## CONCLUSIONS

Two lanostane acids have been isolated in the form of methyl esters from an extract of Siberian fir needles; the structure of one of them corresponds to the known isofirmanoic acid, while for the other the structure of (24E)-lanosta-8,24-diene-3,23-dion-26-oic acid has been established.

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# GLYCOSYLATION OF TRITERPENOIDS OF THE DAMMARANE SERIES.

## IX. β-D-GLUCOPYRANOSIDES OF 20(S),24(R)-EPOXYDAMMARANE-3α,12β,17α,25-TETRAOL


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Glycosides have been synthesized from 20(S),24(R)-epoxy-dammarane-3α,12β,17α,25-tetraol, which was isolated from the leaves of Betula costata. Exhaustive glycosylation of betulafolienetetraol oxide with α-acetobromoglucose in the presence of mercury cyanide gave an acetylated 3,12,25-triglucoside (yield 61%), while glycosylation in the presence of insoluble silver compounds led to the formation of 3- and 12-mono- and 3,12- and 12,25-diglucopyranosides (total yield 57-82%). The structures of the glucosides obtained have been established on the basis of the results of IR and $^1H$ and $^{13}C$ NMR spectroscopy.


Intensive investigations being made of the composition of the saponins of Panax ginseng C. S. Meyer and plants related to it have shown that, in addition to the known ginsenosides $R_{g1}$, $R_e$, $R_{b1}$, $R_{b3}$, and $R_d$, they contain saponins of the ocotillol type which have been called pseudoginsenosides [1, 2].

In order to study the structure-activity interrelationship, we have carried out the synthesis of glucosides from 20(S),24(R)-epoxydammarane-3α,12β,17α,25-tetraol (1), which differs from the genin of the pseudoginsenosides – 20(S),24(R)-epoxydammarane-3β,6α,12β,25-tetraol – by the position of one of the hydroxy groups and the configuration of the hydroxy group at C-3.


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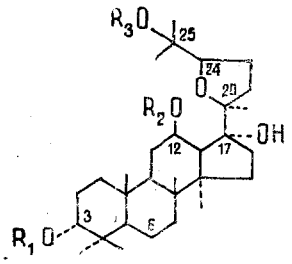

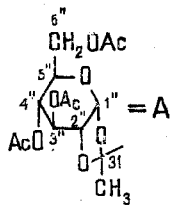

1. $R_1=R_2=R_3=H$
2. $R_1=Glc(Ac)_4$, $R_2=R_3=H$
3. $R_1=R_3=H$, $R_2=Glc(Ac)_4$
4. $R_1=R_2=Glc(Ac)_4$, $R_3=H$
5. $R_1=H$, $R_2=R_3=Glc(Ac)_4$
6. $R_1=A$, $R_2=Glc(Ac)_4$, $R_3=H$
7. $R_1=R_2=R_3=Glc(Ac)_4$
8. $R_1=Ac$, $R_2=R_3=Glc(Ac)_4$

As a result of the interaction of the tetraol (1) with α-acetobromoglucose in the presence of insoluble silver compounds we obtained the 3-O- and 12-O-monoglucosides (2) and (3), the diglucosides (4) and (5), and compound (6). When mercury cyanide was used as the promotor, we obtained the triglucoside (7) and the diglucoside (8), the appearance of which is obviously connected with a transformation of an intermediately formed orthoester of type (6) [3]. The conditions and results of glycosylation are given in Table 1. The structures of the compounds obtained were established on the basis of the results of IR and $^1H$ and $^{13}C$ NMR spectroscopy and elementary analysis. An additional proof of the structure of compound (6) is the ease of its acid hydrolysis, as a result of which it is converted into the monoglucoside (3).

The chemical shifts and spin-spin coupling constants of the anomeric protons of the glucose residues showed the trans-configuration of the glycosidic bonds in compounds (2-8). The positions of attachment of the glucose residues were determined by comparing the $^{13}C$ spectra of the initial tetraol (1) and the newly obtained glucosides (2-8) (Table 2).

## EXPERIMENTAL

IR spectra were recorded on a Specord 75 IR spectrophotometer in chloroform solution, and $^1H$ and $^{13}C$ NMR spectra were measured on a Bruker WM-250 spectrometer with a working frequency of 250 MHz for $^1H$ and 62.9 MHz for $^{13}C$ at 30°C in deuterochloroform. Chemical shifts are expressed on the δ scale relative to TMS. The accuracy of the measurement was ±1.5 Hz for $^{13}C$ and ±0.15 Hz for $^1H$. Optical rotations were measured on a Perkin–Elmer 141 instrument in a cell 10 cm long at 20°C, and the melting points of the substances on a Boëtius stage. Column chromatography was carried out on KSK silica gel (120-150 mesh) in the benzene–methanol (200:1 → 60:1) (A) and hexane–acetone (8:1 → 4:1) (B) systems.

The individuality of the substances was checked with the aid of TLC in the benzene–chloroform–methanol (6:4:1) and hexane–acetone (3:2) systems. The substances were detected with 10% $H_2SO_4$ in ethanol with heating at 100-200°C. The hydrolytic tests for compound (6) were carried out under the conditions of [4]. The elementary analyses for all the newly obtained compounds coincided with the calculated figures. Condensation was carried out by methods described previously [5]. The silver silicate was obtained in accordance with [6]. The deacetylation of compounds (2-5) and (7) with a 0.1 N solution of sodium methanolate in methanol led to the corresponding free glycosides (yields 95-96%).

20(S),24(R)-Epoxydammarane-3α,12β,17α,25-tetraol (1) was isolated from the unsaponifiable part of an ethereal extract of the leaves of Betula costata [7] followed by chromatography on silica gel and crystallization from acetone; mp 250-251.5°C.

20(S),24(R)-Epoxydammarane-3α,12β,17α,25-tetraol 3-O-(2',3',4',6'-Tetra-O-acetyl-β-D-glucopyranoside) (2). $[\alpha]_D^{20}$ −20.1° (c 0.93, $CHCl_3$). IR spectrum (ν, $cm^{-1}$): 1752, 3428. $^1H$ spectrum (δ, ppm): 0.83 (s, 3H), 0.87 (s, 3H), 0.90 (s, 3H), 0.97 (s, 3H), 1.12 (s, 3H), 1.19 (s, 3H), 1.30 (s, 3H), 1.35 (s, 3H), 2.00-2.08 (s, 12H, 4 × OAc), 3.34 (t, 1H, J = 2.7 Hz, $H_e$-3), 3.73 (m, 3H, H-5', $H_a$-12, H-24), 4.14-4.24 (m, 2H, 2 × H-6'), 4.50 (d, 1H, $J_{1',2'}$ = 7.5 Hz, H-1'), 4.90-5.21 (m, 3H, H-2', H-3', H-4').

20(S),24(R)-Epoxydammarane-3α,12β,17α,25-tetraol 12-O-(2',3',4',6'-Tetra-O-acetyl-β-D-glucopyranoside) (3). mp 205-207°C (ethanol).×,$[\alpha]_D^{20}$ −4.8° (c 0.93, $CHCl_3$). IR spectrum (ν, $cm^{-1}$): 1756, 3320, 3520, 3580, 3624. $^1H$ spectrum (δ, ppm): 0.85 (s, 3H), 0.86 (s, 3H), 0.94 (s, 3H), 0.95 (s, 3H), 1.08 (s, 3H), 1.17 (s, 3H), 1.20 (s, 3H), 1.27 (s, 3H), 2.01-2.10 (s, 12H, 4 × OAc), 3.23 (s, 1H, OH), 3.42 (t, 1H, J = 2.7 Hz, $H_e$-3), 3.73 (m, 3H, H-5', $H_a$-12, H-24), 4.12-4.24 (m, 2H, 2H-6'), 4.57 (d, 1H, $J_{1',2'}$ = 7.5 Hz, H-1'), 4.96-5.21 (m, 3H, H-2', H-3', H-4').

TABLE 1. Conditions and Results of the Glycosylation of the Tetraol (1) with α-Acetobromoglucose (ABG)*

| Compound | Starting materials: alcohols (1), mmole | Starting materials: ABG*** mmole × n (times) | Starting materials: HBr acceptor, g × n (times) | Solvent, ml | Reaction products, %**: monoglucosides (2) : (3) | diglucosides: 4 | diglucosides: 5 | diglucosides: 8 | 6 | trigluco-side (7) | Recovery of the starting material, %** |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 1 | 1×4 | $Ag_2O$ 0,234×4 | Dichloroethane 10 | 51,6 (1:3) | 23,8 | 6,3 | — | 12,1 | 1,8 | — |
| 2 | 1 | 1×4 | " | Dichloroethane–nitromethane 10 (1:1) | 56,3 (1:1,5) | Tr. | 1,3 | — | Tr. | — | — |
| 3 | 1 | 1×4 | $Ag_2O$ 0,234×4 4 Å mol. sieve 2,0×4 | Dichloroethane | 41,3 (1:3) | 35,1 | 1,2 | — | 18,5 | — | Tr. |
| 4 | 1 | 1×4 | " | Dichloroethane–nitromethane 10 (1:1) | 45,0 (1:1,5) | 25,3 | 1,6 | — | 8,9 | — | — |
| 5 | 1 | 1×4 | Ag silicate 0,75×4 | Dichloroethane 10 | 51,2 (1:2) | 5,3 | 1,2 | — | 2,7 | — | 20,7 |
| 6 | 1 | 4 | $Hg(CN)_2$ 1,0 | Nitromethane 25 | | — | — | 13,5 | — | 61,1 | — |

*The reaction time in all the experiments was 4 h, and the temperature 20-22°C.
**The yields are given for the chromatographically homogeneous substances.
***ABG – α-acetobromoglucose.

TABLE 2. $^{13}C$ Chemical Shifts of the Tetraol (1) and Its Glucosides (2-7) (δ; ppm relative to TMS)

| C atom | Compound | | | | | | |
|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 7 | 6 |
| 1 | 33,6 | 34,0 | 33,9 | 33,9 | 34,0 | 34,1 | 34,0 |
| 2 | 25,5 | 21,9 | 25,4 | 21,1 | 25,3 | 22,1 | 23,4 |
| 3 | 76,2 | 82,1 | 75,9 | 82,3 | 76,0 | 82,5 | 78,0 |
| 4 | 37,6 | 36,9 | 37,4 | 37,2 | 37,3 | 37,0 | 37,2 |
| 5 | 49,6 | 49,8 | 49,5 | 49,8 | 49,6 | 49,9 | 49,8 |
| 6 | 18,3 | 18,0 | 18,3 | 18,1 | 18,7 | 18,1 | 18,1 |
| 7 | 34,2 | 33,7 | 34,1 | 34,0 | 34,0 | 34,1 | 33,9 |
| 8 | 40,6 | 40,5 | 40 3 | 40,3 | 40,2 | 40,2 | 40,2 |
| 9 | 50,4 | 50,3 | 49,8 | 50,0 | 49,5 | 49,9 | 50,2 |
| 10 | 37,4 | 36,9 | 37,2 | 37,1 | 37,3 | 37,0 | 37,2 |
| 11 | 31,6 | 31,6 | 29,1 | 29,1 | 29,2 | 29,0 | 29,2 |
| 12 | 67,7 | 67,8 | 79,0 | 79,3 | 78,5 | 78,5 | 78,9 |
| 13 | 52,0 | 51,1 | 50,6 | 50 7 | 50,5 | 50,6 | 50,5 |
| 14 | 51,2 | 51,9 | 52,1 | 52,1 | 52,2 | 52,2 | 52,1 |
| 15 | 33,6 | 33,7 | 33,2 | 33,2 | 33,0 | 32,9 | 33,2 |
| 16 | 38,8 | 38,8 | 37,6 | 37,2 | 37,3 | 37,0 | 38,0 |
| 17 | 85,5 | 85,4 | 85,2 | 85,1 | 85,0 | 84,9 | 85,2 |
| 18 | 16,2 | 16,3 | 16,2 | 16,4 | 16,0 | 16,1 | 16,4 |
| 19 | 15,7 | 15,7 | 15 7 | 15,7 | 16,0 | 16,1 | 15,7 |
| 20 | 89,7 | 89,7 | 89,2 | 89,2 | 89,1 | 89,1 | 89,2 |
| 21 | 22,0 | 22,0 | 23,8 | 23,7 | 23,5 | 23,5 | 23,8 |
| 22 | 33,6 | 33,7 | 33,9 | 34,2 | 34,0 | 34,1 | 34,5 |
| 23 | 25,1 | 25,1 | 26 3 | 26,3 | 28,3 | 28,6 | 26,3 |
| 24 | 85,7 | 85,7 | 83,8 | 83,8 | 82,5 | 82,5 | 83,8 |
| 25 | 70,1 | 70,1 | 70,0 | 70,9 | 80,0 | 80,1 | 71,0 |
| 26 | 28,0 | 28,0 | 28,3 | 28,3 | 23,5 | 23,5 | 28,3 |
| 27 | 26,3 | 26,2 | 24,9 | 24,9 | 22,4 | 22,5 | 24,9 |
| 28 | 28,3 | 28,6 | 28,3 | 28,5 | 28,3 | 28,2 | 28,6 |
| 29 | 22,0 | 22,0 | 22,0 | 22,0 | 22,0 | 22,1 | 22,1 |
| 30 | 18,4 | 18,3 | 18,5 | 18 5 | 18,7 | 18,7 | 18,7 |

20(S),24(R)-Epoxydammarane-3α,12β,17α,25-tetraol 3,12-Di-O-(2',3',4',6'-Tetra-O-acetyl-β-D-glucopyranoside) (4). mp 210-211°C (ethanol). $[\alpha]_D^{20}$ = 14° (c 0.93, $CHCl_3$). IR spectrum (ν, $cm^{-1}$): 1756, 3376, 2516. $^1H$ spectrum (δ, ppm): 0.84 (s, 3H), 0.86 (s, 3H), 0.91 (s, 6H), 1.08 (s, 3H), 1.17 (s, 3H), 1.20 (s, 3H), 1.27 (s, 3H), 2.00-2.11 (s, 24H, 8 × OAC), 3.23 (s, 1H, OH), 3.37 (t, 1H, J = 2.7 Hz, $H_e$-3), 3.68 (m, 4H, 2H-5', H-24, $H_a$-12), 4.14-4.24 (m, 4H, 4H-6'), 4.53 (d, 1H, $J_{1',2'}$ = 7.5 Hz, H-1' at C-3), 4.56 (d, 1H, $J_{1',2'}$ = 7.5 Hz, H-1' at C-12), 4.92, 5.23 (m, 6H, 2H-2', 2H-3', 2H-4').

20(S),24(R)-Epoxydammarane-3α,12β,17α,25-tetraol 12,25-Di-O-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranoside) (5). mp 208-212°C (ethanol). $[\alpha]_D^{20}$ −4 (c 0.93, $CHCl_3$). IR spectrum (ν, $cm^{-1}$): 1756, 3376, 3536. $^1H$ spectrum (δ, ppm): 0.78 (s, 3H), 0.89 (s, 3H), 0.95 (s, 3H), 1.00 (s, 3H), 1.14 (s, 3H), 1.17 (s, 3H), 1.20 (s, 3H), 1.27 (s, 3H), 2.00-2.09 (s, 24H, 8 × OAC), 3.11 (s, 1H, OH), 3.42 (t, 1H, J = 2.7 Hz, $H_e$-3), 3.69 (m, 3H, 2H-5', $H_a$-12), 3.99 (m, 1H, H-24), 4.12-4.24 (m, 4H, 4H-6'), 4.53 (d, 1H, $J_{1',2'}$ = 7.5 Hz, H-1' at C-12), 4.95 (d, 1H, $J_{1',2'}$ = 8.0 Hz, H-1' at C-25), 5.01-5.23 (m, 6H, 2H-2', 2H-3', 2H-4').

20(S),24(R)-Epoxydammarane-3α,12β,17α,25-tetraol 12-O(2',3',4',6'-Tetra-O-acetyl-β-D-glucopyranoside) 3-O-(3",4",6"-Tri-O-acetyl-1",2"-O-ethylidene-α-D-glucopyranoside) (6). Amorphous. $[\alpha]_D^{20}$ +3° (c 1.0; benzene). IR spectrum (ν, $cm^{-1}$): 1756, 3376, 3516. $^1H$ spectrum (δ, ppm): 0.84 (s, 3H), 0.85 (s, 3H), 0.87 (s, 3H), 0.91 (s, 3H), 1.08 (s, 3H), 1.17 (s, 3H), 1.20 (s, 3H), 1.27 (s, 3H), 1.77 (s, 3H, $C^{31}$-$CH_3$), 2.00-2.11 (s, 21H, 7 × OAc), 3.23 (s, 1H, OH), 3.38 (t, J = 2.8 Hz, $H_e$-3), 3.70 (m, 3H, H-5', $H_a$-12, H-24), 3.96 (dd, 1H, J = 4.0 Hz, J = 9.2 Hz, H-5"), 4.19 (m, 4H, 2H-6', 2H-6"), 4.33 (dd, 1H, J = 3.0 Hz, J = 5.0 Hz, H-2"), 4.73 (1, 1H, $J_{1',2'}$ = 7.5 Hz, H-1'), 4.90-5.23 (m, 5H, H-2', H-3', H-4', H-3", H-4"), 5.70 (d, 1H, $J_{1",2"}$ = 4.7 Hz, H-1").

20(S),24(R)-Epoxydammarane-3α-12β,17α,25-tetraol 3,12,25-Tri-O-(2',3',4',6'-Tetra-O-acetyl-β-D-glucopyranoside) (7). mp 226-230°C (ethanol). $[\alpha]_D^{20}$ −15.0° (c 1.0; $CHCl_3$). IR spectrum (ν, $cm^{-1}$): 1756, 3408, 3536. $^1H$ spectrum (δ, ppm): 0.85 (s, 3H), 0.88 (s, 3H), 0.92 (s, 3H), 0.98 (s, 3H), 1.13 (s, 3H), 1.15 (s, 3H), 1.18 (s, 3H), 1.20 (s, 3H), 2.00-2.11 (s, 36H, 12 × OAc), 3.10 (s, 1H, OH), 3.37 (t, 1H, J = 2.7 Hz, $H_e$-3), 3.69 (m, 4H, 3H-5', $H_a$-12), 3.99 (m, 1H, H-24), 4.10-4.35 (m, 6H, 6H-6'), 4.48 (d, 1H, $J_{1',2'}$ = 7.5 Hz, H-1' at C-3), 4.54 (d, 1H, $J_{1',2'}$ = 7.5 Hz, H-1' at C-12), 4.94 (d, 1H, $J_{1',2'}$ = 8.0 Hz, H-1 at C-25), 4.97-5.23 (m, 9H, 3H-2', 3H-3', 3H-4').

20(S),24(R)-Epoxydammarane-3α,12β,17α,25-tetraol 3-O-Acetate 12,25-Di-O-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranoside) (8). IR spectrum (ν, $cm^{-1}$): 1756, 3376, 3536. $^1H$ spectrum (δ, ppm): 0.85 (s, 3H), 0.90 (s, 6H), 1.00 (s, 3H), 1.14 (s, 3H), 1.18 (s, 3H), 1.20 (s, 6H), 2.00-2.11 (s, 27H, 9 × OAc), 3.11 (s, 1H, OH), 3.70 (m, 3H, 2H-5', $H_a$-12), 3.99 (m, 1H, H-24), 4.12-4.24 (m, 4H, 4H-6'), 4.56 (d, 1H, $J_{1',2'}$ = 7.5 Hz, H-1' at C-12), 4.66 (t, 1H, J = 1.7 Hz, $H_e$-3), 4.95 (d, 1H, $J_{1',2'}$ = 8.0 Hz, H-1' at C-25), 5.01-5.23 (m, 6H, 2H-2', 2H-3', 2H-4').

## CONCLUSIONS

1. The condensation of 20(S),24(R)-epoxydammarane-3α,12β,17α,25-tetraol(betulafolienetetraol oxide), isolated from birch leaves, with α-acetobromoglucose in the presence of mercury cyanide and of insoluble silver compounds has been studied.

2. Betulafolienetetraol oxide 3- and 12-mono-, 3,12- and 12,25-di-O- and 3,12,25-tri-β-D-glucopyranosides have been obtained for the first time.

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# SYNTHESIS OF A NUMBER OF DERIVATIVES OF ALKALOIDS AND OF NITROGEN-CONTAINING HETEROCYCLES AND THEIR ANTICHOLINESTERASE ACTIVITIES


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N-Methyl- and N-phenylcarbamates based on a number of alkaloids and nitrogen-containing heterocycles have been synthesized, and they have proved to be weak irreversible inhibitors of acetylcholinesterase and butyrylcholinesterase. It has been shown that the choline fragments of the above-mentioned carbamates and their β-methylcholine analogs are reversible inhibitors of both cholinesterases and make a substantial contribution to the anticholinesterase activity. Selective inhibitors of ACE and BuCE have been found among the compounds synthesized.


Many organophosphorus compounds having onium nitrogen in a ring exhibit high anticholinesterase activities [1-3]. A study of the influence of carbamates containing a nitrogen atom in a ring may lead to the creation of highly specific and selective cholinesterase effectors, since it is known [4, 5] that carbamates, like organophosphorus inhibitors, interact chemically with the active sites of the cholinesterases. Furthermore, by studying the laws of the antienzyme activity of carbamates with systematic variations in their structure it will be possible to obtain additional information of the structure and topography of the catalytic site of the cholinesterases.


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