Synergistic TRAIL sensitizers from *Barleria alluaudii* and *Diospyros maritima*

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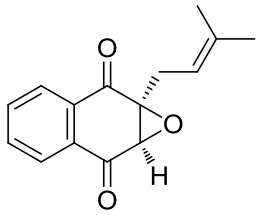
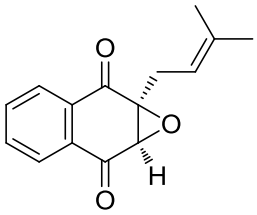
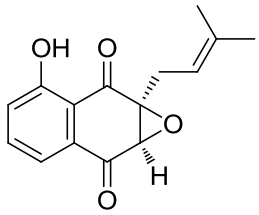
^{1}H NMR spectrum of 2,3-epoxy-2,3-dihydrolapachol (**1**) in $CDCl_3$



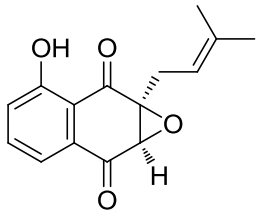
^{13}C NMR spectrum of 2,3-epoxy-2,3-dihydrolapachol (**1**) in $CDCl_3$



^{1}H NMR spectrum of 2,3-epoxy-2,3-dihydro-8-hydroxylapachol (**2**) in $CDCl_3$



^{13}C NMR spectrum of 2,3-epoxy-2,3-dihydro-8-hydroxylapachol (**2**) in $CDCl_3$



Chiral HPLC analysis of **1**

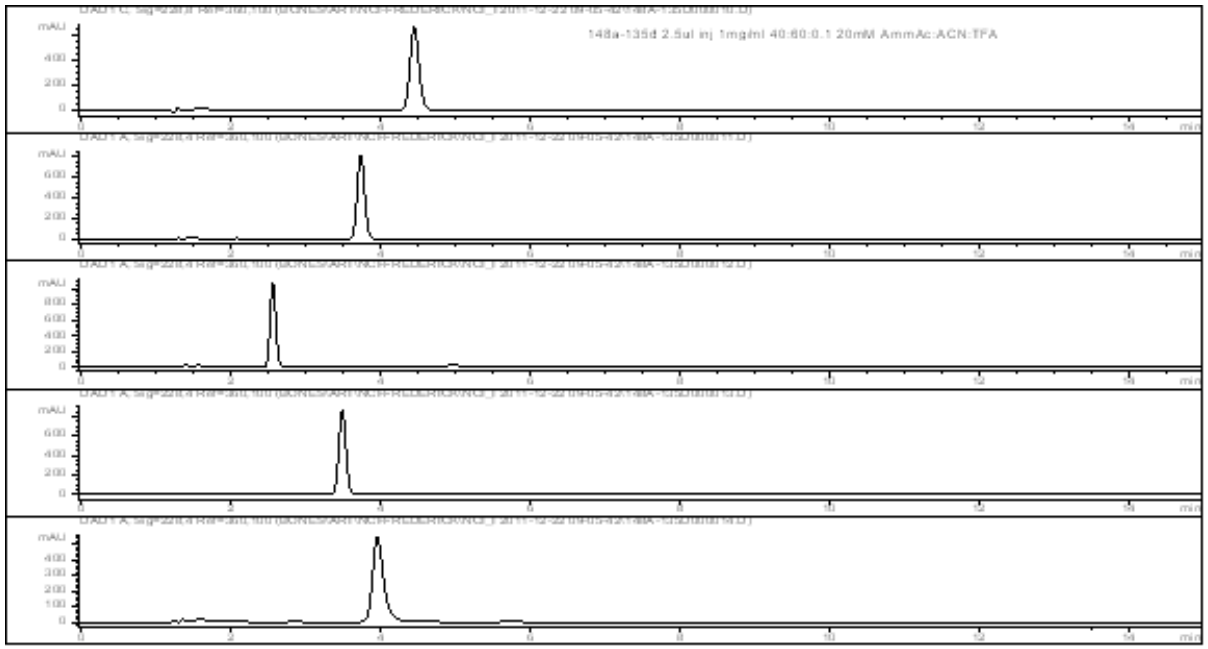
1

2

3

4

5



Columns	Conditions
1, Lux Cellulose-1 (5 μm, 150 x 4.6 mm)	(40:60:0.1) 20 mm NH_4OAc/CH_3CN/TFA
2, Lux Cellulose-2 (5 μm, 150 x 4.6 mm)	(40:60:0.1) 20 mm NH_4OAc/CH_3CN/TFA
3, Lux Cellulose-3 (5 μm, 150 x 4.6 mm)	(40:60:0.1) 20 mm NH_4OAc/CH_3CN/TFA
4, Lux Cellulose-4 (5 μm, 150 x 4.6 mm)	(40:60:0.1) 20 mm NH_4OAc/CH_3CN/TFA
5, Lux Amylose-2 (5 μm, 150 x 4.6 mm)	(40:60:0.1) 20 mm NH_4OAc/CH_3CN/TFA
(S,S)-WHELK-02 (10 μm, 250 x 4.6 mm)	(50:50:0.1) CH_3CN/H_2O/AcOH (data not shown)

The Gaussian09 keywords for calculating ECD are:

td=(nstates=50) rb3lyp/6-31g(d) scrf=(iefpcm,solvent=methanol)

Table S1. Excited energy, wavelength, oscillator strength, rotatory strength in velocity form and rotatory strength in length form of **2a-2f**.[a]

Conformer	ΔE (eV)	λ (nm)	*f*	$R^{vel,b}$	$R^{len,b}$
2a	2.99	414.1	0.001	-5.7	-7.7
	3.38	368.2	0.040	-31.2	-29.9
	3.47	357.2	0.091	2.2	2.9
	3.75	330.8	0.004	26.1	24.9
	4.26	290.8	0.012	-3.9	-7.7
	4.32	287.1	0.039	3.3	3.9
	4.60	269.2	0.019	12.5	13.4
	4.78	259.3	0.013	-29.0	-30.5
	5.04	246.2	0.036	34.3	39.9
	5.20	238.3	0.069	-20.0	-21.4
	5.35	231.7	0.038	15.5	16.0
	5.51	225.2	0.298	-0.8	-1.3
	5.91	209.8	0.061	-8.5	-10.0
	5.96	208.1	0.005	-0.4	-0.4
	6.08	203.9	0.049	-10.7	-10.6
	6.13	202.3	0.108	10.2	8.6
2b	3.11	399.3	0.0003	2.2	1.3
	3.36	369.0	0.024	-31.6	-30.3
	3.47	357.8	0.109	13.7	14.5
	3.71	334.1	0.001	14.9	13.9
	4.30	288.4	0.038	10.2	8.0
	4.36	284.2	0.020	-9.6	-9.3
	4.58	270.5	0.015	14.5	13.4
	4.75	260.9	0.015	-27.1	-28.0
	5.02	247.0	0.035	34.7	39.6
	5.17	239.7	0.056	-22.6	-23.8
	5.37	230.9	0.047	0.8	1.0
	5.51	225.2	0.309	4.6	4.4
	5.91	210.0	0.012	5.7	6.0
	6.06	204.6	0.075	23.3	24.2
	6.09	203.6	0.040	0.7	-0.5
	6.12	202.5	0.041	5.7	5.6

2c	3.17	390.6	0.003	-0.3	-1.0
	3.35	369.6	0.024	-34.2	-32.4
	3.47	357.3	0.115	3.2	3.5
	3.74	331.8	0.003	21.1	19.5
	4.30	288.3	0.044	0.1	-3.0
	4.43	280.0	0.003	2.4	3.4
	4.59	270.0	0.015	12.2	11.7
	4.76	260.7	0.018	-31.7	-32.8
	5.02	247.1	0.036	32.3	38.5
	5.19	239.0	0.056	-20.4	-22.2
	5.38	230.3	0.048	11.5	11.9
	5.52	224.8	0.331	-7.8	-8.4
	5.89	210.5	0.007	8.0	8.0
	6.11	202.9	0.039	-13.7	-15.0
	6.13	202.2	0.080	5.9	5.2
	6.16	201.4	0.021	-2.8	-2.9
2d	3.12	397.8	0.0002	-1.5	-2.5
	3.35	369.7	0.026	-33.7	-32.3
	3.46	358.1	0.112	19.5	20.2
	3.71	334.6	0.002	15.9	15.1
	4.30	288.1	0.045	9.4	7.5
	4.37	283.8	0.029	-3.6	-2.9
	4.58	270.8	0.017	14.3	13.4
	4.74	261.6	0.016	-28.2	-29.0
	5.02	247.0	0.024	26.9	31.9
	5.18	239.4	0.036	-18.3	-19.4
	5.39	230.1	0.061	3.4	3.6
	5.50	225.3	0.327	32.8	34.6
	5.84	212.4	0.005	1.3	1.3
	6.08	203.9	0.009	-18.2	-18.9
	6.09	203.4	0.070	38.3	39.2
	6.12	202.5	0.074	12.5	12.5
2e	3.16	392.4	0.002	0.5	-0.6
	3.36	369.5	0.028	-35.3	-33.6
	3.47	357.3	0.113	11.4	11.9
	3.74	331.6	0.003	19.4	18.3
	4.31	287.8	0.046	-8.9	-12.2
	4.41	281.2	0.005	3.2	3.9
	4.59	270.3	0.017	17.5	17.2
	4.75	261.0	0.017	-30.7	-31.6
	5.02	247.1	0.031	27.4	32.8

	5.19	238.9	0.047	-17.3	-18.6
	5.47	226.7	0.053	-7.0	-7.5
	5.51	224.9	0.340	13.7	14.6
	5.78	214.5	0.002	-1.6	-1.8
	6.09	230.4	0.057	5.6	5.3
	6.13	202.3	0,956	7.1	7.2
	6.15	201.5	0.012	-5.5	-6.3
2f	3.06	405.7	0.002	-8.7	-10.1
	3.36	368.5	0.039	-34.2	-32.6
	3.46	357.9	0.099	-3.8	-3.2
	3.69	336.1	0.003	26.8	24.4
	4.29	288.9	0.032	-5.6	-9.8
	4.34	285.7	0.024	3.8	5.1
	4.60	269.4	0.020	13.4	14.0
	4.77	259.9	0.014	-32.2	-33.8
	4.99	248.6	0.028	26.5	32.1
	5.17	239.9	0.072	-8.5	-9.4
	5.36	231.2	0.029	10.1	10.3
	5.51	225.2	0.319	-33.5	-35.8
	5.96	208.0	0.025	2.4	1.9
	5.99	207.0	0.037	-25.8	-27.3
	6.09	203.6	0.018	-6.0	-5.9
	6.13	202.3	0.120	4.1	2.4

[a] All calculations were performed at the B3LYP/6-31G(d) level using the IEFPCM solvent continuum model with methanol as the solvent. [b] 10^{-40} cgs.

Table S2. Important dihedral angles (deg) of optimized predominant conformers **2a-2f** with DFT at the B3LYP/6-31G(d) using the IEFPCM solvent continuum model with methanol as the solvent.

	2a	**2b**	**2c**	**2d**	**2e**	**2f**
C3-C2-C1'-C2'	126	-82	17	-89	30	133
C2-C1'-C2'-C3'	126	-118	94	115	-120	-101

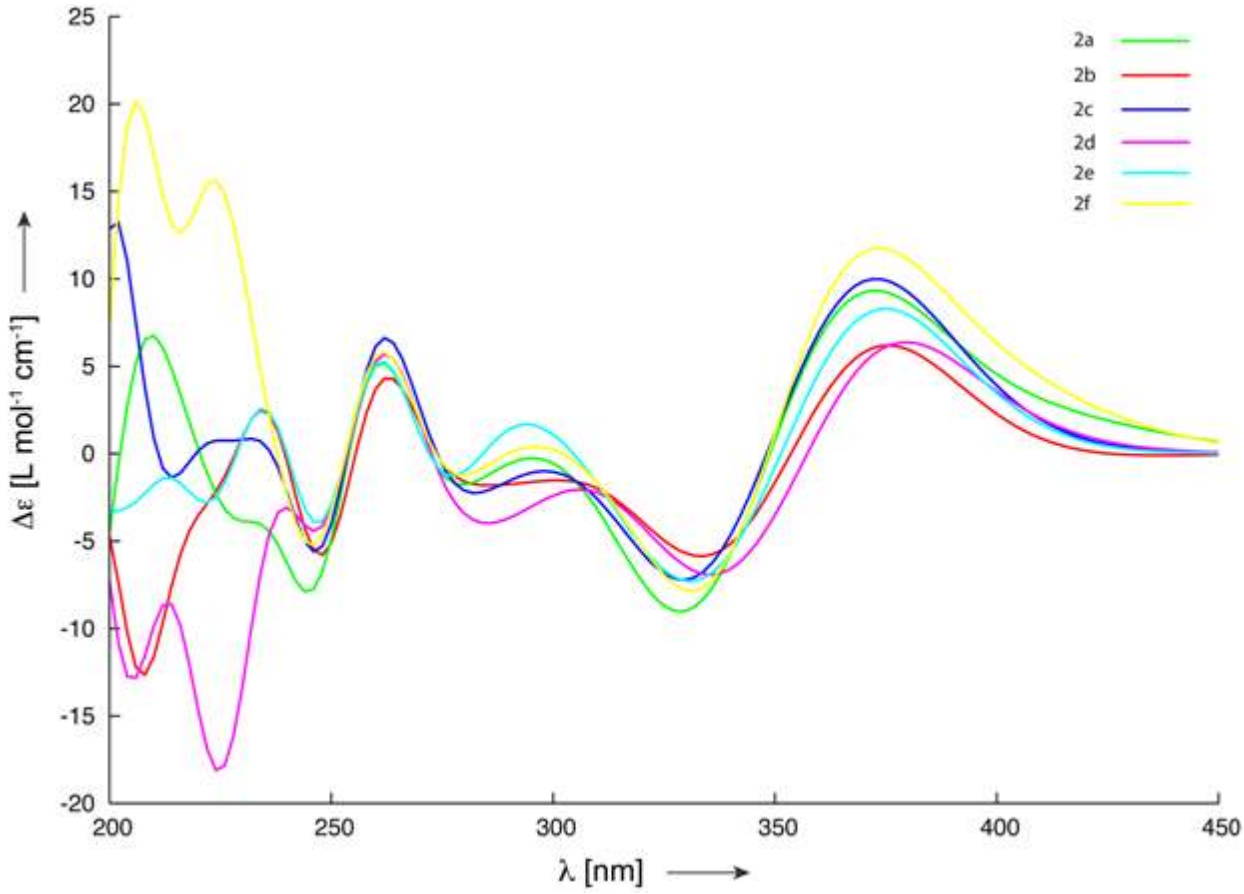


Figure S1. Comparison of the computed ECD spectra for the six energy lowest conformers with a 2*S*,3*R* configuration. The calculations were performed with DFT at the B3LYP/6-31G(d) level using the IEFPCM solvent continuum model with methanol as the solvent.

Table S3. Calculated ORD values for the six lowest energy conformers of (2*S*,3*R*)-**2** at three different wavelengths and their conformational averages compared to experimental values.

Conformer	Population	[α]		
		λ = 546 nm	λ = 578 nm	λ = 589 nm
2a	6.4	+225.0	+136.3	+112.7
2b	26.2	+246.5	+202.8	+189.5
2c	15.4	+276.0	+205.9	+185.8
2d	10.5	-215.5	-210.4	-206.5
2e	29.3	+314.5	+246.1	+225.9
2f	12.2	+873.2	+690.4	+636.3
	Conformational average	+297.5	+227.7	+207.5
	Experimental	+132.5	+103.6	+92.8

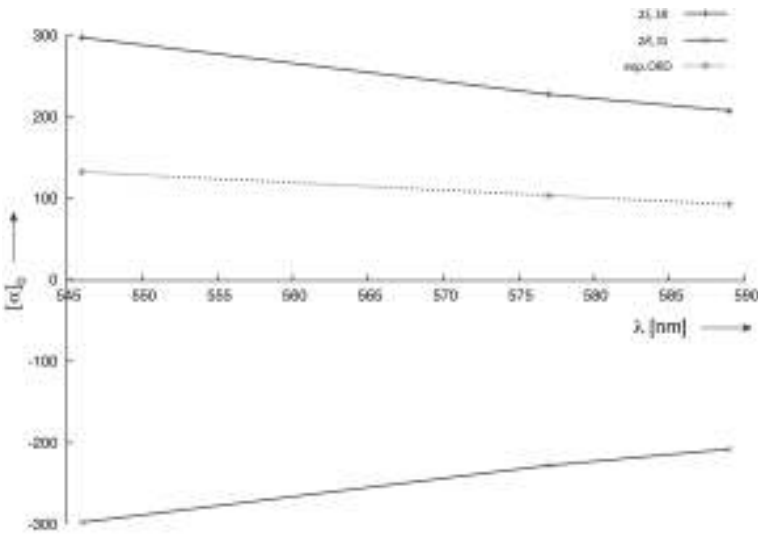


Figure S2. Comparison of experimental ORD values with those calculated for the two possible enantiomers (2*S*,3*R* and 2*R*,3*S*) of **2**. The calculations were performed with DFT at the B3LYP/6-31G(d) level using the IEFPCM solvent continuum model with methanol as the solvent. The calculated ORD values are weighted based on the Gibbs free energy.

Coordinates of conformers (**2a**-**2f**):

Conformer **2a**

1	C1	3.6836	-0.3455	0.2323 C
2	C2	2.3266	-0.5430	0.0083 C
3	C3	1.8286	-1.9291	-0.2065 C
4	O4	2.5688	-2.8705	-0.4560 O
5	C5	0.3476	-2.1465	-0.0939 C
6	C6	-0.6002	-1.0029	-0.1652 C
7	C7	-0.0027	0.3810	-0.3167 C
8	O8	-0.7449	1.3307	-0.6020 O
9	C9	1.4357	0.5612	-0.0827 C
10	C10	1.9663	1.8728	0.0245 C
11	C11	3.3377	2.0528	0.2820 C
12	C12	4.1799	0.9564	0.3870 C
13	H13	4.3419	-1.2055	0.2805 H
14	H14	0.0016	-3.1376	-0.3807 H
15	H15	3.7135	3.0663	0.3777 H
16	H16	5.2380	1.1111	0.5756 H
17	O17	-0.2408	-1.6034	1.0979 O
18	C18	-2.0403	-1.2095	-0.6096 C
19	C19	-3.0435	-0.6711	0.3814 C
20	C20	-4.0416	0.1984	0.1624 C
21	C21	-4.9782	0.5858	1.2830 C
22	H22	-2.1914	-2.2916	-0.7216 H
23	H23	-2.1612	-0.7677	-1.6017 H
24	H24	-2.9343	-1.0795	1.3862 H
25	H25	-4.7261	0.0810	2.2209 H
26	H26	-6.0186	0.3383	1.0300 H
27	H27	-4.9525	1.6702	1.4592 H
28	C28	-4.3386	0.8639	-1.1584 C
29	H29	-4.3250	1.9565	-1.0456 H
30	H30	-5.3475	0.6010	-1.5049 H
31	H31	-3.6314	0.6015	-1.9480 H
32	O32	1.2082	2.9730	-0.1082 O
33	H33	0.2958	2.6685	-0.3481 H

Conformer **2b**

1	C1	3.3744	0.5921	0.7424 C
2	C2	2.0623	0.6522	0.2898 C
3	C3	1.3697	1.9704	0.2833 C
4	O4	1.8051	2.9507	0.8717 O
5	C5	0.0834	2.0676	-0.4843 C

6	C6	-0.6539	0.8446	-0.8813 C
7	C7	-0.0066	-0.4953	-0.5954 C
8	O8	-0.6445	-1.5294	-0.8411 O
9	C9	1.3775	-0.5281	-0.1124 C
10	C10	2.0568	-1.7713	-0.0249 C
11	C11	3.3918	-1.8097	0.4183 C
12	C12	4.0379	-0.6420	0.7931 C
13	H13	3.8674	1.5061	1.0536 H
14	H14	-0.4665	2.9963	-0.3431 H
15	H15	3.8894	-2.7728	0.4660 H
16	H16	5.0662	-0.6870	1.1389 H
17	O17	0.1378	1.5854	-1.8380 O
18	C18	-2.1609	0.8733	-1.0629 C
19	C19	-2.8926	0.7304	0.2494 C
20	C20	-3.7316	-0.2467	0.6289 C
21	C21	-4.3950	-0.2004	1.9855 C
22	H22	-2.4401	0.0953	-1.7771 H
23	H23	-2.4031	1.8400	-1.5233 H
24	H24	-2.7066	1.5399	0.9565 H
25	H25	-4.1391	-1.0901	2.5774 H
26	H26	-5.4894	-0.1990	1.8867 H
27	H27	-4.1030	0.6865	2.5564 H
28	C28	-4.1066	-1.4431	-0.2100 C
29	H29	-3.5575	-1.5025	-1.1510 H
30	H30	-3.9175	-2.3706	0.3469 H
31	H31	-5.1816	-1.4317	-0.4367 H
32	O32	1.4769	-2.9368	-0.3508 O
33	H33	0.5395	-2.7334	-0.6037 H

Conformer **2c**

1	C1	-3.0896	1.6946	0.2481 C
2	C2	-1.8849	1.0489	-0.0002 C
3	C3	-0.6677	1.8715	-0.2437 C
4	O4	-0.7159	3.0704	-0.4830 O
5	C5	0.6585	1.1715	-0.1823 C
6	C6	0.7390	-0.3067	-0.2752 C
7	C7	-0.5650	-1.0766	-0.3370 C
8	O8	-0.5260	-2.2966	-0.5546 O
9	C9	-1.8233	-0.3698	-0.0774 C
10	C10	-3.0222	-1.1125	0.0799 C
11	C11	-4.2286	-0.4424	0.3544 C
12	C12	-4.2565	0.9411	0.4391 C
13	H13	-3.1096	2.7778	0.2877 H
14	H14	1.5146	1.7665	-0.4905 H

15	H15	-5.1280	-1.0357	0.4832 H
16	H16	-5.1961	1.4455	0.6437 H
17	O17	0.8661	0.3697	0.9928 O
18	C18	1.9712	-1.0313	-0.8043 C
19	C19	3.2286	-0.1999	-0.8393 C
20	C20	4.1812	-0.1310	0.1050 C
21	C21	5.3970	0.7432	-0.0901 C
22	H22	1.7303	-1.3765	-1.8170 H
23	H23	2.0964	-1.9355	-0.2006 H
24	H24	3.3607	0.4026	-1.7380 H
25	H25	5.3734	1.2708	-1.0487 H
26	H26	6.3189	0.1468	-0.0488 H
27	H27	5.4756	1.4904	0.7115 H
28	C28	4.1518	-0.8874	1.4098 C
29	H29	3.2715	-1.5235	1.5227 H
30	H30	5.0471	-1.5158	1.5111 H
31	H31	4.1672	-0.1869	2.2556 H
32	O32	-3.0630	-2.4503	-0.0215 O
33	H33	-2.1492	-2.7512	-0.2619 H

Conformer **2d**

1	C1	-3.0672	1.4300	-0.6838 C
2	C2	-1.8385	0.9742	-0.2233 C
3	C3	-0.7229	1.9499	-0.0771 C
4	O4	-0.7537	3.0699	-0.5681 O
5	C5	0.4753	1.5088	0.7126 C
6	C6	0.7100	0.0728	0.9895 C
7	C7	-0.3471	-0.9142	0.5388 C
8	O8	-0.1134	-2.1272	0.6491 O
9	C9	-1.6322	-0.4064	0.0508 C
10	C10	-2.6999	-1.3128	-0.1783 C
11	C11	-3.9438	-0.8293	-0.6244 C
12	C12	-4.1210	0.5235	-0.8693 C
13	H13	-3.1925	2.4855	-0.8971 H
14	H14	1.3244	2.1887	0.6800 H
15	H15	-4.7464	-1.5429	-0.7800 H
16	H16	-5.0842	0.8818	-1.2198 H
17	O17	0.1778	0.9521	2.0059 O
18	C18	2.1158	-0.4576	1.2200 C
19	C19	2.7926	-0.8874	-0.0589 C
20	C20	3.8780	-0.3488	-0.6378 C
21	C21	4.6556	0.8311	-0.1085 C
22	H22	2.0365	-1.3134	1.9024 H
23	H23	2.6750	0.3224	1.7425 H

24	H24	2.3305	-1.7439	-0.5482 H
25	H25	4.2632	1.2318	0.8288 H
26	H26	4.6636	1.6456	-0.8455 H
27	H27	5.7058	0.5545	0.0570 H
28	C28	4.4245	-0.9281	-1.9218 C
29	H29	5.4615	-1.2666	-1.7895 H
30	H30	3.8304	-1.7769	-2.2745 H
31	H31	4.4456	-0.1696	-2.7165 H
32	O32	-2.5793	-2.6355	0.0140 O
33	H33	-1.6398	-2.8057	0.2818 H

Conformer **2e**

1	C1	3.0686	1.7555	-0.1513 C
2	C2	1.8705	1.0559	-0.0815 C
3	C3	0.5919	1.8183	-0.1191 C
4	O4	0.5310	2.9929	-0.4559 O
5	C5	-0.6556	1.0869	0.2815 C
6	C6	-0.6828	-0.3941	0.3322 C
7	C7	0.6110	-1.1289	0.0446 C
8	O8	0.5835	-2.3633	-0.0677 O
9	C9	1.8606	-0.3655	-0.0335 C
10	C10	3.0991	-1.0566	-0.0848 C
11	C11	4.3033	-0.3303	-0.1313 C
12	C12	4.2835	1.0556	-0.1610 C
13	H13	3.0457	2.8382	-0.2006 H
14	H14	-1.5878	1.6211	0.1133 H
15	H15	5.2363	-0.8839	-0.1565 H
16	H16	5.2203	1.6028	-0.2048 H
17	O17	-0.5683	0.3900	1.5388 O
18	C18	-1.9677	-1.1854	0.1287 C
19	C19	-3.2086	-0.4642	0.5824 C
20	C20	-4.2796	-0.1229	-0.1530 C
21	C21	-5.4577	0.5715	0.4895 C
22	H22	-2.0157	-1.4683	-0.9273 H
23	H23	-1.8552	-2.1229	0.6890 H
24	H24	-3.2223	-0.2153	1.6428 H
25	H25	-5.2962	0.7502	1.5570 H
26	H26	-5.6559	1.5375	0.0051 H
27	H27	-6.3736	-0.0251	0.3764 H
28	C28	-4.4423	-0.3857	-1.6302 C
29	H29	-3.5777	-0.8718	-2.0876 H
30	H30	-4.6237	0.5548	-2.1675 H
31	H31	-5.3208	-1.0198	-1.8120 H
32	O32	3.1801	-2.3964	-0.0906 O

33 H33 2.2512 -2.7430 -0.1023 H

Conformer **2f**

1 C1 3.4517 0.9941 0.5263 C
2 C2 2.1415 0.8203 0.0981 C
3 C3 1.3189 2.0247 -0.2004 C
4 O4 1.8002 3.1412 -0.3353 O
5 C5 -0.1631 1.8246 -0.3283 C
6 C6 -0.7366 0.4686 -0.5345 C
7 C7 0.2328 -0.6944 -0.5667 C
8 O8 -0.1734 -1.8047 -0.9398 O
9 C9 1.6129 -0.4824 -0.1162 C
10 C10 2.4617 -1.6018 0.0847 C
11 C11 3.7768 -1.4076 0.5458 C
12 C12 4.2595 -0.1266 0.7651 C
13 H13 3.8327 1.9994 0.6659 H
14 H14 -0.7182 2.6921 -0.6798 H
15 H15 4.3988 -2.2821 0.7070 H
16 H16 5.2797 0.0083 1.1115 H
17 O17 -0.7638 1.1031 0.7592 O
18 C18 -2.0855 0.2895 -1.2194 C
19 C19 -3.0144 -0.6532 -0.4900 C
20 C20 -4.0474 -0.3220 0.3010 C
21 C21 -4.8912 -1.3965 0.9464 C
22 H22 -2.5336 1.2803 -1.3314 H
23 H23 -1.8943 -0.0884 -2.2314 H
24 H24 -2.7971 -1.7095 -0.6325 H
25 H25 -4.5473 -2.4014 0.6824 H
26 H26 -4.8746 -1.3048 2.0413 H
27 H27 -5.9438 -1.3040 0.6443 H
28 C28 -4.4755 1.0876 0.6285 C
29 H29 -5.5135 1.2594 0.3123 H
30 H30 -4.4530 1.2484 1.7149 H
31 H31 -3.8480 1.8538 0.1684 H
32 O32 2.0637 -2.8628 -0.1462 O
33 H33 1.1464 -2.8141 -0.5184 H

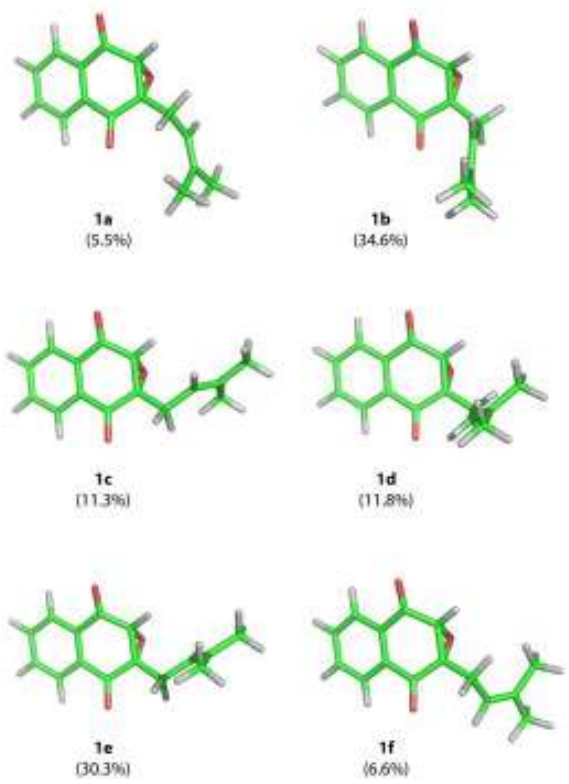


Figure S3. Six energy lowest conformers of (2*S*,3*R)*-epoxy-2,3-dihydrolapachol (**1**). Population of each conformer was calculated using the Gibbs free energy.

Table S4. Excited energy, wavelength, oscillator strength, rotatory strength in velocity form and rotatory strength in length form of **1a-1f**.[a]

Conformer	ΔE (eV)	λ (nm)	f	$R^{vel,b}$	$R^{len,b}$
1a	3.09	400.8	0.001	-5.7	-7.8
	3.47	357.5	0.002	-24.3	-22.7
	3.65	339.6	0.007	33.8	33.3
	4.18	296.5	0.022	-3.6	-4.0
	4.25	292.0	0.047	-3.1	-5.2
	4.38	283.0	0.058	9.2	10.0
	4.76	260.3	0.008	0.6	-1.3
	4.85	255.6	0.007	1.1	4.1
	5.21	237.9	0.082	-0.2	-0.1
	5.41	229.3	0.064	7.6	7.0
	5.44	227.8	0.042	10.4	11.3
	5.49	225.6	0.480	5.7	3.6
	5.91	209.9	0.051	-16.9	-18.1
	6.05	205.0	0.007	2.7	2.5
	6.08	203.9	0.024	-3.9	-3.9
	6.14	201.8	0.012	7.0	6.8
1b	3.16	392.7	0.0003	4.9	3.9
	3.44	359.9	0.001	-23.3	-21.0
	3.61	343.9	0.002	15.2	15.1
	4.20	295.5	0.063	-2.5	-2.4
	4.27	290.3	0.010	12.5	11.5
	4.36	284.5	0.060	-4.4	-4.4
	4.71	263.4	0.004	-1.3	-2.7
	4.84	256.2	0.013	1.0	3.3
	5.17	240.0	0.073	-3.9	-4.0
	5.38	230.3	0.044	-0.5	-1.1
	5.45	227.5	0.080	19.6	19.2
	5.48	226.1	0.482	-3.5	-4.6
	6.00	206.8	0.015	10.2	10.1
	6.05	204.9	0.049	8.1	8.9
	6.09	203.8	0.009	-12.0	-12.1
	6.15	201.6	0.002	2.5	2.6
1c	3.22	385.5	0.001	3.1	1.7
	3.44	360.3	0.001	-22.1	-19.8
	3.66	339.0	0.005	20.6	20.0
	4.20	295.0	0.064	-4.2	-4.2
	4.33	286.2	0.016	-2.7	-5.9

	4.37	283.6	0.046	9.5	12.1
	4.71	263.4	0.004	-0.5	-2.4
	4.85	255.5	0.016	2.7	6.1
	5.18	239.5	0.064	-0.8	-0.8
	5.40	229.6	0.046	3.2	2.9
	5.46	227.0	0.074	19.6	20.4
	5.49	225.7	0.525	-23.1	-24.2
	5.98	207.3	0.009	11.5	11.5
	6.10	203.1	0.014	-4.8	-4.4
	6.14	201.8	0.004	-0.4	-0.3
	6.18	200.5	0.0004	3.6	3.8
1d	3.19	388.6	0.0001	1.0	0.02
	3.44	360.4	0.001	-22.0	-19.7
	3.59	345.8	0.003	16.3	16.3
	4.19	296.0	0.056	-2.5	-2.4
	4.30	288.6	0.034	23.8	23.2
	4.36	284.1	0.063	-10.6	-10.2
	4.69	264.2	0.005	0.1	-1.4
	4.83	256.4	0.007	-3.4	-0.5
	5.17	240.0	0.046	-2.9	-3.0
	5.38	230.6	0.046	-0.9	-1.7
	5.47	226.8	0.198	77.1	77.5
	5.48	226.1	0.402	-26.9	-26.3
	5.95	208.5	0.008	-0.5	-0.7
	6.08	203.9	0.024	2.1	2.5
	6.09	203.6	0.007	-2.0	-1.3
	6.17	201.0	0.003	3.7	3.7
1e	3.22	385.3	0.001	2.2	0.6
	3.45	359.9	0.001	-22.5	-20.1
	3.65	339.8	0.006	20.8	20.6
	4.20	295.2	0.064	-3.5	-3.4
	4.33	286.2	0.014	-4.3	-7.3
	4.38	283.2	0.055	6.1	8.1
	4.71	263.3	0.004	-0.2	-1.8
	4.85	255.8	0.013	2.1	5.3
	5.18	239.6	0.055	-3.1	-3.3
	5.40	229.8	0.034	-0.5	-0.8
	5.49	225.8	0.548	9.3	9.5
	5.54	223.6	0.078	-3.0	-3.4
	5.89	210.3	0.003	-3.2	-3.5
	6.09	203.7	0.017	2.0	2.6

	6.14	201.8	0.004	-4.1	-4.2
	6.18	200.6	0.002	8.1	8.5
1f	3.16	392.4	0.002	-8.5	-10.1
	3.45	359.1	0.003	-20.1	-18.6
	3.60	344.8	0.008	27.3	25.9
	4.20	295.2	0.051	-3.6	-3.6
	4.28	290.0	0.023	-14.0	-16.6
	4.38	283.2	0.061	15.2	16.8
	4.75	261.2	0.012	-1.0	-3.2
	4.80	258.3	0.003	-0.4	2.5
	5.19	238.8	0.087	6.0	6.7
	5.40	229.5	0.055	9.8	9.2
	5.44	228.0	0.040	3.0	3.9
	5.49	225.8	0.496	-46.6	-49.7
	5.99	206.9	0.036	-7.2	-7.8
	6.07	204.1	0.021	0.6	0.4
	6.10	203.3	0.010	-9.4	-10.2
	6.15	201.8	0.009	19.7	20.3

[a] All calculations were performed at the B3LYP/6-31G(d) level using the IEFPCM solvent continuum model with methanol as the solvent. [b] 10^{-40} cgs.

Table S5. Conformational analysis of **1** using the IEFPCM solvent continuum model (methanol)

Conformer	ΔE^a	P_{Eb} (%)[b]	$\Delta E_0{}^a$	P_{E0} (%)[b]	ΔG^a	P_G(%)[b]
1a	0.84	7.0	0.85	6.9	1.09	5.5
1b	0.15	23.0	0.18	21.3	0	34.6
1c	0.45	13.8	0.44	13.8	0.66	11.3
1d	0.29	18.0	0.23	19.8	0.4	11.8
1e	0	29.6	0	29.1	008	30.3
1f	0.73	8.6	0.69	9.0	0.98	6.6

[a] Relative energy, relative zero point energy, and relative Gibbs free energy at the B3LYP/6-31G(d) level, respectively (kcal/mol). [b] Conformational distribution calculated by using the respective parameters above at the B3LYP/6-31G(d) level.

Table S6. Important dihedral angles (deg) of optimized predominant conformers **1a-1f** with DFT at the B3LYP/6-31G(d) using the IEFPCM solvent continuum model with methanol as the solvent.

	1a	**1b**	**1c**	**1d**	**1e**	**1f**
C3-C2-C1'-C2'	129	-81	17	-88	30	135
C2-C1'-C2'-C3'	125	-118	93	116	-120	-102

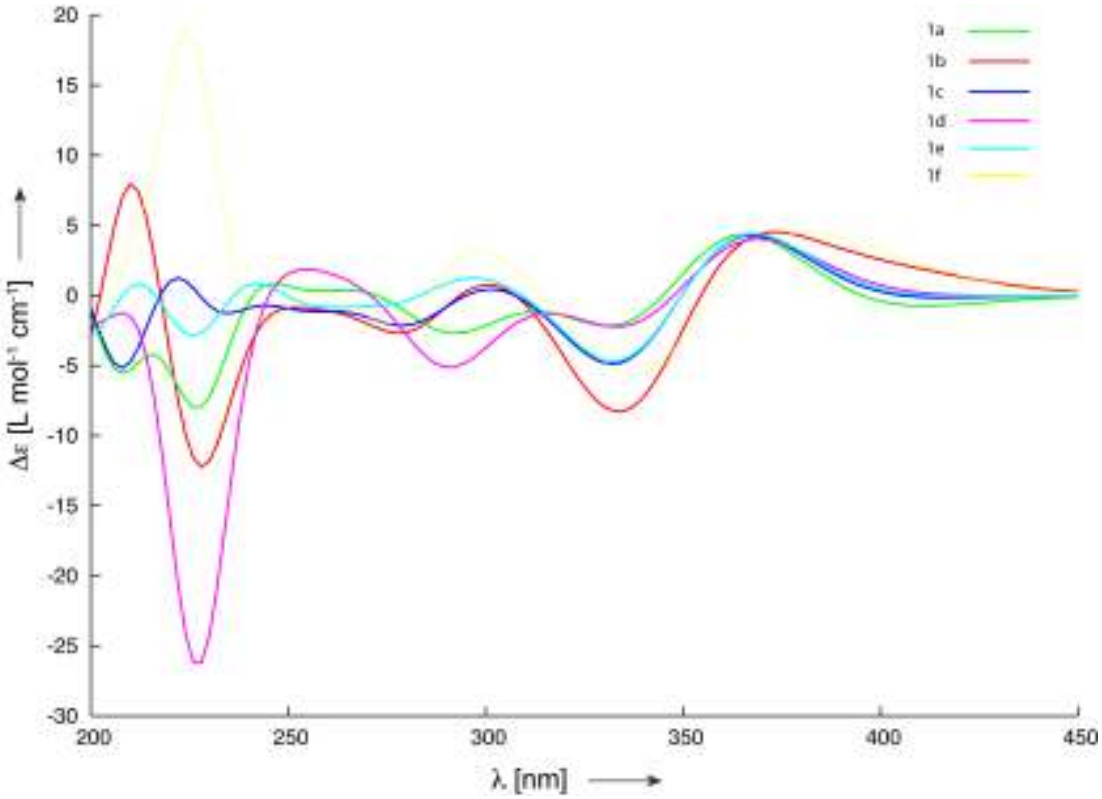


Figure S4. Comparison of the computed ECD spectra for the six energy lowest conformers of **1** with a 2*S*,3*R* configuration. The calculations were performed with DFT at the B3LYP/6-31G(d) level using the IEFPCM solvent continuum model with methanol as the solvent.

Table S7. Calculated ORD values for the six energy lowest conformers of (2*S*,3*R*)-**1** at different wavelengths.

Conformation	Population	[α]		
		λ = 546 nm	λ = 578 nm	λ = 589 nm
1a	5.5	-190.5	-191.5	-185.4
1b	34.6	109.1	114.5	130.6
1c	11.3	-118.1	-122.3	-133.0
1d	11.8	-319.6	-333.0	-370.3
1e	30.3	60.1	66.2	86.9
1f	6.6	293.9	318.1	399.4
	Conformational average	+13.8	+17.0	+28.9
	Experimental	-3.0	-11.3	-9.0

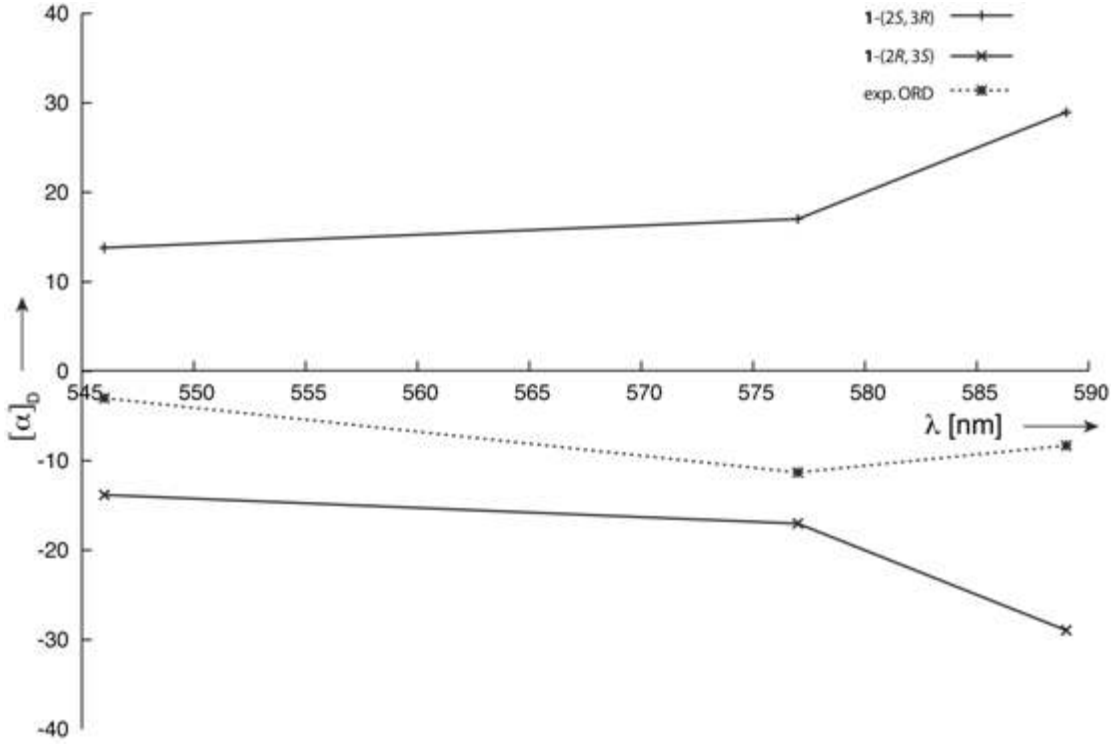


Figure S5. Comparison of experimental ORD values with those calculated for the two possible enantiomers (2*S*,3*R* and 2*R*,3*S*) of **1**. The calculations were performed with DFT at the B3LYP/6-31G(d) using the IEFPCM solvent continuum model with methanol as the solvent. The calculated ORD values are weighted based on the Gibbs free energy.

Coordinate of conformers **1a**-**1f**:

Conformer **1a**:

1	C1	-3.7542	-0.0223	-0.2017 C
2	C2	-2.4006	0.2634	0.0068 C
3	C3	-1.9686	1.6746	0.1859 C
4	O4	-2.7453	2.5852	0.4392 O
5	C5	-0.5018	1.9559	0.0177 C
6	C6	0.5058	0.8632	0.1255 C
7	C7	-0.0256	-0.5309	0.3987 C
8	O8	0.7059	-1.4000	0.8493 O
9	C9	-1.4655	-0.7903	0.0996 C
10	C10	-3.2513	-2.3882	-0.2504 C
11	C11	-4.1772	-1.3426	-0.3412 C
12	H12	-4.4607	0.7998	-0.2525 H
13	H13	-0.1971	2.9770	0.2395 H
14	H14	-3.5826	-3.4171	-0.3541 H
15	H15	-5.2268	-1.5597	-0.5147 H
16	O16	0.0814	1.3722	-1.1562 O
17	C17	1.9441	1.1644	0.5145 C
18	C18	2.9411	0.5595	-0.4438 C
19	C19	3.9673	-0.2597	-0.1679 C
20	C20	4.8874	-0.7316	-1.2696 C
21	H21	2.0601	2.2565	0.5146 H
22	H22	2.1000	0.8260	1.5417 H
23	H23	2.7979	0.8650	-1.4806 H
24	H24	4.5992	-0.3284	-2.2455 H
25	H25	5.9262	-0.4338	-1.0696 H
26	H26	4.8880	-1.8284	-1.3379 H
27	C27	4.3149	-0.7838	1.2032 C
28	H28	4.3322	-1.8822	1.1979 H
29	H29	5.3231	-0.4598	1.4959 H
30	H30	3.6181	-0.4653	1.9812 H
31	C31	-1.9046	-2.1136	-0.0187 C
32	H32	-1.1801	-2.9158	0.0741 H

Conformer **1b**:

1	C1	3.4976	0.2346	-0.7151 C
2	C2	2.1748	0.3643	-0.2780 C
3	C3	1.5176	1.6966	-0.3385 C
4	O4	1.9697	2.6339	-0.9822 O
5	C5	0.2463	1.8633	0.4440 C
6	C6	-0.5390	0.6800	0.8789 C

7	C7	0.0412	-0.6949	0.6010 C
8	O8	-0.6376	-1.6965	0.7752 O
9	C9	1.4685	-0.7731	0.1723 C
10	C10	3.4271	-2.1371	-0.2450 C
11	C11	4.1249	-1.0093	-0.6914 C
12	H12	4.0193	1.1176	-1.0691 H
13	H13	-0.2664	2.8112	0.2899 H
14	H14	3.9150	-3.1071	-0.2307 H
15	H15	5.1544	-1.1031	-1.0235 H
16	O16	0.3001	1.4066	1.8053 O
17	C17	-2.0401	0.7836	1.0822 C
18	C18	-2.7999	0.6781	-0.2176 C
19	C19	-3.6962	-0.2526	-0.5819 C
20	C20	-4.3789	-0.1713	-1.9273 C
21	H21	-2.3462	0.0192	1.8001 H
22	H22	-2.2285	1.7607	1.5463 H
23	H23	-2.5838	1.4767	-0.9288 H
24	H24	-4.1791	-1.0728	-2.5230 H
25	H25	-5.4700	-0.1132	-1.8109 H
26	H26	-4.0504	0.6995	-2.5033 H
27	C27	-4.1200	-1.4275	0.2642 C
28	H28	-3.5538	-1.5199	1.1923 H
29	H29	-3.9963	-2.3631	-0.2976 H
30	H30	-5.1873	-1.3559	0.5152 H
31	C31	2.1040	-2.0202	0.1765 C
32	H32	1.5466	-2.8885	0.5114 H

Conformer **1c**:

1	C1	-3.3809	1.2908	-0.2578 C
2	C2	-2.1225	0.7413	0.0097 C
3	C3	-0.9731	1.6453	0.2804 C
4	O4	-1.1076	2.8320	0.5468 O
5	C5	0.3997	1.0404	0.2007 C
6	C6	0.5899	-0.4304	0.3004 C
7	C7	-0.6570	-1.2888	0.4103 C
8	O8	-0.5684	-2.4620	0.7436 O
9	C9	-1.9665	-0.6611	0.0679 C
10	C10	-4.3216	-0.9315	-0.4300 C
11	C11	-4.4748	0.4584	-0.4864 C
12	H12	-3.4848	2.3706	-0.2835 H
13	H13	1.2158	1.6968	0.4928 H
14	H14	-5.1754	-1.5795	-0.6037 H
15	H15	-5.4474	0.8896	-0.7035 H
16	O16	0.6442	0.2467	-0.9714 O

17	C17	1.8811	-1.0566	0.8129 C
18	C18	3.0760	-0.1371	0.8210 C
19	C19	3.9999	0.0011	-0.1439 C
20	C20	5.1513	0.9637	0.0237 C
21	H21	1.6821	-1.4109	1.8313 H
22	H22	2.0617	-1.9550	0.2137 H
23	H23	3.1831	0.4751	1.7166 H
24	H24	5.1085	1.4914	0.9816 H
25	H25	6.1142	0.4376	-0.0360 H
26	H26	5.1571	1.7119	-0.7808 H
27	C27	3.9981	-0.7584	-1.4474 C
28	H28	3.1645	-1.4575	-1.5405 H
29	H29	4.9347	-1.3197	-1.5675 H
30	H30	3.9440	-0.0609	-2.2940 H
31	C31	-3.0759	-1.4874	-0.1445 C
32	H32	-2.9462	-2.5625	-0.0808 H

Conformer **1d**:

1	C1	-3.3297	1.0351	0.6587 C
2	C2	-2.0556	0.6613	0.2184 C
3	C3	-0.9958	1.6972	0.0919 C
4	O4	-1.0876	2.8089	0.5943 O
5	C5	0.2227	1.3262	-0.7051 C
6	C6	0.5556	-0.0964	-0.9651 C
7	C7	-0.4187	-1.1486	-0.4702 C
8	O8	-0.0924	-2.3274	-0.4516 O
9	C9	-1.7776	-0.6965	-0.0550 C
10	C10	-4.0550	-1.2700	0.5389 C
11	C11	-4.3287	0.0754	0.8100 C
12	H12	-3.5210	2.0804	0.8775 H
13	H13	1.0243	2.0623	-0.6914 H
14	H14	-4.8324	-2.0180	0.6615 H
15	H15	-5.3187	0.3722	1.1430 H
16	O16	-0.0498	0.7296	-1.9848 O
17	C17	1.9941	-0.5255	-1.2044 C
18	C18	2.7256	-0.8453	0.0763 C
19	C19	3.7883	-0.2115	0.5983 C
20	C20	4.4808	0.9829	-0.0115 C
21	H21	1.9680	-1.4146	-1.8478 H
22	H22	2.4828	0.2707	-1.7709 H
23	H23	2.3276	-1.7005	0.6206 H
24	H24	4.0405	1.3126	-0.9553 H
25	H25	4.4614	1.8327	0.6842 H
26	H26	5.5405	0.7586	-0.1949 H

27	C27	4.3969	-0.6872	1.8971 C
28	H28	5.4500	-0.9683	1.7579 H
29	H29	3.8637	-1.5507	2.3068 H
30	H30	4.3870	0.1120	2.6512 H
31	C31	-2.7833	-1.6542	0.1177 C
32	H32	-2.5523	-2.6955	-0.0805 H

Conformer **1e**:

1	C1	3.3771	1.3668	-0.1404 C
2	C2	2.1195	0.7559	-0.0912 C
3	C3	0.8954	1.5984	-0.1515 C
4	O4	0.9097	2.7691	-0.5074 O
5	C5	-0.3947	0.9505	0.2627 C
6	C6	-0.5275	-0.5286	0.2973 C
7	C7	0.7043	-1.3472	-0.0427 C
8	O8	0.6017	-2.5408	-0.2879 O
9	C9	2.0242	-0.6520	-0.0348 C
10	C10	4.4416	-0.8042	-0.0574 C
11	C11	4.5343	0.5910	-0.1141 C
12	H12	3.4304	2.4490	-0.1983 H
13	H13	-1.2898	1.5507	0.1160 H
14	H14	5.3437	-1.4083	-0.0416 H
15	H15	5.5083	1.0702	-0.1425 H
16	O16	-0.3354	0.2322	1.5080 O
17	C17	-1.8699	-1.2206	0.1062 C
18	C18	-3.0480	-0.4252	0.6011 C
19	C19	-4.1011	0.0160	-0.1065 C
20	C20	-5.2156	0.7757	0.5745 C
21	H21	-1.9585	-1.4768	-0.9537 H
22	H22	-1.8127	-2.1766	0.6439 H
23	H23	-3.0282	-0.2071	1.6682 H
24	H24	-5.0285	0.9066	1.6448 H
25	H25	-5.3458	1.7693	0.1241 H
26	H26	-6.1754	0.2539	0.4556 H
27	C27	-4.3031	-0.1897	-1.5880 C
28	H28	-3.4822	-0.7226	-2.0730 H
29	H29	-4.4233	0.7772	-2.0947 H
30	H30	-5.2276	-0.7533	-1.7741 H
31	C31	3.1928	-1.4222	-0.0279 C
32	H32	3.1059	-2.5032	-0.0012 H

Conformer **1f**:

1	C1	3.6216	0.5124	0.5450 C
2	C2	2.2973	0.4823	0.0952 C
3	C3	1.5851	1.7597	-0.1727 C
4	O4	2.1598	2.8330	-0.2932 O
5	C5	0.0874	1.6873	-0.2734 C
6	C6	-0.6014	0.3941	-0.5447 C
7	C7	0.2800	-0.8302	-0.6979 C
8	O8	-0.1444	-1.8365	-1.2482 O
9	C9	1.6660	-0.7568	-0.1503 C
10	C10	3.6857	-1.9063	0.5306 C
11	C11	4.3103	-0.6775	0.7726 C
12	H12	4.0958	1.4740	0.7116 H
13	H13	-0.4030	2.6157	-0.5599 H
14	H14	4.2251	-2.8327	0.7037 H
15	H15	5.3342	-0.6502	1.1329 H
16	O16	-0.5451	0.9490	0.7830 O
17	C17	-1.9750	0.3660	-1.1992 C
18	C18	-2.9316	-0.5948	-0.5321 C
19	C19	-3.9263	-0.2921	0.3174 C
20	C20	-4.8028	-1.3822	0.8887 C
21	H21	-2.3679	1.3861	-1.1972 H
22	H22	-1.8351	0.0791	-2.2487 H
23	H23	-2.7681	-1.6425	-0.7761 H
24	H24	-4.5149	-2.3731	0.5238 H
25	H25	-4.7521	-1.3925	1.9864 H
26	H26	-5.8576	-1.2147	0.6296 H
27	C27	-4.2780	1.0994	0.7841 C
28	H28	-5.3128	1.3488	0.5117 H
29	H29	-4.2250	1.1571	1.8798 H
30	H30	-3.6232	1.8745	0.3804 H
31	C31	2.3745	-1.9452	0.0599 C
32	H32	1.8853	-2.8905	-0.1496 H