Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Chloroformate-Mediated Ring Cleavage of Indole Alkaloids Leads to Re-engineered Antiplasmodial Agents

Daniel C. Schultz[†[a]], Alejandra Chávez-Riveros[†[a]], Michael G. Goertzen II[[a]], Beau R. Brummel[[a]], Raphaella A. Paes[[b]], Natalia M. Santos [[b]], Srinivasarao Tenneti[[a]], Khalil A. Abboud[[c]], James R. Rocca[[a,d]], Gustavo Seabra[[a]], Chenglong Li[[a]], Debopam Chakrabarti[[b]], Robert W. Huigens III[*[a]]

[a]Department of Medicinal Chemistry, Center for Natural Product Drug Discovery & Development (CNPD3), College of Pharmacy, University of Florida, Gainesville, FL.; [b]Division of Molecular Microbiology, Burnett School of Biomedical Sciences, University of Central Florida, Orlando, FL.; [c]Department of Chemistry, University of Florida, Gainesville, FL; [d]McKnight Brain Institute, J H Miller Health Center, University of Florida, Gainesville, FL.

† These authors contributed equally to this work.

* Corresponding Author: rhuigens@cop.ufl.edu

Supporting Information

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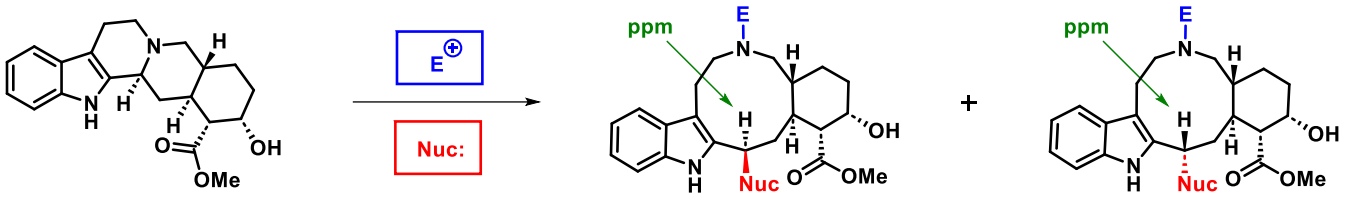
1.) General Information.

All chemical reactions were carried out under an atmosphere of argon unless otherwise specified. Chemical reagents were purchased from commercial sources and used without further purification. Yohimbine hydrochloride was purchased from Acros Organics at ≥ 99% purity. Vincamine was purchased from AK Scientific at ≥ 98% purity. Reserpine was purchased from Thermo Scientific at 99% purity. Apovincamine and vinburnine were synthesized according to our published procedures.[1] Anhydrous solvents were transferred via syringe to flame-dried glassware, which was cooled under a stream of dry argon. All microwave reactions were carried out in microwave vessels in an Anton Paar Monowave 300 Microwave Synthesis Reactor and a constant power was applied during these reactions to ensure reproducibility. Temperature control was automated via IR sensor and all indicated temperatures correspond to the maximal temperature reached during each experiment. Analytical thin layer chromatography (TLC) was performed using 250 μm Silica Gel 60 F254 pre-coated plates (EMD Chemicals Inc.). Flash column chromatography was performed using 230-400 Mesh 60Å Silica Gel (Sorbent Technologies). Melting points were obtained on a Mel-Temp II capillary melting point apparatus and were uncorrected.

NMR experiments were recorded on the following instruments: Bruker Avance III HD and Avance Neo spectrometers (600 MHz and 400 MHz for ^{1}H NMR; 151 MHz and 101 MHz for ^{13}C NMR), and Agilent Systems VNMRS spectrometer (500 MHz for ^{1}H NMR; 126 MHz for ^{13}C NMR). All spectra are presented using MestReNova (Mnova) software and are displayed without the use of the signal suppression function. Spectra were obtained in the following solvents (reference peaks included for ^{1}H and ^{13}C NMRs): $CDCl_3$ (^{1}H NMR: 7.26 ppm; ^{13}C NMR: 77.23 ppm), DMSO-*d6* (^{1}H NMR: 2.50 ppm; ^{13}C NMR: 39.52 ppm), MeOD-*d4* (^{1}H NMR: 3.31 ppm; ^{13}C NMR: 49.00 ppm), and Tetrachloroethane-*d2* (TCE) (^{1}H NMR: 6.00 ppm; ^{13}C NMR: 73.78 ppm). Chemical shift values (δ) are reported in parts per million (ppm) for all ^{1}H NMR and ^{13}C NMR spectra. ^{1}H NMR multiplicities are reported as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br. = broad, appt. = apparent.

Variable temperature (VT) NMR at 100 °C was required for the majority of the ring cleavage compounds reported herein. We believe the ^{1}H and ^{13}C spectra at room temperature for C-N cleavage compounds exhibited broadened signals due to the conformational flexibility of the medium sized rings. Acquiring spectra at 100 °C produced sufficiently sharpened signals for analysis in most cases, though some ^{1}H and ^{13}C signals remained broad even at elevated temperatures or were occasionally not visible in both 1D and 2D spectra. This phenomenon has been reported for medium-size rings in previous literature.[2–5] Proton signals for methoxy groups are singlets, but occasionally some of those resonances and other sharp signals have the appearance of splitting due to slight inhomogeneities of the magnetic field at high temperature. Notes are made at the end of the proton tabulated data when these instances occur.

2.) Supplementary Table 1. Diagnostic ^{1}H NMR Signals of Yohimbine Products.



Yohimbine 7 | Inversion Product (42) | Retention Product (43)

CNBr E^+	Nucleophile Nuc:	Cyanamides*	
		Inversion Product (42)	Retention Product (43)
CNBr	Methanol	4.25 ppm	--
CNBr	Ethanol	4.39 ppm	--
CNBr	Isopropanol	4.46 ppm	4.95 ppm
CNBr	Propargyl-OH	4.66 ppm	5.13 ppm
CNBr	Butanol	4.33 ppm	4.79 ppm
CNBr	Phenol	5.23 ppm	5.68 ppm
CNBr	4-Methoxyphenyl-OH	5.06 ppm	5.58 ppm
CNBr	Benzyl-OH	4.31 ppm	4.91 ppm
CNBr	4-Bromobenzyl-OH	4.39 ppm	4.90 ppm
CNBr	2-Iodobenzyl-OH	4.50 ppm	5.01 ppm
Chloroformate E^+	**Nucleophile Nuc:**	**Carbamates****	
		Inversion Product (42)	**Retention Product (43)**
Methyl	Methanol	4.27 ppm	4.57 ppm
Methyl	2-Iodobenzyl-OH	4.51 ppm	4.88 ppm
Ethyl	Methanol	4.28 ppm	4.58 ppm
Ethyl	2-Iodobenzyl-OH	4.51 ppm	4.89 ppm
Trichloroethyl	Methanol	4.27 ppm	4.62 ppm
Phenyl	Methanol	4.34 ppm	4.66 ppm
Phenyl	*tert*-Butanol	4.75 ppm	5.03 ppm
Phenyl	2-Iodobenzyl-OH	4.54 ppm	4.96 ppm
Phenyl	2-Butyn-1-ol	4.69 ppm	5.09 ppm
Methyl	Ethyl mercaptan	3.93 ppm	4.27 ppm
Methyl	Benzyl mercaptan	4.17 ppm†	3.97 ppm†
Phenyl	Benzyl mercaptan	3.84 ppm	4.02 ppm
Allyl	Methanol	4.27 ppm	4.59 ppm
Propargyl	Methanol	4.28 ppm	4.59 ppm

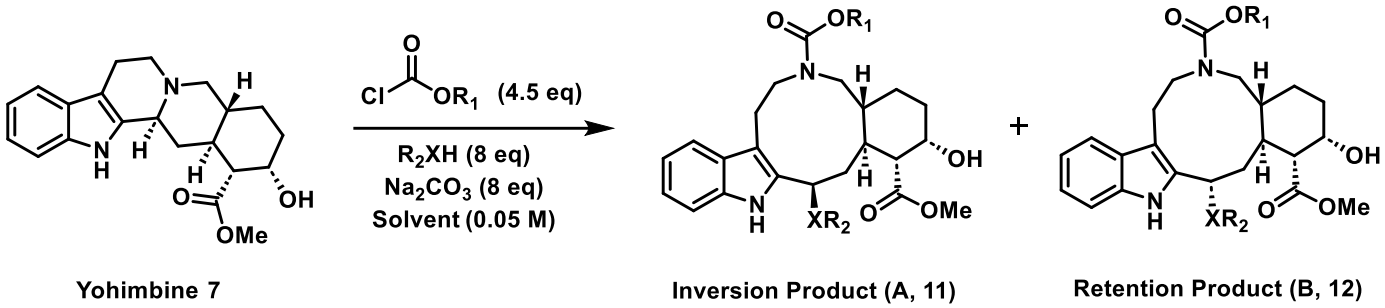
* ^{1}H NMR data of cyanamide compounds in $CDCl_3$ reproduced for reference from previous literature.[6]

** ^{1}H NMR spectra of carbamate compounds were obtained in $C_2D_2Cl_4$.

† ^{1}H NMR conducted in DMSO-d_6 for these compounds as better results were obtained compared to $C_2D_2Cl_4$.

Note: When forming cyanamide products upon reaction with yohimbine and cyanamide bromide / alcohol from our previous work[6], the inversion product for each diastereomeric pair always had a ^{1}H NMR chemical shift upfield (4.25 - 5.23 ppm) compared to the retention product (4.79 - 5.68 ppm). In all but one instance when reacting yohimbine with carbamates / alcohol (or thiol), the inversion products had ^{1}H NMR chemical shifts that are upfield (3.93 - 4.82 ppm) compared to the retention diastereomer (3.97 - 5.09 ppm). The lone exception in this study was using benzyl mercaptan with methyl chloroformate; however, NMRs were taken in DMSO-*d6*.

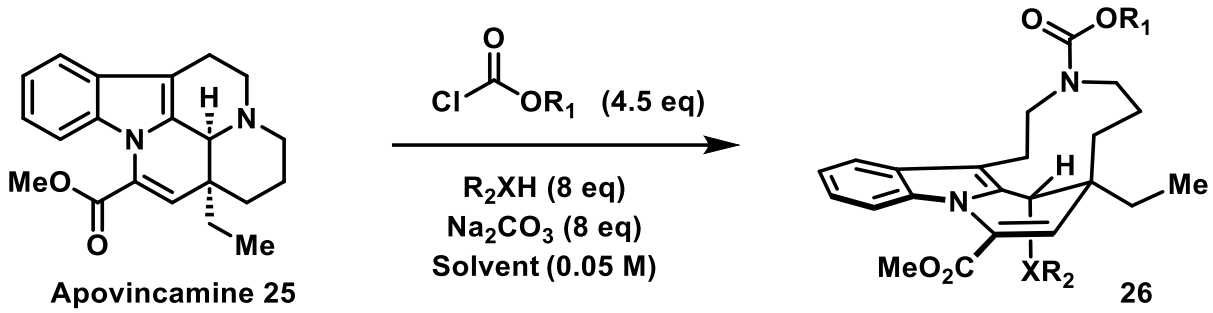
3.) Supplementary Table 2. Yohimbine Ring Cleavage Experimental Findings.



Chloroformate (R)	Nucleophile (R_2XH)	Conditions	Scale (mg)	Time	Combined % Yield (Ratio of 11 / 12)	d.r.
Methyl	**MeOH**	$CHCl_3$, RT	201	4.5 h	78% (30 / 48)	1:1.6
	MeOH	$CHCl_3$, 60 °C, Oil Bath	202	1 h	90% (39 / 51)	1:1.3
	2-I-BnOH	$CHCl_3$, 60 °C, Oil Bath	500	20 h	45% (17 / 28)	1:1.6
	BnSH	$CHCl_3$, 60 °C, Oil Bath	1005	3 h	50% (23 / 27)	1:1.2
	EtSH	$CHCl_3$, RT	500	18 h	44% (11 / 33)	1:3.0
Ethyl	**MeOH**	$CHCl_3$, RT	53	51 h	41% (22 / 19)	1.2:1
	MeOH	$CHCl_3$, 60 °C, Oil Bath	200	3 h	81% (41 / 40)	1.0:1
	MeOH	$CHCl_3$, 60 °C, Microwave	200	15 min	81% (39 / 42)	1:1.1
	MeOH	$CHCl_3$, 100 °C, Microwave	200	5 min	75% (35 / 40)	1:1.1
	MeOH	$CHCl_3$, 100 °C, Microwave	200	1 min	62% (25 / 37)	1:1.5
	MeOH	$CHCl_3$, 200 °C, Microwave	200	1 min	53% (30 / 23)	1.3:1
	2-I-Bn-OH	$CHCl_3$, 60 °C, Microwave	203	15 min	49% (18 / 31)	1:1.7
$-CH_2CCH$	**MeOH**	$CHCl_3$, RT	500	5 h	52% (18 / 34)	1:1.9
$-CH_2CHCH_2$	**MeOH**	$CHCl_3$, RT	150	4 h	60% (29 / 31)	1:1.1
$-CH_2CCl_3$	**MeOH**	$CHCl_3$, RT	52	51 h	71% (30 / 41)	1:1.4
	MeOH	$CHCl_3$, 60 °C, Oil Bath	250	3 h	87% (38 / 49)	1:1.6
	MeOH	$CHCl_3$, 60 °C, Microwave	250	15 min	59% (25 / 34)	1:1.4
	MeOH	CH_2Cl_2, RT	460	3 h	85% (33 / 52)	1:1.6
Phenyl	**MeOH**	$CHCl_3$, RT	50	51 h	58% (27 / 31)	1:1.1
	MeOH	$CHCl_3$, 60 °C, Oil Bath	100	3 h	96% (53 / 43)	1.2:1
	MeOH	$CHCl_3$, 60 °C, Oil Bath	600	3 h	66% (34 / 32)	1.1:1
	MeOH	$CHCl_3$, 60 °C, Oil Bath	203	2 h	64% (30 / 34)	1:1.1
	MeOH	$CHCl_3$, 60 °C, Microwave	200	15 min	66% (31 / 35)	1:1.1
	^{t}BuOH	$CHCl_3$, 60 °C, Oil Bath	201	3 h	33% (13 / 20)	1:1.5
	2-Butyn-1-ol	CH_2Cl_2, RT	500	3 h	89% (27 / 62)	1:2.3
	2-I-Bn-OH	$CHCl_3$, 60 °C, Microwave	202	15 min	75% (21 / 54)	1:2.6
	BnSH	$CHCl_3$, RT	203	9 h	67% (32 / 35)	1:1.1
	BnSH	CH_2Cl_2, RT	201	6 h	90% (27 / 63)	1:2.3

Notes: All yield data are from isolated materials following purification via column chromatography. RT = room temperature. d.r. = diasteromeric ratio.

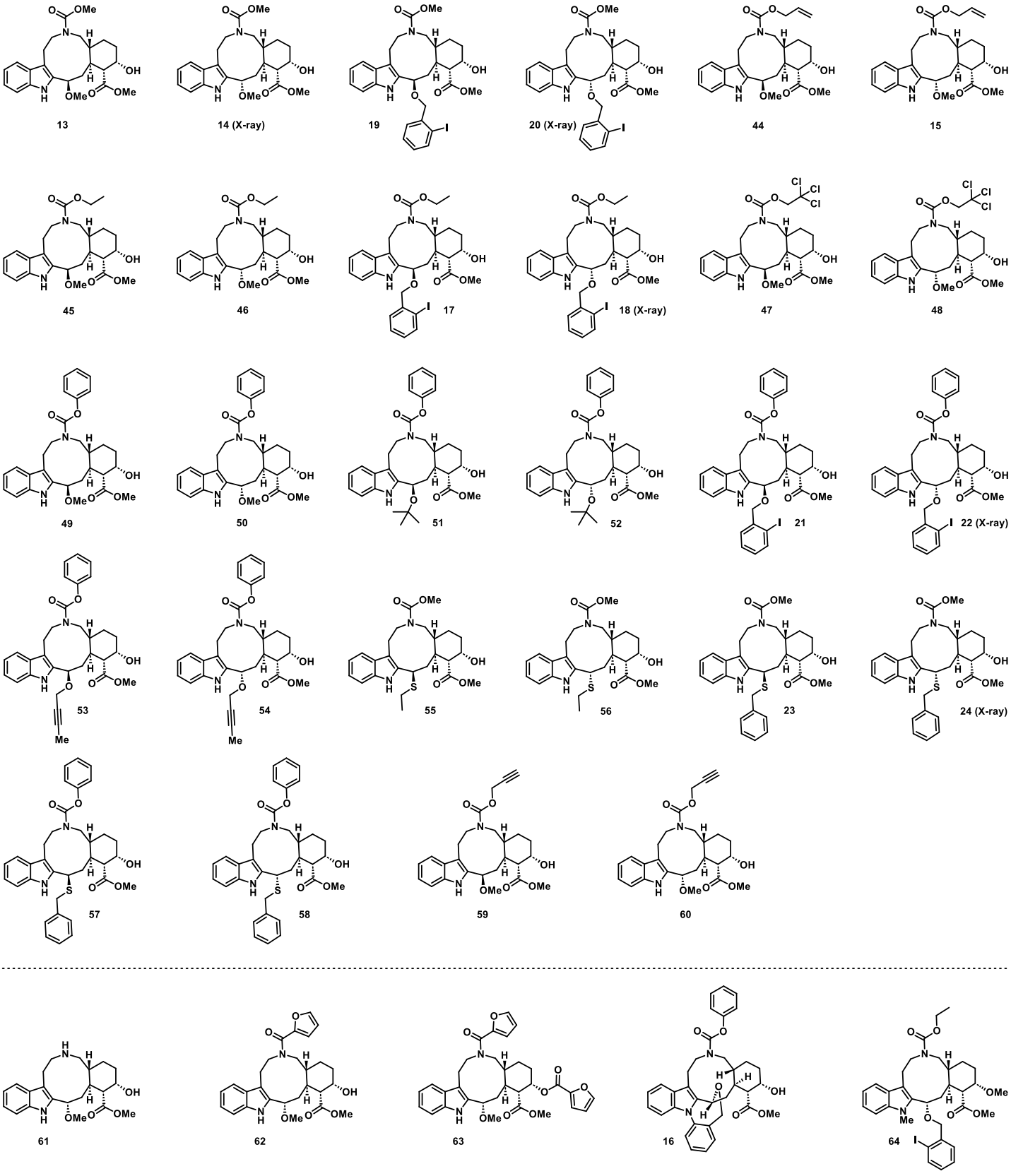
4.) Supplementary Table 3. Apovincamine Ring Cleavage Experimental Findings.



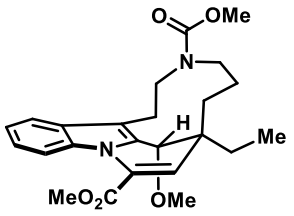
Chloroformate (R)	Nucleophile (R_2XH)	Conditions	Scale (mg)	Time	Yield (%)	Recovered SM
Methyl	**MeOH**	$CHCl_3$, 100 °C, Microwave	229	30 min	15%	n.d.
	MeOH	$CHCl_3$, 100 °C, Microwave	211	1 h	24%	n.d.
	MeOH	CH_2Cl_2, 100 °C, Microwave	211	1 h	35%	n.d.
	MeOH	CH_2Cl_2, 65 °C, Sealed Tube	202	44 h	25%	n.d.
	MeOH	CH_2Cl_2, 100 °C, Sealed Tube	1002	71 h	33%	n.d.
	EtOH	$CHCl_3$, 100 °C, Microwave	195	1 h	30%	n.d.
	Propargyl-OH	$CHCl_3$, 100 °C, Microwave	277	1 h	16%	n.d.
	2-Butyn-1-ol	CH_2Cl_2, 100 °C, Microwave	206	1 h	17%	68%
	Allyl-OH	CH_2Cl_2, 100 °C, Microwave	202	1 h	51%	39%
	Benzyl-OH	CH_2Cl_2, 100 °C, Microwave	200	1 h	24%	31%
	EtSH	CH_2Cl_2, 100 °C, Microwave	200	1 h	25%	n.d.
Ethyl	**MeOH**	$CHCl_3$, 100 °C, Microwave	216	1 h	26%	n.d.
	MeOH	CH_2Cl_2, 100 °C, Sealed Tube	207	68 h	67%	n.d.
-CH_2CCl_3	**MeOH**	$CHCl_3$, 100 °C, Microwave	273	1 h	20%	n.d.
	MeOH	CH_2Cl_2, 100 °C, Sealed Tube	399	71 h	19%	76%
Phenyl	**MeOH**	$CHCl_3$, 100 °C, Microwave	242	1 h	6%	n.d.
Allyl	**MeOH**	$CHCl_3$, 100 °C, Microwave	218	1 h	10%	n.d.

Notes: “Recovered SM” refers to the percent of starting material recovered following the reaction. n.d. = not determined.

5.) Supplementary Figure 1. Yohimbine Ring-Cleaved Compounds Synthesized.



6.) Supplementary Figure 2. Vincamine- and Reserpine-Derived Compounds Synthesized.



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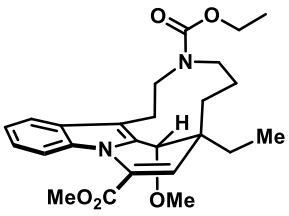

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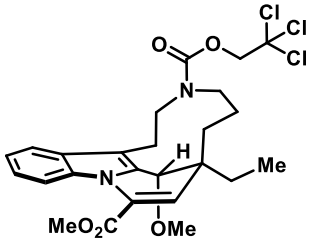

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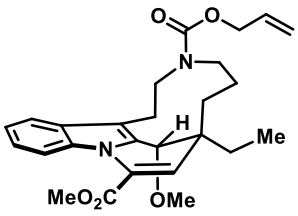

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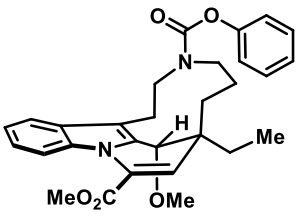

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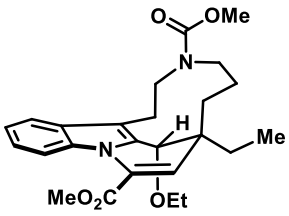

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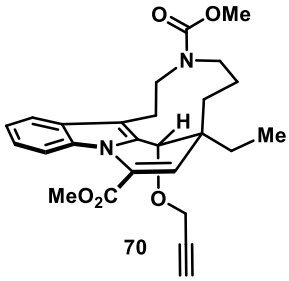

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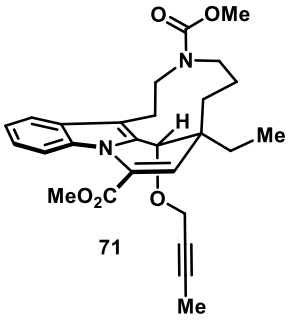

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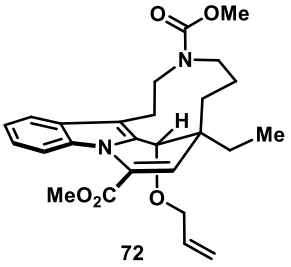

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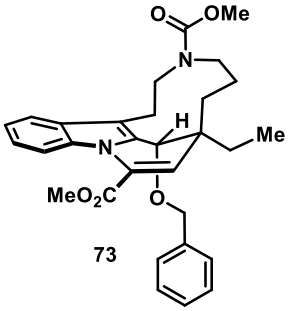

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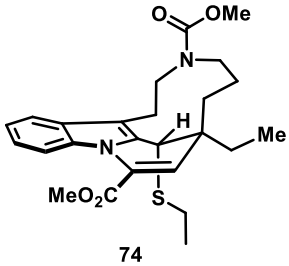

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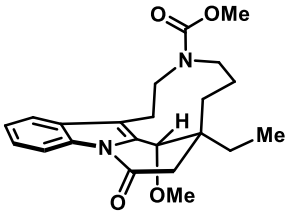

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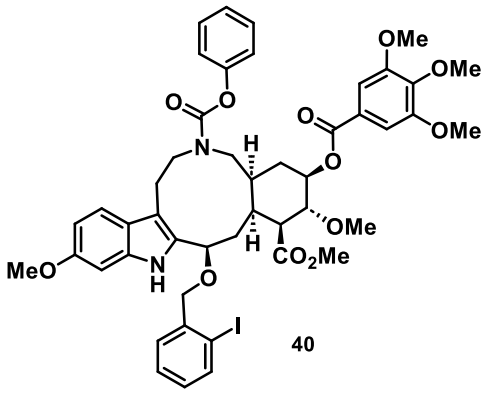

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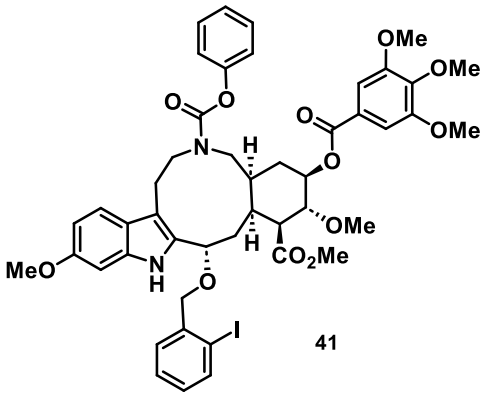

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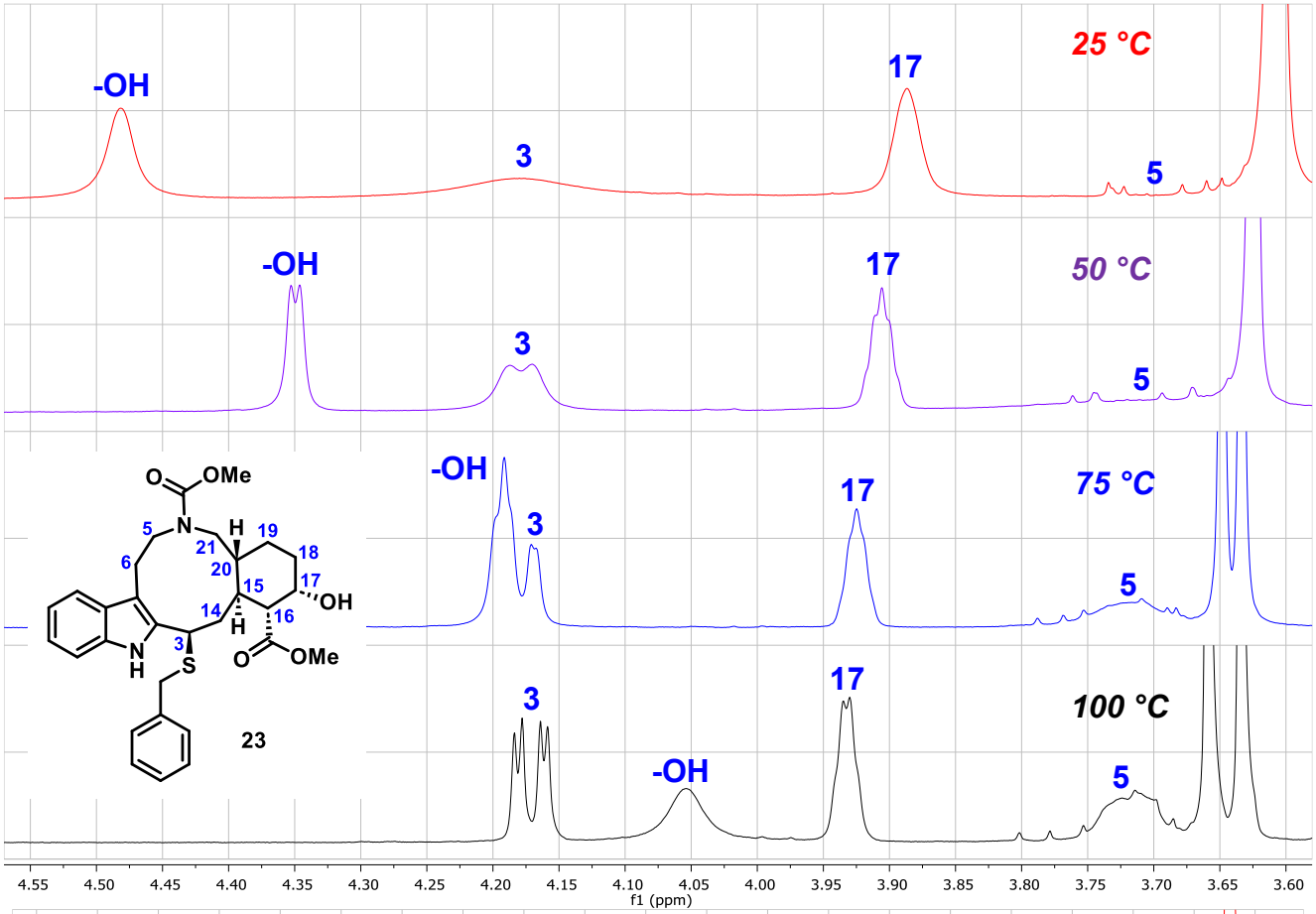
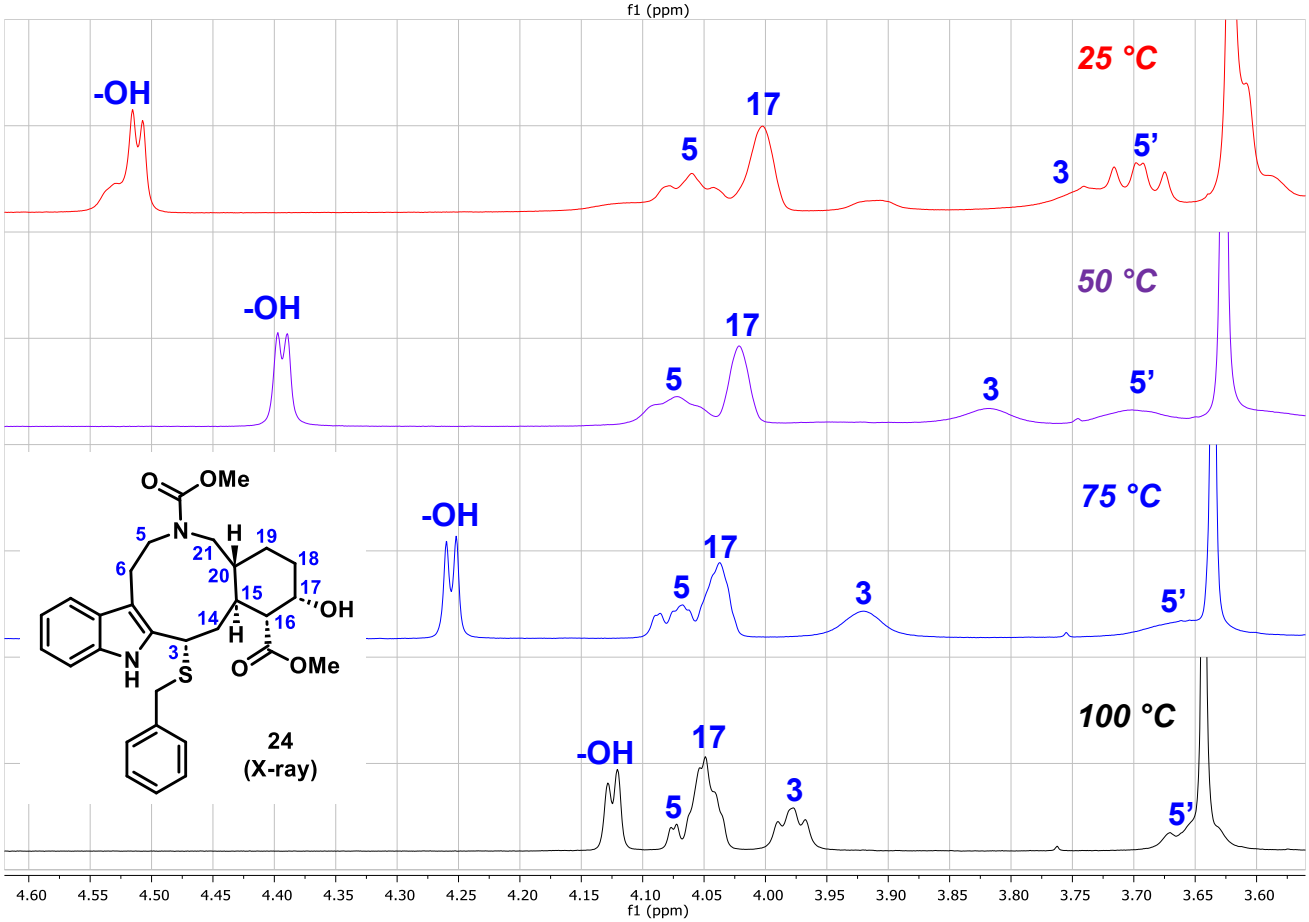
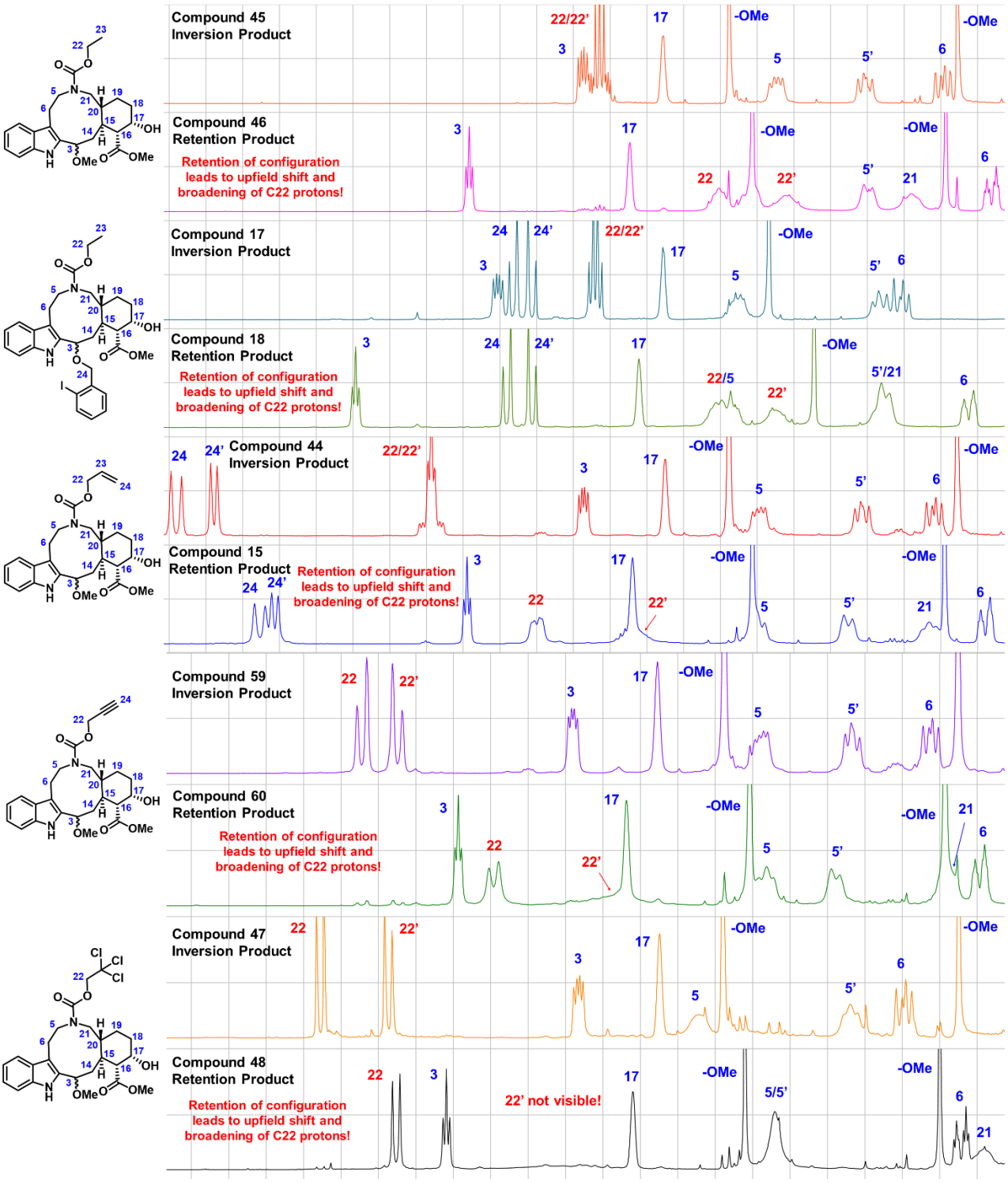
7.) Supplementary Figure 3. Effects of Temperature on 23 and 24 ^{1}H NMR Spectra.





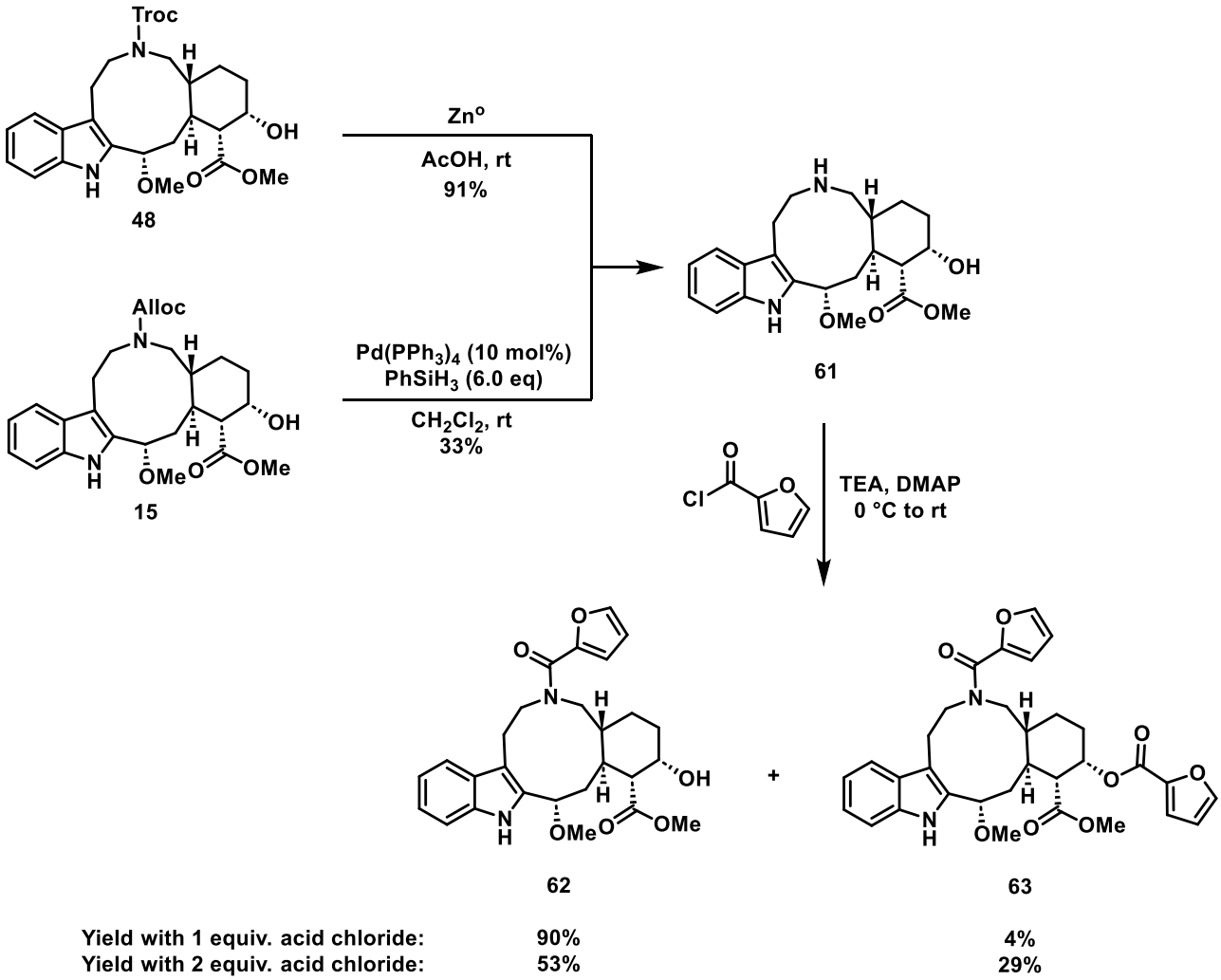
Note: ^{1}H NMR in DMSO-*d6*. Peak shapes and shifts are altered as a function of temperature.

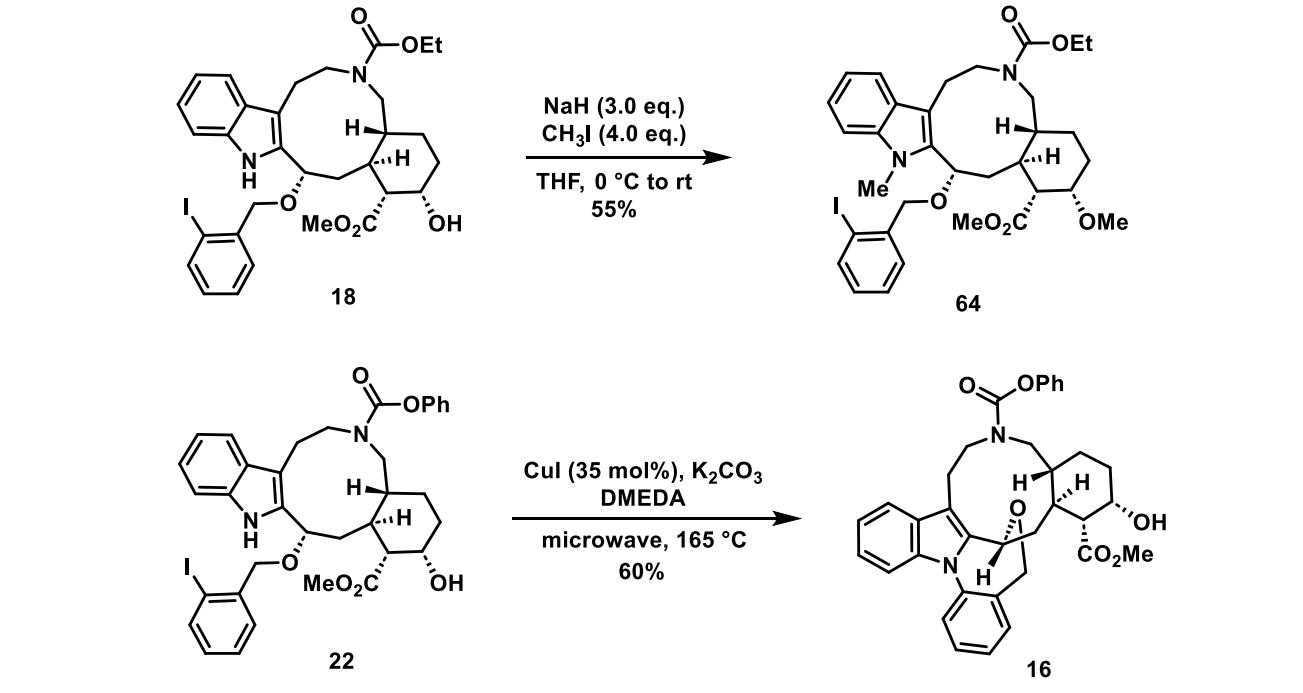
8.) Supplementary Figure 4. Characteristic NMR signals in Select Compounds.



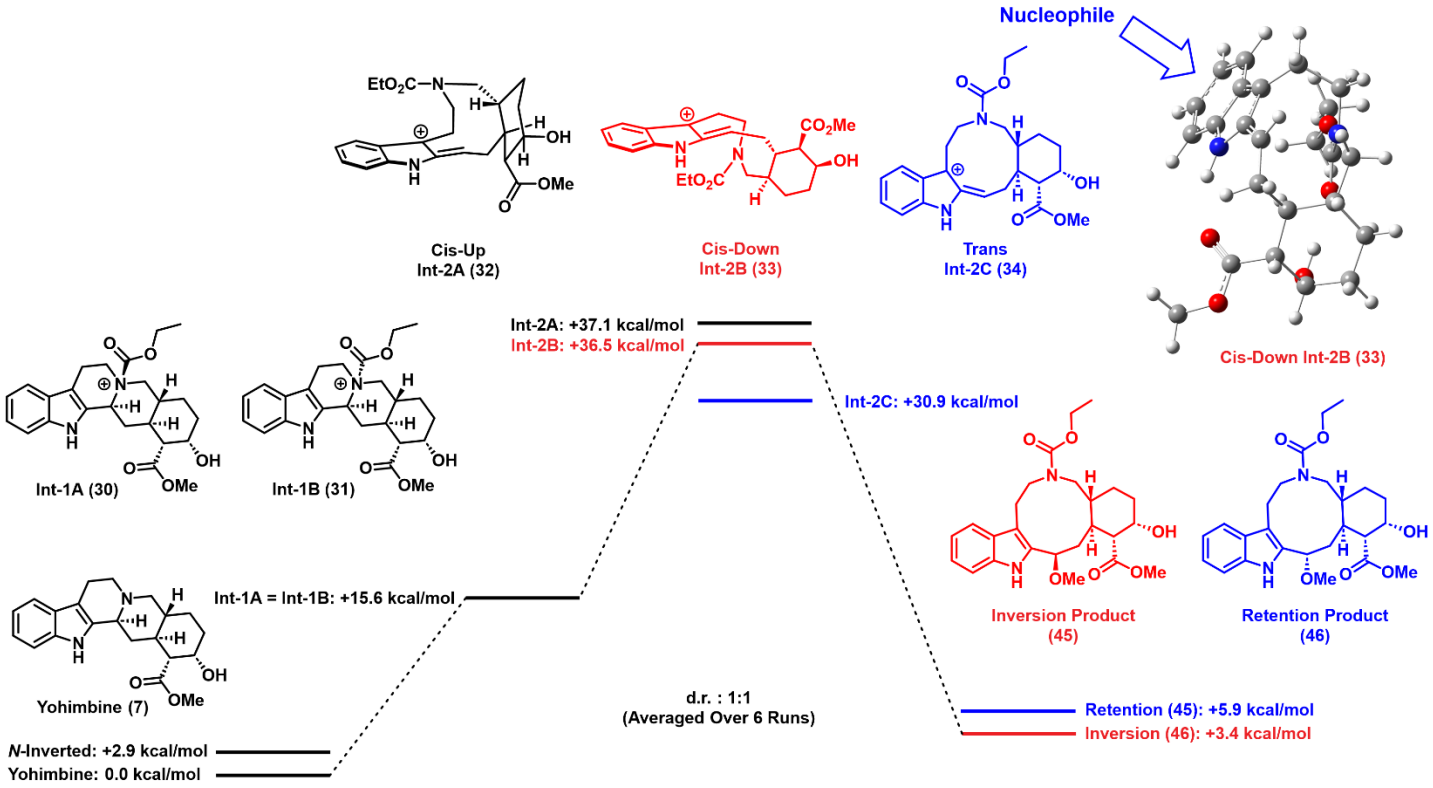
The stereochemistry at C3 has a profound effect on the peak shape and chemical shift of C22 methylene protons in the yohimbine ring cleavage series synthesized during these studies. Inversion products exhibit sharp, clearly-defined C22 diastereotopic proton signals, whereas retention products exhibit broader, weaker signals upfield of their inversion product counterparts. Troc-protected derivative **48** displays a particularly peculiar phenomenon wherein the H22' signal of this retention product was completely absent from the ^{1}H spectrum, with no correlations observed in 2-D NMR experiments. Similar broadening and upfield shift of the C22 singlet of methyl carbamate retention products are observed as well (see spectra).

9.) Supplementary Figure 5. Diversification of Yohimbine Ring-Cleaved Products.



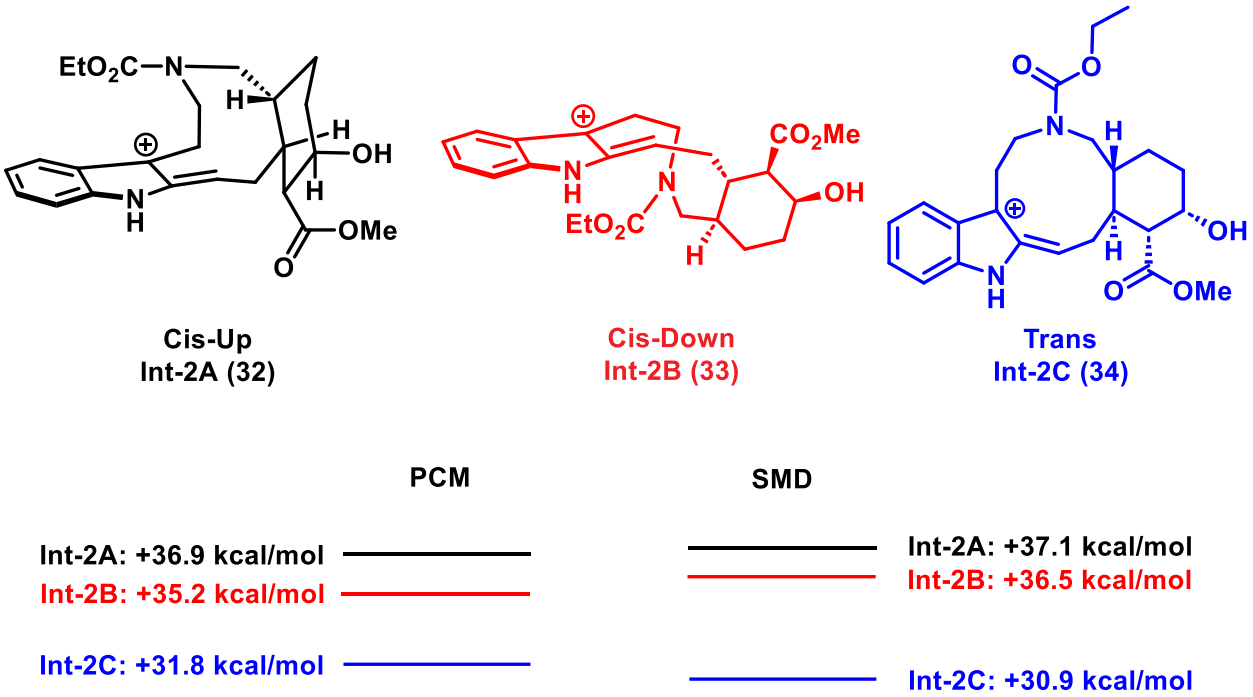


10.) Supplementary Figure 6. Relative Free Energy Diagram for 45 and 46.



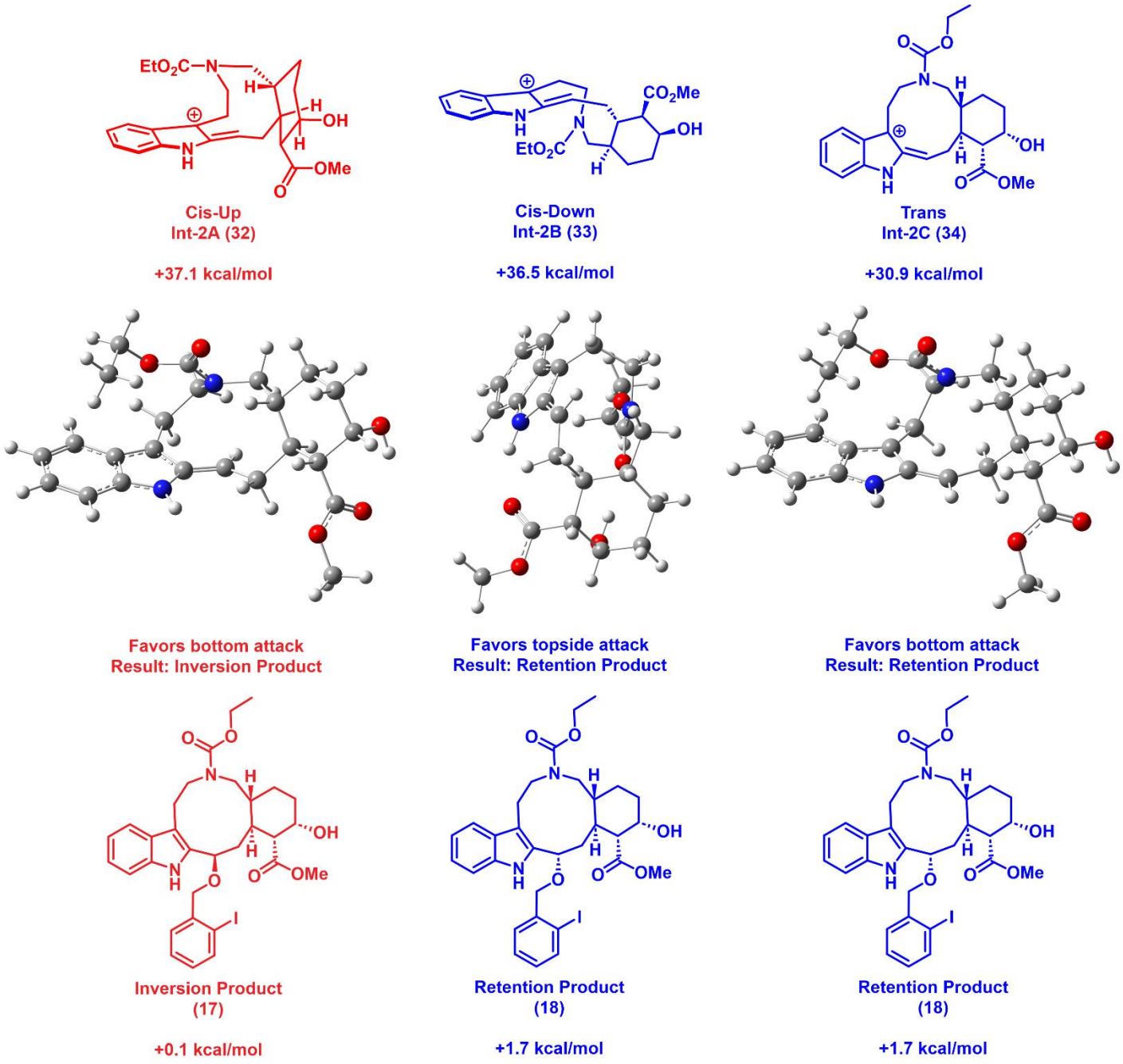
Relative free energy diagram for yohimbine ring cleavage using ethyl chloroformate and methanol. Optimized structure of **Int-2B** shown in top right. Yohimbine proceeds through a quaternary nitrogen intermediate, which then undergoes indole-promoted ring cleavage to form **Int-2B**. **Int-2C** does not form due to a lack of favorable orbital overlap. Nucleophilic attack affords products **A (45)** and **B (46)**.

11.) Supplementary Figure 7. DFT Solvent Model Comparison for Cationic Intermediates.



Note: Energies shown relative to that of the starting materials using the PCM or SMD solvent model.

12.) Supplementary Figure 8. Yohimbine Cationic Intermediate Geometries.

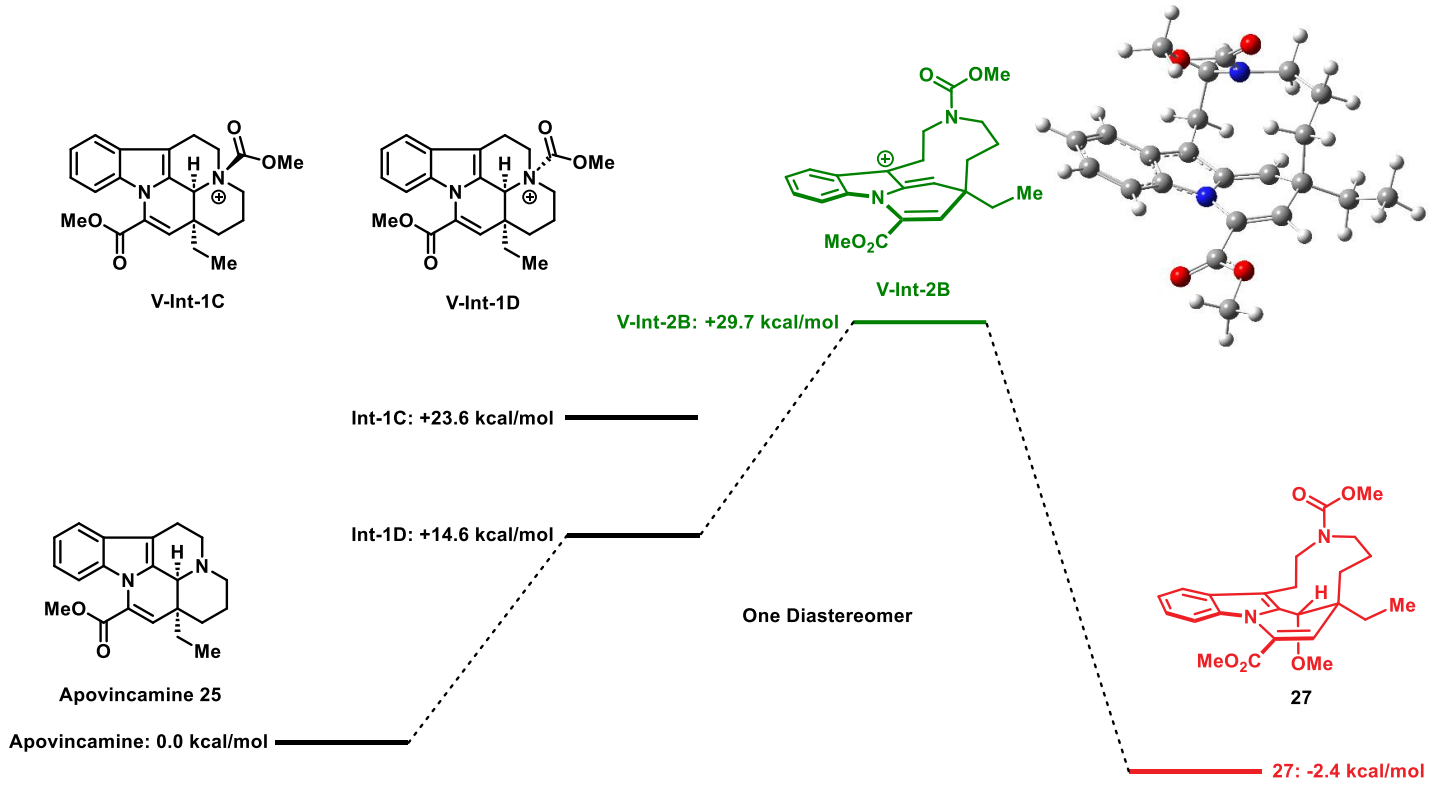


Top Row: Indole-stabilized carbocation intermediates for yohimbine the ring cleavage reaction using ethyl chloroformate and their energies relative to the starting materials.

Middle Row: Geometry optimized structures of each carbocationic intermediate.

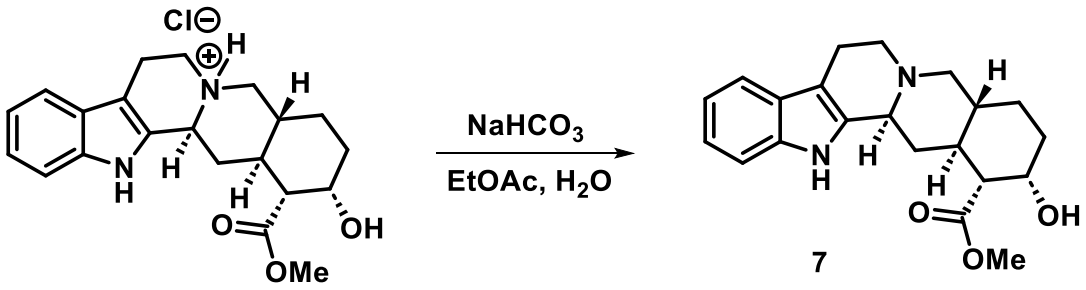
Bottom Row: Preferred products upon nucleophilic attack based on the shielding of the top or bottom face in the carbocationic intermediate along with their energies relative to the starting materials.

13.) Supplementary Figure 9. Relative Free Energy Diagram for 27.



Relative free energy diagram for apovincamine ring cleavage using methyl chloroformate and methanol. Reaction proceeds through quaternary nitrogen intermediate **V-Int-1D**, which undergoes indole-promoted ring cleavage to form **V-Int-2B** (likely exist in equilibrium). Nucleophilic attack affords the sole product **27**. Optimized structure of **V-Int-2B** shown in top right.

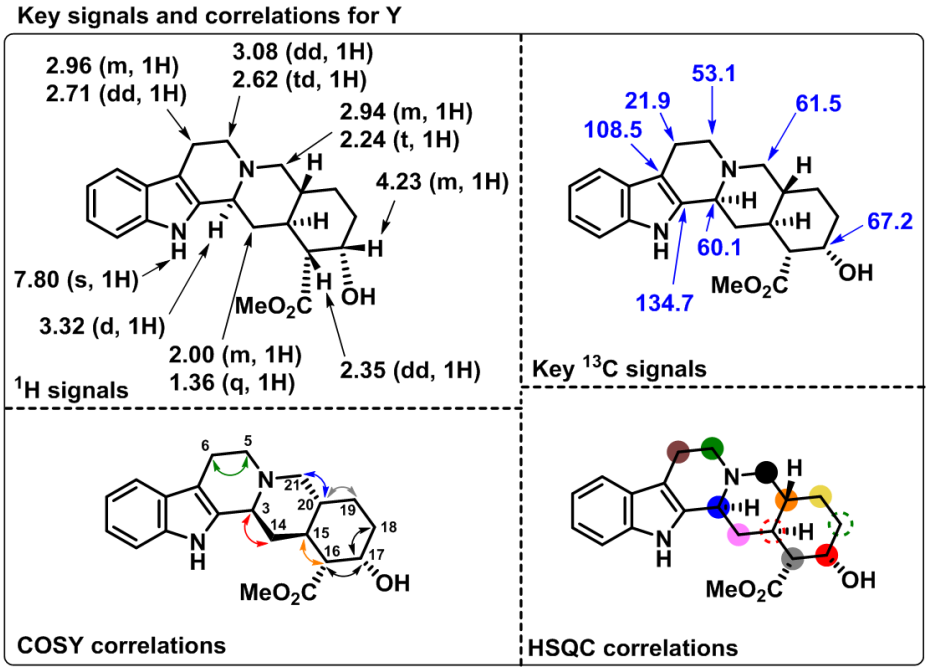
14.) Procedures and Characterization Data.

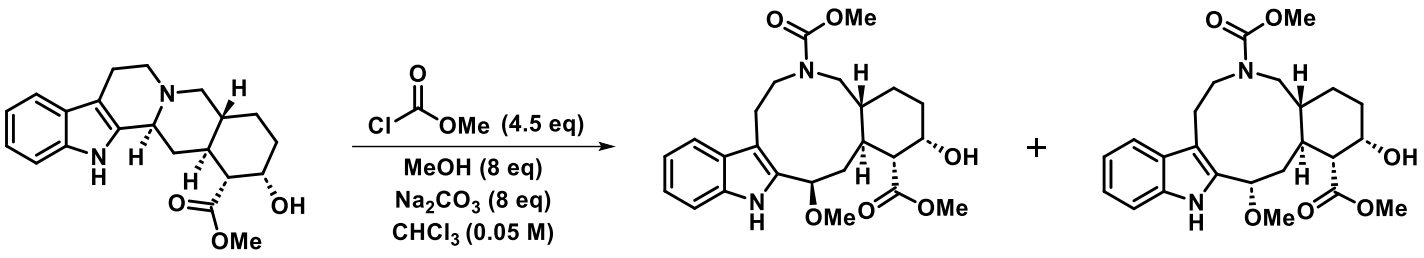


Procedure. Commercially available yohimbine hydrochloride (2.03 g, 5.20 mmol) was added to an Erlenmeyer flask and was dissolved in 200 mL of ethyl acetate. Then, 200 mL of a saturated solution of sodium bicarbonate was added and the resulting mixture was stirred for 10 minutes at room temperature. The reaction mixture was then extracted with ethyl acetate, and dried with sodium sulfate, filtered, and concentrated under reduced pressure to afford pure yohimbine **7** as a free base (1.81 g, 98%, white solid). Note: The tabulated data, NMR spectra, and key signals figure below are reproduced with permission from *Chem. Eur. J.* **2017**, *23,* 4327-4335. This was used as an internal standard for this study.

^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.47 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.30 (d, *J* = 7.9 Hz, 1H), 7.13 (appt. td, *J* = 7.2, 1.4 Hz, 1H), 7.08 (appt. td, *J* = 7.4, 1.2 Hz, 1H), 4.23 (m, 1H), 3.81 (s, 3H), 3.32 (dd, *J* = 11.4, 2.3 Hz, 1H), 3.08 (ddd, *J* = 11.1, 5.9, 1.3 Hz, 1H), 3.04 - 2.90 (m, 2H), 2.71 (dd, *J* = 15.2, 4.0 Hz, 1H), 2.62 (appt. td, *J* = 11.1, 4.3 Hz, 1H), 2.35 (dd, *J* = 11.5, 2.1 Hz, 1H), 2.24 (appt. t, *J* = 10.5 Hz, 1H), 2.09 - 1.94 (m, 3H), 1.64 - 1.49 (m, 3H), 1.42 (m, 1H), 1.36 (appt. q, *J* = 11.9 Hz, 1H).

^{13}C NMR: (101 MHz, $CDCl_3$) δ 175.8, 136.2, 134.7, 127.6, 121.6, 119.6, 118.3, 110.9, 108.5, 67.2, 61.5, 60.1, 53.1, 52.6, 52.2, 41.0, 36.9, 34.5, 31.7, 23.5, 21.9.

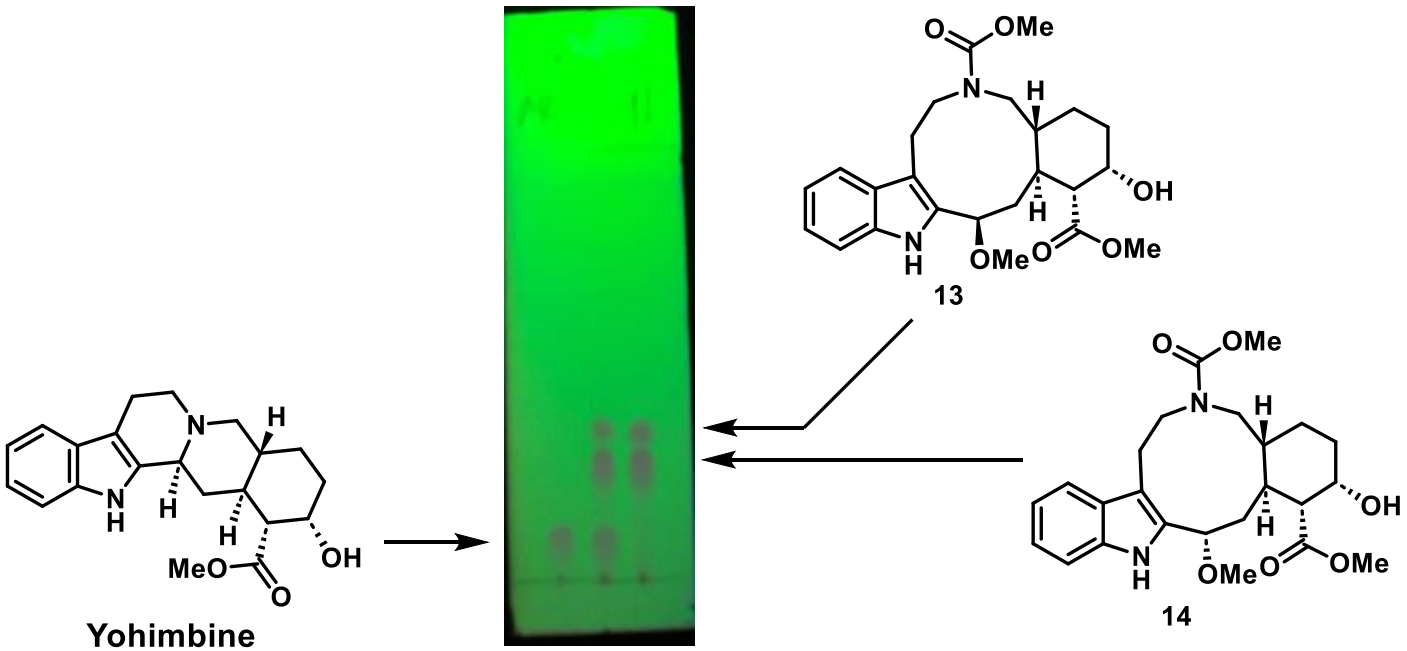




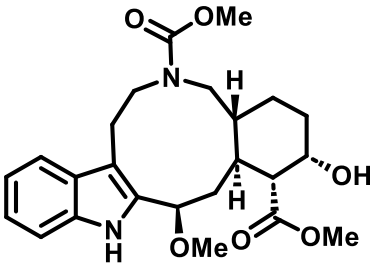
7 13 14

Procedure. Yohimbine **7** (201 mg, 0.56 mmol) was added to a round bottom flask which was then dissolved with the addition of 12 mL of chloroform. Sodium carbonate (474.6 mg, 4.48 mmol), and methyl chloroformate (0.20 mL, 2.52 mmol) were then added to the solution and the mixture stirred at room temperature for 10 minutes before the addition of methanol (0.16 mL, 3.96 mmol). The reaction was then stirred at room temperature for 4.5 hours (reaction progress was monitored by thin layer chromatography, or TLC, analysis). After yohimbine was consumed (based on TLC analysis), the reaction mixture was filtered and concentrated under reduced pressure. The resulting crude product was purified via column chromatography by using 100:0 to 2:3 hexanes:ethyl acetate to afford compound **13** (73 mg, 30%) as a white solid and compound **14** (120 mg, 48%) as a white solid. Note: This procedure was adapted from the literature[7] and successfully applied to a diversity of chloroformates in combination with alcohol / thiol nucleophiles to give two diastereomeric products from yohimbine.

TLC image in 1:1 Hexanes:Ethyl Acetate



Picture Taken By Dr. Alejandra Chávez-Riveros



13

Yield: 30%; 73 mg of **13**; white solid.

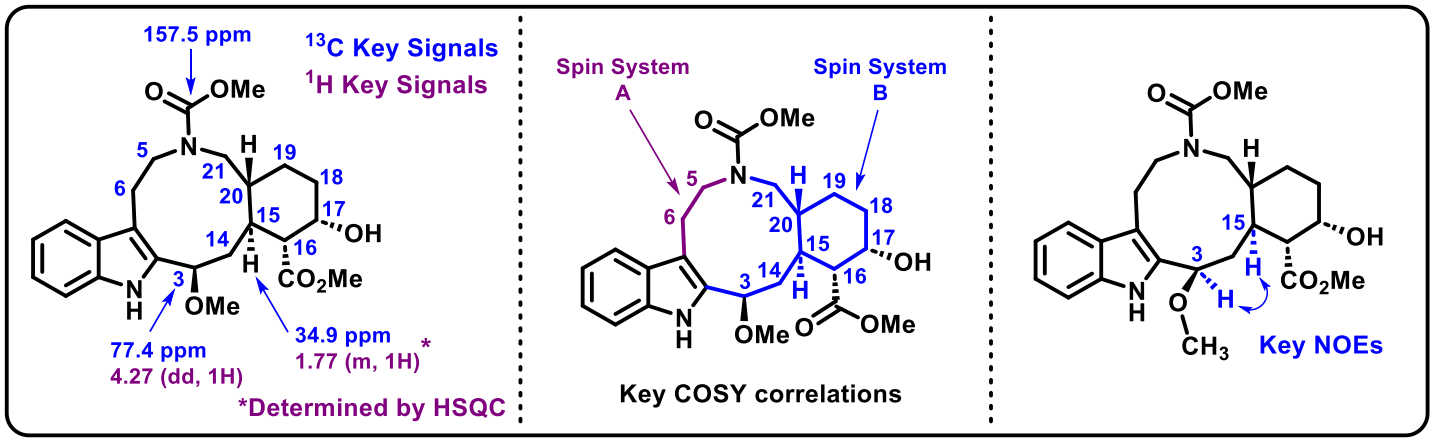
^{1}H NMR: (600 MHz, TCE, 100 °C) δ 8.24 (s, 1H), 7.53 (d, *J* = 7.9 Hz, 1H), 7.42 (dd, *J* = 8.0, 0.5 Hz, 1H), 7.23 (m, 1H), 7.16 (m, 1H), 4.27 (dd, *J* = 9.6, 5.1 Hz, 1H), 4.05 (m, 1H), 3.88 (s, 3H), 3.78 (s, 3H), 3.75 (m, 1H), 3.50 (dd, *J* = 13.9, 9.5 Hz, 1H), 3.30 (dd, *J* = 15.4, 9.6 Hz,1H), 3.26 (s, 3H), 3.00 (dd, *J* = 15.2, 7.1 Hz, 1H), 2.90 (dd, *J* = 13.9, 1.0 Hz, 1H), 2.76 (m, 1H), 2.58 - 2.51 (m, 3H), 2.04 (ddd, *J* = 14.5, 5.2, 5.2 Hz, 1H), 1.81 - 1.73 (m, 2H), 1.60 (m, 1H), 1.42 (m, 1H), 1.19 (appt. dq, *J* = 13.6, 4.4 Hz, 1H), 1.08 (m, 1H). Note: The appearance of the methoxy 3 H signals (3) are due to slight inhomogeneities of the magnetic field at higher temperature. These are singlets despite their appearance.

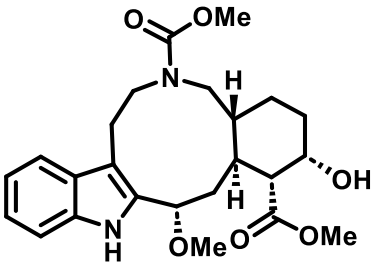
^{13}C NMR: (151 MHz, TCE, 100 °C) δ 176.2, 157.5, 135.4, 135.3, 128.5, 121.8, 119.4, 118.0, 111.2, 111.1, 77.4, 66.6, 57.6, 56.5, 53.8, 52.3, 51.7, 51.4, 39.1, 36.6, 34.9, 30.5, 24.6, 24.1.

HRMS (ESI): calc. for $C_{24}H_{32}N_2O_6Na$ $[M+Na]^+$: 467.2153, found: 467.2157.

Melting point: 178 - 180 °C.

Key Signals for 13





14

Yield: 48%; 120 mg of **14**; white solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 8.19 (s, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.38 (dd, *J* = 8.0, 0.6 Hz, 1H), 7.20 (m, 1H), 7.15 (m, 1H), 4.57 (dd, *J* = 5.1, 5.1 Hz, 1H), 4.15 (m, 1H), 3.82 (m, 1H, buried), 3.81 (s, 3H), 3.48 (m, 1H), 3.37 (m, 1H), 3.28 (s, 3H), 3.25 (br. s, 3H), 3.17 (ddd, *J* = 15.1, 3.6, 3.6 Hz, 1H), 3.01 (ddd, *J* = 14.9, 10.7, 4.1 Hz, 1H), 2.91 (dd, *J* = 14.6, 1.4 Hz, 1H), 2.58 (br. s, 1H), 2.54 (dd, *J* = 11.4, 1.9 Hz, 1H), 2.18 (ddd, *J* = 15.6, 4.2, 4.2 Hz, 1H), 2.13 (ddd, *J* = 15.6, 5.1, 5.1 Hz, 1H), 2.03 (m, 1H), 1.90 (appt. dq, *J* = 13.7, 3.7 Hz, 1H), 1.79 (m, 1H), 1.55 (m, 1H), 1.47 - 1.36 (m, 2H). Note: The appearance

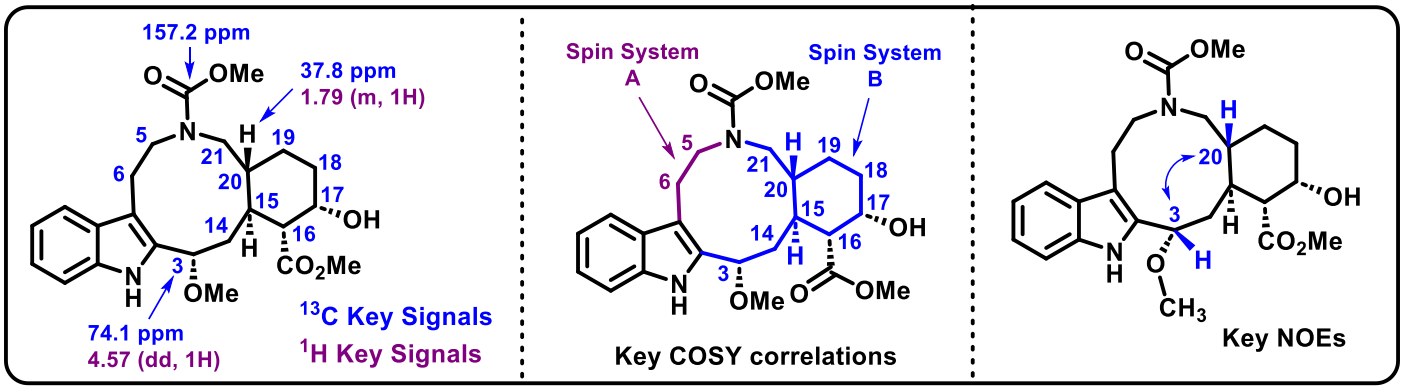
of the methoxy 3 H signals (3) are due to slight inhomogeneities of the magnetic field at higher temperature. These are singlets despite their appearance.

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 174.9, 157.2, 136.4, 135.4, 128.7, 121.5, 119.2, 118.0, 110.8, 109.8, 74.1, 66.7, 57.4, 56.8, 52.0, 51.8, 51.4, 50.2, 38.2, 37.8, 35.6, 30.9, 24.9, 24.8.

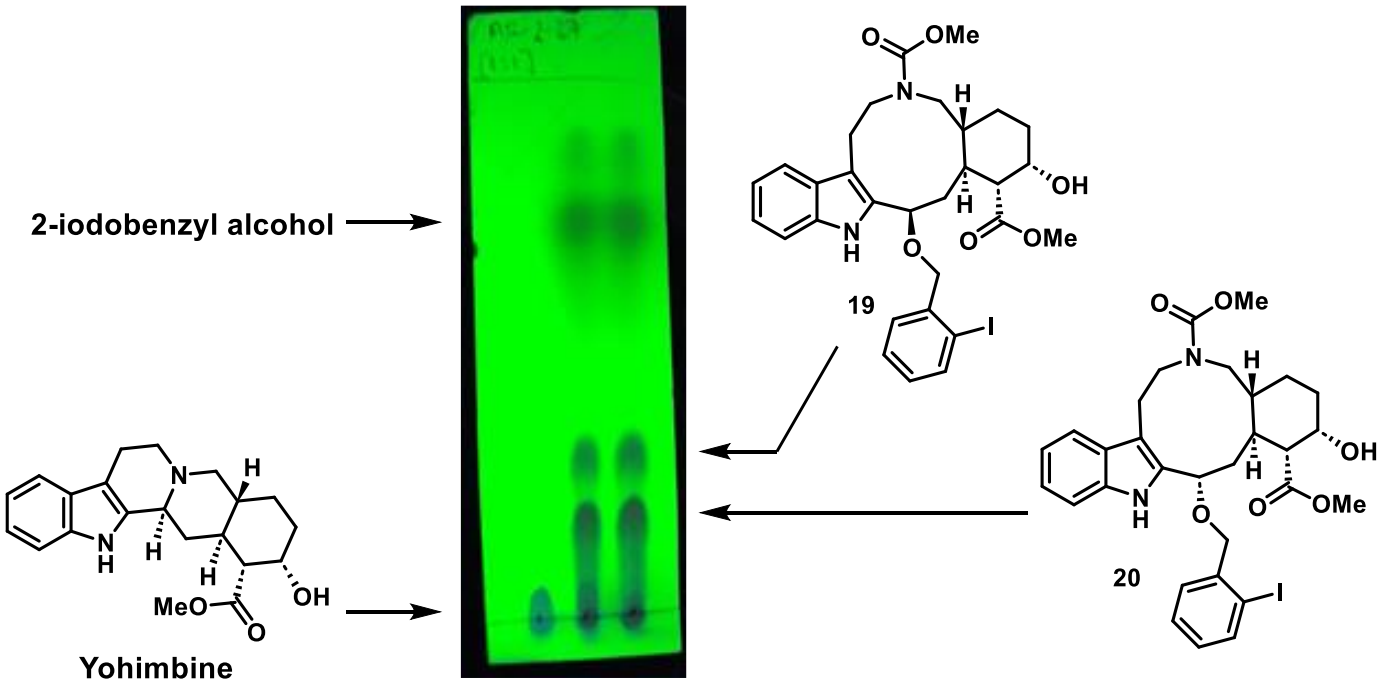
HRMS (ESI): calc. for $C_{24}H_{32}N_2O_6Na$ $[M+Na]^+$: 467.2153, found: 467.2154.

Melting point: 164 - 166 °C.

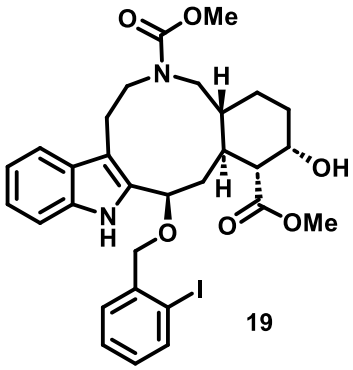
Key Signals for 14 (have X-ray)



TLC image in 1:1 Hexanes:Ethyl Acetate



Picture Taken By Dr. Alejandra Chávez-Riveros



19

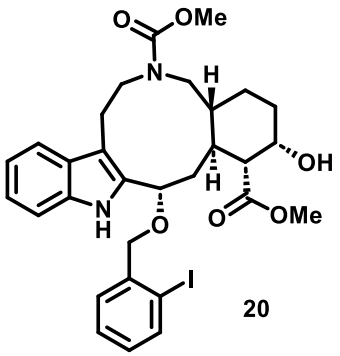
Yield: 17%; 154 mg of **19**; white solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 8.37 (s, 1H), 7.86 (d, *J* = 7.9 Hz, 1H), 7.57 (d, *J* = 7.9 Hz, 1H), 7.44 (d, *J* = 8.1 Hz, 1H), 7.42 - 7.35 (m, 2H), 7.25 (m, 1H), 7.18 (m, 1H), 7.01 (m, 1H), 4.51 (dd, *J* = 9.9, 5.2 Hz, 1H), 4.46 (d, *J* = 12.7 Hz, 1H), 4.41 (d, *J* = 12.7 Hz, 1H), 4.05 (m, 1H), 3.87 (m, 1H), 3.79 (s, 3H), 3.76 (s, 3H), 3.51 - 3.38 (m, 2H), 3.05 (dd, *J* = 14.8, 6.5 Hz, 1H), 2.96 (d, *J* = 13.9 Hz, 1H), 2.75 - 2.61 (m, 3H), 2.55 (dd, *J* = 10.8, 1.0 Hz, 1H), 2.13 (ddd, *J* = 14.5, 5.2, 5.2 Hz, 1H), 1.82 - 1.64 (m, 3H), 1.43 (m, 1H), 1.22 (m, 1H), 1.09 (m, 1H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 176.3, 157.5, 140.6, 139.1, 135.5, 135.0, 129.0, 129.0, 128.5, 128.0 121.9, 119.4, 118.1, 111.5, 111.2, 97.8, 75.5, 74.7, 66.5, 57.7, 54.0, 52.3, 51.8, 51.4, 39.6, 36.8, 34.8, 30.5, 24.7, 24.1.

HRMS (ESI): calc. for $C_{30}H_{35}IN_2O_6Na$ $[M+Na]^+$: 669.1432, found: 669.1425.

Melting point: 93 - 95 °C.



20

Yield: 28%; 257 mg of **20**; tan solid.

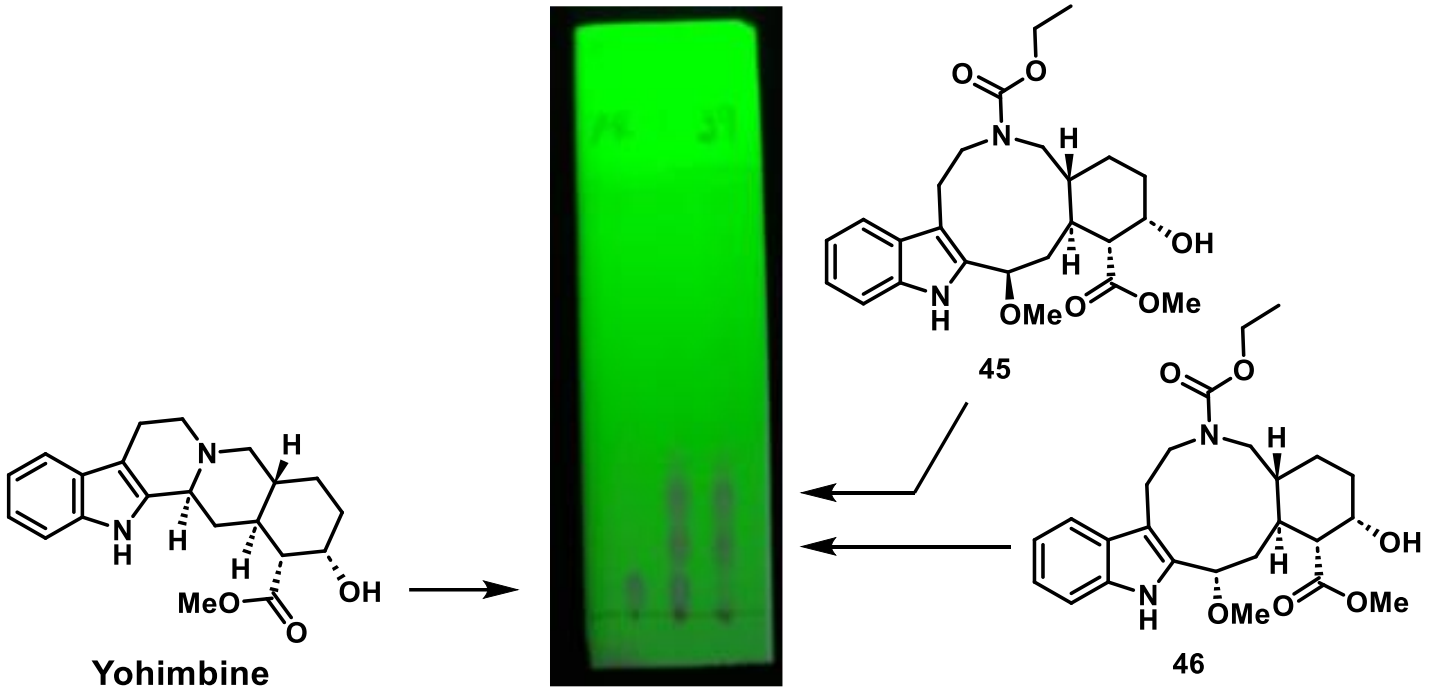
^{1}H NMR: (600 MHz, TCE, 100 °C) δ 8.29 (s, 1H), 7.86 (dd, *J* = 7.9, 0.6 Hz, 1H), 7.58 (d, *J* = 7.8 Hz, 1H), 7.48 (dd, *J* = 7.7, 1.0 Hz, 1H), 7.41 - 7.37 (m, 2H), 7.21 (ddd, *J* = 7.1, 7.1, 0.6 Hz, 1H), 7.16 (m, 1H), 7.02 (ddd, *J* = 7.6, 7.6, 1.4 Hz, 1H), 4.88 (dd, *J* = 5.5, 5.5 Hz, 1H), 4.48 (d, *J* = 12.4 Hz, 1H), 4.42 (d, *J* = 12.4 Hz, 1H), 4.13 (m, 1H), 3.88 (m, 1H), 3.64 (s, 3H), 3.51 - 3.40 (m, 2H), 3.28 (br. s, 3H), 3.23 (ddd, *J* = 15.3, 4.0, 4.0 Hz, 1H, partially buried), 3.06 (ddd, *J* = 15.1, 10.3, 4.0 Hz, 1H), 2.89 (dd, *J* = 14.5, 1.8 Hz, 1H), 2.59 (dd, *J* = 11.5, 2.4 Hz, 1H), 2.53 (br. s, 1H), 2.29 (ddd, *J* = 15.6, 4.7, 4.0 Hz, 1H), 2.22 (ddd, *J* = 15.6, 5.3, 5.3 Hz, 1H), 2.10 (m, 1H), 1.88 (appt. dq, *J* = 13.3, 3.7 Hz, 1H), 1.72 (m, 1H), 1.54 - 1.33 (m, 3H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 174.7, 157.2, 140.5, 139.1, 135.9, 135.6, 129.2, 129.0, 128.7, 127.9, 121.6, 119.2, 118.1, 110.9, 110.5, 97.9, 75.0, 72.2, 66.6, 57.4, 51.8, 51.6, 51.4, 50.3, 38.1, 37.6, 35.6, 30.9, 24.9, 24.6.

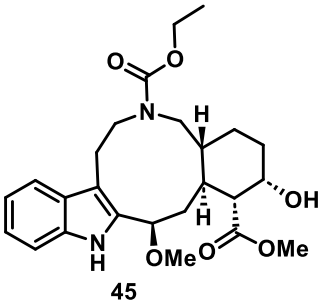
HRMS (ESI): calc. for $C_{30}H_{35}IN_2O_6Na$ $[M+Na]^+$: 669.1432, found: 669.1427.

Melting point: 76 - 78 °C.

TLC image in 1:1 Hexanes:Ethyl Acetate



Picture Taken By Dr. Alejandra Chávez-Riveros



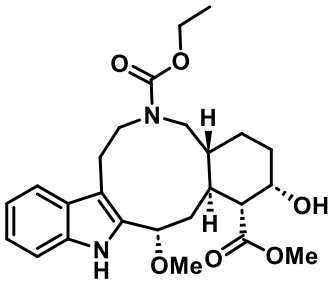
Yield: 39%; 100 mg of **45**; white solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 8.26 (s, 1H), 7.54 (d, *J* = 7.8 Hz, 1H), 7.42 (d, *J* = 8.1 Hz, 1H), 7.23 (m, 1H), 7.16 (m, 1H), 4.28 (dd, *J* = 9.5, 5.1 Hz, 1H), 4.26 - 4.19 (m, 2H), 4.06 (m, 1H), 3.88 (s, 3H), 3.75 (m, 1H), 3.51 (dd, *J* = 13.7, 9.3 Hz, 1H), 3.29 (ddd, *J* = 15.3, 9.2, 1.4 Hz, 1H), 3.25 (s, 3H), 3.00 (ddd, *J* = 15.2, 7.3, 0.9 Hz, 1H), 2.89 (dd, *J* = 14.1, 1.4 Hz, 1H), 2.79 (m, 1H), 2.59 (br. s, 1H), 2.57 - 2.50 (m, 2H), 2.05 (ddd, *J* = 14.5, 5.2, 5.2 Hz, 1H), 1.82 - 1.73 (m, 2H), 1.60 (m, 1H), 1.41 (m, 1H), 1.33 (appt. t, *J* = 7.1 Hz, 3H), 1.19 (appt. dq, *J* = 13.6, 4.4 Hz, 1H), 1.08 (m, 1H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 176.1, 157.1, 135.4, 135.3, 128.5, 121.7, 119.3, 118.0, 111.2, 111.1, 77.4, 66.6, 61.0, 57.4, 56.5, 53.8, 51.6, 51.3, 39.1, 36.7, 34.9, 30.5, 24.5, 24.0, 14.5.

HRMS (ESI): calc. for $C_{25}H_{35}N_2O_6$ $[M+H]^+$: 459.2490, found: 459.2500.

Melting point: 83 - 85 °C.



46

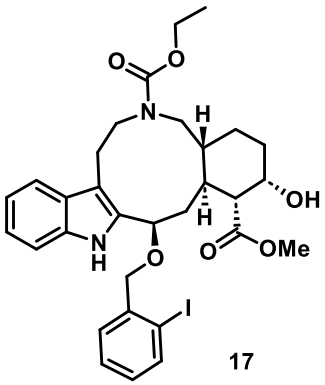
Yield: 42%; 107 mg of **46**; white solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 8.21 (s, 1H), 7.55 (d, *J* = 7.8 Hz, 1H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.20 (m, 1H), 7.14 (m, 1H), 4.58 (dd, *J* = 5.2, 5.1 Hz, 1H), 4.15 (m, 1H), 3.90 (m, 1H), 3.82 (m, 1H, buried), 3.81 (s, 3H), 3.72 (m, 1H), 3.50 (m, 1H), 3.38 (m, 1H), 3.29 (s, 3H), 3.16 (ddd, *J* = 15.2, 3.7, 3.7 Hz, 1H), 3.01 (ddd, *J* = 15.1, 10.8, 3.8 Hz, 1H), 2.91 (dd, *J* = 14.4, 1.2 Hz, 1H), 2.58 (br. s, 1H), 2.54 (dd, *J* = 11.5, 2.1 Hz, 1H), 2.20 (ddd, *J* = 15.6, 4.1, 4.1 Hz, 1H), 2.13 (ddd, *J* = 15.6, 5.1, 5.1 Hz, 1H), 2.04 (m, 1H), 1.90 (appt. dq, *J* = 13.7, 3.7 Hz, 1H), 1.82 (m, 1H), 1.53 (m, 1H), 1.47 - 1.36 (m, 2H), 0.95 (br. m, 3H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 174.9, 156.9, 136.4, 135.4, 128.7, 121.5, 119.2, 118.0, 110.8, 109.9, 74.2, 66.6, 60.9, 57.5, 56.8, 52.0, 51.4, 50.5, 38.3, 37.9, 35.5, 30.9, 24.9, 24.7, 14.0.

HRMS (ESI): calc. for $C_{25}H_{35}N_2O_6$ $[M+H]^+$: 459.2490, found: 459.2498.

Melting point: 72 - 74 °C.



17

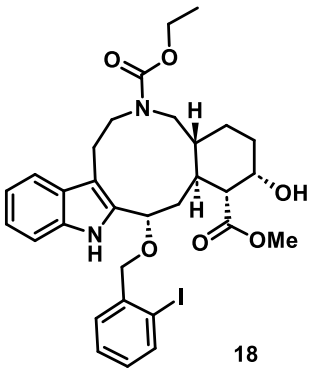
Yield: 18%; 67 mg of **17**; white solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 8.31 (s, 1H), 7.86 (m, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.44 (d, *J* = 8.1 Hz, 1H), 7.41 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.37 (ddd, *J* = 7.4, 7.4, 0.9 Hz, 1H), 7.25 (m, 1H), 7.18 (m, 1H), 7.01 (ddd, *J* = 7.6, 7.6, 1.6 Hz, 1H), 4.51 (dd, *J* = 9.9, 5.3 Hz, 1H), 4.46 (d, *J* = 12.6 Hz, 1H), 4.41 (d, *J* = 12.6 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 4.06 (m, 1H), 3.85 (m, 1H), 3.77 (s, 3H), 3.52 - 3.37 (m, 2H), 3.05 (dd, *J* = 14.4, 6.4 Hz, 1H), 2.96 (d, *J* = 14.0 Hz, 1H), 2.79 - 2.66 (m, 2H), 2.63 (br. s, 1H), 2.54 (dd, *J* = 10.9, 1.8 Hz, 1H), 2.14 (ddd, *J* = 14.5, 5.2, 5.2 Hz, 1H), 1.83 - 1.67 (m, 3H), 1.43 (m, 1H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.22 (m, 1H), 1.10 (m, 1H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 176.3, 157.1, 140.6, 139.1, 135.5, 135.0, 129.0, 128.9, 128.6, 128.0, 121.9, 119.4, 118.1, 111.7, 111.2, 97.8, 75.5, 74.6, 66.5, 61.0, 57.7, 54.0, 51.8, 51.4, 39.6, 36.8, 34.8, 30.5, 24.7, 24.1, 14.5.

HRMS (ESI): calc. for $C_{31}H_{38}IN_2O_6$ $[M+H]^+$: 661.1769, found: 661.1765.

Melting point: 85 - 87 °C.



18

Yield: 31%; 115 mg of **18**; white solid.

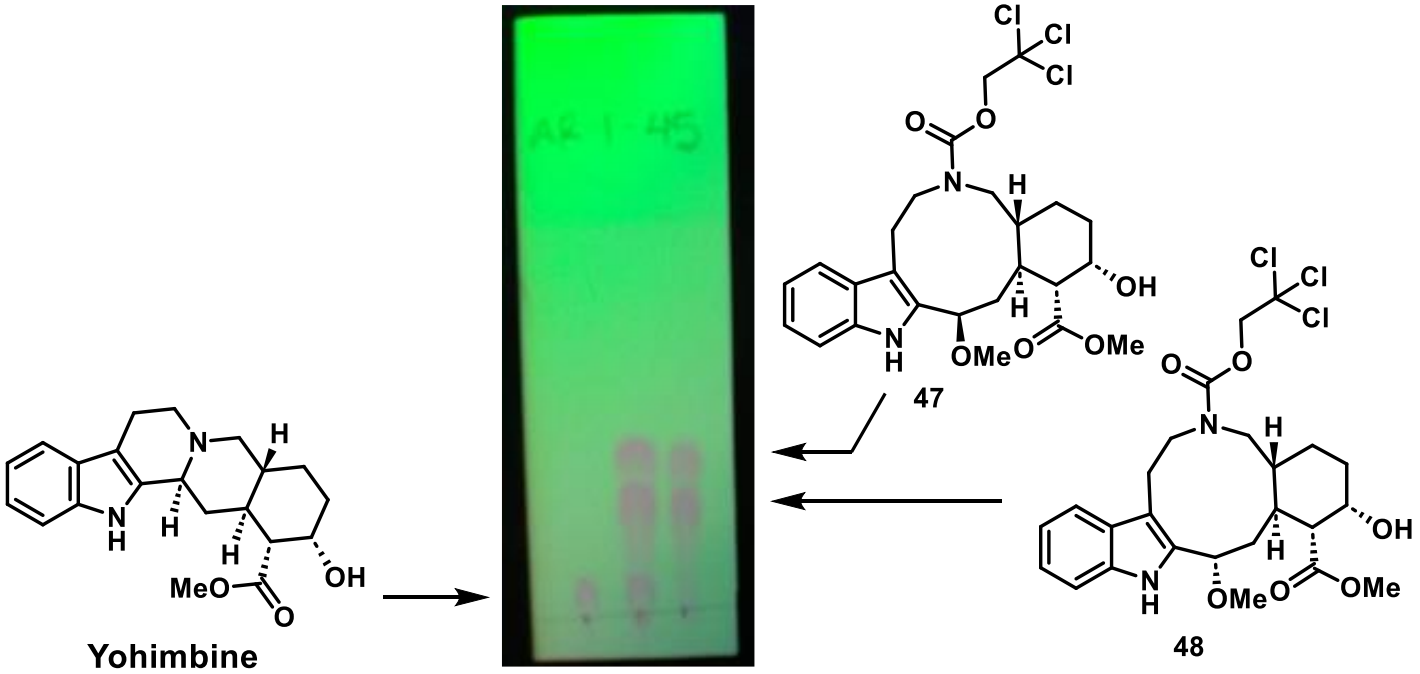
^{1}H NMR: (600 MHz, TCE, 100 °C) δ 8.24 (s, 1H), 7.86 (d, *J* = 7.9 Hz, 1H), 7.58 (d, *J* = 7.8 Hz, 1H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.41 - 7.37 (m, 2H), 7.21 (m, 1H), 7.15 (m, 1H), 7.02 (dd, *J* = 7.6, 7.6 Hz, 1H), 4.89 (dd, *J* = 5.5, 5.5 Hz, 1H), 4.48 (d, *J* = 12.4 Hz, 1H), 4.41 (d, *J* = 12.4 Hz, 1H), 4.12 (m, 1H), 3.96 - 3.83 (m, 2H), 3.75 (m, 1H), 3.64 (s, 3H), 3.51 - 3.41 (m, 2H), 3.22 (ddd, *J* = 15.3, 3.6, 3.6 Hz, 1H), 3.06 (ddd, *J* = 15.1, 10.5, 3.5 Hz, 1H), 2.89 (d, *J* = 14.4 Hz, 1H), 2.57 (dd, *J* = 11.6, 1.6 Hz, 1H), 2.49 (br. s, 1H), 2.30 (ddd, *J* = 15.5, 4.3, 4.3 Hz, 1H), 2.20 (ddd, *J* = 15.5, 5.2, 5.2 Hz, 1H), 2.10 (m, 1H), 1.88 (m, 1H), 1.74 (m, 1H), 1.51 - 1.33 (m, 3H), 0.96 (br. m, 3H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 174.9, 156.9, 140.5, 139.1, 135.9, 135.6, 129.3, 129.0, 128.7, 127.9, 121.7, 119.3, 118.1, 110.9, 110.6, 97.9, 75.0, 72.3, 66.6, 60.9, 57.4, 51.7, 51.4, 50.7, 38.3, 37.7, 35.6, 30.8, 24.9, 24.5, 14.0.

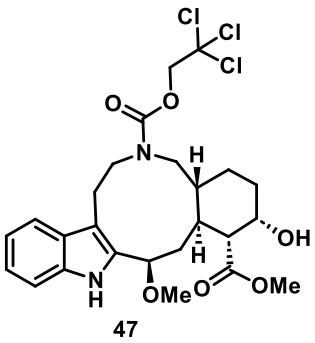
HRMS (ESI): calc. for $C_{31}H_{38}IN_2O_6$ $[M+H]^+$: 661.1769, found: 661.1766.

Melting point: 95 - 97 °C.

TLC image in 1:1 Hexanes:Ethyl Acetate



Picture Taken By Dr. Alejandra Chávez-Riveros



47

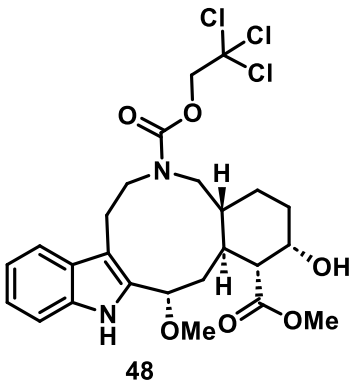
Yield: 38%; 149 mg of **47**; tan solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 8.27 (s, 1H), 7.55 (d, *J* = 7.9 Hz, 1H), 7.43 (dd, *J* = 8.1, 0.5 Hz, 1H), 7.24 (m, 1H), 7.17 (m, 1H), 4.95 (d, *J* = 12.0 Hz, 1H), 4.77 (d, *J* = 12.0 Hz, 1H), 4.27 (dd, *J* = 9.6, 5.1 Hz, 1H), 4.05 (m, 1H), 3.94 (m, 1H), 3.88 (s, 3H), 3.54 (m, 1H), 3.40 (dd, *J* = 15.4, 9.6 Hz, 1H), 3.25 (s, 3H), 3.08 (dd, *J* = 15.4, 7.0 Hz, 1H), 3.04 (d, *J* = 13.8 Hz, 1H), 2.76 (m, 1H), 2.60 - 2.49 (m, 3H), 2.05 (ddd, *J* = 14.6, 4.9, 4.9 Hz, 1H), 1.84 - 1.71 (m, 3H), 1.41 (m, 1H), 1.22 (m, 1H), 1.11 (m, 1H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 176.2, 155.1, 135.4, 135.4, 128.5, 121.8, 119.5, 118.0, 111.2, 110.8, 95.7, 77.5, 75.2, 66.5, 57.9, 56.5, 54.0, 51.8, 51.7, 39.4, 36.7, 34.9, 30.5, 24.3, 24.1.

HRMS (ESI): calc. for $C_{25}H_{32}Cl_3N_2O_6$ $[M+H]^+$: 561.1320, found: 561.1317.

Melting point: 85 - 87 °C.



48

Yield: 49%; 191 mg of **48**; tan solid.

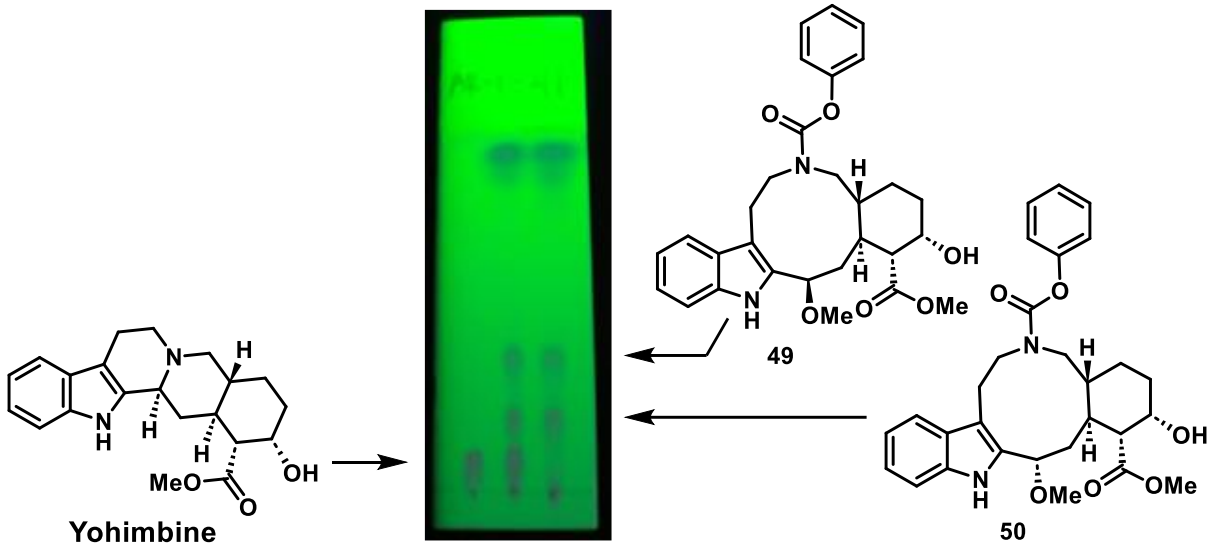
^{1}H NMR: (600 MHz, TCE, 100 °C) δ 8.26 (s, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.22 (m, 1H), 7.15 (dd, *J* = 7.6, 7.3 Hz, 1H), 4.75 (d, *J* = 11.9 Hz, 1H), 4.62 (dd, *J* = 5.4, 5.4 Hz, 1H), 4.12 (m, 1H), 3.82 (s, 3H), 3.78 - 3.68 (m, 2H), 3.30 (s, 3H), 3.24 (ddd, *J* = 15.3, 4.0, 4.0 Hz, 1H), 3.18 (m, 1H), 3.12 - 3.04 (m, 2H), 2.61 (br. s, 1H), 2.52 (dd, *J* = 11.4, 2.0 Hz, 1H), 2.21 (ddd, *J* = 15.6, 5.1, 5.1 Hz, 1H), 2.17 (ddd, *J* = 15.6, 4.4, 4.4 Hz, 1H), 1.99 (m, 1H), 1.91 - 1.82 (m, 2H), 1.49 (m, 1H), 1.45 - 1.36 (m, 2H). Note: While one proton of the Troc group is a sharp doublet (4.75 ppm), the other proton signal does not appear as a clearly discernable peak in either 1D or 2D NMR experiments. It is possible the peak is a broad multiplet hidden in the baseline given the behavior of diastereotopic methylene protons at this position in other yohimbine-derived retention products (i.e., compound **46**). Straightforward NMR theory, however, is insufficient in explaining the general absence of this peak compared to the sharp, clear peak of its geminal proton. Interestingly, all other protons in this compound are characterized similar to other retention products synthesized from yohimbine.

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 175.1, 154.9, 136.0, 135.4, 128.4, 121.7, 119.4, 118.0, 110.9, 109.9, 95.7, 74.8, 74.6, 66.4, 58.2, 56.9, 52.3, 51.5, 51.4, 38.7, 37.8, 35.3, 30.6, 24.6 (2C; confirmed by HSQC).

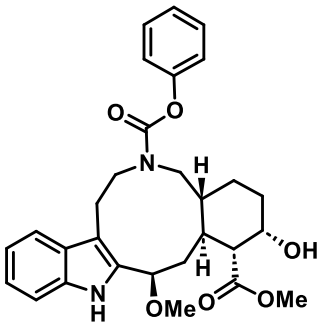
HRMS (ESI): calc. for $C_{25}H_{32}Cl_3N_2O_6$ $[M+H]^+$: 561.1320, found: 561.1306.

Melting point: 87 - 89 °C.

TLC image in 1:1 Hexanes:Ethyl Acetate



Picture Taken By Dr. Alejandra Chávez-Riveros



49

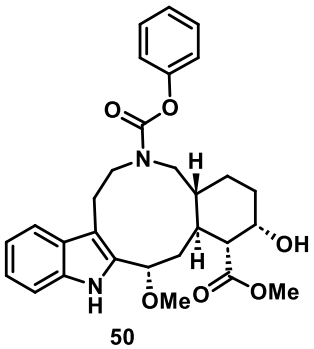
Yield: 34%; 288 mg of **49**; white solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 8.32 (s, 1H), 7.58 (d, *J* = 7.9 Hz, 1H), 7.45 (d, *J* = 8.1 Hz, 1H), 7.44 - 7.40 (m, 2H), 7.28 - 7.24 (m, 2H), 7.23 - 7.16 (m, 3H), 4.34 (dd, *J* = 9.5, 5.2 Hz, 1H), 4.07 (m, 1H), 3.97 (m, 1H), 3.88 (s, 3H), 3.63 (dd, *J* = 13.1, 9.7 Hz, 1H), 3.45 (dd, *J* = 15.2, 9.7 Hz, 1H), 3.29 (s, 3H), 3.14 - 3.06 (m, 2H), 2.86 (m, 1H), 2.65 (ddd, *J* = 14.7, 9.6, 2.4 Hz, 1H), 2.56 (dd, *J* = 10.8, 1.5 Hz, 1H), 2.51 (br. s, 1H), 2.15 (ddd, *J* = 14.3, 5.2, 4.9 Hz, 1H), 1.88 - 1.72 (m, 3H), 1.42 (m, 1H), 1.23 (appt. dq, *J* = 13.6, 4.1 Hz, 1H), 1.14 (m, 1H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 176.2, 155.1, 151.5, 135.4, 129.0, 128.5, 124.9, 121.8, 121.6, 119.5, 118.0, 111.2, 110.8, 77.6, 66.5, 58.0, 56.6, 54.0, 51.8, 51.7, 39.3, 36.6, 35.1, 30.5, 24.4, 24.2. Note: This spectra is missing one carbon signal in the aromatic region likely due to overlap.

HRMS (ESI): calc. for $C_{29}H_{35}N_2O_6$ $[M+H]^+$: 507.2490, found: 507.2497.

Melting point: 105 - 107 °C.



50

Yield: 32%; 274 mg of **50**; white solid.

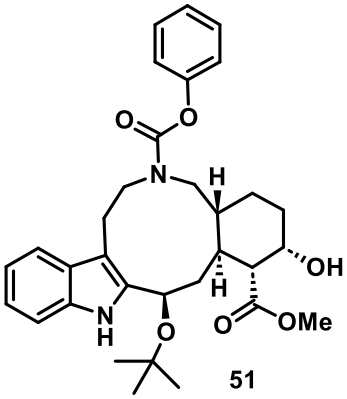
^{1}H NMR: (600 MHz, TCE, 100 °C) δ 8.27 (s, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.40 (d, *J* = 8.1 Hz, 1H), 7.26 (dd, *J* = 7.5, 7.5 Hz, 2H), 7.19 (dd, *J* = 7.6, 7.5 Hz, 1H), 7.14 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.10 (dd, *J* = 7.5, 7.3 Hz, 1H), 6.83 - 6.57 (m, 2H), 4.66 (dd, *J* = 5.3, 5.3 Hz, 1H), 4.16 (m, 1H), 4.01 (m, 1H), 3.81 (s, 3H), 3.67 (m, 1H), 3.49 (m, 1H), 3.33 (s, 3H), 3.28 (ddd, *J* = 15.2, 4.0, 3.7 Hz, 1H), 3.13 (ddd, *J* = 15.3, 10.7, 3.6 Hz,

1H), 3.07 (d, *J* = 14.3 Hz, 1H), 2.57 (dd, *J* = 11.2, 2.1 Hz, 1H), 2.57 (br. s, 1H, buried), 2.29 (ddd, *J* = 15.6, 3.8, 3.8 Hz, 1H), 2.23 (ddd, *J* = 15.6, 5.0, 5.0 Hz, 1H), 2.10 (m, 1H), 1.95 - 1.86 (m, 2H), 1.53 (m, 1H), 1.50 - 1.40 (m, 2H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 174.8, 155.0, 151.2, 136.4, 135.4, 128.7, 128.6, 124.6, 121.6, 121.2, 119.4, 118.0, 110.9, 109.6, 74.3, 66.6, 57.8, 56.9, 52.0, 51.5, 51.0, 38.5, 37.8, 35.6, 30.8, 24.9, 24.8.

HRMS (ESI): calc. for $C_{29}H_{35}N_2O_6$ $[M+H]^+$: 507.2490, found: 507.2498.

Melting point: 118 - 120 ˚C.



51

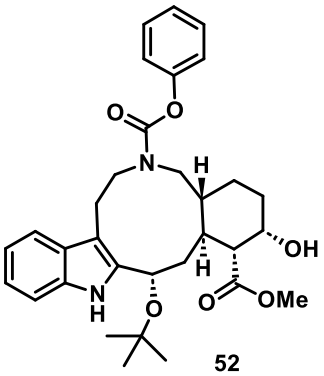
Yield: 13%; 40 mg of **51**; white solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 8.36 (s, 1H), 7.55 (d, *J* = 7.8 Hz, 1H), 7.48 - 7.41 (m, 3H), 7.27 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.26 - 7.21 (m, 3H), 7.17 (dd, *J* = 7.4, 7.4 Hz, 1H), 4.75 (m, 1H), 4.09 (m, 1H), 3.88 (s, 3H), 3.85 - 3.71 (br. m, 2H), 3.51 (br. m, 1H), 3.09 (dd, *J* = 15.2, 8.6 Hz, 1H), 3.05 - 2.88 (br. m, 2H), 2.67 (d, *J* = 10.5 Hz, 1H), 2.55 (br. m, 1H), 2.31 (br. s, 1H), 2.16 (br. m, 1H), 1.90 (br. m, 1H), 1.76 (appt. dq, *J* = 13.8, 3.7 Hz, 1H), 1.52 (br. m, 1H), 1.34 (m, 1H), 1.20 (s, 9H), 1.17 - 1.07 (m, 2H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 175.9, 155.0, 151.6, 138.4, 135.1, 129.0, 128.7, 124.9, 121.6, 121.4, 119.2, 117.8, 111.0, 109.4, 74.2, 67.4, 66.8, 57.8, 53.7, 51.8, 51.6, 41.1, 36.1, 35.2, 30.7, 28.0, 24.4, 24.2.

HRMS (ESI): calc. for $C_{32}H_{41}N_2O_6$ $[M+H]^+$: 549.2959, found: 549.2951.

Melting point: 93 - 95 °C.



52

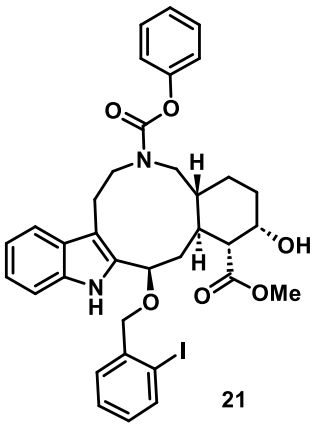
Yield: 20%; 60 mg of **52**; white solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 8.21 (s, 1H), 7.54 (d, *J* = 7.9 Hz, 1H), 7.40 (d, *J* = 8.1 Hz, 1H), 7.30 (dd, *J* = 7.3, 7.3 Hz, 2H), 7.21 - 7.13 (m, 2H), 7.09 (dd, *J* = 7.4, 7.4 Hz, 1H), 6.99 - 6.70 (br. m, 2H), 5.03 (dd, *J* = 5.3, 5.3 Hz 1H), 4.11 (m, 1H), 3.97 (br. m, 1H), 3.78 (s, 3H), 3.69 (br. m, 1H), 3.50 (br. m, 1H), 3.37 (m, 1H), 3.13 (ddd, *J* = 15.3, 9.8, 2.8 Hz, 1H), 3.08 (br. m, 1H, partially buried), 2.69 (dd, *J* = 10.7, 1.7 Hz, 1H), 2.58 (br. s, 1H), 2.24 - 2.12 (br. m, 2H), 2.08 (br. m, 1H), 1.88 (br. m, 1H), 1.53 - 1.39 (m, 3H), 1.20 (s, 9H). Note: This spectrum shows many broad signals. The C20 proton does not appear in ^{1}H NMR spectrum and has no observable correlations in 2D NMR experiments (COSY and HSQC).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 174.8, 155.1, 151.4, 139.2, 135.3, 128.7, 124.6, 121.4, 121.3, 119.2, 118.0, 110.7, 74.5, 66.6, 64.6, 57.4, 51.8, 51.5, 51.2, 40.6, 37.5, 35.5, 30.5, 28.2, 24.8, 24.5. Note: Two aromatic ^{13}C signals are missing in this spectrum.

HRMS (ESI): calc. for $C_{32}H_{40}N_2O_6Na$ $[M+Na]^+$: 571.2779, found: 571.2775.

Melting point: 116 - 118 °C.



21

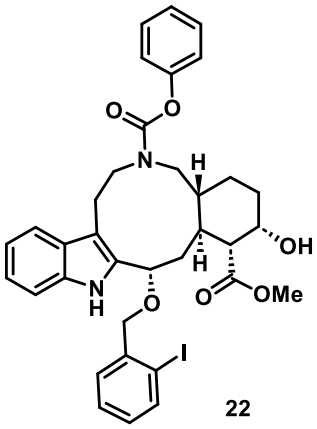
Yield: 21%; 70 mg of **21**; white solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 8.32 (s, 1H), 7.86 (d, *J* = 7.9 Hz, 1H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.47 (d, *J* = 8.1 Hz, 1H), 7.44 - 7.39 (m, 3H), 7.36 (dd, *J* = 7.5, 7.5 Hz, 1H), 7.30 - 7.23 (m, 2H), 7.22 - 7.18 (m, 3H), 7.01 (m, 1H), 4.54 (dd, *J* = 9.9, 5.4 Hz, 1H), 4.50 (d, *J* = 12.6 Hz, 1H), 4.44 (d, *J* = 12.6 Hz, 1H), 4.12 - 4.02 (m, 2H), 3.76 (s, 3H), 3.62 - 3.50 (m, 2H), 3.21 - 3.09 (m, 2H), 2.84 - 2.67 (m, 2H), 2.54 (dd, *J* = 11.1, 1.0 Hz, 1H), 2.52 (br. s, 1H, partially buried), 2.21 (ddd, *J* = 14.5, 5.7, 5.3 Hz, 1H), 1.88 (br. m, 1H), 1.83 - 1.73 (m, 2H), 1.43 (m, 1H), 1.25 (appt. dq, *J* = 13.6, 4.0 Hz, 1H), 1.13 (m, 1H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 176.5, 155.1, 151.5, 140.6, 139.2, 135.5, 135.2, 129.0, 129.0, 129.0 (buried; observed by HSQC), 128.6, 128.0, 124.9, 122.0, 121.6, 119.6, 118.1, 111.3, 111.3, 97.8, 75.6, 74.7, 66.4, 58.3, 54.2, 52.0, 51.9, 39.9, 36.7, 34.9, 30.5, 24.6, 24.2.

HRMS (ESI): calc. for $C_{35}H_{38}IN_2O_6$ $[M+H]^+$: 709.1769, found: 709.1766.

Melting point: 95 - 97 °C.



22

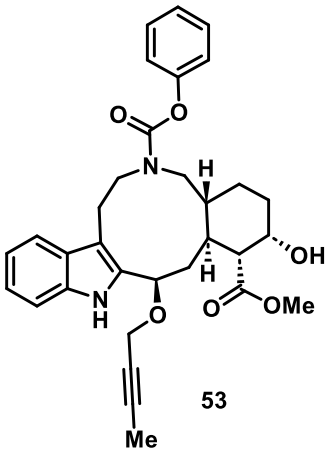
Yield: 54%; 181 mg of **22**; white solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 8.28 (s, 1H), 7.88 (d, *J* = 7.9 Hz, 1H), 7.58 (d, *J* = 7.9 Hz, 1H), 7.49 (d, *J* = 7.6 Hz, 1H), 7.41 (d, *J* = 8.2 Hz, 1H), 7.38 (dd, *J* = 7.5, 7.5 Hz, 1H, partially buried), 7.26 (dd, *J* = 7.3, 7.3 Hz, 2H), 7.20 (dd, *J* = 7.7, 7.3 Hz, 1H), 7.14 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.12 (dd, *J* = 7.3, 7.3 Hz, 1H, partially buried), 7.03 (dd, *J* = 7.6, 7.5 Hz, 1H), 6.89 - 6.57 (m, 2H), 4.96 (dd, *J* = 5.7, 5.7 Hz, 1H), 4.53 (d, *J* = 12.4 Hz, 1H), 4.45 (d, *J* = 12.4 Hz, 1H), 4.13 (m, 1H), 4.07 (m, 1H), 3.64 (s, 3H), 3.63 - 3.53 (m, 2H), 3.35 (ddd, *J* = 15.2, 4.7, 3.3 Hz, 1H), 3.17 (ddd, *J* = 15.2, 10.3, 3.4 Hz, 1H), 3.03 (d, *J* = 14.3 Hz, 1H), 2.60 (dd, *J* = 11.4, 2.2 Hz, 1H), 2.48 (br. s, 1H), 2.40 (dd, *J* = 15.2, 4.0, 4.0 Hz, 1H), 2.30 (ddd, *J* = 15.5, 5.3, 5.3 Hz, 1H), 2.16 (m, 1H), 1.89 (m, 1H), 1.80 (m, 1H), 1.51 - 1.38 (m, 3H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 174.8, 155.0, 151.3, 140.4, 139.2, 135.9, 135.6, 129.3, 129.1, 128.7, 128.6, 128.0, 124.6, 121.9, 121.3, 119.5, 118.1, 111.0, 110.5, 98.0, 75.1, 72.4, 66.6, 57.8, 51.7, 51.5, 51.1, 38.4, 37.5, 35.7, 30.7, 24.9, 24.6.

HRMS (ESI): calc. for $C_{35}H_{38}IN_2O_6$ $[M+H]^+$: 709.1769, found: 709.1759.

Melting point: 182 - 184 °C.



53

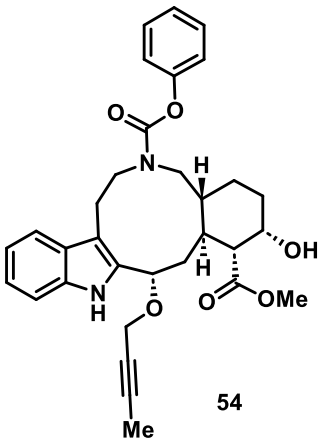
Yield: 27%; 210 mg of **53**; tan solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 8.29 (s, 1H), 7.57 (d, *J* = 7.9 Hz, 1H), 7.46 (d, *J* = 8.1 Hz, 1H), 7.44 - 7.40 (m, 2H), 7.29 - 7.24 (m, 2H), 7.24 - 7.20 (m, 2H), 7.19 (m, 1H), 4.69 (dd, *J* = 10.0, 5.2 Hz, 1H), 4.13 (dq, *J* = 15.5, 2.1 Hz, 1H), 4.06 (m, 1H), 4.03 (m, 1H), 3.94 (dq, *J* = 15.5, 2.1 Hz, 1H), 3.91 (s, 3H), 3.57 (m, 1H), 3.46 (dd, *J* = 15.4, 9.9 Hz, 1H), 3.19 - 3.07 (m, 2H), 2.78 (m, 1H), 2.70 (m, 1H), 2.61 (br. s, 1H), 2.54 (m, 1H), 2.14 (ddd, *J* = 14.4, 5.1, 5.1 Hz, 1H), 1.87 (dd, *J* = 2.1, 2.1 Hz, 3H), 1.87 - 1.75 (m, 3H, partially buried), 1.43 (m, 1H), 1.24 (appt. dq, *J* = 13.5, 4.0 Hz, 1H), 1.14 (m, 1H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 176.5, 155.1, 151.5, 135.5, 134.9, 129.0, 128.5, 124.9, 122.0, 121.6, 119.5, 118.0, 111.3, 111.2, 82.4, 75.4, 73.8 (observed by HSQC, buried in TCE), 66.4, 58.2, 56.2, 54.0, 52.0, 51.8, 39.5, 36.7, 35.0, 30.4, 24.4, 24.2, 3.2.

HRMS (ESI): calc. for $C_{32}H_{36}N_2O_6Na$ $[M+Na]^+$: 567.2466, found: 567.2454.

Melting point: 89 - 91 °C.



54

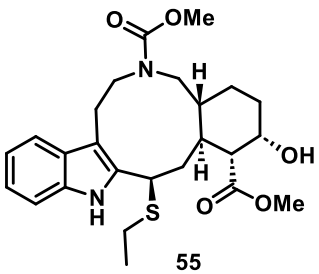
Yield: 62%; 479 mg of **54**; tan solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 8.25 (s, 1H), 7.56 (d, *J* = 7.9 Hz, 1H), 7.39 (d, *J* = 8.1 Hz, 1H), 7.26 (dd, *J* = 7.3, 7.3 Hz, 2H), 7.19 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.14 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.10 (dd, *J* = 7.5, 7.5 Hz, 1H), 6.92 - 6.41 (m, 2H), 5.09 (dd, *J* = 5.5, 5.5 Hz, 1H), 4.18 (m, 1H), 4.14 (dq, *J* = 15.4, 2.1 Hz, 1H), 4.02 (m, 1H), 3.97 (dq, *J* = 15.4, 2.1 Hz, 1H), 3.83 (s, 3H), 3.64 (m, 1H), 3.56 (m, 1H), 3.29 (ddd, *J* = 15.4, 3.9, 3.9 Hz, 1H), 3.17 (ddd, *J* = 15.4, 10.3, 3.6 Hz, 1H), 3.06 (d, *J* = 14.2 Hz, 1H), 2.73 (dd, *J* = 11.4, 2.0 Hz, 1H), 2.52 (br. s, 1H), 2.31 (ddd, *J* = 15.5, 3.9, 3.9 Hz, 1H), 2.23 (ddd, *J* = 15.5, 5.2, 5.2 Hz, 1H), 2.14 (m, 1H), 1.96 - 1.88 (m, 2H), 1.87 (dd, *J* = 2.1, 2.1 Hz, 3H), 1.56 - 1.42 (m, 3H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 174.8, 155.1, 151.2, 135.9, 135.6, 128.6, 128.6, 124.6, 121.8, 121.3, 119.5, 118.0, 110.9, 110.3, 82.6, 75.3, 70.5, 66.7, 57.8, 56.7, 51.7, 51.5, 51.1, 38.1, 37.9, 35.9, 31.0, 24.8 (2 C; one signal is buried, but observed by HSQC), 3.2.

HRMS (ESI): calc. for $C_{32}H_{36}N_2O_6Na$ $[M+Na]^+$: 567.2466, found: 567.2457.

Melting point: 105 - 106 °C.



55

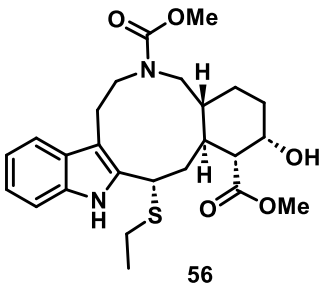
Yield: 11%; 70 mg of **55**; tan solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 8.18 (s, 1H), 7.50 (d, *J* = 7.8 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.22 (m, 1H), 7.15 (dd, *J* = 7.5, 7.5 Hz, 1H), 4.03 (m, 1H), 3.93 (dd, *J* = 12.0, 4.0 Hz, 1H), 3.92 (m, 1H, buried), 3.89 (s, 3H), 3.79 (s, 3H), 3.47 - 3.35 (m, 2H), 3.03 (dd, *J* = 15.0, 7.1 Hz, 1H), 3.00 (d, *J* = 14.3 Hz, 1H), 2.82 (br. s, 1H), 2.71 - 2.57 (m, 2H), 2.47 - 2.40 (m, 2H), 2.36 (dq, *J* = 12.7, 7.4 Hz, 1H), 1.91 (ddd, *J* = 14.4, 4.6, 4.6 Hz, 1H), 1.86 - 1.76 (m, 3H), 1.49 (m, 1H), 1.29 (m, 1H), 1.21 (dd, *J* = 7.4, 7.4 Hz, 3H), 1.11 (m, 1H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 176.6, 157.6, 135.7, 135.3, 128.8, 121.7, 119.4, 117.8, 111.5, 111.0, 66.4, 57.7, 54.0, 52.3, 51.8, 51.6, 41.7, 40.3, 36.9, 30.2, 25.7, 25.1, 24.0, 14.4. Note: Missing one carbon signal in the aliphatic region of this spectrum.

HRMS (ESI): calc. for $C_{25}H_{35}N_2O_5S$ $[M+H]^+$: 475.2261, found: 475.2260.

Melting point: 81 - 83 °C.



56

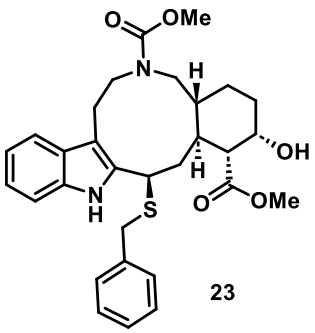
Yield: 33%; 222 mg of **56**; tan solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 8.21 (s, 1H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.19 (m, 1H), 7.14 (m, 1H), 4.27 (dd, *J* = 8.0, 6.0 Hz, 1H), 4.18 (m, 1H), 3.96 (m, 1H), 3.79 (s, 3H), 3.64 (m, 1H), 3.39 - 3.27 (m, 4H), 3.24 (m, 1H), 3.04 (ddd, *J* = 15.1, 9.7, 3.6 Hz, 1H), 2.84 (dd, *J* = 14.6, 2.2 Hz, 1H), 2.68 (dd, *J* = 11.1, 2.6 Hz, 1H), 2.45 (br. s, 1H), 2.40 (dq, *J* = 12.9, 7.4 Hz, 1H), 2.32 (dq, *J* = 12.9, 7.4 Hz, 1H), 2.27 (ddd, *J* = 15.1, 8.3, 2.6 Hz, 1H), 2.14 (m, 1H), 2.00 (ddd, *J* = 15.1, 6.0, 6.0 Hz, 1H), 1.85 (m, 1H), 1.68 (m, 1H), 1.54 - 1.43 (m, 2H), 1.37 (m, 1H), 1.20 (dd, *J* = 7.4, 7.4 Hz, 3H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 174.5, 157.2, 136.0, 135.4, 128.8, 121.6, 119.2, 118.1, 111.1, 110.6, 66.8, 56.9, 51.9, 51.5, 51.0, 50.1, 37.4, 37.1, 36.6, 36.4, 30.4, 25.7, 24.8, 24.3, 14.3.

HRMS (ESI): calc. for $C_{25}H_{35}N_2O_5S$ $[M+H]^+$:475.2261, found: 475.2259.

Melting point: 86 - 88 °C.



23

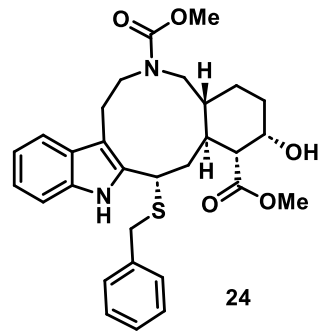
Yield: 23%; 350 mg of **23**; light yellow-white solid.

^{1}H NMR: (600 MHz, DMSO-d_6, 100 °C) δ 10.38 (s, 1H), 7.42 (d, *J* = 7.8 Hz, 1H), 7.39 (d, *J* = 8.1 Hz, 1H), 7.27 - 7.23 (m, 2H), 7.21 - 7.17 (m, 3H), 7.07 (m, 1H), 6.98 (m, 1H), 4.17 (dd, *J* = 11.8, 3.5 Hz, 1H), 4.05 (br. s, 1H), 3.93 (m, 1H), 3.72 (m, 1H), 3.66 (s, 3H), 3.63 (s, 3H), 3.56 (d, *J* = 13.4 Hz, 1H), 3.52 (d, *J* = 13.4 Hz, 1H), 3.33 (dd, *J* = 13.0, 10.4 Hz, 1H), 3.22 (ddd, *J* = 15.1, 10.0, 0.9 Hz, 1H), 2.85 (dd, *J* = 15.1, 6.5 Hz, 1H), 2.76 - 2.64 (m, 2H), 2.54 (ddd, *J* = 14.4, 11.8, 3.4 Hz, 1H), 2.37 (dd, *J* = 9.7, 2.8 Hz, 1H), 1.80 - 1.69 (m, 2H), 1.61 (m, 1H), 1.51 (m, 1H), 1.43 (m, 1H), 1.15 (m, 1H), 1.01 (m, 1H).

^{13}C NMR: (151 MHz, DMSO-d_6, 100 °C) δ 173.5, 156.8, 138.0, 135.3, 135.3, 128.0, 127.7, 127.7, 126.1, 120.5, 118.1, 117.2, 110.9, 110.1, 65.8, 55.9, 54.2, 51.6, 50.7, 50.3, 41.7, 40.2, 37.0, 36.2, 35.3, 30.3, 24.4, 24.0.

HRMS (ESI): calc. for $C_{30}H_{37}N_2O_5S$ $[M+H]^+$: 537.2418, found: 537.2408.

Melting point: 102 - 104 °C.



24

Yield: 27%; 408 mg of **24**; white solid.

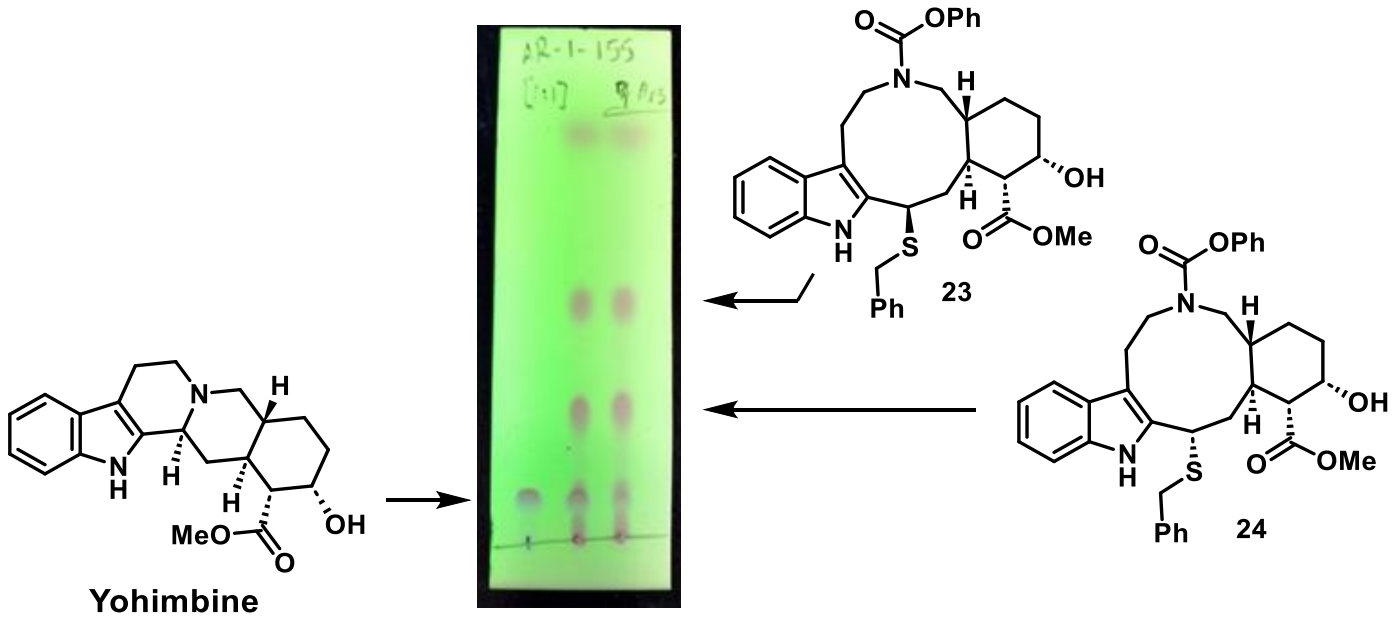
^{1}H NMR: (600 MHz, DMSO-d_6, 100 °C) δ 10.50 (s, 1H), 7.43 (d, *J* = 7.8 Hz, 1H), 7.34 (m, 1H), 7.30 - 7.25 (m, 2H), 7.21 (m, 1H), 7.19 - 7.15 (m, 2H), 7.04 (m, 1H), 6.98 (m, 1H), 4.11 (d, *J* = 4.7 Hz, 1H), 4.08 - 4.02 (m, 2H), 3.97 (dd, *J* = 9.1, 6.4 Hz, 1H), 3.65 (m, 1H, partially buried), 3.64 (s, 3H), 3.50 (d, *J* = 13.5 Hz, 1H), 3.44 (d, *J* = 13.5 Hz, 1H), 3.18 (br. s, 3H, buried), 3.17 (m, 1H), 3.00 (m, 1H, partially buried), 2.87 (ddd, *J* = 15.1, 8.5, 3.1 Hz, 1H), 2.58 (d, *J* = 11.7 Hz, 1H), 2.54 (dd, *J* = 14.4, 1.5 Hz, 1H), 2.28 (dd, *J* = 13.9, 8.5 Hz, 1H), 2.08 (m, 1H), 2.02 (ddd, *J* = 15.0, 5.1, 5.1 Hz, 1H), 1.58 (m, 1H), 1.22 (m, 1H), 1.12 (m, 1H), 1.08 - 0.91 (m, 2H).

^{13}C NMR: (151 MHz, DMSO-d_6, 100 °C) δ 172.3, 155.8, 137.8, 136.1, 135.0, 128.3, 128.1, 127.6, 126.1, 120.1, 117.9, 117.2, 110.5, 109.1, 65.8, 56.0, 51.1, 50.3, 49.2, 36.6, 36.3, 35.3, 34.9, 34.3, 31.1, 24.0, 23.6. Note: This spectrum is missing one carbon signal in the aliphatic region.

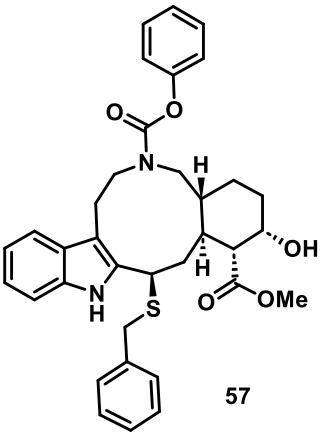
HRMS (ESI): calc. for $C_{30}H_{37}N_2O_5S$ $[M+H]^+$: 537.2418, found: 537.2401.

Melting point: 189 - 190 °C.

TLC image in 1:1 Hexanes:Ethyl Acetate



Picture Taken By Dr. Alejandra Chávez-Riveros



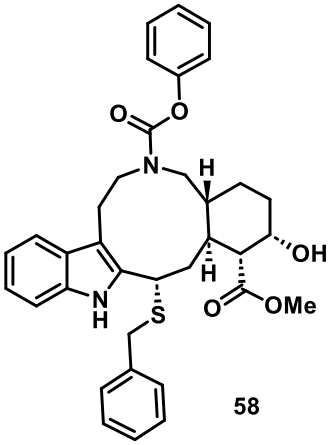
Yield: 32%; 107 mg of **57**; tan solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 8.08 (s, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.46 - 7.40 (m, 3H), 7.34 - 7.29 (m, 2H), 7.29 - 7.23 (m, 5H), 7.23 - 7.16 (m, 3H), 4.19 (dd, *J* = 13.3, 4.4 Hz, 1H), 4.00 (m, 1H), 3.84 (dd, *J* = 12.3, 4.2 Hz, 1H), 3.68 (s, 3H), 3.67 (m, 1H, partially buried), 3.63 (d, *J* = 13.9 Hz, 1H), 3.56 (d, *J* = 13.9 Hz, 1H), 3.44 (dd, *J* = 12.1 Hz, 1H), 3.23 (d, *J* = 13.9 Hz, 1H), 3.10 (dd, *J* = 15.5, 6.2 Hz, 1H), 2.81 - 2.56 (m, 3H), 2.40 (m, 1H), 2.01 (m, 1H), 1.95 (ddd, *J* = 14.5, 5.2, 5.2 Hz, 1H), 1.84 - 1.73 (m, 2H), 1.45 (m, 1H), 1.29 (appt. dq, *J* = 13.6, 4.2 Hz, 1H), 1.14 (m, 1H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 176.6, 155.1, 151.5, 138.1, 135.4, 135.3, 129.0, 128.9, 128.5, 128.2, 126.7, 125.0, 121.9, 121.6, 119.6, 117.8, 111.4, 111.1, 66.3, 58.5, 54.2, 52.2, 51.8, 41.5, 40.2, 37.0, 36.8, 36.1, 30.2, 25.0, 24.1.

HRMS (ESI): calc. for $C_{35}H_{39}N_2O_5S$ $[M+H]^+$: 599.2574, found: 599.2568.

Melting point: 90 - 92 °C.



58

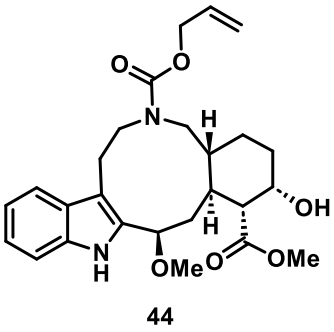
Yield: 35%; 117 mg of **58**; light yellow-white solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 8.25 (s, 1H), 7.56 (d, *J* = 7.9 Hz, 1H), 7.39 - 7.33 (m, 3H), 7.30 (m, 1H), 7.26 - 7.20 (m, 4H), 7.18 (dd, *J* = 7.7, 7.4 Hz, 1H; appt. t), 7.15 - 7.04 (m, 2H), 6.77 - 6.37 (br. m, 2H), 4.28 (m, 1H), 4.12 (m, 1H), 4.02 (dd, *J* = 6.0, 6.0 Hz, 1H), 3.85 (m, 1H), 3.76 (s, 3H), 3.61 (d, *J* = 13.8 Hz, 1H), 3.43 (d, *J* = 13.8 Hz, 1H), 3.39 - 3.30 (m, 2H), 2.99 (m, 1H), 2.87 (d, *J* = 13.7 Hz, 1H), 2.48 (dd, *J* = 11.3, 1.4 Hz, 1H), 2.36 (m, 1H), 2.25 (br. s, 1H), 2.20 (m, 1H), 2.04 (ddd, *J* = 15.5, 5.6, 5.6 Hz, 1H), 1.83 (appt. dq, *J* = 13.9, 3.9 Hz, 1H), 1.46 (m, 1H), 1.37 - 1.28 (m, 3H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 174.1, 154.9, 151.2, 137.8, 136.0, 135.5, 129.0, 128.8, 128.6, 128.1, 126.9, 124.5, 121.7, 121.2, 119.5, 118.1, 110.8, 66.9, 57.1, 51.5, 50.6, 50.3, 36.9, 36.4, 36.4, 36.2, 36.0, 30.7, 24.9, 24.4. Note: One carbon signal is missing from the aromatic region.

HRMS (ESI): calc. for $C_{35}H_{39}N_2O_5S$ $[M+H]^+$: 599.2574, found: 599.2573.

Melting point: 108 - 110 °C.



44

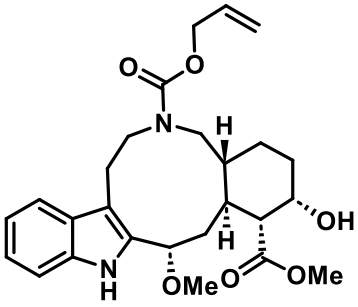
Yield: 29%; 58 mg of **44**; white solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 8.26 (s, 1H), 7.54 (d, *J* = 7.9 Hz, 1H), 7.42 (d, *J* = 8.1 Hz, 1H), 7.23 (m, 1H), 7.16 (m, 1H), 6.03 (m, 1H, partially buried), 5.38 (m, 1H), 5.28 (m, 1H), 4.73 - 4.64 (m, 2H), 4.27 (dd, *J* = 9.4, 5.0 Hz, 1H), 4.05 (m, 1H), 3.88 (s, 3H), 3.80 (dd, *J* = 13.7, 7.2 Hz, 1H), 3.51 (dd, *J* = 13.4, 9.4 Hz, 1H), 3.32 (dd, *J* = 15.2, 9.3 Hz, 1H), 3.26 (s, 3H), 3.02 (dd, *J* = 15.3, 7.2 Hz, 1H), 2.93 (d, *J* = 13.9 Hz, 1H), 2.78 (m, 1H), 2.59 - 2.50 (m, 3H), 2.05 (ddd, *J* = 14.4, 5.1, 5.1 Hz, 1H), 1.81 - 1.73 (m, 2H), 1.64 (m, 1H), 1.41 (m, 1H), 1.19 (m, 1H), 1.09 (m, 1H). Note: The apparent splitting regarding the two methoxy 3H signals in this spectra are due to slight inhomogeneities of the magnetic field at the higher experimental temperature. Despite their appearance, these signals are reported as singlets.

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 176.2, 156.7, 135.4, 135.3, 133.2, 128.5, 121.8, 119.4, 118.0, 116.9, 111.1, 77.4, 66.6, 65.7, 57.6, 56.5, 53.9, 51.7, 51.4, 39.2, 36.6, 34.9, 30.5, 24.5, 24.1. Note: One carbon signal is missing from the aromatic region.

HRMS (ESI): calc. for $C_{26}H_{34}N_2O_6Na$ $[M + Na]^+$: 493.2309, found: 493.2306.

Melting point: 88 - 90 °C.



15

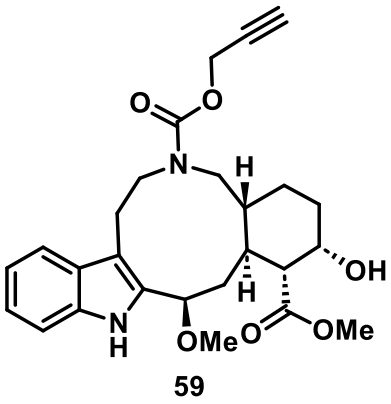
Yield: 31%; 62 mg of **15**; white solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 8.23 (s, 1H), 7.55 (d, *J* = 7.8 Hz, 1H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.20 (m, 1H), 7.14 (m, 1H), 5.65 (m, 1H), 5.15 (d, *J* = 17.4 Hz, 1H), 5.11 (d, *J* = 10.4 Hz, 1H), 4.59 (dd, *J* = 5.2, 5.2 Hz, 1H), 4.40 (dd, *J* = 12.7, 4.3 Hz, 1H), 4.14 (m, 1H), 4.13 (m, 1H, buried), 3.81 (s, 3H), 3.80 (m, 1H, partially buried), 3.55 (m, 1H), 3.33 (m, 1H), 3.29 (s, 3H), 3.18 (ddd, *J* = 15.2, 3.7, 3.7 Hz, 1H), 3.02 (ddd, *J* = 15.1, 10.6, 3.6 Hz, 1H), 2.95 (d, *J* = 14.5 Hz, 1H), 2.59 (br. s, 1H), 2.53 (dd, *J* = 11.4, 1.8 Hz, 1H), 2.19 (ddd, *J* = 15.6, 4.2, 4.2 Hz, 1H), 2.15 (ddd, *J* = 15.6, 5.1, 5.1 Hz, 1H), 2.03 (m, 1H), 1.89 (appt. dq, *J* = 13.7, 3.7 Hz, 1H), 1.81 (m, 1H), 1.52 (m, 1H), 1.46 - 1.36 (m, 2H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 175.0, 156.6, 136.3, 135.4, 133.0, 128.6, 121.5, 119.2, 118.0, 116.8, 110.9, 109.9, 74.3, 66.6, 65.6, 57.6, 56.9, 52.1, 51.4, 50.7, 38.4, 37.9, 35.5, 30.9, 24.9, 24.7.

HRMS (ESI): calc. for $C_{26}H_{34}N_2O_6Na$ $[M + Na]^+$: 493.2309, found: 493.2308.

Melting point: 96 - 98 °C.



59

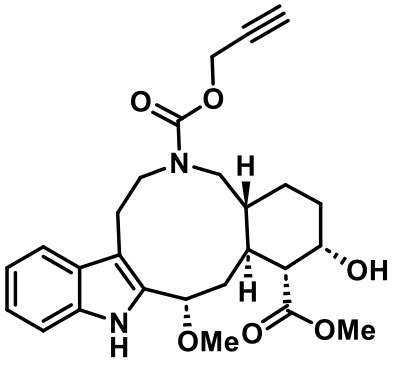
Yield: 18%; 122 mg of **59**; white solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 8.31 (s, 1H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.42 (d, *J* = 8.1 Hz, 1H), 7.23 (m, 1H), 7.16 (m, 1H), 4.84 (dd, *J* = 15.6, 1.5 Hz, 1H), 4.75 (dd, *J* = 15.6, 1.5 Hz, 1H), 4.28 (dd, *J* = 9.2, 5.0 Hz, 1H), 4.05 (m, 1H), 3.88 (s, 3H), 3.78 (m, 1H), 3.53 (dd, *J* = 13.5, 9.6 Hz, 1H), 3.32 (dd, *J* = 15.1, 9.4 Hz, 1H), 3.25 (s, 3H), 3.03 (dd, *J* = 15.3, 7.1 Hz, 1H), 2.91 (d, *J* = 14.1 Hz, 1H), 2.80 (m, 1H), 2.61 - 2.47 (m, 4H), 2.06 (ddd, *J* = 14.6, 4.8, 4.8 Hz, 1H), 1.82 - 1.73 (m, 2H), 1.63 (m, 1H, partially buried under water signal), 1.41 (m, 1H), 1.20 (m, 1H), 1.09 (m, 1H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 176.1, 156.0, 135.4, 135.3, 128.5, 121.8, 119.4, 118.0, 111.1, 111.0, 78.8, 77.4, 74.3, 66.6, 57.5, 56.5, 53.8, 52.7, 51.7, 51.4, 39.1, 36.7, 34.9, 30.5, 24.4, 24.1.

HRMS (ESI): calc. for $C_{26}H_{32}N_2O_6Na$ $[M + Na]^+$: 491.2153, found: 491.2160.

Melting point: 88 - 90 °C.



60

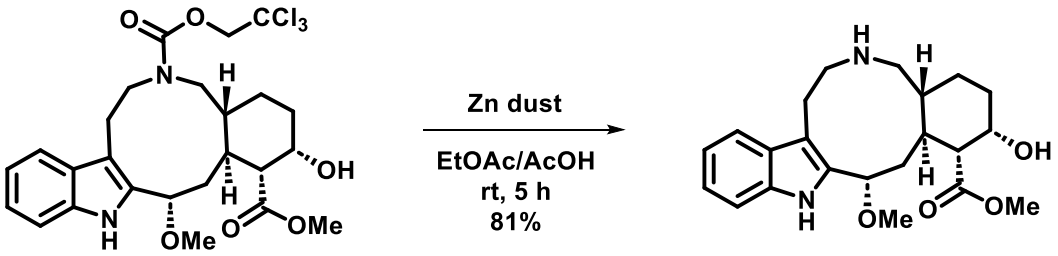
Yield: 34%; 225 mg of **60**; white solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 8.28 (s, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.20 (dd, *J* = 7.5, 7.5 Hz, 1H), 7.15 (m, 1H), 4.59 (dd, *J* = 5.2, 5.2 Hz, 1H), 4.49 (d, *J* = 15.6 Hz, 1H), 4.16 (br. m, 1H, buried), 4.14 (m, 1H), 3.81 (s, 3H), 3.76 (m, 1H), 3.58 (d, *J* = 13.8 Hz, 1H), 3.29 (s, 3H), 3.27 (m, 1H, partially buried), 3.19 (ddd, *J* = 15.3, 3.6, 3.6 Hz, 1H), 3.03 (ddd, *J* = 15.3, 10.4, 3.6 Hz, 1H), 2.97 (d, *J* = 14.4 Hz, 1H), 2.61 (br. s, 1H), 2.54 (dd, *J* = 11.3, 1.8 Hz, 1H), 2.42 (m, 1H), 2.19 - 2.11 (m, 2H), 2.01 (m, 1H), 1.89 (appt. dq, *J* = 13.7, 3.6 Hz, 1H), 1.80 (m, 1H), 1.52 (m, 1H), 1.46 - 1.37 (m, 2H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 175.0, 155.8, 136.2, 135.4, 128.5, 121.6, 119.3, 118.0, 110.9, 109.8, 78.7, 74.3, 66.6, 57.7, 56.9, 52.3, 52.1, 51.5, 50.7, 38.4, 37.9, 35.5, 30.8, 24.7. **Note:** Two ^{13}C signals are missing, likely due to overlap or signal broadening in the following spectral regions (70 - 80 ppm & 20 - 30 ppm regions).

HRMS (ESI): calc. for $C_{26}H_{32}N_2O_6Na$ $[M + Na]^+$: 491.2153, found: 491.2150.

Melting point: 85 - 87 °C.



48 **61**

Procedure. Compound **48** (500 mg, 0.89 mmol) was dissolved in ethyl acetate:acetic acid (17 mL ethyl acetate, 1.7 mL acetic acid), and zinc dust (4.4 g, 66.75 mmol) was then added to the reaction mixture. The resulting mixture was then allowed to stir at room temperature for five hours (the reaction was complete after this time based on TLC analysis), after which the reaction mixture was filtered and the filtrate was diluted with 50 mL ethyl acetate. The solution was then acidified to pH ~ 2 and the aqueous layer was extracted with ethyl acetate. The aqueous layer was then basified to pH ~ 12 and extracted with ethyl acetate. The resulting organic layer was then separated, dried over sodium sulfate, and concentrated to afford 278 milligrams of product **61** (81% yield) as a light tan solid. Note: In some instances, purification of the crude material was conducted via column chromatography using a 99:1 ethyl acetate:triethylamine solvent system instead of an acid-base extraction.

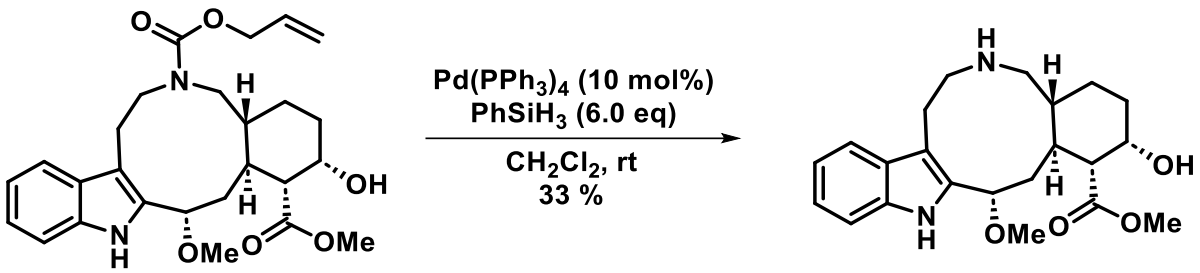
^{1}H NMR: (600 MHz, $CDCl_3$) δ 8.42 (s, 1H), 7.55 (d, *J* = 7.9 Hz, 1H), 7.44 (d, *J* = 8.1 Hz, 1H), 7.22 (ddd, *J* = 8.0, 7.2, 1.1 Hz, 1H), 7.12 (m, 1H), 4.83 (dd, *J* = 9.9, 7.3 Hz, 1H), 4.03 (appt. q, *J* = 2.6 Hz, 1H), 3.72 (s, 3H), 3.12 - 2.99 (m, 2H), 3.09 (s, 3H), 2.96 (m, 1H), 2.93 (dd, *J* = 11.7, 2.3 Hz, 1H), 2.81 (dd, *J* = 12.7, 5.0 Hz, 1H), 2.54

(dd, *J* = 11.7, 3.3 Hz, 1H), 2.31 (dd, *J* = 11.4, 2.7 Hz, 1H), 1.97 (ddd, *J* = 14.4, 10.1, 7.4 Hz, 1H), 1.84 (ddd, *J* = 14.3, 10.1, 0.8 Hz, 1H), 1.76 (appt. dq, *J* = 13.6, 3.4 Hz, 1H), 1.71 (dd, *J* = 13.1, 3.5 Hz, 1H), 1.66 (m, 1H), 1.41 - 1.24 (m, 3H).

^{13}C NMR: (151 MHz, $CDCl_3$) δ 175.5, 137.0, 134.5, 127.0, 122.6, 119.4, 118.8, 111.8, 111.7, 74.4, 67.2, 56.2, 54.7, 52.1, 47.9, 44.6, 42.9, 41.9, 32.0, 30.6, 23.3, 21.3.

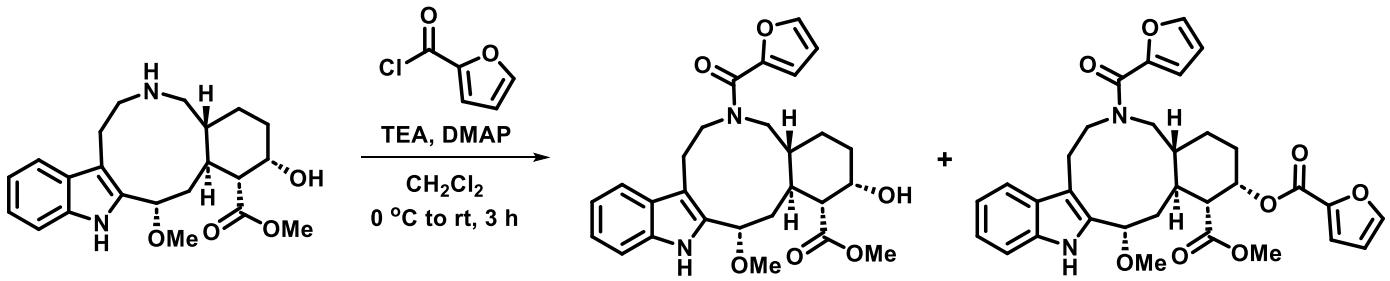
HRMS (ESI): calc. for $C_{22}H_{31}N_2O_4$ $[M+H]^+$: 387.2278, found: 387.2266.

Melting point: 99 - 101 °C.



15 **61**

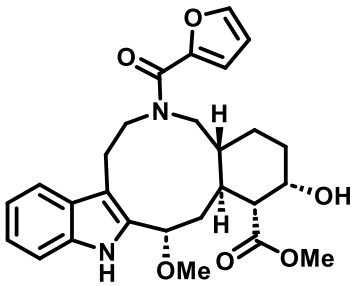
Procedure. Compound **15** (170 mg, 0.36 mmol) was added to a round-bottom flask and was dissolved in 36 mL of dichloromethane. Tetrakis(triphenylphosphine)palladium(0) (41.8 mg, 0.036 mmol) and phenylsilane (0.27 mL, 2.17 mmol) were then added to the reaction mixture, which then stirred at room temperature for 8.5 hours. Upon completion, the reaction was quenched with a saturated solution of sodium bicarbonate. The reaction mixture was then transferred to a separatory funnel and extracted with dichloromethane. The resulting organic layer was then dried with sodium sulfate, filtered, and concentrated under reduced pressure. The crude product was then purified via column chromatography using a gradient of 99:0:1 to 0:99:1 hexanes:ethyl acetate:triethylamine to afford **61** (47 mg, 33%).



61 **62** **63**

Procedure. Compound **61** (150 mg, 0.39 mmol) was dissolved in dichloromethane (3.3 mL). Triethylamine (0.11 mL, 0.78 mmol) was then added to the reaction mixture. The resulting mixture was then cooled to 0 °C before the sequential addition of 2-furoyl chloride (0.077 mL, 0.78 mmol) and 4-dimethylaminopyridine (one crystal). The resulting reaction mixture was then stirred for 25 hours while being allowed to slowly warm to room

temperature. Upon completion, the reaction was quenched with brine and extracted with dichloromethane. The organic layer was separated, dried over sodium sulfate, filtered, and concentrated under reduced pressure. The crude material was then purified via column chromatography using a solvent system of 7:3 hexanes:ethyl acetate to afford **62** (98 mg, 53%) as a white solid and **63** (64 mg, 29%) as a tan solid. Note: When 1 equivalent of 2-furoyl chloride was employed in this reaction, we obtained a 90% yield of **62** and a 4% yield of **63**.



62

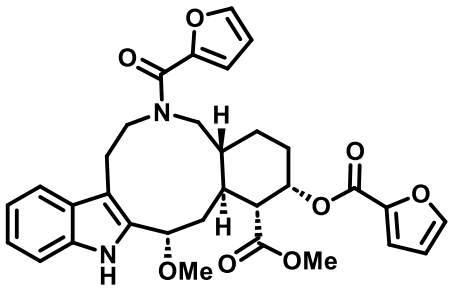
Yield: 90%; 169 mg of **62**; white solid. Yield from using 1 equivalent of 2-furoyl chloride using the acylation procedure.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 8.39 (s, 1H), 7.51 (d, *J* = 7.9 Hz, 1H), 7.46 - 7.42 (m, 2H), 7.22 (m, 1H), 7.15 (m, 1H), 6.95 (m, 1H), 6.47 (m, 1H), 4.72 (dd, *J* = 4.8, 4.8 Hz, 1H), 4.05 (m, 1H), 4.00 (ddd, *J* = 14.7, 3.4, 3.4 Hz, 1H), 3.82 (s, 3H), 3.67 (ddd, *J* = 14.5, 10.3, 2.4 Hz, 1H), 3.36 (s, 3H), 3.29 (d, *J* = 14.0 Hz, 1H), 3.28 - 3.19 (m, 2H), 2.94 (br. s, 1H), 2.80 (m, 1H), 2.40 (dd, *J* = 10.9, 1.7 Hz, 1H), 2.35 (ddd, *J* = 15.5, 4.9, 3.1 Hz, 1H), 2.19 (ddd, *J* = 15.6, 3.5, 3.5 Hz, 1H), 1.91 - 1.80 (m, 3H), 1.48 - 1.39 (m, 2H), 1.33 (m, 1H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 175.7, 162.3, 148.8, 143.4, 135.9, 135.3, 128.2, 121.6, 119.4, 117.7, 115.5, 111.2, 111.0, 109.1, 75.6, 66.2, 58.1, 57.4, 53.3, 52.1, 51.5, 39.2, 37.9, 35.2, 30.6, 25.4, 24.7.

HRMS (ESI): calc. for $C_{27}H_{33}N_2O_6$ $[M+H]^+$: 481.2333, found: 481.2313.

Melting point: 120 - 122 °C.



63

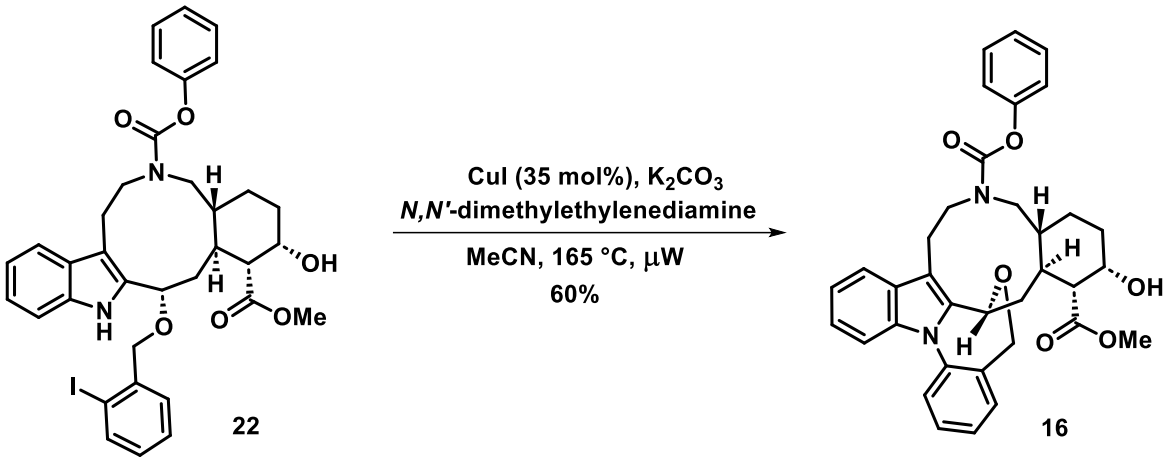
Yield: 29%; 64 mg of **63**; tan solid. Yield from using 2 equivalents of 2-furoyl chloride using the acylation procedure.

^{1}H NMR: (600 MHz, $CDCl_3$, 50 °C) δ 8.71 (s, 1H), 7.53 (m, 1H), 7.51 (d, *J* = 7.9 Hz, 1H), 7.35 (m, 1H), 7.34 (d, *J* = 8.2 Hz, 1H), 7.19 (m, 1H), 7.12 (dd, *J* = 7.4, 7.4 Hz, 1H), 6.96 (d, *J* = 3.4 Hz, 1H), 6.90 (d, *J* = 3.4 Hz, 1H), 6.46 (dd, *J* = 3.4, 1.7 Hz, 1H), 6.40 (dd, *J* = 3.2, 1.6 Hz, 1H), 5.48 (appt. q, *J* = 2.7 Hz, 1H), 4.75 (dd, *J* = 4.7, 4.7 Hz, 1H), 4.00 (d, *J* = 14.1 Hz, 1H), 3.68 (s, 3H), 3.65 (m, 1H, partially buried), 3.31 (d, *J* = 13.8 Hz, 1H), 3.28 (m, 1H, partially buried), 3.24 (s, 3H), 3.23 (m, 1H, partially buried), 2.86 (m, 1H), 2.52 (dd, *J* = 11.5, 2.2 Hz, 1H), 2.31 (ddd, *J* = 15.6, 6.1, 4.9 Hz, 1H), 2.08 (m, 1H), 1.98 - 1.88 (m, 2H), 1.63 - 1.49 (m, 2H), 1.28 - 1.18 (m, 2H).

^{13}C NMR: (151 MHz, $CDCl_3$, 50 °C) δ 172.9, 163.1, 157.8, 149.0, 146.6, 144.9, 143.9, 136.7, 135.8, 128.4, 121.9, 119.6, 118.2, 118.1, 116.6, 111.9, 111.6, 111.6, 109.6, 75.0, 69.9, 59.2, 57.4, 52.9, 52.2, 52.1, 40.2, 38.2, 36.4, 29.4, 25.7. Note: One carbon signal is missing from the aliphatic region.

HRMS (ESI): calc. for $C_{32}H_{35}N_2O_8$ $[M+H]^+$: 575.2388, found: 575.2385.

Melting point: 151 - 153 °C.



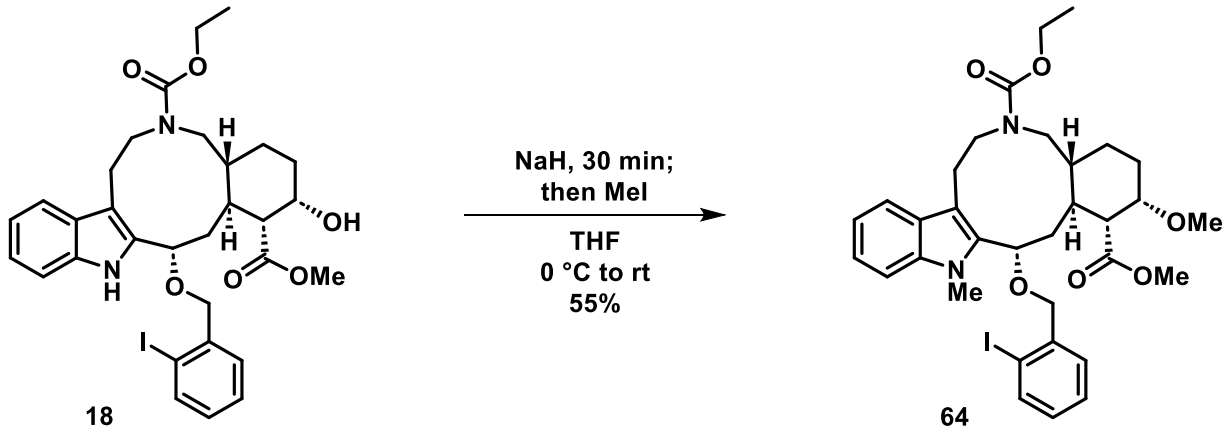
Procedure. Compound **22** (210 mg, 0.30 mmol) was added to a flame-dried microwave vial and was dissolved in anhydrous acetonitrile (4.0 mL). Potassium carbonate (61.4 mg, 0.44 mmol), *N,N'*-dimethylethylenediamine (22 µL, 0.21 mmol), and copper(I) iodide (20 mg, 0.10 mmol) were then added to the solution, and the resulting reaction mixture was subjected to microwave irradiation for 39 minutes at 165 °C. After this time, the reaction mixture was cooled to room temperature, diluted with ethyl acetate, and washed with brine. The organic layer was dried with sodium sulfate, filtered, and concentrated under reduced pressure. The crude product was purified via column chromatography using a gradient of 100% hexanes to 1:4 hexanes:ethyl acetate to afford **16** (104 mg, 60%) as a white solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 7.74 (d, *J* = 8.0 Hz, 1H), 7.69 - 7.64 (m, 2H), 7.56 (m, 1H), 7.43 (m, 1H), 7.34 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.28 - 7.20 (m, 3H), 7.17 (dd, *J* = 7.2, 7.2 Hz, 1H), 7.13 (dd, *J* = 7.3, 7.3 Hz, 1H), 6.74 - 6.50 (m, 2H), 5.63 (m, 1H), 4.75 (d, *J* = 12.2 Hz, 1H), 4.44 (d, *J* = 12.2 Hz, 1H), 4.09 (m, 1H), 4.03 (m, 1H), 3.78 - 3.64 (m, 2H), 3.62 (s, 3H), 3.40 (m, 1H), 3.25 (ddd, *J* = 15.2, 10.0, 4.6 Hz, 1H), 3.13 (d, *J* = 9.4 Hz, 1H), 2.67 (d, *J* = 10.4 Hz, 1H), 2.39 (br. s, 1H), 2.09 (m, 1H), 2.03 (m, 1H), 1.92 (m, 1H), 1.82 (m, 1H), 1.73 - 1.58 (m, 4H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 174.4, 155.0, 151.1, 138.8, 137.0, 135.9, 132.3, 129.8, 129.1, 128.9, 128.6, 125.7, 124.5, 122.7, 122.4, 121.0, 120.7, 119.1, 112.3, 110.4, 68.7, 67.0, 66.8, 57.1, 51.4, 51.2, 50.6, 38.2, 37.8, 35.8, 30.6, 25.0, 24.9.

HRMS (ESI): calc. for $C_{35}H_{37}N_2O_6$ $[M + H]^+$: 581.2646, found: 581.2651.

Melting point: 120 - 122 °C.



18 64

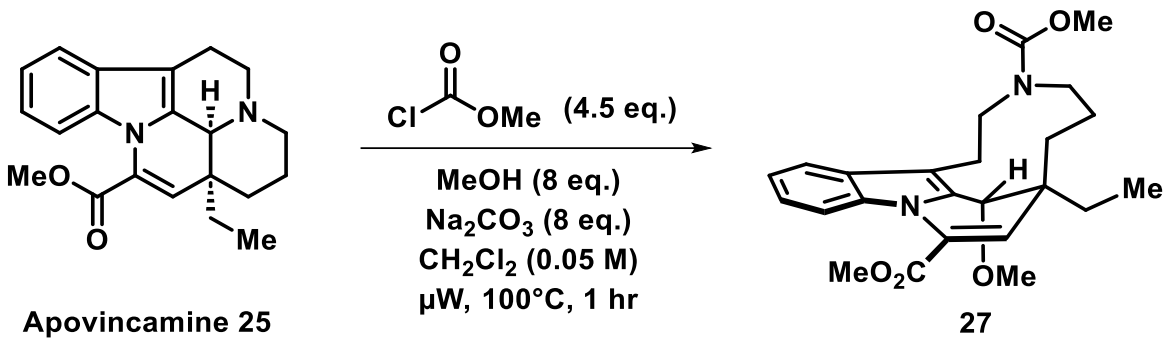
Procedure. Tetrahydrofuran (2 mL) was added to a round-bottom flask followed by sodium hydride (29.8 mg, 0.74 mmol, 60 wt.% dispersion in mineral oil) and the mixture was cooled to 0 °C. Next, a solution of **18** (150 mg, 0.23 mmol) in 0.5 mL of tetrahydrofuran was added to the reaction mixture, which was allowed to stir for 30 minutes at room temperature. Then, the reaction was cooled to 0 °C and methyl iodide (57 µL, 0.92 mmol) was added. The resulting reaction mixture was slowly warmed to room temperature and stirred for 5 hours. Upon completion, the reaction was quenched via brine and extracted with ethyl acetate. The organic layers were collected, dried with sodium sulfate, filtered, and concentrated. The crude mixture was purified via column chromatography using a gradient of 100% hexanes to 7:3 hexanes:ethyl acetate to afford **64** (86 mg, 55%) as a white solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 7.86 (d, *J* = 7.8 Hz, 1H), 7.58 (d, *J* = 7.8 Hz, 1H), 7.42 (d, *J* = 7.4 Hz, 1H), 7.37 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.31 (d, *J* = 8.1 Hz, 1H), 7.24 (m, 1H), 7.15 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.01 (dd, *J* = 7.4, 7.4 Hz, 1H), 5.05 (m, 1H), 4.42 (d, *J* = 12.6 Hz, 1H), 4.37 (d, *J* = 12.6 Hz, 1H), 3.99 (m, 1H), 3.83 (s, 3H), 3.83 - 3.72 (m, 4H), 3.67 (s, 3H), 3.42 - 3.23 (m, 2H), 3.28 (s, 3H), 3.09 (ddd, *J* = 14.6, 10.4, 3.7 Hz, 1H), 2.84 (d, *J* = 8.8 Hz, 1H), 2.62 (d, *J* = 9.7 Hz, 1H), 2.52 (m, 1H), 2.42 - 2.22 (m, 2H), 2.08 (d, *J* = 11.4 Hz, 1H), 1.81 (br. m, 1H), 1.54 - 1.30 (m, 3H), 0.82 (br. s, 3H, methyl group). Note: Broad multiplet at 1.81 ppm aligns with the C20 proton signal observed in compounds **18** (synthetic precursor) and **46**.

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 172.5, 156.6, 140.6, 139.0, 137.8, 136.8, 129.0, 128.9, 128.0, 127.8, 121.3, 118.8, 118.2, 111.2, 108.8, 97.8, 77.0, 74.5, 71.1, 60.7, 56.8, 56.4, 50.8, 50.5, 50.1, 38.3, 36.5, 35.6, 30.5, 27.5, 25.3, 25.1, 13.8.

HRMS (ESI): calc. for $C_{33}H_{42}IN_2O_6$ $[M + H]^+$: 689.2082, found: 689.2082.

Melting point: 134 - 136 °C.



Apovincamine 25 **27**

Procedure. Apovincamine **25** (211 mg, 0.63 mmol) was added to a microwave flask and dissolved in 12.1 mL dichloromethane. Sodium carbonate (532 mg, 5.02 mmol), methyl chloroformate (0.22 mL, 2.82 mmol), and methanol (0.20 mL, 5.02 mmol) were then added to the mixture sequentially. The resulting reaction mixture was then subjected to microwave irradiation for one hour at 100 °C. After completion, the reaction mixture was then filtered to remove excess sodium carbonate and concentrated under reduced pressure. The crude product was then purified via column chromatography using a gradient of 100:0 to 3:1 hexanes:ethyl acetate to afford **27** (92.8 mg, 35%) as a white solid. Notes: We have an X-ray of **27** (see later section for details). During the course of these studies, this procedure was applied to a diversity of alcohol and thiol nucleophiles with chloroformate electrophiles to give ring cleaved products as a single diastereomer.

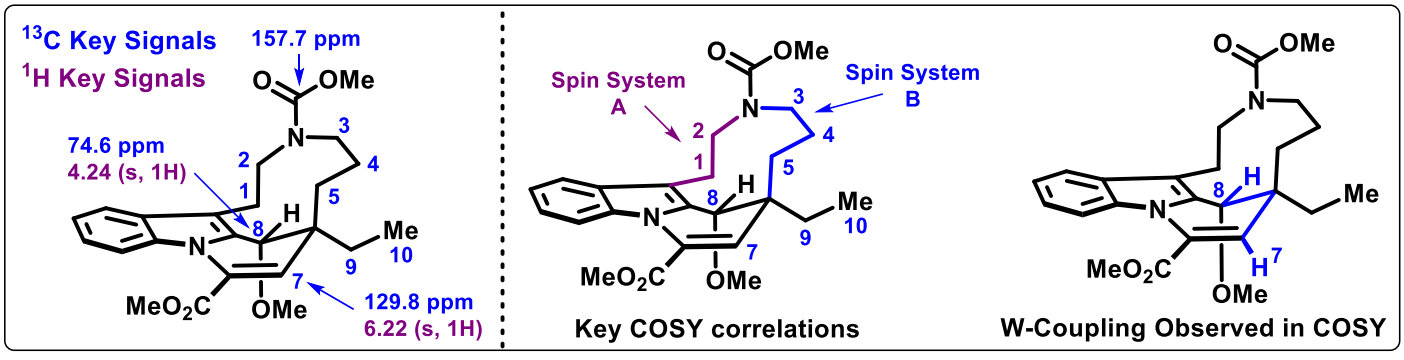
^{1}H NMR: (600 MHz, TCE, 100 °C) δ 7.57 (d, *J* = 7.7 Hz, 1H), 7.33 (m, 1H), 7.26 (m, 1H), 7.21 (m, 1H), 6.22 (s, 1H), 4.24 (s, 1H), 4.11 (m, 1H), 3.99 (s, 3H), 3.80 (s, 3H), 3.72 (ddd, *J* = 14.0, 9.7, 2.0 Hz, 1H), 3.31 (ddd, *J* = 14.6, 11.7, 2.0 Hz, 1H, partially buried), 3.29 (s, 3H), 3.07 (ddd, *J* = 15.1, 3.8, 1.8 Hz, 1H), 2.80 (dd, *J* = 12.5, 12.5 Hz, 1H), 2.28 (ddd, *J* = 14.2, 5.9, 3.2 Hz, 1H), 1.87 - 1.75 (m, 3H), 1.52 (m, 1H), 1.03 (dd, *J* = 7.4, 7.4 Hz, 3H), 0.97 (m, 1H), 0.69 (m, 1H).

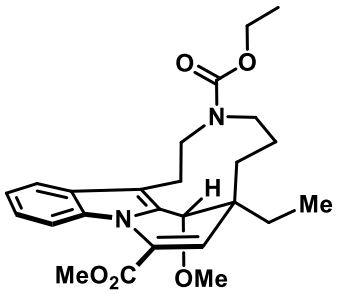
^{13}C NMR: (151 MHz, TCE, 100 °C) δ 163.9, 157.7, 135.7, 133.1, 129.8, 129.1, 128.2, 123.1, 120.4, 118.3, 116.7, 112.6, 74.6, 55.6, 53.2, 52.9, 52.2, 51.9, 43.3, 31.4, 27.0, 23.4, 22.0, 7.5.

HRMS (ESI): calc. for $C_{24}H_{31}N_2O_5$ $[M+H]^+$: 427.2227, found: 427.2241.

Melting point: 164 - 166 °C.

Key Signals for 27 (have X-ray)





65

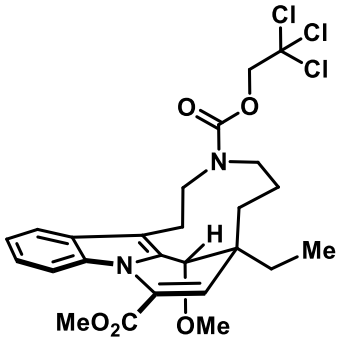
Yield: 67%; 182 mg of **65**; white solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 7.57 (d, *J* = 7.7 Hz, 1H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.26 (m, 1H), 7.22 (m, 1H), 6.22 (d, *J* = 1.2 Hz, 1H), 4.32 - 4.18 (m, 2H, partially buried), 4.26 (d, *J* = 1.2 Hz, 1H), 4.13 (m, 1H), 3.99 (s, 3H), 3.75 (ddd, *J* = 14.1, 9.6, 2.5 Hz, 1H), 3.33 (ddd, *J* = 15.0, 11.7, 2.6 Hz, 1H), 3.30 (s, 3H), 3.07 (ddd, *J* = 15.0, 4.0, 1.9 Hz, 1H), 2.78 (m, 1H), 2.26 (ddd, *J* = 14.3, 5.8, 3.1 Hz, 1H), 1.87 - 1.78 (m, 3H), 1.55 (m, 1H), 1.37 (appt. t, *J* = 7.1 Hz, 3H), 1.04 (dd, *J* = 7.5, 7.5 Hz, 3H), 0.99 (m, 1H), 0.69 (m, 1H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 163.9, 157.3, 135.7, 133.1, 129.7, 129.1, 128.2, 123.1, 120.4, 118.3, 116.8, 112.6, 74.8, 61.1, 55.6, 53.2, 53.0, 51.9, 43.3, 31.4, 27.0, 23.5, 22.1, 14.6, 7.6.

HRMS (ESI): calc. for $C_{25}H_{33}N_2O_5$ $[M+H]^+$: 441.2384, found: 441.2395.

Melting point: 79 - 80 °C.



66

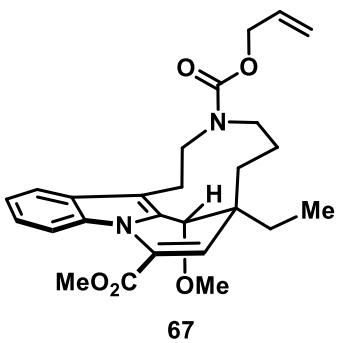
Yield: 20%; 89.9 mg of **66**; white solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 7.57 (d, *J* = 7.7 Hz, 1H), 7.35 (d, *J* = 8.3 Hz, 1H), 7.27 (m, 1H), 7.23 (m, 1H), 6.25 (s, 1H), 4.95 (br. m, 1H), 4.79 (br. m, 1H), 4.30 (m, 1H), 4.24 (ddd, *J* = 14.0, 3.6, 2.5 Hz, 1H), 4.00 (s, 3H), 3.83 (ddd, *J* = 14.0, 9.6, 2.3 Hz, 1H), 3.39 (m, 1H), 3.28 (s, 3H), 3.15 (ddd, *J* = 15.2, 4.1, 1.6 Hz, 1H), 2.89 (m, 1H), 2.34 (d, *J* = 11.1 Hz, 1H), 1.91 - 1.75 (m, 3H), 1.61 (br. m, 1H), 1.02 (dd, *J* = 7.5, 7.5 Hz, 3H), 0.97 (m, 1H), 0.82 (m, 1H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 163.8, 155.4, 135.8, 133.0, 129.6, 129.2, 128.1, 123.2, 120.6, 118.3, 116.5, 112.6, 95.7, 75.2, 74.7, 55.6, 53.8, 53.2, 52.0, 43.5, 31.5, 26.7, 23.5, 21.9, 7.7.

HRMS (ESI): calc. for $C_{25}H_{29}Cl_3N_2O_5Na$ $[M+Na]^+$: 565.1034, found: 565.1056.

Melting point: 68 - 69 °C.



67

Yield: 10%; 29.4 mg of **67**; white solid.

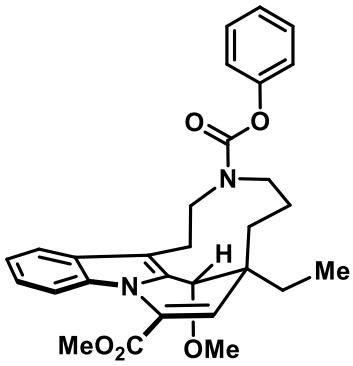
^{1}H NMR: (600 MHz, TCE, 100 °C) δ 7.57 (d, *J* = 7.7 Hz, 1H), 7.34 (d, *J* = 8.3 Hz, 1H), 7.26 (m, 1H), 7.22 (m, 1H), 6.22 (s, 1H), 6.05 (dddd, *J* = 16.4, 10.8, 5.6, 5.6 Hz, 1H), 5.41 (m, 1H), 5.30 (m, 1H), 4.74 (dd, *J* = 13.2, 5.3 Hz, 1H), 4.66 (dd, *J* = 13.2, 5.6 Hz, 1H), 4.25 (s, 1H), 4.16 (ddd, *J* = 13.9, 3.0, 3.0 Hz, 1H), 3.99 (s, 3H), 3.77 (ddd, *J* = 14.1, 9.7, 2.4 Hz, 1H), 3.34 (ddd, *J* = 14.9, 11.7, 2.3 Hz, 1H), 3.29 (s,

3H), 3.08 (m, 1H), 2.81 (dd, *J* = 12.6, 12.6 Hz, 1H), 2.28 (ddd, *J* = 14.2, 5.6, 3.1 Hz, 1H), 1.87 - 1.77 (m, 3H), 1.55 (m, 1H), 1.03 (dd, *J* = 7.5, 7.5 Hz, 3H), 0.99 (m, 1H), 0.70 (m, 1H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 163.9, 156.9, 135.7, 133.1, 133.1, 129.7, 129.1, 128.2, 123.1, 120.5, 118.3, 117.5, 116.7, 112.6, 74.7, 65.8, 55.6, 53.3, 53.0, 51.9, 43.3, 31.4, 27.0, 23.5, 22.1, 7.6.

HRMS (ESI): calc. for $C_{26}H_{32}N_2O_5Na$ $[M+Na]^+$: 475.2203, found: 475.2213.

Melting point: 48 - 50 °C.



68

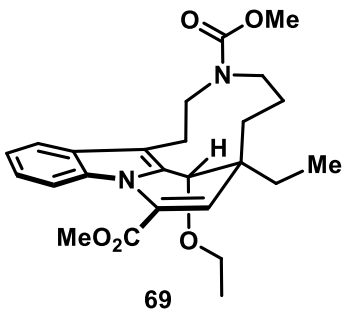
Yield: 6%; 41.2 mg of **68**; white residue.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 7.60 (d, *J* = 7.8 Hz, 1H), 7.46 - 7.40 (m, 2H), 7.38 (d, *J* = 8.3 Hz, 1H), 7.31 - 7.25 (m, 2H), 7.24 (m, 1H), 7.18 - 7.14 (m, 2H), 6.27 (d, *J* = 0.9 Hz, 1H), 4.40 (d, *J* = 0.9 Hz, 1H), 4.27 (ddd, *J* = 13.9, 3.2, 3.2 Hz, 1H), 4.01 (s, 3H), 3.86 (ddd, *J* = 14.2, 9.4, 2.5 Hz, 1H), 3.44 (ddd, *J* = 15.1, 11.8, 2.1 Hz, 1H), 3.35 (s, 3H), 3.19 (ddd, *J* = 15.2, 3.8, 1.9 Hz, 1H), 3.02 (dd, *J* = 12.4, 12.4 Hz, 1H), 2.46 (m, 1H), 1.94 - 1.80 (m, 3H), 1.66 (m, 1H), 1.06 (dd, *J* = 7.5, 7.5 Hz, 3H), 1.02 (m, 1H), 0.87 (m, 1H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 163.8, 155.4, 151.4, 135.8, 133.1, 129.6, 129.2, 129.0, 128.2, 125.0, 123.2, 121.4, 120.6, 118.4, 116.5, 112.6, 75.0, 55.8, 53.5, 53.1, 52.0, 43.5, 31.3, 26.8, 23.4, 21.9, 7.7.

HRMS (ESI): calc. for $C_{29}H_{33}N_2O_5$ $[M+H]^+$: 489.2384, found: 489.2392.

Melting point: 62 - 64 °C.



69

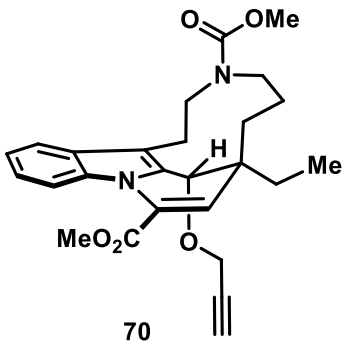
Yield: 30%; 76.7 mg of **69**; white solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 7.55 (d, *J* = 7.7 Hz, 1H), 7.33 (m, 1H), 7.25 (m, 1H), 7.20 (m, 1H), 6.23 (m, 1H), 4.36 (m, 1H), 4.11 (m, 1H), 3.99 (s, 3H), 3.79 (s, 3H), 3.72 (m, 1H), 3.55 (m, 1H), 3.42 (m, 1H), 3.29 (dd, *J* = 13.1, 13.1 Hz, 1H), 3.05 (m, 1H), 2.80 (dd, *J* = 12.5, 12.5 Hz, 1H), 2.28 (m, 1H), 1.87 - 1.77 (m, 3H), 1.54 (m, 1H), 1.15 (m, 3H), 1.03 (m, 3H), 0.95 (m, 1H), 0.73 (m, 1H). Note: Most signals exhibit additional splitting due to inadequate shimming prior to the acquisition of spectral data (e.g., the 3H signals at 1.15 and 1.03 ppm should appear as “dd” or “appt. t” signals).

^{13}C NMR: (101 MHz, TCE, 100 °C) δ 163.9, 157.7, 135.6, 134.0, 130.1, 129.0, 128.2, 123.0, 120.4, 118.2, 116.1, 112.5, 72.4, 63.1, 53.4, 53.0, 52.2, 51.9, 43.3, 31.3, 26.9, 23.5, 22.0, 14.8, 7.6.

HRMS (ESI): calc. for $C_{25}H_{32}N_2O_5Na$ $[M+Na]^+$: 463.2206, found: 463.2206.

Melting point: 53 - 55 °C.



70

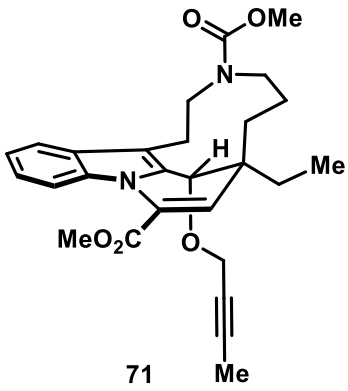
Yield: 16%; 60.6 mg of **70**; white solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 7.57 (d, *J* = 7.7 Hz, 1H), 7.34 (d, *J* = 8.3 Hz, 1H), 7.27 (m, 1H), 7.22 (m, 1H), 6.22 (s, 1H), 4.72 (s, 1H), 4.17 (dd, *J* = 16.2, 2.2 Hz, 1H), 4.12 (m, 1H), 4.05 (dd, *J* = 16.2, 2.1 Hz, 1H), 3.99 (s, 3H), 3.77 (s, 3H), 3.73 (ddd, *J* = 12.9, 9.7, 1.8 Hz, 1H), 3.43 (ddd, *J* = 14.2, 11.3, 1.8 Hz, 1H), 3.08 (ddd, *J* = 15.1, 3.9, 1.6 Hz, 1H), 2.79 (dd, *J* = 12.4, 12.4 Hz, 1H), 2.50 (m, 1H), 2.30 (ddd, *J* = 14.2, 5.4, 3.3 Hz, 1H), 1.92 - 1.74 (m, 3H), 1.50 (m, 1H), 1.07 (dd, *J* = 7.4, 7.4 Hz, 3H), 1.01 (m, 1H), 0.67 (m, 1H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 163.8, 157.7, 135.9, 132.0, 129.7, 129.1, 128.2, 123.4, 120.6, 118.4, 117.8, 112.6, 80.4, 74.2, 70.9, 54.3, 53.1, 52.8, 52.2, 52.0, 43.2, 31.3, 27.1, 23.5, 22.1, 7.5.

HRMS (DART): calc. for $C_{26}H_{31}N_2O_5$ $[M+H]^+$: 451.2227, found: 451.2232.

Melting point: 156 - 158 °C.



71

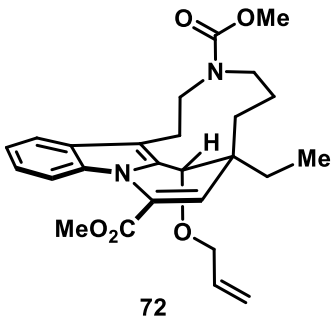
Yield: 17%; 47.3 mg of **71**; white solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 7.56 (d, *J* = 7.7 Hz, 1H), 7.34 (m, 1H), 7.26 (ddd, *J* = 8.3, 7.2, 1.3 Hz, 1H), 7.21 (ddd, *J* = 7.9, 7.0, 1.0 Hz, 1H), 6.21 (d, *J* = 1.0 Hz, 1H), 4.67 (d, *J* = 1.0 Hz, 1H), 4.14 (m, 1H), 4.11 (dq, *J* = 15.6, 2.3 Hz, 1H), 3.99 (s, 3H), 3.98 (dq, *J* = 15.6, 2.3 Hz, 1H, partially buried), 3.78 (s, 3H), 3.71 (ddd, *J* = 14.2, 10.1, 2.7 Hz, 1H), 3.41 (m, 1H), 3.08 (ddd, *J* = 15.1, 4.3, 2.0 Hz, 1H), 2.80 (dd, *J* = 12.2, 12.2 Hz, 1H), 2.30 (ddd, *J* = 14.3, 5.3, 3.4 Hz, 1H), 1.94 (dd, *J* = 2.3, 2.3 Hz, 3H), 1.89 - 1.82 (m, 2H), 1.78 (dq, *J* = 14.7, 7.4 Hz, 1H), 1.46 (m, 1H), 1.06 (dd, *J* = 7.5, 7.5 Hz, 3H), 1.02 (m, 1H), 0.64 (m, 1H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 163.9, 157.7, 135.9, 132.6, 129.9, 129.2, 128.2, 123.2, 120.5, 118.4, 117.6, 112.6, 82.3, 75.7, 70.5, 55.0, 52.9, 52.7 (br.), 52.2, 52.0, 43.2, 31.3, 27.3, 23.4, 22.1, 7.4, 3.2.

HRMS (ESI): calc. for $C_{27}H_{32}N_2O_5Na$ $[M+Na]^+$: 487.2203, found: 487.2215.

Melting point: 161 - 163 °C.



72

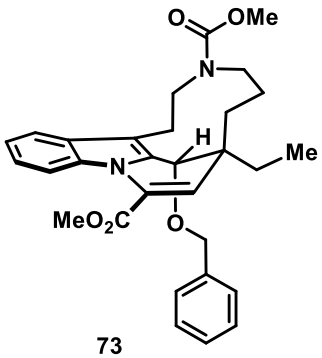
Yield: 51%; 138 mg of **72**; white solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 7.56 (m, 1H), 7.34 (m, 1H), 7.26 (ddd, *J* = 8.2, 7.1, 1.3 Hz, 1H), 7.21 (ddd, *J* = 7.9, 6.9, 1.0 Hz, 1H), 6.26 (d, *J* = 1.2 Hz, 1H), 5.90 (dddd, *J* = 17.3, 10.7, 6.0, 4.9 Hz, 1H), 5.27 (dddd, *J* = 17.3, 1.6, 1.6, 1.6 Hz, 1H; appt. dq), 5.17 (dddd, *J* = 10.5, 1.4, 1.4, 1.4 Hz, 1H; appt. dq), 4.44 (d, *J* = 1.2 Hz, 1H), 4.10 (m, 1H), 4.05 (dddd, *J* = 13.2, 4.8, 1.6, 1.6 Hz, 1H), 3.99 (s, 3H), 3.90 (dddd, *J* = 13.2, 6.1, 1.4, 1.4 Hz, 1H), 3.78 (s, 3H), 3.71 (ddd, *J* = 14.1, 9.4, 2.5 Hz, 1H), 3.28 (ddd, *J* = 14.9, 11.4, 2.4 Hz, 1H), 3.07 (ddd, *J* = 15.1, 4.2, 2.0 Hz, 1H), 2.81 (m, 1H), 2.29 (ddd, *J* = 14.2, 6.2, 3.2 Hz, 1H), 1.92 - 1.78 (m, 3H), 1.53 (m, 1H), 1.05 (dd, *J* = 7.4, 7.4 Hz, 3H), 0.95 (ddd, *J* = 14.8, 9.3, 2.7 Hz, 1H), 0.74 (m, 1H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 163.8, 157.6, 135.7, 135.1, 133.4, 129.9, 129.1, 128.2, 123.1, 120.4, 118.3, 116.5, 116.1, 112.5, 72.2, 68.4, 53.3, 52.8, 52.2, 51.9, 43.5, 31.3, 26.9, 23.5, 22.0, 7.6.

HRMS (ESI): calc. for $C_{26}H_{32}N_2O_5Na$ $[M+Na]^+$: 475.2203, found: 475.2203.

Melting point: 141 - 143 °C.



73

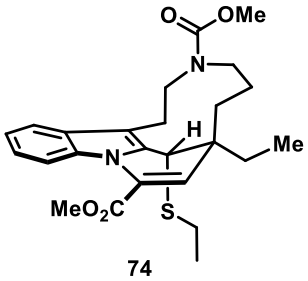
Yield: 24%; 70.2 mg of **73**; white solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 7.57 (d, *J* = 7.7 Hz, 1H), 7.38 - 7.32 (m, 3H), 7.32 - 7.25 (m, 4H), 7.23 (dd, *J* = 7.4, 7.4 Hz, 1H), 6.28 (s, 1H), 4.58 (d, *J* = 12.0 Hz, 1H), 4.48 (s, 1H), 4.40 (d, *J* = 12.0 Hz, 1H), 4.06 (m, 1H), 4.00 (s, 3H), 3.70 (s, 3H), 3.68 (m, 1H, partially buried), 3.19 (dd, *J* = 12.6, 12.6 Hz, 1H), 3.06 (ddd, *J* = 15.1, 3.9, 1.9 Hz, 1H), 2.80 (m, 1H), 2.28 (ddd, *J* = 14.2, 5.9, 3.1 Hz, 1H), 1.96 - 1.78 (m, 3H), 1.49 (m, 1H), 1.04 (dd, *J* = 7.4, 7.4 Hz, 3H), 0.96 (m, 1H), 0.73 (m, 1H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 163.9, 157.6, 138.6, 135.8, 133.2, 129.9, 129.2, 128.2, 128.0, 127.4, 127.1, 123.2, 120.5, 118.4, 116.9, 112.6, 72.5, 69.4, 53.2, 52.7, 52.3, 52.0, 43.6, 31.2, 26.9, 23.6, 22.0, 7.6.

HRMS (ESI): calc. for $C_{30}H_{34}N_2O_5Na$ $[M+Na]^+$: 525.2360, found: 525.2334.

Melting point: 176 - 178 °C.



74

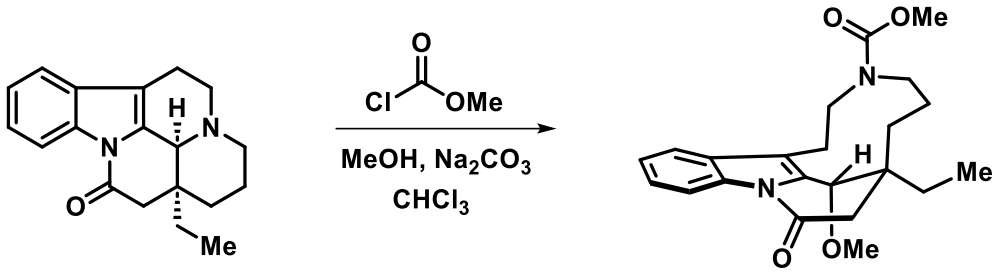
Yield: 25%; 69.0 mg of **74**; white solid.

^{1}H NMR: (600 MHz, TCE, 100 °C) δ 7.51 (m, 1H), 7.27 (m, 1H), 7.25 - 7.18 (m, 2H), 6.23 (d, *J* = 1.2 Hz, 1H), 4.23 (d, *J* = 1.2 Hz, 1H), 4.08 (m, 1H), 4.00 (s, 3H), 3.77 (s, 3H), 3.73 (ddd, *J* = 14.0, 8.6, 2.6 Hz, 1H), 3.22 (ddd, *J* = 15.2, 11.3, 2.6 Hz, 1H), 3.03 (ddd, *J* = 15.2, 4.3, 2.1 Hz, 1H), 2.85 (m, 1H), 2.54 (dq, *J* = 12.6, 7.4 Hz, 1H), 2.46 (dq, *J* = 12.6, 7.4 Hz, 1H), 2.34 (ddd, *J* = 14.2, 6.9, 2.8 Hz, 1H), 1.93 (dq, *J* = 14.7, 7.3 Hz, 1H), 1.86 (ddd, *J* = 15.7, 9.3, 3.9 Hz, 1H), 1.78 (dq, *J* = 14.6, 7.3 Hz, 1H), 1.62 (m, 1H), 1.25 (dd, *J* = 7.4, 7.4 Hz, 3H), 1.06 (dd, *J* = 7.3, 7.3 Hz, 3H), 1.04 - 0.96 (m, 2H).

^{13}C NMR: (151 MHz, TCE, 100 °C) δ 163.6, 157.6, 135.2, 135.2, 129.5, 129.3, 128.3, 122.6, 120.5, 118.0, 113.7, 112.2, 53.7, 52.8, 52.2, 52.0, 44.8, 42.9, 32.5, 28.0, 24.7, 23.7, 22.1, 14.6, 7.8.

HRMS (ESI): calc. for $C_{25}H_{33}N_2O_4S$ $[M+H]^+$: 457.2156, found: 457.2167.

Melting point: 111 - 113 °C.



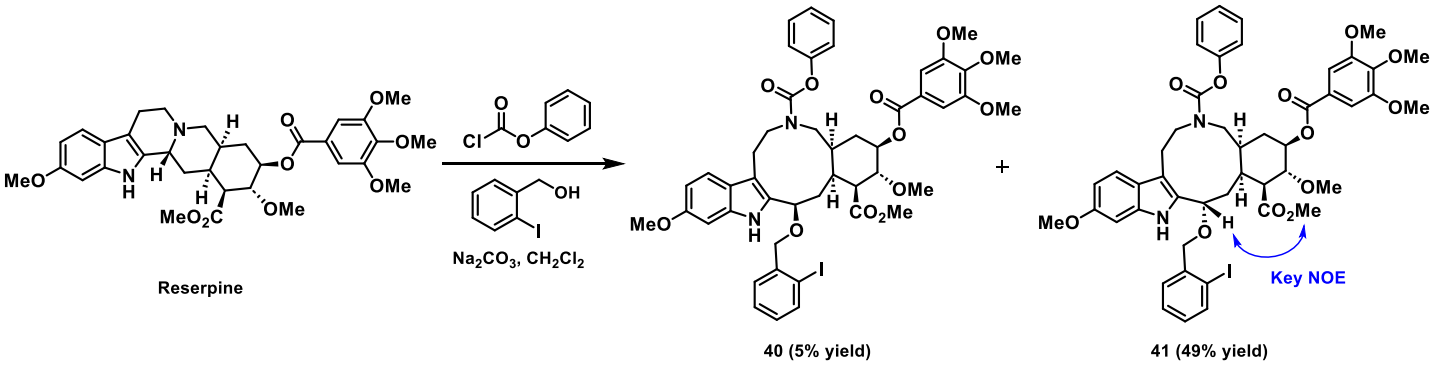
Vinburnine 28 — 29

Procedure. Vinburnine **28** (200 mg, 0.68 mmol) was added to a round bottom flask and dissolved in chloroform (13 mL, 0.05 M). Sodium carbonate (576 mg, 5.43 mmol) and methyl chloroformate (23.6 µL, 3.06 mmol) were added, and the resulting mixture was stirred at room temperature for 10 minutes. After this time, methanol (0.22 mL, 5.43 mmol) was added and the reaction was stirred at 60 °C for 36 hours. Upon completion, the reaction mixture was cooled and diluted with dichloromethane before being filtered. The resulting solvent was then evaporated via rotovap, and the crude material was purified via column chromatography using a gradient of 100% hexanes to 9:2 hexanes:ethyl acetate to afford **29** (10 mg, 4% yield) as a clear-yellow residue.

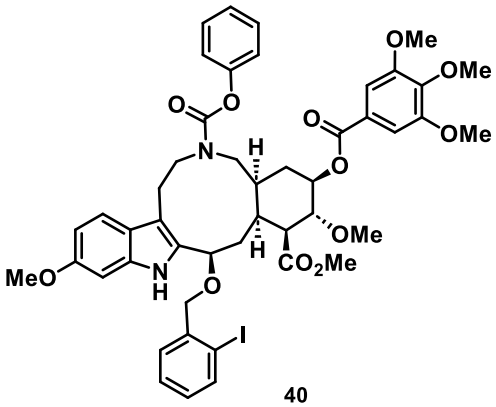
^{1}H NMR: (600 MHz, $CDCl_3$, 50 °C) δ 8.46 (m, 1H), 7.49 (d, *J* = 7.7 Hz, 1H), 7.38 (ddd, *J* = 8.1, 7.4, 1.2 Hz, 1H), 7.31 (ddd, *J* = 8.1, 7.7, 0.9 Hz, 1H), 4.29 (s, 1H), 4.07 (br. m, 1H), 3.76 (s, 3H), 3.71 (dd, *J* = 13.2, 6.7 Hz, 1H), 3.24 (s, 3H), 3.19 (m, 1H), 3.01 (d, *J* = 17.3 Hz, 1H), 3.00 (ddd, *J* = 14.9, 4.3, 1.7 Hz, 1H), 2.72 (dd, *J* = 11.2, 11.2 Hz, 1H), 2.39 (dd, *J* = 17.3, 0.7 Hz, 1H), 2.18 (dd, *J* = 13.7, 8.6 Hz, 1H), 1.91 (dq, *J* = 15.1, 7.6 Hz, 1H), 1.78 (ddd, *J* = 15.5, 10.7, 1.8 Hz, 1H), 1.66 - 1.47 (m, 3H), 0.87 (dd, *J* = 7.6, 7.6 Hz, 3H), 0.82 (m, 1H, partially buried).

^{13}C NMR: (151 MHz, $CDCl_3$, 50 °C) δ 169.6, 158.2, 135.5, 133.5, 129.4, 125.8, 124.0, 119.6 (br.), 118.4, 117.2, 75.6, 56.5, 55.7 (br.), 53.0 (br.), 52.8, 43.5, 41.1, 33.6, 26.8, 24.1, 22.3 (br.), 7.9. Note: This spectrum contained several broad ^{13}C signals, which are indicated in the tabulated data.

HRMS (ESI): calc. for $C_{22}H_{29}N_2O_4$ $[M+H]^+$: 385.2122, found: 385.2134.



Procedure. Reserpine (500 mg, 0.82 mmol) was added to a round-bottom flask and dissolved in methylene chloride (17.6 mL). Then, sodium carbonate (695 mg, 6.56 mmol), 2-iodobenzyl alcohol (1.6 g, 6.56 mmol) and phenyl chloroformate (0.46 mL, 3.69 mmol) were added to the round-bottom flask sequentially and the resulting mixture stirred at room temperature for 2 hours until complete (monitored by TLC). Upon completion of the reaction, the contents of the mixture were filtered and the resulting solvent was evaporated under reduced pressure to give crude materials which were purified via column chromatography using 100% methylene chloride and slowing ramping to a 99.3:0.7 mixture of methylene chloride:methanol to elute pure diastereomers **40** (38.4 mg, 5%) as a cream-colored solid and **41** (387 mg, 49%) as a white solid.



Yield: 5%; 40 mg of **40**; cream-colored solid.

^{1}H NMR: (600 MHz, $CDCl_3$) δ 8.01 (br. s, 1H), 7.85 (d, *J* = 8.0 Hz, 1H), 7.43 (d, *J* = 8.6 Hz, 1H), 7.39 (m, 1H), 7.36 (m, 1H), 7.34 - 7.29 (m, 4H), 7.17 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.02 (ddd, *J* = 7.8, 7.8, 1.8 Hz, 1H), 6.97 - 6.84 (br. m, 2H), 6.82 (s, 1H), 6.77 (dd, *J* = 8.6, 2.2 Hz, 1H), 5.02 (dd, *J* = 7.2, 7.2 Hz, 1H), 4.93 (m, 1H), 4.49 (d, *J* = 12.3 Hz, 1H), 4.44 (d, *J* = 12.3 Hz, 1H), 4.33 (m, 1H), 3.92 (s, 6H), 3.91 (s, 3H), 3.85 (s, 3H), 3.79 (dd, *J* = 11.3, 9.3 Hz, 1H), 3.66 - 3.50 (m, 5H), 3.47 (s, 3H), 3.23 (ddd, *J* = 14.6, 9.5, 3.8 Hz, 1H), 2.95 (ddd, *J* = 16.6, 4.4, 4.4 Hz, 1H), 2.80 - 2.65 (m, 2H), 2.46 (dd, *J* = 11.7, 1.8 Hz, 1H), 2.31 - 2.20 (m, 2H), 2.01 (m, 1H), 1.92 (m, 1H), 1.50 (m, 1H).

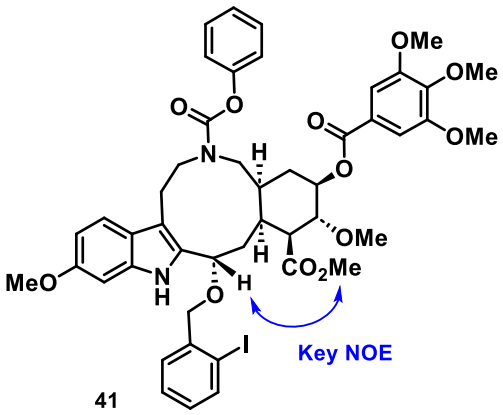
^{1}H NMR: (600 MHz, MeOD-*d4*) δ 7.83 (dd, *J* = 7.9, 0.9 Hz, 1H), 7.51 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.40 - 7.37 (m, 3H), 7.36 (d, *J* = 8.7 Hz, 1H), 7.29 - 7.20 (br. m, 2H), 7.14 (m, 1H), 7.01 (ddd, *J* = 7.7, 7.7, 1.6 Hz, 1H), 6.91 (d, *J* = 1.0 Hz, 1H), 6.67 - 6.57 (br. m, 3H), 5.02 (dd, *J* = 10.2, 5.4 Hz, 1H), 4.91 (ddd, *J* = 10.9, 9.3, 5.9 Hz, 1H), 4.48 (d, *J* = 12.9 Hz, 1H), 4.45 (d, *J* = 12.9 Hz, 1H), 4.35 (br. m, 1H), 3.91 (m, 1H, partially buried), 3.89 (s, 6H),

3.84 (s, 3H), 3.81 (s, 3H), 3.70 (br. s, 3H), 3.49 (s, 3H), 3.47 - 3.36 (br. m, 2H), 3.22 (m, 1H), 3.04 - 2.77 (m, 3H), 2.43 (dd, *J* = 11.3, 3.9 Hz, 1H), 2.36 (ddd, *J* = 14.1, 11.1, 5.6 Hz, 1H), 2.13 (dd, *J* = 12.6, 12.6 Hz, 1H), 1.96 - 1.79 (m, 2H), 1.68 (ddd, *J* = 12.1, 12.1, 12.1 Hz, 1H; "appt. q"). Note: We faced challenges reporting this spectral data due to significant signal broadening. The HSQC for this compound can be found in the spectra section of this document and was critical in the characterization of the following signals: 6.67 - 6.57 (br. m, 3H), 4.35 (br. m, 1H), and 3.47 - 3.36 (br. m, 2H).

^{13}C NMR: (151 MHz, MeOD-*d4*) δ 173.9, 166.8, 158.0, 157.7 (br.), 154.5, 152.4, 143.8, 142.1, 140.5, 139.0, 130.4, 130.4, 130.1 (br.), 129.4, 126.6, 126.3 (br.), 124.1 (br.), 122.8, 122.6, 120.2, 111.9, 109.8, 108.0, 98.8, 95.6, 80.0, 79.5, 75.2, 73.6, 61.2, 61.2, 56.8, 56.1, 55.0, 54.2, 52.4, 49.6, 38.1 (br., observed by HSQC), 34.6, 31.4, 30.4, 24.1 (br.). Note: Signal reported at 38.1 ppm had low intensity and was very broad in our acquired ^{13}C spectrum; however, this signal was observed in the HSQC that can be viewed in the spectra section.

HRMS (ESI): calc. for $C_{47}H_{51}IN_2O_{12}Na$ $[M+Na]^+$: 985.2379, found: 985.2359.

Melting Point: 143 - 145 °C.



41

Yield: 38%; 300 mg of **41**; white solid.

^{1}H NMR: (600 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.9 Hz, 1H), 7.70 (s, 1H), 7.50 (d, *J* = 8.7 Hz, 1H), 7.35 - 7.33 (m, 2H), 7.31 (s, 2H), 7.19 - 7.08 (m, 2H), 7.05 (m, 1H), 6.98 (ddd, *J* = 7.9, 4.5, 4.5 Hz, 1H), 6.89 (s, 1H), 6.69 (d, *J* = 6.7 Hz, 1H), 6.36 - 6.11 (br. m, 2H), 4.93 (m, 1H), 4.70 (ddd, *J* = 13.1, 13.1, 3.1 Hz, 1H), 4.31 (d, *J* = 12.1 Hz, 1H), 4.28 (d, *J* = 12.1 Hz, 1H), 4.25 (br. m, 1H), 3.97 (dd, *J* = 10.1, 10.1 Hz, 1H), 3.91 (s, 6H), 3.91 (s, 3H, buried), 3.83 (s, 3H), 3.75 (s, 3H), 3.51 (s, 3H), 3.46 (dd, *J* = 13.6, 4.6 Hz, 1H), 3.42 (m, 1H), 3.14 (m, 1H), 3.01 (m, 1H), 2.91 (br. m, 1H), 2.74 (dd, *J* = 12.6, 12.6 Hz, 1H), 2.56 (dd, *J* = 11.1, 4.2 Hz, 1H), 2.33 (m, 1H), 2.24 (m, 1H), 2.07 (br. m, 1H), 1.86 (dd, *J* = 11.1, 3.5 Hz, 1H), 1.27 (ddd, *J* = 12.0, 12.0, 12.0 Hz, 1H; "appt q").

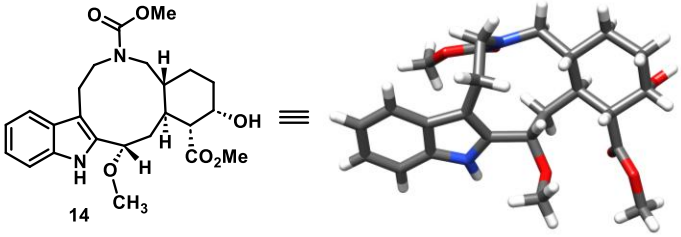
^{13}C NMR: (151 MHz, $CDCl_3$) δ 173.8, 165.3, 156.9, 155.7 (br.), 153.2, 150.8, 142.5, 140.4, 139.6, 136.4, 132.2 (br.), 129.7, 129.7, 128.9 (br.), 128.5, 125.5, 125.1 (br.), 124.0 (br.), 121.7, 120.5 (br.), 110.7 (br.), 110.0, 107.0, 98.8, 95.0, 79.2, 77.6, 76.4, 74.6, 61.1, 60.7, 56.5, 56.0, 52.1, 51.6 (br.), 51.1 (br.), 48.7 (br.), 36.3 (br.), 33.3 (br.), 30.0, 29.7 (br.), 23.6.

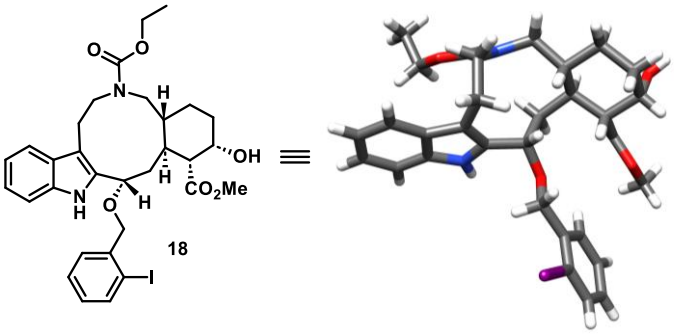
HRMS (ESI): calc. for $C_{47}H_{52}IN_2O_{12}$ $[M+H]^+$: 963.2559, found: 963.2536.

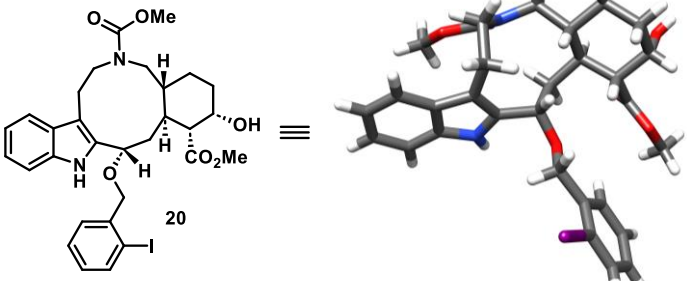
Melting Point: 125 - 127 °C.

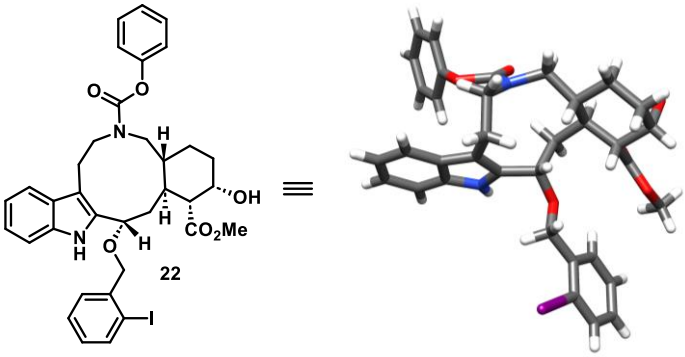
15.) X-Ray Data.

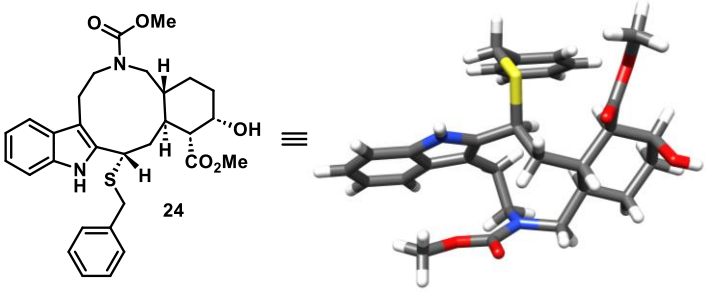
Overview of X-Ray Structures

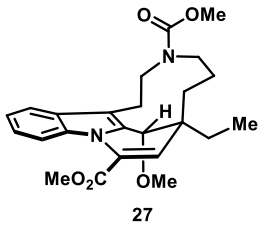


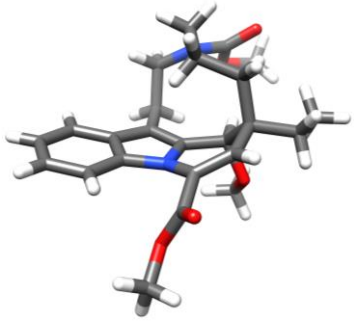




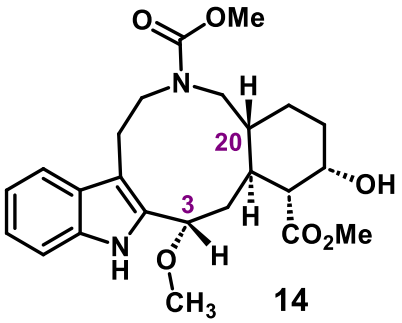






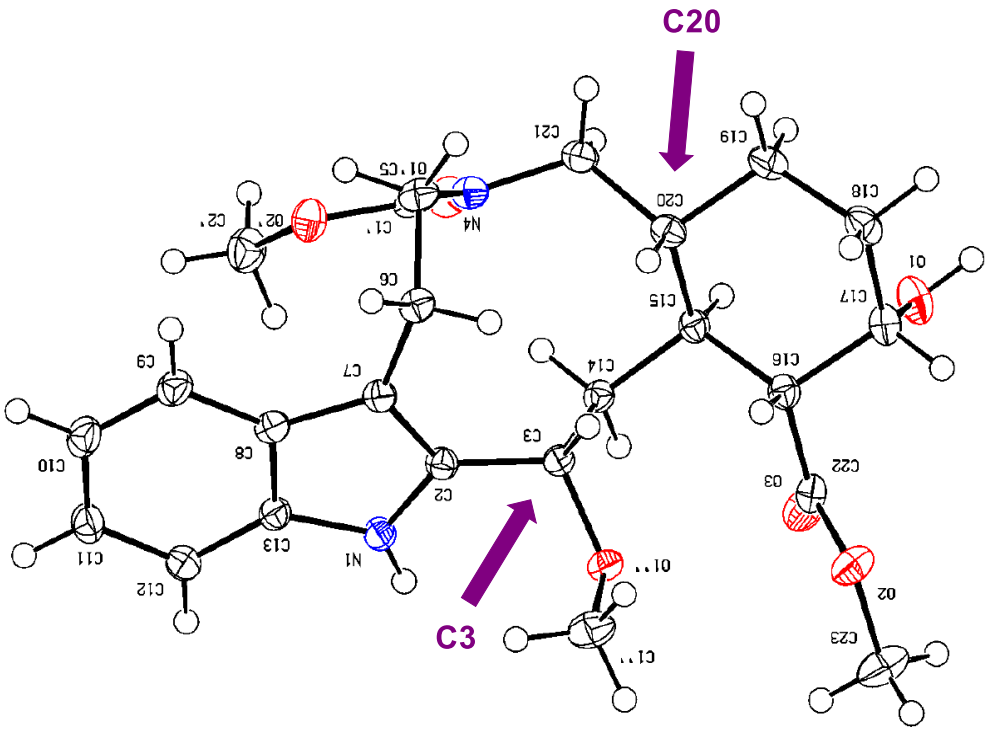


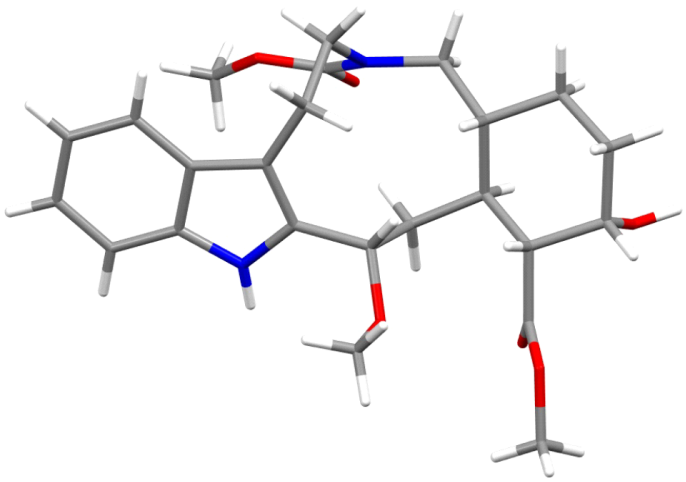
X-Ray Analysis of 14. X-Ray Intensity data were collected at 100 K on a Bruker Dual micro source D8 Venture diffractometer and PHOTON III detector running APEX3 software package of programs and using MoKα radiation (λ = 0.71073 Å). The data frames were integrated and multi-scan scaling was applied in APEX3. Intrinsic phasing structure solution provided all of the non-H atoms. The structure was refined using full-matrix least-squares refinement (SHELXL[8,9]). The non-H atoms were refined with anisotropic displacement parameters and all of the H atoms were calculated in idealized positions and refined riding on their parent atoms. In the final cycle of refinement, 7501 reflections (of which 6384 are observed with I > 2σ(I)) were used to refine 297 parameters and the resulting R_1, wR_2 and S (goodness of fit) were 4.11%, 9.50% and 1.073, respectively. The refinement was carried out by minimizing the wR_2 function using F^2 rather than F values. R_1 is calculated to provide a reference to the conventional R value but its function is not minimized.

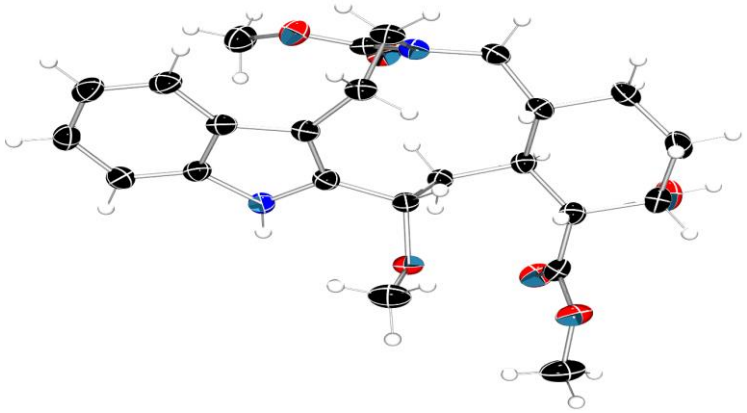


14

Photo by Michael Goertzen





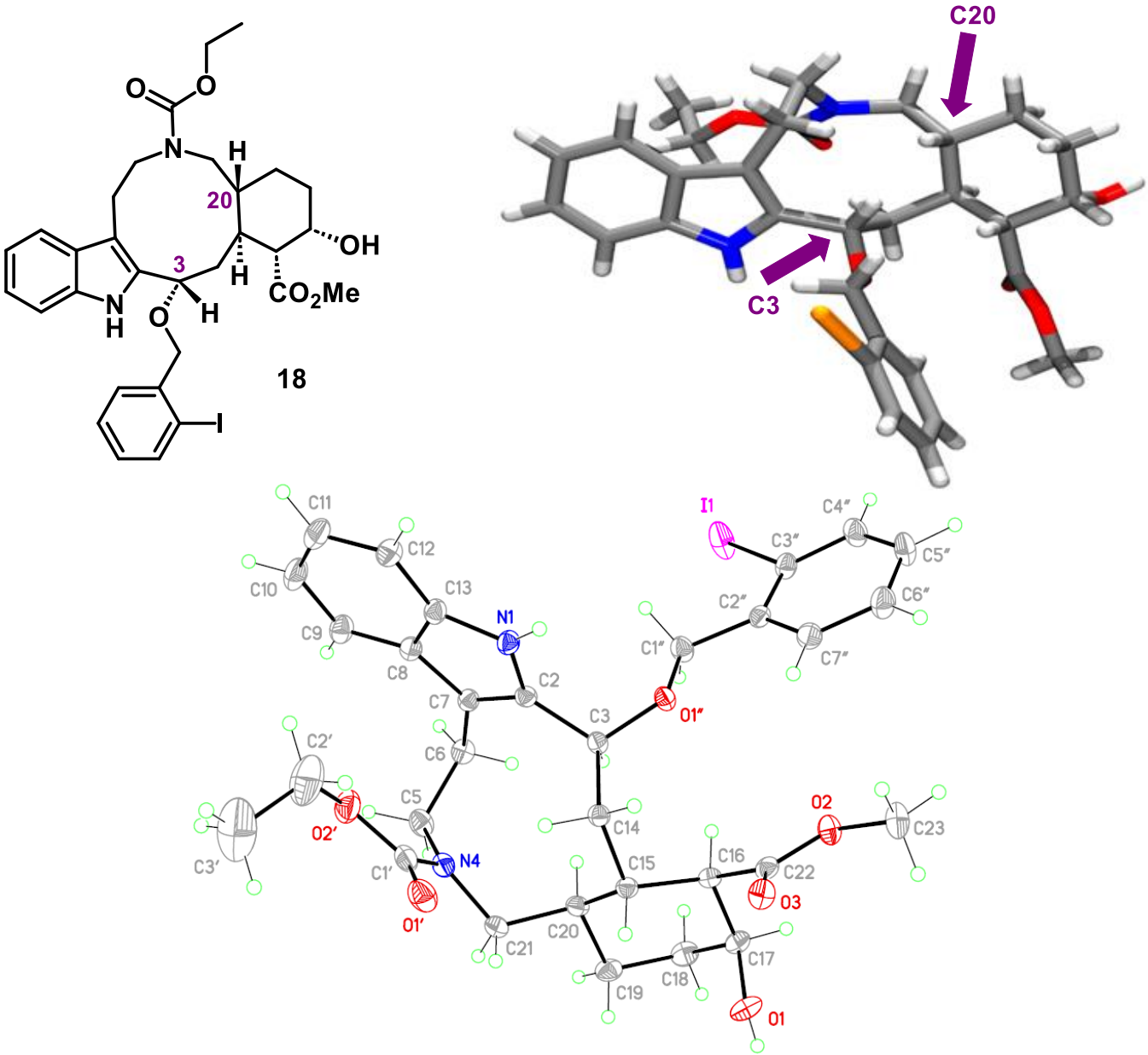


X-Ray Crystallographic Data for 14. Crystallographic data for **14** has been deposited with the Cambridge Crystallographic Data Centre (submission number Y-14; CCDC deposition number 2337941). Copies of the data can be obtained, free of charge at by visiting http://www.ccdc.cam.ac.uk/.

Crystal data and structure refinement for 14.

Identification code	**Y-14** (deposition no. 2337941)	
Empirical formula	C24 H32 N2 O6	
Formula weight	444.51	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 12.0273(3) Å	α = 90°.
	b = 13.1402(4) Å	β = 90°.
	c = 14.3337(4) Å	γ = 90°.
Volume	2265.31(11) $Å^3$	
Z	4	
Density (calculated)	1.303 Mg/m^3	
Absorption coefficient	0.094 mm^{-1}	
F(000)	952	
Crystal size	0.262 x 0.205 x 0.176 mm^3	
Theta range for data collection	2.103 to 32.798°.	
Index ranges	$-18 \le h \le 17$, $-19 \le k \le 19$, $-21 \le l \le 21$	
Reflections collected	39670	
Independent reflections	7501 [R(int) = 0.0539]	
Completeness to theta = 25.242°	99.7 %	
Absorption correction	multi-scan	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	7501 / 0 / 297	
Goodness-of-fit on F^2	1.073	
Final R indices [I>2sigma(I)]	R1 = 0.0411, wR2 = 0.0950 [6384]	
R indices (all data)	R1 = 0.0525, wR2 = 0.1010	
Absolute structure parameter	0.1(3)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.285 and -0.226 $e.Å^{-3}$	

X-Ray Analysis of 18. X-Ray Intensity data were collected at 173 K on a Bruker DUO diffractometer using CuKα radiation (λ = 1.54178 Å), from an ImuS power source, and an APEXII CCD area detector. Raw data frames were read by program SAINT and integrated using 3D profiling algorithms. The resulting data were reduced to produce hkl reflections and their intensities and estimated standard deviations. The data were corrected for Lorentz and polarization effects and numerical absorption corrections were applied based on indexed and measured faces. The structure was solved and refined in SHELXTL2014[8-11], using full-matrix least-squares refinement. The non-H atoms were refined with anisotropic thermal parameters and all of the H atoms were calculated in idealized positions and refined riding on their parent atoms. In the final cycle of refinement, 4534 reflections (of which 4485 are observed with I > 2σ(I)) were used to refine 365 parameters and the resulting R_1, wR_2 and S (goodness of fit) were 2.42%, 6.38% and 1.046, respectively. The refinement was carried out by minimizing the wR_2 function using F^2 rather than F values. R_1 is calculated to provide a reference to the conventional R value but its function is not minimized.

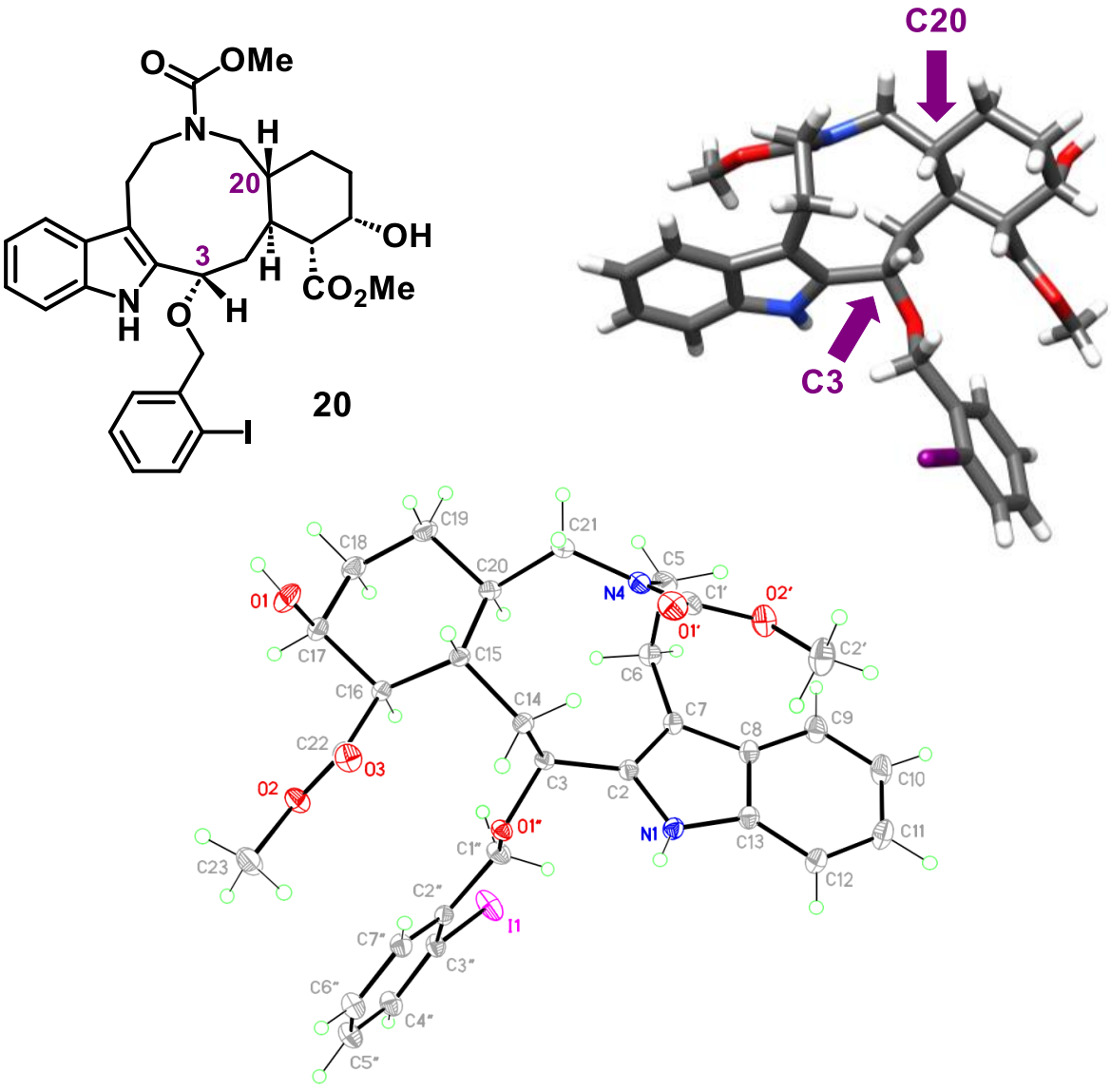


X-Ray Crystallographic Data for 18. Crystallographic data for **18** has been deposited with the Cambridge Crystallographic Data Centre (submission number Y-18; CCDC deposition number 2338890). Copies of the data can be obtained, free of charge at by visiting http://www.ccdc.cam.ac.uk/.

Crystal data and structure refinement for 18.

Identification code	**Y-18** (deposition no. 2338890)	
Empirical formula	C31 H37 I N2 O6	
Formula weight	660.52	
Temperature	173(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 12.2862(2) Å	α = 90°.
	b = 9.7856(2) Å	β = 111.0549(7)°.
	c = 13.1560(3) Å	γ = 90°.
Volume	1476.12(5) $Å^3$	
Z	2	
Density (calculated)	1.486 Mg/m^3	
Absorption coefficient	8.899 mm^{-1}	
F(000)	676	
Crystal size	0.310 x 0.191 x 0.044 mm^3	
Theta range for data collection	3.600 to 71.083°.	
Index ranges	-15 ≤ h ≤ 14, -10 ≤ k ≤ 11, -15 ≤ l ≤ 16	
Reflections collected	18451	
Independent reflections	4534 [R(int) = 0.0248]	
Completeness to theta = 25.000°	99.3 %	
Absorption correction	Multi	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4534 / 1 / 365	
Goodness-of-fit on F^2	1.046	
Final R indices [I>2sigma(I)]	R1 = 0.0242, wR2 = 0.0638 [4485]	
R indices (all data)	R1 = 0.0243, wR2 = 0.0639	
Absolute structure parameter	0.056(4)	
Largest diff. peak and hole	0.904 and -0.803 e.$Å^{-3}$	

X-Ray Analysis of 20. X-Ray Intensity data were collected at 100 K on a Bruker D8 Venture diffractometer using MoKα radiation (λ = 0.71073 Å) and a Photon III area detector. Raw data frames were read by program SAINT and integrated using 3D profiling algorithms. The resulting data were reduced to produce hkl reflections and their intensities and estimated standard deviations. The data were corrected for Lorentz and polarization effects and numerical absorption corrections were applied based on indexed and measured faces. The structure was solved and refined in SHELXTL2014[8-11], using full-matrix least-squares refinement. The non-H atoms were refined with anisotropic thermal parameters and all of the H atoms were calculated in idealized positions and refined riding on their parent atoms. The hydroxyl and amino protons were obtained from a difference Fourier map and refined freely. The molecules also exhibit a network of hydrogen bonding involving bot of the protons. The reported structure and stereochemistry reported here are supported by the value of the Flack x parameter of -0.017(2). In the final cycle of refinement, 9830 reflections (of which 9642 are observed with I > 2σ(I)) were used to refine 362 parameters and the resulting R_1, wR_2 and S (goodness of fit) were 1.98%, 4.77% and 1.039, respectively. The refinement was carried out by minimizing the wR_2 function using F^2 rather than F values. R_1 is calculated to provide a reference to the conventional R value but its function is not minimized.

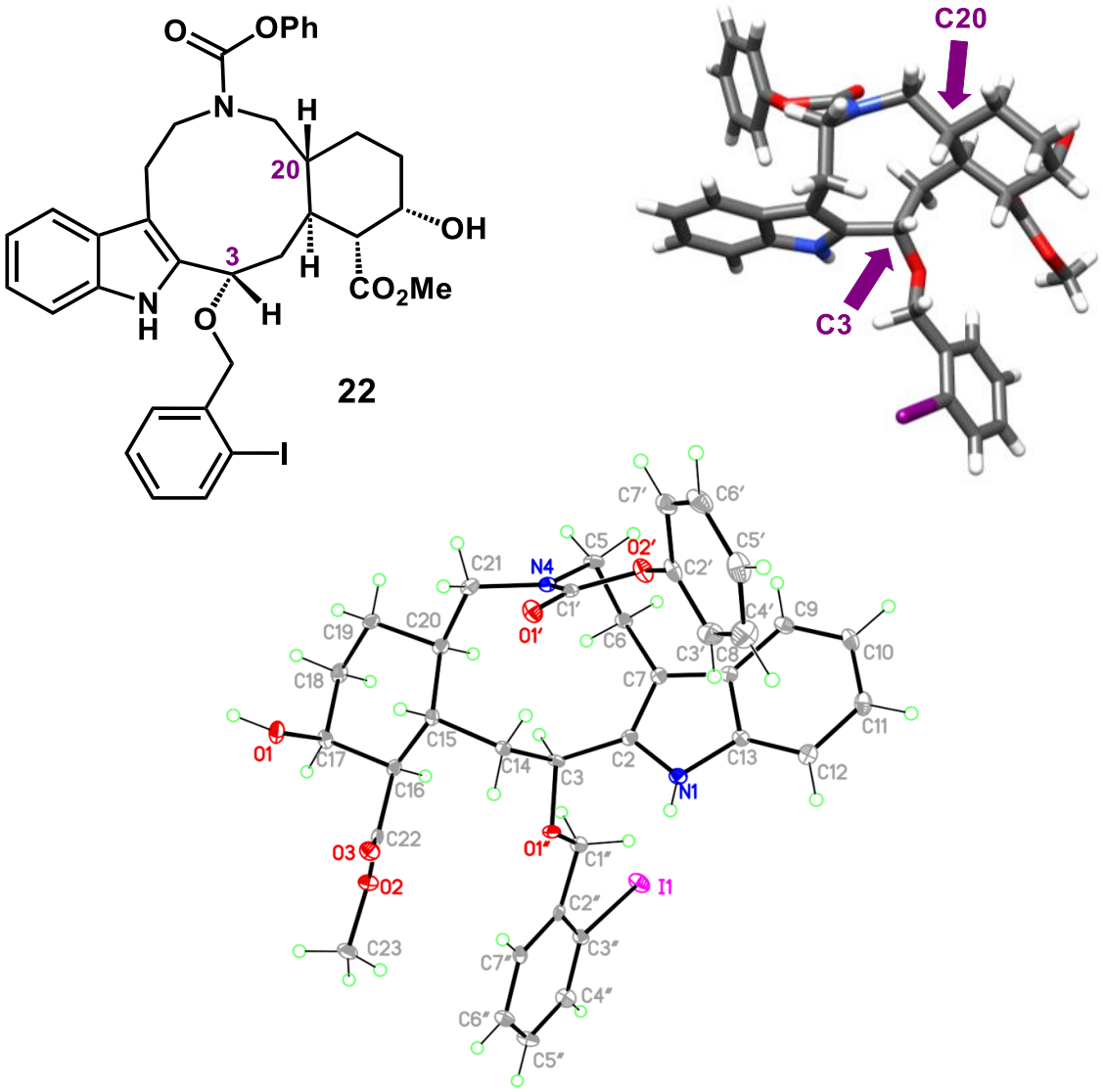


X-Ray Crystallographic Data for 20. Crystallographic data for **20** has been deposited with the Cambridge Crystallographic Data Centre (submission number Y-20; CCDC deposition number 2338892). Copies of the data can be obtained, free of charge at by visiting http://www.ccdc.cam.ac.uk/.

Crystal data and structure refinement for 20.

Identification code	**Y-20** (deposition no. 2338892)	
Empirical formula	C30 H35 I N2 O6	
Formula weight	646.50	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21	
Unit cell dimensions	a = 12.0831(6) Å	α = 90°.
	b = 9.8234(5) Å	β = 111.9770(10)°.
	c = 13.0300(6) Å	γ = 90°.
Volume	1434.24(12) $Å^3$	
Z	2	
Density (calculated)	1.497 Mg/m^3	
Absorption coefficient	1.162 mm^{-1}	
F(000)	660	
Crystal size	0.256 x 0.173 x 0.058 mm^3	
Theta range for data collection	2.672 to 33.356°.	
Index ranges	-18 ≤ h ≤ 18, -15 ≤ k ≤ 14, -20 ≤ l ≤ 19	
Reflections collected	45405	
Independent reflections	9830 [R(int) = 0.0194]	
Completeness to theta = 25.000°	98.3 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	9830 / 1 / 362	
Goodness-of-fit on F^2	1.039	
Final R indices [I>2sigma(I)]	R1 = 0.0198, wR2 = 0.0477 [9642]	
R indices (all data)	R1 = 0.0206, wR2 = 0.0481	
Absolute structure parameter	-0.017(2)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.734 and -0.987 $e.Å^{-3}$	

X-Ray Analysis of 22. X-Ray Intensity data were collected at 100 K on a Bruker DUO diffractometer using MoKα radiation (λ = 0.71073 Å) and an APEXII CCD area detector. Raw data frames were read by program SAINT and integrated using 3D profiling algorithms. The resulting data were reduced to produce hkl reflections and their intensities and estimated standard deviations. The data were corrected for Lorentz and polarization effects and numerical absorption corrections were applied based on indexed and measured faces. The structure was solved and refined in SHELXTL2014[8-11], using full-matrix least-squares refinement. The non-H atoms were refined with anisotropic thermal parameters and all of the H atoms were calculated in idealized positions and refined riding on their parent atoms. The asymmetric unit consists of the molecule and two chloroform solvent molecules. Both solvents have their chlorine atoms disordered and refined in three parts for one and two parts for the second. The correct stereochemistry is refined using this anomalous dispersion method as can be seen from the Flack x parameter of 0.008(6). In the final cycle of refinement, 9134 reflections (of which 8258 are observed with I > 2σ(I)) were used to refine 559 parameters and the resulting R_1, wR_2 and S (goodness of fit) were 2.72%, 5.13% and 1.035, respectively. The refinement was carried out by minimizing the wR_2 function using F^2 rather than F values. R_1 is calculated to provide a reference to the conventional R value but its function is not minimized.

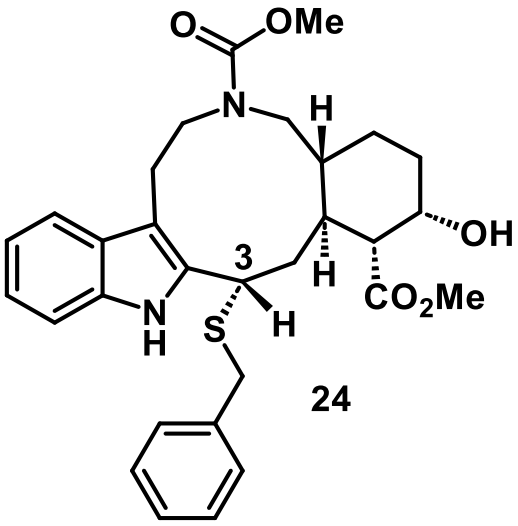


X-Ray Crystallographic Data for 22. Crystallographic data for **22** has been deposited with the Cambridge Crystallographic Data Centre (submission number Y-22; CCDC deposition number 2338891). Copies of the data can be obtained, free of charge at by visiting http://www.ccdc.cam.ac.uk/.

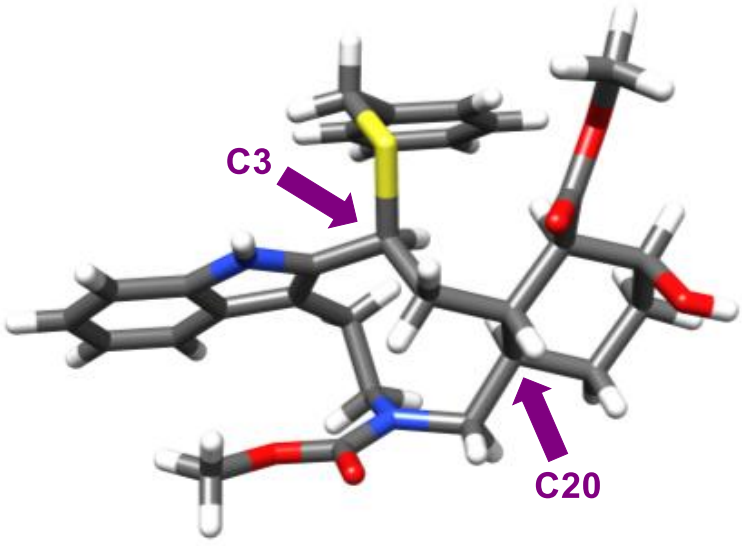
Crystal data and structure refinement for 22.

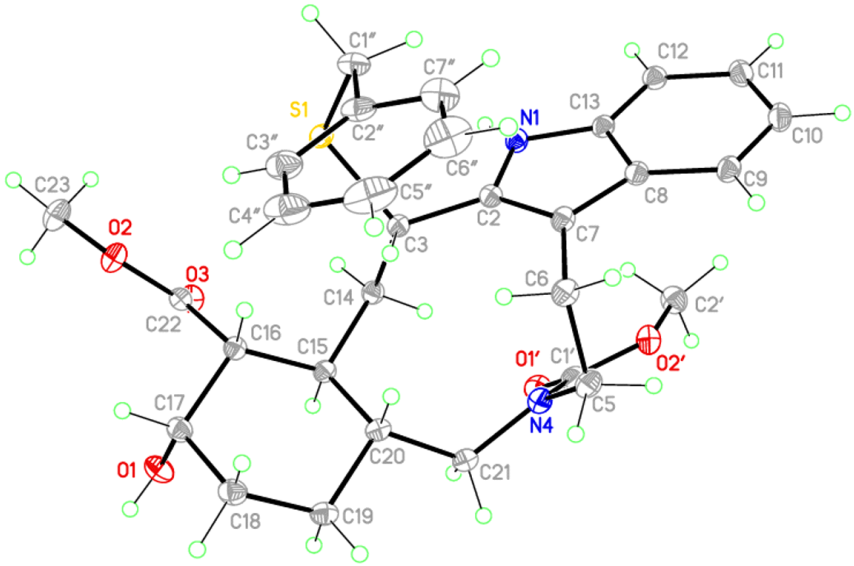
Identification code	**Y-22** (deposition no. 2338891)	
Empirical formula	C37 H39 Cl6 I N2 O6 (2 $CHCl_3$ not shown)	
Formula weight	947.30	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 12.0982(7) Å	α = 90°.
	b = 9.7700(6) Å	β = 98.2052(11)°.
	c = 16.9810(10) Å	γ = 90°.
Volume	1986.6(2) $Å^3$	
Z	2	
Density (calculated)	1.584 Mg/m^3	
Absorption coefficient	1.257 mm^{-1}	
F(000)	956	
Crystal size	0.334 x 0.239 x 0.097 mm^3	
Theta range for data collection	1.212 to 27.500°.	
Index ranges	-15 ≤ h ≤ 13, -12 ≤ k ≤ 12, -18 ≤ l ≤ 22	
Reflections collected	38673	
Independent reflections	9134 [R(int) = 0.0374]	
Completeness to theta = 25.242°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9202 and 0.7697	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	9134 / 2 / 559	
Goodness-of-fit on F^2	1.035	
Final R indices [I>2sigma(I)]	R1 = 0.0272, wR2 = 0.0513 [8258]	
R indices (all data)	R1 = 0.0346, wR2 = 0.0532	
Absolute structure parameter	0.008(6)	
Largest diff. peak and hole	0.688 and -0.470 $e.Å^{-3}$	

X-Ray Analysis of 24. X-Ray Intensity data were collected at 100 K on a Bruker Dual micro source D8 Venture diffractometer and PHOTON III detector running apex3 software package of programs and using MoKα radiation (λ = 0.71073 Å). Raw data frames were read by program SAINT and integrated using 3D profiling algorithms. The resulting data were reduced to produce hkl reflections and their intensities and estimated standard deviations. The data were corrected for Lorentz and polarization effects and numerical absorption corrections were applied based on indexed and measured faces. The structure was solved and refined in SHELXTL2014[8-11], using full-matrix least-squares refinement. The non-H atoms were refined with anisotropic thermal parameters and all of the H atoms were calculated in idealized positions and refined riding on their parent atoms. In the final cycle of refinement, 9474 reflections (of which 8697 are observed with I > 2σ(I)) were used to refine 353 parameters and the resulting R_1, wR_2 and S (goodness of fit) were 3.22%, 7.63% and 1.035, respectively. The refinement was carried out by minimizing the wR_2 function using F^2 rather than F values. R_1 is calculated to provide a reference to the conventional R value but its function is not minimized.



24



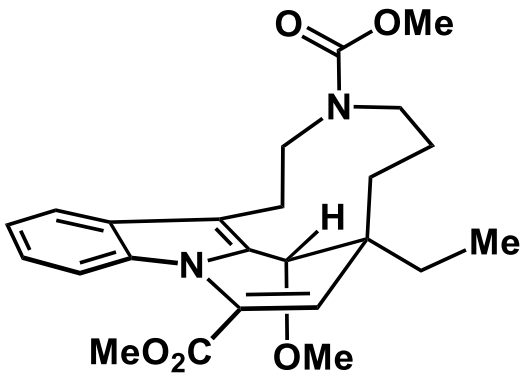


X-Ray Crystallographic Data for 24. Crystallographic data for **24** has been deposited with the Cambridge Crystallographic Data Centre (submission number Y-24; CCDC deposition number 2338909). Copies of the data can be obtained, free of charge at by visiting http://www.ccdc.cam.ac.uk/.

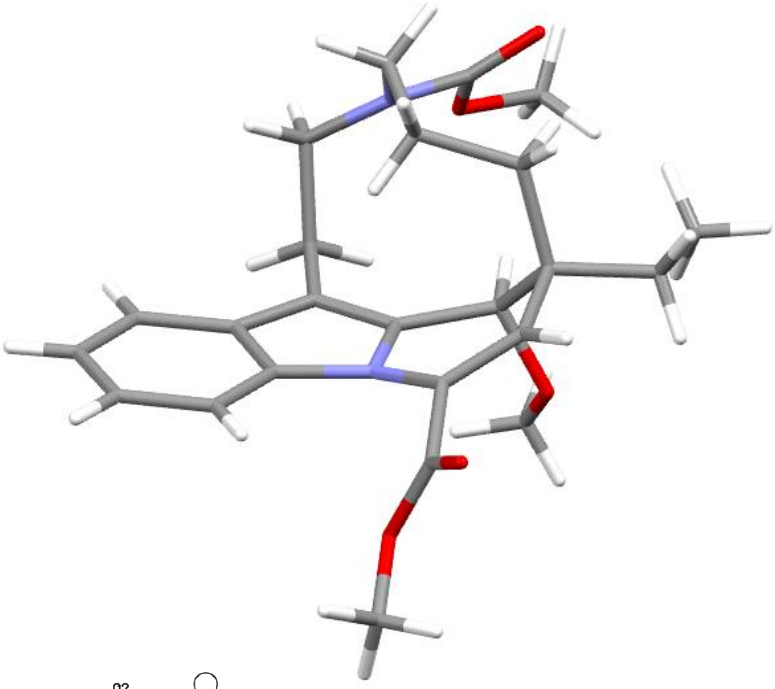
Crystal data and structure refinement for 24.

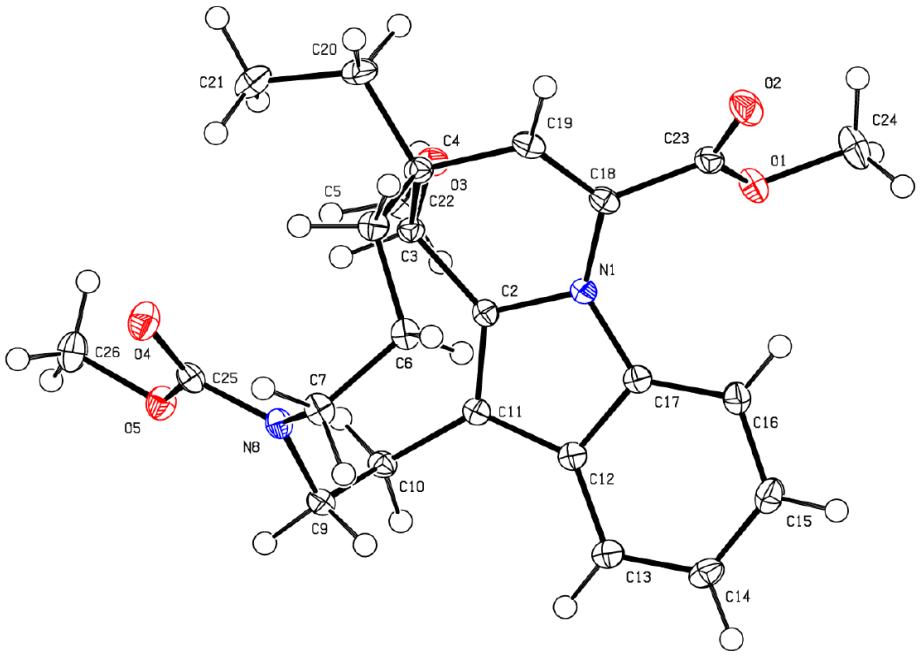
Identification code	**Y-24** (deposition no. 2338909)	
Empirical formula	C30 H36 N2 O5 S	
Formula weight	536.67	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 9.7448(3) Å	α = 90°.
	b = 14.0034(5) Å	β = 90°.
	c = 19.6580(6) Å	γ = 90°.
Volume	2682.54(15) $Å^3$	
Z	4	
Density (calculated)	1.329 Mg/m^3	
Absorption coefficient	0.164 mm^{-1}	
F(000)	1144	
Crystal size	0.187 x 0.119 x 0.046 mm^3	
Theta range for data collection	2.072 to 33.272°.	
Index ranges	$-14 \le h \le 14$, $-21 \le k \le 19$, $-30 \le l \le 30$	
Reflections collected	64890	
Independent reflections	9474 [R(int) = 0.0435]	
Completeness to theta = 25.242°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9948 and 0.9780	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	9474 / 0 / 353	
Goodness-of-fit on F^2	1.035	
Final R indices [I>2sigma(I)]	R1 = 0.0322, wR2 = 0.0763 [8697]	
R indices (all data)	R1 = 0.0372, wR2 = 0.0798	
Absolute structure parameter	0.013(16)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.300 and -0.255 $e.Å^{-3}$	

X-Ray Analysis of 27. X-Ray Intensity data were collected at 100 K on a Bruker Dual micro source D8 Venture diffractometer and PHOTON III detector running APEX3 software package of programs and using CuKα radiation (λ = 1.54178 Å). The data frames were integrated and multi-scan scaling was applied in APEX3. Intrinsic phasing structure solution provided the all of the non-H atoms. The structure was refined using full-matrix least-squares refinement (SHELXL[8-11]). The non-H atoms were refined with anisotropic displacement parameters and all of the H atoms were calculated in idealized positions and refined riding on their parent atoms. The absolute configuration is established by anomalous dispersion giving a value of 0.13(14) for the Flack x parameter. In the final cycle of refinement, 3872 reflections (of which 3861 are observed with $I > 2\sigma(I)$) were used to refine 284 parameters and the resulting R_1, wR_2 and S (goodness of fit) were 3.03%, 8.55% and 1.084, respectively. The refinement was carried out by minimizing the wR_2 function using F^2 rather than F values. R_1 is calculated to provide a reference to the conventional R value but its function is not minimized.



27





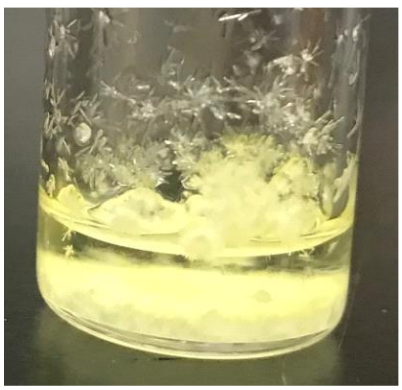


Photo by Michael Goertzen

X-Ray Crystallographic Data for 27. Crystallographic data for **27** has been deposited with the Cambridge Crystallographic Data Centre (submission number V-27; CCDC deposition number 2338889). Copies of the data can be obtained, free of charge at by visiting http://www.ccdc.cam.ac.uk/.

Crystal data and structure refinement for 27.

Identification code	**V-27** (deposition no. 2338889)	
Empirical formula	C24 H30 N2 O5	
Formula weight	426.50	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 9.382(3) Å	α = 90°.
	b = 7.3133(13) Å	β = 104.69(2)°.
	c = 16.086(6) Å	γ = 90°.
Volume	1067.6(6) $Å^3$	
Z	2	
Density (calculated)	1.327 Mg/m^3	
Absorption coefficient	0.728 mm^{-1}	
F(000)	456	
Crystal size	0.418 x 0.100 x 0.066 mm^3	
Theta range for data collection	2.840 to 70.085°.	
Index ranges	$-11 \le h \le 11$, $-8 \le k \le 8$, $-19 \le l \le 19$	
Reflections collected	36941	
Independent reflections	3872 [R(int) = 0.0239]	
Completeness to theta = 67.684°	97.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9567 and 0.8262	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3872 / 1 / 284	
Goodness-of-fit on F^2	1.084	
Final R indices [I>2sigma(I)]	R1 = 0.0303, wR2 = 0.0855 [3861]	
R indices (all data)	R1 = 0.0304, wR2 = 0.0856	
Absolute structure parameter	0.13(14)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.283 and -0.222 $e.Å^{-3}$	

16.) Computational Analysis General Information.

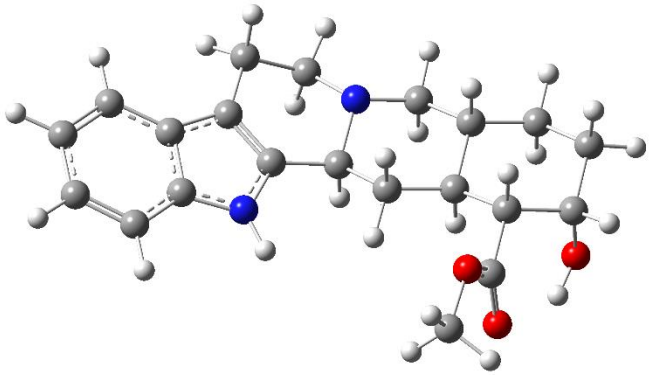
Conformational Search. Structures were drawn in ChemDraw, minimized (MM2[12]) in Chem3D, and then imported into Maestro (part of the Schrödinger Suite[13]). All starting materials, reagents, intermediates, and products were prepared using LigPrep[13] (OPLS3e[14-18] or OPLS4[19], no change of ionization or protonation). Prepared structures were then subjected to a conformational search. For reagents and non-ring-opened starting materials and intermediates, a MacroModel Conformational Search[13] was conducted (OPLS3e or OPLS4; Solvent: $CHCl_3$). The search was first conducted using the Truncated Newton Conjugate Gradient (TNCG) method[20], after which one to three lowest-energy conformers were used as the input for a second round of conformational searching using the Full Matrix Newton Raphson (FMNR) method. For ring-opened intermediates and products, the Macrocycle Conformational Sampling module[13] was used (OPLS3e or OPLS4; GB/SA[21] - water). For each structure, between one and three lowest-energy conformations from these methods were then converted into a Gaussian input file using Avogadro.[22,23]

Geometry Optimization and Energy Calculations. Geometry optimization was performed for each of the saved conformers from the conformational search using Gaussian 09[24] or Gaussian 16.[25] Geometry optimizations were first conducted using the PM6 semi-empirical method[26] (Solvent Model: PCM[27,28] or SMD[29]; Solvent: $CHCl_3$). DFT optimization was then performed using the PM6 result with the M06-2X density functional[30] and the 6-311++(d,p) basis set.[31-34] For structures containing iodine, calculations were performed with a mixed basis set, using MIDI![35] for iodine and 6-311++(d,p) for all other atoms. DFT optimization was performed using the SMD solvent model in $CHCl_3$ with an ultrafine integration grid. Frequency calculations were then conducted on the optimized geometries (same density functional, basis set, solvent, solvent model, and grid size). Results were checked to ensure that a stationary point was found, and all structures displayed zero imaginary frequencies (no transition states discussed here). Note: The location of the cation in the intermediates reflects its initial placement prior to the conformational search and does not indicate a full +1 charge at that location after DFT calculations. The relaxed potential energy scan of **Int-1A** was conducted using the Opt=Modredundant function with the same level of theory, basis sets, and solvent model as previous DFT calculations. All results were visualized using GaussView 6.[36]

17.) DFT Optimized Structures and Sample Input File.

Optimized Structure for Yohimbine

Zero-point correction = 0.449304 (Hartree/Particle)
Thermal correction to Energy = 0.471153
Thermal correction to Enthalpy = 0.472097
Thermal correction to Gibbs Free Energy = 0.398590
Sum of electronic and zero-point Energies = -1150.531886
Sum of electronic and thermal Energies = -1150.510037
Sum of electronic and thermal Enthalpies = -1150.509093
Sum of electronic and thermal Free Energies = -1150.582600



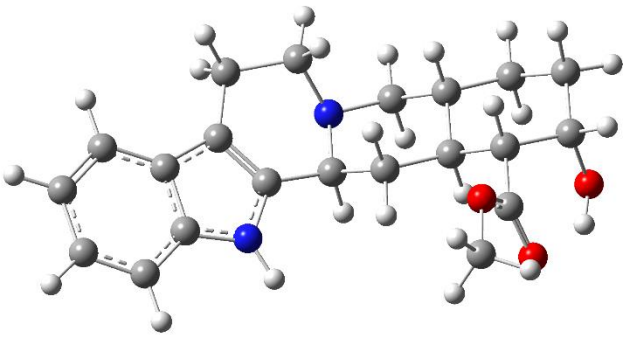
0 1

C	-6.29745900	0.61970400	-0.33636900
C	-5.84639800	1.91099300	-0.00266200
C	-4.51429800	2.15371100	0.29276000
C	-3.63563700	1.06949300	0.24701600
C	-4.06773100	-0.23963300	-0.08683500
C	-5.42293100	-0.45363900	-0.38097200
N	-2.28194200	1.01060000	0.48818000
C	-1.85435500	-0.28898200	0.31727100
C	-2.90657500	-1.08602700	-0.02906200
C	-0.44319400	-0.75300700	0.50405200
N	-0.31325200	-2.07664700	-0.11892500
C	-1.38015400	-2.98248200	0.31420300
C	-2.73316600	-2.55514600	-0.25737500
C	0.58756800	0.21233900	-0.08562500
C	1.99995600	-0.33140100	0.12687900
C	2.11054100	-1.75665000	-0.42910300
C	1.00879000	-2.63249400	0.15718700
C	3.08803700	0.54904100	-0.51691300
C	4.49400500	-0.01800200	-0.22588900
C	4.59476400	-1.44414900	-0.75321100
C	3.49991600	-2.33776000	-0.16708000
O	4.77549700	-0.06049900	1.16549000
H	2.19599200	-0.37174000	1.20671000
H	-0.24237500	-0.83777800	1.59127800
H	1.94634000	-1.70363600	-1.51459900
C	2.97352100	1.96965700	-0.02527800
O	3.33479000	2.34634900	1.06961900
O	2.40962800	2.78418300	-0.91436000
C	2.22342200	4.14429400	-0.49620100
H	-7.34692400	0.46779800	-0.56119400
H	-6.55458100	2.73122200	0.02407900
H	-4.16628300	3.14773100	0.55072700
H	-5.77840200	-1.44531000	-0.64023400
H	-1.70058000	1.79462400	0.74351600
H	-1.12898700	-3.98779800	-0.02972800
H	-1.43757400	-3.01079700	1.41668300
H	-2.77354300	-2.79008700	-1.32644200
H	-3.52998700	-3.12462800	0.23052100
H	0.38476600	0.34455000	-1.15443000
H	0.48334900	1.19010400	0.39919400
H	1.06006600	-3.62989400	-0.28782300
H	1.17063800	-2.74585500	1.24614300

H	2.93849100	0.55662800	-1.60067900
H	5.23557400	0.61444600	-0.73099300
H	5.58542700	-1.83473300	-0.50691700
H	4.51294200	-1.41827900	-1.84489200
H	3.65201800	-2.43557700	0.91296700
H	3.57039600	-3.34131900	-0.59732200
H	4.54297800	0.79872500	1.54198900
H	1.75508700	4.64821600	-1.33770500
H	1.57607600	4.18342300	0.38060700
H	3.18439100	4.60286700	-0.26300000

Optimized Structure for *N*-Inverted Yohimbine

Zero-point correction = 0.449883 (Hartree/Particle)
Thermal correction to Energy = 0.471423
Thermal correction to Enthalpy = 0.472367
Thermal correction to Gibbs Free Energy = 0.400205
Sum of electronic and zero-point Energies = -1150.528357
Sum of electronic and thermal Energies = -1150.506817
Sum of electronic and thermal Enthalpies = -1150.505873
Sum of electronic and thermal Free Energies = -1150.578035



0 1

C	6.24031400	0.46078600	0.54436700
C	5.97063100	1.63805600	-0.17875400
C	4.72259500	1.87122300	-0.73488800
C	3.74132700	0.89462300	-0.55187200
C	3.99246100	-0.30073100	0.16993100
C	5.26512300	-0.50692900	0.72293500
N	2.43302700	0.85349900	-0.97857200
C	1.86385100	-0.32964600	-0.55746200
C	2.77140800	-1.06122100	0.15261900
C	0.44585900	-0.72385900	-0.81791300
N	0.30883200	-2.15204300	-0.49441000
C	0.89373200	-2.51016000	0.80208800
C	2.41862600	-2.38809000	0.75127500
C	-0.54183900	0.18377600	-0.05457100
C	-1.97990700	-0.29509200	-0.25642300
C	-2.10206200	-1.77403500	0.13436000
C	-1.07559100	-2.58762800	-0.66013600
C	-3.00570800	0.53125300	0.54370900
C	-4.44151000	0.03321000	0.27521500
C	-4.55524900	-1.43953200	0.64938400
C	-3.52275300	-2.28845300	-0.09485200
O	-4.80007000	0.15160700	-1.09394800
H	-2.23325300	-0.20509600	-1.32177700
H	0.23030400	-0.62186600	-1.89005800
H	-1.86608600	-1.85747600	1.20566800
C	-2.87485000	1.99532500	0.20916700
O	-3.29789800	2.50636500	-0.80636900
O	-2.22007700	2.68444500	1.14088200
C	-2.00710400	4.07673900	0.86655300
H	7.22818600	0.31299800	0.96530600
H	6.75395800	2.37702100	-0.30286600
H	4.51455800	2.77802000	-1.29193700
H	5.48152300	-1.41268000	1.27952100
H	1.98335100	1.54962600	-1.55457700
H	0.51300000	-1.88057500	1.62093400
H	0.60554900	-3.54076100	1.02044500
H	2.82675900	-2.48307100	1.76195100
H	2.83527800	-3.20556000	0.15297600
H	-0.29377300	0.18379100	1.01316500
H	-0.41886900	1.21316200	-0.41085400
H	-1.13686100	-3.64513600	-0.38792400
H	-1.32633600	-2.51188600	-1.72634800
H	-2.79550700	0.41204200	1.61094000
H	-5.13477400	0.62382200	0.88825700

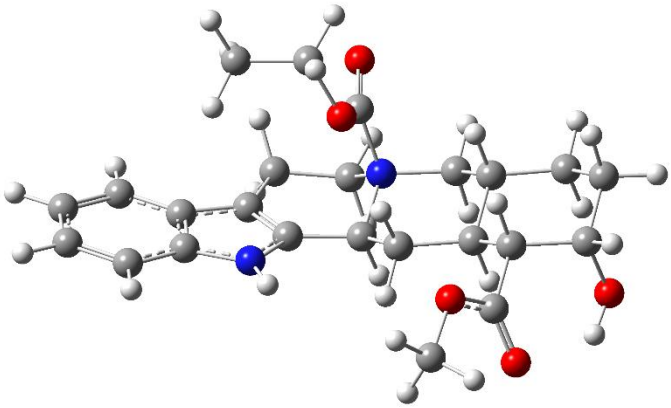
H	-5.56963400	-1.77710300	0.42202700
H	-4.41088400	-1.53550500	1.73063500
H	-3.74124800	-2.26534700	-1.16802500
H	-3.59737200	-3.33150500	0.22725600
H	-4.56901700	1.04424500	-1.38353500
H	-2.96201600	4.59180700	0.76053600
H	-1.45953900	4.46338500	1.72210800
H	-1.42207200	4.19643600	-0.04585900

Optimized Structure for Yohimbine Int-1A (compound 30)

Zero-point correction = 0.535747 (Hartree/Particle)
Thermal correction to Energy = 0.563068
Thermal correction to Enthalpy = 0.564013
Thermal correction to Gibbs Free Energy = 0.478773
Sum of electronic and zero-point Energies = -1418.040810
Sum of electronic and thermal Energies = -1418.013488
Sum of electronic and thermal Enthalpies = -1418.012544
Sum of electronic and thermal Free Energies = -1418.097784

1 1

C	6.02505400	1.18981100	-0.32287800
C	5.49371700	2.44525500	0.03390400
C	4.13045200	2.68286600	0.02195100
C	3.29985200	1.62503800	-0.35705500
C	3.81391000	0.36022100	-0.73031600
C	5.20079900	0.14699400	-0.70507800
N	1.92479400	1.55855800	-0.43105200
C	1.57123300	0.30156000	-0.85519200
C	2.68369800	-0.46658300	-1.05144800
C	0.16654500	-0.19372100	-0.98926800
N	0.22215200	-1.68875200	-0.64616900
C	1.17744700	-2.35913000	-1.63443100
C	2.62336500	-1.91922100	-1.41228300
C	-0.91558900	0.58115100	-0.24410700
C	-2.27897100	-0.09814000	-0.39489800
C	-2.19846800	-1.57206000	0.02729900
C	-1.15755100	-2.29812800	-0.80855200
C	-3.37573700	0.60802700	0.42194700
C	-4.73902300	-0.08496500	0.20917600
C	-4.64498400	-1.54245600	0.64036000
C	-3.54919300	-2.27638400	-0.13210400
O	-5.12940000	-0.07578600	-1.15427800
H	-2.57159000	-0.06852800	-1.45220900
H	-0.12497600	-0.21457300	-2.04395900
H	-1.90869800	-1.61667800	1.08690800
C	0.72260600	-2.02409200	0.74396500
O	1.05644100	-3.14088800	0.97851200
O	0.69448800	-0.99010100	1.52573300
C	1.36393800	-1.12687500	2.82329300
C	2.84979600	-0.93125900	2.63746900
C	-3.45858600	2.06840800	0.04419800
O	-4.00101500	2.48193600	-0.95640300
O	-2.85563000	2.86560600	0.92181800
C	-2.88599500	4.27124800	0.62194200
H	7.09859500	1.04494700	-0.29892700
H	6.16806100	3.24209600	0.32492900
H	3.72224900	3.64792900	0.29922000
H	5.61619200	-0.81547700	-0.98330200
H	1.29133700	2.31993700	-0.23289600
H	1.05434700	-3.43288700	-1.50976800
H	0.80737800	-2.06136700	-2.61480400
H	3.16870500	-2.12707500	-2.33690900
H	3.08839800	-2.52774200	-0.63057300
H	-0.94209300	1.57152500	-0.71123900



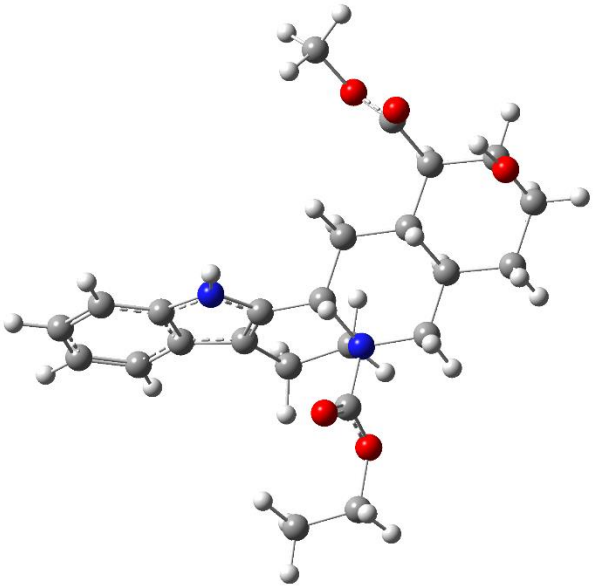
H	-0.66148700	0.71881000	0.80690300
H	-1.38872000	-2.22518700	-1.87421500
H	-1.06758600	-3.34936300	-0.53485900
H	-3.12004500	0.54942700	1.48428600
H	-5.49106400	0.43315600	0.81638100
H	-4.44084500	-1.57998000	1.71502900
H	-5.61177700	-2.02121900	0.47064100
H	-3.81303400	-2.30637900	-1.19395800
H	-3.47048300	-3.30909800	0.21725700
H	-5.09326600	0.83740300	-1.46879400
H	0.91283200	-0.34117000	3.42462500
H	1.10905400	-2.10237600	3.23587700
H	3.33545400	-0.96842300	3.61478900
H	3.27898000	-1.71972800	2.01531200
H	3.05738000	0.03927900	2.18112000
H	-2.35638000	4.75661400	1.43732500
H	-2.38791000	4.46410200	-0.32849800
H	-3.91656300	4.62186300	0.57443400

Optimized Structure for Yohimbine Int-1B (compound 31)

Zero-point correction = 0.536126 (Hartree/Particle)
Thermal correction to Energy = 0.563285
Thermal correction to Enthalpy = 0.564229
Thermal correction to Gibbs Free Energy = 0.479807
Sum of electronic and zero-point Energies = -1418.041410
Sum of electronic and thermal Energies = -1418.014251
Sum of electronic and thermal Enthalpies = -1418.013307
Sum of electronic and thermal Free Energies = -1418.097729

1 1

C	5.43684300	2.60637600	0.81515000
C	5.06341900	3.43402100	-0.26195300
C	3.87539500	3.23985900	-0.94500600
C	3.05954500	2.18688700	-0.52473700
C	3.41718200	1.34301100	0.55340600
C	4.62658400	1.56438900	1.22896500
N	1.84142900	1.75852300	-1.00704800
C	1.43513400	0.67523000	-0.26730300
C	2.35374400	0.38645300	0.69997600
C	0.15764400	-0.06001100	-0.51127700
N	0.34035400	-1.44709000	0.10413200
C	0.80056600	-1.34115800	1.55475600
C	2.20343900	-0.75271600	1.65819800
C	-1.07055500	0.66136100	0.04950500
C	-2.34268700	-0.16953900	-0.09548800
C	-2.15067600	-1.52234600	0.59770300
C	-0.95737500	-2.24417300	-0.00451500
C	-3.57970800	0.53334800	0.48982600
C	-4.83594100	-0.34595200	0.30453100
C	-4.63151200	-1.68825200	0.99546400
C	-3.39317900	-2.40775000	0.45899100
O	-5.09627700	-0.61483900	-1.06321900
H	-2.52872600	-0.35408600	-1.16118700
H	0.00827800	-0.24108300	-1.57744800
H	-1.97519100	-1.34620300	1.66667500
C	1.34958600	-2.21808500	-0.72594000
O	1.60610400	-1.90019600	-1.84060600
O	1.76793600	-3.23984000	-0.03912400
C	2.77991300	-4.08557000	-0.68321000
C	4.14158800	-3.44420400	-0.56825500
C	-3.77214900	1.88449700	-0.15814400
O	-4.21778600	2.04637000	-1.27287900
O	-3.38215500	2.88936800	0.61907300
C	-3.51411000	4.20791700	0.06179500
H	6.37470200	2.79336900	1.32483300
H	5.72095200	4.24150500	-0.56221700
H	3.58927100	3.87698600	-1.77370300
H	4.91831500	0.93065500	2.05942200
H	1.35852900	2.14225100	-1.80712300
H	0.07515400	-0.69689700	2.04475100
H	0.73748000	-2.33902600	1.98269900
H	2.95950100	-1.52203800	1.47664500
H	2.33610500	-0.41934000	2.69103000
H	-1.14155700	1.59472200	-0.51803900



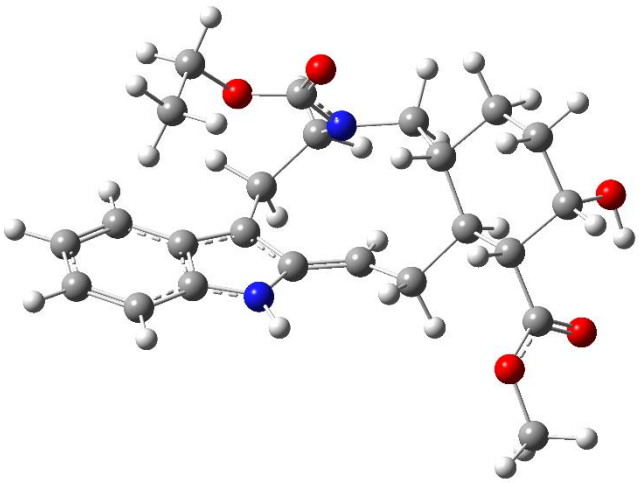
H	-0.91045800	0.94340400	1.09462000
H	-0.77164800	-3.20255900	0.48004900
H	-1.12035900	-2.40742200	-1.07414700
H	-3.42511000	0.69410200	1.56090900
H	-5.69206100	0.17258500	0.75254800
H	-5.52137000	-2.30065000	0.83556100
H	-4.53477100	-1.51982000	2.07262700
H	-3.54575200	-2.65325000	-0.59647800
H	-3.24254700	-3.34687400	0.99784000
H	-5.11410000	0.22767900	-1.53645500
H	2.71329400	-5.02081400	-0.13296400
H	2.47331100	-4.24095800	-1.71699700
H	4.87695100	-4.10405500	-1.03312200
H	4.17449300	-2.48253000	-1.08404200
H	4.41867200	-3.30650500	0.47816400
H	-2.92608300	4.29078300	-0.85248600
H	-4.56108700	4.42095900	-0.15346900
H	-3.13538800	4.88661000	0.82132600

Optimized Structure for Yohimbine Int-2A (Cis-Up; structure 32)

Zero-point correction = 0.533444 (Hartree/Particle)
Thermal correction to Energy = 0.561446
Thermal correction to Enthalpy = 0.562390
Thermal correction to Gibbs Free Energy = 0.475969
Sum of electronic and zero-point Energies = -1418.006036
Sum of electronic and thermal Energies = -1417.978034
Sum of electronic and thermal Enthalpies = -1417.977090
Sum of electronic and thermal Free Energies = -1418.063511

1 1

C	-5.55419700	1.63223300	-0.18164400
C	-4.97271700	2.52586200	-1.13259700
C	-3.61961100	2.73668700	-1.22666900
C	-2.80354900	2.02094200	-0.33158300
C	-3.36528700	1.13671300	0.64526800
C	-4.77274600	0.93888500	0.69686600
N	-1.45803000	1.98917400	-0.22938600
C	-1.10560800	1.15522900	0.83402200
C	-2.31012600	0.59277600	1.37441400
C	-2.36630900	-0.47736400	2.40022700
C	0.14415500	0.78875700	1.20852000
C	1.39664200	1.07769200	0.49205100
C	-1.40472400	-1.70076800	2.19595400
N	-0.70903700	-1.81285700	0.91289900
C	0.72440200	-2.14723700	0.89565300
C	1.61817700	-1.44111600	-0.16242500
C	2.32482200	-0.16104900	0.35347200
C	3.46877600	0.27021100	-0.59689600
C	4.48212900	-0.85793600	-0.85807200
C	3.74875200	-2.01745900	-1.50744100
C	2.63794900	-2.51410400	-0.59280400
H	1.00675300	-1.17218500	-1.03034600
H	2.76336900	-0.37978100	1.33358000
C	-1.41862400	-2.18236700	-0.19536400
O	-0.92784000	-2.62978700	-1.21073800
O	-2.73613300	-1.97824800	-0.02177900
C	-3.58323500	-2.28193000	-1.15052600
C	4.19028100	1.47329900	-0.03536800
O	4.91762800	1.43241800	0.93253800
O	5.07296100	-1.33361600	0.34001000
C	-3.54666800	-1.18093600	-2.18979900
O	3.95047200	2.59294900	-0.71323400
C	4.60087500	3.77765500	-0.22329700
H	-6.63017800	1.51273000	-0.16996600
H	-5.63312200	3.05340700	-1.81161800
H	-3.19499700	3.41023200	-1.96019100
H	-5.20268300	0.25935400	1.42341100
H	-0.81974600	2.58483000	-0.74075500
H	-3.39189700	-0.83872900	2.45389000
H	-2.13009600	-0.03649600	3.37455800
H	0.22186700	0.21447500	2.12629700
H	1.19228100	1.50439700	-0.49407900
H	1.93066500	1.84188600	1.07647300
H	-1.99717100	-2.60055100	2.37183300



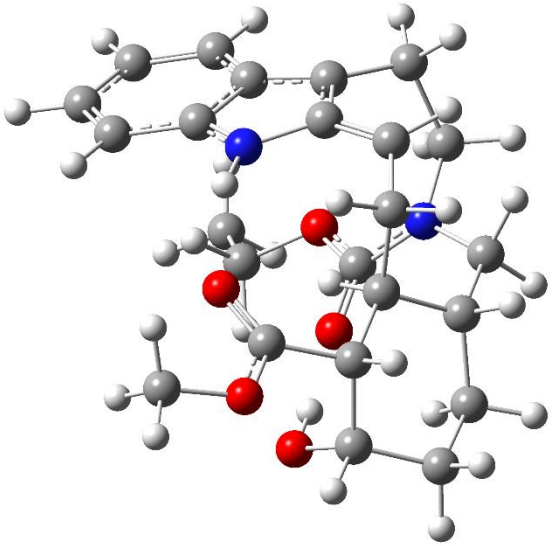
H	-0.63156700	-1.67048800	2.96100000
H	0.81210500	-3.22614200	0.73904500
H	1.11716600	-1.93765400	1.89298300
H	3.03674300	0.55634700	-1.56018000
H	5.26014100	-0.47605900	-1.53090500
H	3.34481100	-1.68549400	-2.46903500
H	4.45797400	-2.82419600	-1.70758500
H	2.08514200	-3.32130300	-1.07962100
H	3.09452200	-2.93645400	0.30866900
H	-3.27389200	-3.23912500	-1.57054600
H	-4.57723300	-2.38824800	-0.71757300
H	5.41269700	-0.57442000	0.83166100
H	-3.91414200	-0.23921300	-1.77725200
H	-2.53442500	-1.04055000	-2.57268400
H	-4.19143500	-1.45741500	-3.02750500
H	4.27592200	3.98932800	0.79590600
H	5.68258200	3.64843900	-0.24538500
H	4.29926600	4.57707600	-0.89481300

Optimized Structure for Yohimbine Int-2B (Cis-Down; structure 33)

Zero-point correction = 0.535085 (Hartree/Particle)
Thermal correction to Energy = 0.562383
Thermal correction to Enthalpy = 0.563327
Thermal correction to Gibbs Free Energy = 0.479789
Sum of electronic and zero-point Energies = -1418.009181
Sum of electronic and thermal Energies = -1417.981883
Sum of electronic and thermal Enthalpies = -1417.980938
Sum of electronic and thermal Free Energies = -1418.064477

1 1

C	-4.43644100	1.99890900	0.40745800
C	-3.46636000	3.00156400	0.72539300
C	-2.18070900	2.97209400	0.24945600
C	-1.84011000	1.89351300	-0.59034400
C	-2.80266700	0.88474400	-0.93848000
C	-4.12004600	0.94871000	-0.40262800
N	-0.65754700	1.59197200	-1.15955500
C	-0.80941300	0.43249300	-1.91806700
C	-2.15983700	-0.03823000	-1.75517700
C	-2.56398600	-1.41675500	-2.13088700
C	0.18130100	-0.27736400	-2.51012700
C	1.61420300	-0.08925400	-2.20894600
C	-2.07606400	-2.46701400	-1.06393700
N	-0.85301000	-2.11965800	-0.33207700
C	0.39687300	-2.72187400	-0.85375800
C	1.78813100	-2.08311300	-0.59606600
C	1.85287500	-0.54062800	-0.72951300
C	3.18007600	0.05487100	-0.24040000
C	3.58632500	-0.49795500	1.14231900
C	3.73994000	-2.00945000	1.05654100
C	2.41654400	-2.66743700	0.68578600
H	2.39962700	-2.47369900	-1.42126800
H	1.06690600	-0.09392900	-0.12045700
C	-0.94488300	-1.50293400	0.87689200
O	-0.00353300	-1.18225800	1.58400300
O	-2.21816200	-1.26153800	1.22406000
C	-2.43866500	-0.43588800	2.38558800
C	3.08416300	1.56556000	-0.13135800
O	2.07416400	2.22409100	-0.26277600
O	2.65488100	-0.09480500	2.13236000
C	-3.84239200	-0.70569000	2.87329600
O	4.25927900	2.10997200	0.15187500
C	4.27642200	3.53371400	0.33956900
H	-5.43146100	2.08844500	0.82542300
H	-3.76491600	3.81558700	1.37643900
H	-1.45365600	3.73183500	0.50673700
H	-4.84435100	0.18136100	-0.65066700
H	0.23126200	2.05960400	-0.98002600
H	-2.15075100	-1.66920500	-3.10907000
H	-3.64938300	-1.49442400	-2.20042200
H	-0.12629100	-1.10940900	-3.13309600
H	2.24333700	-0.67186400	-2.88291900
H	1.87918900	0.96666400	-2.30693100
H	-1.89843600	-3.41228600	-1.57752500



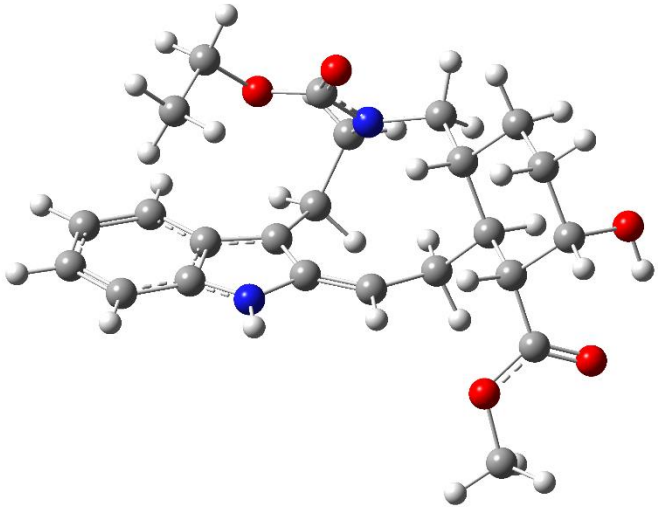
H	-2.87655000	-2.62578600	-0.34894400
H	0.44804300	-3.75623200	-0.49390800
H	0.23784900	-2.79125100	-1.93072400
H	3.99282500	-0.17433200	-0.93925000
H	4.53492300	-0.04228500	1.42874000
H	4.50846500	-2.23592700	0.30944900
H	4.09231500	-2.38852200	2.01869700
H	2.57478300	-3.73605500	0.51667500
H	1.71997500	-2.58750100	1.51976200
H	-2.30287400	0.60657500	2.08206400
H	-1.69689100	-0.68075400	3.14461800
H	1.78957000	-0.49631100	1.95991300
H	-3.94013600	-1.74066300	3.20715100
H	-4.57552200	-0.51652500	2.08772700
H	-4.06418400	-0.04897000	3.71733400
H	5.31047100	3.78639600	0.55838400
H	3.94390200	4.03682500	-0.56855200
H	3.63113700	3.80721800	1.17422300

Optimized Structure for Yohimbine Int-2C (Trans; structure 34)

Zero-point correction = 0.533636 (Hartree/Particle)
Thermal correction to Energy = 0.561610
Thermal correction to Enthalpy = 0.562554
Thermal correction to Gibbs Free Energy = 0.475868
Sum of electronic and zero-point Energies = -1418.015706
Sum of electronic and thermal Energies = -1417.987731
Sum of electronic and thermal Enthalpies = -1417.986787
Sum of electronic and thermal Free Energies = -1418.073473

1 1

C	-5.50796000	1.34710500	0.31542400
C	-5.29006800	2.05982500	-0.91000600
C	-4.04190700	2.31373900	-1.41039300
C	-2.94966400	1.83592100	-0.65547400
C	-3.13872100	1.14512800	0.58940300
C	-4.46173400	0.89921500	1.06313800
N	-1.63974500	1.90162800	-0.91223900
C	-0.91761500	1.28434900	0.12607000
C	-1.89039300	0.80349400	1.08870500
C	-1.61106700	0.11488600	2.37828200
C	0.43679700	1.25184500	0.09864100
C	1.37507400	0.70016700	1.10431800
C	-1.22277300	-1.39496000	2.27400200
N	-0.56675500	-1.81324800	1.03988700
C	0.83423600	-2.25976700	1.03147700
C	1.72599800	-1.57503900	-0.01922800
C	2.39852300	-0.30100800	0.52008500
C	3.30371000	0.30866000	-0.57450500
C	4.39495300	-0.69927700	-0.99221100
C	3.73550000	-1.95924200	-1.53205500
C	2.78494100	-2.57127500	-0.50557600
H	1.09647700	-1.30012400	-0.87430000
H	3.04729400	-0.58592300	1.35582500
C	-1.32233700	-2.25006100	-0.01065000
O	-0.87215900	-2.82104700	-0.98385800
O	-2.62852200	-1.97764900	0.16087100
C	-3.52025100	-2.42762100	-0.87889200
C	3.92766600	1.59867000	-0.09905300
O	4.91472800	1.67067600	0.59643300
O	5.21210300	-1.08044600	0.10215900
C	-3.60159500	-1.42033000	-2.00472800
O	3.25343000	2.67502400	-0.50911700
C	3.76128200	3.94575800	-0.06777100
H	-6.52669500	1.17646700	0.64000100
H	-6.15709000	2.40520200	-1.46193700
H	-3.89098700	2.84360800	-2.34230300
H	-4.61622400	0.36492800	1.99320200
H	-1.21658100	2.33306800	-1.72485900
H	-0.82933800	0.66631500	2.90272300
H	-2.50441800	0.17508100	3.00183700
H	0.89834500	1.72840700	-0.76571300
H	0.86190300	0.23100200	1.93753100
H	1.92330700	1.56019500	1.51574300
H	-0.55345600	-1.62704400	3.10165300



H	-2.12780400	-1.98394700	2.40892300
H	1.23875300	-2.09209100	2.03186900
H	0.84637400	-3.33776700	0.84901200
H	2.70718500	0.53388200	-1.46369200
H	5.01184400	-0.23604100	-1.77230300
H	4.51590300	-2.67358800	-1.80470300
H	3.18800300	-1.70433800	-2.44545600
H	2.27825700	-3.43751600	-0.93906600
H	3.36035800	-2.92850300	0.35568800
H	-3.18449000	-3.40171900	-1.23364100
H	-4.48189400	-2.54174500	-0.37932300
H	5.57507600	-0.27609100	0.49531700
H	-4.25465000	-1.80627300	-2.79113000
H	-4.02012000	-0.47757700	-1.64820700
H	-2.61493600	-1.24108100	-2.43750700
H	3.09367900	4.69165400	-0.49116200
H	3.75230200	3.99804800	1.02122300
H	4.77691400	4.09129200	-0.43470800

Optimized Structure for Compound 45

Zero-point correction = 0.577982 (Hartree/Particle)
Thermal correction to Energy = 0.608655
Thermal correction to Enthalpy = 0.609599
Thermal correction to Gibbs Free Energy = 0.517148
Sum of electronic and zero-point Energies = -1533.293854
Sum of electronic and thermal Energies = -1533.263181
Sum of electronic and thermal Enthalpies = -1533.262237
Sum of electronic and thermal Free Energies = -1533.354688

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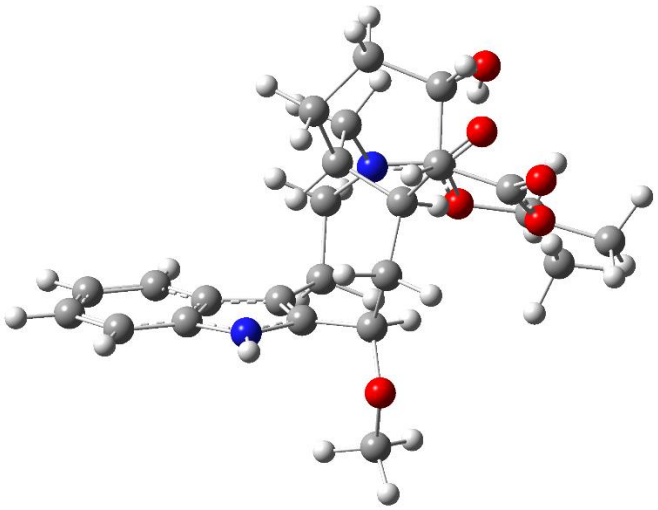
C	5.84332300	-0.00994500	-1.13651200
C	5.98748400	-1.25148100	-0.48667500
C	5.00378400	-1.74364600	0.35493800
C	3.85825200	-0.96242400	0.53142600
C	3.69507300	0.29010800	-0.10624800
C	4.70927700	0.76320500	-0.95337400
N	2.73185000	-1.18301100	1.28368100
C	1.87161100	-0.10966800	1.15350400
C	2.42256900	0.82368300	0.31528200
C	1.84236300	2.11675900	-0.16170000
C	0.55097400	-0.15971200	1.86267500
C	-0.36862100	-1.27586800	1.36033700
C	1.24053200	2.02861200	-1.57172700
N	-0.06350100	1.35893600	-1.62854500
C	-0.20033000	0.02238900	-2.21098700
C	-0.11188600	-1.14158200	-1.20560700
C	-1.06459400	-1.00321400	0.01842600
C	-2.27484400	-1.95699600	-0.08073300
C	-2.86451500	-2.08738100	-1.49657400
C	-1.78480900	-2.58415800	-2.48468700
C	-0.35374200	-2.46329100	-1.94432800
H	0.91552300	-1.15482400	-0.83618900
H	-1.44986800	0.01614100	0.06078300
C	-1.19461700	2.03870200	-1.33633200
O	-2.33025700	1.60615100	-1.48891400
O	-0.95026600	3.26506100	-0.84638100
C	-2.08984900	3.96827100	-0.31152100
C	-3.41832400	-1.61541000	0.85442900
O	-4.27197400	-2.40827000	1.17167100
O	-3.50836600	-0.89231500	-1.90783300
O	0.74878900	-0.41207500	3.25033700
C	-2.47033800	3.41300800	1.04560900
O	-3.42019900	-0.34635800	1.27053500
C	-4.52285000	0.03626100	2.10046900
C	1.46748700	0.61141000	3.91176400
H	6.63555100	0.34185100	-1.78718500
H	6.88766200	-1.83315600	-0.64910000
H	5.11590200	-2.69823800	0.85646200
H	4.60761000	1.72060400	-1.45438700
H	2.58030800	-1.96334400	1.90710000
H	1.07886900	2.48771800	0.52546800
H	2.63516600	2.87190800	-0.18976400
H	0.04708300	0.80907600	1.73582900
H	-1.12825700	-1.40187300	2.13777000



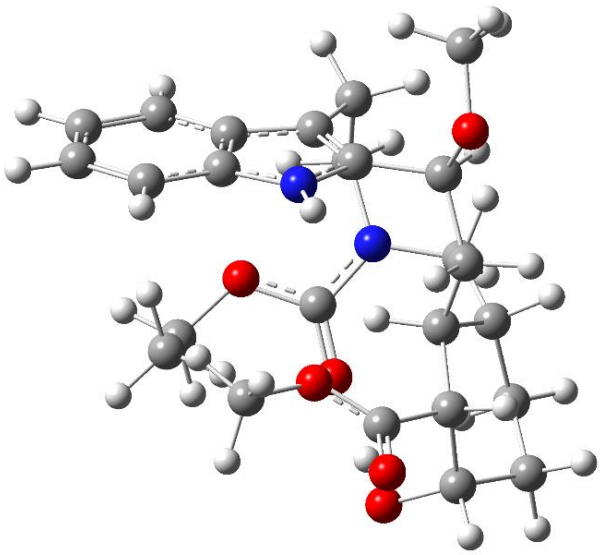
H	0.19032000	-2.21806900	1.30589600
H	1.91217400	1.46946600	-2.22535100
H	1.13224400	3.03222600	-1.98547300
H	0.59777100	-0.09761900	-2.94763400
H	-1.14385900	-0.00390400	-2.75710700
H	-1.96011100	-2.96520700	0.21161100
H	-3.66669200	-2.82612800	-1.45002400
H	-1.98304200	-3.62929500	-2.73447400
H	-1.90224500	-2.01705400	-3.41116500
H	0.36385400	-2.56838100	-2.76348300
H	-0.15214000	-3.28766900	-1.25243200
H	-1.75773700	5.00335300	-0.24359600
H	-2.91456500	3.90272000	-1.02063200
H	-2.97801300	-0.10134300	-1.71287500
H	-3.33226700	3.95814300	1.43770900
H	-2.73747200	2.35704900	0.96462000
H	-1.64424000	3.52277100	1.75216300
H	-4.35659200	1.08130900	2.35123300
H	-5.46089100	-0.07859100	1.55653300
H	-4.54639200	-0.57103700	3.00603000
H	2.50484100	0.66878400	3.56374600
H	0.98817900	1.58663600	3.76072700
H	1.46060900	0.37116600	4.97480800

Optimized Structure for Compound 46

Zero-point correction = 0.578246 (Hartree/Particle)
Thermal correction to Energy = 0.608750
Thermal correction to Enthalpy = 0.609694
Thermal correction to Gibbs Free Energy = 0.518839
Sum of electronic and zero-point Energies = -1533.291204
Sum of electronic and thermal Energies = -1533.260700
Sum of electronic and thermal Enthalpies = -1533.259755
Sum of electronic and thermal Free Energies = -1533.350611

0 1

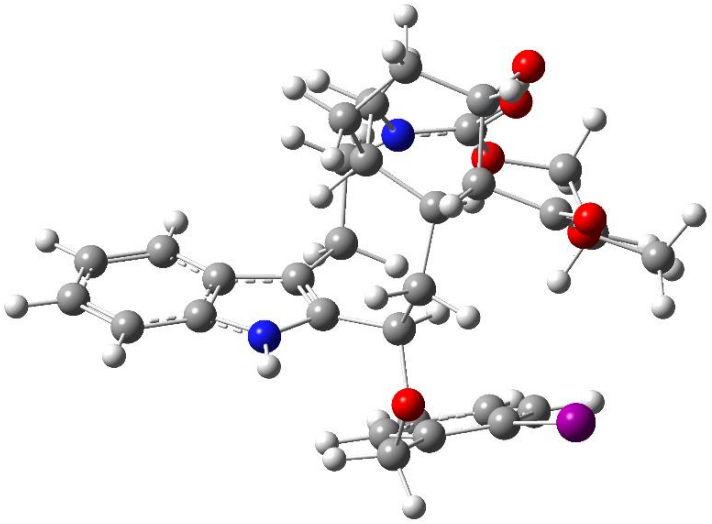
C	-4.59401300	-1.58061200	0.09345100
C	-4.30234900	-1.67525100	1.46921500
C	-3.33353500	-0.87843400	2.05608800
C	-2.65161300	0.02055300	1.23022900
C	-2.94048900	0.14428800	-0.15132100
C	-3.92594600	-0.67867300	-0.71763000
N	-1.63988400	0.90064800	1.51725600
C	-1.27982900	1.57335400	0.36794200
C	-2.06418500	1.15922800	-0.67661900
C	-1.96219600	1.63045200	-2.09170500
C	-0.17194800	2.58203400	0.39888500
C	1.14833100	1.98896100	0.87655300
C	-1.18028900	0.65810100	-2.99001500
N	0.06773200	0.18200300	-2.38700700
C	1.18961300	1.13708200	-2.41700600
C	2.26416200	1.13177200	-1.28933700
C	1.72830200	0.77244700	0.12755900
C	2.80926000	0.21368000	1.08619000
C	3.87364300	-0.69879200	0.45627800
C	4.52766400	0.04375300	-0.70170800
C	3.50310900	0.34931000	-1.78572200
H	2.58931100	2.17857100	-1.22714200
H	0.94690600	0.01794300	0.03351700
C	0.22895600	-1.12044500	-2.07148000
O	1.29377500	-1.64075600	-1.76643600
O	-0.91577700	-1.82198400	-2.11781000
C	-0.87970700	-3.13668400	-1.53006400
C	2.22521500	-0.52671400	2.27543100
O	2.83073400	-0.72163000	3.30187400
O	3.34190200	-1.95562300	0.08012100
O	-0.46109300	3.63757000	1.31108300
C	-0.90003100	-3.04619600	-0.01806100
O	0.98418000	-0.97379600	2.07062400
C	0.39702100	-1.74354300	3.12285700
C	-1.57756100	4.41792000	0.93105100
H	-5.35547300	-2.22496700	-0.33075300
H	-4.84605900	-2.38768900	2.07904500
H	-3.10845000	-0.95070500	3.11444400
H	-4.15588000	-0.61332400	-1.77625900
H	-1.20625500	1.02732400	2.42029700
H	-1.49692600	2.61855200	-2.12063200
H	-2.95871300	1.74936000	-2.52808000
H	-0.06230700	3.00721200	-0.60468400
H	0.99688300	1.71468800	1.92771100



H	1.89069100	2.79401400	0.87599100
H	-0.93313200	1.15025200	-3.93607600
H	-1.79711300	-0.20503200	-3.21891600
H	0.70815900	2.11513200	-2.44244400
H	1.71418400	1.02935100	-3.37456300
H	3.36529000	1.05279200	1.51958600
H	4.61863300	-0.91616700	1.22523600
H	4.97390200	0.96609600	-0.31260500
H	5.33636600	-0.56690900	-1.11145600
H	3.18917800	-0.58458100	-2.25039600
H	3.97094200	0.94506100	-2.57541500
H	-1.77689700	-3.62245100	-1.91249100
H	-0.00065500	-3.66850300	-1.89460800
H	2.61877600	-1.82848600	-0.55509900
H	-1.81080300	-2.54600500	0.32009000
H	-0.03024500	-2.49450000	0.34651200
H	-0.87493400	-4.05134800	0.41071500
H	-0.60416500	-1.99757100	2.77891600
H	0.97860300	-2.65000600	3.29667600
H	0.34842000	-1.15924300	4.04337400
H	-2.50426900	3.83387000	0.94757600
H	-1.65848300	5.23269800	1.65029600
H	-1.43970000	4.84022700	-0.07212200

Optimized Structure for Compound 17

Zero-point correction = 0.650271 (Hartree/Particle)
Thermal correction to Energy = 0.685573
Thermal correction to Enthalpy = 0.686517
Thermal correction to Gibbs Free Energy = 0.583919
Sum of electronic and zero-point Energies = -8654.152572
Sum of electronic and thermal Energies = -8654.117271
Sum of electronic and thermal Enthalpies = -8654.116326
Sum of electronic and thermal Free Energies = -8654.218924



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C	6.39143500	-0.52864500	0.09784700
C	6.45264200	-0.38384600	-1.30215500
C	5.30274300	-0.31400600	-2.07080500
C	4.07718800	-0.38716000	-1.40306800
C	3.99197800	-0.54168100	0.00126100
C	5.17480200	-0.60819100	0.75424700
N	2.79287600	-0.34143900	-1.88496500
C	1.90321600	-0.47724500	-0.83616300
C	2.59154200	-0.60789300	0.34072700
C	2.04701600	-0.72425800	1.72828600
C	0.43414900	-0.41996800	-1.11487100
C	-0.04983600	0.92399500	-1.65842100
C	2.08987200	0.60037800	2.50588000
N	1.05314900	1.56442400	2.11947500
C	1.37880900	2.76406700	1.34581600
C	1.20373400	2.62904100	-0.17989800
C	-0.17178300	2.05020200	-0.62348800
C	-1.08769700	3.13235900	-1.23278400
C	-1.04211500	4.48867500	-0.50655400
C	0.40341100	5.03698000	-0.48205200
C	1.46649000	3.98928600	-0.83786900
H	1.98406200	1.94573900	-0.52102300
H	-0.68491000	1.63020400	0.24230700
C	-0.18977100	1.47552300	2.64249900
O	-1.07001900	2.31514900	2.49973200
O	-0.37886000	0.34929300	3.34749900
C	-1.75179200	0.03584200	3.66101100
C	-2.54204000	2.71965900	-1.34369600
O	-3.32116300	3.24074400	-2.10522500
O	-1.64538300	4.41771500	0.77430500
O	0.08328700	-1.36608000	-2.12352100
C	0.41452600	-2.71645000	-1.85327700
C	-2.48559400	-0.39715400	2.40815600
C	0.01205700	-3.22962500	-0.48706600
C	0.98059500	-3.87427200	0.28672500
C	0.67465100	-4.43608300	1.51978500
C	-0.62569300	-4.35547800	2.00531400
C	-1.60345500	-3.70948400	1.25794100
C	-1.28405200	-3.13912300	0.02682700
I	-2.82210500	-2.17612200	-1.02791100
O	-2.89646200	1.74758100	-0.49918800
C	-4.27735300	1.37248800	-0.52465800
H	7.31371000	-0.57968500	0.66496900
H	7.42008100	-0.32616000	-1.78768400

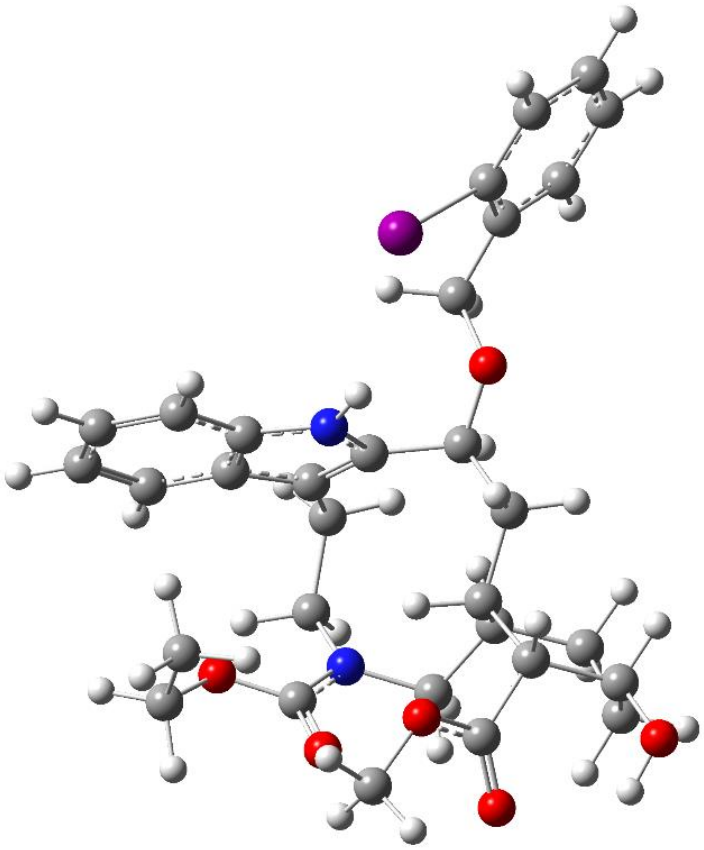
H	5.34931900	-0.20273300	-3.14815400
H	5.13644100	-0.72428800	1.83270100
H	2.52796600	-0.29220900	-2.85850400
H	1.02132100	-1.10262200	1.72072000
H	2.64529100	-1.45358500	2.28556100
H	-0.10937700	-0.64140700	-0.18614100
H	-1.03885600	0.72041200	-2.08202400
H	0.59480300	1.24183400	-2.48708200
H	3.05209700	1.09053800	2.34672500
H	1.99170000	0.39928100	3.57350800
H	2.42247400	3.01484100	1.55034300
H	0.77096400	3.58132400	1.73634700
H	-0.76937800	3.32837200	-2.26312100
H	-1.67348600	5.18044900	-1.06711000
H	0.48142100	5.87224600	-1.18225100
H	0.58022700	5.45090100	0.51362600
H	2.45814300	4.35389600	-0.55356900
H	1.49119200	3.84791400	-1.92333000
H	-1.68011800	-0.77559800	4.38445000
H	-2.21895000	0.89925600	4.13489600
H	-1.33842200	3.64617600	1.28031600
H	1.49149700	-2.87584900	-1.97691100
H	-0.10643500	-3.29030900	-2.62497400
H	-3.49256400	-0.73920100	2.66116200
H	-1.95052500	-1.22182500	1.93483900
H	-2.56439100	0.42812200	1.69736900
H	1.99542900	-3.92749600	-0.09442500
H	1.44702500	-4.93060100	2.09708300
H	-0.88575500	-4.79149000	2.96284100
H	-2.61666900	-3.64229500	1.63549700
H	-4.90418400	2.22945900	-0.27532400
H	-4.55101900	0.99543800	-1.51135700
H	-4.39000700	0.59173400	0.22364800

Optimized Structure for Compound 18

Zero-point correction = 0.650634 (Hartree/Particle)
Thermal correction to Energy = 0.686822
Thermal correction to Enthalpy = 0.687767
Thermal correction to Gibbs Free Energy = 0.581913
Sum of electronic and zero-point Energies = -8654.147633
Sum of electronic and thermal Energies = -8654.111444
Sum of electronic and thermal Enthalpies = -8654.110500
Sum of electronic and thermal Free Energies = -8654.216354

0 1

C	0.47814500	5.05313100	0.63988000
C	-0.29291900	4.91011700	-0.53151700
C	-0.76346700	3.67191500	-0.93553300
C	-0.44440400	2.57064800	-0.13569700
C	0.31130300	2.69339300	1.05444700
C	0.78530000	3.95899800	1.43139500
N	-0.76559400	1.24511900	-0.27987700
C	-0.29329800	0.53950900	0.80546400
C	0.39536400	1.38006200	1.64623600
C	1.08040400	1.02894900	2.93155400
C	-0.62621400	-0.92419800	0.89163700
C	0.19872200	-1.78523400	-0.06922100
C	2.62575600	1.08301600	2.89305700
N	3.27578900	0.43802300	1.75480700
C	3.51066200	-1.00460300	1.77587900
C	2.25425100	-1.82208300	1.44360800
C	1.71860600	-1.57003800	0.01318500
C	2.40175200	-2.43810800	-1.08621100
C	2.63780300	-3.89740500	-0.65936200
C	3.32216600	-4.00839500	0.69547000
C	2.46566500	-3.31069300	1.74853500
H	1.49334800	-1.47277900	2.14024100
H	1.90351800	-0.52045400	-0.23915000
C	3.78682400	1.14574200	0.71473600
O	4.40461200	0.65033300	-0.21122200
O	3.55747800	2.46686200	0.81421600
C	3.96631700	3.25993800	-0.31404100
C	3.66878200	-1.81373500	-1.64282600
O	4.79609000	-2.20804800	-1.44597900
O	3.31400500	-4.62970500	-1.67154500
O	-1.98570900	-1.14648600	0.52731600
C	-2.91911800	-0.52325100	1.39891500
C	3.00331200	3.10919700	-1.47362300
C	-4.28970700	-1.06100200	1.09287200
C	-4.90082200	-1.92359400	2.00451400
C	-6.16084900	-2.45916200	1.76670400
C	-6.83214700	-2.13689300	0.59346900
C	-6.24258700	-1.28163900	-0.33117500
C	-4.98232800	-0.74713300	-0.07962500
I	-4.16915100	0.55395900	-1.50898700
O	3.38342400	-0.81147200	-2.47196600
C	4.50038700	-0.17528900	-3.10416200
H	0.83340100	6.03781000	0.92178800
H	-0.51966100	5.78640900	-1.12802000



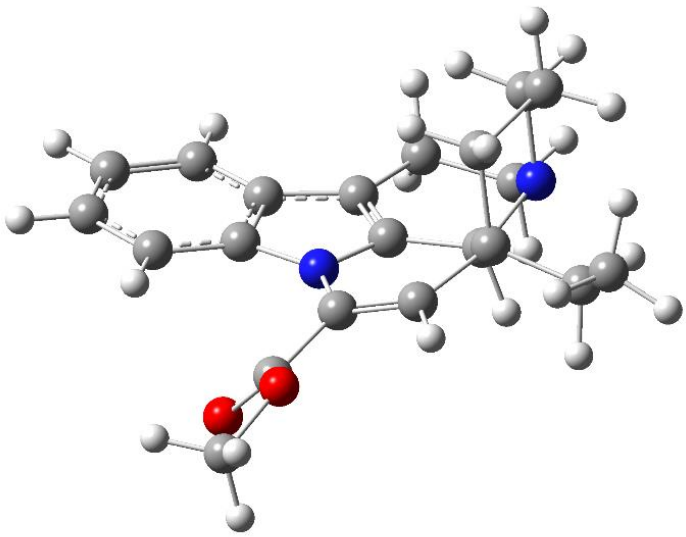
H	-1.35129200	3.55650600	-1.83921800
H	1.38317100	4.07872600	2.32891500
H	-1.41913100	0.86329200	-0.95142300
H	0.74615300	0.04685600	3.27140000
H	0.77483300	1.73554100	3.71174100
H	-0.48712100	-1.25213300	1.92800800
H	-0.06170200	-2.83243400	0.11448000
H	-0.13705900	-1.54255200	-1.08260400
H	3.01122000	0.61124600	3.80207700
H	2.94239600	2.12311500	2.90638400
H	3.84554000	-1.27193800	2.78400200
H	4.32190500	-1.22282500	1.08110200
H	1.71985700	-2.45595200	-1.94211300
H	1.65421000	-4.37103800	-0.57997500
H	3.44206900	-5.06720300	0.93978500
H	4.32026100	-3.56300900	0.64316600
H	2.91529300	-3.41625000	2.74024000
H	1.49033800	-3.80916500	1.79429500
H	3.97019900	4.28197600	0.06494500
H	4.98268800	2.97984100	-0.59445600
H	4.21386600	-4.28310200	-1.71956700
H	-2.66255500	-0.74856600	2.44019300
H	-2.89148100	0.56650200	1.26815700
H	2.92976500	2.06372000	-1.78056500
H	3.36090600	3.69579100	-2.32395500
H	2.01187500	3.47160200	-1.19754400
H	-4.36983000	-2.17596600	2.91627300
H	-6.61300200	-3.12493300	2.49224300
H	-7.81508500	-2.54615600	0.39147300
H	-6.76608500	-1.02813000	-1.24467400
H	5.05200500	-0.90081600	-3.70421000
H	4.07609700	0.59314200	-3.74670000
H	5.15154200	0.26666900	-2.35289000

Optimized Structure for Apovincamine

Zero-point correction = 0.419998 (Hartree/Particle)
Thermal correction to Energy = 0.440552
Thermal correction to Enthalpy = 0.441497
Thermal correction to Gibbs Free Energy = 0.372267
Sum of electronic and zero-point Energies = -1074.093370
Sum of electronic and thermal Energies = -1074.072816
Sum of electronic and thermal Enthalpies = -1074.071872
Sum of electronic and thermal Free Energies = -1074.141101

0 1

C	3.87472400	-2.63756000	0.63389900
C	4.16345800	-1.27855800	0.83706700
C	3.22366300	-0.28919200	0.58396100
C	1.97105500	-0.68831800	0.11474100
C	1.65311400	-2.06136100	-0.06876400
C	2.62542100	-3.03559400	0.18554600
N	0.82734700	0.04306500	-0.20336600
C	0.51617700	1.41145900	-0.12785900
C	-0.76265900	1.80620300	-0.04283900
C	-1.93169800	0.84932200	0.02617100
C	-1.58031600	-0.41738800	-0.79469400
C	-0.17666300	-0.85566700	-0.52315200
N	-2.49330600	-1.55201800	-0.56822900
C	-1.99603000	-2.73248200	-1.28971700
C	-0.64187200	-3.28292600	-0.77779500
C	0.27320600	-2.13353600	-0.48289600
C	1.60940500	2.39143100	-0.38782000
O	2.58191200	2.15110800	-1.05749400
C	-2.72181300	-1.86359800	0.84725200
C	-3.20370400	-0.64280500	1.61724800
C	-2.15817400	0.46167500	1.50355000
C	-3.17759300	1.50562000	-0.60900700
O	1.36674200	3.57679100	0.17090900
C	2.32442000	4.60460000	-0.11790400
C	-3.83146500	2.60494000	0.22298200
H	-1.67234400	-0.14629100	-1.85506500
H	4.63731300	-3.38027200	0.83789500
H	5.14363000	-0.99042900	1.19923800
H	3.46731300	0.75134900	0.74723500
H	2.39492600	-4.08593300	0.04252700
H	-0.96327100	2.87123300	-0.04907100
H	-2.75905700	-3.51262500	-1.23219400
H	-1.88987700	-2.45018000	-2.34128700
H	-0.78382900	-3.89736300	0.11834800
H	-0.21877700	-3.94152200	-1.54216400
H	-1.80921400	-2.23746800	1.33825000
H	-3.46493700	-2.66534400	0.88196800
H	-4.16876500	-0.30653000	1.22563100
H	-3.35018800	-0.91523900	2.66548800
H	-1.21091800	0.09780500	1.91922500
H	-2.43725500	1.34770400	2.07797100
H	-2.87363200	1.91105500	-1.58007200
H	-3.91023900	0.72230100	-0.81941600
H	1.97679800	5.48631200	0.41418000



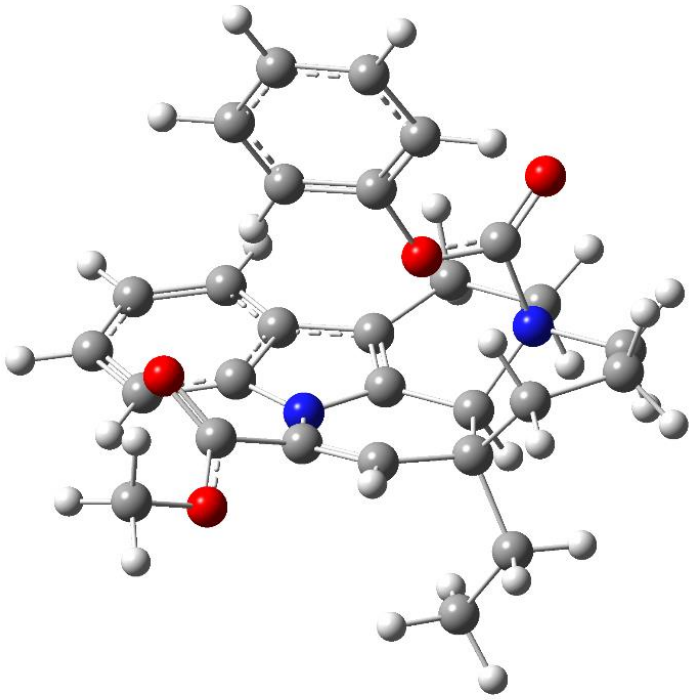
H	3.31232300	4.31036800	0.23691700
H	2.36041000	4.79674700	-1.19062700
H	-3.11114500	3.36473200	0.53976300
H	-4.60494000	3.10907900	-0.36071900
H	-4.30778100	2.20240000	1.11999900

Optimized Structure for V-Int-1A (structure 35)

Zero-point correction = 0.529401 (Hartree/Particle)
Thermal correction to Energy = 0.557823
Thermal correction to Enthalpy = 0.558767
Thermal correction to Gibbs Free Energy = 0.470671
Sum of electronic and zero-point Energies = -1493.963564
Sum of electronic and thermal Energies = -1493.935142
Sum of electronic and thermal Enthalpies = -1493.934198
Sum of electronic and thermal Free Energies = -1494.022294

1 1

C	3.62612900	-0.40534600	3.35741800
C	4.19890300	-0.74904900	2.12121500
C	3.42140900	-1.03411800	1.01024900
C	2.03430000	-0.95513400	1.15381900
C	1.44315600	-0.65869700	2.40706400
C	2.25215300	-0.36784900	3.51255500
N	0.99495300	-1.20524100	0.24588300
C	0.94244400	-1.14950700	-1.15935500
C	-0.21414300	-1.26274200	-1.82205000
C	-1.57431000	-1.47012500	-1.20996800
C	-1.51981300	-1.35329200	0.33888400
C	-0.18785900	-1.14239000	0.96004000
N	-2.45780300	-0.31597700	0.95797300
C	-2.47503500	-0.55858500	2.47309500
C	-1.11004400	-0.34282800	3.13399800
C	0.01625200	-0.77597500	2.24576000
C	2.15138500	-0.69123200	-1.91560300
O	2.87486400	0.19642600	-1.54550200
C	-3.84698200	-0.56462500	0.40573600
C	-3.90646800	-0.32809400	-1.10688000
C	-2.54885000	-0.43929900	-1.82619500
C	-2.06864700	-2.89856500	-1.56550500
C	-2.10114900	1.13385200	0.73698900
O	-2.82178600	1.97951500	1.14958000
O	-0.97242700	1.22245000	0.08651000
C	-0.41136600	2.47224300	-0.25841400
C	-1.17876500	3.47932700	-0.81887100
C	-0.52797100	4.64918100	-1.20045900
C	0.84661000	4.78241300	-1.02541700
C	1.58746100	3.74225900	-0.47097000
C	0.95735000	2.56567500	-0.08037000
O	2.27886100	-1.33029800	-3.07343900
C	3.32143900	-0.84841600	-3.93768800
C	-1.15274500	-4.02689300	-1.09889900
H	-1.94240000	-2.27451600	0.74329700
H	4.27121600	-0.18646800	4.20008400
H	5.27764100	-0.79878700	2.03143900
H	3.88678200	-1.30881100	0.07487300
H	1.80487600	-0.13353000	4.47215400
H	-0.18633000	-1.18426100	-2.90343400
H	-3.22797400	0.11528100	2.87806500
H	-2.81973000	-1.58702500	2.57827100
H	-0.97798900	0.71749600	3.37644600
H	-1.12933500	-0.88034700	4.08567600



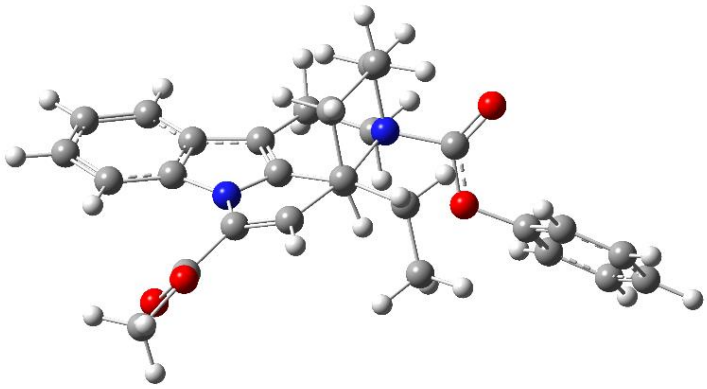
H	-4.52747200	0.08273200	0.95545200
H	-4.05816600	-1.60226800	0.66575400
H	-4.61338200	-1.05385200	-1.51129100
H	-4.32340600	0.66132900	-1.30245800
H	-2.06545600	0.53694100	-1.86235300
H	-2.72070000	-0.72344900	-2.86610200
H	-3.07086700	-3.02314700	-1.13882800
H	-2.17771900	-2.94728600	-2.65245000
H	-2.24632200	3.36179700	-0.95525500
H	-1.10268100	5.45598400	-1.63885600
H	1.34236500	5.69719100	-1.32725300
H	2.65884100	3.83890600	-0.34395200
H	1.50995500	1.73134200	0.33802600
H	3.15444100	0.20192000	-4.17722800
H	4.29239500	-0.96916600	-3.45752800
H	3.26210600	-1.45988200	-4.83392300
H	-1.59496600	-4.99383500	-1.34607200
H	-0.17895500	-3.96917700	-1.58956600
H	-0.98199800	-4.01446100	-0.01823900

Optimized Structure for V-Int-1B (structure 36)

Zero-point correction = 0.530673 (Hartree/Particle)
Thermal correction to Energy = 0.558364
Thermal correction to Enthalpy = 0.559308
Thermal correction to Gibbs Free Energy = 0.474156
Sum of electronic and zero-point Energies = -1493.978896
Sum of electronic and thermal Energies = -1493.951205
Sum of electronic and thermal Enthalpies = -1493.950260
Sum of electronic and thermal Free Energies = -1494.035413

1 1

C	5.11349700	-2.91812800	-0.73311900
C	5.58936600	-1.60111000	-0.61506100
C	4.73047500	-0.52506700	-0.45921900
C	3.36057400	-0.79533800	-0.42322500
C	2.86741400	-2.11938700	-0.51240600
C	3.75762400	-3.18717600	-0.67872400
N	2.26103700	0.04631100	-0.24901200
C	2.17034700	1.42315900	0.00517400
C	1.09111500	1.91542900	0.62045800
C	-0.04867200	1.05471000	1.12408000
C	-0.19832400	-0.13245300	0.13370200
C	1.12865700	-0.74551400	-0.18120200
N	-1.08376100	-1.27725600	0.66938300
C	-0.98507700	-2.48485300	-0.29029800
C	0.39833300	-3.12138300	-0.30374000
C	1.43666900	-2.05261600	-0.36159200
C	3.18583900	2.32205900	-0.62334700
O	3.74882300	2.06468300	-1.65545700
C	-0.68225100	-1.70159500	2.07247800
C	-0.63475600	-0.52924600	3.03360200
C	0.34056300	0.52748400	2.52563000
C	-1.31868500	1.93079400	1.20921800
C	-2.55095900	-0.92826000	0.65632100
O	-3.26549100	-1.20306900	1.55848900
O	-2.84385400	-0.38525700	-0.50330400
C	-4.19370200	-0.04259100	-0.76954700
C	-4.82534900	0.92144500	-0.00447900
C	-6.12860700	1.26973000	-0.34415900
C	-6.76050800	0.66068300	-1.42528000
C	-6.09375100	-0.30307300	-2.17522100
C	-4.79015800	-0.66593300	-1.84894600
O	3.34960200	3.44350700	0.06804700
C	4.24028200	4.41119400	-0.51157000
C	-1.73167100	2.63265300	-0.08340000
H	-0.68446600	0.20586900	-0.78239300
H	5.82071900	-3.72921600	-0.85898100
H	6.65689800	-1.41789800	-0.64606700
H	5.12131300	0.47826100	-0.36762200
H	3.38742600	-4.20372400	-0.75434500
H	1.02287700	2.98556900	0.77203500
H	-1.23844300	-2.08793400	-1.27234400
H	-1.75178000	-3.18930600	0.03357600
H	0.43193000	-3.75859800	-1.19193300
H	0.54566000	-3.77841700	0.55811800



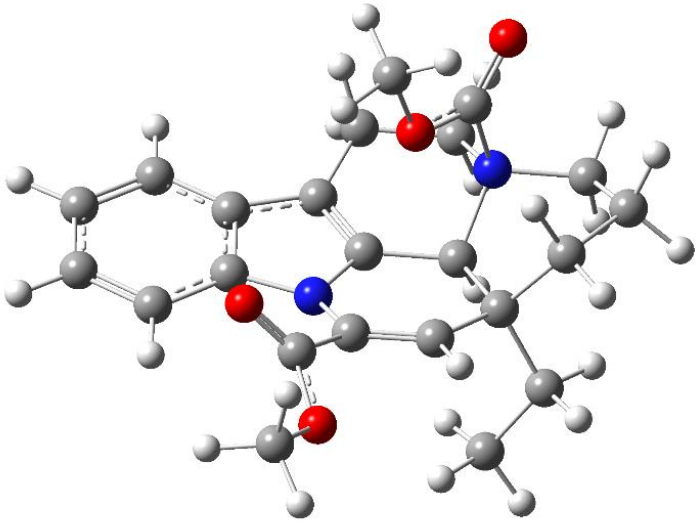
H	-1.38815700	-2.47365400	2.37128600
H	0.31002900	-2.13616500	1.97548200
H	-1.63039000	-0.11789700	3.20565600
H	-0.28685500	-0.92327100	3.99072000
H	1.34472200	0.09309800	2.47986100
H	0.38504200	1.37572600	3.21141600
H	-2.15769400	1.35344000	1.60740600
H	-1.10857300	2.68769500	1.97193700
H	-4.31596400	1.38523400	0.83143500
H	-6.64765500	2.02149600	0.23793200
H	-7.77482400	0.93944600	-1.68405400
H	-6.58389700	-0.77609600	-3.01738900
H	-4.24618200	-1.41055600	-2.41701100
H	3.86698600	4.73201600	-1.48411200
H	4.25635300	5.24462900	0.18526800
H	5.23763400	3.98510800	-0.61944900
H	-0.92899800	3.26761500	-0.46521900
H	-2.59461800	3.27487600	0.10357600
H	-2.01236900	1.93665400	-0.87634800

Optimized Structure for V-Int-1C

Zero-point correction = 0.476817 (Hartree/Particle)
Thermal correction to Energy = 0.502366
Thermal correction to Enthalpy= 0.503310
Thermal correction to Gibbs Free Energy = 0.422227
Sum of electronic and zero-point Energies = -1302.304052
Sum of electronic and thermal Energies = -1302.278504
Sum of electronic and thermal Enthalpies = -1302.277559
Sum of electronic and thermal Free Energies = -1302.358642

1 1

C	3.60303900	-3.30794100	-0.43537900
C	4.22215700	-2.04745200	-0.39030700
C	3.48762800	-0.87273100	-0.41899000
C	2.09733200	-0.98177700	-0.48054000
C	1.46251900	-2.24433900	-0.57459700
C	2.22752900	-3.41625400	-0.53759700
N	1.09911100	-0.00116900	-0.55357300
C	1.07215900	1.33311500	-0.11115600
C	-0.05812900	2.04711000	-0.10164900
C	-1.41025100	1.57246900	-0.56325900
C	-1.39835000	0.05108200	-0.88467700
C	-0.09949800	-0.65915000	-0.76396900
N	-2.43030100	-0.77855800	-0.11934400
C	-2.45176200	-2.18016700	-0.74210500
C	-1.12058300	-2.92524900	-0.60868800
C	0.05208300	-2.00246800	-0.74200200
C	2.26822000	1.88742600	0.60173100
O	2.87843400	1.28475500	1.44613300
C	-3.78256200	-0.12808300	-0.33238000
C	-3.83558600	1.27338800	0.28751300
C	-2.45249500	1.90237800	0.52886600
C	-1.78650800	2.34227300	-1.85816100
C	-2.19995300	-0.94132200	1.36454500
O	-3.06523700	-1.40047100	2.03790700
O	-1.01465500	-0.54145000	1.70816100
C	-0.68807600	-0.63826400	3.11824000
O	2.51955300	3.14139400	0.24403900
C	3.56786600	3.79806300	0.97672200
C	-0.79046800	2.18985900	-3.00424600
H	-1.75751100	-0.06596500	-1.90896800
H	4.21466200	-4.20202800	-0.40920200
H	5.30286000	-1.98848700	-0.33715200
H	3.98769600	0.08516500	-0.39870200
H	1.74786500	-4.38641400	-0.60464400
H	-0.01225400	3.06479300	0.27091800
H	-3.26426400	-2.71722600	-0.25461300
H	-2.71187900	-2.00821200	-1.78541300
H	-1.06753900	-3.41952300	0.36863200
H	-1.12601700	-3.71983800	-1.35945700
H	-3.89887400	-0.10100800	-1.41682600
H	-4.52932700	-0.79803200	0.08769300
H	-4.42719400	1.89923200	-0.38147600
H	-4.36908800	1.23054000	1.23781600
H	-2.06723300	1.59829300	1.50368500



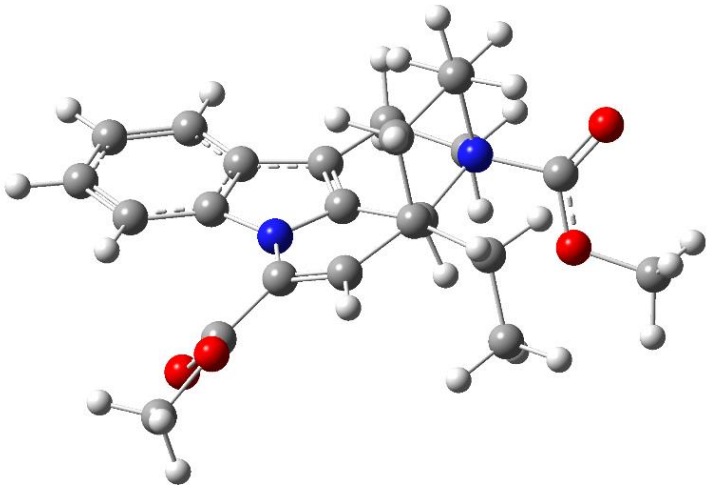
H	-2.55704200	2.98791500	0.57763000
H	-2.77961200	2.00396200	-2.17656000
H	-1.88017900	3.39995200	-1.59533100
H	-1.38250100	-0.02482800	3.69115200
H	0.32750800	-0.26131800	3.19408400
H	-0.74446000	-1.67994200	3.42971500
H	3.62156300	4.80395700	0.56933500
H	4.51211800	3.27432400	0.82819400
H	3.32351900	3.82633100	2.03866000
H	0.17952400	2.61728100	-2.74251900
H	-1.15743400	2.70948900	-3.89135400
H	-0.62919700	1.14405900	-3.28230400

Optimized Structure for V-Int-1D

Zero-point correction = 0.478378 (Hartree/Particle)
Thermal correction to Energy = 0.503067
Thermal correction to Enthalpy = 0.504011
Thermal correction to Gibbs Free Energy = 0.426462
Sum of electronic and zero-point Energies = -1302.321193
Sum of electronic and thermal Energies = -1302.296504
Sum of electronic and thermal Enthalpies = -1302.295560
Sum of electronic and thermal Free Energies = -1302.373110

1 1

C	3.97237900	-3.34654800	-0.05925700
C	4.56362100	-2.08939800	0.15296500
C	3.81936400	-0.92059000	0.14129900
C	2.44718700	-1.03461300	-0.09178600
C	1.83208000	-2.29648100	-0.27851800
C	2.60992000	-3.46067800	-0.27093900
N	1.43865300	-0.07091800	-0.13329600
C	1.45499200	1.31553200	0.08541100
C	0.33827400	1.94131300	0.47158300
C	-0.97104700	1.22787500	0.73832600
C	-1.04831900	0.03691600	-0.25488600
C	0.23298100	-0.72899500	-0.29170500
N	-2.14876900	-0.98245100	0.09109200
C	-2.00935500	-2.21736000	-0.82444200
C	-0.73257400	-3.00631700	-0.56018400
C	0.41613600	-2.06577900	-0.41084700
C	2.66108300	2.08024300	-0.35577000
O	3.39027600	1.71181400	-1.23954600
C	-2.08911600	-1.41546500	1.54647600
C	-2.10081100	-0.23430400	2.49830600
C	-0.93614300	0.70212800	2.19284000
C	-2.12417800	2.24038900	0.54464000
C	-3.52708000	-0.45334900	-0.21687800
O	-4.44318500	-0.64534500	0.51341300
O	-3.51649600	0.14225100	-1.37385600
C	-4.77895300	0.71682700	-1.79795700
O	2.79194900	3.22636000	0.30200400
C	3.85724400	4.08180700	-0.14427500
C	-2.15979800	2.94928400	-0.80908500
H	-1.29231800	0.40510500	-1.25179500
H	4.59307700	-4.23460100	-0.04730100
H	5.63076000	-2.02882900	0.33164700
H	4.29478700	0.03529600	0.31013100
H	2.14787100	-4.43051400	-0.41905800
H	0.36355300	3.01646900	0.59719100
H	-2.90143000	-2.82033600	-0.64844600
H	-2.02205500	-1.82397000	-1.84060900
H	-0.83834400	-3.64879200	0.31874400
H	-0.59729300	-3.66978800	-1.41870300
H	-2.92686500	-2.09350600	1.69601500
H	-1.15611200	-1.96400500	1.65370400
H	-3.06052800	0.28401100	2.47134500
H	-1.99059200	-0.64200200	3.50528800
H	0.00478500	0.16592200	2.35466200



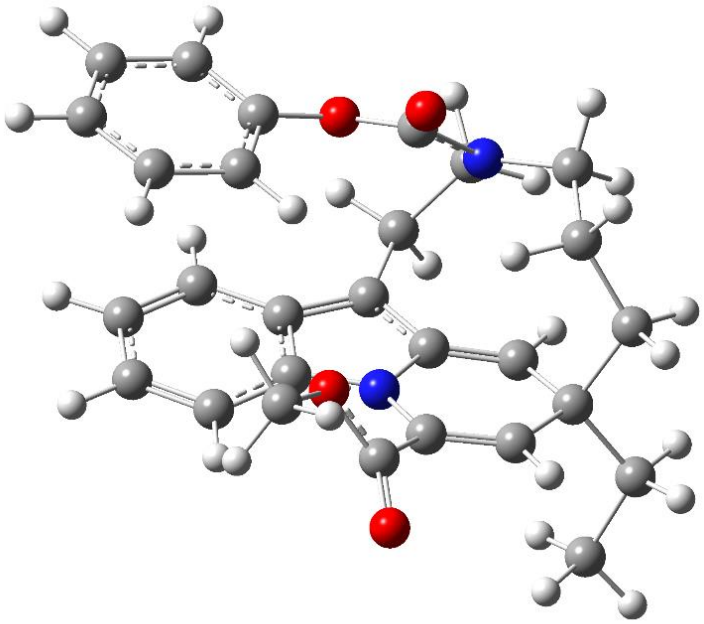
H	-0.94113000	1.55991800	2.86856700
H	-3.09427800	1.77383400	0.74072100
H	-2.00497800	2.98896100	1.33456300
H	-5.10963100	1.44335800	-1.05656700
H	-5.51479000	-0.07739700	-1.91386300
H	-4.56663700	1.19532600	-2.74903800
H	3.80116300	4.96749000	0.48262300
H	3.71381700	4.34349300	-1.19276300
H	4.81773100	3.58314600	-0.01491200
H	-2.27287300	2.25629600	-1.64481600
H	-1.25136600	3.53106500	-0.97961500
H	-3.00320100	3.64237700	-0.84031200

Optimized Structure for V-Int-2A (structure 37)

Zero-point correction = 0.526156 (Hartree/Particle)
Thermal correction to Energy = 0.555201
Thermal correction to Enthalpy = 0.556145
Thermal correction to Gibbs Free Energy = 0.467884
Sum of electronic and zero-point Energies = -1493.959514
Sum of electronic and thermal Energies = -1493.930469
Sum of electronic and thermal Enthalpies = -1493.929525
Sum of electronic and thermal Free Energies = -1494.017786

1 1

C	-2.85675000	1.29963800	2.31226900
C	-2.21372900	2.47175100	1.80586000
C	-0.95819200	2.46463500	1.25244000
C	-0.29199200	1.22369600	1.19391900
C	-0.89768400	0.04146700	1.75957100
C	-2.21602700	0.09890100	2.29931000
N	0.92037500	0.88457900	0.68793400
C	1.88168900	1.58231400	-0.06814600
C	3.05206400	1.00859000	-0.36169000
C	3.43213400	-0.39282900	0.02252500
C	2.37348100	-1.03667500	0.82936400
C	1.17763500	-0.46082300	1.03993000
N	0.26736400	-2.68256000	-0.66091200
C	0.13684400	-3.35508400	0.63535100
C	-0.19898500	-2.45809300	1.87666600
C	-0.00209500	-1.00750300	1.63703600
C	1.51233100	2.86418600	-0.74942300
O	2.22799700	3.82671500	-0.80693200
C	1.45671900	-2.87633500	-1.50905200
C	2.17715200	-1.58346900	-1.96987200
C	3.51623400	-1.27280900	-1.28038800
C	4.80297300	-0.42443400	0.73644000
C	-0.79241500	-2.08834800	-1.25570400
O	-1.85290600	-2.03408100	-0.39434300
O	-0.81832400	-1.65963800	-2.38551100
C	-2.87114800	-1.11509700	-0.59490200
C	-2.63102800	0.17304100	-1.06111500
C	-3.68975400	1.07392600	-1.10041700
C	-4.96314700	0.69706200	-0.68106500
C	-5.18308400	-0.59919400	-0.22351500
C	-4.13552300	-1.51245500	-0.17951400
O	0.32930900	2.75428200	-1.34362700
C	-0.12417400	3.91288400	-2.06568100
C	4.84309100	0.41396700	2.00881000
H	2.54072900	-2.05154400	1.18326200
H	-3.85651800	1.38669900	2.71846400
H	-2.74540900	3.41478300	1.86849500
H	-0.50392300	3.38043500	0.90219800
H	-2.67361100	-0.79778600	2.69991400
H	3.74979000	1.56109700	-0.98269300
H	-0.63422200	-4.12495600	0.57309300
H	1.08500800	-3.86074300	0.80569200
H	0.43990700	-2.78117300	2.70485000
H	-1.23232900	-2.62305500	2.17841000



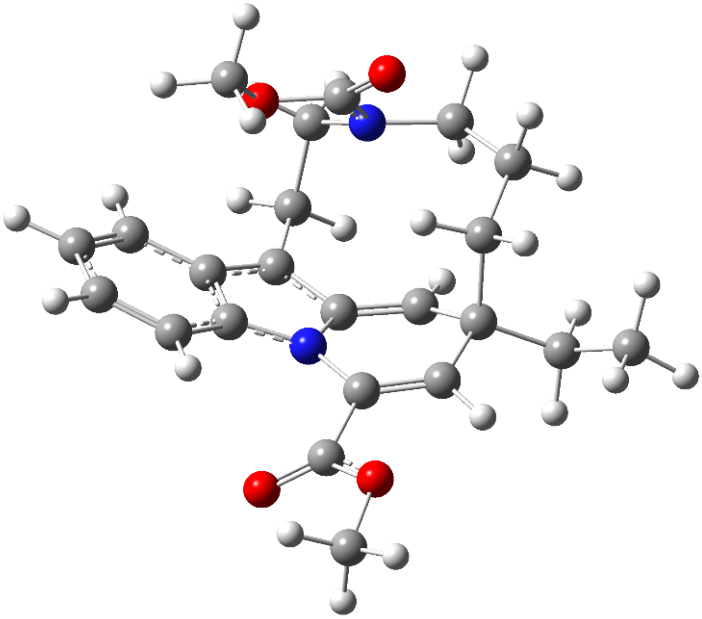
H	2.14256200	-3.51118700	-0.94660900
H	1.14749700	-3.43886100	-2.39263300
H	1.49726100	-0.73085600	-1.88365600
H	2.37376300	-1.69098300	-3.03789000
H	4.03176500	-2.20138000	-1.01568900
H	4.17173500	-0.72774900	-1.96524600
H	5.03868100	-1.46888200	0.96076800
H	5.55190000	-0.07100500	0.02140900
H	-1.63961900	0.47136500	-1.37930900
H	-3.51365900	2.08252300	-1.45651300
H	-5.77987700	1.40830400	-0.71598900
H	-6.17141600	-0.90420300	0.09997600
H	-4.28077000	-2.52476800	0.17909500
H	-0.20894600	4.76627300	-1.39204600
H	0.57211400	4.14384200	-2.87131400
H	-1.09623600	3.64230100	-2.46844700
H	4.09209400	0.07715900	2.72953100
H	5.82155600	0.33486100	2.48592000
H	4.65767700	1.46966900	1.79705300

Optimized Structure for V-Int-2B

Zero-point correction = 0.474931 (Hartree/Particle)
Thermal correction to Energy = 0.500828
Thermal correction to Enthalpy = 0.501772
Thermal correction to Gibbs Free Energy = 0.420535
Sum of electronic and zero-point Energies = -1302.294600
Sum of electronic and thermal Energies = -1302.268704
Sum of electronic and thermal Enthalpies = -1302.267759
Sum of electronic and thermal Free Energies = -1302.348997

1 1

C	-1.72677900	-3.95697200	-0.36358500
C	-0.47687800	-4.03782500	0.32065600
C	0.47148400	-3.04554600	0.27900900
C	0.16441500	-1.89965600	-0.47938400
C	-1.09420900	-1.79633300	-1.16853000
C	-2.04455900	-2.85139700	-1.09453300
N	0.83960200	-0.72788200	-0.63808900
C	2.06758500	-0.24389900	-0.13632300
C	2.25386500	1.07781000	-0.04060800
C	1.19471200	2.07967400	-0.42498000
C	0.25262100	1.47318800	-1.39182200
C	0.02824400	0.14312400	-1.38810300
N	-2.50672600	1.25431800	0.08984300
C	-3.24670100	0.64770200	-1.01822200
C	-2.37966400	0.19155900	-2.22816000
C	-1.18245000	-0.52879600	-1.73264200
C	3.17944800	-1.22360000	0.03920100
O	3.21689900	-2.28508600	-0.52843600
C	-2.21491800	2.69207700	-0.00457600
C	-0.94673400	3.21246600	0.71332700
C	0.28014300	2.30321900	0.85052700
C	1.79831500	3.39481100	-0.95754400
C	-2.50730400	0.67444300	1.32604600
O	-2.78298700	-0.64097200	1.27198600
O	-2.25263200	1.25720400	2.36007000
C	-2.72135200	-1.33694800	2.52050100
O	4.12138500	-0.76547100	0.85076600
C	5.28250800	-1.60241300	0.99220300
C	2.50367800	4.24542800	0.09368700
H	-2.42137000	-4.78379100	-0.28450500
H	-0.26771100	-4.92647400	0.90565700
H	1.40229300	-3.14519500	0.81671000
H	-2.99300400	-2.76055100	-1.61099500
H	3.21720300	1.44072600	0.29630400
H	-0.37252100	2.12014300	-1.99642000
H	-3.78437000	-0.21555600	-0.63698300
H	-3.98071700	1.37057900	-1.38400700
H	-2.08553400	1.04997400	-2.83384600
H	-3.00046700	-0.45731700	-2.84875200
H	-2.16297800	2.90753100	-1.07343500
H	-3.06843500	3.26053900	0.38260400
H	-1.22708400	3.47345800	1.73330800
H	-0.66711200	4.14867600	0.21965800
H	-0.01925200	1.31863400	1.21359200



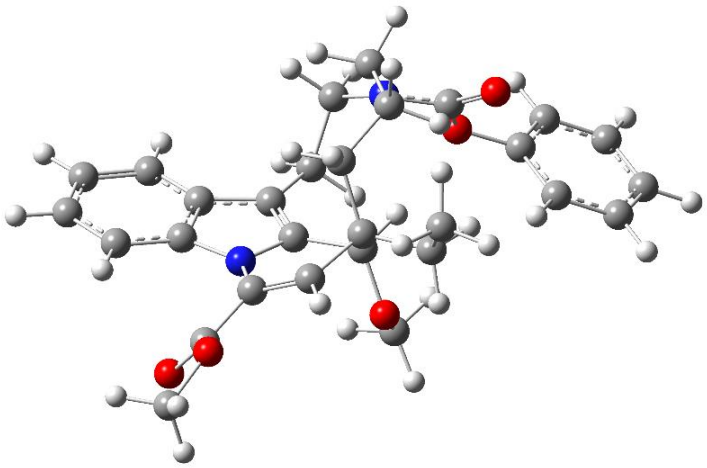
H	0.93944800	2.72914500	1.61076500
H	2.49416800	3.14061700	-1.76236100
H	0.99266200	3.97655500	-1.41504400
H	-2.99334000	-2.36538300	2.29333100
H	-1.71076600	-1.29471400	2.92874400
H	-3.42435200	-0.90891700	3.23522400
H	5.93946600	-1.07402000	1.67734200
H	4.99687300	-2.56979400	1.40471100
H	5.76511700	-1.73898600	0.02462600
H	3.00688800	5.08430700	-0.39049000
H	1.79847400	4.65651700	0.81882200
H	3.26216400	3.68013500	0.64121800

Optimized Structure for Compound 68

Zero-point correction = 0.570325 (Hartree/Particle)
Thermal correction to Energy = 0.602397
Thermal correction to Enthalpy = 0.603341
Thermal correction to Gibbs Free Energy = 0.505916
Sum of electronic and zero-point Energies = -1609.244758
Sum of electronic and thermal Energies = -1609.212686
Sum of electronic and thermal Enthalpies = -1609.211742
Sum of electronic and thermal Free Energies = -1609.309167

0 1

C	-4.40872400	3.37965600	0.12231500
C	-4.18946600	2.02109500	-0.04484300
C	-2.87045600	1.59760700	-0.23063900
C	-1.79062600	2.51251900	-0.21743400
C	-3.35079700	4.30532400	0.10588600
C	-2.04331500	3.88157100	-0.06031900
N	-2.32901100	0.32984900	-0.39662600
C	-0.93939600	0.44517300	-0.43049900
C	-0.56989600	1.75312000	-0.34931300
C	0.82266300	2.30183800	-0.34230900
C	1.46319000	2.32550700	1.05161000
N	1.79280900	0.99422100	1.58554600
C	1.15095700	0.48889100	2.80981800
C	-0.13683900	-0.81948700	-0.40891400
C	-0.76684200	-1.77274200	0.62952000
C	-0.76631400	-1.12555000	2.04296000
C	0.59646900	-0.94035000	2.73841900
C	2.94297300	0.37873000	1.22627500
O	3.43470500	-0.58319000	1.77395600
O	3.50701100	0.97913900	0.13304000
C	4.61735900	0.37921100	-0.44668300
C	4.55319700	-0.92078300	-0.93243000
C	5.66576700	-1.45370900	-1.57303200
C	6.82152700	-0.69170900	-1.73046600
C	6.86413900	0.61039100	-1.24257900
C	5.75820800	1.15301200	-0.59362300
C	-2.93461400	-0.93324900	-0.24918700
C	-2.21398700	-1.95610000	0.22528200
C	-0.02700400	-3.12386700	0.60149100
O	-0.12704600	-1.47743800	-1.66523500
C	0.57390000	-0.75738800	-2.66015900
C	-4.27731600	-1.13007900	-0.86114000
O	-4.72048600	-0.44537900	-1.74850200
O	-4.91732900	-2.17799900	-0.34113200
C	-6.16669100	-2.51093900	-0.96033800
C	-0.40218800	-4.07355100	1.73623900
H	0.89280100	-0.58281900	-0.11811200
H	-5.42266300	3.73417700	0.26764600
H	-5.01692800	1.32527300	-0.03009700
H	-3.56529900	5.36015600	0.23227900
H	-1.22514900	4.59426100	-0.05885400
H	1.46449900	1.73459500	-1.01934000
H	0.80482100	3.33052400	-0.71451300
H	2.37185100	2.92973000	1.02087000



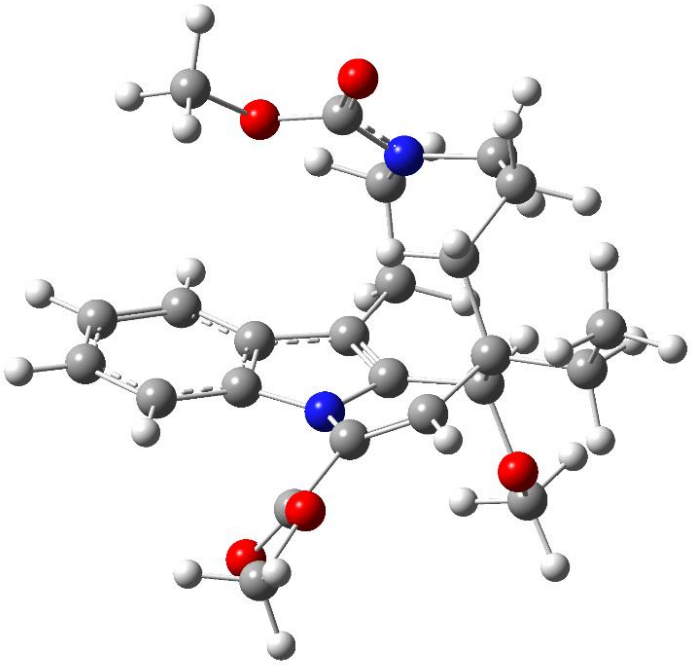
H	0.77835400	2.79184600	1.76087800
H	0.34329400	1.18107100	3.05028700
H	1.88388200	0.53321300	3.62175700
H	-1.29116800	-0.16614100	1.99236300
H	-1.39049000	-1.76676100	2.67000300
H	1.35601500	-1.59865300	2.31562900
H	0.48385900	-1.25499100	3.78014300
H	3.65018200	-1.50505700	-0.79981400
H	5.62755000	-2.46855200	-1.95127000
H	7.68479400	-1.11331400	-2.23151200
H	7.75977200	1.20853000	-1.36333200
H	5.76875800	2.16390700	-0.20381100
H	-2.66525800	-2.94030900	0.26466600
H	-0.23008700	-3.59771600	-0.36128400
H	1.05109600	-2.93323200	0.62395300
H	0.57165900	-1.37066100	-3.56118400
H	0.09089100	0.20076300	-2.88075200
H	1.61229700	-0.57389000	-2.35535200
H	-6.86942100	-1.68284700	-0.86470800
H	-6.01542700	-2.74471700	-2.01458000
H	-6.53345900	-3.38374800	-0.42637700
H	0.06629000	-5.04810900	1.58266400
H	-0.07086500	-3.69732800	2.70711500
H	-1.48314100	-4.23360900	1.78972400

Optimized Structure for Compound 27

Zero-point correction = 0.518736 (Hartree/Particle)
Thermal correction to Energy = 0.547523
Thermal correction to Enthalpy = 0.548467
Thermal correction to Gibbs Free Energy = 0.461099
Sum of electronic and zero-point Energies = -1417.579822
Sum of electronic and thermal Energies = -1417.551036
Sum of electronic and thermal Enthalpies = -1417.550091
Sum of electronic and thermal Free Energies = -1417.637459

0 1

C	-0.62821800	4.15304600	-0.09199400
C	0.36870900	3.19241000	-0.16398500
C	0.13253200	1.96643200	0.46508800
C	-1.08718500	1.70270300	1.13150200
C	-1.83486500	3.91552700	0.58931000
C	-2.07203100	2.69590500	1.19921300
N	0.90381500	0.81131000	0.54422200
C	0.15316100	-0.16855300	1.19487300
C	-1.04978700	0.33328900	1.58433900
C	-2.17758300	-0.44862000	2.17316000
C	-3.28157100	-0.71636600	1.13184600
N	-2.77281100	-1.20553100	-0.14946600
C	-2.28123500	-2.58523300	-0.18878900
C	0.69922000	-1.56296800	1.21303100
C	1.21024100	-1.90352500	-0.20188000
C	0.04244400	-1.83171500	-1.22285200
C	-1.07754000	-2.88135700	-1.10696900
C	-2.97446000	-0.53650500	-1.31107200
O	-2.76835500	-0.99236100	-2.42153100
O	-3.41766600	0.72144600	-1.11432700
C	-3.48014700	1.54110900	-2.28087200
C	2.03967900	0.44598600	-0.20548600
C	2.21267800	-0.83035800	-0.57032800
C	1.89525900	-3.28396000	-0.18636200
O	1.77831700	-1.70606300	2.12249500
C	1.37946400	-1.61935800	3.47581700
C	3.11725900	1.46160300	-0.35998400
O	3.26674900	2.40242000	0.37876600
O	3.92212900	1.19086600	-1.38801000
C	5.04740000	2.06592100	-1.53972200
C	2.24441200	-3.83338000	-1.56764900
H	-0.46909100	5.11164400	-0.57254400
H	1.29075200	3.39775800	-0.68969400
H	-2.58692000	4.69524200	0.62749800
H	-3.01059500	2.50290700	1.70826600
H	-1.80227200	-1.39103700	2.57862400
H	-2.63713200	0.08800900	3.00898000
H	-3.98461500	-1.45508700	1.53166200
H	-3.83352900	0.20004600	0.94573100
H	-2.03561500	-2.83418600	0.84463300
H	-3.09901000	-3.25382800	-0.48508000
H	-0.09600000	-2.26292300	1.49250400
H	-0.38654900	-0.82654800	-1.19759800
H	0.48698800	-1.93217100	-2.21585400



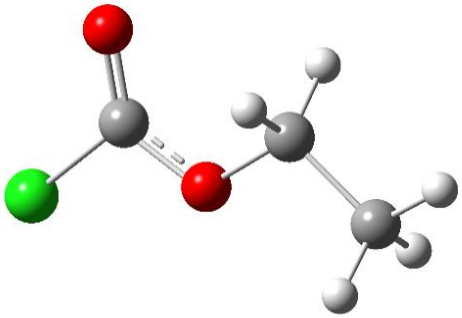
H	-0.66885900	-3.84038800	-0.77261100
H	-1.46265700	-3.04399500	-2.11213700
H	-4.15009700	1.10913800	-3.02497600
H	-2.48510800	1.66637200	-2.71077800
H	-3.86210600	2.50173400	-1.94167900
H	3.12494100	-1.10259700	-1.08757500
H	2.80056100	-3.20365600	0.41919100
H	1.24397600	-3.99240400	0.33620200
H	2.27321400	-1.76594200	4.08205800
H	0.64960900	-2.40185900	3.71942400
H	0.94707300	-0.64009700	3.70788200
H	5.59055200	1.69628100	-2.40579100
H	5.67725800	2.03024200	-0.65040100
H	4.70995400	3.08860700	-1.71036000
H	2.83382000	-3.12030500	-2.15138000
H	1.35128500	-4.07806400	-2.14734300
H	2.83674200	-4.74601600	-1.47070200

Optimized Structure for Ethyl Chloroformate

Zero-point correction = 0.081816 (Hartree/Particle)
Thermal correction to Energy = 0.088524
Thermal correction to Enthalpy = 0.089468
Thermal correction to Gibbs Free Energy = 0.050110
Sum of electronic and zero-point Energies = -727.877986
Sum of electronic and thermal Energies = -727.871278
Sum of electronic and thermal Enthalpies = -727.870334
Sum of electronic and thermal Free Energies = -727.909692

0 1

Cl	-2.03671600	-0.63235600	0.00012300
C	-0.61271700	0.41276900	-0.00014600
O	0.46682700	-0.32678600	-0.00004100
O	-0.70203500	1.59616100	-0.00014400
C	1.72901000	0.40446900	-0.00004200
C	2.82873500	-0.62549300	0.00006900
H	1.75007900	1.03599800	-0.88947300
H	1.75001700	1.03612700	0.88929800
H	3.79383300	-0.11536300	0.00006500
H	2.77083800	-1.25602800	0.88872700
H	2.77089900	-1.25615900	-0.88849900

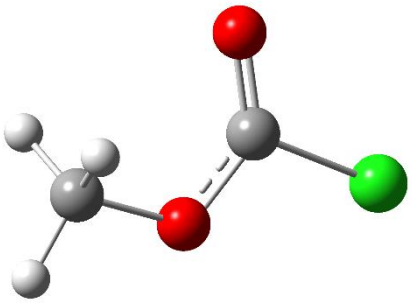


Optimized Structure for Methyl Chloroformate

Zero-point correction = 0.053578 (Hartree/Particle)
Thermal correction to Energy = 0.058946
Thermal correction to Enthalpy = 0.059891
Thermal correction to Gibbs Free Energy = 0.024319
Sum of electronic and zero-point Energies = -688.595575
Sum of electronic and thermal Energies = -688.590207
Sum of electronic and thermal Enthalpies = -688.589263
Sum of electronic and thermal Free Energies = -688.624835

0 1

Cl	1.68708300	-0.30667800	-0.00015000
C	0.03482600	0.30710000	0.00064400
O	-0.80270800	-0.70044800	0.00029000
O	-0.20840300	1.46861600	-0.00011100
C	-2.20051400	-0.33195000	-0.00026300
H	-2.74116200	-1.27361000	-0.00056200
H	-2.42776700	0.24552900	-0.89557400
H	-2.42847200	0.24537300	0.89497100

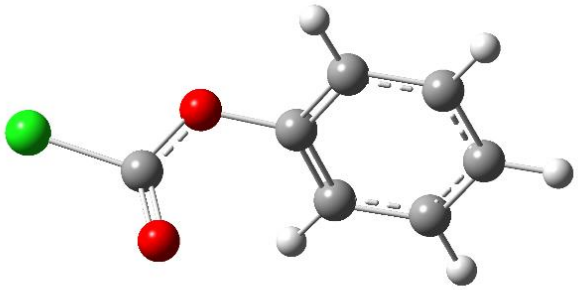


Optimized Structure for Phenyl Chloroformate

Zero-point correction = 0.105835 (Hartree/Particle)
Thermal correction to Energy = 0.114137
Thermal correction to Enthalpy = 0.115081
Thermal correction to Gibbs Free Energy = 0.070681
Sum of electronic and zero-point Energies = -880.254734
Sum of electronic and thermal Energies = -880.246432
Sum of electronic and thermal Enthalpies = -880.245487
Sum of electronic and thermal Free Energies = -880.289888

0 1

Cl	-3.25384000	0.16481500	-0.24480300
C	-1.61729300	-0.15993100	0.30651100
O	-0.76502000	0.36070300	-0.56483100
O	-1.38529800	-0.74970200	1.30451600
C	0.60814500	0.17905300	-0.29819900
C	1.17350300	-1.07339000	-0.46517000
C	2.54108200	-1.21015000	-0.25320200
C	3.30896400	-0.10679200	0.11152100
C	2.71220400	1.14059600	0.26668300
C	1.34359700	1.29325300	0.06156300
H	0.55595000	-1.91651900	-0.75220700
H	3.00554800	-2.18113800	-0.37641200
H	4.37424100	-0.22032200	0.27332400
H	3.30876000	2.00012100	0.54797600
H	0.85211500	2.25216100	0.17325800

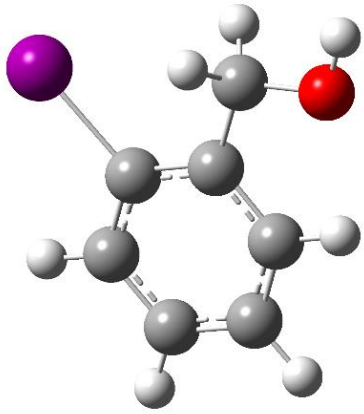


Optimized Structure for 2-Iodobenzyl Alcohol

Zero-point correction = 0.124451 (Hartree/Particle)
Thermal correction to Energy = 0.132945
Thermal correction to Enthalpy = 0.133889
Thermal correction to Gibbs Free Energy = 0.089098
Sum of electronic and zero-point Energies = -7236.504255
Sum of electronic and thermal Energies = -7236.495762
Sum of electronic and thermal Enthalpies = -7236.494817
Sum of electronic and thermal Free Energies = -7236.539608

0 1

C	-0.28525100	-0.54370100	-0.00004900
C	-0.61544300	-1.89451500	-0.00021100
C	-1.95082600	-2.28208800	-0.00023200
C	-2.94907900	-1.31539000	-0.00009400
C	-2.61012300	0.03327000	0.00007900
C	-1.27628200	0.44095100	0.00010800
C	-0.92053000	1.90543500	0.00029100
O	-2.10271100	2.68213700	0.00026800
I	1.74235700	-0.01109300	-0.00003900
H	0.16827400	-2.64207300	-0.00031400
H	-2.20287700	-3.33615400	-0.00035900
H	-3.99277600	-1.60760900	-0.00011900
H	-3.38252000	0.79187300	0.00018300
H	-0.30901900	2.12508900	0.88413100
H	-0.30886900	2.12526400	-0.88339900
H	-1.85025900	3.61068300	0.00046000

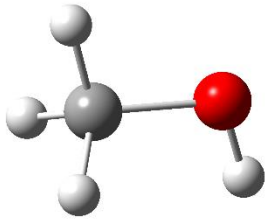


Optimized Structure for Methanol

Zero-point correction = 0.051832 (Hartree/Particle)
Thermal correction to Energy = 0.055120
Thermal correction to Enthalpy = 0.056064
Thermal correction to Gibbs Free Energy = 0.029120
Sum of electronic and zero-point Energies = -115.657849
Sum of electronic and thermal Energies = -115.654560
Sum of electronic and thermal Enthalpies = -115.653616
Sum of electronic and thermal Free Energies = -115.680560

0 1

C	-0.66507200	-0.01995900	0.00000600
O	0.74708100	0.12325600	0.00000800
H	-1.08957000	0.98378600	-0.00135300
H	-1.01827000	-0.54893900	-0.89078900
H	-1.01847800	-0.54668900	0.89205800
H	1.14010200	-0.75445800	-0.00001800

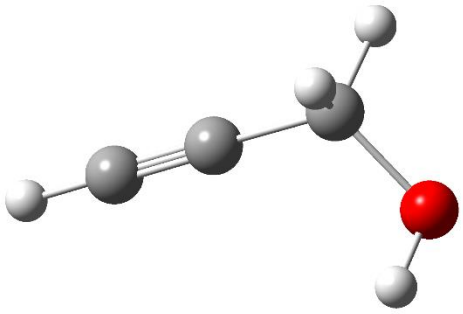


Optimized Structure for Propargyl Alcohol

Zero-point correction = 0.061979 (Hartree/Particle)
Thermal correction to Energy = 0.066650
Thermal correction to Enthalpy = 0.067594
Thermal correction to Gibbs Free Energy = 0.035425
Sum of electronic and zero-point Energies = -191.785842
Sum of electronic and thermal Energies = -191.781171
Sum of electronic and thermal Enthalpies = -191.780227
Sum of electronic and thermal Free Energies = -191.812396

0 1

C	-1.91825600	-0.21585000	-0.01431400
C	-0.77478300	0.15166600	0.00256500
C	0.62781400	0.58775800	0.03476100
O	1.53830200	-0.48736900	-0.11102800
H	-2.93366100	-0.54403700	-0.03183300
H	0.81391100	1.26846900	-0.79713700
H	0.80792100	1.13812700	0.96402700
H	1.39676700	-1.10504700	0.61509600

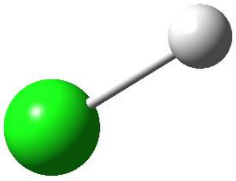


Optimized Structure for HCl

Zero-point correction = 0.006684 (Hartree/Particle)
Thermal correction to Energy = 0.009045
Thermal correction to Enthalpy = 0.009989
Thermal correction to Gibbs Free Energy = -0.011206
Sum of electronic and zero-point Energies = -460.794913
Sum of electronic and thermal Energies = -460.792553
Sum of electronic and thermal Enthalpies = -460.791608
Sum of electronic and thermal Free Energies = -460.812803

0 1

Cl	0.00000000	0.00000000	0.07153700
H	0.00000000	0.00000000	-1.21612500



Optimized Structure for Chloride

Zero-point correction = 0.000000 (Hartree/Particle)
Thermal correction to Energy = 0.001416
Thermal correction to Enthalpy = 0.002360
Thermal correction to Gibbs Free Energy = -0.015023
Sum of electronic and zero-point Energies = -460.354617
Sum of electronic and thermal Energies = -460.353201
Sum of electronic and thermal Enthalpies = -460.352257
Sum of electronic and thermal Free Energies = -460.369640

-1 1
 Cl 0.00000000 0.00000000 0.00000000

Optimized Structure for HBr

Zero-point correction = 0.006052 (Hartree/Particle)
Thermal correction to Energy = 0.008413
Thermal correction to Enthalpy = 0.009357
Thermal correction to Gibbs Free Energy = -0.013171
Sum of electronic and zero-point Energies = -2574.765615
Sum of electronic and thermal Energies = -2574.763255
Sum of electronic and thermal Enthalpies = -2574.762311
Sum of electronic and thermal Free Energies = -2574.784838

0 1
 Br 0.00000000 0.00000000 0.03950400
 H 0.00000000 0.00000000 -1.38262800

Optimized Structure for Bromide

Zero-point correction = 0.000000 (Hartree/Particle)
Thermal correction to Energy = 0.001416
Thermal correction to Enthalpy = 0.002360
Thermal correction to Gibbs Free Energy = -0.016176
Sum of electronic and zero-point Energies = -2574.327641
Sum of electronic and thermal Energies = -2574.326225
Sum of electronic and thermal Enthalpies = -2574.325281
Sum of electronic and thermal Free Energies = -2574.343817

-1 1
 Br 0.00000000 0.00000000 0.00000000

Sample Input File (Propargyl Alcohol)

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%nprocshared=12
%chk=Propargyl_OH-1_DFT_Freq_CHCl3_SMD.chk

#p M062X/GEN OPT=CalcAll freq scrf=(SMD,solvent=chloroform) scf=xqc int=ultrafine Integral=NOXCTest

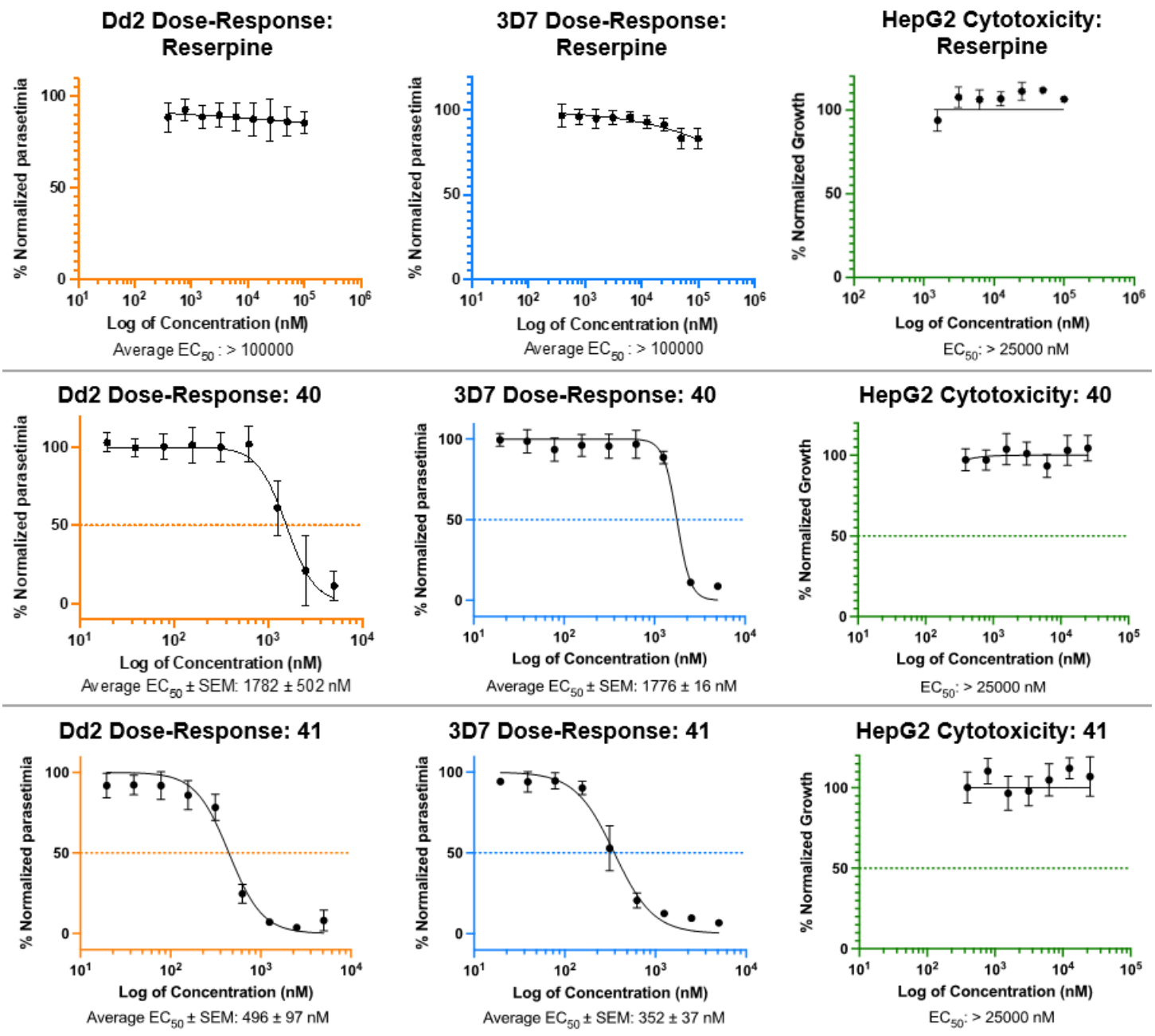
 Propargyl_OH-1_DFT_Freq_SMD

0 1
 C -1.91169300 -0.21965100 -0.01668700
 C -0.76664300 0.15295600 0.00712900
 C 0.60714100 0.60266900 0.03751700
 O 1.53179500 -0.48958600 -0.10920600
 H -2.89966900 -0.53648200 -0.03792100
 H 0.85414600 1.25694000 -0.83104800
 H 0.84108100 1.14505400 0.98129300
 H 1.37724700 -1.16466800 0.59357600

H C O 0
6-311++G(d,p)
****

18.) Antiplasmodial Methods and Results.

Dose-Response Curves



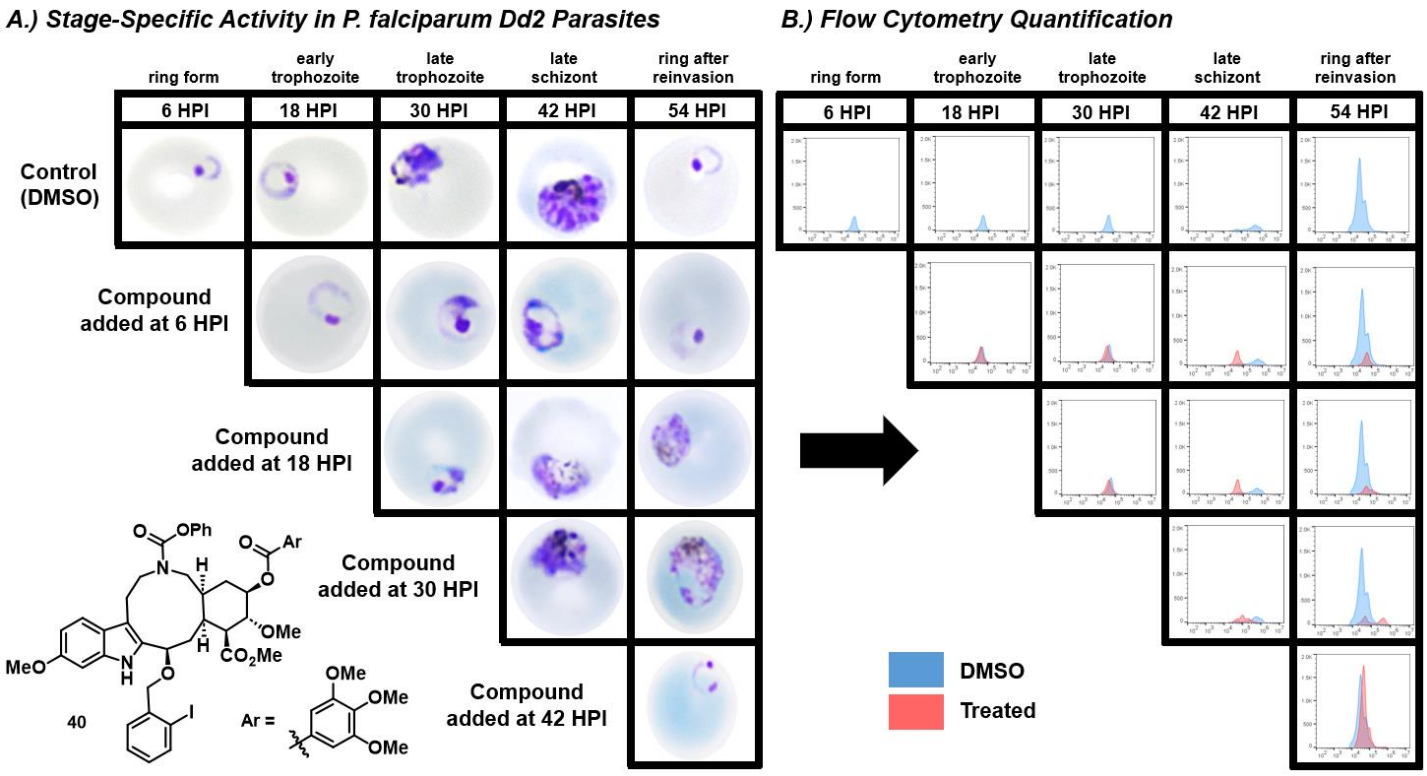
Rate of Killing Assay

Compounds were added at 10 x EC_{50} concentrations to synchronous Dd2 culture at 1% parasitemia and 4% hematocrit starting at six hours post invasion (HPI). Dd2 culture was synchronized by using 5% sorbitol. Cultures were exposed to the compound of interest for 12, 24, and 48 hours, followed by washing steps and continuous monitoring of parasite regrowth over the course of four days. PBS and 0.5% BSA were used for washing and blocking steps. Samples were collected every 24 hours until the 96-hour time point. A mixture of Mitotracker

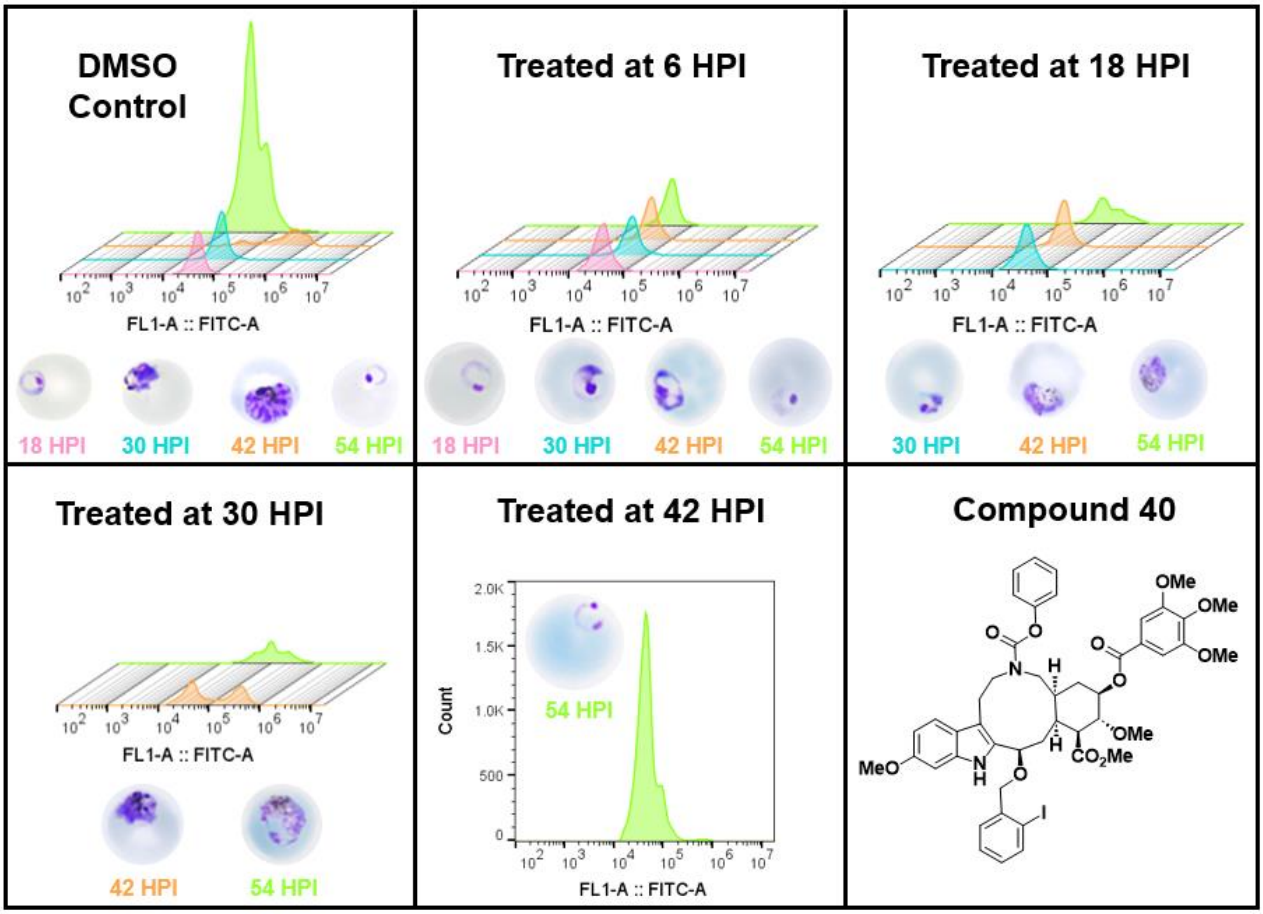
Deep red (MTR) and SYBR Green I dyes were used to stain the culture to track mitochondria content and parasitemia, respectively. Uninfected red blood cells and no mitotracker controls were used to assist with flow-cytometry gating. Dimethyl sulfoxide (DMSO) was used as a negative control. Dihydroartemisinin (DHA) was used as a positive control for rapid parasite killing, and atovaquone was also used as a positive control for late stage killing. GraphPad Prism was used to analyze the flow cytometry data. Results are expressed as the means of triplicate biological experiments and parasite viability.

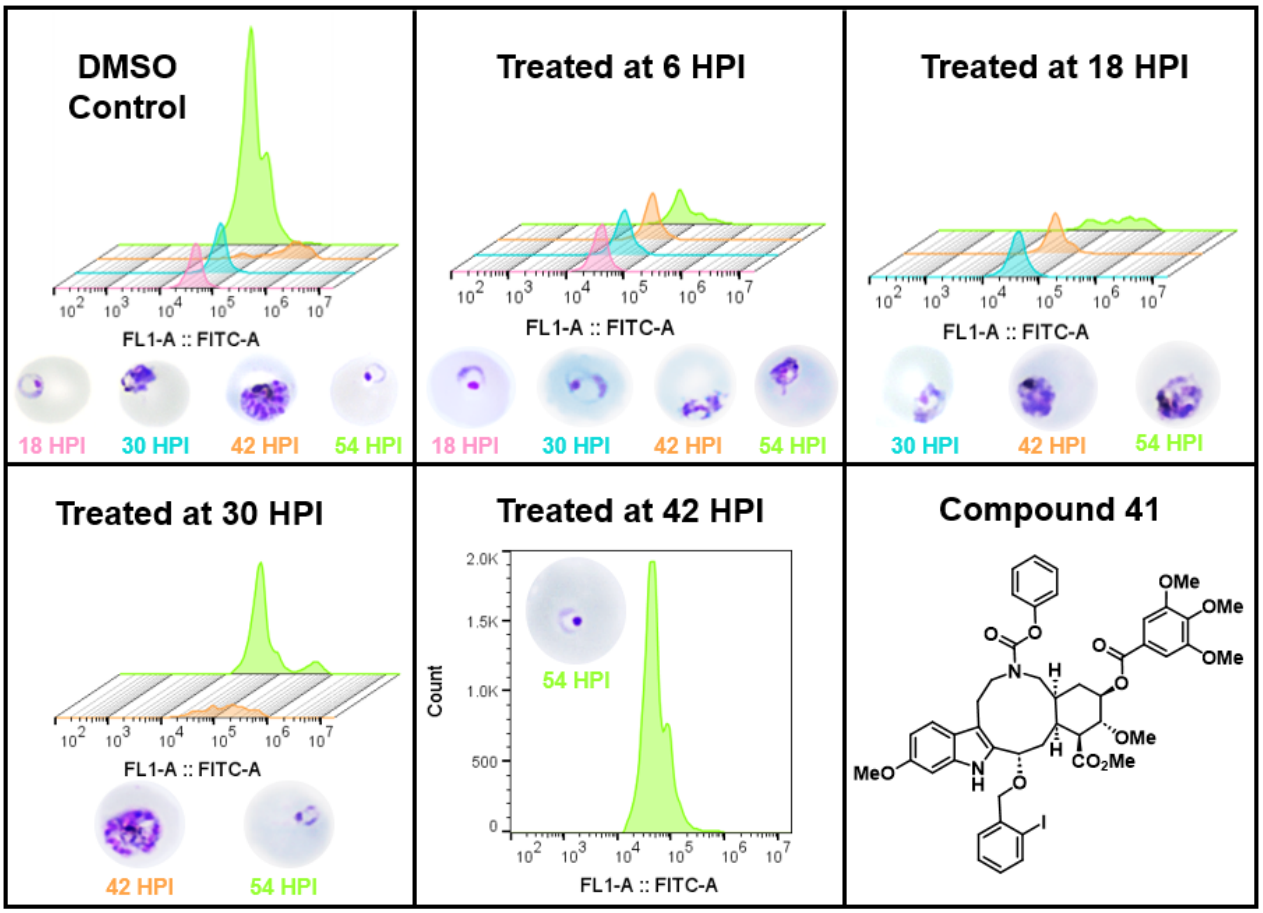
Stage Specific Assay & Supporting Data for Compound 41

Dd2 culture was synchronized by using 5% sorbitol. The culture was then diluted to 1% parasitemia and 2% hematocrit. Compounds of interest were added at 5 x EC_{50} concentrations at 6, 18, 30 and 42 HPI. DMSO and DHA were used as a negative and positive controls, respectively. Samples were collected every 12 hours at every stage until reinvasion at 54 HPI. Giemsa smearing was used to observe the parasite morphology, and flow cytometry was used to observe parasite DNA content. Samples were fixed in 4% paraformaldehyde, and PBS was used for washing steps. Samples were permeabilized in 0.25% Triton X-100 and stained using DNA dye YOYO-1. FlowJo (v 10.8) was used to analyze the flow cytometry data. Results are representative of triplicate biological experiments. Note: Experimental data for compound **40** is shown below (the data for compound **41** is reported in the manuscript).



*Alternative representation of the stage specific assay results for compounds **40** and **41**.*





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Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; and Fox, D. J.; Gaussian, Inc., Wallingford CT, **2013**.

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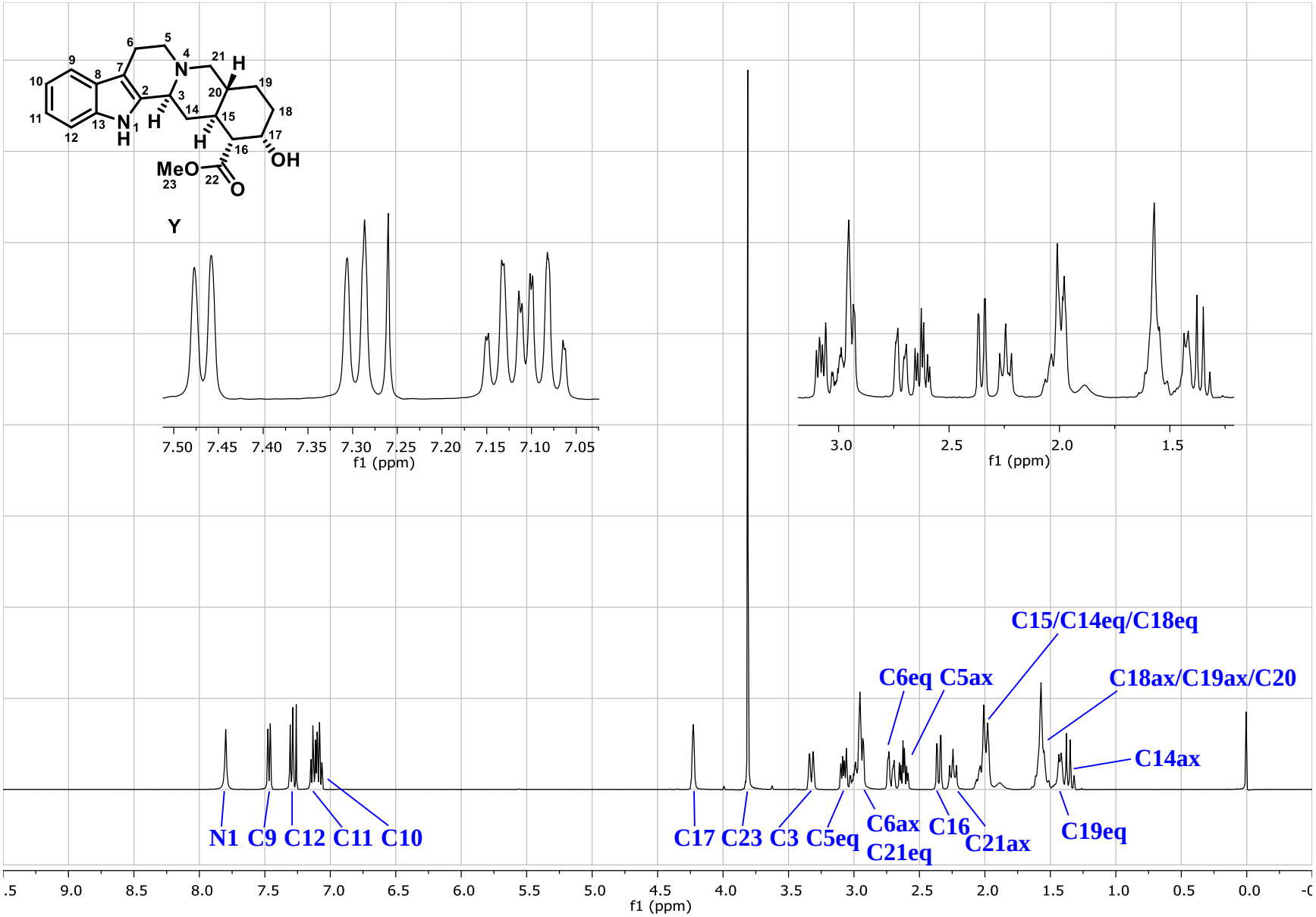
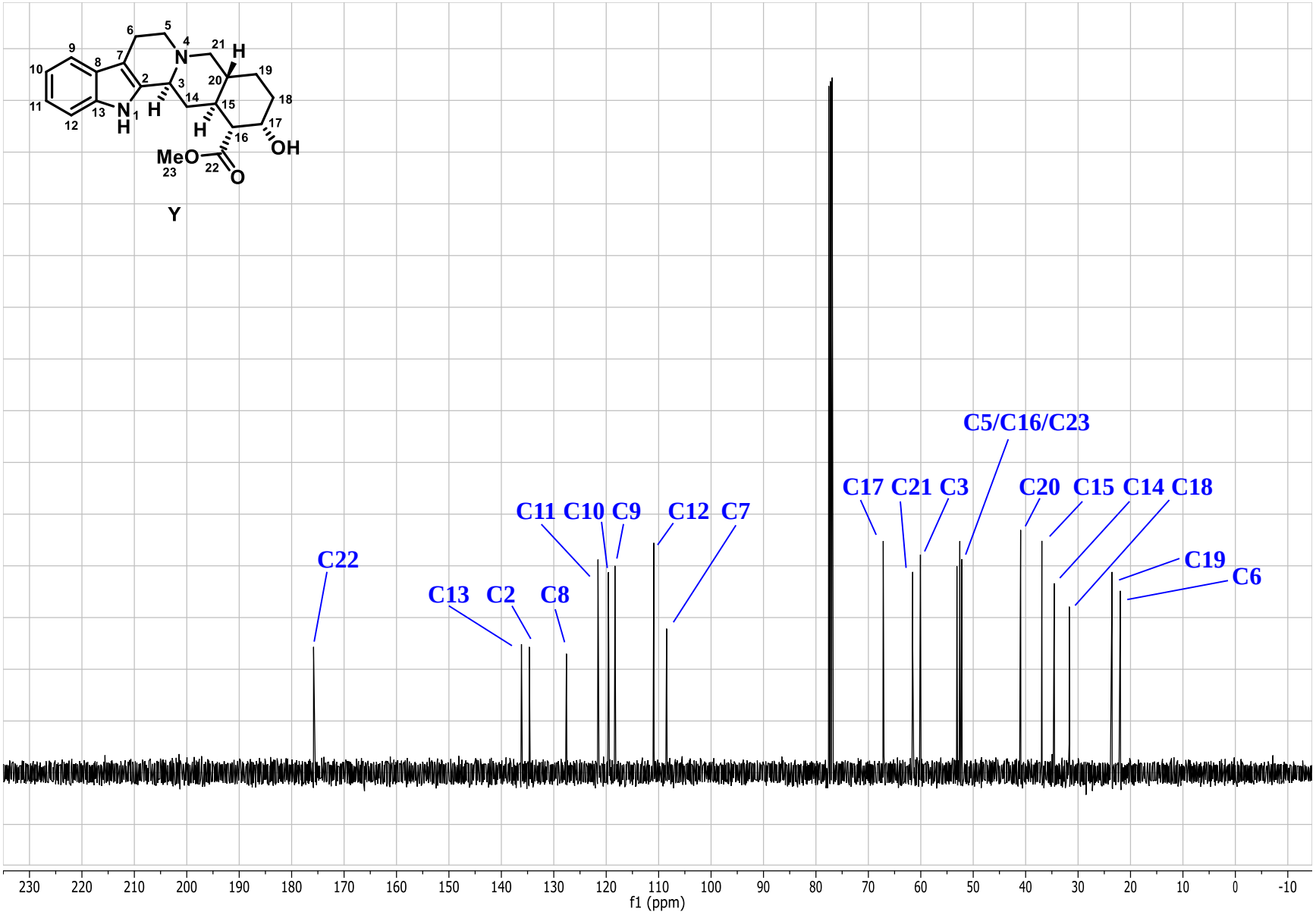
20.) NMR Spectra.

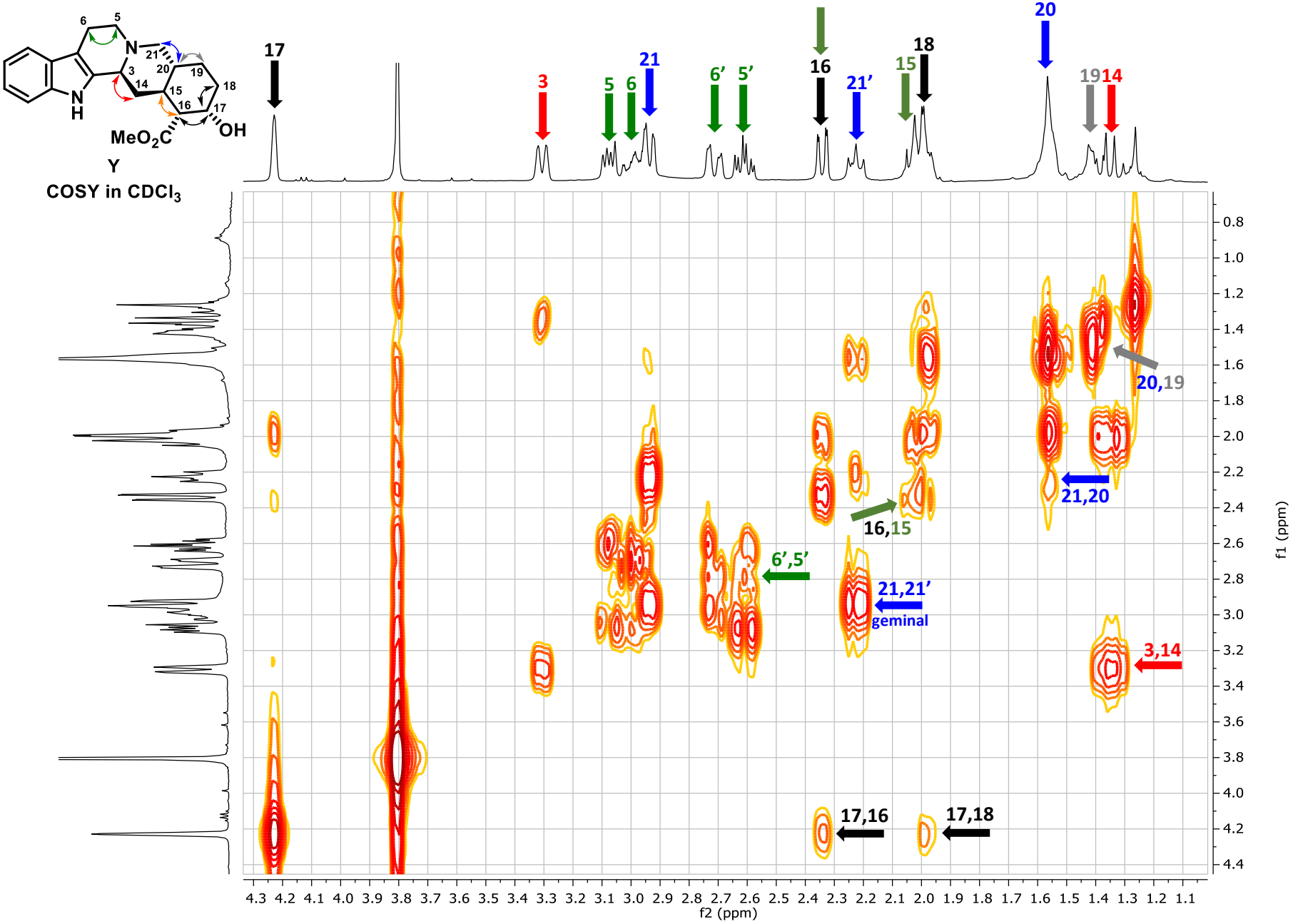
NMR spectra appear in the following order: (1) yohimbine (internal reference for derivatives), (2) ring-cleaved yohimbine derivatives (in the order shown on Supplementary Figure 1), (3) ring-cleaved apovincamine and vinburnine derivatives (in the order shown on Supplementary Figure 2), and (4) ring-cleaved reserpine derivatives (in the order shown on Supplementary Figure 2).



Internal Reference Cited (used with permission):
Chem. Eur. J. **2017,** *23,* 4327-4335.



Internal Reference Cited (used with permission):
Chem. Eur. J. **2017,** *23,* 4327-4335.



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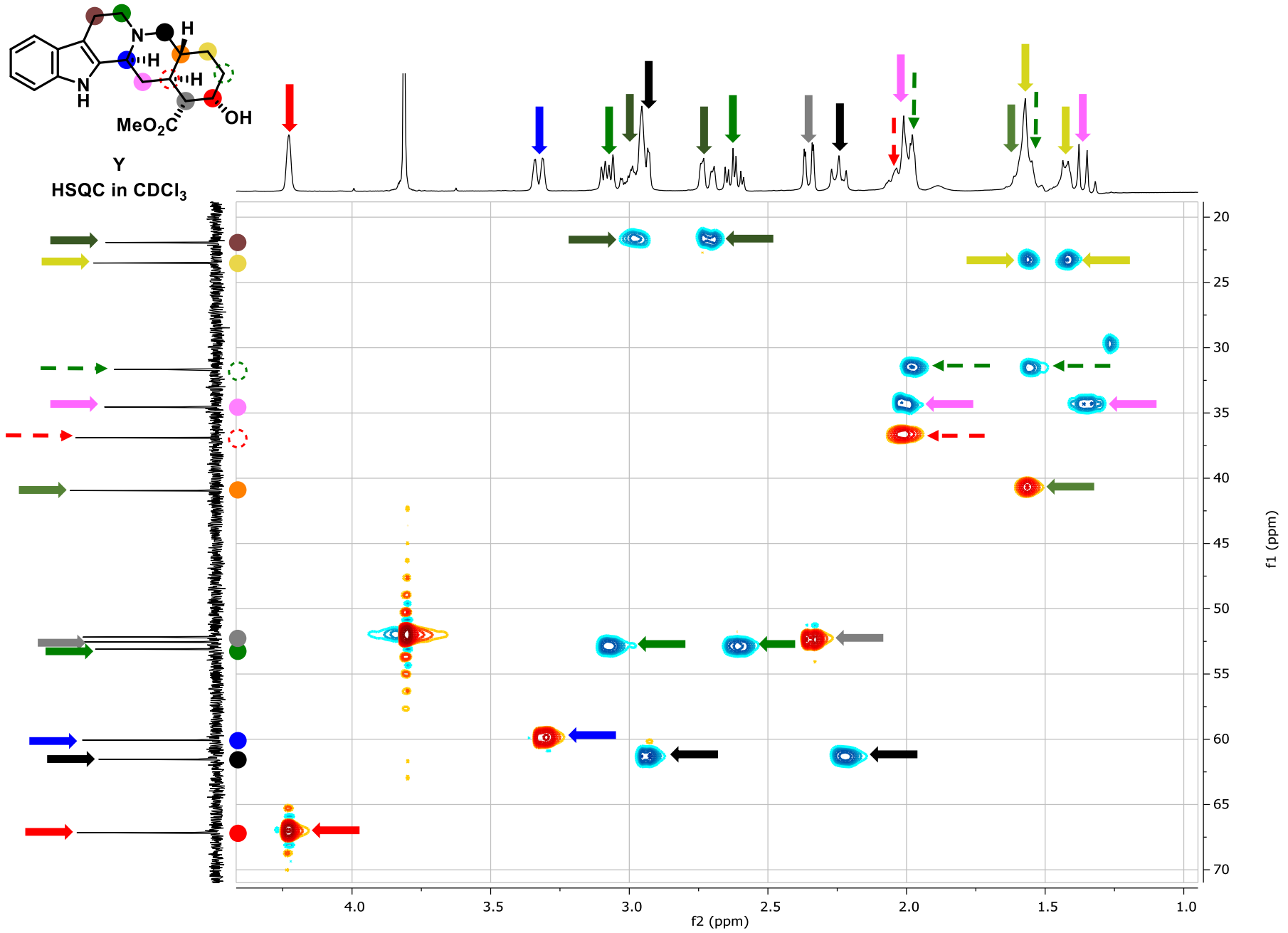
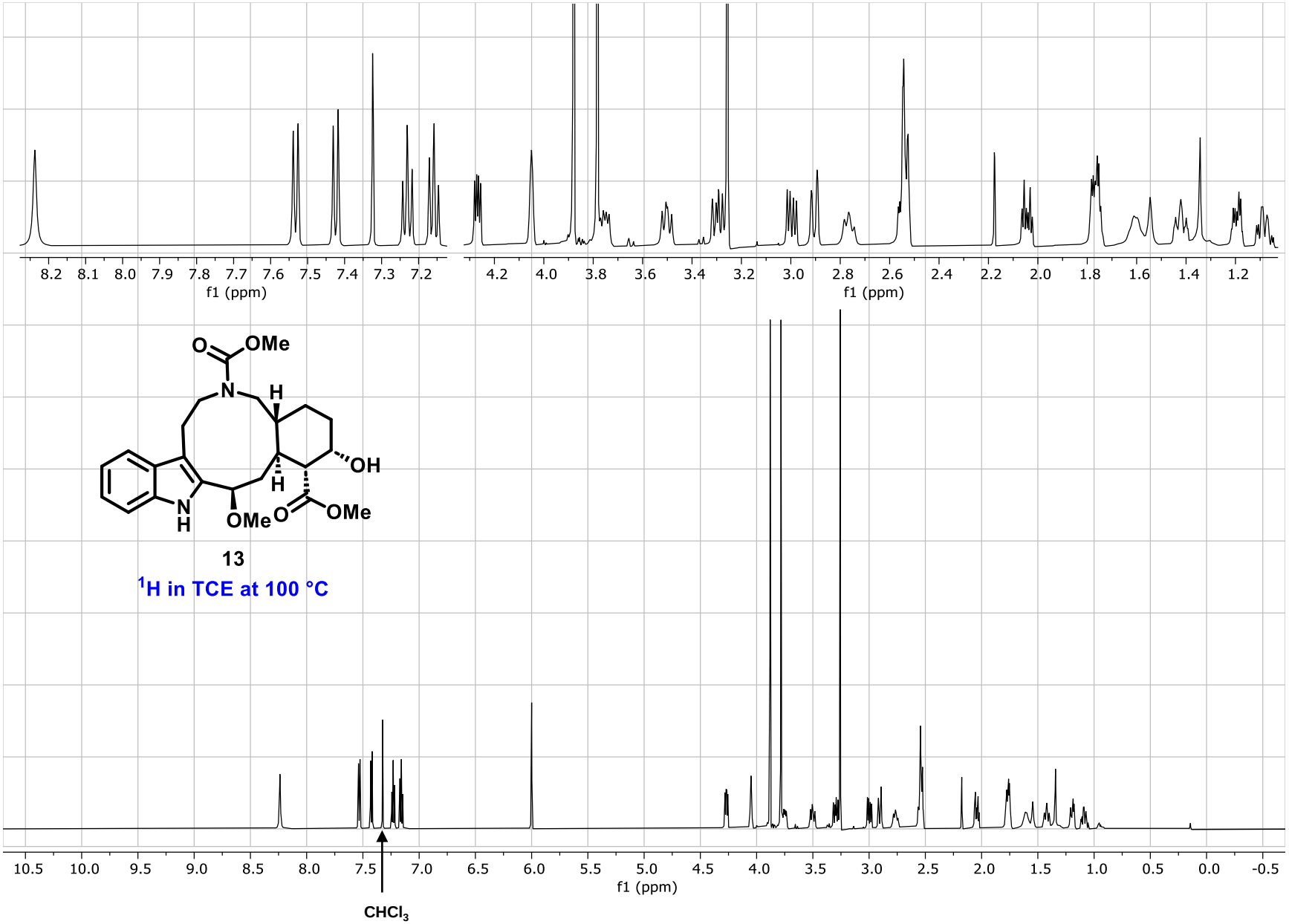
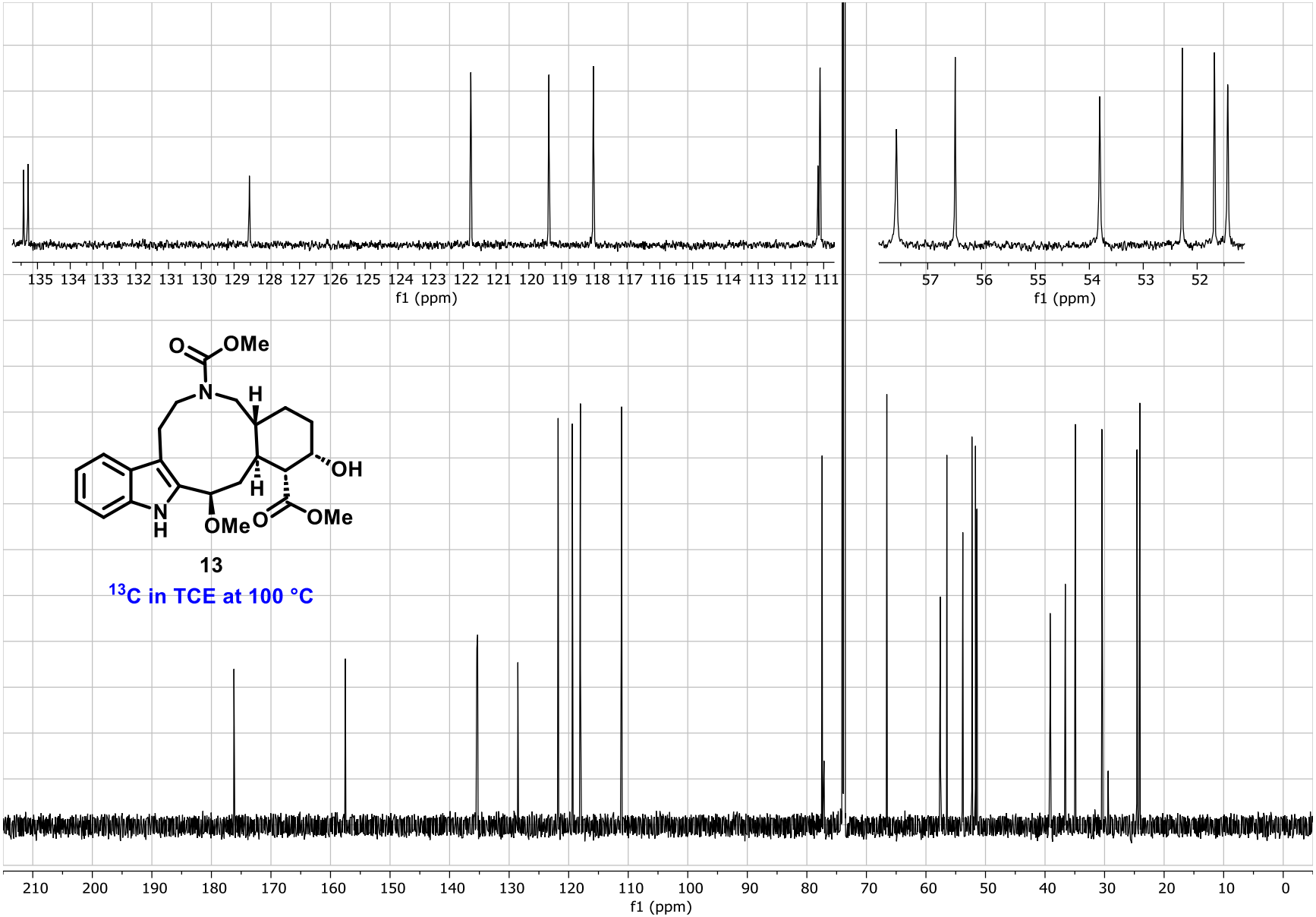
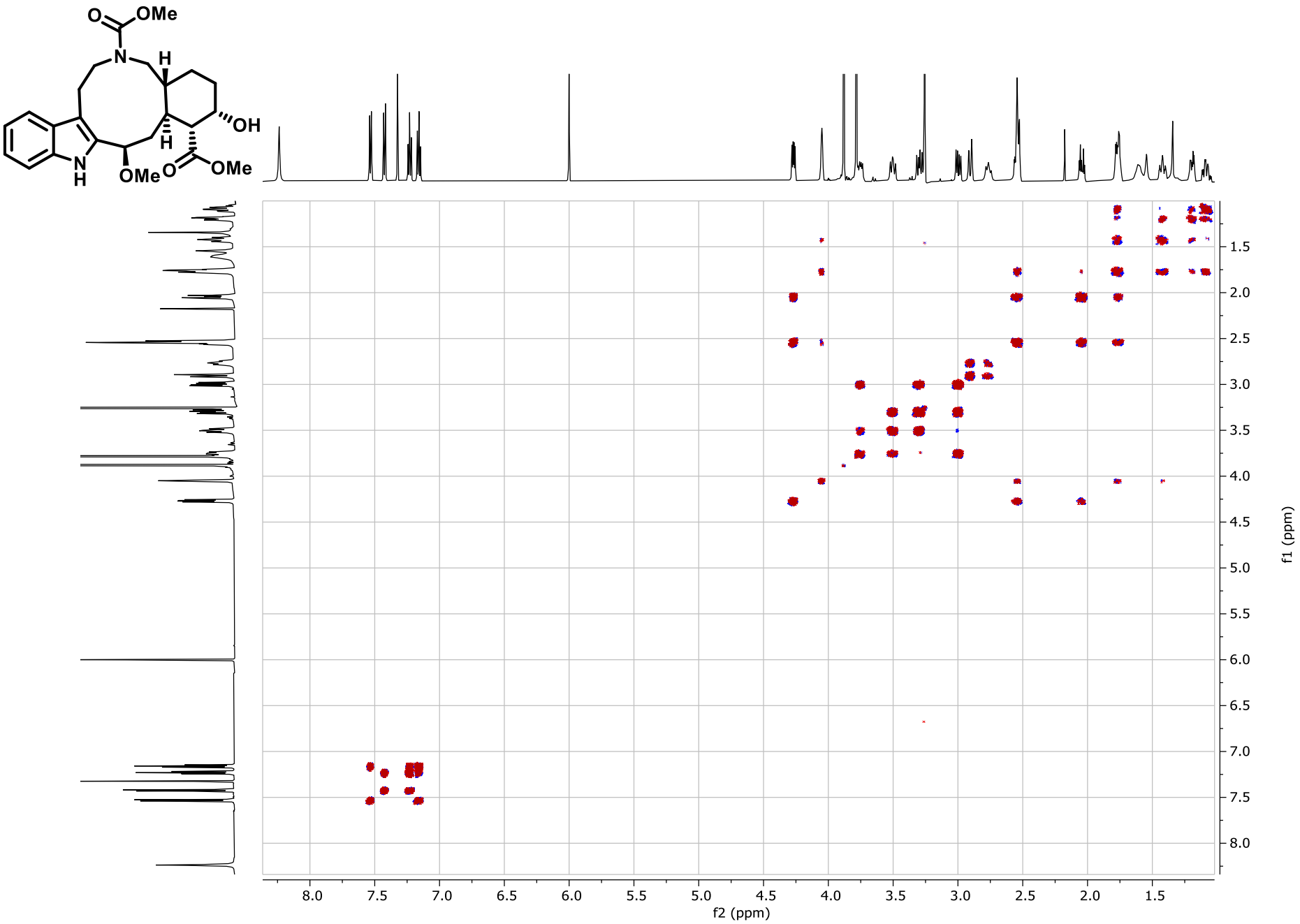
Chem. Eur. J. **2017,** *23,* 4327-4335.



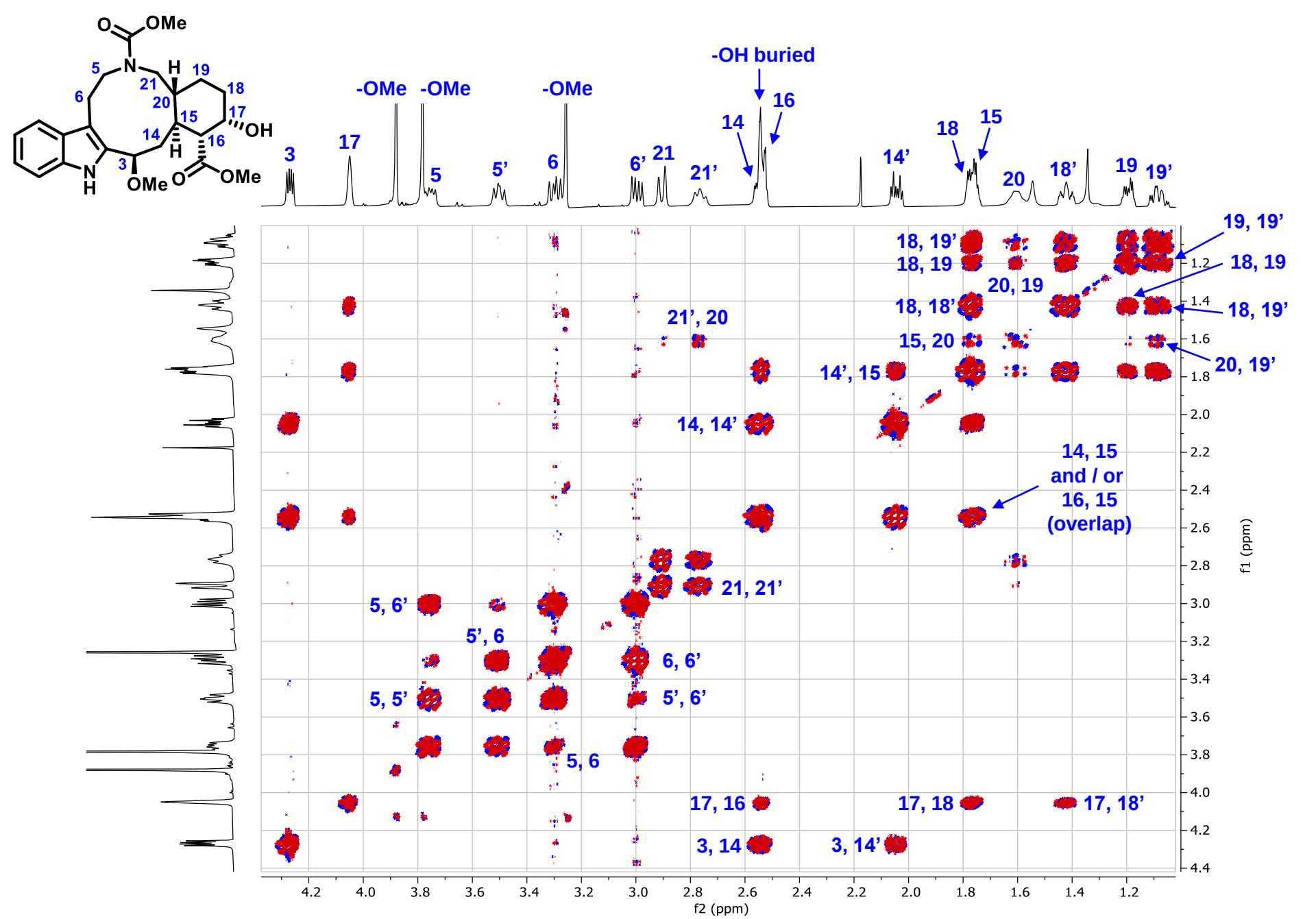
Internal Reference Cited (used with permission):
Chem. Eur. J. **2017,** *23,* 4327-4335.


8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2
f1 (ppm)
4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2
f1 (ppm)
O
OMe
N
H
OH
H
N
H
OMe
O
OMe
13
1H in TCE at 100 °C
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)
CHCl3

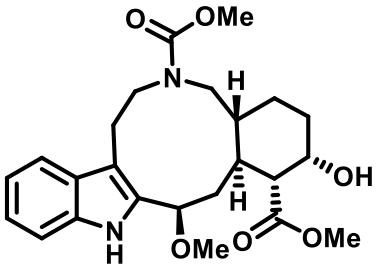

135 134 133 132 131 130 129 128 127 126 125 124 123 122 121 120 119 118 117 116 115 114 113 112 111
f1 (ppm)
57 56 55 54 53 52
f1 (ppm)
O
OMe
N
H
OH
H
N
H
OMe
O
OMe
13
13C in TCE at 100 °C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

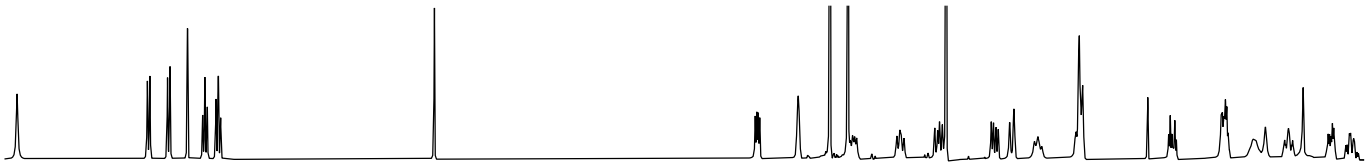


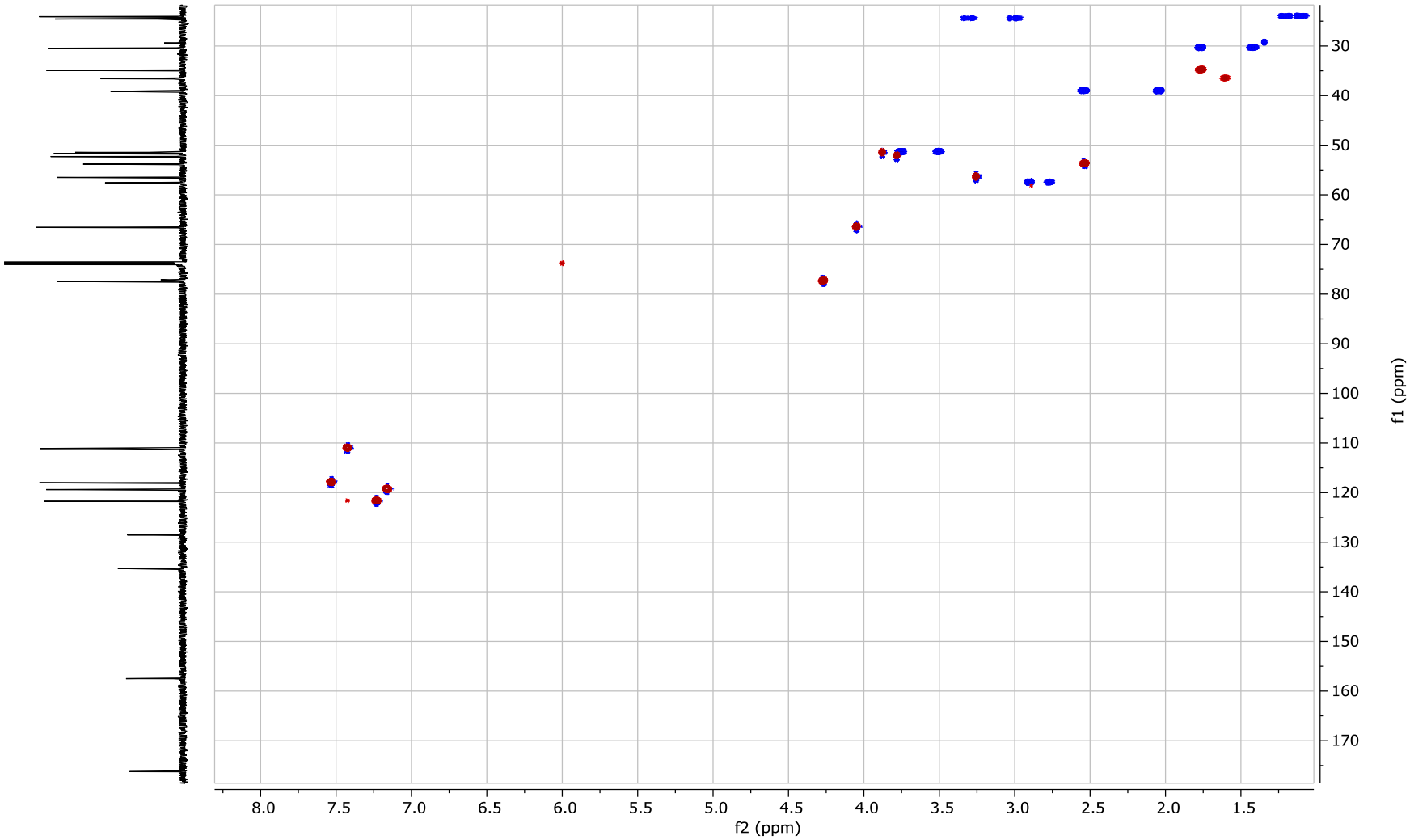
Compound 13: COSY, T = 100 °C, $C_2D_2Cl_4$ (full)



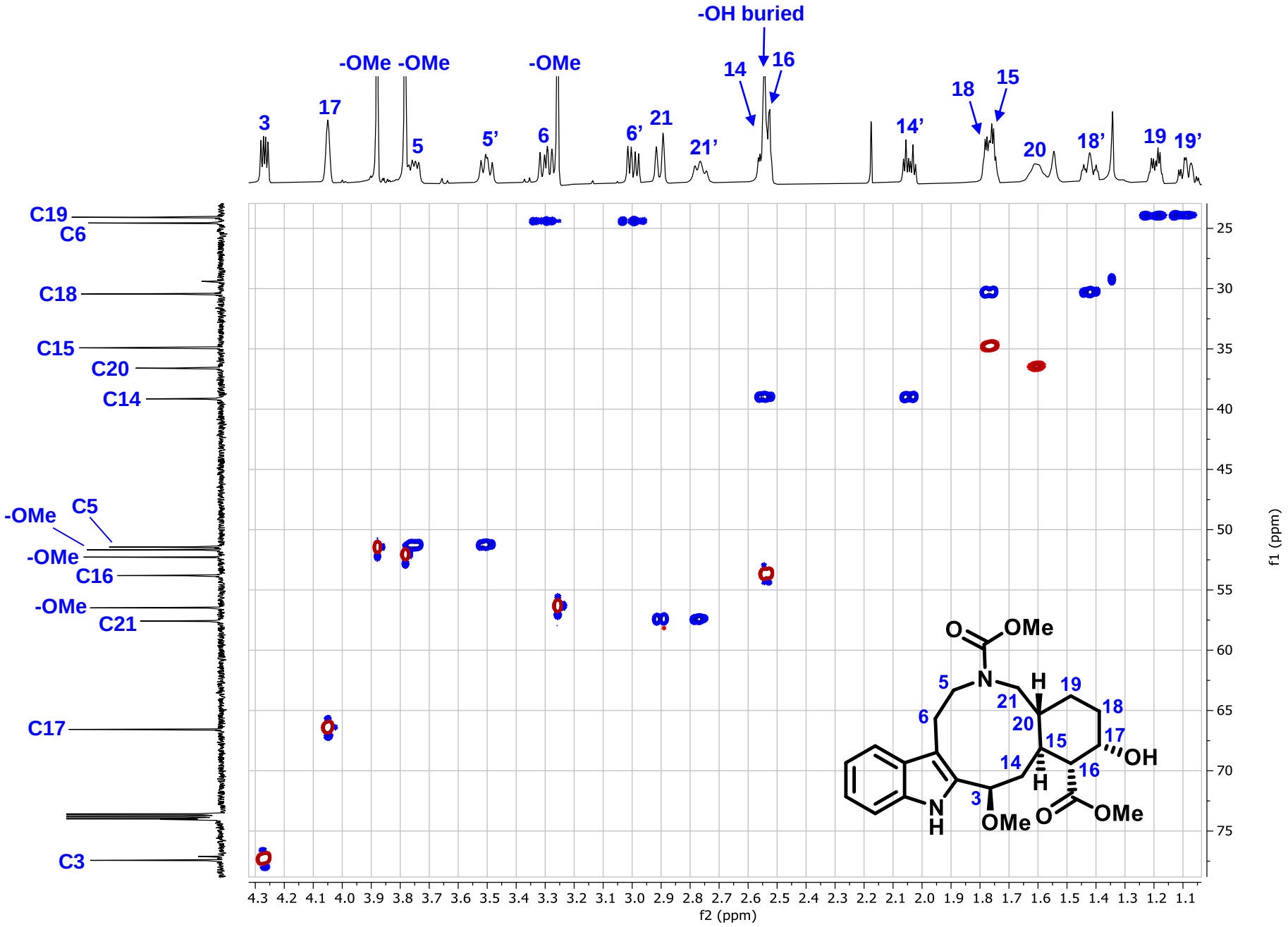
Compound 13: COSY, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in)



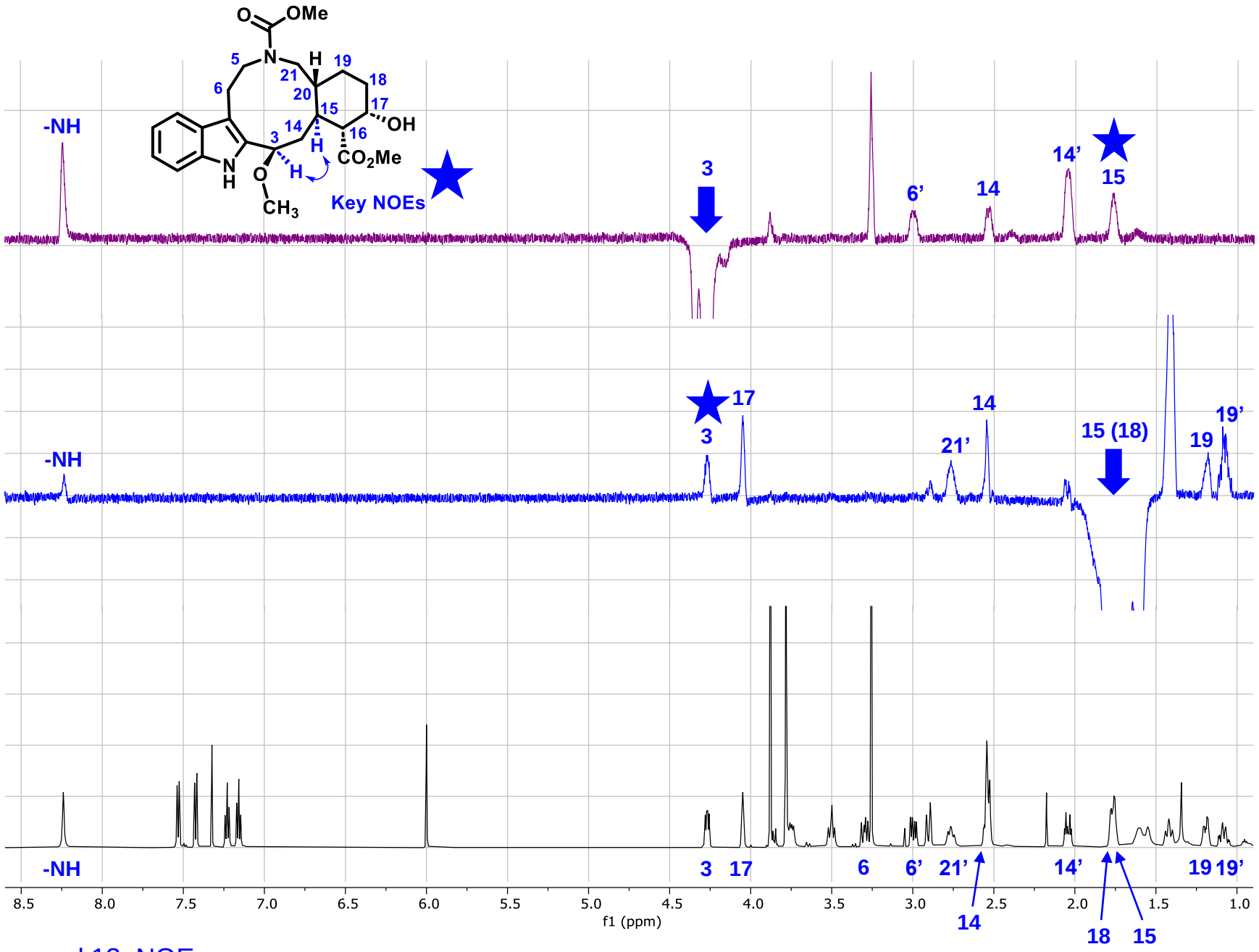




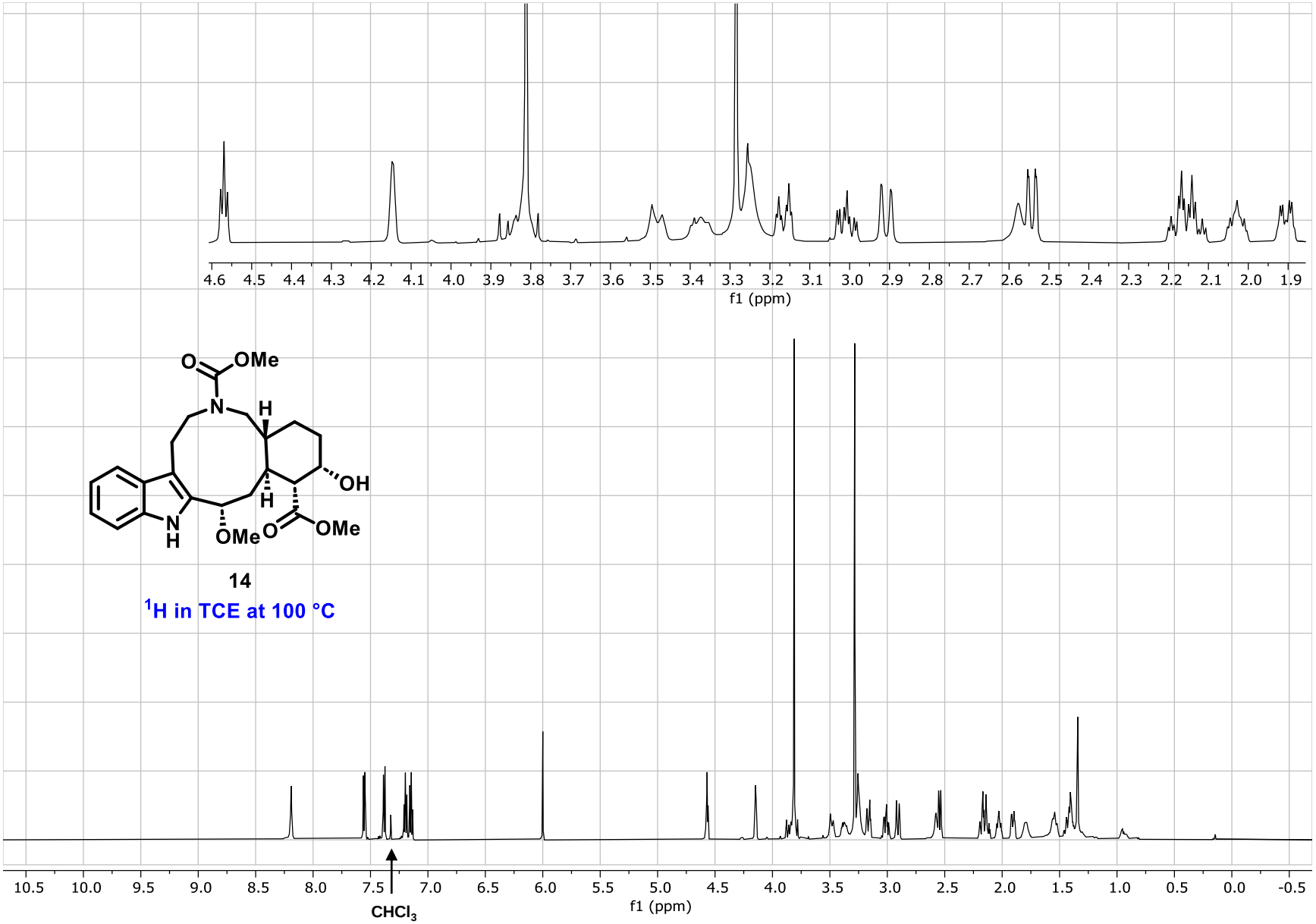
Compound 13: HSQC, T = 100 °C, $C_2D_2Cl_4$ (full)

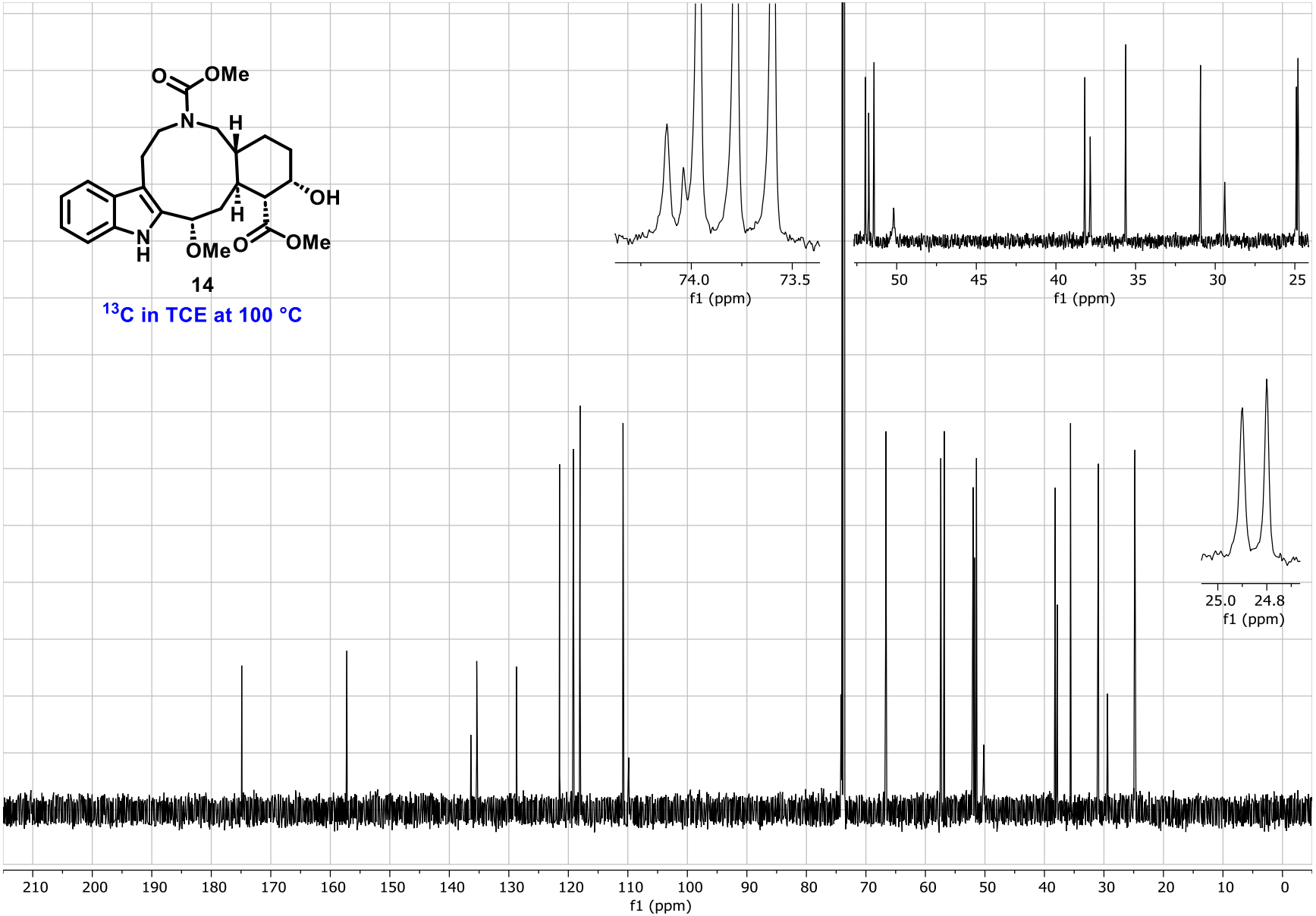


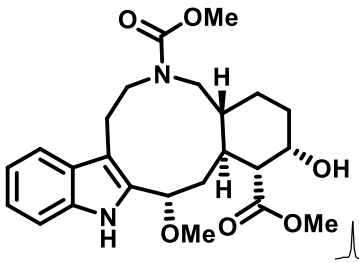
Compound 13: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in)

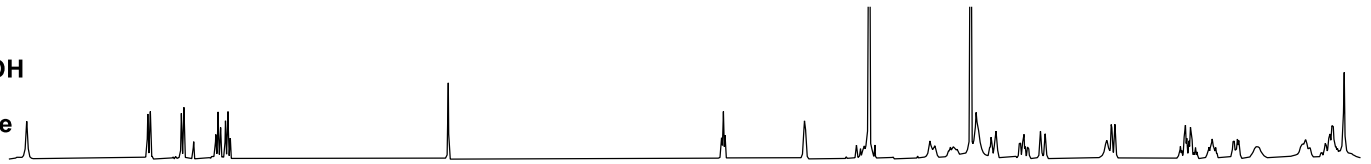


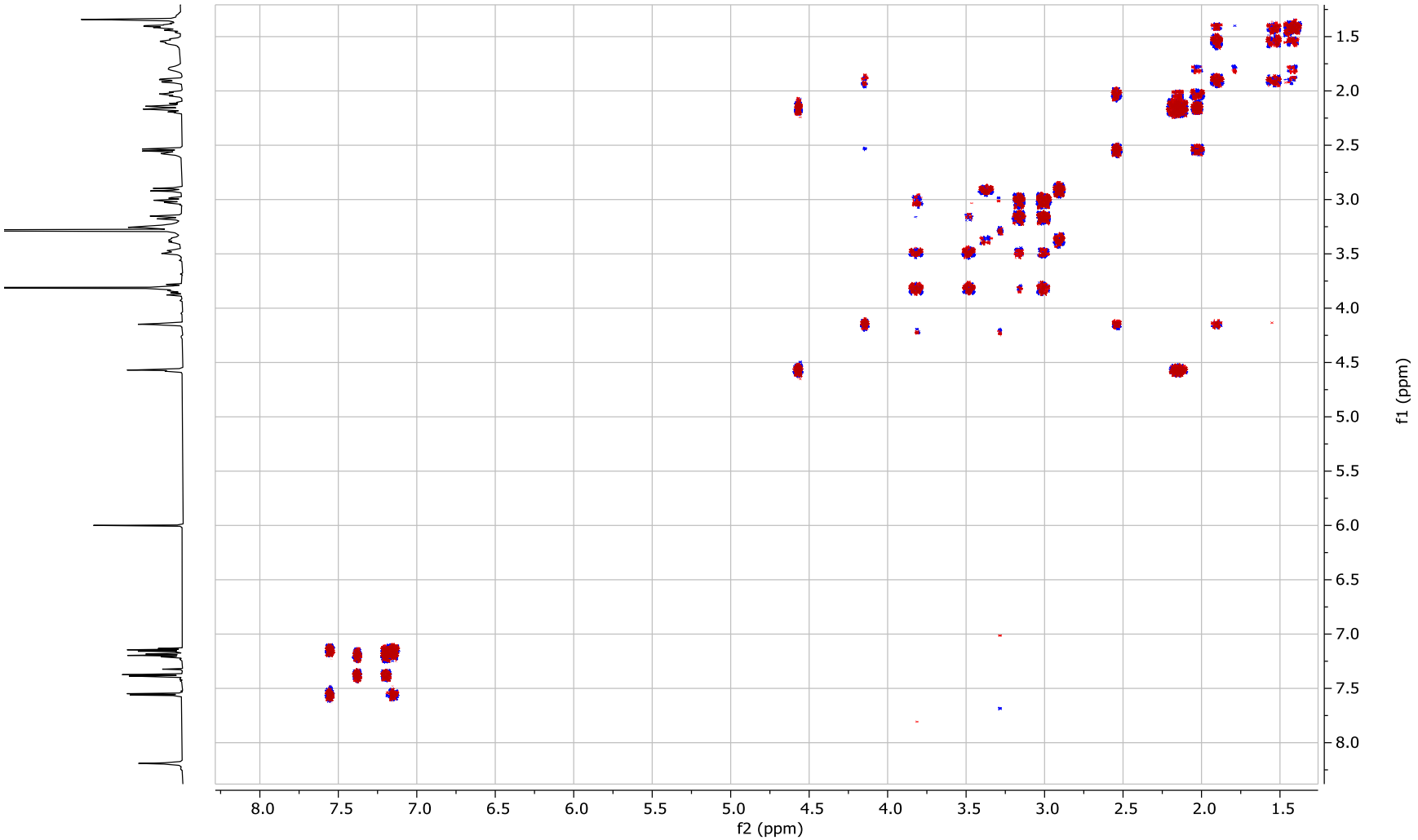
Compound 13: NOE,
T = 100 °C, $C_2D_2Cl_4$


4.6 4.5 4.4 4.3 4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9
f1 (ppm)
O
OMe
N
H
OH
H
N
H
OMe
O
OMe
14
1H in TCE at 100 °C
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
CHCl3
f1 (ppm)

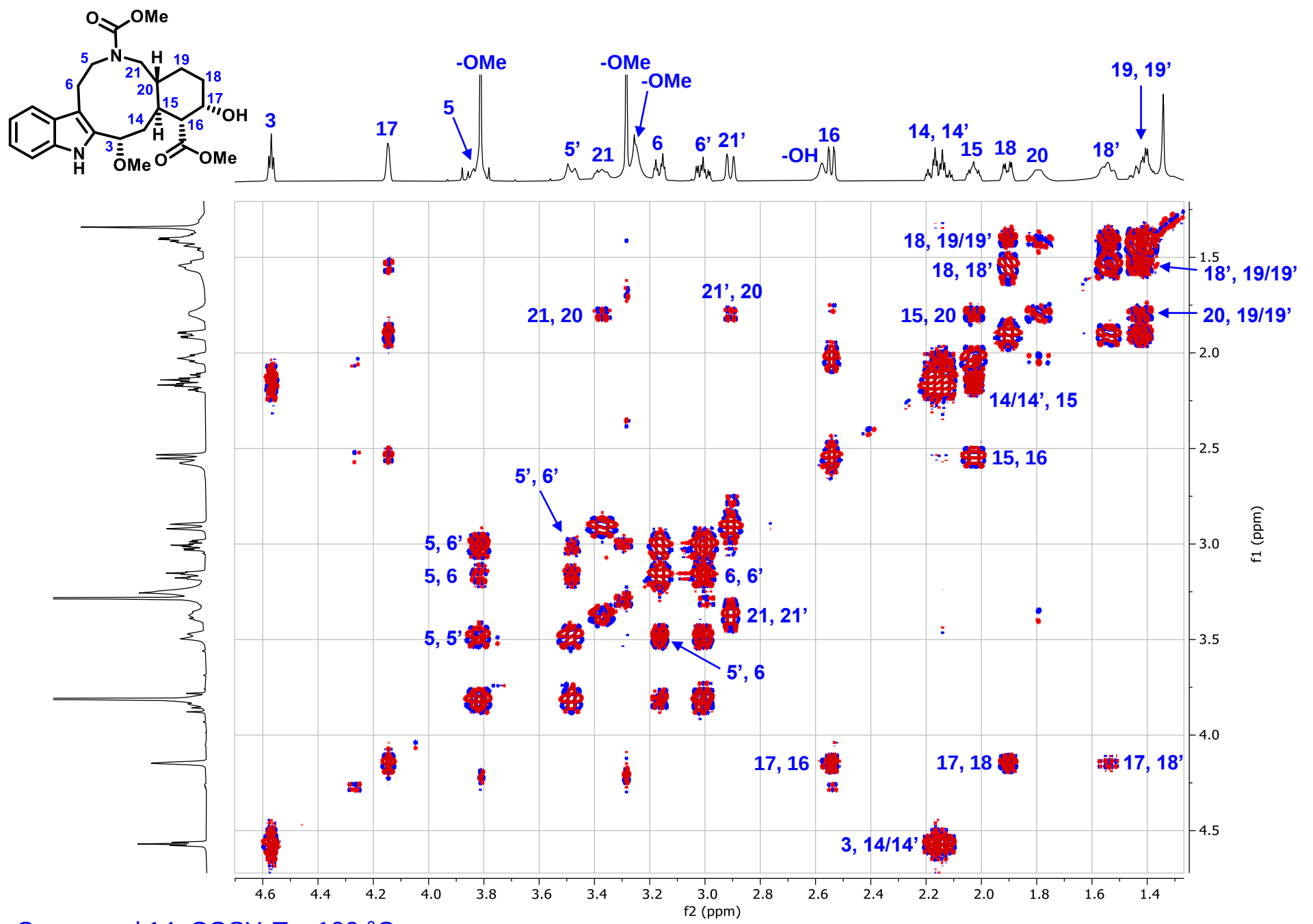

O
OMe
N
H
OH
H
N
H
OMe
O
OMe
14
13C in TCE at 100 °C
74.0
73.5
f1 (ppm)
50
45
40
35
30
25
f1 (ppm)
25.0
24.8
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



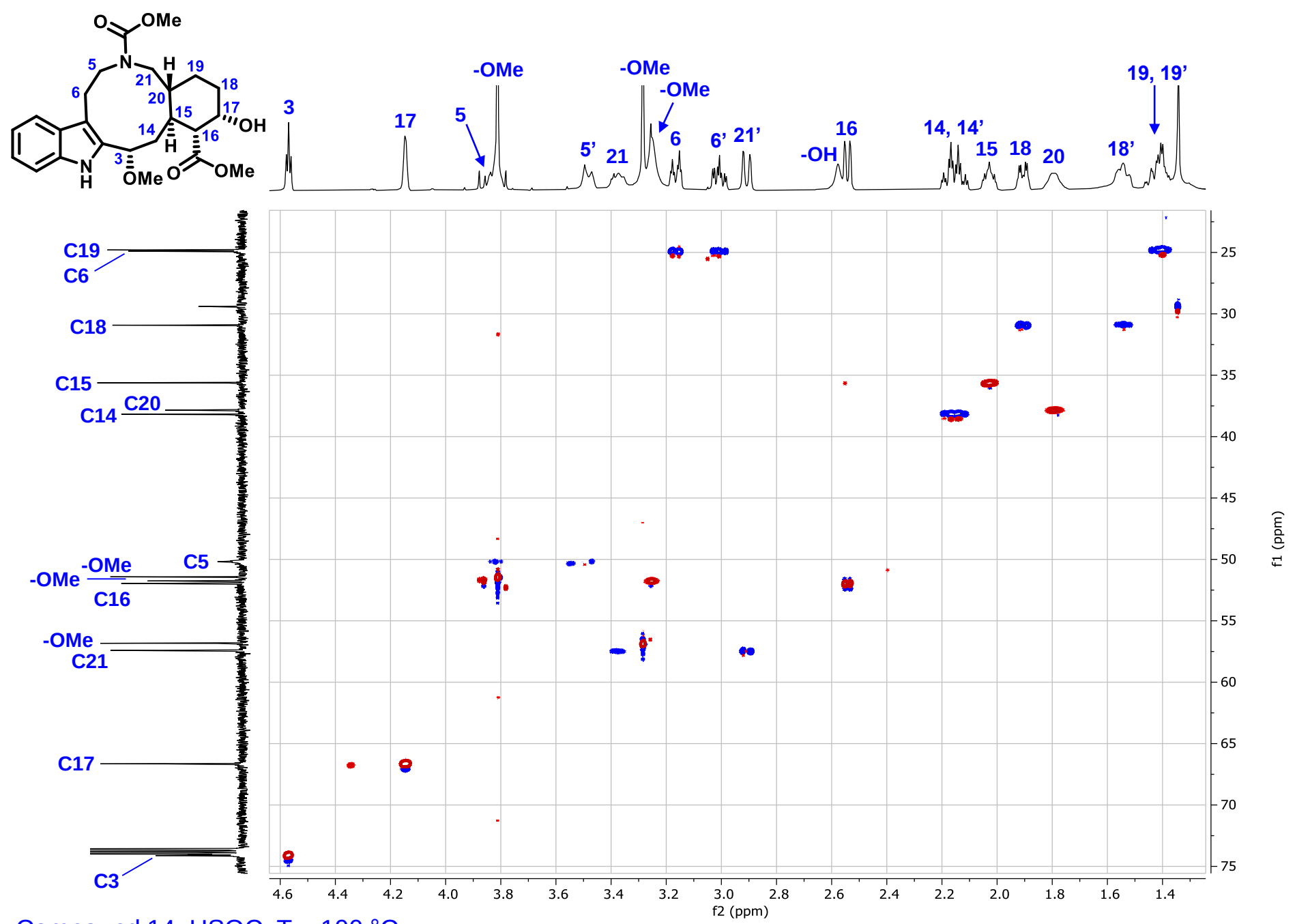




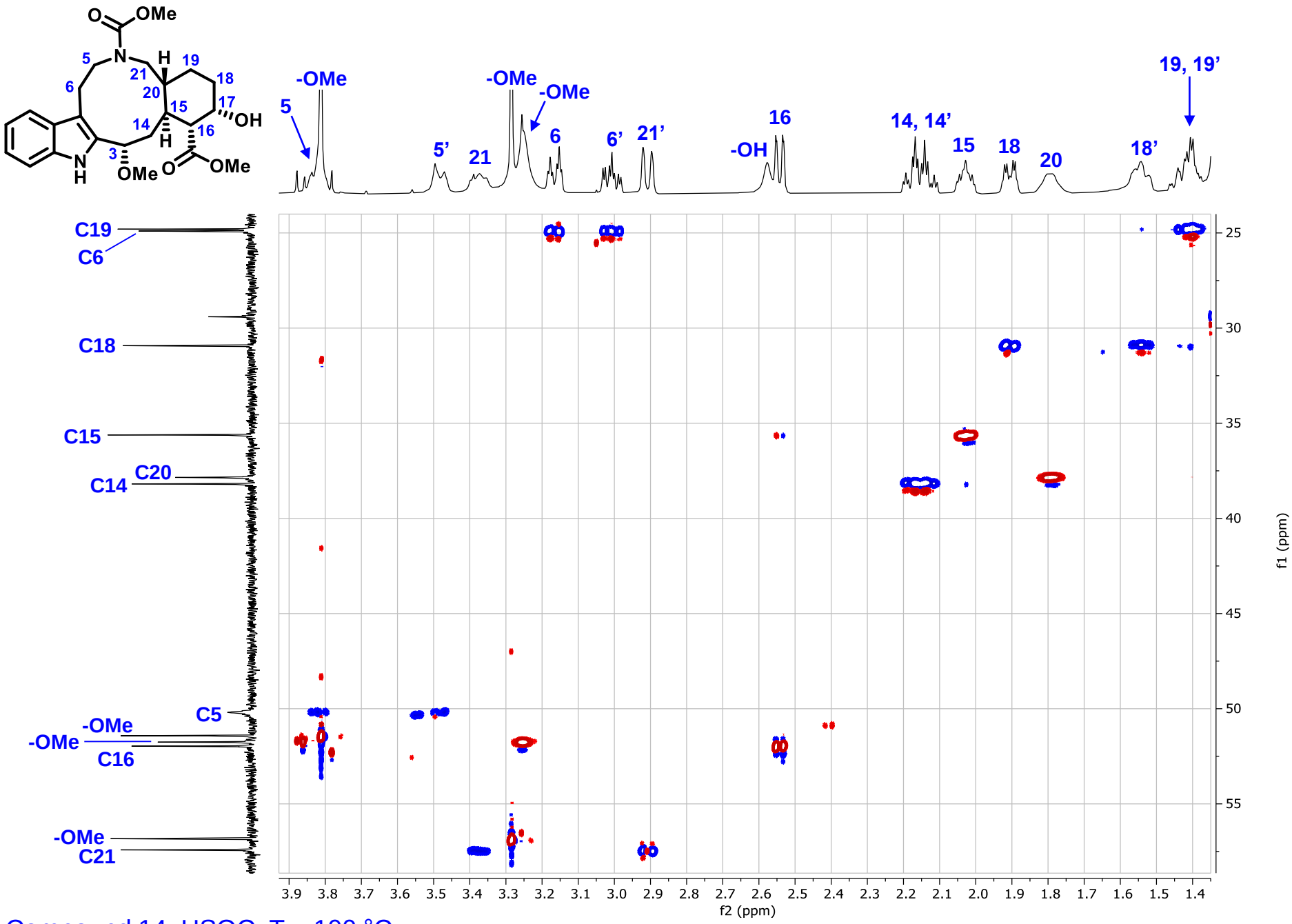
Compound 14: COSY, T = 100 °C,
$C_2D_2Cl_4$ (full)



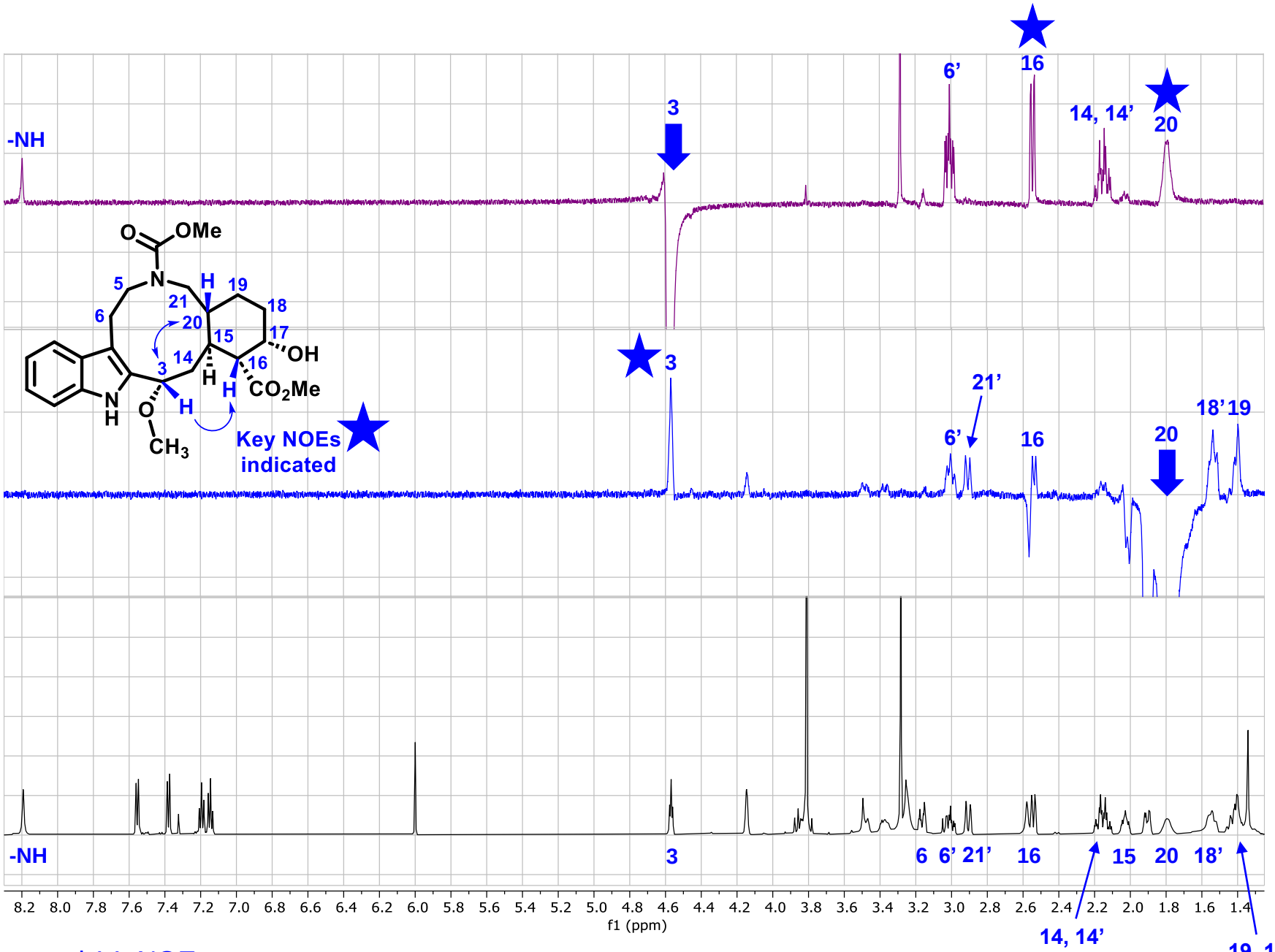
Compound 14: COSY, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in)



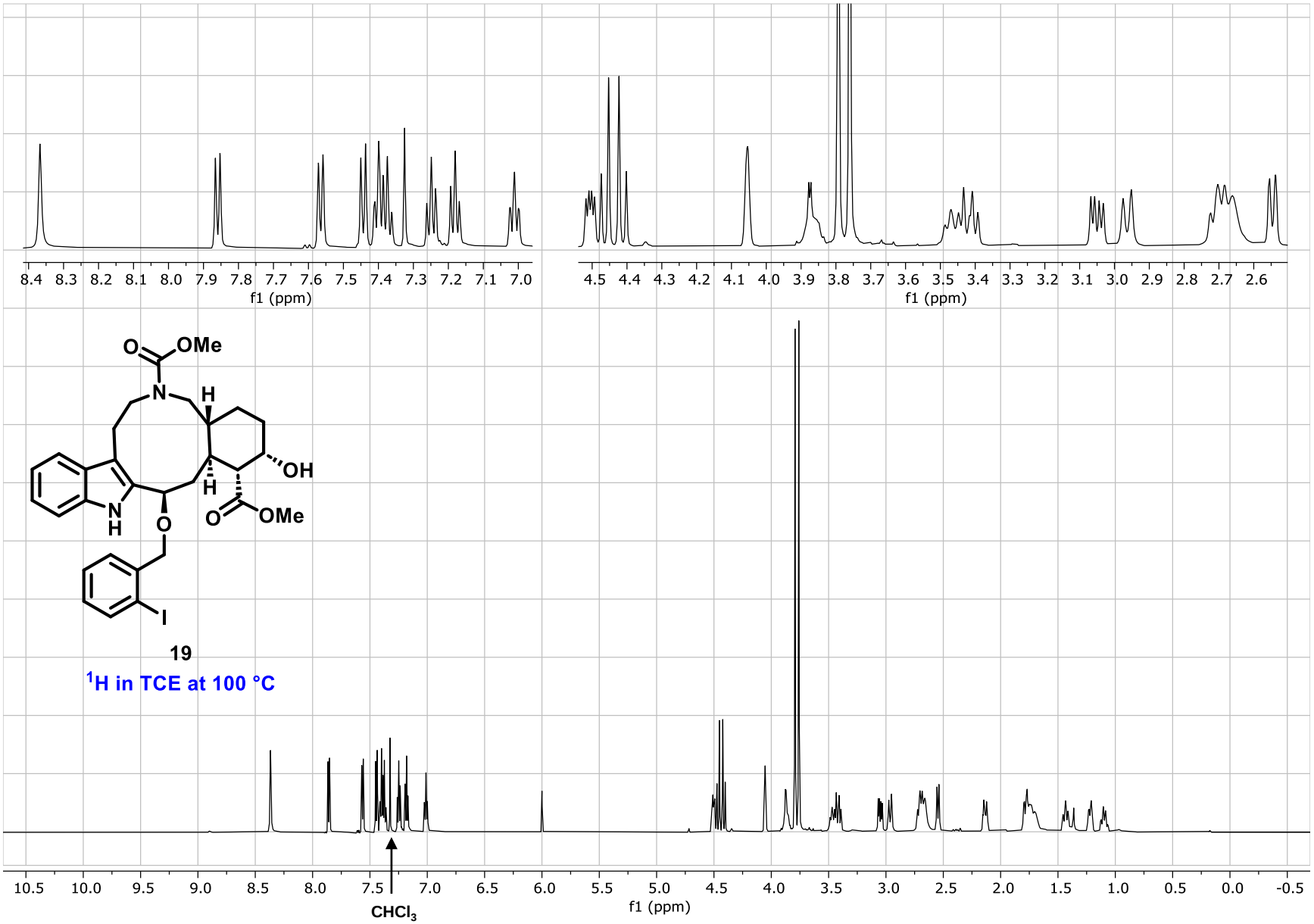
Compound 14: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 1)

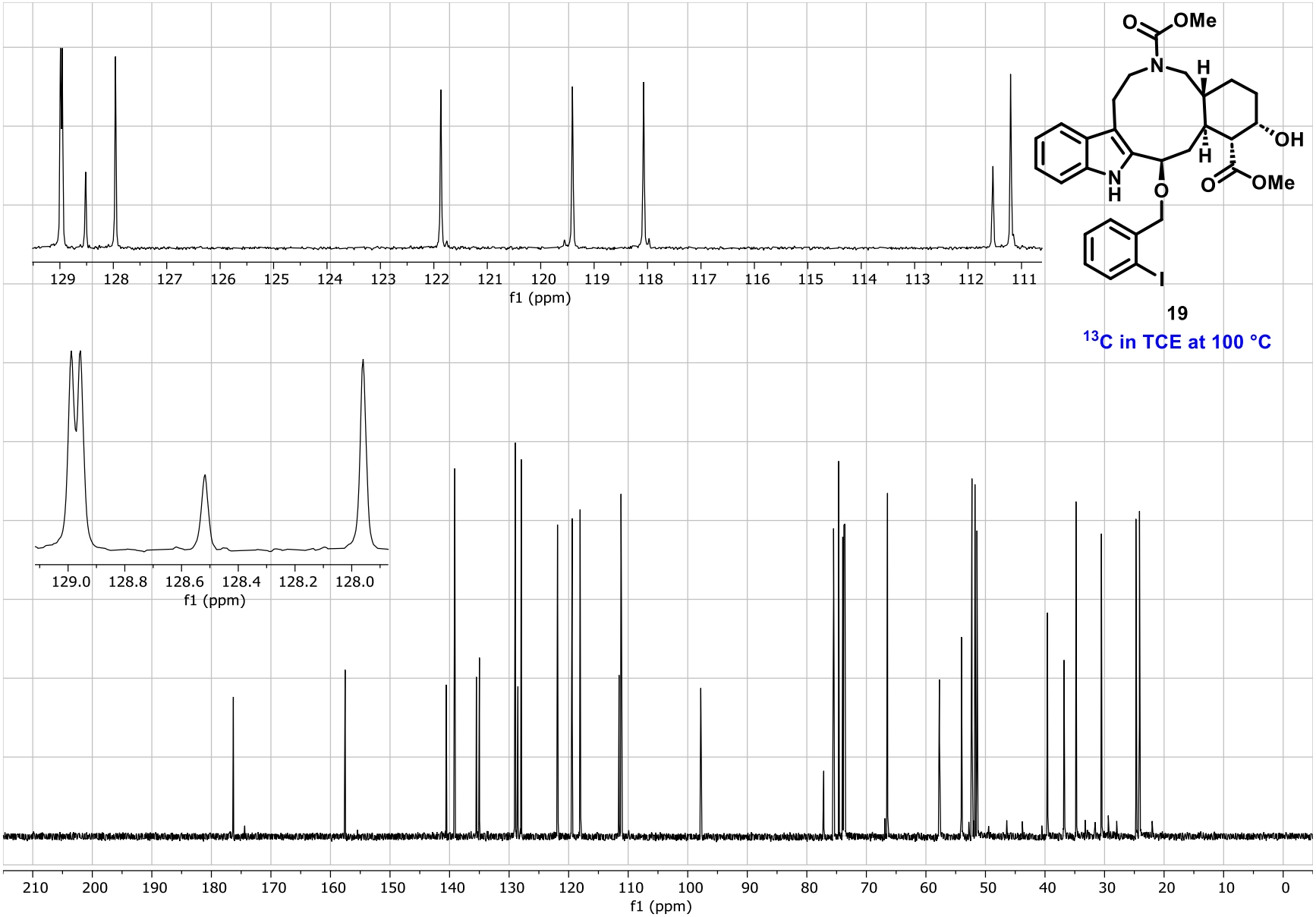


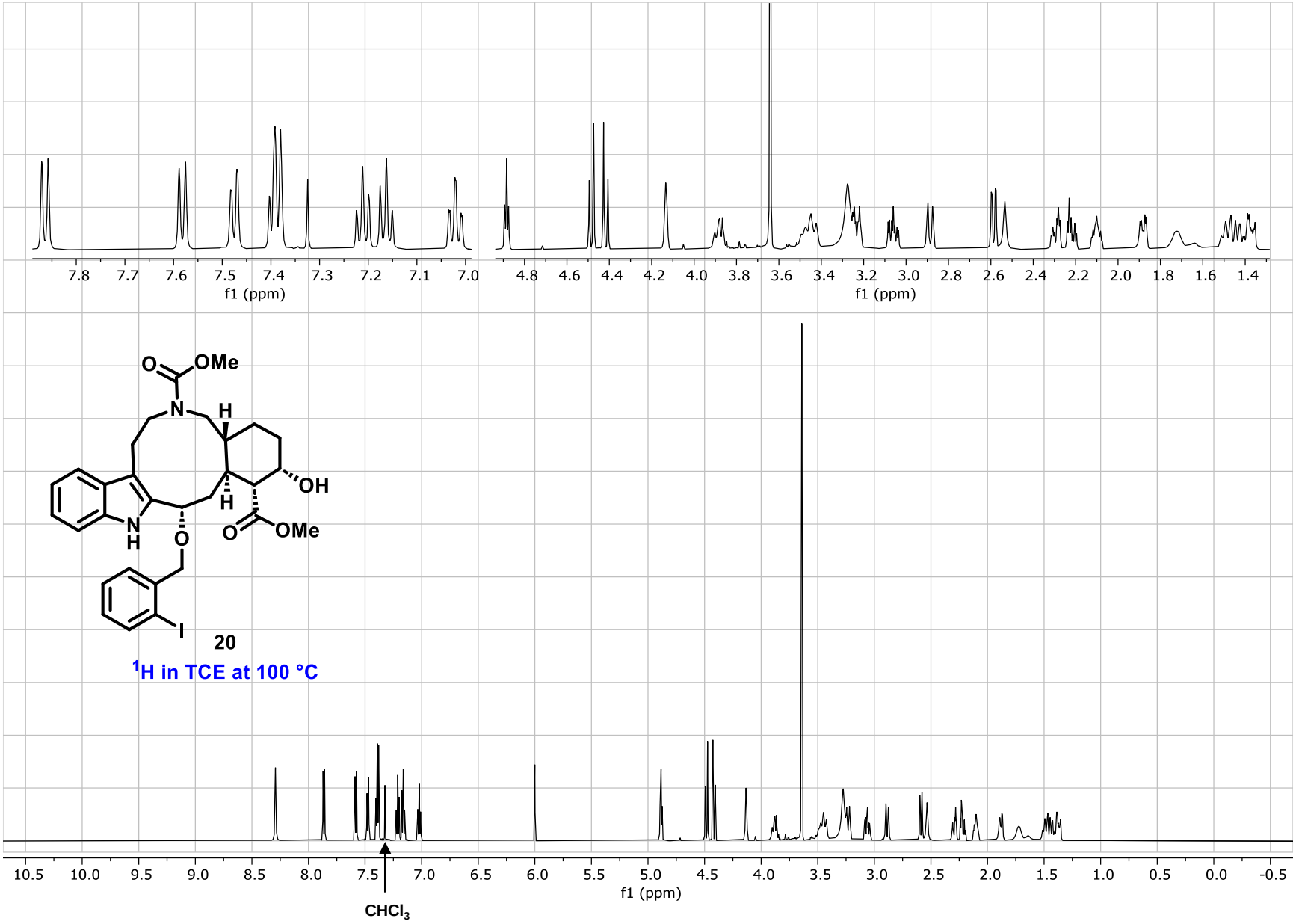
Compound 14: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 2)

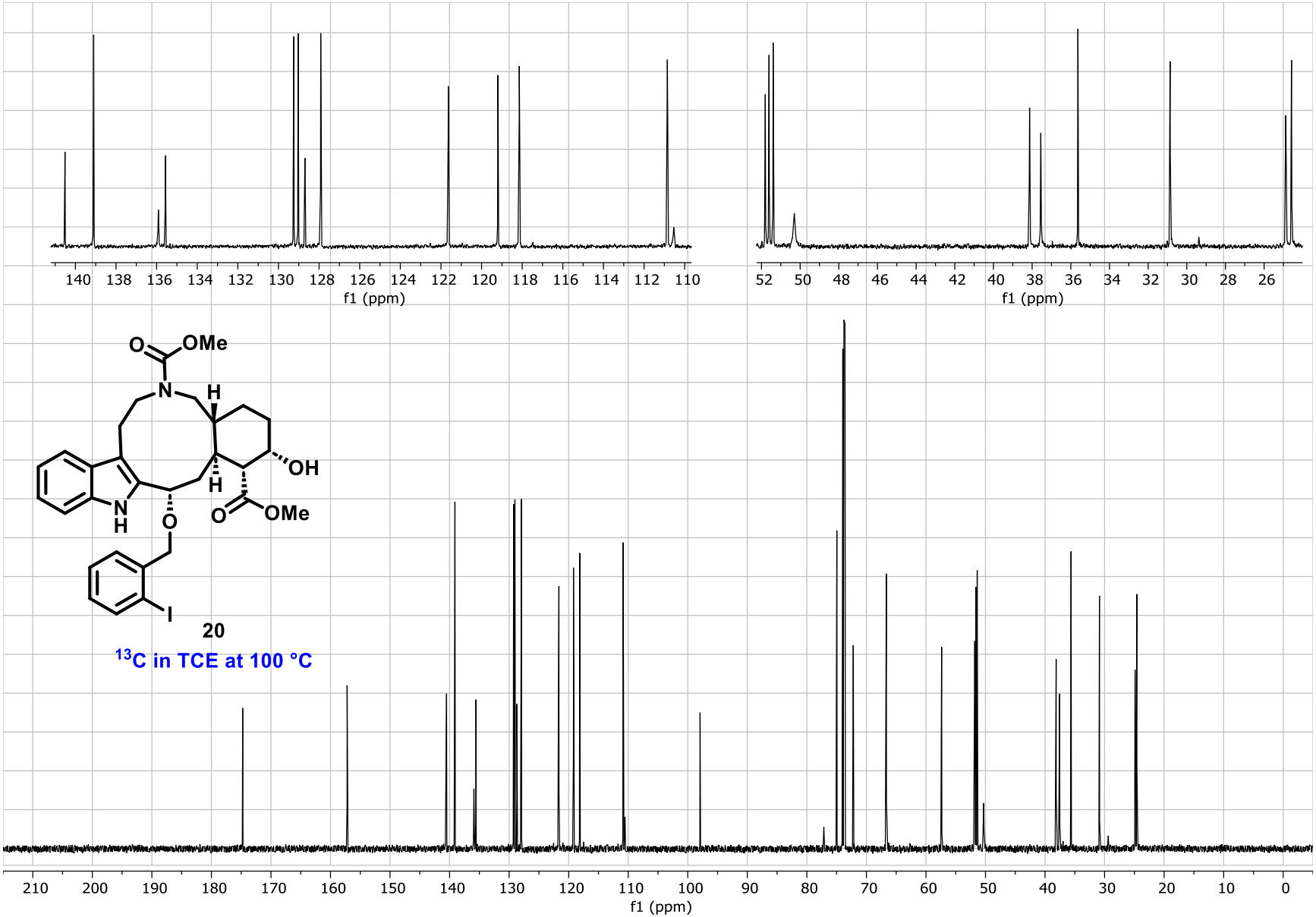


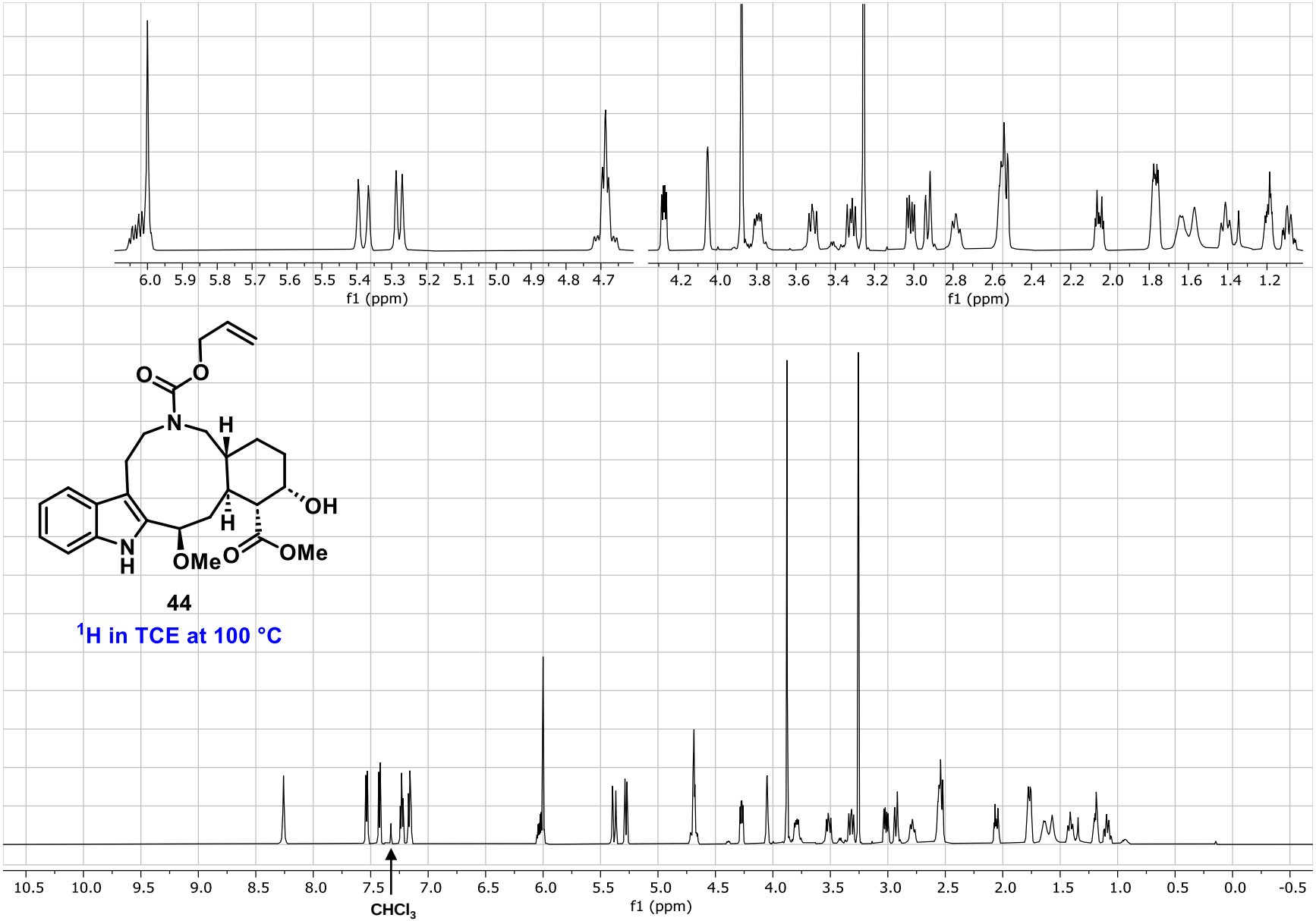
Compound 14: NOE,
T = 100 °C, $C_2D_2Cl_4$

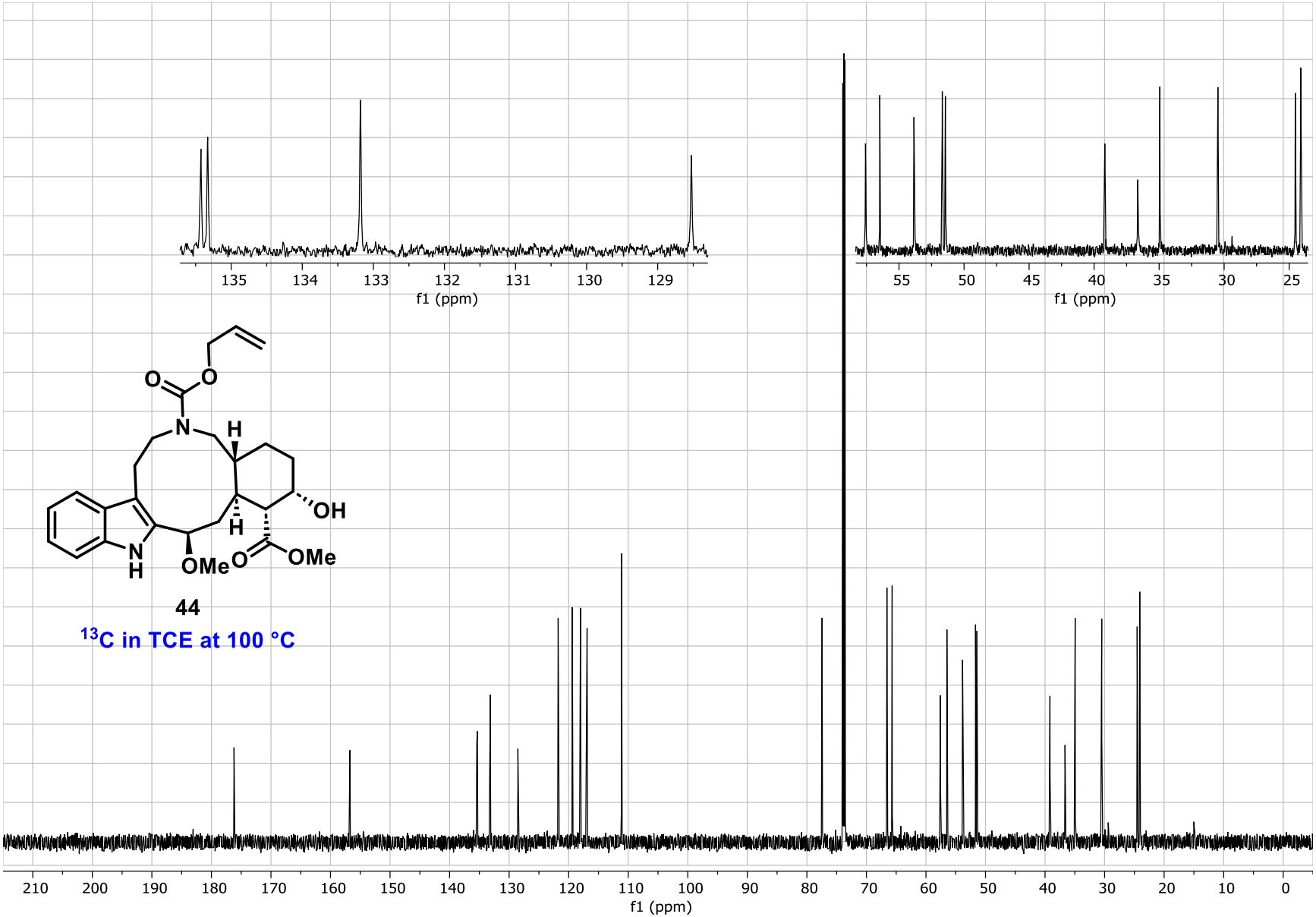

8.4 8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0
f1 (ppm)
4.5 4.4 4.3 4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6
f1 (ppm)
O
OMe
N
H
OH
H
N
H
O
O
OMe
I
19
1H in TCE at 100 °C
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
CHCl3
f1 (ppm)

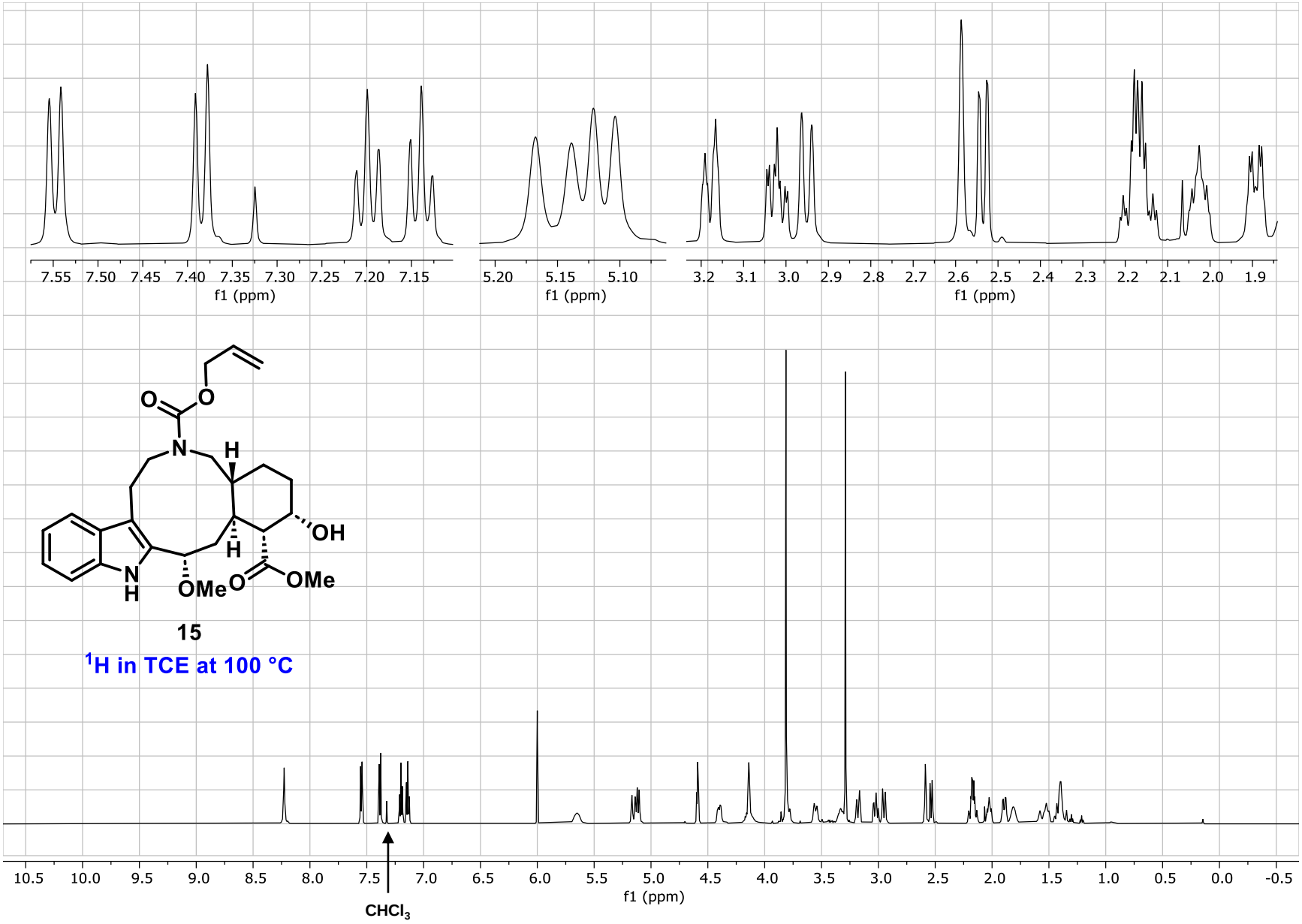

OMe
N
H
OH
H
N
H
O
O
OMe
I
19
13C in TCE at 100 °C
129 128 127 126 125 124 123 122 121 120 119 118 117 116 115 114 113 112 111
f1 (ppm)
129.0 128.8 128.6 128.4 128.2 128.0
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

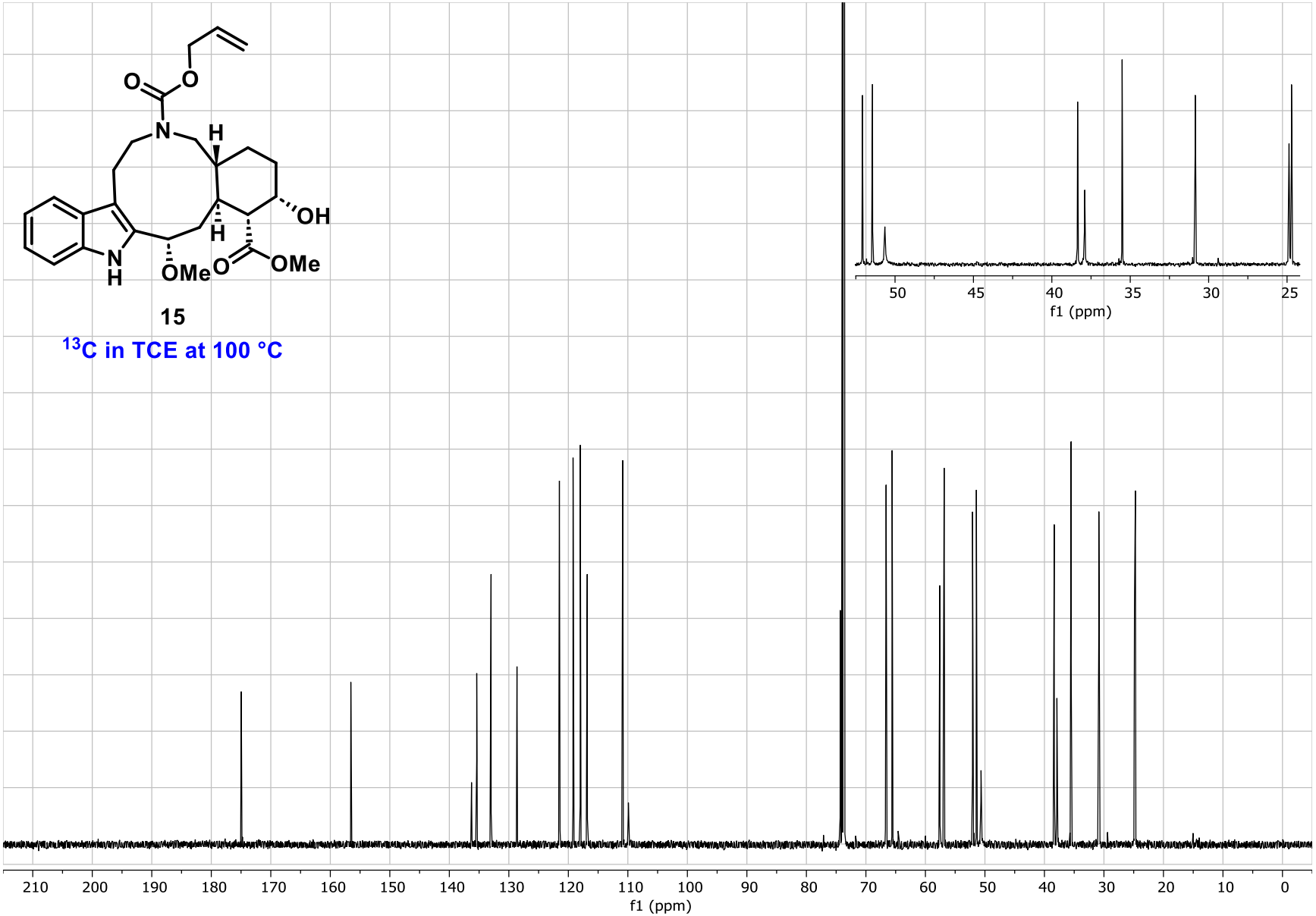

7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0
f1 (ppm)
4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4
f1 (ppm)
O
OMe
N
H
OH
H
N
H
O
O
OMe
I
20
1H in TCE at 100 °C
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)
CHCl3

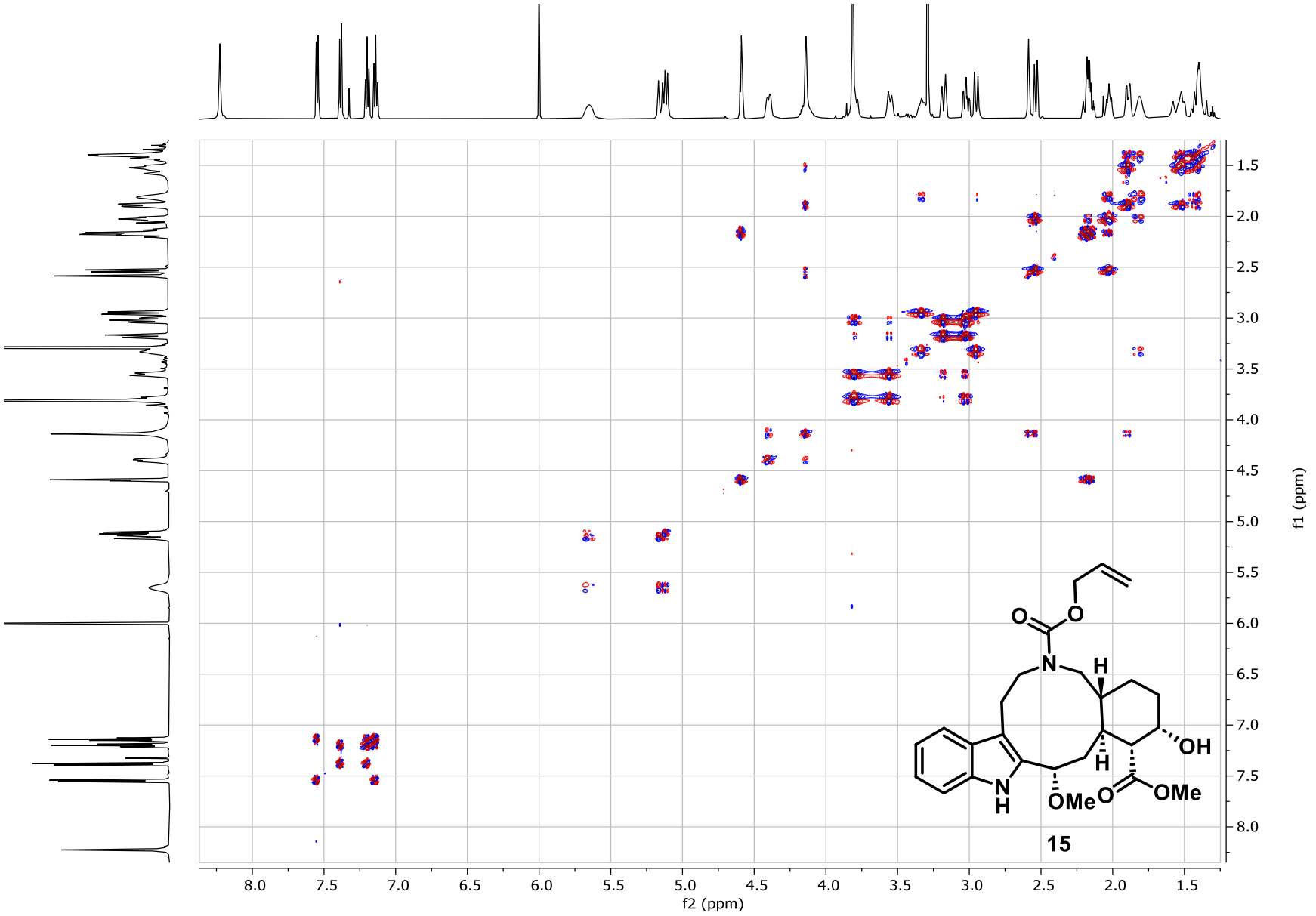

f1 (ppm)
f1 (ppm)
f1 (ppm)
20
13C in TCE at 100 °C


6.0 5.9 5.8 5.7 5.6 5.5 5.4 5.3 5.2 5.1 5.0 4.9 4.8 4.7
f1 (ppm)
4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2
f1 (ppm)
O
O
N
H
OH
H
N
H
OMe
O
OMe
44
1H in TCE at 100 °C
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
CHCl3
f1 (ppm)

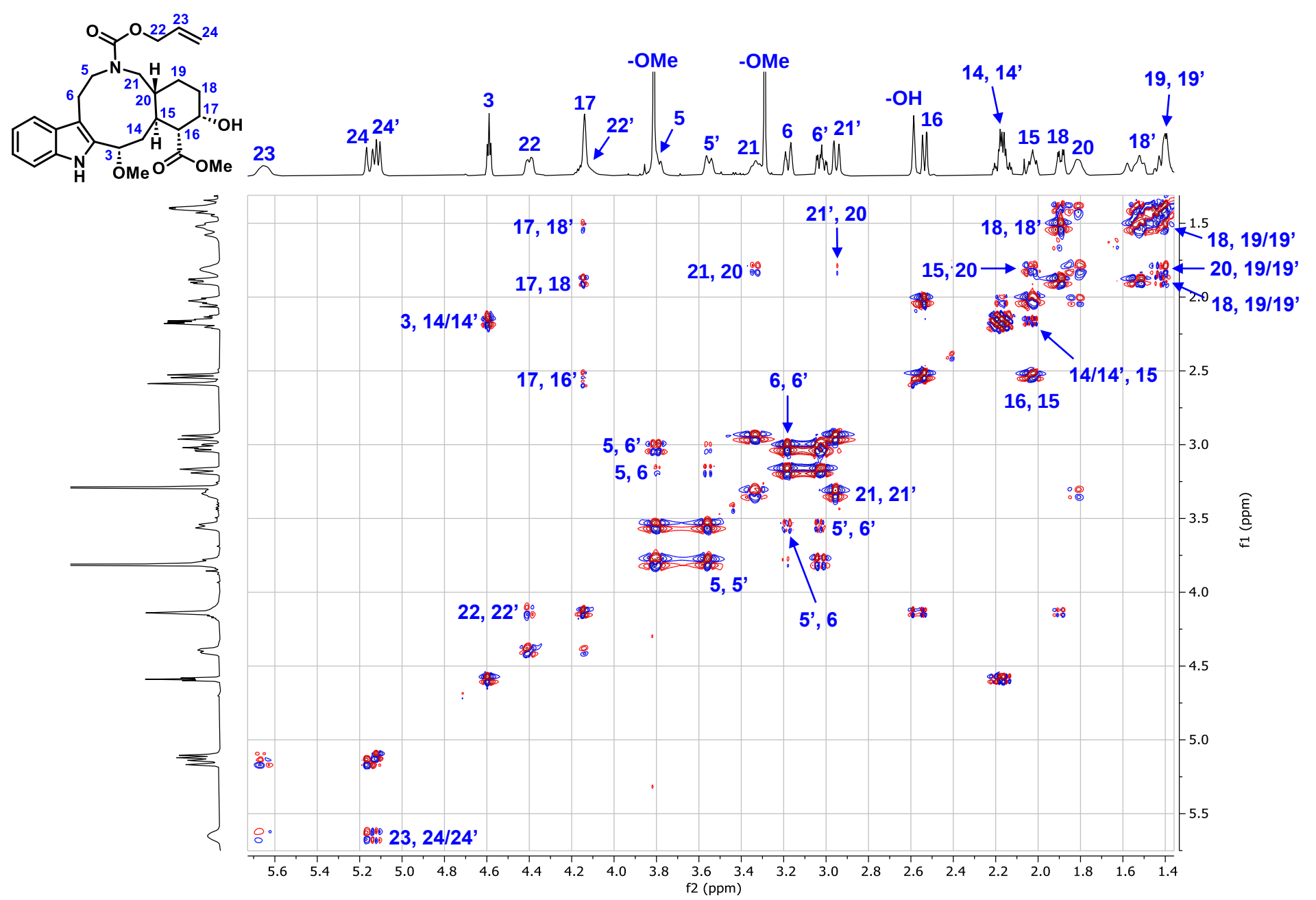

135 134 133 132 131 130 129
f1 (ppm)
55 50 45 40 35 30 25
f1 (ppm)
O
O
N
H
H
OH
N
H
OMe
O
OMe
44
13C in TCE at 100 °C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.55 7.50 7.45 7.40 7.35 7.30 7.25 7.20 7.15
f1 (ppm)
5.20 5.15 5.10
f1 (ppm)
3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9
f1 (ppm)
O
O
N
H
OH
H
N
H
OMe
O
OMe
15
1H in TCE at 100 °C
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)
CHCl3

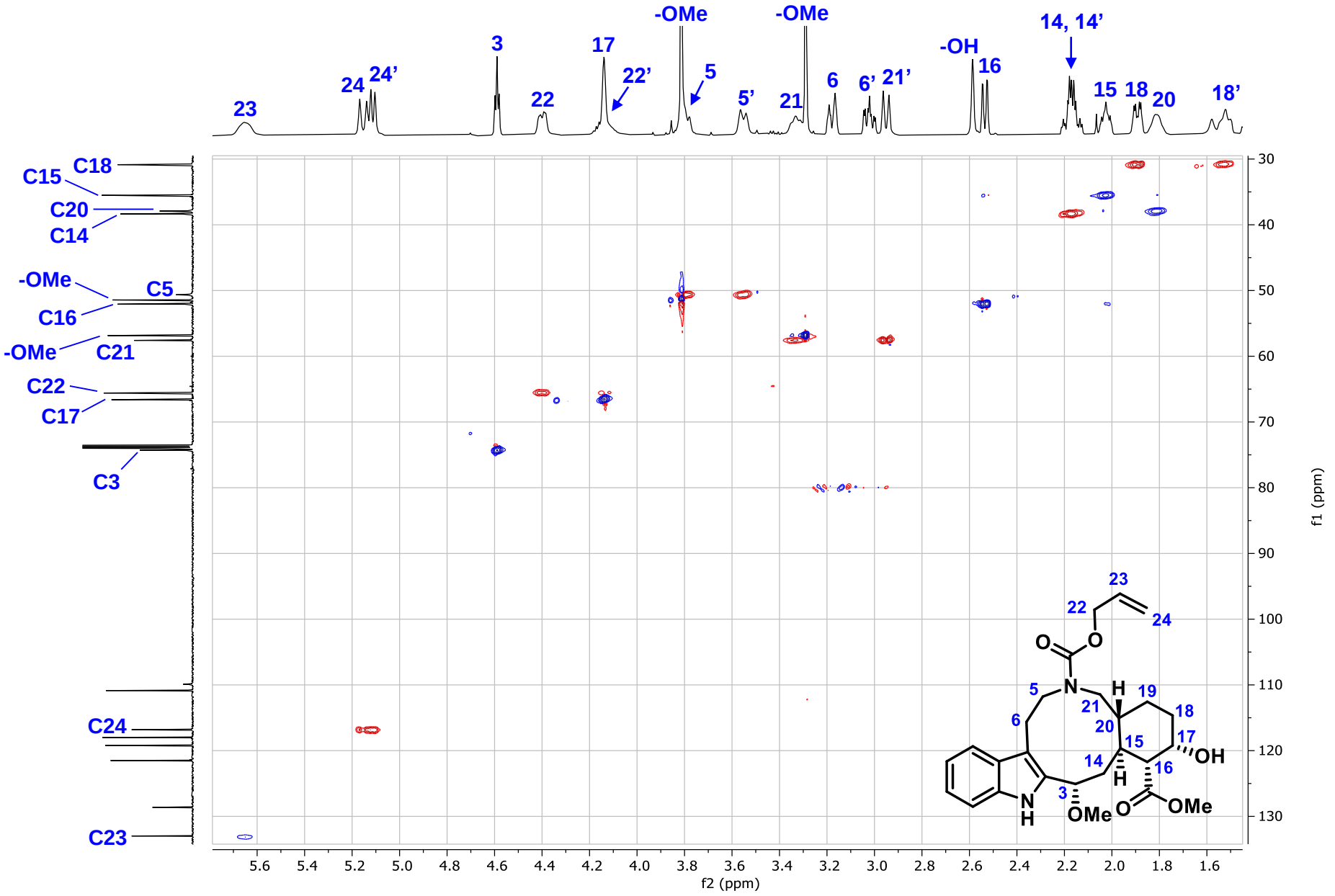

O
O
N
H
OH
H
N
H
OMe
O
OMe
15
13C in TCE at 100 °C
50
45
40
35
30
25
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



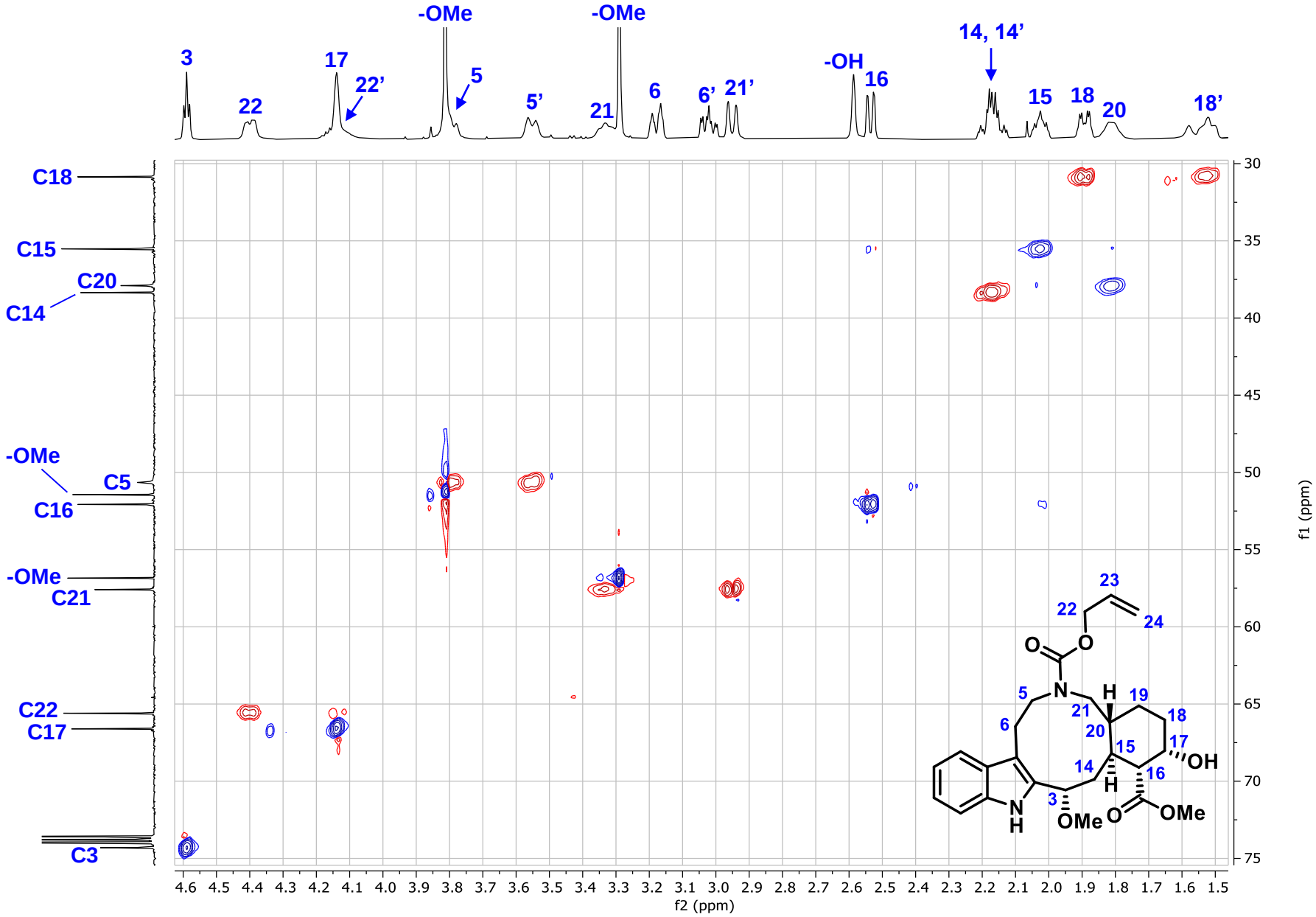
Compound 15: COSY, T = 100 °C,
$C_2D_2Cl_4$ (full)



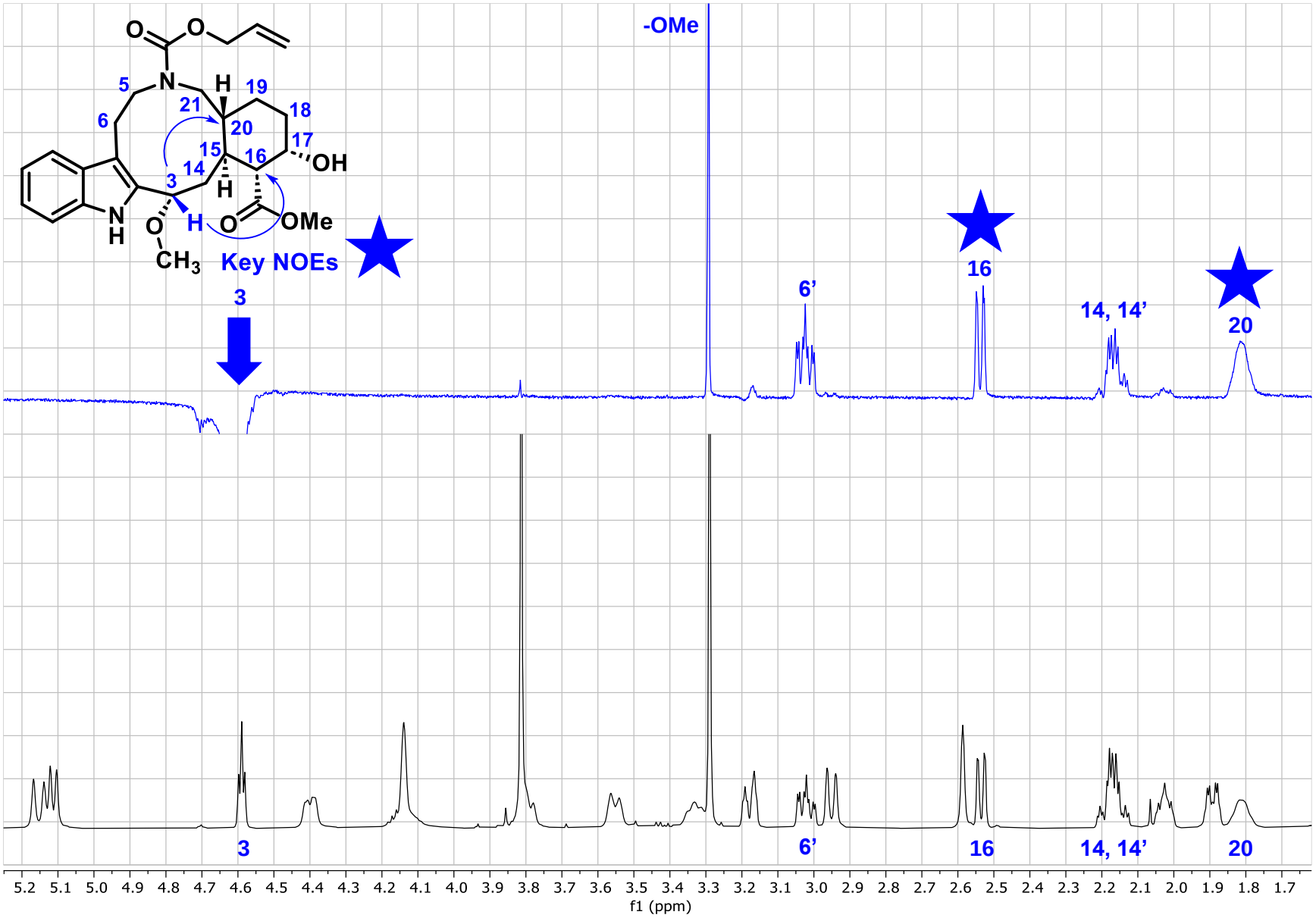
Compound 15: COSY, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in)



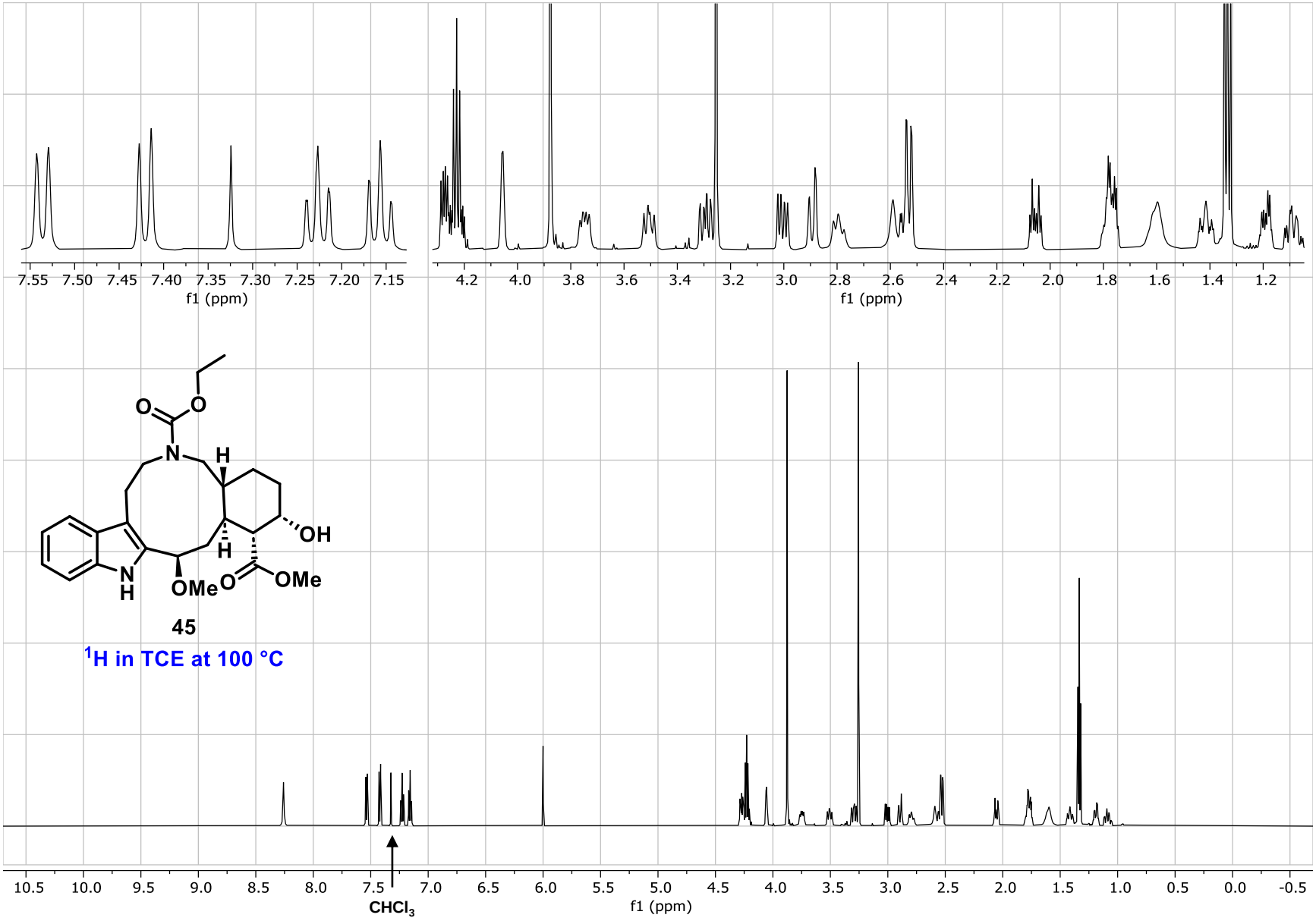
Compound 15: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 1)

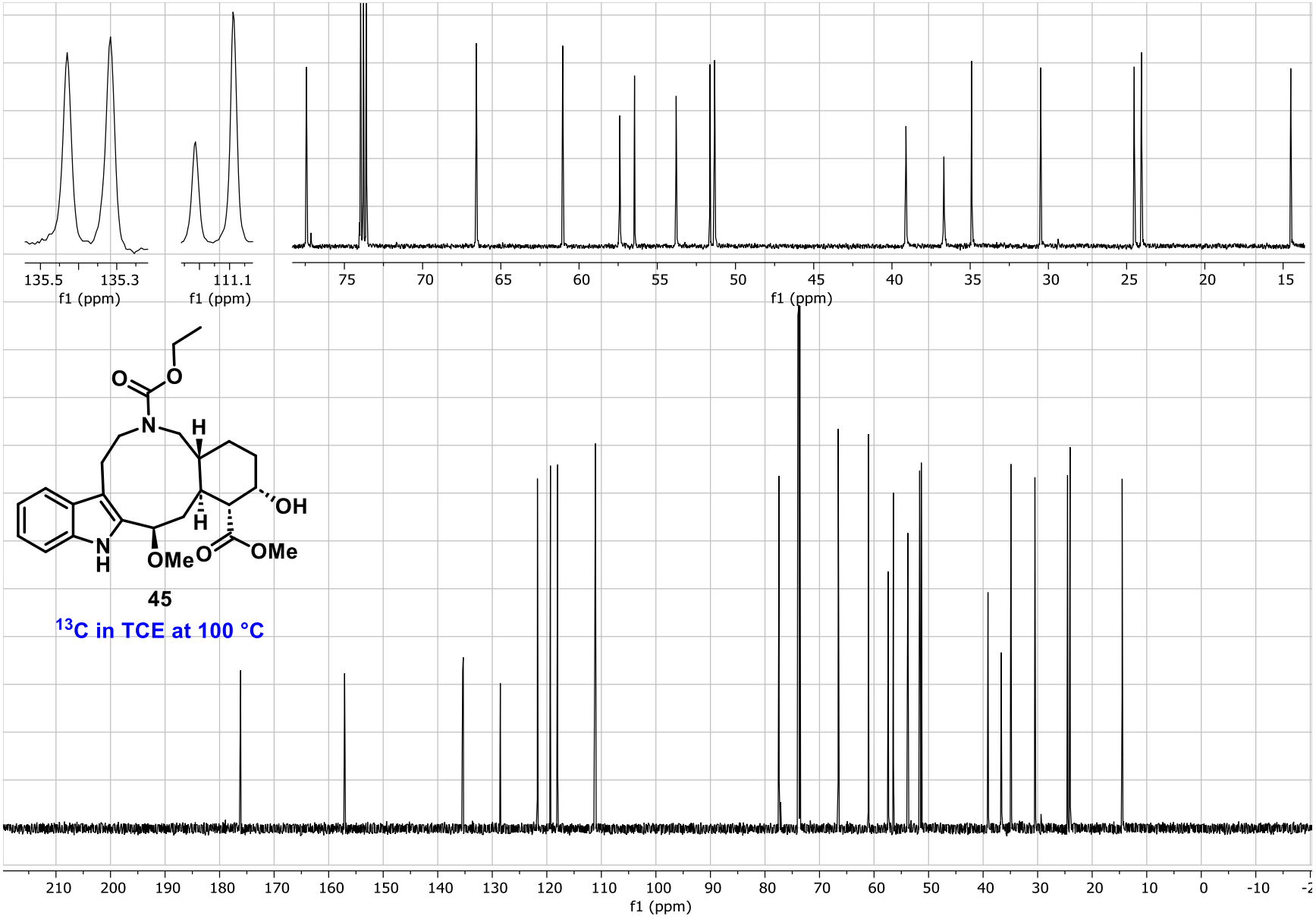


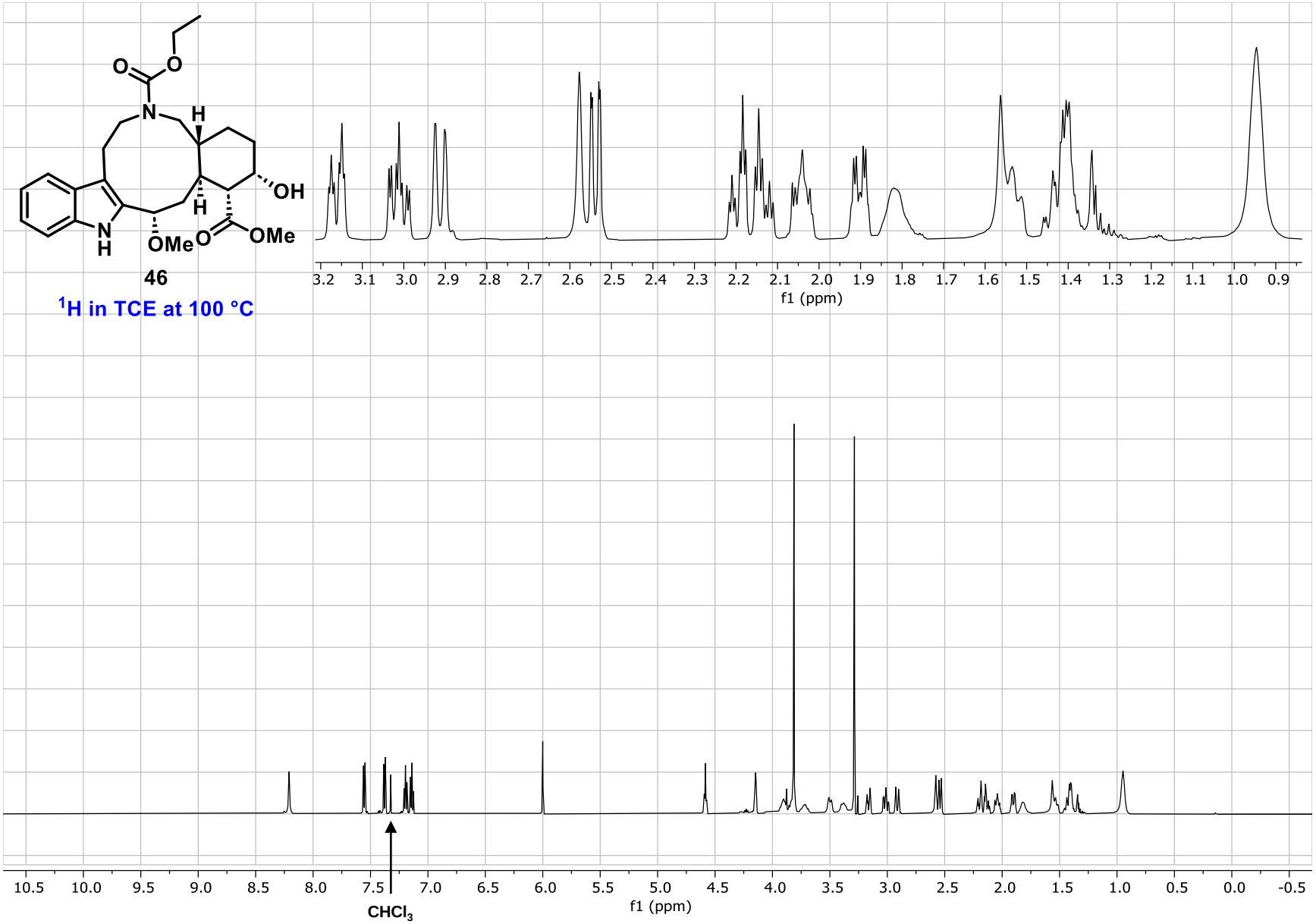
Compound 15: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 2)

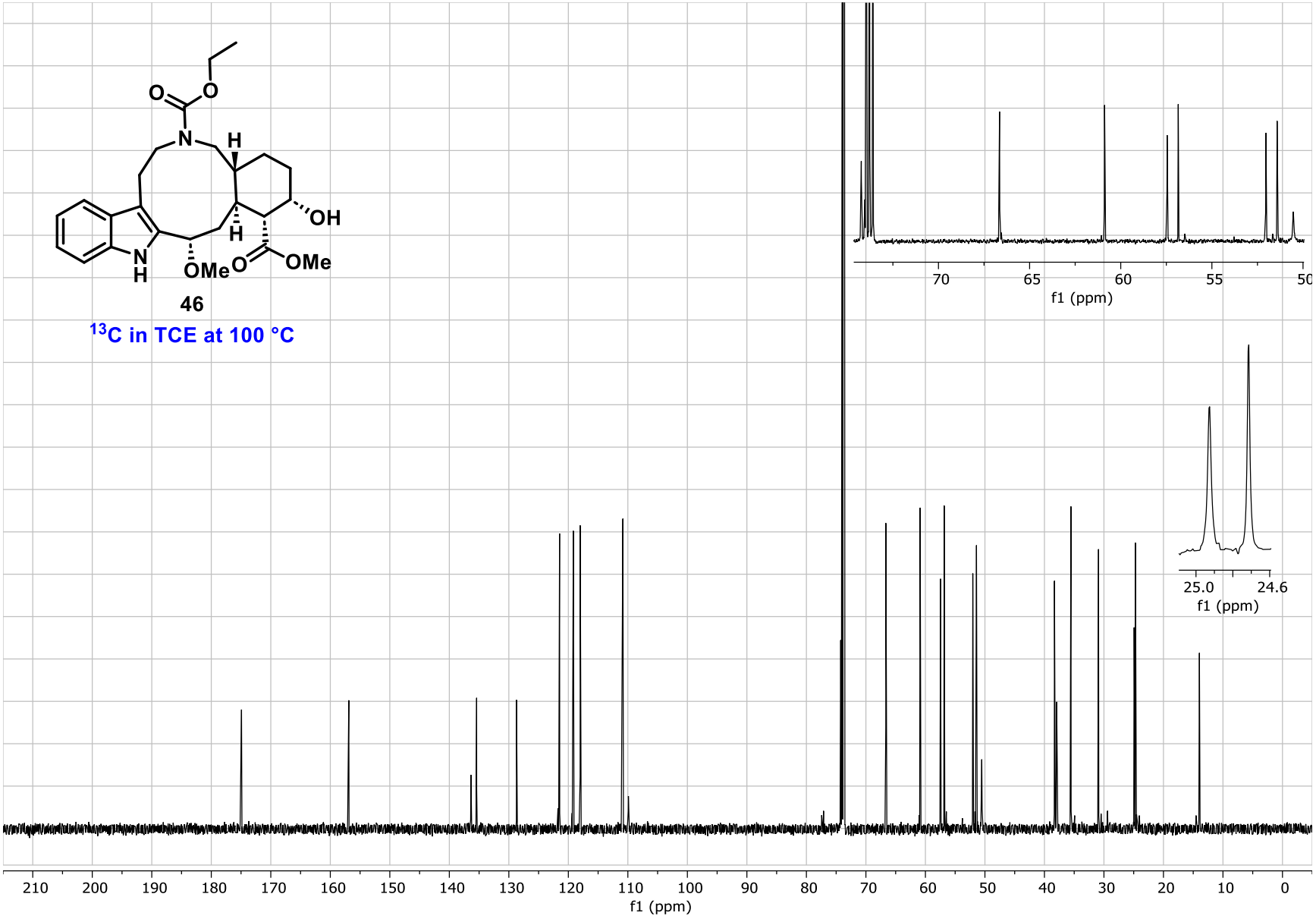


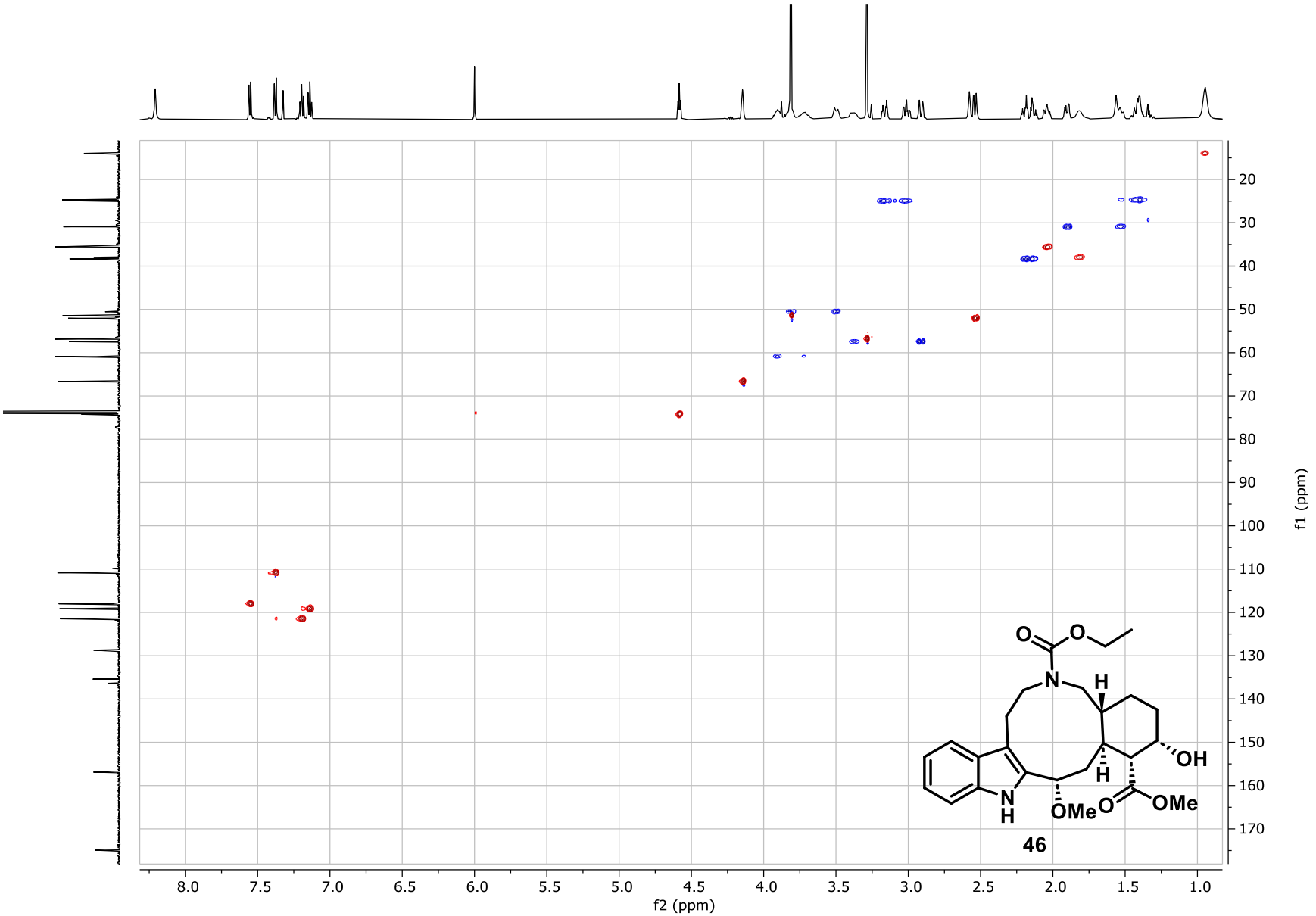
Compound 15: NOE, T = 100 °C, $C_2D_2Cl_4$


7.55 7.50 7.45 7.40 7.35 7.30 7.25 7.20 7.15
f1 (ppm)
4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2
f1 (ppm)
O
O
N
H
OH
H
N
H
OMe
O
OMe
45
1H in TCE at 100 °C
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
CHCl3
f1 (ppm)

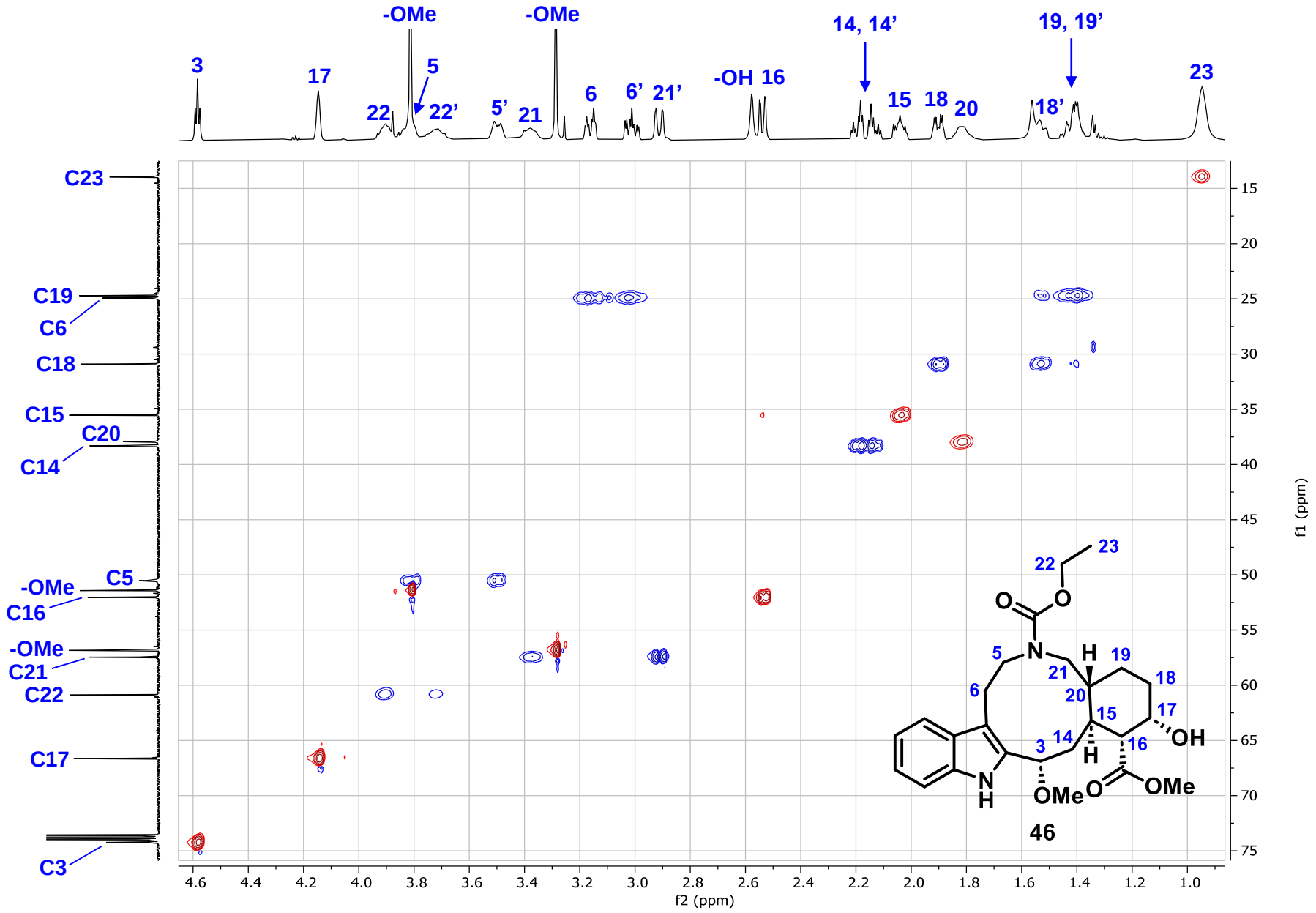

135.5
135.3
f1 (ppm)
111.1
f1 (ppm)
75
70
65
60
55
50
45
40
35
30
25
20
15
f1 (ppm)
O
O
N
H
OH
H
N
H
OMe
O
OMe
45
13C in TCE at 100 °C
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


O
O
N
H
OH
H
N
H
OMe
O
OMe
46
1H in TCE at 100 °C
3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9
f1 (ppm)
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
CHCl3
f1 (ppm)

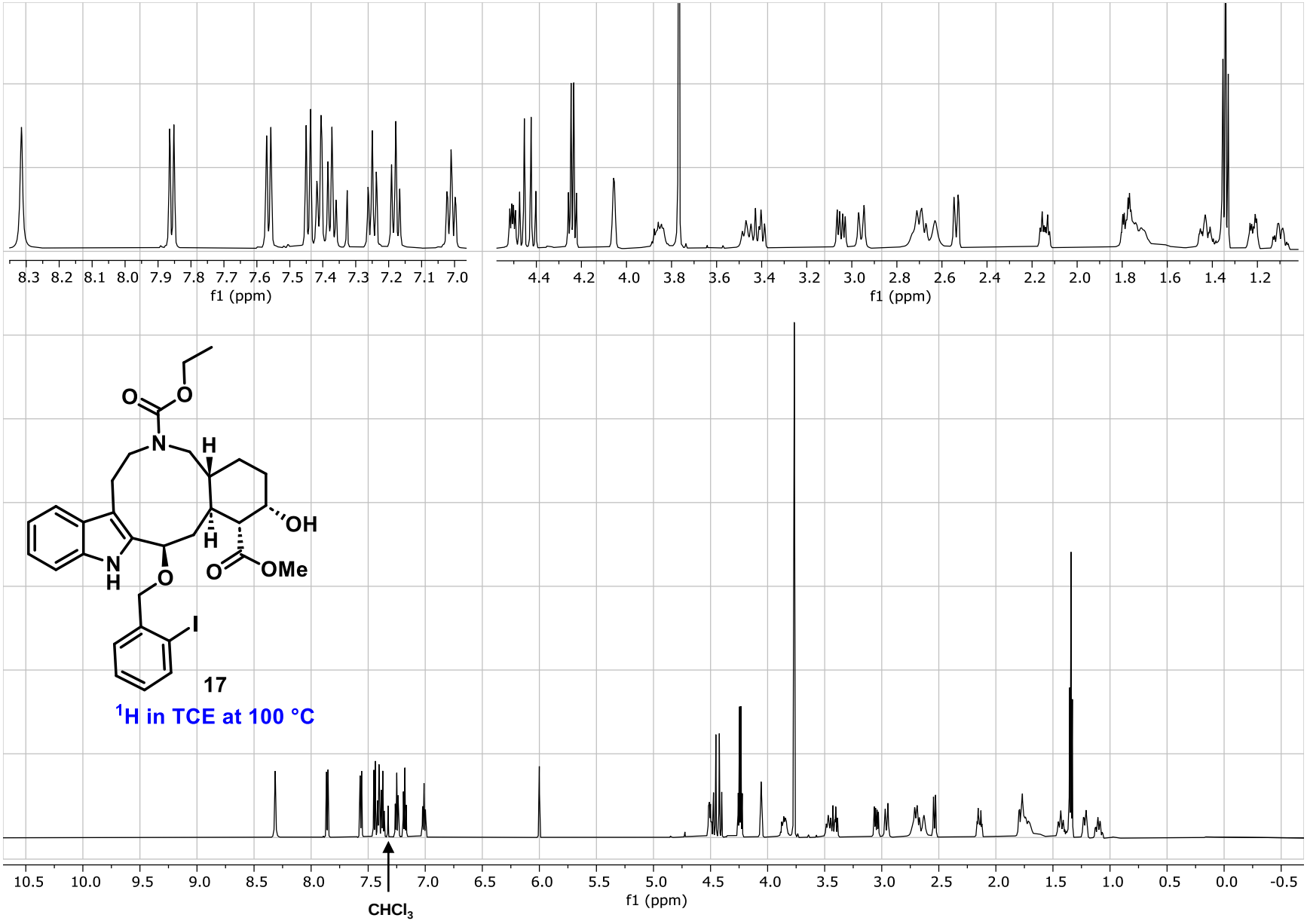

46
13C in TCE at 100 °C
f1 (ppm)
f1 (ppm)
f1 (ppm)

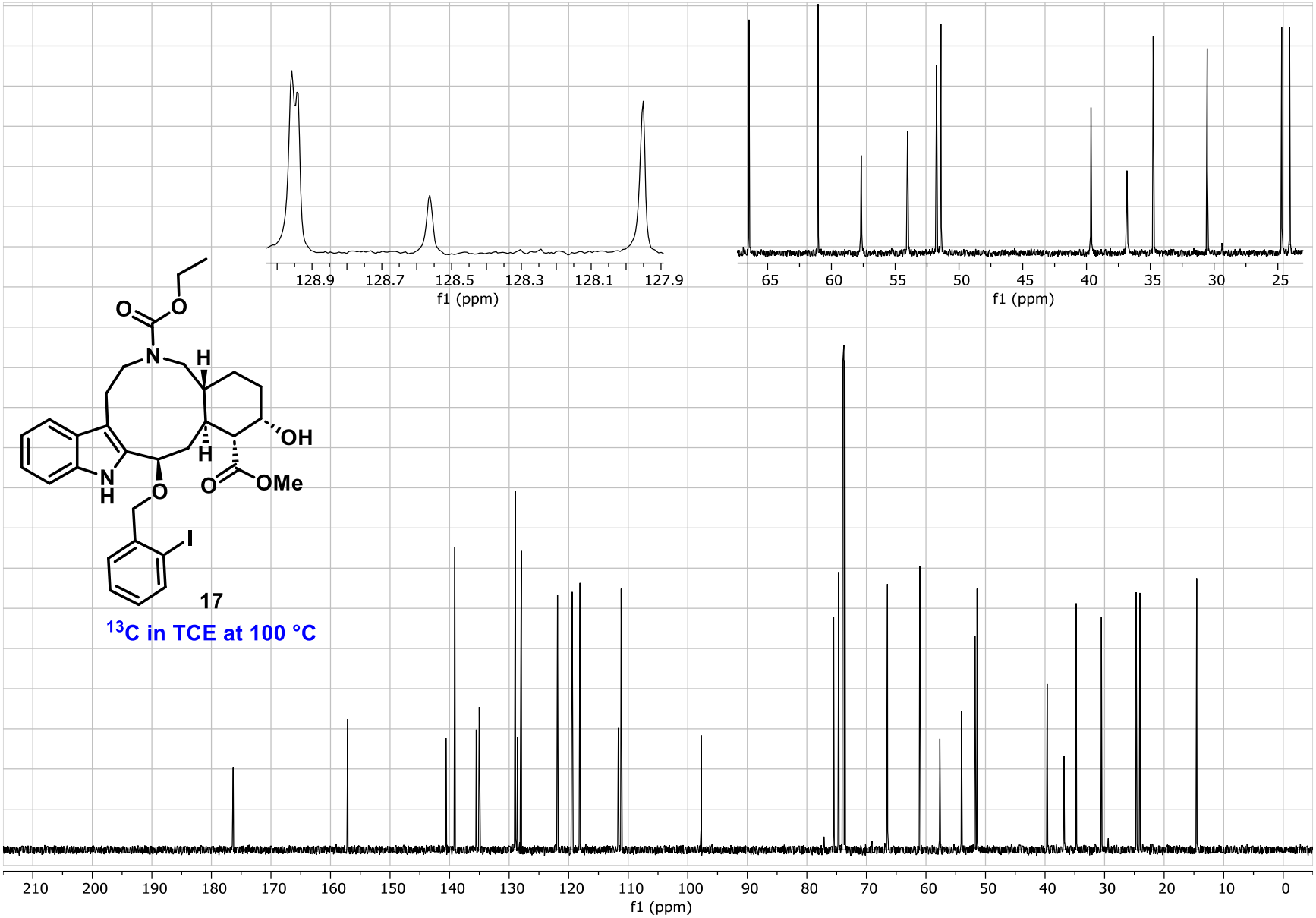


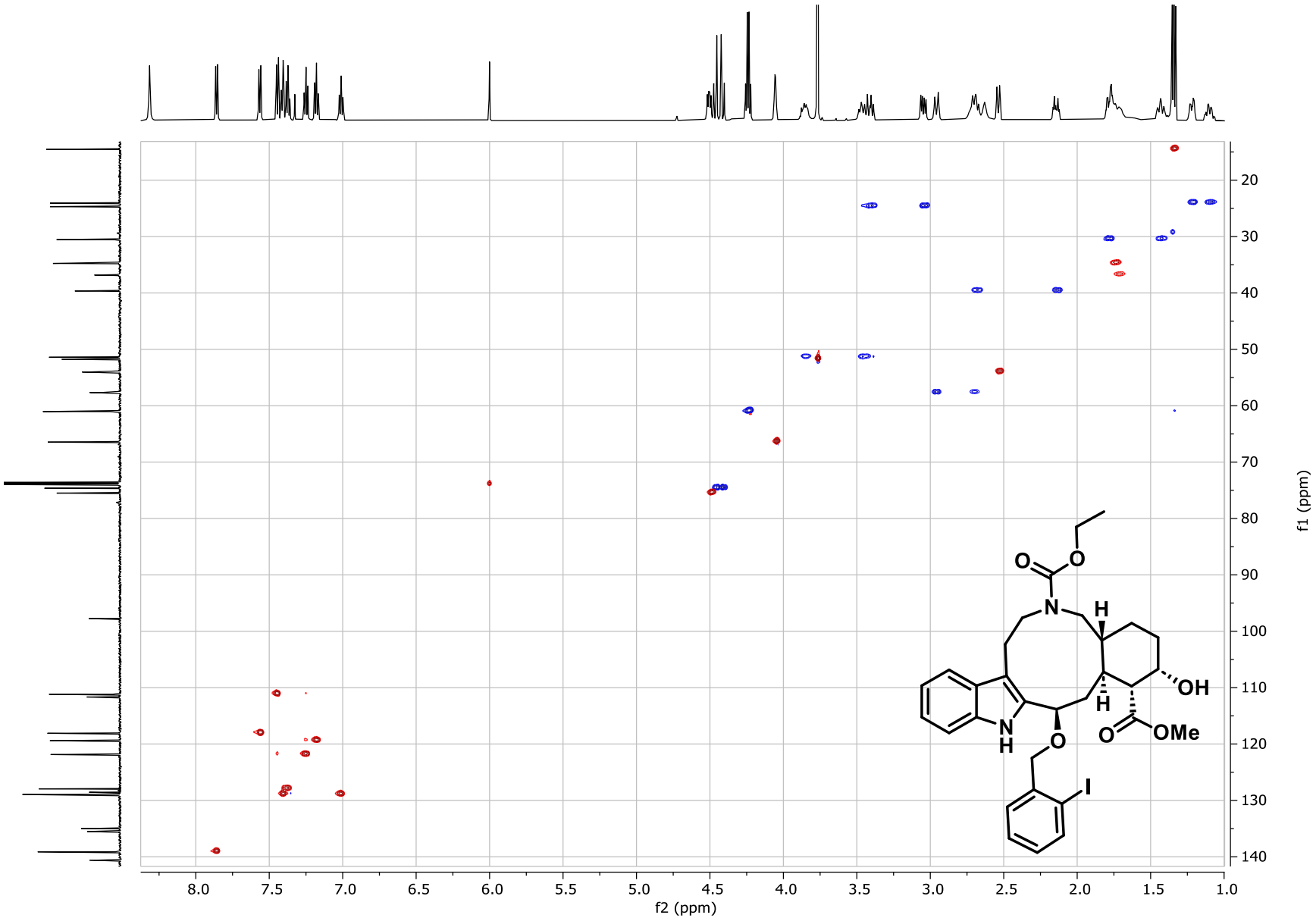
Compound 46: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (full)



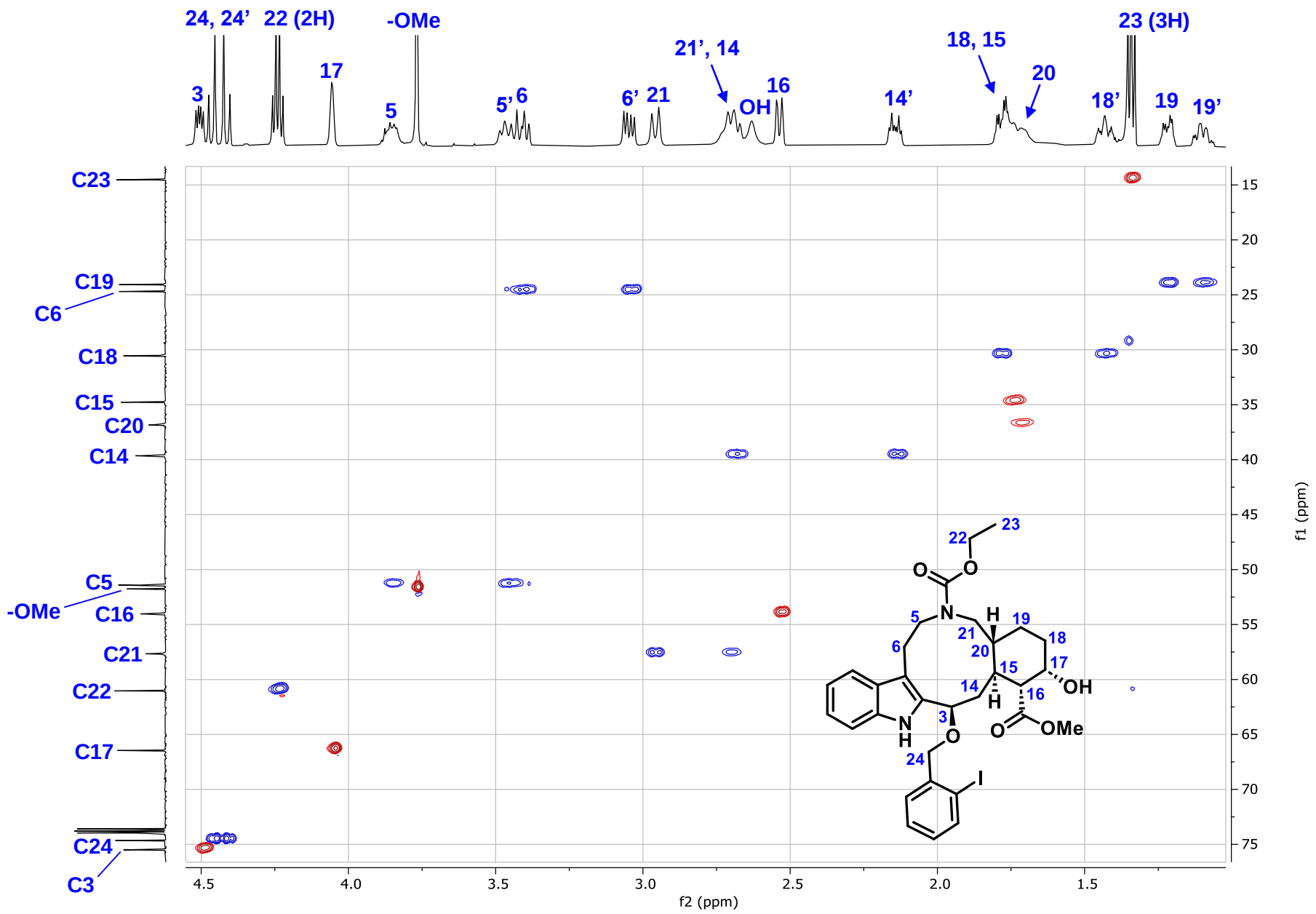
Compound 46: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in)


8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0
f1 (ppm)
4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2
f1 (ppm)
O
O
N
H
OH
H
N
H
O
O
OMe
I
17
1H in TCE at 100 °C
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)
CHCl3

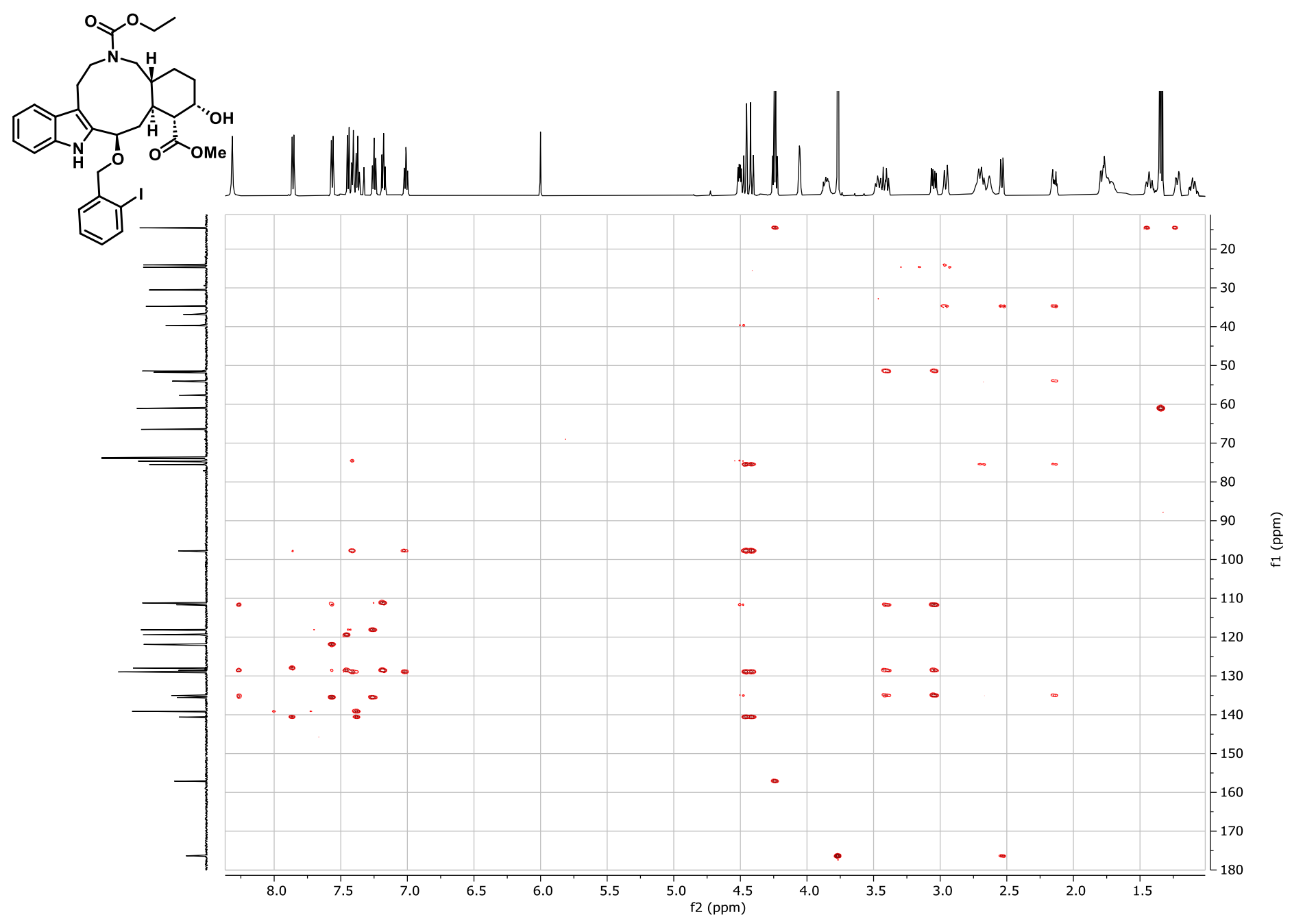

128.9
128.7
128.5
128.3
128.1
127.9
f1 (ppm)
65
60
55
50
45
40
35
30
25
f1 (ppm)
O
O
N
H
OH
H
N
H
O
O
OMe
I
17
13C in TCE at 100 °C
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



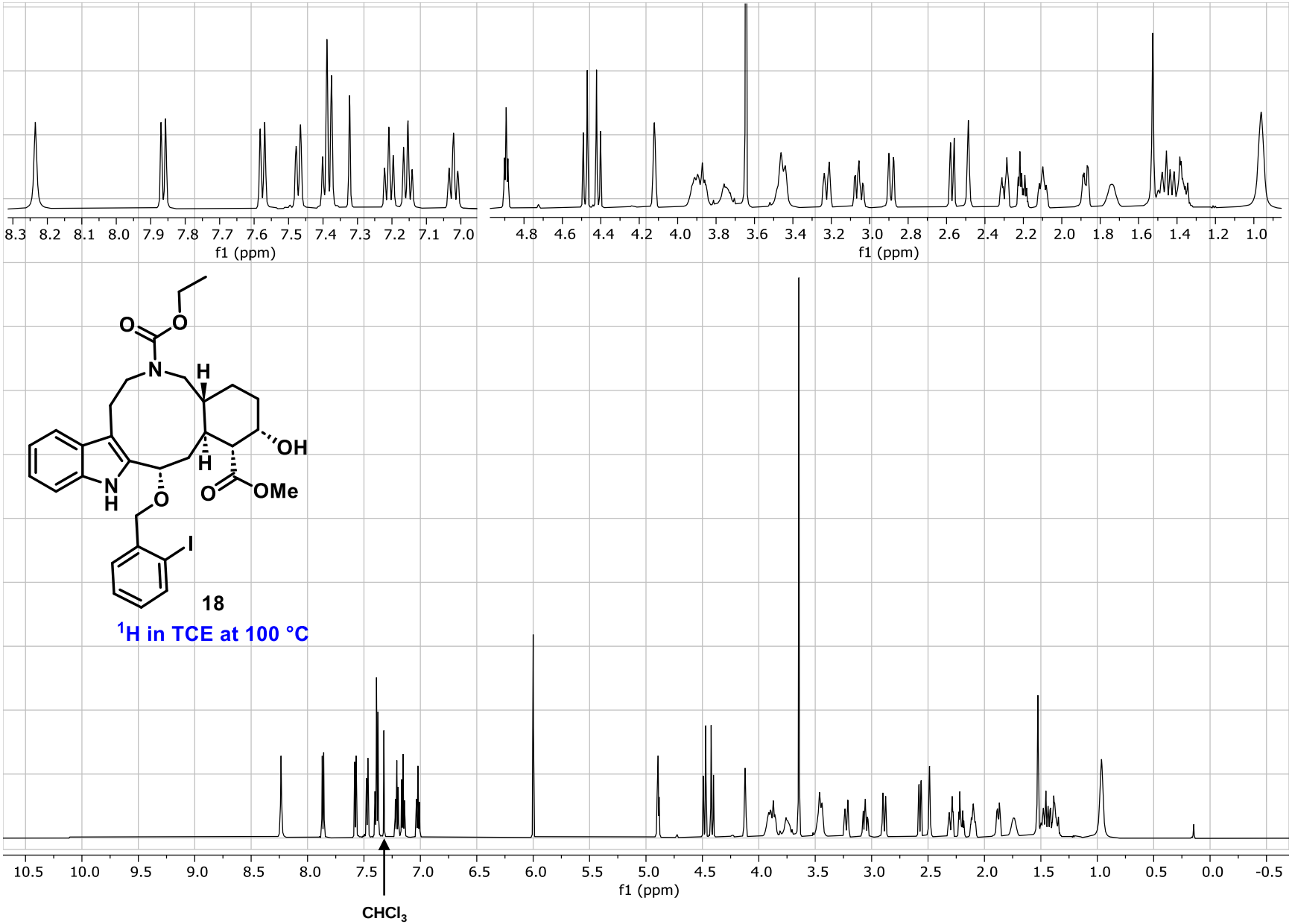
Compound 17: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (full)

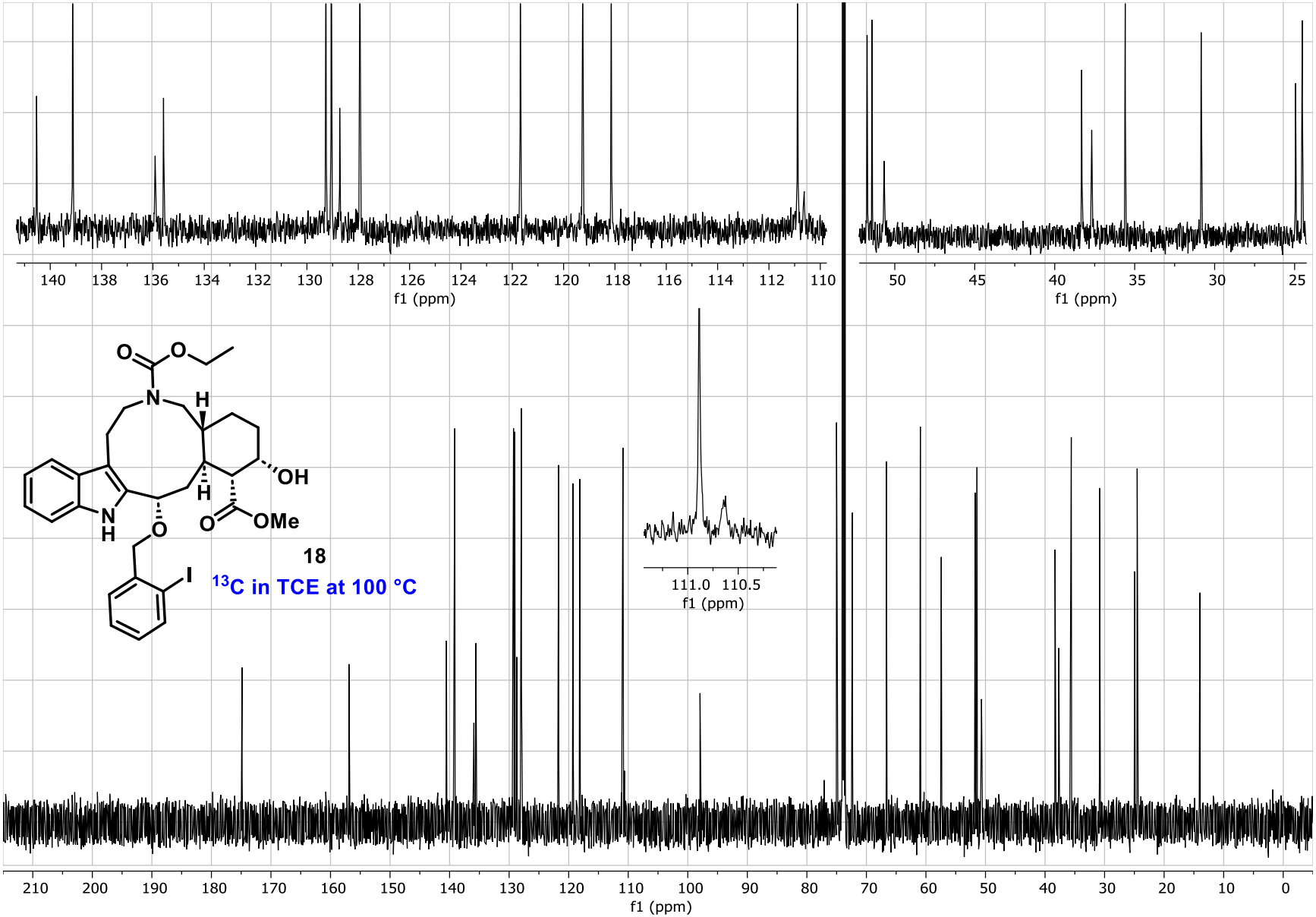


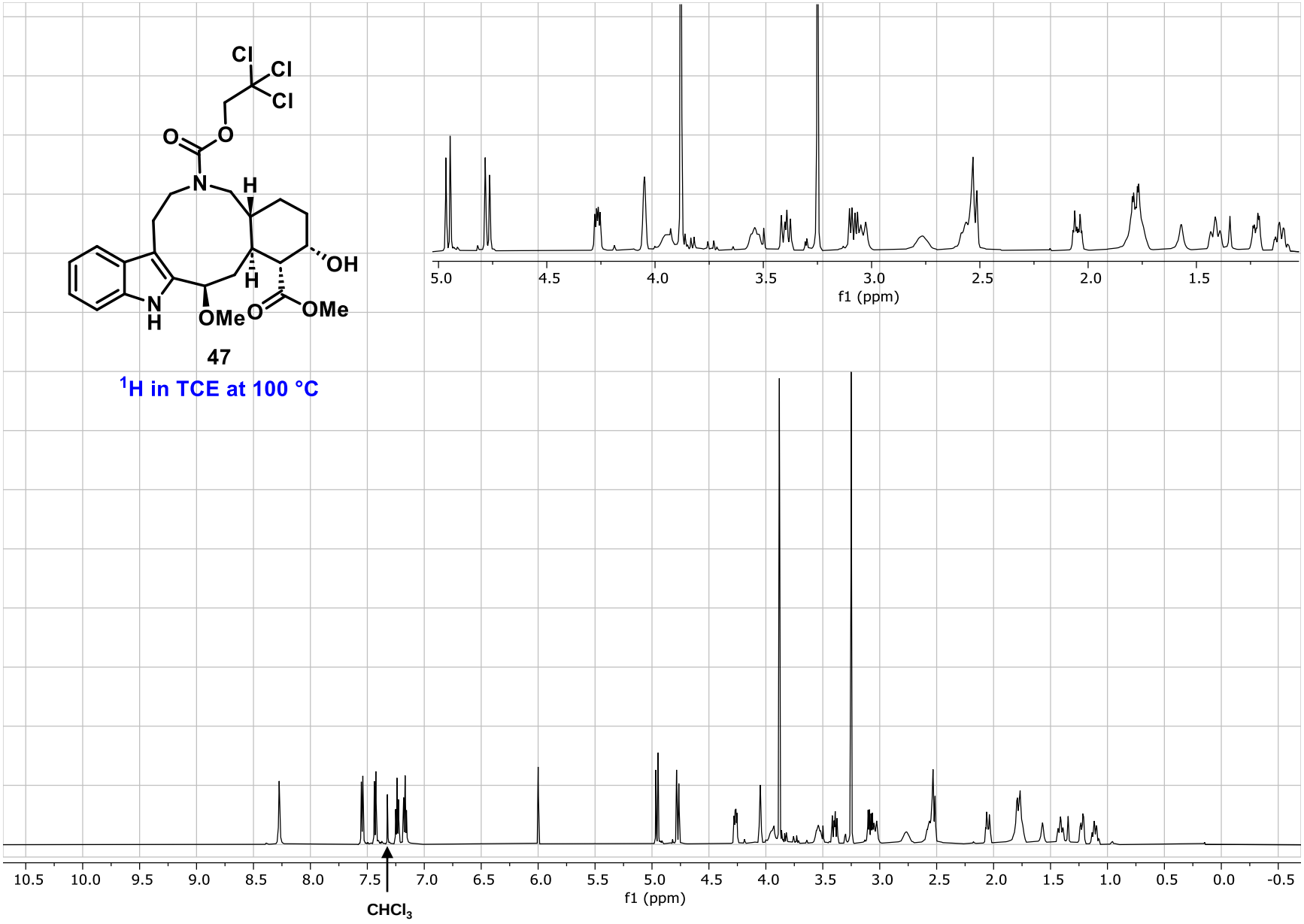
Compound 17: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in)

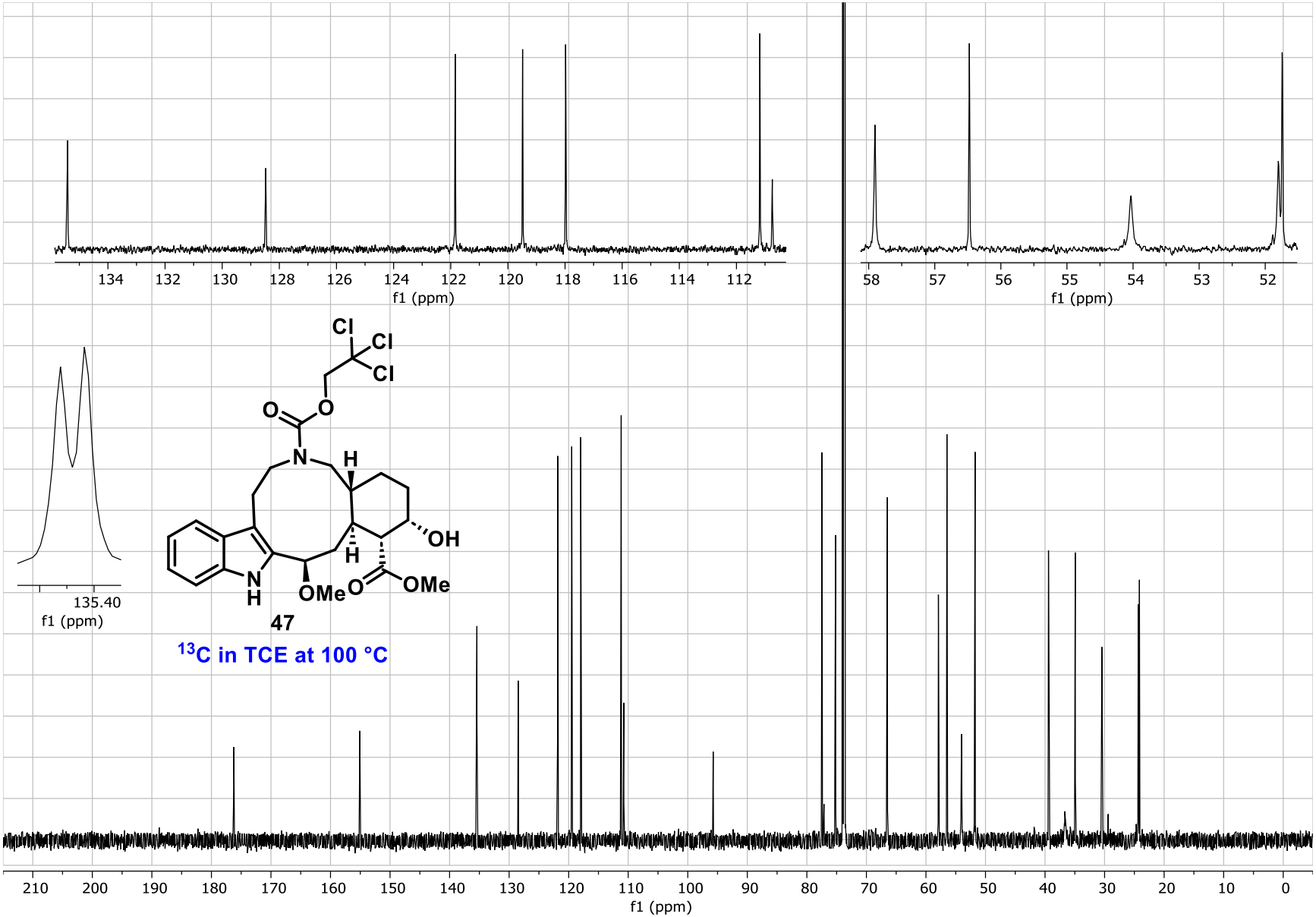


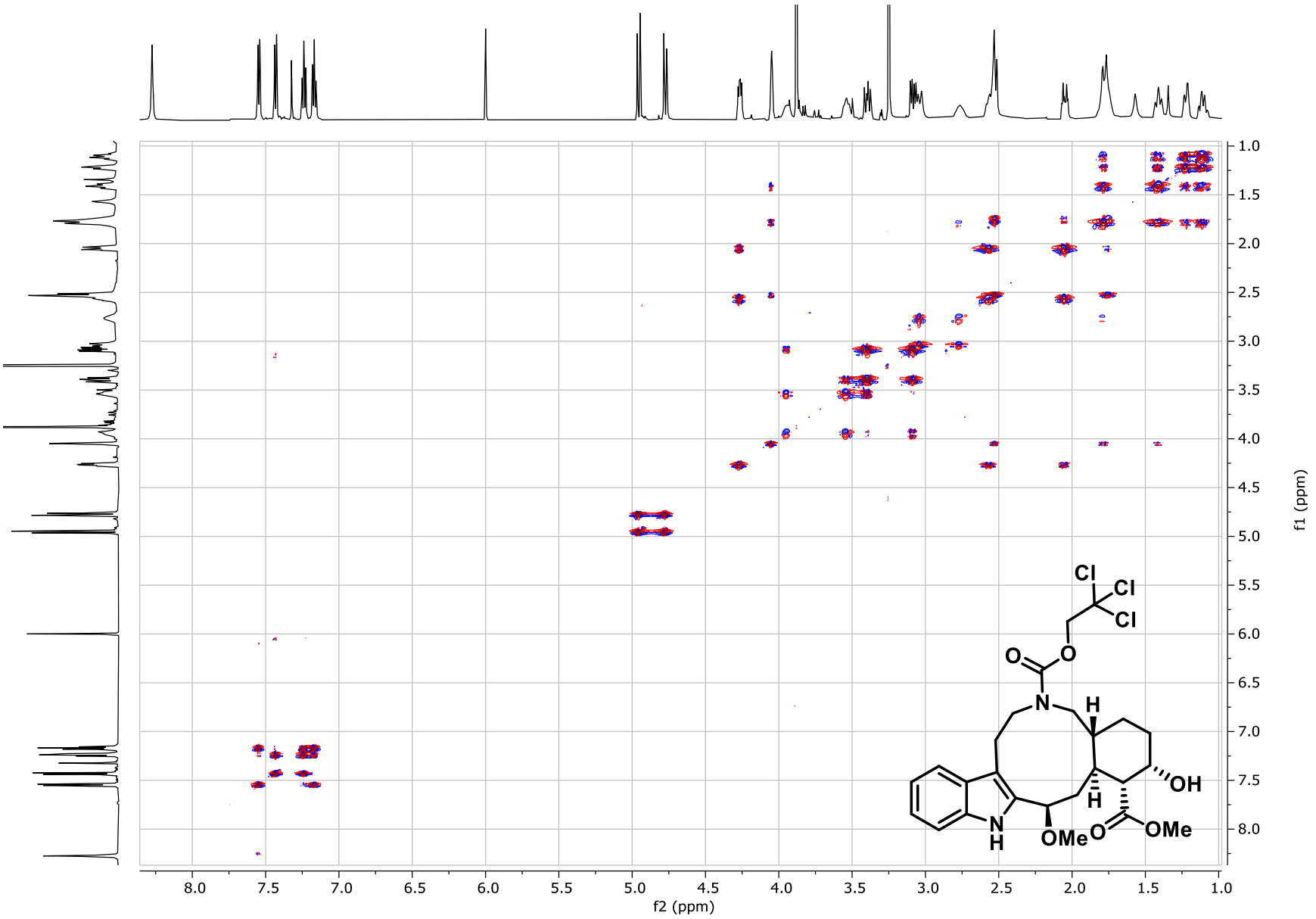
Compound 17: HMBC, T = 100 °C, $C_2D_2Cl_4$ (full)


8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0
f1 (ppm)
4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0
f1 (ppm)
O
O
N
H
OH
H
N
H
O
O
OMe
I
18
1H in TCE at 100 °C
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)
CHCl3

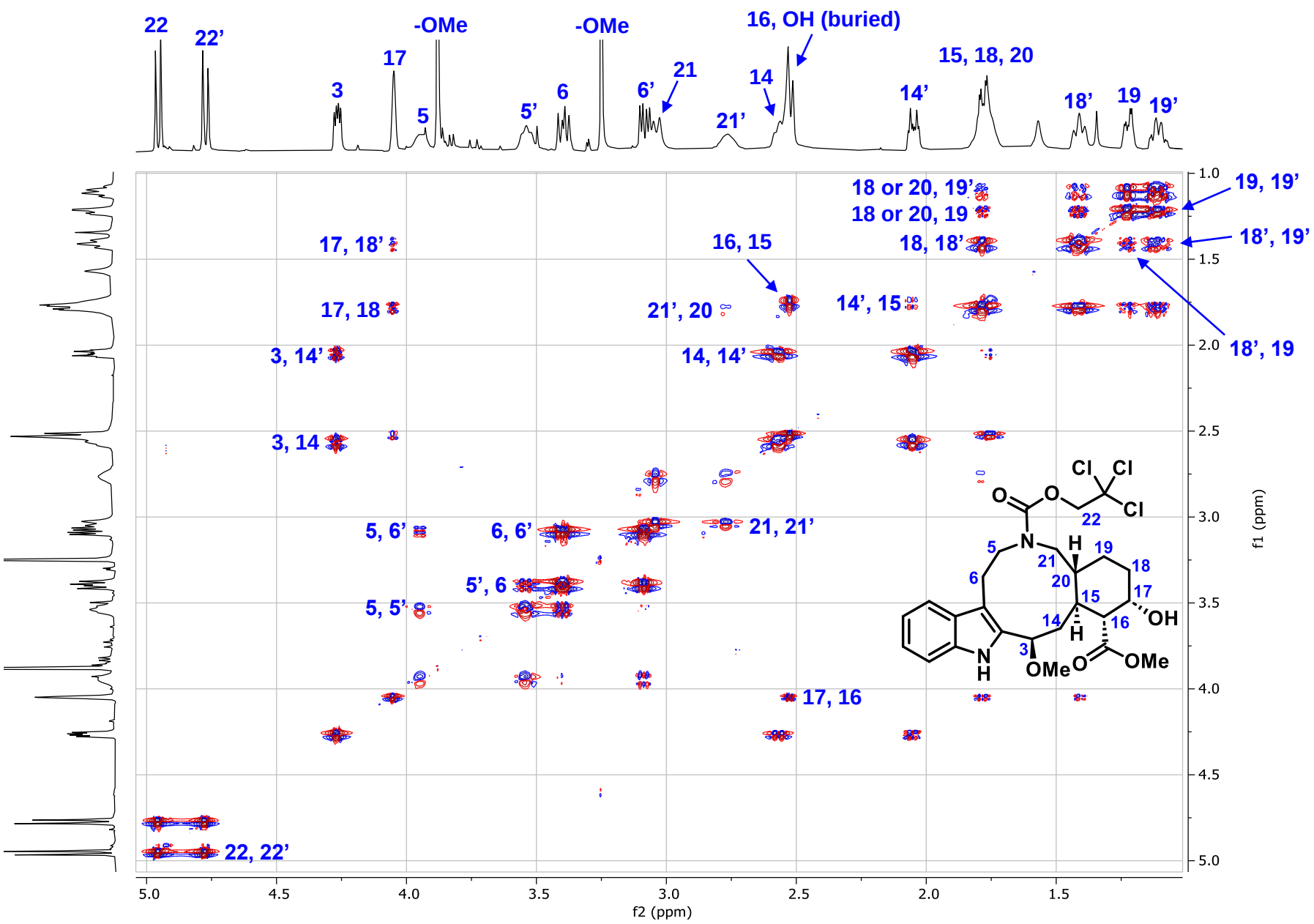

140 138 136 134 132 130 128 126 124 122 120 118 116 114 112 110
f1 (ppm)
50 45 40 35 30 25
f1 (ppm)
O
O
N
H
OH
H
N
H
O
O
OMe
I
18
13C in TCE at 100 °C
111.0 110.5
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


Cl
Cl
Cl
O
O
N
H
OH
H
N
H
OMe
O
OMe
47
^{1}H in TCE at 100 °C
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
f1 (ppm)
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)
CHCl$_3$

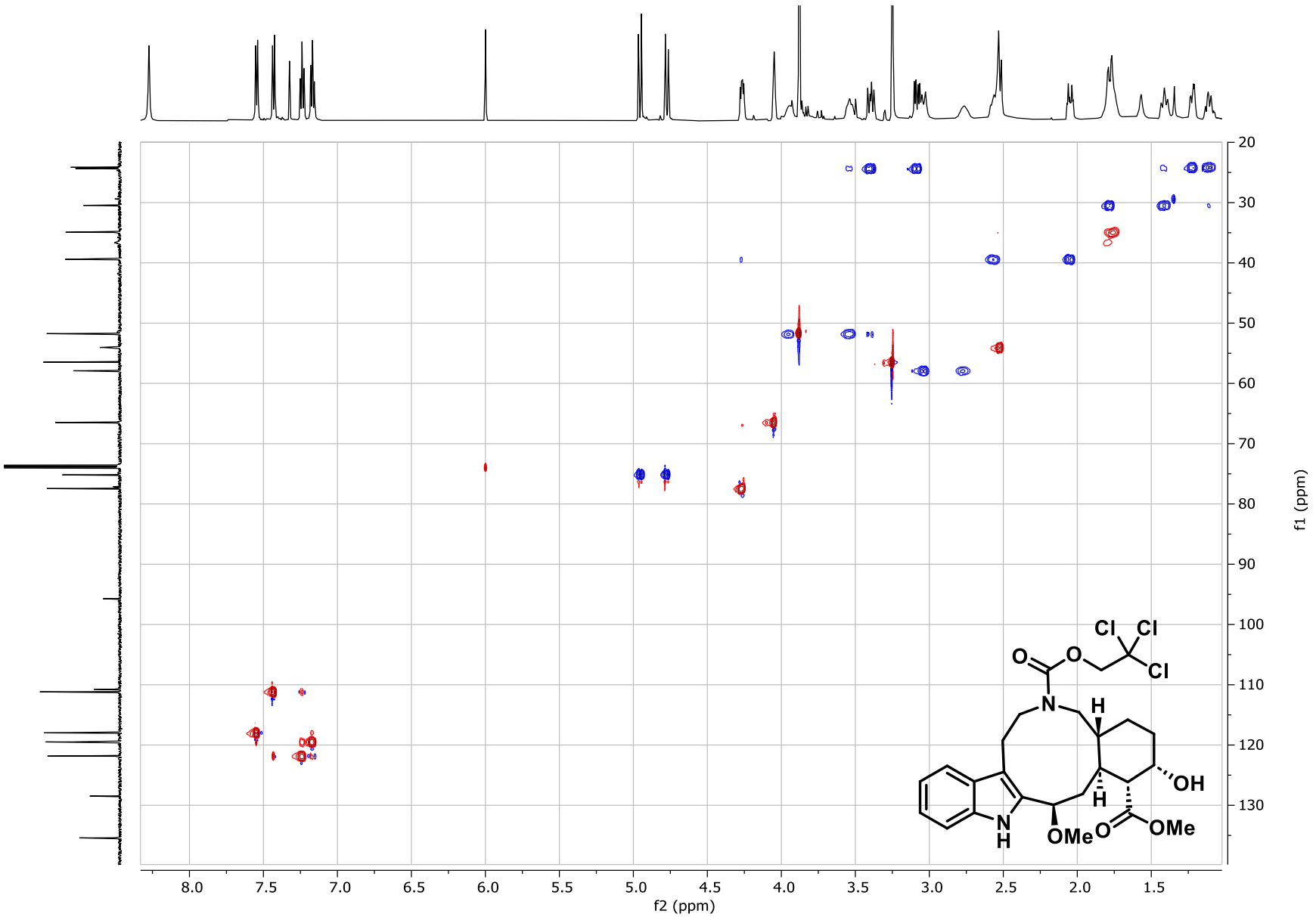

134 132 130 128 126 124 122 120 118 116 114 112
f1 (ppm)
58 57 56 55 54 53 52
f1 (ppm)
135.40
f1 (ppm)
Cl
Cl
Cl
O
O
N
H
H
OH
N
H
OMe
O
OMe
47
13C in TCE at 100 °C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



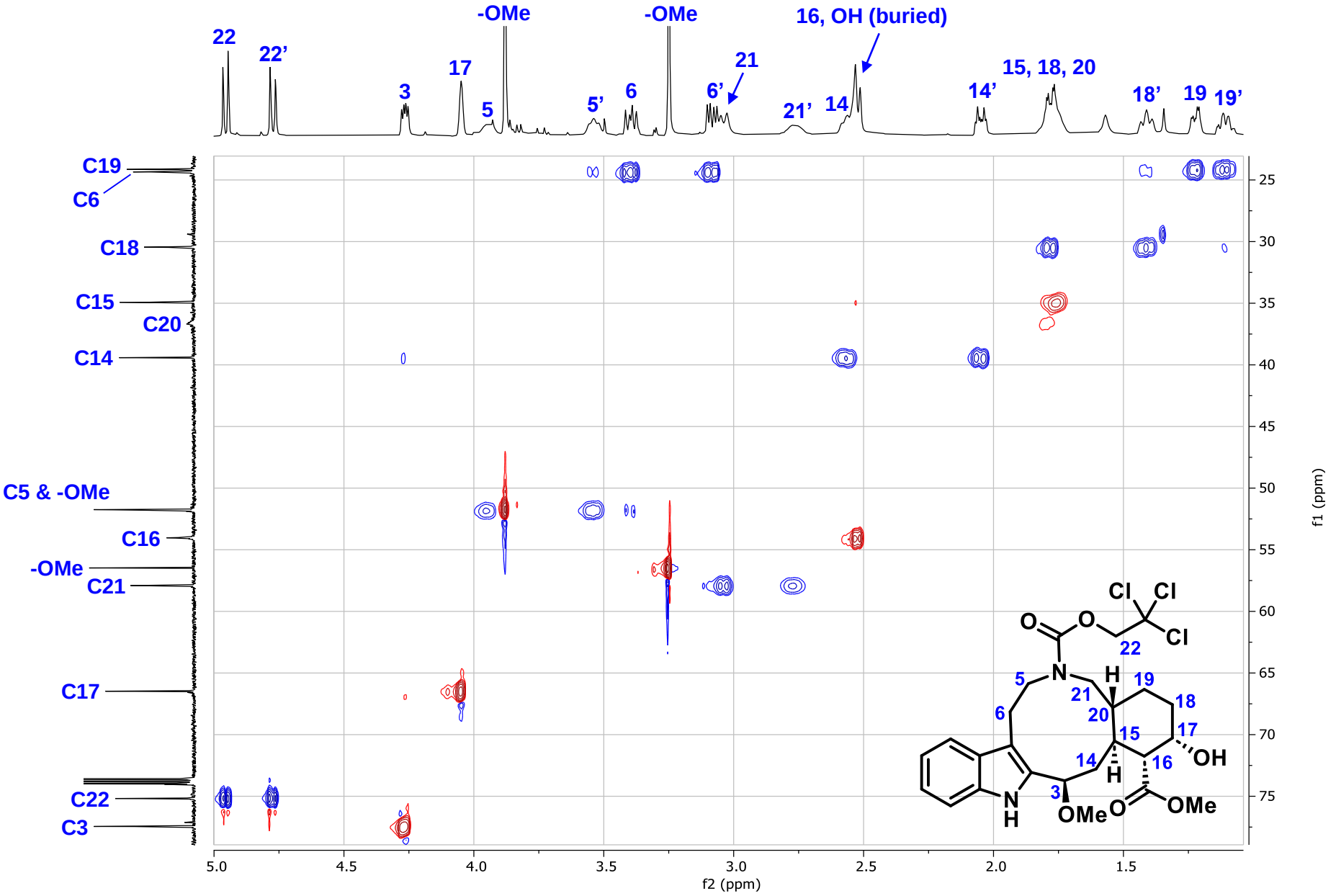
Compound 47: COSY, T = 100 °C, $C_2D_2Cl_4$ (full)



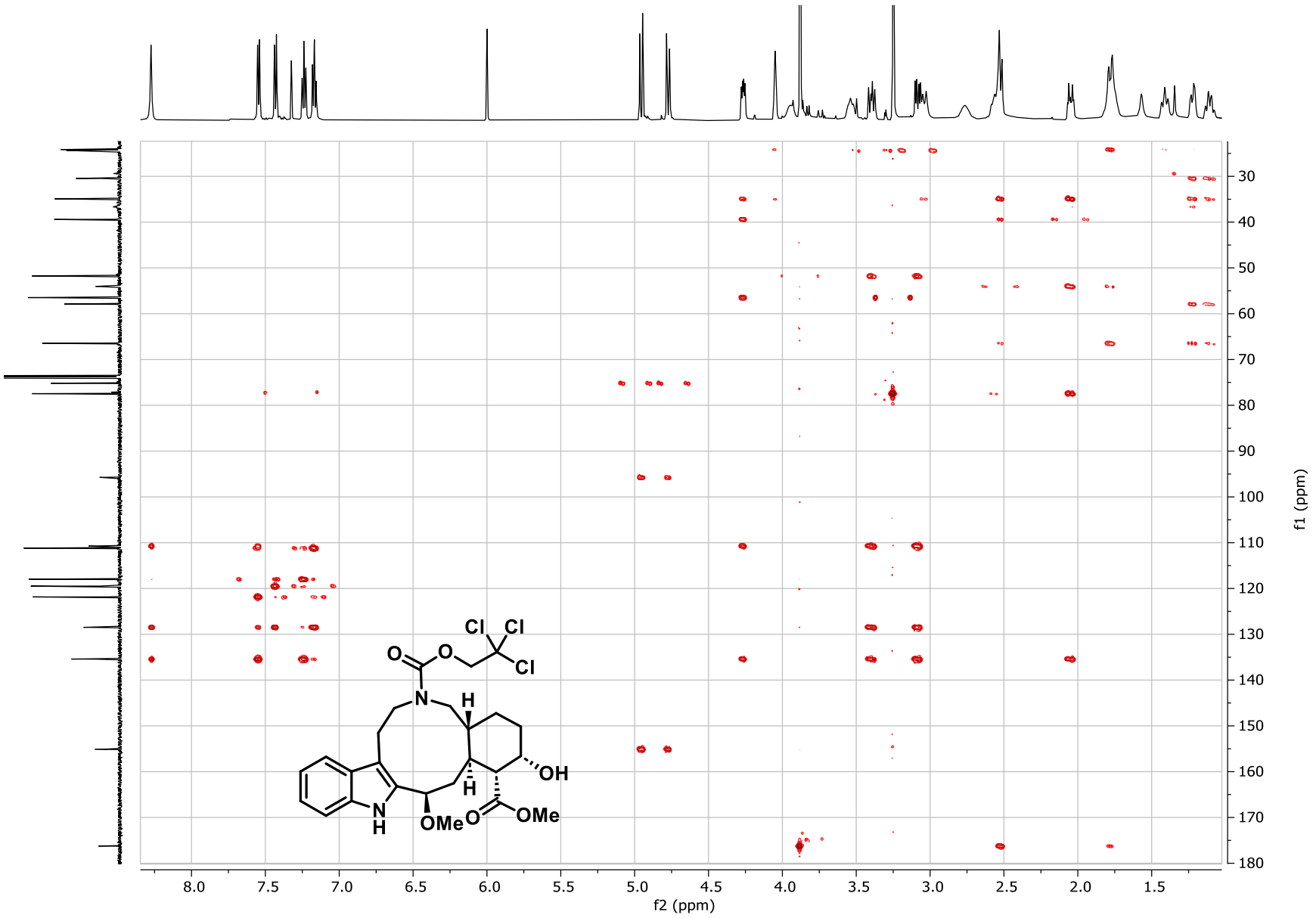
Compound 47: COSY, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in)



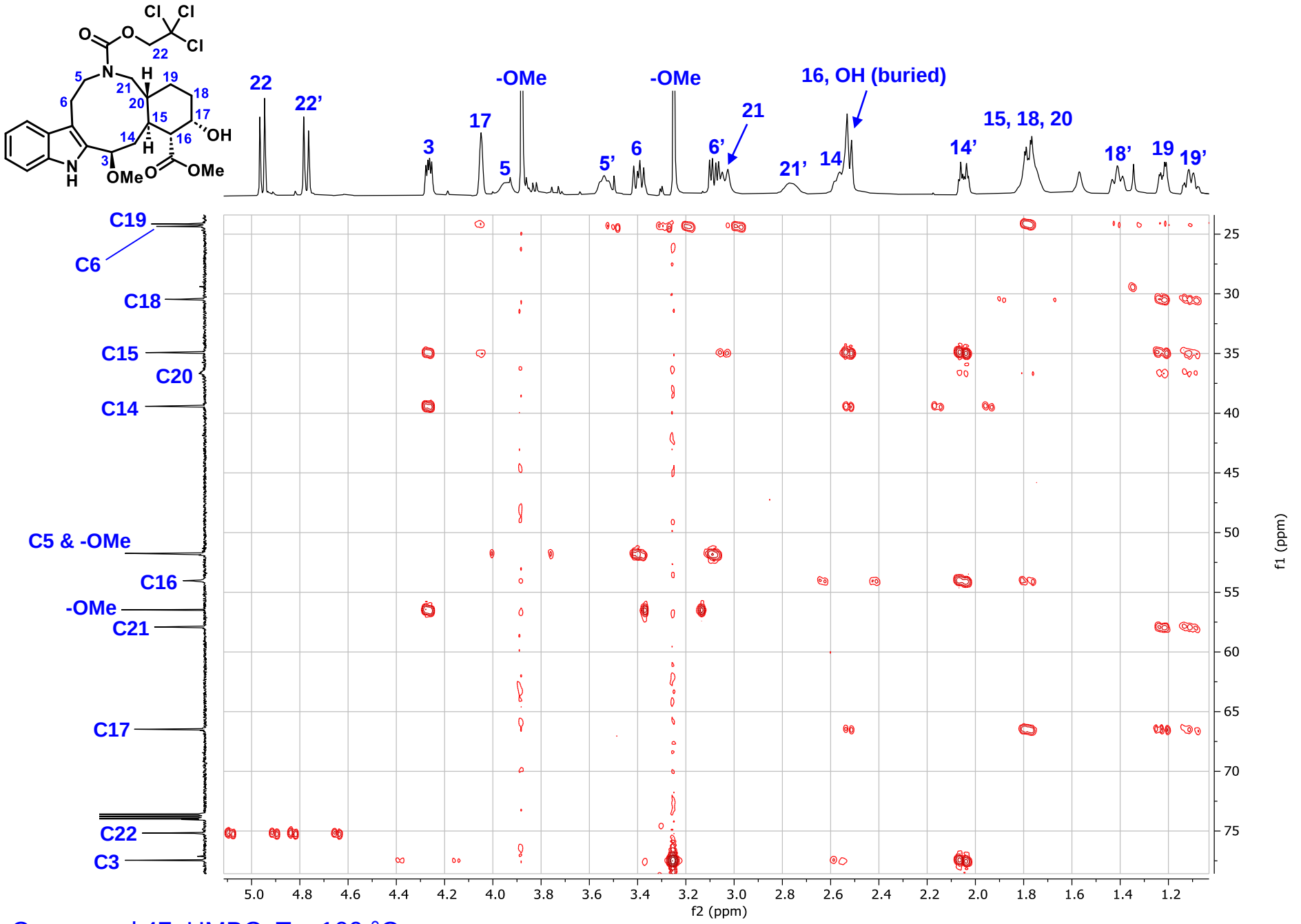
Compound 47: HSQC, T = 100 °C, $C_2D_2Cl_4$ (full)



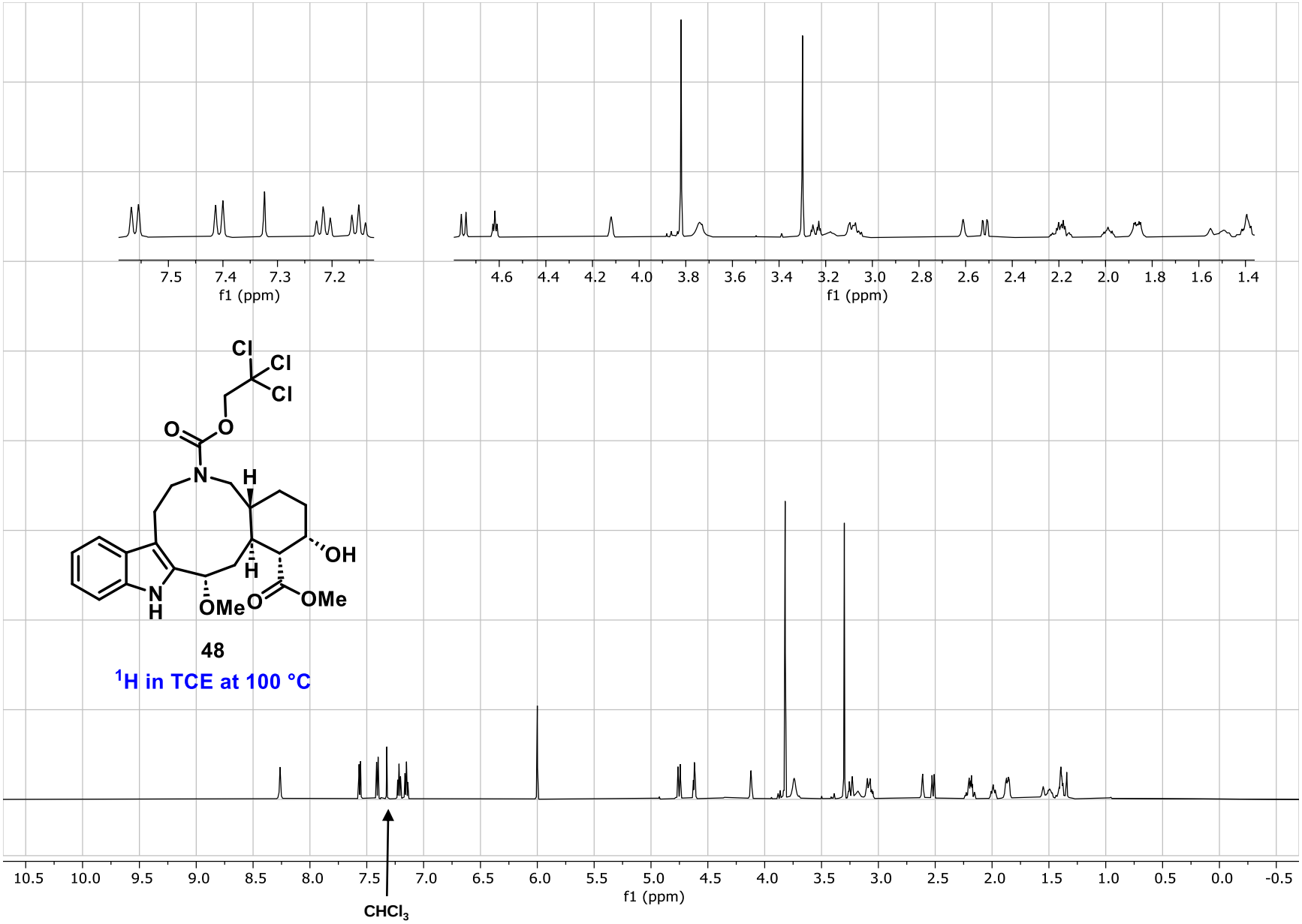
Compound 47: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in)

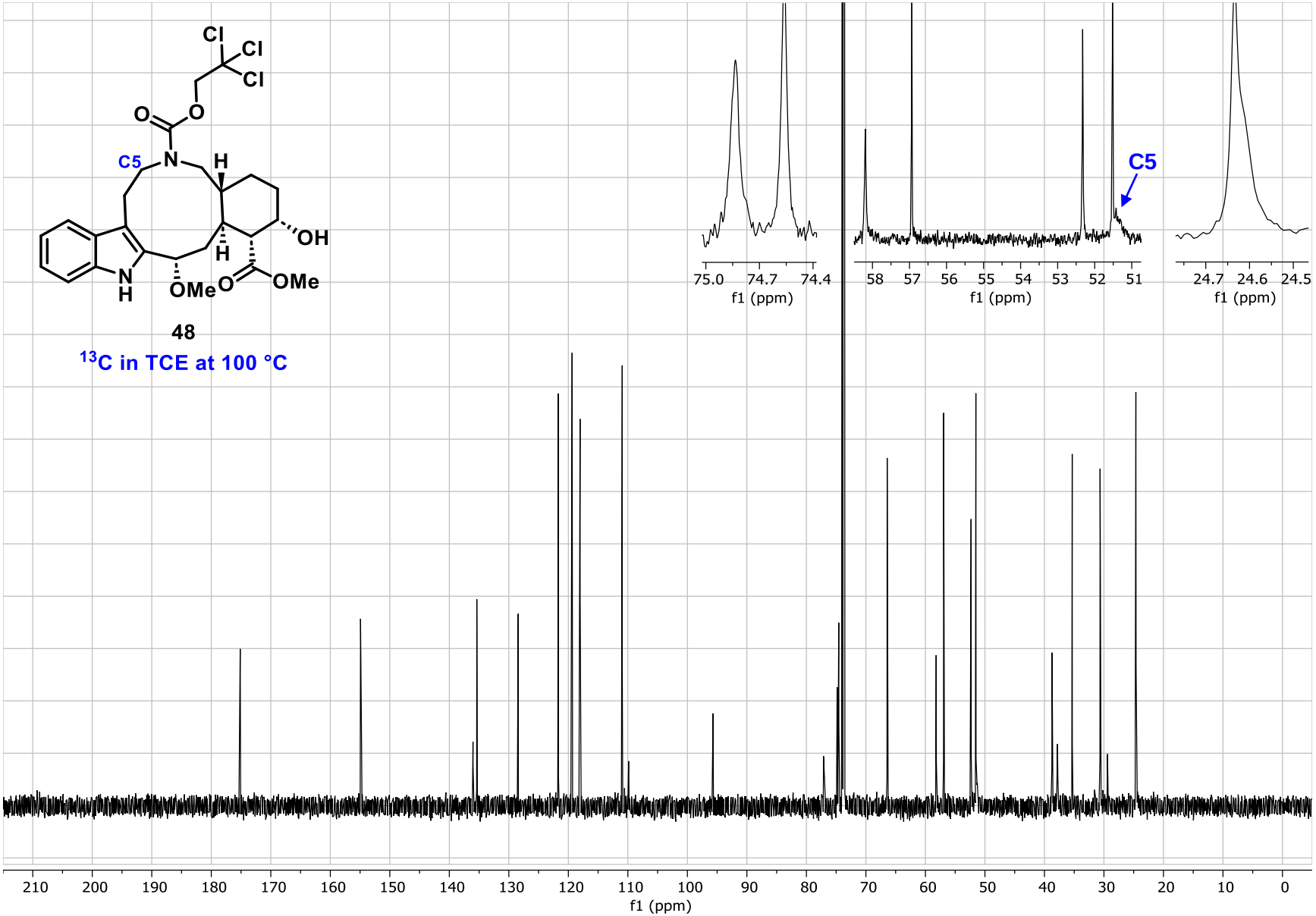


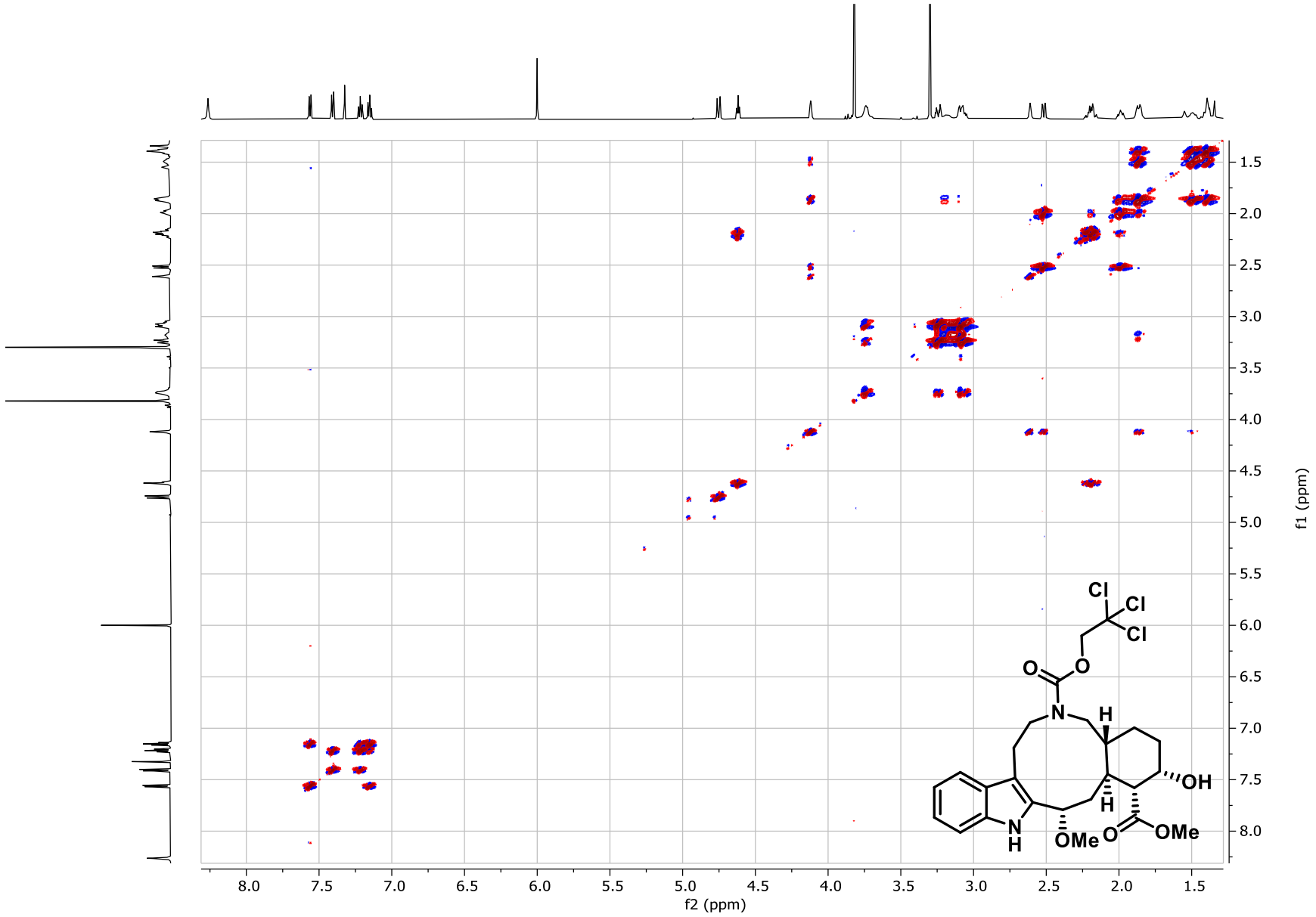
Compound 47: HMBC, T = 100 °C, $C_2D_2Cl_4$ (full)



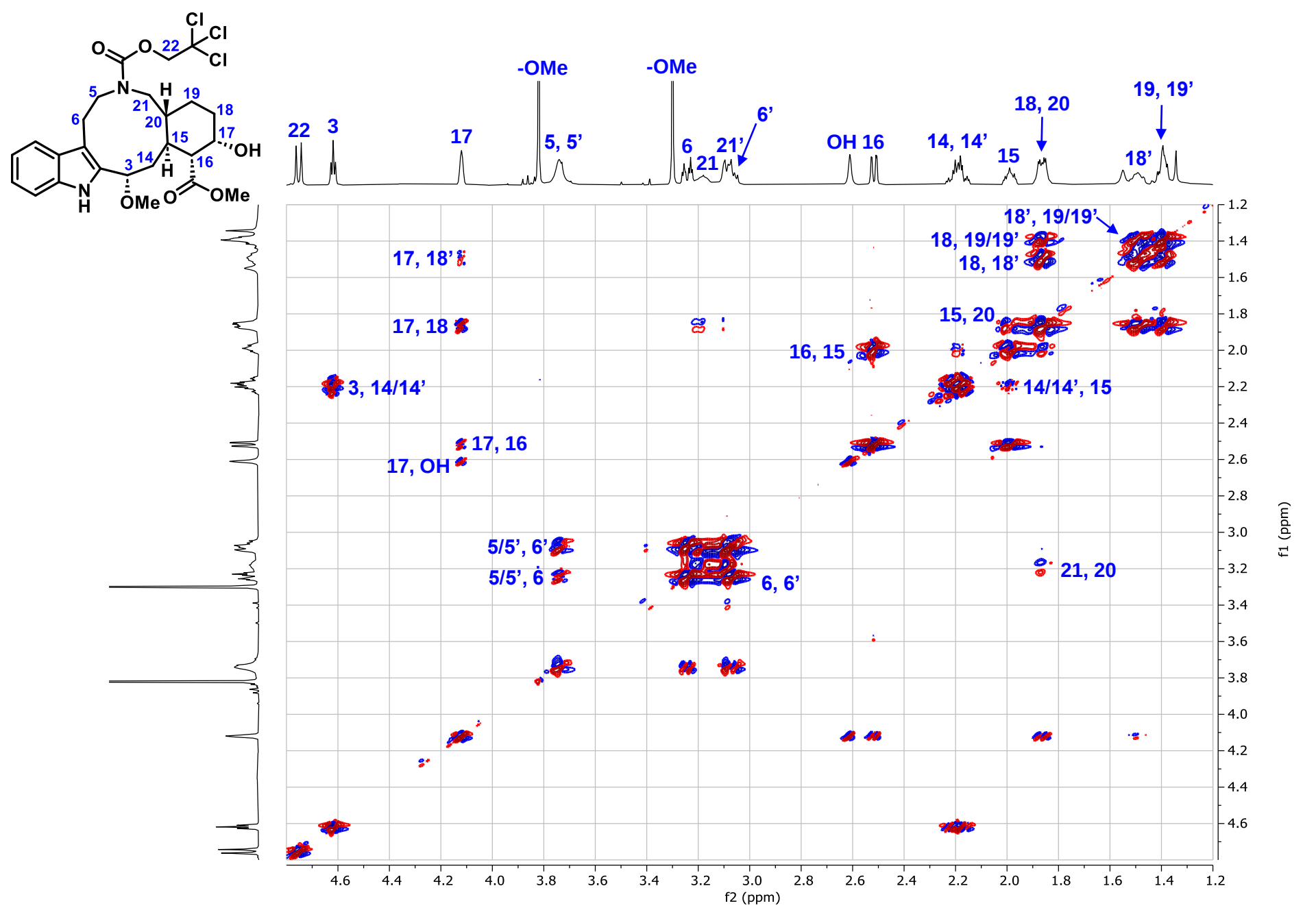
Compound 47: HMBC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in)


7.5 7.4 7.3 7.2
f1 (ppm)
4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4
f1 (ppm)
Cl
Cl
Cl
O
O
N
H
OH
H
N
H
OMe
O
OMe
48
1H in TCE at 100 °C
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)
CHCl3

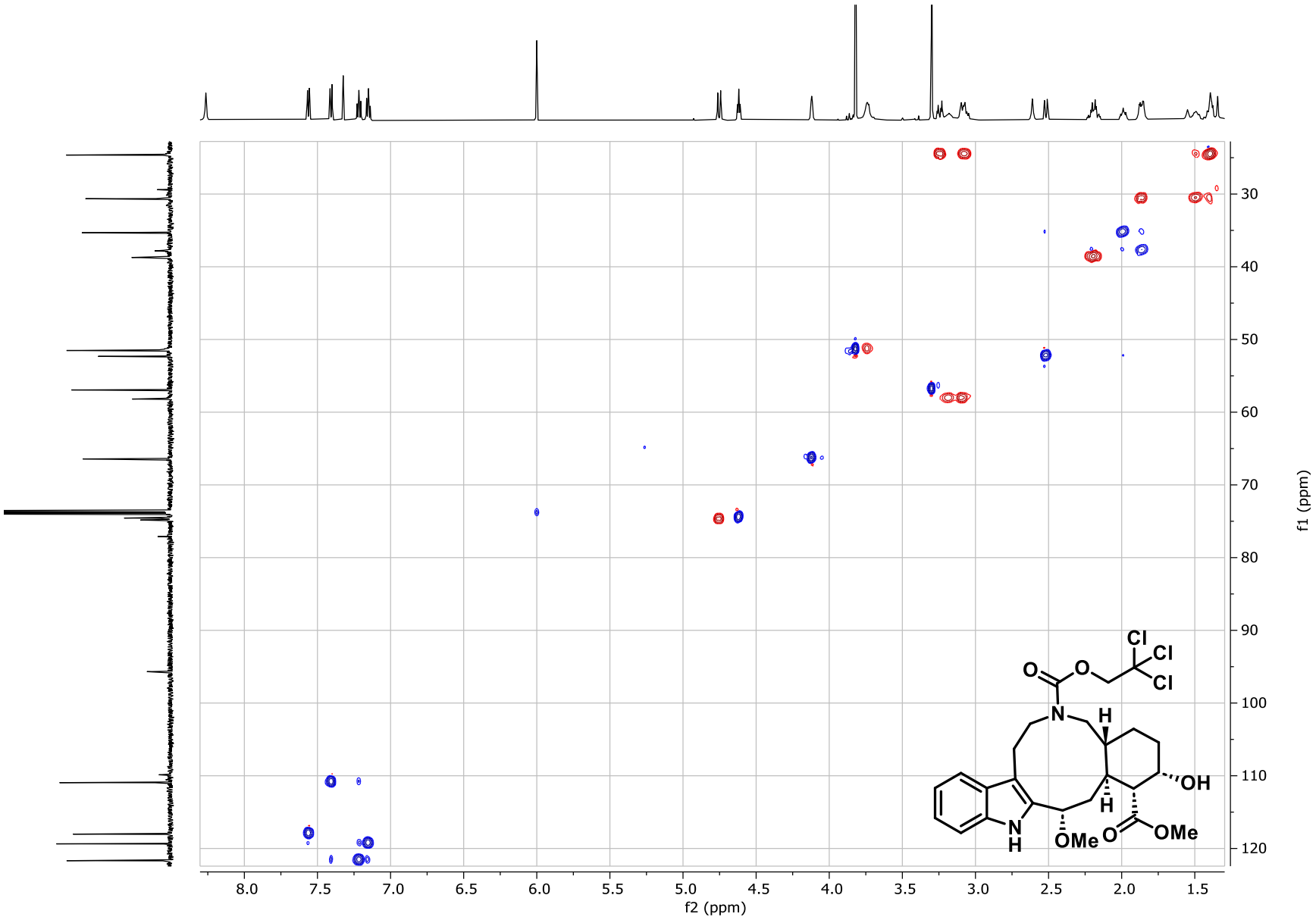

Cl
Cl
Cl
O
O
C5
N
H
OH
H
N
H
OMe
O
OMe
48
13C in TCE at 100 °C
C5
75.0 74.7 74.4
f1 (ppm)
58 57 56 55 54 53 52 51
f1 (ppm)
24.7 24.6 24.5
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



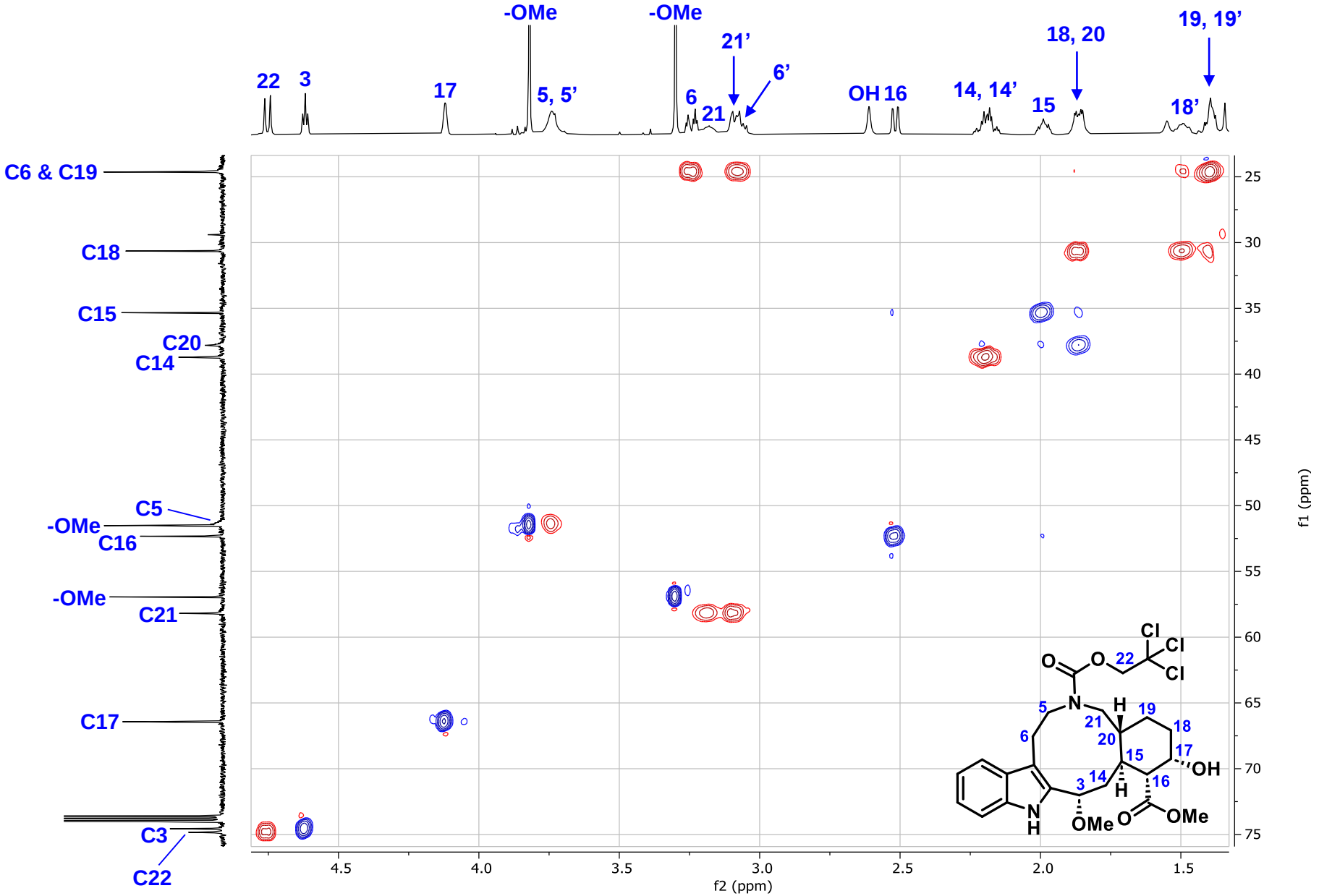
Compound 48: COSY, T = 100 °C, $C_2D_2Cl_4$ (full)



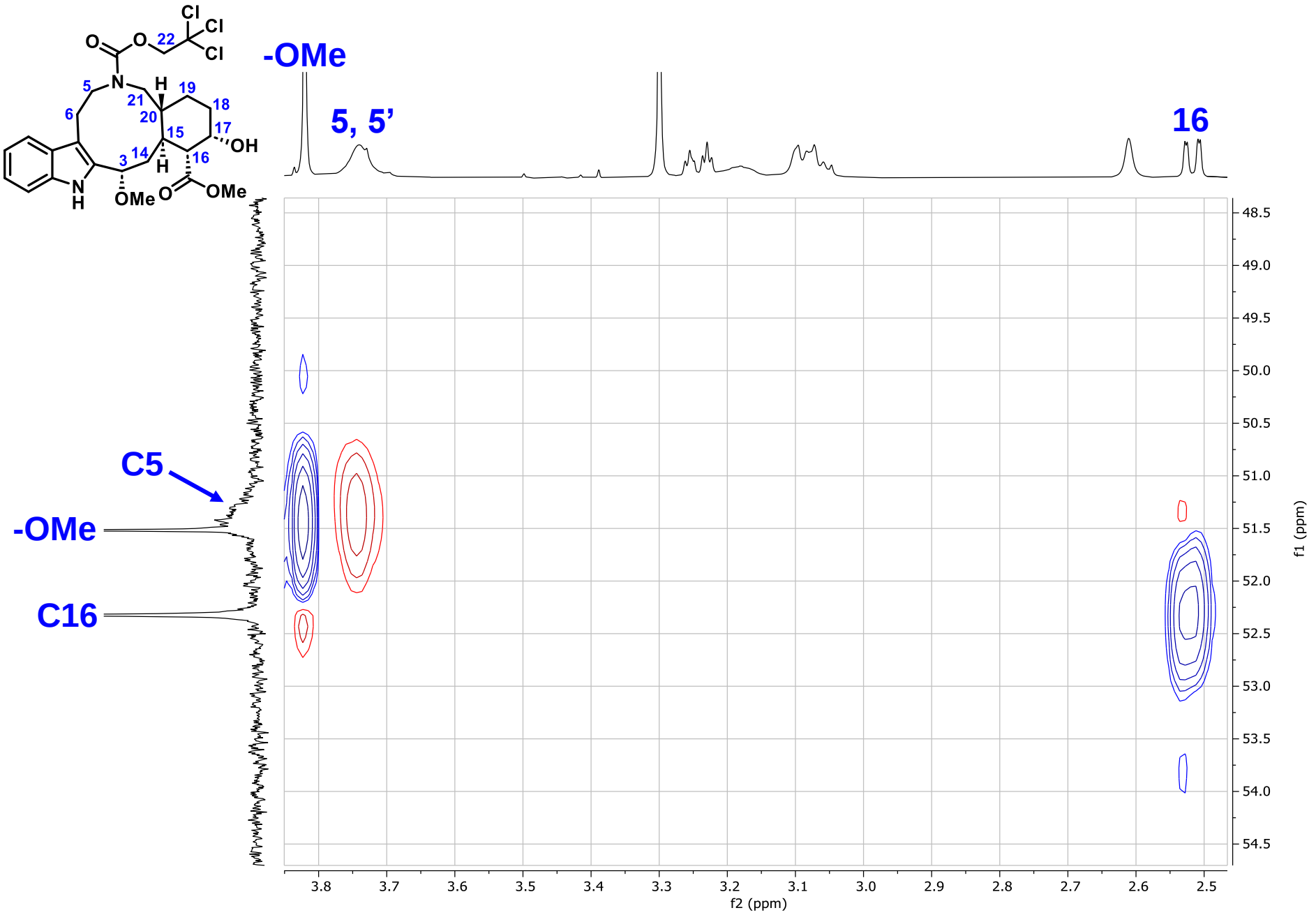
Compound 48: COSY, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in)



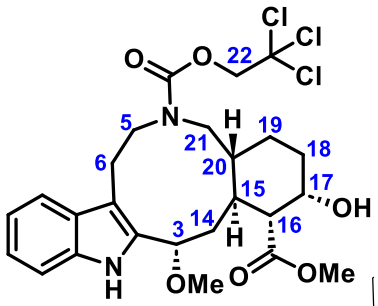
Compound 48: HSQC, T = 100 °C, $C_2D_2Cl_4$ (wide)



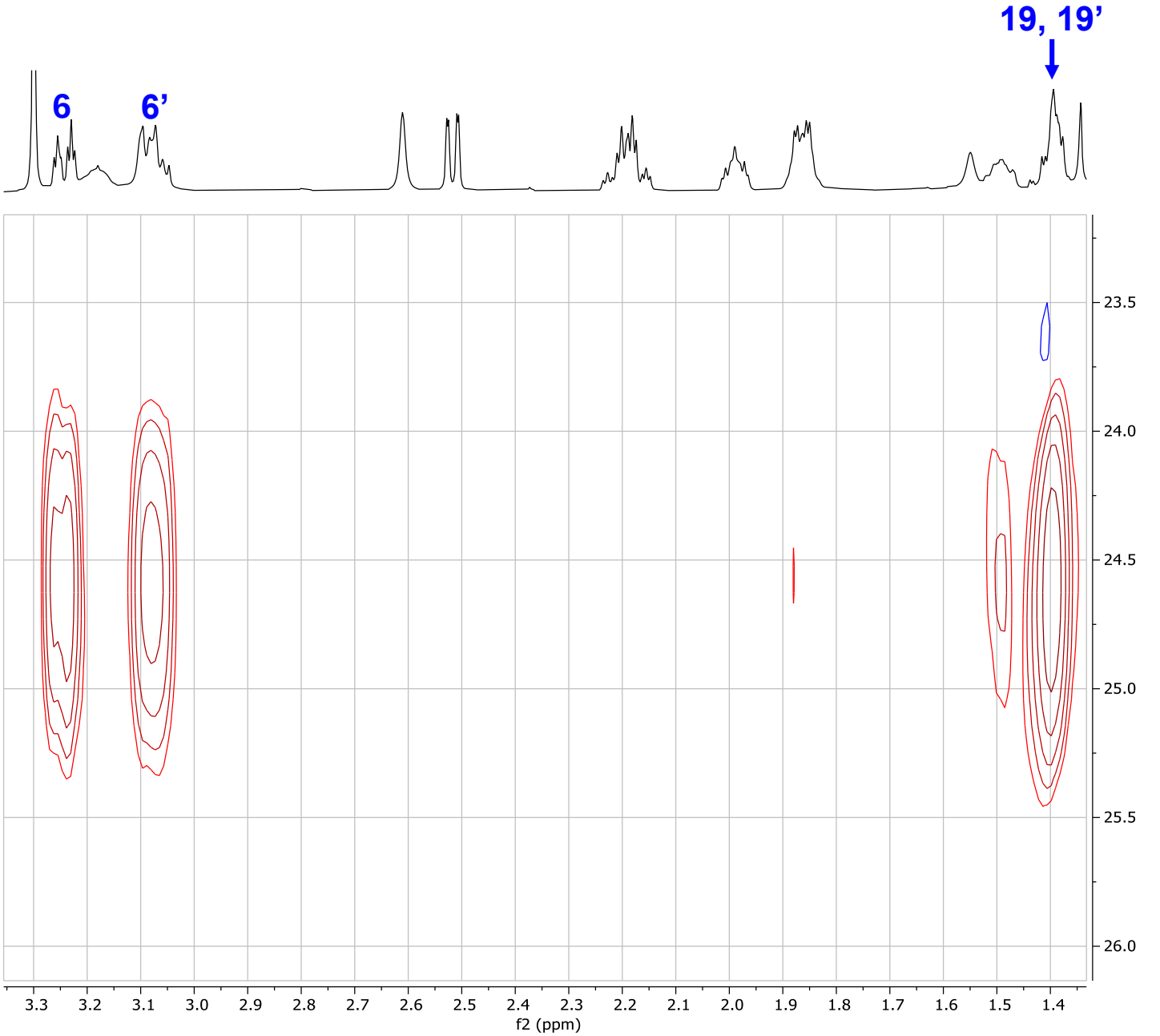
Compound 48: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 1)



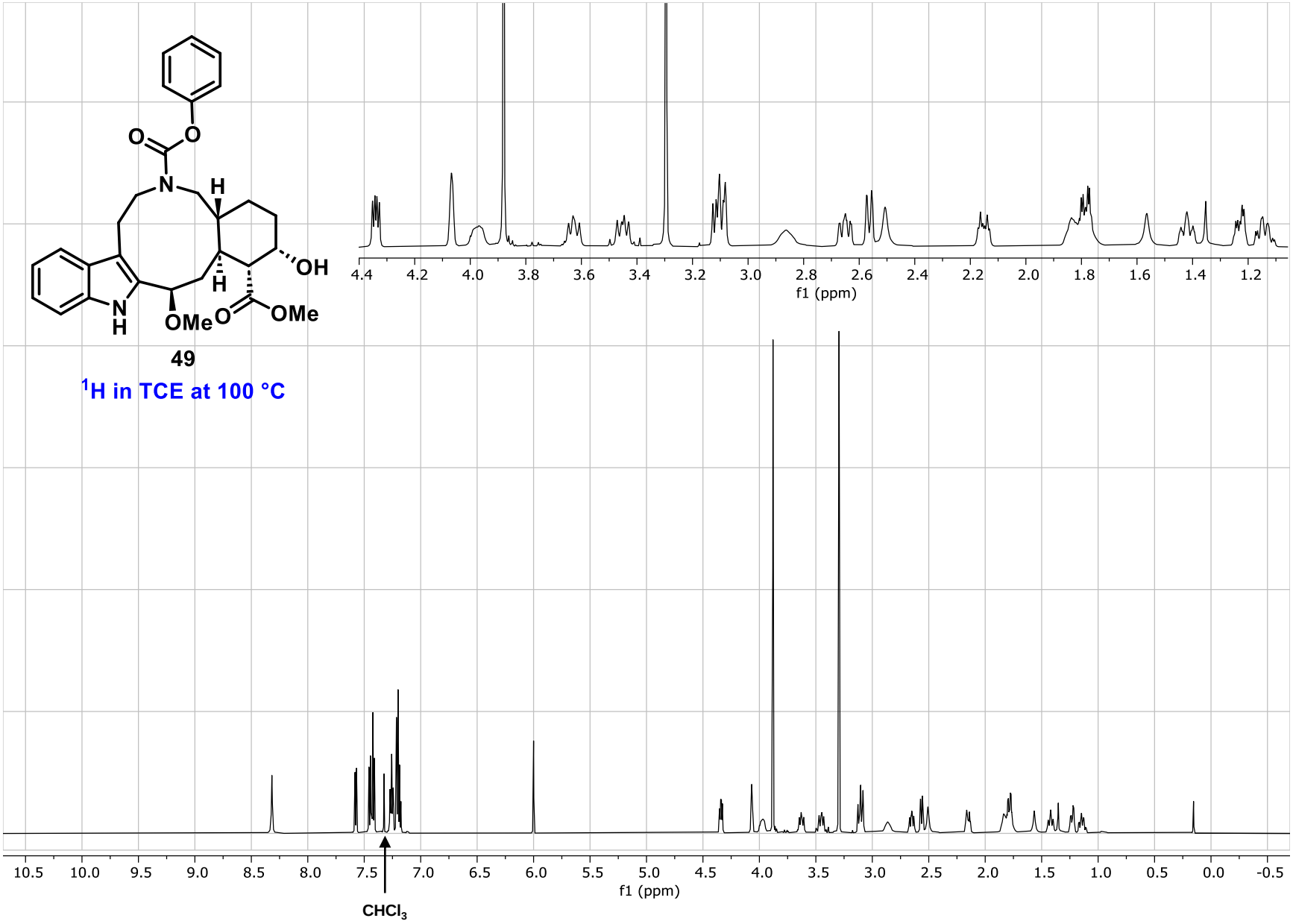
Compound 48: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 2)

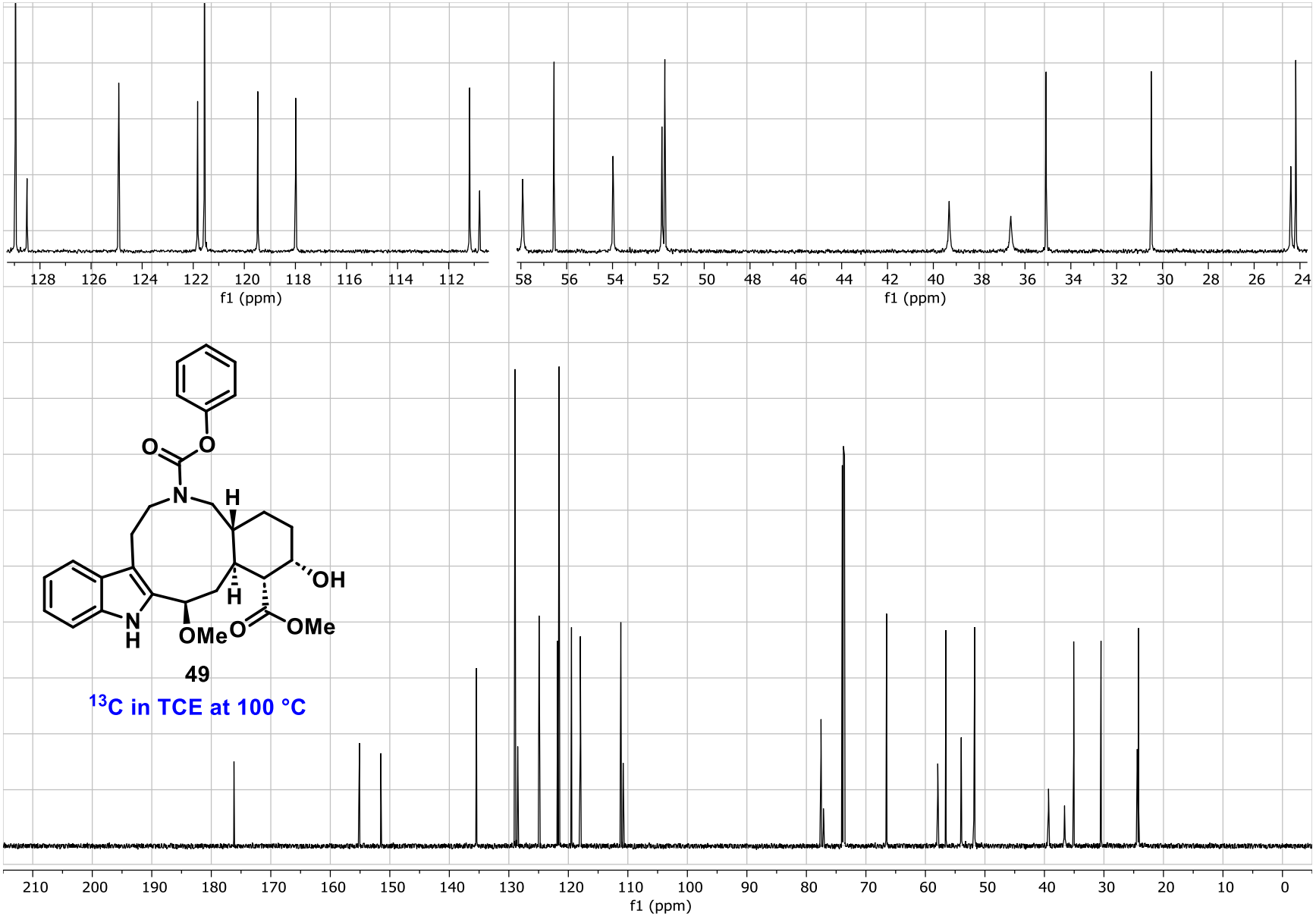


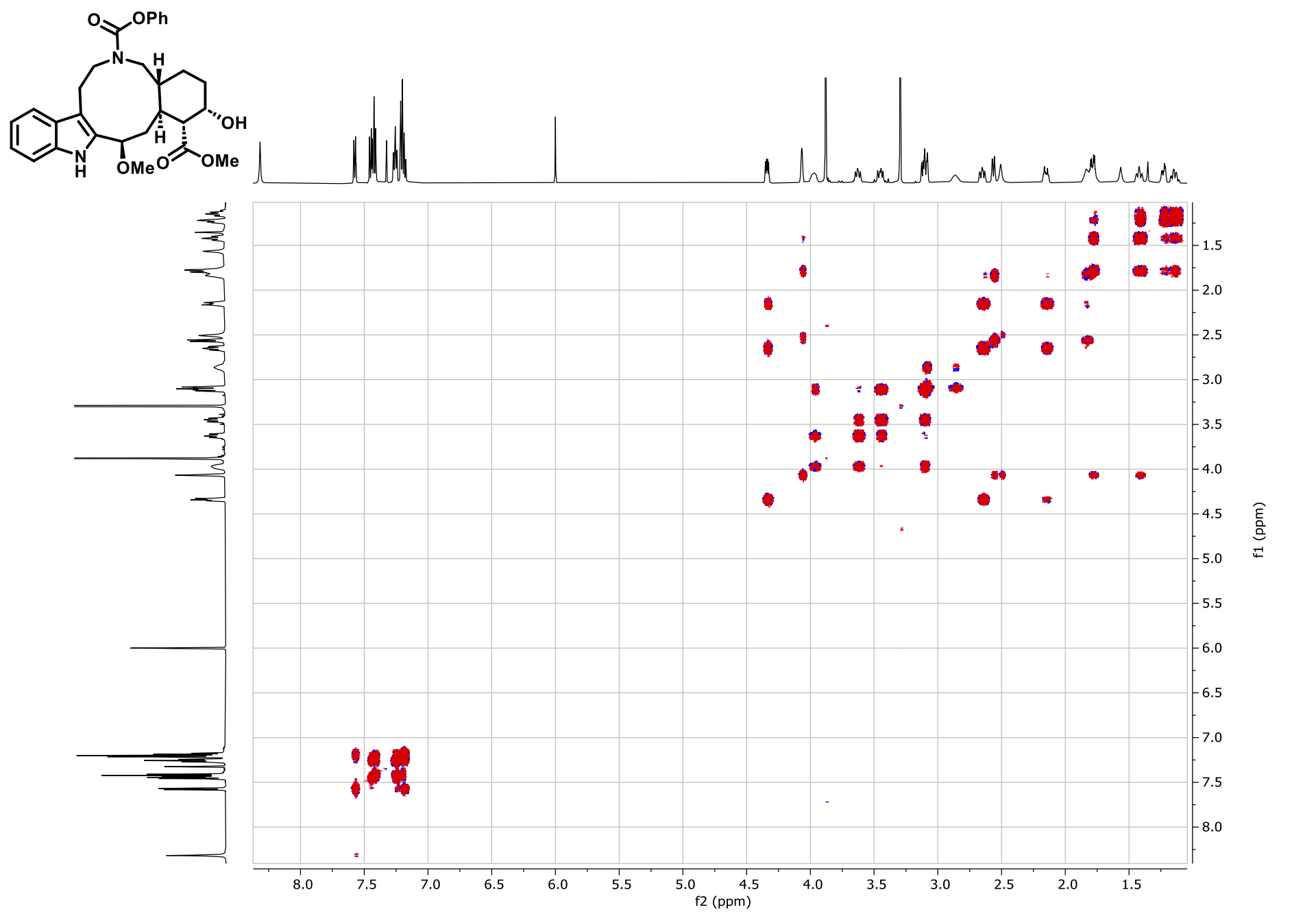
C6 & C19 Signals Overlapping



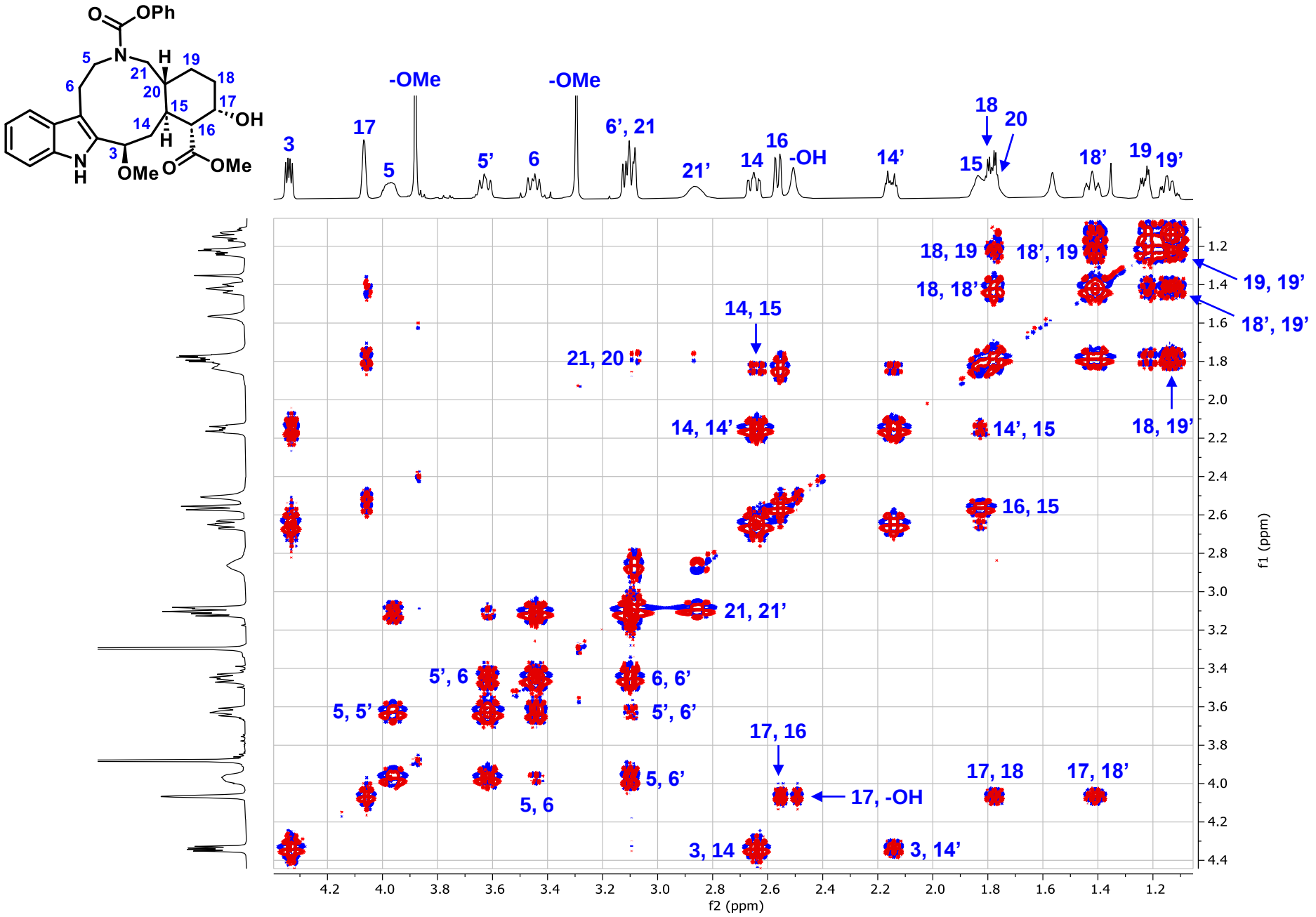
Compound 48: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 3)


O
O
N
H
OH
H
N
H
OMe
O
OMe
49
1H in TCE at 100 °C
4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2
f1 (ppm)
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)
CHCl3

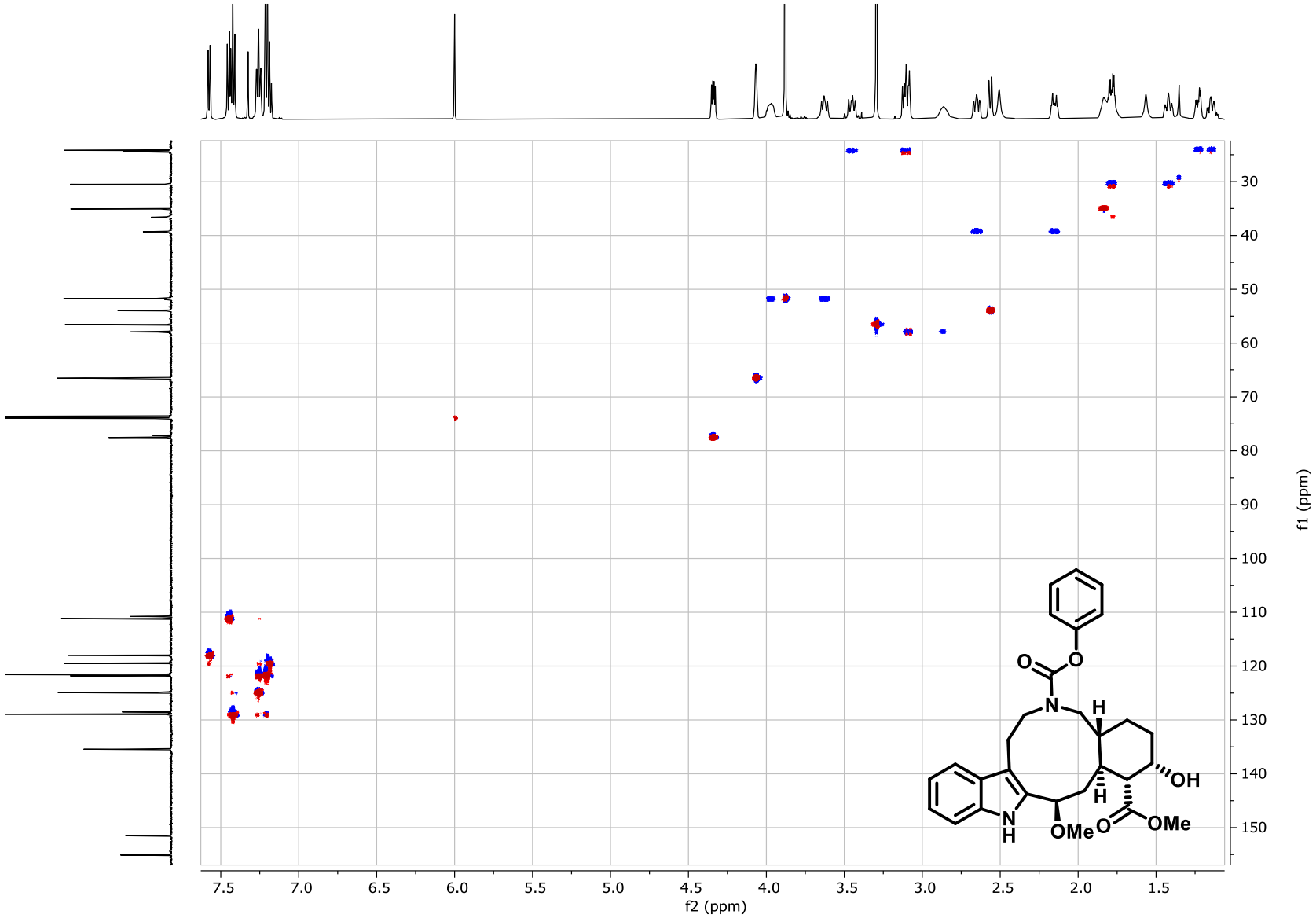

f1 (ppm)
f1 (ppm)
f1 (ppm)
O
O
N
H
H
OH
N
H
OMe
O
OMe
49
13C in TCE at 100 °C



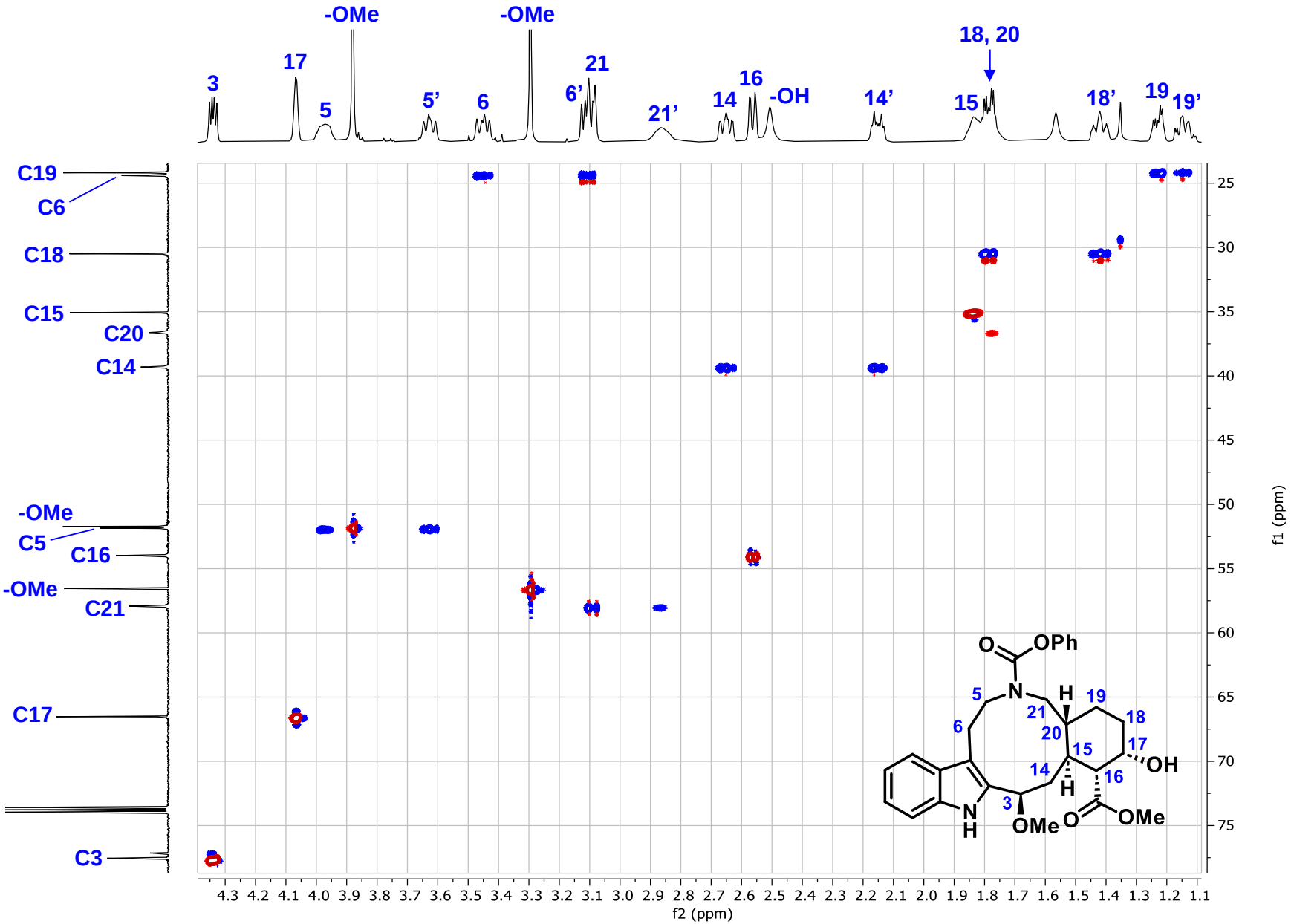
Compound 49: COSY, T = 100 °C, $C_2D_2Cl_4$ (full)



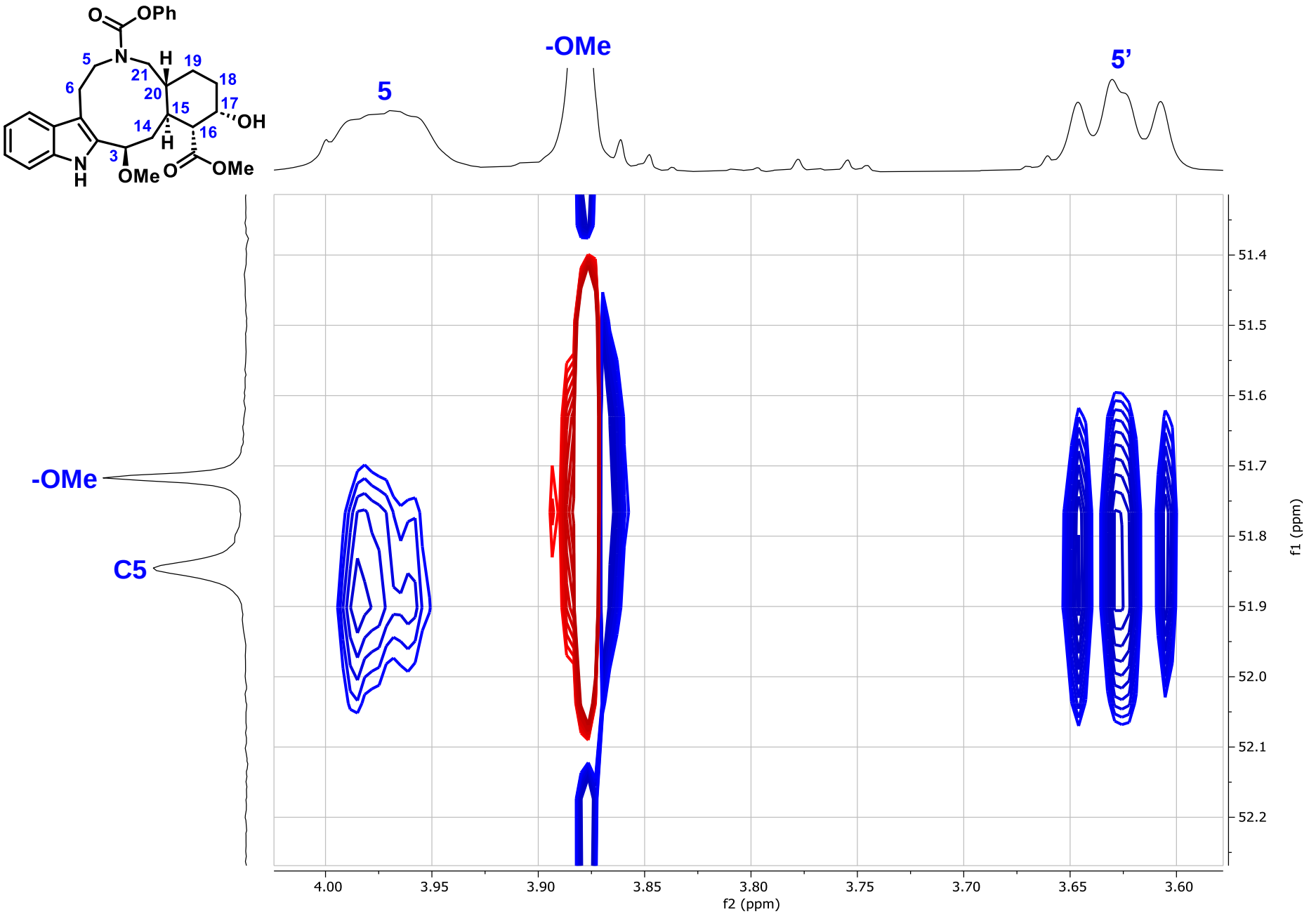
Compound 49: COSY, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in)



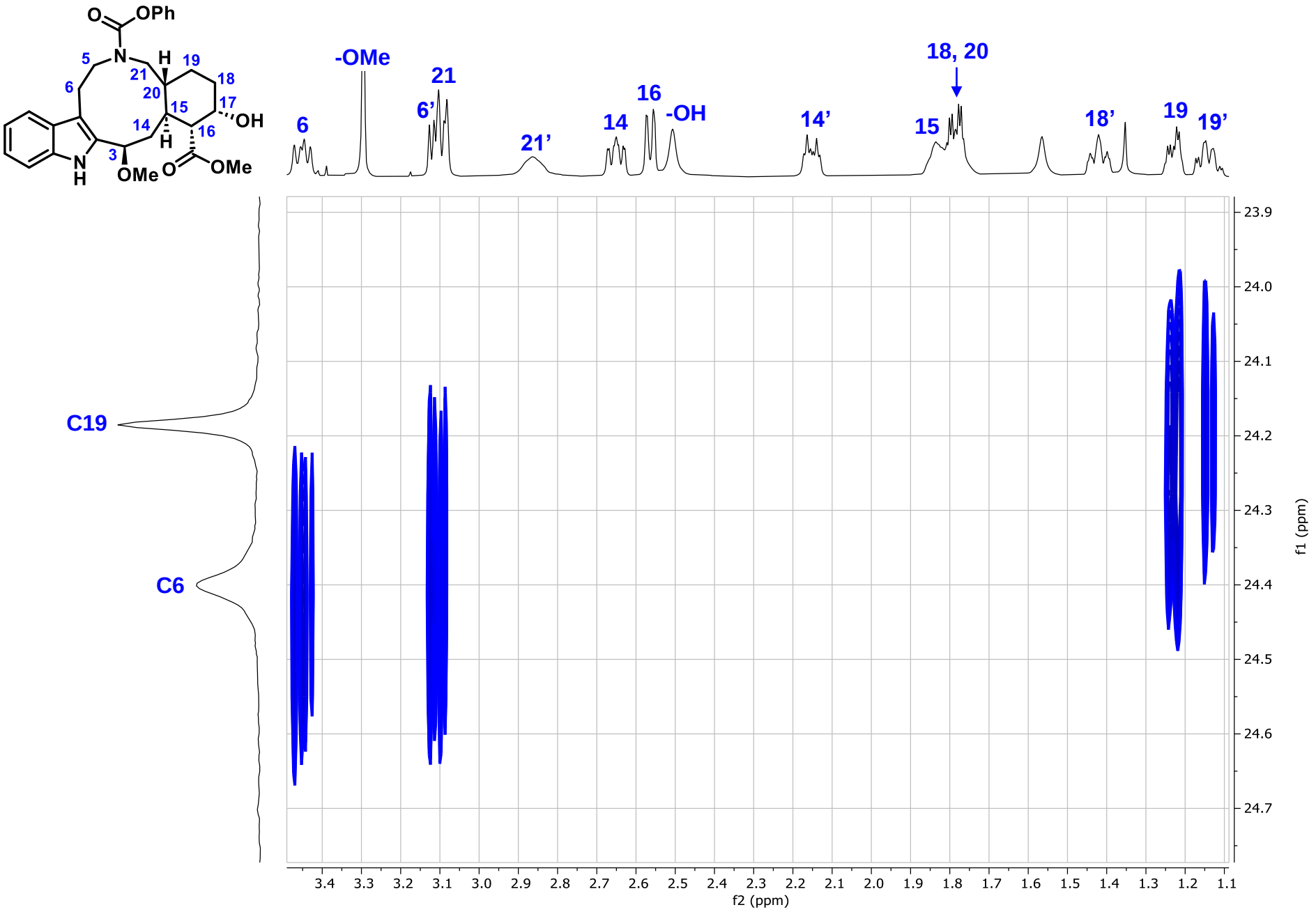
Compound 49: HSQC, T = 100 °C, $C_2D_2Cl_4$ (full)



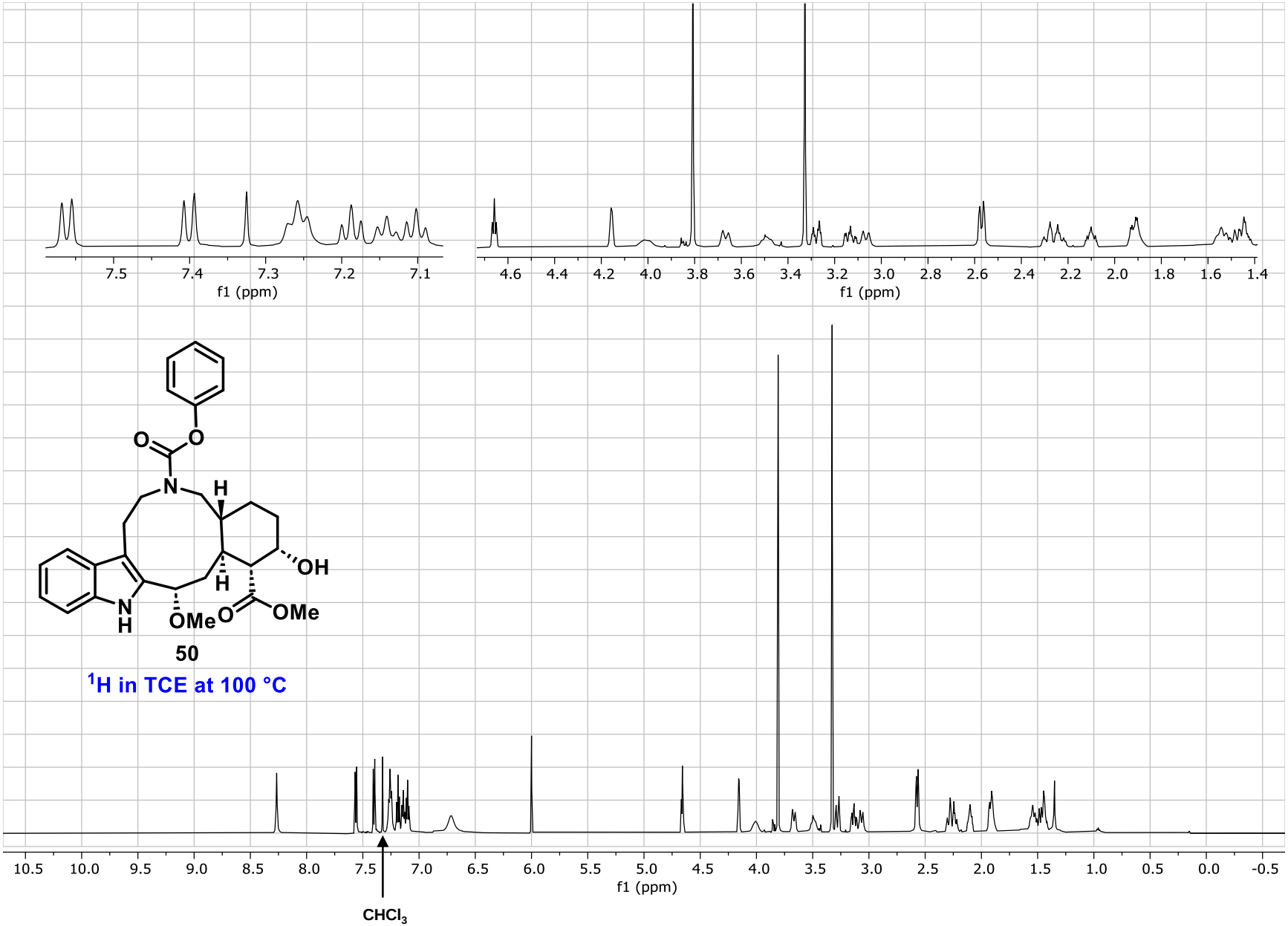
Compound 49: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 1)

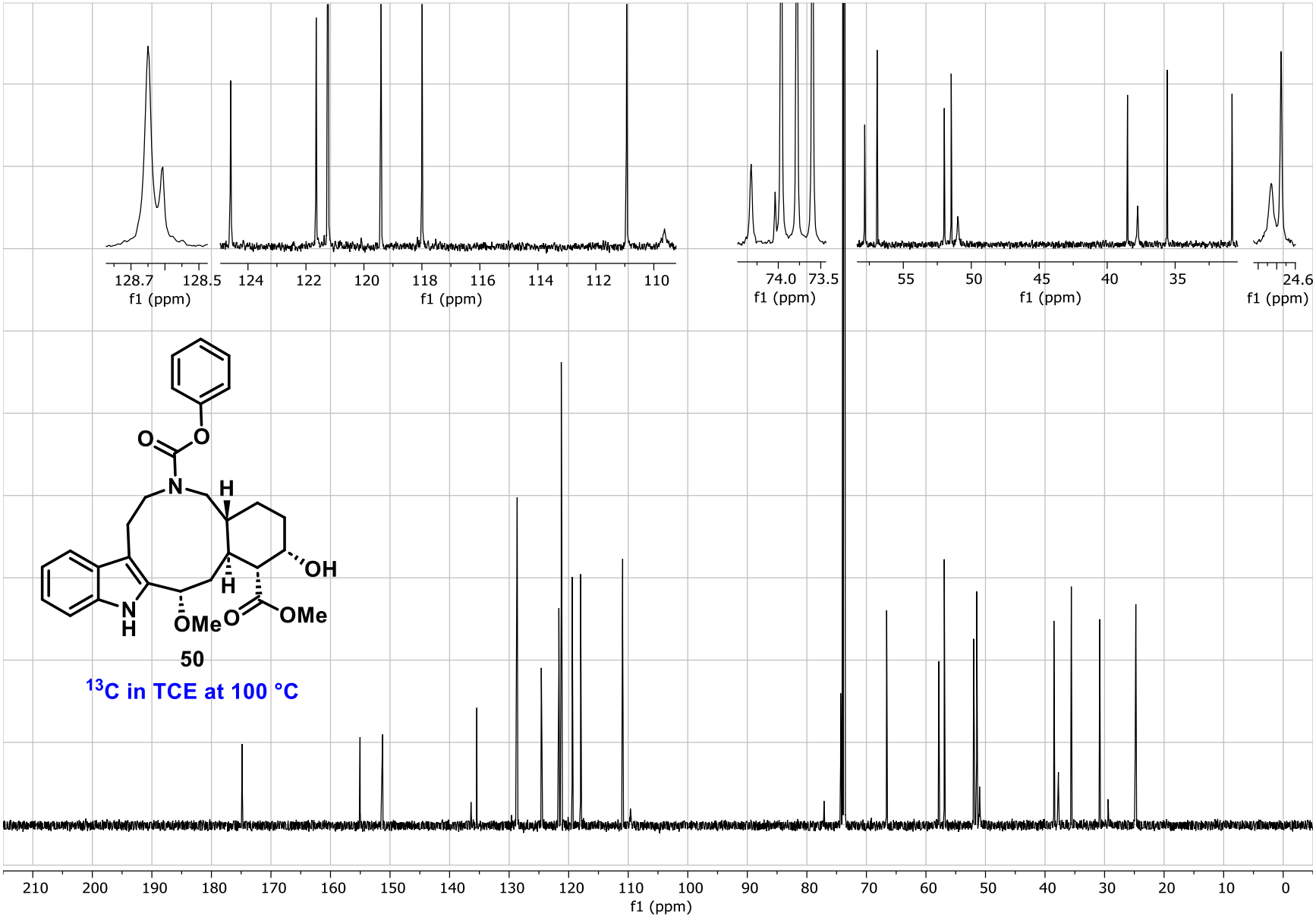


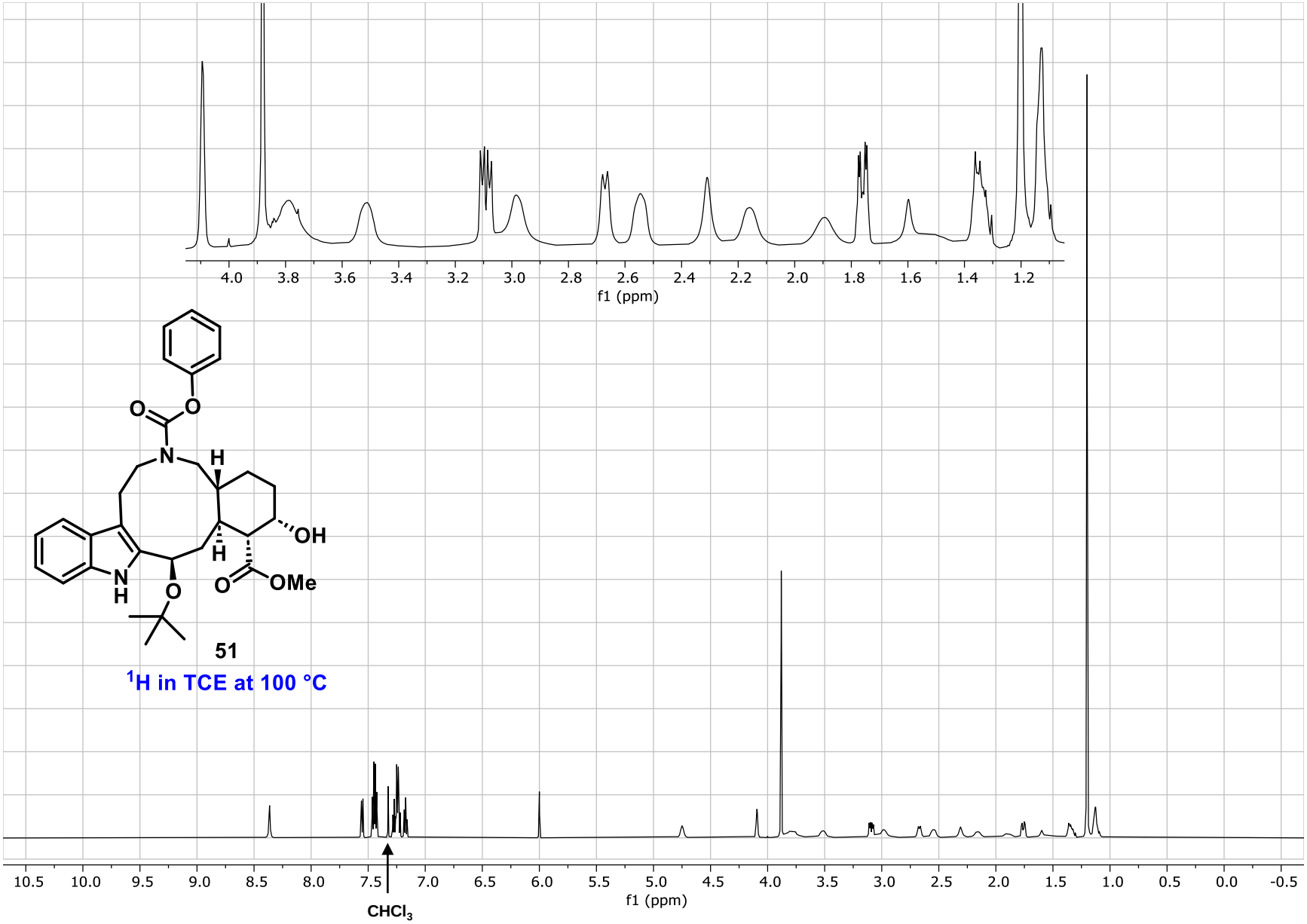
Compound 49: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 2)

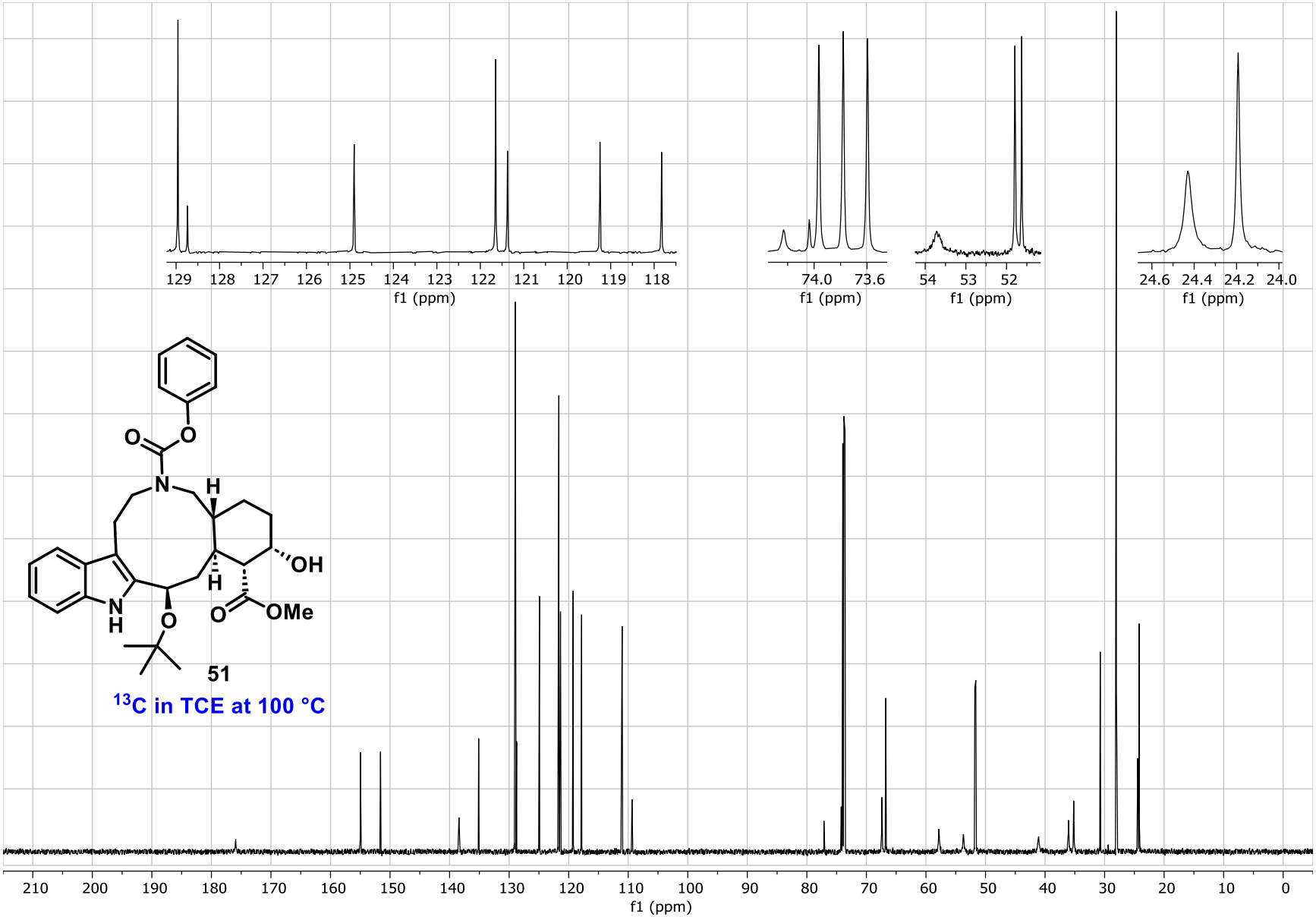


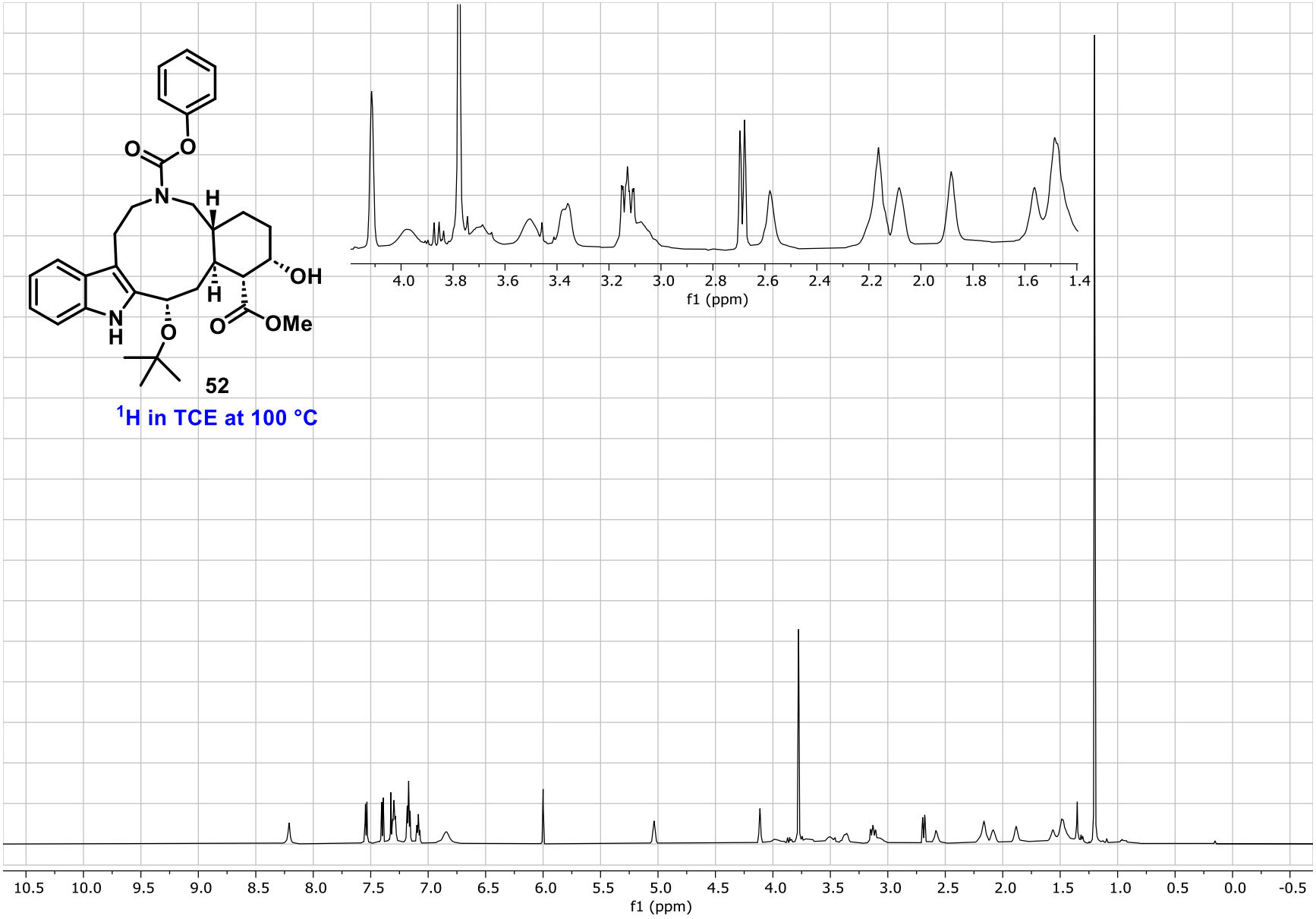
Compound 49: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 3)

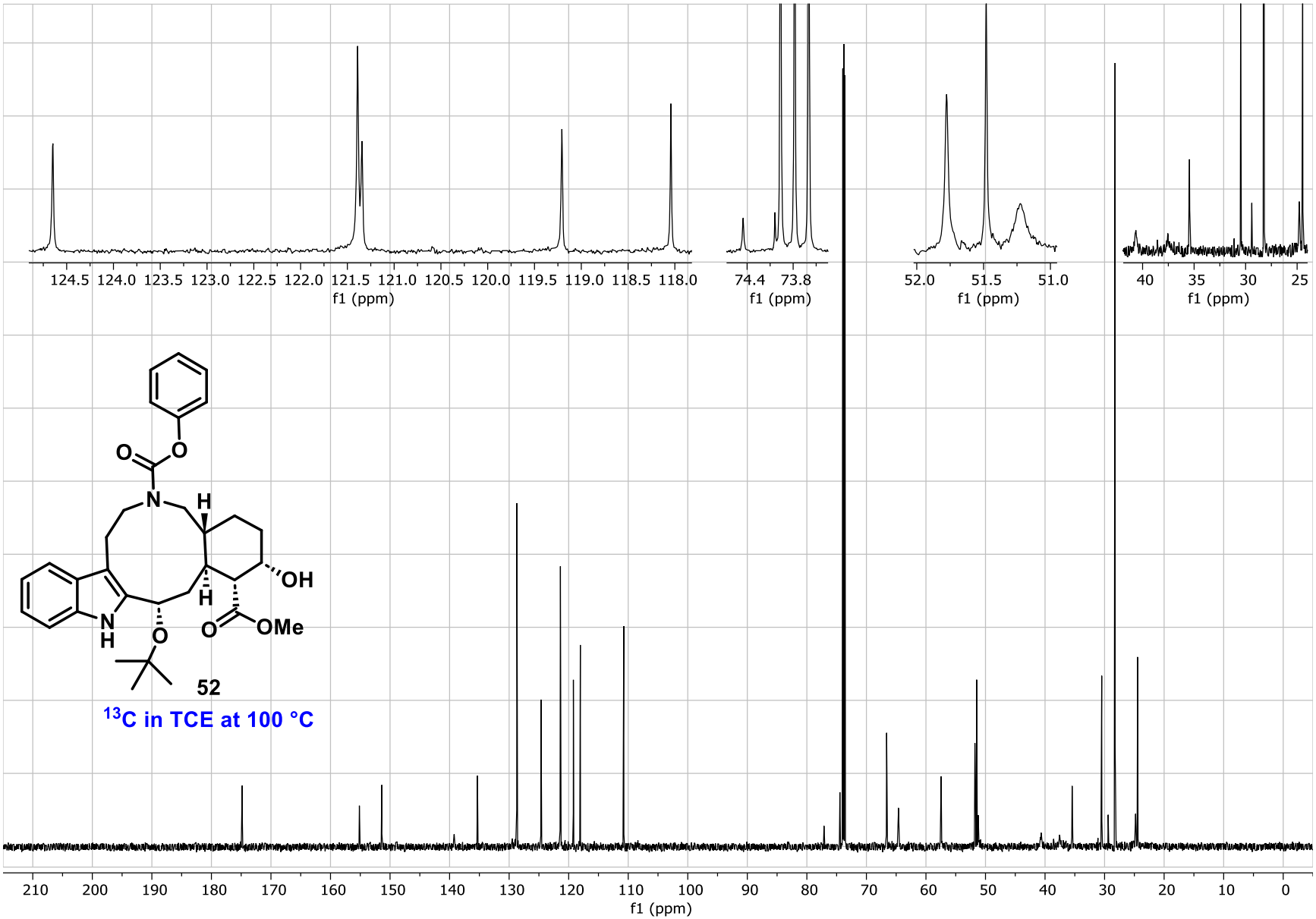

7.5
7.4
7.3
7.2
7.1
f1 (ppm)
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
f1 (ppm)
O
O
N
H
OH
H
N
H
OMe
O
OMe
50
1H in TCE at 100 °C
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)
CHCl3

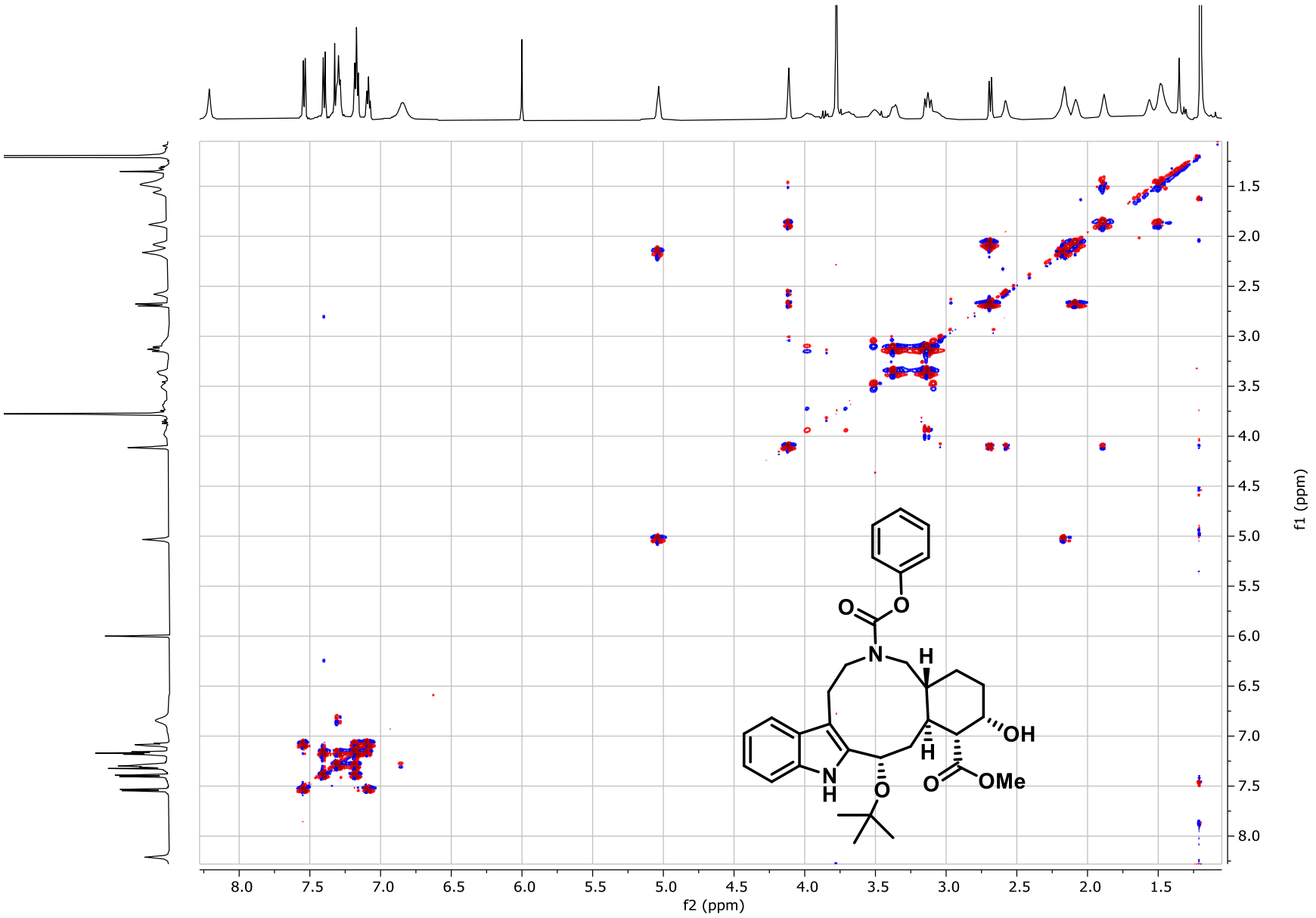

128.7
128.5
f1 (ppm)
124
122
120
118
116
114
112
110
f1 (ppm)
74.0
73.5
f1 (ppm)
55
50
45
40
35
f1 (ppm)
24.6
f1 (ppm)
O
O
N
H
H
OH
N
H
OMe
O
OMe
50
13C in TCE at 100 °C
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
f1 (ppm)
O
O
N
H
OH
H
N
H
O
O
OMe
51
1H in TCE at 100 °C
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)
CHCl3

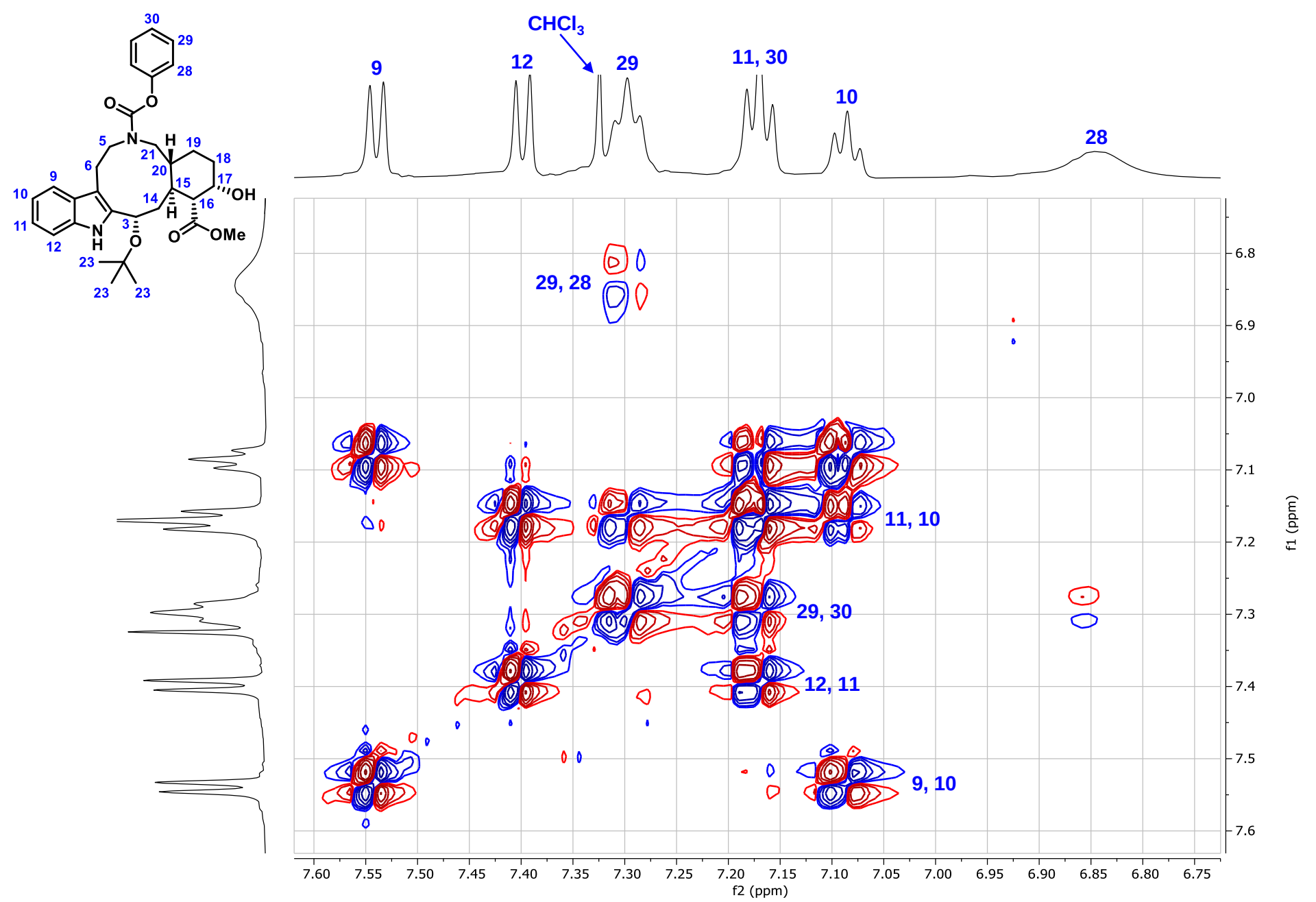

129 128 127 126 125 124 123 122 121 120 119 118
f1 (ppm)
74.0 73.6
f1 (ppm)
54 53 52
f1 (ppm)
24.6 24.4 24.2 24.0
f1 (ppm)
O
O
N
H
OH
H
N
H
O
O
OMe
51
13C in TCE at 100 °C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


O
O
N
H
OH
H
N
H
O
O
OMe
52
1H in TCE at 100 °C
4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4
f1 (ppm)
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

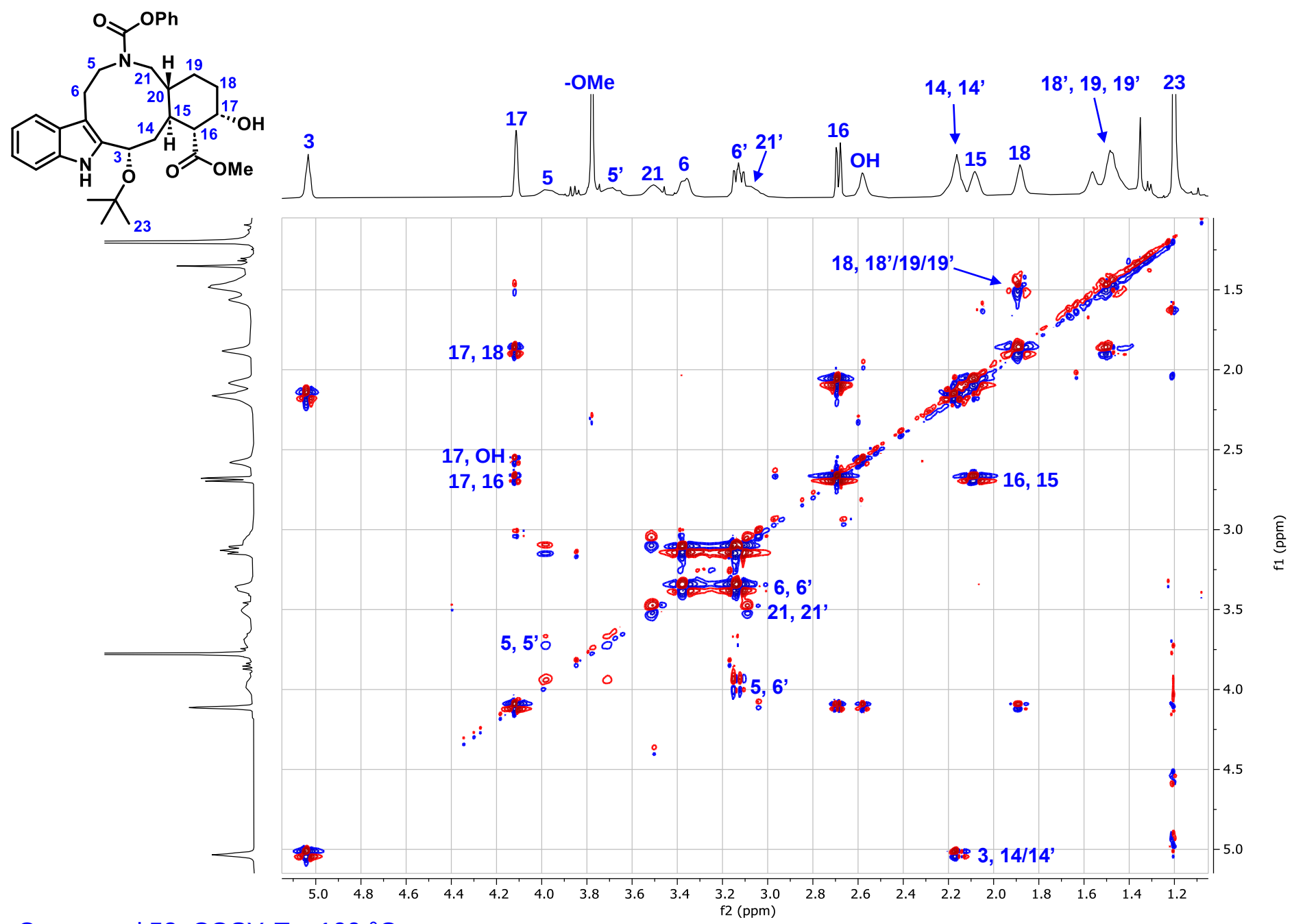

124.5 124.0 123.5 123.0 122.5 122.0 121.5 121.0 120.5 120.0 119.5 119.0 118.5 118.0
f1 (ppm)
74.4 73.8
f1 (ppm)
52.0 51.5 51.0
f1 (ppm)
40 35 30 25
f1 (ppm)
O
O
N
H
OH
H
N
H
O
O
OMe
52
13C in TCE at 100 °C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



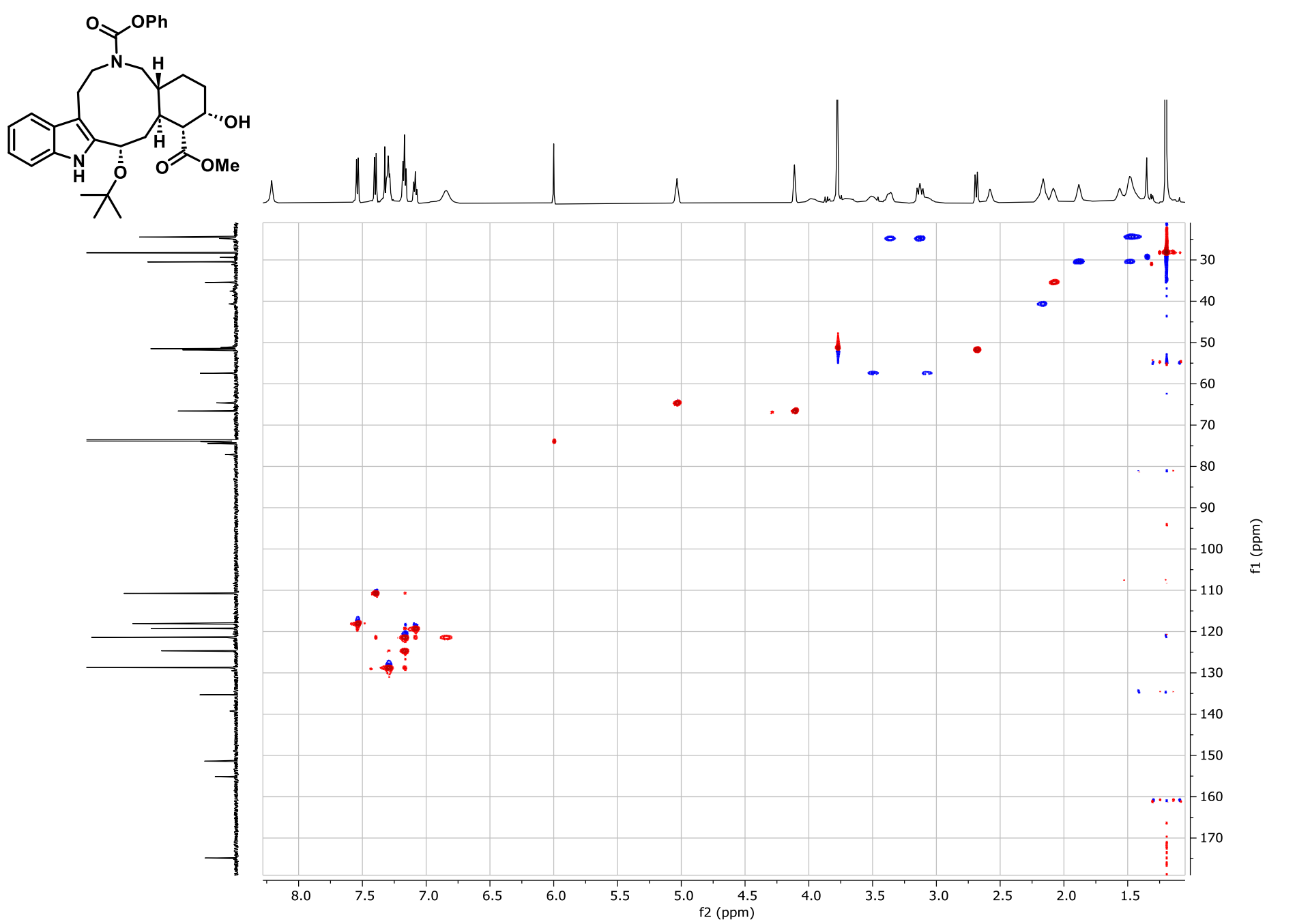
Compound 52: COSY, T = 100 °C, $C_2D_2Cl_4$ (full)



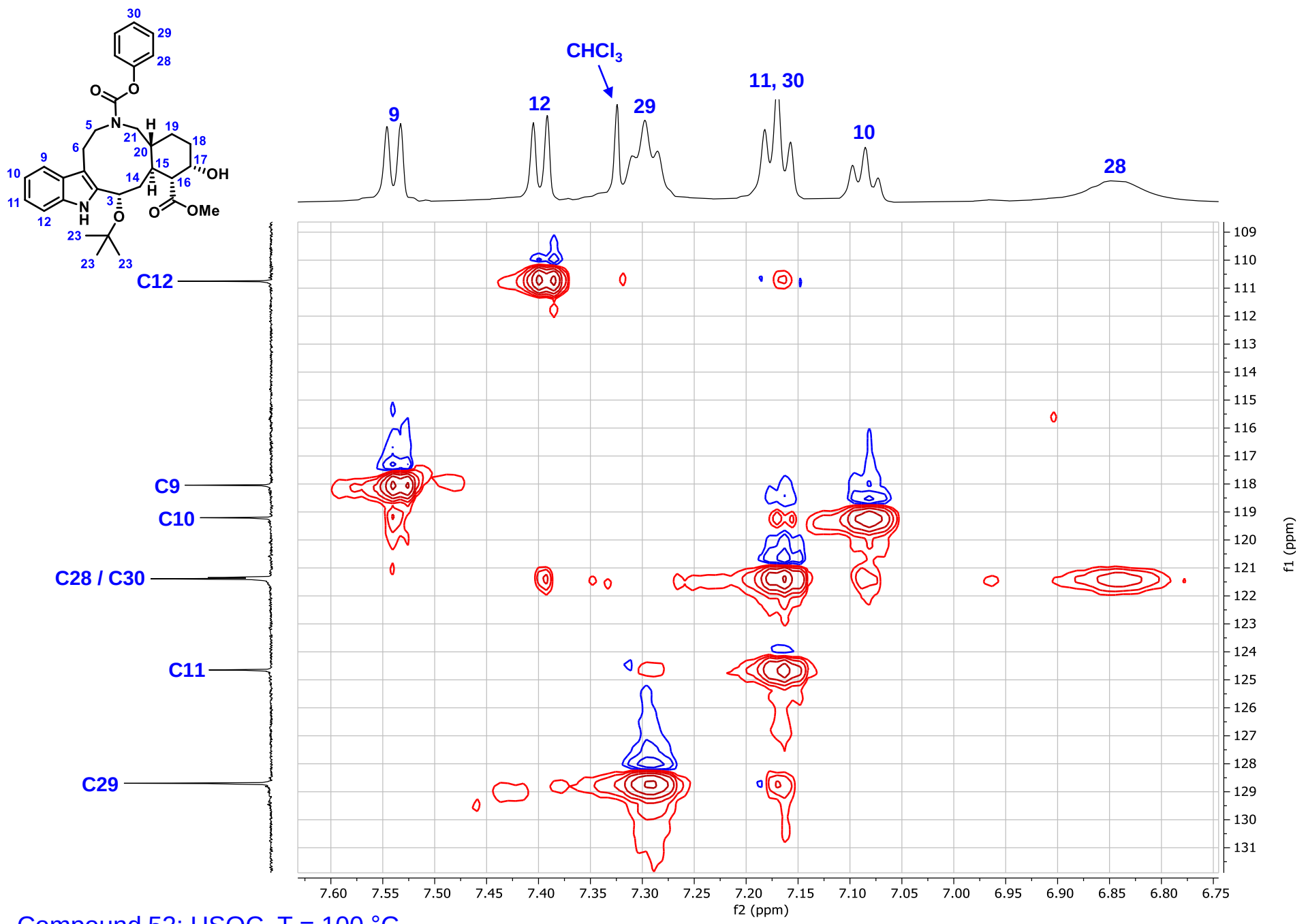
Compound 52: COSY, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 1)



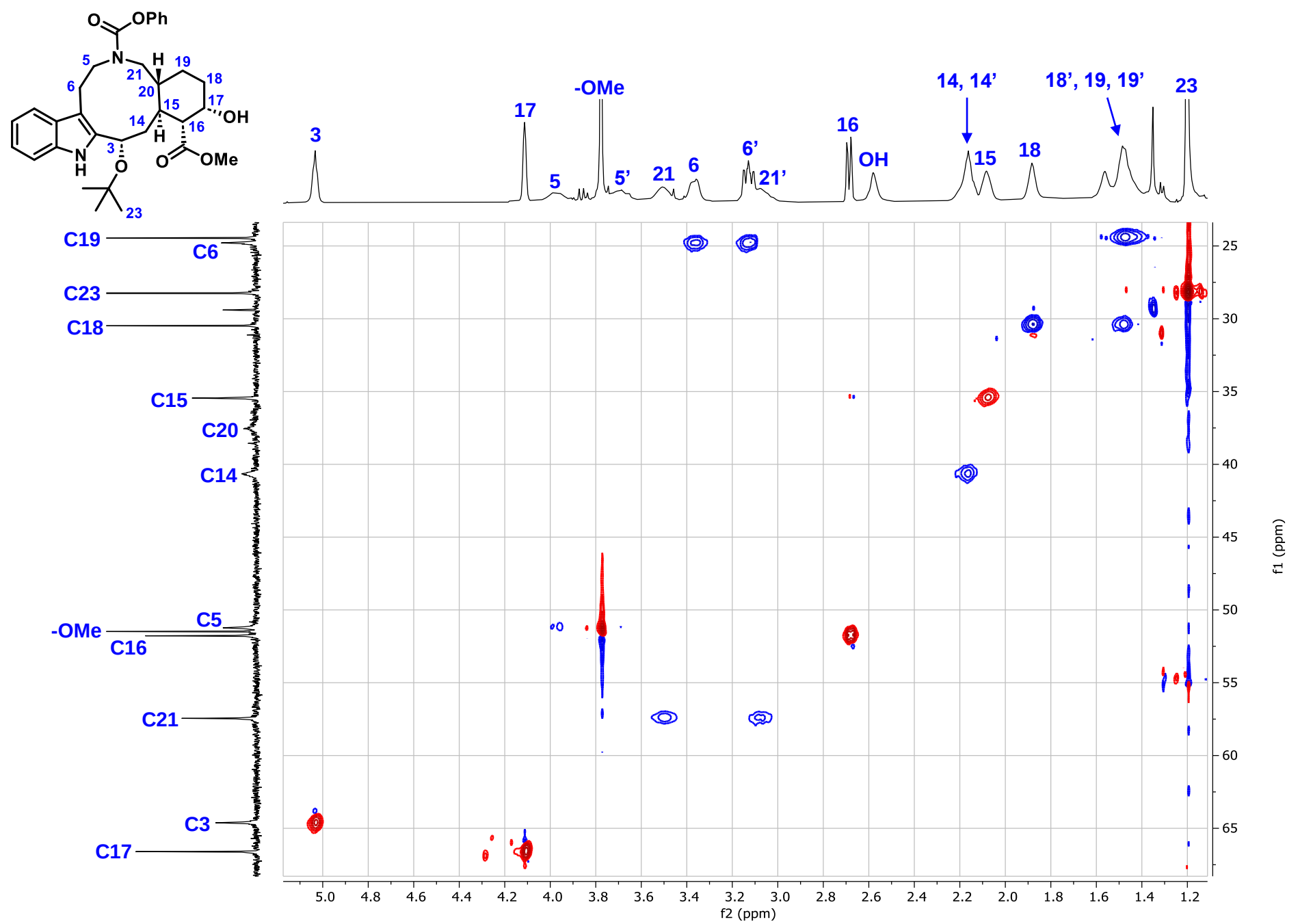
Compound 52: COSY, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 2)



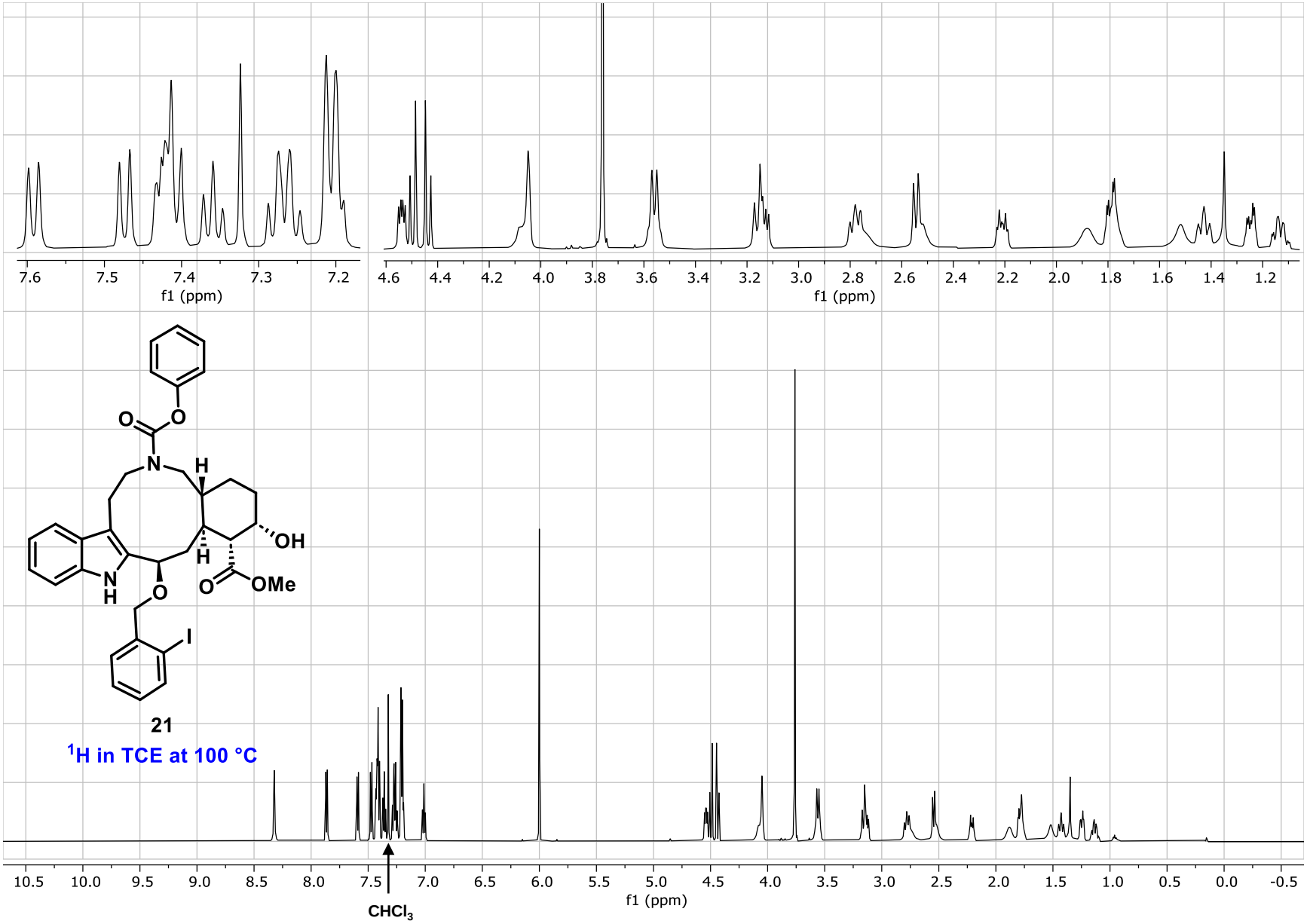
Compound 52: HSQC, T = 100 °C, $C_2D_2Cl_4$ (full)

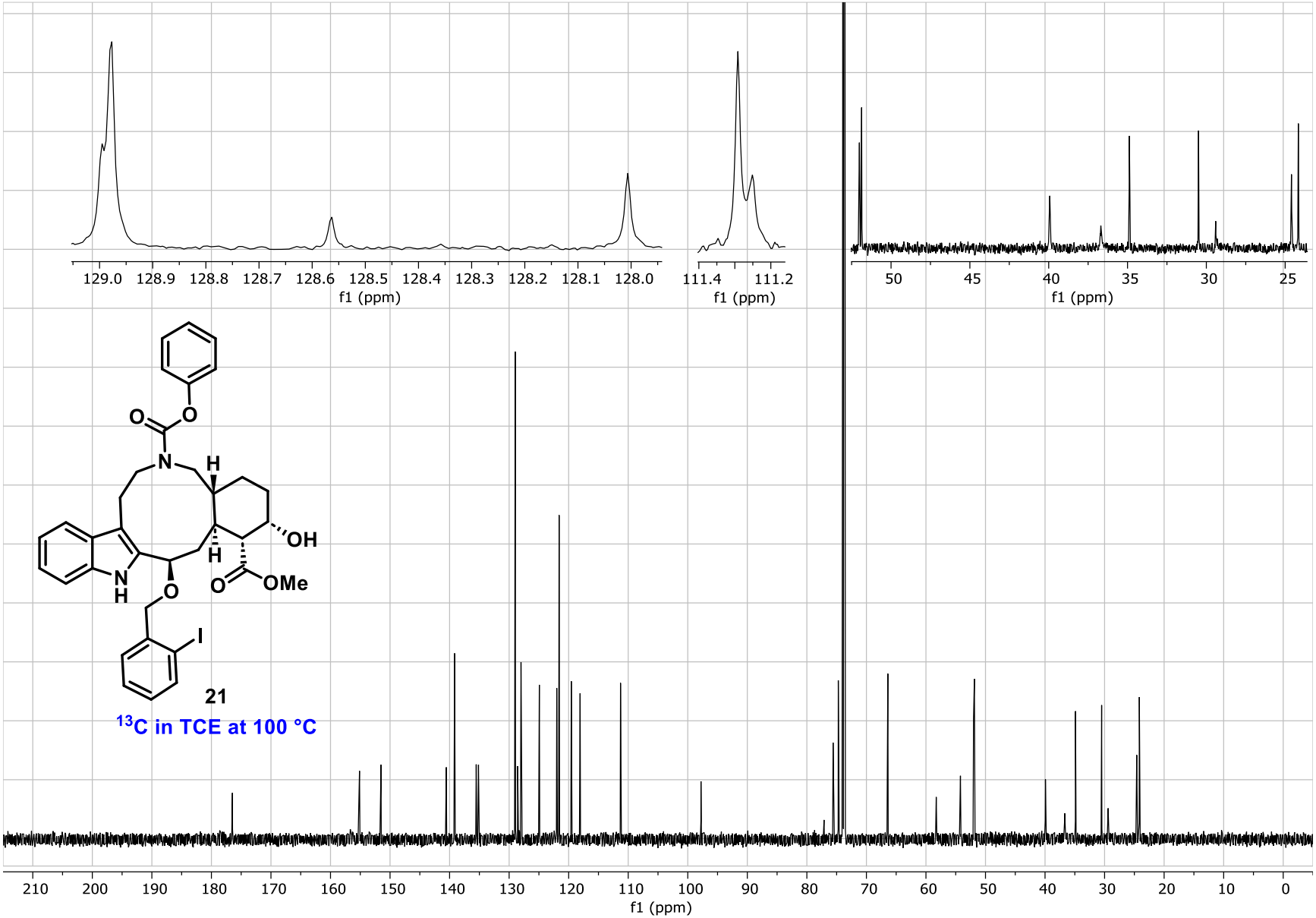


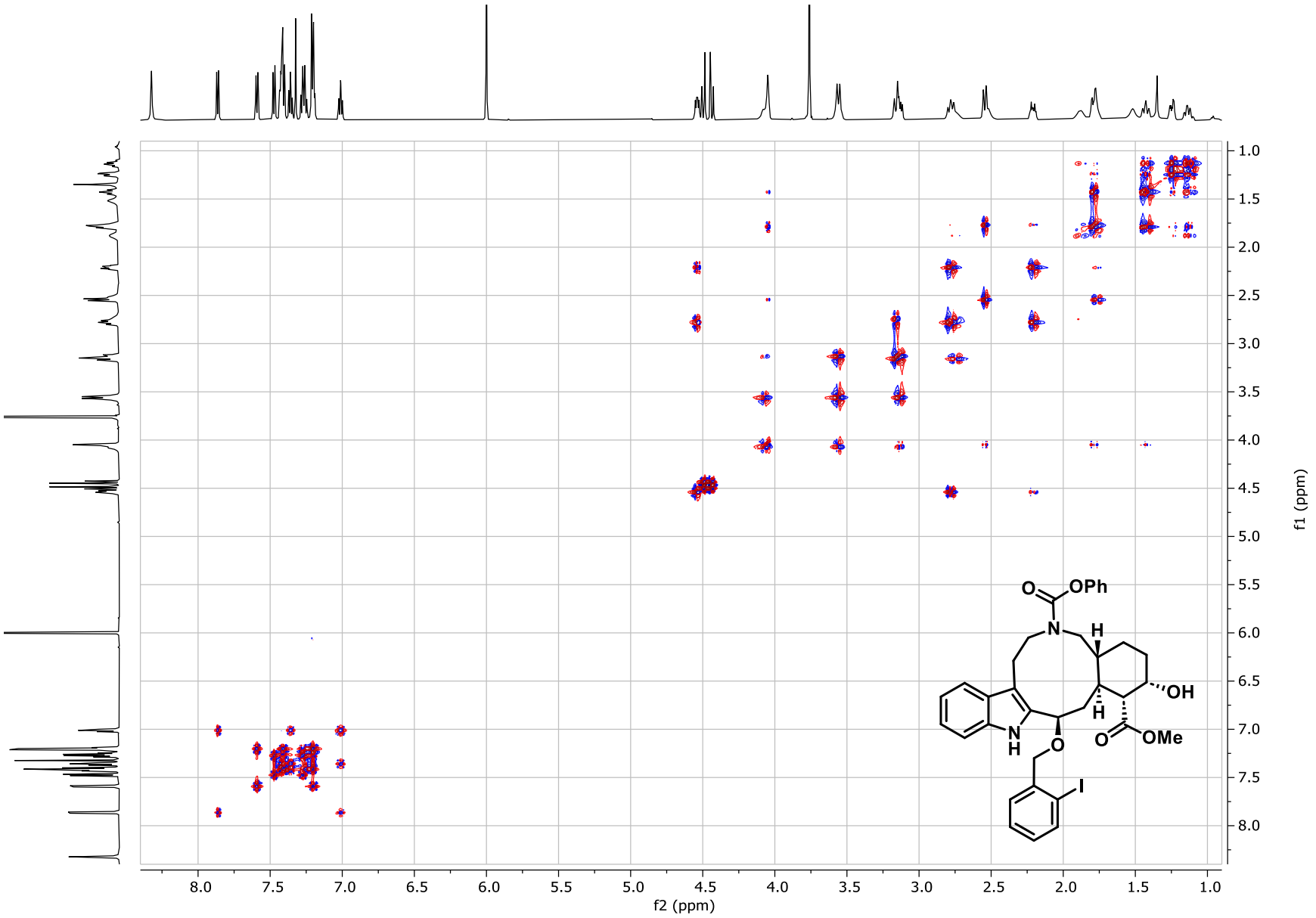
Compound 52: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 1)



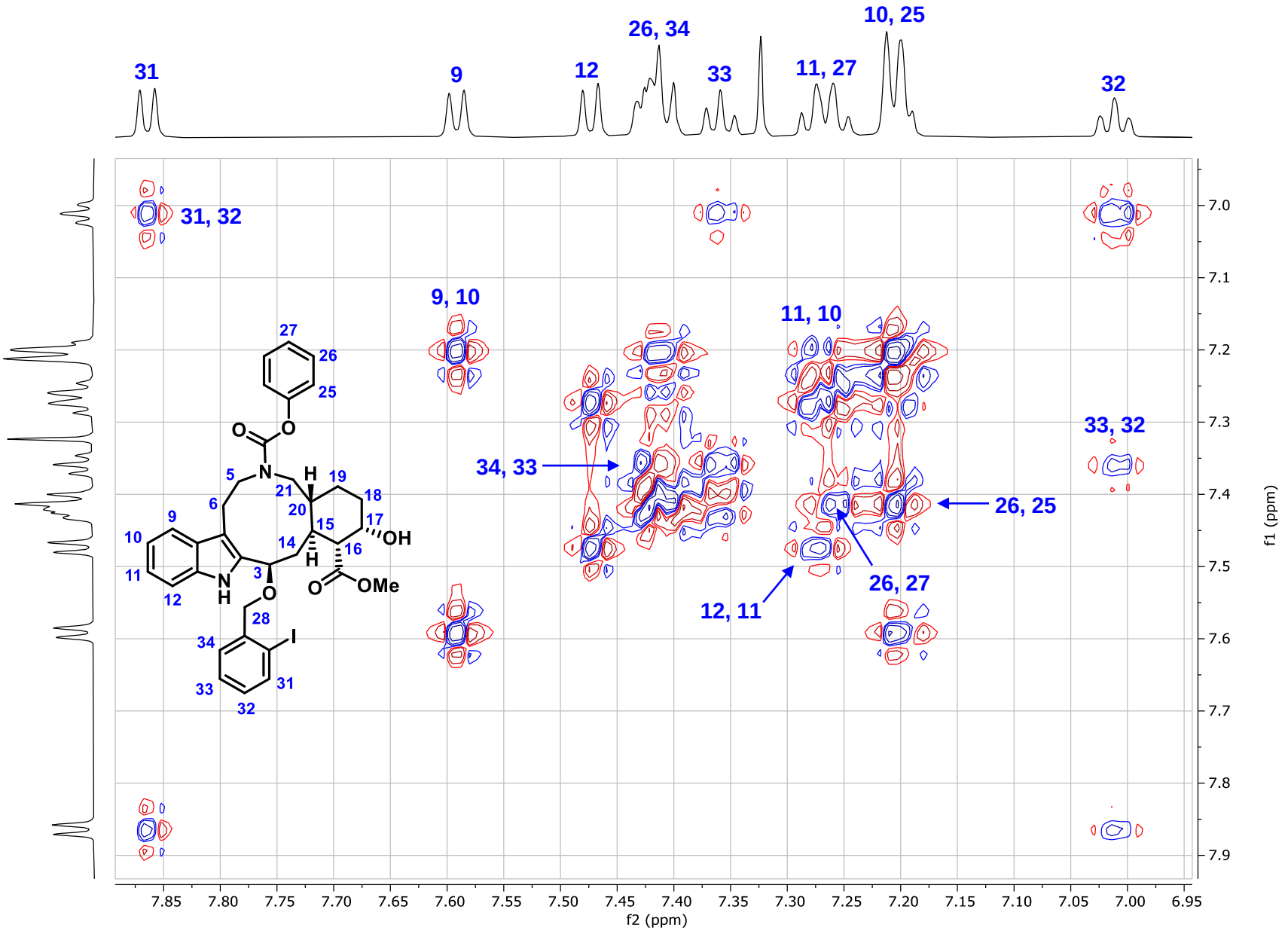
Compound 52: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 2)


7.6
7.5
7.4
7.3
7.2
f1 (ppm)
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
f1 (ppm)
O
O
N
H
OH
H
N
H
O
O
OMe
I
21
1H in TCE at 100 °C
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)
CHCl3

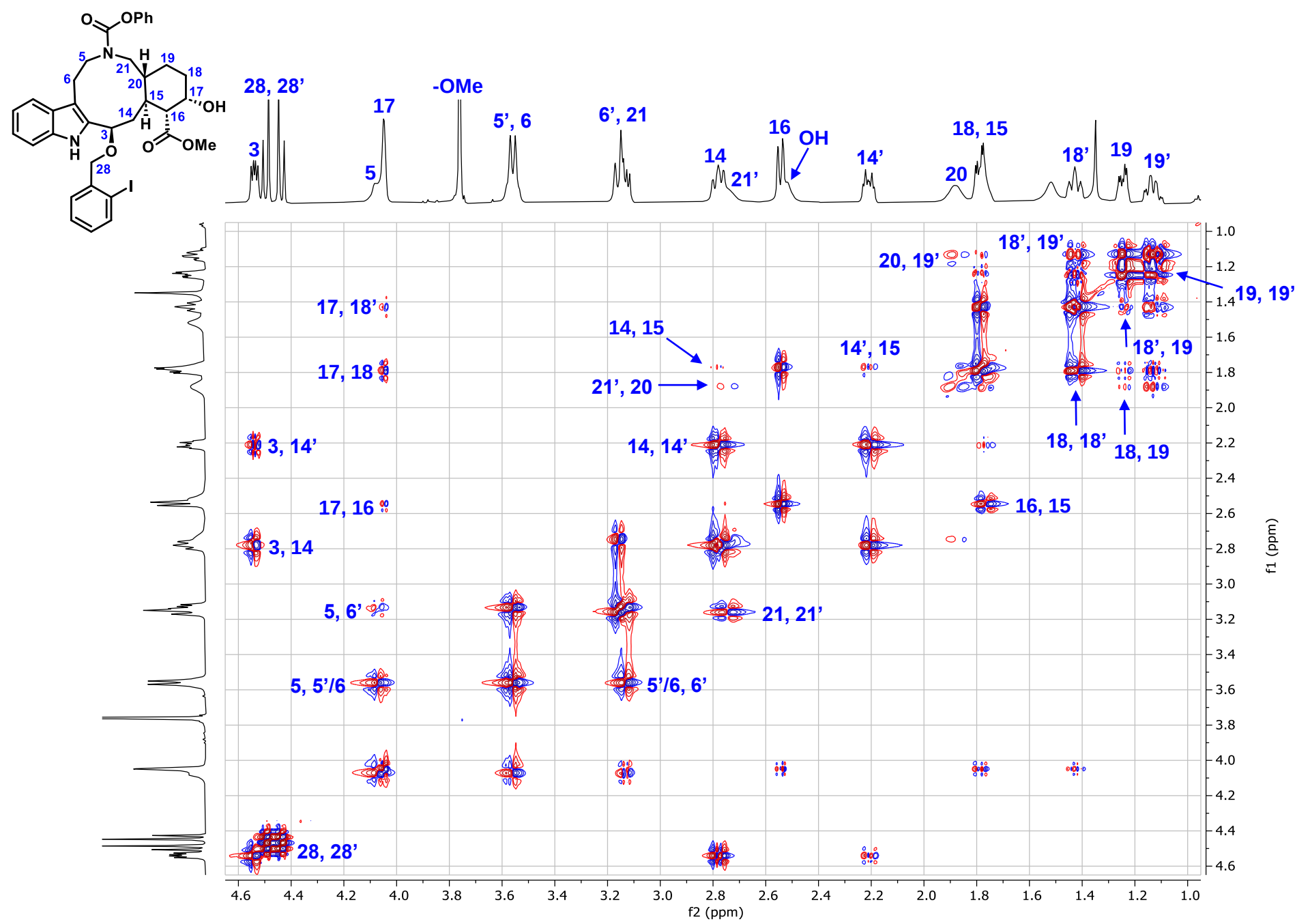

129.0 128.9 128.8 128.7 128.6 128.5 128.4 128.3 128.2 128.1 128.0
f1 (ppm)
111.4 111.2
f1 (ppm)
50 45 40 35 30 25
f1 (ppm)
O
O
N
H
OH
H
N
H
O
O
OMe
I
21
13C in TCE at 100 °C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



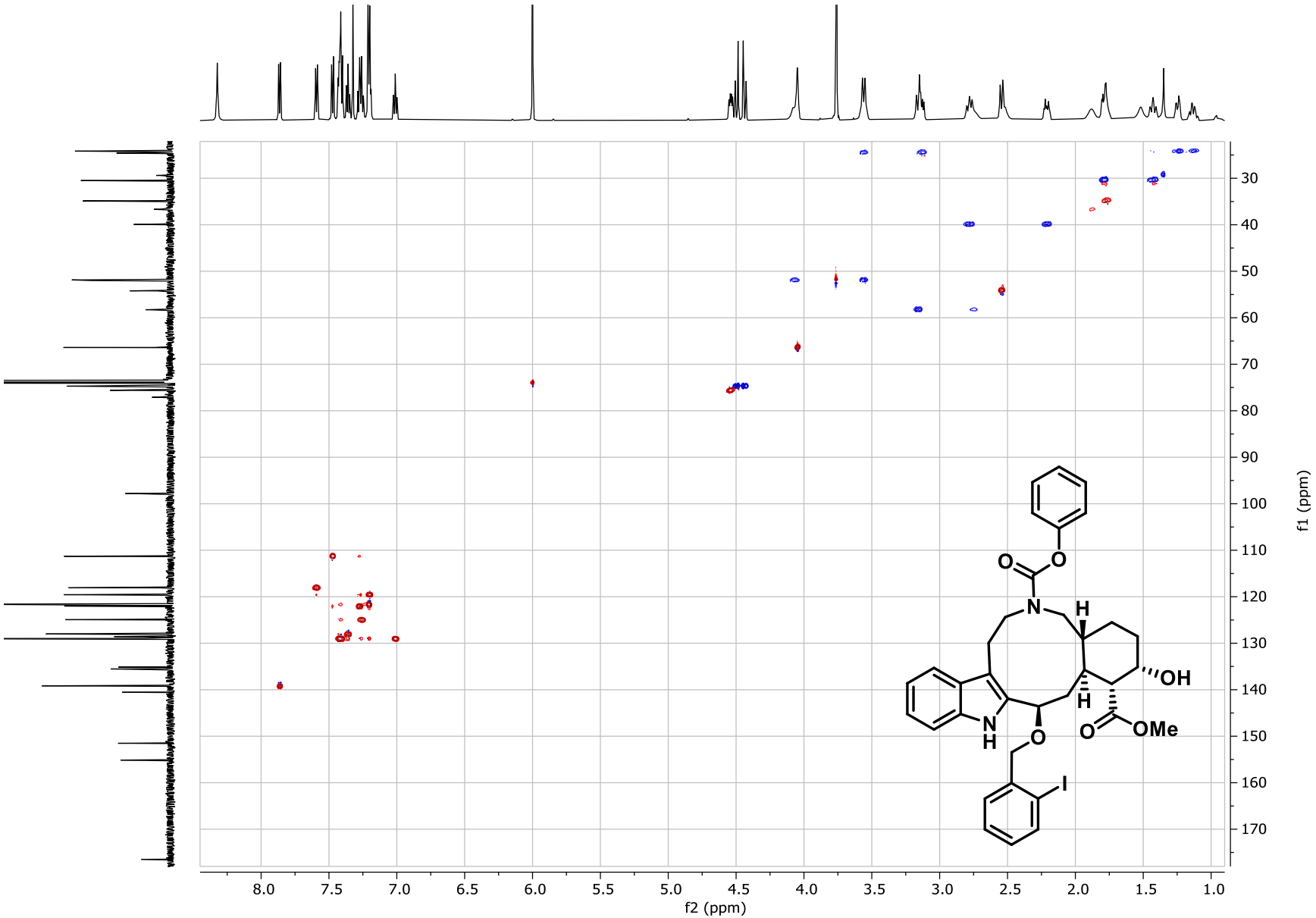
Compound 21: COSY, T = 100 °C, $C_2D_2Cl_4$ (full)



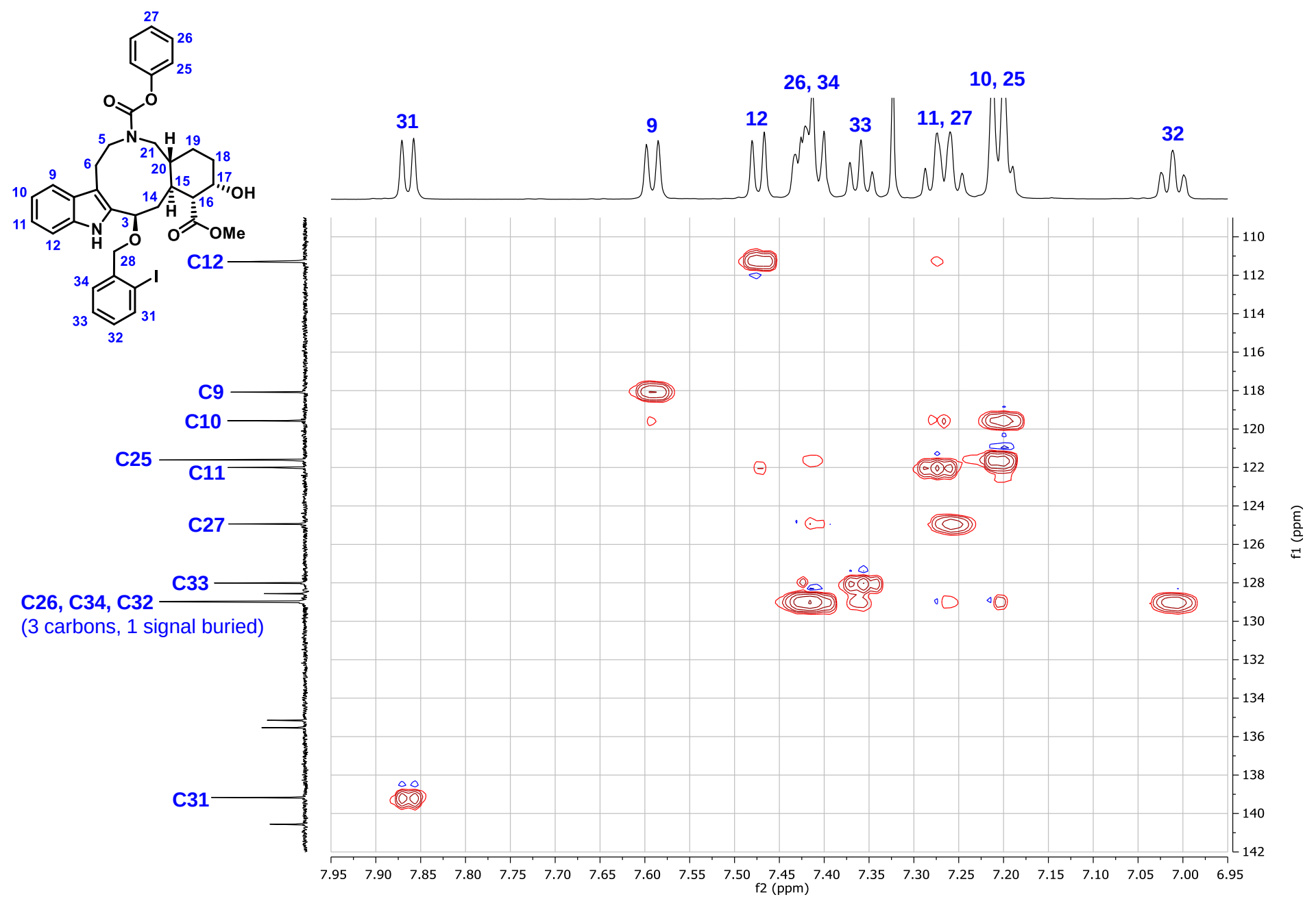
Compound 21: COSY, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 1)



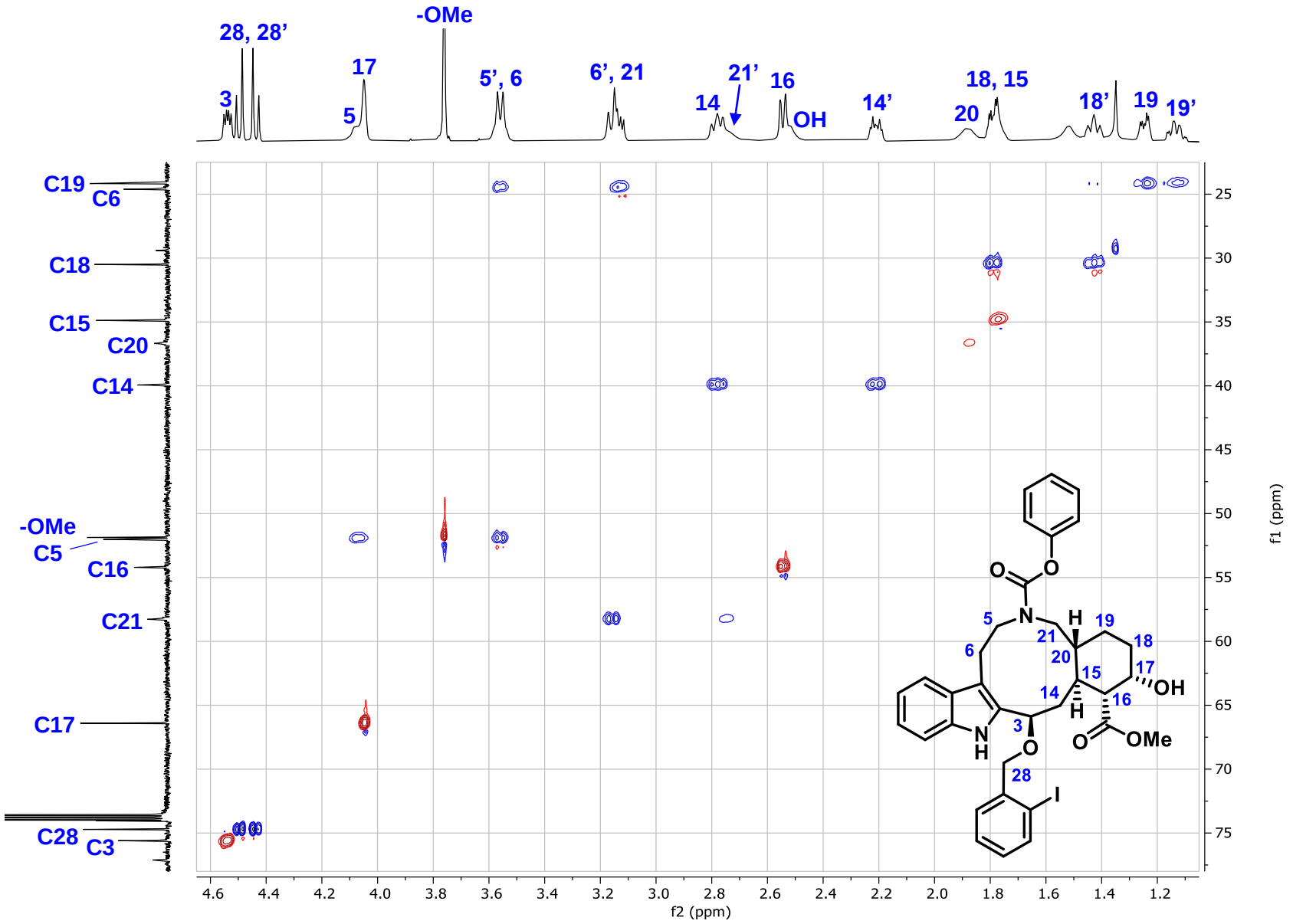
Compound 21: COSY, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 2)



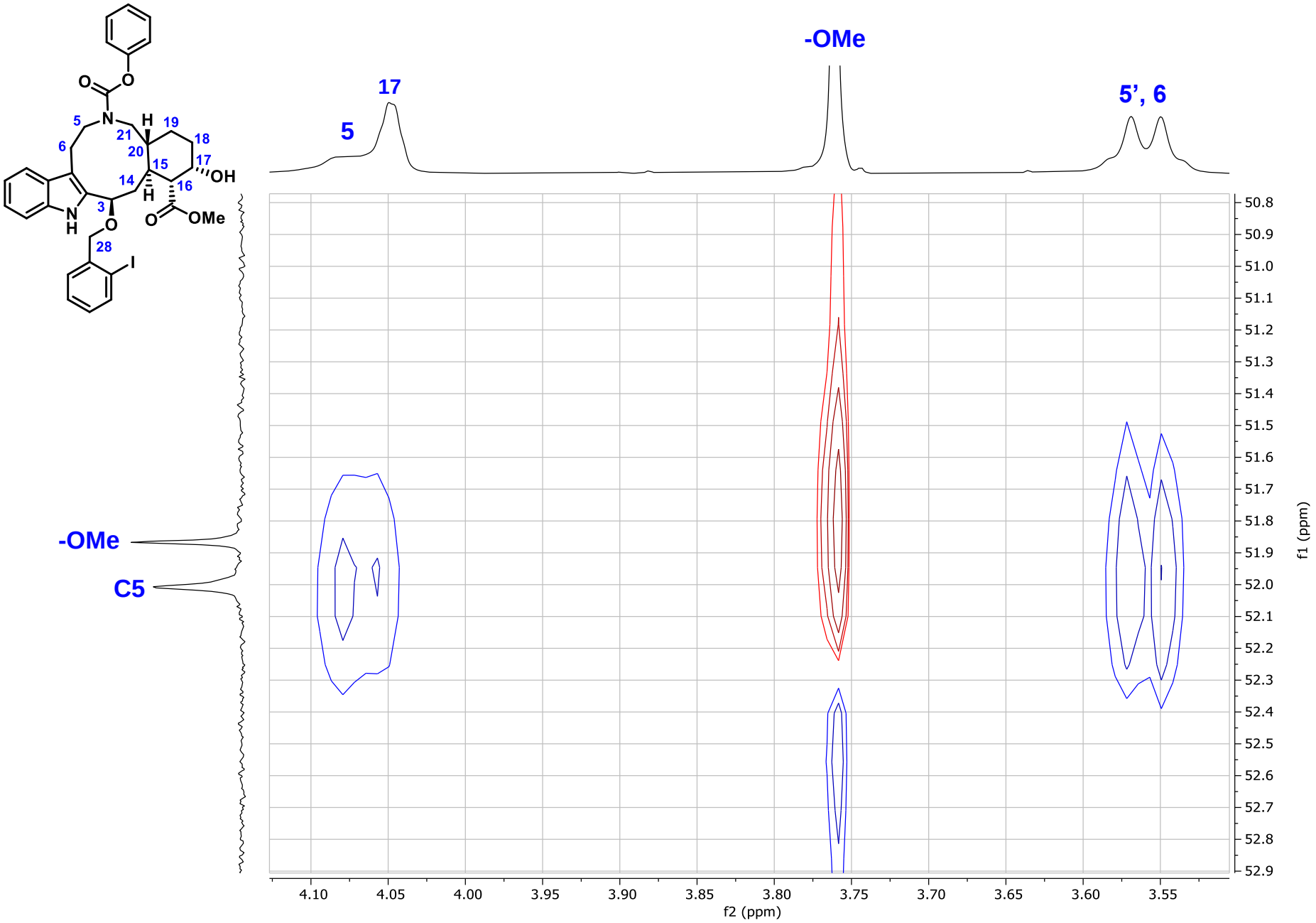
Compound 21: HSQC, T = 100 °C, $C_2D_2Cl_4$ (full)



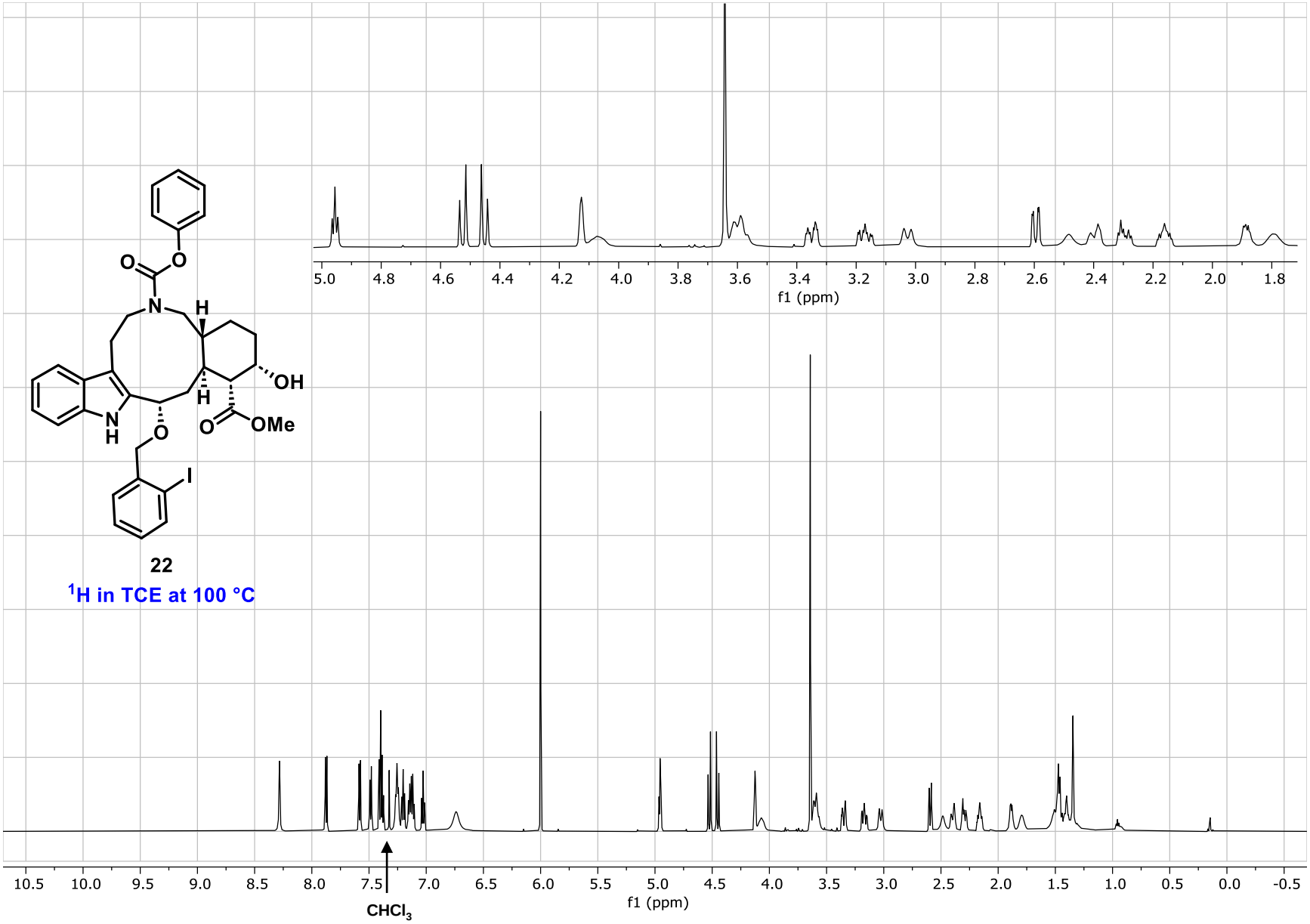
Compound 21: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 1)

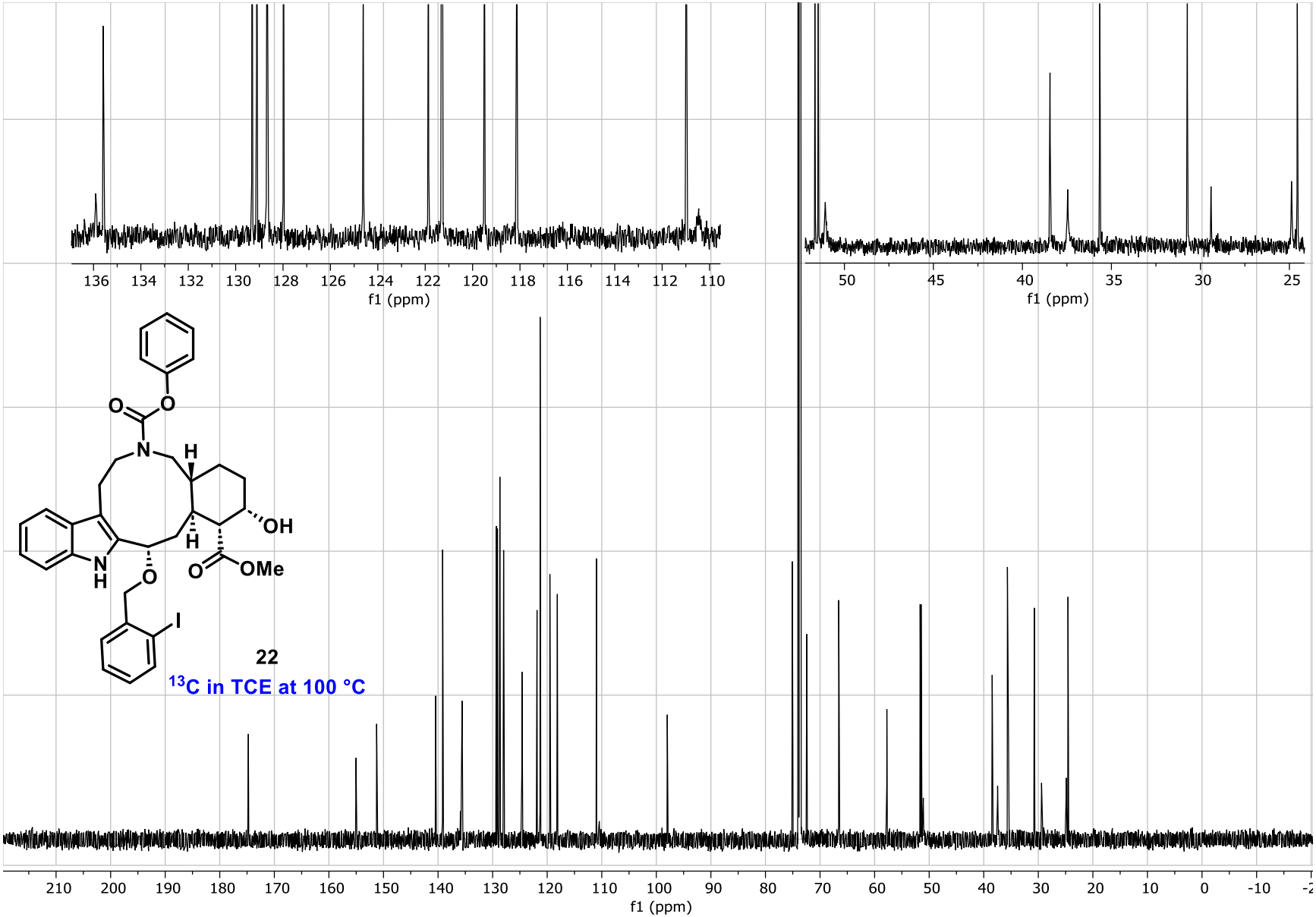


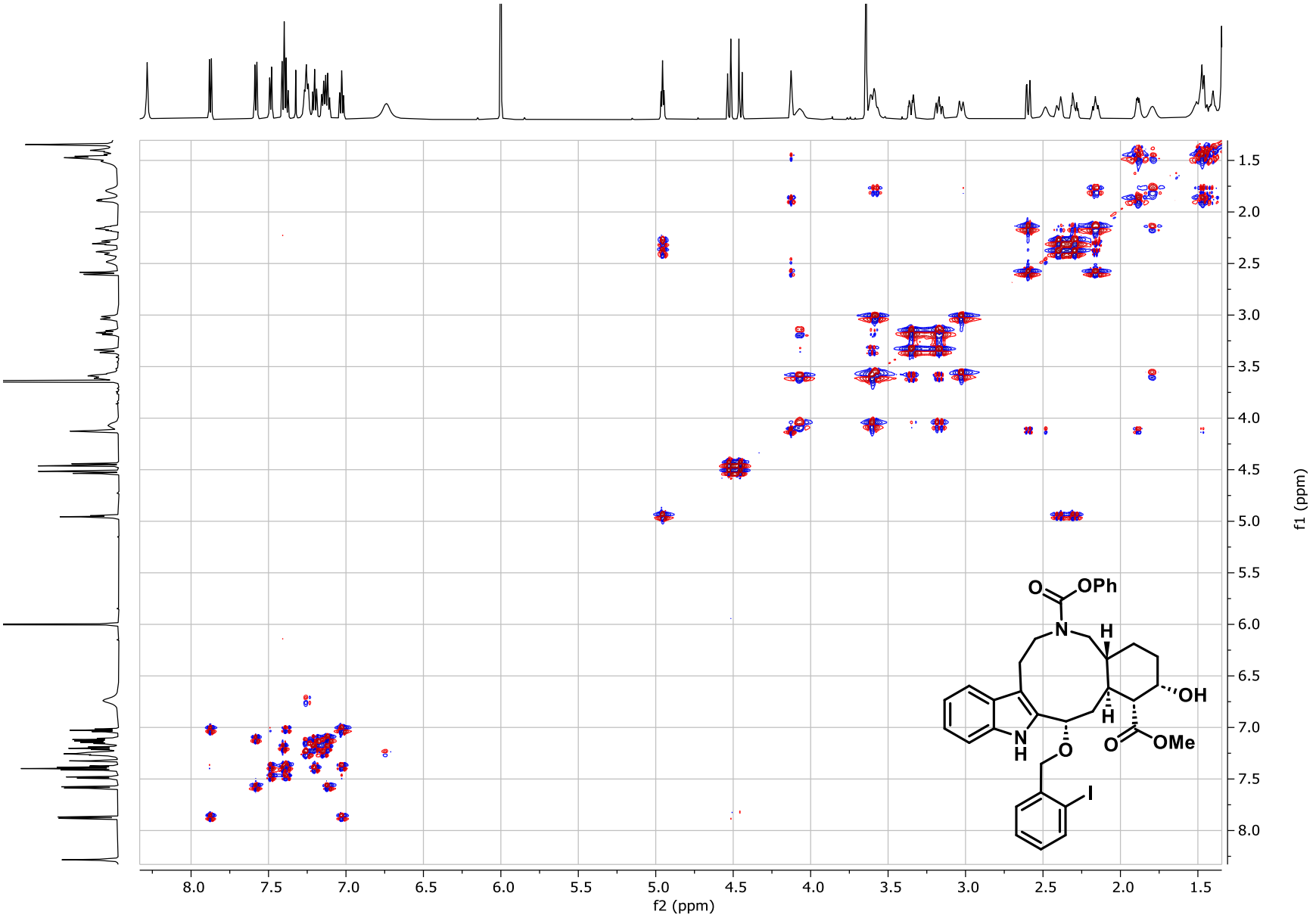
Compound 21: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 2)



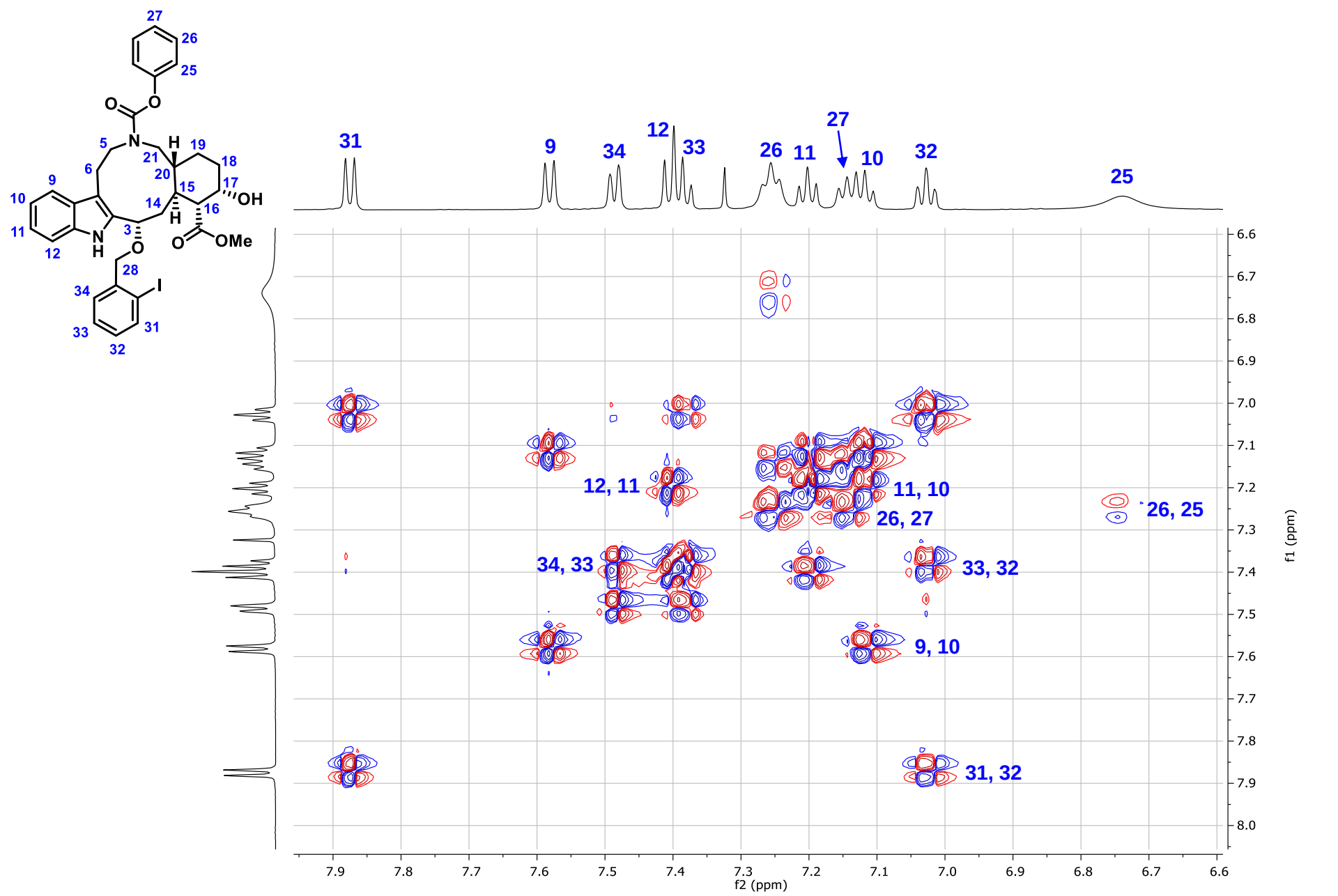
Compound 21: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 3)


O
O
N
H
OH
H
N
H
O
O
OMe
I
22
1H in TCE at 100 °C
5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8
f1 (ppm)
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)
CHCl3

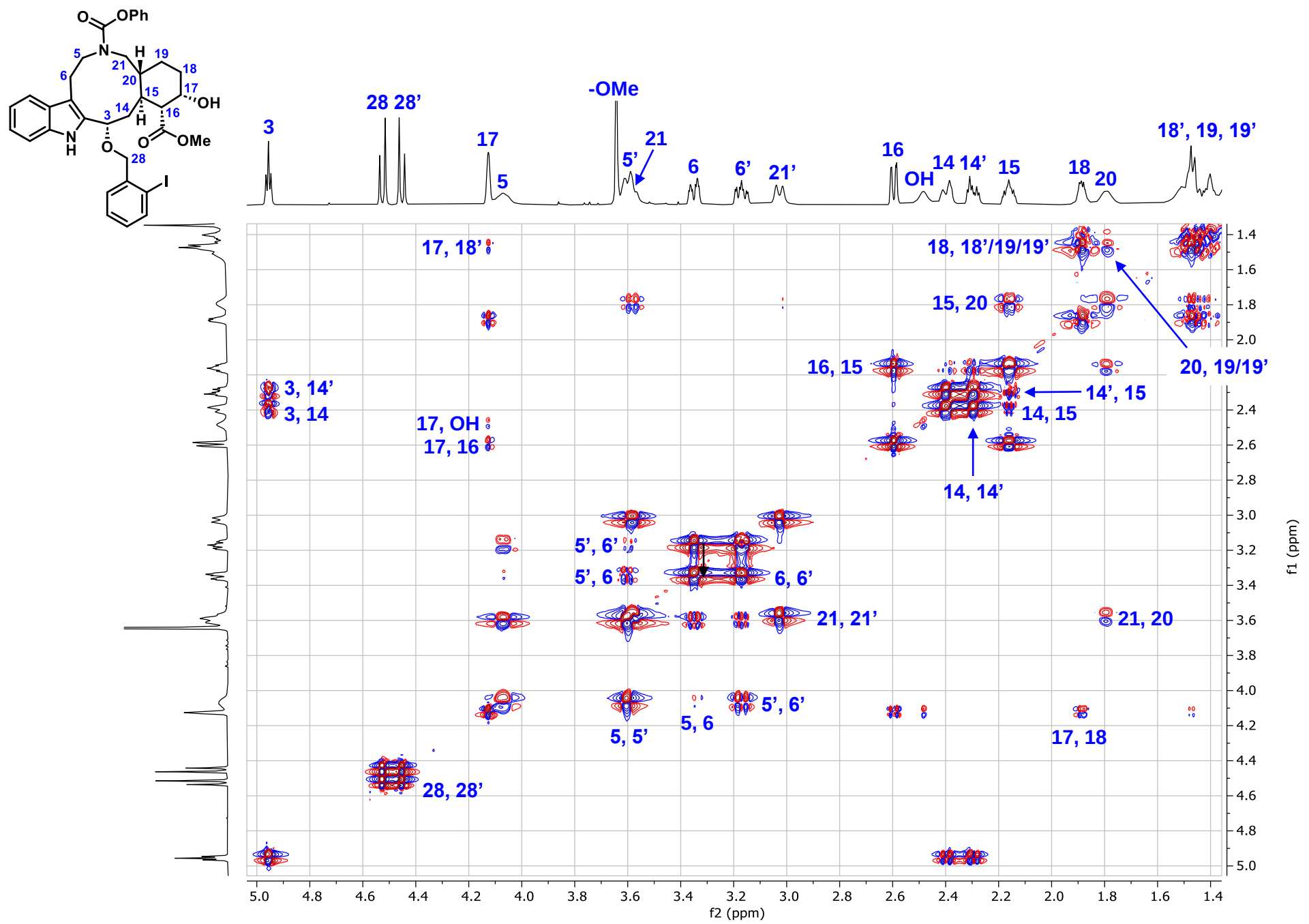

22
13C in TCE at 100 °C
f1 (ppm)
f1 (ppm)
f1 (ppm)



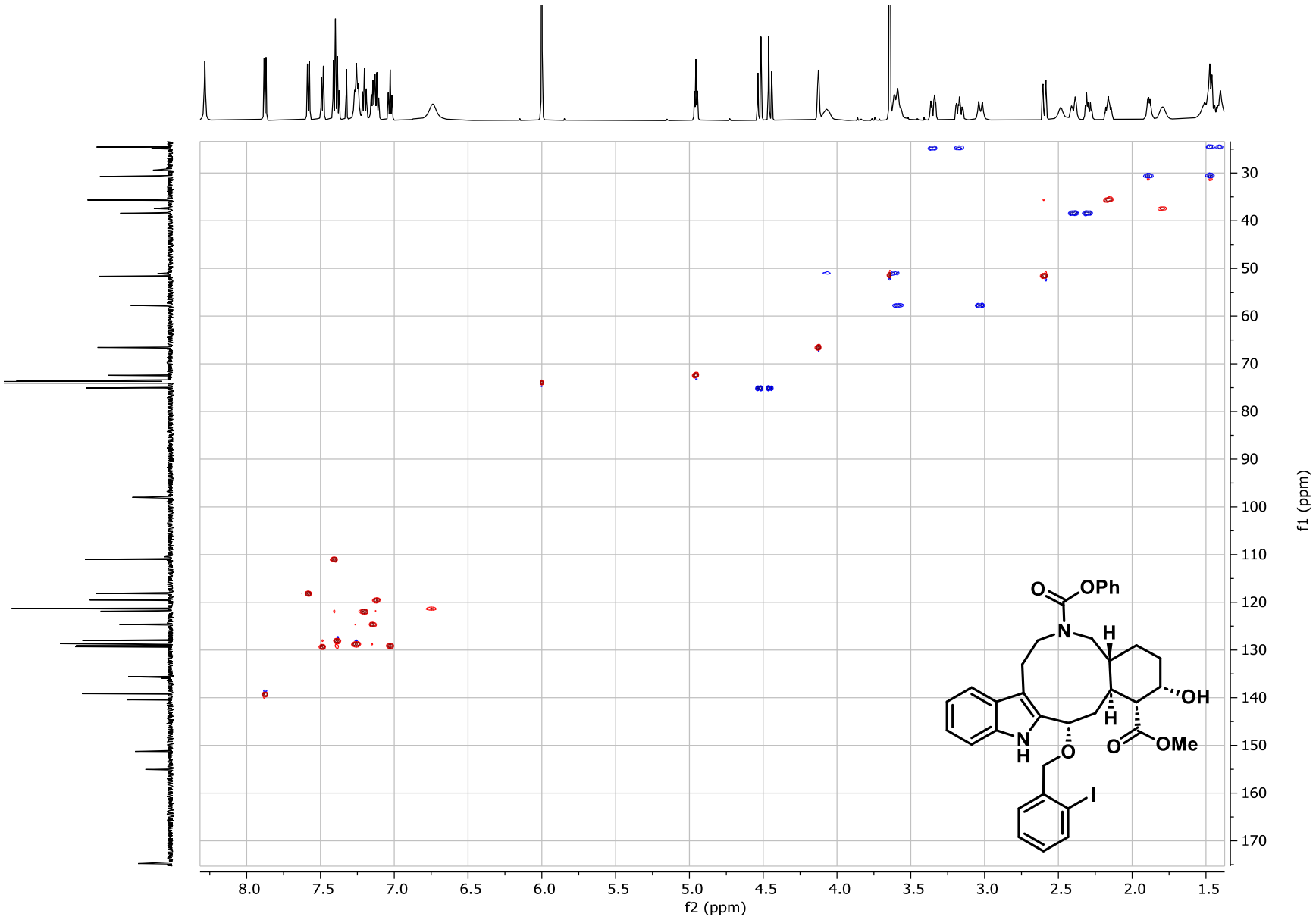
Compound 22: COSY, T = 100 °C, $C_2D_2Cl_4$ (full)



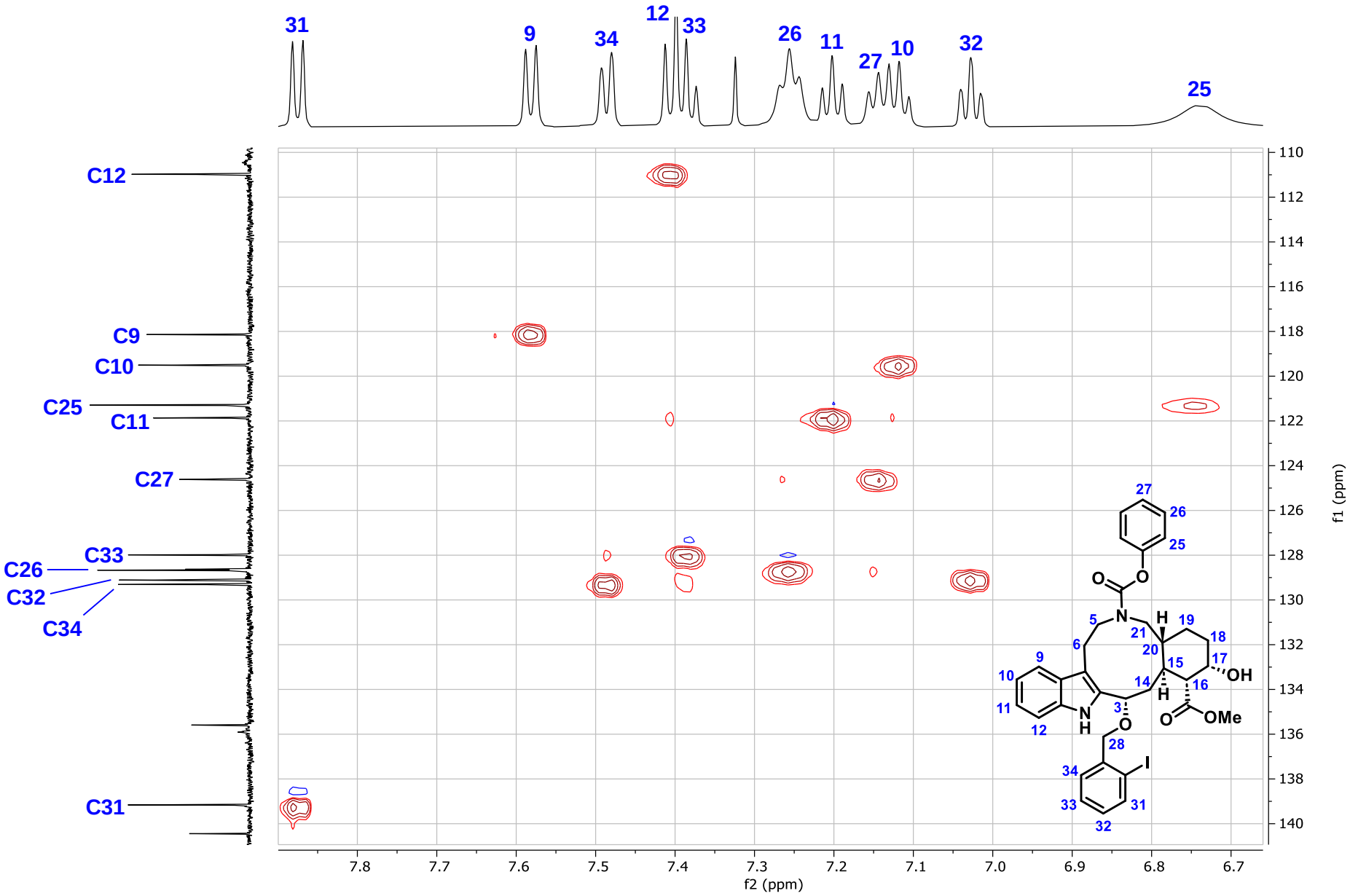
Compound 22: COSY, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 1)



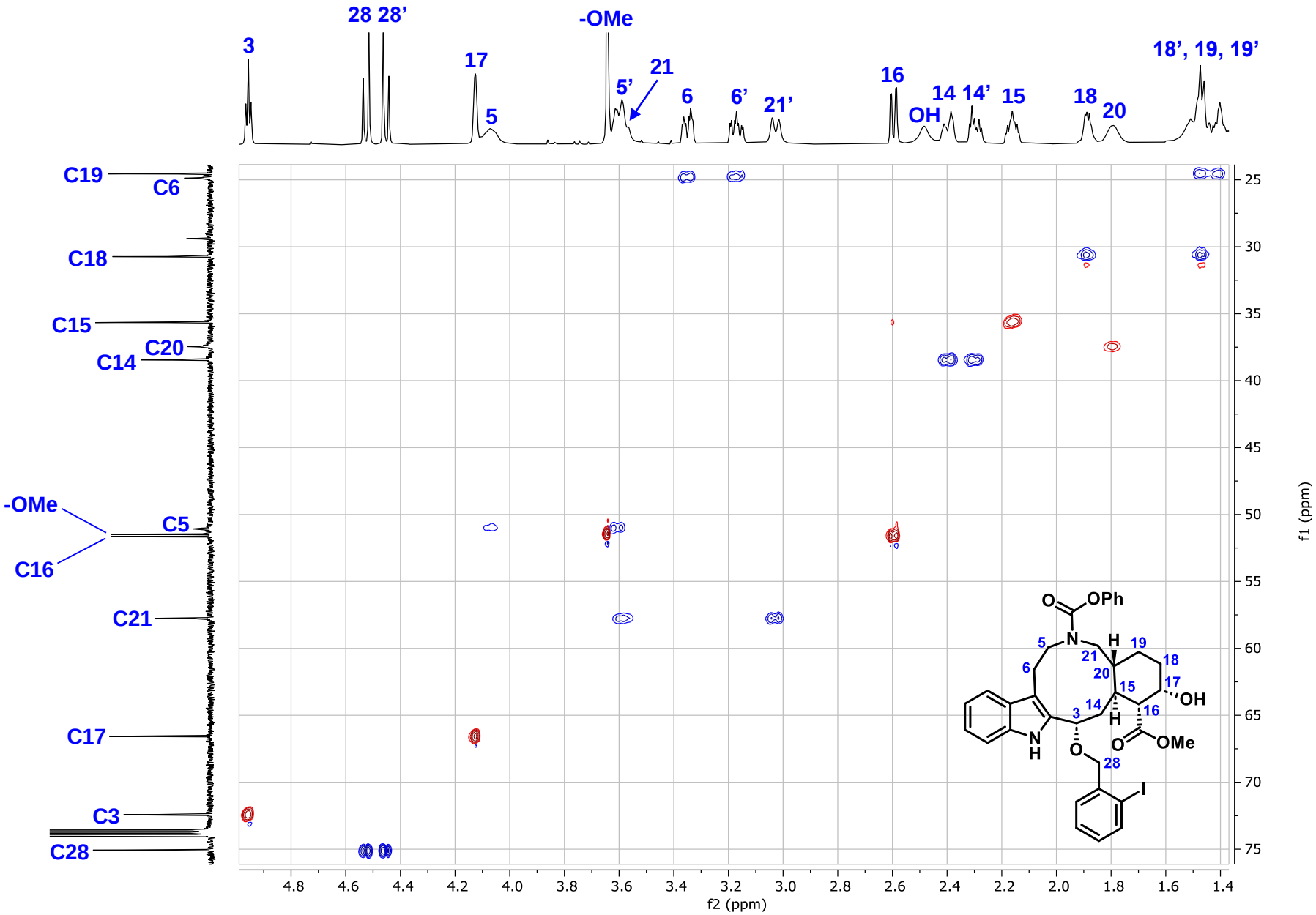
Compound 22: COSY, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 2)



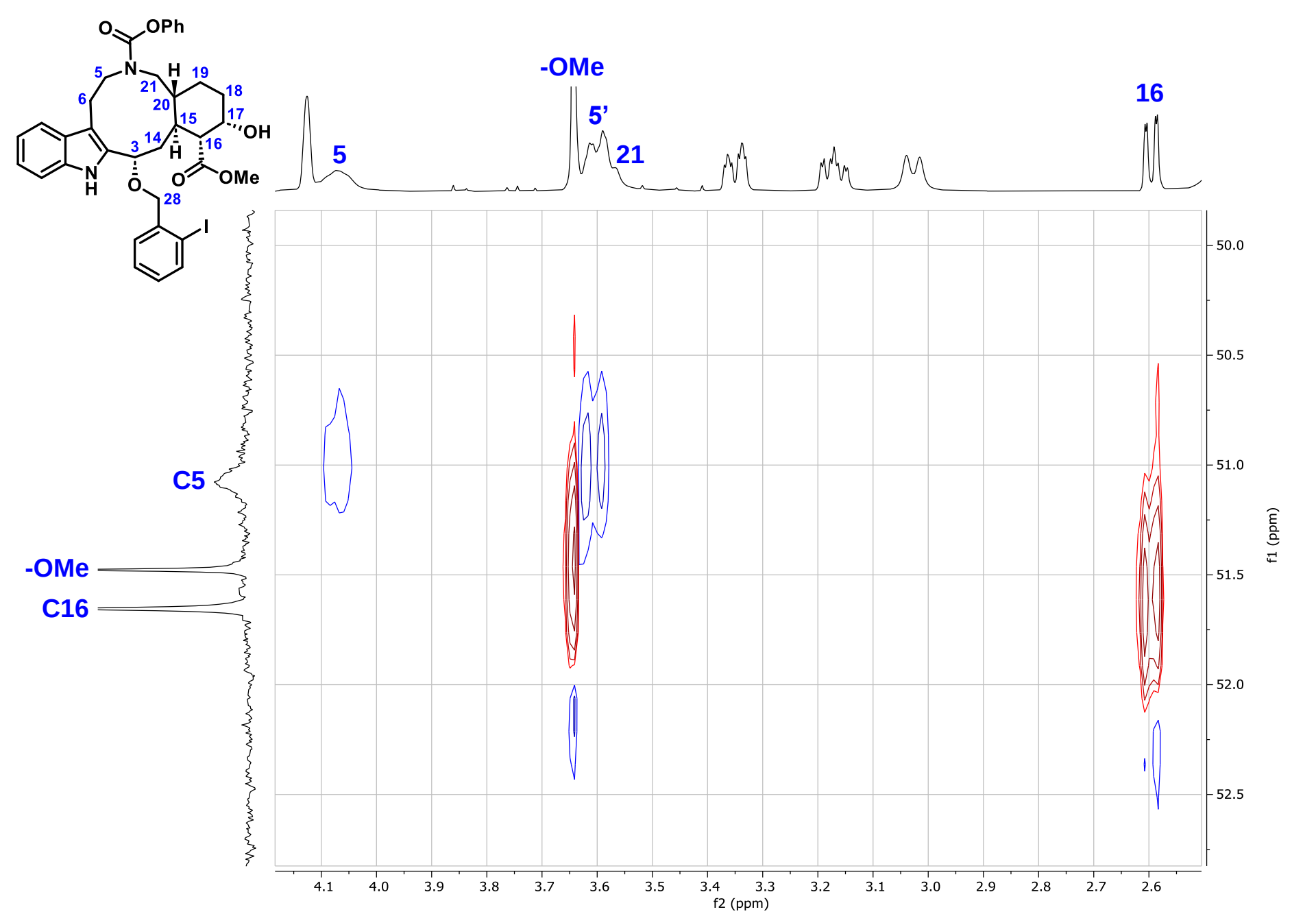
Compound 22: HSQC, T = 100 °C, $C_2D_2Cl_4$ (full)



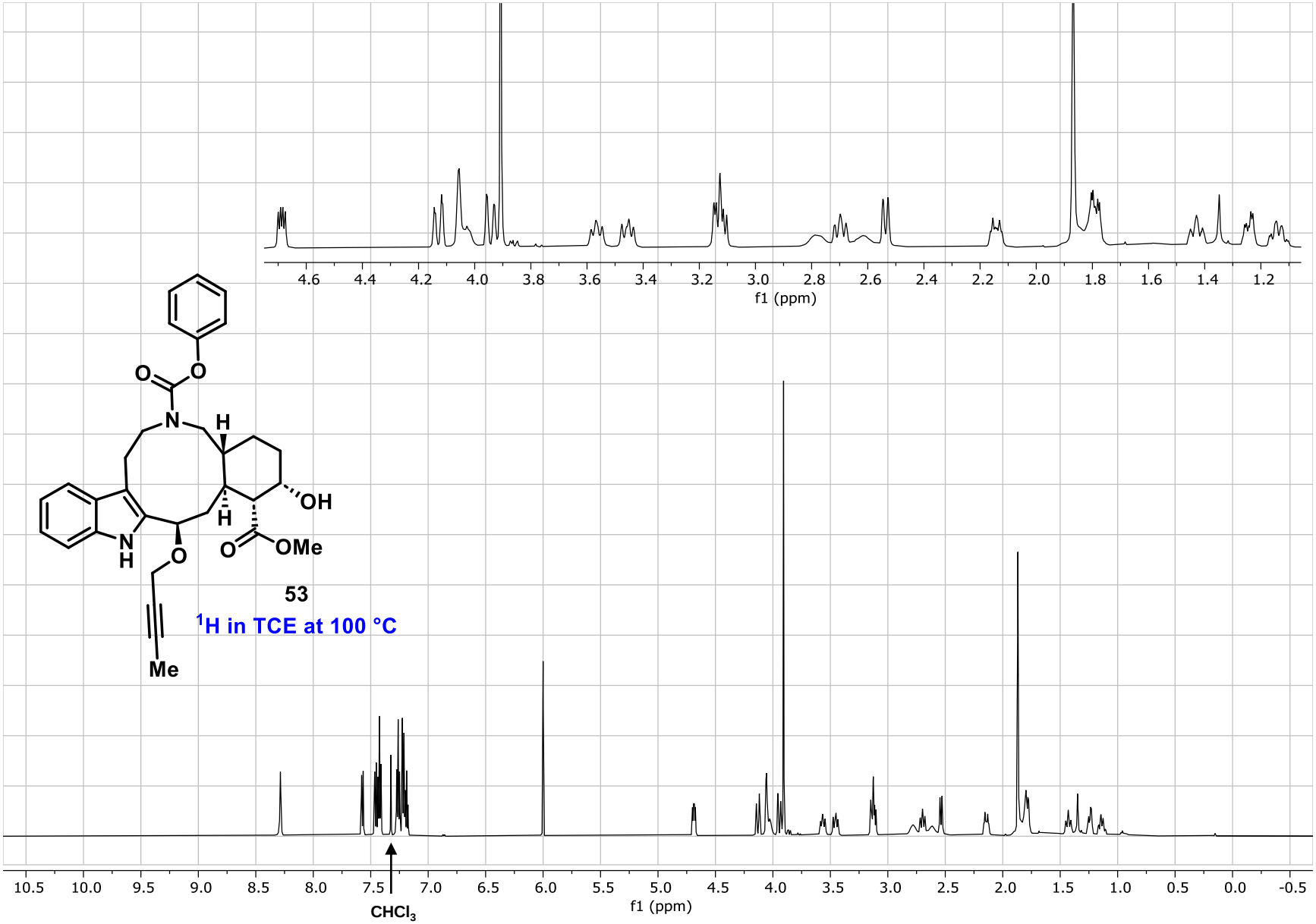
Compound 22: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 1)

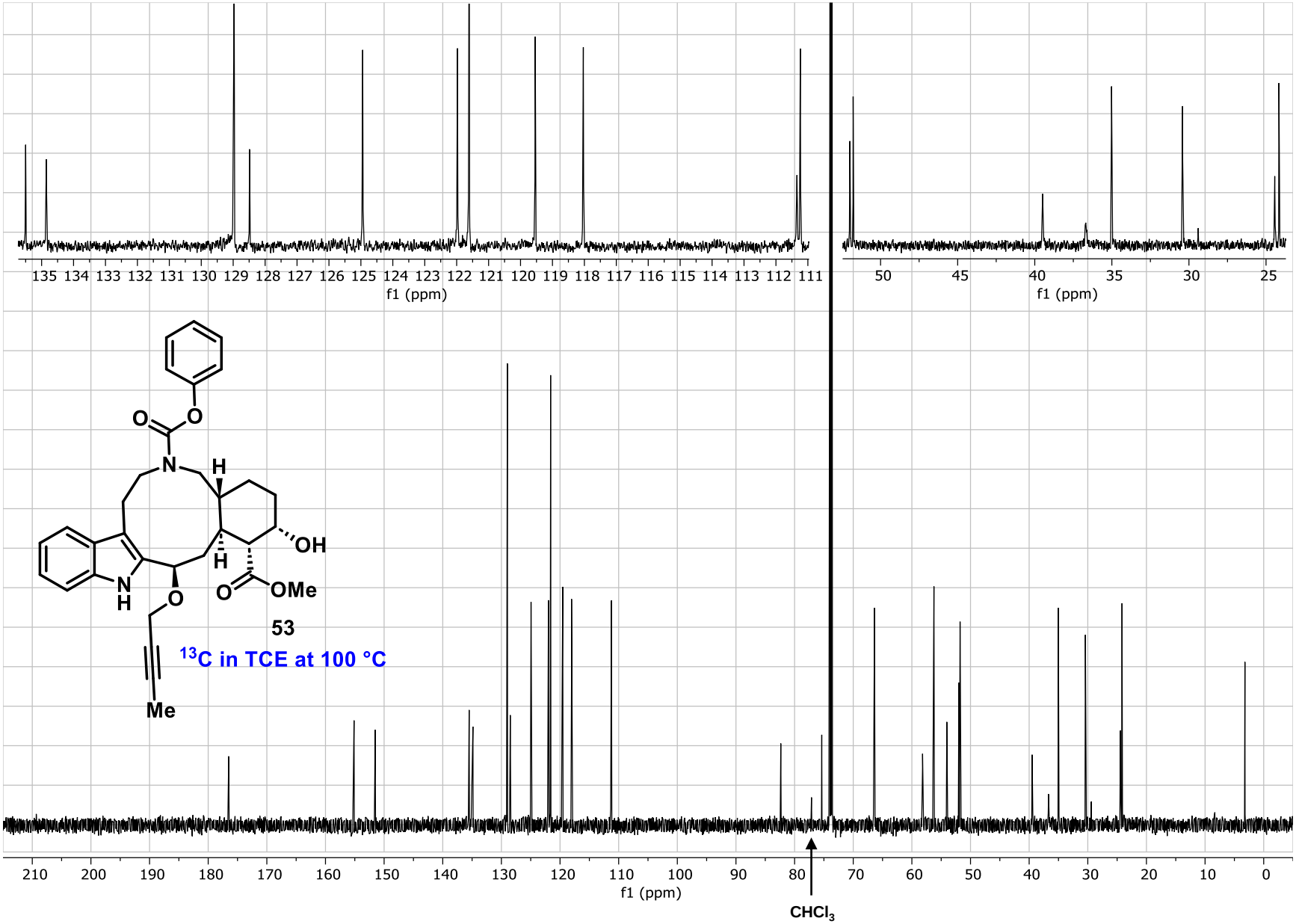


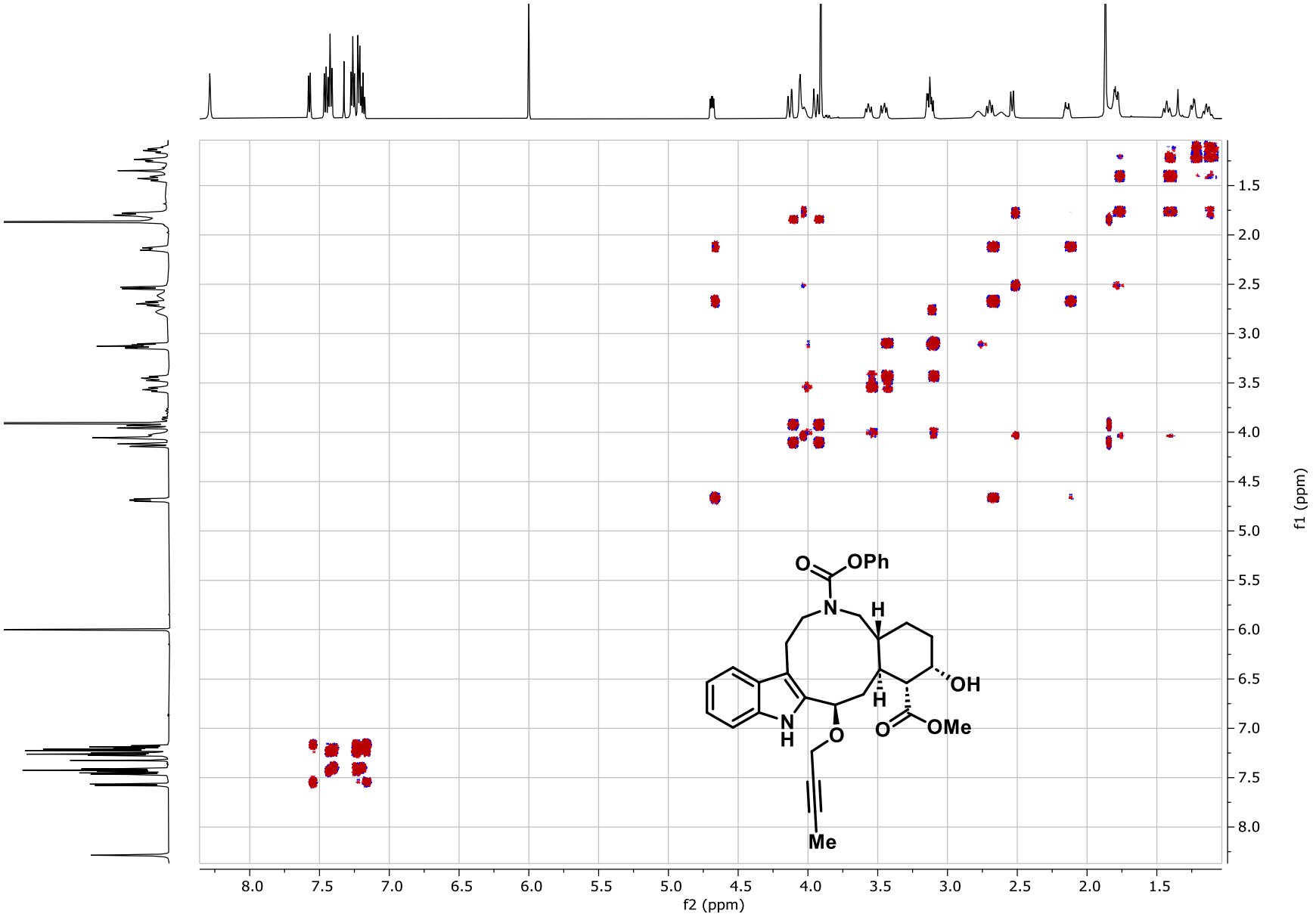
Compound 22: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 2)



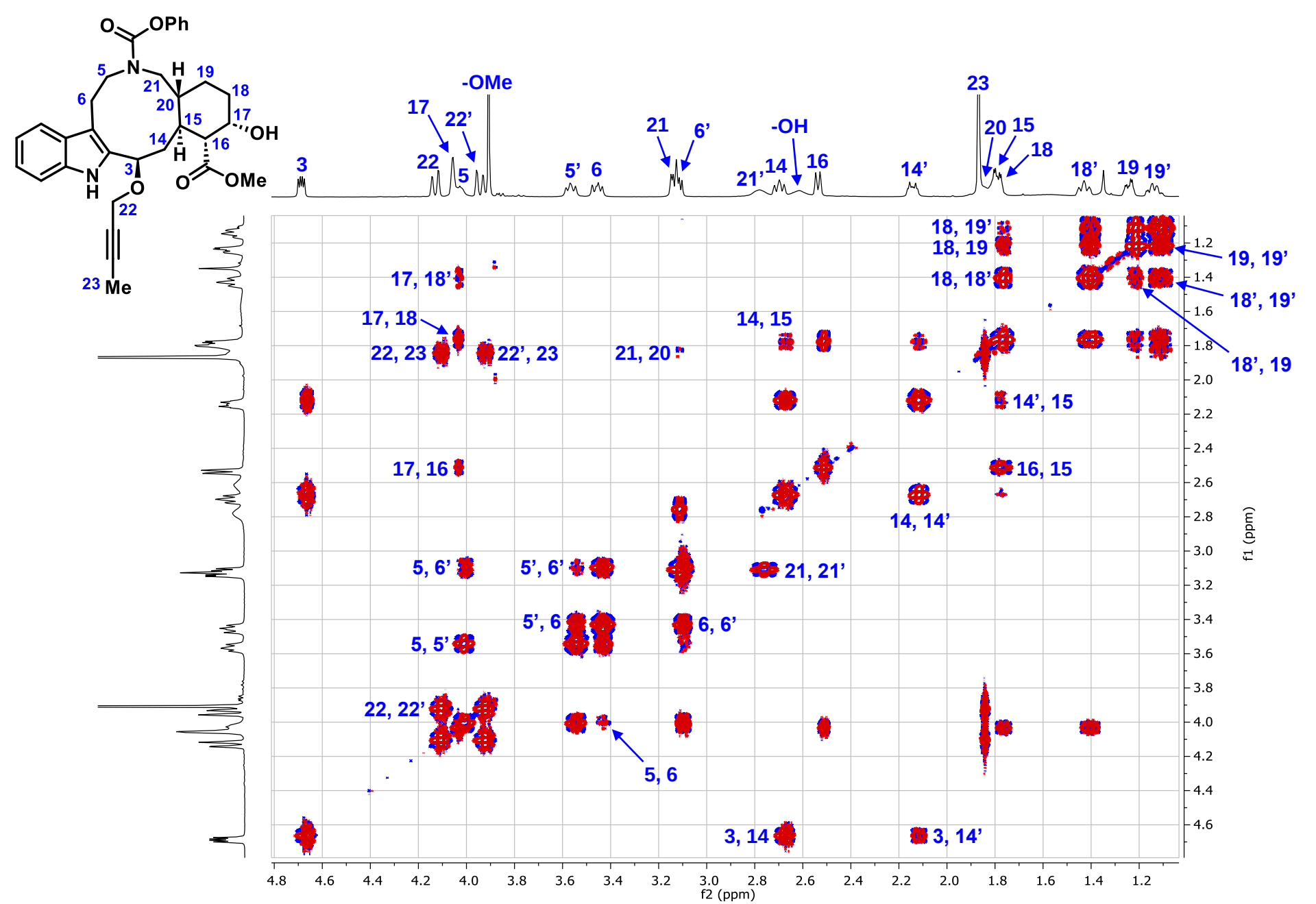
Compound 22: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 3)


4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2
f1 (ppm)
O
O
N
H
OH
H
N
H
O
O
OMe
Me
53
1H in TCE at 100 °C
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
CHCl3
f1 (ppm)

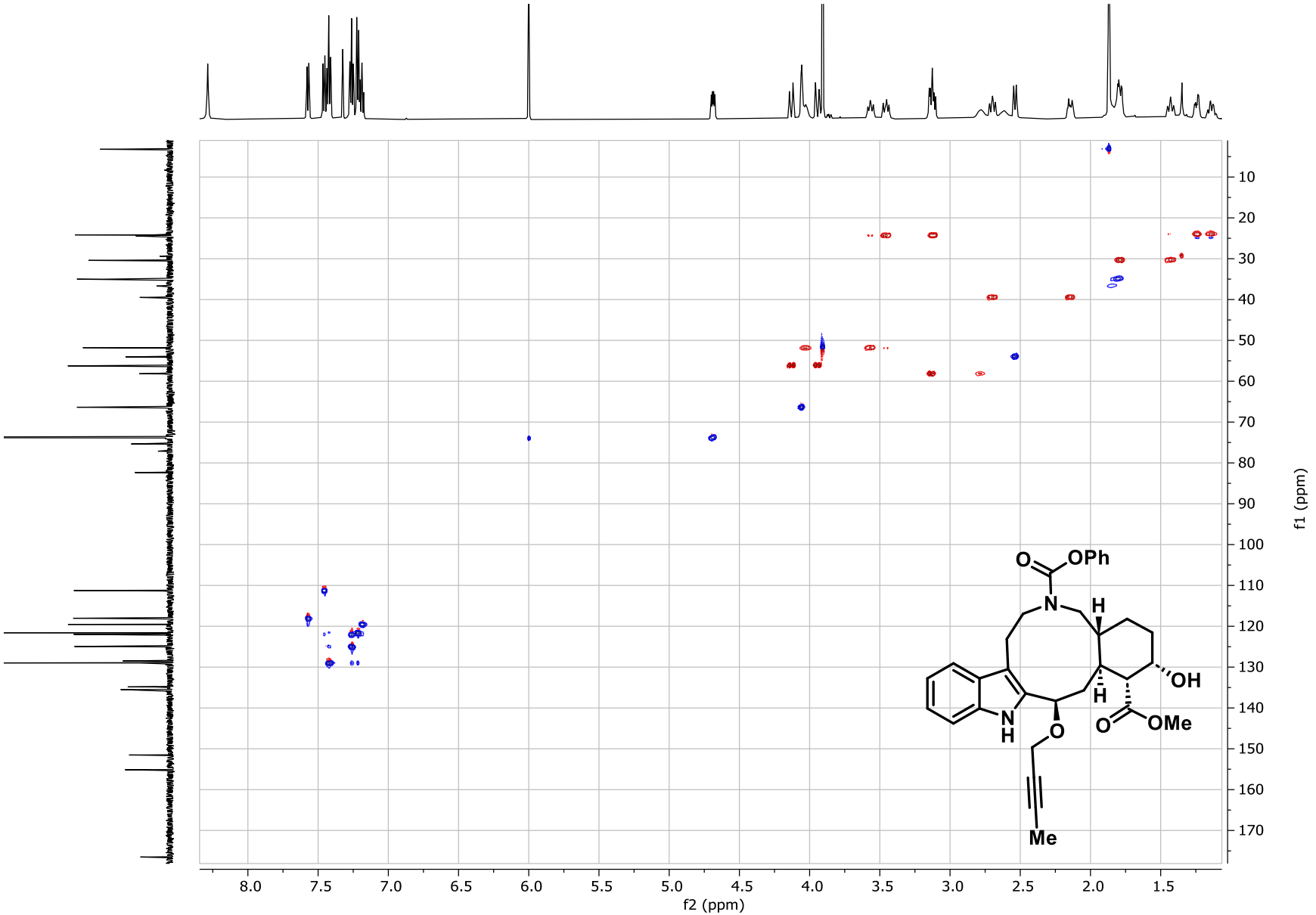

135 134 133 132 131 130 129 128 127 126 125 124 123 122 121 120 119 118 117 116 115 114 113 112 111
f1 (ppm)
50 45 40 35 30 25
f1 (ppm)
O
O
N
H
OH
H
N
H
O
O
OMe
53
13C in TCE at 100 °C
Me
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
CHCl3



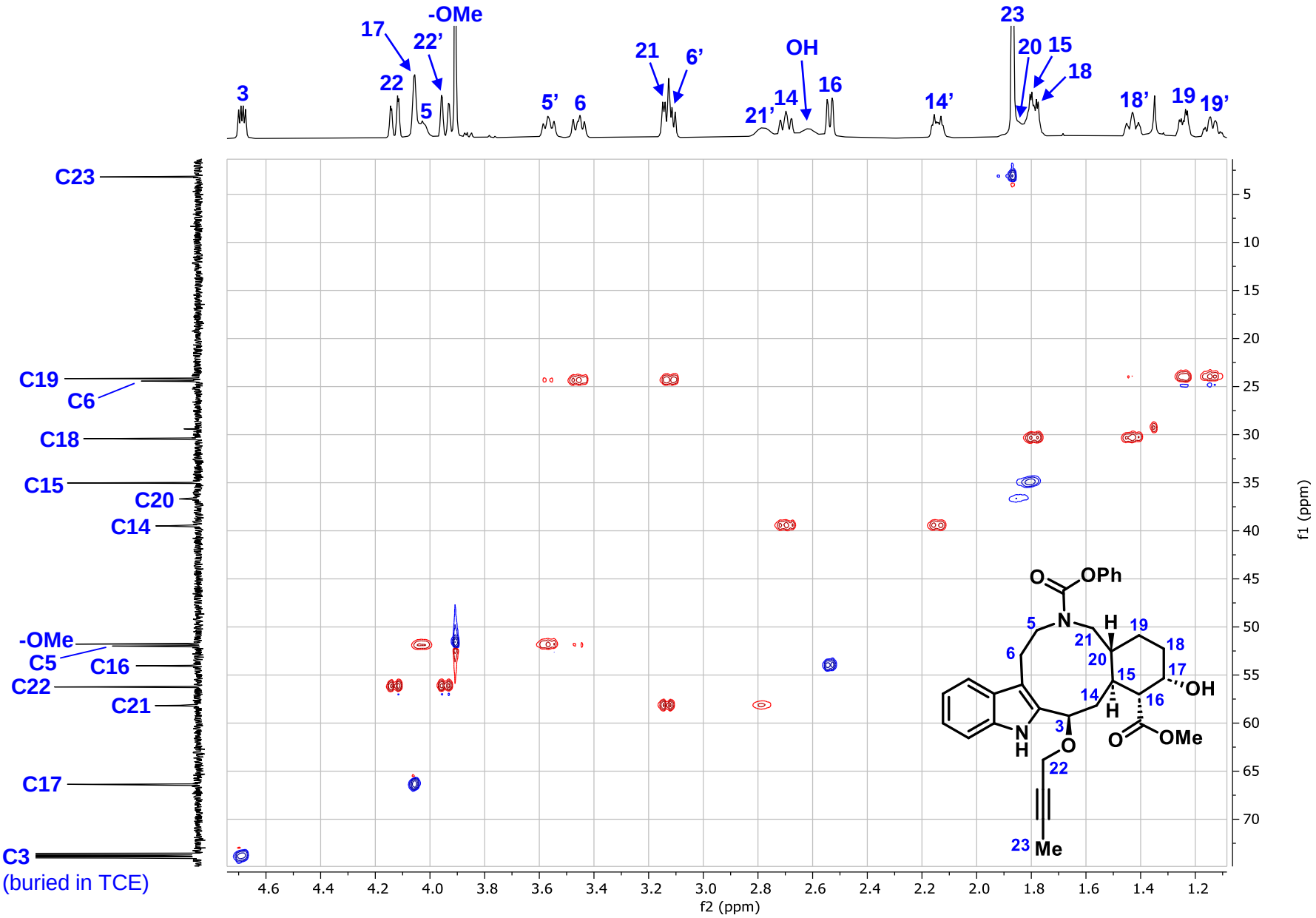
Compound 53: COSY, T = 100 °C, $C_2D_2Cl_4$ (full)



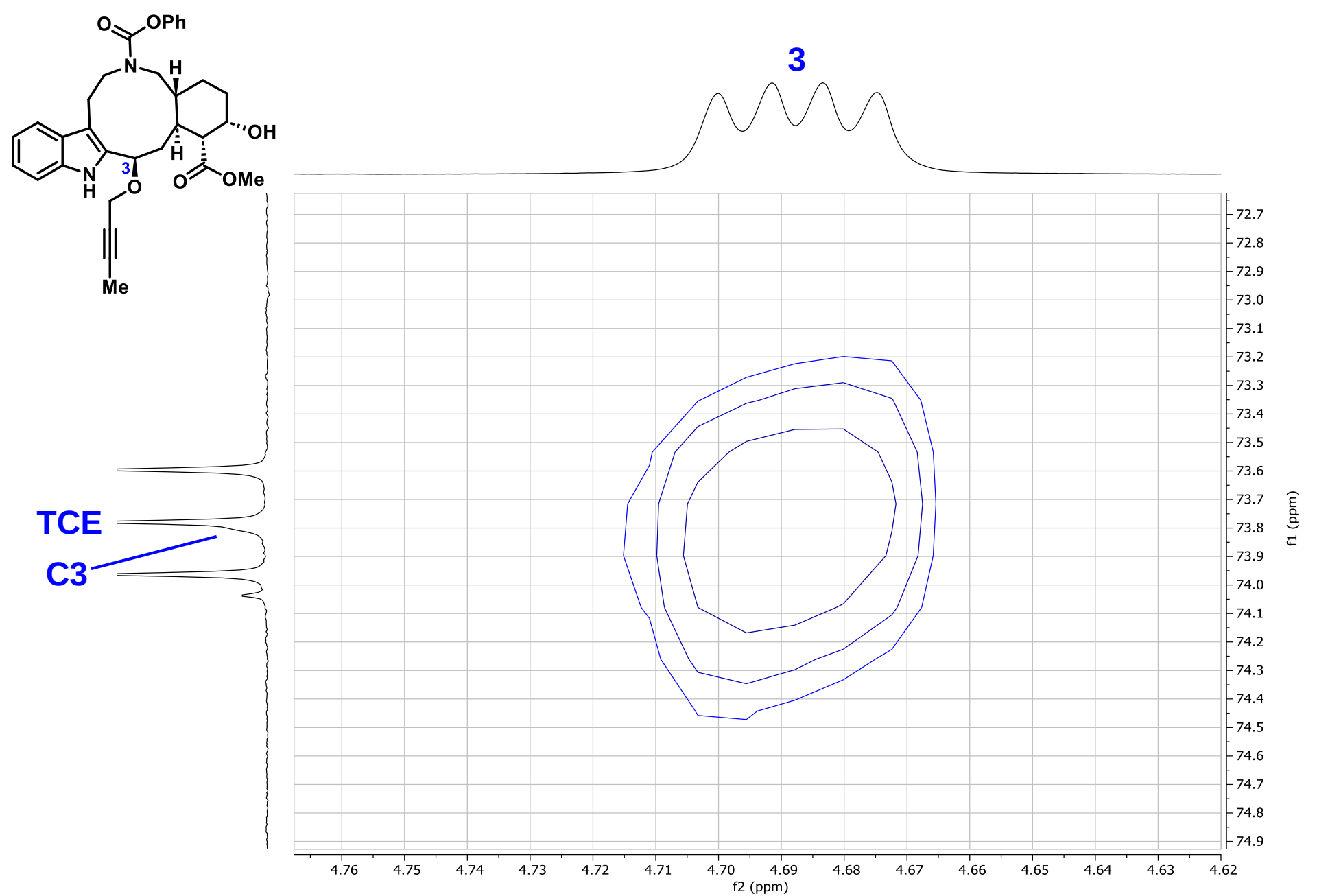
Compound 53: COSY, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in)



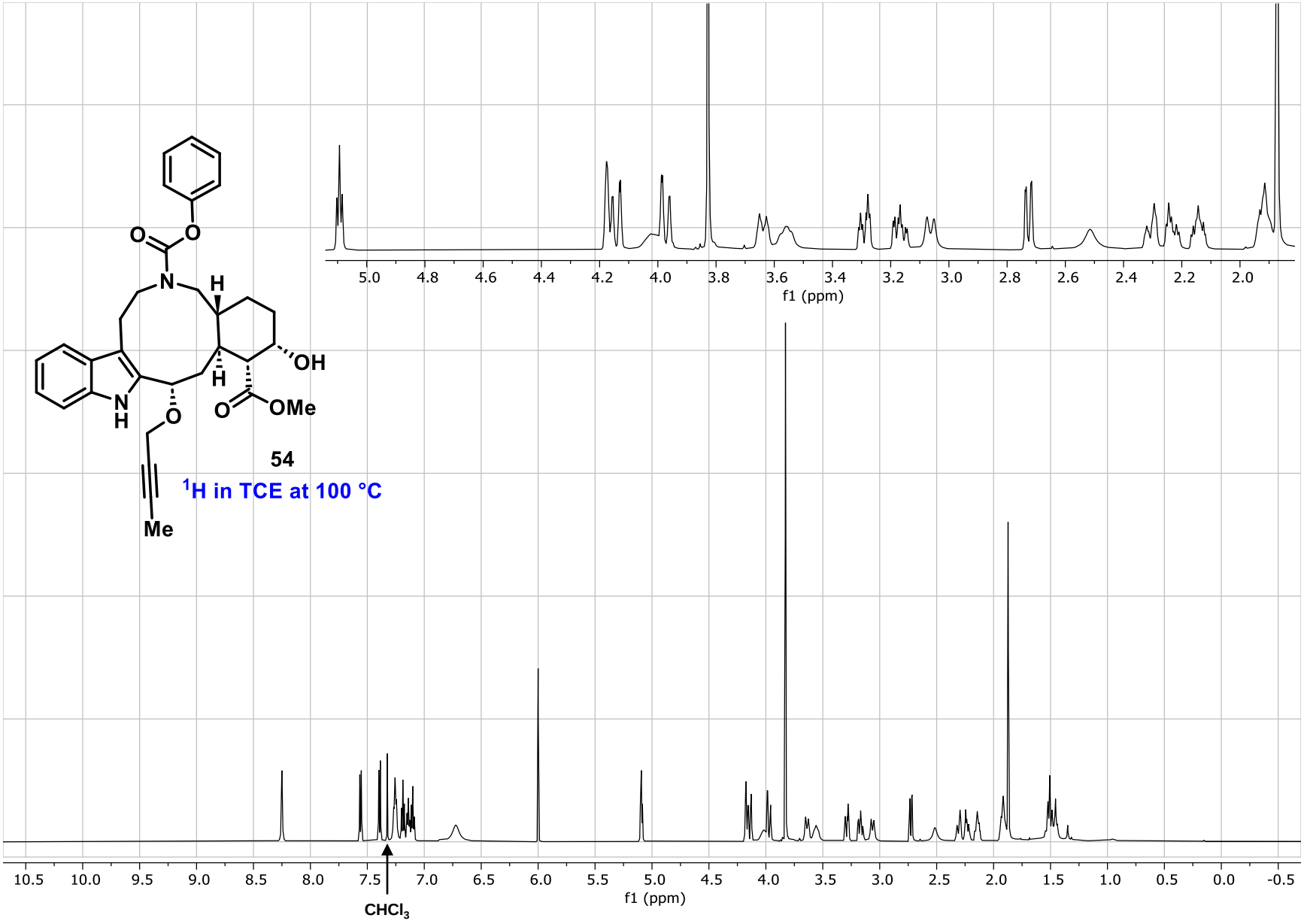
Compound 53: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (full)

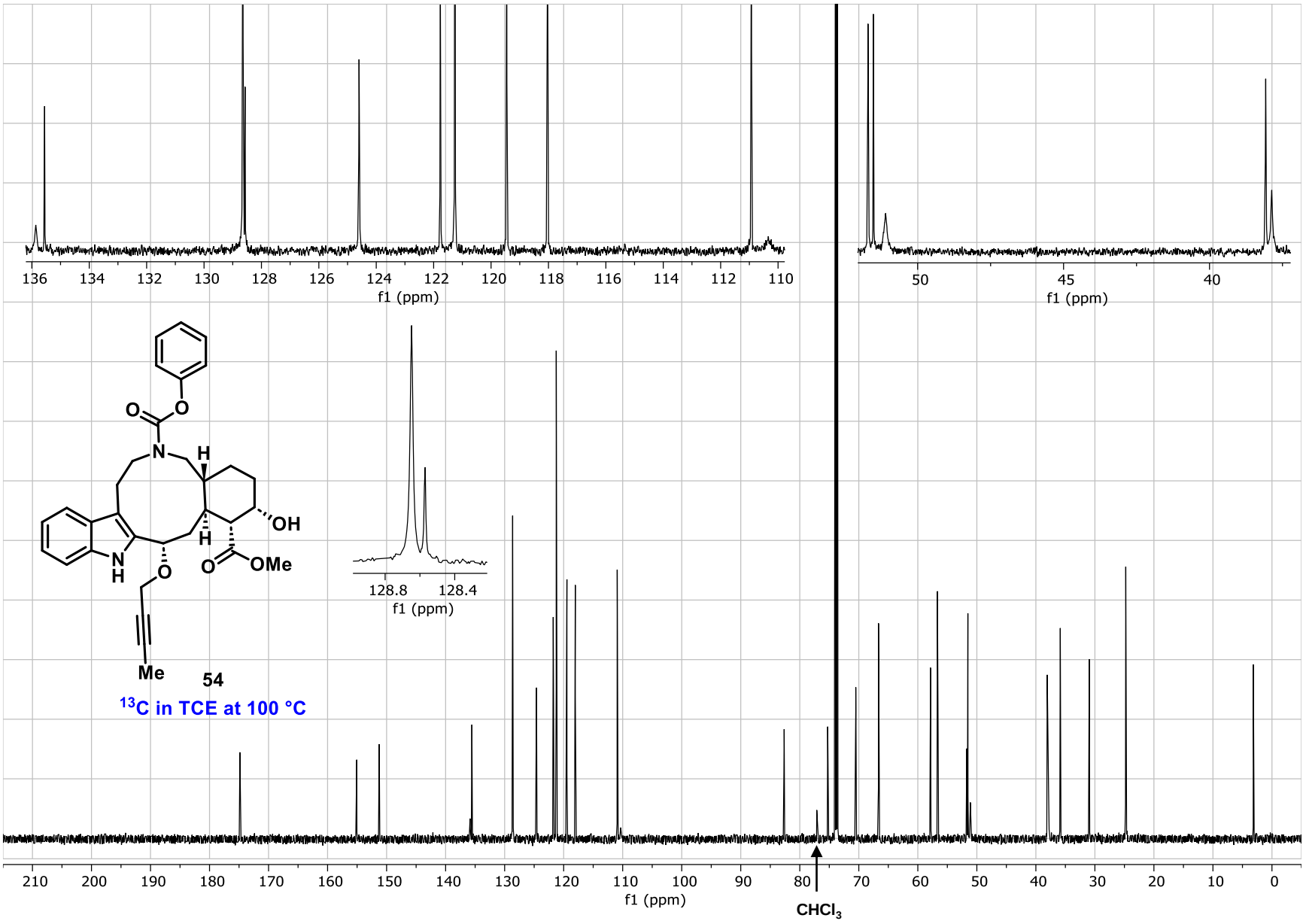


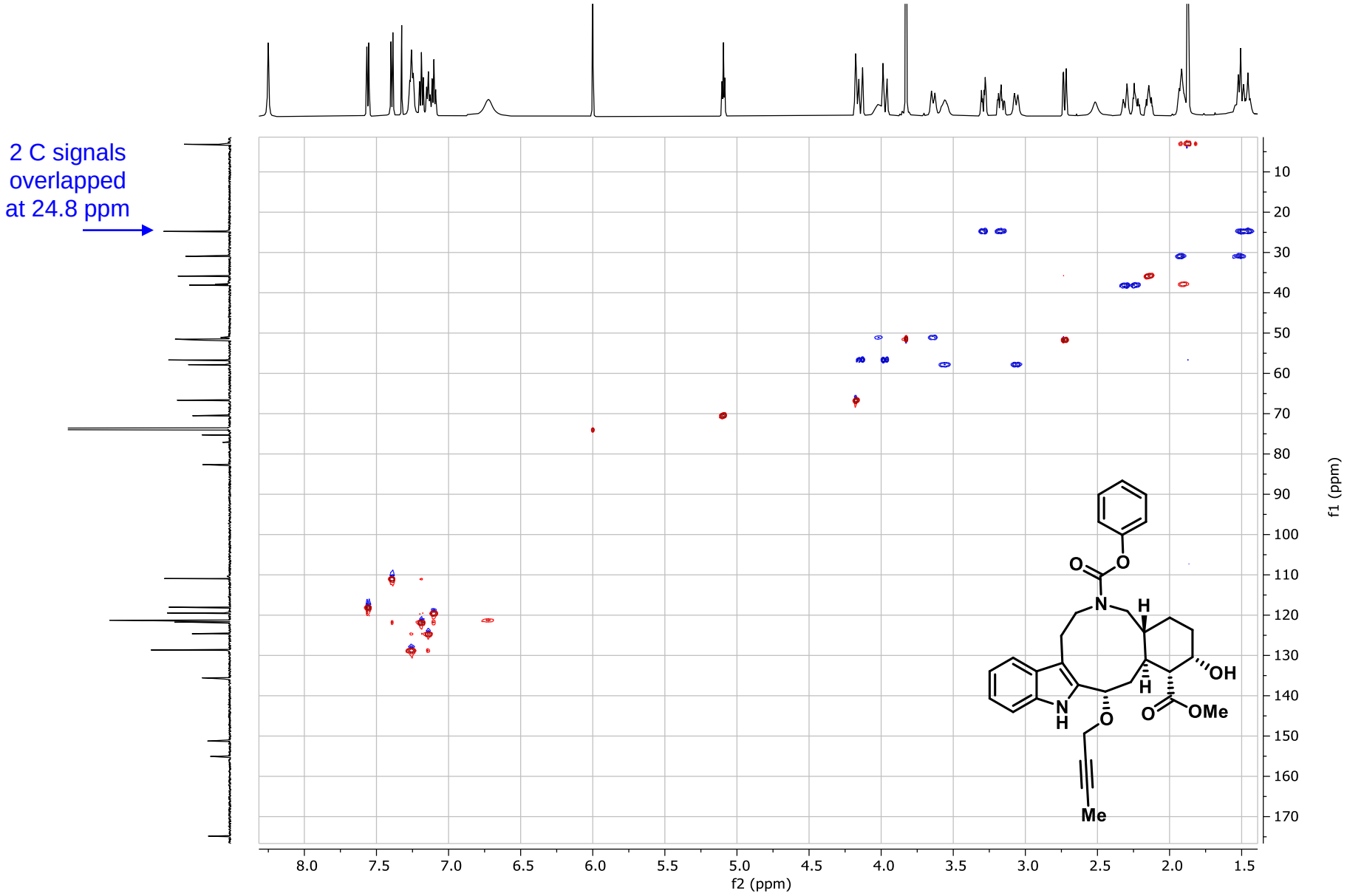
Compound 53: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 1)



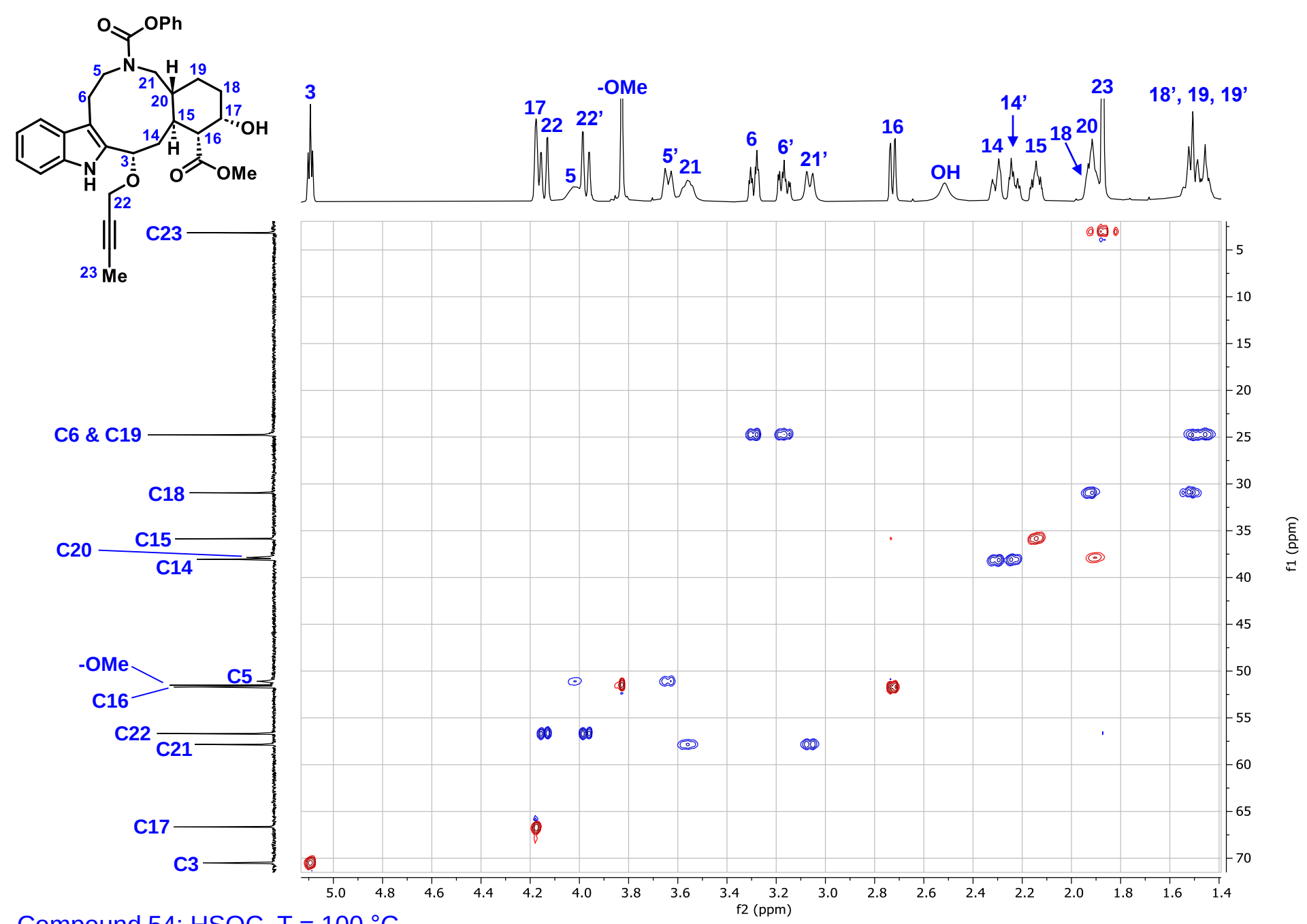
Compound 53: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 2)


54
1H in TCE at 100 °C
Me
OH
OMe
f1 (ppm)
CHCl3

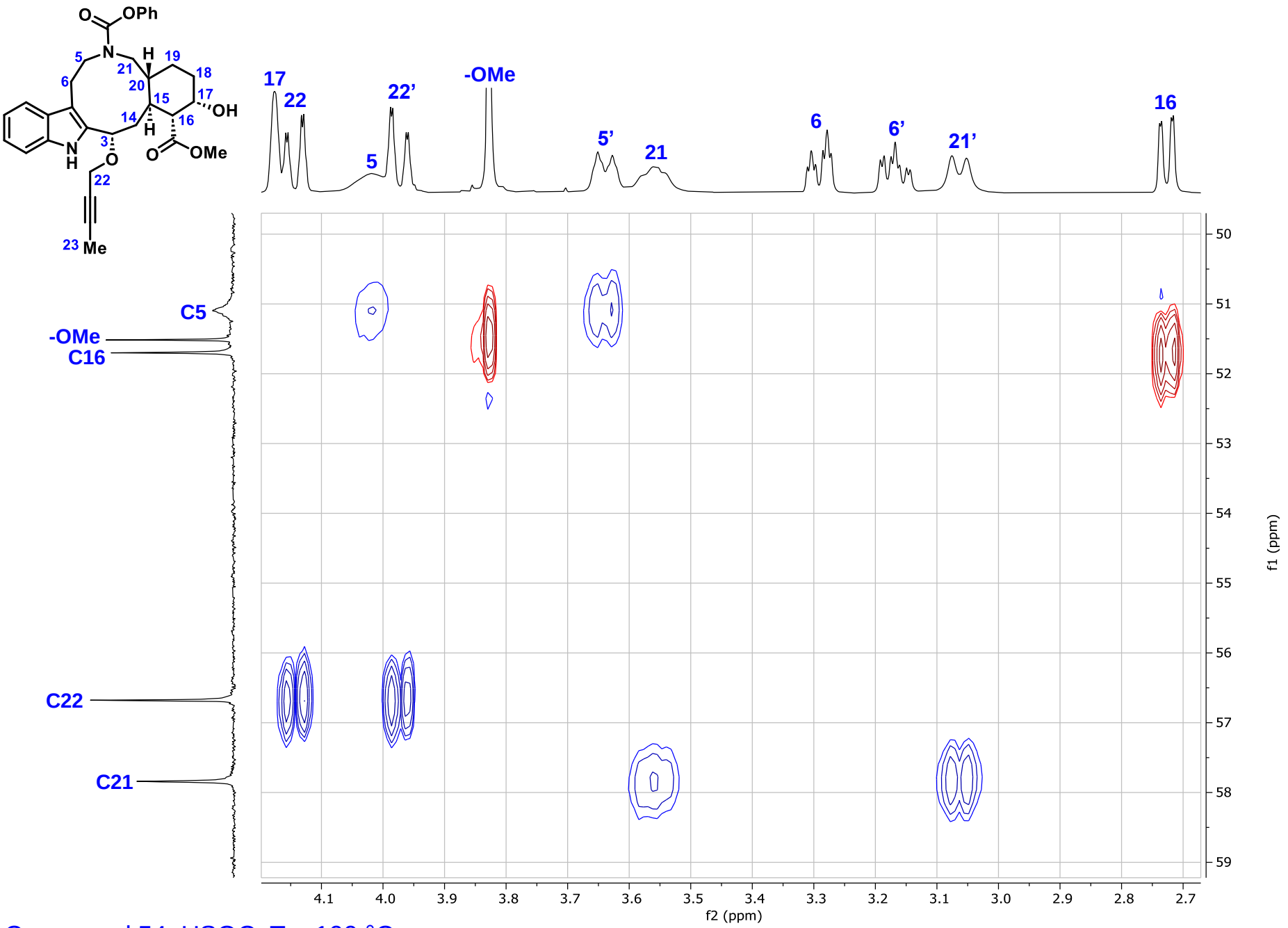

136 134 132 130 128 126 124 122 120 118 116 114 112 110
f1 (ppm)
50 45 40
f1 (ppm)
128.8 128.4
f1 (ppm)
O O N H H OH N H O O OMe Me
54
13C in TCE at 100 °C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
CHCl3



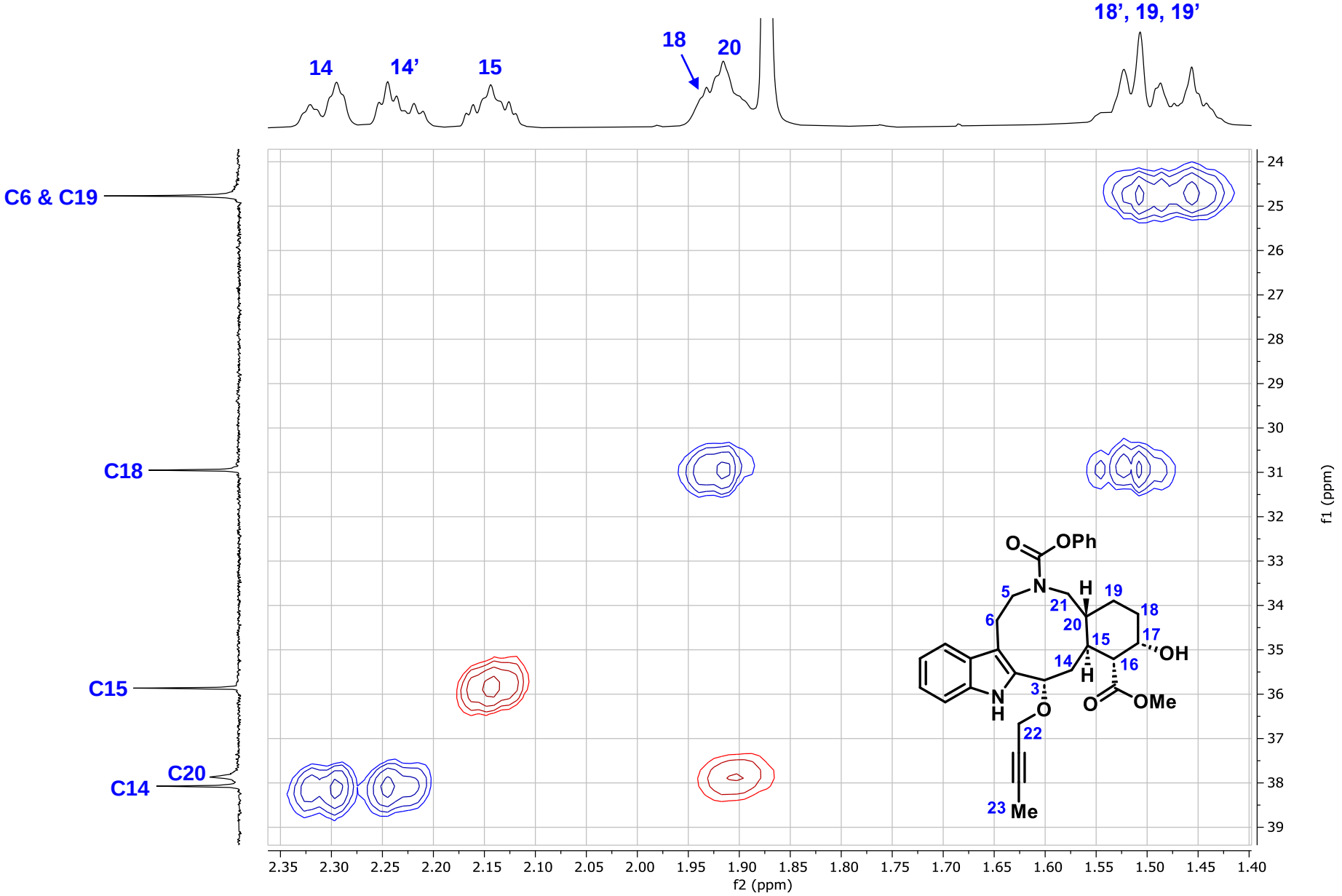
Compound 54: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (full)



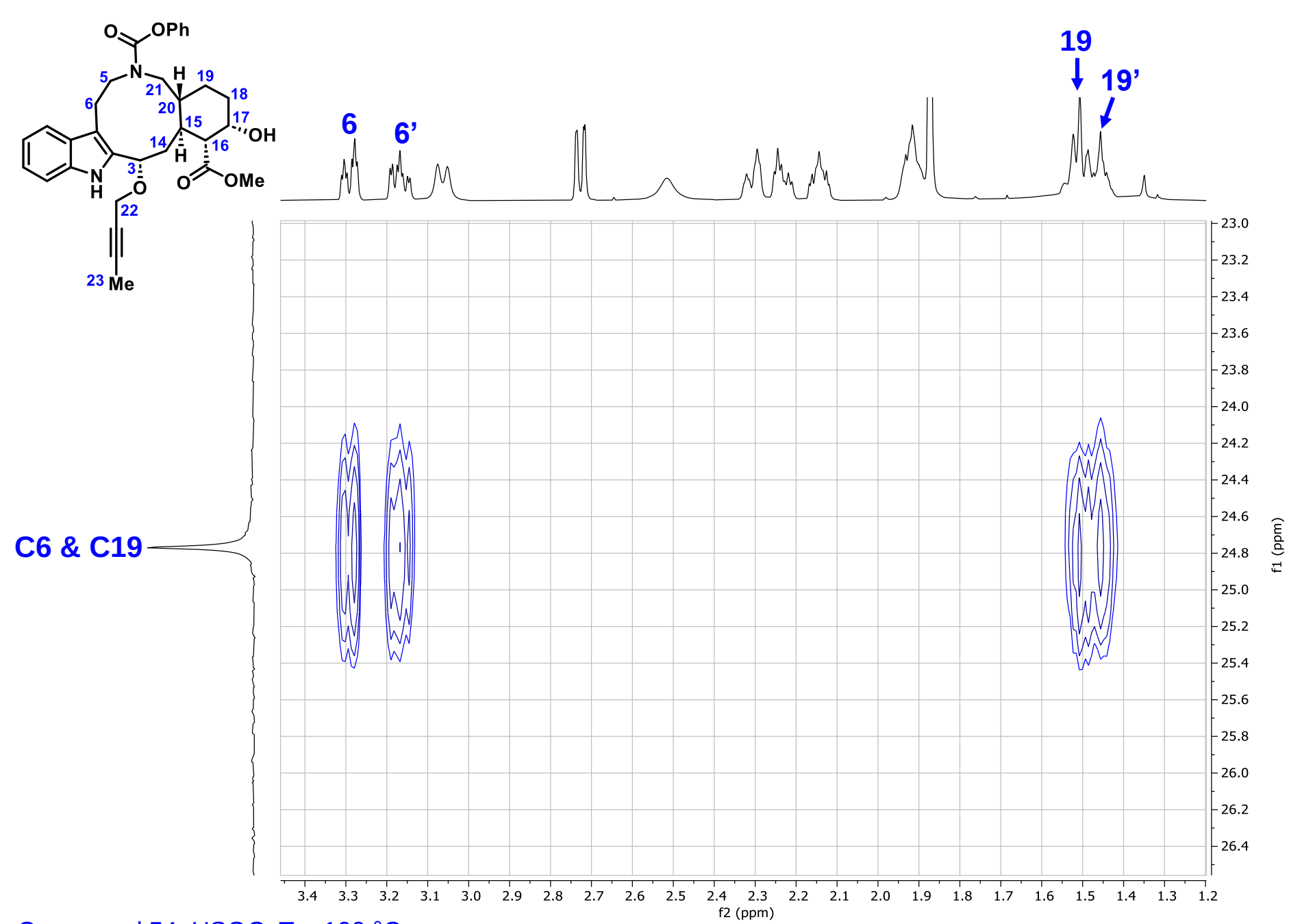
Compound 54: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 1)



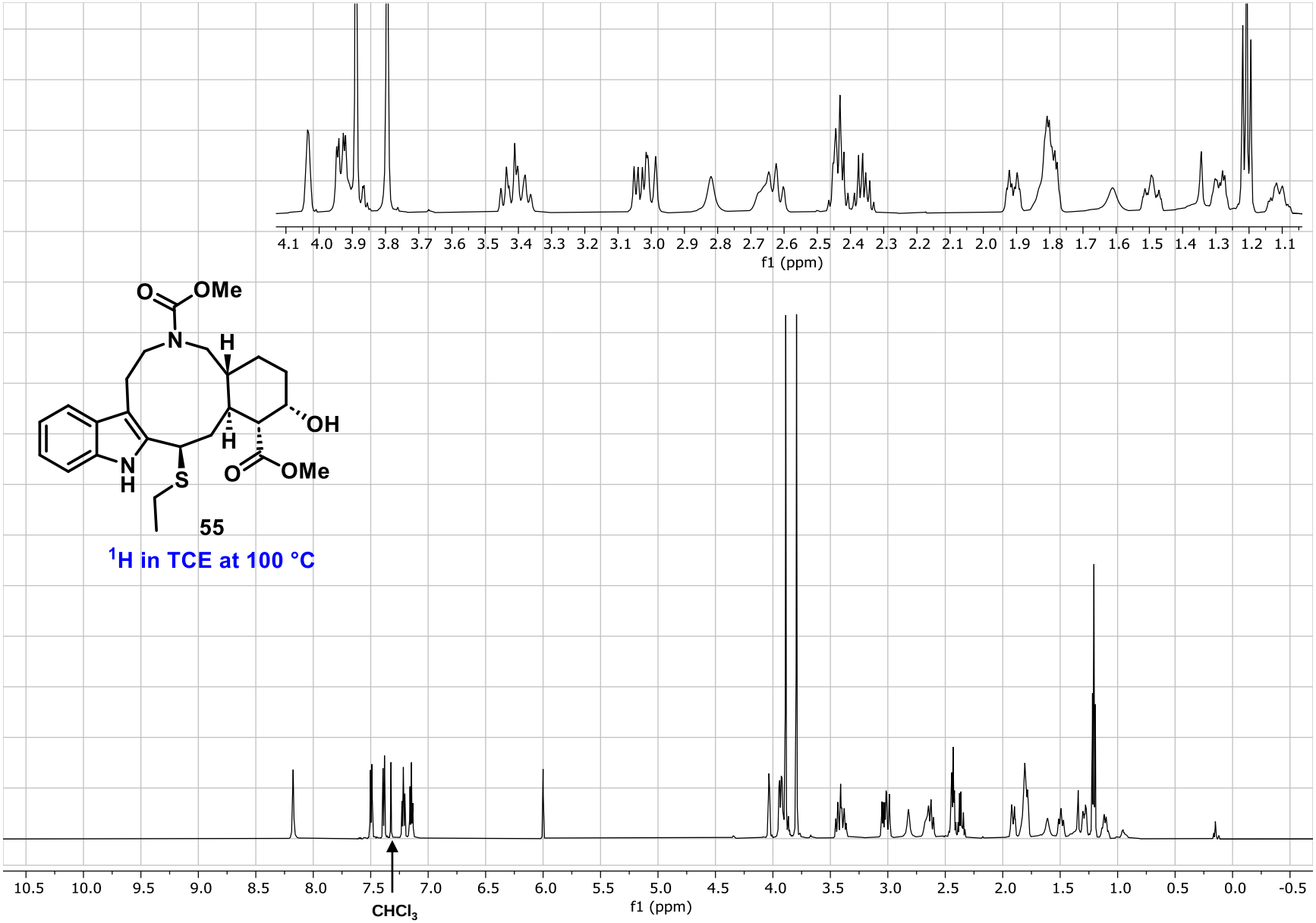
Compound 54: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 2)

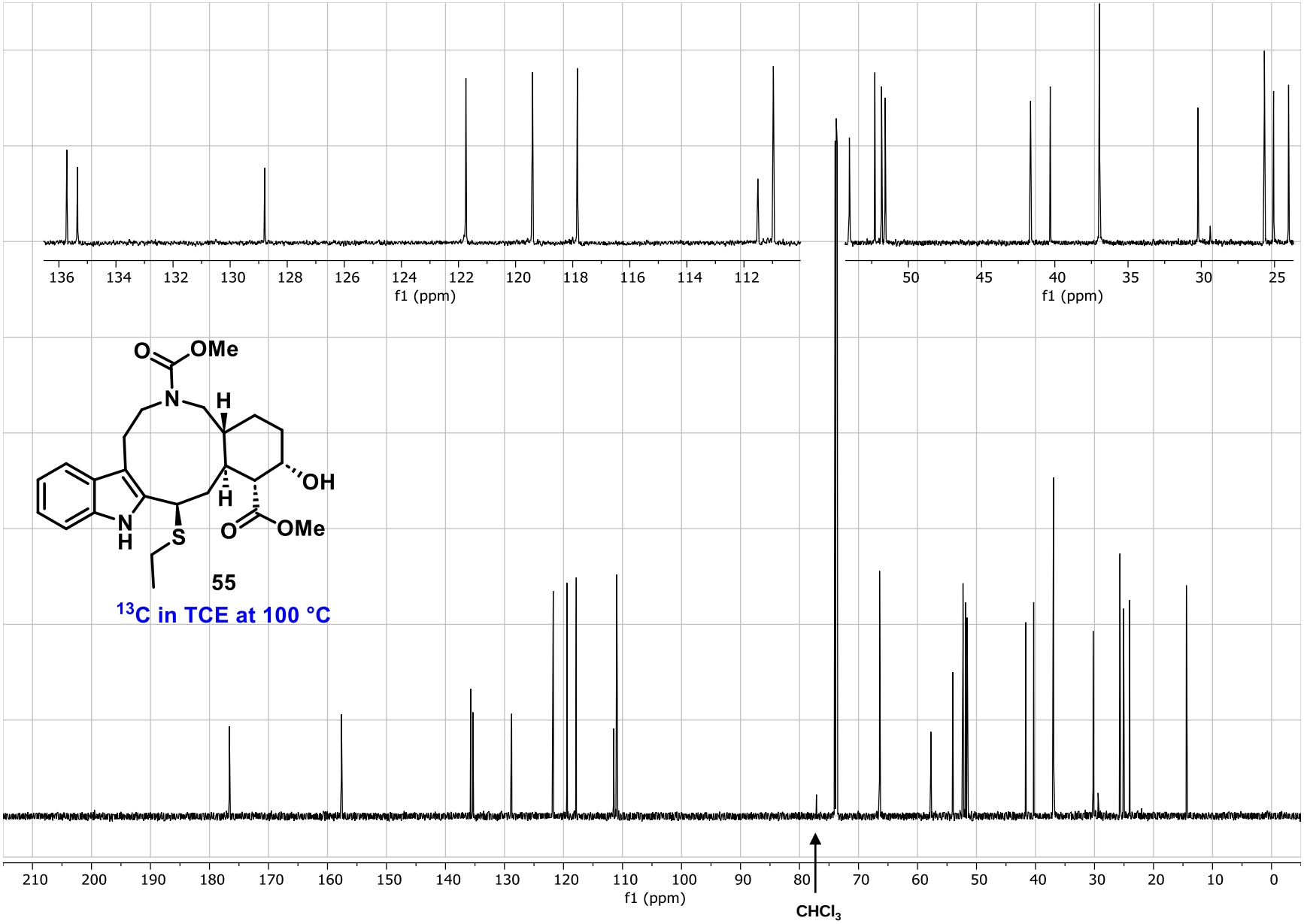


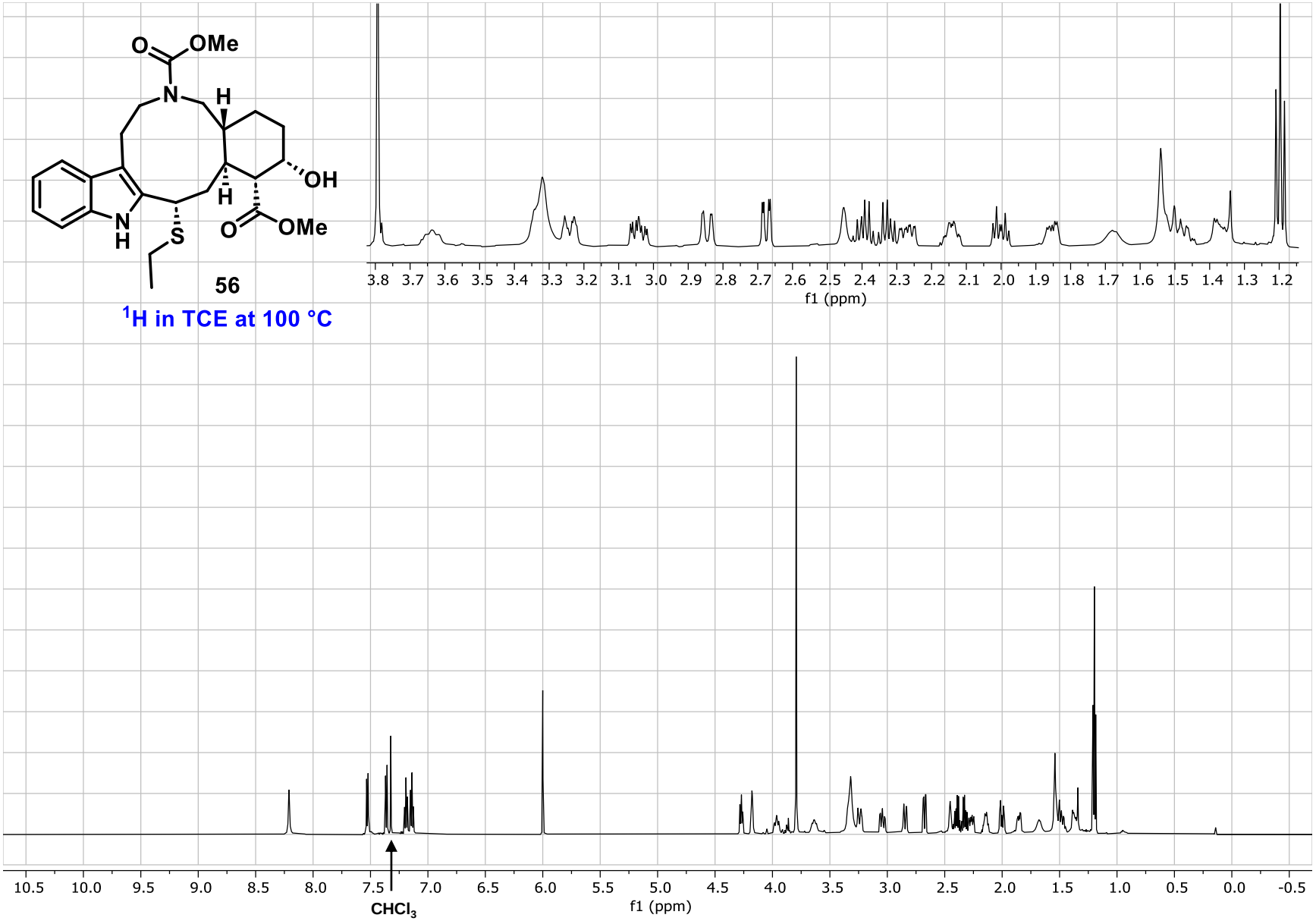
Compound 54: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 3)

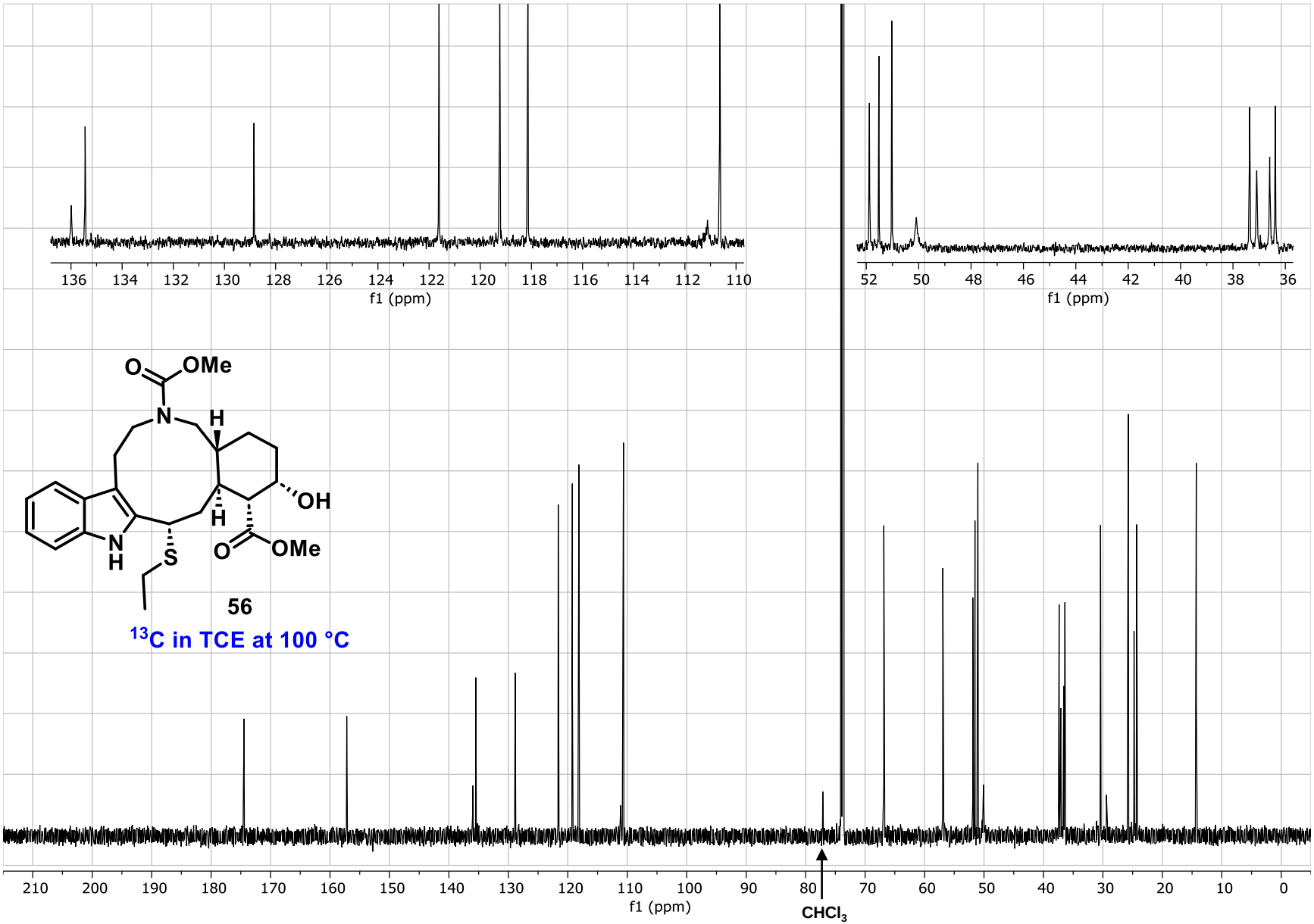


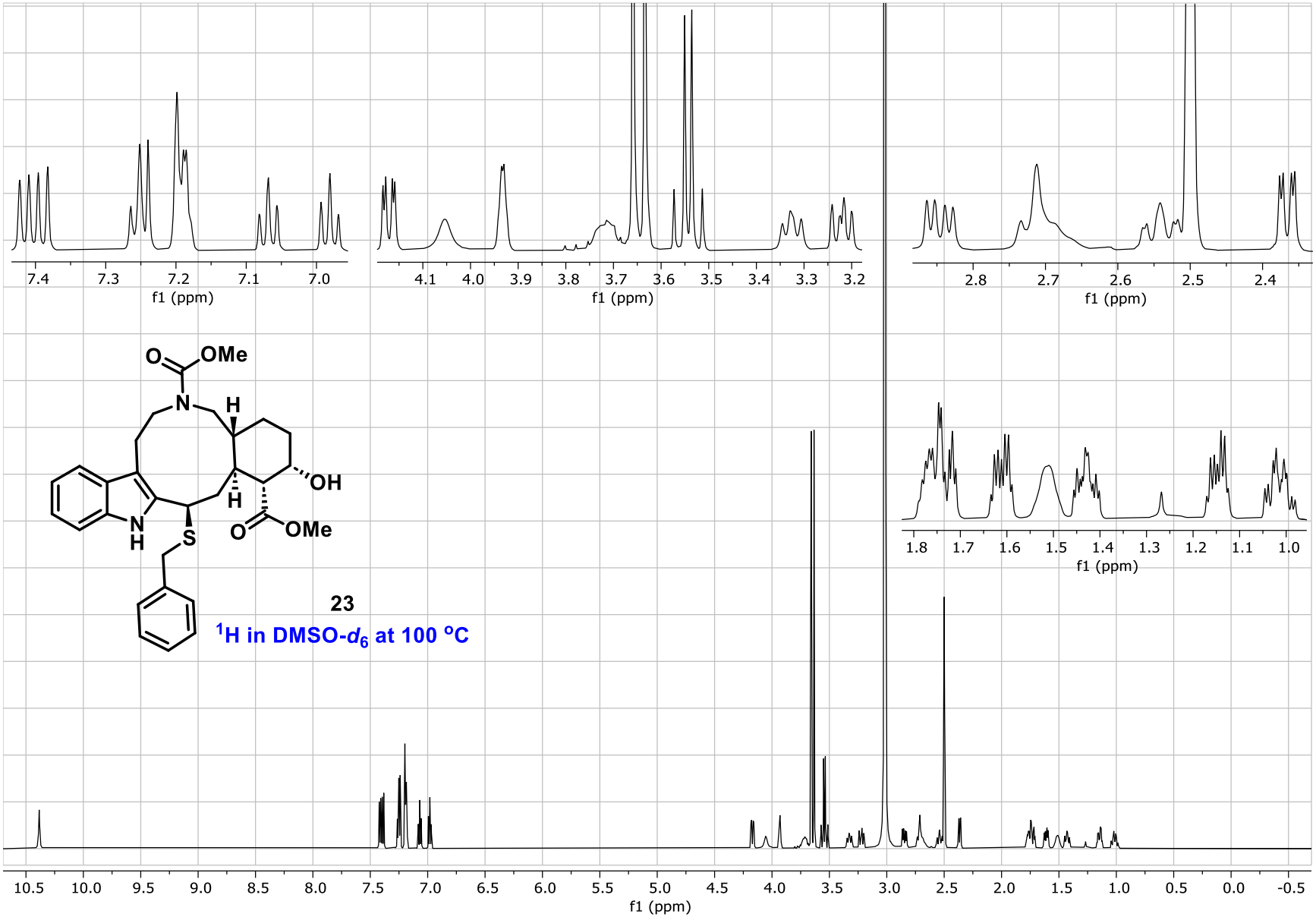
Compound 54: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 4)


4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1
f1 (ppm)
O
OMe
N
H
OH
H
N
H
S
O
OMe
55
1H in TCE at 100 °C
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
CHCl3
f1 (ppm)


136 134 132 130 128 126 124 122 120 118 116 114 112
f1 (ppm)
50 45 40 35 30 25
f1 (ppm)
O
OMe
N
H
OH
H
N
H
S
O
OMe
55
13C in TCE at 100 °C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
CHCl3

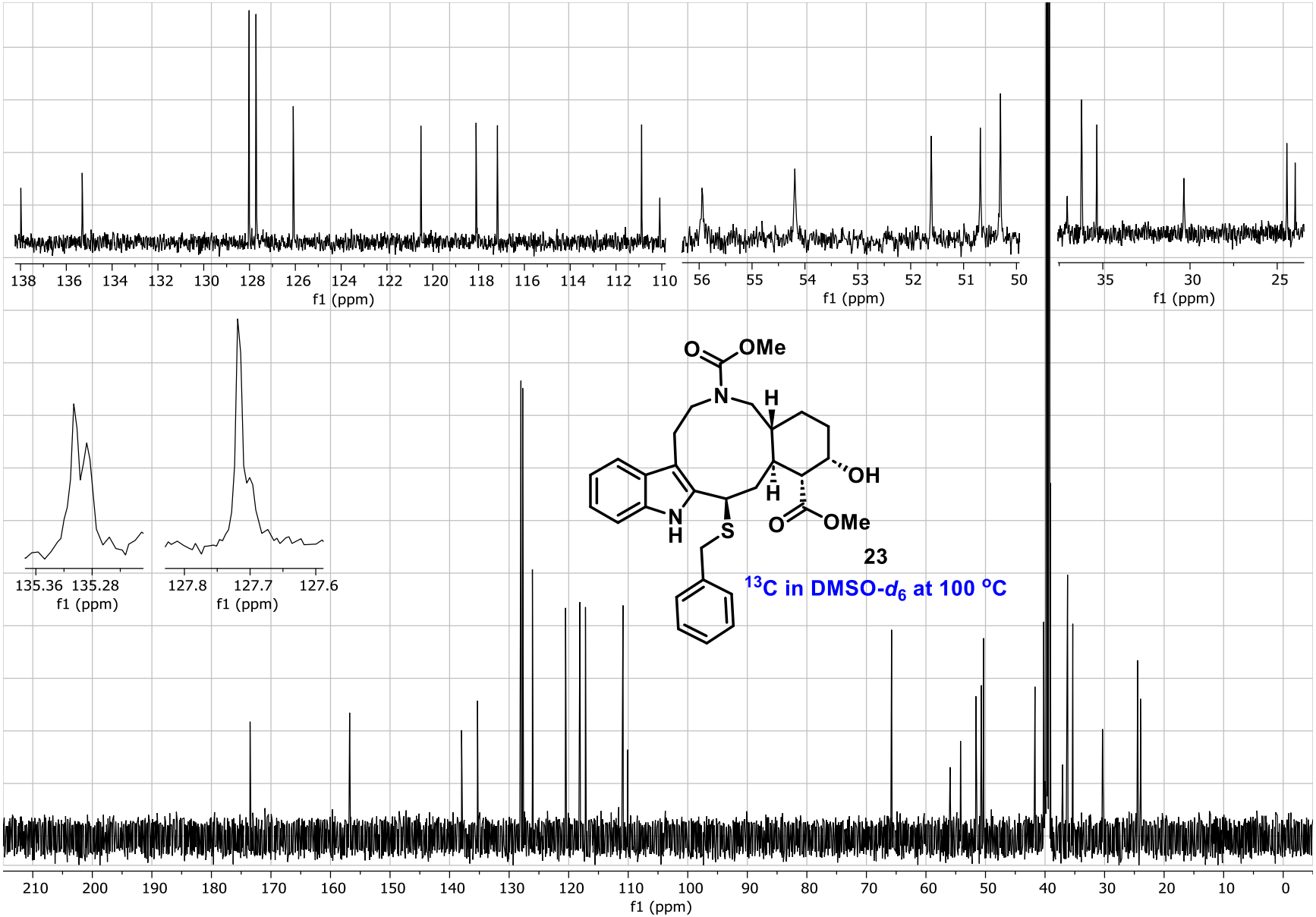

O
OMe
N
H
OH
H
N
H
S
O
OMe
56
1H in TCE at 100 °C
3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2
f1 (ppm)
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
CHCl3
f1 (ppm)

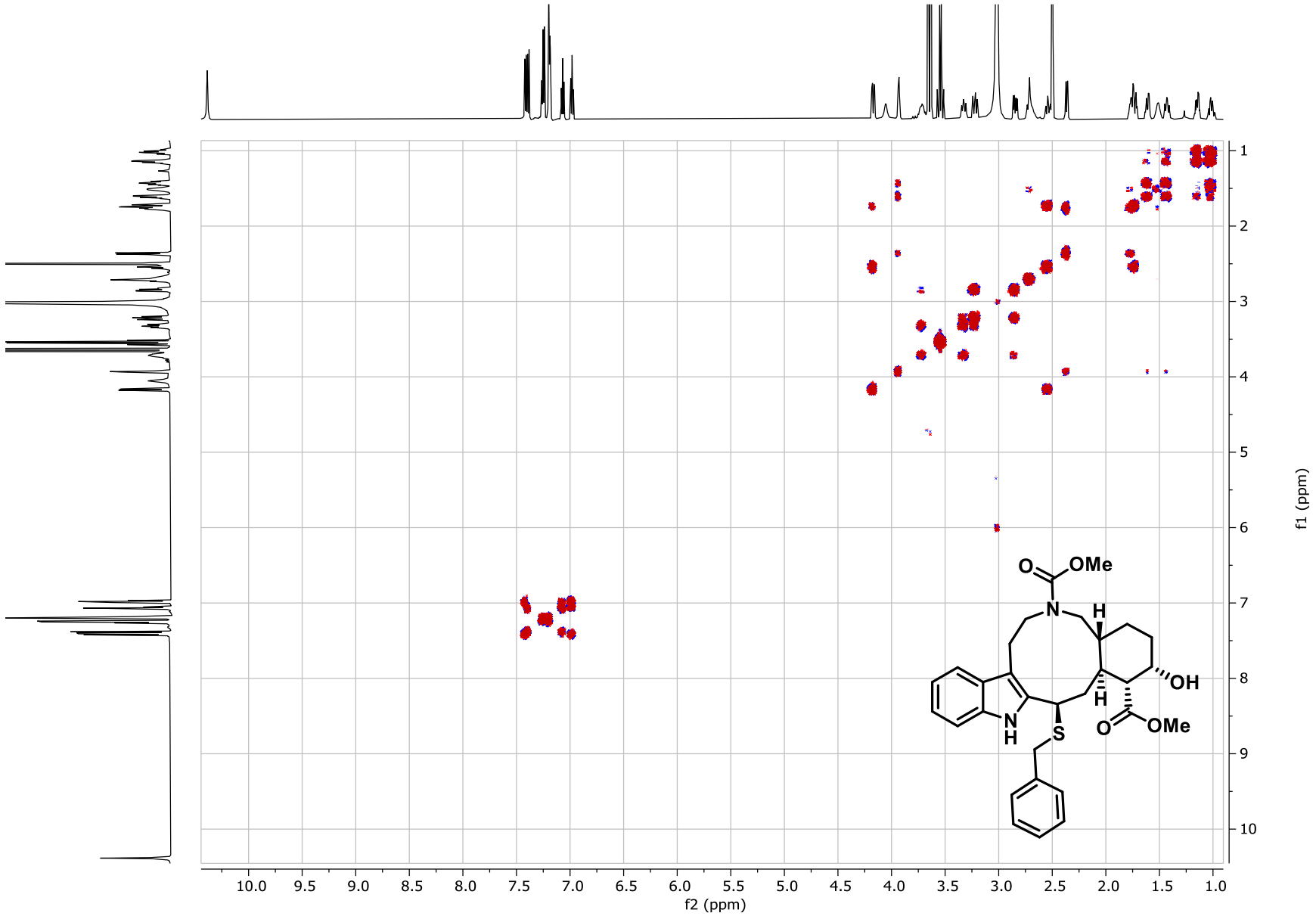

136 134 132 130 128 126 124 122 120 118 116 114 112 110
f1 (ppm)
52 50 48 46 44 42 40 38 36
f1 (ppm)
O
OMe
N
H
OH
H
N
H
S
O
OMe
56
13C in TCE at 100 °C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
CHCl3



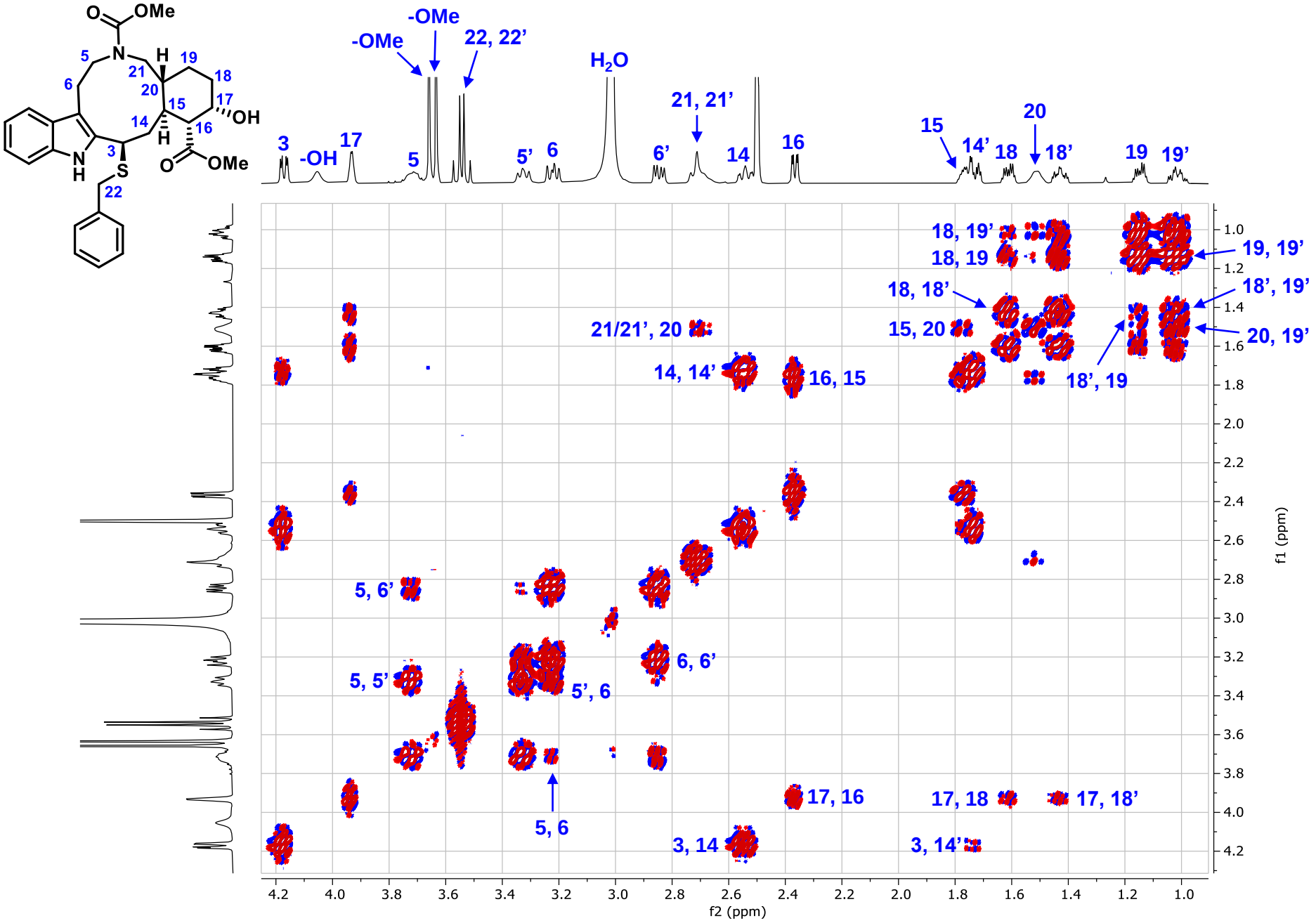
23

^{1}H in DMSO-d_6 at 100 °C

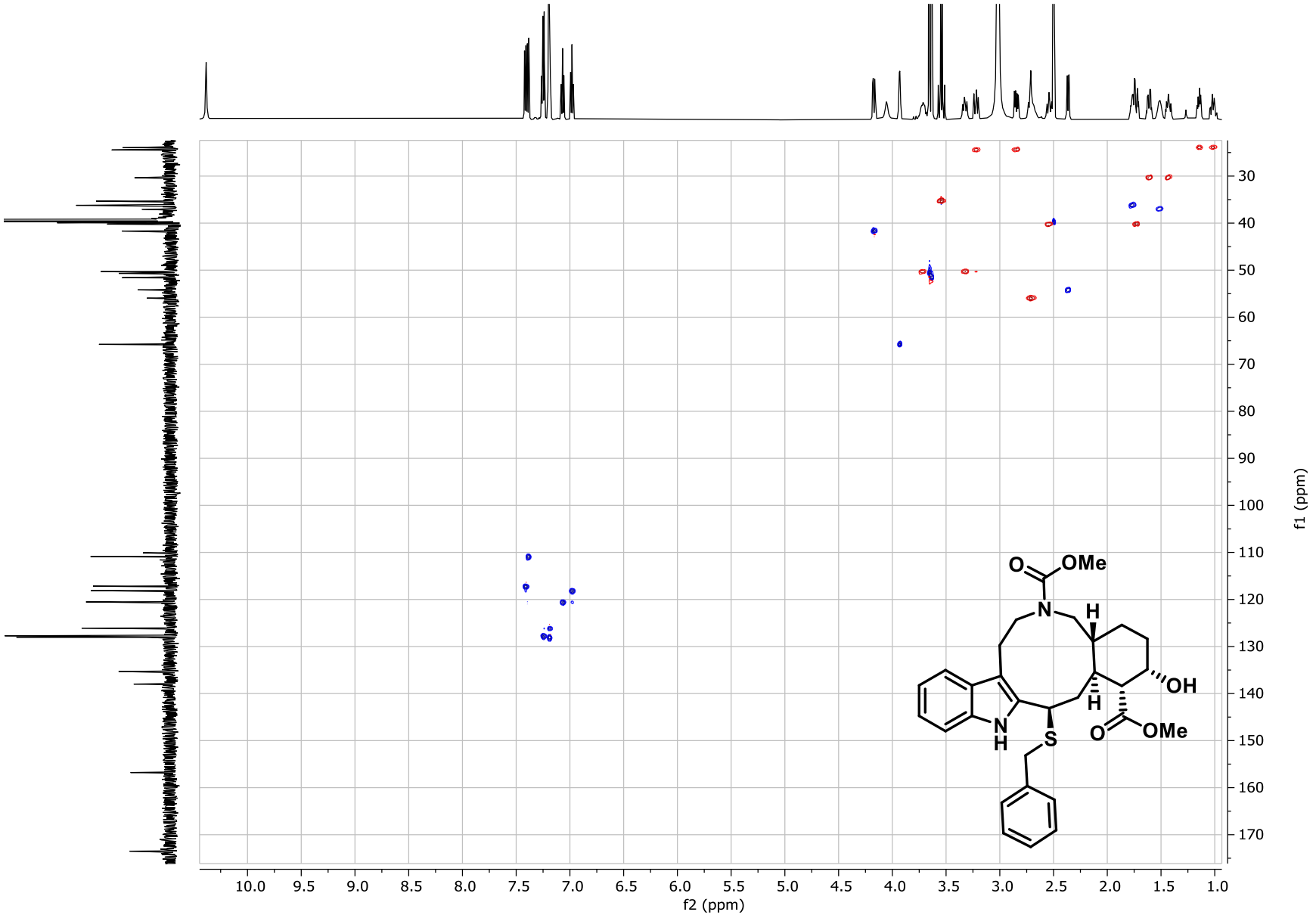

138 136 134 132 130 128 126 124 122 120 118 116 114 112 110
f1 (ppm)
56 55 54 53 52 51 50
f1 (ppm)
35 30 25
f1 (ppm)
135.36 135.28
f1 (ppm)
127.8 127.7 127.6
f1 (ppm)
O
OMe
N
H
OH
H
N
H
S
O
OMe
23
13C in DMSO-d6 at 100 °C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



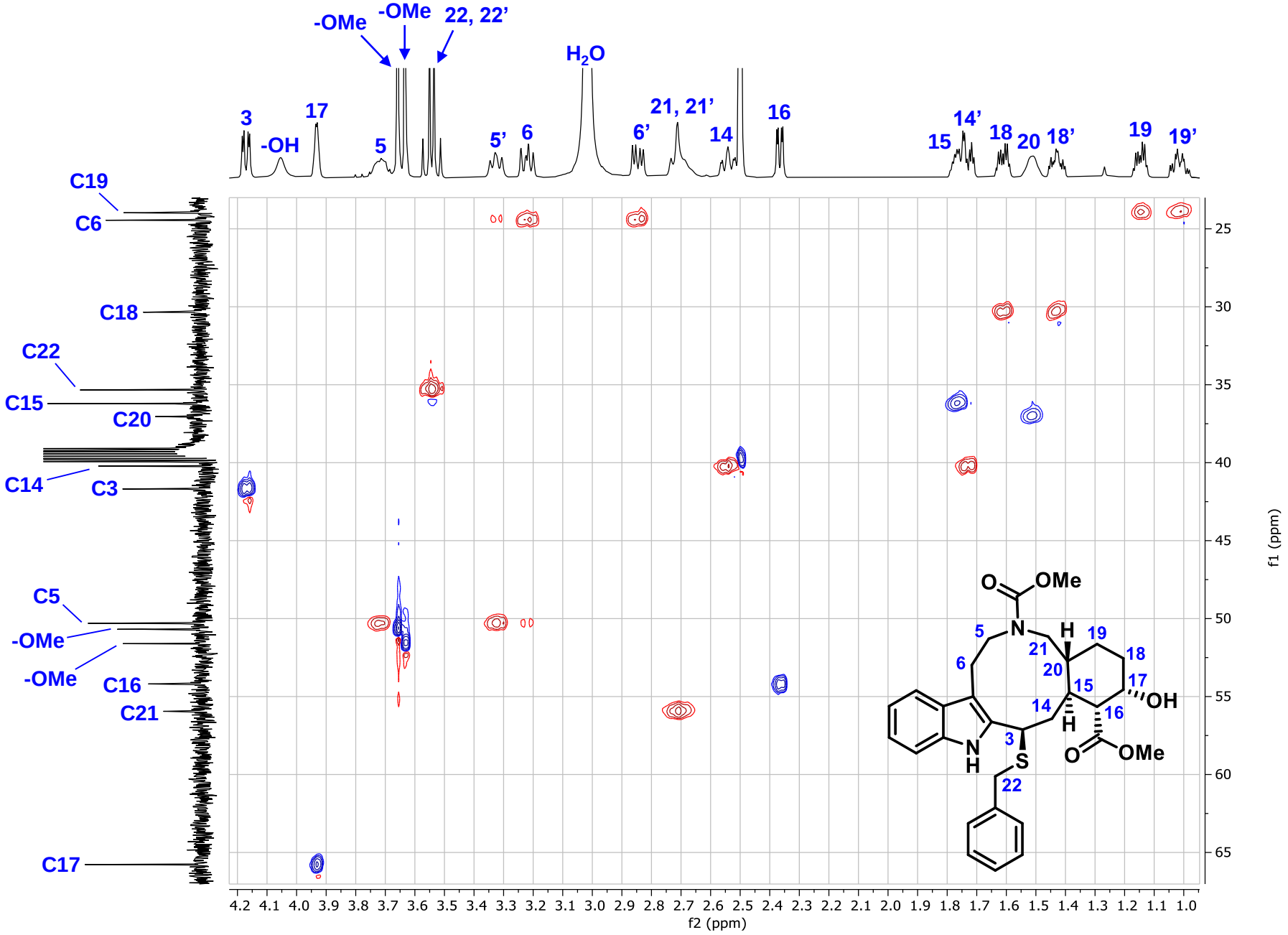
Compound 23: COSY, T = 100 °C,
DMSO-*d6* (full)



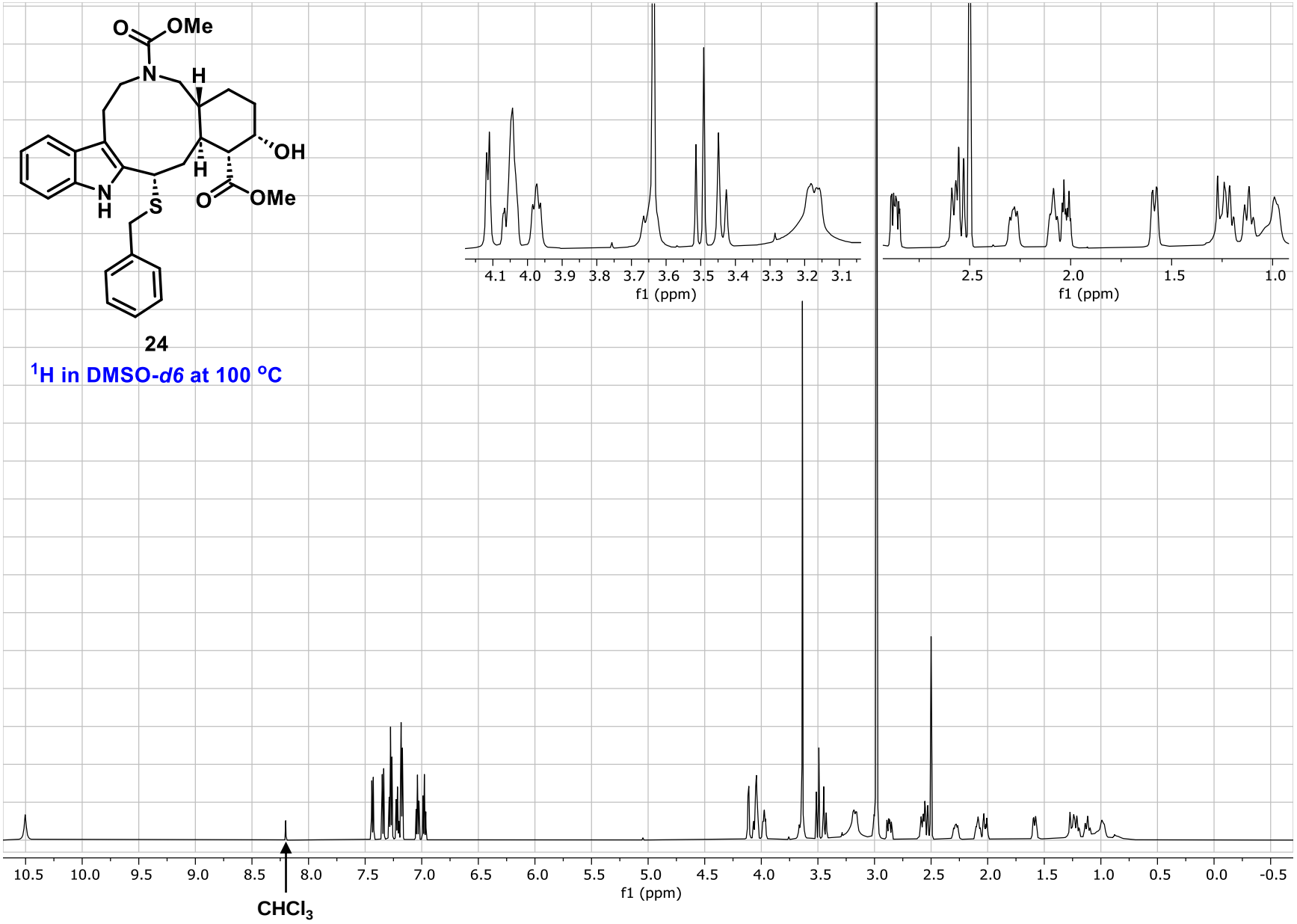
Compound 23: COSY, T = 100 °C,
DMSO-*d6* (zoomed in)

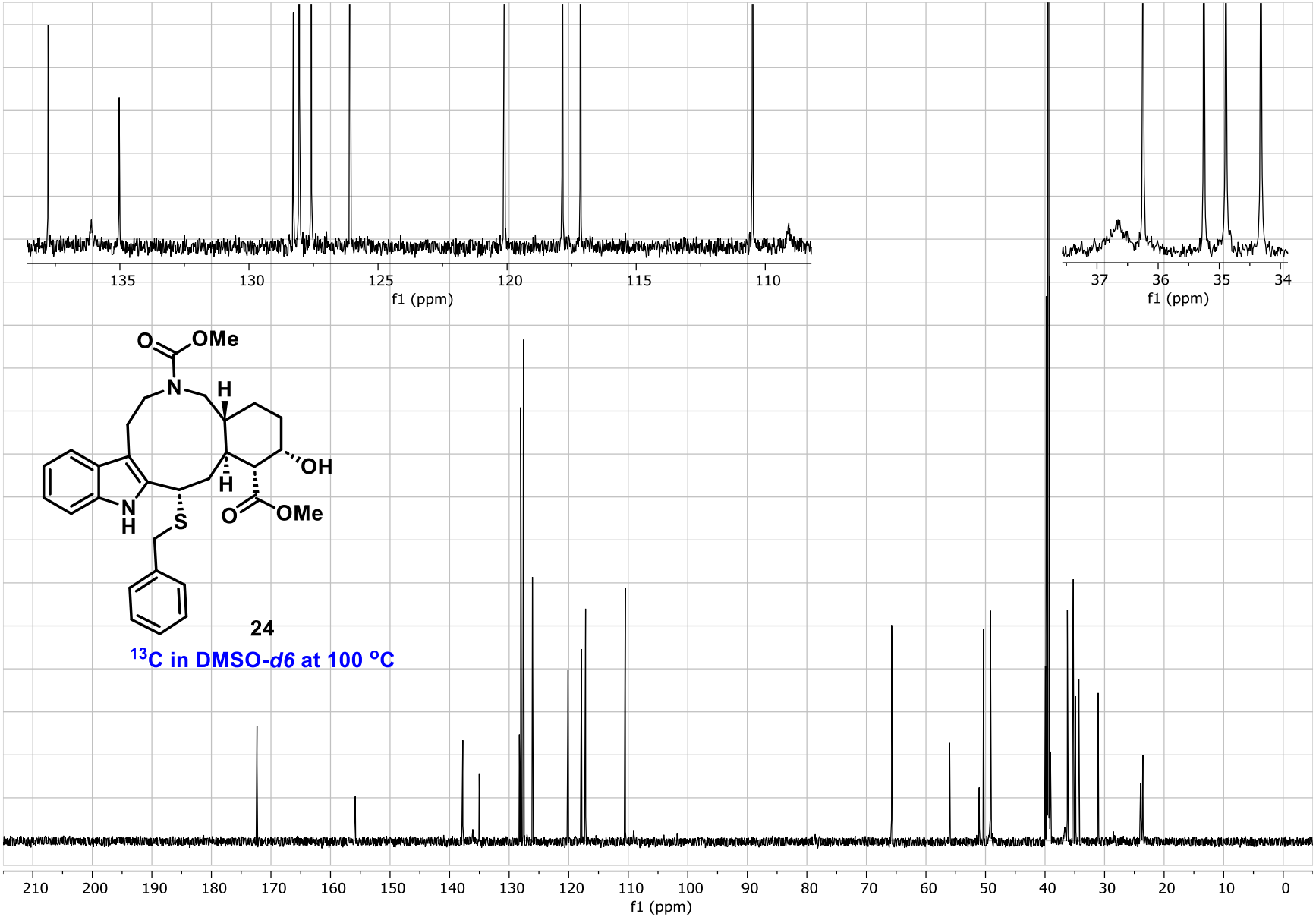


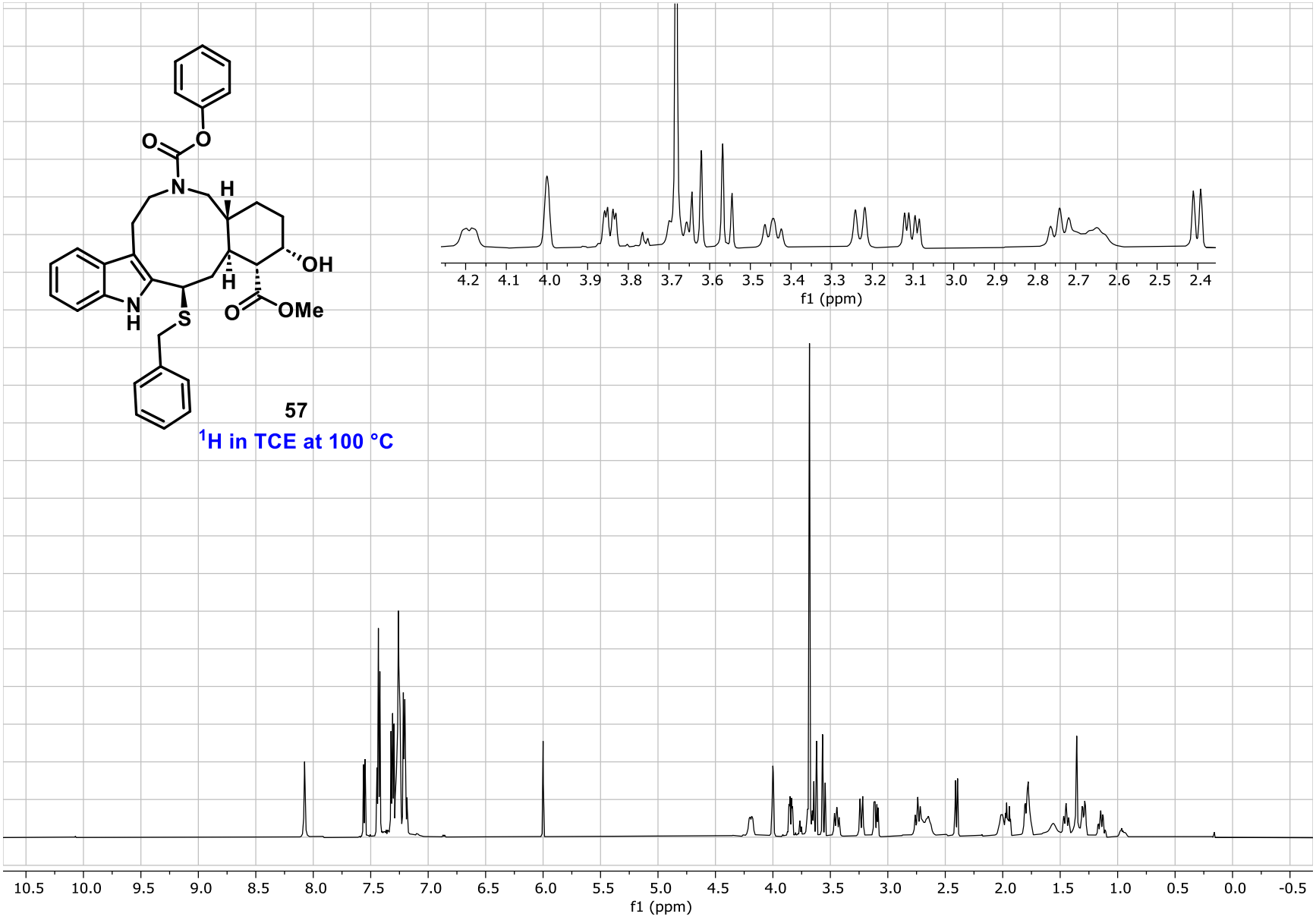
Compound 23: HSQC, T = 100 °C,
DMSO-*d6* (full)

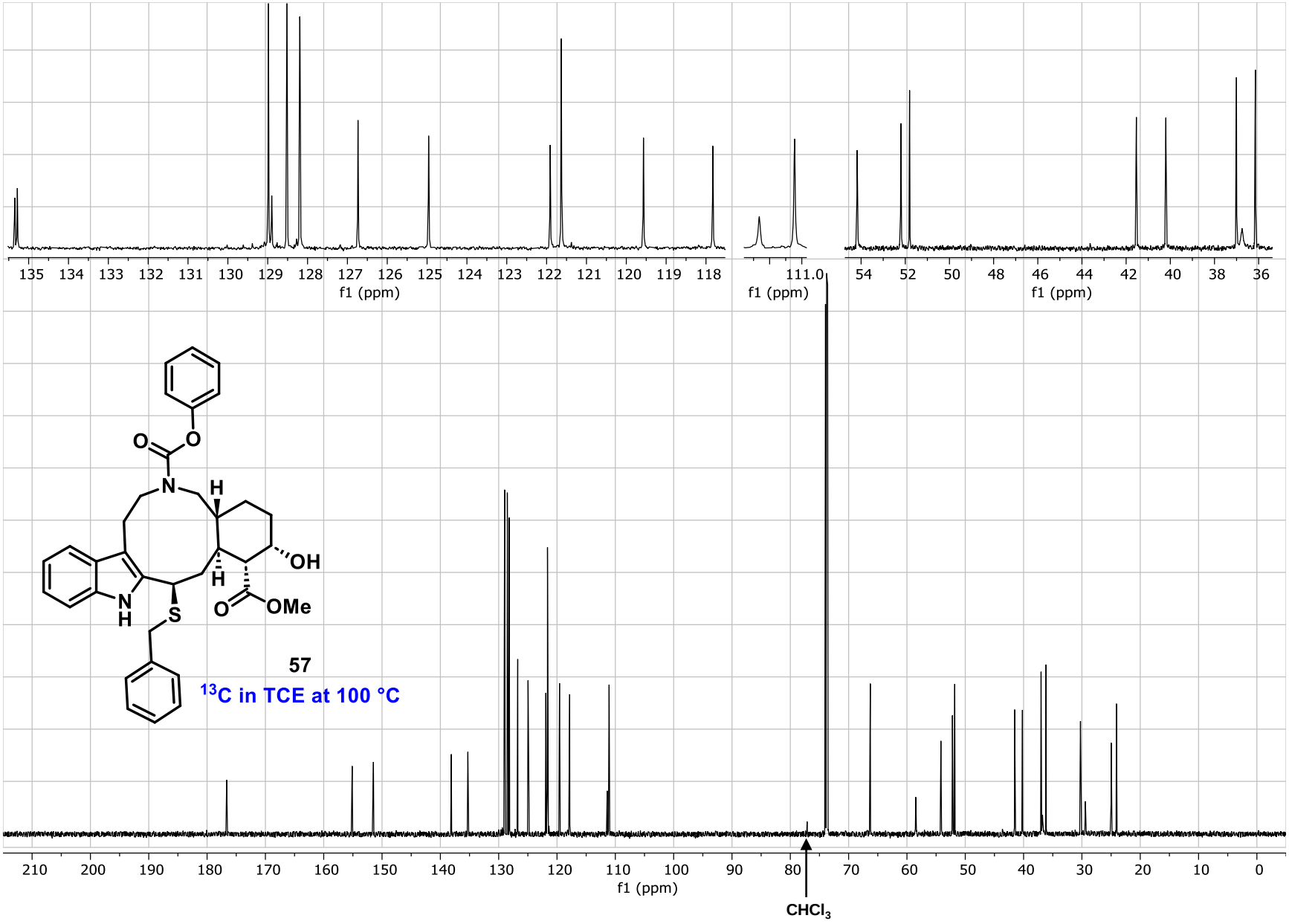


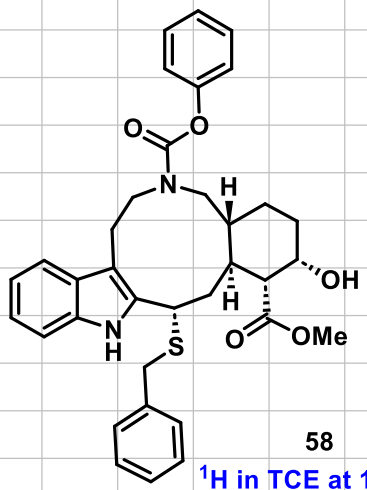
Compound 23: HSQC, T = 100 °C,
DMSO-*d6* (zoomed in)


O
OMe
N
H
OH
H
N
H
S
O
OMe
24
^{1}H in DMSO-*d6* at 100 °C
4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1
f1 (ppm)
2.5 2.0 1.5 1.0
f1 (ppm)
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)
CHCl$_3$


f1 (ppm)
f1 (ppm)
f1 (ppm)
O
OMe
N
H
OH
H
N
H
S
O
OMe
24
13C in DMSO-d6 at 100 °C

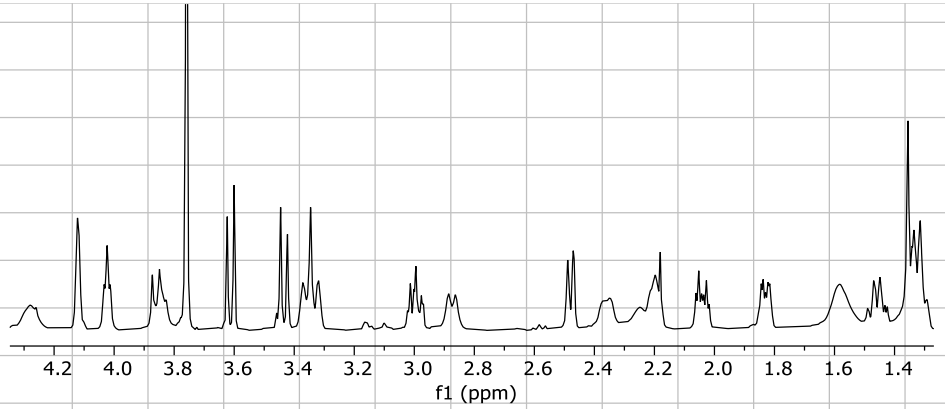

O
O
N
H
OH
H
N
H
S
O
OMe
57
1H in TCE at 100 °C
4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4
f1 (ppm)
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

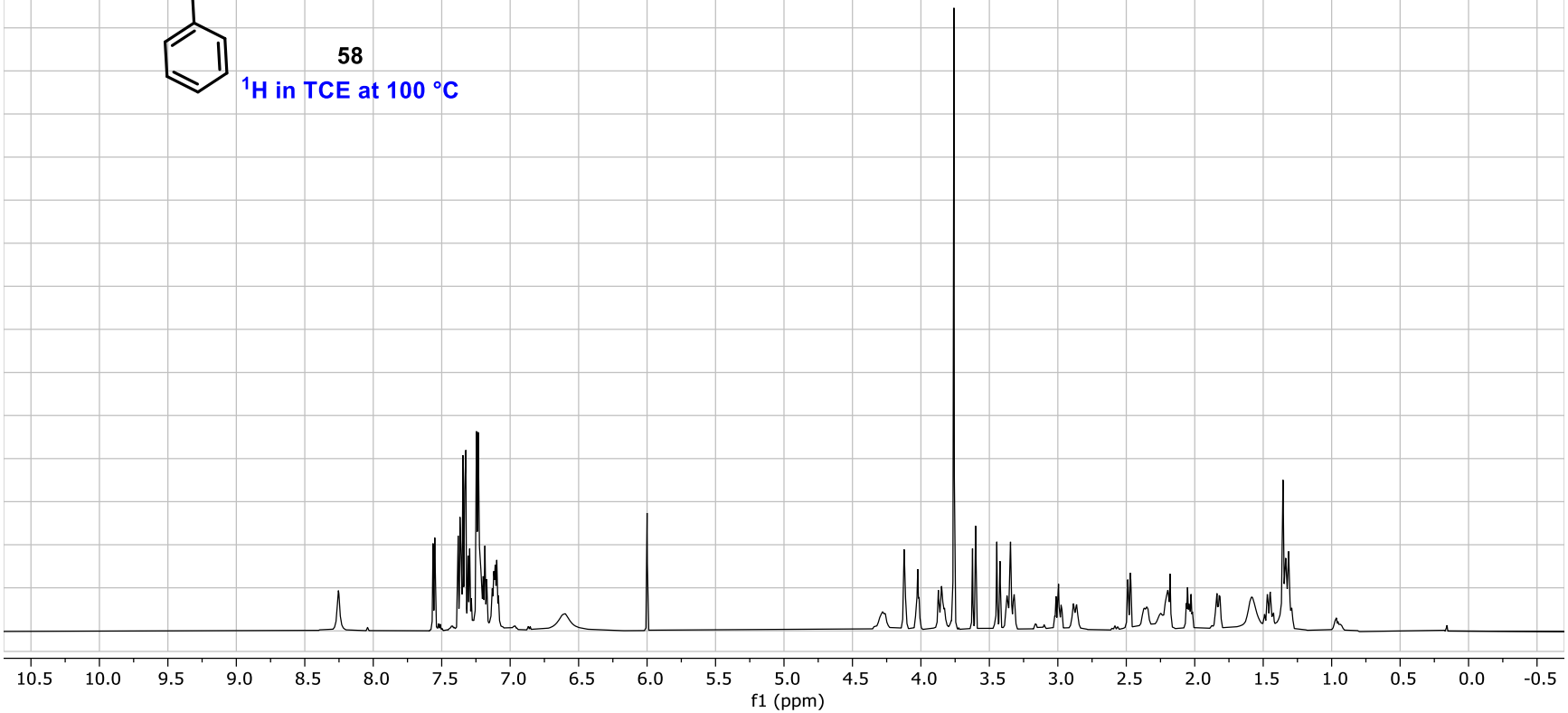

135 134 133 132 131 130 129 128 127 126 125 124 123 122 121 120 119 118
f1 (ppm)
111.0
f1 (ppm)
54 52 50 48 46 44 42 40 38 36
f1 (ppm)
O
O
N
H
OH
H
N
H
S
O
OMe
57
13C in TCE at 100 °C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
CHCl3

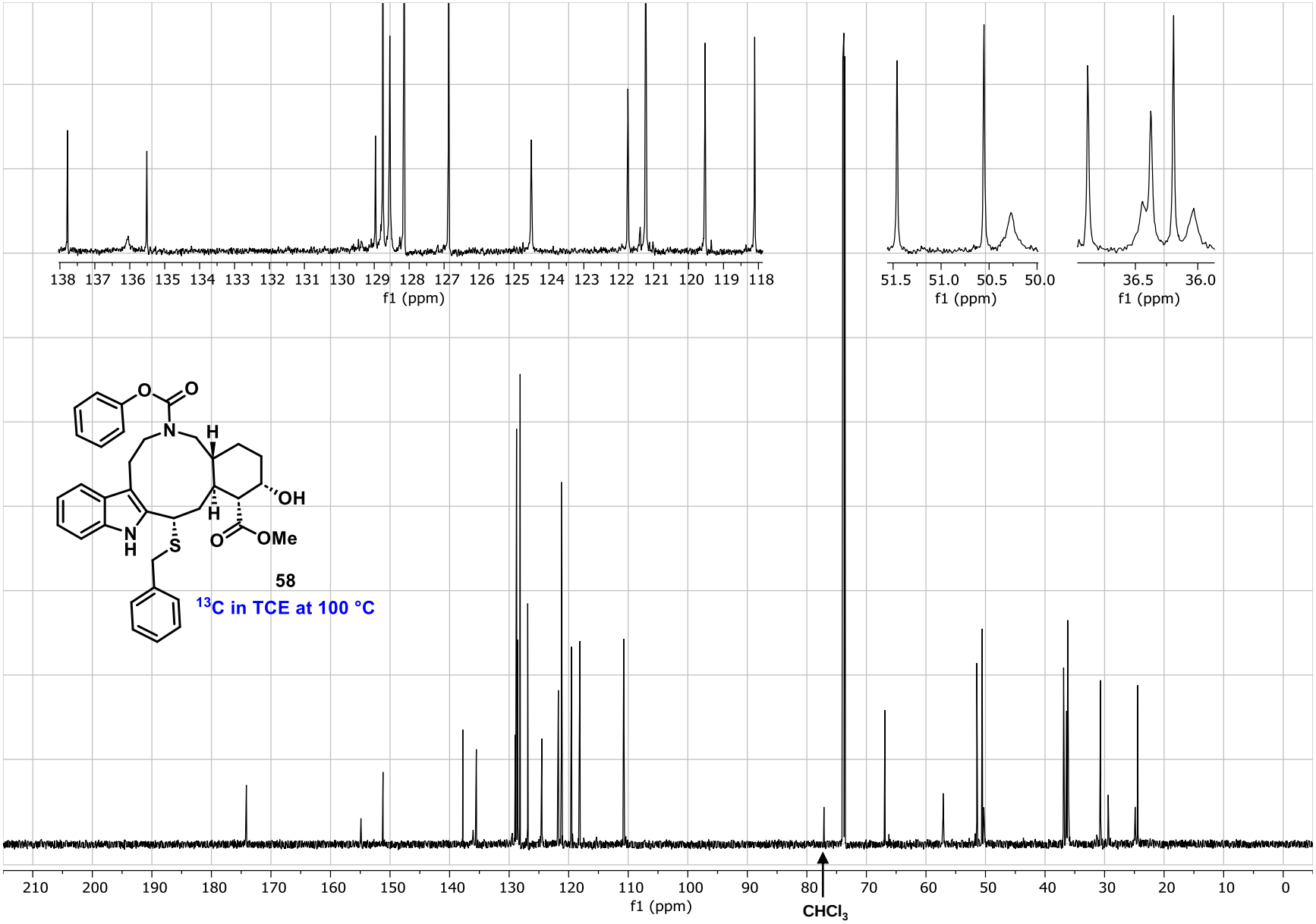


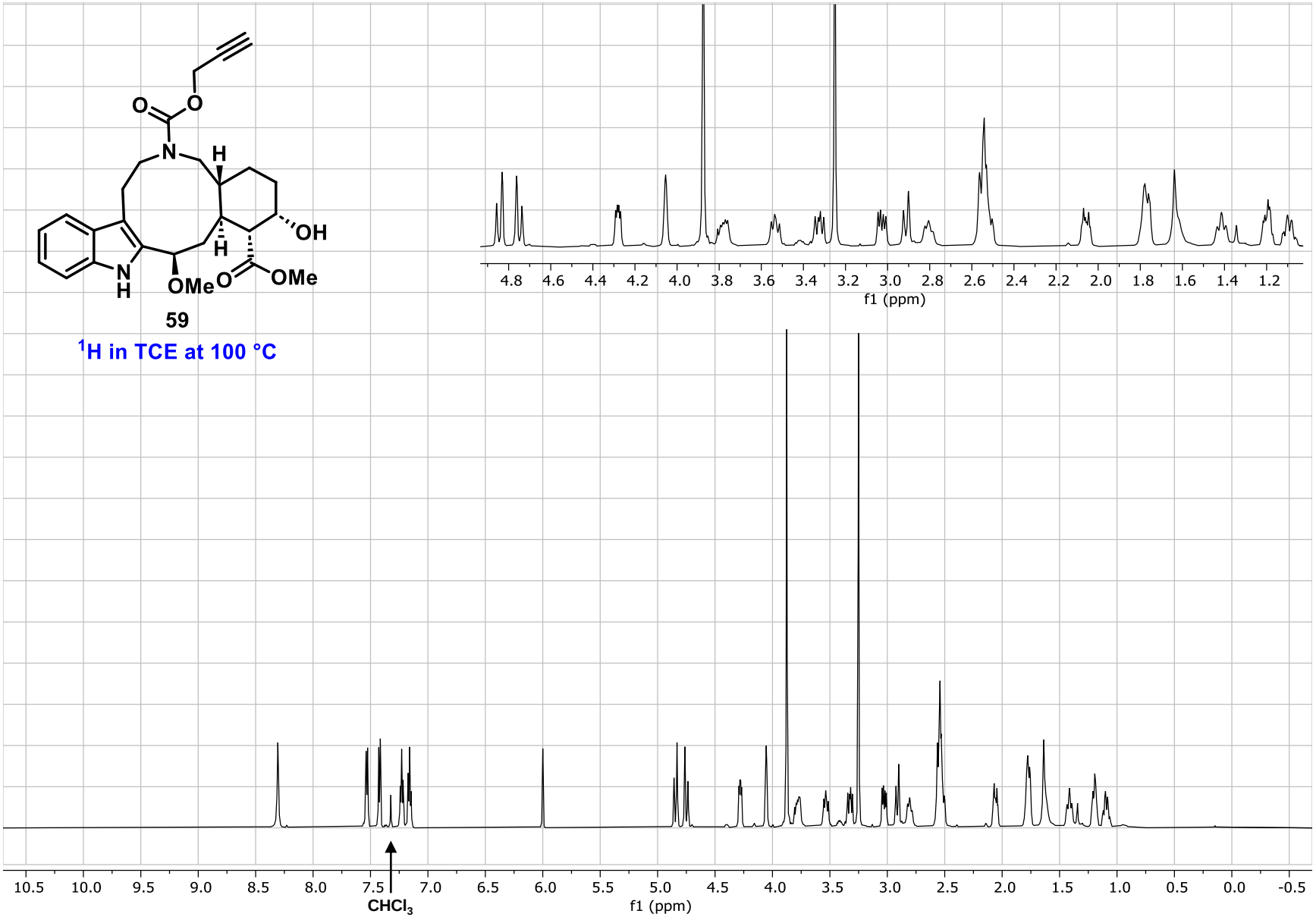
58

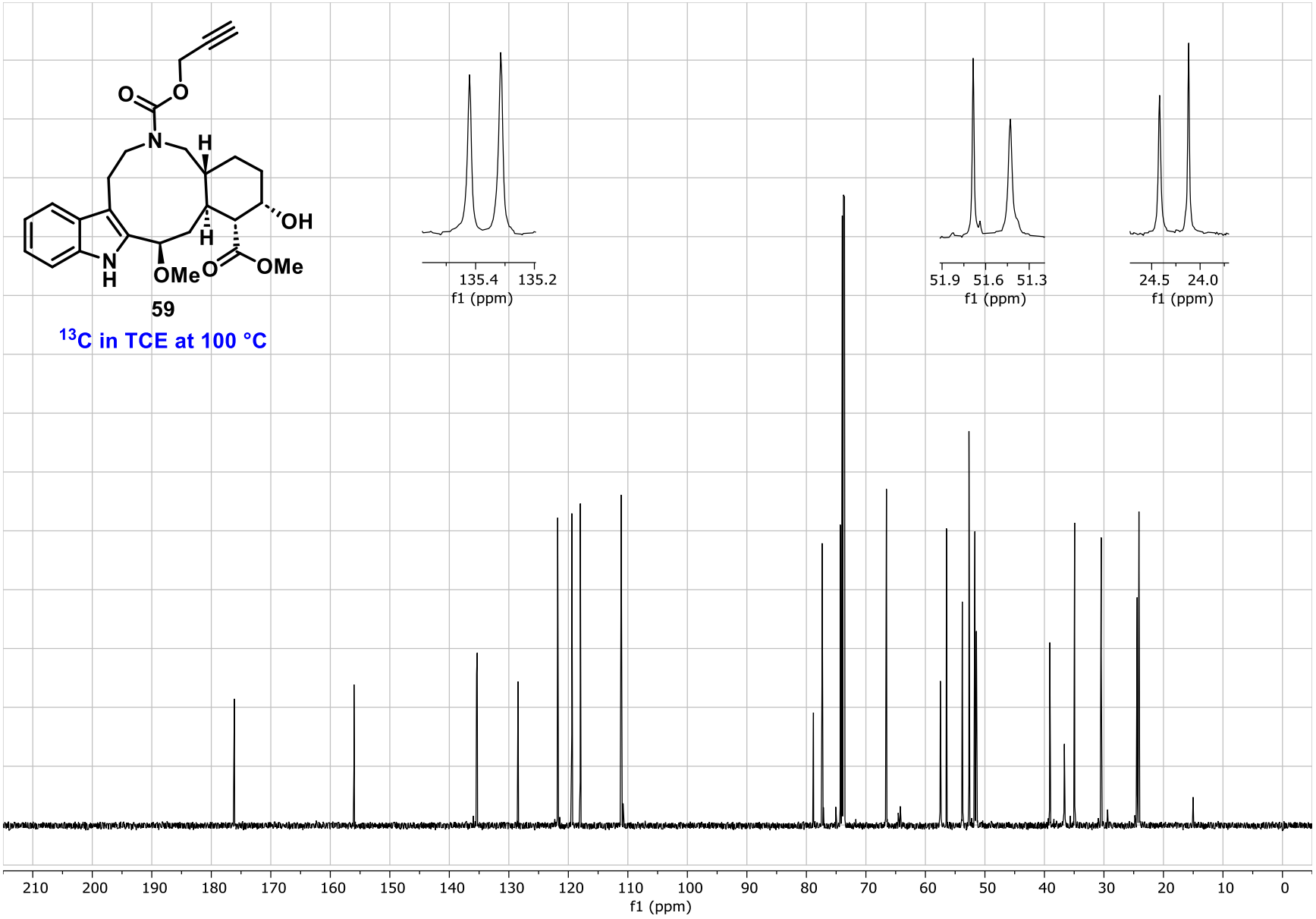
^{1}H in TCE at 100 °C

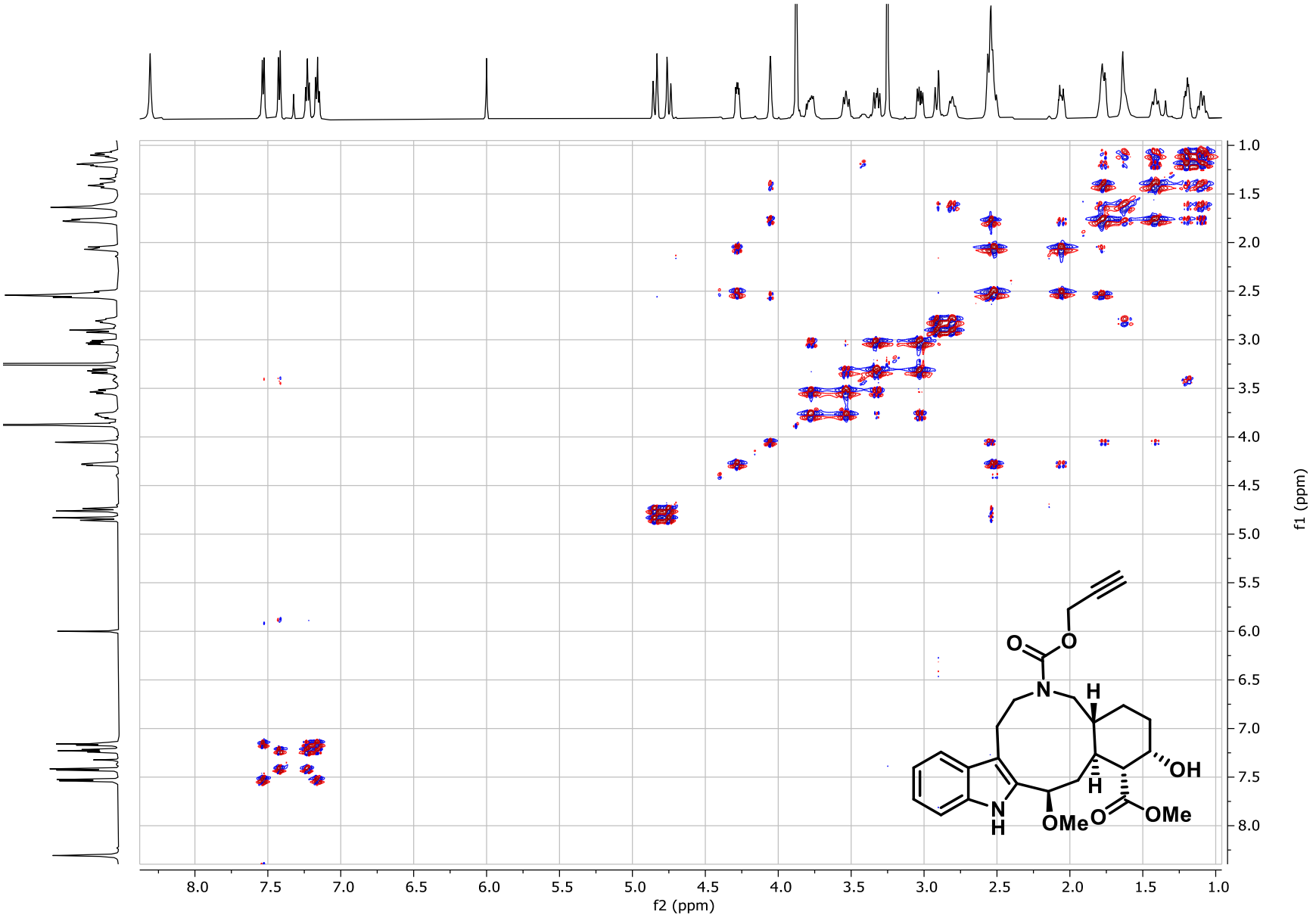




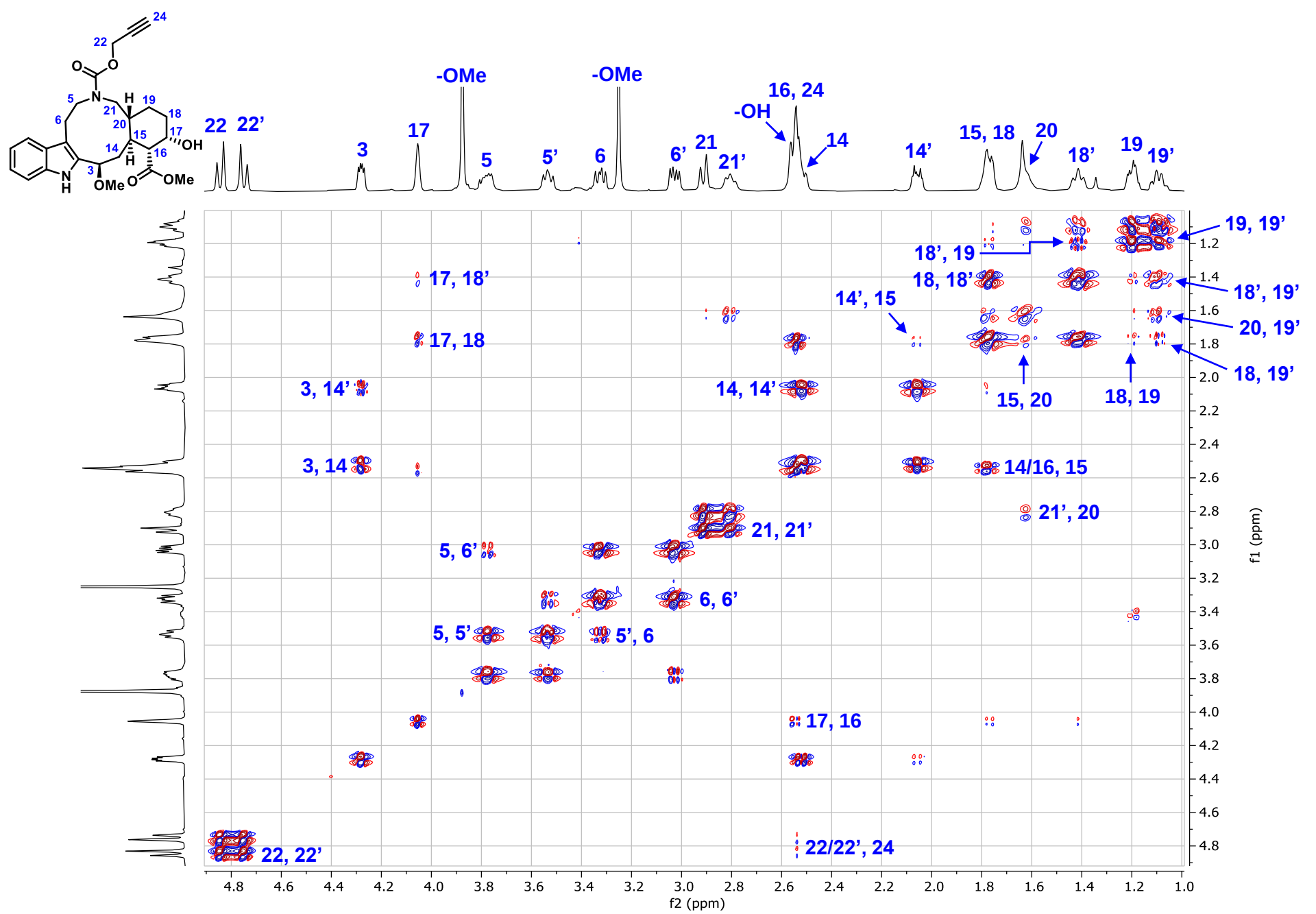

138 137 136 135 134 133 132 131 130 129 128 127 126 125 124 123 122 121 120 119 118
f1 (ppm)
51.5 51.0 50.5 50.0
f1 (ppm)
36.5 36.0
f1 (ppm)
O
O
N
H
OH
H
N
H
S
O
OMe
58
13C in TCE at 100 °C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
CHCl3


O
O
N
H
OH
H
N
H
OMe
O
OMe
59
1H in TCE at 100 °C
4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2
f1 (ppm)
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
CHCl3
f1 (ppm)

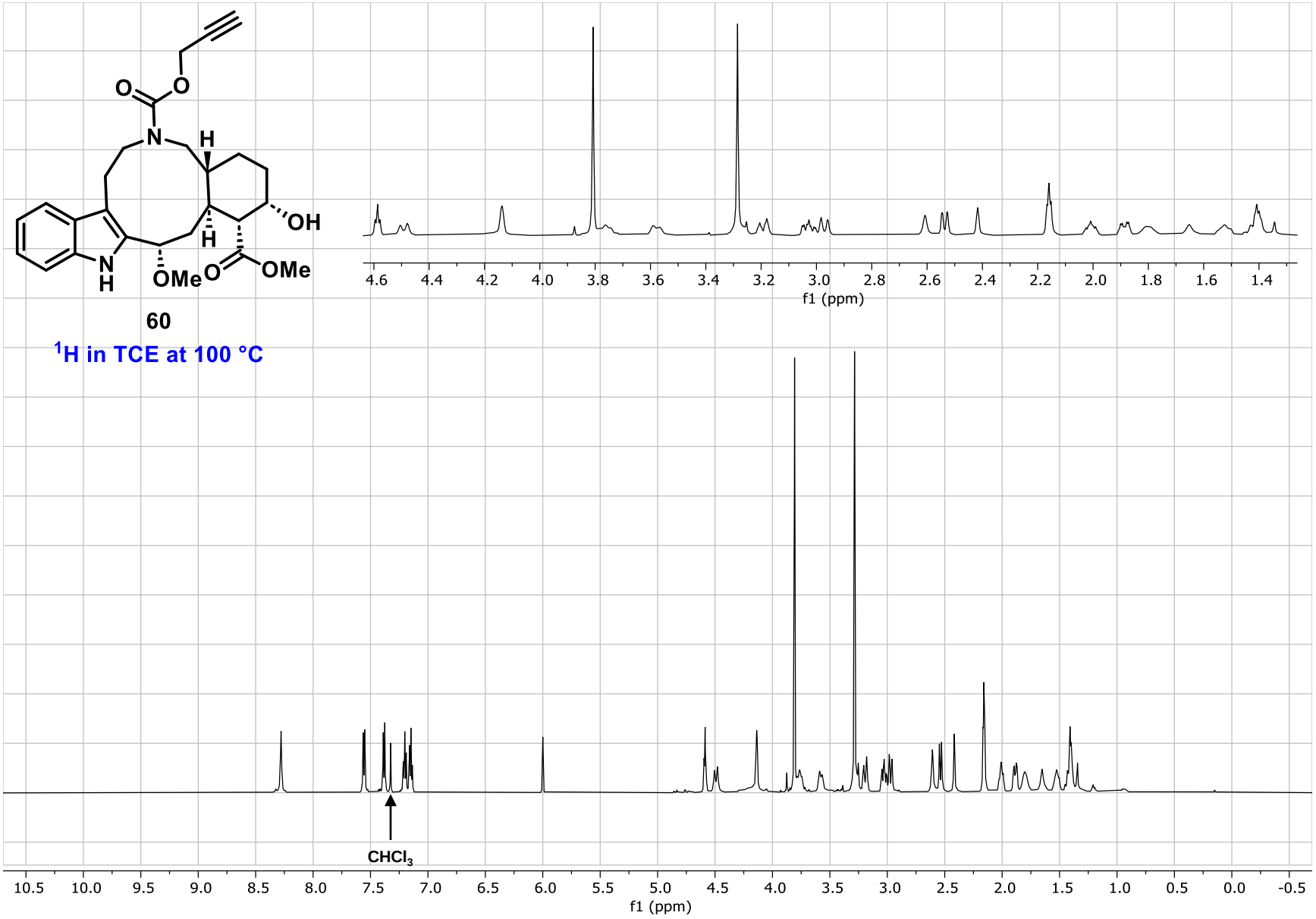

59
^{13}C in TCE at 100 °C
135.4
135.2
f1 (ppm)
51.9
51.6
51.3
f1 (ppm)
24.5
24.0
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

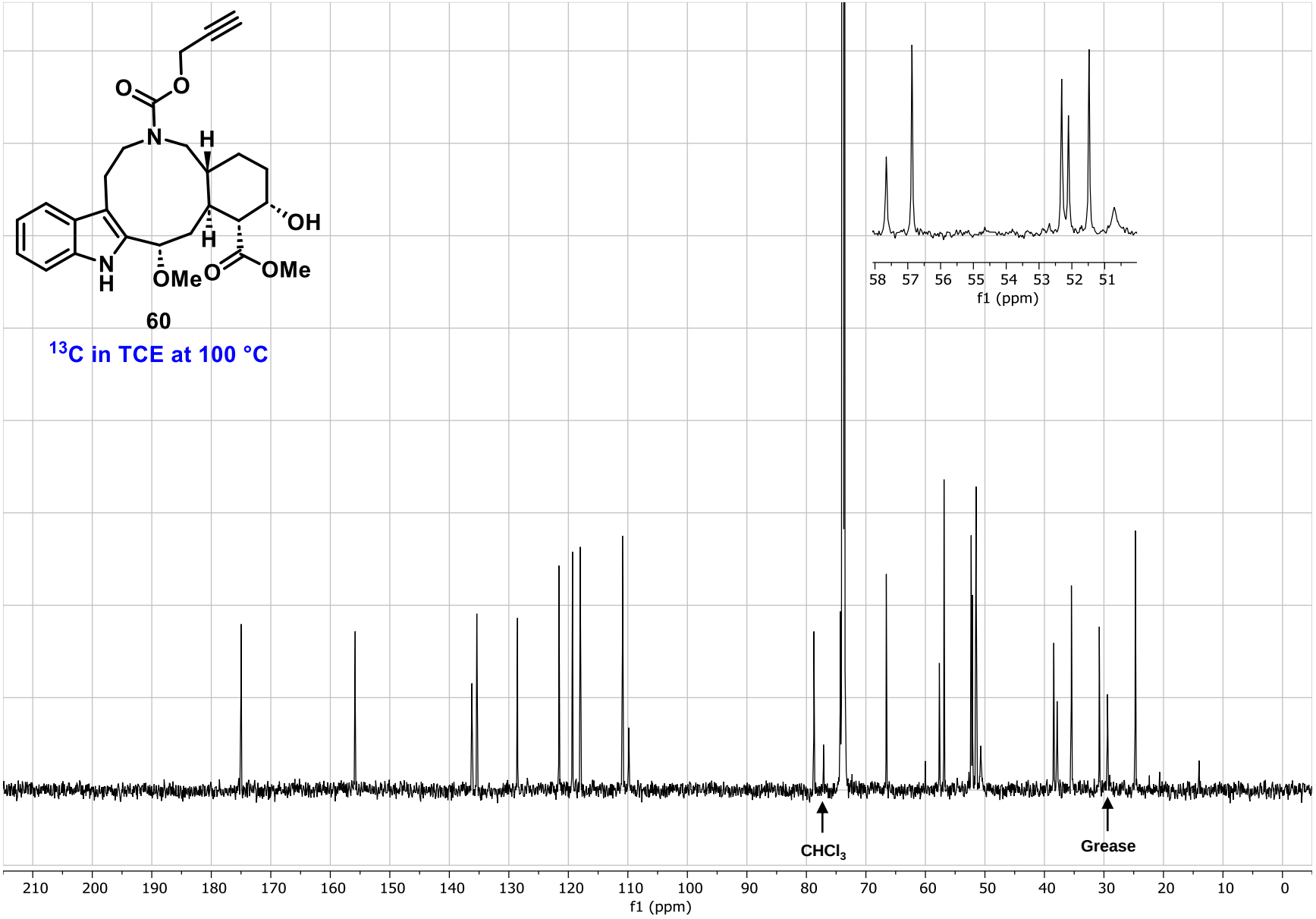


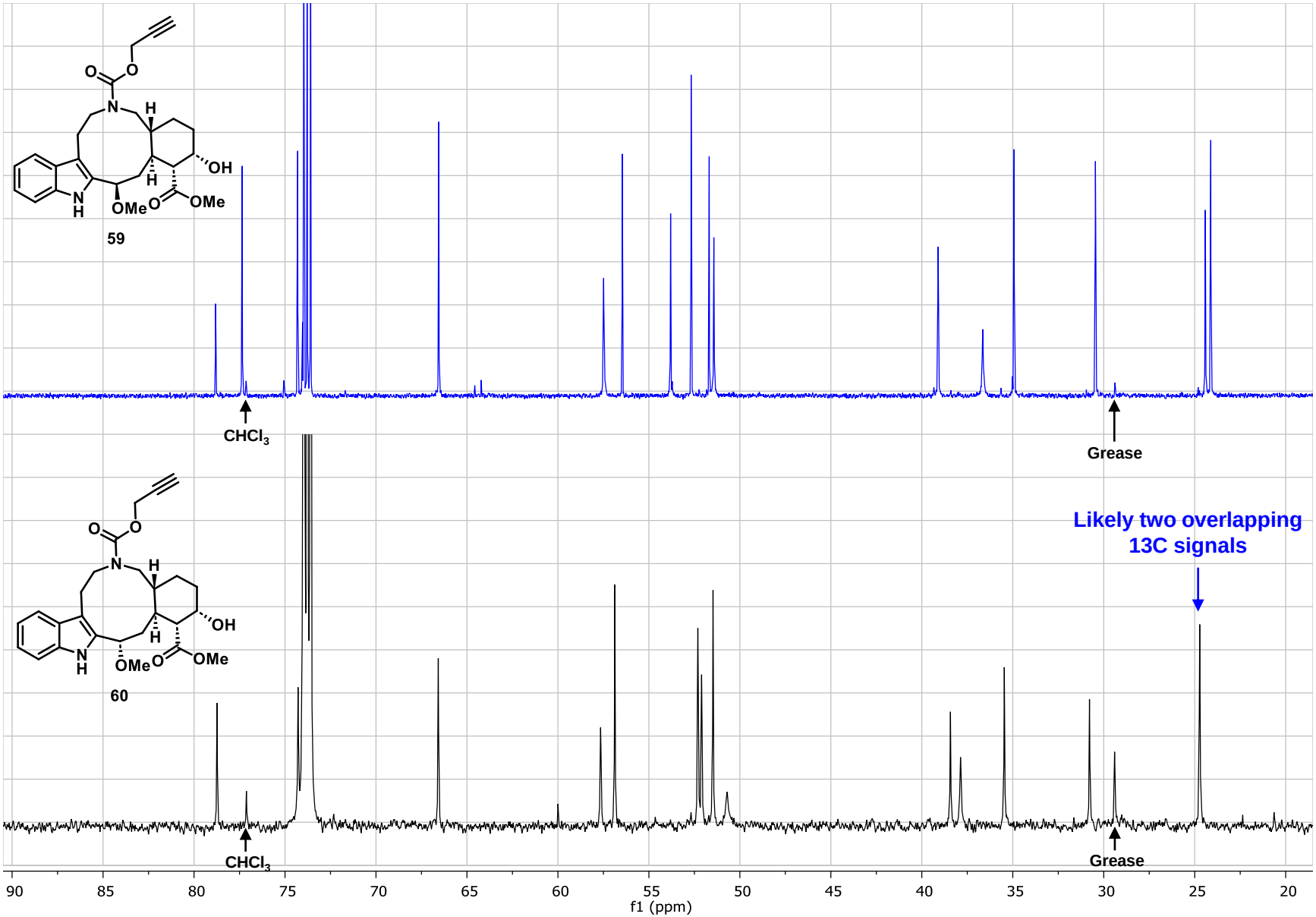
Compound 59: COSY, T = 100 °C, $C_2D_2Cl_4$ (full)



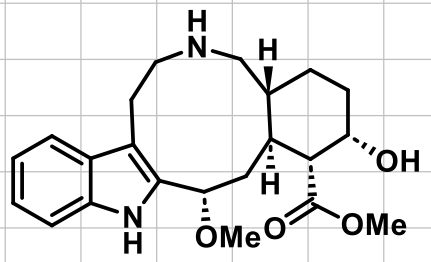
Compound 59: COSY, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in)


O
O
N
H
OH
H
N
H
OMe
O
OMe
60
1H in TCE at 100 °C
4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4
f1 (ppm)
CHCl3
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


60
13C in TCE at 100 °C
58 57 56 55 54 53 52 51
f1 (ppm)
CHCl3
Grease
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

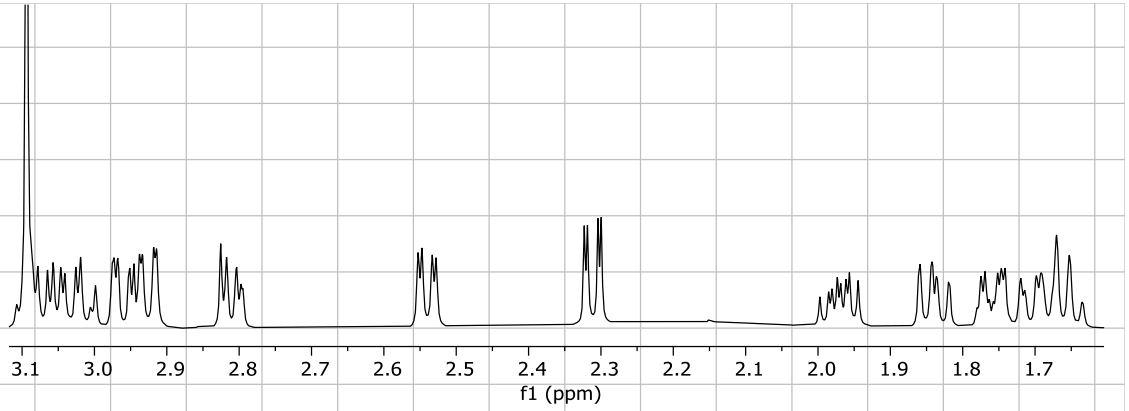


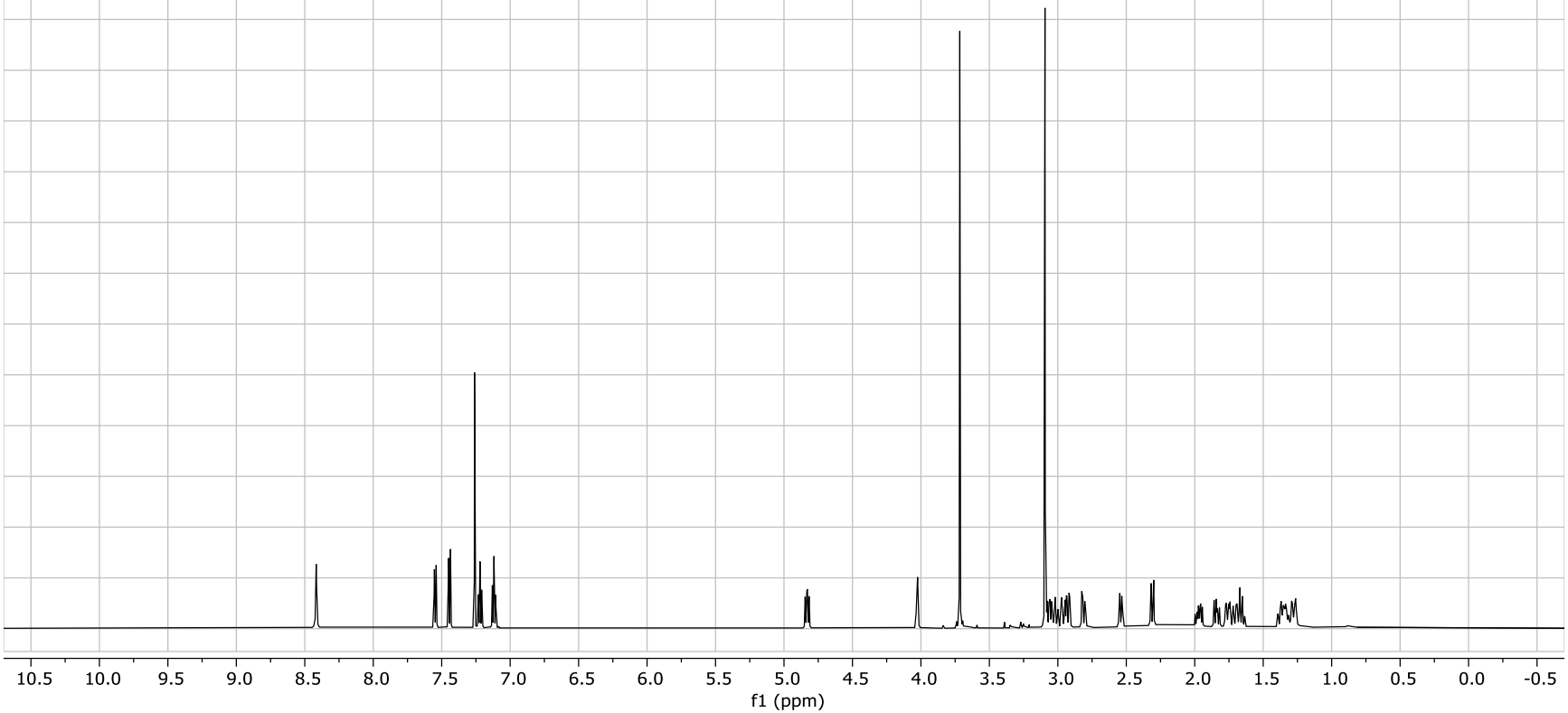
Comparison of ^{13}C NMR profiles for **59** and **60** to support the notion of overlapping carbon peaks at 24.7 ppm (for **60**). T = 100 °C, $C_2D_2Cl_4$

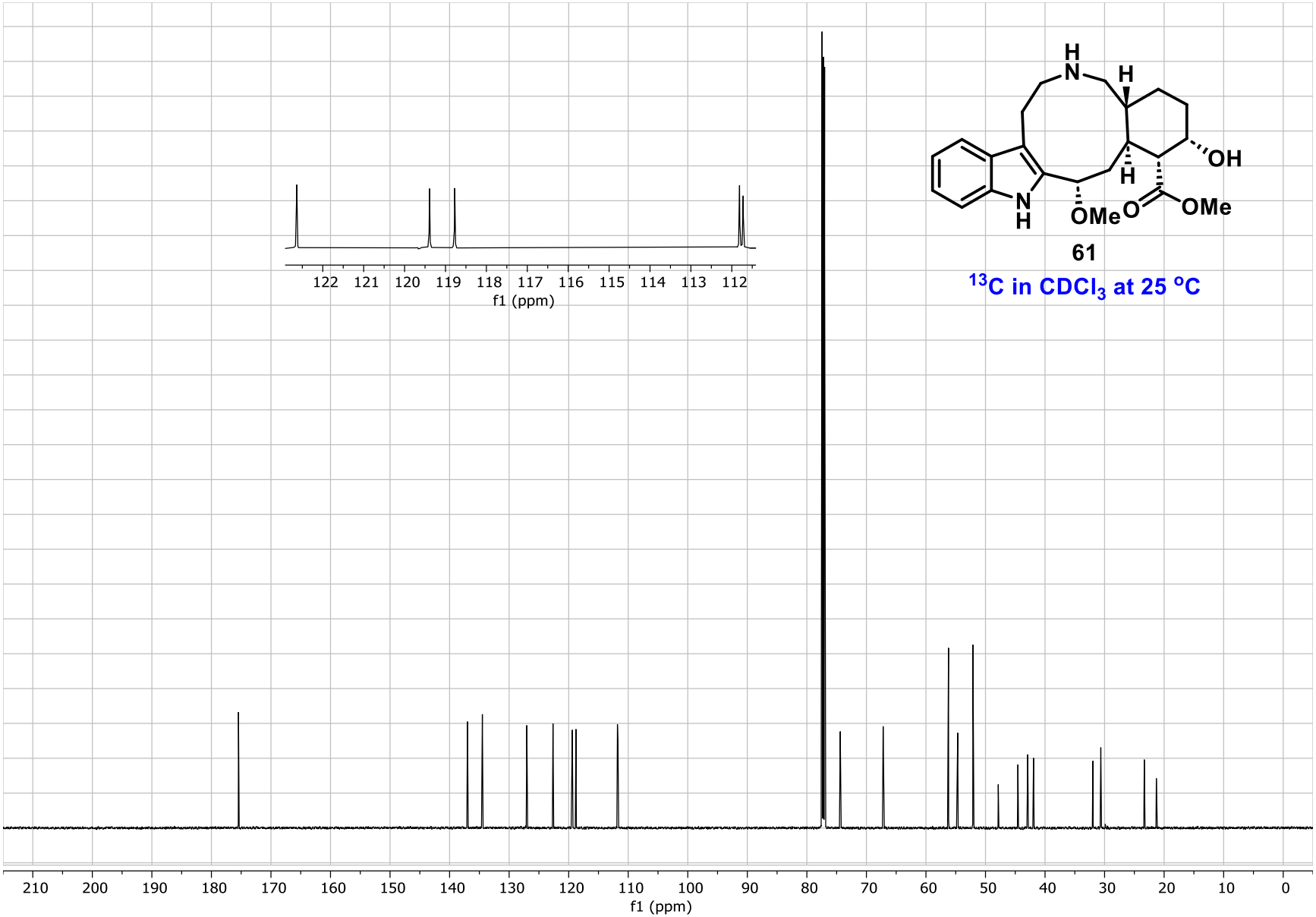


61

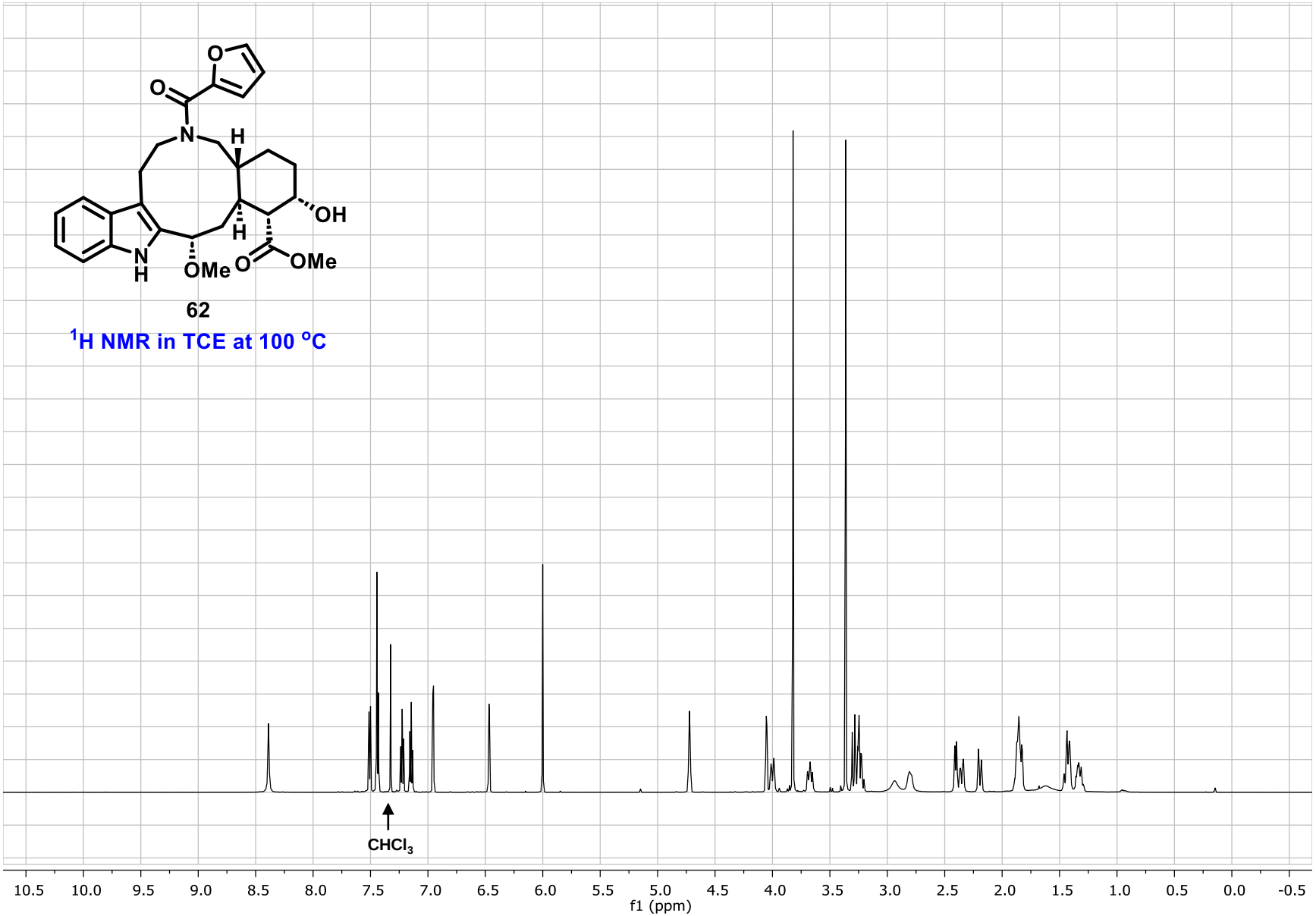
^{1}H in $CDCl_3$ at 25 °C

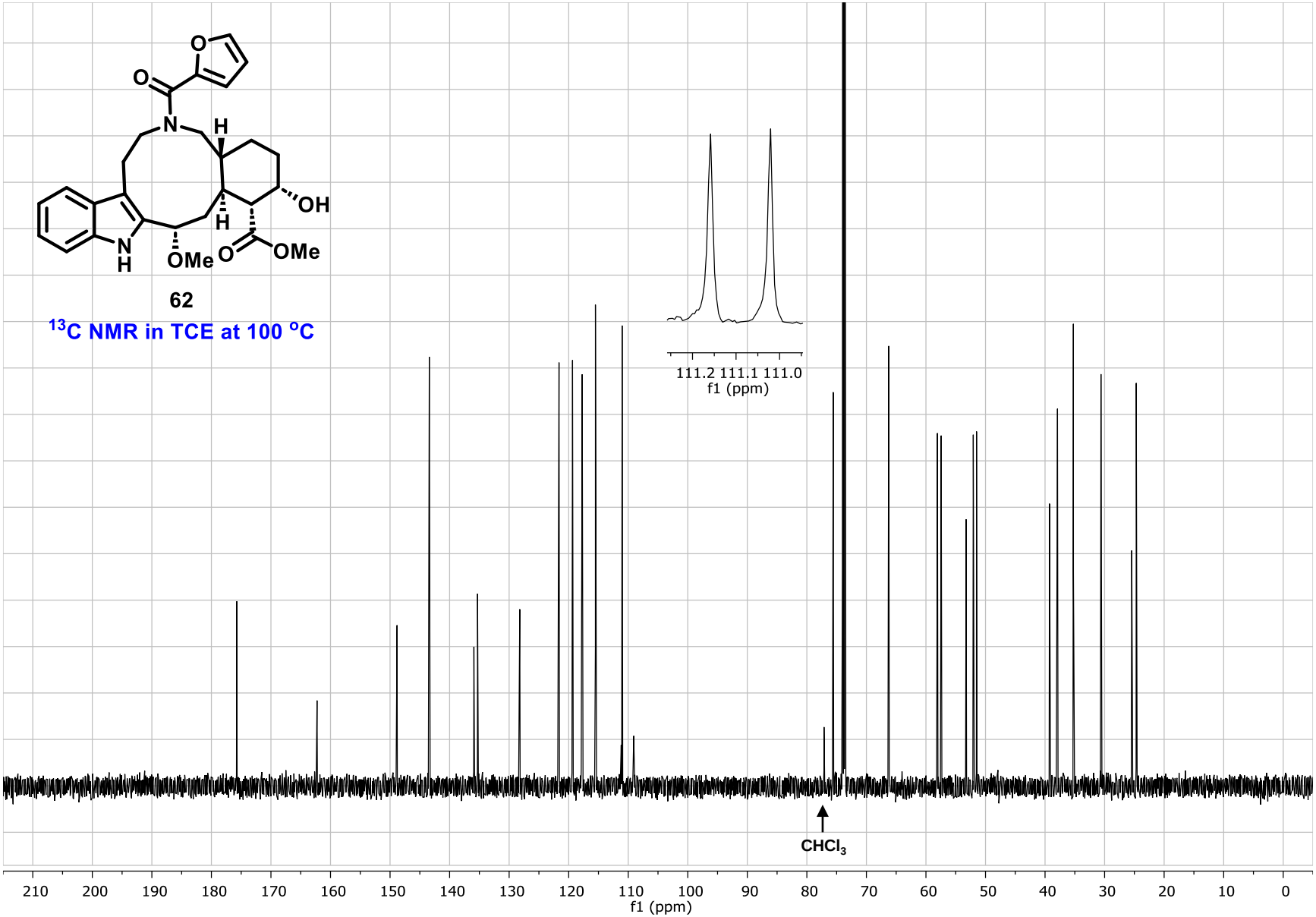


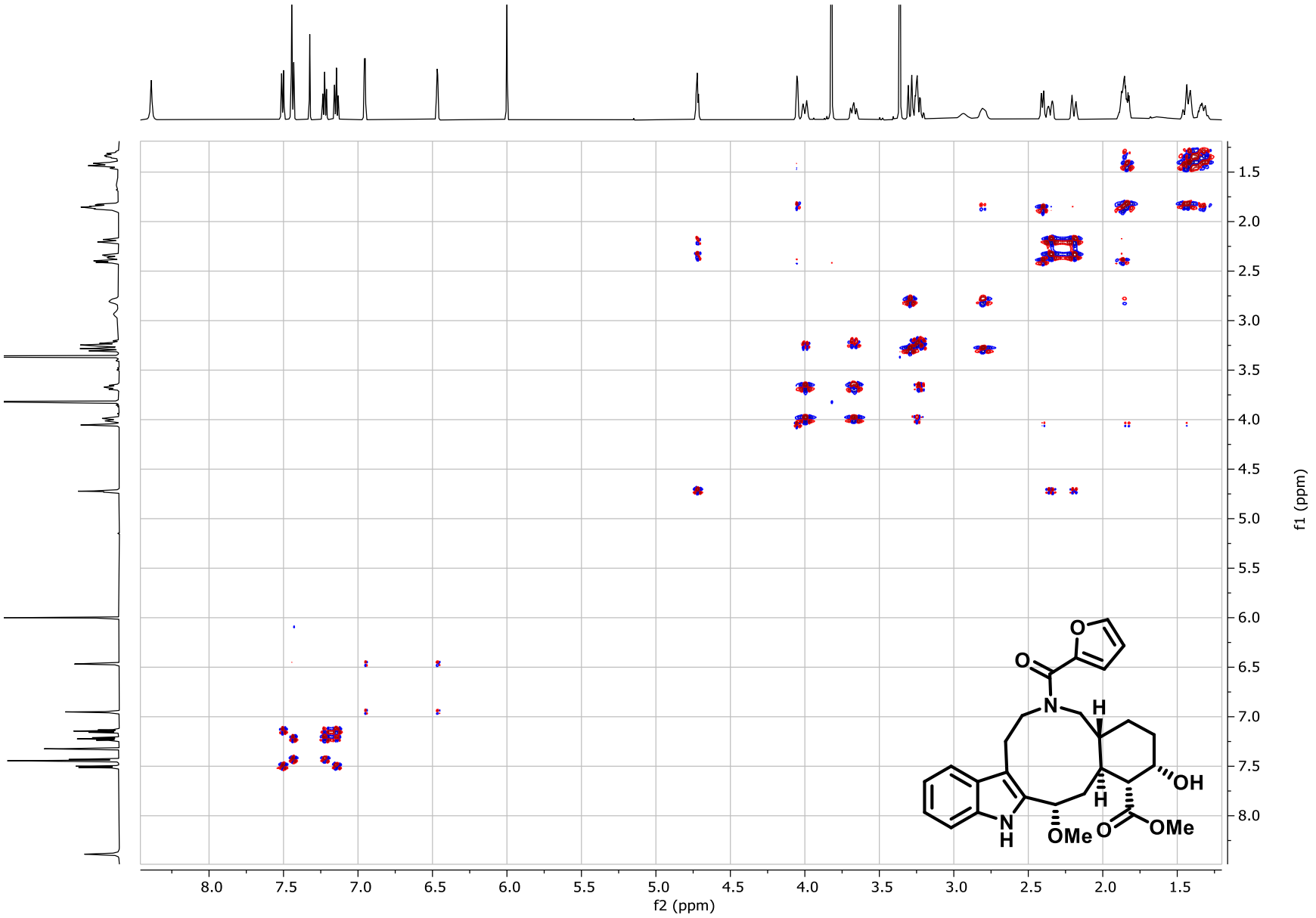



122 121 120 119 118 117 116 115 114 113 112
f1 (ppm)
H
N
H
OH
H
N
H
OMe
O
OMe
61
13C in CDCl3 at 25 °C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

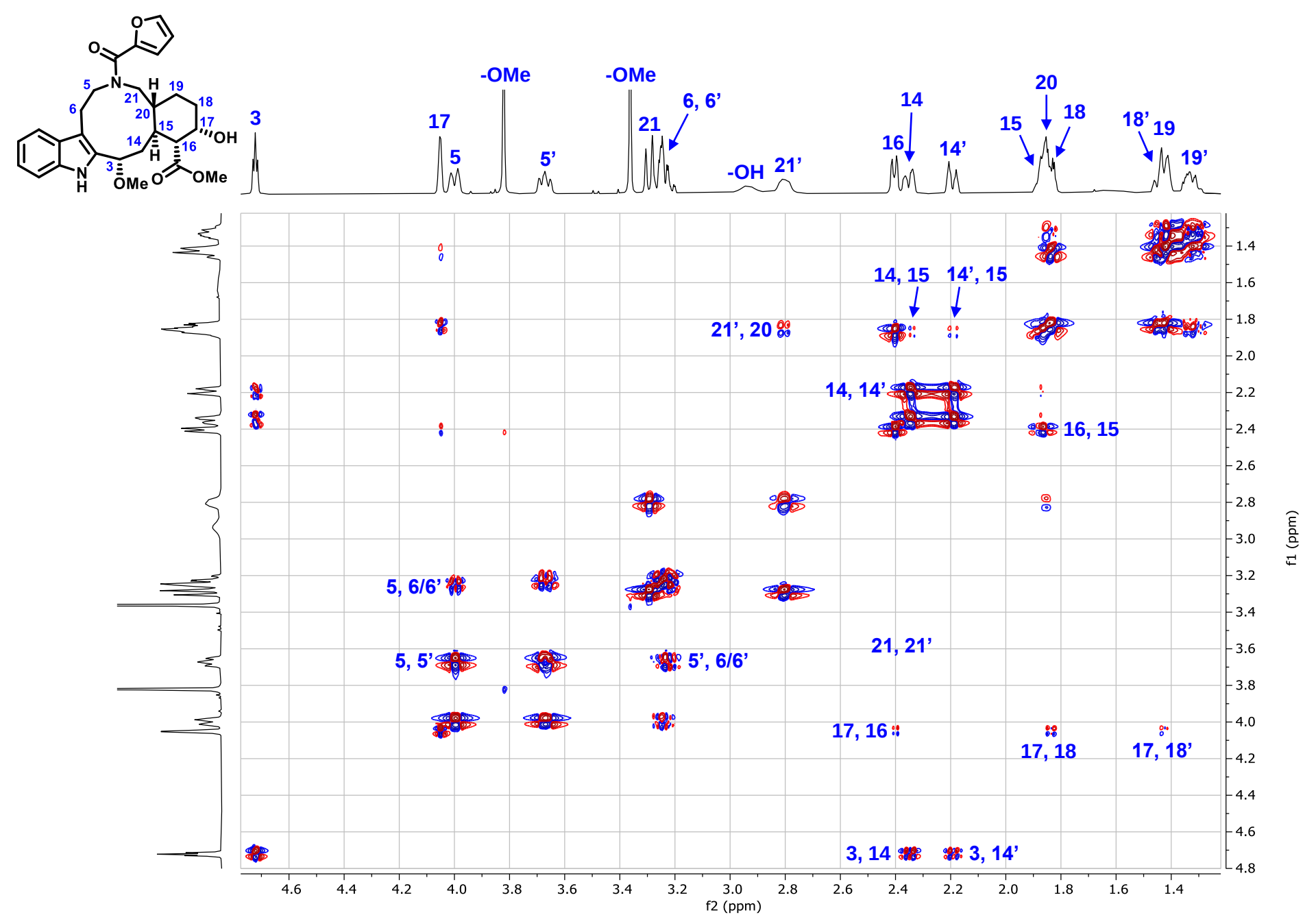
Compound 61: COSY, T = 25 °C, $CDCl_3$ (full)


O
O
N
H
OH
H
N
H
OMe
O
OMe
62
1H NMR in TCE at 100 °C
CHCl3
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

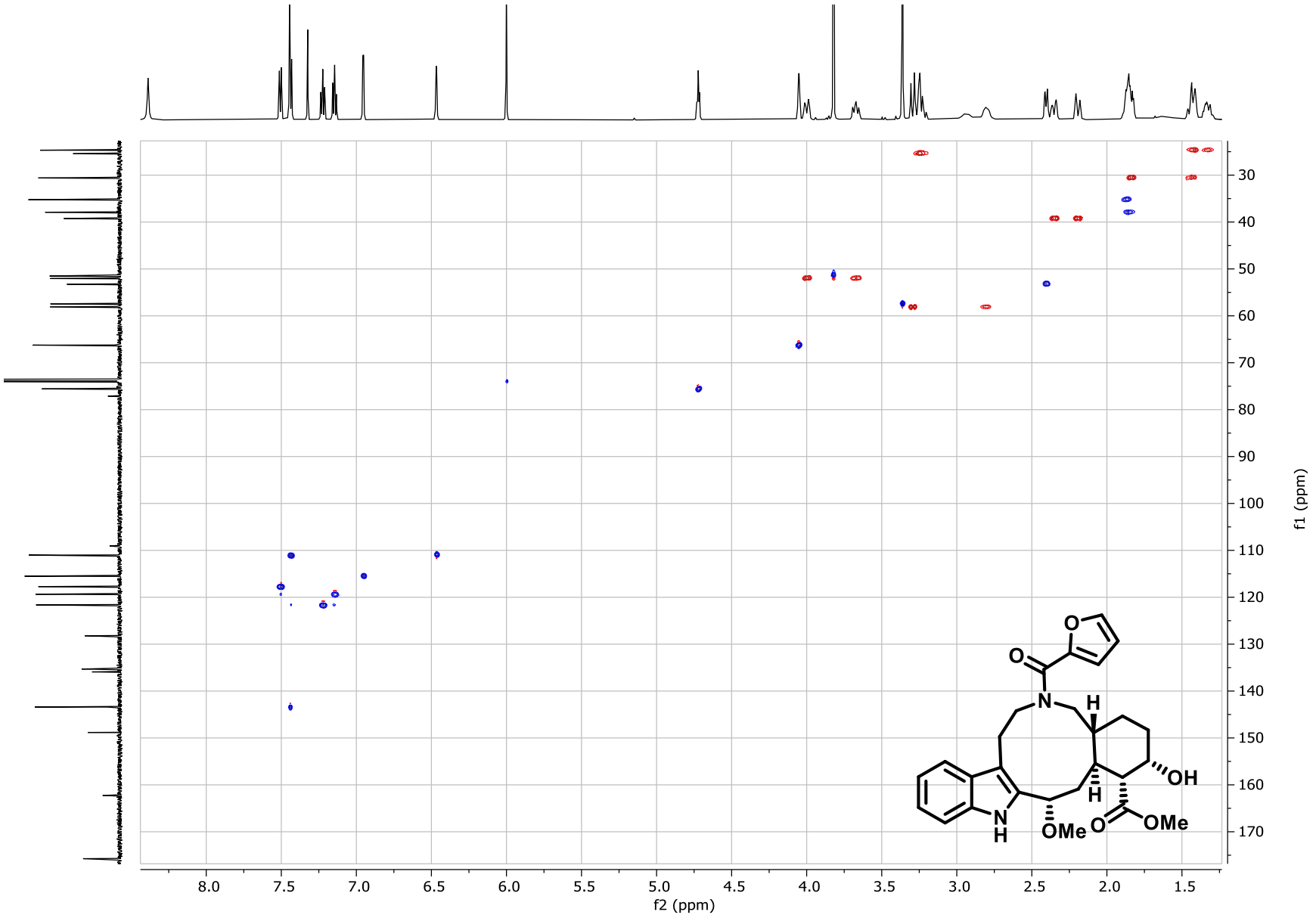

62
^{13}C NMR in TCE at 100 °C
111.2 111.1 111.0
f1 (ppm)
CHCl$_3$
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



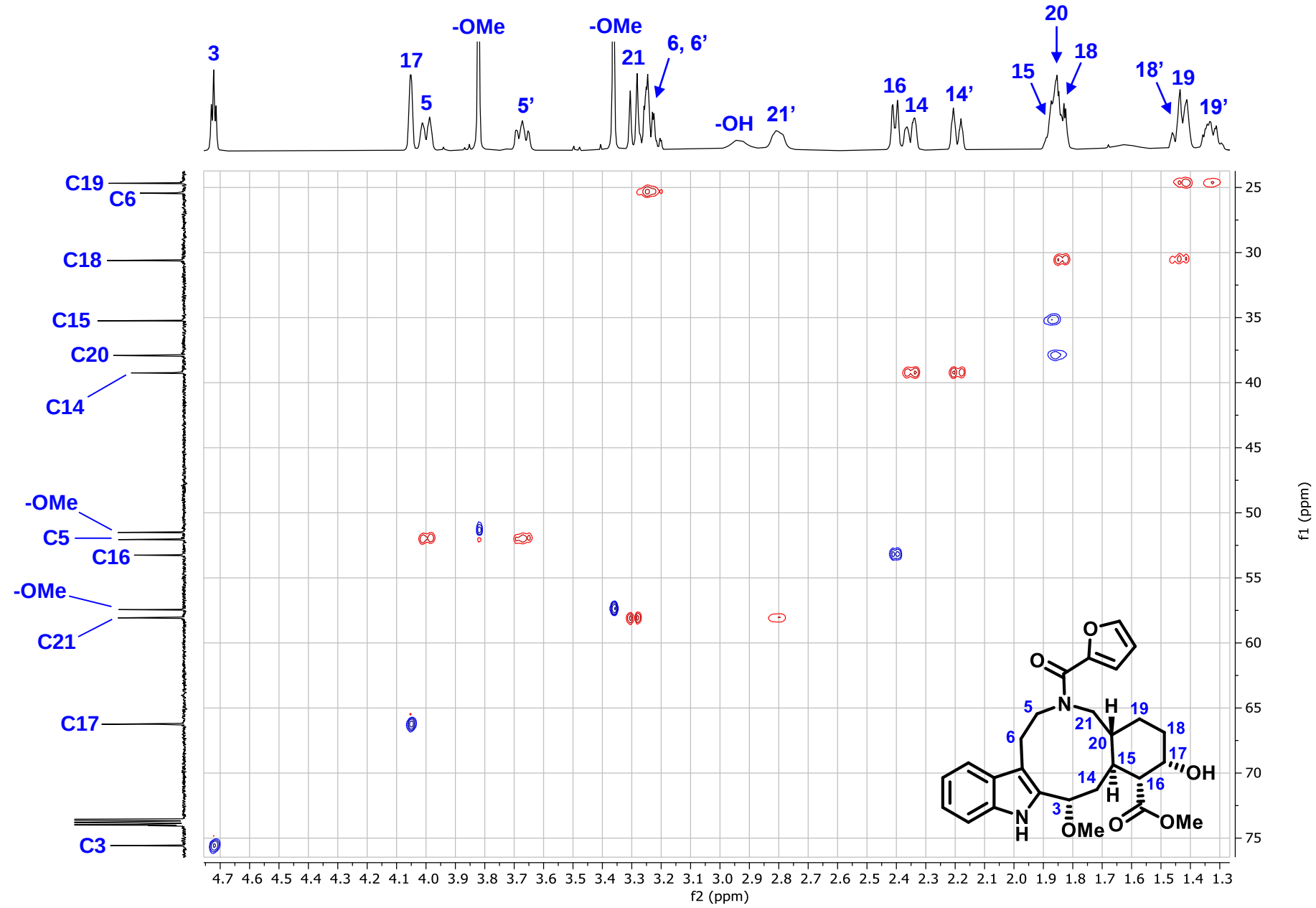
Compound 62: COSY, T = 100 °C, $C_2D_2Cl_4$ (full)



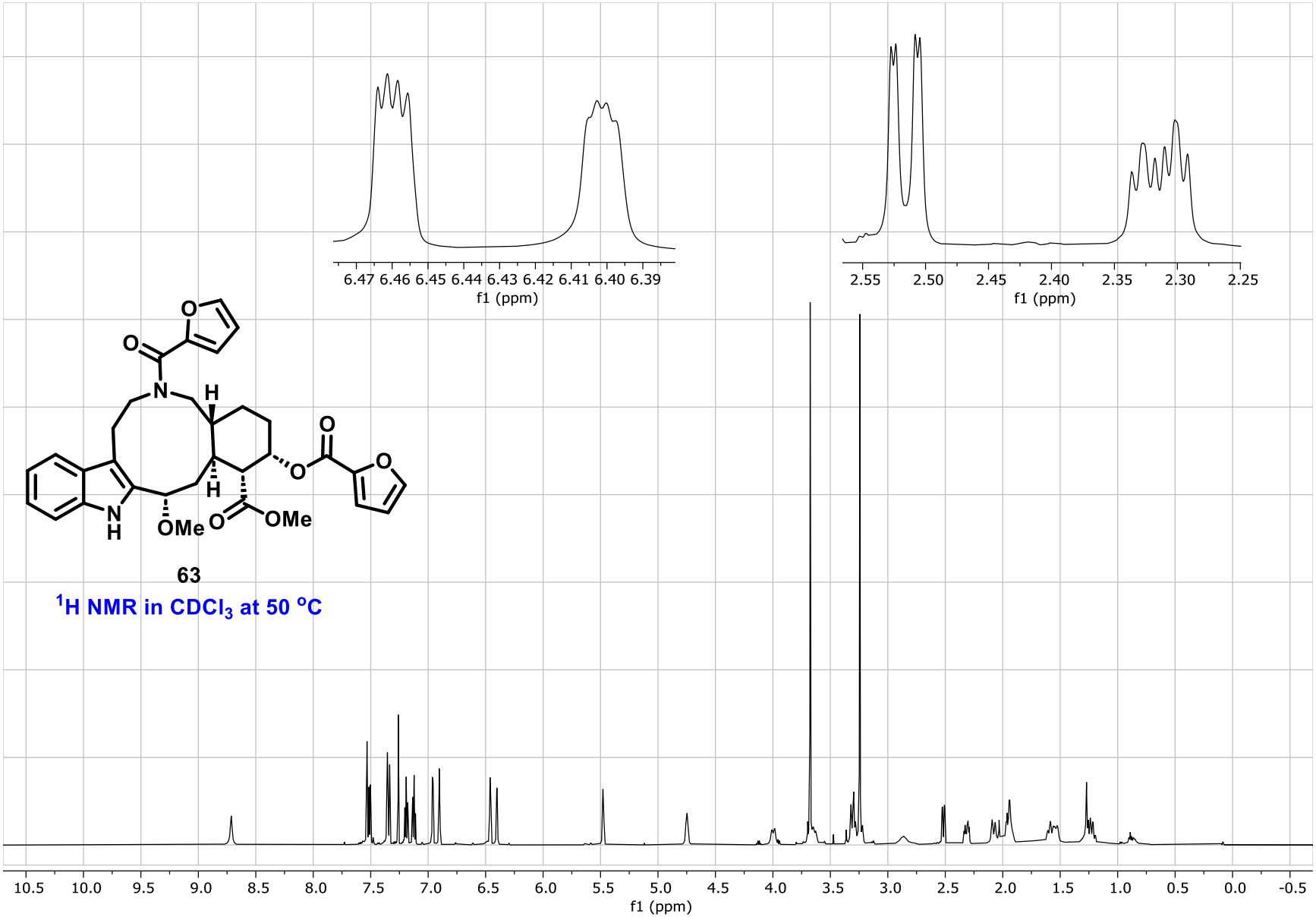
Compound 62: COSY, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in)



Compound 62: HSQC, T = 100 °C, $C_2D_2Cl_4$ (full)

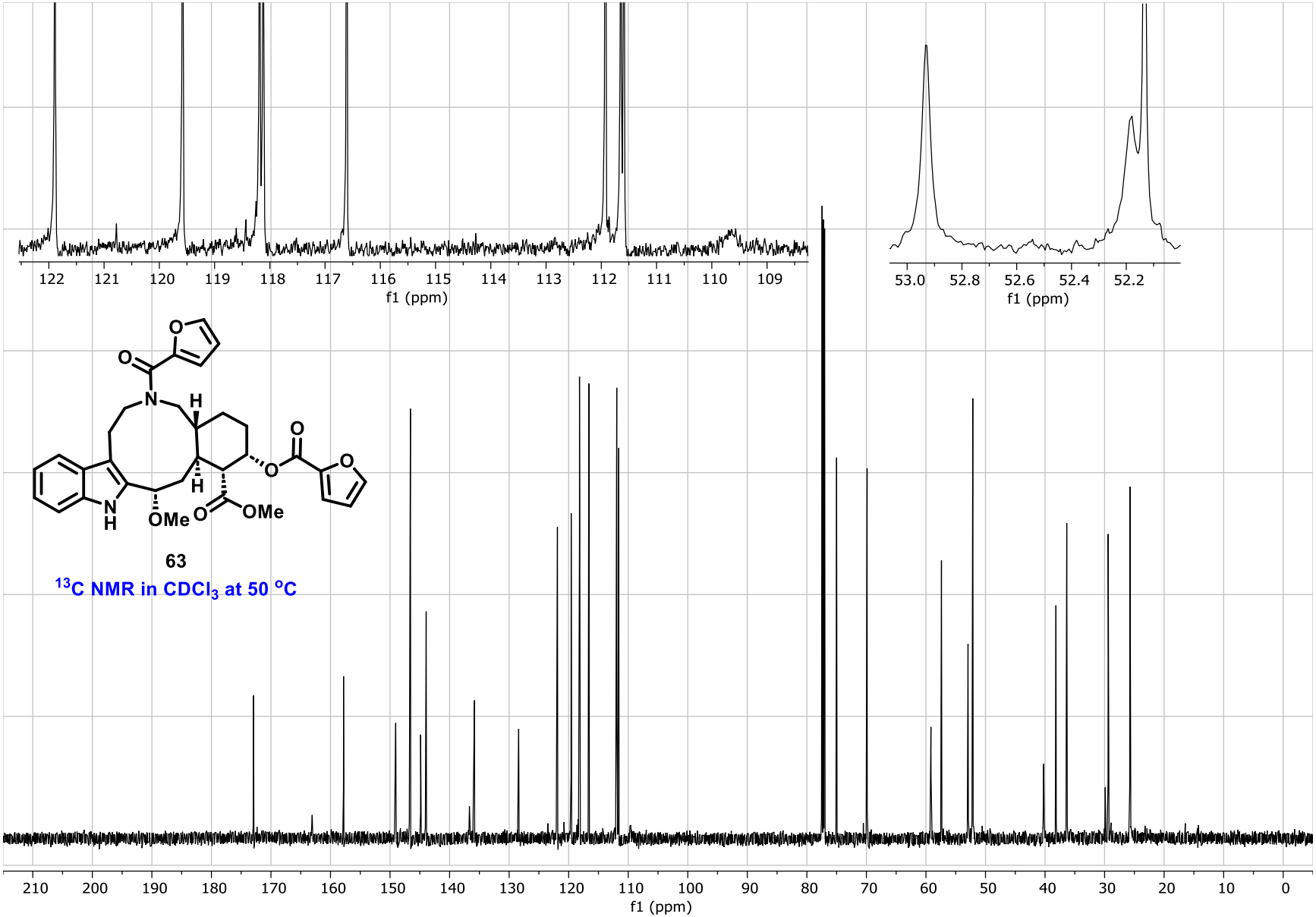


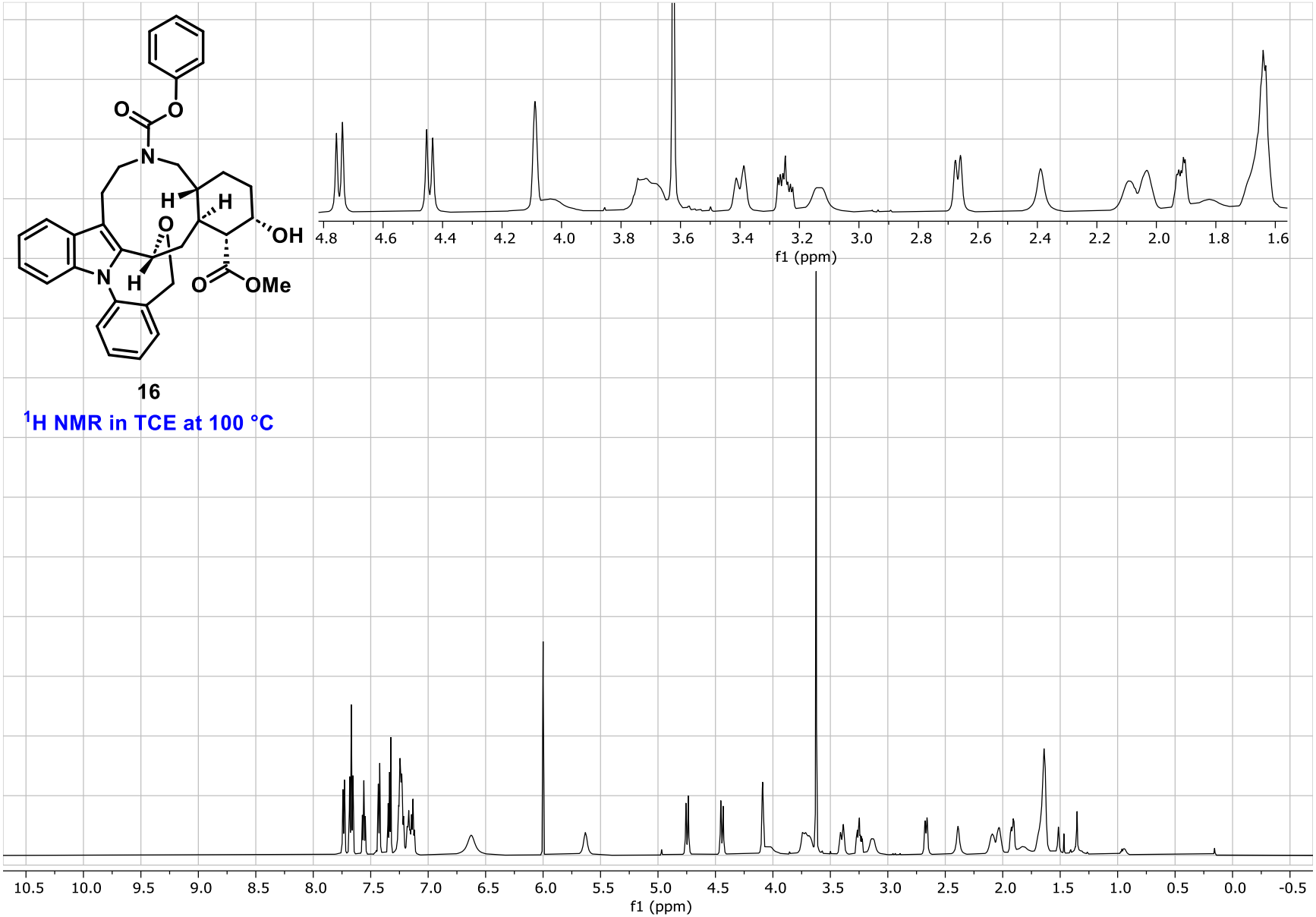
Compound 62: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in)



63

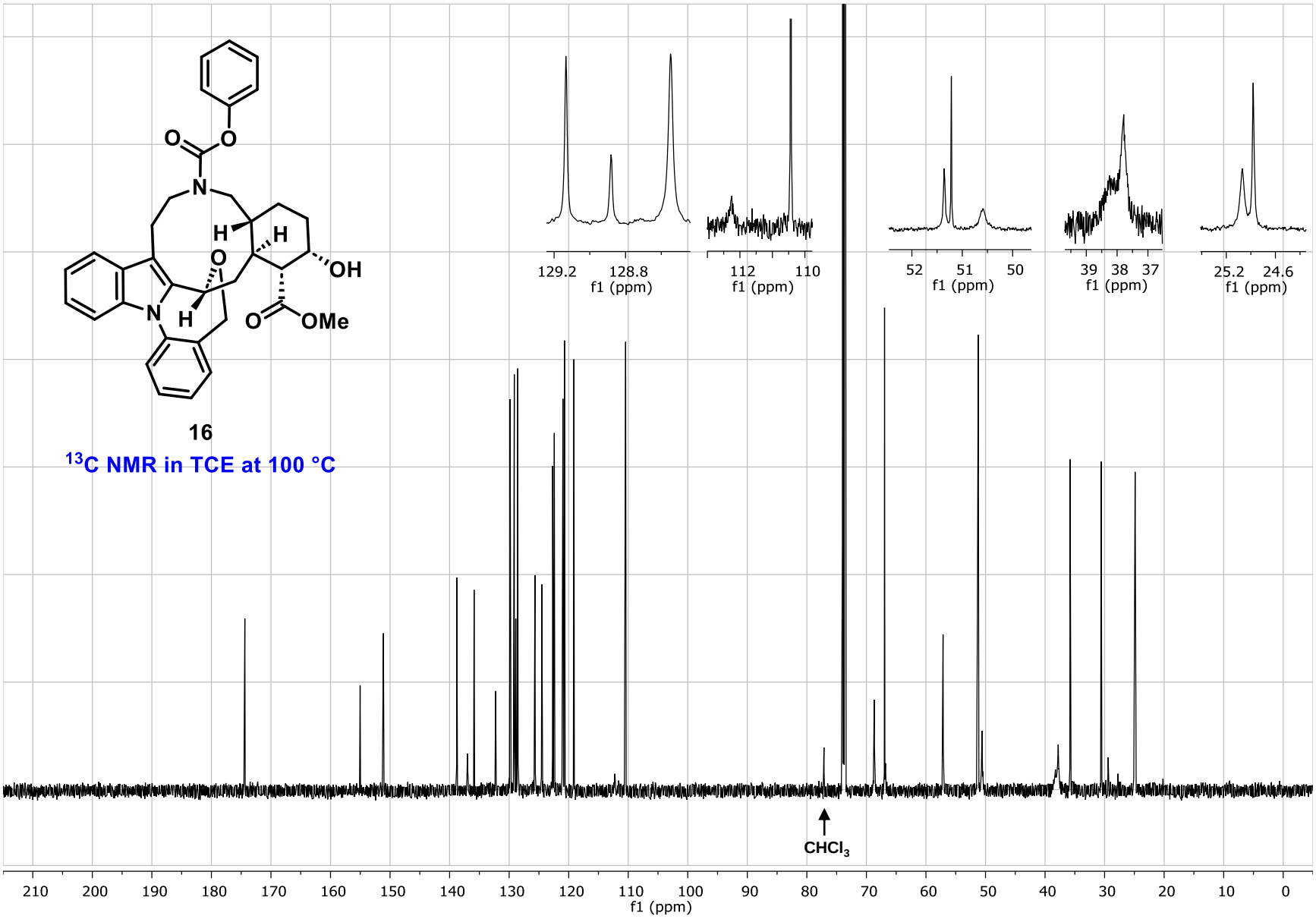
^{1}H NMR in $CDCl_3$ at 50 ^{o}C

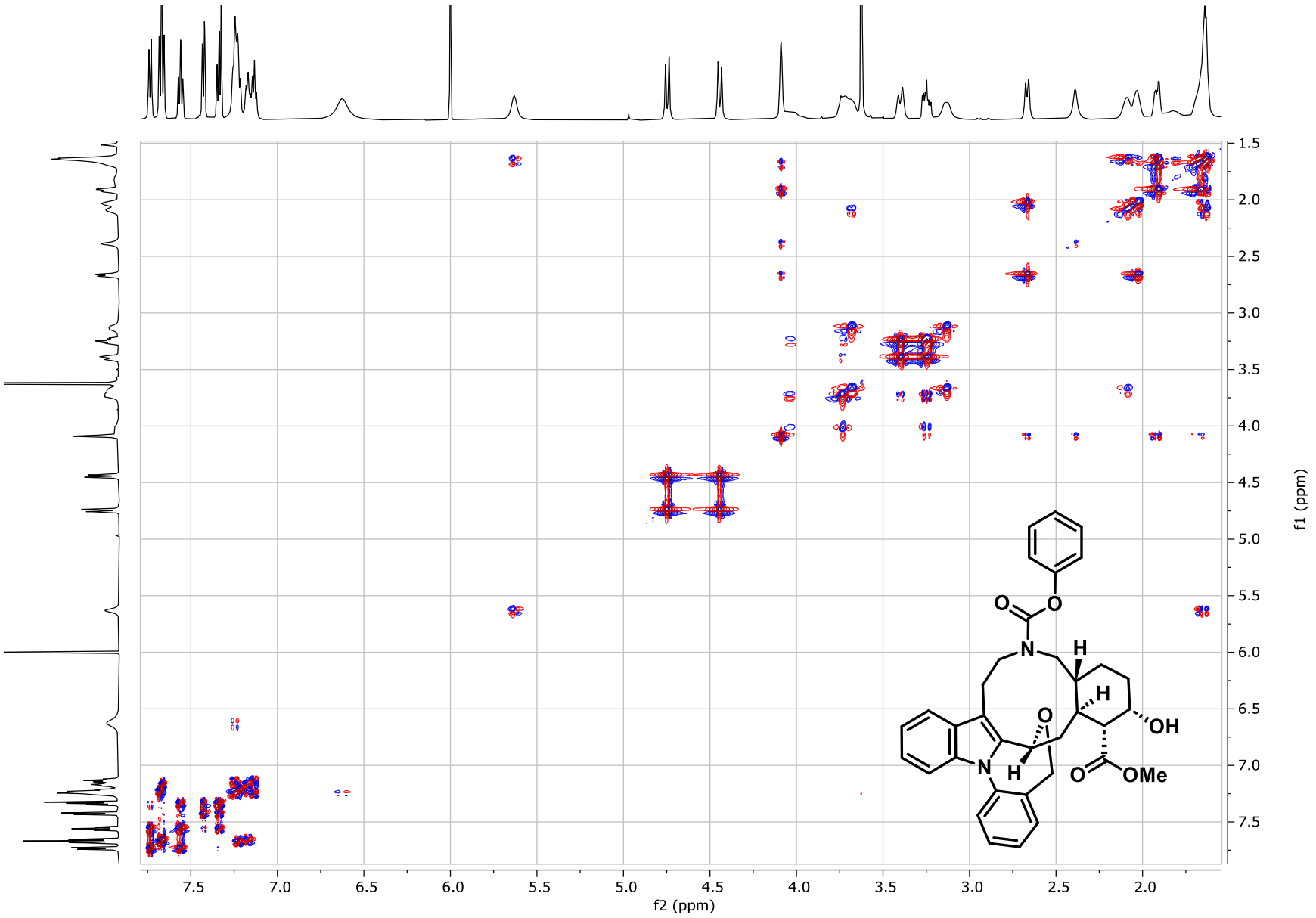

122 121 120 119 118 117 116 115 114 113 112 111 110 109
f1 (ppm)
53.0 52.8 52.6 52.4 52.2
f1 (ppm)
O
O
N
H
O
O
O
H
N
H
OMe
O
OMe
63
13C NMR in CDCl3 at 50 °C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



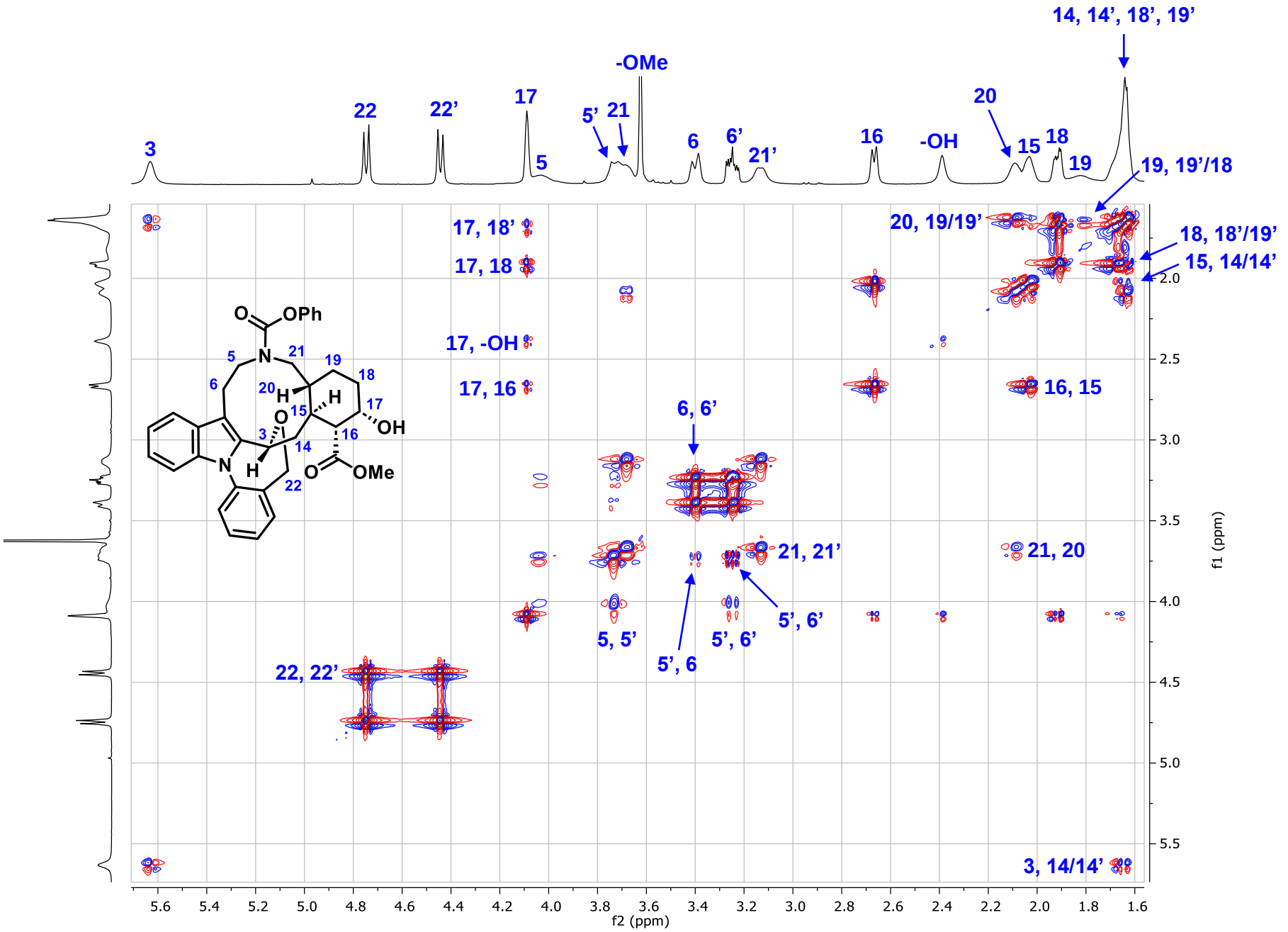
16

^{1}H NMR in TCE at 100 °C

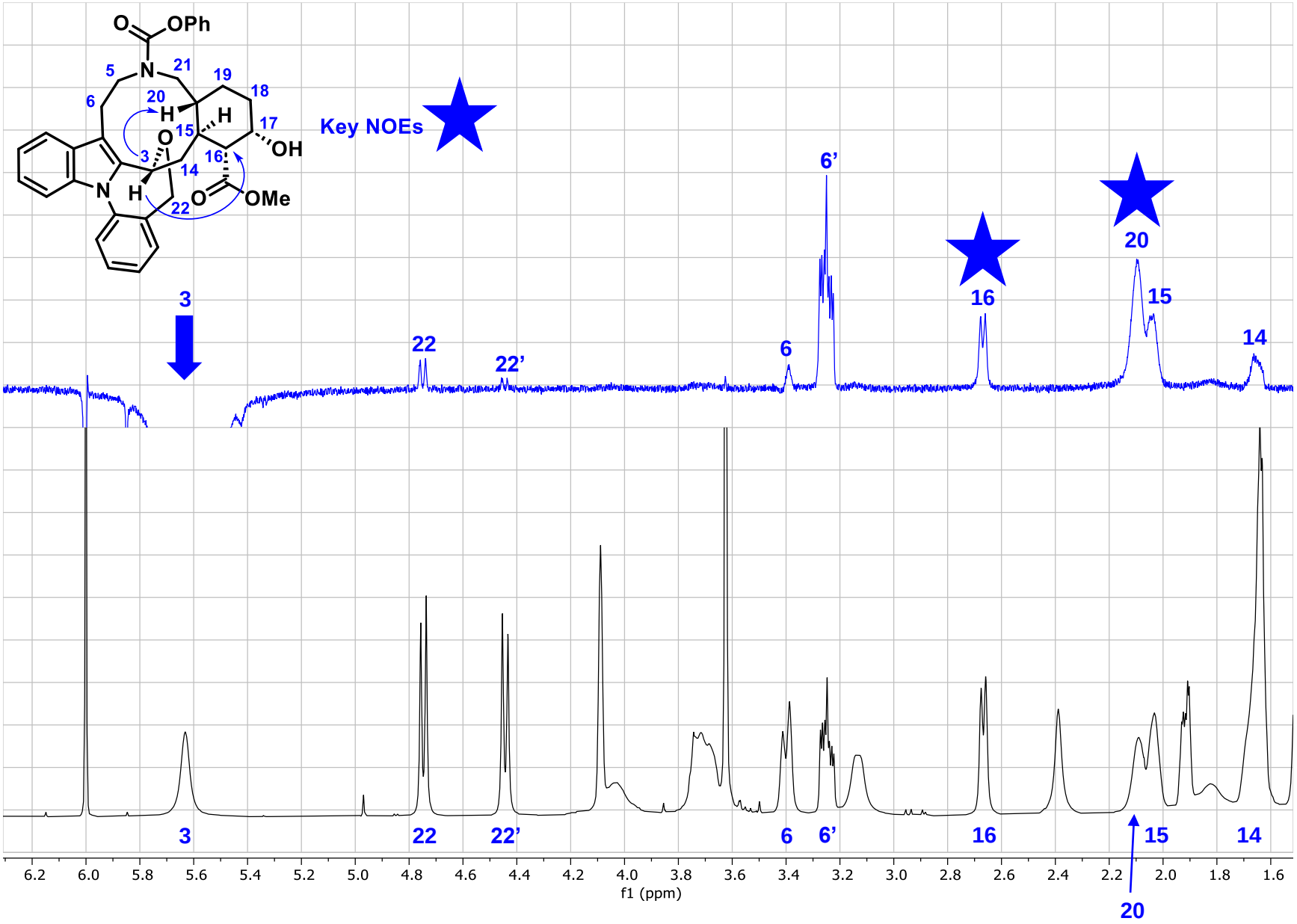

O
O
N
H
H
O
OH
N
H
O
OMe
16
^{13}C NMR in TCE at 100 °C
129.2
128.8
f1 (ppm)
112
110
f1 (ppm)
52
51
50
f1 (ppm)
39
38
37
f1 (ppm)
25.2
24.6
f1 (ppm)
CHCl$_3$
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



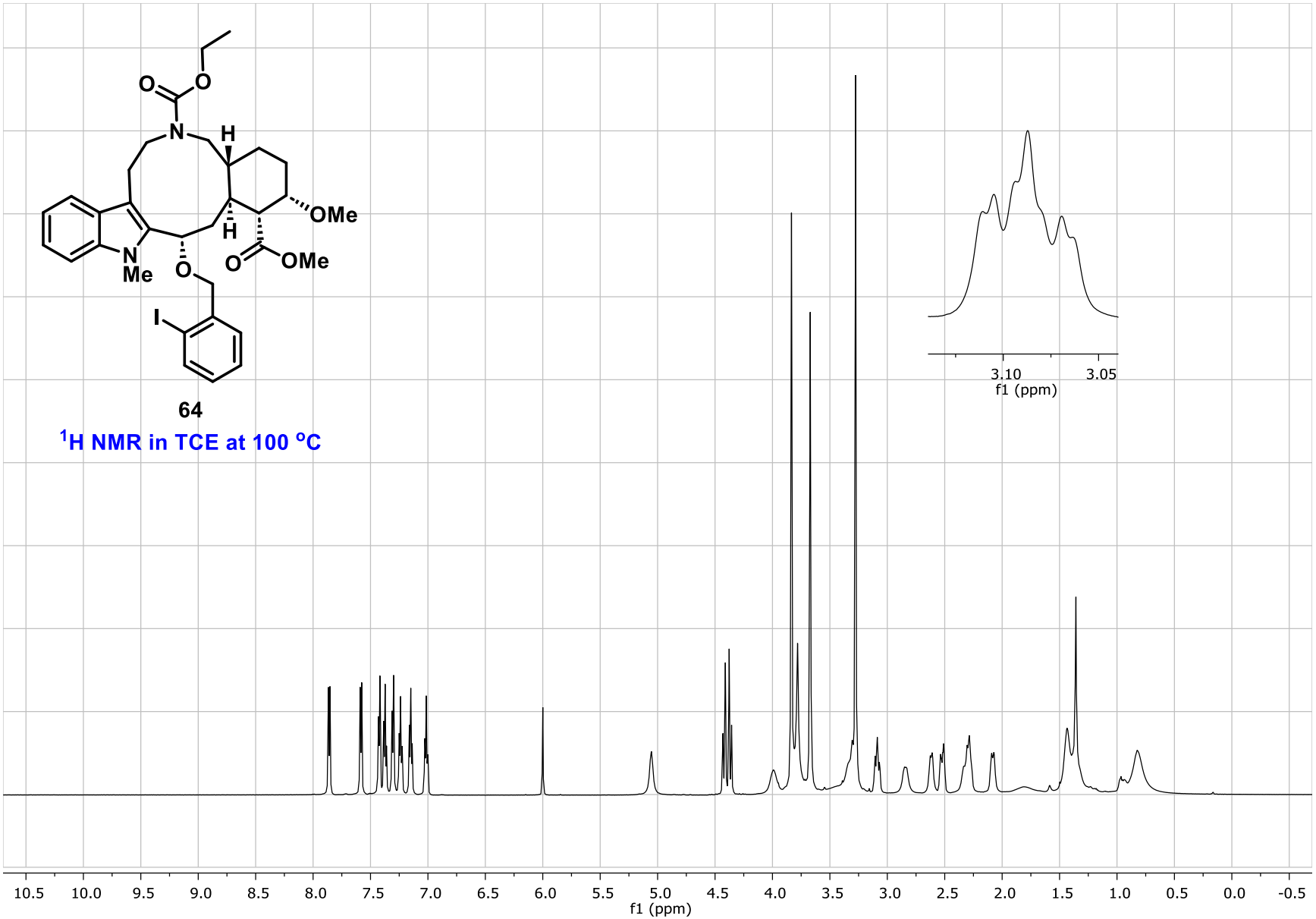
Compound 16: COSY, T = 100 °C, $C_2D_2Cl_4$ (full)

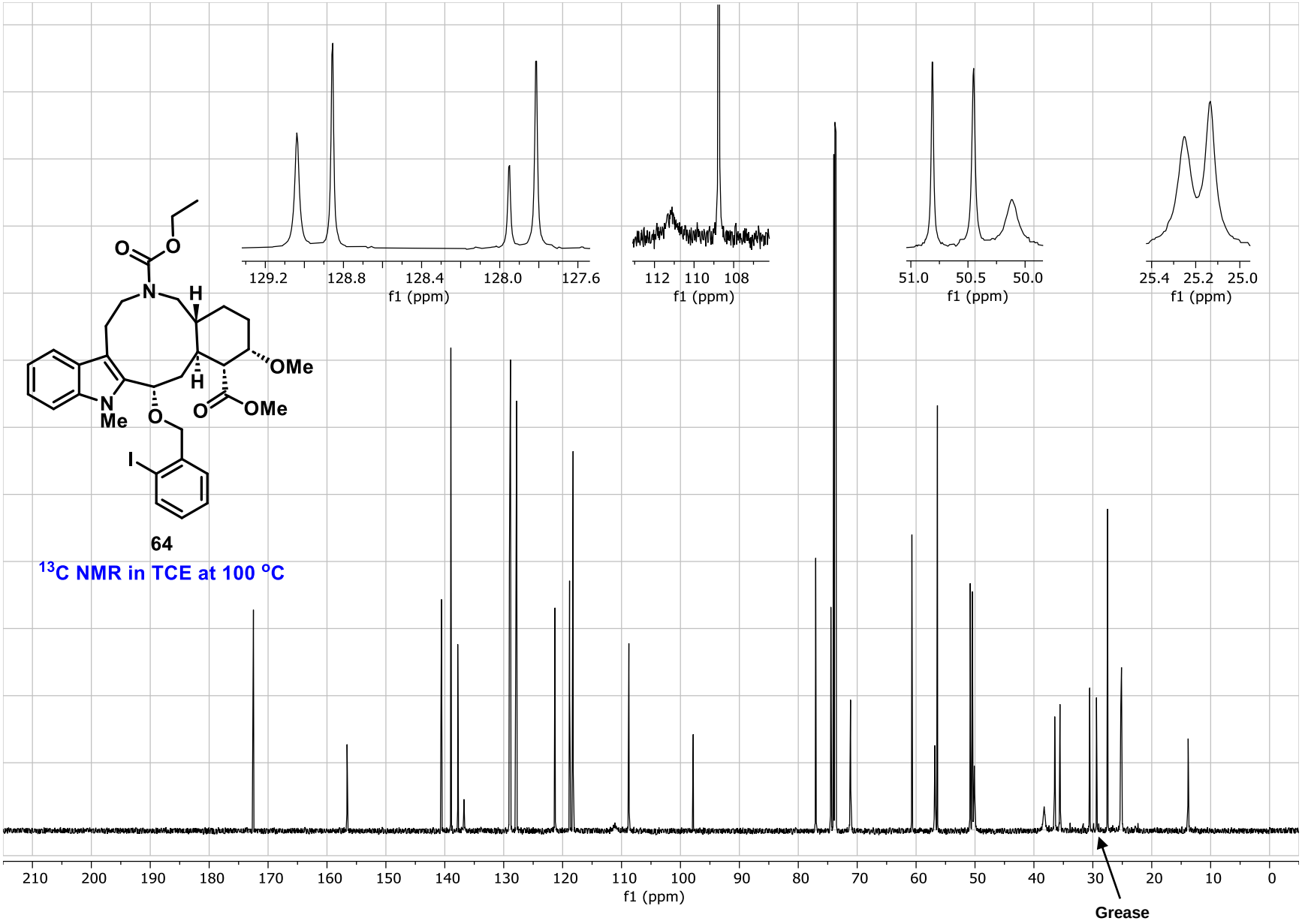


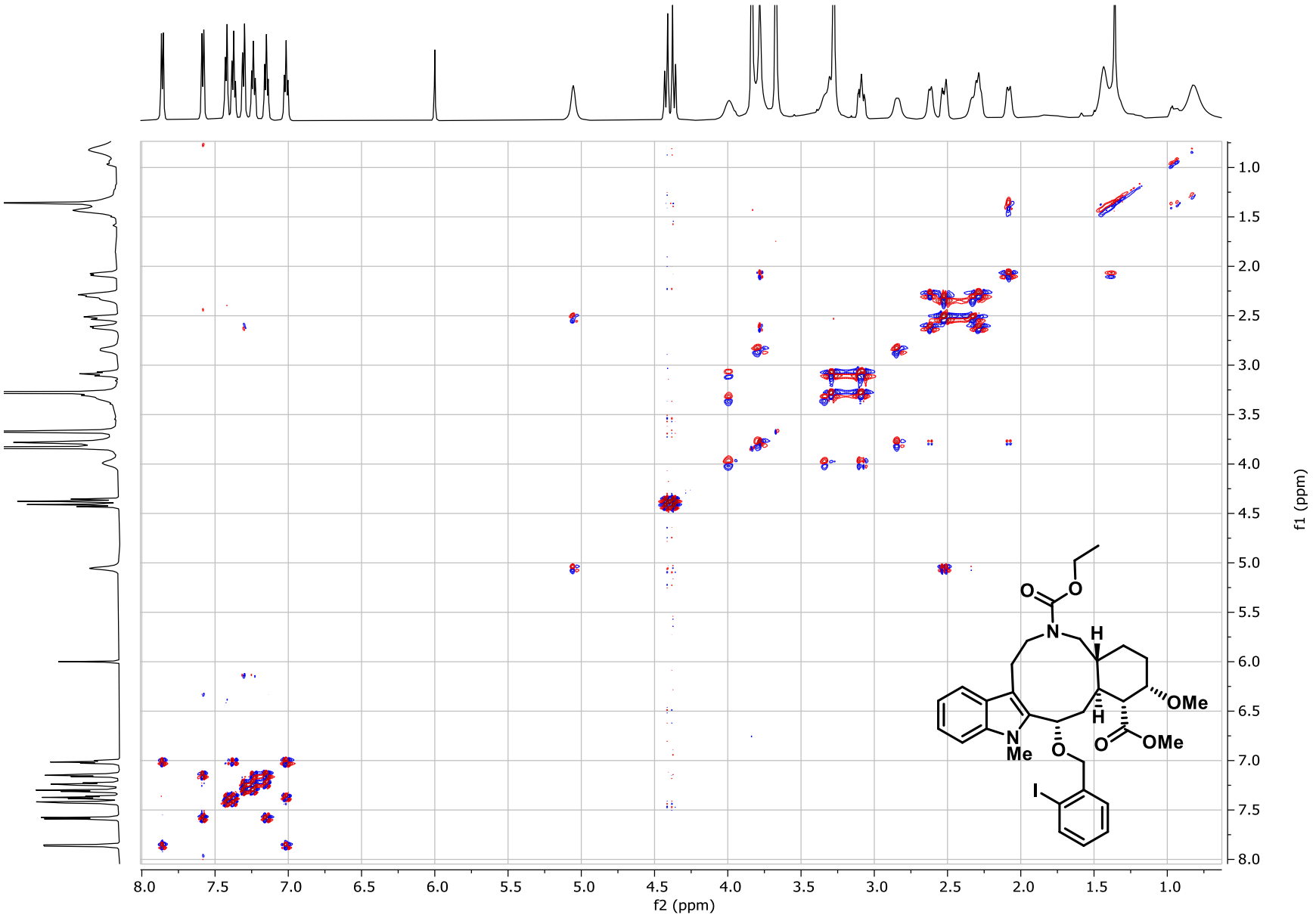
Compound 16: COSY, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in)



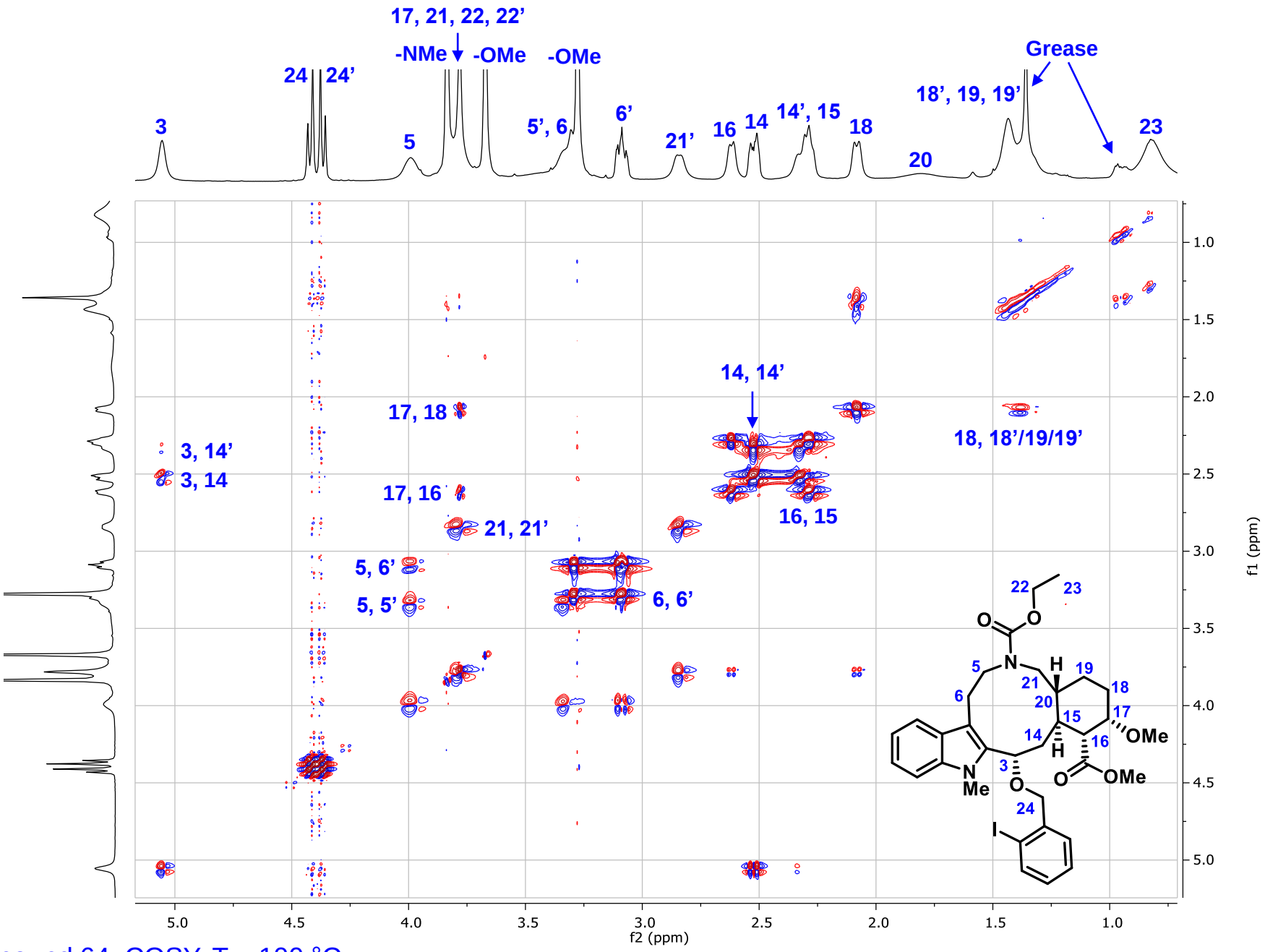
Compound 16: NOE, T = 100 °C, $C_2D_2Cl_4$


O
O
N
H
OMe
H
O
OMe
N
Me
O
I
64
1H NMR in TCE at 100 °C
3.10
3.05
f1 (ppm)
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

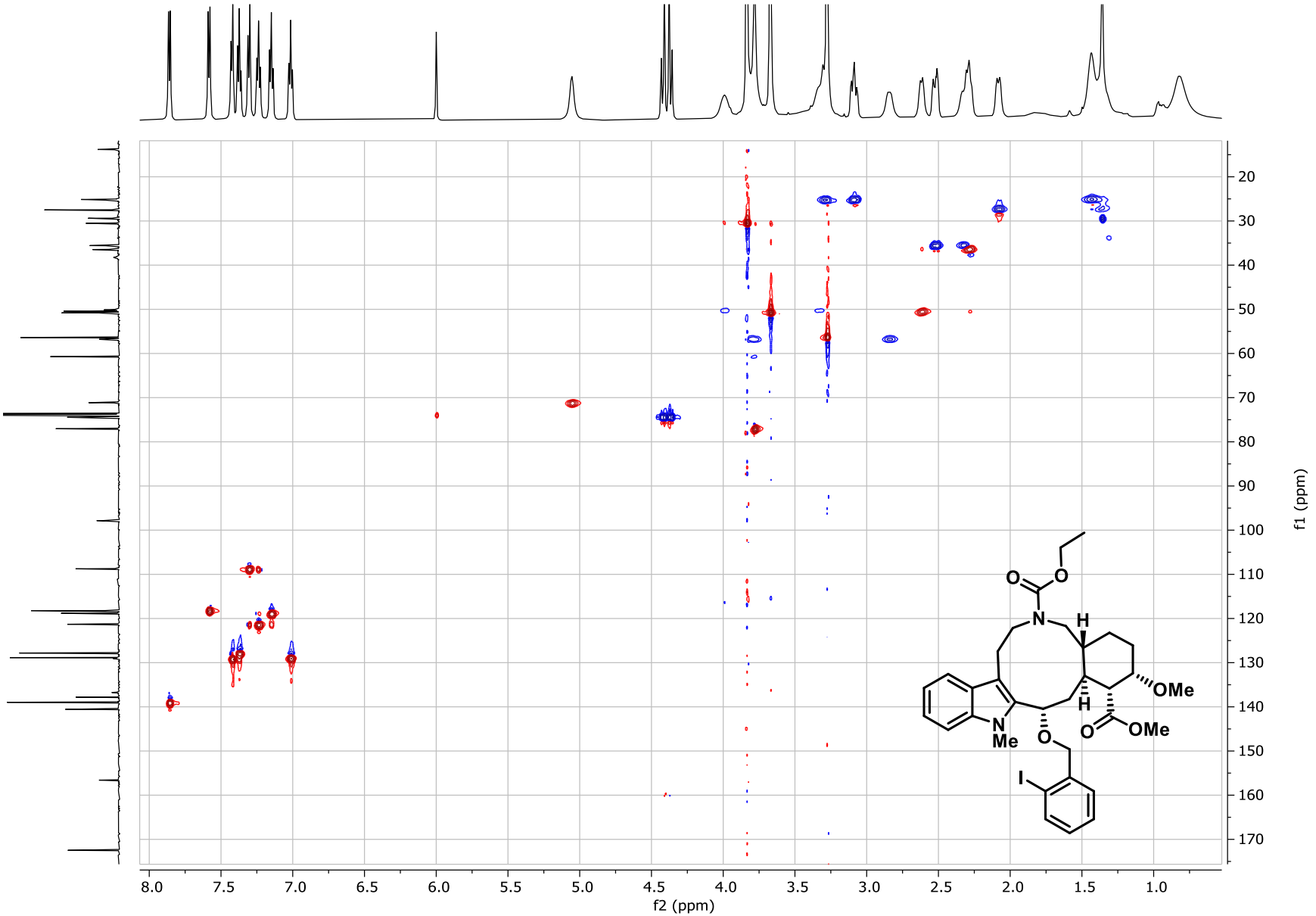

64
^{13}C NMR in TCE at 100 °C
f1 (ppm)
Grease



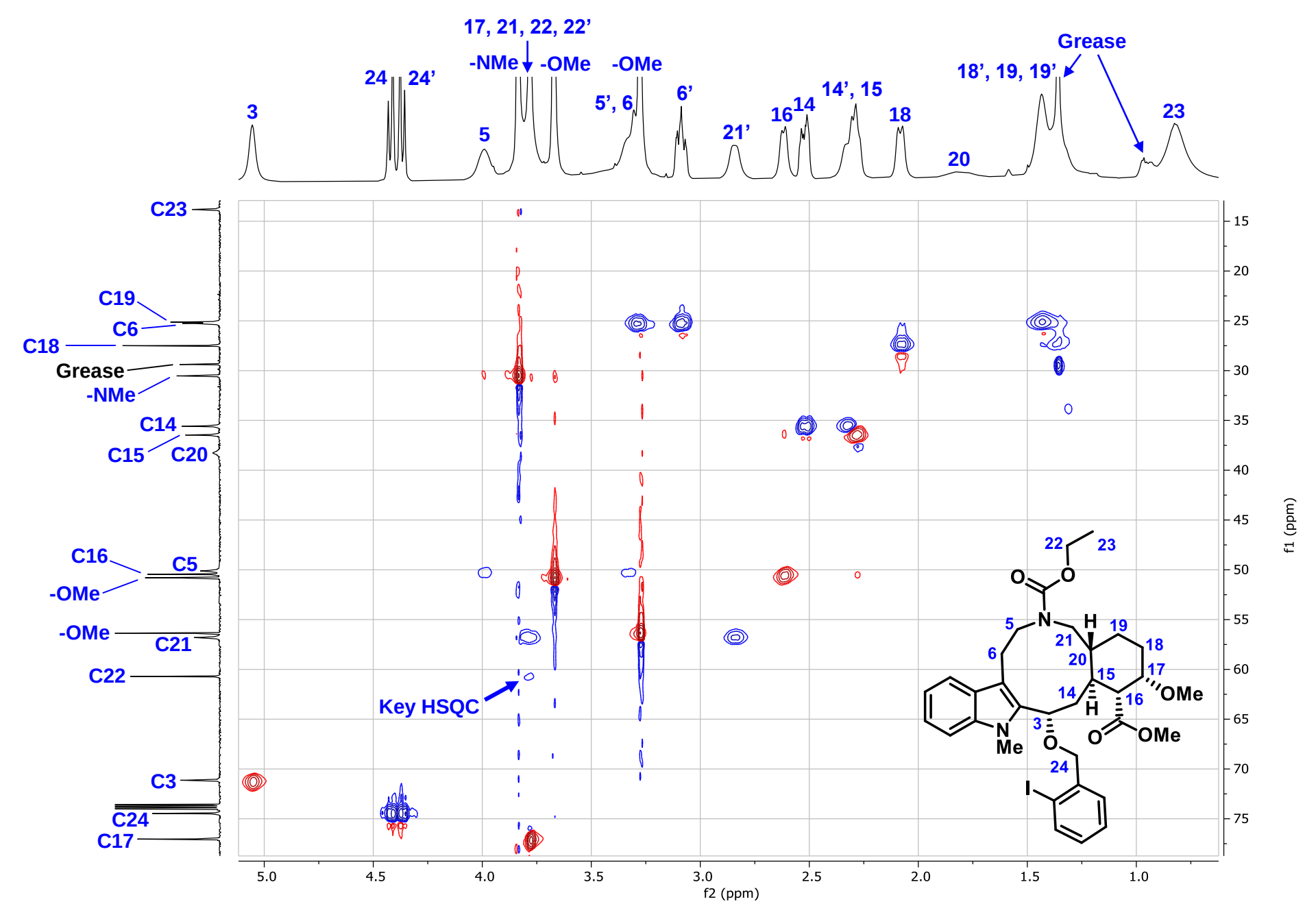
Compound 64: COSY, T = 100 °C, $C_2D_2Cl_4$ (full)



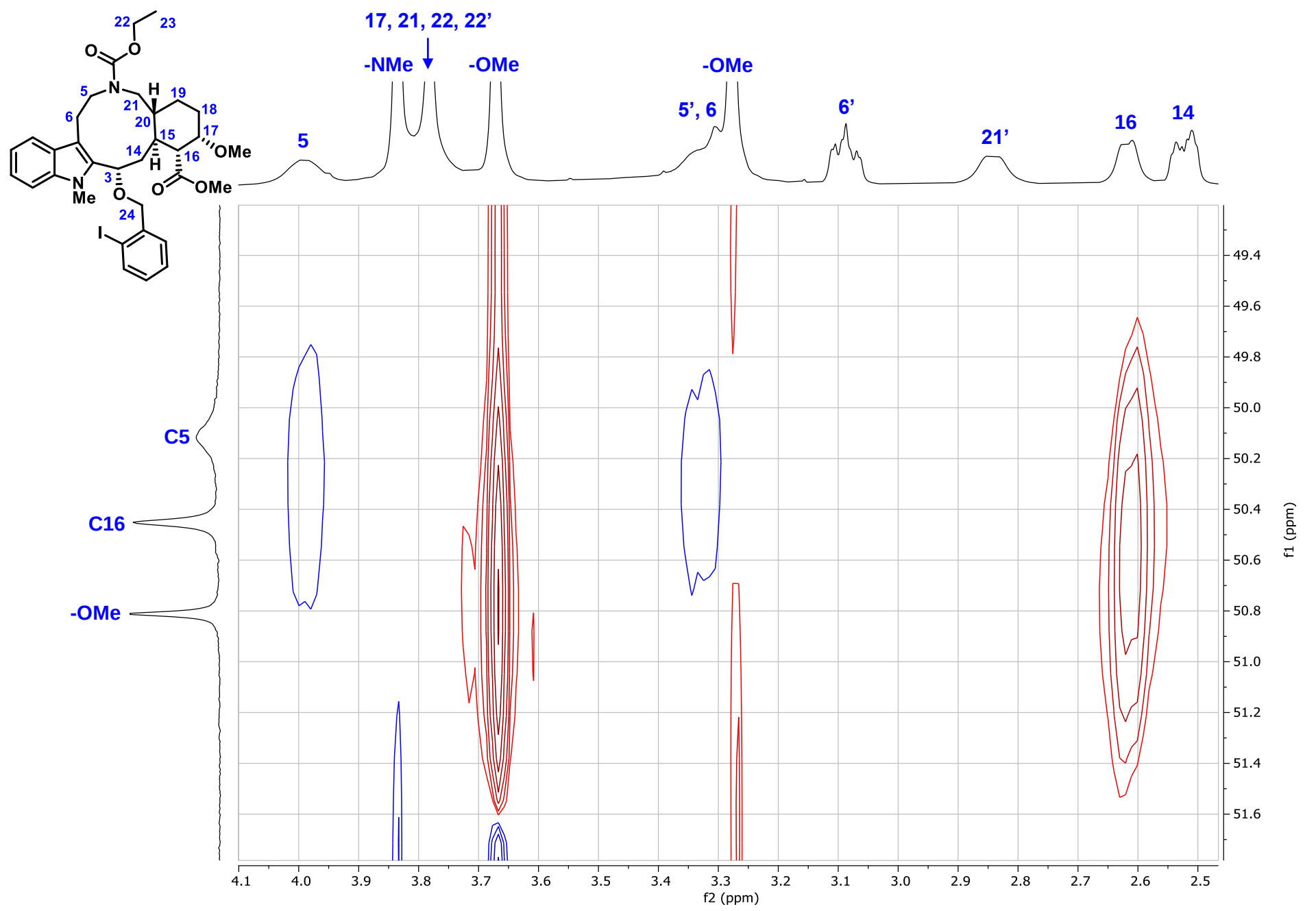
Compound 64: COSY, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in)



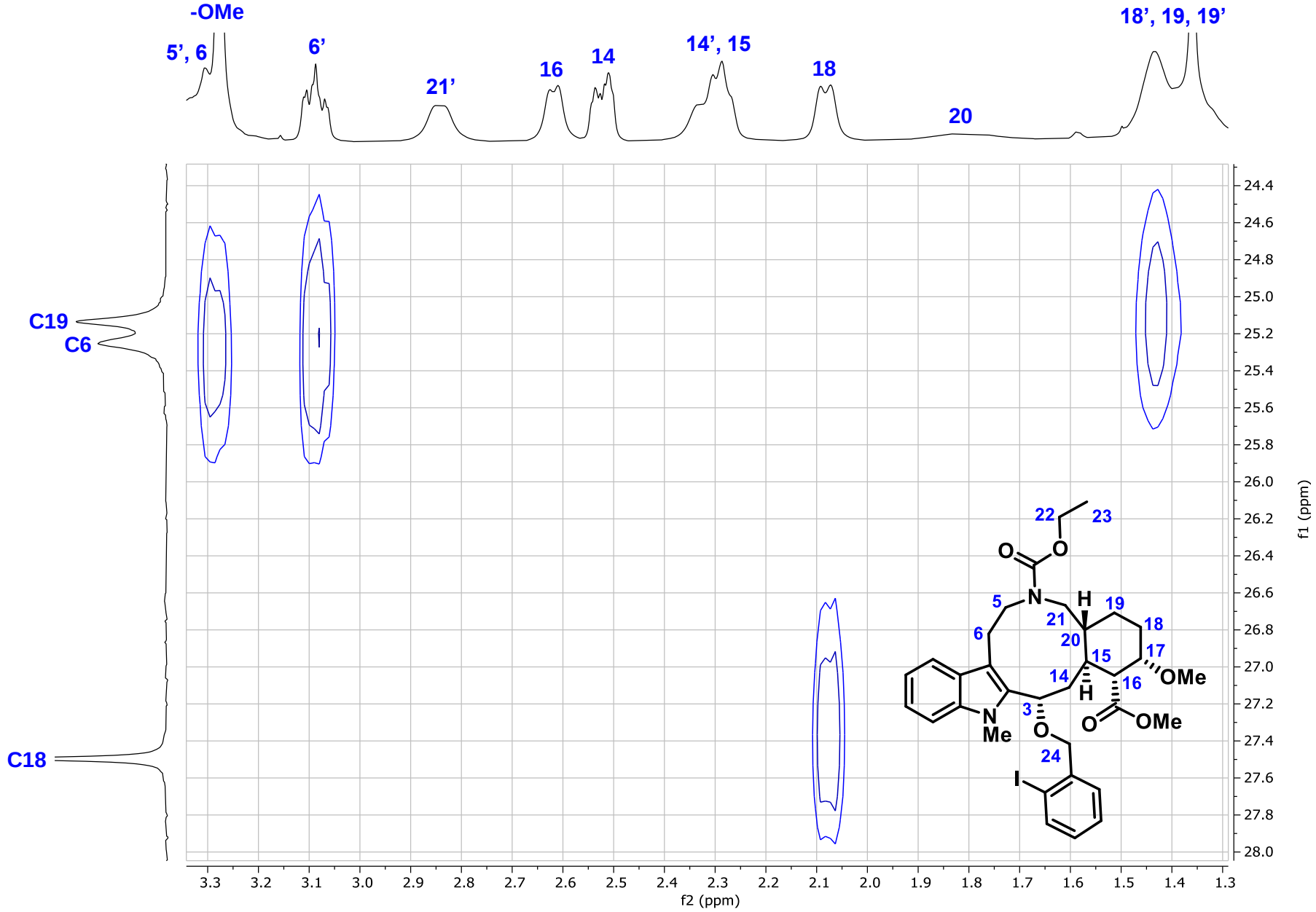
Compound 64: HSQC, T = 100 °C, $C_2D_2Cl_4$ (full)



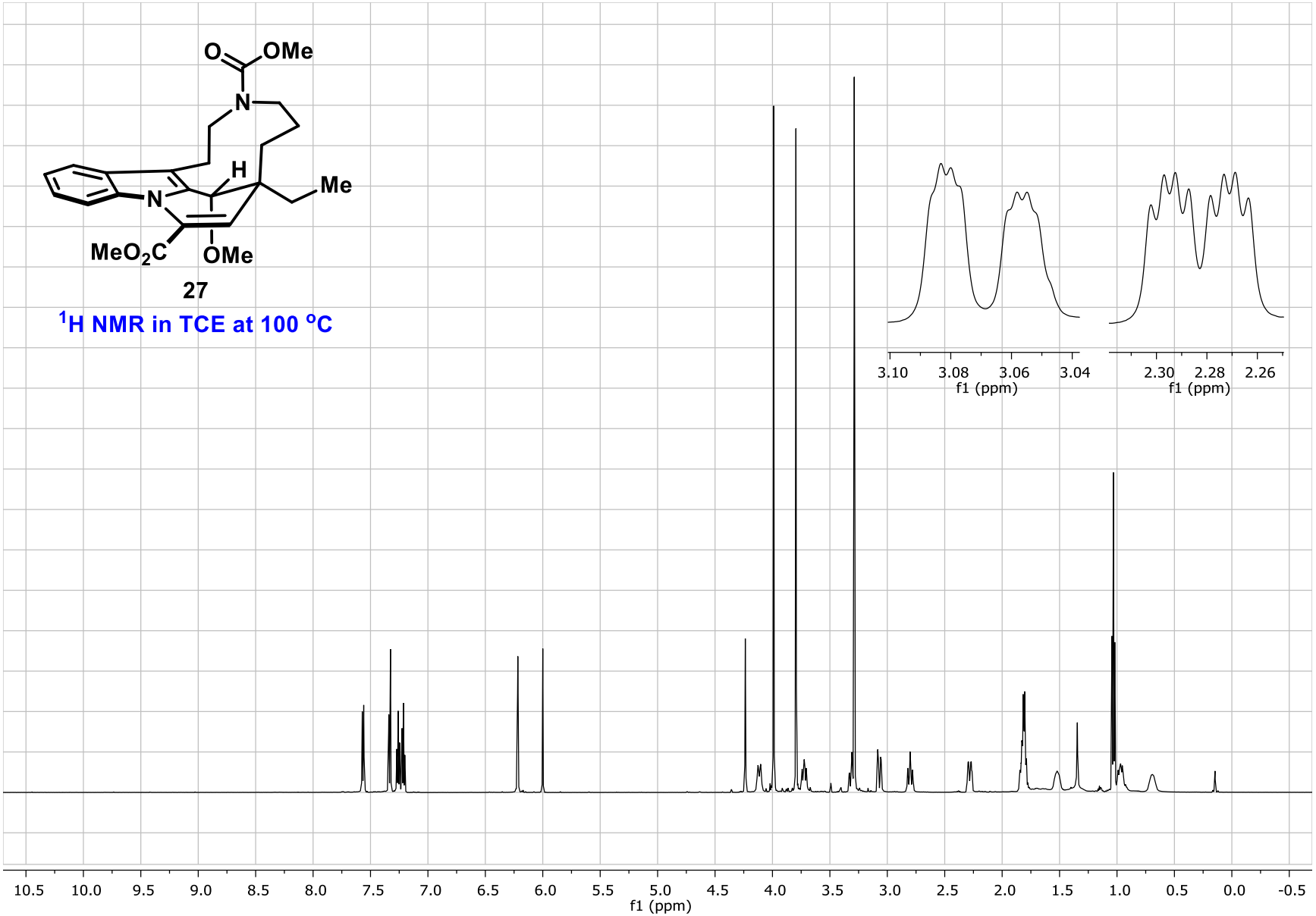
Compound **64**: HSQC, T = 100 °C, $C_2D_2Cl_4$ (zoomed in, version 1). Key correlation to assign 22 & 22'.

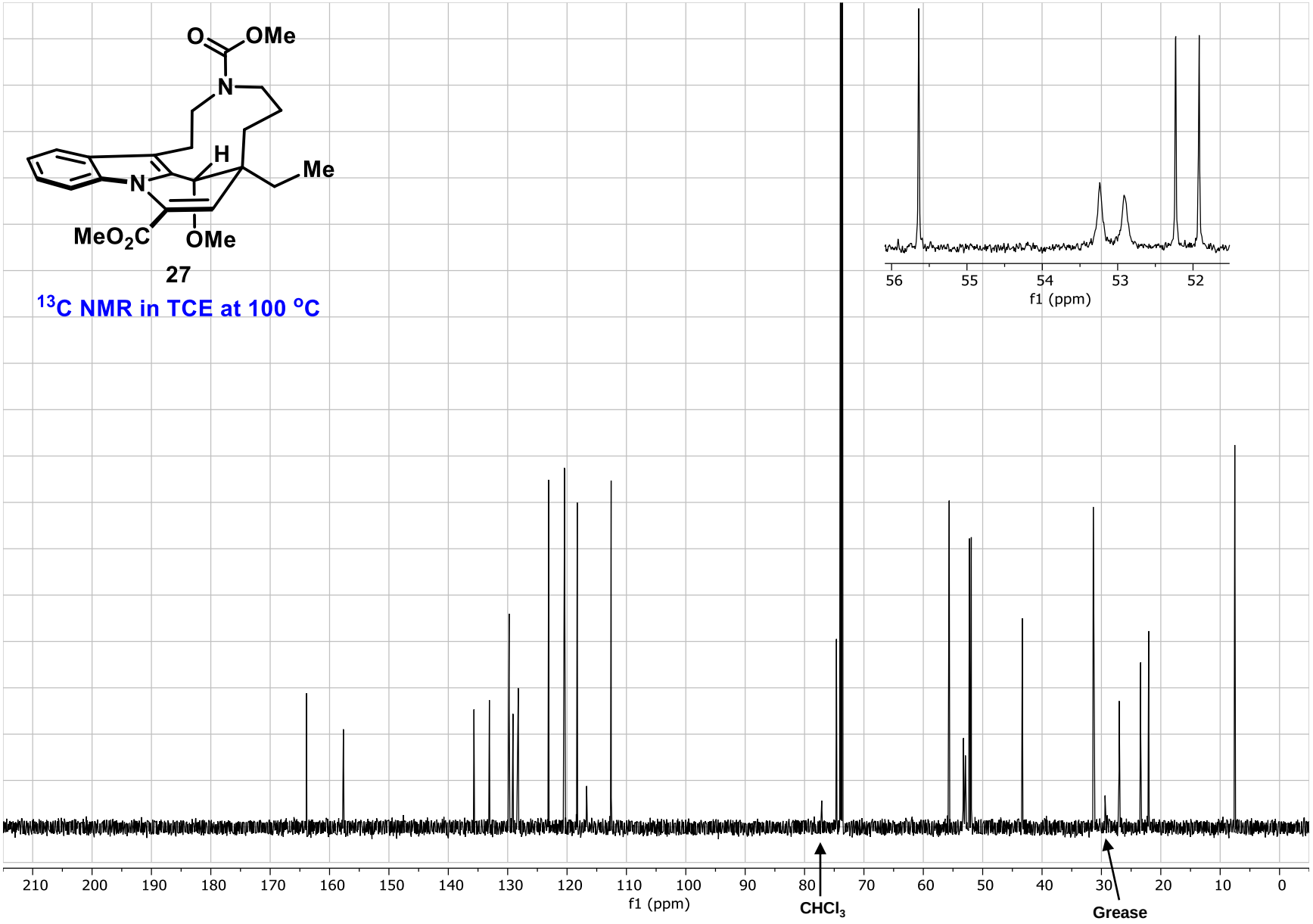


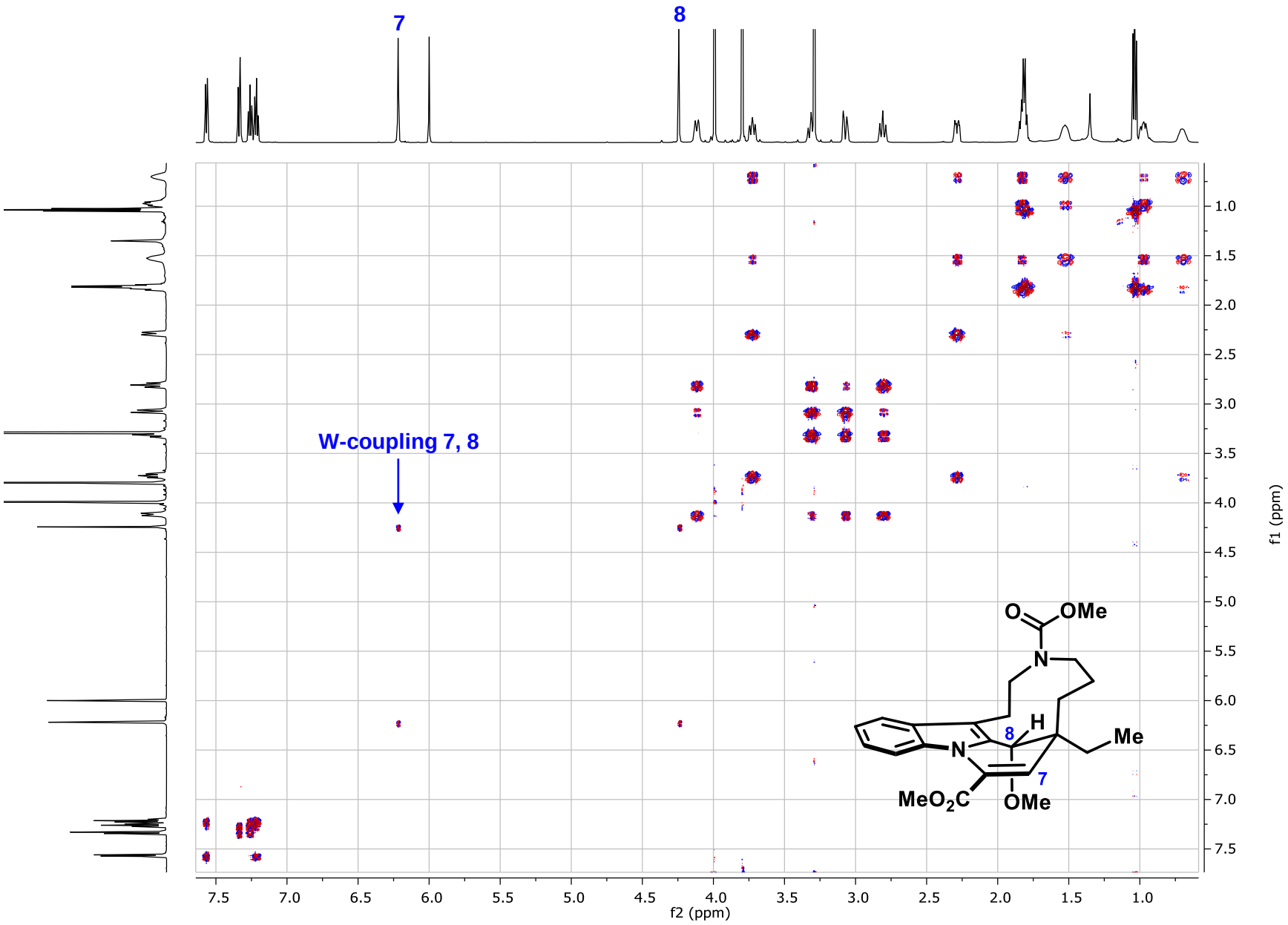
Compound 64: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 2)



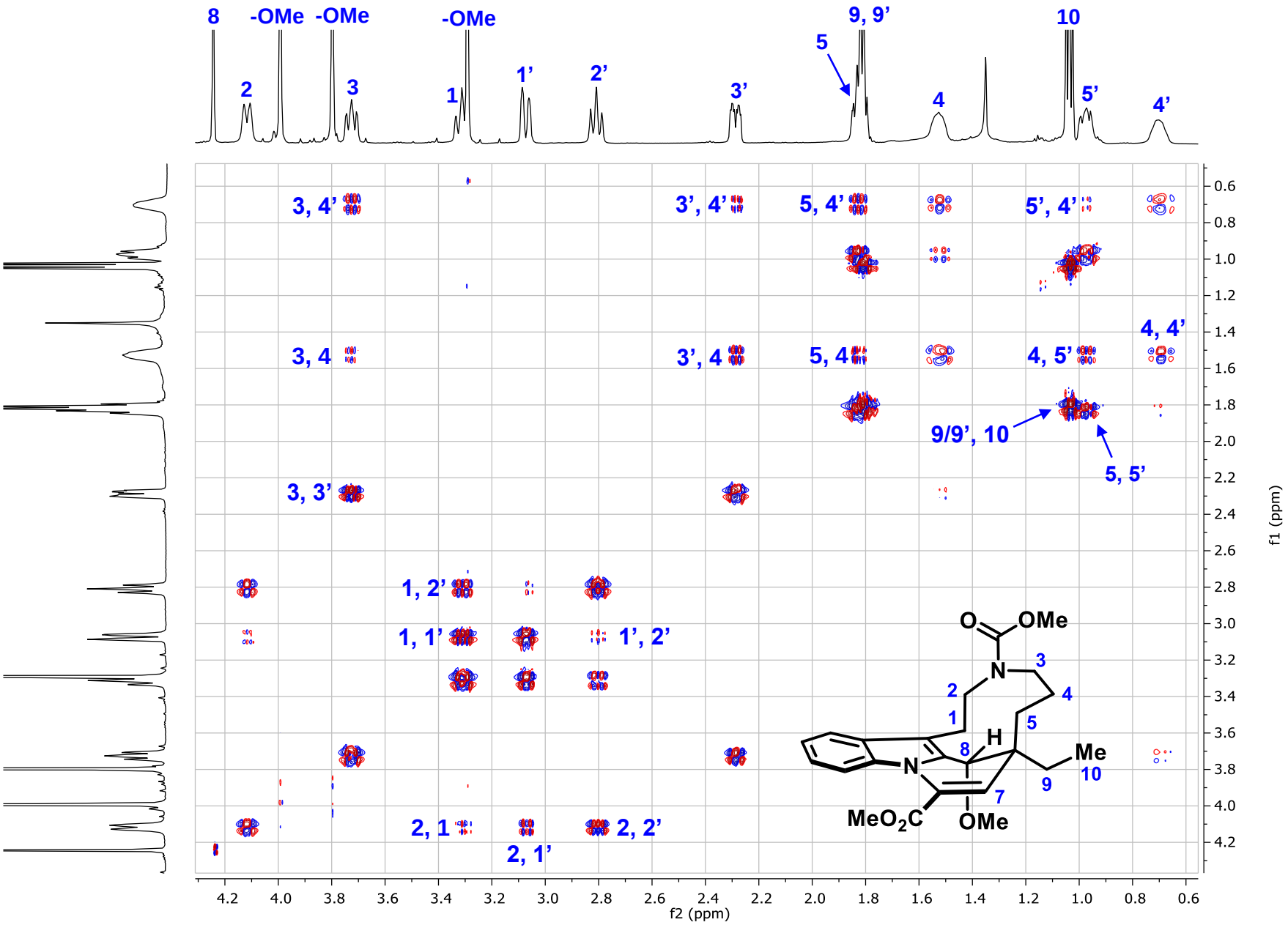
Compound 64: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 3)


O
OMe
N
H
Me
N
MeO2C
OMe
27
1H NMR in TCE at 100 °C
3.10
3.08
3.06
3.04
f1 (ppm)
2.30
2.28
2.26
f1 (ppm)
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

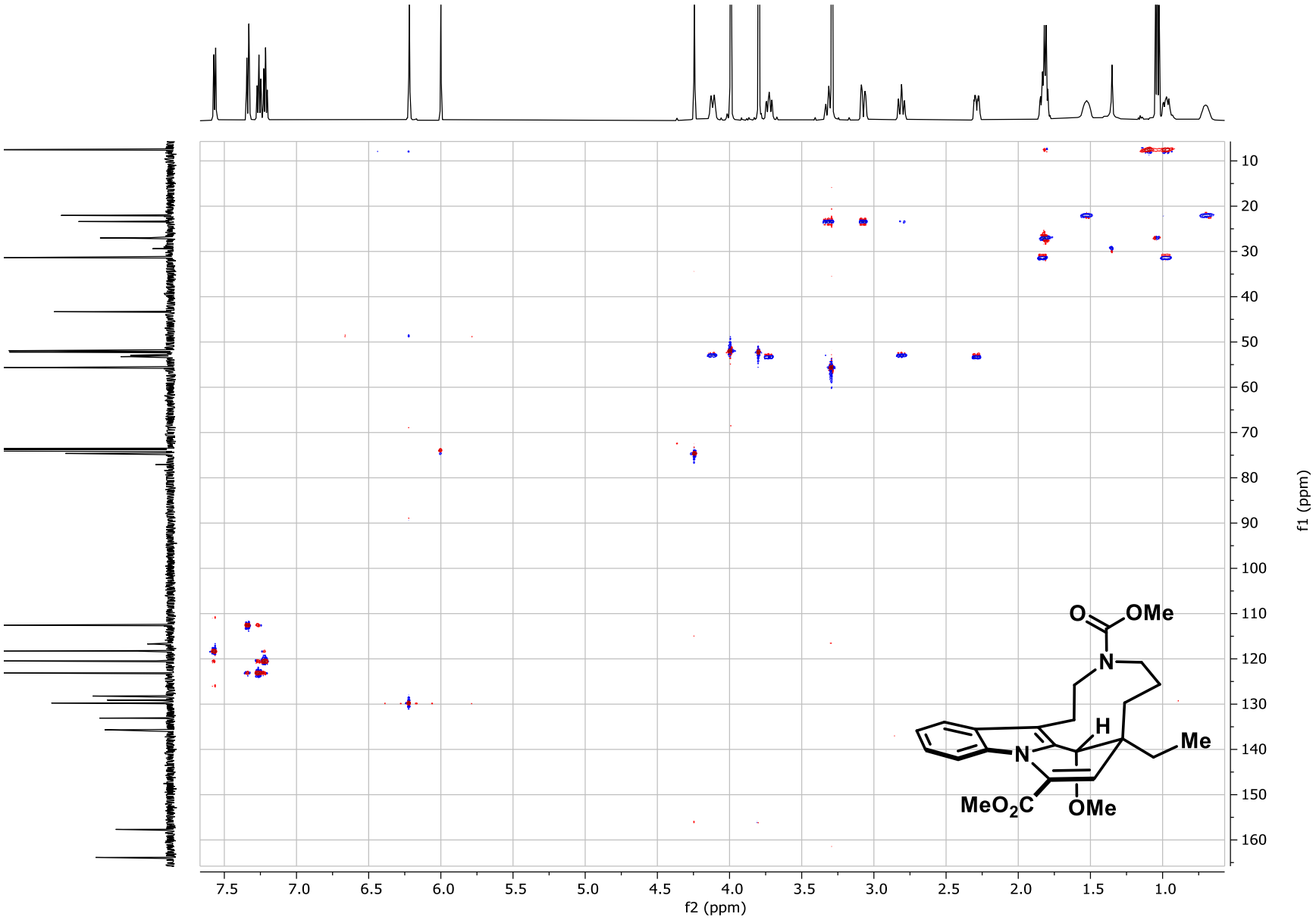

O
OMe
N
H
Me
N
MeO2C
OMe
27
13C NMR in TCE at 100 °C
56
55
54
53
52
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
CHCl3
Grease



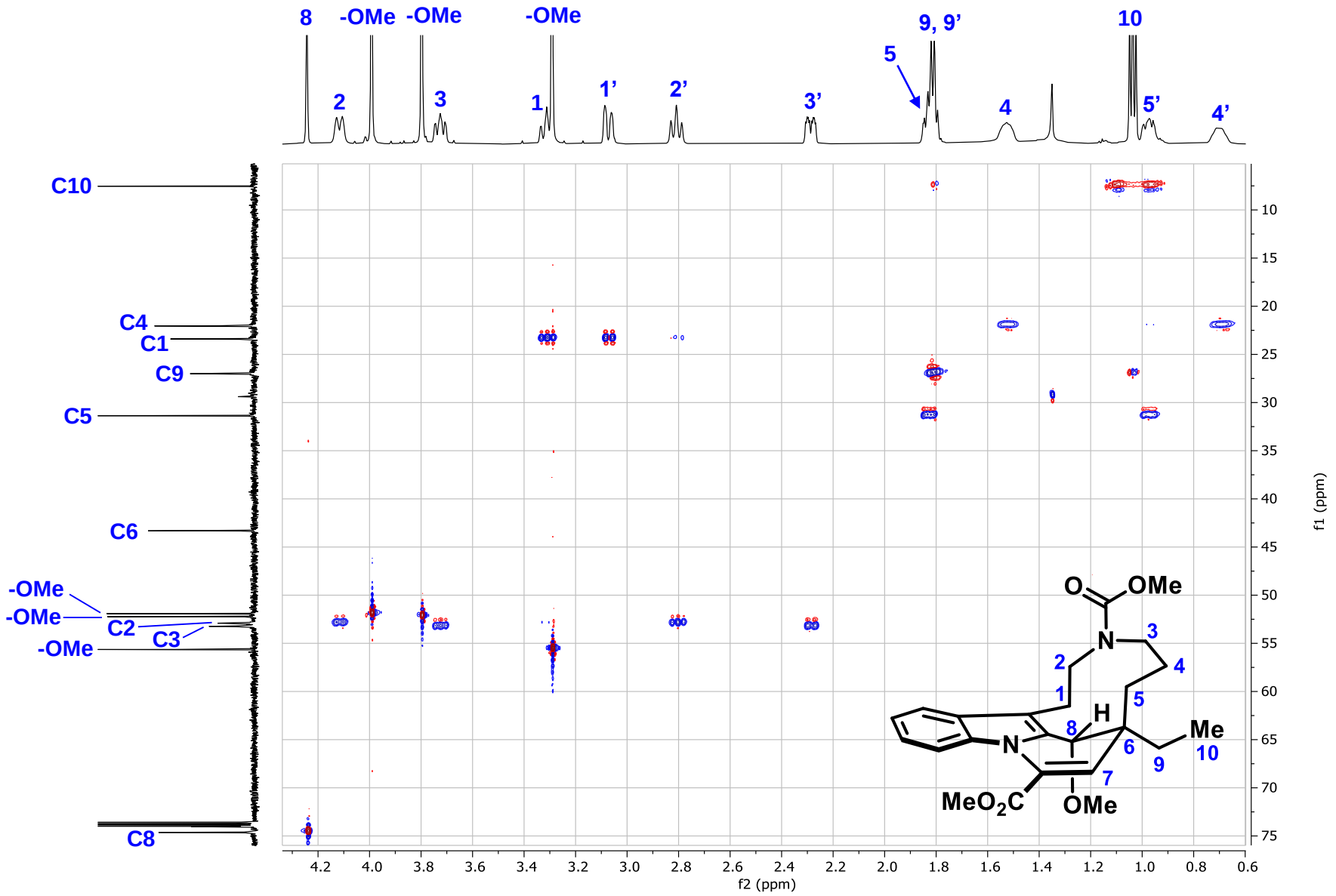
Compound 27: COSY, T = 100 °C, $C_2D_2Cl_4$ (full)



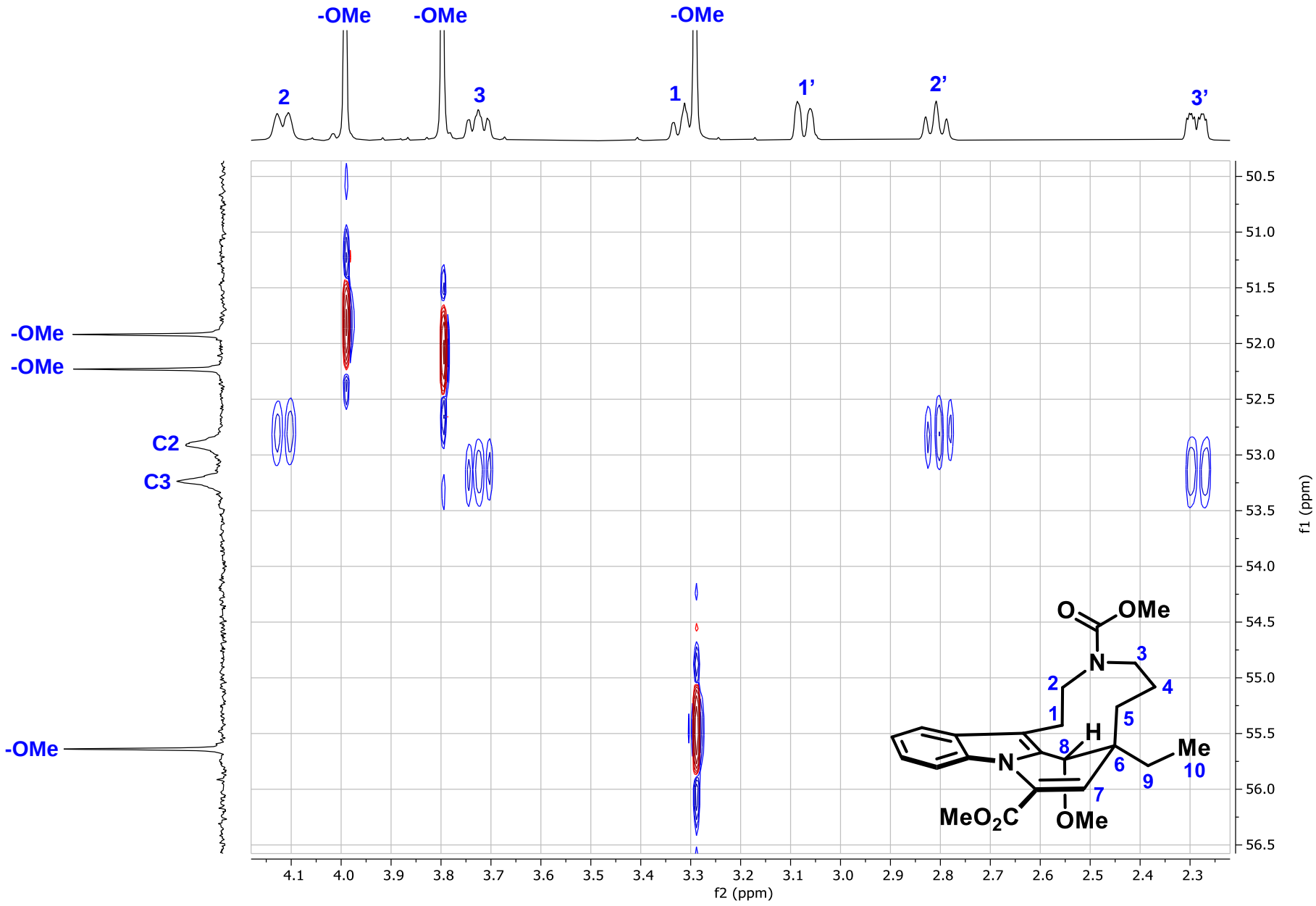
Compound 27: COSY, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in)



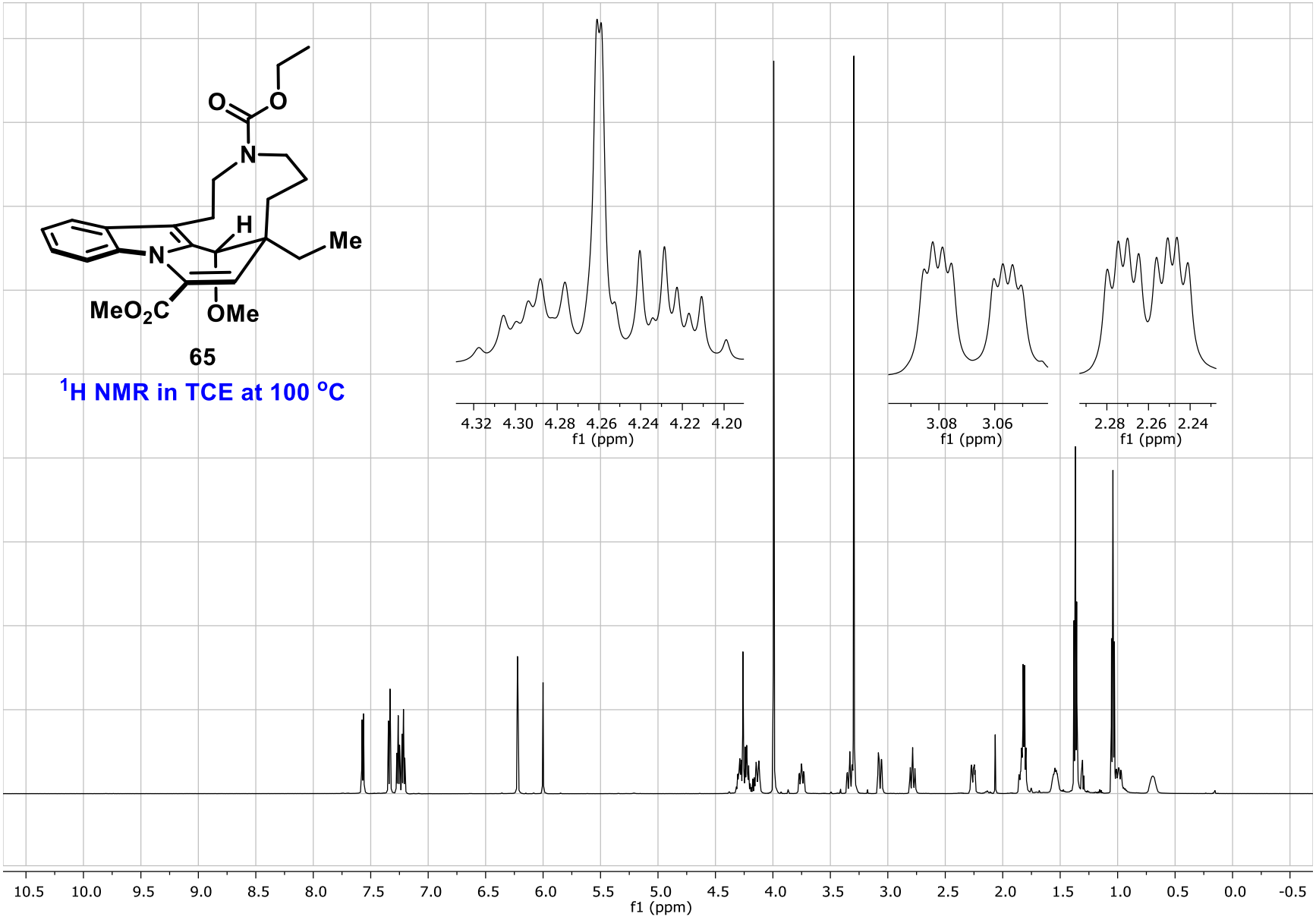
Compound 27: HSQC, T = 100 °C, $C_2D_2Cl_4$ (full)

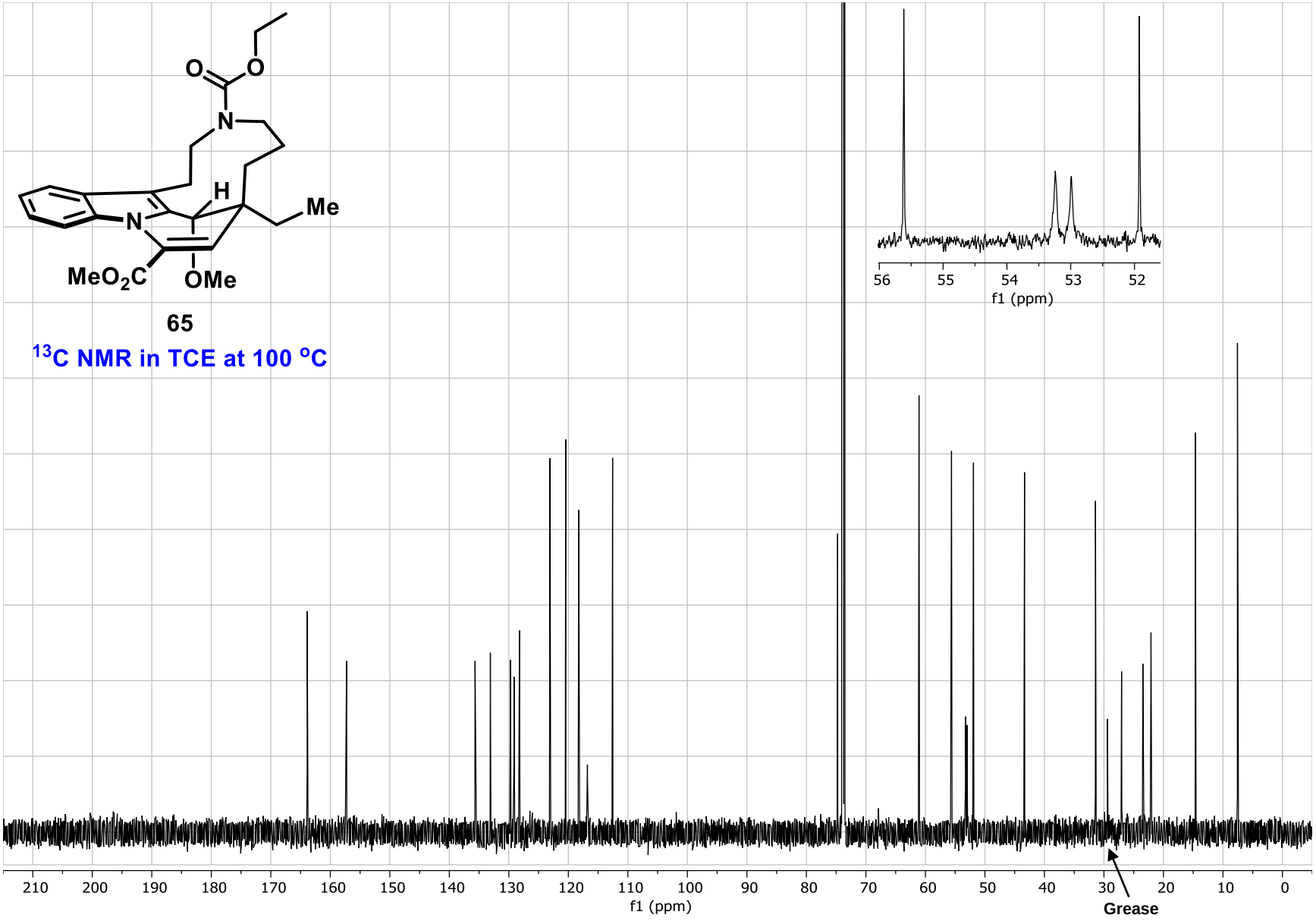


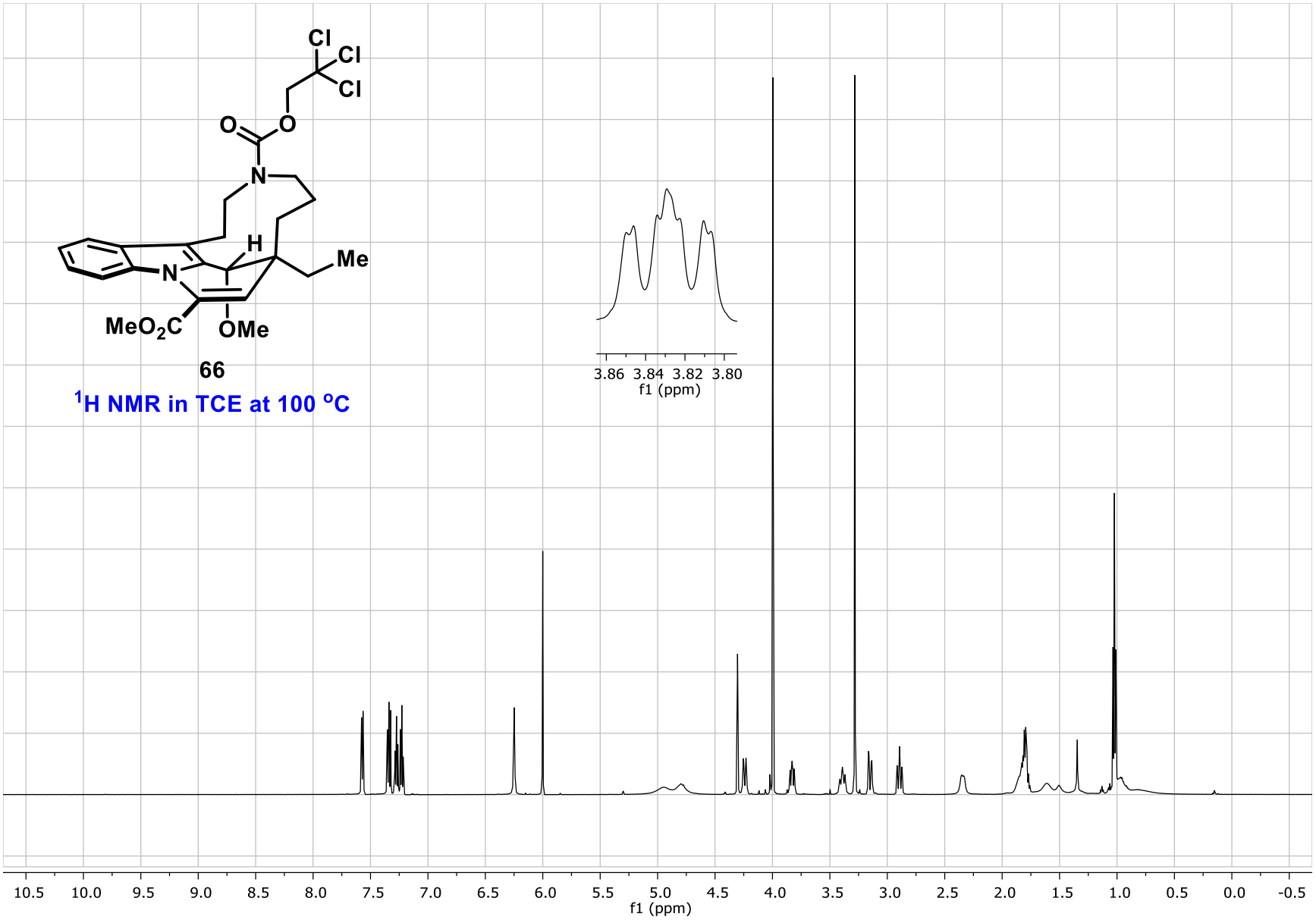
Compound 27: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 1)

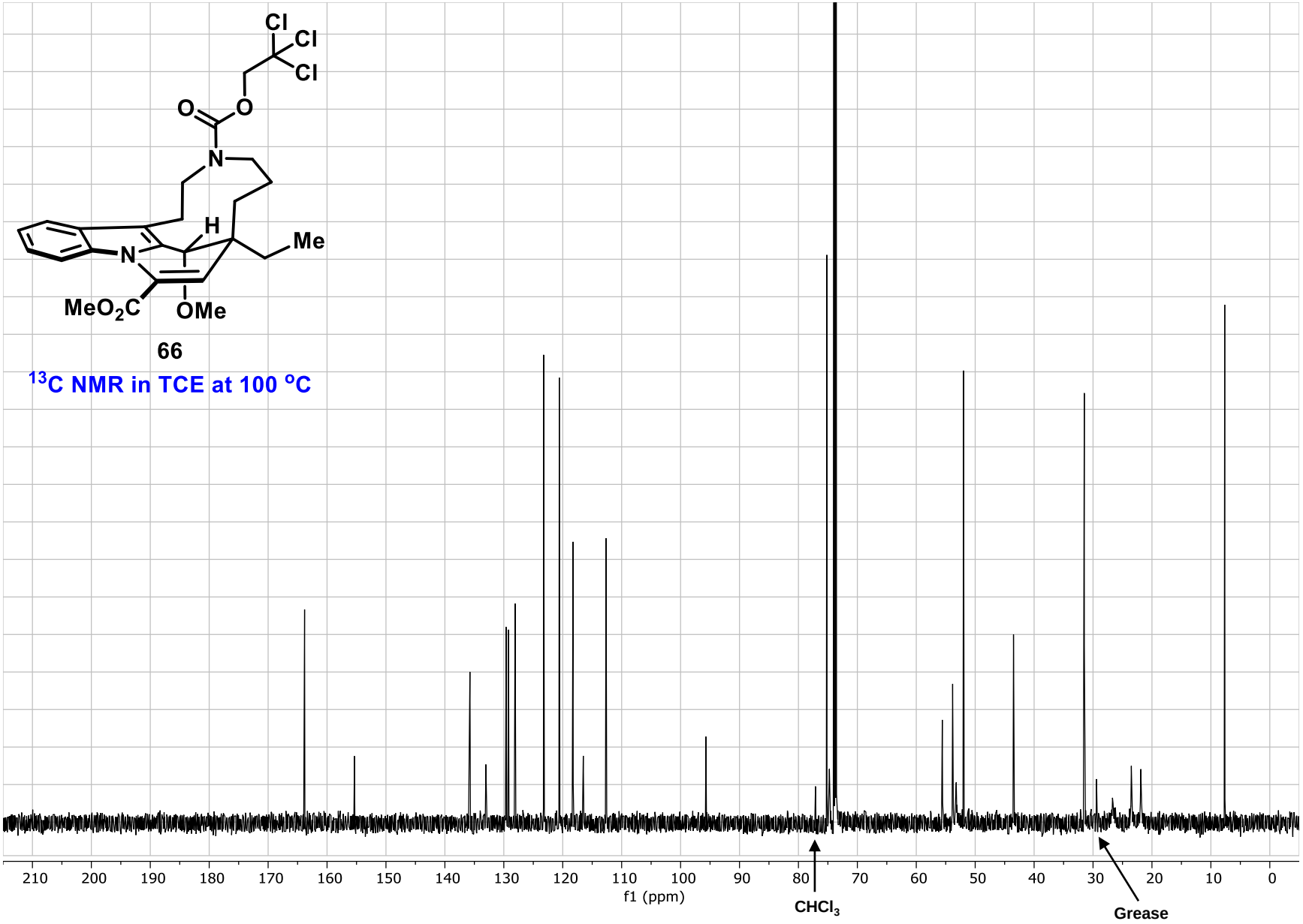


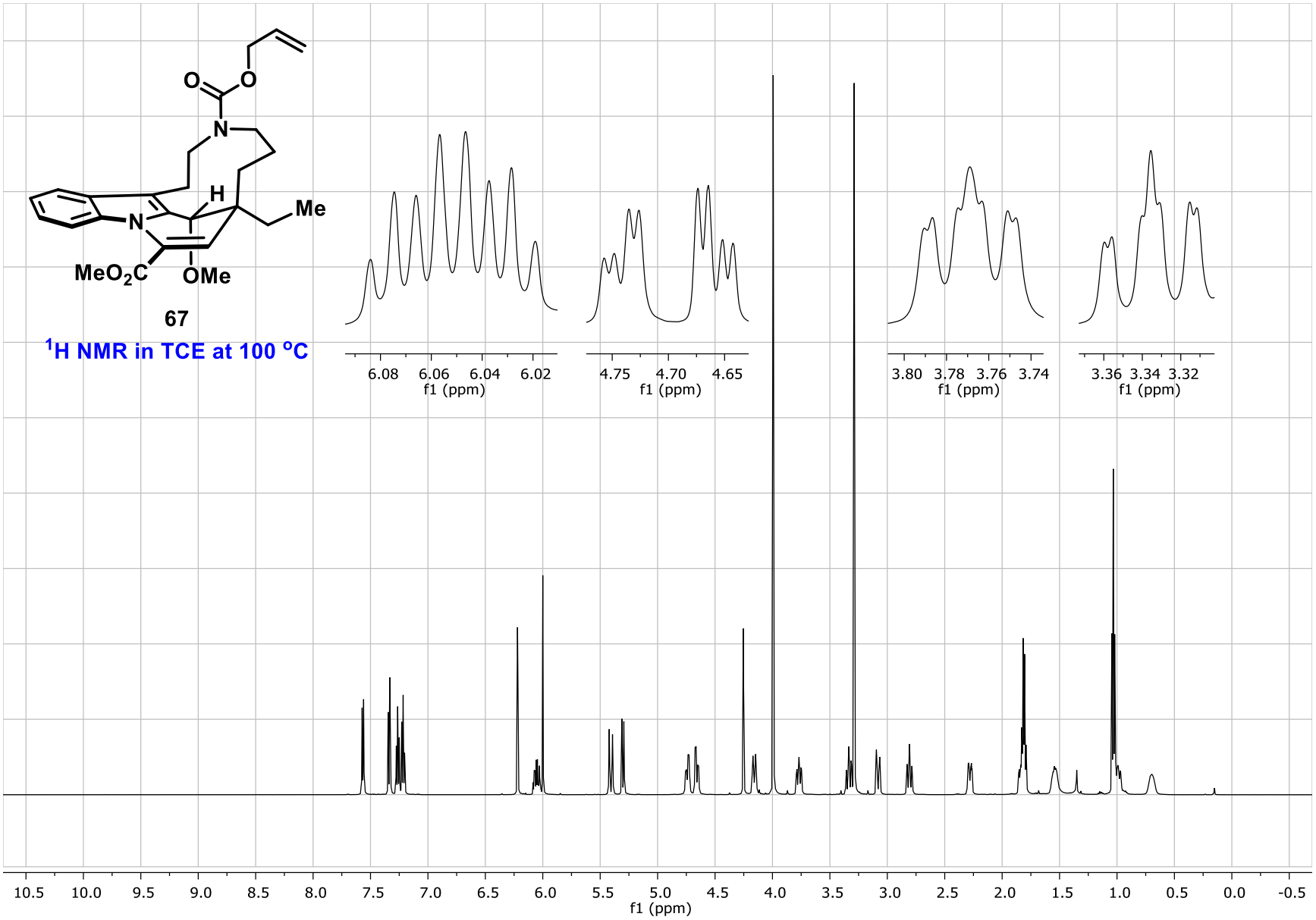
Compound 27: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 2)

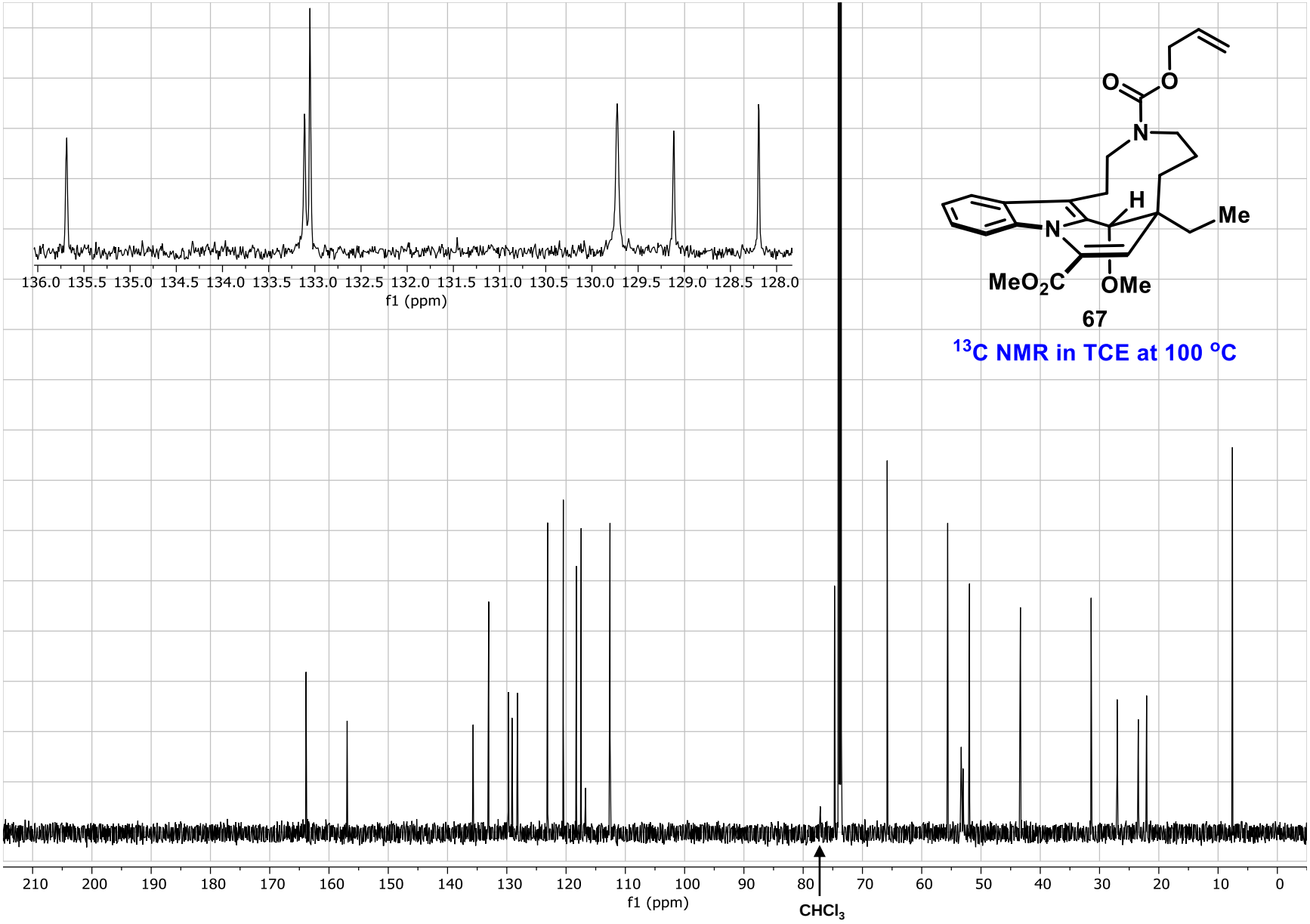

O
O
N
H
Me
N
MeO2C
OMe
65
1H NMR in TCE at 100 °C
4.32 4.30 4.28 4.26 4.24 4.22 4.20
f1 (ppm)
3.08 3.06
f1 (ppm)
2.28 2.26 2.24
f1 (ppm)
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

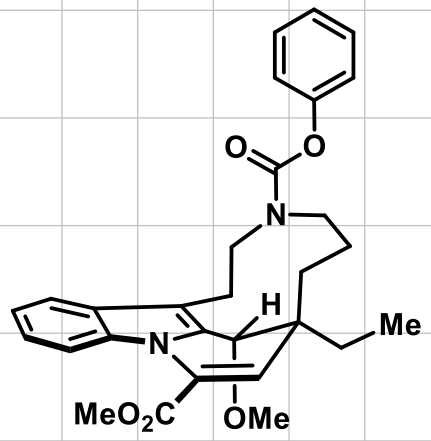

O
O
N
H
Me
N
MeO2C
OMe
65
13C NMR in TCE at 100 °C
56
55
54
53
52
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
Grease


Cl
Cl
Cl
O
O
N
H
N
Me
MeO2C
OMe
66
1H NMR in TCE at 100 °C
3.86 3.84 3.82 3.80
f1 (ppm)
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


Cl
Cl
Cl
O
O
N
H
N
Me
MeO2C
OMe
66
13C NMR in TCE at 100 °C
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
CHCl3
Grease

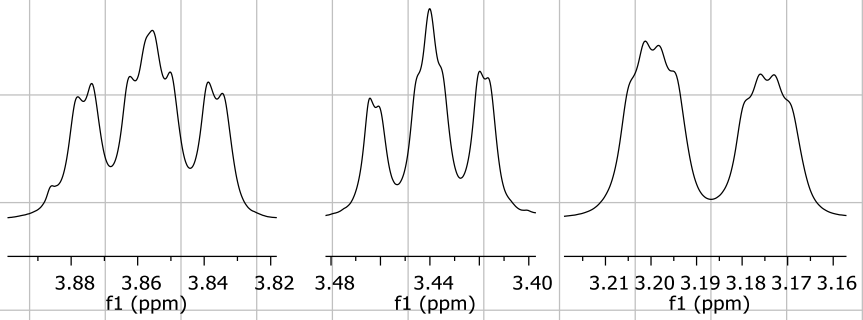

O
O
N
H
Me
N
MeO2C
OMe
67
1H NMR in TCE at 100 °C
6.08 6.06 6.04 6.02
f1 (ppm)
4.75 4.70 4.65
f1 (ppm)
3.80 3.78 3.76 3.74
f1 (ppm)
3.36 3.34 3.32
f1 (ppm)
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

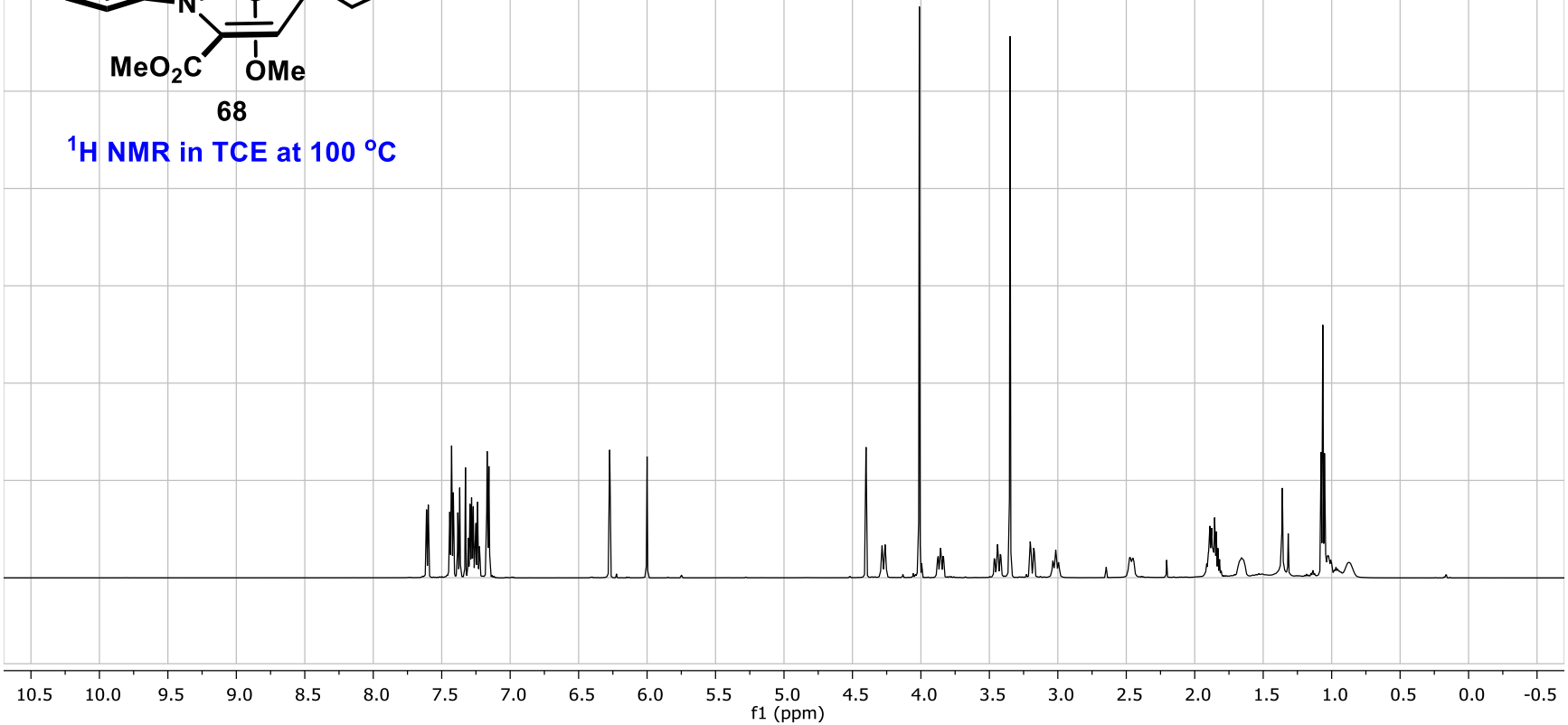

136.0 135.5 135.0 134.5 134.0 133.5 133.0 132.5 132.0 131.5 131.0 130.5 130.0 129.5 129.0 128.5 128.0
f1 (ppm)
O
O
N
H
Me
N
MeO2C
OMe
67
13C NMR in TCE at 100 °C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
CHCl3

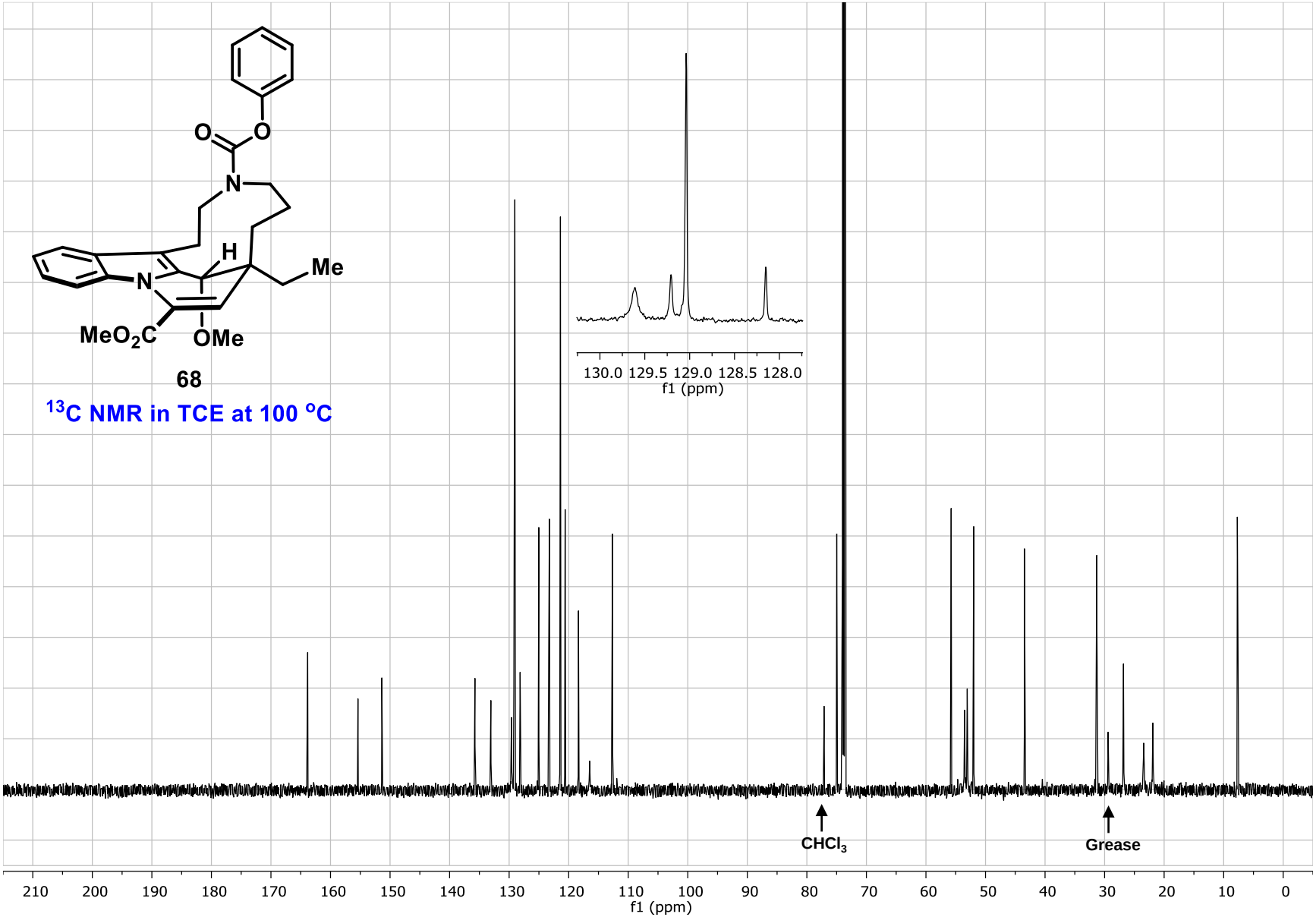


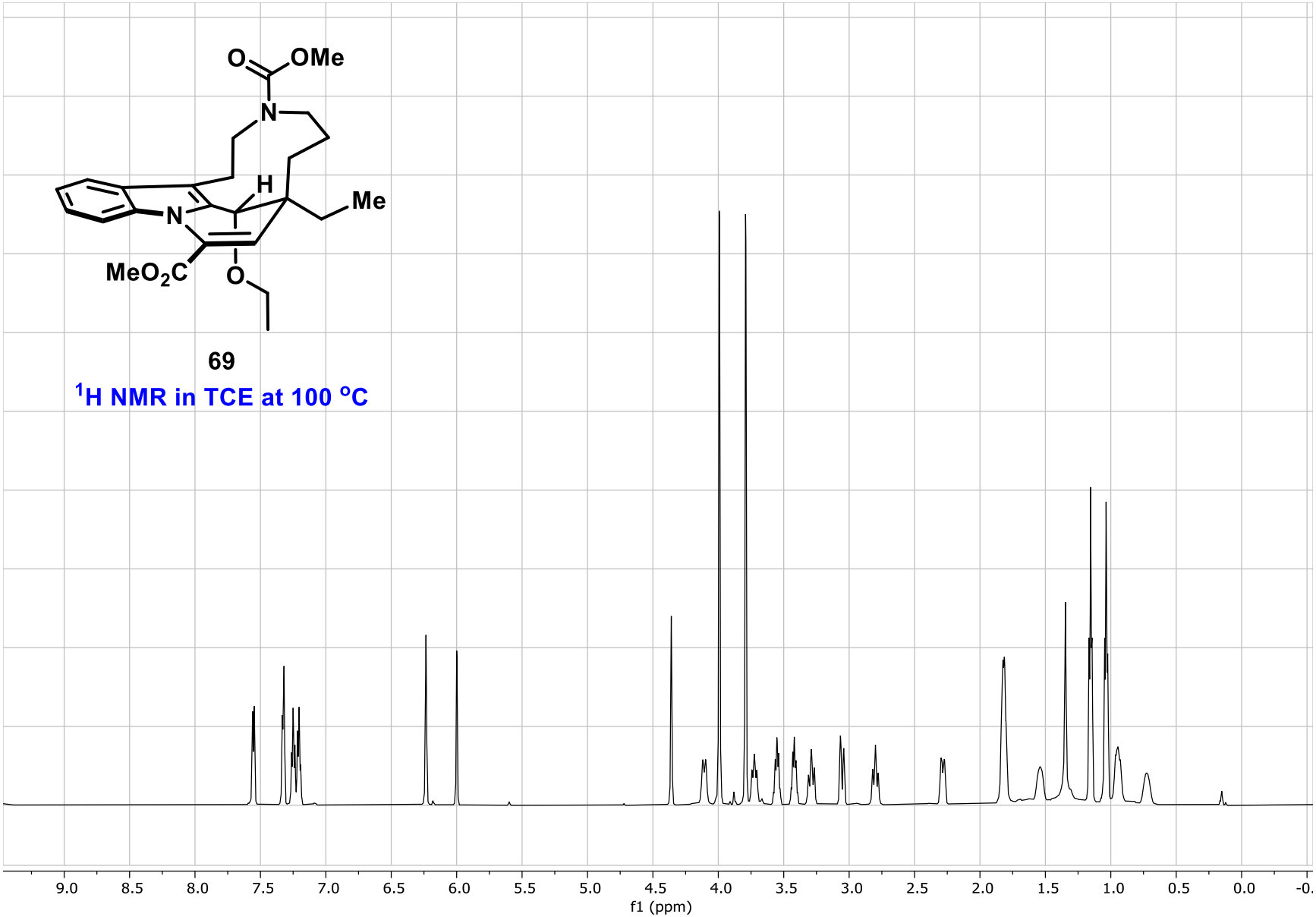
68

^{1}H NMR in TCE at 100 ^{o}C



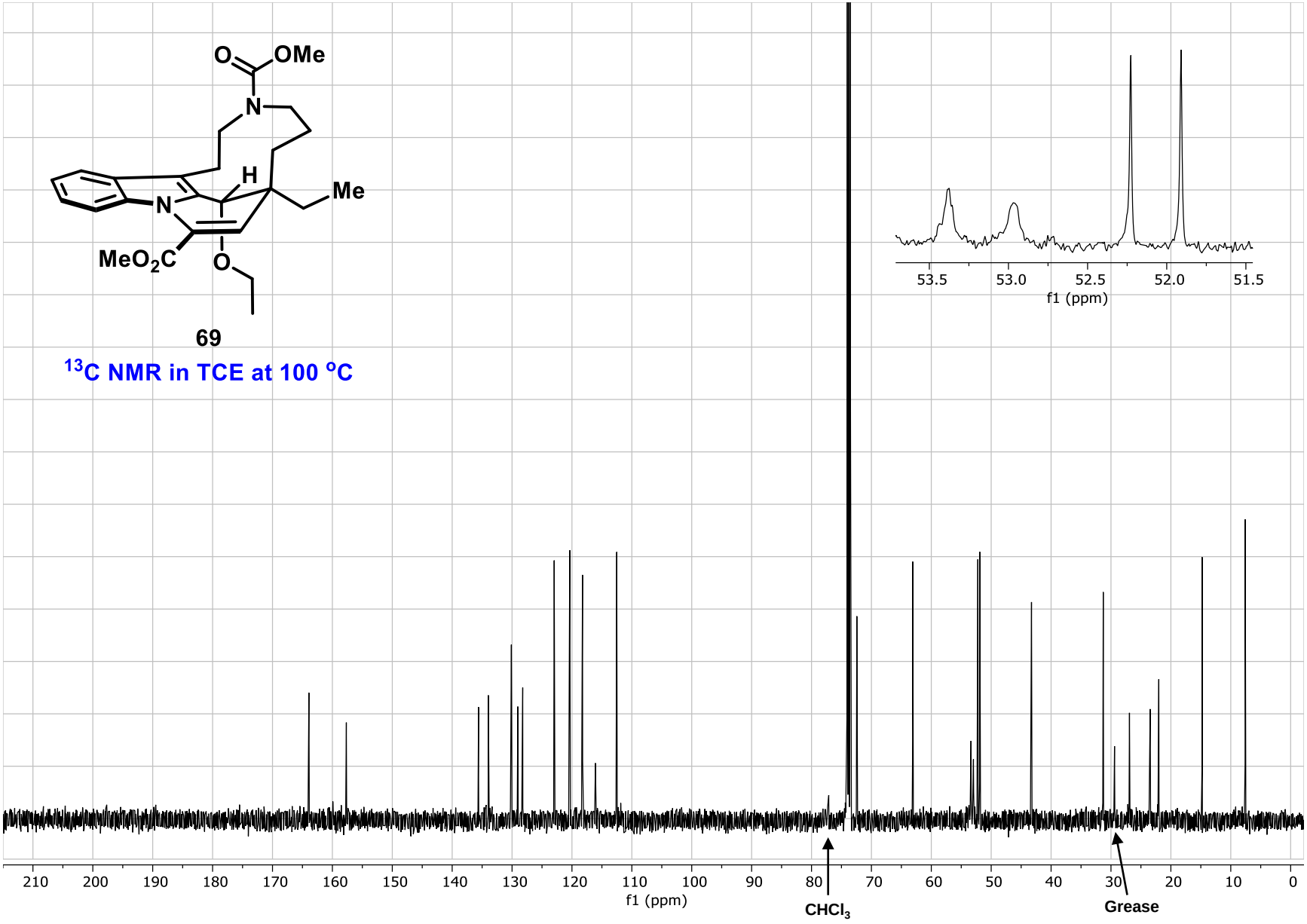


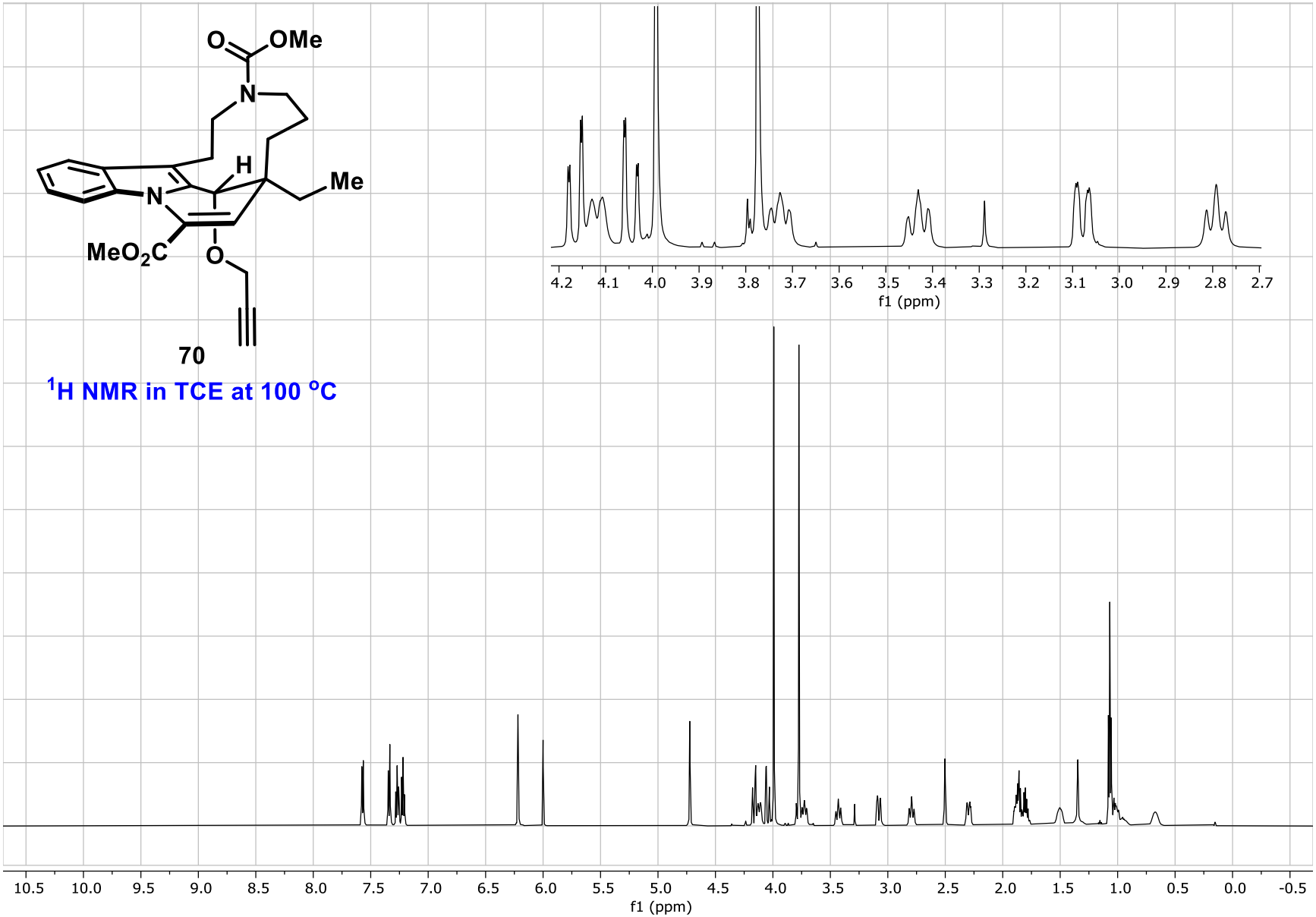

O
O
N
H
Me
N
MeO2C
OMe
68
13C NMR in TCE at 100 °C
130.0 129.5 129.0 128.5 128.0
f1 (ppm)
CHCl3
Grease
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

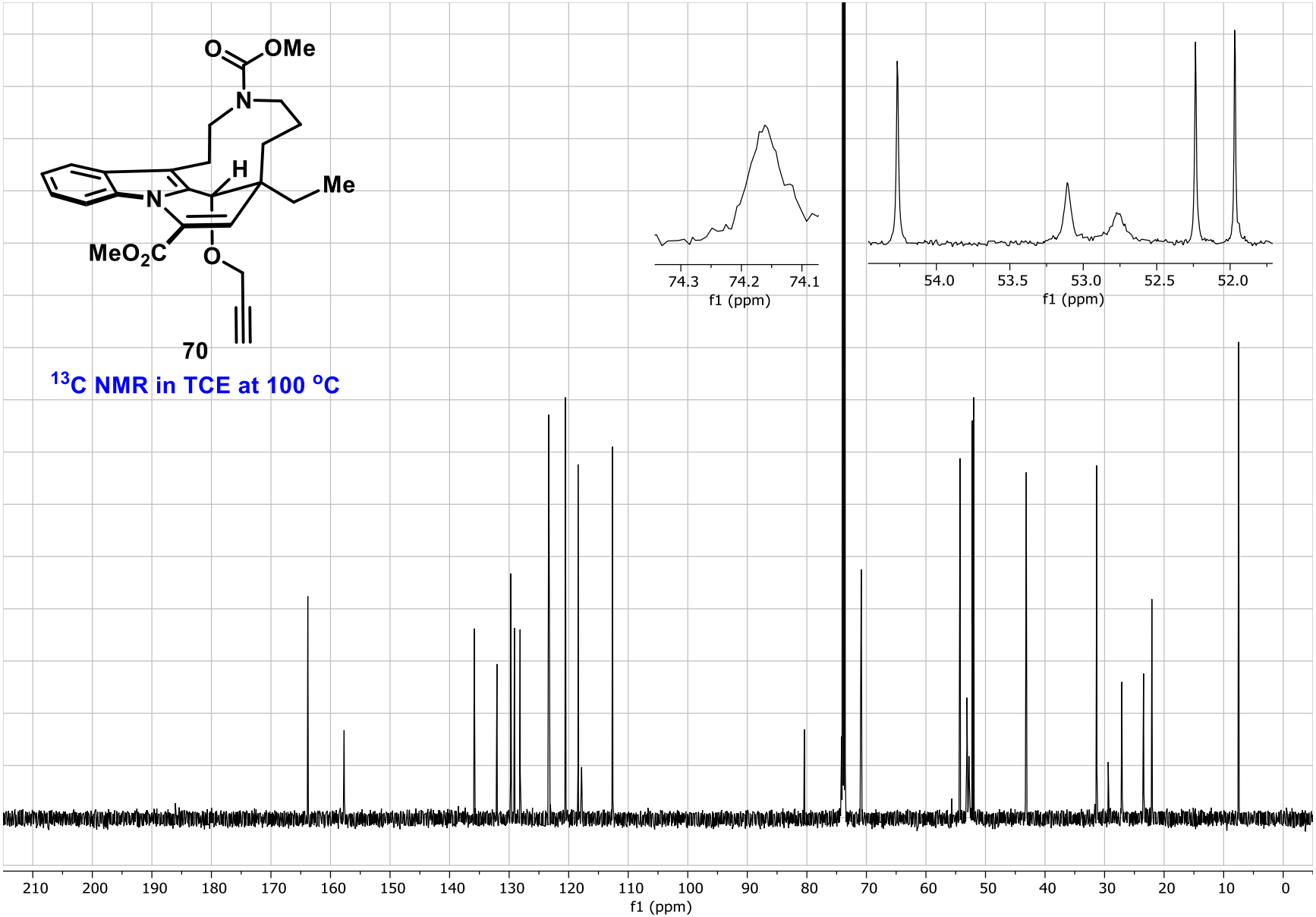


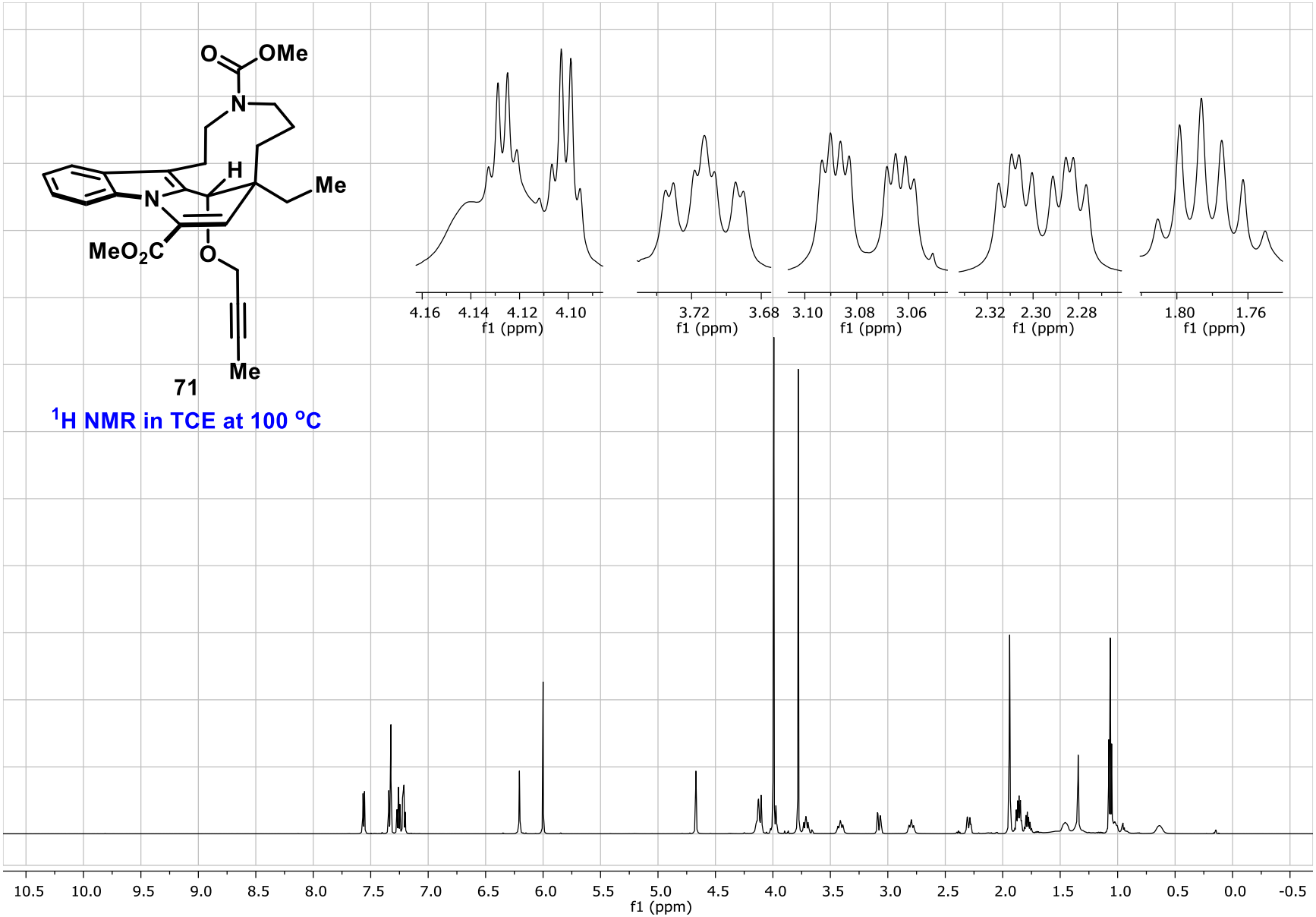
69

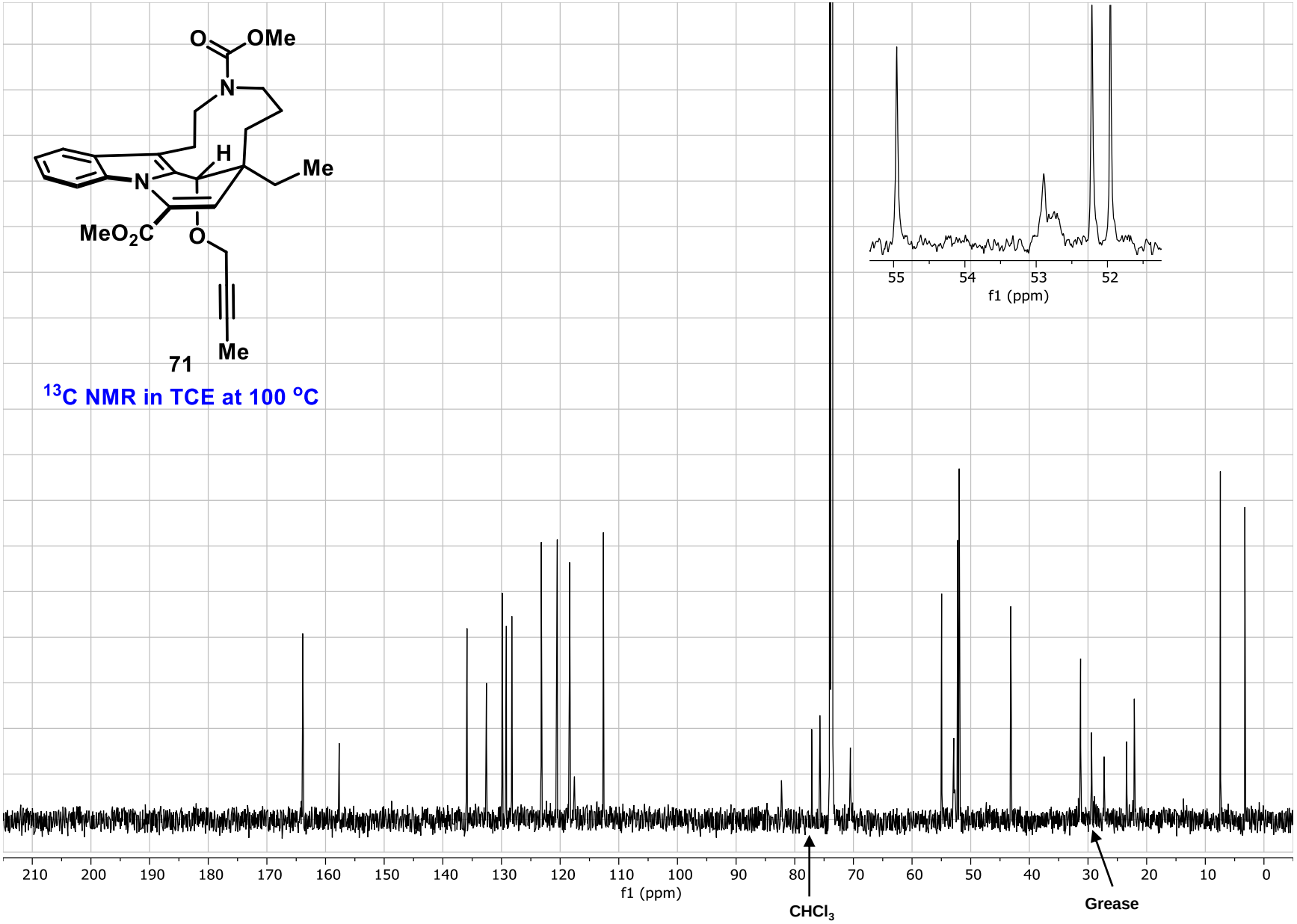
^{1}H NMR in TCE at 100 °C

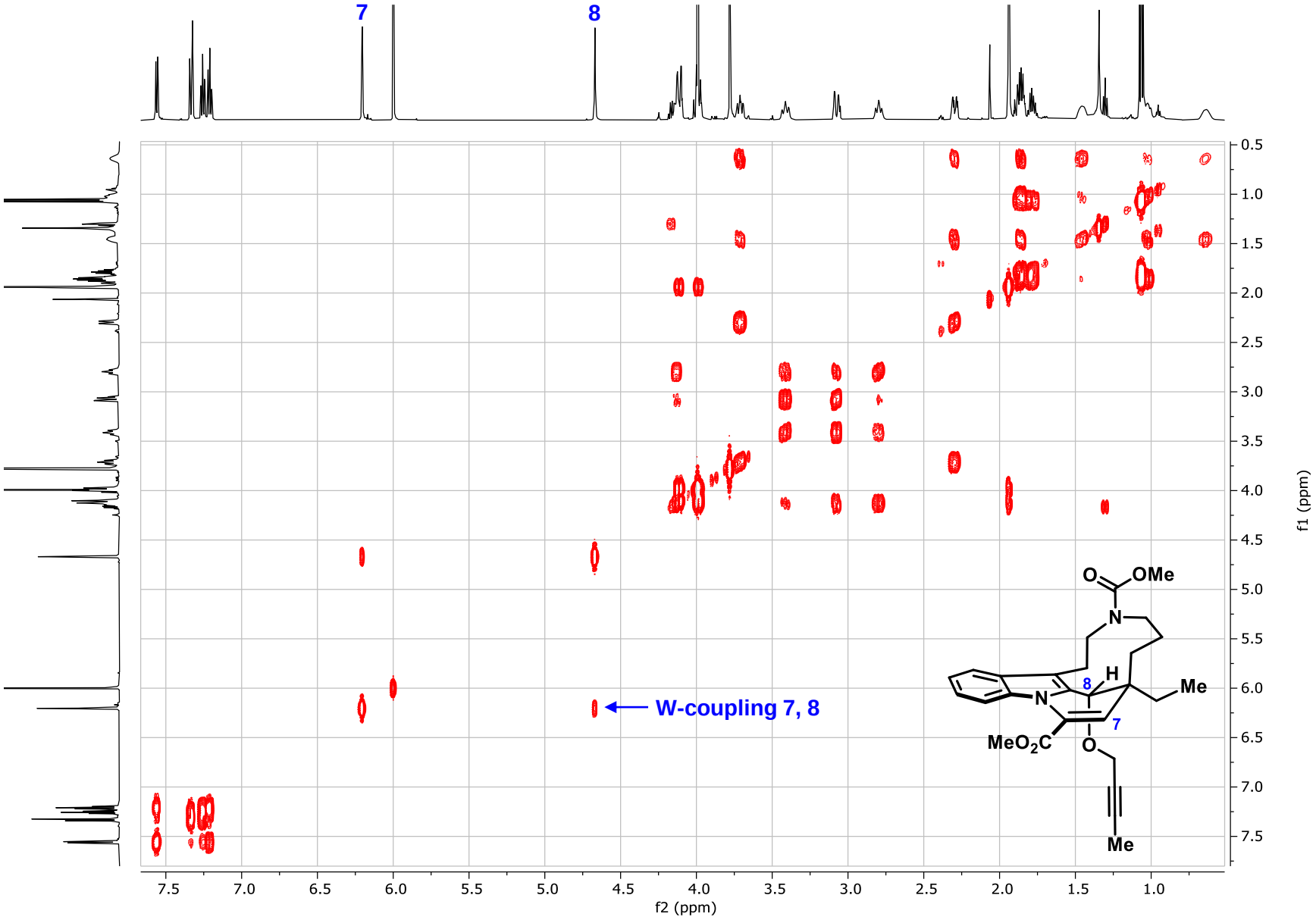

O
OMe
N
H
Me
N
MeO2C
O
69
13C NMR in TCE at 100 °C
53.5
53.0
52.5
52.0
51.5
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
CHCl3
Grease


O
OMe
N
H
Me
N
MeO2C
O
70
1H NMR in TCE at 100 °C
4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7
f1 (ppm)
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

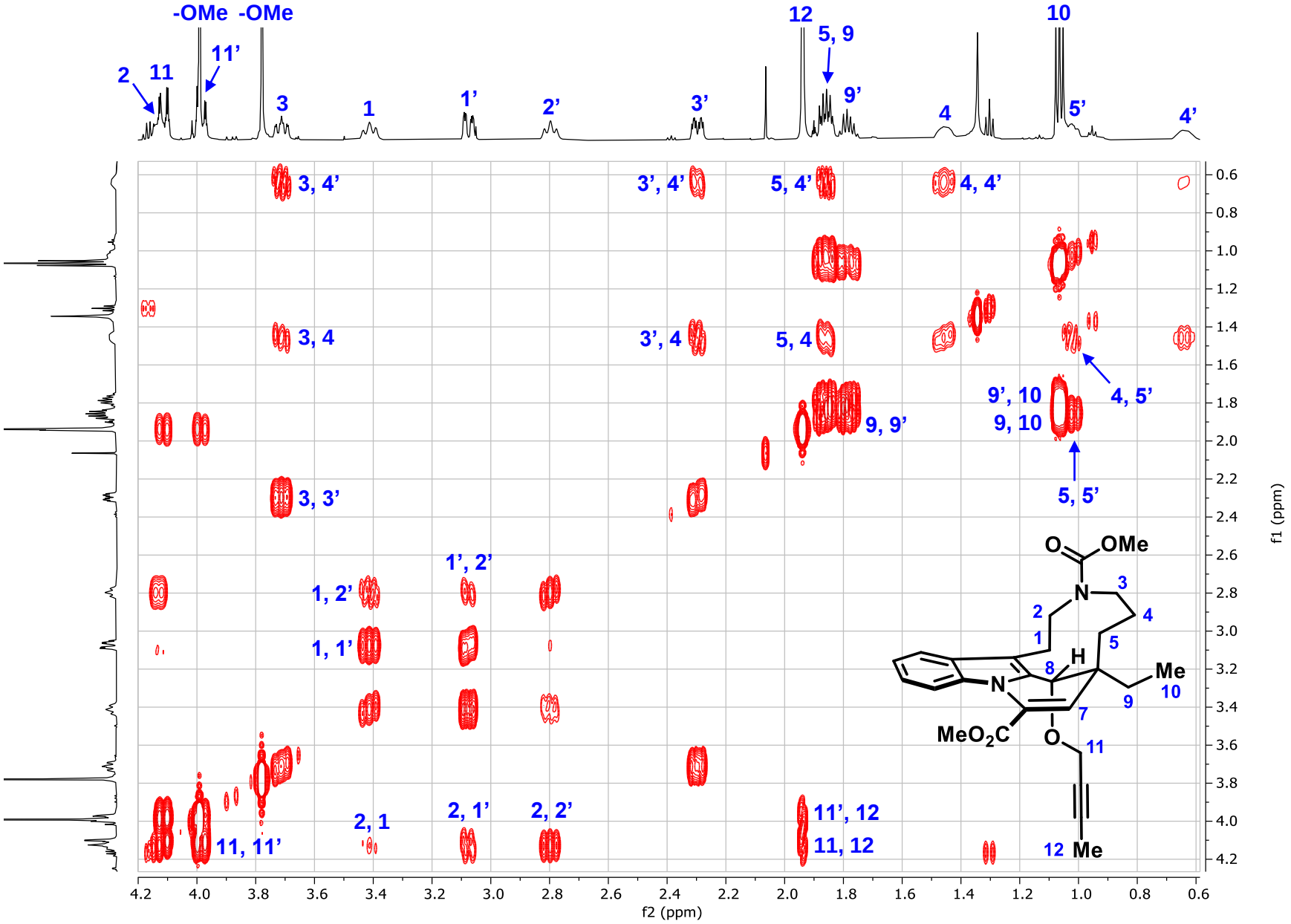

O
OMe
N
H
Me
N
MeO2C
O
70
13C NMR in TCE at 100 °C
74.3
74.2
74.1
f1 (ppm)
54.0
53.5
53.0
52.5
52.0
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


O
OMe
N
H
Me
N
MeO2C
O
Me
71
1H NMR in TCE at 100 °C
4.16 4.14 4.12 4.10
f1 (ppm)
3.72 3.68
f1 (ppm)
3.10 3.08 3.06
f1 (ppm)
2.32 2.30 2.28
f1 (ppm)
1.80 1.76
f1 (ppm)
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

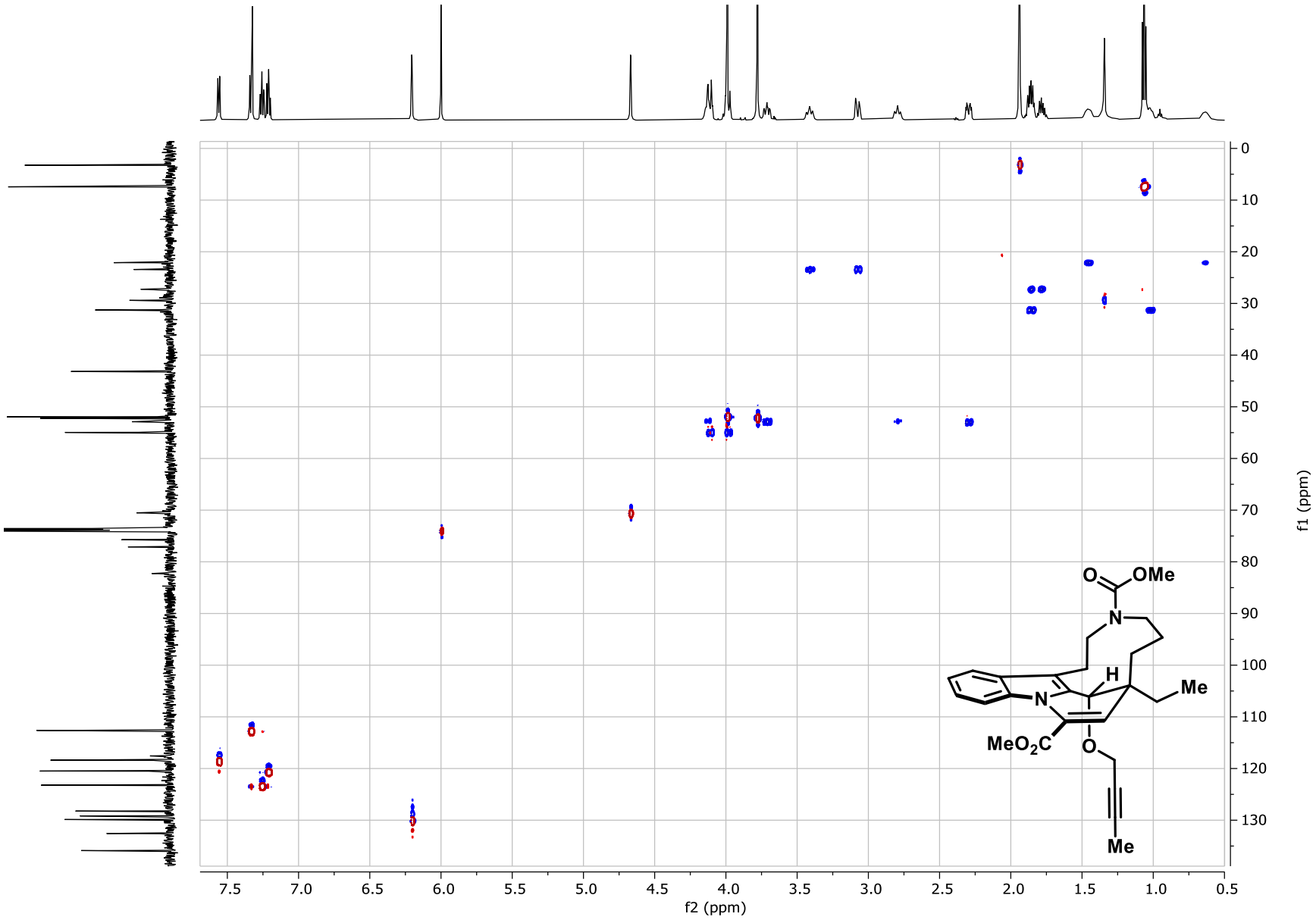

O
OMe
N
H
Me
N
MeO2C
O
Me
71
13C NMR in TCE at 100 °C
55
54
53
52
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
CHCl3
Grease



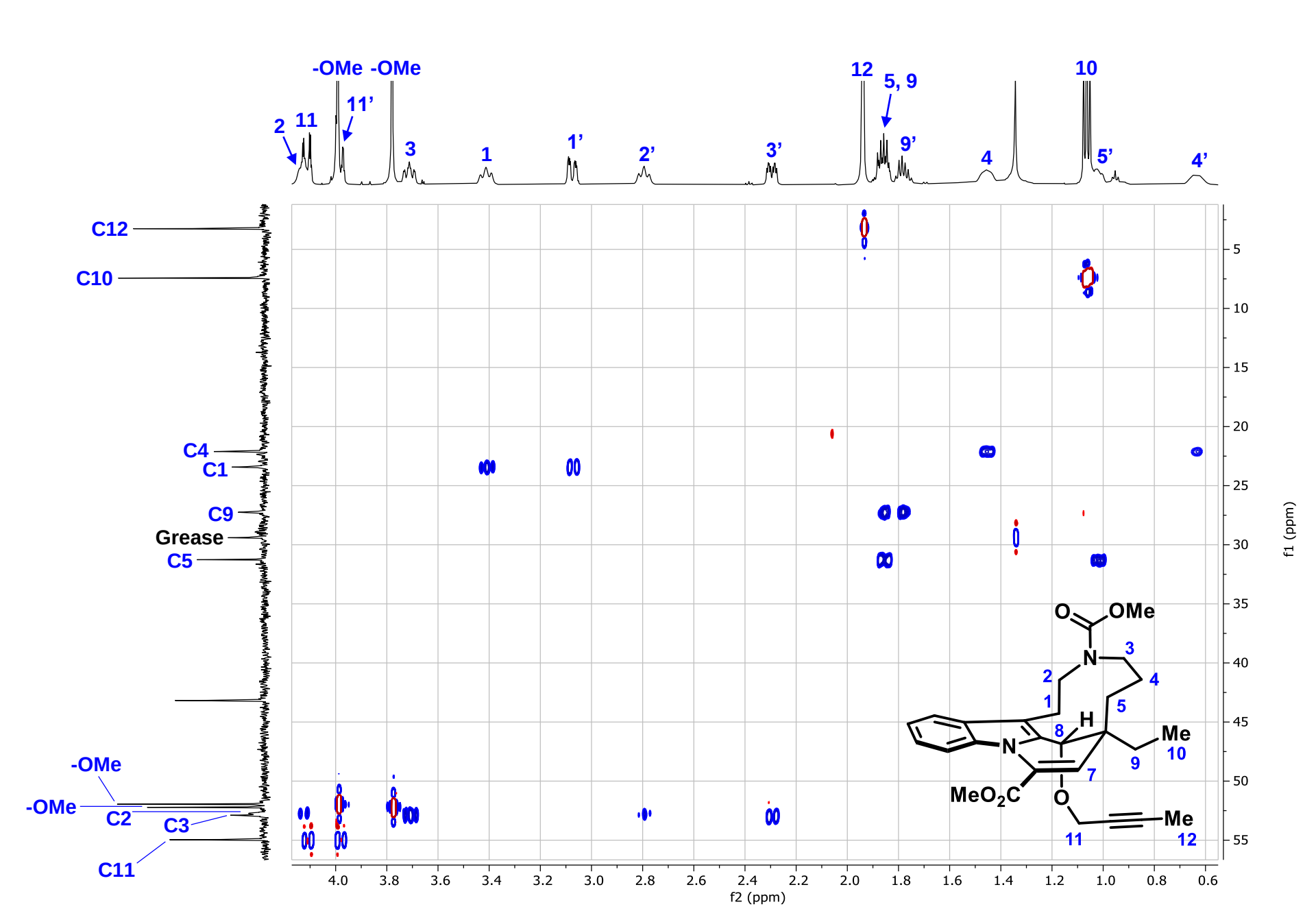
Compound 71: COSY, T = 100 °C, $C_2D_2Cl_4$ (full)



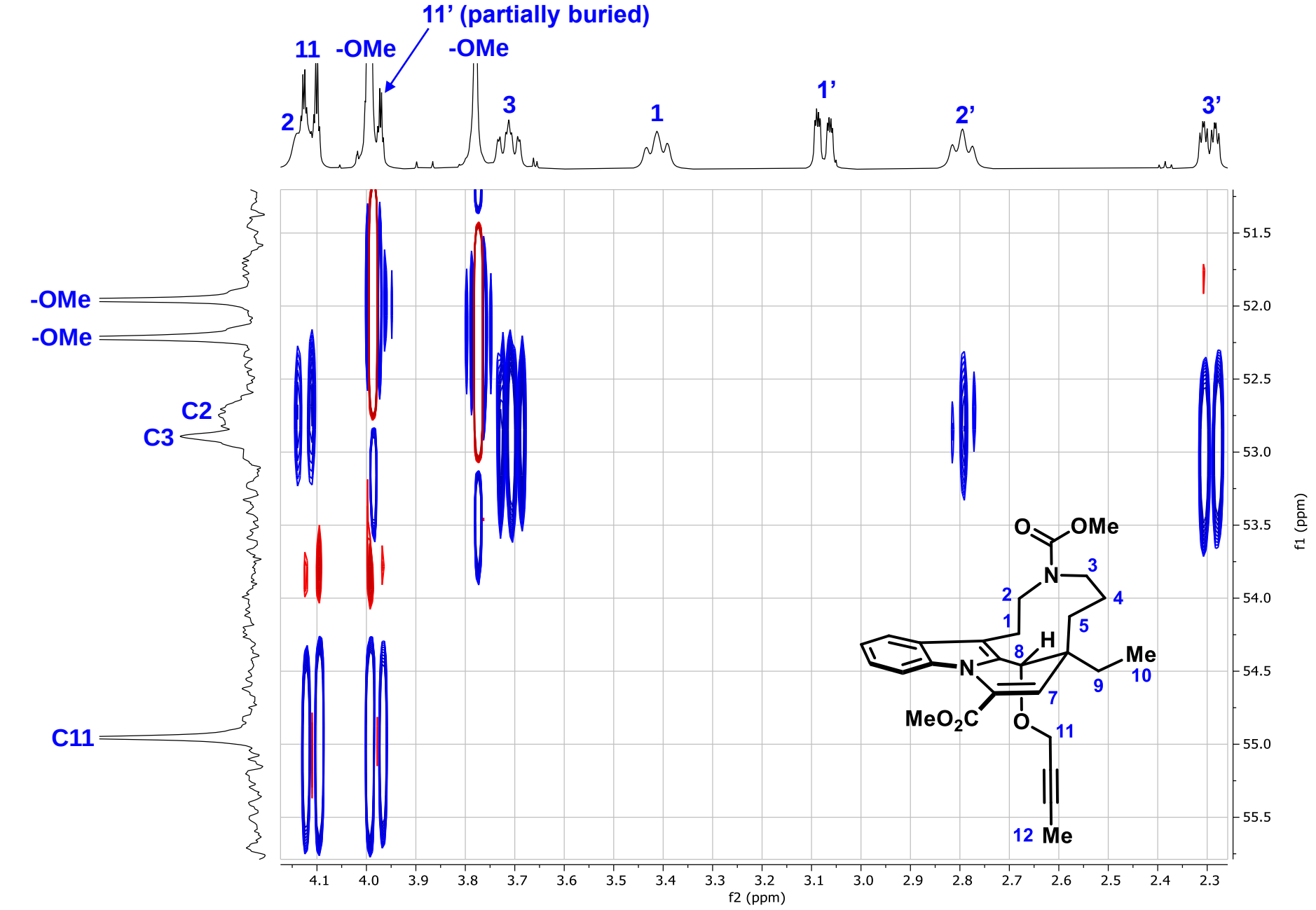
Compound 71: COSY, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in)



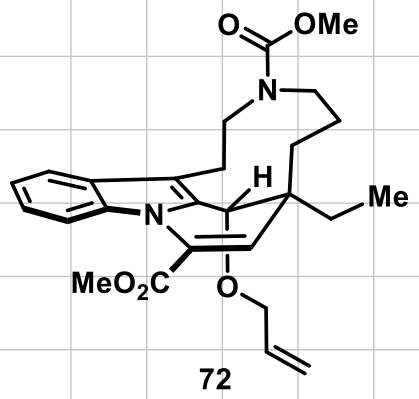
Compound 71: HSQC, T = 100 °C, $C_2D_2Cl_4$ (full)



Compound 71: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 1)

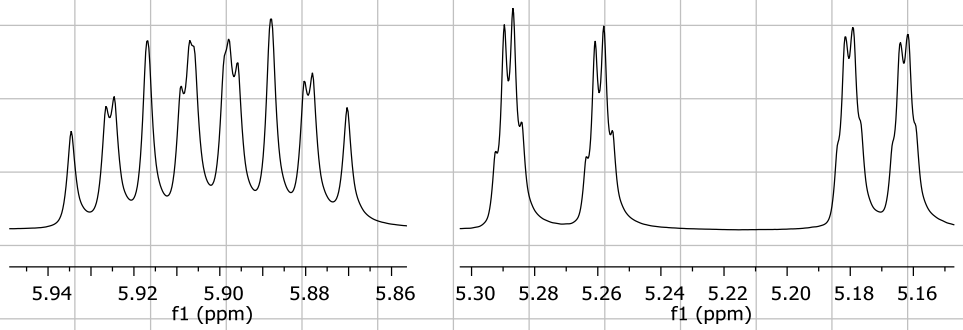


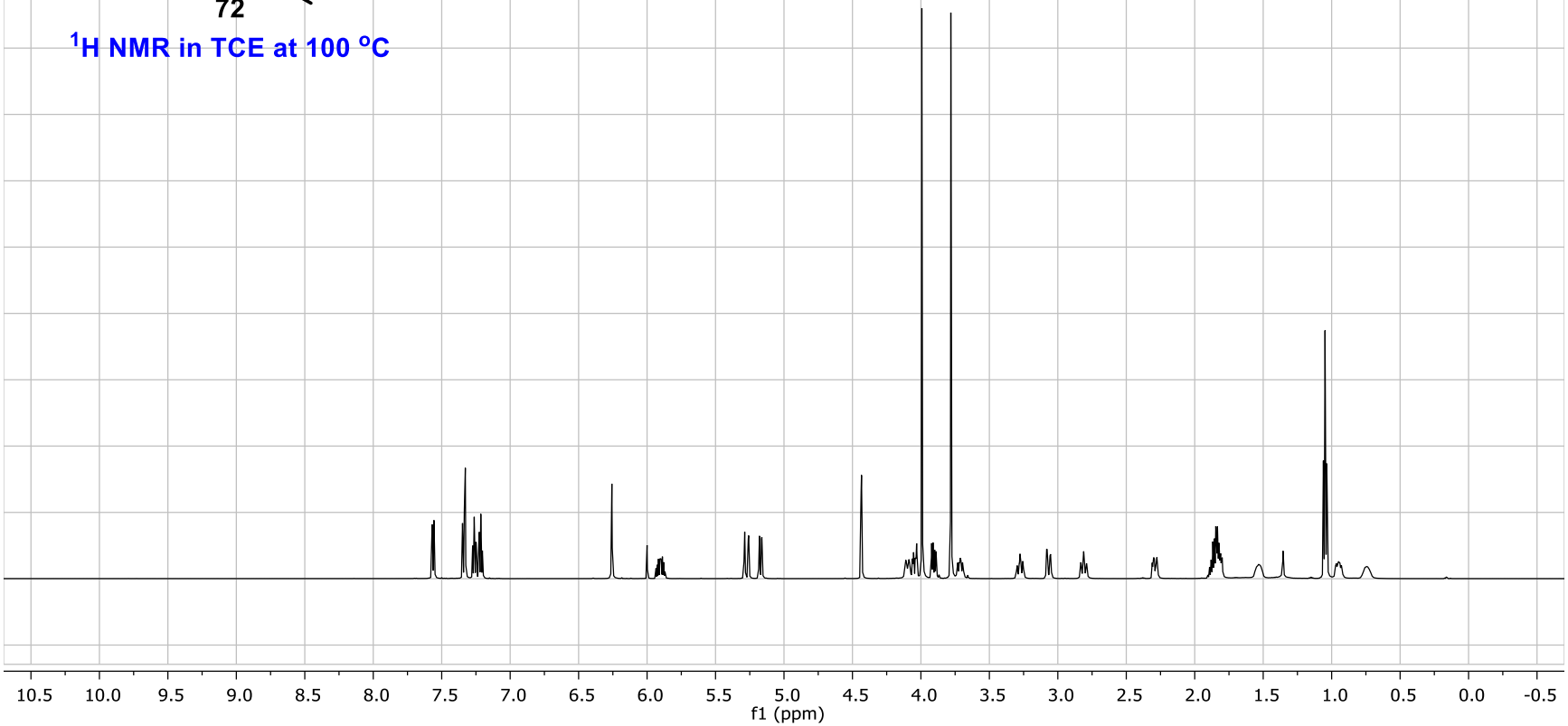
Compound 71: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 2)

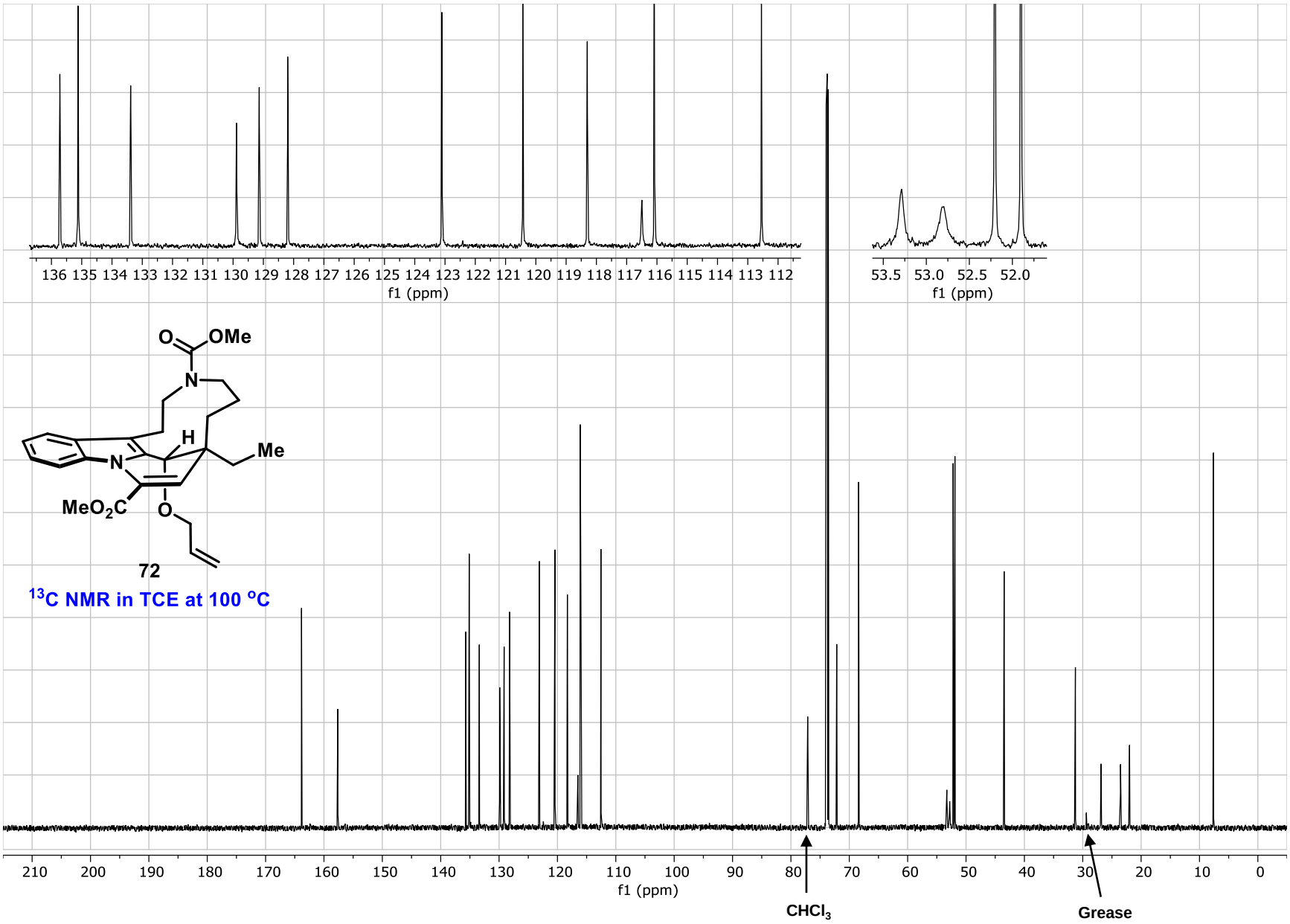


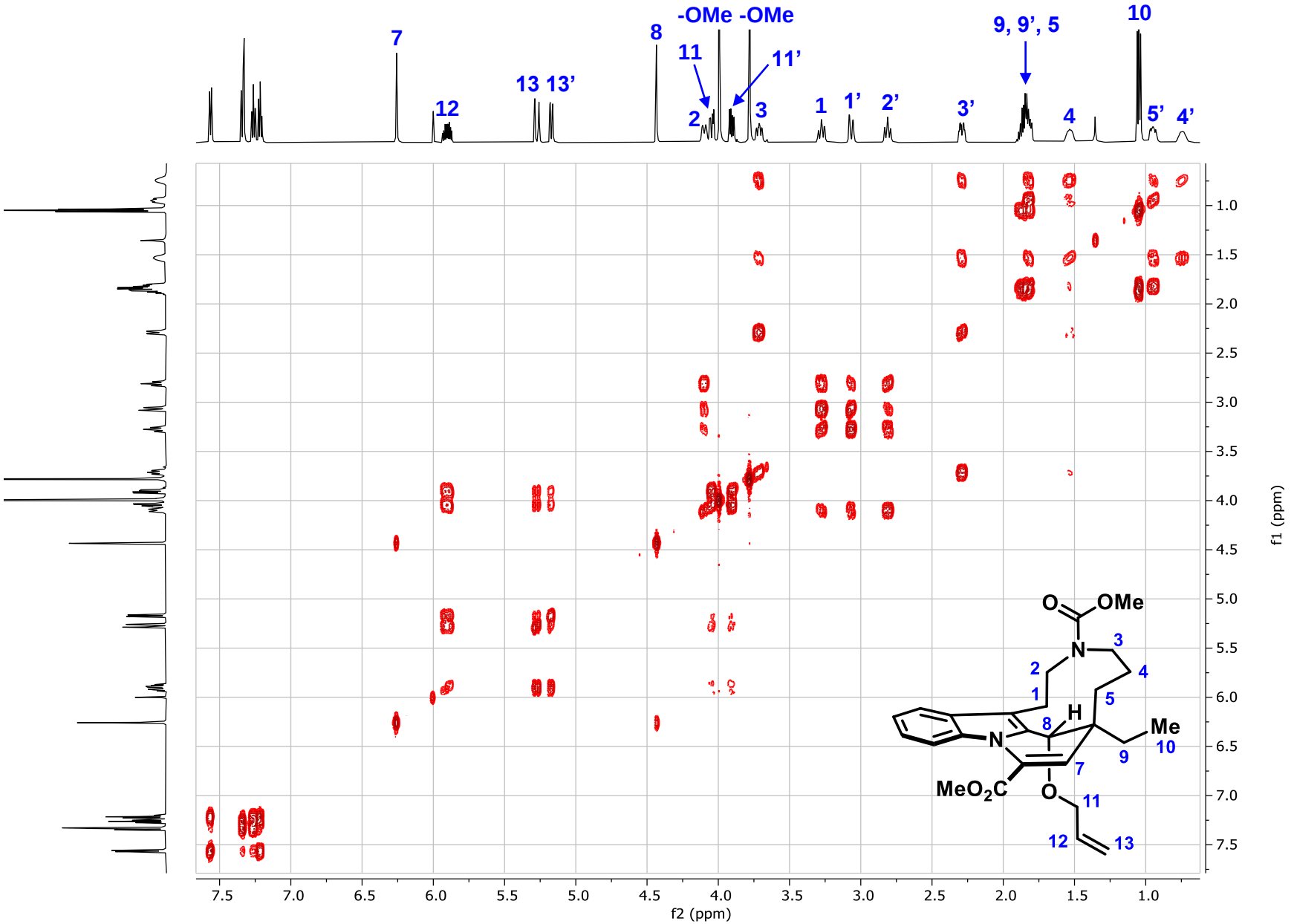
72

^{1}H NMR in TCE at 100 ^{o}C

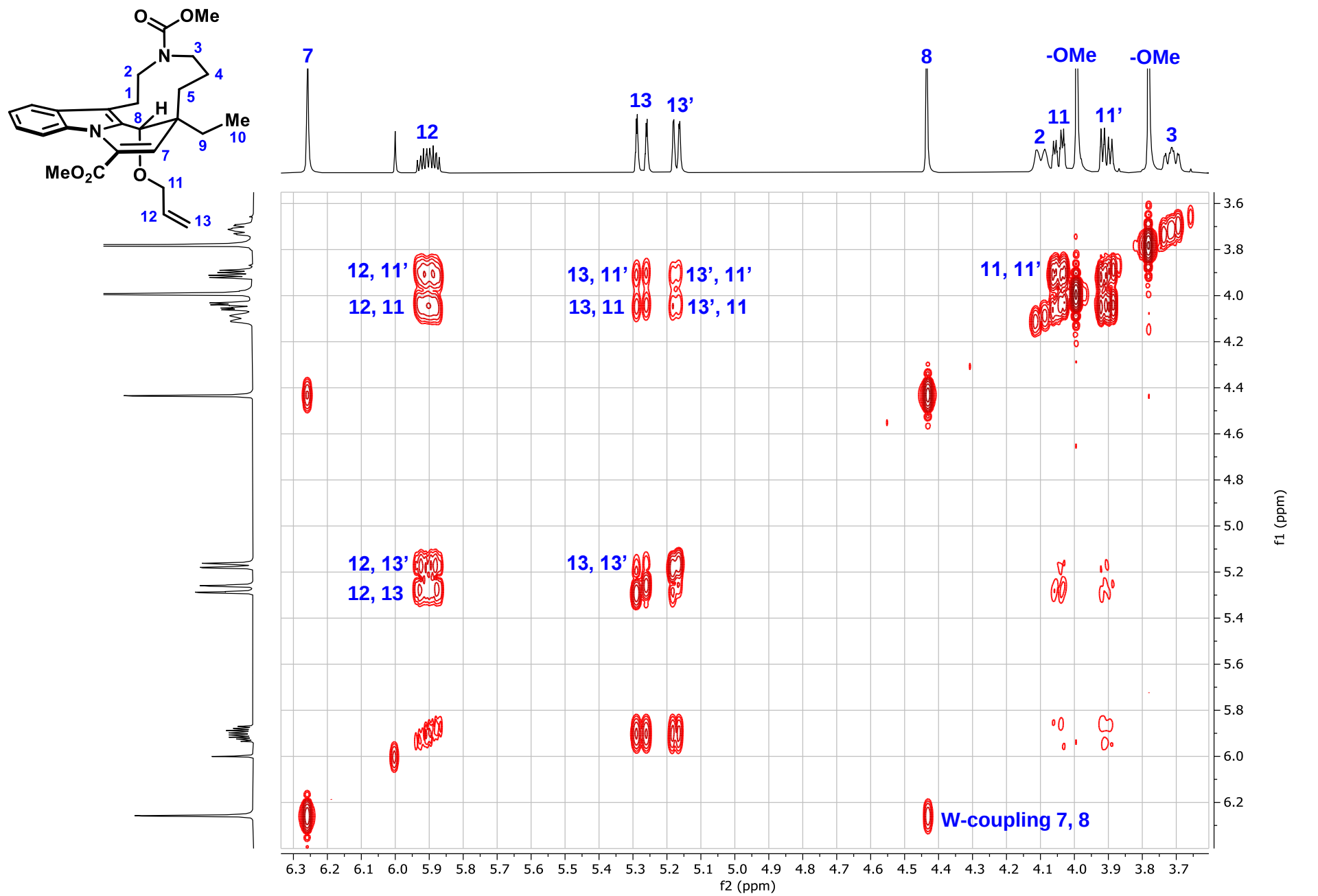




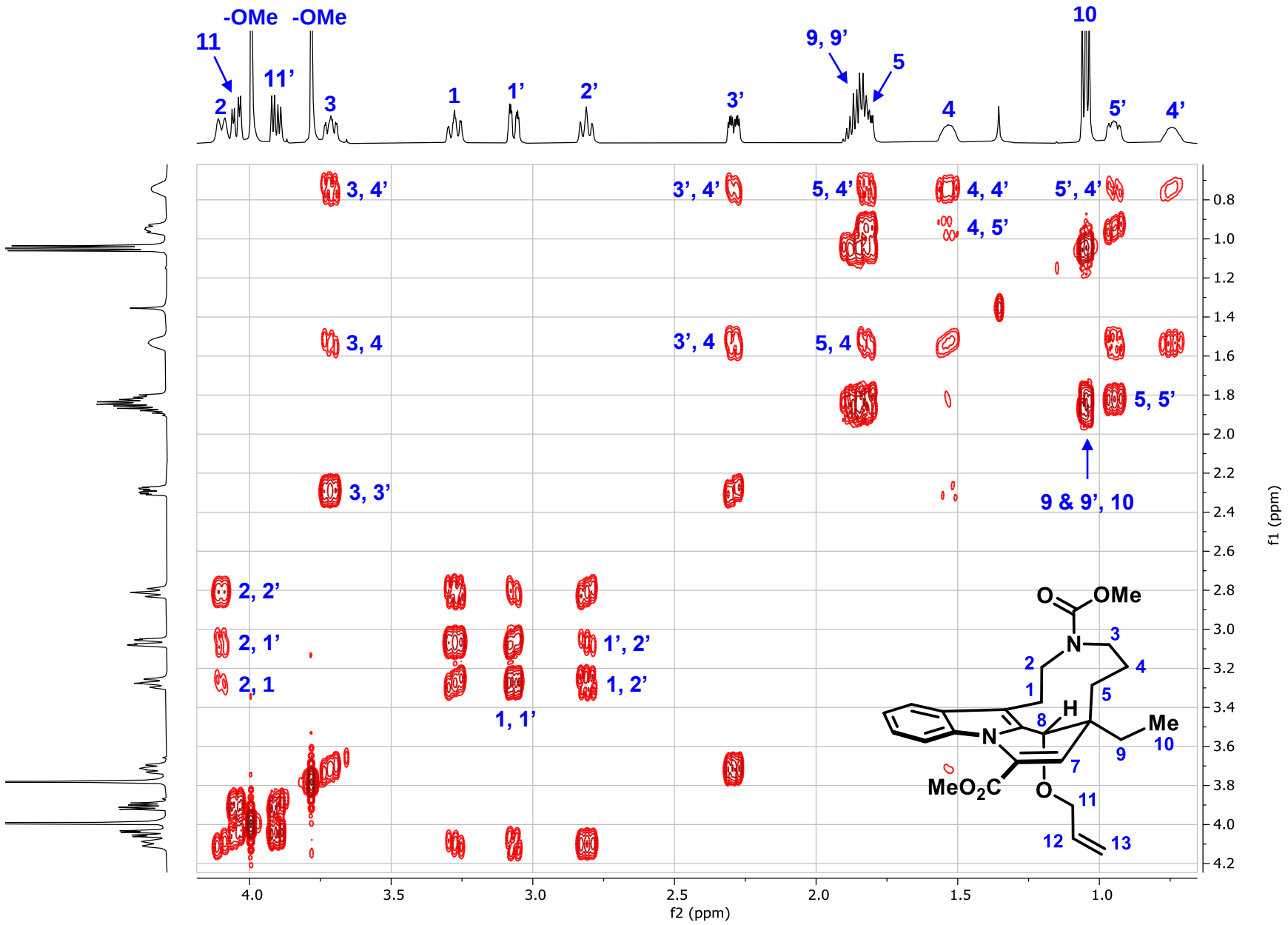

136 135 134 133 132 131 130 129 128 127 126 125 124 123 122 121 120 119 118 117 116 115 114 113 112
f1 (ppm)
53.5 53.0 52.5 52.0
f1 (ppm)
O
OMe
N
H
Me
N
MeO2C
O
72
13C NMR in TCE at 100 °C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
CHCl3
Grease



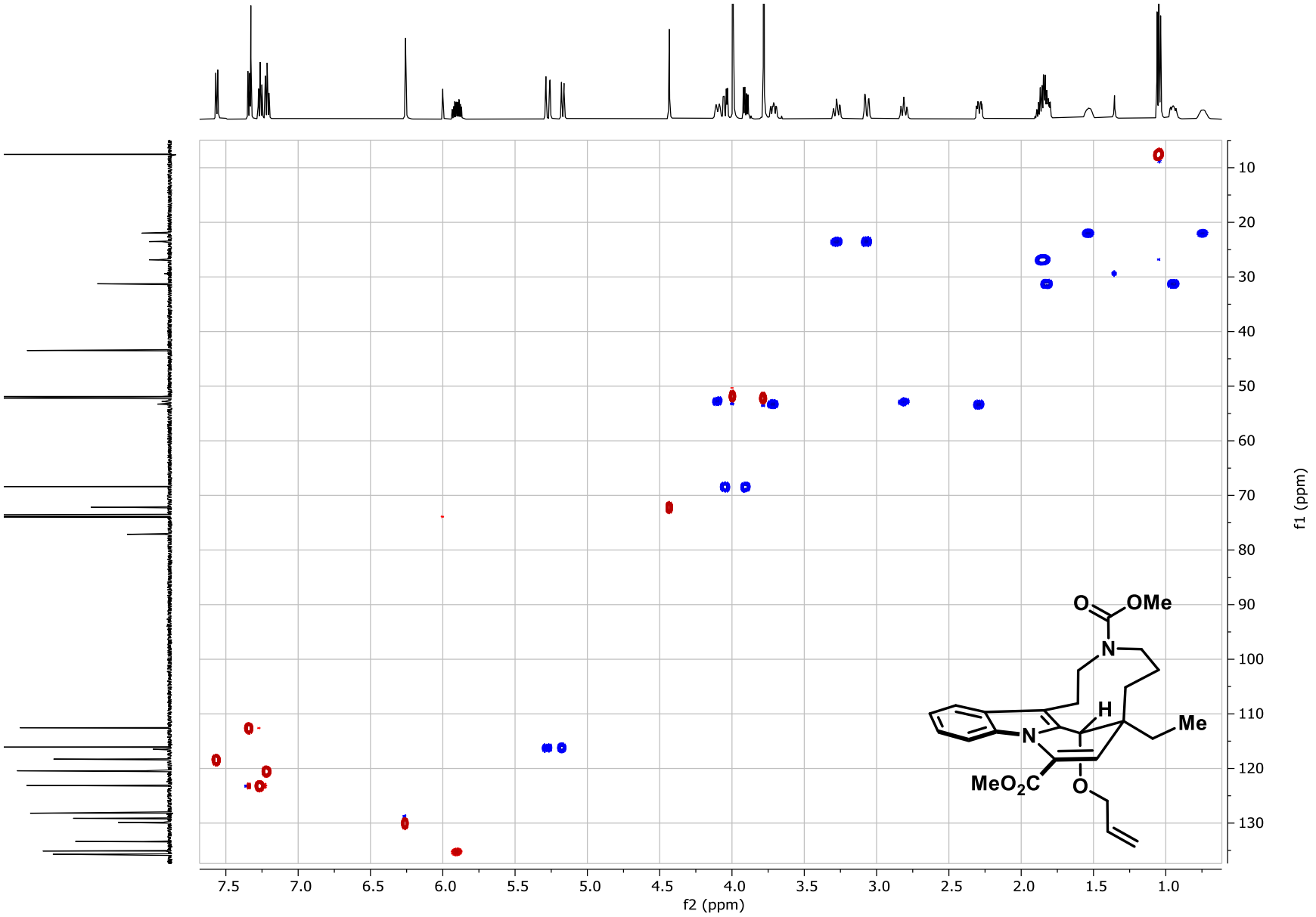
Compound 72: COSY, T = 100 °C,
$C_2D_2Cl_4$ (full)



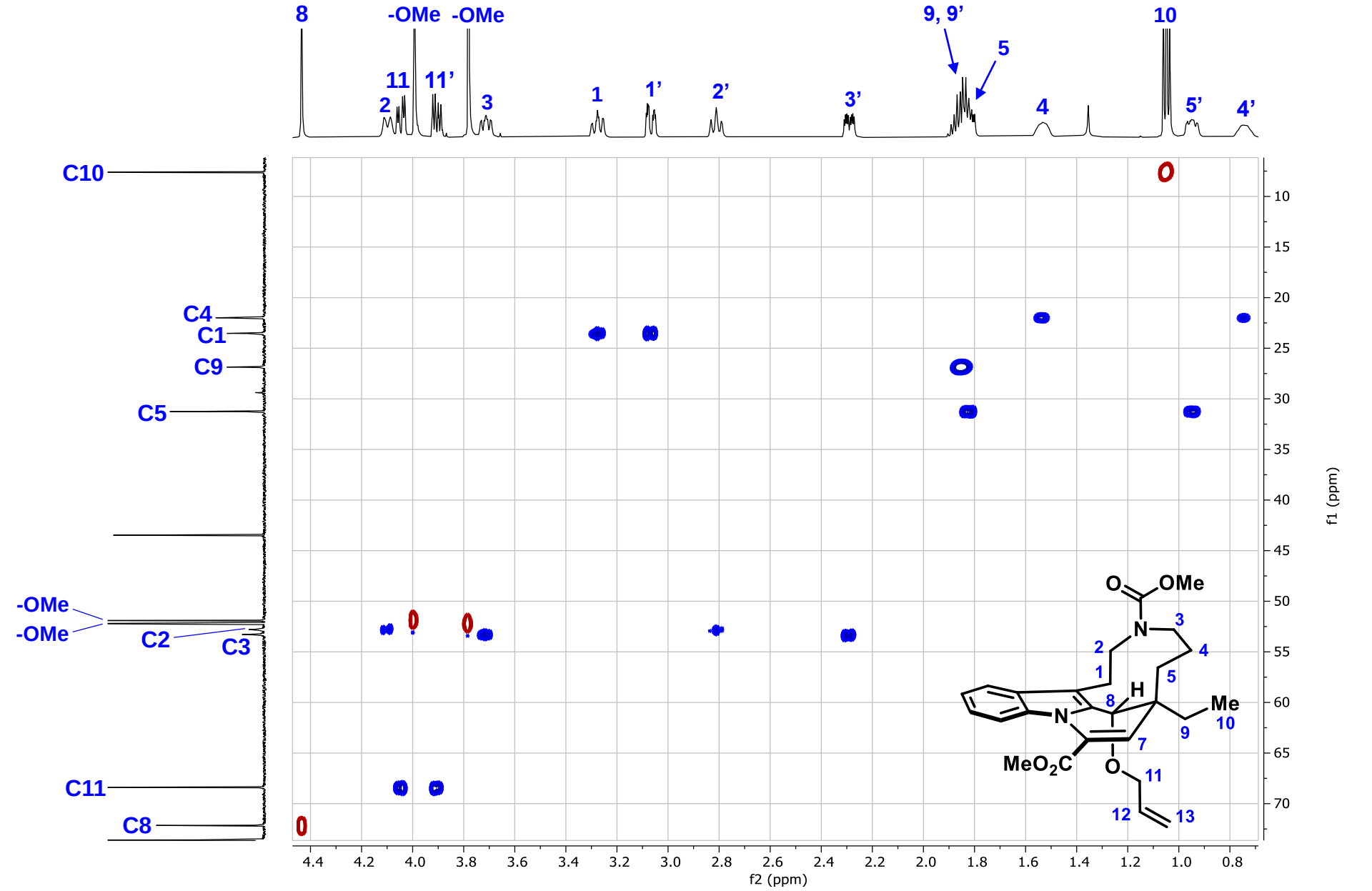
Compound **72**: COSY, T = 100 °C, $C_2D_2Cl_4$ (zoomed in, version 1). Allylic coupling observed between protons at 11 and 13.



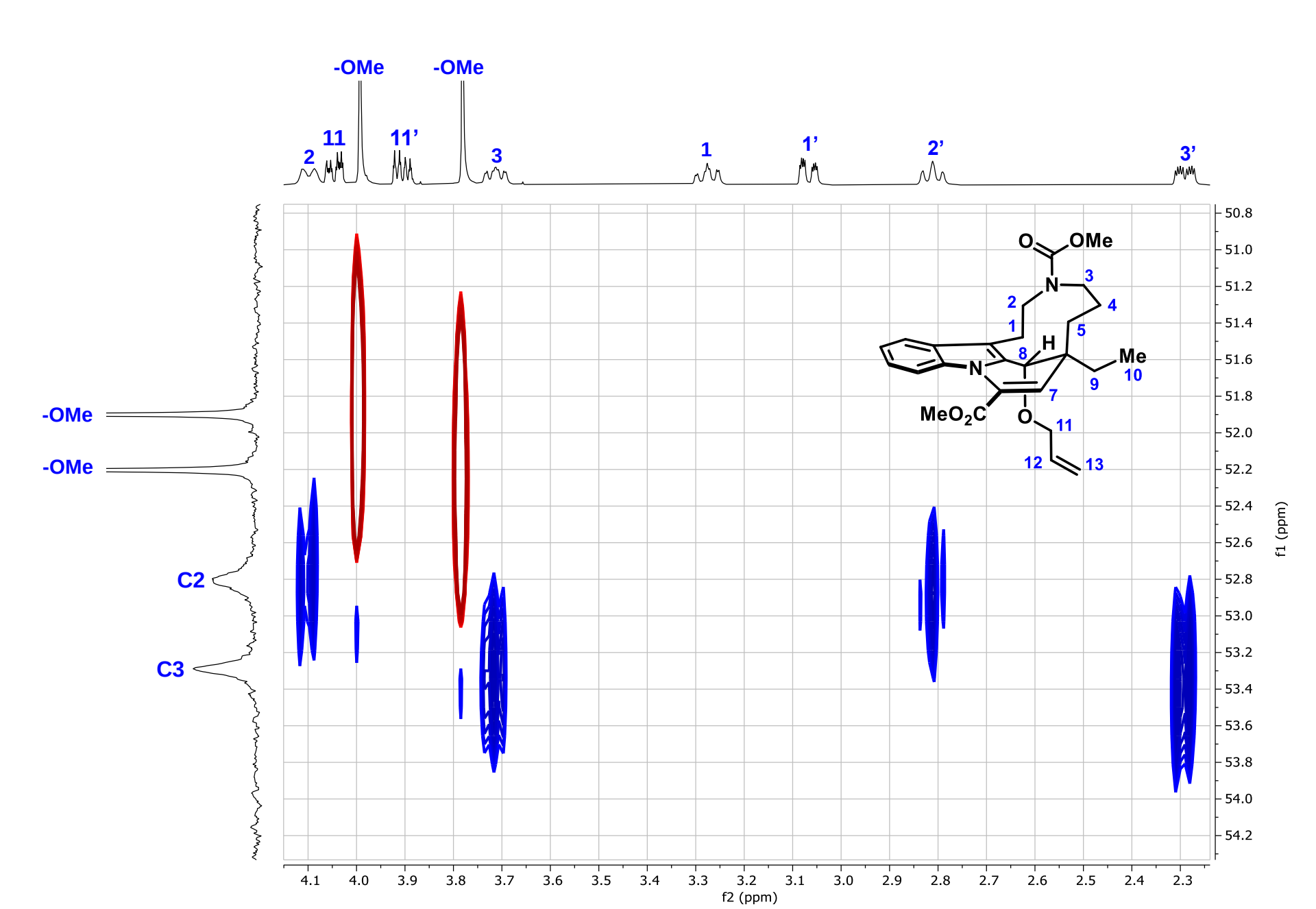
Compound 72: COSY, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 2).



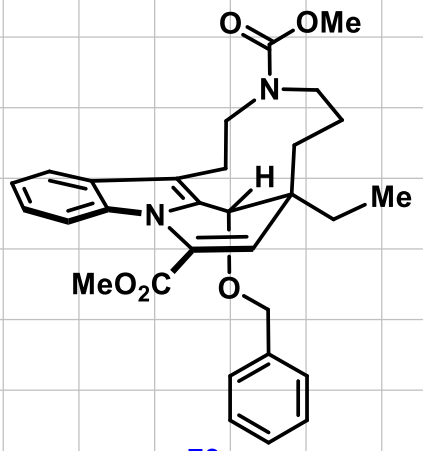
Compound 72: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (full)



Compound 72: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 1)

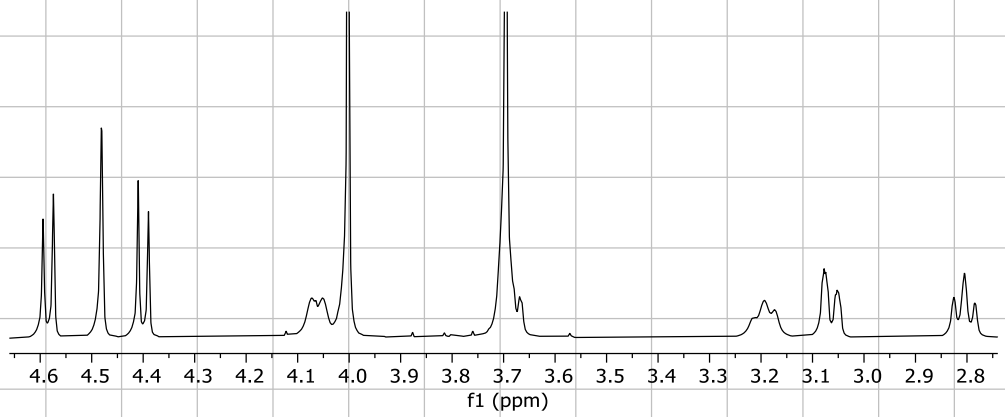


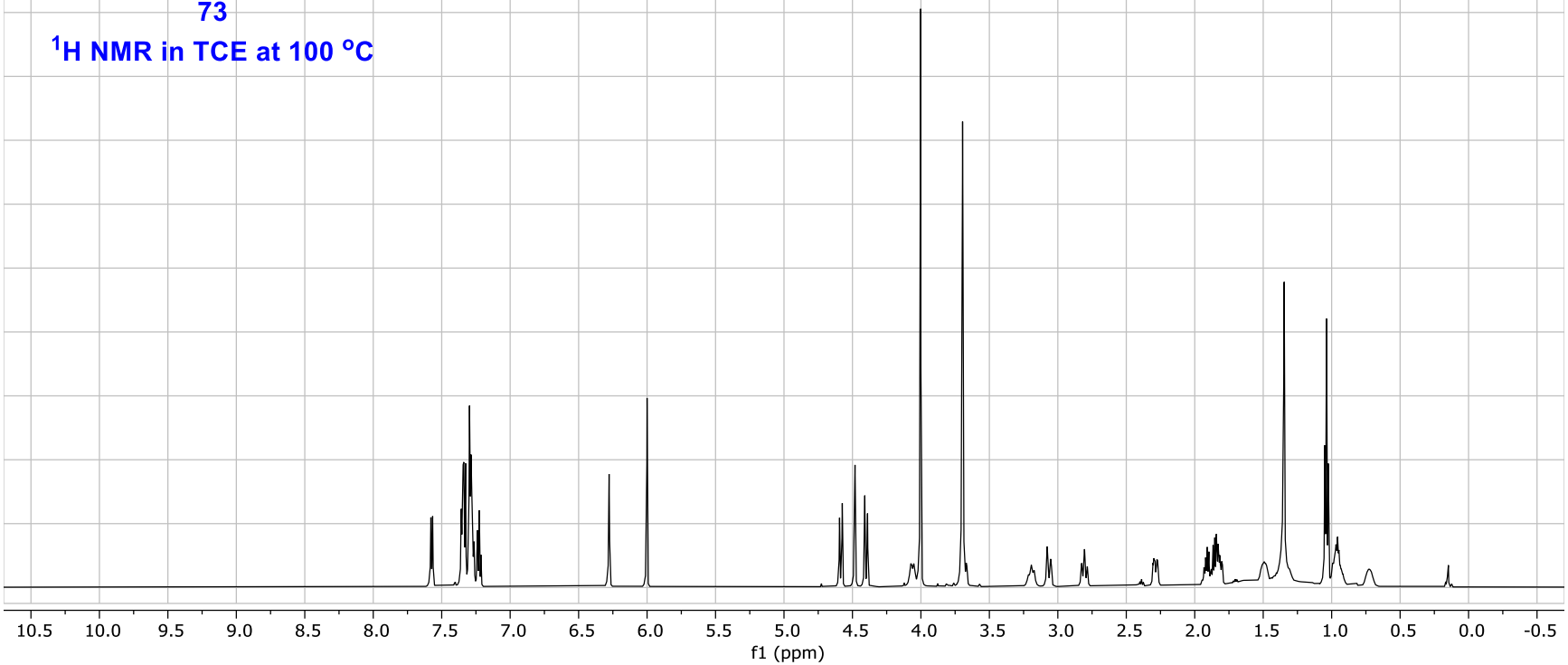
Compound 72: HSQC, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in, version 2)

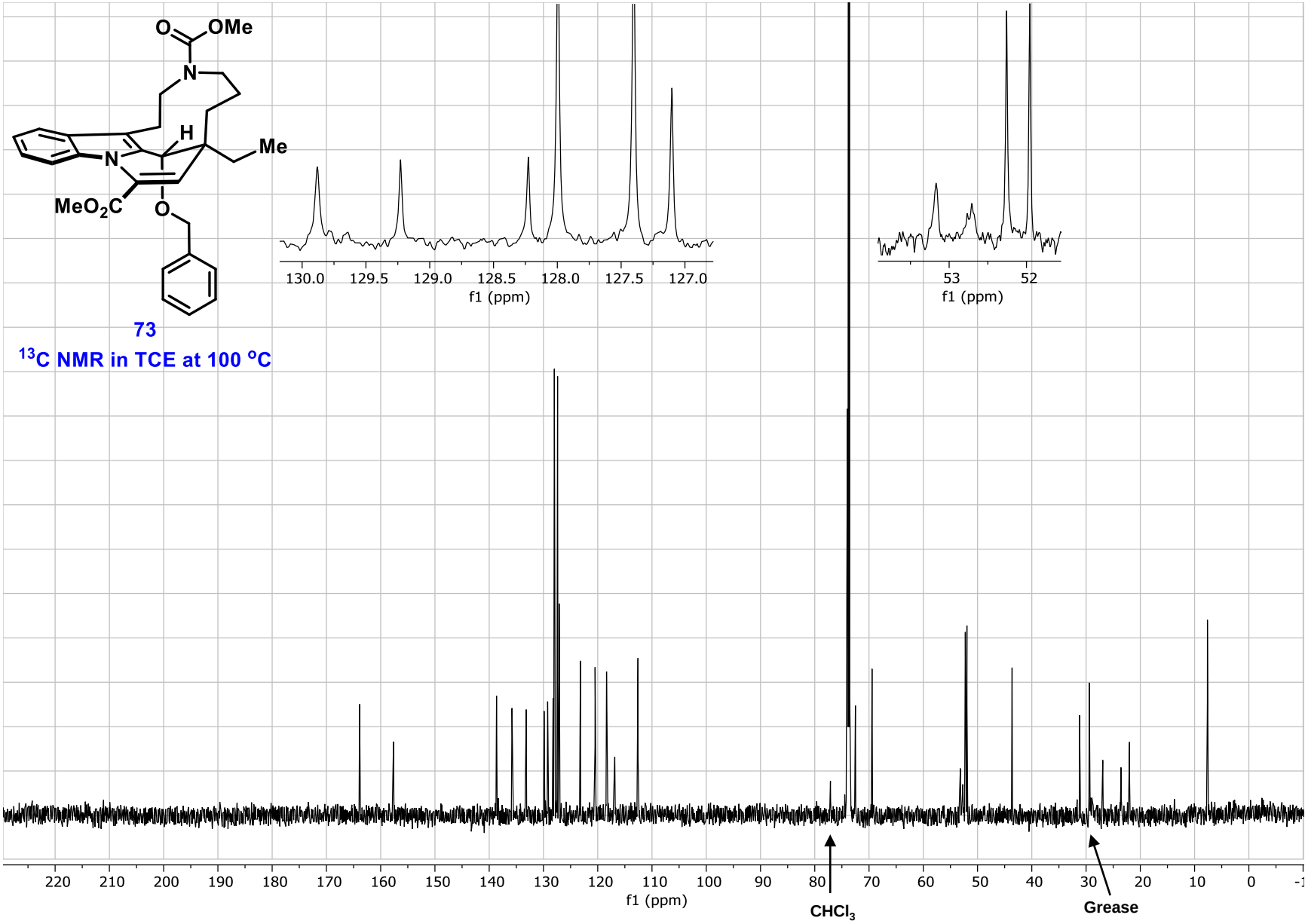


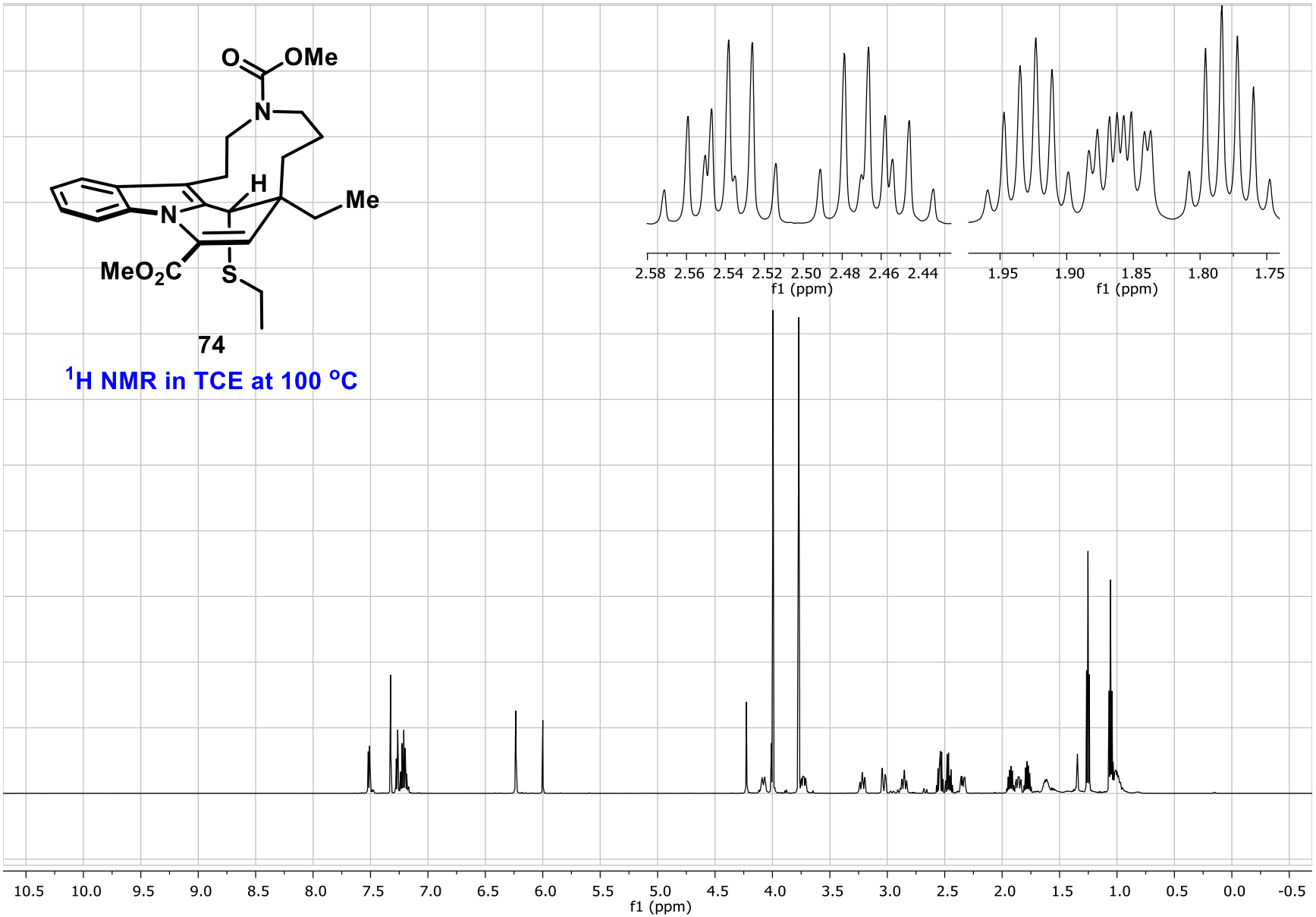
73

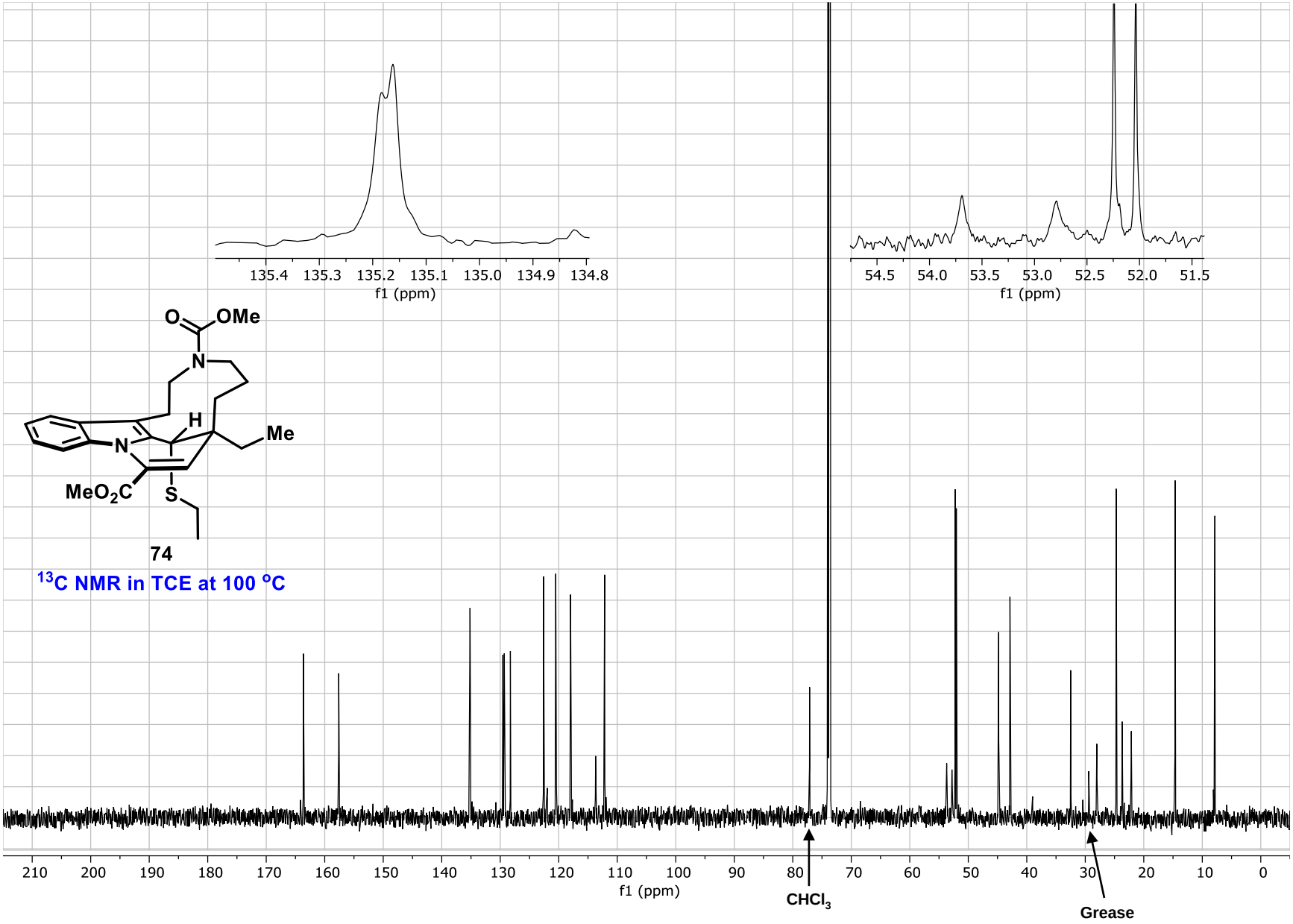
^{1}H NMR in TCE at 100 °C

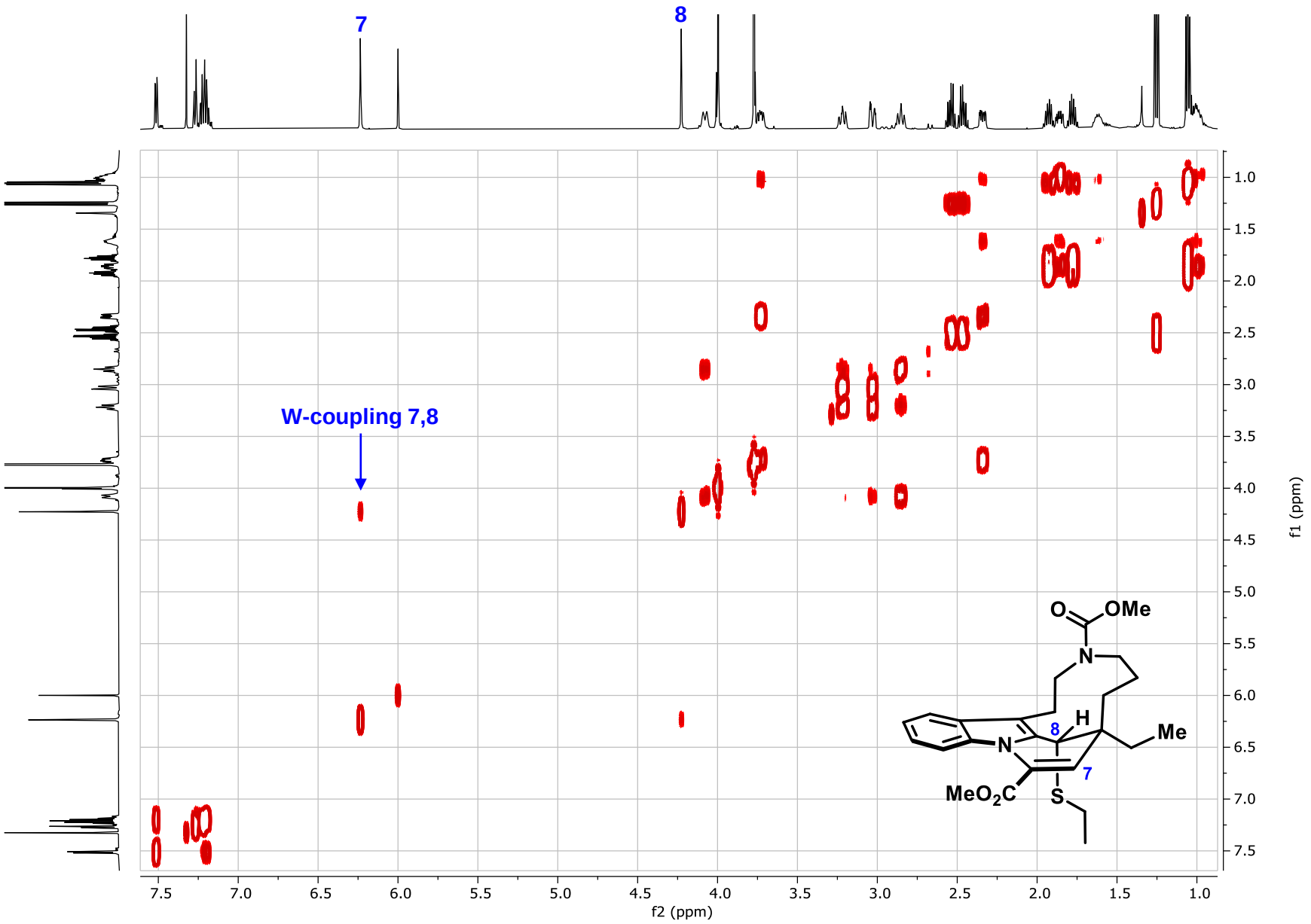




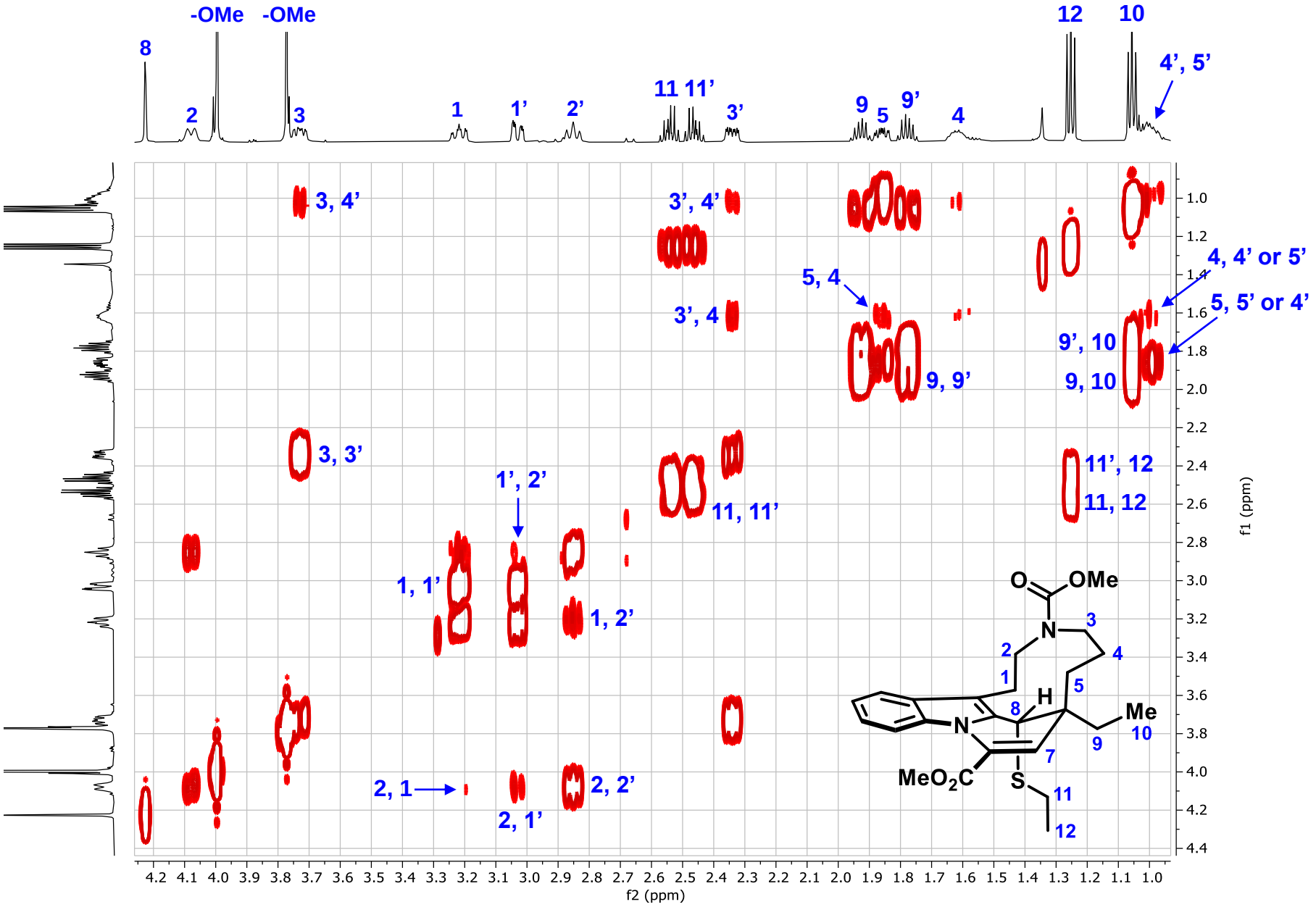

O
OMe
N
H
Me
N
MeO2C
O
73
13C NMR in TCE at 100 °C
130.0
129.5
129.0
128.5
128.0
127.5
127.0
f1 (ppm)
53
52
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
CHCl3
Grease


O
OMe
N
H
Me
N
MeO2C
S
74
1H NMR in TCE at 100 °C
2.58 2.56 2.54 2.52 2.50 2.48 2.46 2.44
f1 (ppm)
1.95 1.90 1.85 1.80 1.75
f1 (ppm)
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

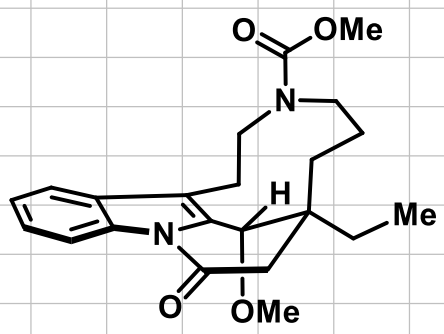

135.4 135.3 135.2 135.1 135.0 134.9 134.8
f1 (ppm)
54.5 54.0 53.5 53.0 52.5 52.0 51.5
f1 (ppm)
O
OMe
N
H
Me
N
MeO2C
S
74
13C NMR in TCE at 100 °C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
CHCl3
Grease



Compound 74: COSY, T = 100 °C, $C_2D_2Cl_4$ (full)

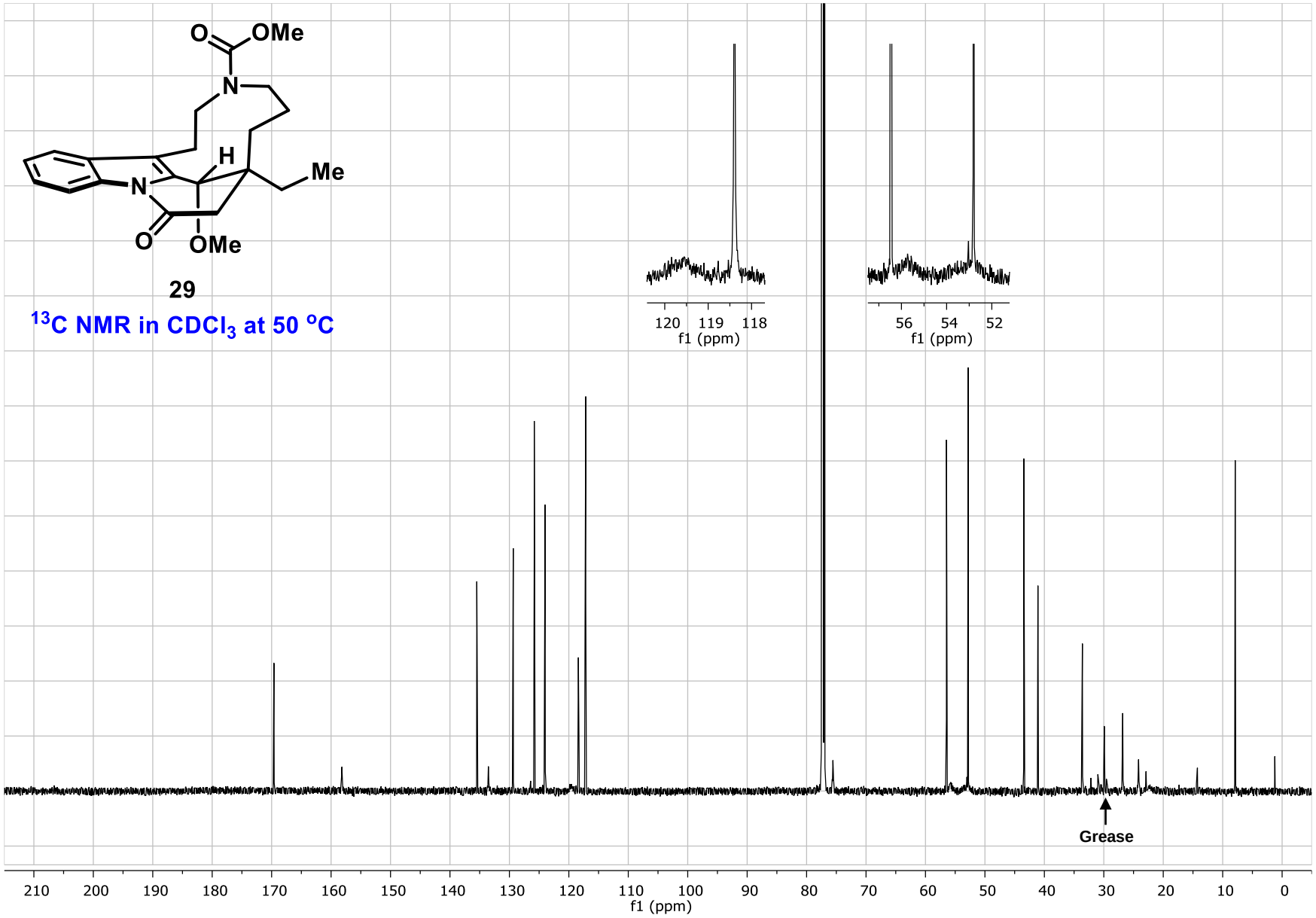


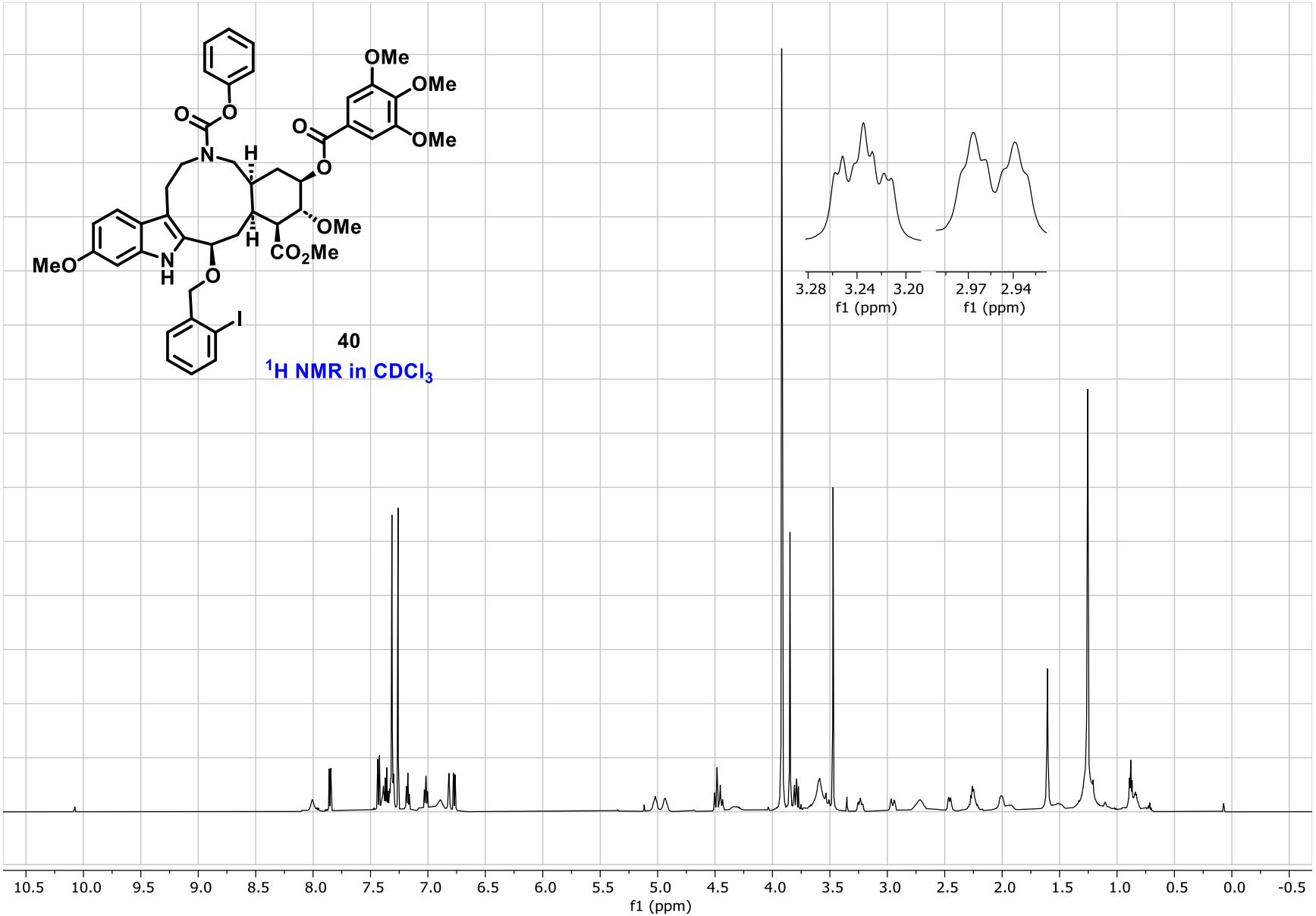
Compound 74: COSY, T = 100 °C,
$C_2D_2Cl_4$ (zoomed in)

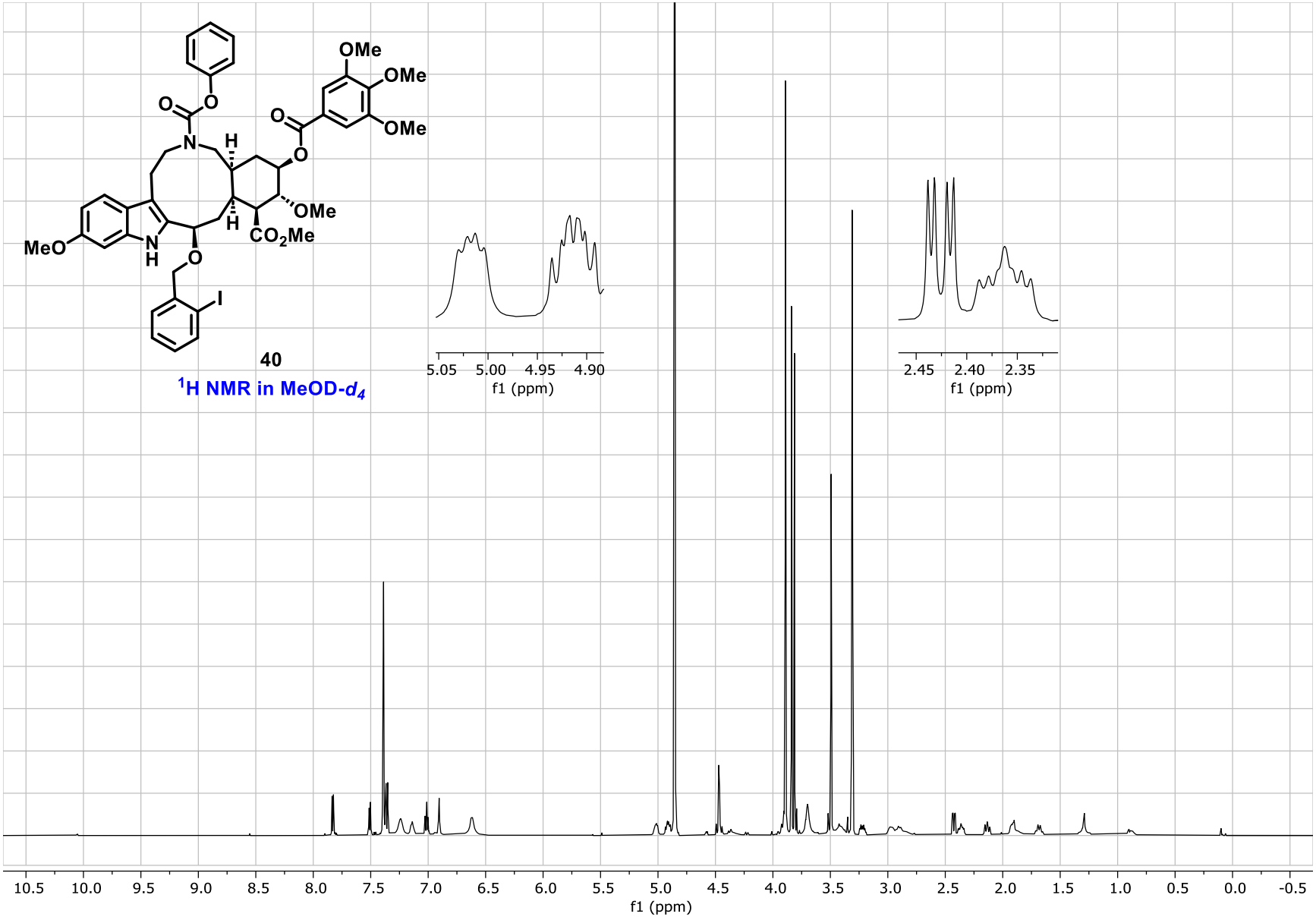


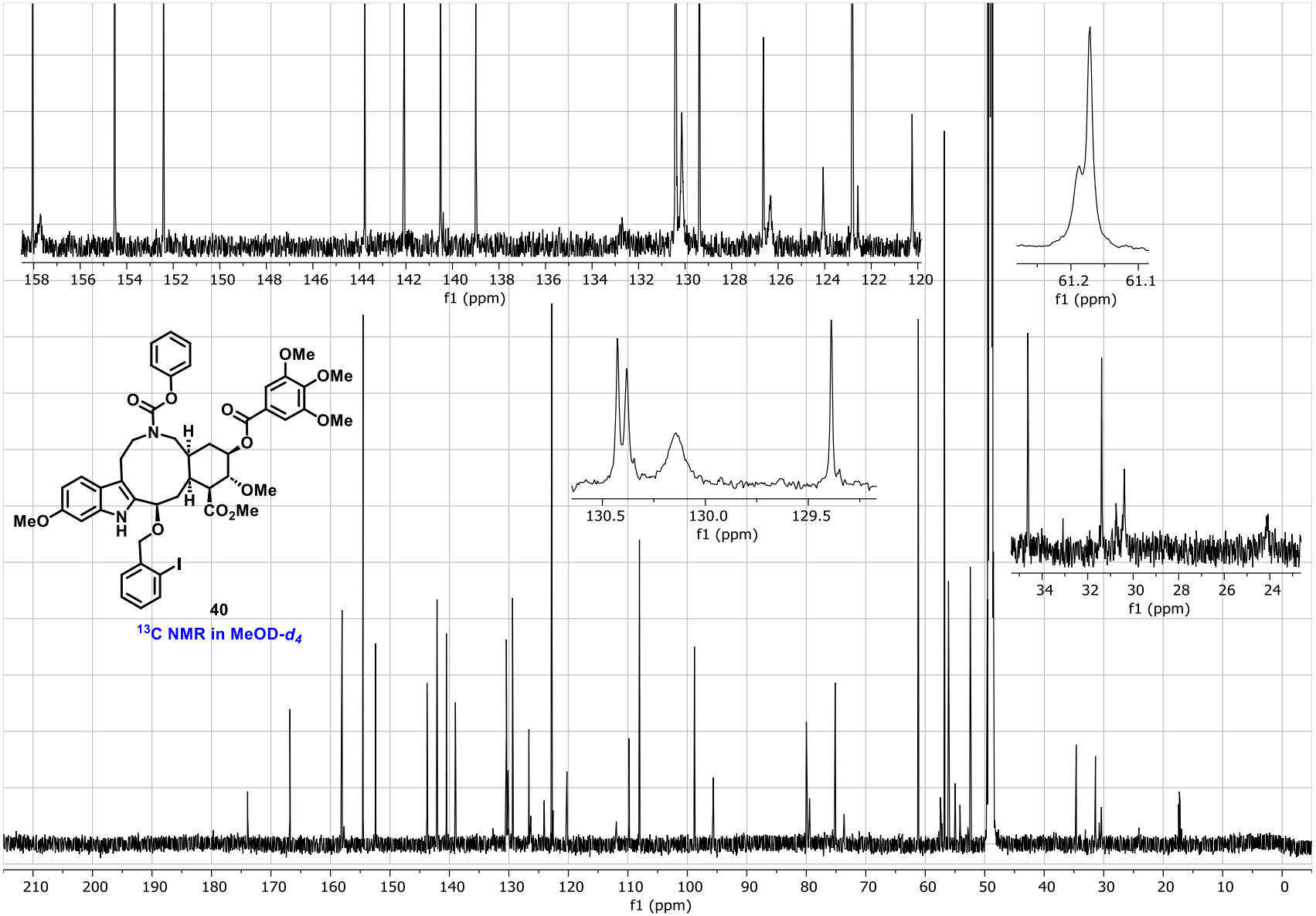
29

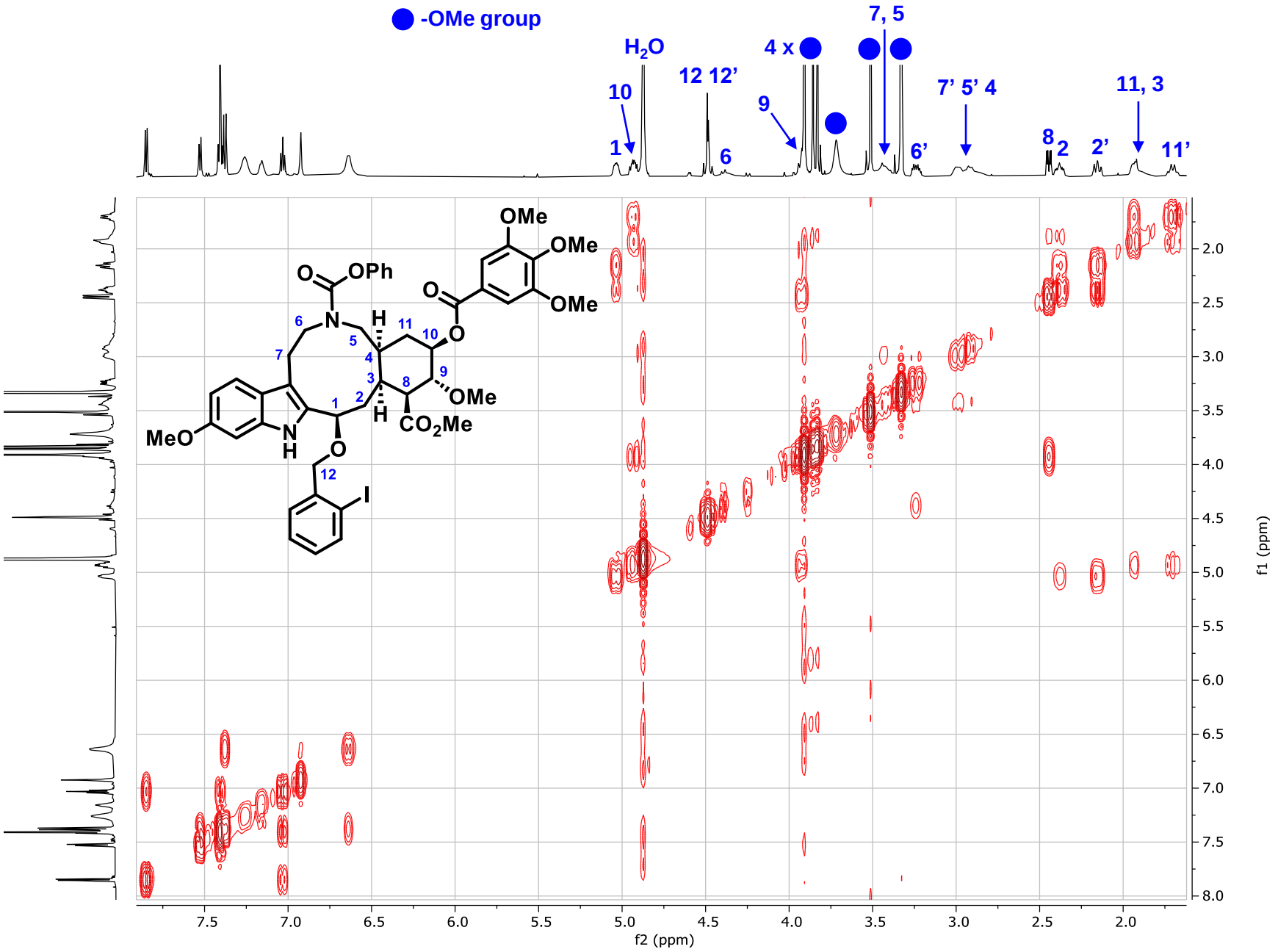
^{1}H NMR in $CDCl_3$ at 50 °C


O
OMe
N
H
Me
N
O
OMe
29
^{13}C NMR in CDCl$_3$ at 50 ^{o}C
120 119 118
f1 (ppm)
56 54 52
f1 (ppm)
Grease
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

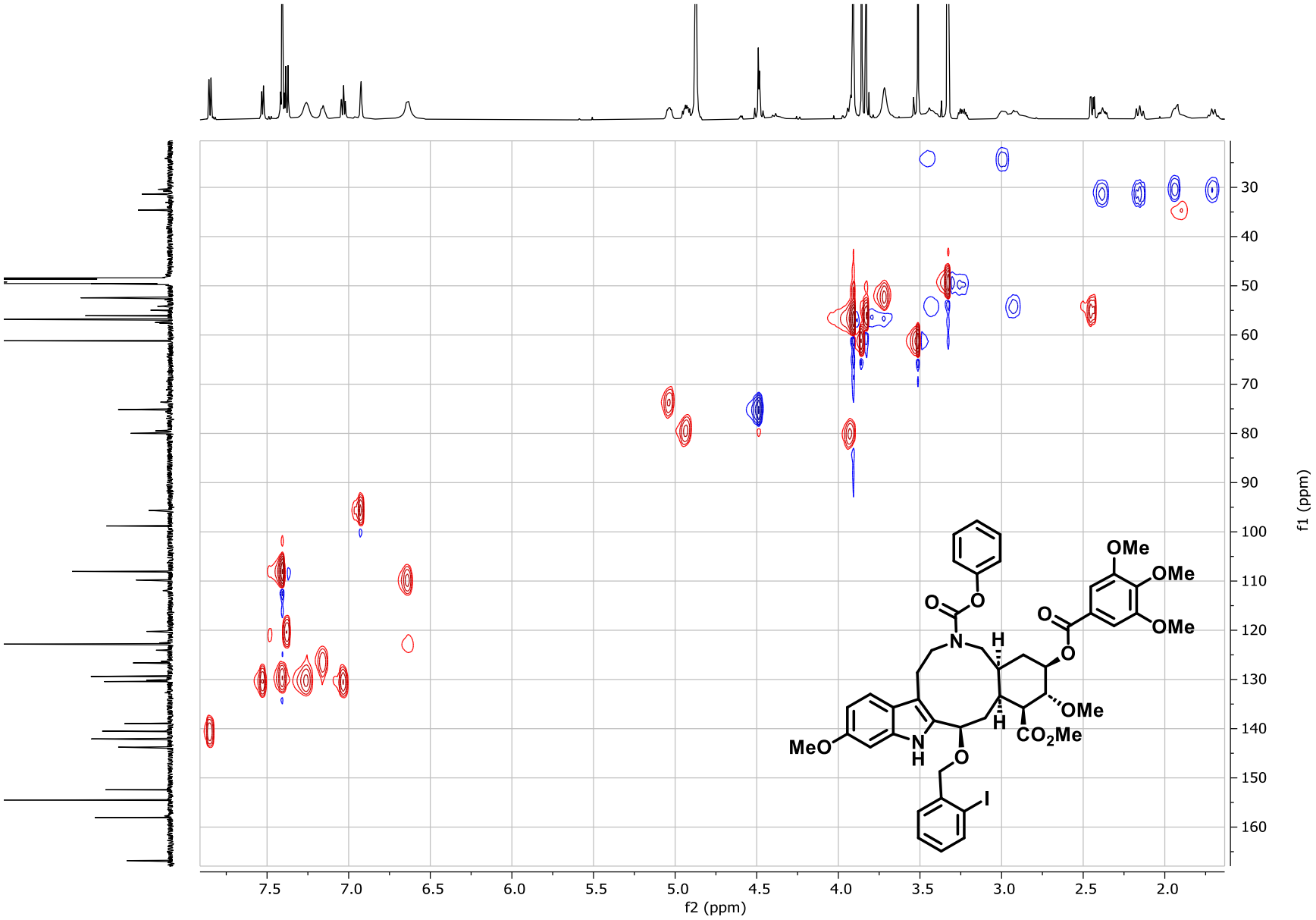

OMe
OMe
OMe
O
O
O
O
N
H
H
OMe
CO2Me
MeO
N
H
O
I
40
1H NMR in CDCl3
3.28
3.24
3.20
f1 (ppm)
2.97
2.94
f1 (ppm)
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


OMe
OMe
OMe
O
O
O
O
N
H
H
OMe
CO2Me
MeO
N
H
O
I
40
1H NMR in MeOD-d4
5.05 5.00 4.95 4.90
f1 (ppm)
2.45 2.40 2.35
f1 (ppm)
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

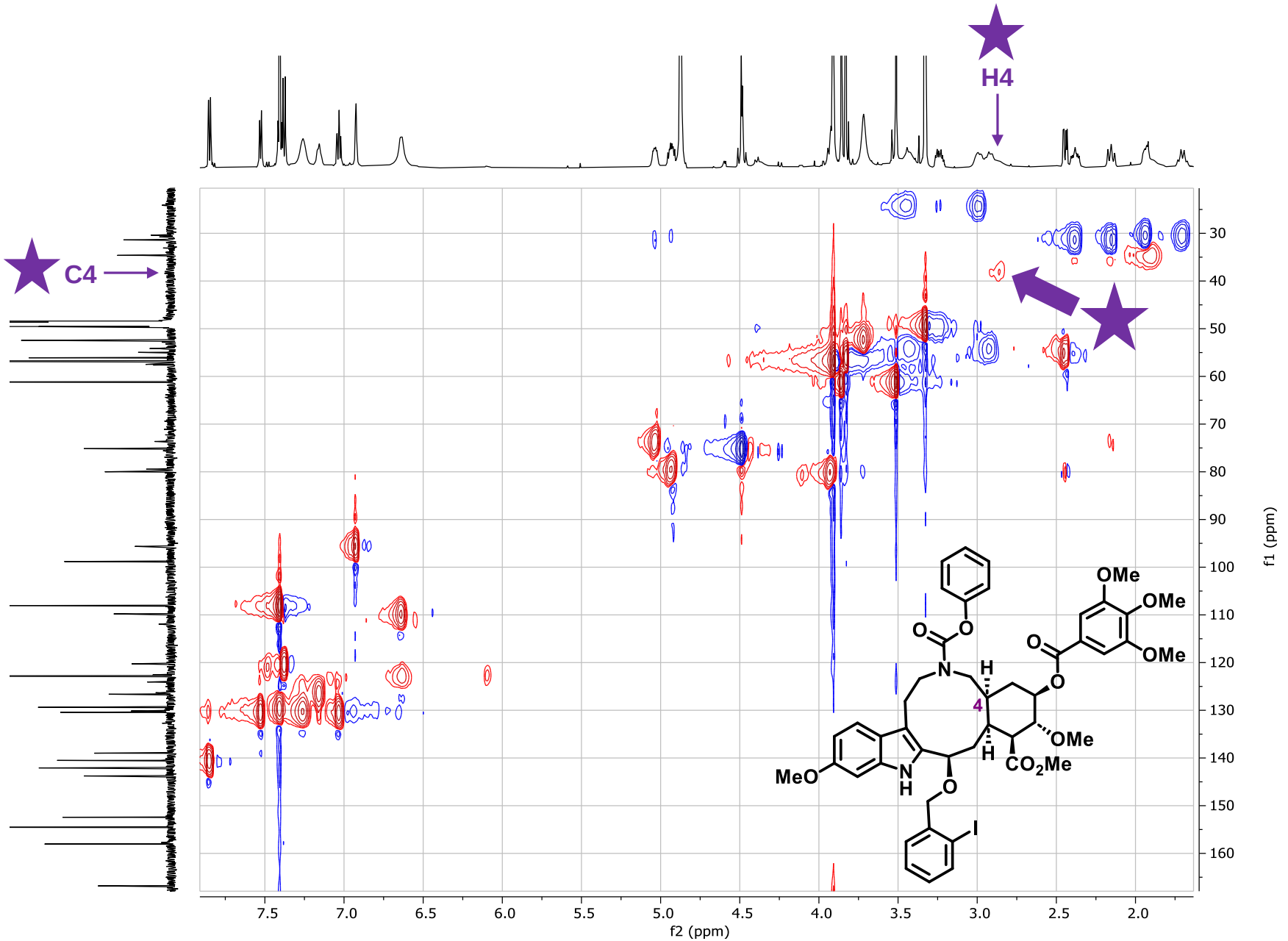

158 156 154 152 150 148 146 144 142 140 138 136 134 132 130 128 126 124 122 120
f1 (ppm)
61.2 61.1
f1 (ppm)
130.5 130.0 129.5
f1 (ppm)
34 32 30 28 26 24
f1 (ppm)
OMe
OMe
OMe
OMe
CO2Me
MeO
I
40
13C NMR in MeOD-d4
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



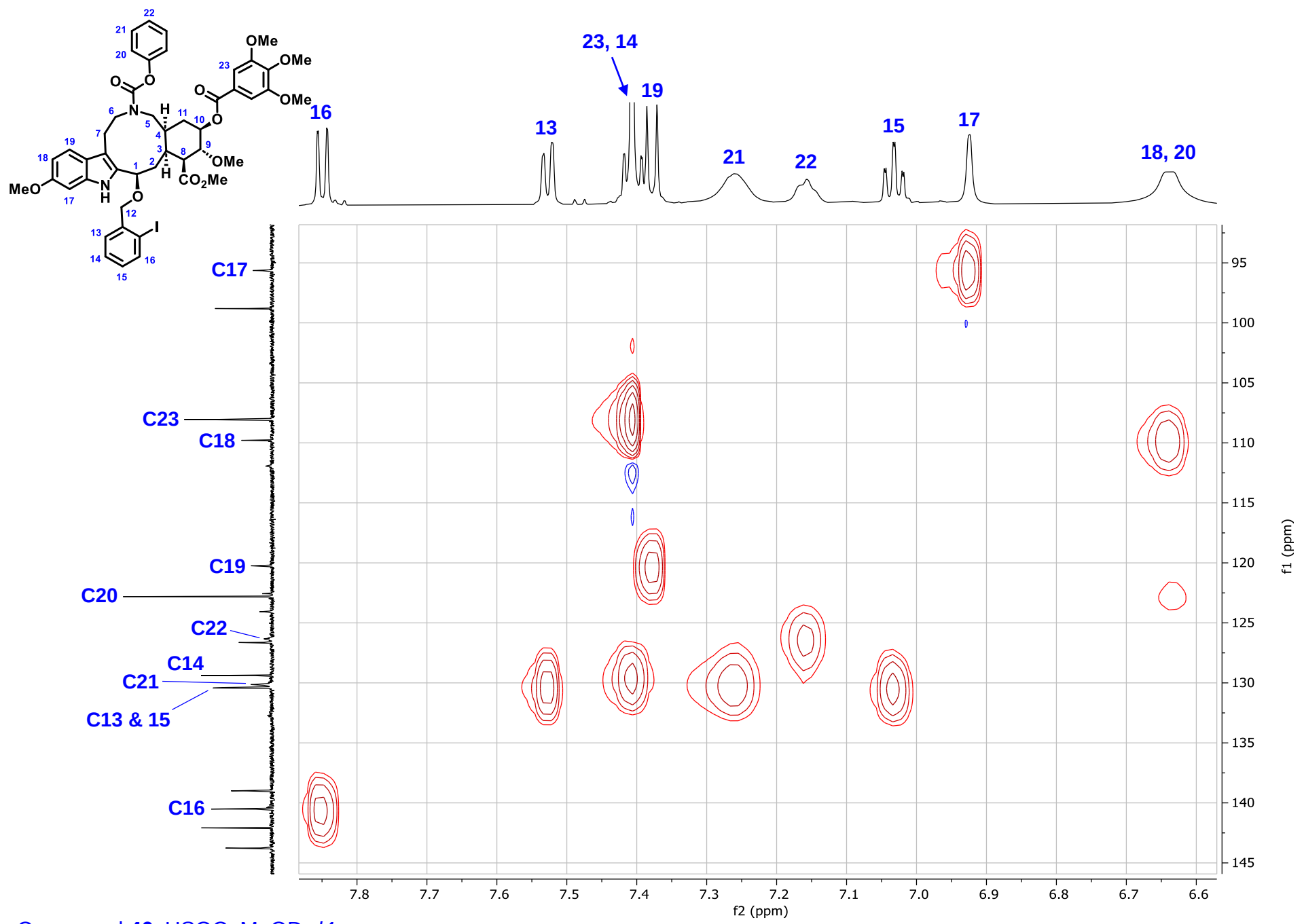
Compound 40: COSY, MeOD-*d4* (full)



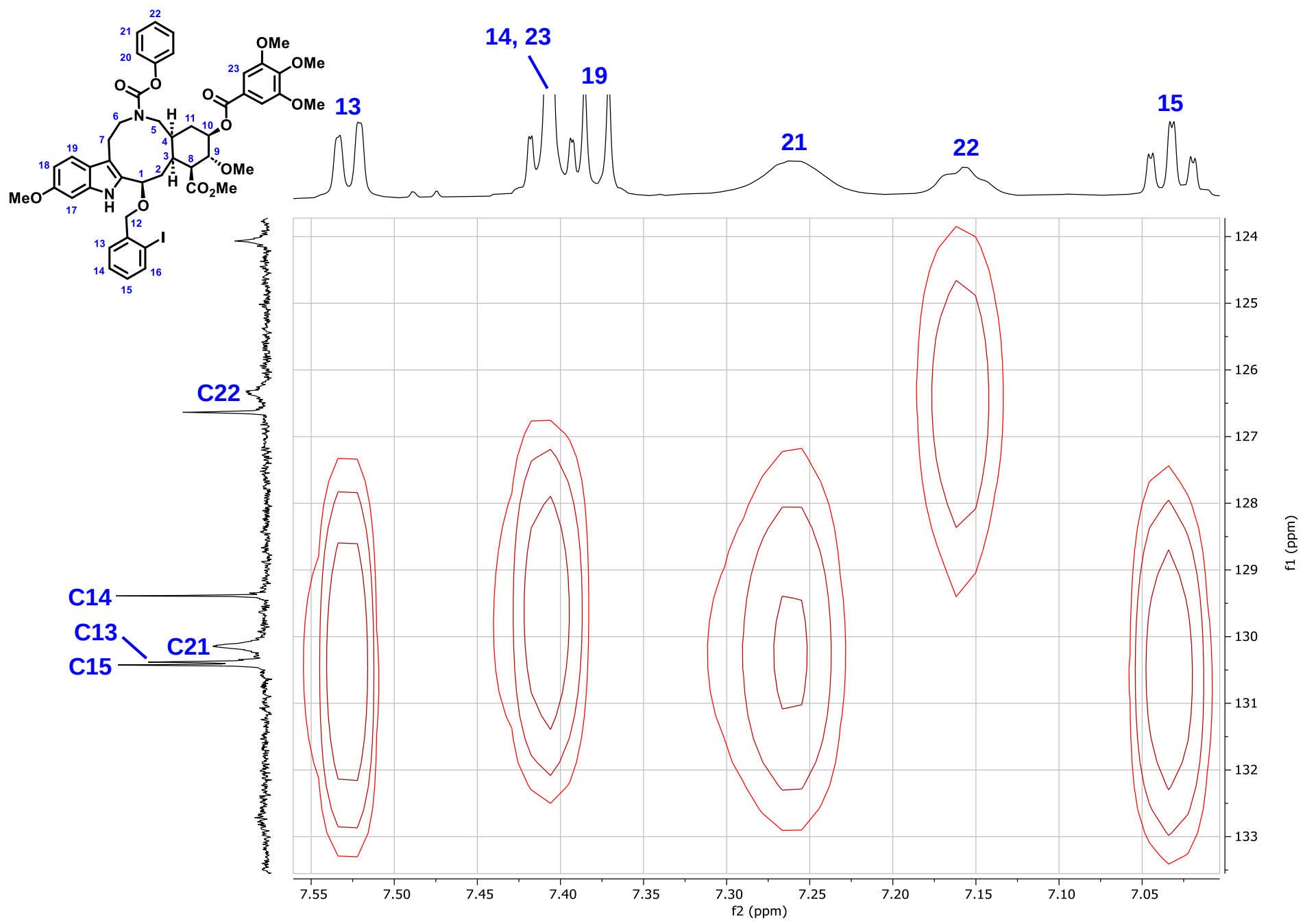
Compound 40: HSQC, MeOD-*d4* (full)



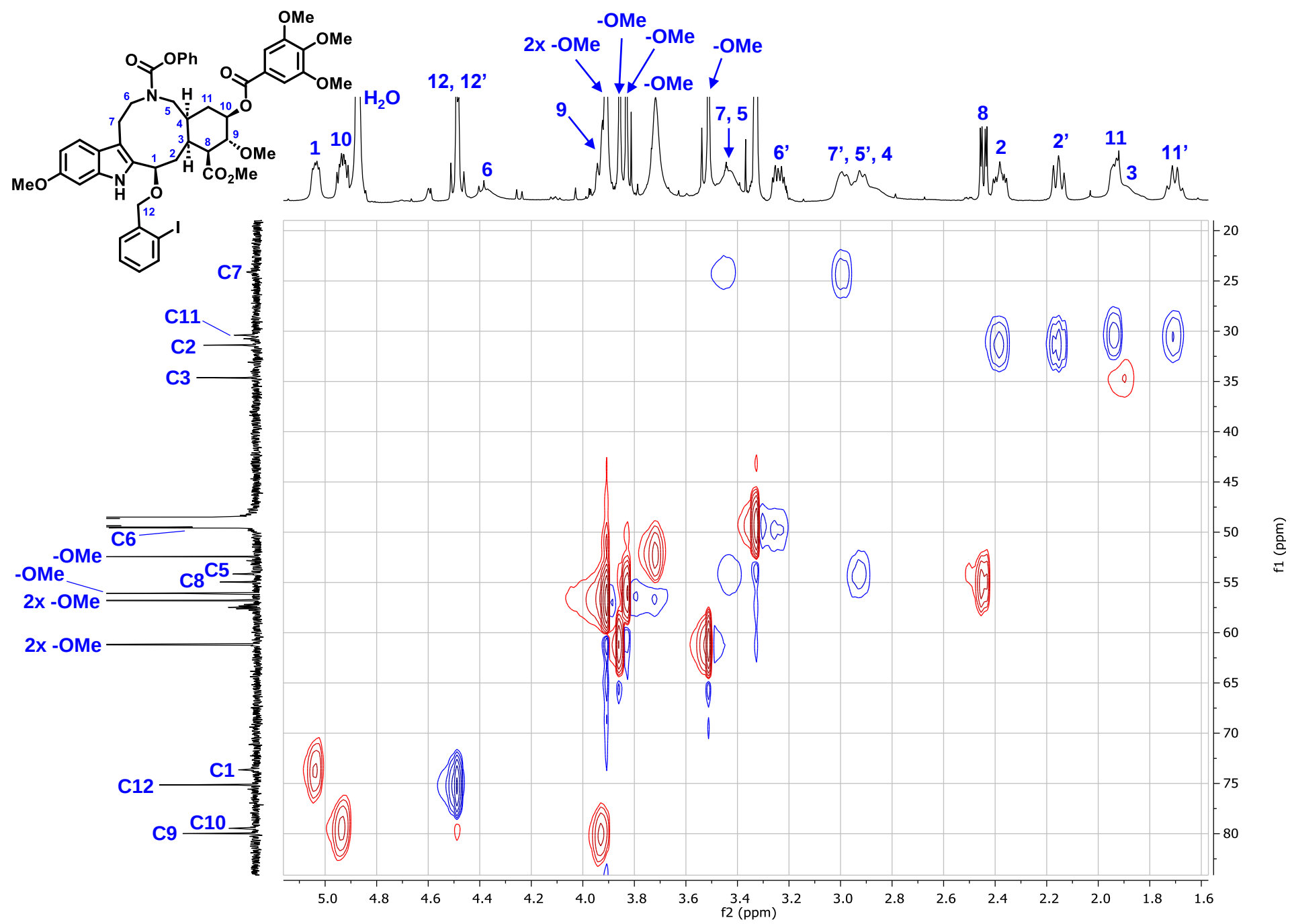
Compound **40**: HSQC, MeOD-*d4* (full, increased signal intensity to characterize the C13 signal for C4)



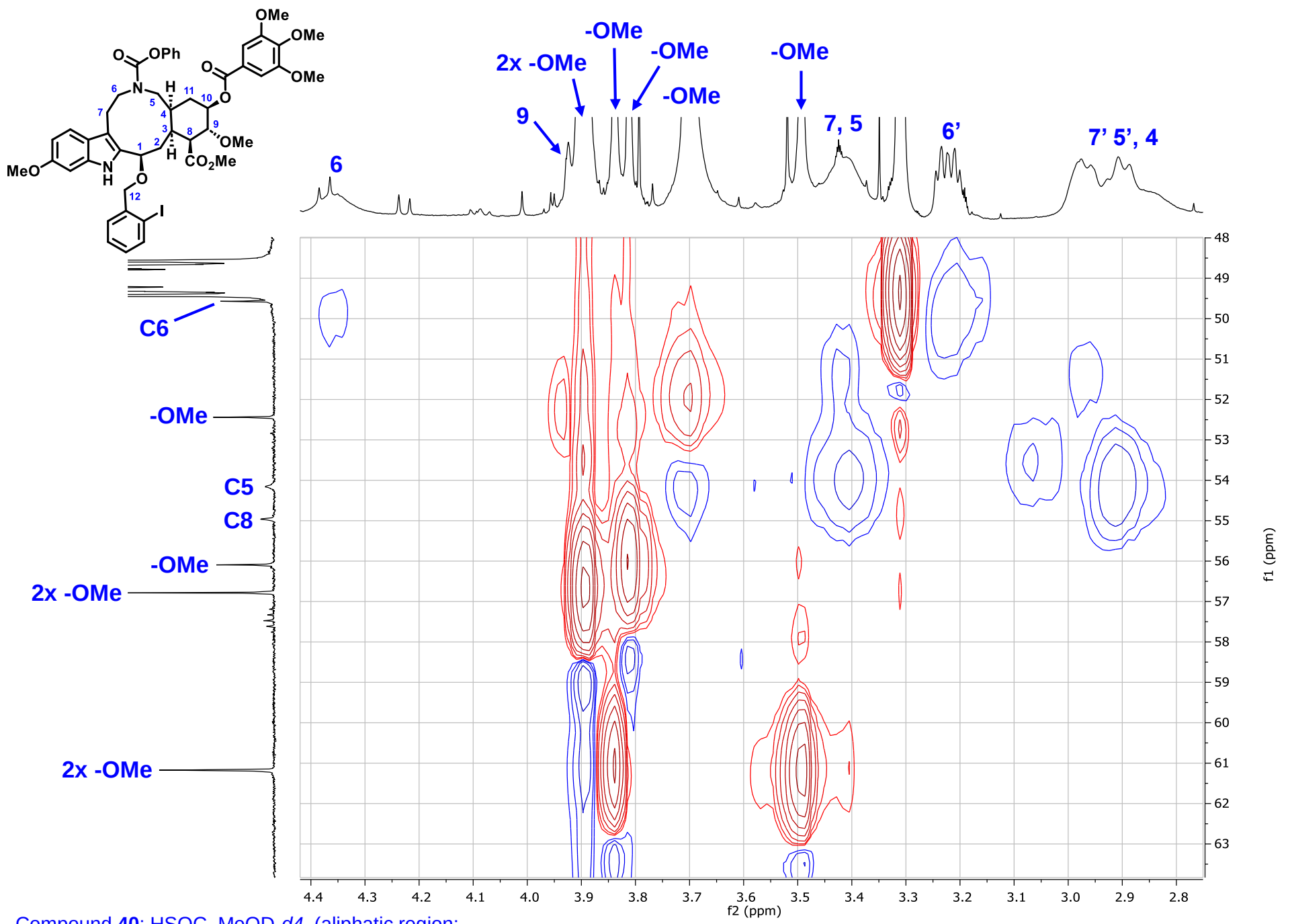
Compound **40**: HSQC, MeOD-*d4*
(aromatic region, version 1)



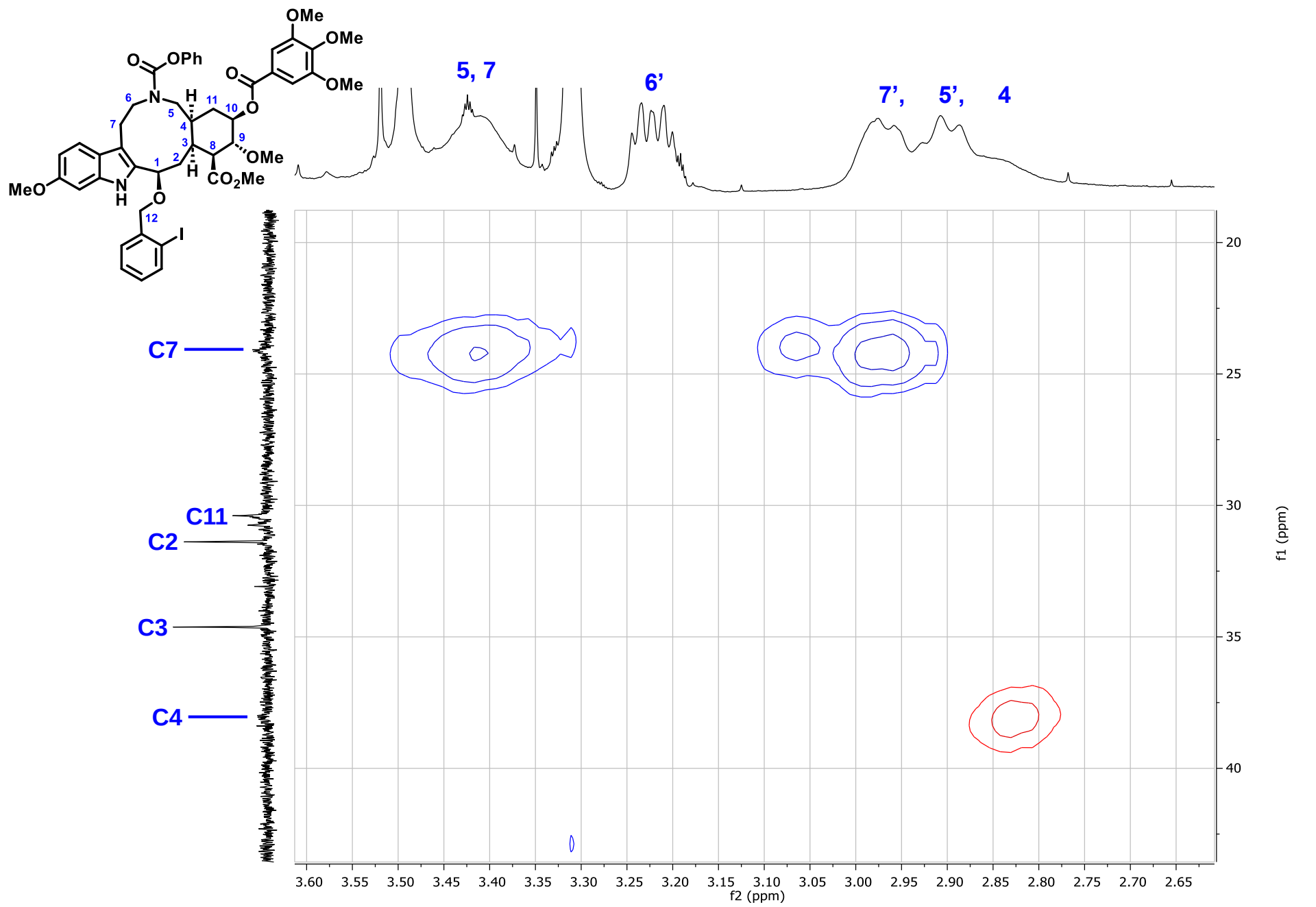
Compound 40: HSQC, MeOD-*d4*
(aromatic region, version 2)



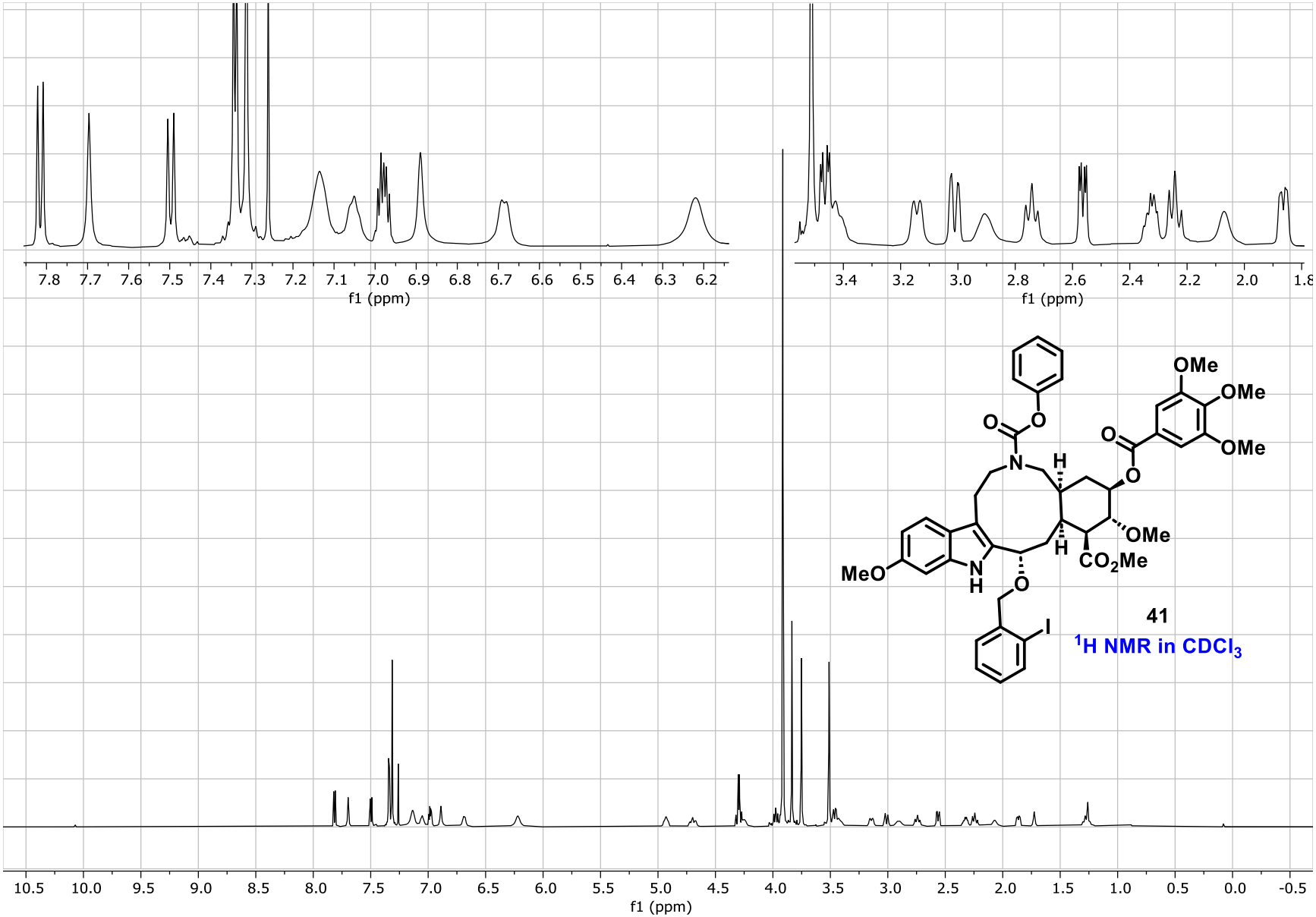
Compound 40: HSQC, MeOD-*d4* (aliphatic region)

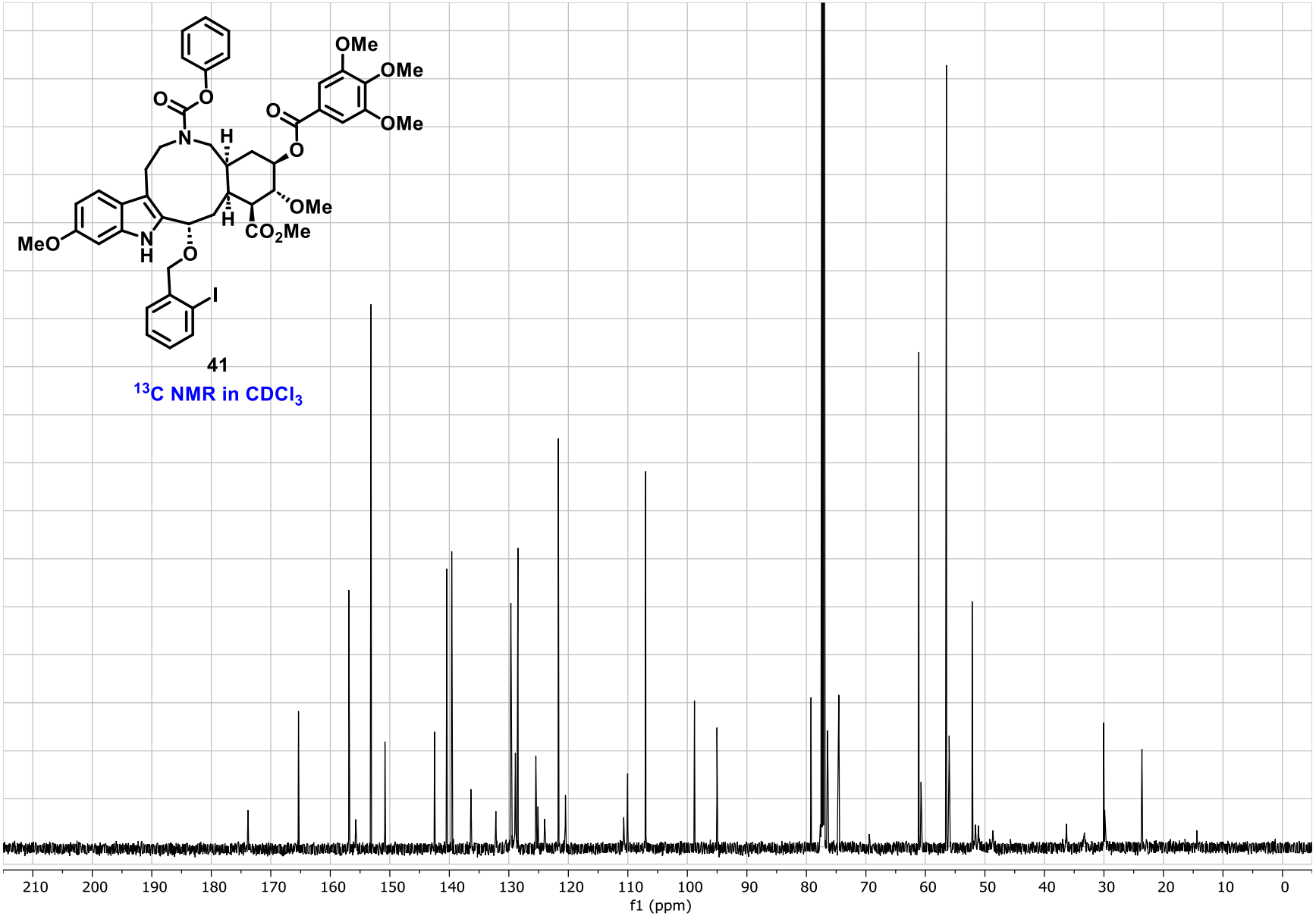


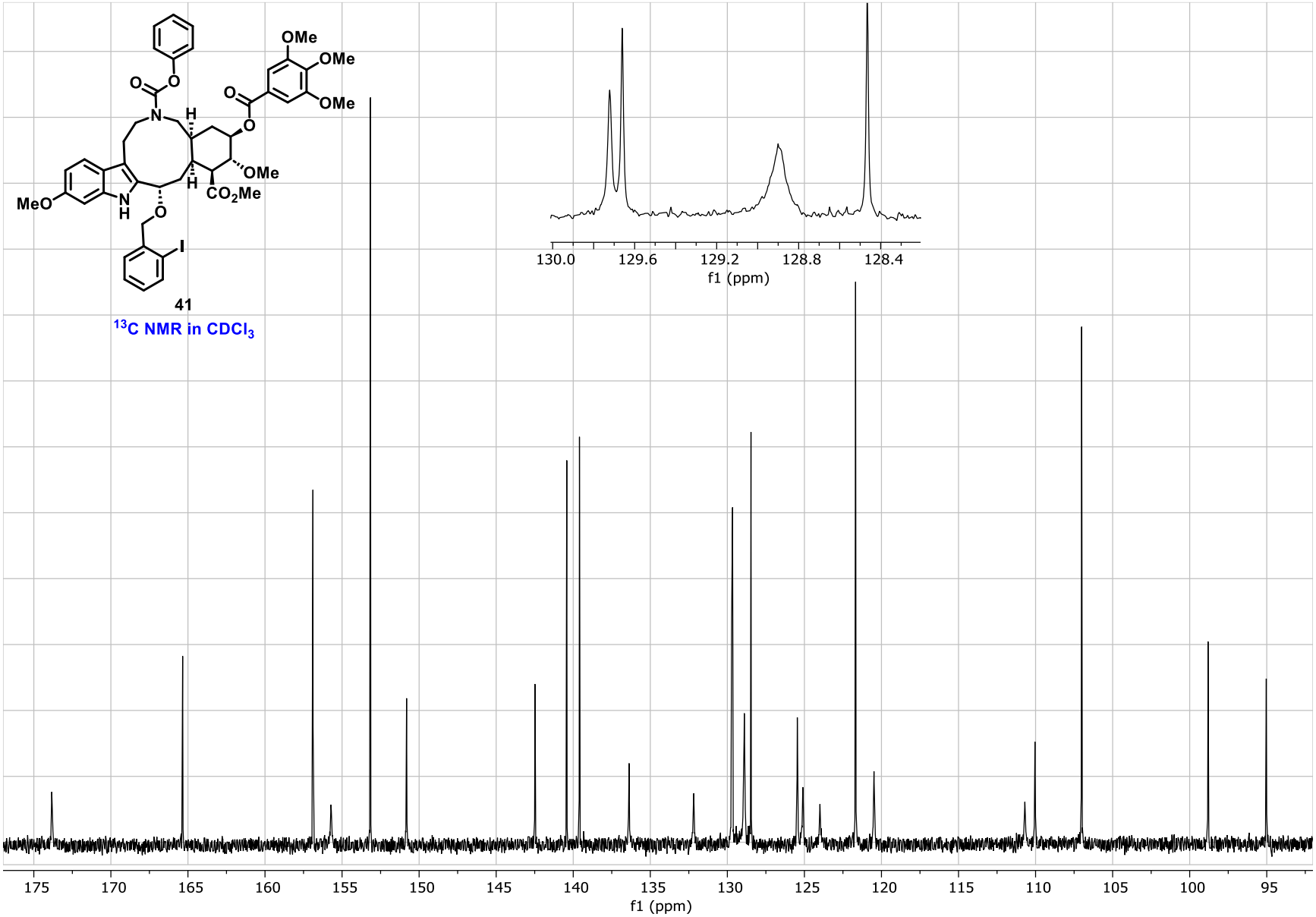
Compound **40**: HSQC, MeOD-*d4* (aliphatic region; zoomed in, version 1 with increased intensity)



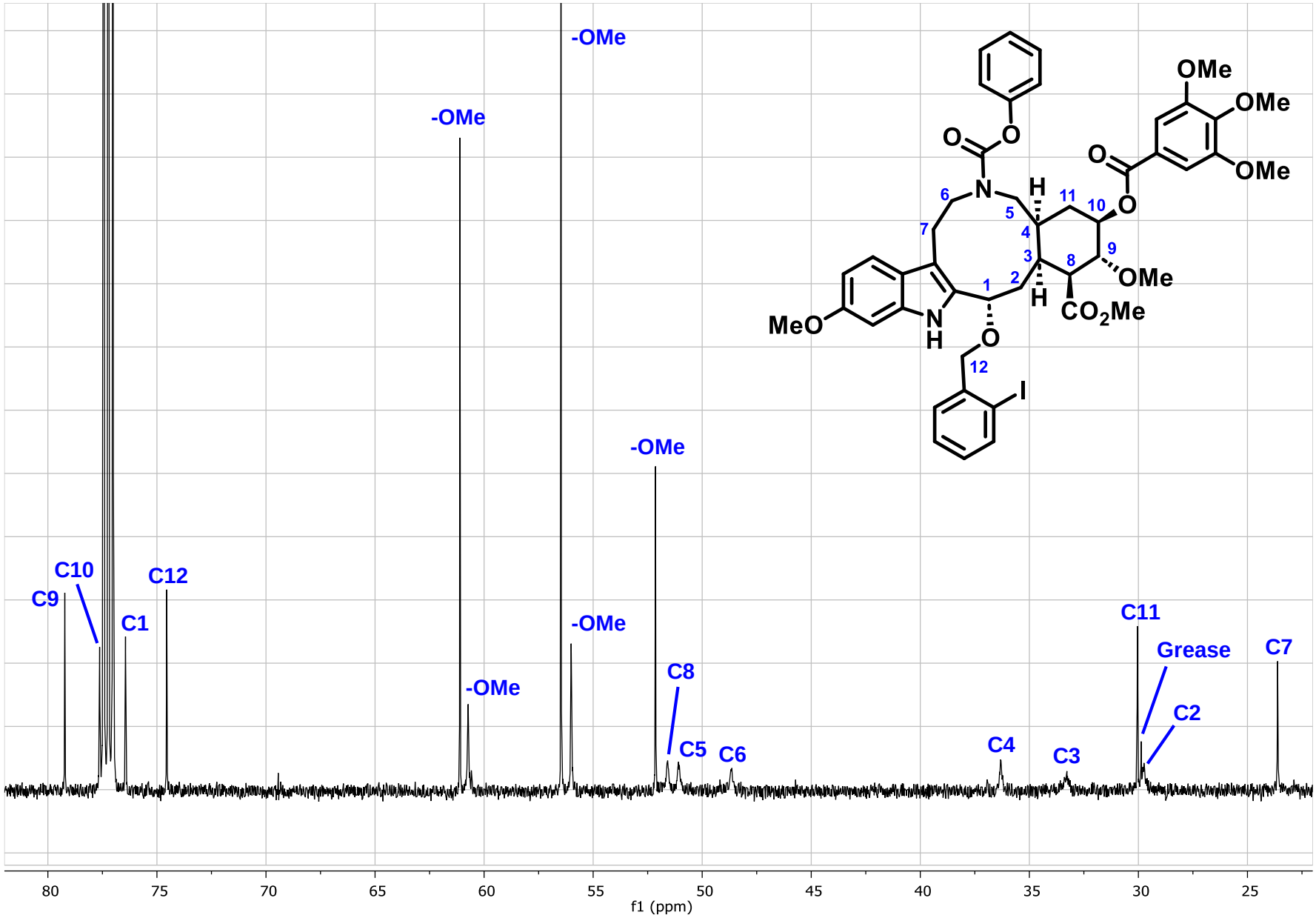
Compound **40**: HSQC, MeOD-*d4* (aliphatic region; zoomed in, version 2 with increased intensity)


7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7 6.6 6.5 6.4 6.3 6.2
f1 (ppm)
3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8
f1 (ppm)
OMe
OMe
OMe
O
O
O
N
H
O
OMe
H
CO2Me
MeO
N
H
O
I
41
1H NMR in CDCl3
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

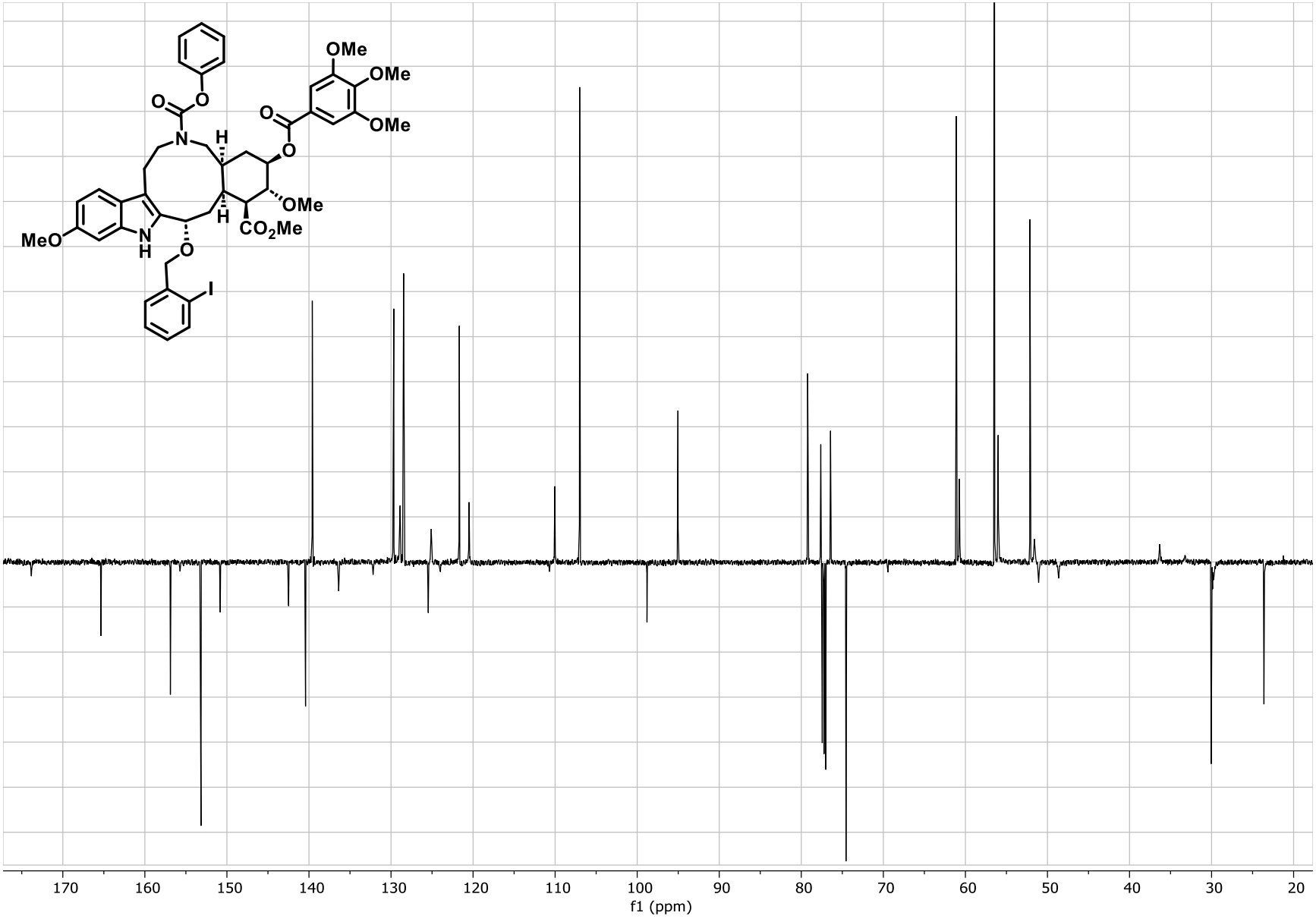

OMe
OMe
OMe
O
O
O
O
N
H
O
OMe
H
CO2Me
MeO
N
H
O
I
41
13C NMR in CDCl3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



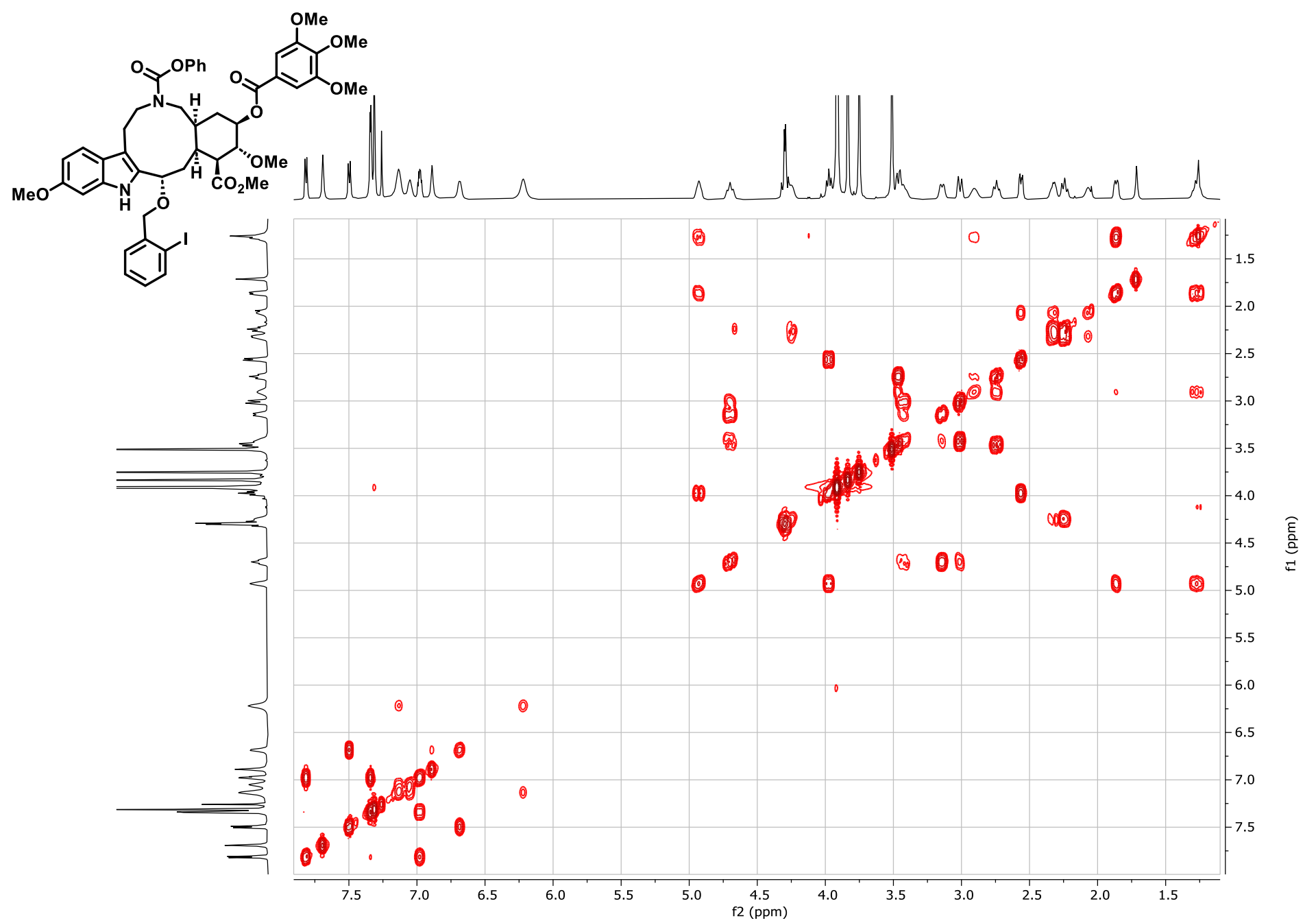
Compound 41: ^{13}C NMR, $CDCl_3$ (aromatic region)



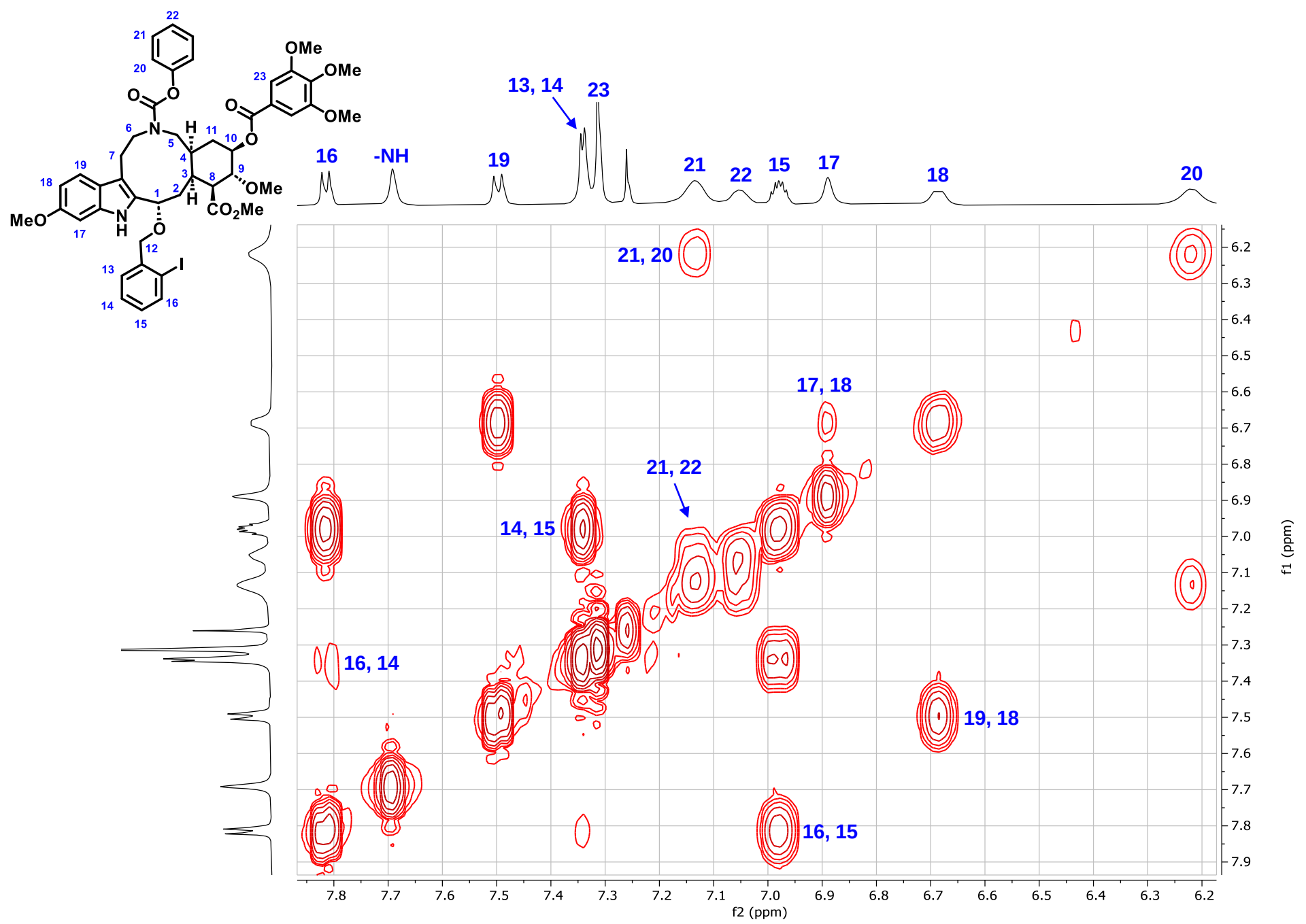
Compound 41: ^{13}C NMR, $CDCl_3$ (aliphatic region)



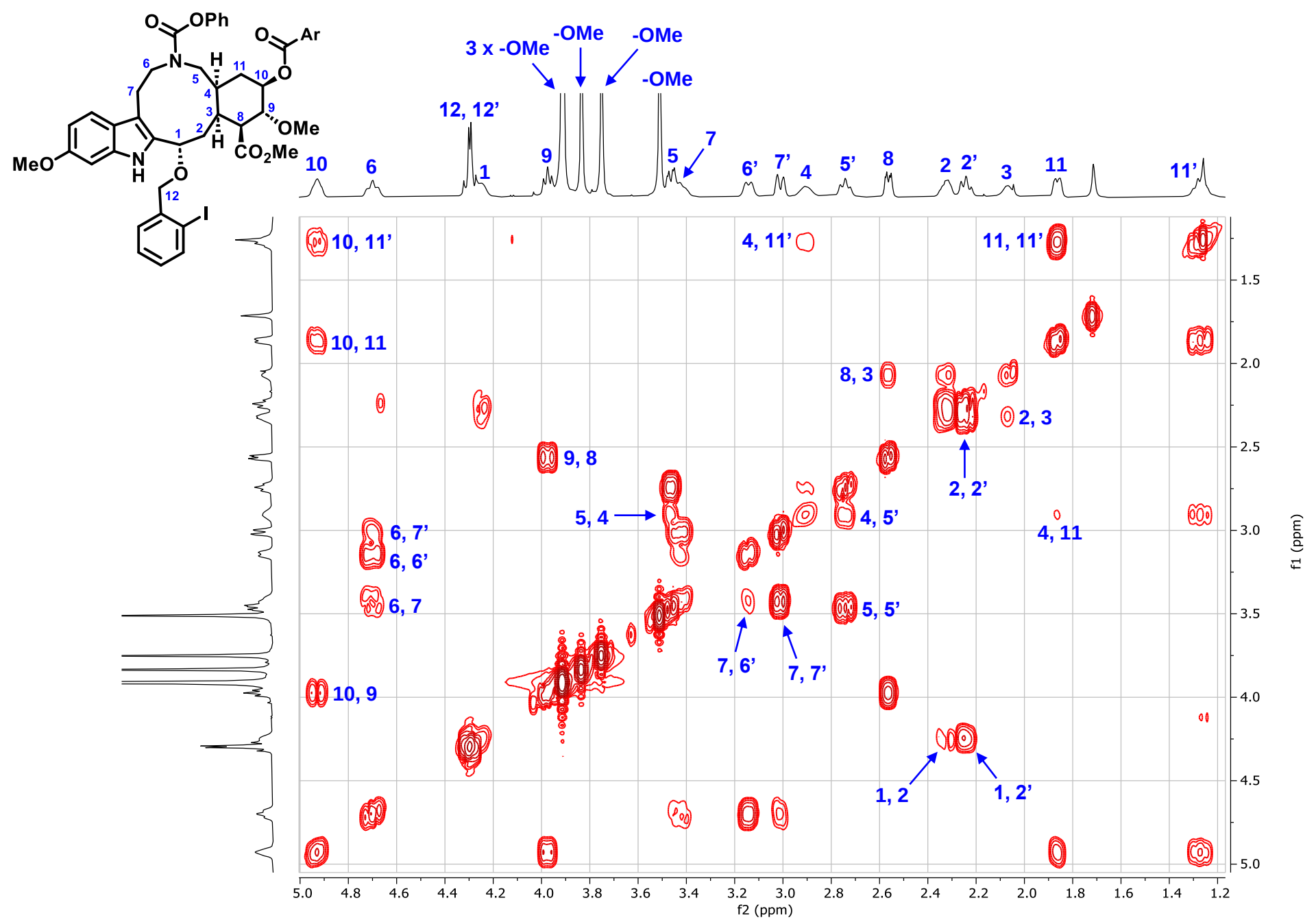
Compound 41: DEPT, $CDCl_3$



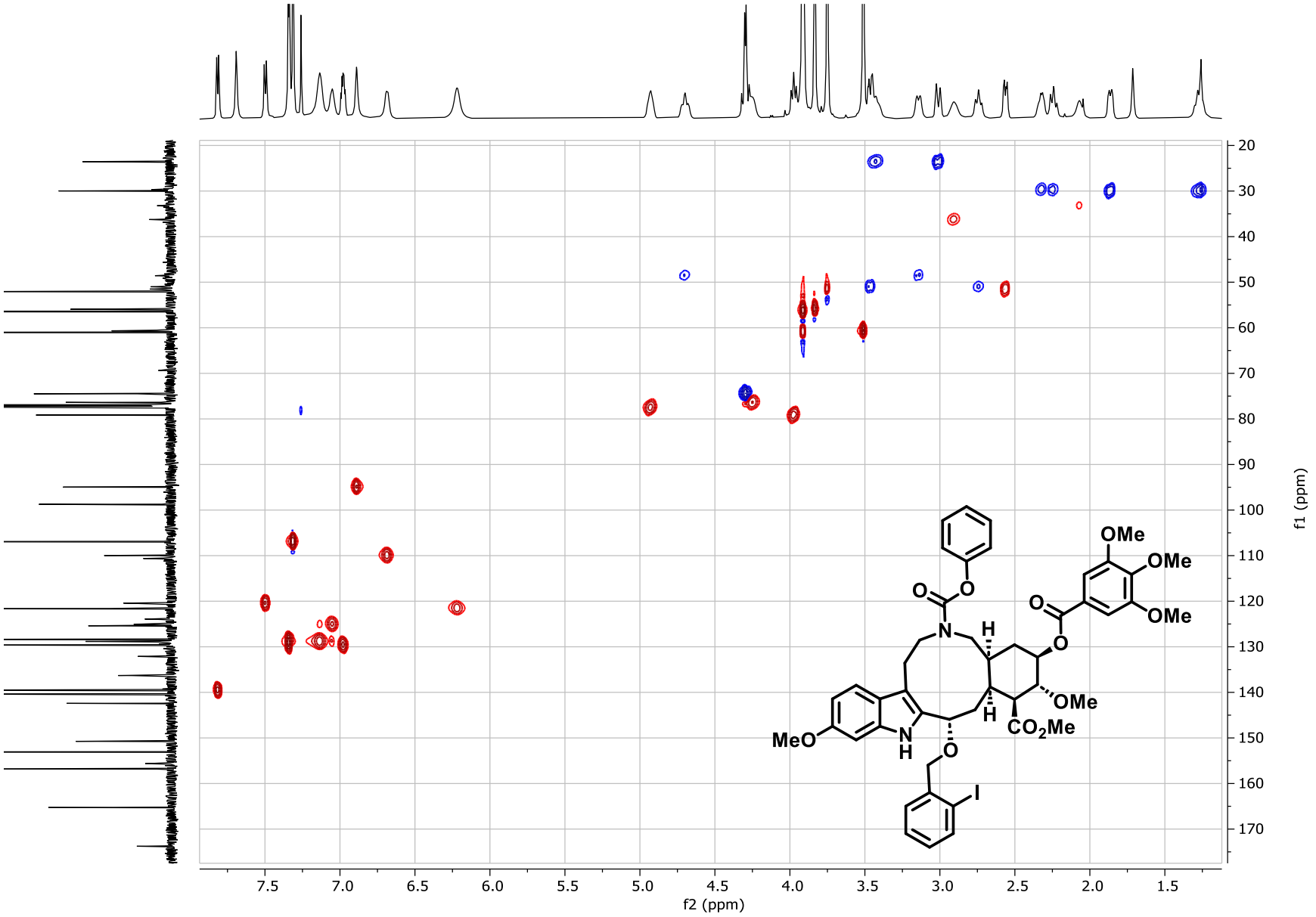
Compound 41: COSY, $CDCl_3$ (full)



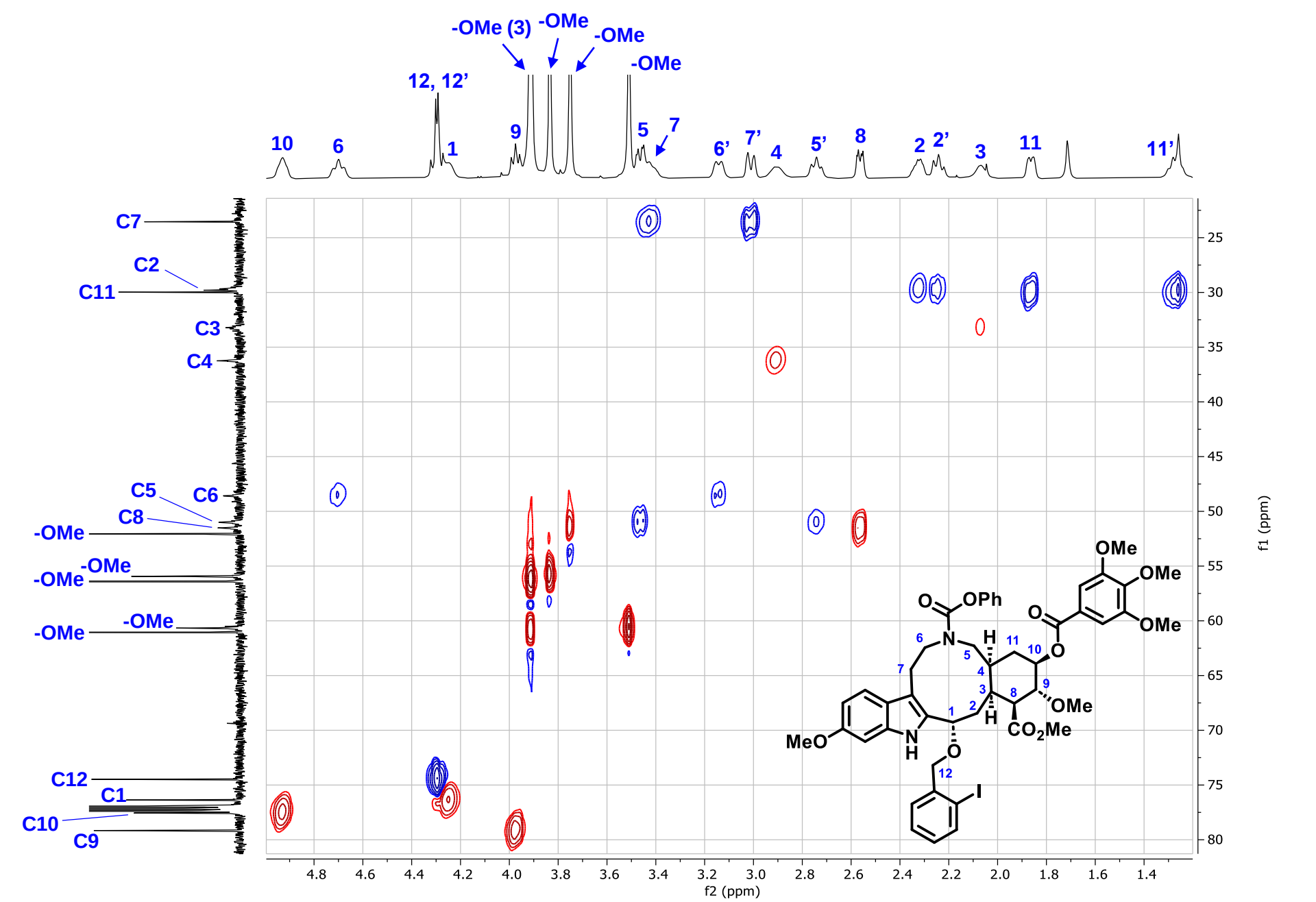
Compound 41: COSY, $CDCl_3$ (aromatic region)



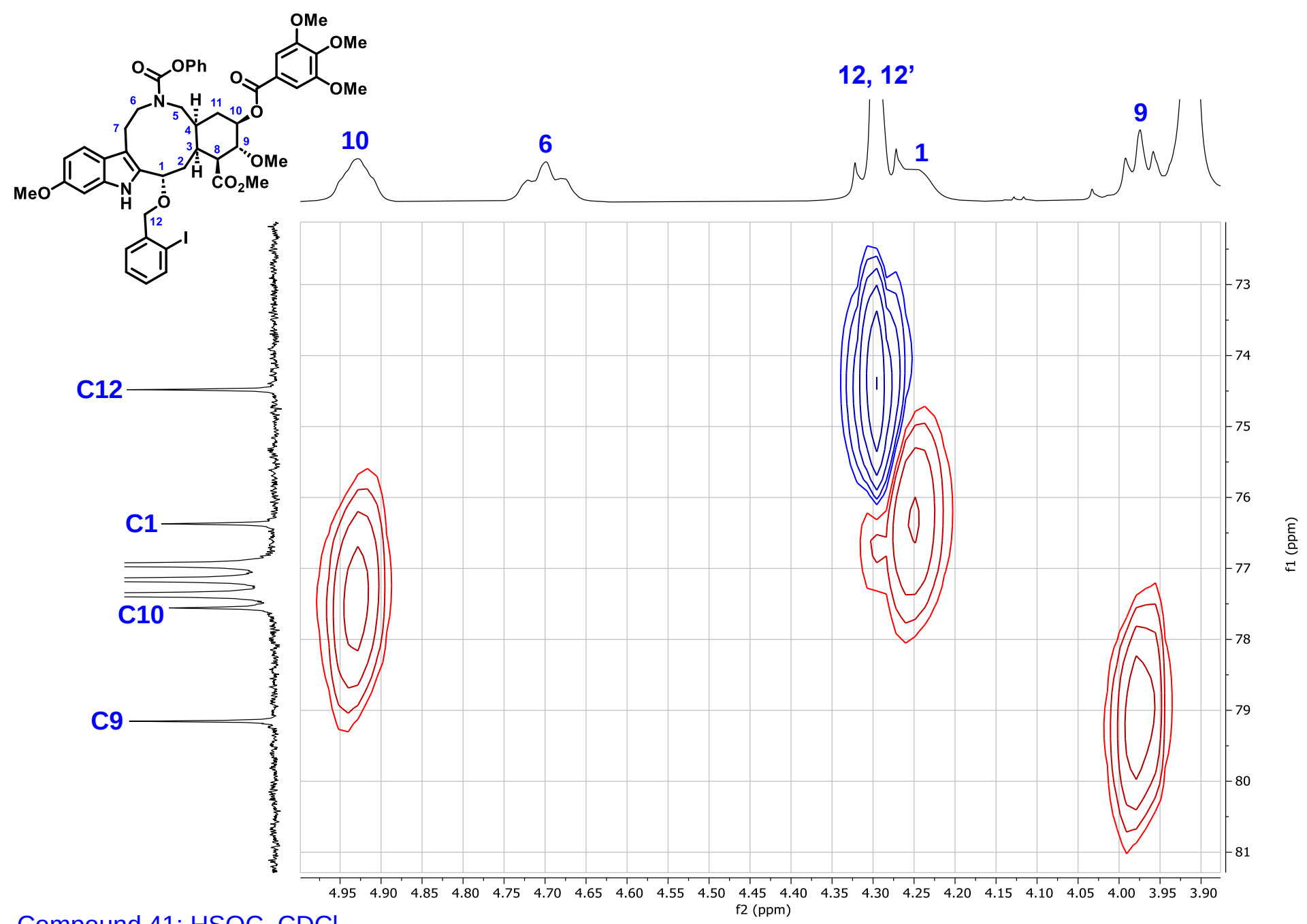
Compound 41: COSY, $CDCl_3$ (aliphatic region)



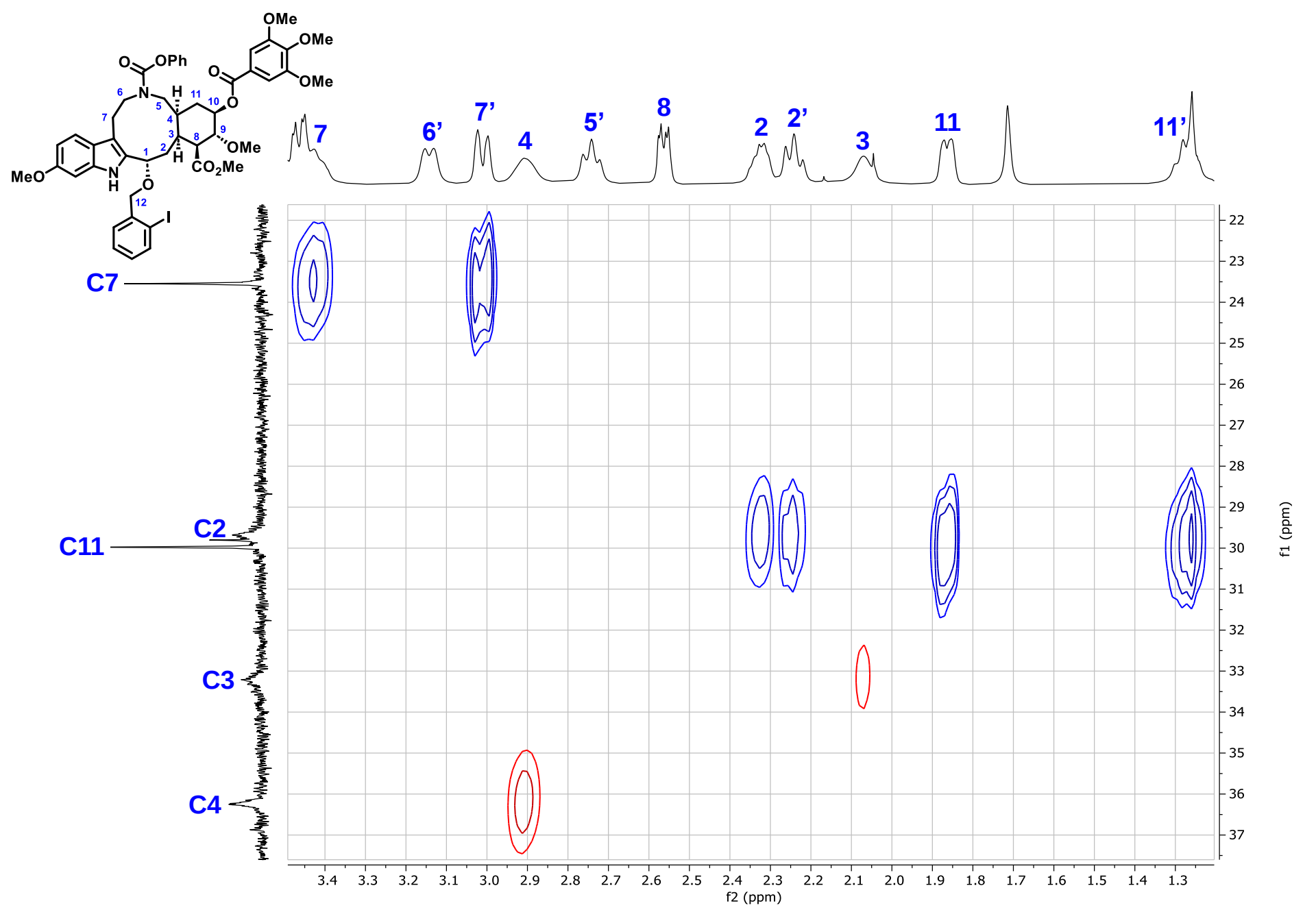
Compound 41: HSQC, $CDCl_3$ (full)



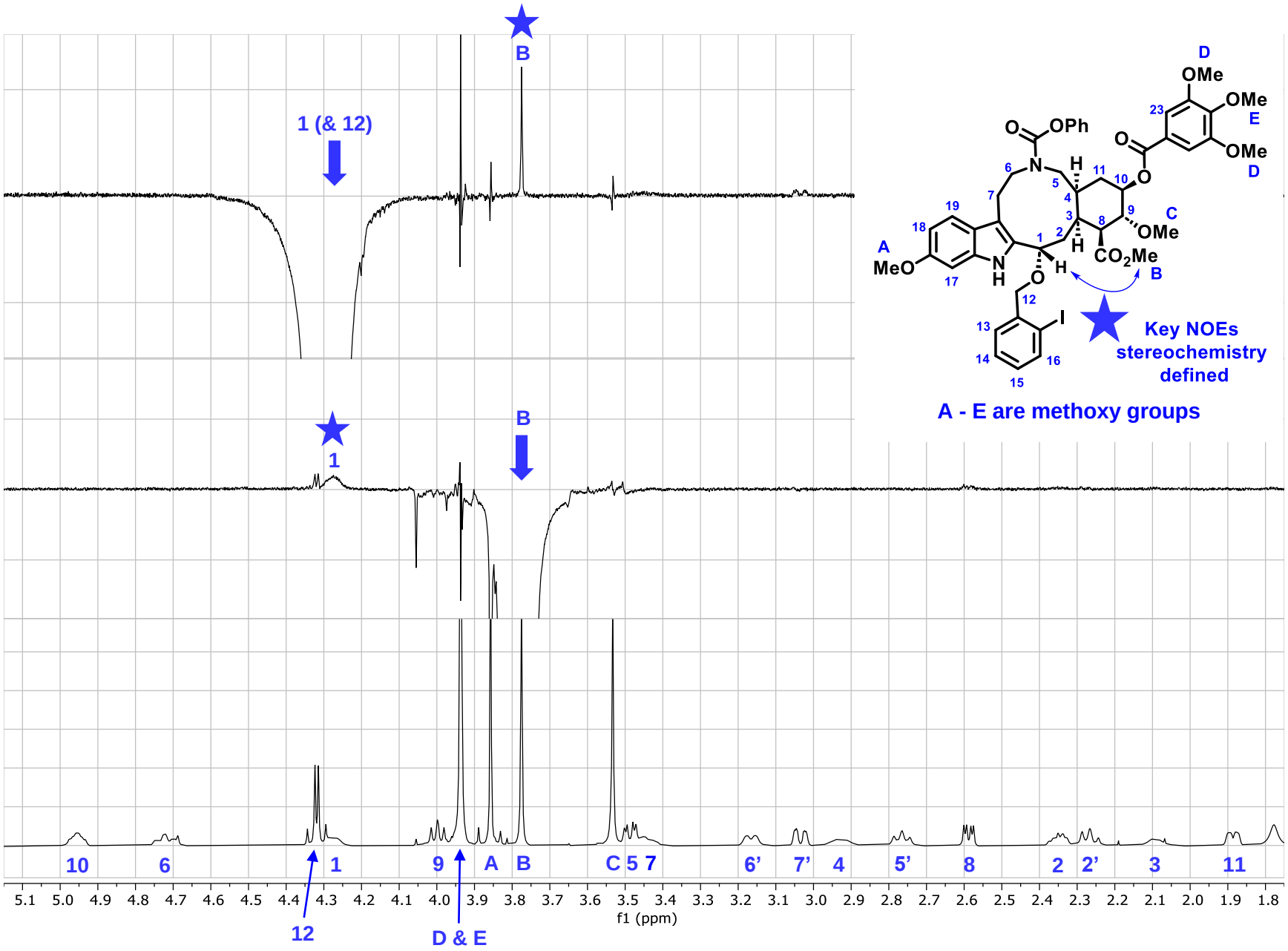
Compound 41: HSQC, $CDCl_3$
(zoomed in, version 1)



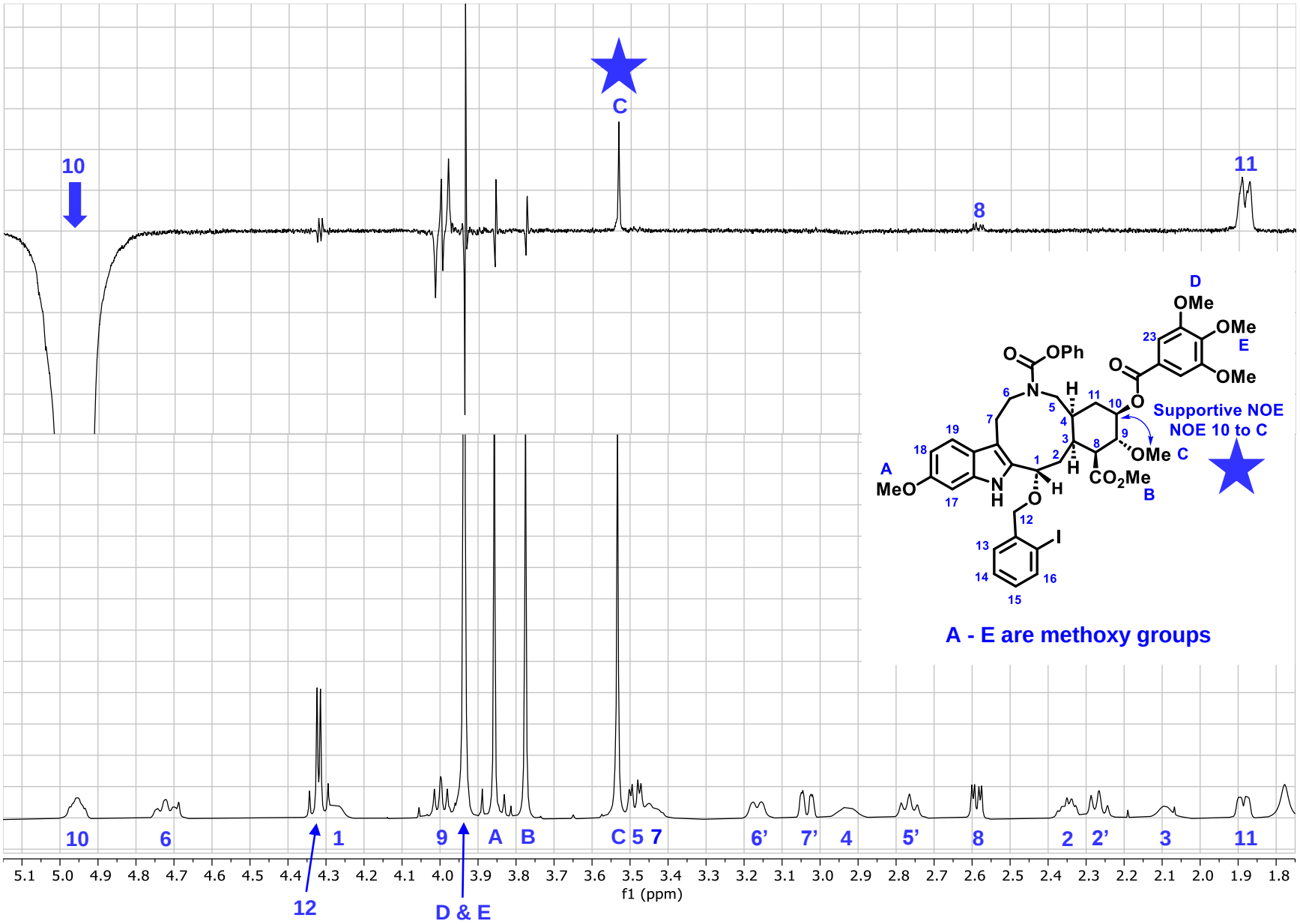
Compound 41: HSQC, $CDCl_3$
(zoomed in, version 2)



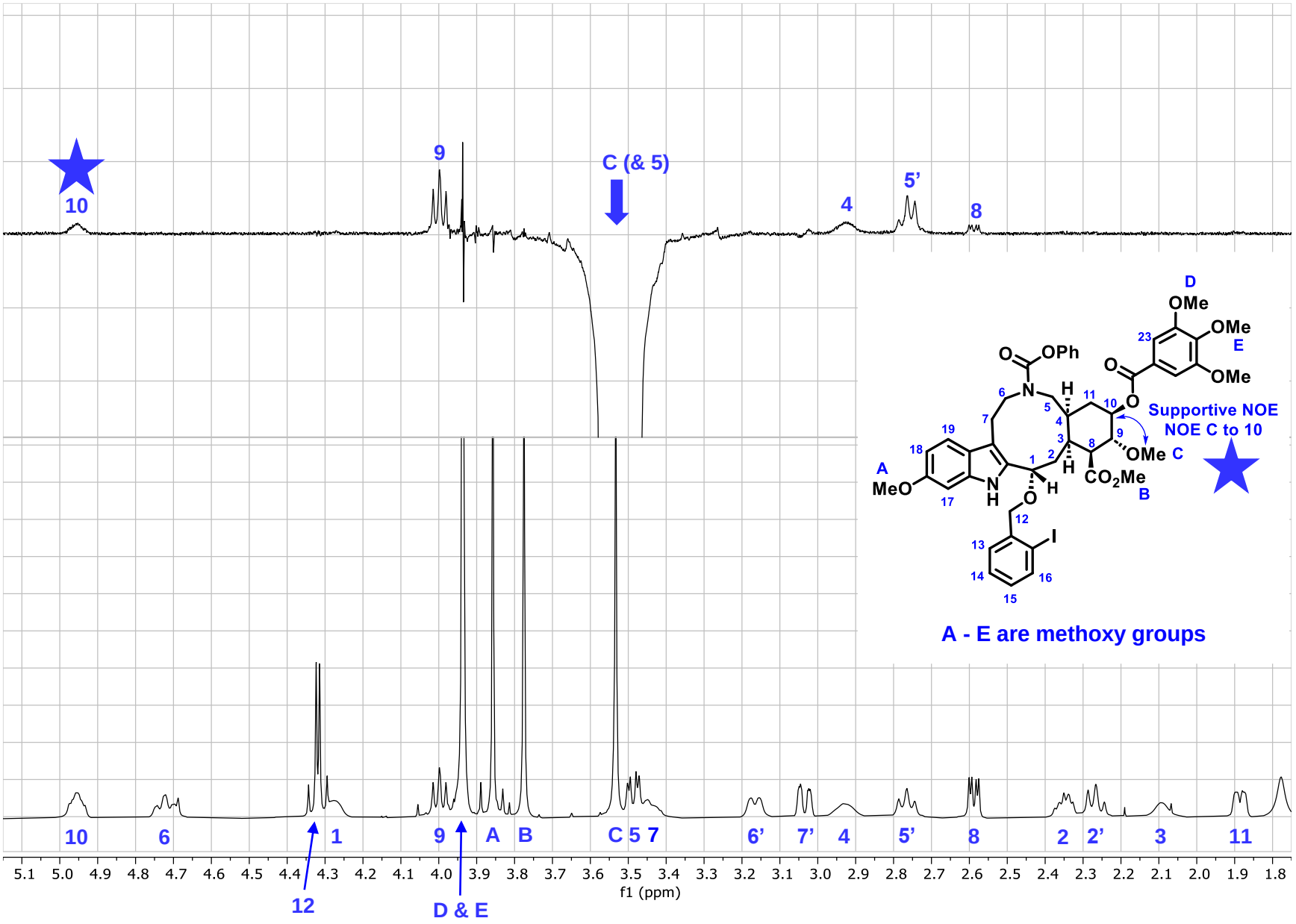
Compound 41: HSQC, $CDCl_3$
(zoomed in, version 3)



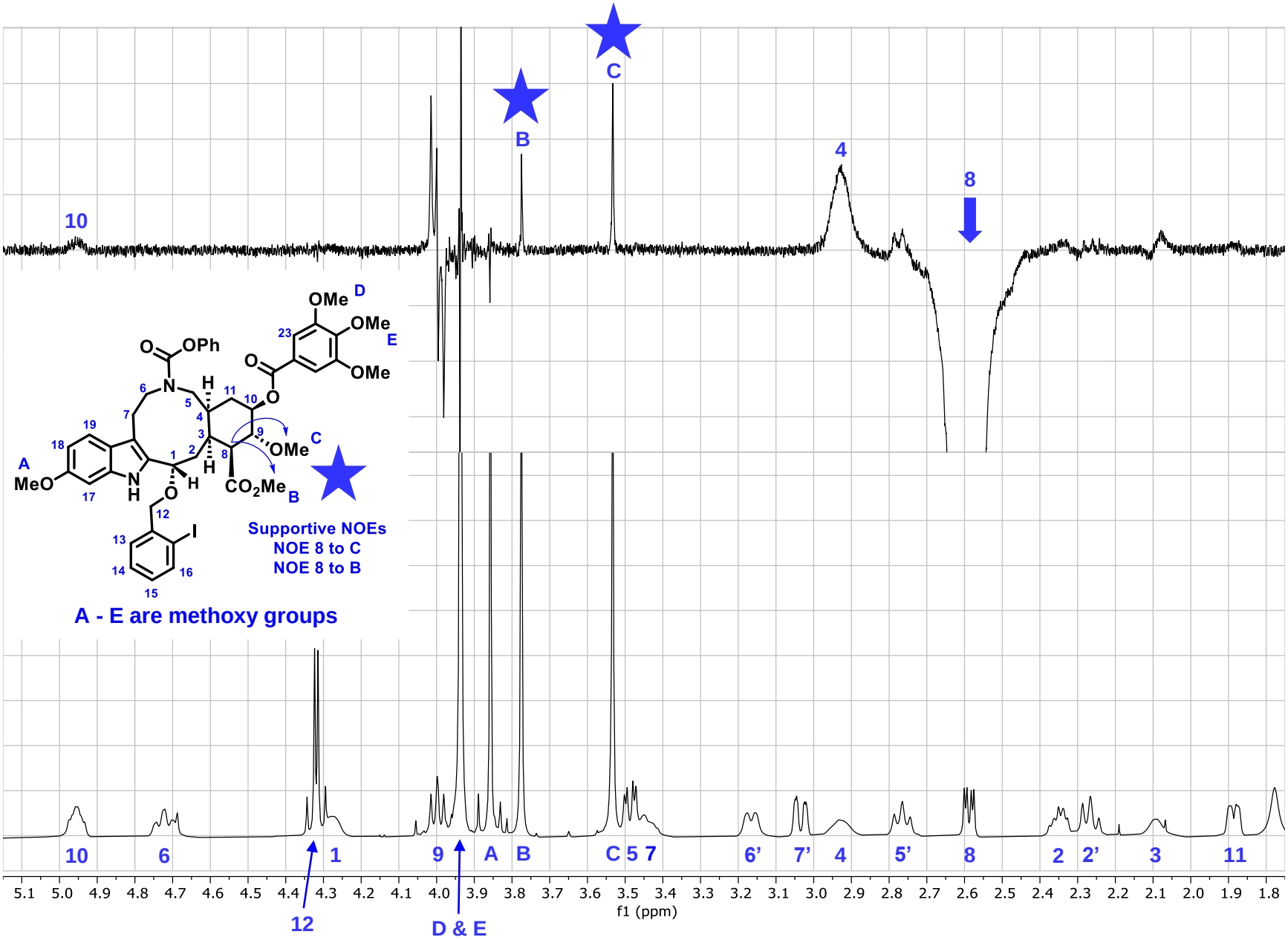
Compound **41**: 1D-NOESY (Key NOEs to define stereochemistry at position 1)



Compound **41**: 1D-NOESY (Supporting NOE to define the "C" methoxy signal, part 1)



Compound **41**: 1D-NOESY (Supporting NOE to define the "C" methoxy signal, part 2)



Compound **41**: 1D-NOESY (Supporting NOE to define the "C" and "B" methoxy signals)