Combining the power of DP4+ and ANN-PRA analysis on stereochemical assignments: Structural validation of bioactive cyclic peroxide from the marine sponge *Plakortis angulospiculatus*.

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Supplementary information

Calculations:

Randomized conformational searches were performed for all the stereoisomers, using the Monte Carlo method and MMFF force field, in the Spartan'10 software package.[1] For isomer 1, 319 conformers with relative energy within 10 kcal mol^{-1} of the lowest energy conformer were selected for further geometry optimized at the B3LYP/6-31G* level. 59 conformers were identified with relative energy < 2.0 kcal mol^{-1}, corresponding to more than 82% of the total Boltzmann distribution. For isomer 2, 334 conformers with relative energy within 10 kcal mol^{-1} of the lowest energy conformer were selected for further geometry optimized at the B3LYP/6-31G* level. 52 conformers were identified with relative energy < 2.0 kcal mol^{-1}, corresponding to more than 87% of the total Boltzmann distribution. For isomer 3, 279 conformers with relative energy within 10 kcal mol^{-1} of the lowest energy conformer were selected for further geometry optimized at the B3LYP/6-31G* level. 94 conformers were identified with relative energy < 2.0 kcal mol^{-1}, corresponding to more than 90% of the total Boltzmann distribution. For isomer 4, 156 conformers with relative energy within 10 kcal mol^{-1} of the lowest energy conformer were selected for further geometry optimized at the B3LYP/6-31G* level. 16 conformers were identified with relative energy < 2.0 kcal mol^{-1}, corresponding

to more than 83% of the total Boltzmann distribution. For isomer 5, 84 conformers with relative energy within 10 kcal mol^{-1} of the lowest energy conformer were selected for further geometry optimized at the B3LYP/6-31G* level. 11 conformers were identified with relative energy < 2.0 kcal mol^{-1}, corresponding to more than 85% of the total Boltzmann distribution. For isomer 6, 255 conformers with relative energy within 10 kcal mol^{-1} of the lowest energy conformer were selected for further geometry optimized at the B3LYP/6-31G* level. 55 conformers were identified with relative energy < 2.0 kcal mol^{-1}, corresponding to more than 86% of the total Boltzmann distribution. For isomer 7, 96 conformers with relative energy within 10 kcal mol^{-1} of the lowest energy conformer were selected for further geometry optimized at the B3LYP/6-31G* level. 40 conformers were identified with relative energy < 2.0 kcal mol^{-1}, corresponding to more than 91% of the total Boltzmann distribution. For isomer 8, 276 conformers with relative energy within 10 kcal mol^{-1} of the lowest energy conformer were selected for further geometry optimized at the B3LYP/6-31G* level. 20 conformers were identified with relative energy < 2.0 kcal mol^{-1}, corresponding to more than 75% of the total Boltzmann distribution. For each selected structure, ^{13}C and ^{1}H NMR chemical shifts were calculated using the GIAO-mPW1PW91/6-31G(d)//B3LYP/6-31G(d)DFT approach, using the tetramethylsilane (TMS) as an internal reference, at the same level of theory. The Gaussian 09 software package was used.[2] The simulations were carried out either in the gas phase or chloroform solutions, using the polarizable continuum model (PCM) in its integral equation formalism version (IEFPCM) in Gaussian. In order to apply the DP4+ parameter, it was used the Excel spreadsheet provided by the authors.[3] For the application of the ANN-PRA method, NMR chemical shifts obtained at the same theoretical level as in the DP4+ method were used, following the instructions of ANN-PRA[4], using the Excel spreadsheet provided by the authors at sarotti-NMR.weebly.com.

Table S1: Lowest energy conformers of isomer 1 of isolated compound at B3LYP/6-31G* level.

Figure S1: The 9 lowest energy conformers of isomer 1 of isolated compound at B3LYP/6-31G* level.

Table S2: Lowest energy conformers of isomer 2 of isolated compound at B3LYP/6-31G* level.

Figure S2: The 9 lowest energy conformers of isomer 2 of isolated compound at B3LYP/6-31G* level.

Table S3: Lowest energy conformers of isomer 3 of isolated compound at B3LYP/6-31G* level.

Figure S3: The 9 lowest energy conformers of isomer 3 of isolated compound at B3LYP/6-31G* level.

Table S4: Lowest energy conformers of isomer 4 of isolated compound at B3LYP/6-31G* level.

Figure S4: The 9 lowest energy conformers of isomer 4 of isolated compound at B3LYP/6-31G* level.

Table S5: Lowest energy conformers of isomer 5 of isolated compound at B3LYP/6-31G* level.

Figure S5: The 9 lowest energy conformers of isomer 5 of isolated compound at B3LYP/6-31G* level.

Table S6: Lowest energy conformers of isomer 6 of isolated compound at B3LYP/6-31G* level.

Figure S6: The 9 lowest energy conformers of isomer 6 of isolated compound at B3LYP/6-31G* level.

Table S7: Lowest energy conformers of isomer 7 of isolated compound at B3LYP/6-31G* level.

Figure S7: The 9 lowest energy conformers of isomer 7 of isolated compound at B3LYP/6-31G* level.

Table S8: Lowest energy conformers of isomer 8 of isolated compound at B3LYP/6-31G* level.

Figure S8: The 9 lowest energy conformers of isomer 8 of isolated compound at B3LYP/6-31G* level.

Table S9: Comparison of calculated δ_{scal} (generalized scaling factor) ^{13}C NMR chemical shifts simulated for the possible stereoisomers of **1** (GIAOmPW1PW91/6-31G(d)//B3LYP/6-31G(d)) with the experimental values (δ_{exp}, 90.5 MHz, $CDCl_3$) of the isolated natural product.

Table S10 Comparison of calculated δ_{scal} (internal scaling factor) ^{13}C NMR chemical shifts simulated for the possible stereoisomers of **1** (GIAOmPW1PW91/6-31G(d)//B3LYP/6-31G(d)) with the experimental values (δ_{exp}, 90.5 MHz, $CDCl_3$) of the isolated natural product.

Table S11: Boltzmann averaged ^{13}C GIAO isotropic magnetic shielding values calculates for all possible stereoisomers of 1 at mPW1PW91/6-31G(d)//B3LYP/6-31G(d).

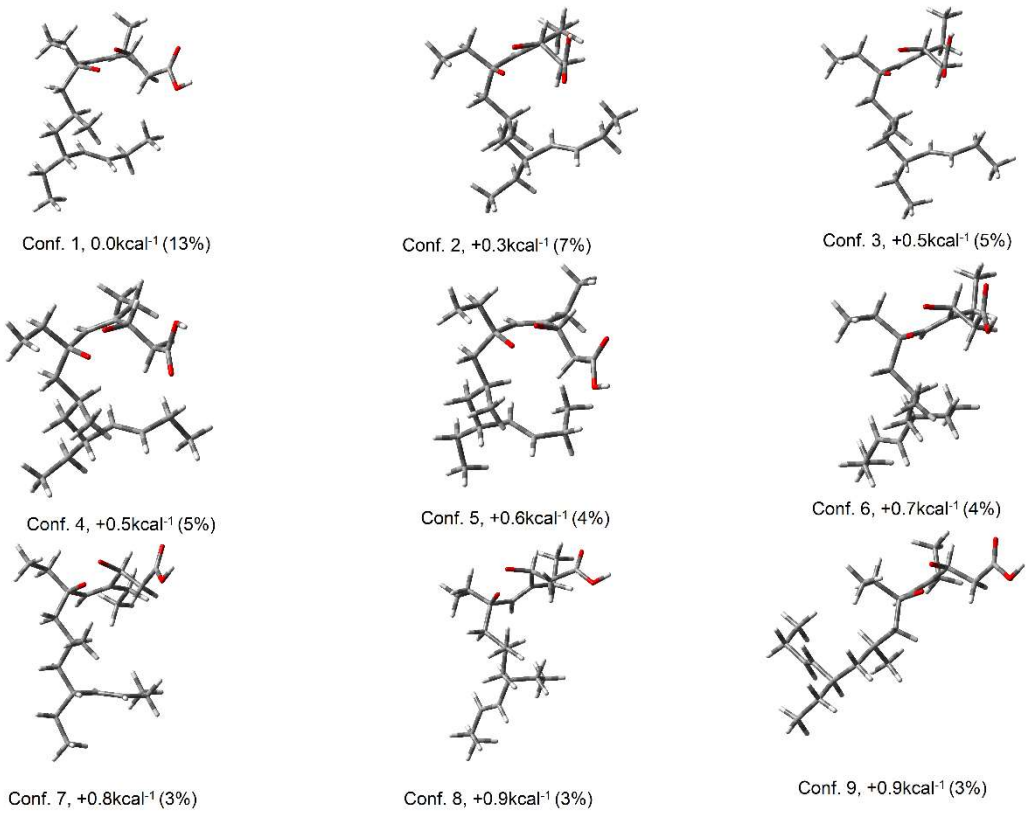
Table S12: Boltzmann averaged ^{1}H GIAO isotropic magnetic shielding values calculates for all possible stereoisomers of 1 at mPW1PW91/6-31G(d)//B3LYP/6-31G(d).

Table S1: Lowest energy conformers of isomer 1 of isolated compound at B3LYP/6-31G* level.

Conformers isomer 1	**Rel. Energy (kcal/mol)**	**Boltzmann population**
isomer1_conf1	0.00	12.73%
isomer1_conf2	0.34	7.21%
isomer1_conf3	0.52	5.28%
isomer1_conf4	0.53	5.19%
isomer1_conf5	0.65	4.25%
isomer1_conf6	0.74	3.65%
isomer1_conf7	0.85	3.01%
isomer1_conf8	0.88	2.88%
isomer1_conf9	0.90	2.78%
isomer1_conf10	0.94	2.58%
isomer1_conf11	1.04	2.20%
isomer1_conf12	1.04	2.18%
isomer1_conf13	1.05	2.16%
isomer1_conf14	1.05	2.14%
isomer1_conf15	1.13	1.89%
isomer1_conf16	1.19	1.70%
isomer1_conf17	1.21	1.65%
isomer1_conf18	1.23	1.60%
isomer1_conf19	1.24	1.56%
isomer1_conf20	1.25	1.54%
isomer1_conf21	1.25	1.54%
isomer1_conf22	1.26	1.51%
isomer1_conf23	1.27	1.49%
isomer1_conf24	1.31	1.39%
isomer1_conf25	1.38	1.23%

isomer1_conf26	1.45	1.11%
isomer1_conf27	1.45	1.11%
isomer1_conf28	1.46	1.09%
isomer1_conf29	1.46	1.08%
isomer1_conf30	1.47	1.07%
isomer1_conf31	1.55	0.93%
isomer1_conf32	1.56	0.91%
isomer1_conf33	1.56	0.91%
isomer1_conf34	1.57	0.91%
isomer1_conf35	1.57	0.89%
isomer1_conf36	1.59	0.87%
isomer1_conf37	1.61	0.83%
isomer1_conf38	1.62	0.82%
isomer1_conf39	1.63	0.81%
isomer1_conf40	1.64	0.80%
isomer1_conf41	1.69	0.74%
isomer1_conf42	1.71	0.71%
isomer1_conf43	1.75	0.67%
isomer1_conf44	1.78	0.63%
isomer1_conf45	1.80	0.61%
isomer1_conf46	1.80	0.61%
isomer1_conf47	1.82	0.59%
isomer1_conf48	1.86	0.55%
isomer1_conf49	1.86	0.55%
isomer1_conf50	1.87	0.54%
isomer1_conf51	1.88	0.54%
isomer1_conf52	1.89	0.52%
isomer1_conf53	1.90	0.51%
isomer1_conf54	1.92	0.50%
isomer1_conf55	1.94	0.48%
isomer1_conf56	1.98	0.45%
isomer1_conf57	1.99	0.44%
isomer1_conf58	1.99	0.44%
isomer1_conf59	2.00	0.44%

Figure S1: The 9 lowest energy conformers of isomer 1 of isolated compound at B3LYP/6-31G* level.



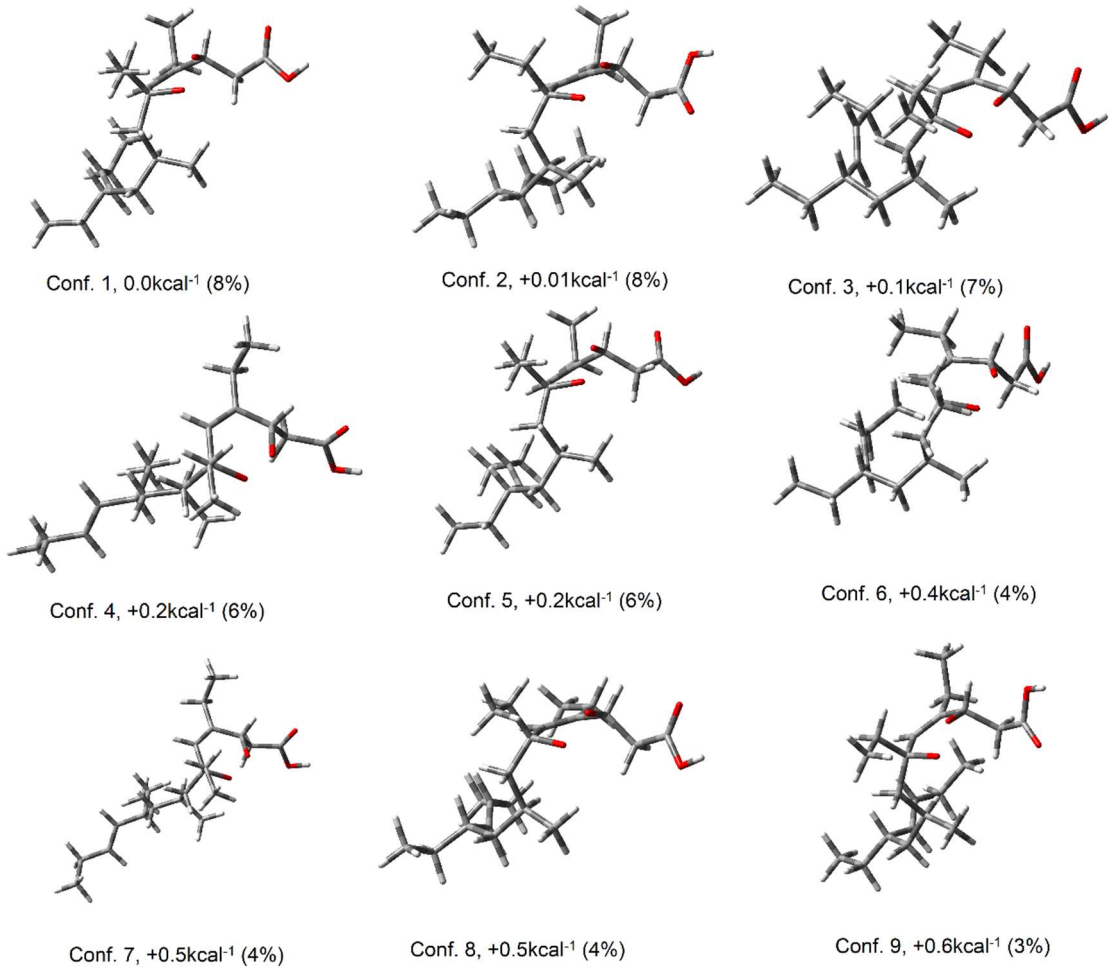
Isomer 1: 319 conformers with relative energy within 10 kcal mol−1 of the lowest energy conformer were selected for further geometry optimized at the B3LYP/6-31G* level. 59 conformers were identified with relative energy < 2.0 kcal mol−1, corresponding to more than 82% of the total Boltzmann distribution.

Table S2: Lowest energy conformers of isomer 2 of isolated compound at B3LYP/6-31G* level.

Conformers isomer 2	Rel. Energy (kcal/mol)	Boltzmann population
isomer2_conf1	0.00	8.45%
isomer2_conf2	0.01	8.33%
isomer2_conf3	0.12	6.93%
isomer2_conf4	0.19	6.10%
isomer2_conf5	0.25	5.50%
isomer2_conf6	0.44	4.00%
isomer2_conf7	0.49	3.71%
isomer2_conf8	0.49	3.68%
isomer2_conf9	0.55	3.36%
isomer2_conf10	0.59	3.10%
isomer2_conf11	0.63	2.89%
isomer2_conf12	0.77	2.30%
isomer2_conf13	0.77	2.30%
isomer2_conf14	0.83	2.09%
isomer2_conf15	0.84	2.03%
isomer2_conf16	0.85	2.03%
isomer2_conf17	0.87	1.94%
isomer2_conf18	0.88	1.92%
isomer2_conf19	0.92	1.78%
isomer2_conf20	0.93	1.77%
isomer2_conf21	0.95	1.70%
isomer2_conf22	0.96	1.67%
isomer2_conf23	0.96	1.67%
isomer2_conf24	1.01	1.52%
isomer2_conf25	1.05	1.42%
isomer2_conf26	1.11	1.30%
isomer2_conf27	1.14	1.24%
isomer2_conf28	1.27	0.99%
isomer2_conf29	1.30	0.94%
isomer2_conf30	1.32	0.91%
isomer2_conf31	1.35	0.86%
isomer2_conf32	1.36	0.85%
isomer2_conf33	1.39	0.80%
isomer2_conf34	1.40	0.80%
isomer2_conf35	1.42	0.77%
isomer2_conf36	1.43	0.76%
isomer2_conf37	1.45	0.73%
isomer2_conf38	1.46	0.72%
isomer2_conf39	1.48	0.69%
isomer2_conf40	1.51	0.66%

isomer2_conf41	1.55	0.61%
isomer2_conf42	1.66	0.51%
isomer2_conf43	1.70	0.48%
isomer2_conf44	1.71	0.47%
isomer2_conf45	1.75	0.44%
isomer2_conf46	1.83	0.38%
isomer2_conf47	1.92	0.33%
isomer2_conf48	1.93	0.32%
isomer2_conf49	1.93	0.32%
isomer2_conf50	1.94	0.32%
isomer2_conf51	1.97	0.30%
isomer2_conf52	1.99	0.29%

Figure S2: The 9 lowest energy conformers of isomer 2 of isolated compound at B3LYP/6-31G* level.



Isomer 2: 334 conformers with relative energy within 10 kcal mol^{-1} of the lowest energy conformer were selected for further geometry optimized at the B3LYP/6-31G* level. 52 conformers were identified with relative energy < 2.0 kcal mol^{-1}, corresponding to more than 87% of the total Boltzmann distribution.

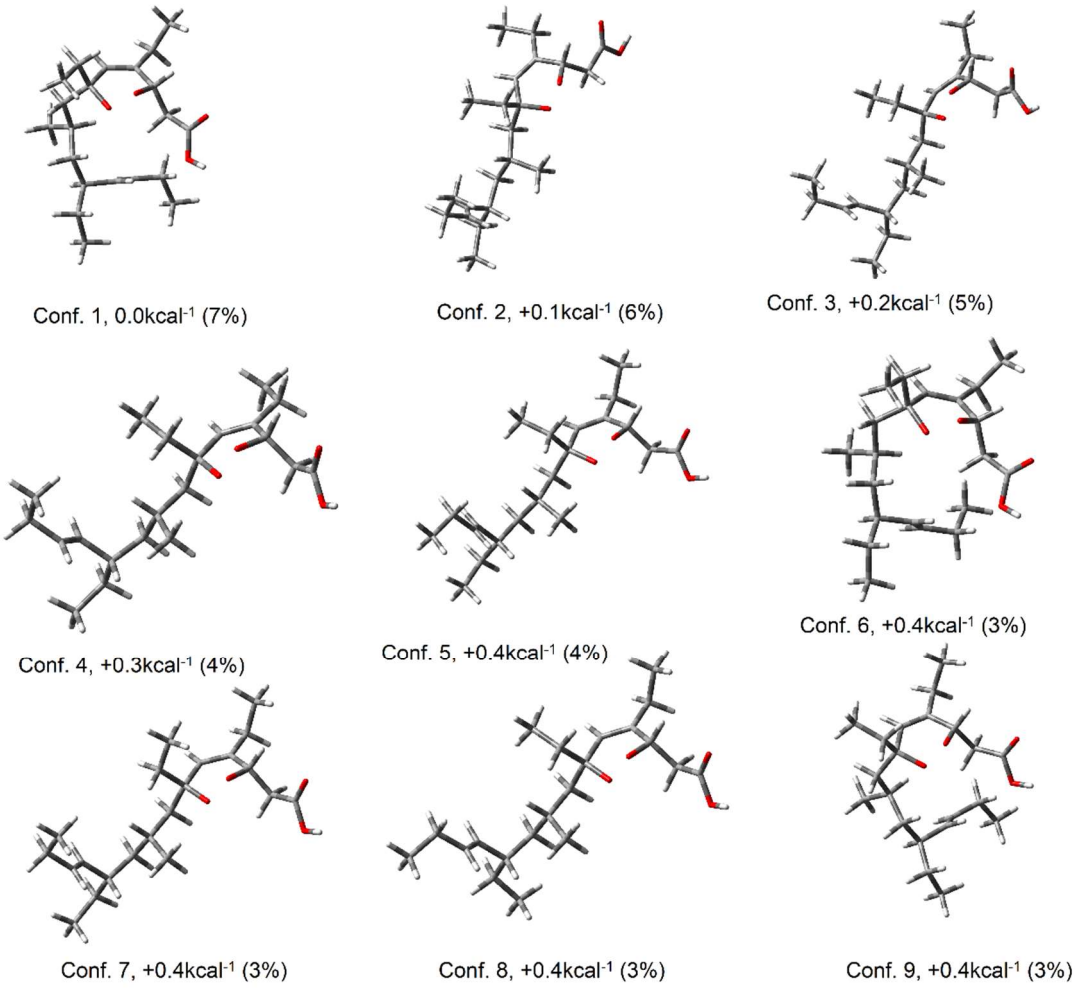
Table S3: Lowest energy conformers of isomer 3 of isolated compound at B3LYP/6-31G* level.

Conformers isomer 3	Rel. Energy (kcal/mol)	Boltzmann population
isomer3_conf1	0.00	6.84%
isomer3_conf2	0.12	5.56%
isomer3_conf3	0.21	4.78%
isomer3_conf4	0.31	4.06%
isomer3_conf5	0.37	3.67%
isomer3_conf6	0.41	3.41%
isomer3_conf7	0.42	3.37%
isomer3_conf8	0.43	3.29%
isomer3_conf9	0.45	3.22%
isomer3_conf10	0.65	2.30%
isomer3_conf11	0.70	2.10%
isomer3_conf12	0.81	1.73%
isomer3_conf13	0.83	1.69%
isomer3_conf14	0.84	1.66%
isomer3_conf15	0.90	1.50%
isomer3_conf16	0.91	1.47%
isomer3_conf17	0.92	1.45%
isomer3_conf18	0.94	1.40%
isomer3_conf19	0.94	1.39%
isomer3_conf20	0.95	1.38%
isomer3_conf21	0.97	1.33%
isomer3_conf22	1.02	1.23%
isomer3_conf23	1.03	1.19%
isomer3_conf24	1.06	1.14%
isomer3_conf25	1.08	1.11%
isomer3_conf26	1.09	1.09%
isomer3_conf27	1.11	1.04%
isomer3_conf28	1.12	1.04%
isomer3_conf29	1.12	1.02%
isomer3_conf30	1.13	1.01%
isomer3_conf31	1.15	0.98%
isomer3_conf32	1.18	0.93%
isomer3_conf33	1.19	0.91%
isomer3_conf34	1.21	0.89%
isomer3_conf35	1.21	0.89%
isomer3_conf36	1.21	0.89%
isomer3_conf37	1.21	0.88%
isomer3_conf38	1.28	0.79%
isomer3_conf39	1.31	0.75%
isomer3_conf40	1.33	0.72%

isomer3_conf41	1.33	0.72%
isomer3_conf42	1.36	0.69%
isomer3_conf43	1.36	0.69%
isomer3_conf44	1.37	0.68%
isomer3_conf45	1.38	0.67%
isomer3_conf46	1.38	0.66%
isomer3_conf47	1.41	0.63%
isomer3_conf48	1.42	0.62%
isomer3_conf49	1.45	0.59%
isomer3_conf50	1.46	0.58%
isomer3_conf51	1.48	0.56%
isomer3_conf52	1.48	0.56%
isomer3_conf53	1.49	0.56%
isomer3_conf54	1.50	0.54%
isomer3_conf55	1.51	0.53%
isomer3_conf56	1.52	0.53%
isomer3_conf57	1.53	0.52%
isomer3_conf58	1.53	0.51%
isomer3_conf59	1.54	0.51%
isomer3_conf60	1.54	0.51%
isomer3_conf61	1.54	0.51%
isomer3_conf62	1.56	0.49%
isomer3_conf63	1.61	0.45%
isomer3_conf64	1.61	0.45%
isomer3_conf65	1.61	0.45%
isomer3_conf66	1.62	0.44%
isomer3_conf67	1.64	0.43%
isomer3_conf68	1.65	0.42%
isomer3_conf69	1.65	0.42%
isomer3_conf70	1.65	0.42%
isomer3_conf71	1.67	0.40%
isomer3_conf72	1.68	0.40%
isomer3_conf73	1.68	0.40%
isomer3_conf74	1.70	0.39%
isomer3_conf75	1.73	0.37%
isomer3_conf76	1.75	0.36%
isomer3_conf77	1.76	0.35%
isomer3_conf78	1.77	0.34%
isomer3_conf79	1.79	0.33%
isomer3_conf80	1.81	0.32%
isomer3_conf81	1.82	0.32%
isomer3_conf82	1.84	0.30%
isomer3_conf83	1.85	0.30%
isomer3_conf84	1.86	0.30%
isomer3_conf85	1.86	0.30%
isomer3_conf86	1.86	0.29%
isomer3_conf87	1.88	0.29%
isomer3_conf88	1.89	0.28%
isomer3_conf89	1.91	0.27%
isomer3_conf90	1.95	0.25%

isomer3_conf91	1.97	0.25%
isomer3_conf92	1.97	0.25%
isomer3_conf93	1.97	0.24%
isomer3_conf94	2.00	0.23%

Figure S3: The 9 lowest energy conformers of isomer 3 of isolated compound at B3LYP/6-31G* level.

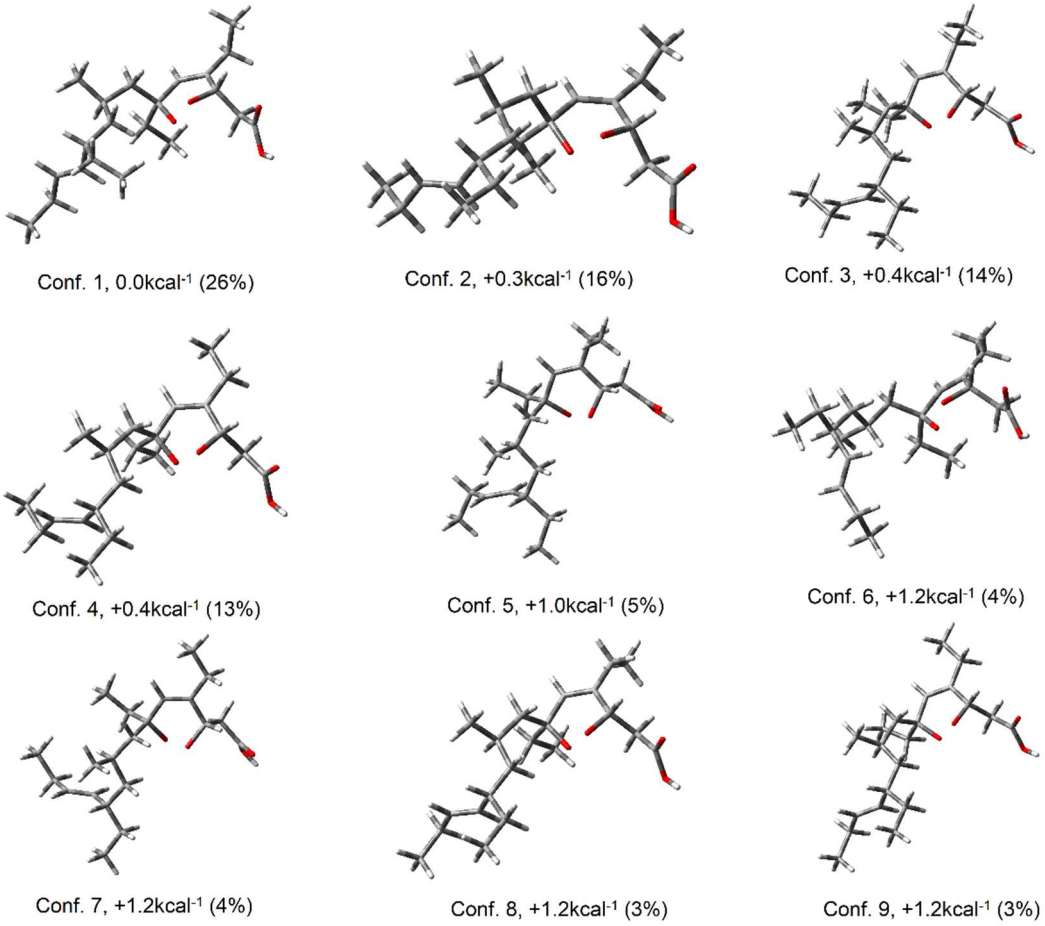


Isomer 3: 279 conformers with relative energy within 10 kcal mol^{-1} of the lowest energy conformer were selected for further geometry optimized at the B3LYP/6-31G* level. 94 conformers were identified with relative energy < 2.0 kcal mol^{-1}, corresponding to more than 90% of the total Boltzmann distribution.

Table S4: Lowest energy conformers of isomer 4 of isolated compound at B3LYP/6-31G* level.

Conformers isomer 2	Rel. Energy (kcal/mol)	Boltzmann population
isomer4_conf1	0.00	26.06%
isomer4_conf2	0.30	15.64%
isomer4_conf3	0.37	14.05%
isomer4_conf4	0.43	12.69%
isomer4_conf5	1.00	4.80%
isomer4_conf6	1.16	3.70%
isomer4_conf7	1.17	3.61%
isomer4_conf8	1.20	3.43%
isomer4_conf9	1.22	3.32%
isomer4_conf10	1.25	3.18%
isomer4_conf11	1.45	2.24%
isomer4_conf12	1.46	2.23%
isomer4_conf13	1.59	1.77%
isomer4_conf14	1.74	1.39%
isomer4_conf15	1.92	1.01%
isomer4_conf16	2.00	0.88%

Figure S4: The 9 lowest energy conformers of isomer 4 of isolated compound at B3LYP/6-31G* level.

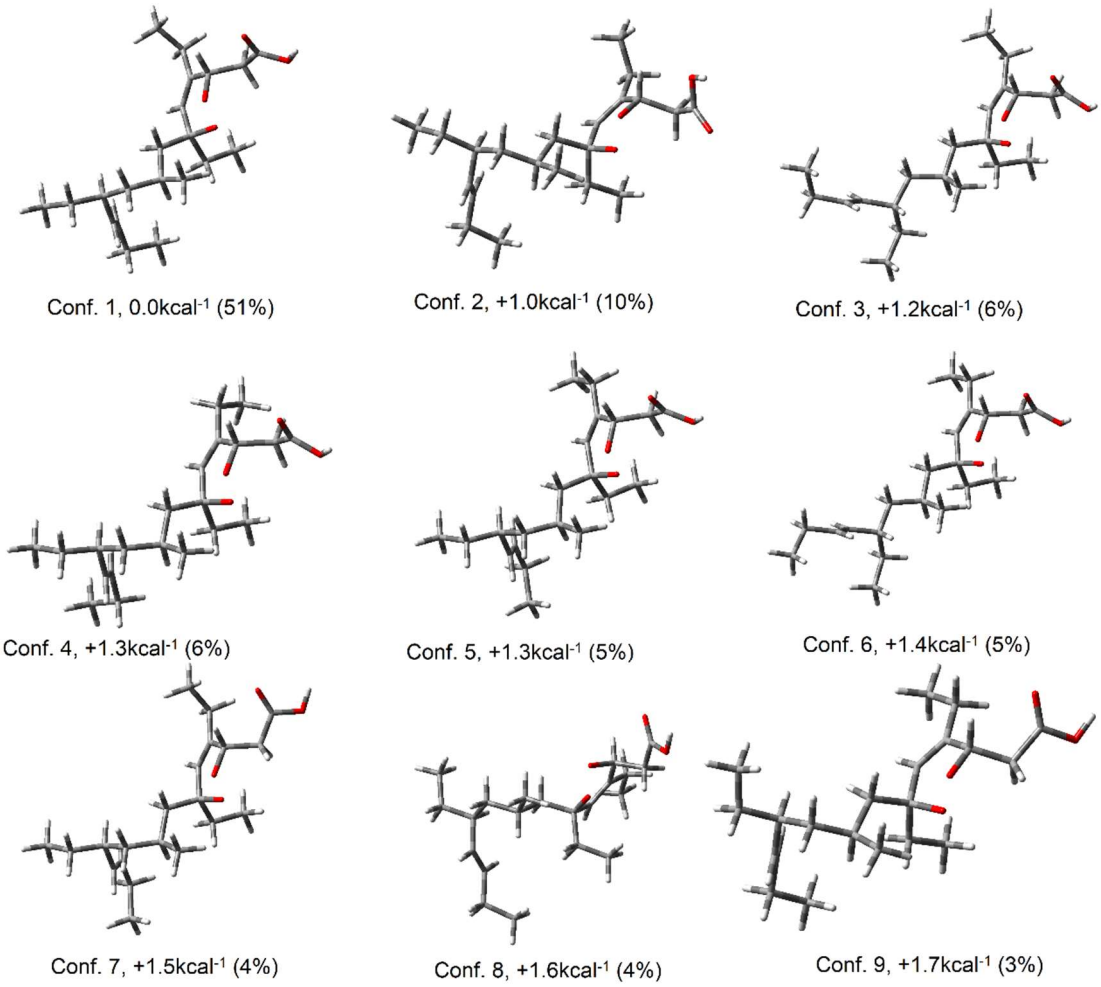


Isomer 4: 156 conformers with relative energy within 10 kcal mol^{-1} of the lowest energy conformer were selected for further geometry optimized at the B3LYP/6-31G* level. 16 conformers were identified with relative energy < 2.0 kcal mol^{-1}, corresponding to more than 83% of the total Boltzmann distribution.

Table S5: Lowest energy conformers of isomer 5 of isolated compound at B3LYP/6-31G* level.

Conformers isomer 2	Rel. Energy (kcal/mol)	Boltzmann population
isomer5_conf1	0.00	51.15%
isomer5_conf2	0.95	10.29%
isomer5_conf3	1.24	6.27%
isomer5_conf4	1.26	6.06%
isomer5_conf5	1.34	5.32%
isomer5_conf6	1.37	5.08%
isomer5_conf7	1.48	4.21%
isomer5_conf8	1.58	3.58%
isomer5_conf9	1.71	2.86%
isomer5_conf10	1.75	2.68%
isomer5_conf11	1.79	2.48%

Figure S5: The 9 lowest energy conformers of isomer 5 of isolated compound at B3LYP/6-31G* level.



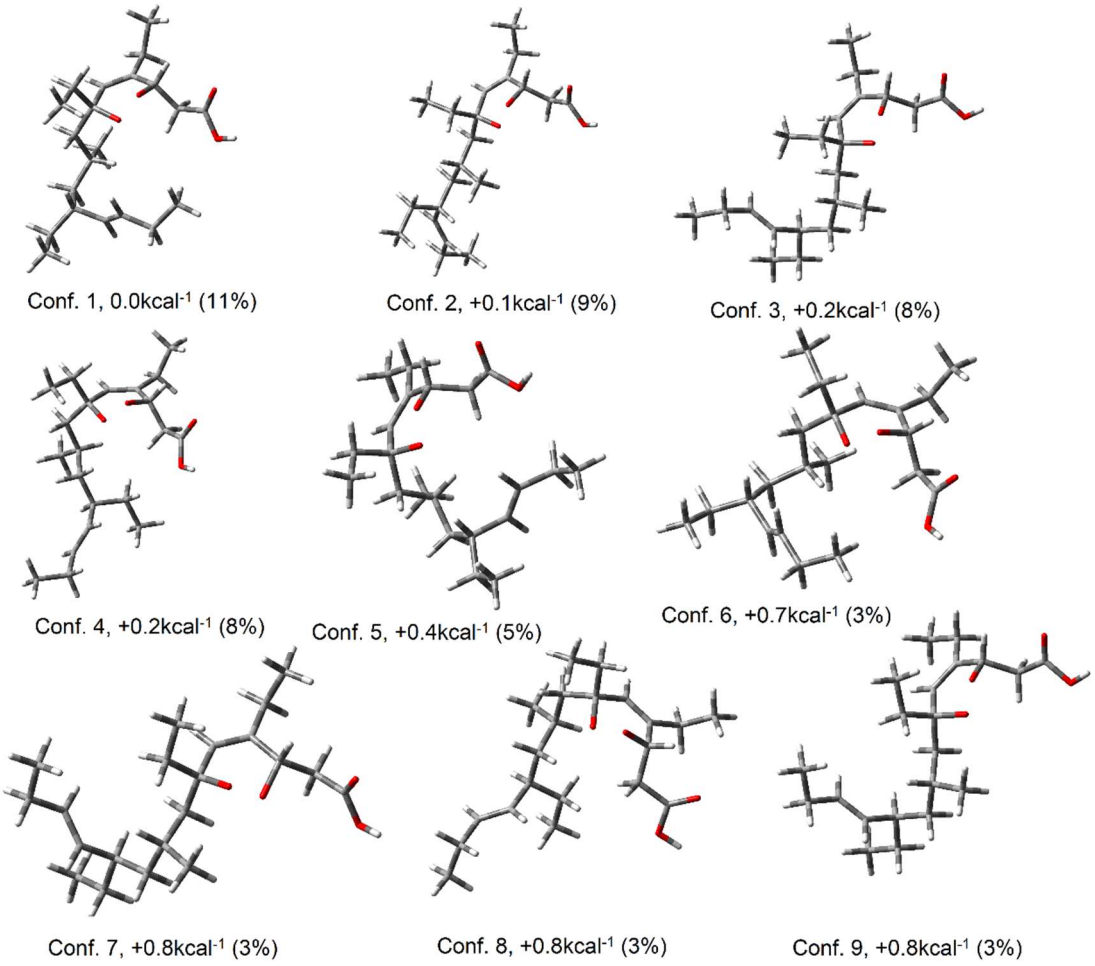
Isomer 5: 84 conformers with relative energy within 10 kcal mol^{-1} of the lowest energy conformer were selected for further geometry optimized at the B3LYP/6-31G* level. 11 conformers were identified with relative energy < 2.0 kcal mol^{-1}, corresponding to more than 85% of the total Boltzmann distribution.

Table S6: Lowest energy conformers of isomer 6 of isolated compound at B3LYP/6-31G* level.

Conformers isomer 2	Rel. Energy (kcal/mol)	Boltzmann population
isomer6_conf1	0.00	10.97%
isomer6_conf2	0.12	8.89%
isomer6_conf3	0.18	8.04%
isomer6_conf4	0.21	7.64%
isomer6_conf5	0.44	5.18%
isomer6_conf6	0.68	3.49%
isomer6_conf7	0.78	2.93%
isomer6_conf8	0.85	2.62%
isomer6_conf9	0.85	2.61%
isomer6_conf10	0.90	2.40%
isomer6_conf11	0.90	2.38%
isomer6_conf12	0.91	2.36%
isomer6_conf13	0.97	2.12%
isomer6_conf14	0.99	2.06%
isomer6_conf15	1.08	1.77%
isomer6_conf16	1.09	1.73%
isomer6_conf17	1.16	1.56%
isomer6_conf18	1.16	1.55%
isomer6_conf19	1.17	1.53%
isomer6_conf20	1.19	1.47%
isomer6_conf21	1.20	1.46%
isomer6_conf22	1.26	1.31%
isomer6_conf23	1.28	1.26%
isomer6_conf24	1.33	1.17%
isomer6_conf25	1.33	1.16%
isomer6_conf26	1.34	1.13%
isomer6_conf27	1.36	1.10%
isomer6_conf28	1.39	1.05%
isomer6_conf29	1.41	1.02%
isomer6_conf30	1.43	0.97%
isomer6_conf31	1.44	0.96%
isomer6_conf32	1.45	0.95%
isomer6_conf33	1.49	0.88%
isomer6_conf34	1.51	0.86%
isomer6_conf35	1.51	0.86%
isomer6_conf36	1.52	0.85%
isomer6_conf37	1.58	0.76%
isomer6_conf38	1.61	0.72%
isomer6_conf39	1.62	0.71%
isomer6_conf40	1.66	0.67%

isomer6_conf41	1.73	0.59%
isomer6_conf42	1.76	0.56%
isomer6_conf43	1.77	0.55%
isomer6_conf44	1.82	0.50%
isomer6_conf45	1.83	0.50%
isomer6_conf46	1.89	0.45%
isomer6_conf47	1.89	0.45%
isomer6_conf48	1.89	0.45%
isomer6_conf49	1.93	0.42%
isomer6_conf50	1.93	0.42%
isomer6_conf51	1.95	0.41%
isomer6_conf52	1.96	0.40%
isomer6_conf53	1.98	0.39%
isomer6_conf54	1.98	0.39%
isomer6_conf55	2.00	0.37%

Figure S6: The 9 lowest energy conformers of isomer 6 of isolated compound at B3LYP/6-31G* level.

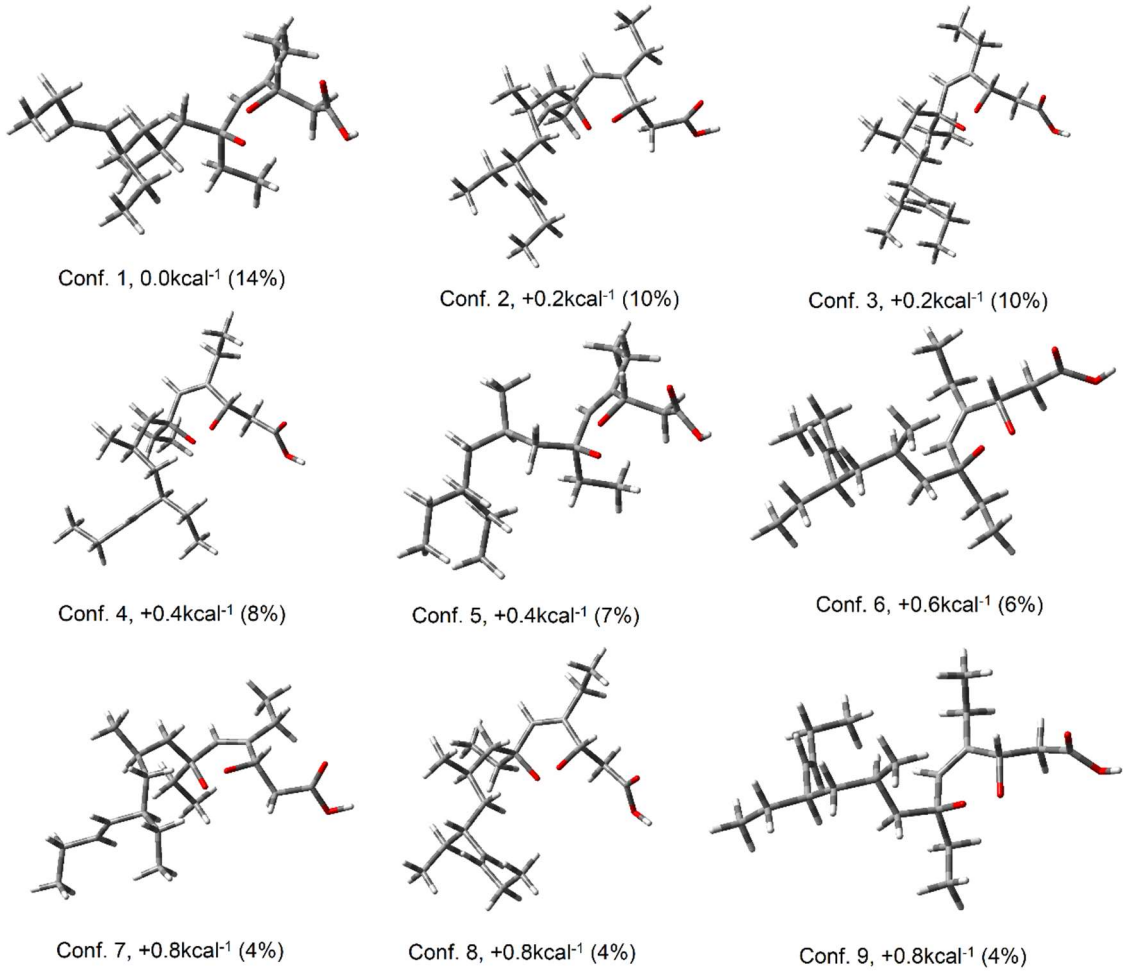


Isomer 6: 255 conformers with relative energy within 10 kcal mol^{-1} of the lowest energy conformer were selected for further geometry optimized at the B3LYP/6-31G* level. 55 conformers were identified with relative energy < 2.0 kcal mol^{-1}, corresponding to more than 86% of the total Boltzmann distribution.

Table S7: Lowest energy conformers of isomer 7 of isolated compound at B3LYP/6-31G* level.

Conformers isomer 2	Rel. Energy (kcal/mol)	Boltzmann population
isomer7_conf1	0.00	14.43%
isomer7_conf2	0.25	9.53%
isomer7_conf3	0.25	9.51%
isomer7_conf4	0.38	7.58%
isomer7_conf5	0.39	7.49%
isomer7_conf6	0.57	5.53%
isomer7_conf7	0.76	3.97%
isomer7_conf8	0.81	3.65%
isomer7_conf9	0.82	3.60%
isomer7_conf10	0.96	2.87%
isomer7_conf11	0.99	2.73%
isomer7_conf12	1.05	2.47%
isomer7_conf13	1.06	2.41%
isomer7_conf14	1.15	2.08%
isomer7_conf15	1.23	1.79%
isomer7_conf16	1.43	1.28%
isomer7_conf17	1.44	1.27%
isomer7_conf18	1.44	1.26%
isomer7_conf19	1.48	1.18%
isomer7_conf20	1.53	1.09%
isomer7_conf21	1.60	0.97%
isomer7_conf22	1.61	0.96%
isomer7_conf23	1.62	0.94%
isomer7_conf24	1.66	0.88%
isomer7_conf25	1.74	0.76%
isomer7_conf26	1.75	0.76%
isomer7_conf27	1.75	0.75%
isomer7_conf28	1.76	0.74%
isomer7_conf29	1.77	0.73%
isomer7_conf30	1.79	0.70%
isomer7_conf31	1.80	0.69%
isomer7_conf32	1.82	0.67%
isomer7_conf33	1.83	0.66%
isomer7_conf34	1.83	0.66%
isomer7_conf35	1.84	0.64%
isomer7_conf36	1.89	0.60%
isomer7_conf37	1.92	0.57%
isomer7_conf38	1.94	0.54%
isomer7_conf39	1.95	0.54%
isomer7_conf40	1.95	0.54%

Figure S7: The 9 lowest energy conformers of isomer 7 of isolated compound at B3LYP/6-31G* level.

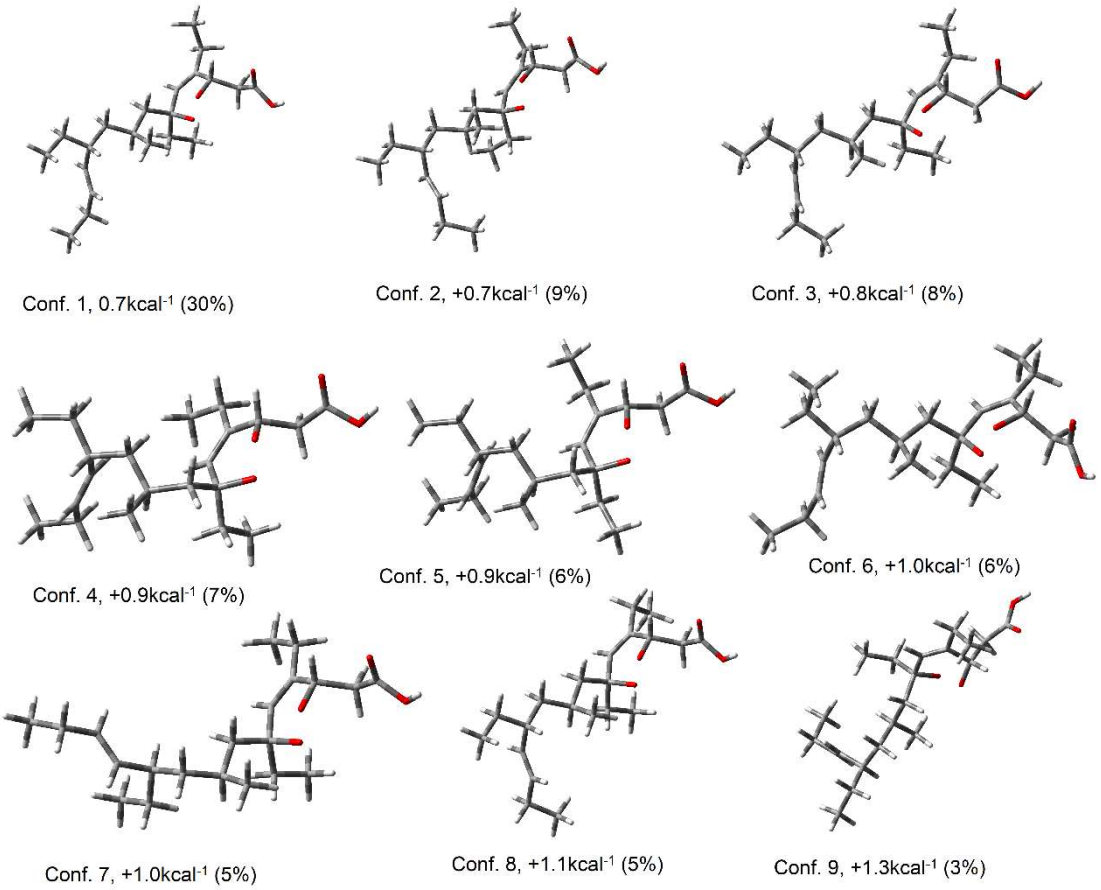


Isomer 7: 96 conformers with relative energy within 10 kcal mol^{-1} of the lowest energy conformer were selected for further geometry optimized at the B3LYP/6-31G* level. 40 conformers were identified with relative energy < 2.0 kcal mol^{-1}, corresponding to more than 91% of the total Boltzmann distribution.

Table S8: Lowest energy conformers of isomer 8 of isolated compound at B3LYP/6-31G* level.

Conformers isomer 2	Rel. Energy (kcal/mol)	Boltzmann population
isomer8_conf1	0.00	30.33%
isomer8_conf2	0.70	9.31%
isomer8_conf3	0.78	8.12%
isomer8_conf4	0.90	6.58%
isomer8_conf5	0.94	6.19%
isomer8_conf6	0.95	6.12%
isomer8_conf7	1.04	5.27%
isomer8_conf8	1.11	4.66%
isomer8_conf9	1.31	3.35%
isomer8_conf10	1.32	3.27%
isomer8_conf11	1.46	2.58%
isomer8_conf12	1.60	2.03%
isomer8_conf13	1.67	1.81%
isomer8_conf14	1.68	1.78%
isomer8_conf15	1.70	1.73%
isomer8_conf16	1.70	1.71%
isomer8_conf17	1.78	1.51%
isomer8_conf18	1.85	1.32%
isomer8_conf19	1.86	1.30%
isomer8_conf20	2.00	1.03%

Figure S8: The 9 lowest energy conformers of isomer 8 of isolated compound at B3LYP/6-31G* level.



Isomer 8: 276 conformers with relative energy within 10 kcal mol^{-1} of the lowest energy conformer were selected for further geometry optimized at the B3LYP/6-31G* level. 20 conformers were identified with relative energy < 2.0 kcal mol^{-1}, corresponding to more than 75% of the total Boltzmann distribution.

Table S9: Comparison of calculated δscal (generalized scaling factor) 13C NMR chemical shifts simulated for the possible stereoisomers of 1 (GIAOmPW1PW91/6-31G(d)//B3LYP/6-31G(d)) with the experimental values (δexp, 90.5 MHz, CDCl3) of the isolated natural product.

Atom number	**Isomer 1** (δ_{scal} ^{13}C, ppm)	**Isomer 2** (δ_{scal} ^{13}C, ppm)	**Isomer 3** (δ_{scal} ^{13}C, ppm)	**Isomer 4** (δ_{scal} ^{13}C, ppm)	**Isomer 5** (δ_{scal} ^{13}C, ppm)	**Isomer 6** (δ_{scal} ^{13}C, ppm)	**Isomer 7** (δ_{scal} ^{13}C, ppm)	**Isomer 8** (δ_{scal} ^{13}C, ppm)	**Isolated compound**[a] (δ_{exp} ^{13}C, ppm)
C1	178.1	178.3	178.4	178.2	178.1	178.3	178.4	178.5	**176.6**
C2	39.9	40.6	39.7	38.5	39.3	39.1	39.2	39.3	**35.3**
C3	80.5	79.9	80.3	80.7	80.4	80.0	81.3	80.2	**76.5**
C4	145.9	146.1	145.9	145.2	145.7	145.1	145.3	145.8	**137.5**
C5	131.9	132.3	131.7	132.4	133.2	132.7	130.9	132.3	**124.9**
C6	89.8	89.8	89.4	89.1	88.8	88.7	88.7	88.6	**83.6**
C7	45.6	43.8	46.7	44.0	42.0	44.1	45.9	45.7	**43.3**
C8	30.6	29.6	30.2	30.3	30.2	29.8	29.7	31.4	**25.9**
C9	46.5	47.9	47.8	42.6	48.1	48.1	46.7	48.0	**44.5**
C10	47.4	47.4	47.8	47.1	47.1	47.5	47.7	47.2	**42.3**
C11	138.5	139.7	139.0	139.1	138.8	139.1	140.0	138.7	**133.2**
C12	137.7	138.1	138.5	138.1	138.3	138.5	137.7	138.8	**132.1**
C13	30.9	31.3	30.7	31.2	31.0	31.2	31.3	31.3	**25.7**
C14	16.4	16.9	16.7	17.1	16.7	16.8	17.1	17.1	**14.2**
C15	30.1	30.7	30.2	30.2	30.1	30.4	29.5	30.2	**24.8**
C16	14.1	14.8	14.1	14.6	14.9	14.6	12.9	15.0	**11.7**
C17	34.6	35.1	33.3	30.3	30.7	33.4	32.4	31.2	**30.9**
C18	9.7	9.6	10.0	9.6	9.4	9.8	9.6	9.7	**8.1**
C19	21.5	24.3	20.7	21.7	21.9	22.9	23.3	18.7	**21.3**
C20	32.2	31.5	32.7	33.6	31.6	31.4	30.1	32.1	**28.9**
C21	13.7	13.8	14.1	12.7	14.0	13.9	13.9	14.2	**11.6**
MAD	**3.95**	**4.22**	**4.10**	**3.73**	**3.83**	**3.93**	**3.75**	**4.12**	

Abbreviations: MAD, mean absolute deviation; RMSD, root mean square deviation.
[a]Data extracted from ref. 5.

Table S10: Comparison of calculated δscal (internal scaling factor) 13C NMR chemical shifts simulated for the possible stereoisomers of 1 (GIAOmPW1PW91/6-31G(d)//B3LYP/6-31G(d)) with the experimental values (δexp, 90.5 MHz, CDCl3) of the isolated natural product.

Atom number	Isomer 1 (δ_{scal} ^{13}C, ppm)	Isomer 2 (δ_{scal} ^{13}C, ppm)	Isomer 3 (δ_{scal} ^{13}C, ppm)	Isomer 4 (δ_{scal} ^{13}C, ppm)	Isomer 5 (δ_{scal} ^{13}C, ppm)	Isomer 6 (δ_{scal} ^{13}C, ppm)	Isomer 7 (δ_{scal} ^{13}C, ppm)	Isomer 8 (δ_{scal} ^{13}C, ppm)	Isolated compound[a] (δ_{exp} ^{13}C, ppm)
C1	172.1	172.0	172.1	172.1	171.8	172.1	172.2	172.1	**176.6**
C2	36.4	36.8	36.0	35.5	36.0	35.6	35.9	35.9	**35.3**
C3	76.2	75.3	76.0	76.8	76.3	75.7	77.2	76.0	**76.5**
C4	140.4	140.4	140.2	139.9	140.2	139.7	139.8	140.2	**137.5**
C5	126.7	126.9	126.3	127.4	127.9	127.5	125.7	127.0	**124.9**
C6	85.4	85.1	84.8	85.0	84.5	84.3	84.4	84.1	**83.6**
C7	42.0	39.8	43.0	40.9	38.7	40.6	42.5	42.2	**43.3**
C8	27.2	26.0	26.9	27.5	27.2	26.4	26.7	28.2	**25.9**
C9	42.9	44.0	44.1	39.5	44.8	44.5	43.3	44.5	**44.5**
C10	43.7	43.6	44.1	44.0	43.8	43.9	44.3	43.7	**42.3**
C11	133.2	134.1	133.4	133.8	133.5	133.7	134.7	133.3	**133.2**
C12	132.4	132.4	132.9	132.9	133.0	133.2	132.4	133.3	**132.1**
C13	27.5	27.7	27.3	28.4	28.0	27.9	28.2	28.0	**25.7**
C14	13.3	13.6	13.6	14.7	14.1	13.8	14.2	14.3	**14.2**
C15	26.7	27.1	26.8	27.4	27.1	27.1	26.4	27.0	**24.8**
C16	11.1	11.4	11.0	12.2	12.3	11.6	10.2	12.2	**11.7**
C17	31.2	31.4	29.8	27.5	27.7	30.0	29.2	27.9	**30.9**
C18	6.7	6.3	7.0	7.3	6.9	6.9	6.9	7.0	**8.1**
C19	18.3	20.8	17.5	19.1	19.1	19.8	20.4	15.8	**21.3**
C20	28.8	27.9	29.2	30.7	28.6	28.0	27.1	28.9	**28.9**
C21	10.6	10.5	11.0	10.3	11.4	10.9	11.1	11.4	**11.6**
MAD	**1.4**	**1.4**	**1.3**	**1.9**	**1.6**	**1.3**	**1.3**	**1.5**	

Table S11: Boltzmann averaged ^{13}C GIAO isotropic magnetic shielding values calculates for all possible stereoisomers of 1 at mPW1PW91/6-31G(d)//B3LYP/6-31G(d).

Atom number	Isomer 1 (σ ^{13}C, ppm)	Isomer 2 (σ ^{13}C, ppm)	Isomer 3 (σ ^{13}C, ppm)	Isomer 4 (σ ^{13}C, ppm)	Isomer 5 (σ ^{13}C, ppm)	Isomer 6 (σ ^{13}C, ppm)	Isomer 7 (σ ^{13}C, ppm)	Isomer 8 (σ ^{13}C, ppm)
C1	25.8	25.7	25.6	25.7	25.9	25.7	25.6	25.5
C2	157.4	156.8	157.7	158.8	158.1	158.2	158.2	158.0
C3	118.8	119.4	119.0	118.6	118.9	119.3	118.0	119.0
C4	56.5	56.4	56.5	57.2	56.7	57.2	57.1	56.6
C5	69.8	69.4	70.1	69.3	68.6	69.0	70.8	69.4
C6	109.9	109.9	110.4	110.6	110.9	111.0	111.0	111.1
C7	152.0	153.8	151.0	153.5	155.5	153.4	151.8	151.9
C8	166.3	167.3	166.7	166.6	166.7	167.1	167.2	165.5
C9	151.2	149.9	149.9	154.9	149.6	149.6	151.0	149.7
C10	150.3	150.3	150.0	150.6	150.6	150.2	150.0	150.5
C11	63.6	62.4	63.1	63.0	63.2	63.0	62.1	63.3
C12	64.3	64.0	63.6	63.9	63.7	63.5	64.3	63.3
C13	166.1	165.6	166.2	165.8	165.9	165.8	165.7	165.7
C14	179.8	179.4	179.6	179.1	179.5	179.5	179.2	179.2
C15	166.8	166.3	166.7	166.7	166.8	166.5	167.4	166.7
C16	182.1	181.4	182.0	181.5	181.3	181.5	183.2	181.1
C17	162.5	162.0	163.8	166.6	166.3	163.7	164.6	165.8
C18	186.2	186.3	185.9	186.4	186.5	186.1	186.4	186.2
C19	175.0	172.3	175.7	174.8	174.6	173.6	173.3	177.7
C20	164.8	165.5	164.3	163.5	165.4	165.6	166.8	164.9
C21	182.4	182.3	182.1	183.4	182.1	182.2	182.2	181.9

Table S12: Boltzmann averaged ^{1}H GIAO isotropic magnetic shielding values calculates for all possible stereoisomers of 1 at mPW1PW91/6-31G(d)//B3LYP/6-31G(d).

Atom number	Isomer 1 (σ ^{1}H, ppm)	Isomer 2 (σ ^{1}H, ppm)	Isomer 3 (σ ^{1}H, ppm)	Isomer 4 (σ ^{1}H, ppm)	Isomer 5 (σ ^{1}H, ppm)	Isomer 6 (σ ^{1}H, ppm)	Isomer 7 (σ ^{1}H, ppm)	Isomer 8 (σ ^{1}H, ppm)
H2	28.72	28.73	28.70	28.68	28.59	28.67	28.76	28.55
H2	28.81	28.67	28.73	28.87	28.96	28.88	28.77	28.96
H3	26.78	26.71	26.76	26.64	26.69	26.70	26.69	26.73
H5	25.68	25.63	25.63	25.70	25.67	25.58	25.69	25.65
H7	30.19	30.09	30.20	30.14	30.07	30.13	30.05	30.06
H8	29.91	29.92	29.86	29.85	29.77	29.79	29.78	29.86
H9	30.35	30.47	30.33	30.64	30.51	30.42	30.43	30.56
H9	30.53	30.59	30.50	29.34	30.49	30.49	30.17	30.45
H10	29.63	29.67	29.61	29.55	29.63	29.62	29.57	29.59
H11	26.16	26.12	25.99	25.97	26.16	26.09	26.06	26.17
H12	25.65	25.68	25.66	25.69	25.73	25.65	25.68	25.64
H13	29.48	29.48	29.42	29.45	29.44	29.45	29.47	29.46
H14	30.60	30.59	30.59	30.59	30.57	30.57	30.58	30.57
H15	29.50	29.51	29.53	29.47	29.47	29.51	29.46	29.49
H16	30.48	30.48	30.49	30.48	30.47	30.49	30.47	30.47
H17	29.92	30.01	29.74	30.05	30.08	29.84	29.81	30.00
H17	29.92	29.77	29.90	29.98	29.80	29.78	30.08	29.99
H18	30.65	30.62	30.67	30.75	30.77	30.66	30.74	30.76
H19	30.68	30.67	30.71	30.80	30.59	30.71	30.76	30.59
H20	30.31	30.46	30.35	30.25	30.32	30.35	30.37	30.46
H20	30.44	30.29	30.34	30.30	30.43	30.33	30.31	30.35
H21	30.74	30.76	30.71	30.72	30.79	30.73	30.75	30.74

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