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Unveiling Chiral Discrimination in Helically Chiral Diastereomers through Reversed Phase HPLC: Insight from Induced Herical Chiralty

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Received: 1 January 1970 Accepted: 1 January 1970 Published: 1 January 1970

Abstract

The most reliable and widely used diastereomer method in chiral discrimination has a fatal problem in that it is impossible to discriminate the diastereomers having chiral centers separated by more than 4 bonds. The problem has been assumed to be intrinsic to the diastereomer method and therefore very difficult to solve. In order to solve the problem, we have developed highly potent chiral discrimination methods by use of helically chiral derivatization reagents (for example A, Fig. 1)1). A has an anthracene-2,3-dicarboximido group on one side (wing) and OH or COOH group for derivatization on the other side (wing). The anthracene-2,3-dicarboximodo group is for highly sensitive fluorescence and long-distance anisotropy for 1H-NMR study

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Index terms—

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1 GJSFR-B Classification: LCC: QD261-272

Strictly as per the compliance and regulations of:

2 By Hiroshi Ohrui Yokohama University

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Abstract-The most reliable and widely used diastereomer method in chiral discrimination has a fatal problem in that it is impossible to discriminate the diastereomers having chiral centers separated by more than 4 bonds. The problem has been assumed to be intrinsic to the diastereomer method and therefore very difficult to solve. In order to solve the problem, we have developed highly potent chiral discrimination methods by use of helically chiral derivatization reagents (for example A, Fig. 1) 1) . A has an anthracene-2,3-dicarboximido group on one side (wing) and OH or COOH group for derivatization on the other side (wing). The anthracene-2,3dicarboximodo group is for highly sensitive fluorescence and long-distance anisotropy for 1 H-NMR study. the two chiral positions (one is the position that tells the helical chirality of the diastereomer and the other is that of methyl branching) of the diastereomer simultaneously so that it gets the two information of the chirality of the diastereomer at the same time. Now, a new question "How can one chiral information of the diastereomer be transmitted to the other interaction position through the methylene chain?" arises.

Here, I would like to propose an idea of "induced helically chiral methylene chain".

The methylene chain of the column is twisted clockwise or counterclockwise depending on the helical chirality of the diastereomer by the interaction with the helically chiral diastereomer, this makes the methylene chain helically chiral. (The difference in affinity for the methylene chain of the column between the anthracene-2,3-dicarboximido group and the alkyl ester group of the diastereomer would be playing an important role for the twisting.) Thus, the information of the helical chirality of the diastereomer can be transmitted throughout the methylene chain as the helical chirality of the methylene chain. The helically chiral methylene chain interacts with the chiral center at the methyl branching of the diastereomer. The interaction is different by the (R)-or (S)-stereochemistry of the chiral center, and therefore chiral discrimination takes place. The chiral discrimination takes place over and over again throughout the column resulting in the separation of the diastereomers.

In conclusion, the normally achiral reversed phase column is changed into a chiral column by the interaction with the eluate. [1]

Figure 1: Global

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Figure 2: Fig. 1

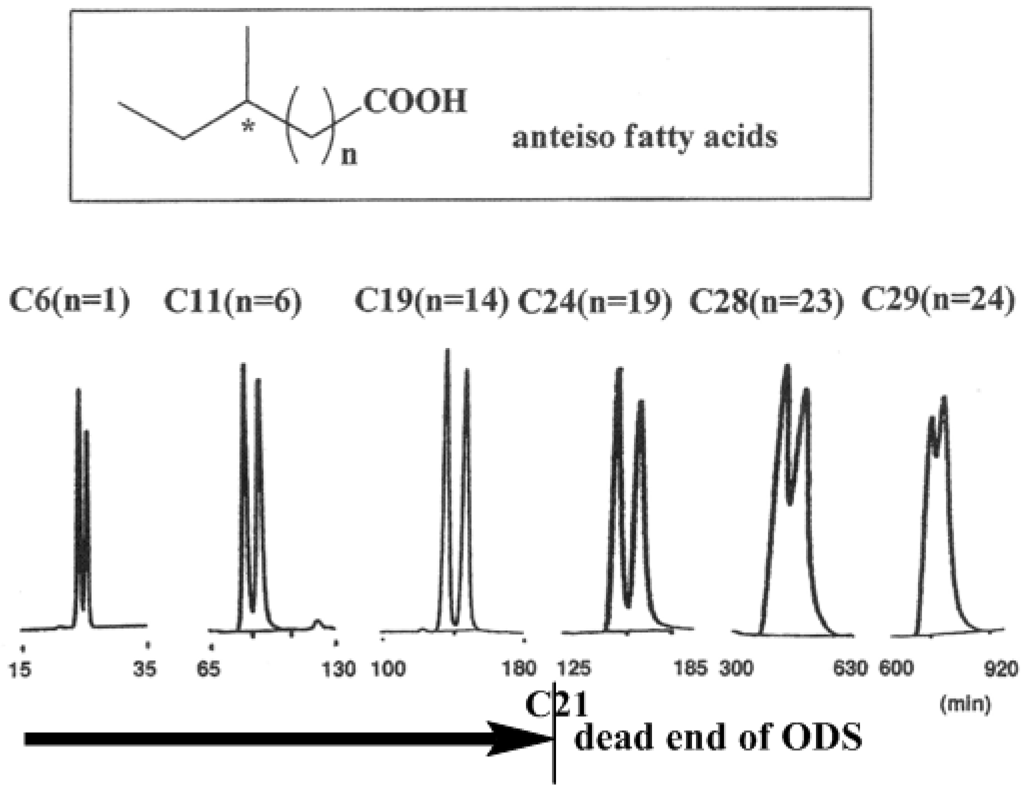

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Figure 3: Fig. 3 :

.1 Acknowledgement

The author would like to dedicate this paper to his two deceased mentors, Dr. Masanao Matsui and Dr. Kenji Mori. 1 Year 2023 Global Journal of Science Frontier Research Volume XXIII Issue ersion I V II (B)

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In this paper, I would like to submit an answer for the question by citing the separation of anteiso fatty acids derivatized with A as an example (Fig. **??**).

I hope that the answer could attract much attention and contribute to the further development of chiral discrimination method. The helically chiral diastereomer derivatized with A and a chiral sample does not have the distance problem of two chiral centers because it has only the chiral center derived from the sample. For example, the helically chiral diastereomer B (Fig. **??**) (derivatized with a helically chiral reagent and a chiral sample having one chiral center) has only one chiral center caused by R' that is derived from the sample, and therefore, B does not have the distance problem. (The chiral center caused by R in B is the one to make the derivatization reagent helically chiral and does not interfere with chiral discrimination.) Therefore, it is expected that the helically chiral diastereomers derivatized with A could be discriminated by some means. In fact, the helically chiral diastereomers (and stereoisomers) derivatized with A can be separated by reversed phase HPLC ?, 2 , and A has been proved to be the most powerful Mosher reagent for 1 H-NMR study. **??**, 3c) The absolute configurations of many natural products have been determined by the HPLC or 1 H-NMR methods. 1,3) However, the question "Why can the helically chiral diastereomers (and stereoisomers), especially those having far remote chiral center(s), be separated by the achiral reversed phase HPLC?" has remained to be answered.

Unveiling Chiral Discrimination in Helically Chiral Diastereomers through Reversed Phase HPLC:

Insight from Induced Herical Chiralty Fig. **??** We showed that the helically chiral diastereomers derivatized with A and anteiso fatty acids up to 21:0 (methyl branching at C18) could be separated by ODS (18 methylene chain) column and those over 18-branching ones could not be separated by ODS column, but they could be separated by C30 column (30 methylene chain) 1,4) (Fig. **??**).

[Akasaka and Ohrui ()] , K Akasaka , H Ohrui . *Biosci. Biotechnol. Biochem* 2004. 68 p. .

[Shudo et al. ()] , H Shudo , H Ohrui , Ihara . *Analytical Sciences* 2007. 23 (3) p. .

[Ohrui ()] , H Ohrui . *Analytical Sciences* 2008. 24 (1) p. .

[Hirota et al. ()] , Y Hirota , K Takada , S Matsunaga , ; K Mori , K Akasaka , S Matsunaga ; Fu -Shuang , Pyae Li , Jing-Ke Phyo , Weng . *Biosci. Biotechnol. Biochem* 2013. 2014. 2019. 2004. 69 p. . (Nature Plants. References Références Referencias)