The Circular Dichroism of Some Lactic Acid Derivatives. A Re-interpretation[1]

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DIRKX and SIXMA[3] demonstrated by o.r.d. that the 210 nm. absorption band of α-hydroxy-acids is optically active. Anand and Hargreaves[3] reported that *S*-(+)-lactic acid exhibits a very weak negative c.d. Cotton effect in the 240—250 nm. region (depending on the solvent) in addition to the strong positive Cotton effect at about 210 nm. Since the negative lower-energy Cotton effect could not be observed in alkaline solution, Anand and Hargreaves[3] attributed it to an n–π^* transition and the stronger positive Cotton effect near 210 nm. to a π–π^* transition. This assignment is in direct conflict with the generally accepted view that the Cotton effect associated with the 210 nm. absorption band of carboxylic acids and esters is of n–π^* origin.[4,5]

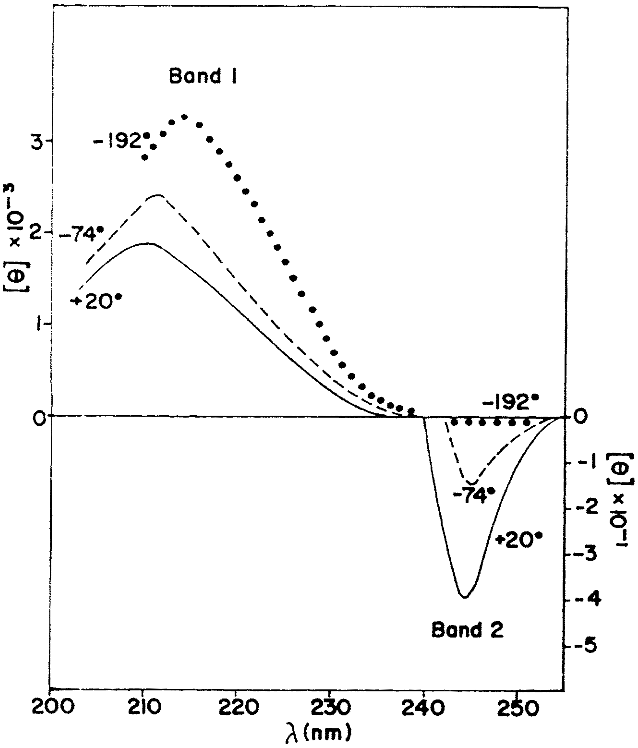


FIGURE 1. *Temperature-dependent circular dichroism of* S-(−)-*ethyl lactate* (II) *in ether–pentane–ethanol,* 5 : 5 : 2); *note scale differences.*

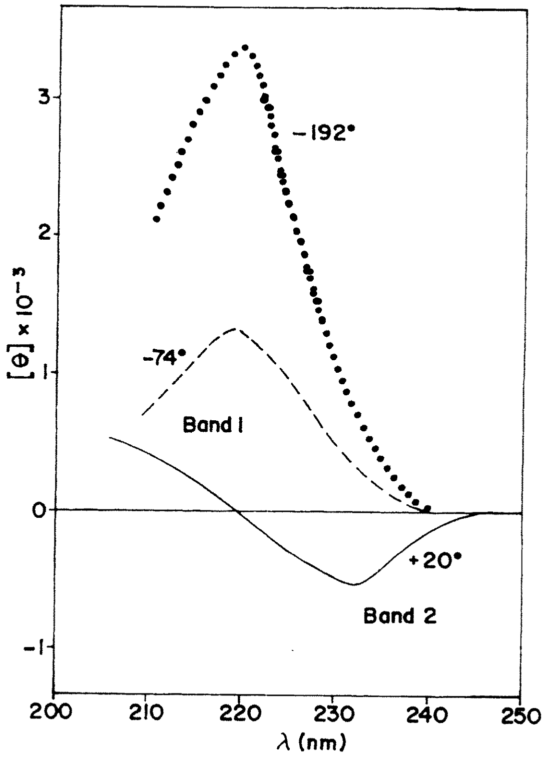


FIGURE 2. *Temperature-dependent circular dichroism of* S-(−)-*ethyl* O-*ethyl-lactate* (IV); (*same solvent systems as in Figure* 1).

Studies in our laboratory on the c.d. spectra of certain α-substituted mandelic acids raised serious doubts about the validity of this recent spectral assignment[3] and prompted us to re-examine this problem by investigating the solvent- and temperature-dependence of the c.d. spectra of several lactic acid derivatives.

The occurrence of two c.d. bands is not peculiar to lactic acid (I) since several ester and ether derivatives (II)—(IV) also exhibit this pattern (Table). Furthermore, the intensity of band 2 increases and shifts hypsochromically in the order [IV(EtOH)] > [III(EtOH)] > [II(EtOH)] > [I(0·5N-HCl)], whereas the variations in position of band 1 are less marked and the intensity progression is different from that of band 2. The results show that the intensity and positions of both bands are highly solvent-dependent. In particular, (III) and (IV) display only band 2 in cyclohexane and for (III) the signs of bands 1 and 2 are reversed in alkaline solution whereas (I) shows only a diminution in the magnitude of band 1. Most important, the low-temperature c.d. spectra of (II) and (IV) (Figures 1 and 2) exhibit an intensity reduction of band 2 and an intensity increase of band 1 together with a bathochromic shift upon lowering the temperature from +20° to −192°.

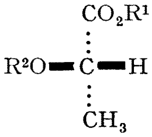
Although the observation of a pair of well separated c.d. bands of opposite signs is frequently diagnostic of the presence of two different electronic transitions, we find it difficult to accommodate our results with the assignment suggested by Anand and Hargreaves.[3] Our data can, however, be readily interpreted by assuming that both c.d. bands have a common origin, namely the n–π^* transition of the carboxy-chromophore and that they are associated either with different rotamers[6] or different solvated species.[7] It should be emphasized that the two c.d. maxima need not necessarily correspond to the maxima of the two absorption bands. In fact, depending on their relative rotational strengths, transitions separated by only 1—20 nm. may

Circular dichroism data at +20°

Compound	Solvent	λ_{max} (nm.), $[\theta]_{max}$ (deg. mole^{-1}cm.^{2}) Band 1	Band 2
S-(+)-Lactic acid (I)[a]	0·5N-HCl	212 (+2200)	243 (− 15)
	Water	214 (+ 600)	—
	0·15N-NaOH	215 (+ 550)	—
S-(−)-Ethyl lactate (II)	EtOH	212 (+2100)	242 (− 47)
	Cyclohexane	211 (+3200)	244 (− 23)
S-(−)-*O*-Ethyl-lactic acid (III)	0·5N-HCl	212 (+1400)	238 (− 96)
	Water	212 (+1000)	237 (− 80)
	0·15 N-NaOH	208 (−1200)	230 (+ 73)
	EtOH	215 (+ 650)	237 (− 200)
	Cyclohexane	—	224 (−1350)
S-(−)-Ethyl *O*-ethyl-lactate (IV)	EtOH	212 (+1350)	235 (− 360)
	Cyclohexane	—	228 (−1100)

[a] Measured as the *R*-(−)-Li salt, and signs reversed for convenience of comparison.

result in c.d. bands which are shifted apart by as much as 35 nm.[8] Although it is not possible to decide, *a priori*, whether solvation or conformational effects predominate, we prefer the latter explanation and will present further evidence in a subsequent and more detailed communication dealing with a larger group of α-hydroxy-acids. In any event, no justification for a reassignment of the n–π^* transition of carboxylic acids is indicated.



$$R^2O-\overset{CO_2R^1}{\underset{CH_3}{C}}-H$$

(I) $R^1 = H; R^2 = H$
(II) $R^1 = Et; R^2 = H$
(III) $R^1 = H; R^2 = Et$
(IV) $R^1 = Et; R^2 = Et$

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[1] For preceding paper on Optical Rotary Dispersion Studies, see W. Voelter, E. Bayer, G. Barth, E. Bunnenberg, and C. Djerassi, *Chem. Ber.*, in the press.

[2] I. P. Dirkx and F. L. J. Sixma, *Rec. Trav. chim.*, 1964, **83**, 523.

[3] R. D. Anand and M. K. Hargreaves, *Chem. Comm.*, 1967, 421.

[4] T. R. Emerson, D. F. Ewing, W. Klyne, D. G. Neilson, D. A. V. Peters, L. H. Roach, and R. J. Swan, *J. Chem. Soc.*, 1965, 4007; D. W. Urry and H. Eyring, *J. Amer. Chem. Soc.*, 1964, **86**, 4574.

[5] W. D. Closson and P. Haug, *J. Amer. Chem. Soc.*, 1964, **86**, 2384.

[6] A. Moscowitz, K. M. Wellmann, and C. Djerassi, *J. Amer. Chem. Soc.*, 1963, **85**, 3515.

[7] A. Rassat, in "Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry," ed. G. Snatzke, Heyden & Son, London, 1967, p. 314; A. Moscowitz, K. M. Wellmann, and C. Djerassi, *Proc. Nat. Acad. Sci.* (*U.S.A.*), 1963, **50**, 799.

[8] K. M. Wellmann, P. H. A. Laur ,W. S. Briggs, A. Moscowitz, and C. Djerassi, *J. Amer. Chem. Soc.*, 1965, **87**, 66.