

Supporting Information

From carbohydrate-derived ketene dithioacetals to 1-C-thioglycals: a synthetic and theoretical insight

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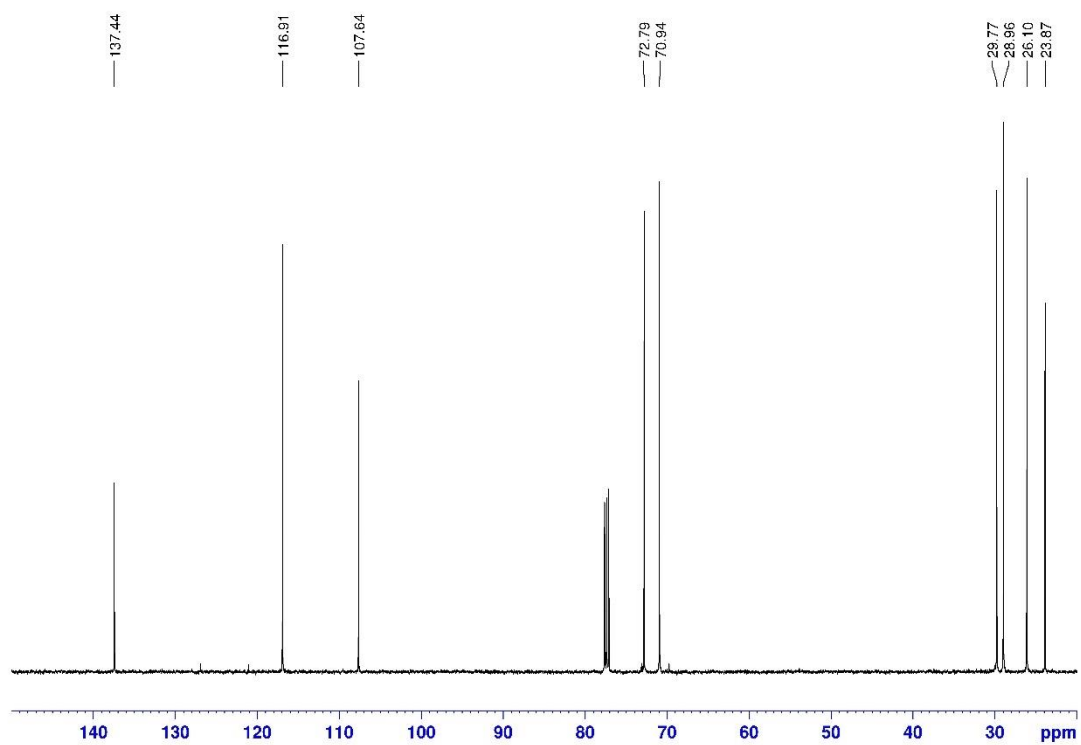
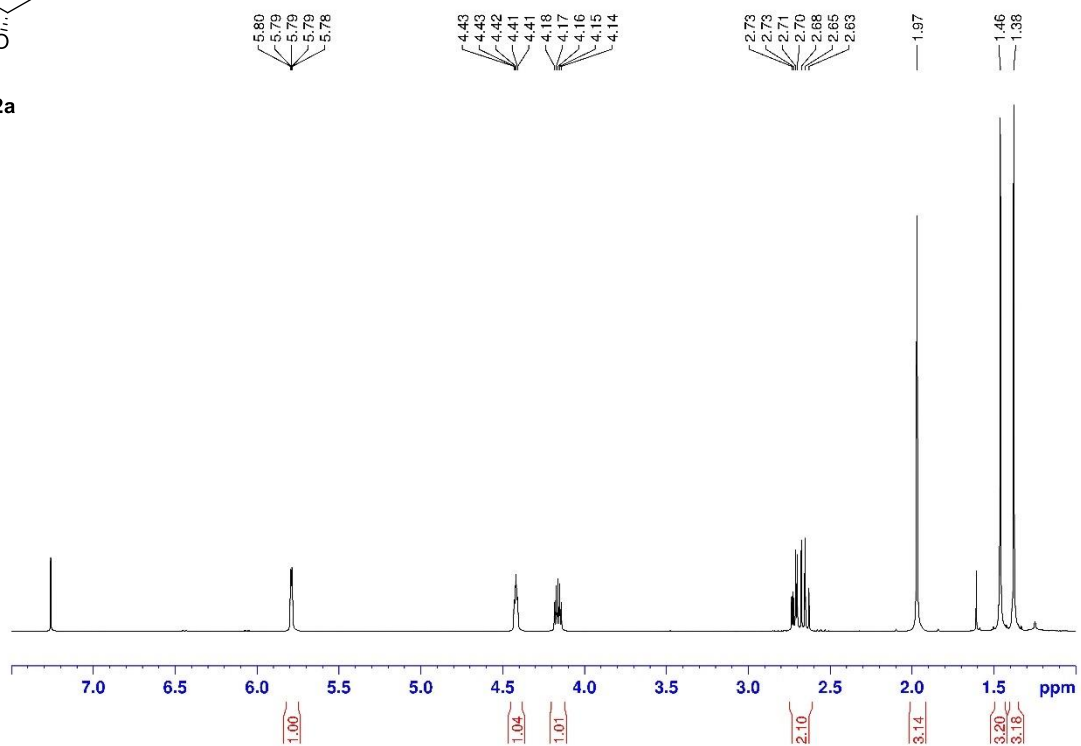
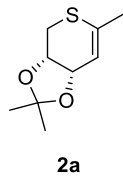
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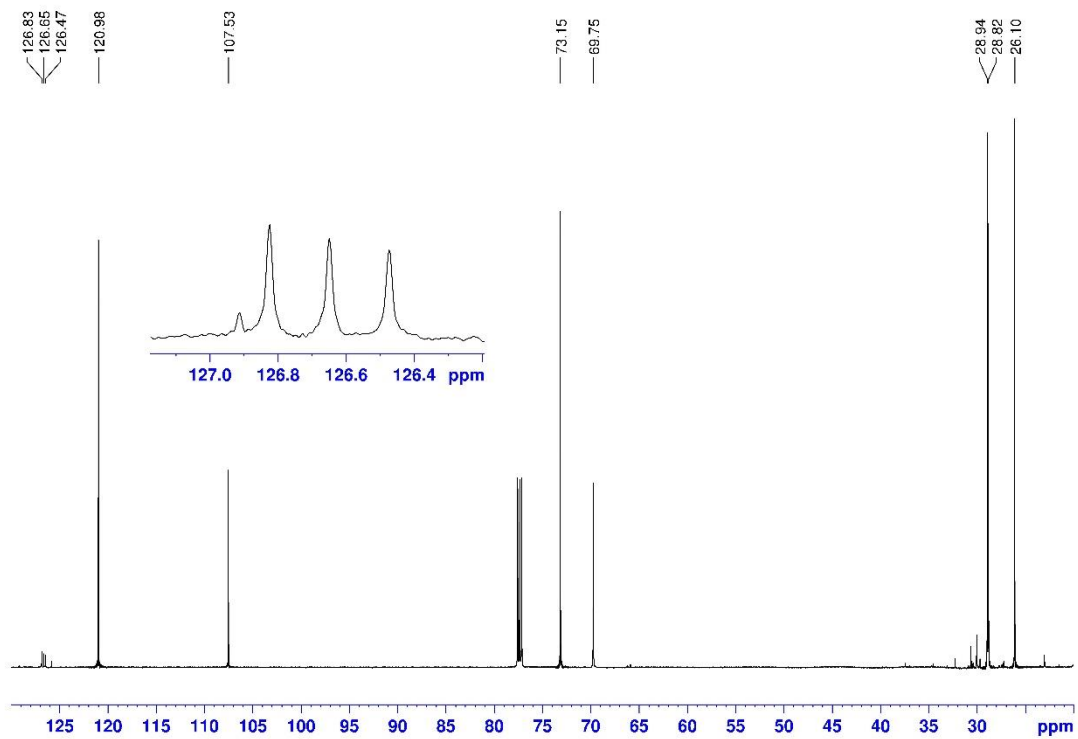
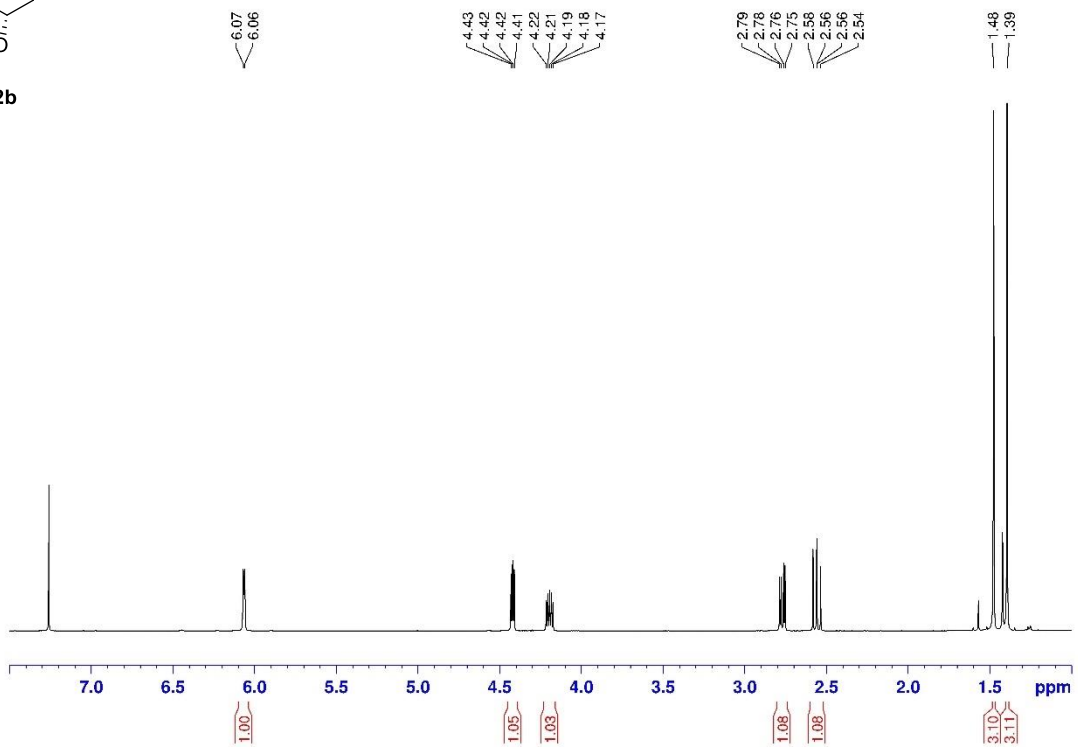
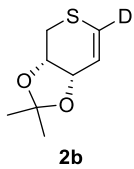
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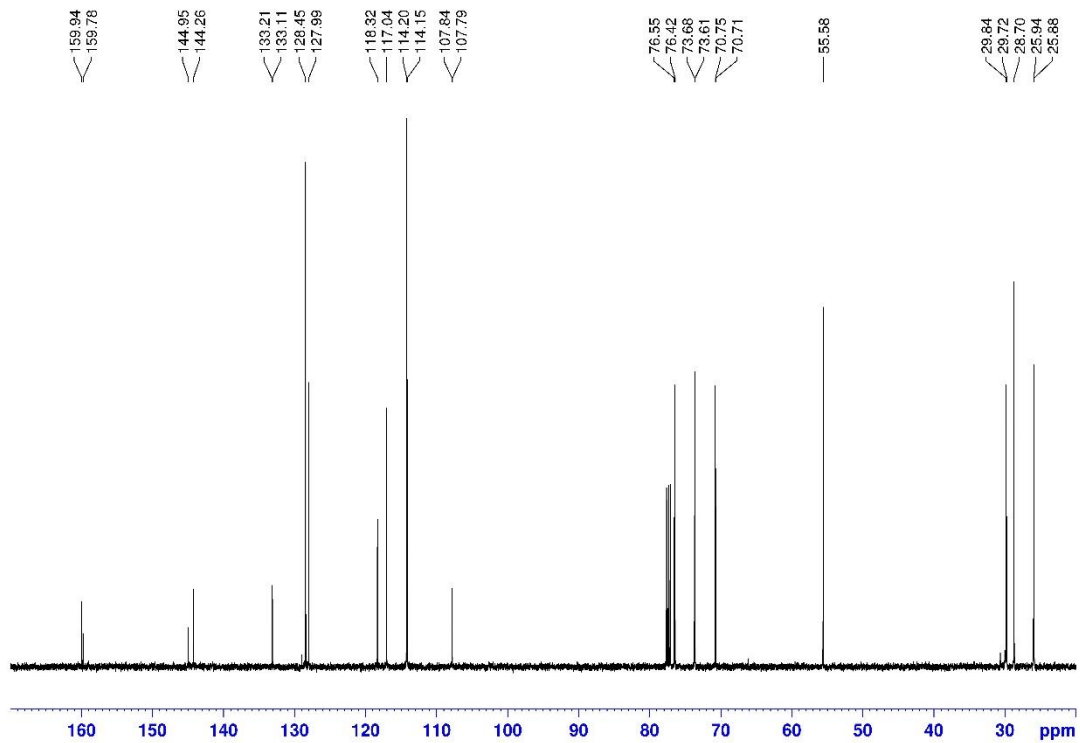
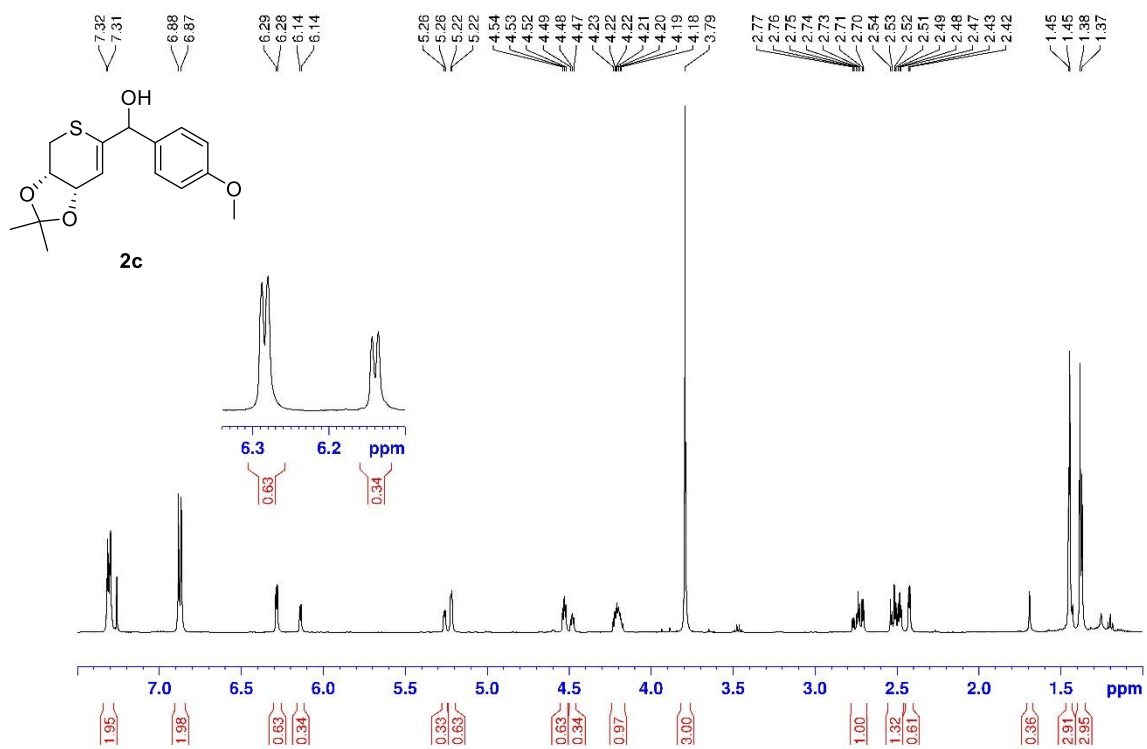
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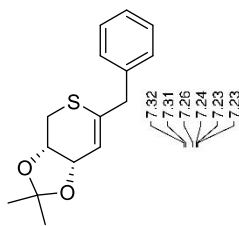
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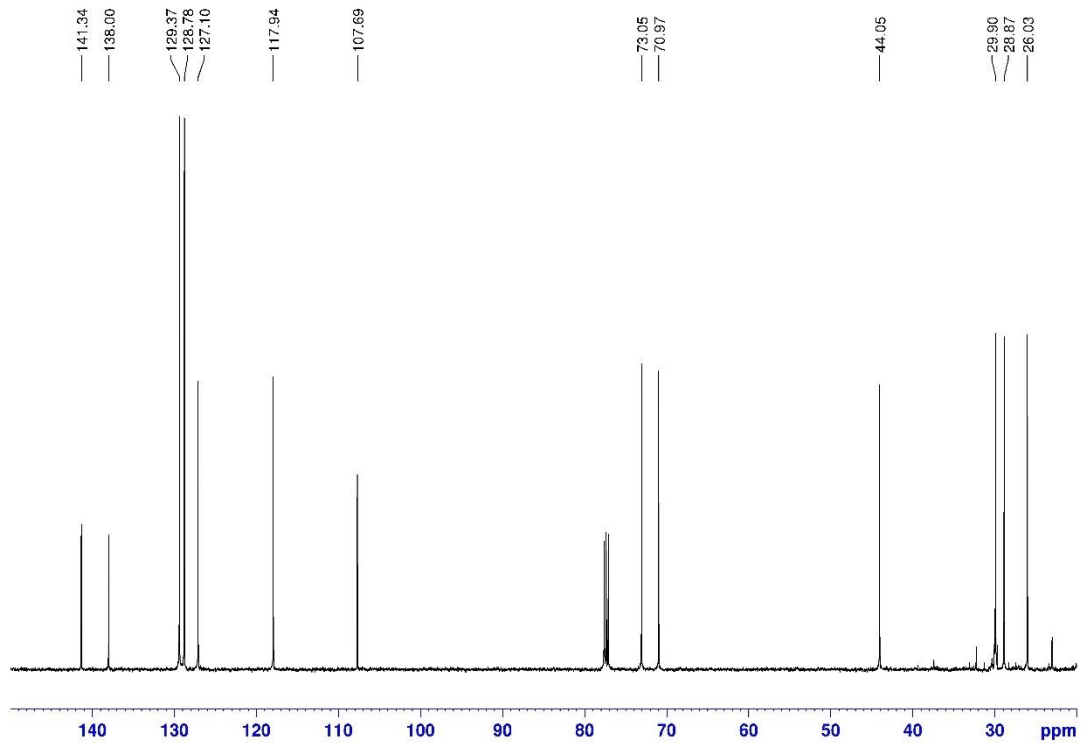
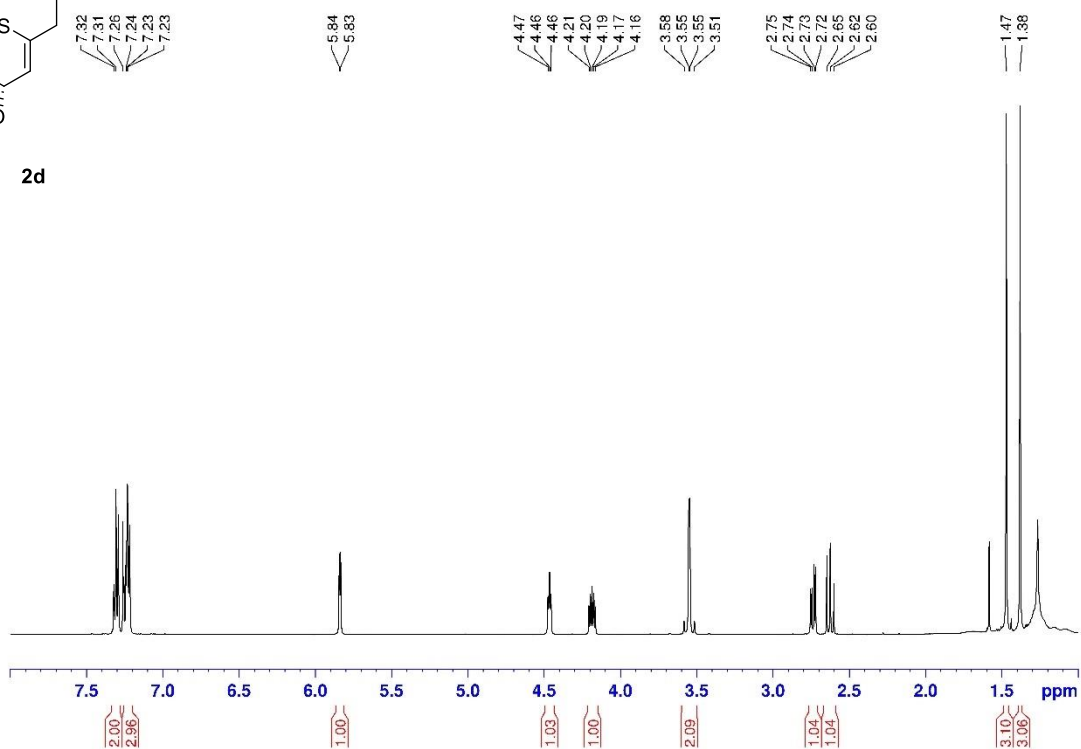


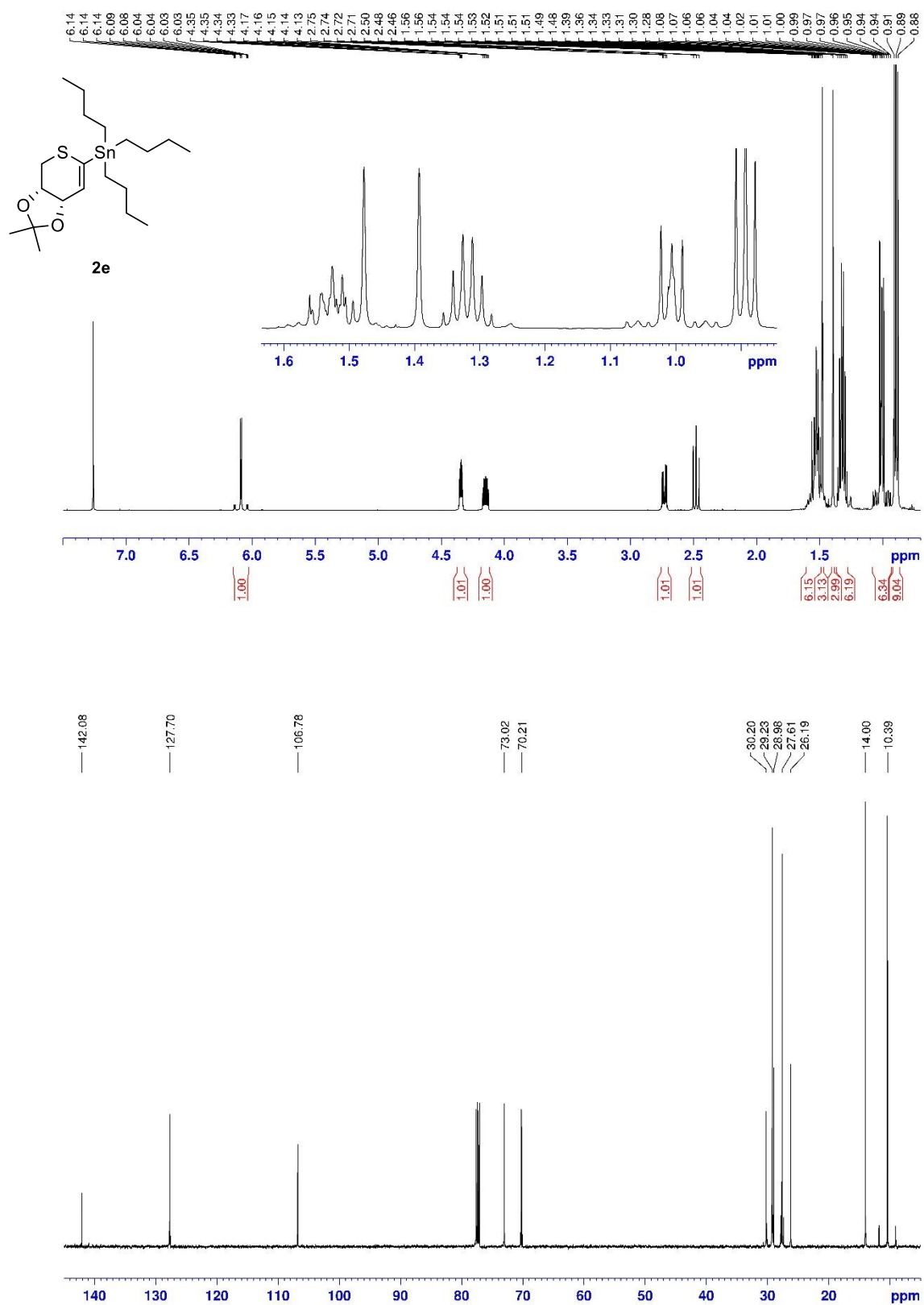


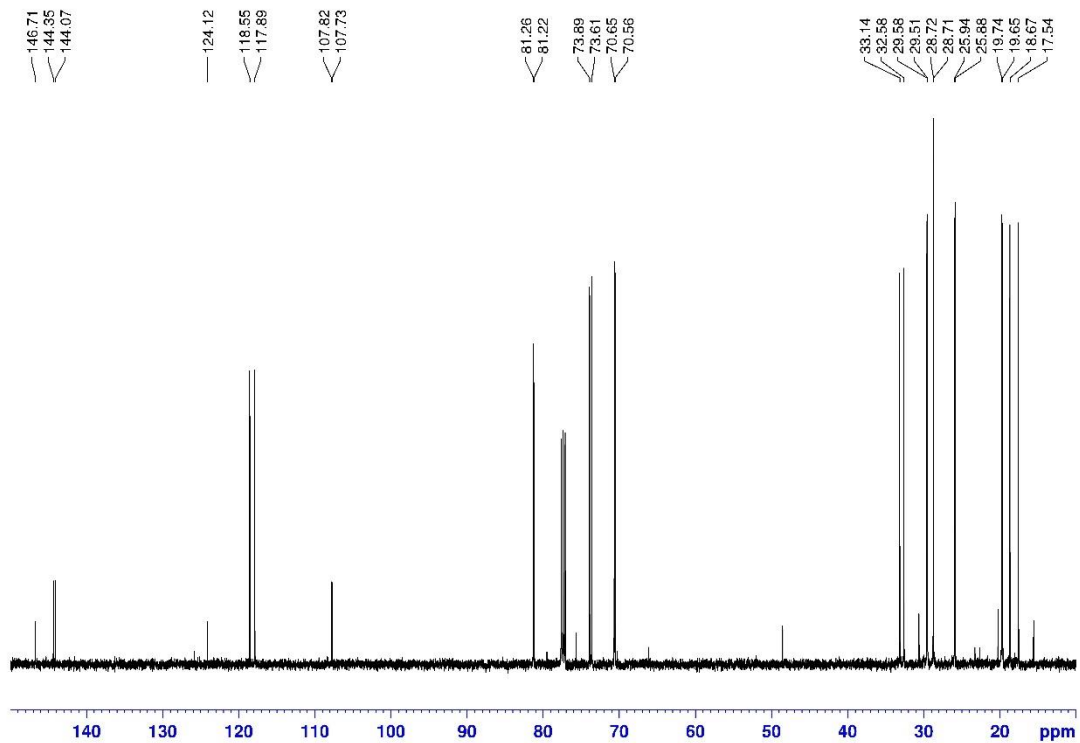
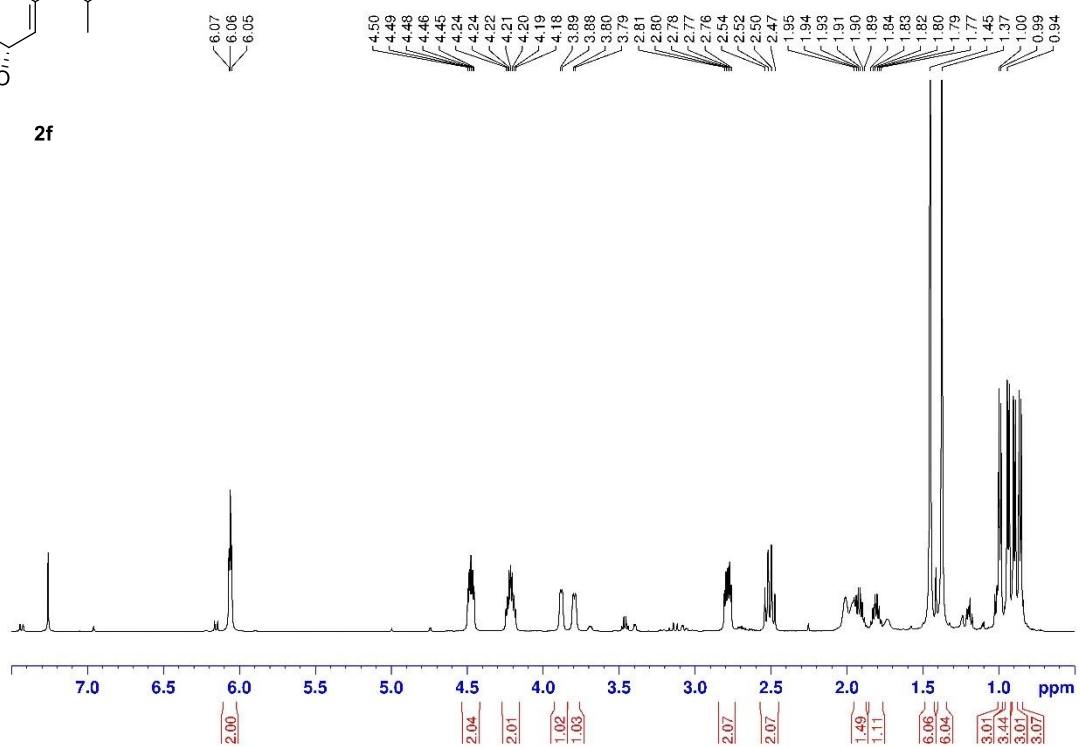
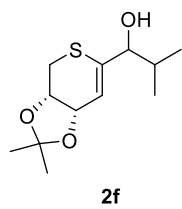


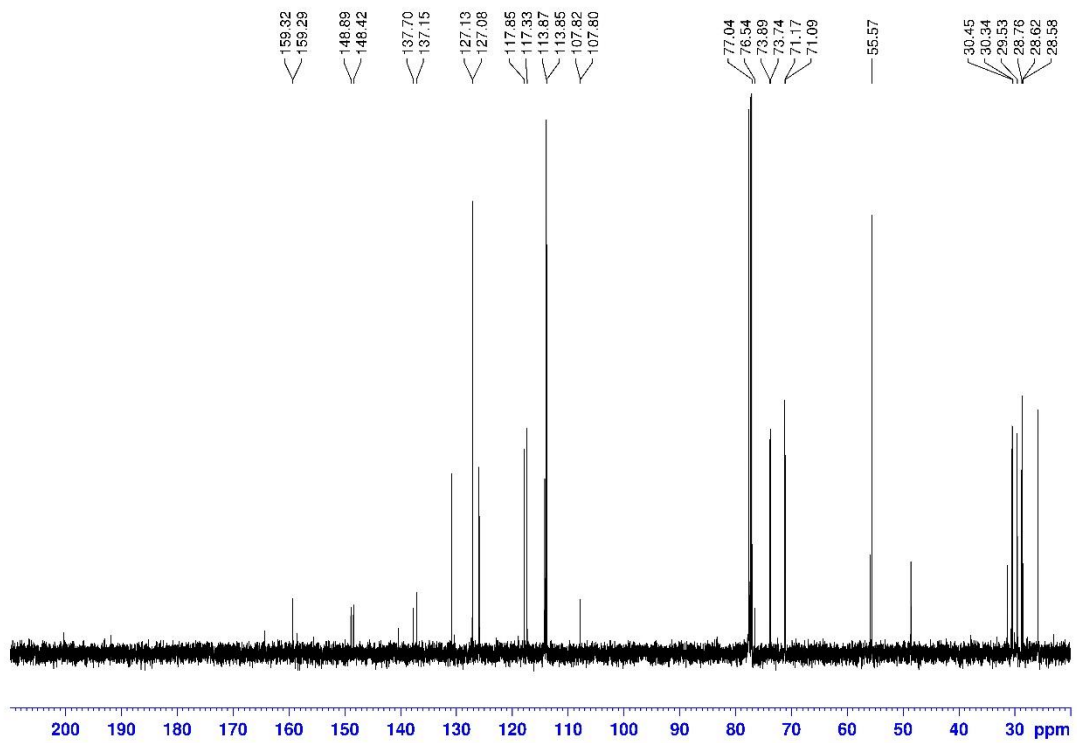
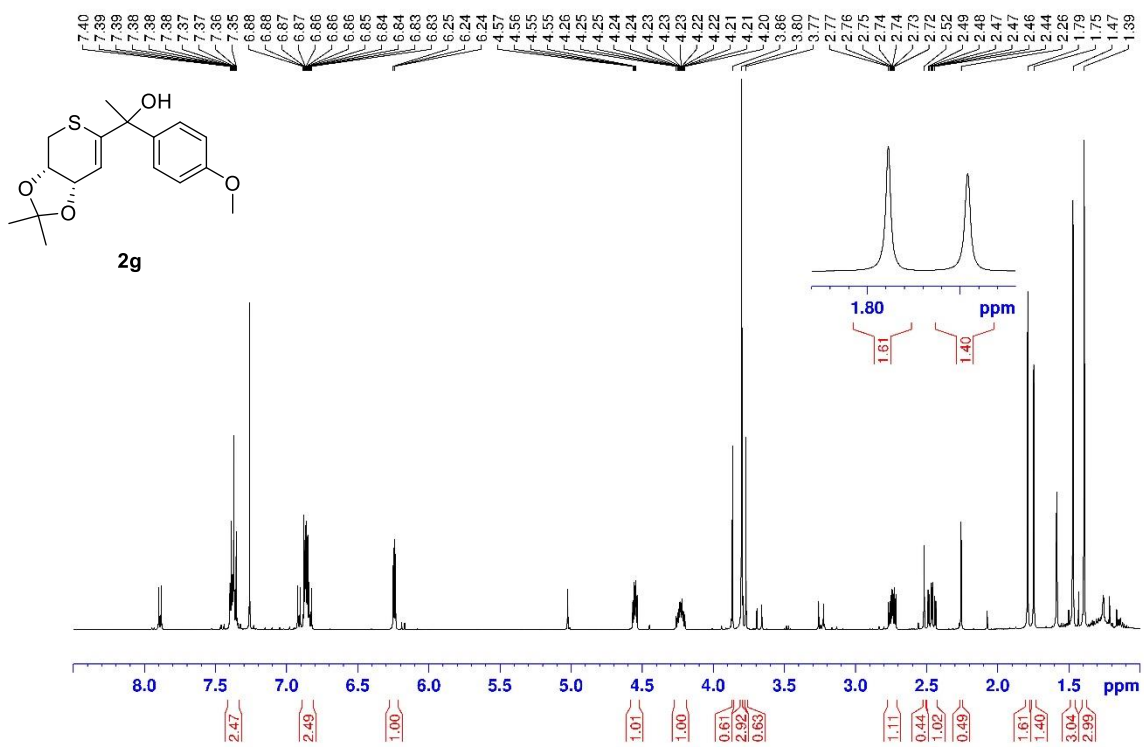


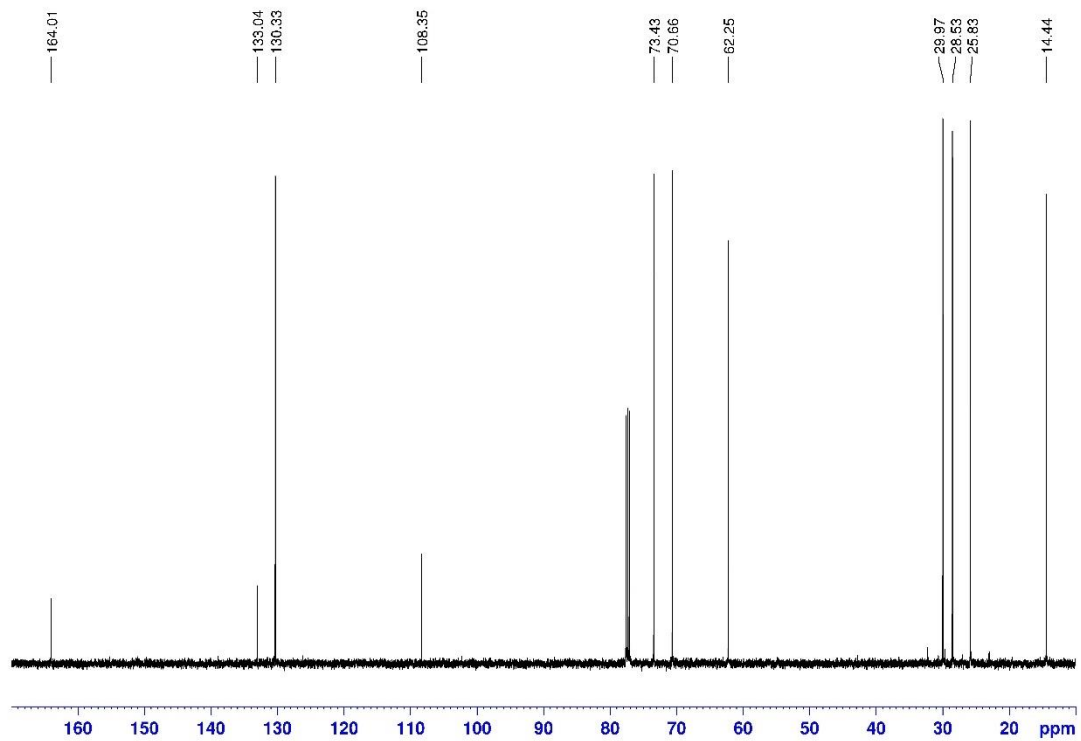
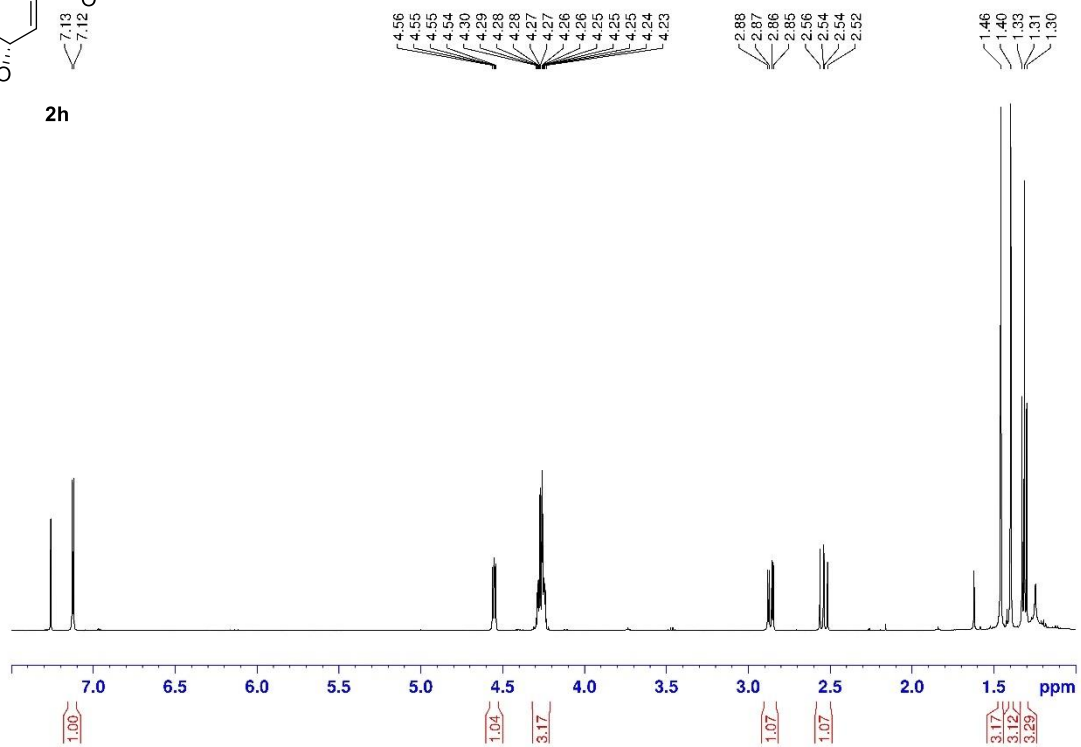
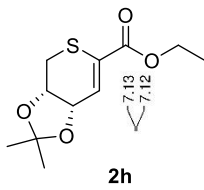
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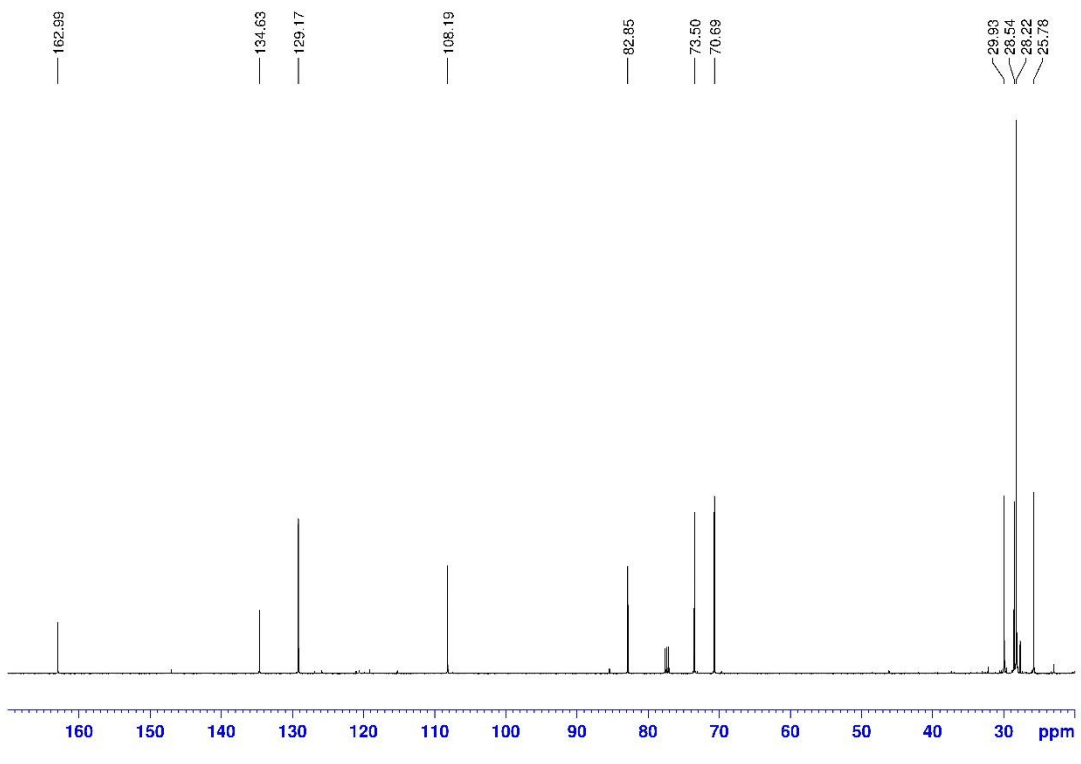
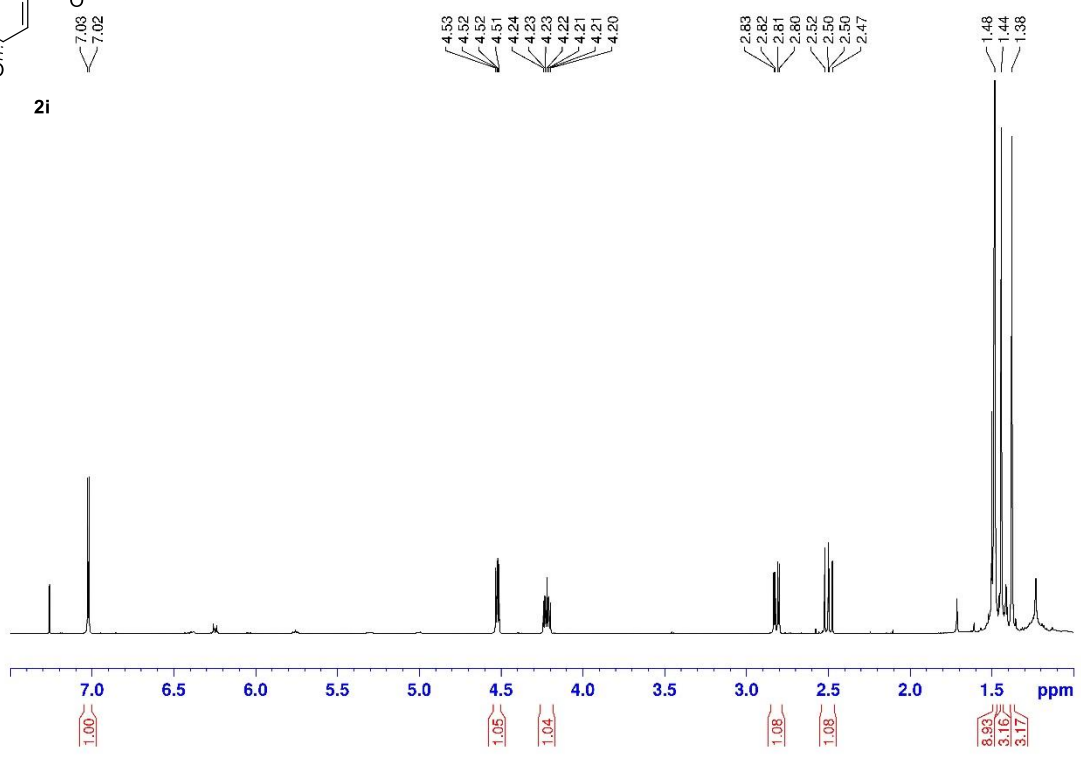
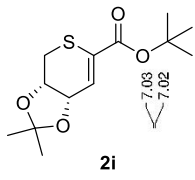


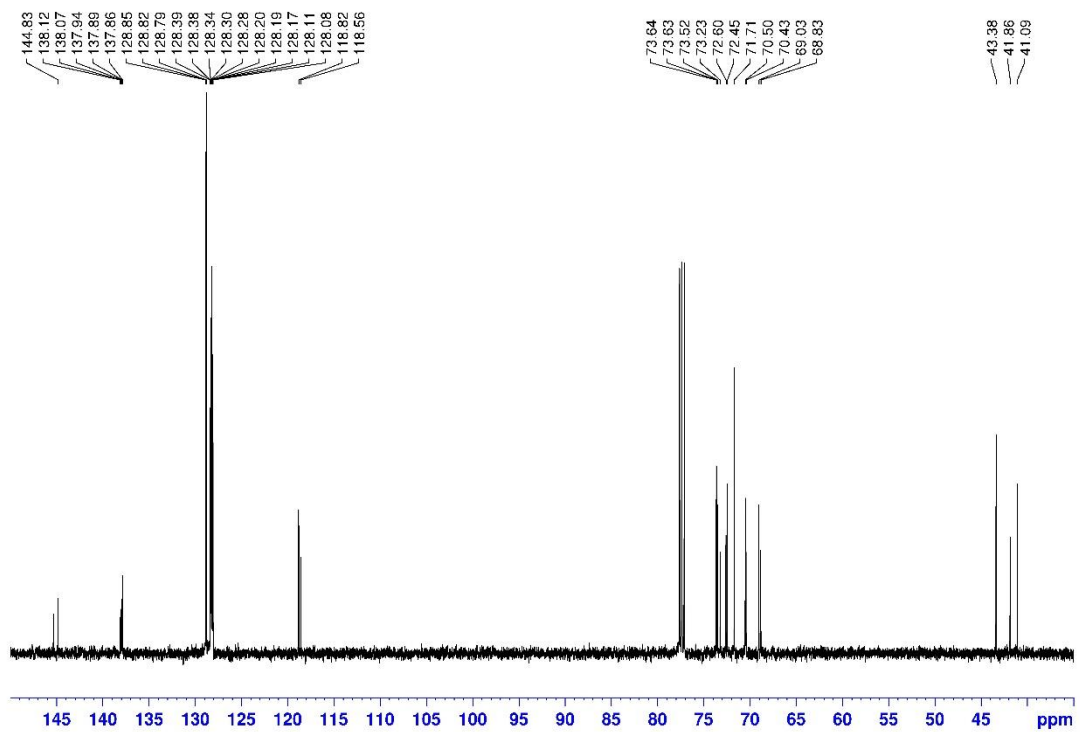
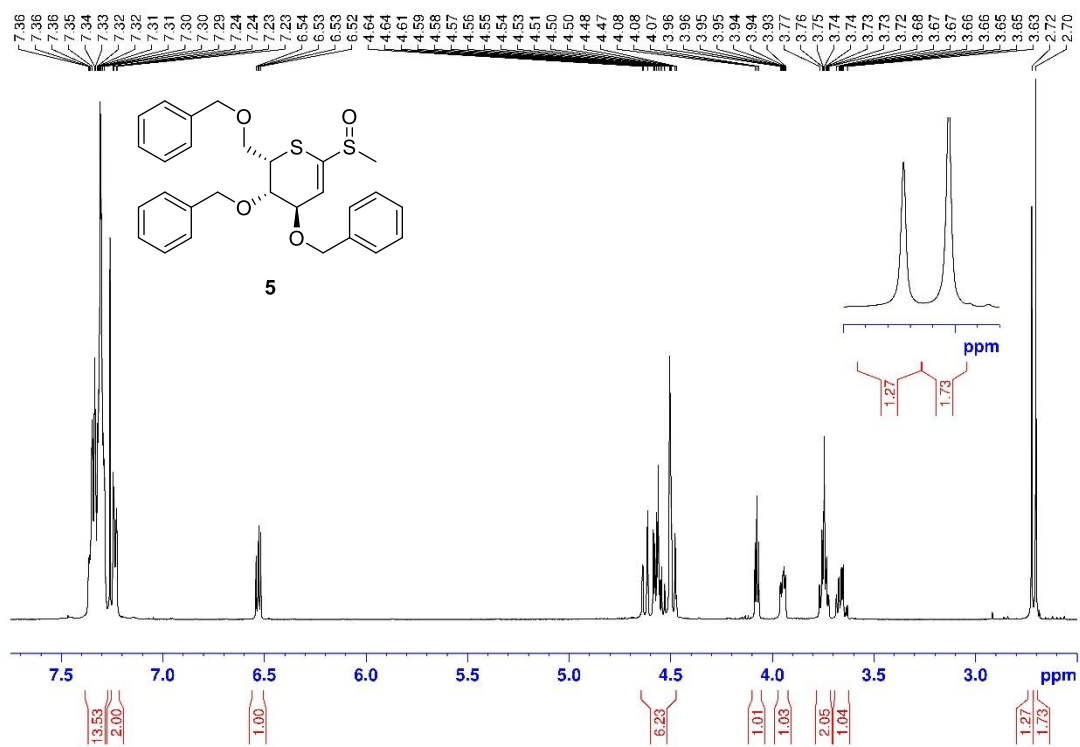


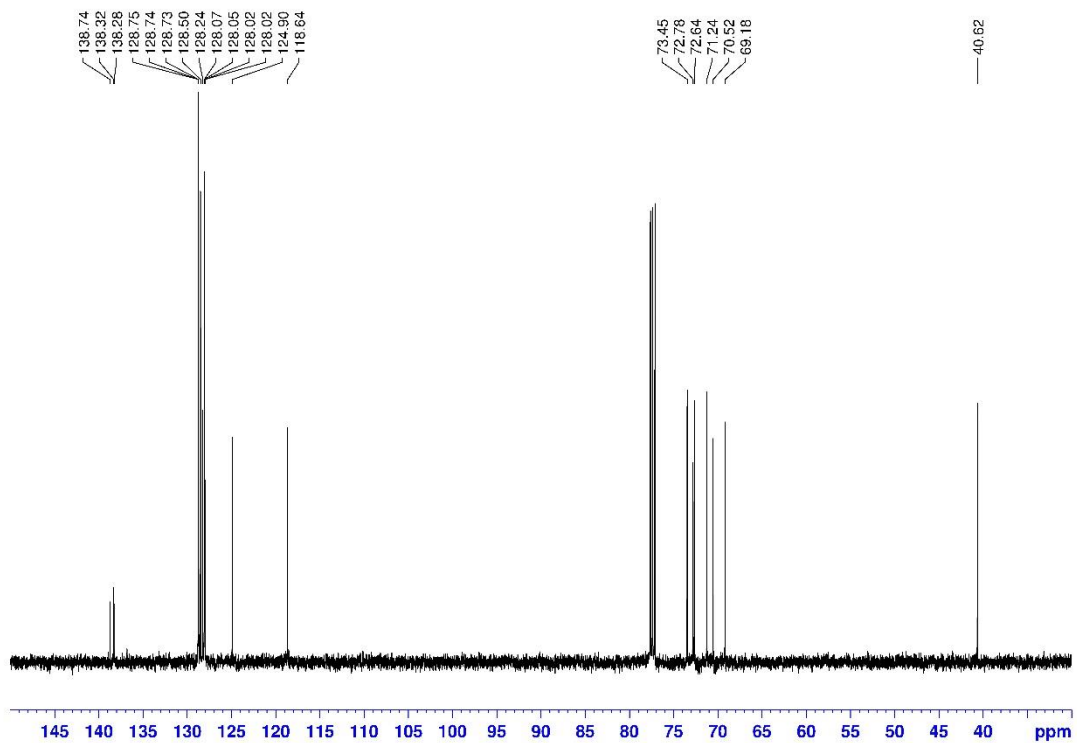
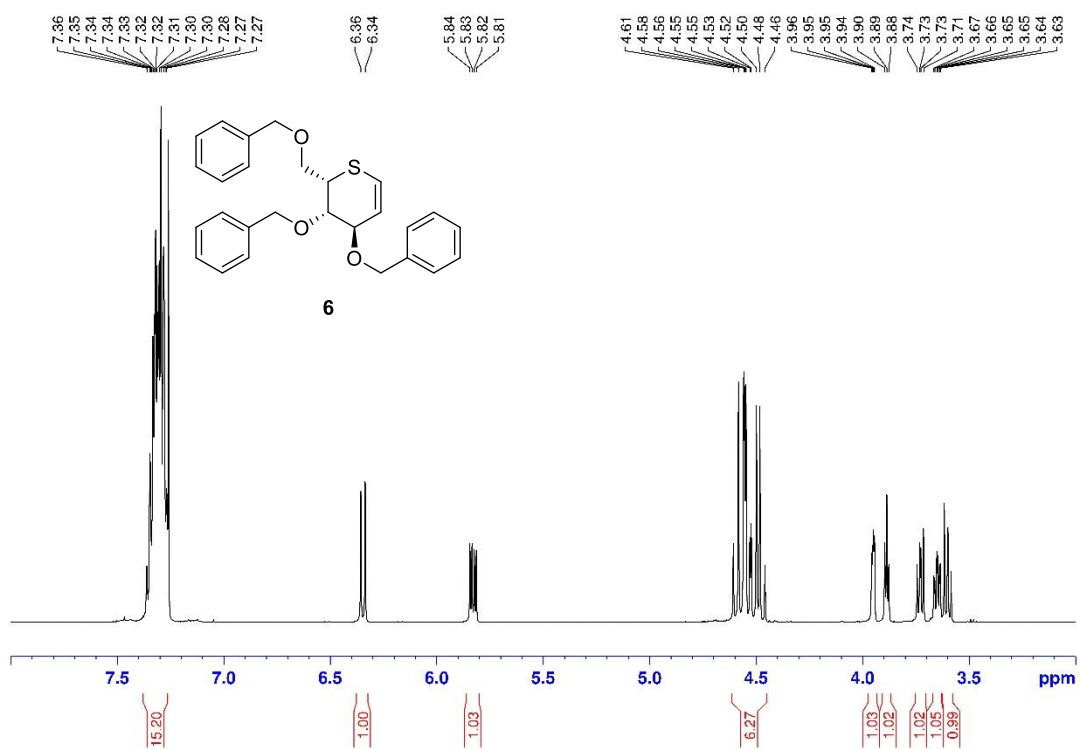


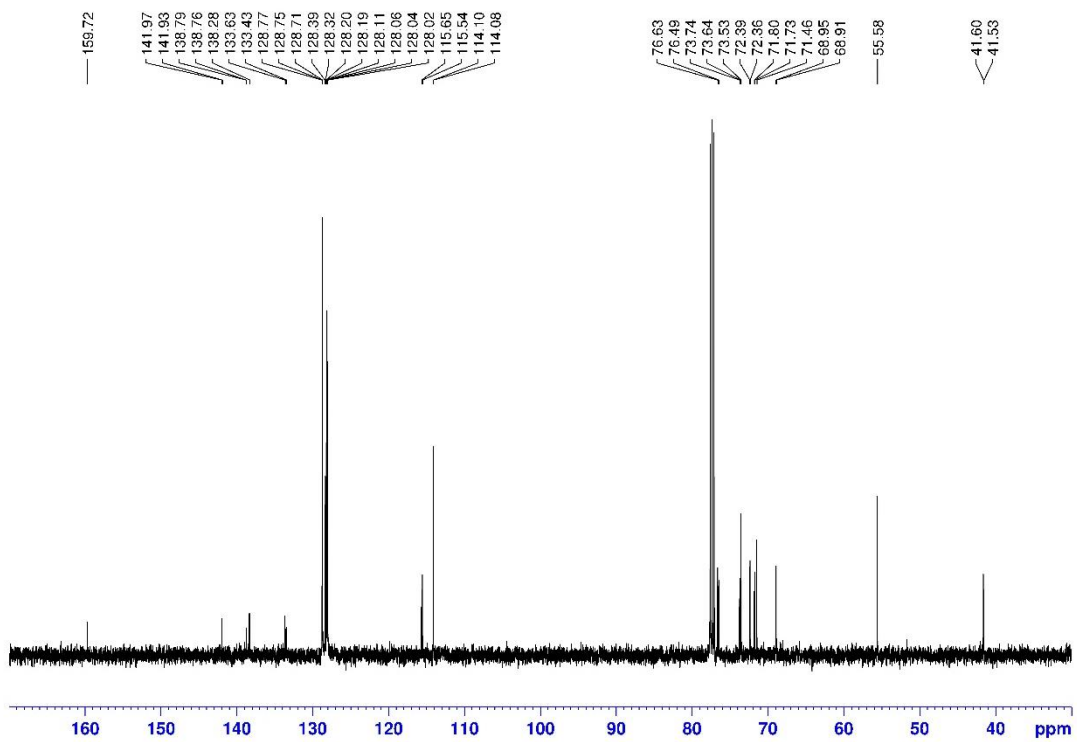
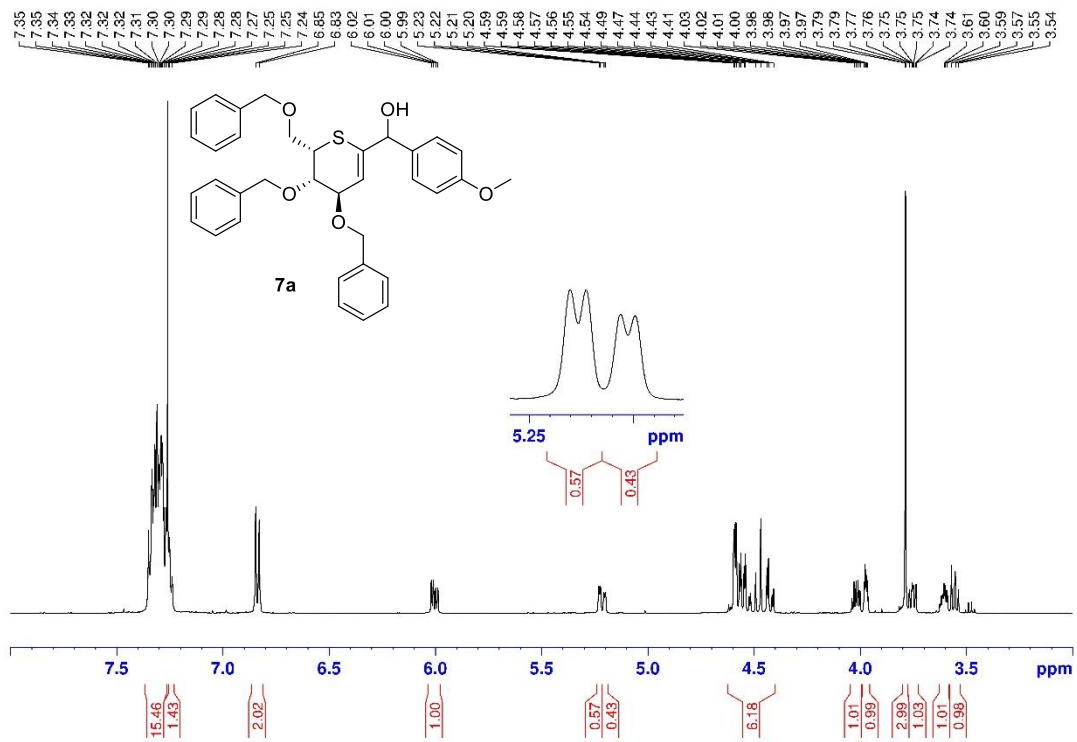


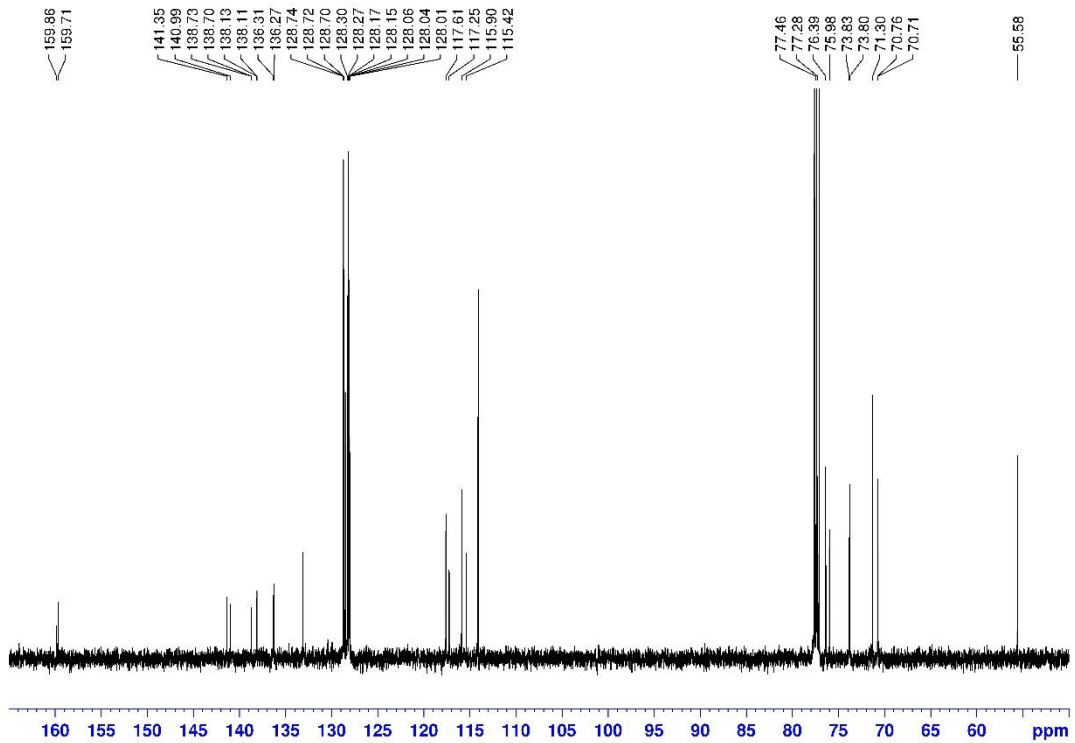
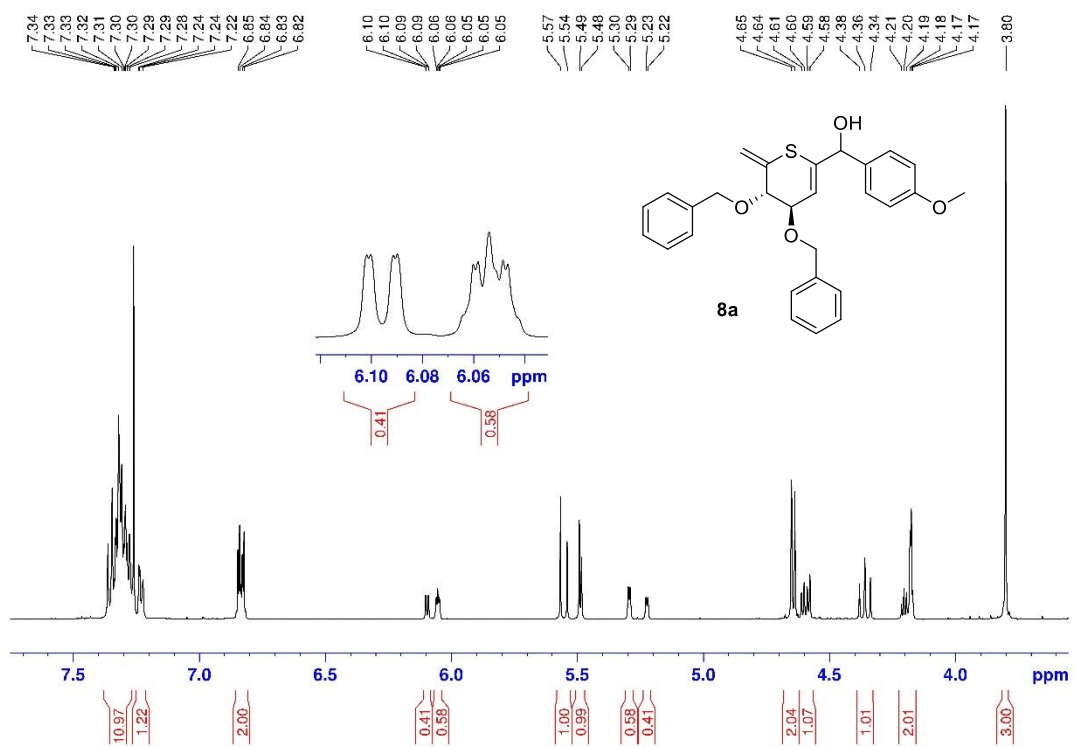


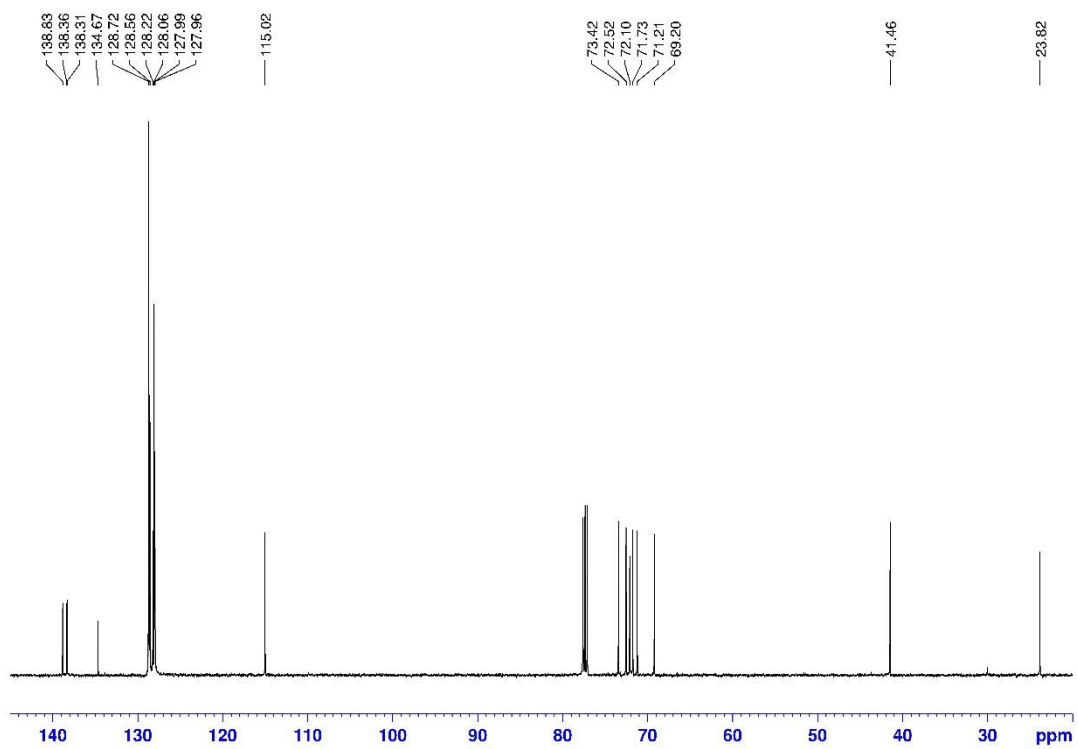
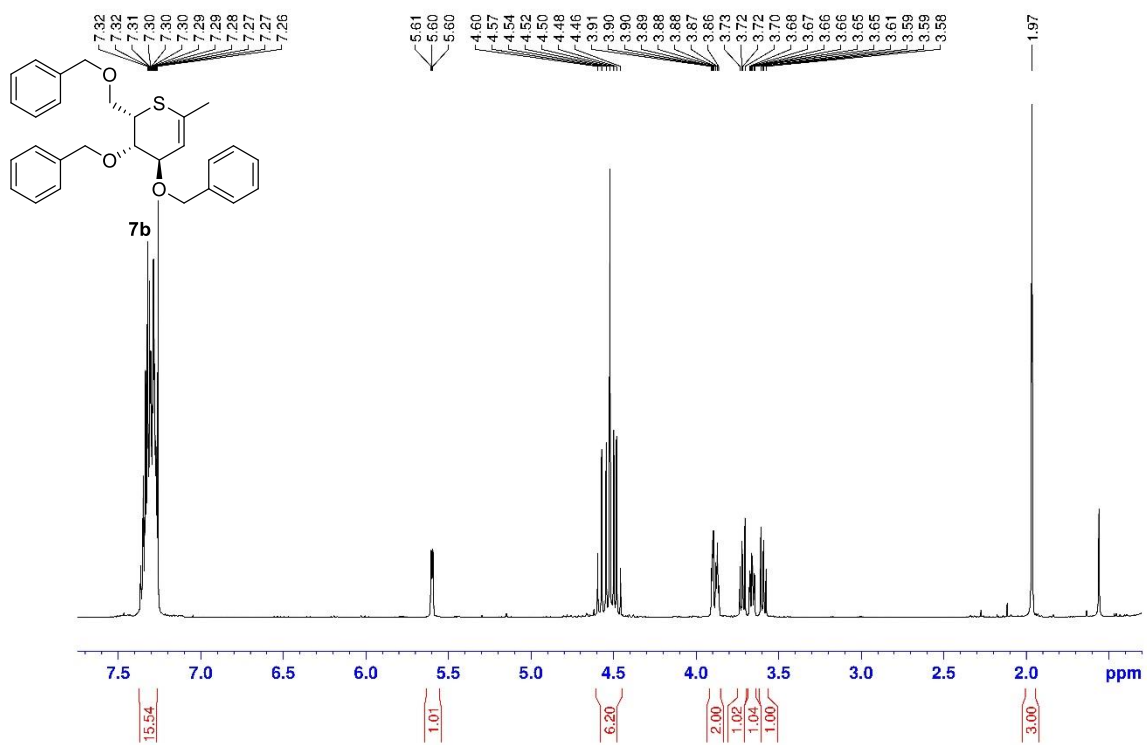


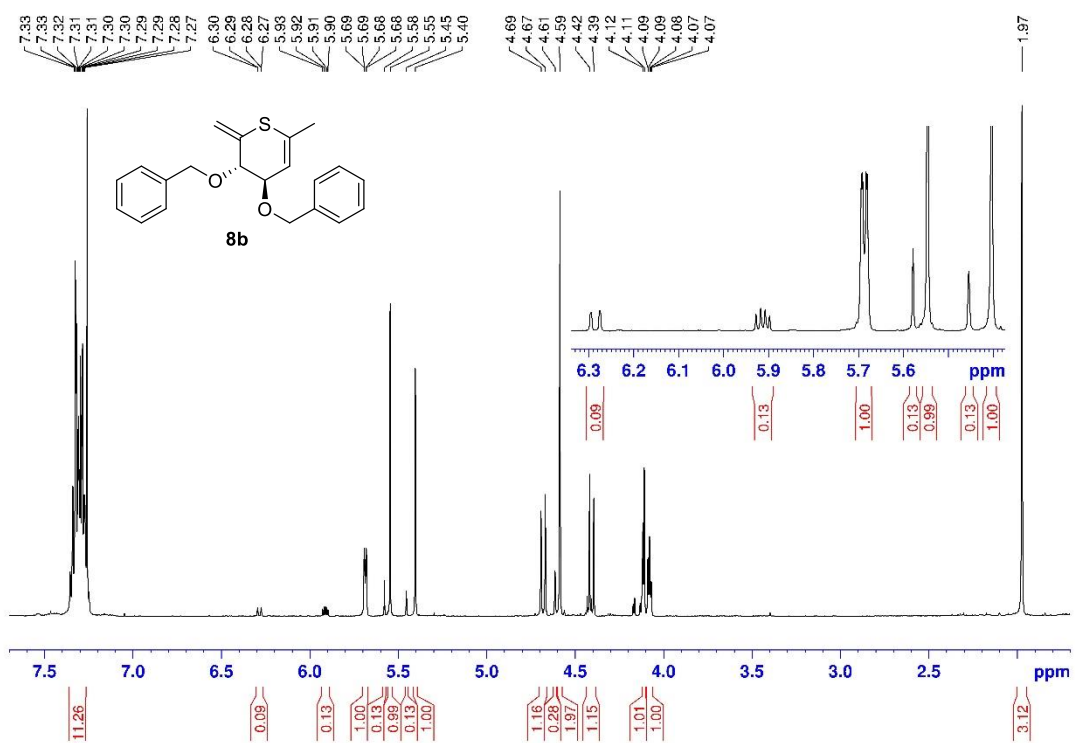


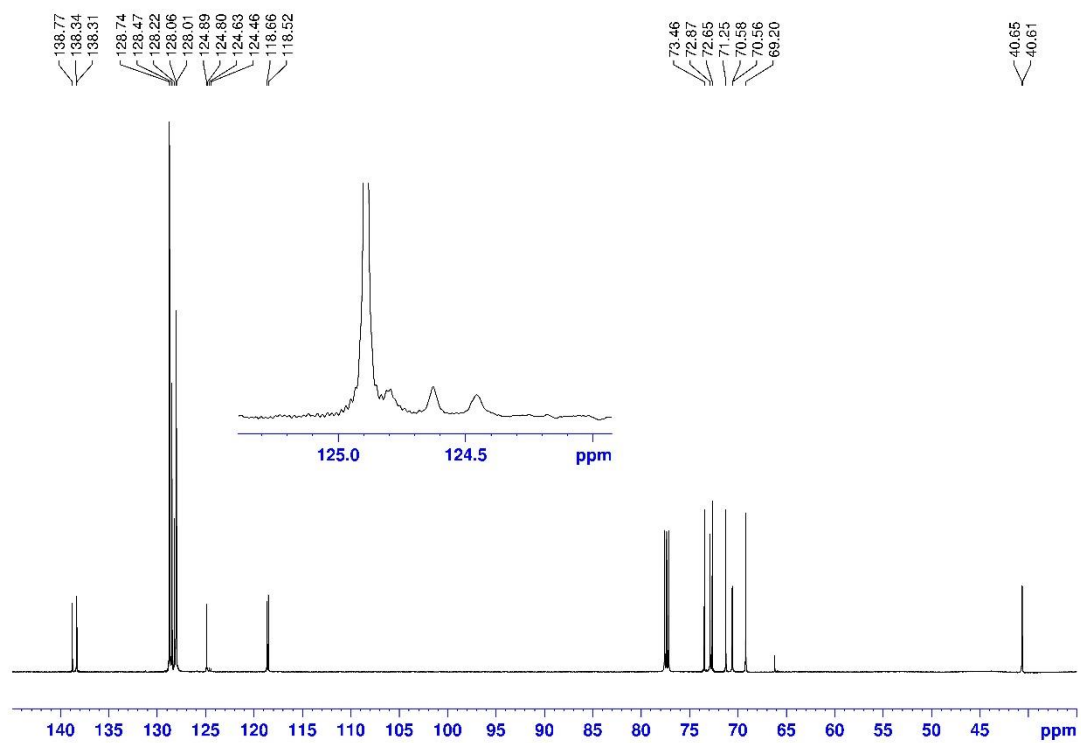
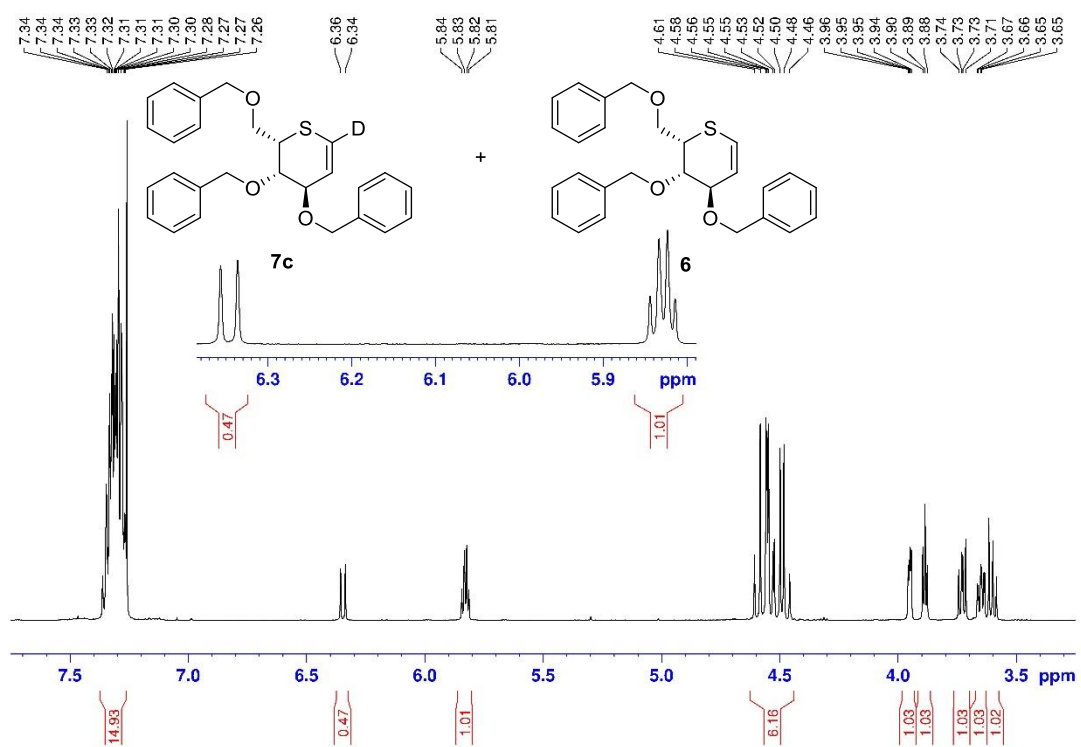


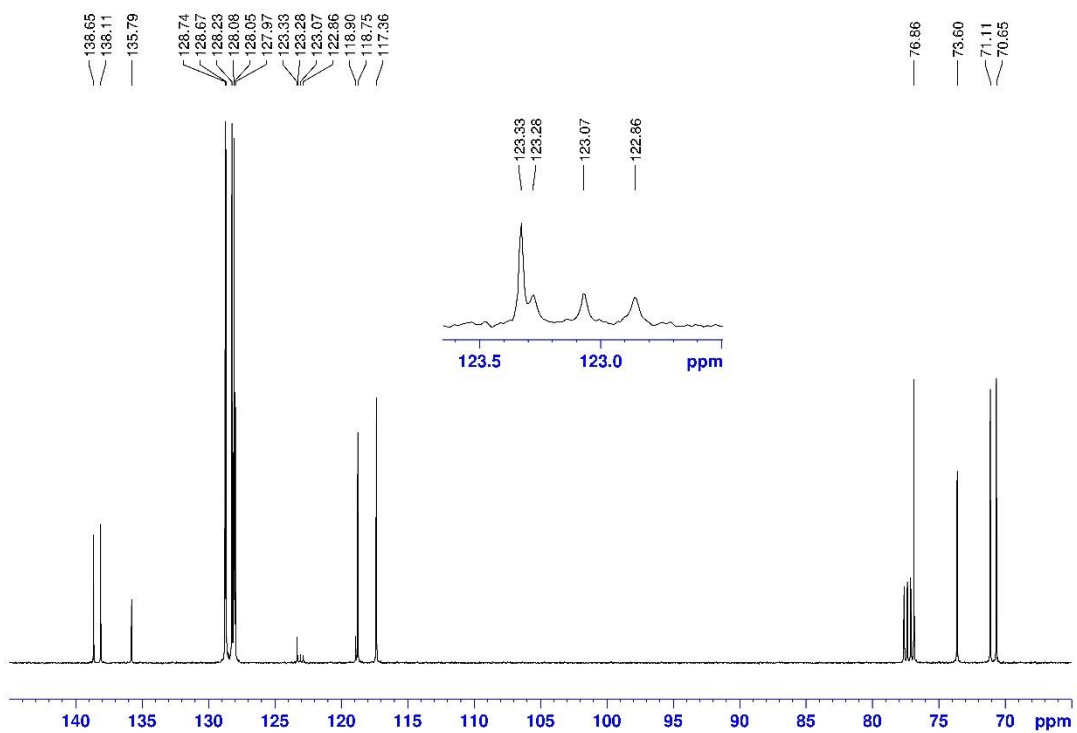
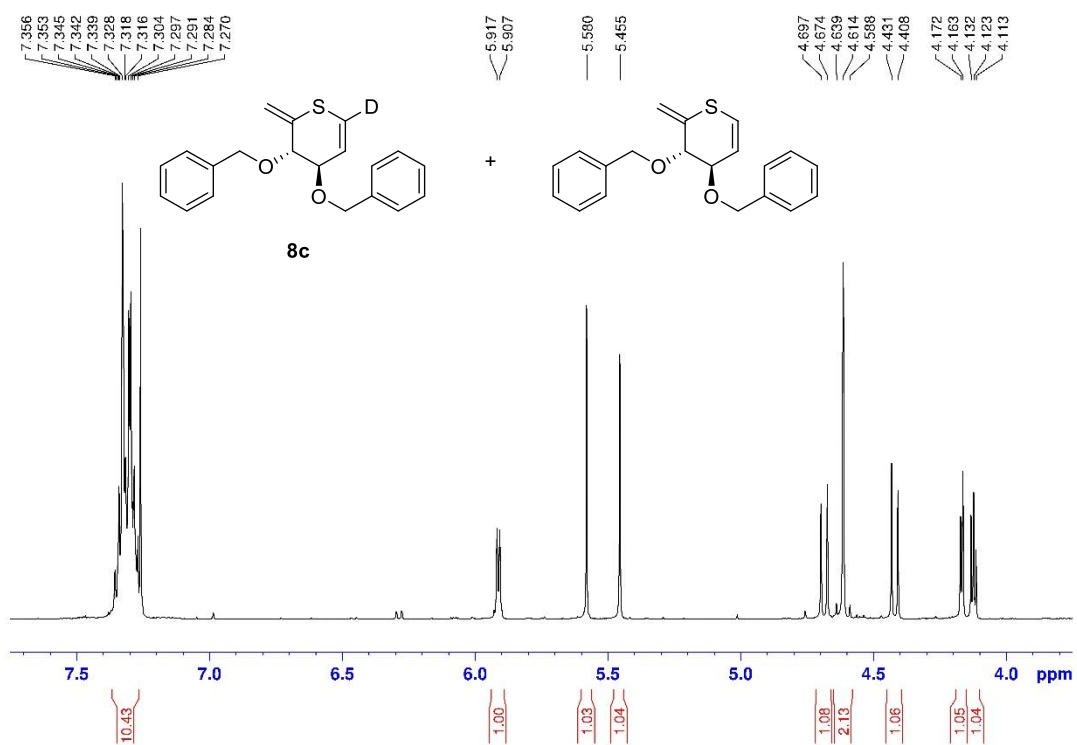


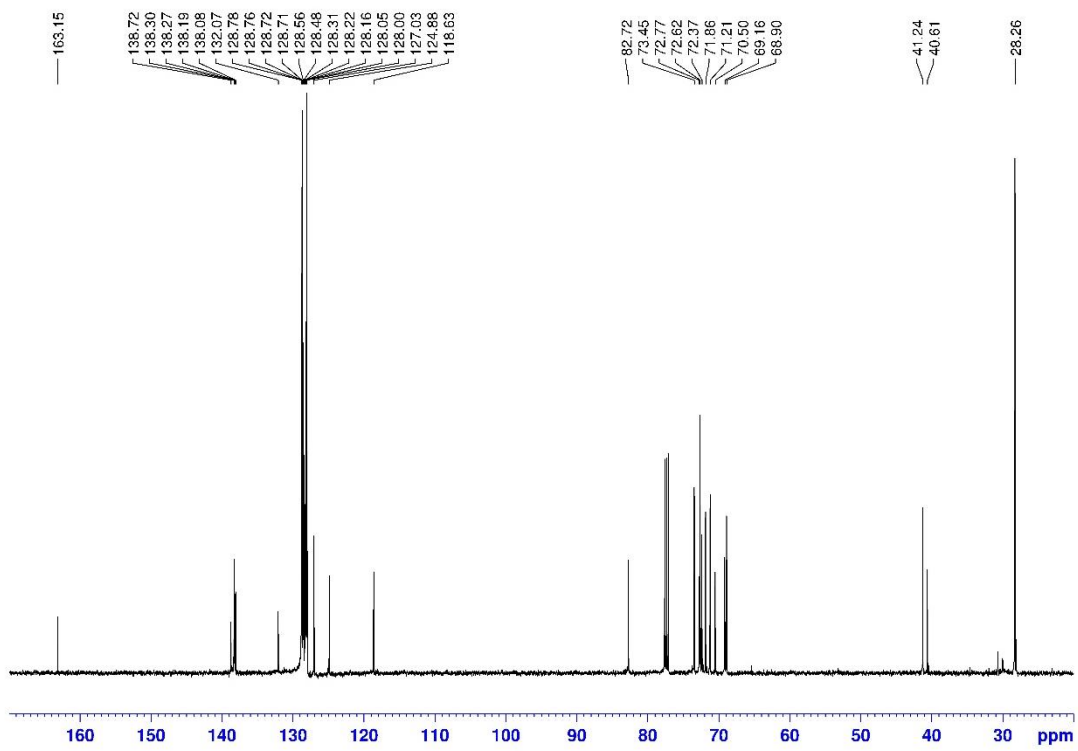
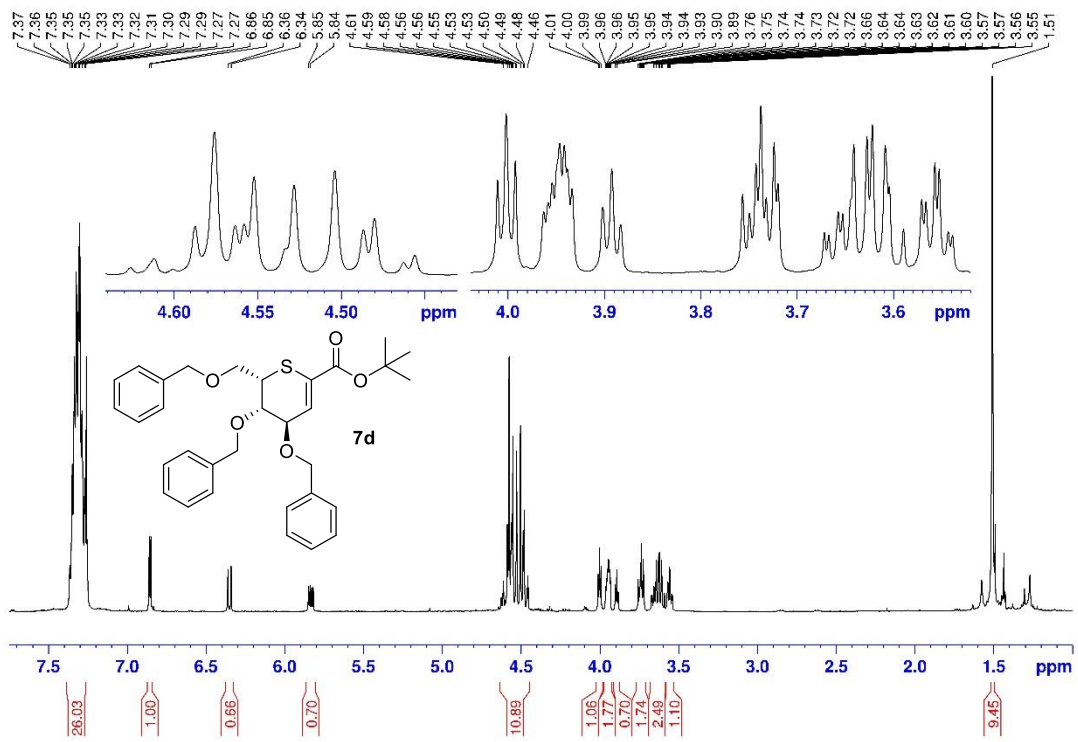


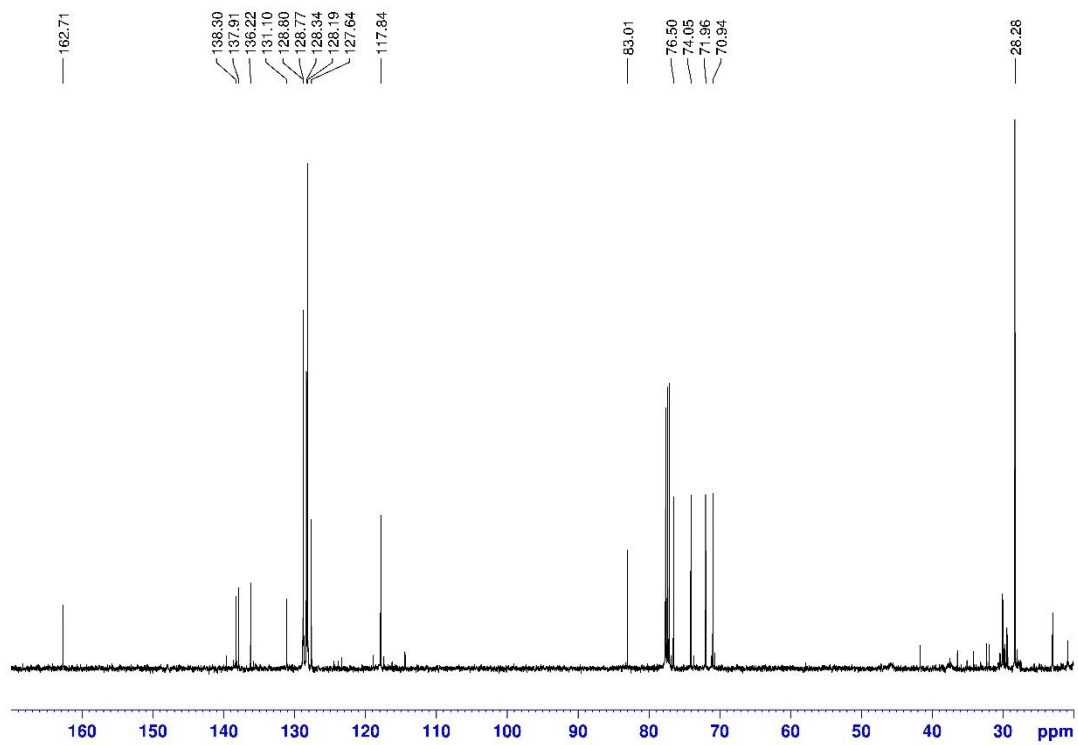
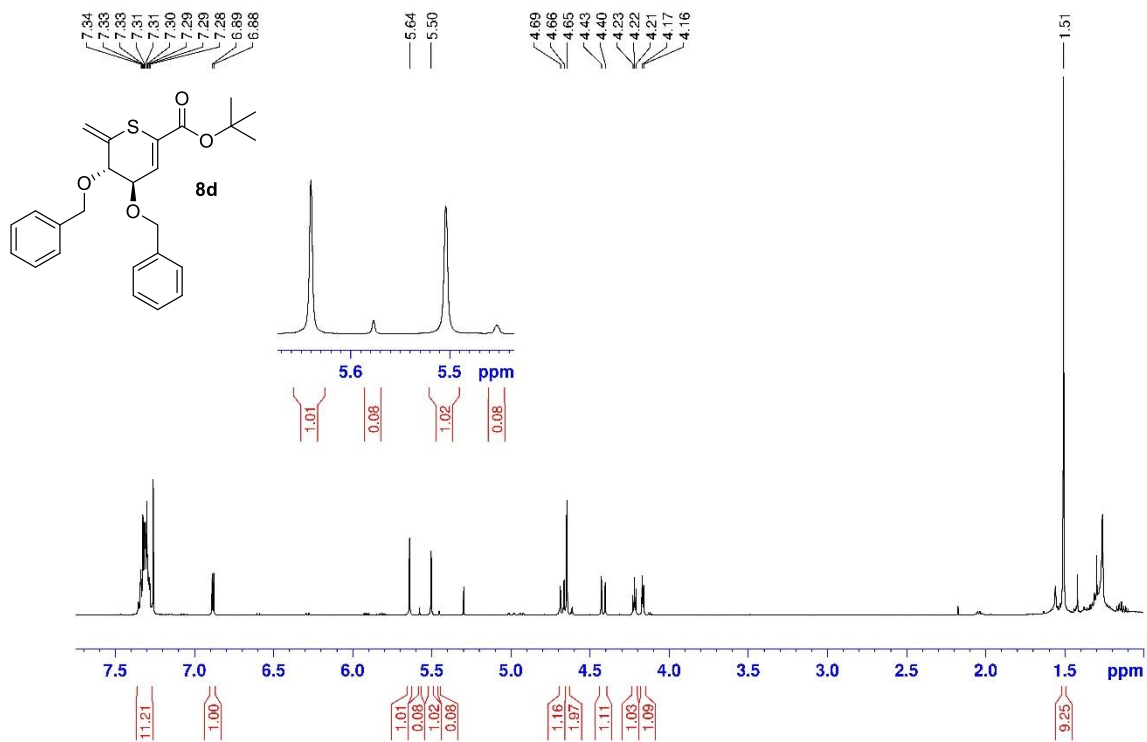








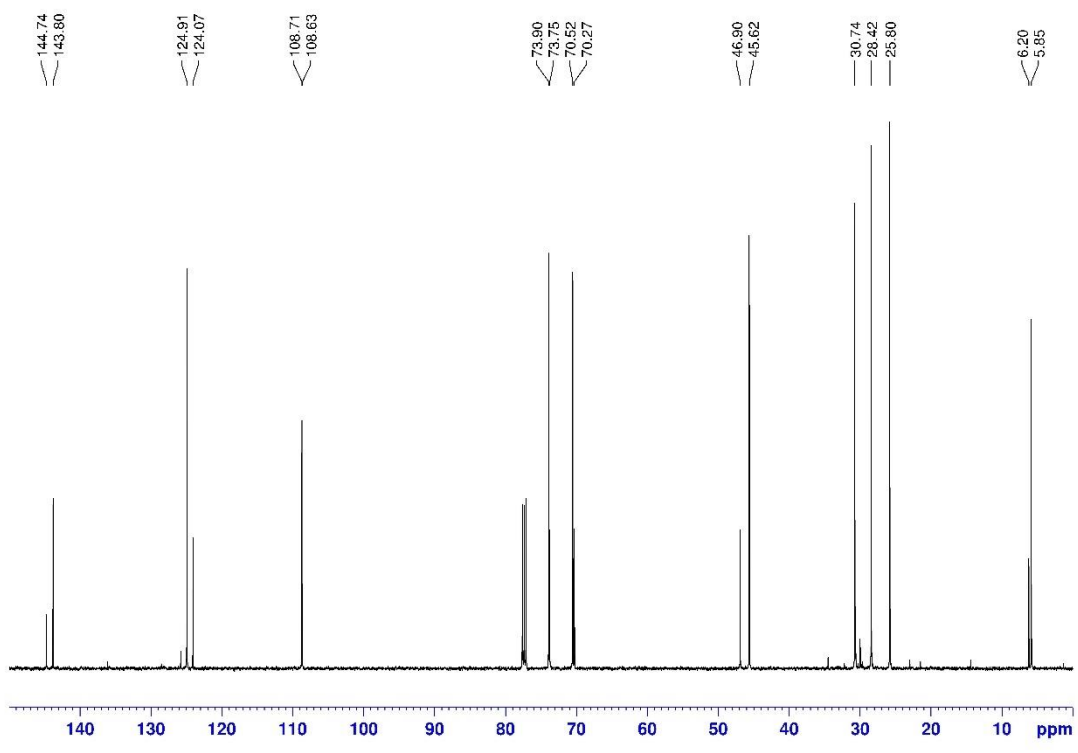
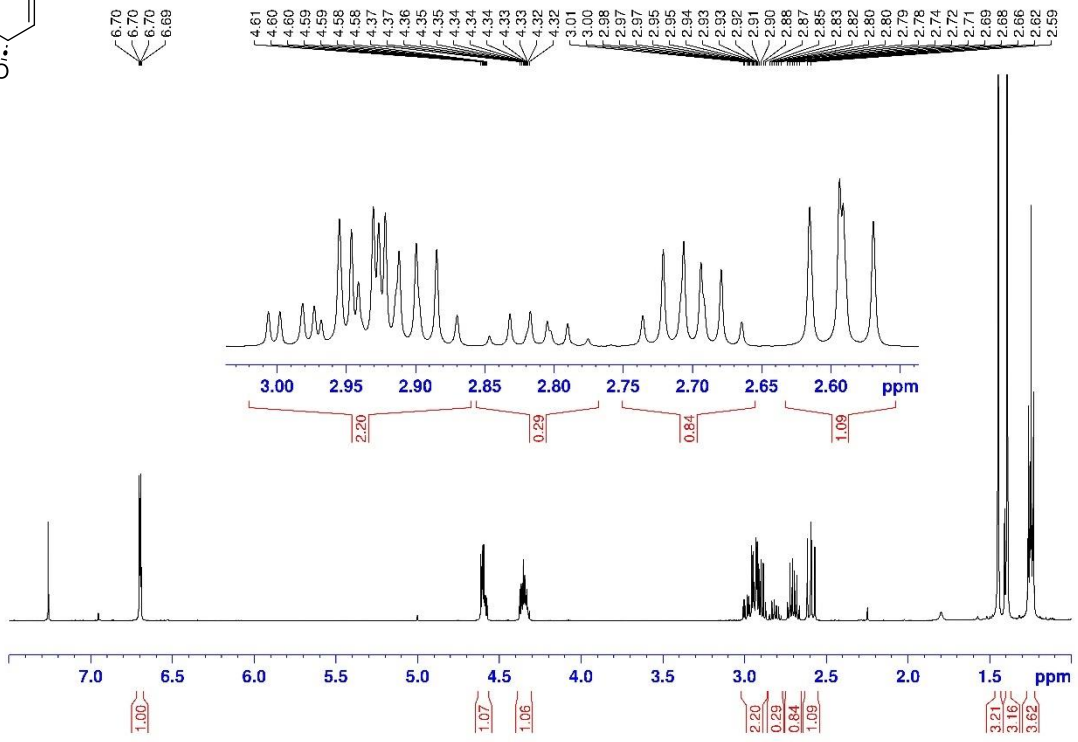
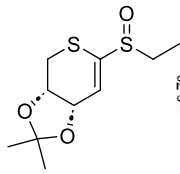




Experimental procedure and characterization of side-products

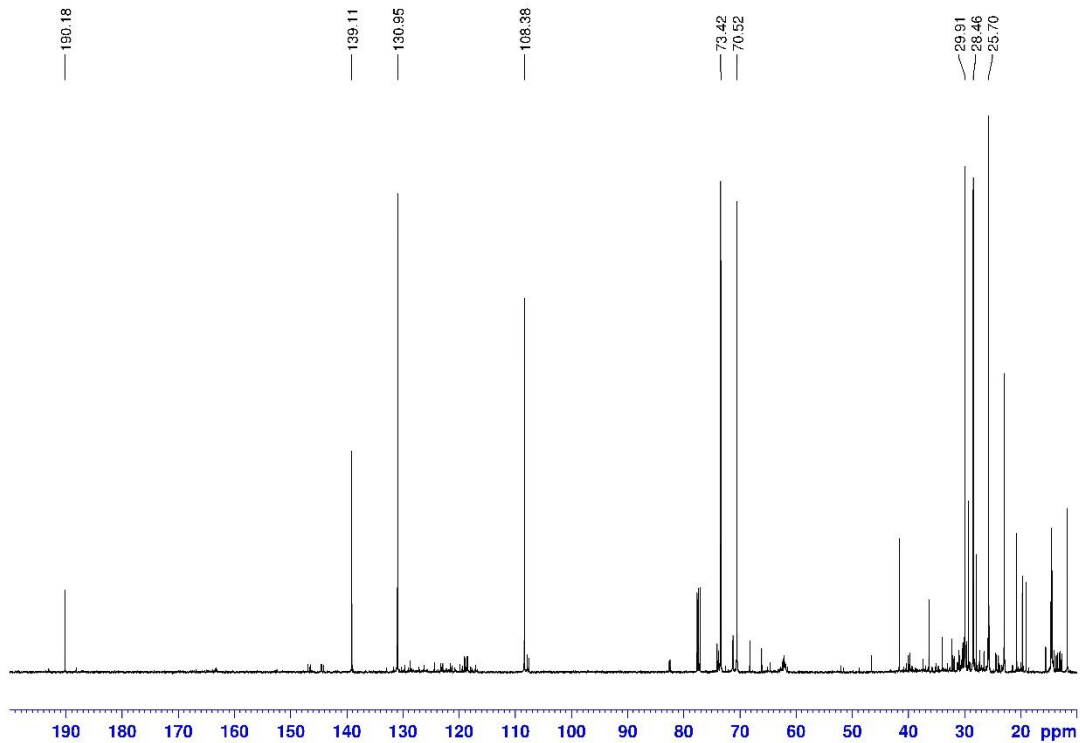
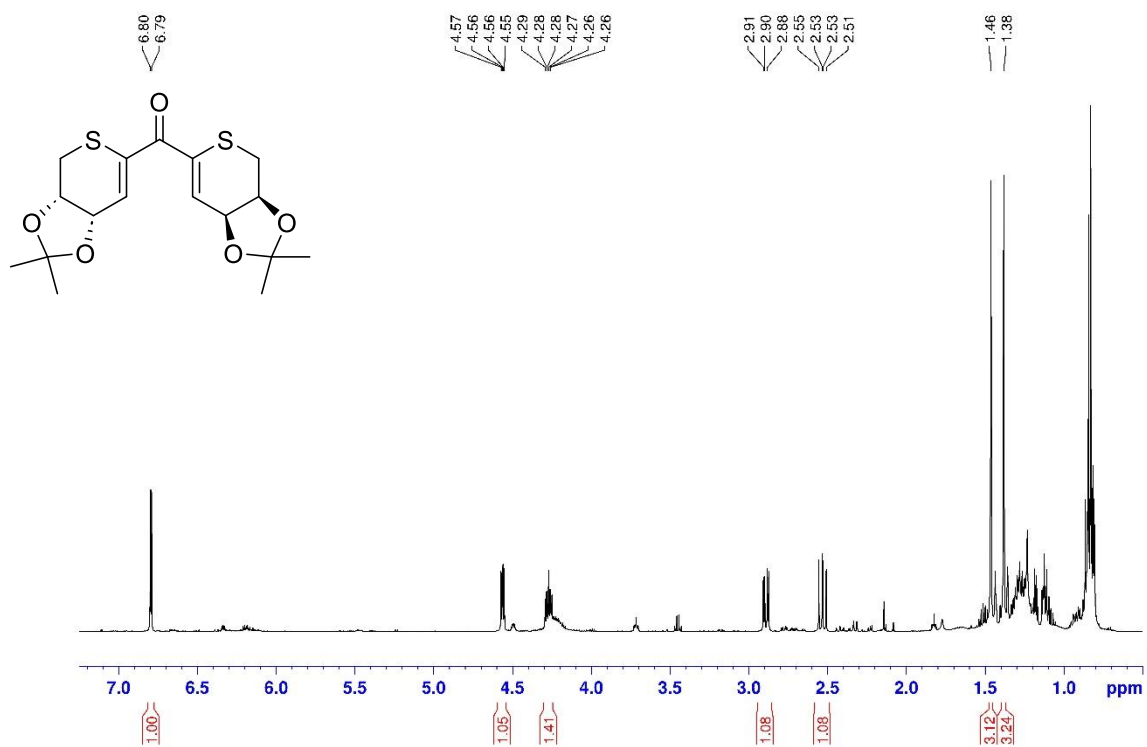
Ethyl 2-deoxy-3,4-O-isopropylidene-1,5-dithio-D-erythropent-1-eno-pyranoside 1-S-oxide

During the synthesis of 3,4-O-isopropylidene-1-methyl-5-thio-D-arabinal **2a** from the corresponding sulfoxide, ethyl 2-deoxy-3,4-O-isopropylidene-1,5-dithio-D-erythropent-1-eno-pyranoside 1-S-oxide was isolated as a yellow solid. Mixture of two diastereoisomers (74:26). m.p. 83.2°C; ¹H NMR δ (500 MHz, CDCl₃) major diastereoisomer: 6.70 (d, *J* = 3.7, 1H, H-2), 4.60 (dd, *J* = 6.0 / 3.7, 1H, H-3), 4.35 (ddd, *J* = 10.6 / 6.0 / 4.4, 1H, H-4), 2.94 (dd, *J* = 12.2 / 4.4, 1H, H-5), 2.91 (dq, *J* = 13.8 / 7.4, 1H, H-1'), 2.70 (dq, *J* = 13.8 / 7.4, 1H, H-1'), 2.59 (dd, *J* = 12.2 / 10.6, 1H, H-5), 1.44 (s, 3H, CH₃), 1.39 (s, 3H, CH₃), 1.24 (t, *J* = 7.4, 3H, H-2') and minor diastereoisomer: 6.69 (d, *J* = 3.9, 1H, H-2), 4.58 (dd, *J* = 6.0 / 3.9, 1H, H-3), 4.33 (ddd, *J* = 10.6 / 6.0 / 4.2, 1H, H-4), 2.99 (dd, *J* = 12.2 / 4.2, 1H, H-5), 2.97-2.92 (m, 1H, H-1'), 2.81 (dq, *J* = 13.6 / 7.5, 1H, H-1'), 2.59 (dd, *J* = 12.2 / 10.6, 1H, H-5), 1.45 (s, 3H, CH₃), 1.40 (s, 3H, CH₃), 1.25 (t, *J* = 7.4, 3H, H-2'); ¹³C NMR δ (125 MHz, CDCl₃) major diastereoisomer: 143.5 (C1), 124.6 (C2), 108.4 (C_{IV}), 73.6 (C4), 70.2 (C3), 45.3 (C1'), 30.4 (C5), 28.1 (CH₃), 25.5 (CH₃), 5.6 (C2') and minor diastereoisomer: 144.4 (C1), 123.8 (C2), 108.3 (C_{IV}), 73.5 (C4), 70.0 (C3), 46.6 (C1'), 30.4 (C5), 28.1 (CH₃), 25.5 (CH₃), 5.9 (C2'); HRMS (ESI+) *m/z* calcd for C₁₀H₁₆O₃NaS₂ [M+Na]⁺ 271.0439, found 271.0435; IR: 2978 (C-H), 2933 (C-H), 2868 (C-H), 1604 (C=C), 1066 (S=O), 1041 (C-O).



Di-3,4-O-isopropylidene-5-thio-D-arabinal ketone

During the purification of the 3,4-O-isopropylidene-1-ethyloxycarbonyl-5-thio-D-arabinal **2h**, di-3,4-O-isopropylidene-5-thio-D-arabinal ketone (0.080 g, 0.22 mmol, 19%) was isolated as a brown oil. ^1H NMR δ (500 MHz, CDCl_3): 6.82 (d, $J = 3.9$, 2H, H-2), 4.58 (dd, $J = 6.0 / 4.0$, 2H, H-3), 4.29 (ddd, $J = 10.7 / 6.0 / 4.4$, 2H, H-4), 2.91 (dd, $J = 12.4 / 4.4$, 2H, H-5), 2.55 (dd, $J = 12.4 / 10.9$, 2H, H-5), 1.49 (s, 6H, CH_3), 1.40 (s, 6H, CH_3); ^{13}C NMR δ (125 MHz, CDCl_3): 189.9 (CO), 138.8 (C1), 130.7 (C2), 108.1 (C_{IV}), 73.1 (C4), 70.2 (C3), 29.6 (C5), 28.2 (CH_3), 25.4 (CH_3); HRMS (ESI+) m/z calcd for $\text{C}_{17}\text{H}_{23}\text{O}_5\text{S}_2$ $[\text{M}+\text{H}]^+$ 371.0987, found 371.0987.



Conformational Search and Ring Inversion

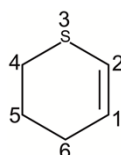
The tetrahydroaromatic rings constitute fundamental structures widely used in organic synthesis. These systems are known to be dynamic (flexible) and rings tend to assume non-planar (warped) conformations. The conformers (three-dimensional shapes) play a crucial role in understanding the molecule's behavior, stability, interactions, and reactivity. A single energy minimum is clearly inappropriate for these flexible systems, and a conformational search is a more suitable tool. In this respect, we performed conformational sampling using the CREST software to find the different low-energy structures of a molecule. The production run in this example yields 686 structures, distributed over two conformers within 6 kcal/mol above the lowest conformer that was found at the search level (GFN2-xTB).



Scheme S1 Thioglycals warped flexible conformations.

We used these two conformers to test the influence of the computational level on structures and to validate our selected computational level (wB97X-D/ Def2TZVP).

Table S1 Influence of the computational level on Bond length (in Å), Torsion angle (in degree) and relative energies of conformers (in kcal/mol) for model compounds.



Calculations level	conformation	Bond length, Å					Torsion angle, deg			
		1-2	2-3	3-4	4-5	5-6	1-2-3-4	2-3-4-5	3-4-5-6	2-1-6-5
MP2/cc-pVTZ	1	1.341	1.751	1.813	1.522	1.524	9.767	-43.391	68.500	15.679
wB97XD/Def2TZVP		1.339	1.757	1.820	1.526	1.529	9.451	-40.910	64.927	16.365
Delta		0.002	-0.006	-0.007	-0.004	-0.005	0.316	2.481	-3.573	0.686
MP2/cc-pVTZ	2	1.342	1.751	1.813	1.522	1.524	-9.721	43.330	-68.487	-15.763
wB97XD/Def2TZVP		1.339	1.757	1.820	1.526	1.529	-9.448	40.893	-64.912	-16.393
Delta		0.003	-0.006	-0.007	-0.004	-0.005	-0.273	2.437	-3.575	0.630

The overall difference for the bond length would be approximately ± 0.0048 Å. This difference is very small, the two calculation levels give similar results for the bond length. Torsion angle between these two calculation levels is also small (the biggest difference is 3.6 deg), the conformation of the ring (spatial orientation of atoms) remains similar. The relative energy of conformers at the tow level is too small also ($2.39 \cdot 10^{-4}$ kcal/mol for MP2 and $8.6 \cdot 10^{-4}$ kcal/mol

for wB97XD). The agreement between the level used in this paper (wB97XD) and the highest-level calculations (MP2) is **very good**.

The investigation of the potential energy surface of the rings results in the localization of transition state with $\Delta E_{\text{inv}}^{\ddagger} = 5.2$ at wB97XD/Def2TZVP (similar transition state was localized in the literature by Shishkina et al. $\Delta E_{\text{inv}}^{\ddagger} = 4.1$ with MP2/6-311G(d,p) method). Energy barrier is slightly underestimated at wB97XD/Def2TZVP level but the agreement between the level used in this paper (wB97XD) and the highest-level calculations (MP2) is still **good**.

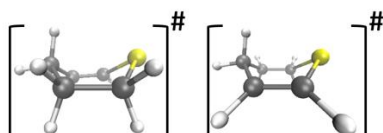


Figure S1 Localization transition states at wB97XD/Def2TZVP level.

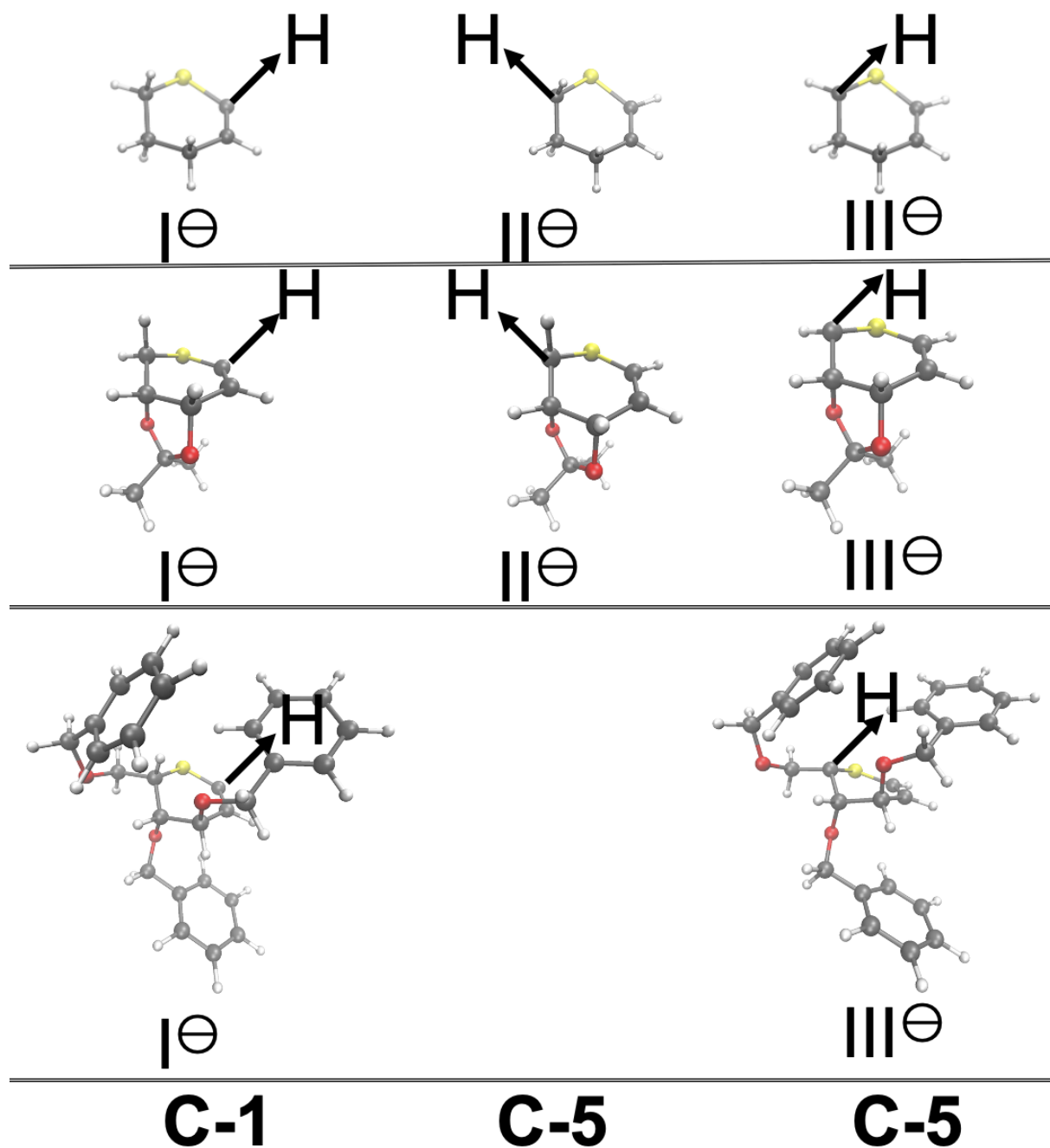


Figure S2 Three different possible anions I-III⁻ for thioglycols at wB97XD/Def2TZVP level.

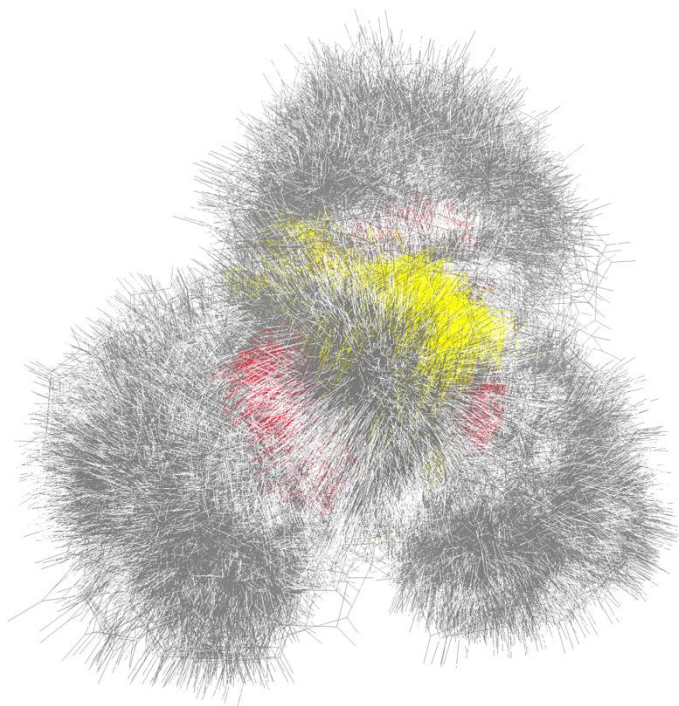
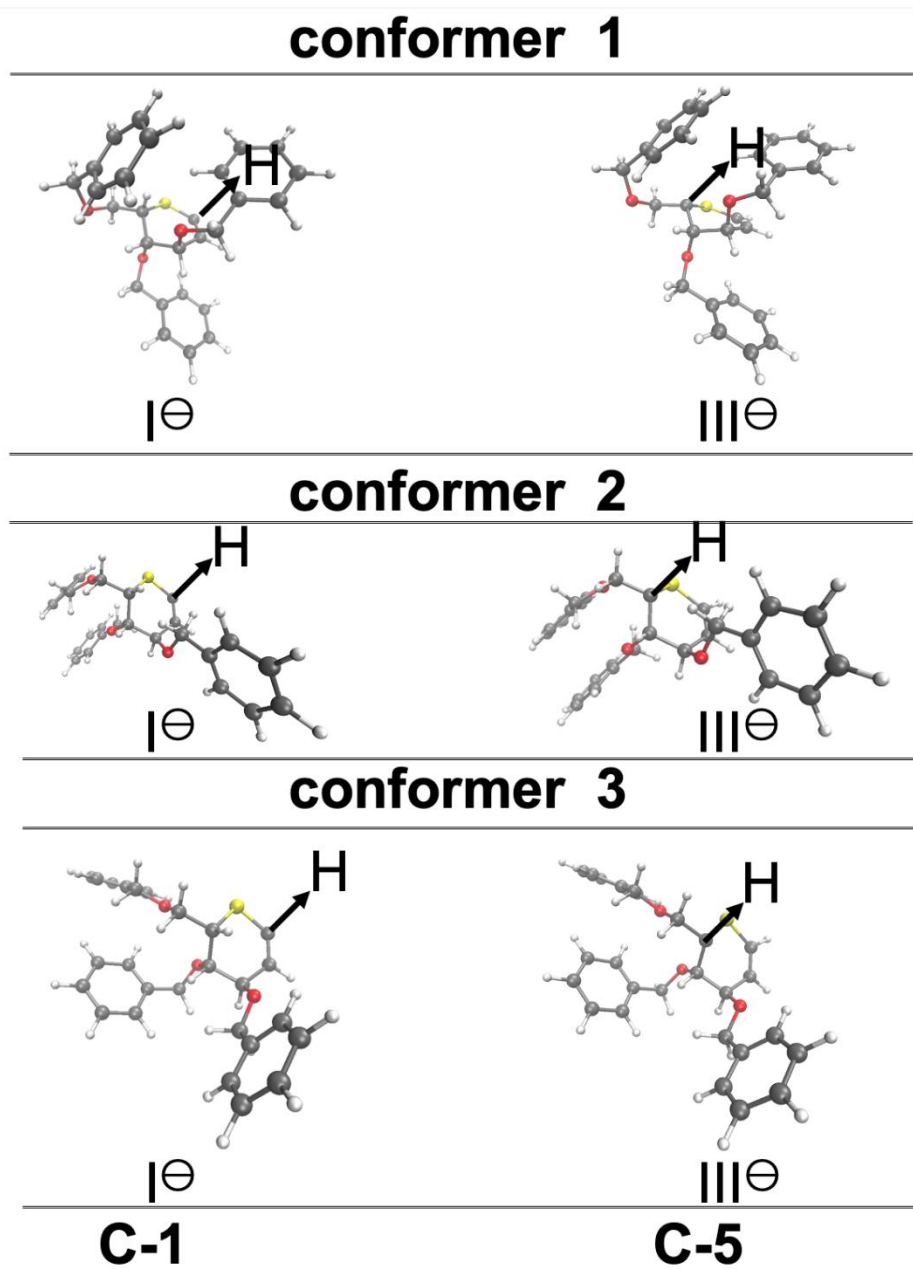


Figure S3 Superposition of atoms for the thioglycal **6** using 4124 snapshots obtained at GFN2-xTB level of theory.



thioglycol 6				
Site	Anion	Conformer 1	Conformer 2	Conformer 3
C-1	I ⁻	0.00	4.87	4.16
C-5	III ⁻	2.86	0.00	0.00

Figure S4 The deprotonation ability of three different conformers of thioglycol 6 system at wB97XD/Def2TZVP level in kcal/mol. The smallest value was chosen as reference for each case. Conformer 1 was the most stable among the 4124 conformers.

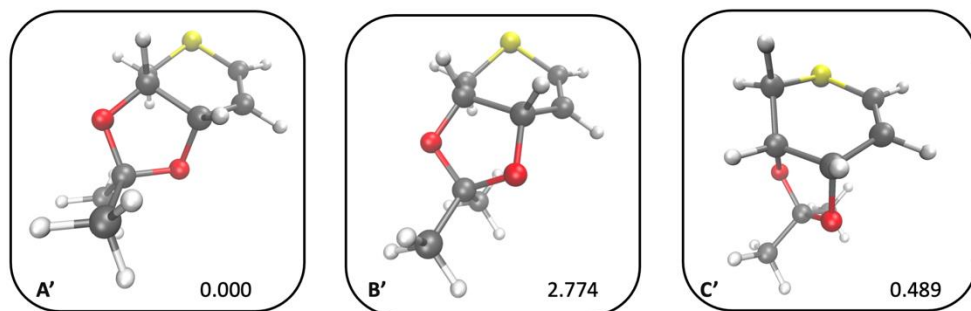


Figure S5 Optimization of three conformers of thioglycolaldehyde **3** localized at wB97X-D/ Def2TZVP level. Six conformers were obtained at the GFN2-xTB level. Full geometry optimizations at the wB97X-D/Def2TZVP level reduced these to three conformers.
