

Synthesis and biological evaluation of a new structural simplified analogue of cADPR, a calcium-mobilizing secondary messenger firstly isolated from sea urchin eggs

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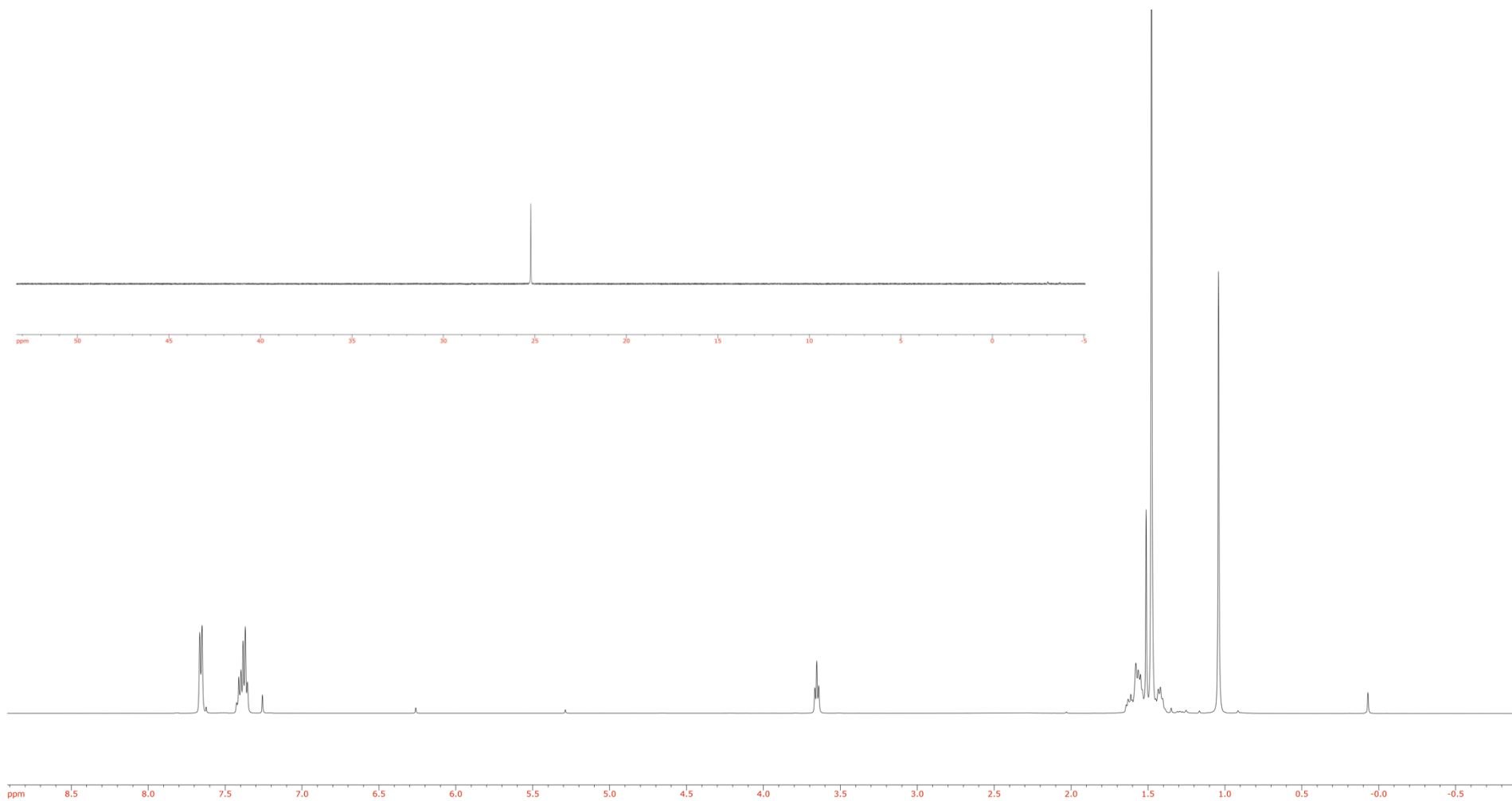
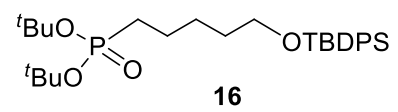
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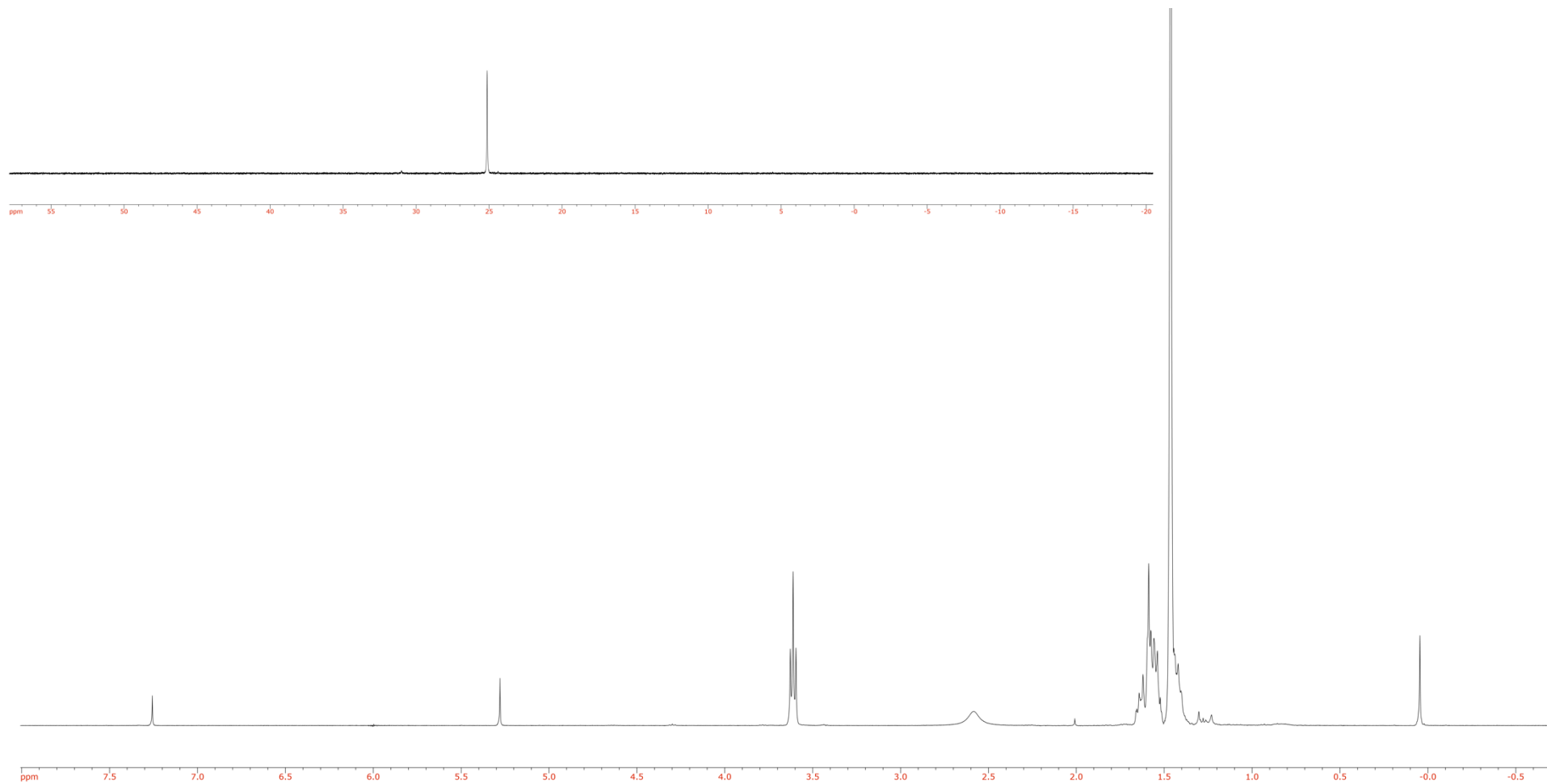
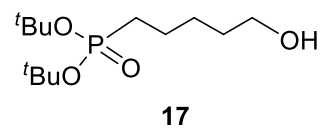
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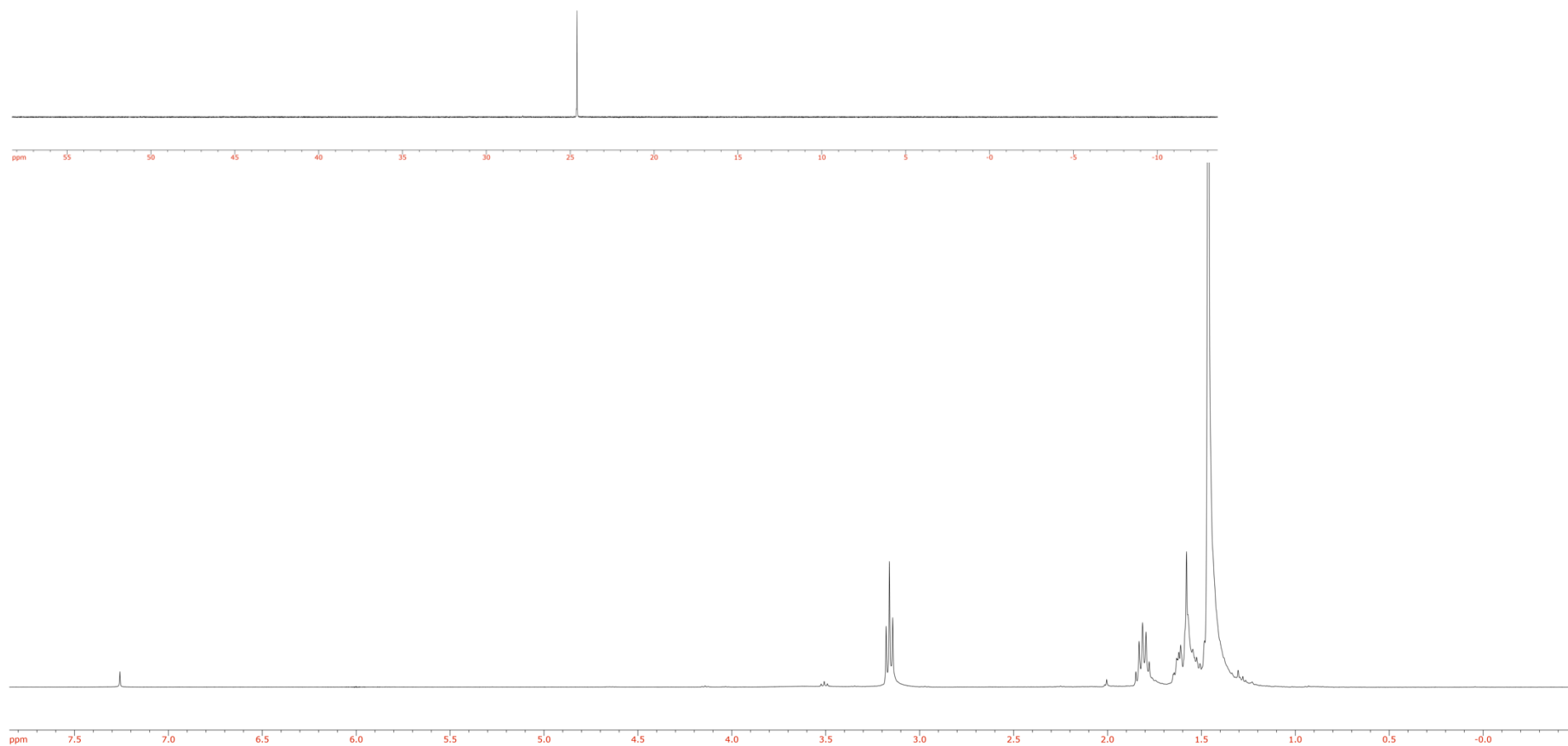
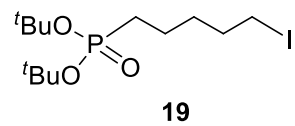
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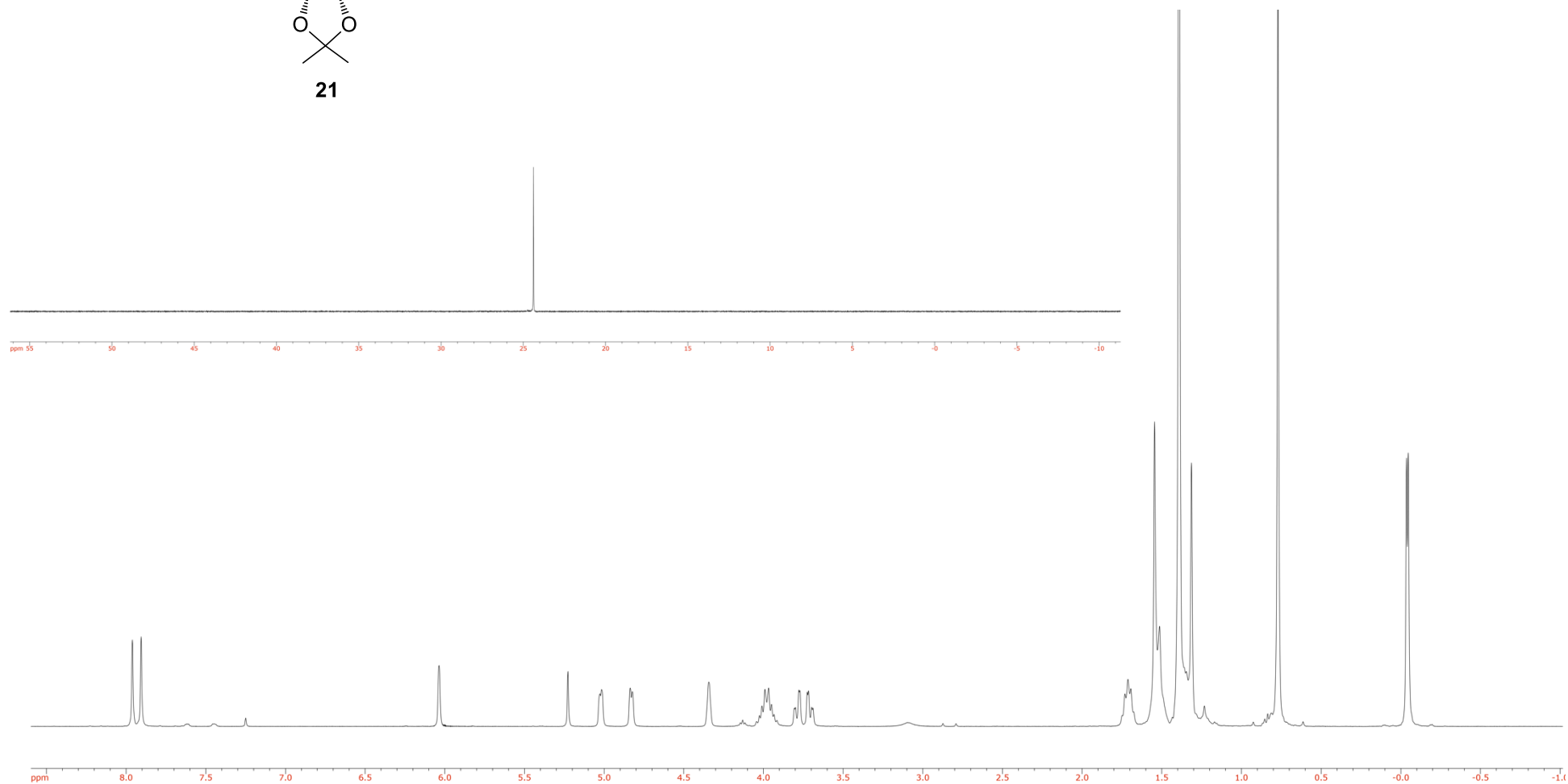
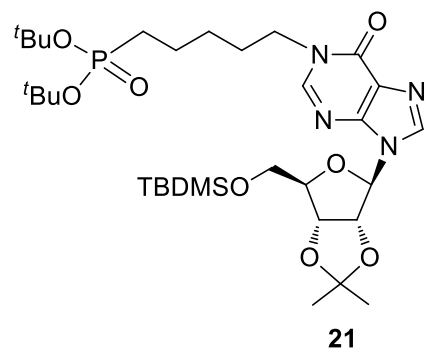
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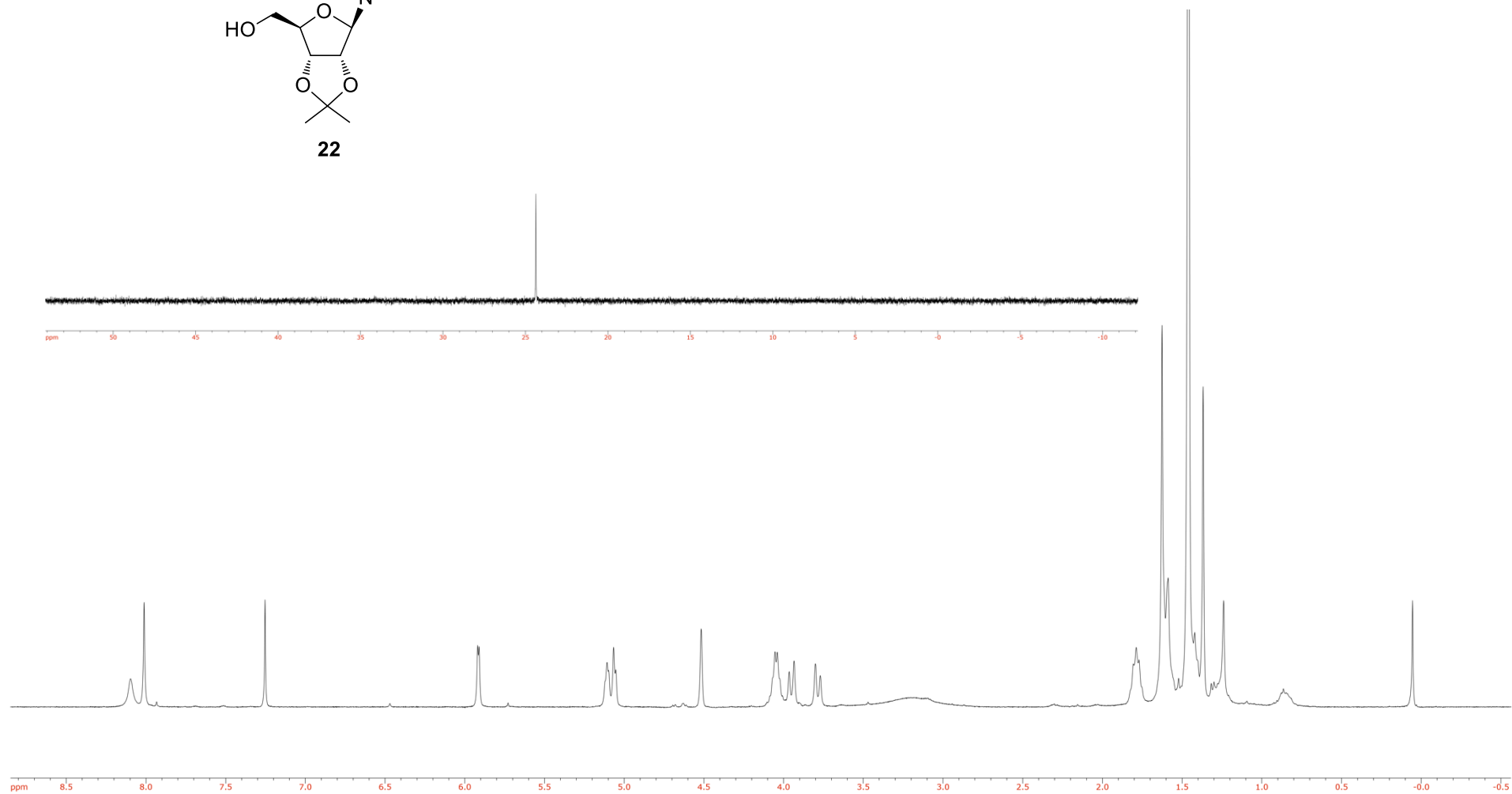
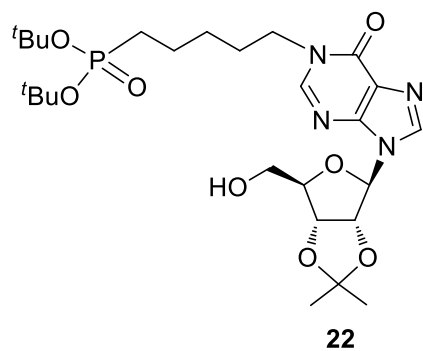
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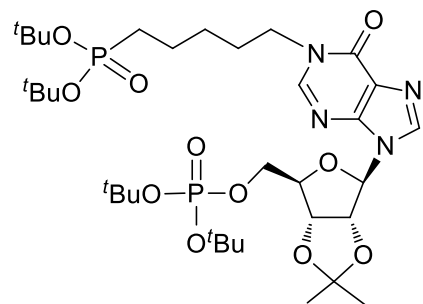




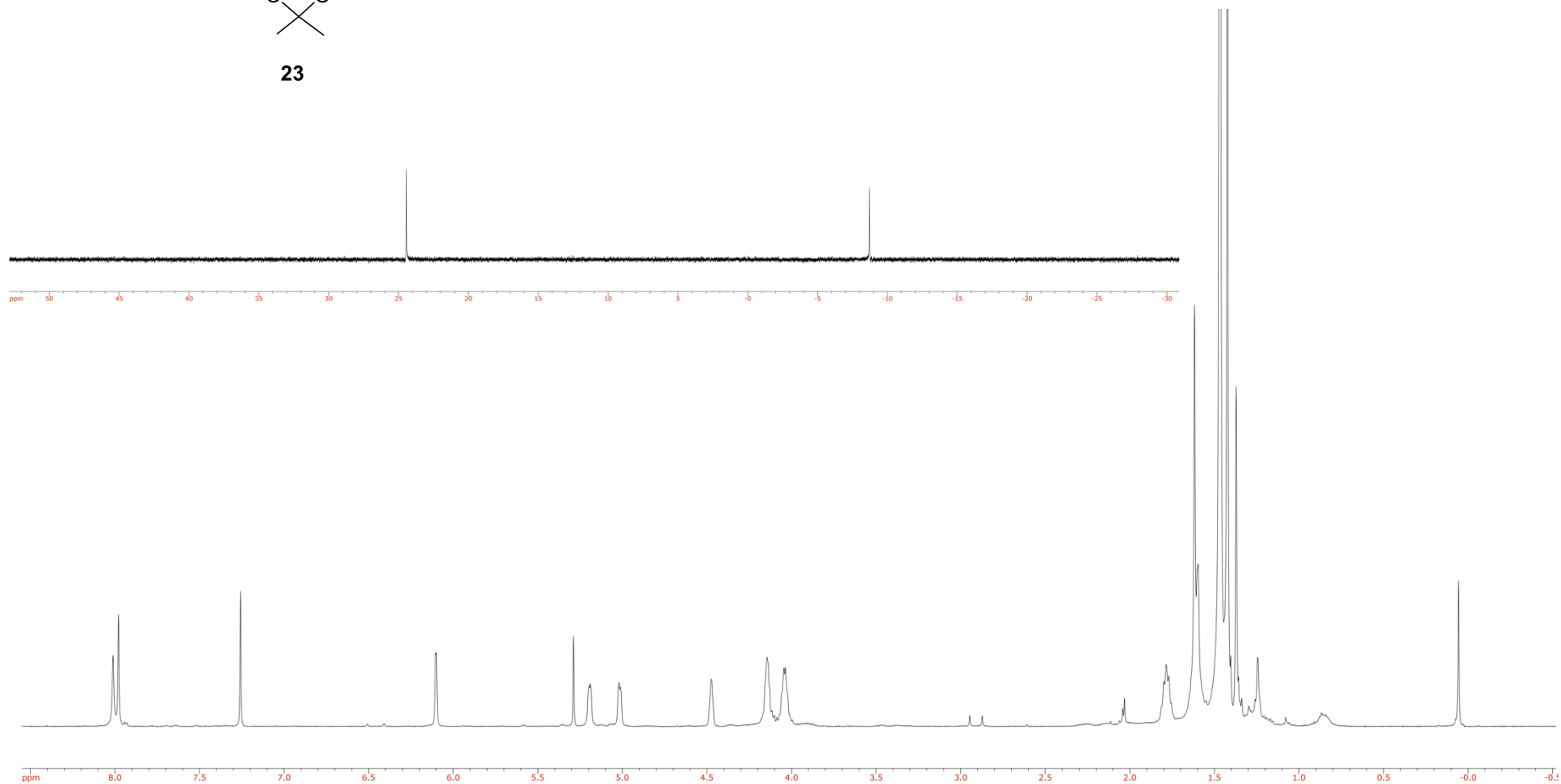


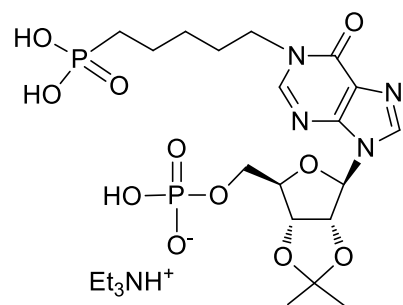




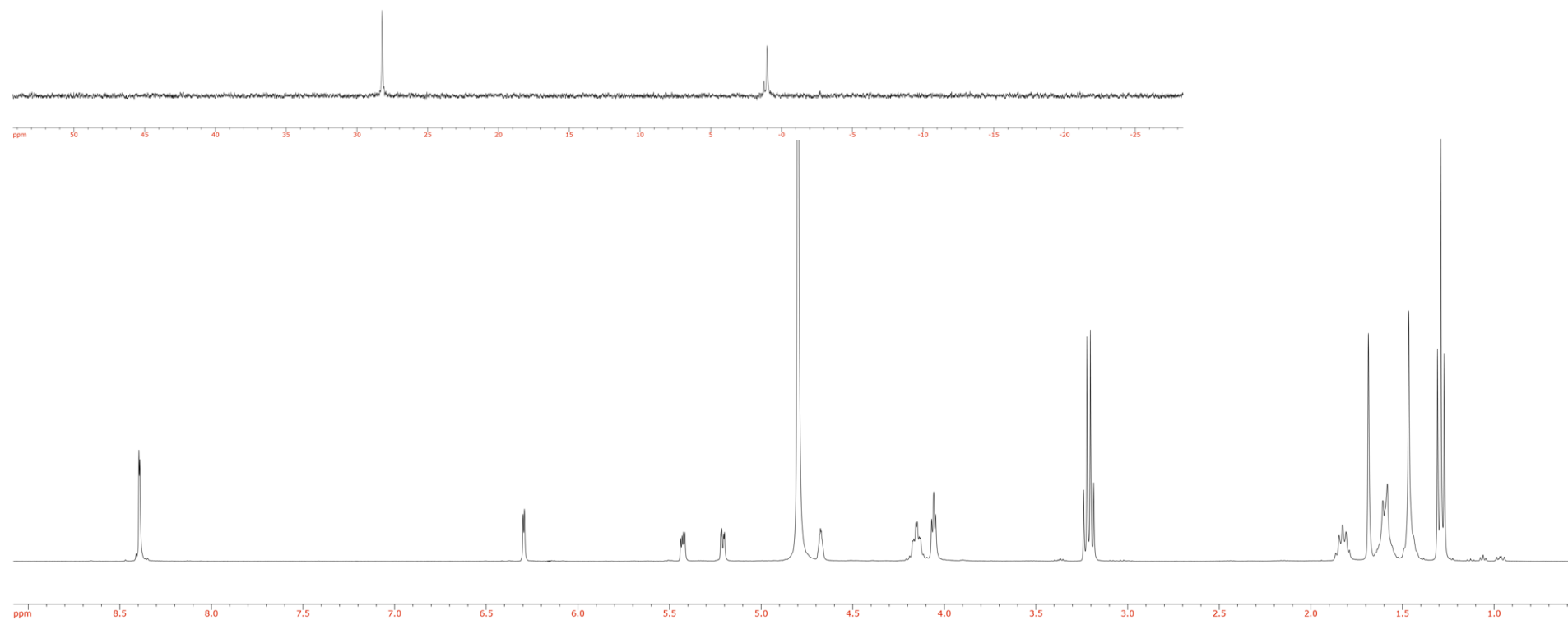


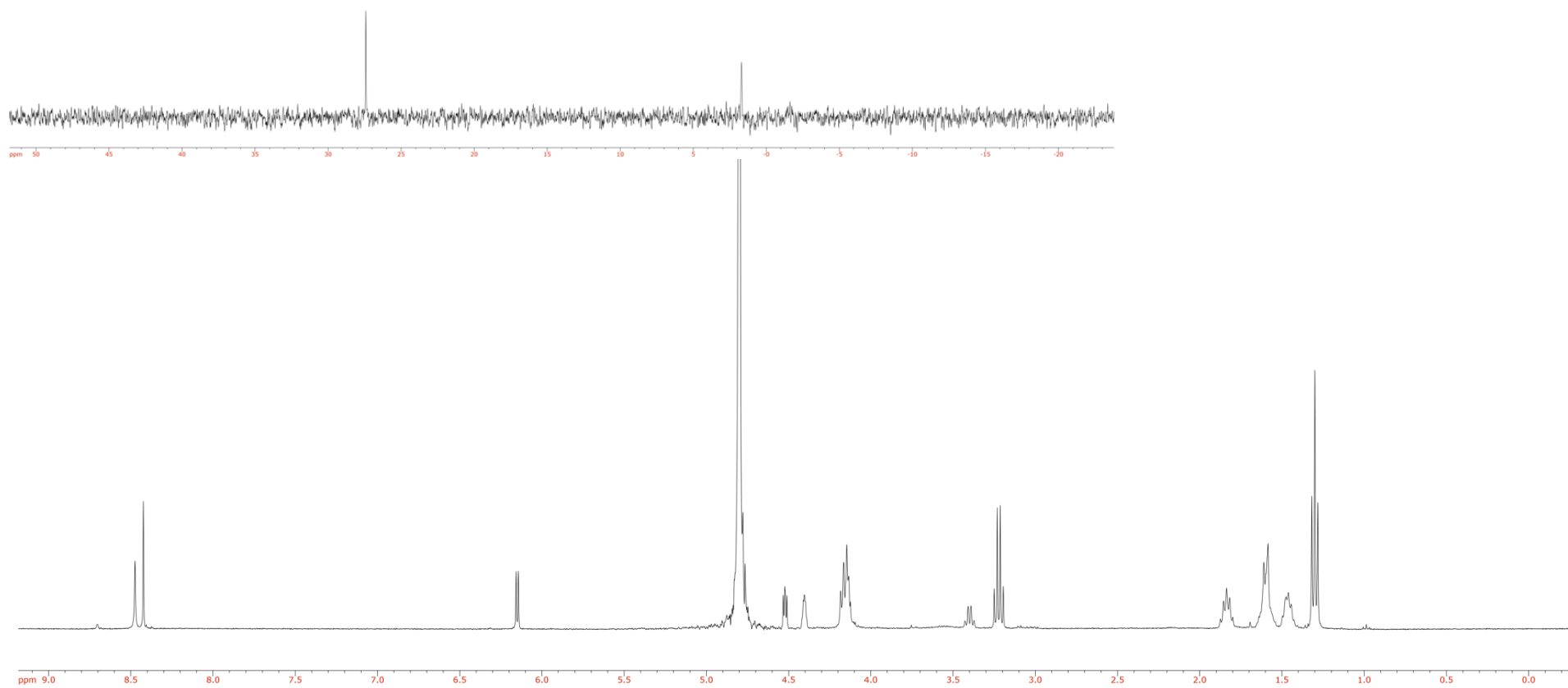
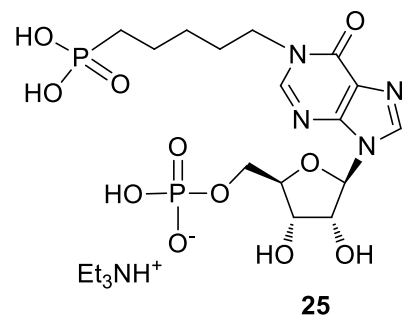
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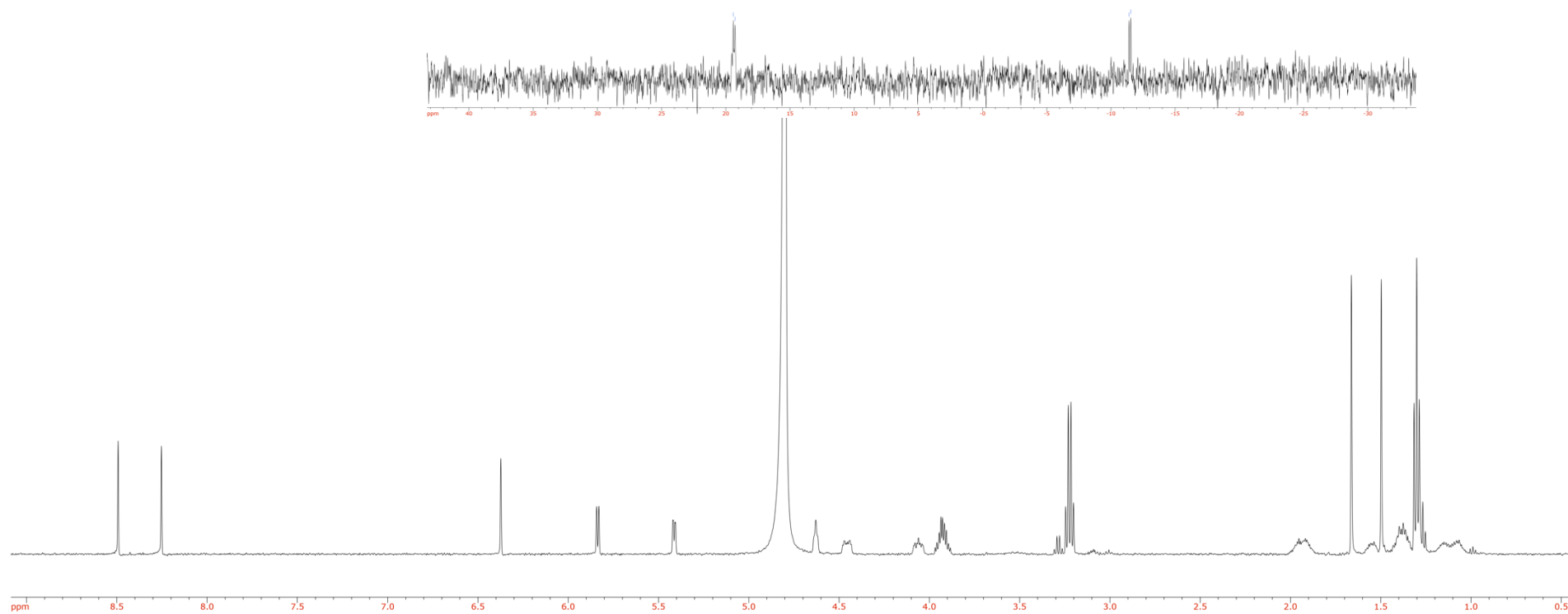
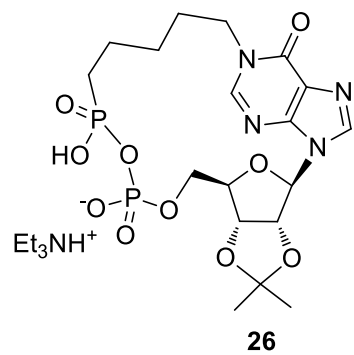


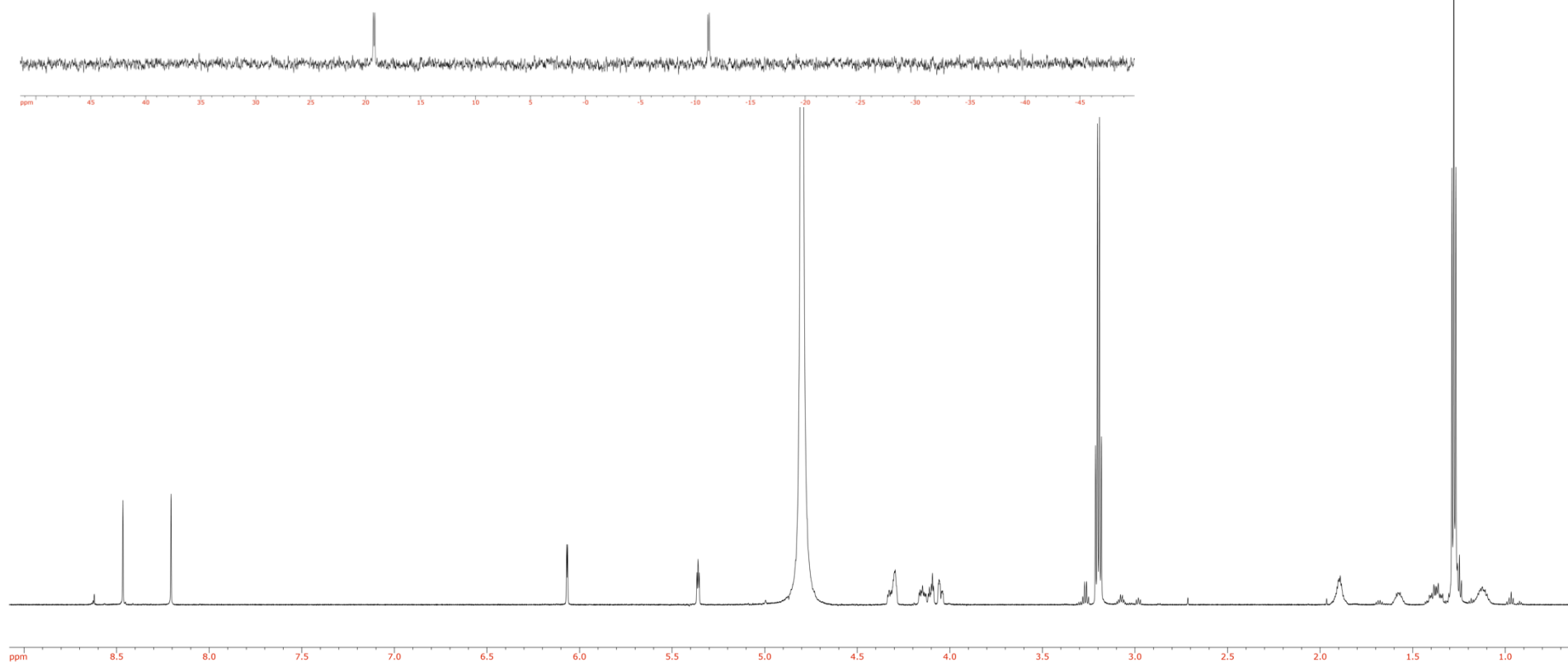
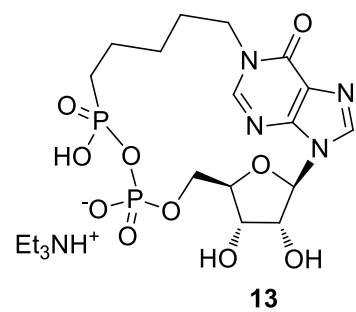


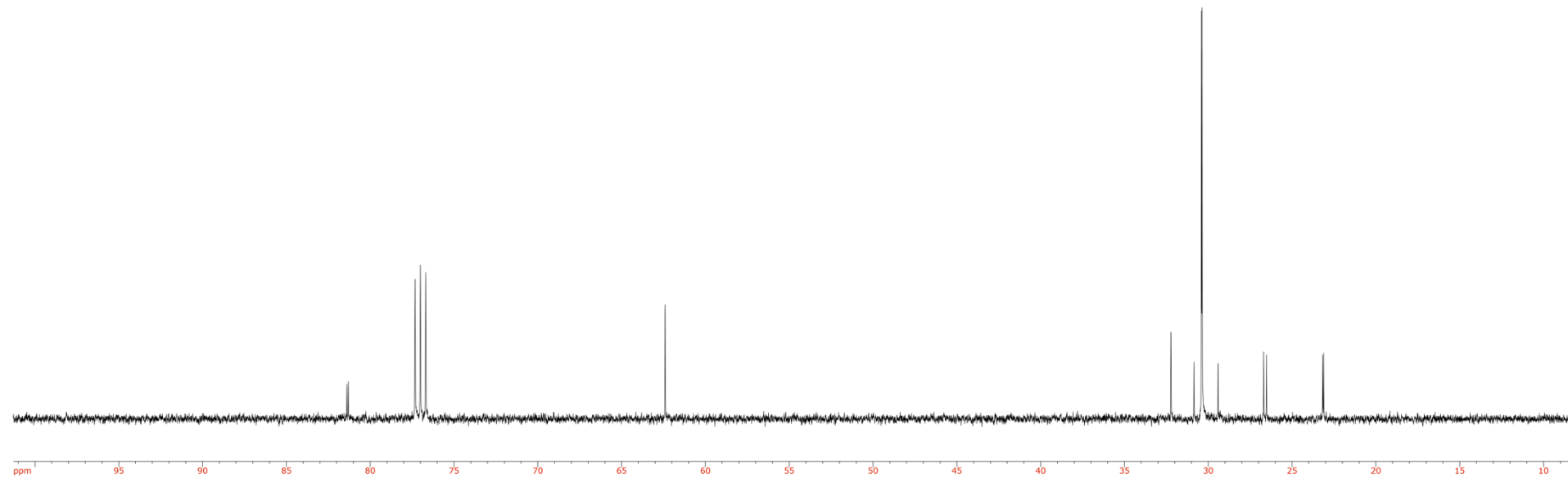
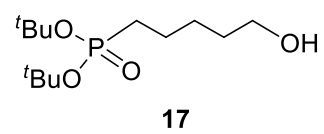
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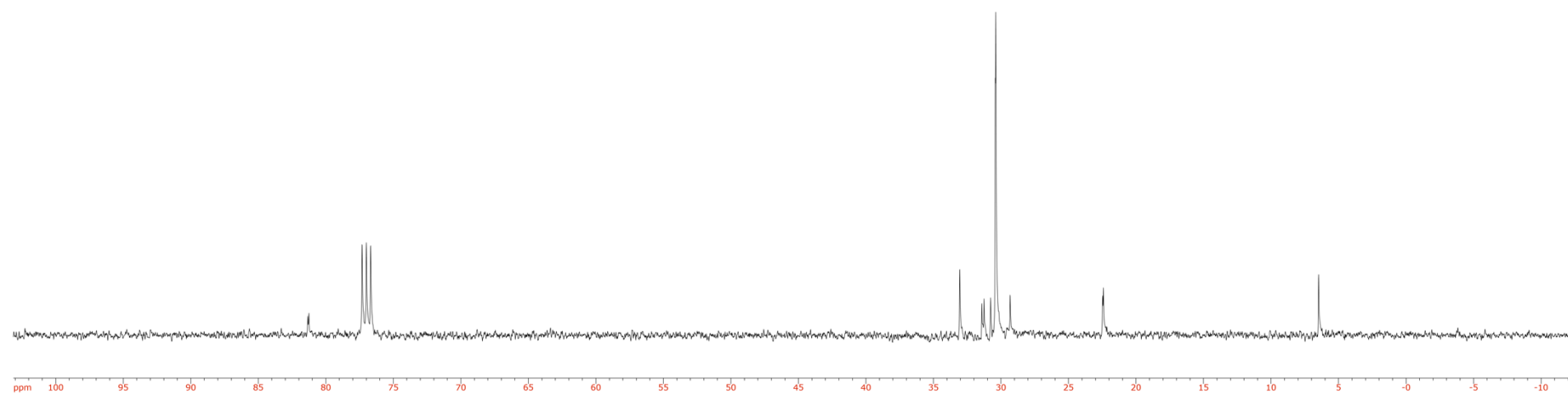
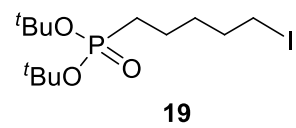


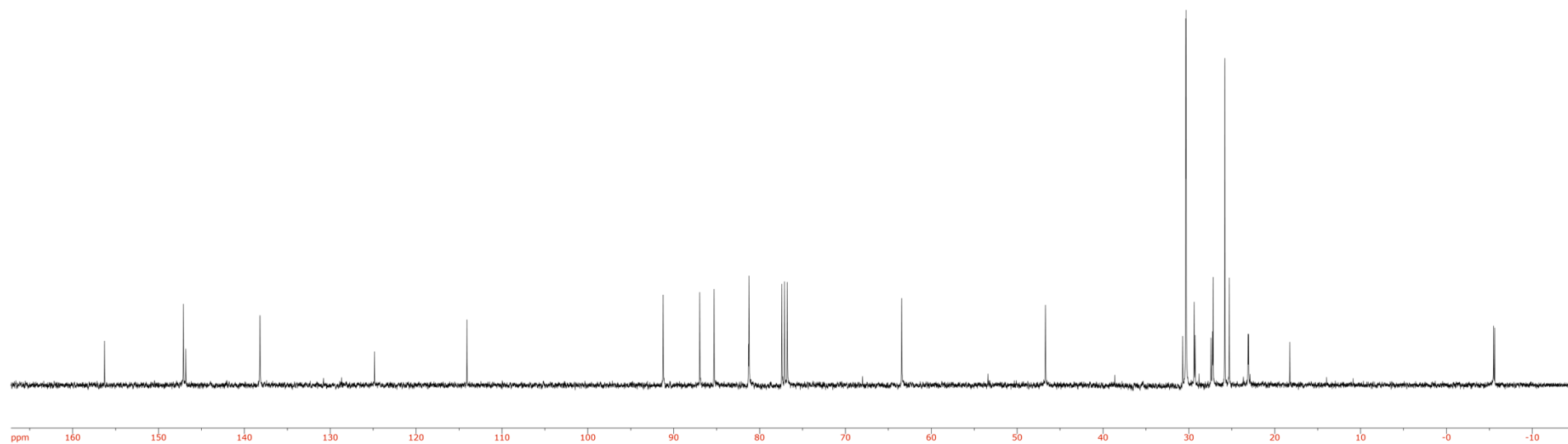
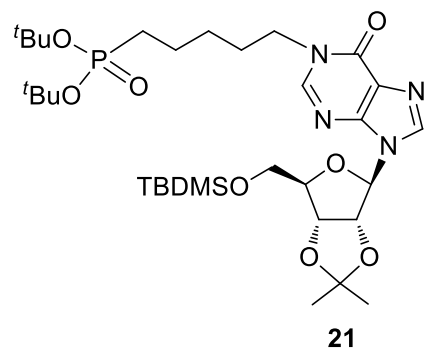


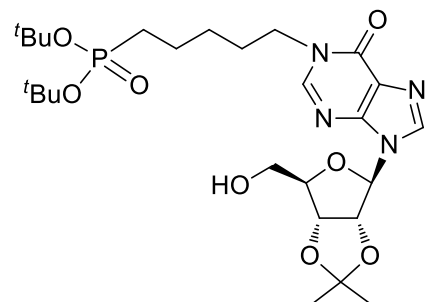




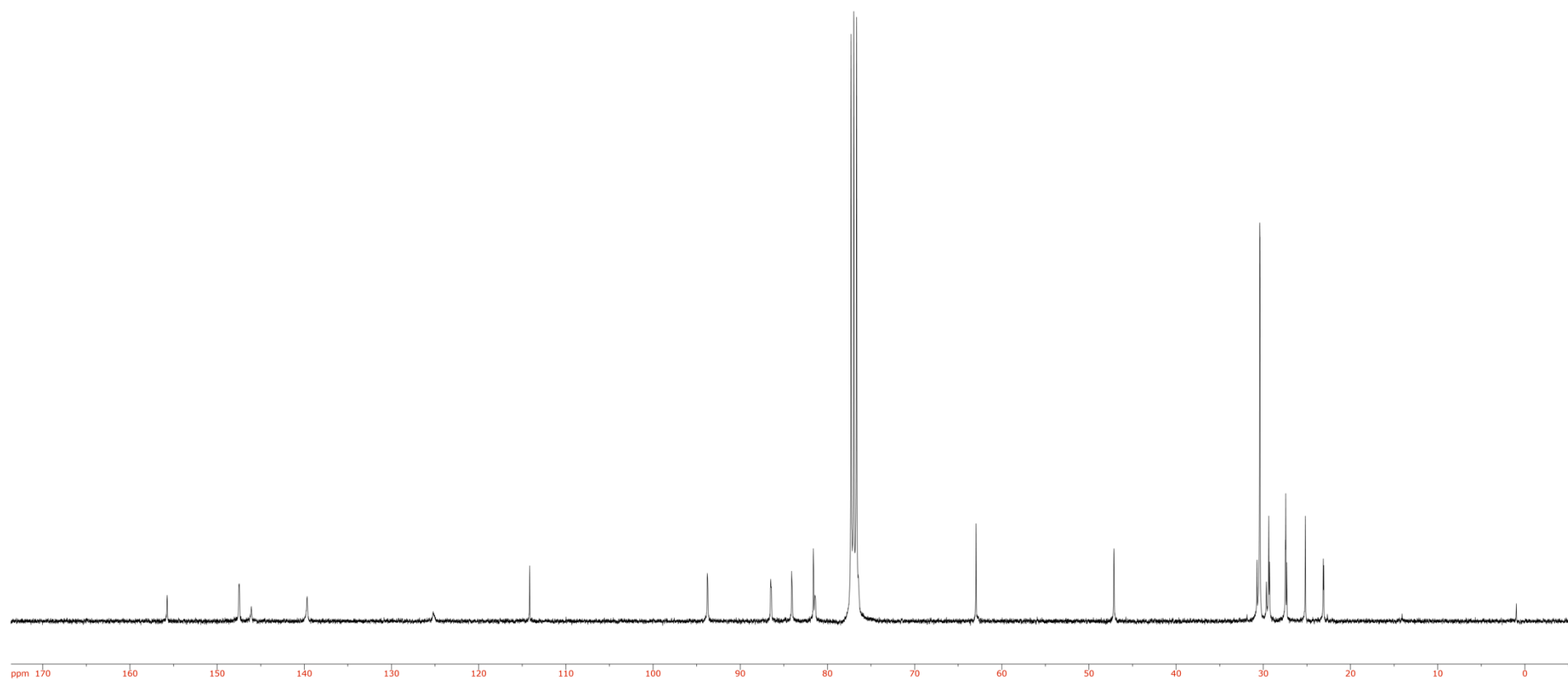


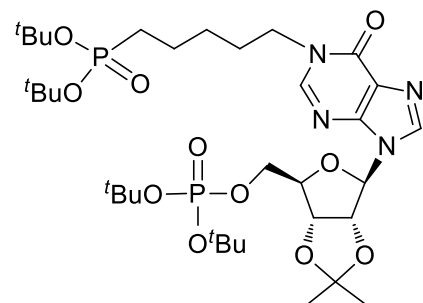




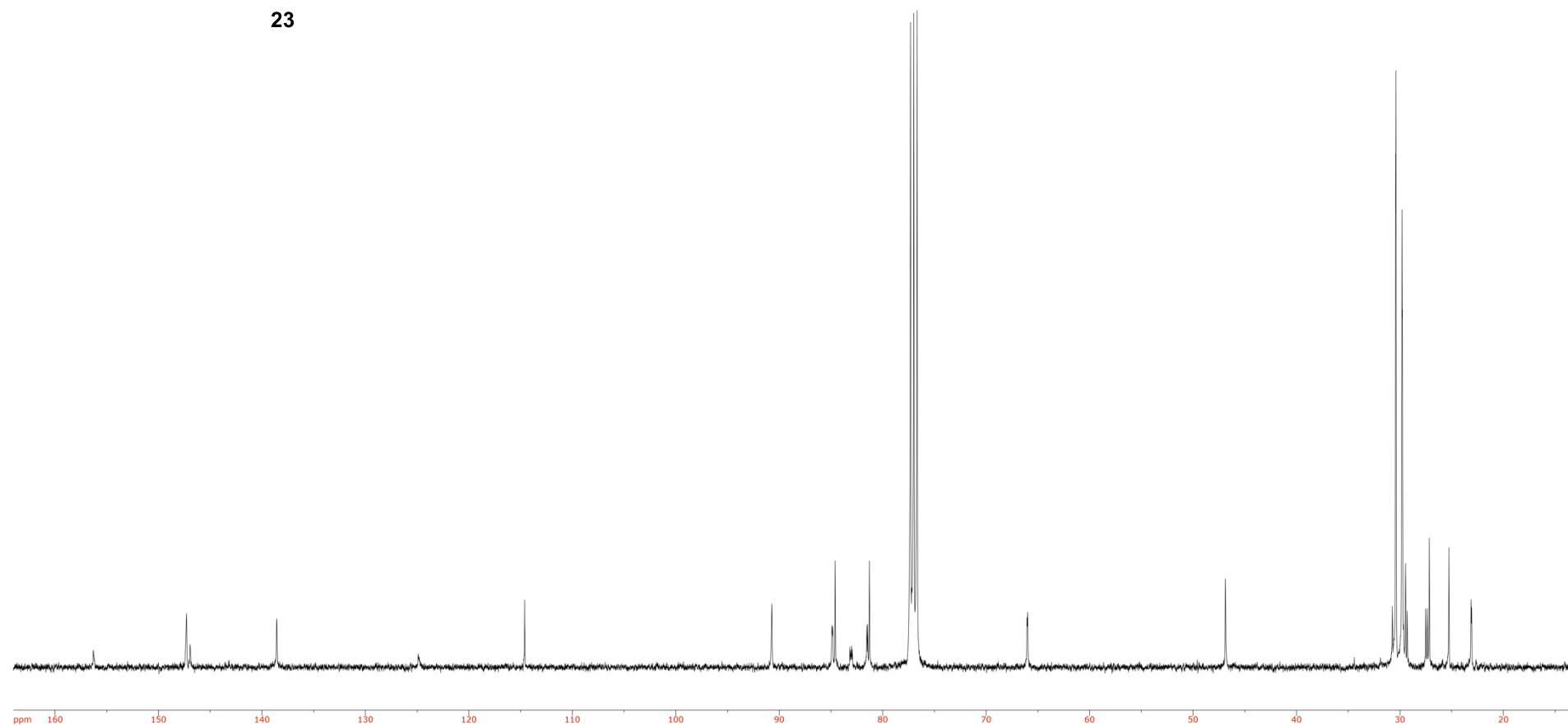


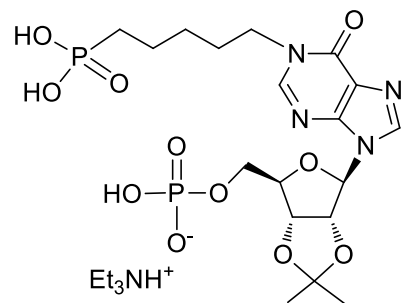
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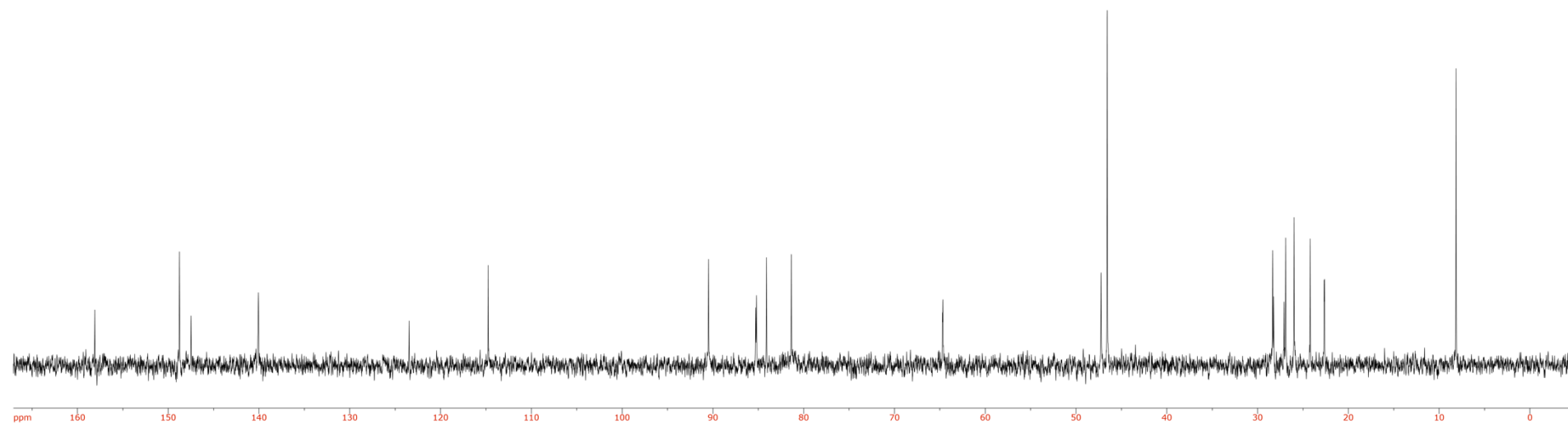


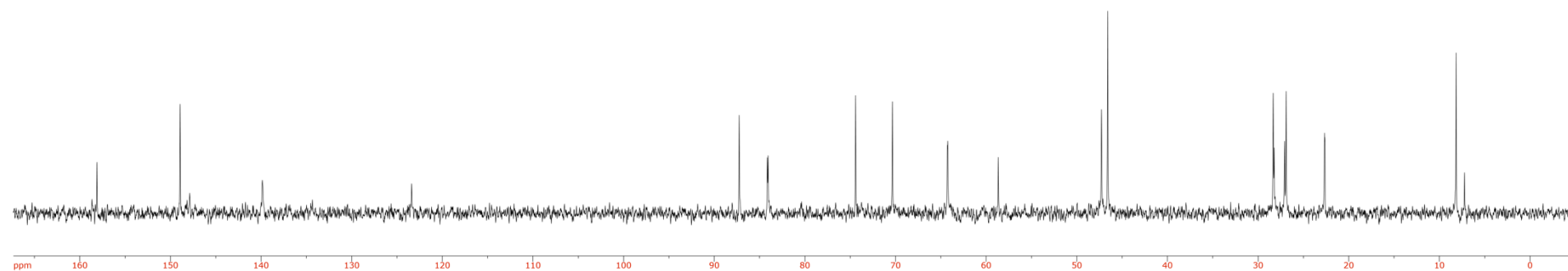
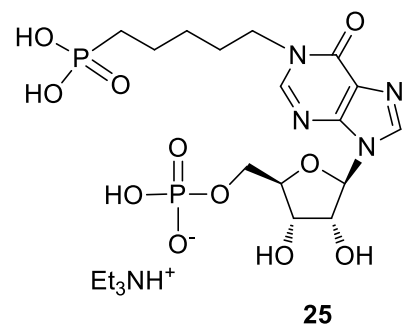
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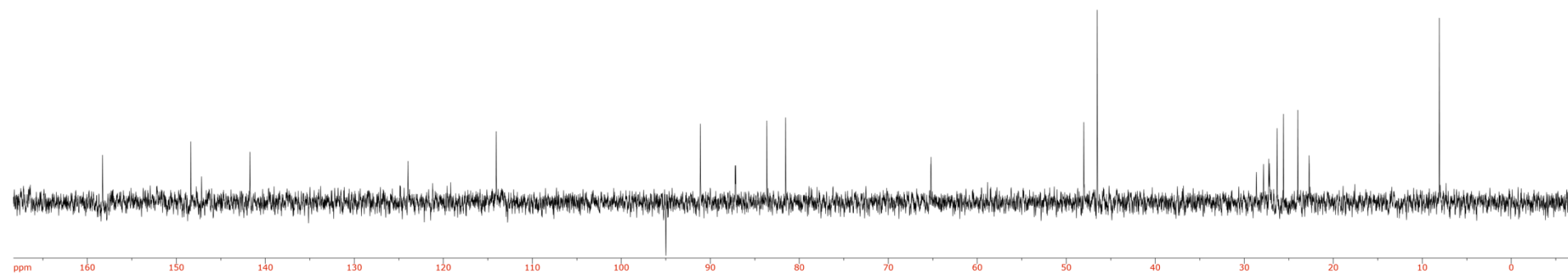
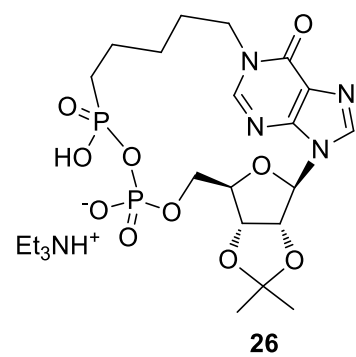


Table S1. Lipophilicity, Relative OPLS 2005 energies and geometrical features of conformers within 5 Kcal/mol from the lowest energy conformation. Atoms used to calculate geometric features are described in Figure 3 of the main text.

Cmpd	AlogP	ΔE (kcal/mol)	d_1 (Å)	d_2 (Å)	d_3 (Å)	θ_1 (°)	θ_2 (°)	θ_3 (°)	θ_4 (°)
cpIPP (13)	-2.4	0.0	8,4	5,6	4,7	73	-38	-54	-140
		4.4	8,2	5,4	6,2	74	67	-56	-113
cbIDP (10)	-2.5	0.0	7,2	4,0	3,9	68	-177	-178	-81
		3.6	7,8	5,4	5,8	65	169	-171	63
		4.4	6,8	4,7	5,9	177	-176	57	-63
		4.7	8,2	5,2	4,7	-46	-54	62	-78
		4.8	7,6	4,2	4,6	69	171	63	80
		4.9	6,6	5,2	4,2	-89	-157	-40	59
cpIDP (11)	-2.0	0	8,9	5,6	5,1	-33	-62	54	51
		4.2	6,5	4,8	4,1	171	-39	79	38
		4.3	9,0	5,5	5,2	-12	-34	85	42
		4.8	8,1	6,2	6,6	-81	-69	50	52

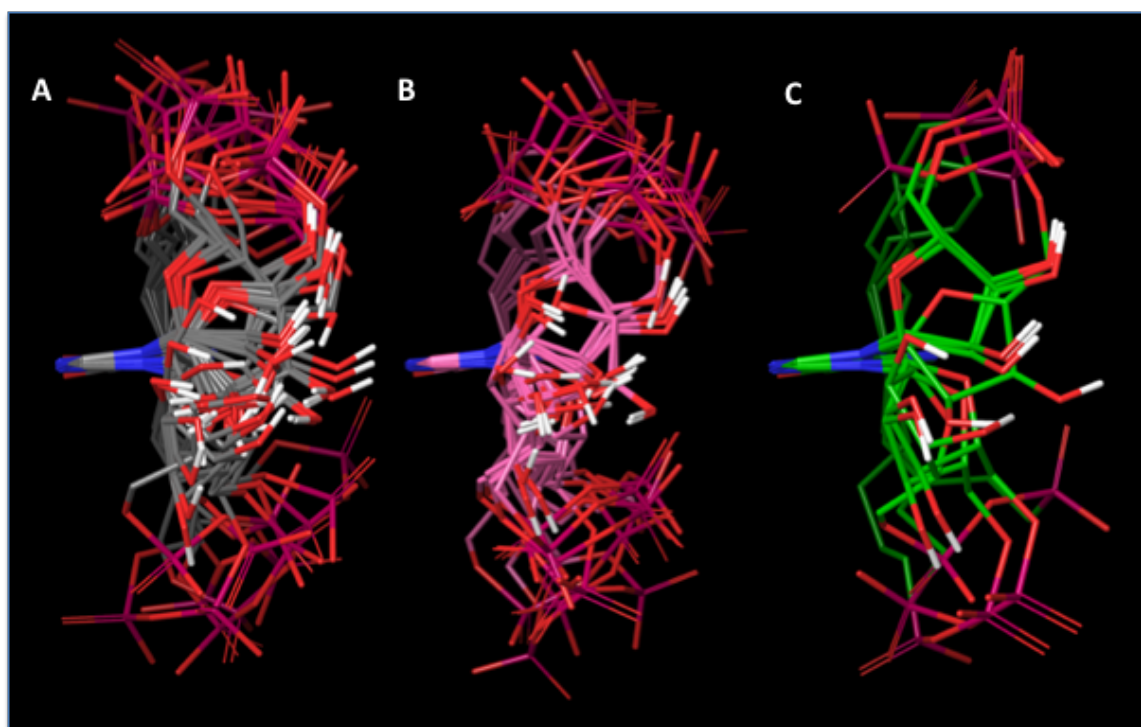


Figure S1. Superimposition on the inosine ring of conformers within 10 kcal/mol from global minimum: A) cbIDP (10, grey), B) cpIDP (11, pink), and C) cpIPP (13, green). Non-polar hydrogens were omitted for sake of clarity. Oxygens were reported in red, nitrogens in blue, phosphates in magenta, hydrogens in white.

Table S2. Lipophilicity, Relative OPLS 2005 energies and geometrical features of conformers within 10 Kcal/mol from the lowest energy conformation. Atoms used to calculate geometric features are described in Figure 3 of the main text.

Cmpd	AlogP	ΔE (kcal/mol)	d ₁ (Å)	d ₂ (Å)	d ₃ (Å)	θ_1 (°)	θ_2 (°)	θ_3 (°)	θ_4 (°)
cpIPP (13)	-2.4	0.0	8,4	5,6	4,7	73	-38	-54	-140
		4.4	8,2	5,4	6,2	74	67	-56	-113
		5.8	8,4	5,8	5,7	82	-41	72	179
		6.9	8,4	5,9	5,6	65	-40	-67	-158
		9.5	8,1	6,0	6,6	68	46	60	-172
		10.0	8,0	5,0	4,4	62	-173	62	171
cbIDP (10)	-2,5	0	7,2	4,0	3,9	68	-177	-178	-81
		3,6	7,8	5,4	5,8	65	169	-171	63
		4,4	6,8	4,7	5,9	177	-176	57	-63
		4,7	8,2	5,2	4,7	-46	-54	62	-78
		4,8	7,6	4,2	4,6	69	171	63	80
		4,9	6,6	5,2	4,2	-89	-157	-40	59
		5,8	7,9	6,1	6,2	73	-53	69	74
		6,5	7,3	4,9	6,8	81	75	168	73
		7,2	6,8	3,6	3,9	-61	-169	166	-84
		7,3	7,9	5,0	4,2	-40	175	58	-86
		7,5	6,3	5,0	5,8	-59	-68	-76	58
		7,8	8,2	5,4	4,5	71	-59	62	77
		8,4	7,0	4,7	6,4	61	164	58	-77
		8,6	7,3	4,6	6,5	89	-55	173	73
		8,7	7,2	4,1	5,5	-74	179	-64	77
		8,9	7,9	6,1	7,0	79	56	52	-78
		9,1	7,4	4,0	4,5	66	164	-67	77
		9,2	7,6	4,4	4,8	167	50	-60	-72
		9,4	7,6	6,1	6,8	64	58	-171	79
		9,5	8,2	5,2	4,6	-46	-53	165	-78
		9,6	7,7	5,5	6,4	71	153	171	60
		9,9	7,2	5,8	6,6	62	167	60	-68
		10,0	7,4	4,7	4,6	-61	63	-159	67

cpIDP (11)	-2.0	0,0	8,9	5,6	5,1	-33	-62	54	51
		4,2	6,5	4,8	4,1	171	-39	79	38
		4,3	9,0	5,5	5,2	-12	-34	85	42
		4,8	8,1	6,2	6,6	-81	-69	50	52
		5,5	8,6	5,9	5,8	-25	-59	57	49
		5,7	8,4	6,4	7,7	89	-168	-53	60
		5,9	8,2	5,0	4,7	-162	-66	49	36
		6,5	8,7	5,8	6,5	68	42	-74	-44
		6,9	7,7	5,7	4,2	-160	-54	64	34
		7,9	8,8	5,5	5,5	175	70	-176	37
		8,5	7,2	4,5	6,4	59	152	35	-55
		9,0	7,8	5,8	4,6	-111	159	44	-52
		9,2	6,4	4,9	4,6	154	174	58	-35
		9,3	7,3	3,9	4,3	-164	172	58	-35
		9,5	8,9	5,3	5,2	81	-168	-54	61
		9,7	8,4	6,1	6,8	86	65	-54	-51
		9,9	7,4	5,0	6,6	-23	-55	61	48
