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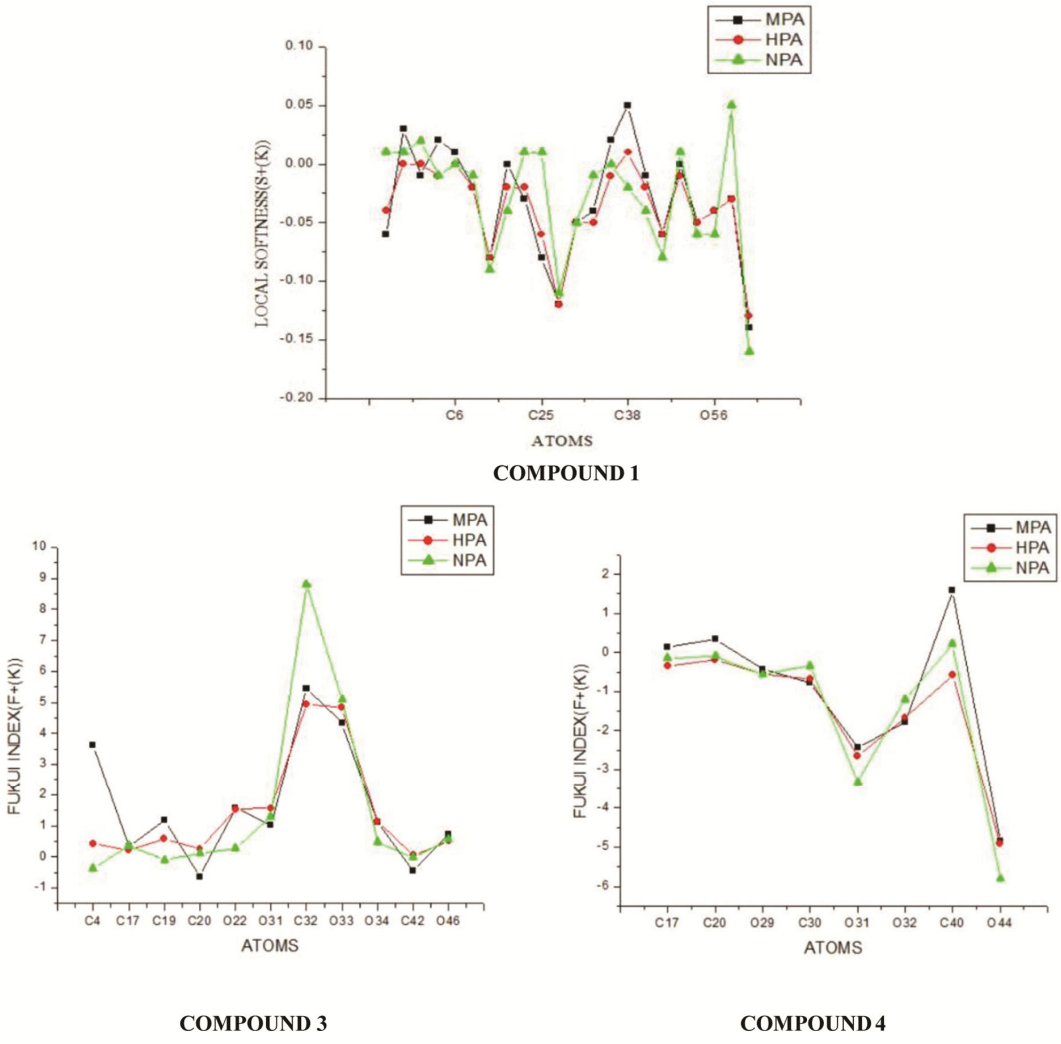
Combined quantum-chemical and *in silico* molecular docking studies on some phytomedicinal compounds reveal potential anti-HIV leads

Avantika Pal[1] and Rahul Kumar[2]*

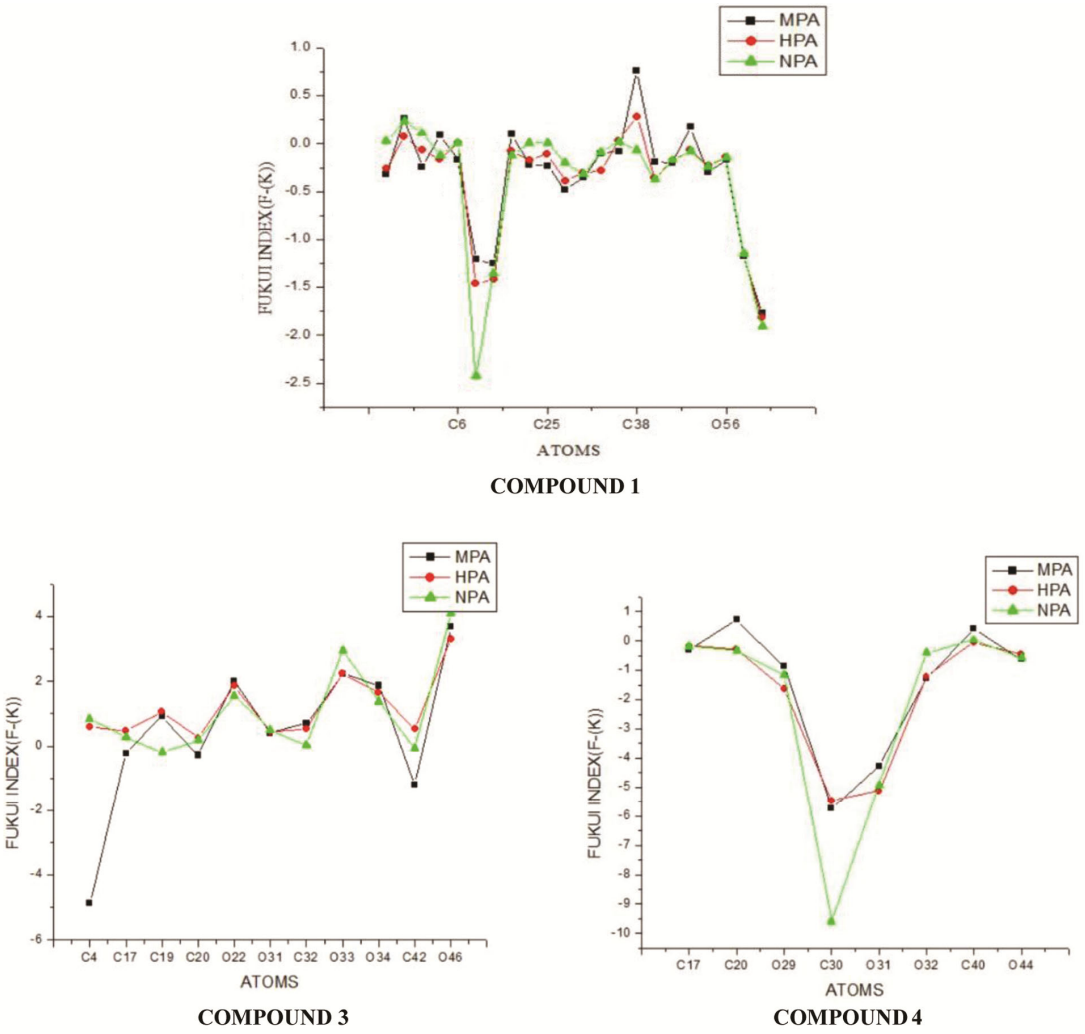
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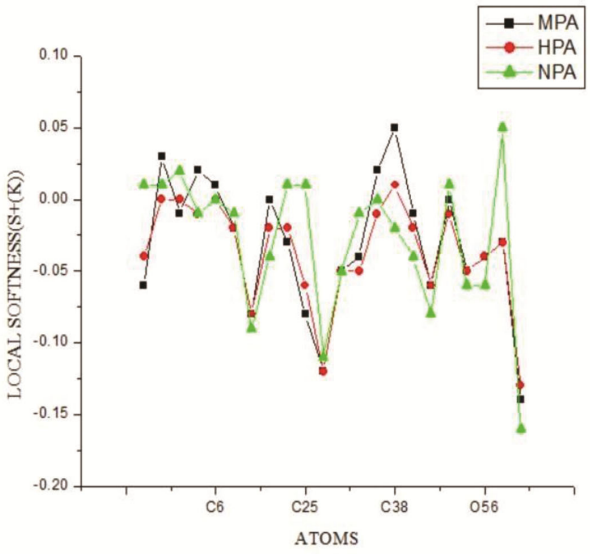
Supplementary data



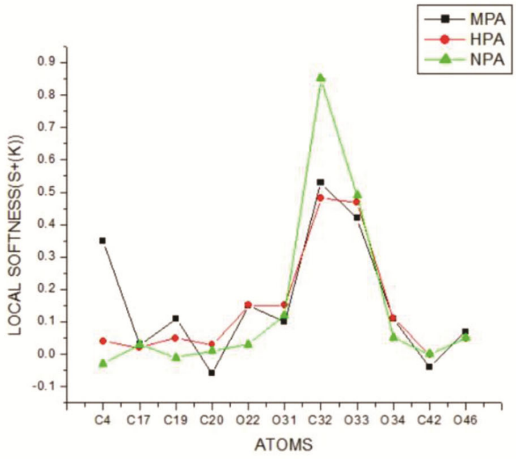
Suppl. Fig. 1 — Variation of Fukui index ($f^{+}(k)$) at the selected atoms (k) in (compound 1, 3, 4) based on NPA, MPA and HPA scheme calculated at B3LYP/6-31G(d, p) level of theory (Molecules 1 and 4 optimized at B3LYP/3-21G level of theory)



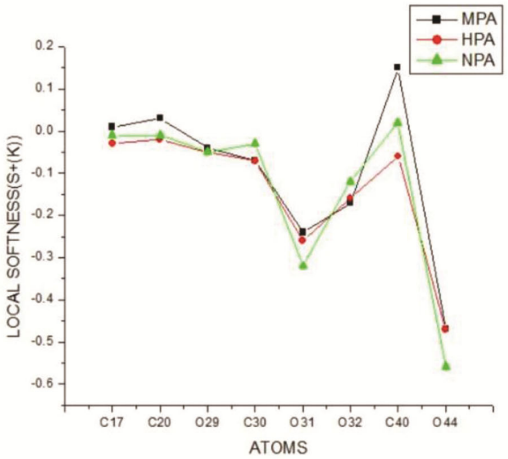
Suppl. Fig. 2 — Variation of Fukui index (f^- (k)) at the selected atoms (k) in (compound 1, 3, 4) based on NPA, MPA and HPA scheme calculated at B3LYP/6-31G(d, p) level of theory (Molecules 1 and 4 optimized at B3LYP/3-21G level of theory)



COMPOUND 1

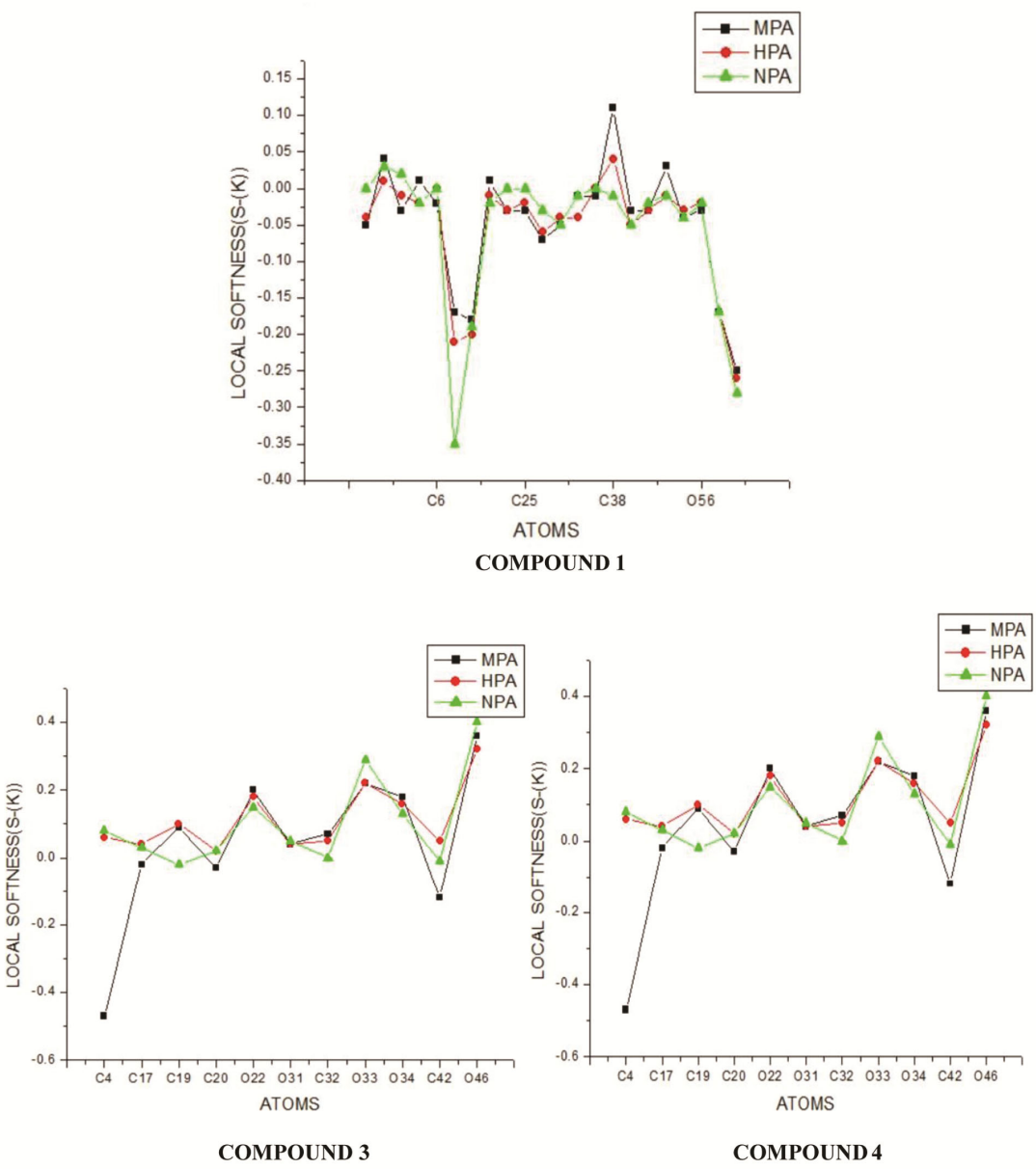


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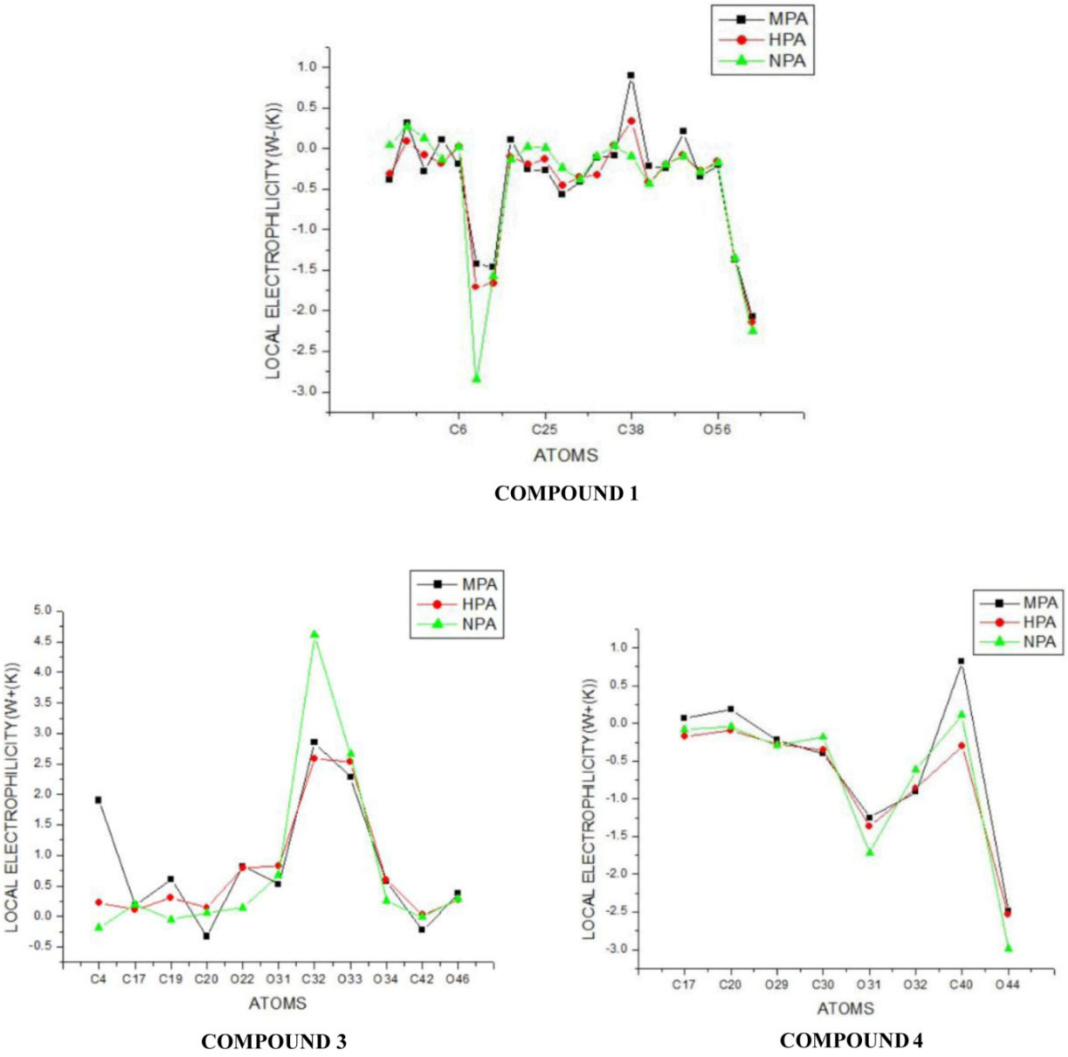


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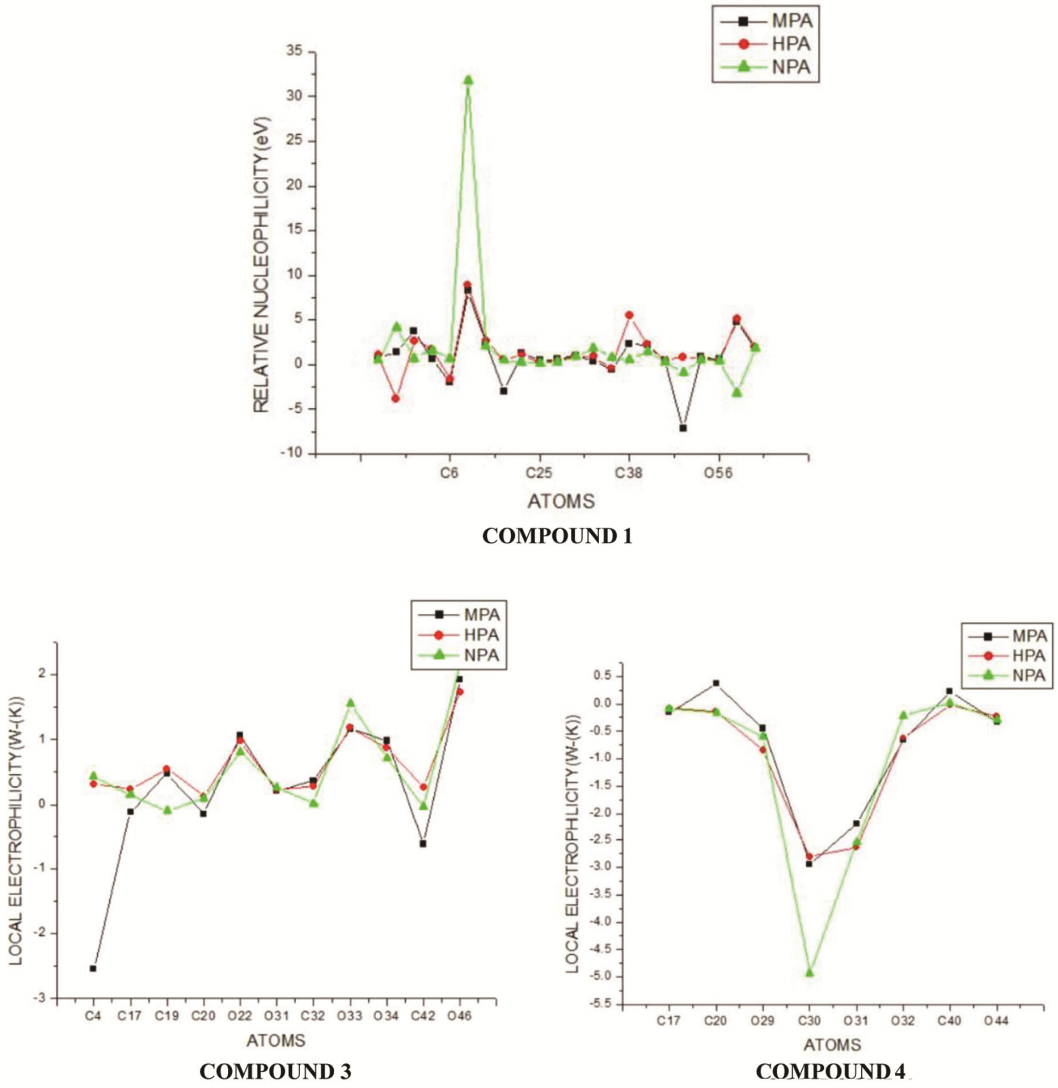
Suppl. Fig. 3 — Variation of Local softness (s+) at the selected atoms in (compound 1, 3, 4) based on NPA, MPA and HPA scheme calculated at B3LYP/6-31G(d, p) level of theory. (Molecules 1 and 4 optimized at B3LYP/3-21G level of theory)



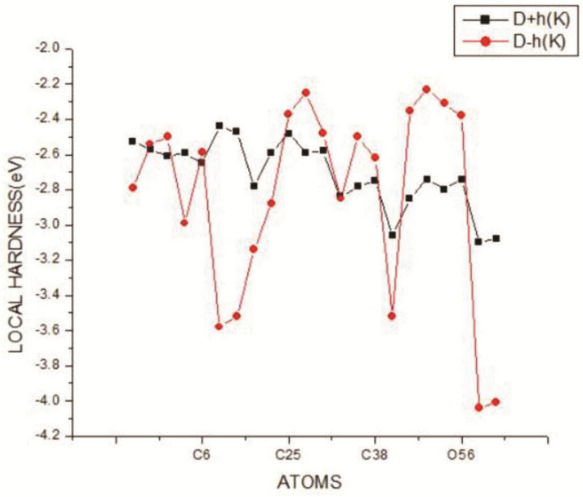
Suppl. Fig. 4 — Variation of Local softness(s-)at the selected atoms in (compound 1, 3, 4) based on NPA, MPA and HPA scheme calculated at B3LYP/6-31G(d, p) level of theory. (Molecules 1 and 4 optimized at B3LYP/3-21G level of theory)



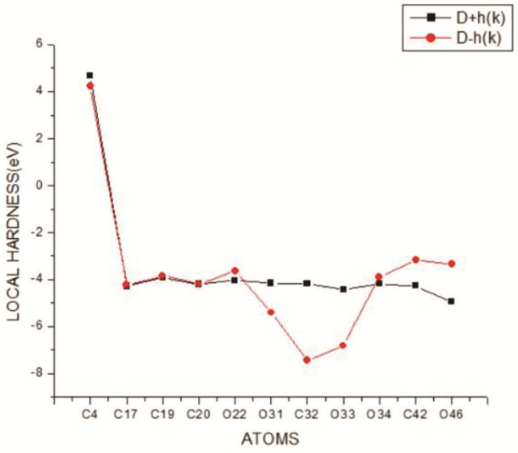
Suppl. Fig. 5 — Variation of Local electrophilicity(ω^{+}) at the selected atoms in (compound 1, 3, 4) based on NPA, MPA and HPA scheme calculated at B3LYP/6-31G(d, p) level of theory. (Molecules 1 and 4 optimized at B3LYP/3-21G level of theory)



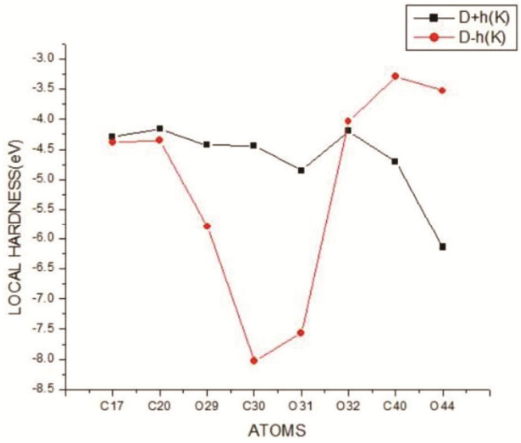
Suppl. Fig. 6 — Variation of Local electrophilicity(ω^-) at the selected atoms in (compound 1, 3, 4) based on NPA, MPA and HPA scheme calculated at B3LYP/6-31G(d, p) level of theory. (Molecules 1 and 4 optimized at B3LYP/3-21G level of theory)



COMPOUND 1

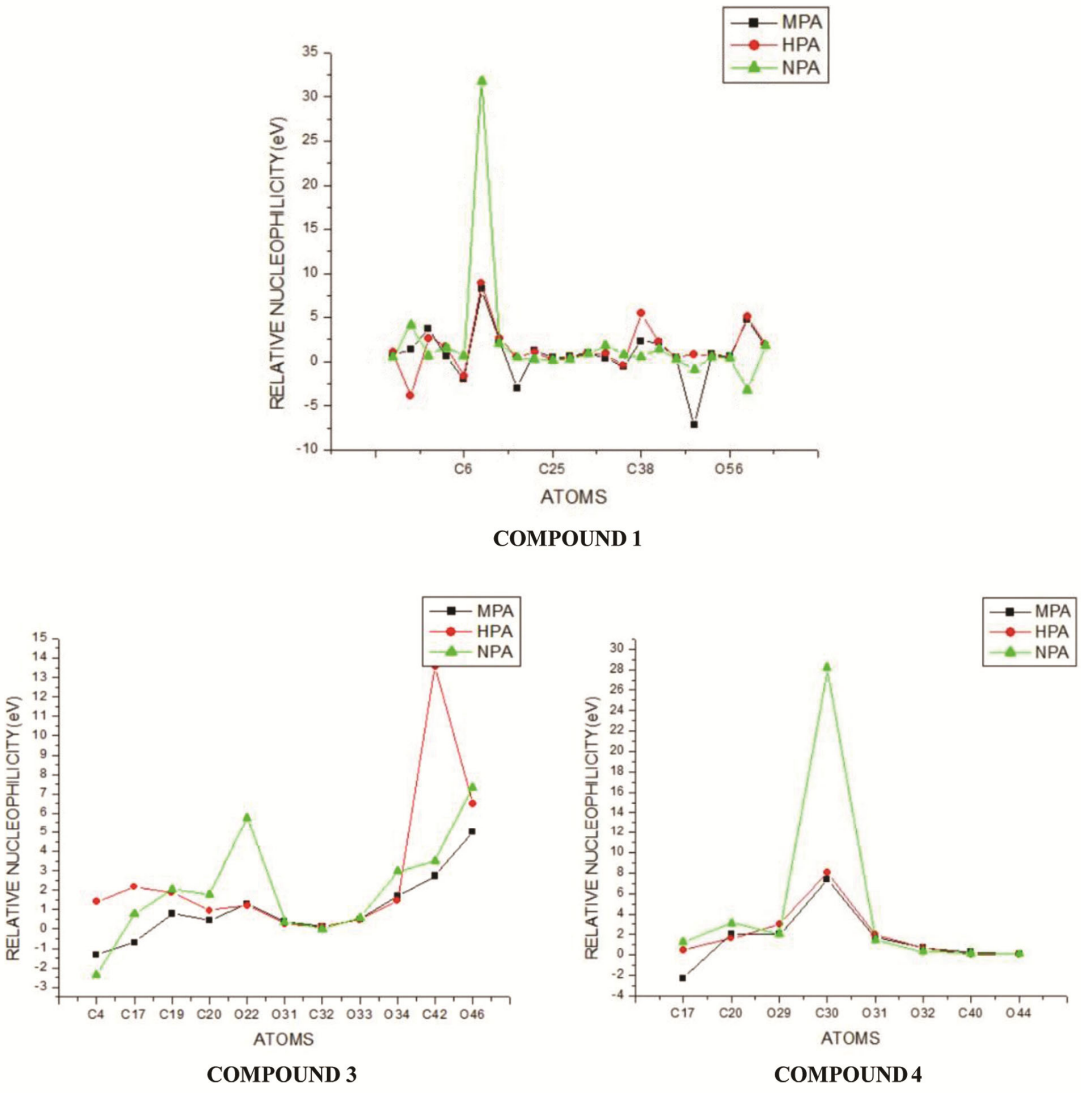


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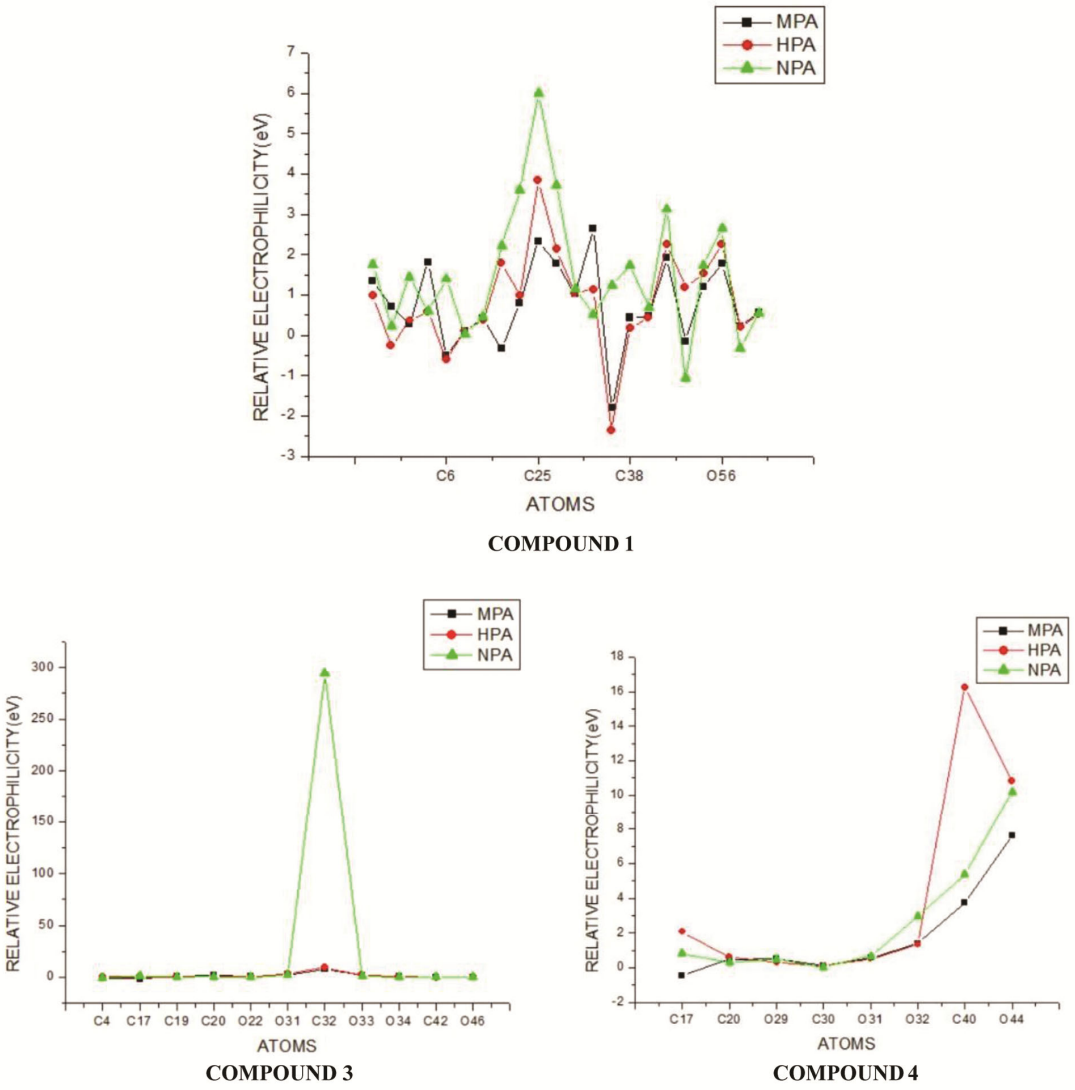


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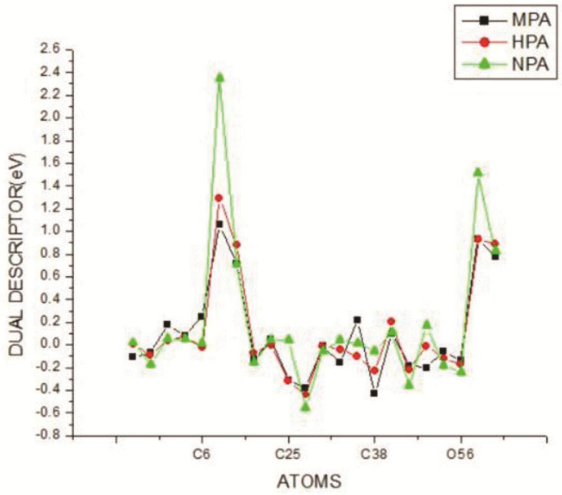
Suppl. Fig. 7 — Variation of Local hardness (Δh) at the selected atoms in (compound 1, 3, 4) based on NPA, MPA and HPA scheme calculated at B3LYP/6-31G(d, p) level of theory. (Molecules 1 and 4 optimized at B3LYP/3-21G level of theory)



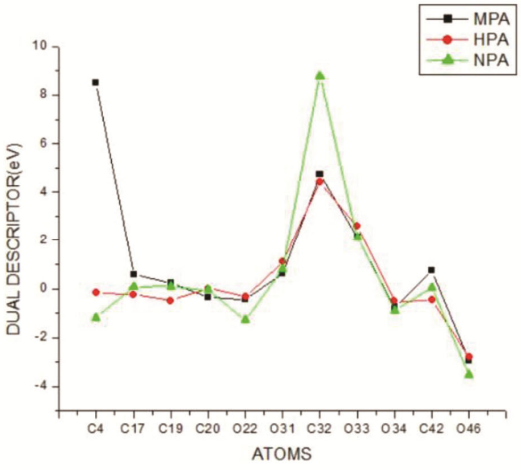
Suppl. Fig. 8 — Variation of Relative nucleophilicity at the selected atoms in (compound 1, 3, 4) based on NPA, MPA and HPA scheme calculated at B3LYP/6-31G(d, p) level of theory. (Molecules 1 and 4 optimized at B3LYP/3-21G level of theory)



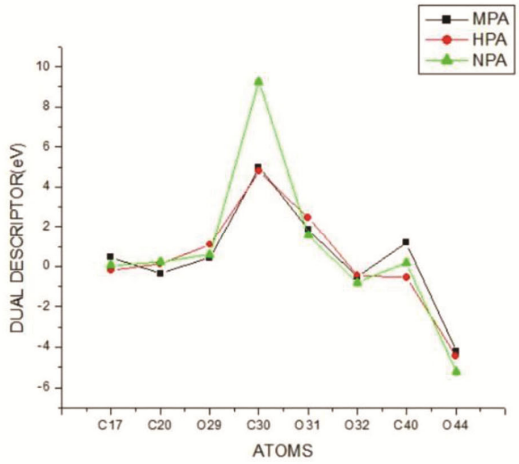
Suppl. Fig. 9 — Variation of Relative electrophilicity at the selected atoms in (compound 1, 3, 4) based on NPA, MPA and HPA scheme calculated at B3LYP/6-31G(d, p) level of theory. (Molecules 1 and 4 optimized at B3LYP/3-21G level of theory)



COMPOUND 1

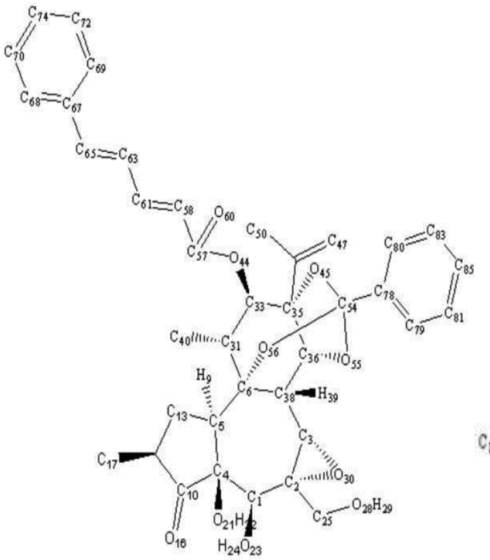


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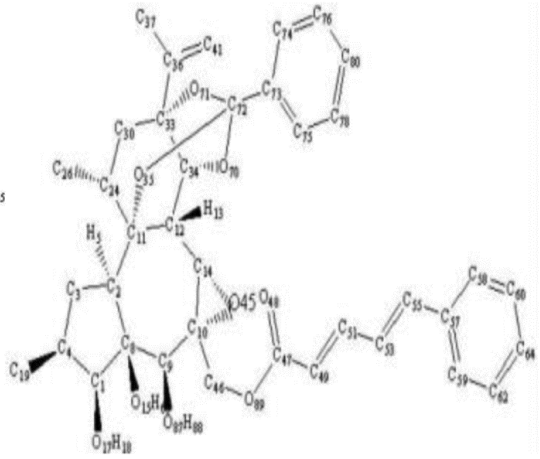


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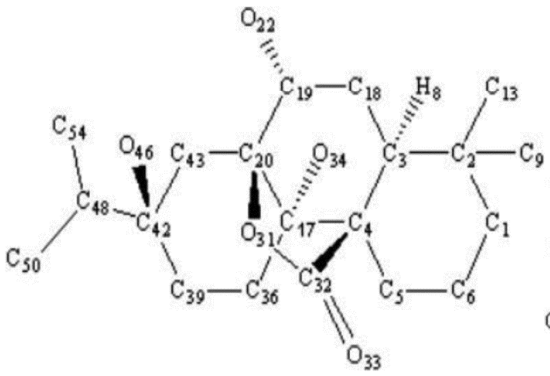
Suppl. Fig. 10 — Variation of Dual descriptor at the selected atoms in (compound 1, 3, 4) based on NPA, MPA and HPA scheme calculated at B3LYP/6-31G(d, p) level of theory. (Molecules 1 and 4 optimized at B3LYP/3-21G level of theory)



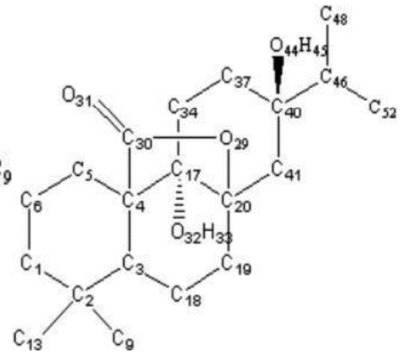
Molecule 1
Onishibarin A
Source: *Daphne pseudomezereum*



Molecule 2
Onishibarin B
Source: *Daphne pseudomezereum*



Molecule 3
Abietamethinol D
Source: *Isodon amethystoides*



Molecule 4
Abietamethinol C
Source: *Isodon amethystoides*

Suppl. Fig. 11 — Structure of anti-HIV molecules (compound 1-4) used for the quantum chemical and *in silico* drug designing studies

Suppl. Table 1 — Natural leads observed from literature survey

Natural Lead	Isolated from	Category	Function	References
Stelleralide A	*Stellerachamaejasme*	Diterpenoid	Turn on protein kinase C and inhibit HIV-1 receptors.	Asada et al., 2011
Trigothysoid N	*Trigonostemon thyrsoideum*	Diterpenoid	HIV-1 RT inhibitor	Cheng et al., 2013
Wikstroechuin A-C	*Wikstroemia chuii*	Diterpene	Repress cytopathic effect of HIV-1	Liu et al., 2020a
Daphneodorins D	*Daphne odora*	Diterpenoid	HIV inhibitor	Otsuki et al., 2019
Wikstroelide M	*Daphne acutiloba*	Diterpenoid	HIV-RT inhibitor	Zhang et al., 2014
Stelleralides F-H	*Stellera chamaejasme*	Diterpenoid	HIV inhibitor	Yan et al., 2015
Daphneodorins A	*Daphne odora*	Diterpenoid	HIV inhibitor	Otsuki et al., 2019
Dapholosericin A	*Wikstroemia scytophylla*	Diterpenoid	HIV-1inhibition in MT4 cells	Otsuki et al., 2020
Stelleracin C	*Wikstroemia scytophylla*	Diterpenoid	HIV-1inhibition in MT4 cells	Zhang et al., 2021
Eurifoloids E	*Euphorbia neriifolia*	Diterpenoid	HIV inhibitor	Zhao et al., 2014
Flueggether A	*Flueggeavirosa*	Alkaloid	HIV-1inhibitor	Zhang et al., 2015
Naucleaoffine A	*Nauclea officinalis*	Alkaloid	HIV-1 RT inhibitor	Liu et al., 2019a
Clausanisumine	*Clausena anism-olens*	Alkaloid	HIV-1 RT inhibitor	Liu et al., 2021
Manizapotins A- C	*Manilkara zapota*	Coumarin	HIV-1 RT inhibitor	Liu et al., 2019b
Clauselenins A-C	*Clausenalenis lenis*	Coumarin	HIV-1 RT inhibitor	Liu et al., 2020b
Ciparasin B	*Cipadessa cinerascens*	Limonoid	HIV inhibitor	Yu et al., 2015
Aspernigin C	*Aspergillus niger*	2-Benzylpyridin-4-one	HIV inhibitor	Zhou et al., 2016
Trigonohowne	*Trigonostemon howii*	Tetrahydrofuran derivative	HIV-1 RT inhibitor	Liu et al., 2018
Artocarheterones A-E	*Artocarpus heterophyllus*	Prenylated chromone	HIV-RT inhibitor	Tao et al., 2022

Suppl. Table 2 — Comparative analysis of functional and basis sets (in gas phase) used for the theoretical studies of molecules (1-4). Self-consistent field energy (ESCF) in gas phase without zero-point energy correction; dipole moment of the system in gas phase (in Debye); CPU runtime for the combined optimization and frequency calculation at respective level of theory; number of steps used for optimization at the respective level of theory

Molecule No.	Parameters	HF/3-21G	B3LYP/3-21G	B3LYP/6-31G(d, p)
1	ESCF (a.u)	-2197.57223924	-2212.08885297	-
	Dipole Moment (Debye)	3.4215	3.4230	-
	CPU Time	10 days, 23 h, 13 min, and 56 sec	9 days, 1 h, 4 min, and 8.0 sec	-
	No. of steps of Optimisation	66	23	-

2	ESCF (a.u)	-2125.26896630	-	-
	Dipole Moment (Debye)	3.1393	-	-
	CPU Time	9 days, 22 h, 59 min, and 14.0 sec	-	-
	No. of steps of Optimisation	96	-	-
3	ESCF (a.u)	-1143.98393315	-1151.24051309	-1157.58136077
	Dipole Moment (Debye)	4.7433	4.3943	4.0385
	CPU Time	3 days, 22 h, 7 min, and 43.0 sec	2 days, 20 h, 55 min, and 36.4 sec	10 days, 2 h, 12 min, and 15 sec
	No. of steps of Optimisation	77	13	13
4	ESCF (a.u)	-1069.55781478	-1076.46016216	-
	Dipole Moment (Debye)	5.0921	4.5148	-
	CPU Time	1day, 19 h, 17 min, and 28 sec	2 days, 3 h, 2min utes, and 23 sec	-
	No. of steps of Optimisation	44	13	-

Suppl. Table 3 — Calculated energies and the thermochemical parameters for the ground state optimized geometries (in gas phase) of compound(1, 3, 4) at B3LYP/6-31G(d, p) level of theory (Molecules 1 and 4 optimized at theory B3LYP/3-21G)

Parameter	Compounds		
	1	3	4
Molecular mass (a.m.u)	656.26215	352.2249	336.2301
a ZPVE (kcal/mol)	453.93971	316.02383	315.5744
Zero point correction (Hartree/Particle)	0.723399	0.503616	0.5029
c Thermal correction to energy (Hartree/Particle)	0.765208	0.527971	0.525408
Thermal correction to enthalpy (Hartree/Particle)	0.766152	0.528915	0.526352
Thermal correction to gibbs free energy(Hartree/Particle)	0.649441	0.454035	0.455562
Sum of electronic and zero point energies (a.u.)	-2211.365	-1157.078	-1075.96
Sum of electronic and thermal energies (a.u.)	-2211.324	-1157.052	-1075.93
Sum of electronic and thermal free enthalpies (a.u.)	-2211.323	-1157.053	--1075.93
Sum of electronic and thermal free energies (a.u.)	-2211.439	-1157.127	-1076
j E (kcal/mol) tot	480.175	331.307	329.698
k S (cal/mol-kelvin) tot	245.64	157.6	148.989

l CV (cal/mol-kelvin) tot	168.189	100.722	94.996

b c d Zero point vibrational energy, Zero point energy(E); is the vibrational energy which a molecule possess in the vibrational ground state (v=0); Correction to internal thermal energy (E = E +E +E +E); H = ZPE tot elec trans rot vib corr e f g E + k T, and it includes zero point energy; G = H – TS , where, S= S + S + S and includes ZPE; Sum of electronic and zero point energy (= E + E); Sum of electronic and thermal energies (= E + E tot B corr corr tot tot elec trans vib, 0 ZPE 0 elec h j + E + E + E); Sumof electronic and thermal enthalpies (= E + H); Sum of electronic and thermal free energies (=E +G). trans rot vib 0 corr 0 corr

Suppl. Table 4 — Energy values for neutral, anionic and cationic systems, and antiradical capacityof the studied compounds (compound 1, 3, 4) at B3LYP/6-31G(d, p) level of theory. (Molecules 1 and 4 optimized at B3LYP/3-21G level of theory)*

Compound no.	1	3	4
I.P.	-0.5642	1.8828	1.9116
E.A.	-7.5149	-8.4685	-8.4446
ω-	-0.65584	-0.07548	-0.07025
ω+	-4.13119	-5.25113	-5.24835
Rd	-0.1901	-0.02188	-0.02036
Ra	-1.19055	-1.51329	-1.51249

Suppl. Table 5 — Frontier molecular orbitals and global reactivity descriptors of the studied compounds (compound 1, 3, 4) at B3LYP/6-31G(d, p)level of theory. (Molecules 1 and 4 optimized at B3LYP/3-21G level of theory

S. No	Property	Molecule-1	Molecule-3	Molecule-4
		Gas phase	Gas phase	Gas phase
1	EN(a.u.)	-2212.088853	-1157.581361	- 1076.460162
2	EN+1(a.u.)	-2211.812688	-1157.27015	- 1076.149831
3	EN-1(a.u.)	-2212.109587	-1157.512169	- 1076.389913
4	aDipole moment (Debye)	3.423	4.0385	4.5148
5	I.P.(a.u.))[EN-1-EN]	-0.0207	0.0692	0.0702
	I.P.(eV) [EN-1-EN]	-0.5642	1.8828	1.9116
6	E.A.(a.u.) [EN-EN+1]	-0.2762	-0.3112	-0.3803
	E.A.(eV) [EN-EN+1]	-7.5149	-8.4685	-8.4446
7	DE(a.u.) (I.P.-E.A.)	0.2554	0.3804	0.3806
	DE(eV) (I.P.-E.A.)	6.951	10.351	10.356
8	EHOMO(eV) [-EHOMO=I.P.]	0.5642	-1.8828	-1.9116
9	ELUMO(eV) [-ELUMO=E.A.]	7.5149	-8.4685	8.4446
10	Electronic chemical potential (m) (eV)	4.0396	3.2929	3.2665
	2m (eV)	16.3180	10.8429	10.6700
11	Electronegativity (c)(eV)	-4.0396	-3.2929	-3.2665

12	Chemical hardness (h)(eV) [ELUMO-EHOMO]	6.9507	10.3514	10.3562
	2h(eV)	13.9014	20.7027	20.7124
13	Global softness (S)(/eV) [1/h]	0.1439	0.0966	0.0966
14	Electrophilicity index (w)(eV) [m2/2h]	1.1738	0.5237	0.5152

b c E , E and E are the total energies of the system containing respectively, N, N+1 and N-1 electrons; Dipole moment for the system containing N number of electrons; I.P. is N N+1 N-1 d e f the ionization potential given by E –E ; E.A. is the electron affinity given by E – E ; ΔE is the band gap given by I.P. – E.A.; Energy of the highest occupied molecular N-1 N N N+1 g h orbital as –E = I.P.; Energy of the lowest unoccupied molecular orbital as –E = E.A.; Electronic chemical potential of the system given by E + E)/2; HOMO LUMO HOMO LUMO j k l Electronegativity of the system given by -μ; Global hardness of the system given by E – E ; Global softness of the system given by 1/η; Electrophilicity index of the LUMO HOMO 2 system given by μ /2η

Suppl. Table 6 — Molecular docking results for all the studied molecules (1-4) using SwissDock

Parameters	Compound No. 1	2	3	4
	HIV-1 Reverse Transcriptase (3DLE)			
Binding Energy	-7.8313	-6.9851	-6.4113	-6.3761
AC Score	317.293574	337.460567	21.726801	6.265070
SP-dG	-7.8313	-6.9851	-6.4113	-6.3761
RMSD	21.2611	38.9346	44.7170	34.7568
XYZ coordinates	-3.702727, -12.215318, 13.921568	8.680955, -34.806561, 19.953121	7.693158, -35.505667, 23.493123	20.468000, -22.58160712.645196
	HIV-1 Envelope Glycoprotein (4RZ2)			
Binding Energy	-8.9475	-6.8058	-6.7431	-6.1273
AC Score	686.045053	340.268815	18.933573	12.095359
SP-dG	-8.9475	-6.8058	-6.7431	-6.1273
RMSD	63.7042	55.9633	58.1137	65.1525
XYZ coordinates	30.410109, 22.967948, 44.312414	28.755258, 21.930288, 43.303333	28.553877, 22.338877, 45.101088	30.338982, -2.445696, 57.352411

Suppl. Table 7 — Molecular docking results for all the studied molecules (1-4) for all the listed proteins using PyRx

Molecule	HIV-1 RT	Gp120
Onishibarin A	-9.3	-8.1
Onishibarin B	-8.5	-6.9
Abietamethinol D	-7.4	-6.7
Abietamethinon C	-7.6	-7.1

APPENDIX-1 — Atomic charges (a.u.) at the selected atoms of studied compounds (1, 3 and 4) based on MPA at B3LYP/6-31G(d, p) level of theory (Molecules 1 and 4 optimized at B3LYP/3-21G level of theory)

System	Atom (k)	Atomic Charge	Gas phase					
			Neutral (N)		Anion (N+1)		Cation (N-1)	
			qN(k)	PN(k)	qN+1(k)	PN+1(k)	qN-1(k)	PN-1(k)
MOLECULE 1	C1	6	0.225	5.7750	0.2411	5.7589	0.2131	5.7869
	C2	6	0.0623	5.9377	0.0553	5.9447	0.072	5.9280
	C3	6	0.2992	5.7008	0.3016	5.6984	0.2903	5.7097
	C4	6	0.0615	5.9385	0.0553	5.9447	0.0649	5.9351
	C6	6	0.2173	5.7827	0.2142	5.7858	0.2112	5.7888
	C10	6	0.54	5.4600	0.5454	5.4546	0.4955	5.5045
	O16	8	-0.4816	8.4816	-0.4622	8.4622	-0.5274	8.5274
	O21	8	-0.1816	8.1816	-0.1804	8.1804	-0.178	8.1780
	O23	8	-0.186	8.1860	-0.1796	8.1796	-0.1941	8.1941
	C25	6	0.3052	5.6948	0.3253	5.6747	0.2966	5.7034
	O28	8	-0.2005	8.2005	-0.1686	8.1686	-0.2183	8.2183
	O30	8	-0.4139	8.4139	-0.4007	8.4007	-0.4268	8.4268
	C33	6	0.2916	5.7084	0.3011	5.6989	0.288	5.7120
	C35	6	0.1072	5.8928	0.102	5.8980	0.1043	5.8957
	C38	6	-0.0076	6.0076	-0.0199	6.0199	0.0205	5.9795
	O44	8	-0.52	8.5200	-0.5168	8.5168	-0.5268	8.5268
	O45	8	-0.4617	8.4617	-0.4476	8.4476	-0.4691	8.4691
	C54	6	0.6622	5.3378	0.6631	5.3369	0.6687	5.3313
	O55	8	-0.4533	8.4533	-0.44	8.4400	-0.4644	8.4644
	O56	8	-0.5112	8.5112	-0.4998	8.4998	-0.5176	8.5176
	C57	6	0.6427	5.3573	0.6516	5.3484	0.5998	5.4002
	O60	8	-0.4847	8.4847	-0.4485	8.4485	-0.5496	8.5496
MOLECULE 3	C17	6	0.2803	5.7197	0.2717	5.7283	0.2679	5.7321
	C19	6	0.2682	5.7318	0.3022	5.6978	0.2253	5.7747
	C20	6	0.2204	5.7796	0.2101	5.7899	0.2436	5.7564
	O22	8	-0.2267	8.2267	-0.1525	8.1525	-0.2839	8.2839
	O31	8	-0.5321	8.5321	-0.5175	8.5175	-0.5695	8.5695
	C32	6	0.6438	5.3562	0.67	5.3300	0.4435	5.5565
	O33	8	-0.4749	8.4749	-0.393	8.3930	-0.6346	8.6346
	O34	8	-0.2466	8.2466	-0.1777	8.1777	-0.2875	8.2875
	C42	6	0.2809	5.7191	0.2371	5.7629	0.297	5.7030
	O46	8	-0.2606	8.2606	-0.1252	8.1252	-0.2876	8.2876

MOLECULE 4	C17	6	0.2257	5.7743	0.2208	5.7792	0.2145	5.7855
	C20	6	0.1653	5.8347	0.1524	5.8476	0.1919	5.8081
	O29	8	-0.5012	8.5012	-0.4852	8.4852	-0.5331	8.5331
	C30	6	0.7411	5.2589	0.7696	5.2304	0.5303	5.4697
	O31	8	-0.4678	8.4678	-0.3784	8.3784	-0.6249	8.6249
	O32	8	-0.2047	8.2047	-0.1397	8.1397	-0.2512	8.2512
	C40	6	0.2064	5.7936	0.1480	5.8520	0.2220	5.7780
	O44	8	-0.2234	8.2234	-0.0456	8.0456	-0.2467	8.2467

Compound numbers as shown in Suppl. Figure 11, P_N (k) is the electronic population on atom (k) in the neutral species (N), the anionic species (N+1), the cationic species (N-1), where N is the number of electrons

APPENDIX-2 — Atomic charges (a.u.) at the selected atoms of studied compounds (1, 3 and 4) based on HPA at B3LYP/6-31G (d, p) level of theory. (Molecules1 and 4 optimized at B3LYP/3-21G levelof theory)

System	Atom(k)	Atomic Charge	Gas phase					
			Neutral (N)		Anion (N+1)		Cation (N-1)	
			qN(k)	PN(k)	qN+1(k)	PN+1(k)	qN-1(k)	PN-1(k)
MOLECULE 1	C1	6	0.0894	5.9106	0.0989	5.9011	0.0797	5.9203
	C2	6	0.0447	5.9553	0.0454	5.9546	0.0474	5.9526
	C3	6	0.0963	5.9037	0.0972	5.9028	0.0939	5.9061
	C4	6	0.0555	5.9445	0.0589	5.9411	0.0497	5.9503
	C6	6	0.0919	5.9081	0.0922	5.9078	0.0924	5.9076
	C10	6	0.1566	5.8434	0.1626	5.8374	0.1031	5.8969
	O16	8	-0.2146	8.2146	-0.1948	8.1948	-0.2667	8.2667
	O21	8	-0.0784	8.0784	-0.073	8.0730	-0.0814	8.0814
	O23	8	-0.0585	8.0585	-0.0522	8.0522	-0.0649	8.0649
	C25	6	0.1202	5.8798	0.1359	5.8641	0.1161	5.8839
	O28	8	-0.0986	8.0986	-0.0681	8.0681	-0.1129	8.1129
	O30	8	-0.179	8.1790	-0.1675	8.1675	-0.19	8.1900
	C33	6	0.0995	5.9005	0.1111	5.8889	0.0892	5.9108
	C35	6	0.0675	5.9325	0.0701	5.9299	0.0686	5.9314
	C38	6	-0.0034	6.0034	-0.0053	6.0053	0.007	5.9930
	O44	8	-0.1441	8.1441	-0.1381	8.1381	-0.1573	8.1573
	O45	8	-0.1717	8.1717	-0.1573	8.1573	-0.1781	8.1781
	C54	6	0.2044	5.7956	0.2074	5.7926	0.2019	5.7981
	O55	8	-0.1837	8.1837	-0.1707	8.1707	-0.1922	8.1922
	O56	8	-0.1754	8.1754	-0.1641	8.1641	-0.1804	8.1804
	C57	6	0.2006	5.7994	0.2091	5.7909	0.1578	5.8422

	O60	8	-0.2494	8.2494	-0.2151	8.2151	-0.3163	8.3163
MOLECULE 3	C17	6	0.0693	5.9307	0.0862	5.9138	0.0615	5.9385
	C19	6	0.0784	5.9216	0.1172	5.8828	0.0576	5.9424
	C20	6	0.077	5.9230	0.0862	5.9138	0.0674	5.9326
	O22	8	-0.0599	8.0599	0.0088	7.9912	-0.1162	8.1162
	O31	8	-0.1289	8.1289	-0.1126	8.1126	-0.1864	8.1864
	C32	6	0.2138	5.7862	0.2332	5.7668	0.0322	5.9678
	O33	8	-0.2591	8.2591	-0.1764	8.1764	-0.4367	8.4367
	O34	8	-0.0414	8.0414	0.0196	7.9804	-0.0833	8.0833
	C42	6	0.0776	5.9224	0.0966	5.9034	0.0762	5.9238
	O46	8	-0.0989	8.0989	0.0225	7.9775	-0.1176	8.1176
MOLECULE 4	C17	6	0.0625	5.9375	0.0749	5.9251	0.0565	5.9435
	C20	6	0.081	5.9190	0.0878	5.9122	0.0700	5.9300
	O29	8	-0.1405	8.1405	-0.1208	8.1208	-0.2003	8.2003
	C30	6	0.2093	5.7907	0.2343	5.7657	0.0087	5.9913
	O31	8	-0.2249	8.2249	-0.1277	8.1277	-0.4131	8.4131
	O32	8	-0.0441	8.0441	0.0172	7.9828	-0.0885	8.0885
	C40	6	0.0772	5.9228	0.0986	5.9014	0.0759	5.9241
	O44	8	-0.1161	8.1161	0.0641	7.9359	-0.1327	8.1327

Compound numbers as shown in Suppl. Figure 11, P_N (k) is the electronic population on atom (k) in the neutral species(N), the anionic species (N+1), the cationic species (N-1), where N is the number of electrons

APPENDIX-3 — Atomic charges (a.u.) at the selected atoms of studied compounds (1, 3 and 4) based on NPA at B3LYP/6-31G (d, p) level of theory. (Molecules1 and 4) optimized at B3LYP/3-21Glevel of theory)

System	Atom(k)	Atomic Charge	Gas phase					
			Neutral(N)		Anion(N+1)		Cation(N-1)	
			$q_N(k)$	$P_N(k)$	$q_{N+1}(k)$	$P_{N+1}(k)$	$q_{N-1}(k)$	$P_{N-1}(k)$
MOLECULE1	C1	6	0.0097	5.9903	0.0076	5.9924	0.0109	5.9891
	C2	6	0.138	5.8620	0.136	5.8640	0.1463	5.8537
	C3	6	0.0289	5.9711	0.0231	5.9769	0.0329	5.9671
	C4	6	0.1323	5.8677	0.1351	5.8649	0.1278	5.8722
	C6	6	0.2748	5.7252	0.2741	5.7259	0.2753	5.7247
	C10	6	0.5485	5.4515	0.5513	5.4487	0.4594	5.5406
	O16	8	-0.4857	8.4857	-0.4622	8.4622	-0.5353	8.5353
	O21	8	-0.6693	8.6693	-0.6595	8.6595	-0.6737	8.6737
	O23	8	-0.6865	8.6865	-0.6883	8.6883	-0.686	8.6860

	C25	6	-0.157	6.1570	-0.1588	6.1588	-0.1567	6.1567
	O28	8	-0.6735	8.6735	-0.6459	8.6459	-0.6809	8.6809
	O30	8	-0.4731	8.4731	-0.4593	8.4593	-0.485	8.4850
	C33	6	0.0397	5.9603	0.0414	5.9586	0.0365	5.9635
	C35	6	0.1822	5.8178	0.1812	5.8188	0.183	5.8170
	C38	6	-0.3596	6.3596	-0.3549	6.3549	-0.3623	6.3623
	O44	8	-0.5146	8.5146	-0.5052	8.5052	-0.5281	8.5281
	O45	8	-0.5104	8.5104	-0.4907	8.4907	-0.5167	8.5167
	C54	6	0.7286	5.2714	0.7254	5.2746	0.7256	5.2744
	O55	8	-0.4974	8.4974	-0.4819	8.4819	-0.5064	8.5064
	O56	8	-0.5187	8.5187	-0.5046	8.5046	-0.524	8.5240
	C57	6	0.6841	5.3159	0.671	5.3290	0.6417	5.3583
	O60	8	-0.5029	8.5029	-0.4632	8.4632	-0.5732	8.5732
MOLECULE3	C17	6	0.2937	5.7063	0.3039	5.6961	0.2806	5.7194
	C19	6	0.091	5.9090	0.0839	5.9161	0.0945	5.9055
	C20	6	0.2648	5.7352	0.2709	5.7291	0.2613	5.7387
	O22	8	-0.7532	8.7532	-0.6962	8.6962	-0.7631	8.7631
	O31	8	-0.5769	8.5769	-0.559	8.5590	-0.6239	8.6239
	C32	6	0.8387	5.1613	0.8398	5.1602	0.5151	5.4849
	O33	8	-0.5659	8.5659	-0.4571	8.4571	-0.7527	8.7527
	O34	8	-0.7418	8.7418	-0.6911	8.6911	-0.759	8.7590
	C42	6	0.2992	5.7008	0.2964	5.7036	0.3	5.7000
	O46	8	-0.7875	8.7875	-0.6366	8.6366	-0.8081	8.8081
MOLECULE4	C17	6	0.2493	5.7507	0.2547	5.7454	0.2427	5.7573
	C20	6	0.2321	5.7679	0.2360	5.7641	0.2201	5.7799
	O29	8	-0.5043	8.5043	-0.4835	8.4835	-0.5470	8.5470
	C30	6	0.7455	5.2545	0.7580	5.2420	0.3929	5.6071
	O31	8	-0.4863	8.4863	-0.3638	8.3638	-0.6673	8.6673
	O32	8	-0.6616	8.6616	-0.6173	8.6173	-0.6766	8.6766
	C40	6	0.2475	5.7525	0.2394	5.7606	0.2490	5.7510
	O44	8	-0.6999	8.6999	-0.4864	8.4864	-0.7209	8.7209

Compound numbers as shown in Suppl. Figure 11, P_N (k) is the electronic population on atom (k) in the neutral species(N), the anionic species (N+1), the cationic species (N-1), where N is the number of electrons

APPENDIX-4 — Table 4.1 Various Reactivity descriptors of the studied compounds (1, 3 and 4) based on MPA calculated at B3LYP/6-31G(d, p) level of theory (Molecules1 and 4 optimized at B3LYP/3-21G level of theory)

System	Atom (k)	Fukui function				Local softness				Local electrophilicity				Relative nucleophilicity	Relative electrophilicity	Dual descriptor
		$f^+(k)$		$f^-(k)$		$s^+(k)$		$s^-(k)$		$w^+(k)$		$w^-(k)$				
		(a.u.)	(eV)	(a.u.)	(eV)	(a.u.)	(eV)	(a.u.)	(eV)	(a.u.)	(eV)	(a.u.)	(eV)			
MOLECULE 1	C1	-0.0161	-0.4381	0.0119	-0.3238	0.0023	0.0630	0.0017	0.0466	-0.0189	-0.5142	0.0140	-0.3801	0.7391	1.3529	-0.1143
	C2	0.0070	0.1905	0.0097	0.2640	0.0010	0.0274	0.0014	0.0380	0.0082	0.2236	0.0114	0.3098	1.3857	0.7216	-0.0735
	C3	-0.0024	-0.0653	0.0089	-0.2422	0.0003	0.0094	0.0013	0.0349	-0.0028	-0.0767	0.0104	-0.2843	3.7083	0.2697	0.1769
	C4	0.0062	0.1687	0.0034	0.0925	0.0009	0.0243	0.0005	0.0133	0.0073	0.1980	0.0040	0.1086	0.5484	1.8235	0.0762
	C6	0.0031	0.0844	-0.0061	-0.1660	0.0004	0.0121	-0.0009	-0.0239	0.0036	0.0990	-0.0072	-0.1948	-1.9677	-0.5082	0.2503
	C10	-0.0054	-0.1469	0.0445	1.2109	-0.0008	-0.0211	-0.0064	-0.1743	-0.0063	-0.1725	-0.0522	-1.4214	8.2407	0.1213	1.0640
	O16	-0.0194	-0.5279	0.0458	1.2463	-0.0028	-0.0760	-0.0066	-0.1793	-0.0228	-0.6197	-0.0538	-1.4629	2.3608	0.4236	0.7184
	O21	-0.0012	-0.0327	0.0036	0.0980	-0.0002	-0.0047	0.0005	0.0141	-0.0014	-0.0383	0.0042	0.1150	-3.0000	-0.3333	-0.1306
	O23	-0.0064	-0.1742	0.0081	0.2204	-0.0009	-0.0251	-0.0012	-0.0317	-0.0075	-0.2044	-0.0095	-0.2587	1.2656	0.7901	0.0463
	C25	-0.0201	-0.5470	0.0086	0.2340	-0.0029	-0.0787	-0.0012	-0.0337	-0.0236	-0.6420	-0.0101	-0.2747	0.4279	2.3372	-0.3129
	O28	-0.0319	-0.8681	0.0178	0.4844	-0.0046	-0.1249	-0.0026	-0.0697	-0.0374	-1.0189	-0.0209	-0.5685	0.5580	1.7921	-0.3837
	O30	-0.013	-0.359	0.012	0.351	-0.001	-0.051	-0.001	-0.050	-0.015	-0.421	-0.015	-0.4120	0.9773	1.0233	-0.0082

		2	2	9	0	9	7	9	5	5	6	1			
	C33	-0.0095	-0.2585	-0.0036	-0.0980	-0.0014	-0.0372	-0.0005	-0.0141	-0.0112	-0.3034	-0.0042	-0.1150	0.3789	2.6389	-0.1605
	C35	0.0052	0.1415	-0.0029	-0.0789	0.0007	0.0204	-0.0004	-0.0114	0.0061	0.1661	-0.0034	-0.0926	-0.5577	-1.7931	0.2204
	C38	0.0123	0.3347	0.0281	0.7646	0.0018	0.0482	0.0040	0.1100	0.0144	0.3929	0.0330	0.8975	2.2846	0.4377	-0.4299
	O44	-0.0032	-0.0871	-0.0068	-0.1850	-0.0005	-0.0125	-0.0010	-0.0266	-0.0038	-0.1022	-0.0080	-0.2172	2.1250	0.4706	0.0980
	O45	-0.0141	-0.3837	-0.0074	-0.2014	-0.0020	-0.0552	-0.0011	-0.0290	-0.0166	-0.4504	-0.0087	-0.2364	0.5248	1.9054	-0.1823
	C54	-0.0009	-0.0245	0.0065	0.1769	-0.0001	-0.0035	0.0009	0.0255	-0.0011	-0.0287	0.0076	0.2076	-7.2222	-0.1385	-0.2014
	O55	-0.0133	-0.3619	-0.0111	-0.3020	-0.0019	-0.0521	-0.0016	-0.0435	-0.0156	-0.4248	-0.0130	-0.3545	0.8346	1.1982	-0.0599
	O56	-0.0114	-0.3102	-0.0064	-0.1742	-0.0016	-0.0446	-0.0009	-0.0251	-0.0134	-0.3641	-0.0075	-0.2044	0.5614	1.7813	-0.1361
	C57	-0.0089	-0.2422	-0.0429	-1.1674	-0.0013	-0.0349	-0.0062	-0.1680	-0.0104	-0.2843	-0.0504	-1.3703	4.8202	0.2075	0.9252
	O60	-0.0362	-0.9851	-0.0649	-1.7660	-0.0052	-0.1418	-0.0093	-0.2541	-0.0425	-1.1563	-0.0762	-2.0730	1.7928	0.5578	0.7810
MOLECULE 3	C17	0.0086	0.2340	-0.0124	-0.3374	0.0008	0.0226	-0.0012	-0.0326	0.0075	0.2034	-0.0108	-0.2933	-1.4419	-0.6935	0.5714
	C19	-0.0340	-0.9252	-0.0429	-1.1674	-0.0033	-0.0894	-0.0041	-0.1128	-0.0295	-0.8041	-0.0373	-1.0146	1.2618	0.7925	0.2422
	C20	0.0103	0.2803	0.0232	0.6313	0.0010	0.0271	0.0022	0.0610	0.0090	0.2436	0.0202	0.5487	2.2524	0.4440	-0.3510
	O22	-0.0742	-2.0191	-0.0572	-1.5565	-0.0072	-0.1950	-0.0055	-0.1504	-0.0645	-1.7548	-0.0497	-1.3528	0.7709	1.2972	-0.4626

	O31	-0.0146	-0.3973	-0.0374	-1.0177	-0.0014	-0.0384	-0.0036	-0.0983	-0.0127	-0.3453	-0.0325	-0.8845	2.5616	0.3904	0.6204
	C32	-0.0262	-0.7129	-0.2003	-5.4505	-0.0025	-0.0689	-0.0193	-0.5265	-0.0228	-0.6196	-0.1741	-4.7370	7.6450	0.1308	4.7375
	O33	-0.0819	-2.2286	-0.1597	-4.3457	-0.0079	-0.2153	-0.0154	-0.4198	-0.0712	-1.9369	-0.1388	-3.7768	1.9499	0.5128	2.1171
	O34	-0.0689	-1.8749	-0.0409	-1.1130	-0.0067	-0.1811	-0.0040	-0.1075	-0.0599	-1.6295	-0.0355	-0.9673	0.5936	1.6846	-0.7619
	C42	0.0438	1.1919	0.0161	0.4381	0.0042	0.1151	0.0016	0.0423	0.0381	1.0359	0.0140	0.3808	0.3676	2.7205	0.7538
	O46	-0.1354	-3.6845	-0.0270	-0.7347	-0.0131	-0.3559	-0.0026	-0.0710	-0.1177	-3.2022	-0.0235	-0.6385	0.1994	5.0148	-2.9497
MOLECULE 4	C17	0.0049	0.1333	-0.0112	-0.3043	0.0005	0.0129	-0.0011	-0.0294	0.0025	0.0687	-0.0058	-0.1568	-2.2832	-0.4380	0.4375
	C20	0.0129	0.3518	0.0266	0.7247	0.0012	0.0340	0.0026	0.0700	0.0067	0.1812	0.0137	0.3734	2.0601	0.4854	-0.3729
	O29	-0.0160	-0.4342	-0.0319	-0.8674	-0.0015	-0.0419	-0.0031	-0.0838	-0.0082	-0.2237	-0.0164	-0.4469	1.9977	0.5006	0.4332
	C30	-0.0285	-0.7746	-0.2108	-5.7356	-0.0027	-0.0748	-0.0204	-0.5541	-0.0147	-0.3990	-0.1086	-2.9550	7.4050	0.1350	4.9610
	O31	-0.0894	-2.4327	-0.1571	-4.2748	-0.0086	-0.2350	-0.0152	-0.4129	-0.0461	-1.2533	-0.0809	-2.2024	1.7572	0.5691	1.8420
	O32	-0.0650	-1.7700	-0.0465	-1.2646	-0.0063	-0.1710	-0.0045	-0.1222	-0.0335	-0.9119	-0.0239	-0.6515	0.7145	1.3996	-0.5053
	C40	0.0584	1.5898	0.0156	0.4240	0.0056	0.1536	0.0015	0.0410	0.0301	0.8190	0.0080	0.2184	0.2667	3.7498	1.1658
	O44	-0.1778	-4.8388	-0.0233	-0.6332	-0.0172	-0.4674	-0.0022	-0.0612	-0.0916	-2.4929	-0.0120	-0.3262	0.1309	7.6419	-4.2056

Table 4.2 — Various Reactivity descriptors of the studied compounds (1, 3 and 4) based on HPA calculated at B3LYP/6-31G (d, p) level of theory (Molecules 1 and 4 optimized at B3LYP/3-21G level of theory)

System	Atom (k)	Fukuifunction				Localsoftness				Localelectrophilicity				Relativenucleophilicity	Relative electrophilicity	Dual descriptor
		$f^+(k)$		$f^-(k)$		$s^+(k)$		$s^-(k)$		$w^+(k)$		$w^-(k)$				
		(a.u.)	(eV)	(a.u.)	(eV)	(a.u.)	(eV)	(a.u.)	(eV)	(a.u.)	(eV)	(a.u.)	(eV)			
MOLECULE 1	C1	-0.0095	-0.2585	-0.0097	-0.2640	-0.0014	-0.0372	-0.0014	-0.0380	-0.0112	-0.3034	-0.0114	-0.3098	1.0211	0.9794	0.0054
	C2	-0.0007	-0.0190	0.0027	0.0735	-0.0001	-0.0027	0.0004	0.0106	-0.0008	-0.0224	0.0032	0.0862	-3.8571	-0.2593	-0.0925
	C3	-0.0009	-0.0245	-0.0024	-0.0653	-0.0001	-0.0035	-0.0003	-0.0094	-0.0011	-0.0287	-0.0028	-0.0767	2.6667	0.3750	0.0408
	C4	-0.0034	-0.0925	-0.0058	-0.1578	-0.0005	-0.0133	-0.0008	-0.0227	-0.0040	-0.1086	-0.0068	-0.1853	1.7059	0.5862	0.0653
	C6	-0.0003	-0.0082	0.0005	0.0136	0.0000	-0.0012	0.0001	0.0020	-0.0004	-0.0096	0.0006	0.0160	-1.6667	-0.6000	-0.0218
	C10	-0.0060	-0.1633	-0.0535	-1.4558	-0.0009	-0.0235	-0.0077	-0.2095	-0.0070	-0.1916	-0.0628	-1.7088	8.9167	0.1121	1.2926
	O16	-0.0198	-0.5388	-0.0521	-1.4177	-0.0028	-0.0775	-0.0075	-0.2040	-0.0232	-0.6324	-0.0612	-1.6641	2.6313	0.3800	0.8789
	O21	-0.0054	-0.1469	-0.0030	-0.0816	-0.0008	-0.0211	-0.0004	-0.0117	-0.0063	-0.1725	-0.0035	-0.0958	0.5556	1.8000	-0.0653
	O23	-0.0063	-0.1714	-0.0064	-0.1742	-0.0009	-0.0247	-0.0009	-0.0251	-0.0074	-0.2012	-0.0075	-0.2044	1.0159	0.9844	0.0027
	C25	-0.0157	-0.4272	-0.0041	-0.1116	-0.0023	-0.0615	-0.0006	-0.0161	-0.0184	-0.5015	-0.0048	-0.1310	0.2611	3.8293	-0.3157
	O28	-0.0305	-0.8300	-0.0143	-0.3891	-0.0044	-0.1194	-0.0021	-0.0560	-0.0358	-0.9742	-0.0168	-0.4568	0.4689	2.1329	-0.4408
	O30	-0.0115	-0.3129	-0.0110	-0.2993	-0.0017	-0.0450	-0.0016	-0.0431	-0.0135	-0.3673	-0.0129	-0.3514	0.9565	1.0455	-0.0136

	C33	-0.0116	-0.3157	-0.0103	-0.2803	-0.0017	-0.0454	-0.0015	-0.0403	-0.0136	-0.3705	-0.0121	-0.3290	0.8879	1.1262	-0.0354
	C35	-0.0026	-0.0708	0.0011	0.0299	-0.0004	-0.0102	0.0002	0.0043	-0.0031	-0.0830	0.0013	0.0351	-0.4231	-2.3636	-0.1007
	C38	0.0019	0.0517	0.0104	0.2830	0.0003	0.0074	0.0015	0.0407	0.0022	0.0607	0.0122	0.3322	5.4737	0.1827	-0.2313
	O44	-0.0060	-0.1633	-0.0132	-0.3592	-0.0009	-0.0235	-0.0019	-0.0517	-0.0070	-0.1916	-0.0155	-0.4216	2.2000	0.4545	0.1959
	O45	-0.0144	-0.3918	-0.0064	-0.1742	-0.0021	-0.0564	-0.0009	-0.0251	-0.0169	-0.4600	-0.0075	-0.2044	0.4444	2.2500	-0.2177
	C54	-0.0030	-0.0816	-0.0025	-0.0680	-0.0004	-0.0117	-0.0004	-0.0098	-0.0035	-0.0958	-0.0029	-0.0799	0.8333	1.2000	-0.0136
	O55	-0.0130	-0.3538	-0.0085	-0.2313	-0.0019	-0.0509	-0.0012	-0.0333	-0.0153	-0.4152	-0.0100	-0.2715	0.6538	1.5294	-0.1225
	O56	-0.0113	-0.3075	-0.0050	-0.1361	-0.0016	-0.0442	-0.0007	-0.0196	-0.0133	-0.3609	-0.0059	-0.1597	0.4425	2.2600	-0.1714
	C57	-0.0085	-0.2313	-0.0428	-1.1647	-0.0012	-0.0333	-0.0062	-0.1676	-0.0100	-0.2715	-0.0502	-1.3671	5.0353	0.1986	0.9334
	O60	-0.0343	-0.9334	-0.0669	-1.8205	-0.0049	-0.1343	-0.0096	-0.2620	-0.0403	-1.0956	-0.0785	-2.1369	1.9504	0.5127	0.8871
MOLECULE 3	C17	-0.0169	-0.4599	-0.0078	-0.2123	-0.0016	-0.0444	-0.0008	-0.0205	-0.0147	-0.3997	-0.0068	-0.1845	0.4615	2.1667	-0.2476
	C19	-0.0388	-1.0558	-0.0208	-0.5660	-0.0037	-0.1020	-0.0020	-0.0547	-0.0337	-0.9176	-0.0181	-0.4919	0.5361	1.8654	-0.4898
	C20	-0.0092	-0.2503	-0.0096	-0.2612	-0.0009	-0.0242	-0.0009	-0.0252	-0.0080	-0.2176	-0.0083	-0.2270	1.0435	0.9583	0.0109
	O22	-0.0687	-1.8694	-0.0563	-1.5320	-0.0066	-0.1806	-0.0054	-0.1480	-0.0597	-1.6247	-0.0489	-1.3315	0.8195	1.2202	-0.3374
	O31	-0.0163	-0.4435	-0.0575	-1.5647	-0.0016	-0.0428	-0.0056	-0.1511	-0.0142	-0.3855	-0.0500	-1.3599	3.5276	0.2835	1.1211
	C32	-0.0194	-0.5279	-0.1816	-4.9416	-0.0019	-0.0510	-0.0175	-0.4774	-0.0169	-0.4588	-0.1578	-4.2948	9.3608	0.1068	4.4137
	O33	-0.0827	-2.2504	-0.1776	-4.8328	-0.0080	-0.2174	-0.0172	-0.46	-0.0719	-1.9558	-0.1544	-4.2002	2.1475	0.4657	2.5824

									68								
	O34	-0.0610	-1.6599	-0.0419	-1.1402	-0.0059	-0.1603	-0.0040	-0.1101	-0.0530	-1.4426	-0.0364	-0.9909	0.6869	1.4558	-0.5197
	C42	-0.0190	-0.5170	-0.0014	-0.0381	-0.0018	-0.0499	-0.0001	-0.0037	-0.0165	-0.4493	-0.0012	-0.0331	0.0737	13.5714	-0.4789
	O46	-0.1214	-3.3035	-0.0187	-0.5089	-0.0117	-0.3191	-0.0018	-0.0492	-0.1055	-2.8711	-0.0163	-0.4422	0.1540	6.4920	-2.7946
MOLECULE4	C17	-0.0124	-0.3385	-0.0060	-0.1630	-0.0012	-0.0327	-0.0006	-0.0157	-0.0064	-0.1744	-0.0031	-0.0840	0.4815	2.0770	-0.1755
	C20	-0.0068	-0.1840	-0.0110	-0.3000	-0.0007	-0.0178	-0.0011	-0.0290	-0.0035	-0.0948	-0.0057	-0.1546	1.6307	0.6132	0.1160
	O29	-0.0197	-0.5359	-0.0598	-1.6261	-0.0019	-0.0518	-0.0058	-0.1571	-0.0101	-0.2761	-0.0308	-0.8377	3.0341	0.3296	1.0901
	C30	-0.0250	-0.6812	-0.2006	-5.4584	-0.0024	-0.0658	-0.0194	-0.5273	-0.0129	-0.3510	-0.1033	-2.8122	8.0127	0.1248	4.7772
	O31	-0.0972	-2.6460	-0.1882	-5.1212	-0.0094	-0.2556	-0.0182	-0.4947	-0.0501	-1.3632	-0.0970	-2.6384	1.9355	0.5167	2.4752
	O32	-0.0613	-1.6669	-0.0444	-1.2072	-0.0059	-0.1610	-0.0043	-0.1166	-0.0316	-0.8588	-0.0229	-0.6220	0.7242	1.3808	-0.4597
	C40	-0.0214	-0.5811	-0.0013	-0.0358	-0.0021	-0.0561	-0.0001	-0.0035	-0.0110	-0.2994	-0.0007	-0.0184	0.0615	16.2519	-0.5453
	O44	-0.1802	-4.9033	-0.0166	-0.4528	-0.0174	-0.4737	-0.0016	-0.0437	-0.0928	-2.5262	-0.0086	-0.2333	0.0923	10.8295	-4.4505

Table 4.3 — Various Reactivity descriptors of the studied compounds (1, 3 and 4) based on NPA calculated at B3LYP/6-31G (d, p) level of theory (Molecules 1 and 4 optimized at B3LYP/3-21G level of theory)

System	Atom (k)	Fukui function				Local softness				Local electrophilicity				Relative nucleophilicity	Relative electrophilicity	Dual descriptor
		$f^+(k)$		$f^-(k)$		$s^+(k)$		$s^-(k)$		$w^+(k)$		$w^-(k)$				
		(a.u.)	(eV)	(a.u.)	(eV)	(a.u.)	(eV)	(a.u.)	(eV)	(a.u.)	(eV)	(a.u.)	(eV)			
MOLECULE1	C1	0.0021	0.0571	0.0012	0.0327	0.0003	0.0082	0.0002	0.0047	0.0025	0.0671	0.0014	0.0383	0.5714	1.7500	0.0245
	C2	0.0020	0.0544	0.0083	0.2259	0.0003	0.0078	0.0012	0.0325	0.0023	0.0639	0.0097	0.2651	4.1500	0.2410	-0.1714
	C3	0.0058	0.1578	0.0040	0.1088	0.0008	0.0227	0.0006	0.0157	0.0068	0.1853	0.0047	0.1278	0.6897	1.4500	0.0490
	C4	-0.0028	-0.0762	-0.0045	-0.1225	-0.0004	-0.0110	-0.0006	-0.0176	-0.0033	-0.0894	-0.0053	-0.1437	1.6071	0.6222	0.0463

C6	0.0007	0.0190	0.0005	0.0136	0.0001	0.0027	0.0001	0.0020	0.0008	0.0224	0.0006	0.0160	0.7143	1.4000	0.0054
C10	-0.0028	-0.0762	-0.0891	-2.42466	-0.00044	-0.01110	-0.00128	-0.34899	-0.00333	-0.00894	-0.01046	-2.84559	31.8214	0.0314	2.3484
O16	-0.0235	-0.6395	-0.0496	-1.34977	-0.00334	-0.00920	-0.00071	-0.01942	-0.00276	-0.07506	-0.00582	-1.58443	2.1106	0.4738	0.7102
O21	-0.0098	-0.26667	-0.00444	-0.11977	-0.00144	-0.00384	-0.00006	-0.00172	-0.00115	-0.03130	-0.00052	-0.14045	0.4490	2.2273	-0.1469
O23	0.0018	0.0490	0.0005	0.0136	0.0003	0.0070	0.0001	0.0020	0.0021	0.0575	0.0006	0.0160	0.2778	3.6000	0.0354
C25	0.0018	0.0490	0.0003	0.0082	0.0003	0.0070	0.0000	0.0012	0.0021	0.0575	0.0004	0.0096	0.1667	6.0000	0.0408
O28	-0.0276	-0.7510	-0.0074	-0.20144	-0.00404	-0.10811	-0.00111	-0.00290	-0.00324	-0.08816	-0.00087	-0.23644	0.2681	3.7297	-0.5497
O30	-0.0138	-0.3755	-0.0119	-0.3238	-0.0020	-0.0540	-0.0017	-0.0466	-0.0162	-0.4408	-0.0140	-0.3801	0.8623	1.1597	-0.0517
C33	-0.0017	-0.0463	-0.0032	-0.08711	-0.0002	-0.0067	-0.0005	-0.0125	-0.0020	-0.0543	-0.0038	-0.1022	1.8824	0.5313	0.0408
C35	0.0010	0.0272	0.0008	0.0218	0.0001	0.0039	0.0001	0.0031	0.0012	0.0319	0.0009	0.0256	0.8000	1.2500	0.0054
C38	-0.0047	-0.1279	-0.0027	-0.07355	-0.0007	-0.0184	-0.0004	-0.0106	-0.0055	-0.1501	-0.0032	-0.0862	0.5745	1.7407	-0.0544
O44	-0.0094	-0.2558	-0.0135	-0.36744	-0.0014	-0.0368	-0.0019	-0.0529	-0.0110	-0.3002	-0.0158	-0.4312	1.4362	0.6963	0.1116
O45	-0.0197	-0.5361	-0.0063	-0.17144	-0.0028	-0.0771	-0.0009	-0.0247	-0.0231	-0.6292	-0.0074	-0.2012	0.3198	3.1270	-0.3646
C54	0.0032	0.0871	-0.0030	-0.08166	0.0005	0.0125	-0.0004	-0.0117	0.0038	0.1022	-0.0035	-0.0958	-0.9375	-1.0667	0.1687
O55	-0.0155	-0.4218	-0.0090	-0.24499	-0.0022	-0.0607	-0.0013	-0.0352	-0.0182	-0.4951	-0.0106	-0.2875	0.5806	1.7222	-0.1769

	O56	-0.0141	-0.3837	-0.0053	-0.1442	-0.0020	-0.0552	-0.0008	-0.0208	-0.0166	-0.4504	-0.0062	-0.1693	0.3759	2.6604	-0.2395
	C57	0.0131	0.3565	-0.0424	-1.1538	0.0019	0.0513	-0.0061	-0.1660	0.0154	0.4184	-0.0498	-1.3543	-3.2366	-0.3090	1.5102
	O60	-0.0397	-1.0803	-0.0703	-1.9130	-0.0057	-0.1555	-0.0101	-0.2753	-0.0466	-1.2681	-0.0825	-2.2455	1.7708	0.5647	0.8327
MOLECULE 3	C17	-0.0102	-0.2776	-0.0131	-0.3565	-0.0010	-0.0268	-0.0013	-0.0344	-0.0089	-0.2412	-0.0114	-0.3098	1.2843	0.7786	0.0789
	C19	0.0071	0.1932	0.0035	0.0952	0.0007	0.0187	0.0003	0.0092	0.0062	0.1679	0.0030	0.0828	0.4930	2.0286	0.0980
	C20	-0.0061	-0.1660	-0.0035	-0.0952	-0.0006	-0.0160	-0.0003	-0.0092	-0.0053	-0.1443	-0.0030	-0.0828	0.5738	1.7429	-0.0708
	O22	-0.0570	-1.5511	-0.0099	-0.2694	-0.0055	-0.1498	-0.0100	-0.2600	-0.0495	-1.3480	-0.0866	-0.2341	0.1737	5.7576	-1.2817
	O31	-0.0179	-0.4871	-0.0470	-1.2789	-0.0017	-0.0471	-0.0045	-0.1235	-0.0156	-0.4233	-0.0408	-1.1115	2.6257	0.3809	0.7919
	C32	-0.0011	-0.0299	-0.0323	-8.8057	-0.0001	-0.0029	-0.0313	-0.8506	-0.0010	-0.0260	-0.2812	-7.6530	294.1818	0.0034	8.7757
	O33	-0.1088	-2.9606	-0.1868	-5.0831	-0.0105	-0.2860	-0.0180	-0.4910	-0.0946	-2.5731	-0.1623	-4.4177	1.7169	0.5824	2.1225
	O34	-0.0507	-1.3796	-0.0172	-0.4680	-0.0049	-0.1333	-0.0017	-0.0452	-0.0441	-1.1990	-0.0149	-0.4068	0.3393	2.9477	-0.9116
	C42	0.0028	0.0762	0.0008	0.0218	0.0003	0.0074	0.0001	0.0021	0.0024	0.0662	0.0007	0.0189	0.2857	3.5000	0.0544
	O46	-0.1509	-4.1062	-0.0206	-0.5606	-0.0146	-0.3967	-0.0020	-0.0541	-0.1311	-3.5687	-0.0179	-0.4872	0.1365	7.3252	-3.5457
MOLECULE 4	C17	-0.0053	-0.1456	-0.0066	-0.1807	-0.0005	-0.0141	-0.0006	-0.0175	-0.0028	-0.0750	-0.0034	-0.0931	1.2411	0.8057	0.0351

	C20	-0.0038	-0.1048	-0.0120	-0.3255	-0.0004	-0.0101	-0.0012	-0.0314	-0.0020	-0.0540	-0.0062	-0.1677	3.1065	0.3219	0.2207
	O29	-0.0208	-0.5660	-0.0427	-1.1628	-0.0020	-0.0547	-0.0041	-0.1123	-0.0107	-0.2916	-0.0220	-0.5990	2.0543	0.4868	0.5968
	C30	-0.0125	-0.3404	-0.3526	9.5956	-0.0012	-0.0329	-0.0341	-0.9269	-0.0064	-0.1754	-0.1817	-4.9437	28.1878	0.0355	9.2552
	O31	-0.1225	-3.3342	-0.1809	-4.9239	-0.0118	-0.3221	-0.0175	-0.4757	-0.0631	-1.7178	-0.0932	-2.5368	1.4768	0.6771	1.5897
	O32	-0.0443	-1.2068	-0.0150	-0.4076	-0.0043	-0.1166	-0.0014	-0.0394	-0.0228	-0.6218	-0.0077	-0.2100	0.3378	2.9606	-0.7992
	C40	0.0081	0.2193	0.0015	0.0405	0.0008	0.0212	0.0001	0.0039	0.0042	0.1130	0.0008	0.0209	0.1849	5.4094	0.1788
	O44	-0.2135	-5.8105	-0.0210	-0.5717	-0.0206	-0.5613	-0.0020	-0.0552	-0.0100	-2.9936	-0.0108	-0.2945	0.0984	10.1633	-5.2388

Table 4.4 — Various Reactivity descriptors of the studied compounds (1, 3and 4) calculated at B3LYP/6-31G (d, p) level of theory. (Molecules1and 4 optimized at B3LYP/3-21G level of theory)

System	Atom(k)	Electrostatic potential (Vel)			Hardness Potential [h(k)]			Local hardness			
		Neutral(N)	Anion(N+1)	Cation(N-1)	Neutral(N)	Anion(N+1)	Cation(N-1)	$D^{+}h(k)$		$D^{-}h(k)$	
		(a.u.)	(a.u.)	(a.u.)	(a.u.)	(a.u.)	(a.u.)	(a.u.)	(eV)	(a.u.)	(eV)
MOLECULE 1	C1	-58.4987	-58.4056	-58.6011	58.4987	58.4056	58.6011	-0.0931	-2.5334	-0.1024	-2.7865
	C2	-59.0229	-58.9285	-59.1161	59.0229	58.9285	59.1161	-0.0944	-2.5688	-0.0932	-2.5361
	C3	-60.6979	-60.6021	-60.7898	60.6979	60.6021	60.7898	-0.0958	-2.6069	-0.0919	-2.5007
	C4	-61.1445	-61.0492	-61.2545	61.1445	61.0492	61.2545	-0.0953	-2.5933	-0.1100	-2.9933
	C6	-64.4458	-64.3485	-64.541	64.4458	64.3485	64.5410	-0.0973	-2.6477	-0.0952	-2.5905
	C10	-55.3663	-55.2768	-55.4979	55.3663	55.2768	55.4979	-0.0895	-2.4354	-0.1316	-3.5810
	O16	-56.4702	-56.3795	-56.5995	56.4702	56.3795	56.5995	-0.0907	-2.4681	-0.1293	-3.5185
	O21	-65.4099	-65.3077	-65.5254	65.4099	65.3077	65.5254	-0.1022	-2.7810	-0.1155	-3.1429
	O23	-60.4777	-60.3826	-60.5836	60.4777	60.3826	60.5836	-0.0951	-2.5878	-0.1059	-2.8817
	C25	-52.184	-52.093	-52.271	52.1840	52.0930	52.2710	-0.0910	-2.4763	-0.0870	-2.3674

	O28	-55.2	-55.105	-55.2827	55.2000	55.1050	55.2827	-0.0950	-2.5851	-0.0827	-2.2504
	O30	-63.1447	-63.0499	-63.236	63.1447	63.0499	63.2360	-0.0948	-2.5797	-0.0913	-2.4844
	C33	-60.924	-60.8195	-61.0286	60.9240	60.8195	61.0286	-0.1045	-2.8436	-0.1046	-2.8463
	C35	-61.5905	-61.4884	-61.6823	61.5905	61.4884	61.6823	-0.1021	-2.7783	-0.0918	-2.4980
	C38	-64.2252	-64.124	-64.3216	64.2252	64.1240	64.3216	-0.1012	-2.7538	-0.0964	-2.6232
	O44	-66.0901	-65.9775	-66.2193	66.0901	65.9775	66.2193	-0.1126	-3.0640	-0.1292	-3.5157
	O45	-65.5772	-65.4725	-65.6635	65.5772	65.4725	65.6635	-0.1047	-2.8491	-0.0863	-2.3484
	C54	-61.204	-61.1034	-61.286	61.2040	61.1034	61.2860	-0.1006	-2.7375	-0.0820	-2.2314
	O55	-65.4531	-65.3503	-65.538	65.4531	65.3503	65.5380	-0.1028	-2.7974	-0.0849	-2.3103
	O56	-67.3334	-67.2328	-67.4208	67.3334	67.2328	67.4208	-0.1006	-2.7375	-0.0874	-2.3783
	C57	-55.0572	-54.9434	-55.2057	55.0572	54.9434	55.2057	-0.1138	-3.0967	-0.1485	-4.0409
	O60	-56.4717	-56.3584	-56.6191	56.4717	56.3584	56.6191	-0.1133	-3.0831	-0.1474	-4.0110
MOLECULE 3	C17	-48.8813	-48.7232	-49.0373	48.8813	48.7232	49.0373	-0.1581	-4.3022	-0.1560	-4.2450
	C19	-45.3435	-45.1987	-45.4855	45.3435	45.1987	45.4855	-0.1448	-3.9402	-0.1420	-3.8640
	C20	-48.902	-48.7473	-49.0563	48.9020	48.7473	49.0563	-0.1547	-4.2096	-0.1543	-4.1987
	O22	-47.6308	-47.4816	-47.7658	47.6308	47.4816	47.7658	-0.1492	-4.0600	-0.1350	-3.6736
	O31	-53.0609	-52.9076	-53.2602	53.0609	52.9076	53.2602	-0.1533	-4.1715	-0.1993	-5.4233
	C32	-47.295	-47.141	-47.5685	47.2950	47.1410	47.5685	-0.1540	-4.1906	-0.2735	-7.4424
	O33	-48.1009	-47.9382	-48.3514	48.1009	47.9382	48.3514	-0.1627	-4.4273	-0.2505	-6.8165
	O34	-50.1847	-50.0303	-50.3283	50.1847	50.0303	50.3283	-0.1544	-4.2015	-0.1436	-3.9076
	C42	-44.8451	-44.6875	-44.9631	44.8451	44.6875	44.9631	-0.1576	-4.2885	-0.1180	-3.2110
	O46	-48.0613	-47.879	-48.1848	48.0613	47.8790	48.1848	-0.1823	-4.9607	-0.1235	-3.3606
MOLECULE 4	C17	-47.5408	-47.3832	-47.7019	47.5408	47.3832	47.7019	-0.1576	-4.2895	-0.1611	-4.3849
	C20	-47.1751	-47.0221	-47.3351	47.1751	47.0221	47.3351	-0.1530	-4.1644	-0.1600	-4.3539
	O29	-51.7211	-51.5584	-51.9340	51.7211	51.5584	51.9340	-0.1627	-4.4275	-0.2129	-5.7938
	C30	-46.2641	-46.1011	-46.5594	46.2641	46.1011	46.5594	-0.1630	-4.4367	-0.2953	-8.0350
	O31	-47.2996	-47.1213	-47.5779	47.2996	47.1213	47.5779	-0.1783	-4.8510	-0.2783	-7.5741
	O32	-48.5420	-48.3878	-48.6903	48.5420	48.3878	48.6903	-0.1542	-4.1968	-0.1483	-4.0350
	C40	-43.9078	-43.7349	-44.0288	43.9078	43.7349	44.0288	-0.1729	-4.7042	-0.1210	-3.2925
	O44	-47.5956	-47.3700	-47.7255	47.5956	47.3700	47.7255	-0.2256	-6.1382	-0.1299	-3.5337

References

1 Asada, Y., Sukemori, A., Watanabe, T., Malla, K. J., Yoshikawa, T., Li, W., ... & Lee, K. H. (2011). Stelleralides A–C, Novel Potent Anti-HIV Daphnane-Type Diterpenoids from Stellera chamaejasm e L. *Organic Letters*, *13*(11), 2904-2907.

2 Cheng, Y. Y., Chen, H., He, H. P., Zhang, Y., Li, S. F., Tang, G. H., ... & Hao, X. J. (2013).

3 Anti-HIV active daphnane diterpenoids from Trigonostemon thyrsoideum. *Phytochemistry*, *96*, 360-369.

4 Liu, Y. Y., Liu, Y. P., Wang, X. P., Qiao, Z. H., Yu, X. M., Zhu, Y. Z., ... & Fu, Y. H.

5 (2020a). Bioactive daphnane diterpenes from Wikstroemia chuii with their potential anti-inflammatory effects and anti-HIV activities. *Bioorganic Chemistry*, *105*, 104388.

6 Otsuki, K., Li, W., Asada, Y., Chen, C. H., Lee, K. H., & Koike, K. (2019). Daphneodorins A–C, anti-HIV gnidimacrin related

macrocyclic daphnane orthoesters from Daphne
7 odora. *Organic letters*, *22*(1), 11-15.
8 Zhang, X., Huang, S. Z., Wan-Gang, G. U., Liu-Meng, Y. A. N. G., Huan, C. H. E. N., Zheng, C. B., ... & Zheng, Y. T. (2014). Wikstroelide M potently inhibits HIV replication by targeting reverse transcriptase and integrase nuclear translocation. *Chinese Journal of Natural Medicines*, *12*(3), 186-193.
9 Yan, M., Lu, Y., Chen, C. H., Zhao, Y., Lee, K. H., & Chen, D. F. (2015). Stelleralides D–J and anti-HIV daphnane diterpenes from Stellera chamaejasme. *Journal of natural*
10 *products*, *78*(11), 2712-2718.
11 Otsuki, K., Li, W., Asada, Y., Chen, C. H., Lee, K. H., & Koike, K. (2019). Daphneodorins A–C, anti-HIV gnidimacrin related macrocyclic daphnane orthoesters from Daphne
12 odora. *Organic letters*, *22*(1), 11-15.
13 Otsuki, K., Zhang, M., Yamamoto, A., Tsuji, M., Tejima, M., Bai, Z. S., ... & Koike, K. (2020). Anti-HIV tigliane diterpenoids from Wikstroemia scytophylla. *Journal of natural products*, *83*(12), 3584-3590.
14 Zhang, M., Otsuki, K., Kikuchi, T., Bai, Z. S., Zhou, D., Huang, L., ... & Li, W. (2021). LC-MS identification, isolation, and structural elucidation of anti-HIV tigliane diterpenoids from Wikstroemia lamatsoensis. *Journal of Natural Products*, *84*(8), 2366-2373.
15 Zhao, J. X., Liu, C. P., Qi, W. Y., Han, M. L., Han, Y. S., Wainberg, M. A., & Yue, J. M.
16 (2014). Eurifoloids A–R, structurally diverse diterpenoids from Euphorbia neriifolia. *Journal of Natural Products*, *77*(10), 2224-2233.
17 Zhang, H., Zhu, K. K., Han, Y. S., Luo, C., Wainberg, M. A., & Yue, J. M. (2015). Flueggether A and virosinine A, anti-HIV alkaloids from Flueggea virosa. *Organic Letters*, *17*(24), 6274-6277.
18 Liu, Y. P., Liu, Q. L., Zhang, X. L., Niu, H. Y., Guan, C. Y., Sun, F. K., ... & Fu, Y. H.
19 (2019a). Bioactive monoterpene indole alkaloids from Nauclea officinalis. *Bioorganic Chemistry*, *83*, 1-5.
20 Liu, Y. P., Guo, J. M., Xie, Z., Suo, X. Y., Liu, Z. Y., Qiao, Z. H., ... & Fu, Y. H. (2021).
21 Clausanisumine, a prenylated bicarbazole alkaloid from the fruits of Clausena anisum-olens and its potential anti-HIV activity. *The Journal of Organic Chemistry*, *86*(24), 17722-17726.
22 Liu, Y. P., Yan, G., Guo, J. M., Liu, Y. Y., Li, Y. J., Zhao, Y. Y., ... & Fu, Y. H. (2019b).
23 Prenylated coumarins from the fruits of Manilkara zapota with potential anti-inflammatory effects and anti-HIV activities. *Journal of agricultural and food chemistry*, *67*(43), 11942-11947.
24 Liu, Y. P., Yan, G., Xie, Y. T., Lin, T. C., Zhang, W., Li, J., ... & Fu, Y. H. (2020b).
25 Bioactive prenylated coumarins as potential anti-inflammatory and anti-HIV agents from Clausena lenis. *Bioorganic Chemistry*, *97*, 103699.
26 Yu, J. H., Wang, G. C., Han, Y. S., Wu, Y., Wainberg, M. A., & Yue, J. M. (2015).
27 Limonoids with anti-HIV activity from Cipadessa cinerascens. *Journal of Natural Products*, *78*(6), 1243-1252.
28 Zhou, X., Fang, W., Tan, S., Lin, X., Xun, T., Yang, B., ... & Liu, Y. (2016). Aspernigrins with anti-HIV-1 activities from the marine-derived fungus Aspergillus niger SCSIO Jcsw6F30. *Bioorganic & medicinal chemistry letters*, *26*(2), 361-365.
29 Liu, Y. P., Zhao, W. H., Feng, X. Y., Zhang, Z. J., Zong, K., Sun, Z. G., ... & Fu, Y. H.
30 (2018). Novel tetrahydrofuran derivatives from Trigonostemon howii with their potential anti-HIV-1 activities. *Bioorganic Chemistry*, *79*, 111-114.
31 Tao, L., Zhuo, Y. T., Qiao, Z. H., Li, J., Tang, H. X., Yu, Q. M., ... & Liu, Y. P. (2022).
32 Prenylated coumarins from the fruits of Artocarpus heterophyllus with their potential anti-inflammatory and anti-HIV activities. *Natural Product Research*, *36*(10), 2526-2533.