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BIOCHEMICAL STUDIES ON "BAKANAE" FUNGUS. PART 75. SYNTHESIS OF SUBSTANCES RELATED TO GIBBERELLINS. PART XVII A SYNTHESIS OF C-19 GIBBANE COMPOUND.*

Tomoya Ogawa, Kenji Mori, Masanao Matsui and Yusuke Sumiki

Dept. of Agricultural Chemistry, Faculty of Agriculture

University of Tokyo, Bunkyo-ku, Tokyo, Japan.

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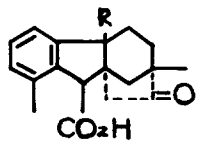
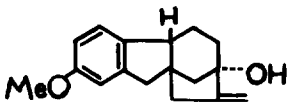
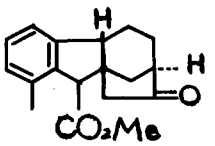
Among many polycyclic terpenes already discovered in Nature, gibberellins are the interesting substances from the synthetic point of view, not only because of their structural characteristics which present a considerable challenge to synthetic organic chemists but also their well known biological activities. In recent years, synthesis of compounds having gibbane skeleton - (±)-gibberic acid (I)[1,2], (±)-epigibberic acid (II)[1], gibbane alcohol (III)[3], (±)-desoxyepiallogibberic acid methyl ester norketone (IV)[4] - have been described.



I R= ---H
II R= —H



III



IV

The present communication describes the synthesis of C-19 gibbane compound (V) from the oily alcohol (VI) which has been prepared from 6-methoxy tetralone[5] according to the synthetic sequence already published[6,7].

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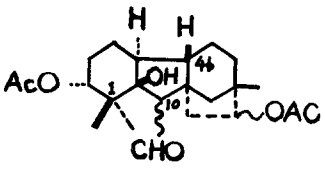
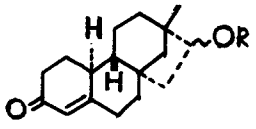
* Part XVI, T. Ogawa, K.Mori, M. Matsui and Y. Sumiki, Agr. Biol. Chem., in press. This paper is also regarded as part V of " Experiments directed toward the total synthesis of polycyclic terpenes.

Acetylation of the alcohol (VI) gave the acetate (VII) which was methylated with methyl iodide and potassium tert. butoxide in tert. butanol. Sodium borohydride reduction of the resulting dimethyl derivative (VIII) and subsequent acetylation in acetic anhydride and pyridine followed by silicic acid - silver nitrate chromatography[8] afforded the diacetate (IX), m.p. 157-172°. The structure was determined by the following spectral data : ν_{max} ; 1735, 1375, 1255, 1031 cm^{-1} τ : 4.56 (1H, diffused doublet, J=5 cps, for C-6 olefinic proton); 5.27 (1H, quartet, J=5, 11 cps), 5.58 (1H, quartet, J=5,12 cps), these two set of quartets for C-3 axial proton[9] and C-16 proton; 7.97 and 7.99 (two 3H singlets for acetate methyls); 9.03 and 9.07 (6H singlet and 3H singlet for three tert. methyls). This diacetate (IX) was also obtained from the diketone (X)[7] by sodium borohydride reduction followed by acetylation.

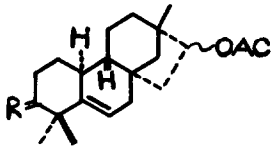
Ozonolysis of the diacetate (IX) and reductive cleavage of the ozonide by zink dust and acetic acid[10] gave the keto aldehyde (XI), m.p. 140-142°, of



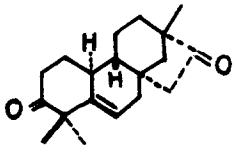
V



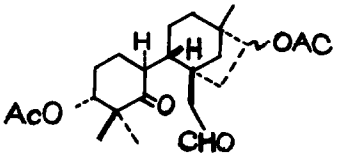
VI R=H
VII R=AC



VIII R=O
IX R=---OAC
—H



X



XI

Satisfactory analyses were obtained for all crystalline compounds.

which structure was determined by the following spectral data : ν_{max}; 1745, 1735, 1700, 1380, 1255, 1235 cm^{-1}. τ: 0.29 (1H, quartet, J= 2,4 cps, for aldehyde proton[11]), 5.36 (2H, overlaping quartets, for two C<u>H</u>OAc), 7.95 (6H, singlet, for two OCO<u>Me</u>), 8.84, 8.96 and 9.02 (three 3H singlets, for three tert. methyls).

Alumina chromatography of this keto aldehyde (XI) gave the gibbane compound (V), m.p. 158 - 162°, by intramolecular aldol condensation. ν_{max}: 3530, 1746, 1720, 1375, 1270, 1250, 1145, 1058, 1039, 970 cm^{-1}. The NMR spectra of this compound showed aldehyde proton at τ 0.22 (1H, doublet, J = 3 cps), C_2<u>H</u>OAc at τ 5.00 (1H, diffused quartet, low field shift of this proton signal was probably due to the deshielding effect of hydroxyl group at C-10a[12], so the hydroxyl group was assigned as β configuration and had 1,3 diaxial relationship with C-2 hydrogen), C_8<u>H</u>OAc at τ 5.39 (1H, quartet, J = 5, 11 cps), C_{10a}<u>OH</u> at τ 6.71 (1H, singlet, disappeared by the addition of deuterium oxide), C_{10}<u>H</u> at τ 7.43 (1H, doublet, J = 3 cps), C_2OCO<u>Me</u> and C_8OCO<u>Me</u> at τ 7.97 and 8.00 (two 3H singlets), C_1di <u>Me</u> and C_7<u>Me</u> at τ 9.02, 9.08 and 9.13 (three 3H singlets). From these spectral data the structure of this compound was determined as ($\pm$)-1,1-Dimethyl-2α, 8β-diacetoxy-10β-formyl-10aβ-oxy-4aα, 4bβ, 7α-gibbane which is a first synthetic C-19 gibbane compound.

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11. This split is probably due to the coupling with protons of adjacent methylene group which are regarded as magnetically non-equivalent. It has been known for some time that the geminal, non-cyclic, protons in compounds of the general type $RCH_2CR^1R^2R^3$ are often magnetically non-equivalent.
cf., G.M.Whiteside, J.I.Grocki, D.Holtz, H.Steinberg, J.D.Roberts, J. Am. Chem. Soc., 87, 1058 (1965)

12. A similar deshielding effect of hydroxyl group are known in steroid field.
cf., S.G.Levine, N.H.Eudy, C.F.Leffler, J. Org. Chem. 3995 (1966)