Pergamon

Tetrahedron Letters, Vol. 35, No. 19, pp. 3127-3128, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $6.00+0.00

0040-4039(94)E0566-G

The Conformation of the 17-*O*-MTPA-Eicosatetraenoyl Chain of a Marine Acylphloroglucinol

Takenori Kusumi,* Takashi Ooi, Hidetaka Uchimura†

Faculty of Pharmaceutical Sciences, The University of Tokushima, Tokushima 770, Japan
†Chugai Pharmaceutical Company, Kyobashi 2-1-9, Chuo-ku, Tokyo 104, Japan

Abstract: *The 17-O-MTPA-eicosatetraenoyl chain of a marine acylphloroglucinol (1) has been proved to have a round conformation by the analysis of NOESY spectrum as well as the modified Mosher's method.*

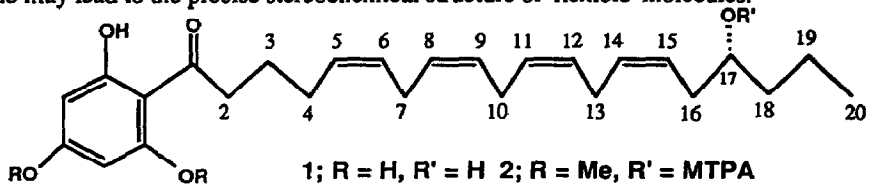
Modified Mosher's method has been developed to elucidate the absolute configurations of organic compounds.[1] In this report, we would like to describe another versatility of this method, which may reveal the conformation of long-chain compounds such as fatty acids.

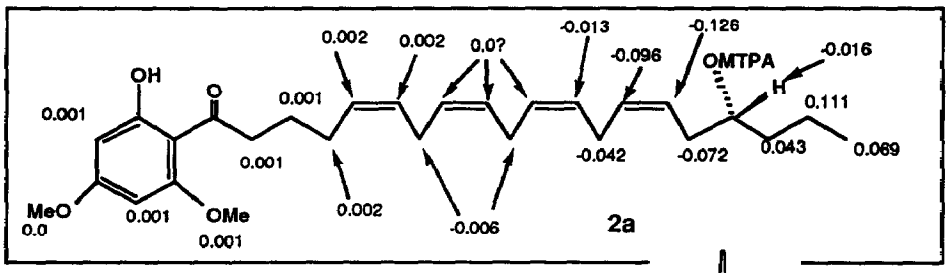
During the course of our continuing works to seek for pharmaceutically significant compounds from marine organisms, we have obtained two acylated phloroglucinol derivatives, **1** and 2-eicosapentaenoyl-phloroglucinol, from the brown alga, *Distromium decumbems* (Dictyotaceae), as moderately cytotoxic compounds. Both the compounds are known,[2] although the absolute configuration of the secondary hydroxy group of **1** has been undetermined. The *R*-configuration of C-17 was easily obtained by applying the modified Mosher's method to the methyl derivative **2** (**1** was treated with CH_2N_2, followed by MTPA acid/DCC-DMAP /CH_2Cl_2.), the results of which are shown in **2a**. Aside from the absolute configuration, we were interested in how long in distance the anisotropy of the phenyl group of the MTPA moiety reaches in this long-chain compound. The negative $\Delta\delta$ value ($\Delta\delta = \delta_S - \delta_R$) is observed even at the protons on C-7, which is ten bonds apart from 17-*O*-MTPA group. It is noteworthy that the sign of $\Delta\delta$ changes from negative to positive at the protons of C-6. The positive $\Delta\delta$ values are also observed for the protons located on farther than position-6, although the values are as small as the instrumental error. Such inversion of the signs of $\Delta\delta$ has been observed in other compounds.[3]

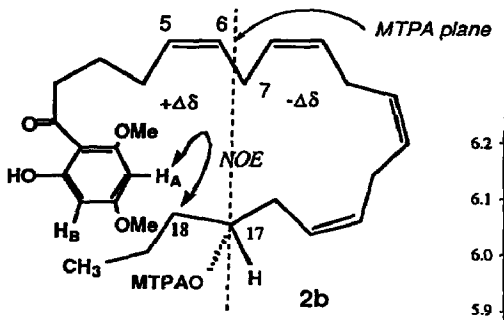
One of the possible interpretation for this phenomenon is that this long-chain compound exists in a round conformation as is shown in **2b**, in which protons on C-16 to 7 are located on the left side, and those on C-6 to the aromatic ring oriented on the right side of MTPA plane. In fact, a distinct NOE cross peak was observed between the methylene protons on C-18 and H_A on the benzene ring in the phase-sensitive NOESY spectra of both (*R*) and (*S*)-MTPA esters (**2**) (Figure 1).

If such round conformations are general for highly unsaturated fatty acid chains, they would give a very important key for biosynthetic consideration of the conformation of arachidonic acid, a precursor of prostaglandins. However, no such NOE was observed for the compound (1). The most convenient interpretation for this fact may be that, although 1 takes a round conformation, the distance between the phenyl and the aliphatic hydrogens is larger than in 2 to some extent. However, it may be still possible that 2 is only the special case: it exists in a round shape because, for instance, some weak attraction between two aromatic rings (of methylated phloroglucinol and of MTPA) may be working.

As pointed out in the previous paper,[1] the absolute value of the $\Delta\delta$ for each proton must be proportional to the distance from the hydrogen to the phenyl group. Also, the sign of $\Delta\delta$ depends on which side of the MTPA plane the proton in question is located. Therefore, analysis of both the absolute values and the signs of $\Delta\delta$ may lead to the precise stereochemical structure of 'flexible' molecules.







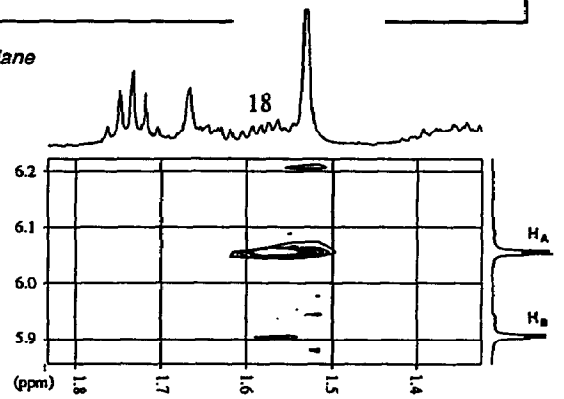


Figure 1. A part of the phase-sensitive NOESY spectrum of (*S*)-MTPA ester 2a ($CDCl_3$, 500 MHz), which was measured using a 0.02 mM solution with the data size 2K x 1/4K, 62 scans and 2 sec mixing time.

REFERENCES AND NOTES

1. I. Ohtani, T. Kusumi, Y. Kashman, H. Kakisawa, *J. Am. Chem. Soc.*, **1991**, *113*, 4092.
2. W. Gerwick, W. Fenical, *Phytochemistry*, **1982**, *21*, 633.
3. (a) I. Ohtani, T. Kusumi, Y. Kashman, H. Kakisawa, *J. Org. Chem.*, **1991**, *56*, 1296. (b) T. Kusumi, T. Hamada, M. O. Ishitsuka, I. Ohtani, H. Kakisawa, *J. Org. Chem.*, **1992**, *57*, 1033.

(*Received in Japan* 7 *December* 1993; *accepted* 1 *March* 1994)