H_5', 2 H_6'); 5.35-5.38 (m, 1 H, H_3); 5.56-5.65 (m, 2 H, H_2', H_4'); 5.88 (d, $J_{1',2'}$ = 3.2 Hz, 1 H, 1 H_1'); 6.54 (s, 1 H, H_3); 7.70-7.80 (m, 2 H, H_6, H_7); 8.04-8.12 (m, 2 H, H_5, H_8). IR spectrum (ν, cm^{-1}): 1748 (CH_3COO), 1681 and 1648 (C=O).

SUMMARY

A method is proposed for the synthesis of acetylated glycosides of hydroxynaphthoquinones.

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SYNTHESIS OF GLUCOSIDES OF 3-ALK[EN]YL-2-HYDROXY-1,4-NAPHTHOQUINONES

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UDC 547.656+547.455+616-006.6

The condensation of D-glucose (tert-butyl orthoacetate) with 3-alk[en]yl-2-hydroxy-1,4-naphthoquinones has yielded a series of acetylated glycosides of hydroxynaphthoquinones. It has been established that the time of the glycosylation reaction lengthens with an increase in the length and in the degree of branching of the side chain of the quinone. It has been shown that when the glycosides obtained are deacetylated cleavage of the glycosidic bond takes place with the formation of glucose and the corresponding quinone methyl ethers. Details of IR and ^1H and ^{13}C NMR spectra are given.

We have previously [1, 2] reported a new method of obtaining acetylated glycosides of hydroxynaphthoquinones which consists in boiling equimolar amounts of a quinone and an orthoester in absolute chlorobenzene without a catalyst. To elucidate the possibilities of the proposed method of glycosylation, a number of 3-alk[en]yl-2-hydroxy-1,4-naphthoquinones have been condensed with the glucose orthoesters (I) and (II). The results are given in Table 1.

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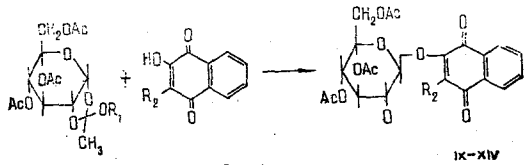
Translated from Khimiya Prirodnykh Soedinenii, No. 3, pp. 328-331, May-June, 1983. Original article submitted April 26, 1982.

0009-3130/83/1903-0310$07.50

TABLE 1. Dependence of the Time of Glycosylation of the Naphthoquinones (III-VIII) by Orthoester (I) on the Nature of R_2

Quinone	Glycoside	R_2	Time, h	Yield of glycoside, % on the quinone: taken in the reaction	Yield of glycoside, % on the quinone: consumed in the reaction	Unchanged quinone recovered, %
III	IX	H	1	64	83	23
IV	X	CH_3	1	75	93	19
V	XI	CH_2CH_3	1	56	71	21
VI	XII	$CH_2-CH=CH_2$	2	52	66	20
VII	XIII	$CH_2CH_2CH(CH_3)_2$	4	52	66	21
VIII	XIV	$CH_2-CH=C(CH_3)_2$	6	72	84	23



I. $R_1 = \tau\text{-}C_4H_9$
II. $R_1 = CH_2CH_3$

III. $R_2 = H$
IV. $R_2 = CH_3$
V. $R_2 = CH_2CH_3$
VI. $R_2 = CH_2-CH=CH_2$
VII. $R_2 = CH_2CH_2CH(CH_3)_2$
VIII. $R_2 = CH_2CH=C(CH_3)_2$

IX-XIV

As can be seen from Table 1, the conversion of the quinones amounted to 75-80%, but the yields of the glycoside differed considerably which is apparently connected with the nature of their isolation. The highest yields were obtained in the case of the readily crystallizing glycosides (X) and (XIV), which were isolated by column chromatography.

In the series of quinones (III-VIII), an increase in the time of the glycosylation reaction with a lengthening of the chain and with an increase in the degree of branching of the substituent R_2 is observed. This relationship is apparently due to the spatial and electronic effects of the substituent R_2. The introduction of an electron-donating alkyl or alkenyl substituent R_2 into the quinone molecule leads to a decrease in the mobility of the proton of the neighboring hydroxy group. This effect is probably shown in the form of a fall in the capacity of the proton of the hydroxy group of the naphthoquinone for catalyzing the formation of an acyloxonium ion from the orthoester [3], which leads to an increase in the time of the glycosylation reaction.

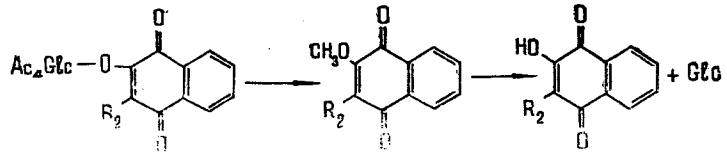
The electronic effect of the substituent R_2 is particularly significant when the orthoester (I) is replaced by the less reactive ester (II) [4]. Boiling the ester (II) with the quinone (III) for 12 h gave the glycoside (IX) with a yield of 70%, while compound (IV) did not react at all under these conditions. In order to evaluate the steric effect of R_2 in lowering the reactivity of the naphthoquinone in the glycosylation of orthoester (II), equimolar amounts of compounds (II), (III), and (IV) were boiled together for 12 h. In this case, the quinone (III) acted as a catalyst for the formation of an acyloxonium ion from the orthoester (II), which then glycosylated both the quinones (III) and (IV). As a result, a mixture of the glycosides (IX) and (X) in a ratio of ~ 2:1 was obtained with a total yield of 70%. The effective inclusion of the quinone (IV) in the reaction on combined glycosylation unambiguously shows that it is just the inductive effect of the methyl group that is responsible for the passivity of quinone (IV) on its glycosylation by the orthoester (II).

A consideration of molecular models of the whole series of naphthoquonones (III-VIII) showed that the greatest steric hindrance for the approach of the quinone to the orthoester is created in the glycosylation of the quinone (VII). Since the electronic and spatial factors act in the same direction and increase with the lengthening and the branching of the radical R_2 [5], the maximum time of the glycosylation reaction must be expected for the quinones (VI-VIII), as was confirmed by the results of the experiments (see Table 1).

The structures of the newly obtained glycosides (X-XIII) were confirmed by the results of investigations by the methods of IR and ^1H and ^{13}C NMR spectroscopy, and also by elementary analysis. It has been shown previously [2] by ^{13}C NMR spectroscopy that, under the conditions of the described method of glycosylation, the glycosides (IX) and (XIV) with a p-quinoid structure of the aglycone are formed. The results of an analysis of the ^1H NMR spectra of the glycosides of 3-alk[en]yl-2-hydroxy-1,4-naphthoquinone (X-XIII) obtained indicate the β configuration of the glycosidic bond in these compounds (the SSCC $J_{1',2'} = 6.8$-7.6 Hz). In the ^1H

NMR spectrum of (XII), the signal of the anomeric proton does not appear in the form of a separate doublet because of the superposition of the signals of the protons at the double bond of the radical R_2, and therefore the configuration of the glycosidic bond was established from the chemical shift of the anomeric carbon atoms in the ^{13}C spectrum [2].

In order to obtain glycosides with free hydroxy groups in the sugar component, compounds (IX)-(XIV) were treated in the cold with a solution of sodium methanolate in methanol. In all cases, the glycosidic bond was broken and, in addition to glucose, the corresponding initial quinone was formed. The reaction apparently takes place through a nucleophilic replacement of the glycoside residue by a methanolate ion and the formation of the methyl ether of the quinone. The corresponding methyl ethers of the quinones (III-VIII) were isolated and characterized by the ^1H NMR method. The presence of glucose in the reaction products was confirmed by TLC.



Such a pattern of cleavage of a glycosidic bond was first observed by Cote and Goodman for the case of the o-naphthoquinone glycosides lawsone and menoctone [6]. Later, de Oliveira [7] reported the deacylation of glycoside (XIV) with 85% yield. A consideration of the possible conformations of the acetylglycoside (XIV) on spatial models, however, permits the conclusion that no energetically favorable conformations in which an alkenyl substituent would prevent the nucleophilic replacement of the glucoside residue by a methanolate ion exist. This conclusion is in complete agreement with the results of the deacetylation of glycosides (IX-XIV).

EXPERIMENTAL

Melting points were determined on a Boëtius stage. Specific rotations were measured on a Perkin-Elmer 141 polarimeter. NMR spectra were taken on a Bruker HX-90 E spectrometer with a working frequency of 90.0 MHz for ^1H and 22.63 MHz for ^{13}C at 30°C in $CDCl_3$. Chemical shifts are expressed in the δ scale relative to TMS. IR spectra were recorded on a Specord IR-75 spectrophotometer in $CHCl_3$. TLC was performed on Silufol plates in the hexane–benzene–acetone (2:1:1), hexane–acetone (2:1), and chloroform–methanol (2:1) systems. The plates were first saturated with ammonia to avoid the decomposition of the orthoester in the process of chromatography. The spots were revealed by heating the plates. Column chromatography was performed on SiO_2 "L" (40-60 μ) in the hexane–acetone (10:1 → 2:1) system. The results of the analysis of all the newly obtained compounds were in satisfactory agreement with the calculated values.

Methods described in the literature were used for obtaining 3,4,6-tri-O-acetyl-α-D-glucopyranosyl 1,2-(tert-butyl orthoacetate) (I) [8]; 3,4,6-tri-O-acetyl-α-D-glucopyranosyl 1,2-(ethyl orthoacetate) (II) [9]; 2 hydroxy- and 2-methoxy-1,4,naphthoquinones [10]; and the 3-alk[en]yl-2-hydroxy-1,4-naphthoquinones (III-VIII) [11]; and the 3-alk[en]yl-2-methoxy-1,4-naphthoquinones were obtained from the corresponding quinones by methylation with diazomethane. The glycosylation of the hydroxynaphthoquinones was carried out as described in the preceding paper [2].

2-(Tetra-O-acetyl-β-D-glycopyranosyloxy)-1,4-naphthoquinone (IX). mp 166.5-168.5°C (MeOH). According to the literature [12]: mp 168.5-170°C (ethanol).

3-Methyl-2-(tetra-O-acetyl-β-D-glucopyranosyloxy)-1,4-naphthoquinone (X). mp 158-159°C (MeOH). ^1H NMR spectrum (ppm): 2.11 (s, 3 H, CH_3); 1.97-2.15 (m, 12 H, 4× OAc); 3.71-3.84 (m, 1 H, 1 H_5'), 4.11-4.19 (m, 2 H, 2 H_6'); 5.03-5.34 (m, 3 H, H_2', H_3', H_4'); 5.69 (d, $J_{1,2}$ = 6.8 Hz, 1 H, 1 H_1'), 7.65-7.76 (m, 2 H, H_6, H_7); 8.00-8.09 (m, 2 H, H_5, H_8); IR spectrum (ν, cm^{-1}): 1755 (CH_3COO); 1670 and 1658 (C=O).

3-Ethyl-2-(tetra-O-acetyl-β-D-glucopyranosyloxy)-1,4-naphthoquinone (XI). mp 163-163.5°C (MeOH). ^1H NMR spectrum (ppm): 1.11 (t, J = 6.7 Hz, 3 H, 3 H_{12}); 1.97-2.13 (m, 12 H, 4× OAc); 2.65 (q, J = 6.7 Hz, 2 H, 2 H_{11}); 3.70-3.85 (m, 1 H, 1 H_5'); 4.10-4.18 (m, 2 H, 2 H_5'); 5.13-5.38 (m, 3 H, H_2', H_3', H_4'); 5.79 (d J=7.6 Hz, 1 H, H_1'); 7.65-7.80 (m, 2 H, H_6, H_7); 7.99-8.12 (m, 2 H, H_5, H_8). IR spectrum (ν, cm^{-1}): 1755 and 1722 (CH_3COO); 1670 and 1658 (C=O).

3-Allyl-2-(tetra-O-acetyl-β-D-glucopyranosyloxy)-1,4-naphthoquinone (XII). mp 98-100°C (ether–hexane). ^1H NMR spectrum (ppm): 1.97-2.12 (m, 12 H, 4× OAc); 3.34-3.41 (m, 2 H, 2 H_{13}); 3.73-3.84 (m, 1 H, H_5); 4.08-4.17 (m, 2 H, 2 H_6'); 5.03-5.36 (m, 5 H, 2 H_{12}, H_2', H_3', H_4'); 5.71-5.92 (m, 2 H, H_{11}, H_1'); 7.66-7.77

(m, 2 H, H_6, H_7); 8.04-8.14 (m, 2 H, H_5, H_8). IR spectrum (ν, cm^{-1}): 1756 (CH_3COO); 1670 (C=O). ^{13}C NMR spectrum (ppm): 180.8 (C_1), 153.0 (C_2), 135.9 (C_3), 184.4 (C_4), 126.5 (C_5), 134.1 (C_6), 133.5 (C_7), 126.1 (C_8), 131.2 (C_9), 131.9 (C_{10}), 28.2 (C_{11}), 117.1 (C_{12}), 133.5 (C_{13}), 99.0 (C_1') 71.6 (C_2'), 72.3 (C_3'), 68.4 (C_4'), 726 (C_5'), 61.6 (C_6), 20.5 ($\underline{C}H_3COO$), 170.0 ($CH_3\underline{C}OO$).

3-(3-Methylbutyl)-2-(tetra-O-acetyl-β-D-glucopyranosyloxy)-1,4-naphthoquinone (XIII). Yellow oil, $[\alpha]_D^{24}$ − 81.9° (c 1; $CHCl_3$). ^1H NMR spectrum (ppm): 0.96 (d, J = 6.2 Hz, 6 H, 6 H_{14}); 1.34-1.59 (m, 3 H, 2 H_{12}, 1 H_{13}); 1.97-2.12 (m, 12 H, 4× OAc); 2.52-2.70 (m, 2 H, 2 H_{11}); 3.82-3.94 (m, 1 H, H_5'); 4.07-4.19 (m, 2 H, 2 H_6'); 5.12-5.36 (m, 3 H, H_2', H_3', H_4'); 5.82 (d, $J_{1',2}$ = 7.6 Hz, 1 H, H_1'); 7.65-7.76 (m, 2 H, H_6, H_7); 8.00-8.13 (m, 2 H, H_5, H_8). IR spectrum, ν, cm^{-1}): 1754 (CH_3COO); 1669 (C=O).

3-(3-Methylbut-2-enyl)-2-(tetra-O-acetyl-β-D-glucopyranosyloxy)-1,4-naphthoquinone (XIV). mp 62-63°C (MeOH). According to the literature [7]: mp 62-65°C (CH_3OH–ethyl acetate).

General Method for the Deacetylation of the Glycosides. A solution of 0.040 g of one of the glycosides (IX-XIV) in 1 ml of absolute CH_3OH was treated at 5°C with 0.1 ml of a 0.1 N solution of CH_3ONa in CH_3OH. After a few minutes the appearance of the corresponding methyl ester was detected by the TLC method in the hexane–benzene–acetone (2:1:1) and hexane–acetone (2:1) systems. The presence of glucose in the reaction mixture was confirmed by the TLC method in the $CHCl_3$–CH_3OH (2:1) system. The initial acetylated glycosides were completely converted into the methyl ethers of the corresponding quinones and glucose in 1.5-3.5 h. The reaction mixtures were diluted with water (10 ml) and extracted with $CHCl_3$ (3× 5 ml), the extracts were dried over Na_2SO_4 and after the elimination of the solvent the methyl ethers of the hydroxynaphthoquinones (III-VIII) were obtained.

According to ^1H NMR, the methyl ethers of the hydroxynaphthoquinones (III-VIII) isolated from the deacetylation reaction products were identical with the samples obtained by the methylation of the quinones (III-VII) with diazomethane.

SUMMARY

1. The condensation of D-glucose (tert-butyl orthoacetate) with 3-alk[en]yl-2-hydroxy-1,4-naphthoquinone has given a series of acetylated glucosides of hydroxynaphthoquinones.

2. It has been established that the time of the glycosylation reaction increases with the length and the degree of branching of the side chain of the quinone.

3. It has been shown that when the glycosides obtained are deacetylated the glycosidic bond is broken with the formation of glucose and the corresponding hydroxyquinone methyl ethers.

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