

## Studies on Triterpenoid Corticomimetics (IV)

### E-Ring Opening of Pomolic Acid by Retrograde Aldol Condensation

Yong Nam Han, Byung Hoon Han, Eun Tae Park\* and Tae Hee Kim\*

Natural Products Research Institute, Seoul National University, Seoul 110, Korea

\*College of Pharmacy, Sookmyung Women's University, Seoul 151, Korea

(Received September 16, 1985)

**Abstract** □ Acetyl-11-ketopomolic acid methyl ester (VI), mp 276~278°, was synthesized from pomolic acid (III). The mild alkaline treatment of VI induced the opening of ring E on carbon skeleton to yield VII, and then VII was deacetylated to give VIII, mp 82~84°. Compound VIII was established as 11,19-diketo-18,19-secoursolic acid methyl ester. The E-ring opening was believed to be due to retrograde aldol condensation.

**Keywords** □ Pomolic acid, 11,19-Diketo-18,19-secoursolic acid, E-Ring opening of triterpenoid, Retrograde aldol condensation.

By introducing C<sub>11</sub>-oxo group to triterpenoids we have synthesized some artificial inhibitors on corticoid-5 $\beta$ -reductase.<sup>1~4)</sup> During these studies, it was found that alkaline treatment of a triterpenoid having both functional groups of  $\alpha$ ,  $\beta$ -unsaturated ketone and  $\delta$ -hydroxy results in cleavage of  $\gamma$ - $\delta$  bond.

Pomolic acid (III) used was prepared by Smith's degradation of Ziyu-glycoside II isolated from *Sanguisorbae radix*. Acetyl-11-oxopomolic acid methyl ester (VI) was synthesized from III through serial reactions of acetylation, methylation and oxidation by chromium trioxide-acetic acid. Treatment of VI under a mild alkaline condition first induced E-ring opening to give compound VII, and then it was deacetylated to yield compound VIII, which was assigned to be 11,19-diketo-18,19-secoursolic acid methyl

ester. The ring opening was thought to be due to retrograde aldol condensation. The present paper reports that the E-ring opening is the first finding in the triterpenoid chemistry.

### EXPERIMENTAL METHODS

#### Isolation of Ziyu-glycoside I

Ziyu-glycoside I was isolated from *Sanguisorbae radix* (the dried roots of *Sanguisorba officinalis*) by a method differing Yosioka's<sup>5)</sup> as follows;

The roots (6Kg) were extracted four times with methanol refluxing. Evaporation of solvent gave a redish-brown residue (1.2kg), which was suspended in a small volume of water and then ether was added to the aqueous solution until its full saturation. After standing at room temp. over one day, needle crystals were formed. They were filtered, washed several times with water-saturated ether, and recrystallized from 50% ethanol to yield Ziyu-glycoside I (needle crystals, 38g). mp: 216~218°, IR  $\nu_{\max}^{\text{KBr}}$  cm<sup>-1</sup>: 3400(OH), 1735(ester), 1635(olefin), PMR $\delta_{\text{ppm}}^{\text{TMS}}$  (in CD<sub>3</sub>OD): 0.77, 0.84, 1.03, 1.19, 1.32 (5 $\times$ 3H, each s, 5 $\times$ CH<sub>3</sub>), 0.95 (6H, s, 2 $\times$ CH<sub>3</sub>), 2.51 (1H, s, C<sub>18</sub>-H), 5.28 (1H, m, C<sub>12</sub>-H).

A solution of Ziyu-glycoside I (1g) in pyridine (3ml) and acetic anhydride (4ml) was kept at room temp. overnight, poured into ice-water, and treated as usual. Crystallization of the

product with 95% methanol yielded colorless fine crystals of the heptaacetate (0.88g), mp: 167~170°, IR $\nu_{\max}^{\text{KBr}}$  cm<sup>-1</sup>: 3560 (OH), 1750(ester), PMR  $\delta_{\text{ppm}}^{\text{TMS}}$  (CDCl<sub>3</sub>): 0.70, 0.77, 0.92, 0.95, 1.20 (18H, totally 6×CH<sub>3</sub>), 1.23(3H, s, C<sub>19</sub>(OH)CH<sub>3</sub>), 2.01 (12H, s, 4×OCOCH<sub>3</sub>), 2.04 (6H, s, 2×OCOCH<sub>3</sub>), 2.12(3H, s, 1×OCOCH<sub>3</sub>), 2.52(1H, s, C<sub>18</sub>-H), 3.08(1H, t-like, C<sub>3</sub>-H), 4.45(1H, d, C'<sub>1</sub>-H, J=7Hz), 5.58(1H, d, C''<sub>1</sub>-H, J=8Hz), 3.68(1H, m, C''<sub>5</sub>-H), 3.50, 3.93, (2H, C'<sub>5</sub>-H<sub>2</sub>), 5.05 ~5.37 (7H, C<sub>12</sub>-H and sugar oxymethine).

#### Preparation of Ziyu-glycoside II

The supernatant after filtering the needle crystals of Ziyu-glycoside I was made to be 10% NaOH solution, and hydrolyzed in a boiling water bath for 10hrs. The reaction mixture was acidified to pH 3 with 10% HCl and extracted with butanol. Evaporation of butanol gave a reddish-brown residue, which was recrystallized from 90% methanol to yield Ziyu-glycoside II (scale-like crystals, 60g). mp: 266~270°, IR $\nu_{\max}^{\text{KBr}}$  cm<sup>-1</sup>, 3560, 3420 (OH), 1695(COOH).

A solution of Ziyu-glycoside II (0.9g) in pyridine (5ml) and acetic anhydride (7ml) was kept at room temp. overnight, poured into ice-water, and treated as usual. Crystallization of the product with benzene yielded colorless crystals of the triacetate (0.41g). IR $\nu_{\max}^{\text{KBr}}$  cm<sup>-1</sup>: 3620 (OH), 1755(ester), 1695(COOH).

The triacetate (0.2g) in ether was treated with diazomethane to give its methyl ester(0.2g, a single spot on TLC, but crystallization did not succeed.). IR $\nu_{\max}^{\text{KBr}}$  cm<sup>-1</sup>: 3620(OH), 1760 (OCOCH<sub>3</sub>), 1736 (OCOCH<sub>3</sub>), PMR $\delta_{\text{ppm}}^{\text{TMS}}$ (CDCl<sub>3</sub>): 0.67, 0.76, 0.90, 0.93, 0.96, 1.10, 1.21(18H, totally 6×CH<sub>3</sub>), 1.24 (3H, s, C<sub>19</sub>(OH)CH<sub>3</sub>), 2.01, 2.04, 2.12 (3×3H, each s, 3×OCOCH<sub>3</sub>), 2.59 (1H, s, C<sub>18</sub>-H), 3.07(1H, t-like, C<sub>3</sub>-H),

3.59 (3H, s, COOCH<sub>3</sub>), 3.77(2H center, AB part in ABX system, C'<sub>5</sub>-H<sub>2</sub>), 4.42 (1H, d, C'<sub>1</sub>-H, J=7Hz), 5.34(1H, m, C<sub>12</sub>-H), 4.81~5.20(3H, C'<sub>2</sub>, C'<sub>3</sub>, C'<sub>4</sub>-H), 2.2~2.75 (1H, m, C<sub>20</sub>-H), MS(m/z): 726 (M<sup>+</sup>-H<sub>2</sub>O), 684 (M<sup>+</sup>-CH<sub>3</sub>COOH, 0.3%), 468(C<sub>31</sub>H<sub>49</sub>O<sub>3</sub><sup>+</sup>, 3.1%), 259(C<sub>11</sub>H<sub>15</sub>O<sub>7</sub><sup>+</sup>, 19.9%).

#### Smith's Degradation of Ziyu-glycoside II Giving Pomolic Acid (III)

Ziyu-glycoside II (3g) was dissolved in pyridine (20ml) and methanol (30ml), and periodic acid (dihydrate, 3g) in 5ml water was added over a period of 1 hr while the solution was being stirred and cooled in an ice bath. The solution was allowed to stand in the dark at room temp. for two days, and water (300ml) was added. A precipitate was taken by centrifugation, and suspended with 30ml water. Then while the suspension was being stirred, potassium iodide (1.2g) was added and then sodium arsenite until iodine color disappeared. An equal volume of 10% potassium hydroxide in ethanol was added. The solution was heated on a boiling water bath under nitrogen for 4 hrs, and carefully acidified with *d*-H<sub>2</sub>SO<sub>4</sub> to pH 4. Ethanol was removed *in vacuo*, and extraction with ether gave a crude sapogenin, which was subjected to chromatography on a silica gel column, using the elution solvent of chloroform/methanol (8 : 1). Pomolic acid (III) obtained was crystallized from methanol(300mg). mp: 260~262°, IR $\nu_{\max}^{\text{KBr}}$  cm<sup>-1</sup>: 3620, 3565(OH), 3000~2500, 1690 (COOH), 1025, 995 (C-OH), 927 (tert. C-OH), PMR $\delta_{\text{ppm}}^{\text{TMS}}$  (CDCl<sub>3</sub>): 0.67, 0.77, 0.88 (15H, 5×CH<sub>3</sub>), 1.12 (3H, s, C<sub>27</sub>-H<sub>3</sub>), 1.18 (3H, s, C<sub>19</sub>(OH)CH<sub>3</sub>), 2.53 (1H, s, C<sub>18</sub>-H), 2.33~2.73 (1H, m, C<sub>20</sub>-H), 3.08 (1H, t, C<sub>3</sub>-H), 5.25 (1H, m, C<sub>12</sub>-H), MS (m/z): 472 (M<sup>+</sup>, C<sub>30</sub>H<sub>48</sub>O<sub>4</sub>, 2.5%), 454 (M<sup>+</sup>-H<sub>2</sub>O, 4.4%), 426(C<sub>29</sub>H<sub>46</sub>O<sub>2</sub>, 11.9%),

264 (C<sub>16</sub>H<sub>24</sub>O<sub>3</sub>, 6.9%), 207 (C<sub>14</sub>H<sub>23</sub>O, 23.9%).

A solution of pomolic acid (III) (270mg) in pyridine (2ml) and acetic anhydride (3ml) was kept at room temp. and treated as usual. Crystallization of the product with methanol gave colorless fine crystals of the monoacetate (IV) (170mg), mp: 251°, IR<sub>ν<sub>max</sub></sub><sup>KBr</sup> cm<sup>-1</sup>: 3620, 3515 (OH), 1735, 1715(ester), 1695 (COOH), PMRδ<sub>ppm</sub><sup>TMS</sup> (CDCl<sub>3</sub>): 0.67, 0.79, 0.88 (15H, 5×CH<sub>3</sub>), 1.24 (3H, s, C<sub>27</sub>-H<sub>3</sub>), 1.28 (3H, s, >C<sub>19</sub>(OH)CH<sub>3</sub>), 1.96 (3H, s, OCOCH<sub>3</sub>), 2.43 (1H, s, C<sub>18</sub>-H), 4.40 (1H, t-like, C<sub>3</sub>-H), 5.25(1H, m, C<sub>12</sub>-H).

Acetylpomolic acid (IV) (650mg) in methanol was treated with diazomethane to yield its methyl ester (V) (600mg). mp: 228~230°, IR<sub>ν<sub>max</sub></sub><sup>KBr</sup> cm<sup>-1</sup>: 3620, 920 (tert. alcohol), 1730 (ester), PMRδ<sub>ppm</sub><sup>TMS</sup> (CDCl<sub>3</sub>): 0.67, 0.84, 0.91, 1.00 (15H, 5×CH<sub>3</sub>), 1.19 (3H, s, C<sub>27</sub>-H<sub>3</sub>), 1.23 (3H, s, >C<sub>19</sub>(OH)CH<sub>3</sub>), 2.00 (3H, s, OCOCH<sub>3</sub>), 2.53 (1H, s, C<sub>18</sub>-H), 3.56 (3H, s, COOCH<sub>3</sub>), 4.45 (1H, t-like, C<sub>3</sub>-H), 5.30 (1H, m, C<sub>12</sub>-H).

#### Chromium Trioxide-Acetic Acid Oxidation of Acetylpomolic Acid Methyl Ester (V)

Acetylpomolic acid methyl ester (V) (750mg) in acetic acid (10ml) and dioxane (10ml) was treated with chromium trioxide (900mg) in acetic acid (10ml). The reaction mixture was stirred at room temp. for 5 hrs and poured into ice-water. The product was extracted with chloroform. The extract was washed with water, dried over sodium sulfate anhydrous, and freed from solvent. The residue was chromatographed on a silica gel column eluting with hexane/ethylacetate(5:1), and crystallized from hexane/chloroform to give VI (250mg). mp: 276~278°, [α]<sub>D</sub><sup>21</sup>: +0.74 (c=0.6, CH<sub>2</sub>Cl<sub>2</sub>), UV (λ<sub>max</sub> in methanol): 252.5nm (ε 11, 200), IR<sub>ν<sub>max</sub></sub><sup>KBr</sup> cm<sup>-1</sup>: 3610 (OH), 1730, 1240 (ester), 1660, 1610(α, β-

unsaturated ketone and olefin), PMR and CMR δ<sub>ppm</sub><sup>TMS</sup> (CDCl<sub>3</sub>): Table I and II, MS (m/z): 542(M<sup>+</sup>, C<sub>33</sub>H<sub>50</sub>O<sub>6</sub>, 5.6%), 483(M<sup>+</sup>-CH<sub>3</sub>-CO<sub>2</sub>, 31.9%), 333(C<sub>20</sub>H<sub>29</sub>O<sub>4</sub>, 8.3%), 292 (C<sub>17</sub>H<sub>24</sub>O<sub>4</sub>, 5.1%), 277(C<sub>16</sub>H<sub>21</sub>O<sub>4</sub>, 11.4%), 273(C<sub>18</sub>H<sub>25</sub>O<sub>2</sub>, 10.0%).

#### Alkaline Hydrolysis of VI

A solution of VI (70mg) in 0.1M K<sub>2</sub>CO<sub>3</sub>-85% methanol (7ml) was kept at 30° for two days, neutralized with d-HCl and extracted with chloroform. The extract was dried over sodium sulfate anhydrous and freed from solvent. The residue was chromatographed on a silica gel column eluting with hexane/ethylacetate(1:1), giving VII (50mg) and VIII. VIII was crystallized from chloroform/ether (500mg).

VII; UV(λ<sub>max</sub> in methanol: 244.5nm(ε 8, 000), IR<sub>ν<sub>max</sub></sub><sup>KBr</sup> cm<sup>-1</sup>: 1730, 1720(ester), 1705 (ketone), 1668, 1635 (α, β-unsaturated ketone and olefin), PMRδ<sub>ppm</sub><sup>TMS</sup> (CDCl<sub>3</sub>): Table I.

VIII; mp: 82~84°, [α]<sub>D</sub><sup>21</sup>: +0.68 (c=0.5, MeOH) UV(λ<sub>max</sub> in methanol): 244.5nm (ε 10, 000), IR<sub>ν<sub>max</sub></sub><sup>KBr</sup> cm<sup>-1</sup>: 3450 (OH), 1725(ester), 1700(ketone), 1690(hydrogen bonded ketone), 1670, 1635 (α, β-unsaturated ketone and olefin), PMR and CMRδ<sub>ppm</sub><sup>TMS</sup> (CDCl<sub>3</sub>): Table I and II, Mass (m/z): 500(M<sup>+</sup>, C<sub>31</sub>H<sub>48</sub>O<sub>5</sub>, 5.5%), 441 (M<sup>+</sup>-CH<sub>3</sub>-CO<sub>2</sub>, 8.1%), 333(C<sub>20</sub>H<sub>29</sub>O<sub>4</sub>, 14.9%), 292 (C<sub>27</sub>H<sub>24</sub>O<sub>4</sub>, 6.9%), 273 (C<sub>18</sub>H<sub>26</sub>O<sub>2</sub>, 4.5%).

#### Instrumental Analysis

All melting points were taken on a Mitamura heat block apparatus and uncorrected. IR absorption spectra were obtained in KBr pellets on Perkin-Elmer Model 281B. NMR spectra were determined in CDCl<sub>3</sub> solution by a varian Model FT80A NMR spectrometer with tetramethylsilane as an internal standard. (<sup>1</sup>H; 80MHz, <sup>13</sup>C; 20MHz) The chemical shifts are recorded in δ. A recording spectrophotometer, Gilford Type

Table I: <sup>1</sup>H-NMR data of compounds VI, -VII and -VIII in CDCl<sub>3</sub>

	VI	VII	VIII
Methyl group	0.86, 0.96(15H)	0.86(6H, s)	0.81(3H, s)
	1:11(3H, s)	0.97(3H, s)	0.99(6H, s)
		1.08(3H, d, J=7Hz)	1.09(3H, d, J=7Hz)
		1.19(3H, s)	1.18(3H, s)
		1.25(3H, s)	1.26(3H, s)
C <sub>20</sub> -H <sub>3</sub>	1.22(3H, s)	2.11(3H, s)	2.11(3H, s)
C <sub>3</sub> -αH	4.51(1H, t-like)	4.48(1H, t-like)	3.21(1H, t-like)
C <sub>0</sub> -H	2.44(1H, s)	2.28(1H, s)	2.28(1H, s)
C <sub>12</sub> -H	5.64(1H, s)	5.64(1H, d, J=2Hz)	5.64(1H, d, J=2Hz)
C <sub>18</sub> -H	2.72(1H, s)	2.59(1H, q-like, H <sub>B</sub> )	2.59(1H, q-like, H <sub>B</sub> )
		2.80(1H, q-like, H <sub>A</sub> )	2.80(1H, q-like, H <sub>A</sub> )
C <sub>3</sub> -OCOCH <sub>3</sub>	2.03(3H, s)	2.03(3H, s)	—
C <sub>28</sub> -OOCH <sub>3</sub>	3.58(3H, s)	3.62(3H, s)	3.65(3H, s)

2600 was used for the measurements of UV-visible absorption spectra. Mass spectra were obtained on a Hewlett Packard GC/MS spectrometer (type 5985B) using an electron impact method.

## RESULTS AND DISCUSSION

Ziyu-glycoside I and ziyu-glycoside II were isolated from Sanguisorbae radix by an advanced method differing from Yosioka's<sup>5)</sup>. The methanol extract of the roots was suspended in a small volume of water and partitioned into ether. Needle-like crystals of I were obtained between both layers.

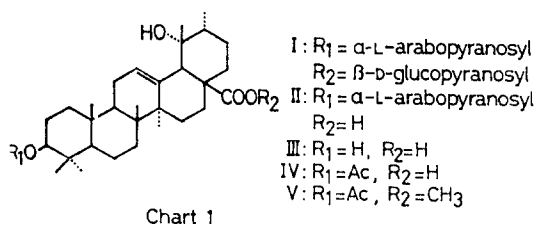
A large amount of I with a small amount of II were still remained in the supernatant, which was hydrolyzed with 10% NaOH to yield II. The IR and PMR spectra of I, II, and their derivatives were identical with those of literature references,<sup>5)</sup> respectively.

Yosioka *et al.* obtained with a low yield pomolic acid (III), the genuine aglycone of the glycosides by the soil bacterial hydrolysis method,

Table II: <sup>13</sup>C-NMR data of compounds VI and -VIII in CDCl<sub>3</sub>

Carbon	VI	VII	Carbon	VI	VIII
1	38.8	39.3	16	25.2	30.4
2	23.5	27.3	17	47.7	47.9
3	80.6	78.6	18	53.8	27.0
4	38.0	39.1	19	73.1	211.5
5	55.1	55.2	20	41.4	47.0
6	17.4	17.5	21	25.8	30.7
7	33.2	33.9	22	36.7	38.7
8	43.5	43.5	23	28.1	28.1
9	61.2	61.2	24	16.6	15.6
10	37.0	37.1	25	16.1	16.3
11	199.8	199.5	26	18.7	18.6
12	133.0	126.9	27	21.1	19.8
13	163.3	161.3	28	177.4	175.3
14	45.7	44.1	29	27.1	28.1
15	28.6	27.8	30	15.8	16.4
			COOCH <sub>3</sub>	51.7	51.6
			OCOCH <sub>3</sub>	170.6	
			OCOCH <sub>3</sub>	21.4	

but they did not isolate it by Smith's degradation method. However, we have carefully undertaken the latter method. Excess reagents (IO<sub>4</sub><sup>-</sup>, IO<sub>3</sub><sup>-</sup>

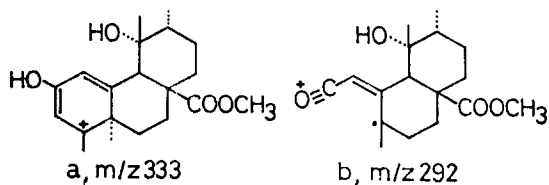


etc) were removed by centrifugation and by reduction of them with KI-As<sub>2</sub>O<sub>3</sub>. Finally, we succeeded in isolating III with a fairly good yield.

Compound III isolated, mp 260~262°, was positive in Libermann-Buchard reaction. Its mass spectrum showed the molecular ion at m/z 472, C<sub>30</sub>H<sub>48</sub>O<sub>4</sub>. The IR spectrum of III showed the presences of a carboxylic acid (3,000~2,500, 1690cm<sup>-1</sup>) and hydroxyl groups (3620, 3565, 1025, 995cm<sup>-1</sup>; 927cm<sup>-1</sup>, tert. C-OH). Compound III afforded the monomethyl ester (IV) with diazomethane treatment, and acetylation of IV yielded the monoacetate (V).

The IR spectrum of V showed an absorption band at 3620, 920cm<sup>-1</sup>, revealing the presence of tertiary hydroxyl group. The PMR spectrum of V exhibited the signals for one carboxy methyl ester at δ3.56 (3H, s), one acetoxy group at δ2.00(3H, s) and a vinyl proton at δ5.30 (1H, m). These data of III were coincided with those of pomolic acid.<sup>5-9)</sup>

Oxidation of V with chromium trioxide-acetic acid yielded VI, mp 276~278°. Compound VI contains an α,β-unsaturated ketone as seen from its UV (252.5nm, ε11,200) and IR (1660, 1610 cm<sup>-1</sup>) spectra, which was further confirmed by the signals at δ5.64 (1H on C<sub>12</sub>, s) and 2.44 (1H on C<sub>9</sub>, s) in its PMR spectrum. The spectrum also exhibited the signals at δ2.03 (3H, s) for the acetoxy group on C<sub>3</sub> and δ1.20 (3H, s) for the angular methyl group (29) on C<sub>19</sub>-



OH, indicating no oxidation except C<sub>11</sub>. (Table I).

The mass spectra of VI showed the molecular ion at m/z 542, giving a possible molecular formula C<sub>33</sub>H<sub>50</sub>O<sub>6</sub>, and two diagnostic ions at m/z 333 (a) by McLafferty rearrangement and at m/z 292 (b) by retro-Diels-Alder fragmentation.

The CMR data of VI exhibited the signals at δ199.7 for the ketone of C<sub>11</sub> and at 132.9, 163.3 for the vinyl group on C<sub>12</sub>, C<sub>13</sub> as shown in Table II. Thus, VI was assigned to be 3-O-acetyl-11-oxopomolic acid methyl ester.

The mild alkaline treatment of VI gave VII by way of VII as shown in Fig. 1.

The UV absorption maximum of VII was blue-shifted to 244.5nm (ε 8,800) by the alkaline

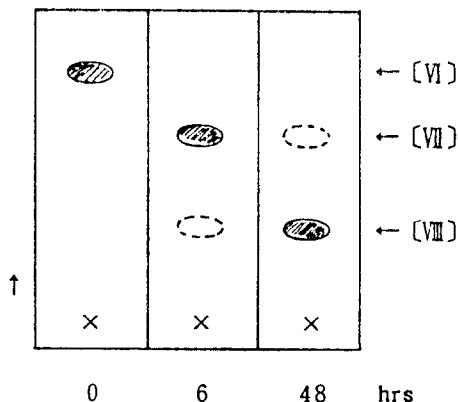


Fig. 1: Mild alkaline treatment of compound VI. A solution of VI in 0.1M K<sub>2</sub>CO<sub>3</sub>-85% methanol was incubated at 30°. At the indicated times, TLC was carried out with the developing solvent of hexane/ethylacetate(1:1). The spots were visualized by UV and d-H<sub>2</sub>SO<sub>4</sub>.

treatment of VI (252.5nm), suggesting a change in carbon skeleton. The IR spectrum of VII exhibited the presences of both of a ketone ( $1705\text{cm}^{-1}$ ) and the  $\alpha, \beta$ -unsaturated ketone ( $1668, 1635\text{cm}^{-1}$ ).

Compound VII possesses two acetyl groups as seen from its PMR spectra ( $\delta 2.03, 2.11$ ). The signal at  $\delta 2.03$  must be for the acetoxy group on  $C_3$ , which was further confirmed by the signal at  $\delta 4.48$  (t-like) for one proton on  $C_3$ . The signal at  $\delta 2.11$  exhibited the same chemical shift as the acetyl on acetone.

These data indicated that the alkaline treatment of VI induced the opening of E-ring on carbon skeleton to yield VII. This was also supported by the signals at  $\delta 2.59$  (1H, q-like) for  $H_B$  on  $C_{18}$  and  $2.80$  (1H, q-like) for  $H_A$  on  $C_{18}$ , and by the signal at  $\delta 5.64$  (d) for one proton on  $C_{12}$  which was splitted by allylic coupling ( $J=2$  Hz). Thus, VII was assigned to be 3-O-acetyl-11, 19-diketo-18, 19-secoursolic acid methyl ester.

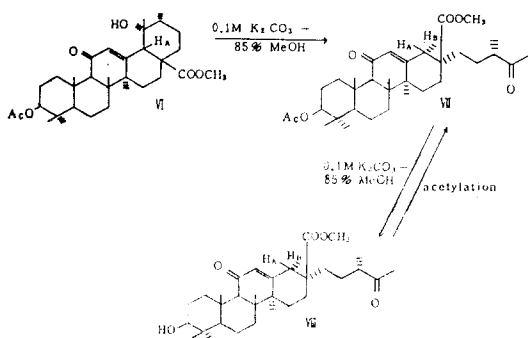
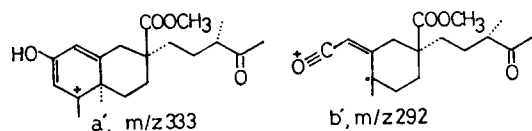


Chart 2

Further incubation of VII under the alkaline condition yielded VIII, mp  $82\sim 84^\circ$ . Compound VIII possesses both of the ketone ( $1,700, 1,690\text{cm}^{-1}$ ) and the  $\alpha, \beta$ -unsaturated ketone ( $1,670, 1,635\text{cm}^{-1}$ ) as seen from its IR spectrum. These were also supported by its UV spectrum ( $\lambda_{\text{max}}$  at  $244.5\text{nm}$ ,  $\epsilon 10,000$ ) and PMR spectrum (3H on

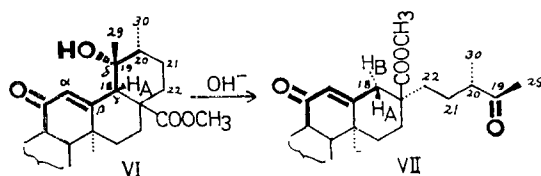
$-\overset{\text{O}}{\parallel}{\text{C}}-\text{CH}_3$ , s, at  $\delta 2.11$ ; 1H on  $C_{12}$ , d,  $J=2$  Hz, at  $5.64$ ). Compound VIII contains no acetoxy group as judged from the signal at  $\delta 3.21$  for one proton (t-like) on  $C_3$  in its PMR spectrum.

The mass spectrum of VIII exhibited the molecular ion at  $m/z 500$ , giving a possible molecular formula  $C_{31}H_{48}O_5$ . The ions at  $m/z 333$  (**a'**) and  $m/z 292$  (**b'**) were thought to be formed by McLafferty rearrangement and by retro-Diels-Alder fragmentation, respectively.



These data indicated that VIII was the deacetylate of VII. The CMR data of VIII provided conclusive assignment for its chemical structure. Application of attached proton test yields the data as shown in Table II, which exhibited the signals at  $\delta 27.0$  for  $C_{18}-H_2$  and at  $\delta 211.5$  for  $C_{19}$  besides the signals at  $\delta 199.5$  for  $C_{11}$ , at  $\delta 126.9$  for  $C_{12}$  and at  $\delta 161.3$  for  $C_{13}$ . Therefore, VIII was established as 11, 19-diketo-18, 19-secoursolic acid methyl ester.

Since VI possesses the active hydrogen (on  $C_{18}$ ) in the  $\gamma$  position of the  $\alpha, \beta$ -unsaturated ketone and the hydroxyl group (on  $C_{19}$ ) in the  $\delta$  position, the treatment with  $\text{OH}^-$  can cleave the  $\gamma$ - $\delta$  bond, of which reaction is known as the retrograde aldol condensation.



A strong alkaline treatment of VI such as 0.1 N NaOH in alcohol did not give VIII because of its decomposition. Reacetylation of VIII only yielded VII without giving VI. Thus, the pathway of VI to VII was turned to be irreversible. To our best knowledge, the E-ring opening is the first finding in the triterpenoid chemistry.

### ACKNOWLEDGEMENTS

This work was supported by a research grant from the Korean Science and Engineering Foundation.

### LITERATURE CITED

- 1) Han, B.H., Lee, H.J. and Han, D.S.: Studies on triterpenoid corticosteroids. (I). Inhibition of corticoid-5 $\beta$ -reductase by 11-oxo-oleanolic acid and 11-oxo-hederagenin. *Yakhak Hoeji* **26**, 1 (1982).
- 2) Han, B.H., Kim-Cho, M.S., Han, Y.N. and Park, M.H.: Studies on triterpenoid corticosteroids. (II). Synthesis of 11-oxo-oleanolic acid derivatives and their anti-inflammatory activities. *Korean Biochem. J.* **17**, 91 (1984).
- 3) Han, B.H., Kim, K.M., Park, J.H., Park, M.H., Kim, T.H. and Han, Y.N.: Studies on triterpenoid corticosteroids. (III). Determination of acetyl-11-keto- $\beta$ -boswellic acid and 11-keto- $\beta$ -boswellic acid in olibanum. *Arch. Pharm. Res.* **8**(4), 213 (1985).
- 4) Han, B.H. and Han, Y.N.: Studies on triterpenoid corticosteroids. (V). Oxidation of presengenin with chromium trioxide-acetic acid to yield 11-keto and 12-keto derivatives. *Arch. Pharm. Res.* **8**(4), 229 (1985).
- 5) Yosioka, I., Sugawara, T., Ohsuka, A. and Kitagawa, I.: Soil bacterial hydrolysis leading to genuine aglycone. III. The structures of glycosides and genuine aglycone of *Sanguisorbae radix*. *Chem. Pharm. Bull.* **19**, 1700 (1971).
- 6) Takahashi, K., Kawaguchi, S., Nishimura, K., Kubota, K., Tanabe, Y. and Takani, M.: Studies on constituents of medicinal plants. XIII. Constituents of the pericarps of the capules of *Euscaphis japonica* Pax. *Chem. Pharm. Bull.* **22**, 650 (1974).
- 7) Takahashi, K. and Takani, M.: Studies on constituents of the medicinal plants, XXI. Constituents of the leaves of *Clethra barbinervis* Sieb. et Zucc. (2) and the <sup>13</sup>C-nuclear magnetic resonance spectra of 19 $\alpha$ -hydroxyur-12-en-28-oic acid type of triterpenoids. *Chem. Pharm. Bull.* **26**, 2689 (1978).
- 8) Bermejo, J. Bretón, J.L., Fuente, G. de'la and Gonzalez, A.G.: Terpenoids of the micromerias.- I. Two new triterpenic acids isolated from *Micromeria benthami* Webb et Berth. *Tetrahedron Letters* **47**, 4649 (1967).
- 9) Brieskorn, C.H. and Wunderer, H.: Über den chemischen Aufbau der Apfelschale, IV. Pomol- und Pomonsäure. *Chem. Ber.* **100**, 1252 (1967).