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SYNTHESIS OF CERTAIN MONOTERPENOID GLUCOSIDES

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The monoterpenols borneol, verbenol, 4-(1-hydroxyethyl)carene-2, and myrtenol were glucosylated using acetobromoglucose. The structures of the prepared derivatives were established using PMR and ^{13}C NMR spectroscopy.

Key words: monoterpenoids, glucosylation.

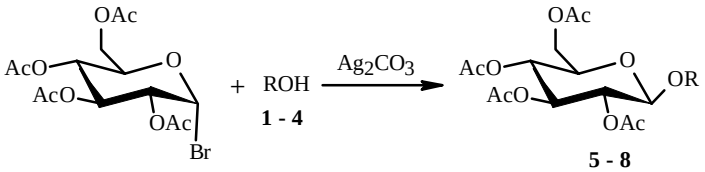
Monoterpenoids are found in essential oils of many medicinal plants and medicinal agents based on them. Monoterpene glucosides have been isolated from the medicinal plants *Origanum vulgare* L., *Rosa gallica*, which possess distinct fungicidal properties [1, 2]; and *Paeona peregrine*, which has a unique structure and possesses adaptogenic activity among others [3, 4].

The physiological activity of monoterpene glucosides was studied by synthesizing glucosides of the terpene alcohols borneol (**1**), verbenol (**2**), 4-(1-hydroxyethyl)carene-2 (**3**), and myrtenol (**4**), which have chemical structures identical to the natural ones except for **3**.

Glucosides were synthesized using the Koenig—Knorr method [5] and silver carbonate catalyst. Unreacted monoterpenoids were removed after the reactions were completed by steam distillation. Then, compounds were purified over silica-gel columns with elution by $CHCl_3$:CH_3OH of increasing polarity.

We believe that the scatter in the product yields is explained by steric hindrances in the structures of the actual monoterpenoids. In particular, the hydroxyl in **2** is more reactive because it is allylic and as far as possible from the *gem*-dimethyl on C-6. Therefore, the yield of verbenol glucoside is slightly greater than that of the other alcohols. The low yield of borneol (**1**) glucoside is explained by the fact that the C-2 hydroxyl has the *endo*-configuration that is known to be sterically shielded. Compounds **3** and **4** give similar yields:

Compound	Yeld, %
5	35
6	58
7	42
8	42



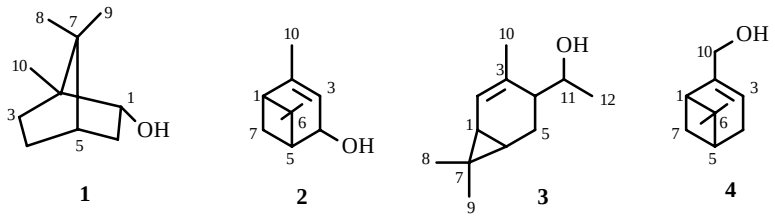


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TABLE 1. ^{13}C NMR and PMR Chemical Shifts of Monoterpenoid Glycosides, ppm*

C atom	Compound							
	5		**6**		**7**		**8**	
	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H
1	49.0	-	47.7	1.8	213.0	0.9	42.1	2.4
2	72.6	3.8	149.7	-	122.4	5.2	142.8	-
3	39.1	1.5	114.8	5.5	137.5	-	123.1	5.6
4	47.9	1.6	76.6	4.0	45.3	2.4	34.7	2.0
5	26.3	1.7	46.6	2.8	27.6	1.7	40.8	3.2
6	28.2	1.5	35.5	-	21.3	0.6	37.6	-
7	47.9	-	27.6	1.6	22.3	-	26.5	1.5
8	20.3	0.8	26.6	1.1	20.0	1.0	24.0	1.0
9	18.8	0.9	22.8	1.2	20.6	1.1	23.4	1.0
10	15.0	1.0	22.4	1.7	68.7	1.6	68.3	3.9
11	-	-	-	-	20.7	3.6	-	-
12	-	-	-	-	20.7	0.7	-	-
1′	102.3	4.7	98.9	4.2	98.8	4.6	101.1	4.4
2′	71.8	4.4	71.0	4.3	69.8	4.5	71.9	4.8
3′	71.2	5.0	69.8	4.8	68.8	5.0	70.9	5.4
4′	68.6	4.7	68.4	4.8	67.2	4.8	67.1	5.0
5′	72.6	3.7	72.9	3.5	71.0	3.5	69.7	4.0
6′	62.0	4.2	61.9	4.0	61.9	4.2	61.9	4.1
O-C=O	169-170	-	169-170	-	169-170	-	169-170	-
OCH_3	19-21	2.0	19-21	2.0	19-21	2.0	19-21	2.0

*Acetates in acylated glycosides were removed by a Zemplen reaction [6].

According to PMR and ^{13}C NMR spectra, the resulting glucosides have a β-D-glucoside bond. This was confirmed by the presence in the spectra of signals at 4.2-4.6 ppm ($J_{1'2'}$ = 8-8.5 Hz) and 99-101 ppm, respectively (Table 1). According to the literature, most glucosides isolated from medicinal plants have the β-D-configuration.

EXPERIMENTAL

^{13}C NMR and PMR spectra were recorded on a Bruker DRX 400 spectrometer at working frequency 400 and 100 MHz, respectively, in $CDCl_3$. TLC was performed on Silufol (Czech Rep.) plates using $CHCl_3$:CH_3OH (9:1 and 6:1); column chromatography, over silica gel L (100/160 μm) using mixtures of $CHCl_3$:CH_3OH (10:1-4:1). Compounds were detected by phosphotungstic acid solution (20%) in ethanol with heating at 120°C for 1 min.

2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosylbromide was prepared by the literature method [7], silver carbonate, by reacting silver nitrate (2 g) with saturated Na_2CO_3 solution (100 mL) in the dark. The resulting yellow powder was dried with anhydrous acetone and then lyophilized. Diethylether was distilled from metallic Na.

Synthesis of 5-8. A weighed portion of starting alcohol (50 mg) in absolute diethylether (20 mL) was stirred and treated with glycosylating agent (2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosylbromide, 0.7 mol amount) and $AgCO_3$ (2-fold excess, 71 mg). The reaction mixture was stirred at room temperature for 1 d. The course of the reaction was monitored by TLC. After the reaction was finished, solvent was evaporated. The excess of monoterpenoids was steam distilled. The solid was placed on a SiO_2 column and eluted by $CHCl_3$:CH_3OH (20:1-6:1).

Removal of Acetates. A solution of acetylated glucoside in anhydrous CH_3OH (25 mL) was treated with a solution prepared by dissolving metallic Na (10 mg, 0.435 mmol) in CH_3OH (absolute, 25 mL) and stirred for 5 h at room temperature. The reaction mixture was neutralized by adding cation-exchanger KU-2 (1 g) in the H-form. Yield 95-97%.

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