

## Supplementary Information

### Synthesis and Biological Activity of Cyclopropyl $\Delta^7$ -Dafachronic Acids as DAF-12 Receptor Ligands

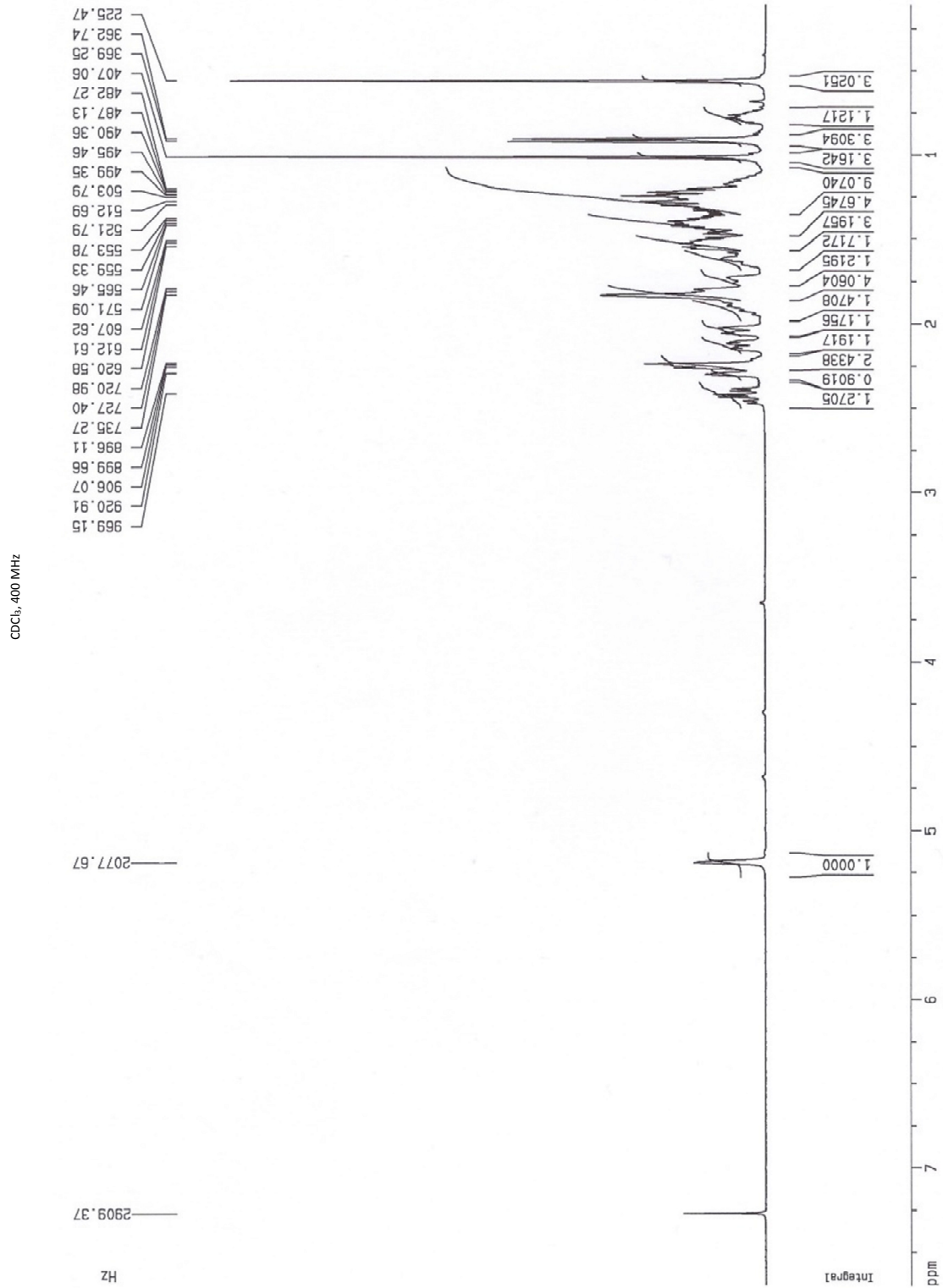
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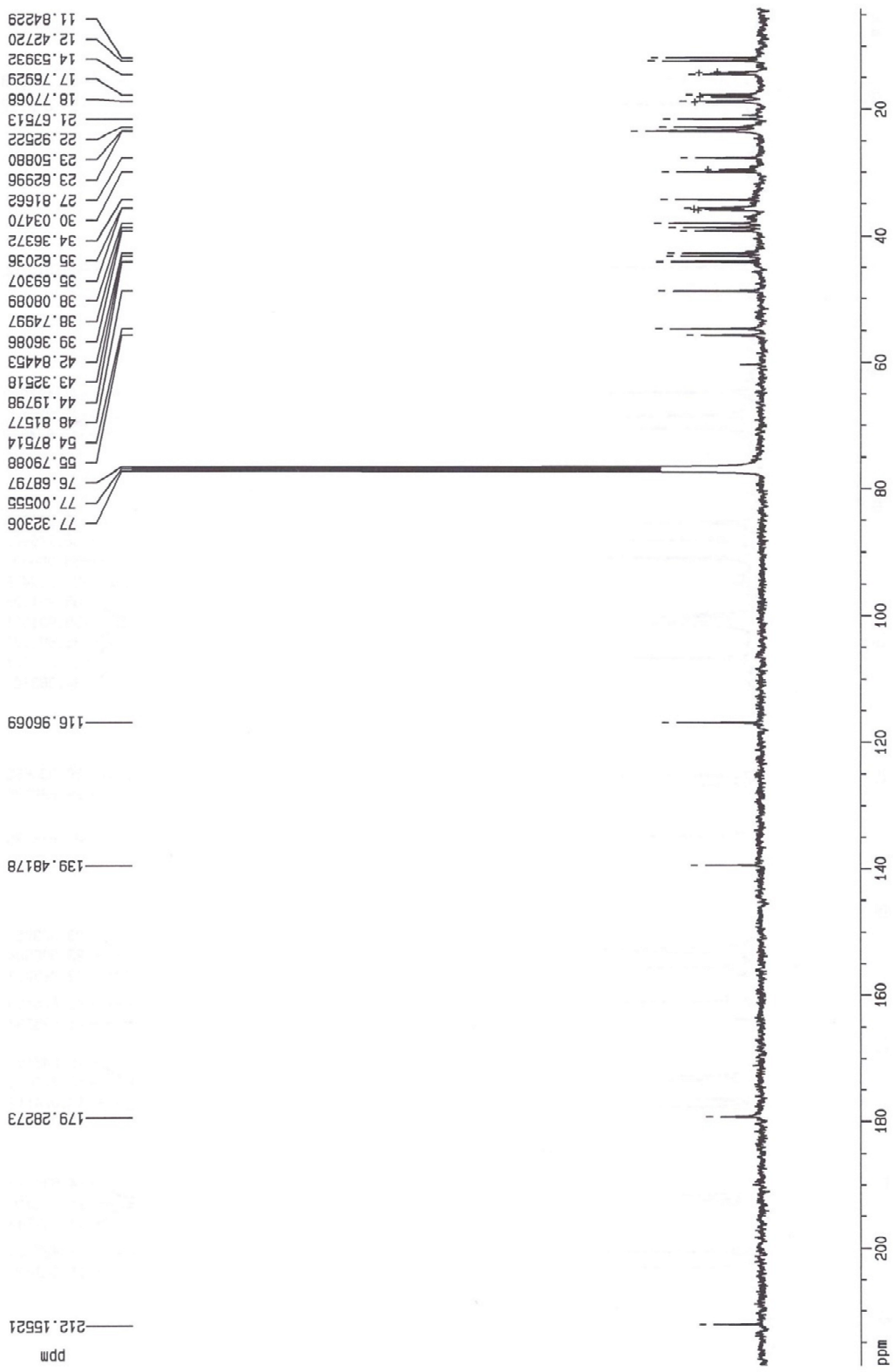
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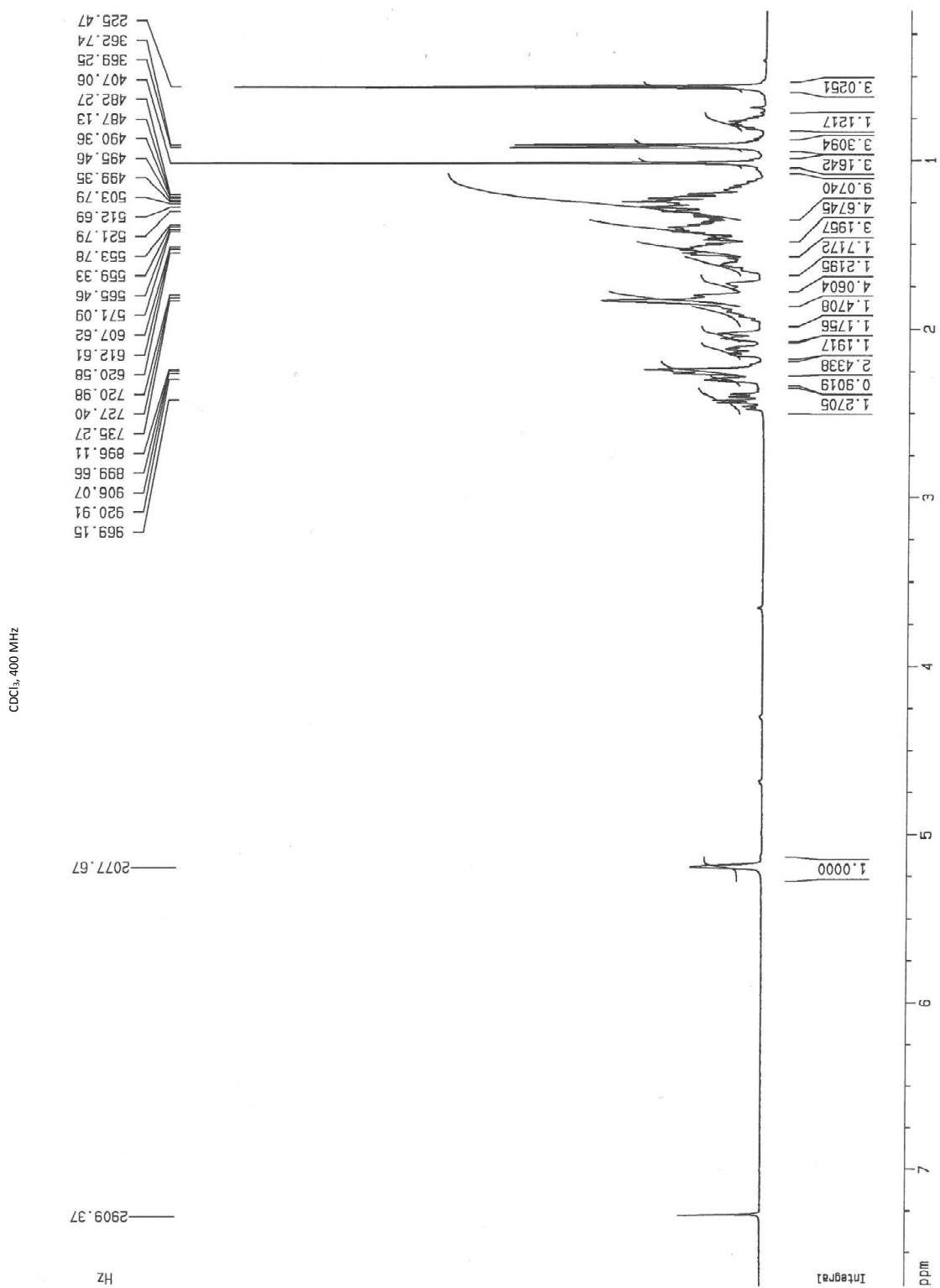
3-keto-24,25-methylen-24-bishomo-5 $\alpha$ -chol-7-en-26-oic acid (5, 6)

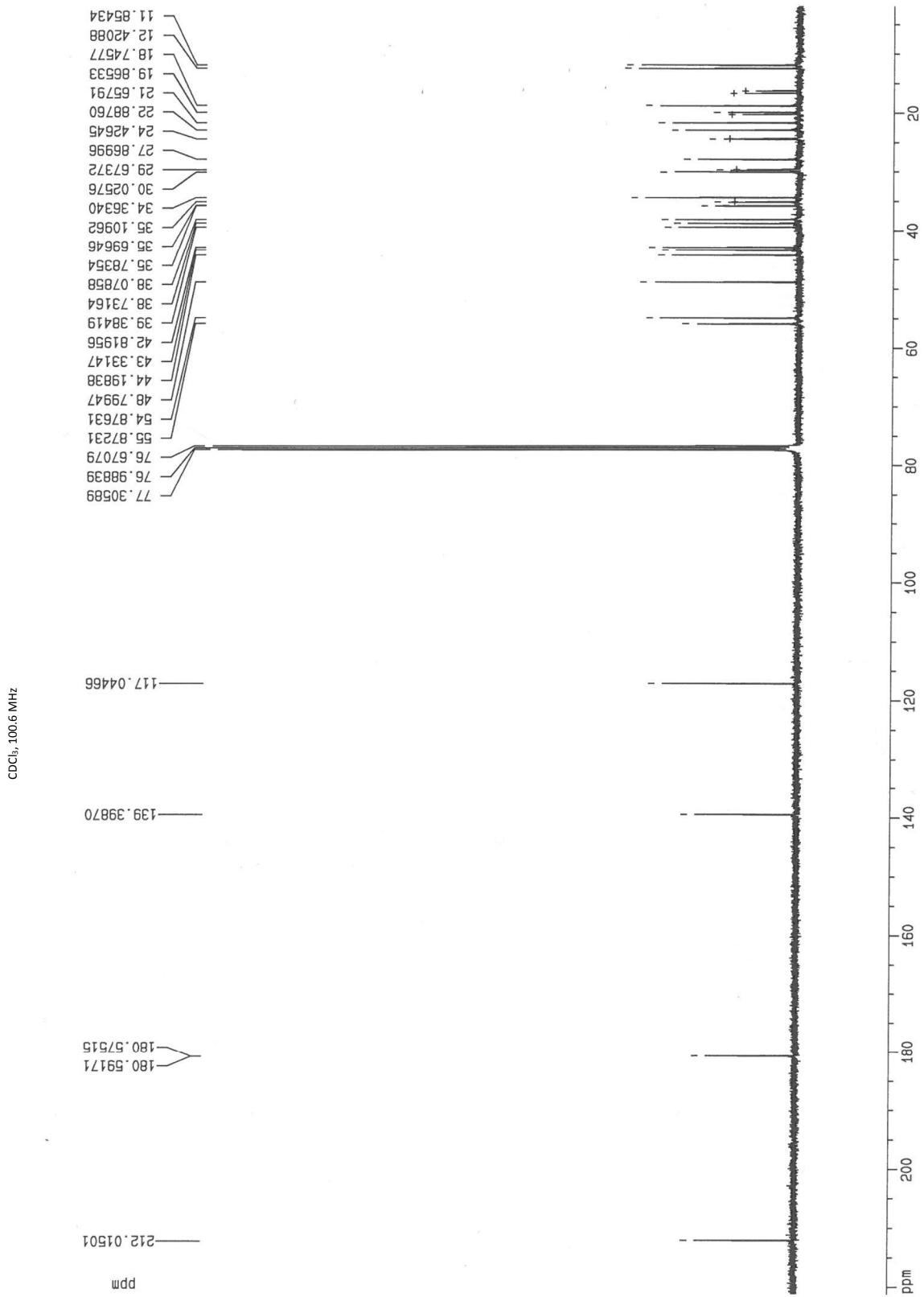


CDCl<sub>3</sub>, 100.6 MHz

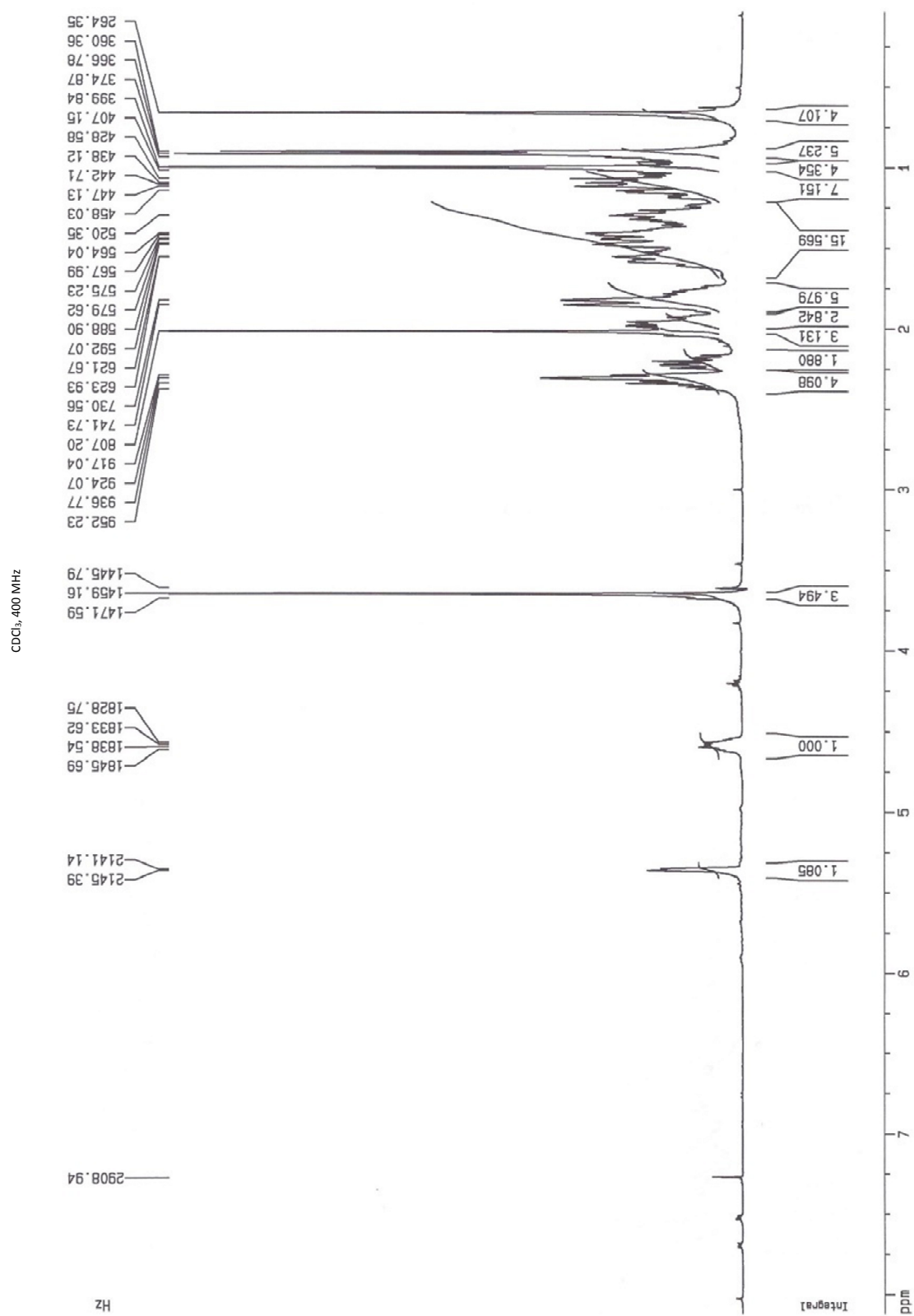


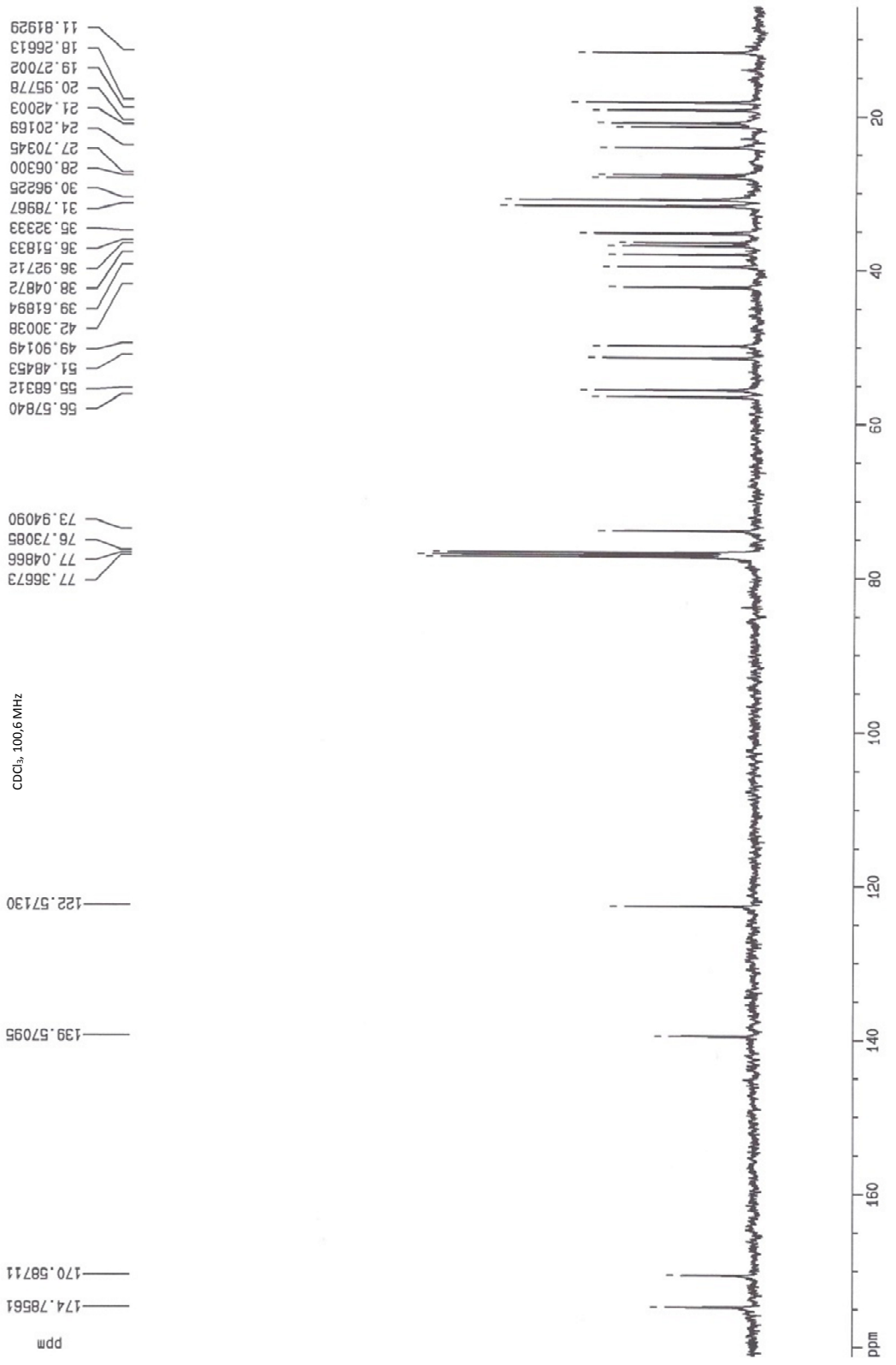
3-keto-24,25-methylen-24-bishomo-5 $\alpha$ -chol-7-en-26-oic acid (7, 8)





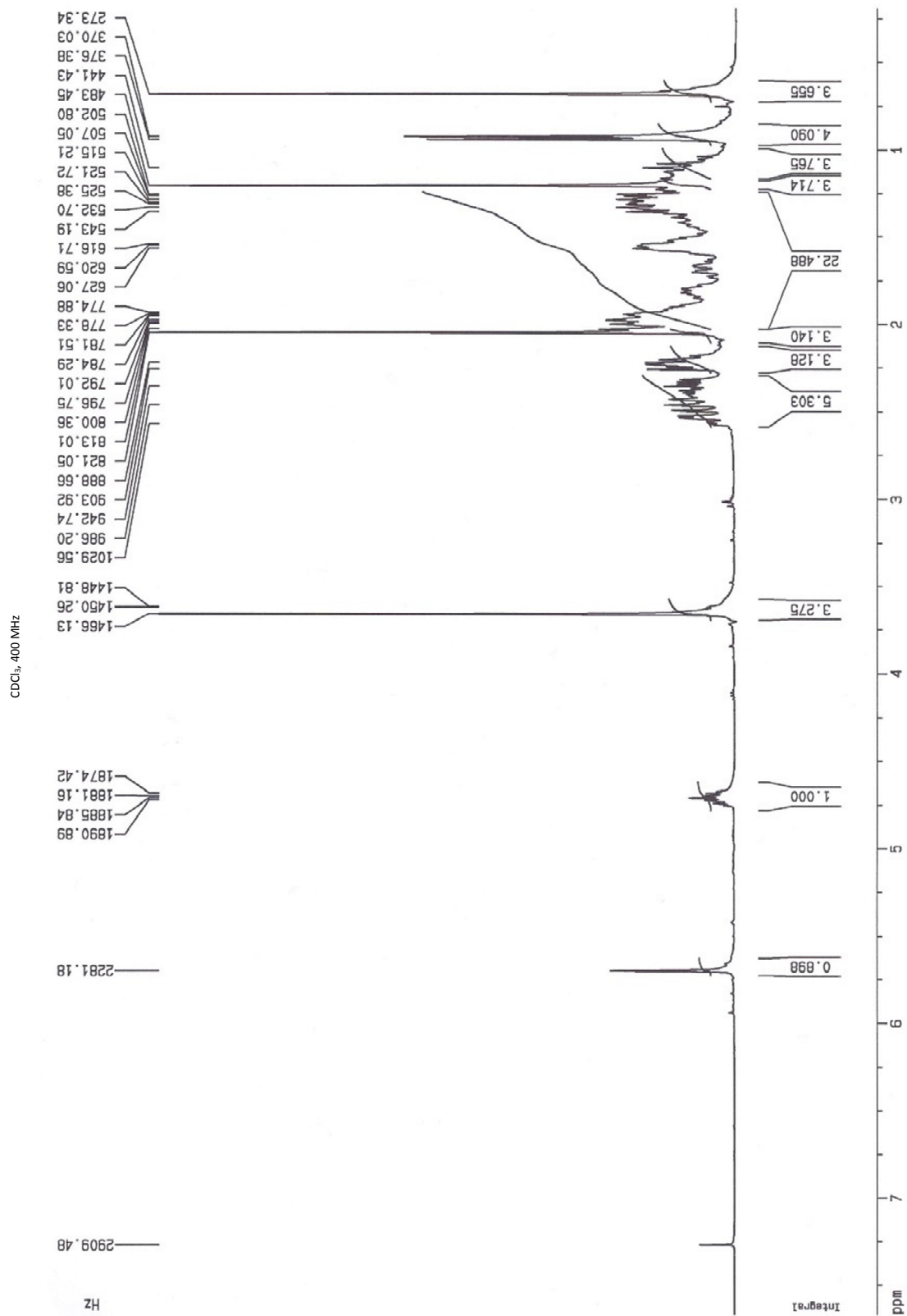
Methyl 3 $\beta$ -acetoxy-chol-5-en-24-oate (11)

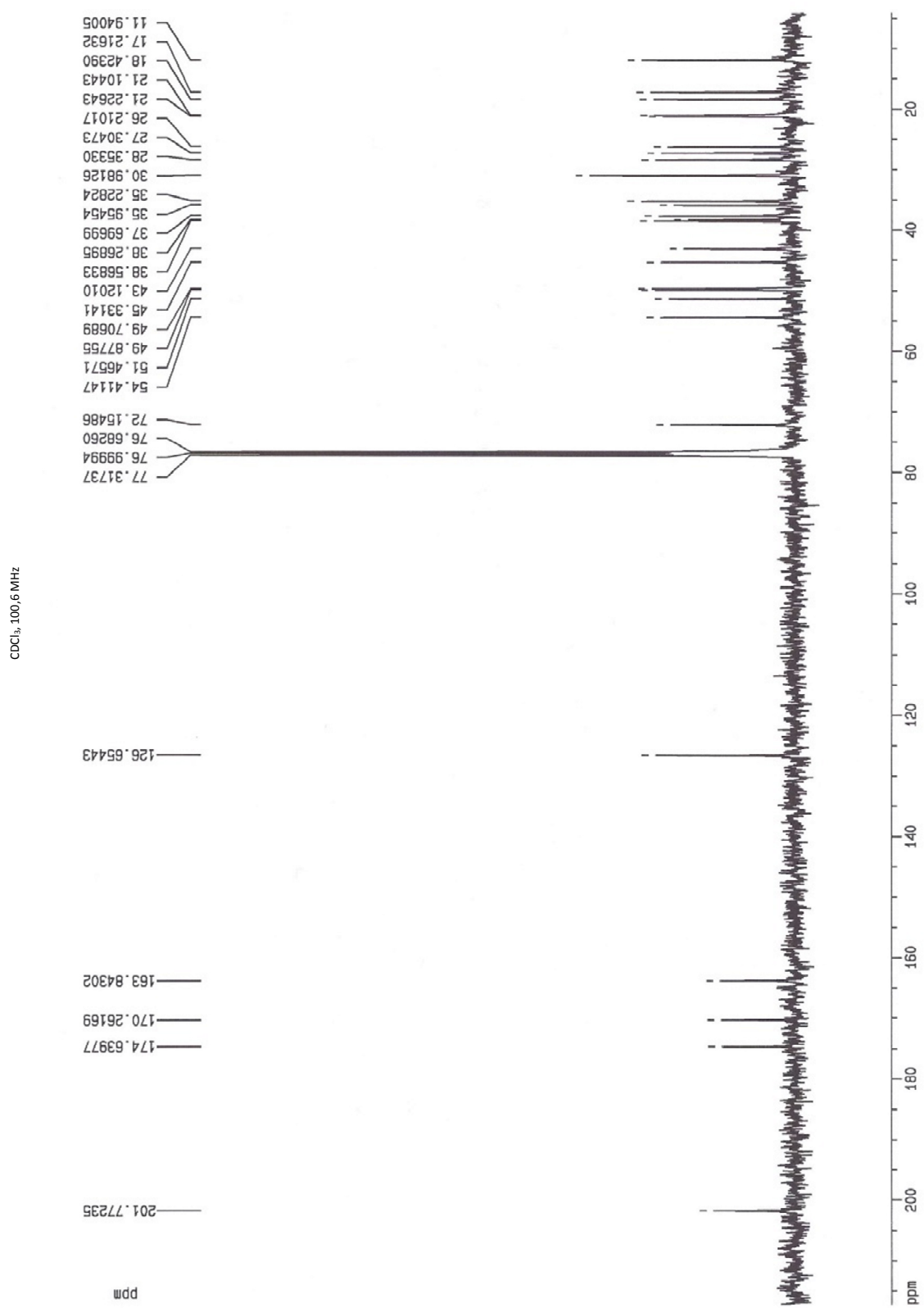




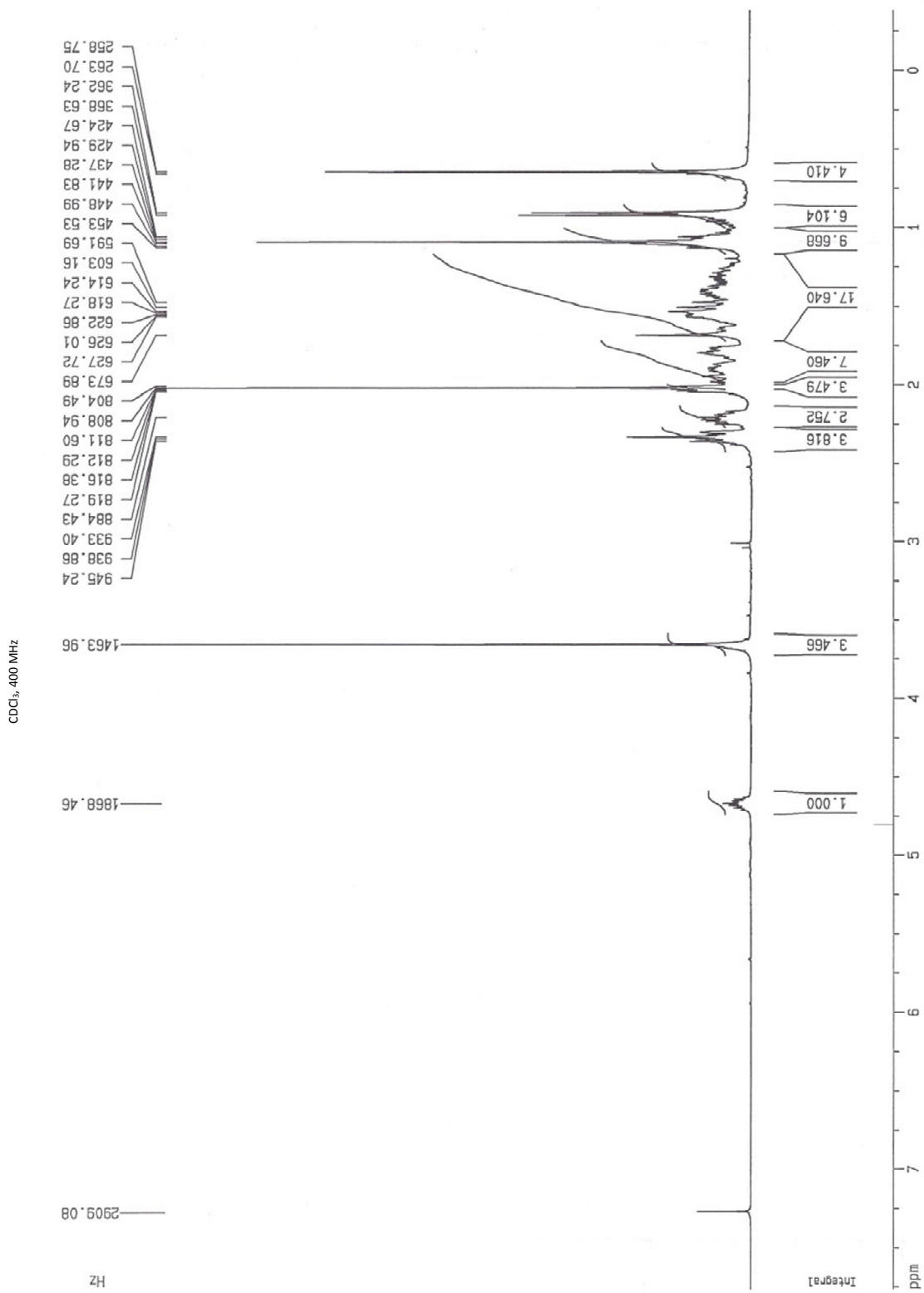


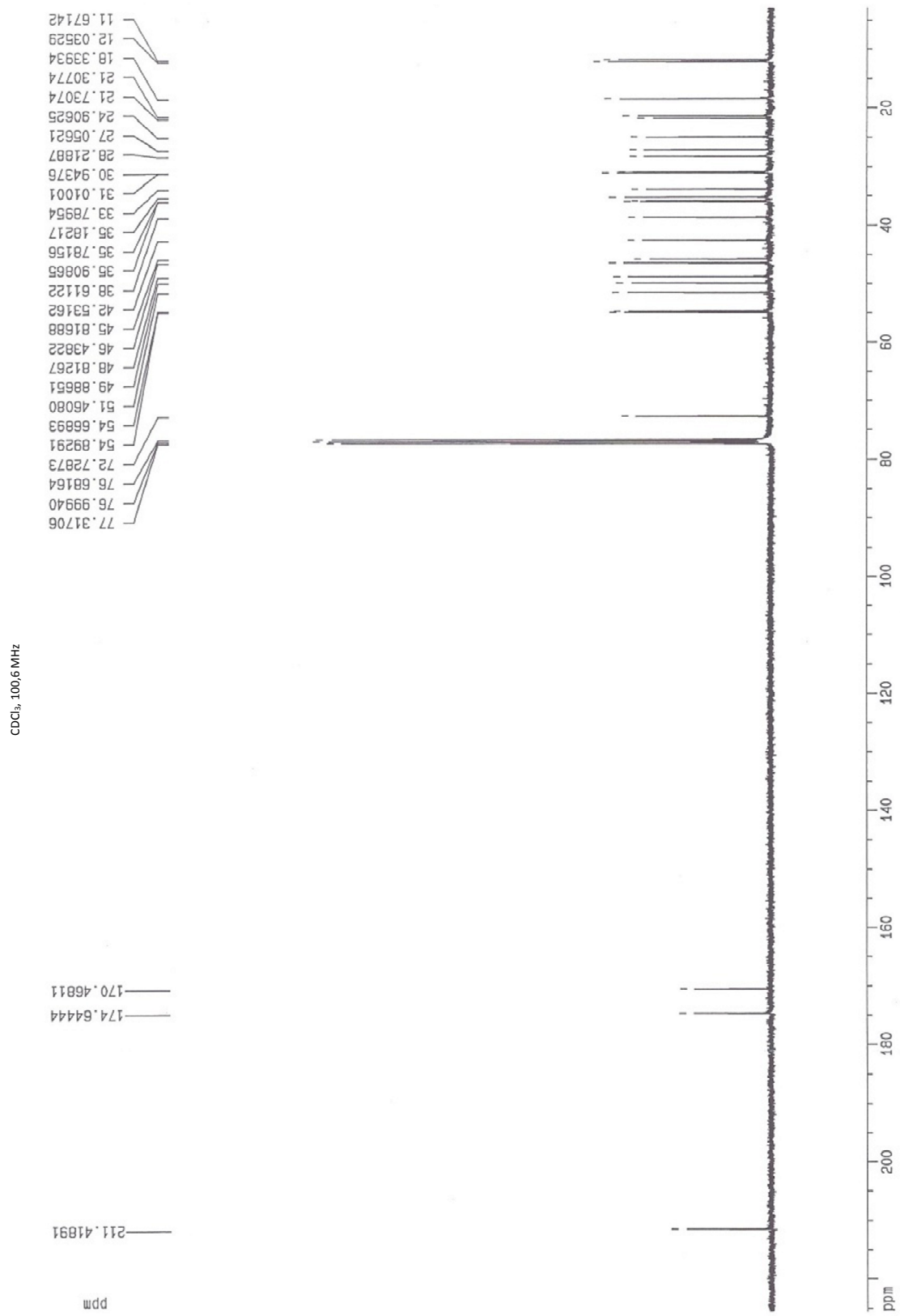
Methyl 3 $\beta$ -acetoxy-7-keto-chol-5-en-24-oate (12)



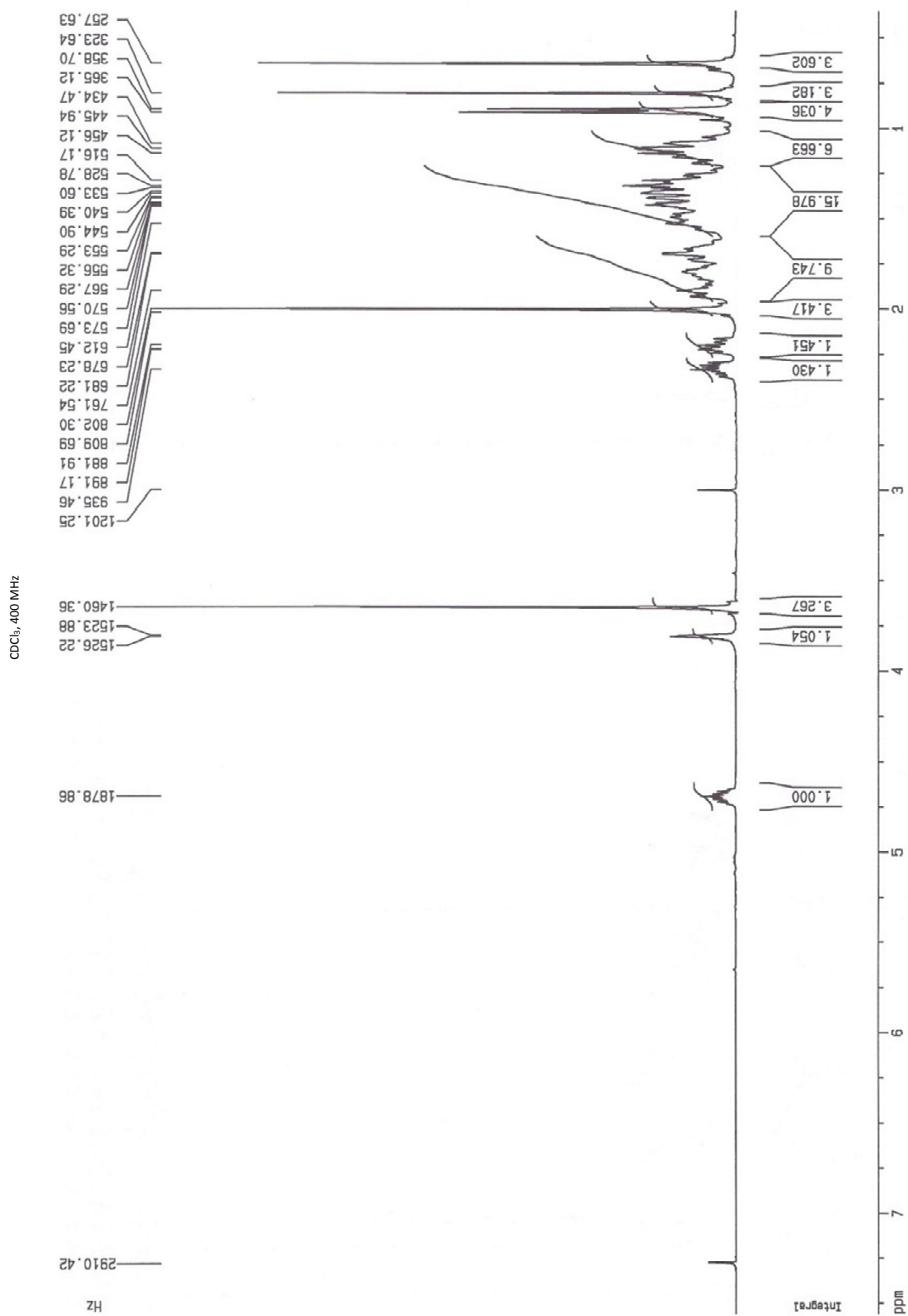


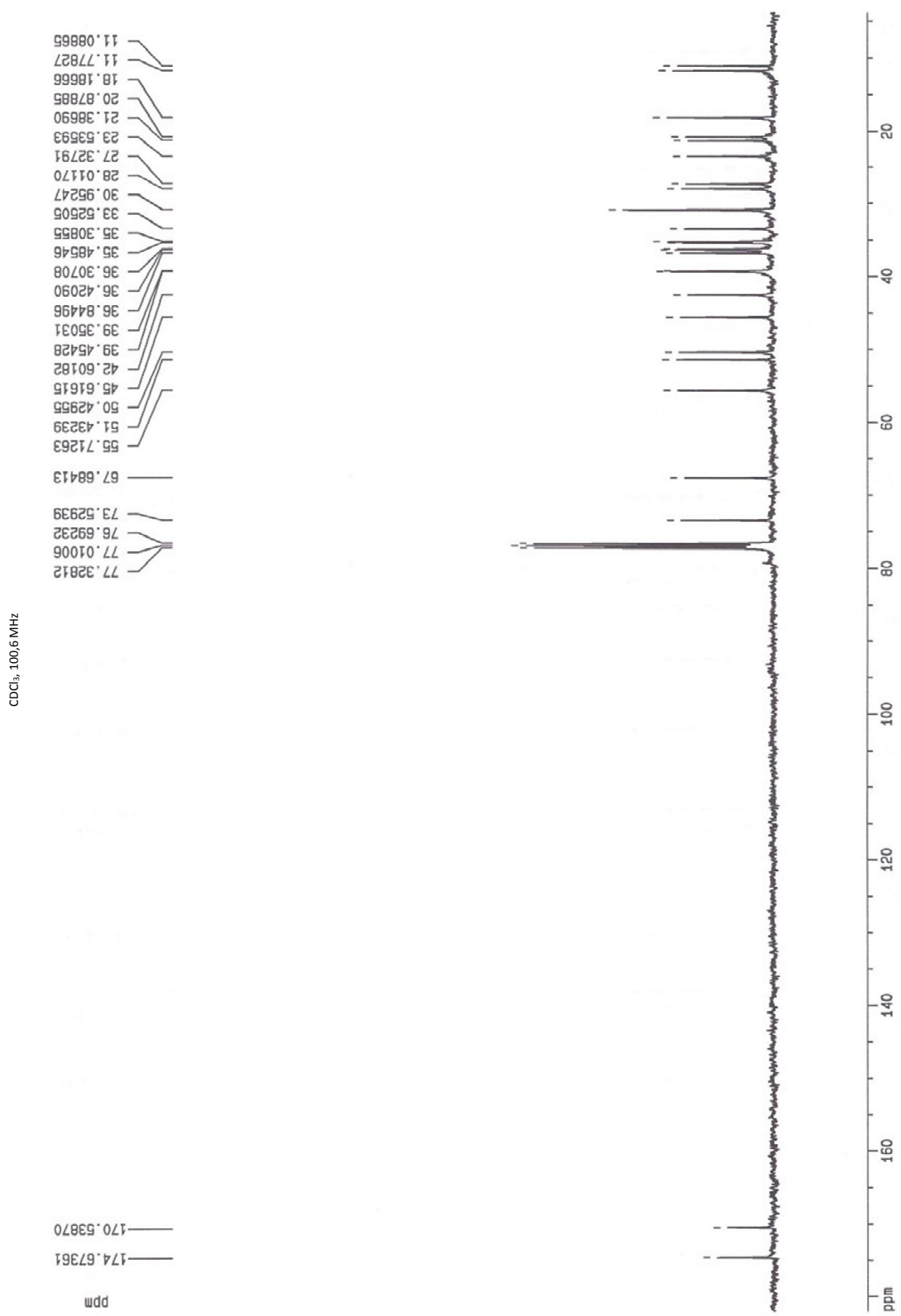
Methyl 3 $\beta$ -acetoxy-7-keto-5 $\alpha$ -cholan-24-oate (13)



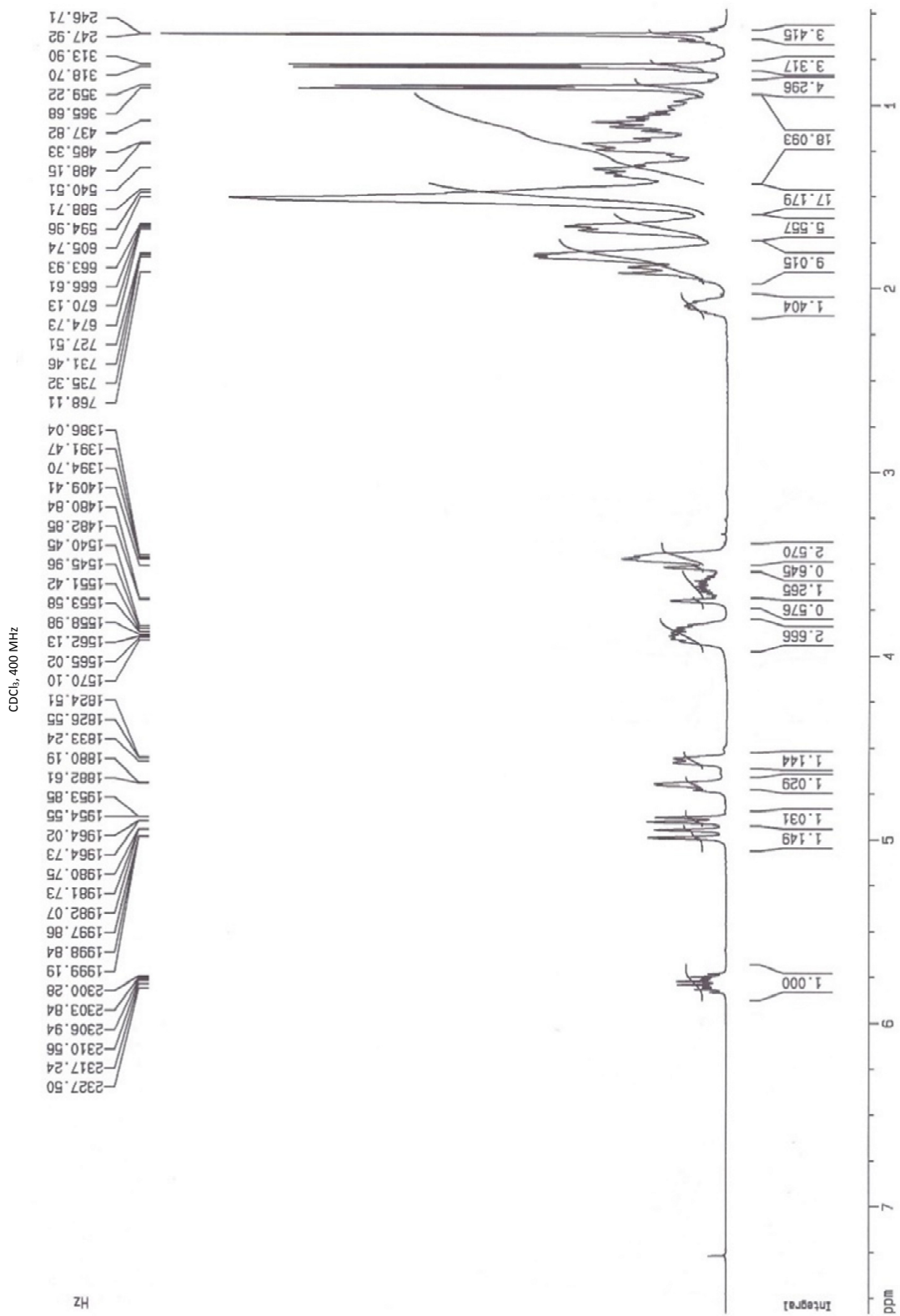


Methyl 3 $\beta$ -acetoxy-7 $\alpha$ -hydroxy-5 $\alpha$ -cholan-24-oate (14)

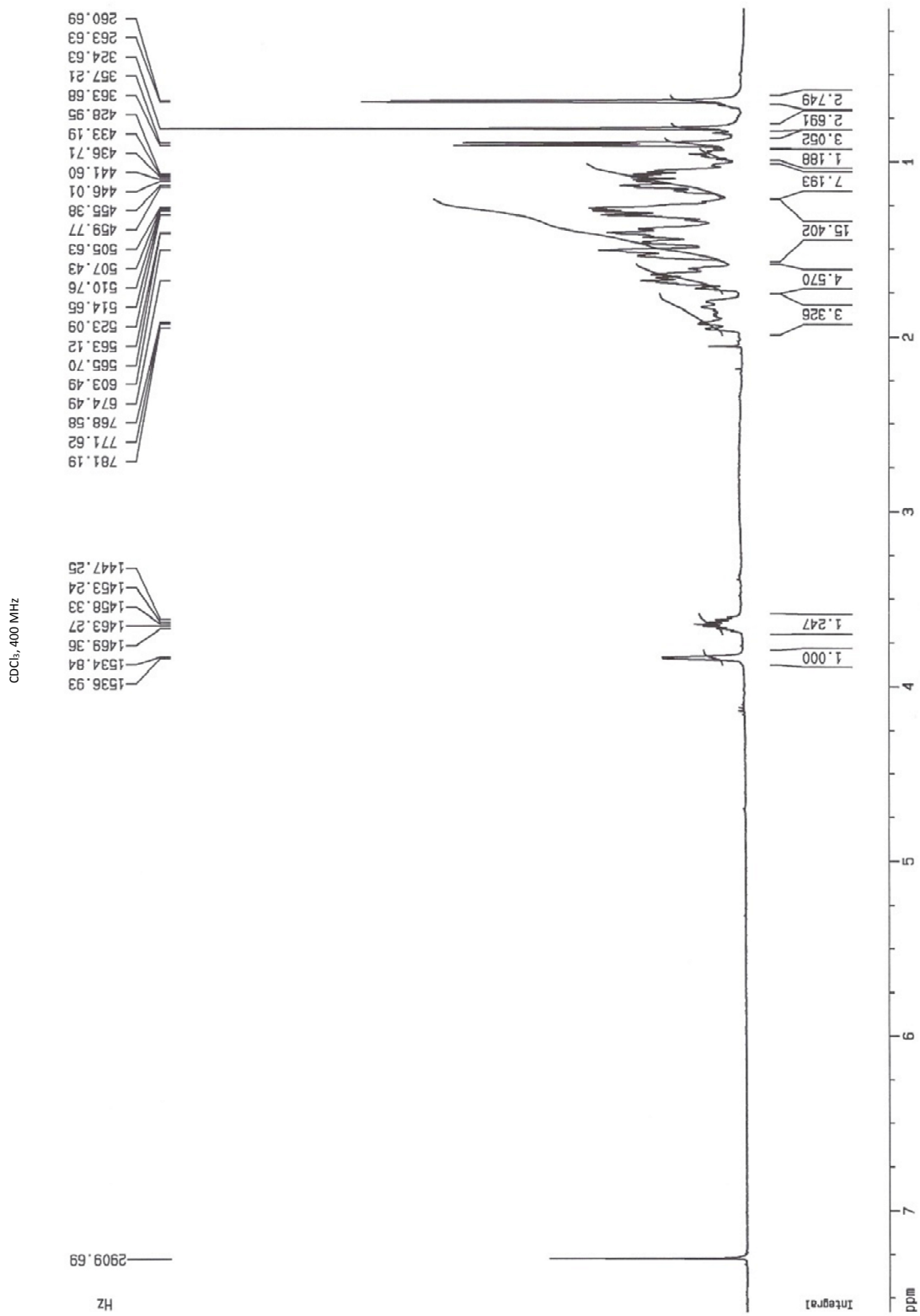




3 $\beta$ ,7 $\alpha$ -ditetrahydropyranyloxy-24-homo-5 $\alpha$ -chol-24-ene (19)

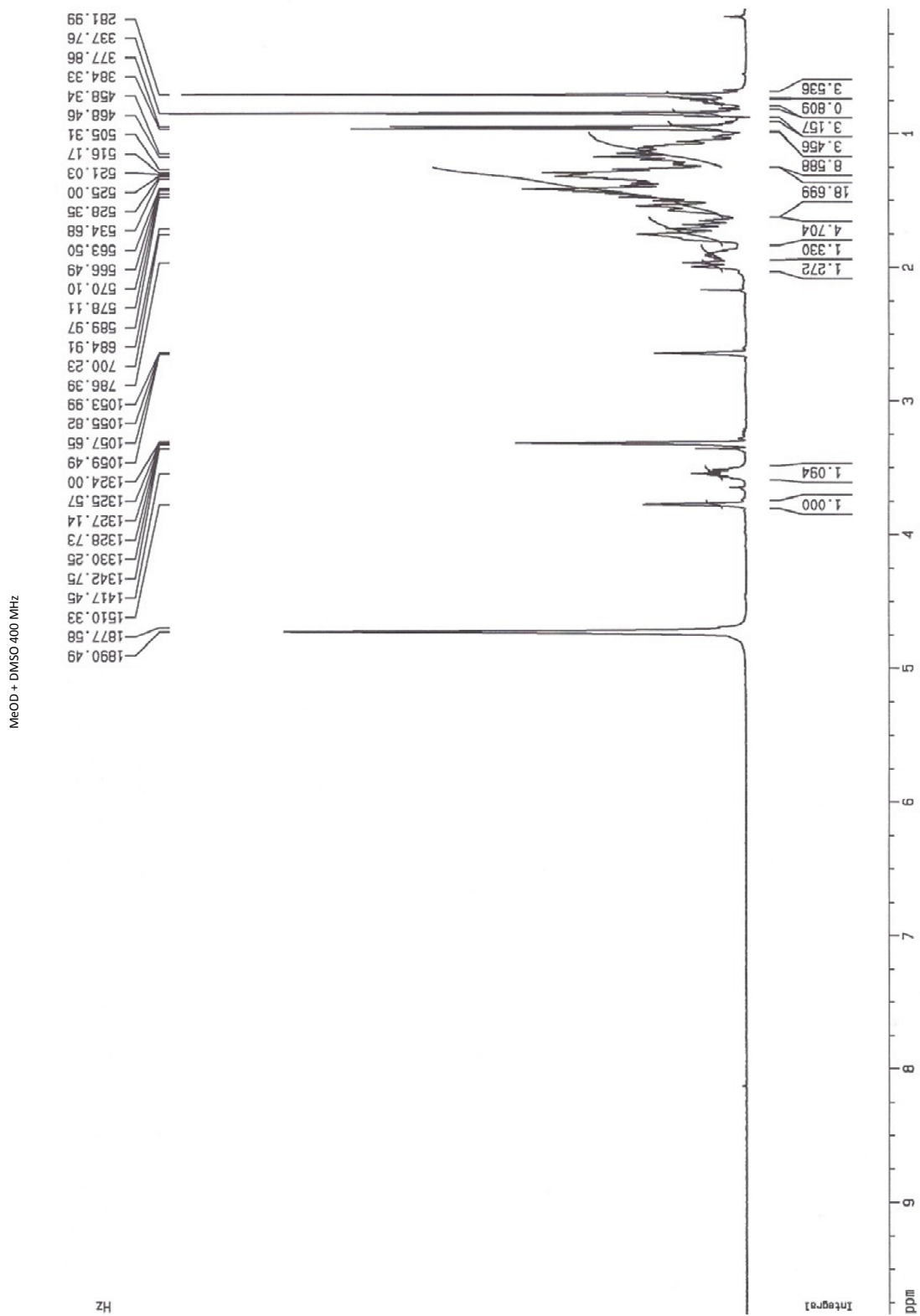


3 $\beta$ ,7 $\alpha$ -dihydroxy-24,25-methylen-24-bishomo-5 $\alpha$ -cholan-26-oic acid (20a)

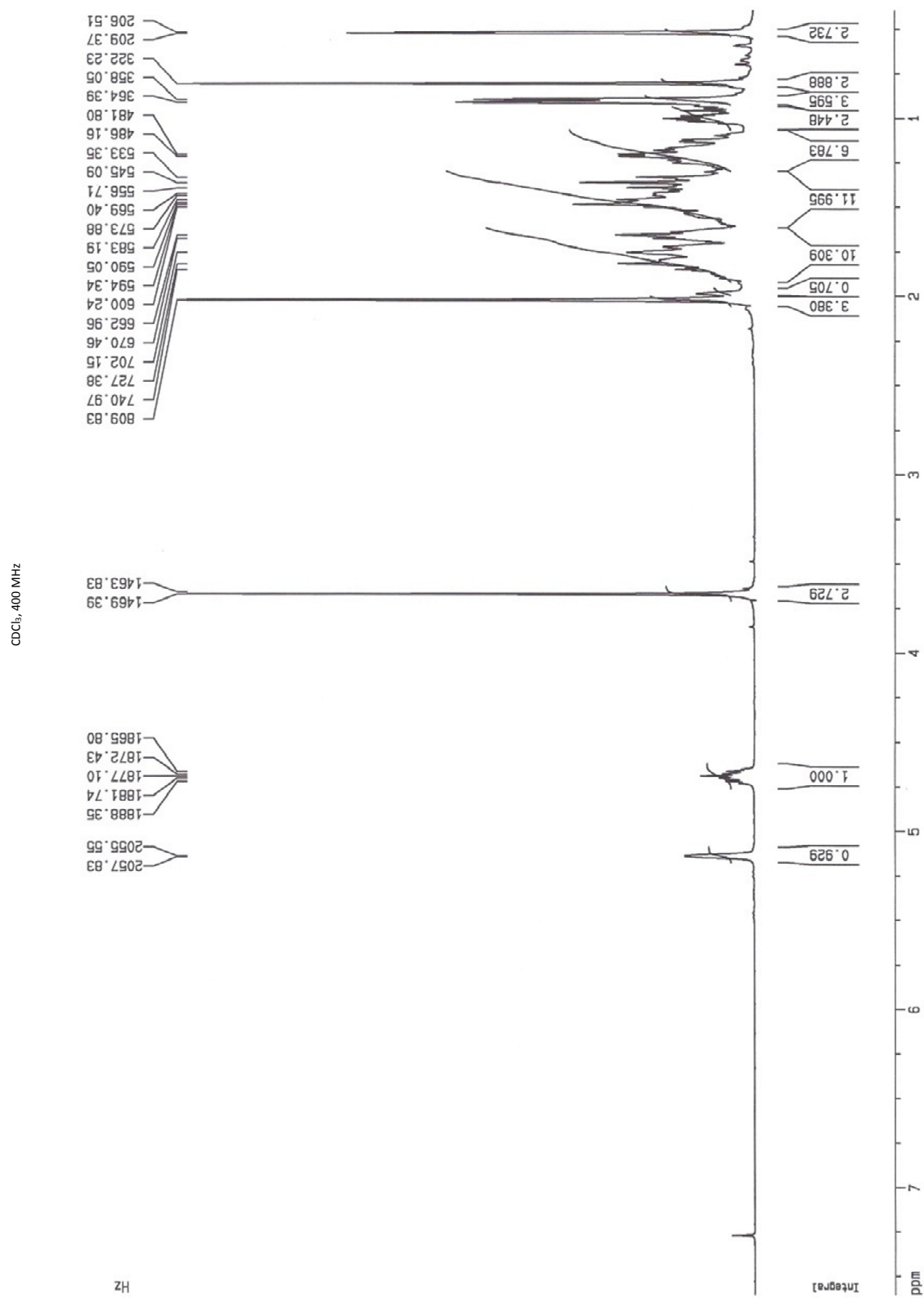


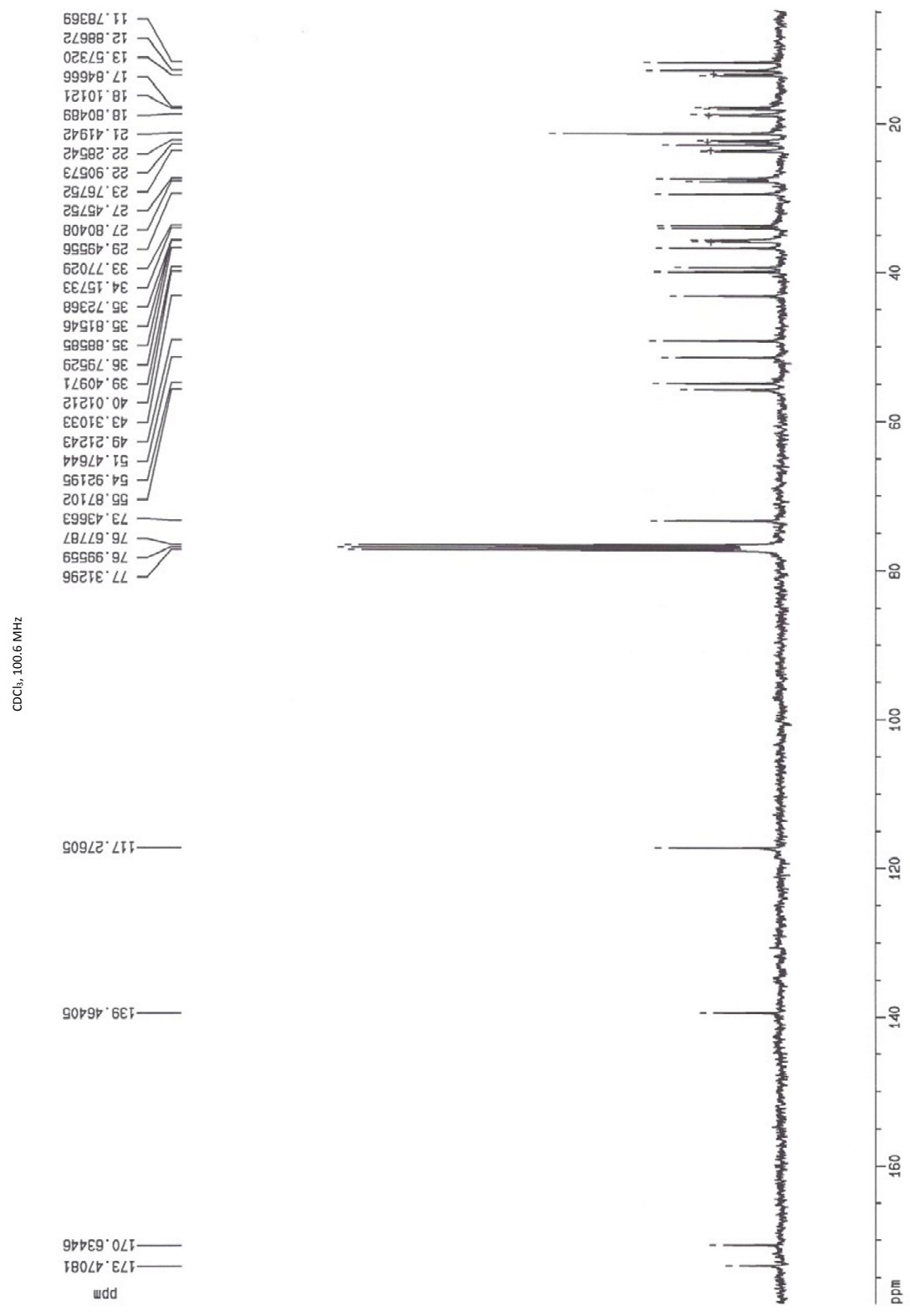


3 $\beta$ ,7 $\alpha$ -dihydroxy-24,25-methylen-24-bishomo-5 $\alpha$ -cholan-26-oic acid (20b)

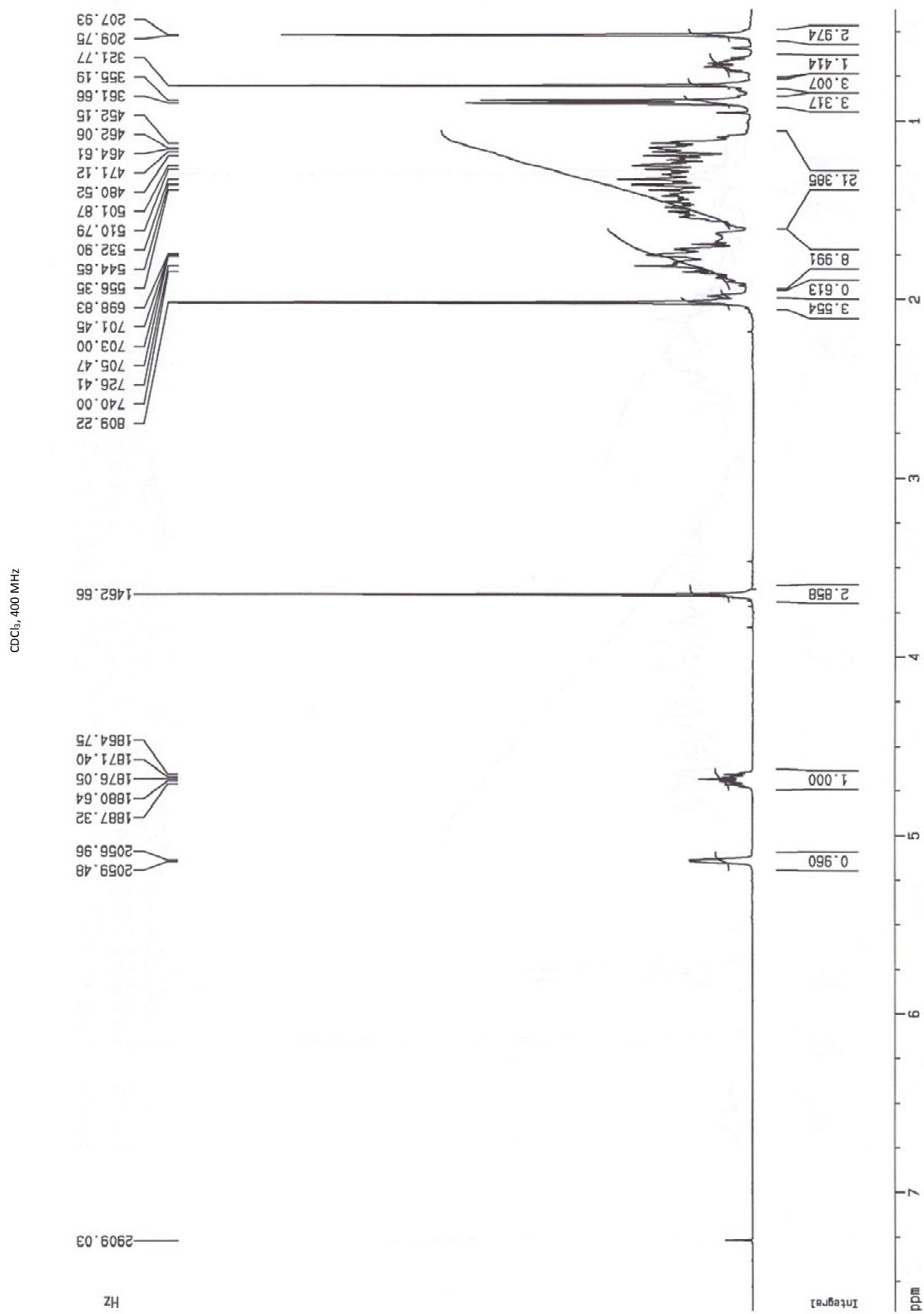


Methyl 3 $\beta$ -acetoxy-24,25-methylen-24-bishomo-5 $\alpha$ -chol-7-en-26-oate (22a)

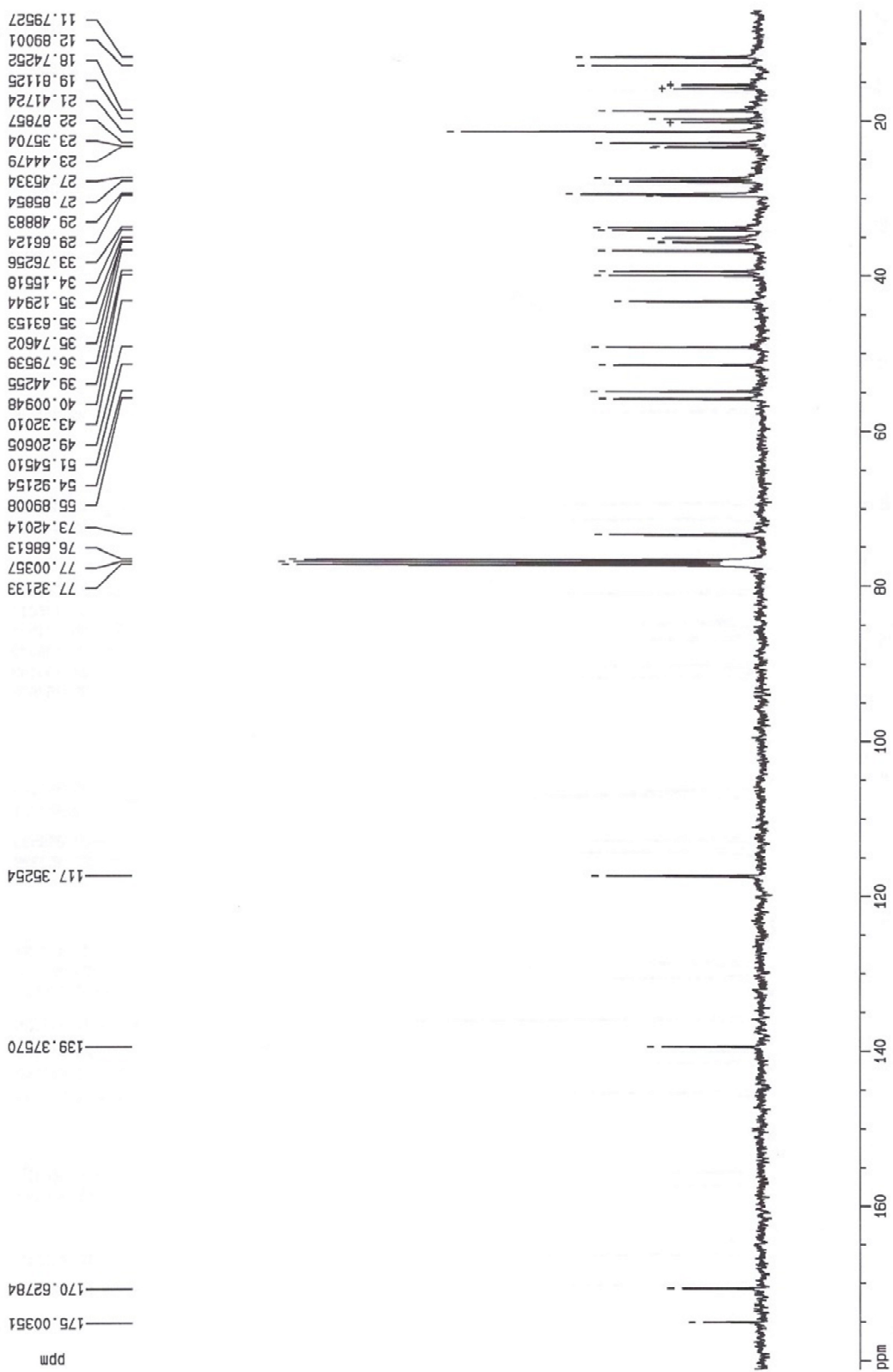




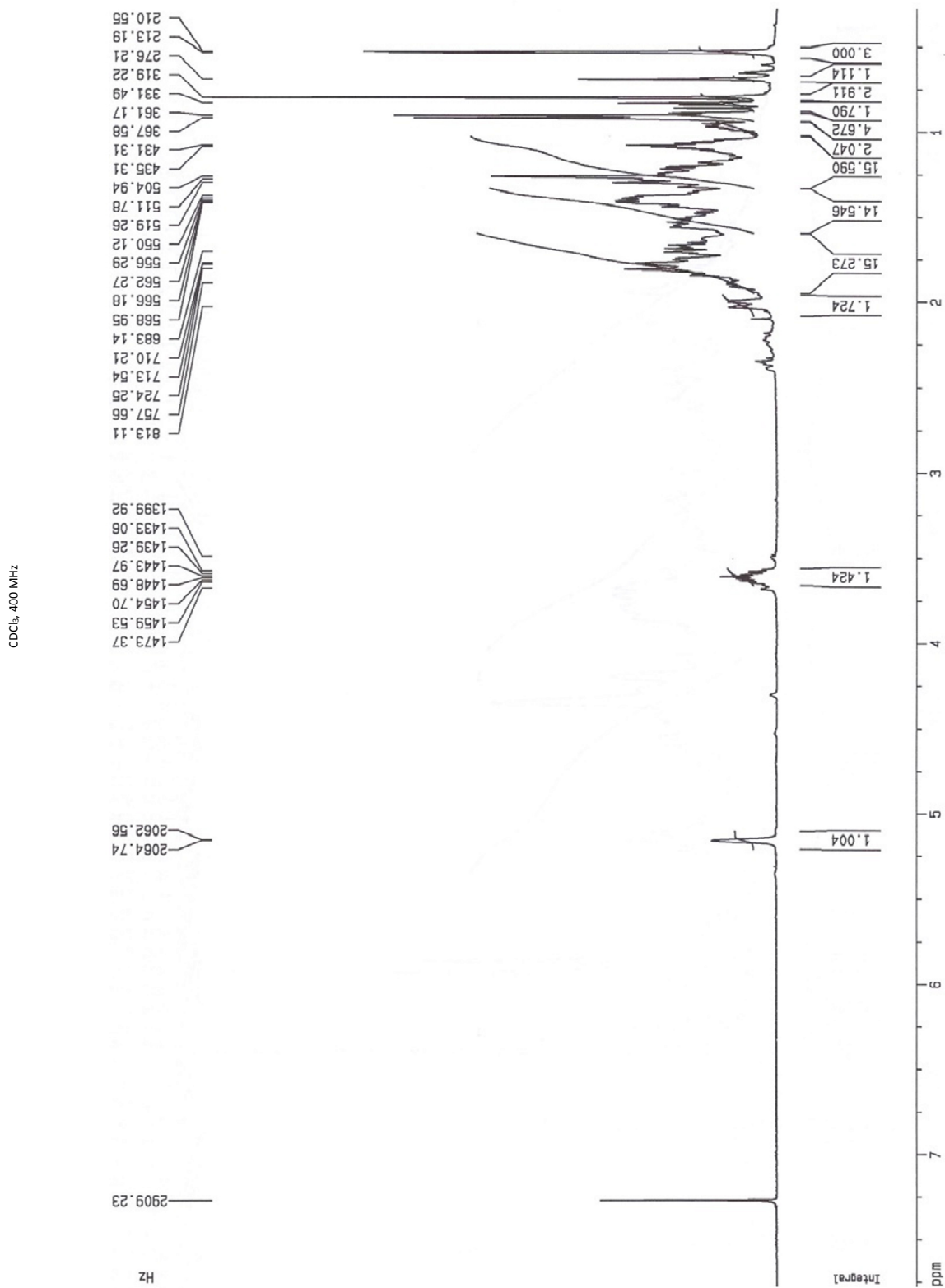
Methyl 3 $\beta$ -acetoxy-24,25-methylen-24-bishomo-5 $\alpha$ -chol-7-en-26-oate (22b)



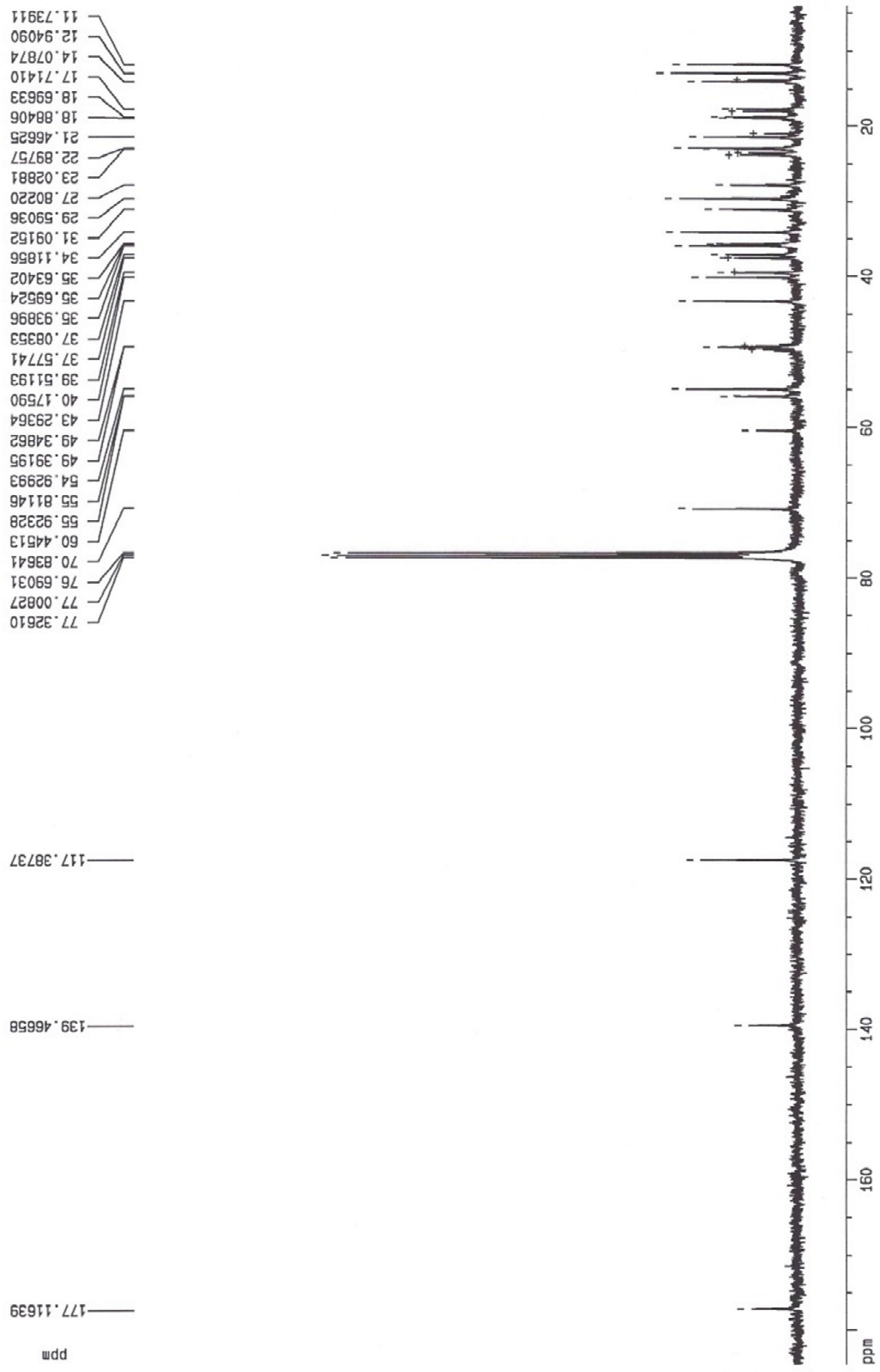
CDCl<sub>3</sub>, 100.6 MHz



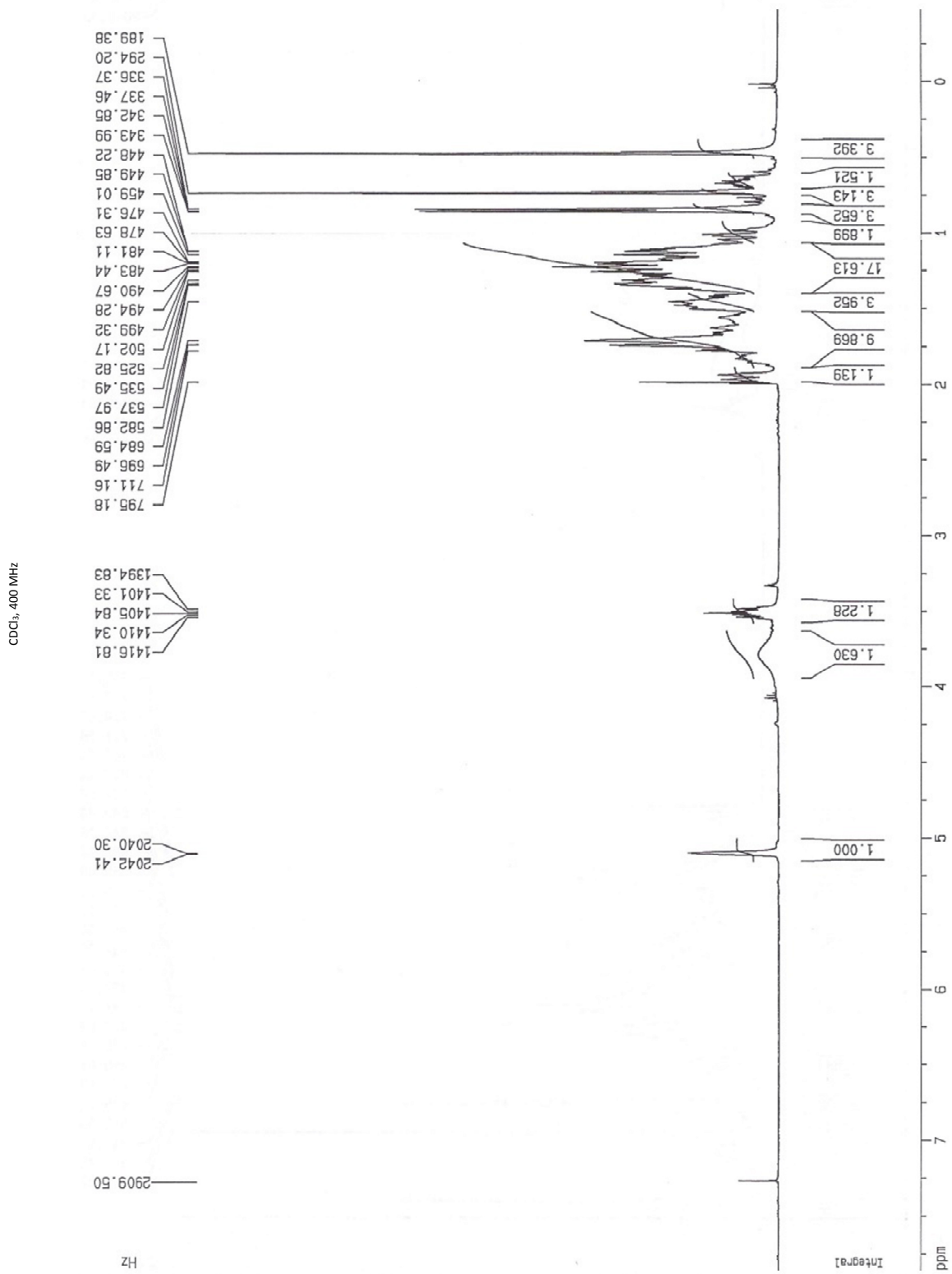
3 $\beta$ -hydroxy-24,25-methylen-24-bishomo-5 $\alpha$ -chol-7-en-26-oic acid (23a)



CDCl<sub>3</sub>, 100.6 MHz

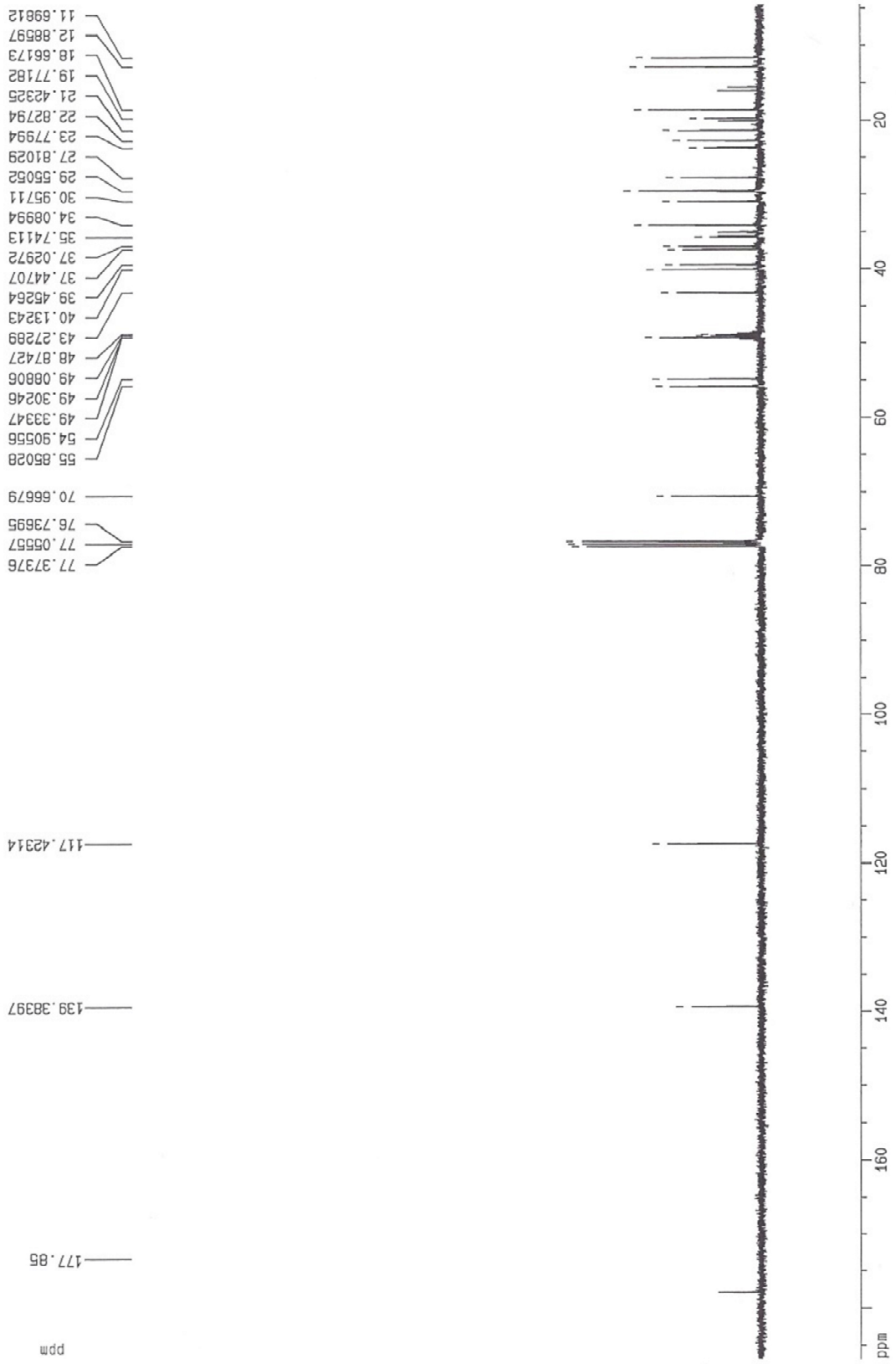


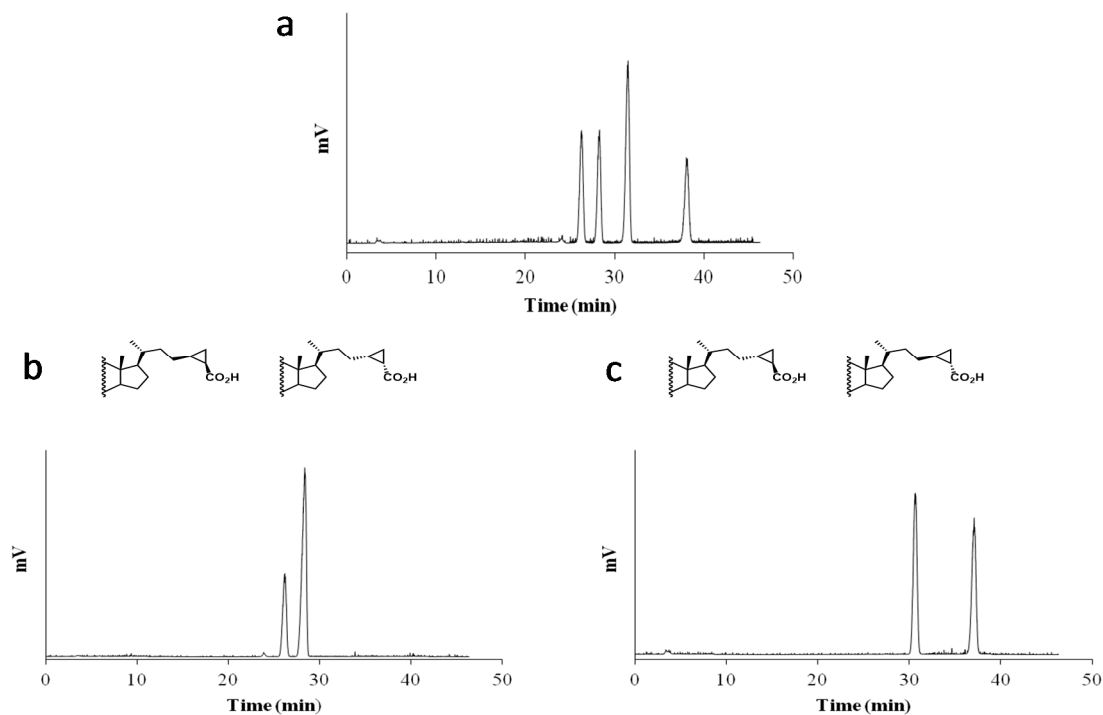
3 $\beta$ -hydroxy-24,25-methylen-24-bishomo-5 $\alpha$ -chol-7-en-26-oic acid (23b)





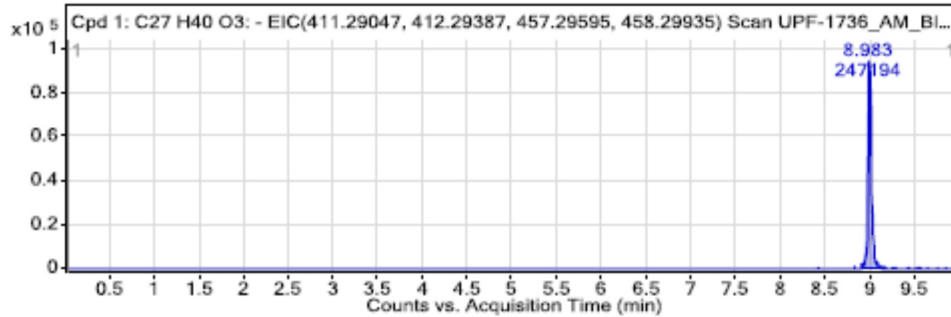
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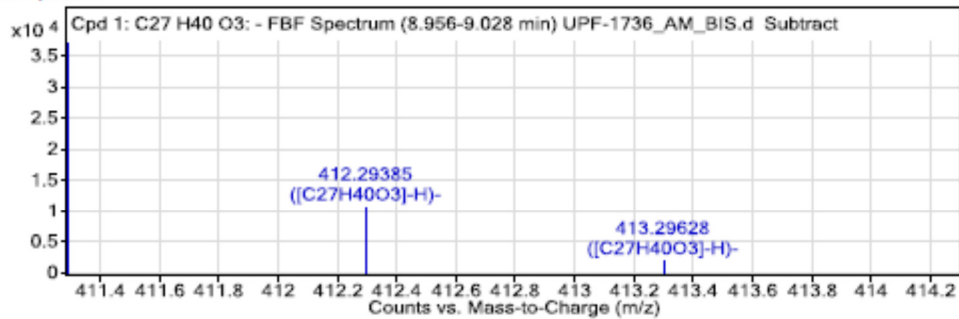


**Fig. 1S** a) HPLC analysis of isomeric mixture of 3 $\beta$ ,7 $\alpha$ -dihydroxy-24,25-methylen-24-bishomo-5 $\alpha$ -cholan-26-oic acid (**20a,b**). b) HPLC analysis of *cisoids* **20a** c) HPLC analysis of *transoids* **20b**. *Analysis conditions*: column Grace Smart RP18 (Grace, Lokeren, Belgium) (250 mm x 4.6 mm I.D., 5 $\mu$ m), column temperature 25  $^{\circ}$ C, eluent H<sub>2</sub>O/CH<sub>3</sub>CN/MeOH 50:40:10 (v/v/v) + NH<sub>4</sub>HCOO 40 mM, pH= 3.5 (this is actually the so-called “apparent pH” of the overall ternary mixture), flow rate= 0.7 mL/min, detector ELSD (T<sub>vap</sub> = 50  $^{\circ}$ C, T<sub>neb</sub> = 30  $^{\circ}$ C, gas flow rate = 1.5 L/min).

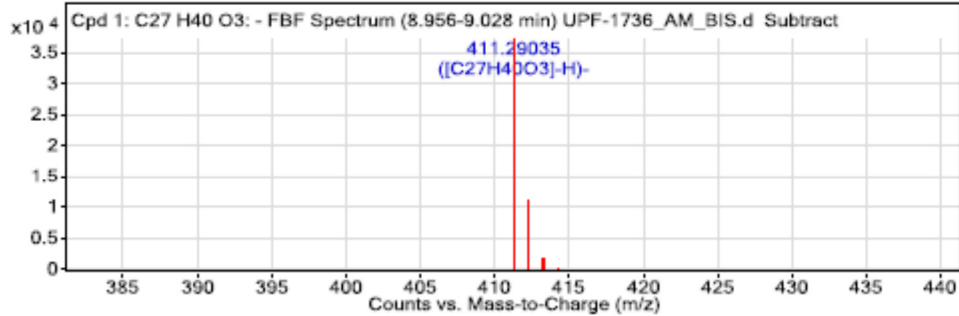
Compound Label	<i>m/z</i>	RT	Algorithm	Mass
Cpd 1: C27 H40 O3	411.29035	8.983	Find By Formula	412.29762



#### MS Spectrum



#### MS Zoomed Spectrum



#### MS Spectrum Peak List

<i>m/z</i>	<i>z</i>	Abund	Formula	Ion
411.29035	1	37222.9	C27H40O3	(M-H)-
412.29385	1	10883.66	C27H40O3	(M-H)-
413.29628	1	2084.2	C27H40O3	(M-H)-
414.29694	1	99.14	C27H40O3	(M-H)-