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CONFIGURATION OF INTERMEDIATES IN THE TOTAL SYNTHESIS OF D(-) SHIKIMIC ACID

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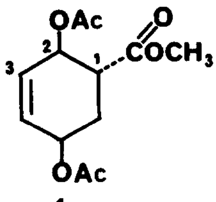
Recently two groups of authors have reported their pmr studies on an intermediate obtained in total synthesis of shikimic acid (1,2). However, since our results were reported previously (3), but not in a primary journal, we feel impelled to record our studies at this time.

The first step in the total synthesis of shikimic acid reported by us was the Diels-Alder condensation of trans, trans-1,4-diacetoxybutadiene and methyl acrylate (4). The stereochemistry of the adduct, as shown in 1, was assigned on the basis of the chemical behavior of the acetonide of the hydroxylated intermediate, 2.

In a similar reaction, McCrindle, *et al.* (5) assigned the opposite stereochemistry at C-1 to their adduct 3 (R = H) and the corresponding acetonide 4. We immediately noticed the discrepancy and reinvestigated the problem. The pmr spectra of the adduct and the acetonide were measured in chloroform-*d* solution, using tetramethylsilane as internal standard, on a 60MHz spectrometer (Fig. 1). The methine proton at C-1 of the acetonide appeared in an eight-lined pattern at τ6.80-7.17, with three coupling constants 11.5, 4, and 3Hz. The same eight-lined pattern was in benzene solution in the 100Hz spectrum. This pattern was accounted for by one axial-axial and two axial-equatorial couplings, with the assumption that the cyclohexane ring was in a slightly deformed chair conformation [the detailed discussion has appeared elsewhere (3)]. Accordingly, our acetonide must have the stereochemistry as assigned by McCrindle, *et al.*, and assume the conformation 5.

The C-1 of the adduct must have the same absolute configuration as that of the acetonide. The adduct, therefore, had the stereochemistry as shown in 3 ($R = CH_3$) instead of 1. The approximately six-lined pattern of H_{C-1} (centered at τ7.2, J = 11.5, 3, and 3Hz) indicated the molecule existed in a half-chair conformation 6 (Fig. 2). Therefore, we have unambiguously established the correct stereochemistry of the Diels-Alder adduct and revised our previous assignments.

We observed that the acetonide 4 underwent facile elimination of acetic acid upon heating in a sealed tube, affording the olefin 7 in excellent yields. The overall reaction is a thermal *trans*-β-elimination, which has been hitherto unknown. Further work to prove this mechanism unequivocally is approaching a conclusion and will be published in a separate paper.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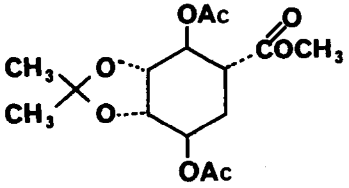
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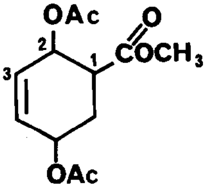
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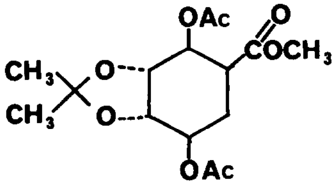
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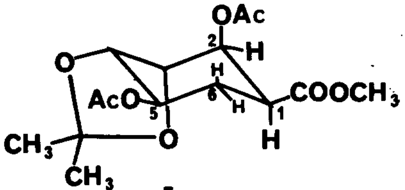
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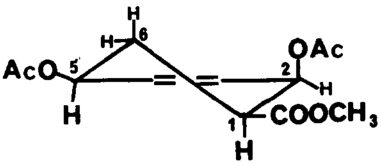
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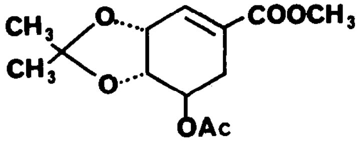
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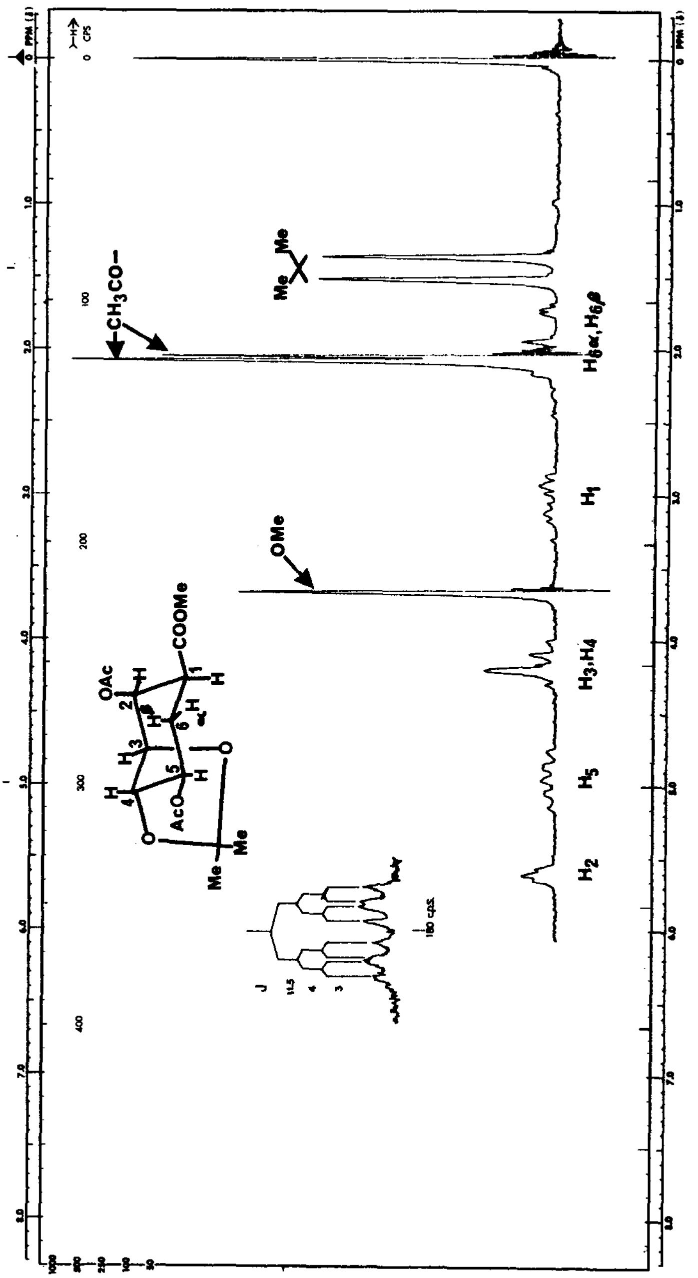
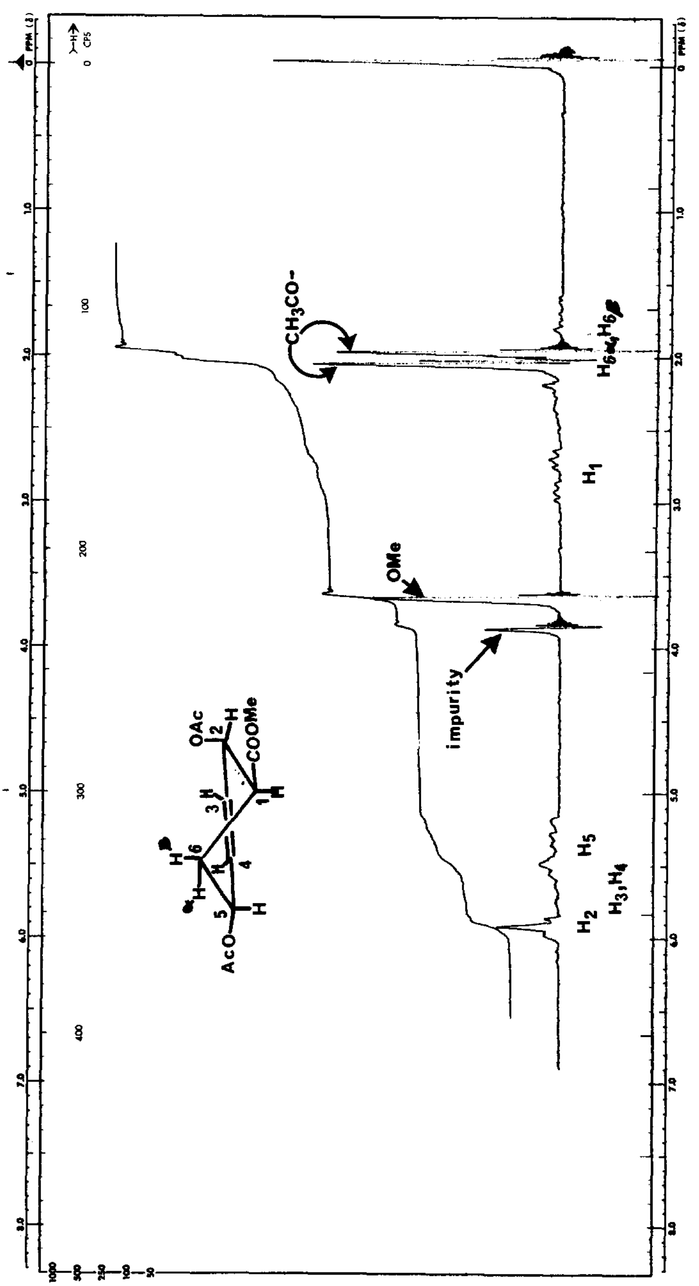

0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
PPM (δ)
0 CPS
100
200
300
400
CH$_3$CO-
Me
Me
OMe
H$_{6α}$, H$_{6β}$
H$_1$
H$_3$;H$_4$
H$_5$
H$_2$
OAc
COOMe
AcO
Me
Me
J
11.5
4
3
180 cps

FIGURE 1

FIGURE 2


PPM (δ)
CPS
0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
100
200
300
400
1000
500
250
100
50
CH3CO-
OMe
impurity
H1
H2
H3,H4
H5
H6α,H6β
OAc
COOMe
AcO
1
2
3
4
5
6
H