Electronic Supplementary Material (ESI) for RSC Advances.

SUPPLEMENTARY MATERIAL

ON THE USE OF ^{1}H NMR CHEMICAL SHIFTS AND THERMODYNAMIC DATA FOR THE PREDICTION OF THE PREDOMINANT CONFORMATION OF ORGANIC MOLECULES IN SOLUTION: The example of the flavonoid Rutin

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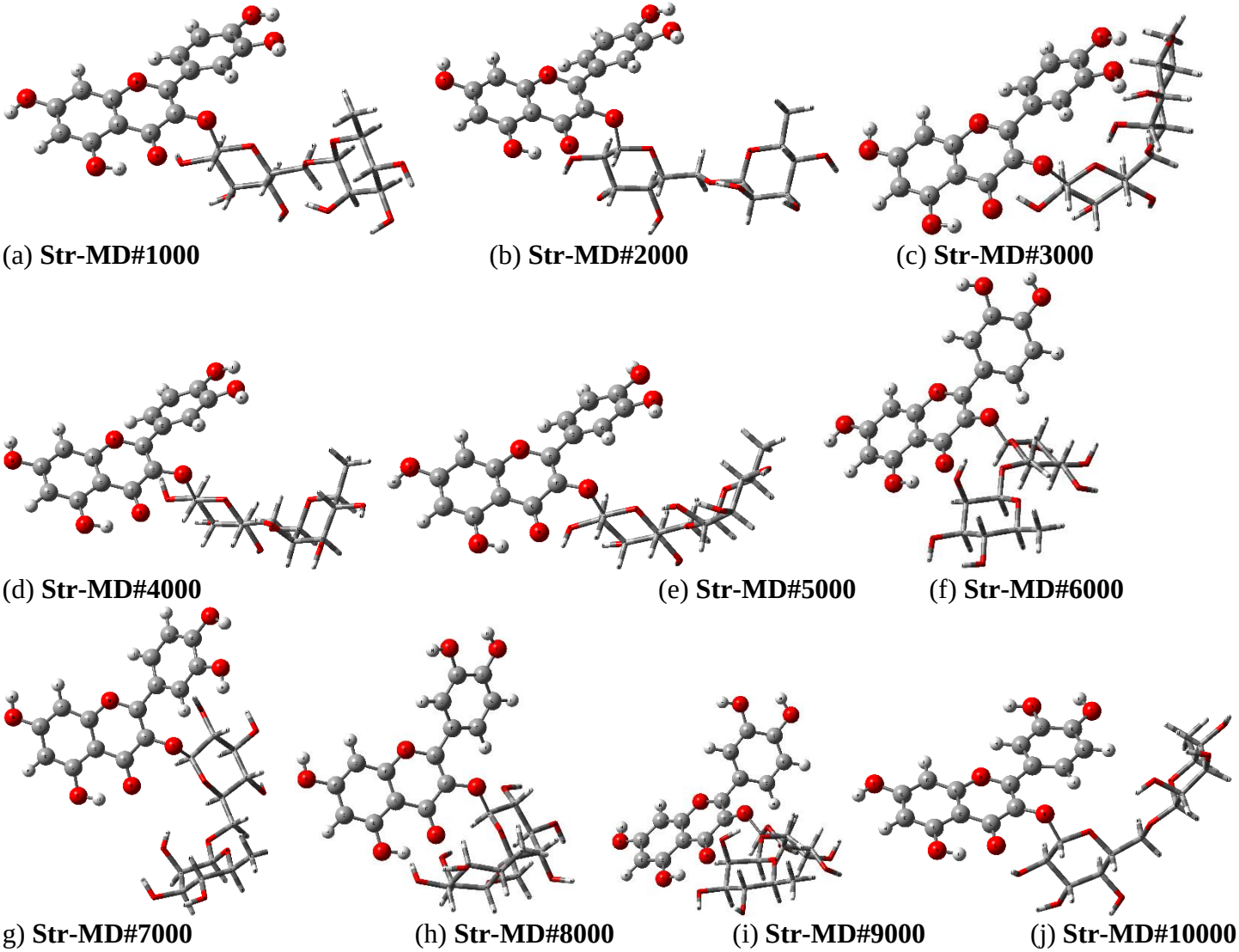


(a) **Str-MD#1000** (b) **Str-MD#2000** (c) **Str-MD#3000**

(d) **Str-MD#4000** (e) **Str-MD#5000** (f) **Str-MD#6000**

g) **Str-MD#7000** (h) **Str-MD#8000** (i) **Str-MD#9000** (j) **Str-MD#10000**

Figure S1. ωB97x-D /6-31G(d,p) new fully optimized structures of rutin obtained from ten frames (from a total of 10000) of MD simulation in DMSO. The optimized torsion angle values are given in Table S1.

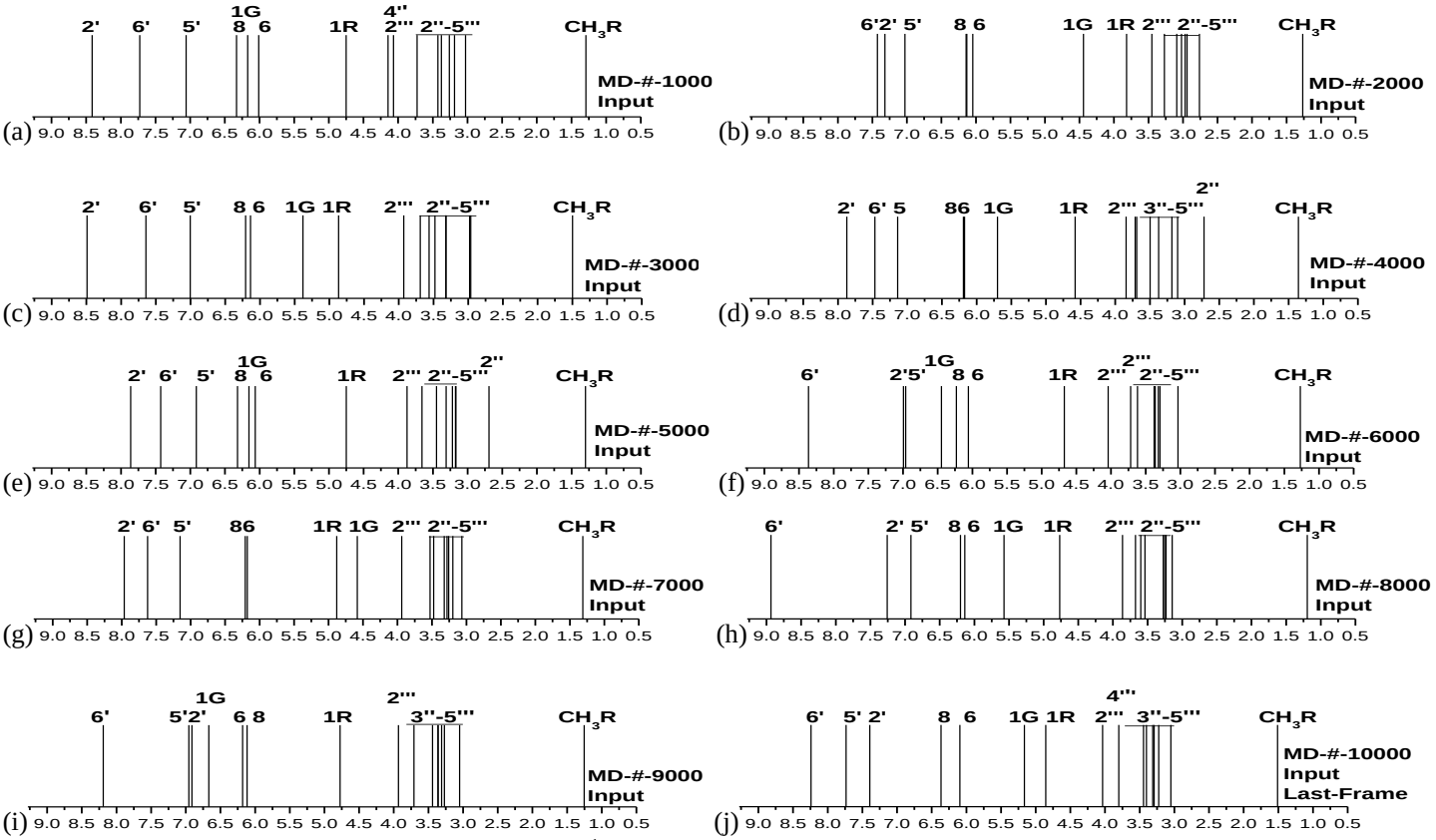


Figure S2. B3LYP/6-31G(d,p)-PCM-DMSO ^{1}H NMR spectra for DFT optimized rutin structures (MD inputs)

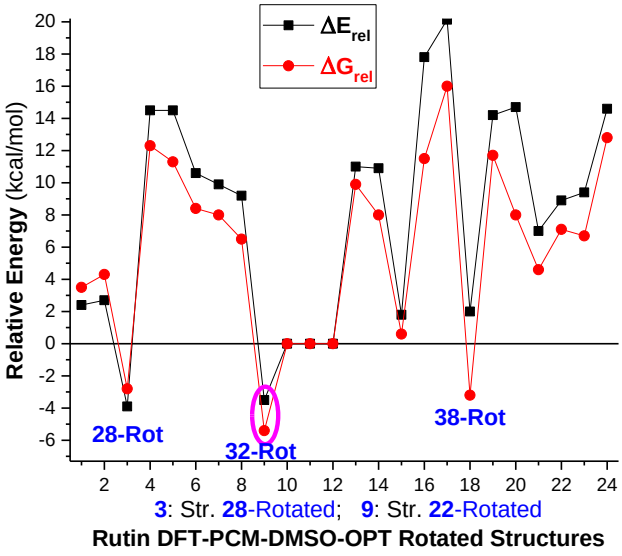


Figure S3. ωB97x-D /6-31G(d,p)-PCM-DMSO relative energies (**ΔE_{rel}** and **ΔG_{rel}** in kcal mol^{-1}) for relevant fully optimized and ϕ_1, ϕ_s rotated structures structures located on the PES for rutin. ΔG_{rel} was estimated using thermal corrections for DFT fully optimized structures (the ϕ_1, ϕ_s rotated structures are not true minimum on the PES, so harmonic frequency calculations, needed for evaluation of thermal correction, are meaningless).

1: Str-**28**-PCM-OPT; **2:** Str-**28** Vacuum-OPT; **3: Str-28-PCM-OPT-Rotated**; **4**: Str-**30**-PCM-OPT; **5:** Str-**30** Vacuum-OPT; **6: Str-30-PCM-OPT-Rotated; 7:** Str-**32**-PCM-OPT; **8:** Str-**32** Vacuum-OPT**; 9: Str-32-PCM-OPT-Rotated; 10**: Str-**34**-PCM-OPT; **11:** Str-**34** Vacuum-OPT; **12: Str-34-PCM-OPT-Rotated**; **13:** : Str-**37**-PCM-OPT; **14:** Str-**37** Vacuum-OPT; **15: Str-37-PCM-OPT-Rotated**; **16:**: Str-**38**-PCM-OPT; **17:** ; Str-**38** Vacuum-OPT; **18: Str-38-PCM-OPT-Rotated**;**19:**: Str-**42**-PCM-OPT; **20:** ; Str-**42** Vacuum-OPT; **21: Str-42-PCM-OPT-Rotated**; **22:** : Str-**44**-PCM-OPT; **23:** Str-**44** Vacuum-OPT; **24: Str-44-PCM-OPT-Rotated**.

Table S1. Deviation between ωB97x-D/6-31G(d,p)-PCM-DMSO and B3LYP/6-31G(d,p)-PCM-DMSO ^{1}H NMR chemical shifts (in ppm) for rotated structures of rutin. MAE (in ppm) values are also given.

CH_n Protons	Str.-28-Rot	Str.-30-Rot	Str.-32-Rot	Str.-34-Rot	Str.-37-Rot	Str.-42-Rot	Str.-44-Rot
H-C6	0.19	0.19	0.17	0.24	0.29	0.16	0.25
H-C8	0.18	0.22	0.2	0.18	0.13	0.16	0.19
H-C2'	0.15	0.18	0.20	0.16	0.08	0.24	0.14
H-C5'	0.22	0.21	0.22	0.20	0.21	0.16	0.16
H-C6'	0.15	0.18	0.25	0.21	0.19	0.13	0.18
H-C1-R	-0.23	-0.12	-0.11	-0.10	-0.07	-0.05	-0.09
H-C1-G	-0.21	-0.05	-0.14	-0.09	-0.09	-0.14	-0.07
H-CH3	-0.05	0.003	-0.006	0.03	0.02	0.04	0.03
H-2"	-0.01	-0.11	0.05	-0.03	-0.24	-0.07	-0.09
H-3"	-0.03	-0.01	-0.01	0.013	0.01	-0.002	0.03
H-4"	0.004	-0.10	-0.01	-0.13	-0.14	-0.02	-0.10
H-5"	-0.13	-0.11	-0.12	-0.04	-0.06	-0.04	-0.06
H-2"'	-0.04	-0.07	-0.02	-0.07	-0.03	-0.04	-0.05
H-3"'	-0.21	0.04	0.03	0.07	0.14	0.12	0.09
H-4"'	0.01	-0.02	-0.04	-0.05	-0.14	-0.12	-0.11
H-5"'	-0.30	-0.05	-0.06	0.04	0.03	0.01	-0.001
MAE	**0.13**	**0.10**	**0.10**	**0.10**	**0.12**	**0.09**	**0.10**

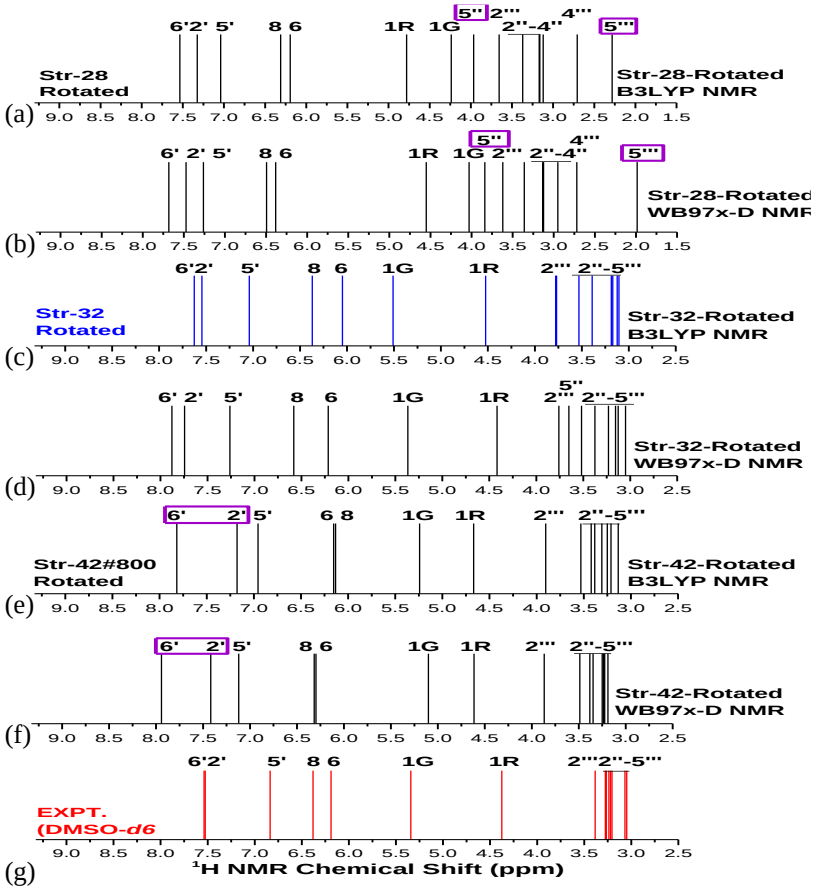
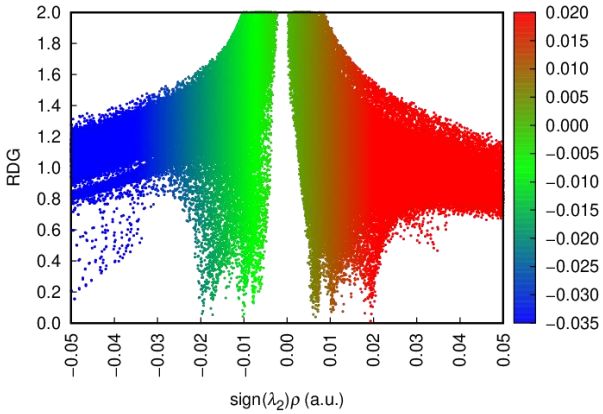
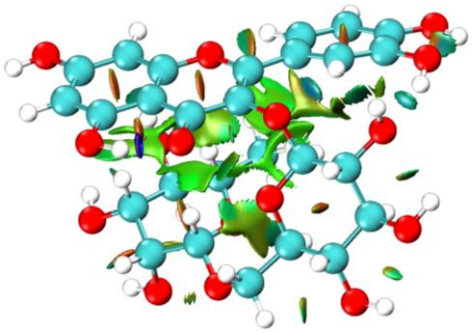


Figure S4. B3LYP/6-31G(d,p)-PCM-DMSO and ωB97x-D /6-31G(d,p)-PCM-DMSO ^{1}H NMR spectra for selected structures of rutin (ωB97x-D /6-31G(d,p)-PCM-DMSO optimized geometries) (a-f) and experimental spectra (in DMSO-*d6*) (g). The protons having large deviation from experimental data are highlighted in pink rectangle.



(a) 28 full opt



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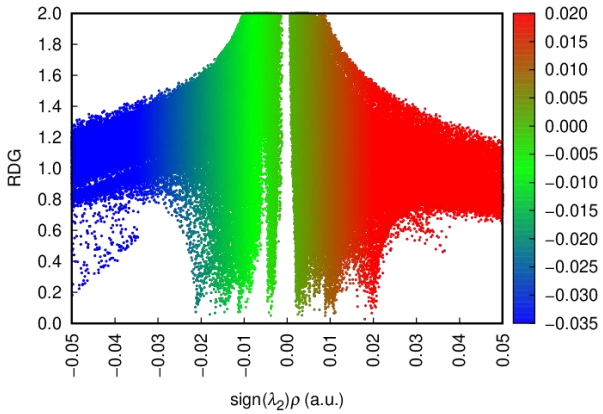
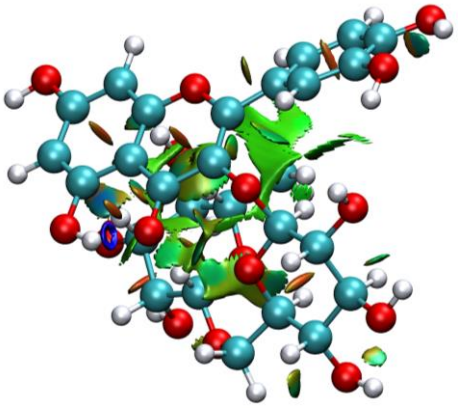
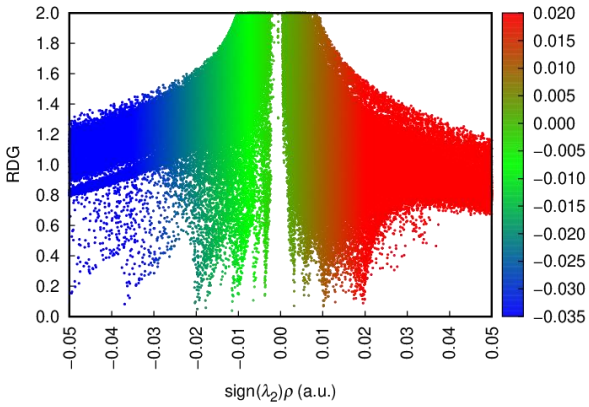


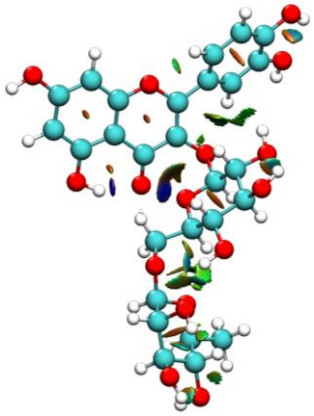
(c) 28 rot



(d) 28 rot



(e) 30 FO



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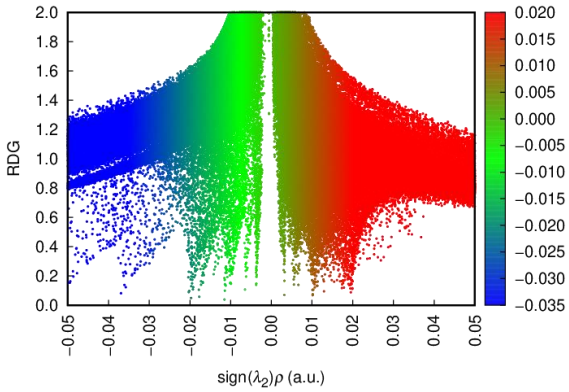

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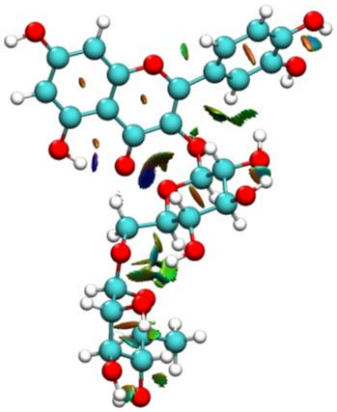

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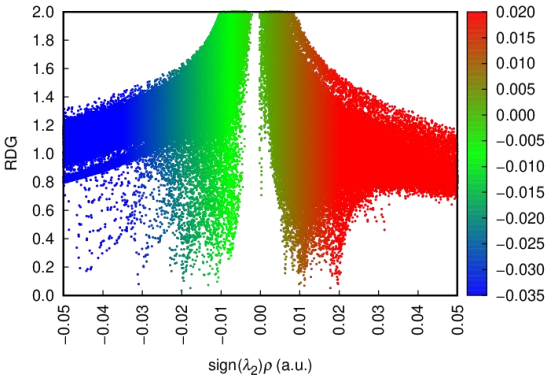

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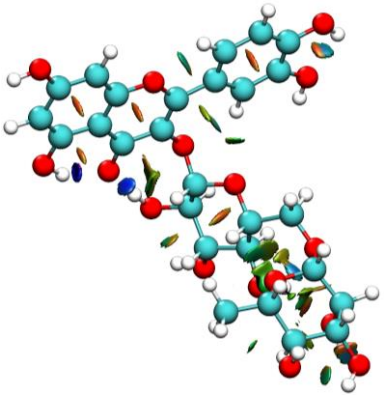

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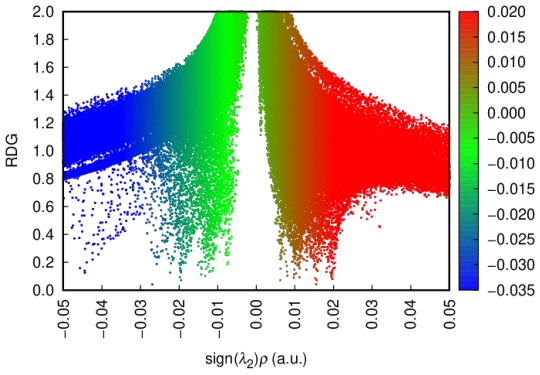

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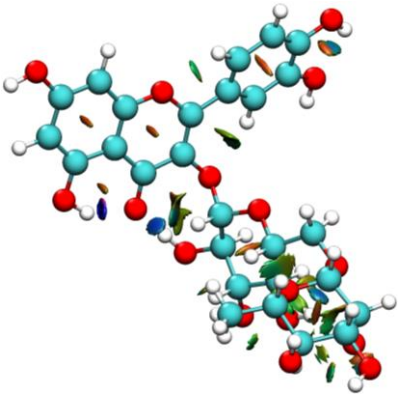

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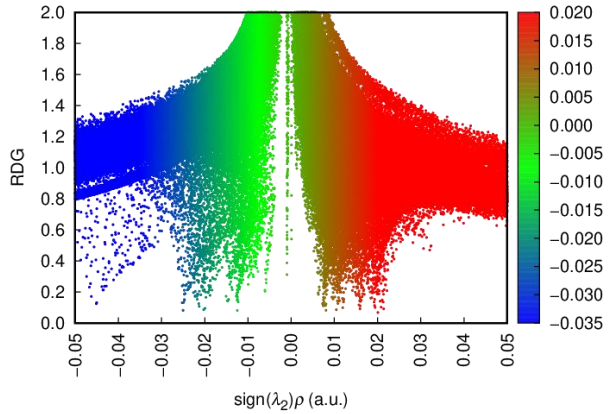
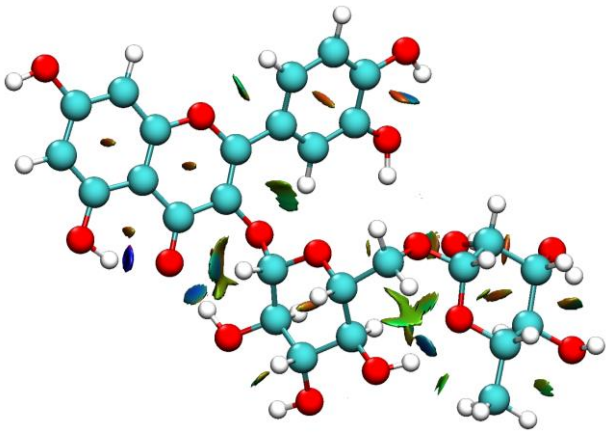


(m) 34 FO



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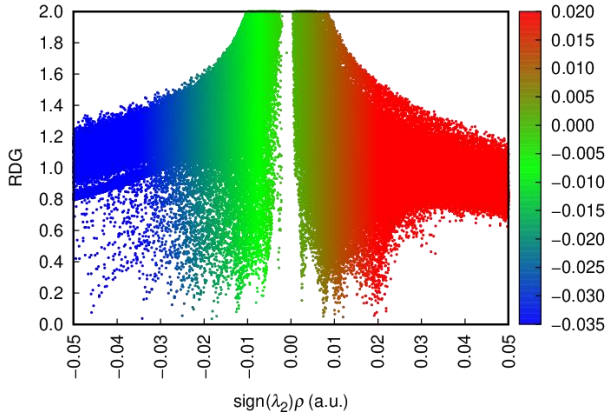

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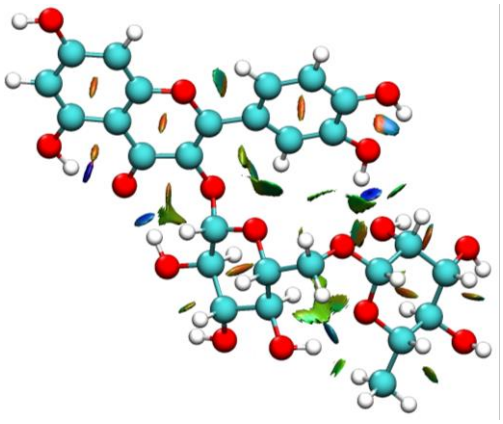
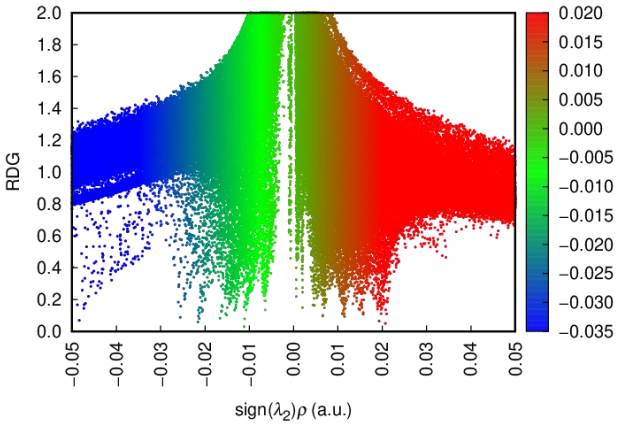
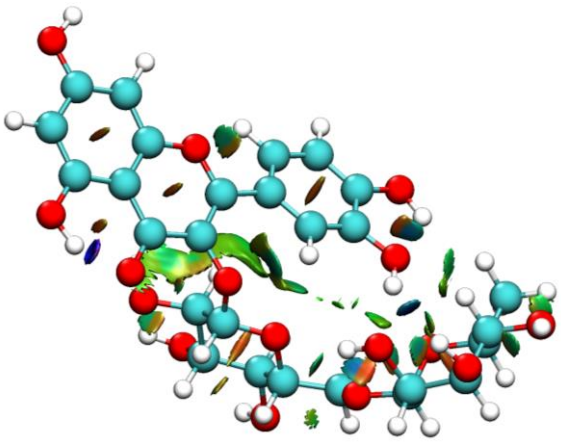


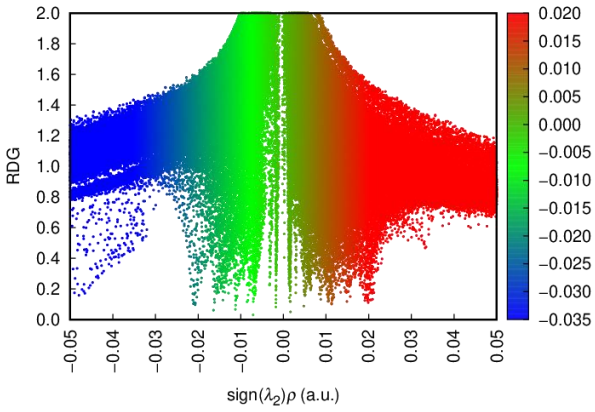
(p) 34 ROT



(q) 37 FO



(r) 37 FO



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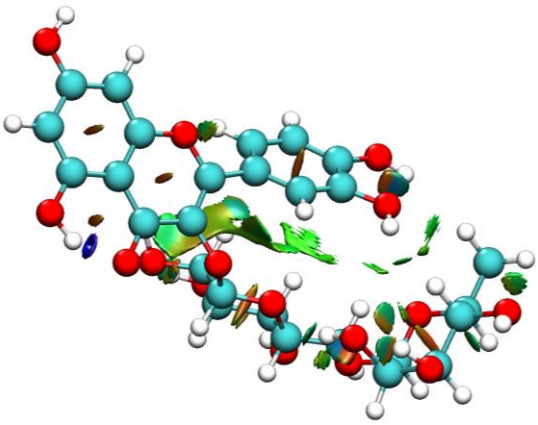

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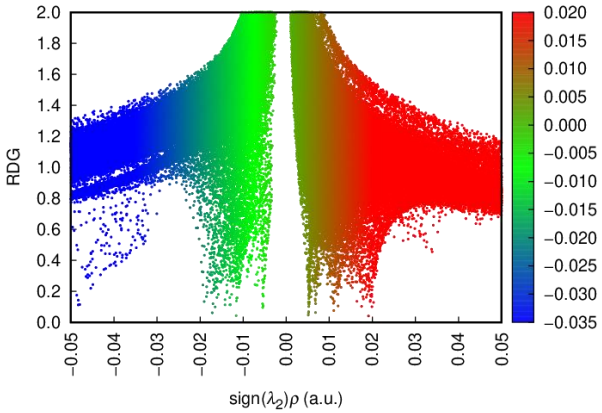

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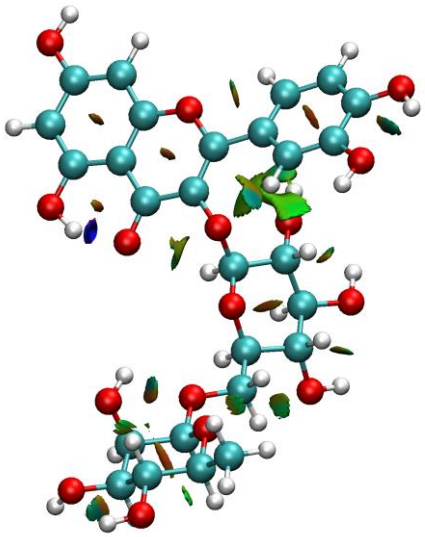

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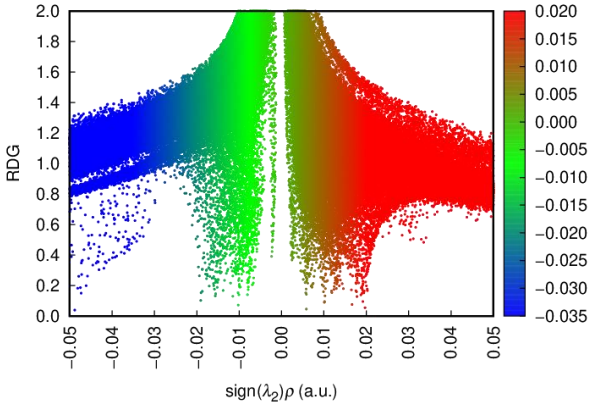

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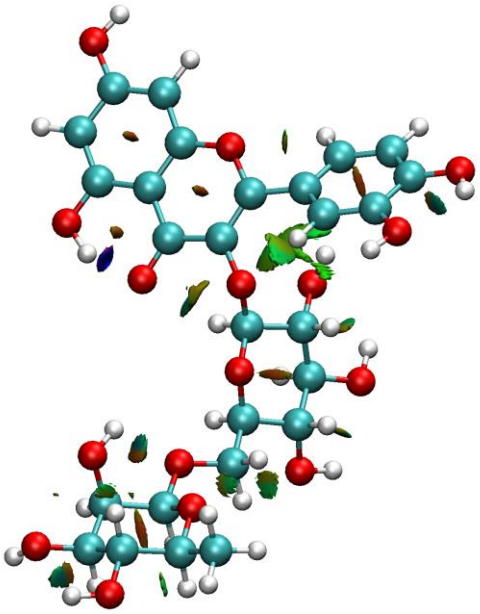
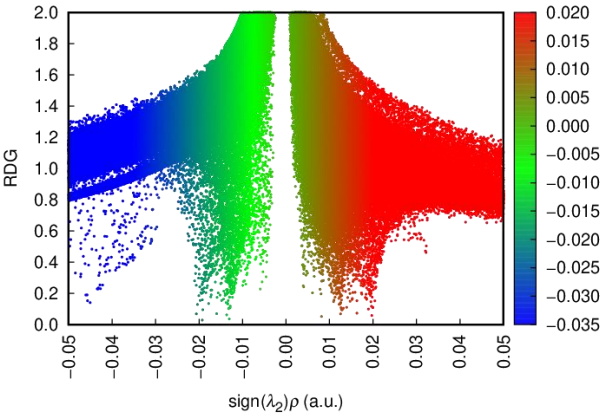
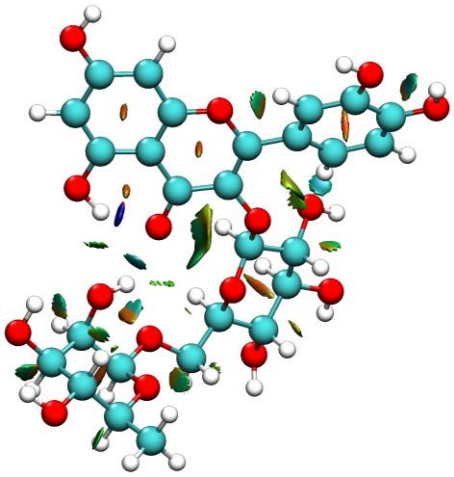


(x) 38 ROT



(y) 42 OPT



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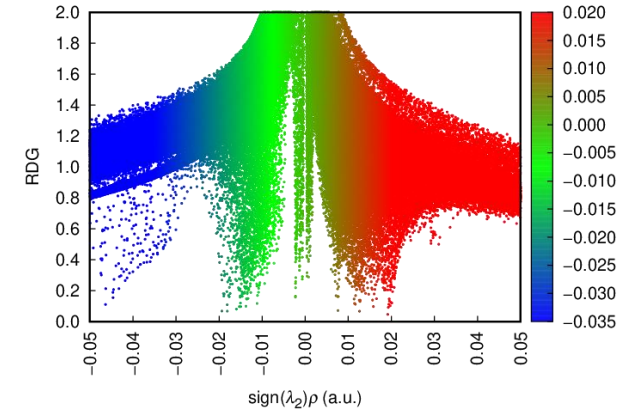
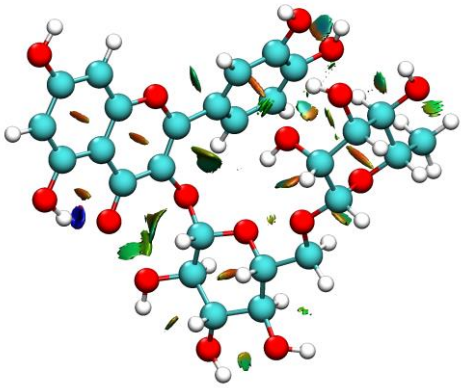
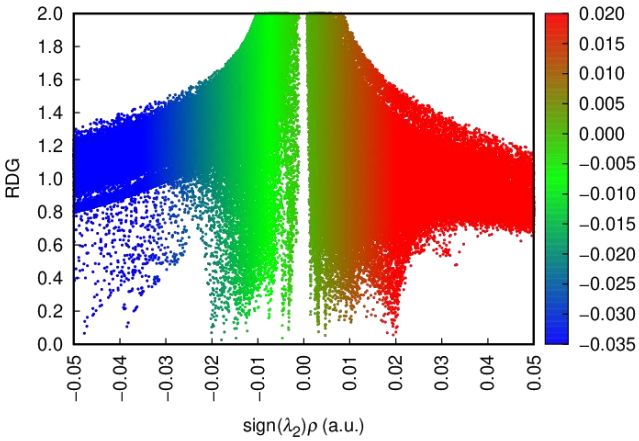


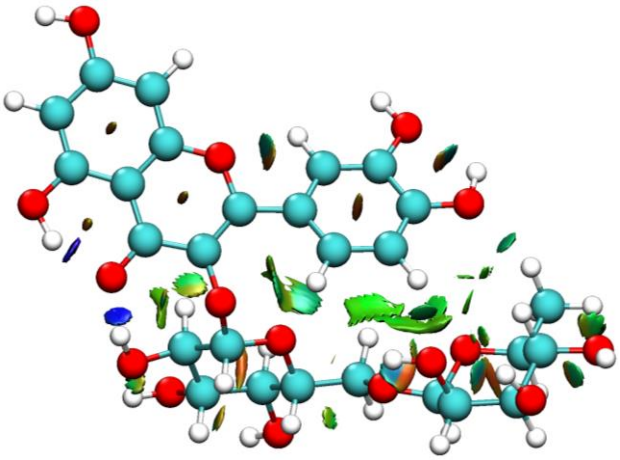
(aa) 42 ROT



(ab) 42 ROT



(ac) 44 FO



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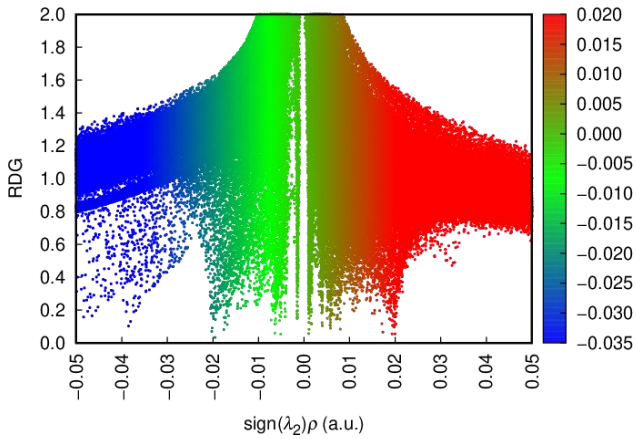
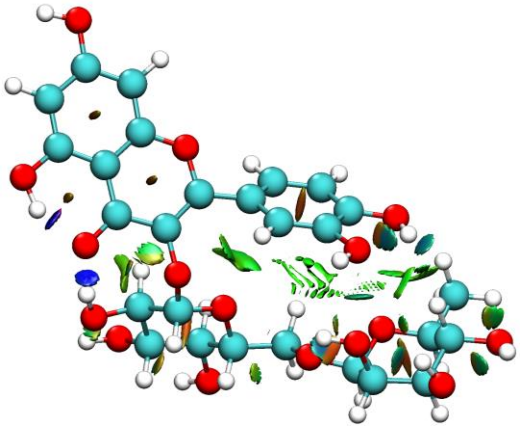


(ae) 44 ROT



(af) 44 ROT

Figure S5. Bi and tridimensional NCI plots calculated at ωB97x-D/6-31G(d,p) – PCM DMSO level of theory (FO = Fully Optimized and ROT = rotated).

Table S2. Selected ωB97x-D /6-31G(d,p)-PCM-DMSO optimized torsion angles (º) for fully optimized structures located on the PES for rutin using relevant MD frames as input and MD original frames (#300, #400, #800 and #1000) not optimized structures. Relative energy values (ΔE_{rel} in kcal mol^{-1}) for DFT-PCM optimized geometries and original MD frames inputs (DFT-PCM single point calculations) are also given.

Structures	**φ1** [O-C2-C1'-C2']	**φ2** [C1''-O-C3-C2]	**φ3** [C2''-C1''-O-C3]	**φ4** [O-C6''-C5''-O]	**φ5** [C1'''-O-C6''-C5'']	**φ6** [C1'''-O-C6''-C5'	**ΔE_{rel}**
37 PCM-DMSO-FULL-OPT (DM-#300) [a]	158.3	-92.5	14.3	57.9	-166.2	168.1	**2.2**
37 DM-#300 Original Frame (non-opt)[b]	**106.0**	-110.0	**57.7**	39.5	-167.6	174.1	**-13.4** [c] (197) [d]
38 PCM-DMSO-FULL-OPT (DM-#400) [a]	153.2	-113.8	93.0	69.4	170.8	-175.2	**8.9**
38 DM-#400 Original Frame (non-opt)[b]	114.4	-117.6	70.8	102.3	-165.0	167.4	**8.6** [c] (194) [d]
42 PCM-DMSO-FULL-OPT (DM-#800) [a]	29.3	-141.2	134.3	67.5	-169.8	175.3	**5.3**
42 DM-#800 Original Frame (non-opt [b]	**72.6**	-141.3	**77.7**	84.9	-157.7	174.8	**-8.7** [c] (133) [d]
44 PCM-DMSO-FULL-OPT (DM (#1000) [a]	-20.9	-92.0	-37.7	68.8	165.6	-179.8	**0.0**
44 DM-#1000 Original Frame (non-opt)[b]	**34.8**	**-141.9**	**65.3**	72.9	-170.1	178.3	**0.0** [c] (0.0) [d]

[a] ωB97x-D /6-31G(d,p)-PCM-DMSO optimized torsion angles (º); [b] DM original frame (non-optimized) torsion angle.
[c] ωB97x-D /6-31G(d,p)-PCM-DMSO relative energy single-point using DM original frame (non-optimized) structure
[d] Classical DM relative energy (using Force Field) using DM original frame (non-optimized) structure

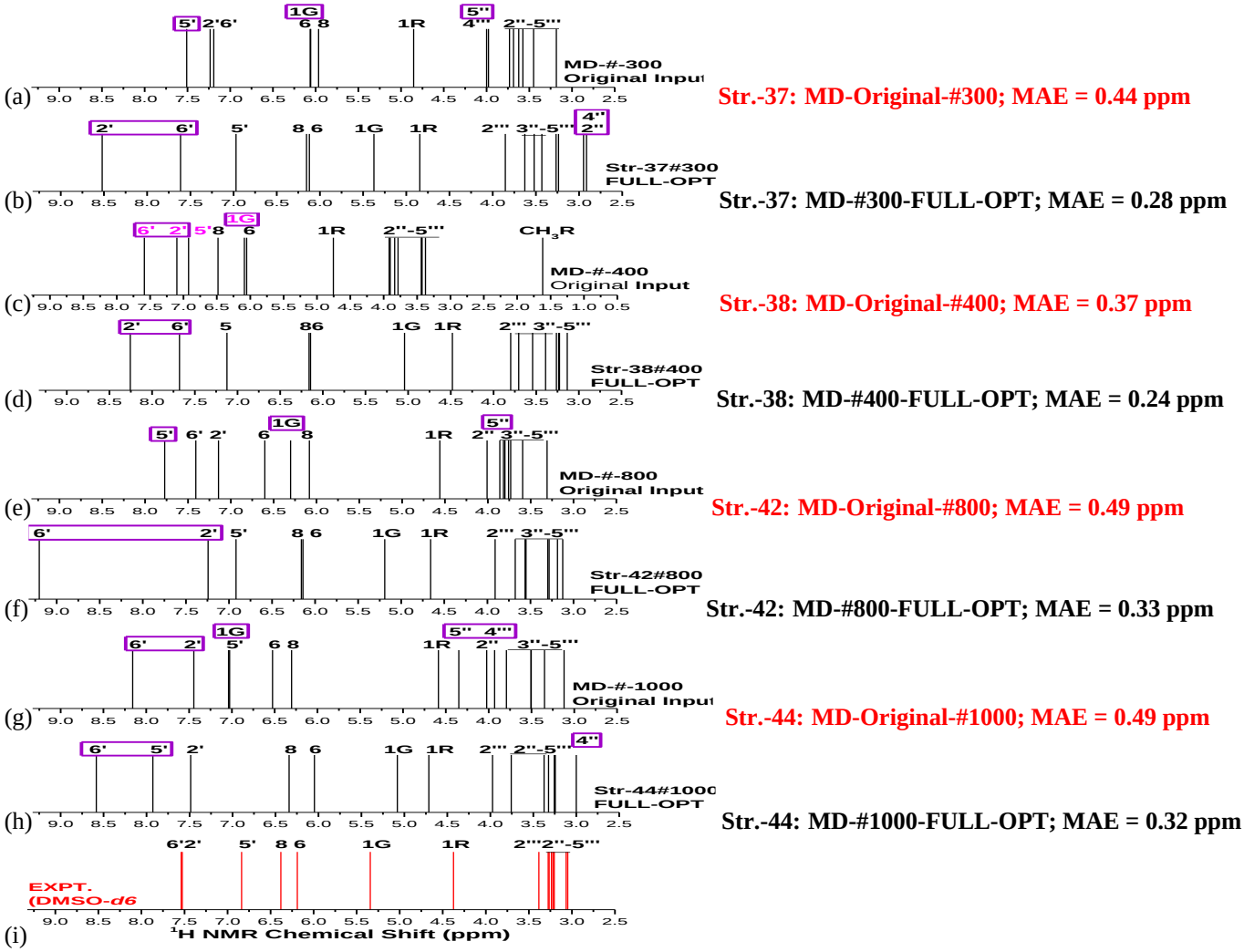


Figure S6. B3LYP/6-31G(d,p)-PCM-DMSO ^{1}H NMR spectra for selected structures **37**, **42** and **44** of rutin obtained from DM frames. Three distinct structures were used in the DFT-PCM NMR calculations: (i) Original DM frames (not optimized) (a,c,e,g) (ii) DFT-PCM-DMSO fully optimized DM inputs (b,d,f,h) and (iii) ϕ_1, ϕ_s torsion angles rotated structures (c,f,i). The experimental ^{1}H NMR spectrum (in DMSO-*d6*) is also shown (i).
The protons having large deviation from experimental data are highlighted in pink rectangle.