Communications to the Editor

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CHEMICAL MODIFICATION OF OLEANENE-OLIGOGLYCOSIDES BY MEANS OF ANODIC OXIDATION

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By utilizing anodic oxidation as the key reaction, various olean-12-ene sapogenols were readily converted into olean-11-en-28,13β-olide, 11α,12α-epoxy-oleanan-28,13β-olide, and 13β,28-epoxy-olean-11-ene derivatives, respectively in high yields. Since previous protection of hydroxyl groups in the starting compounds was not required, the conversion method was directly applied to hederagenin oligoglycosides and corresponding oligoglycosides of olean-11-ene sapogenols, functionalized as above, were successfully synthesized.

KEYWORDS —— anodic oxidation; olean-12-ene sapogenol; olean-11-en-28,13β-olide; 11α,12α-epoxy-oleanan-28,13β-olide; 13β,28-epoxy-olean-11-ene; triterpene oligoglycoside; *Sapindus mukurossi*

During the course of our studies on selective cleavage methods for the glucuronide linkage,[1] we found a new cleavage method by means of an anodic decarboxylation reaction.[2] By utilizing the reaction intermediate in this cleavage procedure, a versatile conversion method from uronic acids leading to cyclitols was developed and aminocyclitol oligoglycosides were conveniently synthesized from glucuronide-saponins.[3] Furthermore, on application of the anodic decarboxylation reaction to some olean-12-ene glucuronide-saponins, we found that the olean-12-ene sapogenol underwent an allylic oxidation at the 11α position. Since only a few examples of anodic allylic oxidation are known (*e.g.* on monoterpenes[4]), we investigated this matter and found that the anodic allylic oxidation was quite useful for converting olean-12-ene sapogenols to 11-en-28,13β-olide, 11α,12α-epoxy-28,13β-olide, and 13β,28-epoxy-11-ene derivatives *via* short reaction steps and in high yields. This communication further deals with successful conversion of hederagenin oligoglycosides (24, 25) by making use of anodic oxidation leading to variously functionalized olean-11-ene oligoglycosides (28, 29, 30, 31, 33, 34), which may be of interest from the viewpoint of their biological activities.[5]

When oleanolic acid (1) or hederagenin (2) in MeOH containing Et_4NBr and PhSeSePh[4c] was subjected to constant current electrolysis (Pt electrode, current density 6.5 mA/cm^2, 1 h, ca. 30 V),[6] a 12α-bromo-28,13β-olide [3[7] (from 1) or 4 (from 2), $C_{30}H_{47}O_4Br$,[8] mp 242-243°C] was quantitatively obtained. On the other hand, constant current electrolysis (glassy carbon, 2.5 mA/cm^2, 8 h, 25-35 V) of 1 or 2 in MeOH-AcOH afforded an 11-en-28,13β-olide [5 (92%), $C_{30}H_{46}O_3$, mp 260-261°C or 6

(90%), $C_{30}H_{46}O_4$, mp 279-280°C]. Treatment of 3 or 4 with DBU at 110°C for 12 h gave 5 or 6 (each in 90% yield), and treatment of 5 or 6 with 9% HCl-dry MeOH at 25°C for 30 min quantitatively gave 7[9] or 8, $C_{30}H_{46}O_4$, mp 300-301°C. Thus the structures of electrochemically prepared compounds were chemically substantiated. Oxidation of 5 or 6 with 30% aq. H_2O_2-P.TsOH at 25°C for 10 h furnished an 11α,12α-epoxy-28,13β-olide [9[10] (from 5) or 10 (from 6), $C_{30}H_{46}O_5$, mp 305-306°C, each in 80% yield] which had the same epoxy-lactone moiety as eupteleogenin.[11]

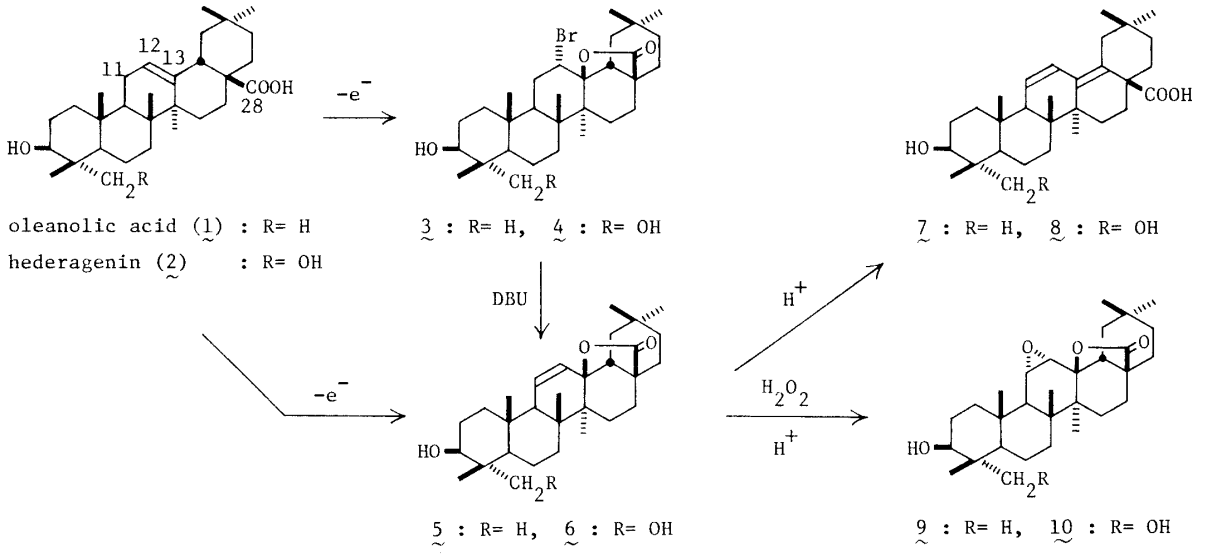
Next, three olean-12-ene alcohols [erythrodiol (11), hederatriol (12), primulagenin A (13)] in MeOH-AcONa were subjected to constant current electrolysis (glassy carbon, 20 mA/cm^2, 6 h, ca. 10 V). An 11α-methoxy derivative (14, 28%), $C_{31}H_{52}O_3$, white powder, and a 13β,28-epoxy-11-ene (17, 55%),[12] $C_{30}H_{48}O_2$, mp 224-226°C, from 11, 15 (28%), $C_{31}H_{52}O_4$, mp 135-137°C, and 18 (56%),[12] $C_{30}H_{48}O_3$, mp 248-250°C, from 12, and 16 (28%), $C_{31}H_{52}O_4$, mp 147-149°C, and 19[12] (54%), $C_{30}H_{48}O_3$, mp 258-260°C, from 13, were respectively obtained. The 11α-methoxy derivatives (14, 15, 16) were quantitatively converted to the 13β,28-epoxy-11-enes (17, 18, 19) by 0.05% p.TsOH·H_2O-dioxane treatment at 25°C for 30 min as experienced in saikogenins.[13] 17, 18, and 19 were further quantitatively converted to 20, $C_{30}H_{48}O_2$, mp 264-265°C, 21,[14] and 22,[15] respectively by 9% HCl-dry MeOH treatment at 25°C for 30 min.

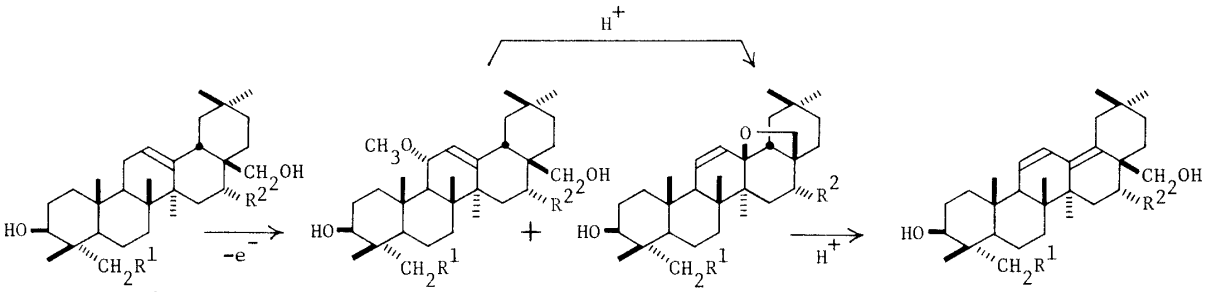
As was shown in our recent work,[2] previous protection of hydroxyl functions in the carbohydrate moiety of the starting oligoglycoside was not required in the anodic oxidation. We next applied the present electrochemical modification to hederagenin oligoglycosides (24,[16] 25[16]), which were abundantly isolated from the pericarps of *Sapindus mukurossi* Gaertn. (Sapindaceae) by Tanaka, et al.[17a] and recently by us.[17b]

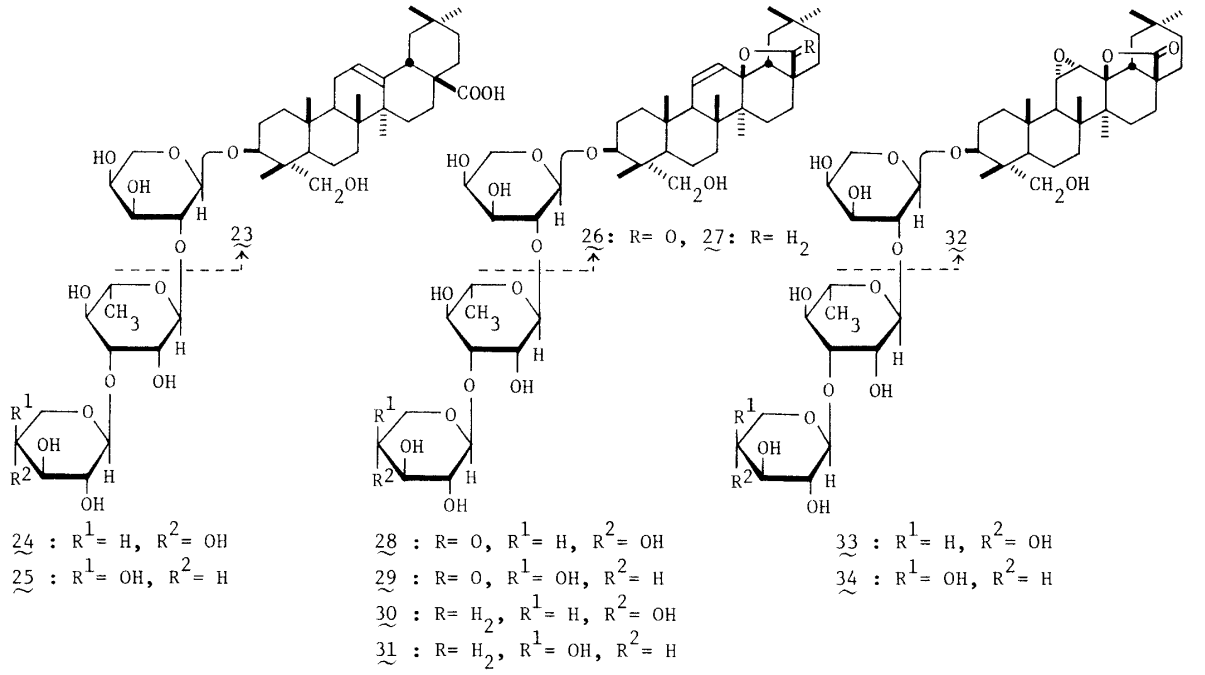
First, hederagenin arabinoside (23), a prosapogenol of 24 and 25, was examined. Constant current electrolysis (glassy carbon, 2.5 mA/cm^2, 15 h, 25-30 V) of 23 in MeOH-AcOH furnished 26 (90%), $C_{35}H_{54}O_8 \cdot H_2O$, mp 205-207°C, ^{1}H NMR (δ)[18]: 4.91 (1H, d, J= 7.5 Hz, 1'-H), 5.48 (1H, dd, J= 3, 10 Hz, 11-H), 6.09 (1H, d, J= 10 Hz,12-H), ^{13}C NMR (δc): 64.6 (t, 23-C), 89.6 (s, 13-C), 106.2 (d, 1'-C), 127.5, 136.2 (both d, 11,12-C), 179.3 (s, 28-C). Oxidation of 26 with 30% aq. H_2O_2-p.TsOH at 25°C for 5 h gave the desired epoxy-lactone arabinoside (32, 80%), $C_{35}H_{54}O_9 \cdot H_2O$, mp 297-298°C, δ: 3.18 (2H, m, 11,12-H), 4.93 (1H, d, J= 7 Hz, 1'-H), δc: 52.9, 57.5 (both d, 11,12-C), 87.7 (s, 13-C), 106.2 (d, 1'-C), 178.7 (s, 28-C).

On the other hand, hederatriol arabinoside, which was prepared from 23 by CH_2N_2 methylation followed by $LiAlH_4$ reduction, was similarly converted to the 13β, 28-epoxy-11-ene (27, 54% from 23), $C_{35}H_{56}O_7 \cdot H_2O$, mp 195-197°C, δ: 4.93 (1H, d, J= 7 Hz, 1'-H), 5.52 (1H, dd, J= 3, 10 Hz, 11-H), 5.95 (1H, d, J= 10 Hz, 12-H), δc: 64.2 (t, 23-C), 77.0 (t, 28-C), 84.9 (s, 13-C), 106.4 (d, 1'-H), 130.0 (d, 12-C), 131.7 (d, 11-C).

We next carried out the same conversion reactions for 24 and 25. Constant current electrolysis of 24 or 25 in MeOH-AcOH afforded the 11-en-28,13β-olide oligoglycoside, 28 (84%), $C_{46}H_{72}O_{16} \cdot 2H_2O$, mp 217-219°C, FD-MS (m/z): 880 (M^+), δc: 63.8 (t, 23-C), 89.6 (s, 13-C), 101.2 (d, 1"-C), 104.4 (d, 1'-C), 107.2 (d, 1"'-C), 127.3, 136.2 (both d, 11,12-C), 179.6 (s, 28-C), or 29 (86%), $C_{46}H_{72}O_{16} \cdot H_2O$, mp 228-230°C, FD-MS: 880 (M^+), δc: 64.2 (t, 23-C), 89.6 (s, 13-C), 101.3 (d, 1"-C), 104.0 (d, 1'-C), 106.7 (d, 1"'-C), 127.5, 136.2 (both d, 11,12-C), 179.4 (s, 28-C).







Oxidation of 28 or 29 with 30% aq. H_2O_2-p.TsOH yielded 33 (81%), $C_{46}H_{72}O_{17}\cdot 2H_2O$, mp 225-227°C, FD-MS: 896 (M^+), δc: 52.8, 57.6 (both d, 11,12-C), 64.3 (t, 23-C), 87.7 (s, 13-C), 101.4 (d, 1"-C), 104.2 (d, 1'-C), 107.1 (d, 1"'-C), 178.7 (s, 28-C), or 34 (82%), $C_{46}H_{72}O_{17}\cdot 2H_2O$, mp 215-217°C, FD-MS: 896 (M^+), δc: 52.8, 57.5 (both d, 11,12-C), 64.4 (t, 23-C), 87.7 (s, 13-C), 101.4 (d, 1"-C), 104.1 (d, 1'-C), 106.8 (d, 1"'-C), 178.7 (s, 28-C).

Successive treatment (esterification, reduction, and electrolysis) of 24 or 25 as described for 23 furnished 30 (50% from 24), $C_{46}H_{74}O_{15}\cdot 2H_2O$, mp 211-213°C, FD-MS: 866 (M^+), δc: 64.0 (t, 23-C), 77.0 (t, 28-C), 84.9 (s, 13-C), 101.4 (d, 1"-C), 104.5 (d, 1'-C), 107.3 (d, 1"'-C), 131.7 (d, 12-C), 132.0 (d, 11-C), or 31 (52% from 25), $C_{46}H_{74}O_{15}\cdot 3H_2O$, mp 218-220°C, FD-MS: 866 (M^+), δc: 64.4 (t, 23-C), 77.2 (t, 28-C), 85.0 (s, 13-C), 101.3 (d, 1"-C), 104.0 (d, 1'-C), 106.8 (d, 1"'-C), 131.7 (d, 12-C), 132.0 (d, 11-C).

Structures of 28, 29, 30, 31, 33, and 34 were further corroborated on the bases of enzymatic degradation and methylation analyses. Among these oligoglycosides, 30 and 31, having a 23-hydroxy-13β,28-epoxy moiety,[19] may be of interest for their anti-inflammatory activity, while 33 and 34, having an 11α,12α-epoxy-28, 13β-olide moiety,[20] may be of interest for their antimicrobial activity.

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