# NOTE

## A CONVENIENT REGIO- AND STEREOSPECIFIC SYNTHESIS OF $^2$H-LABELLED METHYL *trans*-CHRYSANTHEMATE

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**Summary**

The methyl ester of *trans*-chrysanthemic acid (a constituent of natural pyrethrins) has been regio- and stereospecifically deuteriated in the olefinic (76%D) and the cyclopropane ring (67%D) protons in a one stage synthesis as shown by $^1$H nmr spectroscopy.

**Key Words:** [1-$^2$H],2,2-Dimethyl-3-(2-methylprop[1-$^2$H]enyl)cyclopropane carboxylic acid ester, synthesis, pyrethrins, insecticides.

The high insecticidal activity and low mammalian toxicity of the pyrethrins have encouraged the development of synthetic routes to a key parent acid, *trans*-chrysanthemic acid.[1] The increasing interest in chrysanthemic acid (**1**) is due to the fact that flowers of *Chrysanthemum cinerariifolium* (from which pyrethrins and cinerins are extracted) are not readily available and also because of the growing use of pyrethrins as domestic insecticides.[2] Several syntheses of chrysanthemic acid have appeared in the literature.[2] In the present paper, we wish to report on the synthesis of the methyl ester of this important acid, labeled with deuterium in the olefinic part and the cyclopropane ring. [2,4-$^2H_2$]Methyl-4-oxo-2-butenoate, a potential useful intermediate in the synthesis of the labeled acid was stereoselectively prepared in our previous study[3] through the ozonolysis of [2,4-$^2H_2$] methyl sorbate.[4] Using this intermediate as the starting material and isopropylidene

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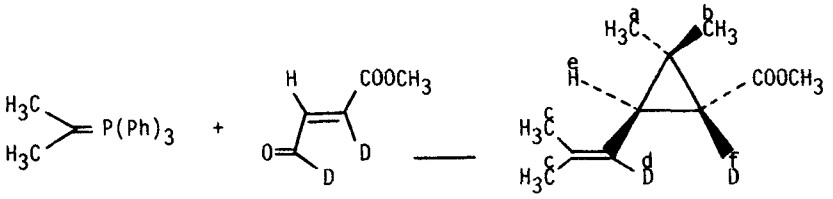
0362-4803/85/101093-03$01.00

Received May 1, 1985
Revised June 4, 1985

triphenyl phosphorane[5] as its complementary partner, we prepared deuteriated methyl trans-chrysanthemate stereospecifically in 66% yield by simply stirring a mixture of THF solutions of the [2,4-$^2H_2$]methyl-4-oxo-2-butenoate (1 equivalent) and the isopropylidene triphenyl phosphorane (2.5 equivalent) for 3 hr at 10°C.



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According to Krief et al.[2], the chrysanthemic ester can arise from two isopropylidenes, and the ylid reacts both at the carbonyl of the aldehyde and at the activated carbon-carbon double bond. However, the $^1H$ nmr spectrum of the deuteriated compound, as compared with that of the authentic sample[7], confirmed the regiospecificity of the deuterium through the marked reduction in intensity of the olefinic and cyclopropane ring protons (Table). The stereospecificity of labelling was also confirmed through the nmr data as shown in the table and compared with the literature values.[8] Synthesis of $^2H$-labeled pyrethrins and cinerins using the target molecule as an intermediate is underway for further studies on these insecticides.

Table: $^1H$ nmr data for deuteriated* and non-deuteriated** methyl trans-chrysanthemate (chemical shifts in ppm).[6]

| | $^aCH_3$ (s) | $^bCH_3$ (s) | $^cCH_3$ d(J≈1.4) | $^dH$ dm(J≈7.8)† | $^eH$ dd(J≈5 and 8) | $^fH$ d(J≈5)† | $-OCH_3$ (s) |
|---|---|---|---|---|---|---|---|
| ** | 1.25 | 1.11 | 1.69 | 4.91 | 2.1 | 1.37 | 5.67 |
| * | 1.27 | 1.12 | 1.70 | 4.96+ | 2.1 | 1.40+ | 5.67 |

† Resonance partly obscured

+ Slight difference in the chemical shifts probably due to the deuterium isotope effects.

**Acknowledgement**

Appreciation is due to Professor J.L. McLaughlin for help in editing this paper.

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7. An authentic sample kindly provided by Dr. M. Shadman, University of Tehran, Iran.
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