

Electronic Supplementary Information

for

Microwave Assisted Cobinamide Synthesis

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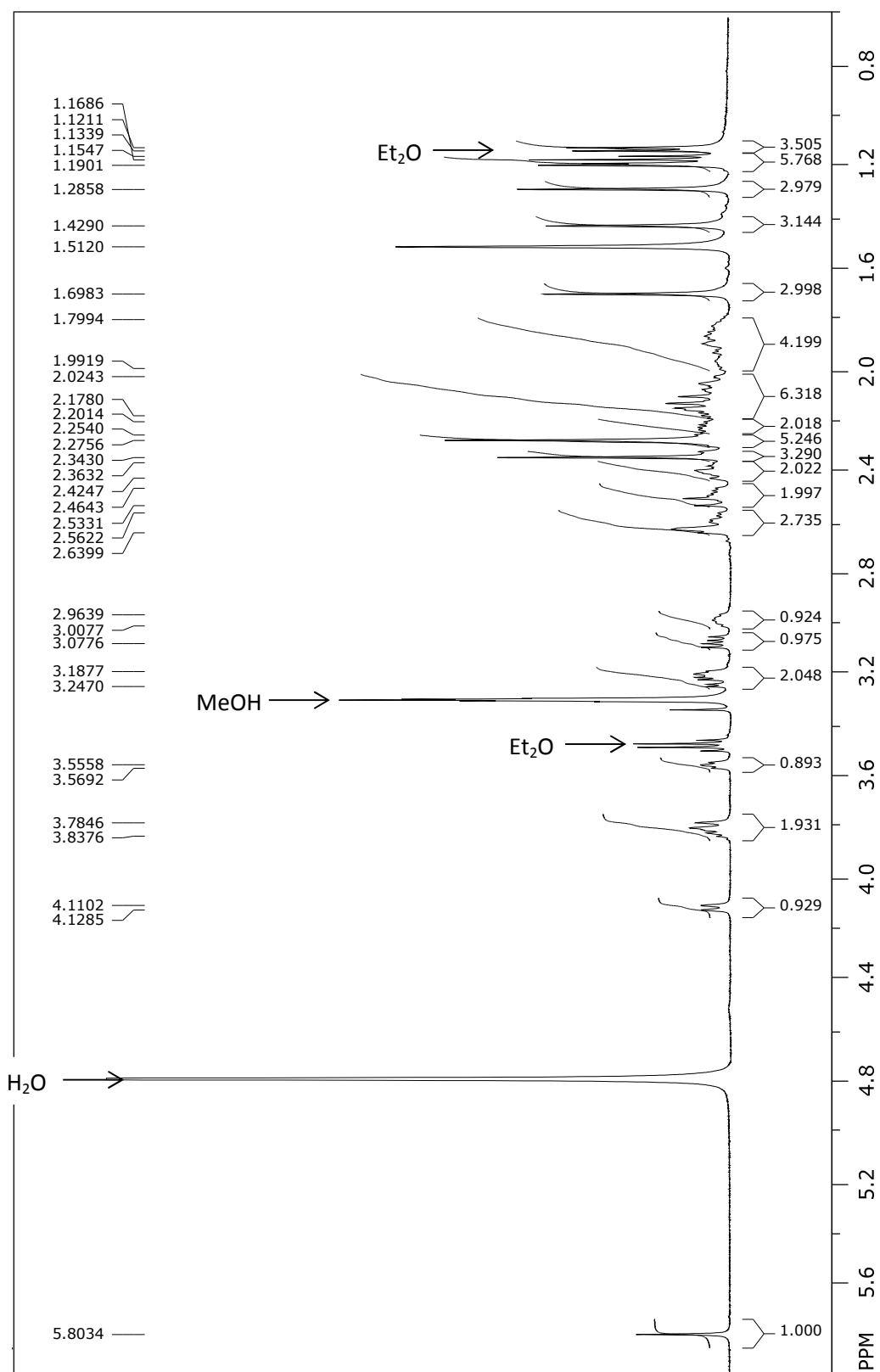
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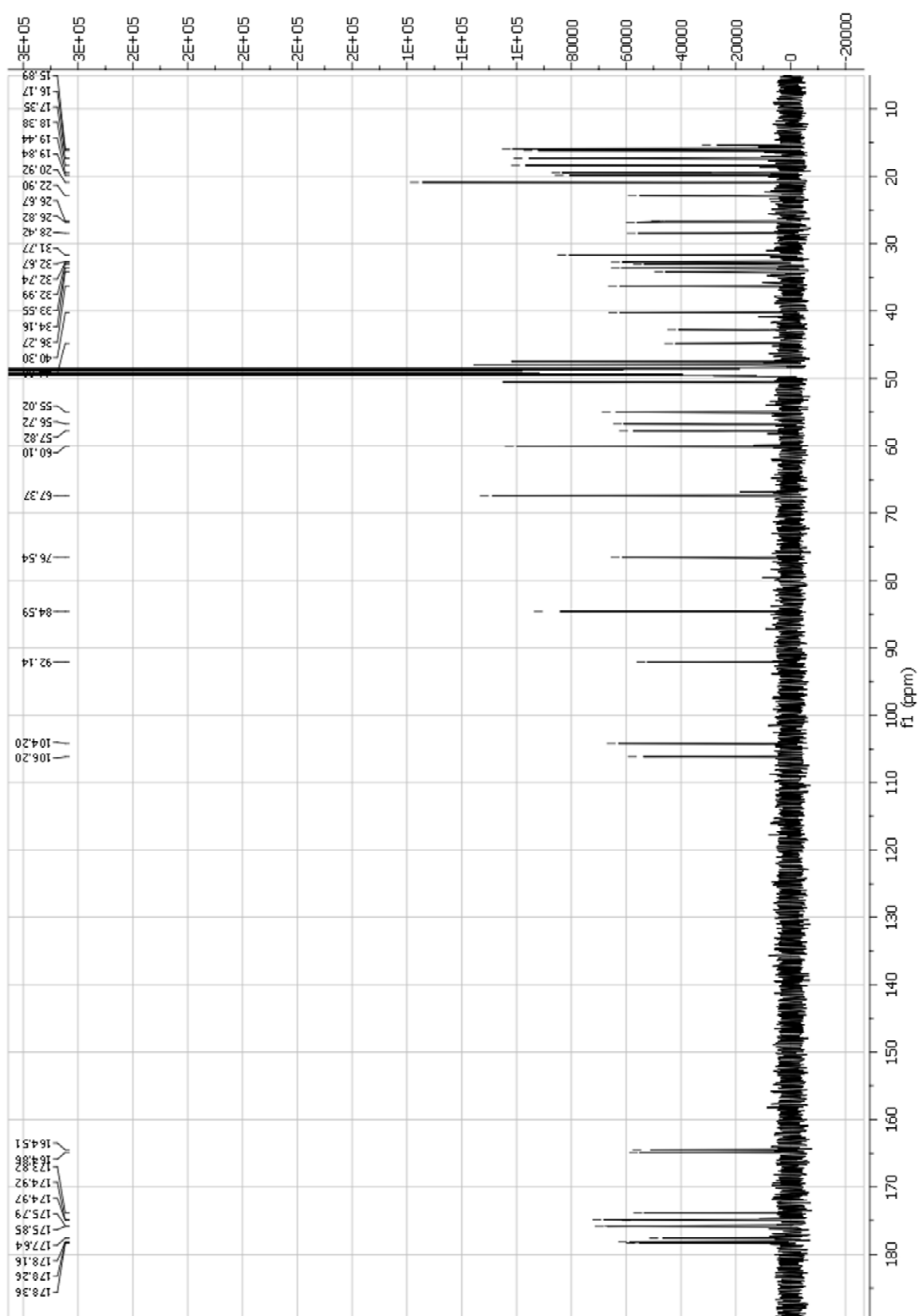
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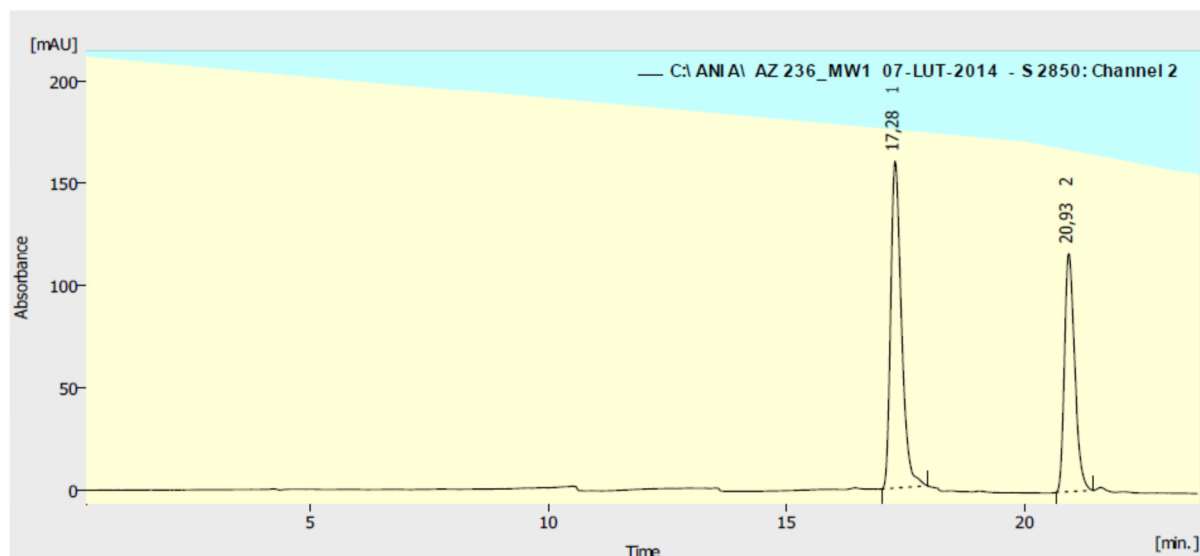
^1H NMR of $(\text{CN})_2\text{Cbi}$ 2 in CD_3OD (NaCN in MW)



^{13}C NMR of $(\text{CN})_2\text{Cbi}$ 2 in CD_3OD (NaCN in MW)



HPLC of (CN)₂Cbi 2 (NaCN in MW)



Result Table (Uncal - C:\ANIA\ AZ 236_MW1 07-LUT-2014 - S 2850: Channel 2)

	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Peak Purity [-]
1	17,283	2507,997	160,075	59,0	57,8	0,25	709
2	20,933	1745,456	116,651	41,0	42,2	0,25	648
	Total	4253,452	276,727	100,0	100,0		

HPLC, t_r 17.3 and 20.9 min. (Eurospher II 100-5 C18 250 mm x 4.6 mm column, MeCN/H₂O 0.05% TFA, 1 mL/min)

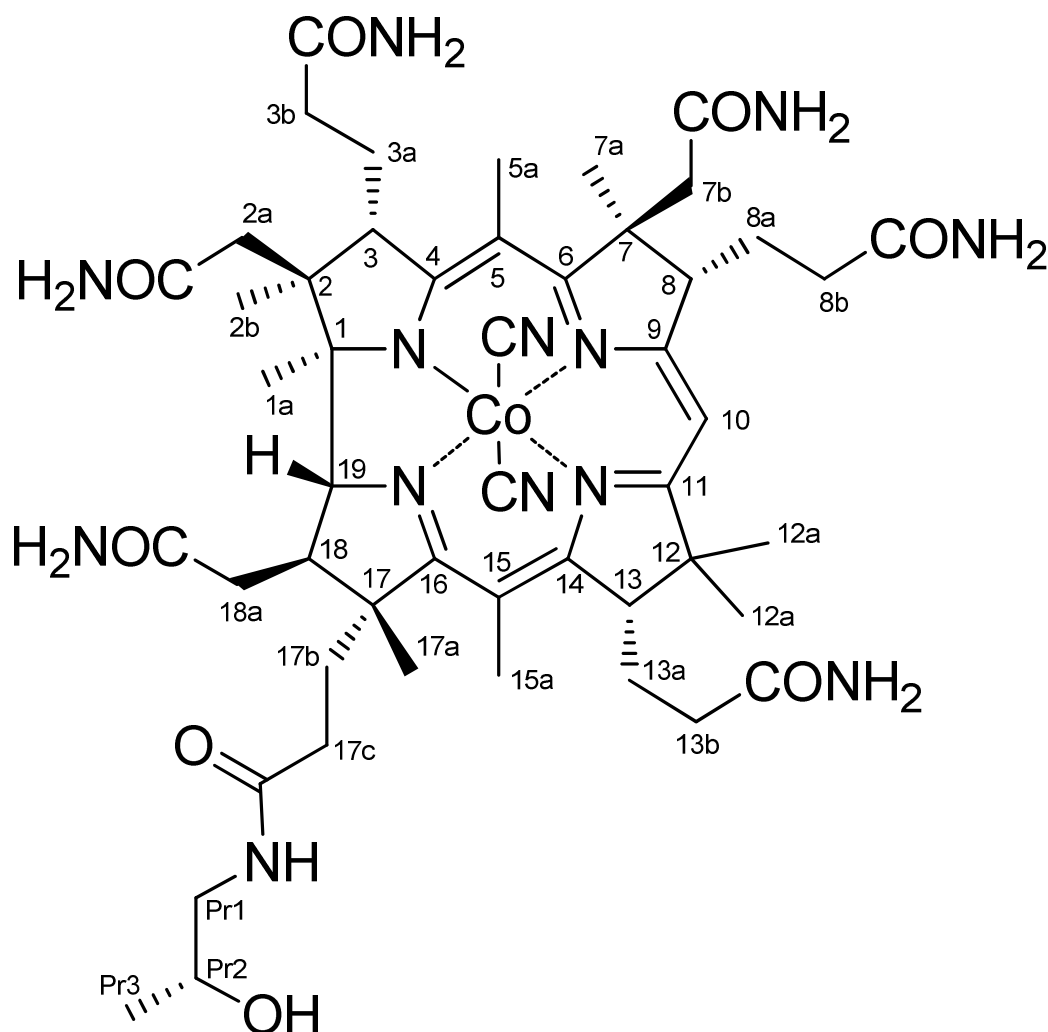
Two signals are observed for dicyano cobinamide: (CN)(H₂O)Cbi at 17.3 min. and (CN)₂Cbi at 20.9 min. This is caused by the acidic conditions on the column.

HPLC gradient for (CN)₂Cbi

HPLC Measurement conditions: Column: Eurospher II 100-5 C18 250 mm x 4.6 mm (Knauer) with a precolumn; detection: UV-Vis, wavelength: $\lambda = 361$ nm; flow rate: 1 mL/min; pressure: 10 Mpa, Temperature: 30 °C. HPLC method:

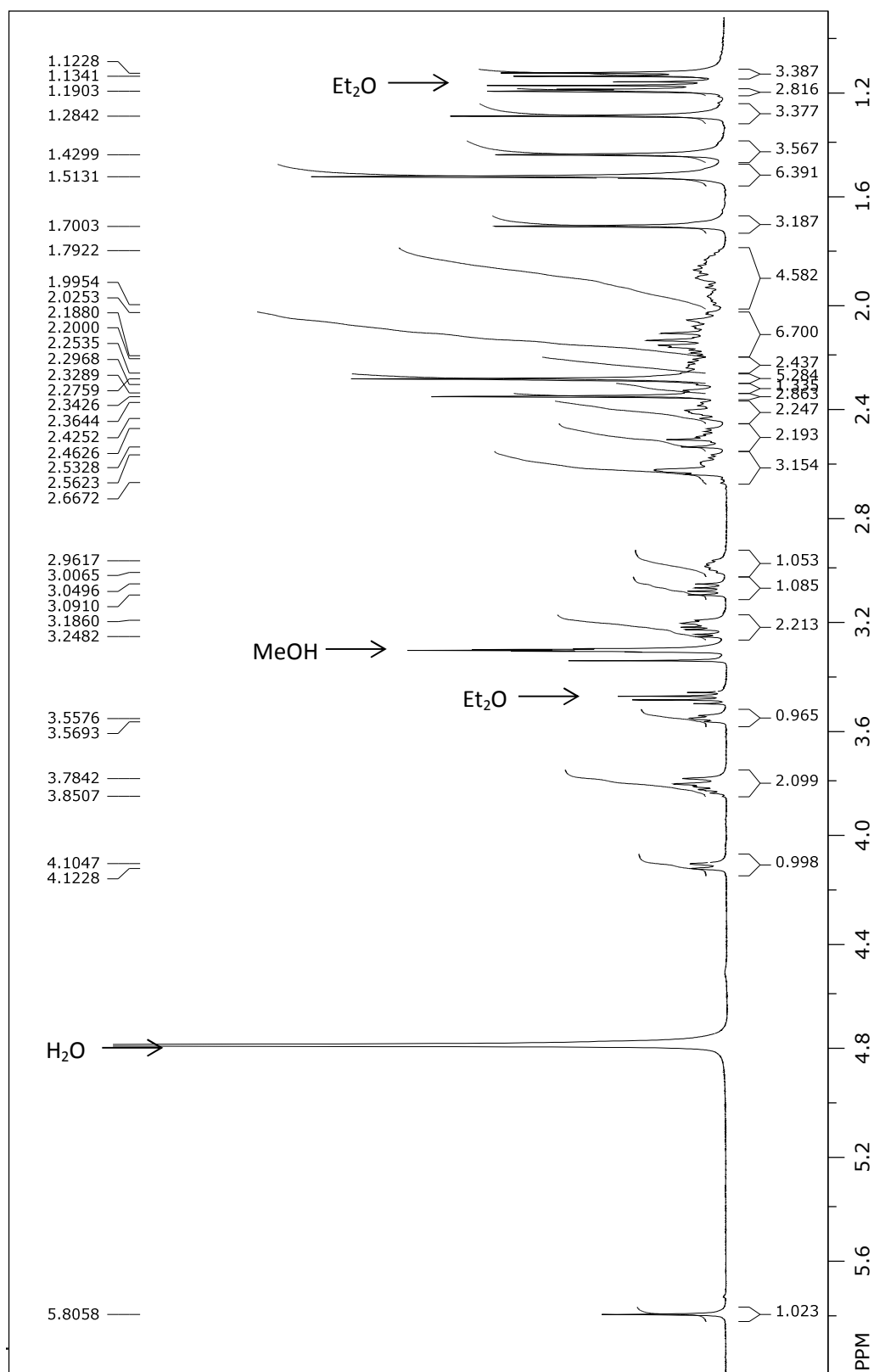
Time [min.]	H ₂ O + 0.05% TFA [%]	MeCN [%]
Initial	99	1
20	80	20
30	60	20

¹H NMR of (CN)₂Cbi 2 in CD₃OD (NaCN in MW large scale)

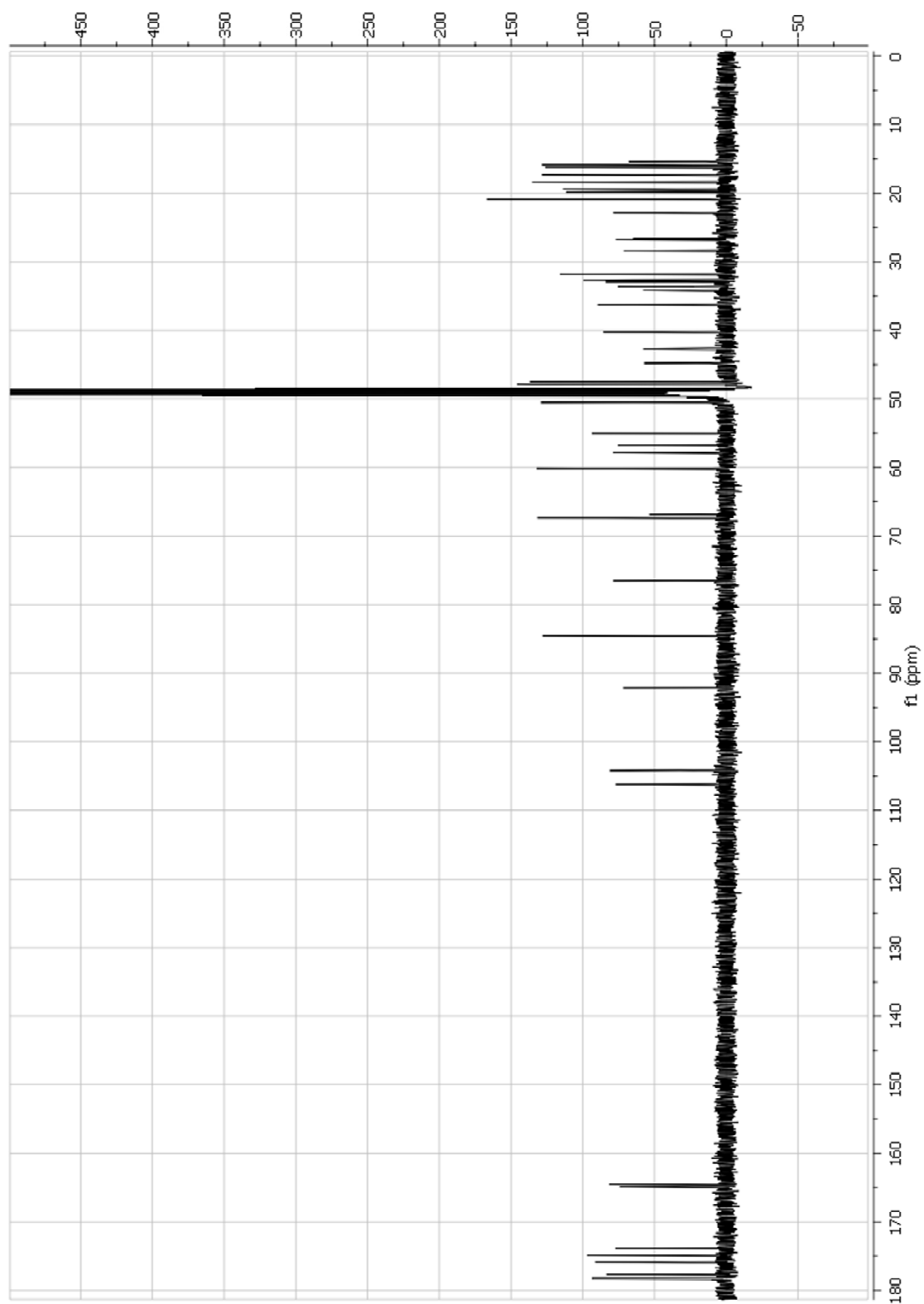


¹H NMR (500 MHz, CD₃OD) δ (ppm): 5.80 (s, 1H, **C10**), 4.11 (d, $J = 8.3$ Hz, 1H, **C3**), 3.81 (m, 2H, **Pr2** and **C19**), 3.55 (t, $J = 5.6$ Hz, 1H, **C8**), 3.24-3.18 (m, 2H, **Pr1** and **C13**), 3.07 (dd, $J = 7.1$ and 6.6 Hz, 1H, **Pr1**), 2.98 (m, 1H, **C18**), 2.66-2.56 (m, 3H, **17b** and **18a**), 2.53-2.46 (m, 2H, **C7a**), 2.42-2.36 (m, 2H, **-CH₂**), 2.34 (s, 3H, **C15a**), 2.32-2.29 (m, 1H, **C3a**), 2.27 (s, 5H, **C5a**, **C2a** and **-CH₂**), 2.24-2.19 (m, 2H, **C3a** and **C2a**), 2.18-2.02 (m, 6H, **C7b**, **C8a** and **-CH₂**), 1.99-1.80 (m, 4H, **C8a** and **-CH₂**), 1.70 (s, 3H, **C7a**), 1.51 (s, 6H, **C2a** and **C1a**), 1.43 (s, 3H, **C17a**), 1.28 (s, 3H, **C12a**), 1.19 (s, 3H, **C12a**), 1.12 (d, $J = 6.2$ Hz, 3H, **Pr3**). ¹³C NMR (125 MHz, CD₃OD) δ (ppm): (178.35, 178.31, 178.2, 178.15, 178.1; **C16**, **C11** and **C4**) 177.6, 175.8, 175.7, 174.96, 174.91, 173.8 (**C9**), 164.8 (**C14**), 164.5 (**C6**), 106.1 (**C12**), 104.1 (**C15**), 92.1 (**C10**), 84.5 (**C1**), 76.5, 67.3 (**C19**), 60.0, 57.8 (**C3**), 56.7 (**C8**), 55.0 (**C13**), 50.5 (**C7**), 47.9 (**C12**), 47.8, 47.4 (**C2**), 44.8 (**C7b**), 42.7, 40.3 (**C18**), 36.2, 34.1, 33.5, 32.9, 32.7, 32.6, 31.7 (**C12a**), 28.4, 26.8, 26.6, 22.9 (**C1a**), 20.9, 19.8, 19.4 (**C7a**), 18.3 (**C12a** and **C17a**), 17.3 (**C2a**), 16.1 (**C5a**), 15.8 (**C15a**).

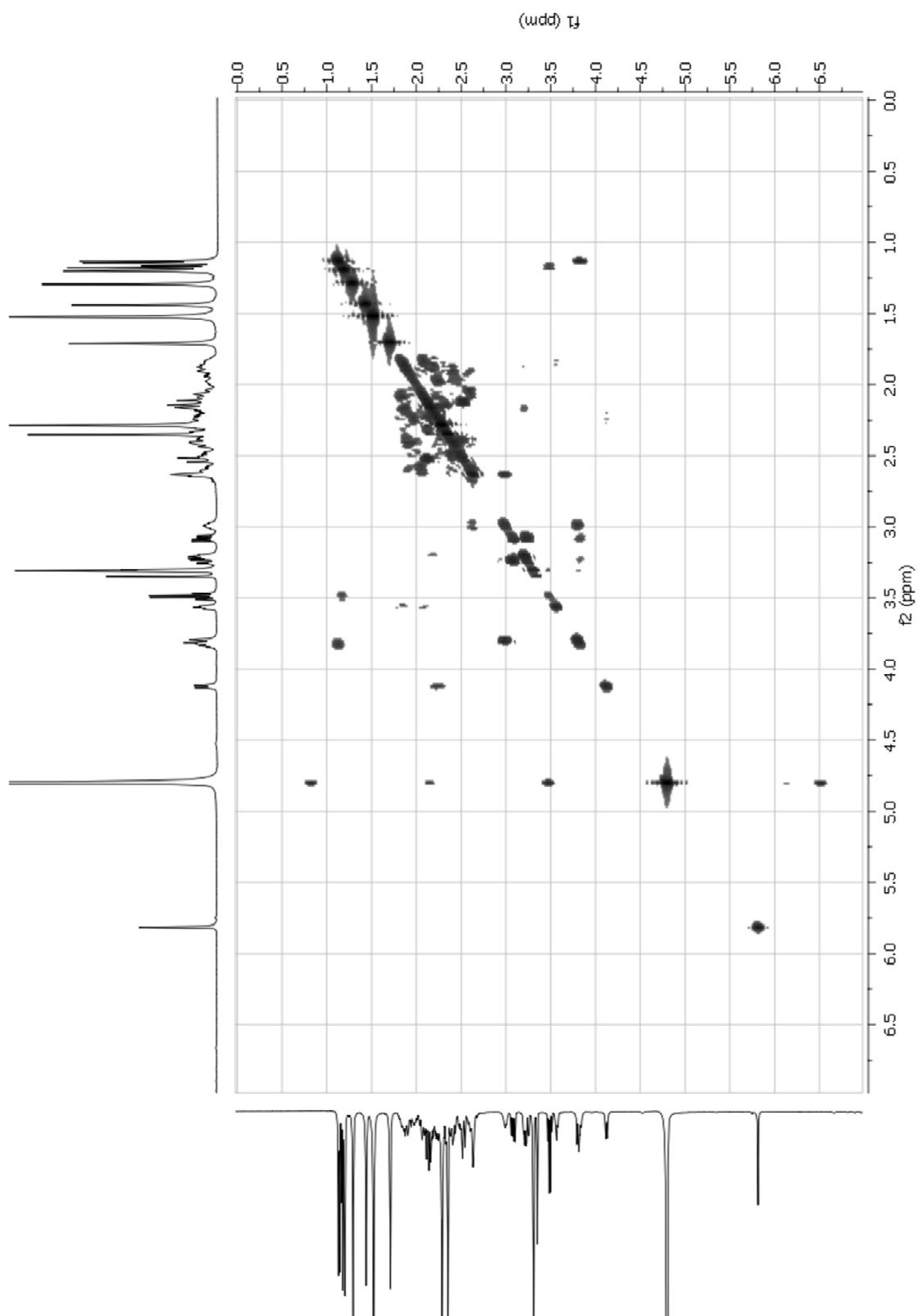
^1H NMR of $(\text{CN})_2\text{Cbi}$ 2 in CD_3OD (NaCN in MW large scale)



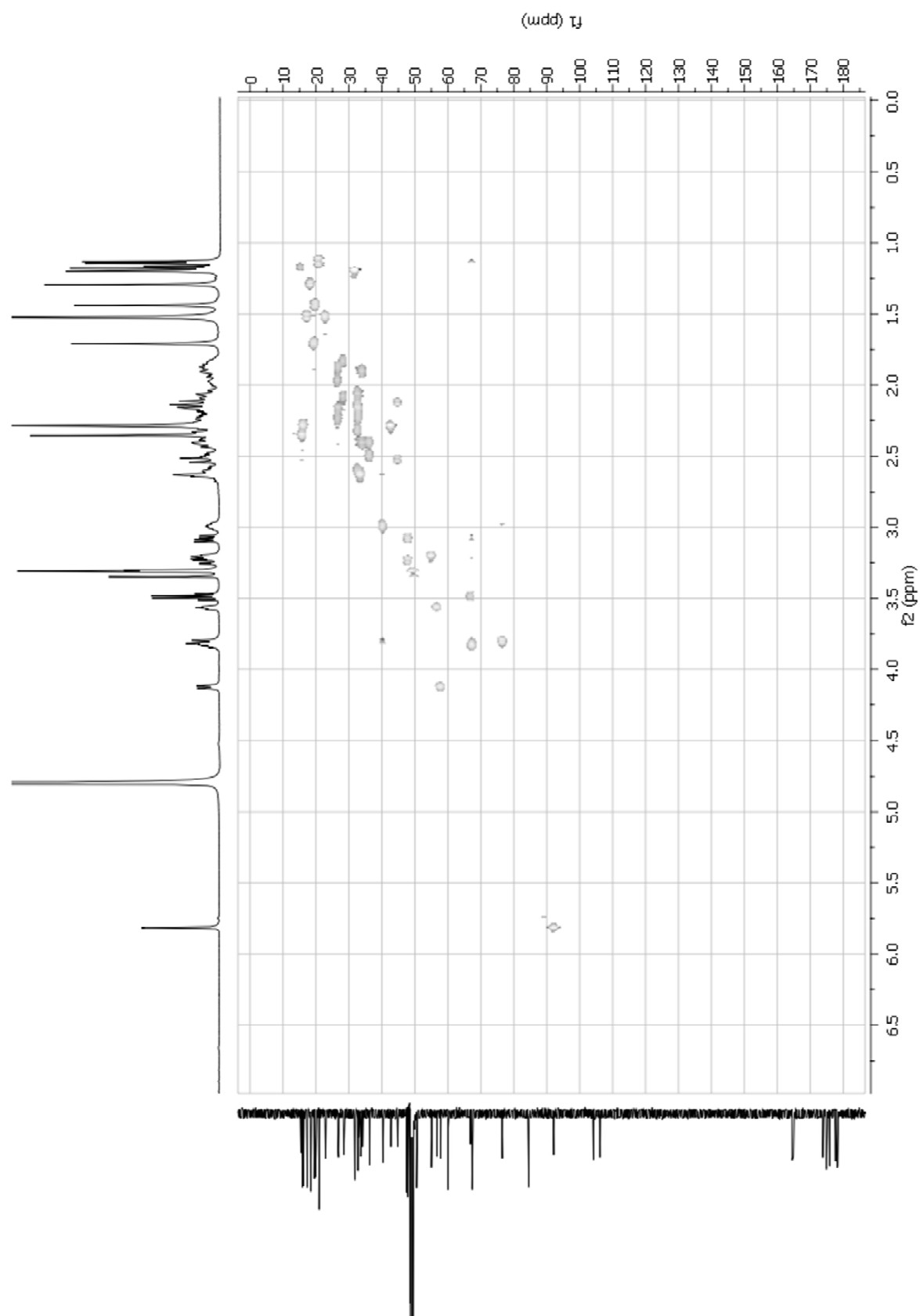
^{13}C NMR of $(\text{CN})_2\text{Cbi}$ 2 in CD_3OD (NaCN in MW large scale)



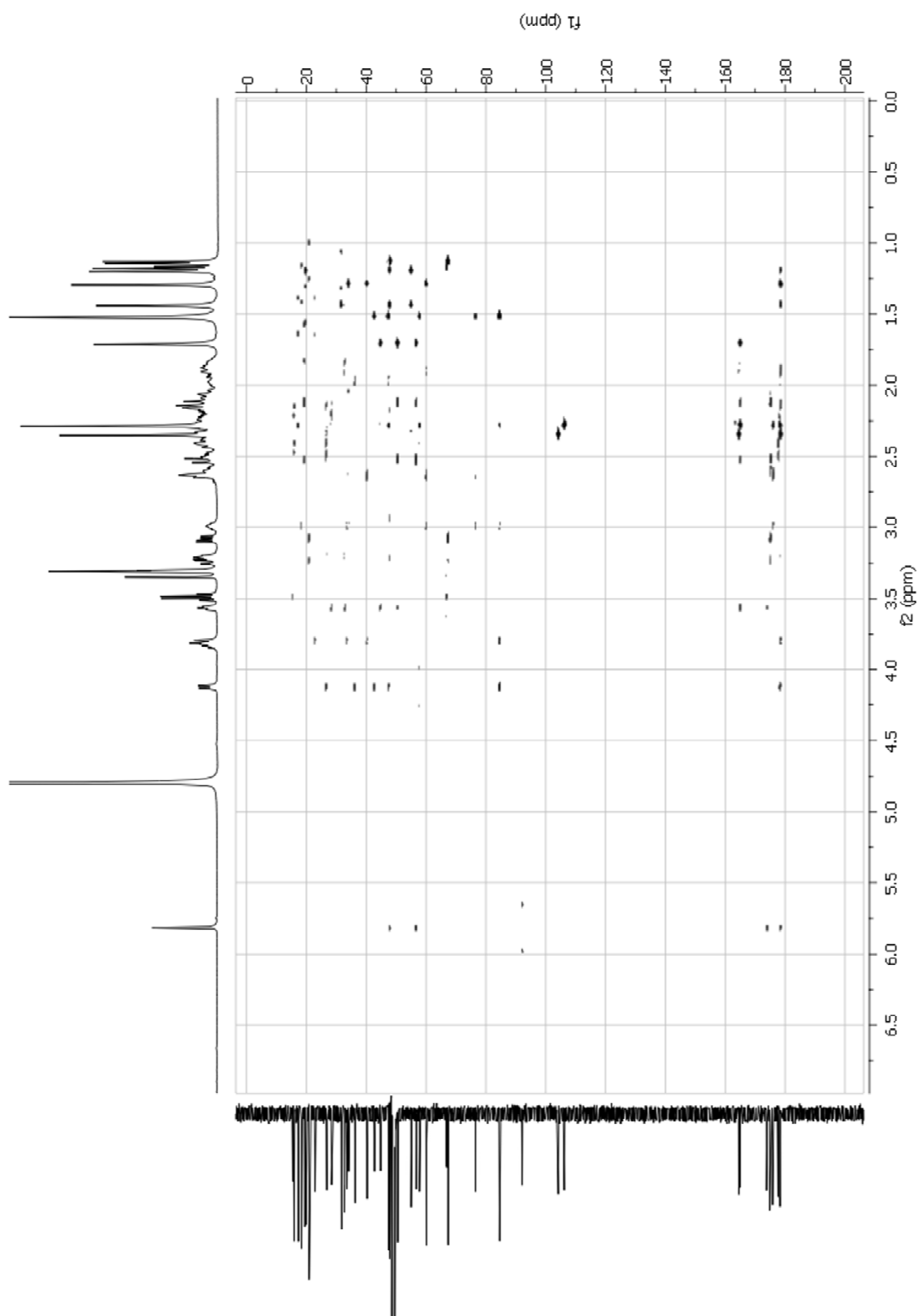
COSY NMR of (CN)₂Cbi 2 in CD₃OD (NaCN in MW large scale)



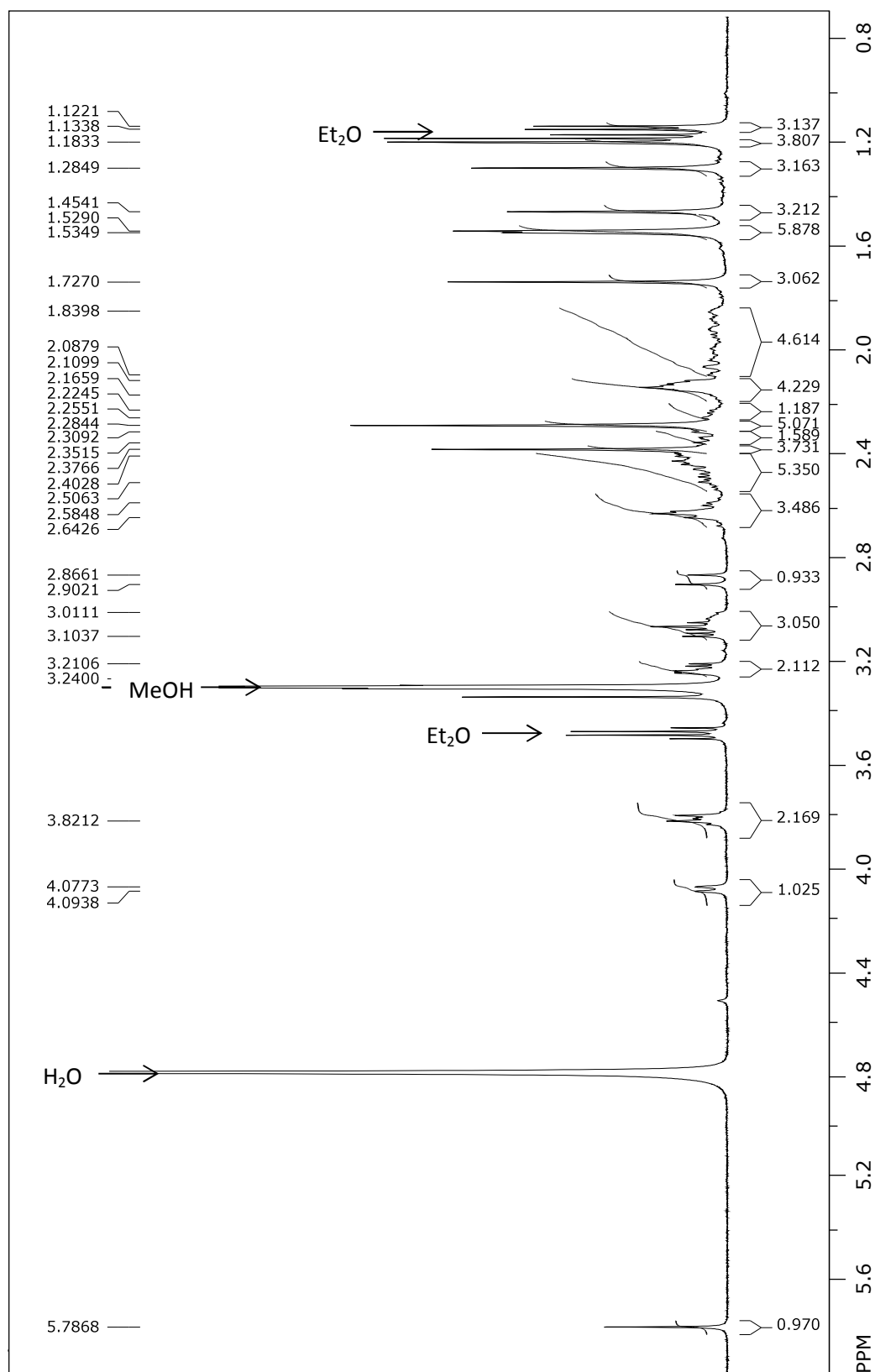
HSQC NMR of (CN)₂Cbi 2 in CD₃OD (NaCN in MW large scale)



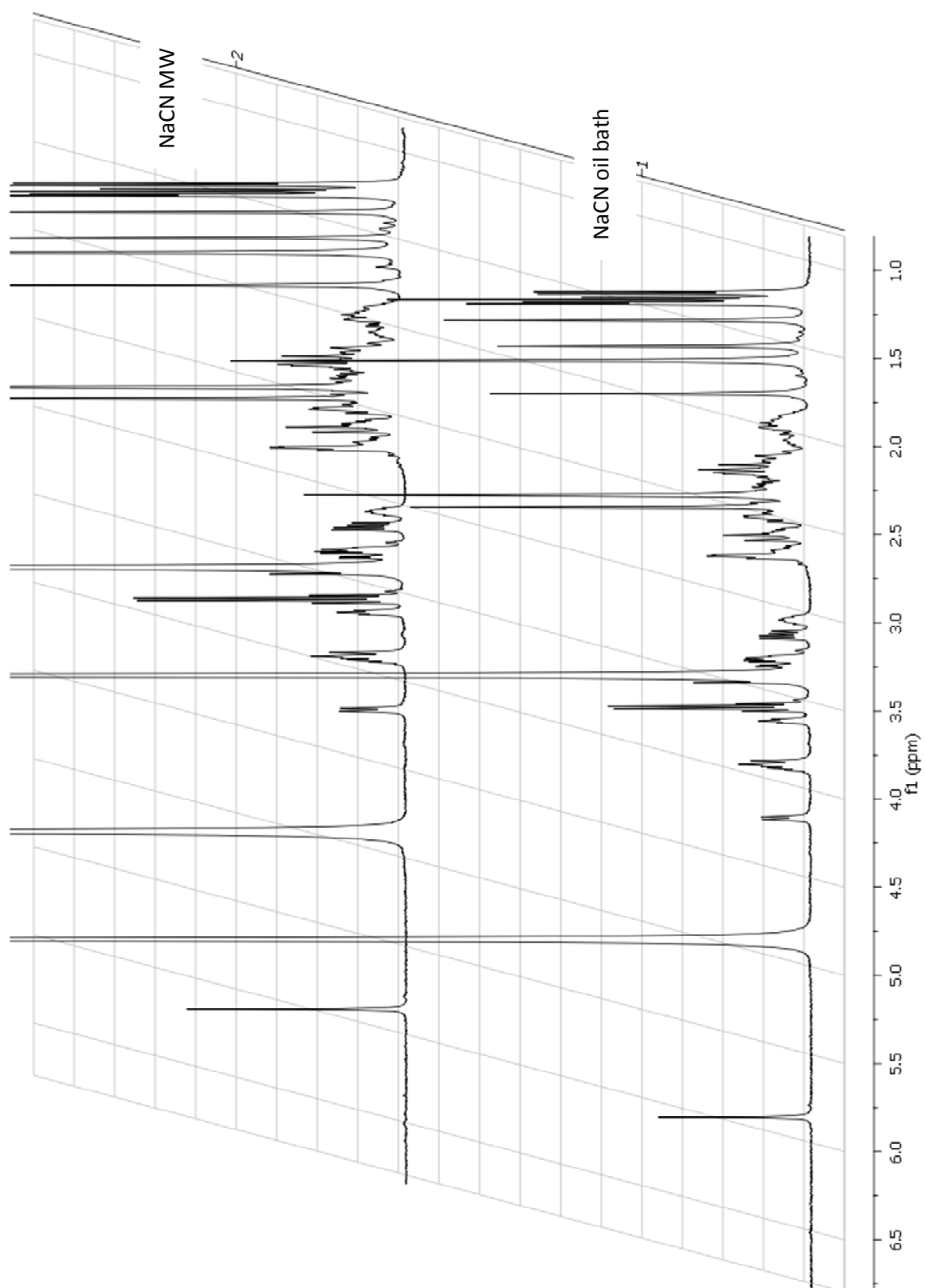
HMBC NMR of (CN)₂Cbi 2 in CD₃OD (NaCN in MW large scale)



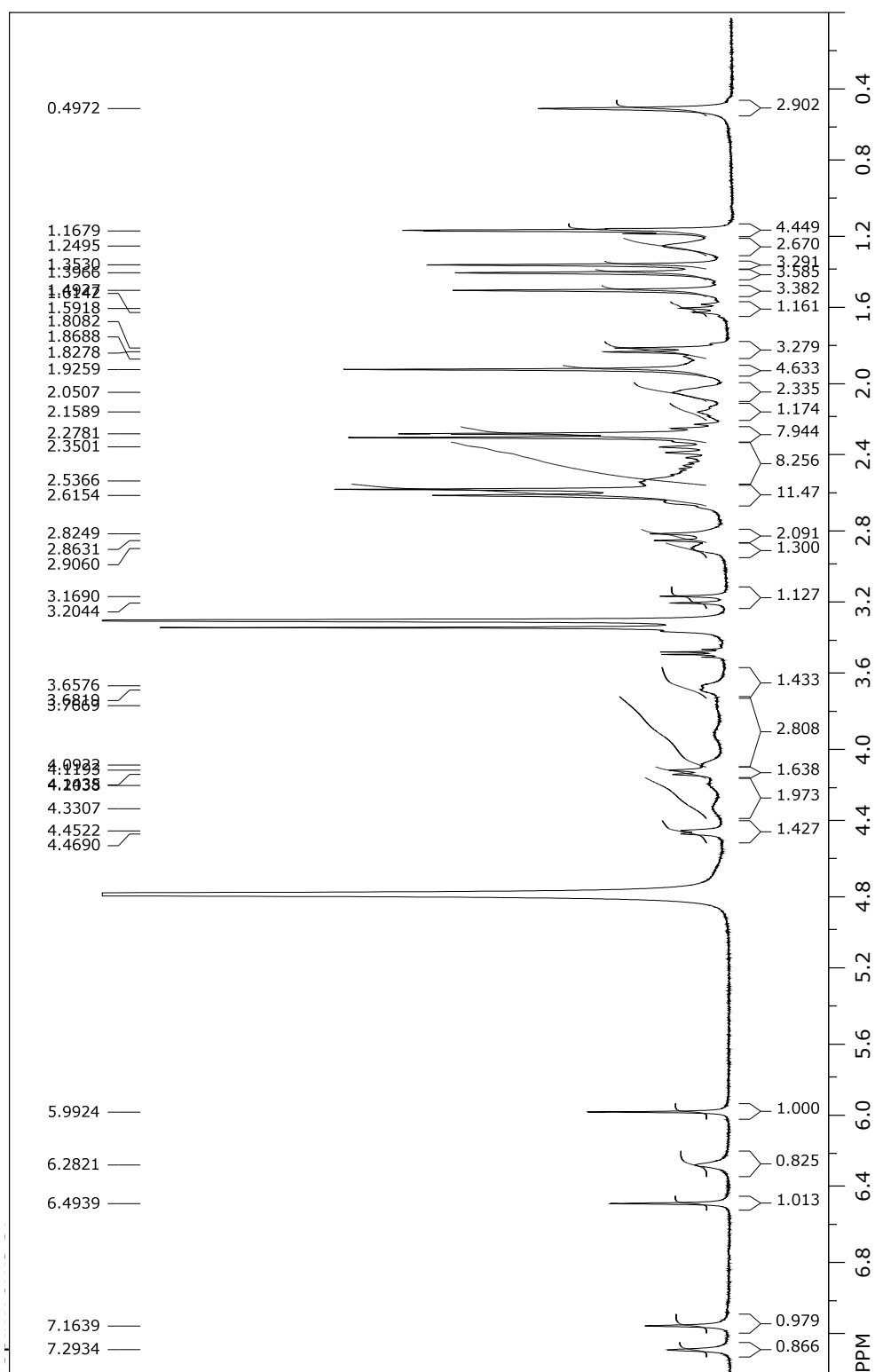
^1H NMR of $(\text{CN})_2\text{Cbi}$ 2 in CD_3OD (NaCN in an oil bath)



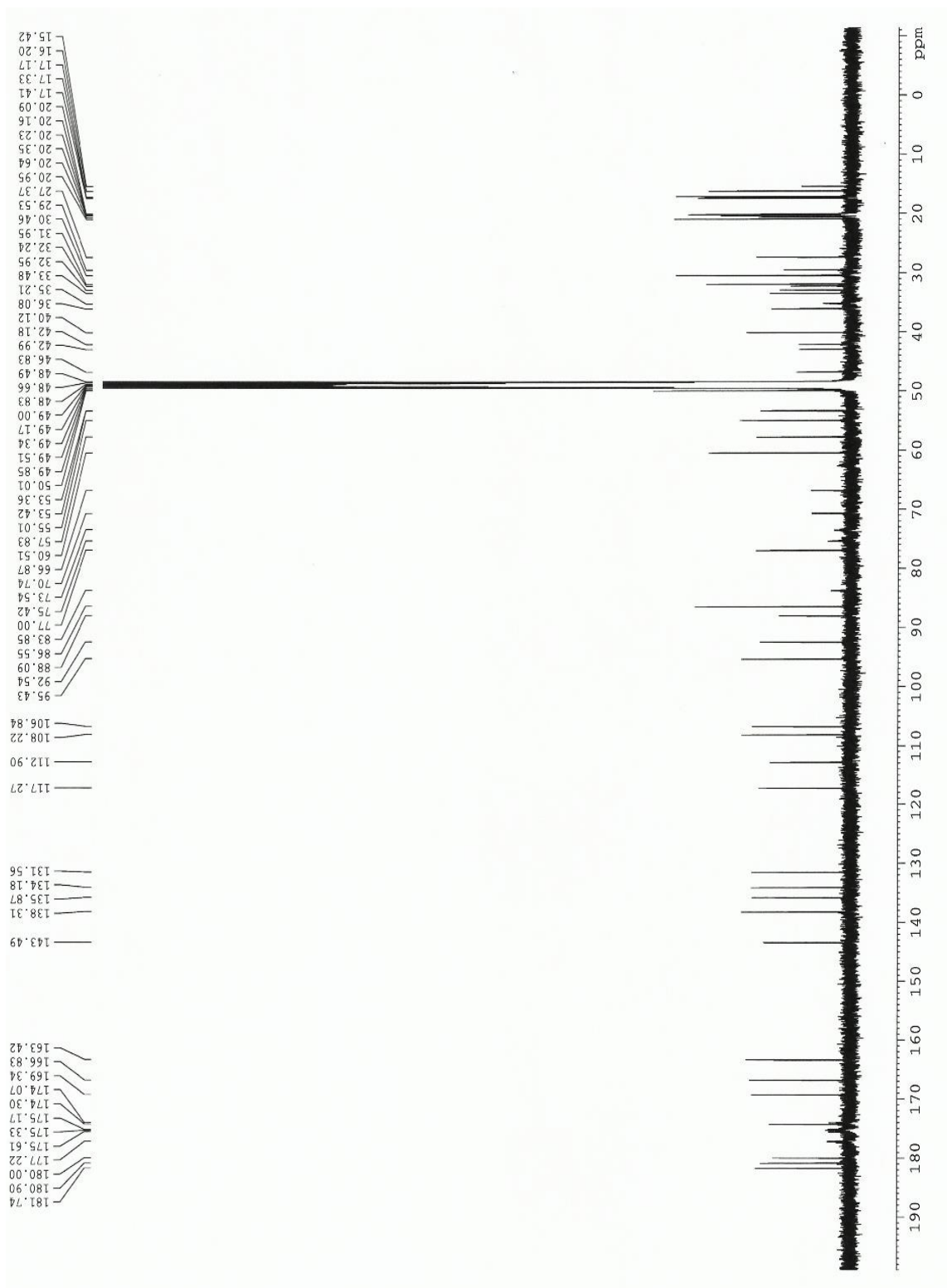
^1H NMR stack of $(\text{CN})_2\text{Cbi}$ 2 in CD_3OD



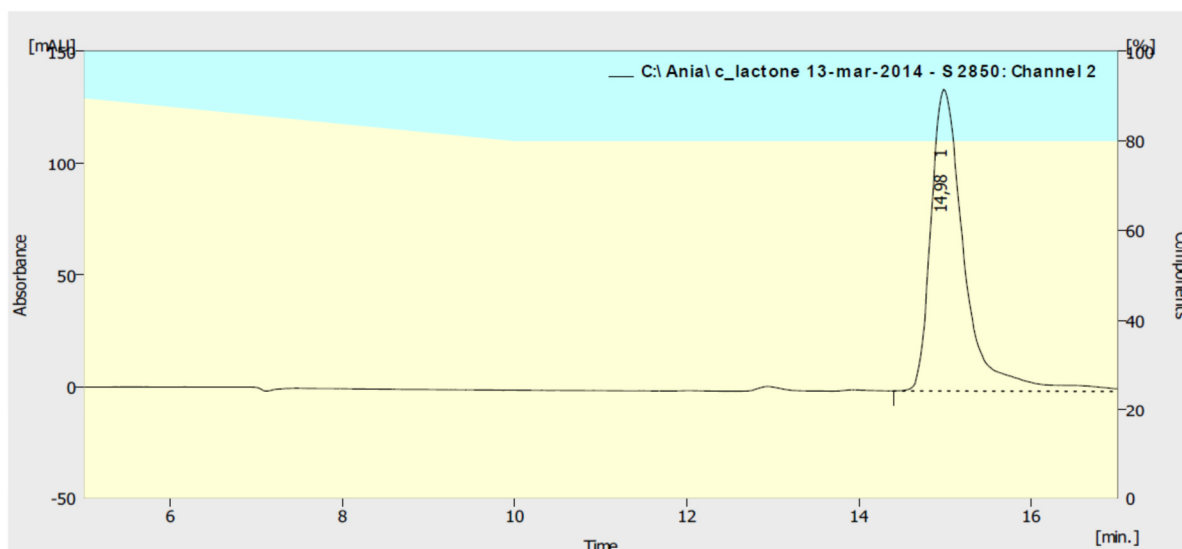
^1H NMR spectrum of (CN)Cbl(*c*-lactone) 3 in CD_3OD



^{13}C NMR spectrum of (CN)Cbl(*c*-lactone) 3 in CD_3OD



HPLC of (CN)Cbl(*c*-lactone) 3



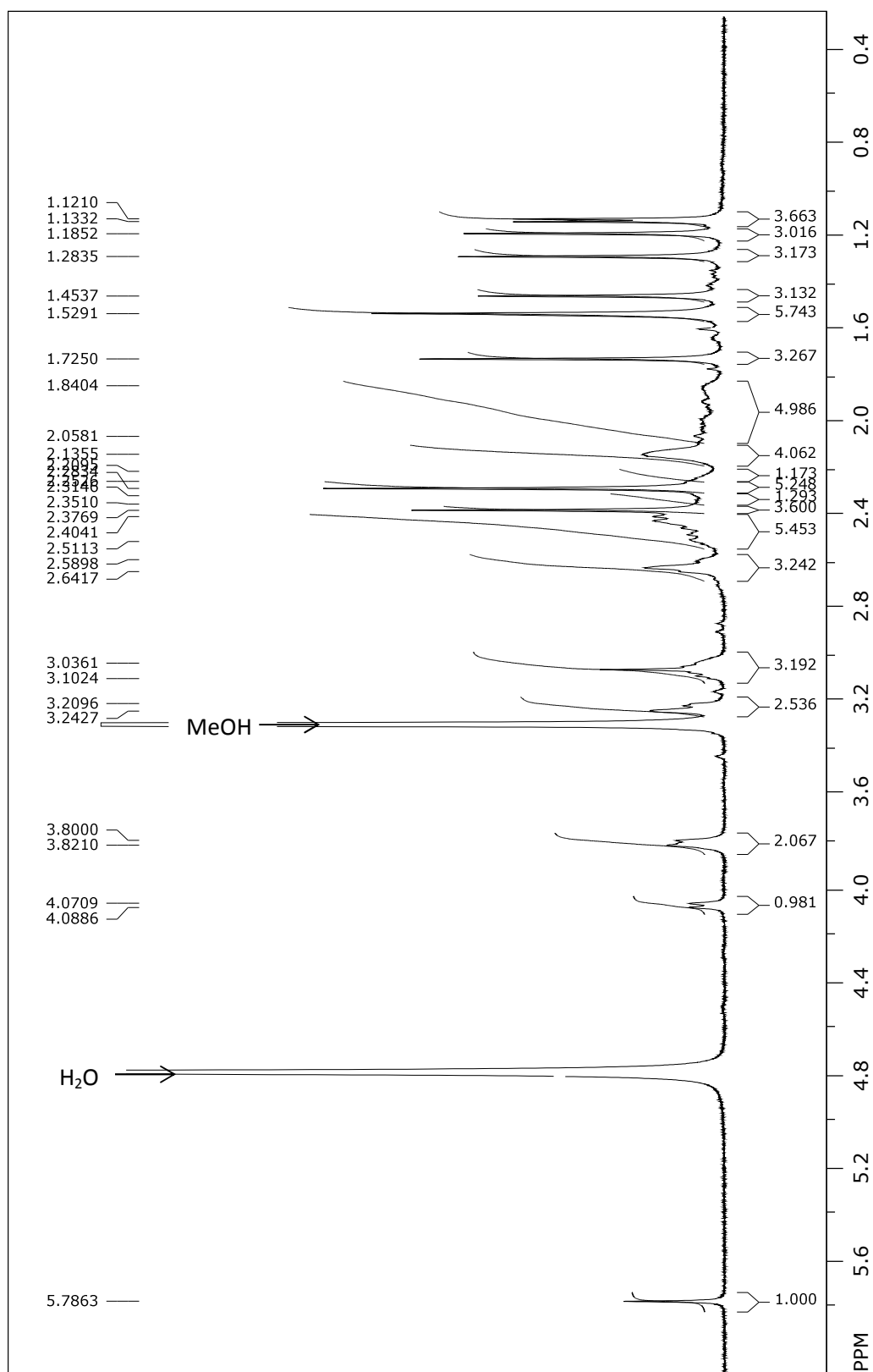
HPLC, t_r 14.9 min. (Eurospher II 100-5 C18 250 mm x 4.6 mm column, MeCN/H₂O 0.05% TFA, 1 mL/min)

HPLC gradient for (CN)Cbl(*c*-lactone) 3

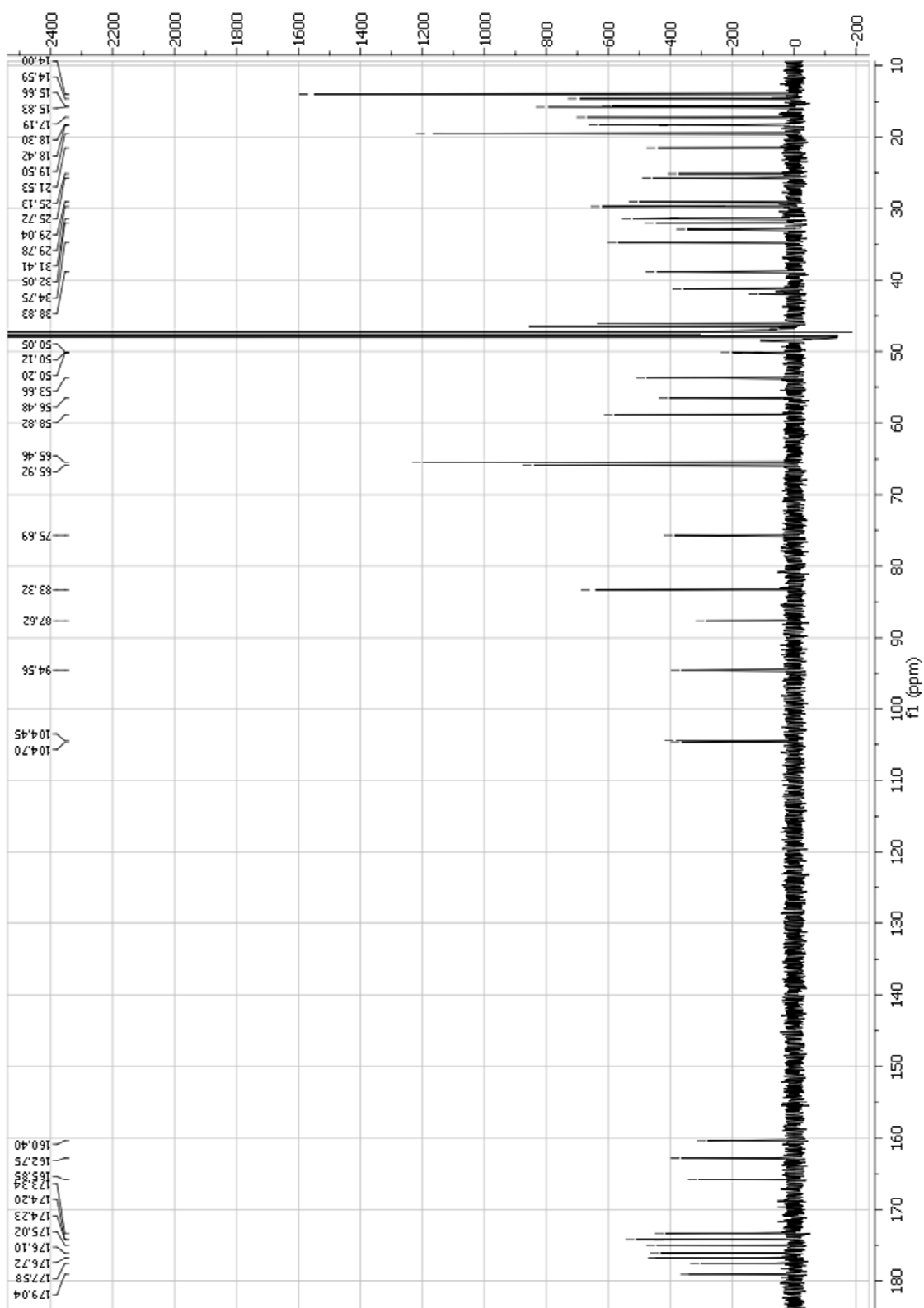
HPLC Measurement conditions: Column: Eurospher II 100-5 C18 250 mm x 4.6 mm (Knauer) with a precolumn; detection: UV-Vis, wavelength: $\lambda = 361$ nm; flow rate: 1 mL/min; pressure: 10 Mpa, Temperature: 30 °C. HPLC method:

Time [min.]	H ₂ O [%]	MeCN [%]
Initial	99	1
10	80	20
20	80	20
30	30	70

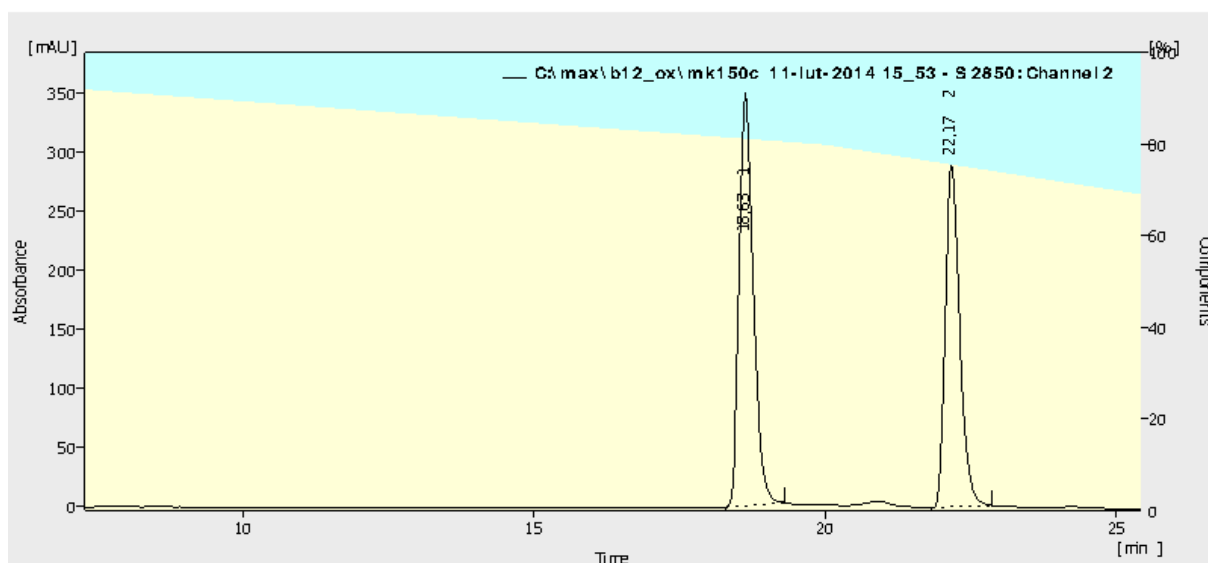
^1H NMR of $(\text{CN})_2\text{Cbi}(c\text{-lactone})$ **5 in CD_3OD (NaCN in MW)**



^{13}C NMR of $(\text{CN})_2\text{Cbi}(c\text{-lactone})$ 5 in CD_3OD (NaCN in MW)



HPLC of (CN)₂Cbi(c-lactone) 5 (NaCN in MW)



Result Table (Uncal C:\max\b12_ox\mk150c 11-jul-2014 15_53 - S 2850: Channel 2)

	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	WCS [min]	Peak Purity []
1	18,633	5902,020	349,472	54,3	54,8	0,28	692
2	22,167	4964,923	288,671	45,7	45,2	0,27	693
	Total	10866,942	638,143	100,0	100,0		

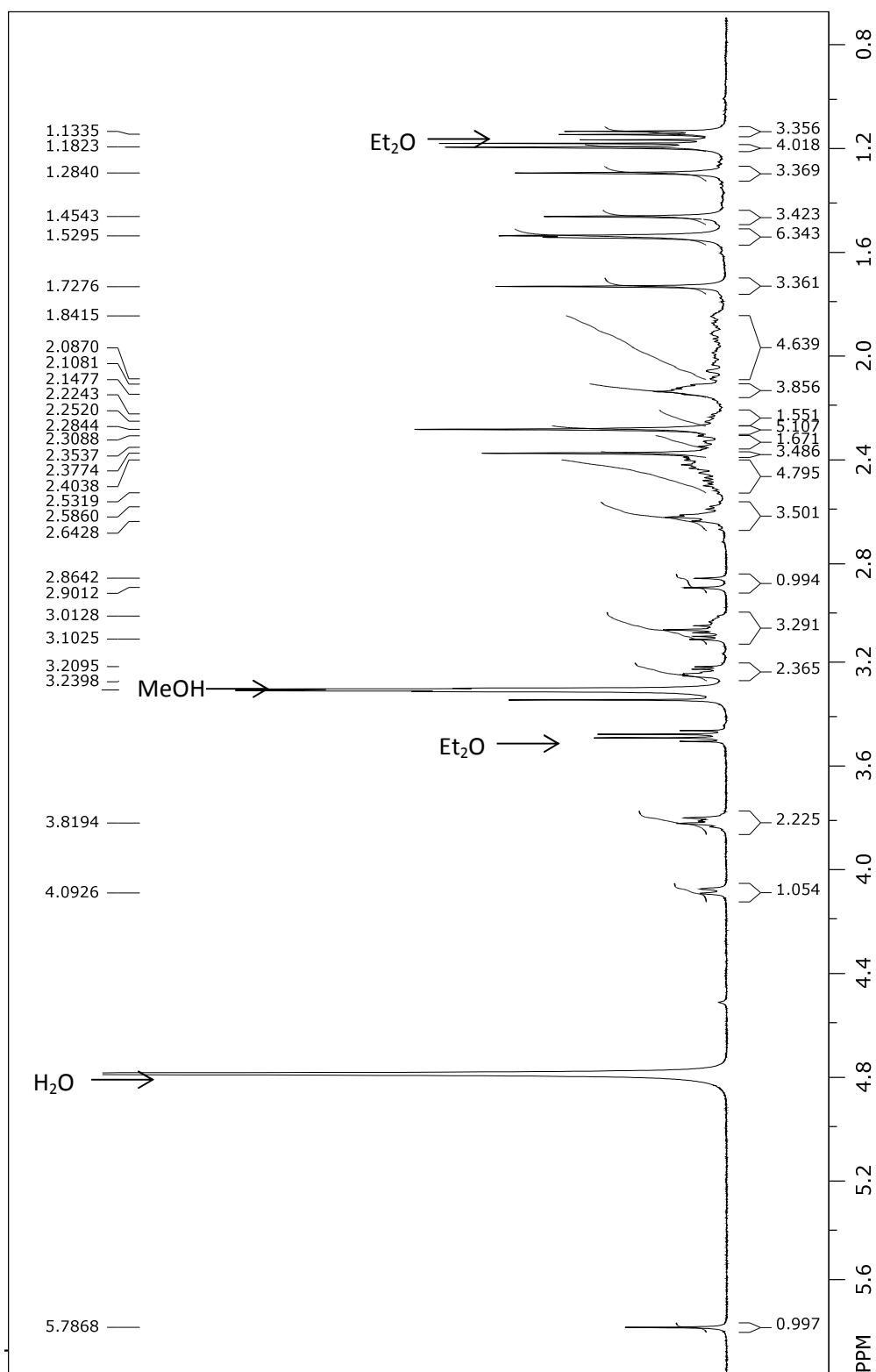
HPLC, t_r 18.6 and 22.1 min. (Eurospher II 100-5 C18 250 mm x 4.6 mm column, MeCN/H₂O 0.05% TFA, 1 mL/min)

HPLC gradient for (CN)₂Cbi(c-lactone)

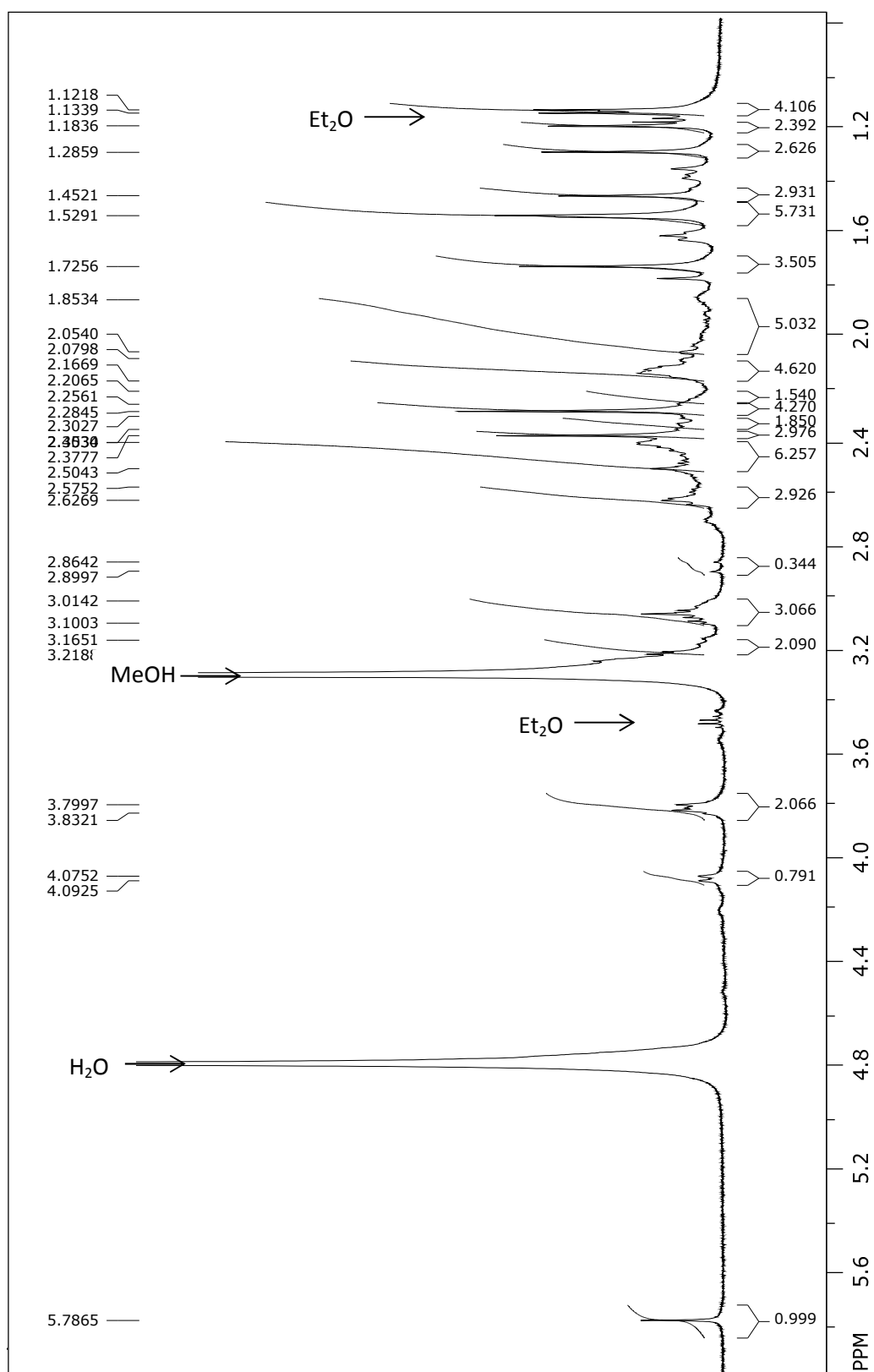
HPLC Measurement conditions: Column: Eurospher II 100-5 C18 250 mm x 4.6 mm (Knauer) with a precolumn; detection: UV-Vis, wavelength: $\lambda = 361$ nm; flow rate: 1 mL/min; pressure: 10 Mpa, Temperature: 30 °C. HPLC method:

Time [min.]	H ₂ O + 0.05% TFA [%]	MeCN [%]
Initial	99	1
20	80	20
30	60	20

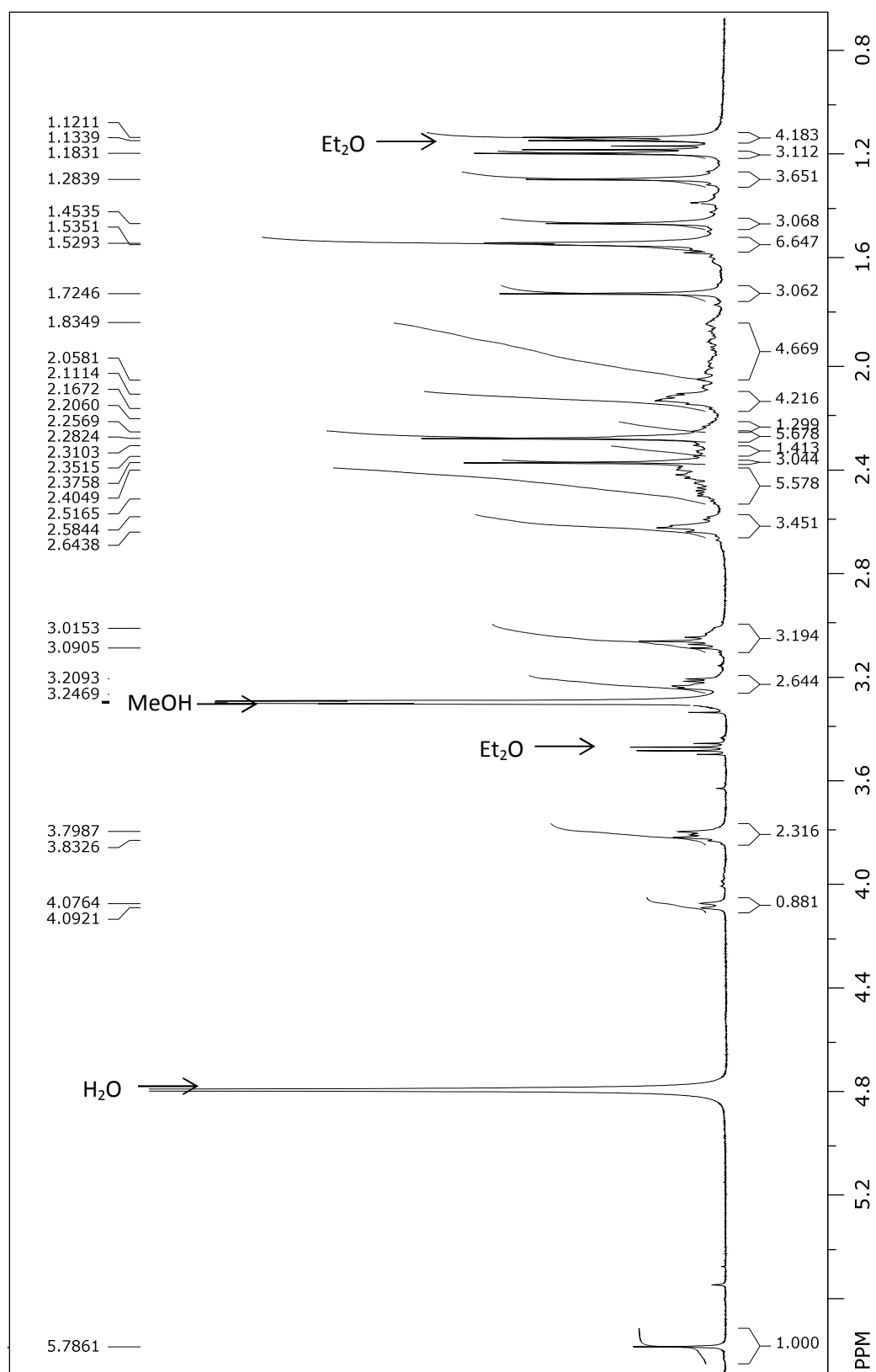
^1H NMR of $(\text{CN})_2\text{Cbi}(c\text{-lactone})$ 5 in CD_3OD (NaCN in an oil bath)



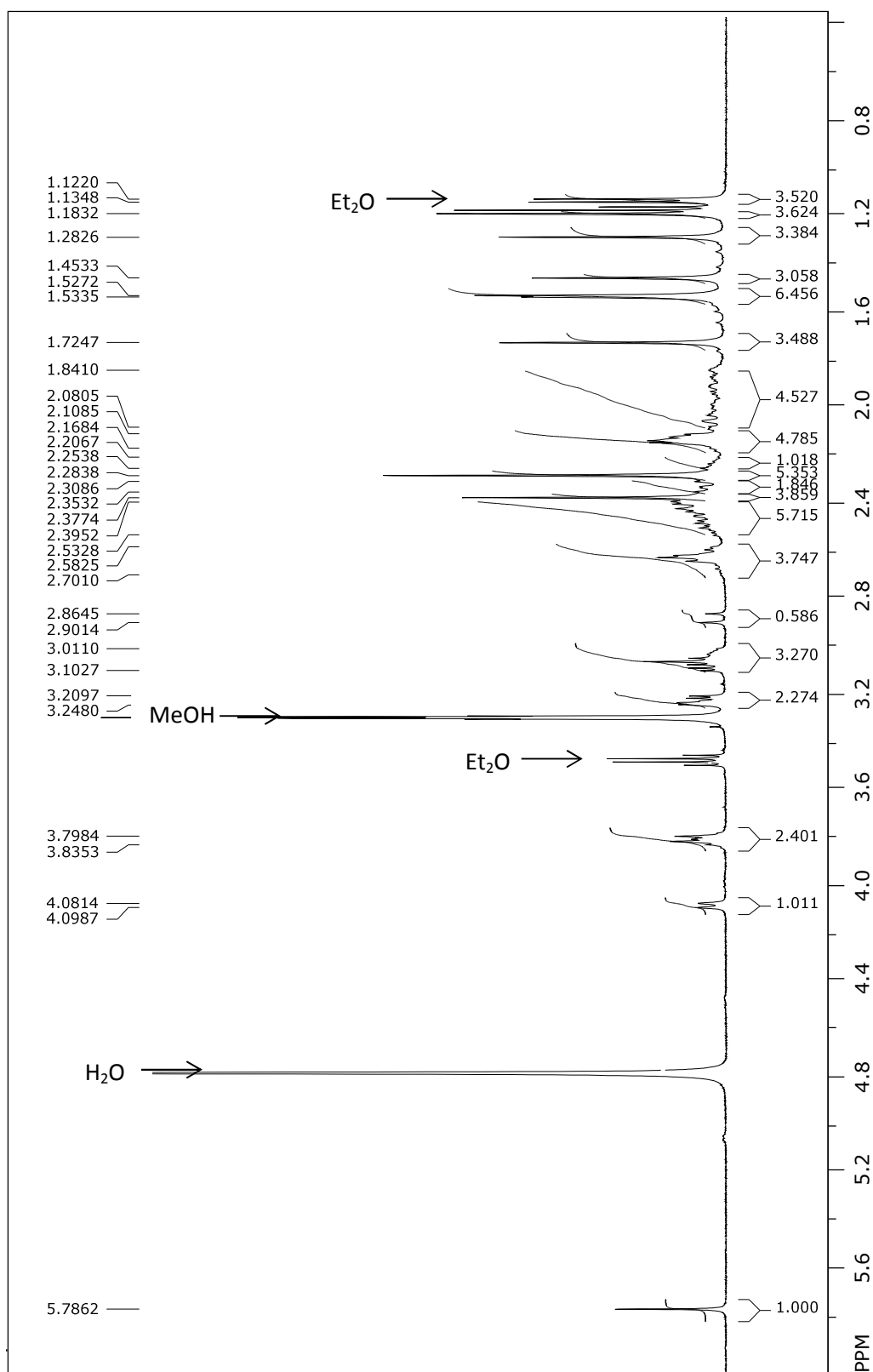
^1H NMR of $(\text{CN})_2\text{Cbi}(c\text{-lactone})$ **5 in CD_3OD from $(\text{CN})\text{Cbl}(c\text{-lactone})$ **3** (CuBr in MW)**



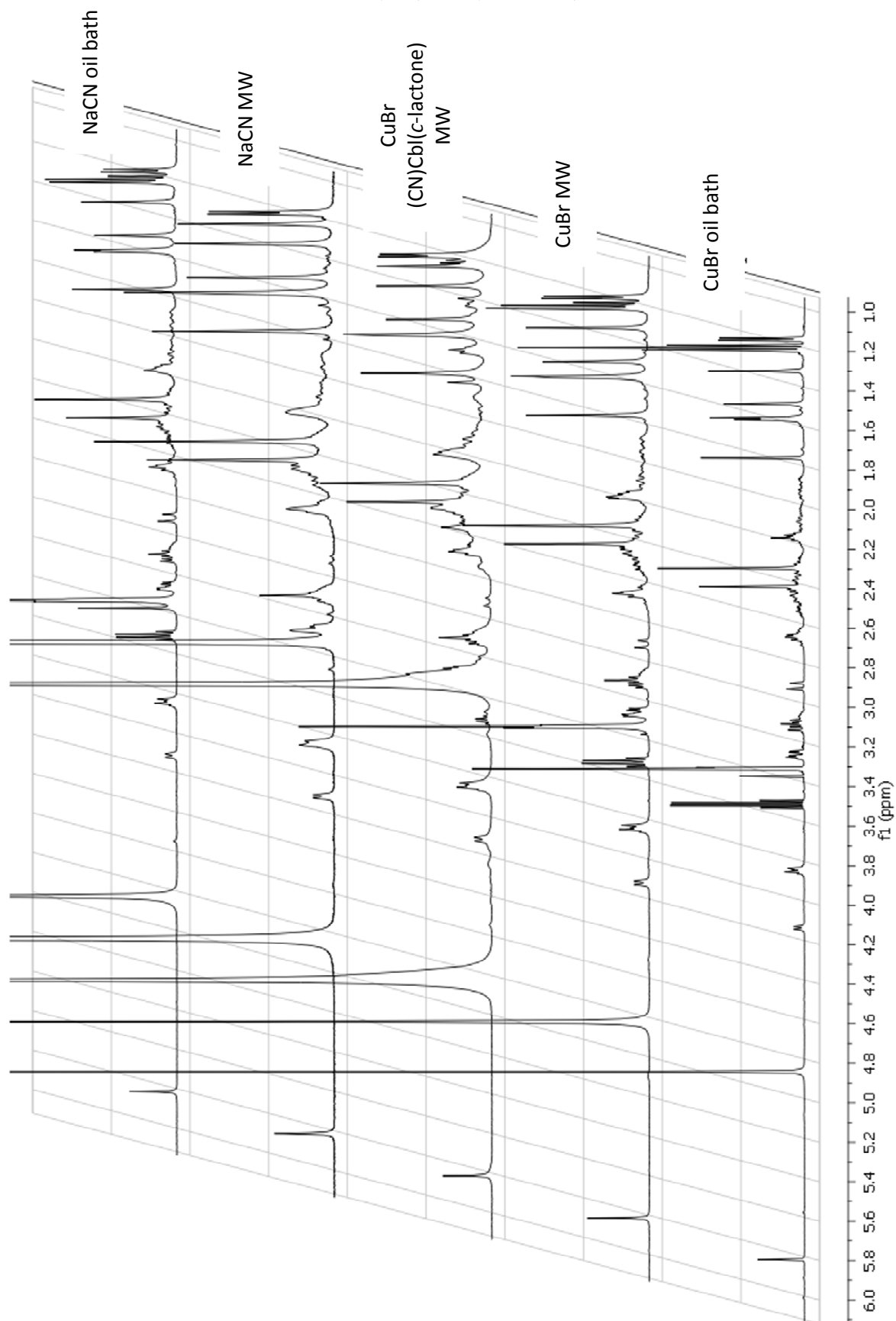
^1H NMR of $(\text{CN})_2\text{Cbi}(c\text{-lactone})$ **5 in CD_3OD from $(\text{CN})\text{Cbi}$ **1** (CuBr and NBS in MW)**



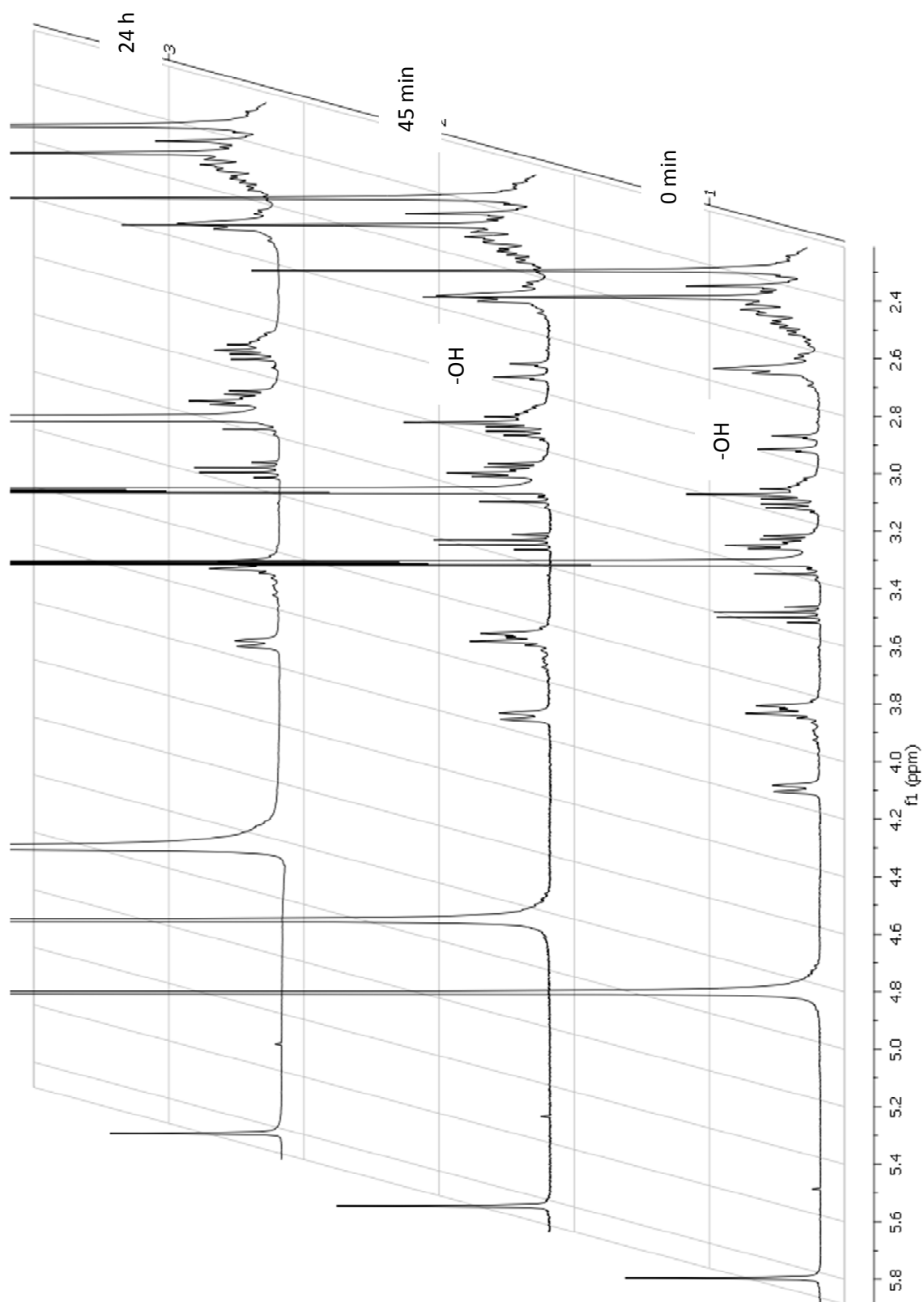
^1H NMR of $(\text{CN})_2\text{Cbi}(c\text{-lactone})$ **5 in CD_3OD from $(\text{CN})\text{Cbl}$ **1** (CuBr and NBS in an oil bath)**



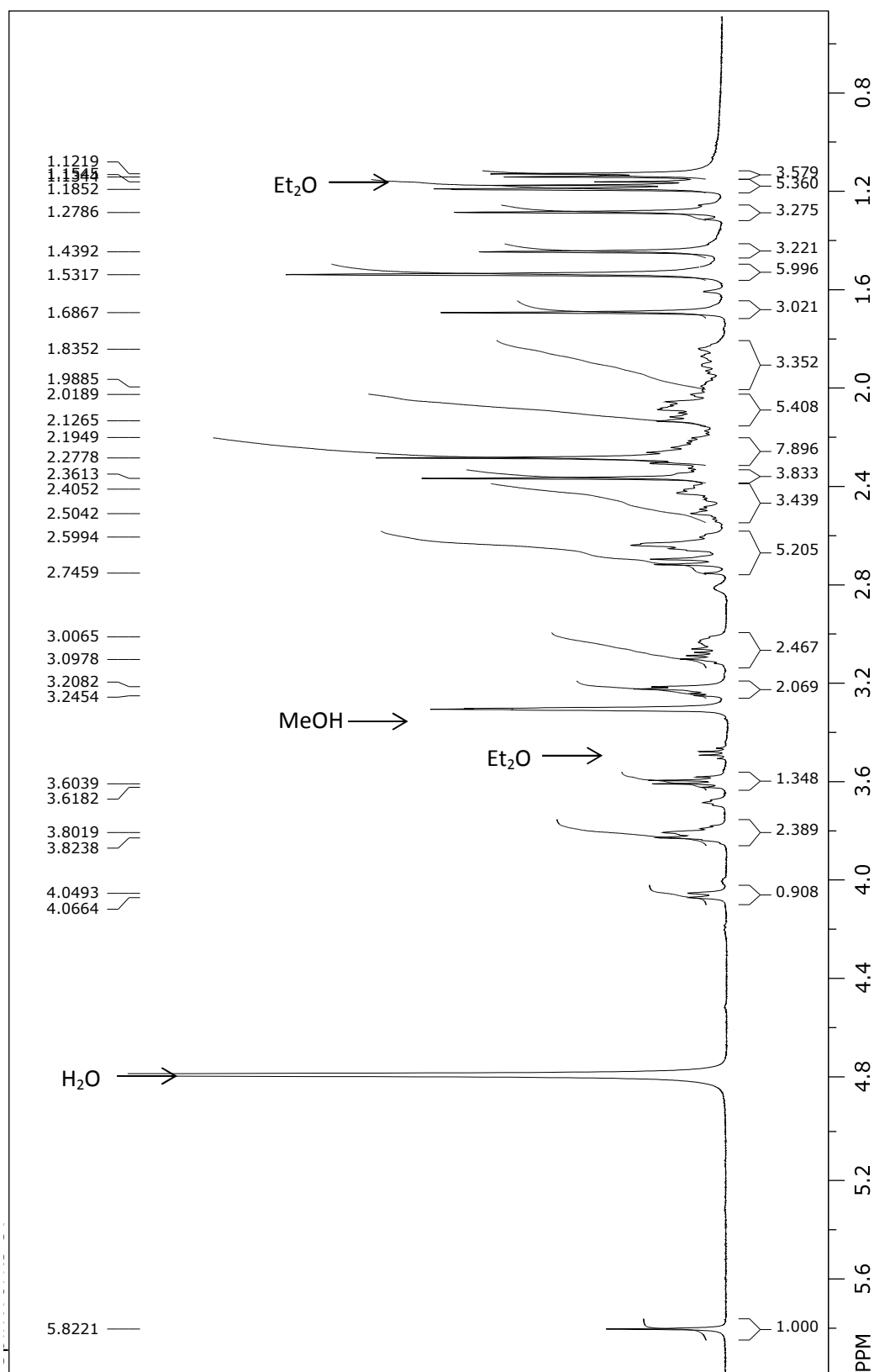
^1H NMR stack of $(\text{CN})_2\text{Cbi}(c\text{-lactone})$ 5 in CD_3OD



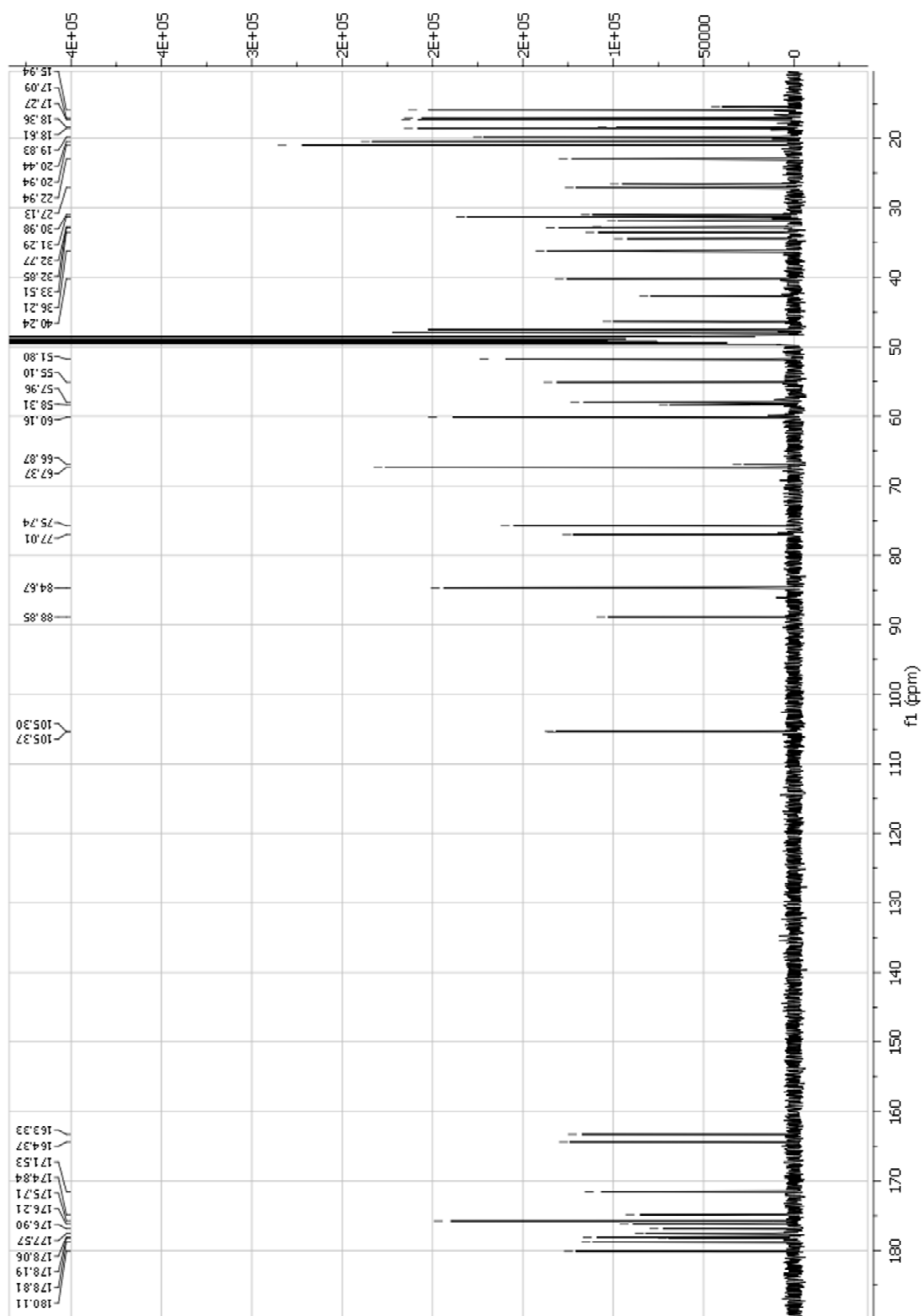
^1H NMR spectra stack of $(\text{CN})_2\text{Cbi}(c\text{-lactone})$ **5** in CD_3OD after 0 min, 45 min and 24 h



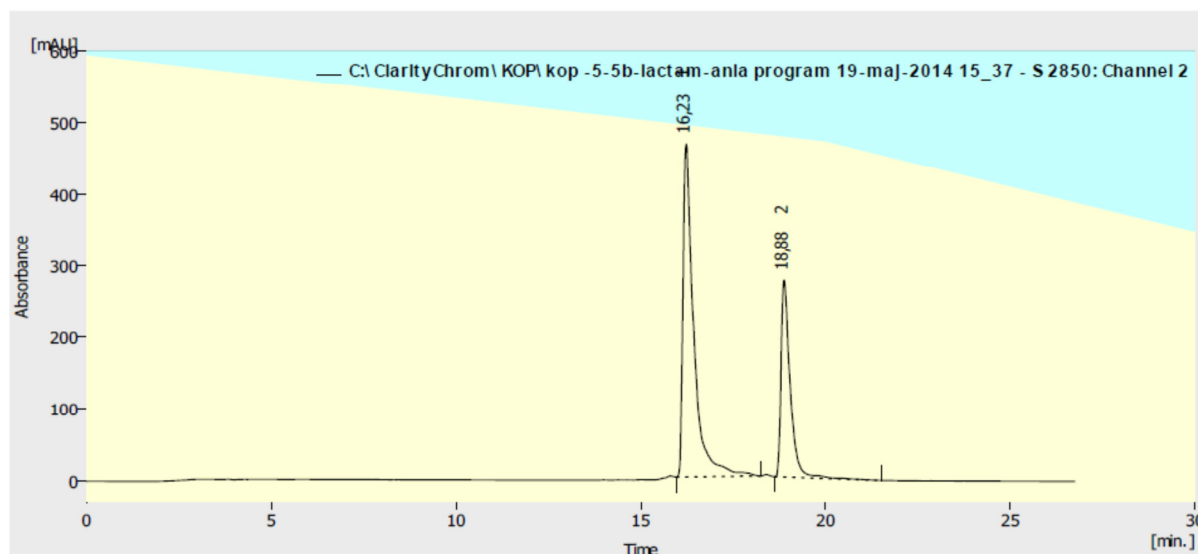
¹H NMR of (CN)₂Cbi(*c*-lactam) **6** in CD₃OD



¹³C NMR of (CN)₂Cbi(*c*-lactam) 6 in CD₃OD



HPLC of (CN)₂Cbi(c-lactam) 6 (NaCN in MW)



Result Table (Uncal - C:\ClarityChrom\KOP\kop -5-5b-lactam-ania program 19-maj-2014 15_37 - S 2850: Channel 2)

	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Peak Purity [-]
1	16,233	9436,413	464,378	66,8	62,9	0,28	840
2	18,883	4686,276	273,948	33,2	37,1	0,25	793
	Total	14122,689	738,326	100,0	100,0		

HPLC, t_r 16.2 and 18.8 min. (Eurospher II 100-5 C18 250 mm x 4.6 mm column, MeCN/H₂O 0.05% TFA, 1 mL/min)

HPLC gradient for (CN)₂Cbi(c-lactam)

HPLC Measurement conditions: Column: Eurospher II 100-5 C18 250 mm x 4.6 mm (Knauer) with a precolumn; detection: UV-Vis, wavelength: $\lambda = 361$ nm; flow rate: 1 mL/min; pressure: 10 Mpa, Temperature: 30 °C. HPLC method:

Time [min.]	H ₂ O + 0.05% TFA [%]	MeCN [%]
Initial	99	1
20	80	20
30	60	20