

Table S1. Relative energies (in kcal/mol) calculated for ATV species present during lactonisation/hydrolysis under acidic conditions in vacuo and in aqueous solution.

Structure	Relative energy B3LYP /6-31+g(d) (isolated)	Hydratation free energy SM5.4A	Hydratation free energy SM5.4P	Relative energy B3LYP & SM5.4A (aqueous)	Relative energy B3LYP & SM5.4P (aqueous)
I	0.0	-8.8	-12.9	0.0	0.0
A_AL2	4.1	-10.0	-14.1	2.8	2.9
A_AL1	11.3	-9.5	-12.9	10.6	11.4
TS	16.5	-9.1	-11.7	16.3	17.8
AL2	35.8	-10.1	-13.6	34.5	35.1
AL1	37.8	-9.2	-13.0	37.3	37.7
II	6.0	-8.4	-12.4	6.4	6.5
TS1_eq	6.2	-8.4	-12.4	6.6	6.8
TS1_ax	8.8	-8.5	-12.3	9.1	9.4
III_eq	5.1	-8.9	-12.7	5.0	5.2
III_ax	6.1	-9.3	-13.2	5.6	5.9
TS2_eq	5.9	-10.3	-14.4	4.4	4.4
TS2_ax	18.4	-11.2	-15.7	16.0	15.7
IV_eq	4.5	-10.4	-14.7	2.9	2.7
IV_ax	5.7	-9.6	-13.8	4.8	4.8
TS3_eq	25.1	-9.4	-13.1	24.5	24.9
TS3_ax	18.7	-9.2	-12.4	18.3	19.2
L_AL2	-1.7	-8.7	-11.0	-1.6	0.3
L_AL1	-4.2	-9.3	-12.8	-4.7	-4.1
V_eq	-1.7	-8.7	-11.0	-1.6	0.3
V_ax	-4.2	-9.3	-12.8	-4.7	-4.1

(B3LYP/6-31+G(d) energy baseline -2053.9435098 Hartree)

Table S2. Relative energies (in kcal/mol) calculated for ATV species present during lactonisation/hydrolysis under basic conditions in vacuo and in aqueous solution.

Structure	Relative energy B3LYP /6-31+g(d) (isolated)	Hydratation free energy SM5.4A	Hydratation free energy SM5.4P	Relative energy B3LYP & SM5.4A (aqueous)	Relative energy B3LYP & SM5.4P (aqueous)
	0.0	-48.8	-53.0	0.0	0.0
	23.9	-44.8	-50.2	27.9	26.8
	22.9	-47.9	-53.5	23.8	22.4
	26.9	-52.9	-57.8	22.8	22.1
	21.0	-51.7	-58.1	18.1	15.9

(B3LYP/6-31+G(d) energy baseline -1940,08620928 Hartree)