Supporting Information

Scalable and Modular Synthesis Enables Pharmacological Diversification of Salvinorins

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I. Supplementary Figures and Tables

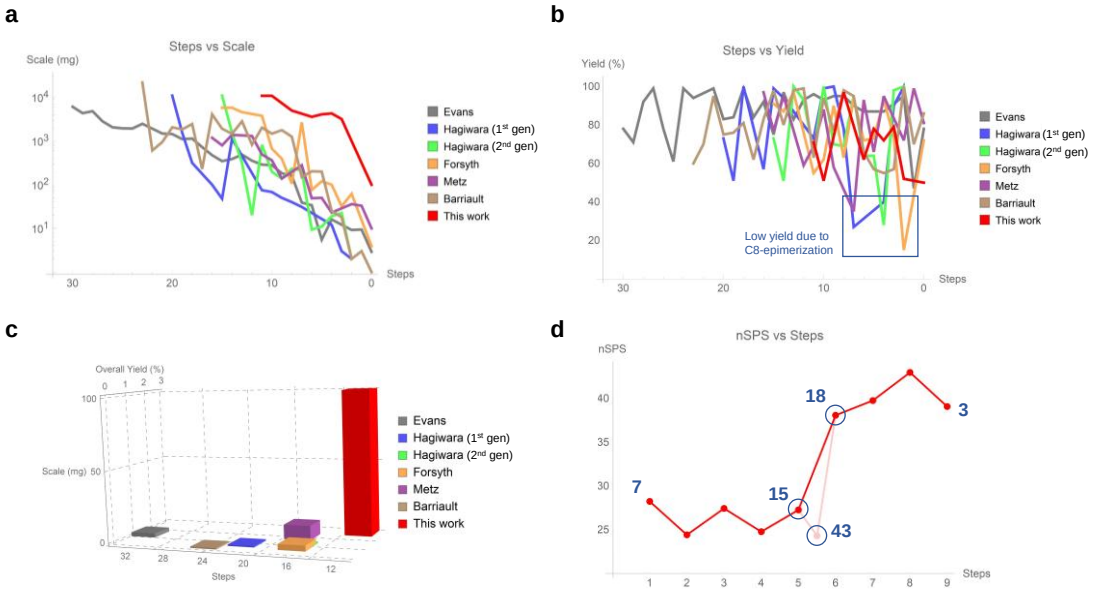


Figure S1. Total syntheses of salvinorin A (**1**). (**a**) Reported total syntheses of SalA and our synthesis of EOM-SalB. The reaction scales required to prepare starting material **7** were taken from the synthesis reported by Shenvi and co-workers.[1] The scale indicated for each step refers to the amount of starting material used. Data for the reported syntheses were obtained from the corresponding Supporting Information. (**b**) Stepwise yields of reported syntheses of SalA and our synthesis of EOM-SalB. The reaction yields required to prepare **7** were taken from ref. 1. Yields are reported without correction for recovered starting material. C8 epimerization substantially compromises synthetic efficiency. (**c**) Comparison of reported syntheses of SalA and our synthesis of EOM-SalB in terms of reaction scale, overall yield and step count. All routes commence from commercially available starting materials. The steps and yields to prepare **7** were taken from ref. 1. (**d**) Normalized spacial score (nSPS)[2] of each intermediate (from **7** to **3**) in our synthesis. The photochemical construction of the quaternary center makes a major contribution to the overall nSPS. A similar comparison among syntheses of salvinorin A has been reported elsewhere.[3]

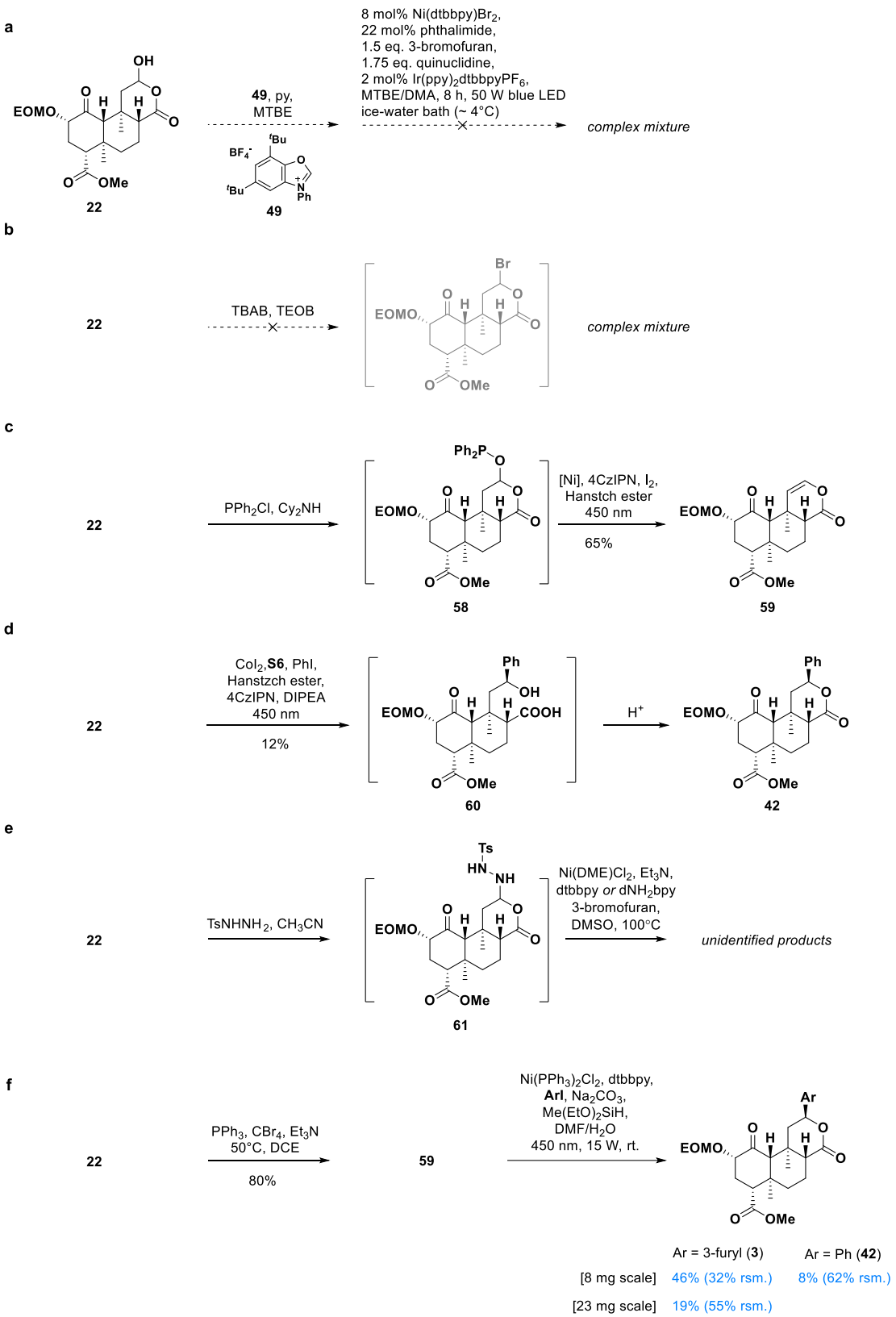
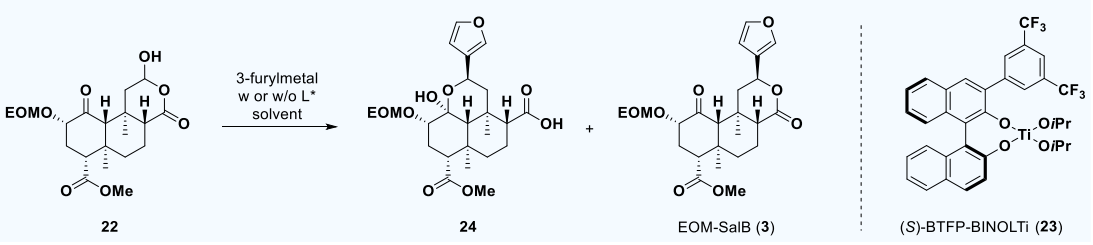


Figure S2. Attempts on deoxygenative arylation of lactol **22** (**a**) Deoxygenative arylation methodology[4] was not successful and gave complex mixture of unidentified products. (**b**) In situ bromination-reductive cross coupling methodology[5] was not

successful as the bromination condition yielded complex mixture. (**c**) Diphenyl phosphinyl group mediated deoxygenative arylation system[6] afforded elimination product **59** upon treatment of **58** with iodine. (**d**) Photoredox aldehyde arylation conditions[7] on **22** led to a low yield of desired product **42** and starting material recovery. (**e**) Putative hydrazine adduct **61** was obtained but the subsequent cross-coupling was unfruitful. (**f**) Appel condition efficiently yielded elimination product **59**. Subsequent hydroarylation conditions[8] effectively afford EOM-SalB (**3**) at 8 mg scale, but were less efficient on larger scales, or for iodobenzene as the coupling partner.

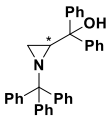
Table S1. Optimization of the aryl metal reagent addition to 22.



22 | 24 | EOM-SalB (**3**) | (*S*)-BTFP-BINOLTi (**23**)

Entry[a]	Reagent	Catalyst or additive	Temp. & time	Solvent[b]	Yields[c] 24	3	22
1	20 equiv 3-furylZnEt	20 mol% **(*R*)-45**	0 °C, 3 h	toluene	75%	0%	0%
2	20 equiv 3-furylZnEt	20 mol% **(*S*)-45**	0 °C, 3 h	toluene	0%	0%	70%
3	2.5 equiv. 3-furylLi	none	–78 °C, 1 h	Et_2O	20%	14%	50%
4	3 equiv 3-furylMgBr	100% $LaCl_3$ $(LiCl)_2$	–46-25 °C, 3 h	THF	low conversion		
5	3 equiv 3-furylTi(O*i*Pr)$_3$	none	0 °C, 3 h	toluene	46%	33%	15%
6	3 equiv 3-furylTi(O*i*Pr)$_3$	none	0 °C, 3 h	THF	0%	0%	20%
7	3 equiv 3-furylTi(O*i*Pr)$_3$	none	0 °C, 3 h	CH_3CN	60%	11%	0%
8	3 equiv 3-furylTi(O*i*Pr)$_3$	none	0 °C, 3 h	benzene	22%	9%	0%
9	3 equiv 3-furylTi(O*i*Pr)$_3$	none	0 °C, 3 h	DCM	low conversion		
10	3 equiv 3-furylTi(O*i*Pr)$_3$	none	0 °C, 3 h	C_6F_6	low conversion		
11	3 equiv 3-furylTi(O*i*Pr)$_3$	none	0 °C, 3 h	$PhCF_3$	30%	39%	n.d.
12[e]	3 equiv 3-furylTi(O*i*Pr)$_3$	none	0 °C, 3 h	$PhCF_3$	45%	30%	n.d.
13	3 equiv 3-furylTi(O*t*Bu)$_3$	none	0 °C, 3 h	toluene	60%	20%	0%
14	3 equiv 3-furylTi(O*i*Pr)$_3$	30 mol% (*R*)-BINOLTi(O*i*Pr)$_2$	0 °C, 3 h	toluene	65%	26%	0%
15	3 equiv 3-furylTi(O*i*Pr)$_3$	80 mol% (*R*)-BINOLTi(O*i*Pr)$_2$	0 °C, 3 h	toluene	complex mixture		
16	3 equiv 3-furylTi(O*i*Pr)$_3$	30 mol% (*S*)-BINOLTi(O*i*Pr)$_2$	0 °C, 3 h	toluene	28%	28%	0%
17	2 equiv 3-furylTi(O*i*Pr)$_3$	30 mol% (*S*)-BINOLTi(O*i*Pr)$_2$	0 °C, 3 h	toluene	33%	21%	0%
18	3 equiv 3-furylTi(O*i*Pr)$_3$	30 mol% (*S*)-BINOLTi(O*i*Pr)$_2$ + 100 mol% 12-crown-4	0 °C, 3 h	toluene	33%	21%	0%
19	3 equiv 3-furylTi(O*i*Pr)$_3$	200 mol% (*S*)-BINOLTi(O*i*Pr)$_2$	0 °C,3 h	toluene	45%	40%	0%
20	3 equiv 3-furylTi(O*i*Pr)$_3$	200 mol% **23**	0 °C,3 h	toluene	32%	32%	n.d.
21	3 equiv 3-furylTi(O*i*Pr)$_3$	200 mol% **23**	–40 °C, 18 h	toluene	40%	45%	0%
22	3 equiv 3-furylTi(O*i*Pr)$_3$	200 mol% **23**	–40 °C, 18 h	$PhCF_3$	low conversion		
23	3 equiv 3-furylTi(O*i*Pr)$_3$	200 mol% **23**	–78 °C, 20 h	toluene	incomplete conversion		
24[f]	3 equiv 3-furylTi(O*i*Pr)$_3$	200 mol% **23**	–40 °C, 24 h	toluene	44%[d]	51%[d]	0%
25	3 equiv 3-furylTi(O*i*Pr)$_3$	100 mol% **23**	–40 °C, 24 h	toluene	32%	51%	14%[h]
26[g]	3 equiv 3-furylTi(O*i*Pr)$_3$	100 mol% **23**	–40 °C, 24 h	toluene	32%[d]	50%[d]	14%[h,d]
27	3 equiv PhTi(O*i*Pr)$_3$	none	0 °C, 3 h	toluene	n.d.	18%[i]	14%[h]

[a] 8 mg scale unless otherwise noted.
[b] Final concentration = 0.04 M.
[c] NMR yield unless otherwise noted.
[d] Isolation yield.
[e] 24 mg scale
[f] 50 mg scale
[g] 100 mg scale
[h] Lactol **20** from the previous step was directly used without purification (see Experimental Procedures); thus the starting material contained ~14% **22** that could be recovered from this step.
[i] The yield of **42** instead of **3.**



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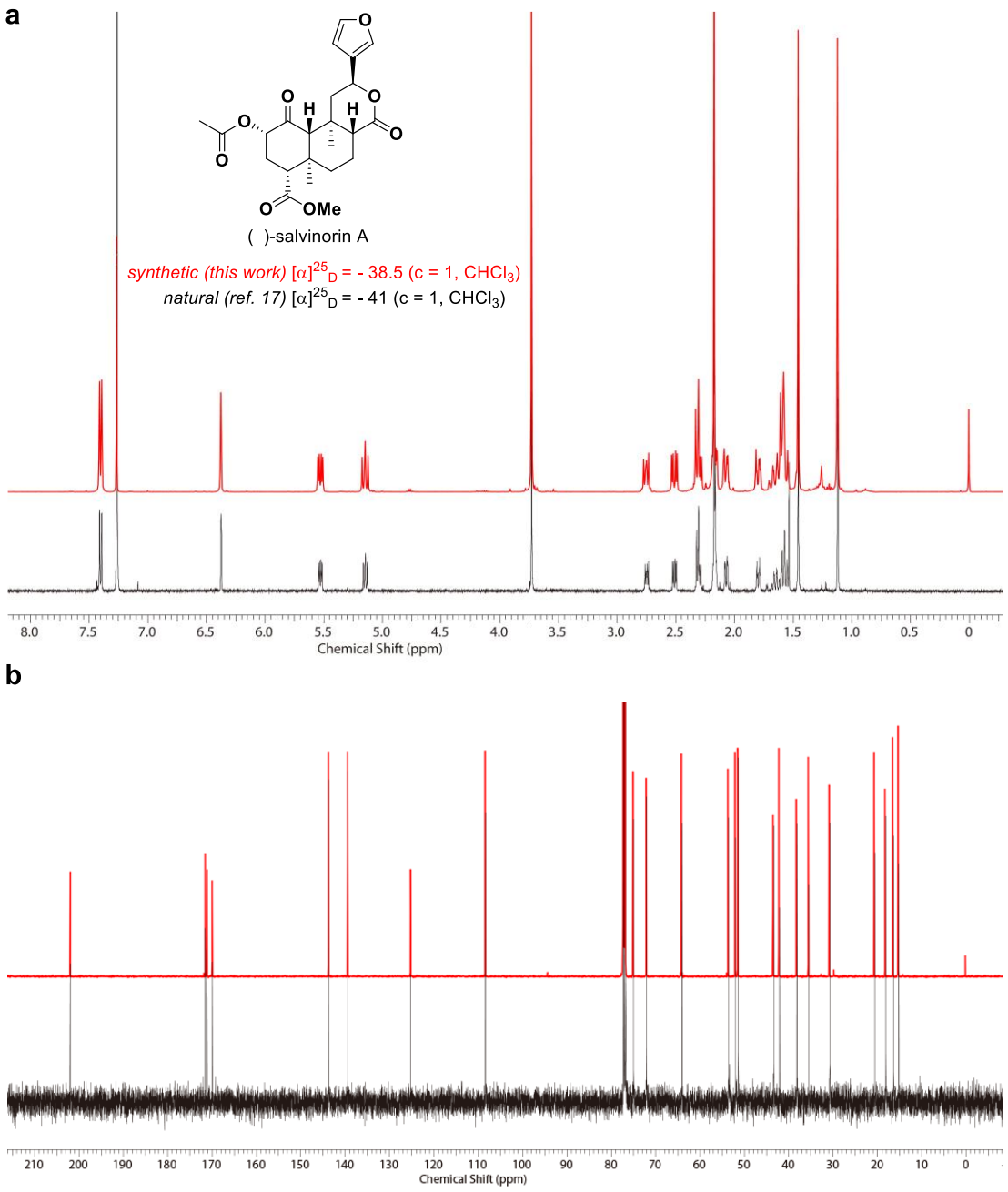


Figure S3. Comparison of NMR and optical rotation data obtained from natural[17] and synthetic (–)-salvinorin A **(a)** ^{1}H NMR and optical rotation data **(b)** ^{13}C NMR data

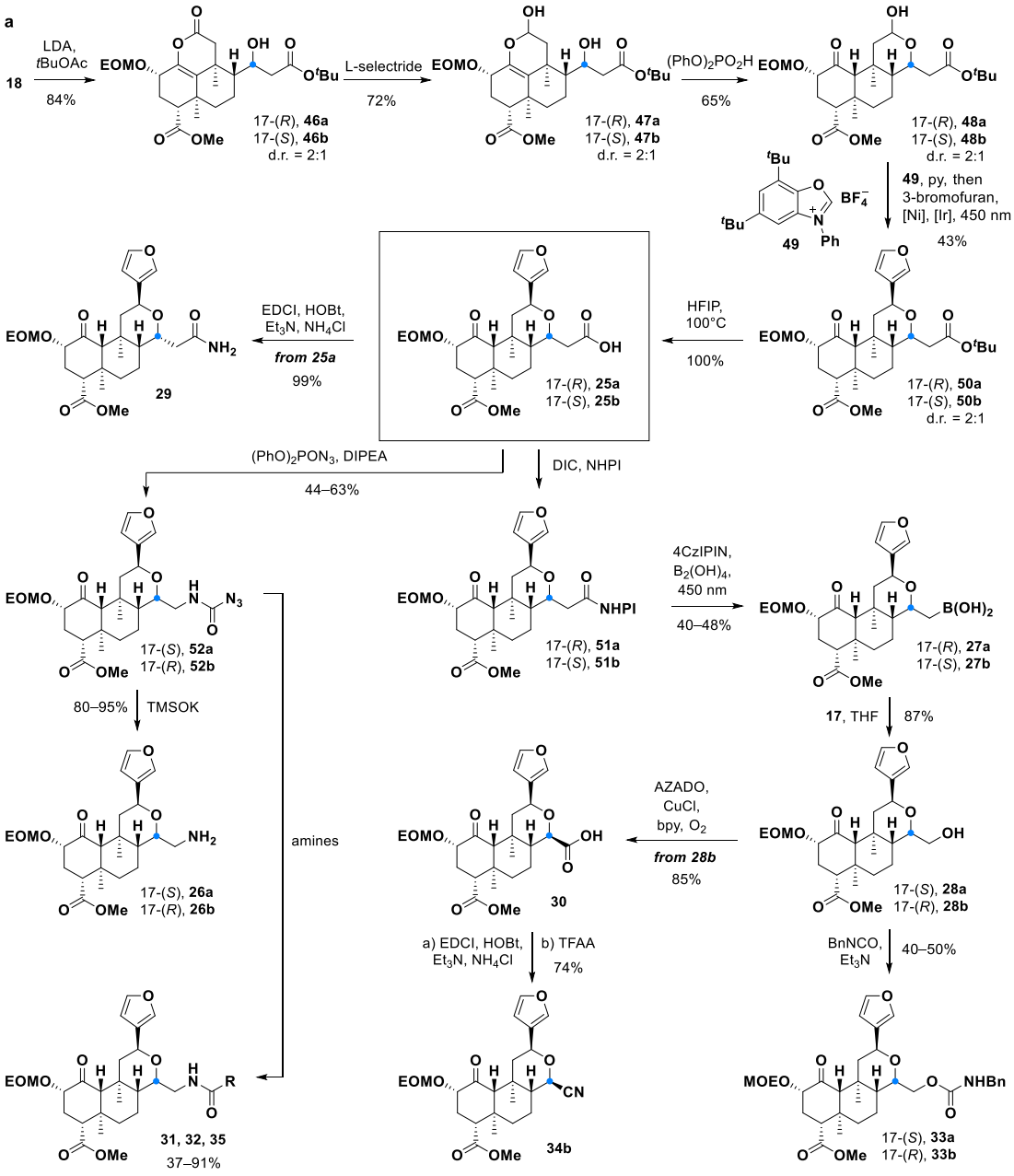


Figure S4. Synthesis of compound **25a** and **25b** and diversifications at C17 therefrom. Yields shown are isolation yields.

Table S2. Functional activity and binding parameters at KOR of salvinorin analogues.

compounds	cAMP pathway			β-arrestin pathway			Bias factor	K_i
	EC_{50}/nM	pEC_{50}	E_{max}%	EC_{50}/nM	pEC_{50}	E_{max}%		
SalA (**1**)	1.70 ± 0.12	8.77 ± 0.03	104.7	7.7 ± 1.5	8.11 ± 0.08	104.8	2.5	1.39 ± 0.17
3	0.30 ± 0.03	9.52 ± 0.05	103.6	0.56 ± 0.09	9.25 ± 0.07	96.7	1.0	0.81 ± 0.13
42	1.60 ± 0.11	8.79 ± 0.03	109.6	9.6 ± 1.0	8.02 ± 0.05	96.6	3.5	*n.d.*
28b	0.62 ± 0.05	9.21 ± 0.03	103.9	5.2 ± 1.3	8.29 ± 0.11	85.6	5.6	*n.d.*
33b	1.63 ± 0.06	8.79 ± 0.02	110.6	27 ± 5	7.56 ± 0.08	77.0	12.2	*n.d.*
28a	0.22 ± 0.03	9.66 ± 0.05	101.3	2.0 ± 0.25	8.69 ± 0.05	97.4	4.8	5.31 ± 0.76
33a	8.54 ± 0.67	8.07 ± 0.03	99.8	97 ± 13	7.01 ± 0.06	71.1	9.8	*n.d.*
26b	0.31 ± 0.03	9.50 ± 0.04	101.2	8.2± 1.3	8.09 ± 0.07	94.3	18.3	*n.d.*
31b	0.73 ± 0.05	9.13 ± 0.03	104.5	9.5 ± 2.2	8.02 ± 0.10	86.9	8.8	*n.d.*
30	0.19 ± 0.02	9.73 ± 0.04	105.7	4.5 ± 0.5	8.35 ± 0.05	86.6	19.1	13.0 ± 1.7
34b	0.03 ± 0.01	10.54 ± 0.09	104.3	0.50 ± 0.05	9.30 ± 0.04	86.4	13.6	1.52 ± 0.29
32b	1.56 ± 0.12	8.81 ± 0.03	98.5	*n.d.*	*n.d.*	*n.d.*	*n.d.*	*n.d.*
25a	6.53 ± 0.43	8.19 ± 0.03	104.3	*n.d.*	*n.d.*	*n.d.*	*n.d.*	*n.d.*
25b	6.71 ± 0.52	8.17 ± 0.03	102.3	*n.d.*	*n.d.*	*n.d.*	*n.d.*	*n.d.*
29	0.34 ± 0.04	9.47 ± 0.05	105.3	3.40 ± 0.62	8.47 ± 0.08	87.3	6.5	10.2 ± 1.5
26a	0.04 ± 0.00	10.44 ± 0.05	104.0	0.09 ± 0.03	10.05 ± 0.12	80.0	2.2	0.20 ± 0.03
31a	6.97 ± 0.68	8.16 ± 0.04	105.5	61 ± 7	7.22 ± 0.05	81.6	5.8	*n.d.*
35a	17.86 ± 0.78	7.75 ± 0.02	103.6	*n.d.*	*n.d.*	*n.d.*	*n.d.*	*n.d.*
34a	1.05 ± 0.13	8.98 ± 0.05	101.9	6.4 ± 0.9	8.19 ± 0.06	88.7	3.7	*n.d.*
40	62.67 ± 2.23	7.20 ± 0.02	105.9	*n.d.*	*n.d.*	*n.d.*	*n.d.*	*n.d.*
38	0.36 ± 0.02	9.45 ± 0.02	111.5	*n.d.*	*n.d.*	*n.d.*	*n.d.*	*n.d.*
27b	1.48 ± 0.08	8.83 ± 0.02	103.0	42 ± 4	7.38 ± 0.04	75.2	21.5	4.21 ± 0.88
36b	0.13 ± 0.02	9.89 ± 0.07	103.4	1.32 ± 0.14	8.88 ± 0.05	92.5	6.7	*n.d.*
36a	1.74 ± 0.11	8.76 ± 0.03	108.8	*n.d.*	*n.d.*	*n.d.*	*n.d.*	*n.d.*
37	2.74 ± 0.16	8.56 ± 0.03	109.2	*n.d.*	*n.d.*	*n.d.*	*n.d.*	*n.d.*
39	0.10 ± 0.01	9.99 ± 0.04	104.0	0.70 ± 0.13	9.15 ± 0.08	74.8	5.3	13.0 ± 3.8
32a	3.14 ± 0.13	8.50 ± 0.02	109.3	*n.d.*	*n.d.*	*n.d.*	*n.d.*	*n.d.*
27a	1.30 ± 0.12	8.89 ± 0.04	102.8	34 ± 3	7.46 ± 0.04	79.8	18.9	2.55 ± 0.56
35b	7.07 ± 0.53	8.15 ± 0.03	108.4	*n.d.*	*n.d.*	*n.d.*	*n.d.*	*n.d.*
41	0.23 ± 0.02	9.63 ± 0.03	107.3	*n.d.*	*n.d.*	*n.d.*	*n.d.*	0.98 ± 0.13
U69593	3.16 ± 0.14	8.50 ± 0.02	108.4	748 ± 15	7.13 ± 0.09	89.7	13.1	*n.d.*

n.d. not determined

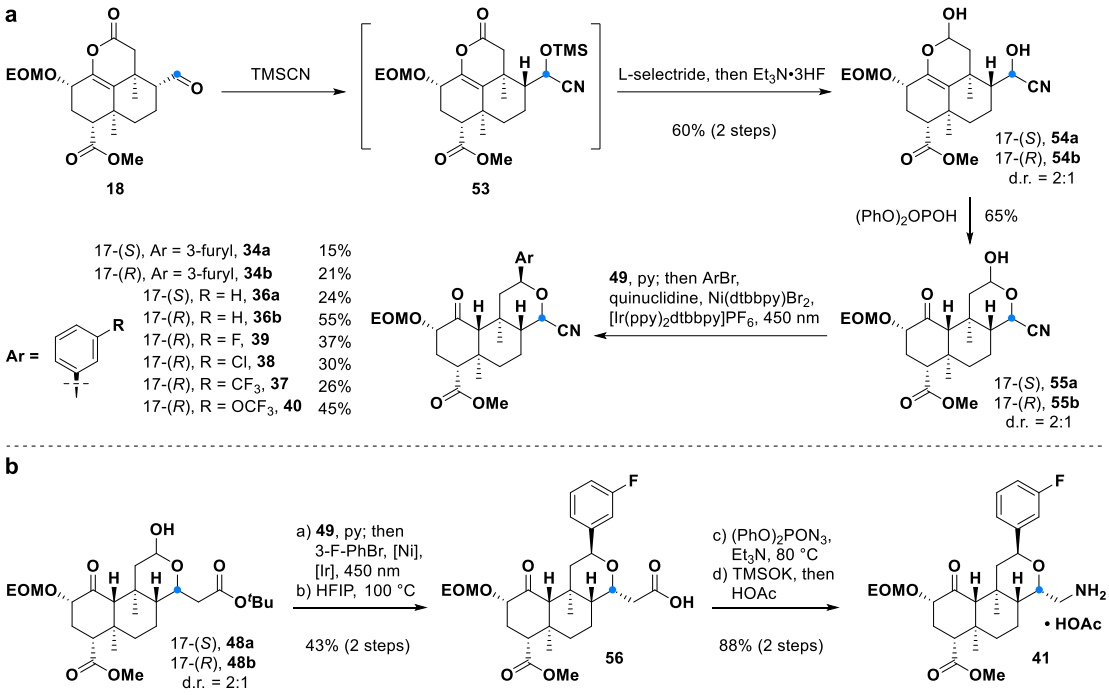


Figure S5. Diversifications at C12. (**a**) Synthesis of C17-cyano-C12-aryl analogues. (**b**) Synthesis of analogue **41**. Yields shown are isolation yields.

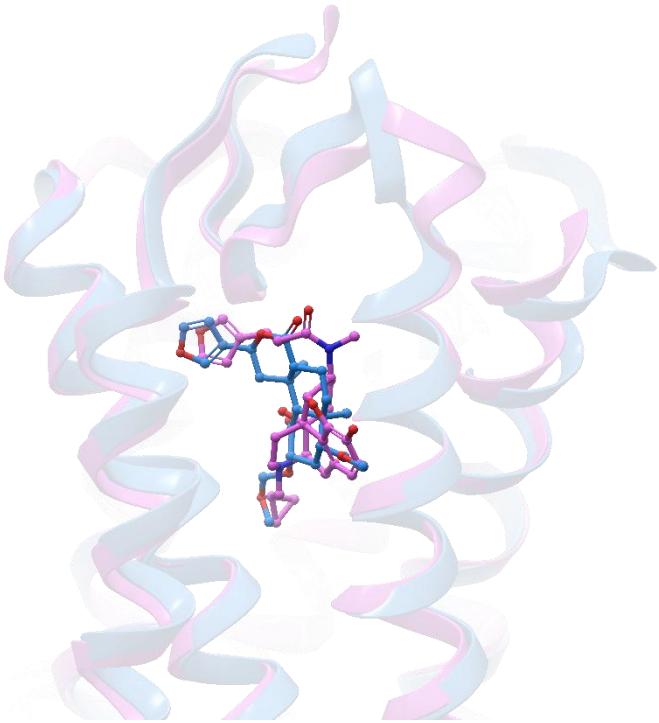
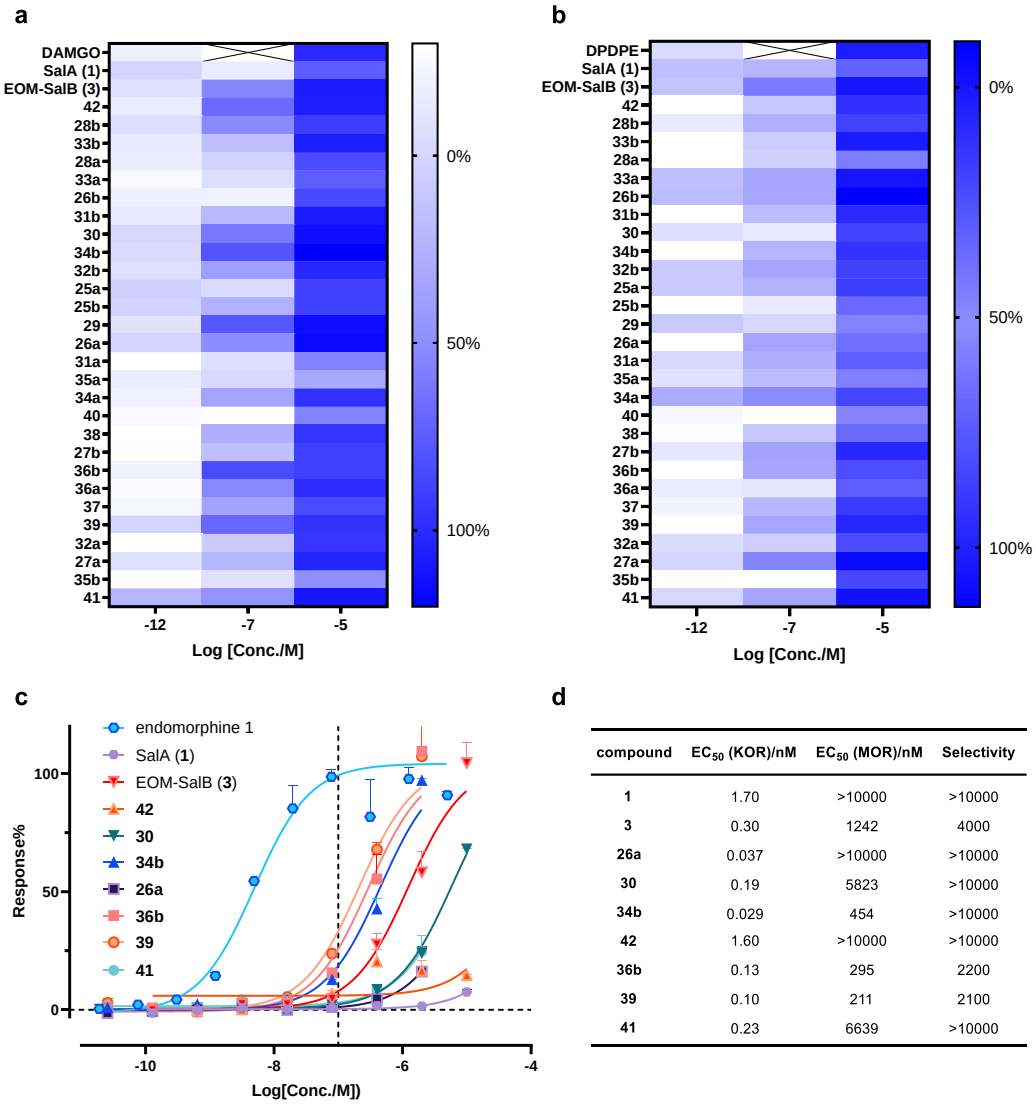


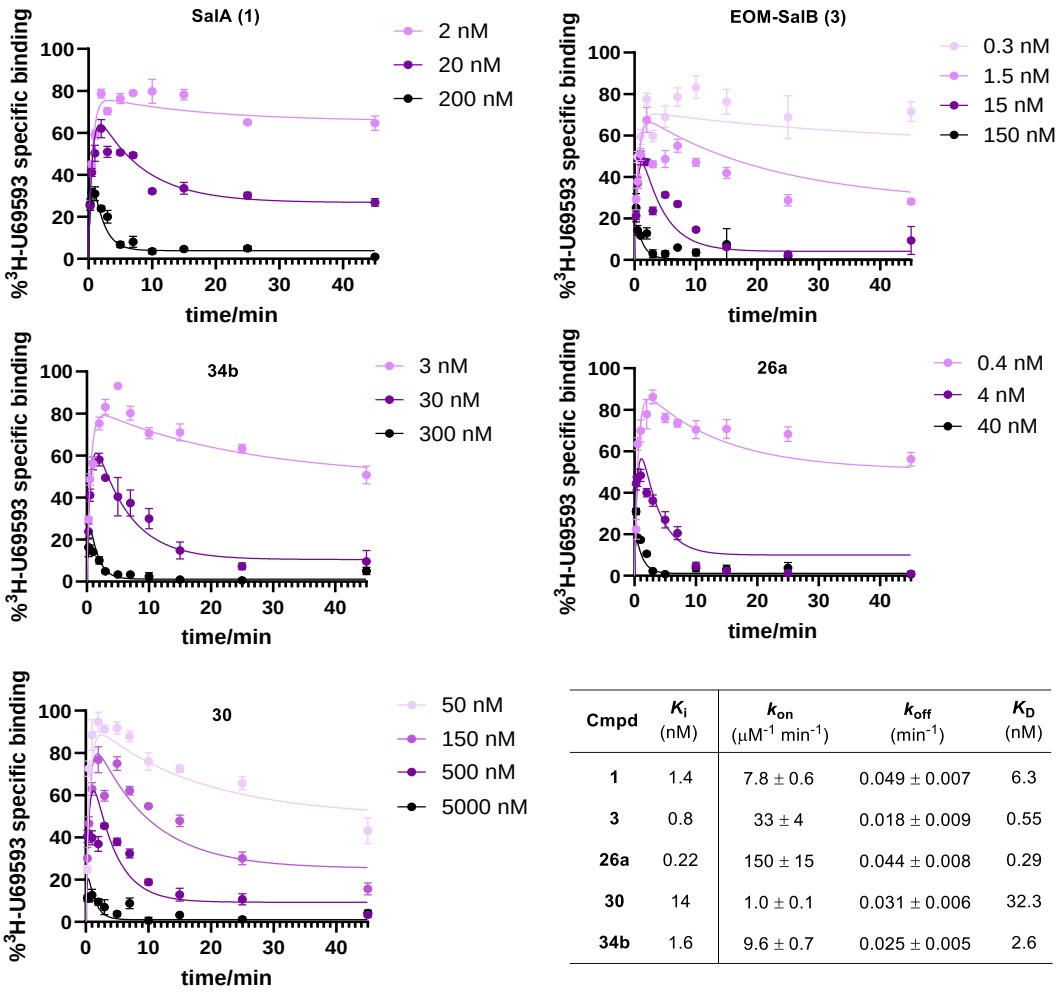
Figure S6. Binding pose of KOR-bound nalfurafine (pink, PDB ID: 7YIT) and MOM-SalB (blue, PDB ID: 8DZP). The RMSD between the furan groups is 1.5 Å



d

compound	EC_{50} (KOR)/nM	EC_{50} (MOR)/nM	Selectivity
1	1.70	>10000	>10000
3	0.30	1242	4000
26a	0.037	>10000	>10000
30	0.19	5823	>10000
34b	0.029	454	>10000
42	1.60	>10000	>10000
36b	0.13	295	2200
39	0.10	211	2100
41	0.23	6639	>10000

Figure S7. Selectivity screening over MOR and DOR. (**a**) MOR selectivity screening. Several compounds showed moderate activation at 10^{-7} M and were selected for dose-response curve measurement. (**b**) DOR selectivity screening. Compounds consistently showed weak activities. (**c**) Dose-response curve of selected compounds at MOR. (**d**) Calculated MOR EC_{50} and corresponding selectivity ($EC_{50,\ MOR}/EC_{50,\ KOR}$). All compounds are highly KOR-selective.



Cmpd	K_i (nM)	k_{on} (μM^{-1} min^{-1})	k_{off} (min^{-1})	K_D (nM)
1	1.4	7.8 ± 0.6	0.049 ± 0.007	6.3
3	0.8	33 ± 4	0.018 ± 0.009	0.55
26a	0.22	150 ± 15	0.044 ± 0.008	0.29
30	14	1.0 ± 0.1	0.031 ± 0.006	32.3
34b	1.6	9.6 ± 0.7	0.025 ± 0.005	2.6

Figure S8. Binding kinetics as measured by competitive binding experiments. The k_{on} values varied with ligand charge while k_{off} values were similar across the tested compounds. The kinetic parameters of SalA well corroborated with reported values.[9] The kinetic dissociation constants (K_D) were consistent with the thermodynamic dissociation constants (K_i).

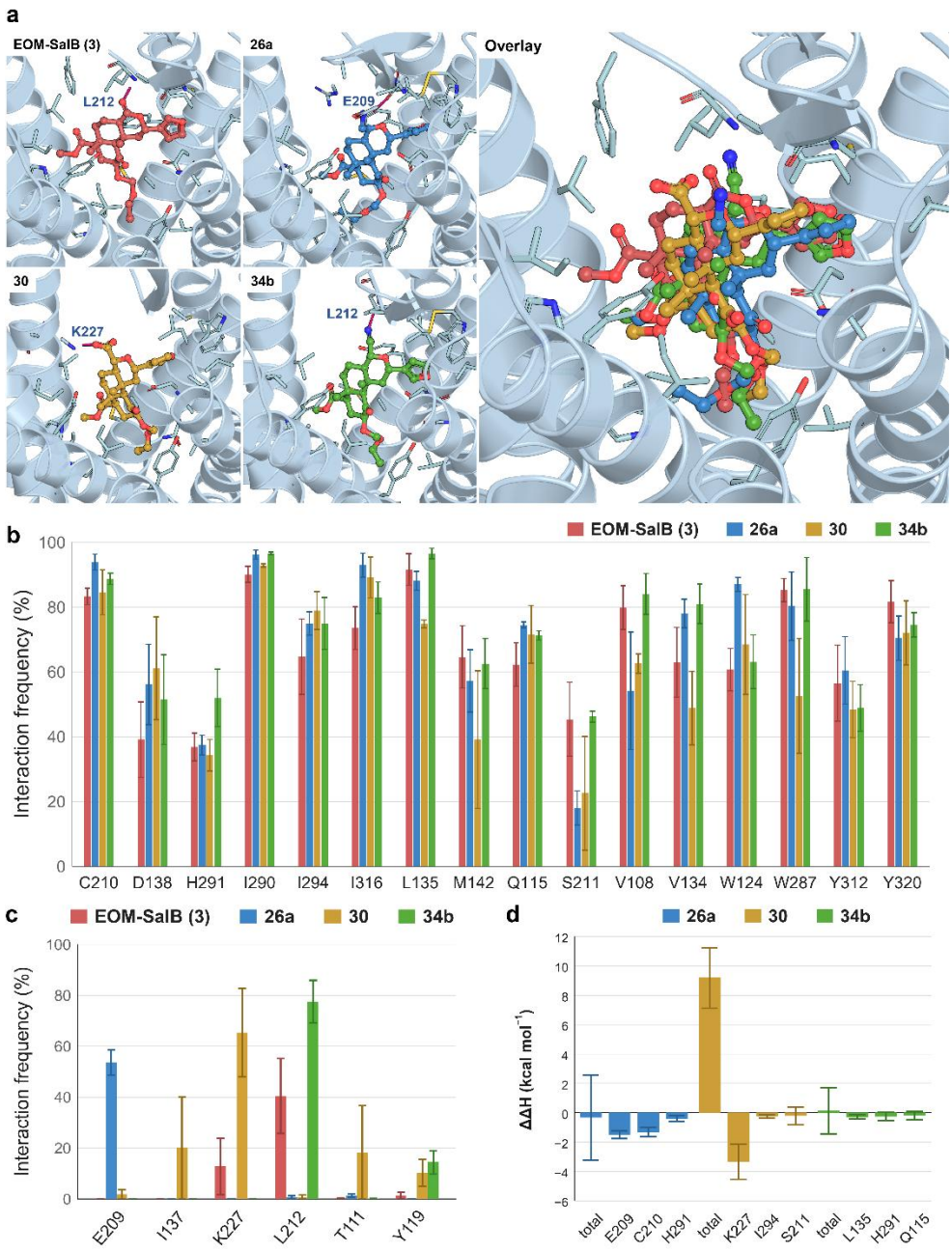


Figure S9. Molecular dynamic simulations revealed C17 substitutions introduce additional interactions while preserving core ligand-receptor engagement. (**a**) Representative simulation snapshots illustrating interactions involving the C17 substituents of **3**, **26a**, **30** and **34b**. (**b**) Interaction-fingerprint analysis of the simulation trajectories identified conserved ligand–receptor contacts shared by the four compounds. (**c**) Compound-specific receptor contacts formed by **3**, **26a**, **30** and **34b**. (**d**) Molecular mechanics Poisson–Boltzmann surface area (MM–PBSA) estimates of total binding free energies ($\Delta\Delta H_{total}$) and per-residue energy contribution ($\Delta\Delta H_{res}$) of

26a, **30** and **34b**, calculated relative to the reference ligand **3** ($\Delta\Delta H = \Delta H_{\mathbf{26a/30/34b}} - \Delta H_{\mathbf{3}}$). For each ligand, the three residues with the most favourable relative contributions—that is, the lowest mean $\Delta\Delta H_{res}$ values—are shown. Negative values indicate stabilization relative to **3**. $E209^{ECL2}$ and $K227^{5.40}$ provided the largest additional stabilizing contributions to the binding of **26a** and **30**, respectively. Data are presented as mean ± s.e.m. from three independent simulations.

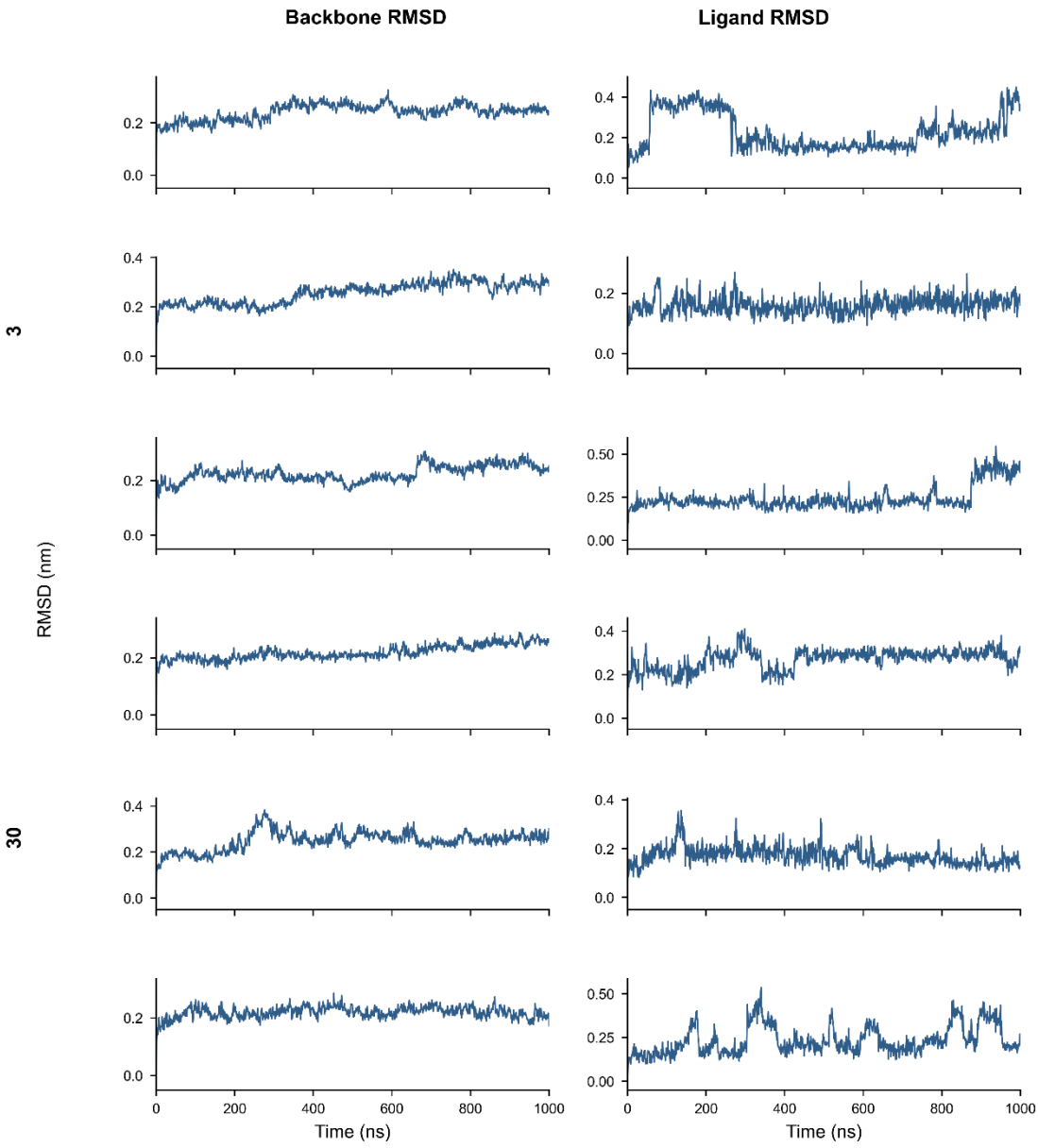


Figure S10. Protein backbone and ligand RMSD of **3** and **30** during simulation.

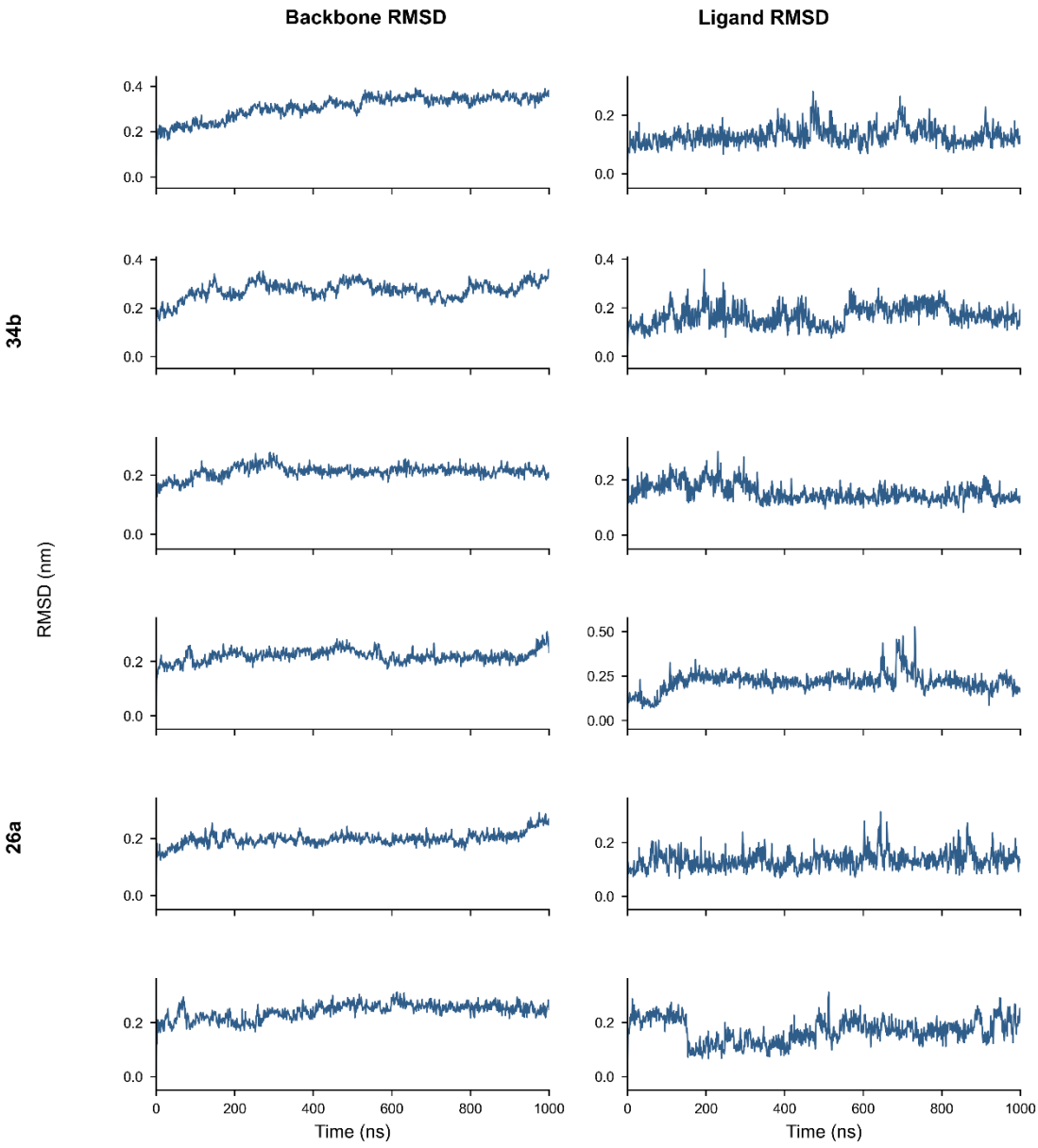


Figure S11. Protein backbone and ligand RMSD of **34b** and **26a** during simulation.

Table S3. MDCK-MDR1 bidirectional permeability assay

Compound	Conc. (μM)	$P_{app\ A→B}$ (10^{-6} cm/s)	$P_{app\ B→A}$ (10^{-6} cm/s)	Efflux Ratio	Recovery A→B%	Recovery B→A%	$TEER_{A→B}$ (Ω × cm^2)	$TEER_{B→A}$ (Ω × cm^2)	$LY_{A→B}$ Leakage (%)	$LY_{B→A}$ Leakage (%)
Metoprolol	5	22.79	18.89	0.83	93.96	94.29	150	155	0.29	0.34
Digoxin	5	1.99	15.47	7.78	93.50	104.80	148	153	0.15	1.10
Imatinib	5	9.53	28.00	2.94	86.24	98.30	141	146	0.35	0.58
1	5	22.79	13.50	0.59	72.58	81.43	148	147	0.30	1.16
3	5	22.77	16.07	0.71	70.47	69.92	150	149	1.12	1.83
34b	5	14.87	10.30	0.69	53.20	57.86	147	149	1.17	0.90
26a	5	0.73	18.76	25.80	86.42	94.96	154	152	1.33	1.58
30	5	0.23	0.69	3.00	86.71	92.87	147	149	2.99	2.36
41	5	1.07	32.18	30.12	64.27	82.84	151	149	1.71	2.07



Figure S12. Photochemical setup with AL1 photoreactor. If the reaction is not very sensitive to temperature (the conversion of **15** to **18**), the commercial 3STech AL1 parallel photoreactor was used (with 410~415 nm light source), and parameters were set as follow: 1000 rpm stirring, 12 W power, full-powered cooling fan. (https://www.3s-tech.net/en/products/al.html)



Figure S13. Photochemical setup with RLH-18CU photoreactor. For reactions requiring strict temperature control (the conversions of **19** to **18**, and **54a/b** to **55a/b**), the Rogertech RLH-18CU multi-position parallel photoreactor was employed. 420 nm and 450 nm light sources were used, respectively. Parameters were set as follow: 1000 rpm stirring, 15 W power, 0~10℃ bath temperature (the low-temperature cooling circulating pump was set to ~ –5℃ correspondingly). (https://www.rogertech.cn/ProductShow.aspx?CatalogId=20&RecordId=30)

II. Experimental Procedures and Data

General Information

Unless otherwise mentioned, all reactions were carried out under a nitrogen atmosphere with ultradry solvents under anhydrous conditions. All the chemicals were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Anhydrous THF and Et_2O were distilled from sodium-benzophenone, toluene was distilled from sodium, and dichloromethane was distilled from calcium hydride. Yields refer to chromatographically and spectroscopically (^1H NMR) pure materials, unless otherwise stated.

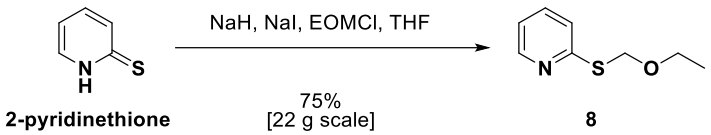
Reactions were monitored by thin layer chromatography (TLC) carried out on 0.25 mm E. Merck silica plates (60F-254), using UV light and an ethanolic solution of ammonium molybdate and heat, or $KMnO_4$ and heat as the visualizing agent and petroleum ether (PE)/EtOAc as developing solvents. If not specially mentioned, flash column chromatography uses silica gel (200-300 mesh) supplied by Tsingtao Haiyang Chemicals (China).

NMR spectra were recorded on Brüker Advance 400 (^1H 400 MHz, ^{13}C 101 MHz), Brüker Advance 500 (^1H 500 MHz, ^{13}C 126 MHz, ^{19}F 471 MHz) or Brüker Advance 600 (^1H 600 MHz, ^{13}C 151 MHz, ^{19}F 565 MHz). TMS was used as the internal standard for ^1H NMR (0.00 ppm), and solvent signal was used as reference for ^1H NMR ($CDCl_3$, 7.26 ppm, CD_3OD, 3.31 ppm, CD_2Cl_2, 5.32 ppm), ^{13}C NMR ($CDCl_3$, 77.16 ppm, CD_3OD, 49.00 ppm, CD_2Cl_2, 53.84 ppm). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad.

Mass spectrometric data were obtained using Brüker Apex IV FTMS using ESI (electrospray ionization). Infrared spectra were recorded on a Thermo Nicolet iS5 spectrometer. Optical rotations were measured on an InsMark IP-digi300 digital polarimeter with a LED light source at ambient temperature and are reported as follows: $[\alpha]\lambda$ (c g/100 mL).

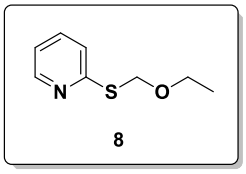
Caution: The conversion of **18** to **53** involves a potential cyanide hazard. All reaction operations, aqueous workup procedures, and purification steps should therefore be conducted in a well-ventilated fume hood. Upon completion of the experiment, all glassware, rotary evaporator components, and waste solutions that may have come into contact with cyanide-containing materials should be decontaminated with an aqueous $KMnO_4$ solution prior to removal from the fume hood. Appropriate personal protective equipment should be worn at all times, and institutional protocols for the handling and disposal of cyanide-containing waste should be strictly followed.

Synthesis of compound 8



To a 2 L RBF (round bottom flask) was added NaH (8.0 g, 200 mmol, 1.0 equiv, 60% dispersion in mineral oil), which was washed 3 times with pentane. After removal of residue pentane under reduced pressure, THF (1000 mL) was added, followed by the portionwise addition of 2-pyridinethione (22.2 g, 200 mmol, 1.0 equiv) (**caution:** exothermic reaction with gas evolution). The resulting mixture was cooled to 0 ℃, and NaI (30 g, 200 mmol, 1.0 equiv) and EOMCl (17.4 mL, 200 mmol, 1.0 equiv) were added sequentially. The reaction mixture was then allowed to warm to 23 ℃ and stirred overnight. The reaction was quenched with saturated NH_4Cl solution (300 mL), and most of the THF was removed under reduced pressure. EtOAc (400 mL) and H_2O (200 mL) were added, and the layers were separated. The aqueous layer was extracted with EtOAc (200 mL), and the combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated to afford a dark-red oil. Purification by flash chromatography on silica gel (~800 mL), eluting with PE followed by 10% EtOAc in PE, afforded product **8** as a colorless oil (25.4 g, 75%).

*The product may gradually develop a yellow coloration upon storage; however, this appears to have minimal impact on the subsequent reaction. Nevertheless, for optimal stability, it is recommended that **8** be stored at –20℃ under a N_2 atmosphere in the dark. Prior to use, the material should be dried under high vacuum for approximately 30 min.*



R_f = 0.6 (PE: EtOAc = 10:1)

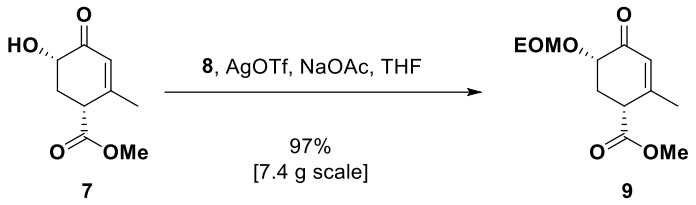
HRMS-ESI (m/z): calc. for $C_8H_{12}NOS$ [M+H$^+$] 170.0634, found 170.0632.

IR (neat, cm^{-1}): 2975, 2876, 1576, 1558, 1452, 1415, 1394, 1306, 1280, 1078, 1012,757, 721, 677.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.47 (ddd, *J* = 4.9, 2.0, 0.9 Hz, 1H), 7.61 – 7.44 (m, 1H), 7.31 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.03 (ddd, *J* = 7.4, 4.9, 1.1 Hz, 1H), 5.37 (s, 2H), 3.65 (q, *J* = 7.0 Hz, 2H), 1.21 (t, *J* = 7.0 Hz, 3H).

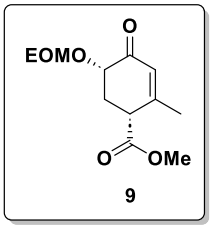
^{13}C NMR (101 MHz, $CDCl_3$): δ 158.3, 149.7, 136.6, 123.0, 120.3, 72.0, 64.8, 15.0.

Synthesis of compound 9



In an oven-dried 1 L RBF, **7** (7.36 g, 40 mmol, 1.0 equiv, prepared according to the reported procedure[1]) and NaOAc (3.28 g, 40 mmol, 1.0 equiv) were added. The flask was evacuated and backfilled with nitrogen three times before THF (300 mL) was introduced. 2-pySEOM (**8**, 13.6 g, 80 mmol, 2.0 equiv) was added via syringe, followed by the cannular transfer of a solution of AgOTf (20.6 g, 80 mmol, 2.0 equiv) in THF (300 mL) over 5 min at 23 ℃ with vigorously stirring. A white precipitate formed upon addition and gradually redissolved as the addition was completed. The reaction mixture was stirred for no longer than 10 min and then quenched with HOAc (2.4 mL, 40 mmol, 1.0 equiv). DCM (400 mL) was added, resulting in the formation of a sticky yellow precipitate. The suspension was filtered through a silica gel pad pre-equilibrated with 1% HOAc in DCM, and the pad was eluted with 0%→50% EtOAc in DCM (containing 1% HOAc). The combined eluents were concentrated under reduced pressure to afford a yellow oil. The crude product was purified by flash column chromatography on silica gel (~800 mL), eluting with 0%→40% EtOAc in PE (containing 1% HOAc), to afford **9** as a yellow oil (9.4 g, 97%).

This reaction is very sensitive to moisture. All glassware should be thoroughly dried before use. NaOAc and AgOTf should be freshly dried in vacuo.



$\boldsymbol{R_f}$ = 0.4 (PE: EtOAc = 2:1)

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\boldsymbol{21.8}}$ = –32.8 (c = 0.636, $CHCl_3$)

HRMS-ESI (m/z): calc. for $C_{12}H_{19}O_5$ $[M+H^+]$ 243.1227, found 243.1228.

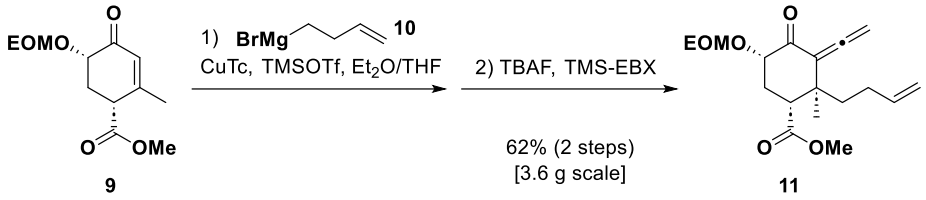
IR (neat, cm^{-1}): 2975, 2885, 1737, 1690, 1635, 1437, 1380, 1269, 1193, 1165, 1120,

1099, 1036, 884

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.18 – 5.77 (m, 1H), 4.84 (d, *J* = 7.0 Hz, 1H), 4.81 (d, *J* = 7.0 Hz, 1H), 4.16 (dd, *J* = 11.2, 5.0 Hz, 1H), 3.76 (s, 3H), 3.64 (dddd, *J* = 16.7, 9.7, 7.1, 2.6 Hz, 2H), 3.47 (dddd, *J* = 9.6, 5.2, 2.2, 1.1 Hz, 1H), 2.54 – 2.29 (m, 2H), 1.97 (t, *J* = 1.3 Hz, 3H), 1.20 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 195.8, 172.1, 156.7, 127.7, 94.6, 74.3, 63.9, 52.6, 46.8, 32.9, 22.5, 15.2.

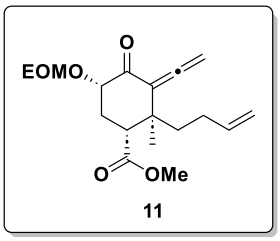
Synthesis of compound 11



The procedure was slightly modified from the literature report.[10] In an oven-dried 1 L RBF, copper (I) thiophene-2-carboxylate (8.64 g, 45 mmol, 3.0 equiv) was suspended in Et_2O (55 mL) and cooled to –65 °C. Grignard reagent **10** (0.8 M in THF, 55 mL, 45 mmol, 3.0 equiv) was then added dropwise over 10 min, and the resulting mixture was stirred at –55 °C for 1.5 h. Subsequently, TMSOTf (5.4 mL, 30 mmol, 2.0 equiv) was then added at –65 °C, followed by slow addition of a solution of **9** (3.6 g in 55 mL Et_2O, 15 mmol, 1.0 equiv) over 30 min. The reaction mixture was stirred for an additional 4 h at –65 °C (monitored by TLC). Upon completion, the reaction was quenched by slow addition of H_2O (200 mL) and Et_2O (200 mL), and the cooling bath was removed. Aqueous Na_2EDTA (sat., 100 mL) and NH_4Cl solutions (sat., 100 mL) were then added, and the mixture was warmed to 20 °C with vigorous stirring. The resulting gray suspension was filtered under reduced pressure and washed with Et_2O. The filtrate was separated, and the aqueous layer was extracted with Et_2O (2×200 mL). The combined organic layers were washed vigorously with saturated $NaHCO_3$ solution (2×20 mL, to remove the thiophene carboxylic acid), followed by brine, dried over Na_2SO_4, filtered, and concentrated to afford a clear colorless oil, which was carried forward without further purification.

To the above oil was added TMS-EBX (5.5 g, 16 mmol, 1.06 equiv). The flask was flushed with N_2 for three times before THF (48 mL) and DCM (25 mL) were added. The solution was cooled to –78 °C, and TBAF (1 M in THF with 5% H_2O, 43 mL, 43 mmol, 2.9 equiv) was added dropwise over 30 min. The reaction mixture was stirred for a further 3 h. The reaction was quenched with saturated NH_4Cl solution (100 mL), and excess THF was removed under reduced pressure. EtOAc (200 mL) and H_2O (100 mL) were added, and the layers were separated. The organic layer was washed with

H_2O (2×50 mL) and saturated $NaHCO_3$ solution (2×20 mL). The aqueous layer was extracted with EtOAc (2×150 mL) and the combined organic layers were washed with brine, and dried over Na_2SO_4. The mixture was concentrated to a red solution (~100 mL), during which any precipitated 2-iodobenzoic acid was removed by filtration. After addition of Et_3N (0.3 mL), the mixture was stored at –20 °C overnight, during which complete isomerization of the alkyne intermediate to the allene was observed by TLC. The crude product was concentrated and purified by flash column chromatography on silica gel (~300 mL), eluting with 0%→25% EtOAc in PE, to afford **11** as an orange oil (3.05 g, 62%).



11

$\boldsymbol{R_f}$ = 0.4 (PE: EtOAc = 4:1)

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\boldsymbol{21.1}}$ = –100.3 (c = 0.561, $CHCl_3$)

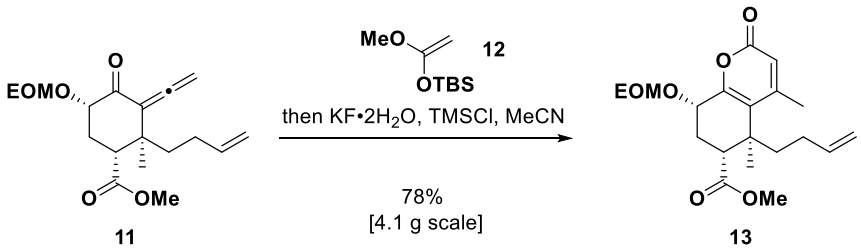
HRMS-ESI (m/z): calc. for $C_{18}H_{27}O_5$ [M+H$^+$] 323.1853, found 323.1855.

IR (neat, cm^{-1}): 2974, 1731, 1699, 1640, 1436, 1373, 1268, 1193, 1158, 1099, 1042, 1012, 916, 846.

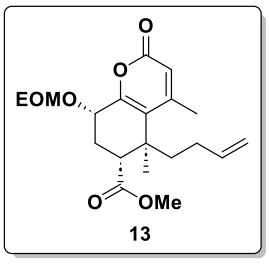
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.78 (ddt, *J* = 16.8, 10.1, 6.6 Hz, 1H), 5.27 (d, *J* = 14.2 Hz, 1H), 5.21 (d, *J* = 14.2 Hz, 1H), 5.13 – 4.91 (m, 1H), 4.85 (q, *J* = 7.1 Hz, 2H), 4.18 (dd, *J* = 12.0, 7.0 Hz, 1H), 3.74 – 3.66 (m, 1H), 3.73 (s, 3H), 3.62 (dq, *J* = 9.6, 7.1 Hz, 1H), 3.02 (dd, *J* = 12.0, 3.9 Hz, 1H), 2.41 – 2.19 (m, 3H), 2.00 (dddd, *J* = 15.7, 7.8, 6.1, 3.4 Hz, 1H), 1.73 – 1.60 (m, 2H), 1.57 (s, 3H), 1.21 (t, *J* = 7.1 Hz, 3H), 1.15 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 209.8, 197.9, 172.5, 138.2, 114.8, 112.7, 94.8, 81.3, 76.8, 64.0, 52.0, 44.9, 42.0, 38.7, 29.7, 28.6, 25.6, 15.3.

Synthesis of compound 13



To a 100 mL RBF was added **11** (4.15 g, 12.8 mmol, 1.0 equiv) and ketene acetal **12** (4.8 g, 25.5 mmol, 2.0 equiv; prepared from methyl acetate according to the literature procedure[11]). The mixture was stirred neat at 100 °C under a nitrogen atmosphere for 4 h. Upon completion, MeCN (30 mL) and KF·$2H_2O$ (2.80 g, 30 mmol, 2.3 equiv, freshly ground to a fine powder prior to use) were added, and the mixture was cooled to 0 °C. TMSCl (3.80 mL, 29 mmol, 2.2 equiv) was then added dropwise over 5 min at 0°C, and the reaction was stirred vigorously for an additional 5 min (monitored by TLC; prolonged reaction may lead to partial EOM deprotection). The reaction was carefully quench with saturated $NaHCO_3$ solution (40 mL) and transferred to a separatory funnel. EtOAc (100 mL) was added, and the layers were separated. The aqueous phase was extracted with EtOAc (2×100 mL), and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by flash column chromatography on silica gel (~300 mL), eluting with 0%→50% EtOAc in PE, to afford **13** as an orange oil (3.65 g, 78%).



R_f = 0.15 (PE: EtOAc = 3:1)

$[\alpha]_D^{22.5}$ = –62.1 (c = 1.00, $CHCl_3$)

HRMS-ESI (m/z): calc. for $C_{20}H_{28}NaO_6$ [M+Na^+] 387.1778, found 387.1790.

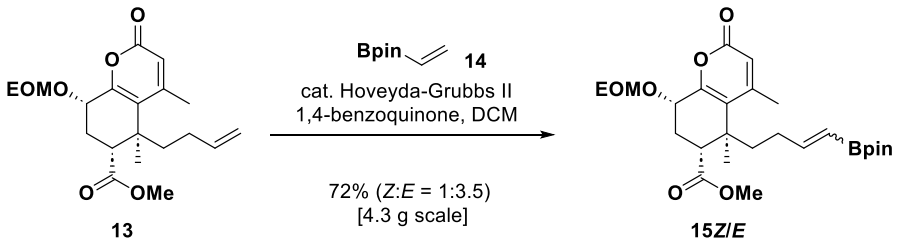
IR (neat, cm^{-1}): 2975, 1728, 1533, 1436, 1378, 1270, 1205, 1166, 1109, 1016, 918.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.16 – 6.02 (m, 1H), 5.75 (dddd, *J* = 17.1, 10.2, 6.9, 6.0 Hz, 1H), 5.01 – 4.93 (m, 3H), 4.84 (d, *J* = 7.2 Hz, 1H), 4.47 (dd, *J* = 9.8, 7.0 Hz, 1H), 3.76 – 3.61 (m, 5H), 2.82 (dd, *J* = 12.6, 3.0 Hz, 1H), 2.31 (d, *J* = 1.2 Hz, 3H), 2.25

(ddd, J = 13.5, 7.1, 3.1 Hz, 1H), 2.19 (dd, J = 12.8, 9.8 Hz, 1H), 2.15 – 2.04 (m, 1H), 1.97 (ddd, J = 14.9, 12.3, 4.0 Hz, 1H), 1.78 (ddd, J = 14.9, 12.0, 5.0 Hz, 1H), 1.62 – 1.52 (m, 1H), 1.36 (s, 3H), 1.23 (t, J = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.9, 160.9, 157.6, 155.5, 137.5, 120.2, 117.0, 115.3, 95.8, 70.6, 63.9, 52.0, 45.4, 40.2, 37.0, 28.7, 28.5, 23.6, 23.2, 15.2.

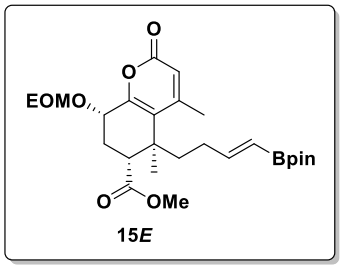
Synthesis of compound 15



To a 100 mL RBF was added **13** (4.3 g, 11.7 mmol, 1.0 equiv), vinylBpin (4.47 g, 29.4 mmol, 2.5 equiv), 1,4-benzoquinone (379 mg, 3.51 mmol, 0.3 equiv) and DCM (40 mL). The flask was sealed with a septum, and nitrogen was bubbled through the solution for 15 min. The mixture was then heated to 60 °C (bath temperature; the RBF was tightly sealed to maintain a slightly positive pressure) before Hoveyda-Grubb II catalyst (1.10 g, 1.76 mmol, 0.15 equiv) in DCM (5 mL) was added slowly over 20 h via syringe pump (*Note: to prevent pressure buildup from produced ethylene, the septum was periodically vented using a fine syringe needle at 1–2 h interval*). The reaction was stirred for an additional 8 h at 60 °C, then cooled to room temperature. The reaction was quenched by addition of DMSO (1 mL)[12] and stirred for 3 h. The mixture was diluted with DCM (30 mL) and washed successively with 10% aqueous ascorbic acid (2×5 mL, to remove 1,4-benzoquinone), H_2O (20 mL) and brine (20 mL). The organic layer was separated, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford a black oil. The crude material was passed through a short pad of silica gel (~80 mL), eluting with 50%→100% EtOAc in PE, to remove residual ruthenium species. The crude product was purified by flash column chromatography on silica gel (~200 mL, 0%→20% EtOAc in PE). Fractions containing products and residual starting material were repurified by a second chromatography (~30 mL silica gel, 0%→20% EtOAc in PE). The combined product fractions were concentrated to afford the products (*Z*:*E* = 1:3.5, 4.15 g, 72% yield) as a dark brown, viscous tar. The pure sample of **15*E*** was obtained via preparative TLC (PTLC) using 20% EtOAc in PE as developing solvent for 4 times.

The purity of product could vary from batch to batch, typically contaminated by minor alkene isomers, which do not interfere with subsequent transformations, and

trace ruthenium residues, which account for the dark coloration and may inhibit the subsequent photo-[2+2] cycloaddition if present at elevated levels. Efficient removal of ruthenium during silica gel purification is therefore essential.



R_f = 0.3 (PE: EtOAc = 2:1)

$[\alpha]_D^{20.1}$ = –86.8 (c = 0.345, $CHCl_3$)

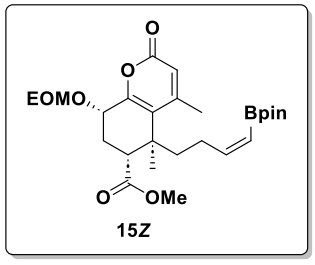
HRMS-ESI (m/z): calc. for $C_{26}H_{40}BO_8$ $[M+H^+]$ 491.2811, found 491.2806.

IR (neat, cm^{-1}): 2977, 1731, 1637, 1533, 1436, 1364, 1322, 1269, 1243, 1206, 1166, 1145, 1110, 1044, 1017, 849.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.55 (dt, *J* = 18.0, 6.2 Hz, 1H), 6.07 (d, *J* = 1.4 Hz, 1H), 5.41 (dd, *J* = 17.8, 1.4 Hz, 1H), 4.97 (d, *J* = 7.1 Hz, 1H), 4.84 (d, *J* = 7.0 Hz, 1H), 4.47 (dd, *J* = 9.8, 7.1 Hz, 1H), 3.85 – 3.46 (m, 5H), 2.80 (dd, *J* = 12.6, 3.1 Hz, 1H), 2.29 (s, 3H), 2.28 – 2.09 (m, 3H), 2.01 (td, *J* = 13.7, 12.6, 3.7 Hz, 1H), 1.79 (ddd, *J* = 14.8, 12.4, 4.7 Hz, 1H), 1.71 – 1.62 (m, 1H), 1.36 (s, 3H), 1.26 (s, 12H), 1.25 – 1.20 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 172.8, 160.9, 157.7, 155.5, 152.4, 120.2, 117.0, 95.8, 83.4 (2C), 70.6, 63.9, 52.0, 45.3, 40.1, 36.5, 30.6, 28.5, 25.0, 24.9 (4C), 23.5, 23.2, 15.2.

The attempts to isolate and purify the minor isomer **15*Z*** were unsuccessful as it always co-eluted with an impurity. Neverthless, its configuration is inferred from the 14.0 Hz *J*-coupling constant (18.0 Hz for **15*E***) corresponding to *cis*-1,2-disubstituted alkene in the mixture ^{1}H NMR spectrum (see NMR spectrum section). Therefore, the data below were obtained by mannually subtracting the signals of **15*E*** from those of the mixture, and deviations may exist.

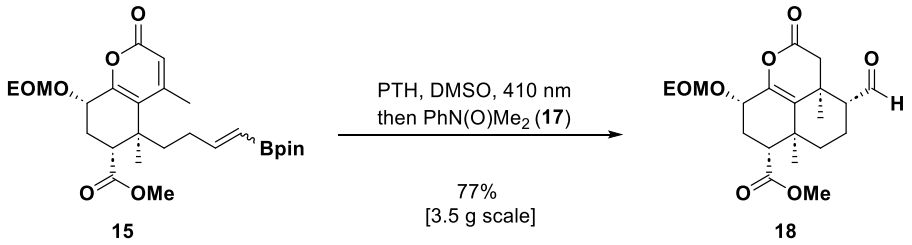


^{1}H NMR (500 MHz, $CDCl_3$): δ 6.32 (dt, *J* = 14.3, 7.4 Hz, 1H), 6.08 (s, 1H), 5.32 (d, *J* = 14.0 Hz, 1H), 4.98 (d, *J* = 6.9 Hz, 1H), 4.85 (d, *J* = 7.0 Hz, 1H), 4.47 (dd, *J* = 9.8, 7.2 Hz, 1H), 3.71 (s, 3H), 3.74 – 3.63 (m, 2H), 2.91 (dd, *J* = 12.5, 2.6 Hz, 1H), 2.36 (s, 3H), 2.27 – 2.12 (m, 3H), 1.97 – 1.87 (m,

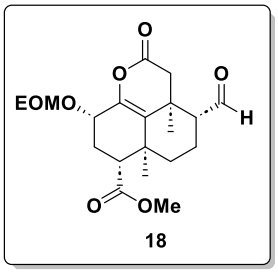
1H), 1.80 – 1.72 (m, 1H), 1.71 – 1.60 (m, 1H), 1.37 (s, 3H), 1.26 (s, 12H), 1.25 – 1.20 (m, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 173.0, 161.1, 157.5, 156.0, 153.2, 120.4, 116.8, 95.8, 83.2 (2C), 70.5, 63.9, 51.9, 45.2, 40.2, 37.5, 28.6, 27.7, 25.0, 24.9 (4C), 23.6, 23.4, 15.2.

Synthesis of compound 18



To a 100 mL Schlenk tube was added **15** (3.5 g, 7.1 mmol, 1.0 equiv), PTH photocatalyst (295 mg, 1.07 mmol, 0.15 equiv) and DMSO (71 mL). The tube was evacuated and backfilled with argon (20 cycles), and irradiated in the 3STech AL1 parallel photoreactor at 410~415 nm (power set to 12 W, full-powered cooling fan, 1000 rpm stirring) until complete conversion was observed by TLC (12 h). $PhN(O)Me_2$ (**17**, prepared from $PhNMe_2$ via oxidation with *m*CPBA followed by recrystallization[13]) was added in one portion, and the reaction mixture was stirred under N_2 at 25 °C for 24 h. The mixture was transferred to a separatory funnel, and H_2O (100 mL), EtOAc (200 mL) and HOAc (1 mL) were added. The layers were separated, the organic layer was washed with H_2O (3×100 mL), and the combined aqueous layers were extracted with EtOAc (3×50 mL). The organic layers were combined, washed with brine and dried over Na_2SO_4. The mixture was filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (~100 mL), eluting with 0%→25% EtOAc in PE, to afford **18** as a yellow oil (2.09 g, 77%).



$\boldsymbol{R_f}$ = 0.4 (PE: EtOAc = 2:1)

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\boldsymbol{24.1}}$ = –73.9 (c = 1.0, $CHCl_3$)

HRMS-ESI (m/z): calc. for $C_{20}H_{28}O_7Na$ [M+Na^+] 403.1727, found 403.1732.

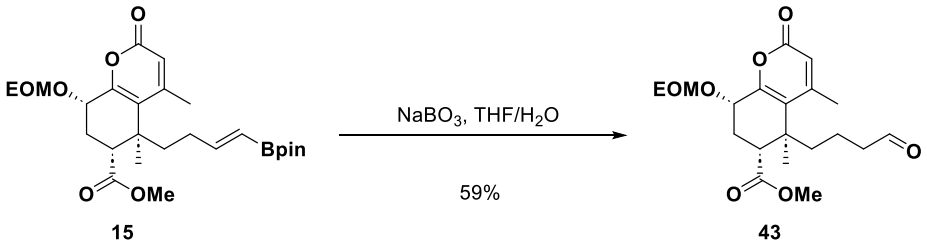
IR (neat, cm^{-1}): 2947, 1764, 1722, 1449, 1385, 1238, 1158, 1107, 1035, 1015, 963, 910, 886, 844.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.75 (d, *J* = 1.7 Hz, 1H), 4.85 (d, *J* = 7.2 Hz, 1H), 4.80 (d, *J* = 7.2 Hz, 1H), 4.34 (t, *J* = 8.7 Hz, 1H), 3.77 – 3.56 (m, 5H), 2.99 (d, *J* = 15.3 Hz,

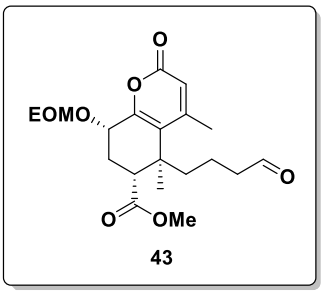
1H), 2.53 (dd, *J* = 13.1, 4.1 Hz, 1H), 2.49 – 2.39 (m, 1H), 2.35 – 2.18 (m, 2H), 2.17 – 2.07 (m, 1H), 1.93 – 1.76 (m, 3H), 1.50 – 1.37 (m, 1H), 1.32 (s, 3H), 1.24 (s, 3H), 1.23 – 1.19 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 202.2, 172.7, 166.5, 144.4, 125.2, 95.4, 70.2, 63.7, 59.0, 51.8, 51.0, 43.8, 36.9, 36.0, 35.6, 29.3, 22.8, 21.8, 18.2, 15.2.

Synthesis of compound 43



To a 15 mL RBF was added **15** (50 mg, 0.1 mmol, 1.0 equiv), THF (1.0 mL) and H_2O (1.0 mL), followed by the addition of $NaBO_3 \cdot 4H_2O$ (32 mg, 0.2 mmol, 2.0 equiv). The reaction mixture was stirred at 25 °C for 1 h, then quenched by addition of EtOAc (2 mL). The mixture was transferred to a separatory funnel, and H_2O (2 mL) and EtOAc (5 mL) were added. The layers were separated, the organic layer was washed with H_2O (3×2 mL), and combined aqueous layers were extracted with EtOAc (3×2 mL). The organic layers were combined, washed with brine and dried over Na_2SO_4. The mixture was filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (~6 mL), eluting with 0%→40% EtOAc in PE, to afford product **43** as a colorless oil (23 mg, 59%).



R_f = 0.1 (PE: EtOAc = 1:1)

$[\alpha]_D^{23.2}$ = –39.7 (c = 0.785, $CHCl_3$)

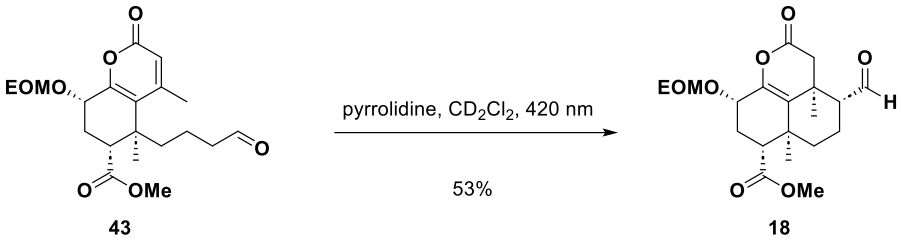
HRMS-ESI (m/z): calc. for $C_{20}H_{32}NO_7$ $[M+NH_4^+]$ 398.2173, found 398.2173.

IR (neat, cm^{-1}): 2974, 1720, 1619, 1532, 1436, 1375, 1280, 1205, 1167, 1109, 1016, 921.

^{1}H NMR (400 MHz, $CDCl_3$):δ 9.75 (s, 1H), 6.08 (s, 1H), 4.97 (d, *J* = 7.2 Hz, 1H), 4.84 (d, *J* = 7.1 Hz, 1H), 4.48 (dd, *J* = 9.7, 6.8 Hz, 1H), 3.72 (s, 3H), 3.79 – 3.58 (m, 2H), 2.82 (dd, *J* = 12.6, 2.9 Hz, 1H), 2.46 (tdd, *J* = 6.9, 3.2, 1.2 Hz, 2H), 2.35 (d, *J* = 1.2 Hz, 3H), 2.34 – 2.21 (m, 1H), 2.16 (td, *J* = 13.0, 9.8 Hz, 1H), 1.97 (ddd, *J* = 15.3, 13.2, 4.7 Hz, 1H), 1.73 – 1.52 (m, 2H), 1.35 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.26 – 1.18 (m, 1H).

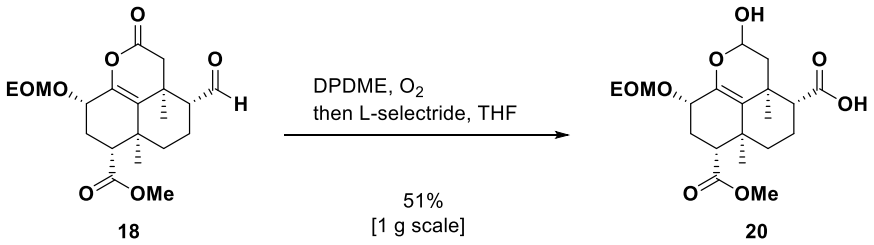
^{13}C NMR (126 MHz, $CDCl_3$): δ 201.6, 172.7, 160.8, 157.7, 155.4, 119.9, 117.0, 95.8, 70.5, 63.9, 52.0, 45.3, 43.9, 40.2, 37.3, 28.4, 23.5, 23.0, 16.9, 15.2.

Synthesis of compound 18 from 43

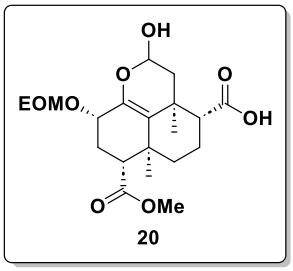


To an NMR tube was added **43** (7.6 mg, 0.02 mmol, 1.0 equiv) and pyrrolidine (1.5 mg, 0.02 mmol, 1.0 equiv), followed by CD_2Cl_2 (0.5 mL). The solution was degassed by bubbling N_2 for 2 min. The tube was then placed in a photoreactor and irradiated at 0 °C (water bath; bath temperature) with 15 W light power. The reaction progress was monitored by ^1H NMR spectroscopy. After 24 h, approximately 90% conversion was observed. The reaction mixture was concentrated under reduced pressure and purified by PTLC (developed with 25% EtOAc in PE) to afford **18** as a colorless oil (4.0 mg, 53%).

Synthesis of compound 20



To **18** (1.0 g, 2.63 mmol, 1.0 equiv) was added dipropylene glycol dimethyl ether[14] (DPDME, mixture of isomers, 1.7 g, 1.9 mL, 10.5 mmol, 4.0 equiv). The reaction mixture was stirred at 80 ℃ for 2 h under an O_2 ballon until complete conversion was confirmed by TLC. The mixture was cooled to room temperature and purged with N_2 (3 cycles). THF (15 mL) was then added, and the solution was cooled to –78 °C. L-selectride (1.0 M in THF, 10.5 mL, 10.5 mmol, 4.0 equiv) was added dropwise, and the reaction mixture was stirred for 4 h. The reaction was carefully quenched with saturated NH_4Cl solution (5 mL), followed by the addition of EtOAc (20 mL). The mixture was transferred to a separatory funnel, and the layers were separated. The aqueous phase was extracted with EtOAc (3 × 10 mL), and the combined organic layers were washed with water, and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel, eluting with 10%→50% EtOAc in PE containing 1% HOAc, to afford lactol **20** (0.51 g, 49% yield) as a white foam.



R_f = 0.4 (PE: EtOAc = 1:1, with 1% HOAc)

$[\alpha]_D^{21.0}$ = –82.2 (c = 0.423, $CHCl_3$)

HRMS-ESI (m/z): calc. for $C_{20}H_{31}O_8$ $[M+H^+]$ 399.2013, found 399.2014.

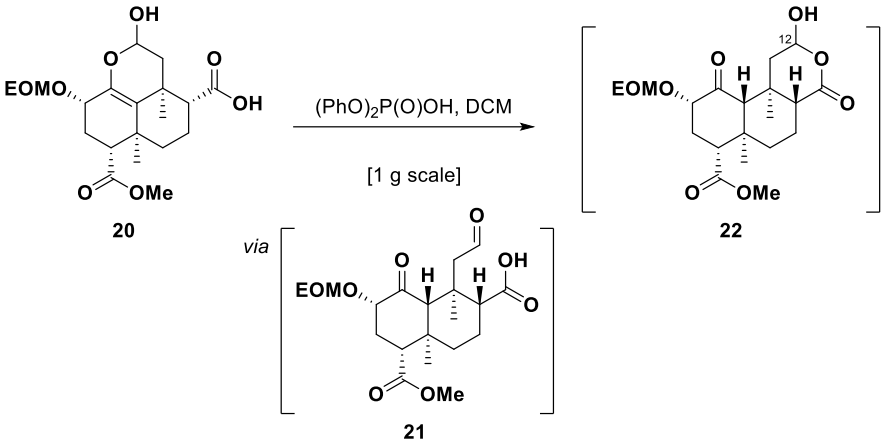
IR (neat, cm^{-1}): 2950, 1731, 1438, 1386, 1285, 1240, 1159, 1129, 1038, 1021, 929, 902, 755

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.34 (dd, *J* = 10.2, 2.4 Hz, 1H), 4.87 (d, *J* = 7.1 Hz, 1H), 4.80 (d, *J* = 7.1 Hz, 1H), 4.23 (dd, *J* = 9.8, 7.8 Hz, 1H), 3.77 – 3.68 (m, 1H), 3.67

(s, 3H), 3.60 (dq, *J* = 9.6, 7.1 Hz, 1H), 2.42 (dd, *J* = 13.2, 3.4 Hz, 1H), 2.23 (dt, *J* = 13.0, 2.9 Hz, 2H), 2.19 – 2.09 (m, 2H), 2.07 – 1.91 (m, 1H), 1.74 (dddd, *J* = 17.7, 14.3, 6.9, 3.5 Hz, 2H), 1.59 (dd, *J* = 13.1, 10.3 Hz, 1H), 1.43 – 1.34 (m, 1H), 1.32 (s, 3H), 1.25 (s, 3H), 1.21 (t, *J* = 7.1 Hz, 3H).

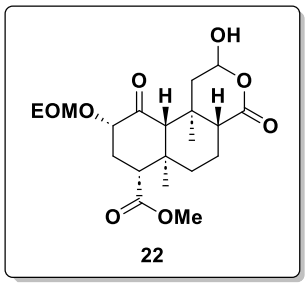
^{13}C NMR (151 MHz, $CDCl_3$): δ 178.4, 173.5, 144.4, 118.0, 95. 5, 91.1, 72.2, 63.5, 53.5, 51.69, 51.65, 45.5, 38.7, 36.1, 35.2, 29.0, 25.9, 22.7, 20.7, 15.2.

Synthesis of compound 22



To **20** (1.0 g, 2.5 mmol, 1.0 equiv) in DCM (100 mL) was added $(PhO)_2P(O)OH$ (6.3 mg, 0.025 mmol, 0.01 equiv), and the resulting solution was stirred at 25 °C for 72-120 h. The reaction progress was monitored by ^1H NMR: an aliquot of the reaction mixture (~ 0.1 mL) was directly transferred to an NMR tube and diluted with $CDCl_3$ (0.4 mL) without prior concentration. Upon completion, Et_3N (2.5 mg, 3.5 μL, 0.025 mmol, 0.01 equiv) was added, and the reaction mixture was concentrated under reduced pressure to afford the crude product, which was used directly in the next step without further purification.

22 *can be purified by repeated PTLC (developed with ~1:5:20 HOAc:acetone:DCM). Alcohol-containing developing solvents should be avoided, as they promote formation of a putative alcohol adduct.* ***22*** *may also be purified by flash column chromatography on silica gel; however, complete separation is challenging. Typically, a single chromatographic purification affords 50% analytically pure* ***22****, together with a fraction consisting of an approximately 3:1 mixture of* ***22/20*** *(accounting for the remaining ~50% of the material). In solution,* ***22*** *exists in equilibration with both its C12 epimer and* ***21*** *(see the NMR Spectrum section).*



22

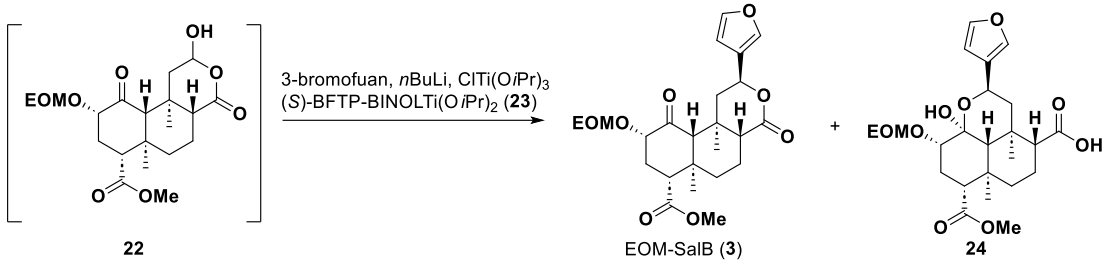
***R**f* = 0.05 (PE: EtOAc = 1:1)

IR (neat, cm^{-1}): 3423, 2951, 1724, 1438, 1392, 1277, 1199, 1159, 1124, 1038, 1019, 755.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.72 (t, *J* = 5.4 Hz, 1H), 4.78 (d, *J* = 7.2 Hz, 1H), 4.74 (d, *J* = 7.2 Hz, 1H), 4.17 (dd, *J* = 12.2, 7.3 Hz, 1H), 4.09 (br, 1H), 3.71 (s, 3H), 3.71 – 3.53 (m, 2H), 2.71 (dd, *J* = 13.3, 3.6 Hz, 1H), 2.62 (dd, *J* = 14.2, 6.3 Hz, 1H), 2.42 (dd, *J* = 11.6, 3.3 Hz, 1H), 2.33 (ddd, *J* = 13.4, 7.3, 3.3 Hz, 1H), 2.25 – 2.10 (m, 2H), 2.05 (dd, *J* = 13.8, 3.6 Hz, 1H), 1.81 – 1.48 (m, 3H), 1.40 (td, *J* = 8.3, 7.2, 4.3 Hz, 2H), 1.33 (s, 3H), 1.19 (t, *J* = 7.0 Hz, 3H), 1.04 (s, 3H).

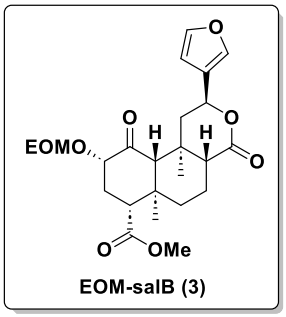
^{13}C NMR (126 MHz, $CDCl_3$): δ 206.1, 172.15, 172.13, 94.8, 94.4, 77.9, 65.4, 64.1, 53.8, 52.0, 48.9, 44.0, 42.2, 38.0, 35.2, 32.6, 18.3, 17.5, 16.2, 15.3.

Synthesis of EOM-SalB (3) and 24



To a 25 mL RBF was added 3-bromofuran (368 mg, 225 μL, 2.5 mmol, 10 equiv) and THF (2.5 mL), and the solution was cooled to –78 °C. *n*BuLi (2.5 M in hexane, 1.0 mL, 2.5 mmol, 10 equiv) was added dropwise, and the mixture was stirred for 1 h. $ClTi(O^iPr)_3$ (1 M in hexane, 2.5 mL, 2.5 mmol, 10 equiv) was then added dropwise. After complete addition, the cooling bath was removed, and the reaction mixture was warmed to 23 °C over 10 min and stirred for an additional 30 min to give a ~ 0.4 M solution of 3-furylTi(O*i*Pr)$_3$, which was used immediately.

In a separate 10 mL RBF charged with (*S*)-BFTP-BINOLTi(O*i*Pr)$_2$ (**23**) (166 mg, 0.25 mmol, 1.0 equiv; prepared according to literature procedure[15]), freshly prepared 3-furylTi(O*i*Pr)$_3$ solution (~ 0.4 M, 2 mL, 0.8 mmol, 3.2 equiv) was added (*5 min prior to use, stirring was stopped to allow complete precipitation of LiCl, and only the clear supernatant was transferred*). The resulting red solution was stirred at 25 °C for 5 min. This solution was then added dropwise to a solution of crude **22** (100 mg, 0.25 mmol, 1.0 equiv) in toluene (2.5 mL) at –40 °C. The reaction mixture was stirred at –40 °C for 24 h, then quenched with 1M HCl (1 mL) and EtOAc (5 mL). The layers were separated, and the aqueous phase was extracted with EtOAc (3×5 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and filtered. The solution was added 5 mg $(PhO)_2P(O)OH$ before being concentrated under reduced pressure, and the residue was stored at 0 °C overnight. The crude material was purified by flash column chromatography on silica gel (~10 mL), eluting with 10% → 50% EtOAc in PE containing 0.5% HOAc, to afford **3** as a white solid (56 mg, 50% over 2 steps) and **24** as a pale yellow foam (33 mg, 33%).



EOM-salB (3)

R_f = 0.5 (PE: EtOAc = 1:1)

Melting point: 146-150 ℃

$[\alpha]_D^{24.4}$ = –71.6 (c = 1.0, $CHCl_3$)

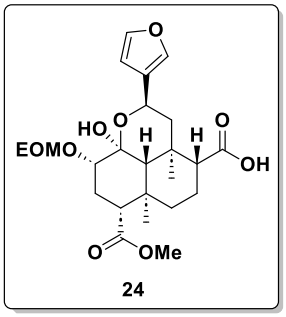
HRMS-ESI (m/z): calc. for $C_{24}H_{33}O_8$ [M+H^+] 449.2170, found 449.2179.

IR (neat, cm^{-1}): 2951, 1724, 1438, 1394, 1368, 1276, 1224, 1159, 1123, 1101, 1073, 1041, 1022, 1003, 940, 875, 785, 754, 602

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (s, 1H), 7.40 (t, *J* = 1.8 Hz, 1H), 6.37 (t, *J* = 1.3 Hz, 1H), 5.54 (dd, *J* = 11.7, 5.1 Hz, 1H), 4.76 (q, *J* = 7.2 Hz, 2H), 4.17 (dd, *J* = 12.2, 7.4 Hz, 1H), 3.71 (s, 3H), 3.75 – 3.64 (m, 1H), 3.58 (dq, *J* = 9.7, 7.1 Hz, 1H), 2.69 (dd, *J* = 13.5, 3.4 Hz, 1H), 2.53 (dd, *J* = 13.3, 5.2 Hz, 1H), 2.34 (ddd, *J* = 13.5, 7.4, 3.4 Hz, 1H), 2.26 – 2.10 (m, 2H), 2.06 (s, 1H), 2.07 – 2.00 (m, 1H), 1.78 (dt, *J* = 13.2, 3.0 Hz, 1H), 1.61 (dddd, *J* = 37.4, 16.2, 10.0, 3.1 Hz, 3H), 1.46 (s, 3H), 1.18 (t, *J* = 7.1 Hz, 3H), 1.11 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 206.0, 171.9, 171.2, 143.8, 139.4, 125.4, 108.3, 94.3, 77.8, 72.0, 64.3, 63.9, 53.9, 51.9, 51.5, 43.6, 42.0, 38.2, 35.5, 32.6, 18.2, 16.4, 15.2, 15.1.

The NMR data were in agreement with literature values.[16]



24

R_f = 0.6 (PE: EtOAc = 1:1)

Melting point: 65-69 °C

$[\alpha]_D^{18.8}$ = –66.3 (c = 0.59, $CHCl_3$)

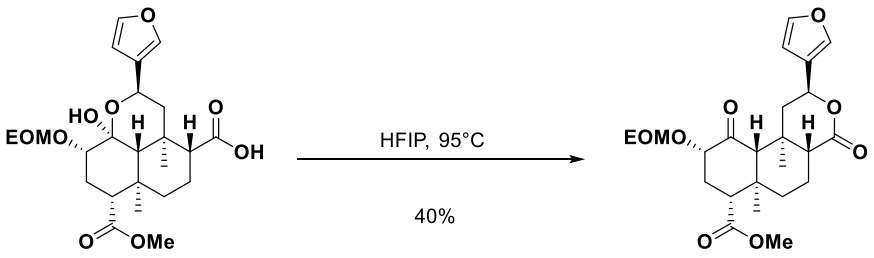
HRMS-ESI (m/z): calc. for $C_{24}H_{34}NaO_9$ [M+Na^+] 489.2095, found 489.2103.

IR (neat, cm^{-1}): 2950, 1728, 1701, 1437, 1394, 1277, 1216, 1161, 1115, 1071, 1022, 989, 940, 875, 772, 601

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (t, *J* = 1.7 Hz, 1H), 7.31 (dt, *J* = 1.7, 0.9 Hz, 1H), 6.33 (dd, *J* = 1.9, 0.9 Hz, 1H), 5.24 – 4.99 (m, 1H), 4.86 (d, *J* = 6.7 Hz, 1H), 4.73 (d, *J* = 6.7 Hz, 1H), 3.73 – 3.62 (m, 4H), 3.62 – 3.57 (m, 1H), 3.54 (dq, *J* = 9.5, 7.1, 6.5 Hz, 1H), 3.41 (d, *J* = 1.6 Hz, 1H), 2.20 (dd, *J* = 13.4, 2.8 Hz, 1H), 2.14 (dd, *J* = 12.8, 3.0 Hz, 1H), 2.01 (dtd, *J* = 15.2, 13.1, 11.4 Hz, 3H), 1.79 (ddd, *J* = 13.3, 5.2, 2.8 Hz, 1H), 1.70 (td, *J* = 16.2, 15.1, 4.5 Hz, 2H), 1.62 (t, *J* = 12.7 Hz, 1H), 1.54 (s, 3H), 1.30 (m, 2H), 1.20 (s, 3H), 1.16 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 178.3, 173.1, 143.0, 138.9, 127.6, 109.1, 97.6, 95.5, 78.2, 63.7, 61.7, 55.5, 54.9, 54.4, 51.6, 49.8, 40.2, 36.8, 36.4, 28.3, 21.1, 18.4, 15.5, 15.2.

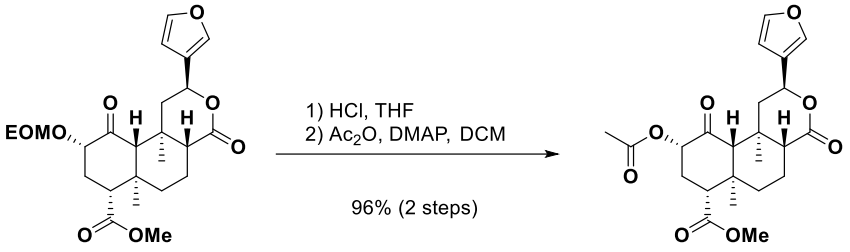
Recycle of compound 24 to EOM-SalB



24 EOM-SalB (**3**)

To a 50 mL sealed glass tube was added **24** (50 mg, 0.11 mmol, 1.0 equiv) and HFIP (0.005 M, 22 mL). The tube was sealed and heated at 95 °C for 48 h (reaction progress monitored by TLC). Upon completion, the solvent was removed under reduced pressure, and the residue was purified by PTLC (developed with 0%→15% EtOAc in DCM) to afford EOM-SalB (**3**) (19 mg, 40% yield) as a pale yellow solid.

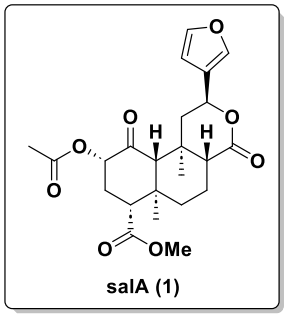
Synthesis of salvinorin A (1)



EOM-SalB (**3**) SalA (**1**)

To a 10 mL RBF was added EOM-SalB (**3**) (20 mg, 0.045 mmol, 1.0 equiv) and THF (0.4 mL), followed by HCl (3 M, 0.2 mL, 0.6 mmol, 14 equiv). The reaction mixture was stirred at 25 °C overnight until TLC indicated complete consumption of starting material. The solvent was then removed under reduced pressure to afford a pale-yellow solid (crude salvinorin B), which was used directly in the next step without further purification.

The crude salvinorin B was dissolved in DCM (1 mL), in which DMAP (0.5 mg, 0.004 mmol, 0.1 equiv) and Ac_2O (0.2 mL, 2 mmol, 50 equiv) were added sequentially. The reaction mixture was stirred at 25 °C for 3 h before concentration under reduced pressure. The residue was purified by PTLC (developed with 0%→40% EtOAc in PE) to afford salvinorin A (**1**) as a white crystalline solid (20 mg, 96%).



R_f = 0.5 (PE: EtOAc = 1:1)

Melting point: 221-225 ℃

$[\alpha]_D^{25.0}$ = –38.5 (c = 1.0, $CHCl_3$)

Lit. $[\alpha]_D^{25}$ = –40.7 (c = 0.12, $CHCl_3$) [17]

Natural $[\alpha]_D^{25}$ = –41 (c = 1, $CHCl_3$)[17]

HRMS-ESI (m/z): calc. for $C_{23}H_{29}O_8$ [M+H$^+$] 433.1857, found 433.1857.

IR (neat, cm^{-1}): 2952, 1724, 1505, 1436, 1377, 1277, 1234, 1203, 1161, 1075, 1051, 1022, 1004, 951, 893, 875, 753, 667, 602, 461

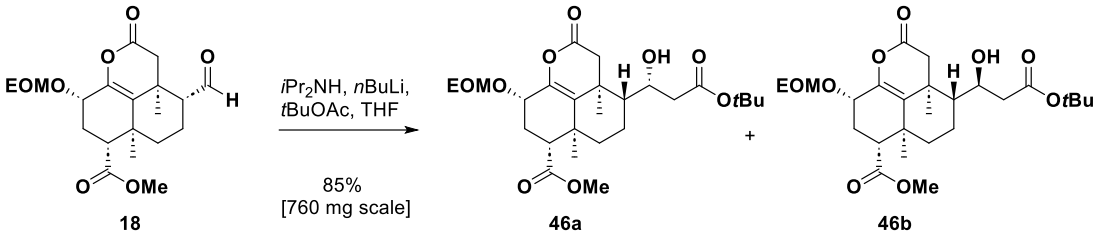
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (d, *J* = 1.3 Hz, 1H), 7.39 (t, *J* = 1.7 Hz, 1H), 6.37 (t, *J* = 1.3 Hz, 1H), 5.52 (dd, *J* = 11.7, 5.1 Hz, 1H), 5.14 (dd, *J* = 11.2, 8.9 Hz, 1H), 3.72

(s, 3H), 2.79 – 2.69 (m, 1H), 2.50 (dd, *J* = 13.4, 5.2 Hz, 1H), 2.36 – 2.21 (m, 2H), 2.17 (s, 3H), 2.21 – 2.12 (m, 1H), 2.07 (dd, *J* = 11.7, 3.0 Hz, 1H), 1.79 (dt, *J* = 13.0, 2.7 Hz, 1H), 1.72 – 1.52 (m, 4H), 1.45 (s, 3H), 1.11 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 202.0, 171.6, 171.1, 170.0, 143.7, 139.4, 125.2, 108.4, 75.0, 72.1, 64.1, 53.6, 52.0, 51.4, 43.4, 42.1, 38.2, 35.5, 30.8, 20.6, 18.2, 16.4, 15.2.

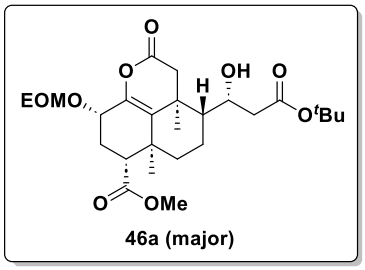
The NMR data were in agreement with literature values.[17]

Synthesis of compounds 46a and 446b



To a 25 mL RBF was added *i*Pr_2NH (532 μL, 3.8 mmol, 1.9 equiv) and THF (12 mL). *n*BuLi (2.5 M, 1.44 mL, 3.6 mmol, 1.8 equiv) was added dropwise at 0 °C, and the mixture was stirred at –78 °C for 40 min. *t*BuOAc (536 μL, 4.0 mmol, 2.0 equiv) was then added dropwise, and the resulting mixture was stirred for an additional 80 min.

In a separate 15 mL pear-shaped flask, aldehyde **18** (760 mg, 2.0 mmol, 1.0 equiv) was dissolved in THF (4 mL) with sonication to afford a homogeneous solution. The aldehyde solution was transferred over 1 min via syringe (with the needle tip touching the wall of the receiving flask) at –78 °C, and the flask was rinsed with THF (2×2 mL) to ensure complete transfer. The reaction mixture was stirred for 30 min at –78 °C, then quenched with saturated NH_4Cl solution (2 mL). The mixture was diluted with H_2O (5 mL) and EtOAc (20 mL), and the layers were separated. The organic layer was washed with H_2O (3×5 mL), and combined aqueous layers were extracted with EtOAc (3×5 mL). The organic layers were combined, washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (~50 mL), eluting with 0%→40% EtOAc in PE, to afford the **46a/b** as a pale yellow gum (*d.r.* = 2:1, 835 mg, 85%). Pure samples of **46a** and **46b** were obtained by repeated PTLC (developed with 35% EtOAc in PE).



R_f = 0.44 (PE: EtOAc = 2:1)

$[\alpha]_D^{23.3}$ = –66.3 (c = 0.72, $CHCl_3$)

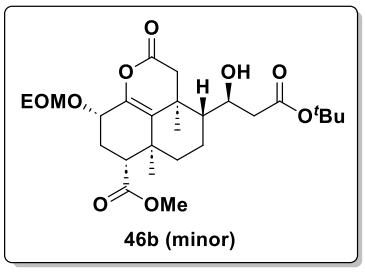
HRMS-ESI (m/z): calc. for $C_{26}H_{44}NO_9$ $[M+NH_4^+]$ 514.3011, found 514.3011.

IR (neat, cm^{-1}): 3507, 2976, 1763, 1727, 1456, 1386, 1368, 1287, 1231, 1156, 1099,

1036, 949, 911, 843, 801, 755, 500, 452, 439, 426, 416, 403

^{1}H NMR (400 MHz, $CDCl_3$):δ 4.86 (d, *J* = 7.2 Hz, 1H), 4.81 (d, *J* = 7.2 Hz, 1H), 4.32 (t, *J* = 8.7 Hz, 1H), 4.18 (dd, *J* = 9.9, 3.5 Hz, 1H), 3.69 (s, 3H), 3.78 – 3.59 (m, 2H), 2.80 (d, *J* = 15.1 Hz, 1H), 2.58 (dd, *J* = 16.4, 9.8 Hz, 1H), 2.51 (dd, *J* = 10.1, 7.0 Hz, 1H), 2.34 – 2.23 (m, 2H), 2.21 (dd, *J* = 16.4, 3.5 Hz, 1H), 2.09 (d, *J* = 15.0 Hz, 1H), 1.93 – 1.81 (m, 1H), 1.76 (dt, *J* = 13.3, 3.3 Hz, 1H), 1.61 – 1.51 (m, 1H), 1.47 (s, 9H), 1.37 (td, *J* = 13.4, 3.1 Hz, 1H), 1.32 (s, 3H), 1.27 (s, 3H), 1.22 (t, *J* = 7.1 Hz, 3H), 1.11 (dd, *J* = 12.5, 3.2 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 173.0, 172.3, 167.6, 143.8, 127.1, 95.4, 81.9, 70.4, 65.7, 63.6, 52.3, 51.7, 51.3, 44.2, 42.2, 38.2, 36.8, 36.3, 29.4, 28.3 (3C), 22.7, 22.0, 16.8, 15.2.



46b (minor)

R_f = 0.45 (PE: EtOAc = 2:1)

$[\alpha]_D^{24.8}$ = –94.53 (c = 0.21, $CHCl_3$)

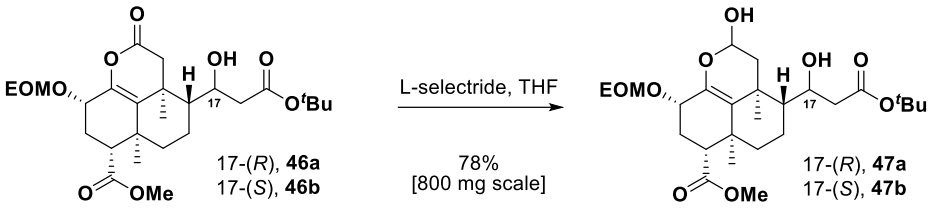
HRMS-ESI (m/z): calc. for $C_{26}H_{44}NO_9$ $[M+NH_4^+]$ 514.3011, found 514.3025.

IR (neat, cm^{-1}): 3504, 2977, 1764, 1732, 1455, 1368, 1230, 1154, 1107, 1078, 1037, 962, 892, 843, 532, 512, 481, 463.

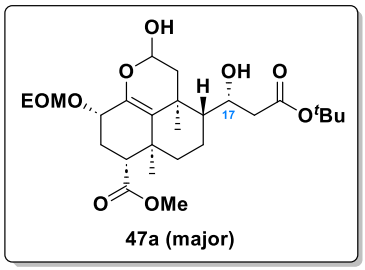
^{1}H NMR (400 MHz, $CDCl_3$): δ 4.87 (d, *J* = 7.2 Hz, 1H), 4.81 (d, *J* = 7.2 Hz, 1H), 4.33 (t, *J* = 8.7 Hz, 1H), 3.95 (s, 1H), 3.68 (s, 3H), 3.78 – 3.58 (m, 2H), 3.56 (d, *J* = 3.8 Hz, 1H), 3.55 (d, *J* = 15.8 Hz, 1H), 2.58 (dd, *J* = 16.7, 2.4 Hz, 1H), 2.51 (dd, *J* = 12.2, 5.1 Hz, 1H), 2.35 (dd, *J* = 16.7, 9.3 Hz, 1H), 2.32 – 2.22 (m, 2H), 2.21 (d, *J* = 15.8 Hz, 1H), 1.76 – 1.67 (m, 1H), 1.47 (s, 9H), 1.39 (m, 4H), 1.27 (s, 3H), 1.24 (s, 3H), 1.26 – 1.18 (t, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 173.0, 172.9, 168.5, 143.8, 127.4, 95.5, 82.2, 70.6, 69.3, 63.6, 51.7, 51.3, 51.2, 44.7, 40.6, 37.6, 36.7, 36.0, 29.4, 28.3 (3C), 22.4, 21.0, 20.5, 15.2.

Synthesis of compounds 47a and 47b



To a 50 mL RBF charged with **46a**/**b** (2:1 mixture, 800 mg, 1.61 mmol total, 1.0 equiv) was added THF (9 mL). The solution was cooled to –78 °C, and L-selectride (1.0 M in THF, 6.4 mL, 6.4 mmol, 4.0 equiv) was added dropwise. The reaction mixture was stirred for 4 h. Saturated NH_4Cl solution (2 mL) was then added dropwise at –78 ºC (**caution:** gas evolution), followed by H_2O (5 mL) and EtOAc (20 mL). The mixture was allowed to warm to room temperature, and the layers were separated. The organic layer was washed with H_2O (3×5 mL), and combined aqueous layers were extracted with EtOAc (3×5 mL). The organic layers were combined, washed with brine, and dried over Na_2SO_4. Filtration and concentration afforded a residue, which was purified by flash column chromatography on silica gel (~50 mL), eluting with 0%→60% EtOAc in PE, to afford **47a**/**b** as a colorless gum (*d.r.* = 2:1 at C17, 625 mg, 78%). Pure samples of **47a** and **47b** were obtained by repeated PTLC (developed with 40% EtOAc in PE).



R_f = 0.25 (PE: EtOAc = 1:1)

$[\alpha]_D^{24.0}$ = –62.1 (c = 0.25, $CHCl_3$)

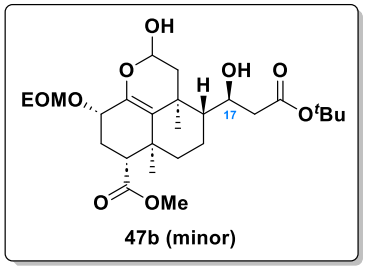
HRMS-ESI (m/z): calc. for $C_{26}H_{42}KO_9$ $[M+K^+]$ 537.2460, found 537.2446.

IR (neat, cm^{-1}): 3430, 2917, 1727, 1636, 1457, 1368, 1290, 1233, 1217, 1156, 1089, 1038, 943, 905, 842, 753, 668, 569.

^{1}H NMR (major C12 diastereoisomer, 400 MHz, $CDCl_3$):δ 5.39 (d, *J* = 9.8 Hz, 1H), 4.86 (d, *J* = 7.0 Hz, 1H), 4.81 (d, *J* = 7.0 Hz, 1H), 4.27 (dd, *J* = 10.0, 3.0 Hz, 1H), 4.21 (dd, *J* = 9.6, 8.1 Hz, 1H), 3.67 (s, 3H), 3.81 – 3.52 (m, 2H), 3.10 (br, 1H), 2.86 (br, 1H), 2.56 (dd, *J* = 16.4, 10.1 Hz, 1H), 2.40 (dd, *J* = 12.1, 4.4 Hz, 1H), 2.24 – 2.02 (m, 4H), 1.93 – 1.76 (m, 2H), 1.47 (s, 9H), 1.34 (s, 3H), 1.24 (s, 3H), 1.21 (t, *J* = 7.1 Hz, 3H),

0.99 (dd, *J* = 12.8, 2.9 Hz, 1H).

^{13}C NMR (major C12 diastereoisomer, 151 MHz, $CDCl_3$): δ 173.7, 172.8, 143.4, 120.1, 95.5, 91.3, 81.7, 72.4, 66.0, 63.4, 52.9, 52.0, 51.6, 45.4, 42.5, 40.1, 36.6, 36.4, 29.0, 28.3 (3C), 25.9, 22.7, 16.8, 15.2.



47b (minor)

R_f = 0.26 (PE: EtOAc = 1:1)

Melting point: 42-46 °C

$[\alpha]_D^{25.7}$ = –85.2 (c = 0.32, $CHCl_3$)

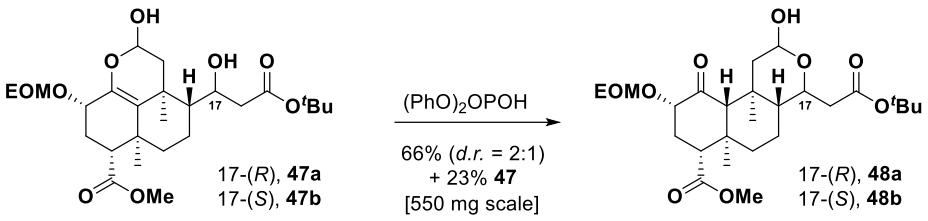
HRMS-ESI (m/z): calc. for $C_{26}H_{42}KO_9$ [M+K$^+$] 537.2460, found 537.2451.

IR (neat, cm^{-1}): 2973, 2901, 1732, 1717, 1700, 1507, 1457, 1394, 1368, 1250, 1155, 1077, 1066, 1043, 419

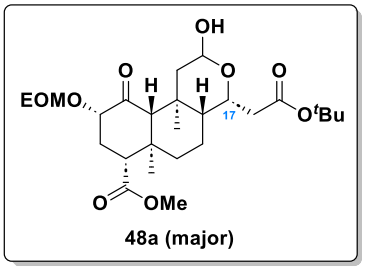
^{1}H NMR (major C12 diastereoisomer, 400 MHz, $CDCl_3$): δ 5.33 (d, *J* = 10.1 Hz, 1H), 4.86 (d, *J* = 7.0 Hz, 1H), 4.80 (d, *J* = 7.1 Hz, 1H), 4.22 (dd, *J* = 9.7, 8.0 Hz, 1H), 4.04 (s, 1H), 3.66 (s, 3H), 3.83 – 3.37 (m, 2H), 3.37 (br, 1H), 2.99 (br, 1H), 2.61 (dd, *J* = 13.0, 2.6 Hz, 1H), 2.50 (dd, *J* = 16.6, 2.4 Hz, 1H), 2.45 – 2.30 (m, 2H), 2.19 – 2.08 (m, 2H), 1.81 – 1.68 (m, 1H), 1.64 – 1.50 (m, 1H), 1.47 (s, 9H), 1.49 – 1.30 (m, 4H), 1.26 (s, 3H), 1.21 (t, *J* = 7.1 Hz, 3H), 1.19 (s, 3H).

^{13}C NMR (major C12 diastereoisomer, 151 MHz, $CDCl_3$): δ 173.6, 173.1, 143.6, 119.9, 95.4, 91.1, 81.7, 72.3, 68.7, 63.3, 52.3, 51.6, 51.4, 45.7, 40.3, 39.5, 36.2, 36.0, 28.9, 28.1 (3C), 25.2, 22.3, 19.6, 15.1.

Synthesis of compounds 48a and 48b



To a 100 mL RBF charged with **47a/b** (2:1 mixture, 550 mg, 1.1 mmol total, 1.0 equiv) was added HPLC-grade DCM (50 mL). $(PhO)_2(O)POH$ (2.5 mg, 0.01 mmol, 0.01 equiv) was then added and the solution was stirred at 25 °C for 36 h (monitored by crude ^1H NMR analysis). Upon completion, a drop of Et_3N was added and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography on silica gel (~30 mL), eluting with 0%→80% EtOAc in PE, to afford **48a/b** as a white foam (*d.r.* = 2:1 at C17, 364 mg, 66%) along with recovered starting material (126 mg, 23%). Pure samples of **48a** and **48b** were obtained through two successive rounds of PTLC (developed with 2% MeOH in DCM for the first separation and 40% EtOAc in PE for the second).



R_f = 0.23 (PE: EtOAc = 1:1)

Melting point: 135-137 °C

$[\alpha]_D^{27.0}$ = –46.8 (c = 0.33, $CHCl_3$)

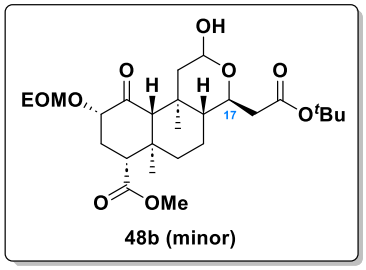
HRMS-ESI (m/z): calc. for $C_{26}H_{43}O_9$ $[M+H^+]$ 499.2902, found 499.2906.

IR (neat, cm^{-1}): 3433, 2975, 2931, 1724, 1437, 1392, 1368, 1274, 1196, 1155, 1122, 1099, 1042, 1016, 985, 931, 903, 868, 845, 787, 754, 666, 545.

^1H NMR (major C12 diastereoisomer, 400 MHz, $CDCl_3$): δ 5.22 (dd, *J* = 8.4, 3.0 Hz, 1H), 4.77 (d, *J* = 7.1 Hz, 1H), 4.71 (d, *J* = 7.2 Hz, 1H), 4.43 (ddd, *J* = 10.4, 6.2, 3.6 Hz, 1H), 4.12 (dd, *J* = 12.3, 7.3 Hz, 1H), 3.69 (s, 3H), 3.73 – 3.52 (m, 2H), 2.70 (dd, *J* = 13.5, 3.4 Hz, 1H), 2.63 (dd, *J* = 15.0, 10.9 Hz, 1H), 2.42 (dd, *J* = 12.9, 3.0 Hz, 1H), 2.35 – 2.24 (m, 2H), 2.14 (q, *J* = 13.1 Hz, 1H), 1.96 (s, 1H), 1.76 – 1.53 (m, 4H), 1.46 (s, 9H), 1.39 (s, 3H), 1.19 (t, *J* = 7.1 Hz, 3H), 1.04 (s, 3H), 0.87 (dd, *J* = 13.0, 8.3 Hz,

1H).

^{13}C NMR (major C12 diastereoisomer, 151 MHz, $CDCl_3$): δ 206.1, 172.4, 171.2, 94.4, 88.7, 81.0, 77.9, 73.9, 66.6, 64.0, 54.06, 51.9, 46.7, 45.4, 42.6, 39.5, 36.9, 35.4, 32.7, 28.3 (3C), 20.2, 17.7, 16.7, 15.3.



48b (minor)

R_f = 0.25 (PE: EtOAc = 1:1)

Melting point: 51-56 °C

$[\alpha]_D^{26.4}$ = –58.6 (c = 0.27, $CHCl_3$)

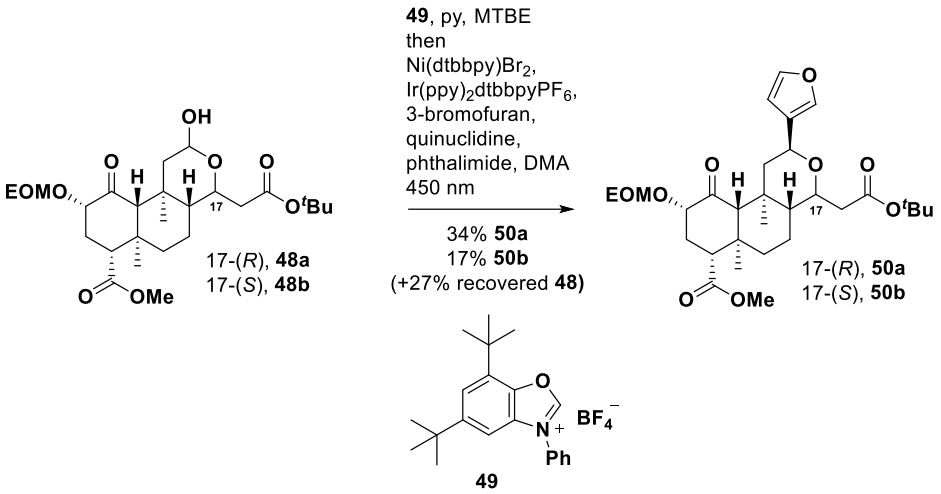
HRMS-ESI (m/z): calc. for $C_{26}H_{42}NaO_9$ [M+Na$^+$] 521.2721, found 521.2716.

IR (neat, cm^{-1}): 3444, 2917, 1725, 1453, 1392, 1368, 1275, 1200, 1153, 1127, 1100, 1066, 1012, 948, 872, 846, 754.

^{1}H NMR (major C12 diastereoisomer, 400 MHz, $CDCl_3$): δ 5.09 (dd, *J* = 9.3, 2.5 Hz, 1H), 4.77 (d, *J* = 7.2 Hz, 1H), 4.71 (d, *J* = 7.1 Hz, 1H), 4.14 (dd, *J* = 12.2, 7.2 Hz, 1H), 3.97 (ddd, *J* = 10.0, 7.7, 4.8 Hz, 1H), 3.69 (s, 3H), 3.74 – 3.50 (m, 2H), 2.74 (br, 1H), 2.69 (dd, *J* = 13.5, 3.5 Hz, 1H), 2.49 (dd, *J* = 15.3, 4.7 Hz, 1H), 2.40 – 2.25 (m, 3H), 2.14 (q, *J* = 13.1 Hz, 1H), 1.96 (s, 1H), 1.69 (d, *J* = 13.5 Hz, 1H), 1.55 (td, *J* = 12.9, 5.0 Hz, 1H), 1.45 (s, 9H), 1.37 (s, 3H), 1.19 (t, *J* = 7.1 Hz, 3H), 1.16 – 1.06 (m, 1H), 1.03 (s, 3H), 0.83 (dd, *J* = 12.6, 9.3 Hz, 1H).

^{13}C NMR (major C12 diastereoisomer, 151 MHz, $CDCl_3$): δ 206.29, 172.3, 170.9, 94.4, 92.4, 81.0, 78.0, 70.8, 65.74, 64.0, 54.2, 51.9, 50.5, 45.8, 42.4, 40.3, 39.4, 35.9, 32.8, 28.3 (3C), 19.0, 16.8, 15.4, 15.3.

Synthesis of compounds 50a and 50b

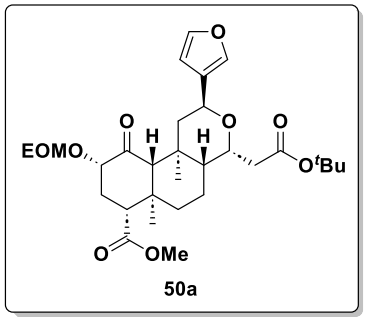


A flame-dried 15 mL RBF equipped with a magnetic stir bar was charged with **48a**/**b** (2:1 mixture, 120 mg, 0.24 mmol, 1 equiv) and **49** (90 mg, 0.228 mmol, 0.95 equiv). In a separate flame-dried 4 mL vial were placed Ni(dtbbpy)Br_2 (9.3 mg, 0.019 mmol, 0.08 equiv), Ir(ppy)$_2$dtbbpyPF_6 (4.4 mg, 5 μmol, 0.02 equiv), quinuclidine (47 mg, 0.42 mmol, 1.75 equiv) and phthalimide (7.8 mg, 0.053 mmol, 0.22 equiv). Both vessels were transferred into a glovebox.

MTBE (1.0 mL) was added to the flask containing the substrate, followed by the slow addition of pyridine (20.5 μL, 0.228 mmol, 0.95 equiv). After stirring for 5 min, the suspension turned faint pink and was filtered through a syringe filter into a flame-dried 8 mL vial. The flask and syringe were rinsed twice with MTBE, and the washings were filtered and combined with the filtrate to give a total MTBE volume of 1.6 mL.

DMA (1.2 mL) was added to the 4 mL vial containing the catalysts, and the mixture was stirred to give a homogeneous dark-green solution. Freshly distilled 3-bromofuran (33 μL, 0.36 mmol, 1.5 equiv; distilled over K_2CO_3 before use) was added, and the mixture was stirred for 5 min. The DMA solution was then transferred to the 8 mL reaction vial containing the substrate-NHC adduct. The catalyst vial was rinsed with DMA (0.4 mL), and the washings were transferred to the reaction vial. The vial was sealed with a screw cap and parafilm, removed from the glovebox, and irradiated in the Rogertech photoreactor at 450 nm (100% power) for 12 h at 5 °C. Upon completion,

the reaction mixture was transferred to a separatory funnel, and H_2O (5 mL), EtOAc (15 mL) and HOAc (0.2 mL) were added. The layers were separated, and the organic phase was washed with H_2O (5×3 mL). The combined aqueous layers were extracted with EtOAc (3×5 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (~15 mL), eluting with 0%→ 40% EtOAc in PE, to afford compounds **50a** (45 mg, 34%) and **50b** (22 mg, 17%) as off-white solids, together with recovered **50a/b** (33 mg, 27%) as a pale-yellow solid.



50a

R_f = 0.5 (PE: EtOAc = 3:2)

Melting point: 52-56 °C

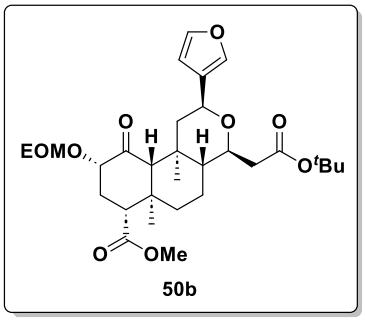
$[\alpha]_D^{24.6}$ = –68.0 (c = 0.61, $CHCl_3$)

HRMS-ESI (m/z): calc. for $C_{30}H_{48}NO_9$ $[M+NH_4^+]$ 566.3324, found 566.3318.

IR (neat, cm^{-1}): 2976, 2930, 1724, 1436, 1392, 1367, 1338, 1272, 1194, 1155, 1124, 1099, 1077, 1043, 1018, 905, 875, 846, 786, 755, 601.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 (t, *J* = 1.7 Hz, 1H), 7.31 (dd, *J* = 1.6, 0.9 Hz, 1H), 6.34 (dd, *J* = 2.0, 0.9 Hz, 1H), 4.85 (d, *J* = 10.8 Hz, 1H), 4.77 (d, *J* = 7.2 Hz, 1H), 4.72 (d, *J* = 7.1 Hz, 1H), 4.32 (ddd, *J* = 11.2, 5.6, 3.6 Hz, 1H), 4.12 (dd, *J* = 12.3, 7.3 Hz, 1H), 3.70 (s, 3H), 3.73 – 3.51 (m, 2H), 2.80 (dd, *J* = 14.4, 11.2 Hz, 1H), 2.71 (dd, *J* = 13.4, 3.4 Hz, 1H), 2.34 – 2.23 (m, 3H), 2.15 (td, *J* = 13.4, 12.2 Hz, 1H), 1.97 (s, 1H), 1.74 – 1.59 (m, 2H), 1.44 (s, 3H), 1.42 (s, 9H), 1.40 – 1.34 (m, 2H), 1.18 (t, *J* = 7.1 Hz, 3H), 1.12 (t, *J* = 12.2 Hz, 1H), 1.06 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 206.3, 172.4, 171.4, 143.0, 139.1, 127.3, 109.1, 94.5, 80.8, 78.1, 74.7, 66.8, 64.0, 61.5, 54.2, 51.8, 48.1, 44.8, 42.9, 39.7, 36.2, 35.0, 32.8, 28.2 (3C), 20.6, 17.1, 16.9, 15.3.



50b

R_f = 0.6 (PE: EtOAc = 3:2)

Melting point: 49-53 °C

$[\alpha]_D^{24.8}$ = –90.2 (c = 0.40, $CHCl_3$)

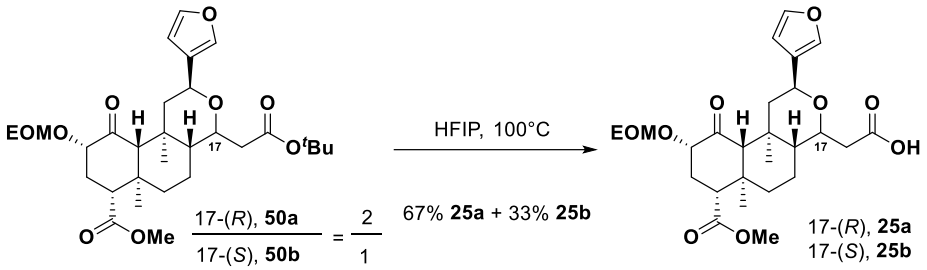
HRMS-ESI (m/z): calc. for $C_{30}H_{48}NO_9$ $[M+NH_4^+]$ 566.3324, found 566.3329.

IR (neat, cm^{-1}): 2933, 1727, 1456, 1392, 1367, 1273, 1199, 1153, 1124, 1100, 1020, 875, 783.

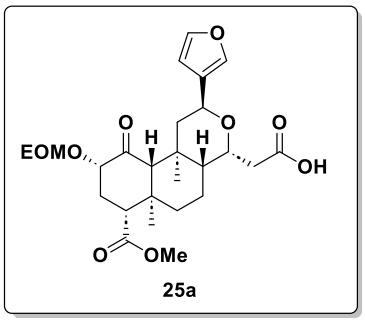
^{1}H NMR (400 MHz, $CDCl_3$):δ 7.32 (t, *J* = 1.7 Hz, 1H), 7.28 (q, *J* = 1.1 Hz, 1H), 6.30 (dd, *J* = 1.8, 0.8 Hz, 1H), 4.81 – 4.73 (m, 2H), 4.73 (d, *J* = 7.1 Hz, 1H), 4.14 (dd, *J* = 12.2, 7.3 Hz, 1H), 3.99 (ddd, *J* = 10.0, 7.7, 4.8 Hz, 1H), 3.69 (s, 3H), 3.75 – 3.51 (m, 2H), 2.69 (dd, *J* = 13.4, 3.4 Hz, 1H), 2.48 (dd, *J* = 14.8, 4.8 Hz, 1H), 2.38 – 2.26 (m, 2H), 2.23 (dd, *J* = 12.8, 2.4 Hz, 1H), 2.16 (q, *J* = 13.3 Hz, 1H), 1.98 (s, 1H), 1.70 (dt, *J* = 13.4, 3.4 Hz, 1H), 1.63 – 1.51 (m, 2H), 1.44 (s, 12H), 1.40 – 1.32 (m, 2H), 1.10 (t, *J* = 12.5 Hz, 1H), 1.07 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 206.6, 172.4, 171.1, 142.9, 138.8, 127.4, 108.9, 94.5, 80.7, 78.2, 72.4, 67.6, 66.0, 64.0, 54.3, 51.8, 51.1, 45.3, 42.5, 40.8, 39.5, 35.4, 32.9, 28.3 (3C), 19.1, 16.8, 15.3, 14.9.

Synthesis of compounds 25a and 25b



To a 50 mL thick-walled glass tube charged with **50a**/**b** (2:1 mixture, 65 mg, 0.058 mmol, 1 equiv) was added HFIP (0.002 M, 30 mL). The tube was sealed and heated at 100 °C for 24 h, with reaction progress monitored by TLC. Upon completion, the solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel (~20 mL), eluting with 0%→50% EtOAc in PE (containing 1% HOAc), to afford compounds **25a** (39 mg, 67% yield) and **25b** (19 mg, 33% yield) as white solids.



R_f = 0.2 (PE: EtOAc = 3:2, containing 1% HOAc)

Melting point: 76-81 °C

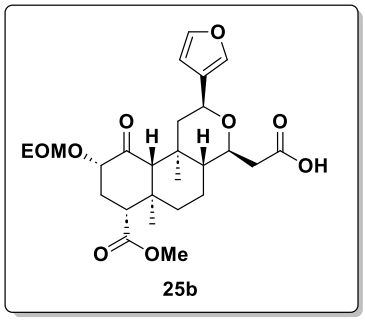
$[\alpha]_D^{22.0}$ = –95.5 (c = 0.57, $CHCl_3$)

HRMS-ESI (m/z): calc. for $C_{26}H_{40}NO_9$ $[M+NH_4^+]$ 510.2698, found 510.2698.

IR (neat, cm^{-1}): 3423, 2931, 1723, 1503, 1436, 1394, 1272, 1193, 1157, 1123, 1099, 1064, 1042, 1017, 930, 904, 875, 785, 750, 666, 601, 470, 408.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (s, 1H), 7.34 (d, *J* = 1.8 Hz, 1H), 6.35 (t, *J* = 1.2 Hz, 1H), 4.85 (d, *J* = 11.3 Hz, 1H), 4.77 (d, *J* = 7.2 Hz, 1H), 4.72 (d, *J* = 7.2 Hz, 1H), 4.33 (dq, *J* = 10.6, 2.7 Hz, 1H), 4.13 (dd, *J* = 12.3, 7.3 Hz, 1H), 3.70 (s, 3H), 3.79 – 3.47 (m, 2H), 2.89 (t, *J* = 13.4 Hz, 1H), 2.71 (dd, *J* = 13.4, 3.4 Hz, 1H), 2.38 (d, *J* = 15.2 Hz, 1H), 2.30 (ddt, *J* = 10.6, 7.3, 3.4 Hz, 1H), 2.24 (d, *J* = 12.8 Hz, 1H), 2.15 (q, *J* = 13.1 Hz, 1H), 1.98 (s, 1H), 1.78 – 1.54 (m, 2H), 1.43 (s, 3H), 1.44 – 1.28 (m, 2H), 1.18 (m, 4H), 1.06 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 206.3, 172.3, 143.1, 139.5, 126.7, 109.1, 94.5, 78.0, 74.4, 66.6, 64.0, 61.6, 54.2, 51.9, 47.7, 46.2 (*visible in HMBC*), 44.7, 42.9, 39.59, 34.9, 32.8, 20.6, 17.0, 16.8, 15.2. (*The carbonyl carbon of carboxylic acid group is invisible in ^{13}C or HMBC.*)



25b

R_f = 0.3 (PE: EtOAc = 3:2, containing 1% HOAc)

Melting point: 113-119 °C

$[\alpha]_D^{22.3}$ = –68.8 (c = 0.45, $CHCl_3$)

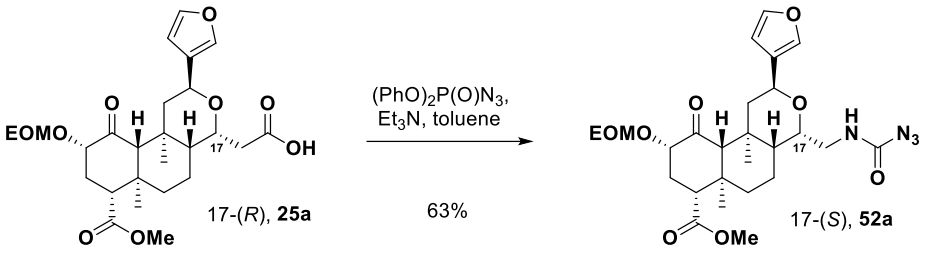
HRMS-ESI (m/z): calc. for $C_{26}H_{36}KO_9$ $[M+K^+]$ 531.1991, found 531.1991.

IR (neat, cm^{-1}): 2950, 1723, 1436, 1393, 1276, 1197, 1156, 1122, 1100, 1014, 948, 902, 875, 782, 752, 666, 601.

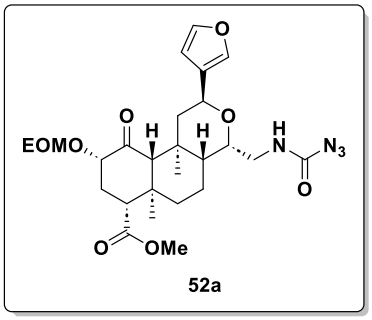
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (d, *J* = 1.8 Hz, 1H), 7.32 (s, 1H), 6.32 (t, *J* = 1.2 Hz, 1H), 4.84 (d, *J* = 11.4 Hz, 1H), 4.77 (d, *J* = 7.2 Hz, 1H), 4.72 (d, *J* = 7.2 Hz, 1H), 4.14 (dd, *J* = 12.2, 7.3 Hz, 1H), 4.00 (td, *J* = 10.9, 9.6, 3.8 Hz, 1H), 3.69 (s, 3H), 3.75 – 3.51 (m, 2H), 2.68 (td, *J* = 14.3, 13.8, 3.2 Hz, 2H), 2.45 (dd, *J* = 15.3, 7.7 Hz, 1H), 2.32 (ddd, *J* = 13.4, 7.3, 3.4 Hz, 1H), 2.23 (dd, *J* = 13.1, 2.4 Hz, 1H), 2.15 (q, *J* = 13.1 Hz, 1H), 2.00 (s, 1H), 1.75 – 1.65 (m, 1H), 1.58 (td, *J* = 12.5, 4.1 Hz, 1H), 1.44 (s, 3H), 1.43 – 1.27 (m, 2H), 1.18 (m, 5H), 1.06 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 206.4, 172.3, 143.3, 139.2, 126.7, 108.7, 94.5, 78.1, 72.0, 67.9, 65.7, 64.0, 54.2, 51.9, 50.6, 45.2, 42.4, 39.2, 35.2, 32.9, 19.0, 16.8, 15.3, 14.7. (*The carbonyl carbon of carboxylic acid group and C9 quaternary carbon are invisible in ^{13}C or HMBC.*)

Synthesis of compound 52a



To a 10 mL RBF was added **25a** (38 mg, 0.075 mmol, 1.0 equiv) and toluene (0.03 M, 2.5 mL), followed by Et_3N (40 μL, 30 mg, 0.30 mmol, 4.0 equiv) and $(PhO)_2P(O)N_3$ (49 μL, 63 mg, 0.23 mmol, 3.0 equiv). The reaction mixture was stirred at room temperature for 30 min then at 80 °C for 12 h. After cooling to room temperature, the solvent was removed under reduced pressure. The residue was purified by PTLC (developed with 35% EtOAc in PE) to afford **52a** (26 mg, 63% yield) as a white foam.



R_f = 0.4 (PE: EtOAc = 3:2)

Melting point: 42-46 °C

$[\alpha]_D^{23.4}$ = –41.3 (c = 0.25, $CHCl_3$)

HRMS-ESI (m/z): calc. for $C_{26}H_{37}N_4O_8$ $[M+H^+]$ 533.2606, found 533.2605.

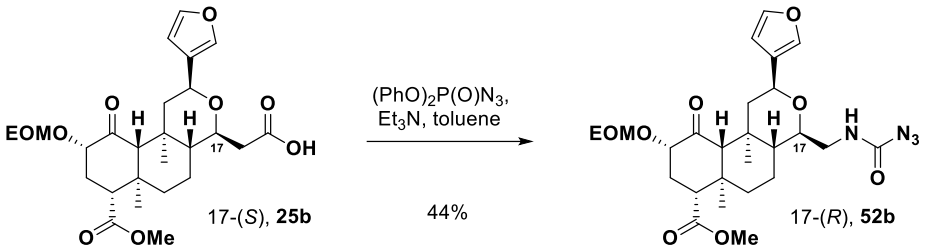
IR (neat, cm^{-1}): 3307, 2918, 2145, 1720, 1526, 1437, 1392, 1273, 1228, 1158, 1123, 1100, 1021, 959, 935, 907, 875, 785, 753, 666, 601, 559.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 – 7.30 (m, 2H), 6.35 (d, *J* = 1.5 Hz, 1H), 5.40 (d, *J* = 7.1 Hz, 1H), 4.81 (d, *J* = 11.3 Hz, 1H), 4.76 (d, *J* = 7.1 Hz, 1H), 4.71 (d, *J* = 7.2 Hz, 1H), 4.12 (dd, *J* = 12.2, 7.3 Hz, 1H), 3.90 – 3.77 (m, 1H), 3.70 (s, 3H), 3.69 – 3.50 (m, 3H), 3.38 (ddd, *J* = 14.2, 7.6, 2.5 Hz, 1H), 2.70 (dd, *J* = 13.5, 3.5 Hz, 1H), 2.30 (ddd, *J* = 13.3, 7.1, 3.3 Hz, 1H), 2.25 – 2.09 (m, 2H), 1.97 (s, 1H), 1.73 (d, *J* = 13.0 Hz, 1H), 1.70 – 1.60 (m, 1H), 1.51 (d, *J* = 3.6 Hz, 1H), 1.41 (s, 3H), 1.18 (t, *J* = 7.0 Hz, 4H), 1.06 (s, 3H).

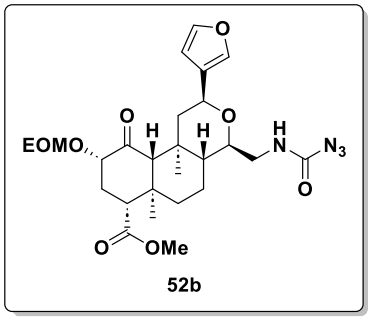
^{13}C NMR (126 MHz, $CDCl_3$): δ 206.2, 172.3, 156.7, 143.4, 139.4, 126.8, 108.8, 94.5,

78.0, 66.5, 64.0, 61.6, 54.2, 51.9, 47.6, 45.3, 42.9, 39.7, 39.3, 34.7, 32.8, 20.5, 17.0, 16.8, 15.3.

Synthesis of compound 52b



To a 10 mL RBF were added **25b** (8 mg, 0.016 mmol, 1.0 equiv) and toluene (0.03 M, 0.5 mL), followed by Et_3N (9 μL, 6.4 mg, 0.064 mmol, 4.0 equiv) and $(PhO)_2P(O)N_3$ (10 μL, 13 mg, 0.048 mmol, 3.0 equiv). The reaction mixture was stirred at room temperature for 30 min then at 80 °C for 12 h. After cooling to room temperature, the solvent was removed under reduced pressure. The residue was purified by PTLC (developed with 35% EtOAc in PE) to afford **52b** (3.8 mg, 44% yield) as a white foam.



R_f = 0.45 (PE: EtOAc = 3:2)

Melting point: 54-59 °C

$[\alpha]_D^{26.1}$ = –92.8 (c = 0.38, $CHCl_3$)

HRMS-ESI (m/z): calc. for $C_{26}H_{37}N_4O_8$ $[M+H^+]$ 533.2606, found 533.2605.

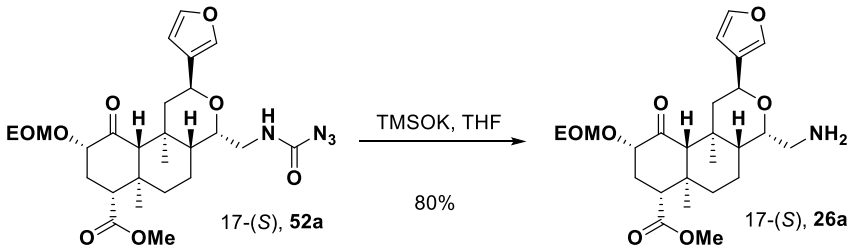
IR (neat, cm^{-1}): 3344, 2950, 2146, 1720, 1507, 1438, 1392, 1351, 1270, 1225, 1156, 1123, 1100, 1081, 1018, 906, 875, 782, 754, 666, 601, 558.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (t, *J* = 1.7 Hz, 1H), 7.32 (dt, *J* = 1.6, 0.8 Hz, 1H), 6.33 (dd, *J* = 1.9, 0.9 Hz, 1H), 5.46 (t, *J* = 5.7 Hz, 1H), 4.81 – 4.73 (m, 2H), 4.71 (d, *J* = 7.2 Hz, 1H), 4.13 (dd, *J* = 12.2, 7.3 Hz, 1H), 3.70 (s, 3H), 3.71 – 3.50 (m, 3H), 3.20 (ddd, *J* = 13.3, 7.0, 5.1 Hz, 1H), 2.69 (dd, *J* = 13.5, 3.5 Hz, 1H), 2.31 (ddd, *J* = 13.3, 7.3, 3.5 Hz, 1H), 2.23 – 2.08 (m, 2H), 1.99 (s, 1H), 1.75 – 1.64 (m, 1H), 1.53 (s, 1H), 1.41 (s, 3H), 1.39 – 1.30 (m, 2H), 1.17 (t, *J* = 7.1 Hz, 3H), 1.13 (d, *J* = 12.1 Hz, 1H), 1.06 (s, 3H).

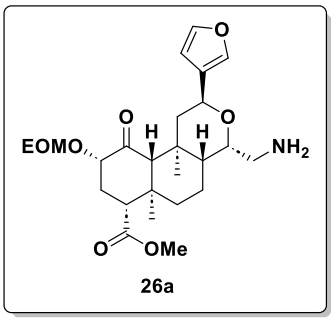
^{13}C NMR (126 MHz, $CDCl_3$): δ 206.5, 172.3, 156.6, 143.2, 139.1, 127.0, 108.8, 94.5,

78.1, 73.3, 67.4, 65.9, 64.0, 54.3, 51.9, 48.3, 45.5, 43.5, 42.4, 39.2, 35.0, 32.9, 18.6, 16.9, 15.3, 14.7.

Synthesis of compound 26a



To a 10 mL RBF was added **52a** (15 mg, 0.028 mmol, 1.0 equiv) and TMSOK (10 mg, 0.07 mmol, 2.5 equiv). The flask was immersed in ice-water bath followed by addition of THF (0.02 M, 1.4 mL). After stirring at 0 °C for 1.5 h, the reaction was quenched with 1 drop of HOAc and then concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (~5 mL), eluting first with 0%→5% MeOH in DCM to remove impurities, and then 5%→10% MeOH/1% NH_4OH in DCM to afford **26a** (10.5 mg, 80% yield) as a pale-yellow solid.



R_f = 0.3 (DCM: MeOH = 10:1, +1% NH_4OH)

Melting point: 155-160 °C

$[\alpha]_D^{22.7}$ = –80.9 (c = 0.27, $CHCl_3$)

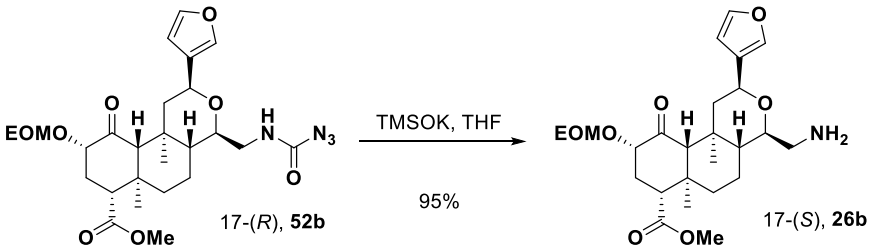
HRMS-ESI (m/z): calc. for $C_{25}H_{37}KNO_7$ $[M+K^+]$ 502.2202, found 502.2198.

IR (neat, cm^{-1}): 2925, 1724, 1439, 1392, 1273, 1198, 1158, 1122, 1100, 1041, 1021, 875, 784, 754, 602.

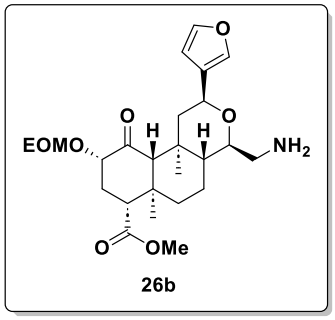
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (s, 1H), 7.34 (t, *J* = 1.7 Hz, 1H), 6.63 – 6.42 (m, 1H), 4.84 (d, *J* = 11.4 Hz, 1H), 4.77 (d, *J* = 7.2 Hz, 1H), 4.72 (d, *J* = 7.2 Hz, 1H), 4.10 (ddd, *J* = 19.2, 11.6, 6.3 Hz, 1H), 3.71 (s, 3H), 3.71 – 3.50 (m, 2H), 3.39 (t, *J* = 12.5 Hz, 1H), 2.86 (d, *J* = 13.1 Hz, 1H), 2.72 (dd, *J* = 13.4, 3.4 Hz, 1H), 2.31 (td, *J* = 7.4, 4.1 Hz, 1H), 2.16 (dt, *J* = 26.0, 12.8 Hz, 2H), 1.91 (s, 1H), 1.68 (d, *J* = 13.1 Hz, 1H), 1.61 – 1.48 (m, 2H), 1.42 – 1.34 (m, 2H), 1.30 (s, 3H), 1.18 (t, *J* = 7.1 Hz, 3H), 1.08 (t, *J* = 12.7 Hz, 1H), 1.03 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 206.2, 172.3, 143.1, 140.1, 126.6, 109.5, 94.5, 78.0, 75.5, 66.3, 64.0, 61.7, 54.0, 51.9, 47.2, 44.6, 42.8, 39.5, 38.4, 34.4, 32.8, 20.2, 16.8, 16.6, 15.3

Synthesis of compound 26b



To a 10 mL RBF was added **52b** (8 mg, 0.015 mmol, 1.0 equiv) and TMSOK (5.2 mg, 0.038 mmol, 2.5 equiv). The flask was immersed in ice-water bath followed by addition of THF (0.02 M, 0.75 mL). After stirring at 0 °C for 1.5 h, the reaction was quenched with 1 drop of HOAc and then concentrated under reduced pressure. The residue was purified by PTLC (developed twice with 5% MeOH/1% NH_4OH in DCM) to afford **26b** (6.6 mg, 95% yield) as a pale-yellow solid.



R_f = 0.3 (DCM: MeOH = 10:1, +1% NH_4OH)

Melting point: 123-127 °C

$[\alpha]_D^{22.8}$ = –107.6 (c = 0.66, $CHCl_3$)

HRMS-ESI (m/z): calc. for $C_{25}H_{38}NO_7$ $[M+H^+]$ 464.2643, found 464.2645.

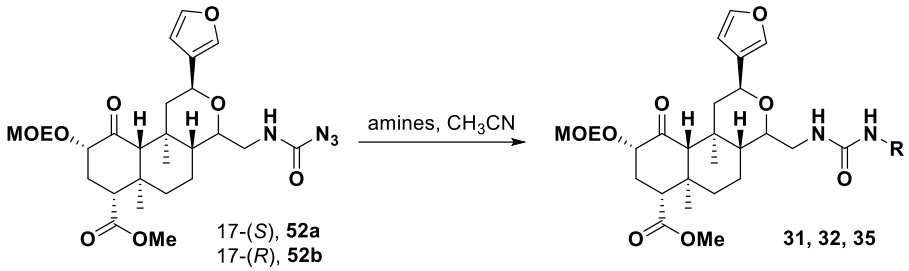
IR (neat, cm^{-1}): 2932, 1723, 1437, 1393, 1270, 1197, 1155, 1123, 1097, 1041, 1014, 875, 783, 752, 602.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (s, 1H), 7.31 (t, *J* = 1.7 Hz, 1H), 6.44 (dd, *J* = 1.9, 0.8 Hz, 1H), 4.81 – 4.73 (m, 2H), 4.71 (d, *J* = 7.2 Hz, 1H), 4.12 (dd, *J* = 12.2, 7.3 Hz, 1H), 3.85 (dd, *J* = 10.8, 7.7 Hz, 1H), 3.70 (s, 3H), 3.76 – 3.63 (m, 2H), 3.57 (dq, *J* = 9.7, 7.0 Hz, 1H), 3.23 (d, *J* = 12.7 Hz, 1H), 2.84 (dd, *J* = 12.7, 9.1 Hz, 1H), 2.69 (dd, *J* = 13.4, 3.4 Hz, 1H), 2.31 (ddd, *J* = 13.3, 7.2, 3.3 Hz, 1H), 2.24 – 2.05 (m, 2H), 1.99 (s, 1H), 1.69 (d, *J* = 13.6 Hz, 1H), 1.58 (q, *J* = 12.8, 10.5 Hz, 1H), 1.39 (s, 3H), 1.38 – 1.28 (m, 2H), 1.18 (t, *J* = 7.0 Hz, 4H), 1.11 (t, *J* = 12.4 Hz, 1H), 1.05 (s, 3H)..

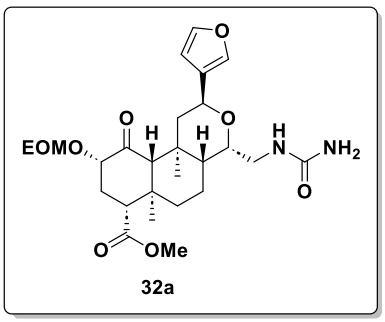
^{13}C NMR (126 MHz, $CDCl_3$): δ 206.4, 172.2, 143.0, 139.6, 126.8, 109.0, 94.5, 78.2,

70.5, 68.0, 65.4, 64.0, 54.2, 51.9, 48.8, 45.4, 42.3, 38.9, 35.0, 32.9, 18.5, 16.9, 15.3, 14.6.

General procedure for the synthesis of compounds 31a, 31b, 32a, 32b, 35a, 35b.



To a 2 mL vial charged with the carbamoyl azide (1.0 equiv) was added CH_3CN (0.1 M) and amine (2.0 equiv), or amine·HCl (2.0 equiv) with Et_3N (3.0 equiv). After stirring at room temperature for 2-12 h (monitored by TLC), the reaction was concentrated under reduced pressure, and the residue was purified by PTLC to afford the corresponding products.



2.3 mg (49% yield) was obtained from 5 mg scale reaction of **52a** with NH_4Cl and Et_3N.

R_f = 0.05 (100% EtOAc)

Melting point: 104-107 °C

$[\alpha]_D^{27.8}$ = –68.6 (c = 0.230, $CHCl_3$)

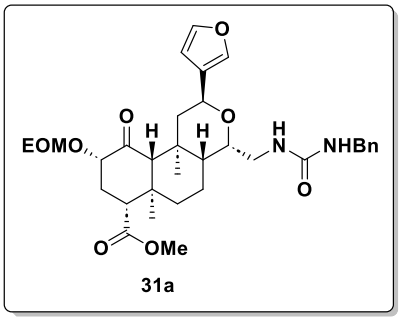
HRMS-ESI (m/z): calc. for $C_{26}H_{38}KN_2O_8$ $[M+K^+]$ 545.2260 found 545.2260.

IR (neat, cm^{-1}): 3359, 2924, 1722, 1652, 1601, 1549, 1436, 1392, 1350, 1273, 1240, 1198, 1157, 1122, 1100, 1082, 1062, 1020, 958, 930, 902, 875, 784, 753, 666, 601.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (d, *J* = 1.6 Hz, 2H), 6.37 (t, *J* = 1.4 Hz, 1H), 4.92 (br, 1H), 4.83 (dd, *J* = 11.7, 2.2 Hz, 1H), 4.76 (d, *J* = 7.2 Hz, 1H), 4.71 (d, *J* = 7.2 Hz, 1H), 4.39 (br, 2H), 4.11 (dd, *J* = 12.3, 7.3 Hz, 1H), 3.83 (ddd, *J* = 11.1, 5.4, 2.1 Hz, 1H), 3.70 (s, 3H), 3.75 – 3.63 (m, 1H), 3.62 – 3.45 (m, 2H), 3.37 (d, *J* = 13.6 Hz, 1H), 2.70 (dd, *J* = 13.4, 3.4 Hz, 1H), 2.29 (ddd, *J* = 13.4, 7.2, 3.4 Hz, 1H), 2.24 – 2.11 (m, 2H), 1.97 (s, 1H), 1.76 – 1.50 (m, 5H), 1.41 (s, 3H), 1.17 (m, 4H), 1.05 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 206.3, 172.3, 143.3, 139.4, 127.0, 108.9, 94.5, 78.2, 78.0, 66.6, 64.0, 61.5, 54.2, 51.9, 47.7, 45.6, 42.9, 39.8, 34.8, 32.8, 20.6, 17.1, 16.8,

15.3.



31a

5.1 mg (91% yield) was obtained from 5 mg scale reaction of **52a** with $BnNH_2$.

$\boldsymbol{R_f}$ = 0.25 (PE: EtOAc = 1:1)

Melting point: 69-73 °C

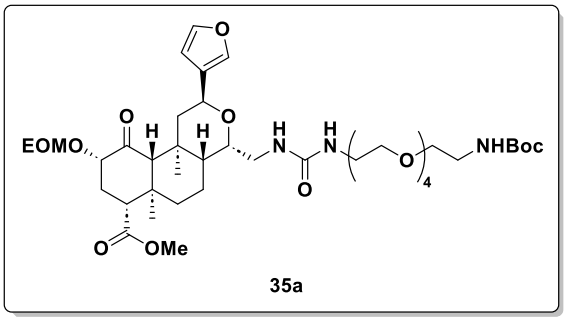
$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{27.8}}$ = –56.2 (c = 0.51, $CHCl_3$)

HRMS-ESI (m/z): calc. for $C_{33}H_{45}N_2O_8$ [M+H$^+$] 597.3170, found 597.3166.

IR (neat, cm^{-1}): 3362, 2926, 1723, 1636, 1559, 1497, 1454, 1436, 1393, 1363, 1272, 1240, 1199, 1157, 1122, 1100, 1039, 1020, 958, 930, 903, 875, 784, 753, 700, 666, 601.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (t, *J* = 1.7 Hz, 1H), 7.34 – 7.20 (m, 6H), 6.30 (dd, *J* = 1.9, 0.9 Hz, 1H), 4.85 (br, 1H), 4.82 – 4.72 (m, 3H), 4.70 (d, *J* = 7.2 Hz, 1H), 4.33 (s, 2H), 4.10 (dd, *J* = 12.3, 7.2 Hz, 1H), 3.80 (dt, *J* = 10.5, 3.8 Hz, 1H), 3.70 (s, 3H), 3.75 – 3.61 (m, 1H), 3.55 (dq, *J* = 9.8, 7.1 Hz, 1H), 3.53 – 3.33 (m, 2H), 2.69 (dd, *J* = 13.4, 3.4 Hz, 1H), 2.29 (ddd, *J* = 13.4, 7.2, 3.4 Hz, 1H), 2.21 – 2.07 (m, 2H), 1.91 (s, 1H), 1.75 – 1.66 (m, 1H), 1.59 – 1.47 (m, 2H), 1.42 (d, *J* = 2.4 Hz, 1H), 1.38 (s, 3H), 1.17 (t, *J* = 7.1 Hz, 3H), 1.13 – 1.05 (m, 1H), 1.04 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 206.3, 172.3, 158.2, 143.3, 139.3, 139.2, 128.8 (2C), 127.7 (2C), 127.5, 127.0, 108.8, 94.5, 78.3, 78.0, 66.5, 64.0, 61.5, 54.2, 51.9, 47.8, 45.5, 44.8, 42.9, 39.7, 38.5, 34.7, 32.7, 20.5, 17.0, 16.8, 15.2.



35a

3.1 mg (37% yield) was obtained from 5 mg scale reaction of **52a** with NH_2-PEG_4-NHBoc.

$\boldsymbol{R_f}$ = 0.01 (100% EtOAc)

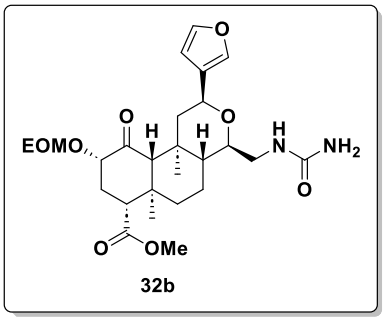
$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25.1}}$ = –45.6 (c = 0.31, $CHCl_3$)

HRMS-ESI (m/z): calc. for $C_{41}H_{67}KN_3O_{14}$ [M+K^+] 864.4255, found 864.4240.

IR (neat, cm^{-1}): 3366, 2871, 1720, 1666, 1557, 1453, 1392, 1365, 1273, 1249, 1156, 1122, 1100, 1037, 1020, 957, 931, 904, 875, 784, 755, 602.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (s, 1H), 7.34 (t, *J* = 1.7 Hz, 1H), 6.37 (dd, *J* = 1.8, 0.9 Hz, 1H), 5.27 (s, 2H), 4.84 (d, *J* = 11.2 Hz, 1H), 4.75 (d, *J* = 7.2 Hz, 1H), 4.70 (d, *J* = 7.1 Hz, 1H), 4.10 (dd, *J* = 12.3, 7.2 Hz, 1H), 3.81 (ddd, *J* = 9.8, 5.2, 2.5 Hz, 1H), 3.70 (s, 3H), 3.70 – 3.39 (m, 20H), 3.35 (s, 2H), 3.26 (d, *J* = 5.5 Hz, 2H), 2.69 (dd, *J* = 13.4, 3.4 Hz, 1H), 2.29 (ddd, *J* = 13.3, 7.2, 3.3 Hz, 1H), 2.22 – 2.07 (m, 2H), 1.96 (s, 1H), 1.70 (d, *J* = 9.5 Hz, 1H), 1.63 (m, 2H), 1.61 – 1.49 (m, 2H), 1.43 (s, 9H), 1.41 (s, 3H), 1.17 (t, *J* = 7.1 Hz, 3H), 1.11 (t, *J* = 12.3 Hz, 1H), 1.05 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 206.4, 172.3, 158.6, 156.2, 143.0, 139.3, 127.4, 109.03, 94.5, 79.3, 78.4, 78.0, 70.66, 70.60, 70.53, 70.46, 70.38, 70.26, 70.19, 70.14, 66.6, 63.9, 61.4, 54.2, 51.9, 47.9, 45.8, 42.9, 40.5, 40.4, 39.8, 38.2, 34.8, 32.8, 28.6 (3C), 20.6, 17.1, 16.8, 15.2.



32b

3.0 mg (69% yield) was obtained from 4 mg scale reaction of **52b** with NH_4Cl and Et_3N.

R_f = 0.05 (100% EtOAc)

Melting point: 81-85 °C

$[\alpha]_D^{27.3}$ = –95.6 (c = 0.30, $CHCl_3$)

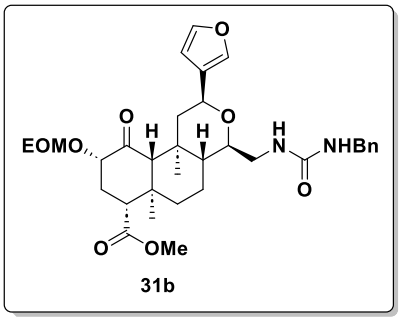
HRMS-ESI (m/z): calc. for $C_{26}H_{39}N_2O_8$ [M+H^+] 507.2701, found 507.2698.

IR (neat, cm^{-1}): 3360, 2929, 1723, 1654, 1601, 1541, 1437, 1392, 1352, 1270, 1200, 1155, 1121, 1098, 1078, 1014, 904, 875, 751, 666, 601.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (t, *J* = 1.7 Hz, 1H), 7.33 (s, 1H), 6.34 (dd, *J* = 1.8, 0.9 Hz, 1H), 4.90 (br, 1H), 4.82 – 4.74 (m, 2H), 4.71 (d, *J* = 7.1 Hz, 1H), 4.49 (br, 1H), 4.13 (dd, *J* = 12.1, 7.3 Hz, 1H), 3.69 (s, 3H), 3.74 – 3.48 (m, 4H), 3.17 – 3.06 (m, 1H),

2.69 (dd, *J* = 13.5, 3.4 Hz, 1H), 2.31 (ddd, *J* = 13.3, 7.2, 3.4 Hz, 1H), 2.22 – 2.08 (m, 2H), 2.00 (s, 1H), 1.73 – 1.65 (m, 2H), 1.62 – 1.47 (m, 2H), 1.41 (s, 3H), 1.38 – 1.27 (m, 1H), 1.17 (t, *J* = 7.1 Hz, 3H), 1.12 (t, *J* = 12.3 Hz, 1H), 1.06 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 206.6, 172.3, 159.0, 143.3, 139.2, 127.2, 108.9, 94.5, 78.1, 74.3, 67.4, 65.9, 64.0, 54.3, 51.9, 48.0, 45.6, 42.4, 39.2, 35.0, 32.9, 29.9, 18.6, 16.9, 15.3, 14.8.



31b

4.1 mg (84% yield) was obtained from 4 mg scale reaction of **52b** with $BnNH_2$.

R_f = 0.20 (PE: EtOAc = 1:1)

Melting point: 85-89 ℃

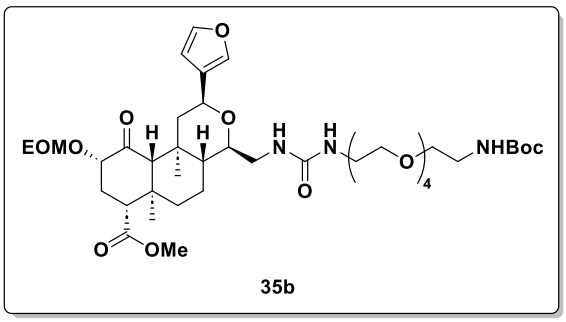
$[\alpha]_D^{23.8}$ = –99.3 (c = 0.41, $CHCl_3$)

HRMS-ESI (m/z): calc. for $C_{33}H_{45}N_2O_8$ [M+H$^+$] 597.3170, found 597.3174.

IR (neat, cm^{-1}): 3370, 2931, 1725, 1635, 1561, 1497, 1453, 1392, 1358, 1271, 1200, 1157, 1122, 1099, 1083, 1018, 875, 782, 753, 700, 665, 601.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 – 7.21 (m, 7H), 6.26 (dd, *J* = 1.9, 0.9 Hz, 1H), 5.02 (br, 1H), 4.76 (d, *J* = 7.2 Hz, 1H), 4.77 – 4.68 (m, 3H), 4.32 (d, *J* = 5.8 Hz, 2H), 4.12 (dd, *J* = 12.2, 7.3 Hz, 1H), 3.70 (s, 3H), 3.75 – 3.63 (m, 1H), 3.61 – 3.51 (m, 3H), 3.16 (dt, *J* = 14.0, 6.2 Hz, 1H), 2.68 (dd, *J* = 13.5, 3.4 Hz, 1H), 2.31 (ddd, *J* = 13.4, 7.3, 3.4 Hz, 1H), 2.22 – 2.08 (m, 2H), 1.94 (s, 1H), 1.71 – 1.62 (m, 1H), 1.53 (td, *J* = 12.2, 11.2, 8.5 Hz, 1H), 1.39 (s, 3H), 1.35 – 1.26 (m, 1H), 1.18 (t, *J* = 7.1 Hz, 3H), 1.13 (t, *J* = 11.1 Hz, 1H), 1.05 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 206.6, 172.3, 158.5, 143.2, 139.4, 139.1, 128.8, 127.6, 127.4, 127.2, 108.9, 94.5, 78.2, 74.3, 67.4, 65.9, 64.0, 54.3, 51.9, 47.9, 45.5, 44.8, 43.2, 42.5, 39.3, 35.0, 33.0, 18.6, 16.9, 15.3, 14.8.



3.5 mg (52% yield) was obtained from 4 mg scale reaction of **52b** with NH_2-PEG_4-NHBoc.

$\boldsymbol{R_f}$ = 0.01 (100% EtOAc)

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\boldsymbol{23.7}}$ = –42.8 (c = 0.35, $CHCl_3$)

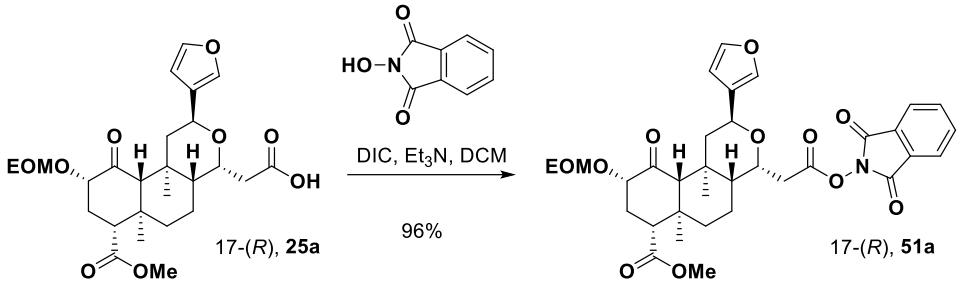
HRMS-ESI (m/z): calc. for $C_{41}H_{67}N_3NaO_{14}$ [M+Na^+] 848.4515, found 848.4507.

IR (neat, cm^{-1}): 3371, 2916, 1724, 1661, 1558, 1453, 1391, 1365, 1273, 1251, 1157, 1101, 1020, 875, 783, 602.

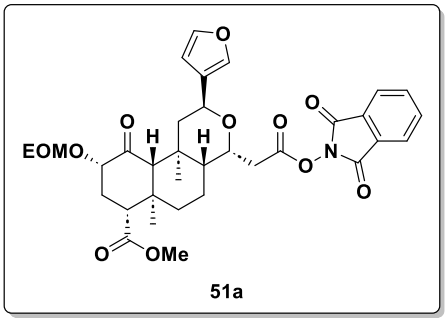
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (dd, *J* = 3.7, 2.0 Hz, 2H), 6.35 (t, *J* = 1.3 Hz, 1H), 5.55 (br, 1H), 5.33 (br, 1H), 5.25 (br, 1H), 4.76 (dd, *J* = 8.2, 2.7 Hz, 2H), 4.71 (d, *J* = 7.2 Hz, 1H), 4.13 (dd, *J* = 12.2, 7.3 Hz, 1H), 3.69 (s, 3H), 3.64 – 3.51 (m, 17H), 3.49 (t, *J* = 5.1 Hz, 2H), 3.37 (dd, *J* = 11.8, 5.6 Hz, 2H), 3.28 (d, *J* = 5.1 Hz, 2H), 3.10 (dd, *J* = 13.8, 6.8 Hz, 1H), 2.70 (dd, *J* = 13.4, 3.4 Hz, 1H), 2.30 (ddd, *J* = 13.4, 7.2, 3.5 Hz, 1H), 2.23 – 2.09 (m, 2H), 2.01 (s, 1H), 1.63 – 1.50 (m, 3H), 1.44 (s, 9H), 1.41 (s, 3H), 1.36 – 1.27 (m, 2H), 1.18 (t, *J* = 7.1 Hz, 3H), 1.11 (t, *J* = 12.4 Hz, 1H), 1.06 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 206.7, 172.4, 159.0, 156.4, 143.0, 139.2, 127.4, 109.04, 94.5, 79.3, 78.2, 74.4, 70.81, 70.62, 70.49, 70.46, 70.43, 70.41, 70.16, 67.3, 65.9, 63.9, 54.2, 51.9, 48.2, 45.7, 43.0, 42.4, 40.5, 40.4, 39.3, 35.0, 33.0, 29.8, 28.6, 18.5, 16.9, 15.2, 14.8.

Synthesis of compound 51a



To a 5 mL RBF charged with **25a** (4 mg, 0.008 mmol, 1.0 equiv) were added N-hydroxyphthalimide (1.5 mg, 0.009 mmol, 1.1 equiv) and DCM (0.05 M, 0.15 mL). DIC (1.6 μL, 1.3 mg, 0.01 mmol, 1.2 equiv) was then added at room temperature. After stirring for 2 h (monitored by TLC), the reaction was concentrated under reduced pressure and the residue was purified by PTLC (developed with 50% EtOAc in PE) to afford **51a** (5.0 mg, 96% yield) as a white foam.



R_f = 0.5 (PE: EtOAc = 1:1)

Melting point: 77-82 °C

$[\alpha]_D^{25.3}$ = –23.4 (c = 0.503, $CHCl_3$)

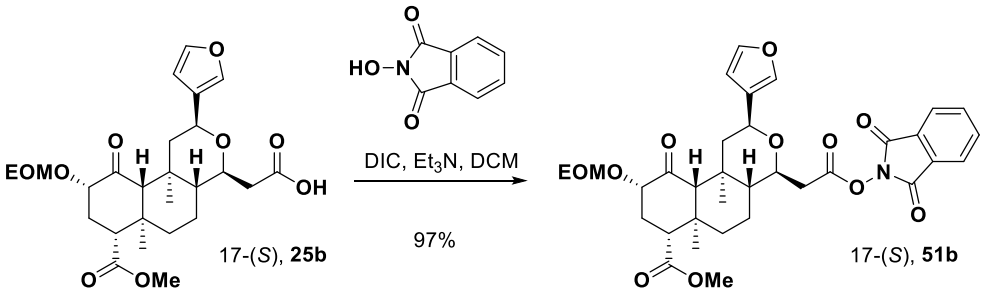
HRMS-ESI (m/z): calc. for $C_{34}H_{40}NO_{11}$ $[M+H^+]$ 638.2596, found 638.2595.

IR (neat, cm^{-1}): 2925, 1816, 1788, 1743, 1725, 1467, 1436, 1367, 1272, 1186, 1157, 1122, 1098, 1082, 1062, 1041, 1014, 965, 931, 902, 875, 785, 752, 697, 667, 601, 518.

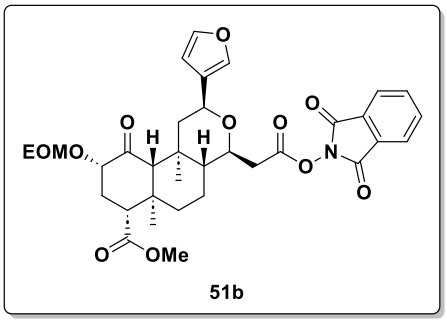
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.86 – 7.69 (m, 2H), 7.41 (dt, *J* = 1.7, 1.0 Hz, 1H), 7.37 (t, *J* = 1.7 Hz, 1H), 6.48 (dd, *J* = 1.9, 0.9 Hz, 1H), 4.92 (d, *J* = 11.1 Hz, 1H), 4.79 (d, *J* = 7.1 Hz, 1H), 4.75 (d, *J* = 7.2 Hz, 1H), 4.49 (dt, *J* = 10.1, 4.3 Hz, 1H), 4.15 (dd, *J* = 12.2, 7.3 Hz, 1H), 3.71 (s, 3H), 3.77 – 3.50 (m, 2H), 3.28 (dd, *J* = 15.5, 10.6 Hz, 1H), 2.82 (dd, *J* = 15.5, 3.7 Hz, 1H), 2.73 (dd, *J* = 13.4, 3.4 Hz, 1H), 2.42 – 2.26 (m, 2H), 2.18 (q, *J* = 13.1 Hz, 1H), 2.01 (s, 1H), 1.80 – 1.71 (m, 2H), 1.66 (td, *J* = 12.9, 12.4, 4.6 Hz, 1H), 1.51 (s, 3H), 1.55 – 1.39 (m, 2H), 1.19 (m, 4H), 1.10 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 206.3, 172.3, 168.0, 161.9 (2C), 143.1, 139.5, 134.9 (2C), 129.1 (2C), 126.7, 124.2 (2C), 109.2, 94.6, 78.1, 73.8, 66.7, 64.0, 61.8, 54.1, 51.9, 47.8, 44.1, 42.9, 39.6, 34.9, 32.8, 31.9, 20.6, 17.0, 16.9, 15.3.

Synthesis of compound 51b



To a 5 mL RBF charged with **25b** (10 mg, 0.02 mmol, 1.0 equiv) were added N-hydroxyphthalimide (3.6 mg, 0.022 mmol, 1.1 equiv) and DCM (0.05 M, 0.4 mL). DIC (3.7 μL, 3.0 mg, 0.024 mmol, 1.2 equiv) was then added at room temperature. After stirring for 2 h (monitored by TLC), the reaction was concentrated under reduced pressure and the residue was purified by PTLC (developed with 50% EtOAc in PE) to afford **51b** (12.6 mg, 97% yield) as a white foam.



R_f = 0.5 (PE: EtOAc = 1:1)

Melting point: 83-87 °C

$[\alpha]_D^{21.4}$ = –87.2 (c = 0.411, $CHCl_3$)

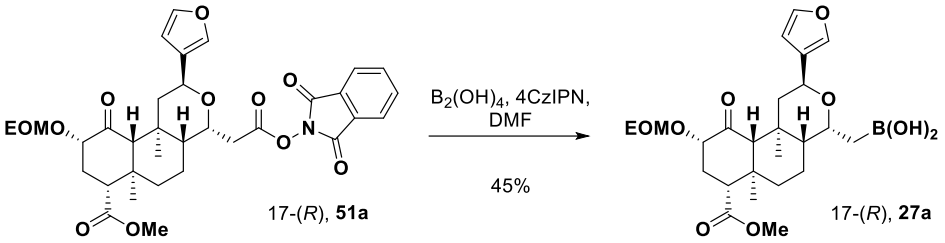
HRMS-ESI (m/z): calc. for $C_{34}H_{39}KNO_{11}$ $[M+K^+]$ 676.2155, found 676.2160.

IR (neat, cm^{-1}): 2950, 1817, 1789, 1742, 1467, 1363, 1276, 1186, 1157, 1123, 1082, 1017, 967, 876, 784, 755, 698, 602.

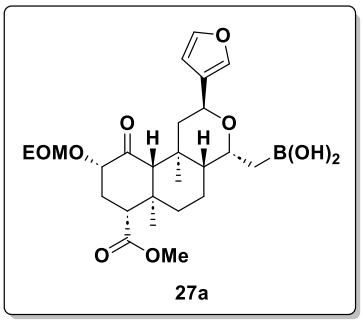
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.80 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.42 (dt, *J* = 1.8, 0.9 Hz, 1H), 7.35 (t, *J* = 1.7 Hz, 1H), 6.44 (dd, *J* = 1.8, 0.8 Hz, 1H), 4.86 (dd, *J* = 12.4, 2.0 Hz, 1H), 4.78 (d, *J* = 7.1 Hz, 1H), 4.73 (d, *J* = 7.2 Hz, 1H), 4.29 – 3.94 (m, 2H), 3.70 (s, 3H), 3.75 – 3.63 (m, 1H), 3.59 (dq, *J* = 9.6, 7.0 Hz, 1H), 2.95 (dd, *J* = 15.1, 4.6 Hz, 1H), 2.80 (dd, *J* = 15.1, 7.2 Hz, 1H), 2.72 (dd, *J* = 13.4, 3.4 Hz, 1H), 2.38 – 2.22 (m, 2H), 2.16 (q, *J* = 13.1 Hz, 1H), 2.04 (s, 1H), 1.79 – 1.69 (m, 1H), 1.63 (td, *J* = 13.3, 12.5, 4.2 Hz, 1H), 1.47 (s, 3H), 1.53 – 1.38 (m, 2H), 1.33 (td, *J* = 11.9, 10.7, 2.9 Hz, 1H), 1.19 (t, *J* = 7.1 Hz, 3H), 1.22– 1.14 (m, 1H), 1.08 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 206.5, 172.3, 167.6, 162.0 (2C), 143.0, 139.1, 134.9 (2C), 129.1 (2C), 127.1, 124.2 (2C), 109.0, 94.5, 78.2, 71.7, 67.9, 65.8, 64.0, 54.2, 51.9, 50.5, 45.1, 42.5, 39.3, 36.4, 35.4, 32.9, 19.2, 16.9, 15.3, 14.7.

Synthesis of compound 27a



To a 2 mL vial charged with **51a** (6 mg, 0.01 mmol, 1.0 equiv) were added $B_2(OH)_4$ (2.7 mg, 0.03 mmol, 3.0 equiv) and 4CzIPN (0.24 mg, 0.3 μmol, 0.03 equiv). The vial was transferred into a glovebox and DMF (0.2 M, 50 μL) was added. The vial was sealed, removed from the glovebox and irradiated at 465 nm in the 3STech AL1 parallel photoreactor (power set to 5 W, with full-powered cooling fan). After stirring at ambient temperature for 1 h (at which time the yellow color of 4CzIPN almost faded out), the reaction was concentrated under reduced pressure and the residue was purified by PTLC (developed with 50% EtOAc in PE containing 1% MeOH) to afford **27a** (2.1 mg, 45% yield) as a white foam.



$\boldsymbol{R_f}$ = 0.25 (PE: EtOAc = 1:1, +1% MeOH)

Melting point: 88-93 °C

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{22.2}}$ = –44.9 (c = 0.187, $CHCl_3$)

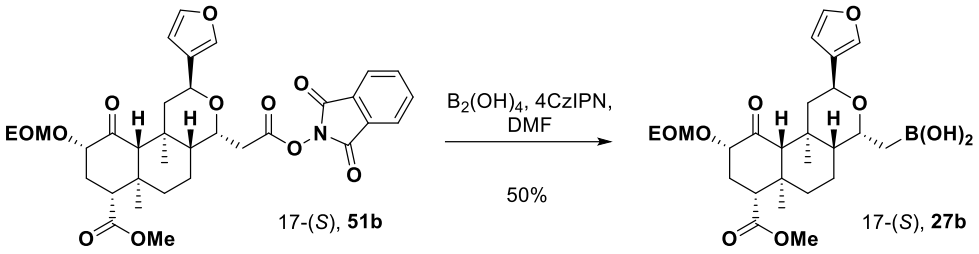
HRMS-ESI (m/z): calc. for $C_{25}H_{41}BNO_9$ $[M+NH_4^+]$ 510.2869, found 510.2877.

IR (neat, cm^{-1}): 3428, 2931, 1725, 1437, 1393, 1344, 1273, 1239, 1193, 1158, 1123, 1100, 1061, 1039, 927, 908, 875, 783, 757, 601.

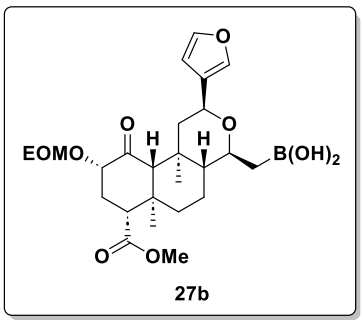
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 – 7.30 (m, 2H), 6.35 (dd, *J* = 1.8, 1.0 Hz, 1H), 5.54 (s, 2H), 4.86 (d, *J* = 11.0 Hz, 1H), 4.77 (d, *J* = 7.1 Hz, 1H), 4.72 (d, *J* = 7.1 Hz, 1H), 4.23 – 4.00 (m, 3H), 3.70 (s, 4H), 3.75 – 3.62 (m, 1H), 3.57 (dq, *J* = 9.7, 7.1 Hz, 1H), 2.71 (dd, *J* = 13.4, 3.4 Hz, 1H), 2.37 – 2.22 (m, 2H), 2.16 (q, *J* = 13.1 Hz, 1H), 1.96 (s, 1H), 1.75 – 1.68 (m, 1H), 1.68 – 1.44 (m, 5H), 1.50 (s, 3H), 1.18 (t, *J* = 7.1 Hz, 3H), 1.21 – 1.13 (m, 1H), 1.08 (s, 3H), 0.97 (dd, *J* = 17.2, 2.9 Hz, 1H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 206.4, 172.4, 143.4, 139.3, 126.8, 108.9, 94.5, 78.0, 76.0, 66.8, 64.0, 61.5, 54.2, 51.9, 48.4, 45.0, 42.9, 39.7, 35.2, 32.7, 20.8, 17.5, 16.9, 15.3, 13.2.

Synthesis of compound 27b



To a 2 mL vial charged with **51b** (12 mg, 0.019 mmol, 1.0 equiv) were added $B_2(OH)_4$ (5.2 mg, 0.057 mmol, 3.0 equiv) and 4CzIPN (0.7 mg, 0.57 μmol, 0.03 equiv). The vial was transferred into a glovebox and DMF (0.2 M, 100 μL) was added. The vial was sealed, removed from the glovebox and irradiated at 465 nm in the 3STech AL1 parallel photoreactor (power set to 5 W, with full-powered cooling fan). After stirring at ambient temperature for 1 h, the reaction was concentrated under reduced pressure and the residue was purified by PTLC (developed with 50% EtOAc in PE containing 1% MeOH) to afford **27b** (4.6 mg, 50% yield) as a white foam.



$\boldsymbol{R_f}$ = 0.4 (PE: EtOAc = 3:2, +1% MeOH)

Melting point: 76-80 °C

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{24.9}}$ = –104.3 (c = 0.46, $CHCl_3$)

HRMS-ESI (m/z): calc. for $C_{25}H_{41}BNO_9$ $[M+NH_4^+]$ 510.2869, found 510.2857.

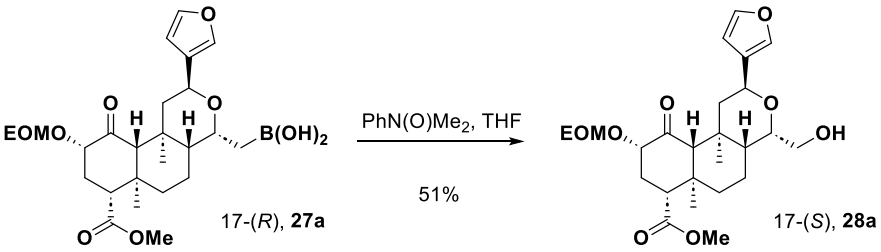
IR (neat, cm^{-1}): 3421, 2932, 1786, 1724, 1437, 1391, 1348, 1316, 1271, 1200, 1156, 1122, 1098, 1079, 1041, 1012, 967, 907, 875, 754, 667, 601.

^{1}H NMR (400 MHz, $CDCl_3$):δ 7.36 (t, *J* = 1.7 Hz, 1H), 7.33 (dt, *J* = 1.6, 0.8 Hz, 1H), 6.33 (dd, *J* = 1.9, 0.9 Hz, 1H), 5.55 (br, 2H), 4.84 (dd, *J* = 11.7, 2.4 Hz, 1H), 4.77 (d, *J* = 7.2 Hz, 1H), 4.72 (d, *J* = 7.2 Hz, 1H), 3.85 (td, *J* = 9.4, 3.8 Hz, 1H), 3.70 (s, 3H), 3.74 – 3.64 (m, 2H), 3.57 (dq, *J* = 9.6, 7.1 Hz, 1H), 2.70 (dd, *J* = 13.5, 3.4 Hz, 1H), 2.32 (ddd, *J* = 13.4, 7.3, 3.5 Hz, 1H), 2.24 – 2.09 (m, 2H), 1.99 (s, 1H), 1.71 (dt, *J* = 14.3, 3.7 Hz, 1H), 1.63 – 1.58 (m, 1H), 1.56 – 1.51 (m, 2H), 1.42 (s, 3H), 1.18 (m, 4H), 1.06

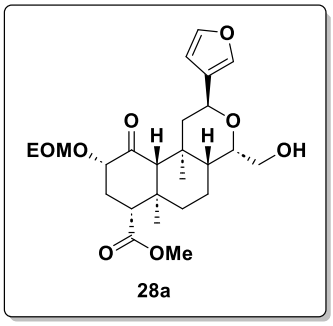
(s, 3H), 0.94 (dd, J = 16.3, 9.1 Hz, 1H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 206.7, 172.4, 143.4, 138.9, 127.0, 108.6, 94.5, 78.1, 73.6, 67.7, 65.8, 64.0, 54.3, 53.6, 53.1, 51.9, 45.5, 42.5, 39.5, 35.2, 32.9, 19.0, 16.9, 15.3, 14.8.

Synthesis of compound 28a



To a 2 mL vial charged with **27a** (2.1 mg, 0.0043 mmol, 1.0 equiv) and THF (0.01 M, 0.4 mL) was added $PhN(O)Me_2$ (1.2 mg, 9 μmol, 2.0 equiv) under ambient atmosphere. The reaction was stirred for 5 h (monitored by TLC) before concentrated under reduced pressure. The residue was purified by PTLC (developed twice with 50% EtOAc in PE) to afford **28a** (1.0 mg, 51% yield) as a white foam.



$\boldsymbol{R_f}$ = 0.1 (PE: EtOAc = 1:1)

Melting point: 124-128 °C

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{20.1}}$ = –87.5 (c = 0.273, $CHCl_3$)

HRMS-ESI (m/z): calc. for $C_{25}H_{37}O_8$ $[M+H^+]$ 465.2483, found 465.2483.

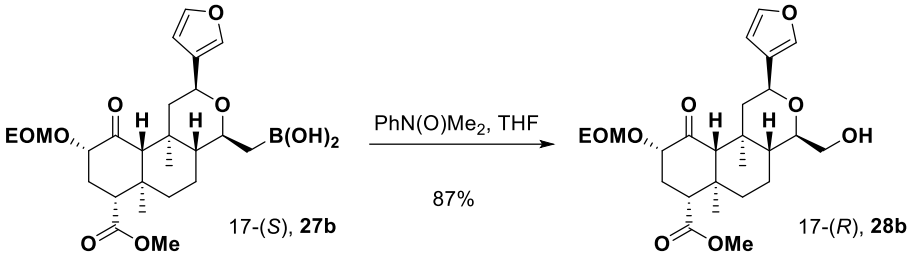
IR (neat, cm^{-1}): 3437, 2930, 1725, 1437, 1393, 1365, 1273, 1238, 1198, 1158, 1123, 1099, 1024, 957, 931, 904, 875, 785, 755, 602.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (d, *J* = 1.7 Hz, 2H), 6.37 (t, *J* = 1.4 Hz, 1H), 4.85 (d, *J* = 10.7 Hz, 1H), 4.76 (d, *J* = 7.1 Hz, 1H), 4.71 (d, *J* = 7.1 Hz, 1H), 4.12 (dd, *J* = 12.0, 8.2 Hz, 2H), 3.96 (dd, *J* = 12.1, 5.6 Hz, 1H), 3.70 (s, 3H), 3.74 – 3.62 (m, 1H), 3.56 (dq, *J* = 9.5, 7.0 Hz, 1H), 3.43 (d, *J* = 11.5 Hz, 1H), 2.71 (dd, *J* = 13.4, 3.5 Hz, 1H), 2.30 (ddd, *J* = 13.4, 7.2, 3.4 Hz, 1H), 2.24 – 2.08 (m, 2H), 1.98 (s, 1H), 1.77 – 1.66 (m, 2H), 1.66 – 1.52 (m, 1H), 1.43 (dd, *J* = 9.5, 5.9 Hz, 2H), 1.35 (s, 3H), 1.17 (t, *J* = 7.0 Hz, 3H), 1.20 – 1.12 (m, 1H), 1.05 (s, 3H).

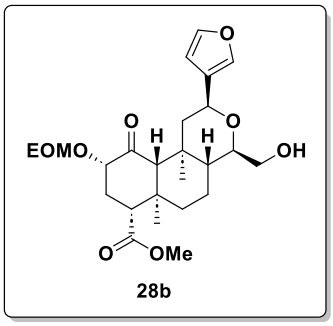
^{13}C NMR (126 MHz, $CDCl_3$): δ 206.3, 172.3, 143.3, 139.3, 127.0, 108.8, 94.5, 79.8, 78.0, 66.4, 64.0, 61.5, 59.5, 54.2, 51.9, 47.5, 45.6, 42.9, 39.8, 34.6, 32.7, 20.4, 16.9,

16.8, 15.3.

Synthesis of compound 28b



To a 2 mL vial charged with **27b** (4.6 mg, 9 μmol, 1.0 equiv) and THF (0.02 M, 0.4 mL) was added $PhN(O)Me_2$ (3 mg, 0.02 mmol, 2.2 equiv) under ambient atmosphere. The reaction was stirred for 5 h (monitored by TLC) before concentrated under reduced pressure. The residue was purified by PTLC (developed twice with 50% EtOAc in PE) to afford **28b** (3.8 mg, 87% yield) as a white foam.



$\boldsymbol{R_f}$ = 0.2 (PE: EtOAc = 3:2)

Melting point: 51-54 °C

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{23.0}}$ = –113.8 (c = 0.380, $CHCl_3$)

HRMS-ESI (m/z): calc. for $C_{25}H_{37}O_8$ $[M+H^+]$ 465.2483, found 465.2482.

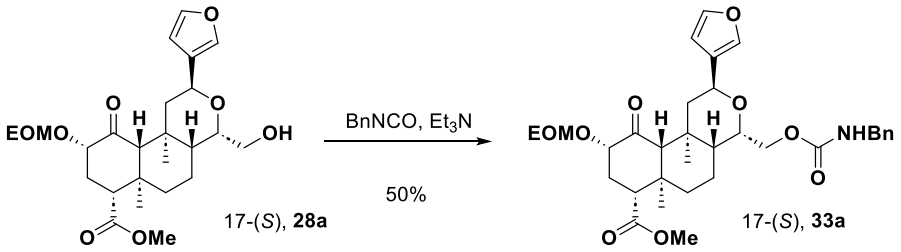
IR (neat, cm^{-1}): 2929, 1724, 1393, 1271, 1200, 1157, 1122, 1100, 1061, 1040, 1019, 875, 782, 754, 602, 405.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (t, *J* = 1.7 Hz, 1H), 7.34 (dt, *J* = 1.6, 0.8 Hz, 1H), 6.35 (dd, *J* = 1.9, 0.9 Hz, 1H), 4.81 (dd, *J* = 11.6, 2.4 Hz, 1H), 4.77 (d, *J* = 7.2 Hz, 1H), 4.72 (d, *J* = 7.2 Hz, 1H), 4.14 (dd, *J* = 12.2, 7.3 Hz, 1H), 3.76 (d, *J* = 11.0 Hz, 1H), 3.69 (s, 3H), 3.73 – 3.48 (m, 4H), 2.70 (dd, *J* = 13.5, 3.5 Hz, 1H), 2.31 (ddd, *J* = 13.3, 7.3, 3.5 Hz, 1H), 2.24 – 2.07 (m, 2H), 2.02 (s, 1H), 1.76 – 1.64 (m, 1H), 1.67 – 1.57 (m, 1H), 1.43 (s, 3H), 1.49 – 1.37 (m, 1H), 1.36 – 1.29 (m, 2H), 1.18 (t, *J* = 7.1 Hz, 3H), 1.13 (d, *J* = 12.3 Hz, 1H), 1.07 (s, 3H).

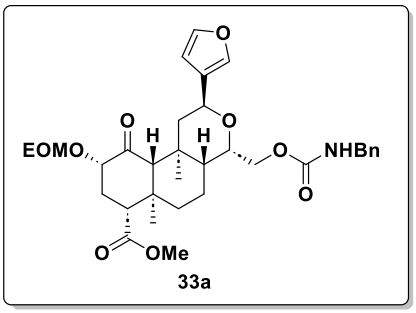
^{13}C NMR (101 MHz, $CDCl_3$): δ 206.6, 172.4, 143.2, 139.1, 127.2, 108.9, 94.5, 78.1, 74.9, 67.4, 66.0, 64.1, 64.0, 54.3, 51.8, 47.2, 45.7, 42.4, 39.2, 35.0, 32.9, 18.5, 16.9,

15.3, 14.7.

Synthesis of compound 33a



To a 5 mL RBF was added **28a** (1.0 mg, 2 μmol, 1.0 equiv) and DCM (0.01 M, 0.2 mL). Et_3N (1.1 μL, 0.8 mg, 8 μmol, 4.0 equiv) and BnNCO (1 μL, 1 mg, 8 μmol, 4.0 equiv) were then added sequentially. The reaction was stirred overnight before being concentrated under reduced pressure. The residue was purified by PTLC (developed with 50% EtOAc in PE) to afford **33a** (0.65 mg, 50% yield) as a colorless wax.



R_f = 0.5 (PE: EtOAc = 1:1)

Melting point: 54-58 °C

$[\alpha]_D^{19.2}$ = –61.8 (c = 0.167, $CHCl_3$)

HRMS-ESI (m/z): calc. for $C_{33}H_{44}NO_9$ $[M+H^+]$ 598.3011, found 598.3016.

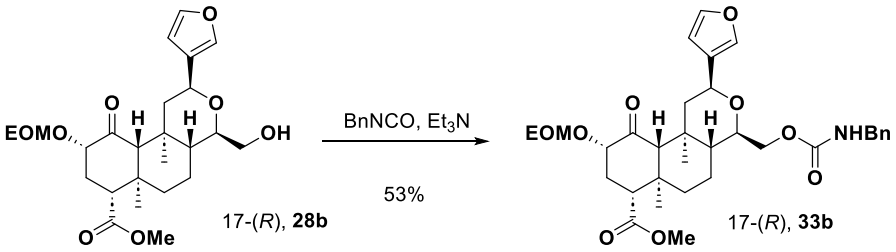
IR (neat, cm^{-1}): 3338, 2925, 1723, 1522, 1455, 1394, 1272, 1241, 1199, 1157, 1124, 1100, 1023, 958, 904, 875, 773, 700, 601.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (s, 1H), 7.33 (t, *J* = 1.7 Hz, 1H), 7.32 – 7.23 (m, 5H) 6.36 (dd, *J* = 1.8, 0.9 Hz, 1H), 5.06 (t, *J* = 5.9 Hz, 1H), 4.92 (d, *J* = 11.4 Hz, 1H), 4.76 (d, *J* = 7.2 Hz, 1H), 4.72 (d, *J* = 7.1 Hz, 1H), 4.67 (d, *J* = 11.3 Hz, 1H), 4.36 (d, *J* = 6.0 Hz, 2H), 4.12 (dd, *J* = 12.3, 7.2 Hz, 1H), 4.05 – 3.97 (m, 2H), 3.70 (s, 3H), 3.74 – 3.62 (m, 1H), 3.56 (dq, *J* = 9.7, 7.1 Hz, 1H), 2.71 (dd, *J* = 13.4, 3.4 Hz, 1H), 2.30 (ddd, *J* = 13.4, 7.5, 3.6 Hz, 1H), 2.25 – 2.08 (m, 2H), 1.99 (s, 1H), 1.71 (d, *J* = 12.8 Hz, 2H), 1.66 – 1.55 (m, 1H), 1.54 – 1.43 (m, 2H), 1.40 (s, 3H), 1.18 (t, *J* = 7.0 Hz, 3H), 1.20 – 1.12(m, 1H) 1.06 (s, 3H).

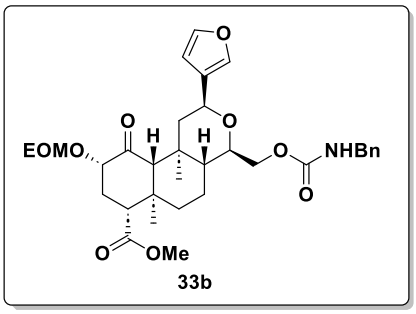
^{13}C NMR (151 MHz, $CDCl_3$): δ 206.3, 172.3, 156.7, 143.1, 139.6, 138.5, 128.8 (2C),

127.6 (3C), 126.9, 109.1, 94.5, 78.0, 77.3, 66.4, 64.0, 61.8, 61.6, 54.2, 51.9, 47.8, 45.3, 45.2, 42.9, 39.7, 34.7, 32.8, 20.7, 16.8, 16.6, 15.3.

Synthesis of compound 33b



To a 5 mL RBF was added **28b** (2.5 mg, 5 μmol, 1.0 equiv) and DCM (0.01 M, 0.5 mL). Et_3N (2.8 μL, 2 mg, 0.02 mmol, 4.0 equiv) and BnNCO (2 μL, 2 mg, 15 μmol, 3.0 equiv) were then added sequentially. The reaction was stirred overnight before being concentrated under reduced pressure. The residue was purified by PTLC (developed with 50% EtOAc in PE) to afford **33b** (1.7 mg, 53% yield) as a white foam.



R_f = 0.5 (PE: EtOAc = 1:1)

Melting point: 47-51 °C

$[\alpha]_D^{26.2}$ = –120.7 (c = 0.098, $CHCl_3$)

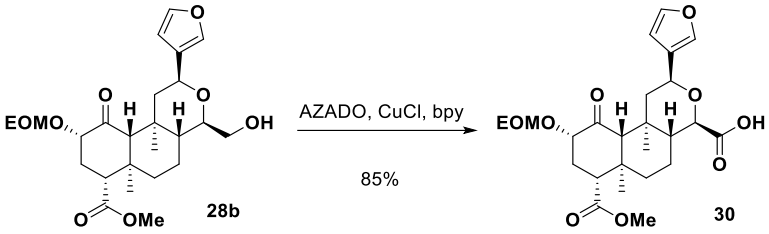
HRMS-ESI (m/z): calc. for $C_{33}H_{44}NO_9$ $[M+H^+]$ 598.3011, found 598.3006.

IR (neat, cm^{-1}): 3352, 2922, 2850, 2357, 1724, 1529, 1454, 1392, 1238, 1201, 1156, 1123, 1100, 1080, 1041, 1019, 875, 782, 700, 668, 601.

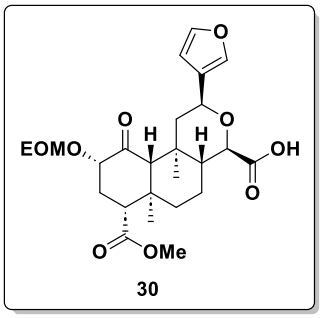
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 – 7.26 (m, 7H), 6.33 (s, 1H), 5.08 (t, *J* = 5.9 Hz, 1H), 4.83 – 4.74 (m, 2H), 4.72 (d, *J* = 7.2 Hz, 1H), 4.38 (d, *J* = 6.0 Hz, 2H), 4.29 (d, *J* = 11.9 Hz, 1H), 4.23 – 4.07 (m, 2H), 3.76 – 3.64 (m, 2H), 3.70 (s, 3H), 3.57 (dq, *J* = 9.6, 7.1 Hz, 1H), 2.69 (d, *J* = 13.4 Hz, 1H), 2.32 (ddd, *J* = 16.8, 7.3, 3.6 Hz, 1H), 2.23 – 2.08 (m, 2H), 2.01 (s, 1H), 1.69 (d, *J* = 13.5 Hz, 1H), 1.43 (s, 3H), 1.40 – 1.29 (m, 2H), 1.18 (t, *J* = 7.1 Hz, 3H), 1.13 (t, *J* = 12.2 Hz, 1H), 1.07 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 206.5, 172.3, 156.6, 143.0, 139.2, 138.5, 128.8 (2C), 127.7 (2C), 127.2, 108.9, 94.5, 78.1, 73.3, 67.5, 66.2, 66.0, 64.0, 54.3, 51.9, 47.4, 45.4, 45.3, 42.4, 39.3, 35.1, 32.9, 29.9, 18.7, 16.9, 15.3, 14.7.

Synthesis of compound 30



To a 2 mL vial charged with **28b** (8 mg, 0.017 mmol, 1.0 equiv) was added CuCl (0.17 mg, 1.7 μmol, 0.1 equiv), 2,2'-bipyridine (0.27 mg, 1.7 μmol, 0.1 equiv) and AZADO (0.26 mg, 1.7 μmol, 0.1 equiv) under ambient atmosphere. MeCN (0.1 M, 0.17 mL) was then added, and the reaction mixture was stirred vigorously in air at room temperature. After 1 h (monitored by TLC), the reaction was quenched with a drop of HOAc and concentrated under reduced pressure. The residue was diluted with EtOAc and filtered through a short silica plug (~ 1 mL), eluting with 1% HOAc in EtOAc. The eluate was concentrated, and the residue was purified by PTLC (developed twice with 40% EtOAc in PE containing 1% HOAc) to afford **30** (7.0 mg, 85% yield) as a white foam.



R_f = 0.25 (PE: EtOAc = 3:2, +1% HOAc)

Melting point: 104-108 °C

$[\alpha]_D^{24.7}$ = –57.3 (c = 0.30, $CHCl_3$)

HRMS-ESI (m/z): calc. for $C_{25}H_{33}O_9$ [M-H^+] 477.2130, found 477.2129.

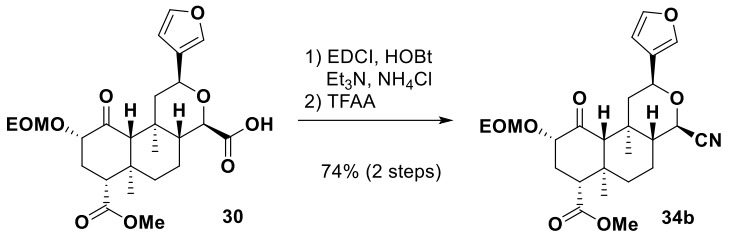
IR (neat, cm^{-1}): 2933, 1725, 1607, 1437, 1393, 1275, 1201, 1158, 1123, 1098, 1041, 1013, 875, 784, 755.

^{1}H NMR (400 MHz, CD_3OD): δ 7.46 (dt, *J* = 1.7, 0.8 Hz, 1H), 7.40 (t, *J* = 1.8 Hz, 1H), 6.45 (dd, *J* = 1.9, 0.8 Hz, 1H), 4.84 (dd, *J* = ~10, 2.4 Hz, 1H), 4.74 (d, *J* = 6.9 Hz, 1H), 4.66 (d, *J* = 7.0 Hz, 1H), 4.31 (dd, *J* = 12.2, 7.3 Hz, 1H), 4.08 (d, *J* = 9.8 Hz, 1H), 3.68 (s, 3H), 3.62 (qd, *J* = 7.1, 4.3 Hz, 2H), 2.91 (dd, *J* = 13.4, 3.5 Hz, 1H), 2.40 (s, 1H), 2.29 (ddd, *J* = 13.2, 7.3, 3.4 Hz, 1H), 2.14 – 1.92 (m, 2H), 1.73 – 1.58 (m, 2H), 1.46 (s,

3H), 1.56 – 1.33 (m, 4H), 1.14 (t, J = 7.1 Hz, 3H), 1.04 (s, 3H).

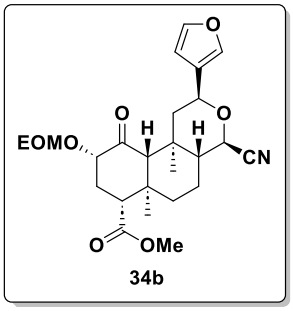
^{13}C NMR (151 MHz, CD_3OD): δ 209.2, 175.6, 174.1, 144.0, 140.8, 128.2, 110.2, 95.5, 79.8, 78.1, 68.8, 65.8, 64.8, 54.6, 52.1, 49.6, 46.1, 43.5, 40.1, 36.2, 34.1, 20.1, 17.1, 15.4, 14.9.

Synthesis of compound 34b



To a 2 mL vial charged with **30** (5 mg, 0.01 mmol, 1.0 equiv) was added HOBt (3.2 mg, 0.024 mmol, 2.4 equiv), EDCI·HCl (4.6 mg, 0.024 mmol, 2.4 equiv), NH_4Cl (5.0 mg, 0.093 mol, 9.3 equiv) and DCM (0.1 M, 0.1 mL) under ambient atmosphere. DIPEA (5.0 μL, 3.7 mg, 0.029 mmol, 2.9 equiv) was then added, and the reaction mixture was stirred vigorously at room temperature. After 2 h (monitored by TLC), the reaction was quenched with a drop of HOAc and concentrated under reduced pressure. The residue was diluted with DCM and filtered through a short silica plug (~ 2 mL), eluting with 50% EtOAc in PE. The eluate was concentrated, and the residue was directly advanced to the next step.

To the above product was added DCM (0.03 M, 0.3 mL), followed by Et_3N (8.0 μL, 5.8 mg, 0.058 mmol, 5.8 equiv) and trifluoroacetic acid anhydride (8.0 μL, 11.9 mg, 0.057 mmol, 5.7 equiv). The reaction mixture was stirred at 0 ℃ for 3 h before quenching with MeOH (1 drop) and concentration under reduced pressure. The residue was purified by PTLC (developed with 30% EtOAc in PE) to afford **34b** (3.5 mg, 74% yield over two steps) as a white foam.



R_f = 0.5 (PE: EtOAc = 3:2)

Melting point: 55-60 °C

$[\alpha]_D^{24.9}$ = –90.0 (c = 0.230, $CHCl_3$)

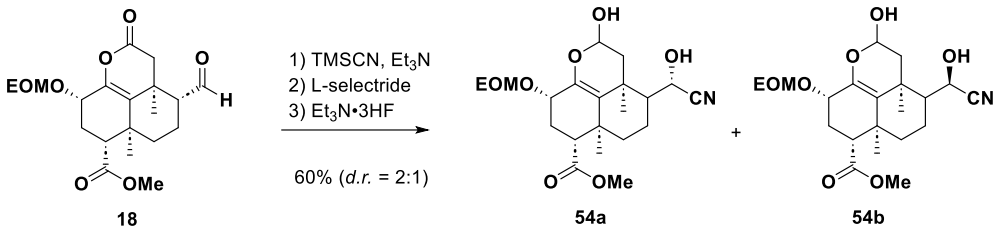
HRMS-ESI (m/z): calc. for $C_{25}H_{34}NO_7$ $[M+H^+]$ 460.2330, found 460.2330.

IR (neat, cm^{-1}): 3675, 2972, 2900, 1725, 1456, 1436, 1394, 1241, 1201, 1157, 1075, 1066, 1057, 1046, 1027, 875.

^{1}H NMR (600 MHz, $CDCl_3$):δ 7.37 – 7.35 (m, 2H), 6.35 (dd, *J* = 1.9, 0.9 Hz, 1H), 4.80 (dd, *J* = 11.6, 2.4 Hz, 1H), 4.77 (d, *J* = 7.2 Hz, 1H), 4.72 (d, *J* = 7.1 Hz, 1H), 4.40 (d, *J* = 11.0 Hz, 1H), 4.15 (dd, *J* = 12.2, 7.3 Hz, 1H), 3.71 (s, 3H), 3.68 (dt, *J* = 9.6, 7.1 Hz, 1H), 3.57 (dq, *J* = 9.6, 7.0 Hz, 1H), 2.72 (dd, *J* = 13.5, 3.4 Hz, 1H), 2.34 (ddd, *J* = 13.5, 7.3, 3.4 Hz, 1H), 2.22 (dd, *J* = 13.3, 2.4 Hz, 1H), 2.17 (q, *J* = 13.4 Hz, 1H), 2.02 (s, 1H), 1.82 – 1.74 (m, 2H), 1.67 (td, *J* = 13.9, 13.0, 4.2 Hz, 1H), 1.60 (ddd, *J* = 13.4, 11.0, 2.5 Hz, 1H), 1.49 – 1.43 (m, 1H), 1.42 (s, 3H), 1.22 (t, *J* = 12.7 Hz, 1H), 1.18 (t, *J* = 7.1 Hz, 3H), 1.09 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 206.0, 172.1, 143.4, 139.4, 125.6, 117.4, 108.7, 94.5, 78.0, 68.6, 66.3, 65.3, 64.0, 54.0, 52.0, 49.2, 44.7, 42.6, 38.7, 35.0, 32.8, 19.3, 16.9, 15.3, 14.0.

Synthesis of compounds 54a and 54b

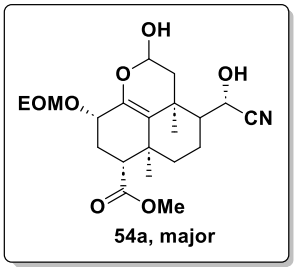


To a 50 mL RBF charged with **18** (760 mg, 2.0 mmol, 1.0 equiv) was added DCM (10 mL). Et_3N (415 μL, 3 mmol, 1.5 equiv) and TMSCN (500 μL, 4 mmol, 2.0 equiv) were added sequentially under ambient atmosphere, and the reaction mixture was stirred at room temperature for 1 h. The solvent was removed under reduced pressure to afford a yellow oil which was used directly in the next step without further purification.

To the above RBF containing the residue was added THF (14 mL) under N_2 and the mixture was cooled to –78 °C. L-selectride (1 M in THF, 6 mL, 6 mmol, 3.0 equiv) was added dropwise, and the reaction mixture was stirred for 4 h. The reaction was then carefully quenched with saturated NH_4Cl solution (5 mL) and diluted with EtOAc (20 mL) and H_2O (5 mL). After warming to room temperature, the layers were separated. The organic layer was washed with H_2O (3×4 mL), and the combined aqueous layers were extracted with EtOAc (3×5 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure to afford a colorless oil, which was used directly in the next step without further purification.

The crude residue was dissolved in THF (10 mL), and $Et_3N{\cdot}3HF$ (1.3 mL, 8 mmol, 4.0 equiv) was added under ambient atmosphere. The reaction mixture was stirred at room temperature for 30 min (monitored by TLC), then filtered through a short silica gel plug (~ 10 mL), eluting with EtOAc. The eluate was concentrated under reduced pressure and purified by flash column chromatography on silica gel (~20 mL), eluting with 0%→70% EtOAc in PE, to afford the products as a white solid (*d.r.* = 2:1, 489 mg, 60%). Pure samples of **54a** and **54b** were obtained by two successive rounds of PTLC (developed with 3% MeOH in DCM for the first separation and 50% EtOAc in PE for

the second).



54a, major

R_f = 0.15 (DCM: MeOH = 20:1)

Melting point: 90-94 °C

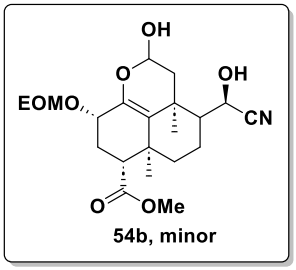
$[\alpha]_D^{24.8}$ = –91.8 (c = 0.14, $CHCl_3$)

HRMS-ESI (m/z): calc. for $C_{21}H_{32}NO_7$ [M+H^+] 410.2173, found 410.2174.

IR (neat, cm^{-1}): 3369, 2927, 1731, 1636, 1456, 1387, 1339, 1291, 1233, 1161, 1097, 1038, 1022, 905, 756.

^{1}H NMR (major C12 diastereoisomer, 400 MHz, $CDCl_3$): δ 5.38 (d, *J* = 10.3 Hz, 1H), 4.86 (d, *J* = 7.0 Hz, 1H), 4.80 (d, *J* = 7.0 Hz, 1H), 4.77 (d, *J* = 5.2 Hz, 1H), 4.22 (dd, *J* = 9.9, 7.8 Hz, 1H), 3.81 – 3.65 (m, 1H), 3.68 (s, 3H), 3.60 (dq, *J* = 9.5, 7.1 Hz, 1H), 3.15 (d, *J* = 6.4 Hz, 1H), 2.43 (dd, *J* = 13.4, 3.2 Hz, 1H), 2.34 (d, *J* = 6.3 Hz, 1H), 2.27 – 2.05 (m, 3H), 2.00 – 1.75 (m, 2H), 1.51 – 1.38 (m, 2H), 1.33 (s, 3H), 1.28 – 1.18 (m, 6H).

^{13}C NMR (major C12 diastereoisomer, 151 MHz, $CDCl_3$): δ 173.5, 144.2, 120.1, 118.9, 95.5, 90.8, 72.1, 63.5, 61.8, 52.4, 51.7, 51.7, 45.3, 39.5, 36.3, 36.3, 29.0, 26.4, 22.7, 18.0, 15.2.



54b, minor

R_f = 0.15 (DCM:MeOH = 20:1)

Melting point: 35-39 °C

$[\alpha]_D^{25.3}$ = –73.8 (c = 0.21, $CHCl_3$)

HRMS-ESI (m/z): calc. for $C_{21}H_{32}NO_7$ [M+H^+] 410.2173, found 410.2174.

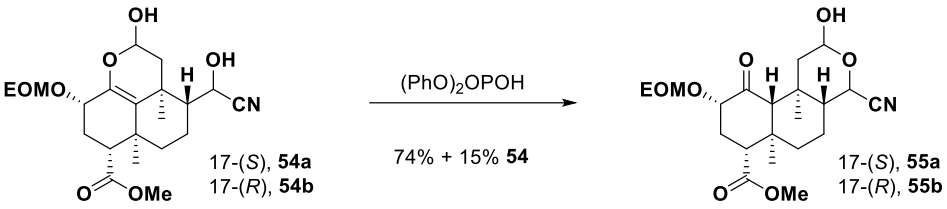
IR (neat, cm^{-1}): 3378, 2926, 1730, 1437, 1386, 1339, 1286, 1221, 1161, 1096, 1037, 1018, 957, 907, 755.

^{1}H NMR (major C12 diastereoisomer, 400 MHz, $CDCl_3$): δ 5.35 (d, *J* = 10.5 Hz, 1H), 4.86 (d, *J* = 7.1 Hz, 1H), 4.83 – 4.75 (m, 1H), 4.58 (t, *J* = 5.0 Hz, 1H), 4.22 (dd, *J* = 9.8,

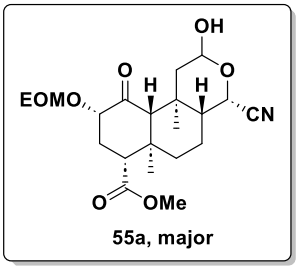
7.8 Hz, 1H), 3.76 – 3.69 (m, 1H), 3.68 (s, 3H), 3.60 (dq, *J* = 9.6, 7.1 Hz, 1H), 3.29 (d, *J* = 6.6 Hz, 1H), 2.71 (d, *J* = 5.6 Hz, 1H), 2.41 (dd, *J* = 13.2, 3.5 Hz, 1H), 2.24 (dd, *J* = 12.7, 2.6 Hz, 1H), 2.20 – 2.05 (m, 2H), 2.00 – 1.68 (m, 2H), 1.68 – 1.59 (m, 1H), 1.49 (dd, *J* = 12.5, 10.1 Hz, 1H), 1.45 – 1.35 (m, 1H), 1.32 (s, 3H), 1.24 – 1.17 (m, 6H).

^{13}C NMR (major C12 diastereoisomer, 151 MHz, $CDCl_3$): δ 173.5, 144.5, 119.4, 118.6, 95.4, 90.8, 72.1, 63.6, 62.8, 52.5, 51.7, 51.7, 45.1, 39.1, 36.2, 35.6, 28.9, 25.2, 22.6, 19.7, 15.2.

Synthesis of compounds 55a and 55b



To a 100 mL RBF was added **54a** and **54b** (2:1 mixture, 350 mg, 0.86 mmol total, 1 equiv) and HPLC grade DCM (43 mL). $(PhO)_2(O)POH$ (4.4 mg, 0.018 mmol, 0.02 equiv) was added and the solution was stirred at 25 °C for 96 h (monitored by TLC). Upon completion, a drop of Et_3N was added and the solvents were removed under reduced pressure. The residue was subjected to silica gel chromatography (~30 mL), eluting with 0%→5% MeOH in DCM to afford the products as a white solid (*d.r.* = 2:1, 260 mg, 74%) and starting material (52 mg, 15%). Pure samples of **55a** and **55b** were obtained by two successive rounds of PTLC (developed with 3% MeOH in DCM for the first separation and 50% EtOAc in PE for the second).



R_f = 0.3 (DCM:MeOH = 20:1)

Melting point: 77-82 °C

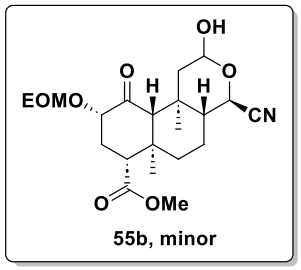
$[\alpha]_D^{26.4}$ = –58.8 (c = 0.53, $CHCl_3$)

HRMS-ESI (m/z): calc. for $C_{21}H_{32}NO_7$ $[M+H^+]$ 410.2173, found 410.2173.

IR (neat, cm^{-1}): 3444, 2932, 1723, 1437, 1396, 1352, 1274, 1240, 1193, 1155, 1122, 1098, 1064, 1040, 999, 958, 936, 892, 862, 843, 753, 667, 547.

^{1}H NMR (major C12 diastereoisomer, 400 MHz, $CDCl_3$): δ 5.39 (d, *J* = 10.0 Hz, 1H), 4.77 (d, *J* = 7.2 Hz, 1H), 4.73 (d, *J* = 7.2 Hz, 1H), 4.66 (d, *J* = 5.1 Hz, 1H), 4.13 (dd, *J* = 12.2, 7.3 Hz, 1H), 3.70 (s, 3H), 3.73 – 3.64 (m, 1H), 3.58 (dq, *J* = 9.7, 7.1 Hz, 1H), 3.23 (d, *J* = 5.7 Hz, 1H), 2.69 (dd, *J* = 13.5, 3.4 Hz, 1H), 2.46 (dd, *J* = 13.0, 2.5 Hz, 1H), 2.31 (ddd, *J* = 13.4, 7.3, 3.4 Hz, 1H), 2.15 (q, *J* = 12.6, 12.0 Hz, 1H), 1.92 (s, 1H), 1.76 (td, *J* = 8.1, 6.9, 3.2 Hz, 1H), 1.73 – 1.61 (m, 3H), 1.60 (s, 3H), 1.19 (t, *J* = 7.1 Hz, 3H), 1.09 (s, 3H), 0.94 (dd, *J* = 13.0, 9.3 Hz, 1H).

^{13}C NMR (major C12 diastereoisomer, 126 MHz, $CDCl_3$): δ 205.5, 172.1, 117.6, 94.4, 91.4, 77.7, 65.7, 64.9, 64.0, 54.1, 52.0, 46.1, 44.4, 42.5, 38.9, 35.7, 32.6, 19.4, 17.0, 15.6, 15.3.



55b, minor

R_f = 0.32 (DCM:MeOH = 20:1)

Melting point: 72-77 °C

$[\alpha]_D^{26.0}$ = –92.9 (c = 0.24, $CHCl_3$)

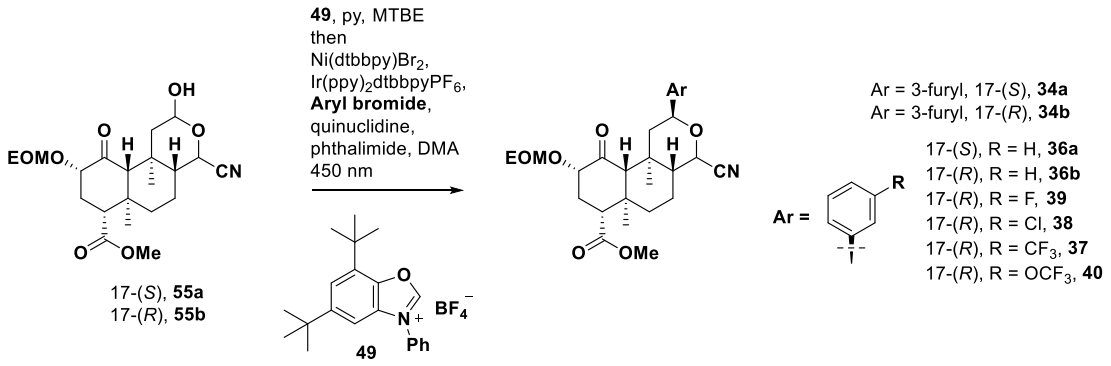
HRMS-ESI (m/z): calc. for $C_{21}H_{32}NO_7$ [M+H$^+$] 410.2173, found 410.2174.

IR (neat, cm^{-1}): 3434, 2931, 1724, 1437, 1395, 1351, 1277, 1155, 1123, 1098, 1061, 1040, 1007, 985, 938, 902, 883, 846, 784, 753, 667, 595.

^{1}H NMR (major C12 diastereoisomer, 400 MHz, $CDCl_3$): δ 5.15 (ddd, *J* = 8.8, 5.9, 3.2 Hz, 1H), 4.82 – 4.74 (m, 1H), 4.72 (d, *J* = 7.2 Hz, 1H), 4.35 (d, *J* = 11.1 Hz, 1H), 4.16 (dd, *J* = 12.5, 7.3 Hz, 1H), 3.71 (s, 3H), 3.74 – 3.52 (m, 2H), 3.04 (d, *J* = 5.9 Hz, 1H), 2.72 (dd, *J* = 13.8, 3.8 Hz, 1H), 2.39 (dd, *J* = 13.2, 3.2 Hz, 1H), 2.37 – 2.26 (m, 1H), 2.22 – 2.08 (m, 1H), 2.02 (s, 1H), 1.82 – 1.72 (m, 2H), 1.73 – 1.57 (m, 2H), 1.53 – 1.35 (m, 1H), 1.35 (s, 3H), 1.19 (t, *J* = 7.1 Hz, 3H), 1.06 (s, 3H), 1.00 (dd, *J* = 13.2, 8.2 Hz, 1H).

^{13}C NMR (major C12 diastereoisomer, 126 MHz, $CDCl_3$): δ 205.8, 172.1, 117.5, 94.4, 92.9, 77.9, 65.3, 64.6, 64.0, 53.9, 52.0, 47.8, 44.8, 42.5, 38.5, 35.0, 32.8, 19.2, 16.8, 15.3, 14.9.

General procedure for the synthesis of compounds 34a, 34b, 36a, 36b, 37, 38, 39, 40

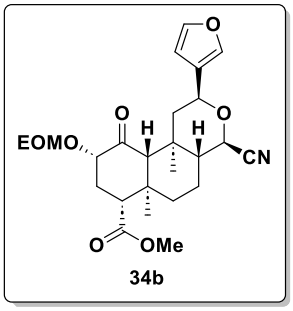


A flame-dried 15 mL RBF equipped with a magnetic stir bar was charged with **55a**/**b** (2:1 mixture, 72 mg, 0.176 mmol, 1.0 equiv) and **49** (66 mg, 0.167 mmol, 0.95 equiv). The flask was transferred into a glovebox, and MTBE (1.0 mL) was added, followed by slow addition of pyridine (15.1 μL, 14.8 mg, 0.167 mmol, 0.95 equiv). The mixture was stirred for 5 min, during which the suspension turned pale pink. The suspension was then filtered through a syringe filter into a flame-dried 4 mL vial. The flask and syringe were rinsed twice with MTBE, and the washings were filtered to the same vial to afford 1.2 mL of a 0.15 M stock solution of the alcohol-NHC adduct in MTBE. This stock solution showed no significant decomposition after storage at –20 °C in the glovebox for one week.

A flame-dried 2 mL vial was charged with Ni(dtbbpy)Br_2 (12 mg, 0.025 mmol, 0.08 equiv) and phthalimide (9.5 mg, 0.065 mmol, 0.22 equiv). The vial was transferred into the glovebox and DMA (1.0 mL) was added to afford a 0.025 M stock solution of the Ni catalyst. This stock solution remained unchanged after storage at –20 °C in the glovebox for one week.

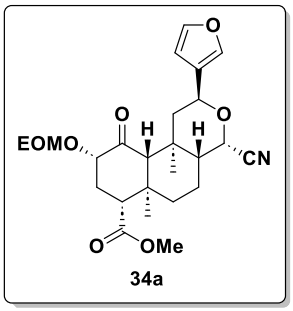
A separate flame-dried 2 mL vial was charged with Ir(ppy)$_2$dtbbpyPF_6 (5.5 mg, 6 μmol, 0.02 equiv) and quinuclidine (60 mg, 0.54 mmol, 1.75 equiv). After transfer into the glovebox, DMA (1.0 mL) was added to afford a 0.006 M stock solution of the Ir catalyst. This stock solution also showed no significant change after storage at –20 °C in the glovebox for one week.

A flame-dried 2 mL vial equipped with a magnetic stir bar was transferred into the glovebox. The Ni catalyst stock solution (85 μL), freshly distilled aryl bromide (0.038 mmol, 1.5 equiv), Ir catalyst stock solution (85 μL), and the alcohol-NHC adduct stock solution (170 μL, containing 10.2 mg **55a/b**) were added sequentially. The vial was sealed with a screw cap and Parafilm, removed from the glovebox, and placed in a 2.5 cm diameter tube containing 1 mL of water as a cooling bath. The reaction mixture was irradiated in the Rogertech RLH-18CU multi-position parallel photoreactor at 450 nm (15 W power, 5°C bath temperature) for 12 h. Upon completion, the reaction mixture was concentrated using a GeneVac evaporator, and the residue was purified by PTLC (developed with 30% EtOAc/PE) to afford the corresponding product.



34b

0.8 mg (7% yield, 21% yield based on **55b**) from 10.2 mg scale reaction of **55** (containing 3.4 mg **55b**) with 3-bromofuran.



34a

1.2 mg (10% yield, 15% yield based on **55a**) from 10.2 mg scale reaction of **55** (containing 6.8 mg **55a**) with 3-bromofuran.

R_f = 0.4 (PE: EtOAc = 3:2)

Melting point: 49-52 ℃

$[\alpha]_D^{20.7}$ = –79.8 (c = 0.217, $CHCl_3$)

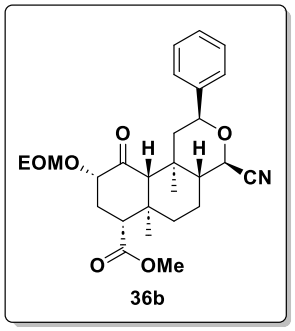
HRMS-ESI (m/z): calc. for $C_{25}H_{34}NO_7$ $[M+H^+]$ 460.2330, found 460.2332.

IR (neat, cm^{-1}): 2931, 1726, 1437, 1395, 1273, 1200, 1158, 1123, 1100, 1073, 1042, 1020, 903, 875, 785, 755, 602, 418.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 (d, *J* = 1.4 Hz, 2H), 6.36 (t, *J* = 1.4 Hz, 1H), 5.09 (dd, *J* = 11.6, 2.2 Hz, 1H), 4.77 (d, *J* = 7.2 Hz, 1H), 4.73 (d, *J* = 7.2 Hz, 1H), 4.62 (d, *J*

= 4.9 Hz, 1H), 4.13 (dd, *J* = 12.2, 7.3 Hz, 1H), 3.71 (s, 3H), 3.78 – 3.63 (m, 1H), 3.57 (dq, *J* = 9.6, 7.1 Hz, 1H), 2.71 (dd, *J* = 13.4, 3.4 Hz, 1H), 2.39 – 2.26 (m, 2H), 2.17 (q, *J* = 13.3 Hz, 1H), 1.93 (s, 1H), 1.82 – 1.73 (m, 1H), 1.75 – 1.67 (m, 2H), 1.67 (s, 3H), 1.67 – 1.59 (m, 1H), 1.49 – 1.39 (m, 1H), 1.24 – 1.18 (m, 1H), 1.18 (t, *J* = 7.0 Hz, 3H), 1.13 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 205.7, 172.1, 143.5, 139.6, 125.6, 117.8, 108.7, 94.5, 77.9, 65.93, 65.84, 65.81, 64.0, 54.2, 52.0, 46.7, 44.2, 42.7, 39.0, 35.1, 32.7, 19.8, 17.04, 15.3, 15.0.



36b

2.2 mg (18% yield, 55% yield based on **55b**) from 10.2 mg scale reaction of **55** (containing 3.4 mg **55b**) with bromobenzene.

R_f = 0.6 (PE: EtOAc = 3:2)

Melting point: 66-70 °C

$[\alpha]_D^{21.0}$ = –138.0 (c = 0.083, $CHCl_3$)

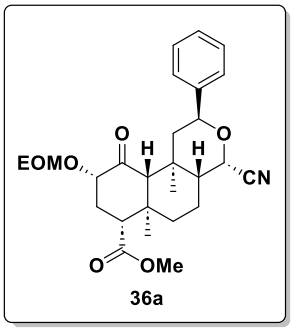
HRMS-ESI (m/z): calc. for $C_{27}H_{36}NO_6$ [M+H$^+$] 470.2537, found 470.2537.

IR (neat, cm^{-1}): 2919, 2849, 1728, 1646, 1456, 1436, 1394, 1280, 1202, 1155, 1123, 1098, 1075, 1041, 1011, 702.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 – 7.27 (m, 5H), 4.81 (dd, *J* = 11.6, 2.5 Hz, 1H), 4.73 (d, *J* = 7.1 Hz, 1H), 4.66 (d, *J* = 7.1 Hz, 1H), 4.45 (d, *J* = 10.9 Hz, 1H), 4.10 (dd, *J* = 12.2, 7.3 Hz, 1H), 3.65 (dq, *J* = 9.6, 7.1 Hz, 1H), 3.53 (dq, *J* = 9.6, 7.0 Hz, 1H), 2.72 (dd, *J* = 13.5, 3.4 Hz, 1H), 2.32 (ddd, *J* = 13.5, 7.3, 3.4 Hz, 1H), 2.27 – 2.08 (m, 2H), 2.01 (s, 1H), 1.84 – 1.74 (m, 2H), 1.75 – 1.57 (m, 1H), 1.54 – 1.41 (m, 1H), 1.48 (s, 3H), 1.21 – 1.13 (m, 1H), 1.15 (t, *J* = 7.1 Hz, 3H), 1.10 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 205.9, 172.1, 140.8, 128.6 (2C), 128.1, 125.8 (2C), 117.5, 94.4, 77.9, 75.4, 66.5, 65.3, 64.0, 54.1, 52.0, 49.3, 46.6, 42.6, 38.8, 35.3, 32.9,

19.3, 16.9, 15.2, 14.0.



36a

1.9 mg (18% yield, 24% yield based on **55a**) from 10.2 mg scale reaction of **55** (containing 6.8 mg **55a**) with bromobenzene.

R_f = 0.5 (PE: EtOAc = 3:2)

Melting point: 74-79 ℃

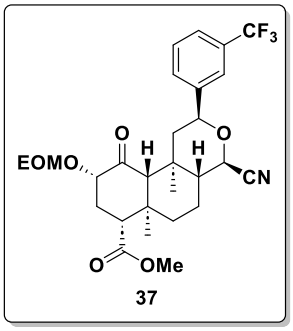
$[\alpha]_D^{21.0}$ = –109.4 (c = 0.168, $CHCl_3$)

HRMS-ESI (m/z): calc. for $C_{27}H_{36}NO_6$ [M+H$^+$] 470.2537, found 470.2536.

IR (neat, cm^{-1}): 2931, 1727, 1453, 1395, 1374, 1273, 1240, 1200, 1156, 1123, 1100, 1074, 1041, 1017, 903, 760, 701.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.26 (m, 5H), 5.09 (dd, *J* = 11.6, 2.2 Hz, 1H), 4.73 (d, *J* = 7.1 Hz, 1H), 4.71 (d, *J* = 4.9 Hz, 1H), 4.66 (d, *J* = 7.2 Hz, 1H), 4.08 (dd, *J* = 12.2, 7.3 Hz, 1H), 3.71 (s, 3H), 3.66 (dq, *J* = 9.6, 7.1 Hz, 1H), 3.53 (dq, *J* = 9.6, 7.1 Hz, 1H), 2.70 (dd, *J* = 13.5, 3.4 Hz, 1H), 2.38 – 2.23 (m, 2H), 2.16 (q, *J* = 13.4 Hz, 1H), 1.93 (s, 1H), 1.84 – 1.76 (m, 1H), 1.76 – 1.65 (m, 3H), 1.72 (s, 4H), 1.51 – 1.43 (m, 1H), 1.20 – 1.14 (m, 1H), 1.15 (t, *J* = 7.1 Hz, 3H), 1.13 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 205.7, 172.1, 140.8, 128.6 (2C), 128.1, 126.1 (2C), 117.9, 94.4, 77.8, 72.7, 66.0, 65.9, 64.0, 54.2, 52.0, 46.8, 46.1, 42.8, 39.0, 35.3, 32.7, 19.8, 17.0, 15.2, 15.1.



37

1.2 mg (8% yield, 26% yield based on **55b**) from 10.2 mg scale reaction of **55** (containing 3.4 mg **55b**) with 3-bromobenzotrifluoride.

R_f = 0.6 (PE: EtOAc = 3:2)

Melting point: 59-63 ℃

$[\alpha]_D^{21.4}$ = –111.6 (c = 0.210, $CHCl_3$)

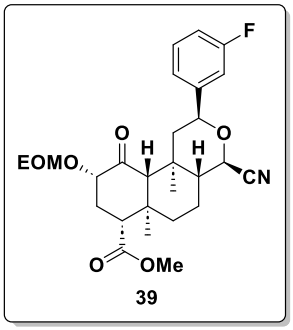
HRMS-ESI (m/z): calc. for $C_{28}H_{35}F_3NO_6$ $[M+H^+]$ 538.2411, found 538.2411.

IR (neat, cm^{-1}): 2933, 1727, 1451, 1394, 1330, 1280, 1204, 1165, 1124, 1100, 1074, 1041, 1013, 904, 806, 703.

^{1}H NMR (400 MHz, $CDCl_3$):δ 7.74 – 7.32 (m, 4H), 4.87 (dd, *J* = 11.6, 2.5 Hz, 1H), 4.73 (d, *J* = 7.2 Hz, 1H), 4.67 (d, *J* = 7.1 Hz, 1H), 4.46 (d, *J* = 11.0 Hz, 1H), 4.11 (dd, *J* = 11.8, 7.3 Hz, 1H), 3.72 (s, 3H), 3.65 (dq, *J* = 9.7, 7.3 Hz, 1H), 3.54 (dq, *J* = 9.7, 7.0 Hz, 1H), 2.72 (dd, *J* = 13.4, 3.5 Hz, 1H), 2.33 (ddd, *J* = 13.4, 7.3, 3.6 Hz, 1H), 2.24 (dd, *J* = 13.4, 2.5 Hz, 1H), 2.22 – 2.10 (m, 1H), 2.02 (s, 1H), 1.87 – 1.76 (m, 2H), 1.75 – 1.59 (m, 3H), 1.49 (s, 3H), 1.14 (m, 4H), 1.10 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 206.0, 172.0, 141.8, 131.0 (q, *J* = 32.4 Hz), 129.2, 129.1, 124.9 (q, *J* = 3.8 Hz), 124.1 (q, *J* = 272.1 Hz), 122.6 (q, *J* = 3.4 Hz), 117.3, 94.48, 78.0, 74.7, 66.5, 65.2, 64.0, 54.0, 52.0, 49.1, 46.5, 42.6, 38.7, 35.3, 32.8, 19.2, 16.9, 15.2, 14.0.

^{19}F NMR (565 MHz, $CDCl_3$) δ -62.56.



39

1.5 mg (12% yield, 37% yield based on **55b**) from 10.2 mg scale reaction of **55** (containing 3.4 mg **55b**) with 3-bromofluorobenzene.

R_f = 0.6 (PE: EtOAc = 3:2)

Melting point: 65-69 ℃

$[\alpha]_D^{22.1}$ = –123.6 (c = 0.250, $CHCl_3$)

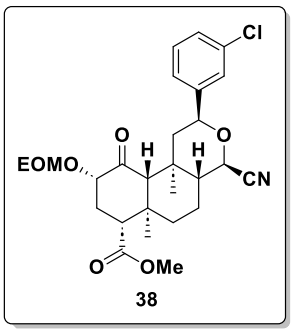
HRMS-ESI (m/z): calc. for $C_{27}H_{35}FNO_6$ [M+H^+] 488.2443, found 488.2444.

IR (neat, cm^{-1}): 2951, 1727, 1617, 1592, 1488, 1449, 1394, 1269, 1200, 1156, 1123, 1098, 1077, 1041, 1012, 903, 871, 781, 755, 694.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 – 7.27 (m, 1H), 7.09 – 7.01 (m, 2H), 6.96 (tdd, *J* = 8.4, 2.6, 1.0 Hz, 1H), 4.81(q, *J* = 11.5, 2.1 Hz, 1H), 4.74 (d, *J* = 7.1 Hz, 1H), 4.67 (d, *J* = 7.1 Hz, 1H), 4.44 (d, *J* = 10.9 Hz, 1H), 4.11 (dd, *J* = 12.1, 7.3 Hz, 1H), 3.71 (s, 3H), 3.66 (dq, *J* = 9.5, 7.1 Hz, 1H), 3.54 (dq, *J* = 9.7, 7.1 Hz, 1H), 2.71 (dd, *J* = 13.5, 3.4 Hz, 1H), 2.32 (ddd, *J* = 13.5, 7.3, 3.4 Hz, 1H), 2.27 – 2.20 (m, 1H), 2.19 – 2.09 (m, 1H), 2.00 (s, 1H), 1.86 – 1.75 (m, 2H), 1.75 – 1.58 (m, 3H), 1.47 (s, 3H), 1.15 (t, *J* = 7.1 Hz, 4H), 1.10 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 206.0, 172.0, 163.0 (d, *J* = 246 Hz), 143.4 (d, *J* = 7.4 Hz), 130.1 (d, *J* = 8.2 Hz), 121.3 (d, *J* = 3.1 Hz), 117.3, 114.9 (d, *J* = 21.0 Hz), 112.9 (d, *J* = 22.3 Hz), 94.4, 77.9, 74.6, 66.5, 65.2, 64.0, 54.0, 52.0, 49.2, 46.5, 42.6, 38.7, 35.3, 32.8, 19.2, 16.9, 15.2, 14.0.

^{19}F NMR (565 MHz, $CDCl_3$) δ –112.66.



38

1.3 mg (10% yield, 30% yield based on **55b**) from 10.2 mg scale reaction of **55** (containing 3.4 mg **55b**) with 3-bromochlorobenzene.

R_f = 0.6 (PE: EtOAc = 3:2)

Melting point: 70-75 ℃

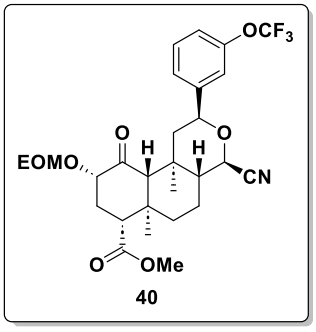
$[\alpha]_D^{21.7}$ = –97.7 (c = 0.182, $CHCl_3$)

HRMS-ESI (m/z): calc. for $C_{27}H_{35}ClNO_6$ [M+H^+] 504.2147, found 504.2148.

IR (neat, cm^{-1}): 2931, 1727, 1436, 1394, 1278, 1202, 1157, 1123, 1099, 1079, 1041, 1012, 904, 785.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (s, 1H), 7.27 – 7.22 (m, 2H), 7.21 – 7.13 (m, 1H), 4.79 (dd, *J* = 11.4, 2.2 Hz, 1H), 4.74 (d, *J* = 7.1 Hz, 1H), 4.67 (d, *J* = 7.2 Hz, 1H), 4.44 (d, *J* = 10.9 Hz, 1H), 4.11 (dd, *J* = 12.3, 7.3 Hz, 1H), 3.71 (s, 3H), 3.66 (dq, *J* = 9.6, 7.1 Hz, 1H), 3.54 (dq, *J* = 9.7, 7.1 Hz, 1H), 2.71 (dd, *J* = 13.5, 3.5 Hz, 1H), 2.33 (ddd, *J* = 13.4, 7.3, 3.5 Hz, 1H), 2.27 – 2.19 (m, 1H), 2.19 – 2.09 (m, 1H), 2.00 (s, 1H), 1.80 (m, 2H), 1.76 – 1.59 (m, 3H), 1.47 (s, 3H), 1.15 (t, *J* = 7.1 Hz, 4H), 1.10 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 206.0, 172.1, 142.8, 134.6, 129.9, 128.2, 126.0, 123.9, 117.3, 94.5, 78.0, 74.6, 66.5, 65.2, 64.0, 54.0, 52.0, 49.2, 46.5, 42.6, 38.7, 35.3, 32.8, 19.3, 16.9, 15.2, 14.0.



40

2.1 mg (15% yield, 45% yield based on **55b**) from 10.2 mg scale reaction of **55** (containing 3.4 mg **55b**) with 1-bromo-3-(trifluoromethoxy)benzene.

R_f = 0.6 (PE: EtOAc = 3:2)

Melting point: 49-54 ℃

$[\alpha]_D^{23.4}$ = –109.2 (c = 0.158, $CHCl_3$)

HRMS-ESI (m/z): calc. for $C_{28}H_{35}F_3NO_7$ [M+H$^+$] 554.2360, found 554.2364.

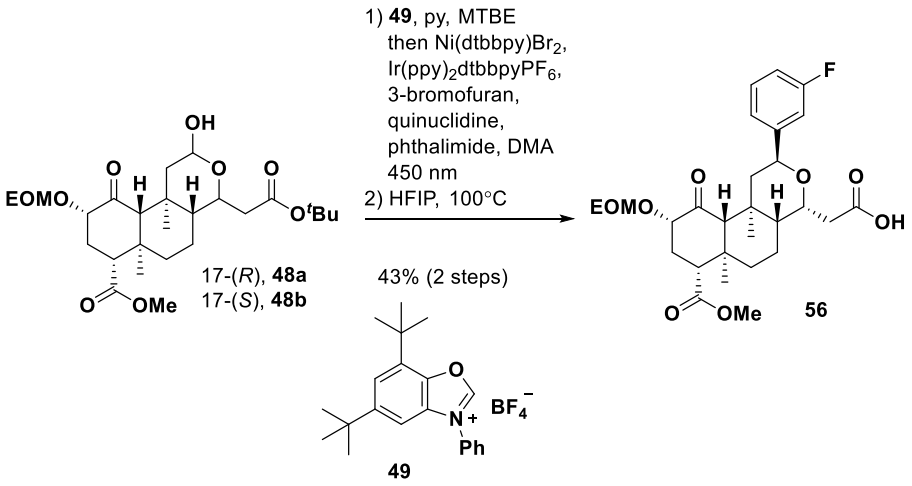
IR (neat, cm^{-1}): 2934, 1727, 1449, 1258, 1216, 1160, 1124, 1099, 1080, 1041, 1013.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (t, *J* = 7.9 Hz, 1H), 7.25 – 7.10 (m, 3H), 4.83 (dd, *J* = 11.6, 2.5 Hz, 1H), 4.74 (d, *J* = 7.2 Hz, 1H), 4.68 (d, *J* = 7.2 Hz, 1H), 4.45 (d, *J* = 11.0 Hz, 1H), 4.11 (dd, *J* = 12.2, 7.3 Hz, 1H), 3.71 (s, 3H), 3.66 (dq, *J* = 9.6, 7.0 Hz, 1H), 3.54 (dq, *J* = 9.6, 7.0 Hz, 1H), 2.72 (dd, *J* = 13.5, 3.5 Hz, 1H), 2.33 (ddd, *J* = 13.6, 7.3, 3.4 Hz, 1H), 2.27 – 2.09 (m, 2H), 2.01 (s, 1H), 1.85 – 1.74 (m, 2H), 1.75 – 1.57 (m, 2H), 1.48 (s, 3H), 1.53 – 1.36 (m, 1H), 1.15 (t, *J* = 7.1 Hz, 4H), 1.10 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 206.0, 172.1, 149.5, 143.2, 129.9, 124.1, 120.6 (q, *J* = 257.3 Hz), 120.4, 118.5, 117.3, 94.5, 78.0, 74.5, 66.5, 65.2, 64.0, 54.0, 52.0, 49.1, 46.5, 42.6, 38.7, 35.3, 32.8, 19.2, 16.9, 15.2, 14.0.

^{19}F NMR (565 MHz, $CDCl_3$) δ –57.69.

Synthesis of compound 56

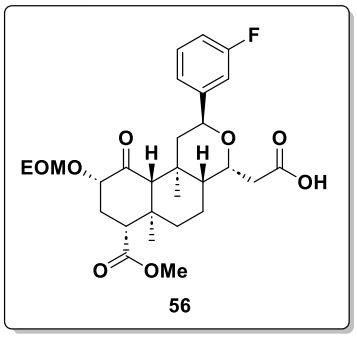


A 15 mL RBF equipped with a magnetic stir bar was charged with **48a**/**b** (2:1 mixture, 84 mg, 0.17 mmol, 1.0 equiv) and **49** (63 mg, 0.16 mmol, 0.95 equiv). MTBE (1 mL) was added to the flask followed by pyridine (14.2 mg, 14.5 μL, 0.16 mmol, 0.95 equiv). The mixture was stirred for 5 min, during which the suspension turned faint yellow. In a separate flame-dried 4 mL vial were placed Ni(dtbbpy)Br_2 (6.5 mg, 0.0135 mmol, 0.08 equiv), Ir(ppy)$_2$dtbbpyPF_6 (3.1 mg, 0.0034 mmol, 0.02 equiv), quinuclidine (33 mg, 0.30 mmol, 1.75 equiv) and phthalimide (5.5 mg, 0.037 mmol, 0.22 equiv). Both vessels were transferred into a glovebox. The suspension containing NHC-adduct was filtered through a syringe filter into an empty flame-dried 4 mL reaction vial. The flask and syringe were rinsed twice with MTBE, and washings were filtered and combined with the filtrate to give a total MTBE volume of ~1.5 mL.

DMA (1.0 mL) was added to the 4 mL vial containing the catalysts, and the mixture was stirred until a homogeneous dark-green solution was obtained. Fresh distilled 3-bromofluorobenzene (28 μL, 44 mg, 0.25 mmol, 1.5 equiv) was added, and the mixture was stirred for 5 min. The DMA solution was then transferred to the 4 mL reaction vial containing the substrate-NHC adduct. The catalyst vial was rinsed with DMA (0.1 mL), and the washings were transferred to the reaction vial. The vial was sealed with a screw cap, and removed from the glovebox. N_2 was bubbled through the reaction mixture until a final solvent volume of 2.2 mL was reached. The vial was then sealed with Parafilm, and irradiated in the Rogertech photoreactor at 450 nm (100% power) for 10 h at 5 °C.

Upon completion, the reaction mixture was transferred to a separatory funnel, and H_2O (5 mL), EtOAc (15 mL) and HOAc (0.2 mL) were added. The layers were separated, and the organic layer was washed with H_2O (5×3 mL). The combined aqueous layers were extracted with EtOAc (3×5 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was filtered through a silica gel plug (~5 mL), first eluting with 10% EtOAc in PE to remove the oxidized NHC, then 25% EtOAc in PE to elute the product, and last with 80% EtOAc in PE to elute the starting material (23 mg, 27%). All fractions containing the product were collected and concentrated to afford a colorless oil (typically contaminated with phthalimide and elimination products), which was directly subjected to the next step without further purification.

The residue from the previous step was dissolved in 12 mL HFIP and heated at 100 ℃ for 48 h. The solvent was removed under reduced pressure, and the residue was purified by PTLC (developed with 40% EtOAc in PE containing 1% HOAc) to afford **56** (25 mg, 43% for 2 steps) as a white foam and its C17 epimer.



56

R_f = 0.25 (PE: EtOAc = 1:1, containing 1% HOAc)

Melting point: 83-88 ℃

$[\alpha]_D^{21.3}$ = –79.90 (c = 0.329, $CHCl_3$)

HRMS-ESI (m/z): calc. for $C_{28}H_{37}FNaO_8$ [M+Na^+] 543.2365, found 543.2375.

IR (neat, cm^{-1}): 2930, 1725, 1591, 1488, 1437, 1394, 1270, 1244, 1193, 1157, 1124, 1099, 1070, 1041, 1016, 986, 931, 904, 864, 784, 754.

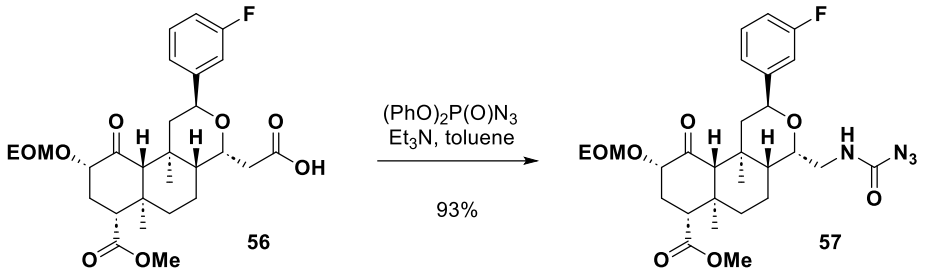
^{1}H NMR (400 MHz, $CDCl_3$):δ 7.23 (dd, *J* = 8.2, 5.9 Hz, 1H), 7.06 (d, *J* = 8.1 Hz, 2H), 6.92 (td, *J* = 8.8, 2.1 Hz, 1H), 4.84 (d, *J* = 11.2 Hz, 1H), 4.73 (d, *J* = 7.1 Hz, 1H), 4.67 (d, *J* = 7.2 Hz, 1H), 4.41 (s, 1H), 4.08 (dd, *J* = 12.3, 7.3 Hz, 1H), 3.70 (s, 3H), 3.66 (dq, *J* = 9.5, 7.1, 6.5 Hz, 2H), 3.53 (dq, *J* = 9.5, 7.0 Hz, 1H), 2.99 – 2.82 (m, 1H), 2.70 (dd, *J* = 13.4, 3.4 Hz, 1H), 2.41 (d, *J* = 15.3 Hz, 1H), 2.29 (ddd, *J* = 13.4, 7.2, 3.3 Hz, 1H),

2.23 (d, J = 12.9 Hz, 1H), 2.14 (q, J = 13.1 Hz, 1H), 1.95 (s, 1H), 1.76 – 1.55 (m, 3H), 1.46 (s, 3H), 1.45 – 1.35 (m, 3H), 1.15 (t, J = 7.1 Hz, 3H) , 1.09 – 1.02 (m, 1H), 1.06 (s, 3H).

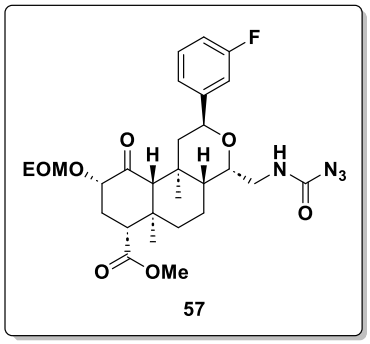
^{13}C NMR (151 MHz, $CDCl_3$): δ 206.3, 176.4, 172.3, 163.0 (d, J = 245.8 Hz), 144.9 (d, J = 7.0 Hz), 129.9 (d, J = 8.1 Hz), 121.9, 114.4 (d, J = 21.1 Hz), 113.3 (d, J = 22.2 Hz), 94.4, 78.0, 74.3, 67.9, 66.5, 64.0, 54.1, 51.9, 47.7, 46.5, 42.9, 39.5, 35.1, 34.4, 32.7, 20.6, 17.0, 16.8, 15.2.

^{19}F NMR (565 MHz, $CDCl_3$) δ –113.00.

Synthesis of compound 57



To a 10 mL RBF charged with **56**(8.0 mg, 0.015 mmol, 1.0 equiv) was added toluene (0.5 mL), followed by Et_3N (7.5 μL, 5.5 mg, 0.054 mmol, 3.6 equiv) and $(PhO)_2P(O)N_3$ (10 μL, 12.8 mg, 0.046 mmol, 3.0 equiv). The solution was stirred at room temperature for 30 min then 80 °C for 8 h. The mixture was cooled to room temperature and concentrated under reduced pressure. The residue was purified by PTLC (developed with 30% EtOAc in PE) to afford **57** (8.0 mg, 93%) as a white foam.



R_f = 0.6 (PE: EtOAc = 1:1)

Melting point: 74-78 °C

$[\alpha]_D^{21.3}$ = –71.6 (c = 0.438, $CHCl_3$)

HRMS-ESI (m/z): calc. for $C_{28}H_{37}FN_4NaO_7$ [M+Na^+] 583.2538, found 583.2543.

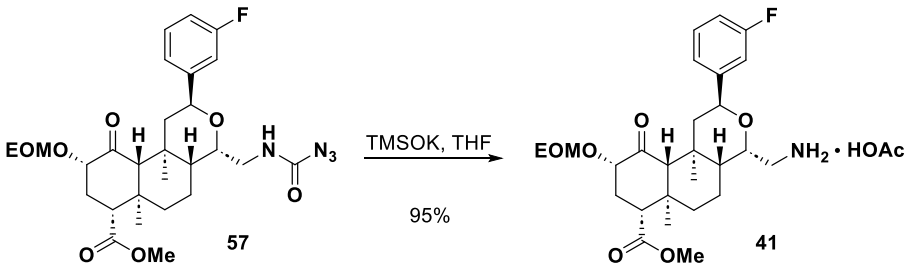
IR (neat, cm^{-1}): 3318, 2930, 2144, 1721, 1616, 1591, 1527, 1487, 1448, 1393, 1367, 1270, 1231, 1157, 1124, 1100, 1016, 956, 934, 899, 879, 785, 755, 694, 549.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 – 7.25 (m, 1H), 7.14 – 7.02 (m, 2H), 7.01 – 6.90 (m, 1H), 5.40 (d, *J* = 6.9 Hz, 1H), 4.78 (dd, *J* = 11.4, 2.3 Hz, 1H), 4.73 (d, *J* = 7.1 Hz, 1H), 4.66 (d, *J* = 7.1 Hz, 1H), 4.07 (dd, *J* = 12.3, 7.3 Hz, 1H), 3.91 (ddd, *J* = 11.5, 5.8, 2.5 Hz, 1H), 3.73 – 3.68 (m, 7H), 3.65 (dq, *J* = 9.7, 7.1 Hz, 1H), 3.62 – 3.46 (m, 2H), 3.42 (ddd, *J* = 14.2, 7.9, 2.6 Hz, 1H), 2.69 (dd, *J* = 13.4, 3.4 Hz, 1H), 2.29 (ddd, *J* = 13.4, 7.2, 3.4 Hz, 1H), 2.25 – 2.07 (m, 2H), 1.95 (s, 1H), 1.79 – 1.67 (m, 2H), 1.63 (td, *J* = 13.2, 12.7, 4.5 Hz, 1H), 1.57 – 1.50 (m, 1H), 1.52 – 1.44 (m, 1H), 1.44 (s, 3H), 1.14 (t, *J* = 7.1 Hz, 3H), 1.06 (s, 3H), 1.10 – 1.00 (m, 1H).

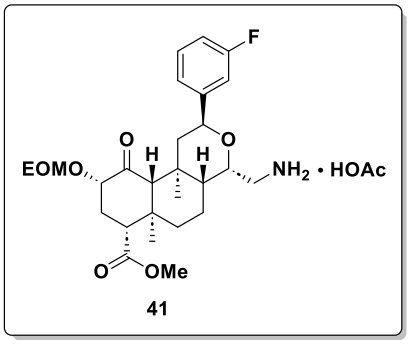
^{13}C NMR (126 MHz, $CDCl_3$): δ 206.2, 172.2, 163.1 (d, J = 246.0 Hz), 156.7, 145.0 (d, J = 7.3 Hz), 130.0 (d, J = 8.2 Hz), 121.8 (d, J = 3.0 Hz), 114.6 (d, J = 21.1 Hz), 113.1 (d, J = 22.1 Hz), 94.4, 77.9, 77.5, 68.0, 66.4, 64.0, 54.2, 51.9, 47.5, 47.1, 42.9, 39.7, 39.3, 34.9, 32.7, 20.5, 17.1, 16.8, 15.2.

^{19}F NMR (565 MHz, $CDCl_3$) δ –112.84.

Synthesis of compound 41



To a 10 mL RBF was added **57** (4.0 mg, 0.007 mmol, 1.0 equiv) and TMSOK (2.5 mg, 0.018 mmol, 2.5 equiv). The flask was immersed in an ice-water bath, and THF (0.5 mL) was added. The reaction mixture was stirred at 0 °C for 1 h and then quenched with one drop of HOAc. The resulting mixture was filtered directly through a syringe filter, and the filtrate was concentrated under reduced pressure. The residue was redissolved in $CHCl_3$ (1 mL) and sonicated for 1 min. The resulting cloudy suspension was filtered through a syringe filter, and the filtrate was concentrated under reduced pressure to afford practically pure **41** as a white solid (3.8 mg, 95%).



R_f = 0.4 (DCM: MeOH = 20:1, containing 1% NH_4OH)

Melting point: 120-125 ℃

$[\alpha]_D^{21.8}$ = –94.7 (c = 0.256, $CHCl_3$)

HRMS-ESI (m/z): calc. for $C_{27}H_{38}FNNaO_6$ [M+Na^+] 514.2575, found 514.2583.

IR (neat, cm^{-1}): 2926, 1723, 1618, 1591, 1528, 1445, 1396, 1272, 1197, 1158, 1124, 1100, 1083, 1043, 1012, 783.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 – 7.23 (m, 1H), 7.09 (d, *J* = 7.5 Hz, 2H), 6.99 – 6.88 (m, 1H), 4.79 (d, *J* = 11.3 Hz, 1H), 4.73 (d, *J* = 7.1 Hz, 1H), 4.66 (d, *J* = 7.1 Hz, 1H), 4.07 (dd, *J* = 12.2, 7.3 Hz, 1H), 3.93 – 3.80 (m, 1H), 3.70 (s, 3H), 3.70 – 3.59 (m, 1H), 3.53 (dq, *J* = 9.7, 7.1 Hz, 1H), 3.27 (t, *J* = 12.4 Hz, 1H), 2.70 (dd, *J* = 13.4, 3.4 Hz, 1H), 2.63 (d, *J* = 13.5 Hz, 1H), 2.28 (ddd, *J* = 13.4, 7.2, 3.4 Hz, 1H), 2.26 – 2.07 (m,

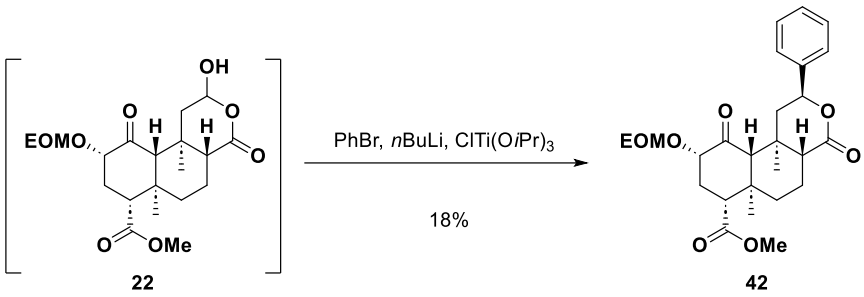
2H), 1.96 (s, 1H), 1.76 – 1.67 (m, 1H), 1.67 – 1.57 (m, 1H), 1.56 – 1.44 (m, 1H), 1.43 (s, 1H), 1.42 (s, 3H), 1.14 (t, *J* = 7.1 Hz, 3H), 1.05 (s, 3H), 1.09 – 0.99 (m, 1H).

^{1}H NMR (400 MHz, $\underline{CD_3OD}$): δ 7.32 (td, *J* = 8.1, 5.9 Hz, 1H), 7.24 – 7.13 (m, 2H), 7.03 – 6.88 (m, 1H), 4.97 (d, *J* = 11.4 Hz, 1H), 4.71 (d, *J* = 6.9 Hz, 1H), 4.61 (d, *J* = 7.0 Hz, 1H), 4.22 (dd, *J* = 12.2, 7.3 Hz, 1H), 4.13 – 3.99 (m, 1H), 3.69 (s, 3H), 3.65 – 3.46 (m, 3H), 2.97 (dd, *J* = 13.5, 2.0 Hz, 1H), 2.91 (dd, *J* = 13.5, 3.4 Hz, 1H), 2.35 (s, 1H), 2.27 (ddd, *J* = 13.2, 7.3, 3.4 Hz, 1H), 2.15 (dd, *J* = 13.4, 2.4 Hz, 1H), 2.01 (q, *J* = 13.1 Hz, 1H), 1.93 (s, 3H), 1.93 – 1.85 (m, 1H), 1.81 – 1.69 (m, 2H), 1.66 – 1.54 (m, 1H), 1.47 (s, 3H), 1.40 (s, 1H), 1.19 (t, *J* = 12.5 Hz, 1H), 1.10 (t, *J* = 7.1 Hz, 3H), 1.05 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 206.3, 174.8, 172.3, 163.0 (d, *J* = 245.5 Hz), 145.4 (d, *J* = 7.0 Hz), 129.9 (d, *J* = 8.2 Hz), 121.7, 114.3 (d, *J* = 21.0 Hz), 113.1 (d, *J* = 24.0 Hz), 94.4, 78.2, 77.7, 67.6, 66.4, 63.9, 54.19, 54.16, 51.9, 47.2, 42.9, 39.1, 35.0, 20.6, 17.2, 16.8, 15.22, 15.19. (*Some carbons are invisible in the spectrum due to the nature of amine salt. Nevertheless, the structure can be unambiguously assigned from ^{1}H NMR and HRMS data.*)

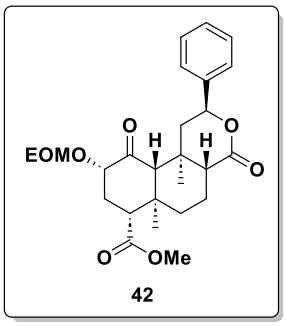
^{19}F NMR (565 MHz, $CDCl_3$) δ –113.08.

Synthesis of compound 42



To a 15 mL RBF was added bromobenzene (39 mg, 26 μL, 0.25 mmol, 10 equiv) and THF (0.25 mL), and the solution was cooled to –78 °C. ^{n}BuLi (2.5 M in hexane, 100 μL, 0.25 mmol, 10 equiv) was added dropwise, and the mixture was stirred for 1 h. $ClTi(O^{i}Pr)_3$ (1 M in hexane, 250 μL, 0.25 mmol, 10 equiv) was then added dropwise. After complete addition, the cooling bath was removed, and the reaction mixture was warmed to 23 °C over 10 min and stirred for an additional 30 min to give a ~ 0.4 M solution of $PhTi(O^{i}Pr)_3$, which was used immediately.

In a separate 5 mL RBF charged with crude **22** (10 mg, 0.025 mmol, 1.0 equiv) and toluene (2.5 mL), freshly prepared $PhTi(O^{i}Pr)_3$ solution was added at –40 °C. The resulting solution was stirred at –40 °C for 24 h, then quenched with 1M HCl (0.4 mL) and EtOAc (1 mL). The layers were separated, and the aqueous layer was extracted with EtOAc (3×2 mL). The combined organic layers were washed with brine, and dried over Na_2SO_4 and filtered. The solution was added 1 mg $(PhO)_2P(O)OH$ before being concentrated under reduced pressure, and the residue was stored at 0 °C overnight. The crude material was purified by PTLC (developed with 2% MeOH in DCM) to afford **42** as a colorless wax (2.0 mg, 18%).



R_f = 0.7 (MeOH: DCM = 1:30)

Melting point: 50-54 °C

$[\alpha]_D^{28.0}$ = –111.89 (c = 0.125, $CHCl_3$)

HRMS-ESI (m/z): calc. for $C_{26}H_{34}NaO_7$ $[M+Na^+]$ 481.2197, found 481.2197.

IR (neat, cm^{-1}): 2918, 1727, 1455, 1377, 1275, 1225, 1201, 1159, 1082, 1041, 1004, 941, 757, 702

^{1}H NMR (400 MHz, $CDCl_3$):δ 7.43 – 7.27 (m, 5H), 5.56 (dd, *J* = 11.8, 5.2 Hz, 1H), 4.76 (d, *J* = 7.2 Hz, 1H), 4.70 (d, *J* = 7.2 Hz, 1H), 4.10 (dd, *J* = 12.2, 7.3 Hz, 1H), 3.72 (s, 3H), 3.70 – 3.62 (m, 1H), 3.55 (dq, *J* = 9.7, 7.1 Hz, 1H), 2.68 (dd, *J* = 13.4, 3.4 Hz, 1H), 2.56 (dd, *J* = 13.5, 5.2 Hz, 1H), 2.33 (ddd, *J* = 13.5, 7.3, 3.4 Hz, 1H), 2.25 – 2.12 (m, 2H), 2.10 (dd, *J* = 11.8, 3.1 Hz, 1H), 2.04 (s, 1H), 1.83 – 1.75 (m, 1H), 1.74 – 1.61 (m, 1H), 1.59 (d, *J* = 4.0 Hz, 1H), 1.52 (s, 3H), 1.51 – 1.40 (m, 1H), 1.16 (t, *J* = 7.1 Hz, 3H), 1.12 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$): δ 206.1, 172.0, 171.6, 140.5, 128.8, 128.4, 125.6, 94.4, 79.0, 77.9, 64.4, 64.0, 54.1, 52.0, 51.8, 45.9, 42.2, 38.4, 35.9, 32.8, 18.4, 16.6, 15.3, 15.2.

III. Biological Experimental Procedures

Statistics and reproducibility

Unless otherwise stated, statistical analyses were performed using GraphPad Prism (version 10.5.0). Animals were randomly assigned to treatment groups. No statistical method was used to predetermine sample size; sample sizes were chosen on the basis of prior studies and are reported in the figure legends. Investigators were not blinded to treatment allocation during data collection or analysis. Animals were excluded only according to prespecified criteria, including overt injury during test, or behavior that prevented valid completion of the assay. Potential outliers in the concentration–response curve were identified using the robust regression and outlier removal (ROUT) method in GraphPad Prism, with the maximum false discovery rate set to Q = 1%. Three independent molecular dynamics (MD) simulations were initialized separately, and all trajectories were included in the analysis.

cAMP inhibition assay (three concentration screening)

HEK293 cells were maintained in high-glucose DMEM supplemented with 10% FBS and 1% penicillin–streptomycin at 37 °C in a humidified 5% CO_2 incubator. One day prior to the experiment, cells were seeded into 6-well plates. At 70–80% confluence, they were co-transfected with pcDNA3.1-hDOR (or pcDNA3.1-hMOR) and pGlosensor-22F (Promega). After 16 h, cells were seeded into 96-well plates at 100,000 cells per well and cultured for a further 16 h. Cells were incubated with 40 μL of 2% GloSensor cAMP reagent for 15 min at room temperature in the dark, followed by test compound at three concentrations for 15 min. Luminescence was measured with a microplate reader, normalized with the plate vehicle control and positive control (10 μM DAMGO or DPDPE), and an inhibition (%)–concentration heatmap was generated using GraphPad Prism 10 software.

cAMP inhibition assay (curve)

The cAMP inhibition dose-response curves were measured by ICE Bioscience Inc. (http://ice-biosci.com) using the LANCE Ultra cAMP kit (PerkinElmer). CHO cells

stably expressing human KOR or MOR were employed. Briefly, CHO-KOR/CHO-MOR cells were seeded into 384-well plates at a density of 2,000 cells per well in 10 μL of medium. Compounds were added and incubated for 10 min at 37 °C before stimulation with 1 μM forskolin for 30 min. Eu-cAMP tracer and ULight anti-cAMP antibody were then added, and plates were incubated for 1 h at room temperature. Fluorescence signals were measured on a PHERAstar FSX microplate reader (BMG Labtech) at 665 nm and 620 nm. The 665 nm/620 nm ratio was plotted against compound concentration, normalized to %Dynorphin A stimulation and fitted using the "log(agonist) versus response" model in GraphPad Prism 10.5.0.

β-arrestin 2 recruitment assay

β-arrestin 2 recruitment to KOR were measured by ICE Bioscience Inc. (http://ice-biosci.com). HEK293T-β-Arrestin2-KOR cells were seeded into 96-well plates at 30,000 cells per well in Opti-MEM medium containing 4% FBS. Nano-Glo Live Cell Substrate was added according to the manufacturer's instructions, followed by a ten-point concentration series of each compound. After 10 min in the dark, luminescence was recorded, normalized to the response to dynorphin B and fitted using the "log(agonist) versus response" model in GraphPad Prism 10.5.0.

Ligand bias quantification

Dose–response data (G protein signaling or arrestin signaling) were fit using the Black and Leff operational model:

$$B=10^{X*n}\cdot 10^{Log\ \tau*n};$$

$$Y=E_{max}\ B/[B+(10^{X}+10^{Log\ KA})^{n}]$$

in Graphpad Prism 10.5.0, where X is the logarithm of the agonist concentration, E_{max} represents the maximum response of the system (shared value for all ligands), K_A is the functional dissociation constant for the agonist, τ is the efficacy of the agonist in the given pathway, and n is shared hill slope. The transduction coefficients $\log(\tau/K_A)$ for each pathway and each ligand were calculated. Using EOM-salvinorin B as the full

agonist reference, $\Delta\log(\tau/K_A)_{ligand}$ was calculated by

$$\Delta\log(\tau/K_A)_{ligand,\ G\ protein} = \log(\tau/K_A)_{ligand,\ G\ protein} - \log(\tau/K_A)_{EOM\text{-}SalB,\ G\ protein};$$

$$\Delta\log(\tau/K_A)_{ligand,\ arrestin} = \log(\tau/K_A)_{ligand,\ arrestin} - \log(\tau/K_A)_{EOM\text{-}SalB,\ arrestin}.$$

The ΔΔlog(τ/KA) was calculated by subtracting the β-Arrestin2 transduction coefficient from the G protein transduction coefficient:

$$\Delta\Delta\log(\tau/K_A)_{ligand} = \Delta\log(\tau/K_A)_{ligand,\ G\ protein} - \Delta\log(\tau/K_A)_{Ligand,\ arrestin}.$$

Bias factor of ligand was calculated by

$$\text{Bias factor} = 10^{\Delta\Delta\log(\tau/KA)ligand}$$

Radioligand competitive binding assay

CHO cells stably expressing human KOR were cultured in DMEM/F12 containing 10% FBS and 1% penicillin–streptomycin at 37 °C and 5% CO_2. Confluent cells were scraped in PBS containing 0.5% EDTA, pelleted and resuspended in 50 mM Tris-HCl (pH 7.4). Competitive binding was measured using [^{3}H]U69593 (46.7 Ci/mmol, K_d = 1.1 nM) and four replicate wells or tubes per condition. The corresponding B_{max} value was 870 ± 80 fmol/mg protein. Samples containing receptor preparation, 2 nM radioligand and serially diluted test compounds were incubated for 30 min at 37 °C. Non-specific binding was defined with 10 μM U69,593. Bound radioligand was collected on GF/C filters, washed with ice-cold buffer and quantified by liquid scintillation counting (Revvity Tri-Carb 4910 TR liquid scintillation counter). Specific radioligand binding% was calculated as

$$(dpm_{test\ compound} - dpm_{non\text{-}specific}) / (dpm_{total\ binding} - dpm_{non\text{-}specific})$$

The half-maximal inhibitory concentration (IC_{50}) was obtained from the competition binding curve, and the K_i of the test compound was determined using the relationship

$$IC_{50} = K_i \times (1 + \text{HotNM}/\text{HotKdNM})$$

where HotNM is the final concentration of the radioligand and HotKdNM is the

dissociation constant of the radioligand. All curve fitting was performed using GraphPad Prism 10.5.0

Kinetics of competitive radioligand binding assay

Association and dissociation kinetics of [^{3}H]U69,593 were determined before competitive kinetic analysis. For association, 2 nM [^{3}H]U69,593 was incubated with membrane at 25 °C for 0.25, 0.5, 1, 2, 3, 5, 7, 10, 15, 25 or 45 min. Non-specific binding was defined with 10 μM U69,593. For dissociation, receptor preparations were equilibrated with [^{3}H]U69,593 for 1 h at 25 °C before addition of 10 μM naloxone, and residual binding was measured at the same time points. Reactions were terminated by GF/C filtration and quantified by liquid scintillation counting. Radioligand k_{on} and k_{off} were obtained in GraphPad Prism 10.5.0. The observed rate constant k_{obs} was derived from the absolute slope of the linear regression of $\ln(Y_{max}/(Y_{max}-Y))$ versus time, and k_{on} was calculated as $k_{on} = \underline{k}_{obs} \times 100 / (Y_{max} \times [L])$; k_{off} was derived from the absolute slope of the linear regression of ln Y versus time, where Y_{max} is the maximal specific binding, Y is specific binding at each time point and [L] is the final radioligand concentration.

Test compounds were analyzed at three or four concentrations spanning 10–1,000 × their estimated K_i. Time courses were globally fitted with the Prism kinetics-of-competitive-binding model using the measured radioligand concentration, k_{on} and k_{off}; fitted k_3 and k_4 values were taken as the association and dissociation rate constants of the test compound.

Animals

ICR mice (18-20 g) were sourced from Shandong Aimaodakang Life Science Co., Ltd. (http://amdocbio.com) Mice were housed in a temperature- and humidity-controlled environment with unrestricted access to food and water, aligned with 12 h light/dark cycle. All animal experiments were performed under the guidelines of the National Institutes of Health Guide for the Care and Use of Laboratory Animals using an approved animal protocol (BARIDD-2026-06-WYJ-03).

Hot Plate Test

To measure thermal nociception, female ICR mice (18–20 g) were acclimated to the testing environment for 1–2 days. On the test day, mice were placed on a hot plate (SA702, JiangSuSansBio) set to 55 °C, and the latency to the first hind-paw licking or jumping was recorded with a 60 s cutoff to prevent tissue injury. Two baseline measurements were taken before the experiment and the average was used as the pre-drug baseline latency; mice with baseline latencies <5 s or >30 s were excluded. For the formal test, mice received the test compound, morphine (positive control), or vehicle in saline intraperitoneally, and hot-plate latencies were measured at selected time points post-administration. Antinociception was quantified as the percentage of maximum possible effect (%MPE) using the formula:

$$\%\text{MPE} = (\text{latency}_{\text{post-drug}} - \text{latency}_{\text{baseline}}) / (\text{cutoff time} - \text{latency}_{\text{baseline}}) \times 100\%.$$

Acetic acid-induced writhing test

Male ICR mice were acclimated for 1–2 days and treated intraperitoneally with vehicle, morphine or test compound in saline. After 20 min, mice received 0.6% acetic acid in saline (0.1 ml per 10 g, i.p.) and were observed for 15 min. A writhe was defined as abdominal constriction with inward concavity, pressing of the forepaws against the bottom, elevation of the hindquarters, and hind-limb extension.

Rotarod Test

Male ICR mice were trained twice daily for 2 days on an accelerating rotarod (KY-ROTD, Shanghai Kuoyunbio; 4–40 rpm over 240 s). Mice meeting the prespecified training criterion of ≥180 s on day 3 entered the experiment. The mean latency from two pre-dose trials was recorded before intraperitoneal administration of vehicle or test compound in saline. Latency to fall was measured 20 min after treatment; the vehicle and **26a** groups were reassessed at 6 h. Motor impairment was calculated for each animal as the percentage decrease from its pre-dose baseline:

$$\%\text{Motor impairment} = (t_{\text{baseline}} - t_{\text{drug}}) / t_{\text{baseline}} \times 100\%,$$

where $t_{baseline}$ denotes mean pre-dose latency, t_{drug} denotes the measured latency after injection.

Open field test

Male ICR mice (18–20 g) were acclimated for 1–2 days. After intraperitoneal administration of vehicle or test compound in saline, mice were placed in 20 × 20 × 40 cm open-field chambers under 3-lux illumination. Movement was recorded for 30 min using an automated video-tracking system (Shanghai Jiliang). The time course of distance moved and the total distance traveled were compared between groups using GraphPad Prism 10.5.0.

MDCK-MDR1 bidirectional permeability assay

The MDCK-MDR1 bidirectional permeability was evaluated by ICE Bioscience, Inc. (http://ice-biosci.com) using MDCK–MDR1 monolayers cultured on Transwell inserts for 3–7 days. Monolayer formation was verified by transepithelial electrical resistance. After equilibration in HBSS containing 10 mM HEPES (pH 7.4), compounds were applied at 5 μM to the apical or basolateral compartment. Samples were collected from both compartments after 2 h at 37 °C and quantified by LC–MS/MS. Apparent permeability and efflux ratio were calculated as

$$P_{app} = (V_{acceptor} \times C_{acceptor})/(A \times t \times C_{initial,donor})$$

where $V_{acceptor}$ is the acceptor-compartment volume, $C_{acceptor}$ is the compound concentration in the acceptor compartment at the end of incubation, A is the membrane surface area, t is the transport time, and $C_{initial,donor}$ is the initial compound concentration in the donor compartment. The efflux ratio was calculated as follows:

$$\text{Efflux ratio} = P_{app(B\rightarrow A)}/P_{app(A\rightarrow B)}$$

Post-experiment monolayer integrity was assessed with Lucifer Yellow.

In vitro plasma stability assay

The in vitro plasma stability was evaluated by Shanghai Medicilon, Inc.

(https://medicilon.com). Plasma stability was measured by Shanghai Medicilon using ICR mouse plasma. Compounds were incubated at 1 μM and 37 °C for 0, 5, 15, 30, 60 or 120 min. Reactions were quenched with four volumes of ice-cold methanol/acetonitrile (1:1) containing internal standard, centrifuged and analyzed by LC–MS/MS. Percentage remaining was calculated relative to the 0-min sample. Each compound was analyzed in two technical wells in one experiment.

In vivo pharmacokinetics

The in vivo plasma/brain concentrations were evaluated by Shanghai Medicilon, Inc. (https://medicilon.com) and SIMM-SERVIER Joint Biopharmacy Laboratory (http://english.simm.cas.cn/Organization/resear/rd/paksf/202012/t20201209_256307.html). Female ICR mice received **3**, **34b**, **26a** or **30** intraperitoneally at 2 mg/kg for plasma sampling or 4 mg/kg for brain sampling dose. Blood was collected into K_2-EDTA tubes, and plasma was isolated by centrifugation and stored at −80 °C. Independent groups of mice ($N = 3$ per compound per time point) were euthanized and whole brains were collected, rinsed with ice-cold PBS, divided into hemispheres and stored at −80 °C. Plasma proteins were precipitated with methanol containing internal standard; brain hemispheres were homogenized in four volumes of acetonitrile/methanol (1:1). Compounds were quantified by validated LC–MS/MS methods.

Data availability

The data supporting the findings of this study are available within the Article and its Supplementary Information. Source data underlying Figs. 1 and 5, Figs. S1, 7 and 8 and Table S2 are provided with this paper. NMR spectra and characterization data for all reported compounds are included in the Supplementary Information. The MD input files and processed trajectories have been deposited in Zenodo and are available to editors and reviewers through a private link. The record will be made publicly available upon publication.

IV. Molecular Dynamics Simulations

System setup for molecular dynamics simulations

Molecular dynamics simulations were initiated using the KOR structure from the MOM-SalB-bound KOR (PDB ID: 8DZQ).[18] The bound G protein was removed to allow free movement of the intracellular domain. The missing extracellular loops 1 and 3 (ECL1, ECL3) and intracellular loop 3 (ICL3) were modelled and refined using MODELLER.[19-20] The missing helix 8 was built by homology modeling based on the nalfurafine-bound KOR structure (PDB ID: 7YIT).[21] Initial binding poses of the small molecules were generated by Autodock suite,[22-25] and the pose most similar to the MOM-SalB binding mode was selected. Conserved water molecules within the GPCR structure were added using the HomolWat web server.[26]

Systems were prepared with CHARMM-GUI web server.[27] Force field parameters and topology files for the ligands were generated via the CHARMM-GUI built-in ParamChem service. The CHARMM36m force field was applied to the proteins, the CHARMM36 force field to lipids and ions, and the CHARMM-modified TIP3P water model was used.[28,29] All ionizable residues were assigned their default protonation states at pH 7.4, with the exception of D105$^{2.50}$ and D155$^{3.49}$, which were maintained in the protonated form. The initial membrane orientation was determined with the PPM 2.0 server,[30] after which the complex was embedded by CHARMM-GUI into a pure POPC bilayer. The resulting system contained 153 POPC lipids and approximately 10,000 water molecules, with a NaCl concentration of 0.15 M. The final system dimensions were approximately 80 Å × 80 Å × 90 Å, comprising approximately 54,000 atoms.

Molecular dynamics simulation

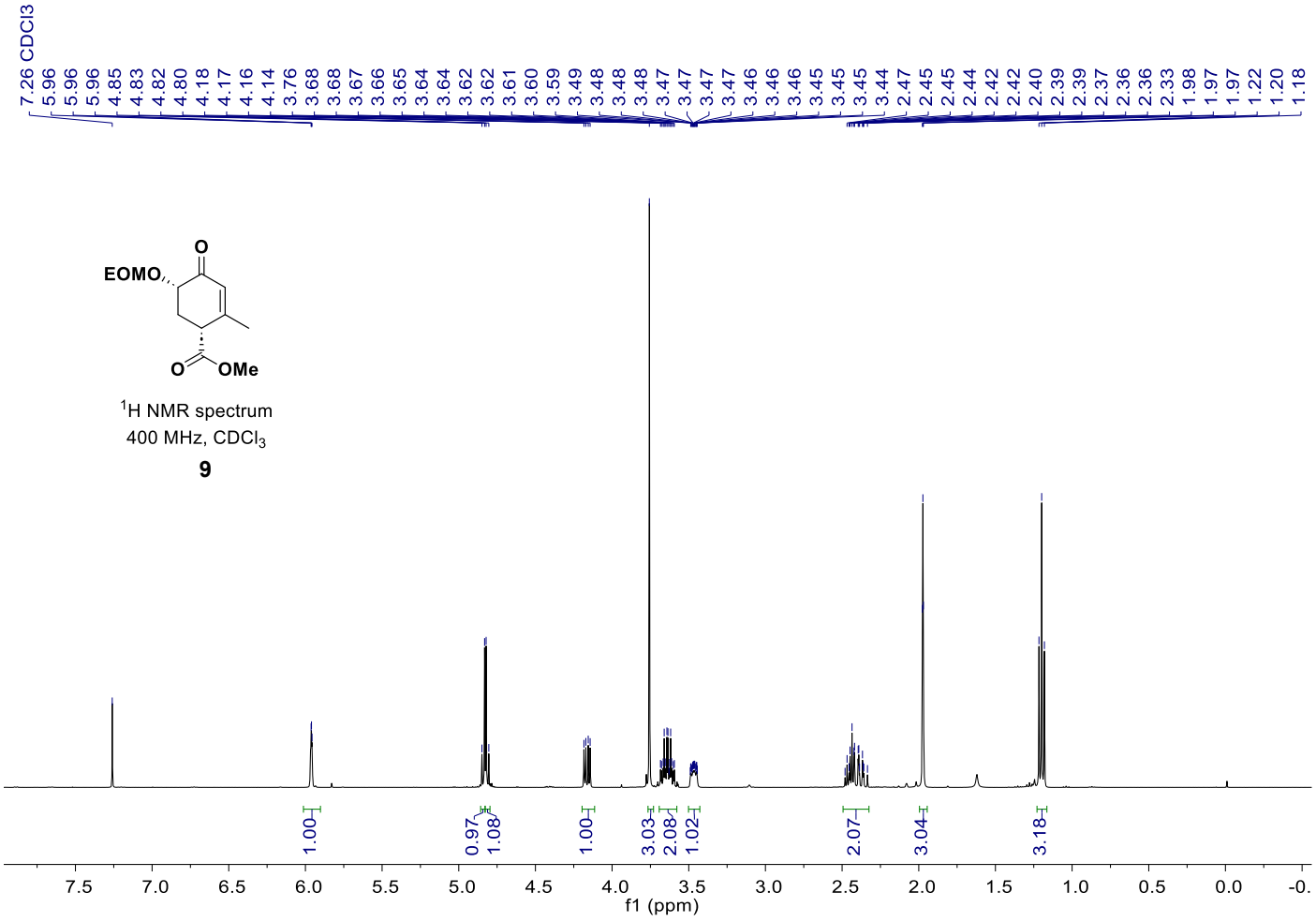
All simulations were performed with GROMACS 2025.3[31] on GPU nodes of the Weiming-II High-Performance Computing Platform at Peking University. Following the default CHARMM-GUI protocol with minor optimizations, a single round of energy minimization (5,000 steps) was performed, followed by five stages of gradual

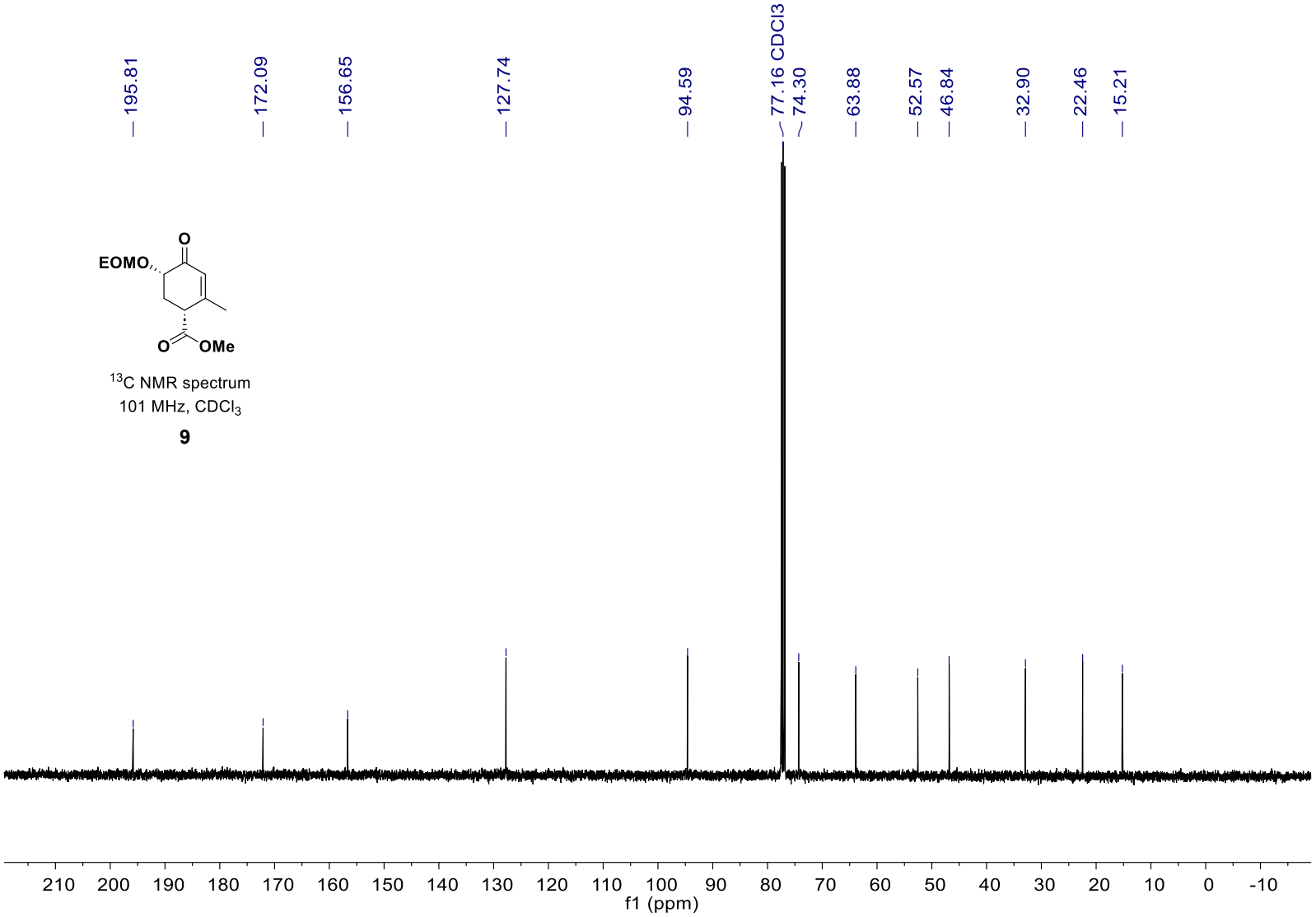
equilibration with progressively reduced harmonic restraints. During the first two equilibration stages, the temperature was raised gradually from 0 K to 310 K in the NPT ensemble, and thereafter held at 310 K.

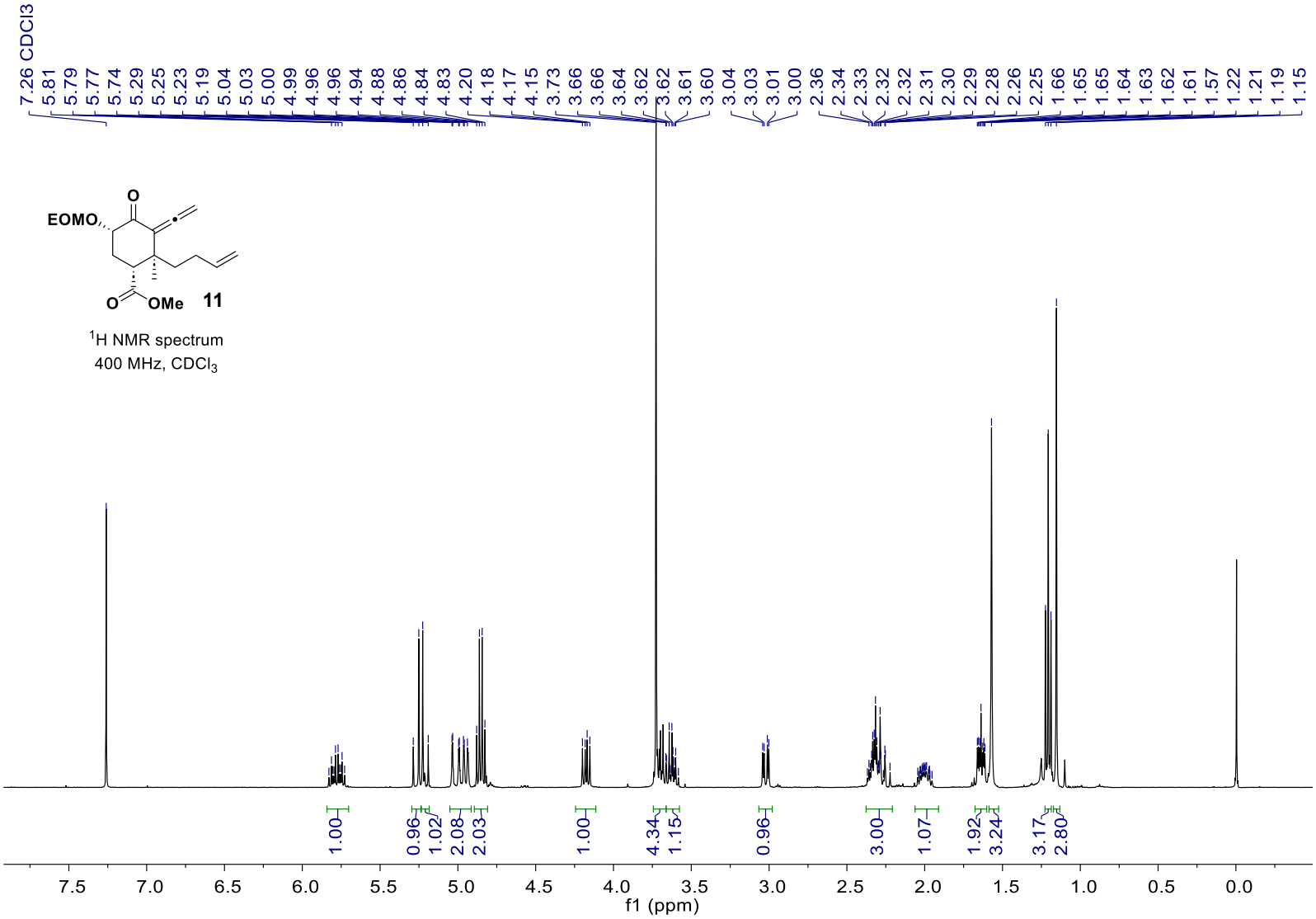
Production simulations were conducted without restraints at 310 K and 1 bar in the NPT ensemble with a 2.0 fs time step. The v-rescale algorithm with a time constant of 1 ps was used to maintain the temperature at 310 K, and the C-rescale algorithm with a time constant of 5 ps was used to maintain the pressure at 1 bar. Bonds involving hydrogen atoms were constrained with the LINCS algorithm.[32] The van der Waals interactions were smoothly switched off between 1.0 and 1.2 nm, and the long-range electrostatic interactions were treated by the particle-mesh Ewald (PME) method. Trajectory frames were saved every 200 ps. Each production simulation was 1,000 ns in length, and three independent replicates were performed for every ligand.

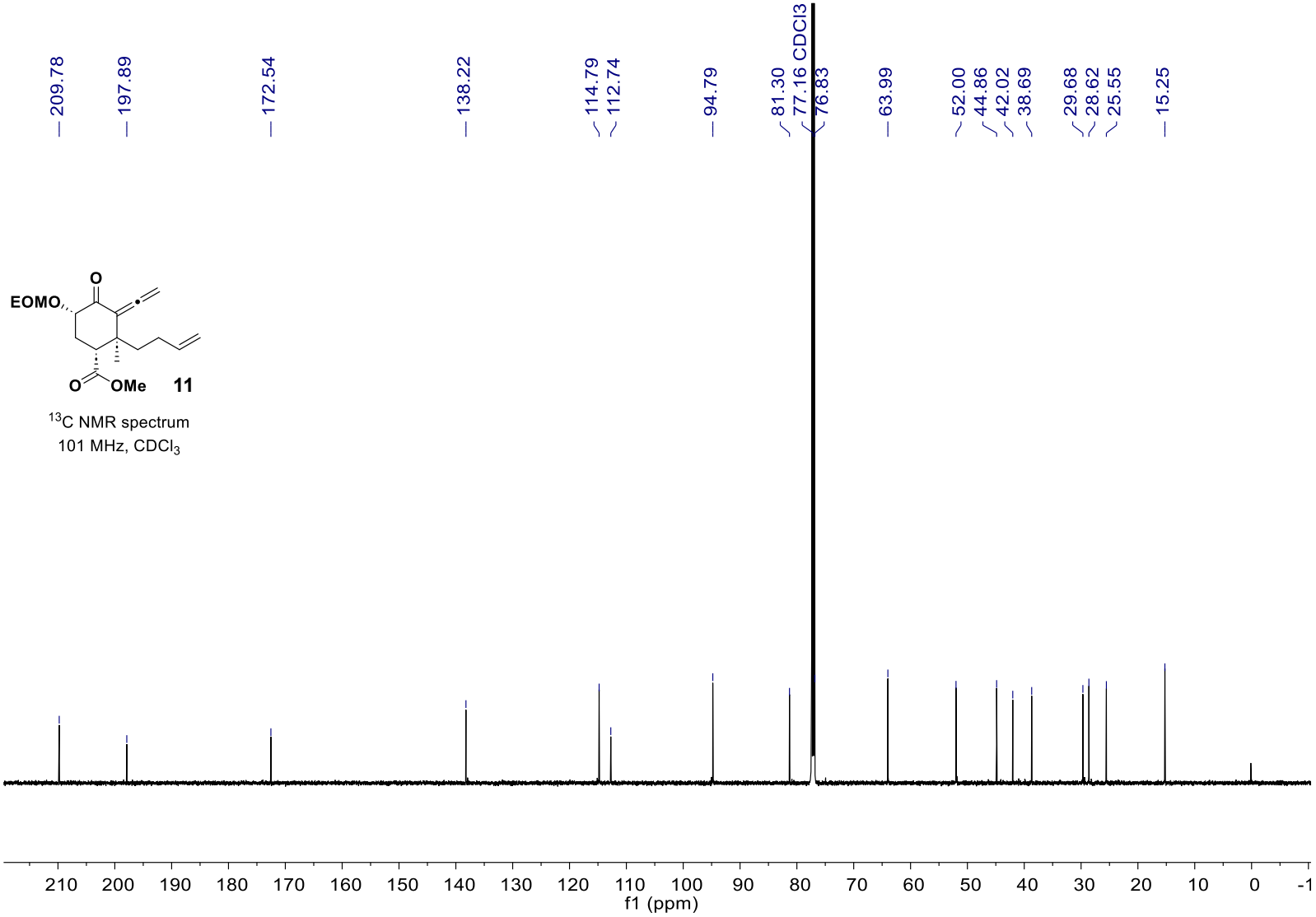
Trajectory analysis was carried out with GROMACS tools. MM-PBSA calculations were performed using the gmx_MMPBSA package.[33] Ligand–receptor interaction fingerprints were analyzed with ProLIF.[34] Root-mean-square deviations (RMSDs) were calculated relative to the initial structure of each simulation after alignment of all protein Cα atoms to the reference.

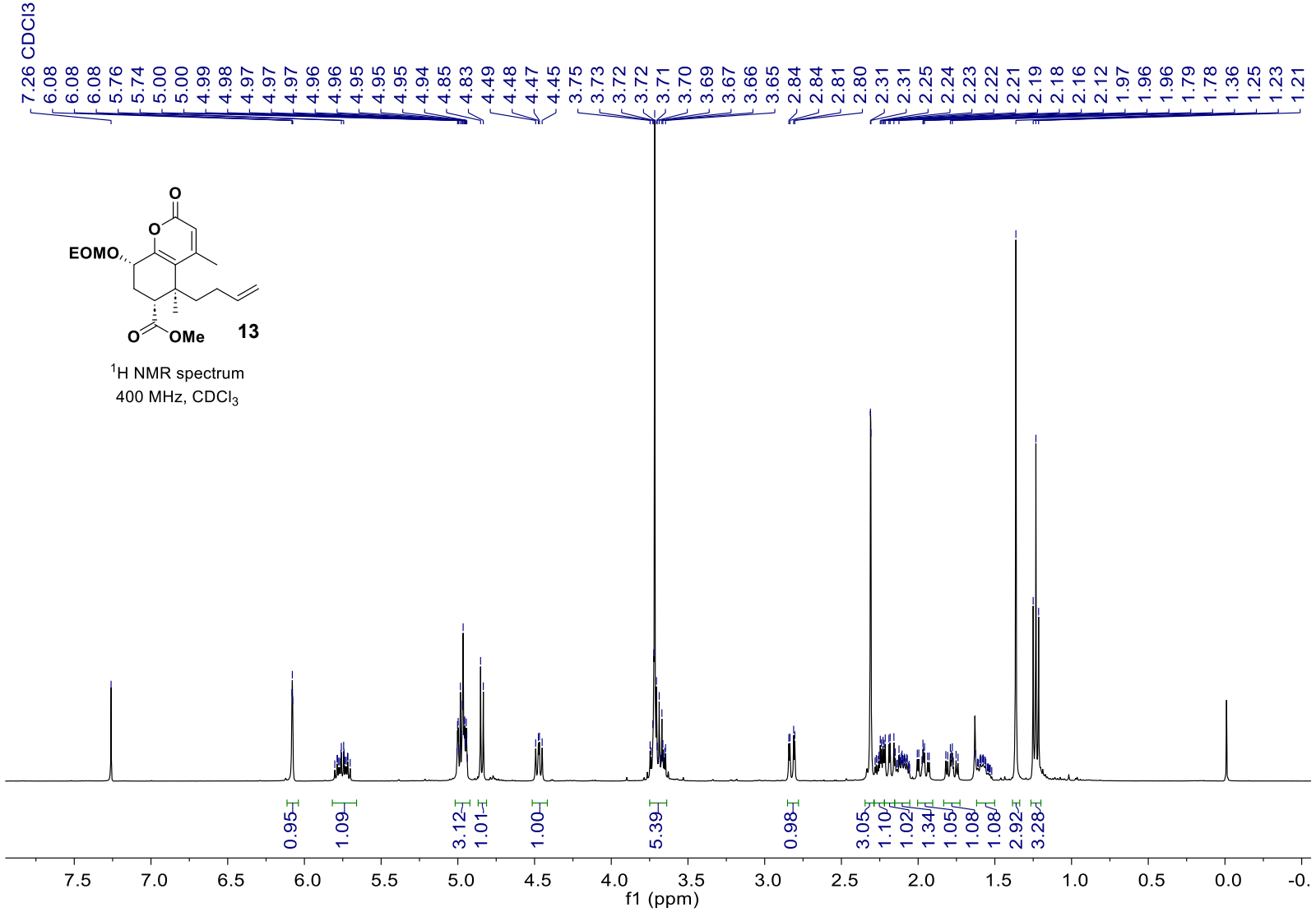
V. NMR Spectra

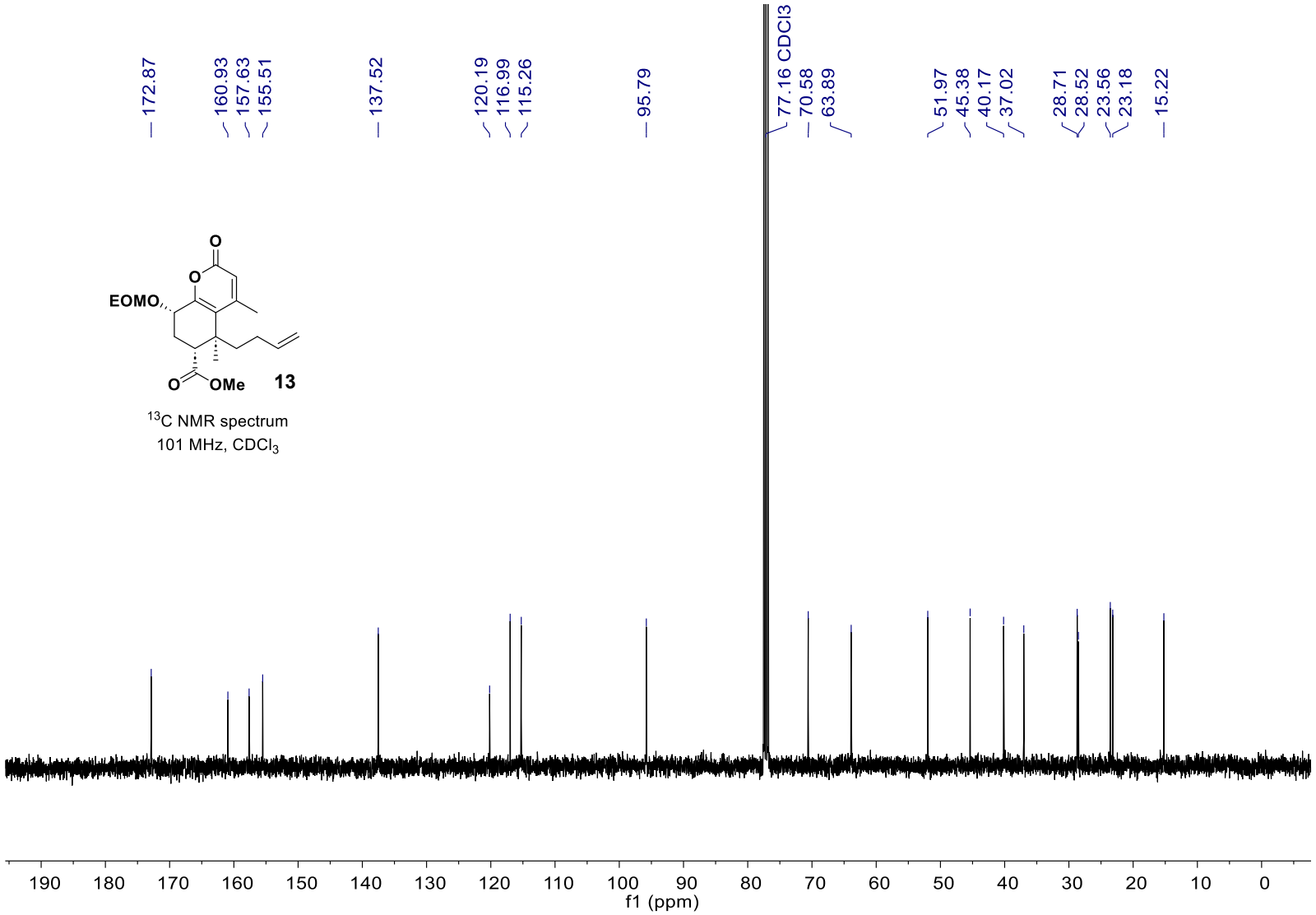



195.81
172.09
156.65
127.74
94.59
77.16 CDCl3
74.30
63.88
52.57
46.84
32.90
22.46
15.21
EOMO
O
O
OMe
13C NMR spectrum
101 MHz, CDCl3
9
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

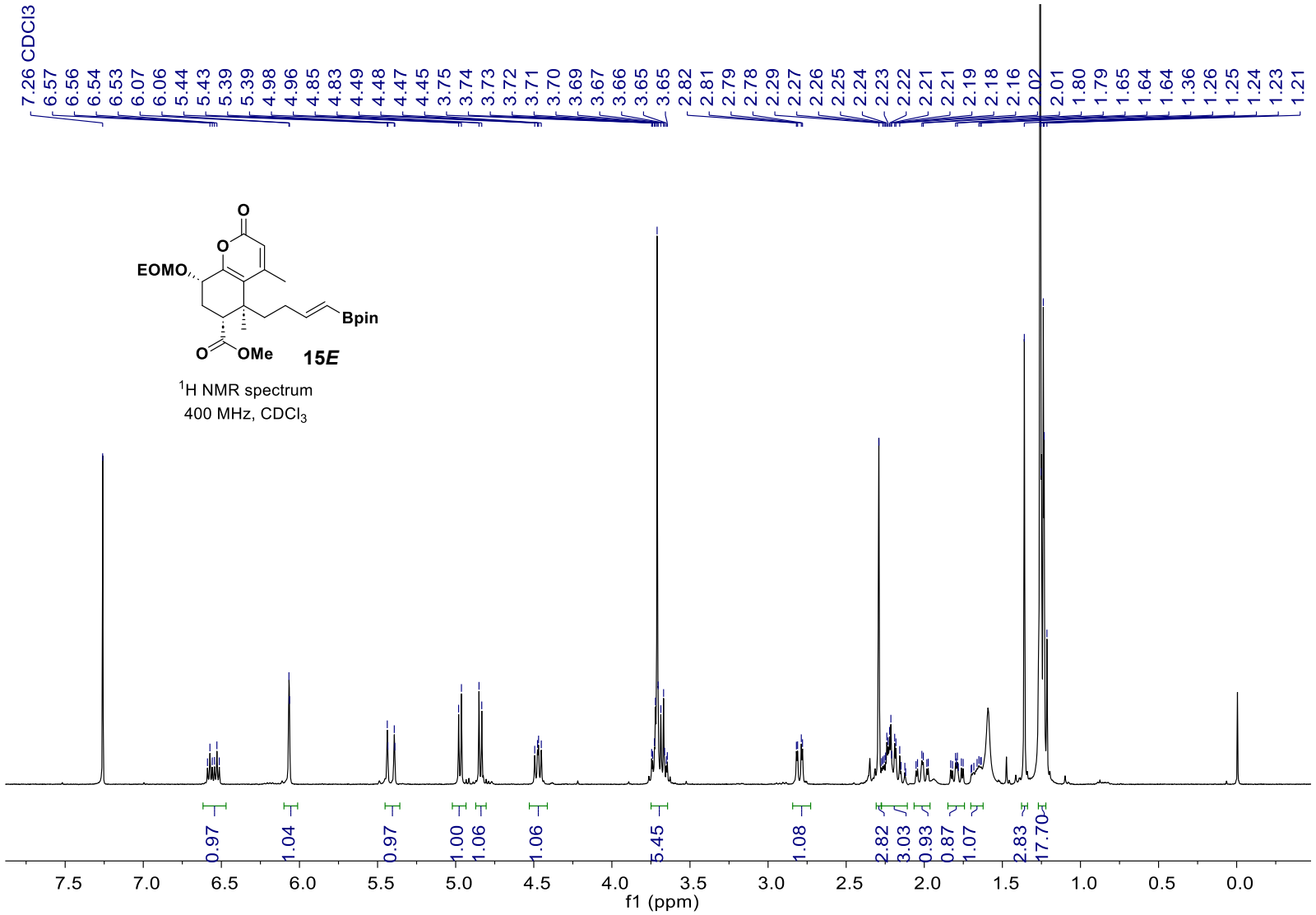

7.26 CDCl3
5.81 5.79 5.77 5.74 5.29 5.25 5.23 5.19 5.04 5.03 5.00 4.99 4.96 4.96 4.94 4.88 4.86 4.84 4.83 4.20 4.18 4.17 4.15 3.73 3.66 3.66 3.64 3.62 3.62 3.61 3.60 3.04 3.03 3.01 3.00 2.36 2.34 2.33 2.32 2.32 2.31 2.30 2.29 2.28 2.26 2.25 1.66 1.65 1.65 1.64 1.63 1.62 1.61 1.57 1.22 1.21 1.19 1.15
EOMO
O
O
OMe
11
1H NMR spectrum
400 MHz, CDCl3
1.00 0.96 1.02 2.08 2.03 1.00 4.34 1.15 0.96 3.00 1.07 1.92 3.24 3.17 2.80
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
f1 (ppm)

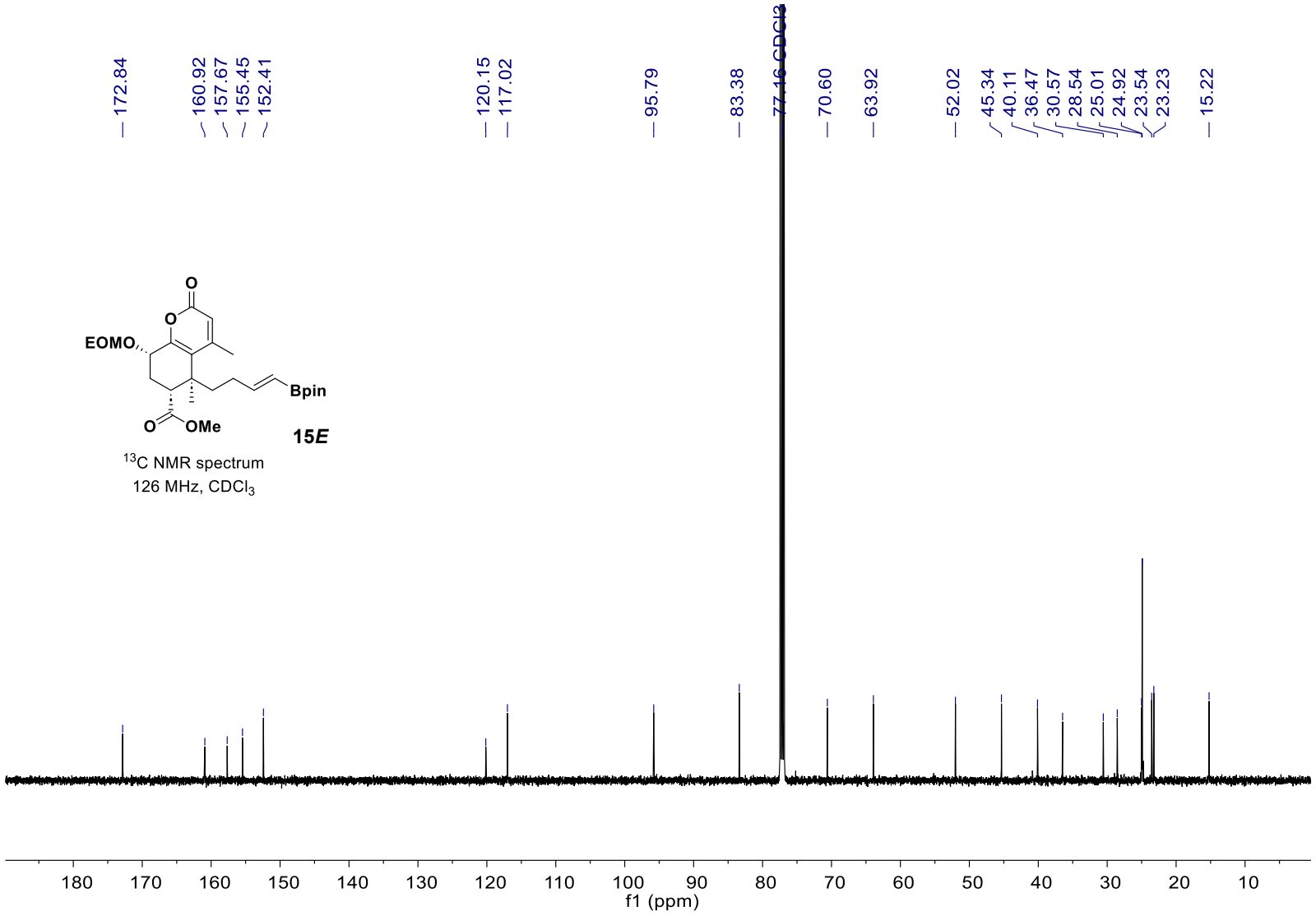

209.78
197.89
172.54
138.22
114.79
112.74
94.79
81.30
77.16 CDCl3
76.83
63.99
52.00
44.86
42.02
38.69
29.68
28.62
25.55
15.25
EOMO
O
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OMe
11
13C NMR spectrum
101 MHz, CDCl3
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f1 (ppm)

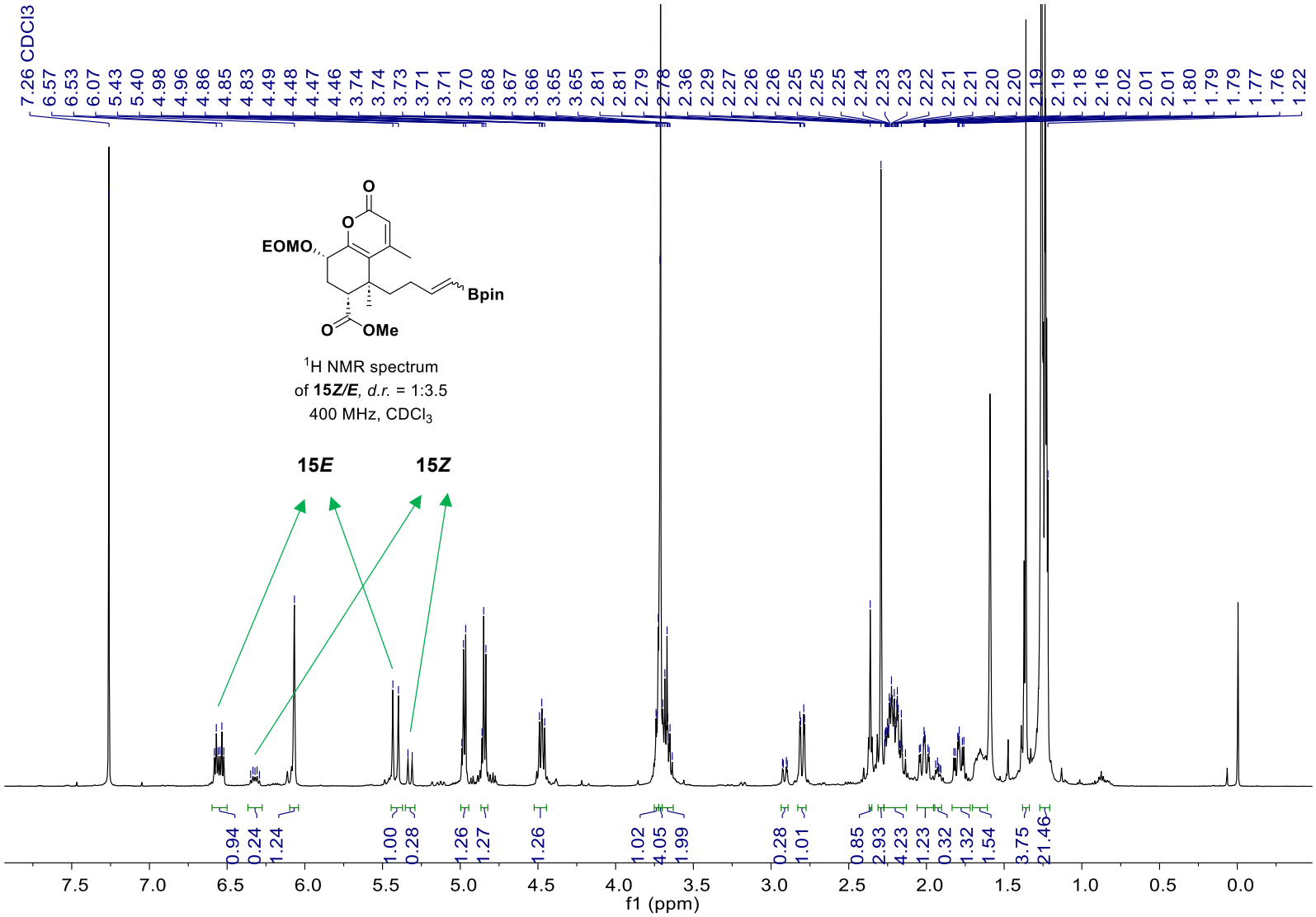

7.26 CDCl3
6.08 6.08 6.08 5.76 5.74 5.00 5.00 4.99 4.98 4.97 4.97 4.97 4.96 4.96 4.95 4.95 4.95 4.94 4.85 4.83 4.49 4.48 4.47 4.45 3.75 3.73 3.72 3.72 3.71 3.70 3.69 3.67 3.66 3.65 2.84 2.84 2.81 2.80 2.31 2.31 2.25 2.24 2.23 2.22 2.21 2.19 2.18 2.16 2.12 1.97 1.96 1.96 1.79 1.78 1.36 1.25 1.23 1.21
EOMO
O
OMe
13
1H NMR spectrum
400 MHz, CDCl3
0.95 1.09 3.12 1.01 1.00 5.39 0.98 3.05 1.10 1.02 1.34 1.05 1.08 1.08 2.92 3.28
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.
f1 (ppm)



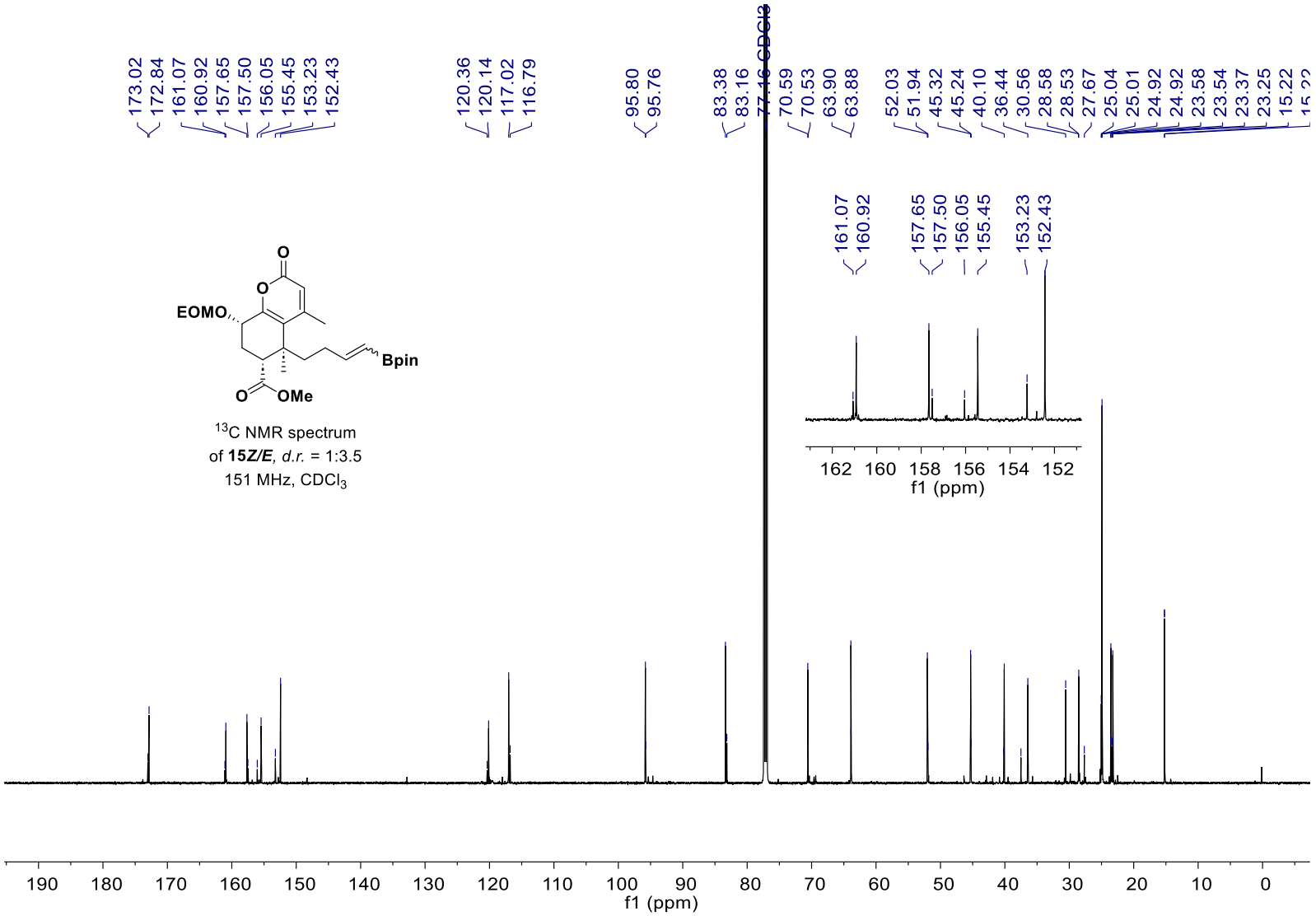
^{13}C NMR spectrum
101 MHz, $CDCl_3$


7.26 CDCl3
6.57 6.56 6.54 6.53 6.07 6.06 5.44 5.43 5.39 5.39 4.98 4.96 4.85 4.83 4.49 4.48 4.47 4.45 3.75 3.74 3.73 3.72 3.71 3.70 3.69 3.67 3.66 3.65 3.65
2.82 2.81 2.79 2.78 2.29 2.27 2.26 2.25 2.24 2.23 2.22 2.21 2.21 2.19 2.18 2.16 2.02 2.01 1.80 1.79 1.65 1.64 1.64 1.36 1.26 1.25 1.24 1.23 1.21
EOMO
Bpin
O
OMe
15E
1H NMR spectrum
400 MHz, CDCl3
0.97 1.04 0.97 1.00 1.06 1.06 5.45 1.08 2.82 3.03 0.93 0.87 1.07 2.83 17.70
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
f1 (ppm)

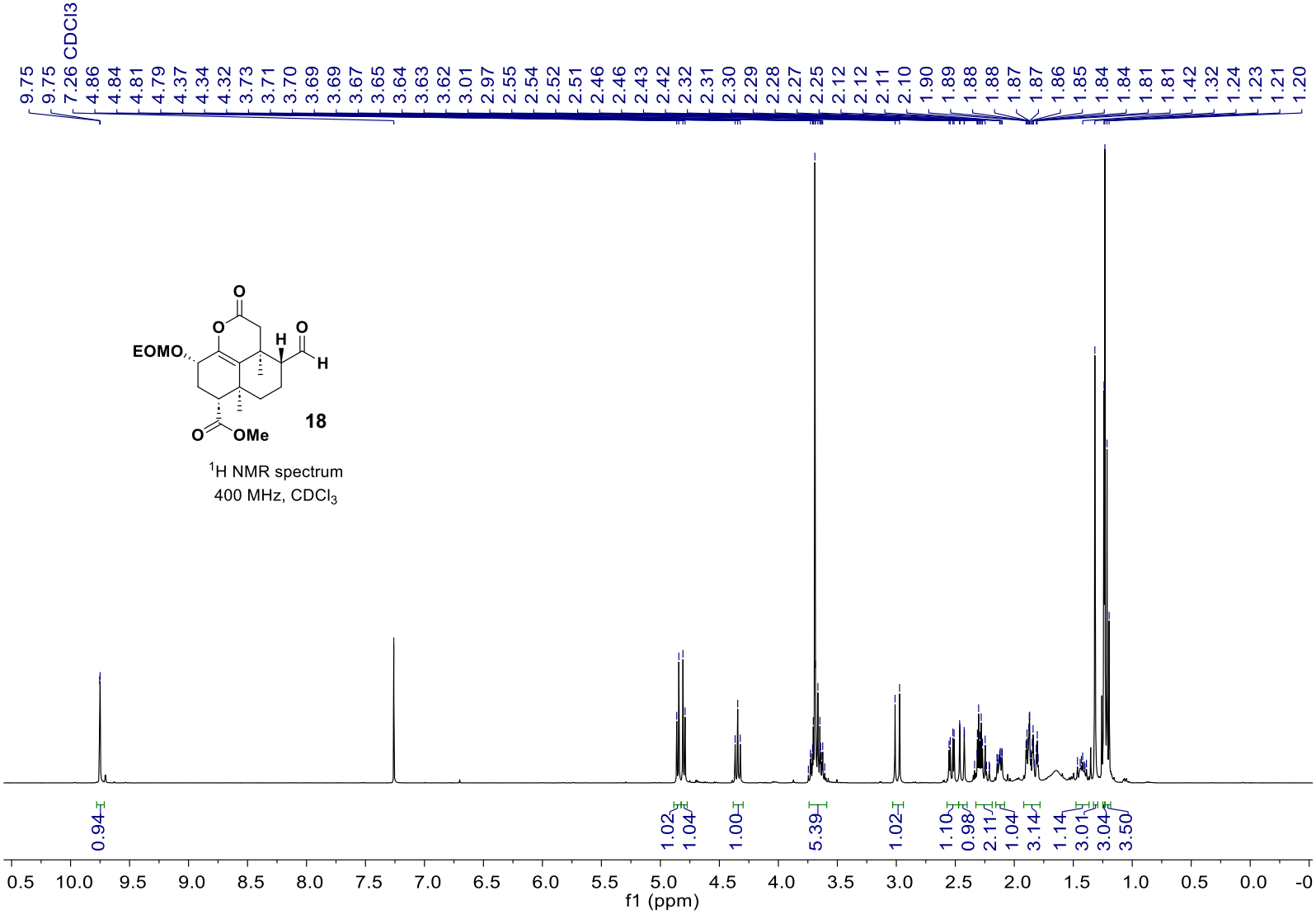

172.84
160.92
157.67
155.45
152.41
120.15
117.02
95.79
83.38
77.16 CDCl3
70.60
63.92
52.02
45.34
40.11
36.47
30.57
28.54
25.01
24.92
23.54
23.23
15.22
EOMO
Bpin
OMe
15E
13C NMR spectrum
126 MHz, CDCl3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)



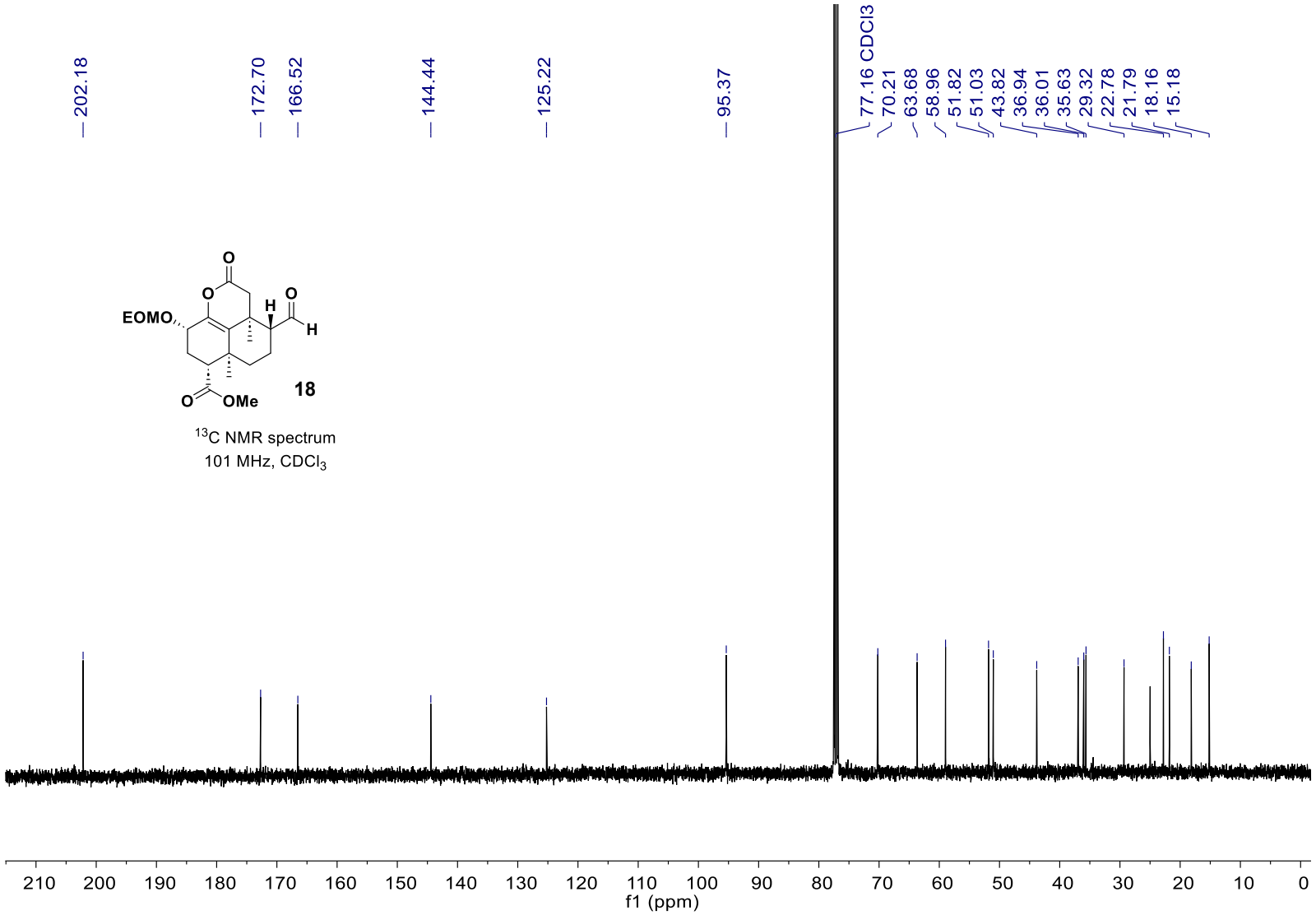
^{1}H NMR spectrum
of **15*Z*/*E***, *d.r.* = 1:3.5
400 MHz, $CDCl_3$



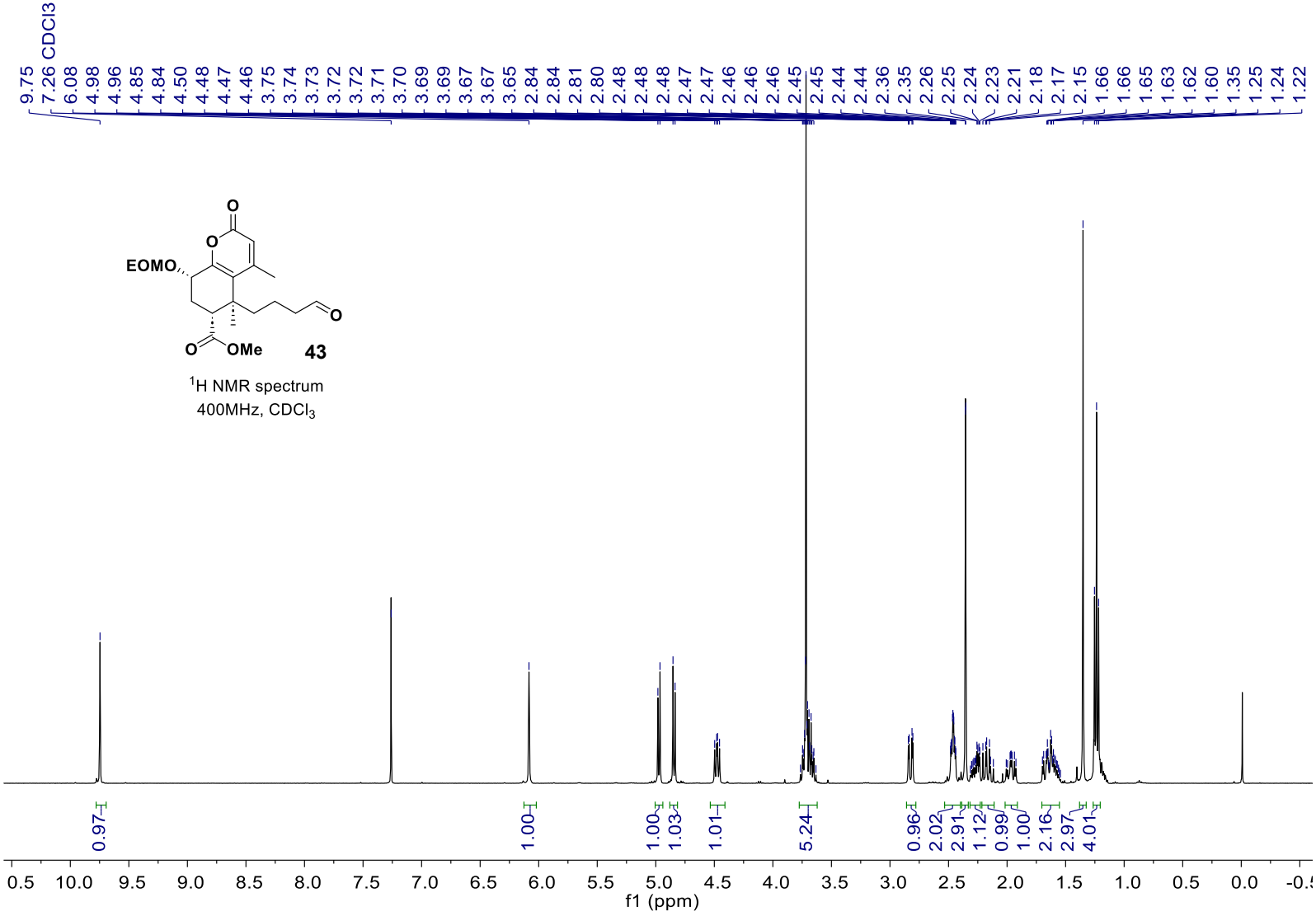
^{13}C NMR spectrum
of **15*Z*/*E***, *d.r.* = 1:3.5
151 MHz, $CDCl_3$

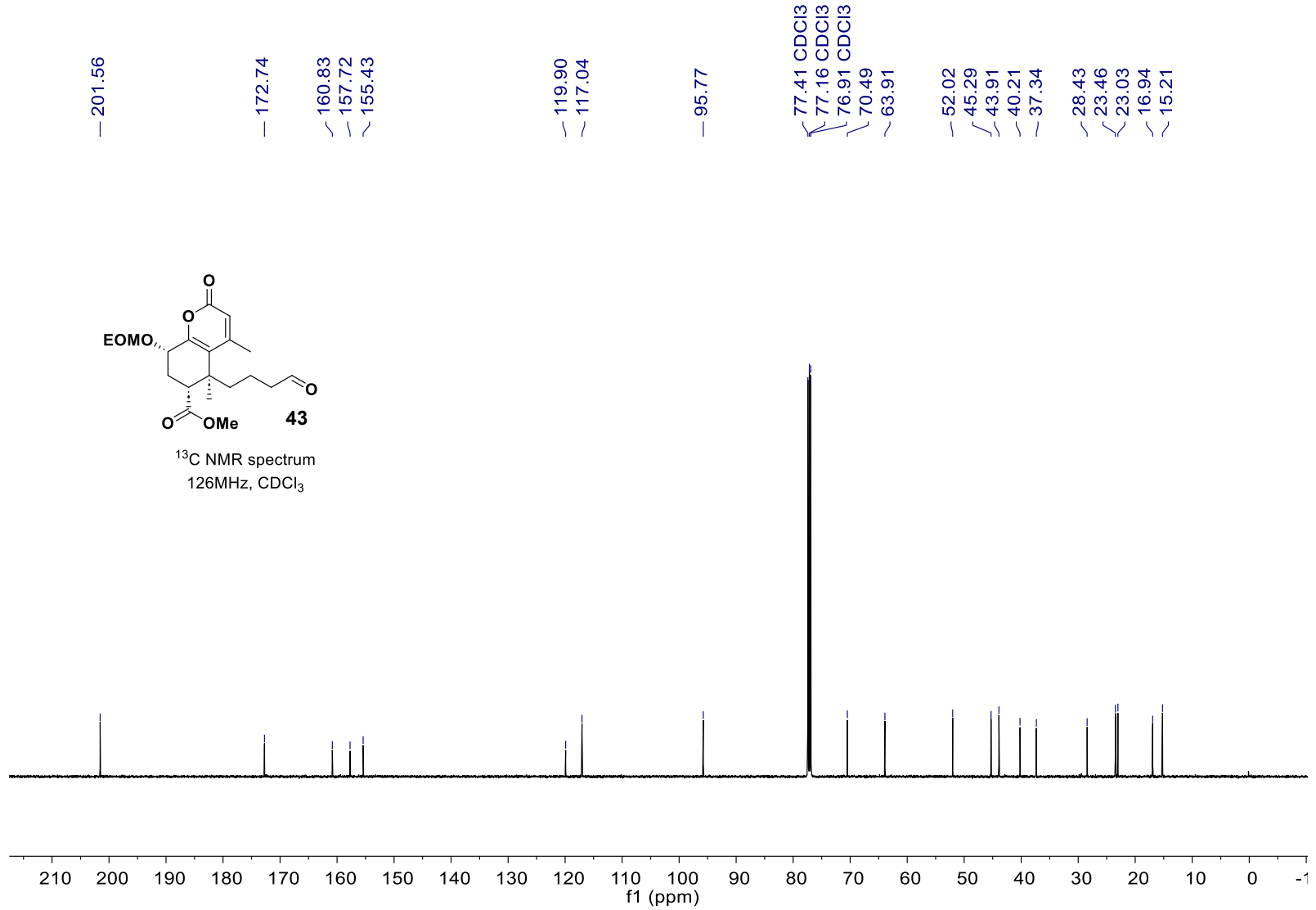


^{1}H NMR spectrum
400 MHz, $CDCl_3$

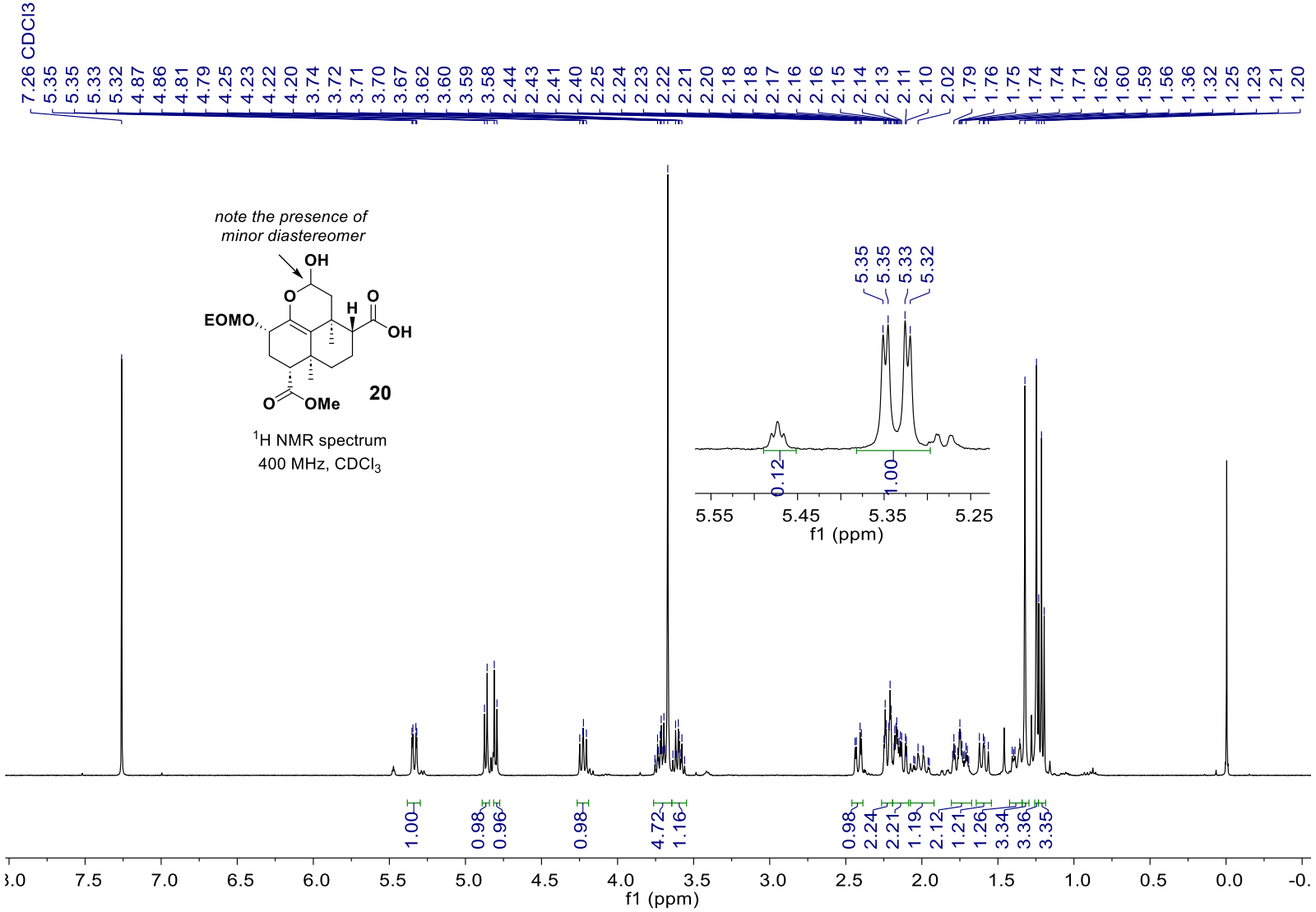


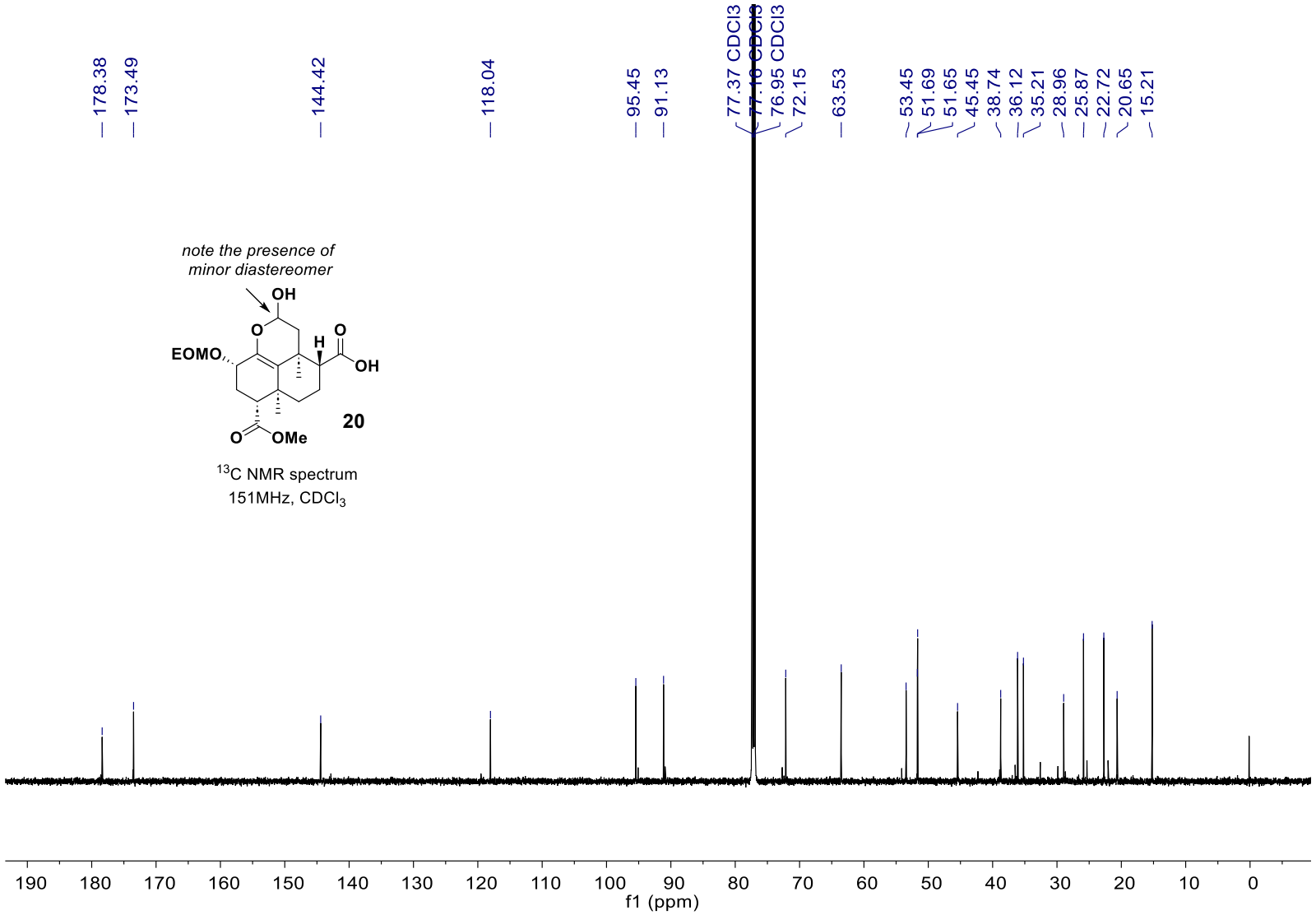
^{13}C NMR spectrum
101 MHz, $CDCl_3$

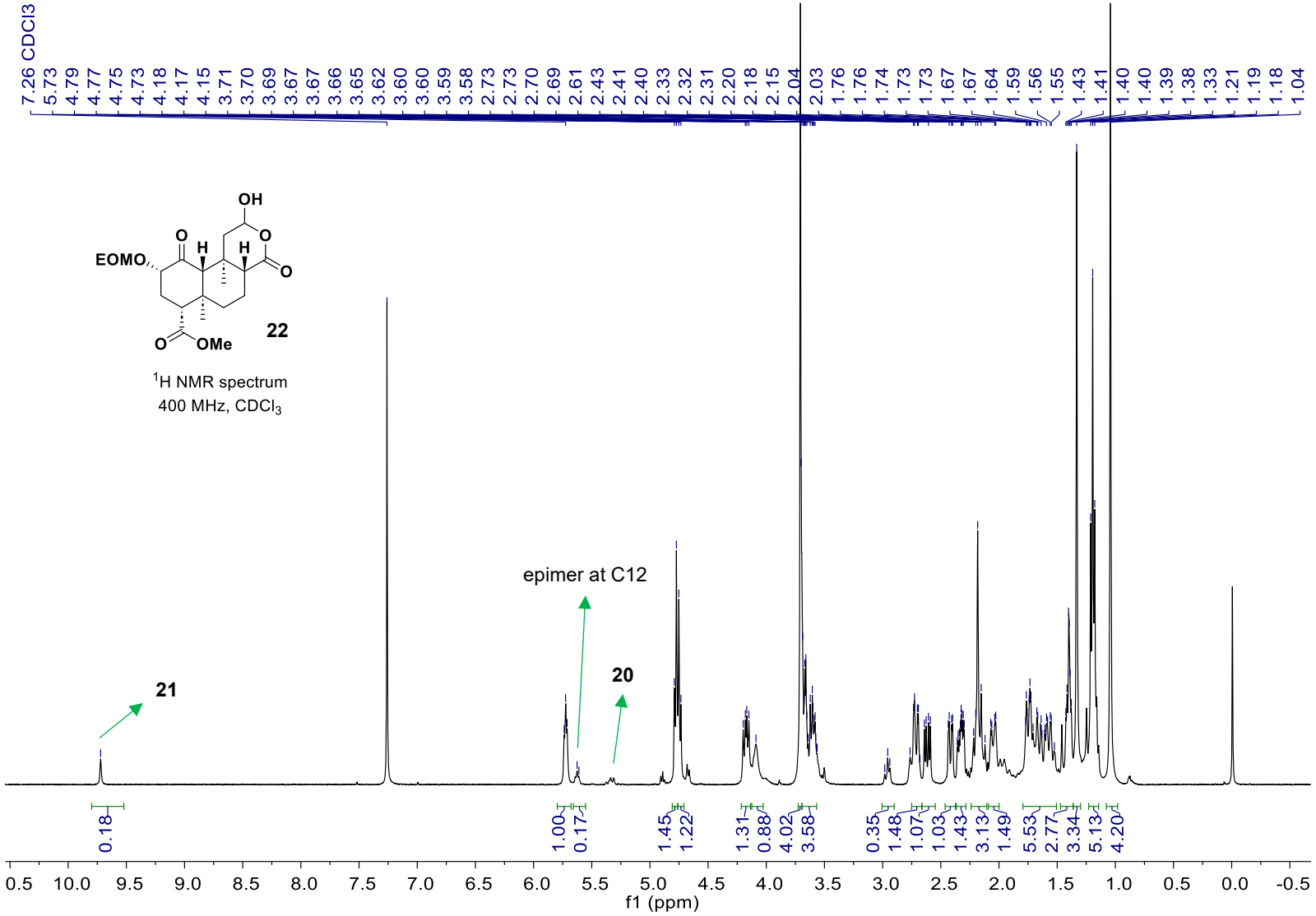

9.75 7.26 CDCl3 6.08 4.98 4.96 4.85 4.84 4.50 4.48 4.47 4.46 3.75 3.74 3.73 3.72 3.72 3.71 3.70 3.69 3.69 3.67 3.67 3.65 2.84 2.84 2.81 2.80 2.48 2.48 2.48 2.47 2.47 2.46 2.46 2.46 2.45 2.45 2.44 2.44 2.36 2.35 2.26 2.25 2.24 2.23 2.21 2.18 2.17 2.15 1.66 1.66 1.65 1.63 1.62 1.60 1.35 1.25 1.24 1.22
EOMO
O
OMe
43
1H NMR spectrum
400MHz, CDCl3
0.97 1.00 1.00 1.03 1.01 5.24 0.96 2.02 2.91 1.12 0.99 1.00 2.16 2.97 4.01
0.5 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
f1 (ppm)

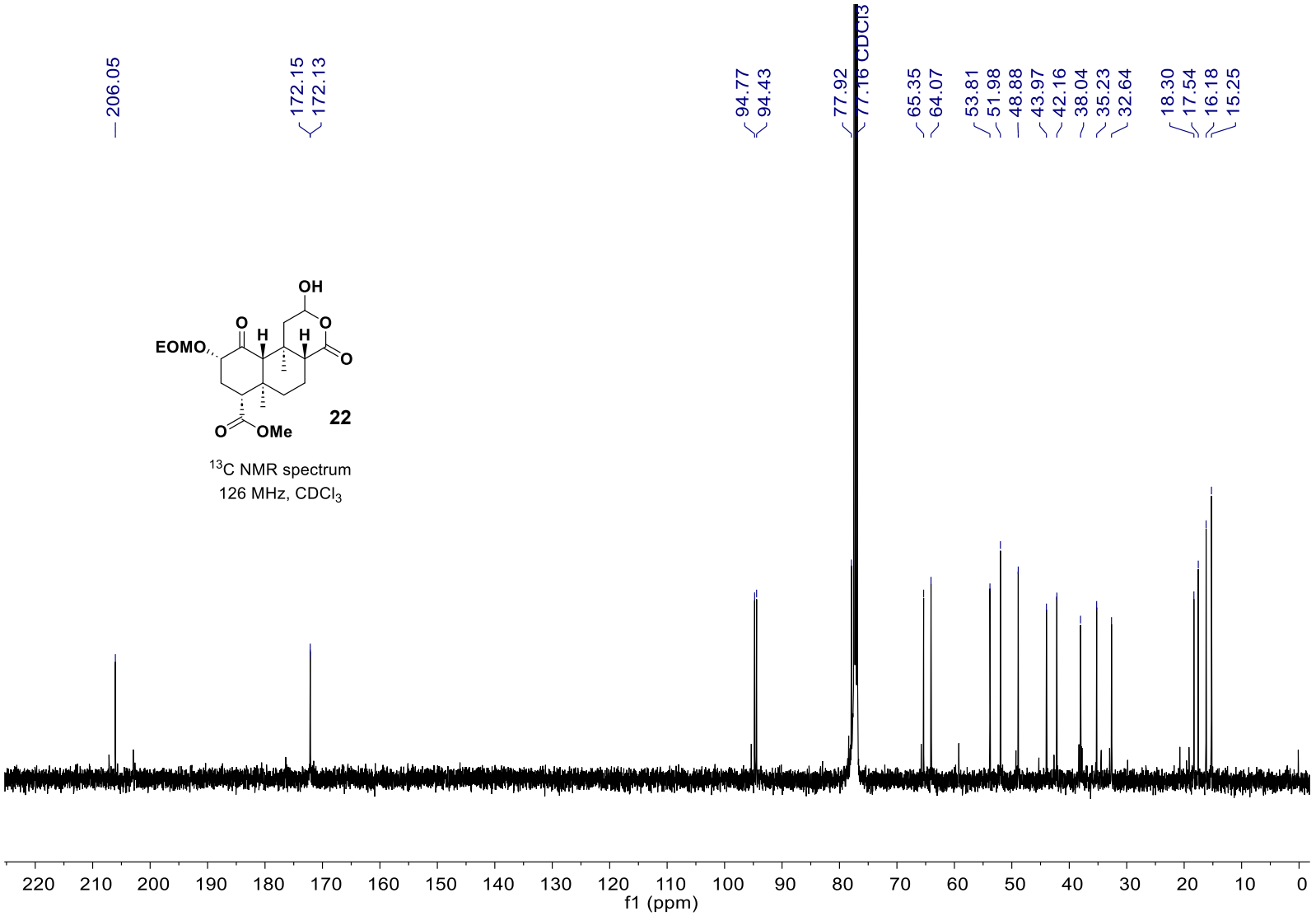


^{13}C NMR spectrum
126MHz, $CDCl_3$

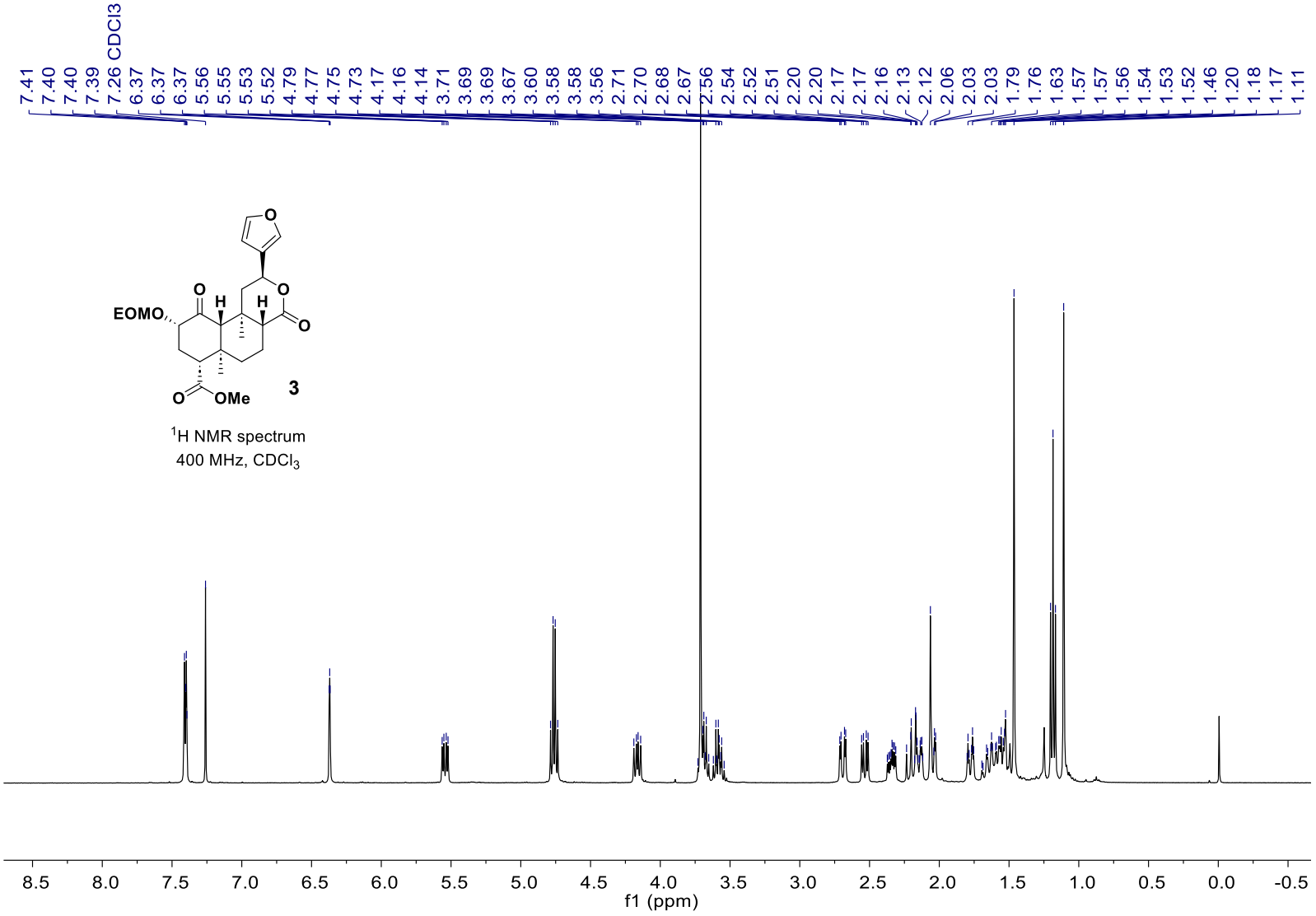

7.26 CDCl3
5.35 5.35 5.33 5.32 4.87 4.86 4.81 4.79 4.25 4.23 4.22 4.20 3.74 3.72 3.71 3.70 3.67 3.62 3.60 3.59 3.58 2.44 2.43 2.41 2.40 2.25 2.24 2.23 2.22 2.21 2.20 2.18 2.18 2.17 2.16 2.16 2.15 2.14 2.13 2.11 2.10 2.02 1.79 1.76 1.75 1.74 1.74 1.71 1.62 1.60 1.59 1.56 1.36 1.32 1.25 1.23 1.21 1.20
note the presence of
minor diastereomer
OH
O
H
O
OH
EOMO
O
OMe
20
1H NMR spectrum
400 MHz, CDCl3
5.35 5.35 5.33 5.32
0.12
1.00
5.55 5.45 5.35 5.25
f1 (ppm)
1.00 0.98 0.96 0.98 4.72 1.16 0.98 2.24 2.21 1.19 2.12 1.21 1.26 3.34 3.36 3.35
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
f1 (ppm)

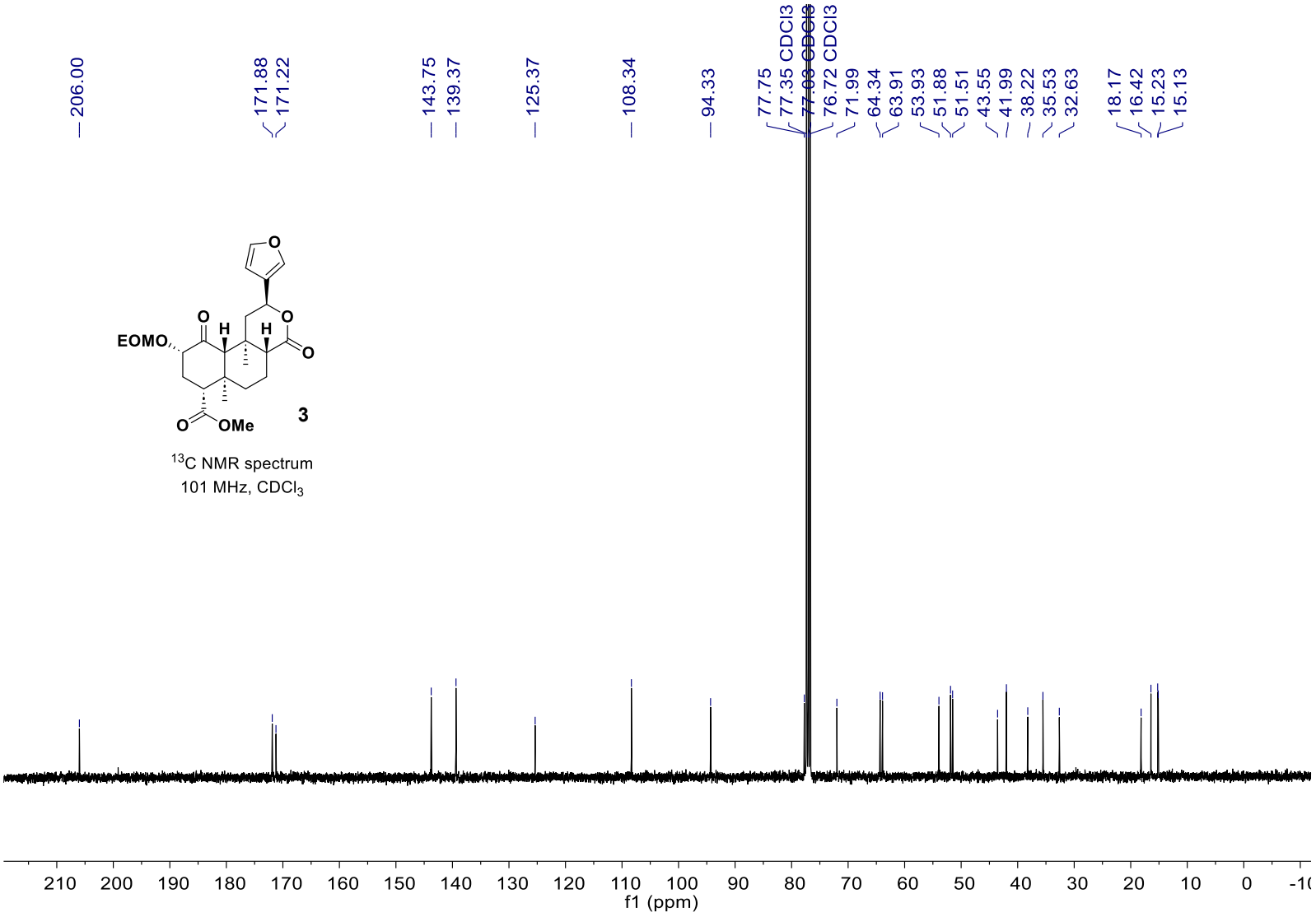

178.38
173.49
144.42
118.04
95.45
91.13
77.37 CDCl3
77.16 CDCl3
76.95 CDCl3
72.15
63.53
53.45
51.69
51.65
45.45
38.74
36.12
35.21
28.96
25.87
22.72
20.65
15.21
note the presence of
minor diastereomer
OH
O
H
O
EOMO
OH
O
OMe
20
13C NMR spectrum
151MHz, CDCl3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.26 CDCl3
5.73 4.79 4.77 4.75 4.73 4.18 4.17 4.15 3.71 3.70 3.69 3.67 3.67 3.66 3.65 3.62 3.60 3.60 3.59 3.58 2.73 2.73 2.70 2.69 2.61 2.43 2.41 2.40 2.33 2.32 2.31 2.20 2.18 2.15 2.04 2.03 1.76 1.76 1.74 1.73 1.73 1.67 1.67 1.64 1.59 1.56 1.55 1.43 1.41 1.40 1.40 1.39 1.38 1.33 1.21 1.19 1.18 1.04
OH
O
H
H
O
EOMO
O
O
OMe
22
1H NMR spectrum
400 MHz, CDCl3
epimer at C12
21
20
0.18
1.00
0.17
1.45
1.22
1.31
0.88
4.02
3.58
0.35
1.48
1.07
1.03
1.43
3.13
1.49
5.53
2.77
3.34
5.13
4.20
0.5 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)

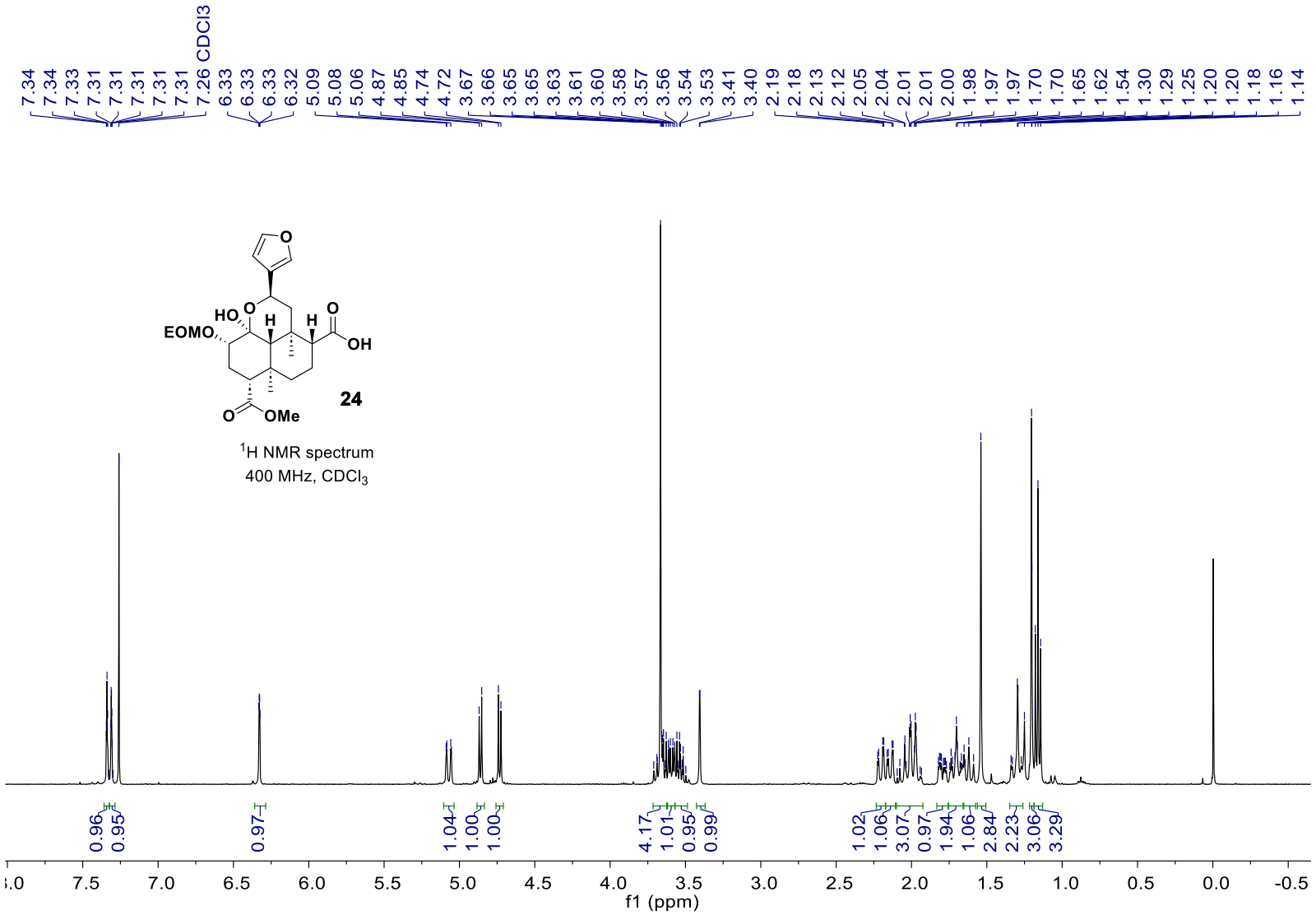


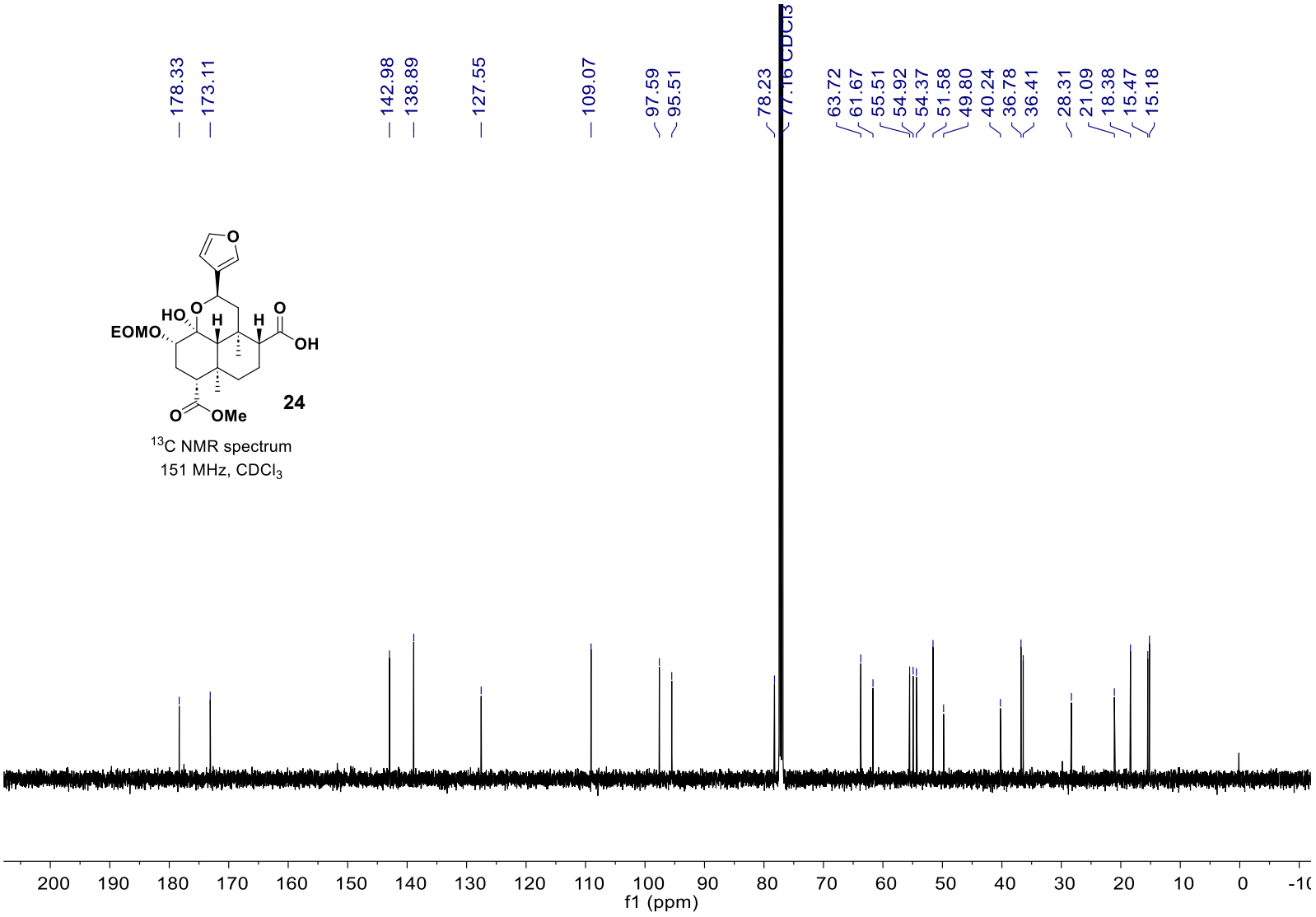
^{13}C NMR spectrum
126 MHz, $CDCl_3$


7.41
7.40
7.40
7.39
7.26 CDCl3
6.37
6.37
6.37
5.56
5.55
5.53
5.52
4.79
4.77
4.75
4.73
4.17
4.16
4.14
3.71
3.69
3.69
3.67
3.60
3.58
3.58
3.56
2.71
2.70
2.68
2.67
2.56
2.54
2.52
2.51
2.20
2.20
2.17
2.17
2.16
2.13
2.12
2.06
2.03
2.03
1.79
1.76
1.63
1.57
1.57
1.56
1.54
1.53
1.52
1.46
1.20
1.18
1.17
1.11
EOMO
O
H
H
O
O
O
O
OMe
3
1H NMR spectrum
400 MHz, CDCl3
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)

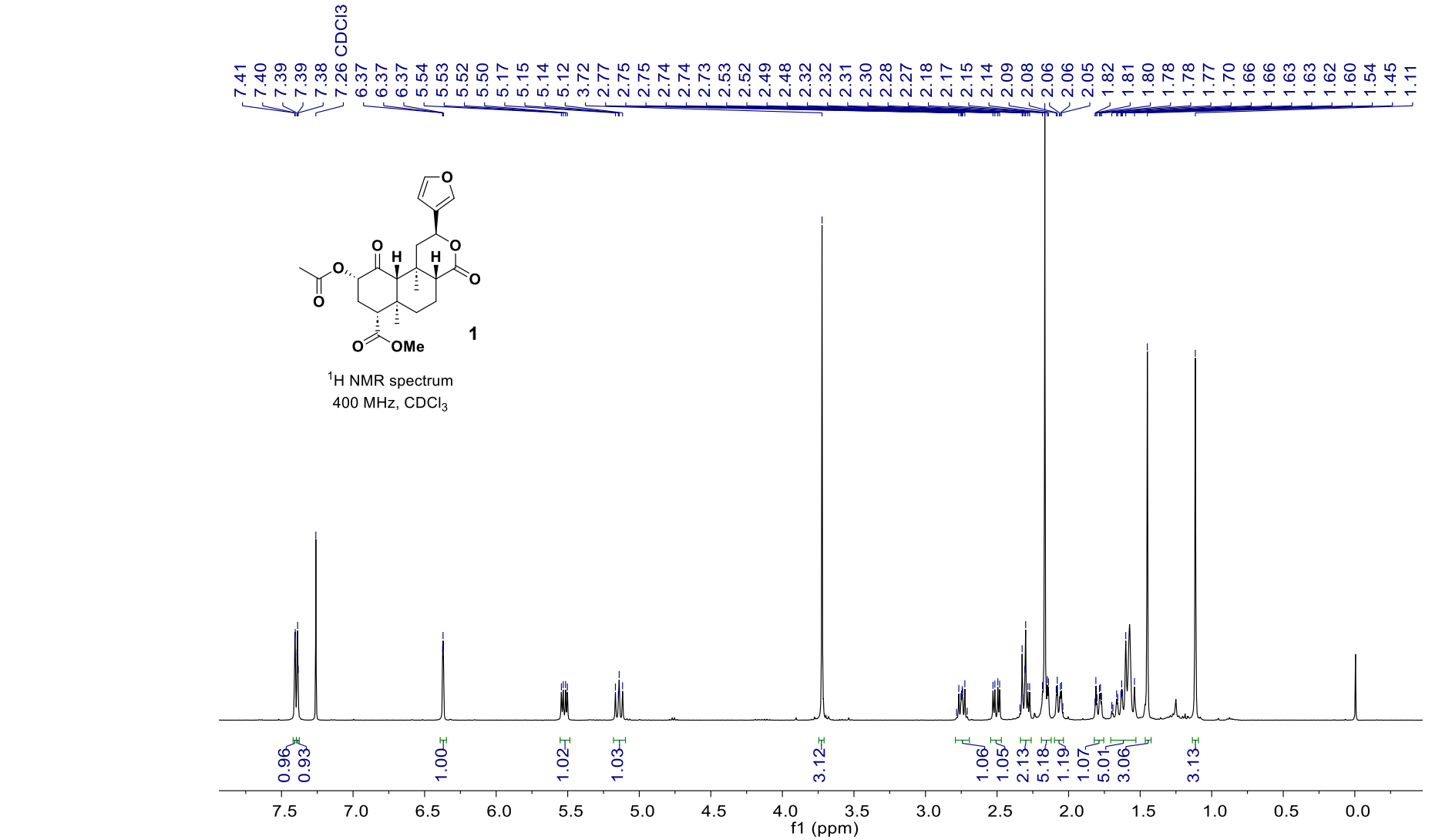


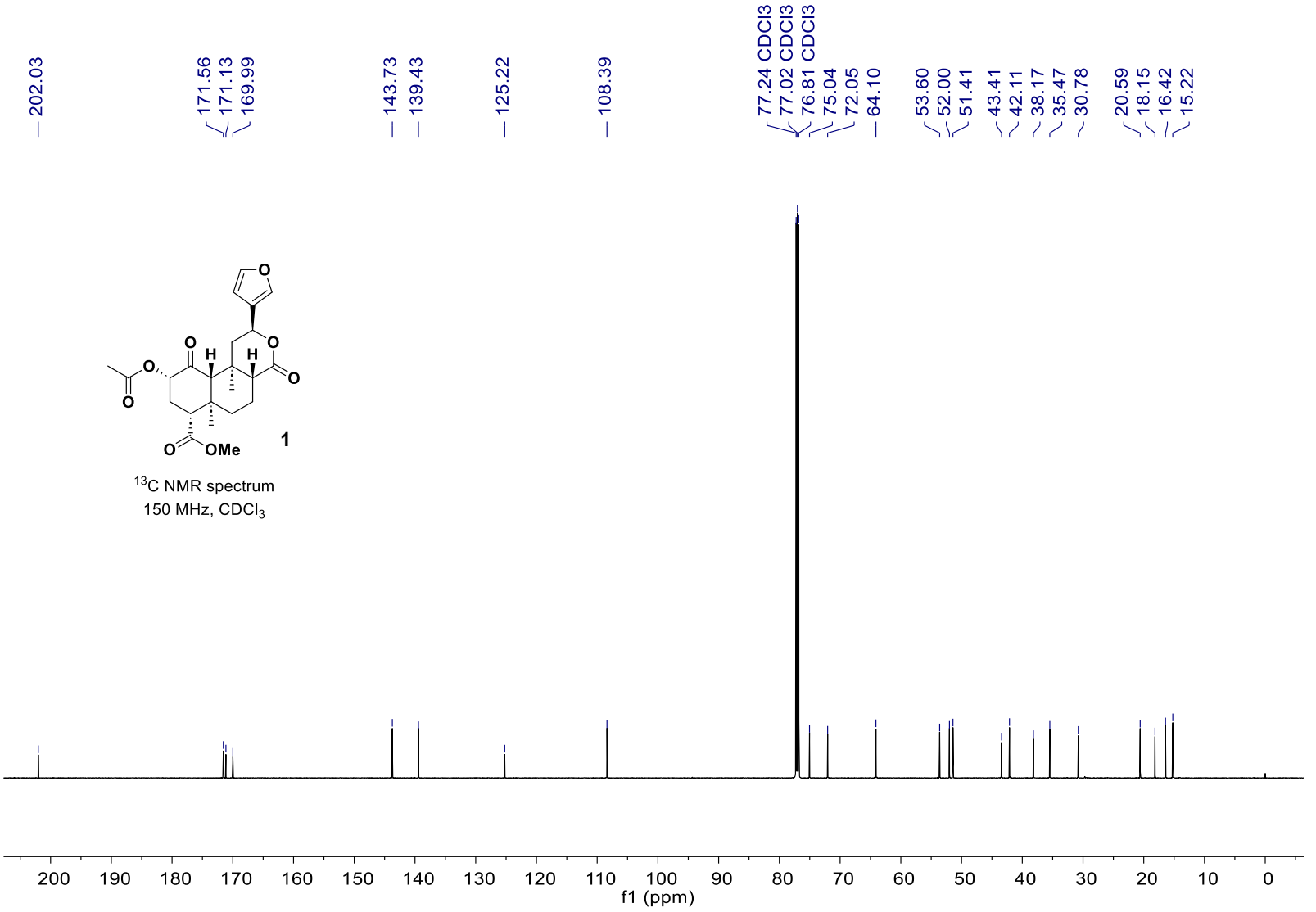
^{13}C NMR spectrum
101 MHz, $CDCl_3$


7.34 7.34 7.33 7.31 7.31 7.31 7.31 7.31 7.26 CDCl3 6.33 6.33 6.33 6.32 5.09 5.08 5.06 4.87 4.85 4.74 4.72 3.67 3.66 3.65 3.65 3.63 3.61 3.60 3.58 3.57 3.56 3.54 3.53 3.41 3.40 2.19 2.18 2.13 2.12 2.05 2.04 2.01 2.01 2.00 1.98 1.97 1.97 1.70 1.70 1.65 1.62 1.54 1.30 1.29 1.25 1.20 1.20 1.18 1.16 1.14
HO
EOMO
H
H
O
OH
O
OMe
24
1H NMR spectrum
400 MHz, CDCl3
0.96 0.95 0.97 1.04 1.00 1.00 4.17 1.01 0.95 0.99 1.02 1.06 3.07 0.97 1.94 1.06 2.84 2.23 3.06 3.29
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)

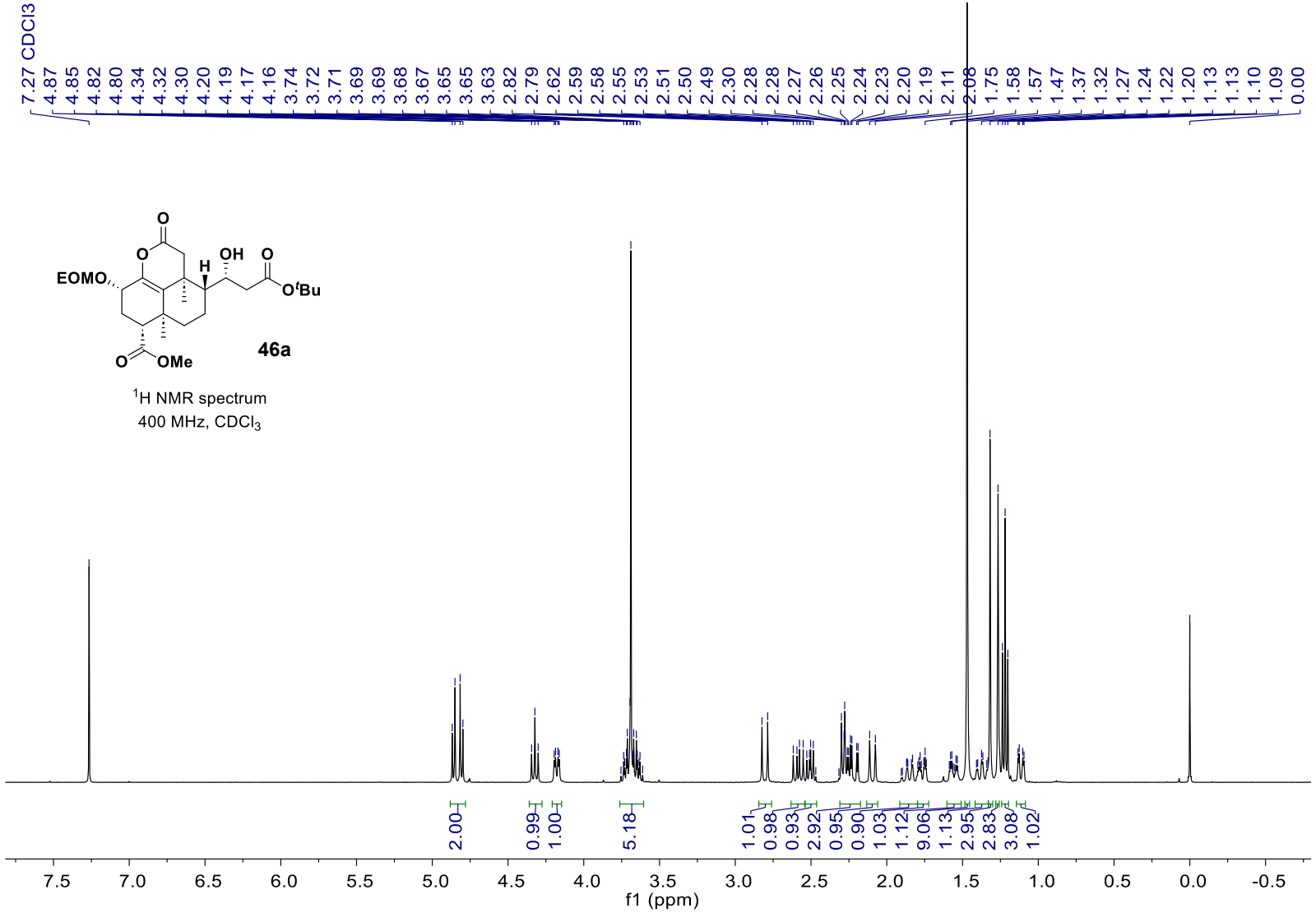


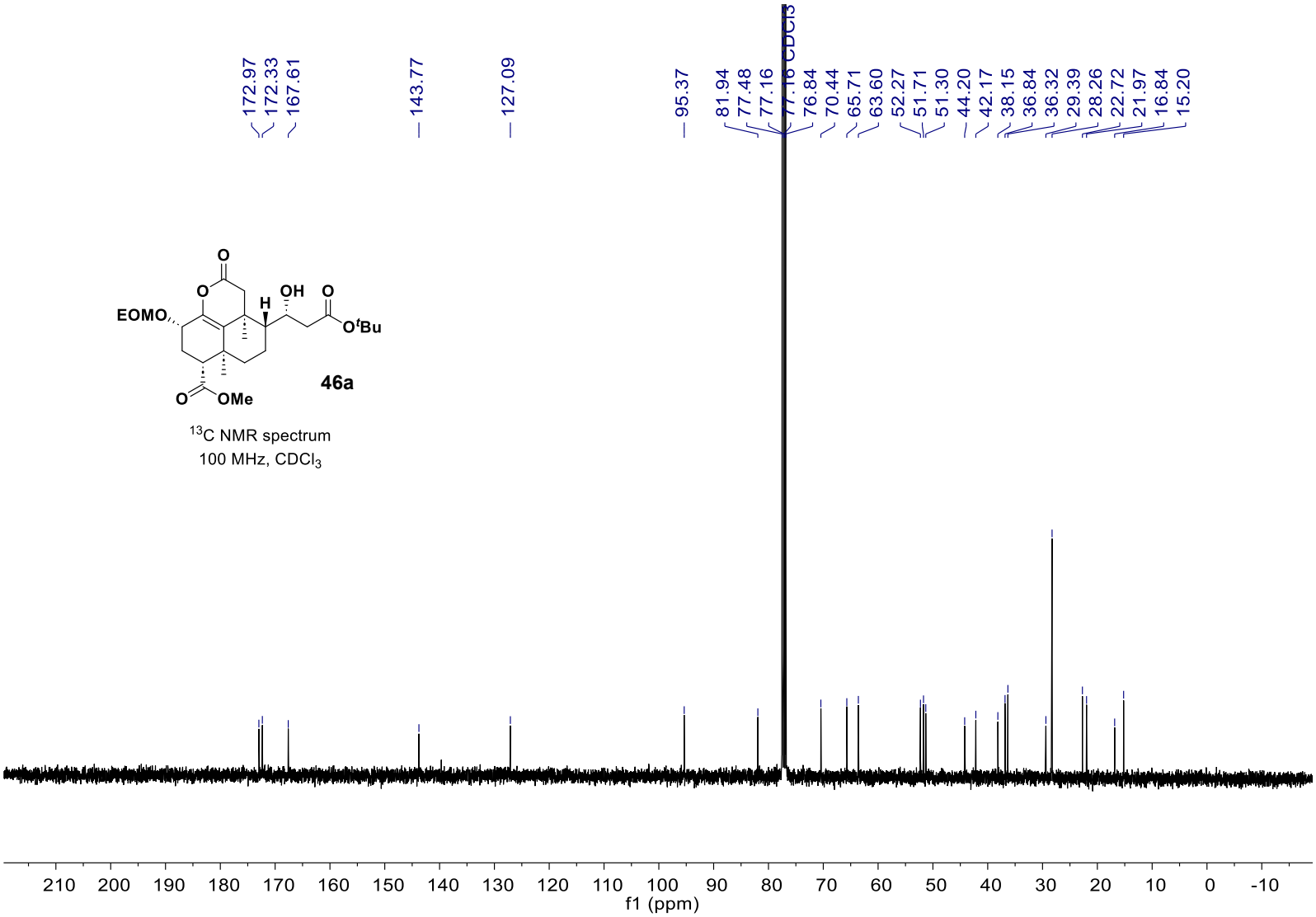
^{13}C NMR spectrum
151 MHz, $CDCl_3$

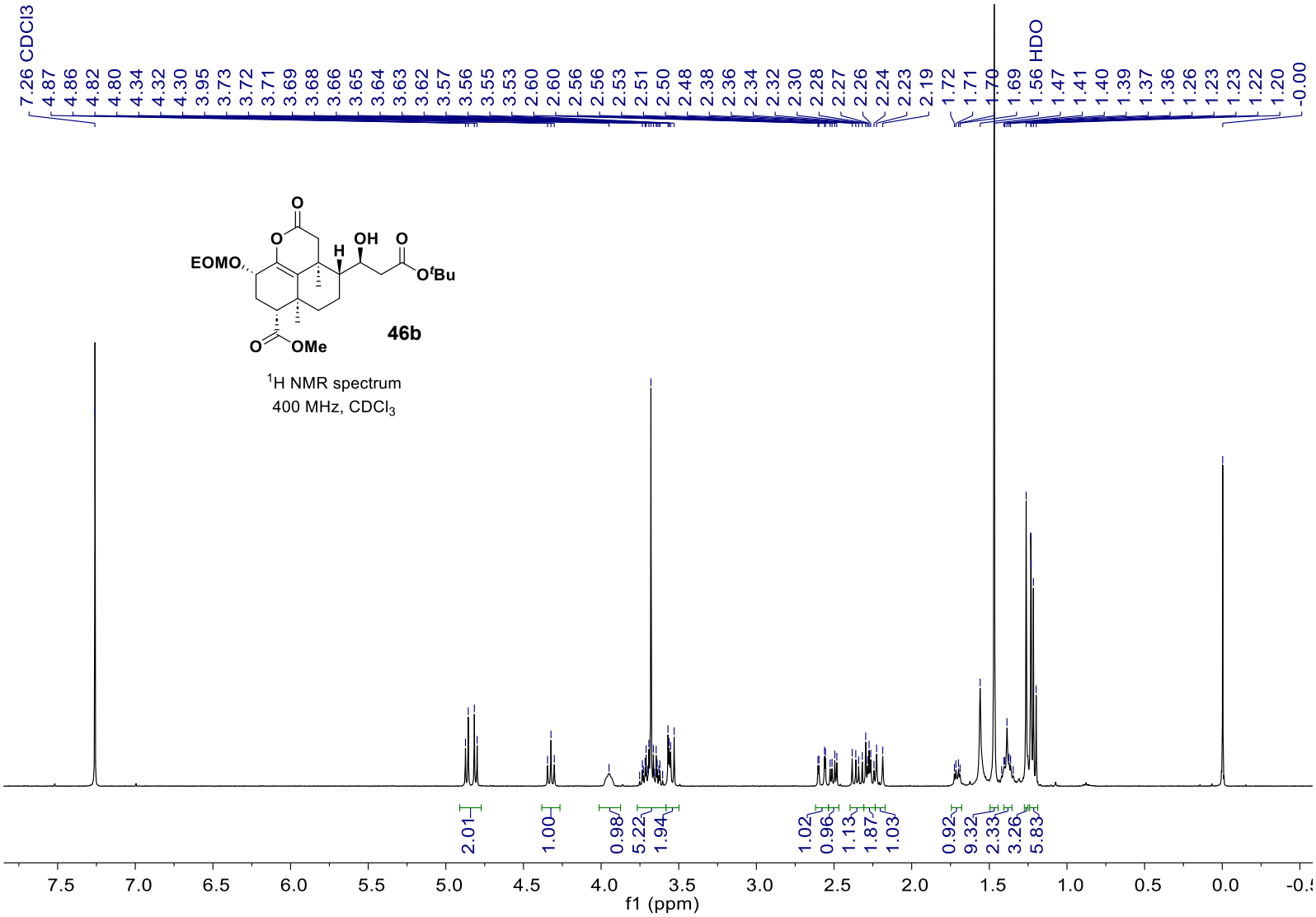

7.41 7.40 7.39 7.39 7.38 7.26 CDCl3 6.37 6.37 6.37 5.54 5.53 5.52 5.50 5.17 5.15 5.14 5.12 3.72 2.77 2.75 2.75 2.74 2.74 2.73 2.53 2.52 2.49 2.48 2.32 2.32 2.31 2.30 2.28 2.27 2.18 2.17 2.15 2.14 2.09 2.08 2.06 2.06 2.05 1.82 1.81 1.80 1.78 1.78 1.77 1.70 1.66 1.66 1.63 1.63 1.62 1.60 1.54 1.45 1.11
O
O
H
H
O
O
O
O
O
O
OMe
1
1H NMR spectrum
400 MHz, CDCl3
0.96 0.93 1.00 1.02 1.03 3.12 1.06 1.05 2.13 5.18 1.19 1.07 5.01 3.06 3.13
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
f1 (ppm)

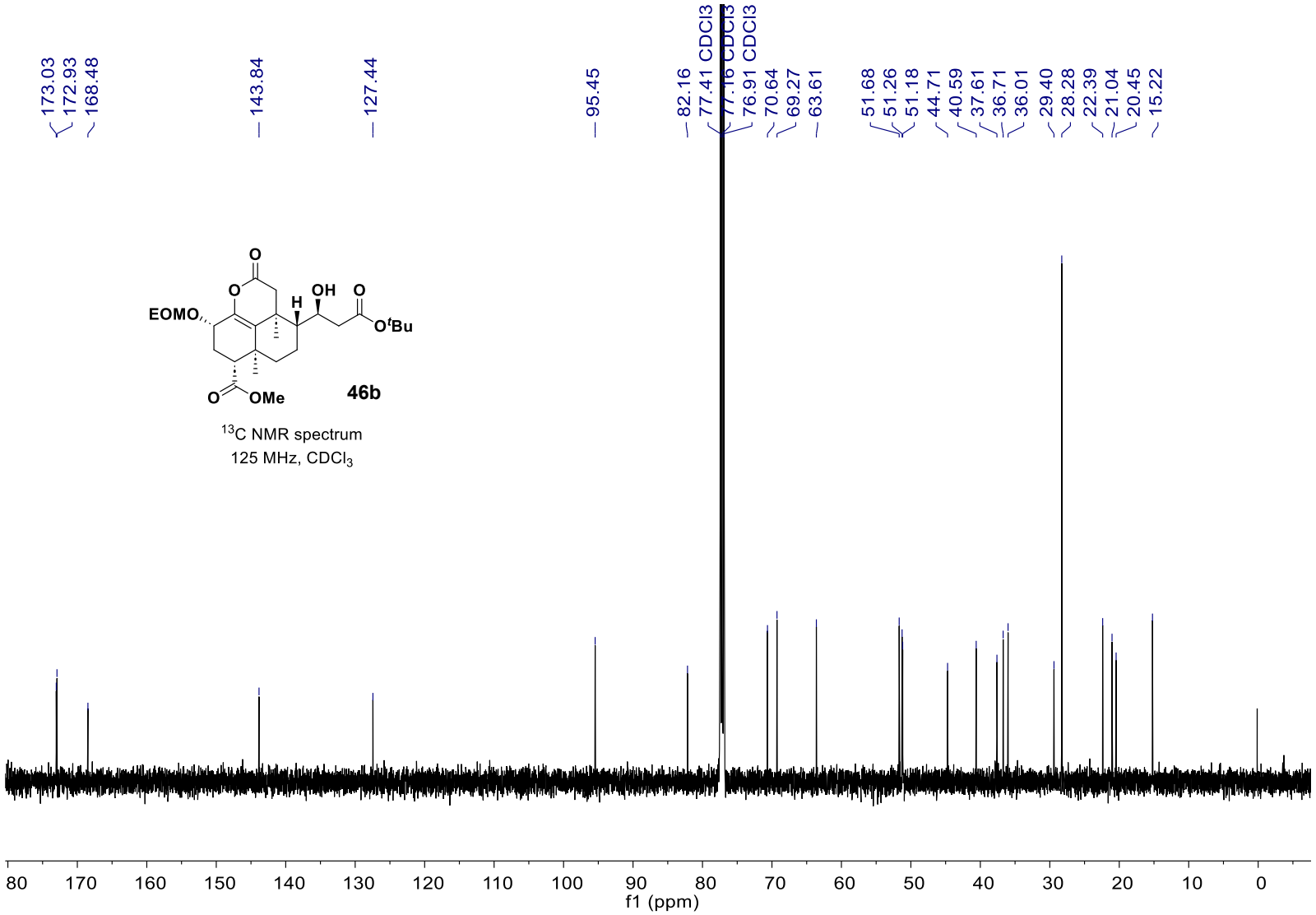


^{13}C NMR spectrum
150 MHz, $CDCl_3$

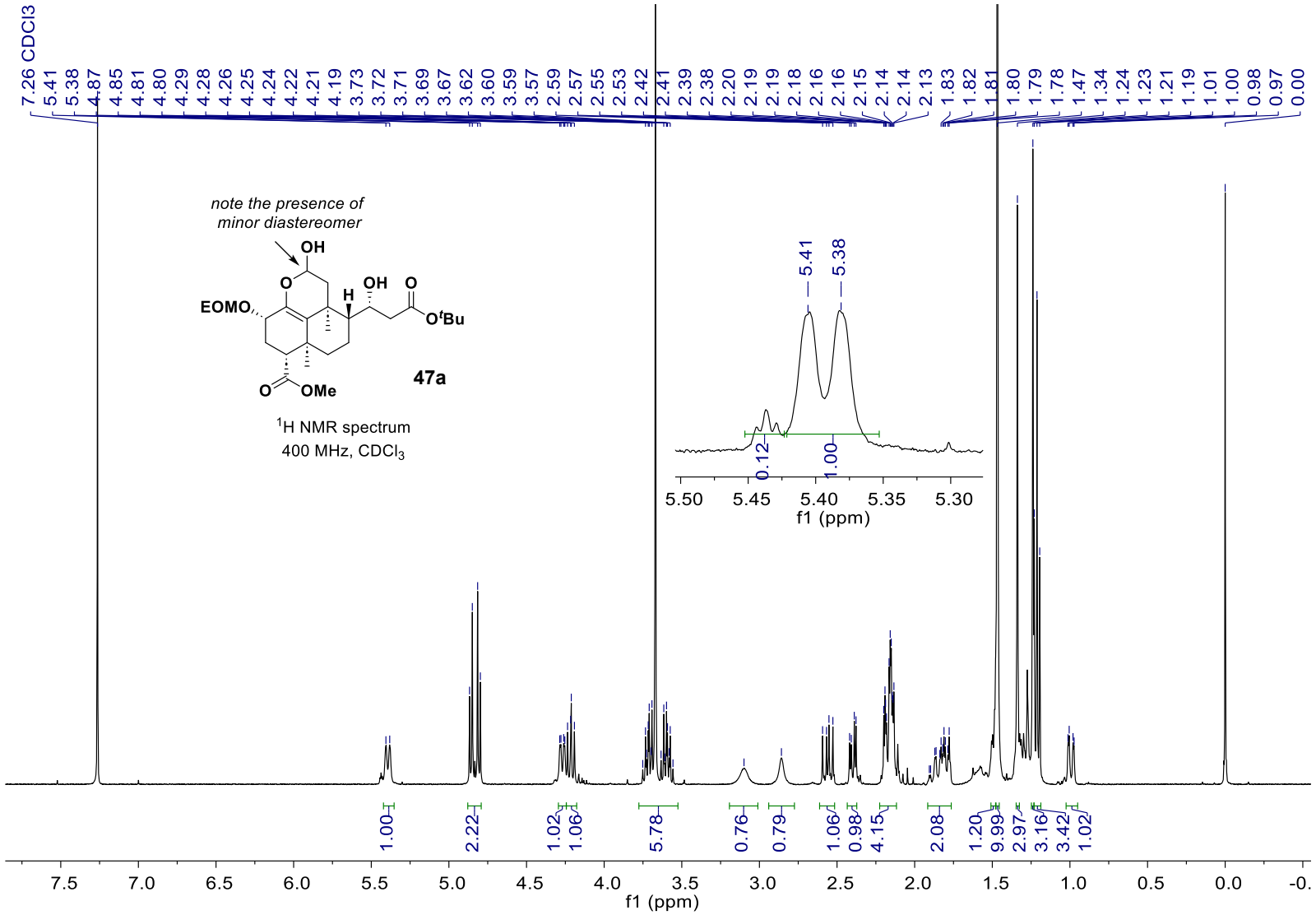

7.27 CDCl3
4.87
4.85
4.82
4.80
4.34
4.32
4.30
4.20
4.19
4.17
4.16
3.74
3.72
3.71
3.69
3.69
3.68
3.67
3.65
3.65
3.63
2.82
2.79
2.62
2.59
2.58
2.55
2.53
2.51
2.50
2.49
2.30
2.28
2.28
2.27
2.26
2.25
2.24
2.23
2.20
2.19
2.11
2.08
1.75
1.58
1.57
1.47
1.37
1.32
1.27
1.24
1.22
1.20
1.13
1.13
1.10
1.09
0.00
EOMO
H
OH
O
O
O
O
O
tBu
O
OMe
46a
1H NMR spectrum
400 MHz, CDCl3
2.00
0.99
1.00
5.18
1.01
0.98
0.93
2.92
0.95
0.90
1.03
1.12
9.06
1.13
2.95
2.83
3.08
1.02
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)

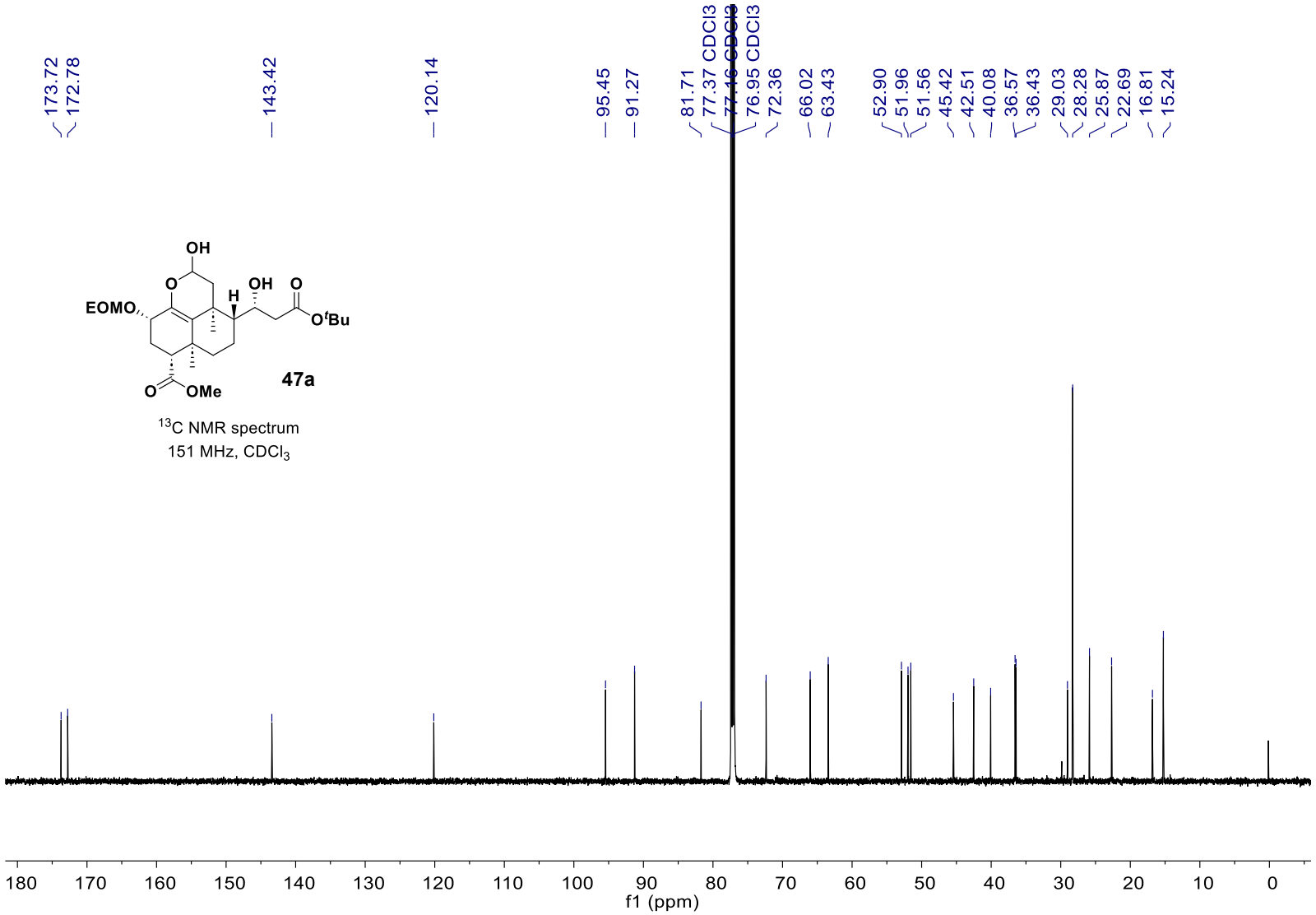

172.97
172.33
167.61
143.77
127.09
95.37
81.94
77.48
77.16
77.16 CDCl3
76.84
70.44
65.71
63.60
52.27
51.71
51.30
44.20
42.17
38.15
36.84
36.32
29.39
28.26
22.72
21.97
16.84
15.20
EOMO
O
O
H
OH
O
O
tBu
O
OMe
46a
13C NMR spectrum
100 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.26 CDCl3
4.87
4.86
4.82
4.80
4.34
4.32
4.30
3.95
3.73
3.72
3.71
3.69
3.68
3.66
3.65
3.64
3.63
3.62
3.57
3.56
3.55
3.53
2.60
2.60
2.56
2.56
2.53
2.51
2.50
2.48
2.38
2.36
2.34
2.32
2.30
2.28
2.27
2.26
2.24
2.23
2.19
1.72
1.71
1.70
1.69
1.56 HDO
1.47
1.41
1.40
1.39
1.37
1.36
1.26
1.23
1.23
1.22
1.20
-0.00
EOMO
O
O
H
OH
O
O
tBu
O
OMe
46b
1H NMR spectrum
400 MHz, CDCl3
2.01
1.00
0.98
5.22
1.94
1.02
0.96
1.13
1.87
1.03
0.92
9.32
2.33
3.26
5.83
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
f1 (ppm)

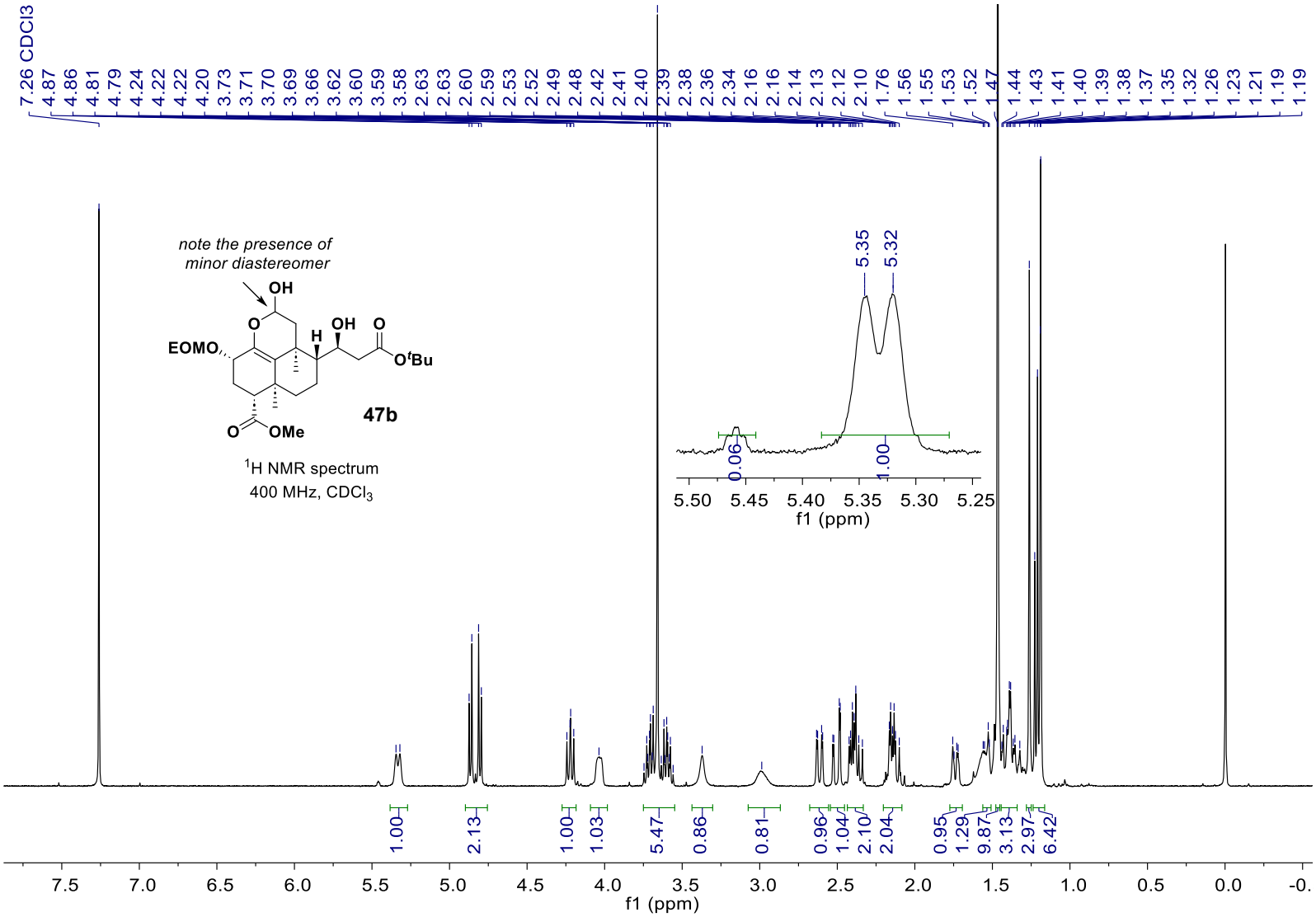


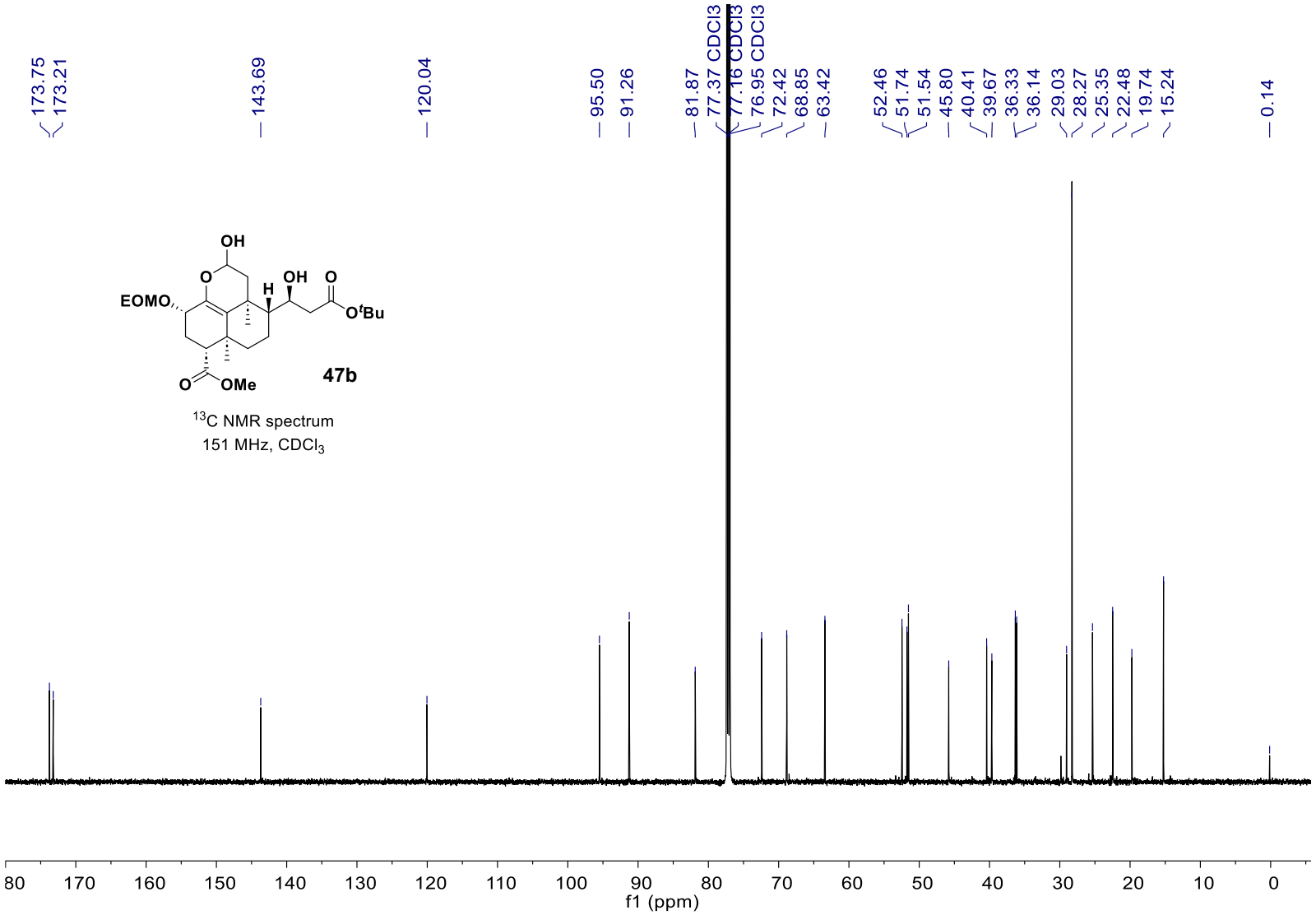
^{13}C NMR spectrum
125 MHz, $CDCl_3$

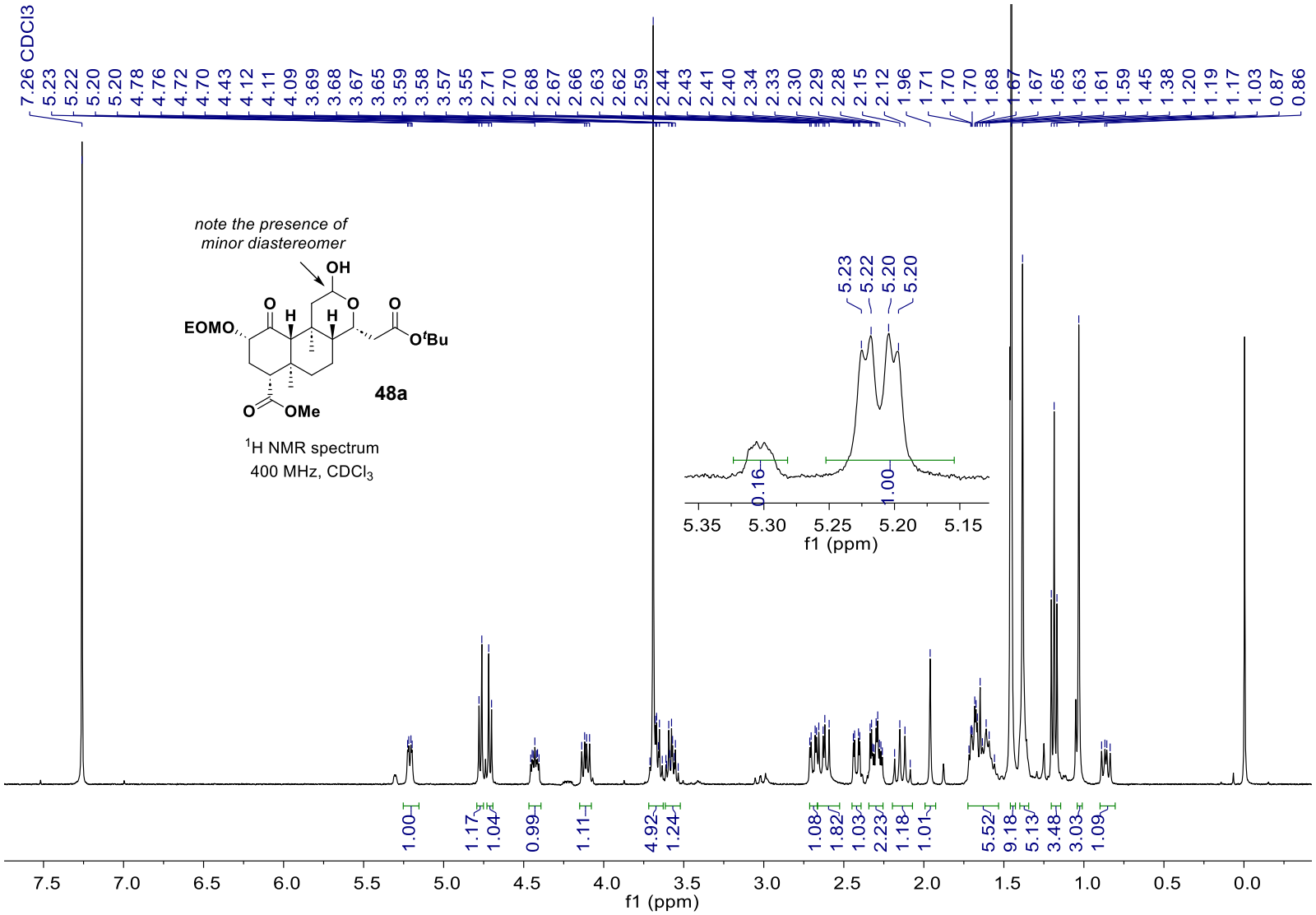

note the presence of
minor diastereomer
OH
O
OH
O
H
EOMO
O
tBu
O
OMe
47a
1H NMR spectrum
400 MHz, CDCl3
5.41
5.38
0.12
1.00
5.50
5.45
5.40
5.35
5.30
f1 (ppm)
7.26 CDCl3
1.00
2.22
1.02
1.06
5.78
0.76
0.79
1.06
0.98
4.15
2.08
1.20
9.99
2.97
3.16
3.42
1.02
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

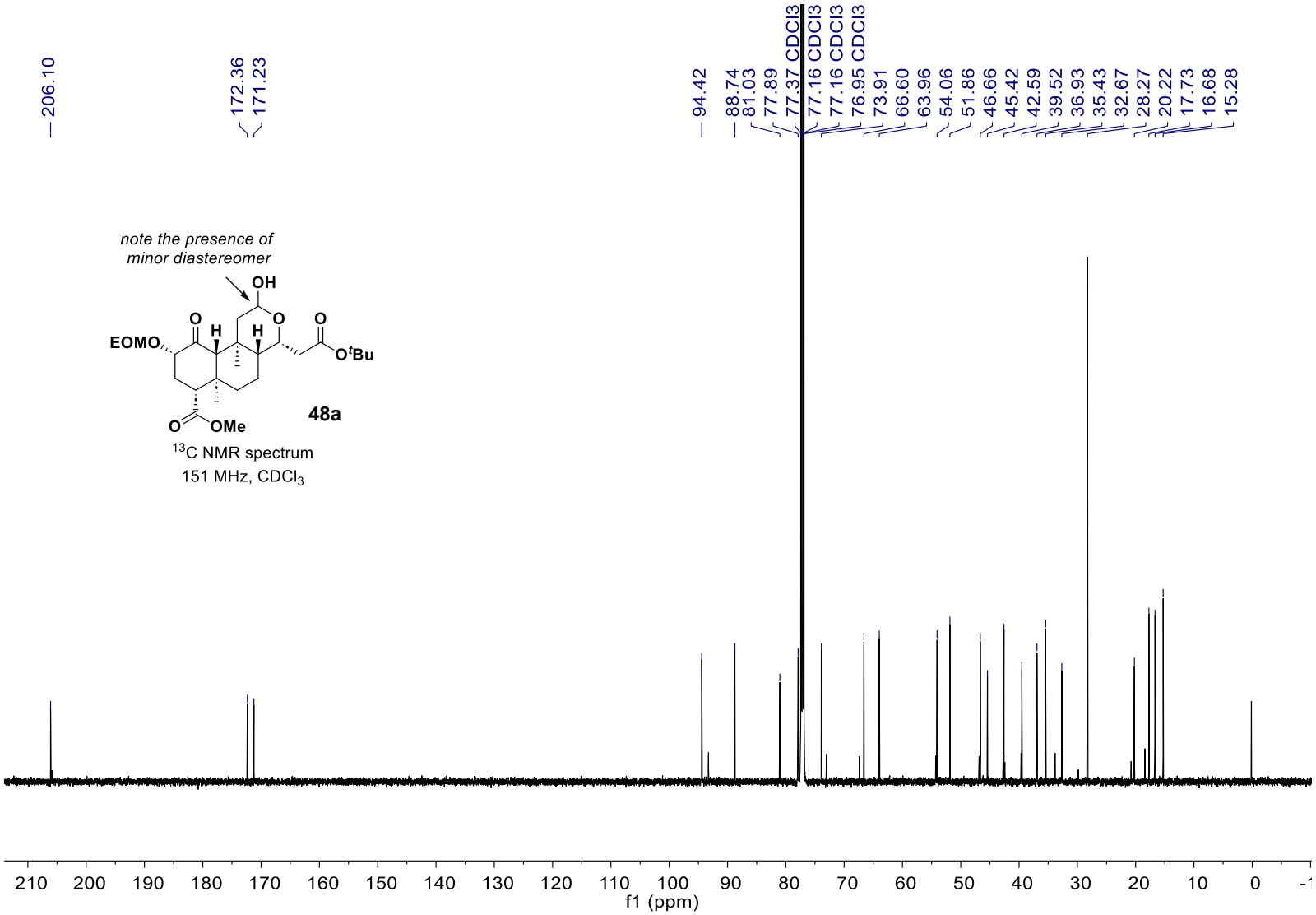


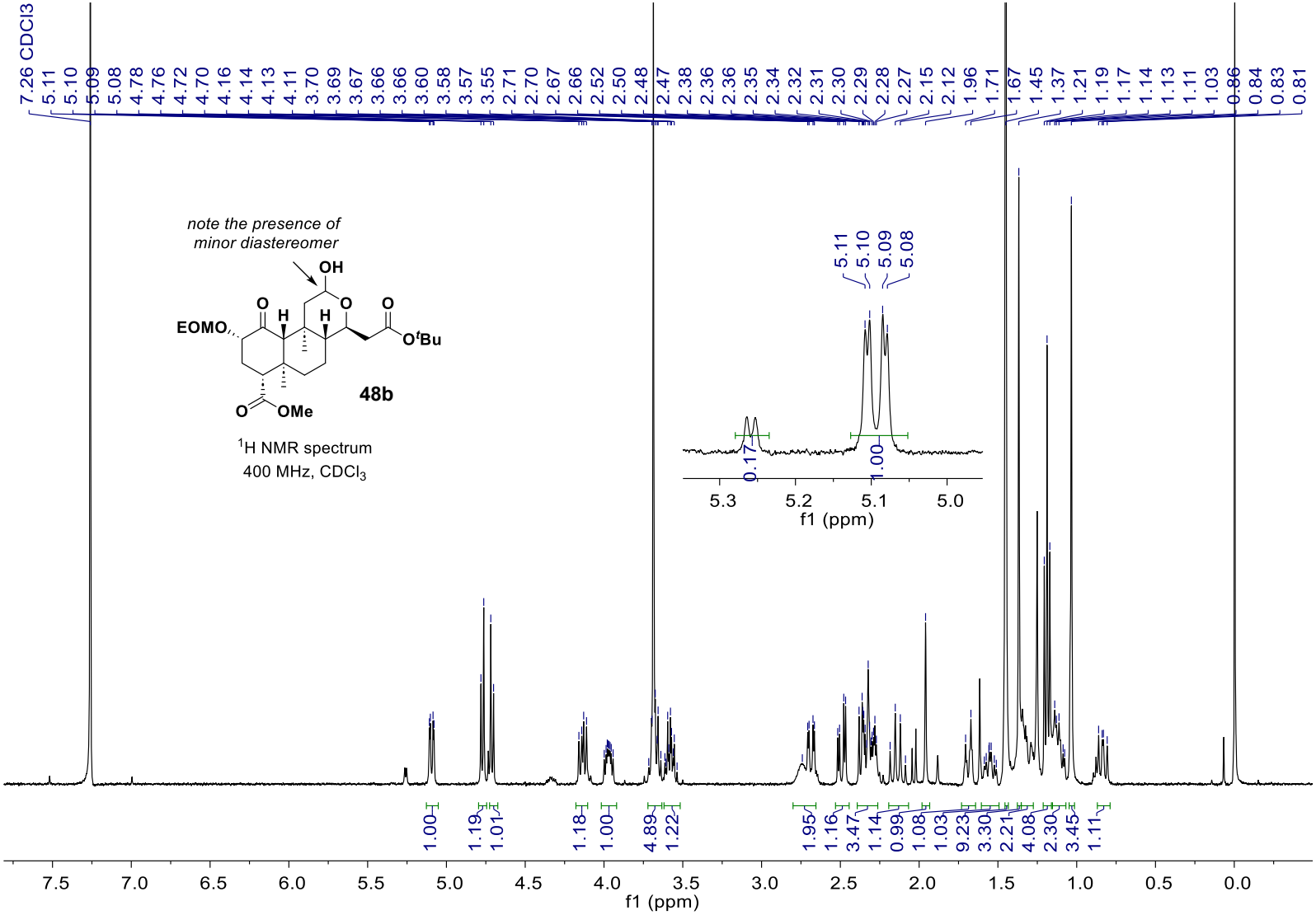
^{13}C NMR spectrum
151 MHz, $CDCl_3$

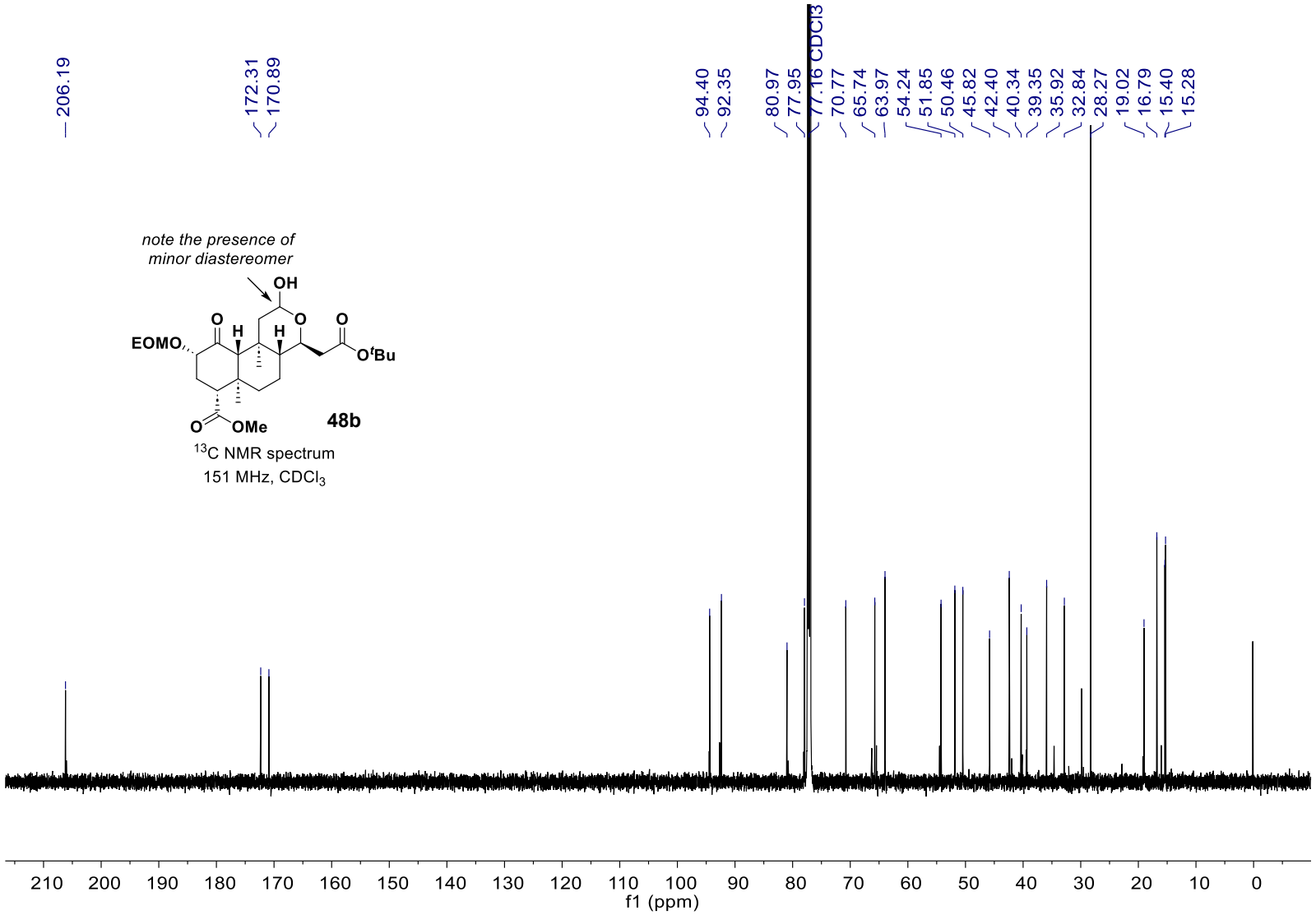

7.26 CDCl3
4.87 4.86 4.81 4.79 4.24 4.22 4.22 4.20 3.73 3.71 3.70 3.69 3.66 3.62 3.60 3.59 3.58 2.63 2.63 2.60 2.59 2.53 2.52 2.49 2.48 2.42 2.41 2.40 2.39 2.38 2.36 2.34 2.16 2.16 2.14 2.13 2.12 2.10 1.76 1.56 1.55 1.53 1.52 1.47 1.44 1.43 1.41 1.40 1.39 1.38 1.37 1.35 1.32 1.26 1.23 1.21 1.19 1.19
note the presence of
minor diastereomer
OH
O
H
OH
O
EOMO
O
tBu
O
OMe
47b
1H NMR spectrum
400 MHz, CDCl3
5.35
5.32
0.06
1.00
5.50 5.45 5.40 5.35 5.30 5.25
f1 (ppm)
1.00 2.13 1.00 1.03 5.47 0.86 0.81 0.96 1.04 2.10 2.04 0.95 1.29 9.87 3.13 2.97 6.42
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.
f1 (ppm)

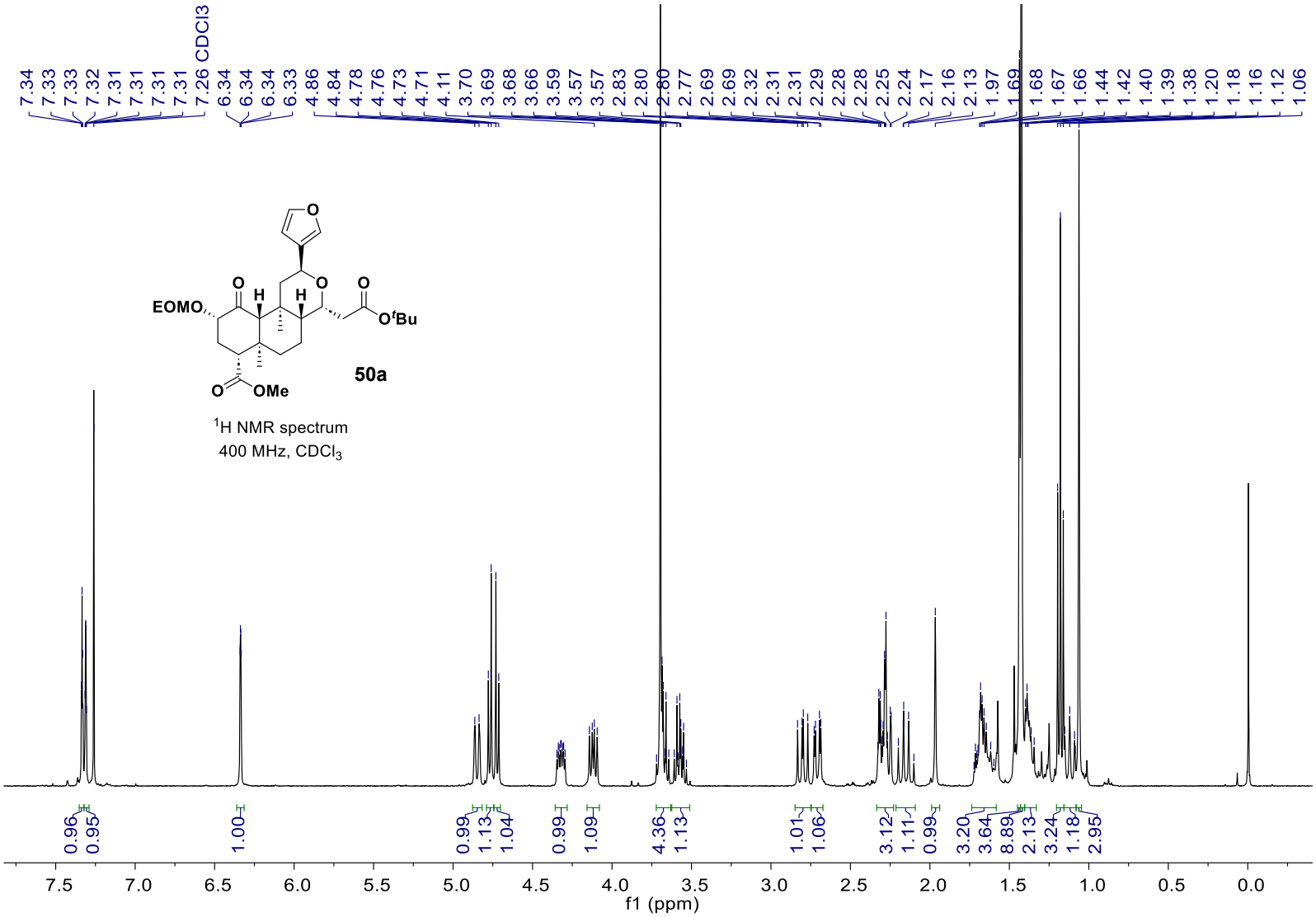

173.75
173.21
143.69
120.04
95.50
91.26
81.87
77.37 CDCl3
77.16 CDCl3
76.95 CDCl3
72.42
68.85
63.42
52.46
51.74
51.54
45.80
40.41
39.67
36.33
36.14
29.03
28.27
25.35
22.48
19.74
15.24
0.14
OH
O
OH
O
H
EOMO
O
tBu
O
OMe
47b
13C NMR spectrum
151 MHz, CDCl3
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

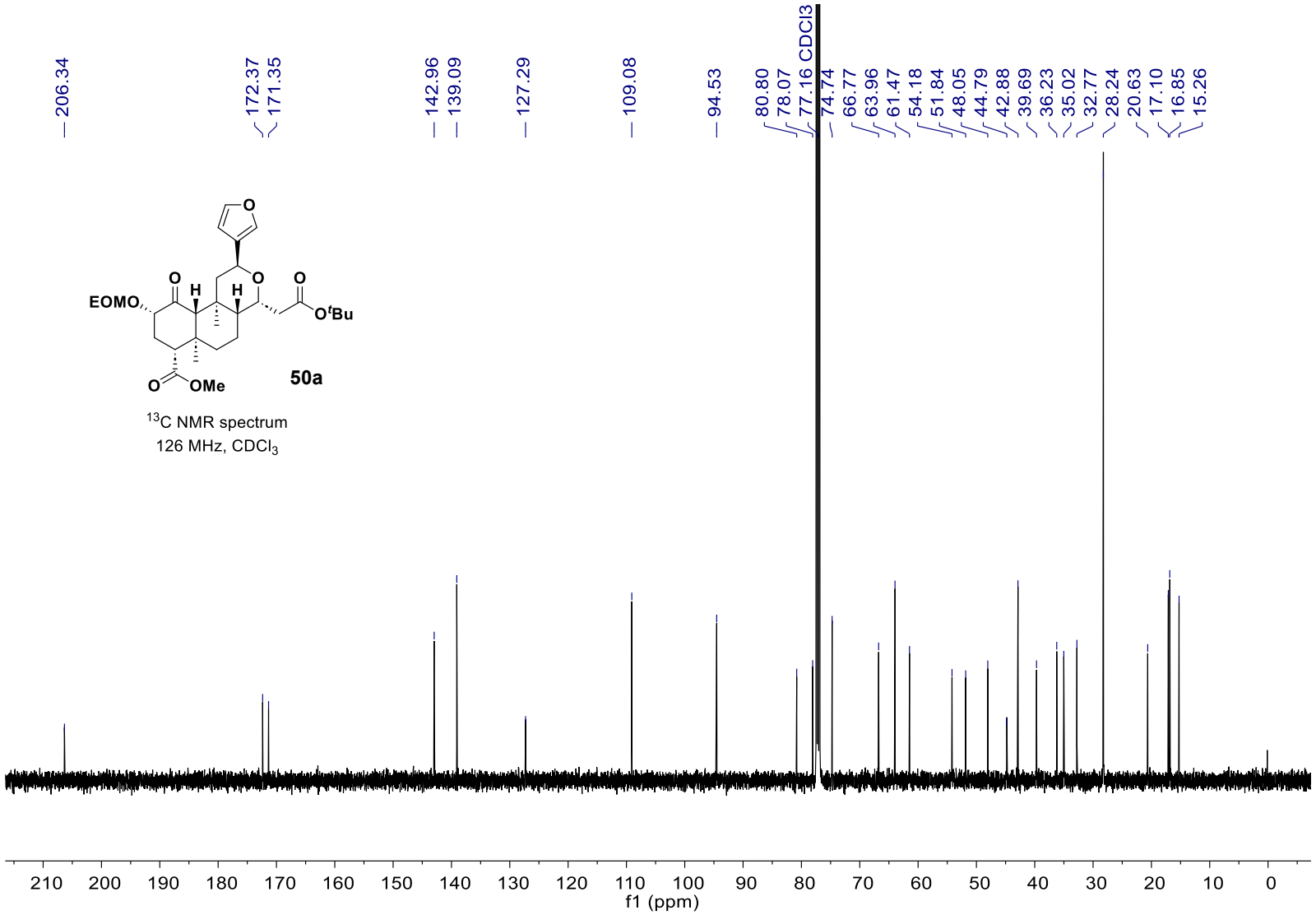

7.26 CDCl3
5.23 5.22 5.20 5.20 4.78 4.76 4.72 4.70 4.43 4.12 4.11 4.09 3.69 3.68 3.67 3.65 3.59 3.58 3.57 3.55 2.71 2.70 2.68 2.67 2.66 2.63 2.62 2.59 2.44 2.43 2.41 2.40 2.34 2.33 2.30 2.29 2.28 2.15 2.12 1.96 1.71 1.70 1.70 1.68 1.67 1.67 1.65 1.63 1.61 1.59 1.45 1.38 1.20 1.19 1.17 1.03 0.87 0.86
note the presence of
minor diastereomer
OH
O
H
O
H
O
O
EOMO
O
tBu
O
OMe
48a
1H NMR spectrum
400 MHz, CDCl3
5.23 5.22 5.20 5.20
0.16
1.00
5.35 5.30 5.25 5.20 5.15
f1 (ppm)
1.00 1.17 1.04 0.99 1.11 4.92 1.24 1.08 1.82 1.03 2.23 1.18 1.01 5.52 9.18 5.13 3.48 3.03 1.09
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
f1 (ppm)

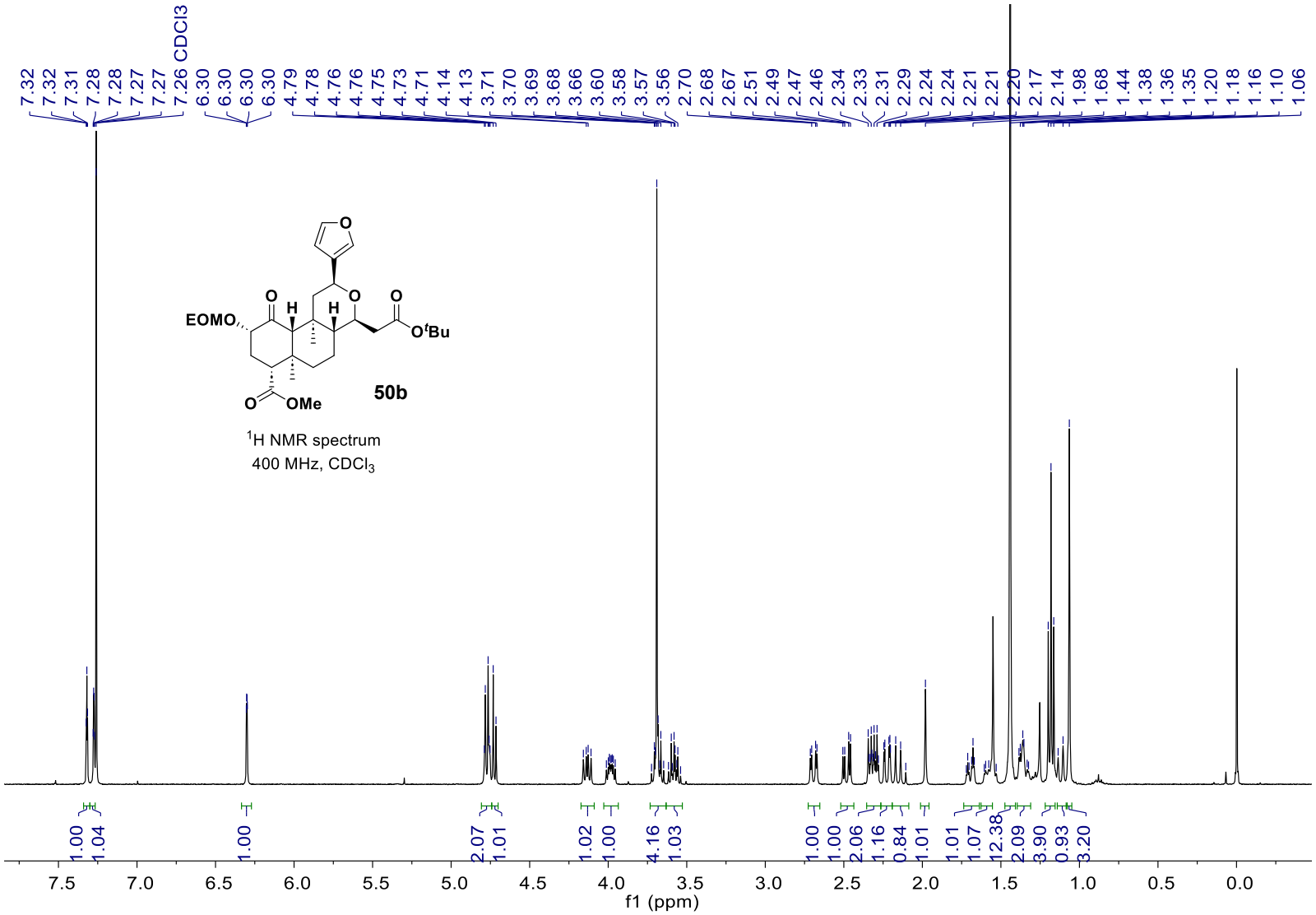

206.10
172.36
171.23
94.42
88.74
81.03
77.89
77.37 CDCl3
77.16 CDCl3
77.16 CDCl3
76.95 CDCl3
73.91
66.60
63.96
54.06
51.86
46.66
45.42
42.59
39.52
36.93
35.43
32.67
28.27
20.22
17.73
16.68
15.28
note the presence of
minor diastereomer
OH
O
H
H
O
O
EOMO
O
tBu
O
OMe
48a
13C NMR spectrum
151 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

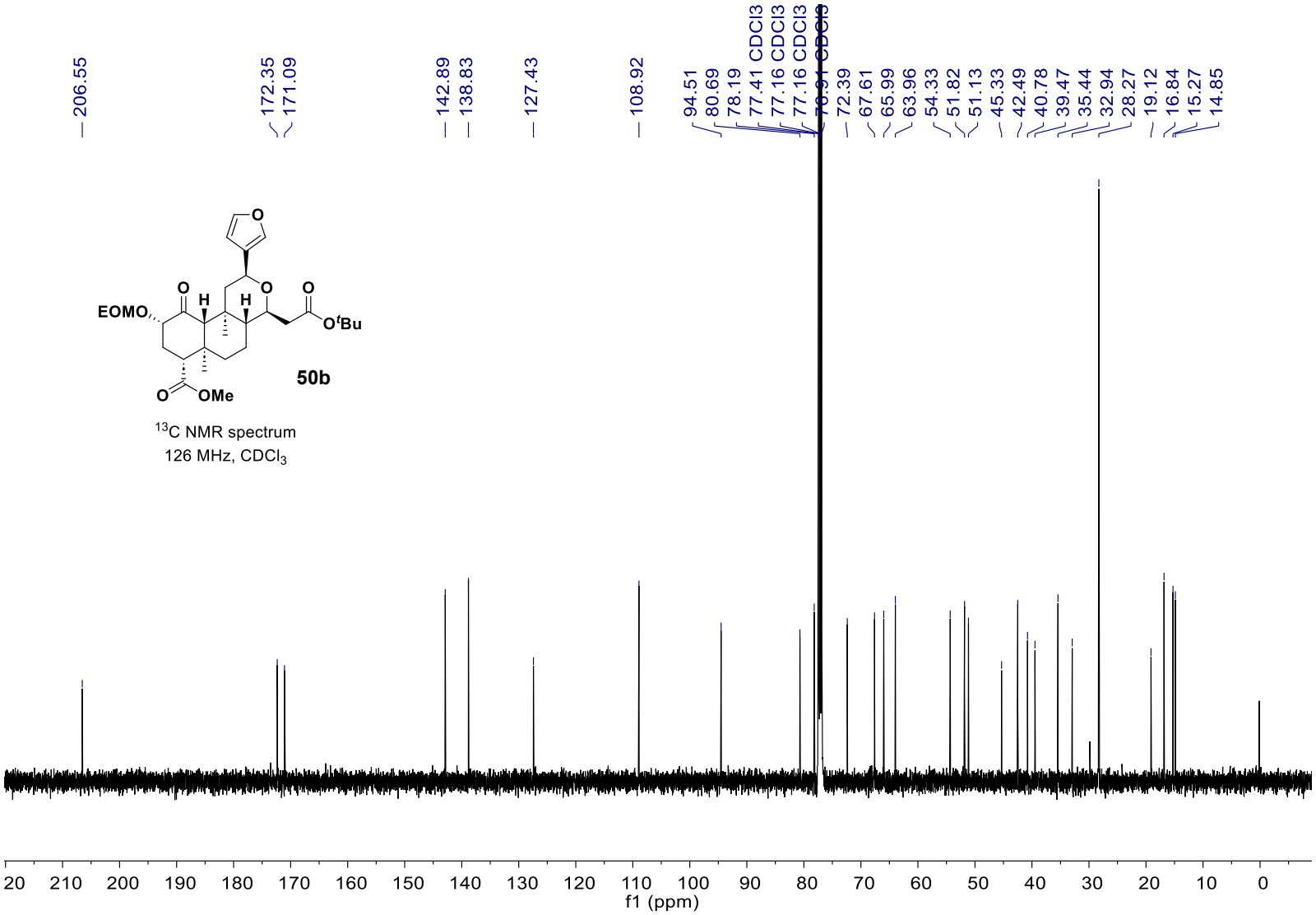

note the presence of
minor diastereomer
OH
EOMO
O
H
H
O
O
O
O
tBu
OMe
48b
1H NMR spectrum
400 MHz, CDCl3
7.26 CDCl3
5.11
5.10
5.09
5.08
4.78
4.76
4.72
4.70
4.16
4.14
4.13
4.11
3.70
3.69
3.67
3.66
3.66
3.60
3.58
3.57
3.55
2.71
2.70
2.67
2.66
2.52
2.50
2.48
2.47
2.38
2.36
2.36
2.35
2.34
2.32
2.31
2.30
2.29
2.28
2.27
2.15
2.12
1.96
1.71
1.67
1.45
1.37
1.21
1.19
1.17
1.14
1.13
1.11
1.03
0.86
0.84
0.83
0.81
0.17
1.00
5.3
5.2
5.1
5.0
f1 (ppm)
1.00
1.19
1.01
1.18
1.00
4.89
1.22
1.95
1.16
3.47
1.14
0.99
1.08
1.03
9.23
3.30
2.21
4.08
2.30
3.45
1.11
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
f1 (ppm)

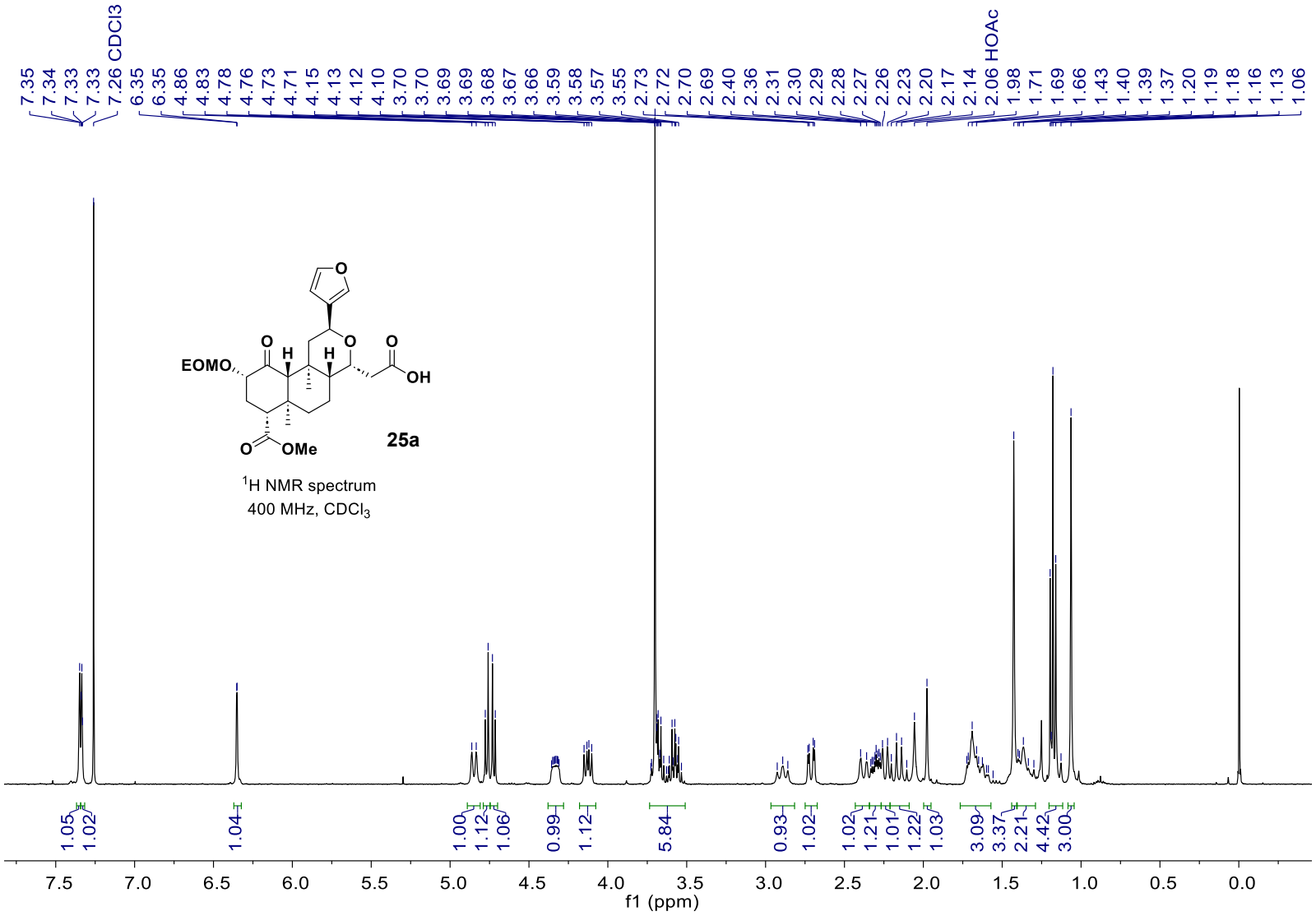

206.19
172.31
170.89
94.40
92.35
80.97
77.95
77.16 CDCl3
70.77
65.74
63.97
54.24
51.85
50.46
45.82
42.40
40.34
39.35
35.92
32.84
28.27
19.02
16.79
15.40
15.28
note the presence of
minor diastereomer
OH
O
H
H
O
O
EOMO
O
tBu
O
OMe
48b
13C NMR spectrum
151 MHz, CDCl3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

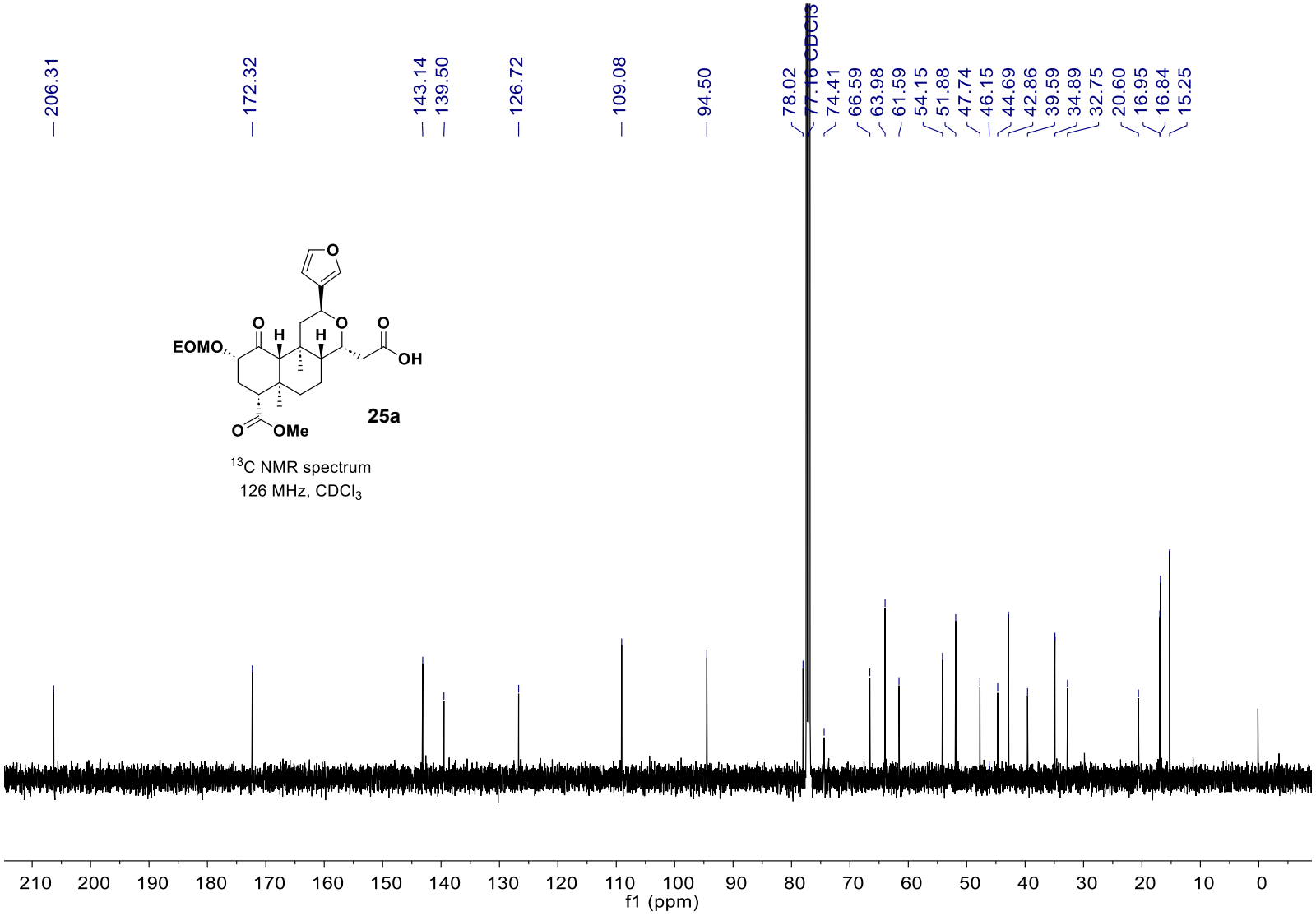

7.34 7.33 7.33 7.32 7.31 7.31 7.31 7.31 7.26 CDCl3
6.34 6.34 6.33
4.86 4.84 4.78 4.76 4.73 4.71 4.11 3.70 3.69 3.68 3.66 3.59 3.57 3.57 2.83 2.80 2.80 2.77 2.69 2.69 2.32 2.31 2.31 2.29 2.28 2.28 2.25 2.24 2.17 2.16 2.13 1.97 1.69 1.68 1.67 1.66 1.44 1.42 1.40 1.39 1.38 1.20 1.18 1.16 1.12 1.06
EOMO
O
H
H
O
O
O
O
tBu
O
OMe
50a
1H NMR spectrum
400 MHz, CDCl3
0.96 0.95 1.00 0.99 1.13 1.04 0.99 1.09 4.36 1.13 1.01 1.06 3.12 1.11 0.99 3.20 3.64 8.89 2.13 3.24 1.18 2.95
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
f1 (ppm)

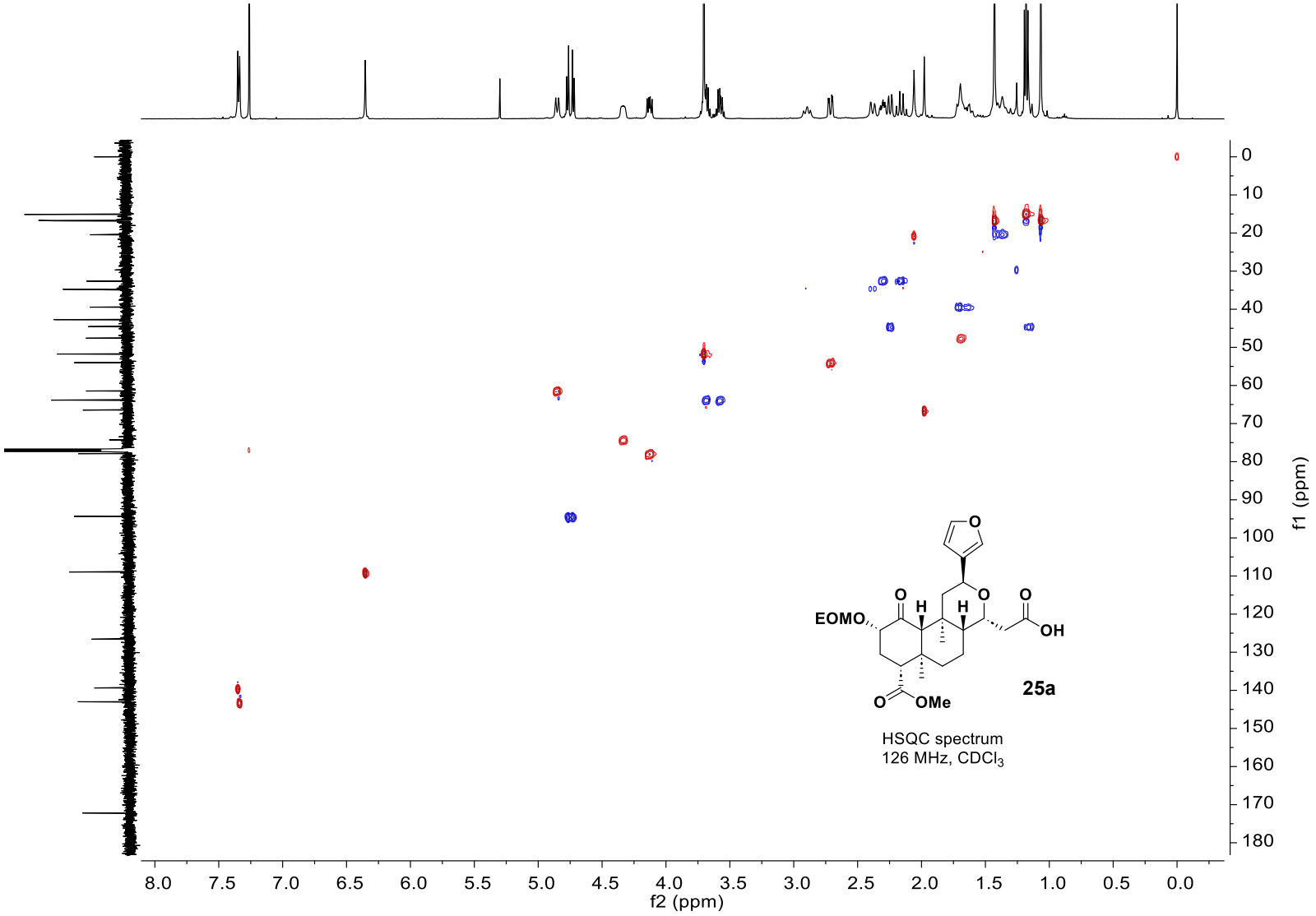

206.34
172.37
171.35
142.96
139.09
127.29
109.08
94.53
80.80
78.07
77.16 CDCl3
74.74
66.77
63.96
61.47
54.18
51.84
48.05
44.79
42.88
39.69
36.23
35.02
32.77
28.24
20.63
17.10
16.85
15.26
EOMO
O
H
H
O
O
O
O
tBu
O
OMe
50a
13C NMR spectrum
126 MHz, CDCl3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

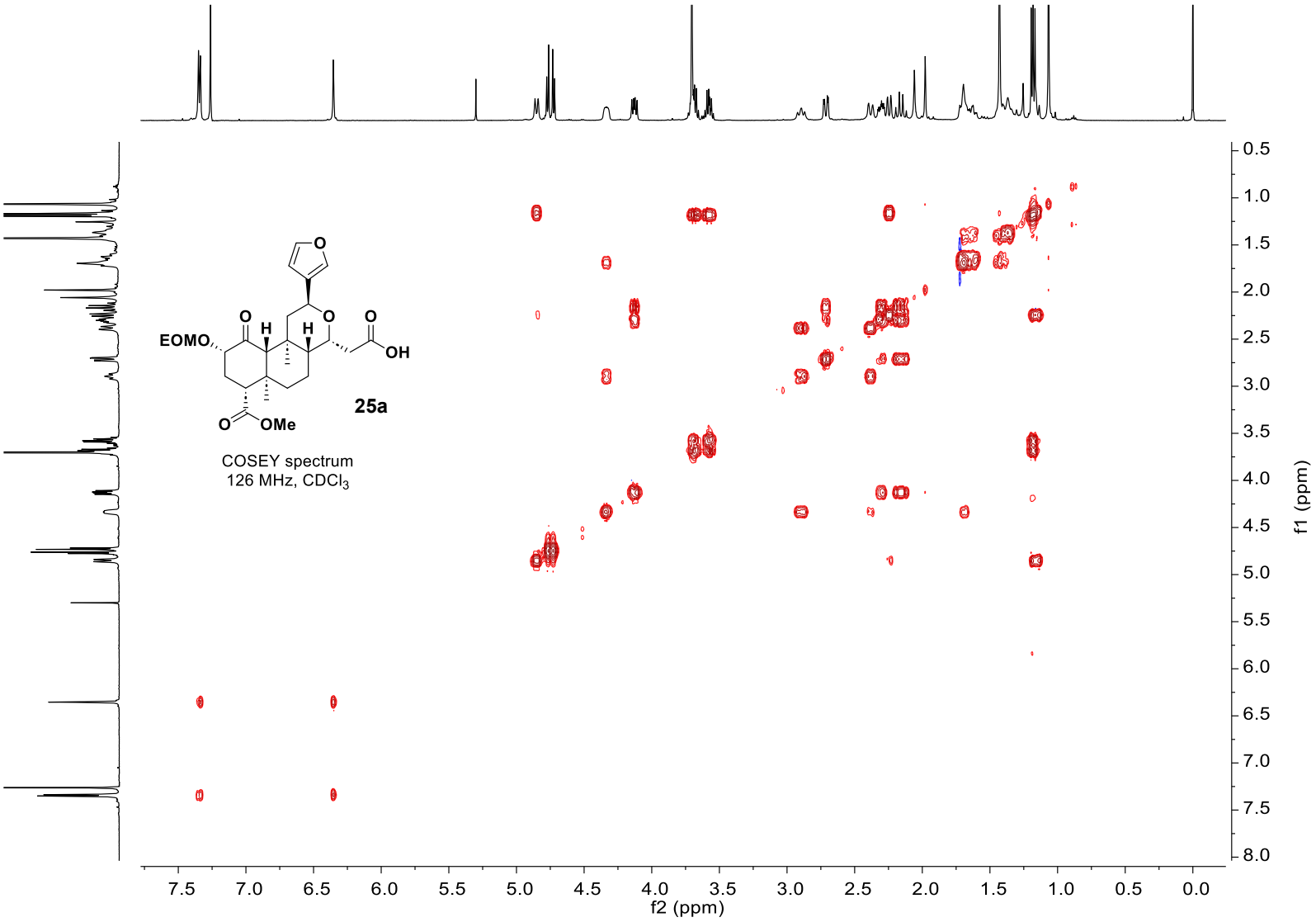

7.32 7.32 7.31 7.28 7.28 7.27 7.27 7.26 CDCl3 6.30 6.30 6.30 4.79 4.78 4.76 4.76 4.75 4.73 4.71 4.14 4.13 3.71 3.70 3.69 3.68 3.66 3.60 3.58 3.57 3.56 2.70 2.68 2.67 2.51 2.49 2.47 2.46 2.34 2.33 2.31 2.29 2.24 2.24 2.21 2.21 2.20 2.17 2.14 1.98 1.68 1.44 1.38 1.36 1.35 1.20 1.18 1.16 1.10 1.06
EOMO
O
H
H
O
O
O
O
tBu
O
OMe
50b
1H NMR spectrum
400 MHz, CDCl3
1.00 1.04 1.00 2.07 1.01 1.02 1.00 4.16 1.03 1.00 1.00 2.06 1.16 0.84 1.01 1.01 1.07 12.38 2.09 3.90 0.93 3.20
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
f1 (ppm)

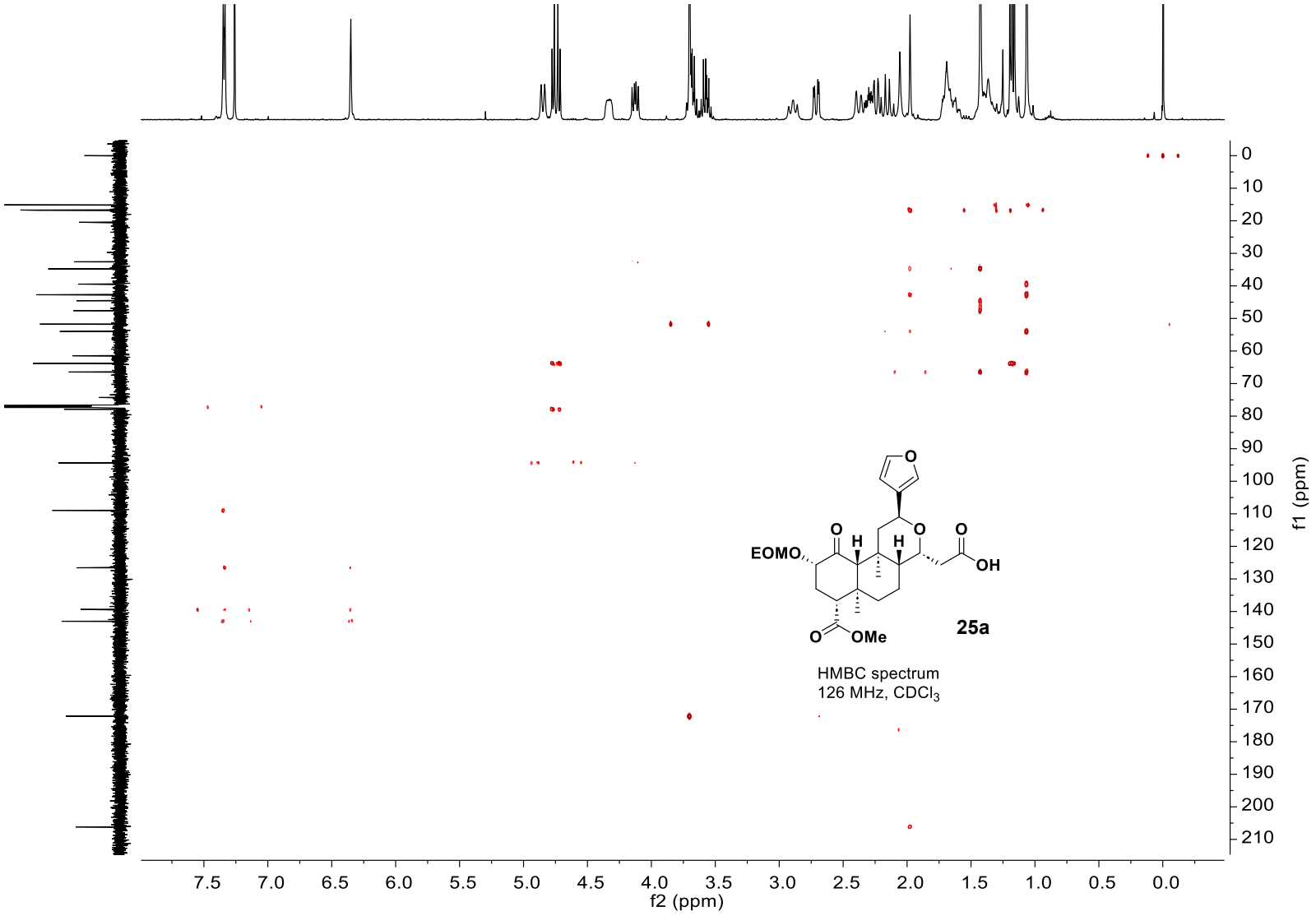

206.55
172.35
171.09
142.89
138.83
127.43
108.92
94.51
80.69
78.19
77.41 CDCl3
77.16 CDCl3
77.16 CDCl3
76.91 CDCl3
72.39
67.61
65.99
63.96
54.33
51.82
51.13
45.33
42.49
40.78
39.47
35.44
32.94
28.27
19.12
16.84
15.27
14.85
EOMO
O
H
H
O
O
O
O
tBu
O
OMe
50b
13C NMR spectrum
126 MHz, CDCl3
20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

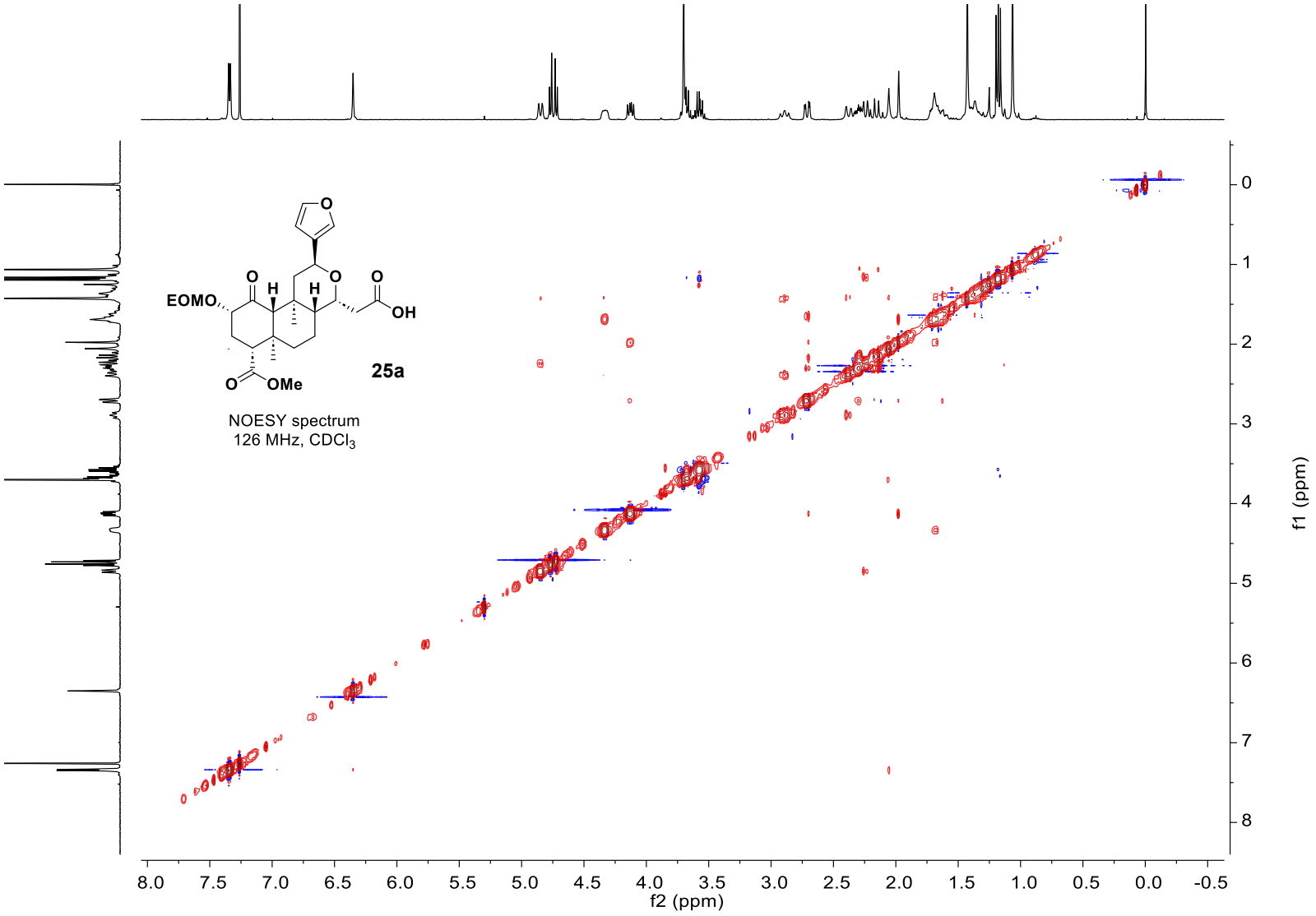

7.35
7.34
7.33
7.33
7.26 CDCl3
6.35
6.35
4.86
4.83
4.78
4.76
4.73
4.71
4.15
4.13
4.12
4.10
3.70
3.70
3.69
3.69
3.68
3.67
3.66
3.59
3.58
3.57
3.55
2.73
2.72
2.70
2.69
2.40
2.36
2.31
2.30
2.29
2.28
2.27
2.26
2.23
2.20
2.17
2.14
2.06 HOAc
1.98
1.71
1.69
1.66
1.43
1.40
1.39
1.37
1.20
1.19
1.18
1.16
1.13
1.06
EOMO
O
H
H
O
O
OH
O
OMe
25a
1H NMR spectrum
400 MHz, CDCl3
1.05
1.02
1.04
1.00
1.12
1.06
0.99
1.12
5.84
0.93
1.02
1.02
1.21
1.01
1.22
1.03
3.09
3.37
2.21
4.42
3.00
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
f1 (ppm)

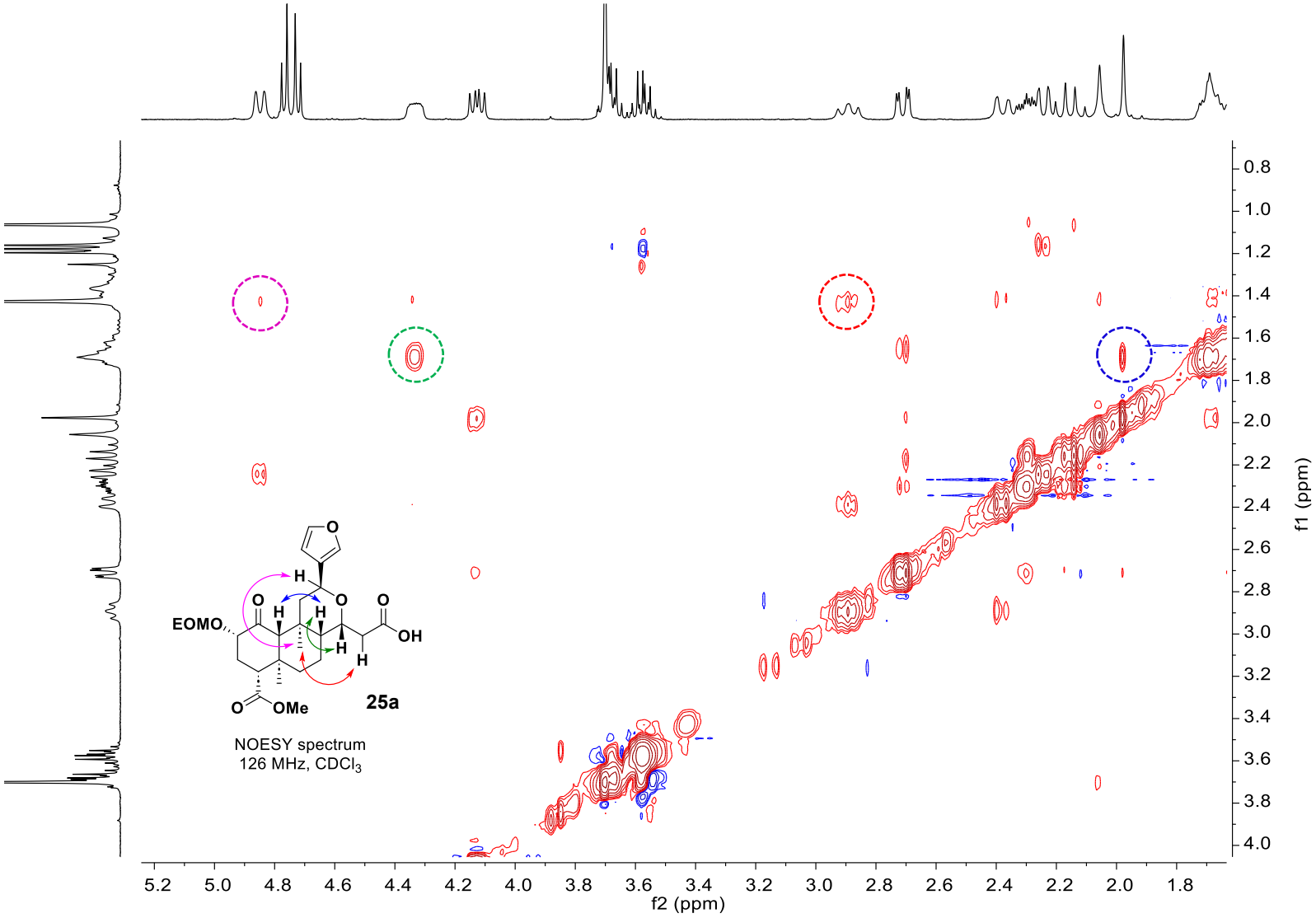

206.31
172.32
143.14
139.50
126.72
109.08
94.50
78.02
77.16 CDCl3
74.41
66.59
63.98
61.59
54.15
51.88
47.74
46.15
44.69
42.86
39.59
34.89
32.75
20.60
16.95
16.84
15.25
EOMO
OH
OMe
25a
13C NMR spectrum
126 MHz, CDCl3
f1 (ppm)

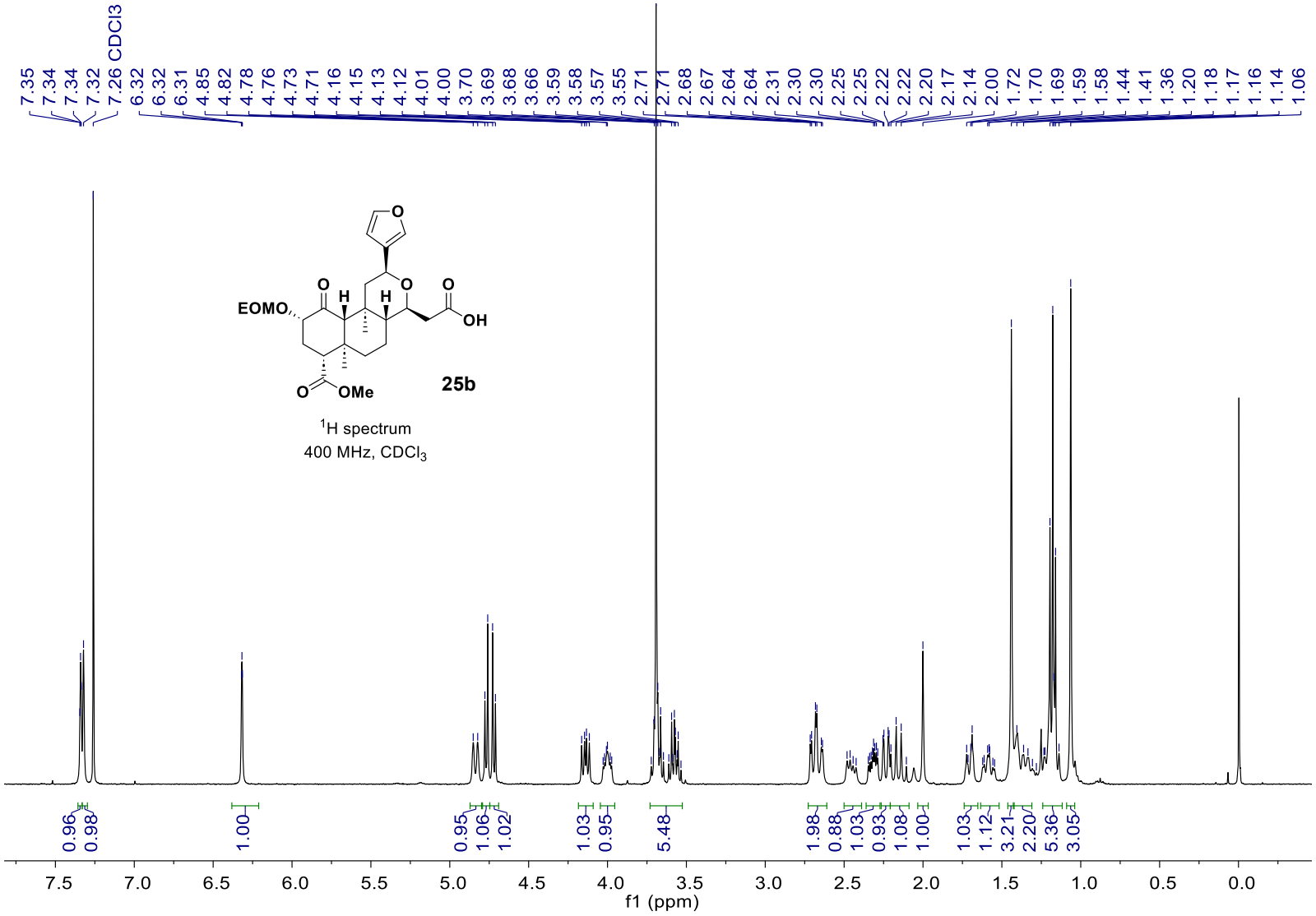

f2 (ppm)
f1 (ppm)
EOMO
OH
OMe
25a
HSQC spectrum
126 MHz, CDCl3


EOMO
O
H
H
O
O
OH
O
OMe
25a
COSEY spectrum
126 MHz, CDCl3
f2 (ppm)
f1 (ppm)

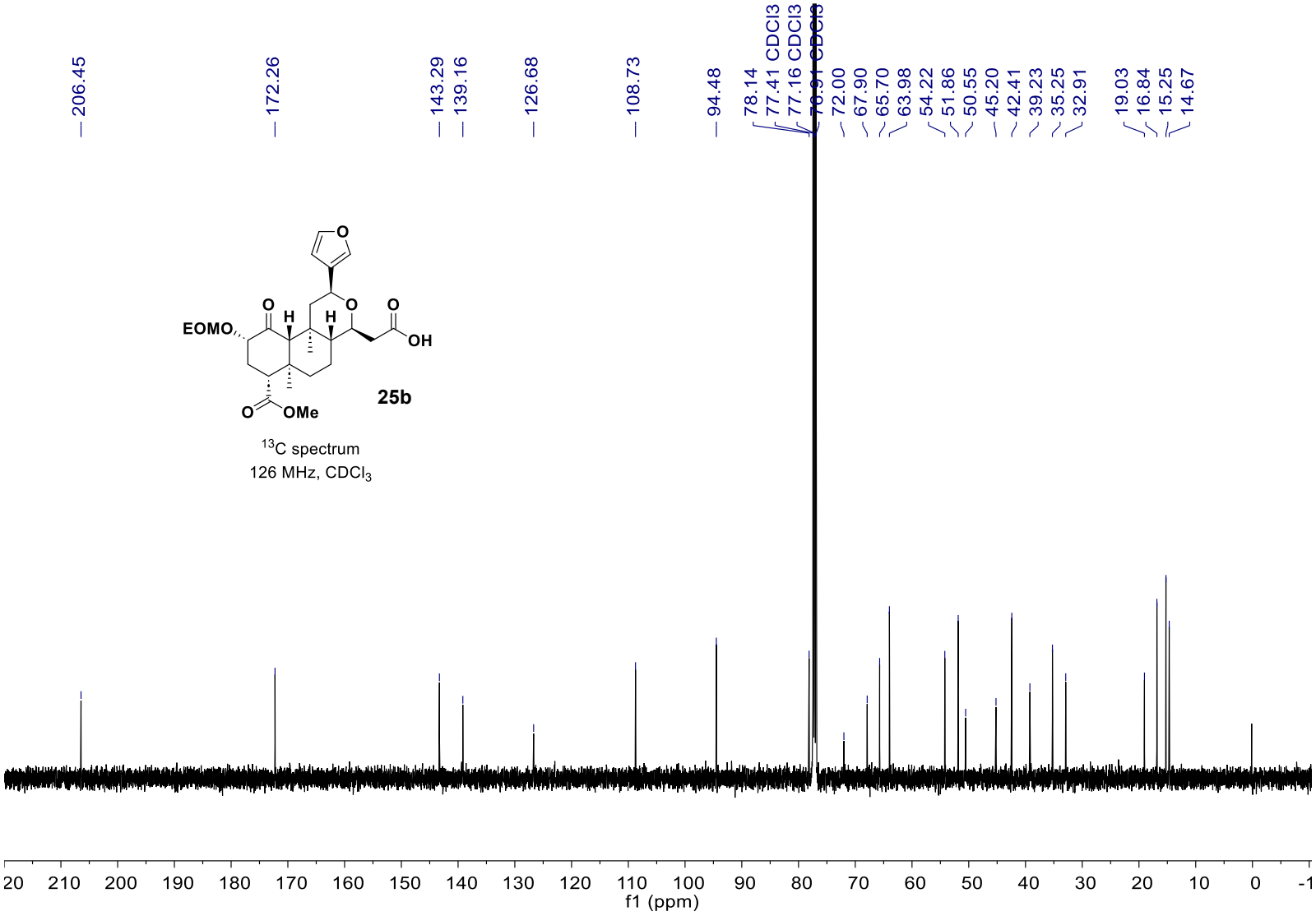

EOMO
O
H
H
O
O
OH
O
O
OMe
25a
HMBC spectrum
126 MHz, CDCl3
f2 (ppm)
f1 (ppm)

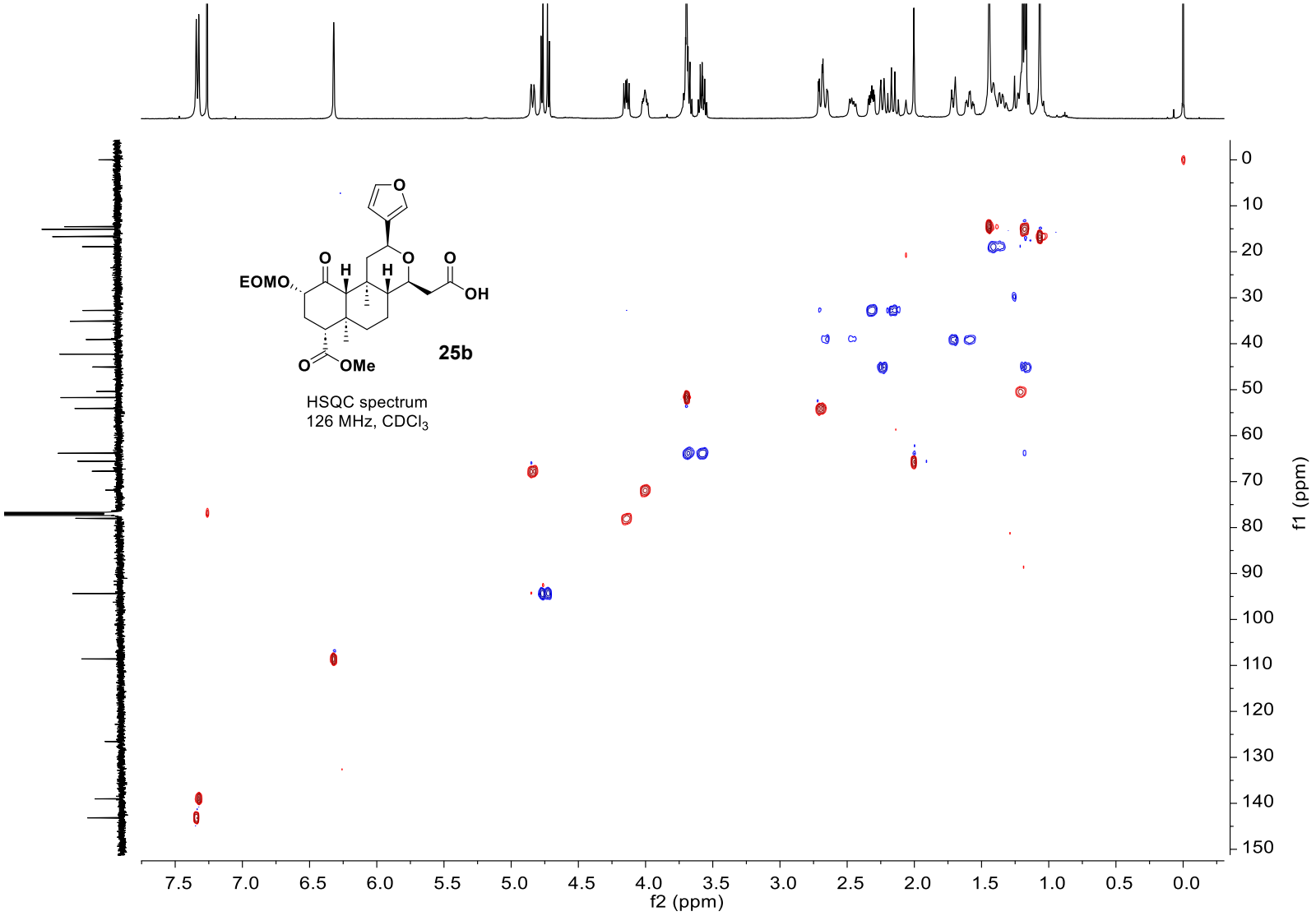

EOMO
O
H
H
O
O
OH
O
OMe
25a
NOESY spectrum
126 MHz, CDCl3
f2 (ppm)
f1 (ppm)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
0
1
2
3
4
5
6
7
8

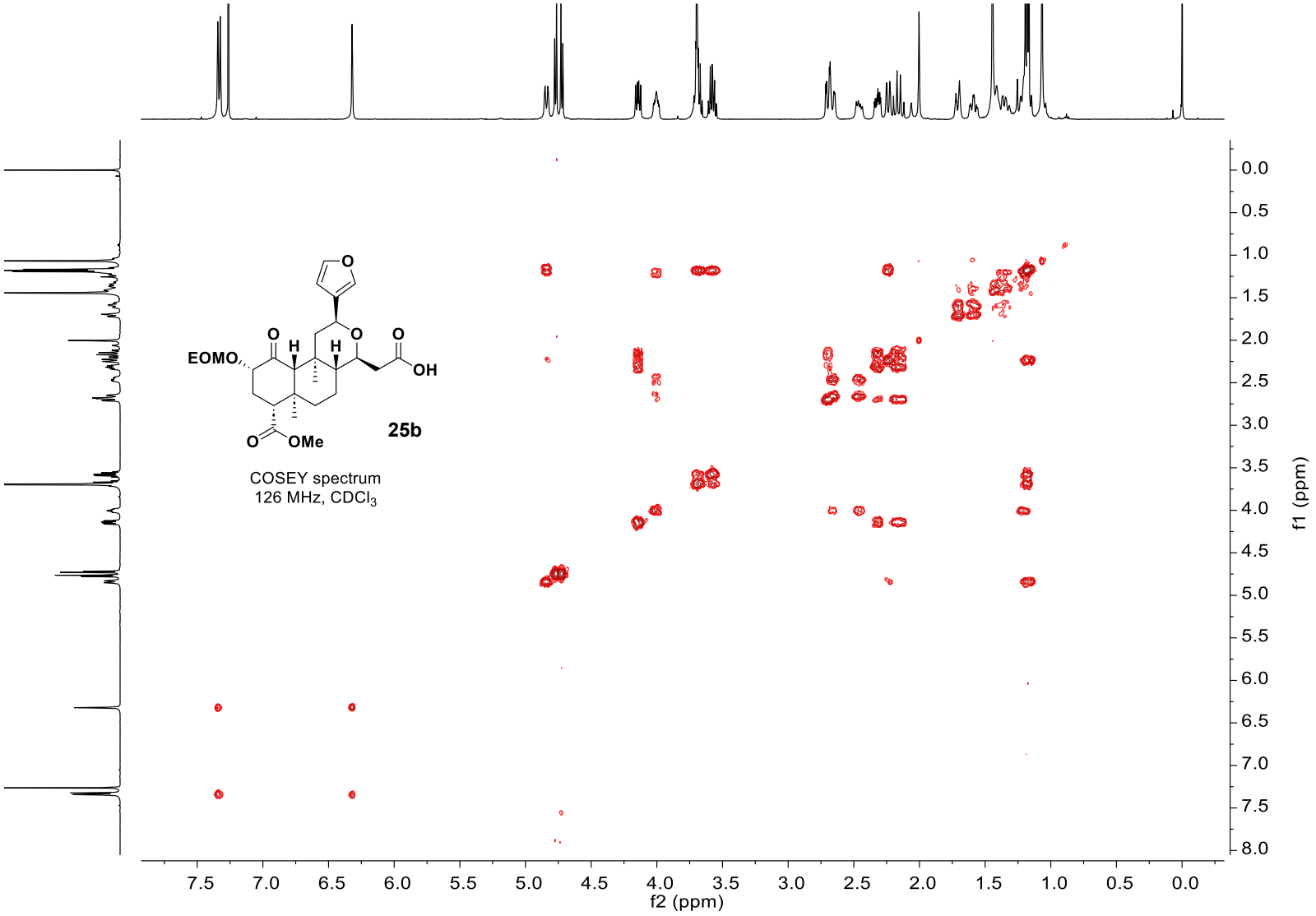

EOMO
OH
OMe
25a
NOESY spectrum
126 MHz, CDCl3
f2 (ppm)
f1 (ppm)

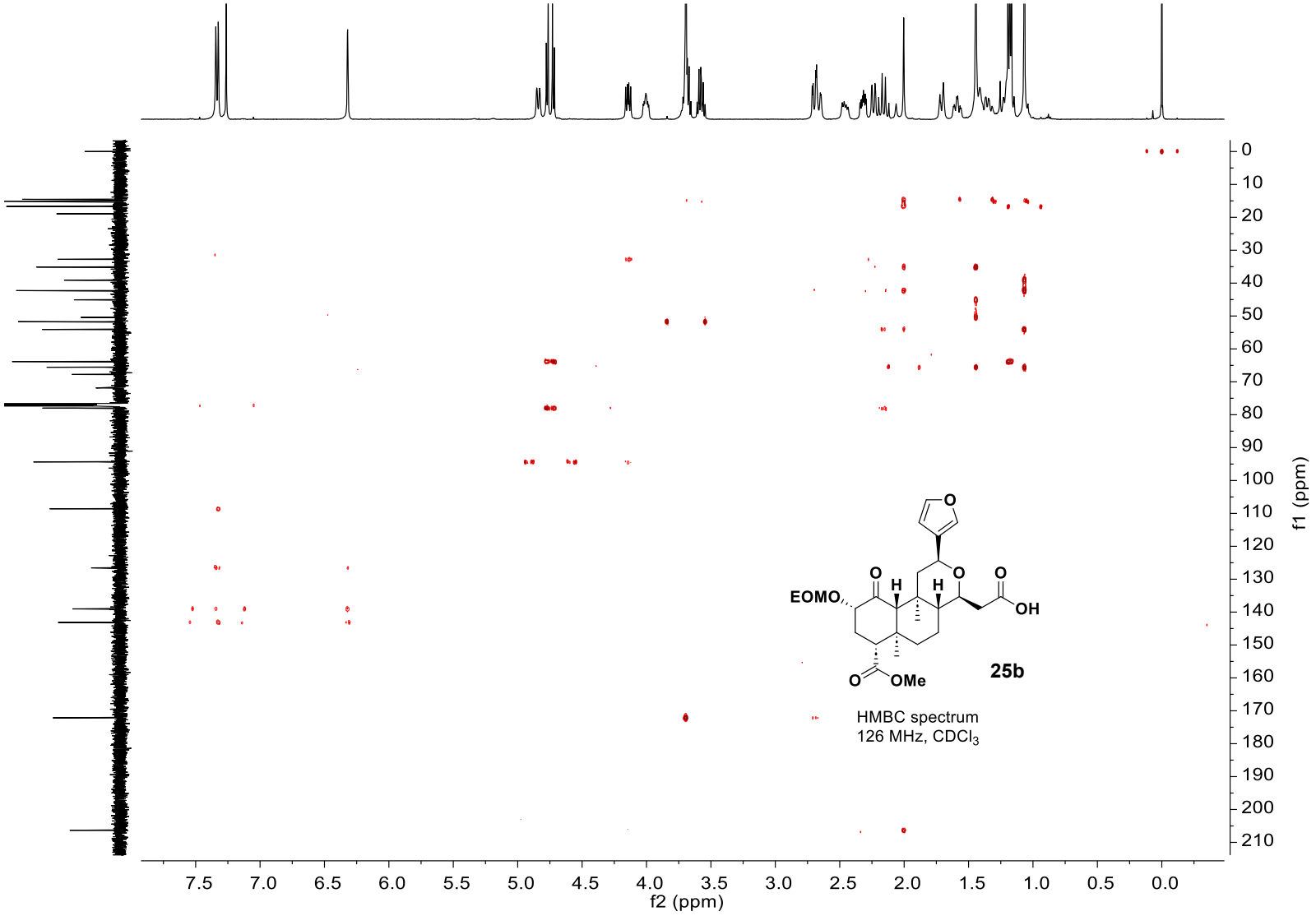


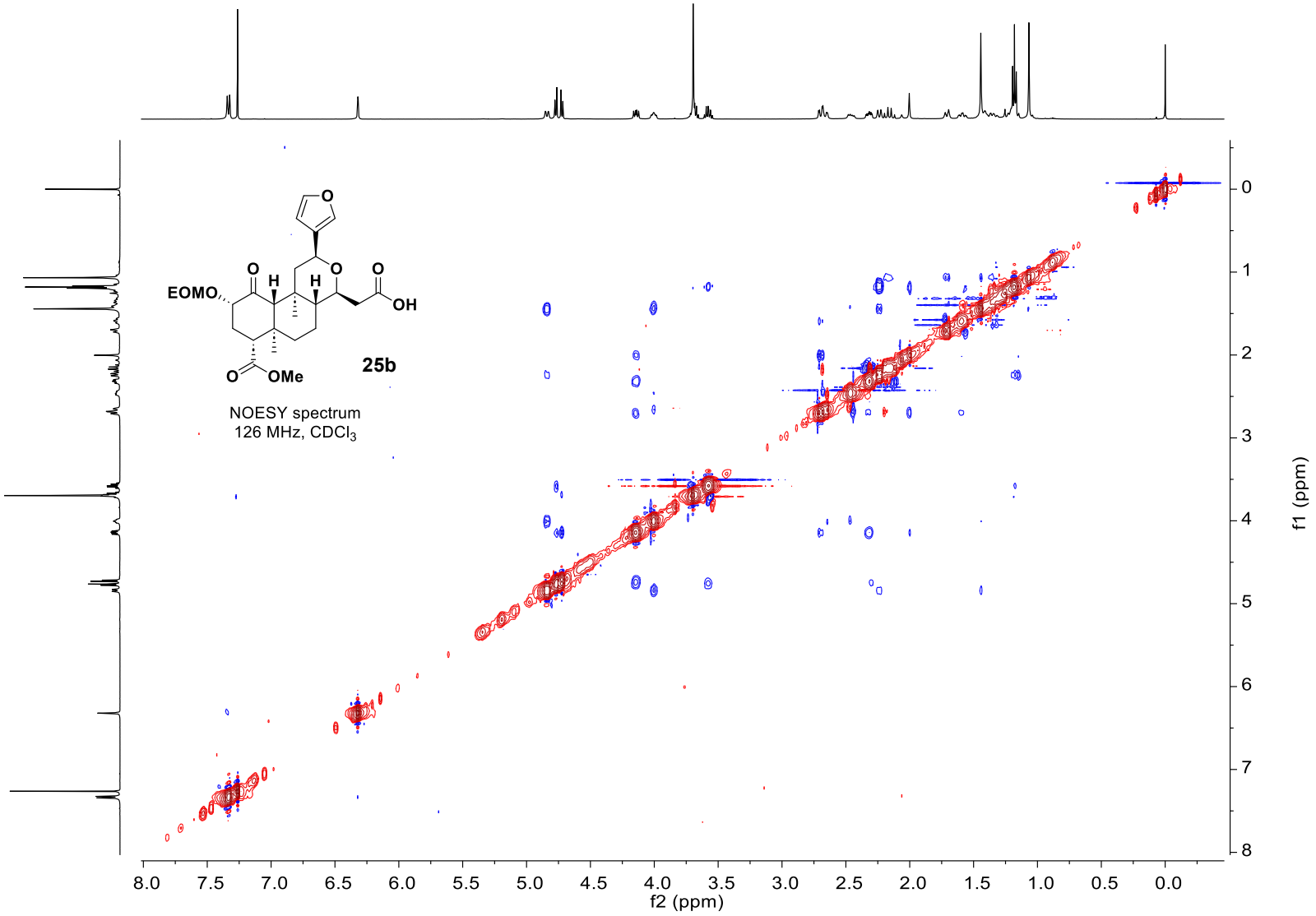
^{1}H spectrum
400 MHz, $CDCl_3$

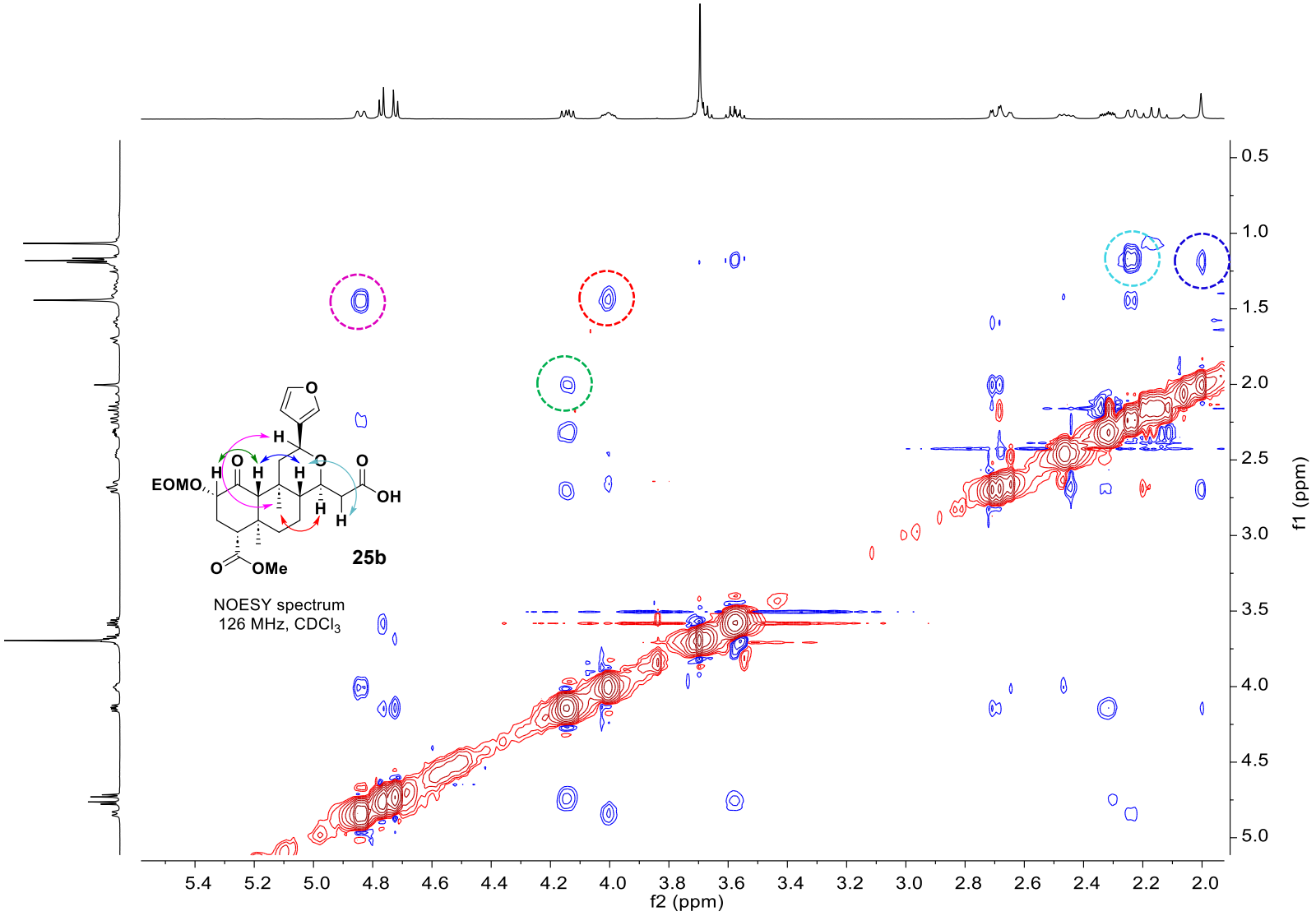

206.45
172.26
143.29
139.16
126.68
108.73
94.48
78.14
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
72.00
67.90
65.70
63.98
54.22
51.86
50.55
45.20
42.41
39.23
35.25
32.91
19.03
16.84
15.25
14.67
EOMO
OH
OMe
25b
13C spectrum
126 MHz, CDCl3
f1 (ppm)

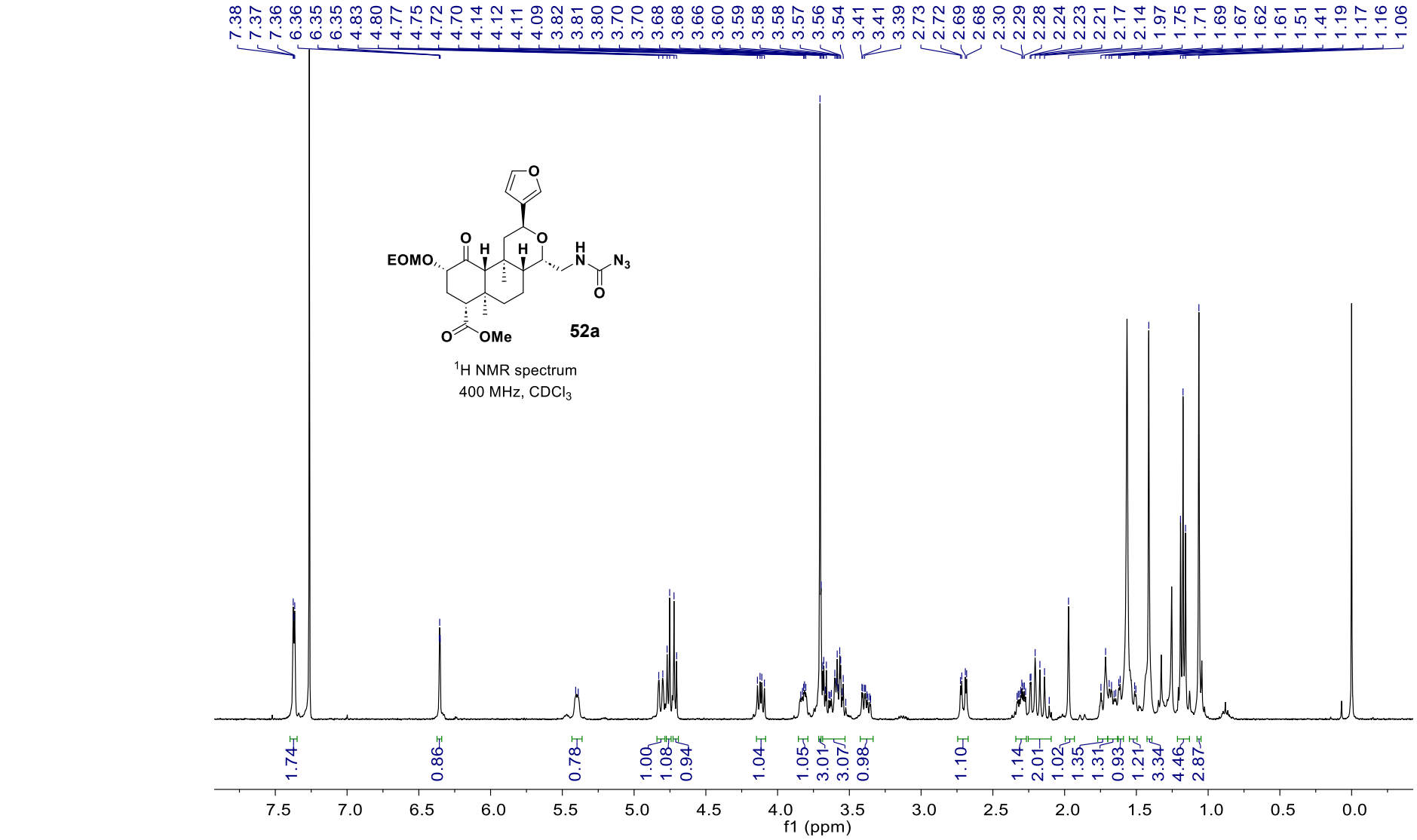

EOMO
O
H
H
O
O
OH
O
OMe
25b
HSQC spectrum
126 MHz, CDCl3
f2 (ppm)
f1 (ppm)

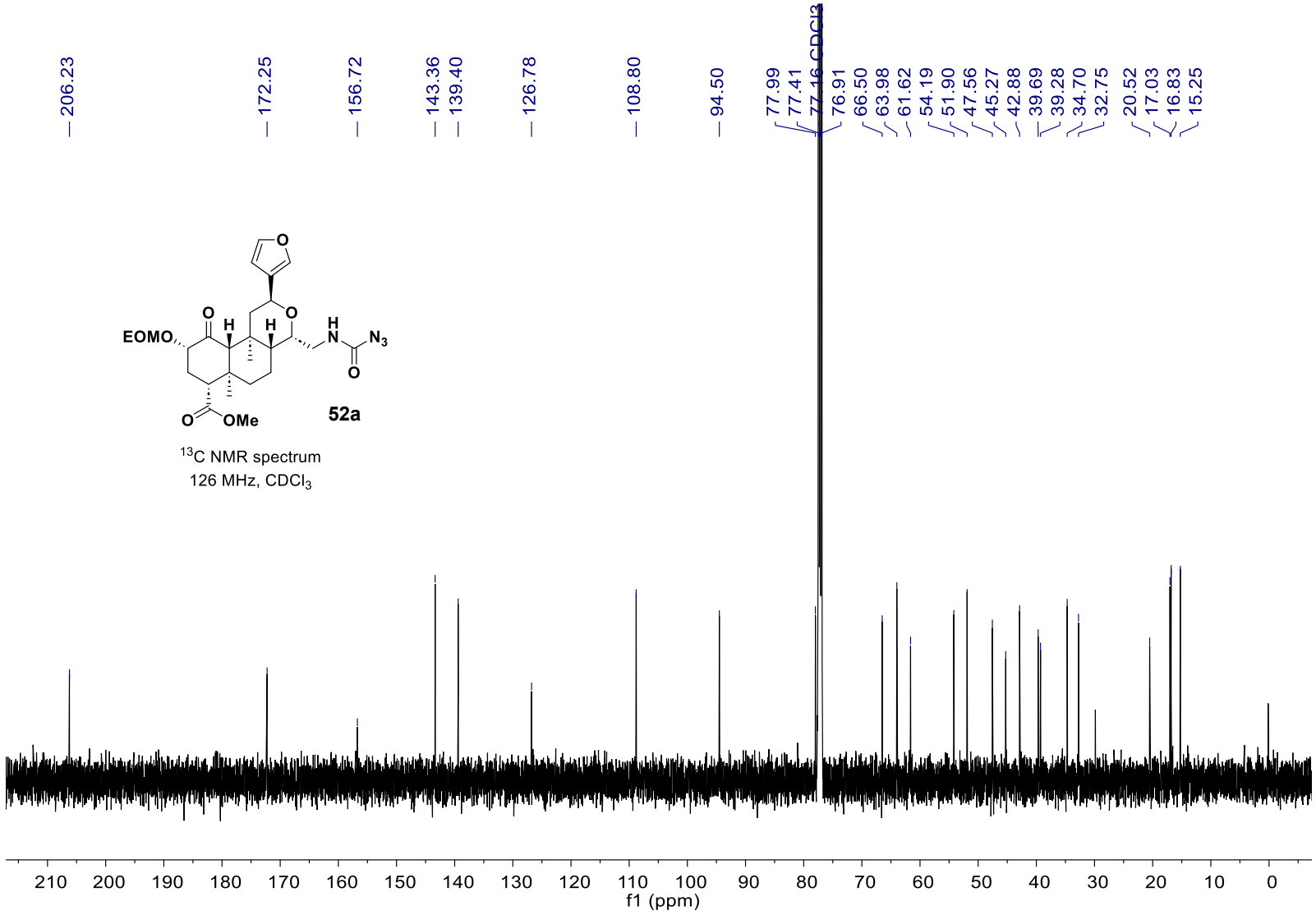

EOMO
OH
OMe
25b
COSEY spectrum
126 MHz, CDCl3
f2 (ppm)
f1 (ppm)

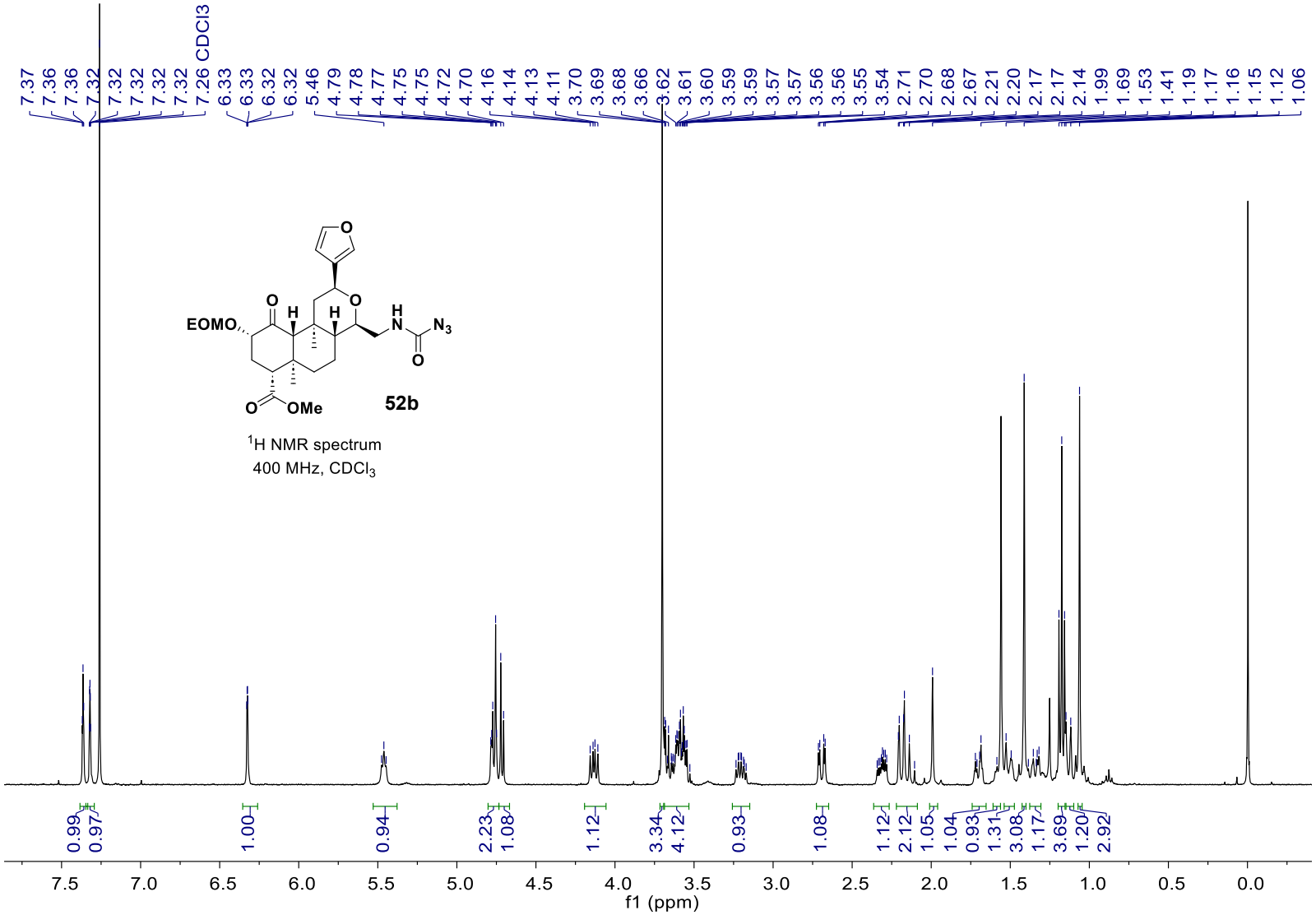

f2 (ppm)
f1 (ppm)
EOMO
OH
OMe
25b
HMBC spectrum
126 MHz, CDCl3

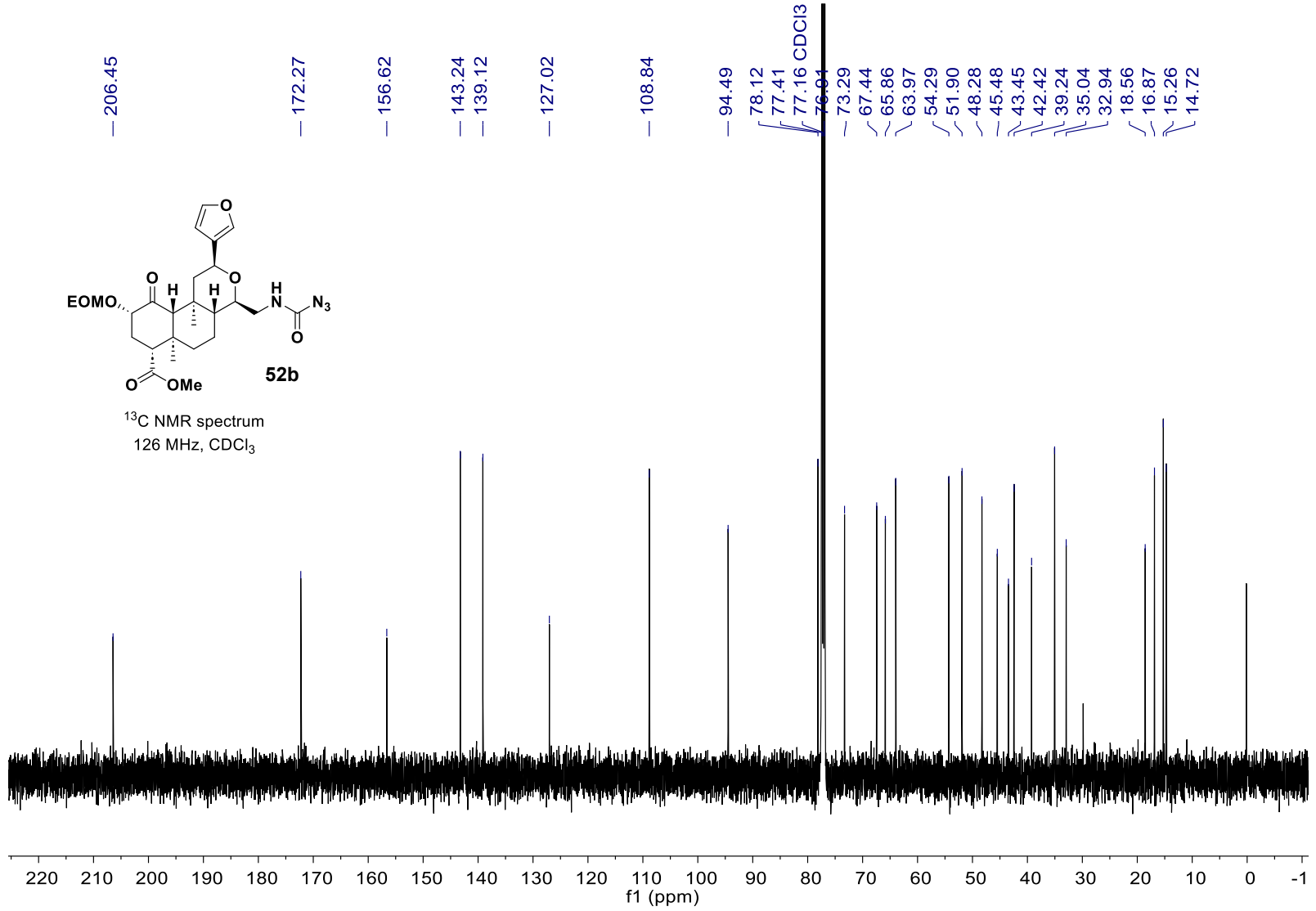

EOMO
O
H
H
O
O
OH
O
OMe
25b
NOESY spectrum
126 MHz, CDCl3
f2 (ppm)
f1 (ppm)

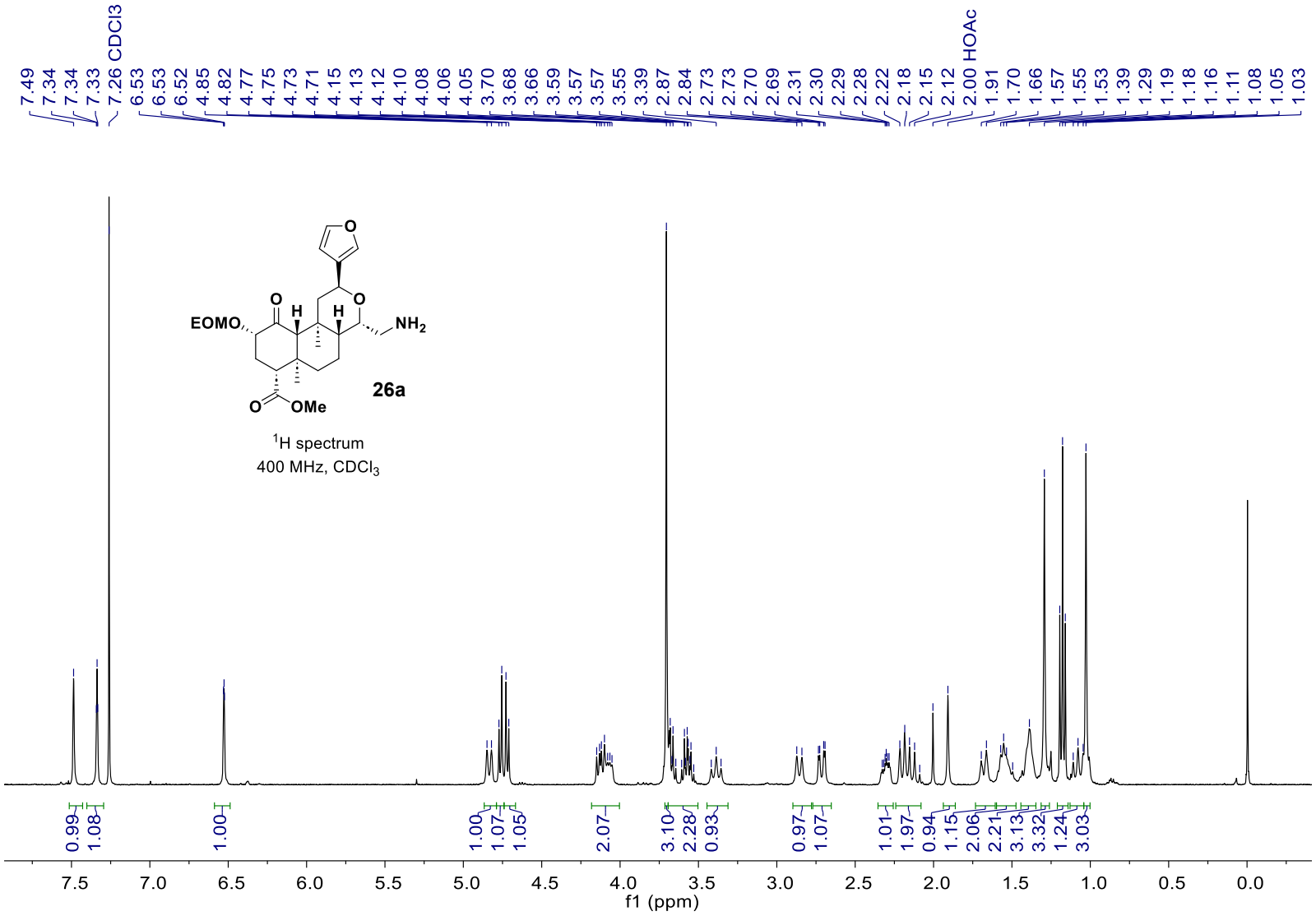

EOMO
OH
OMe
25b
NOESY spectrum
126 MHz, CDCl3
f2 (ppm)
f1 (ppm)
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0

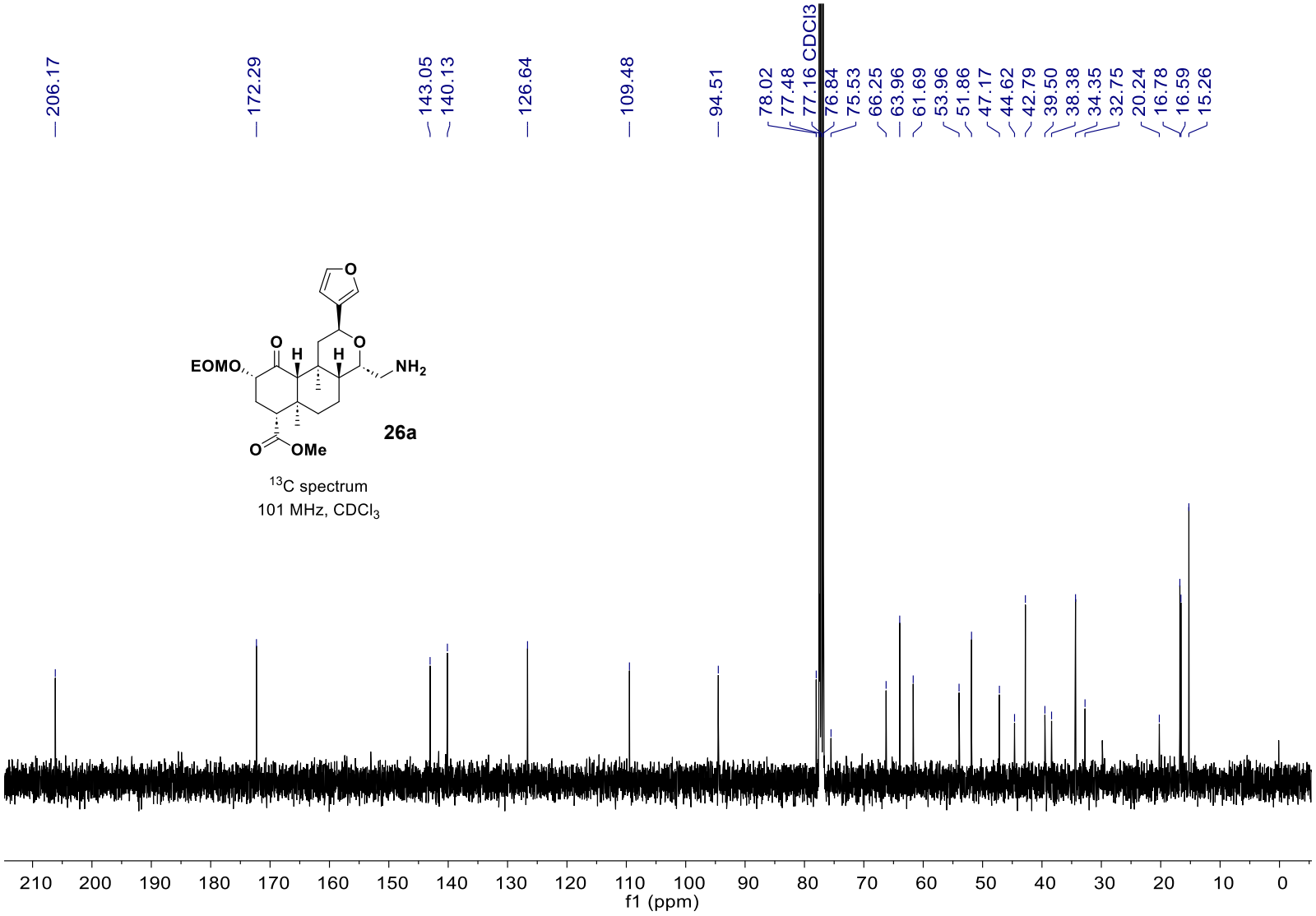

7.38 7.37 7.36 6.36 6.35 6.35 4.83 4.80 4.77 4.75 4.72 4.70 4.14 4.12 4.11 4.09 3.82 3.81 3.80 3.70 3.70 3.68 3.68 3.66 3.60 3.59 3.58 3.58 3.57 3.56 3.54 3.41 3.41 3.39 2.73 2.72 2.69 2.68 2.30 2.29 2.28 2.24 2.23 2.21 2.17 2.14 1.97 1.75 1.71 1.69 1.67 1.62 1.61 1.51 1.41 1.19 1.17 1.16 1.06
EOMO
O
H
H
O
H
N
N3
O
O
OMe
52a
1H NMR spectrum
400 MHz, CDCl3
1.74 0.86 0.78 1.00 1.08 0.94 1.04 1.05 3.01 3.07 0.98 1.10 1.14 2.01 1.02 1.35 1.31 0.93 1.21 3.34 4.46 2.87
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
f1 (ppm)

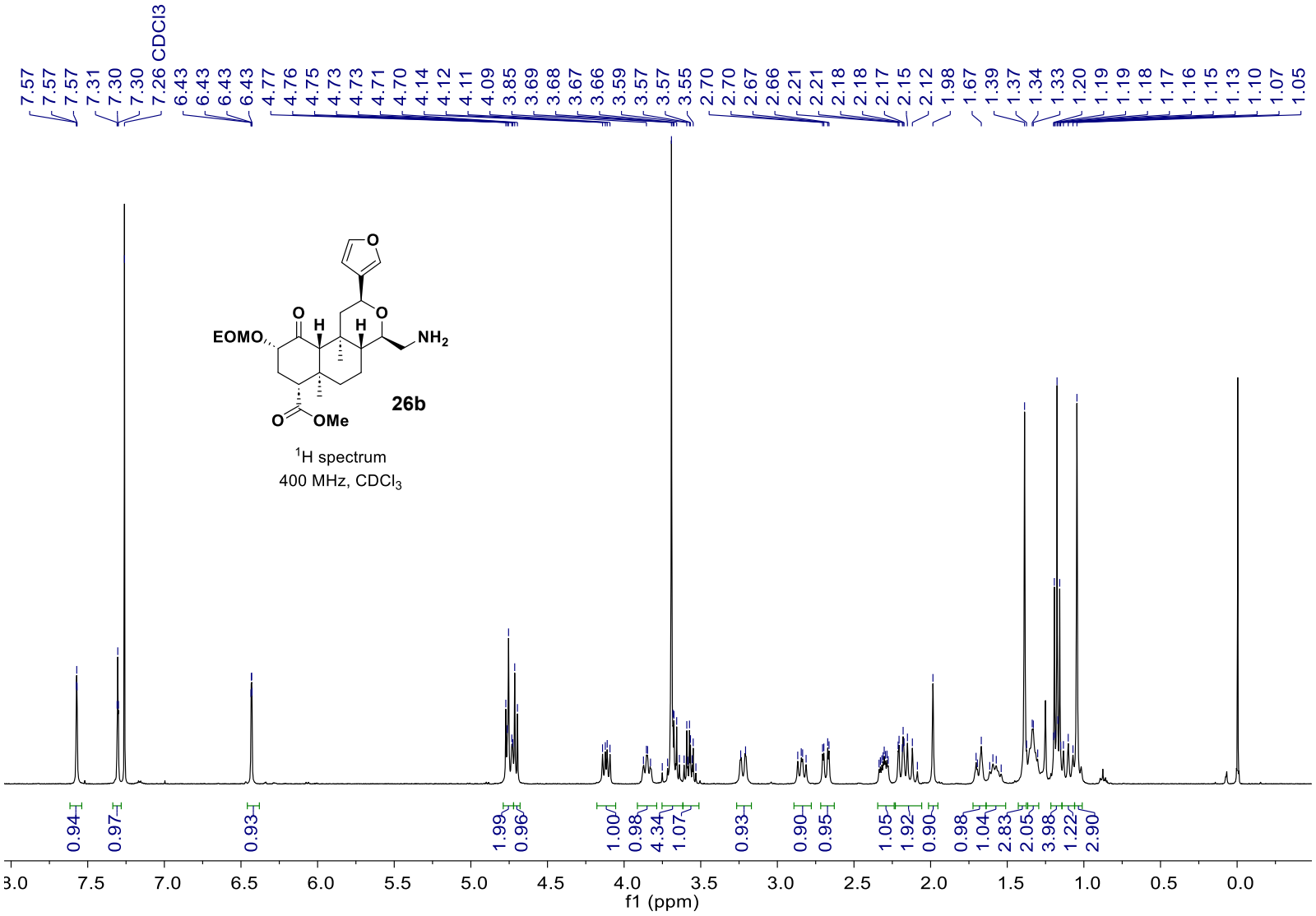

206.23
172.25
156.72
143.36
139.40
126.78
108.80
94.50
77.99
77.41
77.16 CDCl3
76.91
66.50
63.98
61.62
54.19
51.90
47.56
45.27
42.88
39.69
39.28
34.70
32.75
20.52
17.03
16.83
15.25
EOMO
O
H
H
O
H
N
N3
O
O
OMe
52a
13C NMR spectrum
126 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

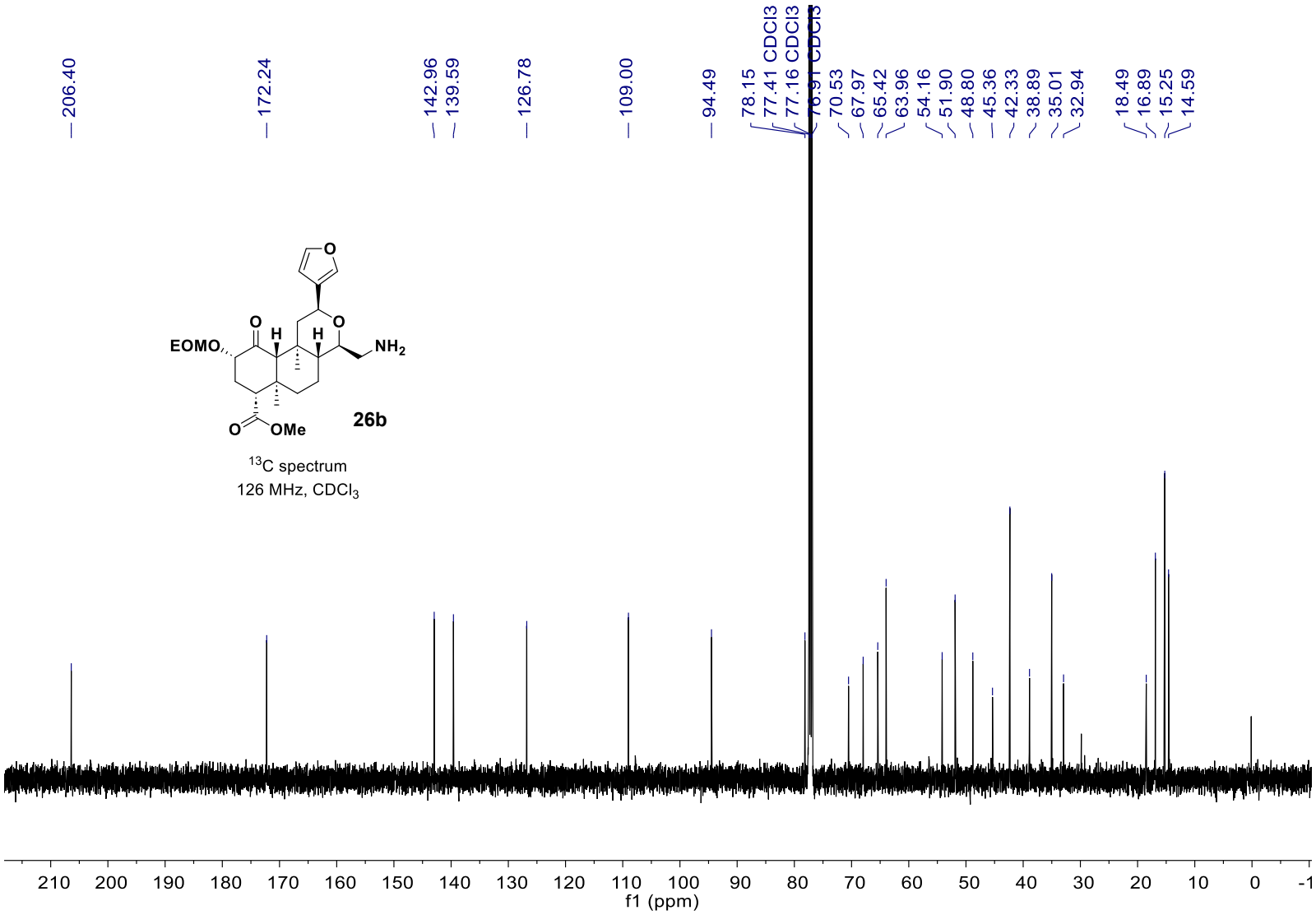

7.37
7.36
7.36
7.32
7.32
7.32
7.32
7.32
7.26 CDCl3
6.33
6.33
6.32
6.32
5.46
4.79
4.78
4.77
4.75
4.75
4.72
4.70
4.16
4.14
4.13
4.11
3.70
3.69
3.68
3.66
3.62
3.61
3.60
3.59
3.59
3.57
3.57
3.56
3.56
3.55
3.54
2.71
2.70
2.68
2.67
2.21
2.20
2.17
2.17
2.14
1.99
1.69
1.53
1.41
1.19
1.17
1.16
1.15
1.12
1.06
EOMO
O
H
H
O
H
N
N3
O
O
OMe
52b
1H NMR spectrum
400 MHz, CDCl3
0.99
0.97
1.00
0.94
2.23
1.08
1.12
3.34
4.12
0.93
1.08
1.12
2.12
1.05
1.04
0.93
1.31
3.08
1.17
3.69
1.20
2.92
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
f1 (ppm)

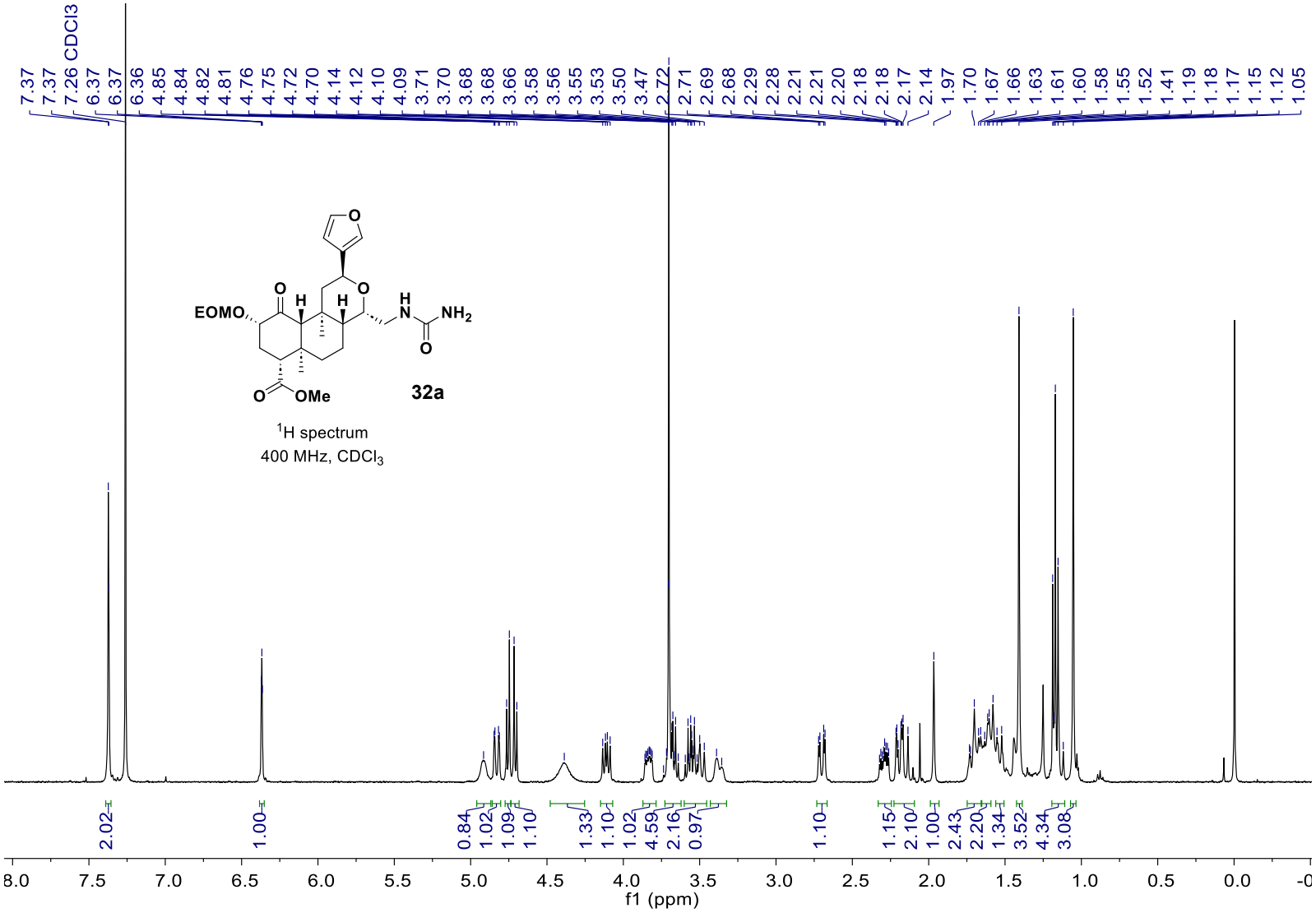

206.45
172.27
156.62
143.24
139.12
127.02
108.84
94.49
78.12
77.41
77.16 CDCl3
76.91
73.29
67.44
65.86
63.97
54.29
51.90
48.28
45.48
43.45
42.42
39.24
35.04
32.94
18.56
16.87
15.26
14.72
EOMO
O
H
H
O
H
N
N3
O
O
OMe
52b
13C NMR spectrum
126 MHz, CDCl3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

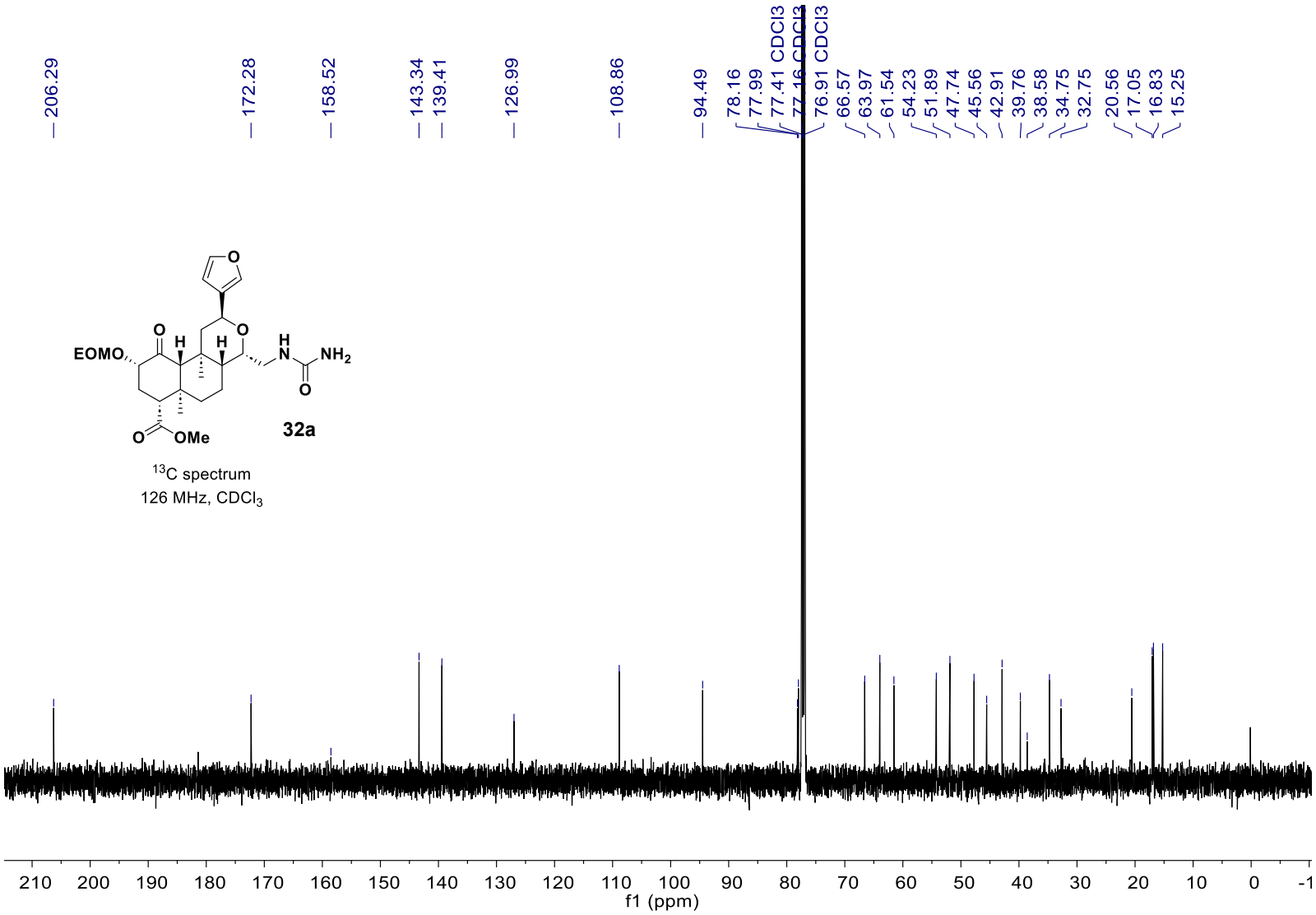

7.49
7.34
7.34
7.33
7.26 CDCl3
6.53
6.53
6.52
4.85
4.82
4.77
4.75
4.73
4.71
4.15
4.13
4.12
4.10
4.08
4.06
4.05
3.70
3.68
3.66
3.59
3.57
3.57
3.55
3.39
2.87
2.84
2.73
2.73
2.70
2.69
2.31
2.30
2.29
2.28
2.22
2.18
2.15
2.12
2.00 HOAc
1.91
1.70
1.66
1.57
1.55
1.53
1.39
1.29
1.19
1.18
1.16
1.11
1.08
1.05
1.03
EOMO
O
H
H
O
O
NH2
O
OMe
26a
1H spectrum
400 MHz, CDCl3
0.99
1.08
1.00
1.00
1.07
1.05
2.07
3.10
2.28
0.93
0.97
1.07
1.01
1.97
0.94
1.15
2.06
2.21
3.13
3.32
1.24
3.03
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
f1 (ppm)

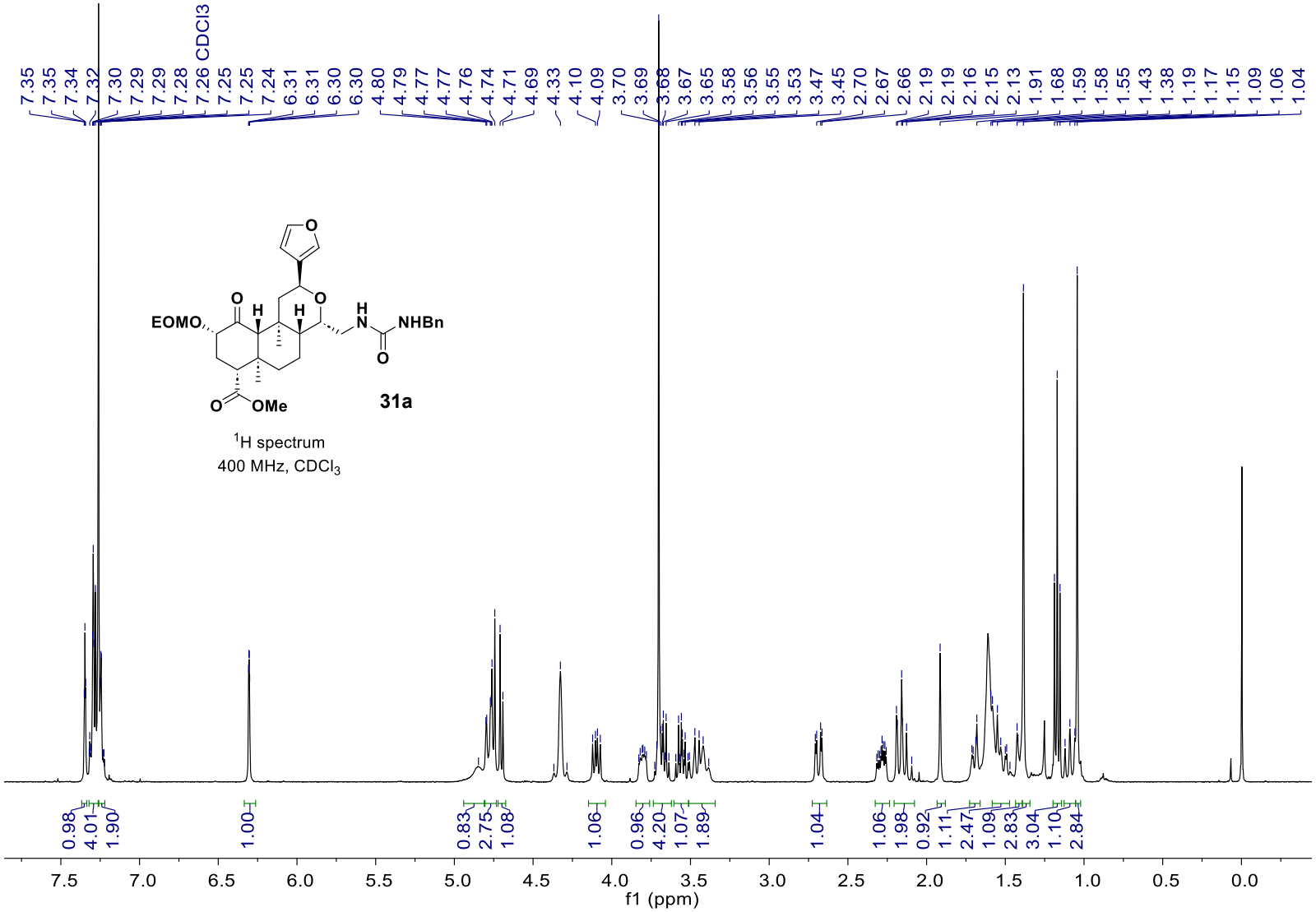

206.17
172.29
143.05
140.13
126.64
109.48
94.51
78.02
77.48
77.16 CDCl3
76.84
75.53
66.25
63.96
61.69
53.96
51.86
47.17
44.62
42.79
39.50
38.38
34.35
32.75
20.24
16.78
16.59
15.26
EOMO
O
H
H
O
NH2
O
OMe
26a
13C spectrum
101 MHz, CDCl3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

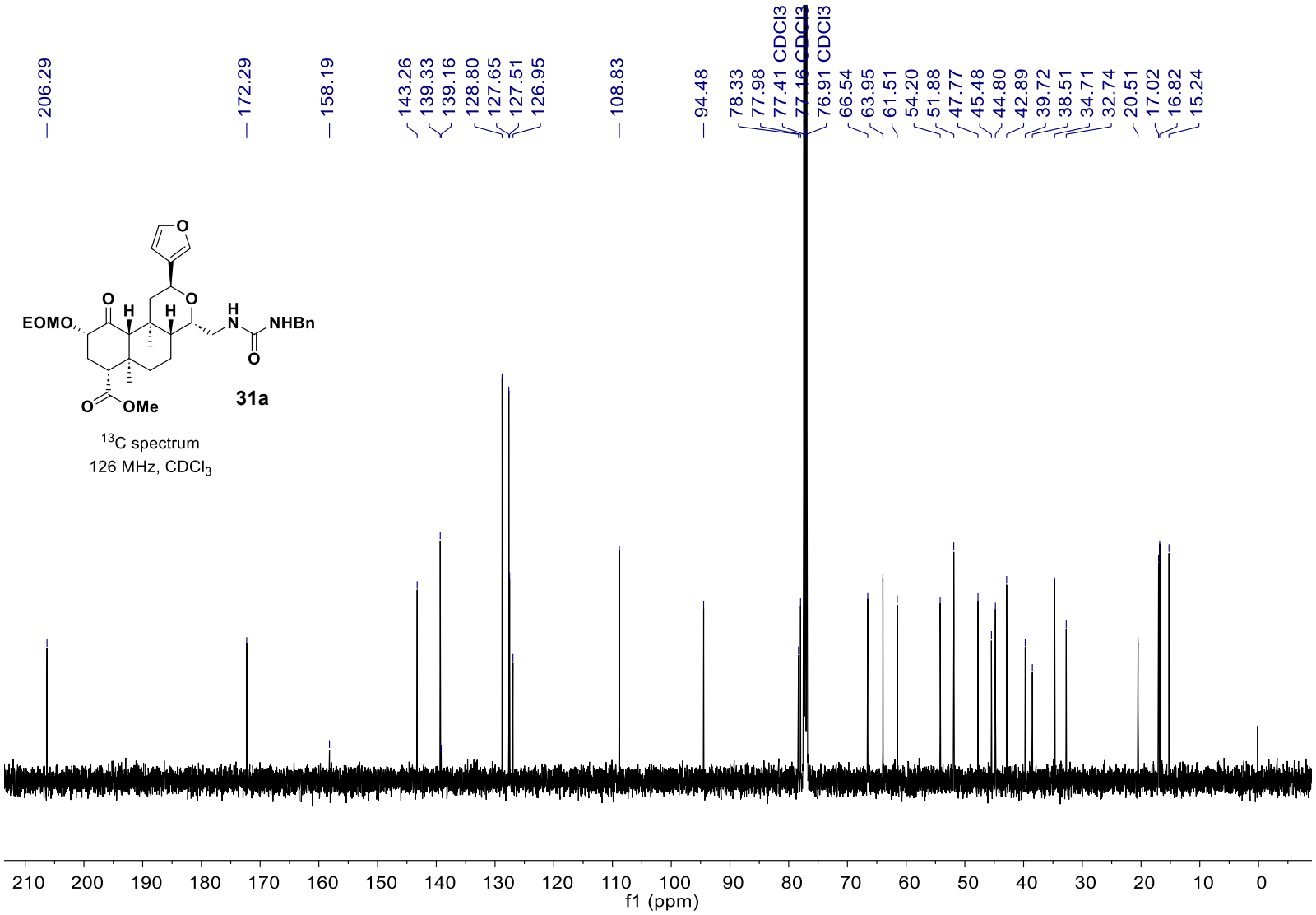

7.57 7.57 7.57 7.31 7.30 7.30 7.26 CDCl3 6.43 6.43 6.43 6.43 4.77 4.76 4.75 4.73 4.73 4.71 4.70 4.14 4.12 4.11 4.09 3.85 3.69 3.68 3.67 3.66 3.59 3.57 3.57 3.55 2.70 2.70 2.67 2.66 2.21 2.21 2.18 2.18 2.17 2.15 2.12 1.98 1.67 1.39 1.37 1.34 1.33 1.20 1.19 1.19 1.18 1.17 1.16 1.15 1.13 1.10 1.07 1.05
EOMO
O
H
H
O
NH2
O
OMe
26b
1H spectrum
400 MHz, CDCl3
0.94 0.97 0.93 1.99 0.96 1.00 0.98 4.34 1.07 0.93 0.90 0.95 1.05 1.92 0.90 0.98 1.04 2.83 2.05 3.98 1.22 2.90
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
f1 (ppm)

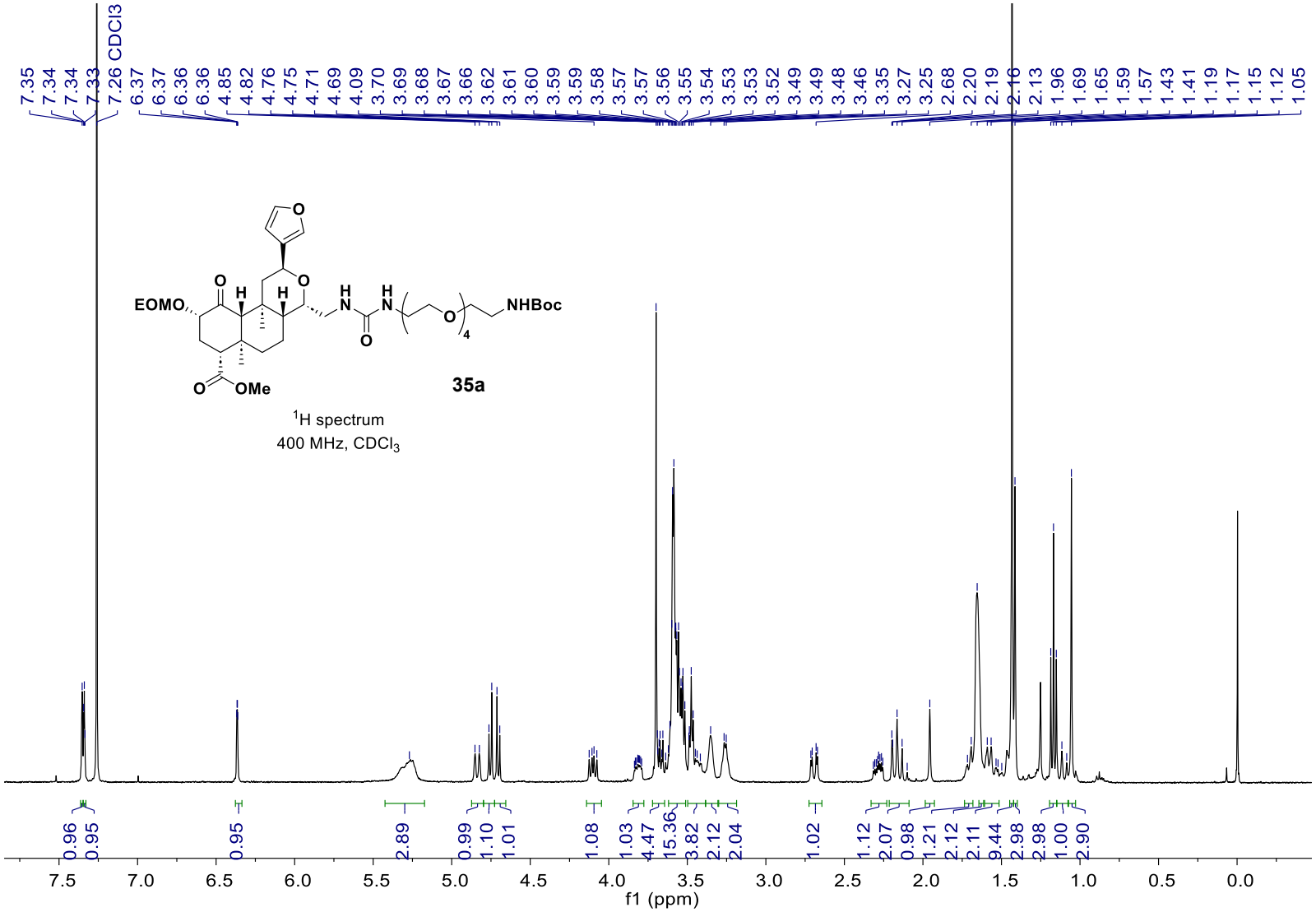

206.40
172.24
142.96
139.59
126.78
109.00
94.49
78.15
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
70.53
67.97
65.42
63.96
54.16
51.90
48.80
45.36
42.33
38.89
35.01
32.94
18.49
16.89
15.25
14.59
EOMO
O
H
H
O
NH2
O
OMe
26b
13C spectrum
126 MHz, CDCl3
f1 (ppm)

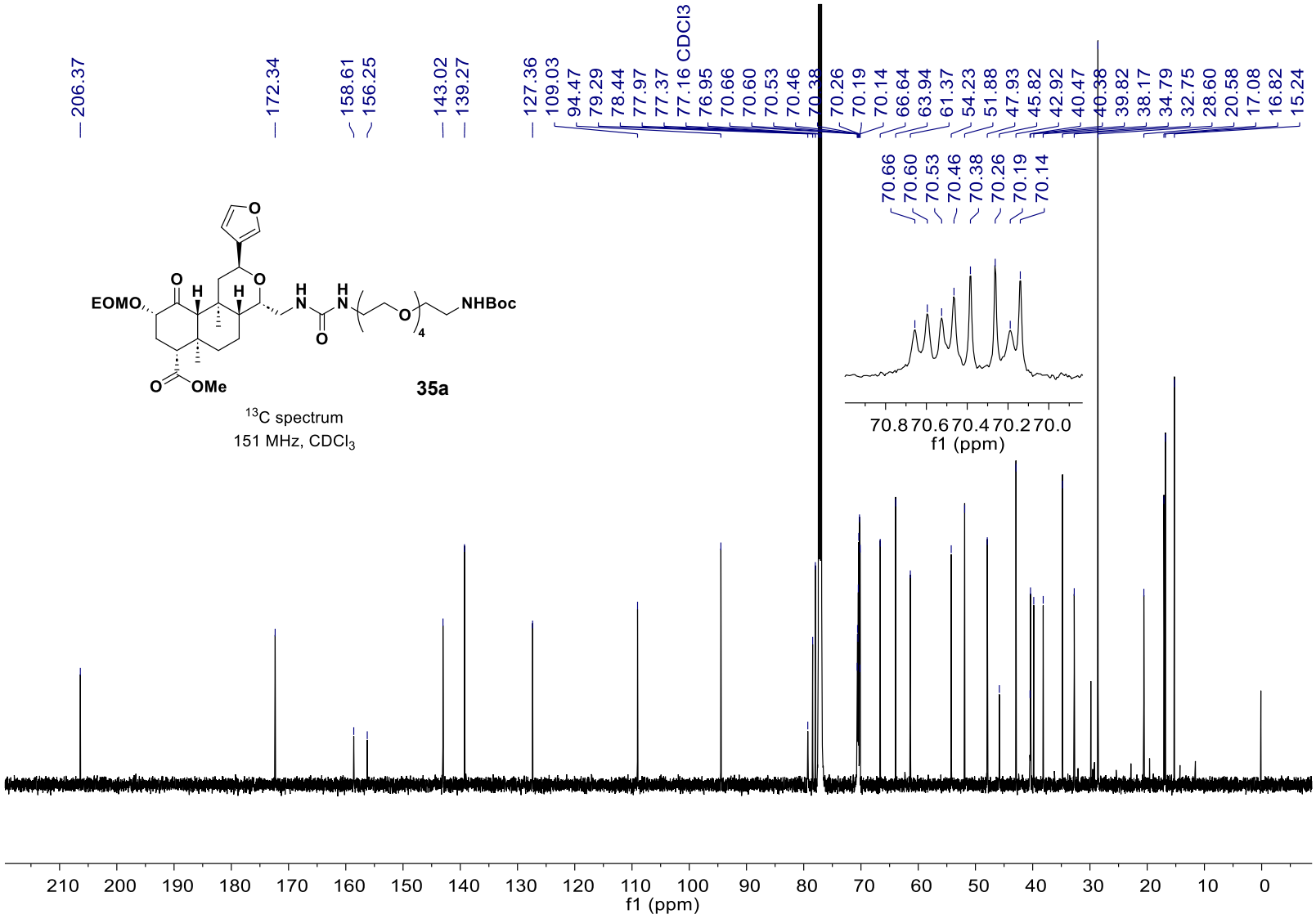

7.37
7.37
7.26 CDCl3
6.37
6.37
6.36
4.85
4.84
4.82
4.81
4.76
4.75
4.72
4.70
4.14
4.12
4.10
4.09
3.71
3.70
3.68
3.68
3.66
3.58
3.56
3.55
3.53
3.50
3.47
2.72
2.71
2.69
2.68
2.29
2.28
2.21
2.21
2.20
2.18
2.18
2.17
2.14
1.97
1.70
1.67
1.66
1.63
1.61
1.60
1.58
1.55
1.52
1.41
1.19
1.18
1.17
1.15
1.12
1.05
EOMO
O
H
H
O
H
N
NH2
O
O
OMe
32a
1H spectrum
400 MHz, CDCl3
2.02
1.00
0.84
1.02
1.09
1.10
1.33
1.10
1.02
4.59
2.16
0.97
1.10
1.15
2.10
1.00
2.43
2.20
1.34
3.52
4.34
3.08
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
f1 (ppm)

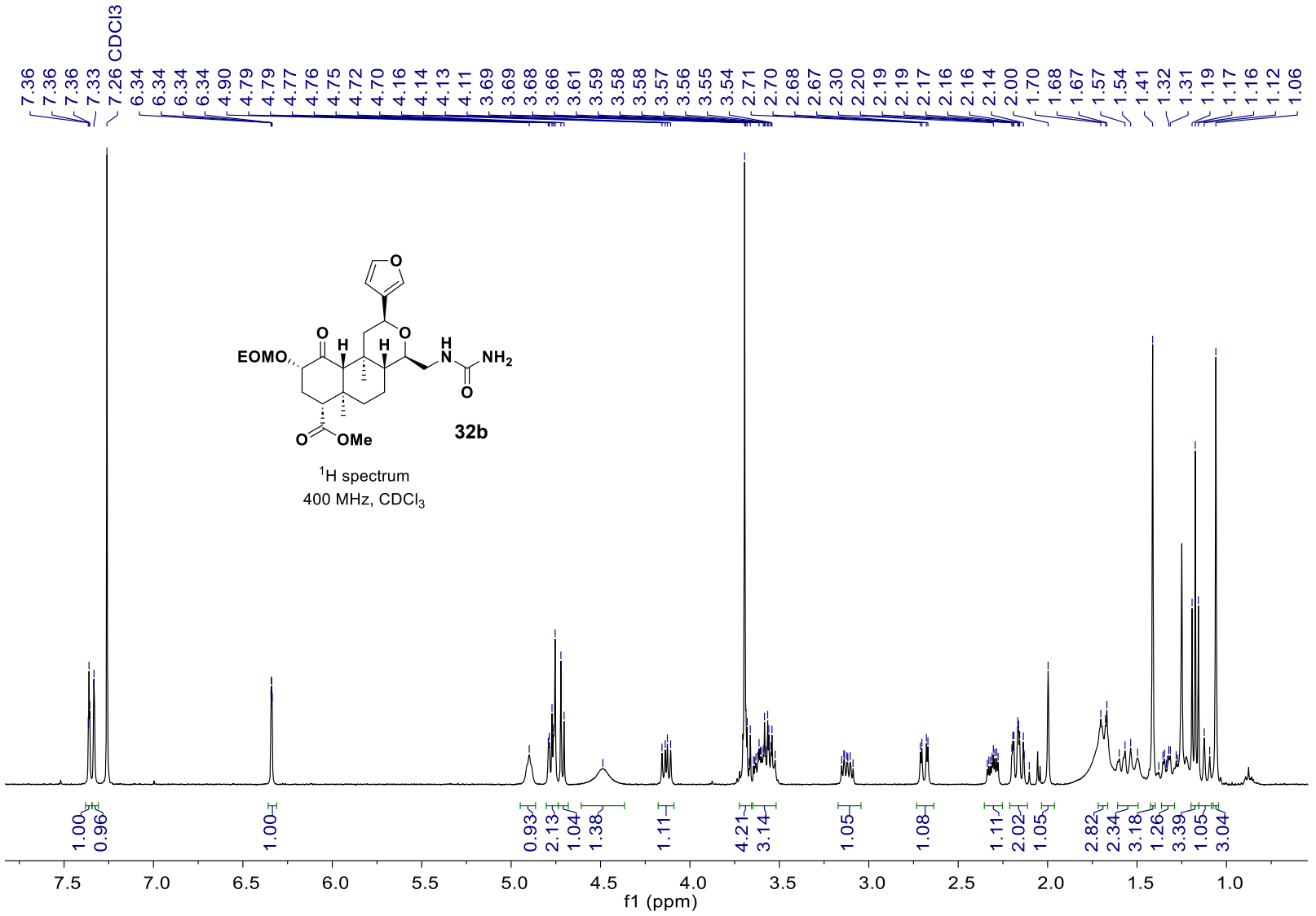

206.29
172.28
158.52
143.34
139.41
126.99
108.86
94.49
78.16
77.99
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
66.57
63.97
61.54
54.23
51.89
47.74
45.56
42.91
39.76
38.58
34.75
32.75
20.56
17.05
16.83
15.25
EOMO
O
H
H
O
H
N
NH2
O
O
OMe
32a
13C spectrum
126 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

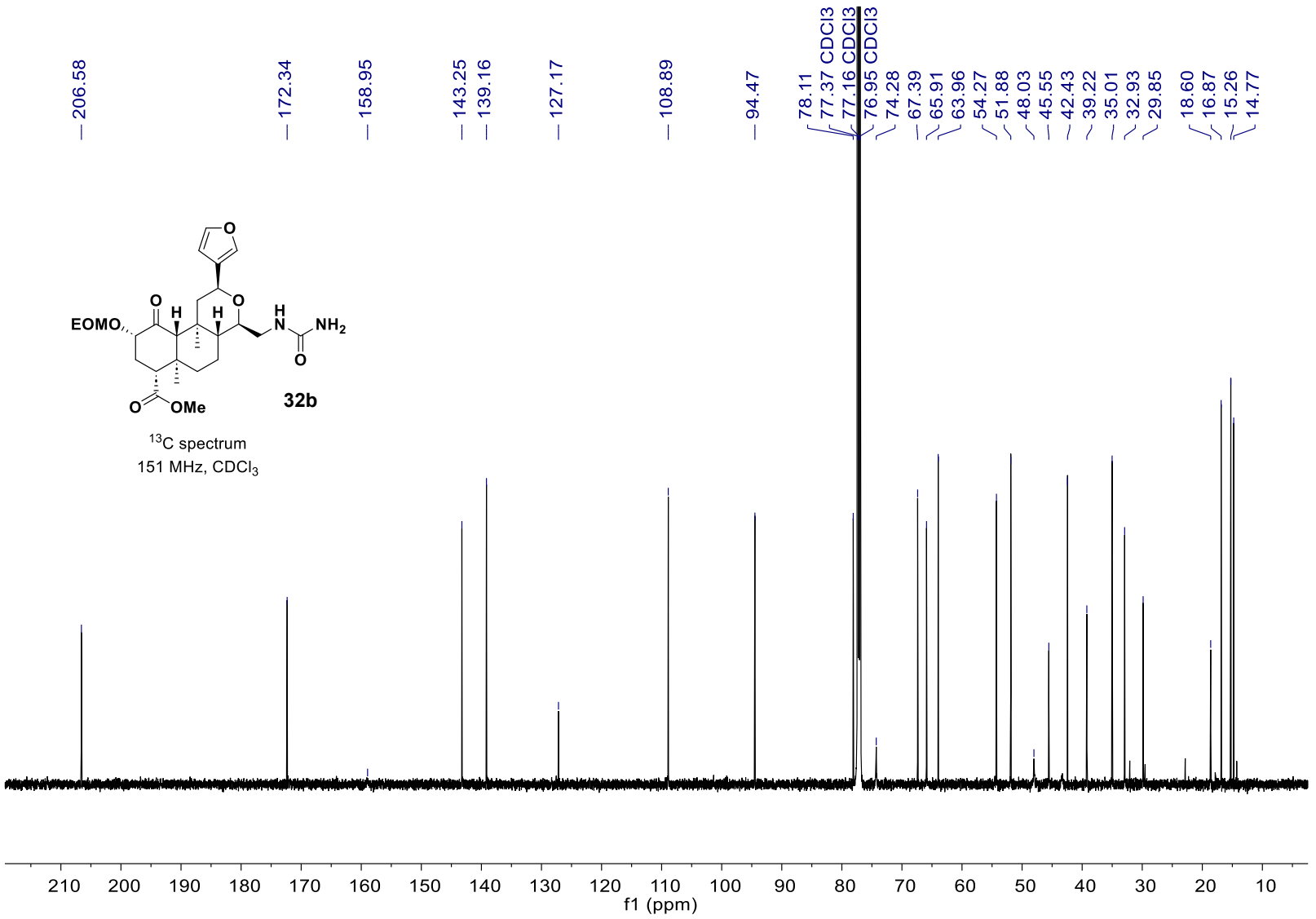

7.35 7.35 7.34 7.32 7.30 7.29 7.29 7.28 7.26 CDCl3 7.25 7.25 7.24 6.31 6.31 6.30 6.30
4.80 4.79 4.77 4.77 4.76 4.74 4.71 4.69 4.33 4.10 4.09 3.70 3.69 3.68 3.67 3.65 3.58 3.56 3.55 3.53 3.47 3.45 2.70 2.67 2.66 2.19 2.19 2.16 2.15 2.13 1.91 1.68 1.59 1.58 1.55 1.43 1.38 1.19 1.17 1.15 1.09 1.06 1.04
EOMO
O
H
H
O
H
N
NHBn
O
O
OMe
31a
1H spectrum
400 MHz, CDCl3
0.98 4.01 1.90 1.00 0.83 2.75 1.08 1.06 0.96 4.20 1.07 1.89 1.04 1.06 1.98 0.92 1.11 2.47 1.09 2.83 3.04 1.10 2.84
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
f1 (ppm)

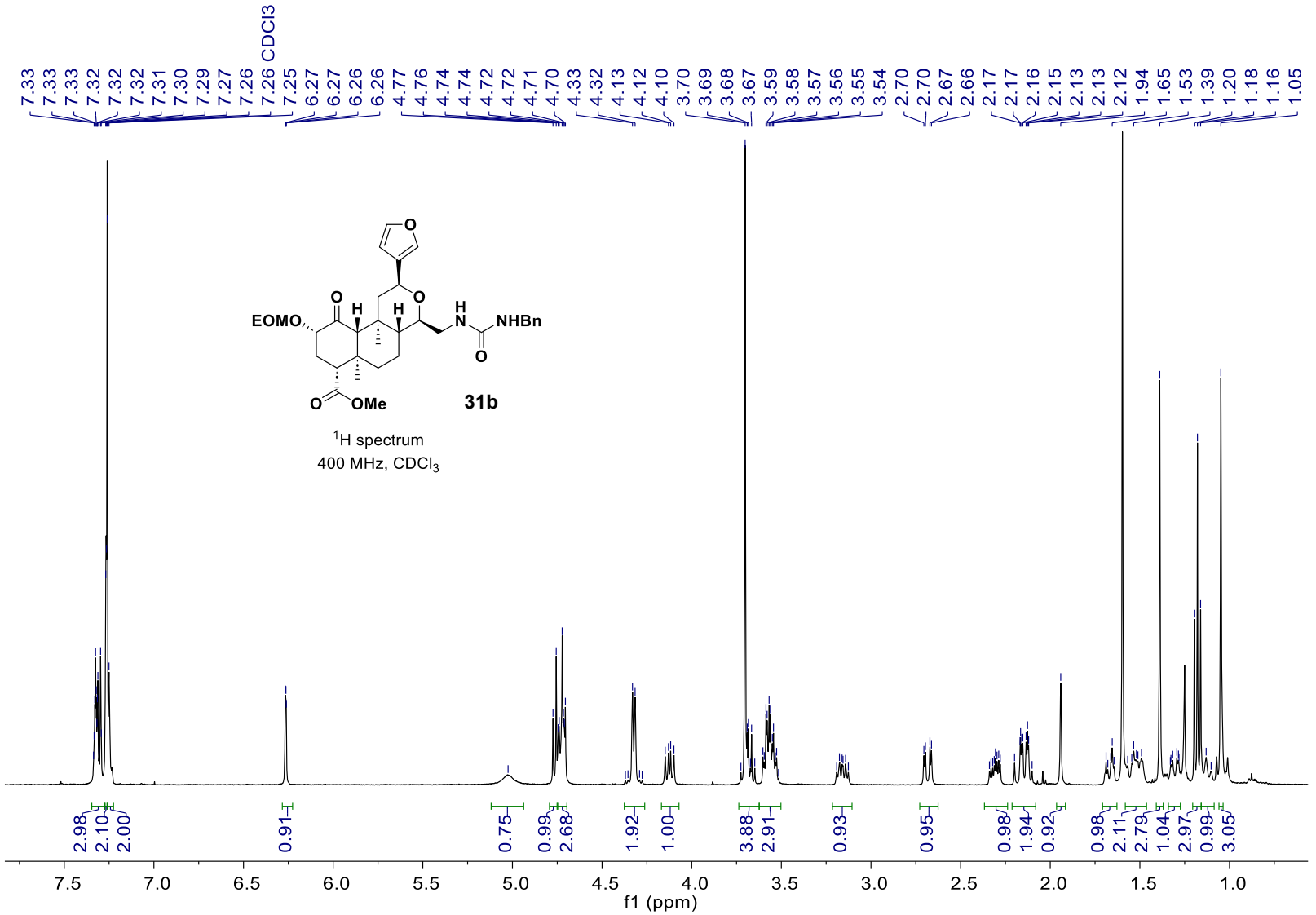

206.29
172.29
158.19
143.26
139.33
139.16
128.80
127.65
127.51
126.95
108.83
94.48
78.33
77.98
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
66.54
63.95
61.51
54.20
51.88
47.77
45.48
44.80
42.89
39.72
38.51
34.71
32.74
20.51
17.02
16.82
15.24
EOMO
NHBn
OMe
31a
13C spectrum
126 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

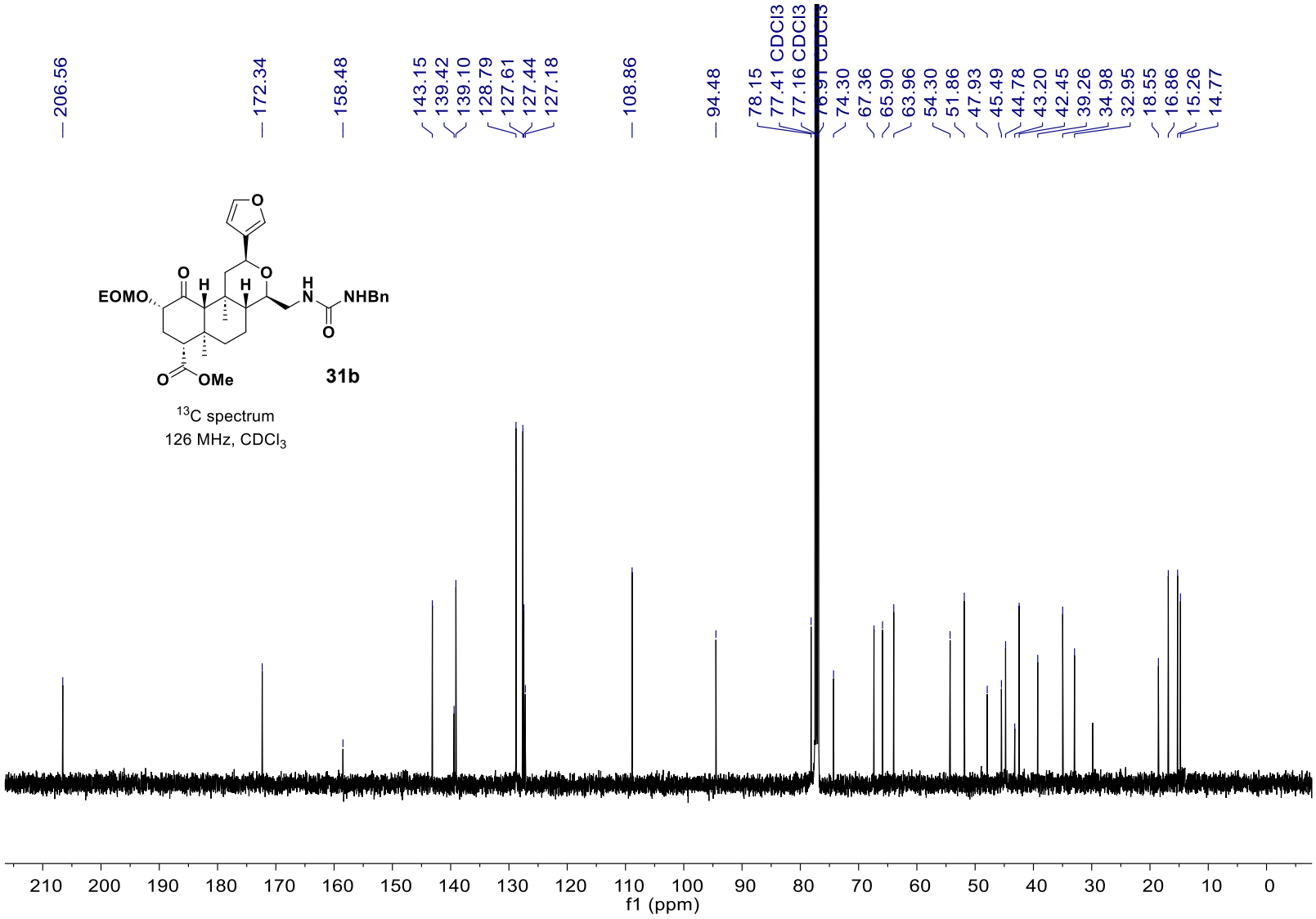

7.35 7.34 7.34 7.33 7.26 CDCl3 6.37 6.37 6.36 6.36 4.85 4.82 4.76 4.75 4.71 4.69 4.09 3.70 3.69 3.68 3.67 3.66 3.62 3.61 3.60 3.59 3.59 3.58 3.57 3.57 3.56 3.55 3.54 3.53 3.53 3.52 3.49 3.49 3.48 3.46 3.35 3.27 3.25 2.68 2.20 2.19 2.16 2.13 1.96 1.69 1.65 1.59 1.57 1.43 1.41 1.19 1.17 1.15 1.12 1.05
EOMO
NHBoc
OMe
35a
1H spectrum
400 MHz, CDCl3
0.96 0.95 0.95 2.89 0.99 1.10 1.01 1.08 1.03 4.47 15.36 3.82 2.12 2.04 1.02 1.12 2.07 0.98 1.21 2.12 2.11 9.44 2.98 2.98 1.00 2.90
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
f1 (ppm)

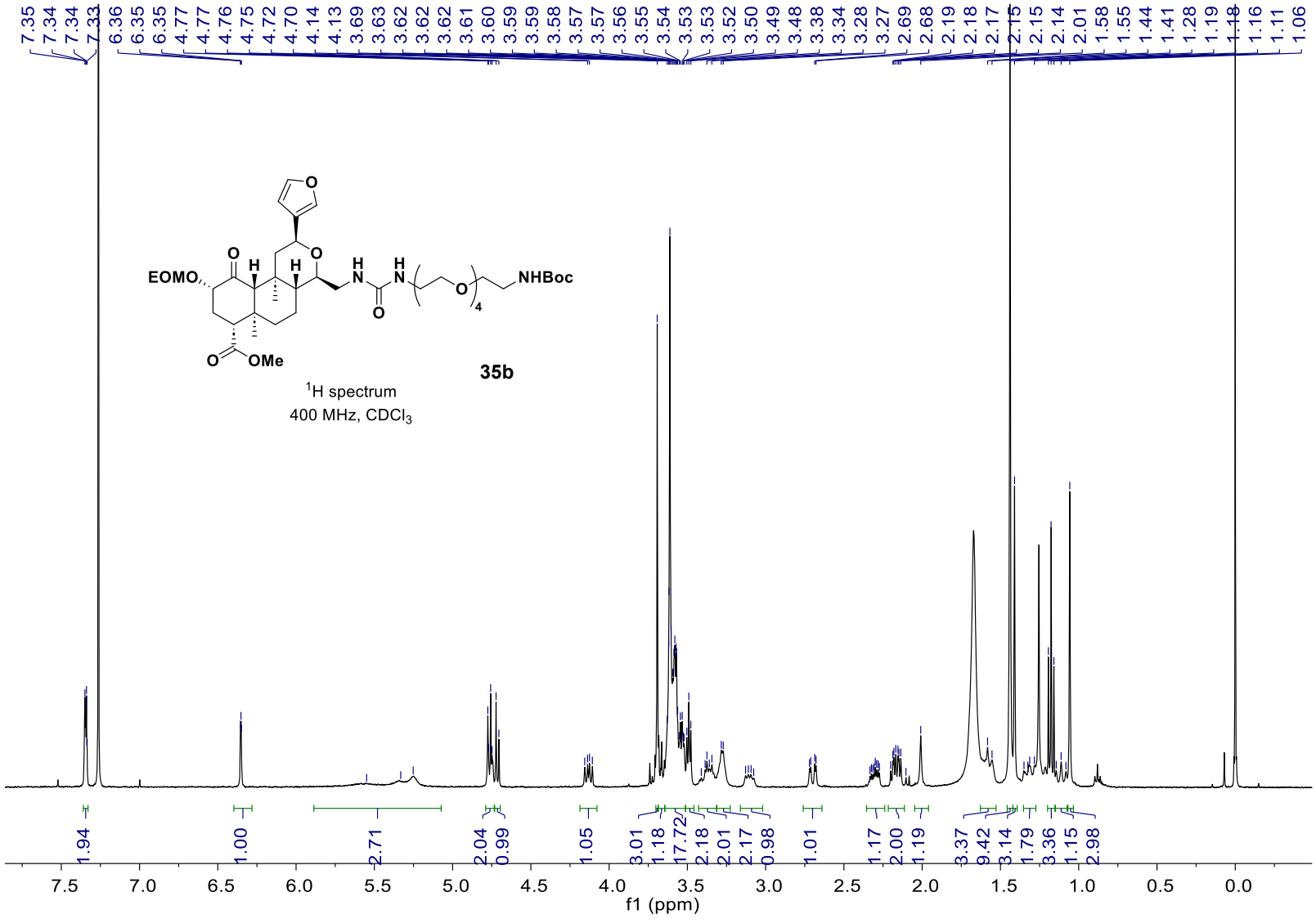

206.37
172.34
158.61
156.25
143.02
139.27
127.36
109.03
94.47
79.29
78.44
77.97
77.37
77.16 CDCl3
76.95
70.66
70.60
70.53
70.46
70.38
70.26
70.19
70.14
66.64
63.94
61.37
54.23
51.88
47.93
45.82
42.92
40.47
40.38
39.82
38.17
34.79
32.75
28.60
20.58
17.08
16.82
15.24
EOMO
NHBoc
OMe
35a
13C spectrum
151 MHz, CDCl3
70.8 70.6 70.4 70.2 70.0
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)

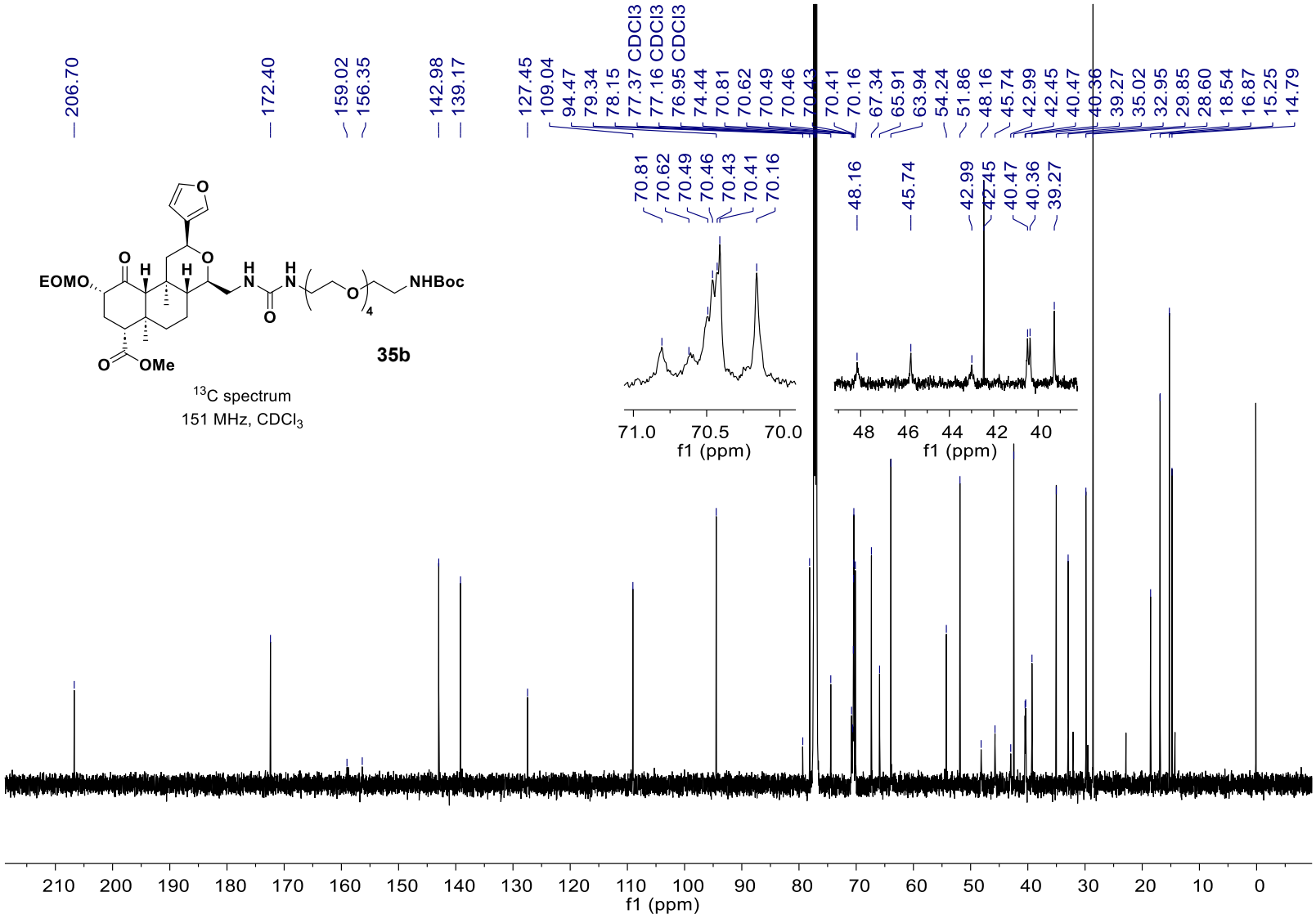

7.36
7.36
7.36
7.33
7.26 CDCl3
6.34
6.34
6.34
6.34
4.90
4.79
4.79
4.77
4.76
4.75
4.72
4.70
4.16
4.14
4.13
4.11
3.69
3.69
3.68
3.66
3.61
3.59
3.58
3.58
3.57
3.56
3.55
3.54
2.71
2.70
2.68
2.67
2.30
2.20
2.19
2.19
2.17
2.16
2.16
2.14
2.00
1.70
1.68
1.67
1.57
1.54
1.41
1.32
1.31
1.19
1.17
1.16
1.12
1.06
EOMO
O
H
H
O
H
N
NH2
O
O
OMe
32b
1H spectrum
400 MHz, CDCl3
1.00
0.96
1.00
0.93
2.13
1.04
1.38
1.11
4.21
3.14
1.05
1.08
1.11
2.02
1.05
2.82
2.34
3.18
1.26
3.39
1.05
3.04
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
f1 (ppm)

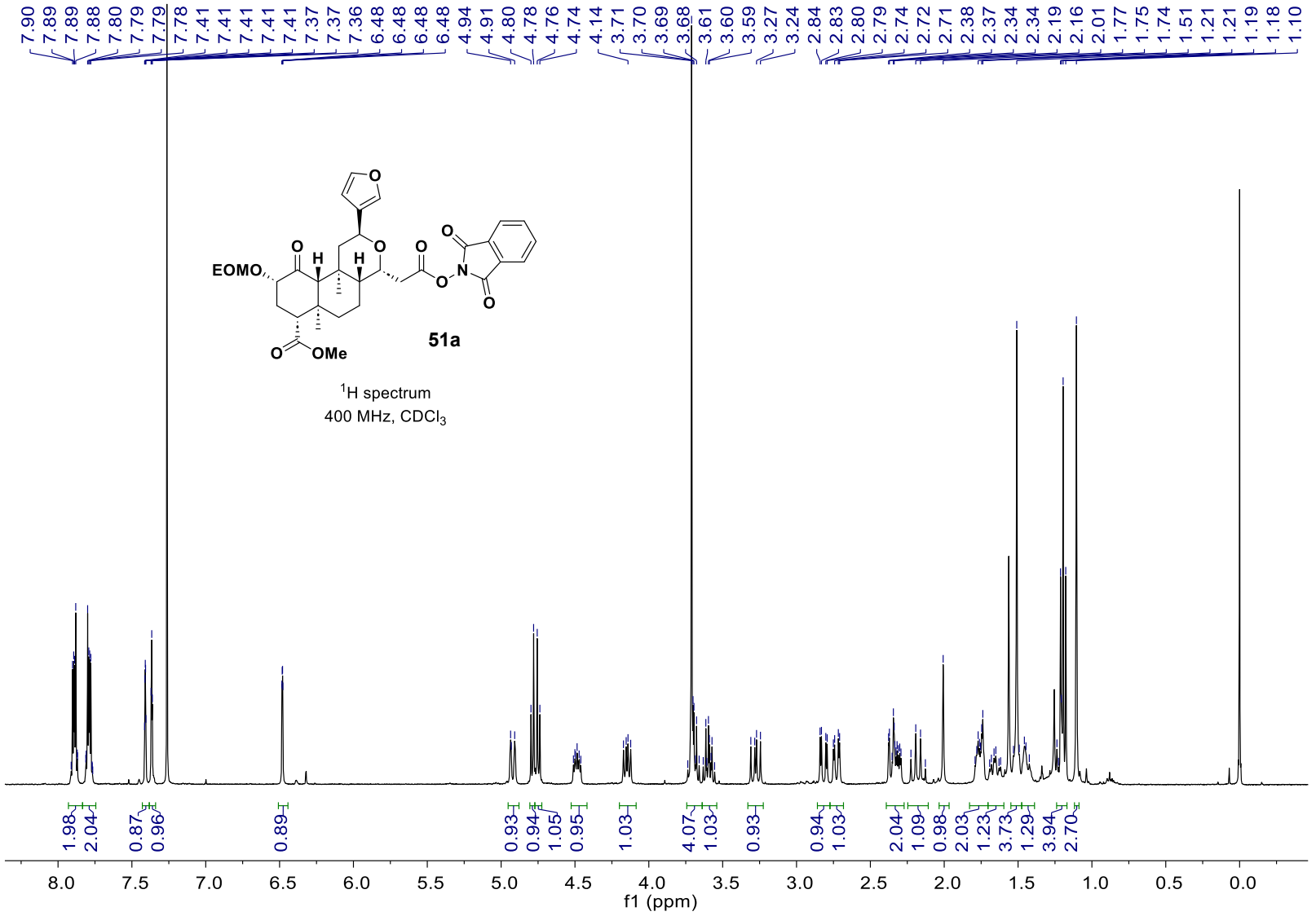

206.58
172.34
158.95
143.25
139.16
127.17
108.89
94.47
78.11
77.37 CDCl3
77.16 CDCl3
76.95 CDCl3
74.28
67.39
65.91
63.96
54.27
51.88
48.03
45.55
42.43
39.22
35.01
32.93
29.85
18.60
16.87
15.26
14.77
EOMO
OMe
NH2
32b
13C spectrum
151 MHz, CDCl3
f1 (ppm)

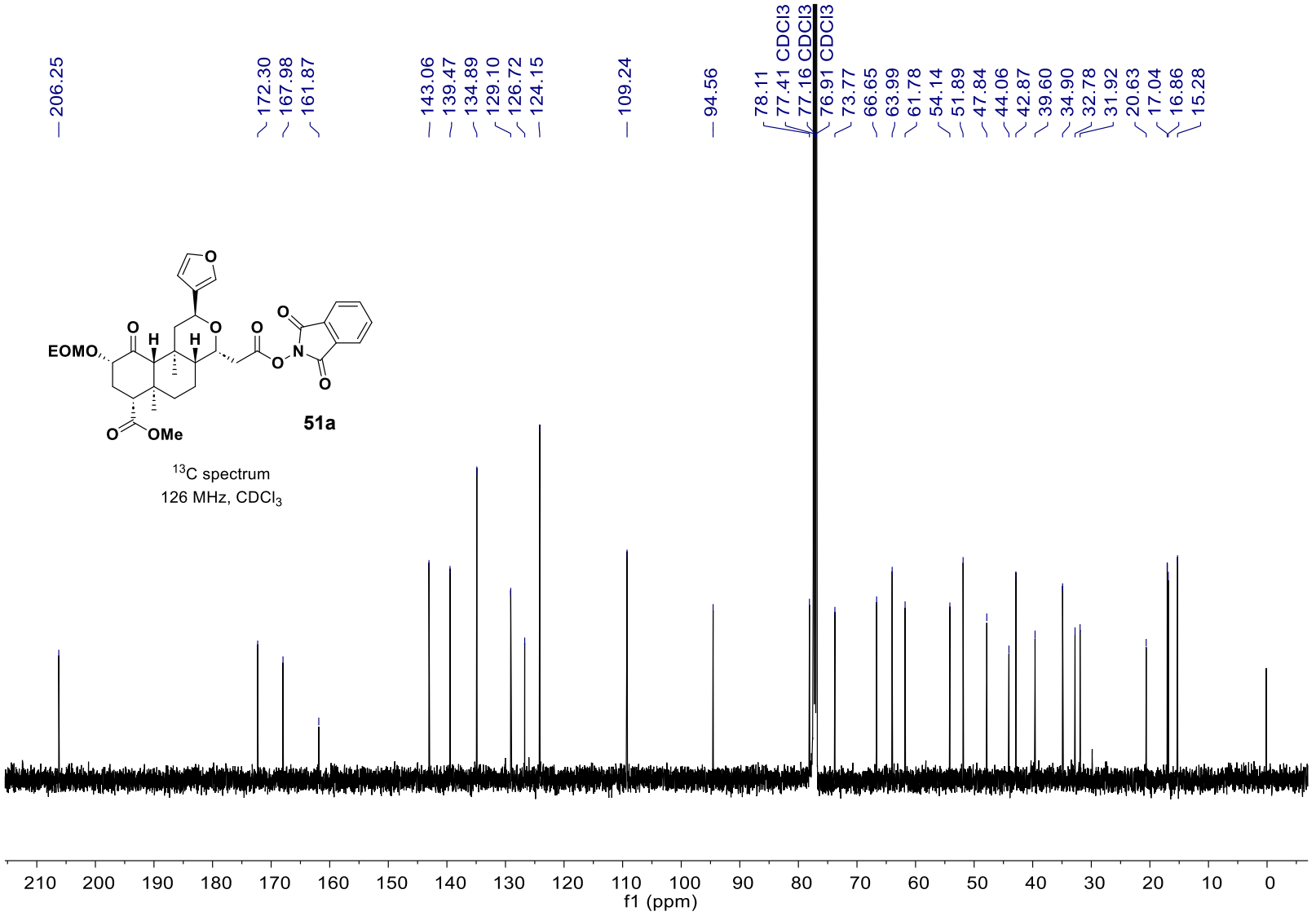

7.33 7.33 7.33 7.32 7.32 7.32 7.31 7.30 7.29 7.27 7.26 7.26 CDCl3 7.25 6.27 6.27 6.26 6.26 4.77 4.76 4.74 4.74 4.72 4.72 4.71 4.70 4.33 4.32 4.13 4.12 4.10 3.70 3.69 3.68 3.67 3.59 3.58 3.57 3.56 3.55 3.54 2.70 2.70 2.67 2.66 2.17 2.17 2.16 2.15 2.13 2.13 2.12 1.94 1.65 1.53 1.39 1.20 1.18 1.16 1.05
EOMO
O
H
H
O
H
N
NHBn
O
O
OMe
31b
1H spectrum
400 MHz, CDCl3
2.98 2.10 2.00 0.91 0.75 0.99 2.68 1.92 1.00 3.88 2.91 0.93 0.95 0.98 1.94 0.92 0.98 2.11 2.79 1.04 2.97 0.99 3.05
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
f1 (ppm)

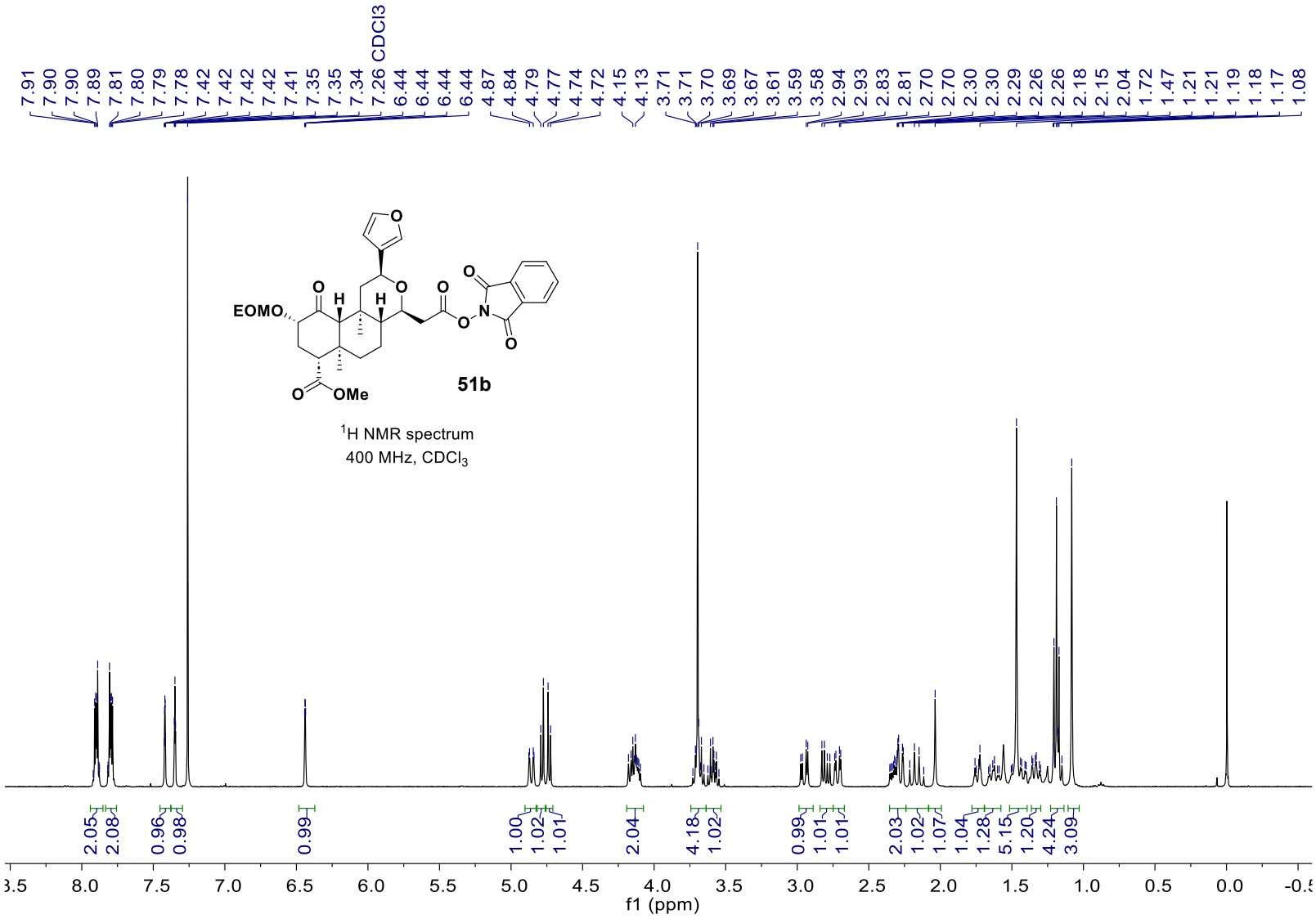

206.56
172.34
158.48
143.15
139.42
139.10
128.79
127.61
127.44
127.18
108.86
94.48
78.15
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
74.30
67.36
65.90
63.96
54.30
51.86
47.93
45.49
44.78
43.20
42.45
39.26
34.98
32.95
18.55
16.86
15.26
14.77
EOMO
NHBn
OMe
31b
13C spectrum
126 MHz, CDCl3
f1 (ppm)

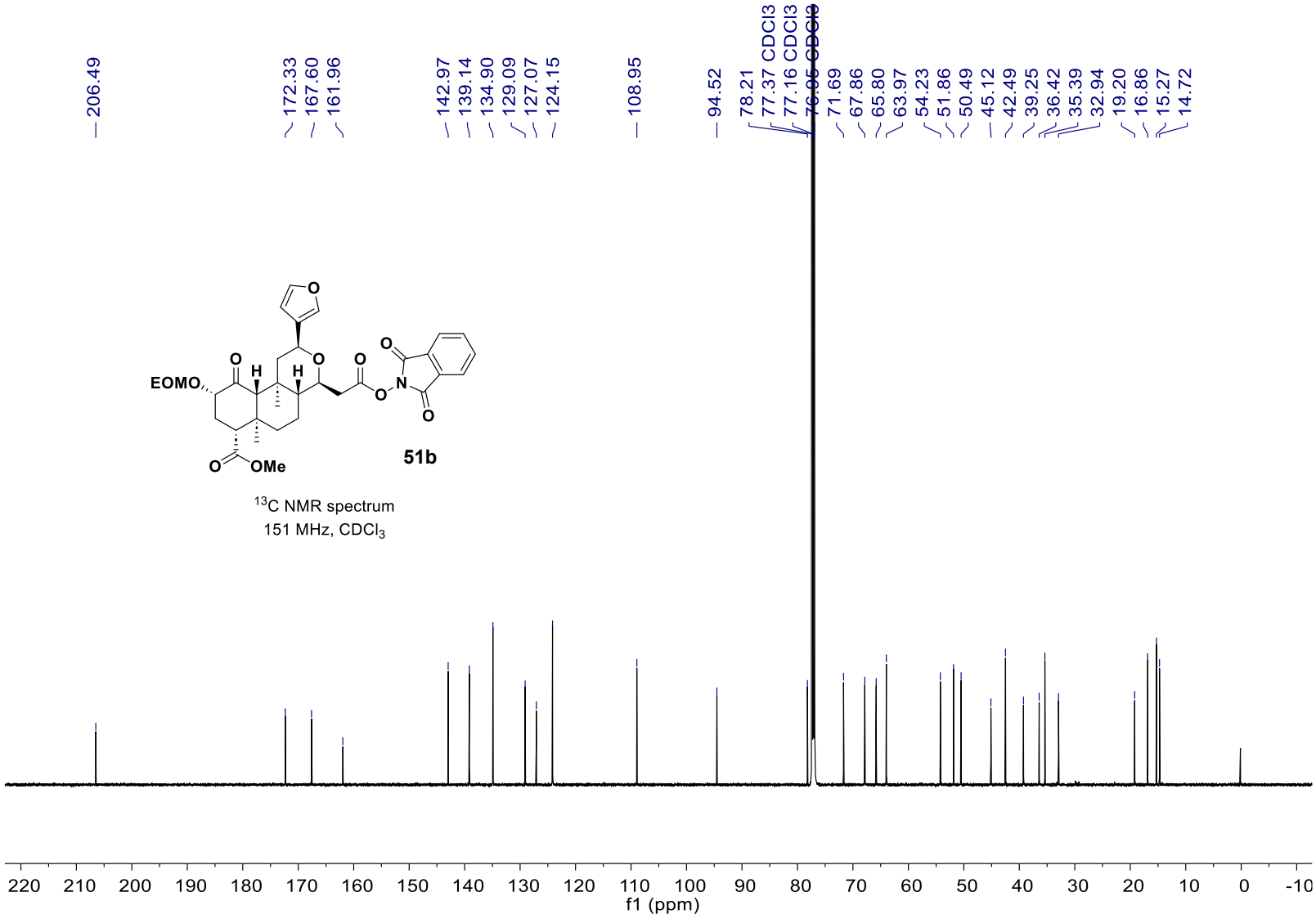

7.35 7.34 7.34 7.33 6.36 6.35 6.35 4.77 4.77 4.76 4.75 4.72 4.70 4.14 4.13 3.69 3.63 3.62 3.62 3.62 3.61 3.60 3.59 3.59 3.58 3.57 3.57 3.56 3.55 3.54 3.53 3.53 3.52 3.50 3.49 3.48 3.38 3.34 3.28 3.27 2.69 2.68 2.19 2.18 2.17 2.15 2.15 2.14 2.01 1.58 1.55 1.44 1.41 1.28 1.19 1.18 1.16 1.11 1.06
EOMO
NHBoc
OMe
35b
1H spectrum
400 MHz, CDCl3
1.94 1.00 2.71 2.04 0.99 1.05 3.01 1.18 17.72 2.18 2.01 2.17 0.98 1.01 1.17 2.00 1.19 3.37 9.42 3.14 1.79 3.36 1.15 2.98
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
f1 (ppm)


206.70
172.40
159.02
156.35
142.98
139.17
127.45
109.04
94.47
79.34
78.15
77.37 CDCl3
77.16 CDCl3
76.95 CDCl3
74.44
70.81
70.62
70.49
70.46
70.43
70.41
70.16
67.34
65.91
63.94
54.24
51.86
48.16
45.74
42.99
42.45
40.47
40.36
39.27
35.02
32.95
29.85
28.60
18.54
16.87
15.25
14.79
EOMO
NHBoc
35b
13C spectrum
151 MHz, CDCl3
f1 (ppm)

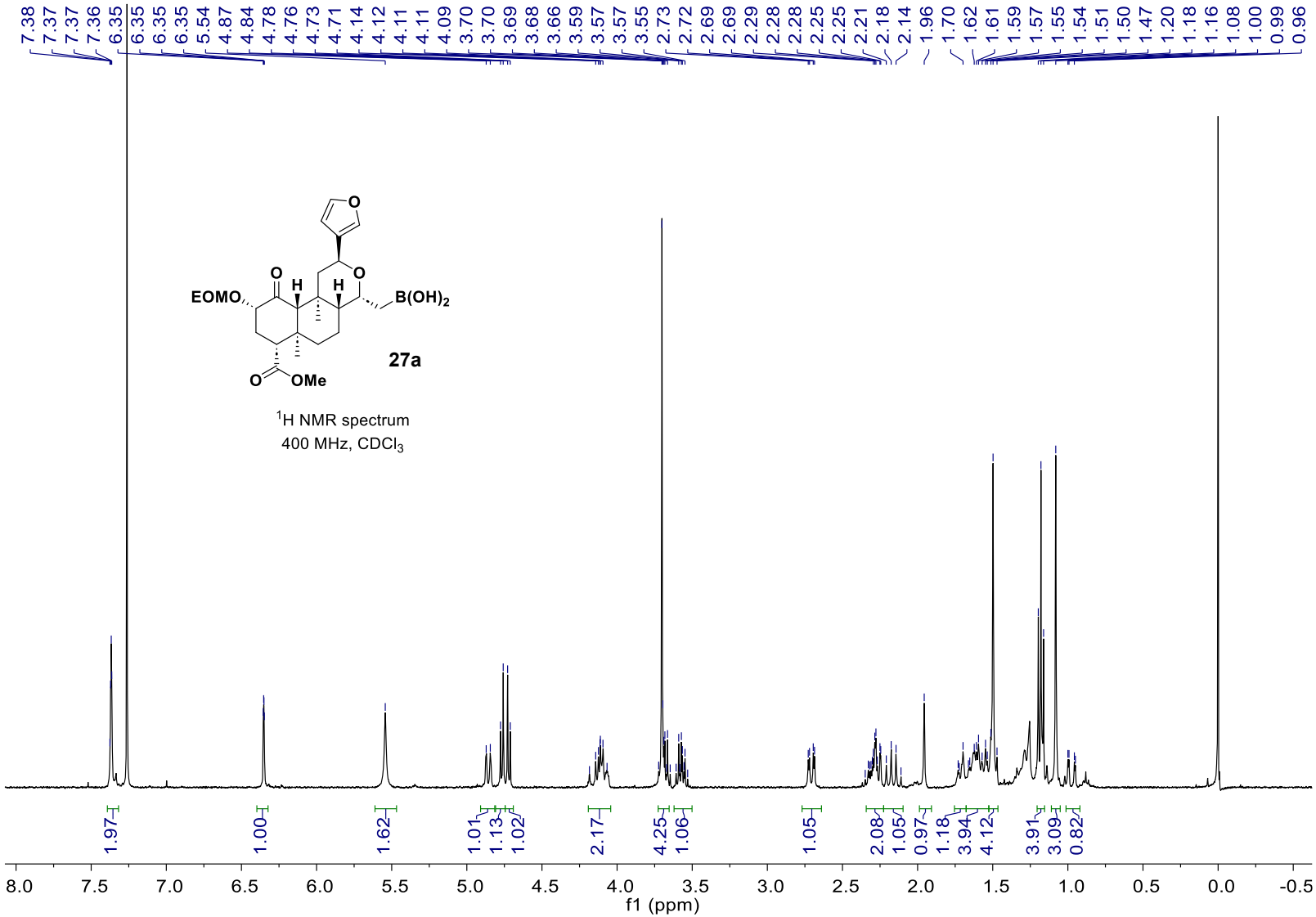

7.90 7.89 7.89 7.88 7.80 7.79 7.79 7.78 7.41 7.41 7.41 7.41 7.41 7.37 7.37 7.36 6.48 6.48 6.48 6.48 4.94 4.91 4.80 4.78 4.76 4.74 4.14 3.71 3.70 3.69 3.68 3.61 3.60 3.59 3.27 3.24 2.84 2.83 2.80 2.79 2.74 2.72 2.71 2.38 2.37 2.34 2.34 2.19 2.16 2.01 1.77 1.75 1.74 1.51 1.21 1.21 1.19 1.18 1.10
EOMO
O
H
H
O
O
O
N
O
O
O
OMe
51a
1H spectrum
400 MHz, CDCl3
1.98 2.04 0.87 0.96 0.89 0.93 0.94 1.05 0.95 1.03 4.07 1.03 0.93 0.94 1.03 2.04 1.09 0.98 2.03 1.23 3.73 1.29 3.94 2.70
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
f1 (ppm)

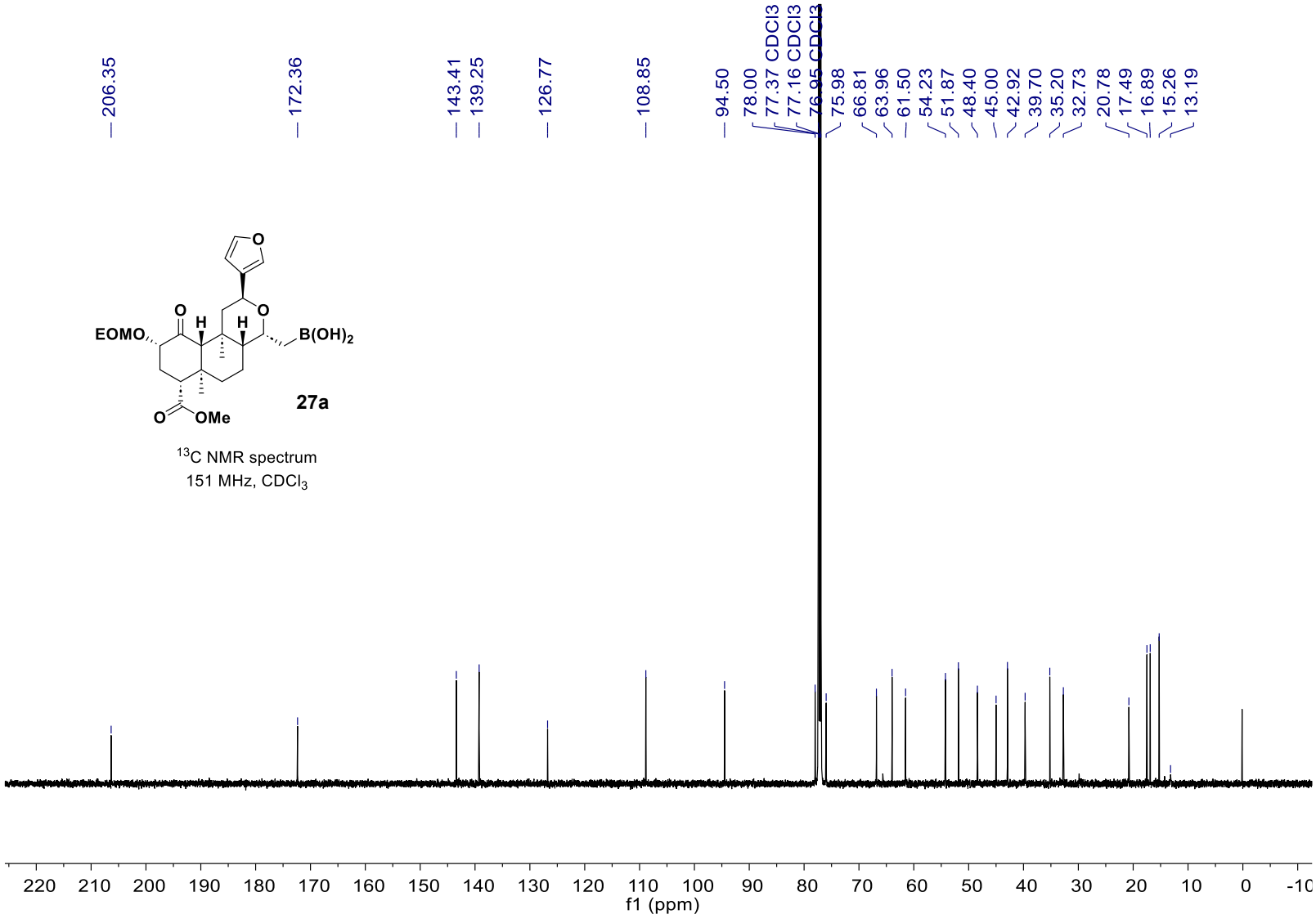

206.25
172.30
167.98
161.87
143.06
139.47
134.89
129.10
126.72
124.15
109.24
94.56
78.11
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
73.77
66.65
63.99
61.78
54.14
51.89
47.84
44.06
42.87
39.60
34.90
32.78
31.92
20.63
17.04
16.86
15.28
EOMO
OMe
51a
13C spectrum
126 MHz, CDCl3
f1 (ppm)


7.91 7.90 7.90 7.89 7.81 7.80 7.79 7.78 7.42 7.42 7.42 7.42 7.41 7.35 7.35 7.34 7.26 CDCl3 6.44 6.44 6.44 6.44 4.87 4.84 4.79 4.77 4.74 4.72 4.15 4.13 3.71 3.71 3.70 3.69 3.67 3.61 3.59 3.58 2.94 2.93 2.83 2.81 2.70 2.70 2.30 2.30 2.29 2.26 2.26 2.18 2.15 2.04 1.72 1.47 1.21 1.21 1.19 1.18 1.17 1.08
EOMO
OMe
51b
1H NMR spectrum
400 MHz, CDCl3
2.05 2.08 0.96 0.98 0.99 1.00 1.02 1.01 2.04 4.18 1.02 0.99 1.01 1.01 2.03 1.02 1.07 1.04 1.28 5.15 1.20 4.24 3.09
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
f1 (ppm)

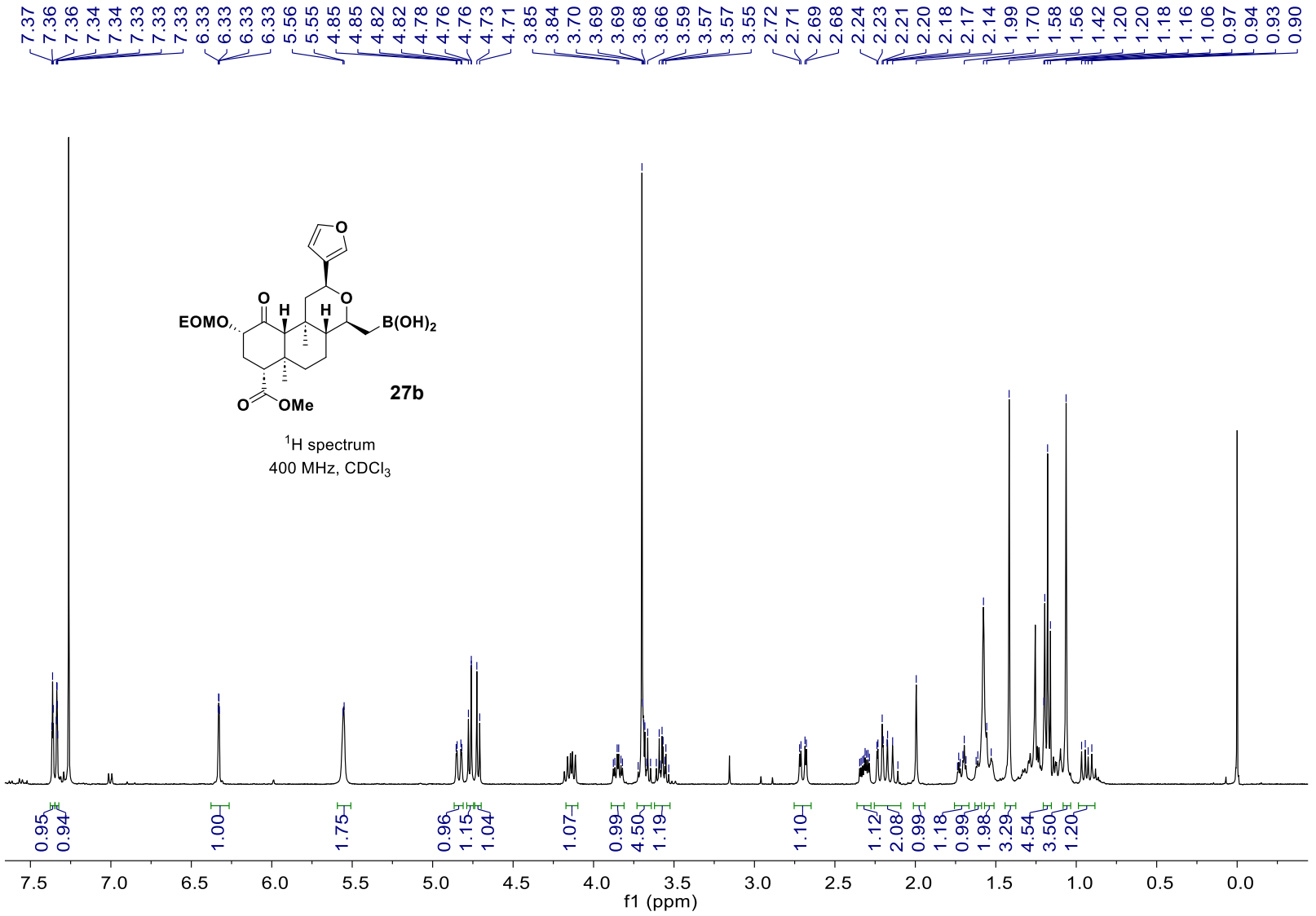


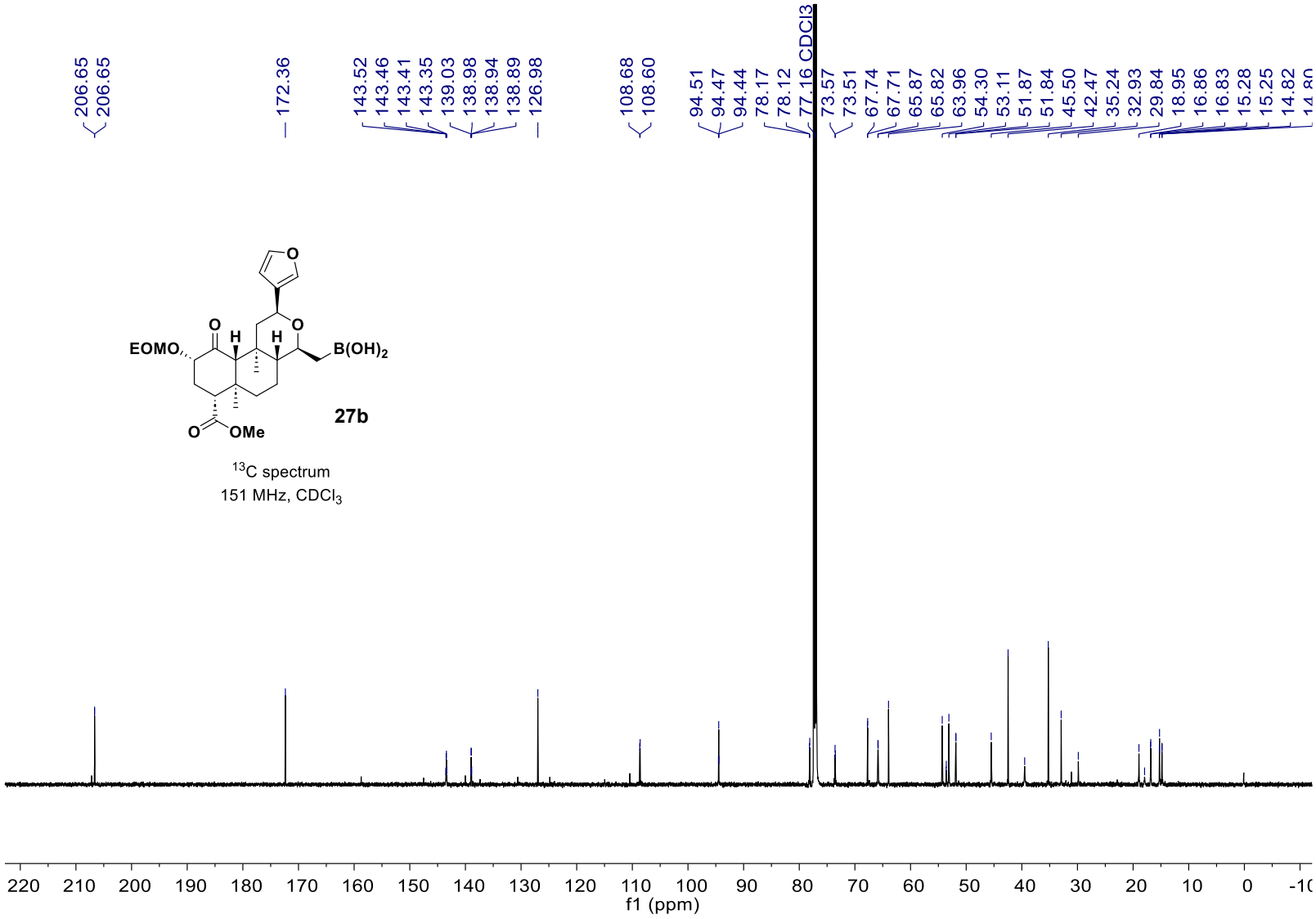
^{13}C NMR spectrum
151 MHz, $CDCl_3$

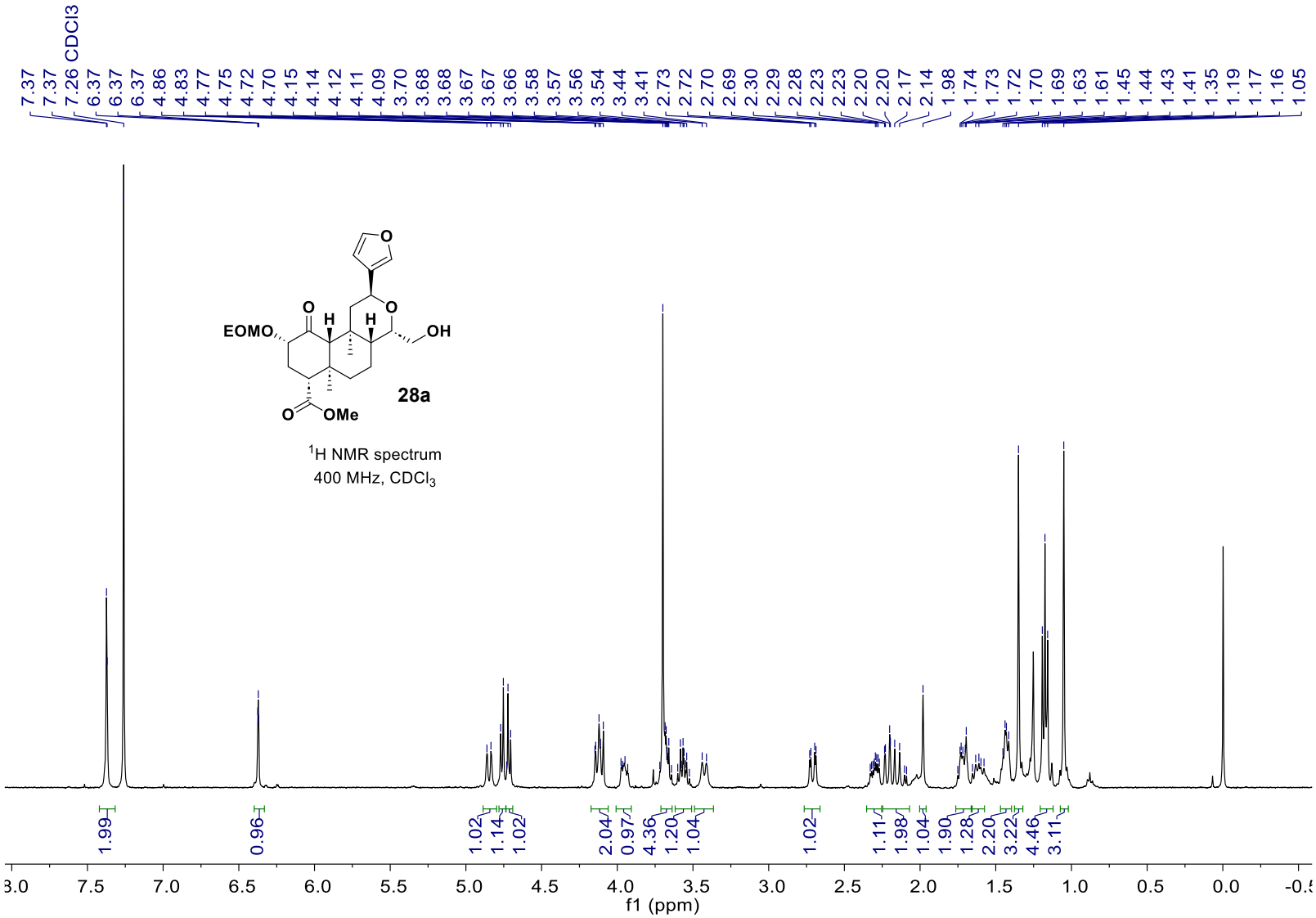

7.38 7.37 7.37 7.36 6.35 6.35 6.35 6.35 5.54 4.87 4.84 4.78 4.76 4.73 4.71 4.14 4.12 4.11 4.11 4.09 3.70 3.70 3.69 3.68 3.66 3.59 3.57 3.57 3.55 2.73 2.72 2.69 2.69 2.29 2.28 2.28 2.25 2.25 2.21 2.18 2.14 1.96 1.70 1.62 1.61 1.59 1.57 1.55 1.54 1.51 1.50 1.47 1.20 1.18 1.16 1.08 1.00 0.99 0.96
EOMO
B(OH)2
27a
OMe
1H NMR spectrum
400 MHz, CDCl3
1.97 1.00 1.62 1.01 1.13 1.02 2.17 4.25 1.06 1.05 2.08 1.05 0.97 1.18 3.94 4.12 3.91 3.09 0.82
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)

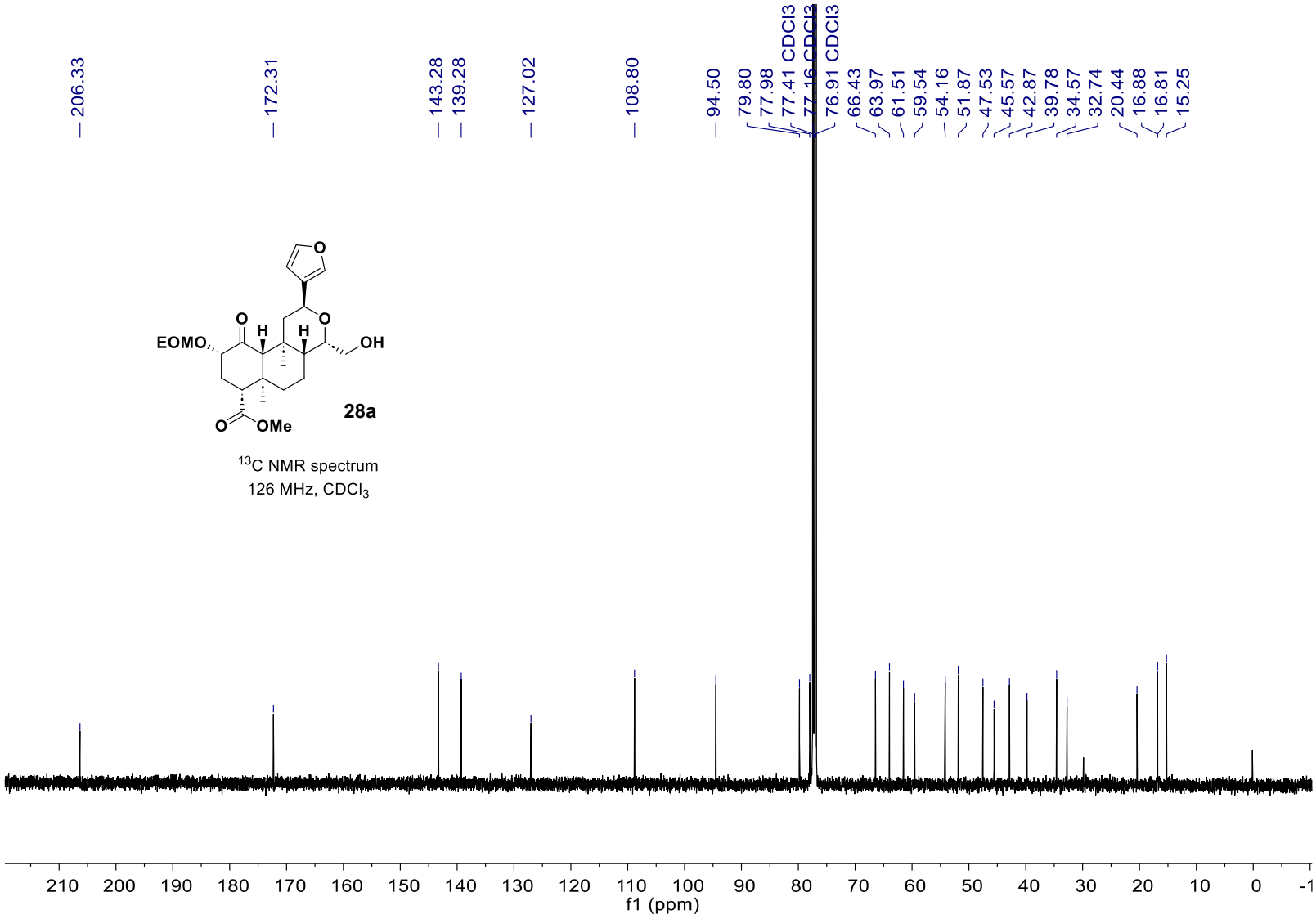


^{13}C NMR spectrum
151 MHz, $CDCl_3$

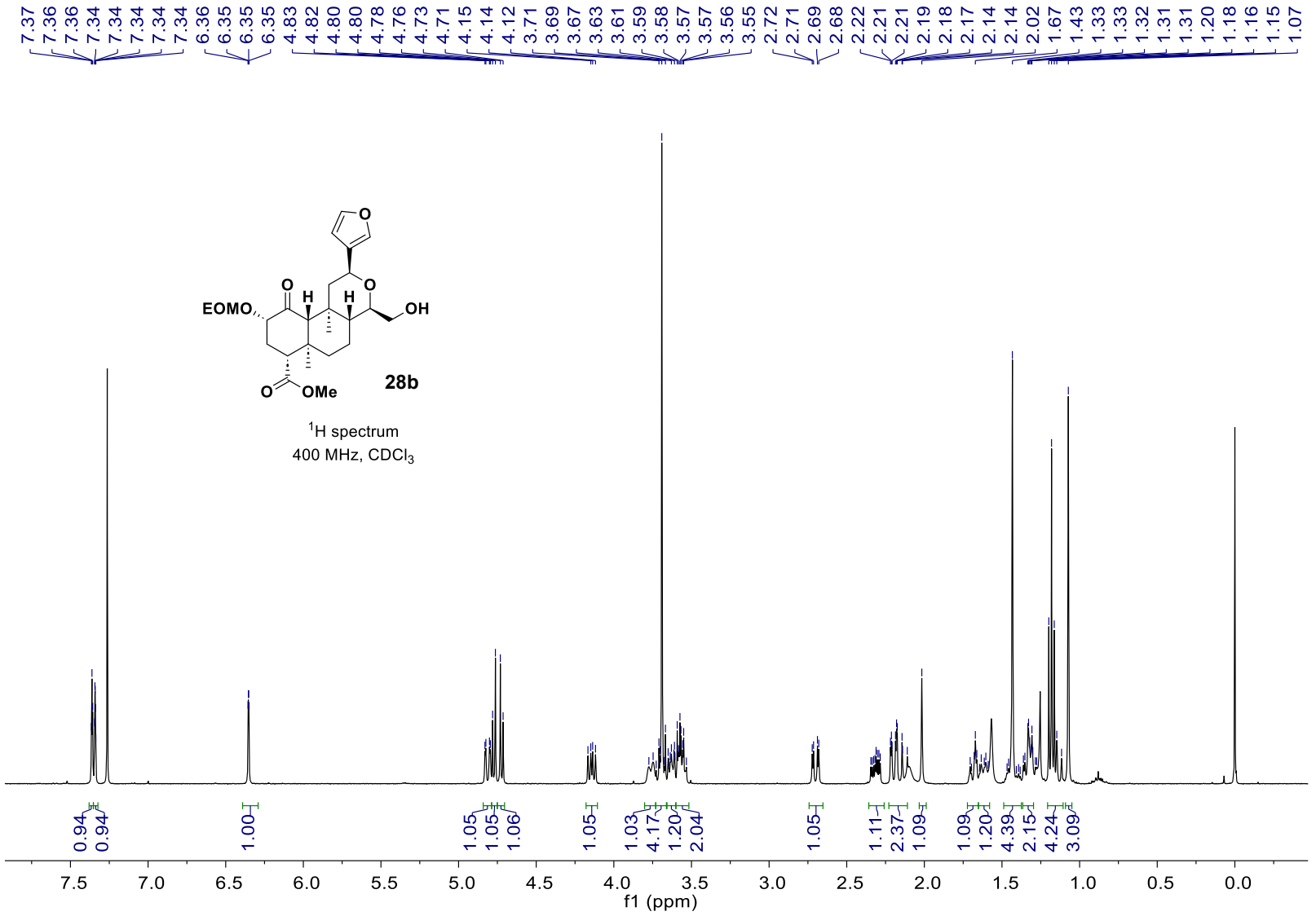

7.37 7.36 7.36 7.34 7.34 7.33 7.33 7.33 6.33 6.33 6.33 6.33 5.56 5.55 4.85 4.85 4.82 4.82 4.78 4.76 4.76 4.73 4.71 3.85 3.84 3.70 3.69 3.69 3.68 3.66 3.59 3.57 3.57 3.55 2.72 2.71 2.69 2.68 2.24 2.23 2.21 2.20 2.18 2.17 2.14 1.99 1.70 1.58 1.56 1.42 1.20 1.20 1.18 1.16 1.06 0.97 0.94 0.93 0.90
EOMO
B(OH)2
27b
1H spectrum
400 MHz, CDCl3
0.95 0.94 1.00 1.75 0.96 1.15 1.04 1.07 0.99 4.50 1.19 1.10 1.12 2.08 0.99 1.18 0.99 1.98 3.29 4.54 3.50 1.20
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
f1 (ppm)

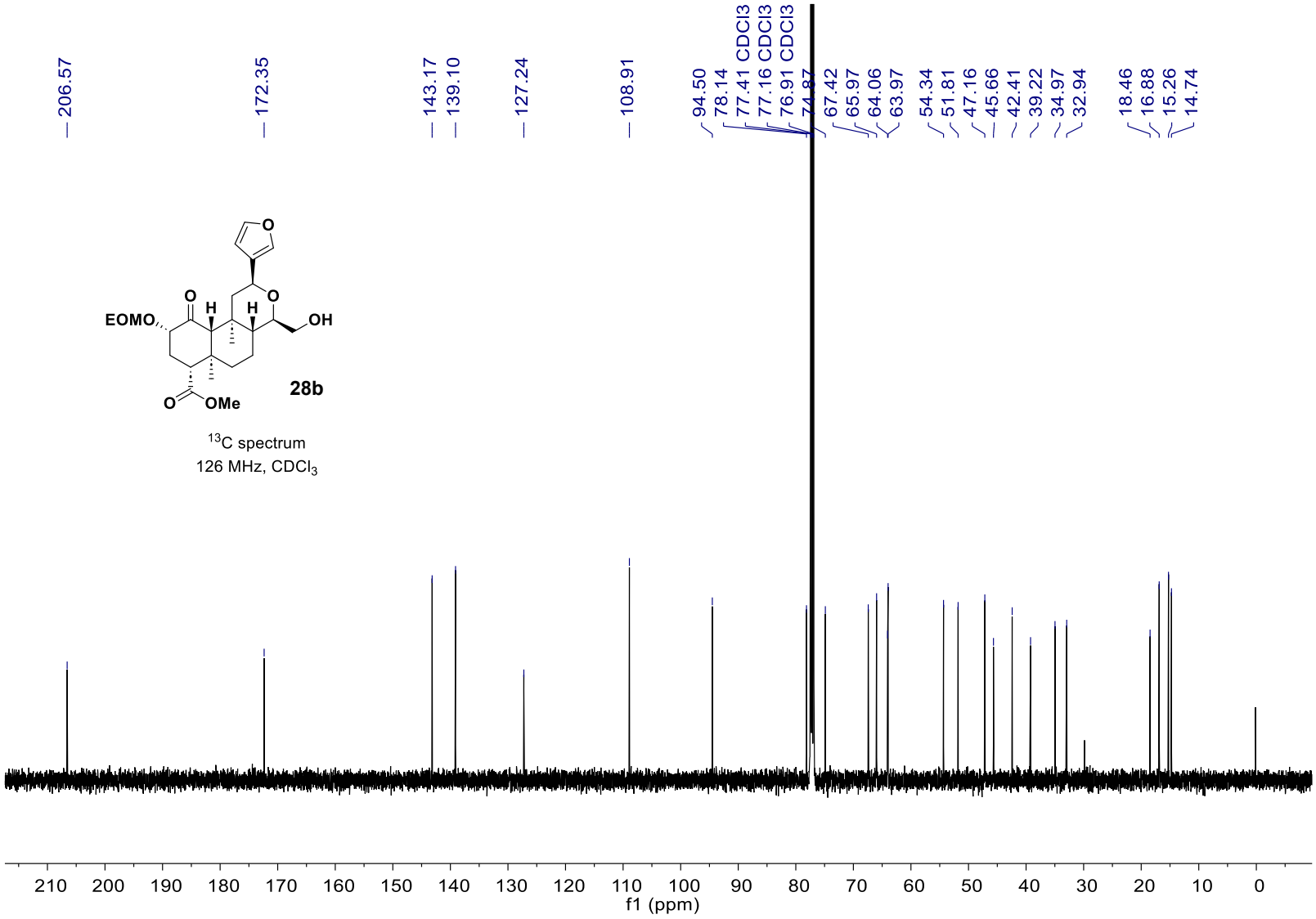

206.65
206.65
172.36
143.52
143.46
143.41
143.35
139.03
138.98
138.94
138.89
126.98
108.68
108.60
94.51
94.47
94.44
78.17
78.12
77.16 CDCl3
73.57
73.51
67.74
67.71
65.87
65.82
63.96
54.30
53.11
51.87
51.84
45.50
42.47
35.24
32.93
29.84
18.95
16.86
16.83
15.28
15.25
14.82
O
O
H
H
O
EOMO
B(OH)2
O
OMe
27b
13C spectrum
151 MHz, CDCl3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

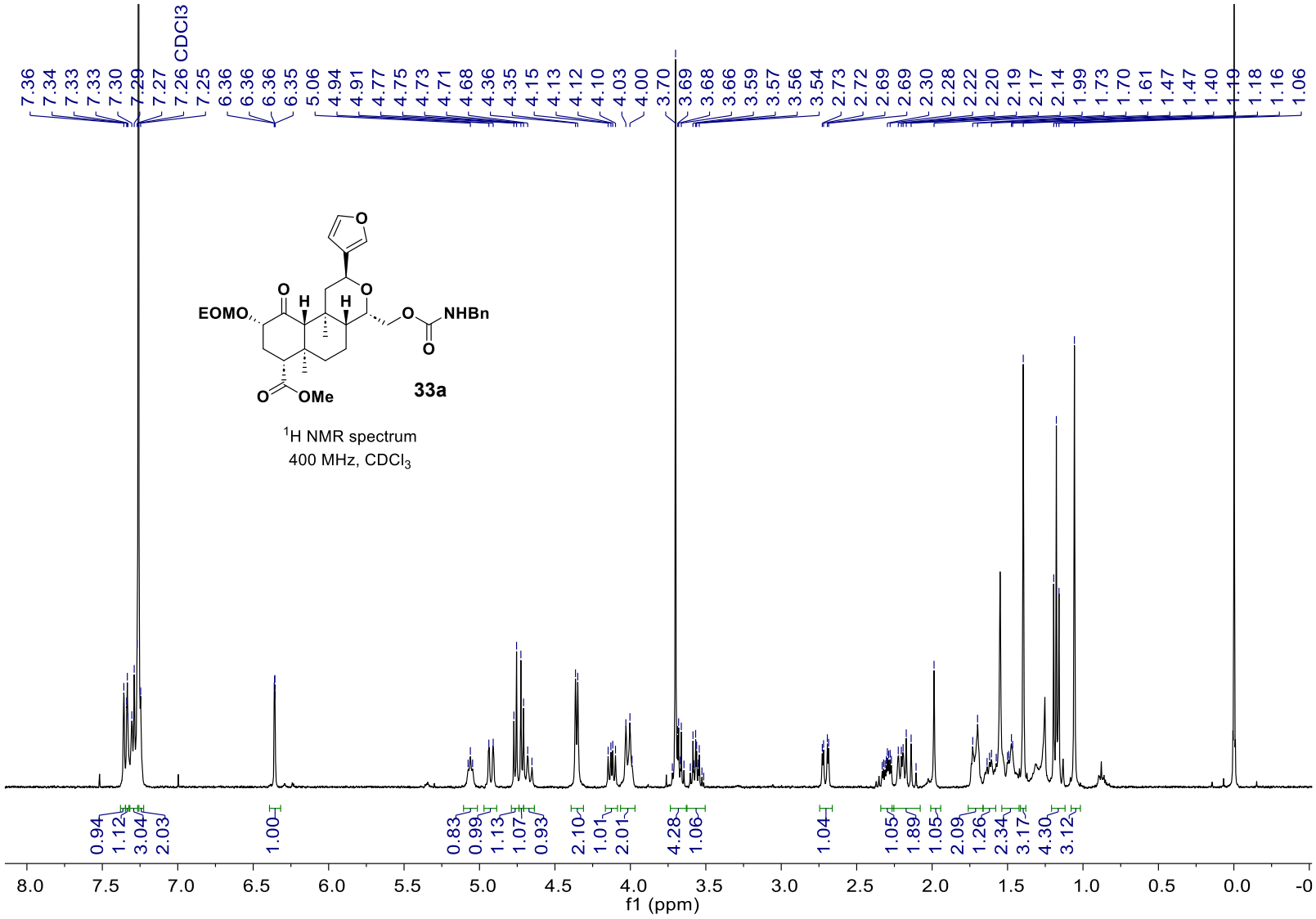

7.37
7.37
7.26 CDCl3
6.37
6.37
6.37
4.86
4.83
4.77
4.75
4.72
4.70
4.15
4.14
4.12
4.11
4.09
3.70
3.68
3.68
3.67
3.67
3.66
3.58
3.57
3.56
3.54
3.44
3.41
2.73
2.72
2.70
2.69
2.30
2.29
2.28
2.23
2.23
2.20
2.20
2.17
2.14
1.98
1.74
1.73
1.72
1.70
1.69
1.63
1.61
1.45
1.44
1.43
1.41
1.35
1.19
1.17
1.16
1.05
EOMO
O
H
H
O
OH
O
OMe
28a
1H NMR spectrum
400 MHz, CDCl3
1.99
0.96
1.02
1.14
1.02
2.04
0.97
4.36
1.20
1.04
1.02
1.11
1.98
1.04
1.90
1.28
2.20
3.22
4.46
3.11
f1 (ppm)

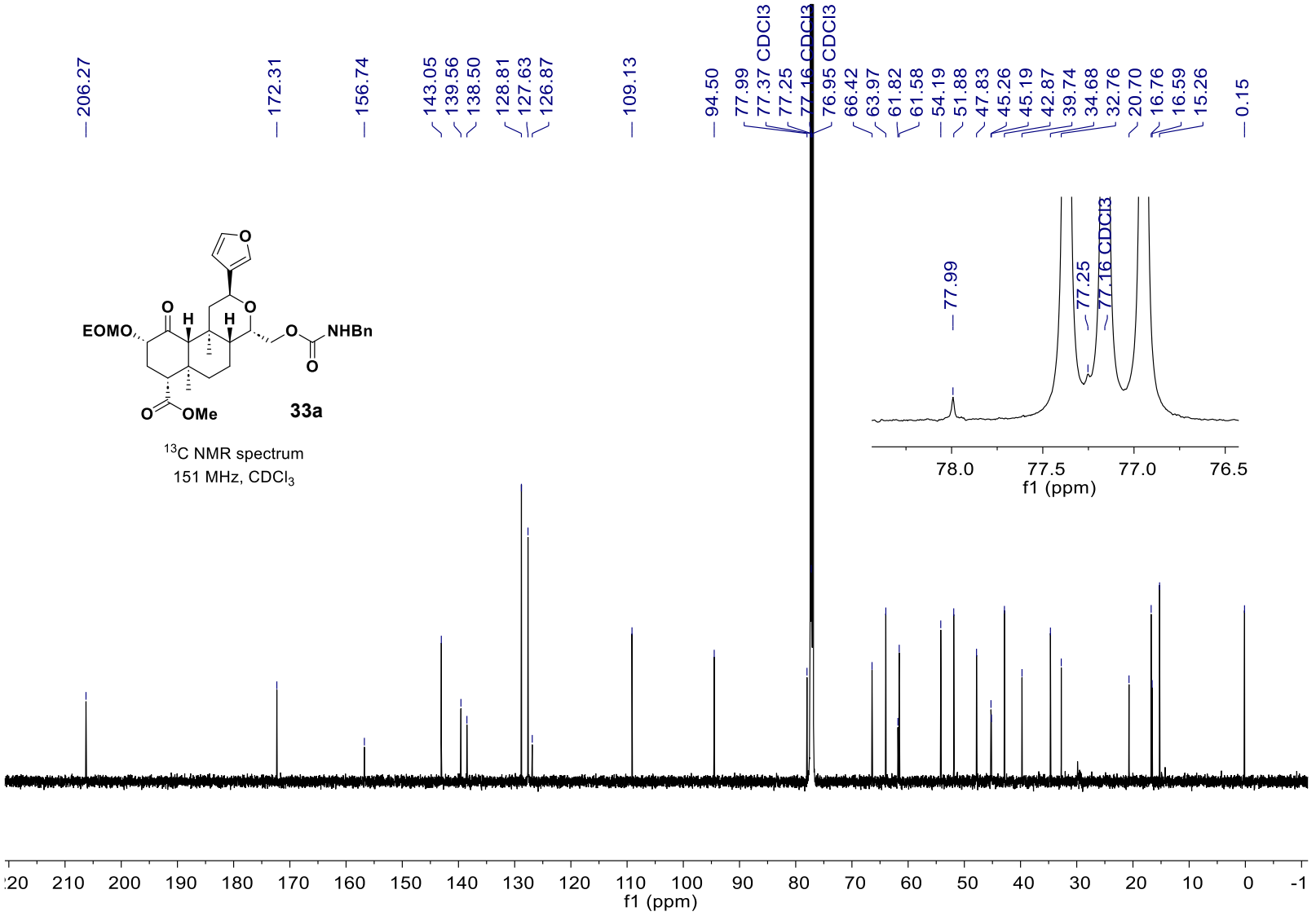


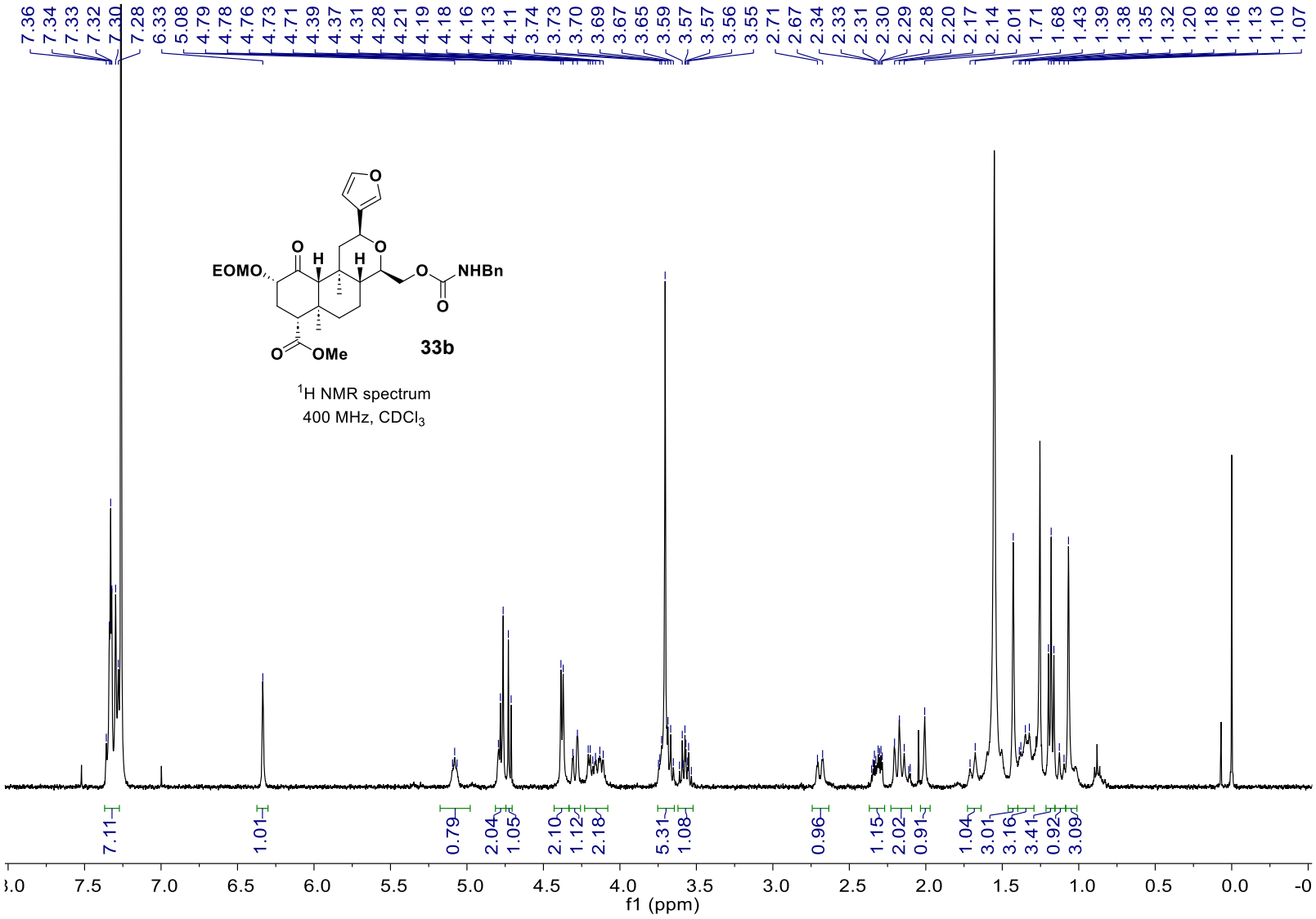
^{13}C NMR spectrum
126 MHz, $CDCl_3$

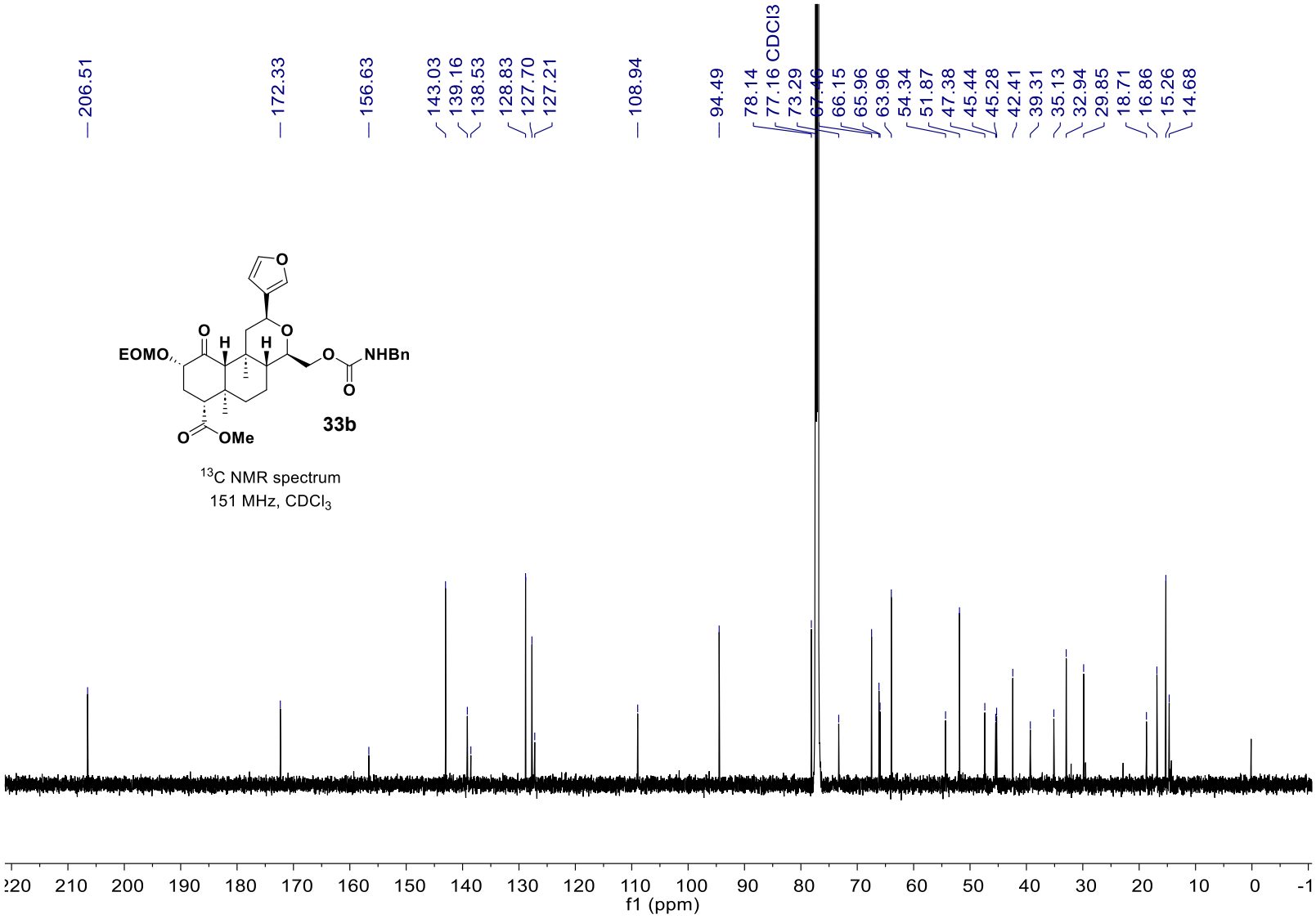

7.37 7.36 7.36 7.34 7.34 7.34 7.34 7.34 6.36 6.35 6.35 6.35 4.83 4.82 4.80 4.80 4.78 4.76 4.73 4.71 4.15 4.14 4.12 3.71 3.69 3.67 3.63 3.61 3.59 3.58 3.57 3.57 3.56 3.55 2.72 2.71 2.69 2.68 2.22 2.21 2.21 2.19 2.18 2.17 2.14 2.14 2.02 1.67 1.43 1.33 1.33 1.32 1.31 1.31 1.20 1.18 1.16 1.15 1.07
EOMO
OH
OMe
28b
1H spectrum
400 MHz, CDCl3
0.94 0.94 1.00 1.05 1.05 1.06 1.05 1.03 4.17 1.20 2.04 1.05 1.11 2.37 1.09 1.09 1.20 4.39 2.15 4.24 3.09
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
f1 (ppm)

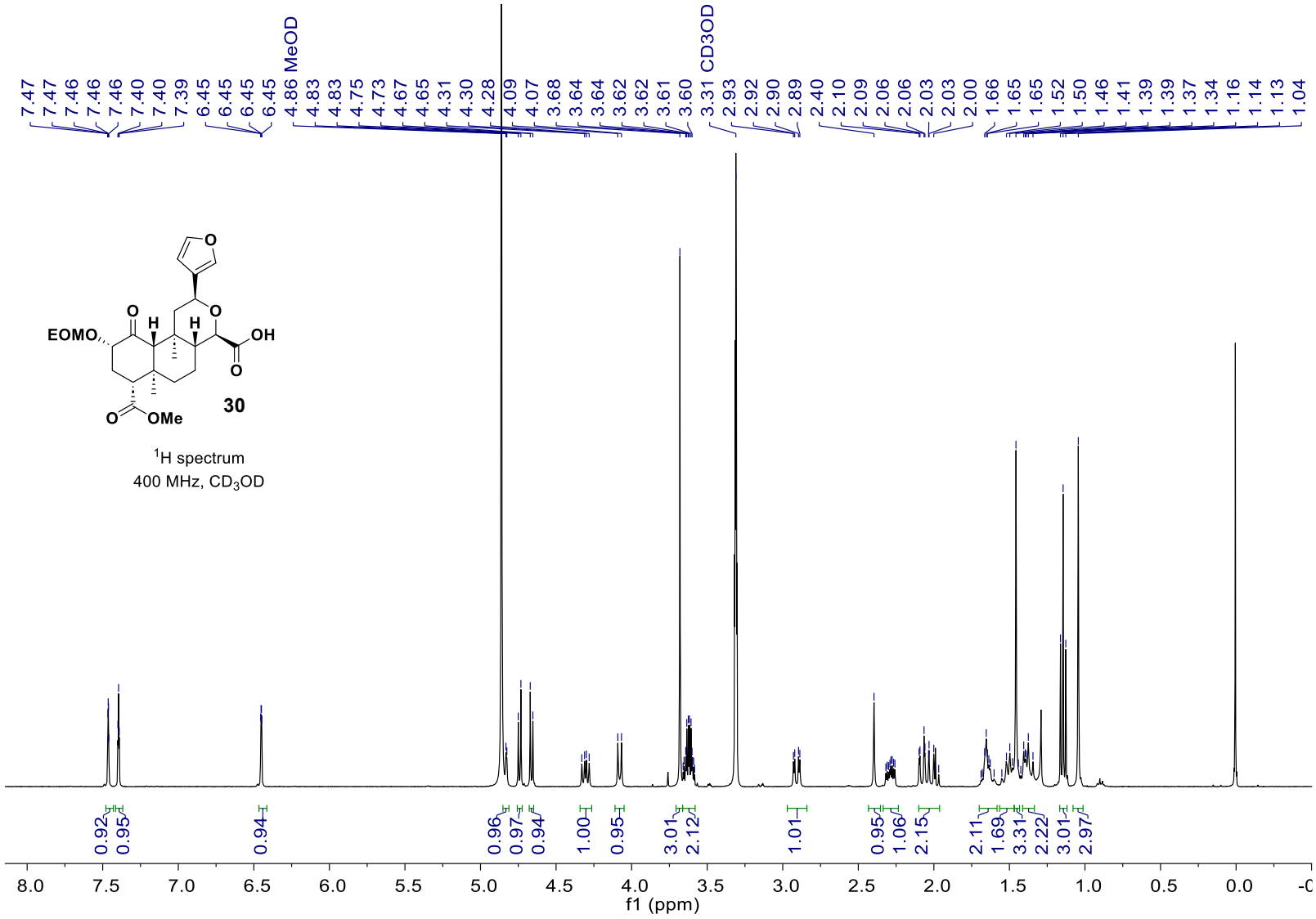

206.57
172.35
143.17
139.10
127.24
108.91
94.50
78.14
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
74.87
67.42
65.97
64.06
63.97
54.34
51.81
47.16
45.66
42.41
39.22
34.97
32.94
18.46
16.88
15.26
14.74
EOMO
OH
OMe
28b
13C spectrum
126 MHz, CDCl3
f1 (ppm)

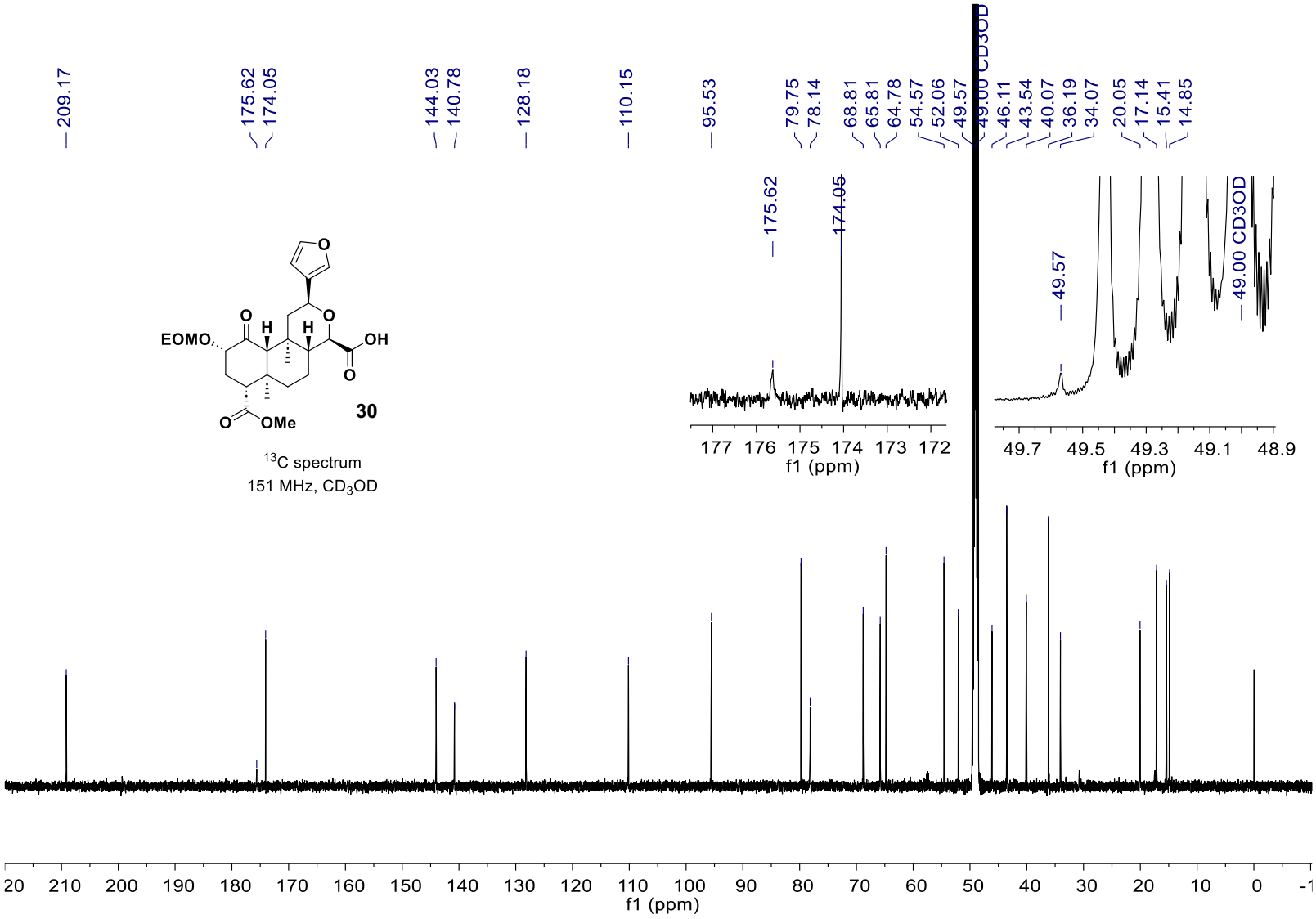

7.36 7.34 7.33 7.33 7.30 7.29 7.27 7.26 CDCl3 7.25 6.36 6.36 6.36 6.35 5.06 4.94 4.91 4.77 4.75 4.73 4.71 4.68 4.36 4.35 4.15 4.13 4.12 4.10 4.03 4.00 3.70 3.69 3.68 3.66 3.59 3.57 3.56 3.54 2.73 2.72 2.69 2.69 2.30 2.28 2.22 2.20 2.19 2.17 2.14 1.99 1.73 1.70 1.61 1.47 1.47 1.40 1.19 1.18 1.16 1.06
EOMO
O
H
H
O
O
NHBn
O
O
OMe
33a
1H NMR spectrum
400 MHz, CDCl3
0.94 1.12 3.04 2.03 1.00 0.83 0.99 1.13 1.07 0.93 2.10 1.01 2.01 4.28 1.06 1.04 1.05 1.89 1.05 2.09 1.26 2.34 3.17 4.30 3.12
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
f1 (ppm)

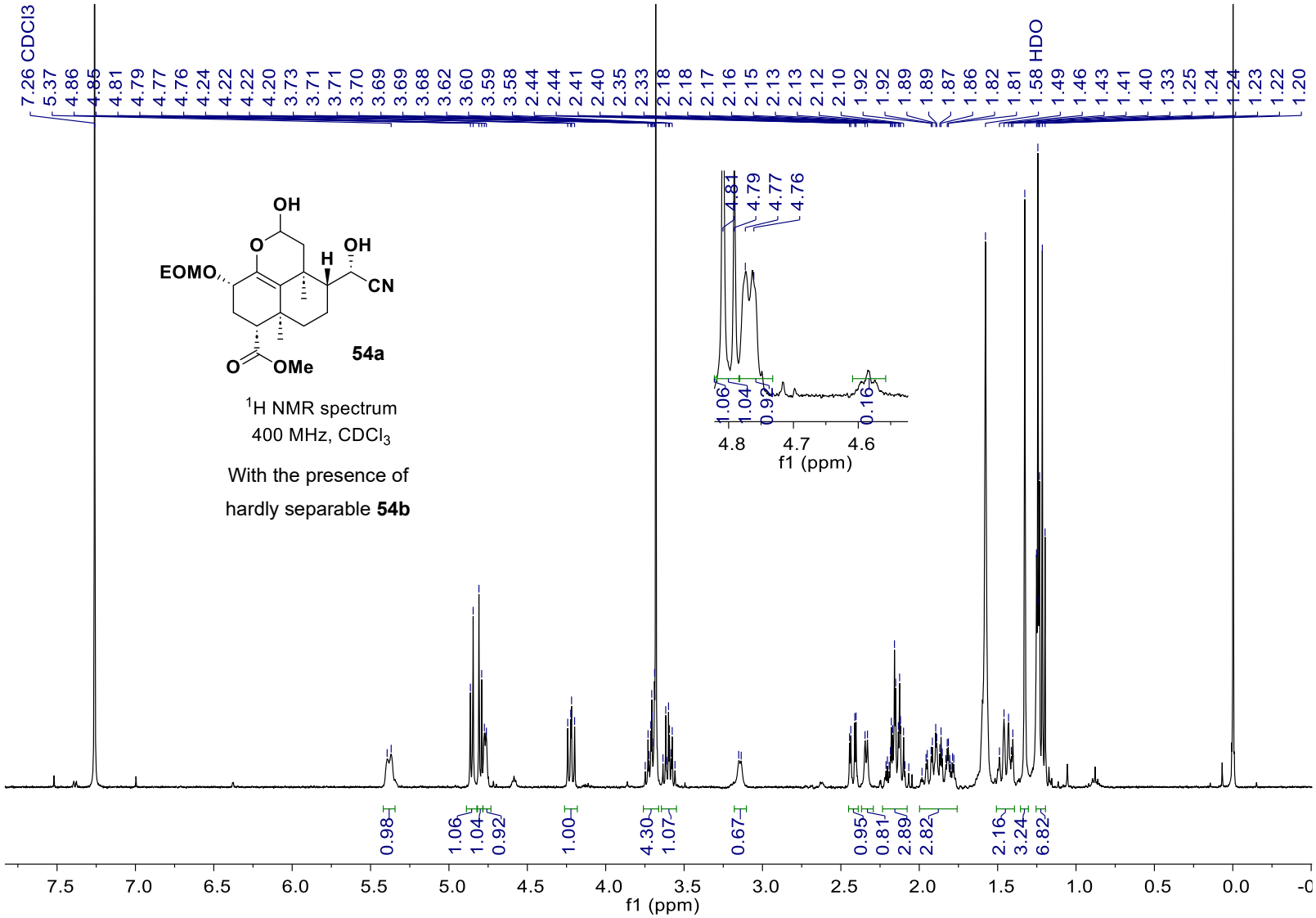

206.27
172.31
156.74
143.05
139.56
138.50
128.81
127.63
126.87
109.13
94.50
77.99
77.37 CDCl3
77.25
77.16 CDCl3
76.95 CDCl3
66.42
63.97
61.82
61.58
54.19
51.88
47.83
45.26
45.19
42.87
39.74
34.68
32.76
20.70
16.76
16.59
15.26
0.15
EOMO
O
H
H
O
O
NHBn
O
O
OMe
33a
13C NMR spectrum
151 MHz, CDCl3
77.99
77.25
77.16 CDCl3
78.0
77.5
77.0
76.5
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 -1
f1 (ppm)

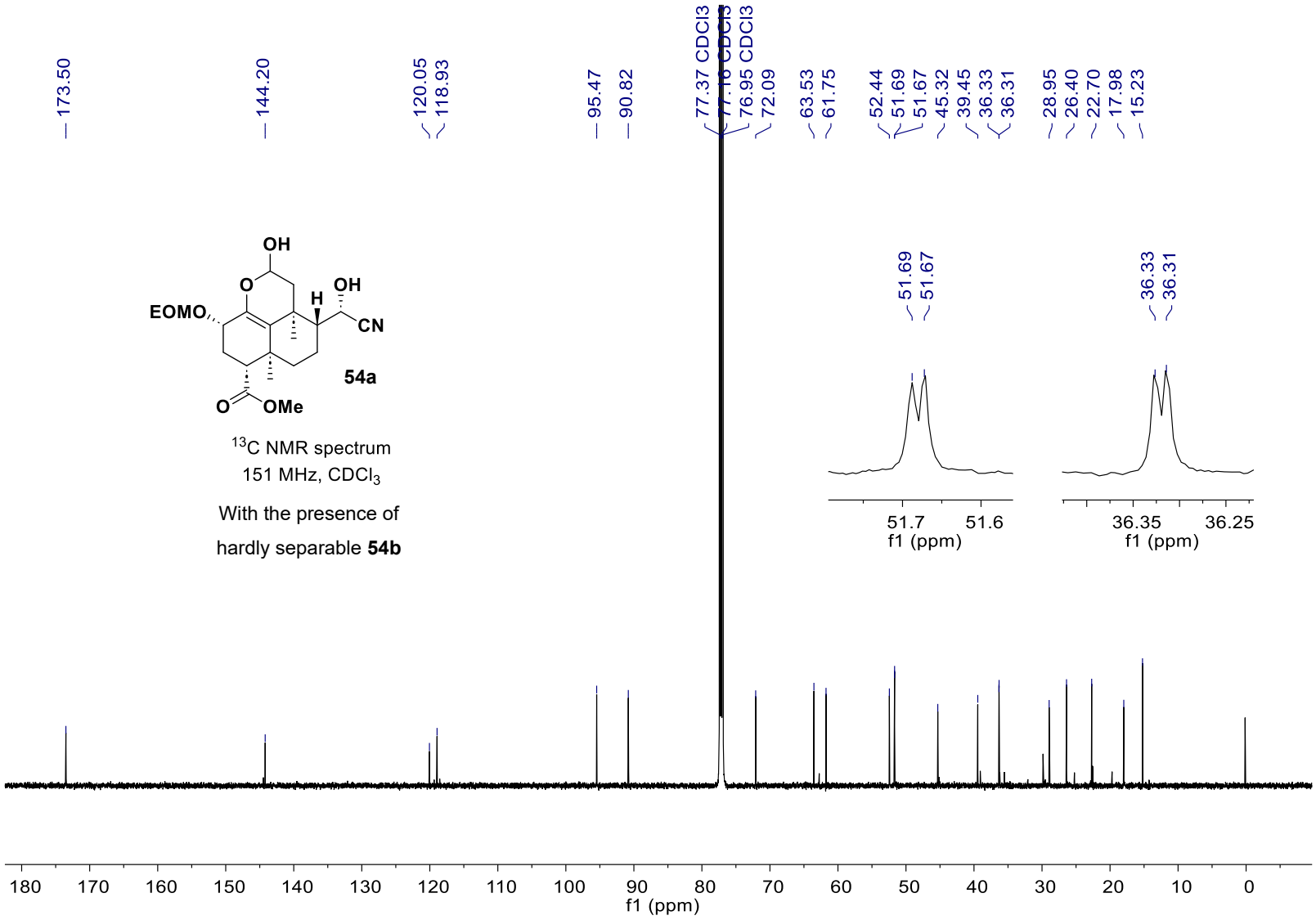

7.36 7.34 7.33 7.32 7.30 7.28 6.33 5.08 4.79 4.78 4.76 4.73 4.71 4.39 4.37 4.31 4.28 4.21 4.19 4.18 4.16 4.13 4.11 3.74 3.73 3.70 3.69 3.67 3.65 3.59 3.57 3.57 3.56 3.55 2.71 2.67 2.34 2.33 2.31 2.30 2.29 2.28 2.20 2.17 2.14 2.01 1.71 1.68 1.43 1.39 1.38 1.35 1.32 1.20 1.18 1.16 1.13 1.10 1.07
EOMO
O
H
H
O
O
NHBn
O
O
OMe
33b
1H NMR spectrum
400 MHz, CDCl3
7.11 1.01 0.79 2.04 1.05 2.10 1.12 2.18 5.31 1.08 0.96 1.15 2.02 0.91 1.04 3.01 3.16 3.41 0.92 3.09
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
f1 (ppm)


206.51
172.33
156.63
143.03
139.16
138.53
128.83
127.70
127.21
108.94
94.49
78.14
77.16 CDCl3
73.29
67.46
66.15
65.96
63.96
54.34
51.87
47.38
45.44
45.28
42.41
39.31
35.13
32.94
29.85
18.71
16.86
15.26
14.68
EOMO
O
H
H
O
O
NHBn
O
O
OMe
33b
13C NMR spectrum
151 MHz, CDCl3
f1 (ppm)


7.47 7.47 7.46 7.46 7.46 7.40 7.40 7.39 6.45 6.45 6.45 6.45 4.86 MeOD 4.83 4.83 4.75 4.73 4.67 4.65 4.31 4.30 4.28 4.09 4.07 3.68 3.64 3.64 3.62 3.62 3.61 3.60 3.31 CD3OD 2.93 2.92 2.90 2.89 2.40 2.10 2.09 2.06 2.06 2.03 2.03 2.00 1.66 1.65 1.65 1.52 1.50 1.46 1.41 1.39 1.39 1.37 1.34 1.16 1.14 1.13 1.04
EOMO
OH
OMe
30
1H spectrum
400 MHz, CD3OD
0.92 0.95 0.94 0.96 0.97 0.94 1.00 0.95 3.01 2.12 1.01 0.95 1.06 2.15 2.11 1.69 3.31 2.22 3.01 2.97
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
f1 (ppm)

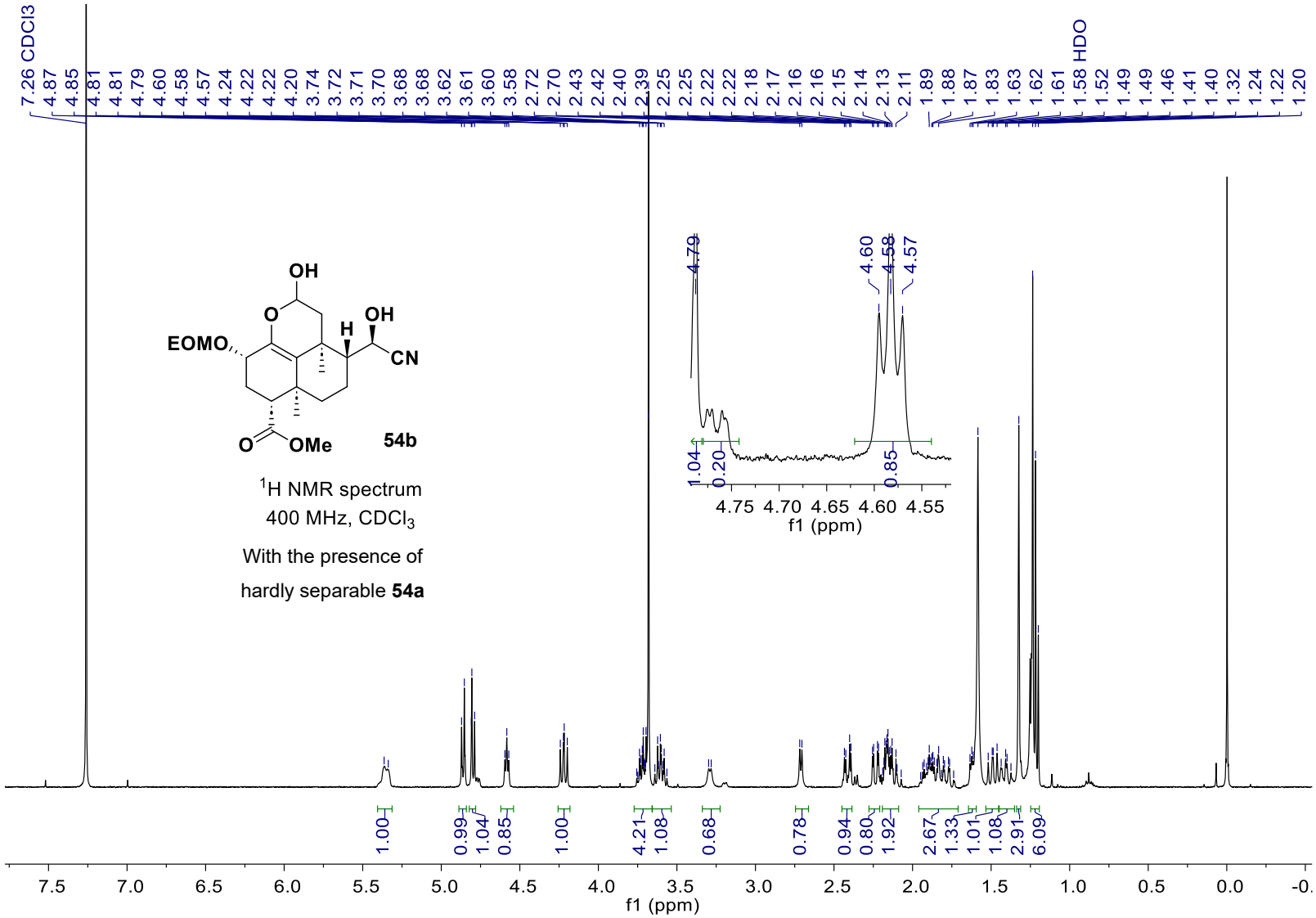

209.17
175.62
174.05
144.03
140.78
128.18
110.15
95.53
79.75
78.14
68.81
65.81
64.78
54.57
52.06
49.57
49.00 CD3OD
46.11
43.54
40.07
36.19
34.07
20.05
17.14
15.41
14.85
EOMO
OH
OMe
30
13C spectrum
151 MHz, CD3OD
f1 (ppm)
f1 (ppm)
f1 (ppm)

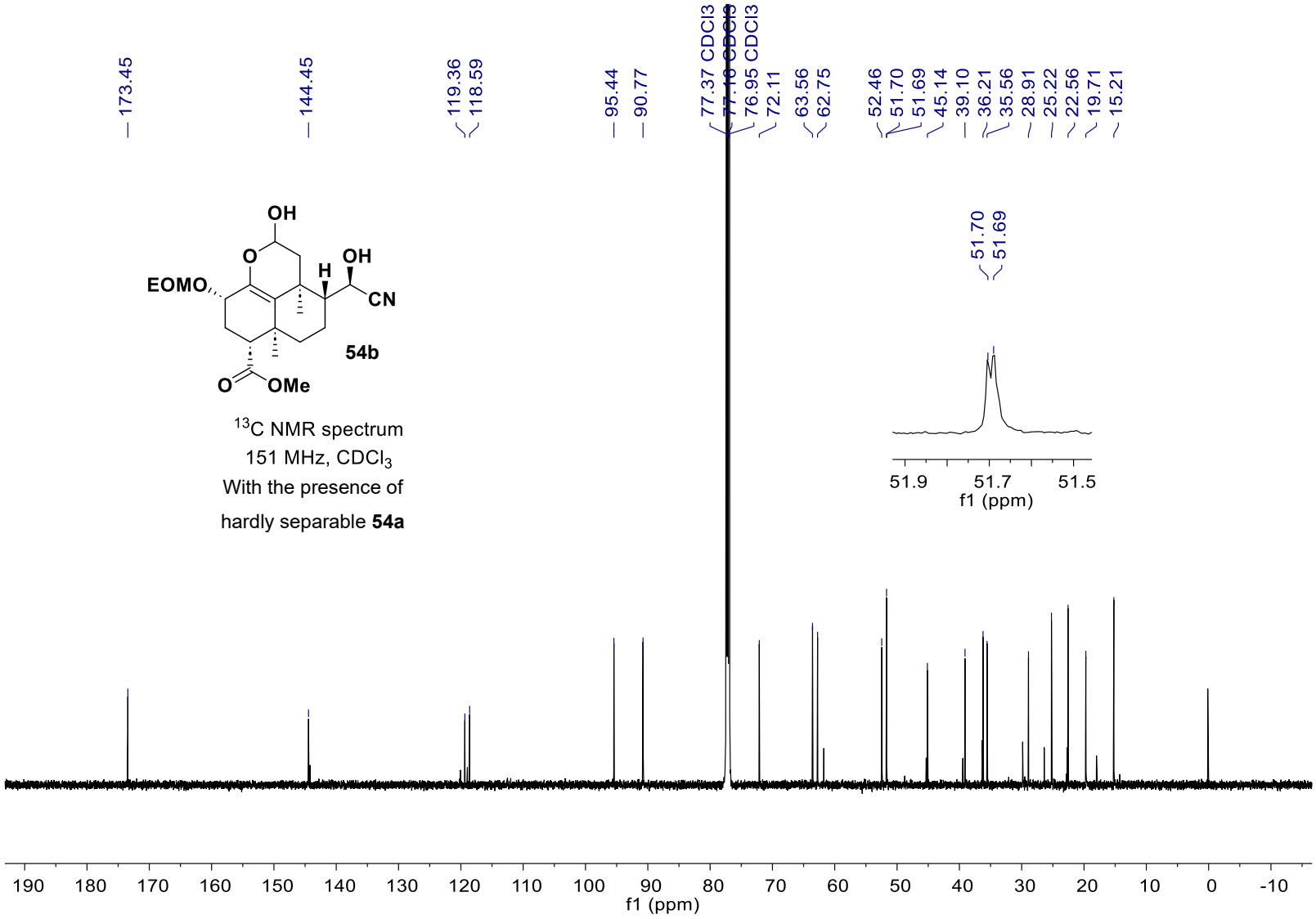

7.26 CDCl3
1.58 HDO
OH
O
OH
H
EOMO
CN
O
OMe
54a
1H NMR spectrum
400 MHz, CDCl3
With the presence of
hardly separable 54b
f1 (ppm)
f1 (ppm)



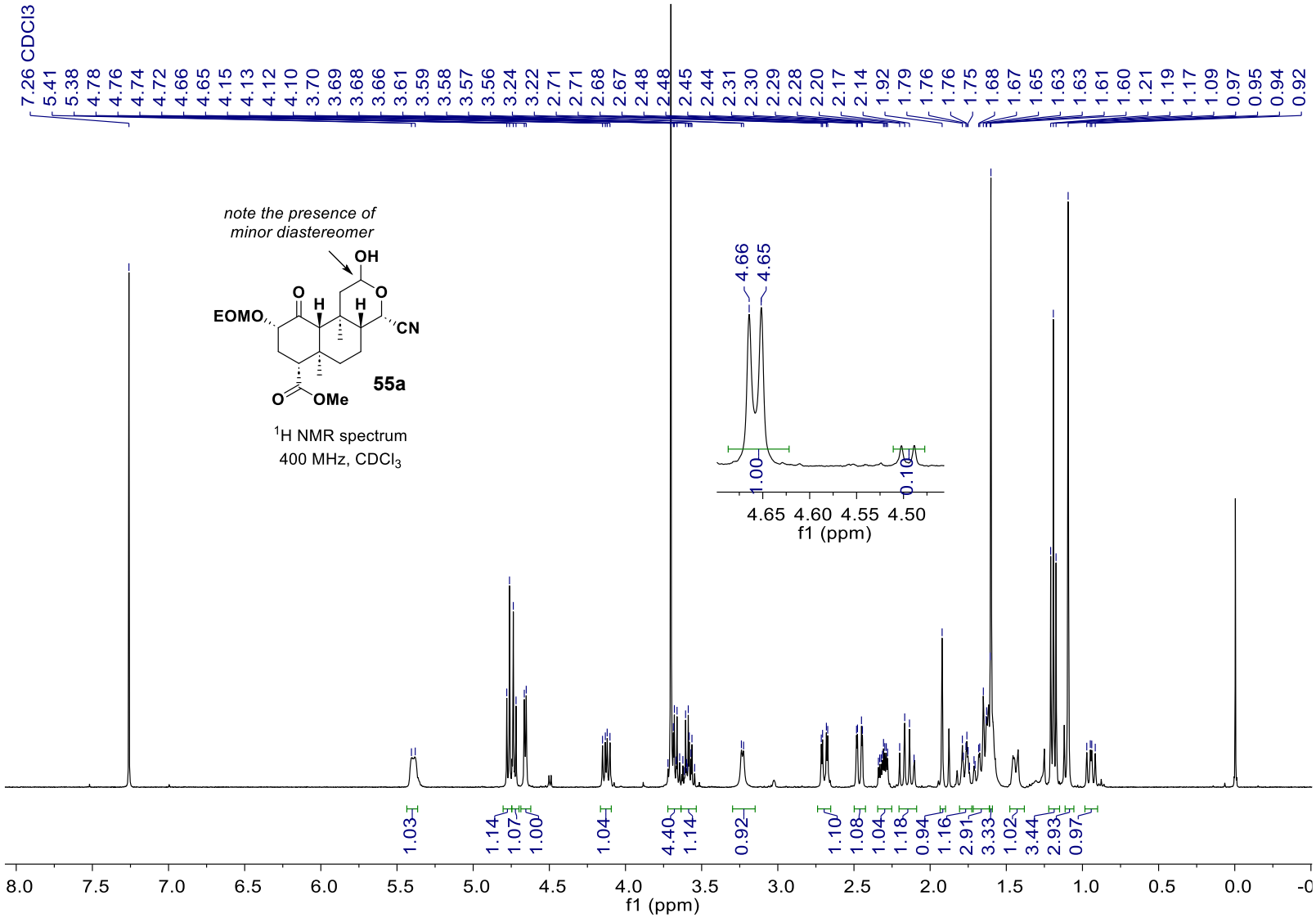
^{13}C NMR spectrum
151 MHz, $CDCl_3$

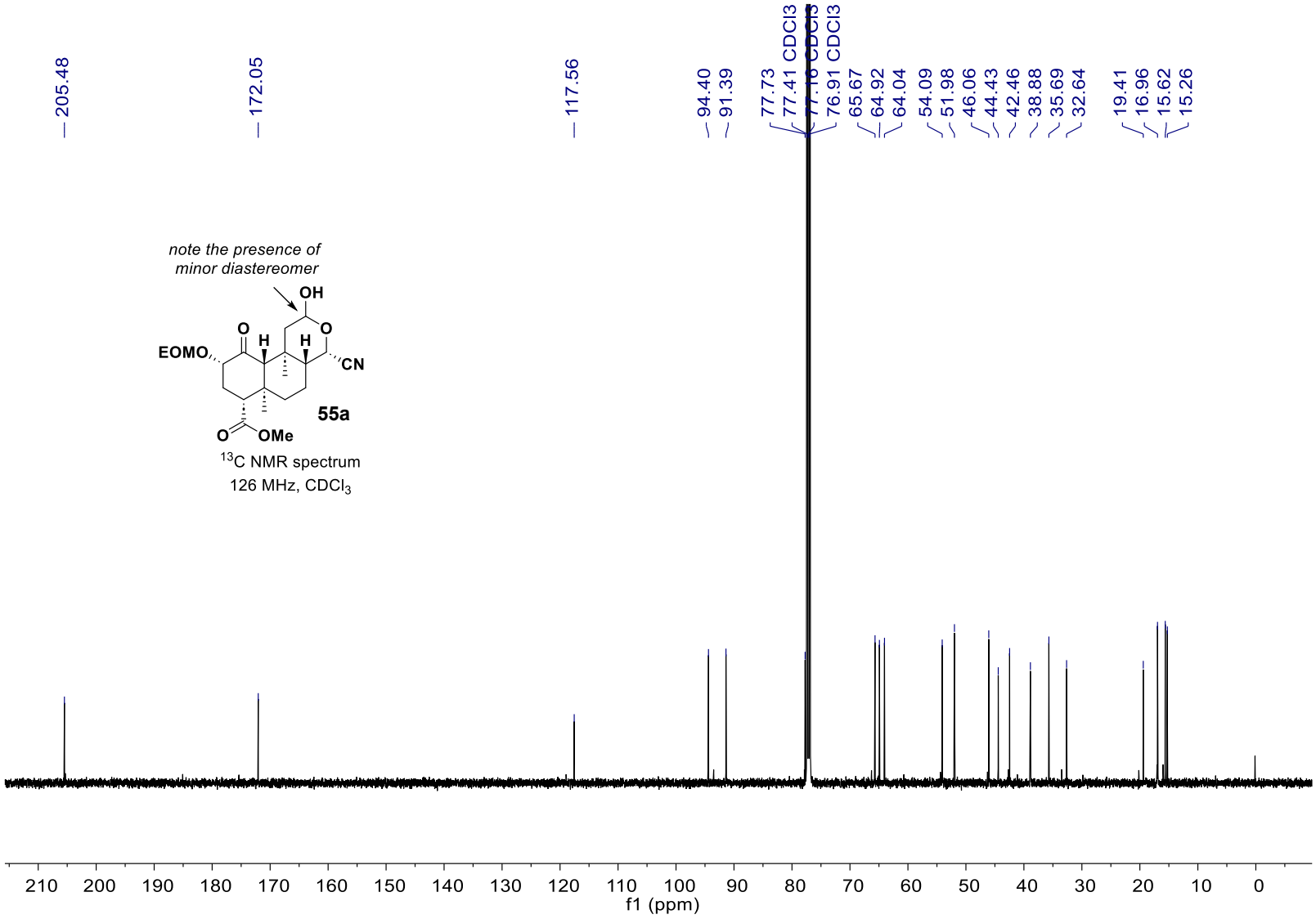
With the presence of
hardly separable **54b**

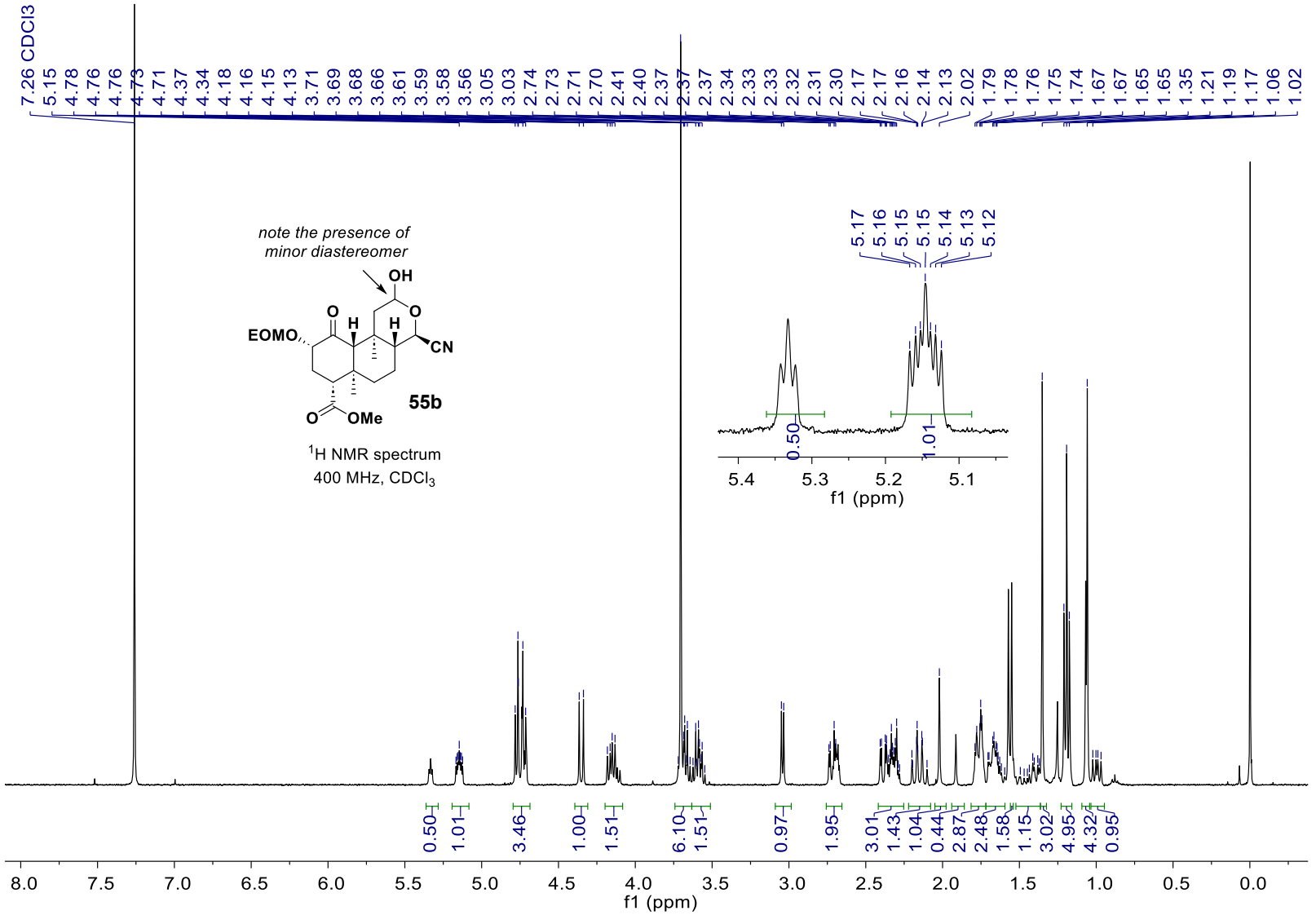

7.26 CDCl3
1.58 HDO
OH
O
H
OH
EOMO
CN
O
OMe
54b
1H NMR spectrum
400 MHz, CDCl3
With the presence of
hardly separable 54a
4.79
4.60
4.58
4.57
1.04
0.20
0.85
4.75 4.70 4.65 4.60 4.55
f1 (ppm)
1.00
0.99
1.04
0.85
1.00
4.21
1.08
0.68
0.78
0.94
0.80
1.92
2.67
1.33
1.01
1.08
2.91
6.09
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

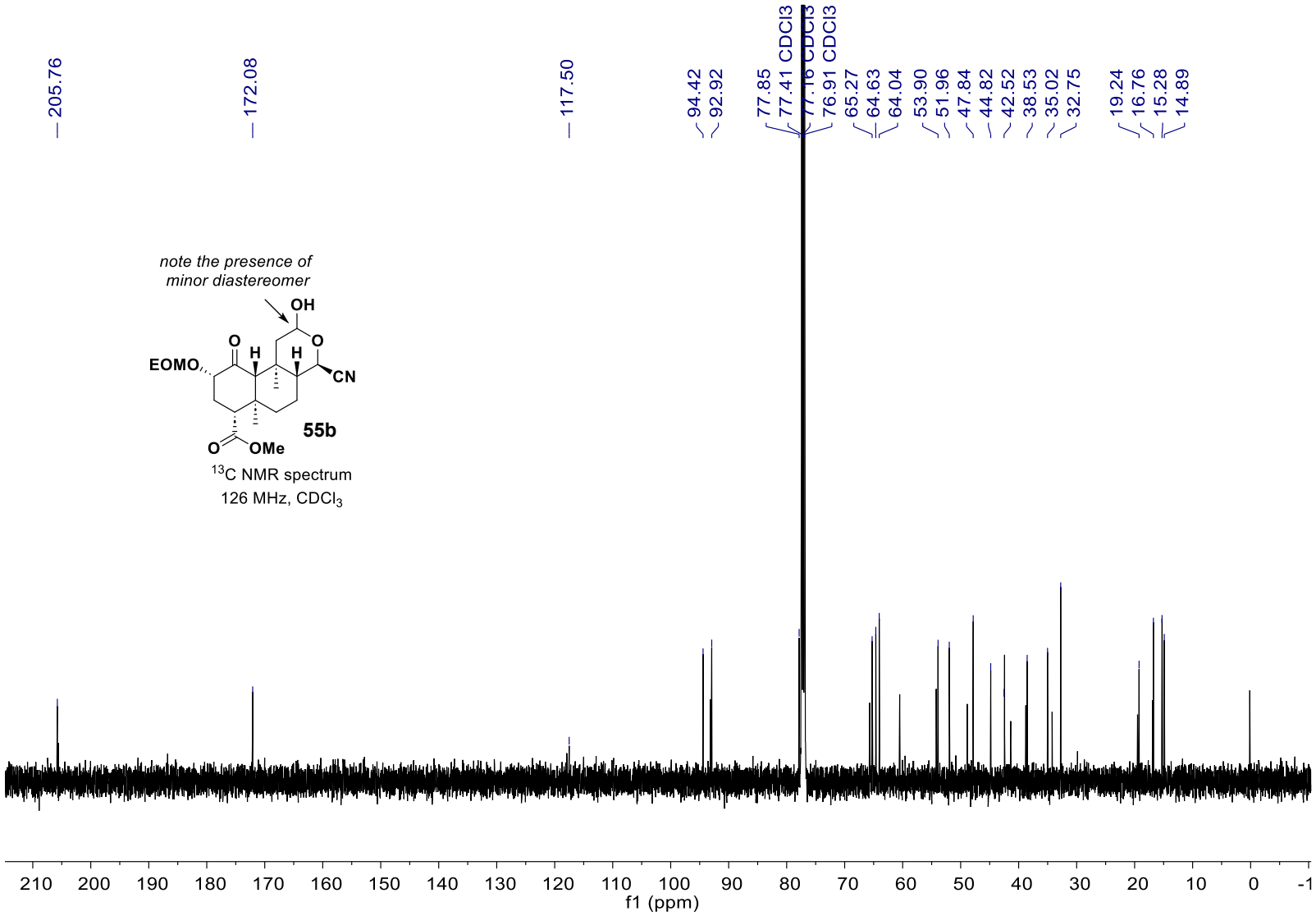


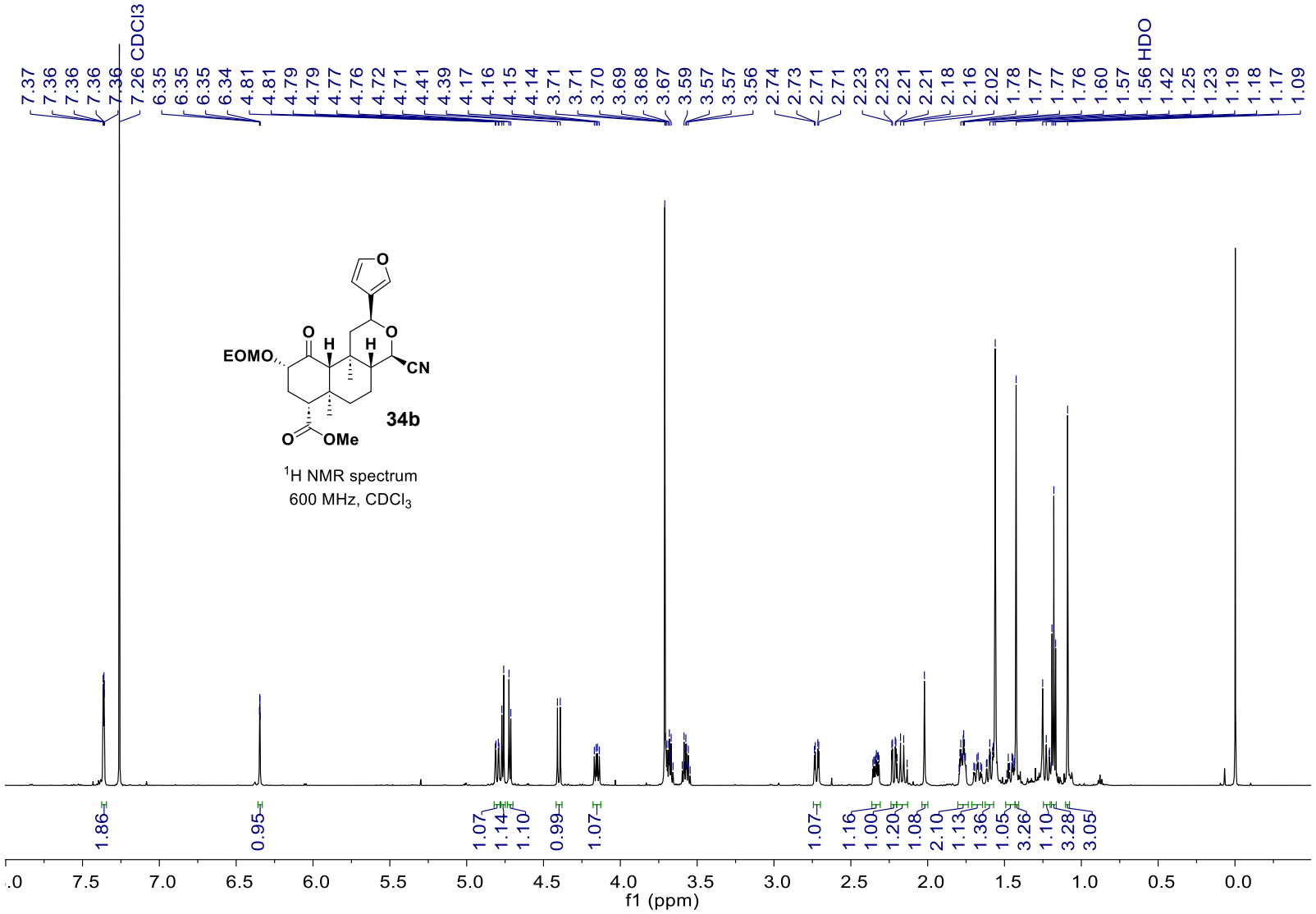
^{13}C NMR spectrum
151 MHz, $CDCl_3$
With the presence of
hardly separable **54a**

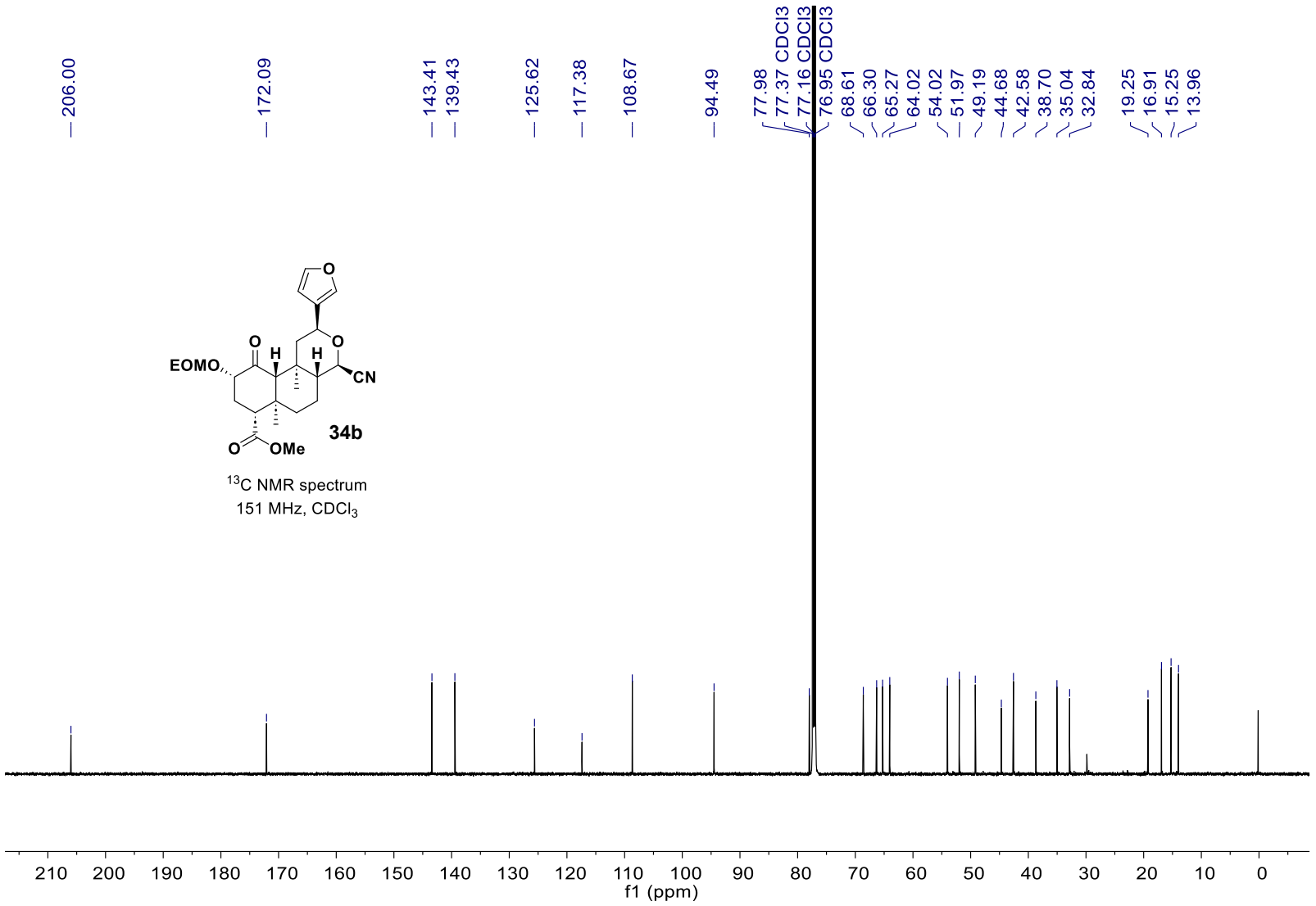

7.26 CDCl3
5.41 5.38 4.78 4.76 4.74 4.72 4.66 4.65 4.15 4.13 4.12 4.10 3.70 3.69 3.68 3.66 3.61 3.59 3.58 3.57 3.56 3.24 3.22 2.71 2.71 2.68 2.67 2.48 2.48 2.45 2.44 2.31 2.30 2.29 2.28 2.20 2.17 2.14 1.92 1.79 1.76 1.76 1.75 1.68 1.67 1.65 1.63 1.63 1.61 1.60 1.21 1.19 1.17 1.09 0.97 0.95 0.94 0.92
note the presence of minor diastereomer
OH
O
H
H
O
EOMO
CN
O
OMe
55a
1H NMR spectrum
400 MHz, CDCl3
4.66
4.65
1.00
0.10
4.65 4.60 4.55 4.50
f1 (ppm)
1.03 1.14 1.07 1.00 1.04 4.40 1.14 0.92 1.10 1.08 1.04 1.18 0.94 1.16 2.91 3.33 1.02 3.44 2.93 0.97
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
f1 (ppm)


205.48
172.05
117.56
94.40
91.39
77.73
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
65.67
64.92
64.04
54.09
51.98
46.06
44.43
42.46
38.88
35.69
32.64
19.41
16.96
15.62
15.26
note the presence of
minor diastereomer
OH
O
H
H
O
EOMO
CN
55a
O
OMe
13C NMR spectrum
126 MHz, 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)

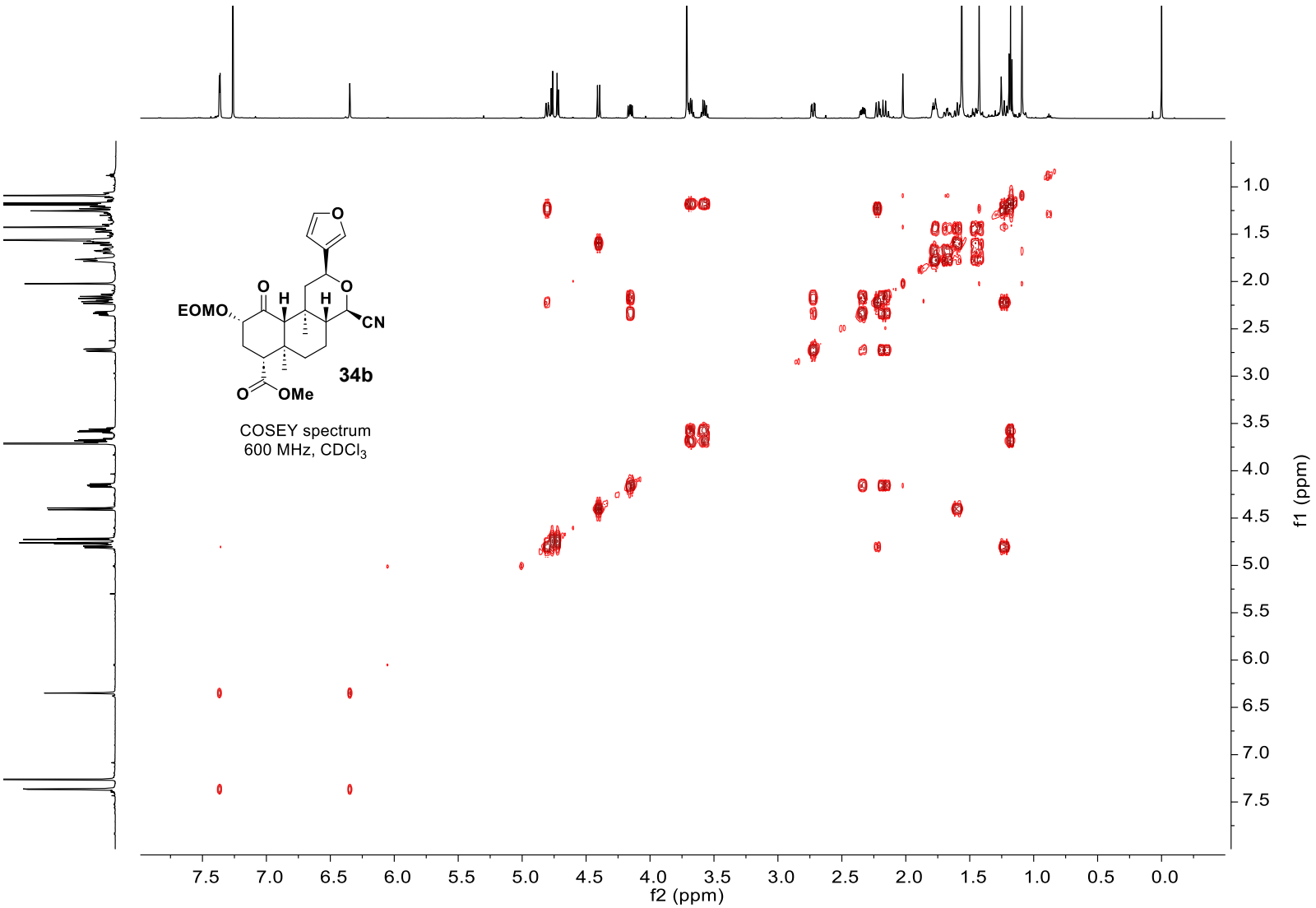

note the presence of
minor diastereomer
OH
O
H
H
O
EOMO
CN
O
OMe
55b
1H NMR spectrum
400 MHz, CDCl3
f1 (ppm)
f1 (ppm)

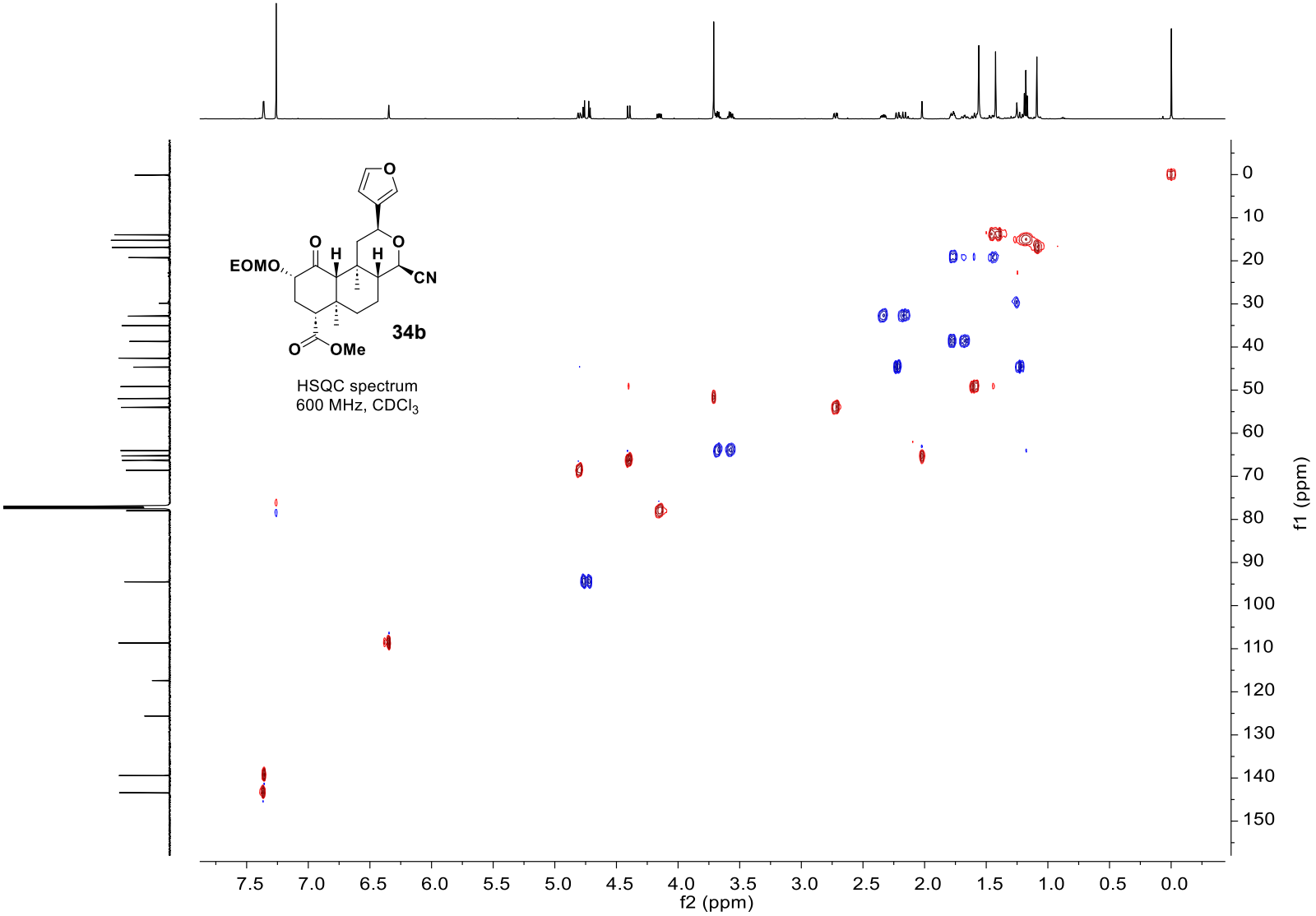

205.76
172.08
117.50
94.42
92.92
77.85
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
65.27
64.63
64.04
53.90
51.96
47.84
44.82
42.52
38.53
35.02
32.75
19.24
16.76
15.28
14.89
note the presence of
minor diastereomer
OH
O
H
H
O
EOMO
CN
55b
O
OMe
13C NMR spectrum
126 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

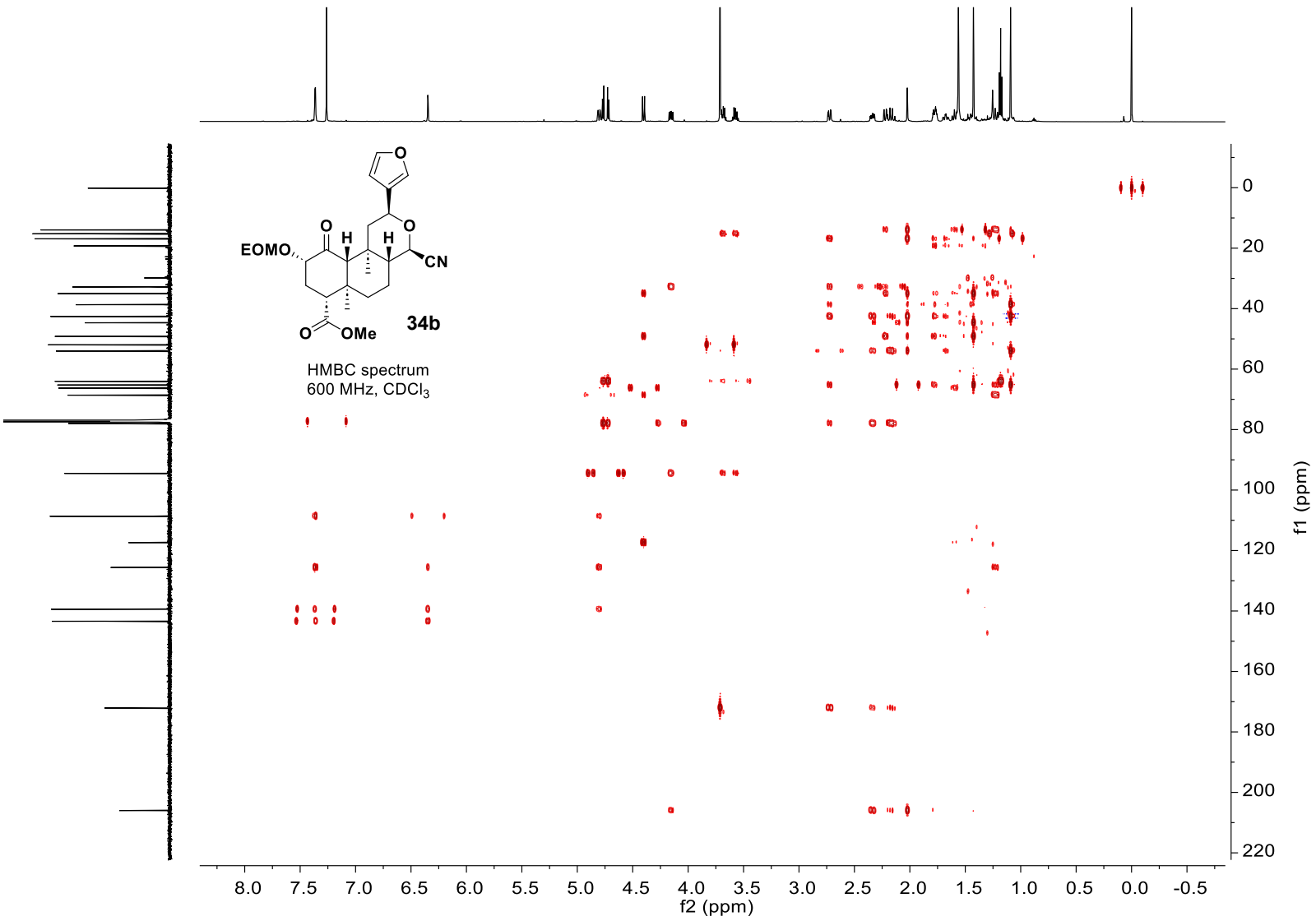

7.37
7.36
7.36
7.36
7.36
7.26 CDCl3
6.35
6.35
6.35
6.34
4.81
4.81
4.79
4.79
4.77
4.76
4.72
4.71
4.41
4.39
4.17
4.16
4.15
4.14
3.71
3.71
3.70
3.69
3.68
3.67
3.59
3.57
3.57
3.56
2.74
2.73
2.71
2.71
2.23
2.23
2.21
2.21
2.18
2.16
2.02
1.78
1.77
1.77
1.76
1.60
1.57
1.56 HDO
1.42
1.25
1.23
1.19
1.18
1.17
1.09
EOMO
O
H
H
O
CN
O
O
OMe
34b
1H NMR spectrum
600 MHz, CDCl3
1.86
0.95
1.07
1.14
1.10
0.99
1.07
1.07
1.16
1.00
1.20
1.08
2.10
1.13
1.36
1.05
3.26
1.10
3.28
3.05
.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
f1 (ppm)

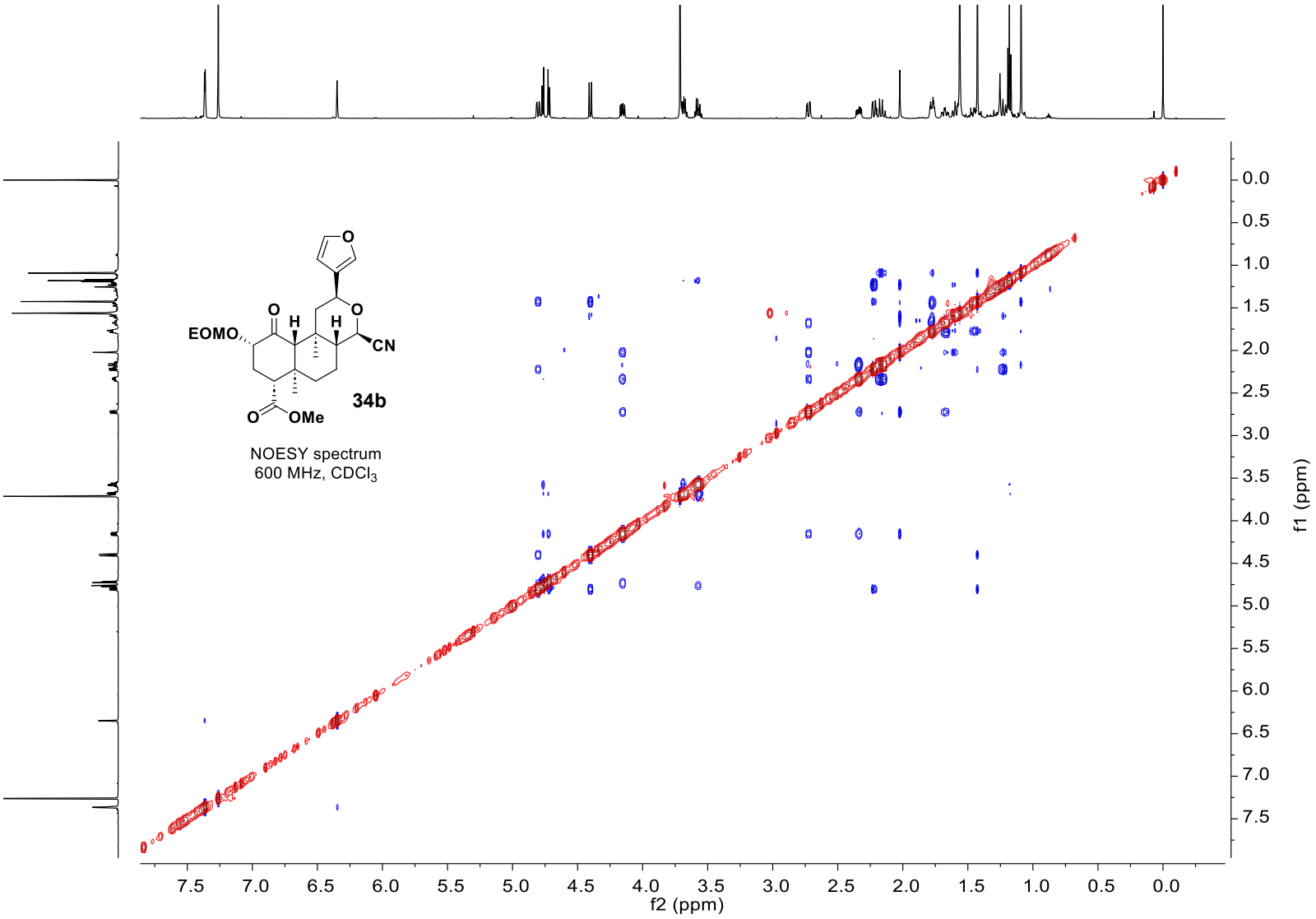


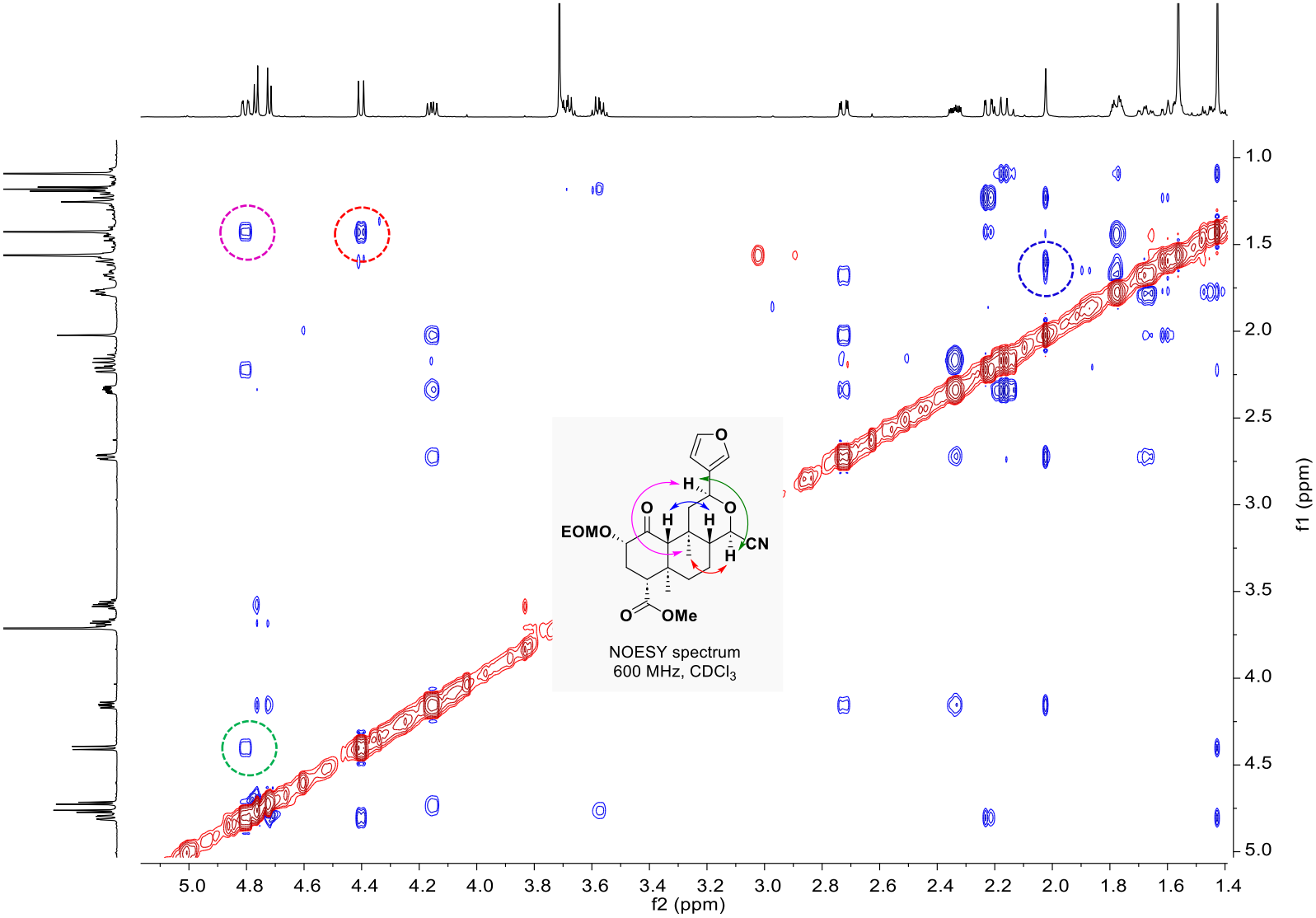
^{13}C NMR spectrum
151 MHz, $CDCl_3$

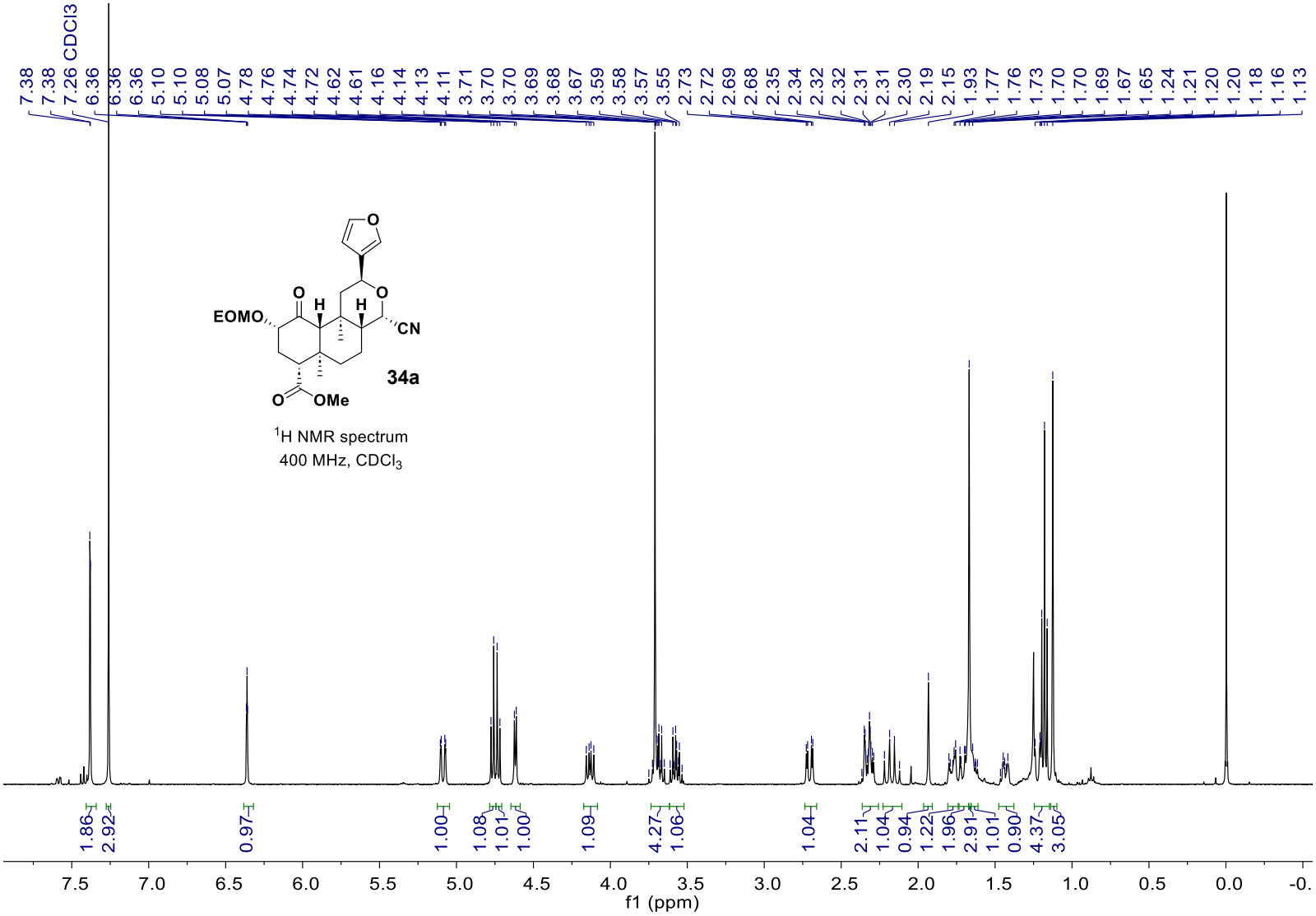

EOMO
O
H
H
O
CN
O
O
OMe
34b
COSEY spectrum
600 MHz, CDCl3
f2 (ppm)
f1 (ppm)

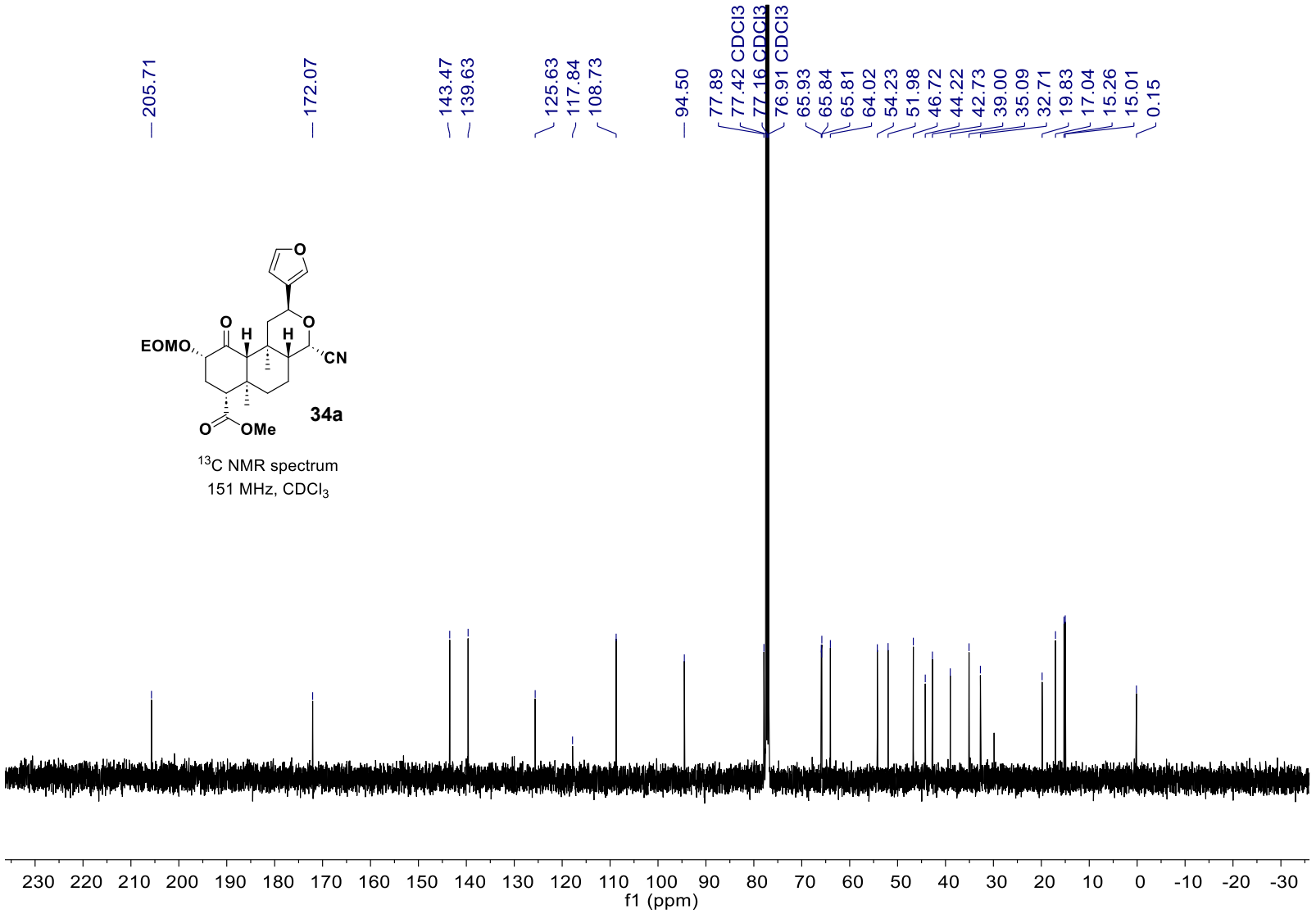

EOMO
O
H
H
O
CN
O
OMe
34b
HSQC spectrum
600 MHz, CDCl3
f2 (ppm)
f1 (ppm)


EOMO
O
H
H
O
CN
O
OMe
34b
HMBC spectrum
600 MHz, CDCl3
f2 (ppm)
f1 (ppm)

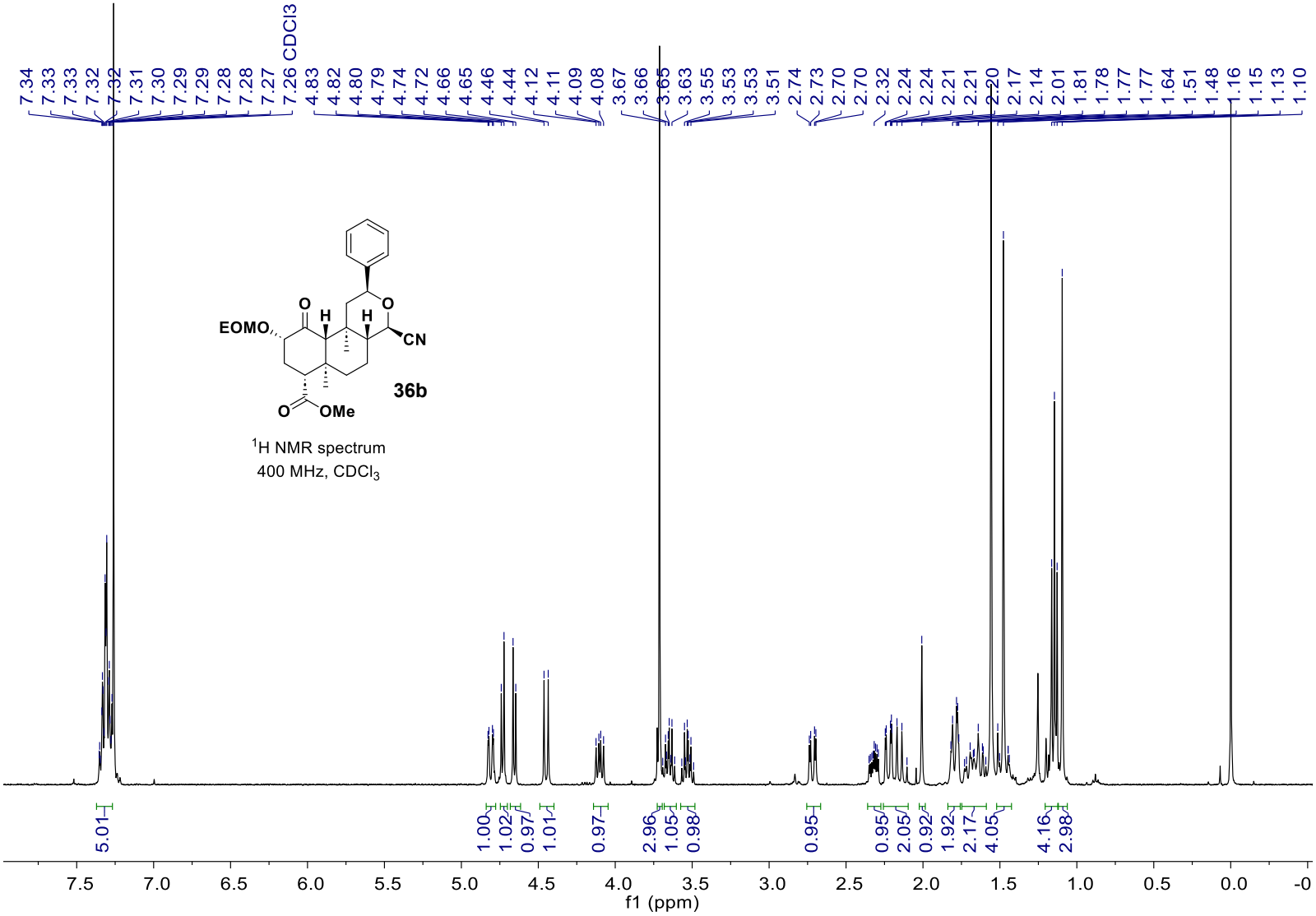

EOMO
O
H
H
O
CN
O
OMe
34b
NOESY spectrum
600 MHz, CDCl3
f2 (ppm)
f1 (ppm)

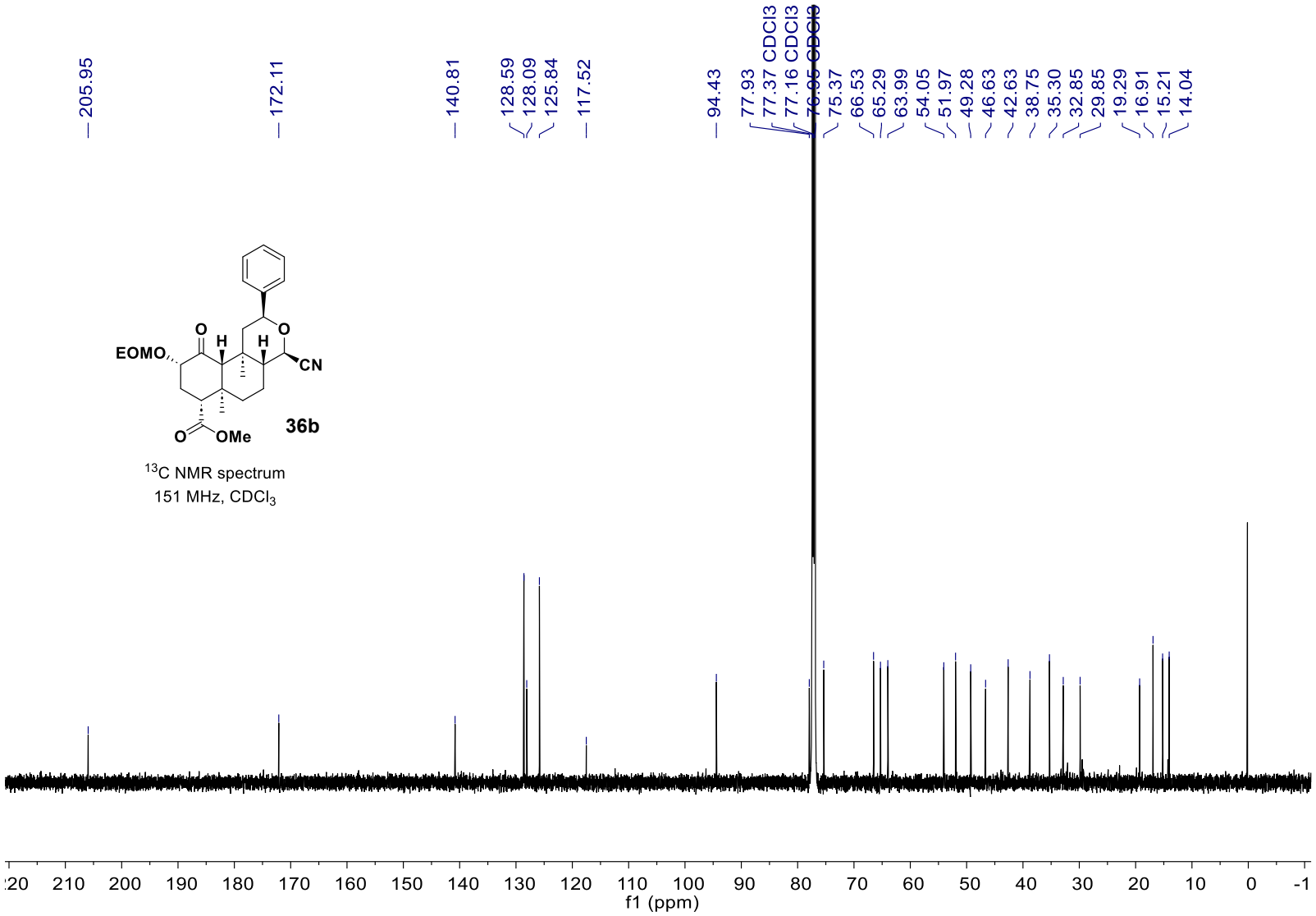

EOMO
CN
OMe
NOESY spectrum
600 MHz, CDCl3
f2 (ppm)
f1 (ppm)

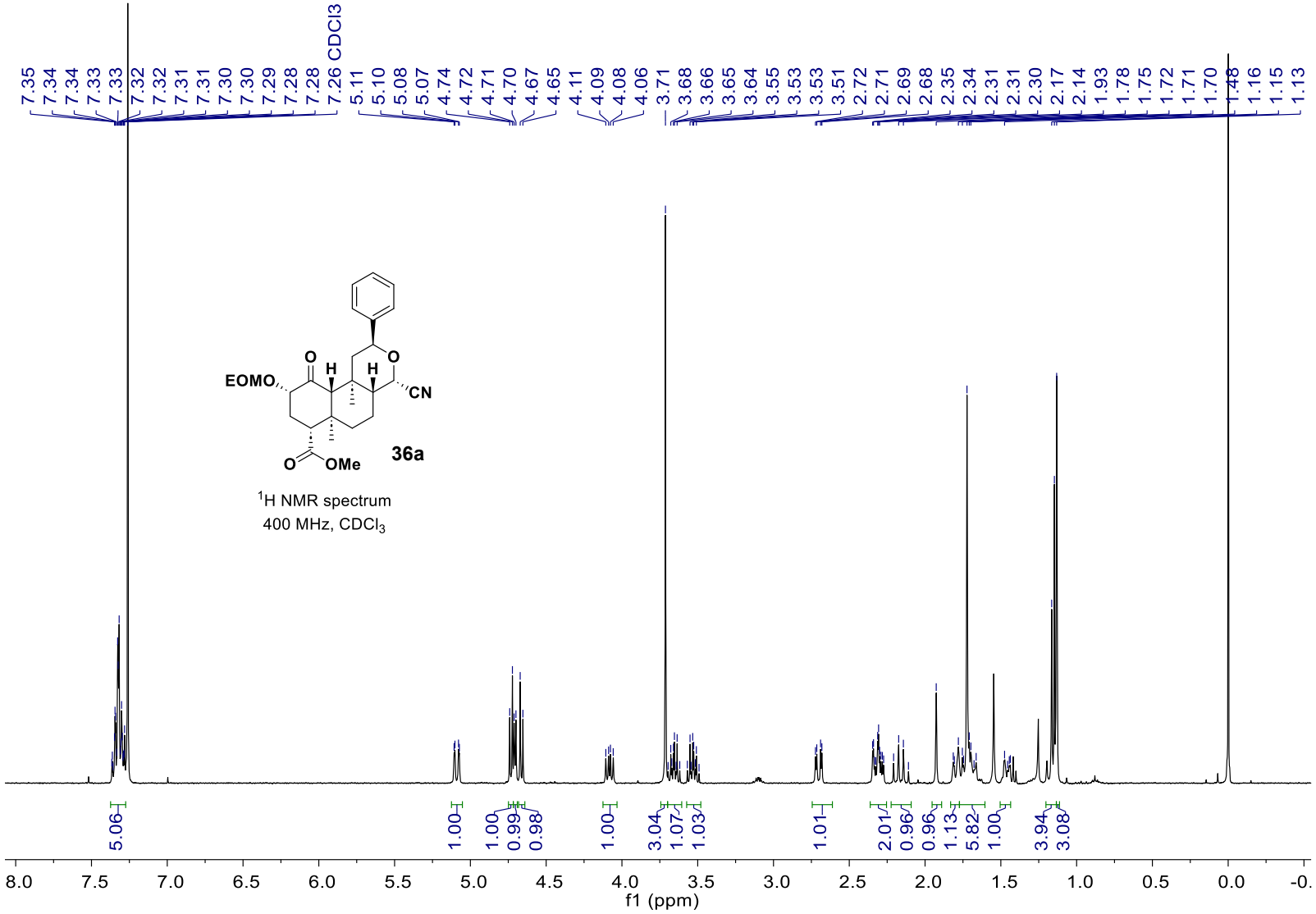

7.38 7.38 7.26 CDCl3 6.36 6.36 6.36 5.10 5.10 5.08 5.07 4.78 4.76 4.74 4.72 4.62 4.61 4.16 4.14 4.13 4.11 3.71 3.70 3.70 3.69 3.68 3.67 3.59 3.58 3.57 3.55 2.73 2.72 2.69 2.68 2.35 2.34 2.32 2.32 2.31 2.31 2.30 2.19 2.15 1.93 1.77 1.76 1.73 1.70 1.70 1.69 1.67 1.65 1.24 1.21 1.20 1.20 1.18 1.16 1.13
EOMO
H
H
CN
34a
O
OMe
1H NMR spectrum
400 MHz, CDCl3
1.86 2.92 0.97 1.00 1.08 1.01 1.00 1.09 4.27 1.06 1.04 2.11 1.04 0.94 1.22 1.96 2.91 1.01 0.90 4.37 3.05
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.
f1 (ppm)

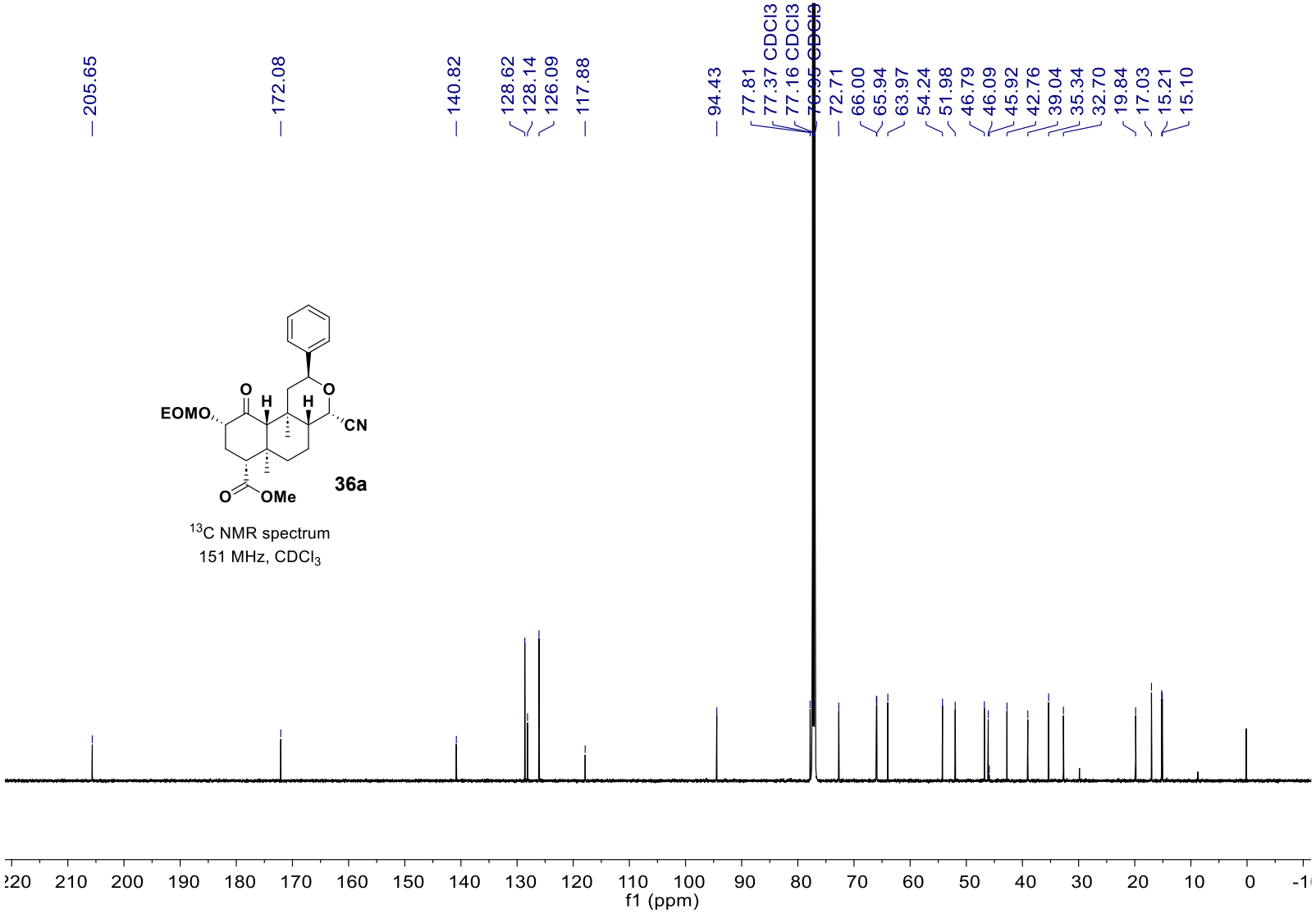


^{13}C NMR spectrum
151 MHz, $CDCl_3$

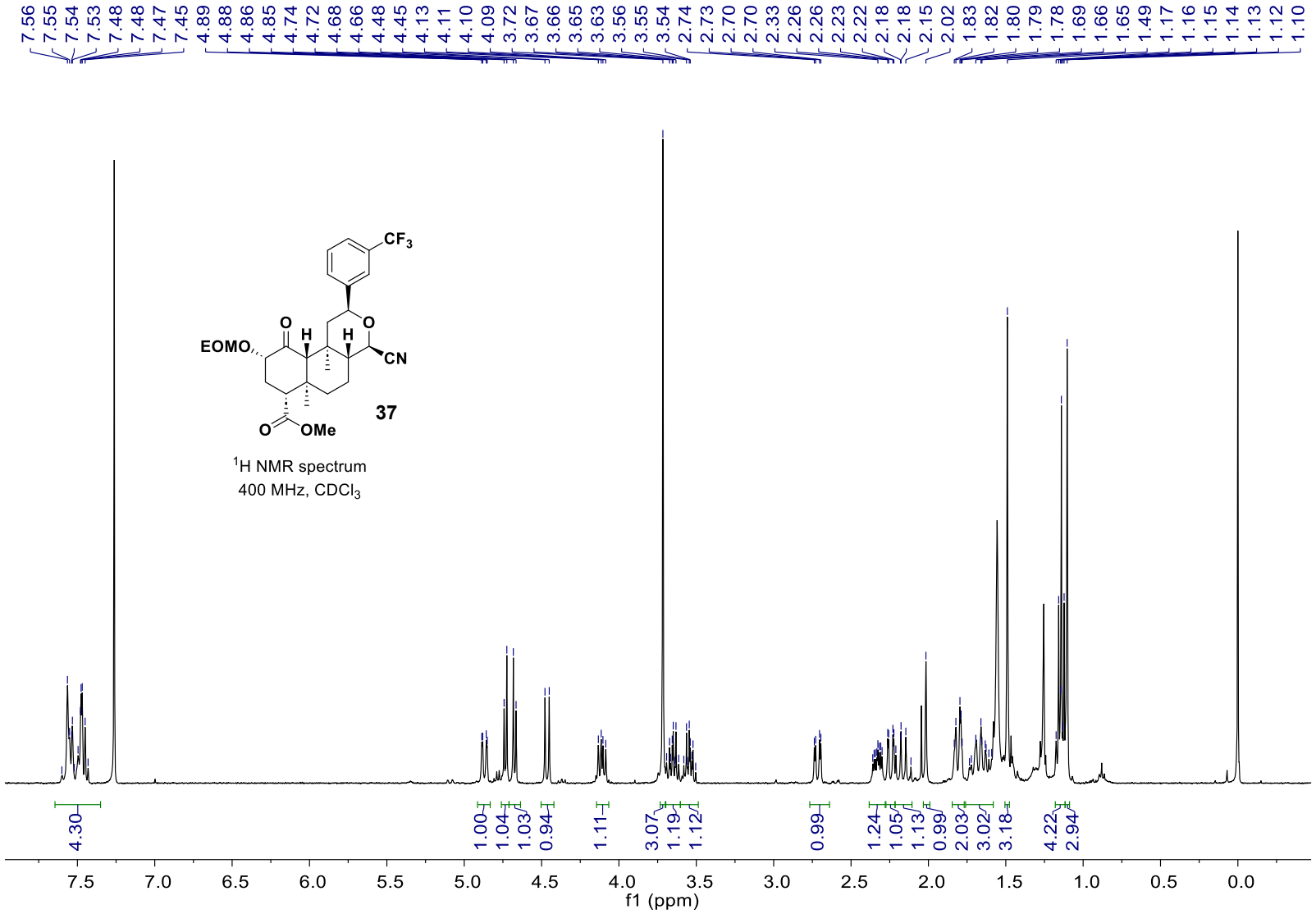

7.34 7.33 7.33 7.32 7.32 7.31 7.30 7.29 7.29 7.28 7.28 7.27 7.26 CDCl3
4.83 4.82 4.80 4.79 4.74 4.72 4.66 4.65 4.46 4.44 4.12 4.11 4.09 4.08
3.67 3.66 3.65 3.63 3.55 3.53 3.53 3.51
2.74 2.73 2.70 2.70 2.32 2.24 2.24 2.21 2.21 2.20 2.17 2.14 2.01
1.81 1.78 1.77 1.77 1.64 1.51 1.48 1.16 1.15 1.13 1.10
EOMO
O
H
H
O
CN
O
OMe
36b
1H NMR spectrum
400 MHz, CDCl3
5.01
1.00 1.02 0.97 1.01 0.97 2.96 1.05 0.98 0.95 0.95 2.05 0.92 1.92 2.17 4.05 4.16 2.98
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
f1 (ppm)

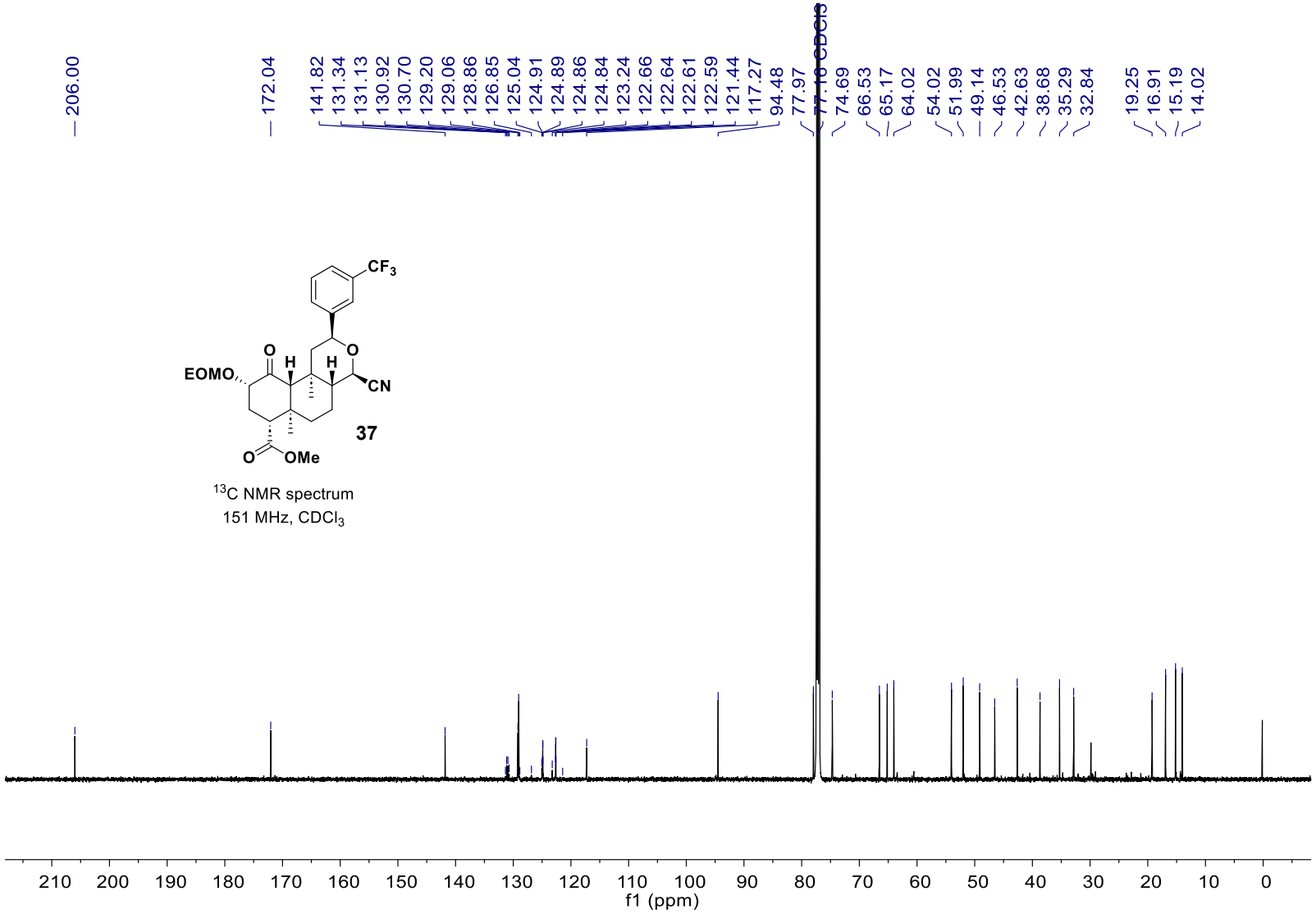

205.95
172.11
140.81
128.59
128.09
125.84
117.52
94.43
77.93
77.37 CDCl3
77.16 CDCl3
76.95 CDCl3
75.37
66.53
65.29
63.99
54.05
51.97
49.28
46.63
42.63
38.75
35.30
32.85
29.85
19.29
16.91
15.21
14.04
EOMO
O
H
H
O
CN
O
OMe
36b
13C NMR spectrum
151 MHz, CDCl3
f1 (ppm)


7.35 7.34 7.34 7.33 7.33 7.32 7.32 7.31 7.31 7.30 7.30 7.29 7.28 7.28 7.26 CDCl3 5.11 5.10 5.08 5.07 4.74 4.72 4.71 4.70 4.67 4.65 4.11 4.09 4.08 4.06 3.71 3.68 3.66 3.65 3.64 3.55 3.53 3.53 3.51 2.72 2.71 2.69 2.68 2.35 2.34 2.31 2.31 2.30 2.17 2.14 1.93 1.78 1.75 1.72 1.71 1.70 1.48 1.16 1.15 1.13
EOMO
O
H
H
O
CN
O
OMe
36a
1H NMR spectrum
400 MHz, CDCl3
5.06 1.00 1.00 0.99 0.98 1.00 3.04 1.07 1.03 1.01 2.01 0.96 0.96 1.13 5.82 1.00 3.94 3.08
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
f1 (ppm)

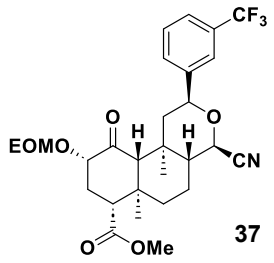


^{13}C NMR spectrum
151 MHz, $CDCl_3$


7.56 7.55 7.54 7.53 7.48 7.48 7.47 7.45 4.89 4.88 4.86 4.85 4.74 4.72 4.68 4.66 4.48 4.45 4.13 4.11 4.10 4.09 3.72 3.67 3.66 3.65 3.63 3.56 3.55 3.54 2.74 2.73 2.70 2.70 2.33 2.26 2.26 2.23 2.22 2.18 2.18 2.15 2.02 1.83 1.82 1.80 1.79 1.78 1.69 1.66 1.65 1.49 1.17 1.16 1.15 1.14 1.13 1.12 1.10
CF3
O
H
H
O
EOMO
CN
37
O
OMe
1H NMR spectrum
400 MHz, CDCl3
4.30 1.00 1.04 1.03 0.94 1.11 3.07 1.19 1.12 0.99 1.24 1.05 1.13 0.99 2.03 3.02 3.18 4.22 2.94
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
f1 (ppm)

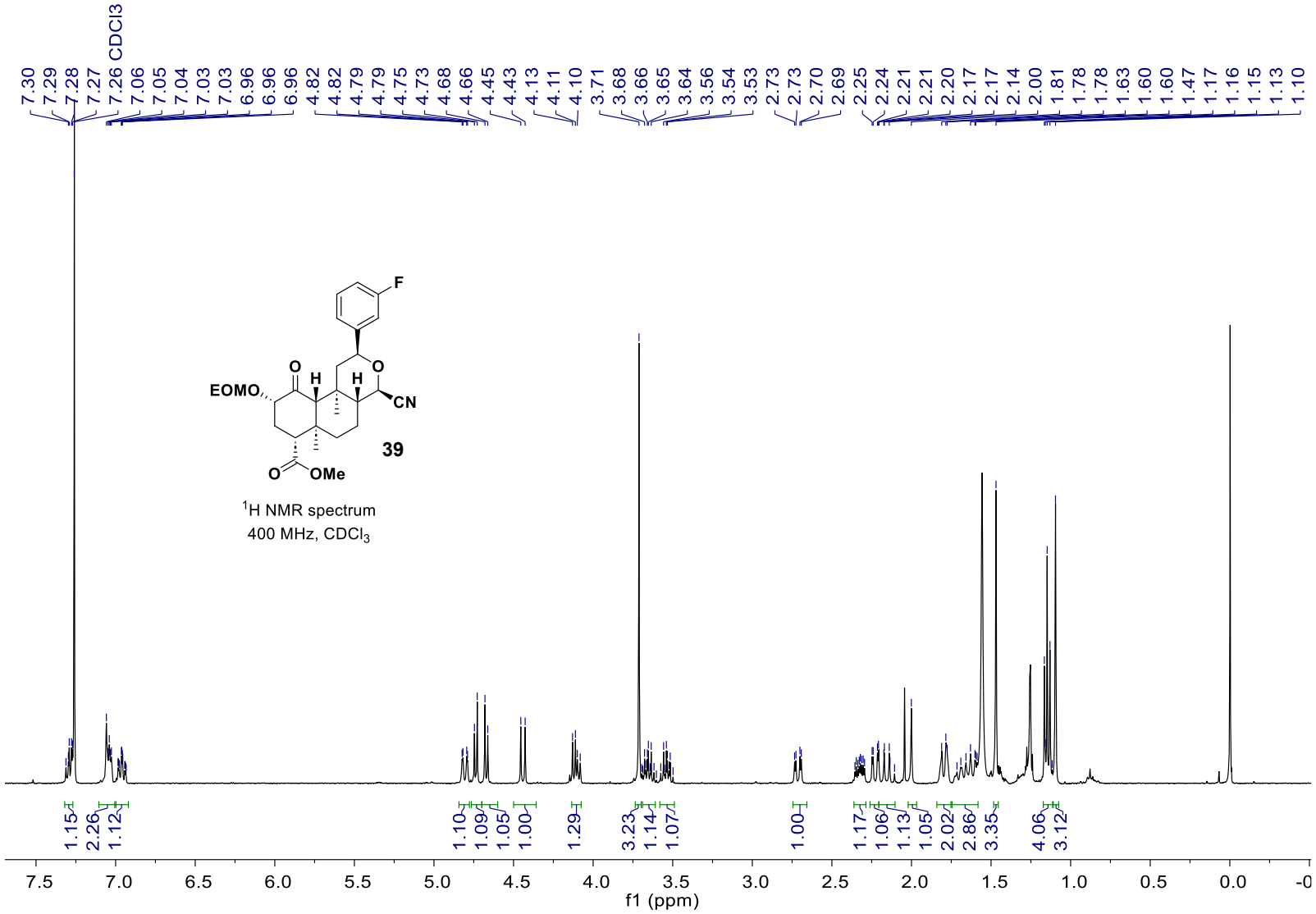


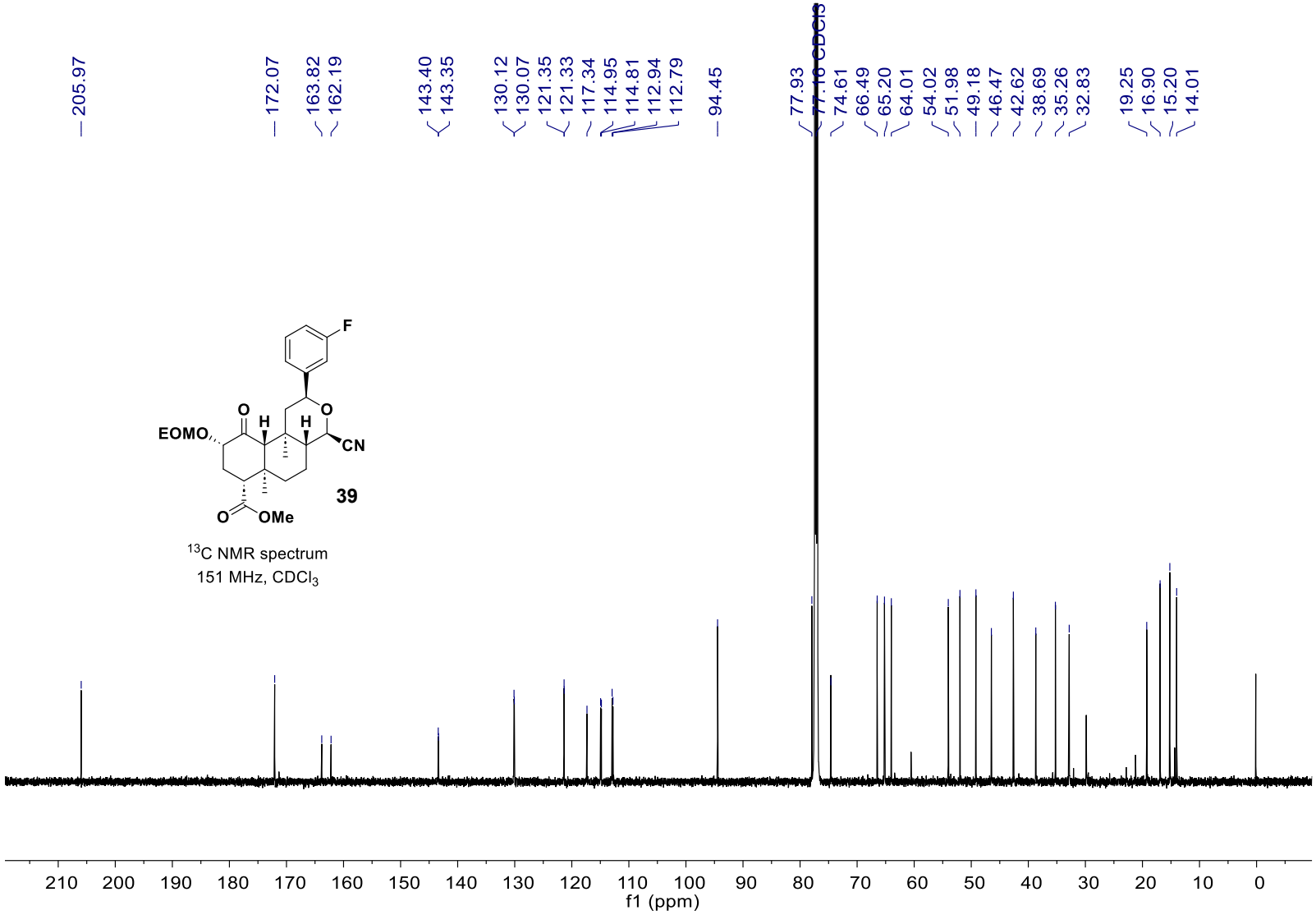
^{13}C NMR spectrum
151 MHz, $CDCl_3$



37

^{19}F NMR spectrum
565 MHz, $CDCl_3$

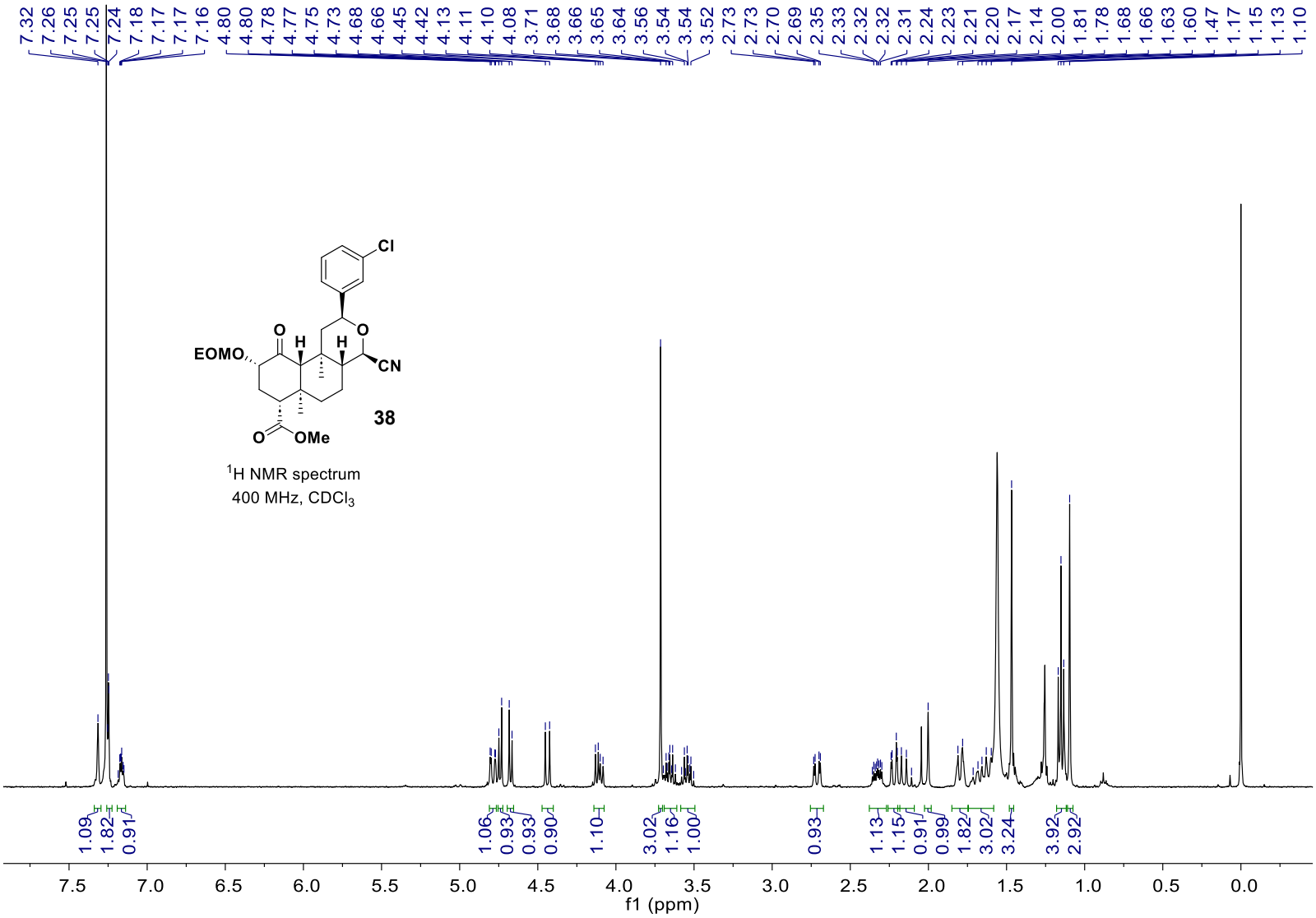

7.30 7.29 7.28 7.27 7.26 CDCl3 7.06 7.05 7.04 7.03 7.03 6.96 6.96 6.96 4.82 4.82 4.79 4.79 4.75 4.73 4.68 4.66 4.45 4.43 4.13 4.11 4.10 3.71 3.68 3.66 3.65 3.64 3.56 3.54 3.53 2.73 2.73 2.70 2.69 2.25 2.24 2.21 2.21 2.20 2.17 2.17 2.14 2.00 1.81 1.78 1.78 1.63 1.60 1.60 1.47 1.17 1.16 1.15 1.13 1.10
F
O
H
H
O
EOMO
CN
39
O
OMe
1H NMR spectrum
400 MHz, CDCl3
1.15 2.26 1.12 1.10 1.09 1.05 1.00 1.29 3.23 1.14 1.07 1.00 1.17 1.06 1.13 1.05 2.02 2.86 3.35 4.06 3.12
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
f1 (ppm)

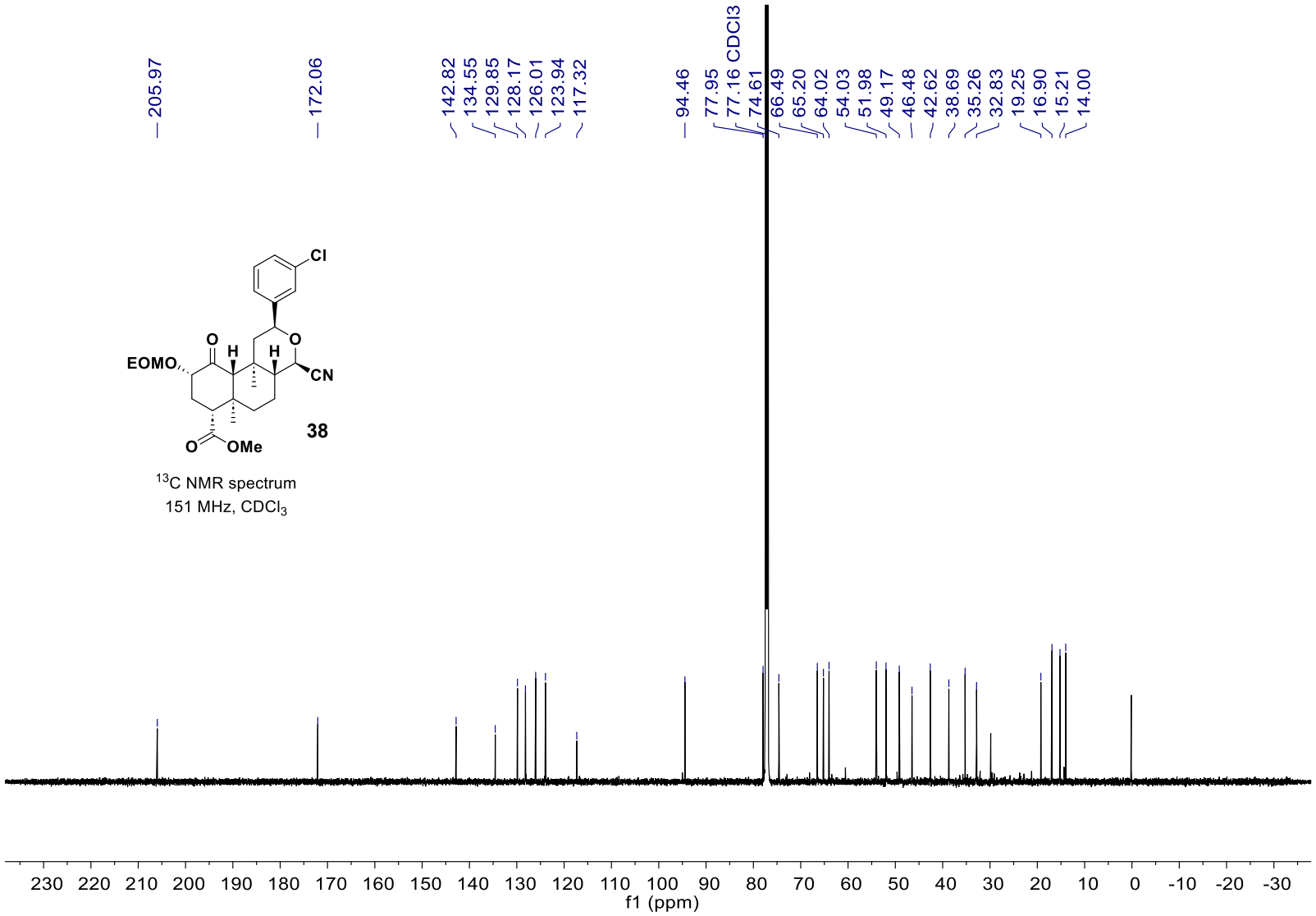


^{13}C NMR spectrum
151 MHz, $CDCl_3$

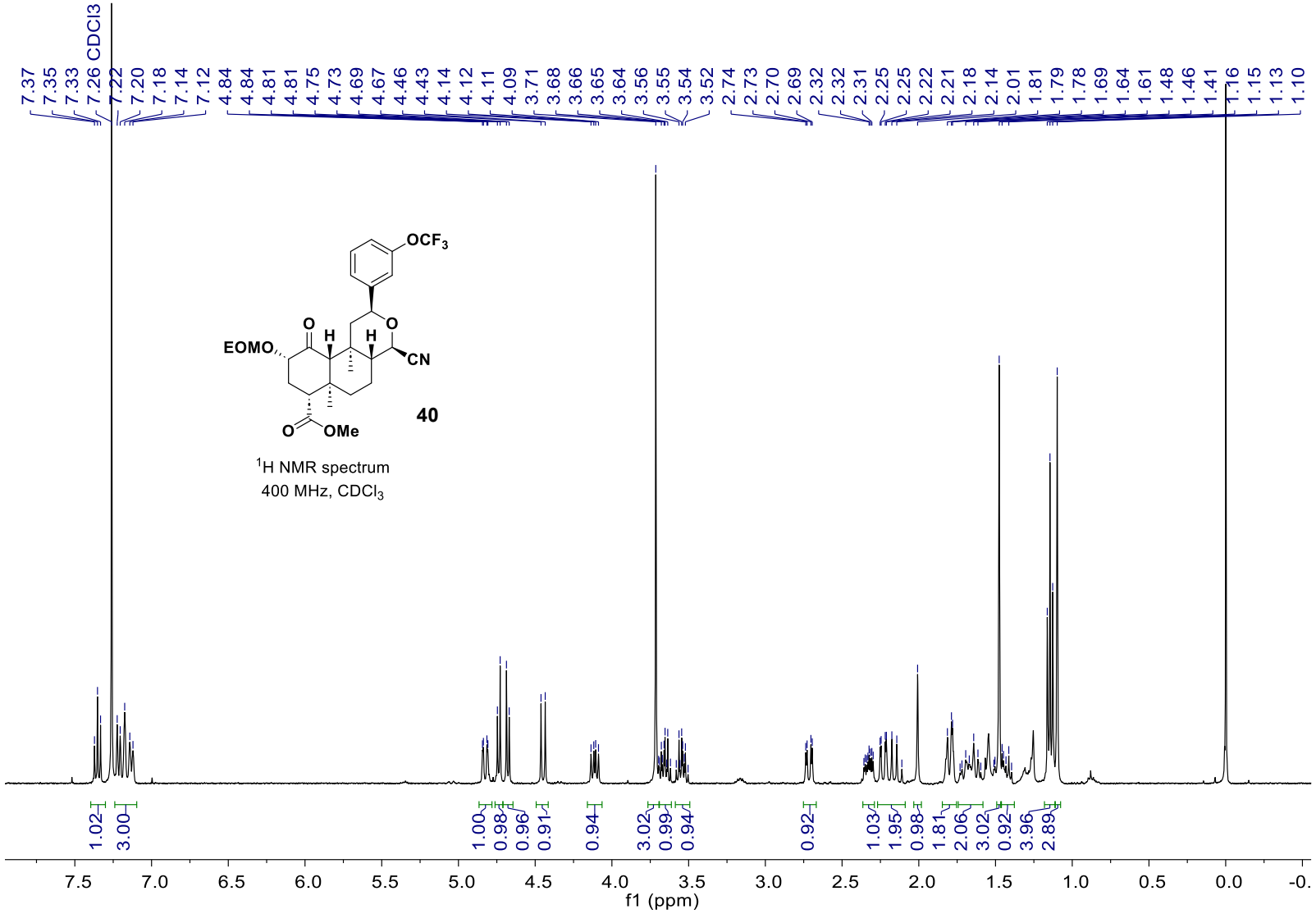


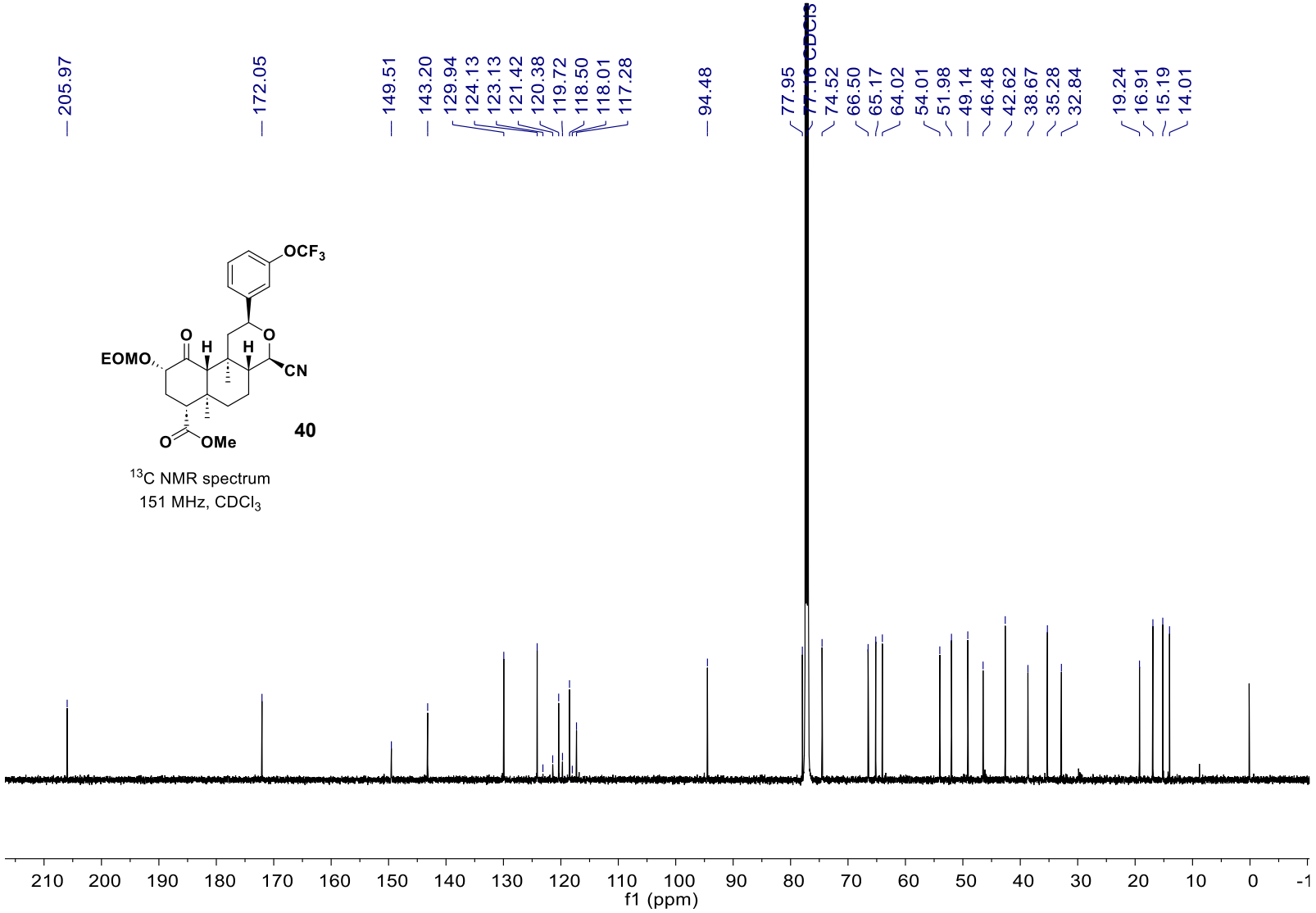
^{19}F NMR spectrum
565 MHz, $CDCl_3$


7.32 7.26 7.25 7.25 7.24 7.18 7.17 7.17 7.16 4.80 4.80 4.78 4.77 4.75 4.73 4.68 4.66 4.45 4.42 4.13 4.11 4.10 4.08 3.71 3.68 3.66 3.65 3.64 3.56 3.54 3.54 3.52 2.73 2.73 2.70 2.69 2.35 2.33 2.32 2.32 2.31 2.24 2.23 2.21 2.20 2.17 2.14 2.00 1.81 1.78 1.68 1.66 1.63 1.60 1.47 1.17 1.15 1.13 1.10
Cl
O
H
H
O
EOMO
CN
38
O
OMe
1H NMR spectrum
400 MHz, CDCl3
1.09 1.82 0.91 1.06 0.93 0.93 0.90 1.10 3.02 1.16 1.00 0.93 1.13 1.15 0.91 0.99 1.82 3.02 3.24 3.92 2.92
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
f1 (ppm)

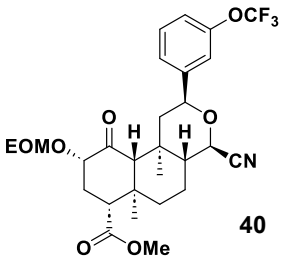


^{13}C NMR spectrum
151 MHz, $CDCl_3$


7.37
7.35
7.33
7.26 CDCl3
7.22
7.20
7.18
7.14
7.12
4.84
4.84
4.81
4.81
4.75
4.73
4.69
4.67
4.46
4.43
4.14
4.12
4.11
4.09
3.71
3.68
3.66
3.65
3.64
3.56
3.55
3.54
3.52
2.74
2.73
2.70
2.69
2.32
2.32
2.31
2.25
2.25
2.22
2.21
2.18
2.14
2.01
1.81
1.79
1.78
1.69
1.64
1.61
1.48
1.46
1.41
1.16
1.15
1.13
1.10
OCF3
O
H
H
O
EOMO
CN
O
OMe
40
1H NMR spectrum
400 MHz, CDCl3
1.02
3.00
1.00
0.98
0.96
0.91
0.94
3.02
0.99
0.94
0.92
1.03
1.95
0.98
1.81
2.06
3.02
0.92
3.96
2.89
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.
f1 (ppm)

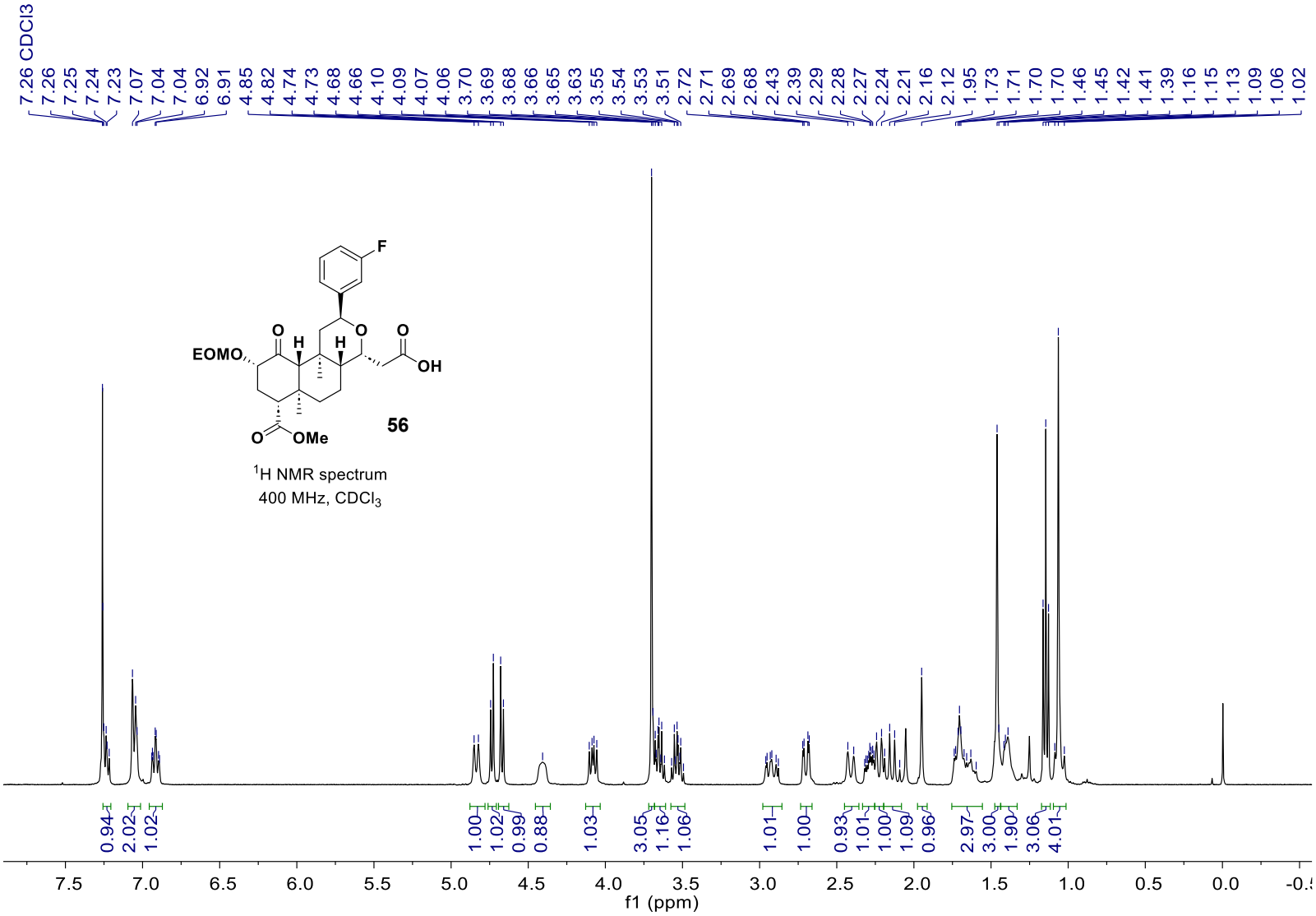


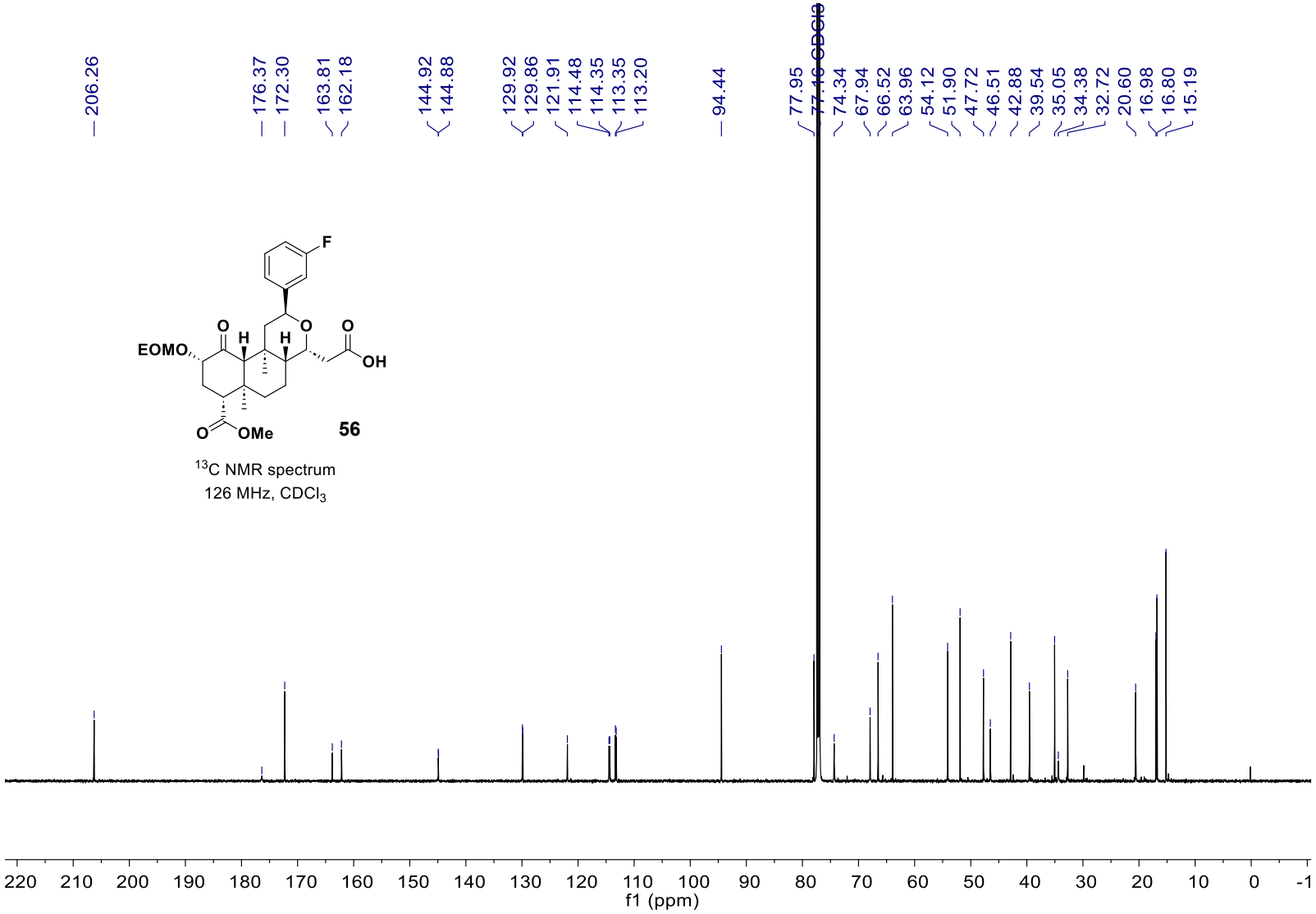
^{13}C NMR spectrum
151 MHz, $CDCl_3$



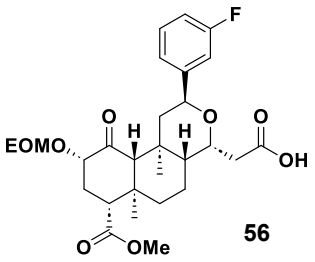
40

^{19}F NMR spectrum
565 MHz, $CDCl_3$


7.26 CDCl3
7.26 7.25 7.24 7.23 7.07 7.04 7.04 6.92 6.91 4.85 4.82 4.74 4.73 4.68 4.66 4.10 4.09 4.07 4.06 3.70 3.69 3.68 3.66 3.65 3.63 3.55 3.54 3.53 3.51 2.72 2.71 2.69 2.68 2.43 2.39 2.29 2.28 2.27 2.24 2.21 2.16 2.12 1.95 1.73 1.71 1.70 1.70 1.46 1.45 1.42 1.41 1.39 1.16 1.15 1.13 1.09 1.06 1.02
F
O
H
H
O
O
EOMO
OH
O
OMe
56
1H NMR spectrum
400 MHz, CDCl3
0.94 2.02 1.02 1.00 1.02 0.99 0.88 1.03 3.05 1.16 1.06 1.01 1.00 0.93 1.01 1.00 1.09 0.96 2.97 3.00 1.90 3.06 4.01
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
f1 (ppm)

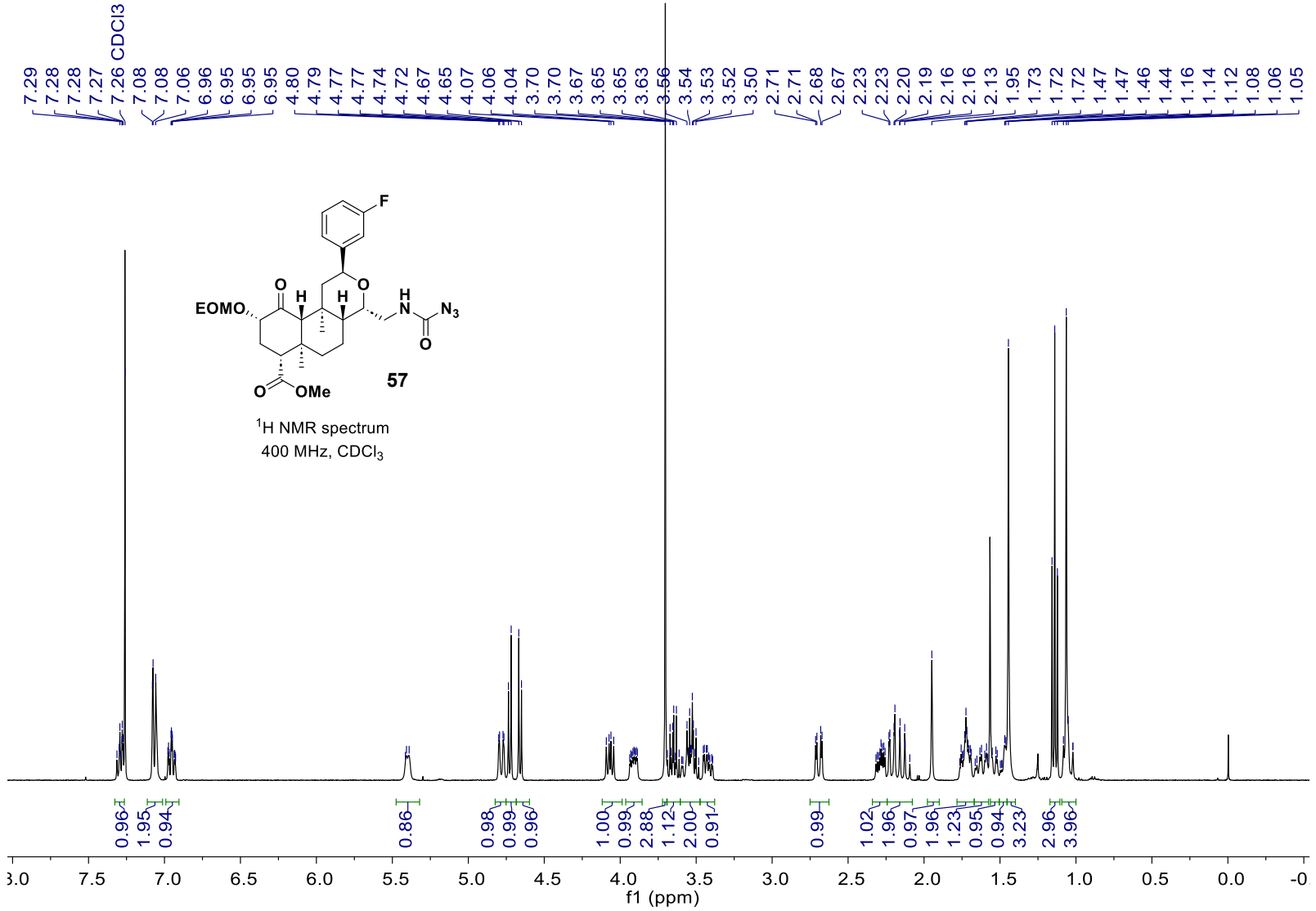


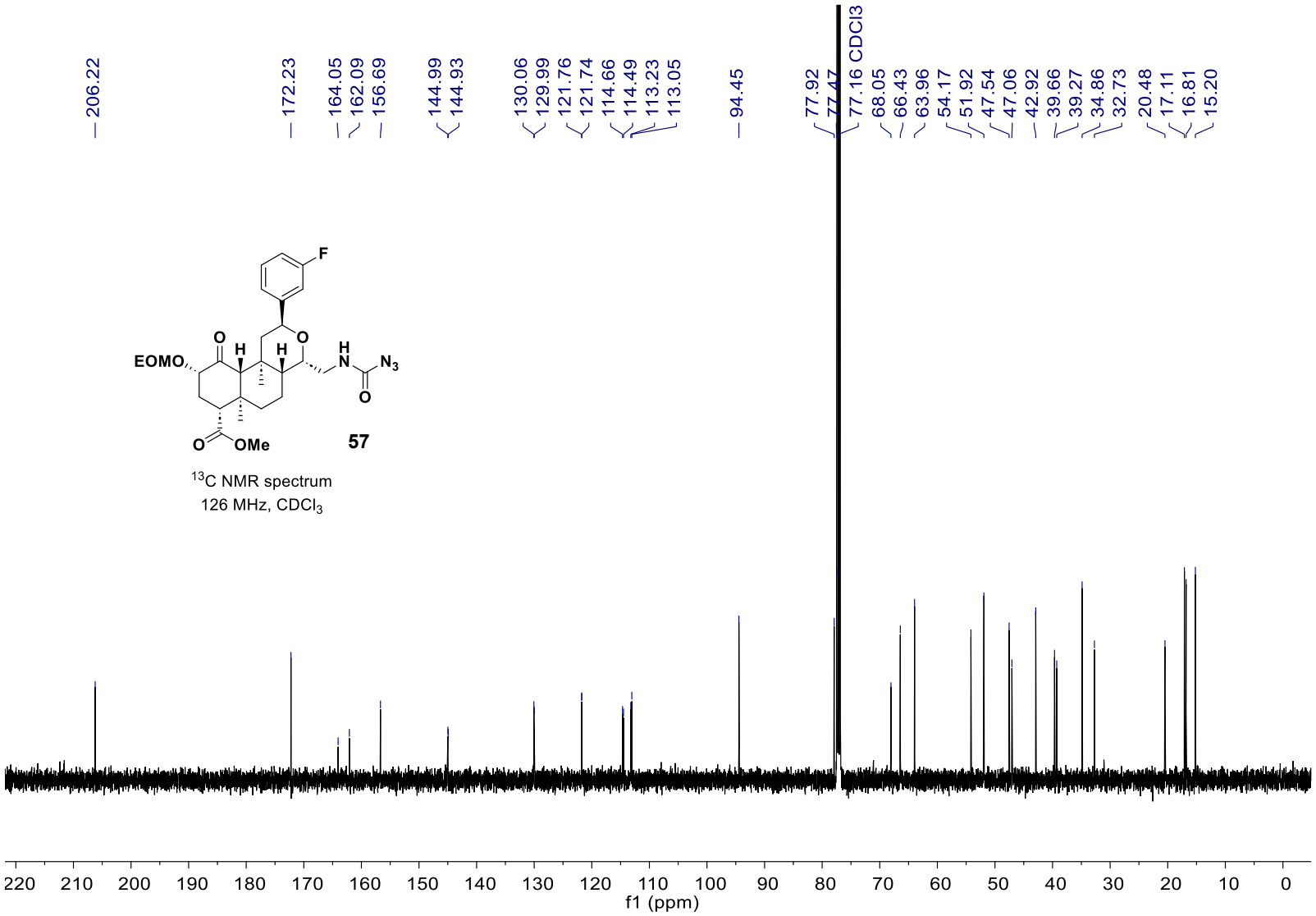
^{13}C NMR spectrum
126 MHz, $CDCl_3$



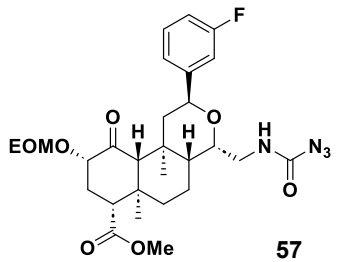
56

^{19}F NMR spectrum
565 MHz, $CDCl_3$


7.29 7.28 7.28 7.27 7.26 CDCl3 7.08 7.08 7.06 6.96 6.95 6.95 6.95 4.80 4.79 4.77 4.77 4.74 4.72 4.67 4.65 4.07 4.06 4.04 3.70 3.70 3.67 3.65 3.65 3.63 3.56 3.54 3.53 3.52 3.50 2.71 2.71 2.68 2.67 2.23 2.23 2.20 2.19 2.16 2.16 2.13 1.95 1.73 1.72 1.72 1.47 1.47 1.46 1.44 1.16 1.14 1.12 1.08 1.06 1.05
F
O
H
H
O
EOMO
H
N
N3
O
O
OMe
57
1H NMR spectrum
400 MHz, CDCl3
0.96 1.95 0.94 0.86 0.98 0.99 0.96 1.00 0.99 2.88 1.12 2.00 0.91 0.99 1.02 1.96 0.97 1.96 1.23 0.95 0.94 3.23 2.96 3.96
3.0 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
f1 (ppm)

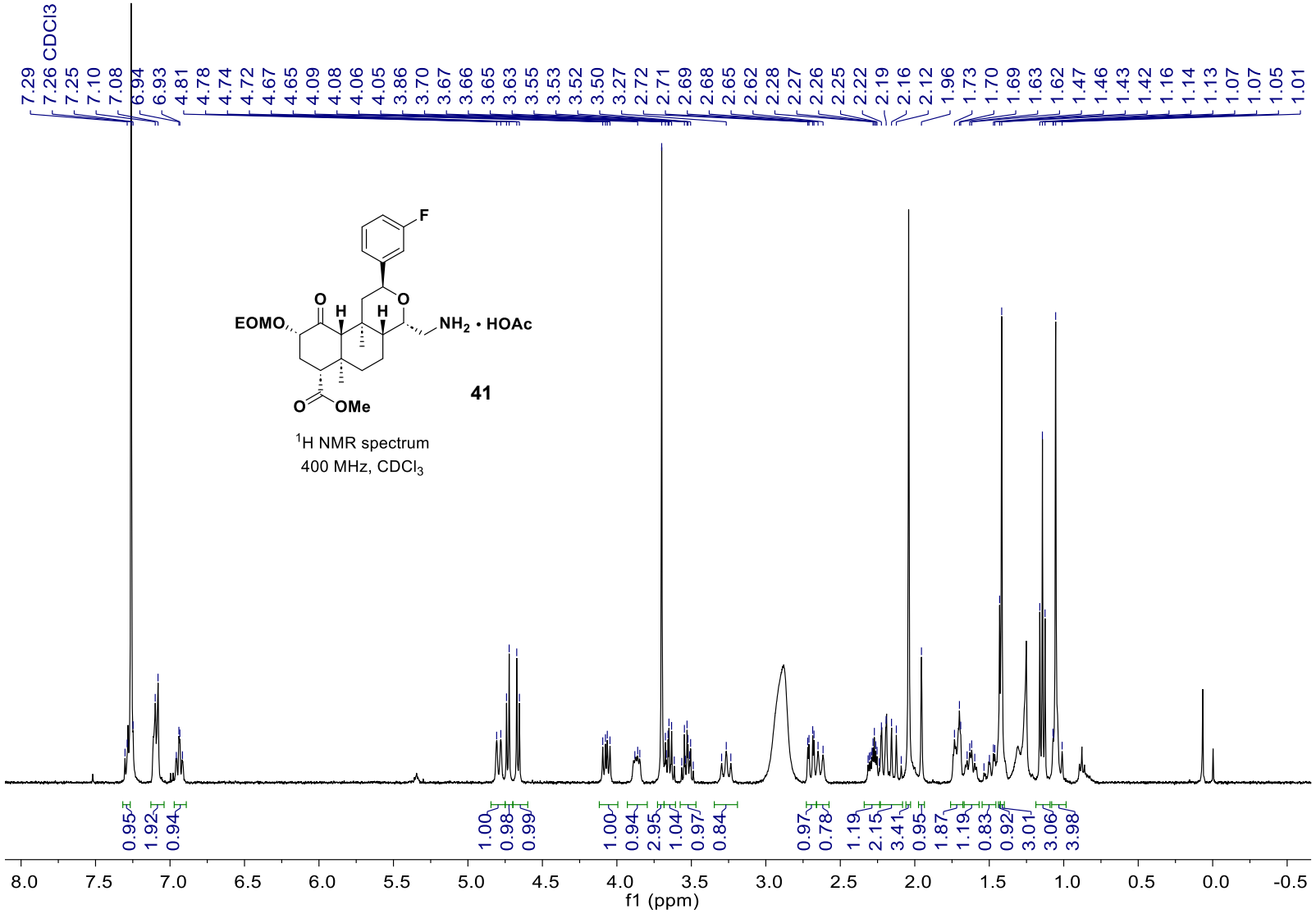


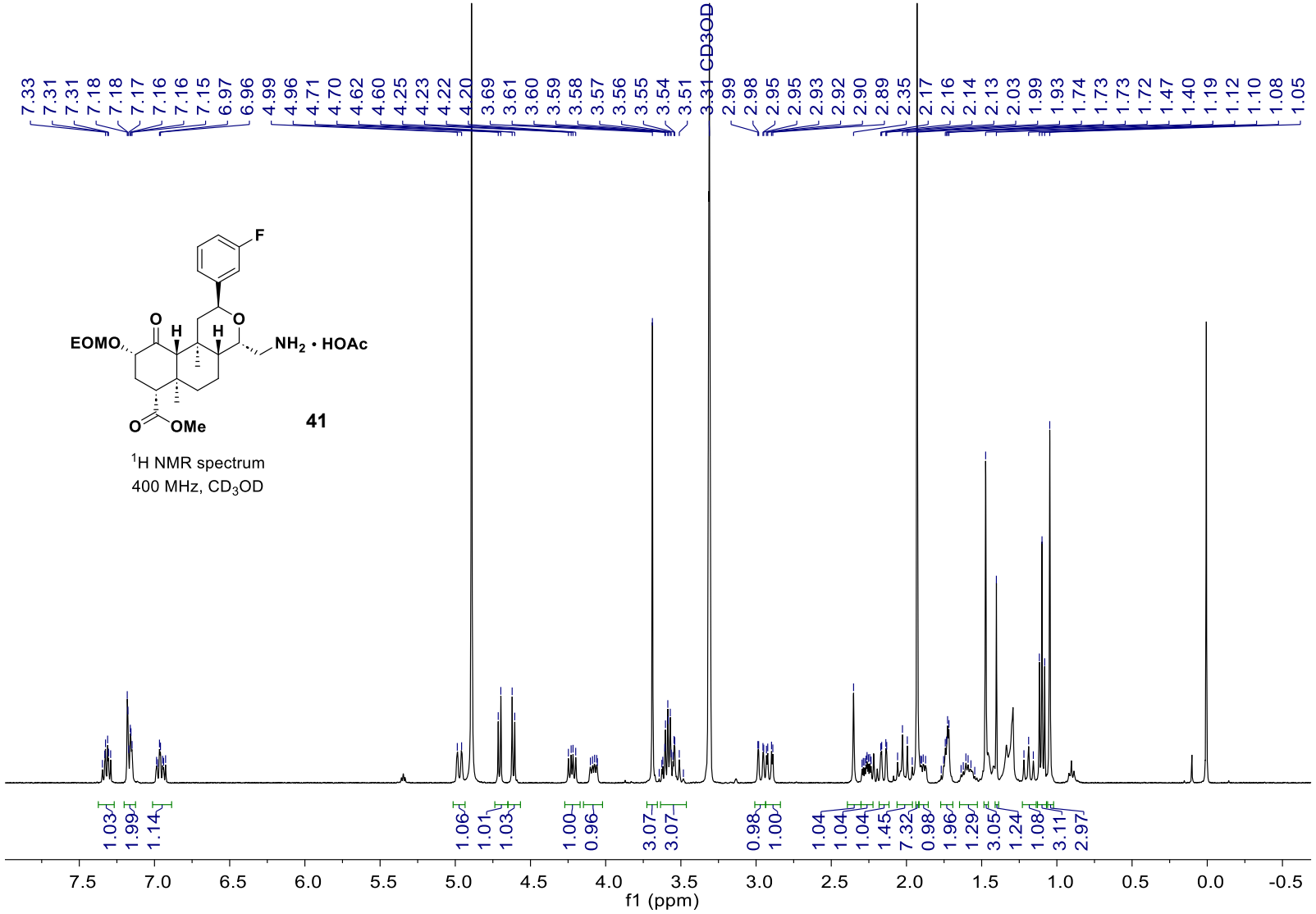
^{13}C NMR spectrum
126 MHz, $CDCl_3$

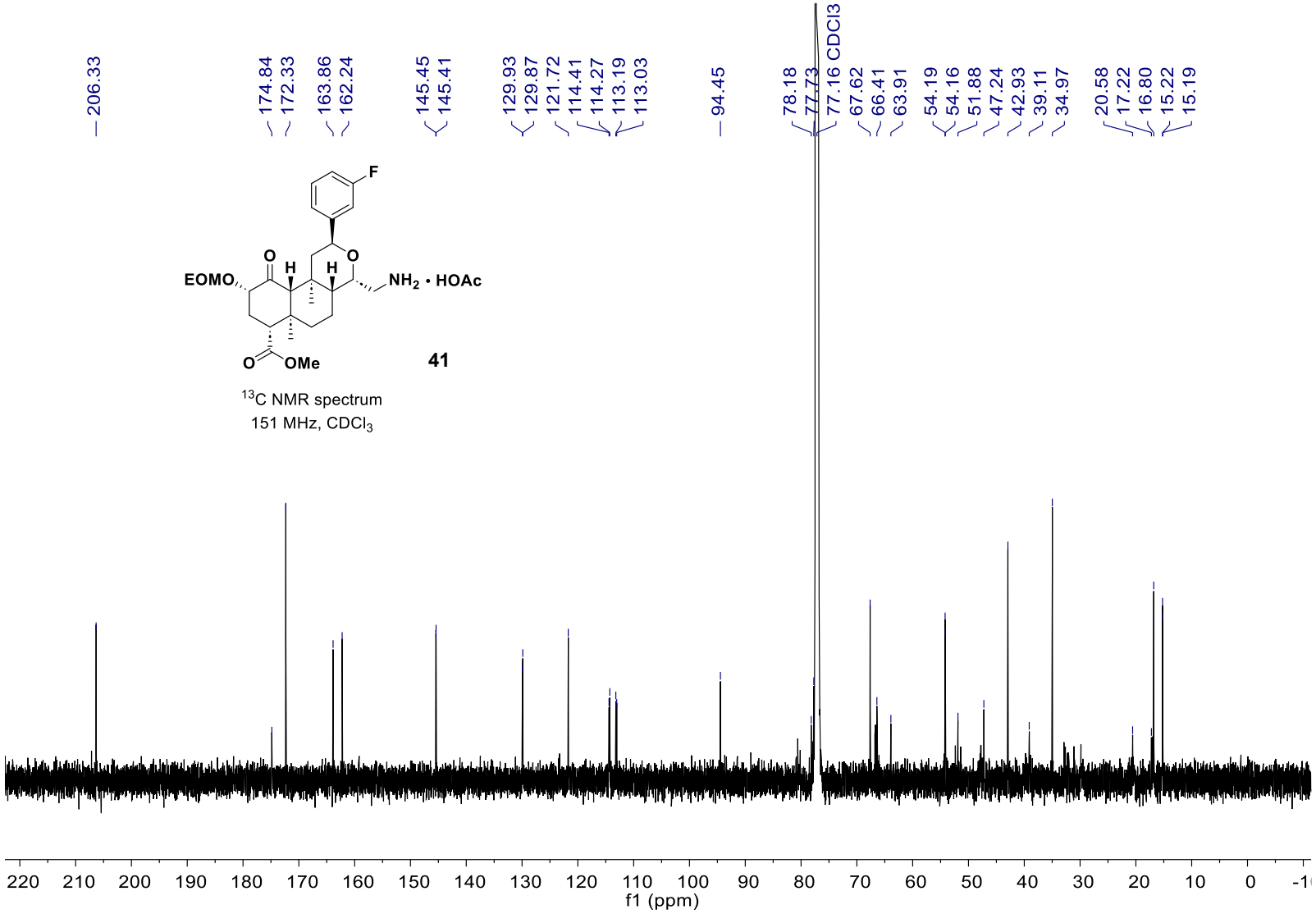


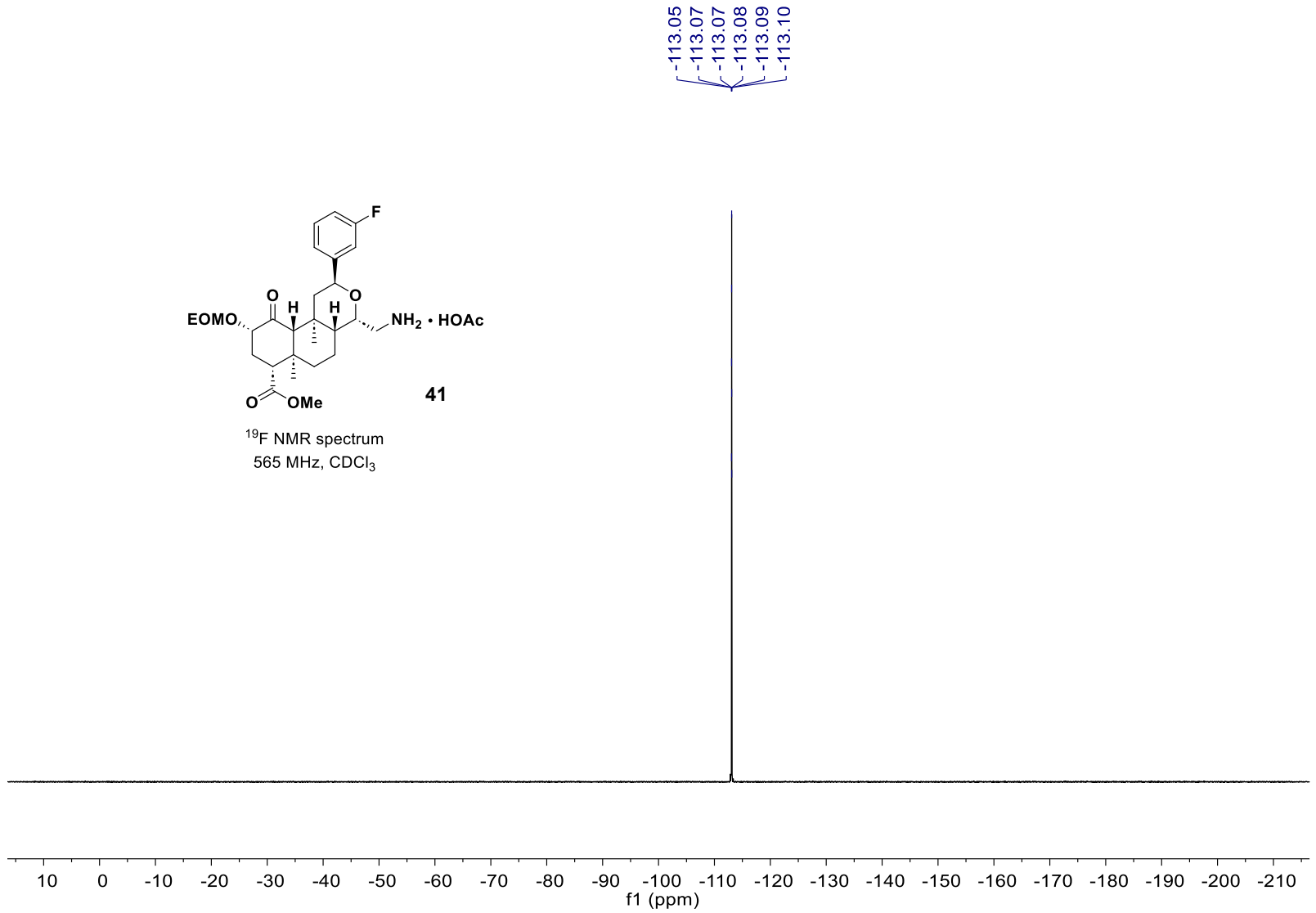
57

^{19}F NMR spectrum
565 MHz, $CDCl_3$

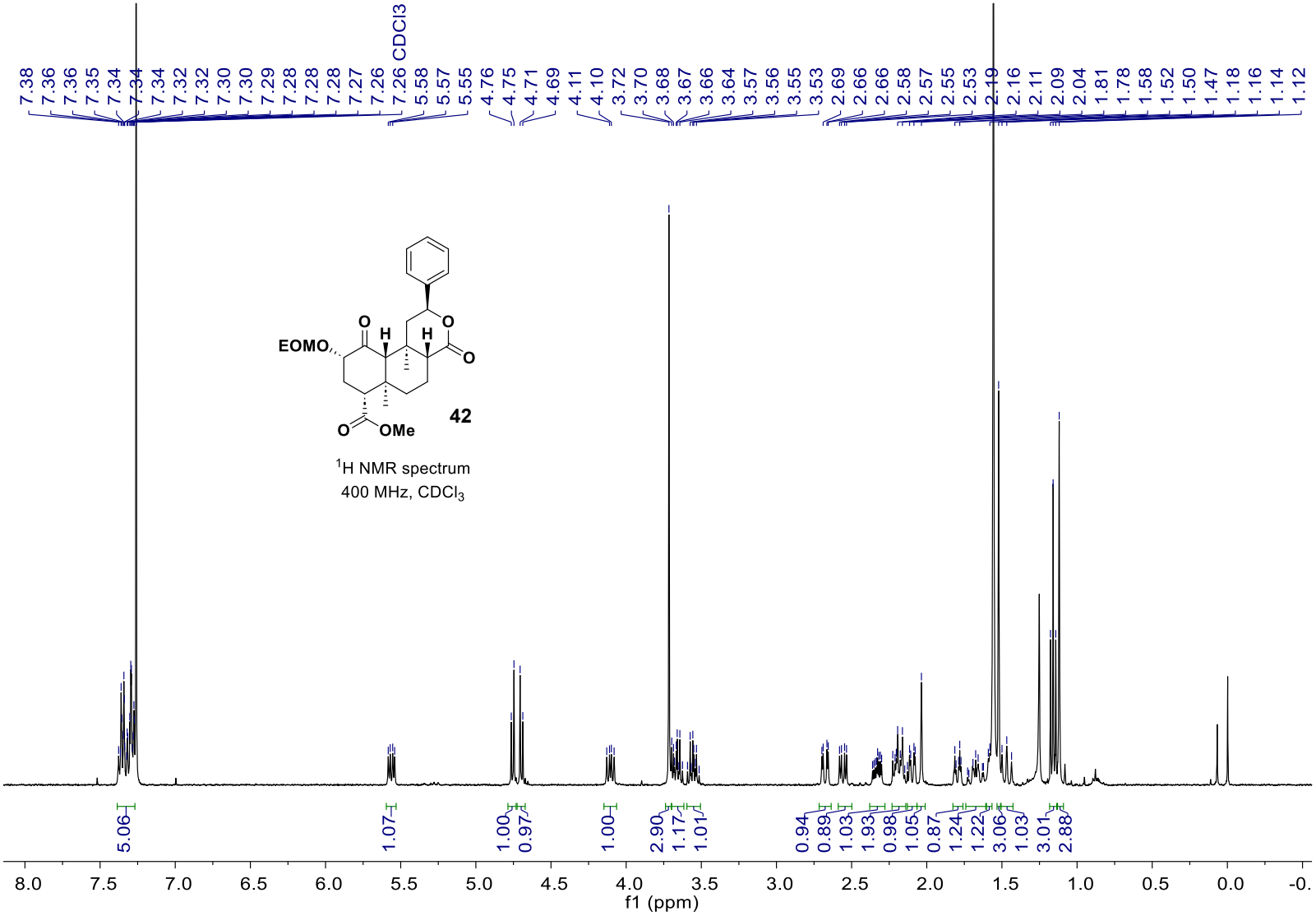

7.29
7.26 CDCl3
7.25
7.10
7.08
6.94
6.93
4.81
4.78
4.74
4.72
4.67
4.65
4.09
4.08
4.06
4.05
3.86
3.70
3.67
3.66
3.65
3.63
3.55
3.53
3.52
3.50
3.27
2.72
2.71
2.69
2.68
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2.62
2.28
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2.26
2.25
2.22
2.19
2.16
2.12
1.96
1.73
1.70
1.69
1.63
1.62
1.47
1.46
1.43
1.42
1.16
1.14
1.13
1.07
1.07
1.05
1.01
F
O
H
H
O
EOMO
NH2 • HOAc
O
OMe
41
1H NMR spectrum
400 MHz, CDCl3
0.95
1.92
0.94
1.00
0.98
0.99
1.00
0.94
2.95
1.04
0.97
0.84
0.97
0.78
1.19
2.15
3.41
0.95
1.87
1.19
0.83
0.92
3.01
3.06
3.98
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)

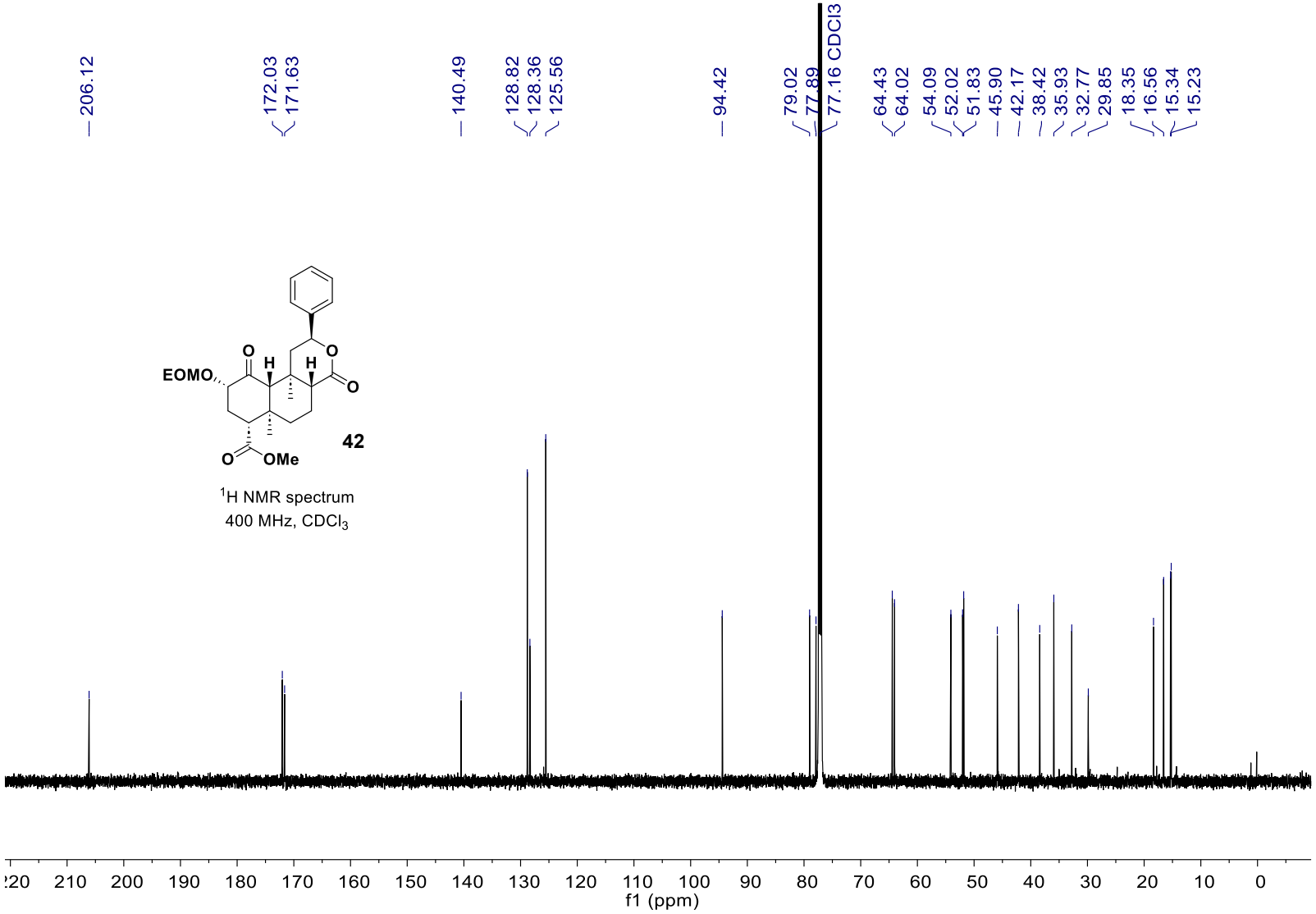

7.33
7.31
7.31
7.18
7.18
7.17
7.16
7.16
7.15
6.97
6.96
4.99
4.96
4.71
4.70
4.62
4.60
4.25
4.23
4.22
4.20
3.69
3.61
3.60
3.59
3.58
3.57
3.56
3.55
3.54
3.51
3.31 CD3OD
2.99
2.98
2.95
2.95
2.93
2.92
2.90
2.89
2.35
2.17
2.16
2.14
2.13
2.03
1.99
1.93
1.74
1.73
1.73
1.72
1.47
1.40
1.19
1.12
1.10
1.08
1.05
F
O
H
H
O
EOMO
NH2 • HOAc
O
OMe
41
1H NMR spectrum
400 MHz, CD3OD
1.03
1.99
1.14
1.06
1.01
1.03
1.00
0.96
3.07
3.07
0.98
1.00
1.04
1.04
1.04
1.45
7.32
0.98
1.96
1.29
3.05
1.24
1.08
3.11
2.97
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)


206.33
174.84
172.33
163.86
162.24
145.45
145.41
129.93
129.87
121.72
114.41
114.27
113.19
113.03
94.45
78.18
77.73
77.16 CDCl3
67.62
66.41
63.91
54.19
54.16
51.88
47.24
42.93
39.11
34.97
20.58
17.22
16.80
15.22
15.19
F
O
H
H
O
EOMO
NH2 • HOAc
O
OMe
41
13C NMR spectrum
151 MHz, CDCl3
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)



^{19}F NMR spectrum
565 MHz, $CDCl_3$


7.38 7.36 7.36 7.35 7.34 7.34 7.34 7.32 7.32 7.30 7.30 7.29 7.28 7.28 7.28 7.27 7.26 7.26 CDCl3 5.58 5.57 5.55 4.76 4.75 4.71 4.69 4.11 4.10 3.72 3.70 3.68 3.67 3.66 3.64 3.57 3.56 3.55 3.53 2.69 2.66 2.66 2.58 2.57 2.55 2.53 2.19 2.16 2.11 2.09 2.04 1.81 1.78 1.58 1.52 1.50 1.47 1.18 1.16 1.14 1.12
EOMO
O
H
H
O
O
O
O
OMe
42
1H NMR spectrum
400 MHz, CDCl3
5.06 1.07 1.00 0.97 1.00 2.90 1.17 1.01 0.94 0.89 1.03 1.93 0.98 1.05 0.87 1.24 1.22 3.06 1.03 3.01 2.88
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.
f1 (ppm)


206.12
172.03
171.63
140.49
128.82
128.36
125.56
94.42
79.02
77.89
77.16 CDCl3
64.43
64.02
54.09
52.02
51.83
45.90
42.17
38.42
35.93
32.77
29.85
18.35
16.56
15.34
15.23
EOMO
O
H
H
O
O
O
OMe
42
1H NMR spectrum
400 MHz, CDCl3
f1 (ppm)

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