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ENANTIOMERIC SHIFT DIFFERENCE INDUCED BY THE LANTHANIDE SHIFT REAGENT : ITS CORRELATION WITH ABSOLUTE CONFIGURATION OF α-AMINO ACIDS

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Chiral lanthanide shift reagents have been found to be applicable to the absolute configurational problem as well as to the direct determination of optical purities of α-amino acids.

Recently, chiral lanthanide shift reagents were found to resolve the ^1H[1-6] as well as the ^{13}C nmr[6] spectra of enantiotopic nuclei by both external and internal comparisons.[5,6] Thus the direct determination of optical purity can easily be performed by use of them.[1-4] Whitesides and Lewis,[2] however, suggested that the use of chiral shift reagents for correlating absolute configurations seems very dim. On the contrary to their prospect, we here wish to show that the chiral shift reagents may be useful for such problems, at least, in a series of compounds of analogous structures, similarly to the well-known chiral-solvent methods.[7]

The enantiomers of α-amino acid methyl esters showed readily observable shift differences in the presence of tris[3-(trifluoromethylhydroxymethylene)-d-camphorato]europium(III) (I).[3] For example, a mixture of L- and D-methyl alanates (L : D = 2 : 1), prepared by Fisher-Speier esterification, gave a pair of signals for the O-methyl (δ 5.18 and 5.24), the C-methyl (δ 4.36 and 4.31), and for the C^{α}-H (δ 6.22 and 6.46) in the presence of 0.5 molar equivalent of I. The relative intensities of each set of peaks given in parentheses agreed well with an expected ratio of 2 : 1. The enantiomeric shift differences, ΔΔδ, for nine common α-amino acid methyl esters, shown in Table 1, suggest that the resonance of α-methoxycarbonyl protons should be best suited for the prediction of absolute configurations of α-amino acid esters.

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Table 1. Enantiomeric shift differences, $\Delta\Delta\delta$, of α-amino acid methyl esters in the presence of 0.5 molar equivalent of I (100 MHz, 0.1M CCl_4).

Parent α-amino acid	molar ratio (L:D)	Assignment	$\Delta\Delta\delta$, Hz	Nonequivalence sense of L-isomer
Alanine	(2:1)	OCH_3	5.4	high
		CH	26.0	high
		CH_3	6.0	low
Phenylalanine	(5:1)	OCH_3	6.0	high
Valine	(2:1)	OCH_3	40.5	high
		CH_3	17.5, 15.0	high, low
Norleucine	(2:1)	OCH_3	6.5	high
Isoleucine	(2:1)	OCH_3	4.5	high
Tryptophane	(2:1)	OCH_3	21.0	high
Aspartic acid	(2:1)	C^1-OCH_3	23.0	high
		C^4-OCH_3	15.5	high
Glutamic acid	(5:1)	C^1-OCH_3	26.0	high
		C^5-OCH_3	5.5	high
Prolin	2:1)	OCH_3	10.5	low

The prolin case which is an exception in the Table, indicates that the sense of the enantiomeric shift difference depends strongly on the geometry around the coordination site. Thus, much caution must be excercised for the application of method to α-amino acids other than glycine derivatives. More extensive studies may hopefully establish some empirical rules between the sense of the shift and the geometry of the coordinated substrate.

References

1) G. M. Whitesides and D. W. Lewis, J. Amer. Chem. Soc., 92, 6979 (1970).
2) idem., ibid., 93, 5914 (1971).
3) H. L. Goering, J. N. Eikenberry, and G. S. Koermer, ibid., 93, 5913 (1971).
4) R. R. Fraser, M. A. Petit, and J. K. M. Saunders, Chem. Commun., 1450 (1971).
5) R. R. Fraser, M. A. Petit, and M. Miskow, J. Amer. Chem. Soc., 94, 3253 (1972).
6) M. Kainosho, K. Ajisaka, W. H. Pirkle, and S. D. Beare, ibid., in the press.
7) W. H. Pirkle and S. D. Beare, ibid., 91, 5150 (1969); ibid., 90, 6250 (1968), and references therein.

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