9. Bond Angles in Lactones and Lactams

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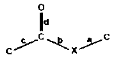
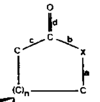
The carbonyl group in lactones and, to a lesser extent, in lactams tends to show a C–C=O angle that is larger than the O–C=O or N–C=O angle, the difference increasing in magnitude as the ring size decreases. The observed trend provides information on ratios of force constants characterising the flexibility of the s-*cis*-ester group and may be interpreted in terms of incipient chemical reaction to $^{-}O-(CH_2)_n-C\equiv O^{+}$. Molecular orbital calculations (MINDO/3, MNDO, EH) for model compounds provide an electronic interpretation of this angle difference in terms of an anomeric interaction between the p-type lone pair on the carbonyl O-atom and the antibonding C–O or C–N orbital.

Introduction. – *Dunitz et al.* have recently described structural characteristics of the carboxylic ester and carboxylic amide groups [1] [2]. The crystal structure data used by these authors show the angle *cd* to be larger than *bd* by 2° for open chain esters **I**, by 4.5° for δ-lactones, and by 6.9° for γ-lactones **II** (X=O). We wanted to know whether these numbers are indicative of a general trend relating the difference *cd* – *bd* to ring size.



I



X=O,NH

II

Data Selection. – The Cambridge Structural Database (version of May 1983 with 37,367 entries [3]) was searched for β- and ε-lactones (X=O), β-, γ- and ε-lactams of primary amines (X=NH), and cyclic and non-cyclic thio-esters (X=S). β-Lactams of secondary amines (X=NR, *e.g.* penicillins) were also searched for to compensate for paucity of data. Both C-atoms adjacent to the X–C=O unit were required to be four-coordinate, and entries with $R > 0.09$ or $\sigma(C-C)_{av} > 0.03$ Å were rejected. If the ester or amide group is contained in more than one ring, the molecule is classified according to the size of the smallest of them. Averaging of distances and angles is based on unit weights since we assumed environmental effects (packing, C-atom substitution, *etc.*) to cause more scatter of the data than is produced by experimental error [4]. A list of reference codes [3] is available from the authors. Average values are marked by brackets (⟨⟩).

Discussion. – In most classes of compounds the carbonyl O-atom deviates from the C—C—X bisector, the deviation depending on the lactone or lactam ring size *(Table)*. A scatterplot of $\langle cd \rangle - \langle bd \rangle$ *vs.* $\langle bc \rangle$ shows positive differences for all lactones (*Fig. 1;* linear regression: $\langle cd \rangle - \langle bd \rangle = -0.334 \langle bc \rangle + 44.0°$, $r^2 = 0.99$). The acyclic esters (labeled ω in *Fig. 1*) deviate significantly from the trend observed for the cyclic molecules. As far as the lactams are concerned the differences $\langle cd \rangle - \langle bd \rangle$ are smaller and their dependence on $\langle bc \rangle$ is less pronounced (linear regression: $\langle cd \rangle - \langle bd \rangle = -0.187 \langle bc \rangle + 20.2°$, $r^2 = 0.81$). Unlike the acyclic esters, the acyclic amides do not show a significant deviation from the trend observed for the lactams. The number of acyclic thioesters and thiolactones (X=S) in the database is very limited; for these $\langle cd \rangle - \langle bd \rangle$ shows an even weaker or possibly reversed dependence on $\langle bc \rangle$.

The average angles $\langle ab \rangle$ and $\langle bc \rangle$ are determined mainly by the size of the lactone or lactam ring. On average, the angles $\langle ab \rangle$ for the lactones are smaller by 4.6° than those for the corresponding lactams. The average bond lengths found in this study for esters and amides are similar to those reported before [1] [2].

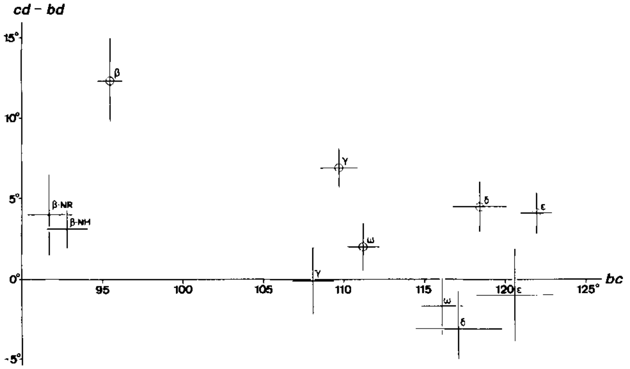


Fig. 1. *Difference of angles at the carbonyl group* ⟨bd⟩ – ⟨cd⟩ vs. *C—C—X angle* ⟨bc⟩. Averaged experimental value, error bars indicate standard deviations of the populations. Esters and lactones (X=O) are marked by a circle; the remaining points refer to amides and lactams (X=NH, NR); ω indicates acyclic functionality.

Force Field Interpretation. – The observed linear dependence of $\langle cd \rangle - \langle bd \rangle$ on $\langle bc \rangle$ may be rationalized in terms of a simple model; it is assumed that the magnitude of ring angle *bc* is almost completely determined by the ring constraints. With this assumption the dependence of potential energy on the variable angles at a planar carbonyl C-atom may be expressed as

$$V = k_{cd}(cd - cd_o)^2/2 + k_{bd}(bd - bd_o)^2/2$$

$$2\pi = bc + bd + cd$$

The minimum energy position of the carbonyl O-atom is determined by the condition $\partial V/\partial(cd - bd) = 0$; this leads to a linear relationship:

$$cd - bd = bc(k_{cd} - k_{bd})/(k_{cd} + k_{bd}) + 2\{k_{bd}(\pi - bd_o) - k_{cd}(\pi - cd_o)\}/(k_{cd} + k_{bd})$$

Table. *Averaged Bond Lengths* ([Å]) *and Angles* ([°]) *with Standard Deviations for Lactones, Lactams and Thiolactones*

	N	⟨*a*⟩	⟨*b*⟩	⟨*c*⟩	⟨*d*⟩	⟨*ab*⟩	⟨*bc*⟩	⟨*cd*⟩	⟨*bd*⟩	⟨*cd*⟩ − ⟨*bd*⟩	⟨*abc*⟩[a]
β-Lactones	2	1.484(7)	1.371(2)	1.504(2)	1.197(4)	90.3(5)	95.5(8)	138.4(17)	126.1(9)	+12.3(27)	0(4.1)
γ-Lactones[b]	10	1.462(8)	1.350(9)	1.515(13)	1.198(7)	110.2(14)	109.7(12)	128.6(8)	121.7(9)	+6.9(12)[c]	0[d]
δ-Lactones[b]	6	1.462(13)	1.337(8)	1.514(15)	1.204(7)	122.9(29)	118.4(17)	123.0(12)	118.5(10)	+4.5(16)[c]	0[d]
ε-Lactones	4	1.468(8)	1.342(20)	1.504(7)	1.207(11)	122.5(45)	120.2(9)	121.9(10)	117.8(4)	+4.1(13)	0(21.1)
Acyclic esters[b]	118	1.447(13)	1.340(14)	1.495(19)	1.195(7)	117.4(16)	111.2(10)	125.4(12)	123.4(9)	+2.0(15)[c]	180[d]
β-Lactams (N–H)	2[e]	1.479(2)	1.339(3)	1.529(25)	1.227(13)	95.8(17)	92.8(13)	135.2(1)	132.0(12)	+3.1(12)	0(6.9)
β-Lactams (N–R)	54	1.473(19)	1.383(21)	1.534(18)	1.199(13)	94.4(17)	91.7(14)	136.1(12)	132.1(16)	+4.0(25)	0(8.2)
γ-Lactams	41	1.455(13)	1.335(13)	1.514(24)	1.232(11)	114.9(13)	108.4(13)	125.7(11)	125.8(14)	−0.1(21)	0(5.3)
δ-Lactams[f]	38	1.462(13)	1.332(11)	1.516(13)	1.234(11)	124.8(33)	117.1(27)	120.2(21)	122.7(11)	−3.1(24)[c]	0[d]
ε-Lactams	7	1.456(26)	1.323(15)	1.533(34)	1.243(18)	128.9(37)	120.6(24)	119.2(26)	120.2(6)	−1.0(29)	0(4.1)
Acyclic amides[f]	158	1.451(14)	1.331(11)	1.515(14)	1.231(11)	122.0(19)	116.1(13)	121.1(13)	122.8(12)	−1.7(18)[c]	180[d]
β-Thiolactone	1	1.840	1.792	1.516	1.187	77.6	93.8	133.0	133.1	−0.0	7.3
γ-Thiolactones	3	1.829(14)	1.769(37)	1.549(15)	1.182(36)	95.1(8)	108.1(19)	126.1(22)	125.7(6)	+0.4(25)	0(4.4)
ζ-Thiolactone (8-ring)	1	1.763	1.770	1.468	1.218	102.7	120.3	124.1	115.6	+8.5	3.4
Acyclic thioesters	5	1.827(8)	1.774(6)	1.497(26)	1.206(12)	99.5(10)	113.5(10)	124.1(5)	122.4(6)	+1.8(6)	180(4.2)

[a] Torsion angle given as: ideal (e.s.d).

[b] Taken from [1].

[c] Standard deviation calculated assuming no correlation between *cd* and *bd*.

[d] Deviation from planarity not available.

[e] Includes one structure determination with $R = 0.10$ but $\sigma(\mathrm{C{-}C})_{\mathrm{av}} < 0.01$ Å.

[f] Taken from [2].

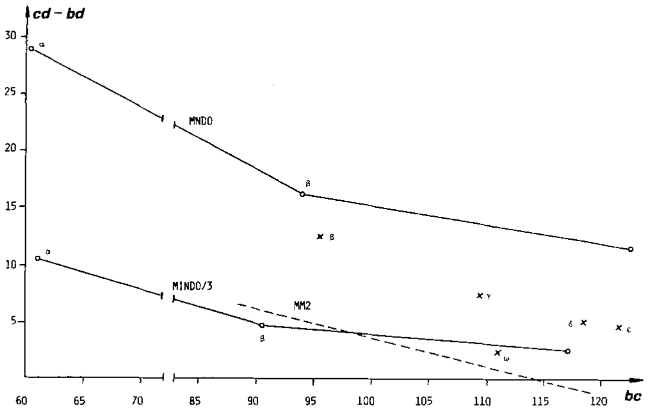


Fig. 2. *Difference of angles at the carbonyl group* cd – bd vs. *C–C–O angle* bc. Circles: calculated for **III–V** (see *Fig. 3*) by MNDO and MINDO/3; broken line: calculated for a collection of medium-ring lactones by the MM2 force field; crosses: observed values for β-, γ-, δ- and ε-lactones; ω indicates acyclic functionality.

Force constants and reference angles taken from the MM2 ester force field [5] yield the relationship *cd* – *bd* = –0.270 *bc* +31.7°. This relationship is in fair agreement with the structural data for acyclic esters but yields differences *cd* – *bd* for the lactones which are too small. This simple model has neglected effects due to *van der Waals'* interactions, partial charges on atoms, and other anharmonic contributions to the molecular force field. However, the minimum-energy structures of unsubstituted β-, γ-, δ- and ε-lactones have been calculated with the full MM2 force field considering 1, 1, 2 and 2 conformations, respectively [6]. Linear regression based on the bond angles obtained in these calculations yields the relationship *cd* – *bd* = –0.256 *bc* +29.0° ($r^2 = 0.99$, line labeled MM2 in *Fig. 2*), which is close to the one obtained from the simple model but which still deviates by ~ 7° from the regression line describing the experimental lactone data.

The empirical relationships reported here for bond angles cover a large range of experimental values and can be used to formulate restraints on potential constants. These restraints may then – with appropriate weighting – be introduced into least-squares optimization of model force fields¹).

The experimental data clearly show that with respect to angle bending lactones with their s-*cis*-conformation behave differently from acyclic esters with s-*trans*-conformation. The corresponding difference is smaller in the case of amides. At present, we cannot offer a rationalization for this observation.

Electronic Interpretation. – There is no *a priori* reason why the angle *cd* should equal the angle *bd*; nevertheless we were surprised to find the above mentioned trends. In an attempt to rationalize them one could invoke an anomeric effect [8] involving an orbital interaction between the in-plane p-type lone pair on the carbonyl O-atom and the σ^*_{CO}-orbital of the adjacent C–O single bond. Such an interaction would obviously benefit from a decrease in the *bd* angle and the associated increase in p-σ^*_{CO} overlap.

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¹) For similar relationships see [7].

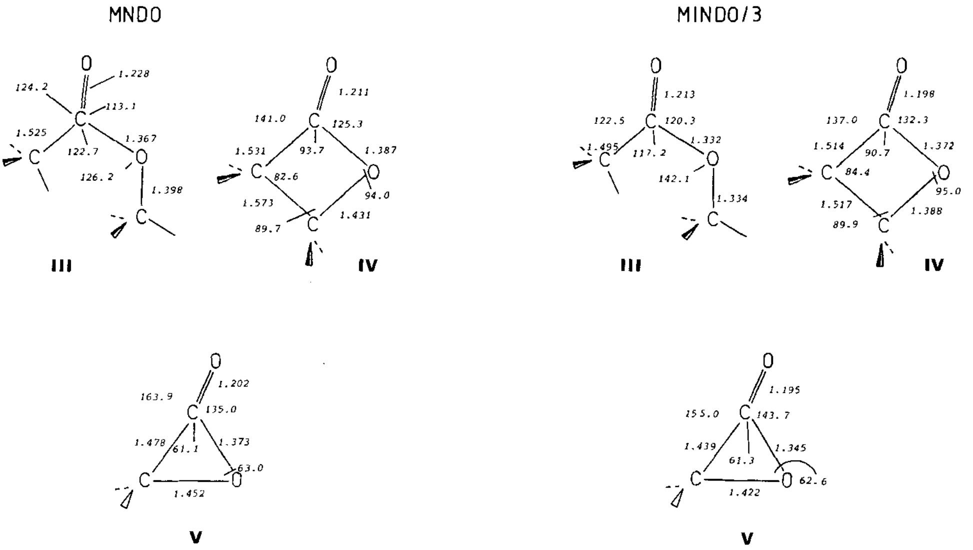
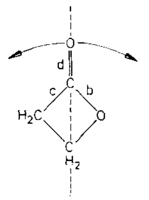


Fig. 3. *MNDO and MINDO/3 ground-state geometries for model systems* **III–V**. Only bond distances and angles relevant in the context of this work are given. C_s symmetry.

This model predicts less angle deformation for lactams and thiolactones since their σ^*_{CX}-orbitals are expected at higher energies than that of lactones; the expectation is borne out by the experimental data.

The qualitative argument has been tested using MO calculations. MINDO/3[9] and MNDO[10] semi-empirical techniques were used to obtain geometry-optimized ground-state structures **III–V** *(Fig. 3)*. Compound **III** serves as a model for lactones with medium rings unaffected by geometric constraints characteristic of small rings. All three systems show coplanar heavy atoms (C_s symmetry). For α-lactones **V** no experimental structure determination comparable to the computed date is available; the fleeting existence of such oxiranones has been demonstrated [11], however.

Fig. 2 compares the MINDO/3 and MNDO values of $cd - bd$ and bc with MM2 and experimental values for lactones and esters. The general trends are the same for computed and experimental values. Not unexpectedly, the absolute values of structural parameters are different for MINDO/3 and MNDO. The former underestimates the angle difference $cd - bd$ much as MM2 does. The latter overestimates it. Extended *Hückel* calculations [12] (EHT) were performed for simplified model geometries of **III**,

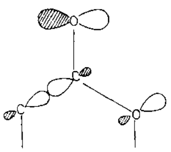


VI

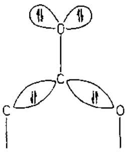
IV and **V**[2]). Only the angle difference $cd - bd$ was optimized (**VI**) and found to be 16, 36 and 60° for **III**, **IV** and **V**, respectively. The trend is the same as before, even though C–O pivoting is unrealistically strong.

In going from the ester **III** to the lactones **IV** and **V** the optimized C–O bond length *(Fig. 3)* decreases, in agreement with the well-known, observed increase in the C–O stretching frequency as ring size decreases. The lactone C–O distance in **IV** and **V** increases compared to **III**. The variations in optimized bond-distances are also reflected in the reduced overlap populations calculated by EHT for the optimal value of $cd - bd$.

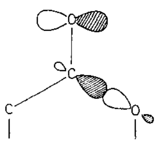
All of these observations are in qualitative agreement with the postulated anomeric effect, as may be seen from an analysis of the pertinent molecular orbitals (MO). The highest occupied MO (HOMO) of the lactones is always dominated by the p-type lone pair on the carbonyl O-atom, and destabilized by anti-bonding admixtures of C–C and C–O bonding orbitals (**VIIa**). As predictable from simple perturbation arguments, the admixture of the energetically higher C–C bonding orbital is larger than that of the lower C–O bonding orbital. The overlap and therefore the destabilizing interaction with the C–C bonding orbitals may be decreased by bending C=O towards C–O. Moreover, the HOMO is stabilized by admixture of the empty antibonding σ^*(C–O) orbital (**VIII**). The overlap and therefore the stabilization increases as the O–C–O angle decreases towards 90°. Thus there are two driving forces in the direction of the observed deformation. For small rings the σ(C–C) and σ^*(C–O) orbitals are higher and lower in energy, respectively, due to their similarity to *Walsh* orbitals in cyclopropane. The interactions with the oxygen p-type lone pair are correspondingly stronger and the driving force larger in agreement with the experimentally observed increase in the difference $cb - bd$.



VIIa



VIIb



VIII

An analogous set of calculations has been performed on β-propiolactam. The angle difference is 6.6° from MINDO/3, 10.3° from MNDO and 16° from ETH calculations. The numbers are about the same as or smaller than those found for β-propiolactone. This is understandable, since the σ^*(C–N) orbital is higher in energy than σ^*(C–O), the interaction with the p-type oxygen lone pair is smaller, and so is the driving force for angle deformation.

Interpretation in Terms of Incipient Reaction. – The correlated angle changes displayed in *Fig. 1* and *3* portray the early stages of a reaction which starts at the esters RCOOR and leads to linear oxocarbonium ions $R{-}C{\equiv}O^+$ by expelling ^-OR[3]). A more

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[2]) All C–C and C–O distances kept at 1.4 Å, C=O 1.2 Å; planar four- and three-membered rings, C–H 1.1 Å, H–C–H angles 109.5°; Ester: C–C–O angle 120°, tetrahedral CH_3-groups, C–O–C angle 120°.

[3]) Crystal structures for several oxocarbonium ions have been reported [13].

detailed investigation of this aspect which includes RCOX compounds with a wide variety of X-groups is underway.

Molecular structures of Li-ester enolates RR'C=C(OLi) (OR') show C–OR' distances (~ 1.4 Å) to be larger than C–OLi distances (~ 1.3 Å) and C=C–OR' angles (~ 116°) to be smaller than C=C–OLi angles (~ 128). This has been interpreted in an analogous way as an incipient stage of a reaction that leads to ketene RR'C=C=O (+LiOR') [14]. The same type of anomeric effect may be held responsible for the observed pattern of correlated structural differences between the two C–O bonds.

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