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LETTERS TO THE EDITOR

Convenient Synthesis of Allobetulin

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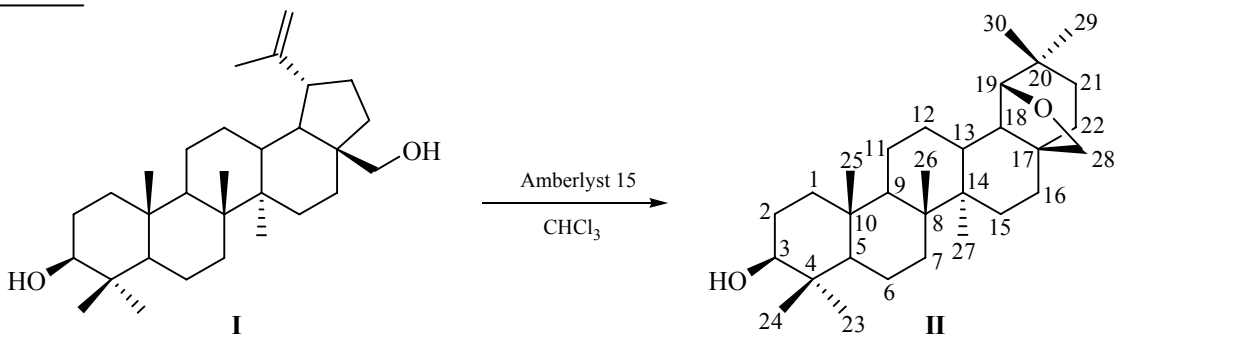
Synthetic transformations of plant triterpenoid betulin **I** widespread in nature and easily isolated in the pure form are promising for creating new and effective medicines [1]. Betulin **I** and its derivatives possess antiinflammatory, hepatoprotective, antiviral, antitumor and anti-HIV activity [2–4]. Allobetulin **II**, an isomerization product of betulin **I**, also exhibits diverse biological activity (antifeedant, antiulcer, antiviral, cytotoxic, etc.) and is used in the synthesis of pharmaceutically valuable and natural products [5–16].



I **II**

Betulin **I** was found to isomerize into allobetulin **II** in the presence of Amberlyst 15 cation resin in chloroform at room temperature in almost quantitative yield. The rate of betulin conversion increases significantly, when the reaction is carried out in boiling chloroform, but the yield of allobetulin decreses due to the formation of unidentified by-products.

The cation exchange resin Amberlyst 15 is easy to handle, non-toxic and provides an almost quantitative yield. When it is used, separation of the desired product involves only filtering and removing the solvent. An important advantage of this cation exchanger is its ability to be reused and to make on its basis a flow synthesis technology of allobetulin from betulin.

Since the content of allobetulin **II** in natural sources is insignificant, the isomerization of readily available betulin **I** is the most promising approach to its synthesis.

The isomerization of betulin **I** into allobetulin **II** is carried out in the presence of inorganic and organic acids, dimethyl sulfate, Fe(III) salts, and other acid agents [17–22].

We investigated the possibility of obtaining allobetulin **II** via betulin **I** isomerization under the influence of industrial ion-exchange resin Amberlyst 15.

The structure and purity of the obtained allobetulin were confirmed by GLC analysis, NMR data, and GC-MS method.

The ^{1}H and ^{13}C NMR spectra ($CDCl_3$) were recorded on a Bruker AM-500 instrument operating at 500.13 and 125.76 MHz, respectively. TMS was used as an internal reference. Chromatographic analysis was carried out on the hardware-software complex Chromatec-Crystal 5000 with a flame ionization detector [capillary column Restek Rtx-1 (30 m × 0.25 mm × 0.25 mm), evaporator temperature 300°C, detector temperature 300°C, column temperature 310°C, carrier gas – helium (2.4 ml min^{-1}). Chromatography-mass spectrometry analysis was performed on a GCMS-

QP2010S Shimadzu gas chromatography-mass spectrometer [EI, 70 eV, range of the detected masses 33–550 Da; capillary column HP-1MS (30 m × 0.25 mm × 0.25 μm), evaporator temperature 300°C, temperature of the ionization chamber 200°C. The analysis was carried out in the temperature programming mode from 200 to 310°C at a rate of 15 deg min^{-1}, and then at 310°C for 20 min, carrier gas – helium (1.1 ml min^{-1}).

Allobetulin (II). To a suspension of 0.1 g of betulin **I** in 3 ml of chloroform was added 0.15 g of Amberlyst 15 cation resin. The reaction mixture was stirred for 5 h. The reaction progress was monitored by GLC. After complete conversion of the substrate the cation exchange resin was filtered off, and the solvent was evaporated in a vacuum. Yield 0.094 g (94%), mp 263–265°C. ^{1}H NMR spectrum, δ, ppm: 0.77 s (3H, CH_3), 0.80 s (3H,CH_3), 0.84 s (3H, CH_3), 0.91 s (3H, CH_3), 0.93 s (3H, CH_3), 0.97 s (6H, CH_3), 1.20–1.73 m (24H, CH_2, CH), 3.20 d.d (1H, C^3H, *J* 11.6, 4.9 Hz), 3.44 d (1H, $C^{28}H_2$, *J* 7.8 Hz), 3.53 s (1H, $C^{19}H$), 3.77 d.d (1H, $C^{28}H_2$, *J* 7.8, 1.2 Hz). ^{13}C NMR spectrum, δ_C, ppm: 13.51 (C^{27}), 15.38 (C^{24}), 15.70 (C^{26}), 16.48 (C^{25}), 18.25 (C^6), 20.98 (C^{11}), 24.55 (C^{29} or C^{30}), 26.25 (CH_2), 26.43 (CH_2), 26.44 (CH_2), 27.40 (C^2), 27.97 (C^{23}), 28.81 (C^{29} or C^{30}), 32.70 (C^{21}), 33.90 (C^7), 34.14 (C^{13}), 36.26 (C^{17}), 36.74 (C^{16}), 37.25 (C^{10}), 38.88 (C^4), 38.91 (C^1), 40.60 (C), 40.70 (C), 41.47 (C), 46.82 (C^{18}), 51.07 (C^9), 55.48 (C^5), 71.26 (C^{28}), 78.96 (C^3), 87.93 (C^{19}). Mass spectrum, *m*/*z* (I_{rel}, %): 443 (2) $[M]^+$, 135 (67), 121 (70), 107 (73), 95 (100), 93 (71), 81 (93), 69 (80), 55 (67), 43 (90), 41 (60).

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