Computational details. All calculations were performed using the Gaussian09 suite of codes (revision D.01).[1] Geometries were fully optimised without any symmetry or geometry constraints using various functional (ωB97XD,[2] B3LYP-D3[3] and M06-2X[4]). Calculations were carried out using a temperature of 398.15 K and solvent effects in 1,4-dioxane were considered using a conductor-like polarisable continuum model (CPCM).[5] The nature of all the stationary points as minima was verified by calculations of the vibrational frequency spectrum. Free energies were calculated within the harmonic approximation for vibrational frequencies. Only the most stable conformational isomers are reported for all intermediates.

Thermodynamics of the hydrolysis of 4-alkyl-caprolactones

The decreased intrinsic reactivity of 4-R-Caprolactones against ε-Caprolactone was also evaluated using Density Functional Theory by calculating the thermodynamics of the hydrolysis reaction for each substrate. Geometry optimisation were performed at the ωB97XD, B3LYP-D3 and M06-2X levels and 398.15 K, using a mixed valence triple ζ basis set 6-311++g(2d,p) for all atoms, and a conductor-like polarisable continuum model of 1,4-dioxane. The results of these calculations are summarised in Table S2.
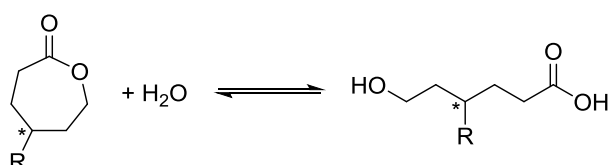

Table S2. DFT computed Free Gibbs energies of the hydrolysis of 4-R-caprolactone[a]

Functional used		Structure	G (Hartree)	ΔΔG (kcal mol^{-1})
ωB97XD	Staring materials	H_2O	-76.439011	-
		Capr	-385.006241	-
		4-Me-Capr	-424.296656	-
		4-Et-Capr	-463.582975	-
		4-iPr-Capr	-502.870424	-
		4-tBu-Capr	-542.157551	-
	Acid formation	6-Hydroxyhexanoic acid	-461.437381	+4.9
		6-Hydroxy-,4-Me-hexanoic acid	-500.724048	+7.3
		6-Hydroxy-,4-Et-hexanoic acid	-540.009374	+7.9
		6-Hydroxy-,4-iPr-hexanoic acid	-579.297143	+7.7
		6-Hydroxy-,4-tBu-hexanoic acid	-618.578256	+11.5
B3LYP-D3	Staring materials	H_2O	-76.465539	-
		Capr	-385.144706	-
		4-Me-Capr	-424.449538	-
		4-Et-Capr	-463.750893	-
		4-iPr-Capr	-503.051926	-
		4-tBu-Capr	-542.353891	-
	Acid formation	6-Hydroxyhexanoic acid	-461.60305	+4.5
		6-Hydroxy-,4-Me-hexanoic acid	-500.904733	+6.5
		6-Hydroxy-,4-Et-hexanoic acid	-540.203162	+8.3
		6-Hydroxy-,4-iPr-hexanoic acid	-579.504003	+8.4
		6-Hydroxy-,4-tBu-hexanoic acid	-618.807199	+7.7

M06-2X	Staring materials	H_2O	-76.427747	-
		Capr	-384.960018	-
		4-Me-Capr	-424.241981	-
		4-Et-Capr	-463.519136	-
		4-iPr-Capr	-502.798009	-
		4-tBu-Capr	-542.077042	-
	Acid formation	6-Hydroxyhexanoic acid	-461.379786	+ 5.0
		6-Hydroxy-,4-Me-hexanoic acid	-500.659641	+ 6.3
		6-Hydroxy-,4-Et-hexanoic acid	-539.933900	+ 8.2
		6-Hydroxy-,4-iPr-hexanoic acid	-579.212336	+ 8.4
		6-Hydroxy-,4-tBu-hexanoic acid	-618.493117	+ 6.7

[a] Protocol: Functional used/6-311++g(2d,p)/ 398.15K/cpcm=1,4-dioxane; the smallest value found from both enantiomers (if any) is reported.

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