On the Strain Energy of 5-Ring and 6-Ring Lactones

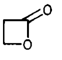
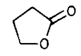
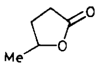
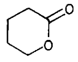
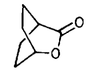
John M. Brown,[a] Alistair D. Conn,[a] Geoffrey Pilcher,[b] M. Luisa P. Leitão,[b] and Yang Meng-Yan[b]

[a] *Dyson Perrins Laboratory, South Parks Road, Oxford OX1 3QY, U.K.*
[b] *Department of Chemistry, University of Manchester, Manchester M13 9PL, U.K.*

Values of the heats of combustion of γ-butyrolactone, γ-valerolactone, and δ-valerolactone have been determined; uniquely among alicyclic compounds, the strain energy of the 6-ring lactone is greater than that for the 5-ring lactones.

The classic studies of Huisgen and Ott[1] quantified an enhanced reactivity of simple lactones over esters towards hydrolysis. This was connected with an intrinsically higher ground-state energy of the (*E*)-conformer about the –O–C(=O)– linkage, estimated to be 15.5 kJ mol^{-1} above the (*Z*)-conformer. In formate esters, where steric effects should be minimised, the (*Z*)-conformer is always predominant; for methyl formate the (*Z*)/(*E*) energy difference is 17 kJ mol^{-1}.[2] This difference is supported by recent theoretical calculations.[3]

Table 1.[a]

		$\Delta_f H_m(l)$	$\Delta_f H_m(g)$	Strain energy Lactones	Hydrocarbons	Ethers	Ketones
	**(4)**		−282.6	97.6	110.3	105.8	93.9
	**(1)**	−420.9 ± 0.7	−366.5 ± 0.8	32.2	25.9	23.4	23.9
	**(2)**	−461.3 ± 1.0	−406.5 ± 1.1	30.5	26.3		
	**(3)**	−437.6 ± 0.8	−379.6 ± 1.1	39.7	0.0	4.6	11.0
	**(5)**		−396.6	41.5	39.2		

[a] Values in kJ mol^{-1}. Enthalpies of formation were determined by static-bomb calorimetry: J. Bickerton, G. Pilcher, and G. Al-Takhin, *J. Chem. Thermodyn.*, 1984, **16**, 373. Enthalpies of vaporisation were determined by microcalorimetry.

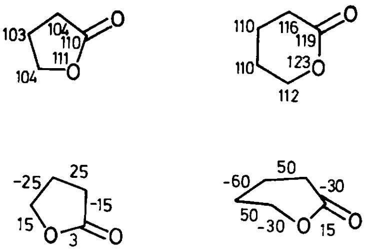
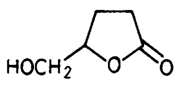


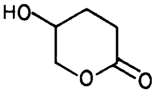
Figure 1. Average internal bond angles and torsion angles for 5- and 6-ring monocyclic lactones, based on the CSSR database.

The origin of this stability variation has been widely debated. Since the dipole moments of simple esters are around 1.9 D and of lactones around 4.5 D, interaction between the C–O and O–C dipole favours the (*Z*)-conformer.[1] It has been suggested that the (*Z*)-conformer is stereoelectronically favoured since it alone has a lone pair antiperiplanar to the C=O bond, which elicits a stabilising n–σ* interaction.[4] In view of this interest, there have been surprisingly few direct measurements of the enthalpy of lactones. We report accurate $\Delta_f H_m^\circ$ values for γ-butyrolactone (**1**), 2-methyl-γ-butyrolactone (**2**), and δ-valerolactone (**3**), which help in assessing the magnitude of these effects (Table 1). Comparative strain energies for β-propiolactone (**4**)[5] and 2-oxabicyclo[2.2.2]octan-3-one[6] are recorded, along with the standard derivation[7] of the strain energy in related alicyclic compounds.

Considering the 5-ring lactones (**1**) and (**2**), the additional strain energy in comparison to the corresponding hydrocarbon, ether, and ketone is relatively modest (<10 kJ mol^{-1}).[8] The total strain energy of (**1**) is substantially less than the 42 kJ mol^{-1} computed by molecular mechanics.[9] These calculations indicate that a single envelope conformation is preferred (Figure 1). *Ab initio* calculations at the 3-21G level, however, suggest that envelope and twist conformations of (**1**) are close in energy.[10] The structures of monocyclic ring lactones contained in the CSSR database† were examined and for the 5-ring case (Figure 1) the lactone moiety is close to coplanarity, enforcing the envelope conformation. The internal angle at the carbonyl group is 110 ± 2° and that at the ring oxygen 111 ± 2° with little deviation between structures. For (*Z*)-esters, values of 112 and 116° are typical in *X*-ray structures and supported by theoretical calculations at the 6-311 + G** level, so that a component of angle strain is likely.



(6)



(7)

δ-Valerolactone (**3**) exhibits very different characteristics. The strain energy of 39.7 kJ mol^{-1} is substantially greater than that in other 6-ring alicyclic compounds. Molecular mechanics calculations[9] indicate a smaller value, the 'calculated inherent strain' being 20 kJ mol^{-1}. They predict two conformations of similar energy with the half-chair 2 kJ mol^{-1} below the boat. The CSSR file provides ten examples of monocyclic 6-ring lactones in half-chair conformation and two of boat conformations. For the half-chair, the average torsion angle about C–C(=O)–O–C is 15° (distorted towards the chair) and the internal angles at the carbonyl and ring oxygen are respectively 119 and 123°. Thus strain is manifested by deviation of both bond and torsional angles from ideality.

The large strain of 6-ring lactones is in accord with several experimental observations. For example, compound (**6**) is readily formed but its isomer (**7**) remains uncharacterised, although it is clearly an intermediate in the acid-catalysed rearrangement of the former.[11] The ease of cyclisation to 5-ring lactones is conspicuously greater than to their 6-ring counterparts.[12] δ-Valerolactone undergoes reversible polymerisation under conditions where γ-butyrolactone does not and this is consistent with a larger strain energy in the former.[13]

In summary, these results demonstrate that there is a small intrinsic strain associated with 5-ring lactones, but it is unsufficient to account for their 500-fold faster rate of hydrolysis relative to esters. Other factors such as enhanced Coulombic stabilisation of the lactone/OH$^-$ transition state must be important. Among lactones of related ring-size,

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† A search of the CSSR database was conducted to obtain data on all monocyclic lactones with 4—9 membered rings, except that only the latest fifteen 5-ring lactone structures were retrieved. For comparison, fifteen recent saturated ester structures were retrieved.

δ-valerolactone (**3**) is anomalously strained, simply because the combined requirements of the bond lengths around the C–C(=O)–O–C moiety and coplanarity of these atoms are not readily accommodated by the 6-ring geometry. A significant conclusion is that stereoelectronic effects are not required to explain the data, or any observations concerning the reactivity of lactones compared with esters.

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