

Supporting Information for

**Vitamin B₁₂ derived cobryketone via
palladium catalyzed cleavage of the sp³-sp³ carbon-carbon bond**

Sylwester Kurcoń, Keith ó Proinsias, Dorota Gryko*

Institute of Organic Chemistry Polish Academy of Sciences, Kasprzaka 44/52, 01-224 Warsaw, Poland.

Table of Contents

	Page
<i>Catalyst screening table</i>	S3
<i>Oxidant screening table</i>	S3
<i>Mechanistic consideration</i>	S3
(CN)₂Cby(III)(OMe)₇ (1)	
¹ H NMR	S4
(CN)₂Cby(III)(8-CO)(OMe)₆ (2a)	
<i>Correlation table</i>	S5
<i>Full ¹H and ¹³C assignments for cobryketone 2a.</i>	S6
¹ H NMR	S7
¹³ C NMR	S8
COSY	S9
HSQC	S11
HMBC	S13
(CN)₂Cby(III)(8-CO)(O-<i>n</i>-Bu)₆ (2b)	
¹ H NMR	S17
¹³ C NMR	S18
(CN)₂Cby(III)(c-lactone)(O-<i>n</i>-Bu)₆ (3b)	
¹ H NMR	S19
¹³ C NMR	S20
(CN)₂-8-<i>nor</i>-Cby(III)(c-acid)(OMe)₅ (4)	
¹ H NMR	S21
ESI MS	S22
(CN)₂-8-<i>nor</i>-Cby(III)(OMe)₆ (5a)	
<i>Correlation table</i>	S23
<i>Full ¹H and ¹³C assignments for hexamethyl cobyrinate 5a.</i>	S24
¹ H NMR	S25
¹³ C NMR	S26
COSY	S27
HSQC	S29
HMBC	S31
(CN)₂-8-<i>nor</i>-Cby(III)(c-2-propylamide)(OMe)₅ (5b)	
¹ H NMR	S35
¹³ C NMR	S36
(CN)₂-8-<i>nor</i>-Cby(III)(c-2-hydroxyethylamide)(OMe)₅ (5c)	
¹ H NMR	S37
¹³ C NMR	S38
(CN)₂-8-<i>nor</i>-Cby(III)(c-propargylamide)(OMe)₅ (5d)	
¹ H NMR	S39
¹³ C NMR	S40
GC/MS chromatogram	S41
GC/MS spectra comparison	S42

Table S1 Catalyst screening.^a

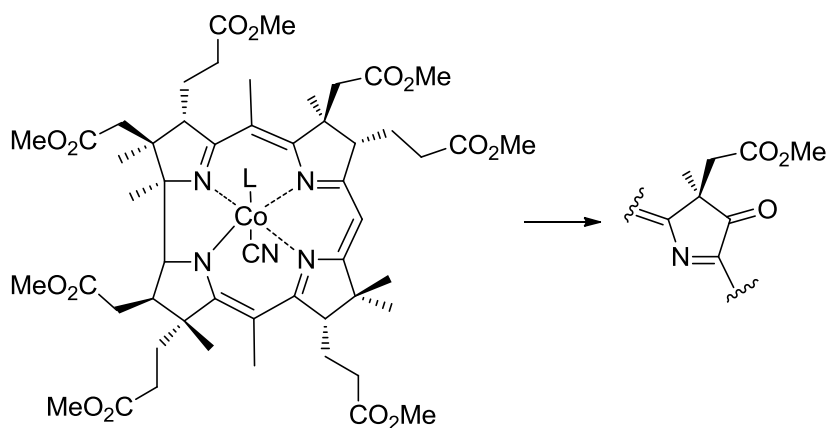
Entry	Catalyst	Time [h]	Yield of cobryketone 2 [%]
1	PdCl ₂ (COD)	72	trace
2	Na ₂ PdCl ₄	72	trace
3	Pd ₂ dba ₃ ·CHCl ₃	16	24
4	PdCl ₂	72	trace
5	Pd(PPh ₃) ₂ Cl ₂	192	23
6	Rh ₂ (COD) ₂ Cl ₂	3.5	14
7	Pd(acac) ₂	4.5	21

^a Reaction condition: (CN)₂Cby(III)(OMe)₇ **1** (14 μmol), Pd source 20% mol, PPh₃ 40% mol, H₂O 1equiv., DMF saturated O₂, conc. 0.07 M, 80 °C.

Table S2 Oxidant screening.^a

Entry	Oxidant	Result
1	DDQ	n. d.
2	Ag ₂ O	n. d.
3	Cu(OAc) ₂	trace
4	Sc(OTf) ₂	n. d.
5	FeCl ₃	n. d.
6	CAN	n. d.

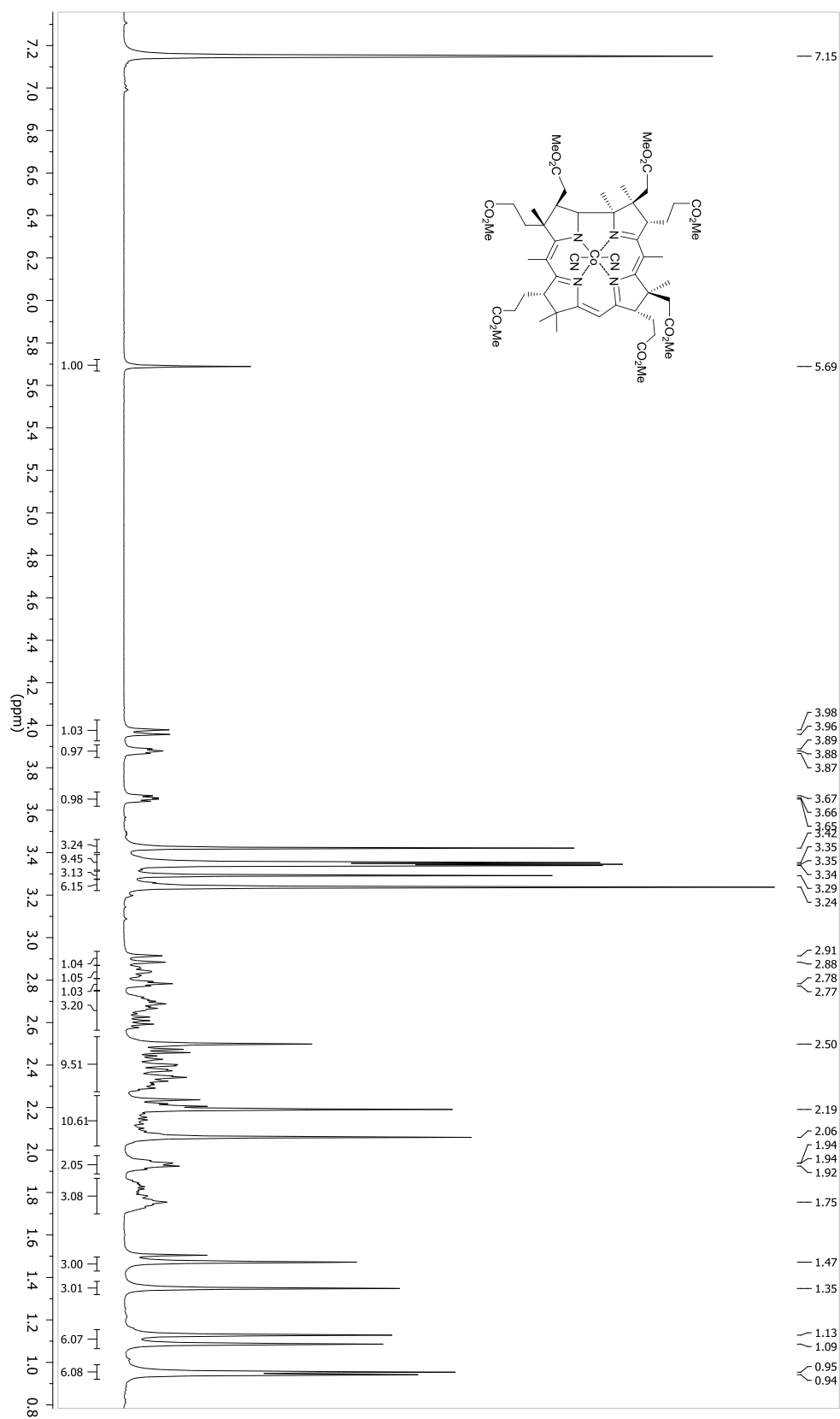
^a Reaction condition: (CN)₂Cby(III)(OMe)₇ **1** (14 μmol), Pd(OAc)₂ 20% mol, PPh₃ 40% mol, oxidant 1equiv., DMF, conc. 0.07 M, 80 °C, 24 h; n.d. – not detected.

Table S3 Mechanistic considerations.^a

Entry	L	Additive	Time [h]	Yield [%]
1	CN	NaCN	48	17
2	H ₂ O ⁺ /ClO ₄ ⁻	-	48	traces
3	CN	TEMPO	4	29

^a Reaction condition: Pd(OAc)₂ 20% mol, PPh₃ 40% mol, H₂O 1 equiv., additive 1 equiv., DMF conc. 0.07 M, 80 °C.

(CN)₂Cby(III)(OMe)₇ (1a) ¹H NMR (500 MHz) measured in C₆D₆ at 303.0 K



(CN)₂Cby(III)(8-CO)(OMe)₆ (2a)

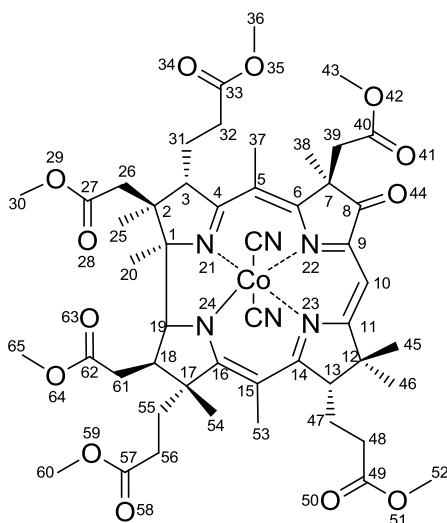


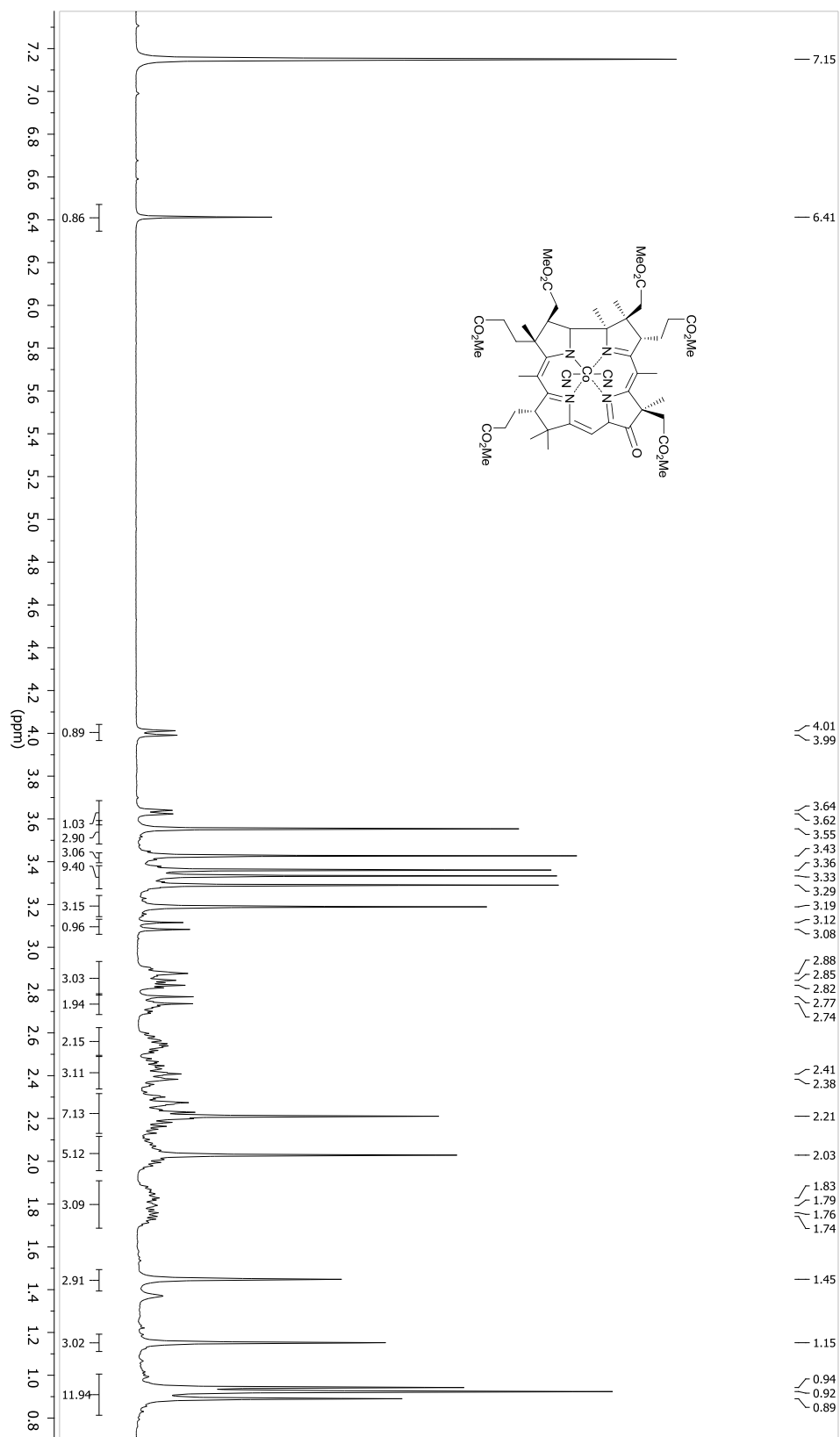
TABLE S4. Full correlation table for compound 5a.

Resonance	HSQC correlation	HMBC correlation
6.41	C10	C12; C9; C11; C8
4.00	C19	C2; C18; C61; C20; C1; C15; C14; C16
3.63	C3	C31; C32; C26; C2; C1; C5; C4
3.55	C43	C40
3.43	C36	C33
3.36	C60	C57
3.33	C65	C62
3.29	C52	C49
3.19	C30	C27
3.10	C39	C38; C7; C6; C40; C8
2.75	C39	C38; C7; C40; C8
2.88	C18	C54; C61; C55; C17; C19; C1
2.86	C26	C25; C2; C3; C1; C27
2.22	C26	C25; C2; C3; C1; C27
2.82	C13	C47; C45 or C46; C48; C12; C15; C14; C16; C11
2.72	C56	C55; C57
2.38	C56	C55; C57
2.57	C48	C47; C13; C49
2.26	C48	C47; C13; C49
2.54	C32	C31; C3; C33
2.46	C32	C31; C3; C33
2.40	C55	C54; C56; C18; C17; C57
1.80	C55	C54; C56; C18; C17; C16
2.28	C61	C18; C17; C19; C62
2.17	C61	C18; C17; C62
2.05	C31	C32; C2; C3; C33
1.85	C31	C32; C2; C3; C33
2.01	C47	C48; C12; C13; C14; C49
1.74	C47	C48; C12; C13; C14; C49
2.21	C53	C15; C14; C16
2.03	C37	C7; C5; C6; C4
1.45	C20	C18; C2; C19; C1
1.15	C25	C26; C2; C3; C1
0.94	C38	C39; C7; C6; C40; C8
0.92	C45 or C46; C54	C45 or C46 and/or C56; C55; C18; C12; C13; C17; C16; C11; C47
0.89	C45 or C46	C45 or C46; C12; C13; C11

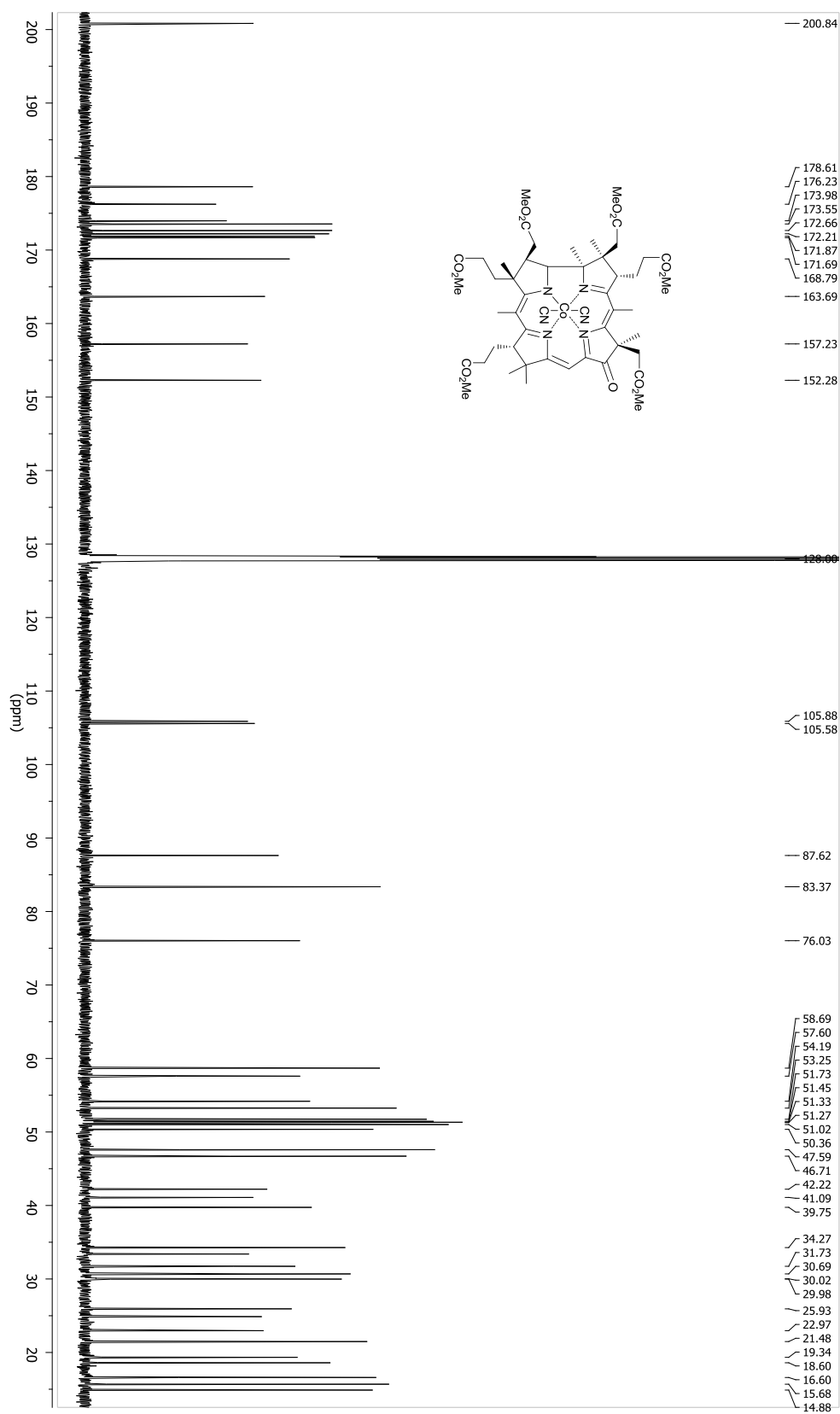
TABLE S5. Full ^1H and ^{13}C assignments for cobryketone **2a**.

group	$\delta^{13}\text{C}/\text{ppm}$	$\delta^1\text{H}/\text{ppm}$
C10	87.62	6.41
C19	76.03	4.00
C3	57.60	3.63
C43	53.25	3.55
C36	51.33	3.43
C60	51.45	3.36
C65	51.74	3.33
C52	51.02	3.29
C30	51.27	3.19
C39	42.22	3.10, 2.75
C18	39.75	2.88
C26	41.10	2.86, 2.22
C13	54.19	2.82
C56	30.03 or 29.99	2.72, 2.38
C48	30.69	2.57, 2.26
C32	34.27	2.54, 2.46
C55	33.39	2.40, 1.80
C61	31.73	2.28, 2.17
C31	24.88	2.05, 1.85
C47	25.94	2.01, 1.74
C53	15.96	2.21
C37	14.89	2.03
C20	22.97	1.45
C25	16.60	1.15
C38	21.49	0.94
C45 or C46	19.34	0.92
C54	18.60	0.92
C45 or C46	30.03 or 29.99	0.89
C1	83.37	
C2	46.71	
C4	173.98	
C5	105.59	
C6	157.24	
C7	50.37	
C8	200.84	
C9	152.30	
C11	178.62	
C12	47.60	
C14	163.69	
C15	105.88	
C16	176.24	
C17	58.69	
C27	171.87	
C33	172.21	
C40	168.79	
C49	173.55	
C57	172.66	
C62	171.69	

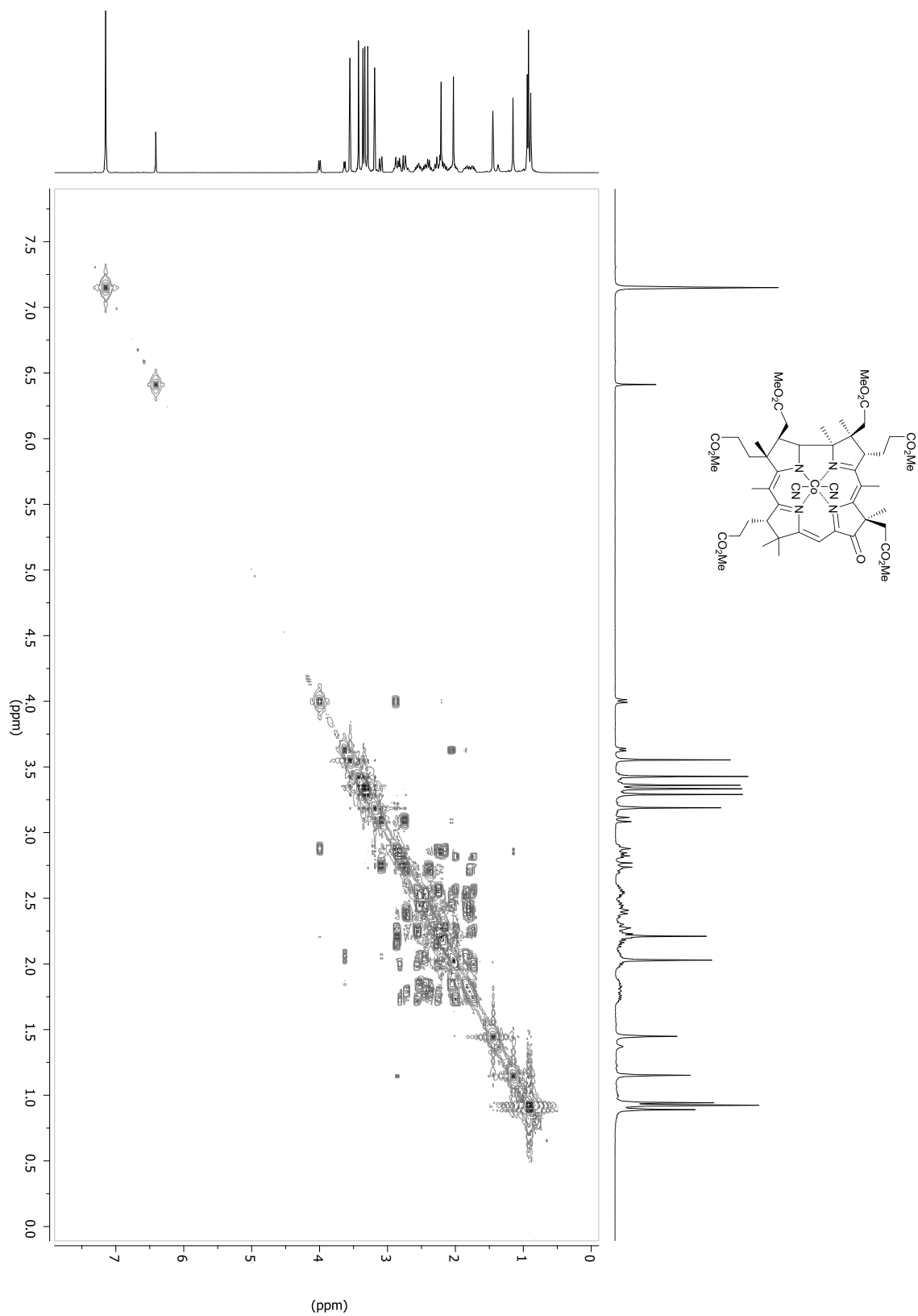
(CN)₂Cby(III)(8-CO)(OMe)₆ (2a) – ¹H NMR (500 MHz) measured in C₆D₆ at 303.0 K



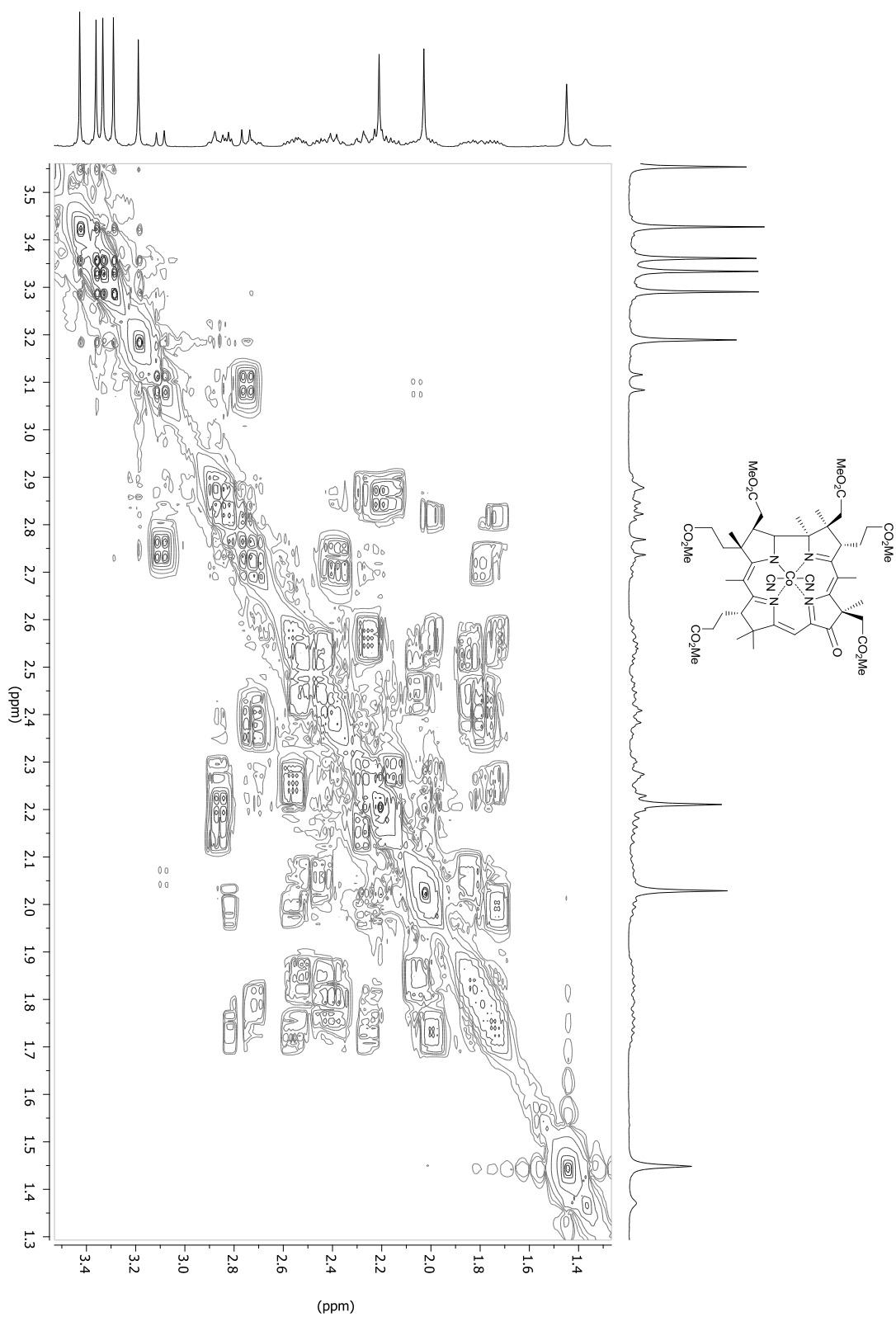
(CN)₂Cby(III)(8-CO)(OMe)₆ (2a) – ¹³C NMR (125 MHz) measured in C₆D₆ at 303.0 K



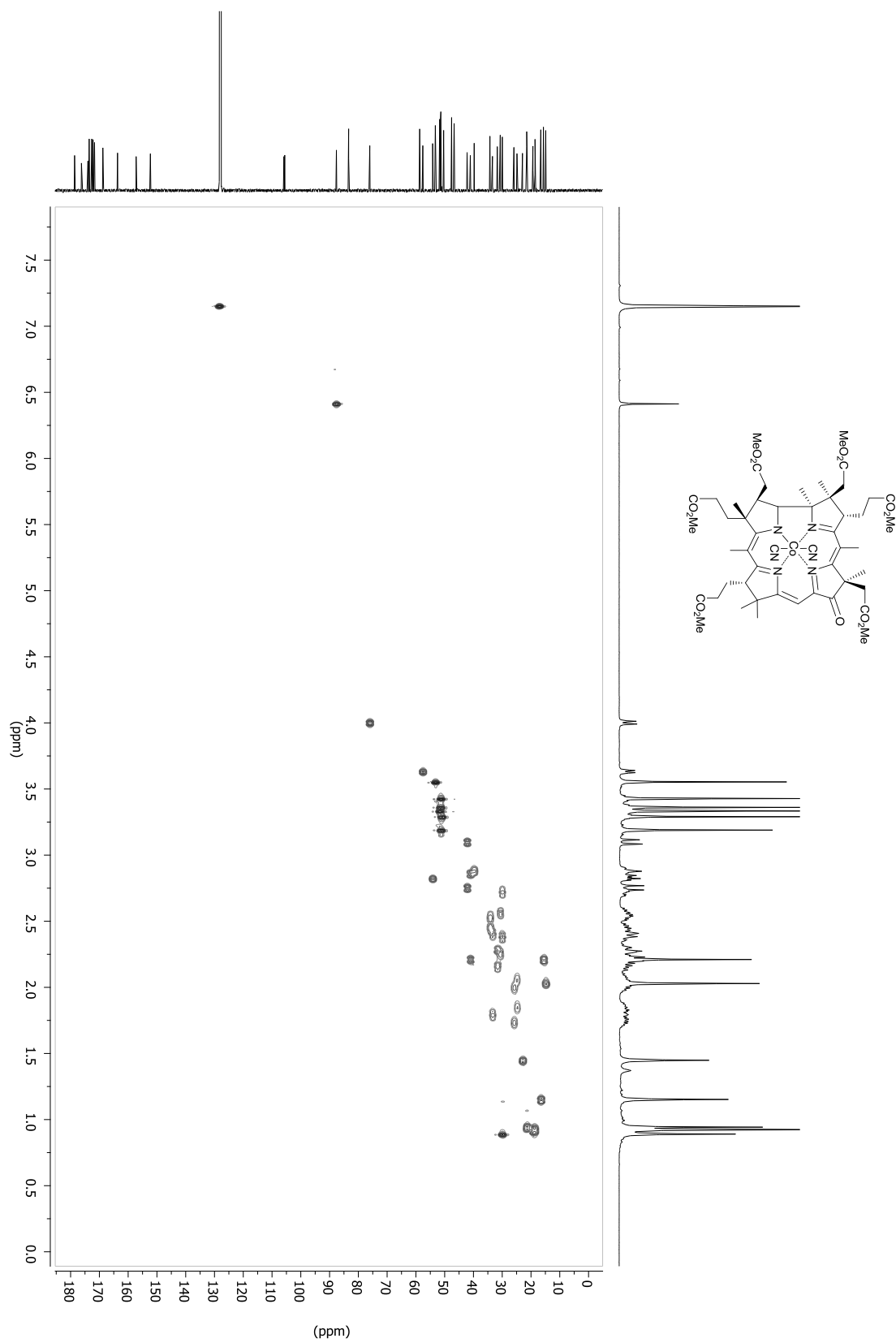
(CN)₂Cby(III)(8-CO)(OMe)₆ (2a) – ¹H/¹H COSY NMR measured in C₆D₆ at 303.0 K



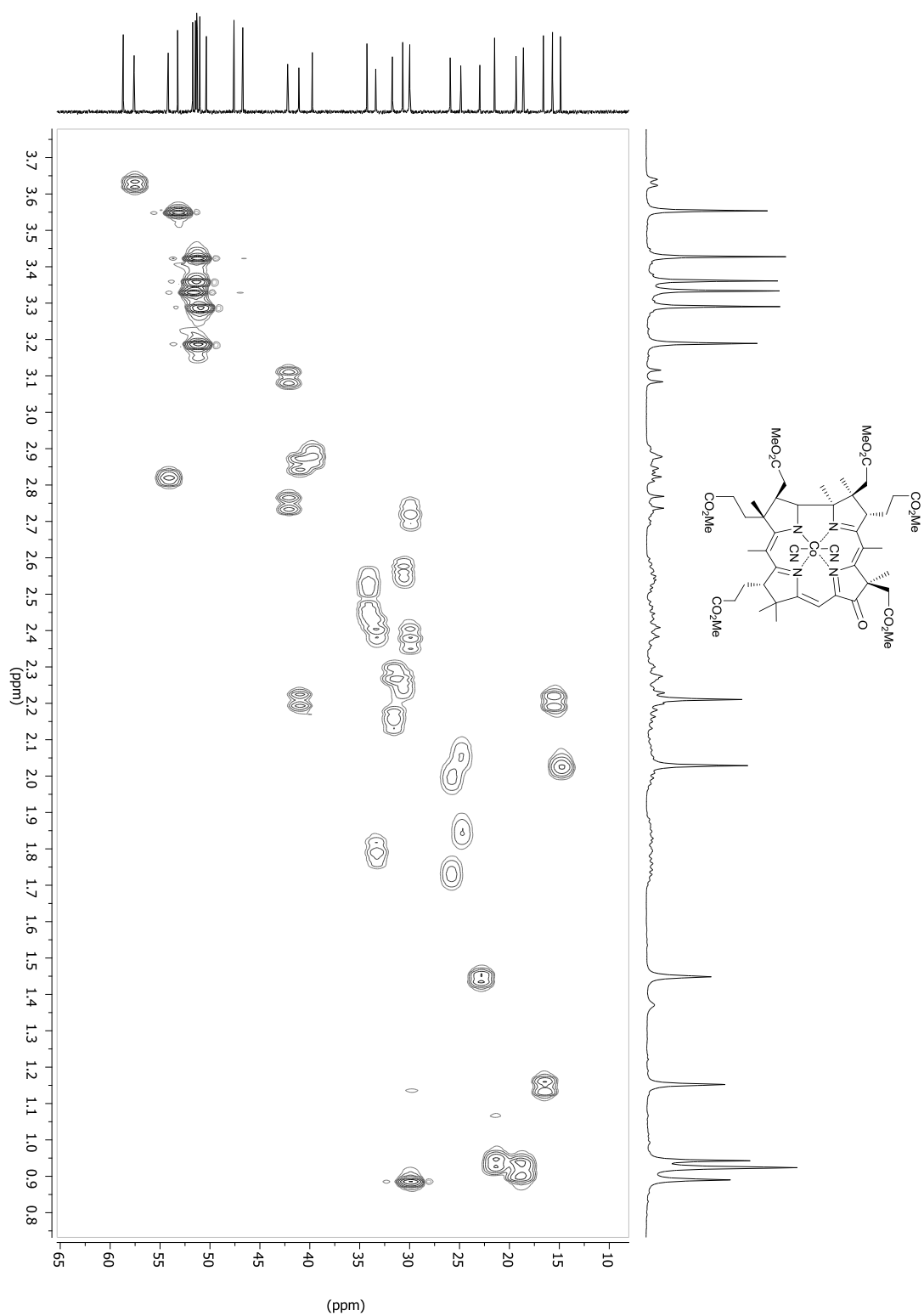
(CN)₂Cby(III)(8-CO)(OMe)₆ (2a) – expansion of ¹H/¹H COSY NMR measured in C₆D₆ at 303.0 K

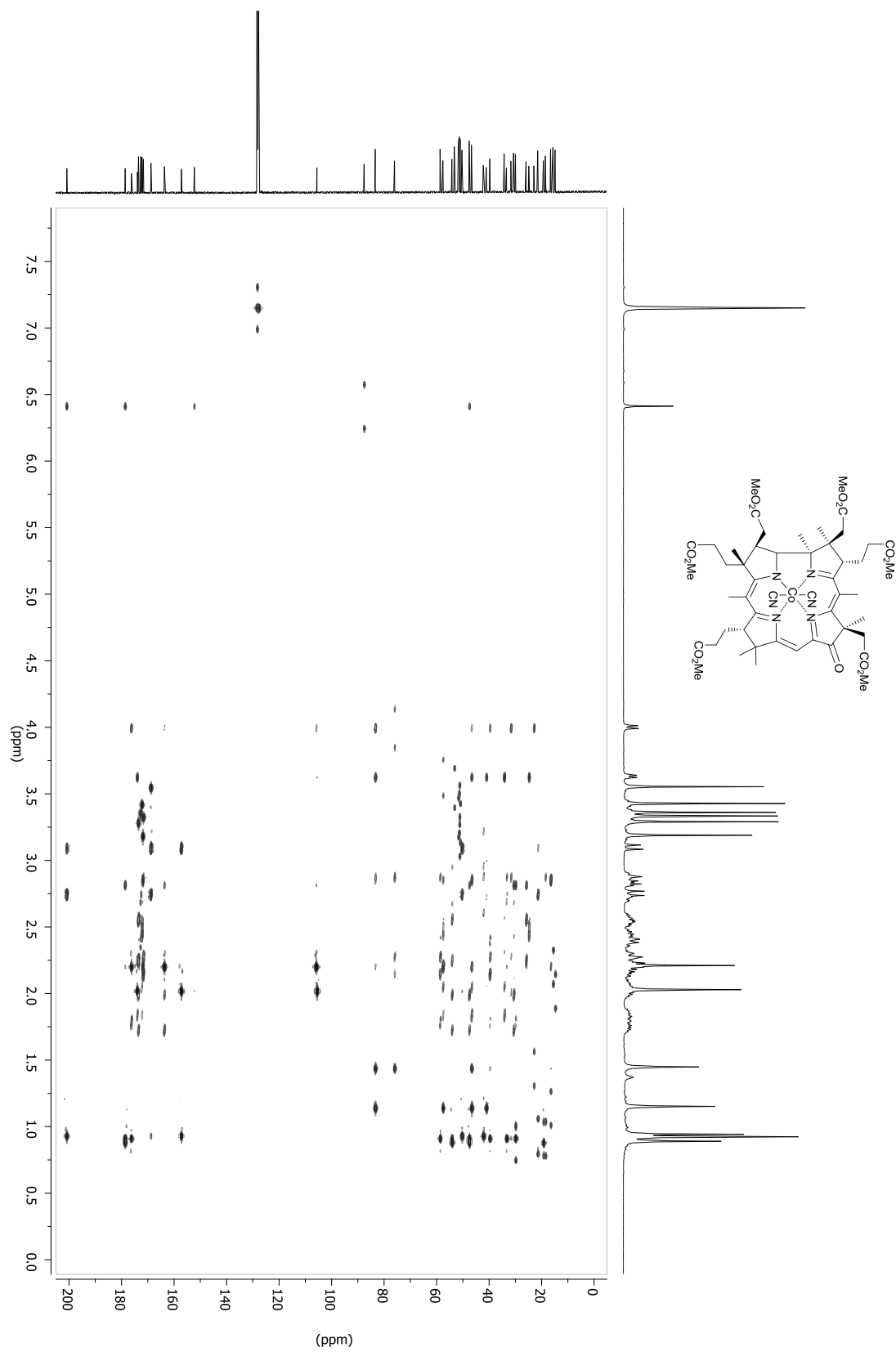


(CN)₂Cby(III)(8-CO)(OMe)₆ (2a) – ¹³C/¹H HSQC NMR measured in C₆D₆ at 303.0 K

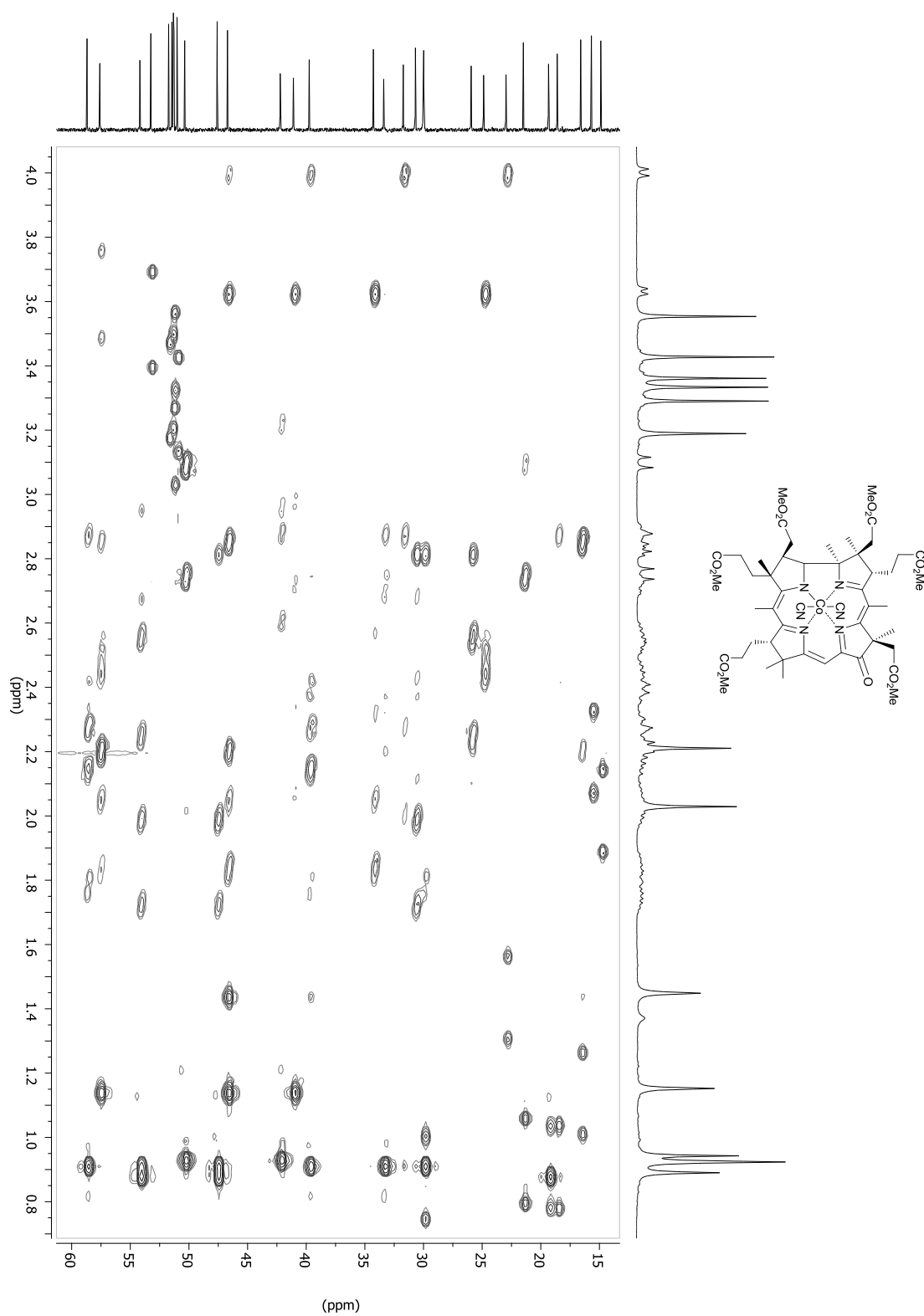


(CN)₂Cby(III)(8-CO)(OMe)₆ (2a) – expansion of ¹³C/¹H HSQC NMR measured in C₆D₆ at 303.0 K

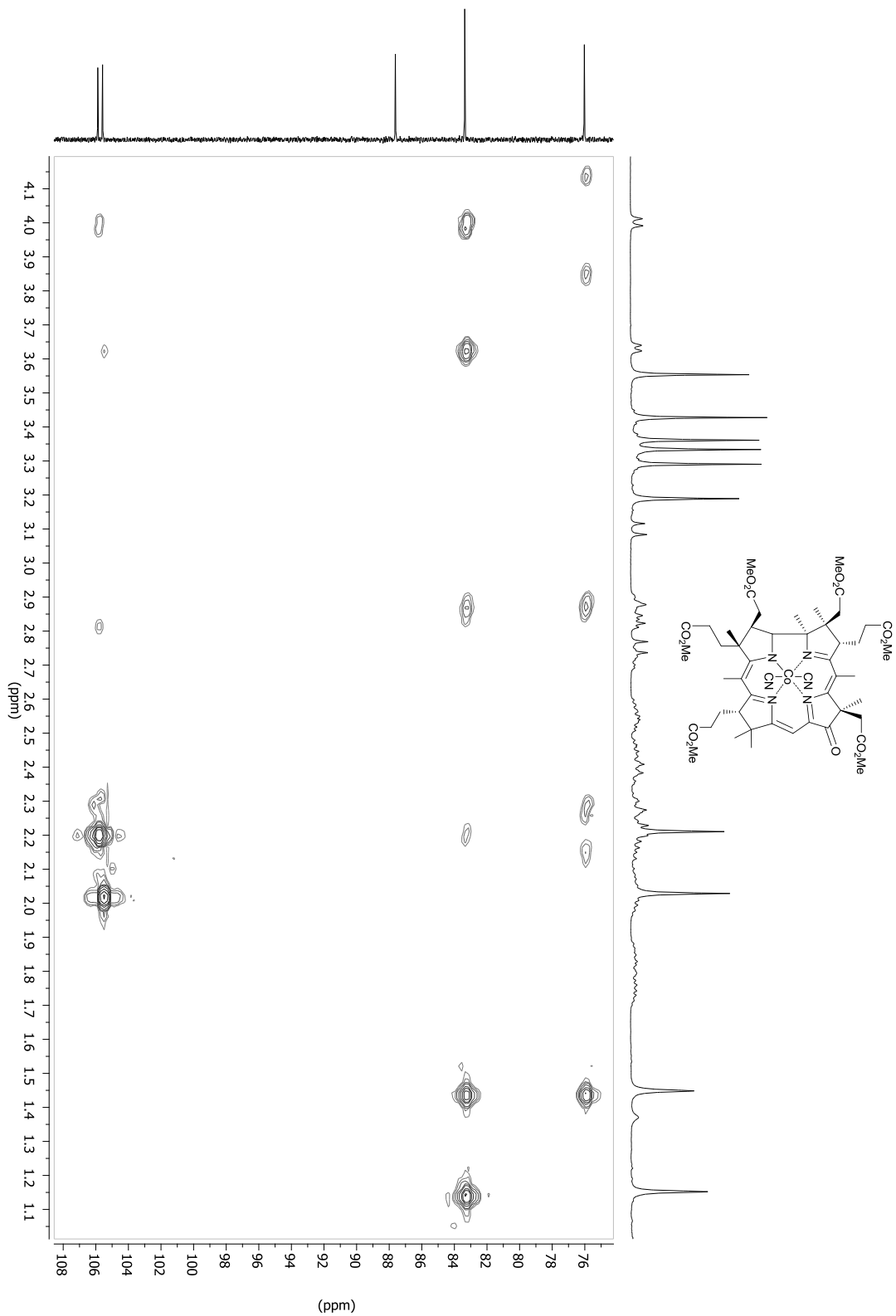




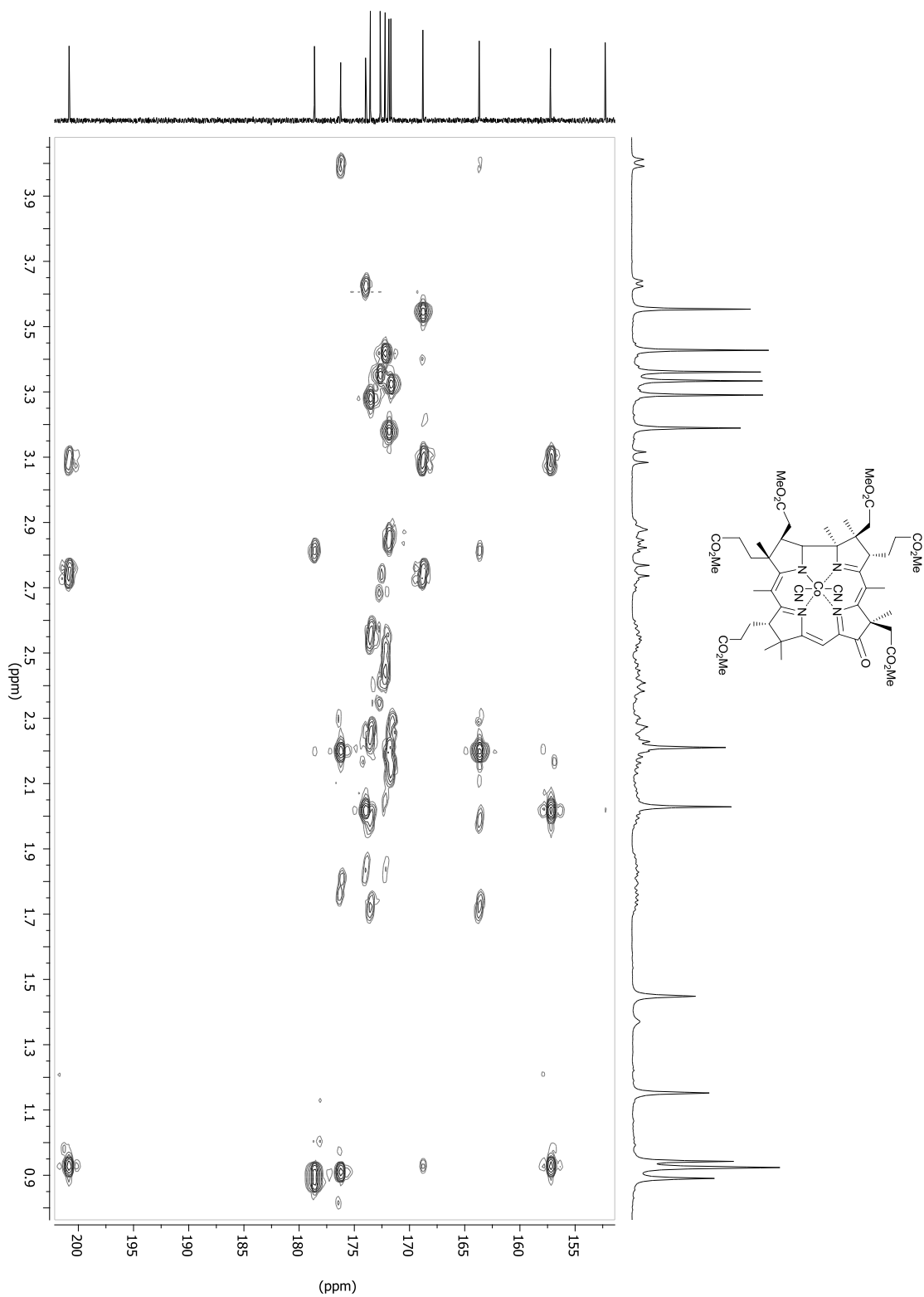
(CN)₂Cby(III)(8-CO)(OMe)₆ (2a) – expansion of ¹³C/¹H HMBC NMR measured in C₆D₆ at 303.0 K



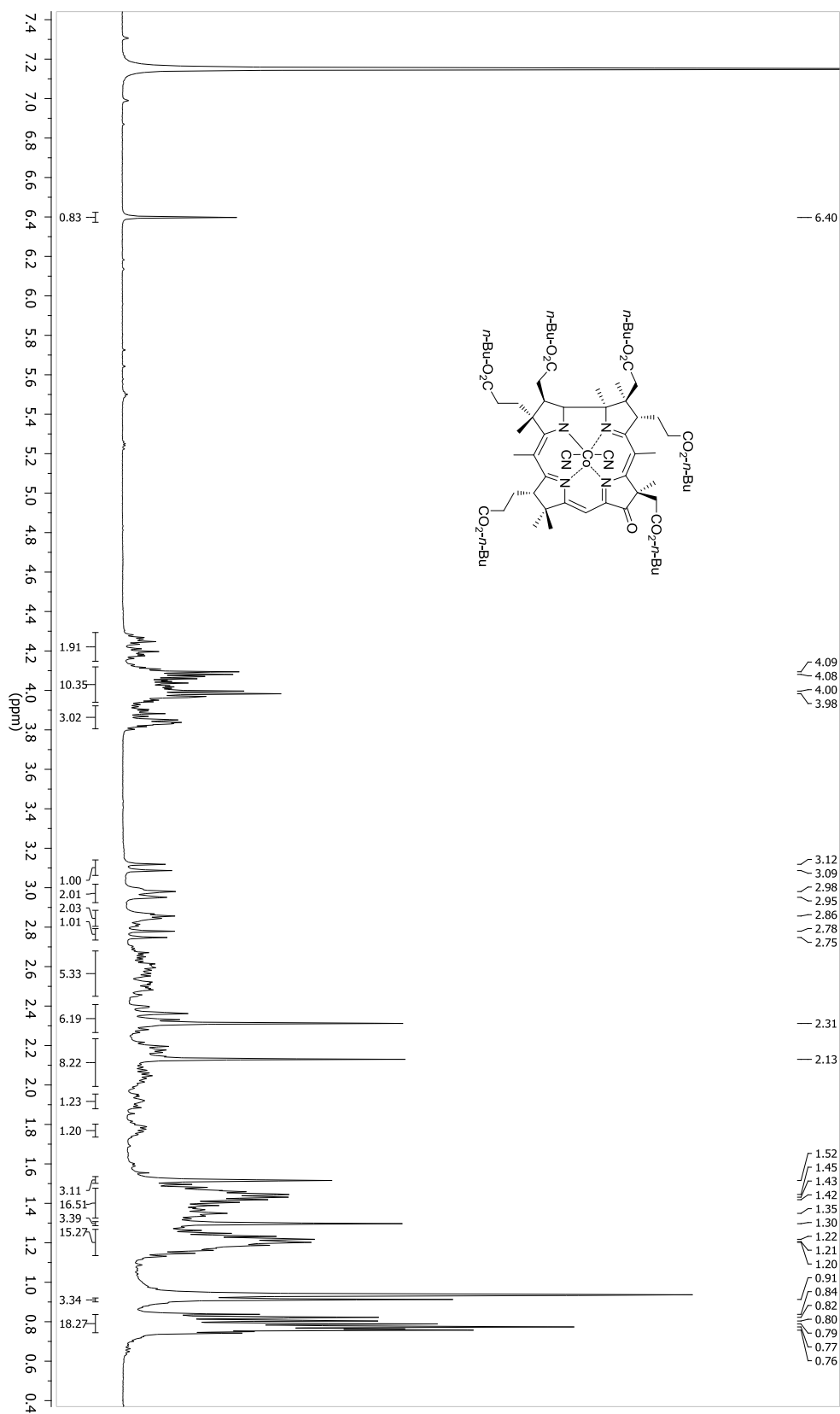
(CN)₂Cby(III)(8-CO)(OMe)₆ (**2a**) – expansion of ¹³C/¹H HMBC NMR measured in C₆D₆ at 303.0 K



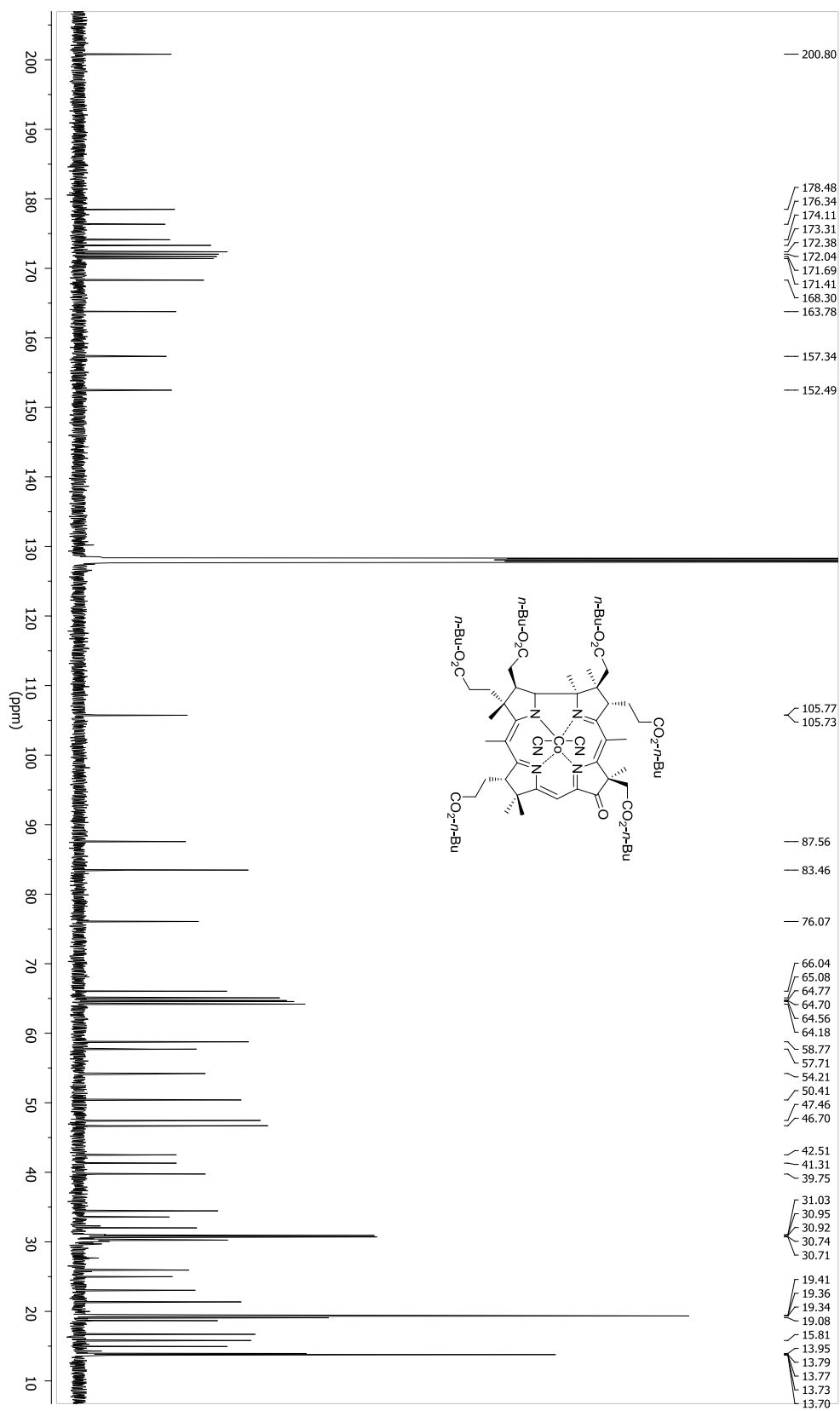
(CN)₂Cby(III)(8-CO)(OMe)₆ (2a) – expansion of ¹³C/¹H HMBC NMR measured in C₆D₆ at 303.0 K



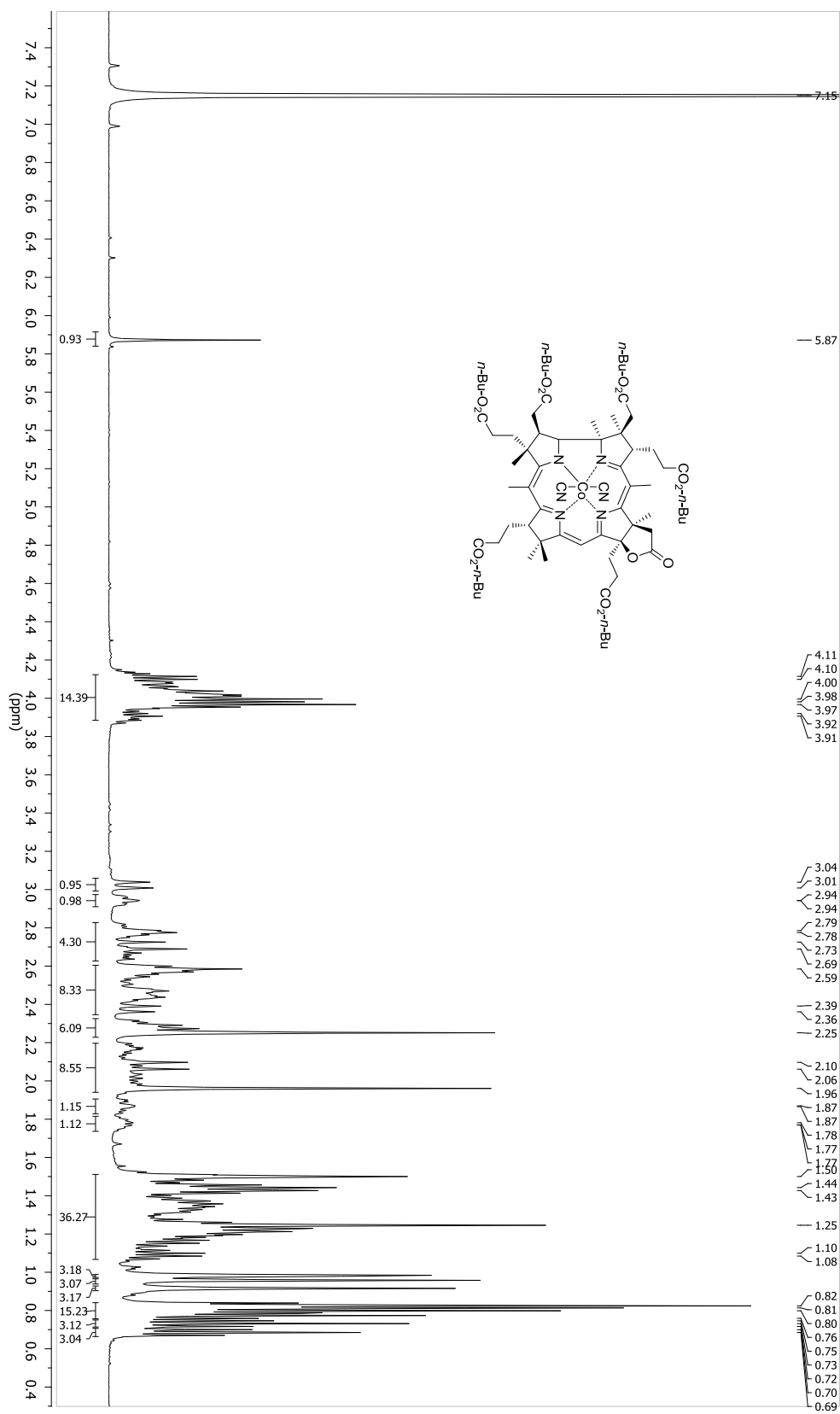
(CN)₂Cby(III)(8-CO)(O-*n*-Bu)₆ (2b) – ¹H NMR (500 MHz) measured in C₆D₆ at 303.0 K



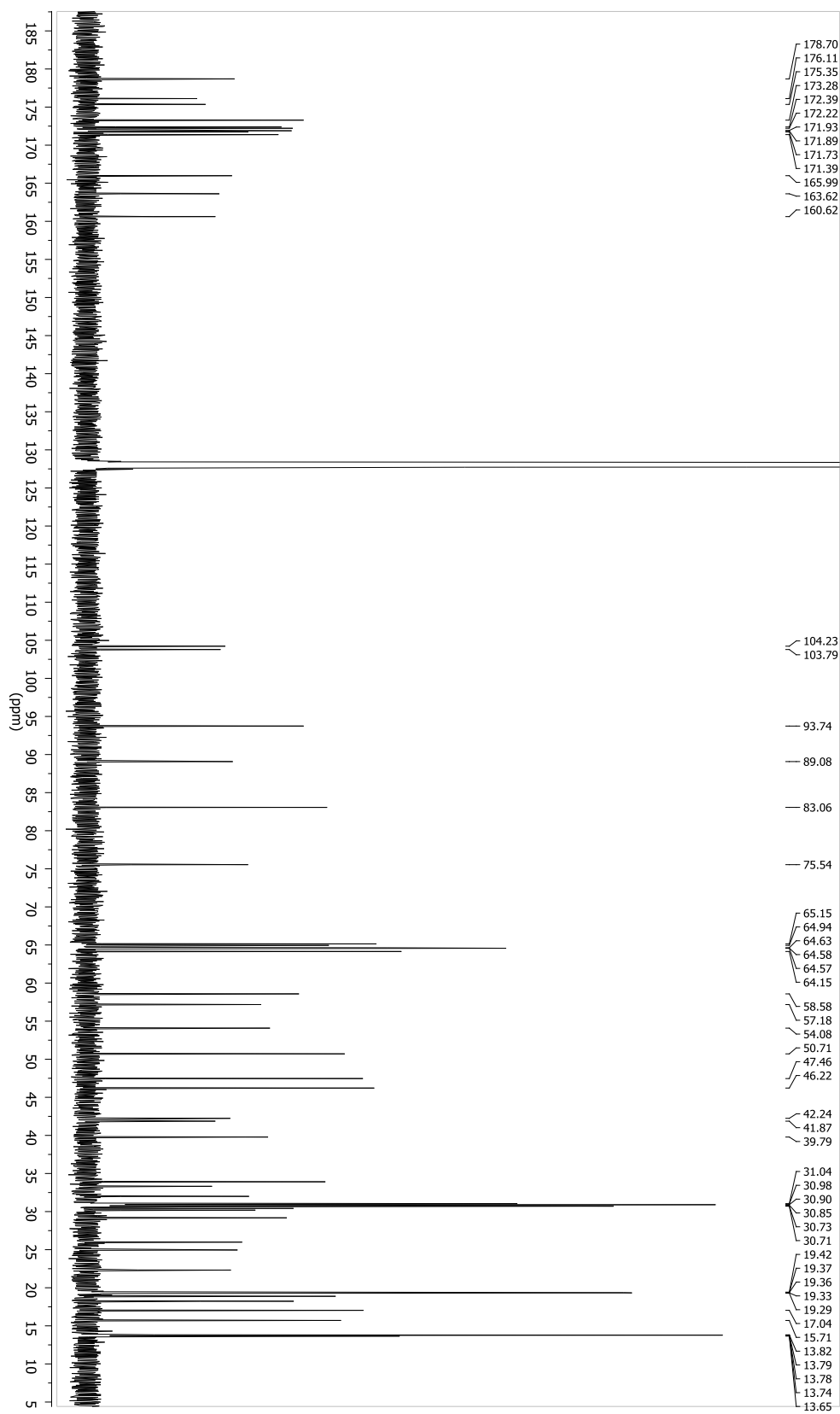
(CN)₂Cby(III)(8-CO)(O-*n*-Bu)₆ (2b) – ¹³C NMR (125 MHz) measured in C₆D₆ at 303.0 K



(CN)₂Cby(III)(c-lactone)(O-*n*-Bu)₆ (3b) – ¹H NMR (500 MHz) measured in C₆D₆ at 303.0 K

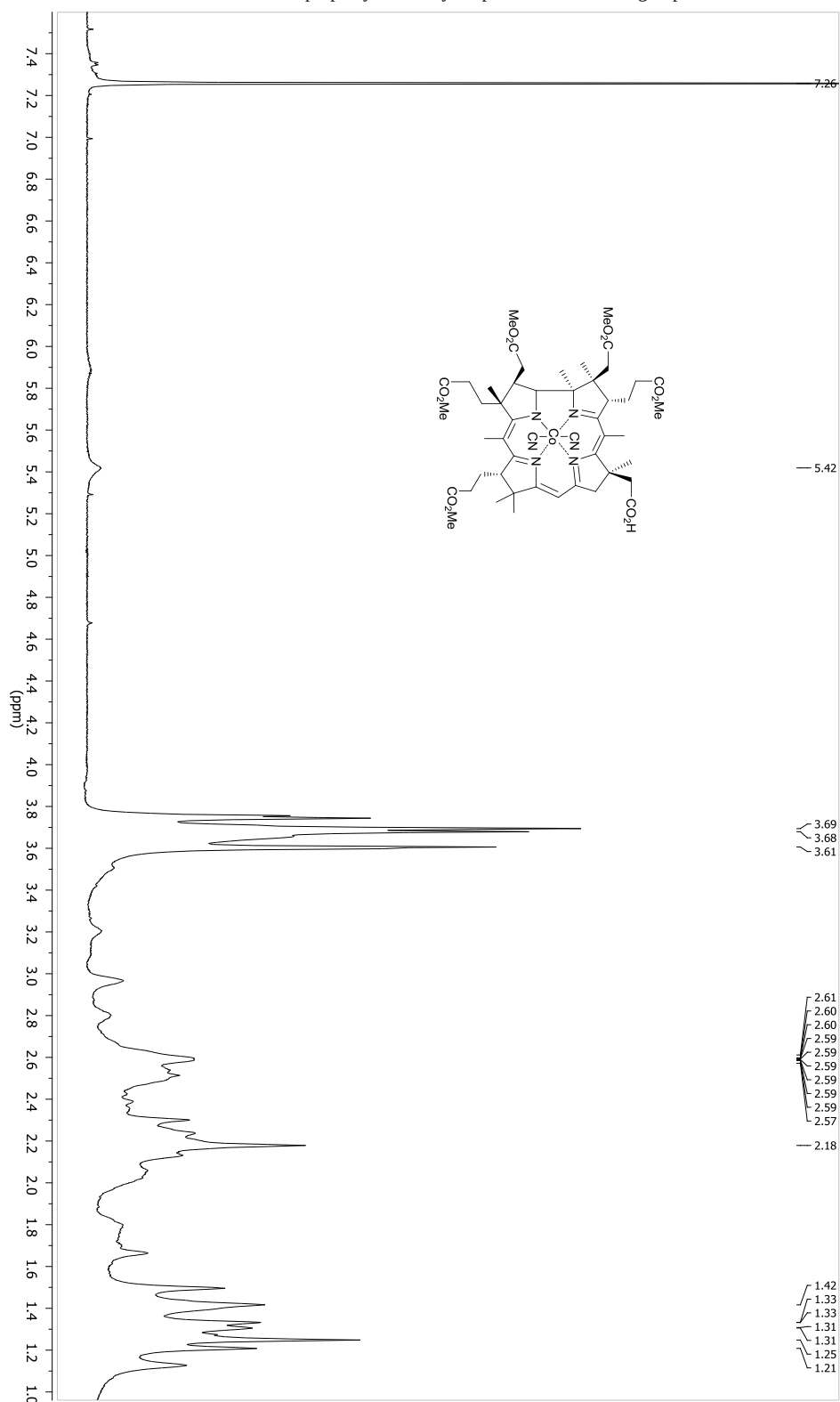


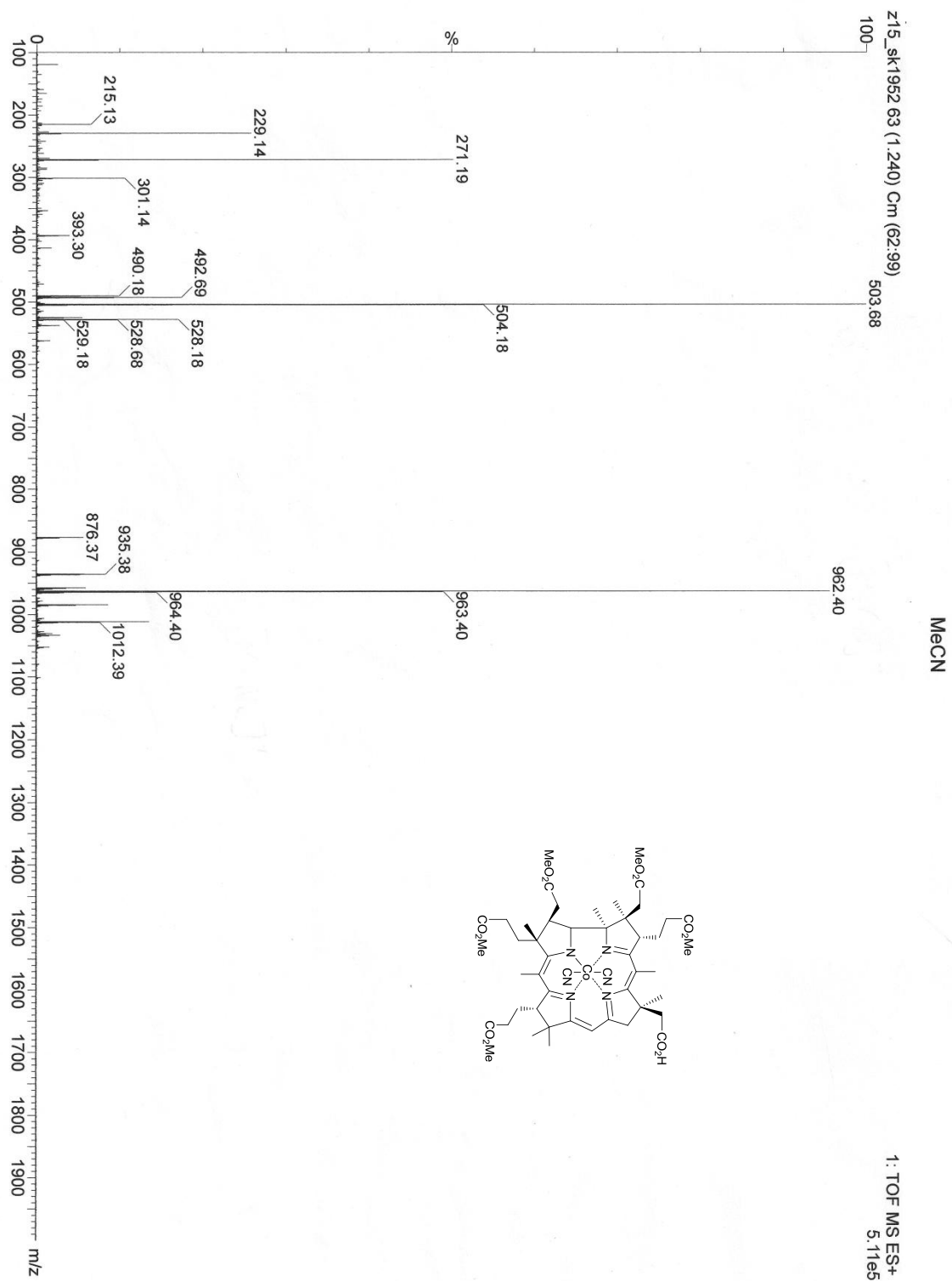
(CN)₂Cby(III)(*c*-lactone)(O-*n*-Bu)₆ (**3b**) – ¹³C NMR (125 MHz) measured in C₆D₆ at 303.0 K



(CN)₂-8-*nor*-Cby(III)(c-acid)(OMe)₅ (4) – ¹H NMR (400 MHz) measured in CDCl₃ at 303.0 K

Note: The broadening of peaks in the ¹H NMR spectrum made it impossible to decipher and consequently high resolution ¹³C spectra could not be obtained. This was probably caused by the presence of the acid group.





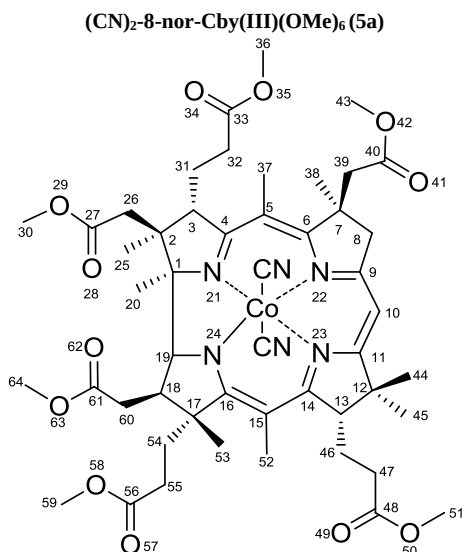


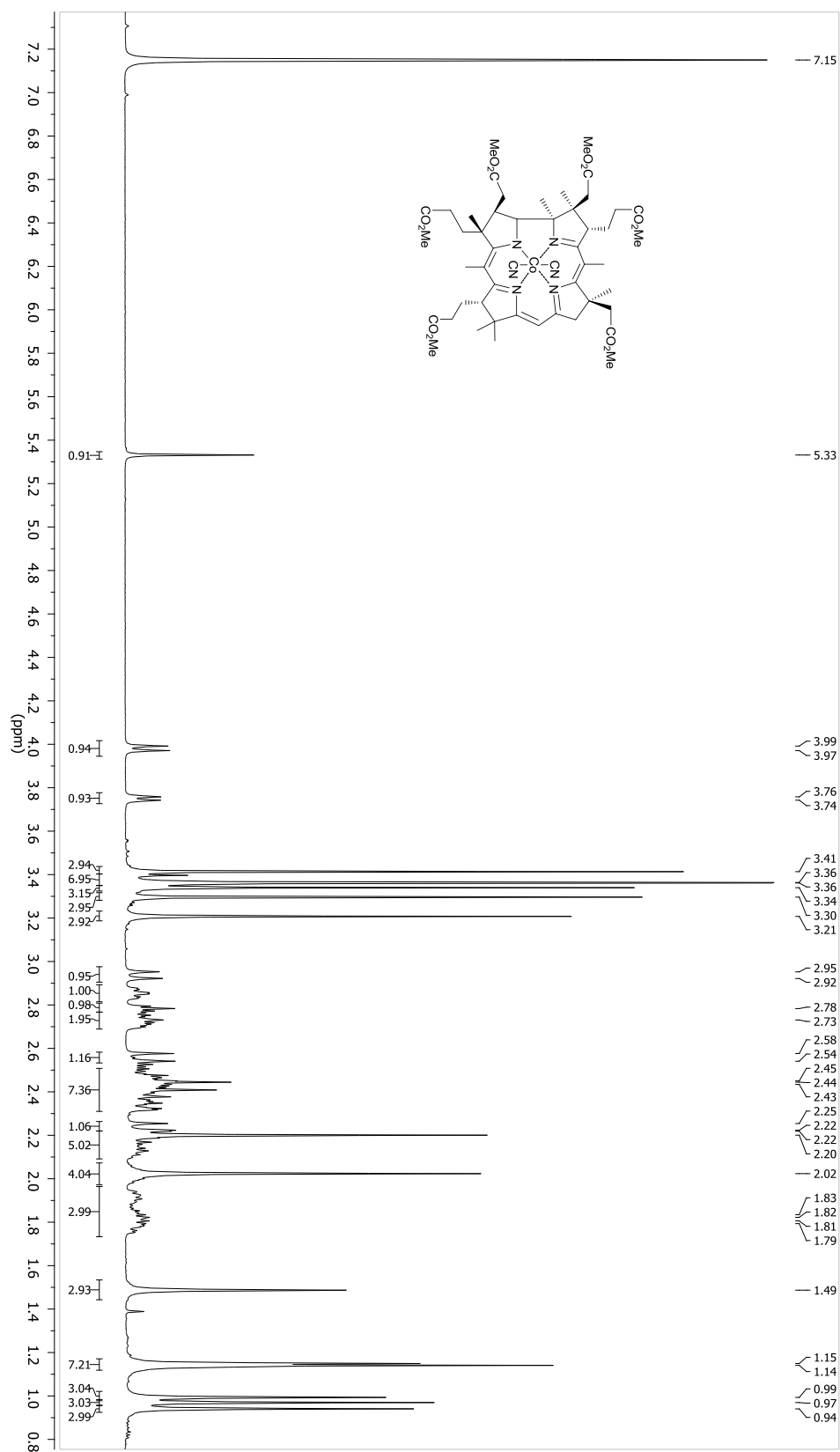
TABLE S6. Full correlation table for compound **5a**.

Resonance	HSQC correlation	HMBC correlation
5.33	C10	C12; C8; C9; C11
3.98	C19	C20; C60; C54; C18; C2; C1; C15; C14; C16
3.75	C3	C31; C32; C26; C2; C1; C5; C4
3.42	C36	C33
3.38	C8	C38; C39; C7; C10; C6; C9
2.56	C8	C38; C39; C7; C10; C9
3.364	C59	C56
3.362	C43	C40
3.34	C64	C61
3.30	C51	C48
3.21	C30	C27
2.94	C26	C25; C2; C3; C1; C27
2.24	C26	C25; C2; C3; C1; C27
2.86	C18	C53; C60; C54; C17; C19; C1; C61
2.78	C13	C46; C47; C44 or C45; C12; C15; C14; C11
2.74	C47	C46; C13; C48
2.35	C47	C46; C13; C48
2.71	C55	C54; C17; C56
2.43	C55	C54; C17; C56
2.50	C32	C31; C3; C33
2.46	C39	C38; C7; C8; C6; C40
2.40	C39	C38; C7; C8; C6; C40
2.44	C54	C55; C18; C17
1.78	C54	C55; C18; C17; C16
2.34	C60	C18; C17; C19; C61
2.19	C60	C18; C17; C19; C61
2.20	C52	C15; C14; C16
2.14	C46	C47; C12; C13; C14; C48
1.83	C46	C47; C12; C13; C14; C48
2.02	C37	C5; C6; C4
2.01	C31	C32; C2; C3; C33
1.92	C31	C32; C2; C3; C33; C4
1.49	C20	C18; C2; C19; C10
1.15	C25	C26; C2; C3; C1
1.14	C38	C39; C7; C8; C6
0.99	C45 or C44	C44 or C45; C12; C11; C13
0.97	C53	C54; C18; C17; C16
0.94	C44 or C45	C45 or C44; C12; C11; C13

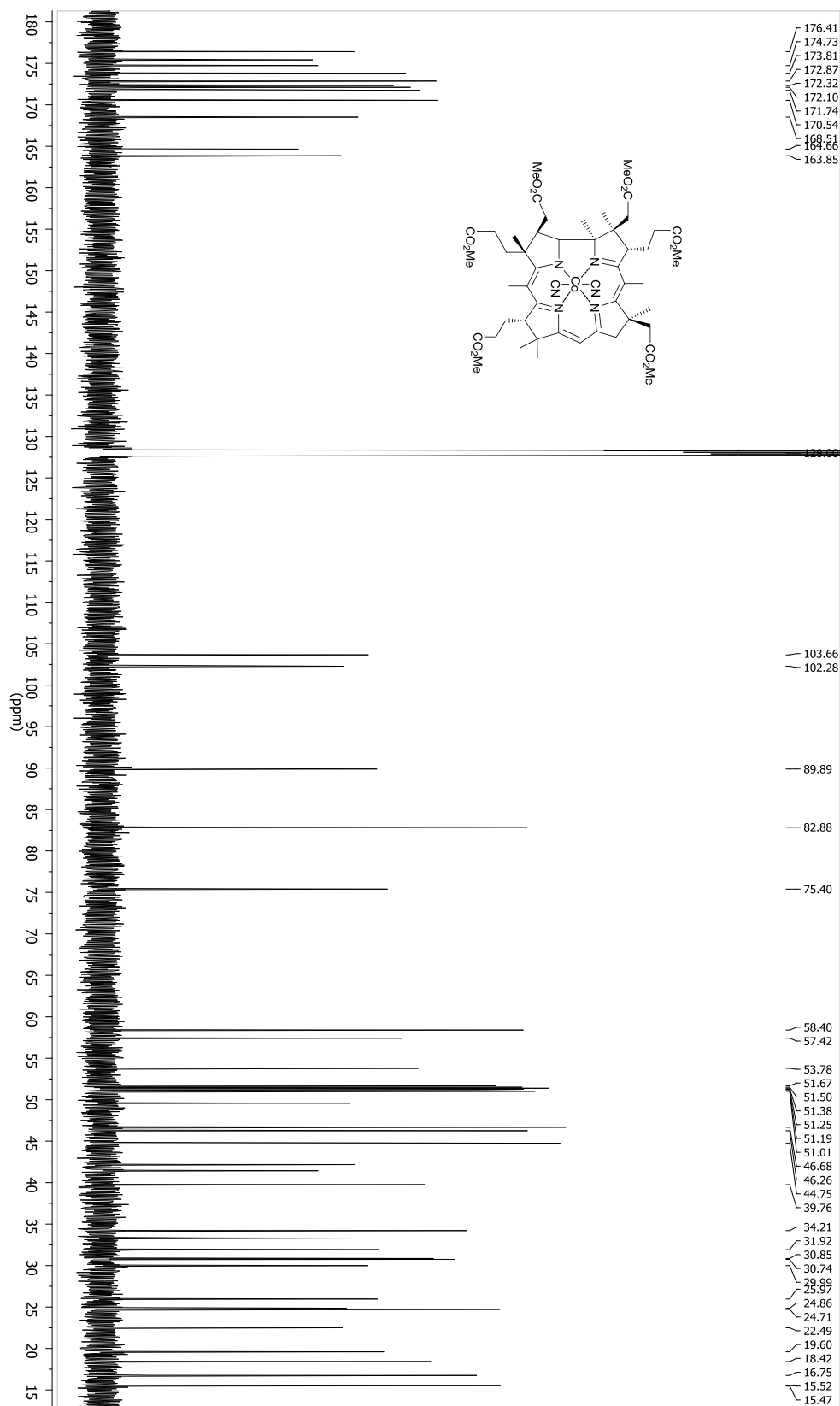
TABLE S7. Full ^1H and ^{13}C assignments for hexamethyl cobyrinate **5a**.

group	$\delta^{13}\text{C}/\text{ppm}$	$\delta^1\text{H}/\text{ppm}$
C10	89.89	5.33
C19	75.40	3.98
C3	57.42	3.75
C36	51.26	3.42
C8	49.58	3.38, 2.56
C59	51.50	3.364
C43	51.38	3.362
C64	51.68	3.34
C51	51.02	3.30
C30	51.19	3.21
C26	41.44	2.94, 2.24
C18	39.76	2.86
C13	53.79	2.78
C47	30.74	2.74, 2.35
C55	29.99	2.71, 2.43
C32	34.22	2.50
C39	42.18	2.46, 2.40
C54	33.32	2.44, 1.78
C60	31.92	2.34, 2.19
C52	15.52	2.20
C46	25.97	2.14, 1.83
C37	15.47	2.02
C31	24.86	2.01, 1.92
C20	22.50	1.49
C25	16.75	1.15
C38	24.71	1.14
C45 or C44	19.60	0.99
C53	18.42	0.97
C44 or C45	30.85	0.94
C1	82.88	
C2	46.26	
C4	174.73	
C5	103.66	
C6	164.66	
C7	44.75	
C9	168.51	
C11	176.41	
C12	46.69	
C14	163.86	
C15	102.28	
C16	175.41	
C17	58.40	
C27	172.10	
C33	172.32	
C40	170.54	
C48	173.81	
C56	172.87	
C61	171.74	

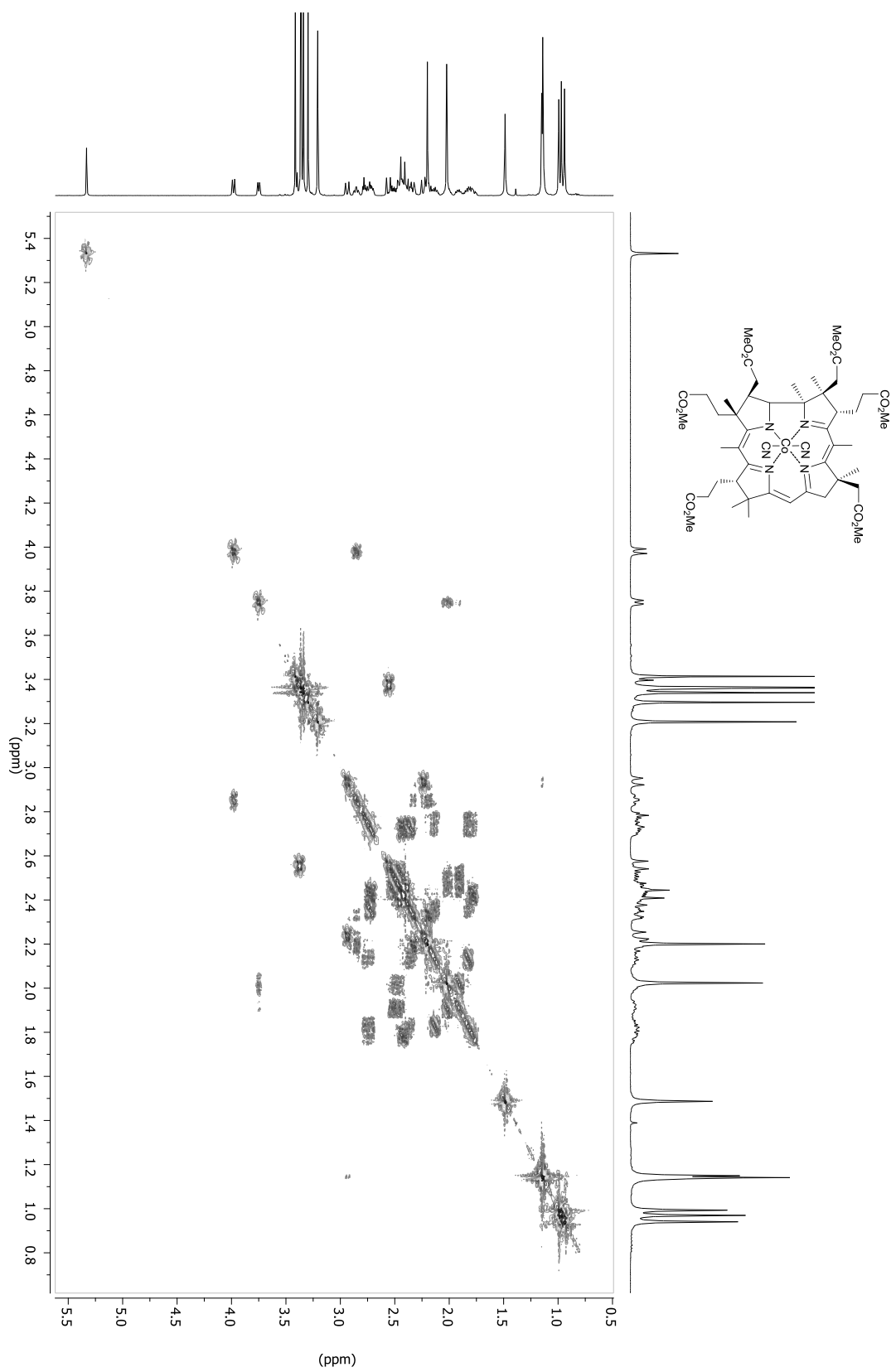
(CN)₂-8-*nor*-Cby(III)(OMe)₆ (5a) – ¹H NMR (500 MHz) measured in C₆D₆ at 303.0 K



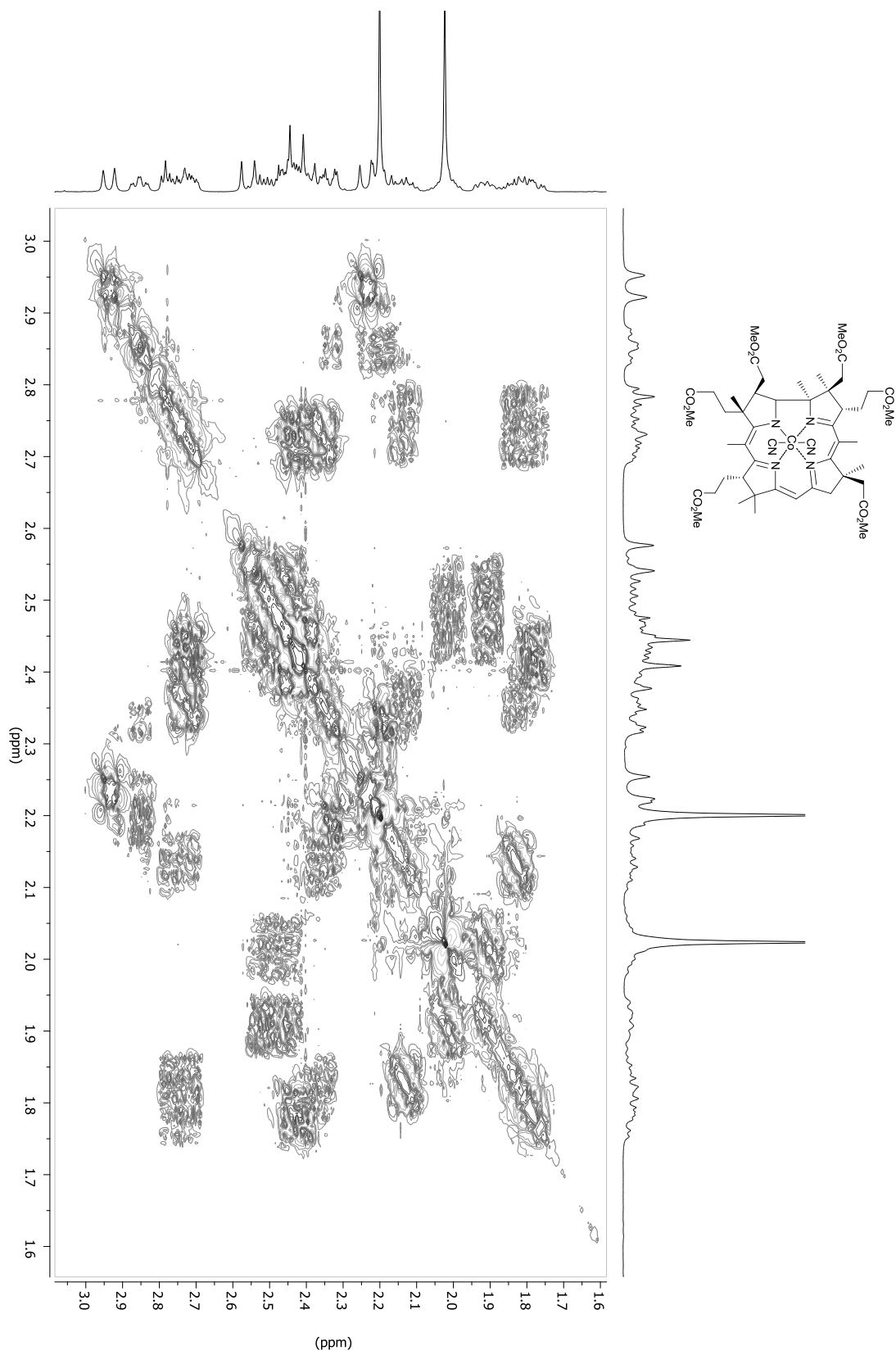
(CN)₂-8-*nor*-Cby(III)(OMe)₆ (5a) – ¹³C NMR (125 MHz) measured in C₆D₆ at 303.0 K



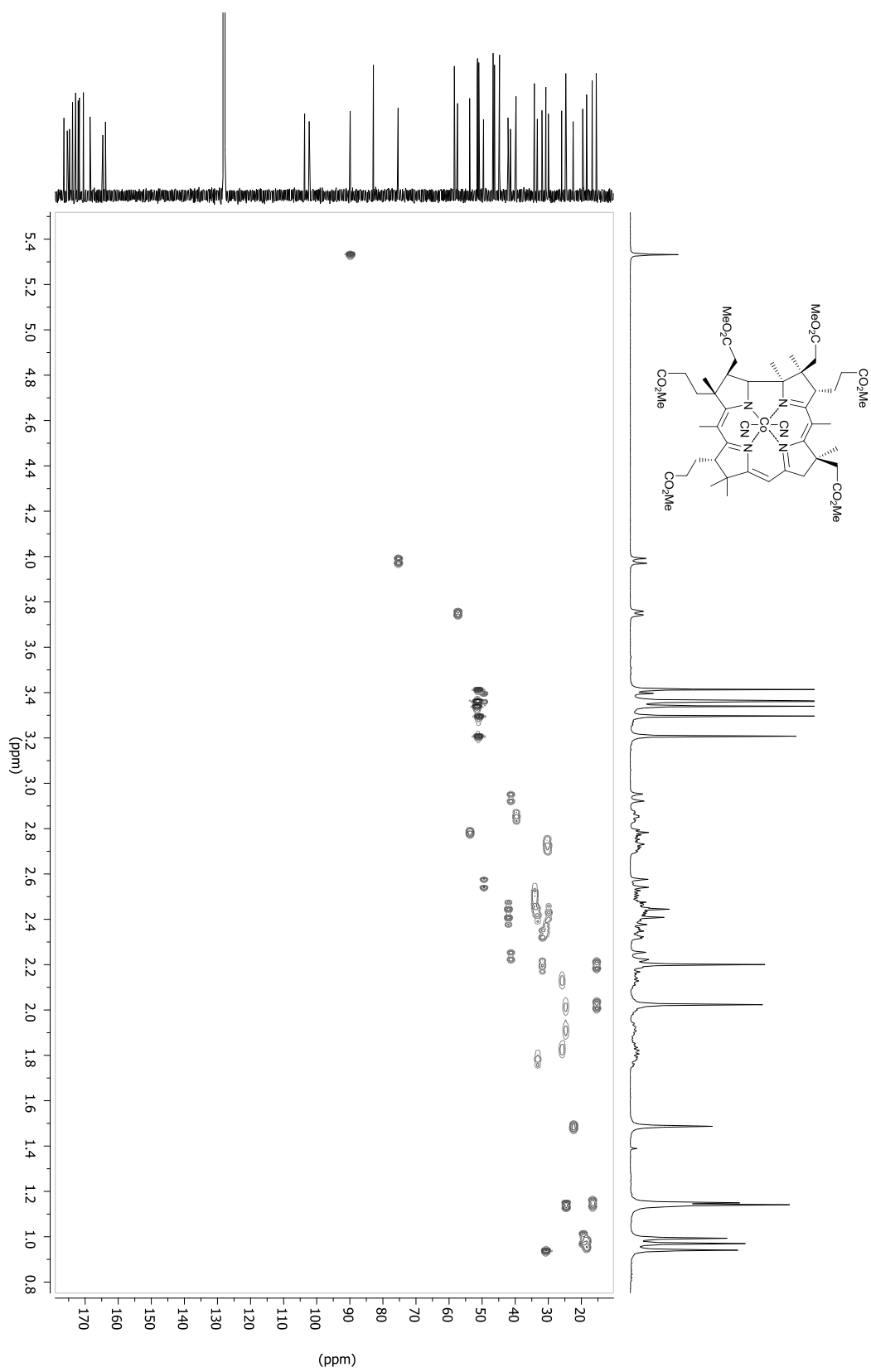
(CN)₂-8-*nor*-Cby(III)(OMe)₆ (5a) – ¹H/¹H COSY NMR measured in C₆D₆ at 303.0 K



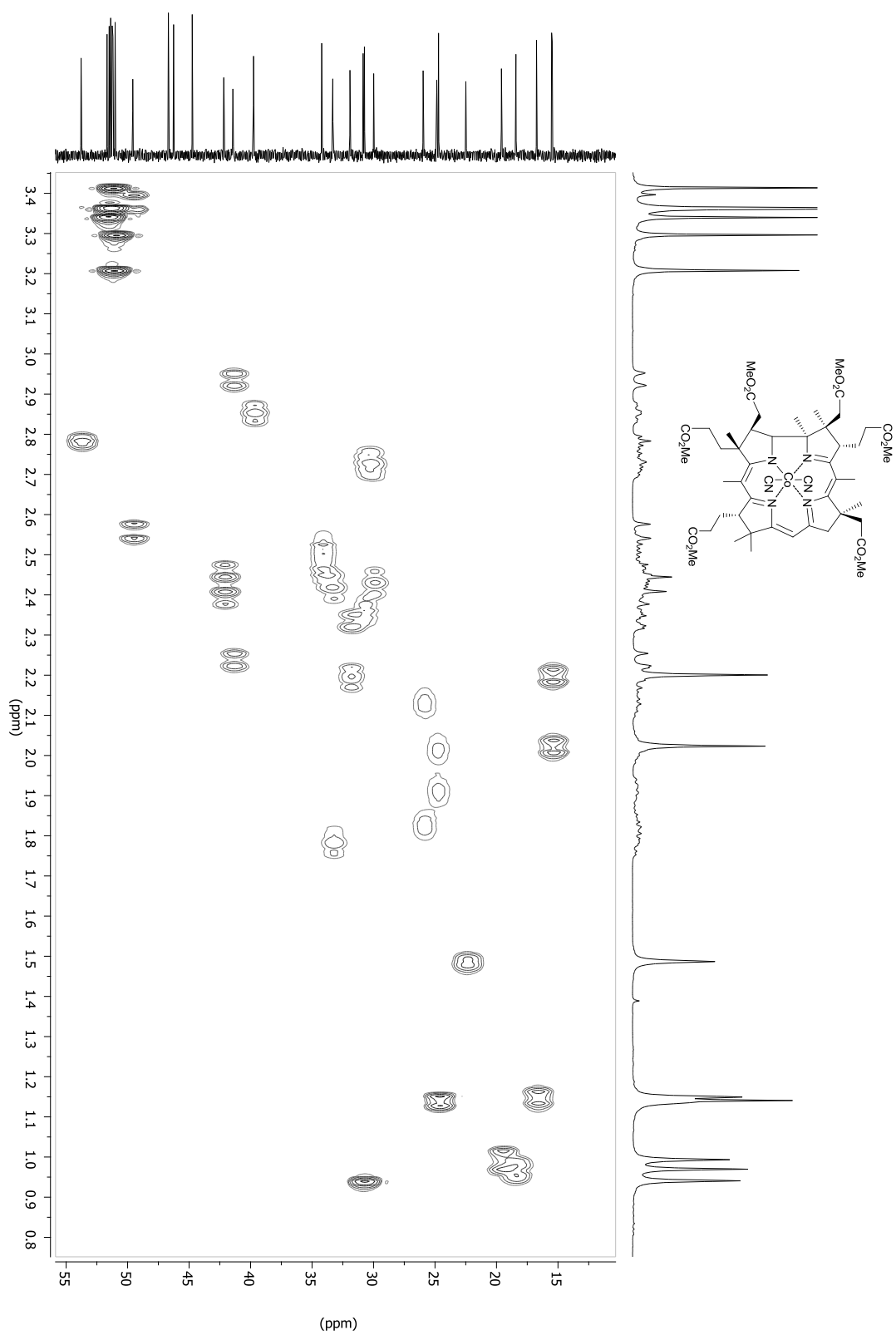
(CN)₂-8-*nor*-Cby(III)(OMe)₆ (5a) – expansion of ¹H/¹H COSY NMR measured in C₆D₆ at 303.0 K



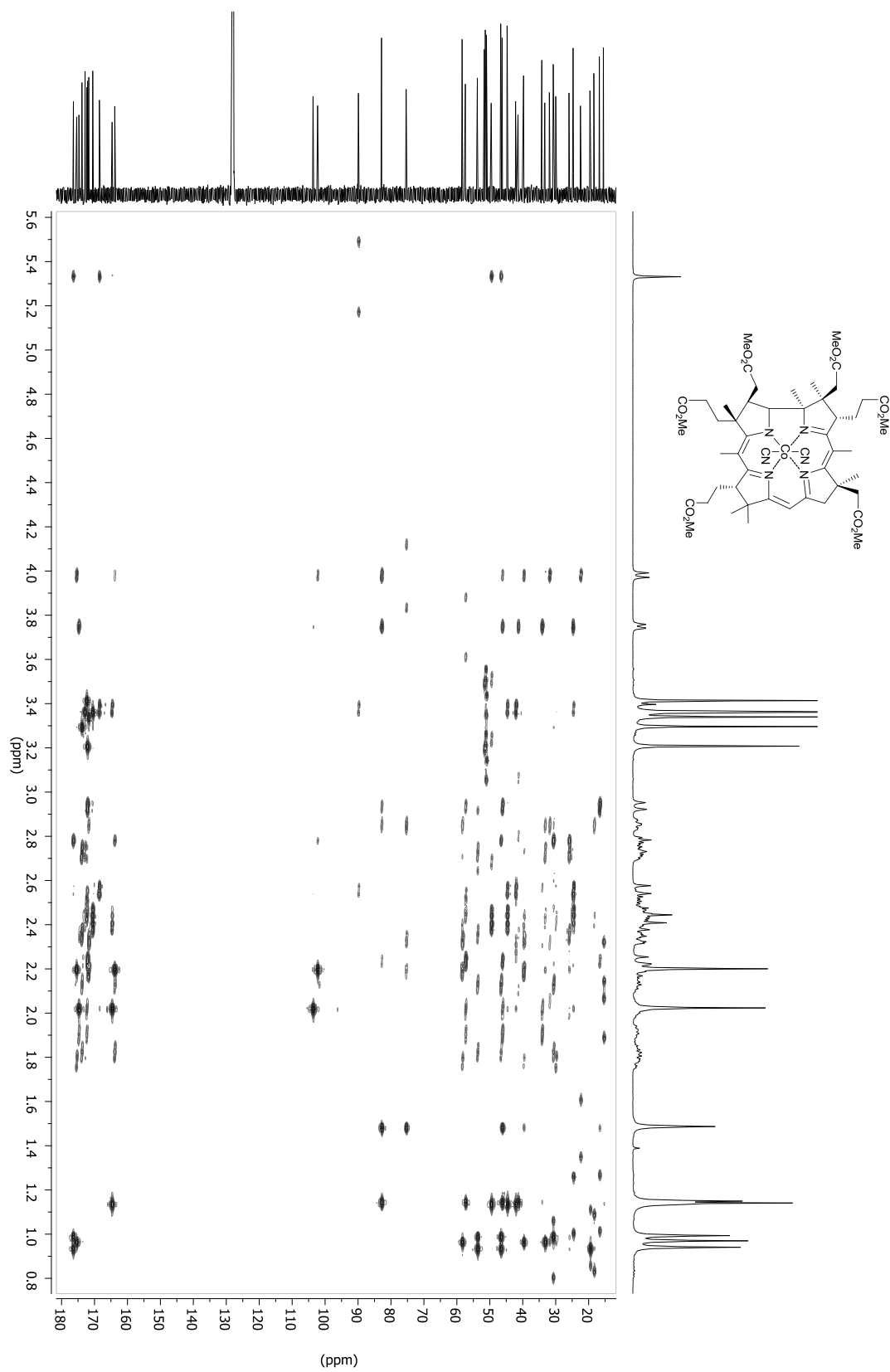
(CN)₂-8-*nor*-Cby(III)(OMe)₆ (5a) – ¹³C/¹H HSQC NMR measured in C₆D₆ at 303.0 K



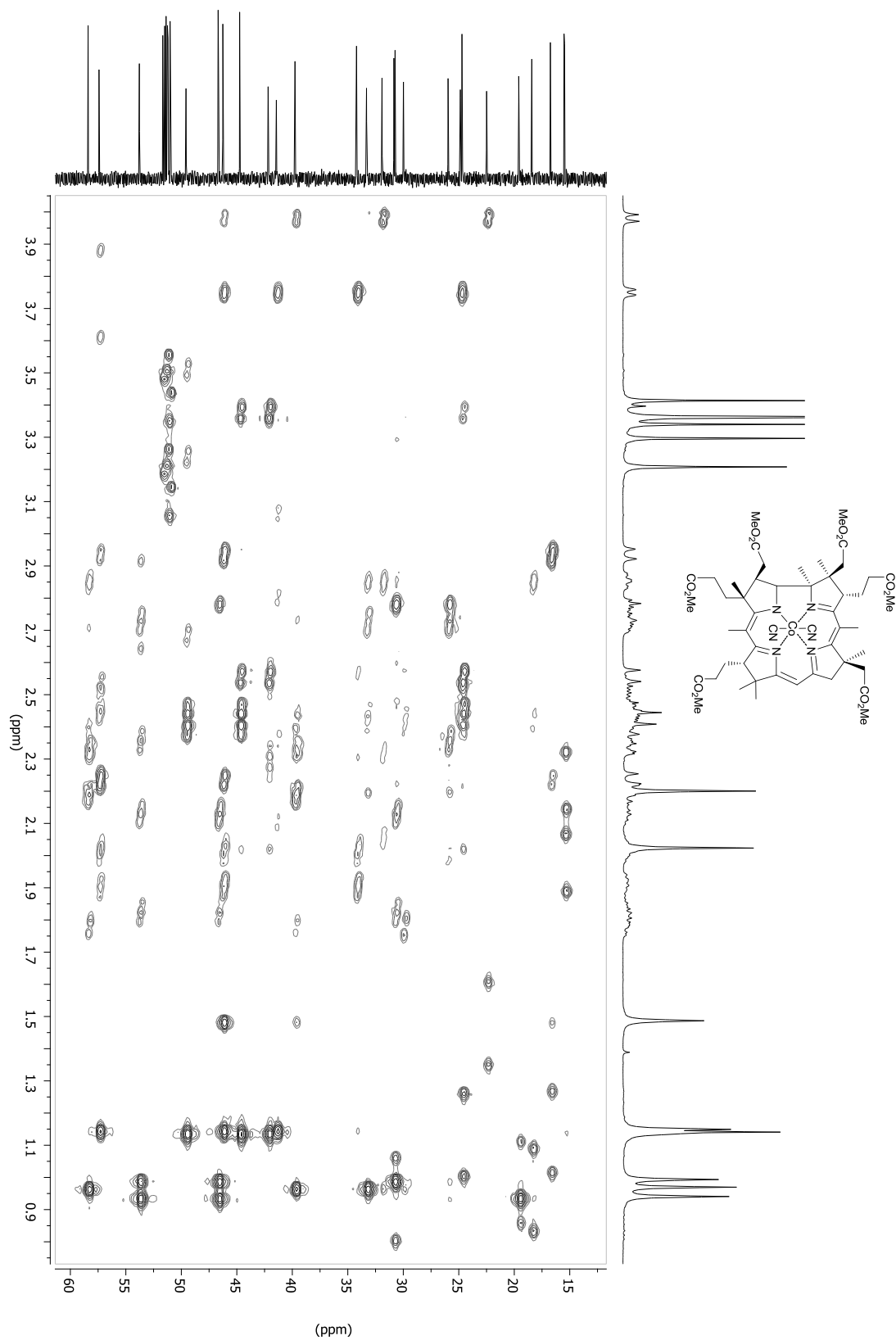
(CN)₂-8-*nor*-Cby(III)(OMe)₆ (5a) – expansion of ¹³C/¹H HSQC NMR measured in C₆D₆ at 303.0 K



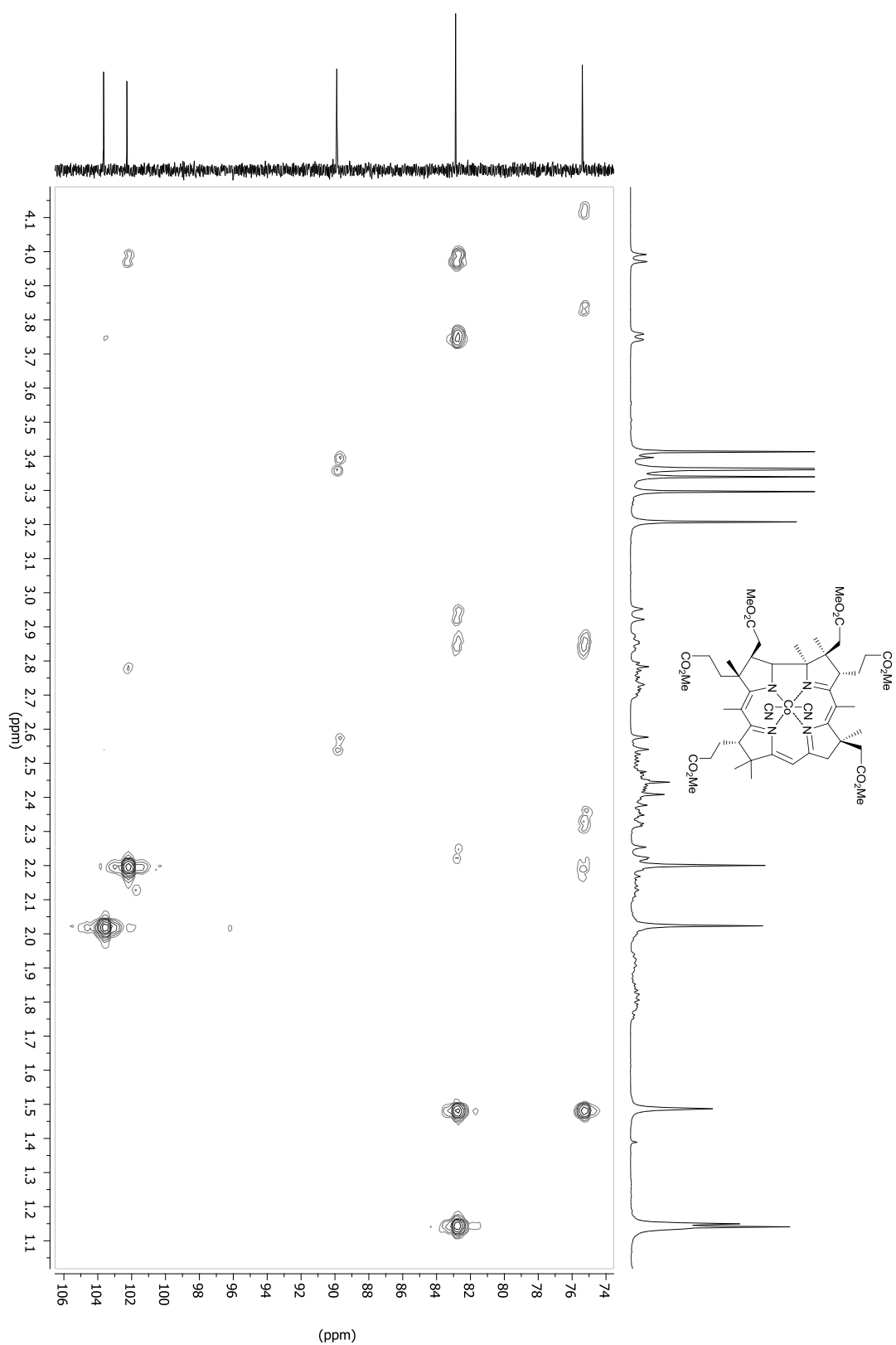
(CN)₂-8-*nor*-Cby(III)(OMe)₆ (5a) – ¹³C/¹H HMBC NMR measured in C₆D₆ at 303.0 K



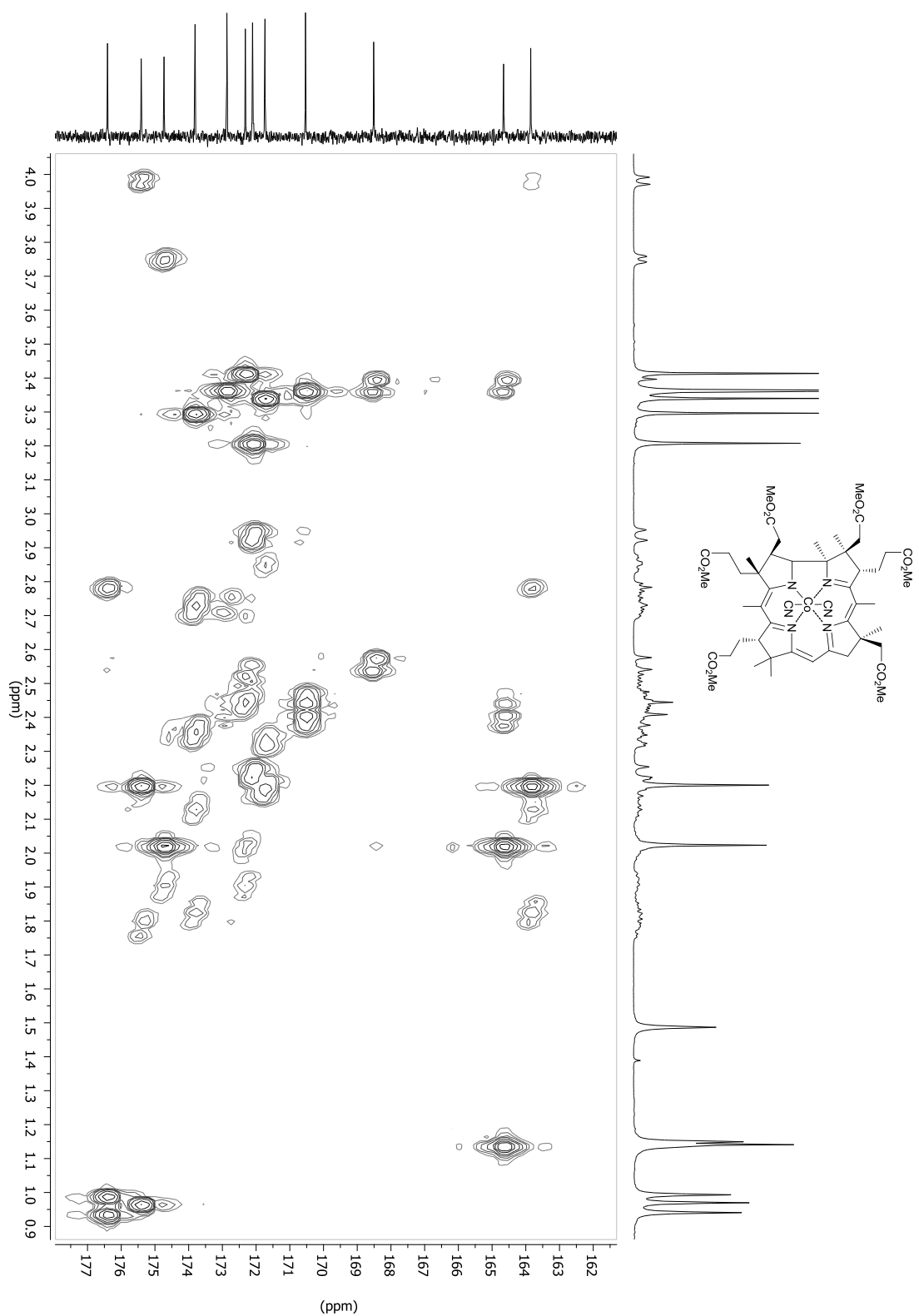
(CN)₂-8-*nor*-Cby(III)(OMe)₆ (5a) – expansion of ¹³C/¹H HMBC NMR measured in C₆D₆ at 303.0 K



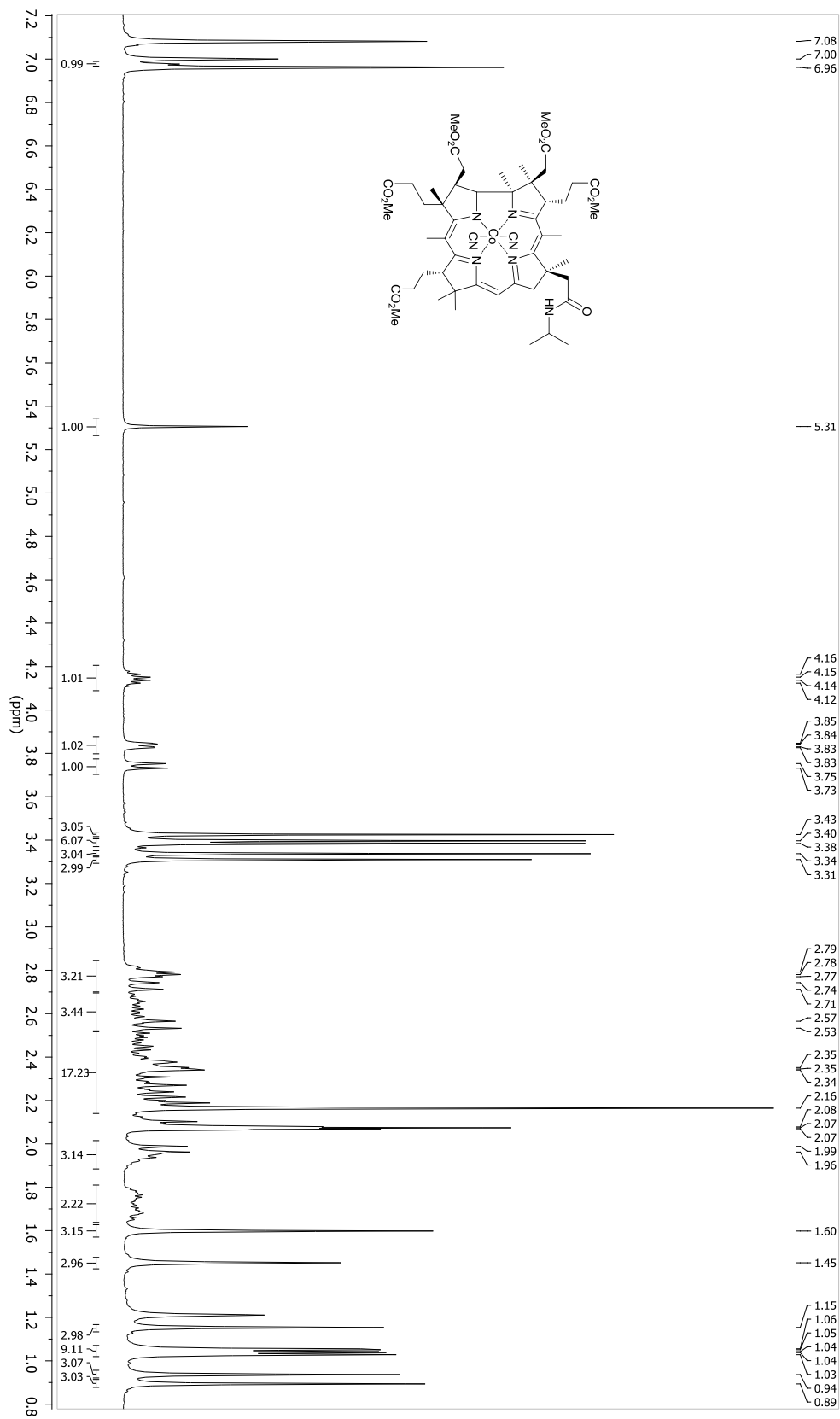
(CN)₂-8-*nor*-Cby(III)(OMe)₆ (5a) – expansion of ¹³C/¹H HMBC NMR measured in C₆D₆ at 303.0 K



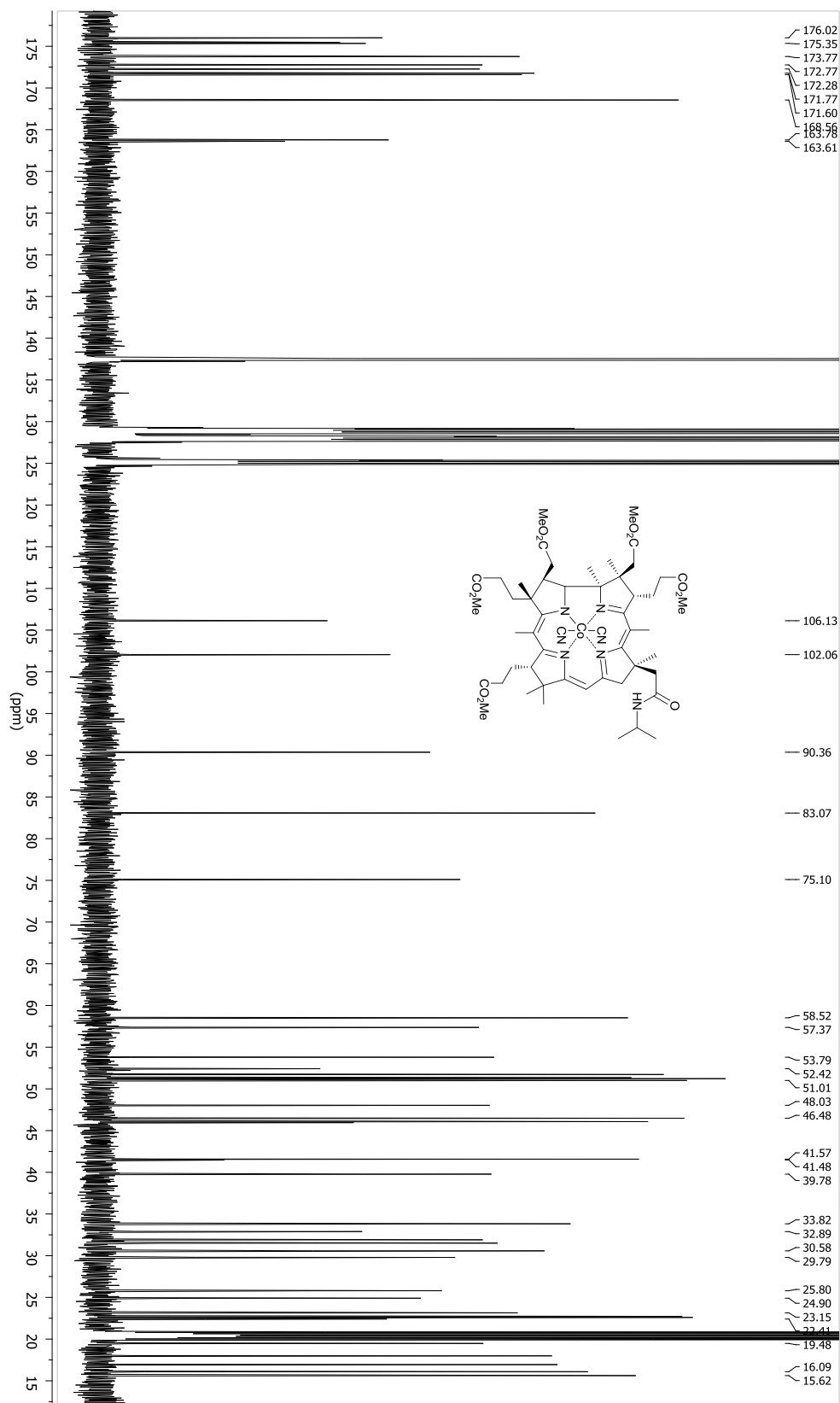
(CN)₂-8-*nor*-Cby(III)(OMe)₆ (5a) – expansion of ¹³C/¹H HMBC NMR measured in C₆D₆ at 303.0 K



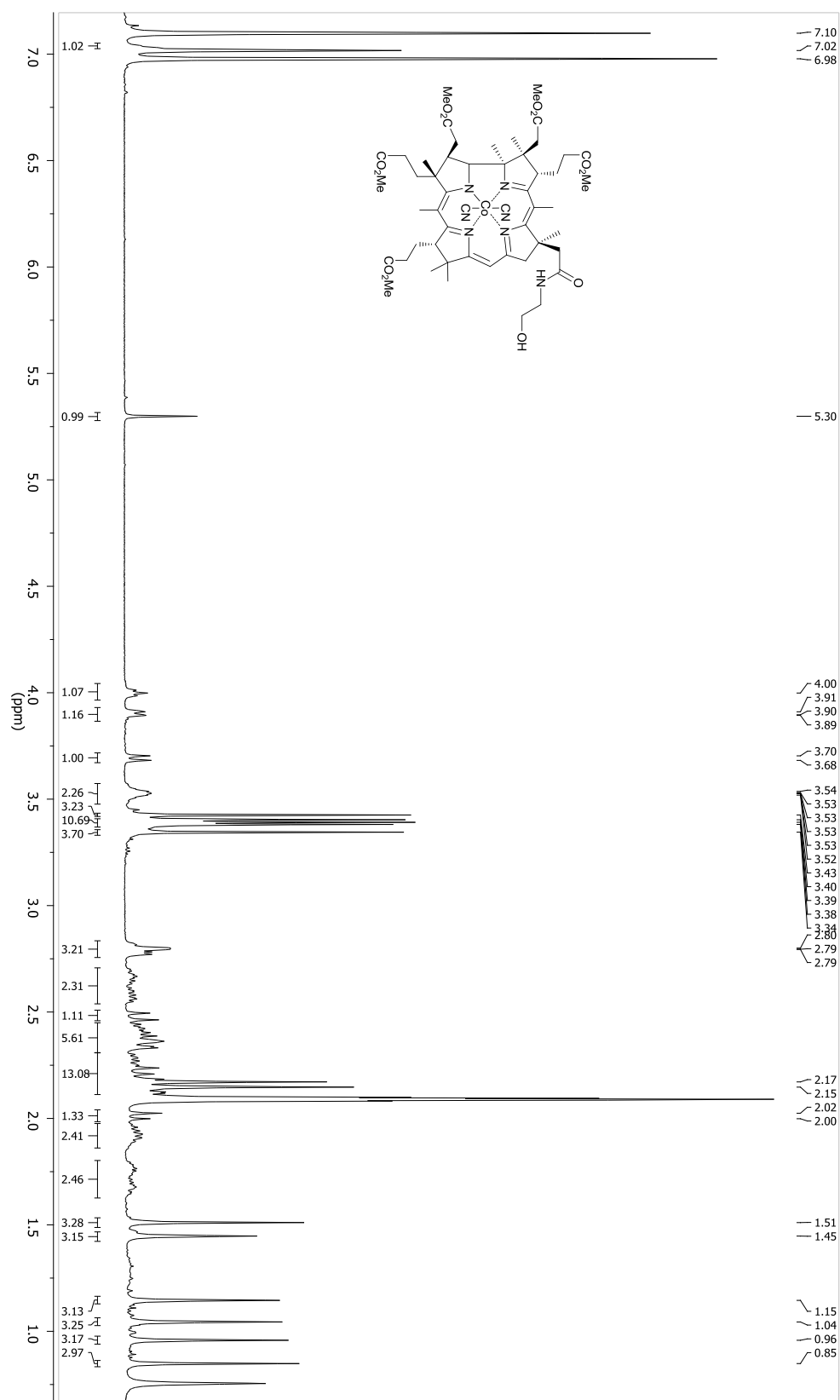
(CN)₂-8-nor-Cby(III)(c-2-propylamide)(OMe)₅ (5b) – ¹H NMR (500 MHz) measured in toluene-*d*₈ at 303.0 K



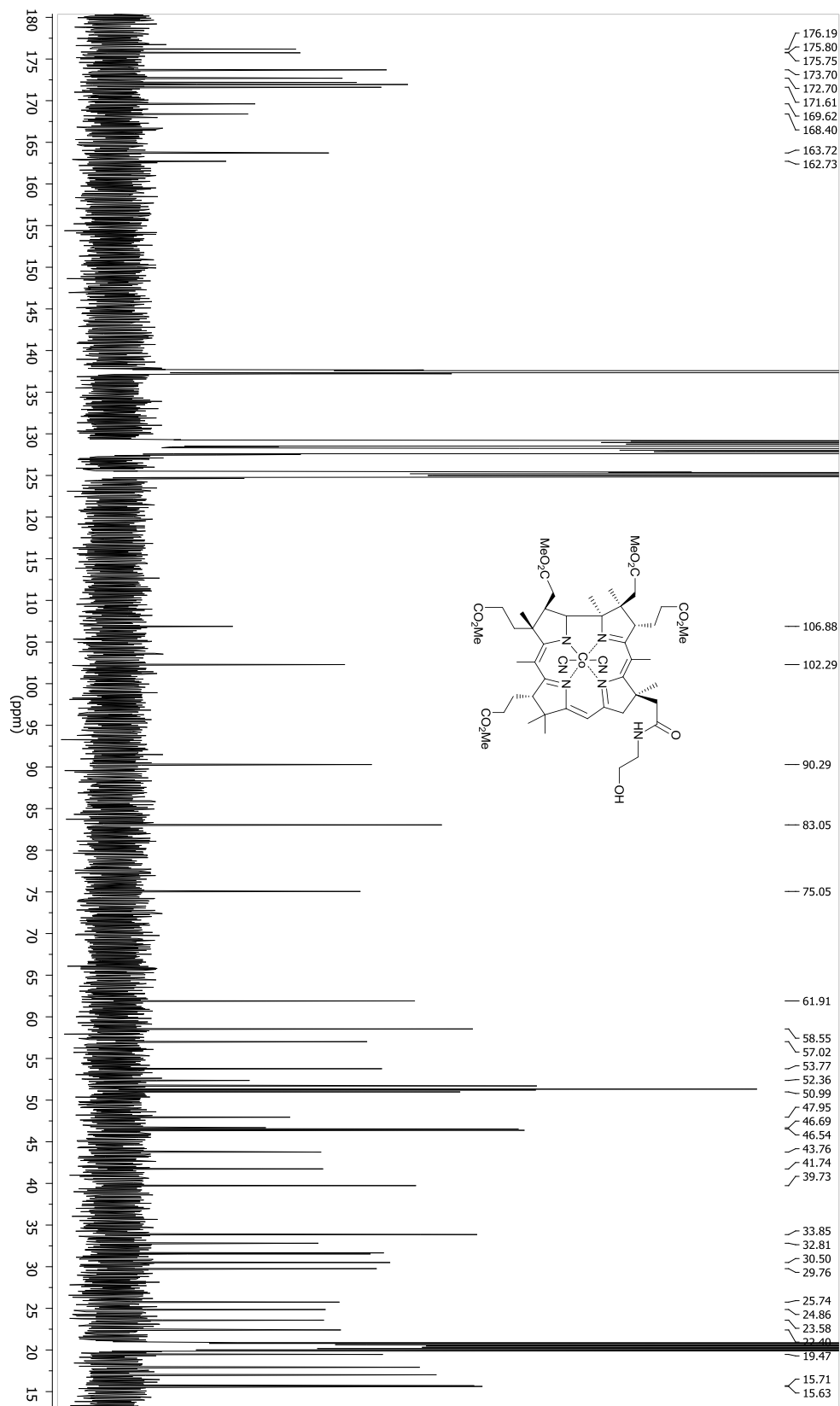
(CN)₂-8-nor-Cby(III)(c-2-propylamide)(OMe)₅ (5b) – ¹³C NMR (125 MHz) measured in toluene-*d*₈ at 303.0 K



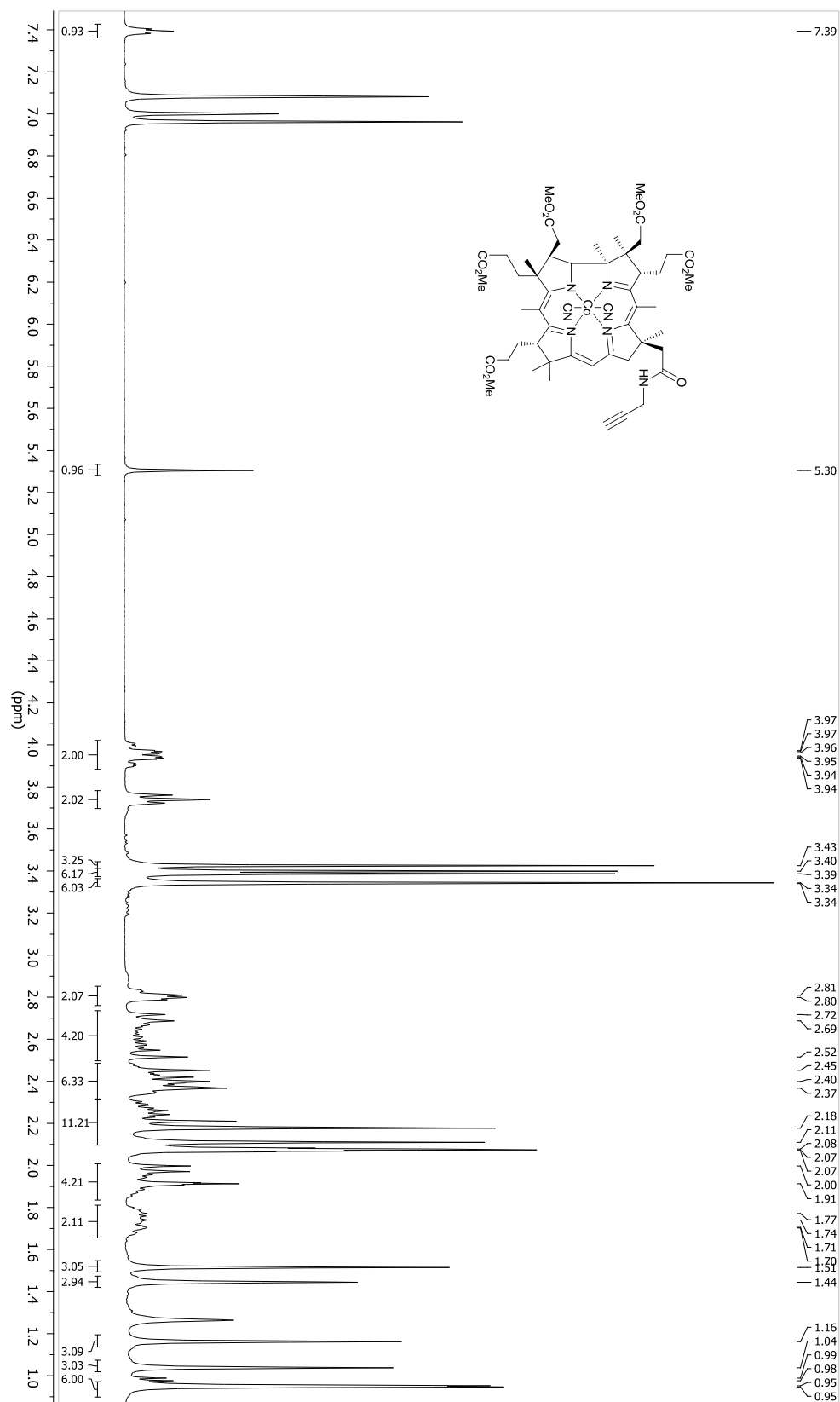
(CN)₂-8-*nor*-Cby(III)(*c*-2-hydroxyethylamide)(OMe)₅ (5c) – ¹H NMR (500 MHz) measured in toluene-*d*₈ at 303.0 K



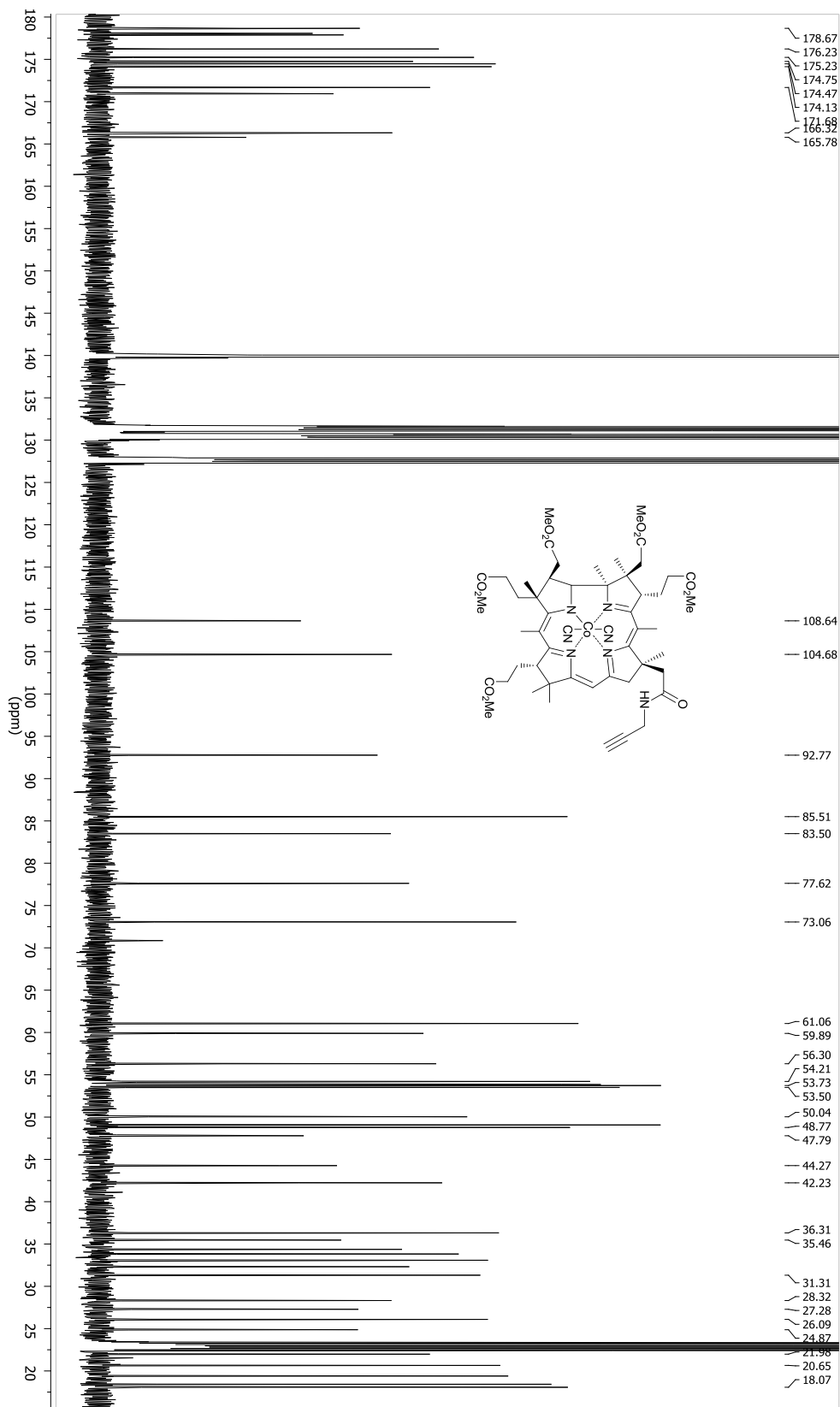
(CN)₂-8-nor-Cby(III)(c-2-hydroxyethylamide)(OMe)₅ (5c) – ¹³C NMR (125 MHz) measured in toluene-*d*₈ at 303.0 K



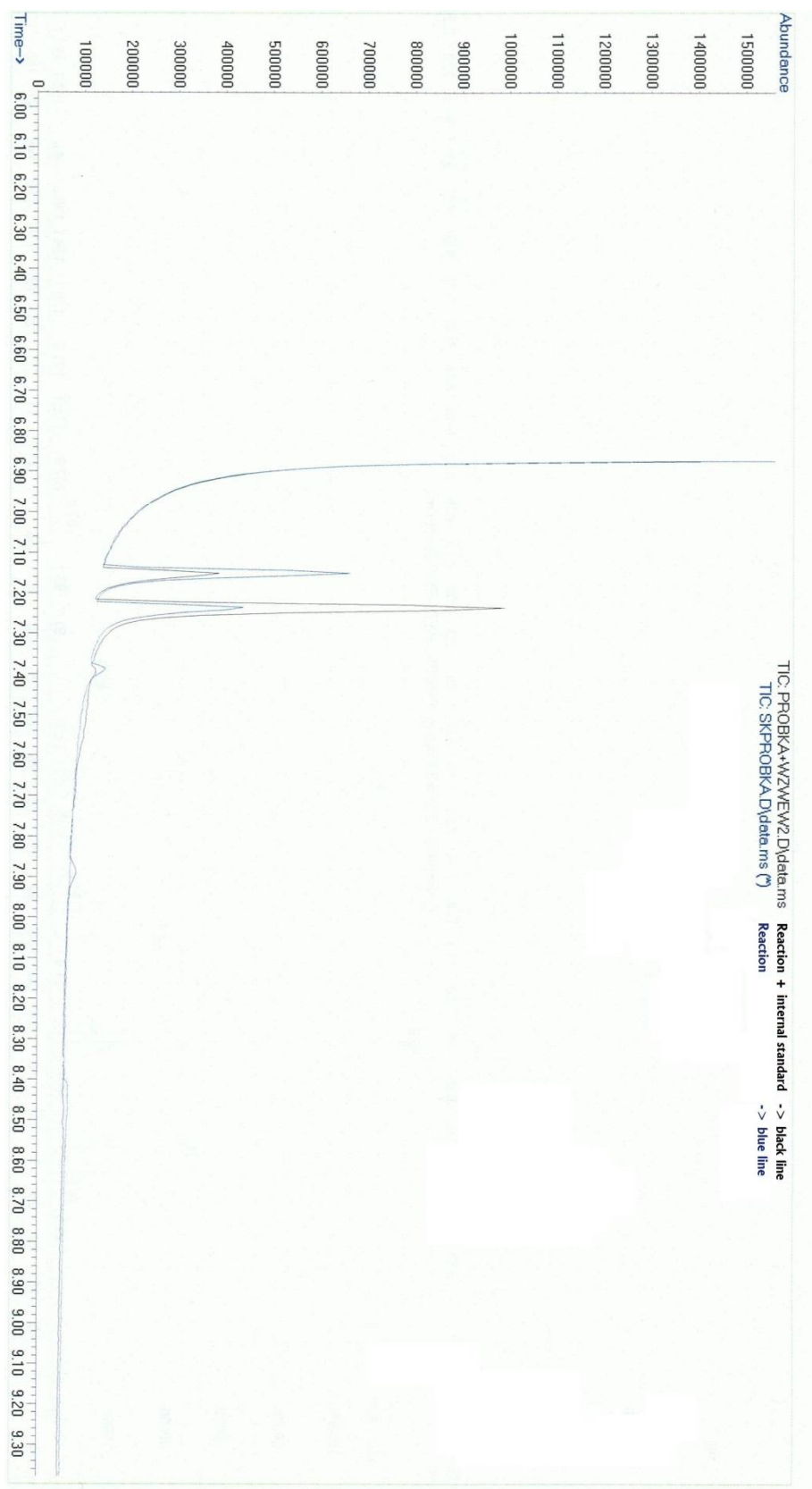
(CN)₂-8-nor-Cby(III)(c-propargylamide)(OMe)₅ (5d) – ¹H NMR (500 MHz) measured in toluene-*d*₈ at 303.0 K



(CN)₂-8-nor-Cby(III)(c-propargylamide)(OMe)₅ (5d) – ¹³C NMR (125 MHz) measured in toluene-*d*₈ at 303.0 K



Overlapped GC/MS chromatograms of the crude reaction of cobryketone 2a formation and the reaction with internal standard



Comparison of the experimental and database patterns for methyl 3-hydroxypropanoate

