

CIRCULAR DICHROISM SPECTRA OF *N,N*-DIMETHYL-L-AMINO ACIDS

By C. J. HAWKINS* and G. A. LAWRENCE*

[Manuscript received 2 April 1973]

Abstract

The circular dichroism spectra in the region 190–300 nm have been measured at pH 1 and pH 13 in aqueous solution for a series of *N,N*-dimethyl-L-amino acids. A dominant positive Cotton effect is generally observed between 205 and 225 nm as has been found previously for the parent L-amino acids. These results are consistent with the same conformer being dominant for both series of compounds.

Most naturally occurring and synthetic L- α -amino acids show positive Cotton effects in the region 200–220 nm originating from the $n \rightarrow \pi^*$ transition of the carboxyl group.^{1–4} The sign and amplitude of the observed Cotton effects have been related to the absolute configuration and conformation of the α -amino acids.⁵

Structural studies of α -amino acids suggest that the preferred conformation has the amine group in the C(α)-COO plane.^{6,7} In this conformation the amine is in a nodal plane of the carboxyl chromophore, and should not play a major part in determining the size of the observed Cotton effect. Substitution on this amine group would be expected to induce only a secondary effect, provided the same conformer is dominating in the *N*-substituted amino acid. In order to investigate further the conformations of α -amino acids in solution, a series of *N,N*-dimethyl-L- α -amino acids has been prepared and the compounds' solution circular dichroism (c.d.) spectra compared with those previously reported for the parent L- α -amino acids.

Experimental

The *N,N*-dimethyl-L- α -amino acids were prepared from standard L- α -amino acids using essentially the method of Bowman and Stroud.⁸ The compounds, which had all been prepared previously,^{8–10} were characterized by their melting points and specific rotations. The rotation data, which are included in Table 1, were determined in a 0.1-m cell at the sodium D line using a Perkin-Elmer 141 polarimeter.

* Department of Chemistry, University of Queensland, St. Lucia, Qld. 4067.

¹ Legrand, M., and Viennet, R., *Bull. Soc. chim. Fr.*, 1965, 679.

² Legrand, M., and Viennet, R., *Bull. Soc. chim. Fr.*, 1966, 2798.

³ Fowden, L., Scopes, P. M., and Thomas, R. N., *J. chem. Soc. (C)*, 1971, 833.

⁴ Fric, J., Spirko, V., and Bláha, K., *Colln Czech. chem. Commun.*, 1968, 33, 4008.

⁵ Jorgensen, E. C., *Tetrahedron Lett.*, 1971, 863.

⁶ Ponnuswamy, P. K., and Sasisekharan, V., *Int. J. Protein Res.*, 1970, 2, 37.

⁷ Freeman, H. C., *Adv. Protein Chem.*, 1967, 22, 257.

⁸ Bowman, R. E., and Stroud, H. H., *J. chem. Soc.*, 1950, 1342.

⁹ Suyama, T., and Kanao, S., *J. pharm. Soc. Japan*, 1965, 85, 284.

¹⁰ Dahn, H., and O'Murchu, C., *Helv. chim. Acta*, 1970, 53, 1379.

The c.d. spectra were measured in aqueous 0.1M HCl and 0.1M KOH at concentrations of approximately 1 mg/ml in 1-mm quartz cells. A Cary 61 instrument was used for the measurements between 190 and 300 nm. The results are tabulated in Table 1 together with the previously reported data for the parent α -amino acids.

TABLE 1
CHIROPTICAL DATA FOR L- α -AMINO ACIDS IN AQUEOUS SOLUTION
Rotations were measured in water at 1-3 g/100 ml at 20°

Amino acid	[α] _D		pH 1		pH 13	
	measured	lit.	λ (nm)	$\Delta\epsilon$	λ (nm)	$\Delta\epsilon$
Alanine ^a			208	+1.04	214	+0.33
N,N-Dimethylalanine	+8.6°	+8.7° ^c	207	+0.92	222	+0.87
Valine ^a			209	+1.45	217	+0.29
N,N-Dimethylvaline	+41.4°	+40.6° ^c	210	+0.48	225	+0.18
Leucine ^a			209	+1.79	212	+0.90
N,N-Dimethylleucine	+49.2°	+49.6° ^c	207	+1.30	220	+1.39
Methionine ^a			208	+1.53	212	+0.81
N,N-Dimethylmethionine	+56.0°	+57.9° ^d	202	+0.59	221	+0.78
			220	+0.54		
			244	-0.02		
Phenylalanine ^b			218	+4.50	216	+2.80
			252	+0.02	253	+0.02
			257	+0.02	258	+0.03
			263	+0.02	266	+0.03
N,N-Dimethylphenylalanine	+78.0°	+77.1° ^c	216	+4.65	217	+4.58
			259	+0.02	258	+0.03
			266	+0.03	264	+0.01
					268	-0.02
Phenylglycine ^b			218	+10.20		
			254	-0.19		
			261	-0.28		
			267	-0.23		
N,N-Dimethylphenylglycine	+134°	+133° ^e	217	+8.71	209	+3.34
			255	-0.22	226	-1.20
			262	-0.39	237	+0.22
			268	-0.33	255	-0.13
					262	-0.22
					268	-0.16

^a Ref. 1. ^b Ref. 2. ^c Ref. 8. ^d Ref. 9. ^e Ref. 10.

Results and Discussion

The general observation of only one c.d. band in the range 200-220 nm for aliphatic amino acids has been interpreted in terms of one dominant conformer in which the N-C(α)-COO atoms are coplanar.⁵ Other α -substituted acids, for example lactic acid and 2-chloropropionic acid, show an additional band of opposite sign at approximately 240 nm.¹¹⁻¹³ Both bands have been attributed to the $n \rightarrow \pi^*$ transition with the high energy band associated with the conformer possessing the non-alkyl

¹¹ Barth, G., Voelter, W., Bunnenberg, E., and Djerassi, C., *Chem. Commun.*, 1969, 355.

¹² Listowsky, I., Avigad, G., and England, S., *J. org. Chem.*, 1970, **35**, 1080.

¹³ Gaffield, W., and Galetto, W. G., *Tetrahedron*, 1971, **27**, 915.

substituent in the C(α)-COO plane and the other band associated with the conformer where the alkyl group is in the plane.

The *N,N*-dimethyl derivatives of alanine, valine, and leucine show one positive Cotton effect in the region of interest in both acidic (at about 210 nm) and alkaline media (at about 220 nm). In acid the c.d. bands occur in approximately the same positions as the parent amino acids but the rotational strengths are reduced somewhat. In alkaline solution the positive bands for the *N,N*-dimethyl derivatives are about 8 nm to longer wavelength than the parent compounds. The relatively small changes are consistent with no change occurring in the dominant conformer on methylating the amine group.

Methionine and its *N,N*-dimethyl derivative follow the normal pattern for aliphatic amino acids in alkaline solution but in acid *N,N*-dimethylmethionine shows three bands at 202, 220, and 244 nm whereas only one band at 208 nm has been reported¹ for methionine. The additional bands, which are probably hidden by the large $n \rightarrow \pi^*$ carboxyl Cotton effect for methionine, are assigned to the R-S-R chromophore because asymmetric open-chain thioethers are known to exhibit c.d. bands at about 201, 210, 230, and between 235 and 255 nm.¹⁴

Phenylalanine, phenylglycine, and their dimethyl derivatives show a series of Cotton effects between 250 and 270 nm which are vibrational in origin based on the transition which is designated in Platt's terminology¹⁵ as the 1L_b band.¹⁶⁻¹⁹ Except for *N,N*-dimethyl-L-phenylglycine these compounds also exhibit a very large c.d. band at about 217 nm in both acid and alkali. *N,N*-Dimethyl-L-phenylglycine has this band in acid but in alkali has three Cotton effects in this region at 209 (+), 226 (-), and 237 (+) nm. The analysis of this region is complicated by the overlap of the $n \rightarrow \pi^*$ carboxyl transition and the 1L_a $\pi-\pi^*$ phenyl transition.¹⁶⁻¹⁹ Further work is needed before an assignment of these bands can be made.

Acknowledgments

The authors gratefully acknowledge financial support from the Australian Research Grants Committee, and also wish to express their appreciation to Professor Runciman of the Research School of Physical Sciences, Australian National University, for the use of the Cary 61 dichrograph.

¹⁴ Salvadori, P., *Chem. Commun.*, 1968, 1203.

¹⁵ Platt, J. R., *J. chem. Phys.*, 1949, 17, 484.

¹⁶ Barth, G., Voelter, W., Mosher, H. S., Bunnenberg, E., and Djerassi, C., *J. Am. chem. Soc.*, 1970, 92, 875.

¹⁷ Moscowitz, A., Rosenberg, A., and Hansen, A. E., *J. Am. chem. Soc.*, 1965, 87, 1813.

¹⁸ Horwitz, J., Strickland, E. H., and Billups, C., *J. Am. chem. Soc.*, 1969, 91, 184.

¹⁹ Klyne, W., Scopes, P. M., Thomas, R. N., and Dahn, H., *Helv. chim. Acta*, 1971, 54, 2420.