

CIRCULAR DICHROISM OF THIOLO- γ -LACTONES AND THEIR CONFIGURATIONS AND CONFORMATIONS

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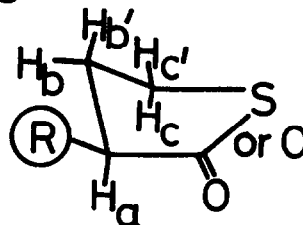
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It has been suggested that the sign of the circular dichroism (CD) maximum (C=O at 220-230 nm) of the γ -lactones might be determined by the two factors. That is, configuration at C-2 (1) (2-(S)-configuration gave positive sign and 2-(R)-configuration gave negative sign) and the conformation of the five membered lactone ring (2) (an envelope C-3 carbon above the nodal plane in Fig.1 gave positive sign.) In thiol- γ -lactones, few CD or ORD has

Fig.1



been reported corresponding to their configurations and conformations. Here we report CD of the five thiol- γ -lactones with different substituent at C-2. They were prepared from (S)-2-amino-thiol- γ -butyrolactone (1) (3) by reactions which have been known to proceed with the retention of the configuration (4). In order to determine the ring conformation their PMR were also studied. In CD₃OD the chemical shift (δ) of the protons at C-2 (Ha), C-3 (Hb and Hb') and C-4 (H_C and H_C') were 4.3-4.7, 2.1-2.9 and 3.1-3.9 respectively. The Ha of (I), (II) and (III) gave quartet and that of (IV) and (V) gave triplet. The coupling constants are shown in Table. Tentative calculations of the dihedral angles between Ha and Hb or Hb' according to Karplus (5) are 20° or 180° in (I), (II) and (III) and 30° or 130° in (IV) and 45° or 120° in (V). Although the considerable deviation due to the differences of the C-2 substituents should be counted to the calculation, it suggests that in all of the five compounds the C-2 substituent should project quasi-equatorial or the ring conformation

should be written in Fig.1 and that the degree of the ring puckering in (I), (II) and (III) might be different from those in (IV) and (V).

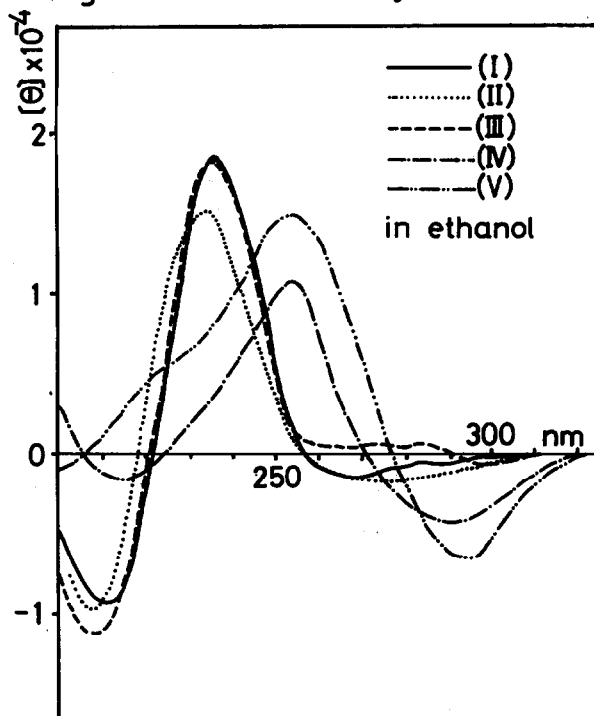
The CD curves of the compounds in ethanol are shown in Fig.2. They gave three bands at the wavelength region of 270-310 nm (Band I), 230-260 nm (Band II) and 210-215 nm (Band III), Kuriyama (6) has reported Cotton effect corresponding to Band I and Band II in steroidal thiol acetate and in one steroidal bridged γ -thiololactone.

He assumed that the Band I with very weak UV absorption might be due to $n-\pi^*$ and the Band II with strong UV peak might be due to $\pi-\pi^*$ of the $-S-C=O$. As well as the thiol acetate our thio- γ -lactones gave strong UV absorption peak ($\epsilon=3000-4000$) and (I), (II) and (III) gave λ_{max} at 240 nm, (IV) at 248 nm and (V) at 254 nm corresponding to Band II. Corresponding to the Band I UV absorption peak was not observed under the strong background absorption. On Band III the nature of the chromophore has not yet been identified.

Table. CD, PMR and Physical Constant of Thio- γ -butyrolactones

Substituent at C-2	CD ($[\theta] \times 10^{-3}$) at max.				PMR H_a (δ ppm)	$J_{ab,ab'}$	Phys. Const. mp.	[α] ₂₅ ²⁵ 589
	BandI	BandII	BandIII	BandI/II				
(I) NH_3^+Cl	-1.3 (268)	+18 (236)	-9.6 (211)	0.072	4.30 (Q)	7, 13 cps	188d	+20.4 (2.5%, H_2O)
(II) $NHAc$	-2.0 (279)	+15 (234)	-9.6 (208)	0.133	4.70 (Q)	7, 13	134	+98.2 (2.4%, $CHCl_3$)
(III) $NHSO_2CH_3$	+0.7 (276)	+18 (235)	-11 (208)	0.039	4.38 (Q)	7, 13	117	-10.6 (2%, $CHCl_3$)
(IV) Cl	-5.1 (290)	+11 (254)	-1.8 (216)	0.463	4.60 (T)	6	liq.	+28.8 (3%, $EtOH$)
(V) Br	-6.9 (295)	+15 (254)		0.460	4.48 (T)	5	liq.	+40.1 (2.4%, $EtOH$)

() ; wavelength nm, (Q); quartet, (T); triplet.

Fig.2. CD of thio- γ -butyrolactones

The relation between sign and magnitude of these bands and the configurations and the conformation are briefly summarized as follows.

(A) Band II; The band gave the strongest peak among the three bands and the magnitudes were almost the same in the compounds independent of the nature of C-2 substituents though the halogen at C-2 gave considerable red shift. All the 2-S compounds gave positive sign. The results suggest that the sign can be applicable to determine the configuration at C-2.

(B) Band I; The band I gave smaller CD maximum than Band II. The sign of this band in our compounds were negative except (II) and the magnitude were varied in individual compound. Because of the lower magnitude and more anomalous sign of CD peak, the Band I was less useful for the determination of the configuration at C-2 than Band II. However it should be noted that the magnitude seems to be related to the coupling patterns of H_a in PMR.

In Table relative strength of the $[\theta]$ of the Band I to Band II are shown. Thus (I), (II) and (III) which gave H_a quartet showed a very weak Band II compared with the relatively strong Band II of (IV) and (V) which gave H_a triplet. It suggests that the band may be more sensitive to the degree of the ring puckering as well as the nature of the C-2 substituents than the Band I.

(C) Band III; The band was observed in (I), (II) and (III) with strong negative magnitude and in (IV) and (V) the magnitude was rather smaller or entirely disappeared.

On the possibility of the extension of the rules obtained in $n-\pi^*$ of γ -lactones to γ -thiololactones, the sign of Band II accorded with the rule, while the sign of the Band I and III gave opposite or anomalous signs.

References

- (1) T. Okuda, S. Harigaya and A. Kiyomoto, Chem. Pharm. Bull. Japan. 12, 504 (1964).
- (2) A.F. Beecham, Tetrahedron Letters, 2355 (1968); *ibid.* 3591 (1968); *ibid.* 4897 (1969).
- (3) du Vigneaud and Brown, Biochem. Preps. 5, 93 (1957).
- (4) (II) and (III) was prepared from (I) with acetyl chloride or methanesulfonyl chloride in pyridine, (IV) and (V) was prepared from (I) with nitrosyl chloride and nitrosyl bromide respectively. All the compounds gave correct elementary analysis results. However their optical purity was not yet checked except (I).
- (5) M. Karplus, J. Chem. Phys., 30, 11 (1959).
- (6) K. Kuriyama, Physical Methods in Organic Chemistry, vol 5, Optical Rotatory Dispersion (in Japanese) Kyoritsu Press Ltd., Tokyo, p. 113 (1965). K. Takeda, K. Kuriyama, T. Komeno, D. A. Lightner, R. Records and C. Djerassi, Tetrahedron, 21, 1203 (1965).
- (7) CD and ORD was measured by JASCO ORD/UV-5 recording polarimeter at 27°C using quartz cells (1 mm or 1 cm) in 95 % ethanol.
- (8) PMR of (I) in D_2O , (II) in pyridine, (III), (IV) and (V) in CCl_4 gave almost same coupling patterns of H_a in CD_3OD . It suggests that the ring conformations in methanol should be kept in these solvents. The CD in various solvents gave similar results which will be reported elsewhere.
- (9) We thank Mr. Y. Kobayashi for the preparation of some of the samples and Mrs. A. Tagiri for the preparation of the manuscript.