SYNTHESIS OF METHYL [3,2-*c*]-PYRAZOL-LUP-20(29)-EN-28-OATE

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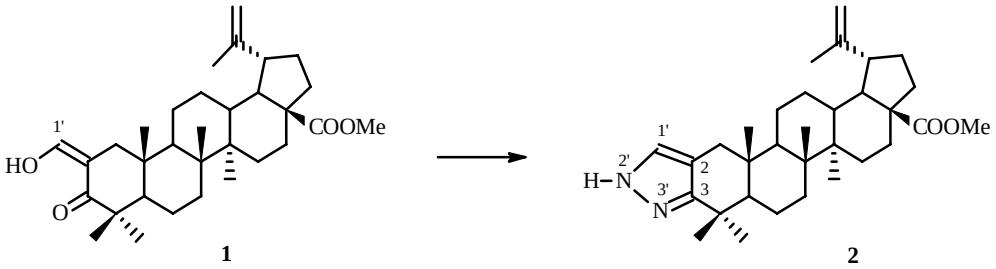
Reaction of 2-hydroxymethylenebetulonic acid with hydrazine hydrate produced methyl-[3,2-c]-pyrazol-lup-20(29)-en-28-oate.

Key words: betulonic acid methyl ester, pyrazole.

The synthesis of derivatives of lupanoic acids is interesting owing to their variety of biological activities [1-5], including antiviral and antitumor.

This work describes the synthesis of methyl-[3,2-*c*]-pyrazol-lup-20(29)-en-28-oate (**2**), a new N-containing heterocyclic derivative of betulonic acid. A convenient method for introducing the additional heterocyclic fragments into the triterpenoid structures is the reaction of their 2-hydroxymethylene-3-ketones with hydrazine and urea derivatives [6-9].

We found that reaction of 2-hydroxymethylene-methylbetulonate (**1**) with hydrazine hydrate and boiling in ethanol forms pyrazole **2** in 80% yield.



The structure of **2** was determined using NMR spectroscopy. Thus, the ^{13}C NMR spectrum exhibits strong-field shifts for C-3 to 177 ppm and C-1′ to 134.3 ppm. The signal of C-2 is shifted to weak field by 7 ppm. The PMR spectrum lacks a signal for the OH group of the hydroxymethylene fragment at 8.8 ppm [10] whereas signals are observed for H-2′ at weak field (10.3 ppm) and H-1′ (7.1 ppm).

It is interesting that the reaction of **1** with urea and thiourea in alcohol did not form the N-heterocycles [10].

EXPERIMENTAL

IR spectra were recorded on Specord M80 and UR-20 spectrometers in mineral oil. PMR and ^{13}C NMR spectra were recorded on a Bruker AM-300 spectrometer (300 and 75.5 MHz, respectively) in $CDCl_3$ with TMS internal standard. Melting points were measured on a Boetius microstage.

TLC was perfromed on Silufol plates (Chemapol, Czech Rep.) using $CHCl_3$—CH_3OH (25:1). Compounds were developed by phosphotungstic acid in ethanol (10%) with subsequent heating at 100-120°C for 2-3 min.

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Solvents were prepared using standard methods [11]. 2-Hydroxymethylene-methybetulonate was prepared as before [10]. Elemental analyses agreed with those calculated.

Methyl-[3,2-*c*]-pyrazol-lup-20(29)-en-28-oate (2). Compound **1** (0.47 g, 1 mmole) in ethanol (50 mL) was treated with hydrazine hydrate (0.1 mL) and refluxed for 2 h. The reaction mixture was poured into cold saturated $NaHCO_3$ solution (50 mL). The solid was washed with water, dried, and chromatographed over Al_2O_3 with elution by $CHCl_3$. Yield 0.39 g (80%), R_f 0.42, mp 270-272°C. $C_{32}H_{48}N_2O_2$. IR spectrum (ν, cm^{-1}): 1710, 1660, 1616, 1480, 1450, 1364, 1312, 1263, 1228, 1188, 1040, 1006, 968, 916, 896, 833, 728. PMR spectrum (δ, ppm): 0.72, 0.91, 0.93, 0.99, 1.04 (5s, 15H, $5CH_3$), 1.00-2.00 (m, H, CH_2, CH), 1.64 (s, 3H, CH_3), 2.52-2.57 (m, 1H, H13), 2.90-3.00 (m, 1H, H19), 3.61 (s, 3H, OCH_3), 4.56 and 4.69 (both br., 1H each, H29), 7.10 (br.s, 1H, H1′), 10.32 (s, 1H, H2′). ^{13}C NMR spectrum (δ, ppm): 14.8 (C-27), 15.8 (C-24), 16.0 (C-25), 16.7 (C-26), 19.2 (C-6), 19.5 (C-30), 21.5 (C-11). 25.7 (C-12), 26.9 (C-15), 27.4 (C-23), 29.9 (C-16), 30.7 (C-21), 34.1 (C-7), 34.4 (C-22), 36.8 (C-13), 37.1 (C-10), 38.3 (C-1), 40.7 (C-8), 42.5 (C-14), 43.1 (C-4), 47.0 (C-19), 49.3 (C-18), 49.6 (C-9), 51.3 (OMe), 53.6 (C-5), 56.7 (C-17), 109.7 (C-29), 112.5 (C-2), 134.3 (C-1′), 150.6 (C-20), 176.7 (C-28), 177.0 (C-3).

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