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EXPERIMENTS DIRECTED TOWARD THE TOTAL SYNTHESIS OF POLYCYCLIC TERPENES. PART VI. STEREOSELECTIVE OXIDATION OF METHYL GROUP.

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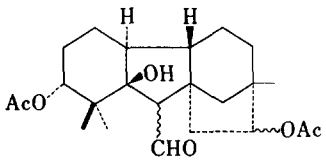
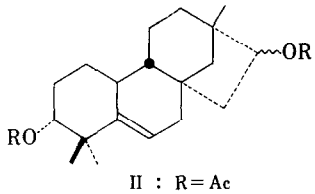
In the previous paper (1), we reported the synthesis of C-19 gibbane compound (I) from tetracyclic diacetate (II).

In this communication we wish to report the oxidative modification of C-4 methyl group of II by using the hydroxyl function which is to be attached axially at C-6. The compound having C-4 α oxygenated methyl group like IX seems to be a promising intermediate for the synthesis of gibberellins.



I

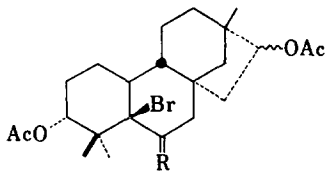


II : R=Ac
III : R=H

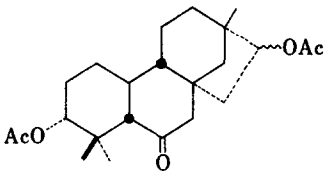
Treatment of diacetate (II) with NBA and perchloric acid in aq. dioxane (2) gave bromohydrin (IV), ν_{max} 3540, 1743, 1720, 1376, 1272, 1250 and 1028 cm^{-1}. Since some skeletal rearrangement seemed possible during bromohydrin formation, following chemical transformation were carried out to confirm the structure.

The oxidation of IV by chromic anhydride in pyridine gave bromoketone (V), m.p. 209-211°, ν_{max} 1743, 1714, 1380, 1370, 1260, 1030 cm^{-1}, which was reduced by zinc dust in acetic acid (2) to keto diacetate (VI), m.p. 199-201°. The structure was determined by the following spectral data: ν_{max} 1738, 1720, 1380, 1255, 1033 cm^{-1}. τ 5.26 (1H, quartet, J=5, 11 cps); 5.65 (1H, quartet, J=5, 12 cps); 7.57 (1H, doublet, J=12 cps, for C-5 β proton (3) which is coupled with C-10 α hydrogen); 7.98 (6H, singlet, for two acetate methyls); 8.90, 9.00, and 9.06 (three 3H singlets for three tert. methyls).

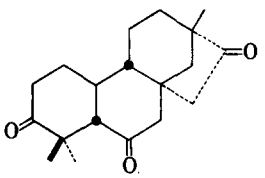
Saponification by sodium hydroxide in methanol and subsequent oxidation by Jones reagent gave the triketone (VII), m.p. 151-153°, which was identified with the triketone obtained from diol (III) by hydroboration (4) followed by alkaline hydrogen peroxide treatment and subsequent Jones oxidation. The spectral data are as follows: ν_{max} 1748, 1710, 1165 cm^{-1}. τ 8.70, 8.80, and 8.97 (three 3H singlets for three tert. methyls).



IV : R=—OH, —H
V : R=O



VI



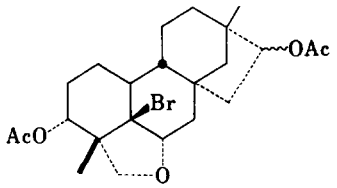
VII

By these transformations it was demonstrated that during the bromohydrin formation no skeletal rearrangement was occurred and that the hydroxyl group was attached to C-6.

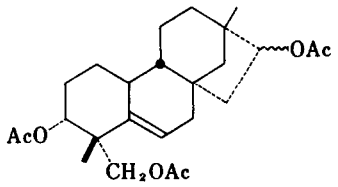
Treatment of IV with lead tetraacetate, calcium carbonate and iodine in boiling benzene (5) afforded bromo ether (VIII), m.p. 185-193°. The structure was determined by the following spectral data: ν_{max} 1740, 1375, 1250, 1030 and 970 cm^{-1}. δ (in benzene) 5.05 (1H, quartet, J=7, 10 cps); 4.80 (1H, quartet, J=5, 11 cps); 4.10 (1H, triplet, J=3 cps, for C-6 β equatorial (6) proton);

3.93 and 3.44 (2H, AB type signals, J=8 cps, for C-4 α methylene); 1.65 and 1.55 (two 3H singlets for two acetate methyls); 1.08 and 0.88 (two 3H singlets for two tert. methyls).

By treatment with zinc dust in acetic acid (5) VIII was transformed into triacetate (IX), m.p. 152-154°, the structure of which was determined by the following spectral data: ν_{max} 1740, 1375, 1250 and 1030 cm^{-1}. τ 4.47 (1H, multiplet, for C-6 olefinic proton); 5.37 (2H, overlapping quartets for C-3 β and C-16 protons); 5.46 and 6.16 (2H, AB type signals, J=12 cps, for C-4 α methylene); 7.97, 7.99 and 8.08 (three 3H singlets, for three acetate methyls); 8.93 and 9.06 (two 3H singlets, for two tert. methyls).



VIII



IX

REFERENCES

Satisfactory analyses were obtained for all crystalline compounds. NMR spectra were determined at 100 Mc in deuterochloroform, unless otherwise noted.

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3. The splitting is consistent with that expected for the proton at C-5 with an axial-axial interaction with hydrogen at C-10, and a dihedral angle of about 180°, thus confirming the structure of VI.

cf., N.S.Bhacca and D.H.Williams, Application of NMR Spectroscopy in Organic Chemistry, Holden-Day, Inc. San Francisco, London, Amsterdam. 1964 pp. 63-76.

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6. The splitting is consistent with that expected for the proton at C-6 with equatorial-axial and equatorial-equatorial interactions with C-7 methylene hydrogens, thus confirming the stereochemistry of tetrahydrofuran part structure of VIII.
cf., N.S.Bhacca and D.H.Williams, Application of NMR Spectroscopy in Organic Chemistry, Holden-Day, Inc. San Francisco, London, Amsterdam. 1964, pp. 77-85.

IR spectra were determined as nujol mulls for solid samples and as films for liquid samples.