Table S1 Geometrical bond length parameters of tretinoin

Bond length Parameters	Experimental bond lengths (Å)	Theoretical B3LYP/6-311++G(d,p)		Bond length Parameters	Experimental bond lengths (Å)	Theoretical B3LYP/6-311++G(d,p)	
		conf. **A** (Å)	conf. **B** (Å)			conf. **A** (Å)	Conf. **B** (Å)
C1–C8	1.5397	1.5416	1.5433	C10–H33	0.9272	1.0955	1.0970
C1–C9	1.5303	1.5436	1.5424	C10–H34	1.1527	1.0903	1.0979
C1–C12	1.5521	1.5415	1.5420	C11–C20	1.5039	1.5071	1.5071
C1–C17	1.5334	1.5419	1.5421	C11–H35	0.8397	1.0889	1.0890
C2–C3	1.4412	1.4342	1.4341	C11–H36	0.9877	1.0956	1.0955
C2–C20	1.3505	1.3641	1.3641	C11–H37	1.1209	1.0955	1.0956
C2–H48	0.9656	1.0886	1.0886	C12–C14	1.5024	1.5246	1.5250
C3–C4	1.3391	1.3569	1.3569	C12–H21	1.0560	1.0956	1.0954
C3–H22	0.9985	1.0839	1.0840	C12–H32	1.1613	1.0973	1.0976
C4–C5	1.4543	1.4505	1.4505	C13–H38	0.9691	1.0860	1.0860
C4–H23	1.0467	1.0880	1.0880	C13–H39	1.0290	1.0956	1.0955
C5–C6	1.3398	1.3606	1.3606	C13–H40	1.0136	1.0955	1.0956
C5–C13	1.4963	1.5071	1.5070	C14–C15	1.5094	1.5281	1.5271
C6–C7	1.4679	1.4648	1.4649	C14–H42	1.0953	1.0944	1.0943
C6–H24	1.0050	1.0844	1.0844	C14–H43	1.1394	1.0950	1.0953
C7–O49	1.3201	1.3680	1.3680	C15–C16	1.5025	1.5146	1.5123
C7–O50	1.2229	1.2148	1.2148	C15–H44	1.0352	1.0962	1.0978
C8–H25	1.0773	1.0943	1.0947	C15–H45	1.0681	1.1009	1.1005
C8–H26	0.9852	1.0933	1.0929	C16–C17	1.3566	1.3540	1.3537
C8–H27	1.0476	1.0954	1.0949	C17–C18	1.4631	1.4667	1.4684
C9–H28	0.9618	1.0938	1.0939	C18–C19	1.3390	1.3502	1.3505
C9–H29	0.9318	1.0957	1.0958	C18–H46	0.9850	1.0863	1.0847
C9–H30	0.9544	1.0928	1.0933	C19–C20	1.4550	1.4512	1.4508
C10–C16	1.5183	1.5092	1.5086	C19–H47	0.9610	1.0855	1.0861
C10–H31	1.0483	1.0984	1.0900	H41–O49	1.0354	0.9681	0.9681

Table S2 Geometrical bond angle parameters of tretinoin

Bond angle Parameters	Experimental bond angle (º)	Theoretical B3LYP/6-311++G(d,p)		Bond angle Parameters	Experimental bond angle (º)	Theoretical B3LYP/6-311++G(d,p)	
		conf. **A** (º)	conf. **B** (º)			conf.**A** (º)	conf. **B** (º)
C8–C1–C9	109.6	108.6	108.3	C20–C11–H37	105.1	110.3	110.2
C8–C1–C12	104.5	107.4	107.1	H35–C11–H36	114.7	108.1	108.3
C8–C1–C17	111.2	110.6	111.3	H35–C11–H37	100.1	108.3	108.1
C9–C1–C12	110.1	109.6	109.9	H36–C11–H37	111.2	107.0	106.9
C9–C1–C17	111.2	109.4	108.9	C1–C12–C14	112.3	112.2	112.2
C12–C1–C17	110.1	111.2	111.3	C1–C12–H21	109.5	108.6	108.5
C3–C2–C20	127.3	127.4	127.5	C1–C12–H32	110.2	108.7	108.8
C3–C2–H48	115.1	115.6	115.5	C14–C12–H21	110.0	111.2	111.4
C20–C2–H48	117.6	117.0	117.0	C14–C12–H32	105.0	108.8	108.6
C2–C3–C4	123.4	123.1	123.1	H21–C12–H32	109.9	107.1	107.2
C2–C3–H22	117.7	118.4	118.5	C5–C13–H38	111.6	111.8	111.8
C4–C3–H22	118.8	118.4	118.5	C5–C13–H39	109.6	109.6	109.6
C3–C4–C5	126.7	125.3	125.3	C5–C13–H40	112.0	109.6	109.6
C3–C4–H23	115.8	118.3	118.3	H38–C13–H39	119.0	109.3	109.3
C5–C4–H23	117.2	116.4	116.4	H38–C13–H40	95.8	109.3	109.3
C4–C5–C6	117.4	117.5	117.5	H39–C13–H40	108.1	107.0	107.0
C4–C5–C13	118.5	118.2	118.2	C12–C14–C15	109.5	109.4	108.8
C6–C5–C13	124.1	124.2	124.2	C12–C14–H42	107.2	110.8	110.9
C5–C6–C7	128.8	127.1	127.1	C12–C14–H43	109.5	109.9	109.9
C5–C6–H24	116.4	118.4	118.4	C15–C14–H42	107.7	110.2	110.3
C7–C6–H24	114.7	114.5	114.5	C15–C14–H43	107.8	109.5	109.7
C6–C7–O49	112.1	110.1	110.1	H42–C14–H43	115.0	107.1	107.2
C6–C7–O50	125.9	129.0	129.0	C14–C15–C16	113.7	114.1	113.9

O49–C7–O50	122.0	120.9	120.9	C14–C15–H44	111.1	110.3	110.6
C1–C8–H25	112.2	110.6	110.9	C14–C15–HH45	109.0	109.6	109.9
C1–C8–H26	111.1	111.9	112.3	C16–C15–H44	107.0	108.8	108.3
C1–C8–H27	110.4	109.5	109.0	C16–C15–HH45	110.2	108.2	108.4
H25–C8–H26	111.2	108.1	108.8	H44–C15–HH45	105.6	105.6	105.4
H25–C8–H27	103.7	108.5	108.3	C10–C16–C15	112.6	113.1	112.5
H26–C8–H27	107.9	108.1	107.4	C10–C16–C17	123.6	124.4	124.7
C1–C9–H28	113.4	111.3	110.5	C15–C16–C17	123.8	122.5	122.7
C1–C9–H29	114.7	109.8	110.1	C1–C17–C16	121.6	122.5	122.3
C1–C9–H30	110.6	111.2	111.1	C1–C17–C18	120.7	113.9	115.0
H28–C9–H29	103.5	107.8	108.5	C16–C17–C18	117.7	123.6	122.7
H28–C9–H30	107.4	107.9	107.9	C17–C18–C19	131.5	127.2	125.7
H29–C9–H30	106.8	108.7	108.6	C17–C18–H46	111.7	115.1	116.5
C16–C10–H31	110.4	111.1	112.8	C19–C18–H46	116.8	117.6	117.7
C16–C10–H33	111.3	109.8	109.2	C18–C19–C20	125.0	125.4	125.6
C16–C10–H34	110.7	112.7	111.1	C18–C19–H47	121.3	118.8	118.6
H31–C10–H33	114.1	106.6	109.0	C20–C19–H47	113.7	115.8	115.8
H31–C10–H34	107.3	107.7	108.0	C2–C20–C11	122.3	123.5	123.6
H33–C10–H34	102.7	108.8	106.4	C2–C20–C19	119.3	118.4	118.3
C20–C11–H35	118.8	112.9	112.9	C11–C20–C19	118.4	118.1	118.1
C20–C11–H36	106.5	110.2	110.3	C7–O49–H41	109.9	106.6	106.7

Table S3 Geometrical dihedral angle parameters of tretinoin

Dihedral angle Parameters	Experimental[a] Dihedral angle (º)	Theoretical B3LYP/6-311++G(d,p)		Dihedral angle Parameters	Experimental[a] Dihedral angle (º)	Theoretical B3LYP/6-311++G(d,p)	
		conf. **A** (º)	conf. **B** (º)			conf. **A** (º)	conf. **B** (º)
C9–C1–C8–H25	174.7	176.6	172.8	C5–C6–C7–O49	173.8	-180.0	-180.0
C9–C1–C8–H26	49.6	56.0	50.9	C5–C6–C7–O50	-6.9	0.0	0.0
C9–C1–C8–H27	-70.1	-63.8	-68.0	H24–C6–C7–O49	-1.9	0.1	0.0
C12–C1–C8–H25	-67.3	-64.9	-68.8	H24–C6–C7–O50	177.4	-179.9	180.0
C12–C1–C8–H26	167.5	174.5	169.3	C6–C7–O49–H41	175.0	180.0	180.0
C12–C1–C8–H27	47.9	54.6	50.4	O50–C7–O49–H41	-4.3	0.0	0.0
C17–C1–C8–H25	51.4	56.6	53.1	H31–C10–C16–C15	121.9	79.8	160.9
C17–C1–C8–H26	-73.8	-64.0	-68.8	H31–C10–C16–C17	-58.0	-100.5	-17.3
C17–C1–C8–H27	166.6	176.1	172.3	H33–C10–C16–C15	-6.0	-37.9	39.5
C8–C1–C9–H28	-67.0	-63.1	-64.1	H33–C10–C16–C17	174.1	141.9	-138.7
C8–C1–C9–H29	51.5	56.3	55.8	H34–C10–C16–C15	-119.5	-159.3	-77.6
C8–C1–C9–H30	172.4	176.6	176.2	H34–C10–C16–C17	60.6	20.4	104.2
C12–C1–C9–H28	178.6	179.8	179.3	H35–C11–C20–C2	-11.6	1.1	-1.1
C12–C1–C9–H29	-62.9	-60.8	-60.8	H35–C11–C20–C19	166.5	-179.0	179.1
C12–C1–C9–H30	58.0	59.5	59.5	H36–C11–C20–C2	119.6	122.1	120.2
C17–C1–C9–H28	56.3	57.7	57.1	H36–C11–C20–C19	-62.3	-58.1	-59.7
C17–C1–C9–H29	174.8	177.0	177.0	H37–C11–C20–C2	-122.3	-120.1	-122.0
C17–C1–C9–H30	-64.3	-62.7	-62.7	H37–C11–C20–C19	55.7	59.8	58.1
C8–C1–C12–C14	166.9	167.6	166.5	C1–C12–C14–C15	-63.4	-61.2	-62.5
C8–C1–C12–H21	-70.6	-69.0	-70.0	C1–C12–C14–H42	-180.0	177.1	176.0
C8–C1–C12–H32	50.3	47.2	46.3	C1–C12–C14–H43	54.6	59.0	57.7
C9–C1–C12–C14	-75.5	-74.6	-76.1	H21–C12–C14–C15	174.5	176.9	175.6
C9–C1–C12–H21	47.0	48.8	47.4	H21–C12–C14–H42	57.9	55.2	54.1

C9–C1–C12–H32	167.9	165.0	163.7	H21–C12–C14–H43	-67.6	-62.9	-64.2
C17–C1–C12–C14	47.5	46.5	44.7	H32–C12–C14–C15	56.3	59.1	57.8
C17–C1–C12–H21	169.9	169.9	168.1	H32–C12–C14–H42	-60.3	-62.6	-63.7
C17–C1–C12–H32	-69.1	-73.9	-75.6	H32–C12–C14–H43	174.3	179.3	178.0
C8–C1–C17–C16	-128.7	-136.4	-130.5	C12–C14–C15–C16	43.3	45.2	45.8
C8–C1–C17–C18	49.5	46.2	50.4	C12–C14–C15–H44	164.1	168.0	168.1
C9–C1–C17–C16	108.9	104.0	110.2	C12–C14–C15–HH45	-80.0	-76.3	-75.9
C9–C1–C17–C18	-72.9	-73.4	-68.9	H42–C14–C15–C16	159.6	167.2	167.7
C12–C1–C17–C16	-13.4	-17.2	-11.1	H42–C14–C15–H44	-79.6	-70.0	-70.0
C12–C1–C17–C18	164.8	165.4	169.8	H42–C14–C15–HH45	36.3	45.8	45.9
C20–C2–C3–C4	176.0	179.9	-179.7	H43–C14–C15–C16	-75.8	-75.2	-74.4
C20–C2–C3–H22	-6.2	0.0	0.2	H43–C14–C15–H44	45.0	47.5	47.8
H48–C2–C3–C4	-5.5	0.0	0.1	H43–C14–C15–HH45	161.0	163.3	163.8
H48–C2–C3–H22	172.3	-179.8	180.0	C14–C15–C16–C10	169.6	162.6	167.9
C3–C2–C20–C11	2.0	0.2	-0.2	C14–C15–C16–C17	-10.4	-17.2	-13.9
C3–C2–C20–C19	-176.1	-179.7	179.6	H44–C15–C16–C10	46.6	39.0	44.4
H48–C2–C20–C11	-176.4	-180.0	180.0	H44–C15–C16–C17	-133.5	-140.8	-137.4
H48–C2–C20–C19	5.5	0.2	-0.2	HH45–C15–C16–C10	-67.7	-75.2	-69.5
C2–C3–C4–C5	-177.2	-179.8	179.7	HH45–C15–C16–C17	112.2	105.0	108.7
C2–C3–C4–H23	-3.4	0.1	-0.1	C10–C16–C17–C1	175.1	-177.0	173.7
H22–C3–C4–C5	5.0	0.1	-0.1	C10–C16–C17–C18	-3.2	0.2	-7.3
H22–C3–C4–H23	178.8	180.0	-180.0	C15–C16–C17–C1	-4.8	2.8	-4.3
C3–C4–C5–C6	174.5	179.9	-179.8	C15–C16–C17–C18	176.9	179.9	174.7
C3–C4–C5–C13	-4.9	0.0	0.1	C1–C17–C18–C19	15.9	-140.5	137.3
H23–C4–C5–C6	0.7	0.0	0.0	C1–C17–C18–H46	-164.8	35.2	-39.3
H23–C4–C5–C13	-178.6	-179.9	180.0	C16–C17–C18–C19	-165.8	42.1	-41.8
C4–C5–C6–C7	178.3	-179.9	179.9	C16–C17–C18–H46	13.5	-142.1	141.6
C4–C5–C6–H24	-6.1	0.1	-0.1	C17–C18–C19–C20	179.6	179.1	-179.7

C13–C5–C6–C7	-2.5	0.1	-0.1	C17–C18–C19–H47	-1.0	0.2	-0.4
C13–C5–C6–H24	173.1	-180.0	180.0	H46–C18–C19–C20	0.3	3.4	-3.1
C4–C5–C13–H38	-170.6	-179.9	179.9	H46–C18–C19–H47	179.6	-175.4	176.2
C4–C5–C13–H39	55.4	58.7	58.5	C18–C19–C20–C2	176.2	-179.5	179.9
C4–C5–C13–H40	-64.5	-58.5	-58.7	C18–C19–C20–C11	-1.9	0.6	-0.2
C6–C5–C13–H38	10.1	0.1	-0.1	H47–C19–C20–C2	-3.1	-0.6	0.6
C6–C5–C13–H39	-123.9	-121.2	-121.5	H47–C19–C20–C11	178.8	179.5	-179.5
C6–C5–C13–H40	116.2	121.5	121.3				

Table S4 Fukui functions, electrophilicity (f_k^+/f_k^-) and nucleophilicity(f_k^-/f_k^+) indices of tretinoin at DFT-D functional with B3LYP/6-311++G(d,p) method

Atoms	f_k^+	f_k^-	fk^0	f_k^+/f_k^-	f_k^-/f_k^+
		conformer **A**			
C3	-0.3254	-0.0048	-0.1651	67.7126	0.0148
C4	0.1272	0.1536	0.1404	0.8277	1.2082
C5	-0.0870	-0.0494	-0.0682	1.7594	0.5684
C8	0.0061	0.0043	0.0052	1.4084	0.7100
C9	0.0211	0.0002	0.0107	89.7957	0.0111
O49	0.0062	0.0248	0.0155	0.2508	3.9878
		conformer **B**			
C1	0.0007	0.0028	0.0017	0.2625	3.8094
C5	0.0460	0.0121	0.0290	3.7915	0.2637

C7	0.0518	0.0198	0.0358	2.6115	0.3829
C17	0.0067	0.0338	0.0202	0.1981	5.0473
C1	0.0007	0.0028	0.0017	0.2625	3.8094