

Supporting Information

Synthesis and structure-activity relationship of berkeleylactone A-derived antibiotics

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1. Table 1: Screening of susceptibility of clinical isolate *S. aureus* L12 and standard strain *S. aureus* CCM3953 to different groups of antimicrobial agents using disk diffusion method
2. Table 2: Characteristic ¹H NMR shifts of sulfa-Michael adducts and related compounds.
3. ¹H and ¹³C NMR of prepared compounds

Table 1: Screening of susceptibility of clinical isolate *S. aureus* L12 and standard strain *S. aureus* CCM3953 to different groups of antimicrobial agents using disk diffusion method (EUCAST version 11.0) (28).

Antibiotic agent (Disk content in µg)		L12	CCM 3953
Penicillins	Oxacillin 10µg	R	S
	Ampicillin 10µg	R	S
Cephalosporins	Cefotaxime 30µg	R	S
	Cefoxitin 30µg	R	S
	Ceftriaxone 30µg	R	S
Carbapenems	Ertapenem 10µg	R	S
Fluoroquinolones	Ciprofloxacin 5µg	R	S
	Ofloxacin 5µg	R	S
	Moxifloxacin 5µg	R	S
	Levofloxacin 5µg	R	S
Aminoglycosides	Gentamicin 10µg	S	S
	Tobramycin 10µg	R	S
Glycopeptides	Vancomycin 30µg	S	S
Macrolides and lincosamides	Erythromycin 15µg	R	S
	Clindamycin 2µg	R	S
Tetracyclines	Tetracycline 30µg	S	S
	Doxycycline 30µg	S	S
Oxazolidinones	Linezolid 10µg	S	S
Streptogramins	Quinupristin-dalfopristin 15µg	S	S
	Rifampicine 5µg	S	S
Sulfonamides	Trimethoprim-Sulfamethoxazole 5µg	S	S

S susceptible

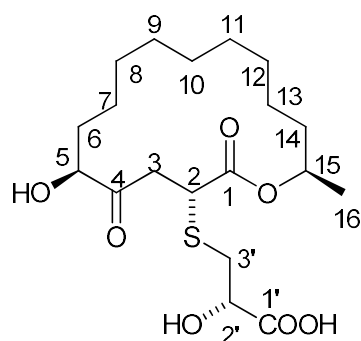
R resistant

Table 2: Characteristic ^1H NMR signals of sulfa-Michael adducts and related compounds (chemical shift, multiplicity and coupling constant in Hertz)

Compound	H2**	H3**
berkeleylactone A	4.03, t (6.6)	3.23, dd (18.3, 7.4) 2.82, dd (18.3, 5.9)
<i>epi</i> -berkeleylactone A	3.72-3.79, m*	3.27, dd (19.0, 3.8) 3.04-3.15, m*
1	6.79, d (15.8)	7.25, d (15.8)
2a	3.89, dd (7.9, 6.2)	3.34 – 3.17, m* 2.79, dd (18.2, 6.0)
2b	3.71, dd (7.5, 5.7)	3.25, dd (18.7, 5.7) 3.05, dd (18.8, 8.1)
3a	3.83, dd (9.3, 5.0)	3.30, dd (18.4, 9.3) 2.75 – 2.65, m*
3b	3.67, t (7.0)	3.13, dd (18.6, 6.5)* 3.09, dd (18.6, 7.6)*
4a	3.97, dd (9.0, 5.4)	3.27, dd (18.5, 9.1)* 2.77, dd (18.4, 5.4)
4b	3.87, "t" (6.8)	3.18, dd (18.4, 6.3) 3.12, dd (18.4, 7.3)
5a	4.64 – 4.56, m*	3.30, dd (18.4, 6.9) 2.85, dd (18.4, 7.2)
5b	4.64 – 4.56, m*	3.47, dd (18.8, 5.0) 2.96, dd (18.7, 4.5)
6	2.79, dt (15.6, 7.4) 2.45, ddd (15.6, 7.7, 5.9)	3.02, dt (18.2, 7.4) 2.63, ddd (18.2, 7.6, 5.9)

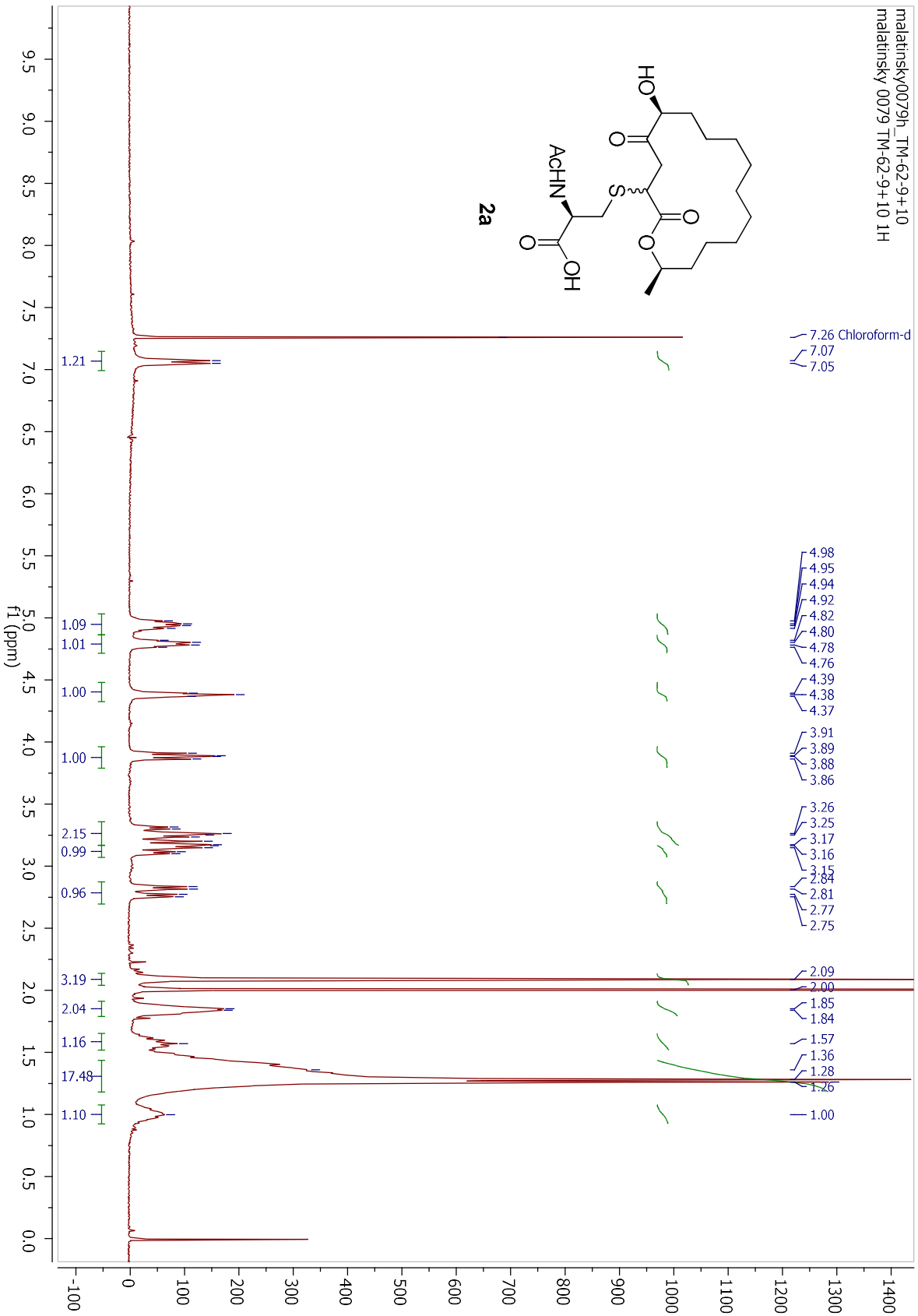
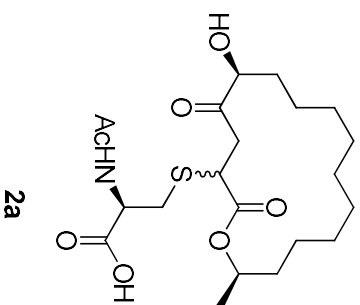
* Overlapping with other signals

** Signals were assigned based on analogy with berkeleylactone A and *epi*-berkeleylactone A

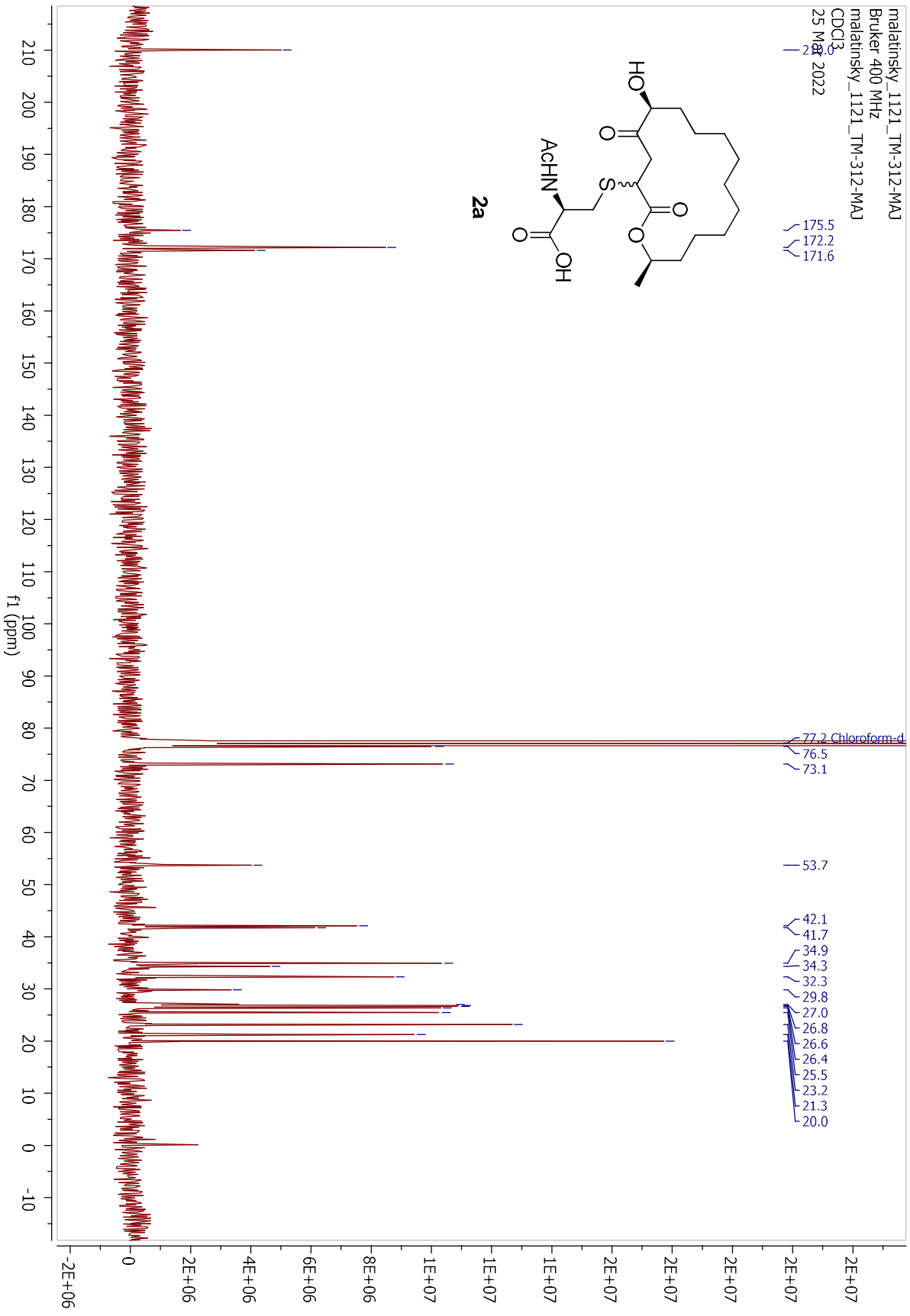
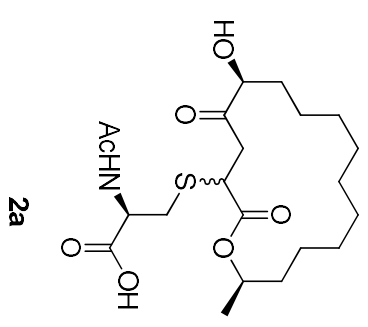


Berkeleylactone A

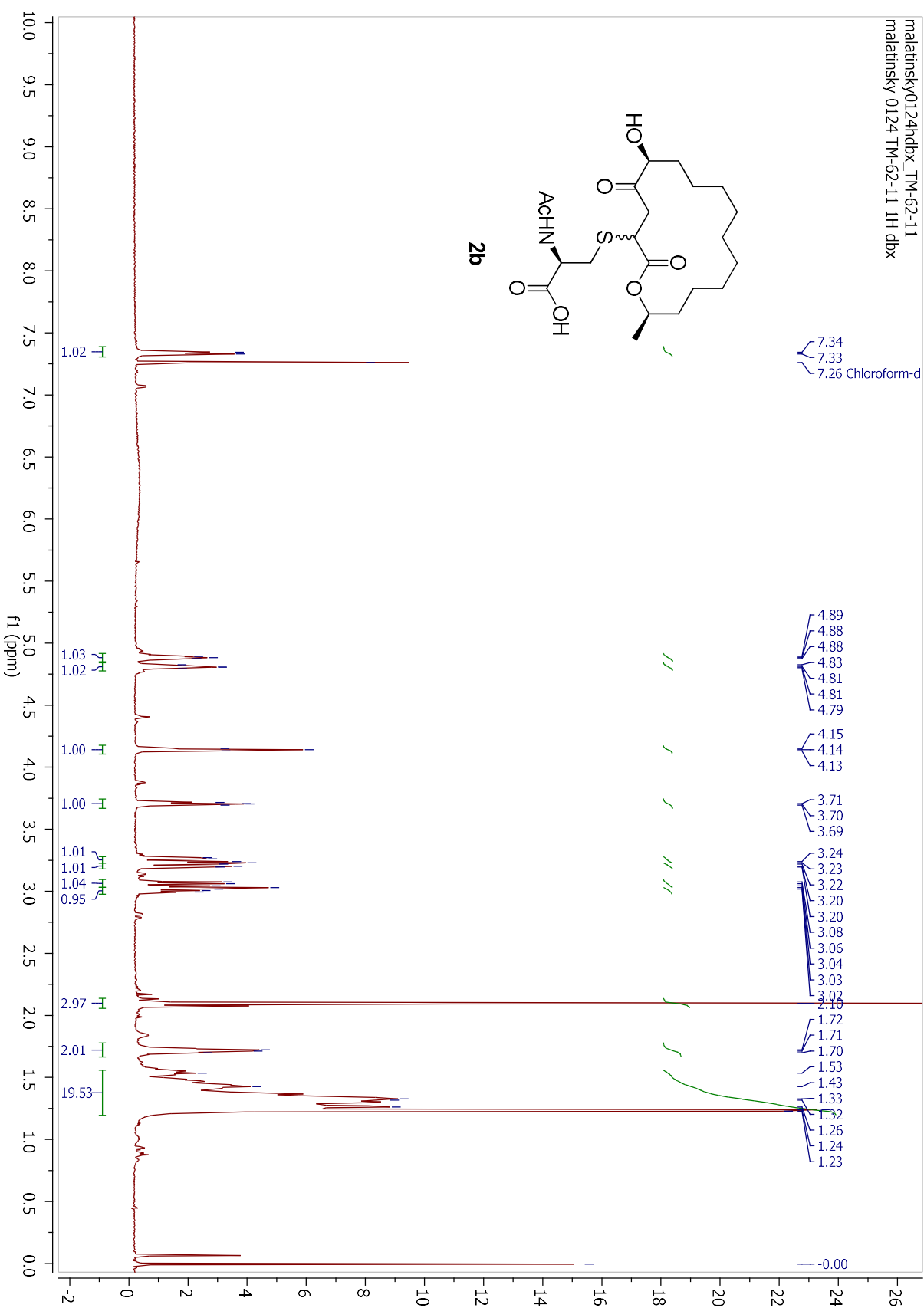
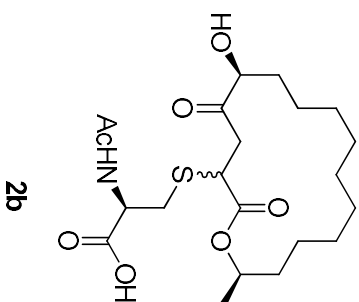
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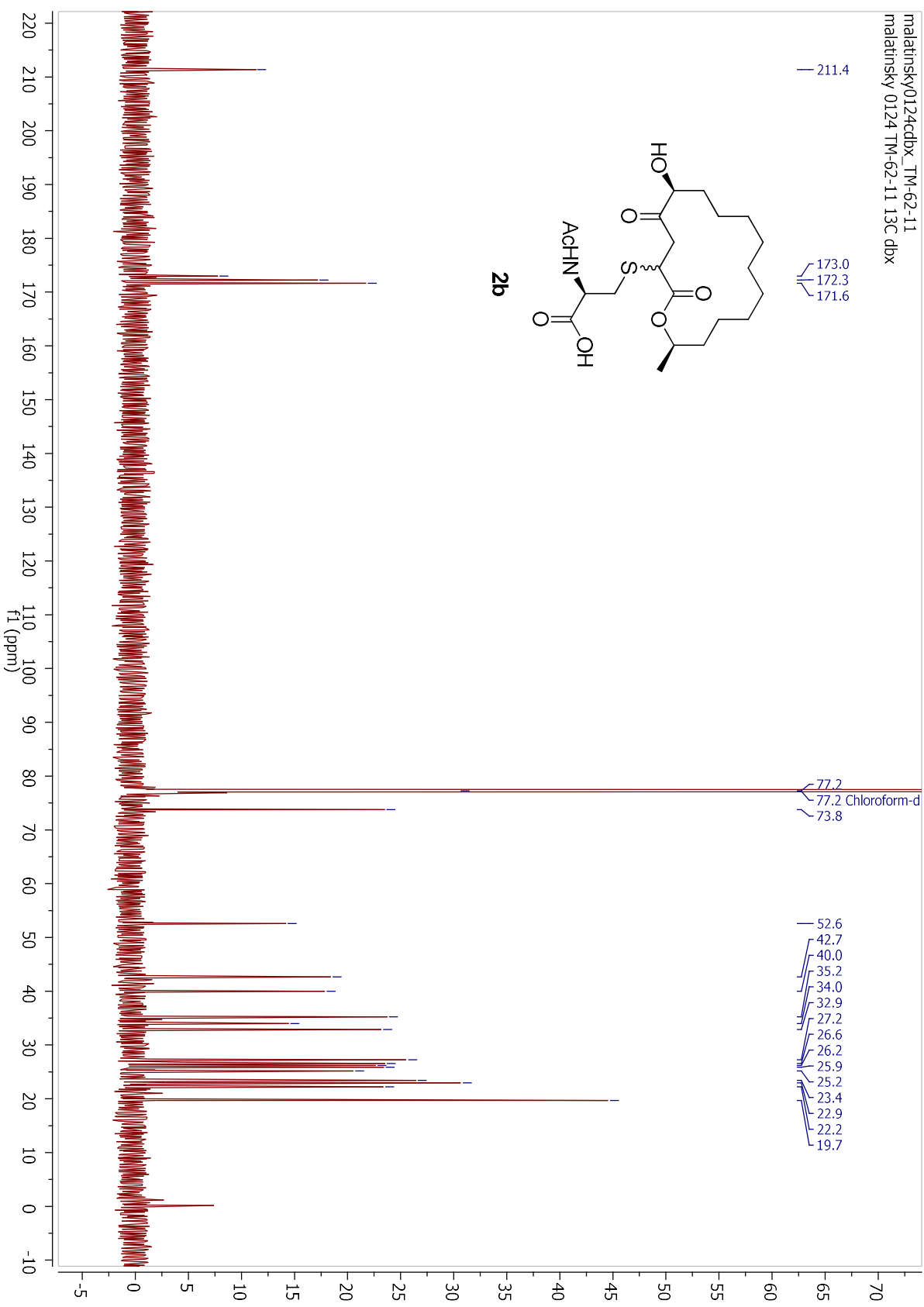
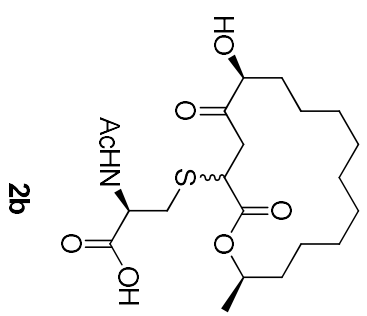
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25 Mar 2022

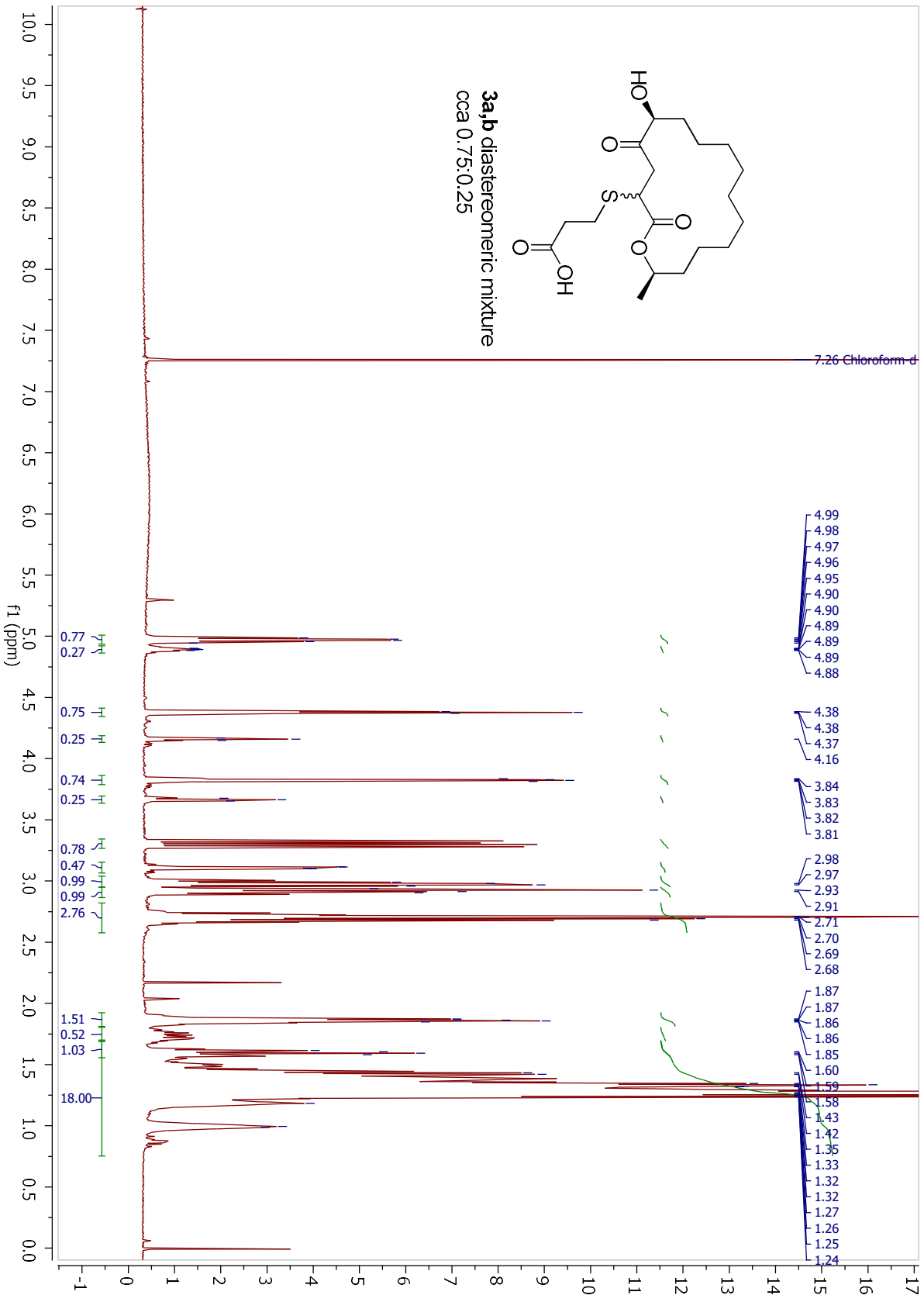


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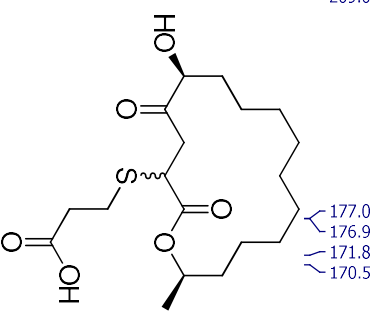


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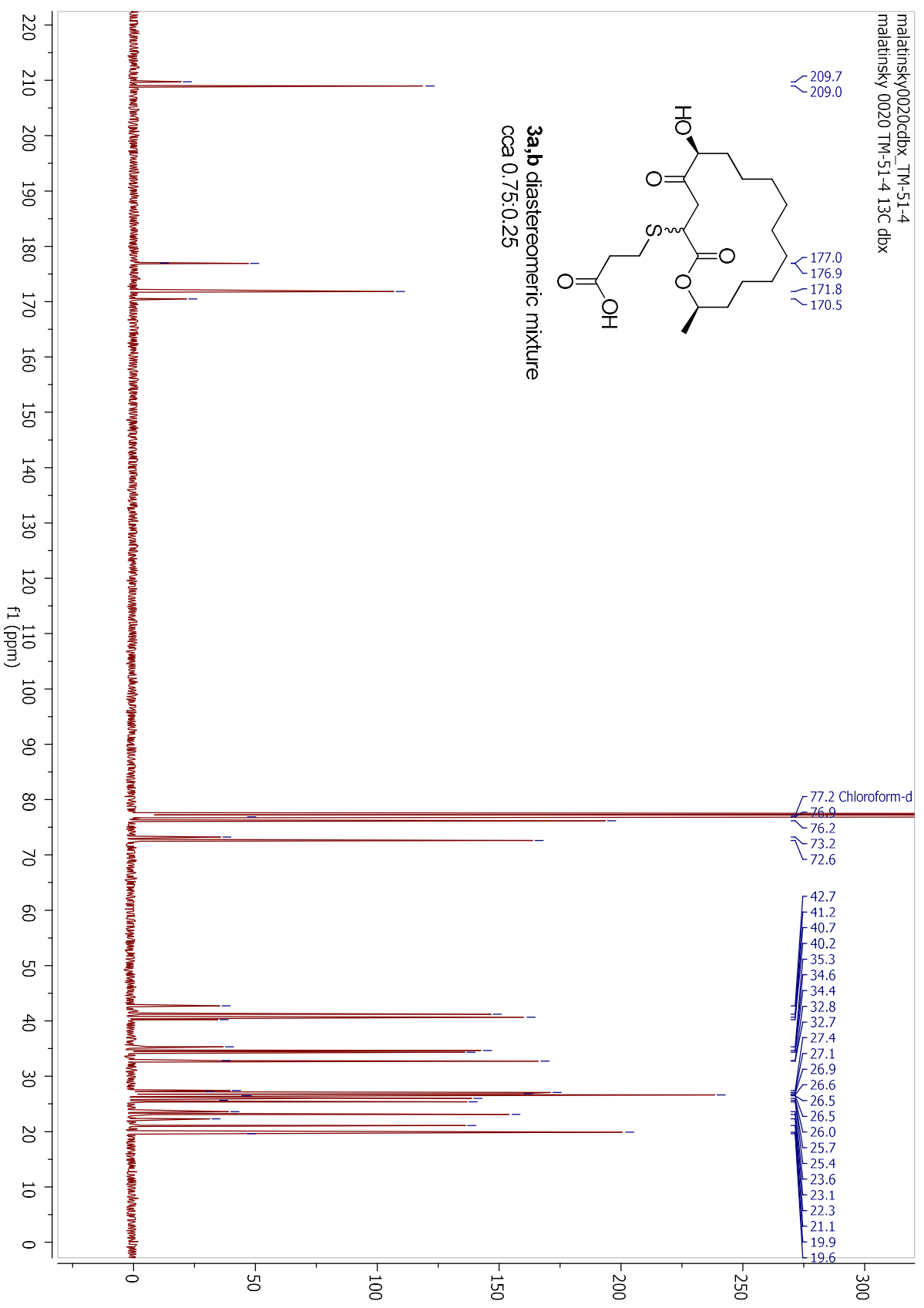




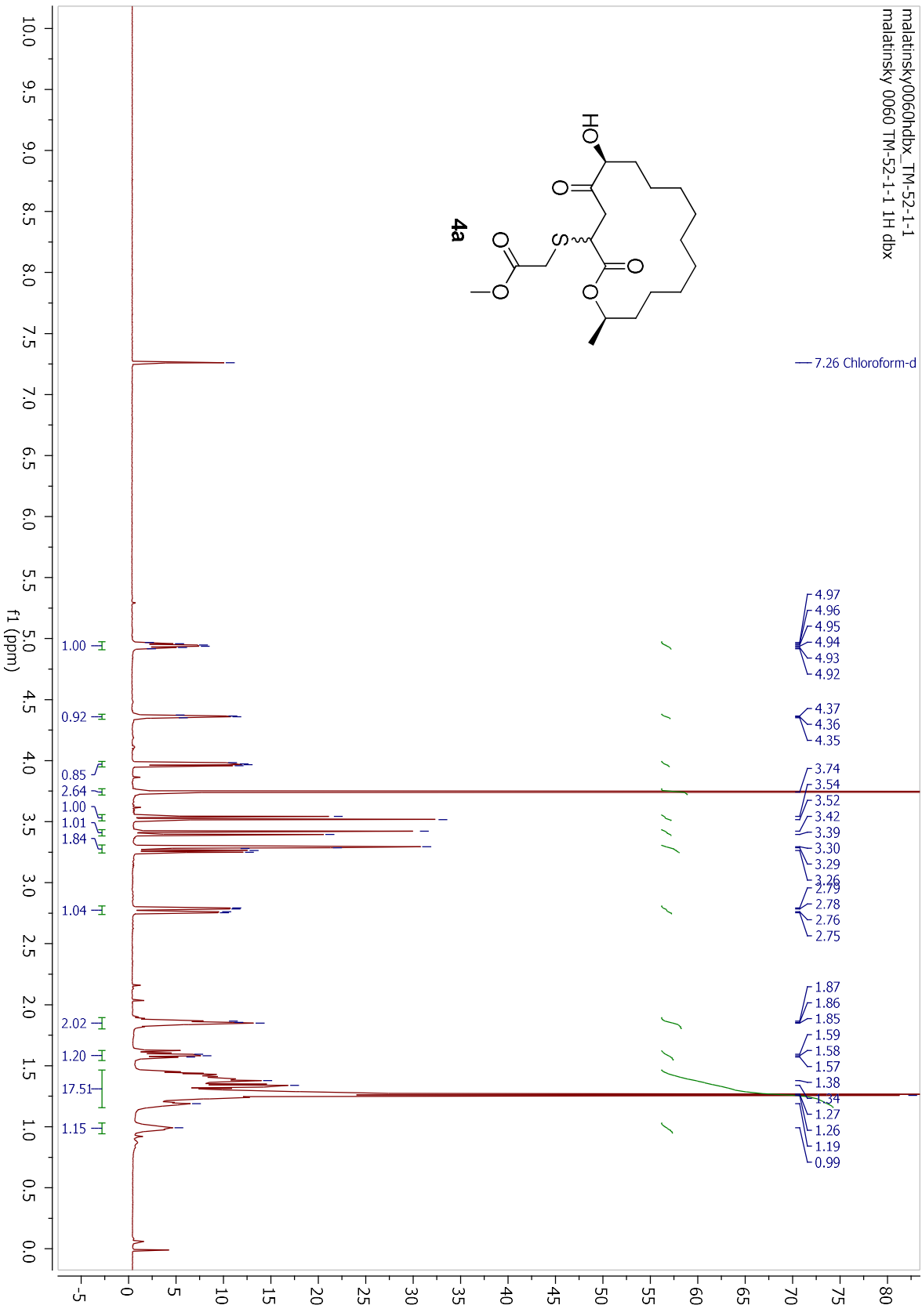
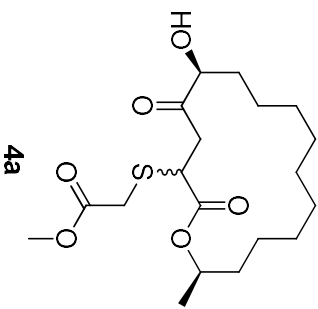
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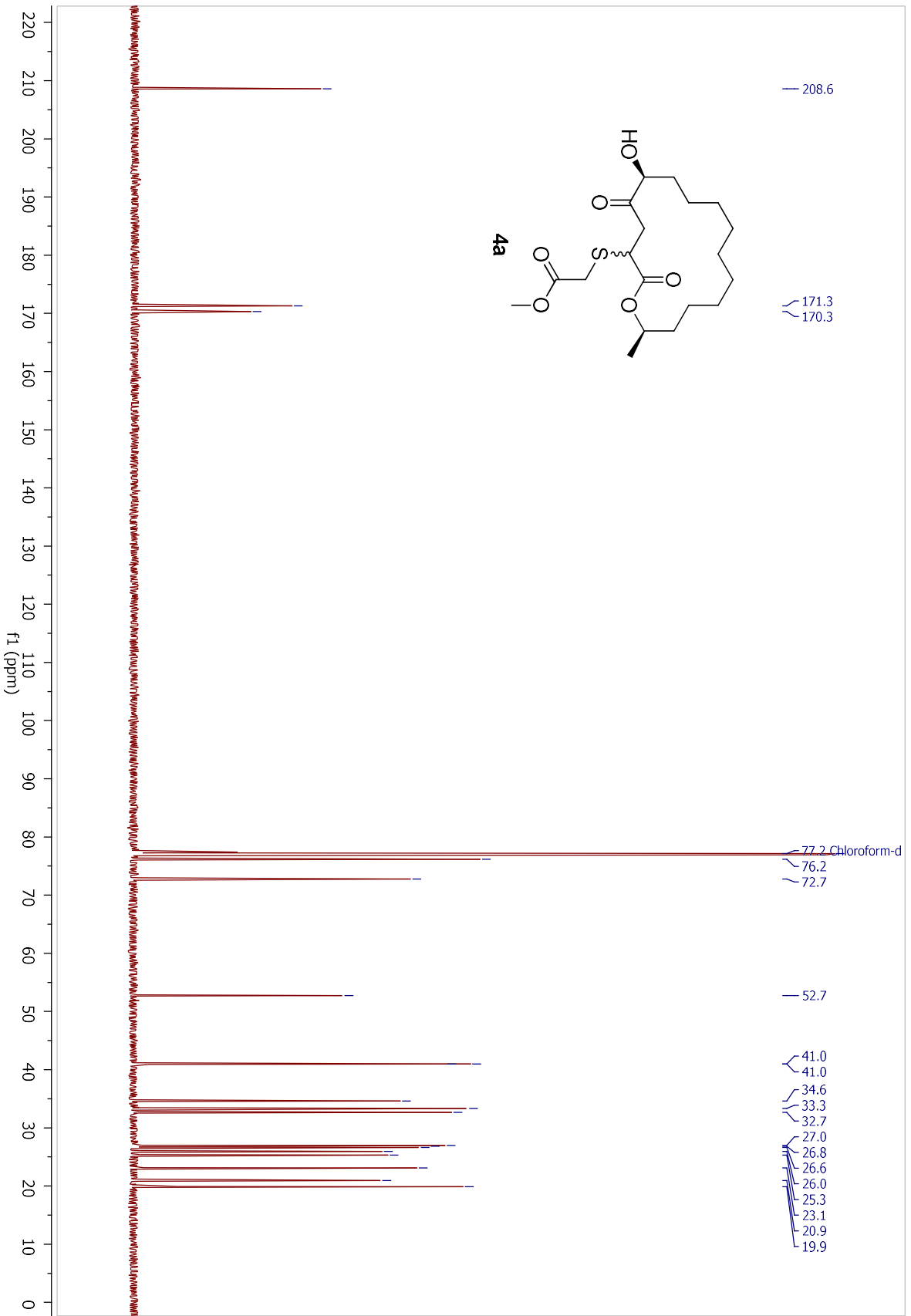


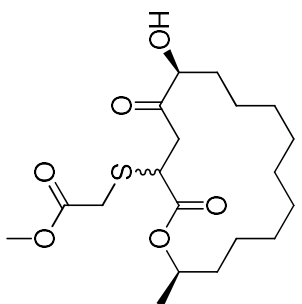
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cca 0.75:0.25



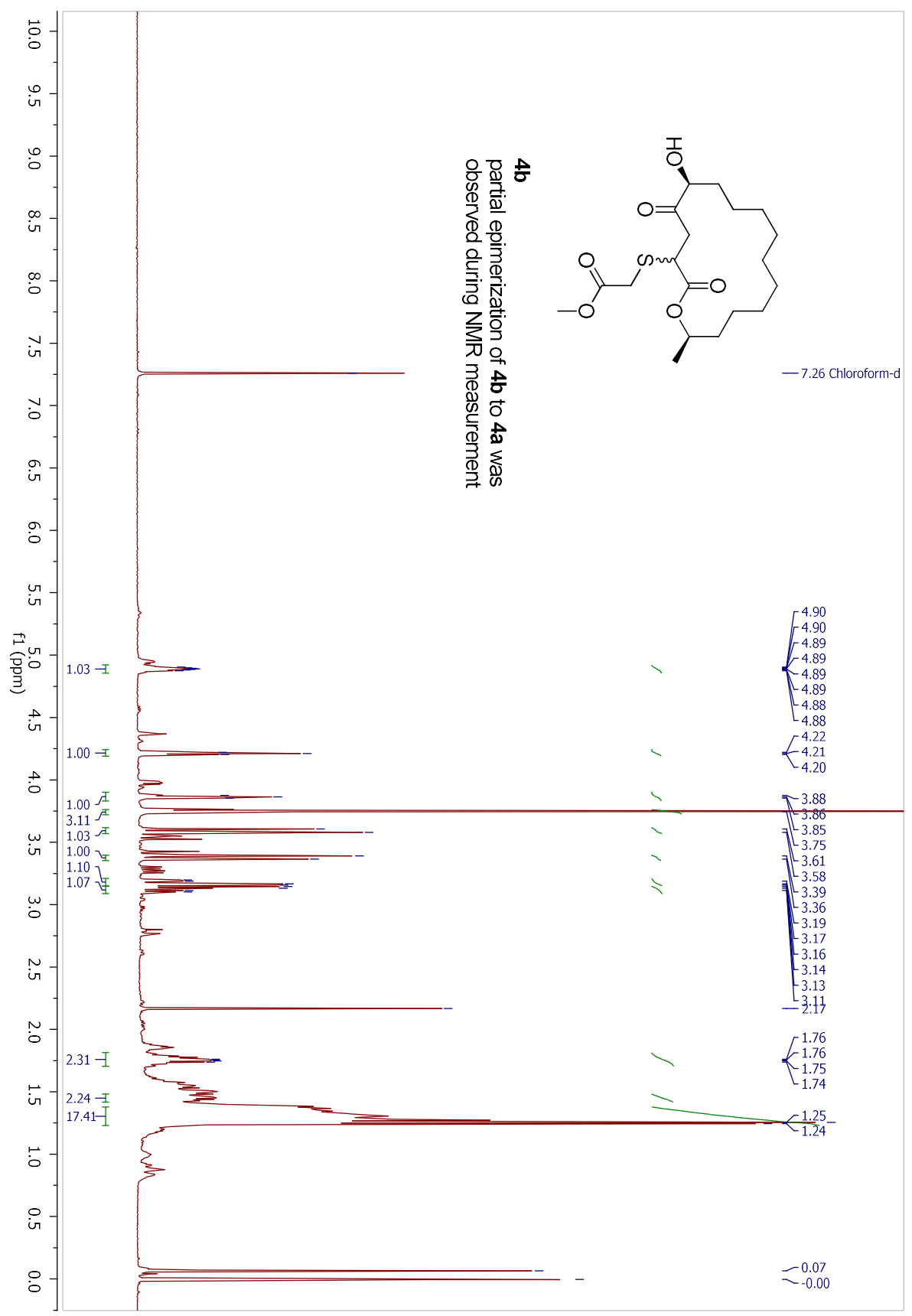
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4b
 partial epimerization of **4b** to **4a** was
 observed during NMR measurement

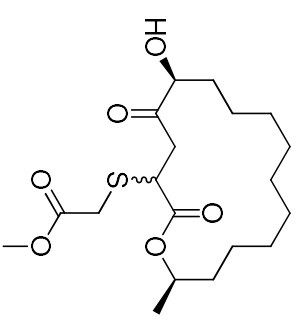


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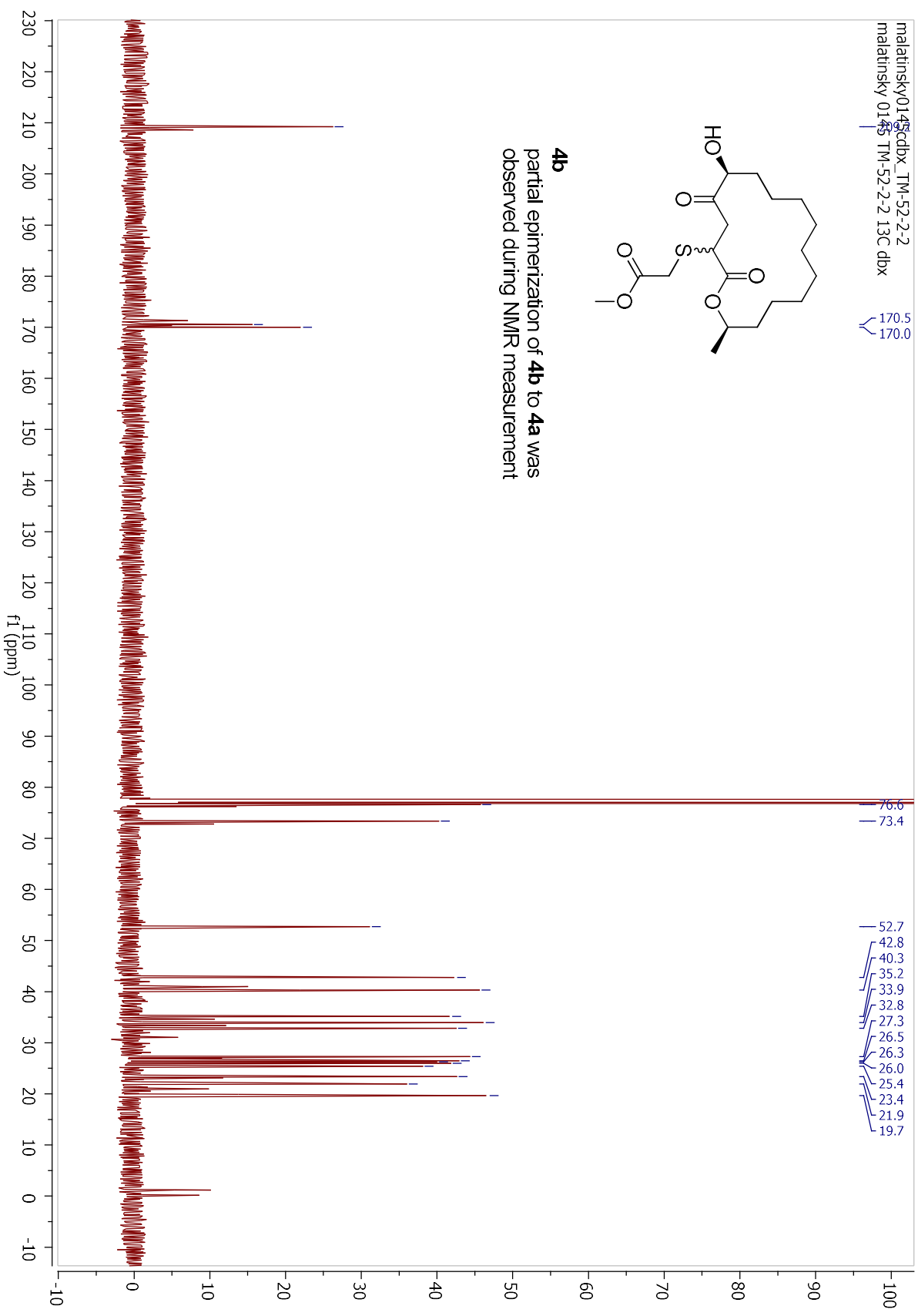
170.5
170.0

76.6
73.4

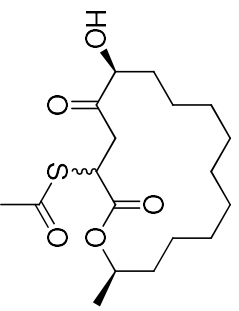
52.7
42.8
40.3
35.2
33.9
32.8
27.3
26.5
26.3
26.0
25.4
23.4
21.9
19.7



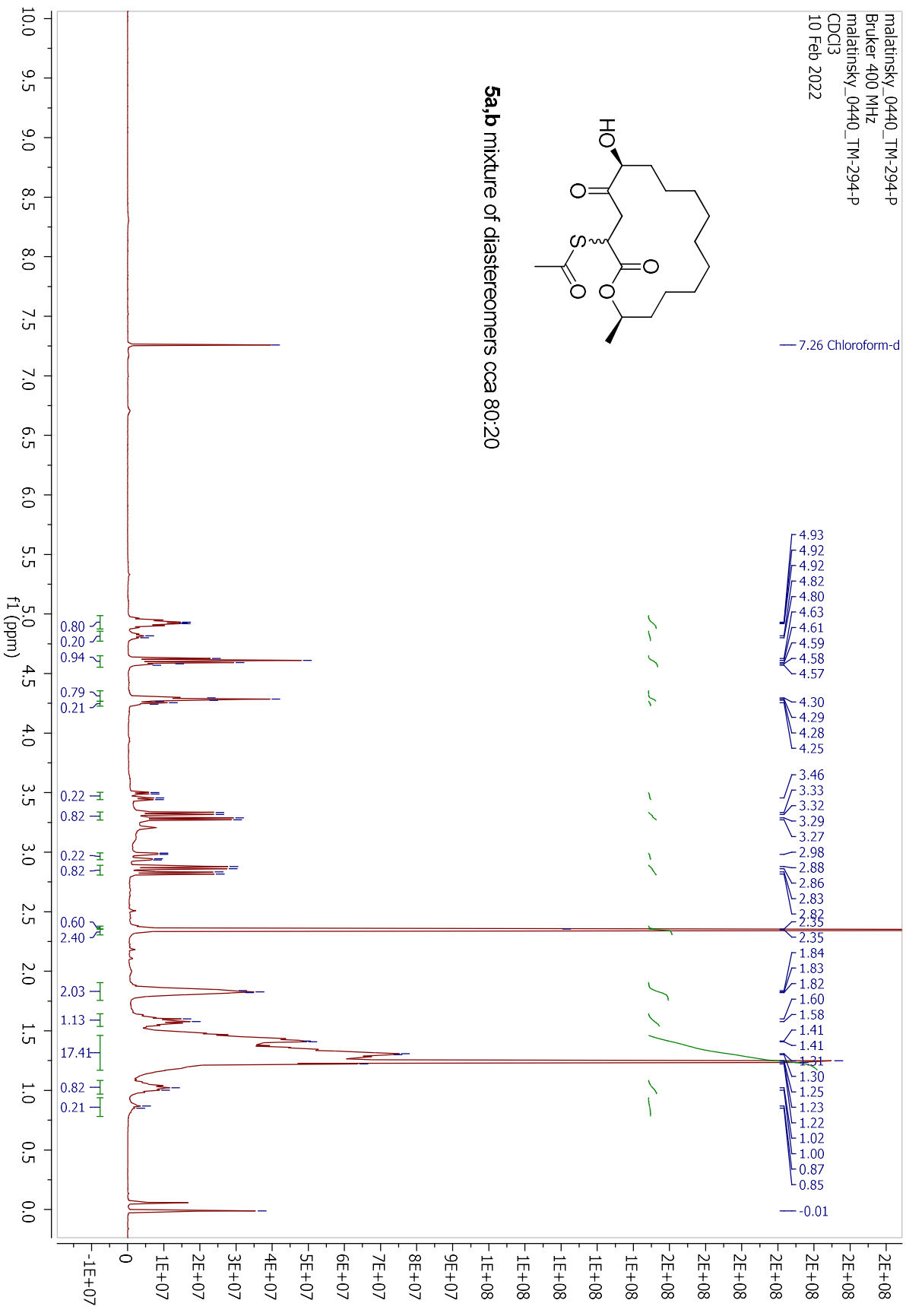
4b
partial epimerization of **4b** to **4a** was
observed during NMR measurement



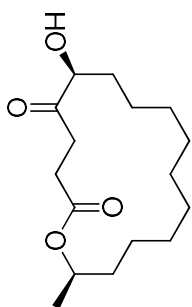
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10 Feb 2022



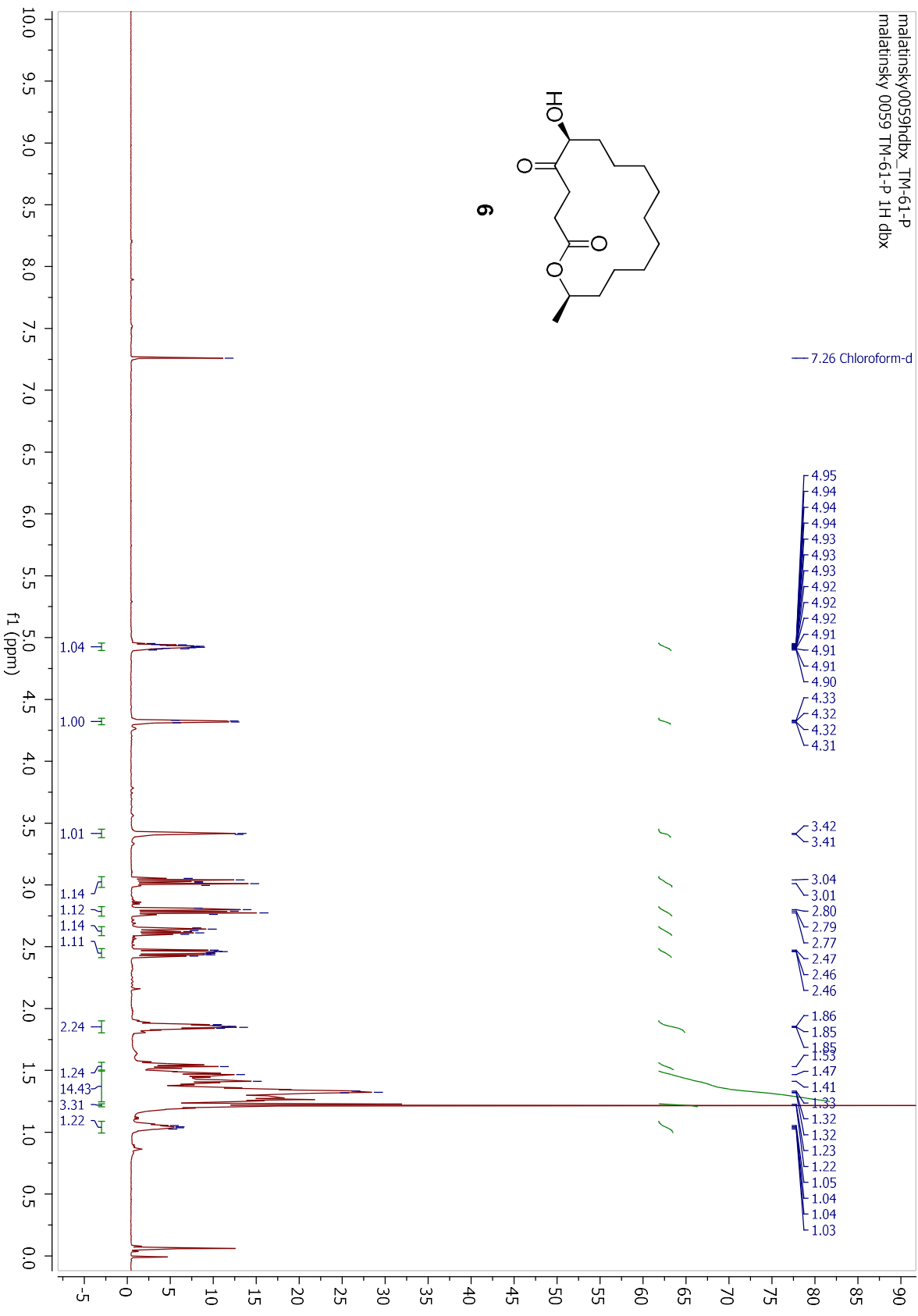
5a,b mixture of diastereomers cca 80:20



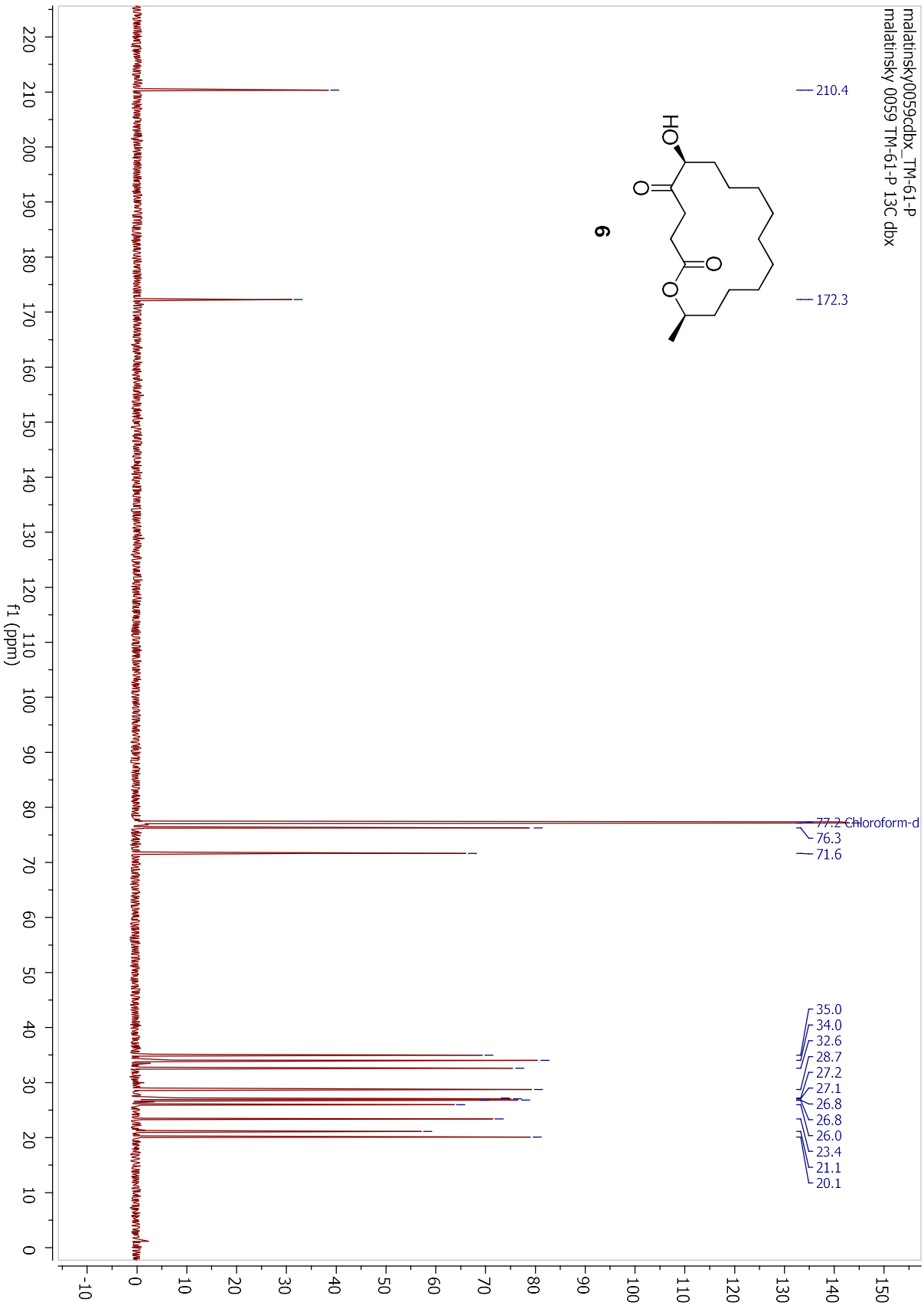
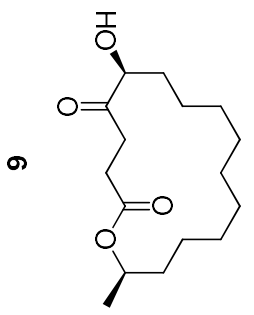
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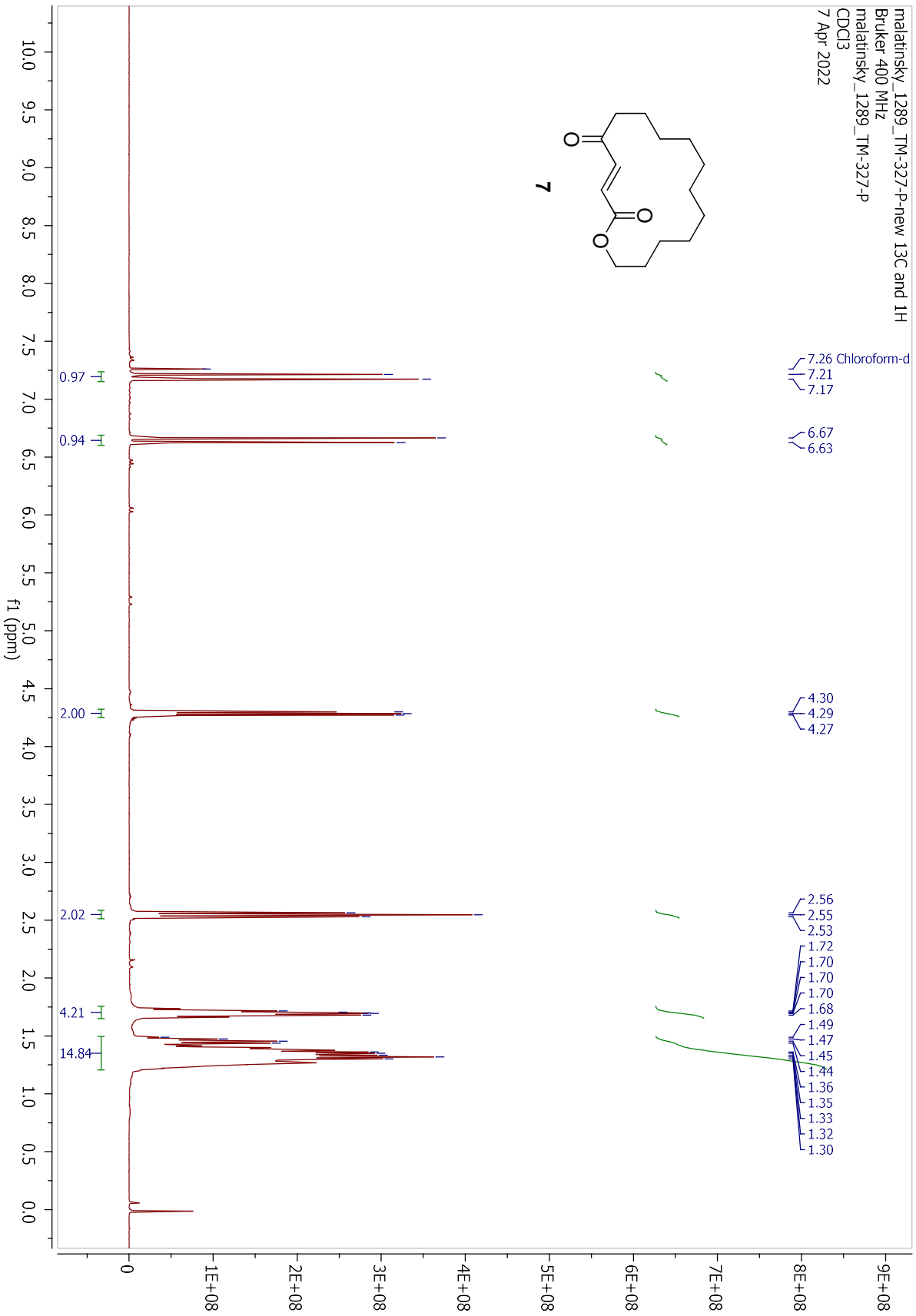
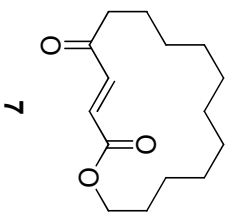
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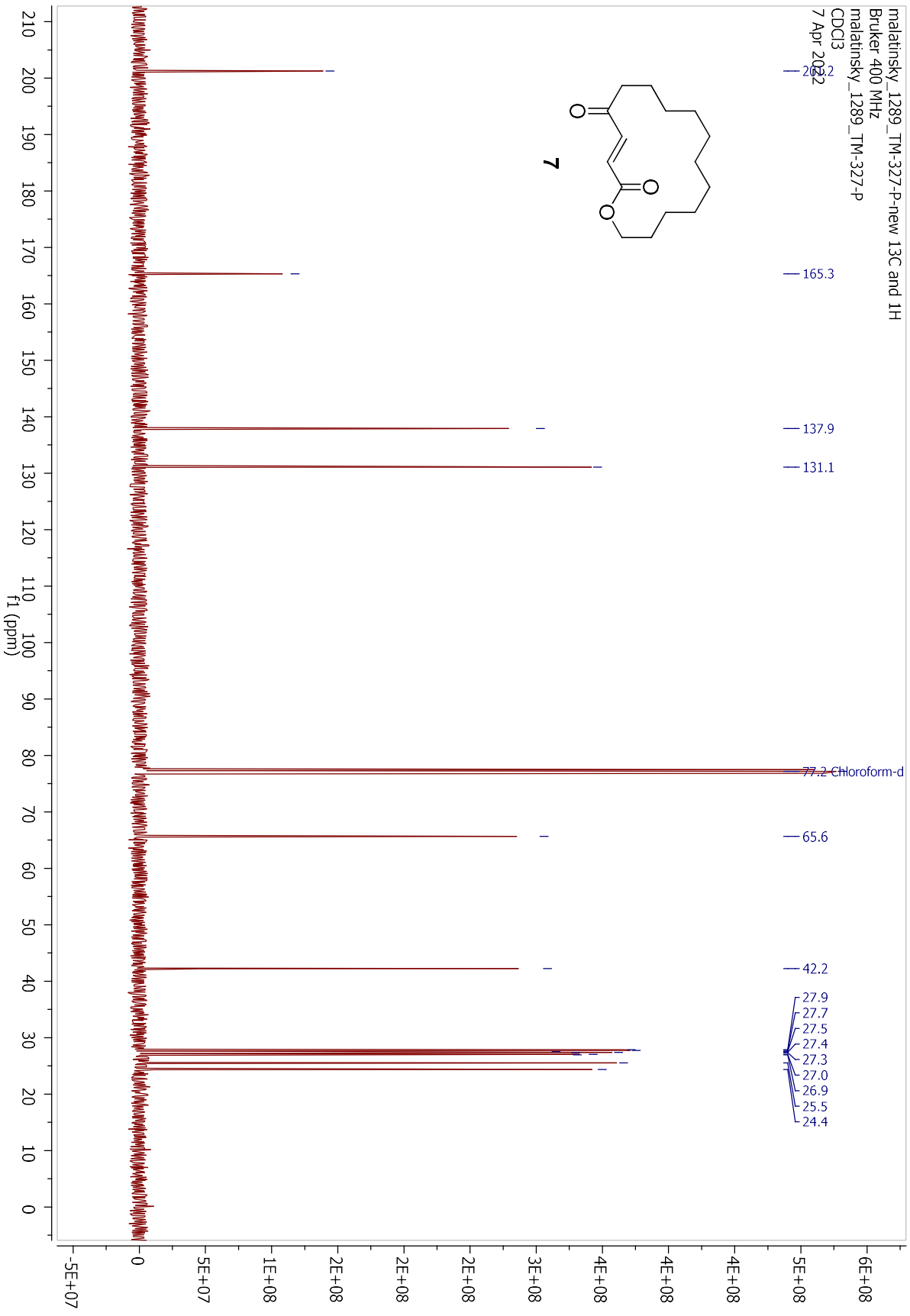
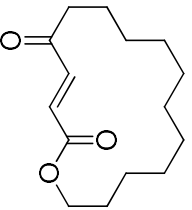
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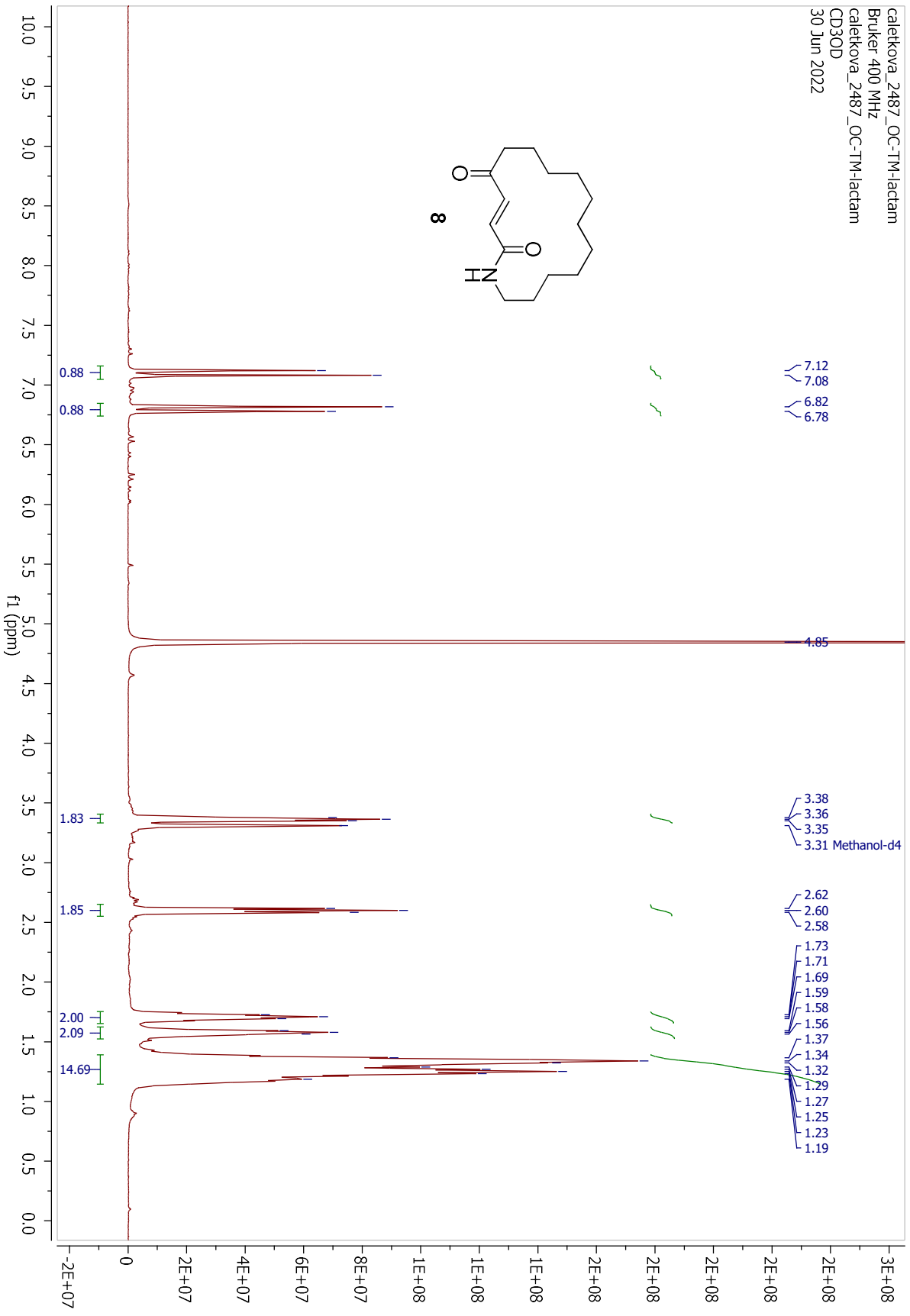
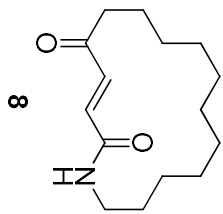
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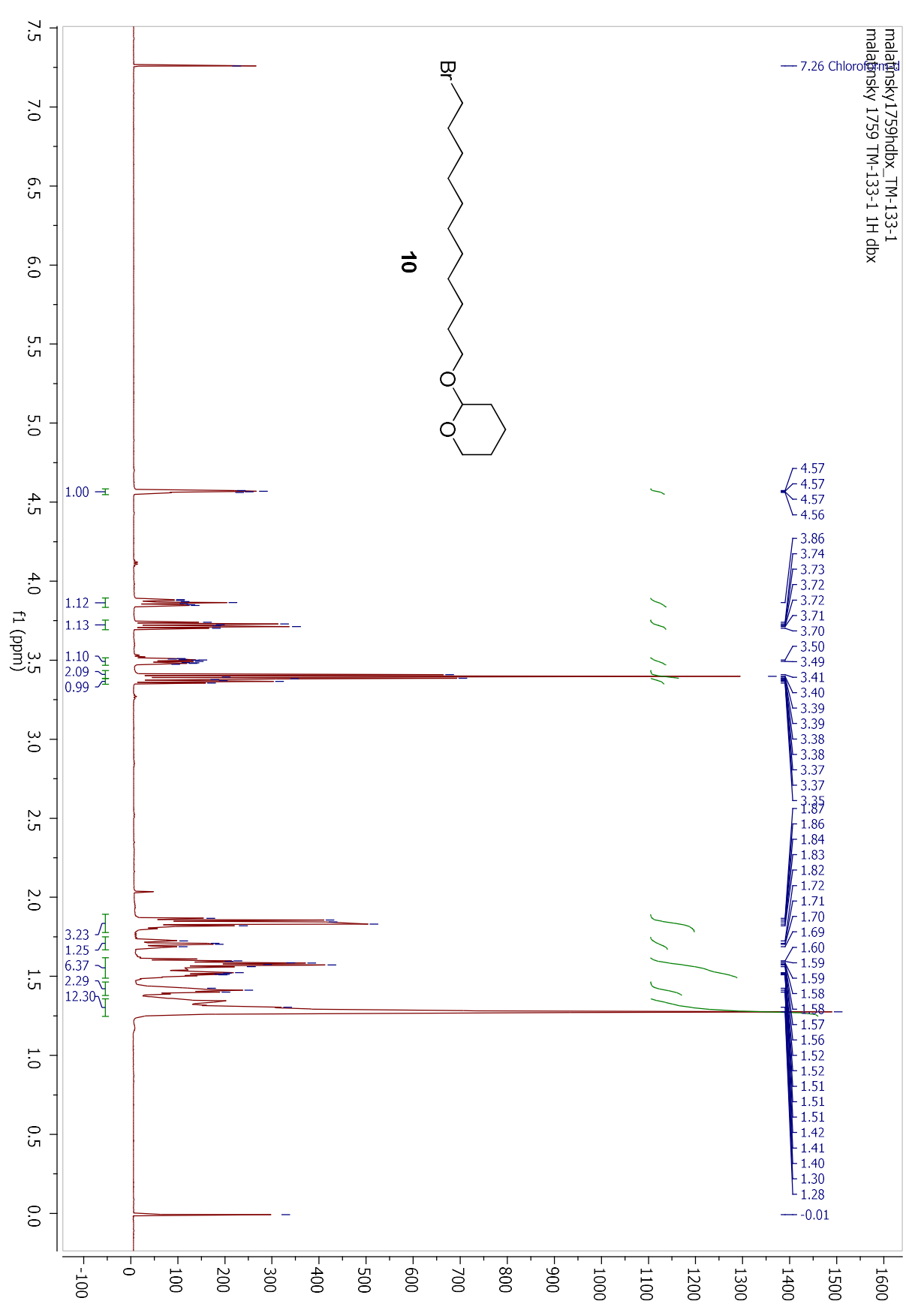
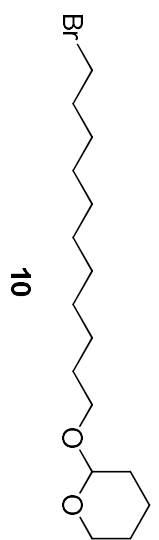
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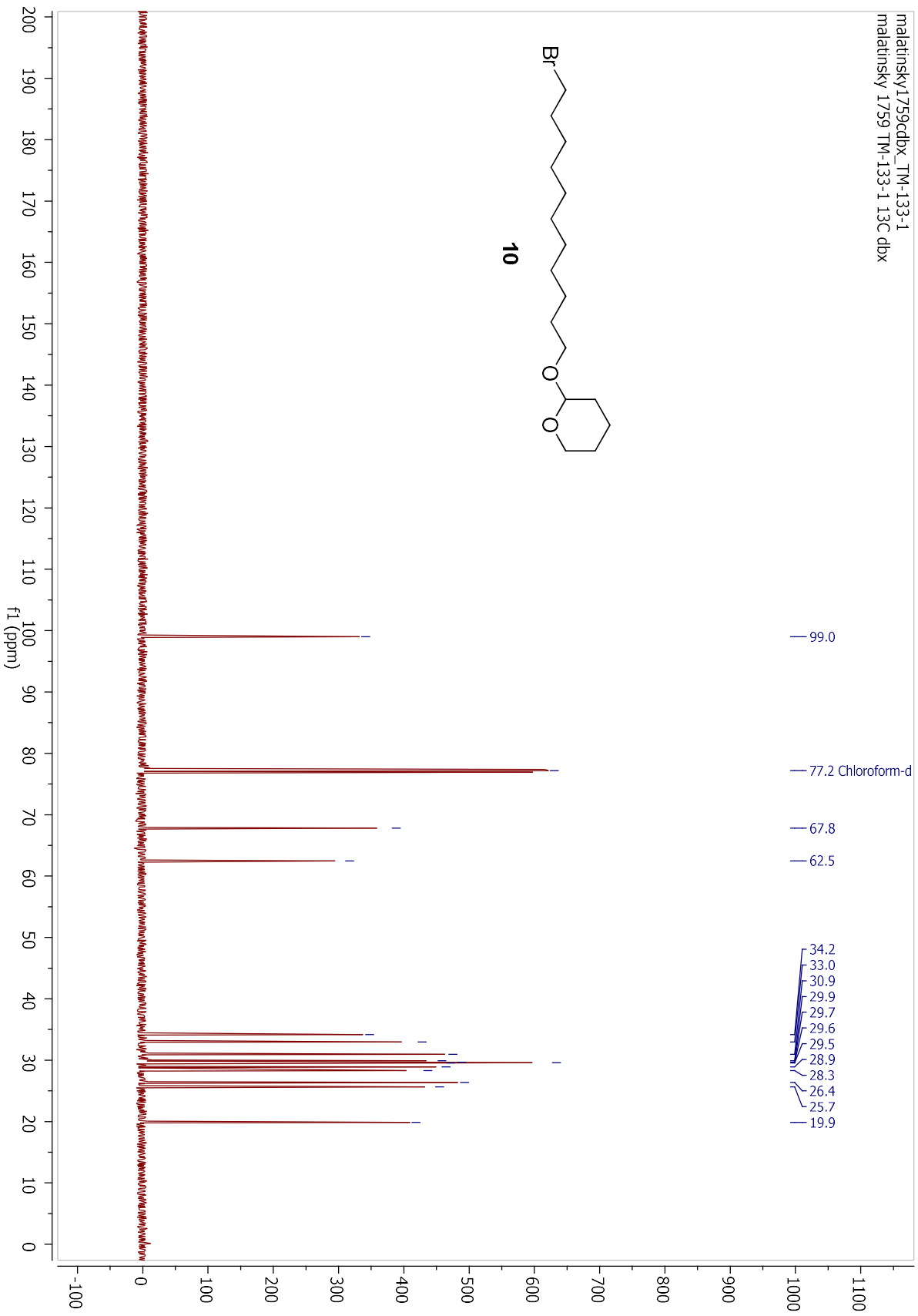
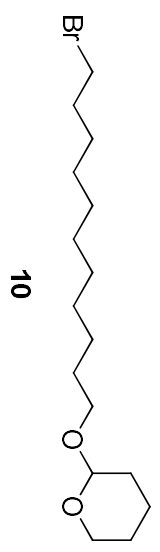
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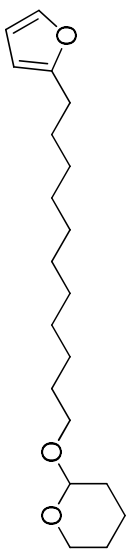
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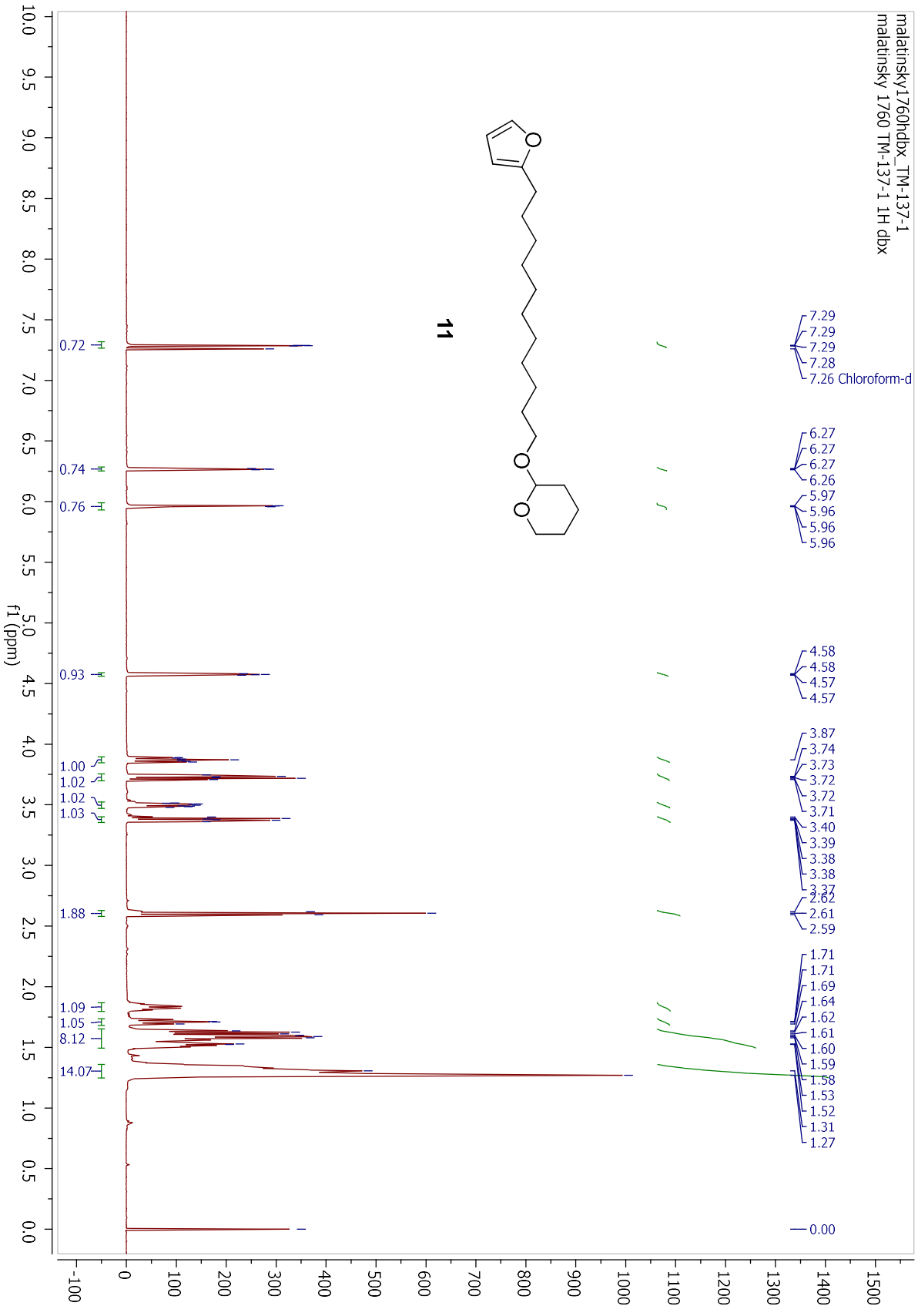
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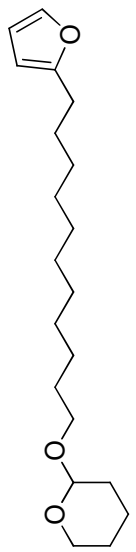
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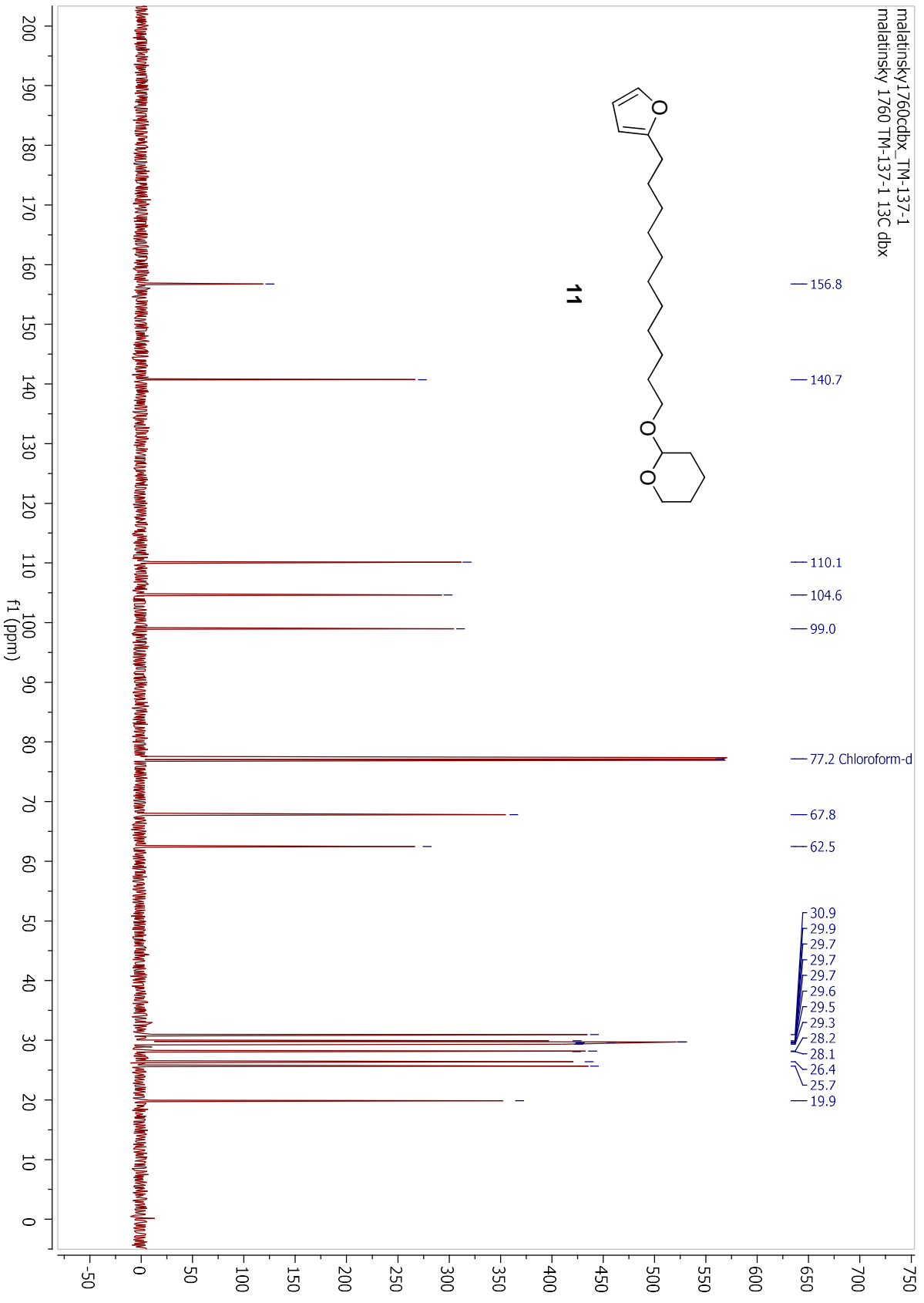
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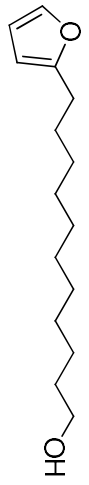
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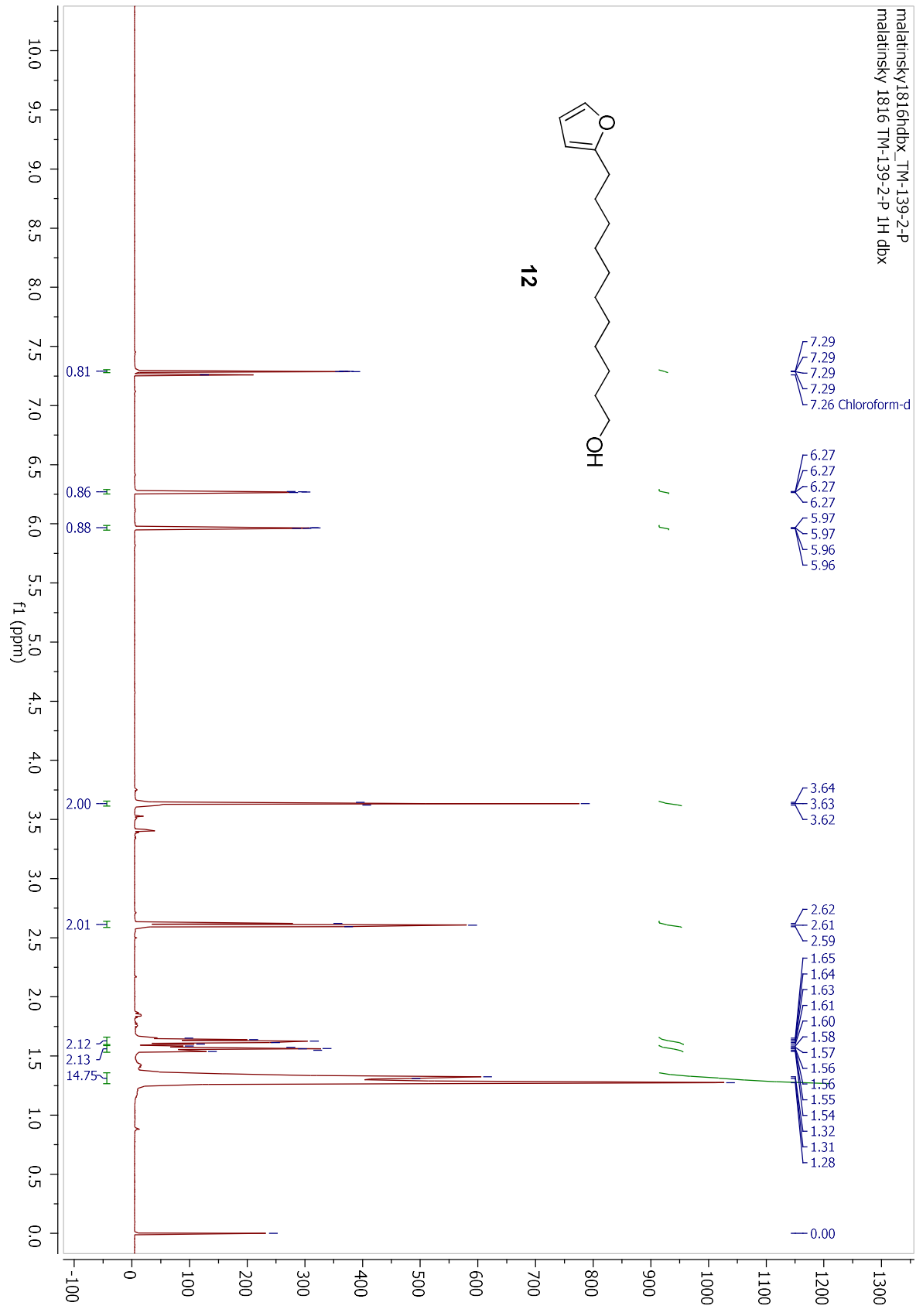
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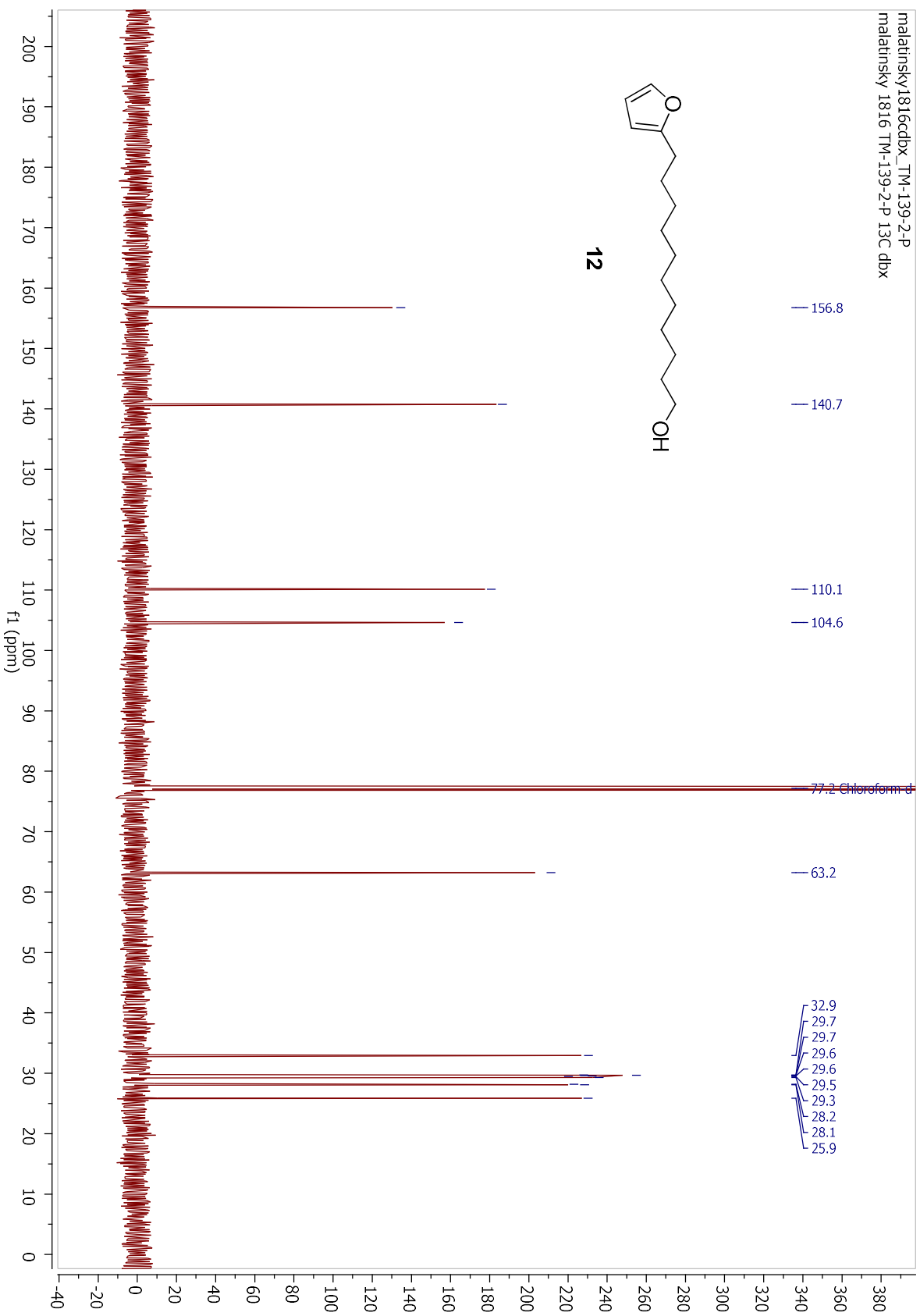
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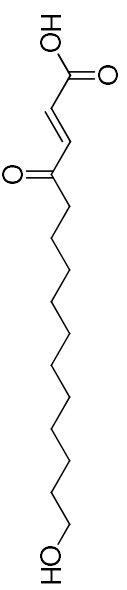
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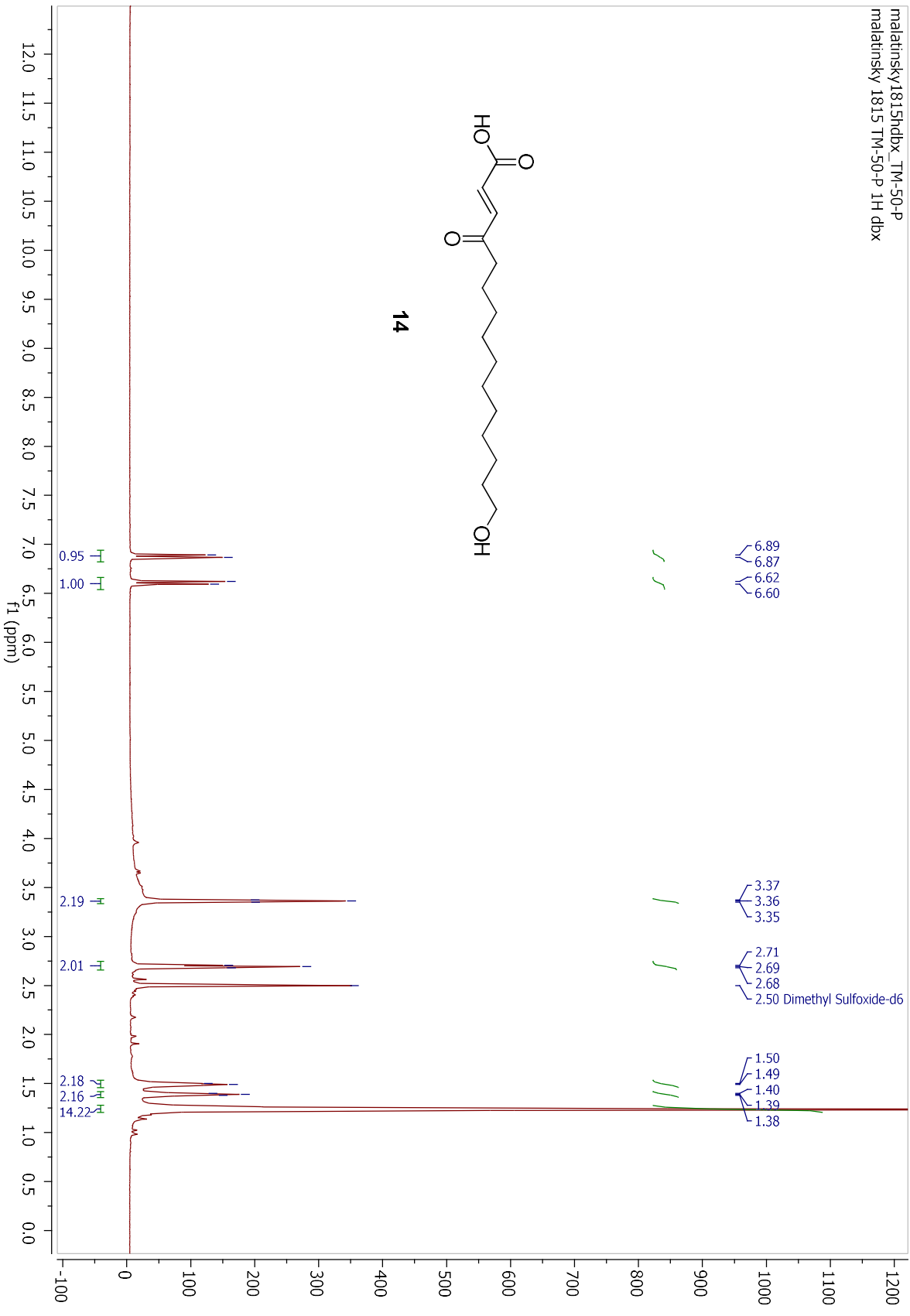
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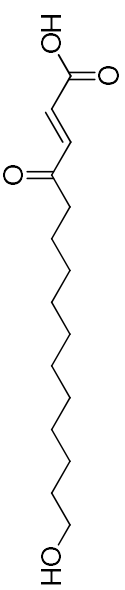
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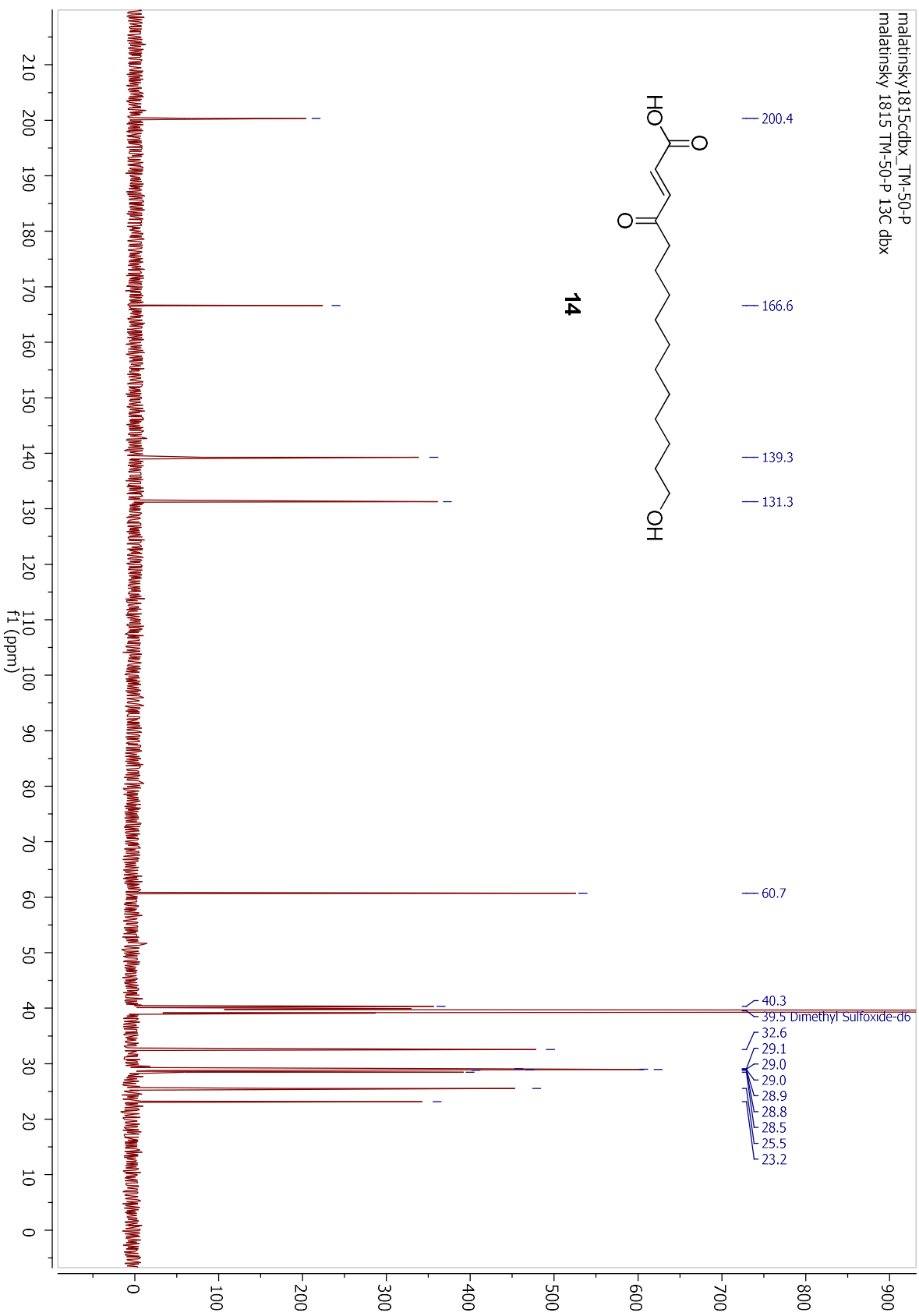
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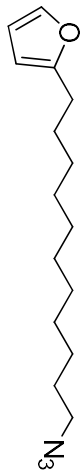


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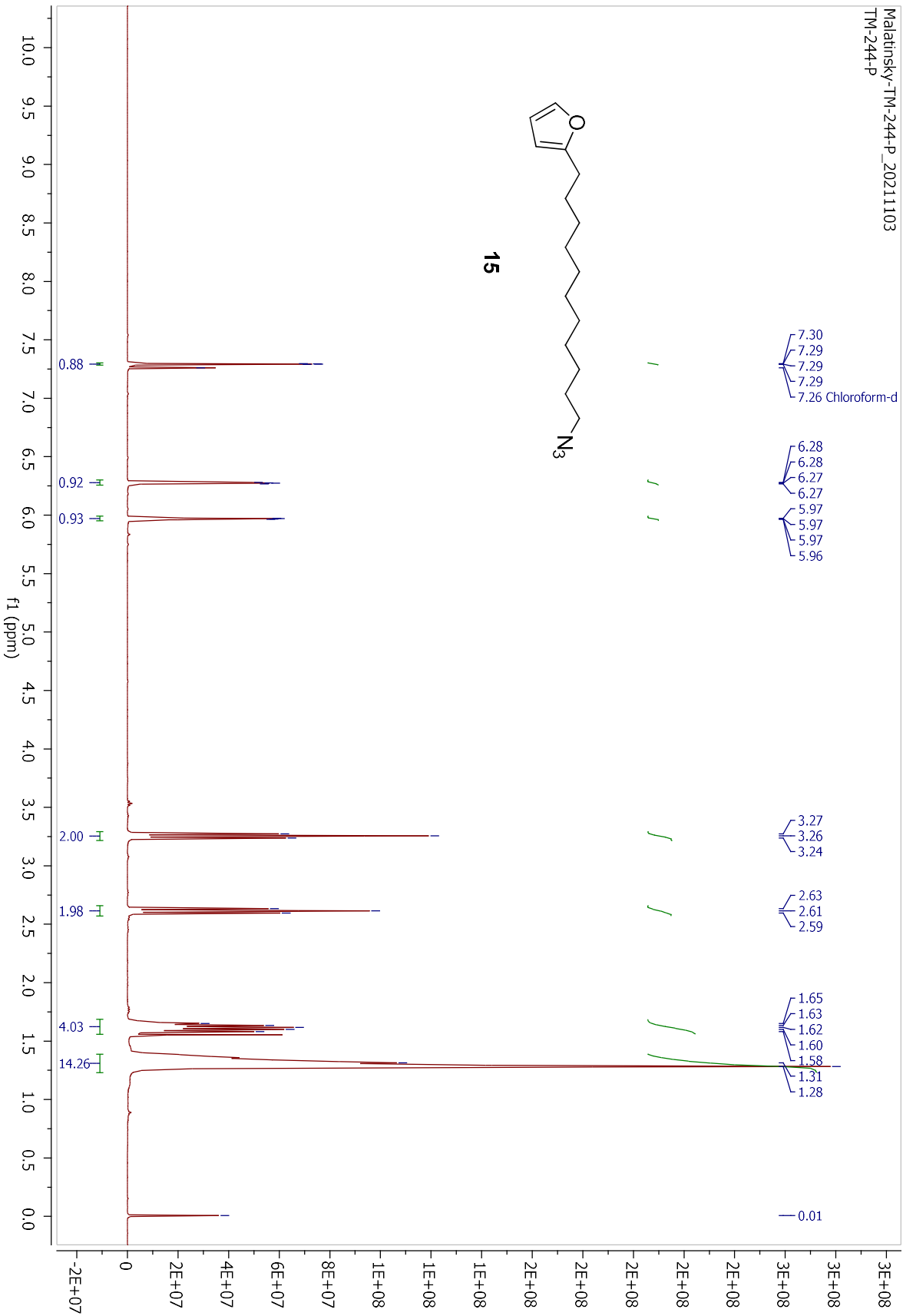


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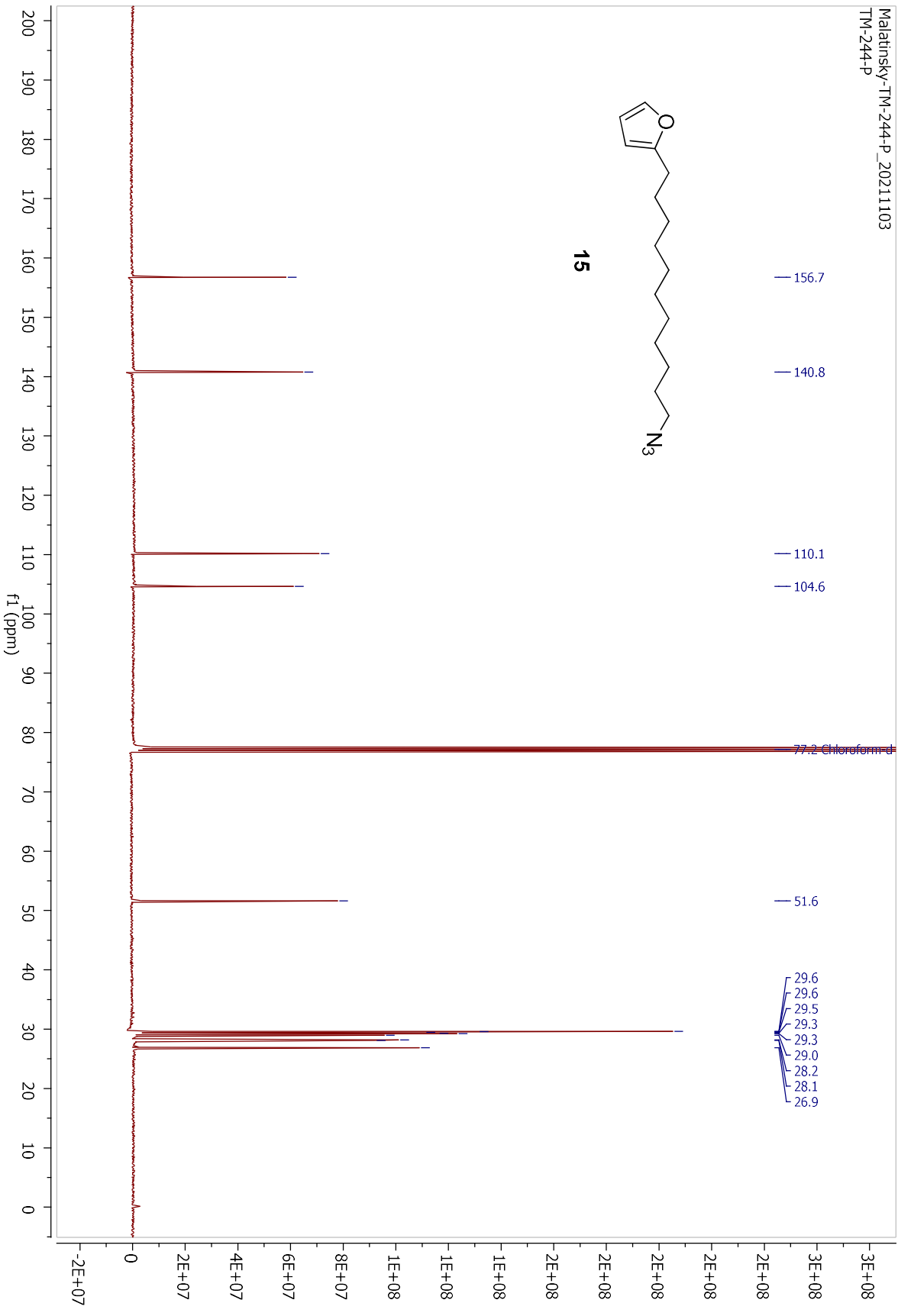


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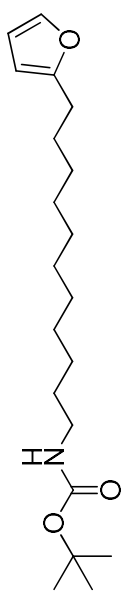




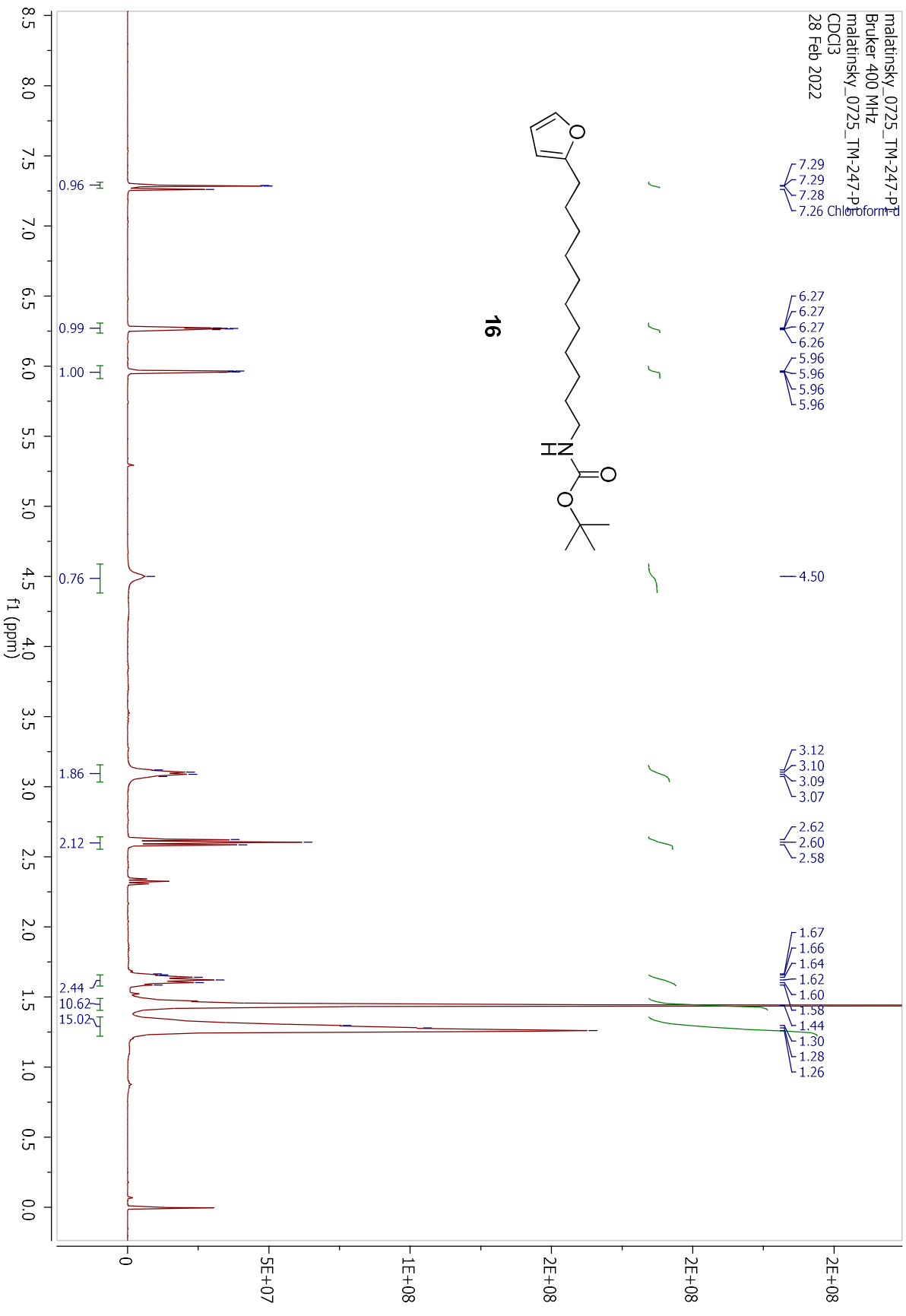
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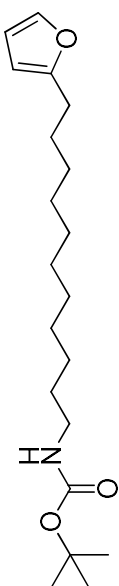
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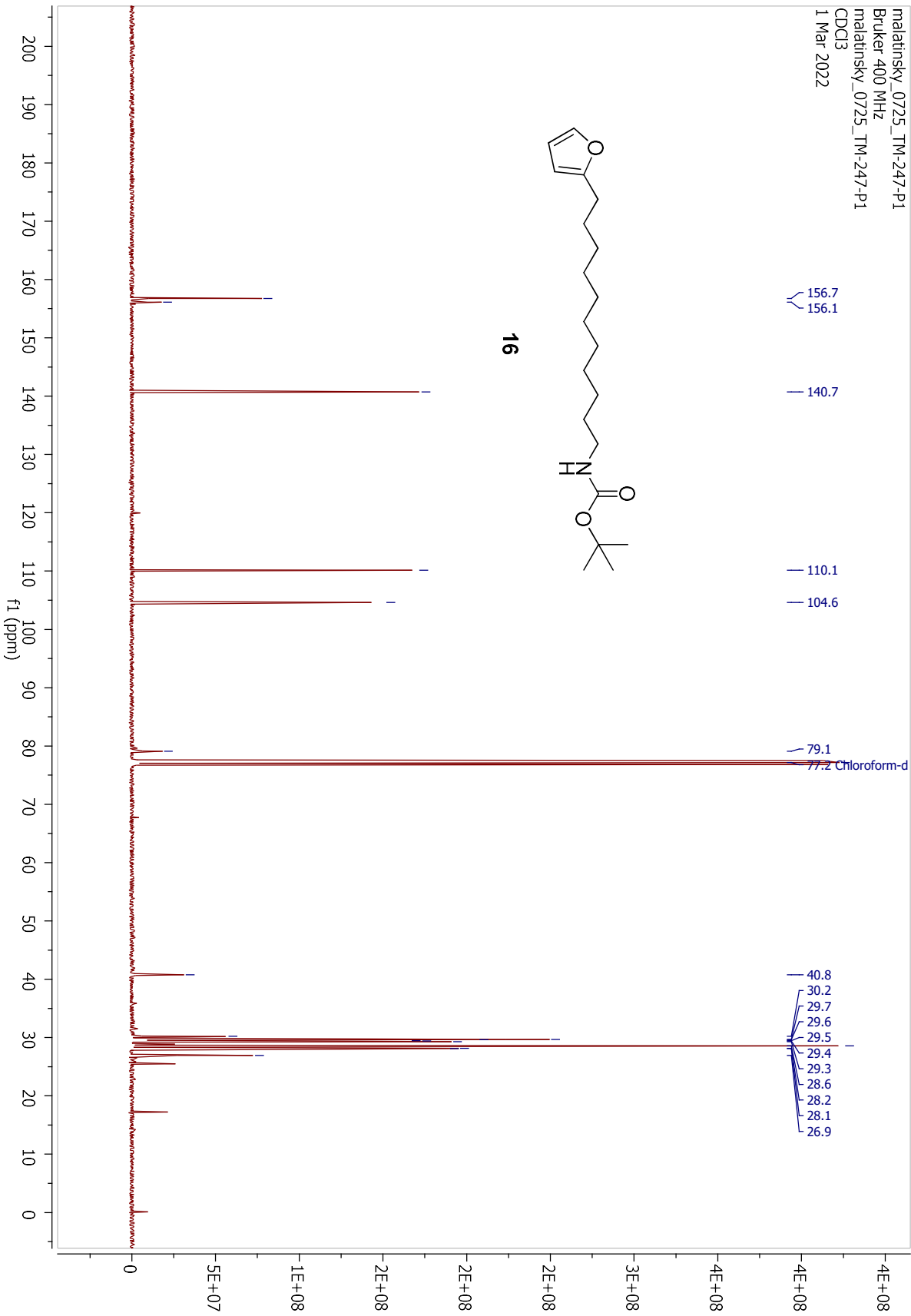
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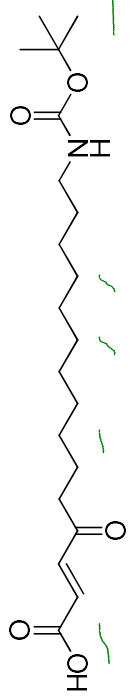
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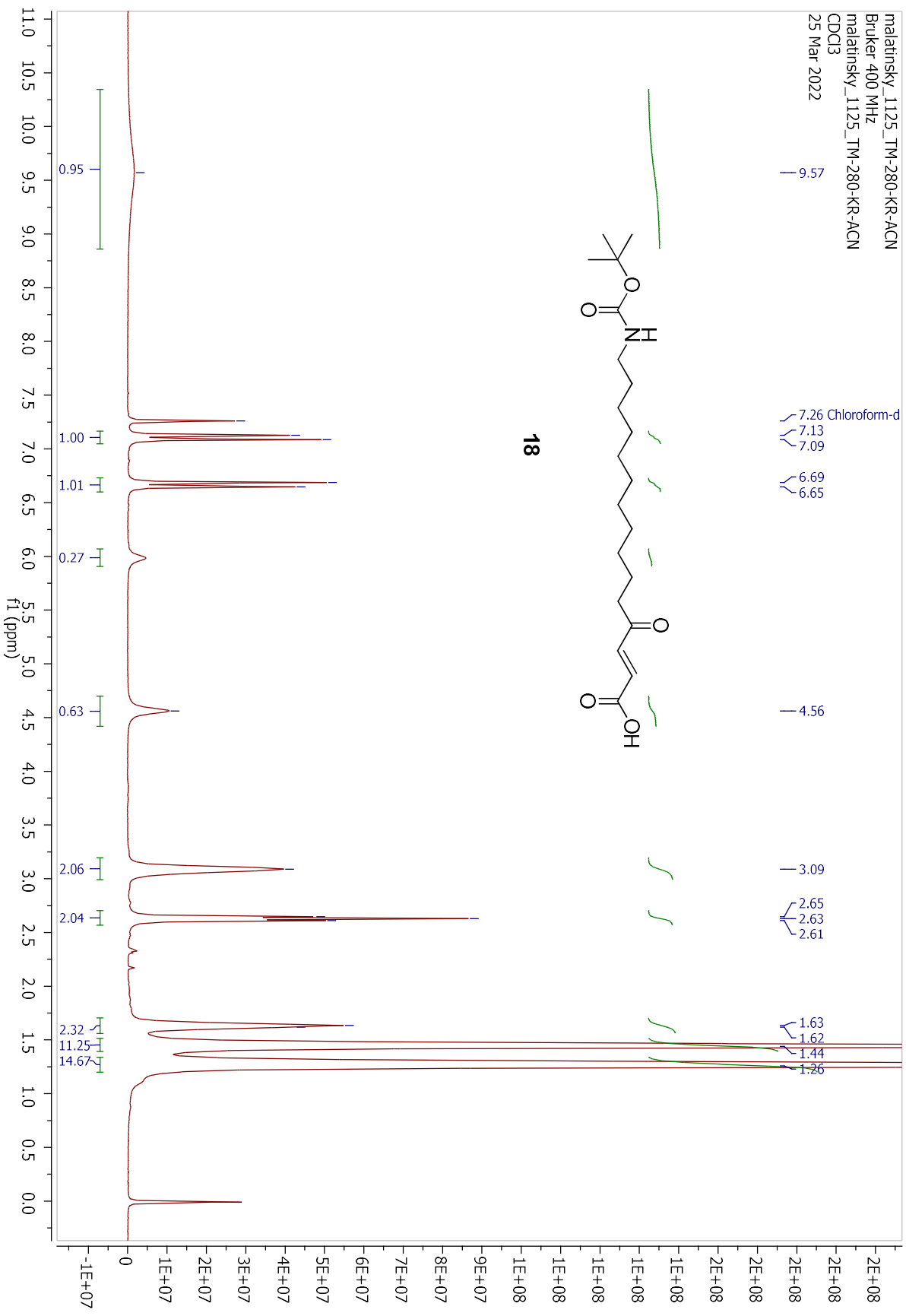
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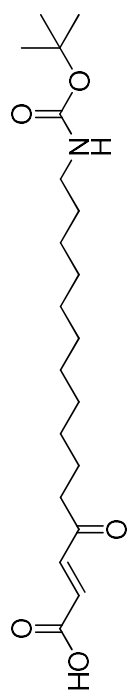
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25 Mar 2022



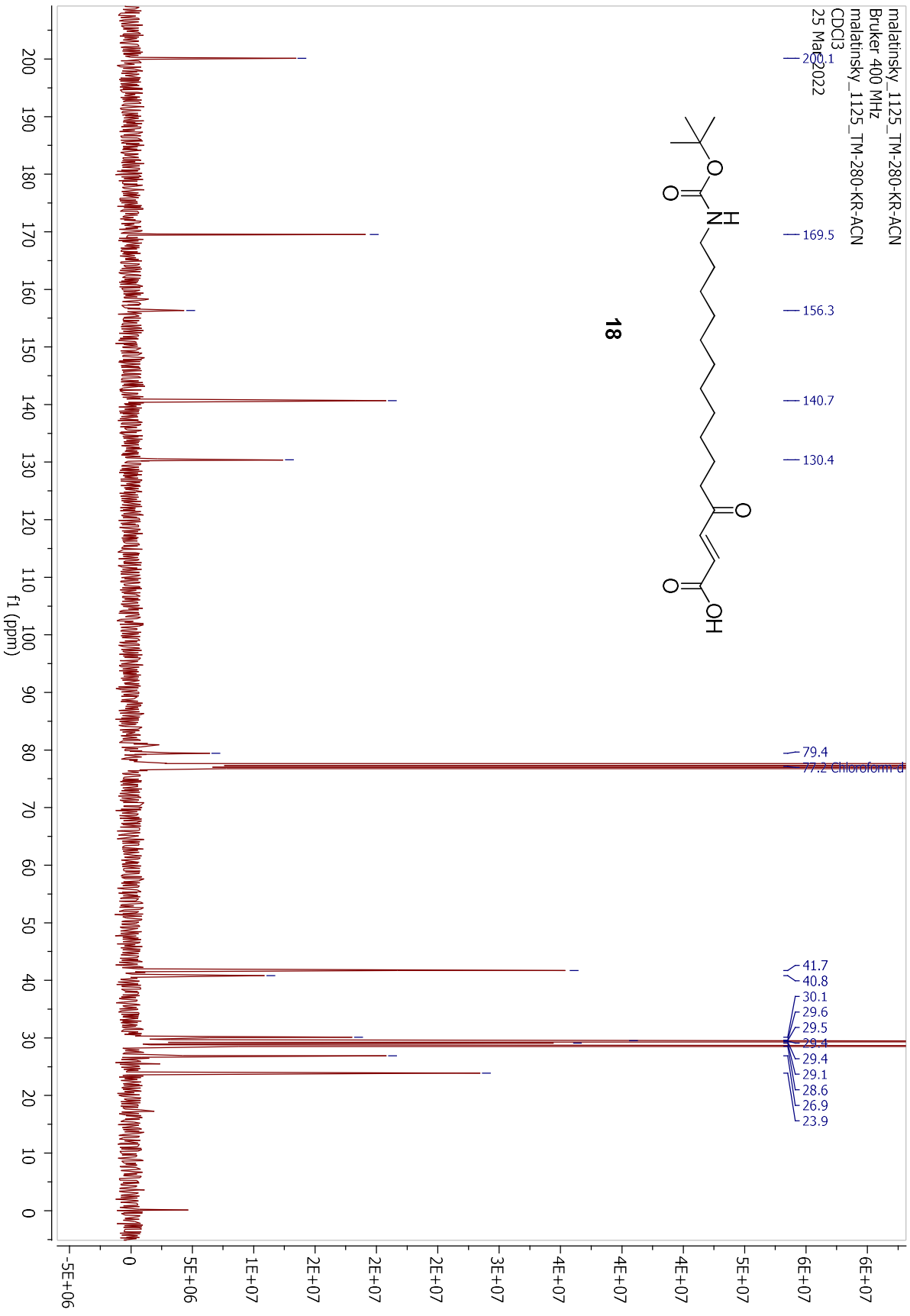
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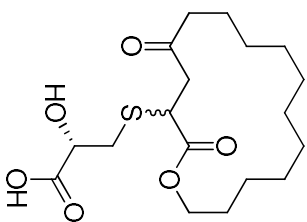
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25 Mar 2022



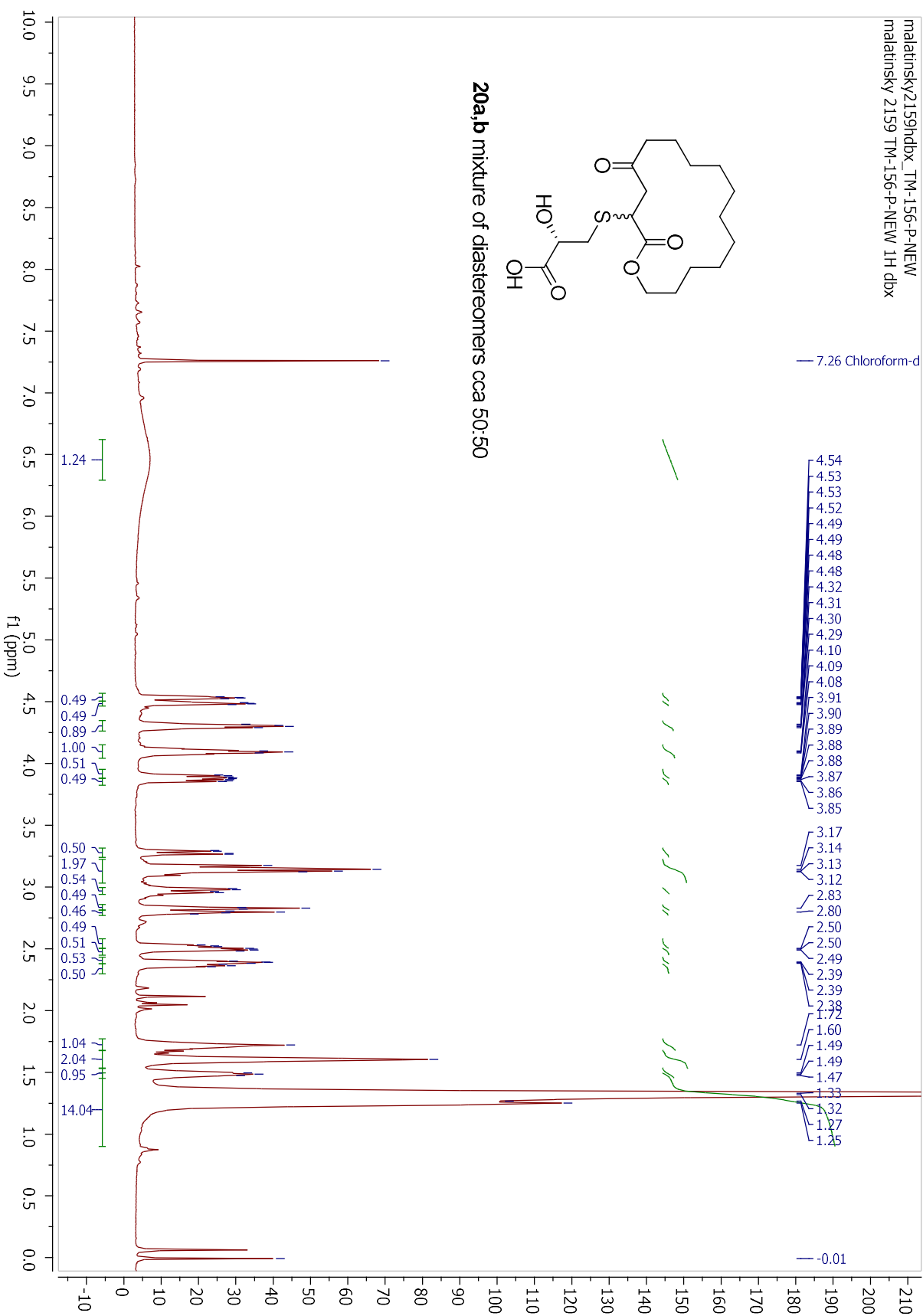
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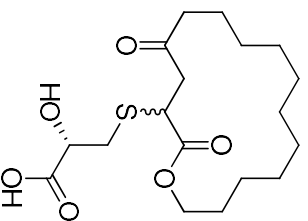
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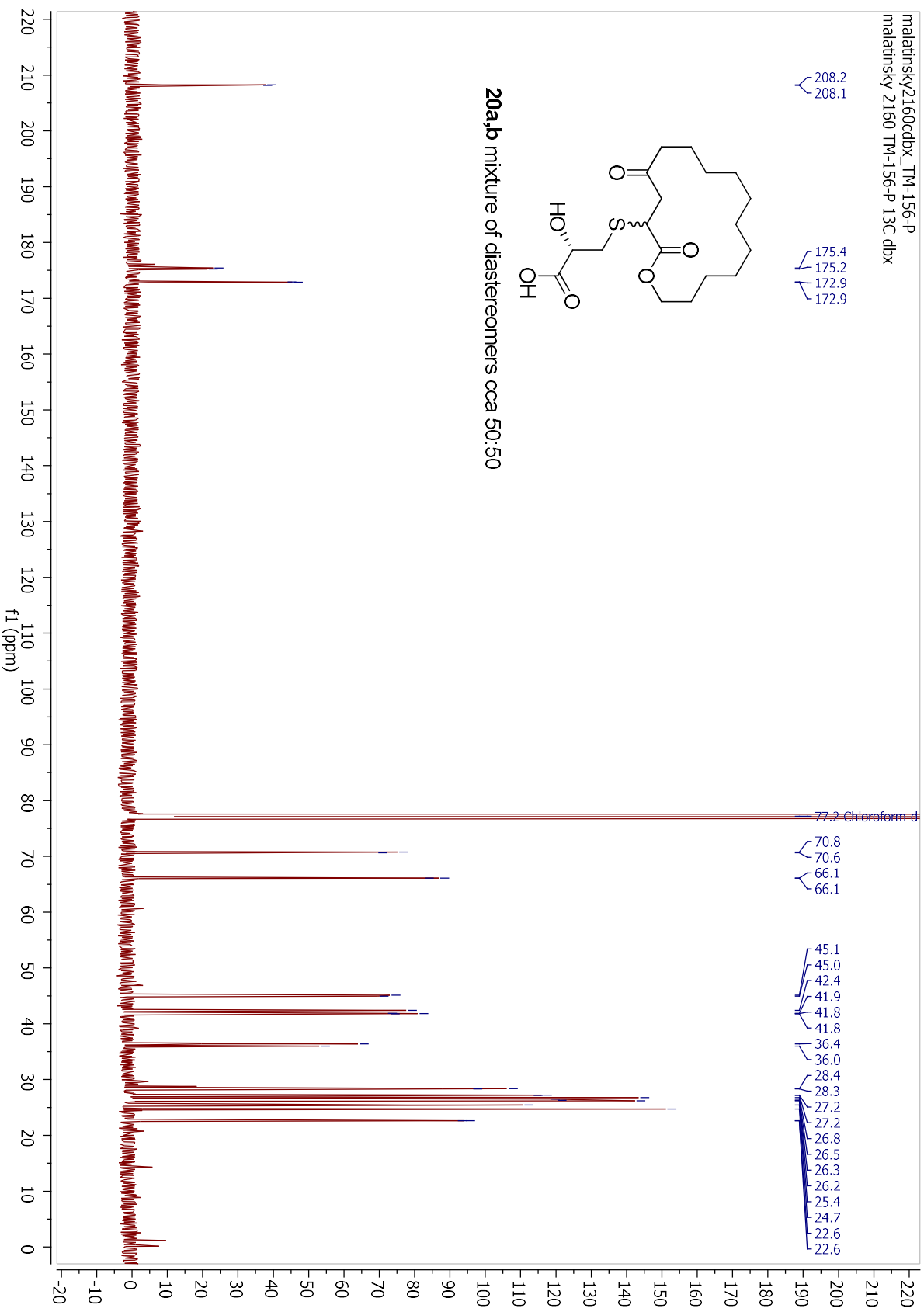
20a,b mixture of diastereomers cca 50:50



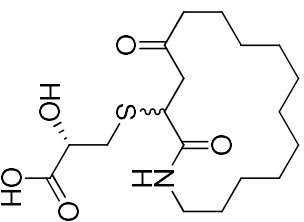
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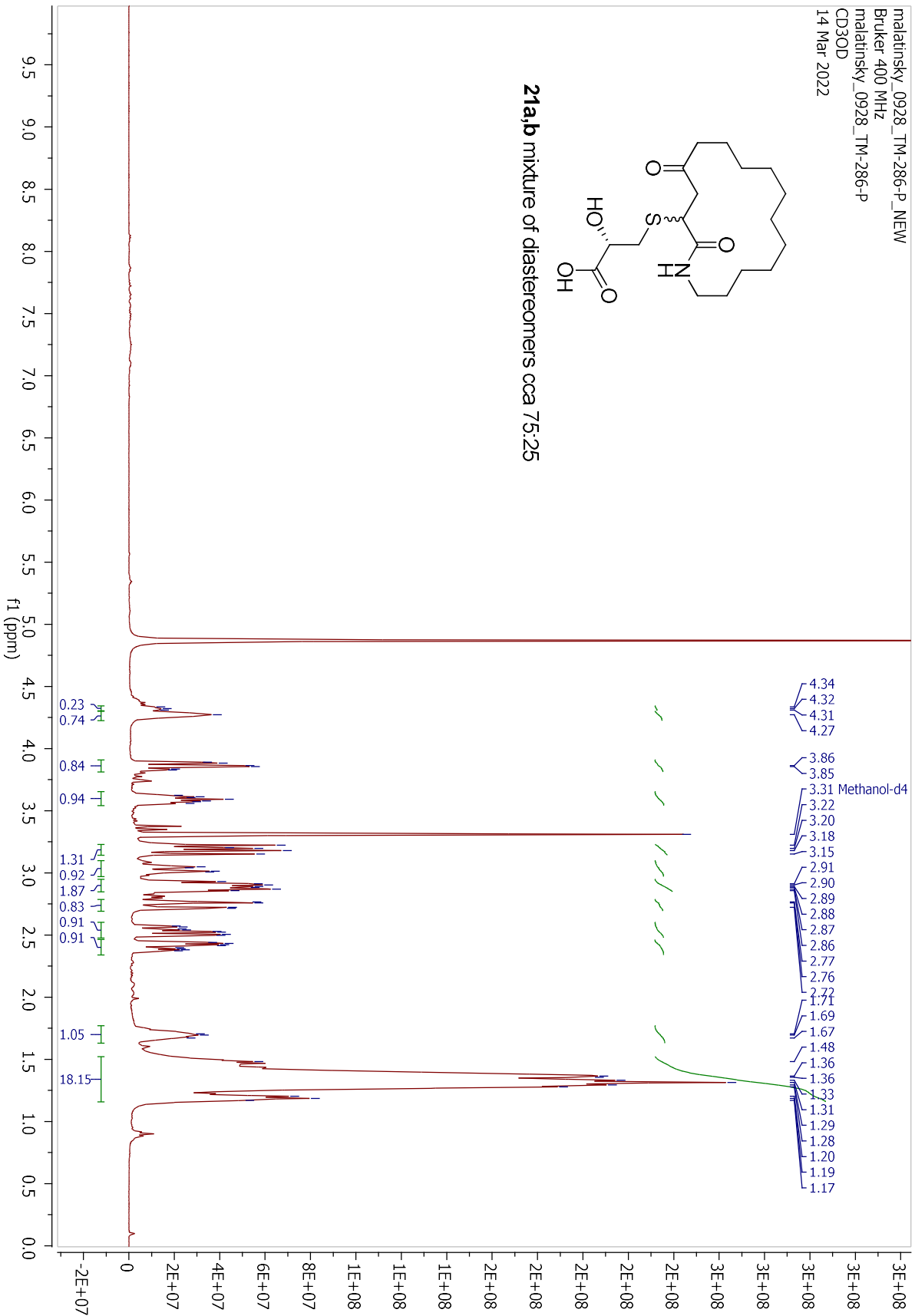
20a,b mixture of diastereomers cca 50:50



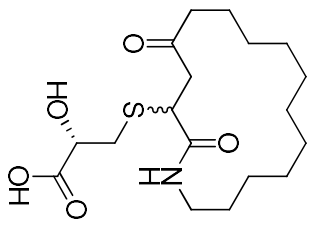
malatinsky_0928_TM-286-P_NEW
Bruker 400 MHz
malatinsky_0928_TM-286-P
CD3OD
14 Mar 2022



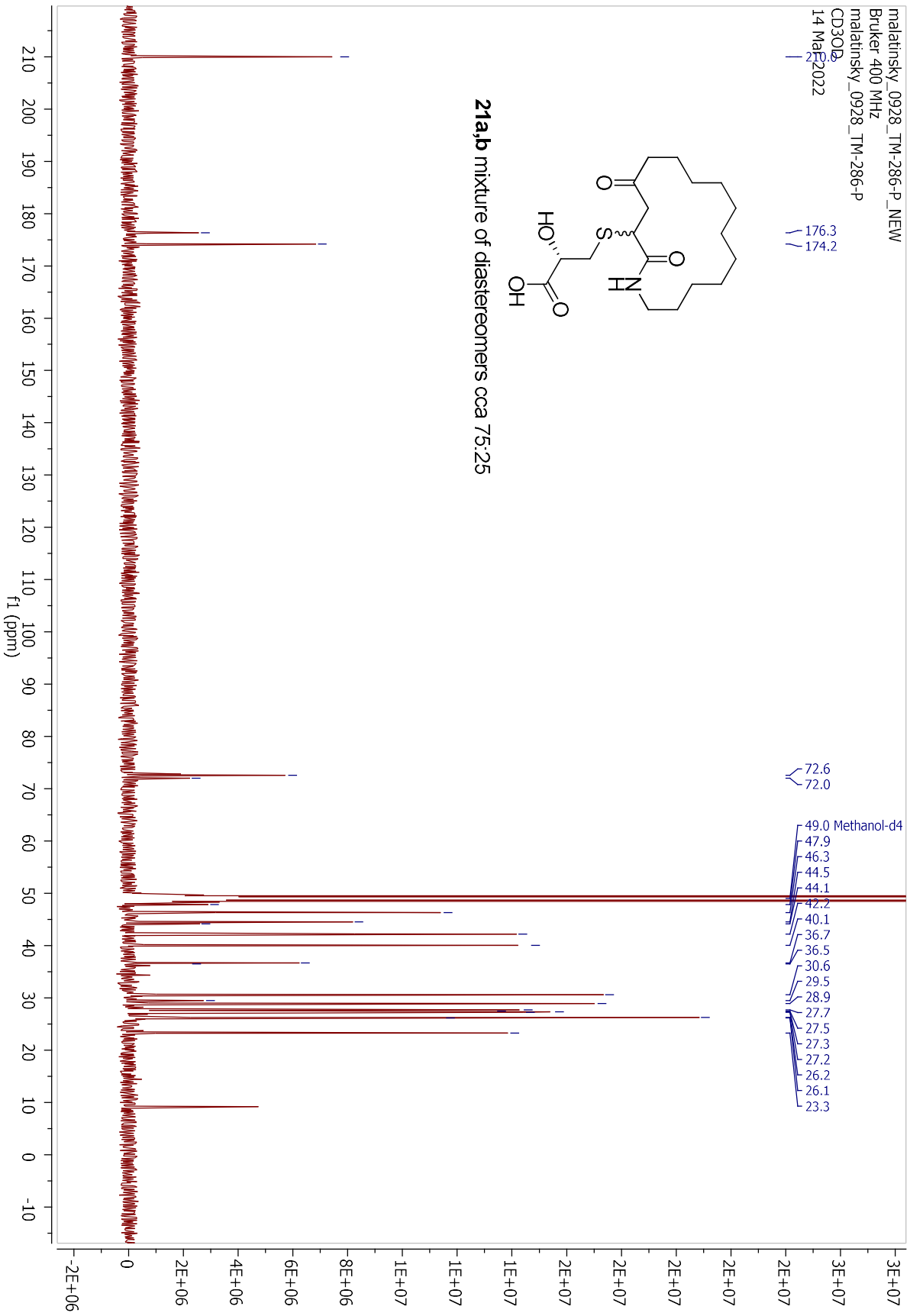
21a,b mixture of diastereomers cca 75:25

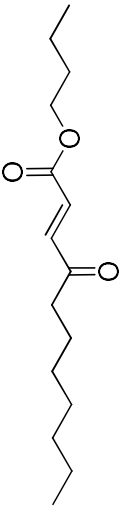


malatinsky_0928_TM-286-P_NEW
Bruker 400 MHz
malatinsky_0928_TM-286-P
CD3OD
14 Mar 2022

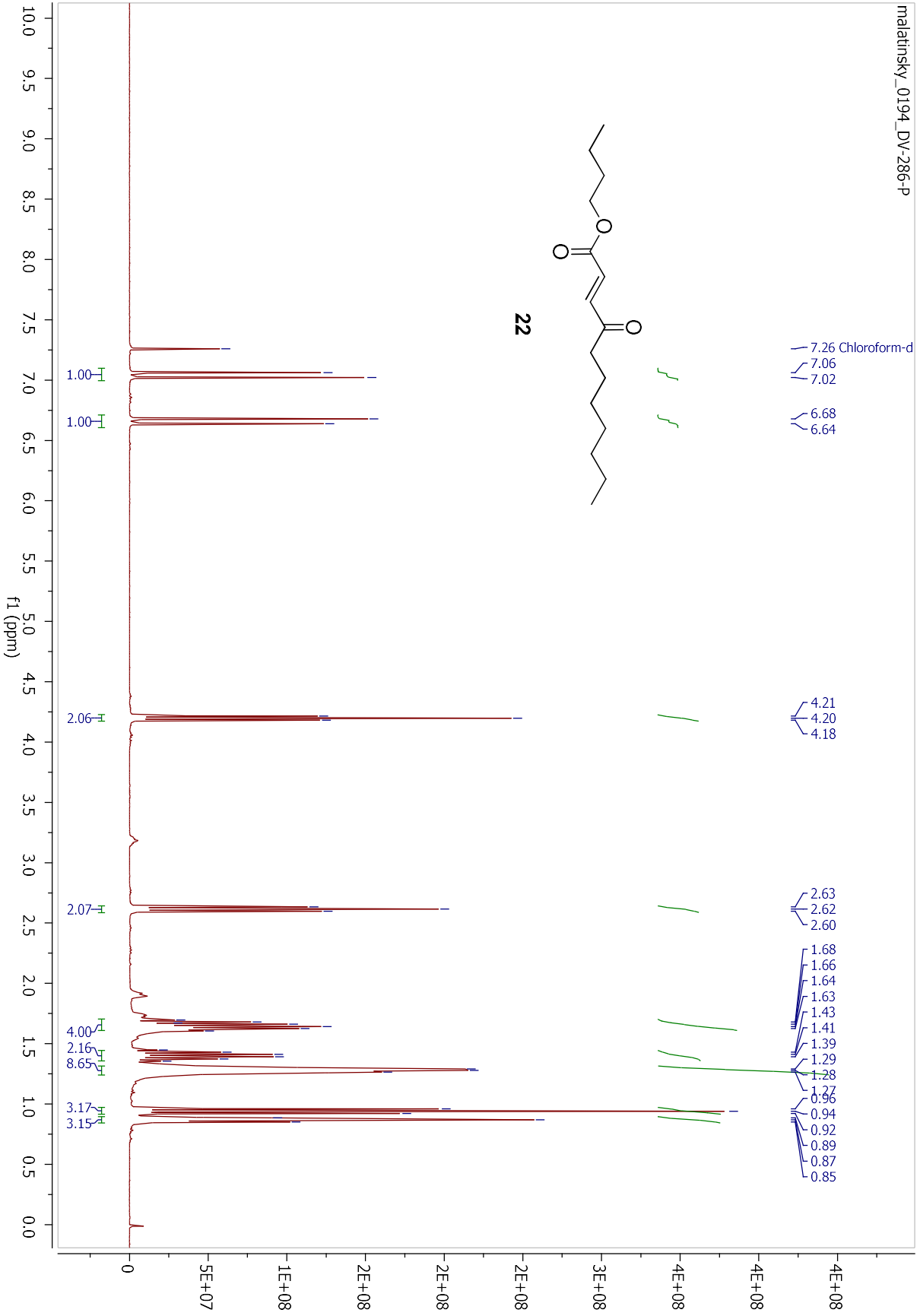


21a,b mixture of diastereomers cca 75:25

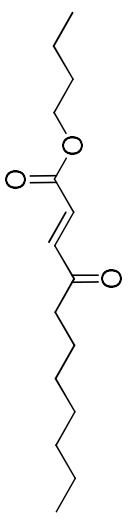




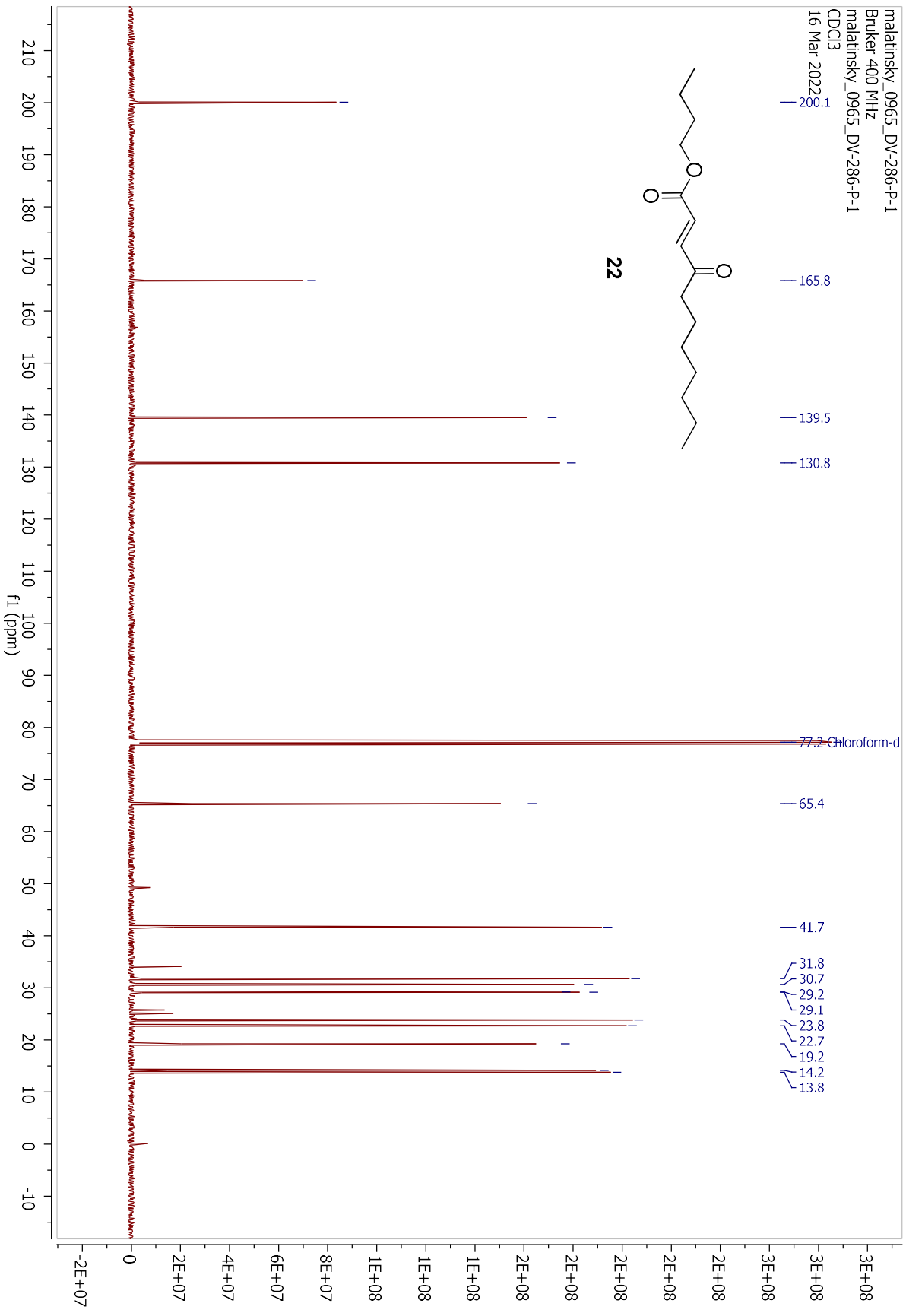
22

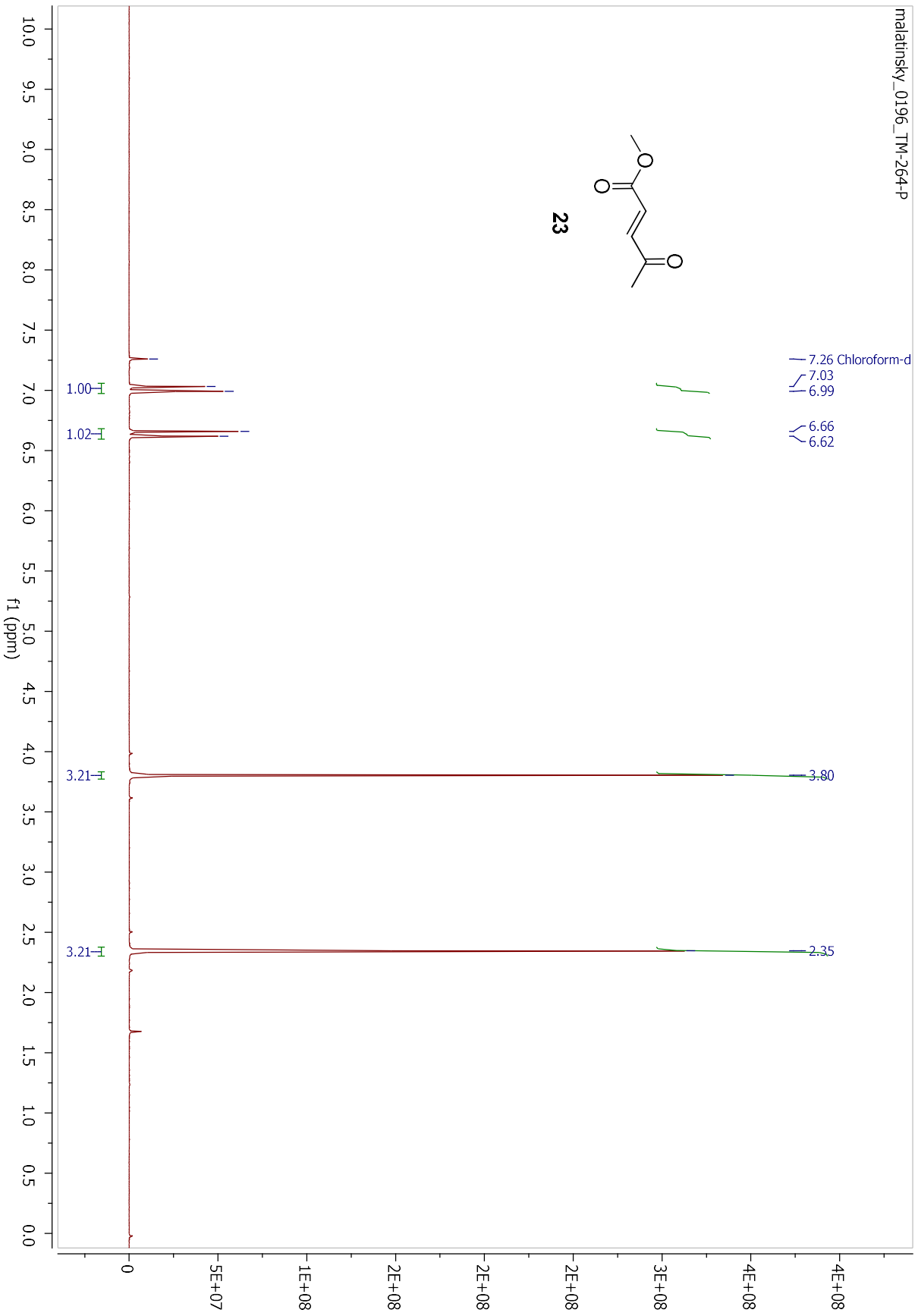
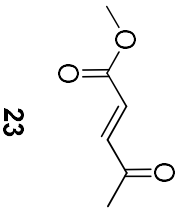


malatinsky_0965_DV-286-P-1
Bruker 400 MHz
malatinsky_0965_DV-286-P-1
CDCl3
16 Mar 2022

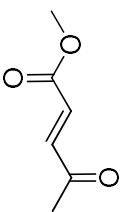


22

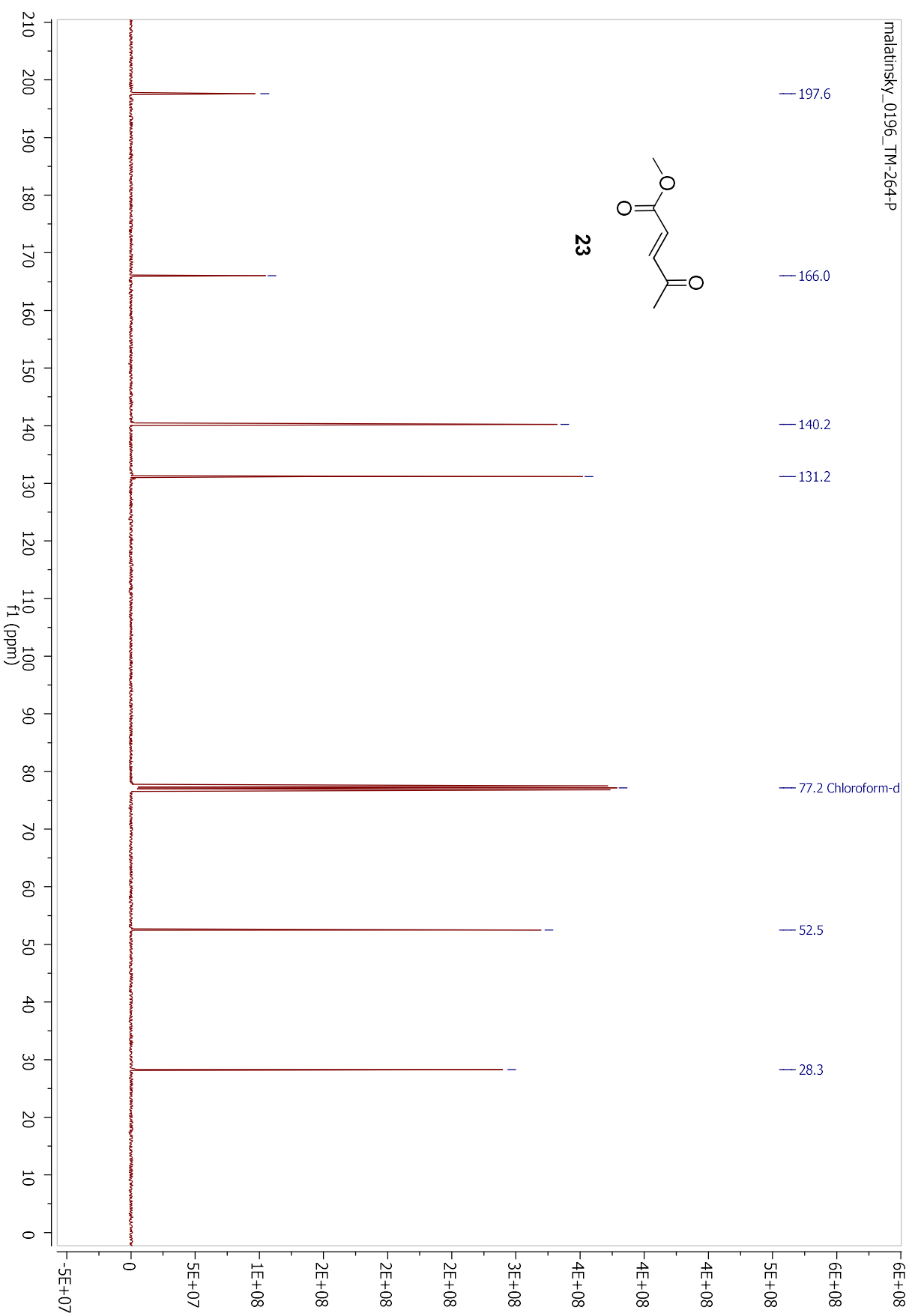




malatinsky_0196_TM-264-P



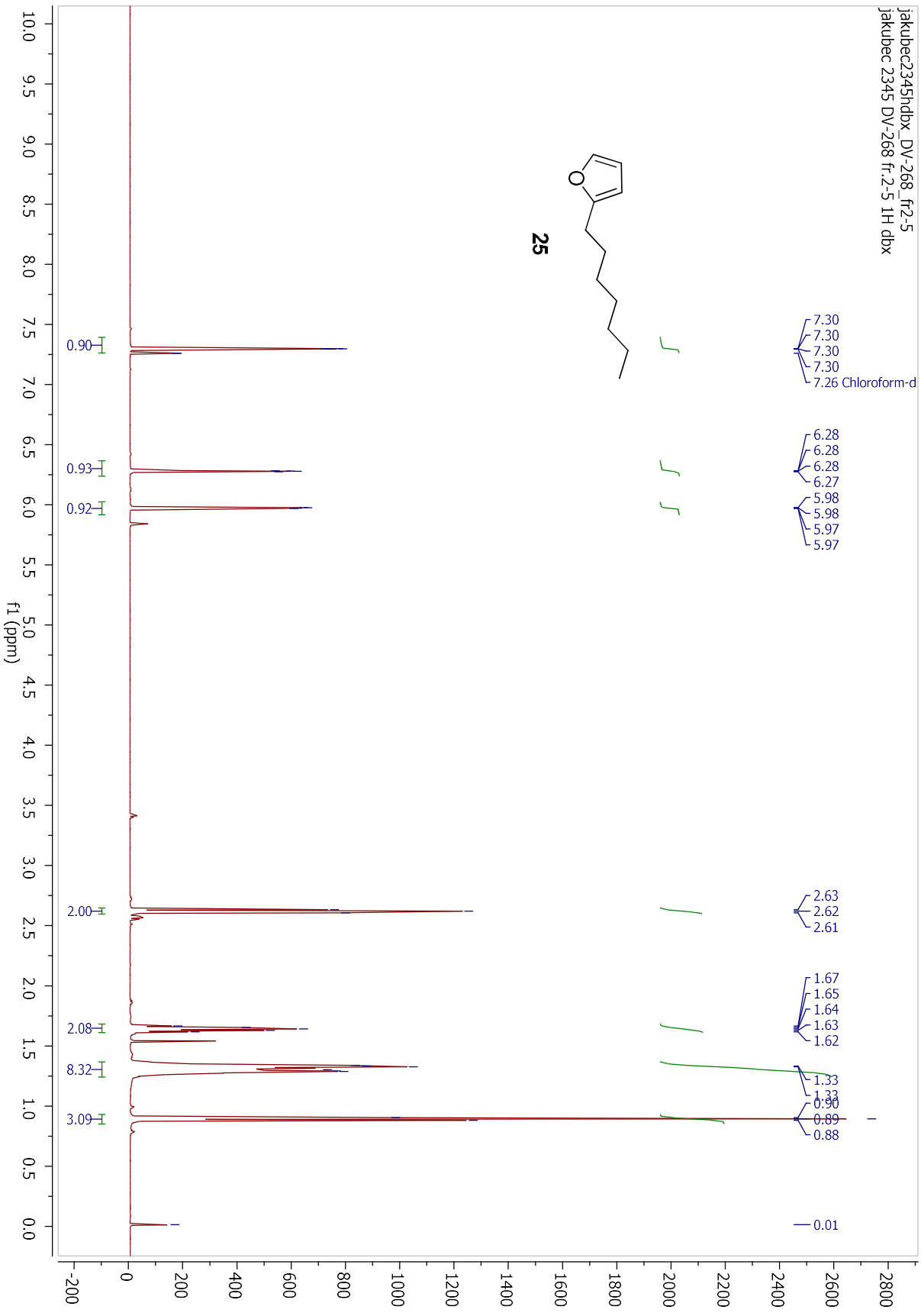
23



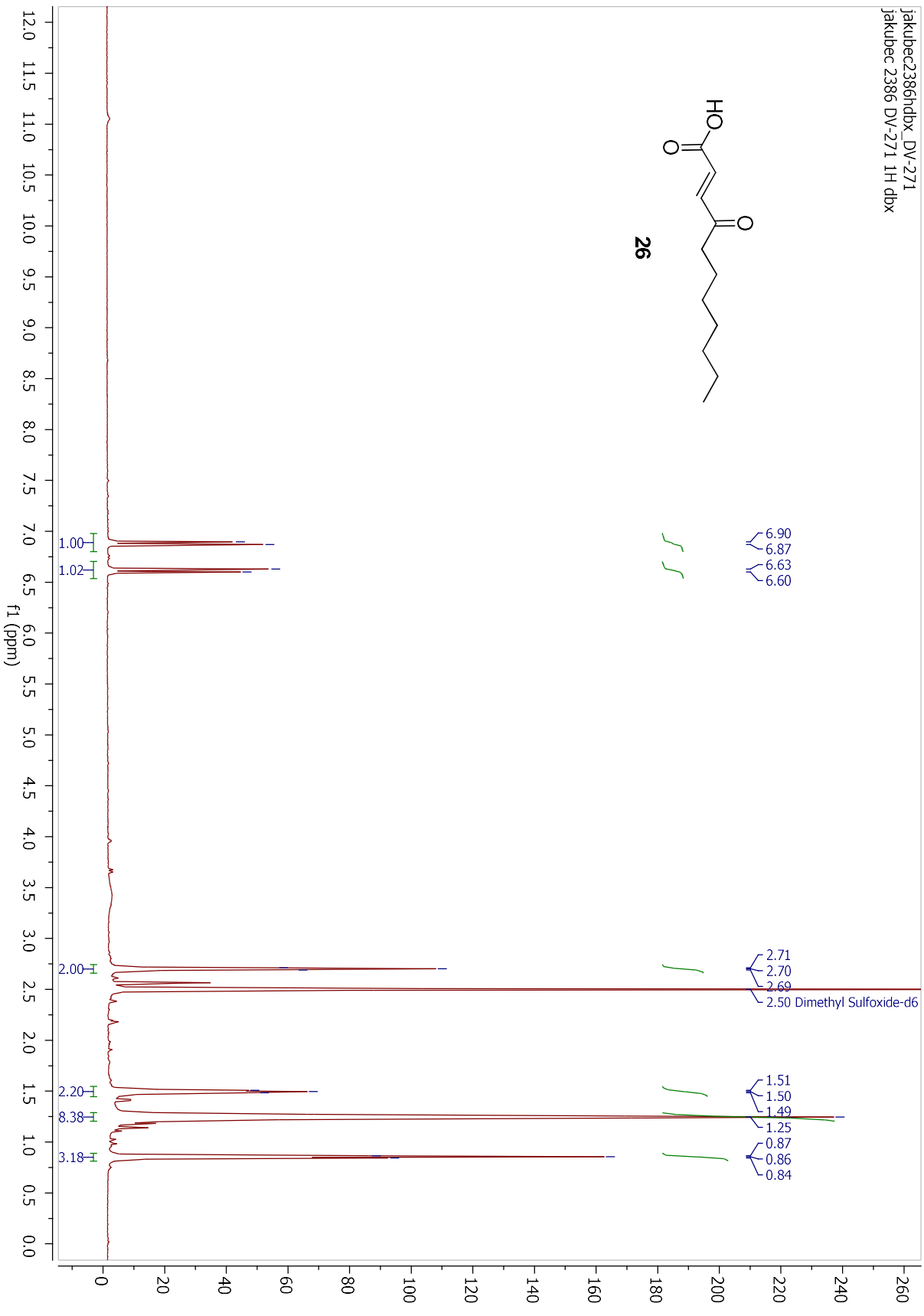
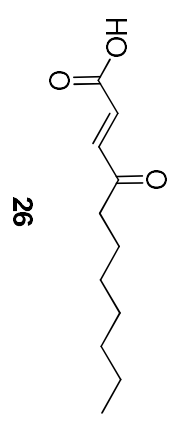
jakubec2345hdbx_DV-268_fr2-5
jakubec 2345 DV-268 fr.2-5 1H dbx

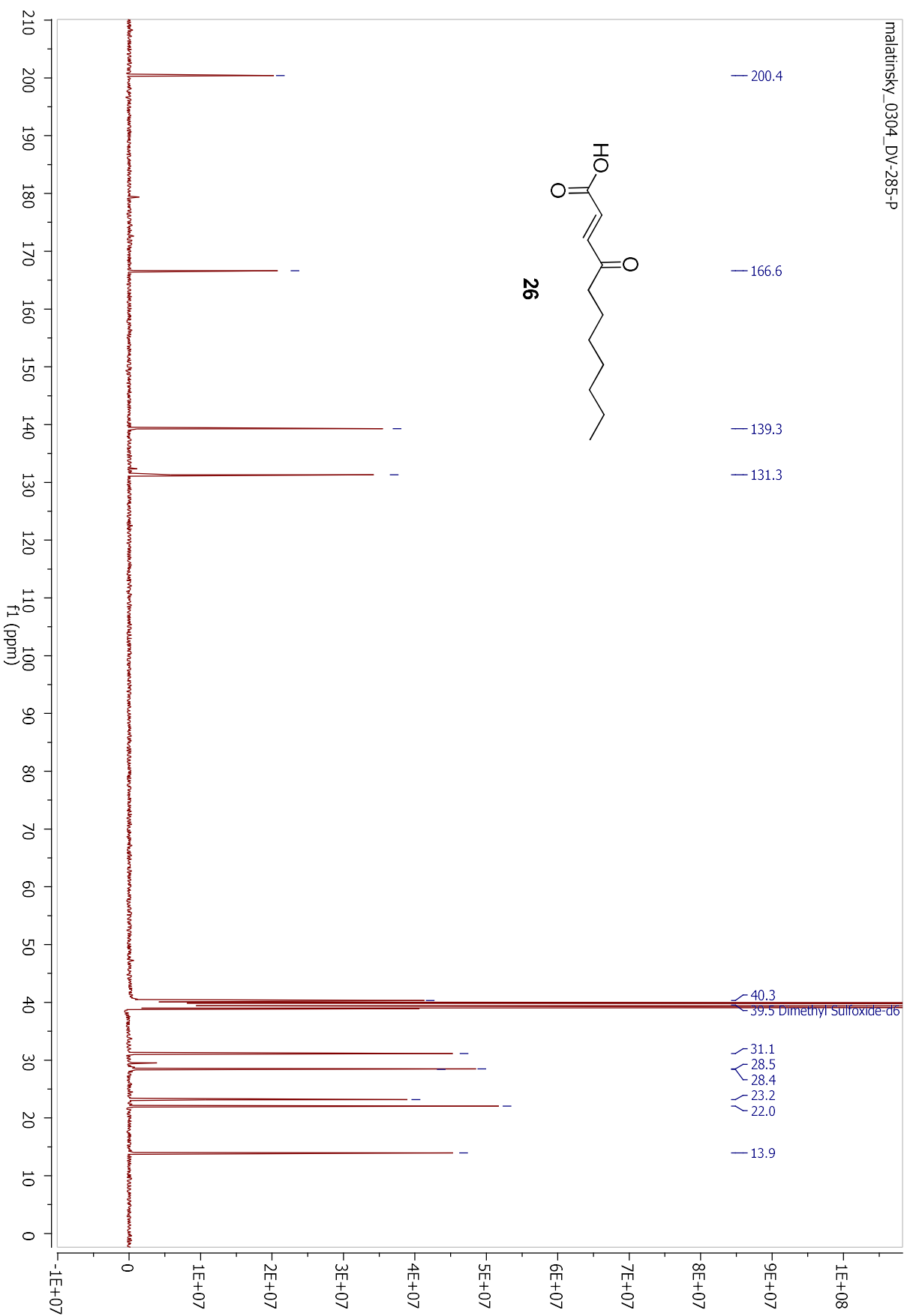
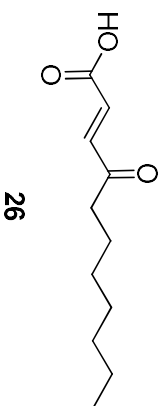


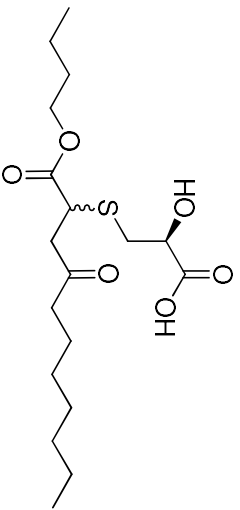
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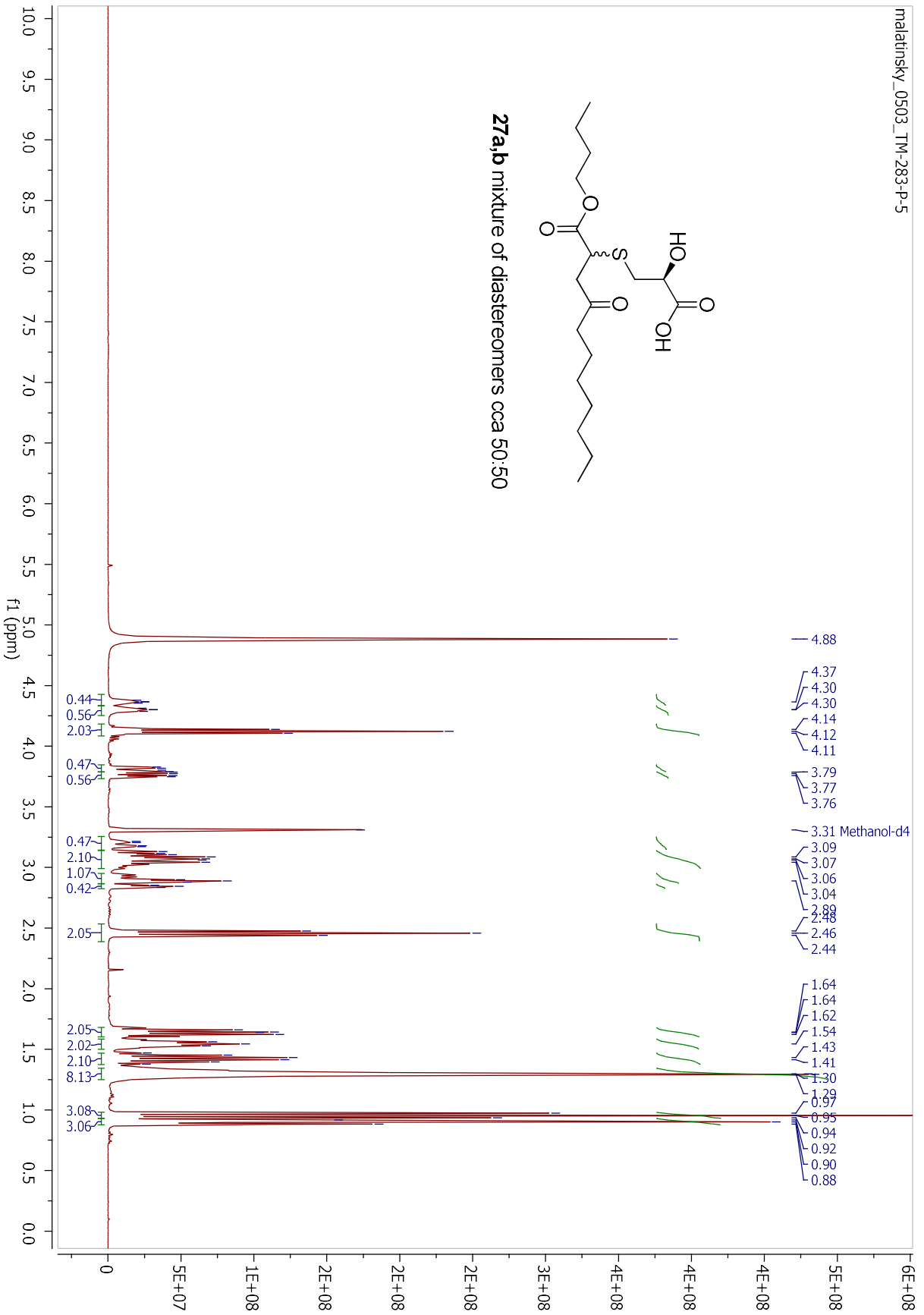
jakubec2386hdbx_DV-271
jakubec 2386 DV-271 1H dbx

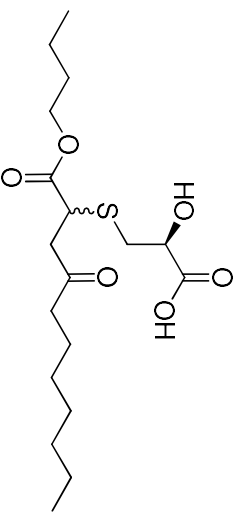




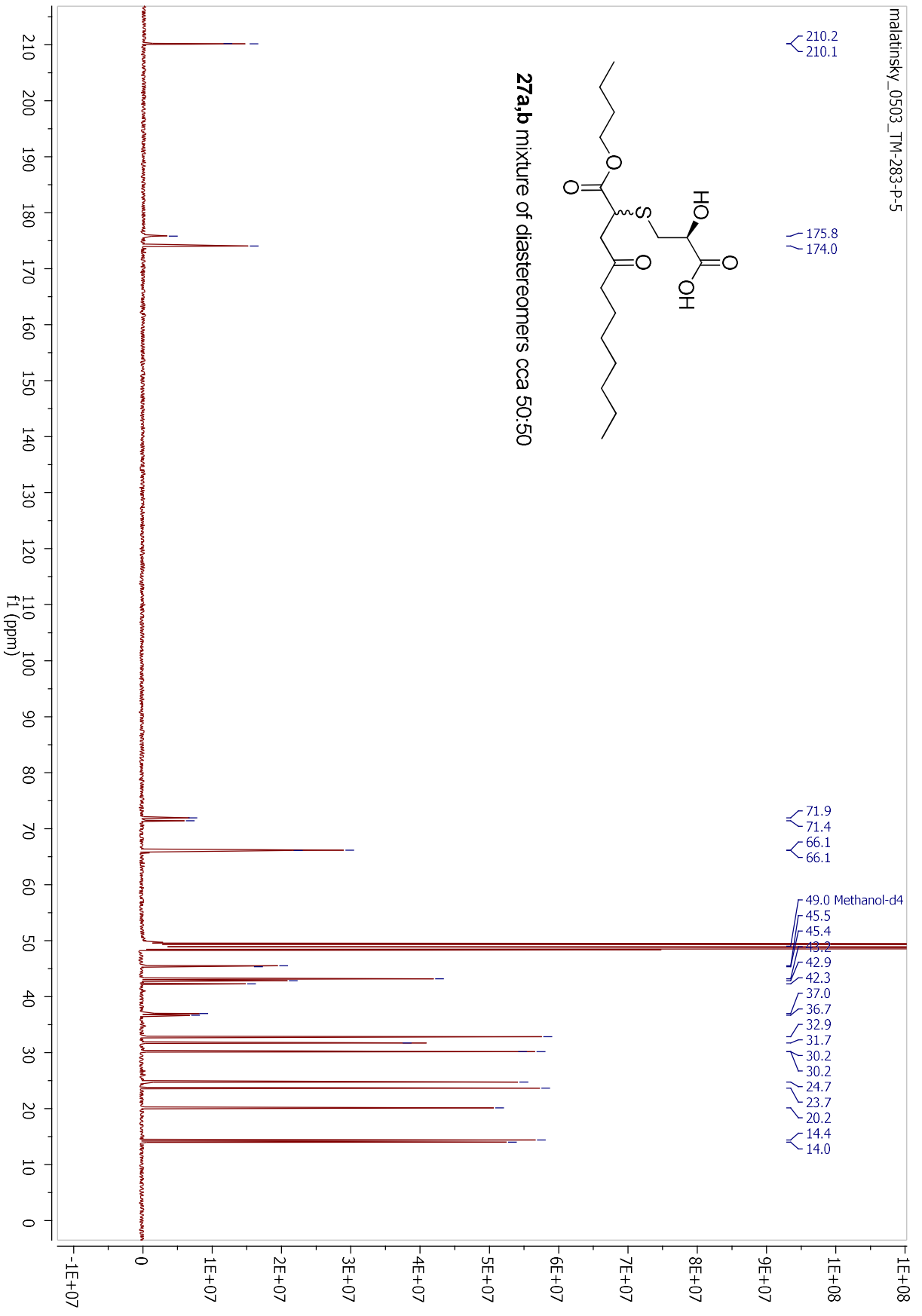


27a,b mixture of diastereomers cca 50:50

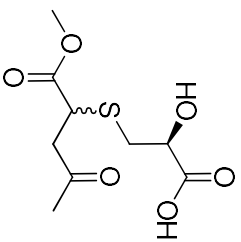




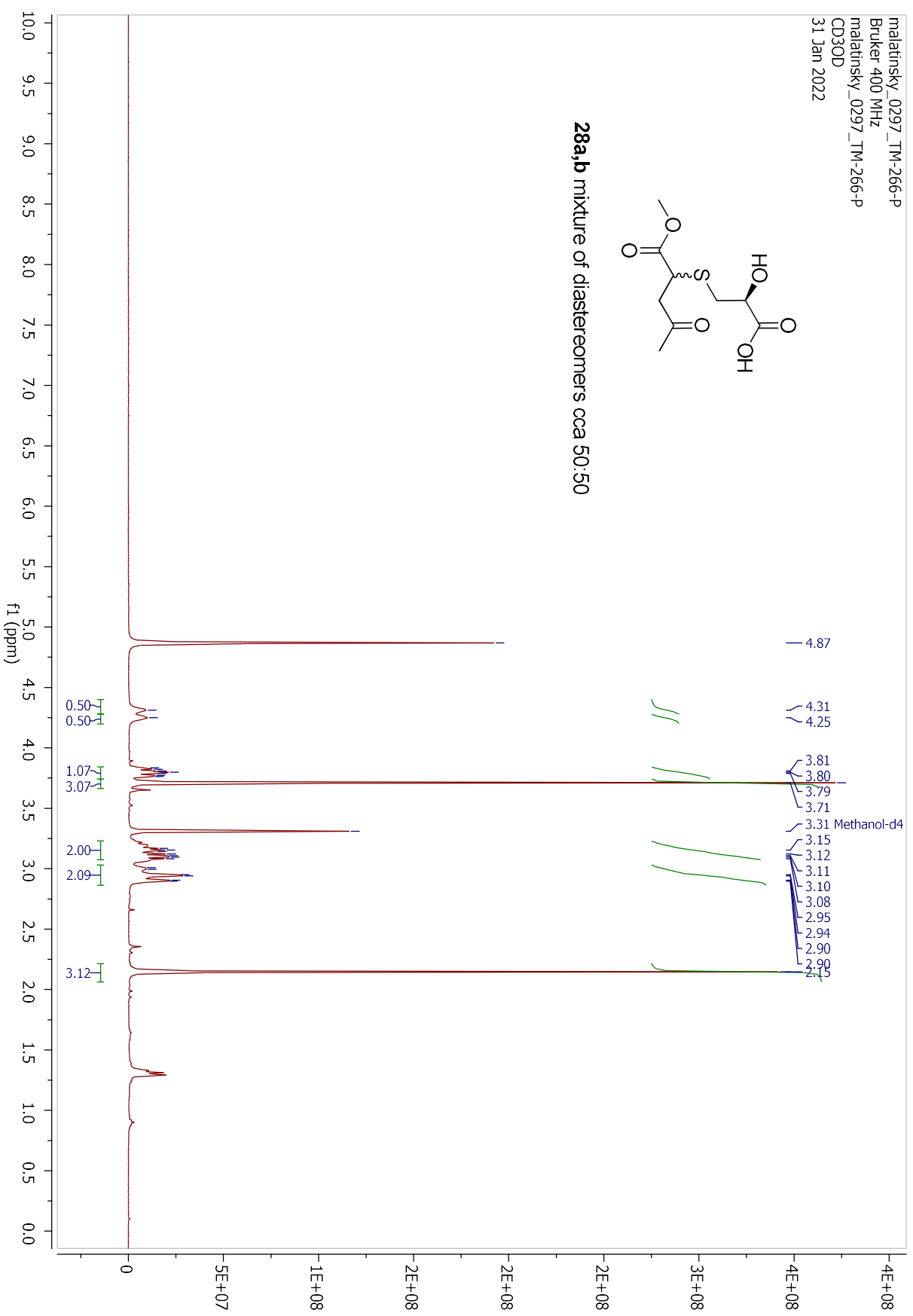
27a,b mixture of diastereomers cca 50:50



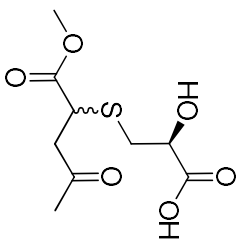
malatinsky_0297_TM-266-P
Bruker 400 MHz
malatinsky_0297_TM-266-P
CD3OD
31 Jan 2022



28a,b mixture of diastereomers cca 50:50



malatinsky_0332_TM-266-P_carbon
Bruker 400 MHz
malatinsky_0332_TM-266-P
CD3OD
3 Feb 2022



28a,b mixture of diastereomers cca 50:50

