Biochemical Studies on "Bakanae" Fungus. Part 74.
Synthesis of Substances Related to Gibberellins.
Part XVI. An Alternate Synthetic Route to a Gibbane-10-Carboxylic Acid.

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Synthesis of the C-10 epimer of racemic desoxogibberic acid is described.

After the completion of the synthesis of (±)-epigibberic acid (I) and (±)-gibberic acid (II),1 other synthetic approaches to tetracyclic gibbane compounds were also investigated. This paper describes the alternate synthesis of C-10 epimer of (±)-desoxo-gibberic acid (V) by the application of the Barbier-Wieland degradation of an ester (III).

The treatment of the ester (VI) obtained previously2 with boron trifluoride etherate and ethanedithiol in chloroform at room temperature gave an oily thioketal (VII). The structure was proved by the disappearance of five-membered ring ketone function in IR spectrum (1740 cm⁻¹). This oily thioketal was converted into an oily C-10 epimer of methyl (±)-desoxohomogibberate (III) by refluxing in dioxane containing Raney nickel W-7. Crystalline acid (IV), m.p. 156~157°C, was obtained from this oily ester by saponification with methanolic potassium hydroxide. The above oily ester was subjected to the Barbier-Wieland degradation to give a gummy acid. The chromatography on silicic acid gave a crystalline acid by elution with benzene-ethyl acetate. This acid was identified to the C-10 epimer of (±)-desoxogibberic acid (V) by the comparison of IR spectrum and the mixed melting point determination with the authentic sample.3

EXPERIMENTAL

All melting points were uncorrected. Infrared spectra were measured as Nujol mulls for solid samples and as films for liquid samples, unless otherwise stated. Ultraviolet spectra were determined for ethanol solution.

8-Dithioethylene ketal of C-10 epimer of (±)methyl 6-oxo-dehydrohomogibberate (VII). C-10 Epimer of methyl (±) 6-oxodehydrohomogibberate (VI, 250 mg) in chloroform (5 ml) was allowed to stand at room temperature overnight with boron trifluoride etherate (0.6 ml) and ethanedithiol (0.6 ml), and then poured into ice water. Organic layer was washed with saturated saline and dried over sodium sulfate.

Evaporation of the solvent gave an oil (VII, 240 mg). $\nu_{\text{max}}$ (liq. film) 1726, 1660, 1628, 1600, 1430, 1165, 866, 790 cm$^{-1}$. This oil was used for the next reaction without further purification.

**C-10 Epimer of methyl \((\pm)\) desoxohomogibberate (III).** The above thioketal (VII, 220 mg) in dioxane (20 ml) was refluxed for 16 hrs with Raney nickel W-7 (5 g). The catalyst was filtered off. Evaporation gave oily ester (III, 160 mg). $\nu_{\text{max}}$ 1736, 1600, 1256, 1155, 756 cm$^{-1}$. The corresponding acid was obtained as follows. The oily ester (III, 50 mg) in methanol (3 ml) containing potassium hydroxide (300 mg) was refluxed for 4 hrs and methanol was evaporated. The residue was diluted with water. Acidification with dil. hydrochloric acid gave C-10 epimer of \((\pm)\) desoxohomogibberic acid as crystals (40 mg). Needles from ethyl acetate-petroleum ether, m.p. 156~157°C. Anal. Found: C, 80.05; H, 8.17. Calcd. for C$_{19}$H$_{24}$O$_2$: C, 80.24; H, 8.51%. $\nu_{\text{max}}$ 1695, 1600, 955, 760 cm$^{-1}$.

**C-10 Epimer of \((\pm)\) desoxogibberic acid (V).** To phenyl magnesium bromide from bromobenzene (0.6 g) and magnesium (0.1 g) in ether (15 ml) was added the ester (III, 150 mg) in ether (5 ml), and the mixture was refluxed with stirring for 3 hrs. To the resulting solution were added 5N-hydrochloric acid (14 ml) and ice. Organic layer was washed with dil. hydrochloric acid, water, 5% aq. sodium hydroxide and water successively. After evaporation, the residue was steam-distilled for 2 hrs to remove biphenyl and then extracted with ether. Ether layer was dried over sodium sulfate. Concentration gave an oil. This oil was refluxed in acetic acid (5 ml) and acetic anhydride (2 ml) for 1 hr. Solvent was evaporated. To the residue in acetic acid (5 ml) was added chromic anhydride (100 mg) in aq. acetic acid (10 ml acetic acid and 0.5 ml water) with ice cooling, and then the reaction mixture was heated at 50°C for 20 min. After cooling and decomposition of excess chromic anhydride with methanol, solvent was evaporated in vacuo. The residue was diluted with water and extracted with ether. Working up of the acidic fraction gave an oily acid. The acid in ethyl acetate was chromatographed over silica gel (81 cm) in benzene. Eluted successively with; (1) benzene, 50 ml. (2) benzene-ethyl acetate (1:1), 50 ml. (3) benzene-ethyl acetate (1:2), 50 ml. (4) benzene-ethyl acetate (1:2), 50 ml. (5) benzene-ethyl acetate (1:5), 50 ml. (6) ethyl acetate, 50 ml. The fraction (5) after evaporation afforded crystalline acid (V, 7 mg), identified with the authentic specimen$^3$ by mixed m.p. determination and infrared measurement. Evaporation of the solvent of other fraction afforded oily product (30 mg).