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CIRCULAR DICHROISM OF δ-LACTAMS

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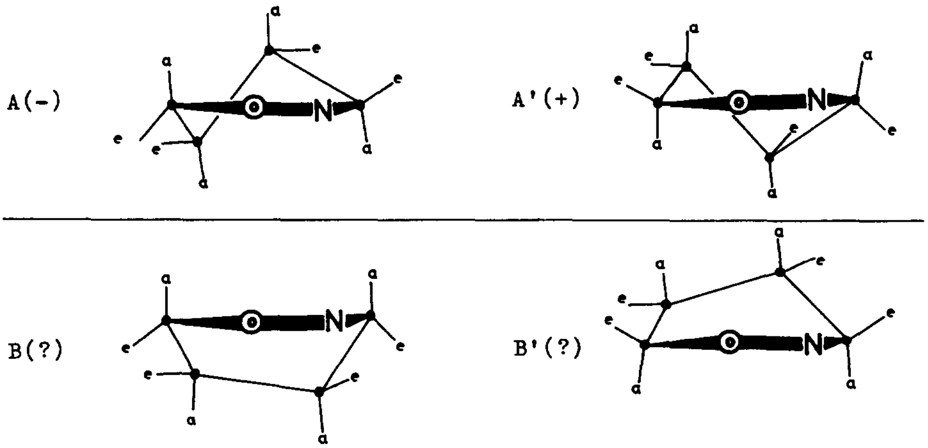
On the CD of six-$^{1)}$and seven-membered$^{2)}$lactams it has been reported that the ring chirality might determine the CD sign. However these CD rules has been derived from CD of the lactams in which their ring conformations were fixed with ring fusion and had no heteroatom substituents at Cα. In another report we revealed that in five-membered lactams$^{3)}$ as well as γ-lactones$^{4)}$the CD sign and magnitude might be determined by two factors: (1) configuration at Cα and (2) ring chirality and their molar ellipticities might be addition of the two effects. The effect of Cα configuration is considered as an extention of axial-haloketone rule$^{5)}$and result of the formation of a kind of inherently dissymmetric chromophore between carbonyl and lone pair electrons of heteroatom at Cα substituents which experimentally are known to cause red shift of CD extremum and gave CD sign due to configuration at Cα(S gave positive and R gave negative). In this communication we present some CD data which suggest to extend the above hypotheses to six-membered lactams.

The ring conformations of δ-lactams are known to take half-boat and half-chair forms both have two enantiomers and are shown in Fig.(A,A' and B,B'). Among them A is reported to give positive sign(hence A' is negative)$^{1)}$. However the signs of B and B' are still left ambiguous.

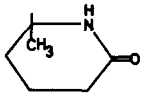
In II and IV the spin-spin coupling(Jab,ab':6.0/11.0 and 6.0/10.0 cps) suggest the Cα substituents hold quasi-equatorial which shows their conformations as A' or B' or an equilibrium mixture of A' and B'. However both A' and B' conformations are expected to give similar Hcc' and Hdd' coupling pattern and were impossible to differenciate from their PMR results.In V$^{6)}$the coupling const.(Jab,Jbc,Jcd,cd':7.5,2.4,4.9,7.5) suggest conformation A. In VI$^{6)}$Jcd,cd'

Fig. Ring chirality of δ-lactams



(6.3,10.0 cps) suggest Hc quasi axial or ring conformation A or B'.In VII7)and VIII7)the chemical shift of Ha,Hb,Hc and Hd were too close to study their coupling const. The conformations(axial or equatorial) of the substituents in each compounds at α,β,γ and δ are also shown in Fig. In sugars hydroxyl group is reported to be more preferable in equatorial than in axial.8) So it is highly plausible for VIII to take ring conformation A in which all the three hold equatorial and one hold axial, and for VII A or B in which three hold equatorial and one hold axial. Similarly in I,III and IX9)their preferable equatorial substituent suggest A' or B'.

IX

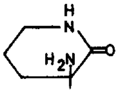
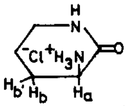
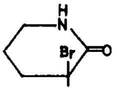
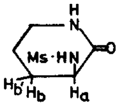
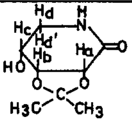
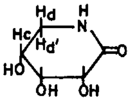
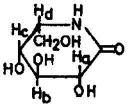
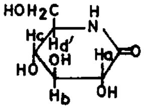


$[\theta]_{222}=+4.72\times10^3$

The results are shown in Table together with the Cα configuration and the ring chirality and the prediction of the signs according to the respective rules in parenthesis.

(1) Sign and red shift: All the δ-lactams with heteroatom substituent at Cα gave CD signs according with the prediction from Cα configuration. It suggests the CD sign can be used to determine the Cα configuration. They also gave red shift of CD maximum from II about 1-4 nm. It is smaller compared with five-membered lactams and lactones but the order of the red shift due to functional group are almost same: Br > O-isopropylidene ether > OH, N-mesyl > NH_2 > NH_3^+ . It together with CD sign and magnitude suggests the formation of the similar inherently dissymmetric chromophore in δ-lactams.

Table CD sign, magnitude and red shift of δ-lactams.

No.	compd.	C_α-config.	ring chirality	$[\theta]\times10^{-3}(\lambda_{max})$	shift	solv.
I		S(+)	A'(+)orB'(?)	+1.53 (218)	+1	W
				+1.68 (225)**		M
II		S	A'(+)orB'(?)	+2.19 (217)	0	W
				+2.09 (225)**		M
III		S(+)	A'(+)orB'(?)	+2.31 (227)		M
IV		S(+)	A'(+)orB'(?)	+7.71 (218)	+1	W
				+8.29 (221)		M
V		R(-)	A(-)	-10.9 (221)	+4	W
				-7.58 (224)		M
VI		R(-)	A(-)	-21.9 (219)	+2	W
				-23.7 (221)		M*
VII		R(-)	B(?)	-18.2 (219)	+2	W
				-15.3 (220)		M*
VIII		R(-)	A(-)	-16.6 (219)	+2	W
				-18.8 (222)		M

Solvent(W:Water,M:Methanol,M*:90%Methanol). CD measurements: On a Jasco J-20A,1 mm cell,about 1 mg/ml. [θ] corrected relatively using D-pantolactone($[\theta]_{222} = -12.8\times10^3$in 95% ethanol) at 25°C. **: at the shortest wavelength measured.

(2) CD magnitude:(a) The lower CD magnitude of II and IX in which no Cα effect is expected suggested that the effect of ring chirality is not so large in six-membered lactams([θ] =2000-5000) compared with five- or seven-membered lactams.

(b) The CD magnitude varied according to Cα substituents and the order of their strength in δ-lactams is principally the same in those of γ-lactones and γ-lactams within the range of deviation from ring chirality. That is OH > O-isopropylidene ether,N-mesyl > NH_2, NH_3^+ . The hydroxyl group of VI,VII and VIII gave similar and the strongest CD magnitude which is about ten times higher than ring chirality effect of II suggesting the Cα configuration might determine the sign independent of the ring conformation. The O-isopropylidene ether of V and N-mesyl group of IV gave about 7000 lower [θ] than hydroxyl, and still three times higher than that of II suggesting the Cα configuration of these functional group might determine the sign independent of the ring chirality. The amino group in I gave lower CD magnitude than all of the functional group cited above. The exception of the order smaller [θ] of I than II can be explaied by the change of ring chirality.

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