

Supplementary Material

Synthesis, antiproliferative evaluation and QSAR analysis of novel halogen- and amidino-substituted benzothiazoles and benzimidazoles

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Table S1. *In vitro* growth-inhibitory effects of compounds **15a–26a**, **15b–26b**, and **15c–26c** on selected tumor cell lines with calculated selectivity index.

Cpd	IC ₅₀ (μM) ¹										
	MDCK1	BJ	HeLa	SI (MDCK)	SI (BJ)	CaCo-2	SI (MDCK)	SI (BJ)	HuT78	SI (MDCK)	SI (BJ)
15a	>100	>100	>100	-	-	>100	-	-	>100	-	-
15b	>100	>100	>100	-	-	>100	-	-	>100	-	-
15c	79.3 ± 14.4	100	>100	-	-	>100	-	-	>100	-	-
16a	87.3 ± 6.9	>100	>100	-	-	>100	-	-	>100	-	-
16b	25.8 ± 9.4	>100	>100	-	-	89.3 ± 15.8	-	-	69.8 ± 15.5	-	1.43
16c	6.8 ± 6.2	>100	>100	-	-	>100	-	-	>100	-	-
17a	100	>100	>100	-	-	>100	-	-	>100	-	-
17b	>100	>100	>100	-	-	>100	-	-	>100	-	-
17c	78.0 ± 27.8	>100	>100	-	-	>100	-	-	>100	-	-
18a	17.6 ± 5.7	>100	42.4 ± 7.5	-	-	100	-	-	13.2 ± 1.2	-	3.2
18b	29.8 ± 17.7	>100	>100	-	-	>100	-	-	100	-	-
18c	41.4 ± 8.1	>100	67.3 ± 7.8	-	-	>100	-	-	55.6 ± 34.6	-	-
19a	1.1 ± 0.2	>100	>100	-	-	>100	-	-	>100	-	-
19b	16.3 ± 11.5	>100	>100	-	-	>100	-	-	100	-	-
19c	1.1 ± 0.2	>100	>100	-	-	>100	-	-	>100	-	-
20a	65.7 ± 11.8	>100	>100	-	-	>100	-	-	>100	-	-
20b	94.2 ± 18.4	>100	>100	-	-	28.7 ± 16.7	3.28	3.48	>100	-	-
20c	85.9 ± 15.7	100	>100	-	-	89.2 ± 16.8	-	1.12	64.7 ± 11.3	1.33	1.55
21a	12.6 ± 4.8	>100	100	-	-	>100	-	-	6.8 ± 6.2	1.85	14.7
21b	10.1 ± 4.5	84.1 ± 24.7	100	-	-	>100	-	-	3.6 ± 3.1	2.8	23.36
21c	43.2 ± 12.4	>100	100	-	-	>100	-	-	24.3 ± 6.5	1.78	4.11
22a	1.1 ± 0.2	>100	54.5 ± 29.4	-	-	73.5 ± 4.5	-	-	14.9 ± 10.8	-	6.71
22b	1.0 ± 0.0	86.4 ± 20.9	50.6 ± 19.3	-	-	100	-	-	9.1 ± 2.8	-	9.49
22c	0.7 ± 0.3	>100	100	-	-	>100	-	-	38.1 ± 23.4	-	2.62
23a	40.7 ± 5.7	>100	52.4 ± 18.4	-	-	95.6 ± 6.6	-	-	19.0 ± 4.0	2.14	5.26
23b	27.4 ± 4.2	40.5 ± 17.2	34.9 ± 14.8	-	-	56.0 ± 14.6	-	-	17.1 ± 7.7	1.6	2.34
23c	29.5 ± 7.2	100	45.7 ± 16.3	-	-	96.4 ± 13.3	-	-	20.0 ± 8.7	-	5.0
24a	11.4 ± 14.5	>100	>100	-	-	>100	-	-	>100	-	-
24b	8.8 ± 8.3	>100	>100	-	-	>100	-	-	>100	-	-
24c	41.1 ± 17.2	>100	82.8 ± 32.3	-	-	>100	-	-	49.6 ± 38.0	-	2.0
25a	8.2 ± 5.8	10 ± 0.01	>100	-	-	>100	-	-	>100	-	-
25b	51.3 ± 4.6	>100	>100	-	-	>100	-	-	19.7 ± 10.6	2.6	5.07
25c	22.8 ± 4.9	>100	>100	-	-	77.6 ± 43.3	-	-	>100	-	-
26a	36.7 ± 18.0	>100	>100	-	-	>100	-	-	>100	-	-
26b	64.8 ± 38.5	>100	>100	-	-	>100	-	-	>100	-	-
26c	8.5 ± 6.4	76.7 ± 27.7	23.3 ± 15.3	-	-	100	-	-	23.7 ± 5.2	-	3.24
5-FU	55.0 ± 8.7	74.0 ± 3.1	8.2 ± 1.9	6.7	9.02	5.9 ± 0.7	9.32	7.94	>100	-	-

¹ IC₅₀ – Compound concentration that inhibited cell growth by 50 %. Data represents mean IC₅₀ (μM) values ± standard deviation (SD) of three independent experiments. Exponentially growing cells were treated with compounds during 72 hrs. Cytotoxicity was analysed using MTT survival assay. **5-FU**: 5-Fluorouracil. SI = IC₅₀ normal cell line (MDCK1 or BJ)/IC₅₀ for respective cancerous cell line.

Table S2. *In vitro* growth-inhibitory effects of benzothiazoles **34a–38a**, **40a**, **41a**, **34b**, **36b–38b**, **40b**, **34c–37c**, **39c–41c** and benzimidazoles **42a–49a**, **42b–45b**, **47b–49b**, **42c–46c**, **48c**, and **49c** on selected tumor and normal cell lines with calculated selectivity index.

Cpd	IC ₅₀ (μM) ¹										
	MDCK1	BJ	HeLa	SI (MDCK)	SI (BJ)	CaCo-2	SI (MDCK)	SI (BJ)	HuT78	SI (MDCK)	SI (BJ)
34a	2.8 ± 0.3	3.9 ± 0.3	3.4 ± 0.2	-	-	4.0 ± 0.2	-	-	2.2 ± 0.3	-	-
34b	2.2 ± 0.3	11.2 ± 6.0	4.5 ± 4.3	-	-	7.0 ± 5.4	-	-	2.1 ± 0.2	-	-
34c	2.1 ± 0.3	4.0 ± 0.1	3.1 ± 0.2	-	-	6.3 ± 3.0	-	-	1.8 ± 0.7	-	-
35a	2.7 ± 0.3	3.2 ± 0.3	18.9 ± 3.6	-	-	26.7 ± 2.1	-	-	1.4 ± 0.2	-	-
35c	7.5 ± 3.5	6.7 ± 4.9	21.8 ± 5.5	-	-	18.2 ± 3.3	-	-	6.2 ± 2.7	-	-
36a	31.8 ± 4.0	38.5 ± 4.6	62.6 ± 22.0	-	-	24.8 ± 9.2	-	-	4.4 ± 3.9	7.23	8.75
36b	25.2 ± 1.3	32.6 ± 3.4	30.0 ± 1.0	-	-	38.3 ± 1.2	-	-	1.8 ± 0.4	14	18.11
36c	100	>100	>100	-	-	>100	-	-	1.6 ± 0.8	62.5	62.5
37a	1.5 ± 0.3	4.3 ± 3.6	3.6 ± 0.1	-	-	3.7 ± 1.5	-	-	1.6 ± 0.8	-	2.69
37b	2.4 ± 0.3	5.3 ± 2.9	4.0 ± 0.4	-	-	6.1 ± 2.7	-	-	2.1 ± 0.2	-	2.52
37c	2.6 ± 0.1	4.8 ± 3.5	3.4 ± 0.2	-	-	4.5 ± 2.7	-	-	3.0 ± 1.0	-	1.6
38a	27.1 ± 3.4	22.6 ± 4.6	19.7 ± 3.1	-	-	25.4 ± 3.5	-	-	16.2 ± 5.5	1.67	1.39
38b	26.6 ± 3.1	32.2 ± 2.8	22.1 ± 1.2	-	-	19.4 ± 4.7	1.37	1.66	4.0 ± 0.9	6.65	8.05
39c	100	38.1 ± 1.4	>100	-	-	34.7 ± 2.8	2.87	-	12.7 ± 0.9	7.87	3
40a	59.4 ± 18.8	>100	100	-	-	100	-	-	100	-	-
40b	>100	>100	>100	-	-	>100	-	-	37.3 ± 12.8	2.68	2.68
40c	>100	100	>100	-	-	>100	-	-	100	-	-
41a	58.2 ± 17.3	27.3 ± 6.0	25.8 ± 0.8	-	-	29.2 ± 4.2	1.99	-	4.1 ± 3.6	14.19	6.65
41c	>100	>100	>100	-	-	>100	-	-	>100	-	-
42a	100	100	>100	-	-	>100	-	-	7.0 ± 5.2	14.29	14.29
42b	67.3 ± 12.7	47.0 ± 3.3	100	-	-	100	-	-	11.9 ± 3.6	5.66	3.95
42c	100	32.8 ± 4.1	>100	-	-	>100	-	-	24.9 ± 4.6	4.0	1.32
43a	100	33.0 ± 20.3	>100	-	-	>100	-	-	28.6 ± 3.9	3.5	-
43b	100	>100	>100	-	-	>100	-	-	43.3 ± 4.4	2.3	2.3
43c	63.4 ± 8.9	30.9 ± 8.7	>100	-	-	>100	-	-	17.7 ± 6.1	3.58	1.75
44a	100	73.3 ± 3.2	100	-	-	>100	-	-	89.2 ± 20.6	1.2	-
44b	>100	45.1 ± 20.9	>100	-	-	>100	-	-	65.6 ± 17.3	1.52	-
44c	100	>100	>100	-	-	>100	-	-	100	-	-
45a	100	55.6 ± 13.4	>100	-	-	100	-	-	4.8 ± 3.6	20.83	11.58
45b	46.1 ± 14.8	82.1 ± 0.4	>100	-	-	100	-	-	5.5 ± 4.0	8.36	14.9
45c	68.5 ± 22.7	>100	>100	-	-	>100	-	-	4.1 ± 3.3	16.7	24.39
46a	100	100	>100	-	-	>100	-	-	63.0 ± 15.1	1.59	1.59
46c	>100	>100	>100	-	-	>100	-	-	5.1 ± 4.2	19.6	19.6
47a	100	>100	>100	-	-	>100	-	-	100	-	-
47b	>100	100	>100	-	-	>100	-	-	100	-	-
48a	100	>100	>100	-	-	>100	-	-	100	-	-
48b	>100	100	>100	-	-	>100	-	-	100	-	-
48c	>100	100	>100	-	-	>100	-	-	69.6 ± 25.9	1.44	1.44
49a	100	80.4 ± 9.9	100	-	-	>100	-	-	100	-	-
49b	82.9 ± 6.6	64.8 ± 9.2	100	-	-	>100	-	-	100	-	-
49c	>100	>100	100	-	-	>100	-	-	100	-	-
5-FU	55.0 ± 8.7	74.0 ± 3.1	8.2 ± 1.9	6.7	9.02	5.9 ± 0.7	9.32	7.94	>100	-	-

¹ IC₅₀ – Compound concentration that inhibited cell growth by 50 %. Data represents mean IC₅₀ (μM) values ± standard deviation (SD) of three independent experiments. Exponentially growing cells were treated with compounds during 72 hrs. Cytotoxicity was analysed using MTT survival assay. **5-FU**: 5-Fluorouracil. SI = IC₅₀ normal cell line (MDCK1 or BJ)/IC₅₀ for respective cancerous cell line.

Table S3. Additional antiproliferative testing of selected compounds with calculated selectivity index.

Cpd	IC ₅₀ (μM) ¹													
	MDCK1	BJ	SW620	SI (MDCK)	SI (BJ)	MDA-MB-231	SI (MDCK)	SI (BJ)	HL60	SI (MDCK)	SI (BJ)	THP1	SI (MDCK)	SI (BJ)
36a	2.7 ± 0.3	3.2 ± 0.3	5.6 ± 1.2	-	-	33.0 ± 4.9	-	-	18.8 ± 1.1	-	-	20.4 ± 3.3	-	-
36c	100	>100	100	-	-	>100	-	-	100	-	-	>100	-	-
38b	26.6 ± 3.1	32.2 ± 2.8	30.5 ± 9.2	-	-	42.4 ± 7.2	-	-	15.8 ± 2.3	1.68	2.04	14.7 ± 4.1	1.8	2.19
39c	100	38.1 ± 1.4	34.2 ± 7.1	2.92	-	38.5 ± 1.6	2.6	-	31.1 ± 3.0	3.22	-	69.7 ± 6.3	1.43	-
42a	100	100	100	-	-	76.3 ± 11.8	1.31	1.31	33.2 ± 1.8	3.01	3.01	44.5 ± 5.3	2.25	2.25
42b	67.3 ± 12.7	47.0 ± 3.3	92.7 ± 34.3	-	-	84.5 ± 18.3	-	-	44.4 ± 12.6	1.51	-	100	-	-
42c	100	32.8 ± 4.1	29.8 ± 3.0	3.36	-	38.9 ± 4.2	2.57	-	19.5 ± 0.8	5.13	1.68	19.7 ± 2.4	5.13	1.68
43a	100	33.0 ± 20.3	>100	-	-	100	-	-	40.4 ± 12.0	2.48	-	29.7 ± 8.6	3.37	-
45a	100	55.6 ± 13.4	>100	-	-	100	-	-	48.1 ± 16.4	2.07	1.15	0.8 ± 0.1	125	69,5
45b	46.1 ± 14.8	82.1 ± 0.4	100	-	-	100	-	-	30.0 ± 12.3	1.54	2.74	2.5 ± 1.5	18.44	32.84
45c	68.5 ± 22.7	>100	100	-	-	100	-	-	25.1 ± 16.0	2.73	4.0	>100	-	-
46c	>100	>100	>100	-	-	>100	-	-	50.7 ± 20.5	1.97	1.97	100	-	-

¹ IC₅₀ – Compound concentration that inhibited cell growth by 50 %. Data represents mean IC₅₀ (μM) values ± standard deviation (SD) of three independent experiments. Exponentially growing cells were treated with compounds during 72 hrs. Cytotoxicity was analysed using MTT survival assay. **5-FU**: 5-Fluorouracil. SI = IC₅₀ normal cell line (MDCK1 or BJ)/ IC₅₀ for respective cancerous cell line.

Table S4. Experimental and calculated $\log IC_{50}$ by Eqs. (1 and 1a), as well as values of descriptors included in QSAR model (Eq. 1 and 1a) antiproliferative activity against MDCK-1 cells.

Code	Status	Exp. endpoint	Pred. eq.(1)	Pred. eq.(1a)	<i>SIC1</i>	<i>GATS4p</i>	<i>BEHv6</i>	<i>BELp1</i>	<i>R7m</i>
15a	Training	2.00	1.96	1.96	0.577	1.241	2.725	1.954	0.199
15b	Training	2.00	2.00	1.97	0.624	1.201	2.725	1.955	0.249
15c	Training	1.89	1.87	1.83	0.61	1.216	2.844	1.963	0.245
16a	Training	1.91	1.31	1.29	0.577	1.498	2.715	1.955	0.182
16b	Training	1.41	1.57	1.53	0.605	1.421	2.715	1.955	0.232
16c	Training	0.83	1.34	1.29	0.61	1.421	2.842	1.964	0.232
17a	Prediction	2.00	2.10	2.12	0.529	1.271	2.713	1.955	0.162
17b	Training	2.00	2.11	2.10	0.577	1.238	2.713	1.955	0.214
17c	Prediction	1.89	1.99	1.96	0.569	1.25	2.842	1.964	0.219
18a	Training	1.25	1.40	1.41	0.609	1.194	2.724	1.957	0.126
18b	Prediction	1.47	1.37	1.36	0.659	1.177	2.724	1.958	0.179
18c	Training	1.62	1.40	1.37	0.639	1.187	2.843	1.967	0.187
19a	Training	0.04	0.62	0.61	0.609	1.516	2.714	1.958	0.112
19b	Training	1.21	0.90	0.88	0.638	1.436	2.714	1.958	0.166
19c	Training	0.04	0.78	0.74	0.639	1.43	2.842	1.967	0.176
20a	Prediction	1.82	1.61	1.65	0.559	1.218	2.713	1.958	0.097
20b	Training	1.97	1.55	1.56	0.609	1.214	2.713	1.958	0.151
20c	Training	1.93	1.54	1.53	0.595	1.22	2.842	1.967	0.164
21a	Training	1.10	1.08	1.08	0.736	0.795	2.724	1.939	0.139
21b	Training	1.00	0.90	0.85	0.785	0.907	2.724	1.94	0.212
21c	Training	1.64	1.35	1.32	0.745	0.887	2.758	1.953	0.208
22a	Training	0.04	0.13	0.10	0.736	1.199	2.713	1.941	0.124
22b	Training	0.00	0.35	0.29	0.762	1.217	2.713	1.942	0.198
22c	Prediction	-0.15	0.62	0.57	0.745	1.189	2.754	1.954	0.197
23a	Training	1.61	1.36	1.38	0.685	0.8	2.711	1.941	0.108
23b	Training	1.44	1.11	1.09	0.736	0.935	2.711	1.942	0.182
23c	Training	1.47	1.53	1.52	0.703	0.909	2.753	1.954	0.185
24a	Prediction	1.06	1.39	1.37	0.62	0.968	2.948	1.952	0.159
24b	Training	0.94	1.39	1.33	0.659	1.023	2.948	1.952	0.23
24c	Prediction	1.61	1.55	1.50	0.638	1.027	2.948	1.956	0.22
25a	Prediction	0.91	0.57	0.52	0.62	1.287	2.946	1.952	0.143

25b	Training	1.71	0.89	-	0.643	1.275	2.946	1.952	0.221
25c	Training	1.36	0.96	0.90	0.638	1.273	2.947	1.957	0.213
26a	Training	1.56	1.49	1.49	0.581	0.978	2.946	1.952	0.127
26b	Training	1.81	1.50	1.46	0.62	1.047	2.946	1.952	0.205
26c	Training	0.93	1.72	1.69	0.603	1.049	2.947	1.957	0.208
34a	Training	0.45	0.76	0.71	0.609	1.221	3.085	1.968	0.154
34b	Training	0.34	0.77	0.71	0.644	1.201	3.085	1.969	0.192
34c	Prediction	0.32	0.93	0.87	0.622	1.218	3.091	1.972	0.19
35a	Training	0.43	0.82	0.81	0.637	1.178	2.934	1.969	0.121
35c	Training	0.88	1.11	1.08	0.646	1.191	2.935	1.974	0.172
36a	Training	1.50	1.19	1.21	0.717	0.869	2.766	1.967	0.109
36b	Prediction	1.40	1.26	1.23	0.753	0.955	2.766	1.967	0.198
36c	Training	2.00	1.51	1.48	0.715	0.946	2.844	1.969	0.213
37a	Prediction	0.18	0.75	0.71	0.636	1.016	3.127	1.967	0.132
37b	Training	0.38	0.70	0.63	0.666	1.058	3.128	1.967	0.179
37c	Prediction	0.41	0.91	0.85	0.643	1.067	3.134	1.97	0.181
38a	Training	1.43	1.56	1.54	0.609	1.229	3.113	2.02	0.173
38b	Training	1.42	1.46	1.43	0.641	1.208	3.113	2.02	0.191
39c	Training	2.00	1.88	1.88	0.64	1.199	2.946	2.021	0.183
40a	Training	1.77	2.02	2.07	0.707	0.873	2.826	2.02	0.128
40b	Training	2.00	1.98	1.99	0.74	0.959	2.826	2.02	0.196
40c	Training	2.00	2.28	2.29	0.703	0.951	2.861	2.021	0.205
41a	Prediction	1.76	1.46	1.46	0.632	1.021	3.169	2.02	0.134
41c	Training	2.00	1.64	1.62	0.638	1.073	3.175	2.021	0.19
42a	Training	2.00	1.58	1.57	0.609	1.328	3.111	2.039	0.166
42b	Training	1.83	1.54	1.50	0.641	1.323	3.112	2.039	0.199
42c	Training	2.00	1.69	1.66	0.618	1.359	3.115	2.04	0.205
43a	Prediction	2.00	1.67	1.70	0.633	1.256	2.946	2.039	0.118
43b	Training	2.00	1.52	1.53	0.666	1.291	2.946	2.039	0.151
43c	Training	1.80	1.95	1.94	0.64	1.327	2.946	2.04	0.195
44a	Training	2.00	2.34	2.41	0.703	0.854	2.826	2.039	0.123
44b	Training	2.00	2.15	2.17	0.735	1.025	2.826	2.039	0.196
44c	Training	2.00	2.39	2.41	0.699	1.022	2.861	2.04	0.198
45a	Training	2.00	1.77	1.78	0.632	1.043	3.166	2.039	0.145

45b	Training	1.66	1.52	1.50	0.66	1.131	3.166	2.039	0.173
45c	Training	1.84	1.71	1.69	0.637	1.152	3.172	2.04	0.181
46a	Training	2.00	2.25	2.26	0.642	0.899	3.167	2.039	0.183
46c	Training	2.00	2.09	2.07	0.637	1.023	3.173	2.04	0.195
47a	Prediction	2.00	1.77	1.77	0.639	1.18	3.047	2.039	0.155
47b	Prediction	2.00	1.92	1.89	0.664	1.232	3.047	2.039	0.231
48a	Training	2.00	1.97	1.99	0.618	1.122	3.038	2.039	0.135
48b	Training	2.00	1.98	1.97	0.642	1.201	3.038	2.04	0.194
48c	Training	2.00	2.23	2.23	0.614	1.211	3.039	2.04	0.202
49a	Training	2.00	1.90	1.94	0.601	1.222	2.984	2.039	0.117
49b	Training	1.92	1.84	1.85	0.625	1.259	2.984	2.039	0.151
49c	Training	2.00	2.17	2.18	0.597	1.297	2.985	2.04	0.18

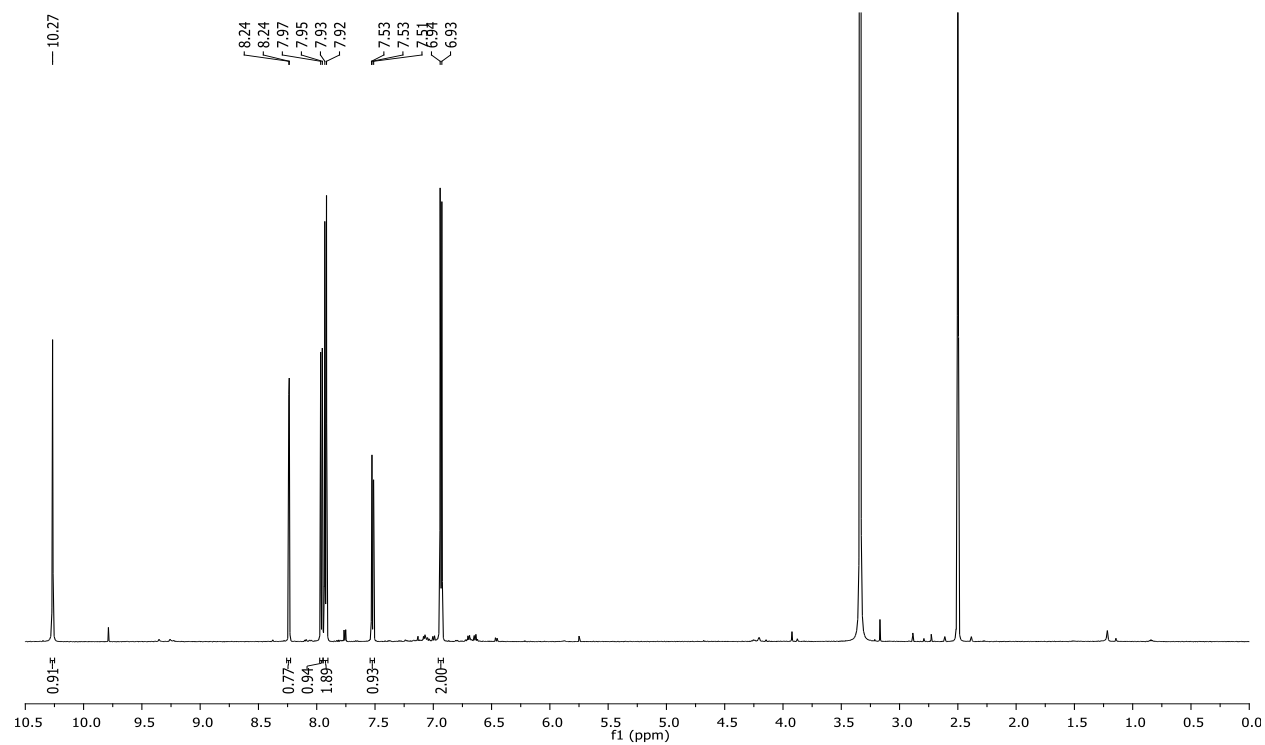
Table S5. Experimental and calculated $\log IC_{50}$ by Eqs. (1 and 1a), as well as values of descriptors included in QSAR model (Eq. 2 and 2a) for antiproliferative activity on T-cell lymphoma (HuT78).

Code	Status	Exp. endpoint	Pred. eq.(2)	Pred. eq.(2a)	<i>MATS8v</i>	<i>Mor30m</i>	<i>Mor09p</i>	<i>E2u</i>
15c	Training	2	1.52	1.6	-0.33	0.469	-1.288	0.36
16b	Training	1.84	1.47	1.45	-0.289	0.087	-1.498	0.484
18a	Training	1.12	1.31	1.41	-0.134	0.215	-1.039	0.5
18b	Training	2	1.63	1.65	-0.255	0.21	-1.075	0.512
18c	Training	1.75	1.57	1.69	-0.183	0.297	-1.006	0.443
19b	Prediction	2	1.99	1.96	-0.343	0.082	-1.229	0.511
20c	Training	1.81	1.82	1.93	-0.209	0.154	-1.123	0.44
21a	Training	0.83	0.82	0.82	-0.258	0.489	-1.144	0.516
21b	Training	0.56	0.83	0.77	-0.329	0.517	-1.226	0.525
21c	Training	1.39	0.97	1.01	-0.312	0.633	-1.172	0.428
22a	Training	1.17	1.45	1.37	-0.407	0.347	-1.29	0.513
22b	Prediction	0.96	1.52	1.4	-0.461	0.331	-1.352	0.524
22c	Training	1.58	1.38	1.37	-0.401	0.505	-1.298	0.427
23a	Training	1.28	1.2	1.16	-0.331	0.374	-1.243	0.514
23b	Prediction	1.23	1.33	1.24	-0.407	0.371	-1.307	0.521
23c	Prediction	1.3	1.35	1.35	-0.369	0.515	-1.245	0.425
24c	Training	1.7	1.7	1.76	-0.312	0.232	-1.5	0.36
25b	Training	1.29	0.58	-	-0.374	0.478	-1.667	0.47
26c	Training	1.37	1.13	1.17	-0.344	0.548	-1.473	0.348
34a	Training	0.34	0.08	0.08	-0.142	0.414	-1.473	0.515
34b	Prediction	0.34	0.11	0.05	-0.254	0.434	-1.771	0.47
34c	Training	0.26	0.2	0.26	-0.195	0.533	-1.681	0.376
35a	Training	0.15	0.5	0.49	-0.203	0.368	-1.466	0.495
35c	Training	0.79	0.95	1.04	-0.22	0.424	-1.42	0.383
36a	Training	0.64	0.76	0.7	-0.301	0.364	-1.502	0.5
36b	Training	0.26	0.62	0.53	-0.338	0.472	-1.488	0.506
36c	Training	0.2	0.76	0.75	-0.329	0.534	-1.518	0.415
37a	Prediction	0.2	0.51	0.43	-0.281	0.262	-1.836	0.473
37b	Training	0.32	0.3	0.19	-0.333	0.383	-1.892	0.472
37c	Training	0.48	0.71	0.72	-0.33	0.56	-1.647	0.362
38a	Training	1.21	0.92	0.98	-0.154	0.23	-1.331	0.486
38b	Training	0.6	0.73	0.75	-0.254	0.483	-1.41	0.435
39c	Training	1.1	1.77	-	-0.227	0.41	-0.9	0.404
40a	Training	2	2.08	2.09	-0.304	0.067	-1.11	0.513
40b	Training	1.57	1.86	1.84	-0.332	0.151	-1.188	0.509
40c	Training	2	1.93	1.99	-0.327	0.313	-1.097	0.427
41a	Prediction	0.61	0.77	0.75	-0.286	0.412	-1.494	0.459
42a	Training	0.85	0.86	0.87	-0.183	0.14	-1.553	0.49
42b	Training	1.08	1.39	1.37	-0.29	-0.003	-1.817	0.43

42c	Prediction	1.4	1.91	2.01	-0.225	-0.004	-1.517	0.371
43a	Training	1.46	1.36	1.37	-0.26	0.092	-1.558	0.458
43b	Prediction	1.64	1.77	1.73	-0.332	-0.048	-1.644	0.467
43c	Training	1.25	1.2	1.23	-0.259	0.184	-1.655	0.405
44a	Training	1.95	2.03	1.99	-0.364	-0.049	-1.567	0.462
44b	Training	1.82	1.72	1.66	-0.387	0.069	-1.61	0.468
44c	Training	2	1.71	1.7	-0.374	0.149	-1.628	0.405
45a	Training	0.68	0.79	0.71	-0.327	0.115	-2.131	0.413
45b	Training	0.74	0.78	0.66	-0.372	0.152	-2.114	0.437
45c	Training	0.61	1.03	0.98	-0.367	0.271	-1.871	0.397
46a	Training	1.8	1.4	1.43	-0.218	0.077	-1.44	0.47
46c	Prediction	0.71	1.12	1.02	-0.286	-0.027	-1.769	0.527
47a	Training	2	2.08	2.13	-0.261	0.051	-1.082	0.497
47b	Prediction	2	2.69	-	-0.363	-0.032	-1.096	0.478
48a	Training	2	1.92	1.97	-0.271	0.071	-1.299	0.447
48b	Training	2	1.8	1.76	-0.372	0.154	-1.4	0.471
48c	Prediction	1.84	2.24	2.29	-0.292	0.071	-1.092	0.47
49a	Training	2	2.22	2.32	-0.24	0.03	-1.124	0.442
49b	Training	2	2.18	2.18	-0.354	0.051	-1.312	0.459
49c	Training	2	1.83	1.85	-0.277	0.104	-1.229	0.483

Fig. S1 a) ^1H NMR and b) ^{13}C NMR of compd. **9a**

a)



b)

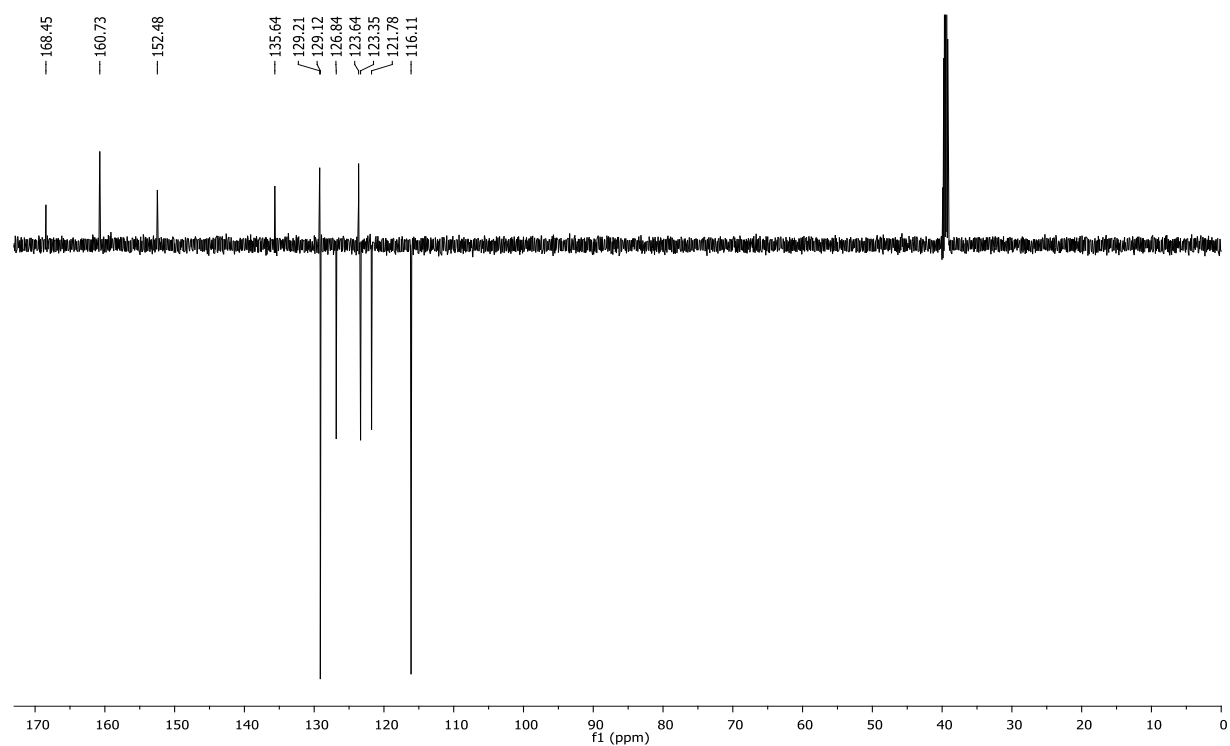
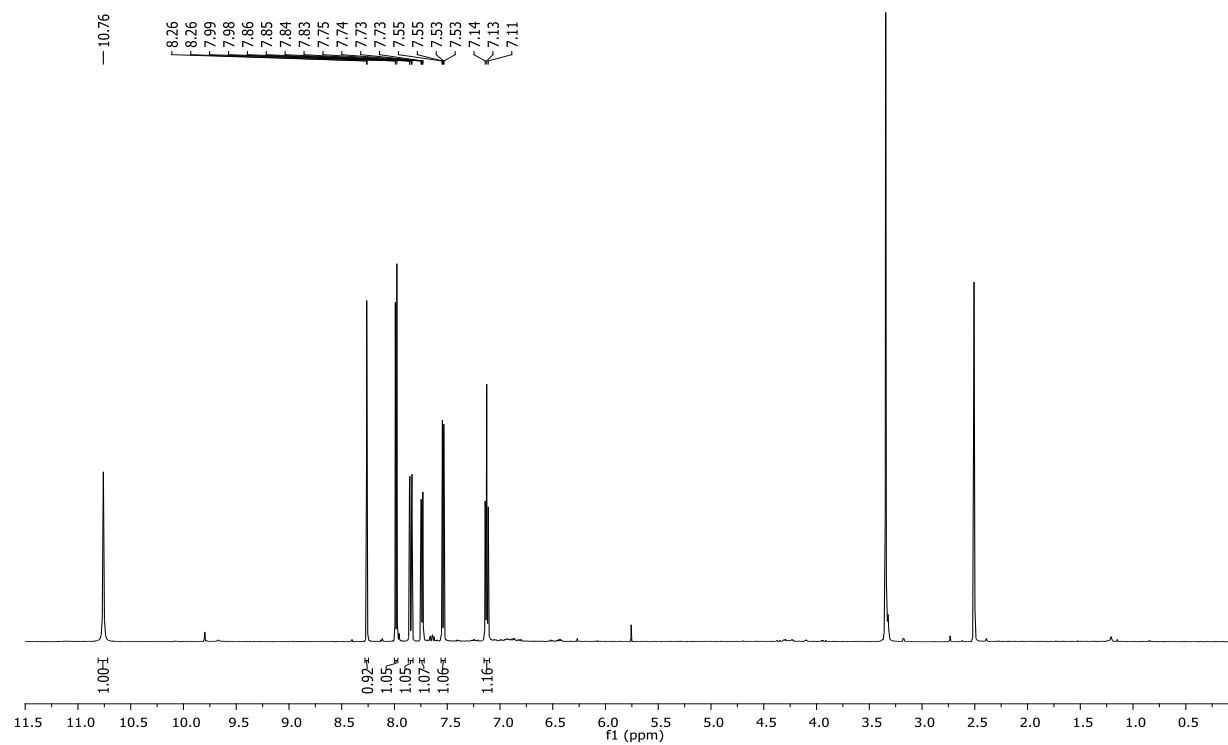


Fig. S2 a) ^1H NMR and b) ^{13}C NMR of compd. **9b**

a)



b)

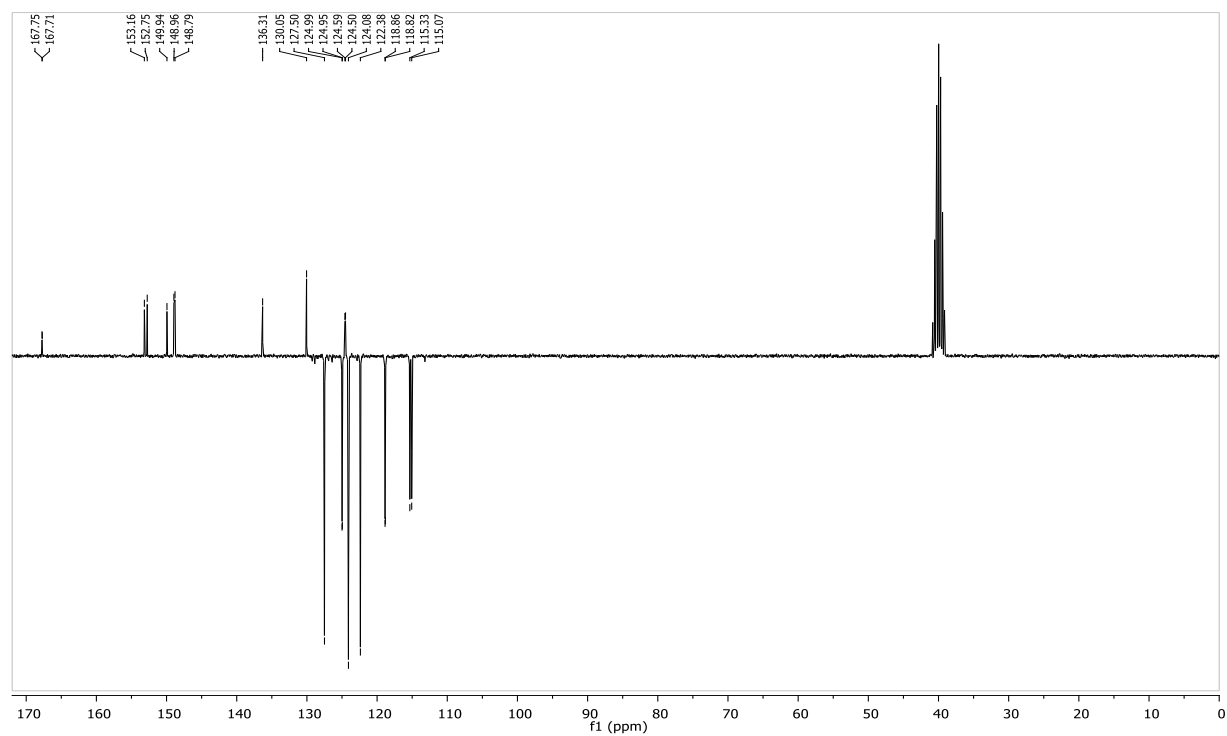
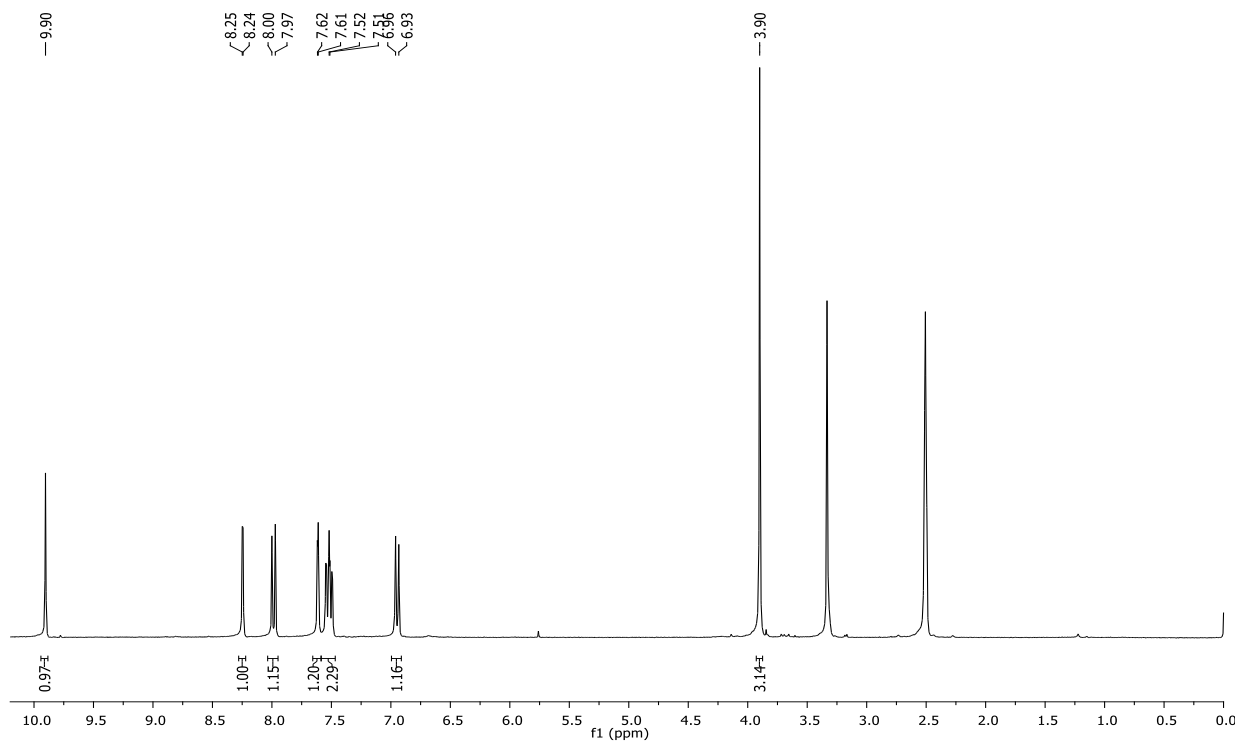


Fig. S3 a) ^1H NMR and b) ^{13}C NMR of compd. **9c**

a)



b)

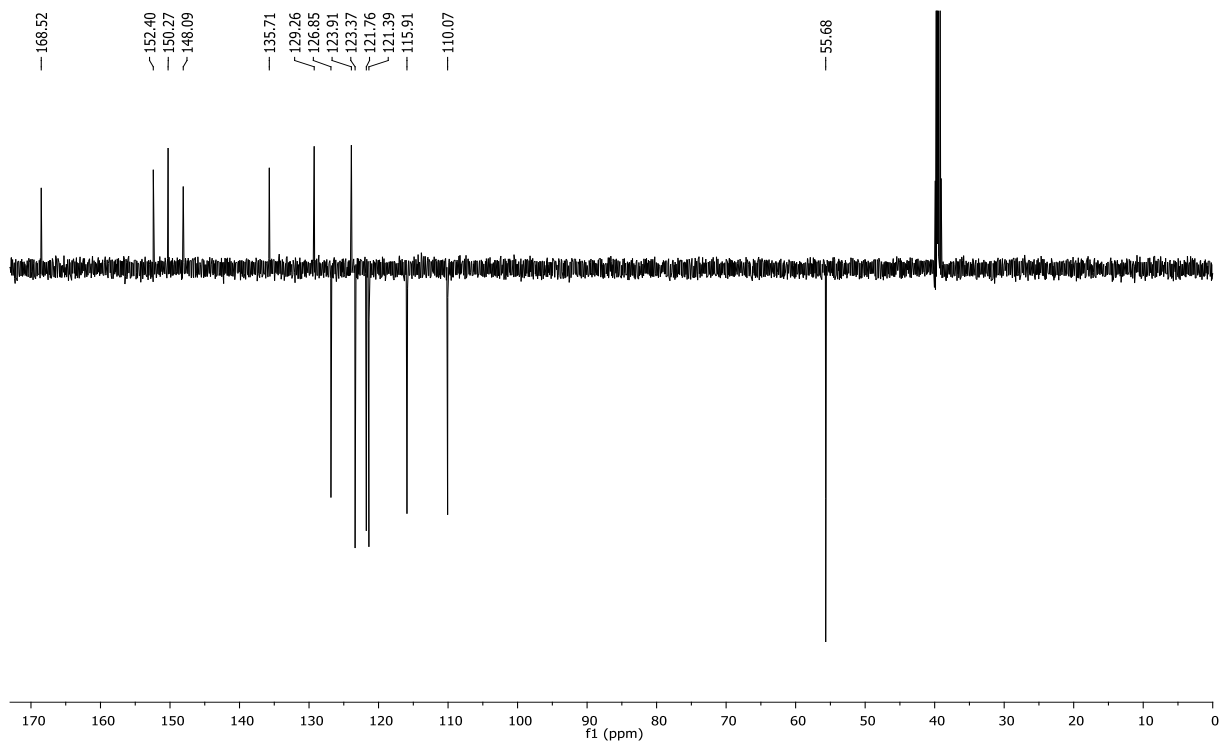
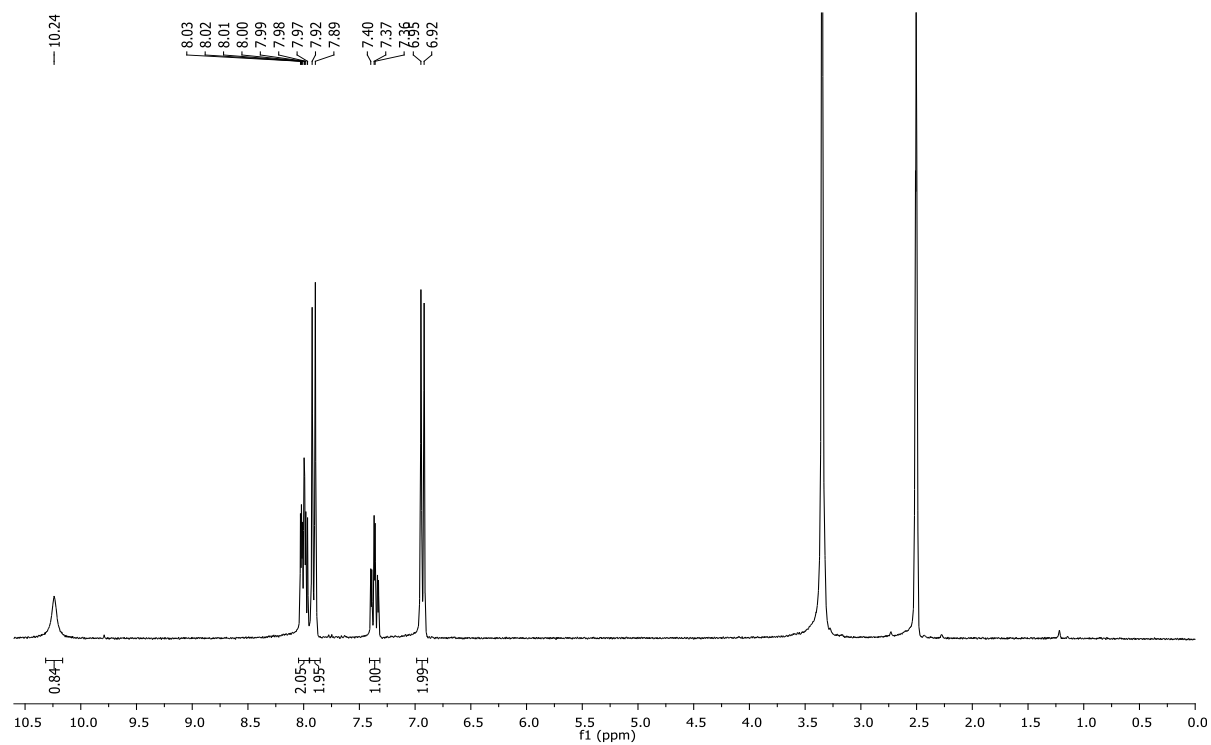


Fig. S4 a) ^1H NMR and b) ^{13}C NMR of compd. **10a**

a)



b)

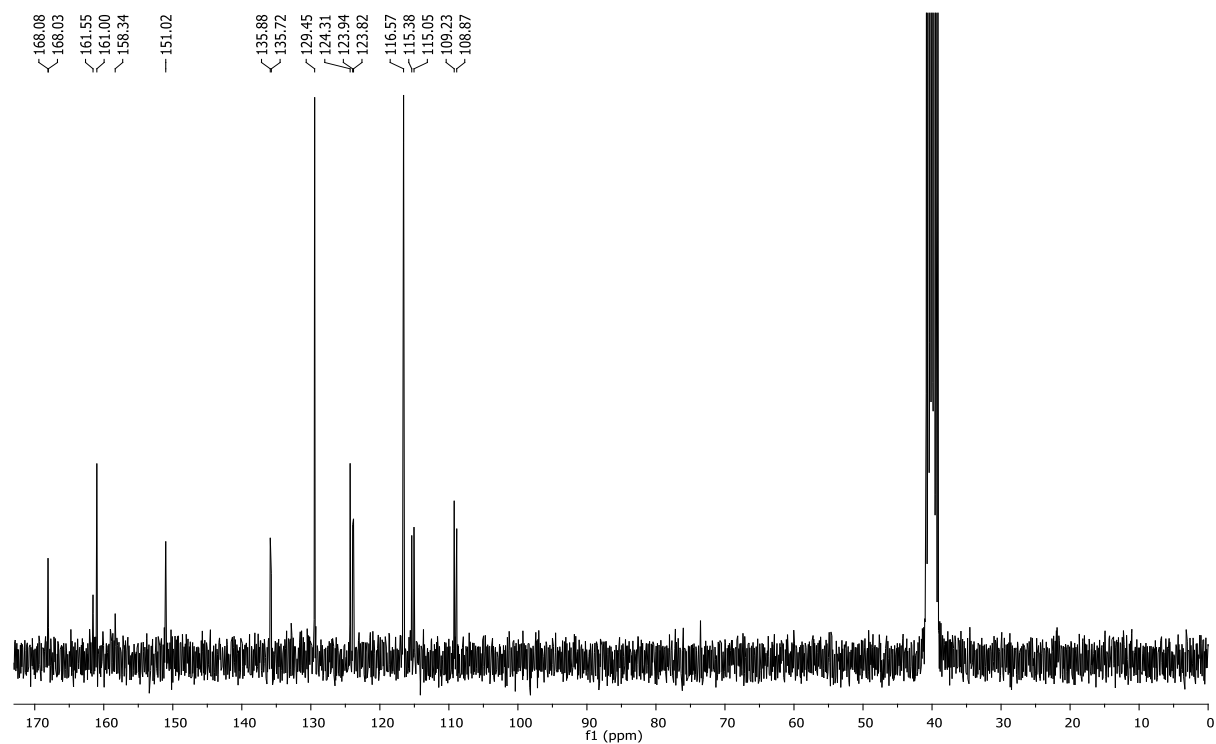
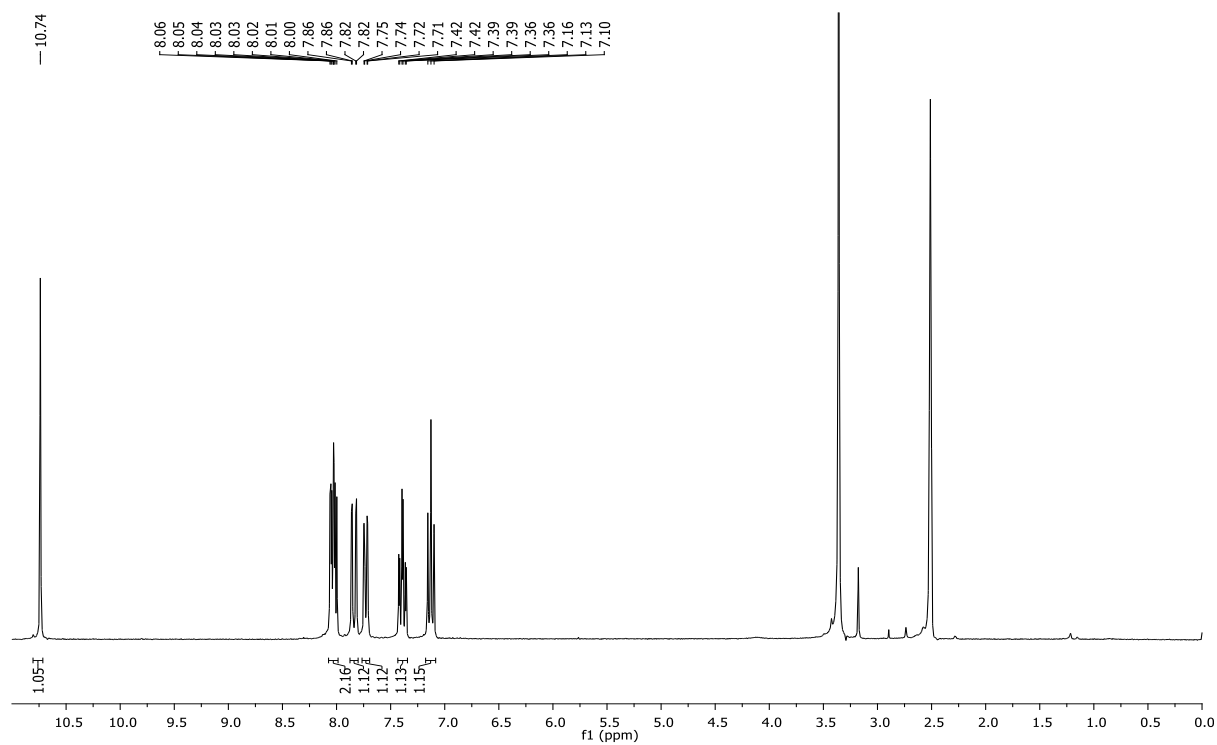


Fig. S5 a) ^1H NMR and b) ^{13}C NMR of compd. **10b**

a)



b)

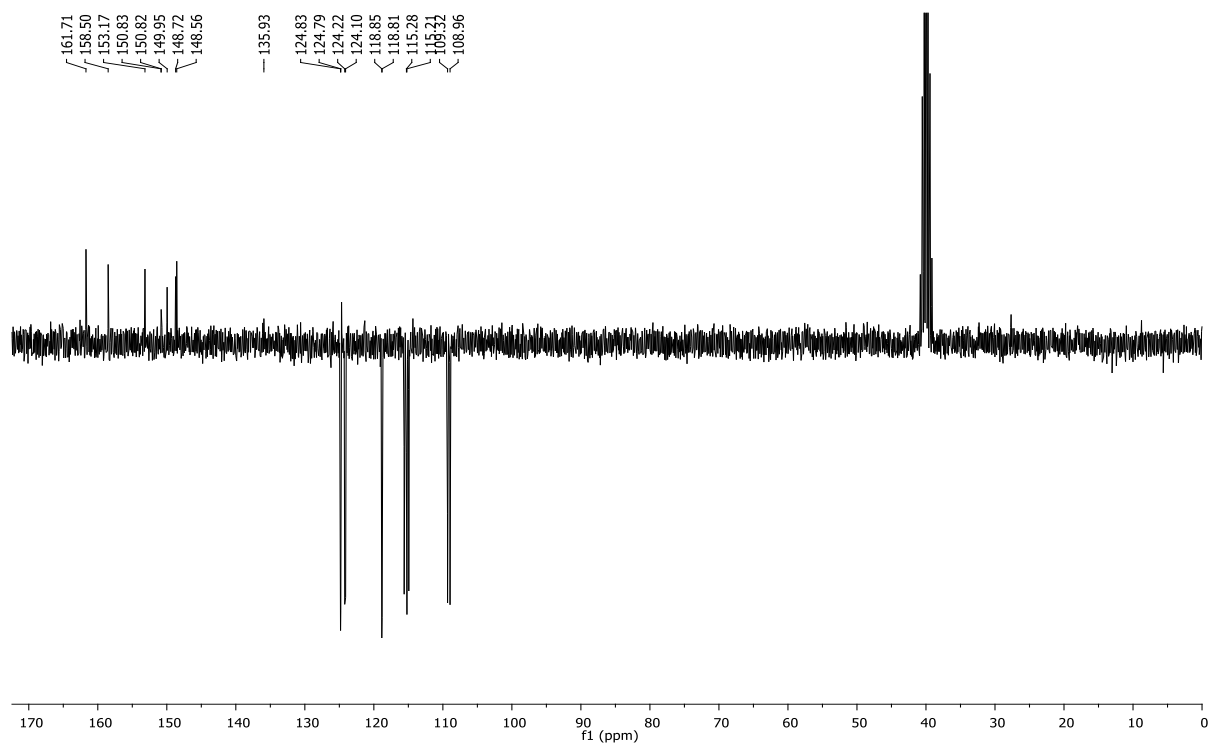
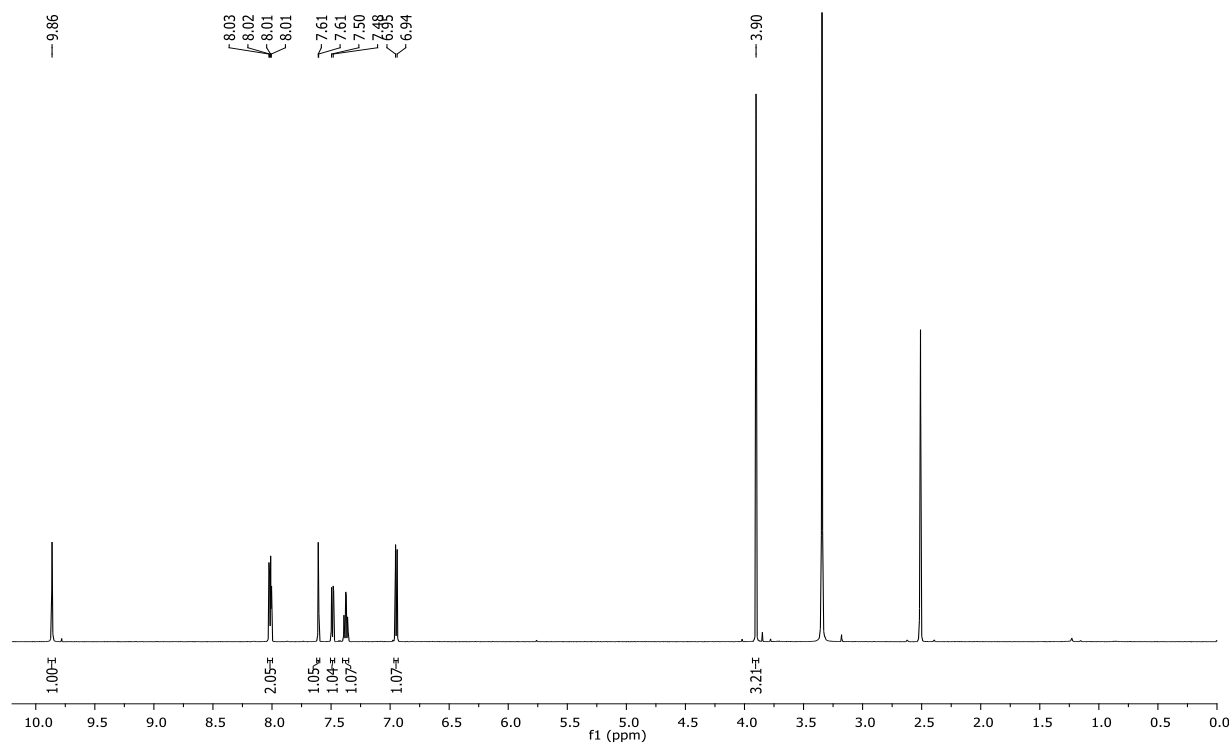


Fig. S6 a) ^1H NMR and b) ^{13}C NMR of compd. **10c**

a)



b)

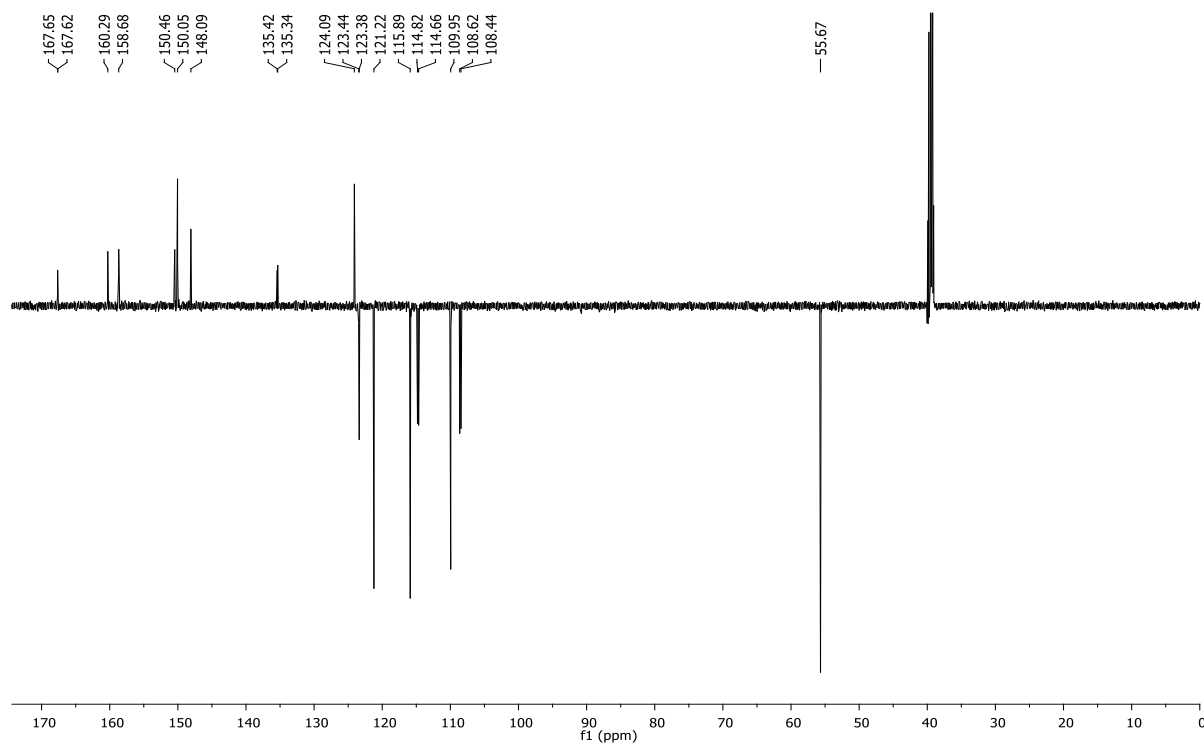
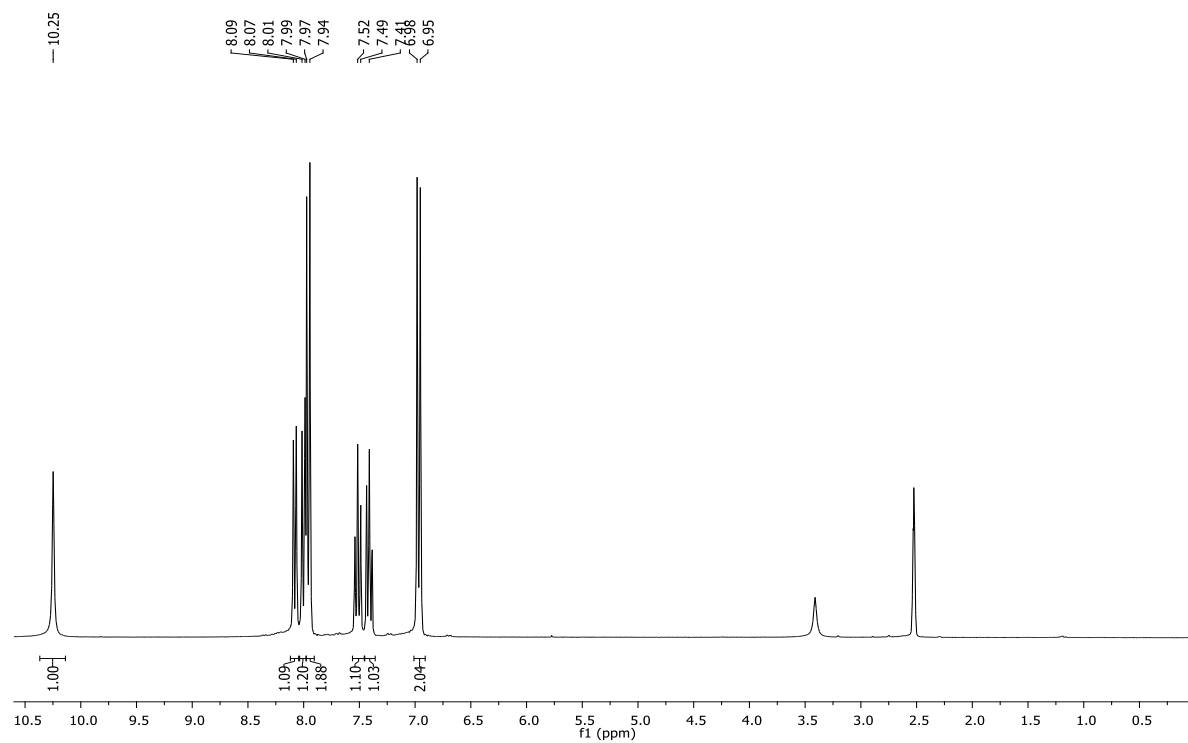


Fig. S7 a) ^1H NMR and b) ^{13}C NMR of compd. **11a**

a)



b)

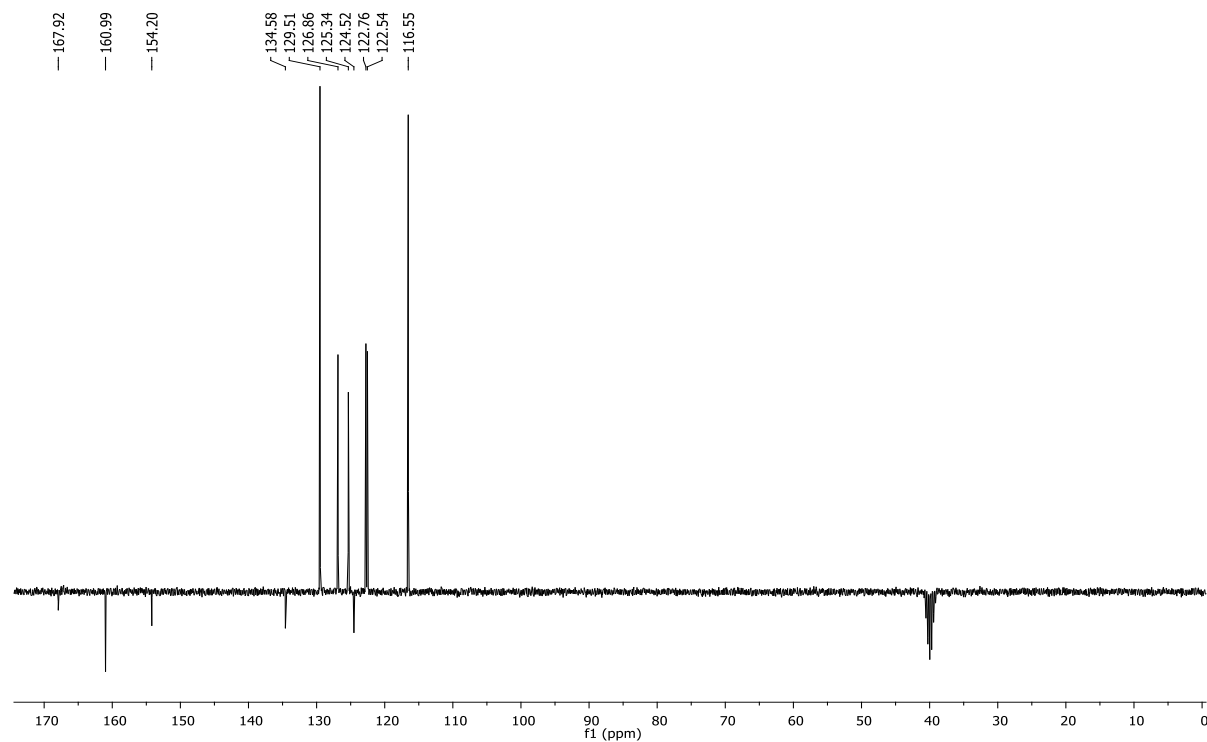
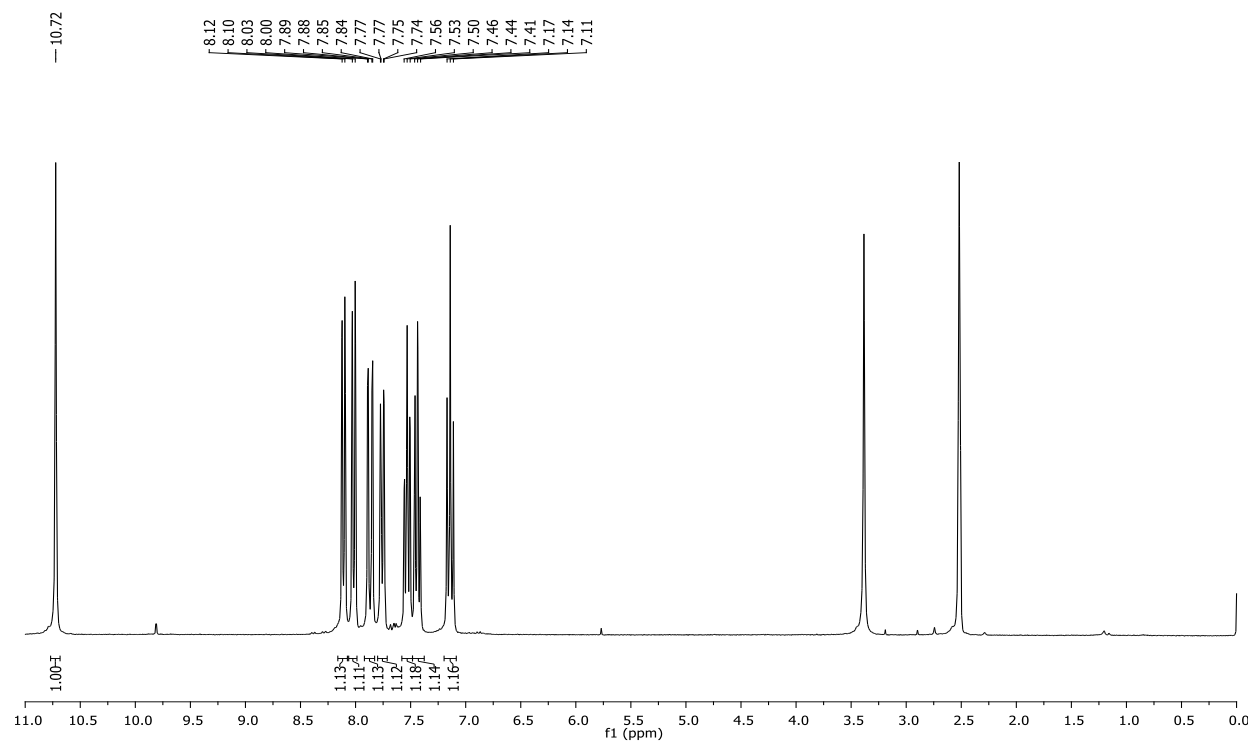


Fig. S8 a) ^1H NMR and b) ^{13}C NMR of compd. **11b**

a)



b)

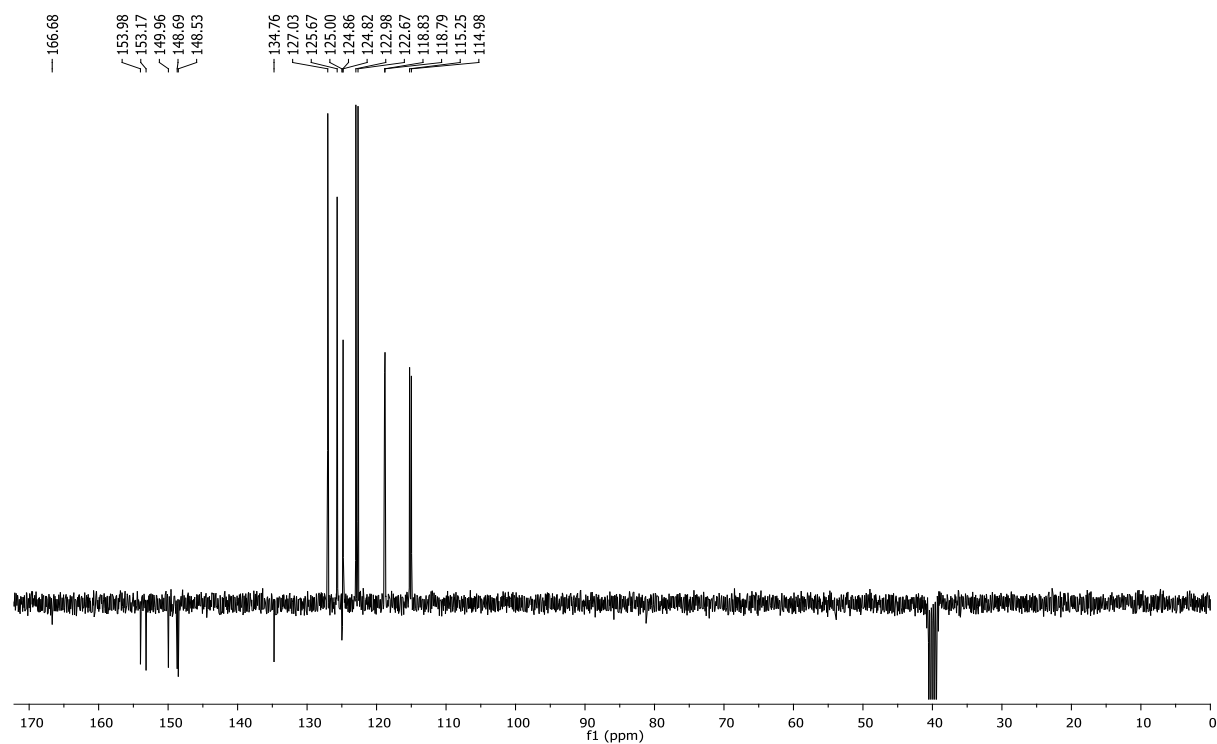
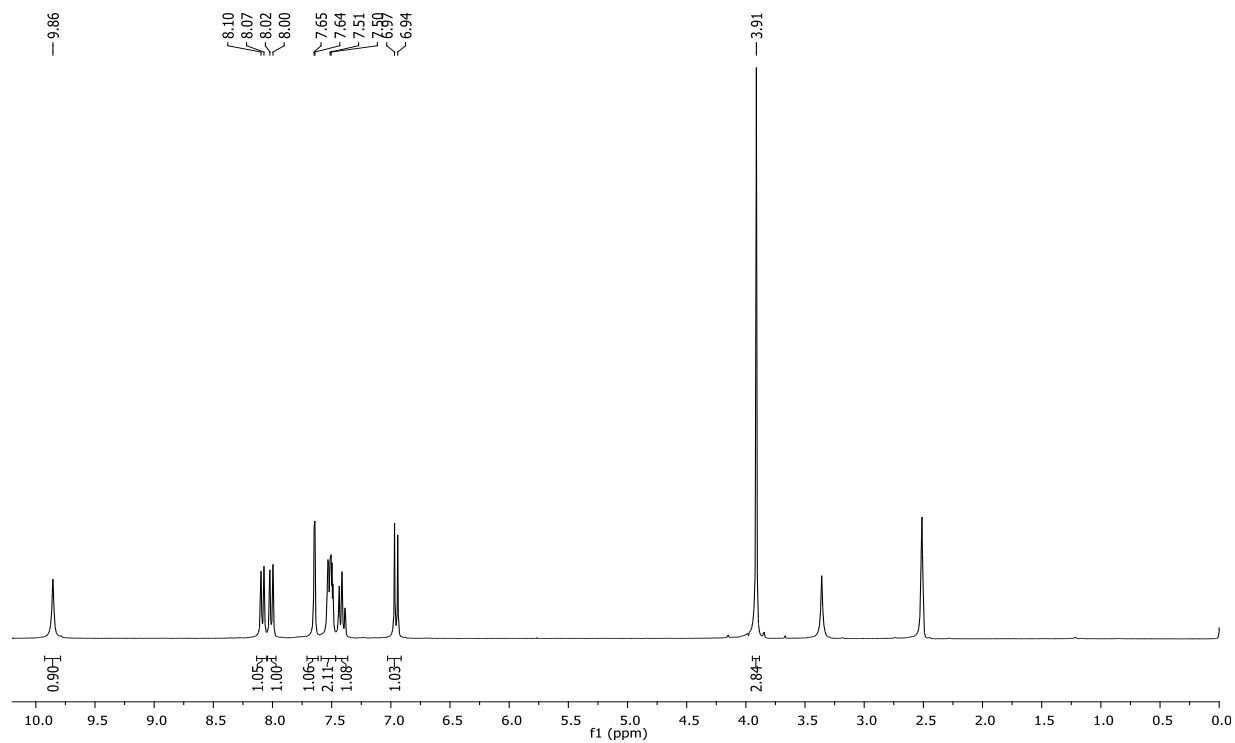


Fig. S9 a) ^1H NMR and b) ^{13}C NMR of compd. **11c**

a)



b)

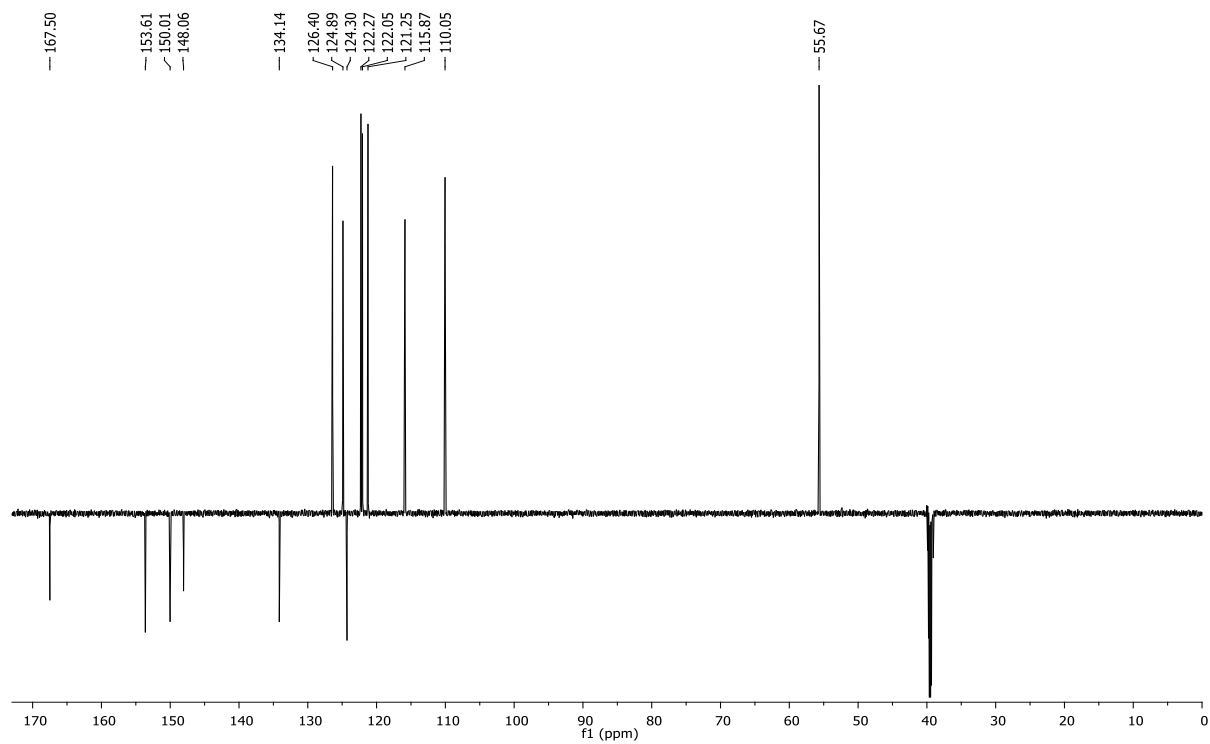
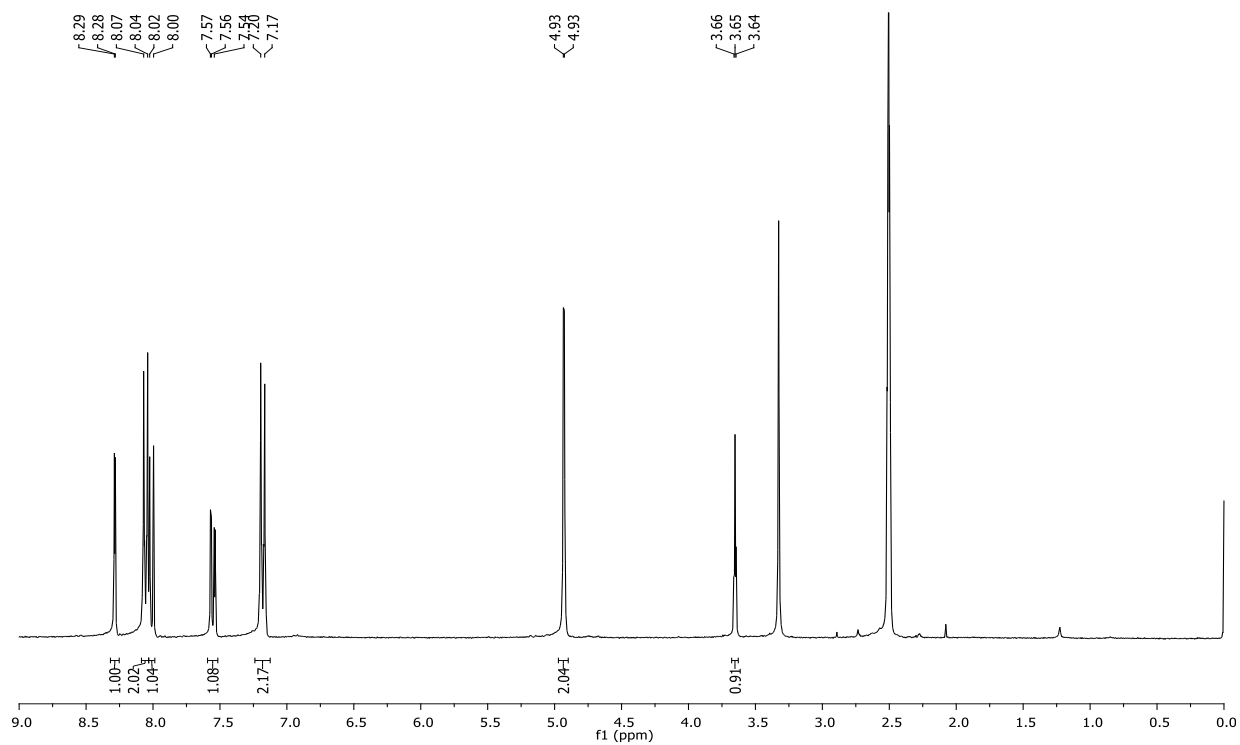


Fig. S10 a) ^1H NMR and b) ^{13}C NMR of compd. **12a**

a)



b)

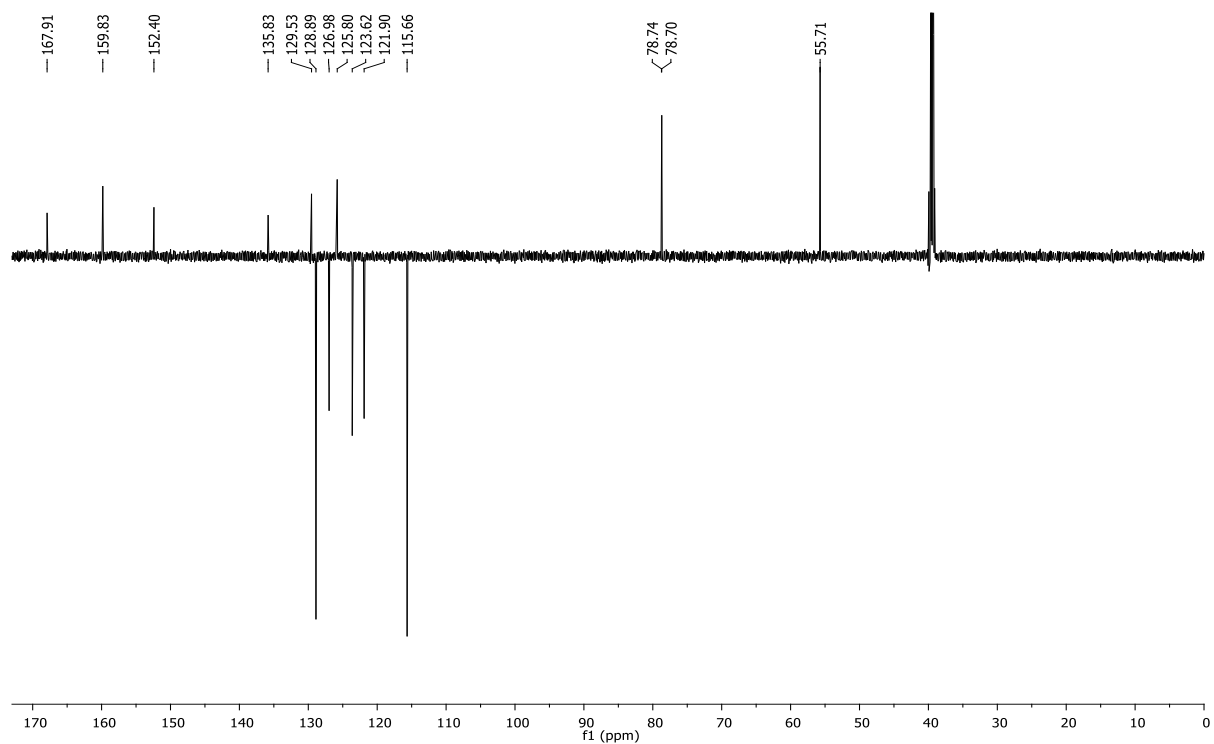
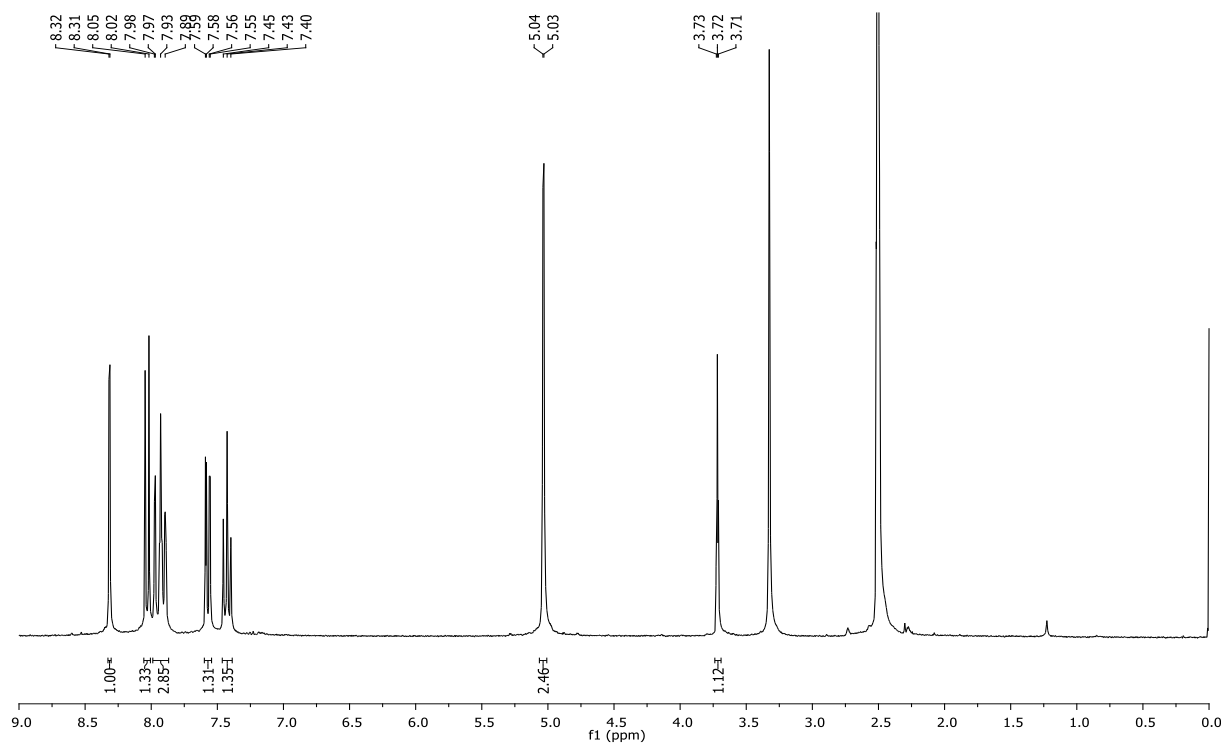


Fig. S11 a) ^1H NMR and b) ^{13}C NMR of compd. **12b**

a)



b)

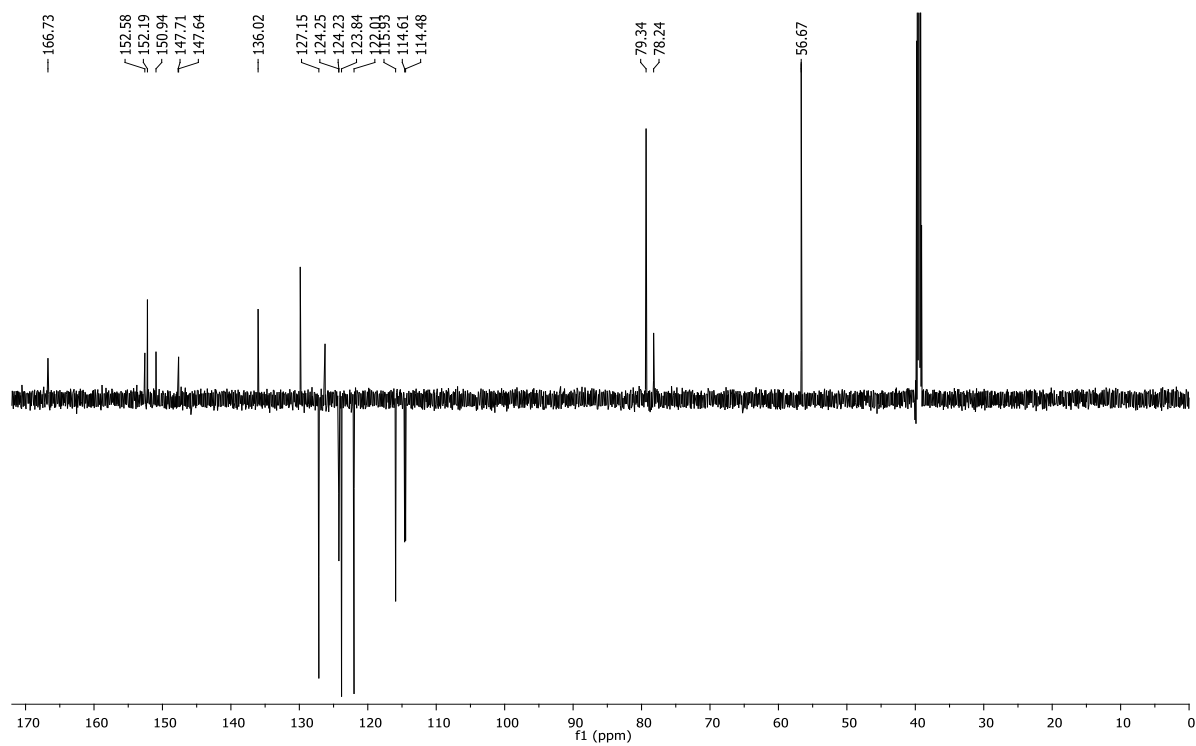
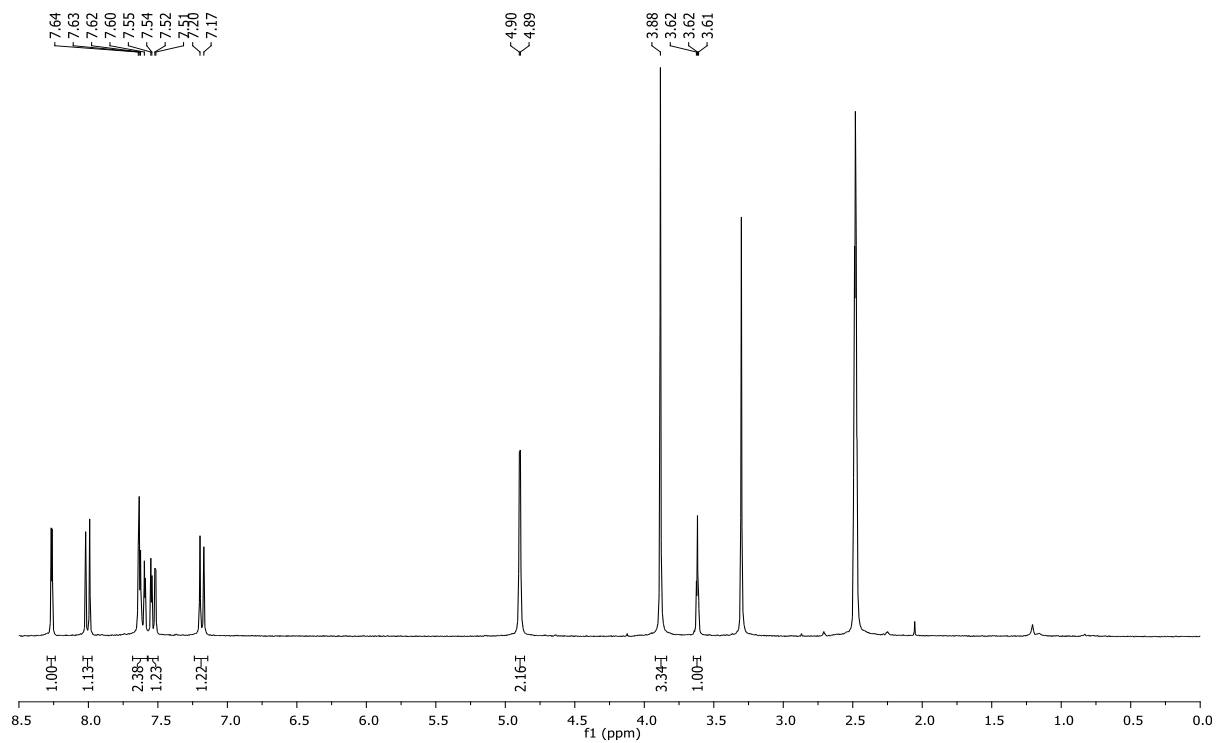


Fig. S12 a) ^1H NMR and b) ^{13}C NMR of compd. **12c**

a)



b)

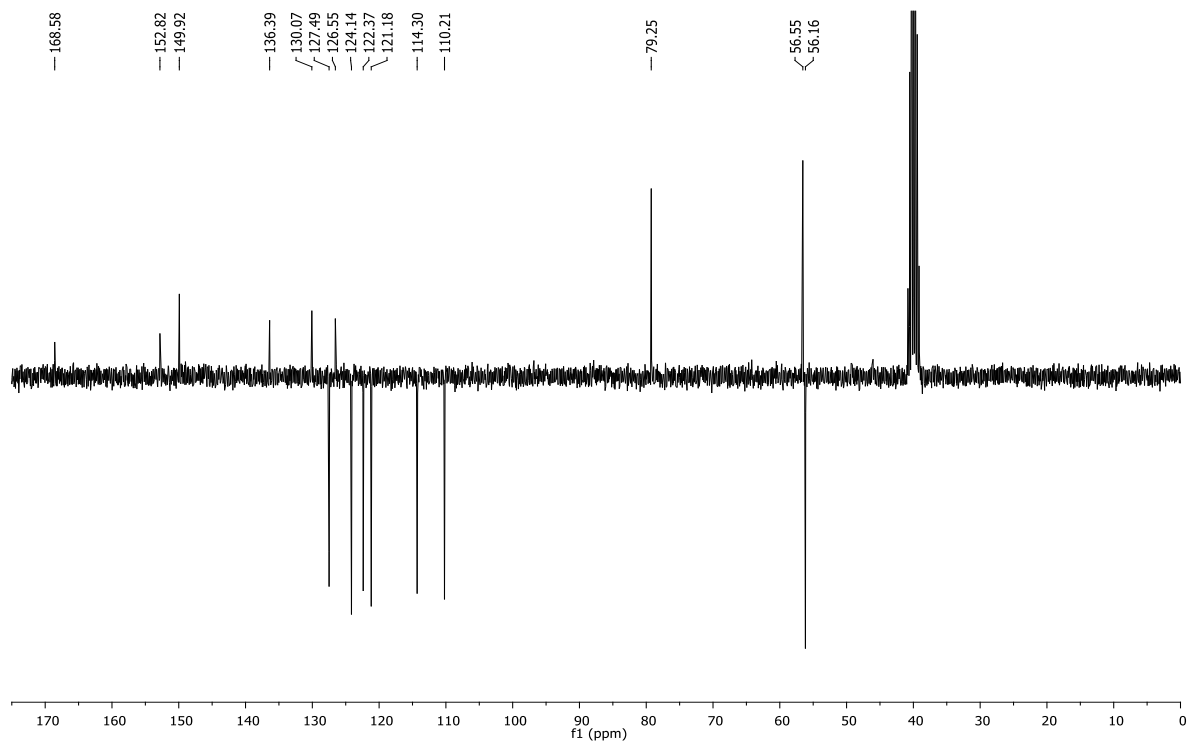
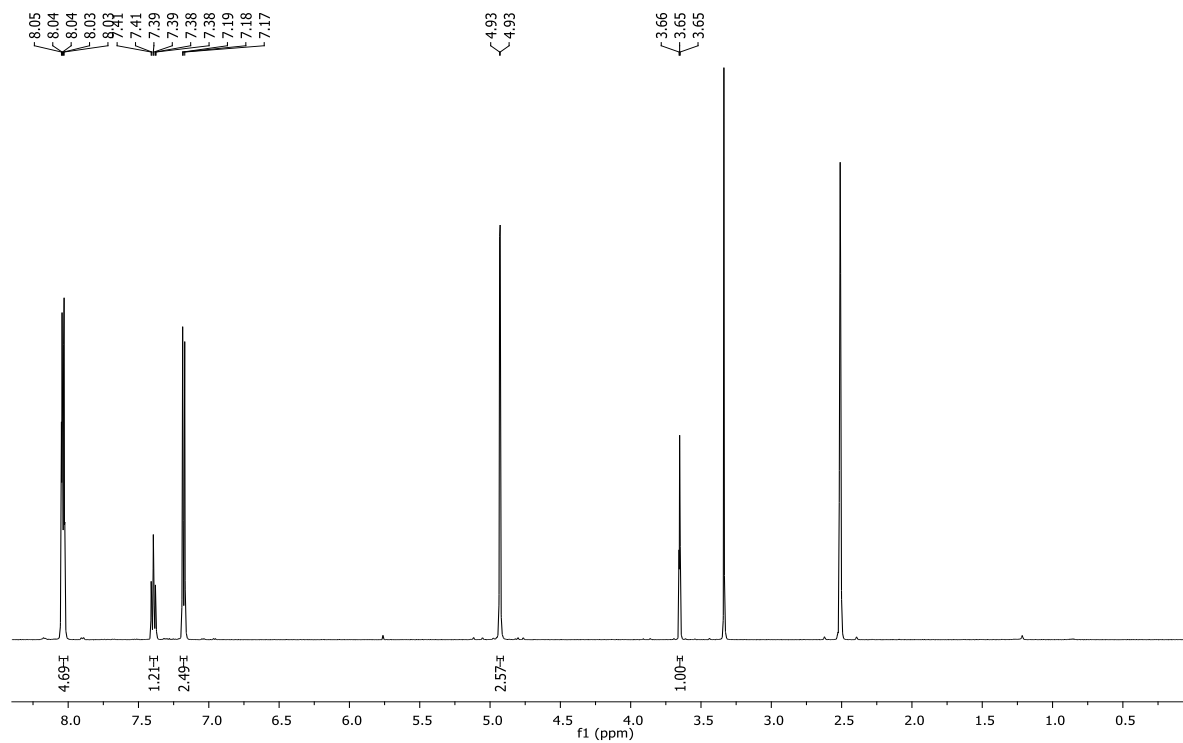


Fig. S13 a) ^1H NMR and b) ^{13}C NMR of compd. **13a**

a)



b)

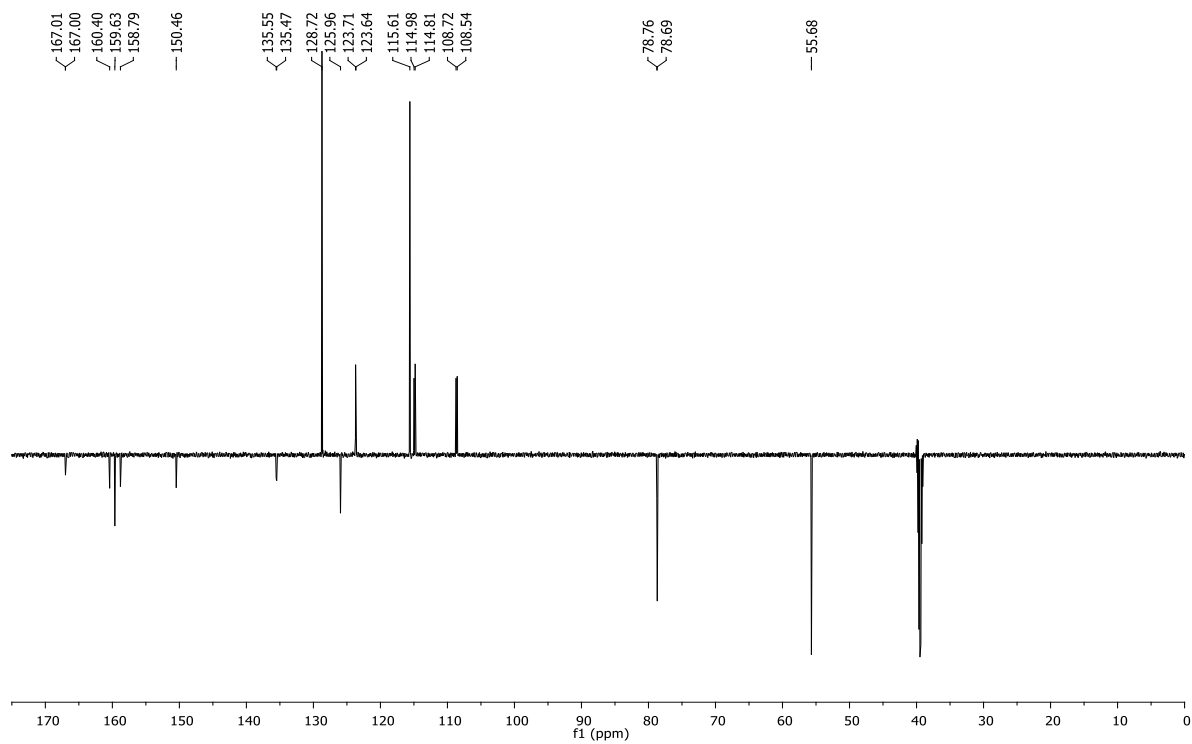
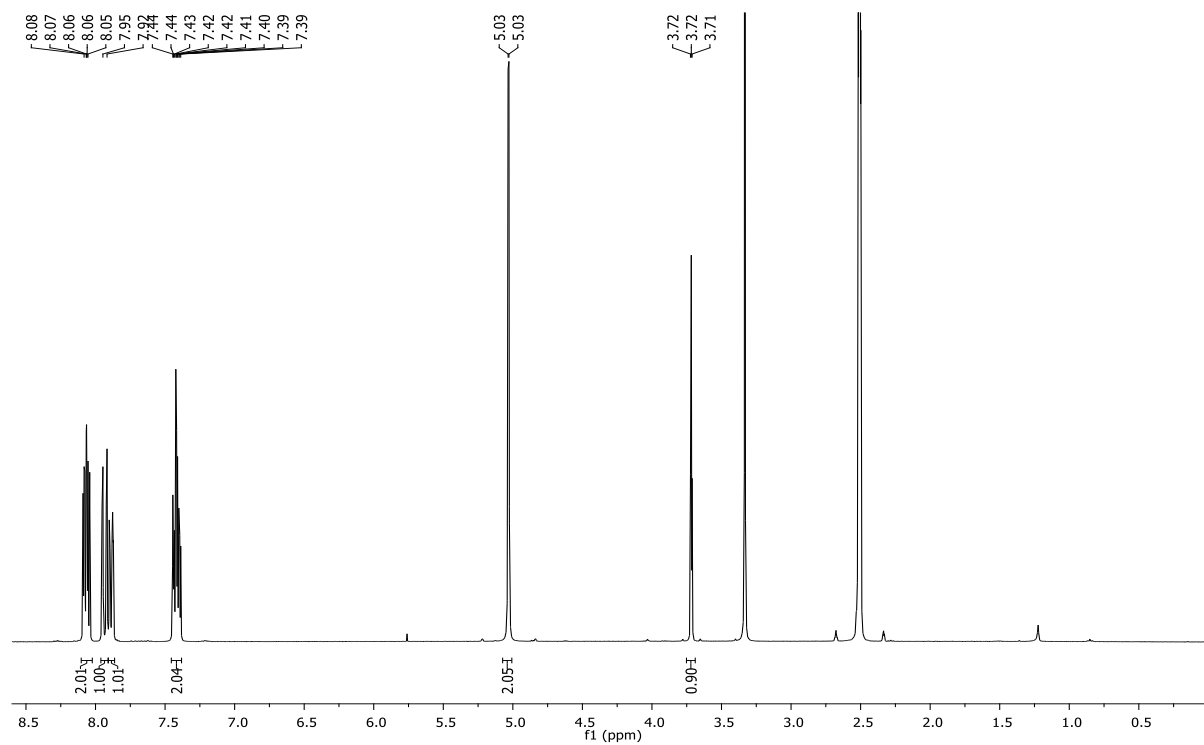


Fig. S14 a) ^1H NMR and b) ^{13}C NMR of compd. **13b**

a)



b)

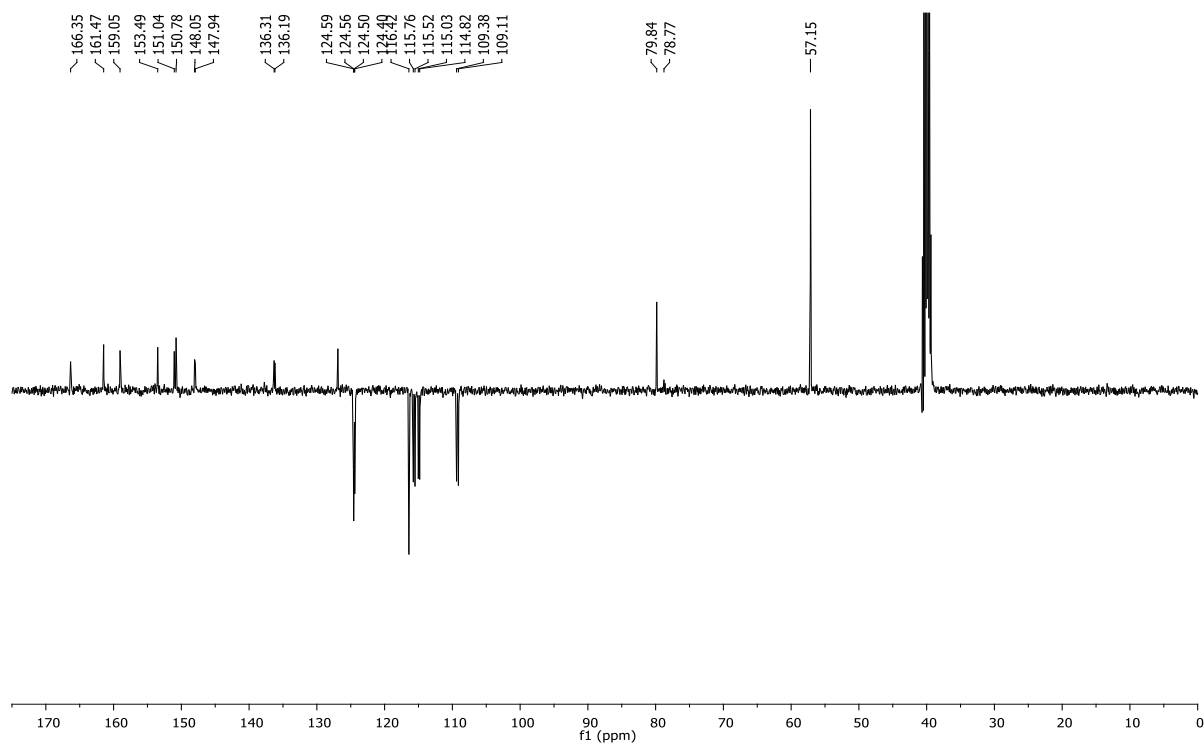
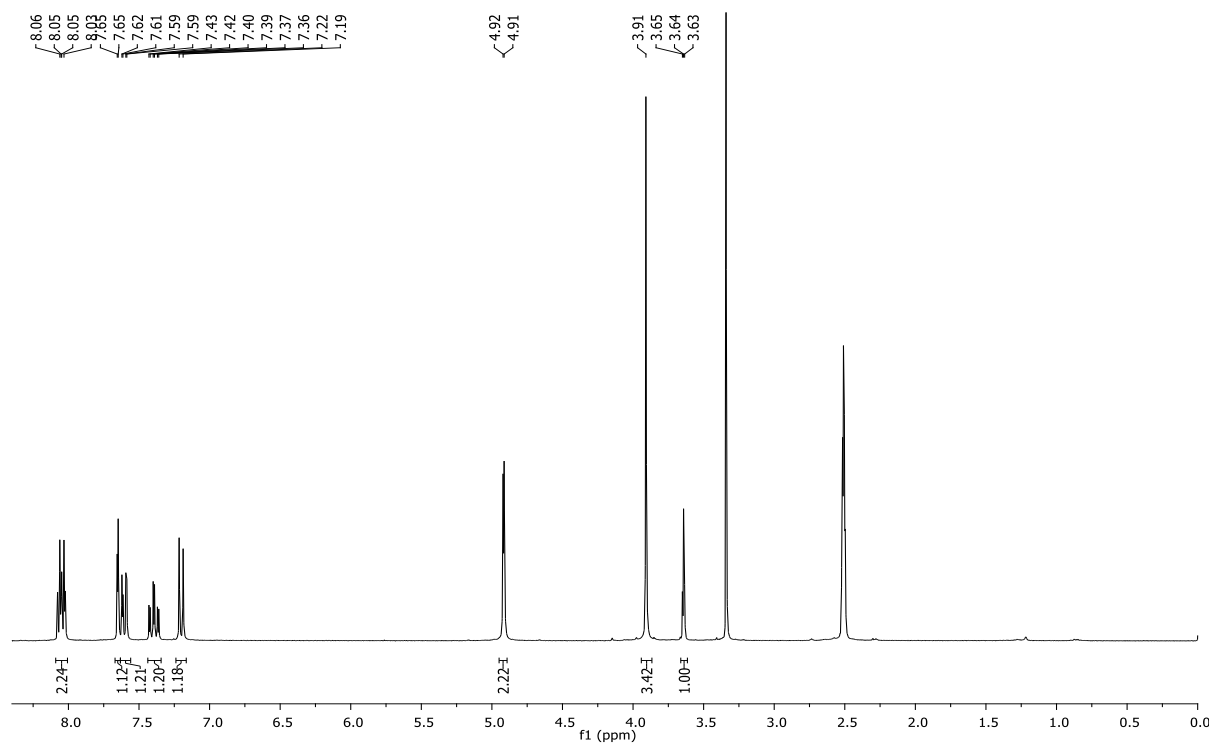


Fig. S15 a) ^1H NMR and b) ^{13}C NMR of compd. **13c**

a)



b)

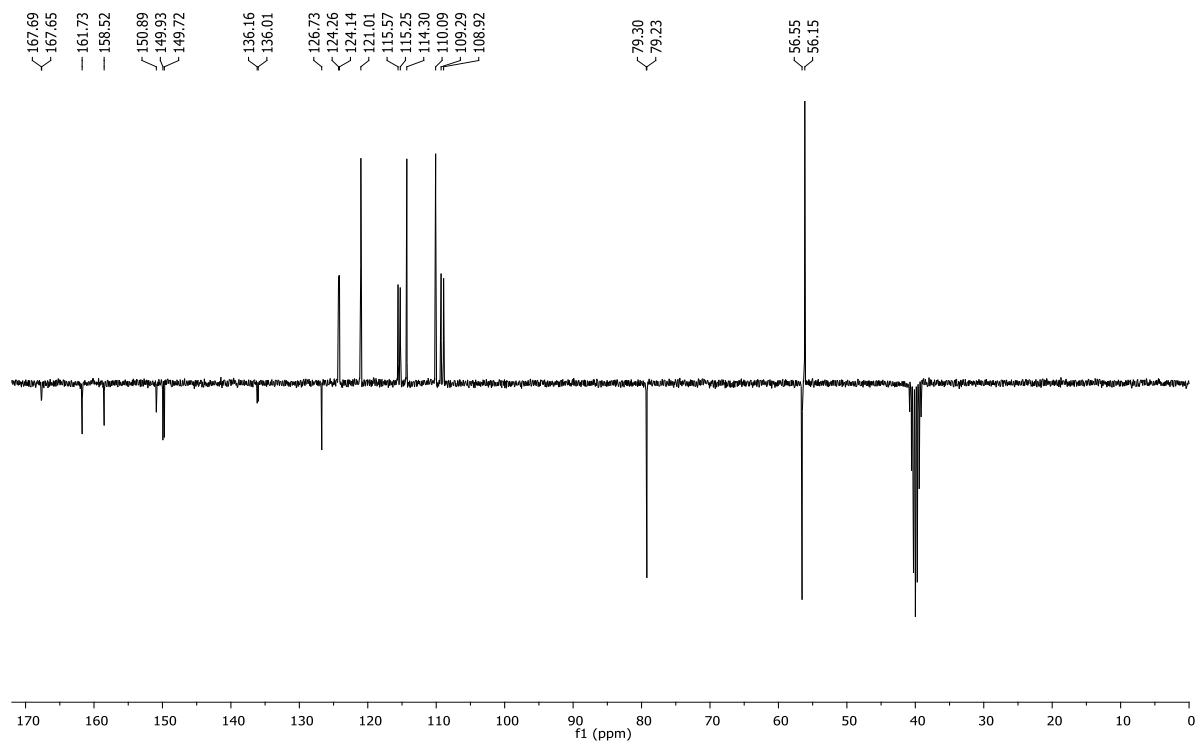
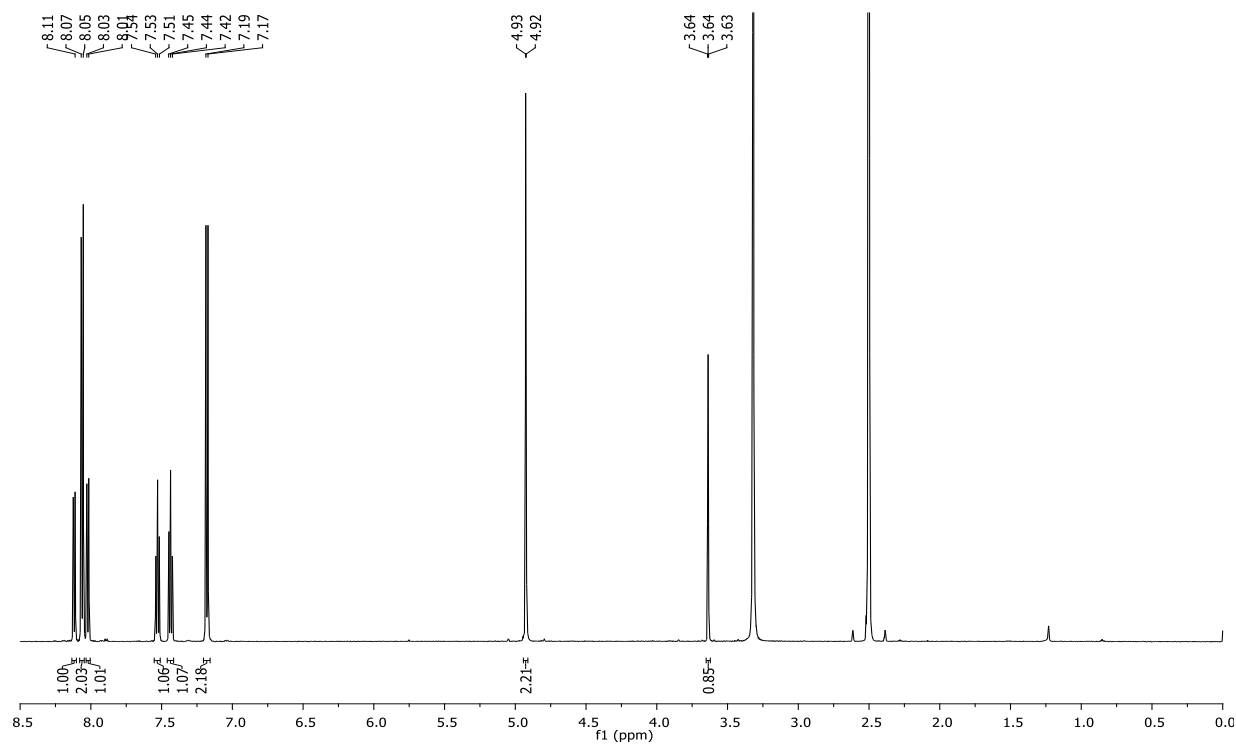


Fig. S16 a) ^1H NMR and b) ^{13}C NMR of compd. **14a**

a)



b)

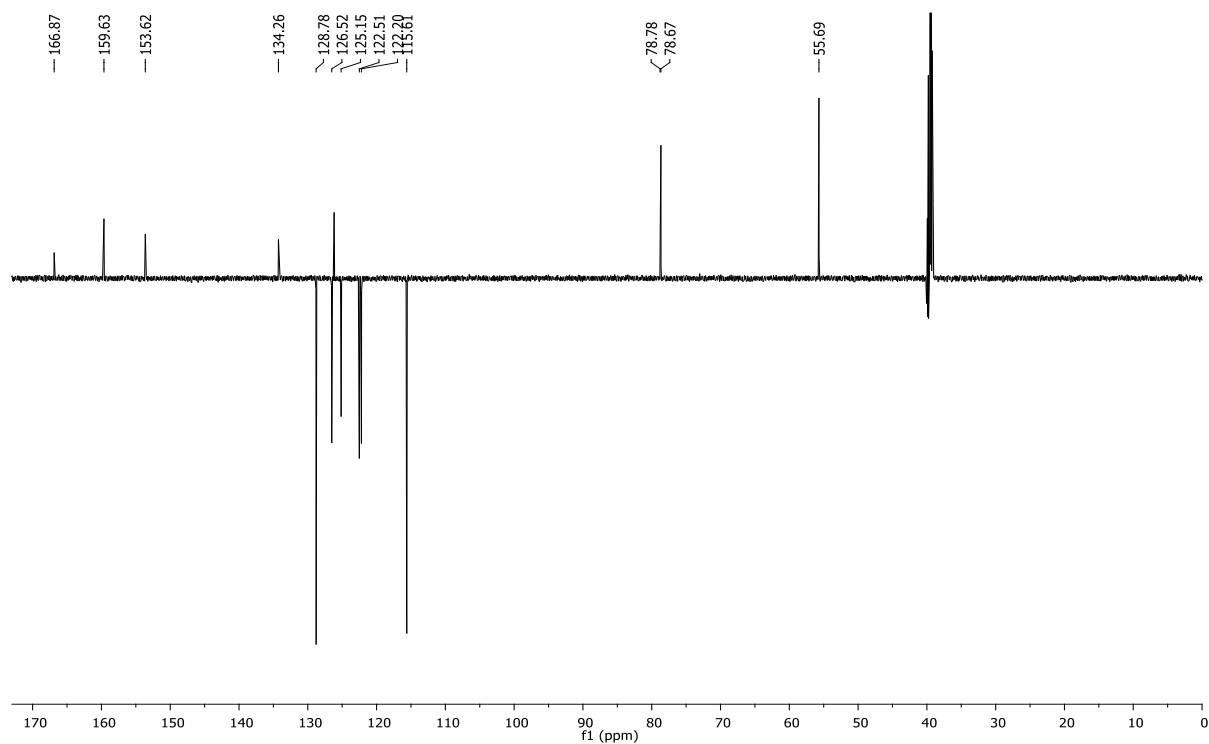
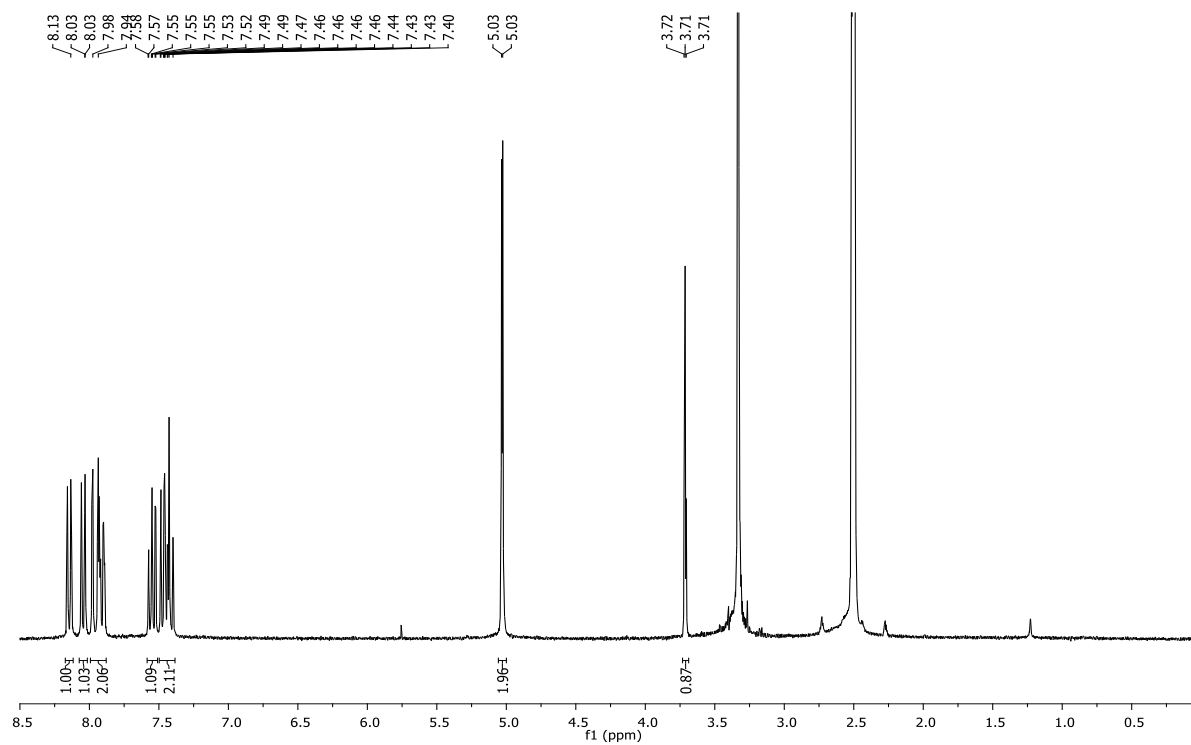


Fig. S17 a) ^1H NMR and b) ^{13}C NMR of compd. **14b**

a)



b)

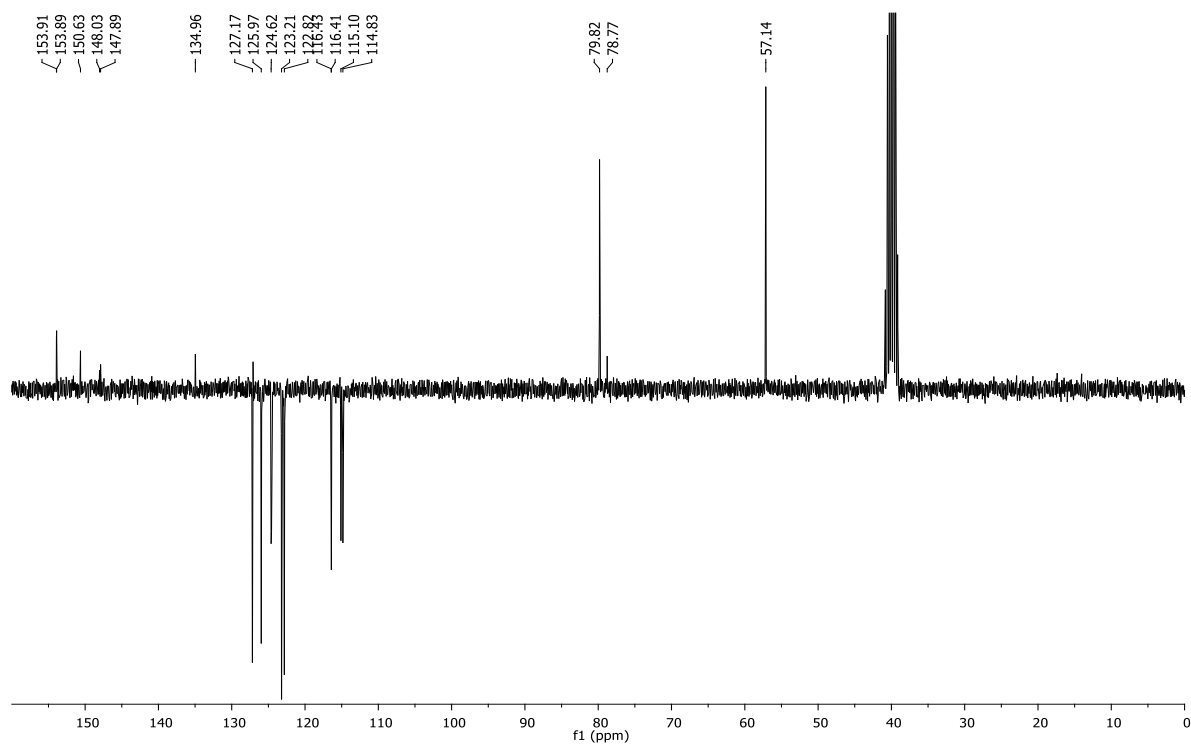
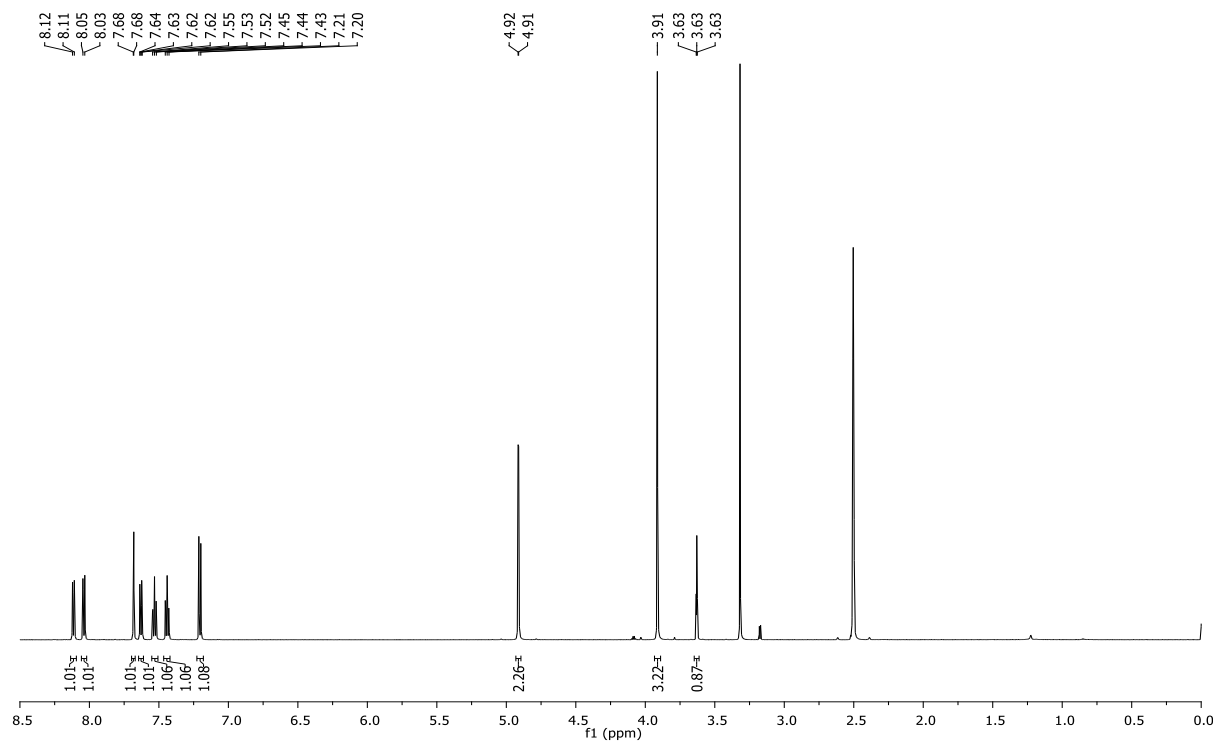


Fig. S18 a) ^1H NMR and b) ^{13}C NMR of compd. **14c**

a)



b)

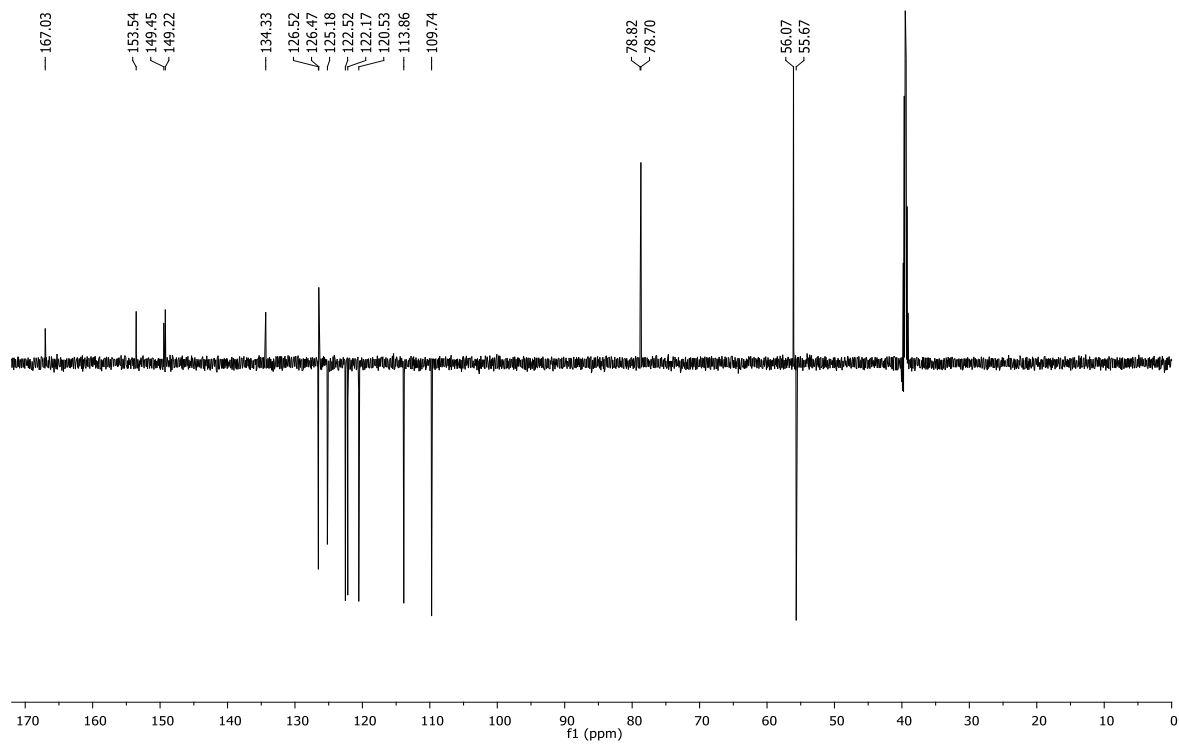
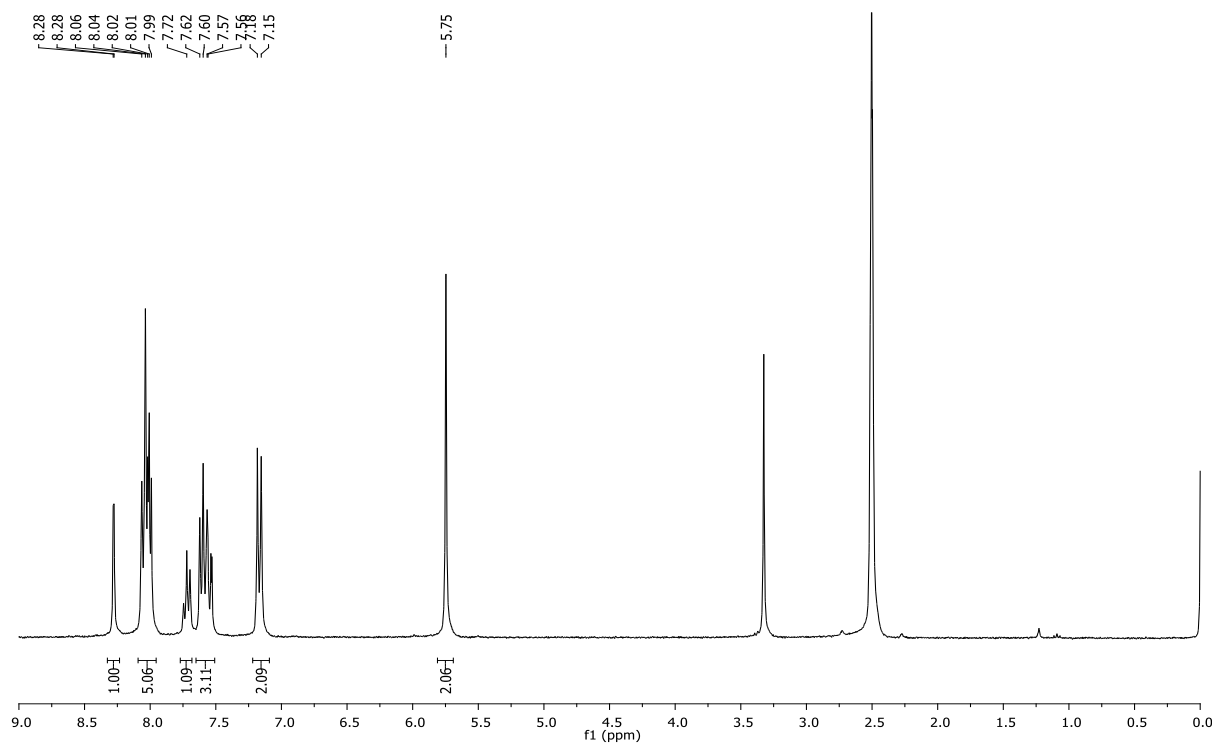


Fig. S19 a) ^1H NMR and b) ^{13}C NMR of compd. **15a**

a)



b)

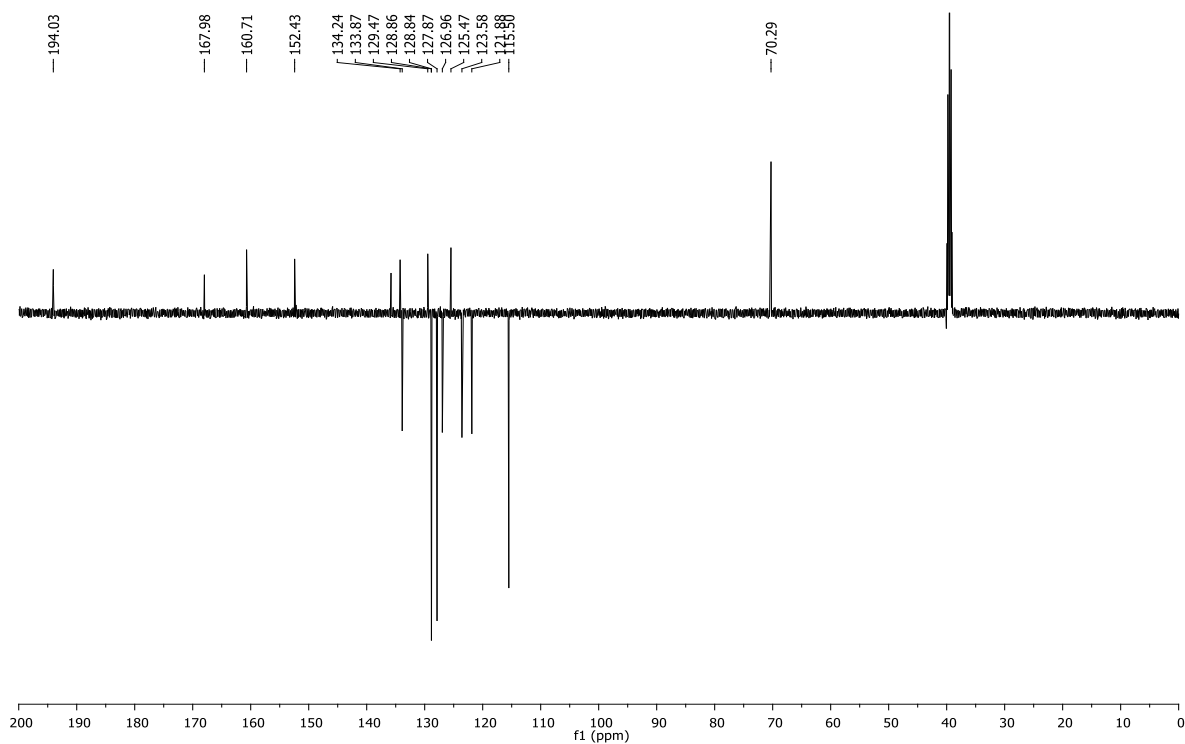
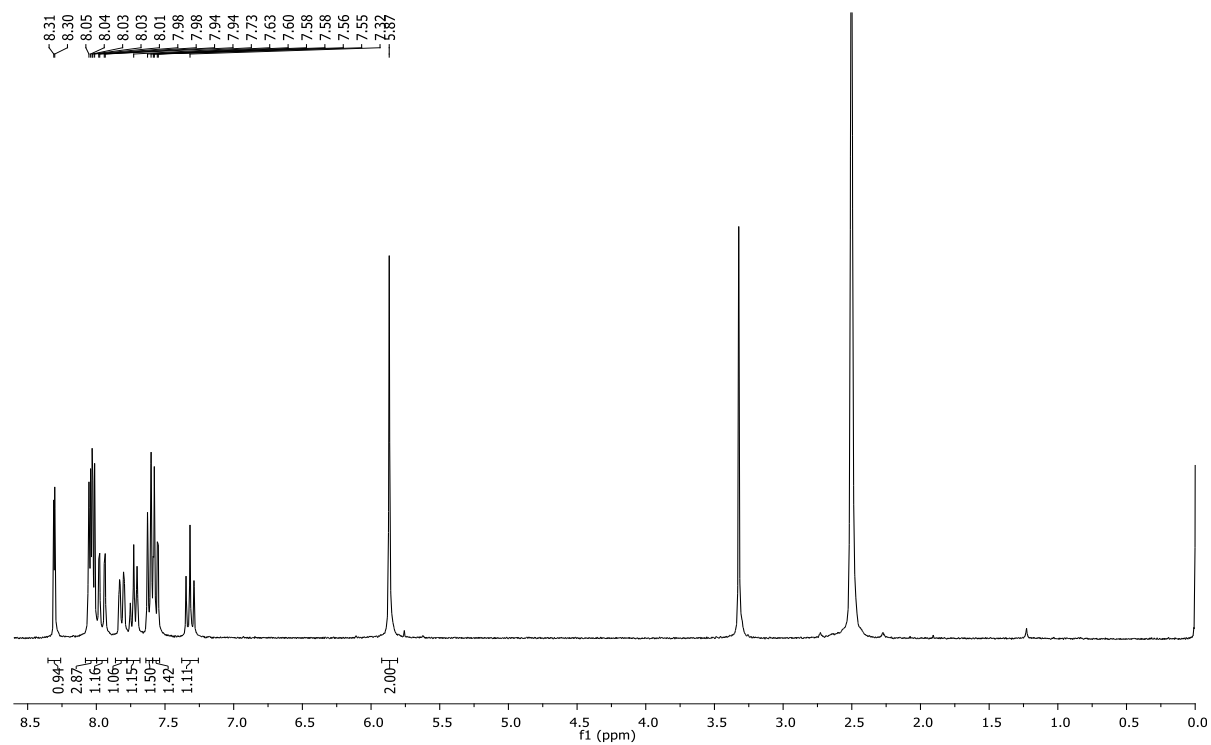


Fig. S20 a) ^1H NMR and b) ^{13}C NMR of compd. **15b**

a)



b)

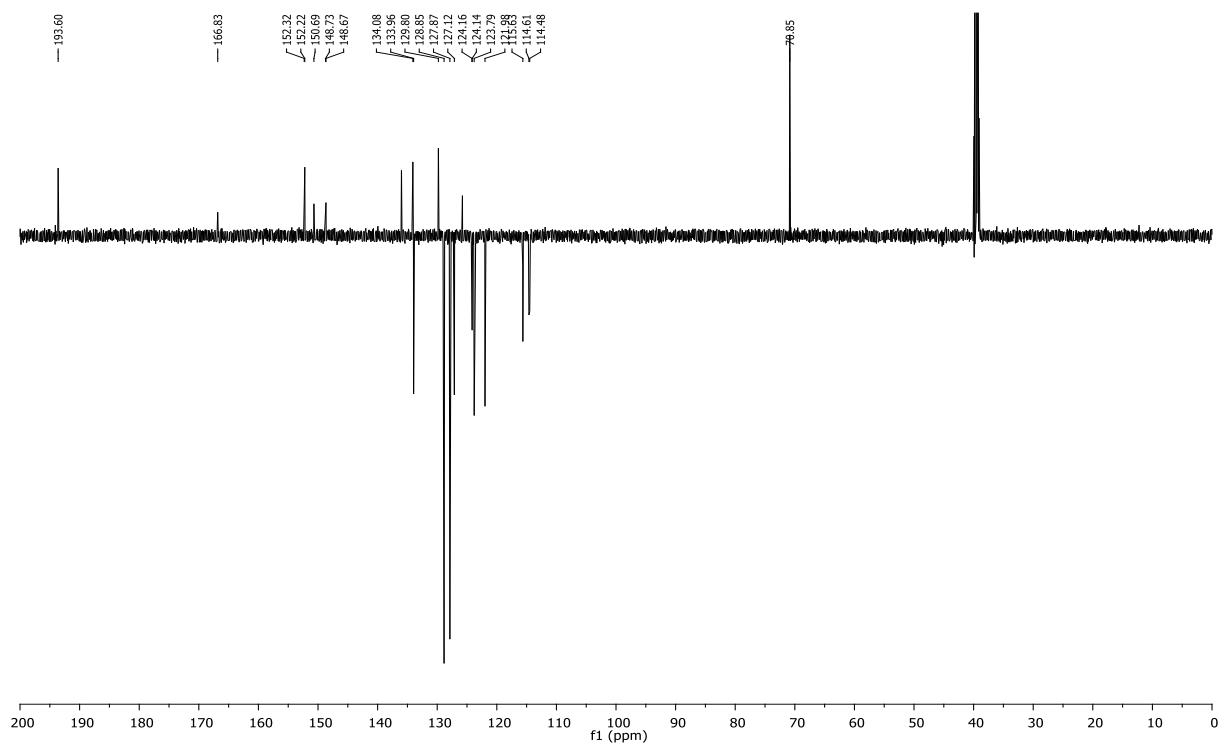
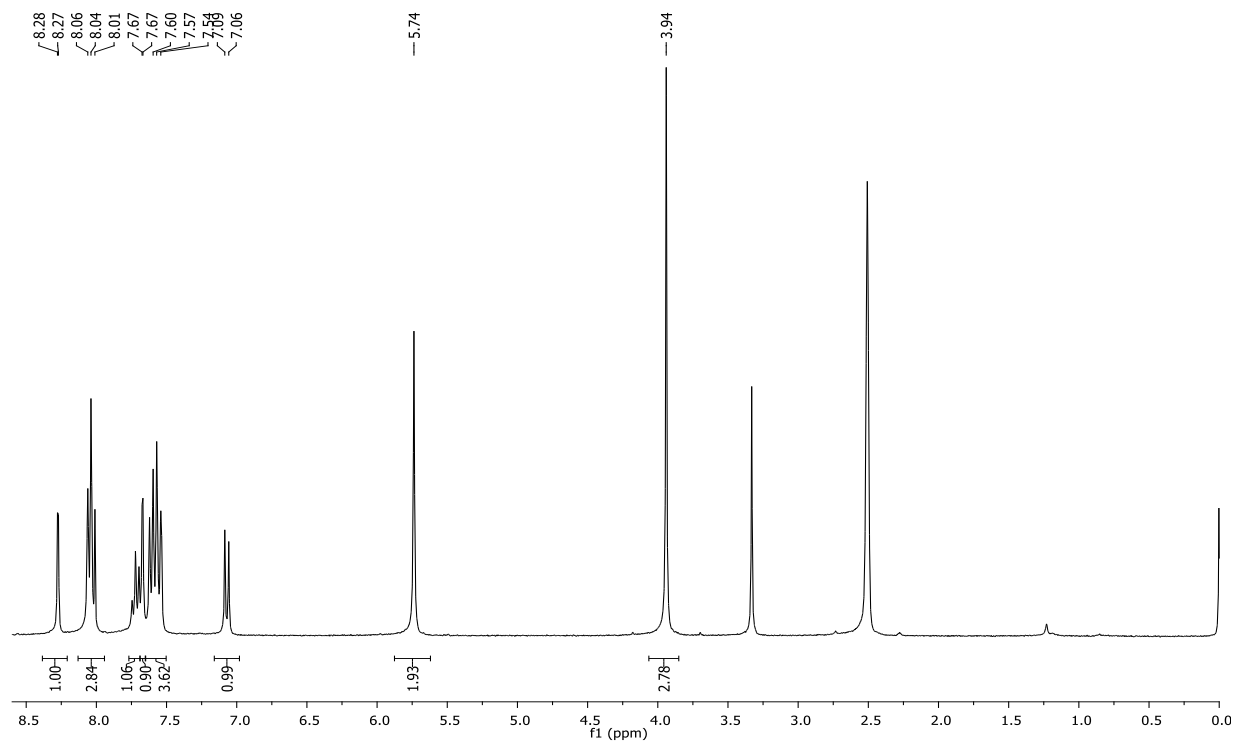


Fig. S21 a) ^1H NMR and b) ^{13}C NMR of compd. **15c**

a)



b)

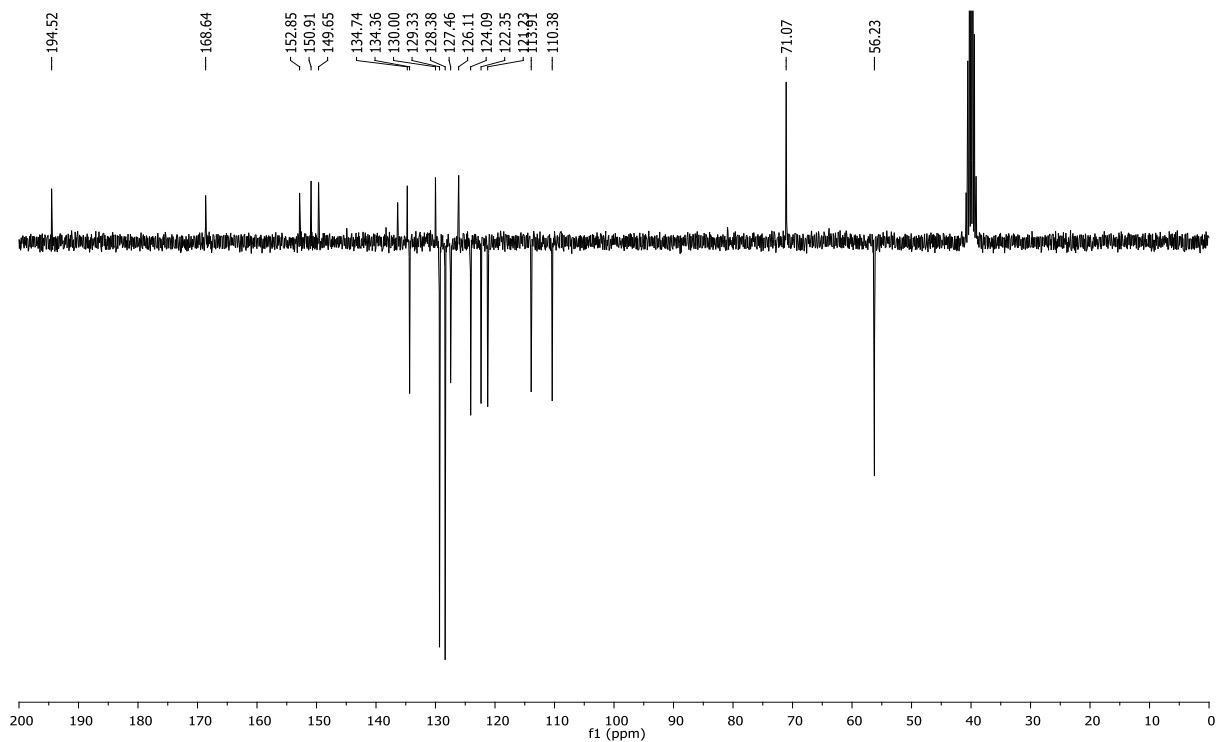
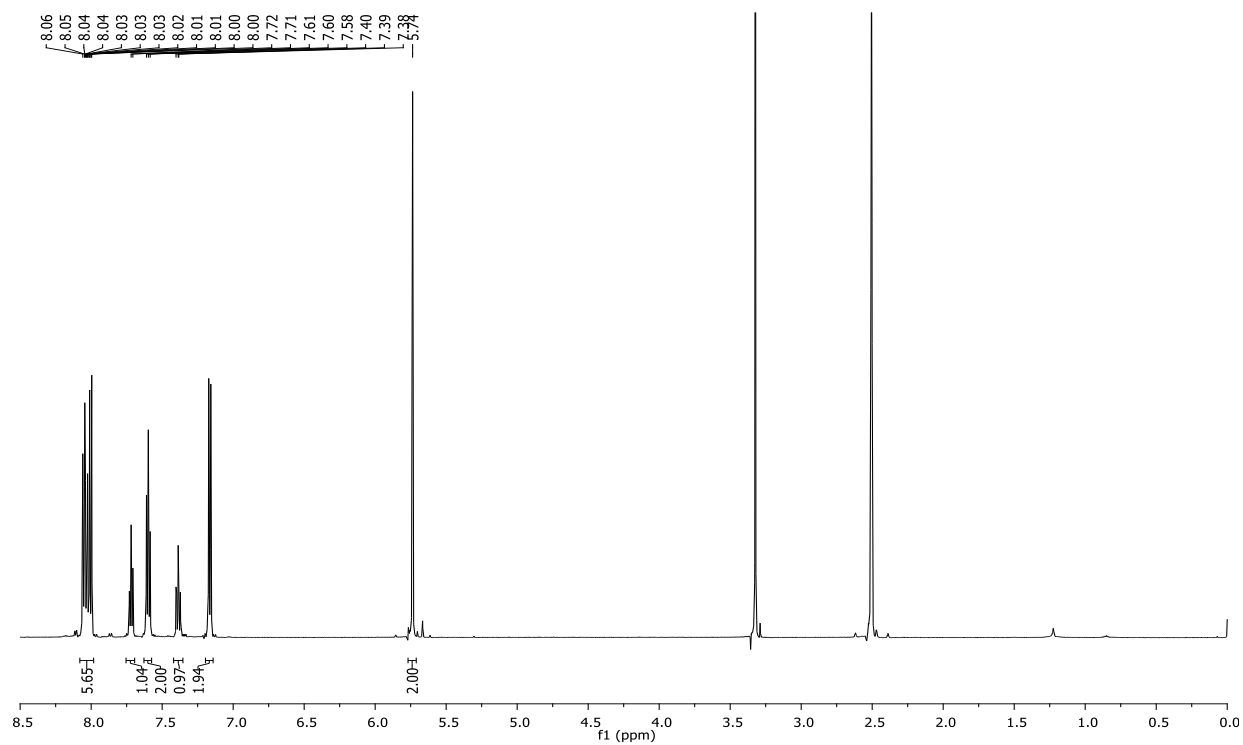


Fig. S22 a) ^1H NMR and b) ^{13}C NMR of compd. **16a**

a)



b)

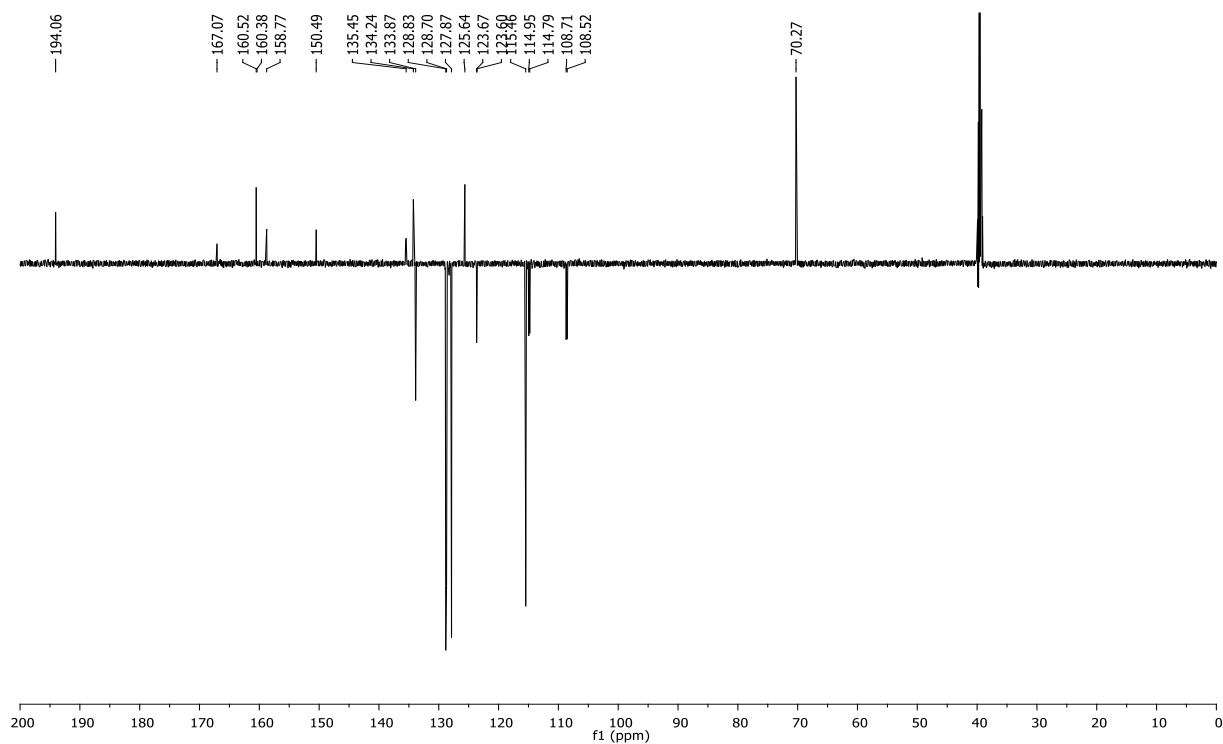
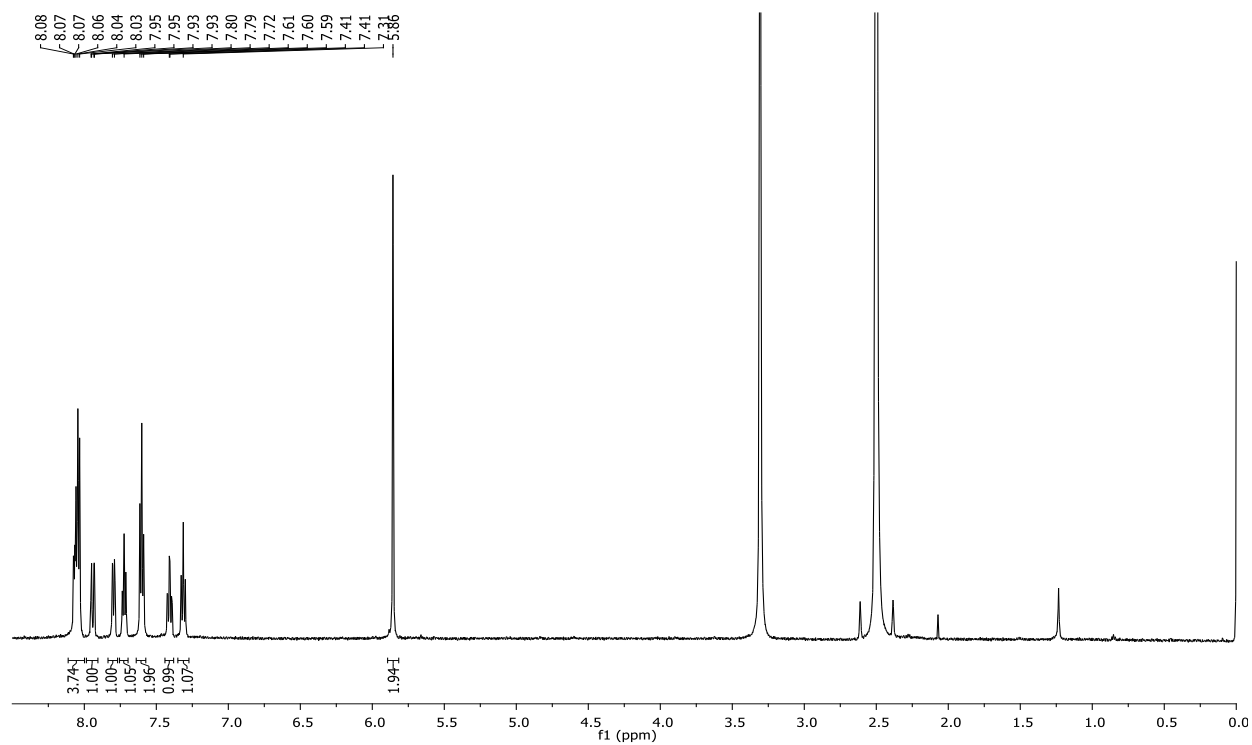


Fig. S23 a) ^1H NMR and b) ^{13}C NMR of compd. **16b**

a)



b)

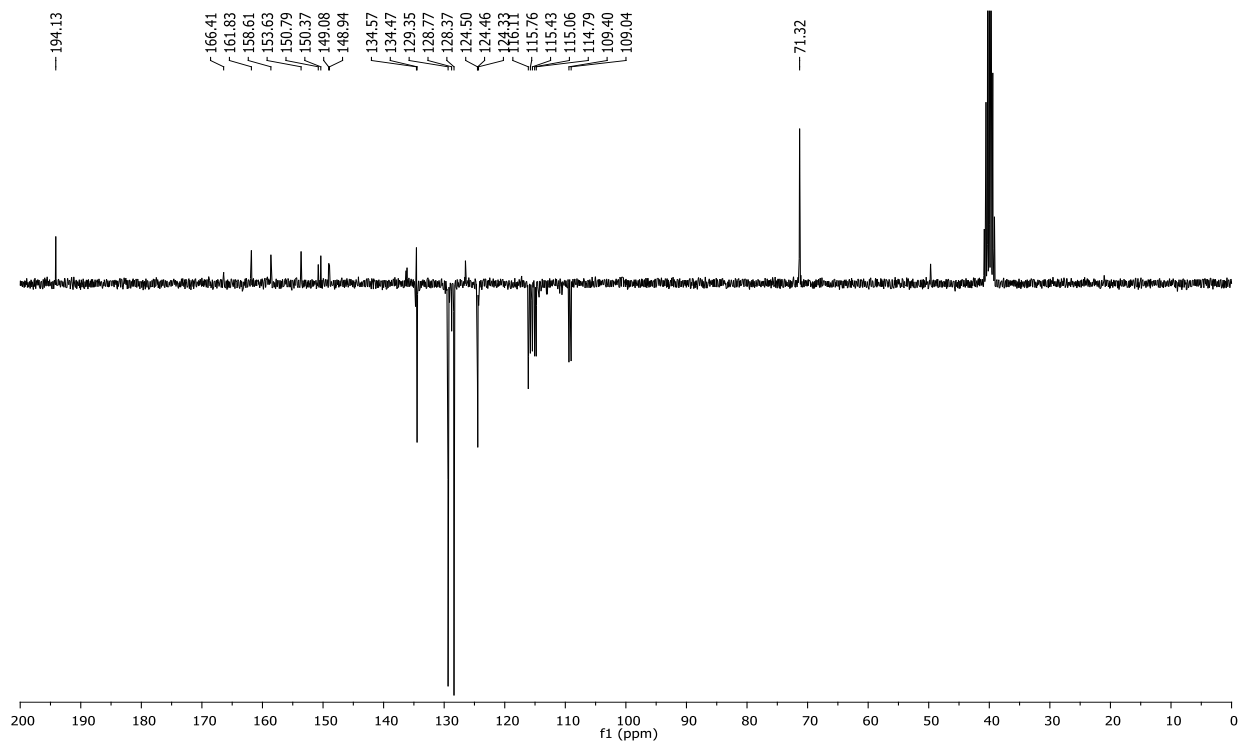
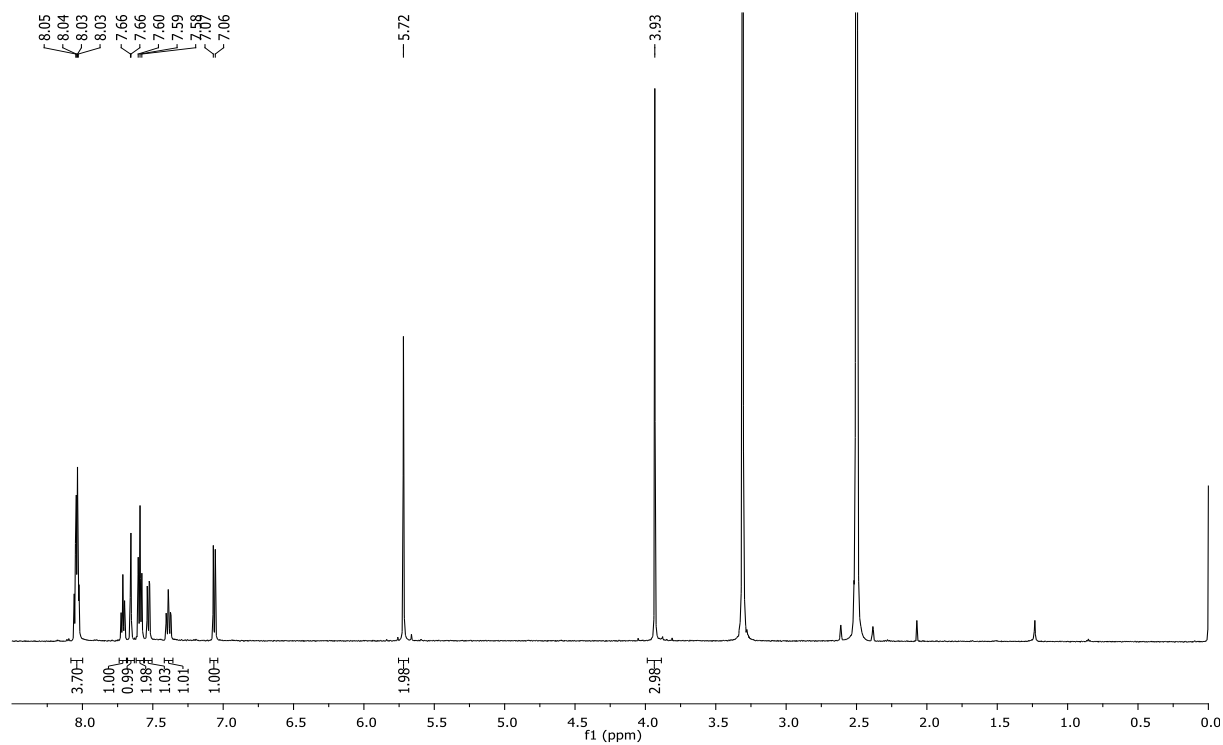


Fig. S24 a) ^1H NMR and b) ^{13}C NMR of compd. **16c**

a)



b)

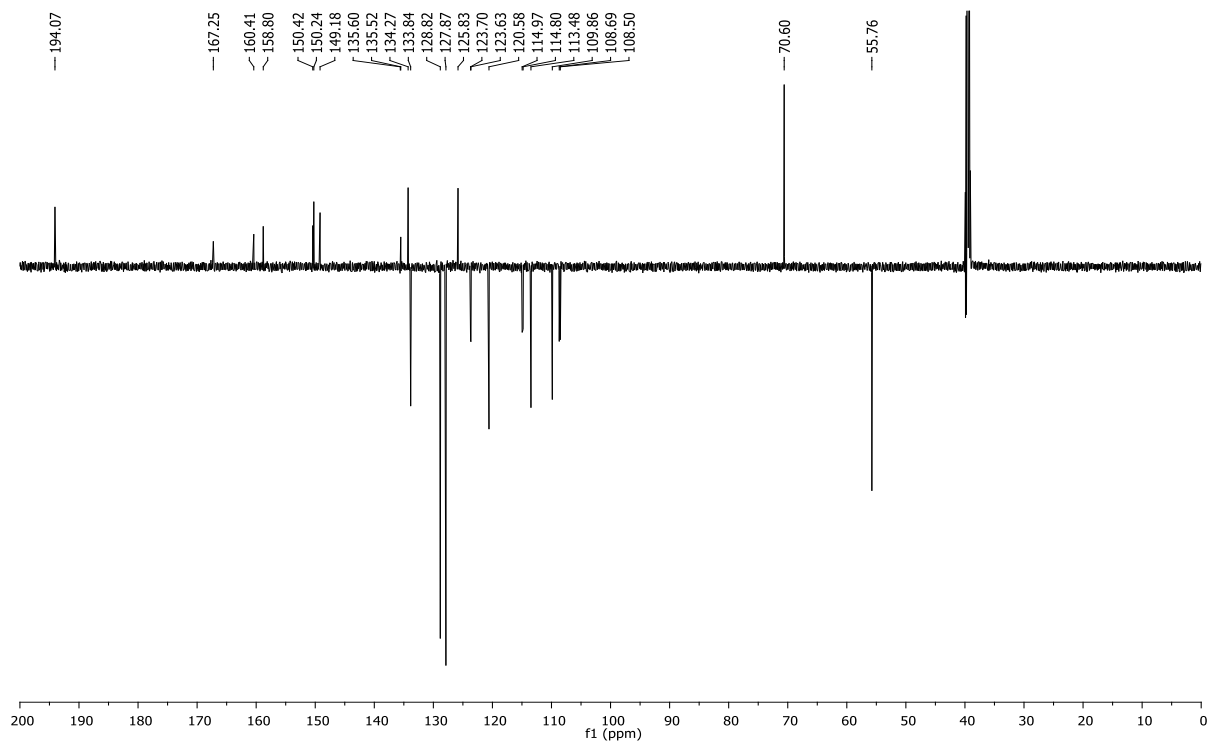
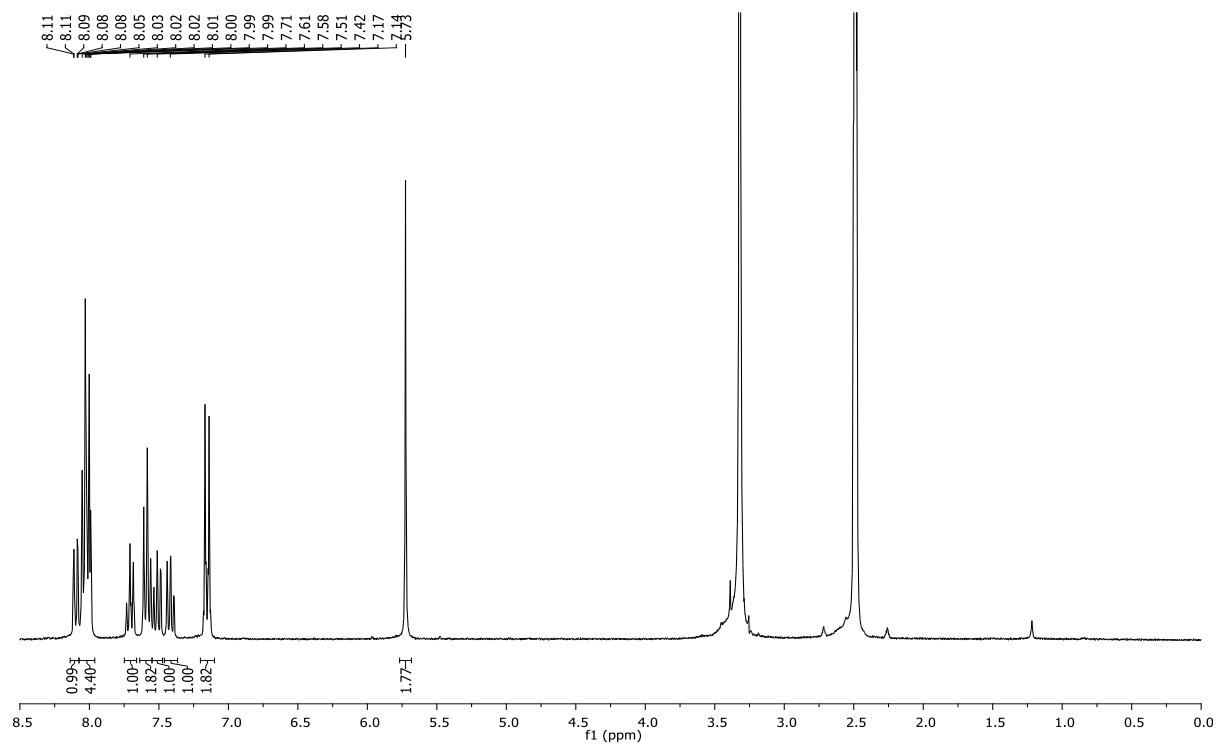


Fig. S25 a) ^1H NMR and b) ^{13}C NMR of compd. **17a**

a)



b)

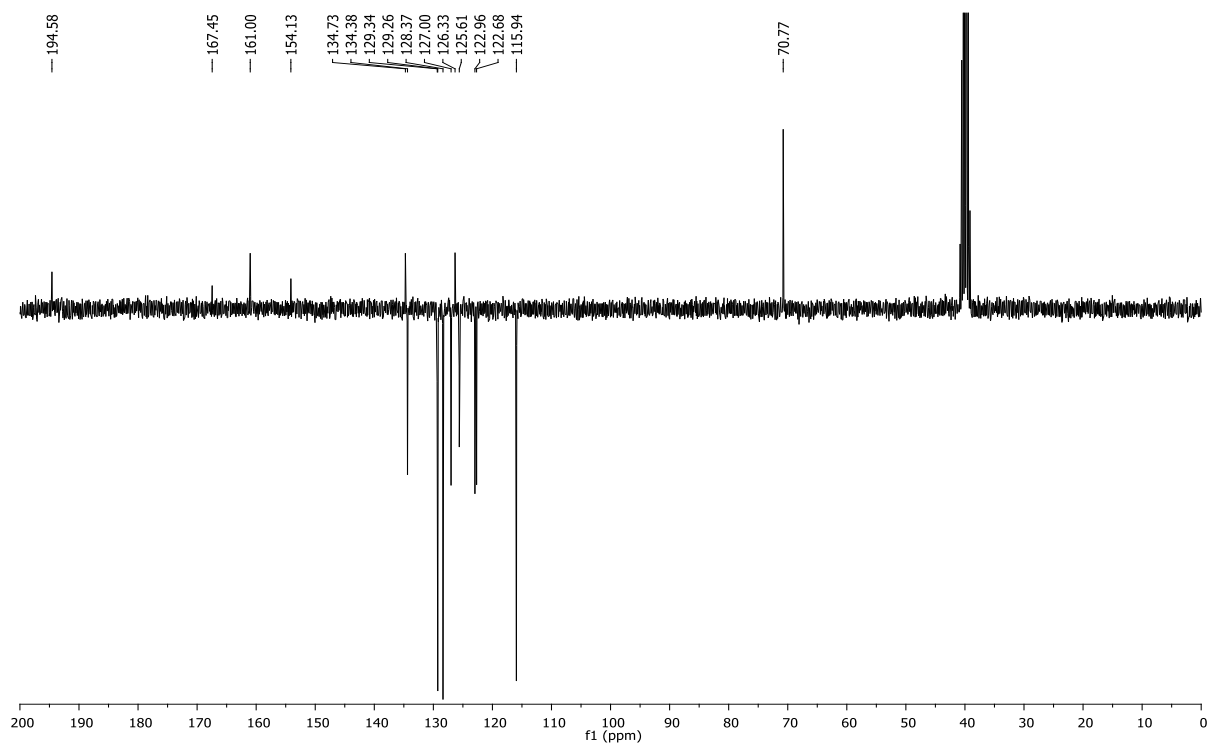
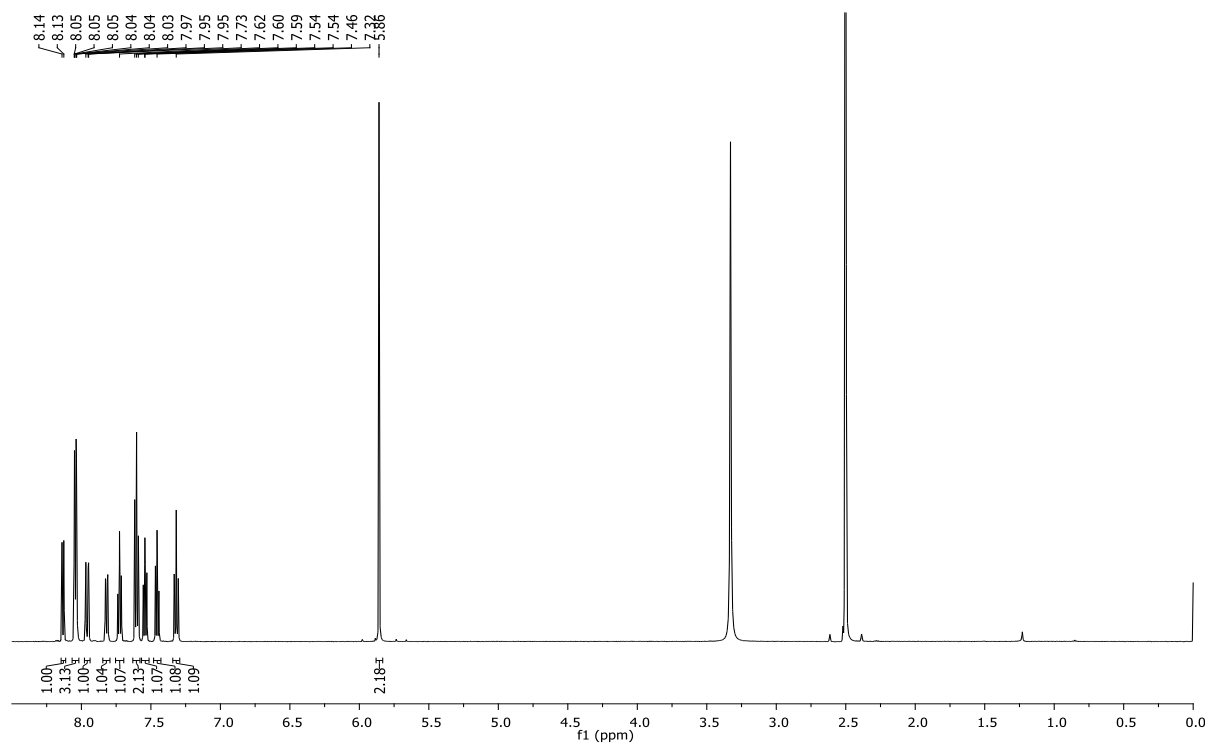


Fig. S26 a) ^1H NMR and b) ^{13}C NMR of compd. **17b**

a)



b)

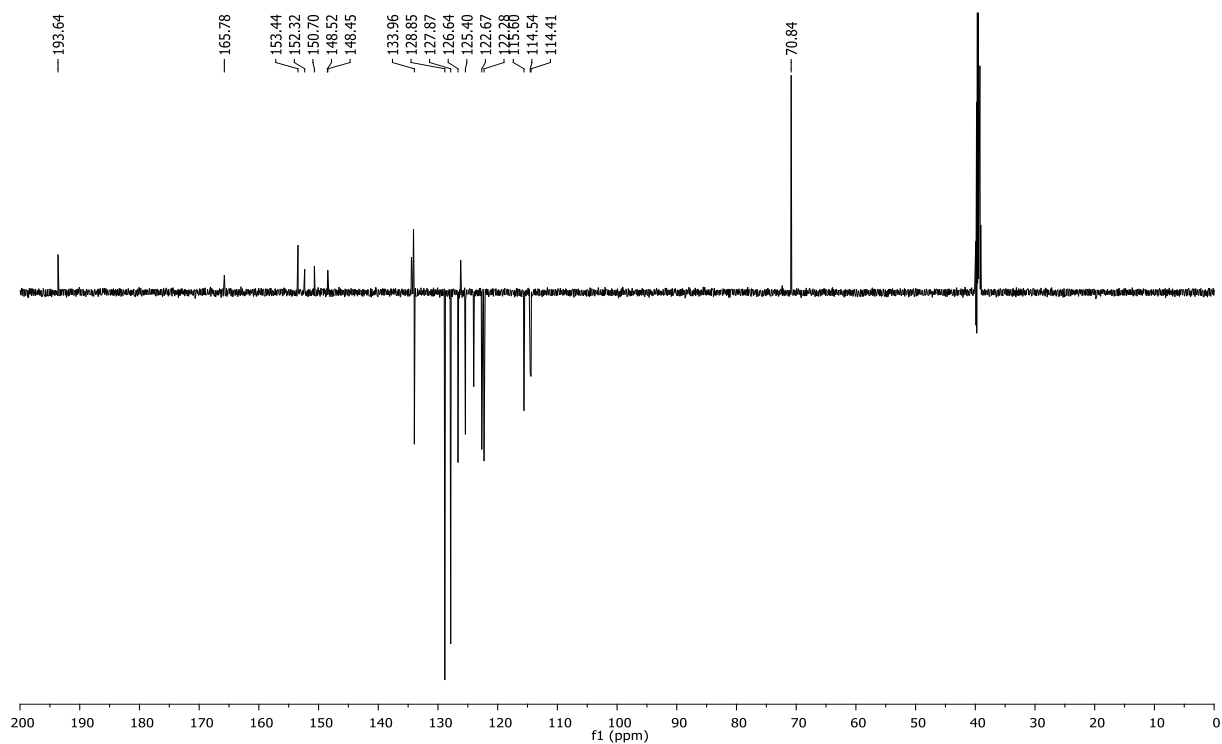
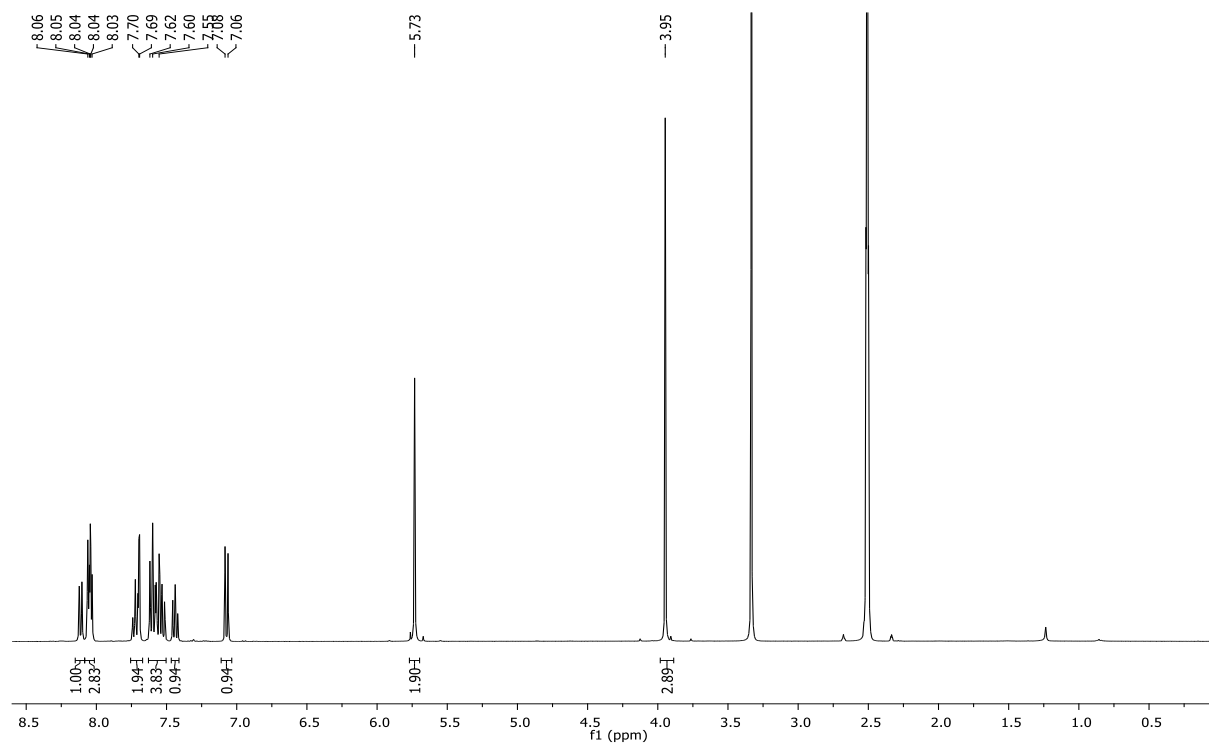


Fig. S27 a) ^1H NMR and b) ^{13}C NMR of compd. **17c**

a)



b)

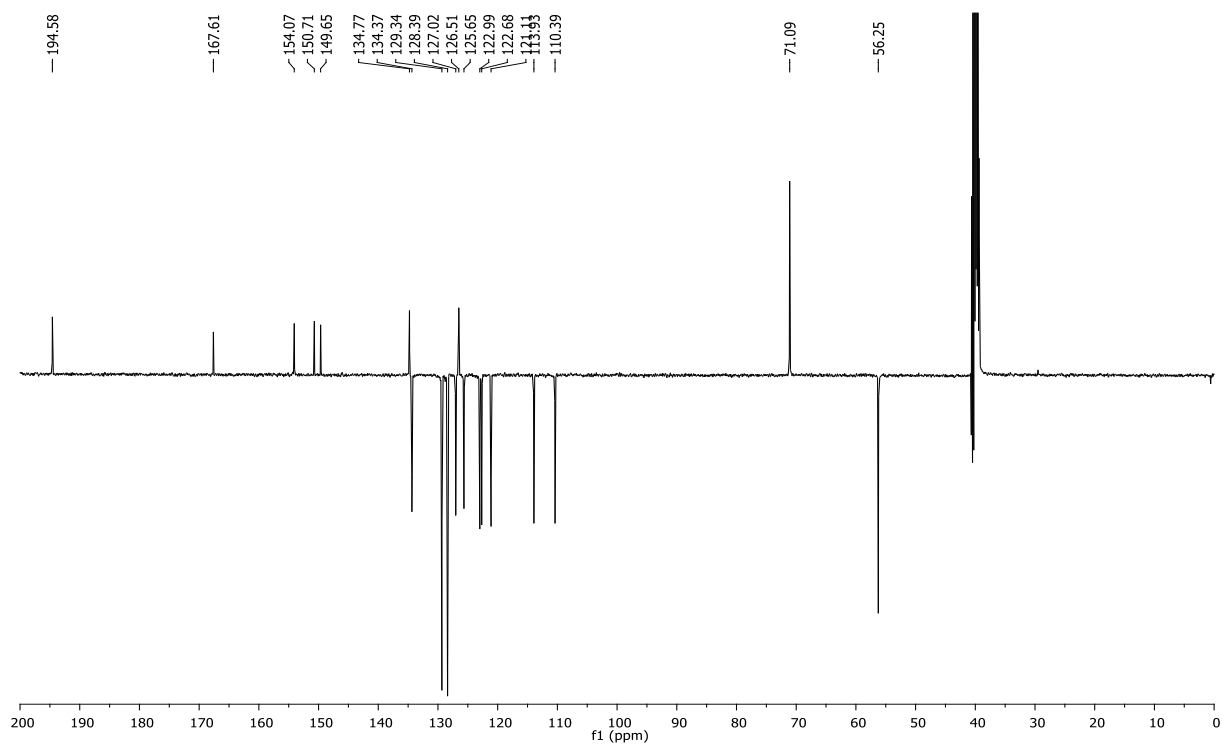
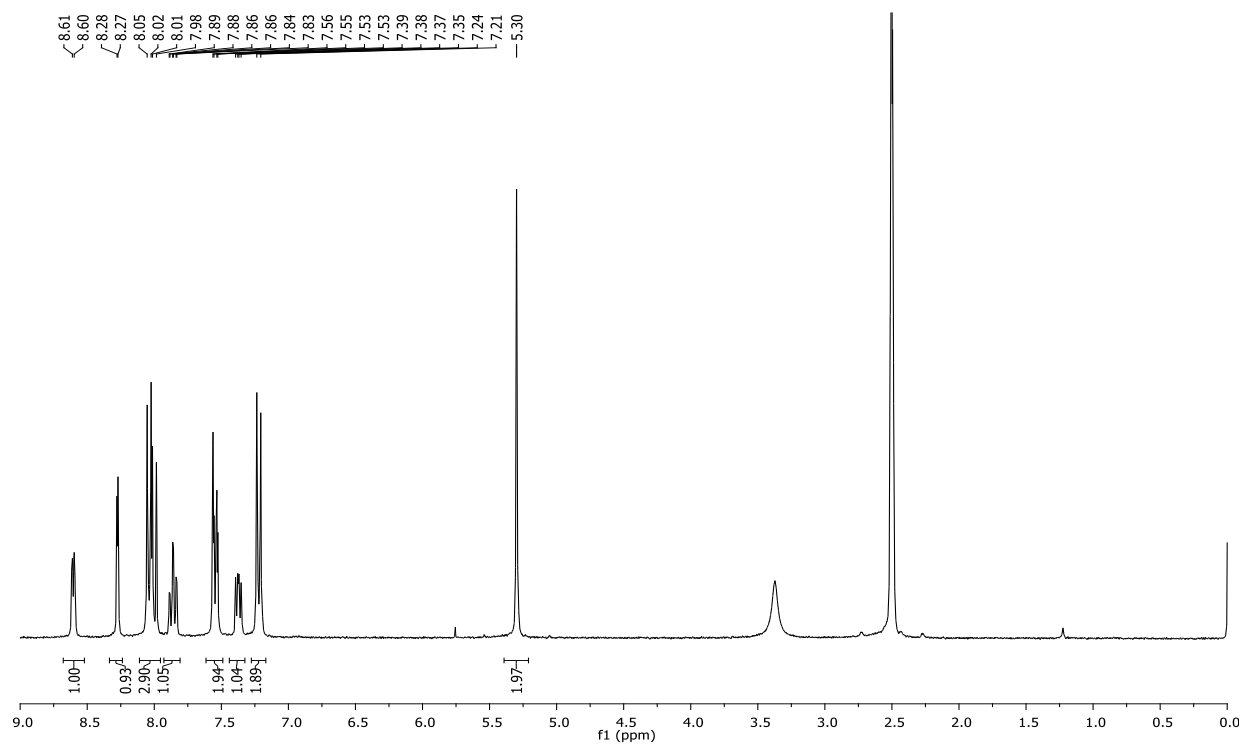


Fig. S28 a) ^1H NMR and b) ^{13}C NMR of compd. **18a**

a)



b)

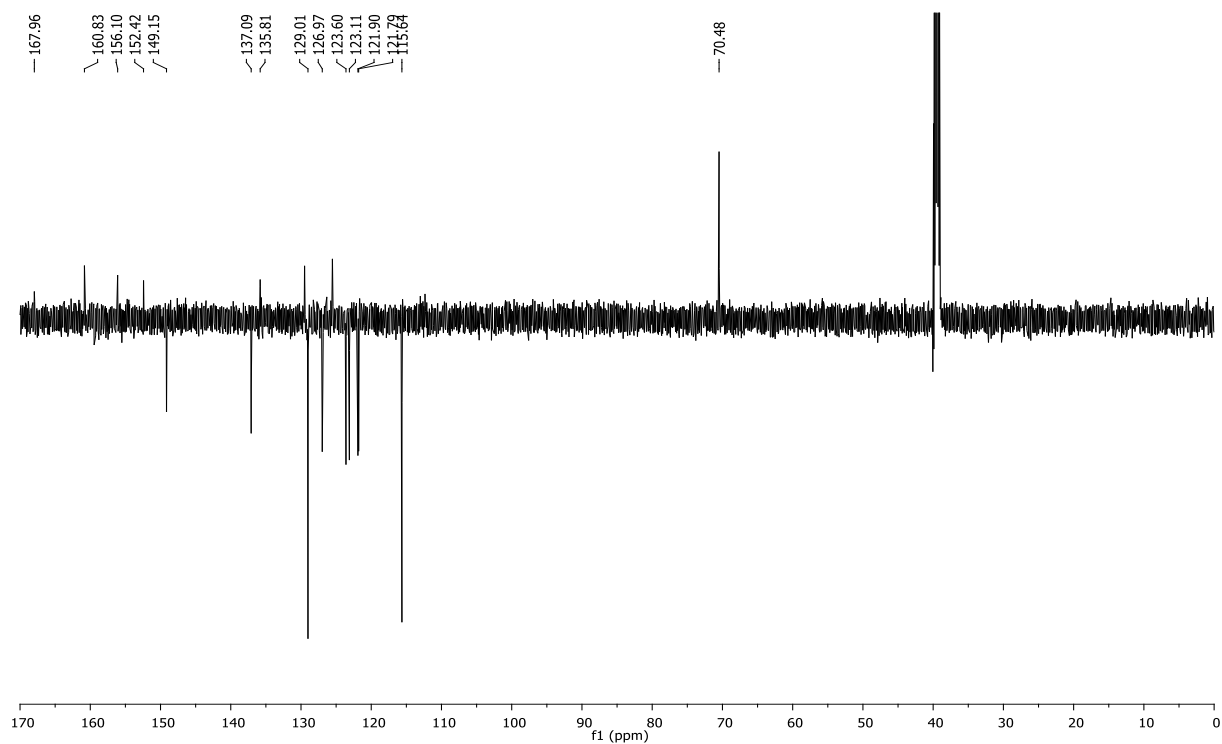
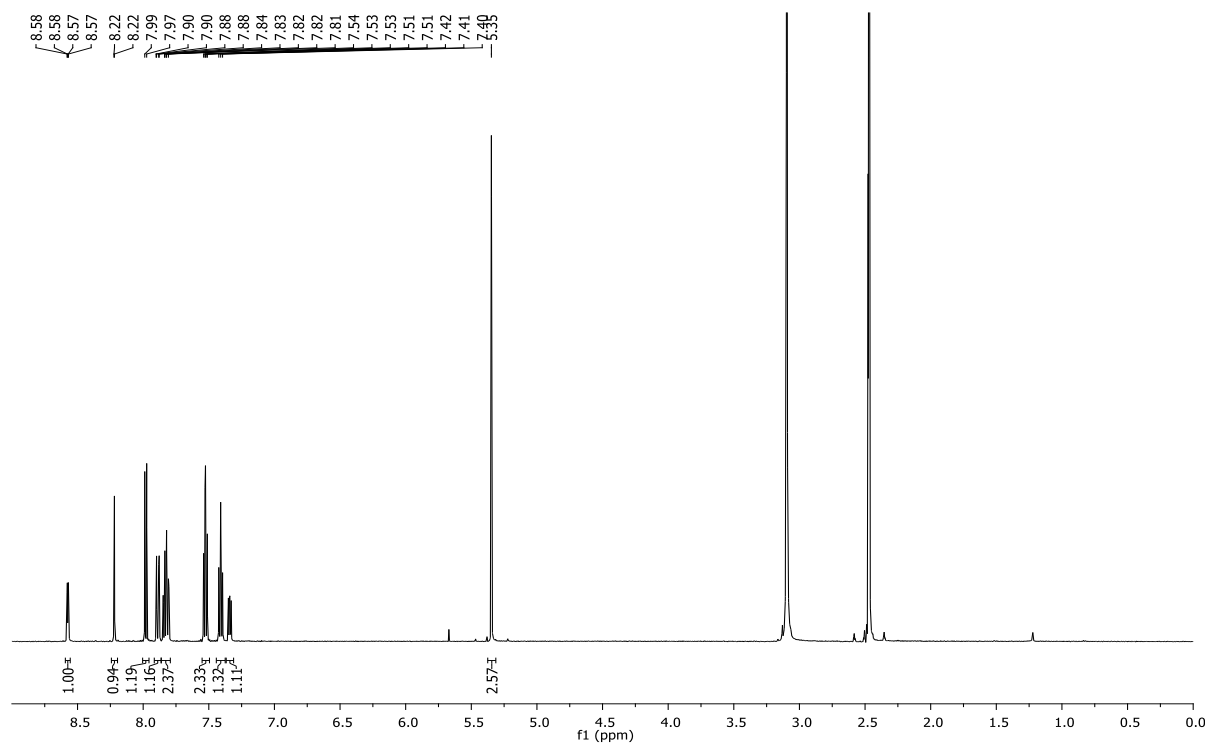


Fig. S29 a) ^1H NMR and b) ^{13}C NMR of compd. **18b**

a)



b)

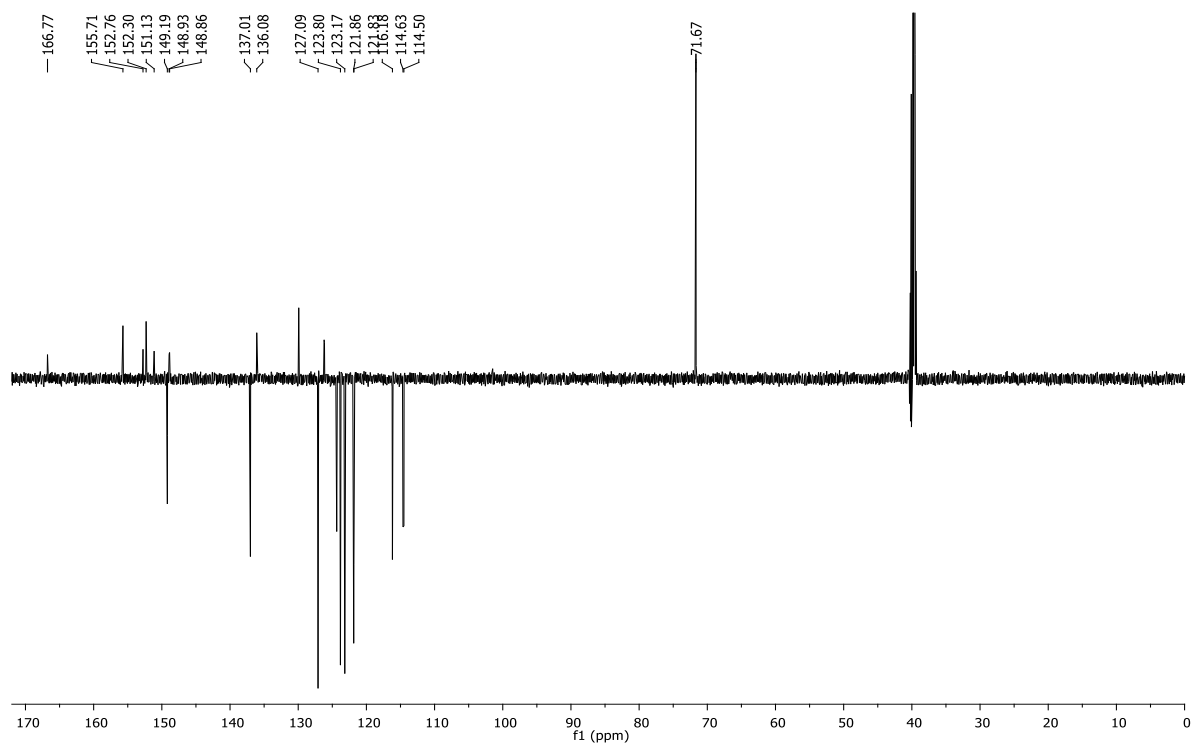
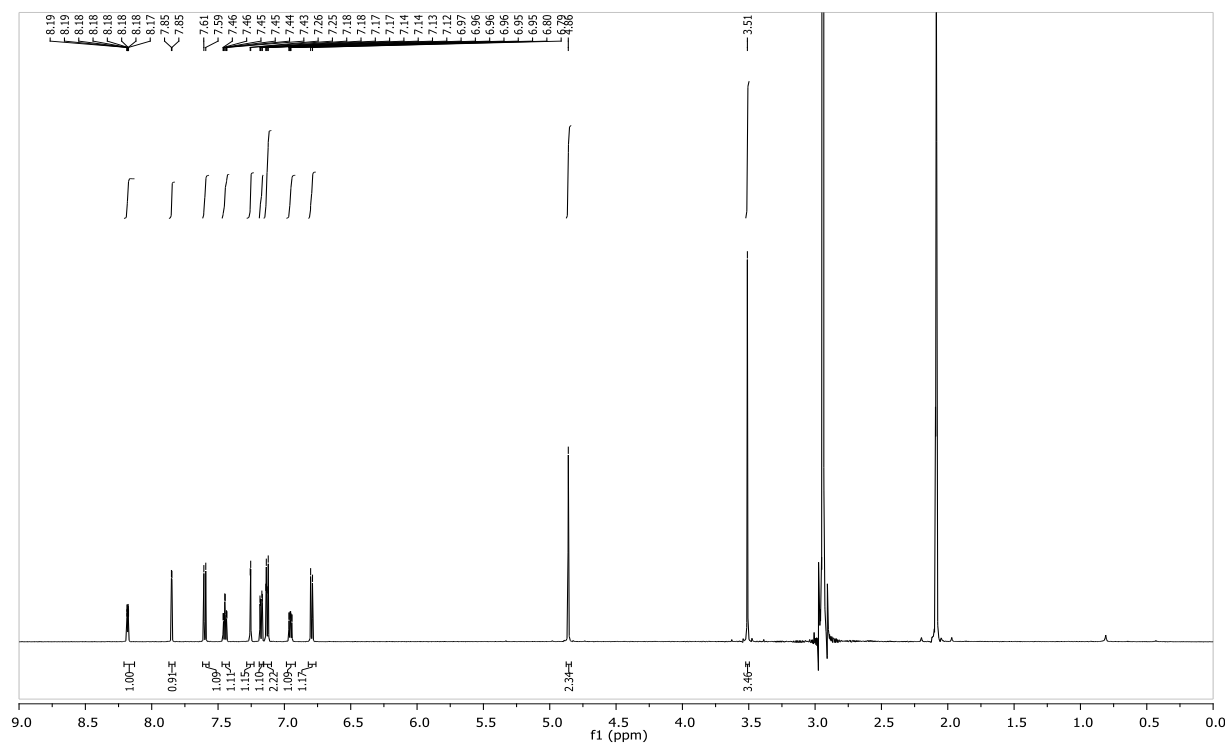


Fig. S30 a) ^1H NMR and b) ^{13}C NMR of compd. **18c**

a)



b)

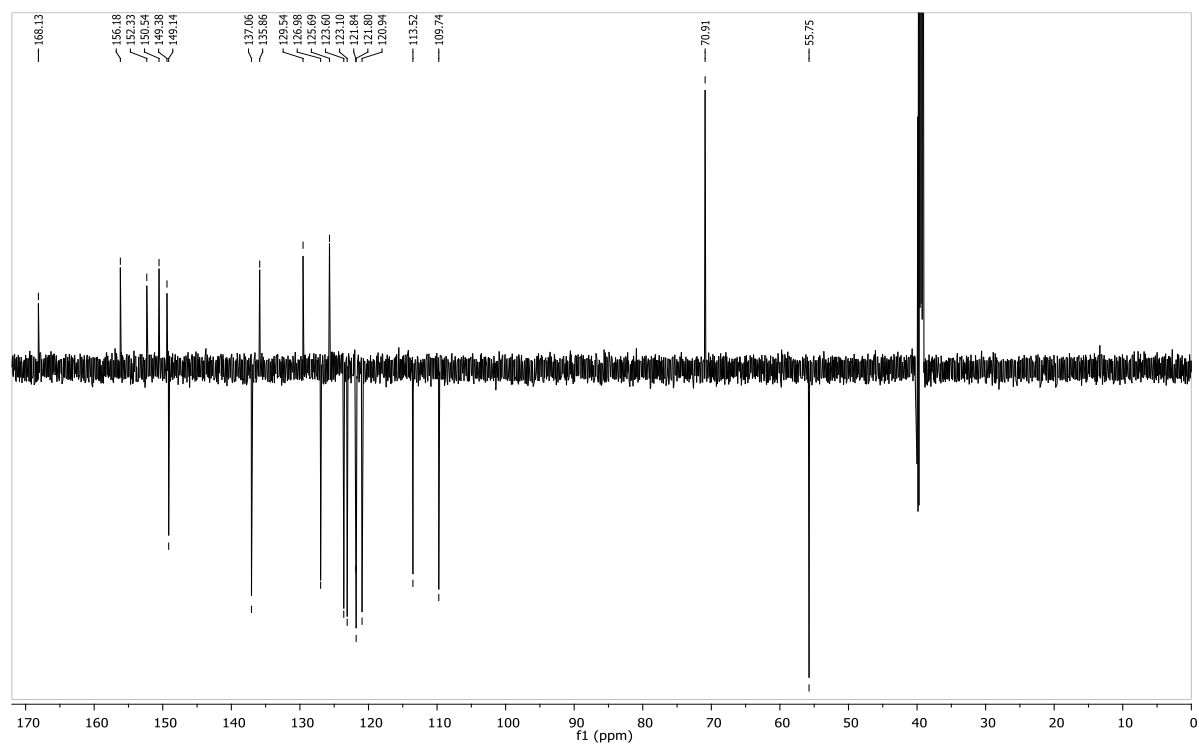
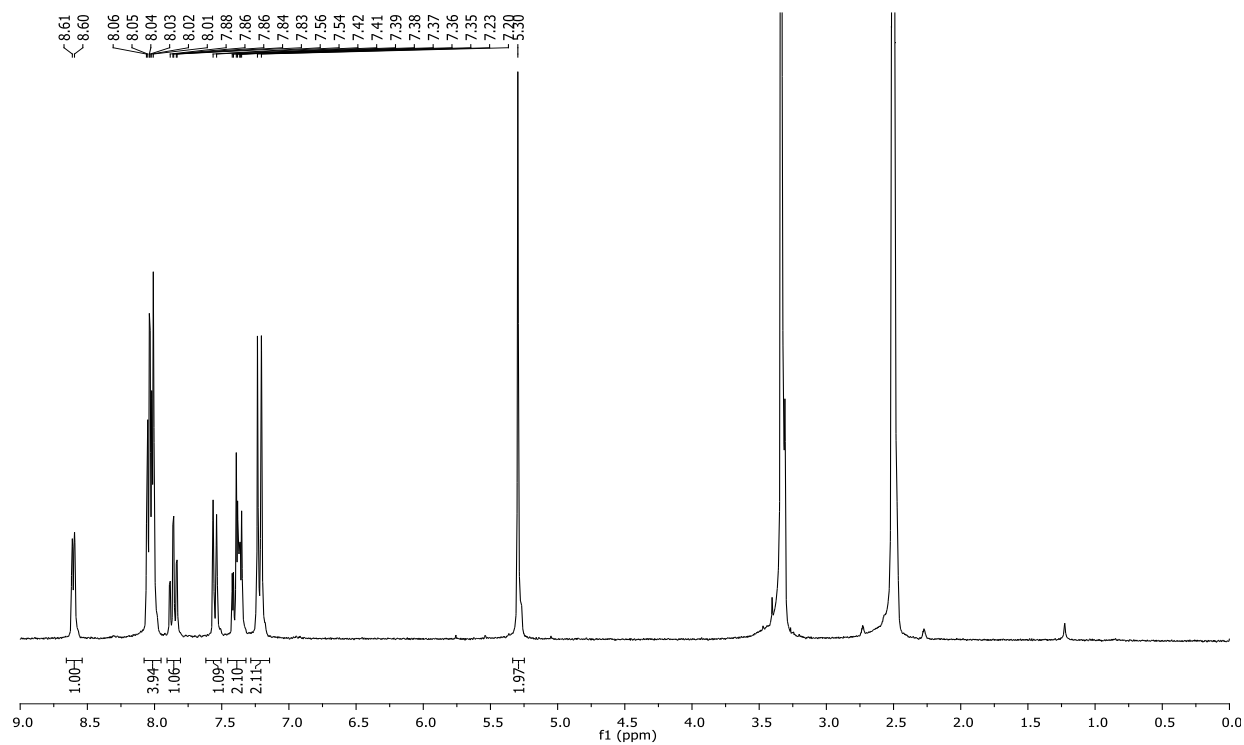


Fig. S31 a) ^1H NMR and b) ^{13}C NMR of compd. **19a**

a)



b)

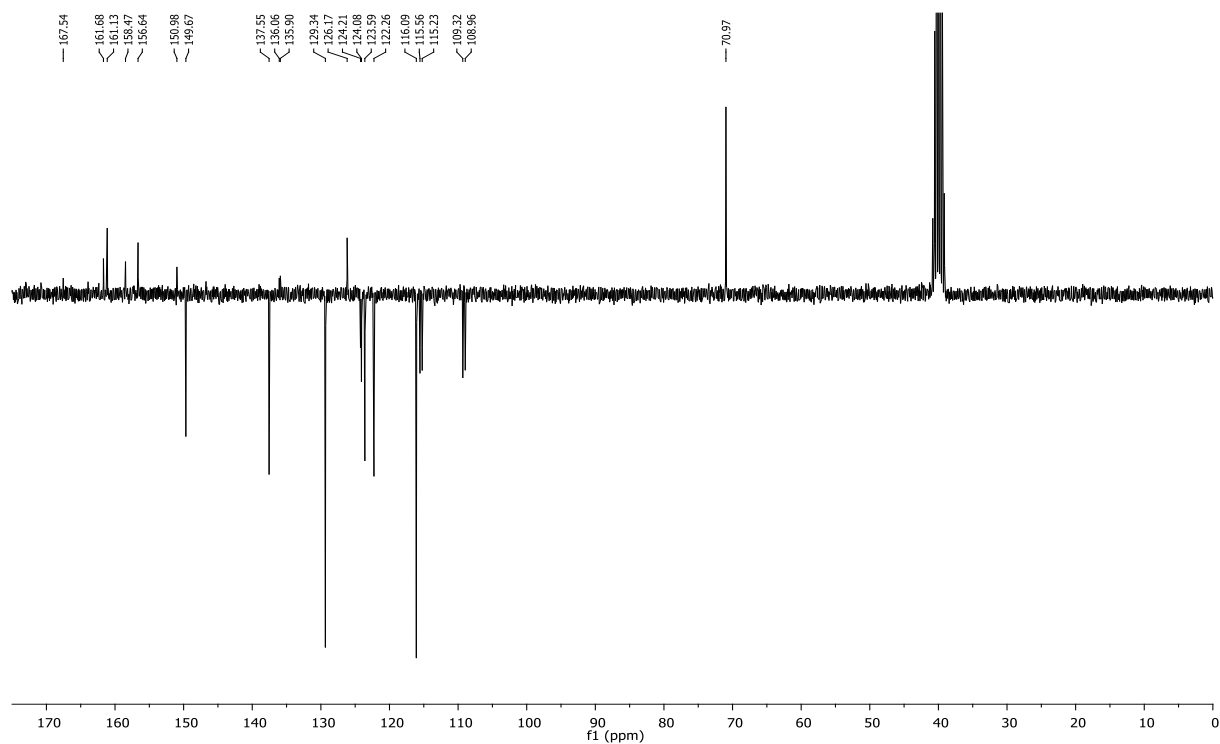
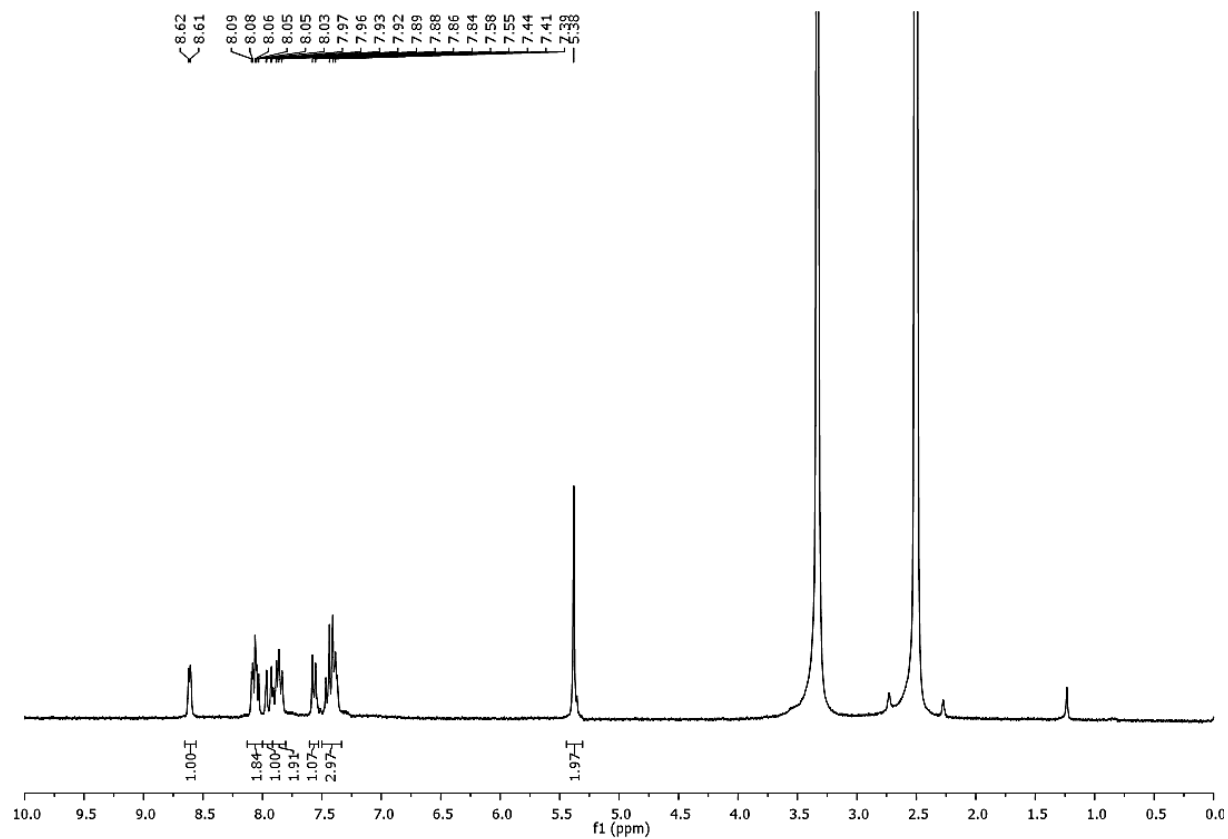


Fig. S32 a) ^1H NMR and b) ^{13}C NMR of compd. **19b**

a)



b)

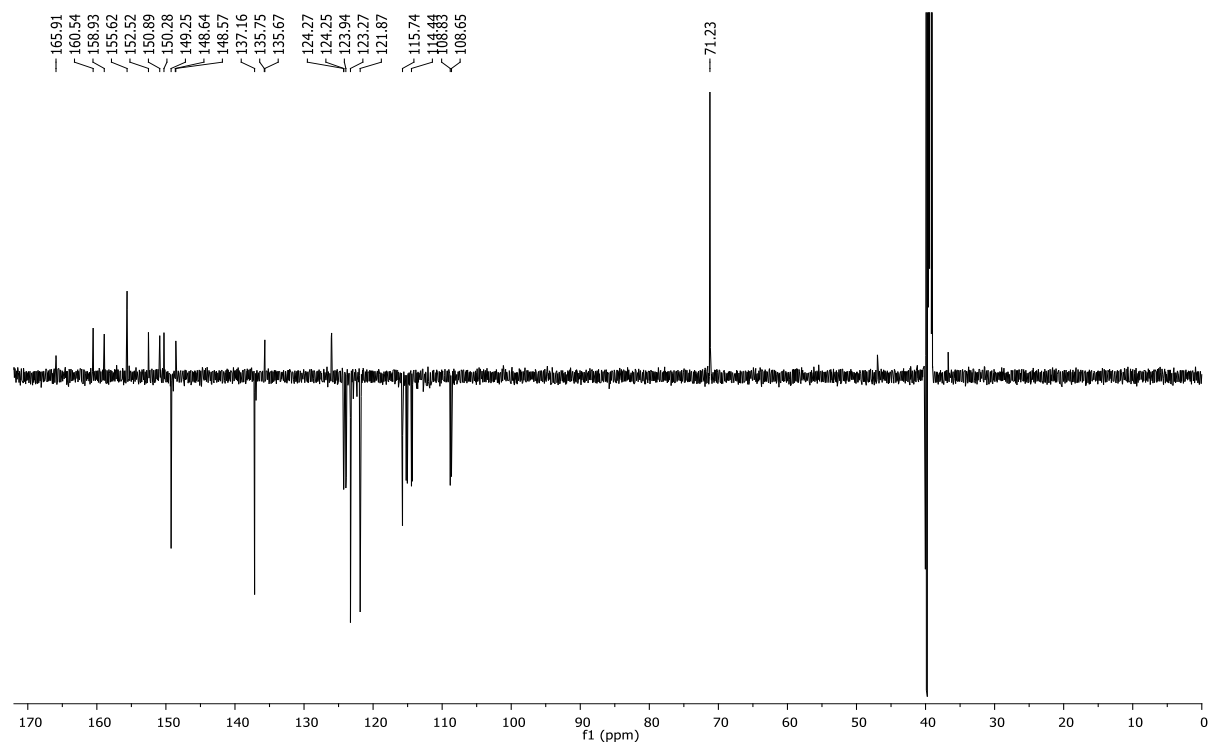
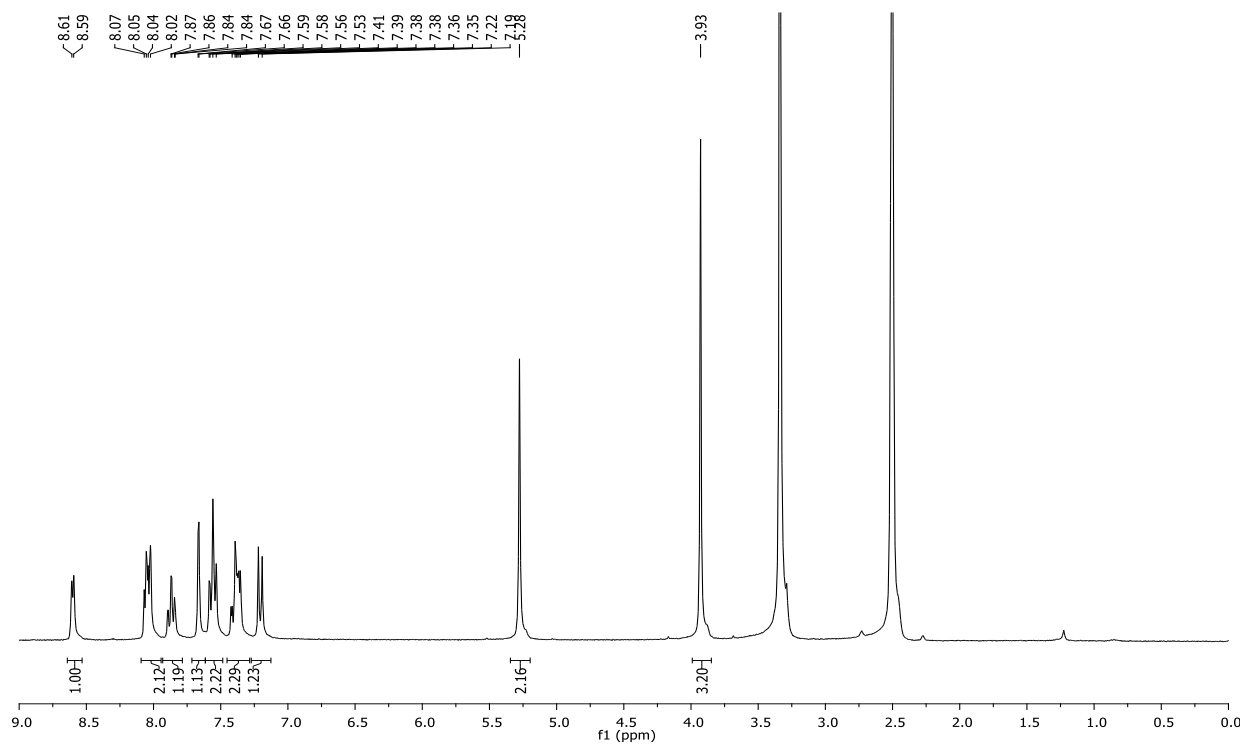


Fig. S33 a) ^1H NMR and b) ^{13}C NMR of compd. **19c**

a)



b)

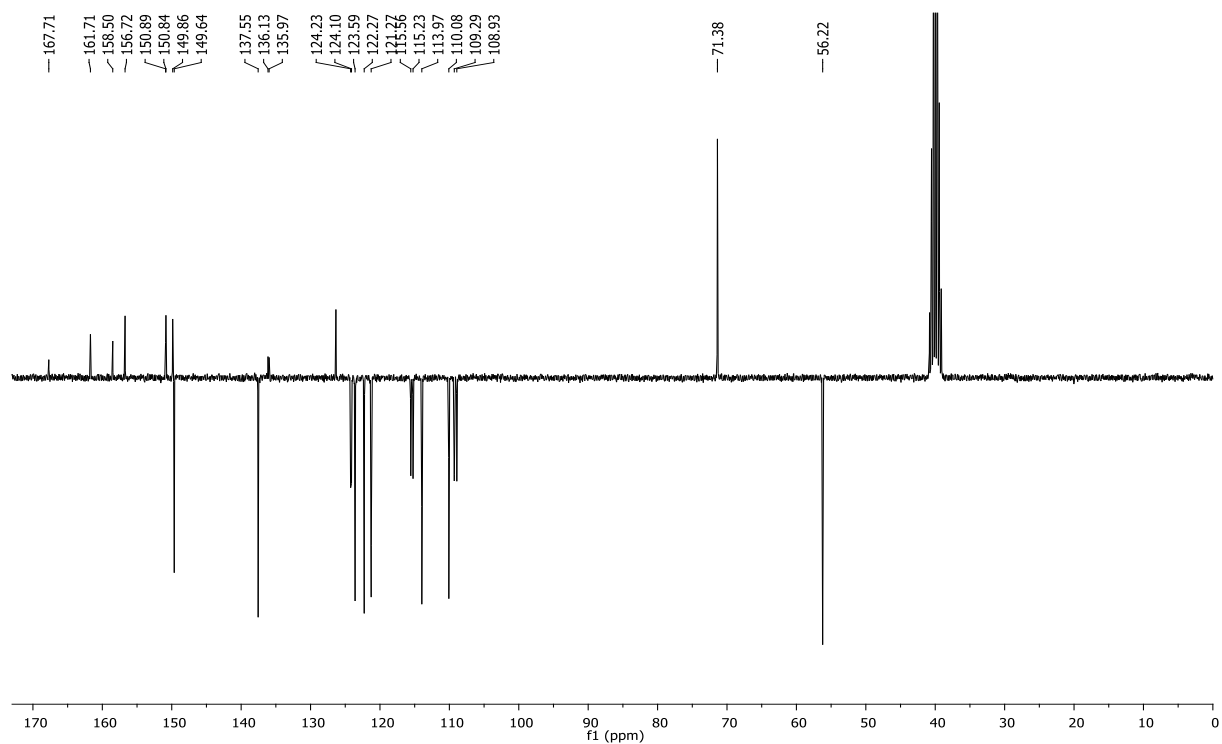
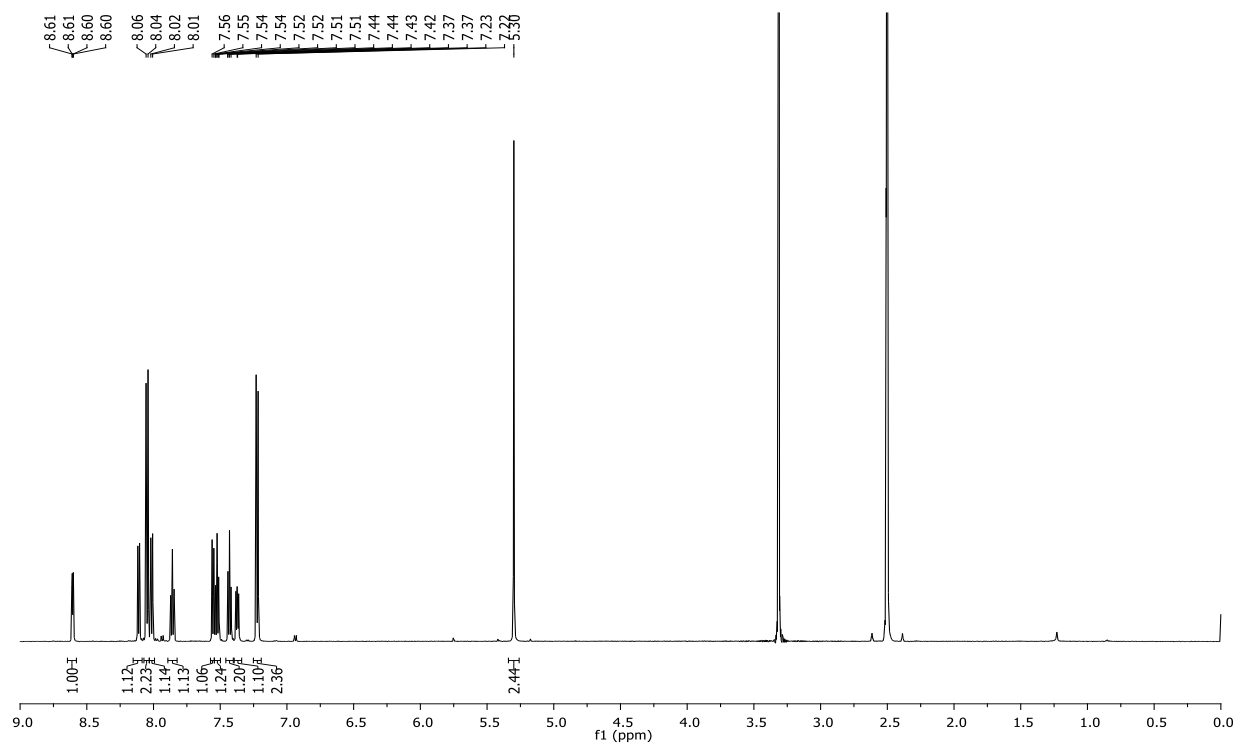


Fig. S34 a) ^1H NMR and b) ^{13}C NMR of compd. **20a**

a)



b)

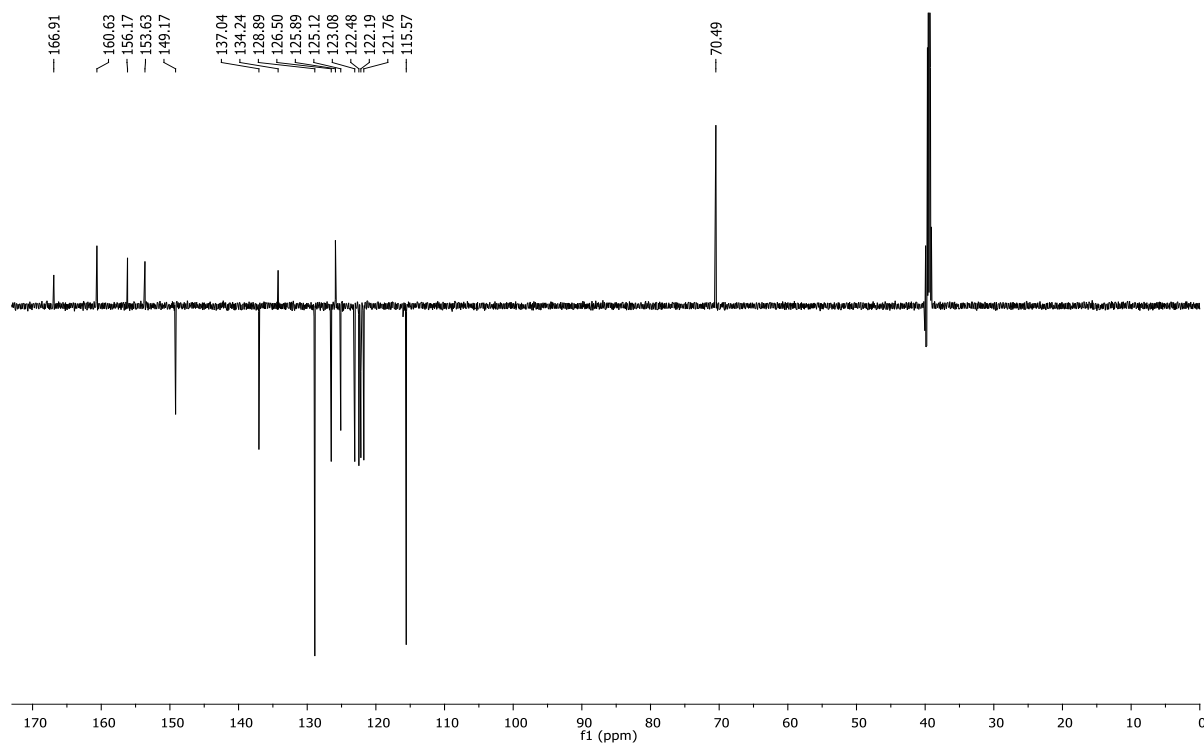
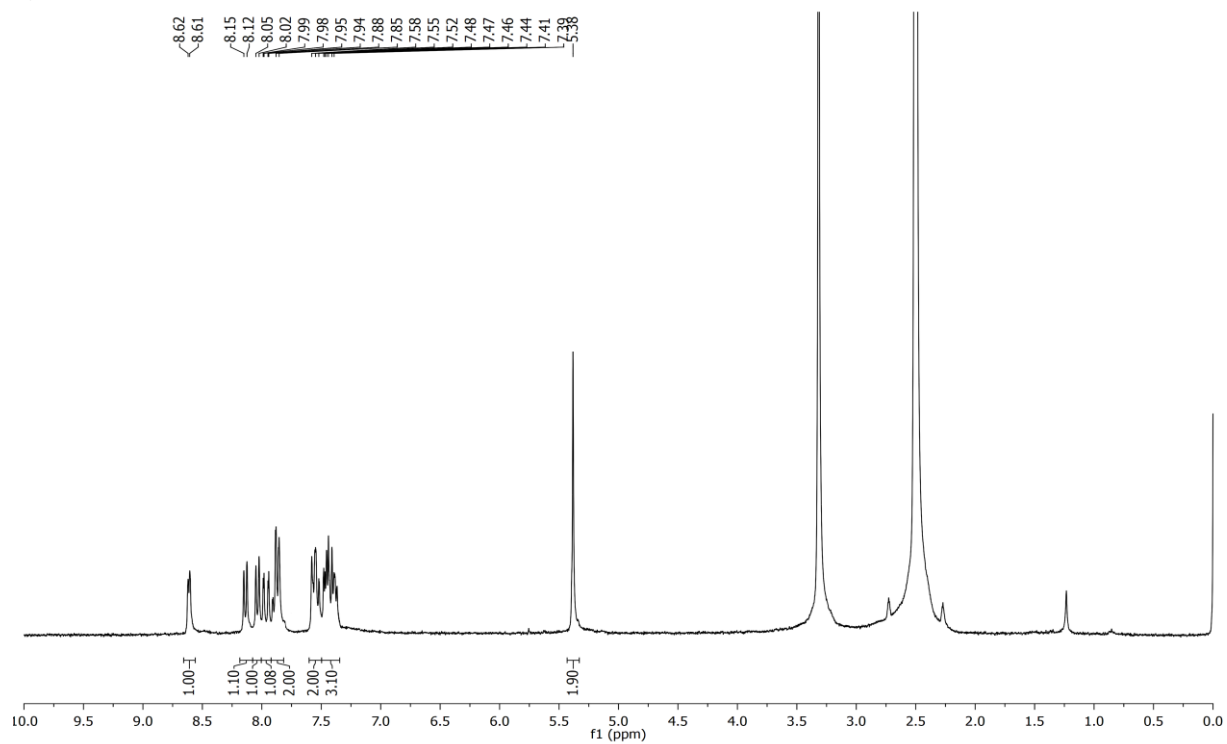


Fig. S35 a) ^1H NMR and b) ^{13}C NMR of compd. **20b**

a)



b)

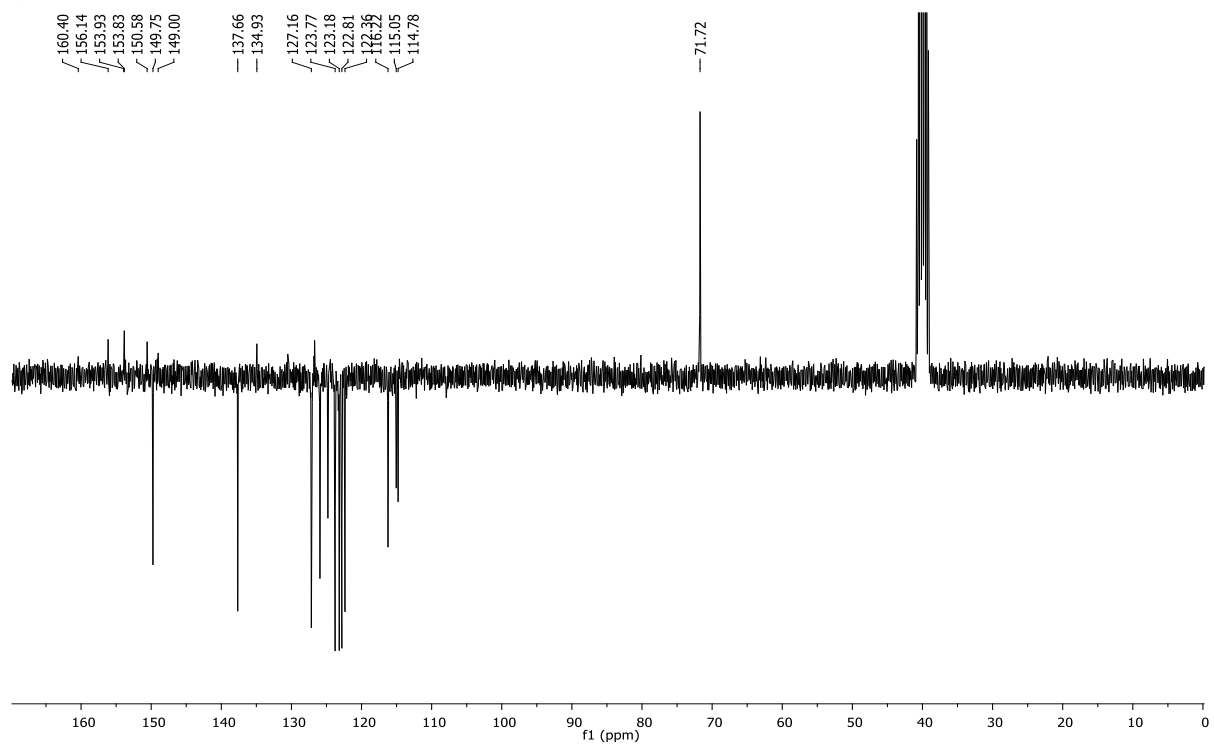
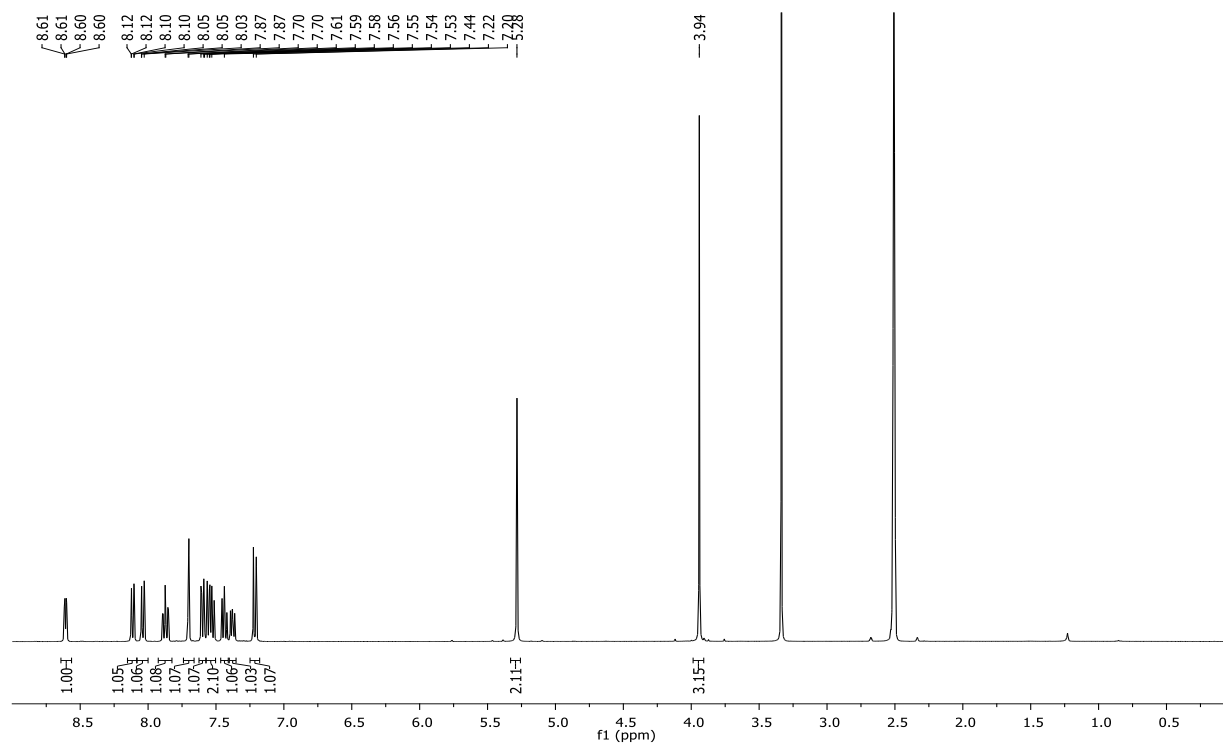


Fig. S36 a) ^1H NMR and b) ^{13}C NMR of compd. **20c**

a)



b)

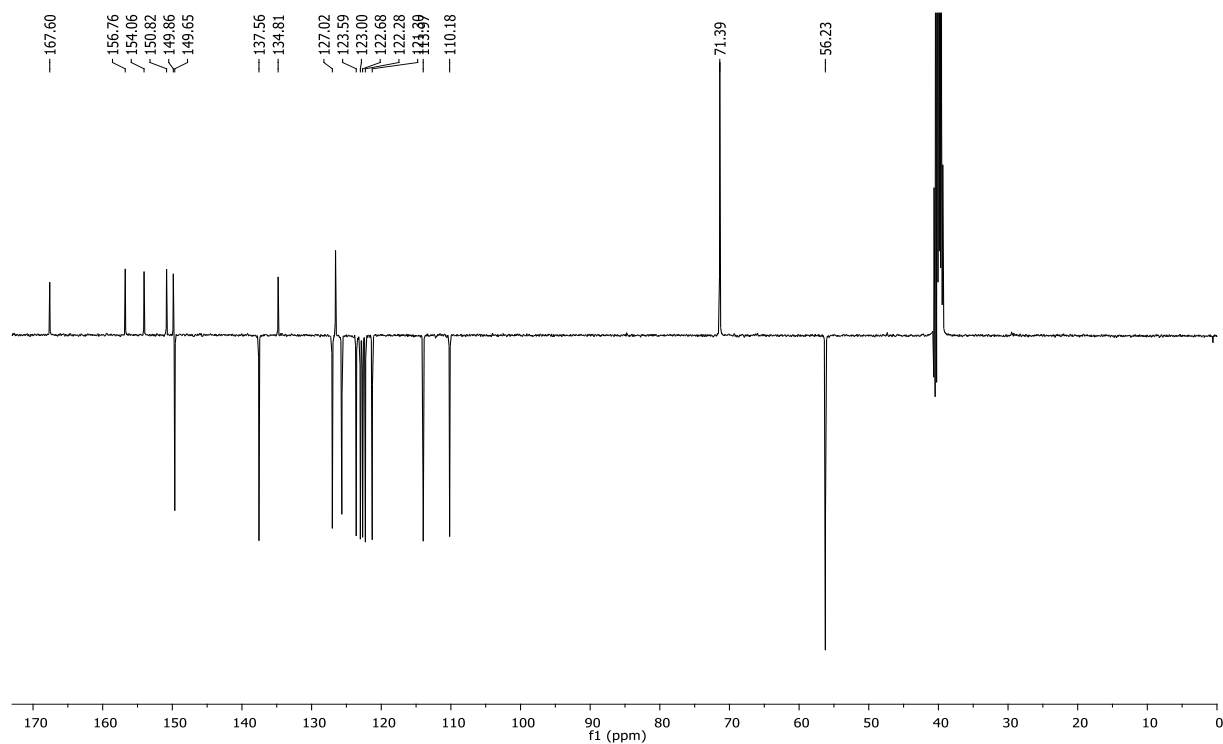
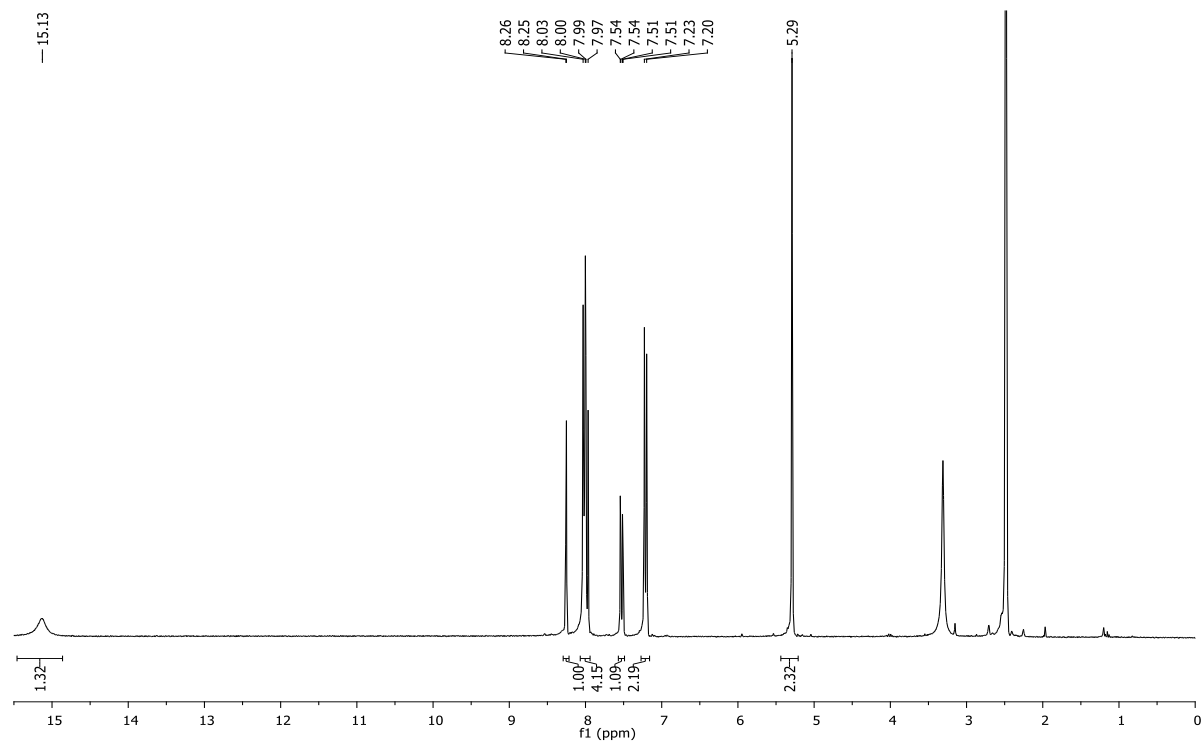


Fig. S37 a) ^1H NMR and b) ^{13}C NMR of compd. **21a**

a)



b)

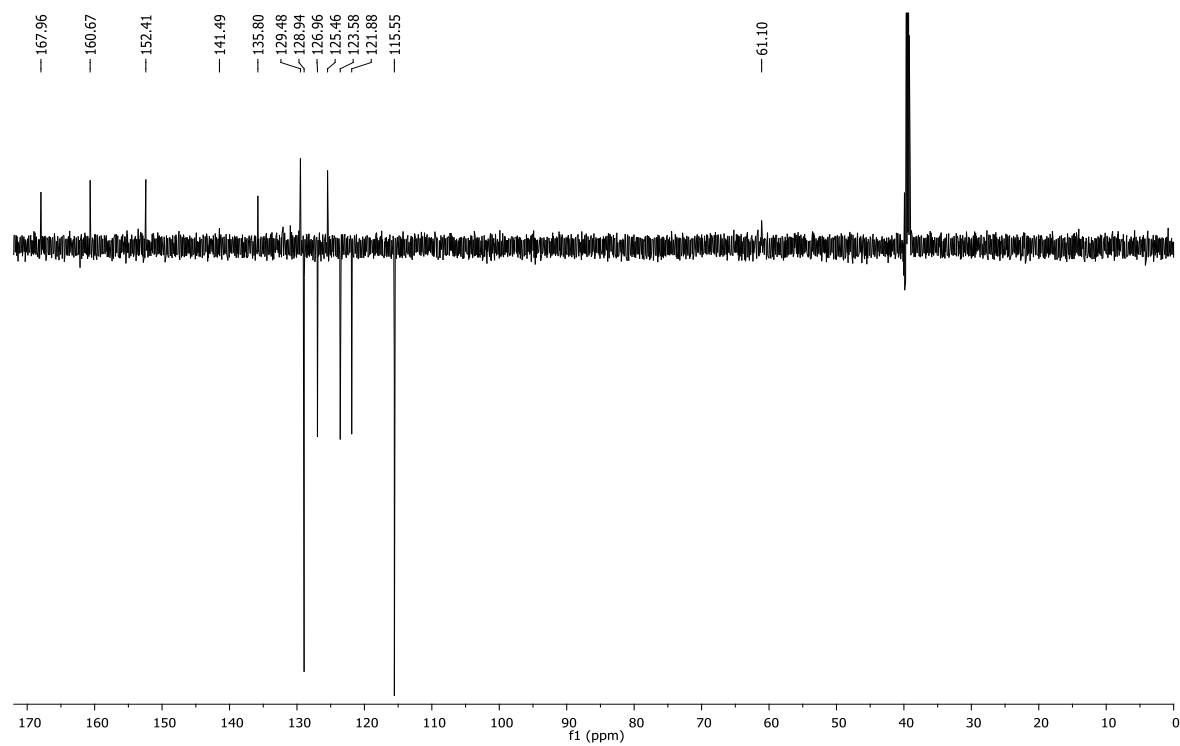
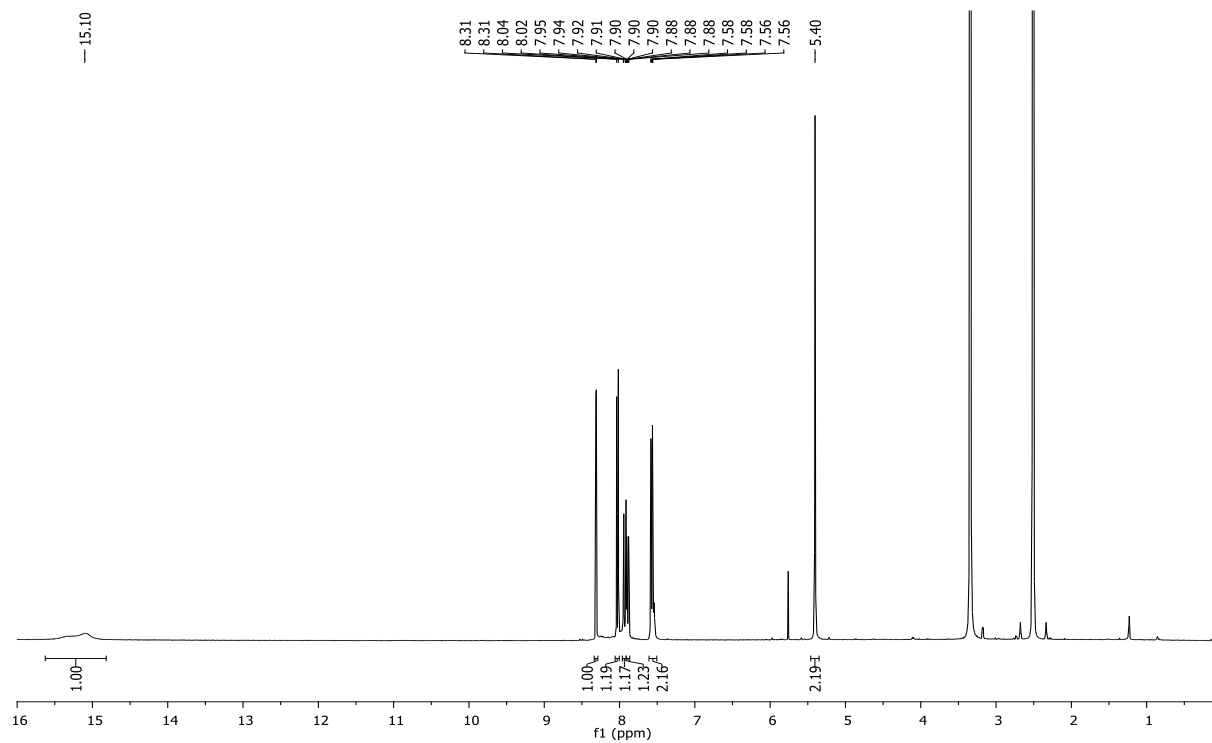


Fig. S38 a) ^1H NMR and b) ^{13}C NMR of compd. **21b**

a)



b)

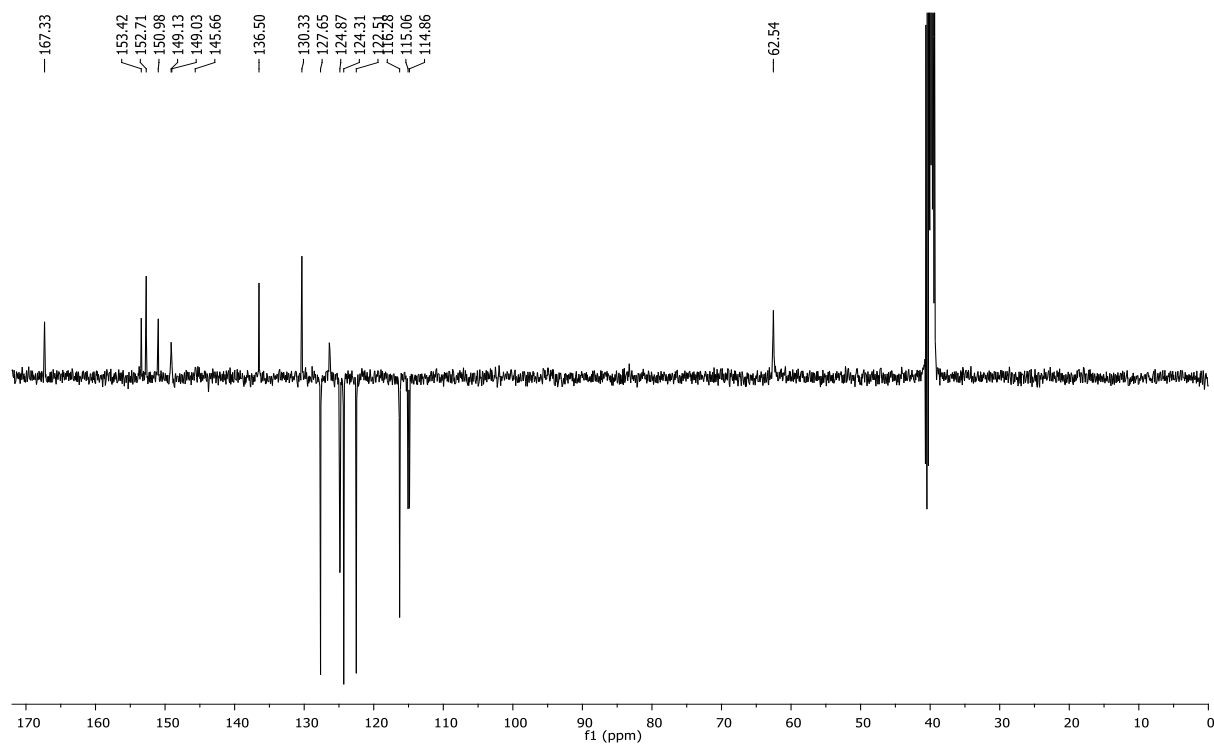
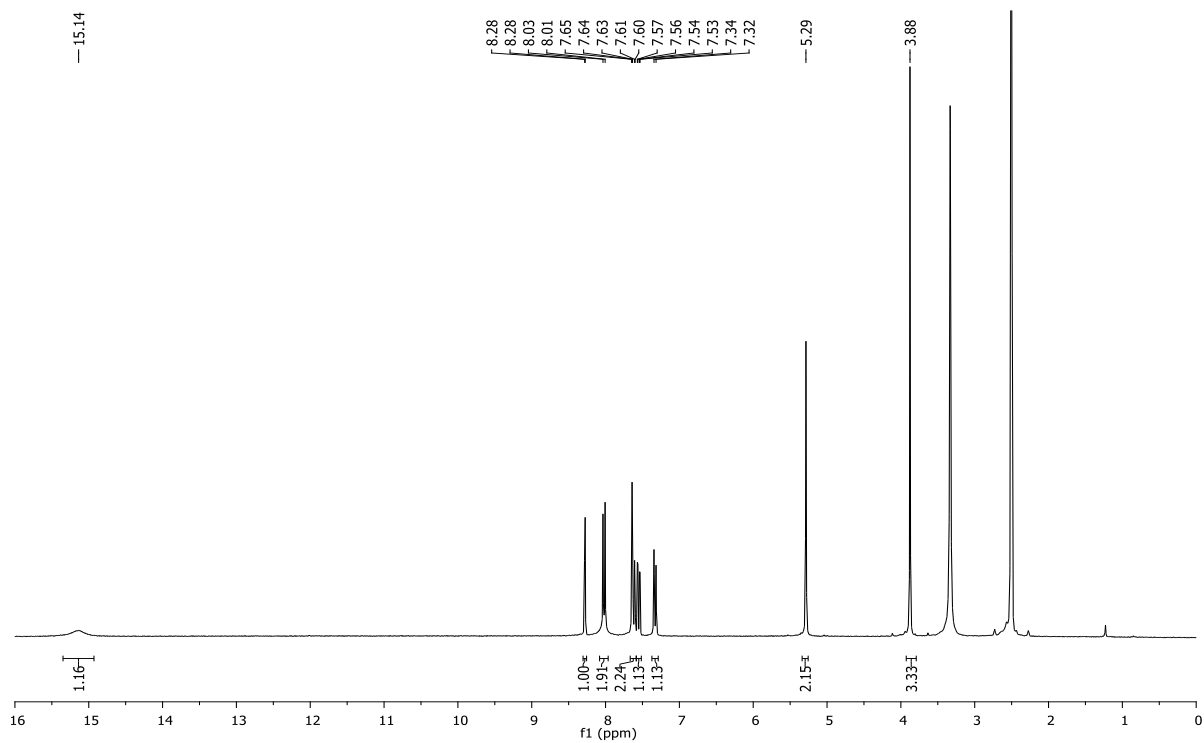


Fig. S39 a) ^1H NMR and b) ^{13}C NMR of compd. **21c**

a)



b)

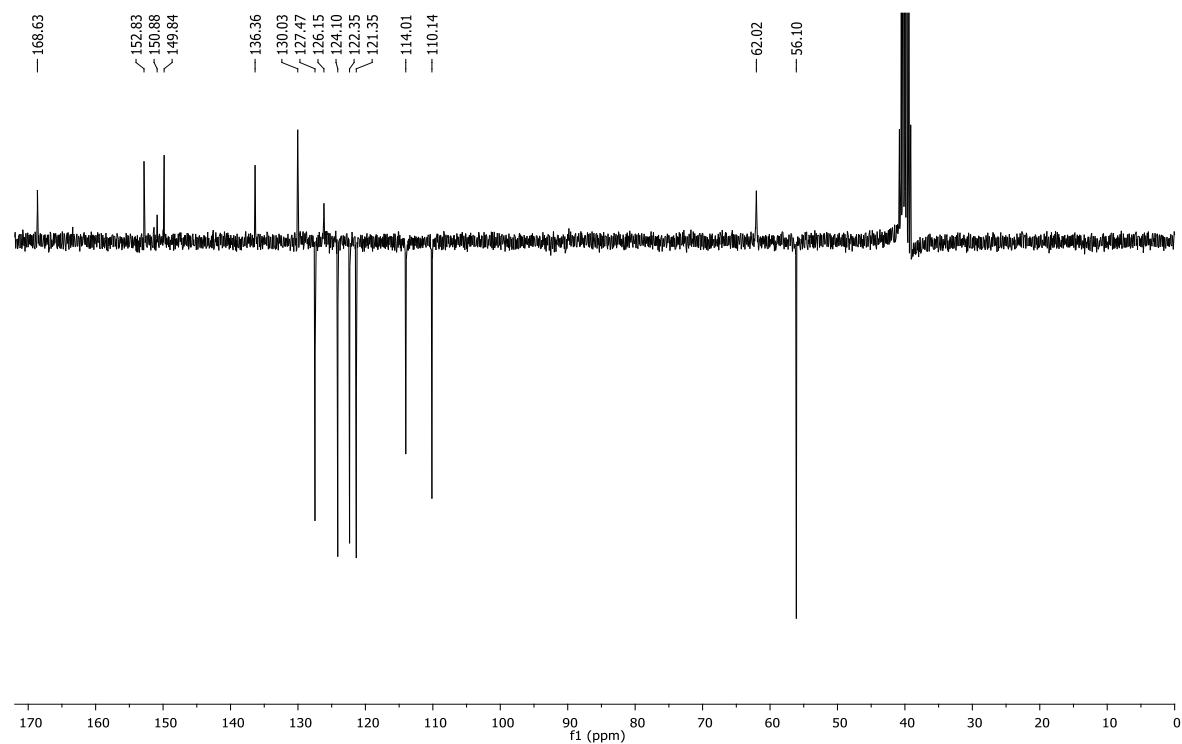
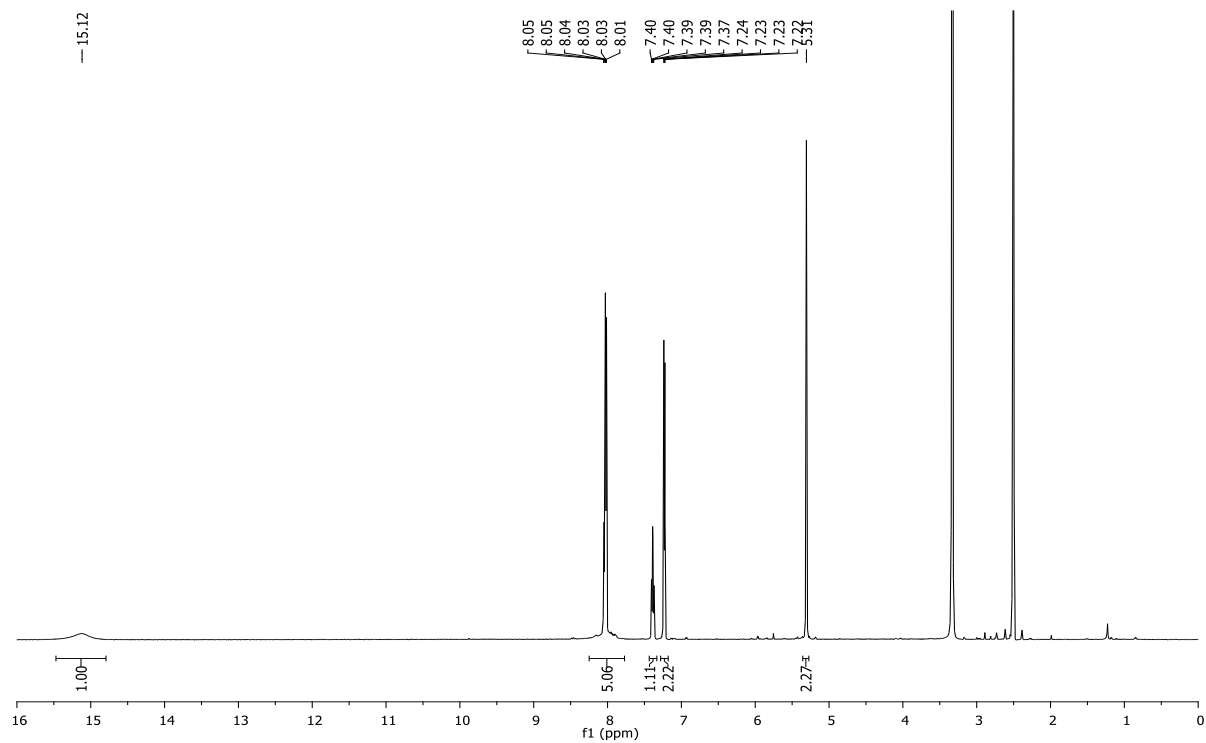


Fig. S40 a) ^1H NMR and b) ^{13}C NMR of compd. **22a**

a)



b)

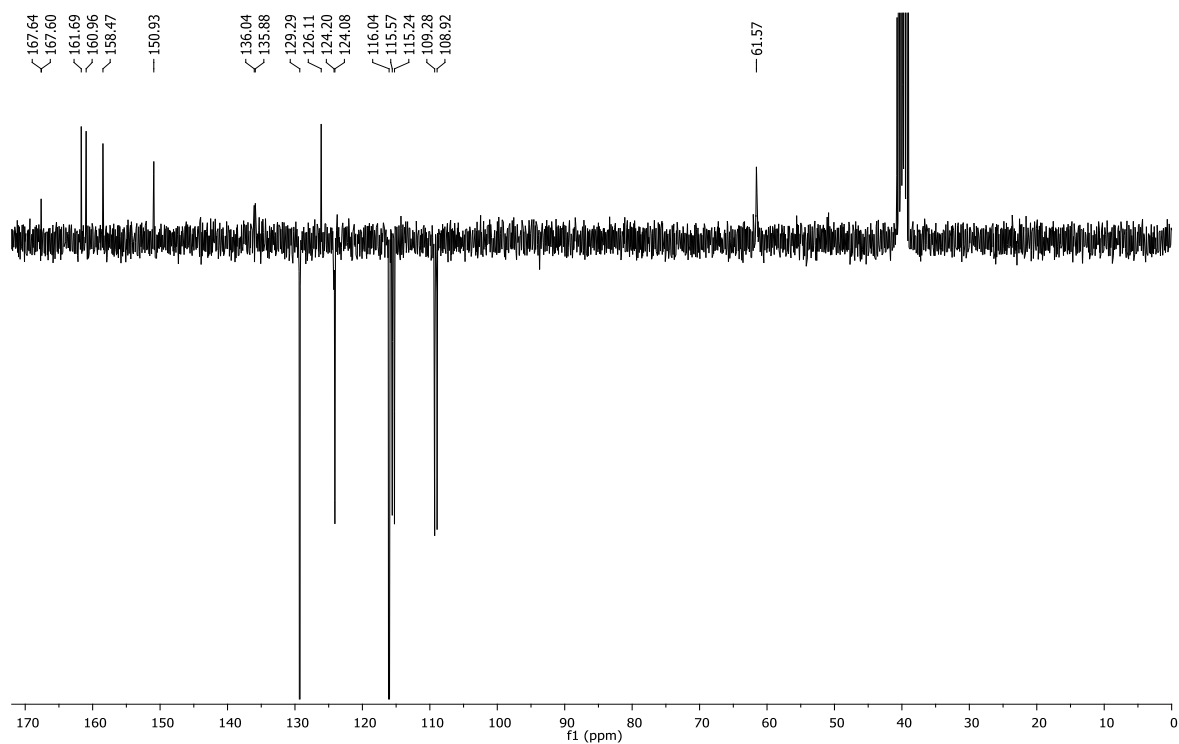
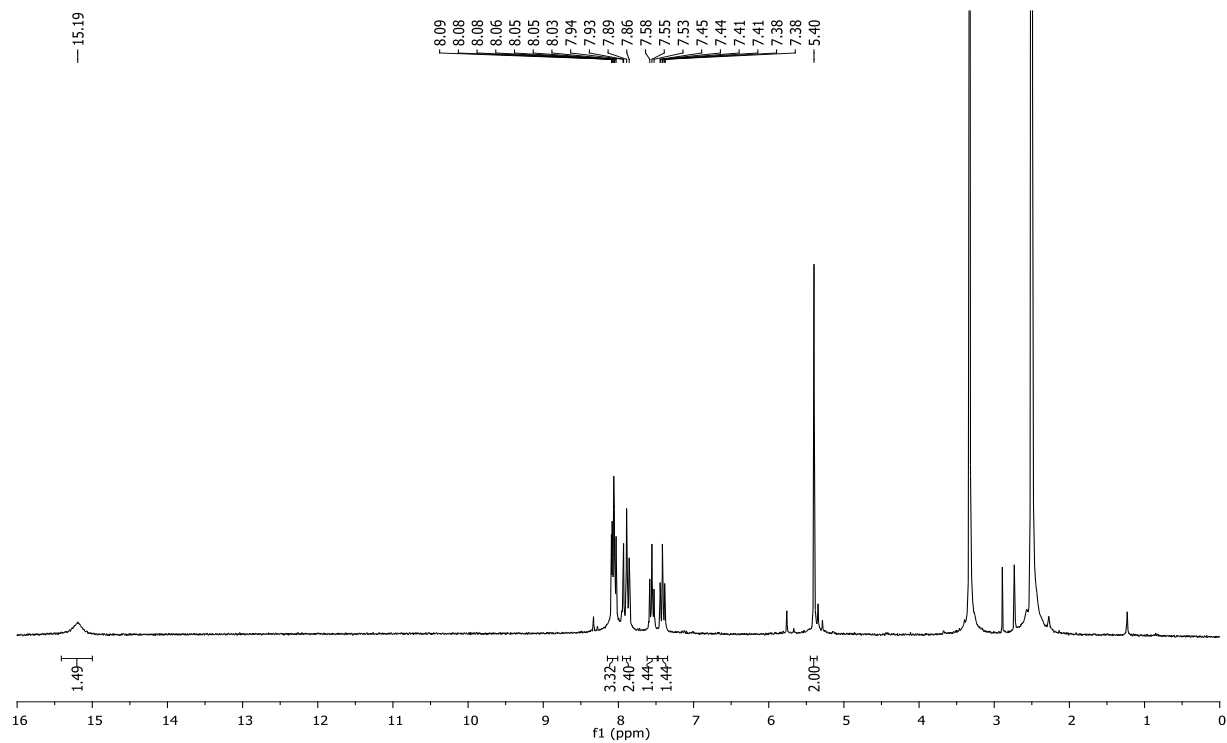


Fig. S41 a) ^1H NMR and b) ^{13}C NMR of compd. **22b**

a)



b)

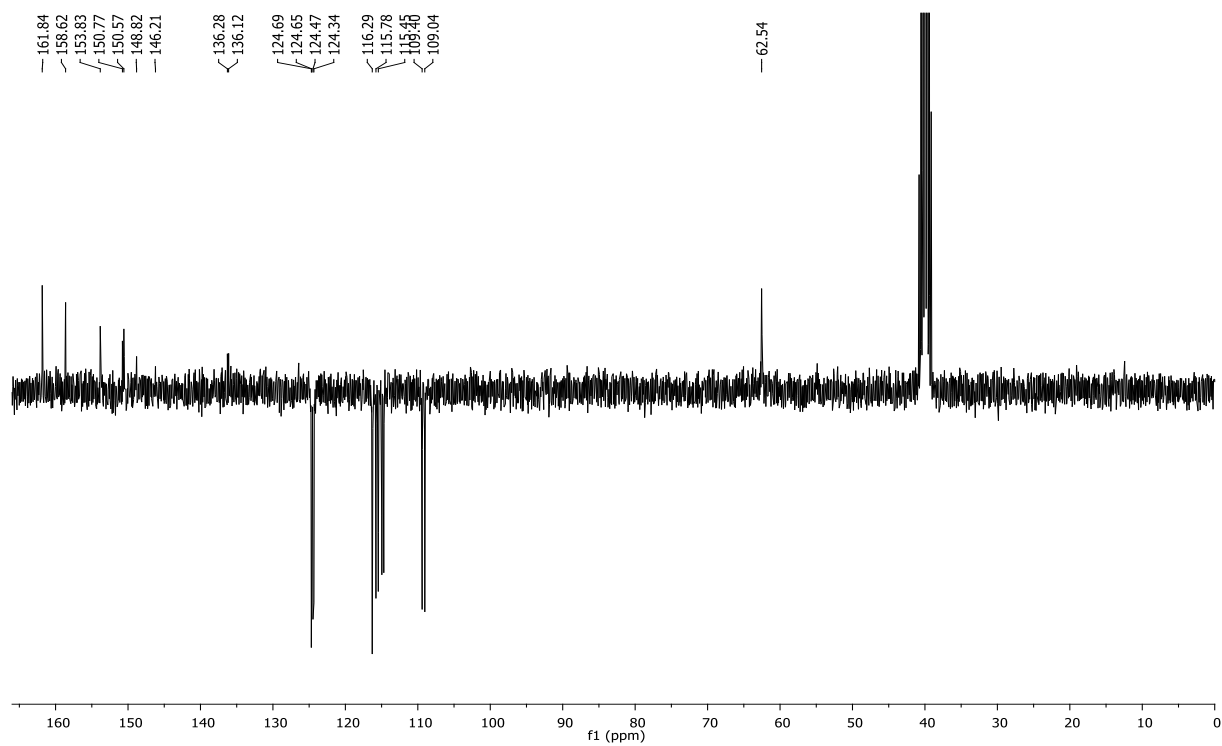
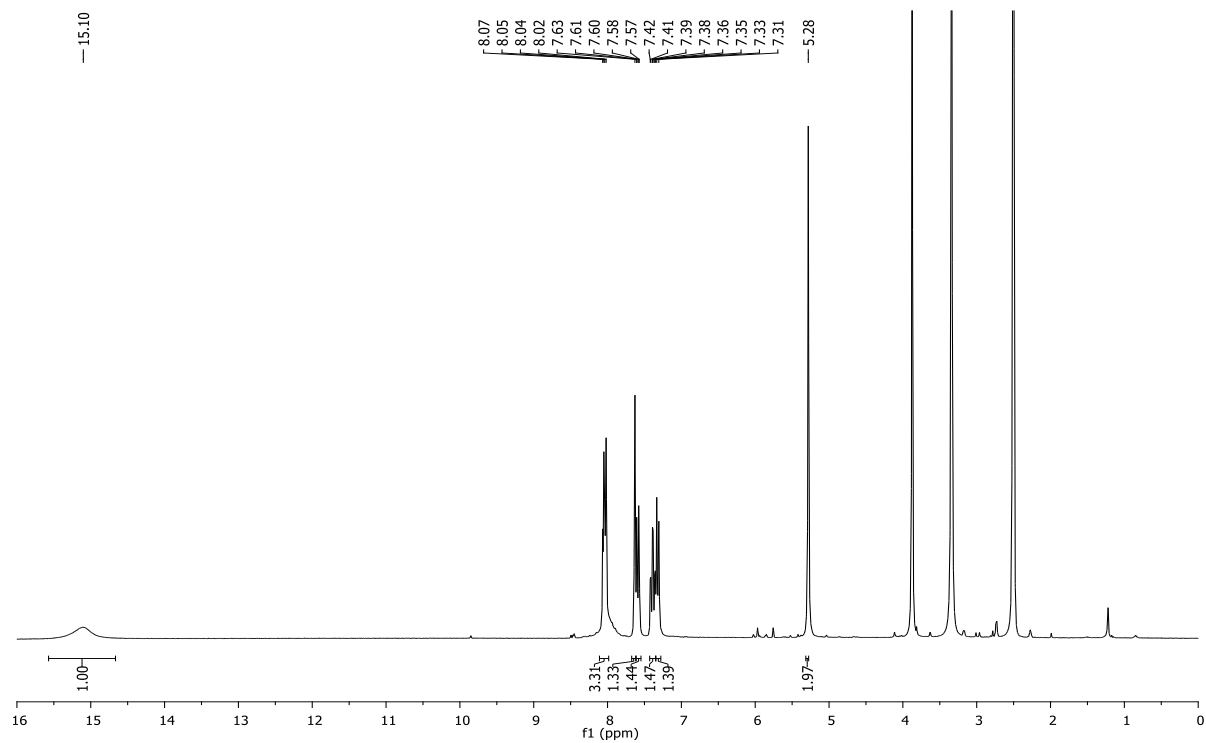


Fig. S42 a) ^1H NMR and b) ^{13}C NMR of compd. **22c**

a)



b)

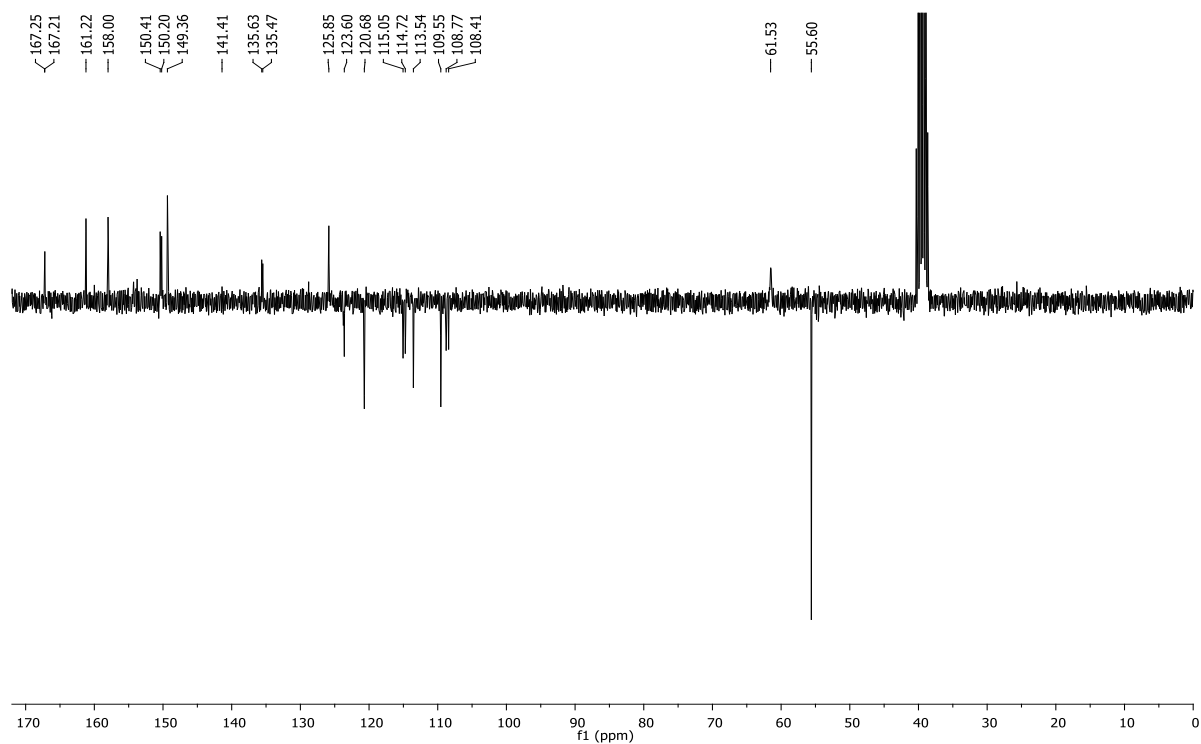
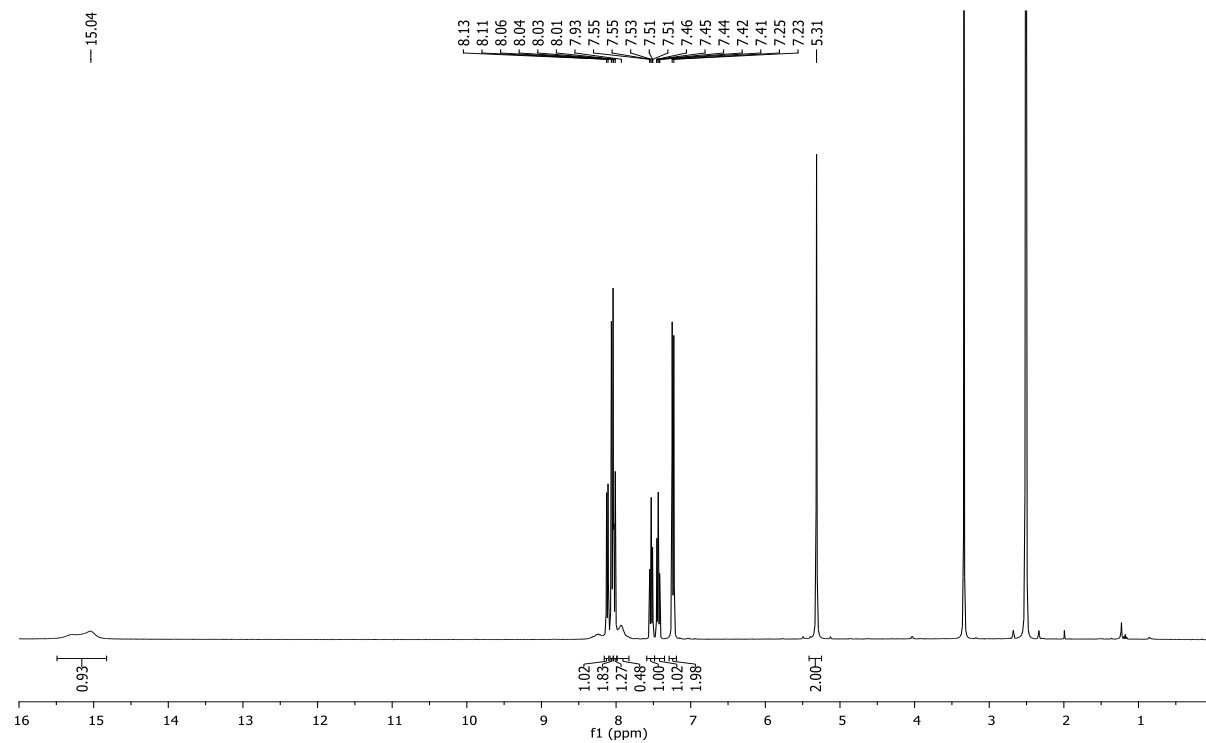


Fig. S43 a) ^1H NMR and b) ^{13}C NMR of compd. **23a**

a)



b)

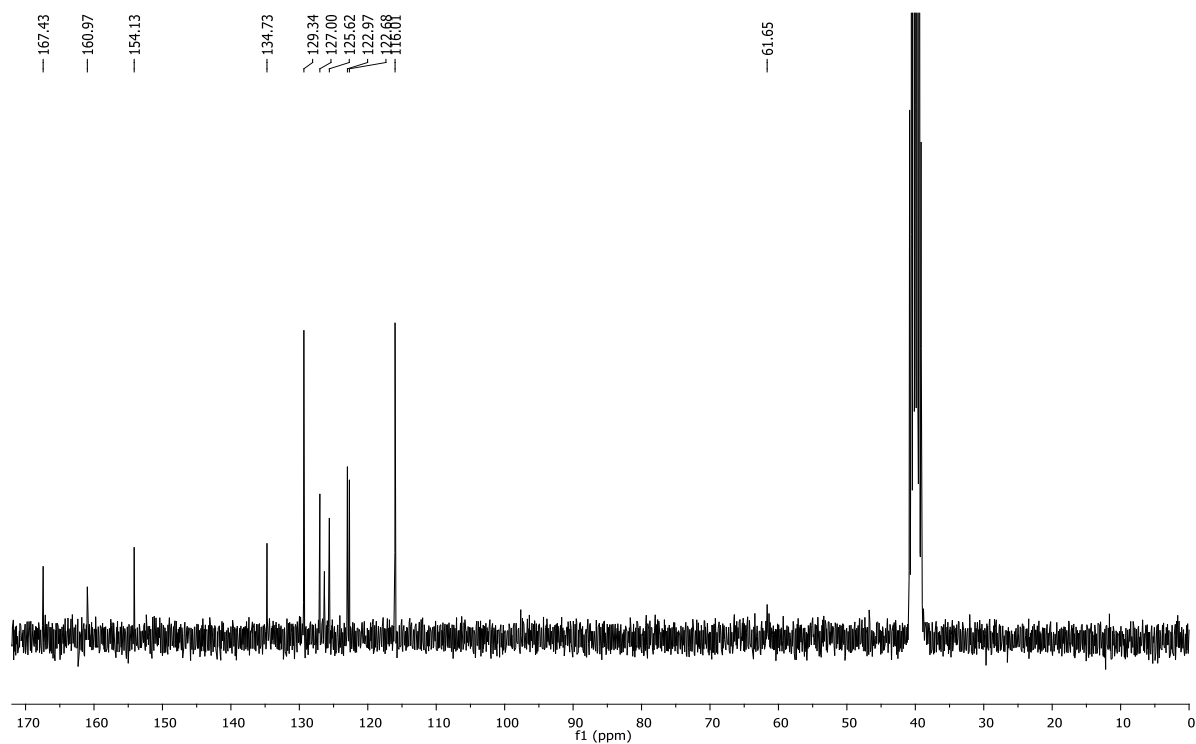
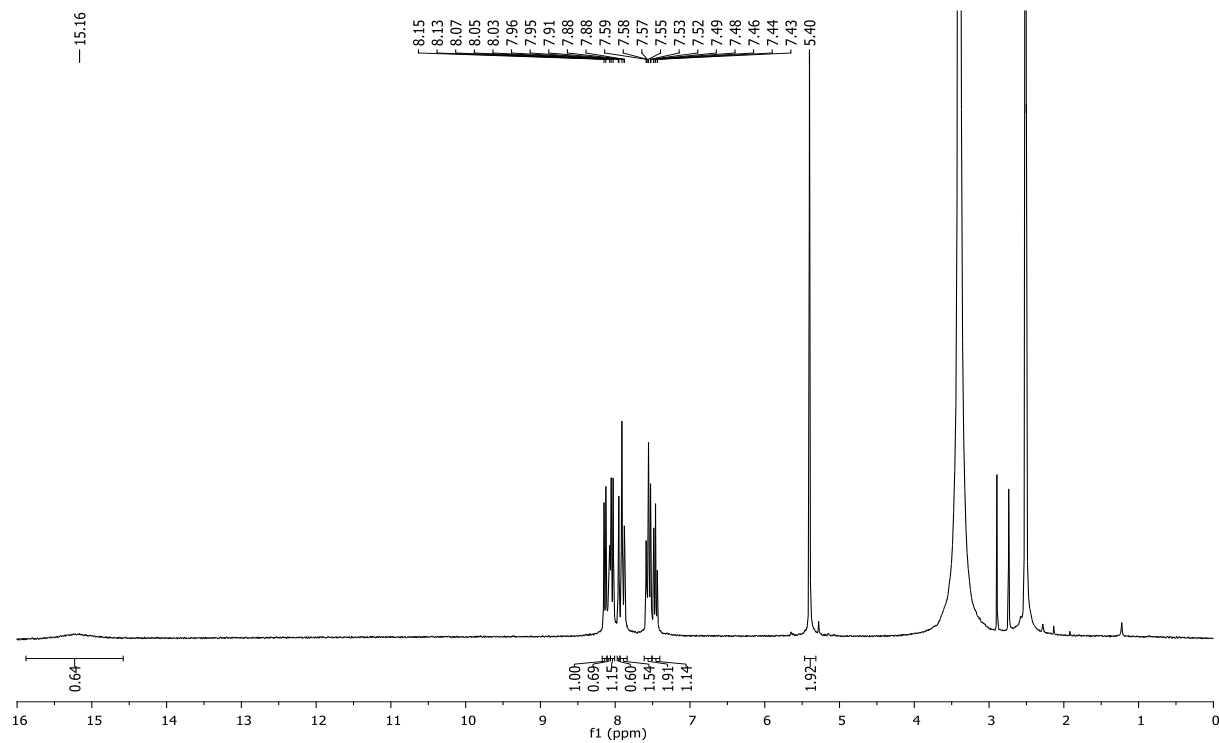


Fig. S44 a) ^1H NMR and b) ^{13}C NMR of compd. **23b**

a)



b)

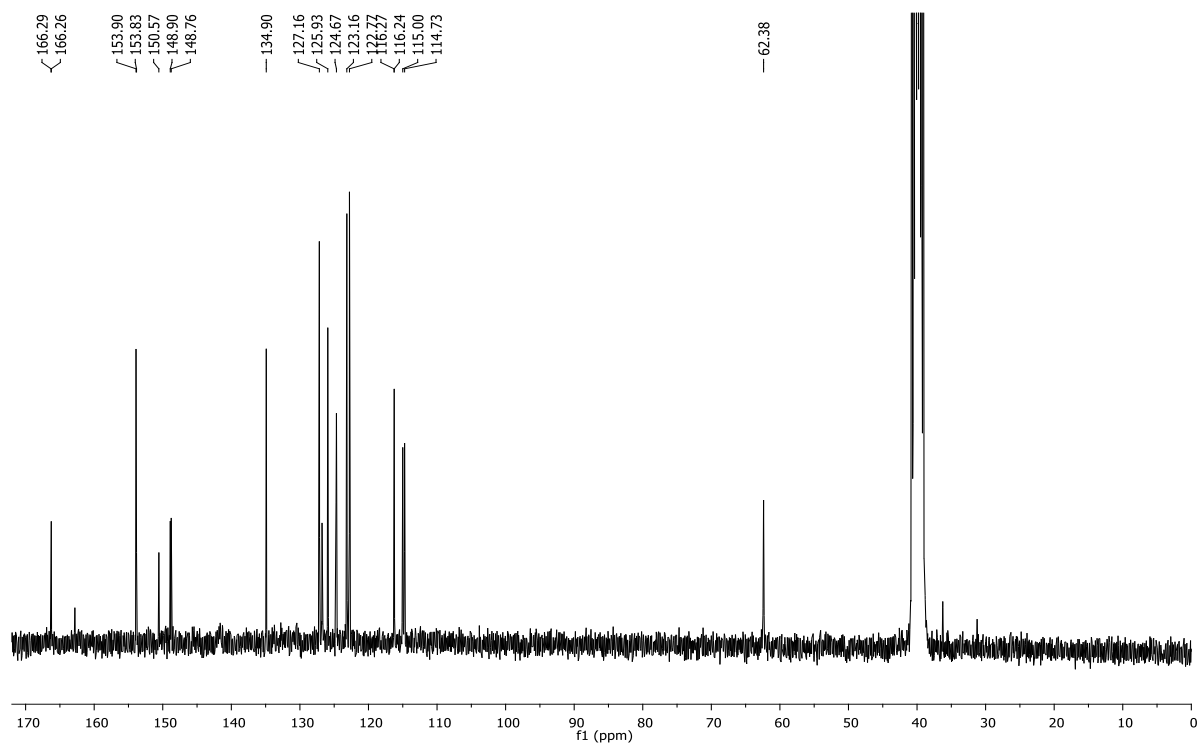
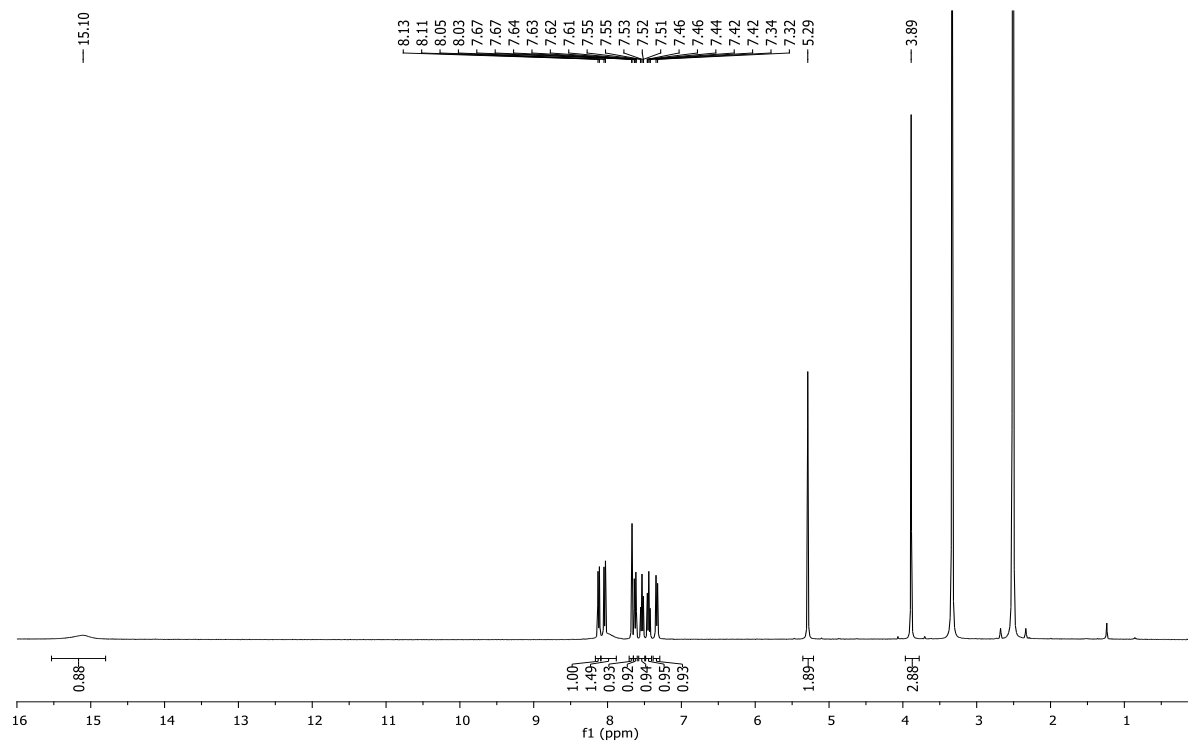


Fig. S45 a) ^1H NMR and b) ^{13}C NMR of compd. **23c**

a)



b)

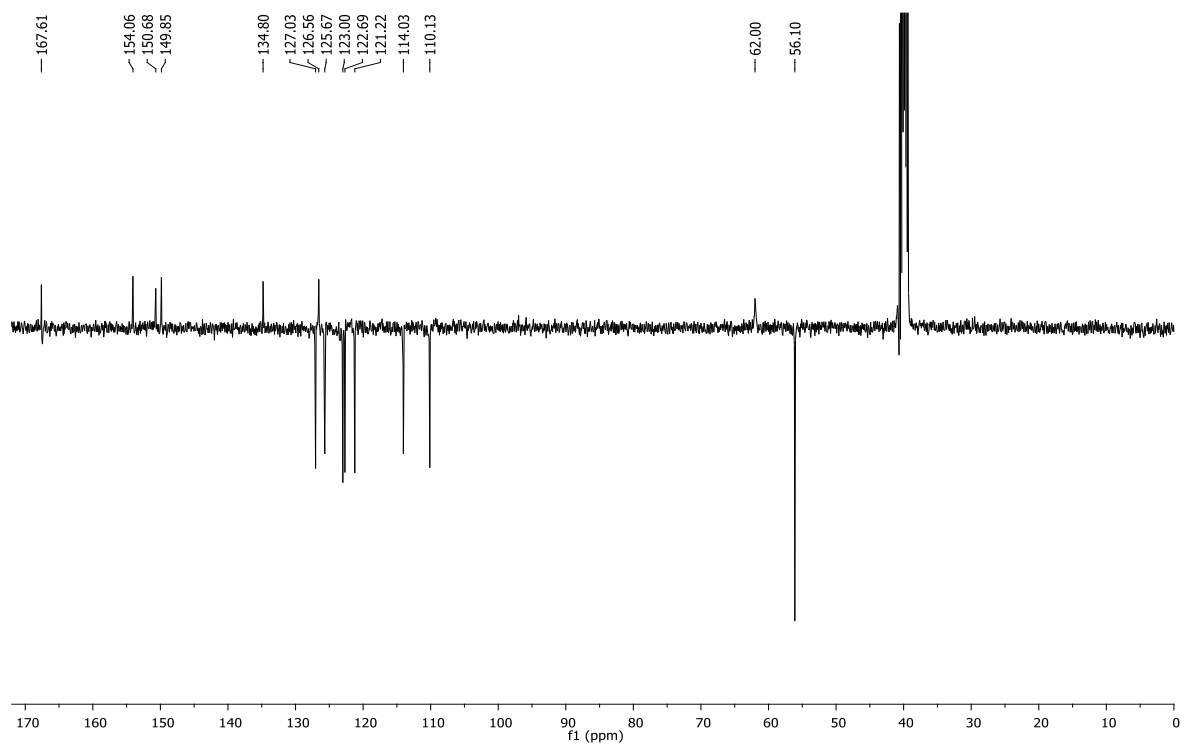
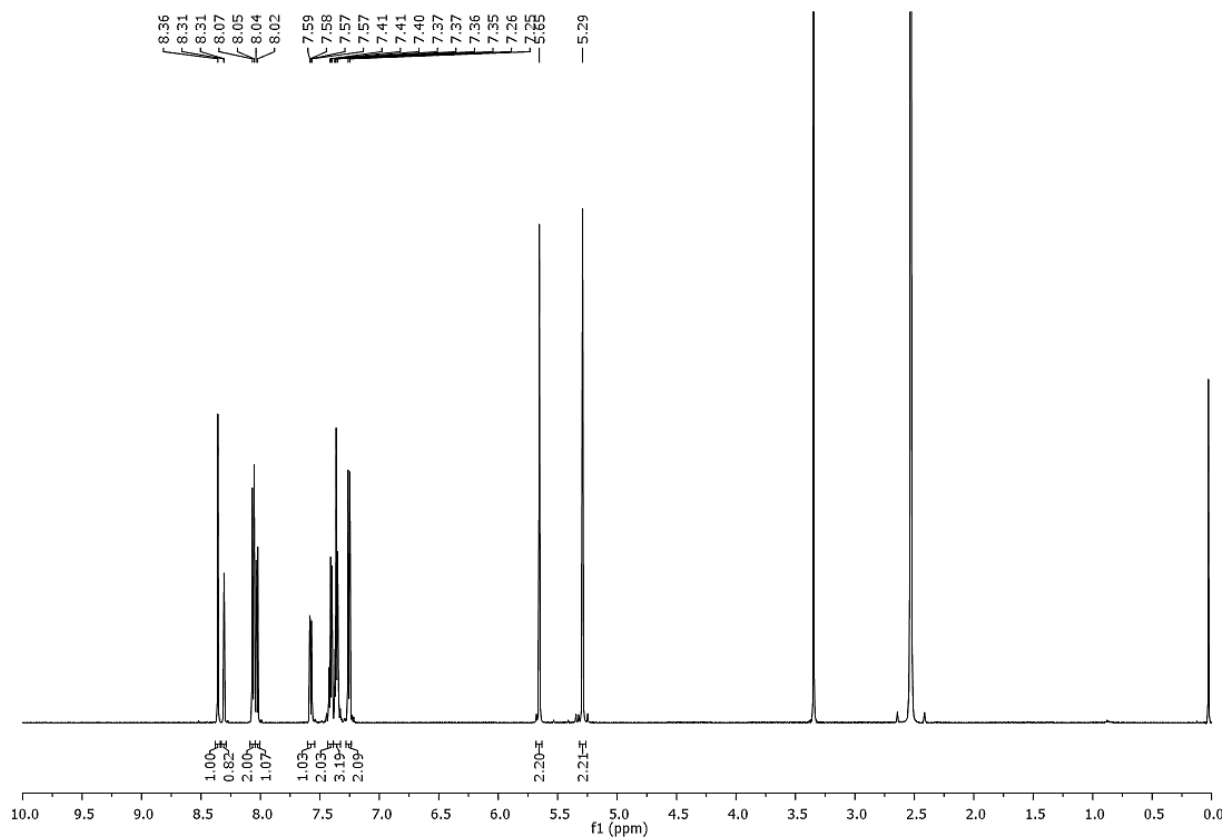


Fig. S46 a) ^1H NMR and b) ^{13}C NMR of compd. **24a**

a)



b)

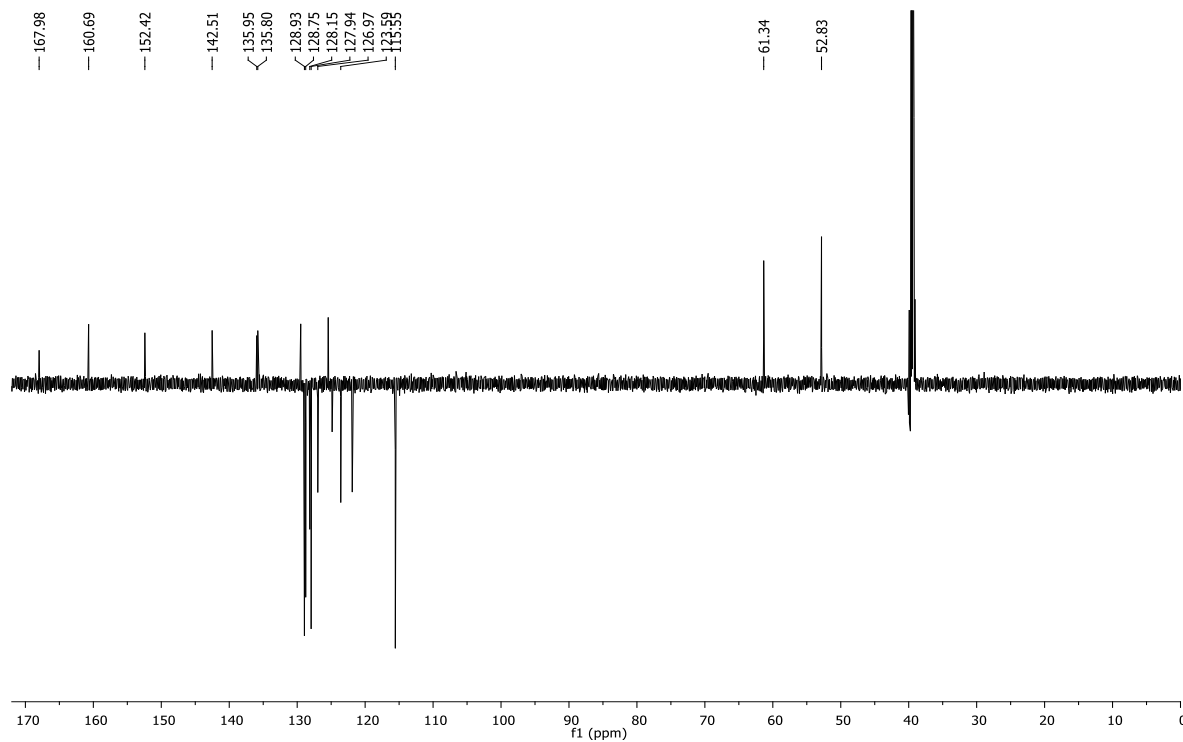


Fig. S47 a) ^1H NMR and b) ^{13}C NMR of compd. **24b**

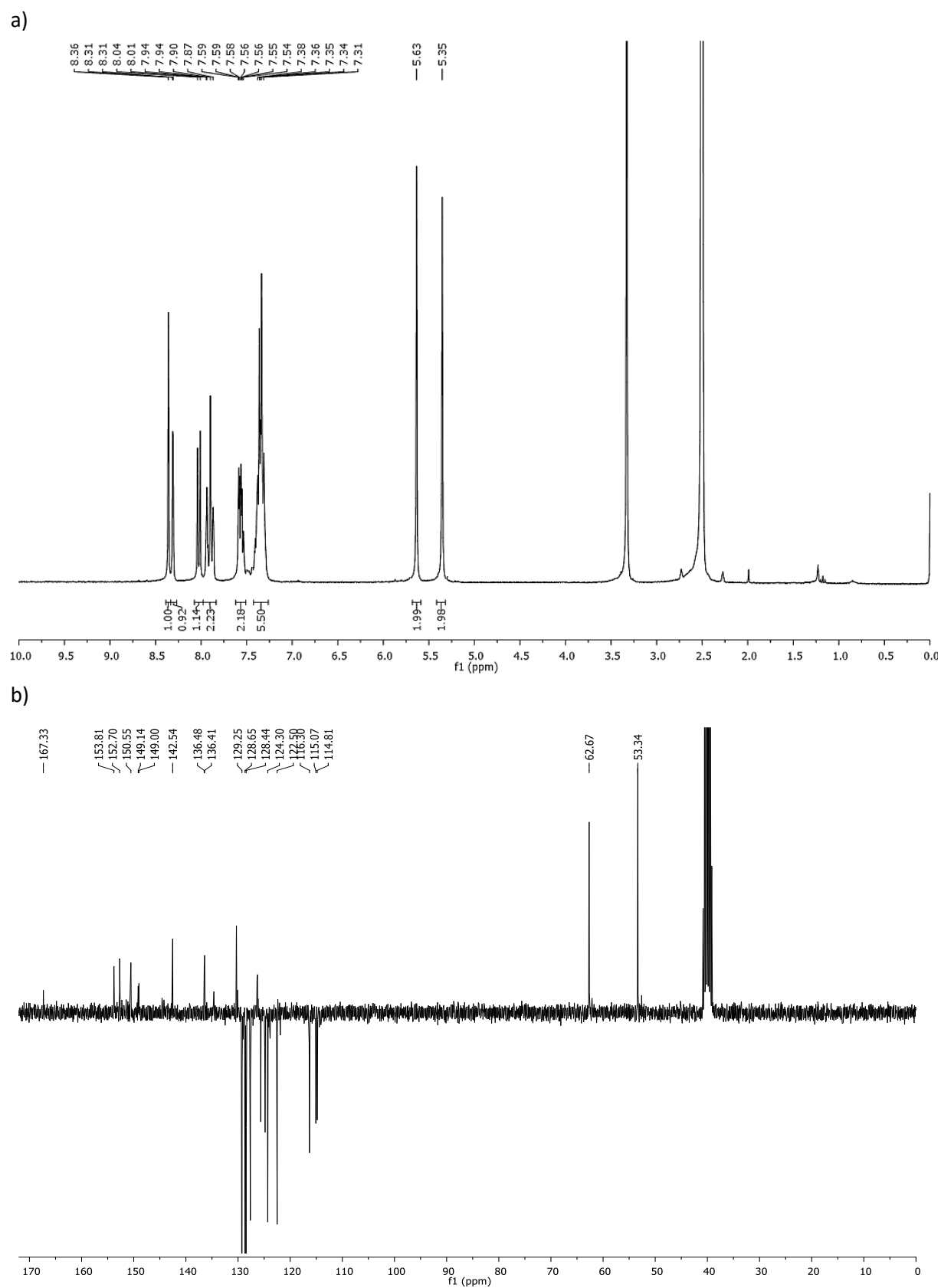
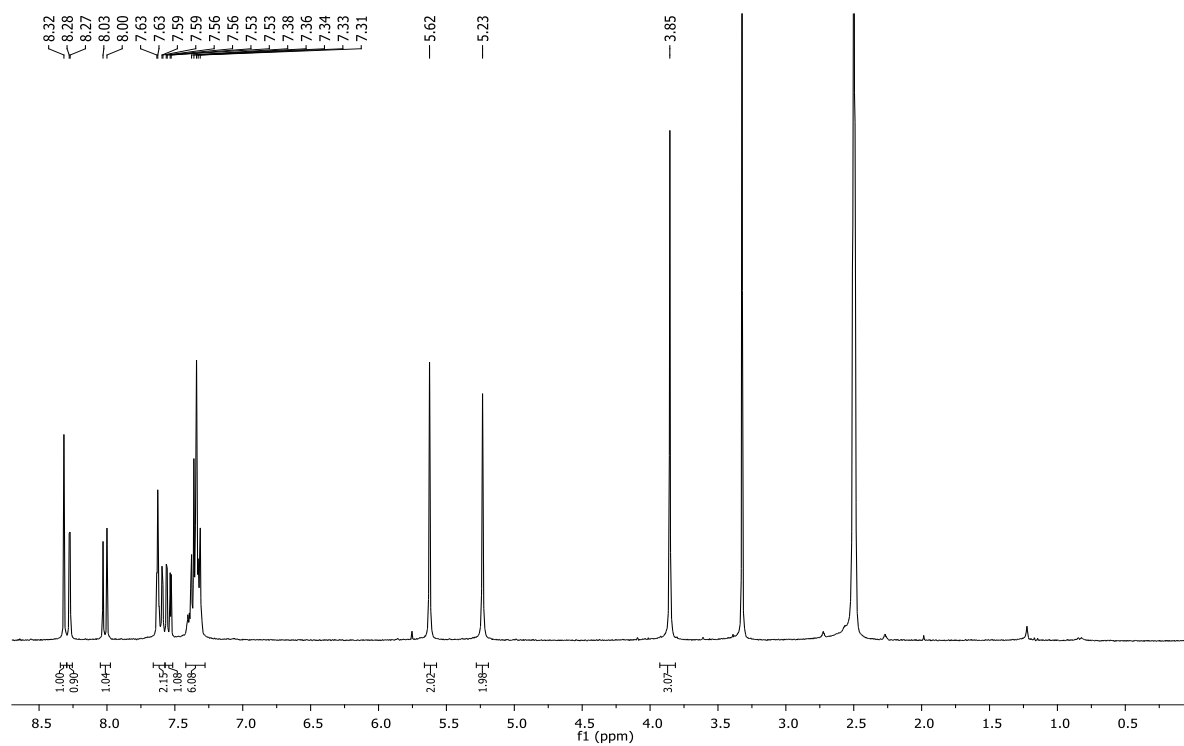


Fig. S48 a) ^1H NMR and b) ^{13}C NMR of compd. **24c**

a)



b)

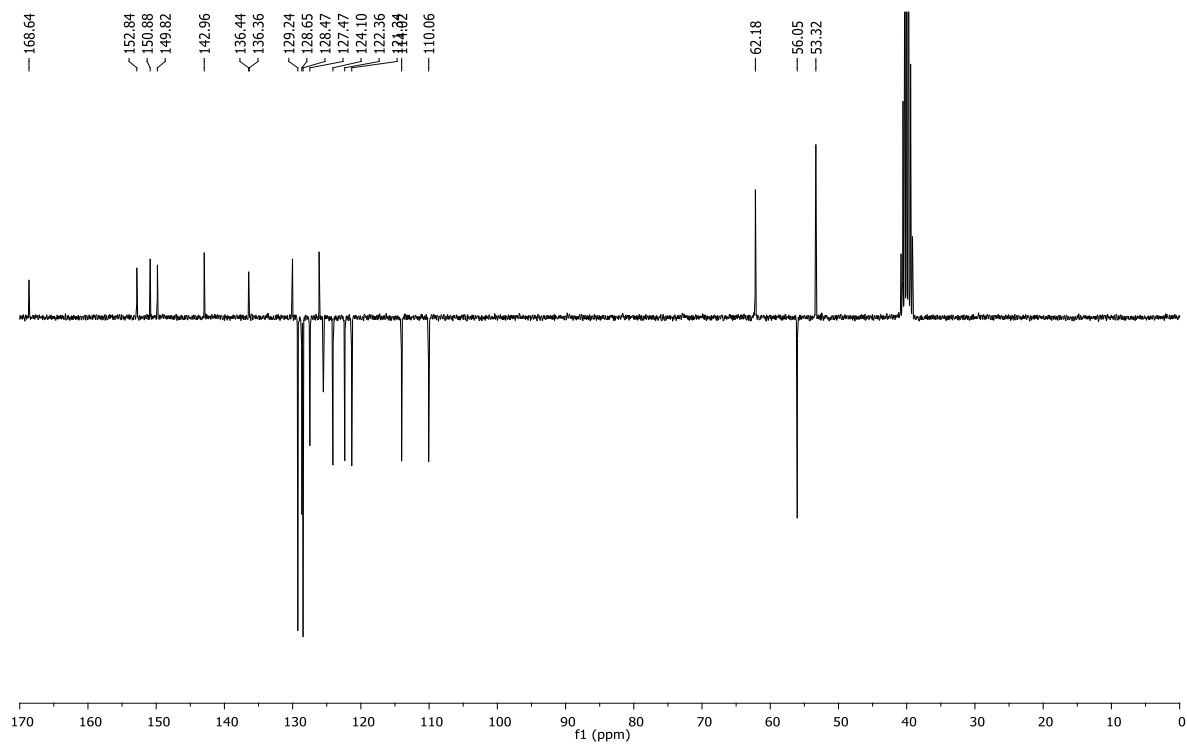
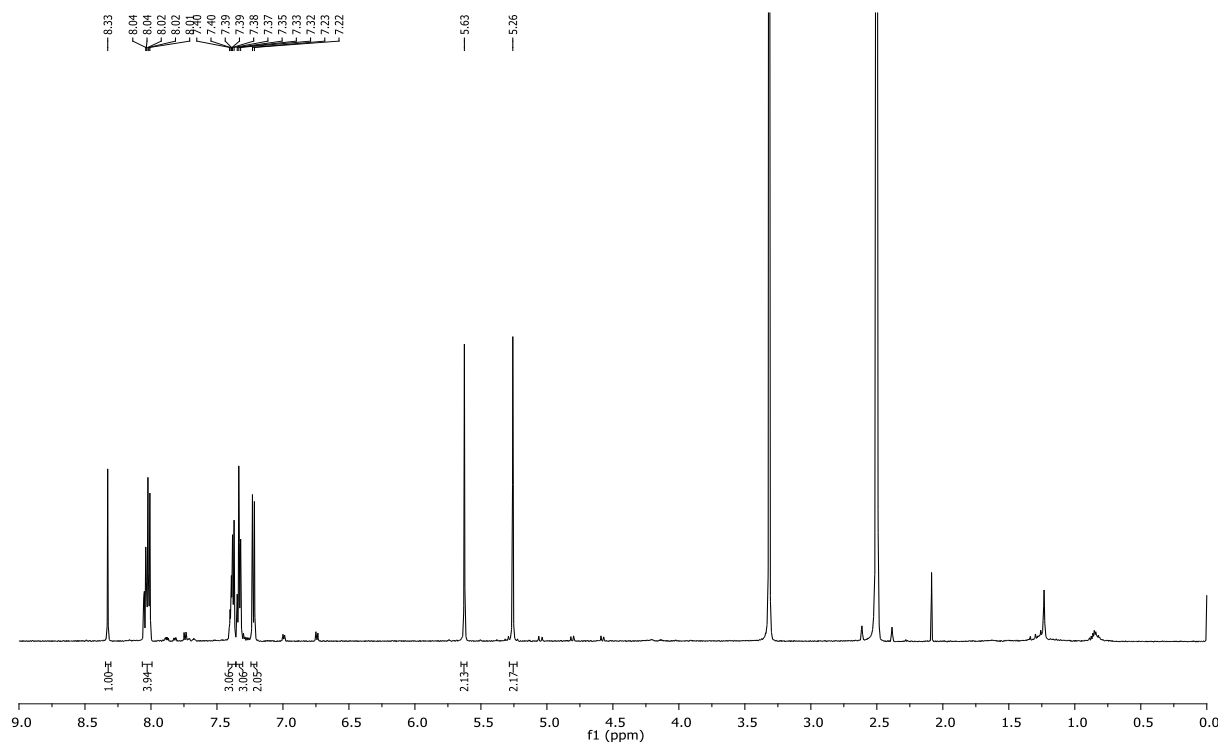


Fig. S49 a) ^1H NMR and b) ^{13}C NMR of compd. **25a**

a)



b)

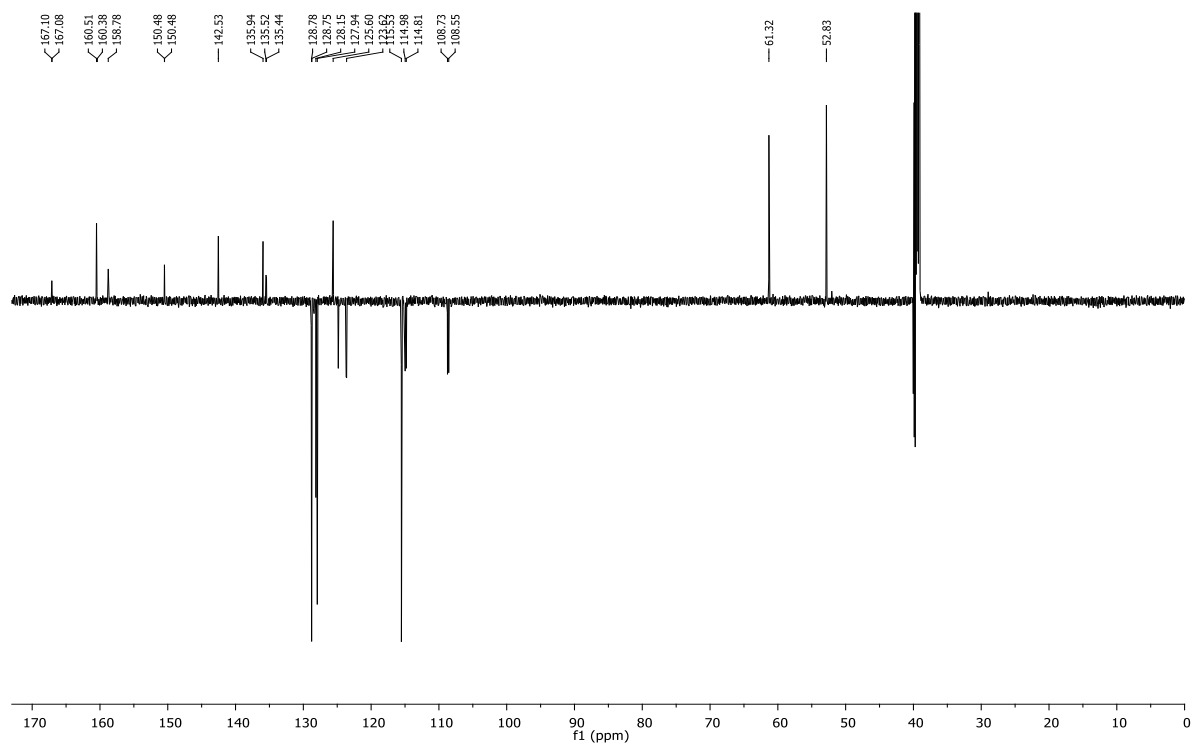
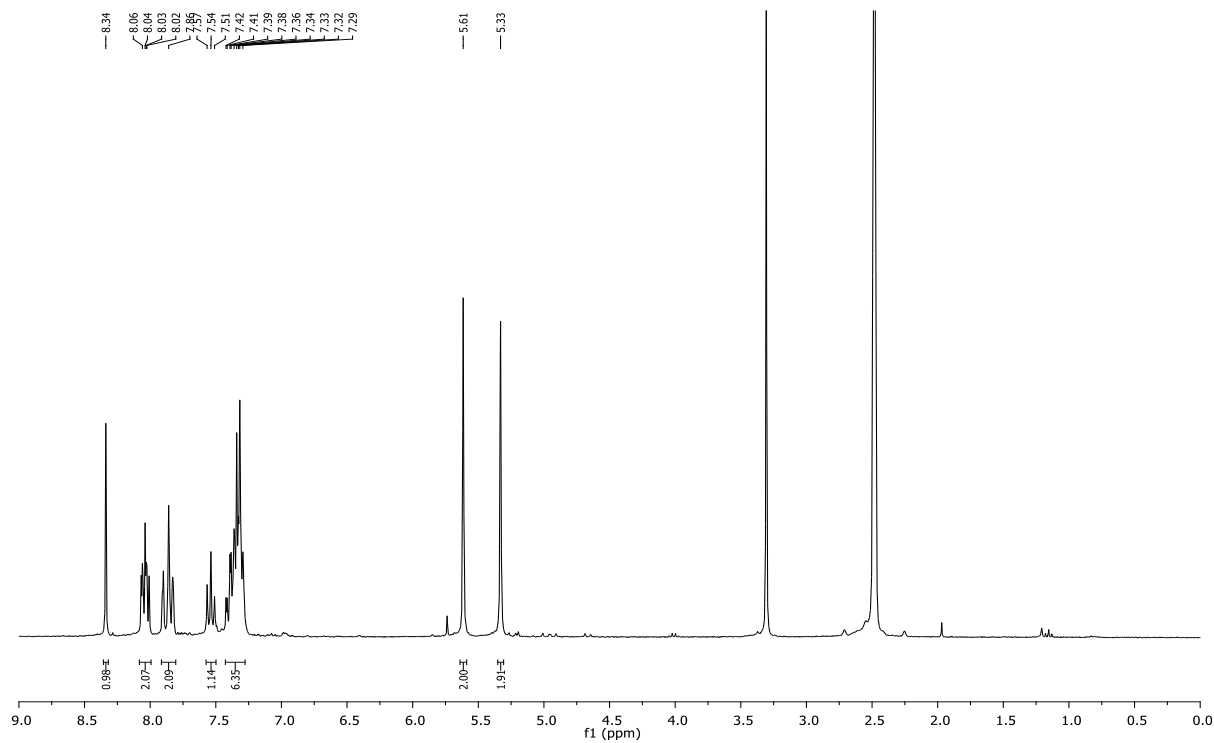


Fig. S50 a) ^1H NMR and b) ^{13}C NMR of compd. **25b**

a)



b)

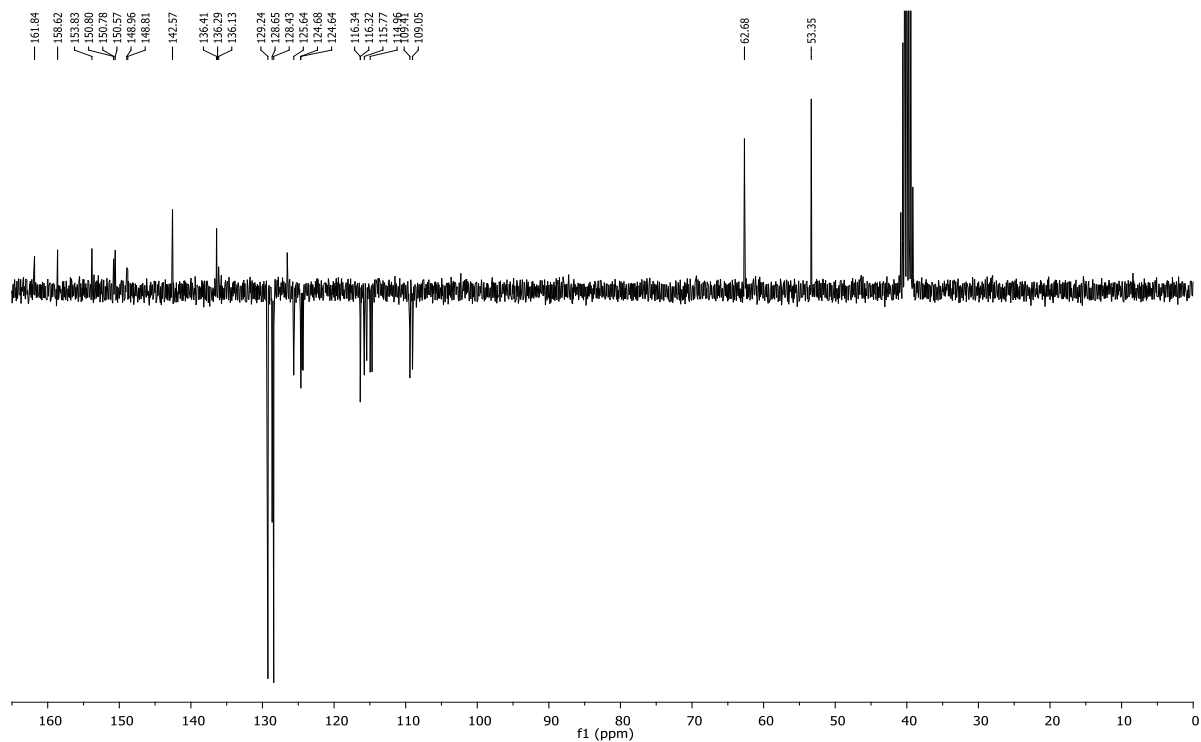
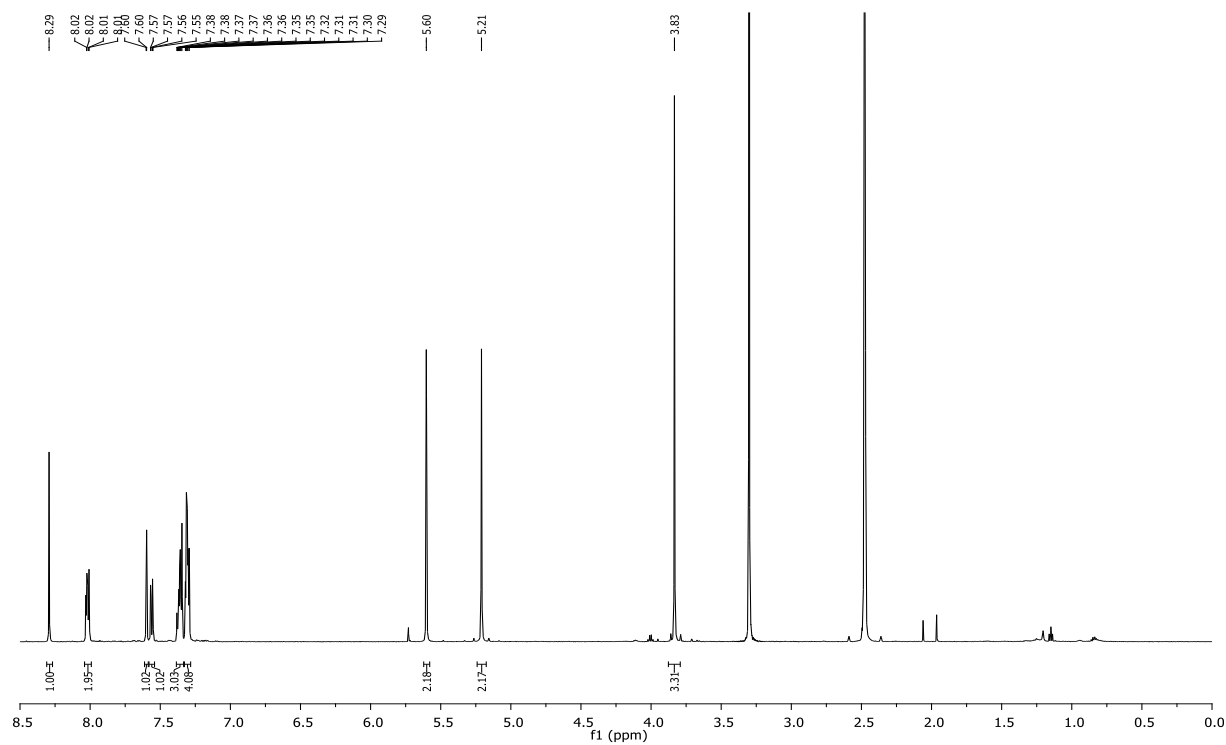


Fig. S51 a) ^1H NMR and b) ^{13}C NMR of compd. **25c**

a)



b)

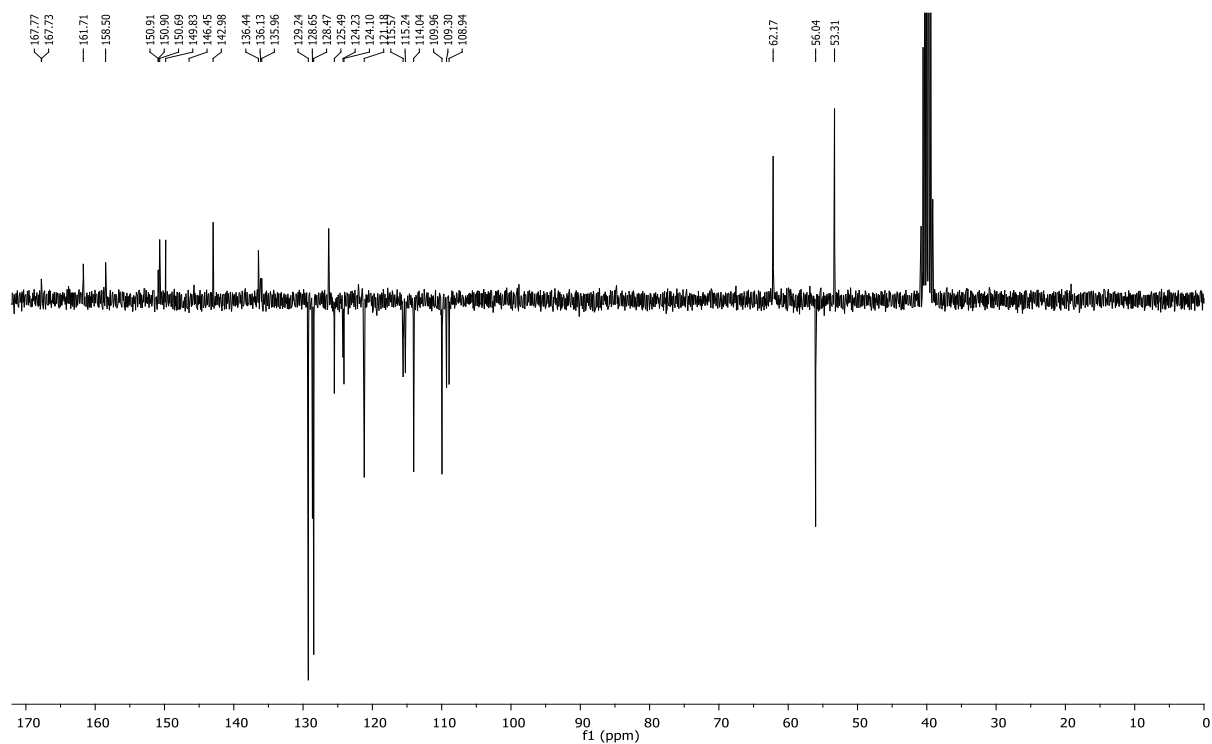
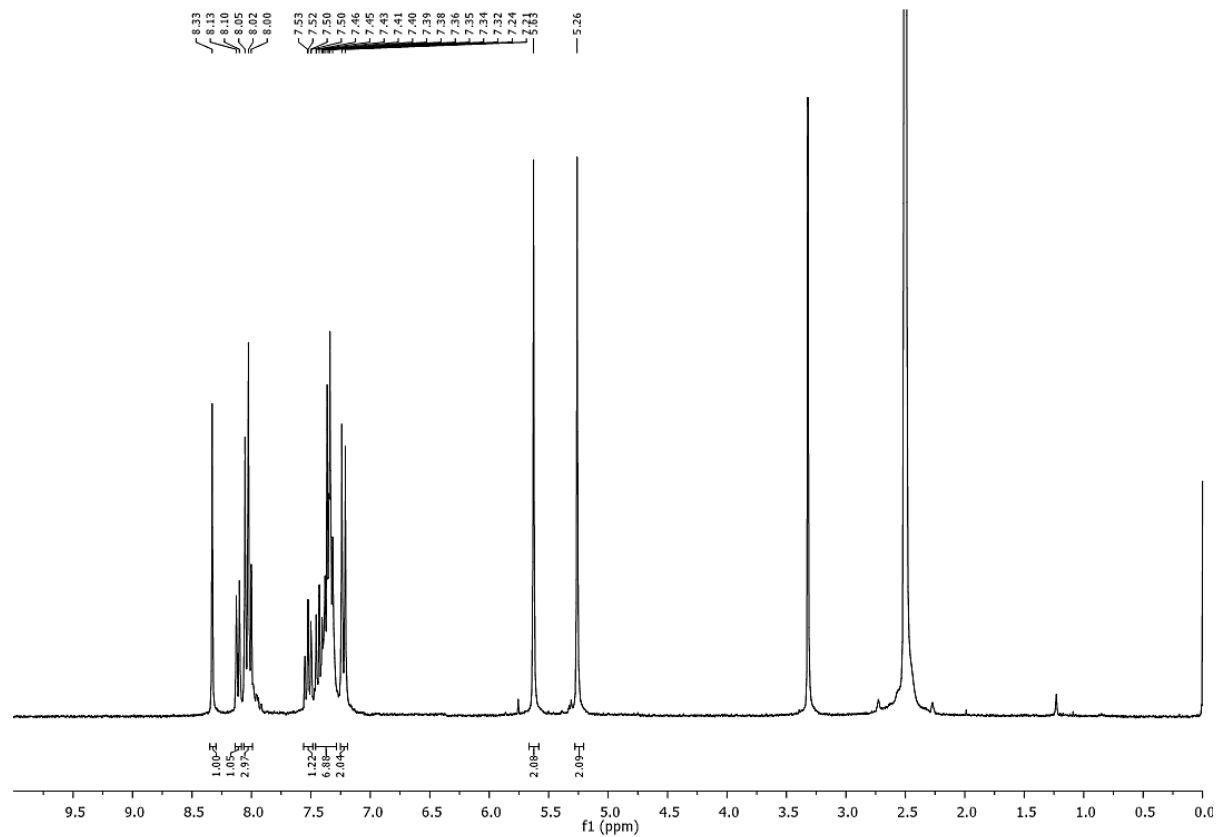


Fig. S52 a) ^1H NMR and b) ^{13}C NMR of compd. **26a**

a)



b)

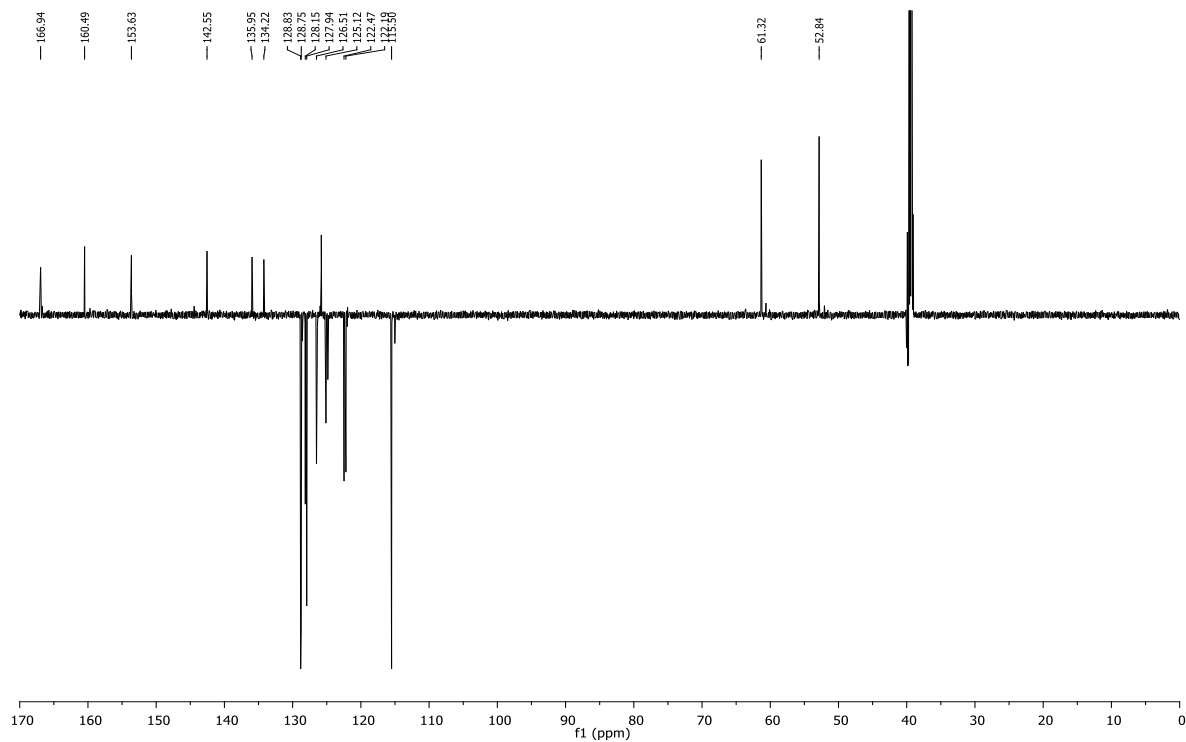
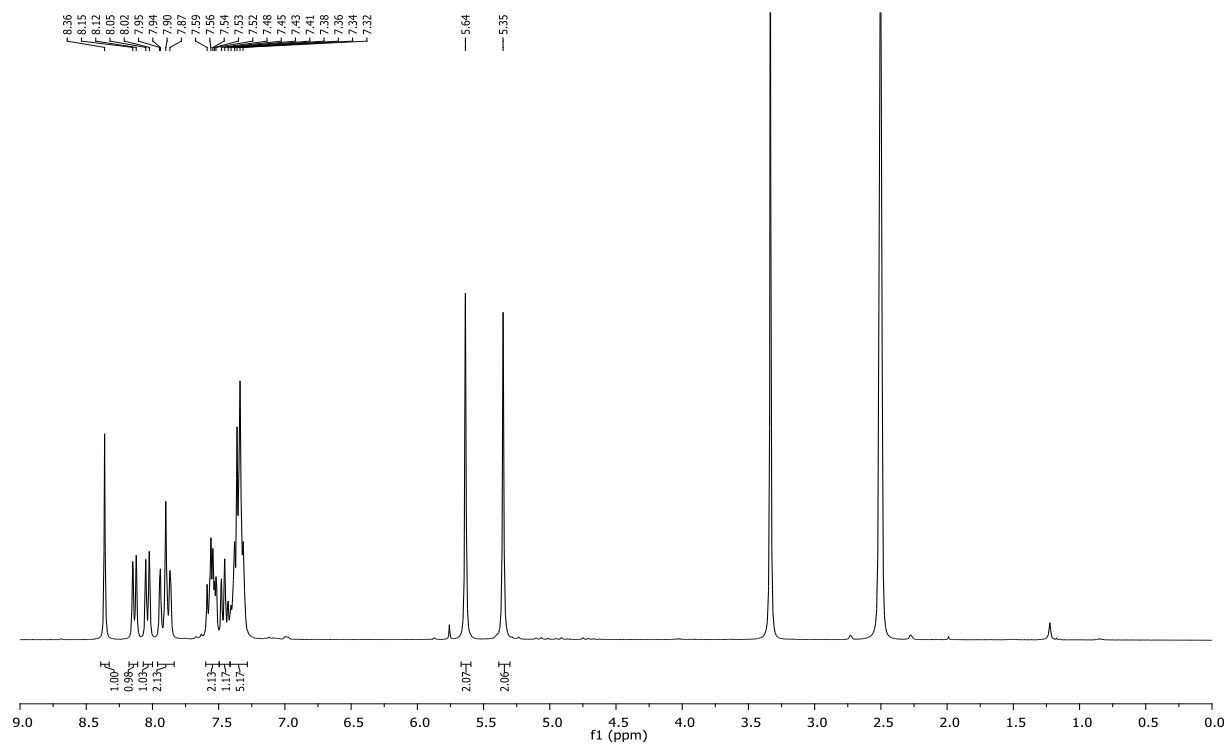


Fig. S53 a) ^1H NMR and b) ^{13}C NMR of compd. **26b**

a)



b)

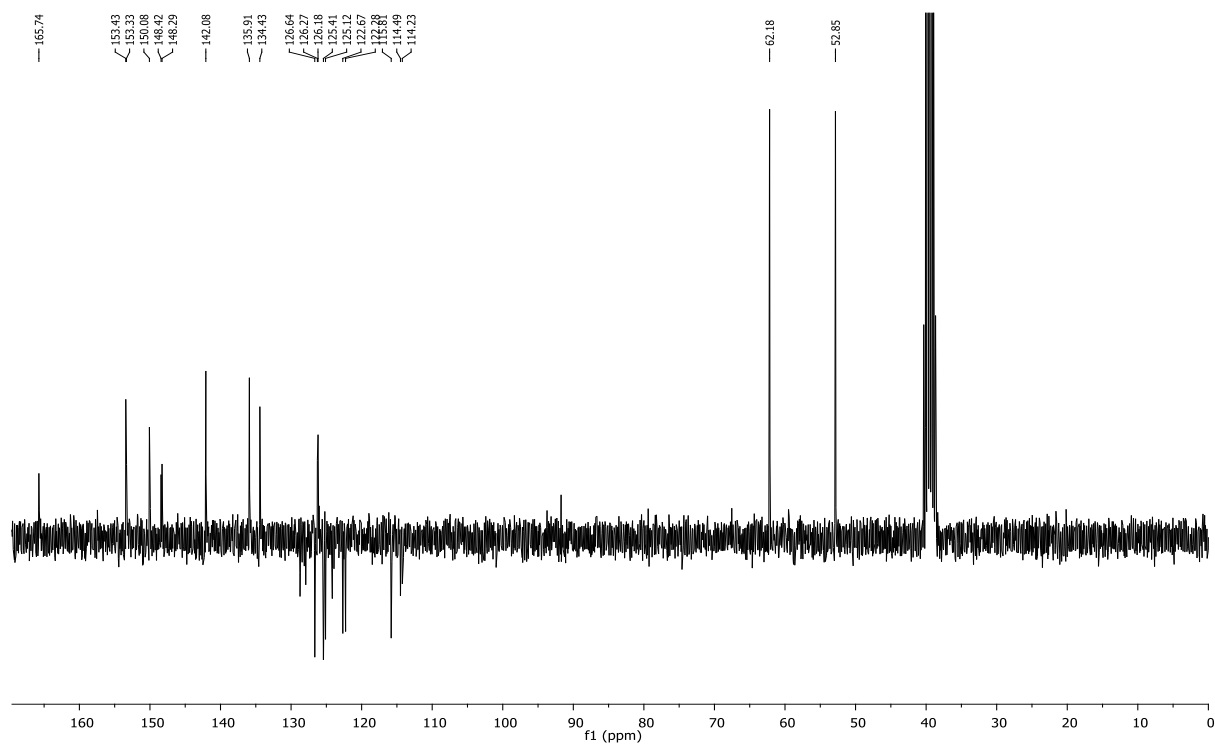
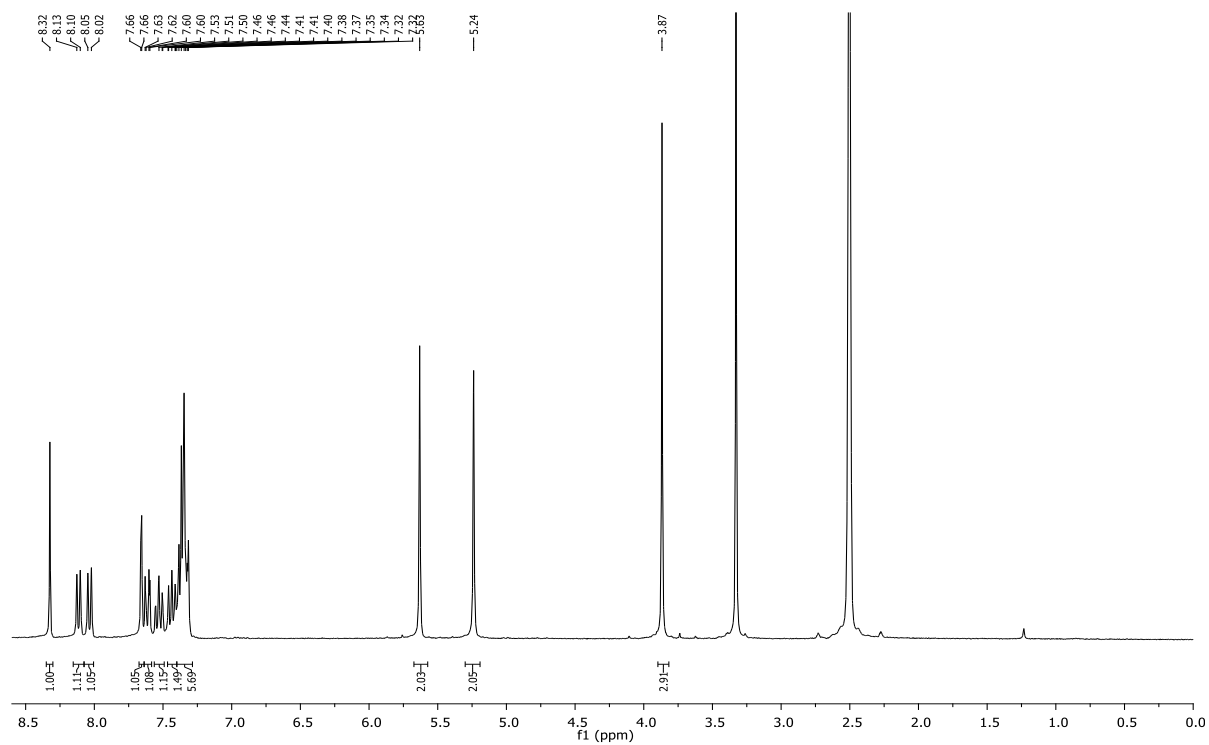


Fig. S54 a) ^1H NMR and b) ^{13}C NMR of compd. **26c**

a)



b)

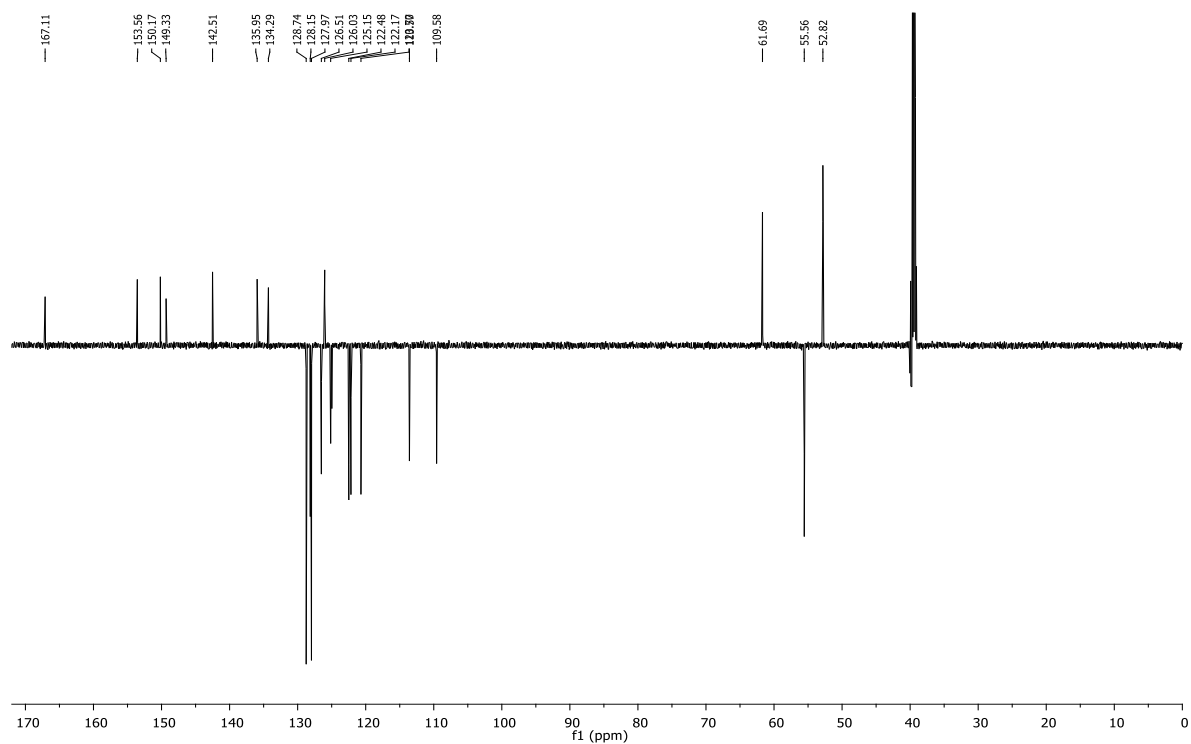
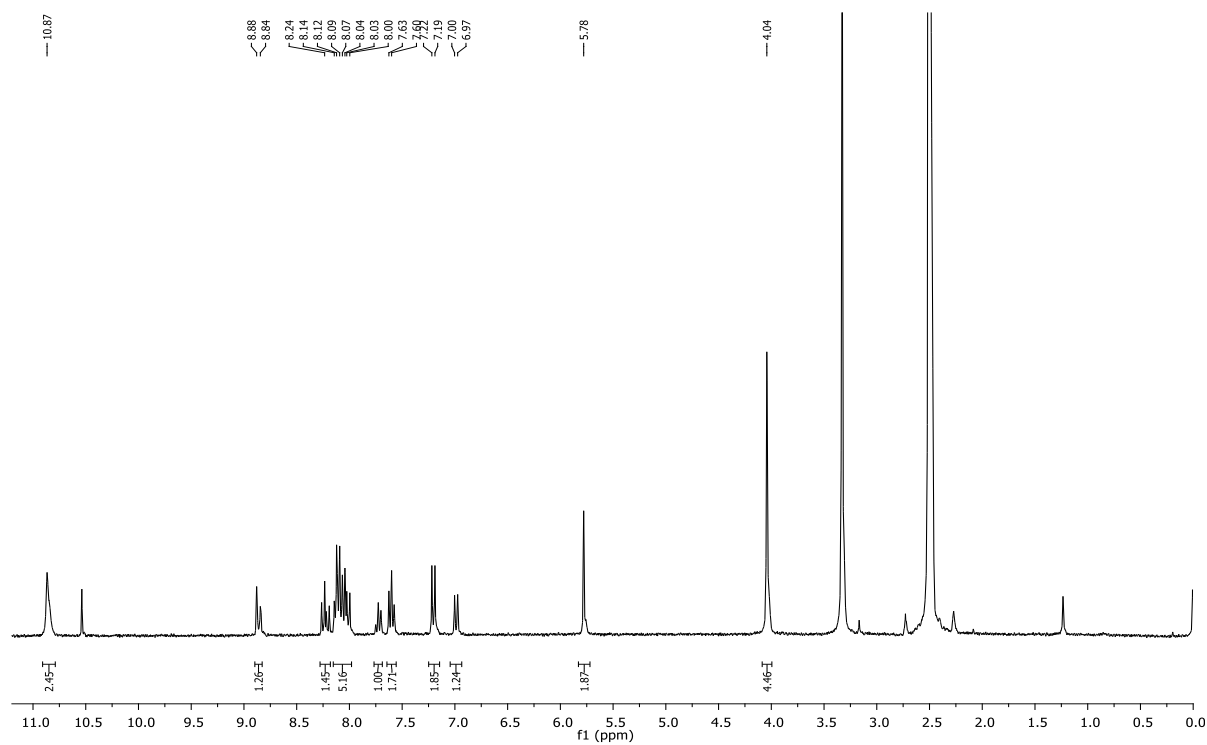


Fig. S55 a) ^1H NMR and b) ^{13}C NMR of compd. **34a**

a)



b)

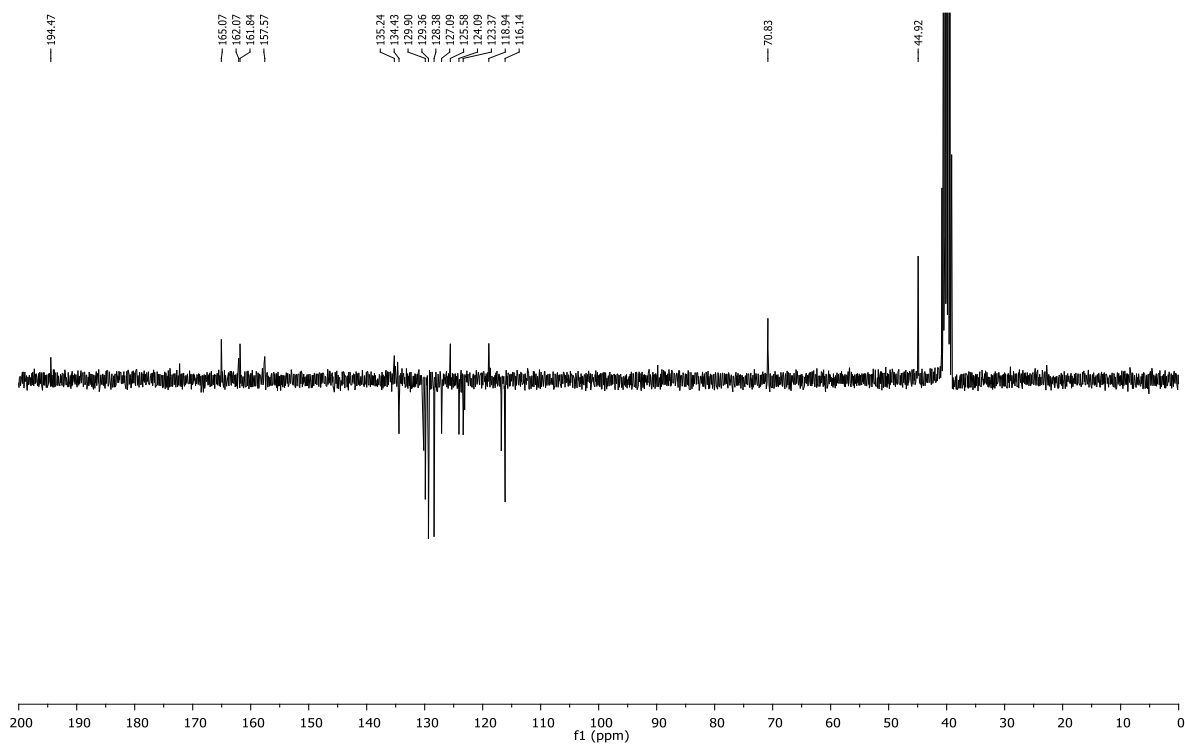
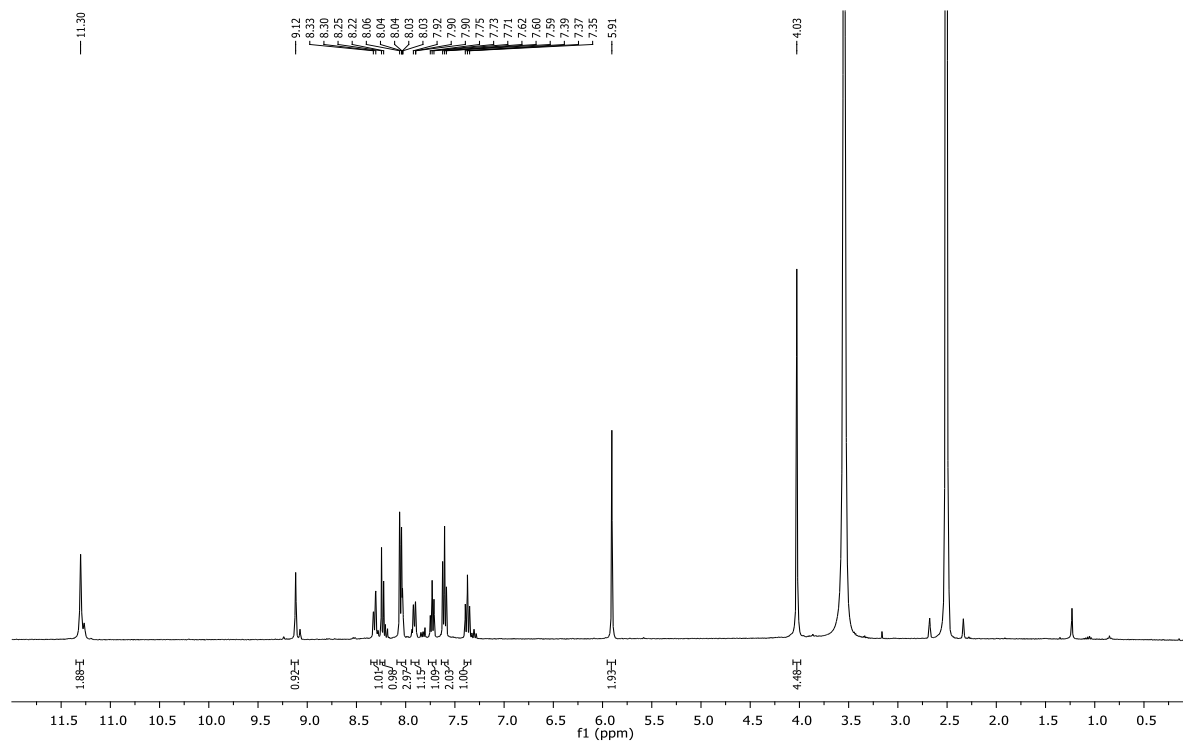


Fig. S56 a) ^1H NMR and b) ^{13}C NMR of compd. **34b**

a)



b)

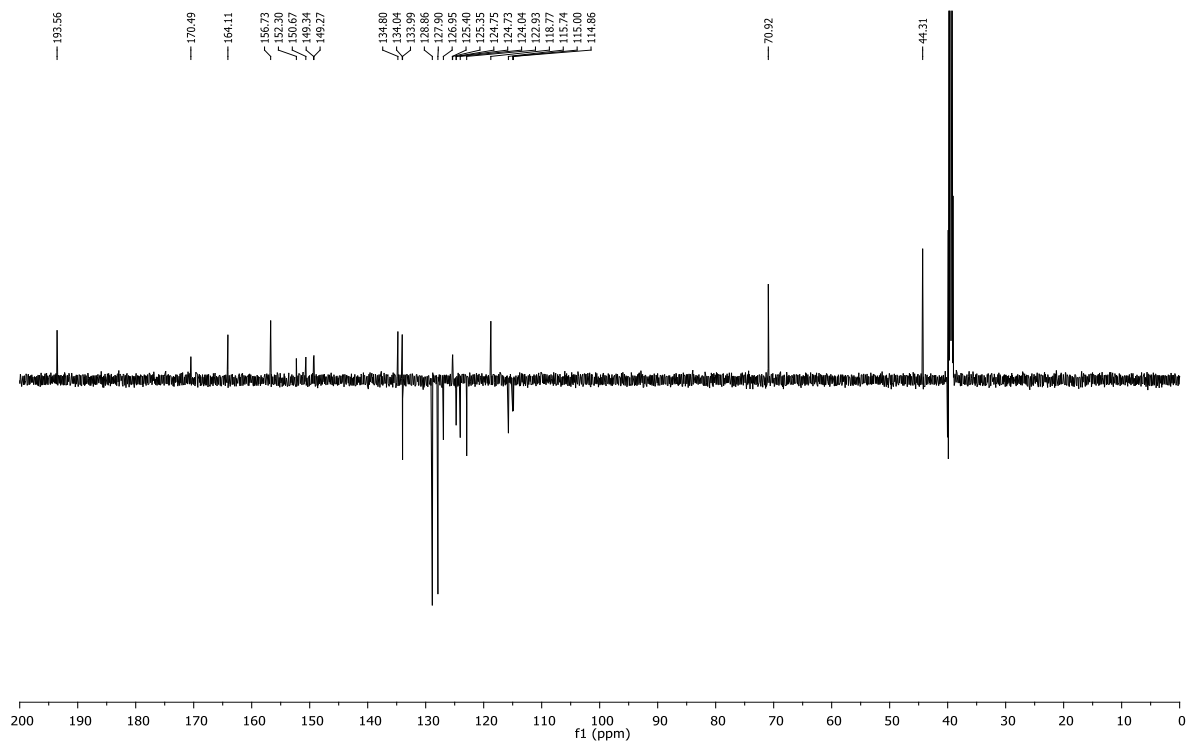
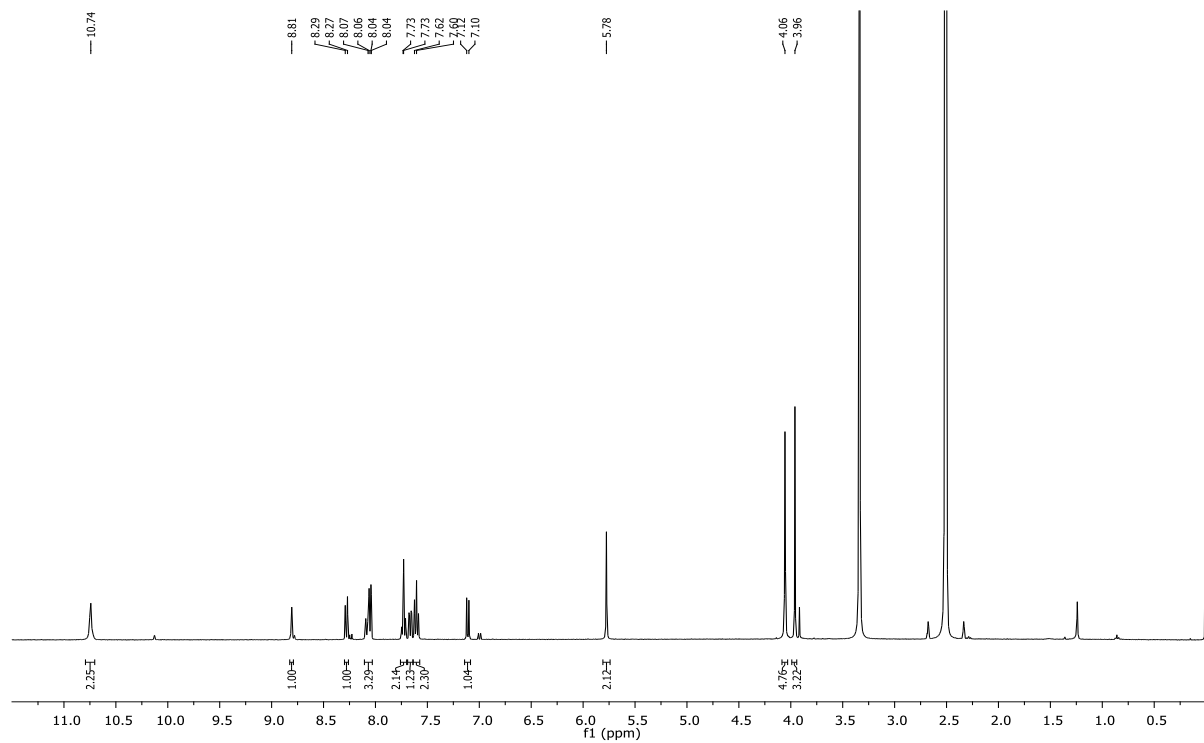


Fig. S57 a) ^1H NMR and b) ^{13}C NMR of compd. **34c**

a)



b)

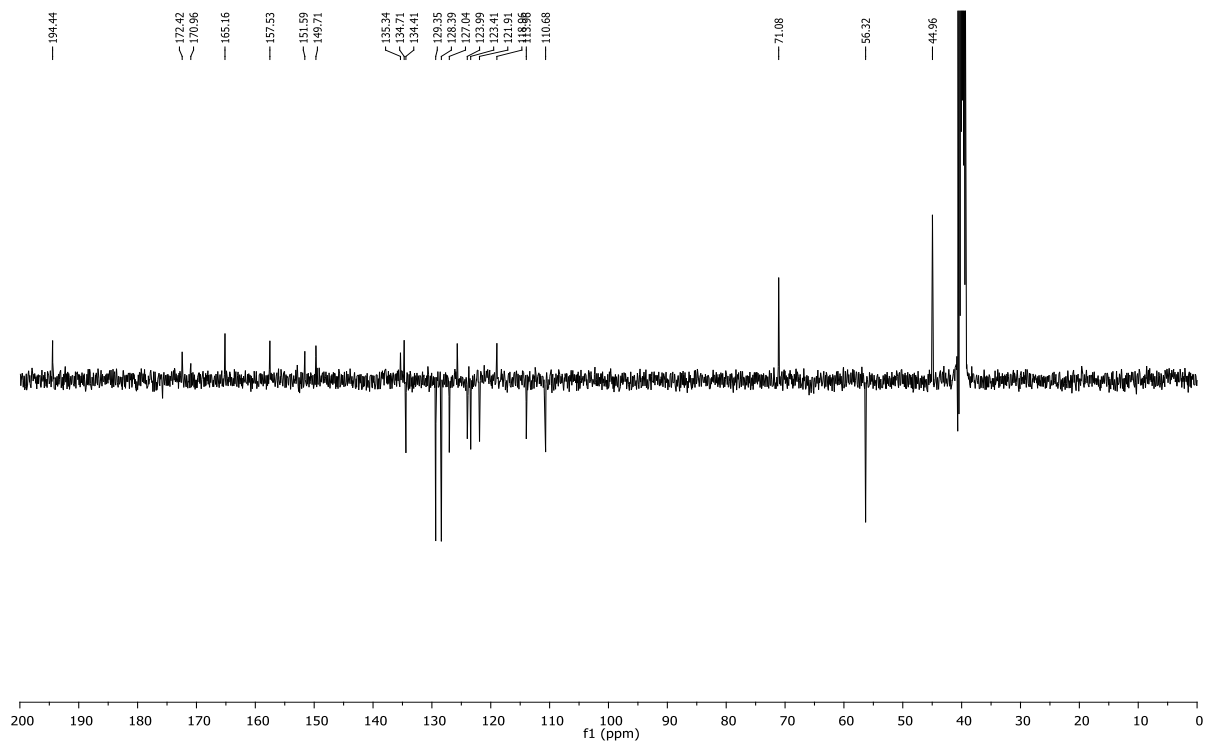
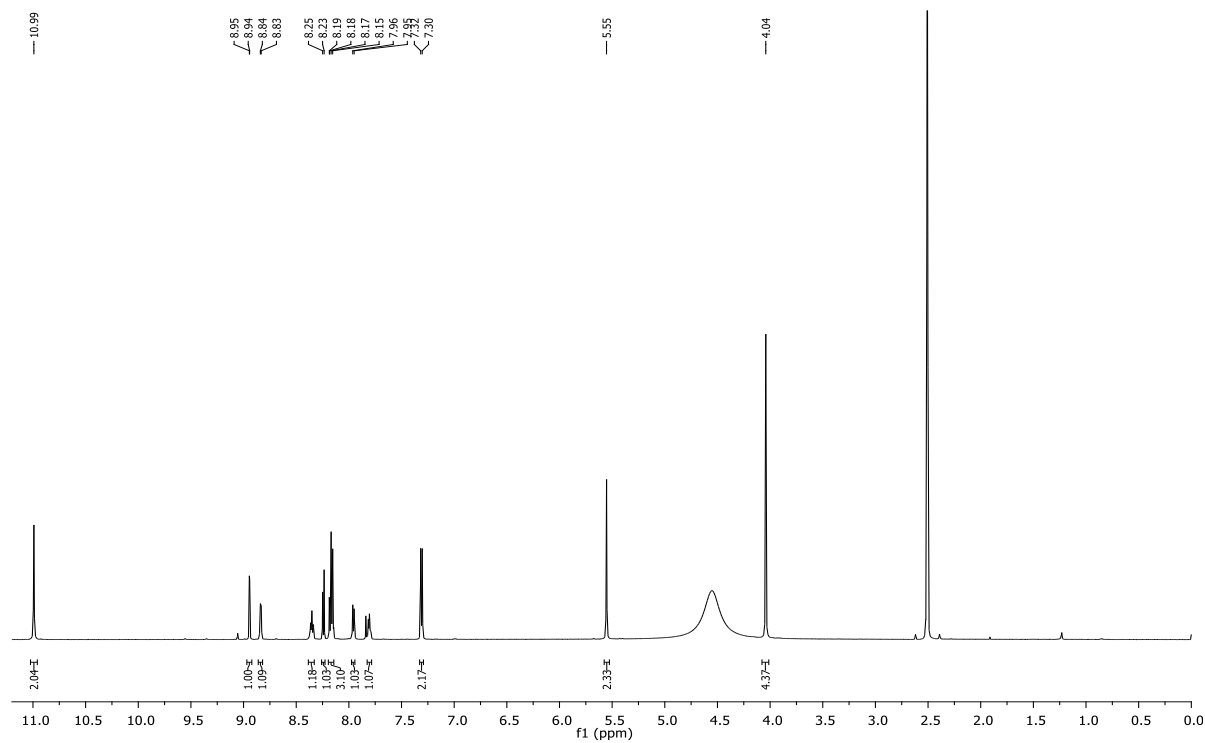


Fig. S58 a) ^1H NMR and b) ^{13}C NMR of compd. **35a**

a)



b)

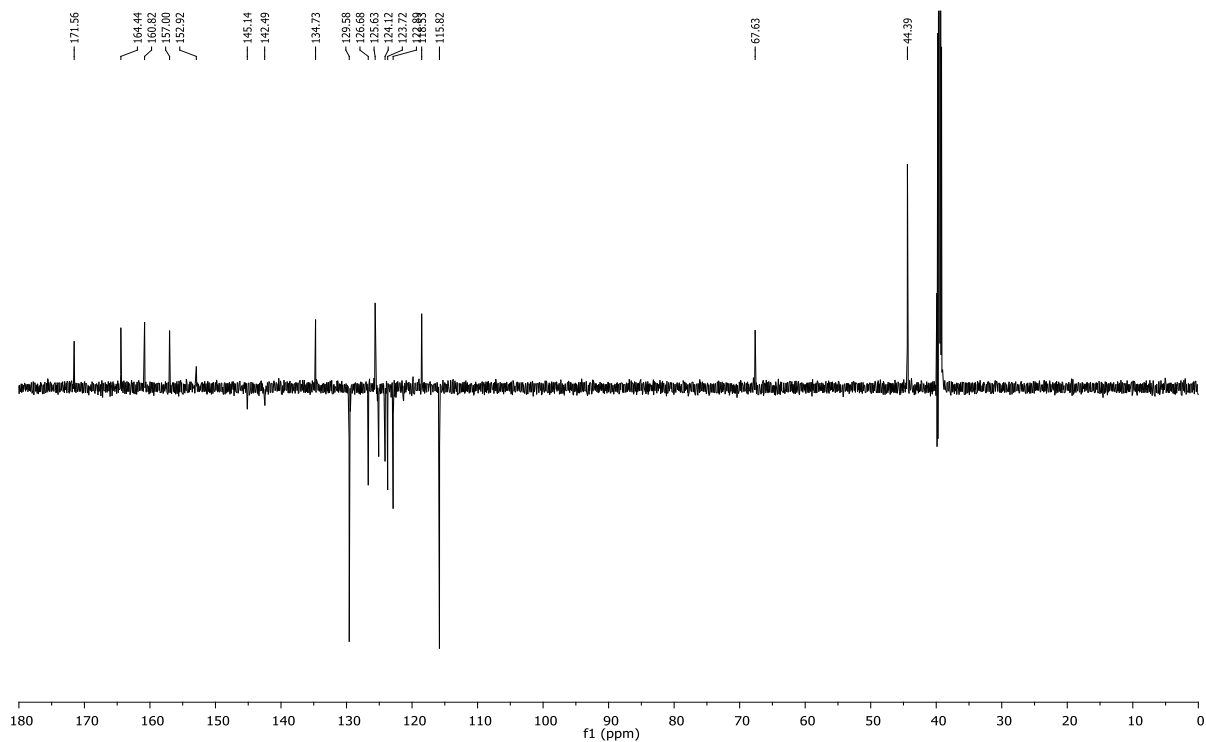
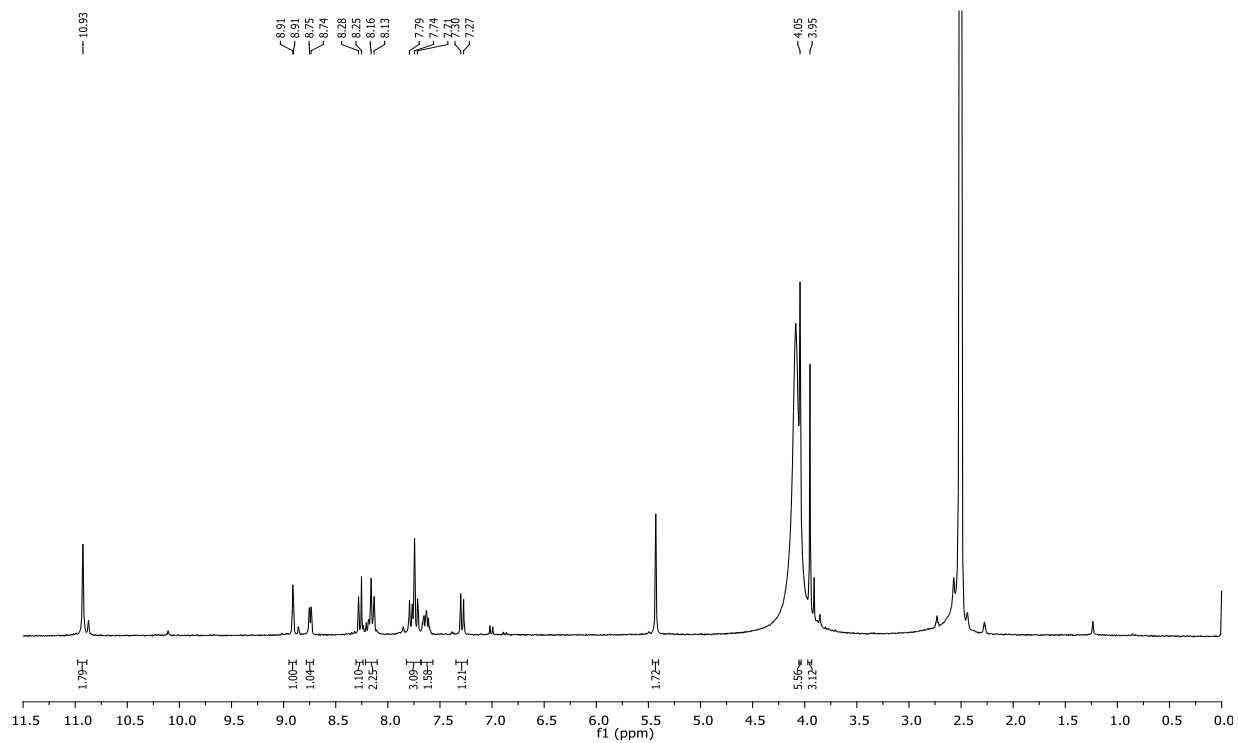


Fig. S59 a) ^1H NMR and b) ^{13}C NMR of compd. **35c**

a)



b)

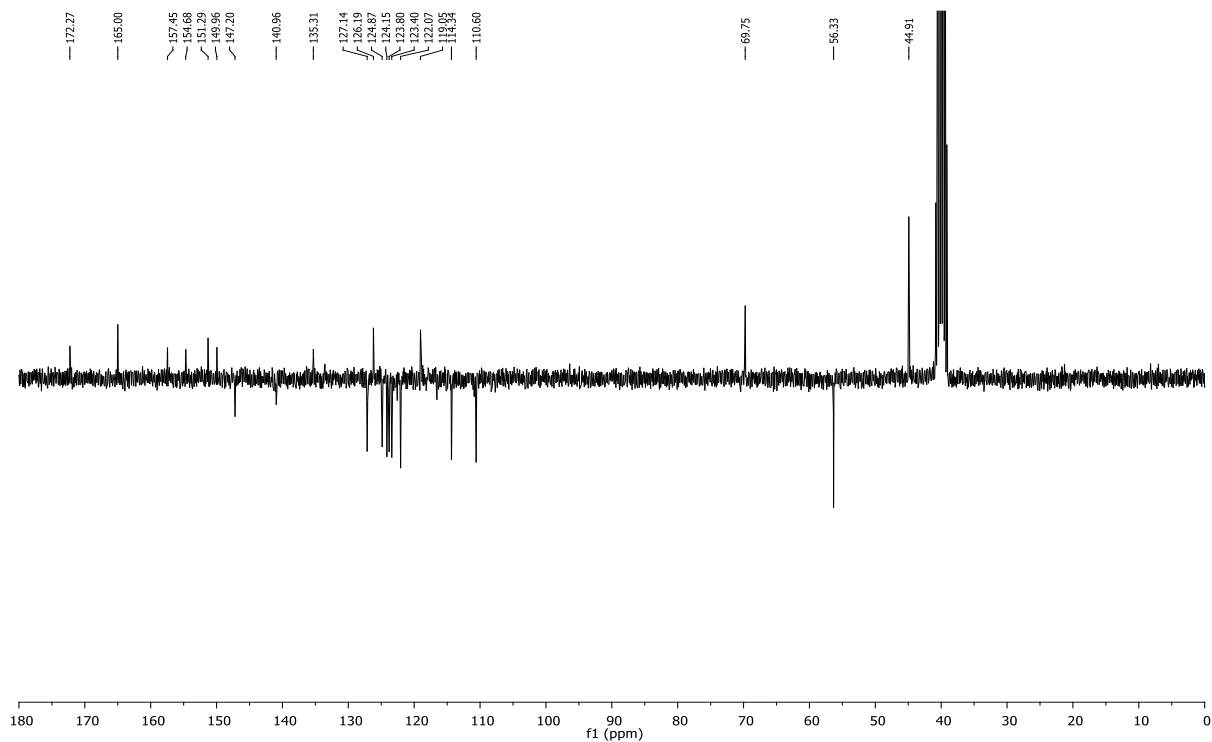
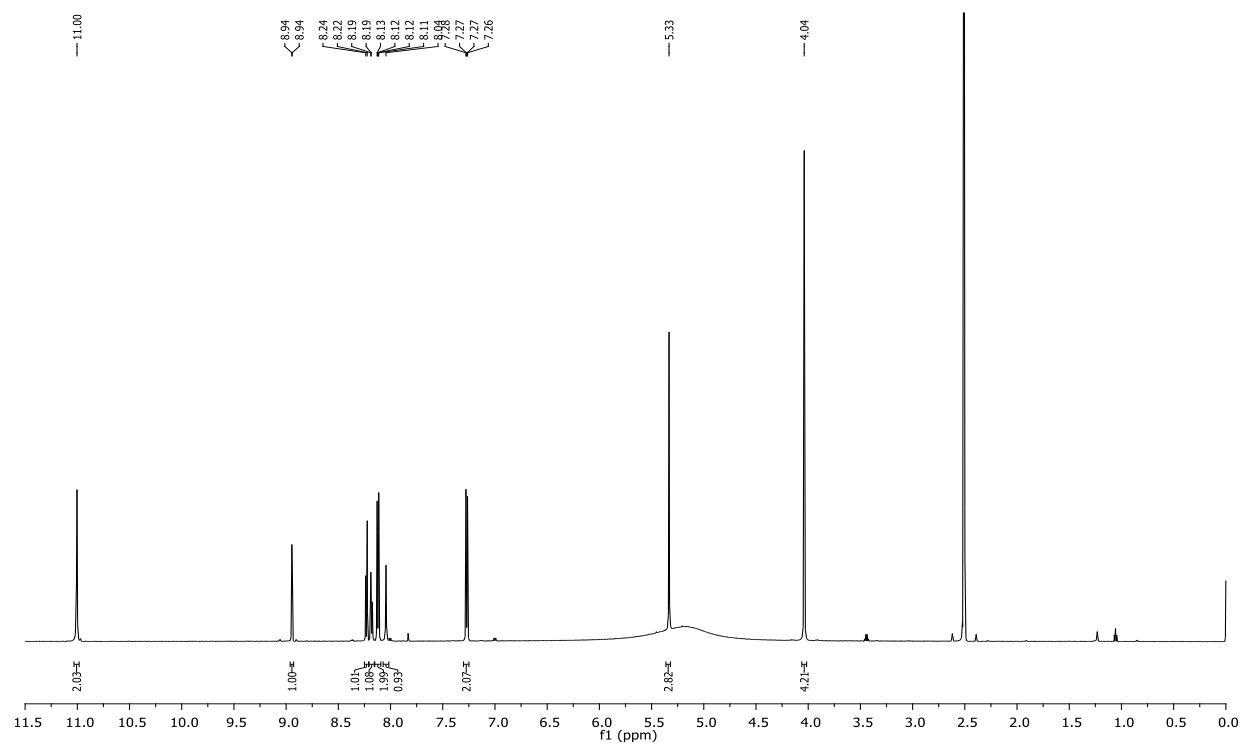


Fig. S60 a) ^1H NMR and b) ^{13}C NMR of compd. **36a**

a)



b)

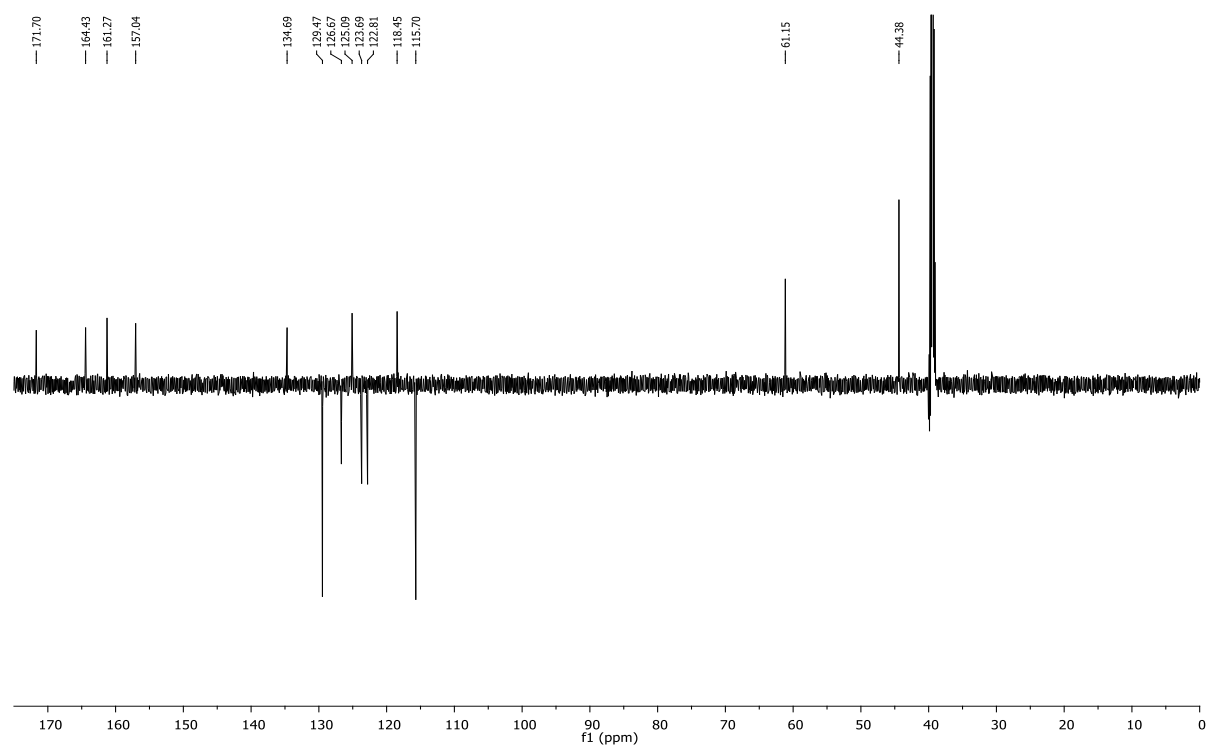
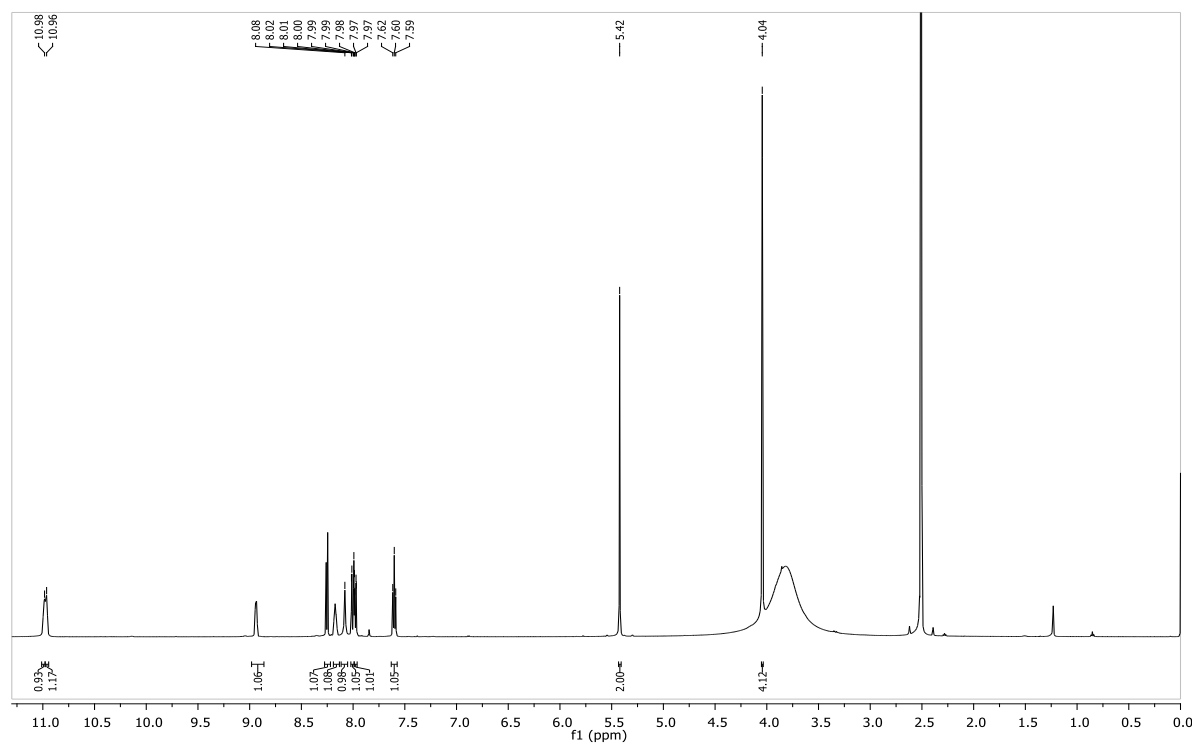


Fig. S61 a) ^1H NMR and b) ^{13}C NMR of compd. **36b**

a)



b)

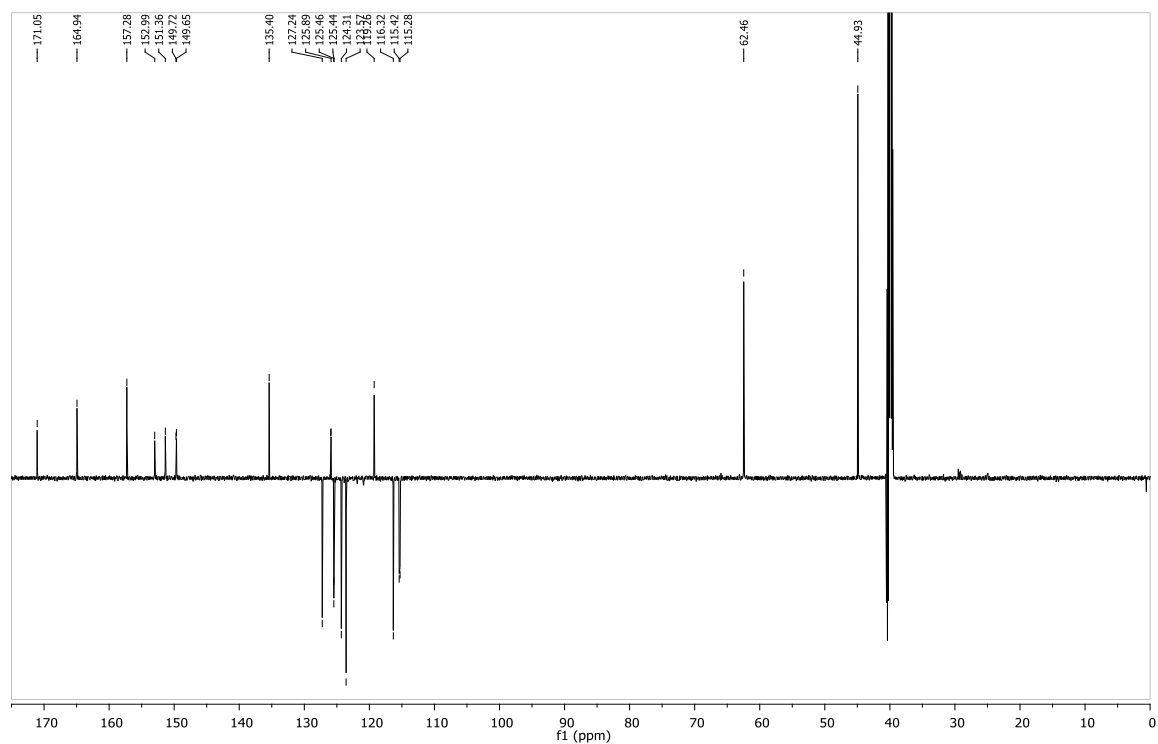
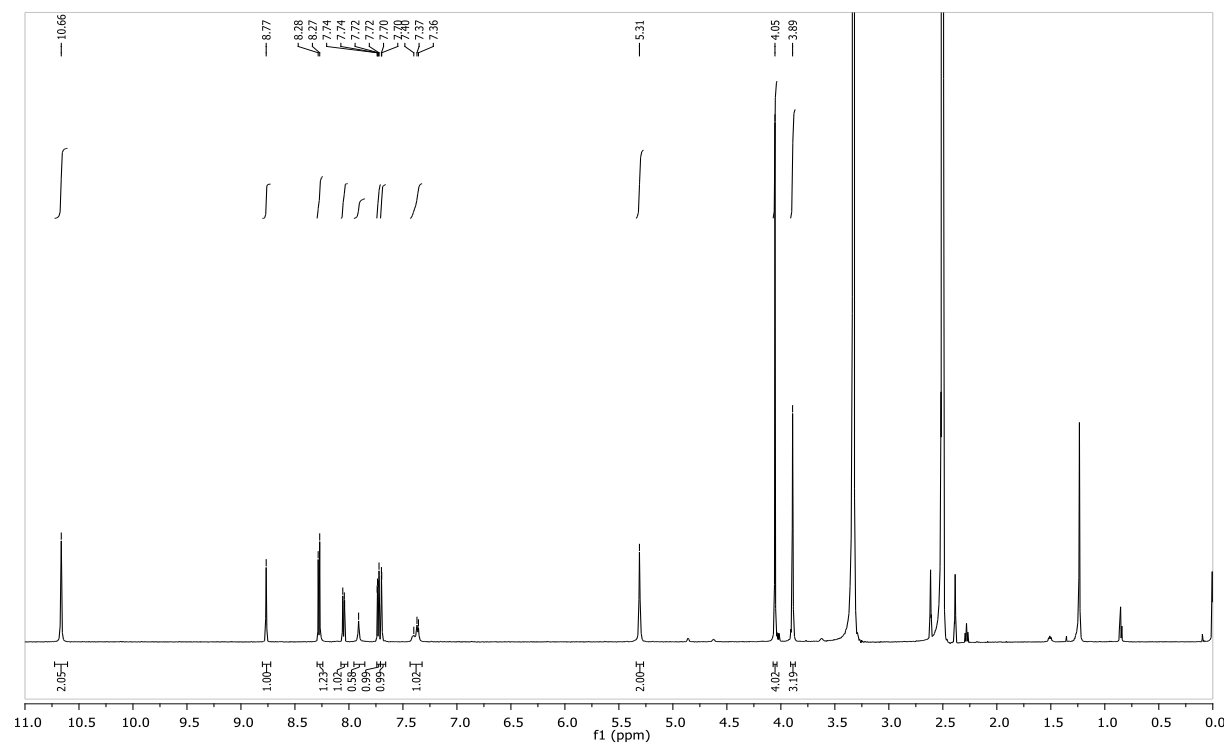


Fig. S62 a) ^1H NMR and b) ^{13}C NMR of compd. **36c**

a)



b)

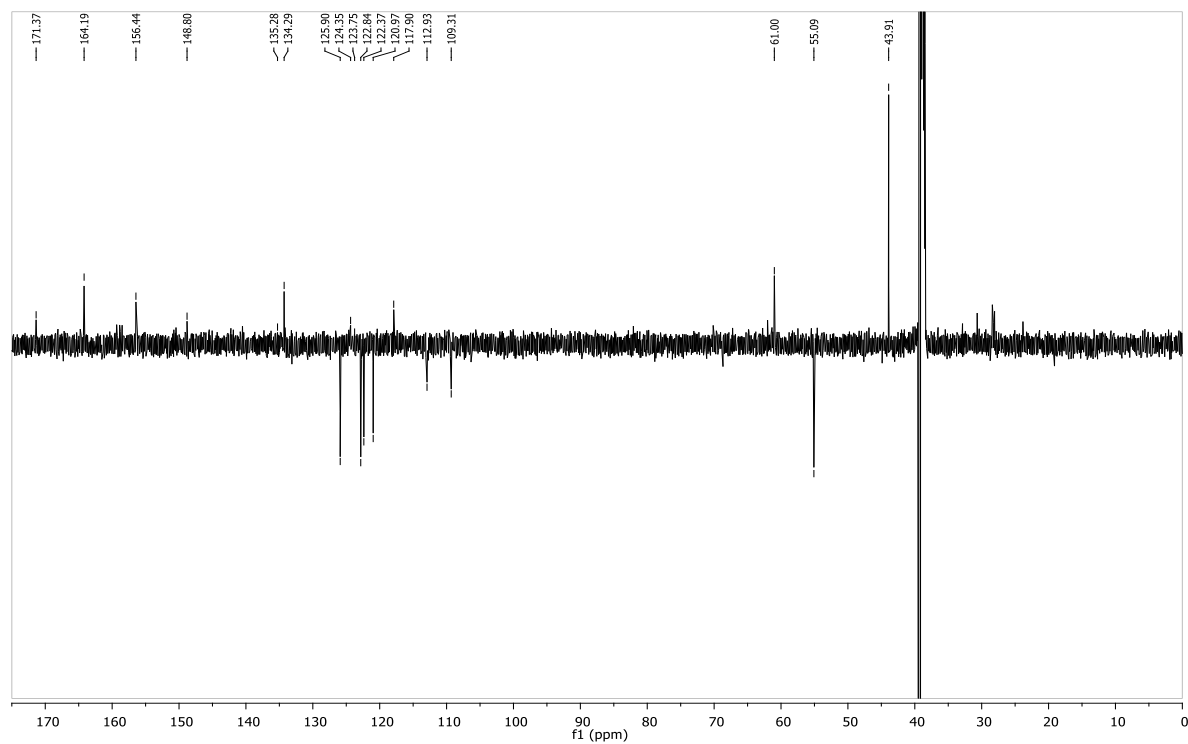
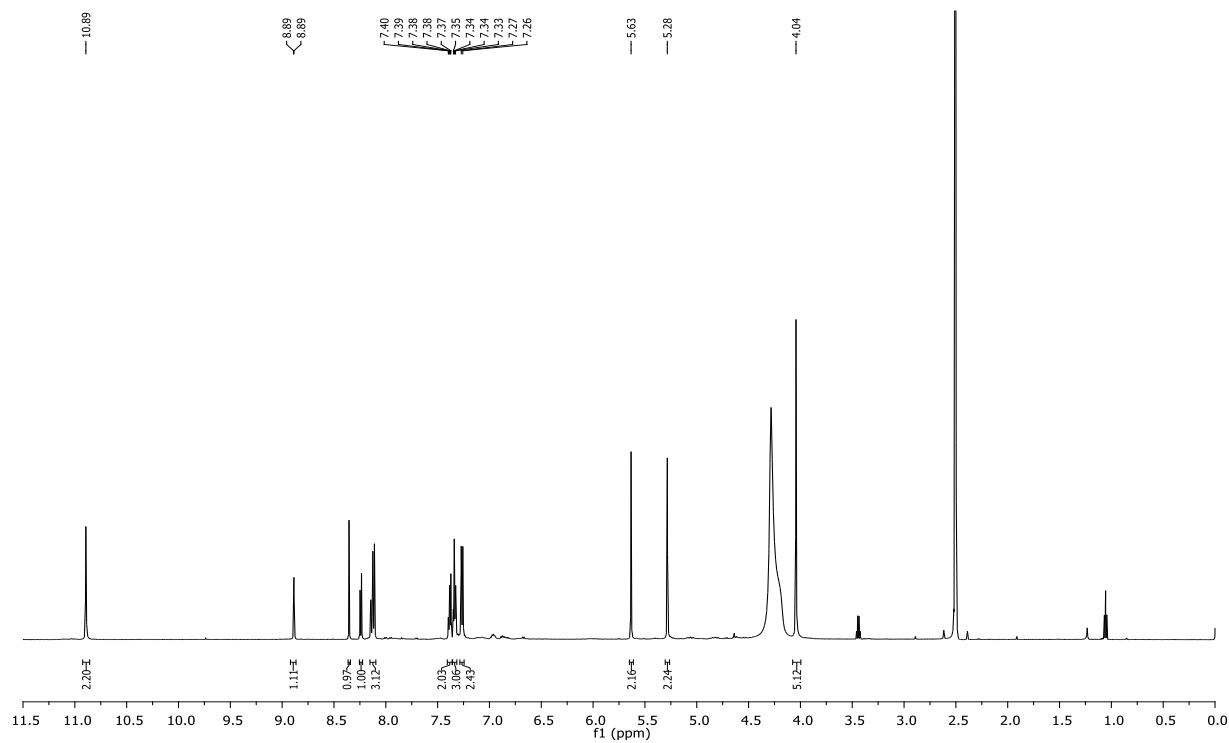


Fig. S63 a) ^1H NMR and b) ^{13}C NMR of compd. **37a**

a)



b)

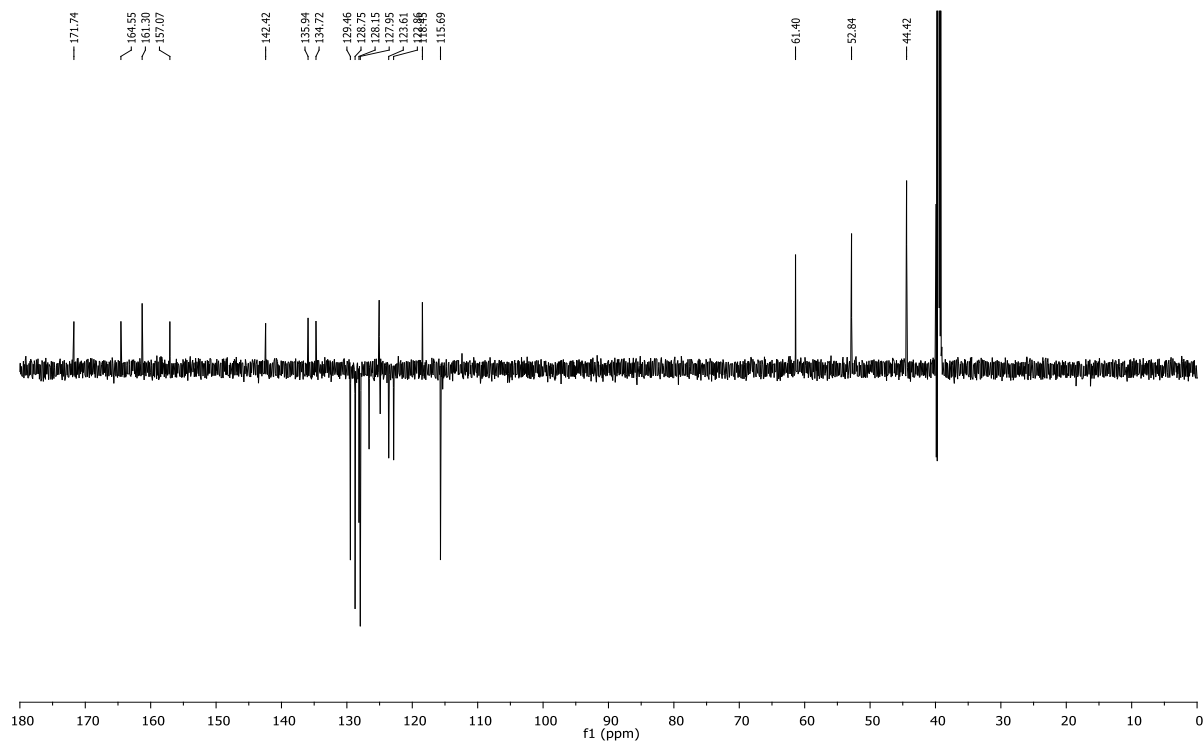
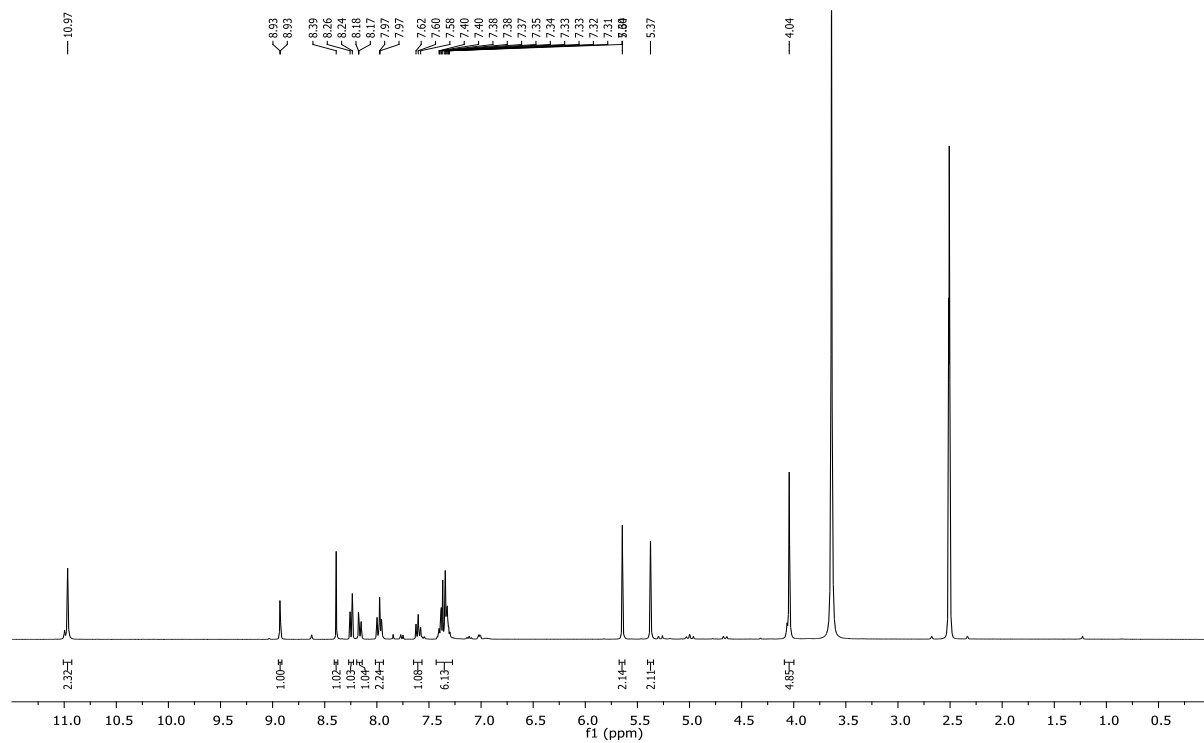


Fig. S64 a) ^1H NMR and b) ^{13}C NMR of compd. **37b**

a)



b)

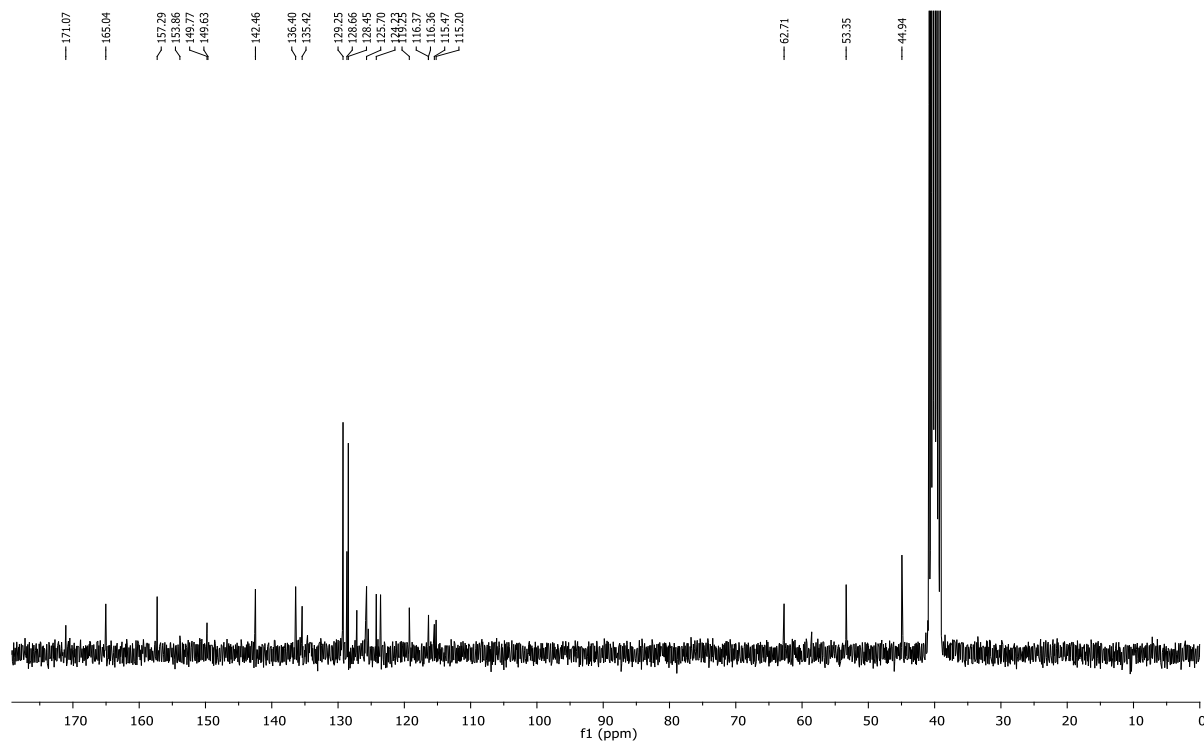
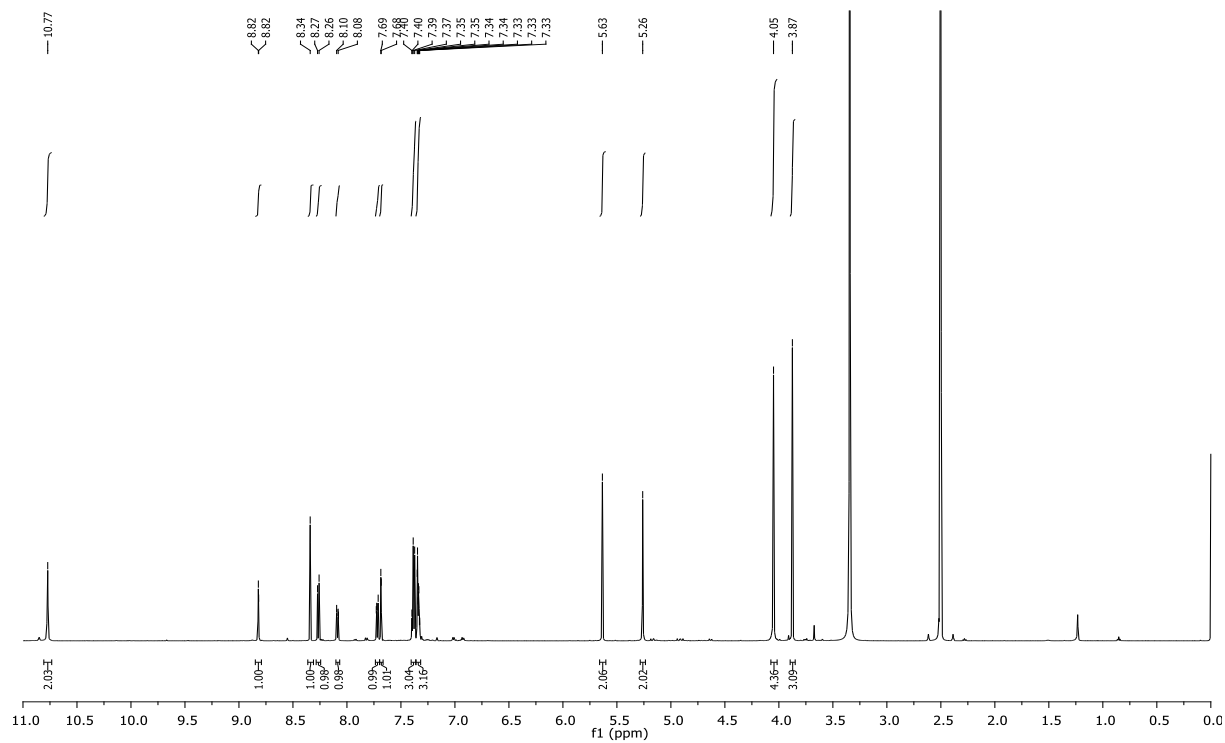


Fig. S65 a) ^1H NMR and b) ^{13}C NMR of compd. **37c**

a)



b)

