

Absolute Configuration of Aldonic Acids and Lanthanoid Induced Shift by the Chiral Shift Reagent Propylenediaminetetraacetatoeuropium(III) in Aqueous Solution

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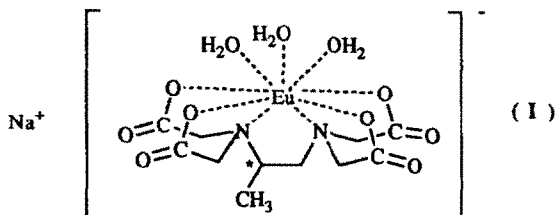
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Abstract: Consistent relation was observed between the absolute configuration of seventeen aldonic acids and their ¹H NMR shifts induced by chiral propylenediaminetetraacetatoeuropium(III) in aqueous solution.

Recent advance in NMR methods for determining absolute configuration has made it possible to apply them to natural products with complex structures.¹ However, no NMR methods have verified their usefulness for carbohydrates and related compounds. We wish to show in this communication that the chiral shift reagents, Na[Eu^{III}(R-pdta)(H₂O)₃] ((R)-(I), pdta=propylenediaminetetraacetate)² and its enantiomer (S)-(I), can be used to determine the absolute configuration of aldonic acids (carboxylic acids related to aldoses) which possess an α-hydroxy acid moiety.



We reported previously that reagent (I) afforded a consistent relation between absolute configuration of various α-hydroxy acids and their relative shifts. The five-membered chelate ring formation to europium ion by carboxyl and α-hydroxyl groups^{2c,3} is suggested to play a key role for the consistent relation. Aldonic acids which we examined here are challenging targets for the chiral shift reagent method since their additional hydroxyls other than the α-one may disturb the chelation and could cause violation of the rule.

We have examined seventeen aldonic acids shown in Figure 1 which include two disaccharide aldonic acids. For the sake of convenience, only (S)_α-isomers (α denotes α-carbon) are shown. Consistent relation was observed between the absolute configuration of these aldonic acids and the shifts of their α, β, and γ protons induced by (I).

Table 1. $\Delta\Delta\delta$ and the sense of nonequivalence of H_α , H_β , and H_γ signals in the presence of (R)-(I).^a

Aldonic acids ^b	pH ^c	$\Delta\Delta\delta$ (Hz)			Sense of nonequivalence of the signals due to (S) _α -isomer		
		H_α	H_β	H_γ	H_α	H_β	H_γ
Glyceric acid (1) ^{d,e}	3.4	28	f)	-	high	-	-
Erythronic acid (2)	3.5	38	71	68g)	high	low	low
Threonic acid (3) ^e	3.3	20	33	68g)	high	low	low
Ribonic acid (4)	3.9	50	16	20	high	low	low
Lyxonic acid (5)	3.6	44	92	76	high	low	low
Xylonic acid (6) ^e	3.2	h)	42	80	-	low	low
Arabonic acid (7) ^e	3.2	46	8	48	high	low	low
Allonic acid (8)	3.6	41	47	60	high	low	low
Talonic acid (9)	4.3	75	26	64	high	low	low
Gulonic acid(10)	3.6	39	93	64	high	low	low
Mannonic acid (11) ^d	3.6	40	112	20	high	low	low
Gluconic acid (12) ^{d,i}	3.8	15	43	j)	high	low	-
Idonic acid (13)	3.7	28	65	138	high	low	low
Galactonic acid (14)	3.7	44	35	120	high	low	low
Altronic acid (15)	3.7	46	33	68	high	low	low
Lactobionic acid (16) ^e	3.1	27	43	46	high	low	low
Melibionic acid (17)	3.9	19	55	j)	high	low	-

a) The NMR spectra were taken for 0.094M D₂O solution at 400 MHz, 22°C, molar ratio of I = 0.11, using t-butyl alcohol as an internal standard unless otherwise stated. b) D-Isomers and Na salts were used unless otherwise stated. c) Adjusted by ca. 6M DCl. d) L-Isomer was used. e) Ca salt. f) One of the H_β signals (not assigned) due to D-isomer(config. R at C_α) shifted most downfield in the presence of (S)-(I). g) The chemical shift difference between the centers of the H_β signals. h) Little chemical shift difference(ca. 1 Hz). i) Data from the reference 2c. j) The signal position was not clear because of overlapping and line-broadening.

the presence of (R)-(I). A distinct regularity was observed throughout all the substrates examined: the sense of H_α signals due to (S)_α-isomers is always high as observed on a series of simple α-hydroxy acids,^{2c} whereas that of H_β and H_γ signals due to them is always low. This means the sense of these signals is ruled solely by the configuration of C_α, regardless the presence and the stereochemistry of the additional hydroxyl groups. This relation is shown in Figure 2.

When consistent relation between shift and absolute configuration is observed, it is generally considered that the formation of a complex between a substrate and a reagent proceeds in a single stoichiometry and the mode of coordination is kept unchanged throughout a series of substrates. In the present case, the reversal of the shift direction found for some substrates indicates stoichiometric changes occur with increasing amount of the shift reagents. In

addition, it is highly probable for the mode of coordination to be perturbed by other hydroxyl groups than the α -one.⁵ It is noteworthy that in spite of these problems of the stoichiometry in complexation and of the coordination with additional hydroxyls, a consistent regularity was observed. To our knowledge this is the first example that a chiral shift reagent afforded a consistent relation between shift and absolute configuration of carbohydrate related compounds.

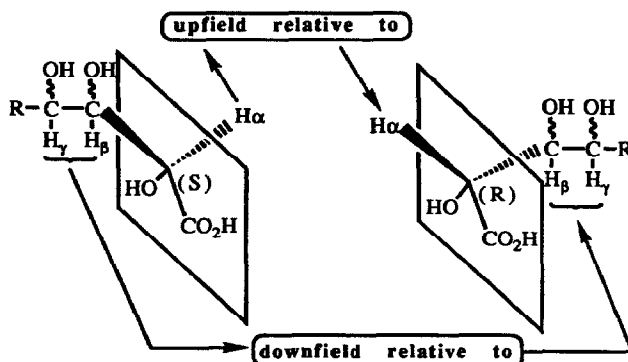


Figure 2. Relative position of H_α , H_β , and H_γ signals of aldonic acid enantiomers in the presence of (R)-(I).

References and Notes

- (1) (a) Adamczeski, M.; Quinoa, E.; Crews, P. *J. Org. Chem.*, **1990**, *55*, 240. (b) Kitagawa, I.; Kobayashi, M.; Katori, T.; Yamashita, M.; Tanaka, J.; Doi, M.; Ishida, T. *J. Am. Chem. Soc.*, **1990**, *112*, 3710. (c) Ohtani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. *J. Am. Chem. Soc.*, **1991**, *113*, 4092.
- (2) (a) Kabuto, K.; Sasaki, Y. *J. Chem. Soc., Chem. Commun.*, **1984**, 316. (b) Kabuto, K.; Sasaki, Y. *ibid.*, **1987**, 670. (c) Kabuto, K.; Sasaki, Y. *Chem. Lett.*, **1989**, 385. (d) Kabuto, K.; Sasaki, Y. *Tetrahedron Lett.*, **1990**, *31*, 1031. Recently, the X-ray analysis of (I) has been accomplished. The result will be published elsewhere.
- (3) Choppin, G. R.; Friedman, H. G. *Inorg. Chem.*, **1966**, *5*, 1599.
- (4) If a sample available is partially active, a measurement using either (R)- or (S)-(I) on it should allow direct comparison of the shifts of the enantiomer signals.
- (5) Participation of the β -hydroxyl group with the coordination was revealed by an analysis of the lanthanoid induced shift of the complex between some aldonic acids and lanthanoid salts in aqueous solution: Taga, T.; Kuroda, Y.; Ohashi, M. *Bull. Chem. Soc. Jpn.*, **1978**, *51*, 2278. Moreover, participation of γ -hydroxyl group can be also conceivable in some specific cases from the comparison of the shifts of H_β and H_γ signals induced by (I). The larger downfield shift was usually observed on the latter, and exceptionally on the former for (2), (5), (10), and (11). These compounds have the common relative stereochemistry between their α , β , and γ -hydroxyls: α , β -erythro for all and β , γ -threo except (2) whose γ -carbon was not asymmetric center. The compounds, (4), (8), and (9), having the stereochemistry of α , β -erythro, β , γ -erythro showed usual shift behavior, therefore it can be considered that the reversal of the shift magnitude arises from participation of γ -hydroxyls.