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# Determination of the Absolute Configuration of Ginnol, a Long-chain Aliphatic Alcohol, by Use of a New Chiral Anisotropic Reagent

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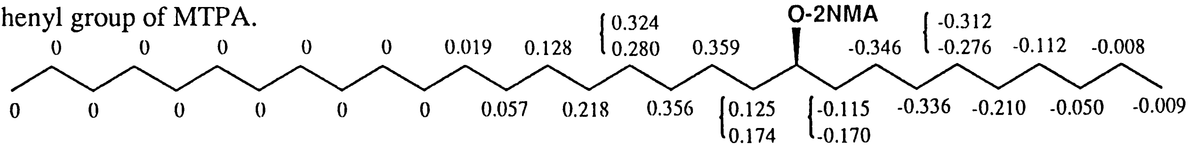
The absolute configuration of ginnol, 10-nonacosanol, has been determined by use of a new chiral anisotropic reagent, 2NMA (2-naphthylmethoxyacetic acid), which results in the marked upfield shifts of the protons located on the same side of the aromatic ring.

Ginnol, 10-nonacosanol (**1**)1), is a component of wax produced by higher plants. Its structure has been determined by mass spectrum and synthesis.2) Its stereochemistry, however, has not been elucidated yet. As in the case of **1**, the absolute configurations of many similar aliphatic alcohols have remained undetermined, because there have been no good methods to establish the configurations of such a hydroxy group that is included in a long aliphatic chain, especially when the alcoholic group is located deep in the middle of the chain. We herein describe the elucidation of the absolute configuration of **1**, mp 81.0-82.0°, $[\alpha]_D$ +1.7° (c=1.50, $CHCl_3$), obtained from the pulverized dry leaves of *Ginkgo biloba* L.

We have previously demonstrated the versatility of new chiral anisotropic reagents, 1NMA (1-naphthylmethoxyacetic acid), 2NMA (**2**: 2-naphthylmethoxyacetic acid), and 9NMA (9-anthranylmethoxyacetic acid),3) the analogues of *O*-methylmandelic acid.4) Among them, **2** is a useful reagent for long-chain compounds because the anisotropic effect of 2-naphthyl group reaches farther than others.3,5)

Ginnol (**1**) was converted into (*R*) and (*S*)-2NMA derivatives (DCC/DMAP/$CHCl_3$). The $^1H$-NMR spectra (600 MHz, $CDCl_3$) of the respective diastereomers are shown in Fig. 1. Spectrum (a) of (*R*)-2NMA derivative shows well-separated signals assignable to methylene protons from 9 to 2 positions, which must be the same side of 2-naphthyl group when the (*S*)-configuration of the 10-hydroxy group is assumed. These methylene signals are easily correlated with a terminal methyl (1-$CH_3$) by analyzing the COSY spectrum. The terminal methyls show the signals separately, one at δ 0.87 (1: upfield shift) and the other at δ 0.88 (29: normal shift). On the contrary, the chemical shifts of the two methyls are the same in the (*S*)-2NMA diastereomer since the 2-naphthyl group directs toward the longer-chain side, but 29-$CH_3$ is too far to be affected by the anisotropy. Yet there are observed the remarkable upfield shifts of the methylene protons from 11 to 17 positions. The Δδ values, which verify the (*S*)-configuration of the hydroxy group, are shown in **1a**. It is noteworthy that only one diastereomer was necessary to determine the absolute configuration: For the long-chain aliphatic alcohols, when one (within 9 bonds from 2NMA-oxycarbon) of the methyl signals shifts upfield in the (*R*)-2NMA diastereomer, the configuration of the hydroxy group is *S* (*vice versa*).

The different chemical shifts of the two methyls are still detectable in (*R*)-2NMA-**1** even at 200 MHz (Fig. 1c). The conventional MTPA method[6] was not applicable to **1** because of the smaller anisotropy of the phenyl group of MTPA.



**1a**

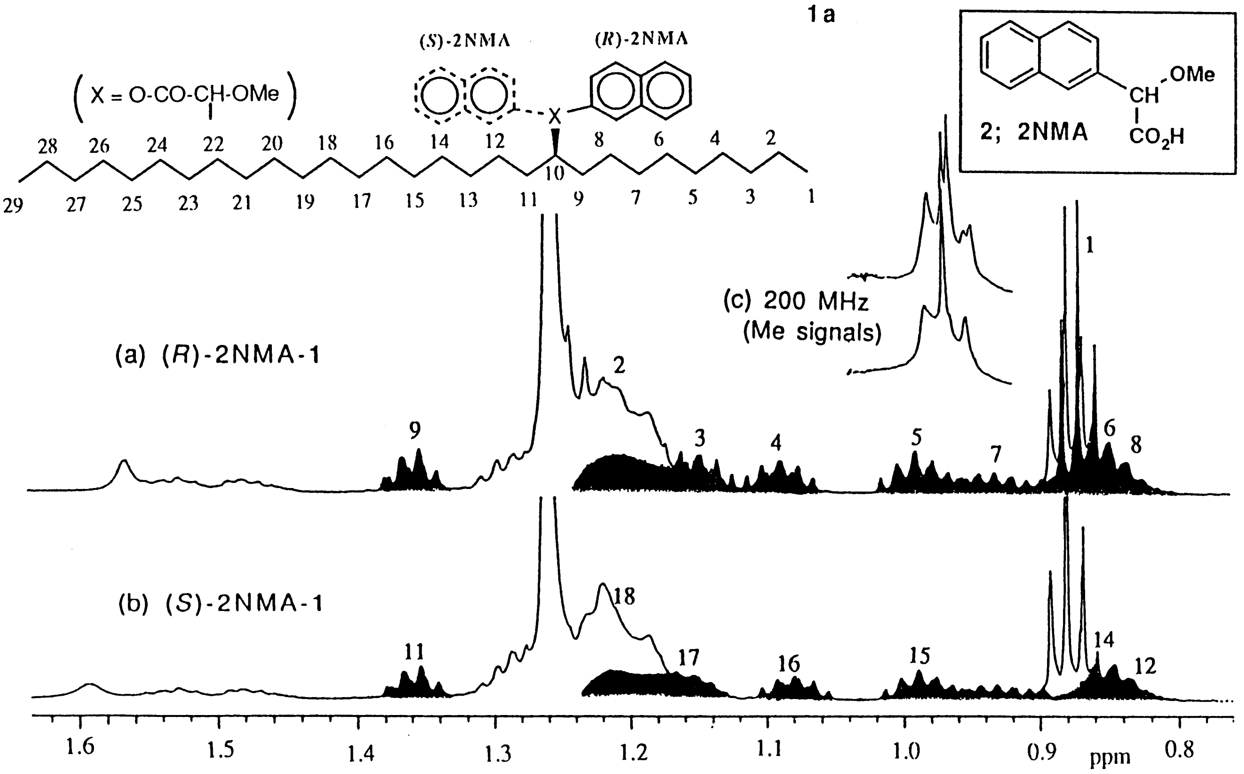


Fig. 1. Parts of the $^1$H-NMR spectra (600 MHz, $CDCl_3$) of (a) (*R*)-2NMA-**1** and (b) (*S*)-2NMA-**1**. (c) The methyl signals of (*R*) (above) and (*S*) (below)-2NMA-**1** measured at 200 MHz.

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