GLYCOSYLATION OF 20(S),24(R)-EPOXYDAMMARANE-3α,12β,25-TRIOL IN THE PRESENCE OF INSOLUBLE SILVER COMPOUNDS

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The glycosylation of 20(S),24(R)-epoxydammarane-3α,12β,25-triol (betulafolienetriol oxide; BFTO) in the presence of silver oxide and a silver zeolite has been studied. It has been established that in contrast to the glycosylation of BFTO in nitromethane in the presence of mercuric bromide (orthoester method) and the Helferich method, glycosylation in the presence of insoluble silver catalysts takes place nonregioselectively and leads to the formation of a mixture of glucoside acetates.

The differences in the reactivities of the hydroxy groups of triterpenoids of the dammarane series makes them a suitable object for the study of regioselective and exhaustive methods of glycosylation. This, in its turn, will permit a set of synthetic analogs of the panaxosites — ginseng glycosides — to be obtained for the subsequent study of their biological action as a function of their chemical structure.

We have previously performed the synthesis of glycosides of **betulafolienetriol oxide** (BFT) (I) and its derivatives under the conditions of the Helferich and the orthoester methods [1]. It has also been shown that the catalytic rearrangements of the 3-mono- and 3,12-diorthoacetates of β-D-glucosides obtained from (I) lead to the formation of the corresponding 12-mono- and 12,25-diglucosides [2]. The anomalous regioselectivity of these rearrangements is due to the influence of intramolecular hydrogen bonds between the C-12 hydroxyl and the oxygen of the tetrahydrofuran ring of (I) [2]. We then showed the possibility of the regioselective glycosylation of the polyol (I) under Helferich's conditions [3]. It must be mentioned that in the methods of glycosylating 20(S),24(R)-epoxydammarane-3,12β,25-triols that have been studied no formation of 3-mono- and 3,12-diglucosides was observed [2, 3].

In the search for a more universal method of glycosylating triterpenoids of the dammarane series, we have investigated silver oxide and a silver zeolite [4, 5] as catalysts. It has been established that the use of silver oxide in the glycosylation of (I) in a 1:1 mixture of the solvents methylene chloride and nitromethane leads to the formation of a complex mixture of glucosides in which the tetraacetates of the 3α- and 12β-monoglycosides (II) and (III) and the octaacetate of the 3,12-diglucoside (IV) predominate (Table 1, experiment 1). The total glycosylation yield amounted to 78.7% with an 89.6% conversion of the polyol (I). In spite of the complex reaction mixture, the isolation of glycosides (II-IV) took place completely satisfactorily because of the considerable differences in their polarity. The addition of 4 Å molecular sieves to the reaction mixture did not appreciably affect the total glycosylation yield, but it changes the ratio of the glucosides (II-IV) in the direction of increasing the yield of the diglucoside (IV). The use of a silver zeolite as condensation catalyst [4] directed the reaction to the formation of the diglucoside (IV) (experiment 3). When (I) was glycosylated in methylene chloride solution a mixture of the monoglucosides (II) and (III) in approximately equal amounts was formed (experiment 4). The results obtained show the great dependence of the glycosylation of (I) on the conditions of performing condensation.

The structures of glucosides (II) and (IV) were confirmed by the results of investigations by ^{13}C and ^{1}H NMR methods and of elementary analysis. The position of attachment of the carbohydrate component was established by comparing the ^{13}C spectra of the triol (I) and the glucosides (II) and (IV) (Table 2). The trans configuration of the glycosidic bonds in (II)

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TABLE 1. Conditions and Results of the Glycosylation of 20(S),24(R)-Epoxydammarane-3α,12β,25-triol (I)

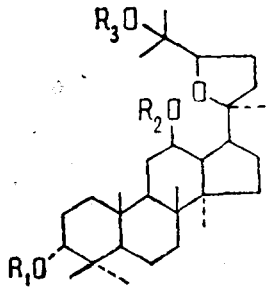
Experiment No.	Initial alcohol (I), mmole	α-ABG, mmole	Catalyst, g	Solvent, ml	Time, h	Reaction product, %
1	1	1×6	Ag_2O 0,234×6	CH_2Cl_2, 5 CH_3NO_2, 5	6	(I) 10,4 (II) 33,6 (III) 20,3 (IV) 13,2 (V) 8 8 (VI) 2.8
2	1	2×3	Ag_2O 0,4 8×3, molecular sieves* 4Å, 4₂×3	CH_2Cl_2, 10 CH_3NO_2, 10	3	(I) 4 (II) 24,7 (III) 17,3 (IV) 26,4 (V) 8,2 (VI) 4,1
3	1	1×6	Ag/zeolite 1, ₂×6	CH_2Cl_2, 5 CH_3NO_2, 5	6	(II) 1,8 (III) 6 (IV) 46 (V) 9,8 (VI) 11
4	1	4,5	Ag/zeolite 4,5	CH_2Cl_2, 10	24	(II) 26 (III) 24,7 (IV) 12

*Molecular sieves were treated with dilute acetic acid, washed with water, dried at 200°C, and calcined at ~3000°C in vacuum.

TABLE 2. ^{13}C Chemical Shifts of Compounds (I), (II), and (IV), ppm relative to TMS

C atom	Compound			^{13}C chemical shifts of the sugar components of compounds (II) and (IV)		
	I	II	IV	C atom	II	IV
1	33,7	33,9	34 0	1′	98,1	97,4; 98,0
2	25,5	20,9	20,9	2′	71,6	71,8; 71,8
3	75,9	82,3	82,1	3′	73,1	73,0; 73,0
4	37,5	37.1	37,1	4′	69,1	69,0; 68,7
5	49,5	50,0	50,0	5′	71,6	71 8; 71,8
6	18,3	18.2	17,9	6′	62,3	62,0; 62,1
7	34,8	34,8	34,6			
8	40,0	40,1	39,9			
9	50 3	50,5	50,0			
10	37,3	37.1	37,2			
11	31,2	31,3	27,5			
12	71,0	71,2	77,8			
13	47,9	49,5	47,8			
14	52.2	52,2	52,3			
15	31.2	31.3	31.8			
16	28,6	28,7	26,9			
17	49,3	48,1	50,0			
18	16,2	16,4	16,3			
19	15,4	15,5	15,6			
20	86,5	86,6	86,6			
21	26,1	26,2	22,0			
22	32,6	32,7	39,0			
23	25.0	25.1	26,2			
24	85,4	85,5	83 5			
25	70,1	70.2	71,3			
26	27.8	28,0	27,5			
27	27,6	26,2	24,3			
28	28.4	28.7	28,6			
29	22,0	22.0	22 2			
30	18,3	18,2	17.9			

and (IV) was shown by the values of the chemical shifts and the spin-spin coupling constants of the anomeric protons of the carbohydrate components of 4.45-4.52 ppm ($J_{1,2}$ = 7.0 Hz), and 4.5 ppm ($J_{1,2}$ = 7.0 Hz), respectively. The IR spectrum of compound (II) showed a broad band of hydroxylic absorption at 3415 cm^{-1} which did not disappear when the solution was diluted 20-fold.



I. $R_1=R_2=R_3=H$
II. $R_1=Glc(OAc)_4$; $R_2=R_3=H$
III. $R_1=H$; $R_2=Glc(OAc)_4$; $R_3=H$
IV. $R_1=R_2=Glc(OAc)_4$; $R_3=H$
V. $R_1=H$; $R_2=R_3=Glc(OAc)_4$
VI. $R_1=R_2=R_3=Glc(OAc)_4$

EXPERIMENTAL

IR spectra were recorded on a IR-75 spectrophotometer in $CHCl_3$ solution, and ^1H and ^{13}C NMR spectra on a Bruker HX-90E spectrometer in the Fourier regime at 30°C using 8% solutions of the substances in $CDCl_3$ with a working frequency of 90.0 MHz for ^1H and 22.63 MHz for ^{13}C. The accuracy of the measurements was +0.15 Hz for ^1H and ±1.5 Hz for ^{13}C. The assignment of the signals in the ^{13}C spectra was made by analogy with [1]. Optical rotations were determined on a Perkin-Elmer instrument in a cell 10 cm long. The melting points of the substances were determined on a Boëtius stage. Solvents were prepared by standard methods [6, 7]. Column chromatography was performed on KSK SiO_2, 100-115 mesh, treated in accordance with [8], in the petroleum ether—acetone (20:1—3:1) system, and TLC in a fixed layer of SiO_2 in the petroleum ether—acetone (2:1) system.

The triterpene (I) was isolated from the leaves of the Far Eastern species *Betula platyphilla*. mp 235-237°C (acetone). According to the literature [9]: mp 237-240°C. Catalysts were prepared by methods described in the literature [4, 10]. The elementary analyses of the compounds newly obtained corresponded to the calculated figures.

Experiment 1. A solution of 0.477 g (1 mmole) of the triterpene (I) in a mixture of 5 ml of CH_2Cl_2 and 5 ml of CH_3NO_2 was stirred while 0.234 g (1 mmole) of Ag_2O and 0.410 g (1 mmole) of α-acetobromoglucose (α-ABG) were added. The reaction was monitored with the aid of TLC until the α-ABG and the initial alcohol had disappeared. The reaction mixture was stirred with a magnetic stirrer for 6 h and it was then filtered and evaporated and the residue was washed free from excess of sugars with hot water. After column separation in SiO_2 the following products were obtained: 50 mg of (I), identical with the initial substance, 271 mg of (II); 164 mg of (III), identical for an authentic sample; 150 mg of (IV); 100 mg of (V), identical with an authentic sample; and 42 mg of (VI), identical with an authentic sample.

Compound (II) — $C_{44}H_{70}O_{13}$, mp 112-120°C (amorphous powder), $[\alpha]_D^{20}$ —22,3° (*c* 0,87; $CHCl_3$). ^1H spectrum (δ, ppm): 4.45-4.52 (d, 1 H, J = 7.0 Hz, H_1'); 2.0 (s, 3 H, OAc); 2.01 (s, 6 H, 2 × OAc); 2.1 (s, 3 H, OAc).

Compound (IV) — $C_{58}H_{88}O_{22}$, mp 196-198°C, $[\alpha]_D^{20}$—27.2° (*c* 0.77; $CHCl_3$. ^1H spectrum (δ, ppm): 4.51 (d, 1 H, J = 7.0 Hz, H_1'); 4.59 (d, 1 H, J = 8.0 Hz, H_1'); 2.01 (s, 6 H, 2 × OAc); 2.03 (s, 9 H, 3 × OAc); 2.06 (s, 1 H, OAc); 2.07 (s, 1 H, OAc); 2.1 (s, 1 H, OAc).

Experiment 2. To a solution of 1 mmole of (1) in 10 ml of CH_2Cl_2 and 10 ml of CH_3NO_2. were added 2 mmole of Ag_2O, 4 g of treated 4 Å molecular sieves, and 2 mmole of α-ABG. The reaction was performed with stirring for 3 h. Then the reaction mixture was worked up as in the previous experiment. The following products were obtained: 19 mg of (I), 200 mg of (II); 140 mg of (III); 300 mg of (IV), 94 mg of (V); and 60 mg of (VI).

Experiment 3. The triterpene (I) (1 mmole) was dissolved in a mixture of 5 ml of CH_2Cl_2 and 5 ml of CH_3NO_2, and 1.5 g of silver zeolite and 1 mmole of α-ABG was added. The reaction mixture was stirred at room temperature for 6 h until the α-ABG and the initial alcohol had disappeared, as monitored by TLC) and was then worked up by the method described. This gave: 15 mg of (II); 50 mg of (III), 524 mg of (IV), 106 mg of (V) and 162 mg of (VI).

Experiment 4. The triterpene (I) (1 mmole) was dissolved in 10 ml of CH_2Cl_2, and 4.5 g of silver zeolite and, with stirring, 4.5 mmole of αABG were added. The mixture was stirred for 24 h and was worked up by the usual method. This gave 232 mg of (II), 200 mg of (III), and 114 mg of (IV).

SUMMARY

1. The glycosylation of 20(S),24(R)-epoxydammarane-3α,12β,25-triol in the presence of insoluble silver compounds has been studied.

2. 20(S),24(R)-Epoxydammarane-3α,12β,25-triol 3-O-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranoside) and its 3,12-di-O-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranoside) have been synthesized for the first time.

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WITHASTEROIDS OF *Physalis*.

V. A STUDY OF THE ^1H AND ^{13}C NMR SPECTRA OF THE WITHASTEROIDS VISCONOLIDE AND 28-HYDROXYWITHAPERUVIN C

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The PMR and ^{13}C NMR spectra of new withasteroids — visconolide and 28-hydroxywithaperuvin C, isolated from *Physalis viscosa* L. — have been investigated. A detailed analysis of the spectral characteristics obtained is given. For visconolide is proposed the structure of 4β,12α,17β,20R,28-pentahydroxy-1-oxo-5β,6β-epoxy-22R-witha-2,24-dienolide, and for 28-hydroxywithaperuvin C that of 6β,14α,17β,20R,28-pentahydroxy-1-oxo-22R-witha-2,4,24-trienolide.

Continuing a study of the withasteroids of *Physalis viscosa* L. [1-4], we have isolated three new compounds from this plant.

A withasteroid with the composition $C_{28}H_{38}O_7$, mp 172-173°C, $[\alpha]_D^{22}$ —83±2° was identified on the basis of a comparison of spectral characteristics and physicochemical constants of the compound itself and of its acetyl derivative as withaperuvin C isolated previously from the roots of *Physalis periviana* L. [6]. The other two compounds were present in the plant in minor amounts and are new. A withasteroid with the composition $C_{28}H_{38}O_9$, we have called visconolide (I), and the second compound, with the composition $C_{28}H_{38}O_8$, is 28-hydroxywithaperuvin C (III).

Visconolide (I). An intense maximum in the UV spectrum at 220 nm (log ε 4.14) and an absorption band in the IR spectrum at 1690 cm^{-1} showed that compound (I) contained an α,β-unsaturated lactone ring. The mass spectrum contained the peaks of ions with m/z 185 (24%)

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