

THE FORMATION OF 3,10 β -EPOXY-B-HOMOTRITERPENES FROM
8 β -HYDROXYCYCLOARTANYL DERIVATIVES

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Abstract- Treatment of 3 β ,8 β -dihydroxycycloartan-7-one (1b) with p-toluenesulfonic acid gave 3 β ,10 β -epoxy-9,10-seco-cycloart-8-en-7-one(2), 3 β -hydroxy-9,10-seco-cycloarta-1(10),8(9)-dien-7-one(3) and an unidentified compound(4).

In addition, transformations of tetrahydropyranyl and ethoxyethyl derivatives (1c and 1d) into 2 with acid catalysts are described.

There are many natural products such as baccharis oxide,¹ epoxyglutinane,² cantharidin,³ and samandarin⁴ having ether linkage(1,4-epoxy) in their molecules. Recently glycinoclepin A,⁵ a natural hatching stimulus for soybean cyst nematode, was reported to have 3,10-epoxy structure in its A-ring. 3,10-Epoxy-B-homotriterpenes as 26-O-methylcimicifugenin A⁶ seem to be synthetically useful intermediates for the AB-ring formation of glycinoclepins.

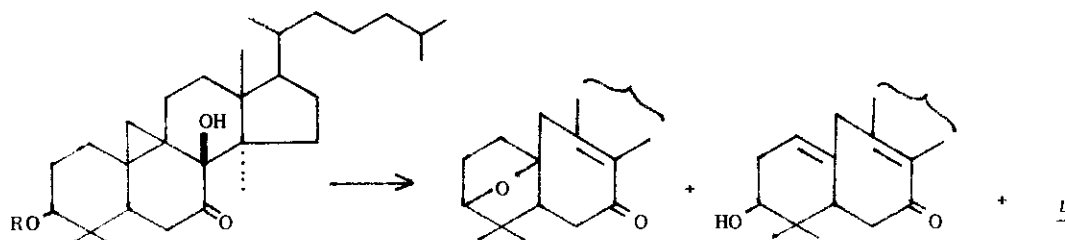
In the previous paper,⁷ we described that catalytic transformation of 3 β -acetoxy-8 β -hydroxycycloartan-7-one(1a) gave 3 β -acetoxy-9,10-seco-cycloarta-1(10),8(9)-dien-7-one and 3 β -acetoxy-9,10-seco-cycloarta-5(10),8(9)-dien-7-one.

This paper presents catalytic transformation of 3 β ,8 β -dihydroxycycloartan-7-one(1b) and its derivatives(1c, 1d) into 3,10 β -epoxy-B-homotriterpenes.

Ozone oxidation of cycloartanyl acetate gave 3 β -acetoxy-8 β -hydroxycycloartan-7-one

1a and 3 β -acetoxycycloartan-7-one. 3 β ,8 β -Dihydroxycycloartan-7-one 1b was obtained quantitatively by hydrolysis of 1a.

Treating 1b with p-toluenesulfonic acid in benzene at 80 °C for half an hour, followed by chromatography over silica gel, gave (2), (3) and (4) in a yield of 19%, 35% and 29% respectively. Compound 2 (mp 102-103 °C, $[\alpha]_D -19^\circ$, M^+ m/z 440.3667



1a ; R=Ac

1b ; R=H

1c ; R=THP

1d ; R=EE

($C_{30}H_{48}O_2$)) has bands at 1645 cm^{-1} (C=O), and 1605 cm^{-1} (C=C) in its ir spectrum. The absorption maximum at 250 nm in the uv spectrum indicated that 2 contained α,β -unsaturated carbonyl system in the molecule. The signals centered at 0.64 ppm(d, $J=6\text{Hz}$) and 0.33 ppm (d, $J=6\text{Hz}$) due to cyclopropane methylene protons in the ^1H -nmr spectrum of 1b were not observed in the spectrum of 2. Moreover, in the ^1H -nmr spectrum of 2, like O-methyl cimiacerol,⁸ a methine proton signal at C-3 appears at 3.75 ppm(d) and the allylic methylene proton signals at 3.00(d) and 2.05 ppm(d). The ^{13}C -nmr spectrum of 1b showed a signal at 81.8 ppm(s) due to C-8. This signal disappeared and additional signals appeared at 142.6(s) and 145.1 ppm(s) in the spectrum of 2. These spectral changes indicated that the double bond in 2 is located at C-8 and C-9. On the basis of these spectral data, it seems reasonable to assume that compound 2 is 3 β ,10 β -epoxy-9,10-secocycloart-8(9)-en-7-one.

Compound 3 (mp 159-160 °C, $[\alpha]_D -35^\circ$, M^+ m/z 440.3641 ($C_{30}H_{48}O_2$)) was obtained as a major product. Compound 3 had bands at 3352 cm^{-1} (OH), 1644 cm^{-1} (C=O) and 1602 cm^{-1} (C=C) in its ir spectrum. In the uv spectrum, the absorption maximum at 253 nm indicated that 3 contains α,β -conjugated carbonyl group in the molecule. In the ^1H -nmr spectrum of 3, the cyclopropane methylene proton signal was not observed, while the olefinic proton signal appeared at 5.43 ppm(br, w/2=11 Hz). Furthermore,

in the both uv and ^1H -nmr spectrum of 2, no evidence for the $\alpha\beta,\gamma\delta$ -conjugated dienone system was observed. On the basis of these spectral data, compound 2 was considered to be 3 β -hydroxy-9,10-secocycloart-1(10),8(9)-dien-7-one.

Experiments to improve the yield of 2 were carried out. Each reactions were attempted three times and the average yield of the products are given in Table 1.

Table 1 Composition of the reaction products

Substrates	Catalysts	Solvents	Yield of the products(%)			
			<u>2</u>	<u>3</u>	<u>4</u>	Others
1b	p-TsOH	C_6H_6	19	35	29	17
	p-TsOH	CH_3CN	20	45	17	18
	BF_3	DMF	26	26	25	23
1c	p-TsOH	C_6H_6	17	43	18	22
	p-TsOH	CH_3CN	22	46	20	12
	BF_3	DMF	30	29	27	14
1d	p-TsOH	C_6H_6	24	50	1	25
	p-TsOH	CH_3CN	37	52	1	10
	BF_3	DMF	31	40	8	21

Reaction conditions; temp. : 80 $^\circ\text{C}$, time : 0.5 h

Generally, the yield of 2 increased slightly in polar aprotic solvent rather than a nonpolar solvent. The compound 2 had also a tendency to increase with the Lewis acid catalyst rather than in the Brönsted one except the cases of 1d.

While 3-acetoxy derivative was reported to give no 3,10-cyclic ether,⁷ 3-hydroxy-cycloartanyl derivative, 1b, gave 2 in yield of 19-26%. These facts suggested that electron-attracting substituent lowered yield of cyclization products. Thus we assumed that introduction of tetrahydropyranyl(THP) or ethoxyethyl(Ee) group to C-3, which are electron-donating in comparison with hydroxy group, would given the 3,10-ether in better yield. The assumption was supported by the experimental results. Among the above runs, treatment of 1d with p-toluenesulfonic acid in CH_3CN afforded 2 in the best yield.

Structure elucidation of product 4 is in progress, and the result will be reported shortly.

EXPERIMENTAL SECTION

All melting points are uncorrected. Ir spectra were obtained in KBr on a Hitachi 270-50 ir-instrument. Uv spectra were recorded in CHCl_3 on a Hitachi 320 spectrophotometer. ^1H -Nmr and ^{13}C -nmr spectra were measured at 100 MHz, in CDCl_3 as solvent. Chemical shifts are given in ppm from tetramethylsilane(TMS) as an internal standard(JNM-FX100 and GX400 instruments). Mass spectra were recorded on a Hitachi M-80B system at 70 eV. Optical rotations were measured in CHCl_3 on a Horiba SEPA-200 polarimeter. Glc was performed on a Shimadzu GC-9A gas chromatography equipped 2% OV-17(3m x 5mm) at 300 °C.

Materials. Hydrolysis of 1a gave 3,8 β -dihydroxycycloartan-7-one(1b)(mp 164-165 °C; ir(KBr) ν : 3450(OH), 1685(C=O) cm^{-1} ; ^1H -nmr δ : 3.55(1H, br, w/2=17Hz, CH-OH), 3.29(1H, s, CH-OH), 0.64(1H, d, J=6Hz, $-\text{CH}_2-$) and 0.33(1H, d, J=6Hz, $-\text{CH}_2-$); ms m/z 458.3710, $\text{C}_{30}\text{H}_{50}\text{O}_3$, Calcd 458.3747), quantitatively. Tetrahydropyranyl(THP) ether(1c) and ethoxyethyl(Ee) ether(1d) derivatives were prepared by the method of the literatures.^{9,10}

Reaction of 1b with p-toluenesulfonic acid. To a solution of 1b(100 mg) in dry benzene(20 ml) was added p-toluenesulfonic acid(4 mg) and the mixture was stirred at 80 °C for 0.5 h. After cooling to room temperature, water was added to the solution, and the products were extracted with benzene. After washing with water, the organic layer was dried over Na_2SO_4 , and the solvent was removed in vacuo. Disappearance of the starting material was confirmed by thin layer chromatography on silica gel. The yields on the products were determined by means of glc(Table 1).

The residue was chromatographed on silica gel, and elution with benzene gave 3,10-epoxy-9,10-secocycloart-8(9)-en-7-one(2)(18mg, 18%): mp 102-103 °C; $[\alpha]_D$ -19° (c=0.3, CHCl_3); ir(KBr) ν : 1645(C=O), 1605 cm^{-1} (C=C); uv(CHCl_3) : 250 nm(ϵ =3500); ^1H -nmr(CDCl_3) δ : 3.75(1H, d, J=5.4 Hz, CH-O), 3.00(1H, d, J=13 Hz, allylic H), 2.05(1H, d, J=13 Hz, allylic H); ^{13}C -nmr(CDCl_3) δ : 203.7(s, C-7), 145.1(s, C-9), 142.6(s, C-8), 87.5(s, C-10), 86.2(d, C-3); ms m/z : 440.3667, $\text{C}_{30}\text{H}_{48}\text{O}_2$, calcd 440.3642. Elution with benzene-ethyl acetate(20:1) afforded 3 β -hydroxy-9,10-secocycloarta-1(10),8(9)-dien-7-one(3)(30mg, 31%); mp 159-160 °C; $[\alpha]_D$ -35° (c=0.2, CHCl_3); ir(KBr) ν : 3352(OH), 1644(C=O), 1602 cm^{-1} (C=C); uv(CHCl_3): 253 nm(ϵ =6600);

$^1\text{H-nmr}(\text{CDCl}_3)$ δ : 5.43(1H, br, $w/2=11$ Hz, $\text{CH}=\text{C}$), 3.53(1H, br, $w/2=20$ Hz, CH-OH); ms m/z : 440.3641, $\text{C}_{30}\text{H}_{48}\text{O}_2$, calcd 440.3642. Elution with benzene-ethyl acetate(15:1) gave an unidentified product(4)(24mg); mp 152-153 $^\circ\text{C}$; $[\alpha]_{\text{D}}^{20} +20^\circ$ ($c=0.2$, CHCl_3); ir(KBr) ν : 3356(OH), 1638(C=O), 1600 cm^{-1} (C=C); $^1\text{H-nmr}(\text{CDCl}_3)$ δ : 5.43(1H, br, $w/2=10$ Hz, $\text{CH}=\text{C}$), 3.54(1H, br, $w/2=20$ Hz, CH-OH); ms m/z : 440.3641, $\text{C}_{30}\text{H}_{48}\text{O}_2$.

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