Pergamon

Tetrahedron Letters, Vol. 35, No. 7, pp. 993-994, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $6.00+0.00

0040-4039(93)E0390-6

STEREOCHEMISTRY OF ENYNOLS - A CAVEAT ON THE EXCITON CHIRALITY METHOD

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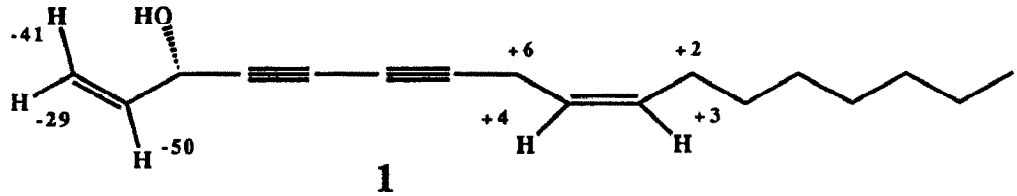
Abstract: The exciton chirality method, as applied to secondary allylic alcohols, cannot be extended to secondary alcohols flanked by two chromophores.

As part of our search for natural products with differential cytotoxicity toward human tumor cell lines,[1,2] we have been investigating falcarinol, **1**, and a series of related compounds from the tropical plant *Dendropanax arboreus* (unpublished data). As part of that study, we sought to define the absolute configuration of our isolate. Our compound was dextrorotatory ($[\alpha]_D$ + 29°, c 0.57, $CHCl_3$), suggesting that it had the 3S configuration, since Lemmich *et al.* proposed the 3R configuration for (-)-falcarinol.[3] Because all previous reports of the optical activity of falcarinol (panaxynol) indicated a levorotatory compound,[3-6] we sought independent confirmation of our assignment via the modified Mosher's method.[7,8] Both the R -and S-MTPA esters of **1** were prepared and the δ_s-δ_R values,-as illustrated in **1**, confirmed the 3S configuration.



1

We then discovered a report in this journal[9] that panaxynol possessed the 3S configuration. This assignment was based on CD spectra of the *p*-bromobenzoate and *p*-dimethylaminobenzoate derivatives of panaxynol. The authors based their assignment on an extension of the application of the exciton chirality method for secondary allylic alcohols.[10] However, the chiral secondary alcohol in **1** (either enantiomer) is flanked by two chromophores, an isolated olefin and a conjugated diyne. It is not readily apparent which, if either, chromophore would couple preferentially to the benzoate chromophore. To complete our analyses of falcarinol and to relate our isolate to the panaxynol of Shim, *et al.*,[9] we prepared the *p*-bromobenzoate of **1** and recorded its CD spectrum ($\Delta\epsilon_{248}$ +8.7, $\Delta\epsilon_{239}$ +7.6, see Figure 1). The spectrum matched that of Shim in wavelength and intensity, but was opposite in sign.

We have clearly established the absolute configuration of our falcarinol as 3S; its optical rotation is opposite in sign to that reported in the literature for (-)-falcarinol[3] and the Mosher method strongly

supported the 3S stereochemistry. Therefore, Shim's panaxynol must be 3R and the exciton chirality method cannot be used to assign unequivocally the stereochemistry of secondary alcohols flanked by two chromophores. We are aware of two subsequent reports of stereochemical determinations based on reference 9.[11,12] In view of the results presented here, those assignments should be reconsidered.[13]

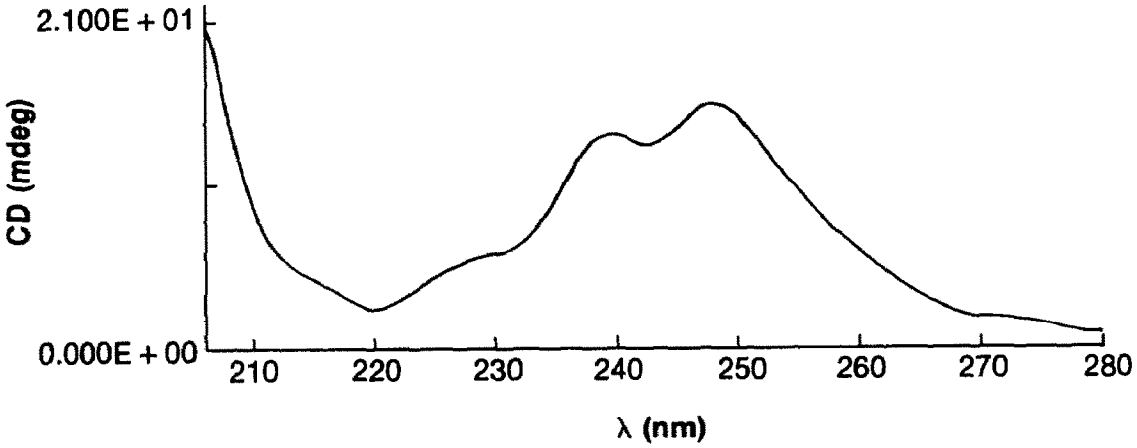


Figure 1. CD Spectrum of the *p*-Bromobenzoate of (+)-Falcarinol (**1**).

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13. We thank Dr. Jane Fayer, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, and Dr. Anthony Dipple, Advanced BioScience Laboratories, Inc., for use of their CD spectropolarimeters.

(Received in USA 26 October 1993; revised 24 November 1993; accepted 10 December 1993)