Tetrahedron Letters No. 18, pp 1563-1565, 1970. Pergamon Press. Printed in Great Britain.

ABNORMAL CIRCULAR DICHROISM OF α-AMINO ACID ESTERS

J. Cymerman Craig and W. E. Pereira, Jr. (1)
Department of Pharmaceutical Chemistry, School of
Pharmacy, University of California, San Francisco,
California 94122

(Received in USA 16 February 1970; received in UK for publication 17 March 1970)

We have observed for α-amino acid esters of the S-configuration the occurrence of a substantial abnormal negative circular dichroism (CD) band in the 230 nm region, in addition to the strong positive CD maximum at 209 nm (Table). While the latter maximum (2) corresponds to the known n—π* transition of the carbonyl group in α-amino acid esters, no transition in the 230 nm region has been reported in the ultraviolet spectra of such compounds.

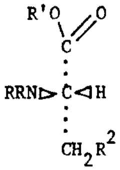
The possibility that intra- or intermolecular hydrogen bonding is the reason for the abnormal band is excluded by the presence of the 230 nm band in α-amino acid esters containing a primary, a secondary, or a tertiary amino group (Table). The 230 nm band could, however, be caused by an interaction through space between the non-bonding orbital of the nitrogen atom and the chromophoric transition of the ester carbonyl group.

This proposed explanation was verified by the observation (Table) that the CD spectra of the corresponding α-amino acid ester hydrochlorides no longer showed either the abnormal negative band at 230 nm or the positive band at 200 nm which is due to the optically active n—σ* transition of nitrogen (3) and which has not previously been observed in CD spectra. On basification of the solution, both CD bands are restored. The normal (209 nm) CD band corresponding to the n—π* transition remains unaffected by these changes.

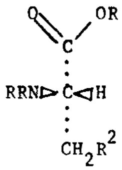
The abnormal negative high-wavelength CD band observed in α-amino acid esters is thus consistent with the existence of two rotamers in solution, in which the more stable form I (maximum angle between dipoles) may be responsible for the strong positive CD at 209 nm, while in form II orbital interaction between the nitrogen and carbonyl moieties causes the weaker long wavelength negative CD reported here.

Similar coupling of an oxygen non-bonding orbital with the carbonyl chromophore satisfactorily explains the weak negative CD band at 240 nm recently reported for S-lactic acid (4,5), and its ethyl ester and O-ethyl ether ethyl ester (5). Indeed, the ratio of the molecular ellipticities (and hence of the rotational strengths) (6) of the abnormal and normal bands increases with the nucleophilicity of the heteroatom α-substituent (Table) in the expected manner.

Furthermore, the absence of the 240 nm negative band in a non-hydroxylic aliphatic acid and in a β-hydroxy acid ester (Table) show that the abnormal CD maximum is not caused by the n—π^* transition of the carbonyl group alone.



I



II

REFERENCES

1. From the Ph.D. dissertation of W. E. Pereira, Jr., University of California, 1968. Support by the U.S.Public Health Service through research grant HE-5881 is gratefully acknowledged.
2. W. D. Closson and P. Haug, *J. Am. Chem. Soc.*, **86**, 2384 (1964); M. Legrand and R. Viennet, *Bull. Soc. Chim.*, 679 (1965).
3. E. Tannenbaum, E. M. Coffin and A. J. Harrison, *J. Chem. Phys.*, **21**, 311 (1953); L. W. Pickett, M. E. Corning, G. M. Wieder, D. A. Semenor and J. M. Buckley, *J. Amer. Chem. Soc.*, **75**, 1618 (1953).
4. R. D. Anand and M. K. Hargreaves, *Chem. Comm.*, 421 (1967).
5. G. Barth, W. Voelter, E. Bunnenberg, and C. Djerassi, *Chem. Comm.*, 355 (1969).
6. W. Moffitt, *J. Chem. Phys.*, **25**, 1189 (1956).

TABLE: Circular Dichroism Spectra in 95% Ethanol

	λ_{max} nm, ($[\theta]_{max}$)		
Compound	200 nm	210 nm	235 nm
S(+) Alanine methyl ester	199(3564)	209(3227)	236(-395)
S(+) Alanine methyl ester hydrochloride	0	208(2987)	0
S(-) Proline methyl ester	202(3788)	209(2889)	232(-604)
S(-) Proline methyl ester hydrochloride	0	208(3148)	0
S(-) N-Methylproline methyl ester	199(3593)	209(1891)	226(-643)
S(-) N-Methylproline methyl ester hydrochloride	0	209(1722)	0
S(-) Methyl lactate	-	211(2545)	240(-66)
S(-) Methyl α-methoxy-succinate	-	216(2230)	242(-219)
S(+) α-Methylbutyric acid	-	212(267)	0
S(+) n-Butyl β-hydroxy isobutyrate	-	215(192)	0