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SYNTHESIS OF HEXAACETYLTETRAHYDROAUCUBIN A

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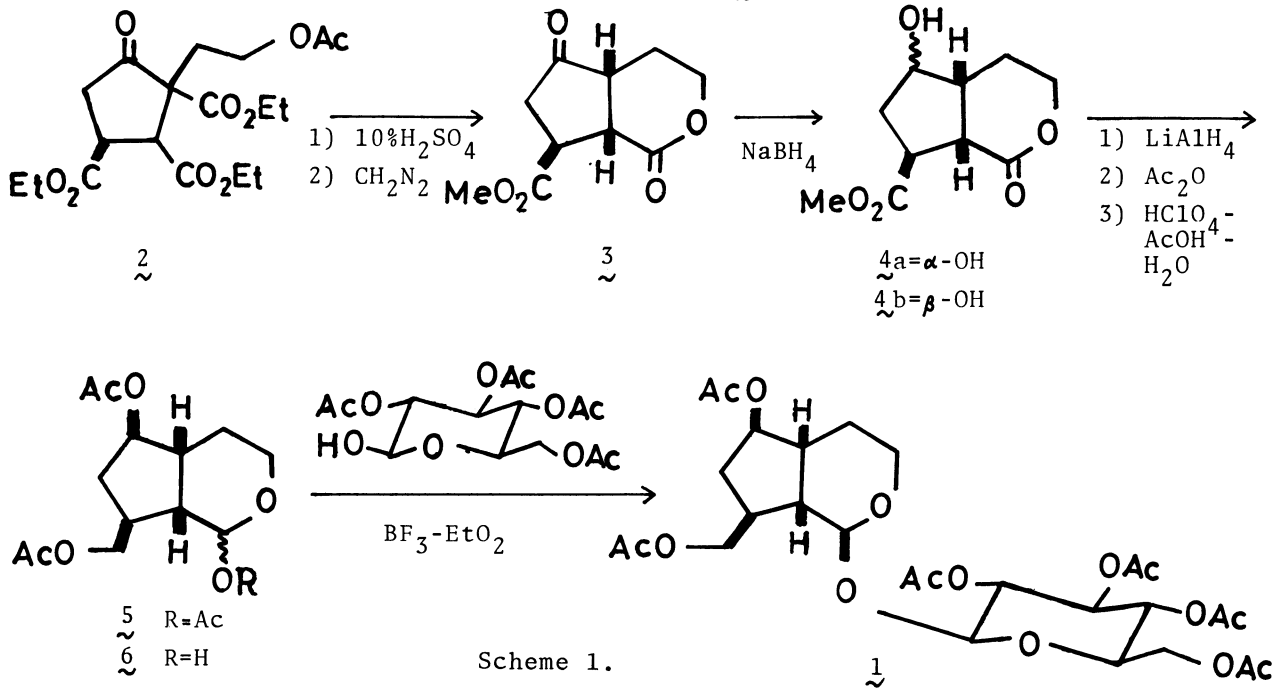
The synthesis of hexaacetyltetrahydroaucubin A, (1S,4aR,5R,7S,7aR)-5-acetoxy-7-acetoxymethyl-1-(2,3,4,6-tetraacetyl-β-D-glucopyranosyloxy)-octahydrocyclopenta[c]pyran, has been carried out.

Hexaacetyltetrahydroaucubin A, one of the derivatives of aucubin,[1] was first obtained by Fujise et al.,[2,3] in 1955. The structure of this derivative is presumed to be 1, (1S,4aR,5R,7S,7aR)-5-acetoxy-7-acetoxymethyl-1-(2,3,4,6-tetra-acetyl-β-D-glucopyranosyloxy)octahydrocyclopenta[c]pyran, on the basis of the structure of aucubin.[4] In connection with our synthetic studies of aucubin, we investigated the synthesis of 1 via a bilding block, (4aRS,7SR,7aSR)-7-(methoxy-carbonyl)octahydrocyclopenta[c]pyran-1,5-dione (3), as shown in Scheme 1.



2 3 4a=α-OH 4b=β-OH

5 R=Ac
6 R=H

Scheme 1.

Hydrolysis and decarboxylation of 2[5] by heating with 10% sulfuric acid, followed by methylation with diazomethane gave 3, mp 118-119 °C, in a 13% yield. Although the reduction of 3 with $NaBH_4$ in tetrahydrofuran gave a mixture of two alcohols, 4a, mp 107-108 °C, and 4b, mp 60-61 °C, in 12% and 48% yields, respectively, the compound 4a was only obtained by the catalytic hydrogenation of 3 using Raney nickel catalyst. Provided that the approach of the catalyst occurs from the less hindered β-side, 4a is assigned as α-alcohol.[8]

The partial reduction of 4b with $LiAlH_4$ in tetrahydrofuran at 0 – 5 °C (10 h) followed at room temperature (5 h) to afford triol (37%), which was immediately acetylated with acetic anhydride-pyridine to give triacetate (5) as an anomeric mixture in a 95% yield. The partial hydrolysis of 5 to 6, an anomeric mixture of racemic aglycons of 1, was accomplished in aqueous acetic acid containing perchloric acid in a 72% yield. The idea of Büchi's loganin synthesis[9] has been applied to the final glucosylation of 6, that is, rather than to resolve the aglycon 6 into enantiomers and to combine the correct enantiomer with suitable derivative of glucose, we decided to transform racemic 6 to a glucoside and separate the resulting mixture of diasteromers. Effort to combine the hemiacetal 6 with 2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl bromide using the original Koenigs-Knorr conditions gave no trace of 1. Then we attempted the glucosylation of 6 with 2,3,4,6-tetra-O-acetyl-β-D-glucopyranose in the presence of BF_3-Et_2O at low temperature. The reaction product was chromatographed on silica gel using chloroform-benzene (3:2) as an eluent to give 1, mp 158-159 °C, in a 6.5% yield. The IR and ^{1}H-NMR spectra of this compound were completely identical with those of natural sample.

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References

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2) Y. Iwanami, Y. Hotta, T. Kubota, S. Fujise, T. Ishikawa, and H. Uda, Nippon Kagaku Zasshi, 76, 77 (1955).
3) Hexaacetyltetrahydroaucubin B, a stereoisomer of 1, has also been obtained.[2]
4) H. Uda, M. Maruyama, K. Kabuki, and S. Fujise, Nippon Kagaku Zasshi, 85, 279 (1964); N. Masaki, M. Hirabayashi, K. Fuji, K. Osaki, and H. Inouye, Tetrahedron Lett., 25, 2367 (1967).
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6) The configuration of 3 was confirmed by the oxidative derivation into c-2,t-3-dicarboxy-5-oxo-r-1-cyclopentylacetic acid, mp 142-143 °C, which easily isomerized into the known c-3,t-2-dicarboxy-5-oxo-r-1-cyclopentylacetic acid.[7] The C_7-epimer of 3 has already been synthesized by us.[5]
7) K. Kurosawa and H. Obara, Bull. Chem. Soc. Jpn., 39, 529 (1966).
8) The C_6-proton signals of the acetates, 4a (mp 67-68 °C, δ 4.82, ddd, $J_{6,5}=J_{6,7A}=J_{6,7B}=6.0$ Hz) and 4b (mp 78.5-79.5 °C, δ 5.27, dt, $J_{6,5}=J_{6,7A}=4.2$ Hz, $J_{6,7B}=1.2$ Hz), in their ^{1}H-NMR spectra (200 Mz) also support the α- and β-alcohol configurations of 4a and 4b, respectively.
9) G. Büchi, L. A. Carlson, J. E. Powell, Jr., and L. F. Tietze, J. Am. Chem. Soc., 95, 545 (1973).

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