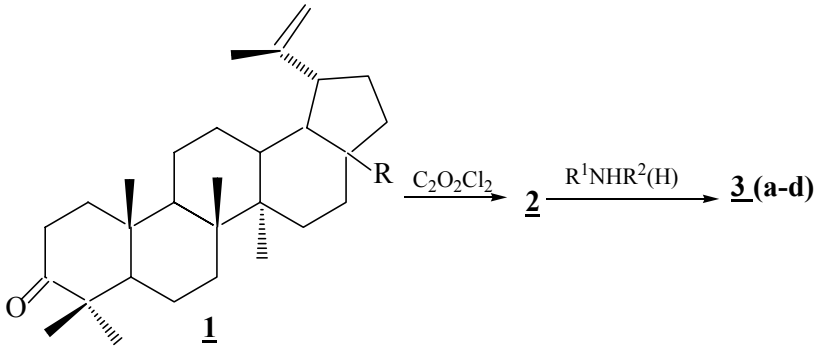
International Conference on Natural Products and Physiologically Active Substances (ICNPAS-2004)
September 12-17, 2004, Novosibirsk, Russia
Poster Presentation

Synthesis of N-substituted Amides of Betulonic Acid

Tamara I. Kogay, Boris N. Kuznetsov

Institute of Chemistry and Chemical Technology SB RAS,
Akademgorodok, Krasnoyarsk, 660036, Russia
E-mail: kogay@lan.krasu.ru

Betulonic acid is being intensively investigated as a therapeutic agent for a variety of diseases. It is established that betulonic acid and some of its derivatives have anti-cancer and anti-HIV activity. Betulonic acid (**1**) can be derived rather easily from betulin by oxidation with chromium trioxide. This invention provides novel betulonic acid N-substituted amides. The novel amides of betulonic acid was synthesized as shown in the scheme:



1 R = COOH
2 R = COCl
3 R= $CONR^1R^2(H)$

3(a) R^1 = 1- adamantyl, R^2 = H
3(b) R^1 = 1-(1-adamantyl)ethyl, R^2 = H
3(c) R^1, R^2 = $-(CH_2)_2$-O-$(CH_2)_2-$
3(d) R^1, R^2 = $-(CH_2)_5-$

Chloranhydride of betulonic acid (**2**) have been prepared from betulonic acid (**1**) and oxalil chloride in anhydrous dichloromethane at room temperature with the yield 95%. The following procedures were used to produce N-substituted amides of betulonic acid (**3 a-d**). Chloranhydride (**2**) was treated with the suitable amine (for preparation **3a** 1-adamantylamine; **3b** – 1-(1-adamantyl)ethylamine; **3c** – morpholine; **3d** – piperidine) in anhydrous dichloromethane in the presence of triethylamine during 6–8 hours at room temperature. Amides (**3 a-d**) were obtained with yield 65-75% and purified with thin-layer chromatography. The structure of these amides have been confirmed by elemental analysis and IR-spectroscopy. Typical for an amide group the band at 1665 – 1625 cm^{-1} was detected in spectra of the amides. The band at 1500 and 1533 was assigned to the mono substituted amides (**3 a,b**).