Tetrahedron Letters No.29, pp. 2469-2471, 1969. Pergamon Press. Printed in Great Britain.

SKELETAL TRANSFORMATION OF PODOCARPIC ACID TYPE DITERPENE.*

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(Received in Japan 8 May 1969; received in UK for publication 19 May 1969)

In our research course on the chemical transformation of the representative diterpenes, as resin acids, their skeletal conversion has aroused our interest and has been undertaken since a few years ago.

Previously, aldol condensation of dioxo ester (II) obtained from methyl tetrahydro-deoxy-enantio-podocarpate (I) by oxidative cleavage of its B/C-ring juncture, selectively gave c-homofluorene type compound (III)[1], even though two other possible routes can be considered. The cyclization mode is consistent with analogous case in steroid field (IV⟶V)[2].

Besides the general-typed conversion as mentioned before, a synthesis of 6-7-5-membered fused ring system regarded as basic skeleton of poisonous aconitine (VI), also attracts our attention and is reported herein. For the synthetic purpose, deoxypodocarpic acid type compound (VII)[3] having 6α,17-epoxy bridge was chosen. Two advantages for the compound (VII) can be recognized: i) The rigid epoxy bridge could stereochemically suppress the general route (II⟶III), and ii) the bridge could assure a foothold to make a nitrogen bridge characterized in the structure of diterpene alkaloid.

Benzene ring of the acid (VII)[3] derived from l-abietic acid, was reduced by Li-$EtNH_2$-t-AmOH to give tetrahydro acid (VIII), m.p. 247-252°(dec.), τ 8.79(C_4-Me), 7.80(allylic H), 6.29 and 5.91(1H each, d.(J=7.8cps), C-C$\underline{H}_2$-O), 5.05(1H, broad, O-C$\underline{H}$-), no olefinic proton. Double bond of the corresponding ester (IX), m.p. 112-113°,

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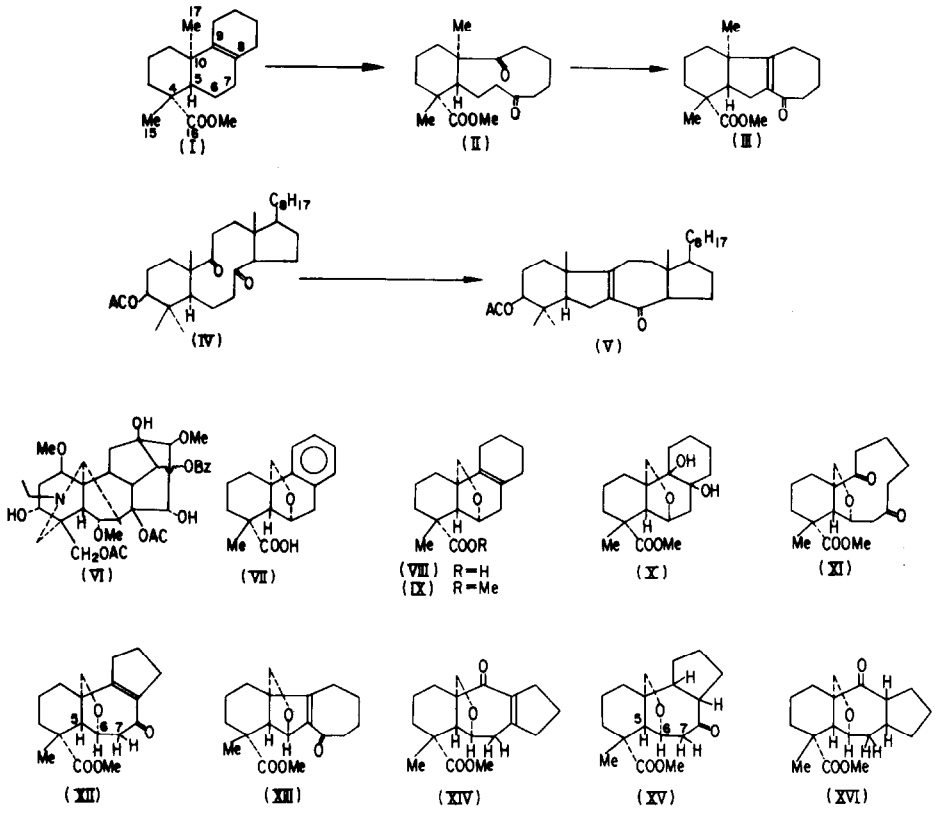
* New compounds indicated by m.p. gave satisfactory analytical values and had gas-liquid chromatographic purity. All NMR spectra were measured at 60Mc in $CDCl_3$ vs Me_4Si as internal reference. The NMR spectrometer was magnetic field sweep type.[4]



obtained by CH_2N_2-treatment of (VIII), was hydroxylated by osmiumtetroxide to give dihydroxyl ester (X), m.p. 153-155°, $\nu_{max}^{CCl_4}$ 3600, 3500, 1730cm^{-1}, τ 6.39 and 6.04(1H each, d.(J=9.6cps)), 5.50(1H, broad). Absence of NMR absorption due to proton attached to the same carbon atom as hydroxyl function in (X), evidently shows that two hydroxyl groups locate at the ring juncture C_8 and C_9. Cis β-configuration of the dihydroxyl groups can be assumed on the basis of stereochemical reaction mechanism. Vic-glycol cleavage of (X) by lead tetraacetate afforded dioxo ester (XI), m.p. 75-76.5°, $\nu_{max}^{CCl_4}$ 1740, 1705cm^{-1}.

The condensation in question of dioxo ester (XI) was performed under acidic condition. The reaction mixture consists of two components in ratio of 4 : 1, both of which are different from the starting material (XI). Main product (XII), m.p. 134-142°, ν_{max}^{KBr} 1725, 1640, 1610cm^{-1}, τ 8.76(3H, s., C_4-Me), 7.05-7.55(about

6H, active methylene), 6.28(3H, s., COOMe), 6.40 and 5.87(1H each d.(J=7.8cps), C-C$\underline{H}_2$-O), 5.36(1H, sextet, O-C$\underline{H}$-). Catalytic hydrogenation (10% Pd-C, 4.2kg/cm^2) of the cyclized compound (XII) gave mixed dihydro compound, GLC; two peaks(10 : 1), whose minor product was epimerized with mineral acid to major product (XV), m.p. 79°, ν_{max}^{KBr} 1730, 1695cm^{-1}, τ 8.79(3H, s., C_4-Me), 7.17(1H, q.(J=16.2, 3.0cps)) and 7.64(1H, q.(J=16.2, 3.6cps)), CO-C$\underline{H}_2$-CH-O, 6.30(3H, s., COOMe), 6.06(2H, t.(J=9cps), C-C$\underline{H}_2$-O), 5.46(1H, sextet, O-C$\underline{H}$-).

In order to elucidate the compound as (XII) exclusive of two other possible structures, nuclear magnetic double resonance method was applied. NMR pattern due to C_6-proton (5.36τ, sextet) changes into doublet (J=1.5cps) and triplet (J=3.6cps) by irradiation at one position (7.23τ, C_7-active methylene; 112cps higher from C_6-H) and the other (8.03τ, C_5-H; 160cps higher from C_6-H) respectively. In consideration of the coupling with C_5-methine proton, it can be ascertained that C_6-proton should be adjacent to and coupled with active methylene protons and, accordingly, the structure (XIII) having no adjacent methylene group can be canceled among three possible structures (XII), (XIII) and (XIV). Appearance of six protons in active methylene field also supports the above assumption.

Successively, similar decoupling experiment was also applied to the reduced compound (XV). Each irradiation at C_6-proton signal (5.46τ, sextet) sharpened the signal, 110cps higher from that of C_6-H, and also the other, 121cps higher, both composing the inner two doublets of the AB octet part (7.30 and 7.51τ, active methylene region) in the ABX system. The fact that C_6-proton of the reduced compound is still situated at adjacent position to active methylene, is only understandable by the former between the survived two structures (XV) and (XVI).

Conclusively, resin acid diterpene can be now transformed into the type (XII) in addition to the synthesis of the other type (III) previously reported.

Financial support from the Ministry of Education (Grant-in-Aid for Scientific Research, No. 8745) are gratefully acknowledged.

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