Kinetic Modelling of Acyl Glucuronide and Glucoside Reactivity and Development of Structure-Property Relationships

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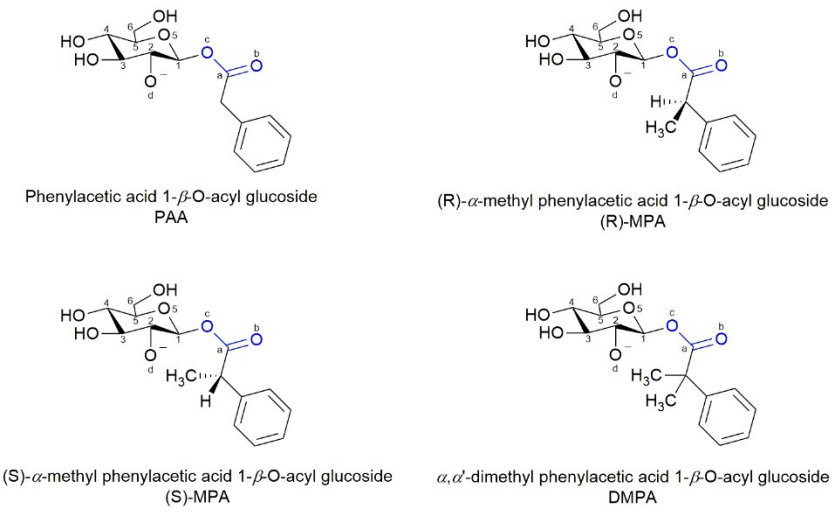
1. Structures of Acyl Glucosides, Molecular Descriptors and Atomic Distances of Optimised of Acyl Glucosides



Supplementary Figure 1. Chemical structures of acyl glucoside conjugates, the ester bond (blue), carbonyl carbon (a), carbonyl oxygen (b), acyl carbon (c) and alkoxide oxygen (d) are highlighted

Supplementary Table 1. Physicochemical descriptors for each acyl glucoside ground state and transition structures

	Ground States				Transition Structures			
Property	PAA	(R)-MPA	(S)-MPA	DMPA	PAA	(R)-MPA	(S)-MPA	DMPA
Partial atomic charge:								
Carbonyl Carbon (a)	0.849	0.853	0.853	0.855	0.819	0.824	0.820	0.827
Carbonyl Oxygen (b)	-0.617	-0.628	-0.629	-0.611	-0.698	-0.711	-0.719	-0.723
Acyl Oxygen (c)	-0.543	-0.536	-0.536	-0.552	-0.655	-0.625	-0.632	-0.678
Alkoxide Oxygen (d)	-0.893	-0.892	-0.895	-0.893	-0.731	-0.745	-0.741	-0.698
E_{HOMO} (Hartree)	-0.203	-0.203	-0.203	-0.203	-0.226	-0.226	-0.220	-0.223
E_{LUMO} (Hartree)	-0.023	-0.026	-0.027	-0.026	-0.015	-0.013	-0.014	-0.011
Activation energy (kcal/mol)	N/A	N/A	N/A	N/A	8.53	8.70	9.82	11.41
Electron affinity (KJ/mol)	95.08	84.14	87.38	68.48	86.56	54.66	54.88	58.24
Electronegativity (χ)	-0.1131	-0.1145	-0.1149	-0.1143	-0.1205	-0.1195	-0.1169	-0.1171
Hardness (η)	0.0902	0.0888	0.0883	0.0886	0.1060	0.1061	0.1032	0.1057
Electrophilicity (ω)	0.0709	0.0738	0.0748	0.0737	0.0686	0.0673	0.0662	0.0649
Softness (S)	5.5448	5.6291	5.6638	5.6418	4.7190	4.7143	4.8471	4.7324
f^N (Carbonyl C)	-8.668	-21.585	-23.484	-24.306	-58.251	-75.283	-30.648	-142.389
f^E (Alkoxide O)	-2.347	-2.343	-2.352	-2.351	-0.730	-0.813	-1.069	-0.642
PSA/CMSA	0.429	0.407	0.403	0.395	0.442	0.424	0.423	0.410

Supplementary Table 2. Key atomic distances (Å) for each acyl glucoside in the ground and transition structures optimised at the B3LYP/6-31G(d,p) level of theory. Distance **a** between the carbonyl carbon (a) and the alkoxide oxygen (d). Distance **b** between the carbonyl carbon (a) and carbon oxygen (b), refer to supplementary figure 1 for atom labels

					PAA					
Bond Length	GS1	GS2	**GS3**	GS4	GS5	GS6		**TS1**	TS2	TS3
Distance **a**	3.69	4.11	**4.18**	3.50	3.50	3.35		**1.76**	1.77	1.87
Distance **b**	1.21	1.21	**1.21**	1.21	1.21	1.21		**1.22**	1.22	1.22
					(R)-MPA					
	GS1	**GS2**	GS3	GS4	GS5			TS1	TS2	**TS3**
Distance **a**	3.39	**4.19**	3.13	3.36	3.44			1.82	1.81	**1.84**
Distance **b**	1.21	**1.22**	1.21	1.21	1.21			1.22	1.22	**1.23**
					(S)-MPA					
	GS1	**GS2**	GS3	GS4	GS5			**TS1**	TS2	TS3
Distance **a**	3.30	**4.04**	3.38	3.73	3.17			**1.84**	1.64	1.86
Distance **b**	1.21	**1.22**	1.21	1.21	1.21			**1.23**	1.22	1.22
					DMPA					
	GS1	GS2	GS3	GS4	GS5	GS6	GS7	GS8	GS9	**GS10**
Distance **a**	2.96	3.53	3.51	2.95	3.22	3.40	3.44	2.95	3.73	**4.10**
Distance **b**	1.22	1.21	1.21	1.21	1.21	1.21	1.21	1.21	1.21	**1.21**
	TS1	TS2	TS3	**TS4**	TS5	TS6				
Distance **a**	1.77	1.75	1.80	**1.66**	1.92	1.91				
Distance **b**	1.23	1.23	1.23	**1.23**	1.22	1.22				

Lowest energy conformers indicated in bold in the table. GS - Ground state, TS - Transition structure

2. Cartesian Coordinates of the Lowest Energy Ground States and Transition Structures for the Series of Acyl Glucosides

PAA Ground state

Energy: -1070.481480 Hartree (B3LYP/6-31++G(d,p) SCRF=water) 0 imaginary freq (B3LYP/6-31G(d,p))

C	-3.41482500	-1.19909800	-0.43576400	O	-1.77637800	-2.88093800	-0.22646800
C	-2.05339000	-1.64574300	0.19451300	C	1.23173100	0.00058300	0.13113500
C	-1.08354200	-0.49905800	-0.15759200	O	1.26816700	0.78102400	-0.79758000
C	-2.85600300	1.15504900	-0.16530000	C	2.40694000	-0.29372700	1.06805500
C	-3.92213600	0.09728600	0.15351600	H	2.28950700	0.40302100	1.91055000
H	-2.17978400	-1.52916500	1.31308700	H	2.27128400	-1.29537900	1.48209100
H	-3.24368700	-1.02298300	-1.51826600	O	0.16307500	-0.70006700	0.53237300
H	-2.80317100	1.26959000	-1.26035600	C	3.77886200	-0.13896900	0.45390300
H	-4.02253100	-0.00352900	1.24595000	C	4.18906500	1.07134400	-0.12481600
H	-0.87815900	-0.43367900	-1.23357800	C	4.68291200	-1.20788200	0.47473200
O	-1.57147000	0.75395100	0.33847200	C	5.46855800	1.20396200	-0.66231000
C	-3.09884400	2.52442300	0.45247800	H	3.48877200	1.89752400	-0.17186100
H	-4.03199800	2.94124100	0.06224200	C	5.96558200	-1.07680600	-0.06098200
H	-3.20448500	2.40735900	1.54436600	H	4.37583200	-2.15421000	0.91306100
O	-2.04241000	3.42066400	0.13220700	C	6.36374500	0.13213700	-0.63084000
O	-5.17293900	0.51407900	-0.41472600	H	5.76697900	2.14815100	-1.11045000
H	-5.64447300	-0.31808000	-0.56800400	H	6.64995000	-1.92077900	-0.03472800
O	-4.28587500	-2.29371800	-0.26367000	H	7.36092700	0.23856900	-1.04980500
H	-3.56114700	-3.00090200	-0.26038500	H	-1.24311800	2.87229400	0.18685100

PAA transition structure

Energy: -1070.467791 Hartree (B3LYP/6-31++G(d,p) SCRF=water) 1 imaginary freq (B3LYP/6-31G(d,p))

C	-1.83073400	1.57323400	0.33972900	O	0.45460100	0.69788800	0.60371300
C	-0.78302500	0.51809300	0.02824100	C	1.08084600	-0.94470400	0.75955200
C	-1.28828500	-0.82010600	0.54984400	O	1.52880700	-1.14670900	1.87517800
C	-3.51981500	-0.28155800	0.03327300	C	1.94318900	-1.08514100	-0.51310000
C	-3.12839400	1.15921600	-0.35625800	H	2.05290400	-2.16087500	-0.69667100
H	-0.73612300	0.41883500	-1.07966100	H	1.39390600	-0.67398100	-1.36636400
H	-2.00451500	1.60146500	1.42836500	O	-0.24464400	-1.69320200	0.39190500
H	-3.78132500	-0.28361500	1.10498500	C	3.31047900	-0.44780000	-0.41307900
H	-2.94947400	1.19280200	-1.44336500	C	3.45119600	0.91703100	-0.11177100
H	-1.60018900	-0.73572800	1.61225100	C	4.47267100	-1.19324000	-0.64714000
O	-2.45466600	-1.20935500	-0.20288900	C	4.71192500	1.50822900	-0.05528300
C	-4.70394300	-0.82025600	-0.76254000	H	2.54905800	1.48500700	0.09337700
H	-5.59757500	-0.22759700	-0.54715100	C	5.73826000	-0.60357200	-0.59297500
H	-4.47948000	-0.72318700	-1.83863800	H	4.38339400	-2.25363800	-0.87296400
O	-4.97118600	-2.16949900	-0.41332600	C	5.86352900	0.75354000	-0.29840200
O	-4.21149400	2.02639600	-0.01239800	H	4.79910500	2.56590800	0.18423500
H	-3.83557900	2.91775000	-0.04980500	H	6.62444900	-1.20684400	-0.77815200
O	-1.47067500	2.88015600	-0.11898000	H	6.84591600	1.21801600	-0.25286000
H	-0.52801200	2.95293600	0.09607300	H	-4.08979700	-2.57044500	-0.33983200

(R)-MPA Ground state

Energy: -1109.797739 Hartree (B3LYP/6-31++G(d,p) SCRF=water) 0 imaginary freq (B3LYP/6-31G(d,p))

C	-3.26427700	-1.51412200	-0.31312500	C	1.10344400	0.51293800	0.09267100
C	-1.85727000	-1.65238800	0.36025200	O	1.00310000	1.20172400	-0.90547800
C	-1.08291500	-0.41351000	-0.13465400	C	2.33205100	0.52719100	1.00972300
C	-3.10063700	0.91489900	-0.33251200	O	0.17165500	-0.32087000	0.56769400
C	-3.98562400	-0.25663200	0.11608200	H	2.12406500	-0.15837800	1.83502300
H	-2.01768100	-1.42118000	1.45644900	C	3.59445900	0.05403600	0.30071000
H	-3.10844400	-1.44434500	-1.41008400	C	4.00690800	0.60668800	-0.92118800
H	-3.04996300	0.90453700	-1.43355700	C	4.39771900	-0.92817400	0.89367800
H	-4.08664400	-0.24039900	1.21302800	C	5.19223900	0.18790800	-1.52489600
H	-0.87475400	-0.44476800	-1.21177200	H	3.37376000	1.34368500	-1.40297100
O	-1.77639600	0.79133500	0.21054300	C	5.58612200	-1.34542000	0.29216400
C	-3.57055500	2.29104200	0.11629900	H	4.08402300	-1.37528300	1.83362400
H	-4.55433500	2.49967900	-0.31437000	C	5.98959400	-0.78620400	-0.92026700
H	-3.66895400	2.29097600	1.21512000	H	5.49153500	0.62158400	-2.47563600
O	-2.67027900	3.30192700	-0.31864500	H	6.19097600	-2.11249600	0.76868500
O	-5.27791700	-0.12109700	-0.49454700	H	6.91229400	-1.11120800	-1.39372500
H	-5.60643600	-1.03114600	-0.54144000	C	2.50305000	1.95429300	1.57460800
O	-3.94666600	-2.70775500	-0.00440400	H	2.64661300	2.67009700	0.76106700
H	-3.11530500	-3.28005900	0.08232300	H	1.61512300	2.25438900	2.14052600
O	-1.37856700	-2.86825600	0.09312700	H	3.37146400	2.00036100	2.23904400
				H	-1.79263100	2.90262700	-0.20491900

(R)-MPA Transition structure

Energy: -1109.783814 Hartree (B3LYP/6-31++G(d,p) SCRF=water) 1 imaginary freq (B3LYP/6-31G(d,p))

C	-2.63857400	-1.31418600	-0.49751100	O	1.39022800	-1.31240700	1.89829700
C	-1.39483800	-1.10208800	0.34893800	C	1.97574400	-1.04509800	-0.43459800
C	-0.87144300	0.29747500	0.06499900	O	0.32518300	0.38964700	0.73963000
C	-3.03823600	1.16374600	-0.22567100	H	1.39847100	-0.81026600	-1.33381200
C	-3.65803900	-0.24449700	-0.10590900	C	3.13665300	-0.06417700	-0.34704500
H	-1.71549000	-1.10292700	1.41372200	C	3.52748700	0.67138700	-1.47446200
H	-2.38194700	-1.18504500	-1.56317500	C	3.87590600	0.10146300	0.83590900
H	-2.84074700	1.35807200	-1.29382200	C	4.62097600	1.53902100	-1.43393200
H	-3.93795300	-0.41700900	0.94572600	H	2.96218200	0.56217700	-2.39766900
H	-0.74247300	0.45058900	-1.02853000	C	4.96578000	0.97009100	0.88078000
O	-1.81843100	1.27953500	0.51733900	H	3.55262900	-0.44087500	1.71850500
C	-3.94094700	2.26771100	0.31417700	C	5.34856800	1.69108100	-0.25341000
H	-4.85904800	2.31860500	-0.27783400	H	4.90013700	2.09923500	-2.32372500
H	-4.21602800	2.02141000	1.35378200	H	5.51838800	1.08944500	1.81022100
O	-3.29511200	3.52904200	0.23815500	H	6.19941200	2.36734700	-0.21510700
O	-4.82143000	-0.29081600	-0.93640900	C	2.48381300	-2.49301200	-0.54957300
H	-5.03570200	-1.23206100	-1.00889400	H	3.00351600	-2.77849900	0.36920800
O	-3.22430800	-2.60450200	-0.30428100	H	1.63049500	-3.16184800	-0.68212000
H	-2.45856300	-3.18880300	-0.18592500	H	3.17234700	-2.60625500	-1.39543000
O	-0.34441700	-1.95068700	0.11117400	H	-2.38737200	3.34653500	0.53026200
C	1.03115900	-0.94030300	0.78620500				

(S)-MPA Ground state

Energy: -1109.798900 Hartree (B3LYP/6-31++G(d,p) SCRF=water) 0 imaginary freq (B3LYP/6-31G(d,p))

C	-3.63001700	-0.78162600	0.10796500	O	1.04631800	-0.63848100	-1.87932400
C	-2.27360000	-1.43819400	0.52427000	C	2.40089700	-1.52497400	-0.07569900
C	-1.21773200	-0.66732100	-0.29250800	O	0.09722100	-1.05426900	0.14858900
C	-2.54552400	1.36350700	-0.30601000	C	3.37709800	-0.38797600	0.20502600
C	-3.68382500	0.68439900	0.47034600	C	3.71564000	0.54861500	-0.78301900
H	-2.07641500	-1.09188700	1.58311700	C	3.99013900	-0.28573300	1.46008000
H	-3.71619200	-0.85213700	-0.99645400	C	4.64494800	1.55440600	-0.51894100
H	-2.76865600	1.28139000	-1.38225300	H	3.22558300	0.49211100	-1.74955600
H	-3.51255600	0.80620000	1.55186800	C	4.92310600	0.71832800	1.72459900
H	-1.29494700	-0.86304400	-1.36849300	H	3.72908900	-0.99855800	2.23838300
O	-1.28053100	0.73990300	-0.02850600	C	5.25546500	1.64243800	0.73395900
C	-2.33485400	2.83180400	0.03712900	H	4.88854100	2.27635800	-1.29405300
H	-3.23265500	3.39925200	-0.22445500	H	5.38383400	0.78105000	2.70706300
H	-2.17599500	2.92160600	1.12498600	H	5.97784300	2.42835700	0.93777900
O	-1.23986000	3.37684700	-0.68736700	C	3.03075300	-2.59711200	-0.98740200
O	-4.92524000	1.30443400	0.10103500	H	3.96498900	-2.96658000	-0.55322200
H	-5.58325000	0.61047500	0.25501900	H	2.34734600	-3.44238700	-1.11572900
O	-4.63164700	-1.56651700	0.71450200	H	3.24262800	-2.17762900	-1.97396600
H	-4.09226500	-2.42284800	0.73416700	H	2.12298100	-1.98143700	0.87779400
O	-2.37129100	-2.75932000	0.36057900	H	-0.56539300	2.67995300	-0.65273500
C	1.11012900	-1.01073100	-0.72235200				

(S)-MPA Transition structure

Energy: -1109.782819 Hartree (B3LYP/6-31++G(d,p) SCRF=water) 1 imaginary freq (B3LYP/6-31G(d,p))

C	2.74139800	-1.39453400	-0.01242800	O	-1.27173800	-1.10904600	1.91931700
C	1.28878600	-1.00218900	-0.23609300	C	-2.04577800	-1.08264800	-0.37961000
C	1.02170700	0.25268800	0.58267000	O	-0.33927800	0.46394200	0.45825000
C	3.18686800	1.08003000	0.22680000	C	-3.20172400	-0.09323200	-0.31787300
C	3.61401100	-0.22774500	-0.47474500	C	-3.85412400	0.20064800	0.89082500
H	1.19644400	-0.69393300	-1.30362900	C	-3.67638200	0.51717800	-1.48682100
H	2.91084700	-1.56065100	1.06481000	C	-4.94377500	1.07019600	0.92082800
H	3.42233100	0.98134600	1.29977400	H	-3.46395900	-0.24295800	1.80132300
H	3.46756200	-0.10862300	-1.56062800	C	-4.76964800	1.38552800	-1.46071300
H	1.30680800	0.10263500	1.64242600	H	-3.17662700	0.30938000	-2.43052700
O	1.78666400	1.34741700	0.06759700	C	-5.41198900	1.66446300	-0.25405700
C	3.89296500	2.31519600	-0.32080300	H	-5.42872300	1.29008700	1.86949800
H	4.96873200	2.23765000	-0.13994700	H	-5.11539300	1.84752300	-2.38296000
H	3.73078000	2.35918400	-1.41133800	H	-6.26231700	2.34195400	-0.22765600
O	3.42052600	3.49150200	0.31701800	C	-2.55603300	-2.53111800	-0.29134700
O	4.99759400	-0.45186100	-0.19044500	H	-3.30548300	-2.73553600	-1.06528600
H	5.15151000	-1.37711700	-0.42986700	H	-1.71039300	-3.21197900	-0.41160800
O	3.11657900	-2.56834200	-0.73894400	H	-3.00431300	-2.71044000	0.68982800
H	2.33674700	-3.14079900	-0.66012100	H	-1.53228700	-0.94547900	-1.33550200
O	0.34432900	-1.92061300	0.14499000	H	2.46009800	3.36096000	0.37169900
C	-1.01791200	-0.84232700	0.74627300				

DMPA Ground state

Energy: -1149.110398 Hartree (B3LYP/6-31++G(d,p) SCRF=water) 0 imaginary freq (B3LYP/6-31G(d,p))

C	3.59716700	-0.76569700	-0.18770800	C	-2.47030600	-1.44687600	0.22572800
C	2.22902500	-1.40792900	-0.58830900	O	-0.11715600	-1.11924300	-0.03448400
C	1.21291100	-0.76073700	0.37332400	C	-3.12740500	-0.11058000	-0.18293800
C	2.50347200	1.29329800	0.53054500	C	-2.39080400	0.84072700	-0.91099500
C	3.59990300	0.73249400	-0.38746100	C	-4.46452800	0.18428500	0.11404800
H	1.95573400	-0.94885100	-1.58669600	C	-2.97461700	2.03689900	-1.32476600
H	3.75743900	-0.95488400	0.89410600	H	-1.34643900	0.65088100	-1.13655400
H	2.79631900	1.09717700	1.57463800	C	-5.05217500	1.37992600	-0.30675500
H	3.35469100	0.96772400	-1.43563500	H	-5.06307400	-0.51842800	0.68270200
H	1.35628800	-1.07083300	1.41476700	C	-4.31078400	2.31284100	-1.02876000
O	1.23510900	0.67060300	0.26388200	H	-2.37766300	2.75789400	-1.87654600
C	2.24244200	2.78443800	0.36912300	H	-6.09222000	1.58026100	-0.06128500
H	3.14644500	3.34237000	0.62985700	H	-4.76464000	3.24610700	-1.35130000
H	2.00631300	2.98858200	-0.68913200	C	-3.28910600	-2.21552000	1.27855600
O	1.19296000	3.21963000	1.22265700	H	-4.25961600	-2.52149500	0.87574000
O	4.85137400	1.33949800	-0.03236600	H	-2.75076800	-3.12172000	1.57070300
H	5.51056900	0.68421700	-0.30505100	H	-3.44140300	-1.61542600	2.17750500
O	4.57142100	-1.45136800	-0.94106900	C	-2.29711000	-2.33056500	-1.03210600
H	4.04945800	-2.31420400	-1.02397900	H	-1.77498100	-3.25930200	-0.78340400
O	2.36119700	-2.73536900	-0.58364600	H	-3.28221900	-2.57830900	-1.44310200
C	-1.10466200	-1.11361900	0.87490700	H	-1.71437100	-1.82389300	-1.80137200
O	-0.97182500	-0.87159100	2.05651400	H	0.52896600	2.51453600	1.16352300

DMPA Transition structure

Energy: -1149.092148 Hartree (B3LYP/6-31++G(d,p) SCRF=water) 1 imaginary freq (B3LYP/6-31G(d,p))

C	-2.73514200	-1.42297200	-0.27124900	C	0.94957400	-0.72784400	-0.66137300
C	-1.35592400	-0.95834400	0.15547600	O	1.22615900	-0.80340500	-1.85299100
C	-1.10171900	0.40638500	-0.46998100	C	2.06950300	-0.99481100	0.40998600
C	-3.34900800	1.03564200	-0.22253300	O	0.21952100	0.65289200	-0.22299400
C	-3.73829000	-0.38526100	0.23952300	C	3.23816500	-0.01783000	0.17416200
H	-1.37812000	-0.80108300	1.25290900	C	4.54478400	-0.45494100	-0.08709100
H	-2.78598000	-1.45856200	-1.37165200	C	3.03400300	1.37210000	0.26625500
H	-3.46884900	1.08001700	-1.31796200	C	5.60368200	0.44480800	-0.24115900
H	-3.71300700	-0.41475700	1.34120400	H	4.75097700	-1.51513000	-0.17892900
H	-1.31639600	0.38801400	-1.55830700	C	4.08632100	2.27198900	0.11137200
O	-1.99777000	1.36398800	0.12478200	H	2.02728500	1.73991900	0.42579100
C	-4.20356500	2.12831900	0.41037800	C	5.38295600	1.81598500	-0.13879300
H	-5.24606500	2.01073900	0.10124500	H	6.60309700	0.06561500	-0.44445000
H	-4.15733400	2.02187400	1.50778000	H	3.88991300	3.33967600	0.18137000
O	-3.76135400	3.41256400	-0.00015300	H	6.20376200	2.51933300	-0.25904600
O	-5.06103000	-0.65948200	-0.22597400	C	2.49327100	-2.46058700	0.19388000
H	-5.16677800	-1.61617900	-0.12156600	H	3.28081600	-2.76267200	0.89524000
O	-3.10813200	-2.69804100	0.26463500	H	1.62313300	-3.10062100	0.35113200
H	-2.31862800	-3.24748600	0.14869400	H	2.84110500	-2.61288300	-0.83074900
O	-0.28874600	-1.75174000	-0.23613200	C	1.57309800	-0.83635000	1.86133200

H	0.75758000	-1.54025300	2.04726700	H	1.20170400	0.17265700	2.04602800
H	2.38533300	-1.04656800	2.56892100	H	-2.79297500	3.34642600	0.02459000