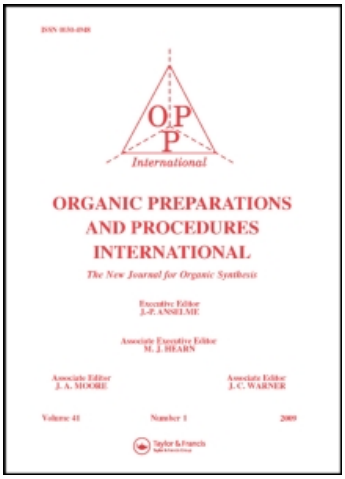

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A CONVENIENT REGIOSPECIFIC AND STEREOSELECTIVE SYNTHESIS OF [2,4-$^2H_2$]METHYL-*trans*-4-OXO-2-BUTENOATE

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A CONVENIENT REGIOSPECIFIC AND STEREOSELECTIVE SYNTHESIS OF [2,4-$^2H_2$]METHYL-trans-4-OXO-2-BUTENOATE

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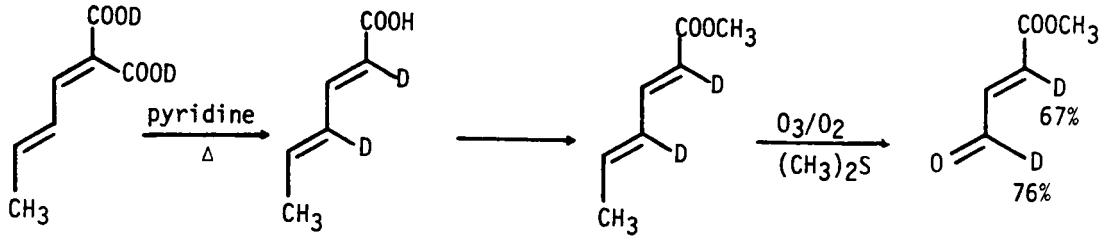
In the course of our studies on natural pyrethrins as domestic insecticides, we required some stereospecific deuteriated chrysanthemic acid. We took advantage of the condensation of crotonaldehyde with $CH_2(CO_2D)_2$ to give the dicarboxy-deuteriated crotonylidenemalonic acid (1), which upon heating in pyridine, afforded sorbic acid (2) bearing a label at both the 2- and 4-positions.[1,2]



1 2 3 4

The ^1H nmr spectrum confirmed the regiospecificity of deuterium through the marked reduction in intensity of the 2- and the 4-positions. The two-site labeling also occurred when a mixture of crotonaldehyde, pyridine, malonic acid, and a trace of tritiated water was kept at room temperature and later heated at 110° for 6 hrs. In this case, the labeling of sorbic acid was demonstrated unambiguously by the two-line ^3H nmr spectrum obtained with ^1H decoupling. We proposed that in boiling pyridine, the monodecarboxylation of crotonylidenemalonic acid in good yield is accompanied by lactonization followed by ring opening,[3] thus resulting in

transfer of the carboxy deuteron to both 2- and 4-positions. In the present study, the labeled acid was methylated[4] and subjected to ozonolysis according to the procedure described by Stotter and Eppner.[5] [2,4-$^2H_2$]Methyl sorbate gave excellent results and afforded as high as 90% yield of [2,4-$^2H_2$]methyl trans-4-oxo-2-butenoate (4) by ozonolytic cleavage (method A).[5,6] The stereoselective preparation of the target molecule is made possible by the highly electrophilic ozone which selectively attacks the Δ^4 double bond of the deuterated methyl sorbate because of the lower electron density at the Δ^2 double bond due to π-conjugation and σ-induction by the carbonyl group.[5]

REFERENCES

• Visiting Assistant Professor, Department of Medicinal Chemistry and Pharmacognosy, School of Pharmacy and Pharmacal Sciences, Purdue University, West Lafayette, Indiana 47907.

1. J. A. Elvidge, J. R. Jones, R. B. Mane and M. Saljoughian, J. Chem. Soc. Perkin Trans. I, 1191 (1978).

2. [2,4-$^2H_2$]Sorbic acid [0.35 g. from crotonaldehyde (0.50 g.), malonic acid-D_2 (0.6 g.) and pyridine (0.5 ml)],[1] mp. 133-134°; MS: M^+ 114; nmr ($CDCl_3$): δ 5.77 (d, J = 15.5 Hz, 2-^1H, 33% ⟷ 2-^2H, 67%) and 6.25 (m, 4-^1H, 24% ⟷ 4-^2H, 76% incorporation); a Varian FT-80 MHz Spectrometer was used for these studies.

3. A. Riedel, Ann., 361, 96 (1908).

4. A. B. Sen and V. S. Misra, J. Indian Chem. Soc., 26, 149 (1949).

5. P. L. Stotter and J. B. Eppner, Tetrahedron Lett., 2417 (1973).

6. [2,4-$^2H_2$]Methyl trans-4-oxo-2-butenoate, mp. 41°; MS: M^+ 116; nmr ($CDCl_3$): δ 6.90 (d, J = 15.8, 2-^1H, 33% ⟷ 2-^2H, 67%) and 9.75 (d, J = 7.8, 4-^1H ⟷ 4-^2H, 76% incorporation).