Synthesizing Betulin Vinyl Ethers via Direct Vinylation by Acetylene in Superbasic KOH/DMSO Medium

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Abstract

Basing on betulin vinylation by acetylene in superbasic medium KOH/DMSO, mono- and divinyl esters of betulin, valuable monomers and intermediates for the synthesis of polymers and biologically active compounds were obtained.

Key words: betulin, acetylene, vinyl esters, superbasic medium

INTRODUCTION

Vinyl ethers are widely used as monomers in polymer chemistry and intermediates in the synthesis of biologically active compounds [1–10]. Among the existing methods for producing O-vinyl ethers [11, 12] there is a method considered to be the most available that consists in the direct vinylation of alcohols by acetylene in superbasic media MOR/DMSO (M = K, Na; R = H, t-Bu) [13, 14]. In recent years, there are reports appeared in the literature concerning successful applying this method to the synthesis of the vinyl esters of hydroxyl-containing natural compounds such as sugars [15, 16], steroids [17, 18] and alkaloids [19].

Higher pentacyclic triterpenoids those represent, as a rule, high oxygenated compounds could be used as promising substrates for this reaction. The transformation of hydroxyl functions into the oxyvinyl ones allows significantly expanding the synthetic potential of this class of compounds. One of the promising applications of triterpene oxyvinyl derivatives could be presented by the synthesis of biologically active homo- and copolymers.

The purpose of this work consisted in developing a method for direct vinylation of betulin ¹ (the most accessible representative of pentacyclic triterpenoids from lupane series) by acetylene in superbasic media.

RESULTS AND DISCUSSION

Initially, the interaction of betulin ¹ with acetylene in superbasic media KOH/DMSO was carried out in an autoclave at a pressure of 16–19 atm at 80 °C during 1 h. The reaction proceeded with the formation of product of complete vinylation such as divinyl ether ², a small amount of monovinyl ether ³ and by unidentified polymerization products. Ethers ² and ³ were isolated by means of column chromatography on SiO₂ impregnated with Et₃N, with the yields equal to 58 and 4 %, respectively. An increase either in the reaction time or in the temperature up to 100 °C resulted in an increase in the percentage of polymerization products, whereas a decrease in the duration of the process leads to increasing the content of monovinyl ether ³ in the mixture (Scheme 1).
It should be noted that the secondary vinyloxy group of the ether 2 very readily undergo hydrolysis in the course of chromatographing on silica gel, not treated by Et₃N, which made difficult to isolate divinyl ether 2. In the case of prolonged contact time of compounds 2 and 3 with the sorbent, both vinyloxy groups underwent the hydrolysis. The selective hydrolysis of the secondary vinyloxy group of diether 2 could be realized under the action n-TsOH/SiO₂ in a benzene solution for three weeks.

It is known that the vinylation of a primary hydroxyl group in some sugars [17, 18] and alkaloid lupinine [19] by acetylene takes place at atmospheric pressure in superbasic media KOH/DMSO or t-BuOK/DMSO. In the case of betulin 1 the selective vinylation primary 28-OH group occurred at an atmospheric pressure in superbasic medium KOH/DMSO at 80 °C.

The ¹H NMR spectrum of divinyl ether 2 contained the entire set of signals inherent in the protons of the vinyloxy group: two-single proton doublets at 6.35 and 6.55 ppm (J 14.4 and 6.8 Hz), located in the α-position with respect to the oxygen atom, and four one-proton doublets at 3.94 ppm (Hα-2’, J = 6.8 and 1.8 Hz), 4.17 ppm (Hβ-2’, J = 14.4 and 1.8 Hz), 3.97 ppm (Hα-2″, J = 6.8 and 1.3 Hz), 4.27 ppm (Hβ-2″, J = 14.4 and 1.3 Hz) related to β-protons. In the spectrum of monovinyl ether 3, there was one set of similar signals: two doublets at 6.55 ppm (J = 14.4 and 6.8 Hz) as well as two doublets at 3.95 ppm (J = 6.8 and 1.8 Hz) and 4.17 ppm (J = 14.4 and 1.8 Hz). The ¹³C NMR spectra of ethers 2 and 3 were completely consistent with the proposed structure.

**EXPERIMENTAL**

The ¹H and ¹³C NMR spectra were registered at a room temperature using a Bruker AM-300 spectrometer with the operating frequency of 300 and 75 MHz as well as CDCl₃ as a solvent with no standard. The chemical shift values are presented with respect to the signal of solvent: δH = 7.27 ppm and δC = 77.1 ppm, the multiplicity of ¹³C signals was found from carbon spectra with the modulation of C–H interactions. The assignment of the ¹³C NMR spectral signals was performed using a JMOD mode and heteronuclear correlation. The angles of rotation were determined using a PerkinElmer 141 polarimeter. The column chromatography was carried out on SiO₂ (L grade, 100/160 mesh, Russia). For the TLC we used Sorfil plates (Sorbpolymer Co., Krasnodar, Russia). Melting point values were determined with the help of a Kofler bench. Betulin was isolated from birch bark by means of the method described in [20]. DMSO was held above KOH and distilled then above CaH₂ under vacuum, in argon atmosphere [21].

**Vinylation of betulin 1**

**Method A.** A mixture of 2.0 g (4.52 mmol) of betulin 1, 0.88 g (13.55 mmol) of
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Methods are developed for synthesizing the vinyl ethers and epoxides belonging to the lupane series by means of acetylene in superbasic KOH/DMSO media. Thus, by the example of betulin it was first demonstrated that it is possible to perform the direct O-vinylolation of triterpene alcohols belonging to the lupane series by means of acetylene in superbasic KOH/DMSO media.

Methods are developed for synthesizing the comprehensive and selective vinylation prod-
ucts of betulin hydroxy functional groups such as di- and monovinyl ethers, promising intermediates and monomers for the synthesis of biologically active compounds and polymers.

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