Chemistry of Natural Compounds, Vol. 46, No. 4, 2010

REACTION OF DEOXYVASICINONE WITH ORGANOLITHIUM COMPOUNDS

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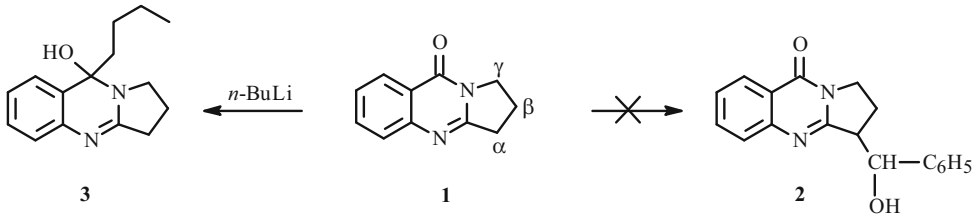
UDC 547.944/945

4-Butyl-4-hydroxydeoxypeganine was prepared by lithiation of deoxyvasicinone. Deoxypeganine and 1,2-dihydrodeoxypeganine were produced by reduction of deoxyvasicinone with lithium aluminum hydride.

Keywords: deoxyvasicinone, deoxypeganine, 4-butyl-, 4-hydroxydeoxypeganine, 1,2-dihydrodeoxypeganine, *n*-butyllithium.

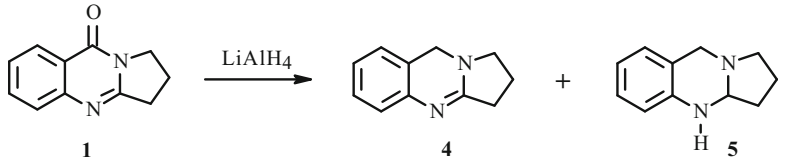
We have previously shown that deoxyvasicinone (**1**) and its analogs react with carbonyl compounds (aromatic aldehydes, acid chlorides) to give derivatives substituted in the α-position [1–4]. The course of the reaction along this direction was explained by the lability of the H atoms in the α-position due to withdrawal of electrons from the α-C by the N=C bond [1]. Furthermore, it was observed that attempts to reduce the carbonyl with $LiAlH_4$ in the absence of inert gas gave small quantities of vasicinone in addition to the reduction product [5]. This results from oxidation of the α-C atom. Therefore, it was assumed that it formed through an intermediate bonded to a lithium cation. Based on this, we hypothesized that the reaction of **1** could be carried out with organolithium compounds, e.g., butyllithium, in order to prepare this intermediate. Then, this reaction could be used to prepare α-substituted deoxyvasicinones, which are difficult to obtain by other methods. Thus, we decided to study the reaction of **1** with *n*-BuLi with subsequent work up of the reaction mixture by electrophilic reagents in order to prepare **2**.



3 **1** **2**

Carrying out the reaction of **1** with *n*-BuLi in THF or anhydrous ether at –78 or 0°C with subsequent addition of benzaldehyde unexpectedly did not form **2**. The reaction took a different direction, i.e., *n*-BuLi added to the carbonyl. Therefore, **2** did not form through the action of an electrophile. Instead, 4-butyl-4-hydroxydeoxypeganine (**3**) was obtained.

We carried out the reduction of **1** by $LiAlH_4$ under an N_2 atmosphere. The reaction went in two directions to form deoxypeganine (**4**) and 1,2-dihydrodeoxypeganine (**5**) in a 2:3 ratio, i.e., the carbonyl group was reduced to methylene, giving **4**, which was further reduced to **5**.



1 **4** **5**

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 0009-3130/10/4604-0598

The structures of the synthesized compounds were proven using PMR, IR, and mass spectra.

This reaction with other organolithium compounds is still being studied.

EXPERIMENTAL

IR spectra were obtained on a Model 2000 Fourier IR-spectrometer (Perkin–Elmer). PMR spectra were recorded in $CDCl_3$ on a Unity Plus instrument at operating frequency 400 MHz. Mass spectra were recorded on a Kratos MS-30 spectrometer (England) at ionizing potential 70 eV and source temperature 220°C. The purity of products was monitored by TLC on Silufol UV-254 plates (Czech Rep.).

Synthesis of 4-butyl-4-hydroxydeoxypeganine (3): A. A cold solution (–78°C) of deoxyvasicinone (**1**, 100 mg, 0.537 mmol) in THF (5 mL) was treated dropwise with a solution of *n*-BuLi (2.6 M, 0.644 mmol, 0.25 mL) under N_2, stirred at –78°C for 1 h, and treated with MeOH (2 mL) to destroy the remaining *n*-BuLi. Solvent was distilled off. The solid was separated over a column (petroleum ether:EtOAc, 7:3) to afford **3** (95 mg), yield 73%, R_f 0.86 (EtOAc:MeOH:petroleum ether, 7:2:1), mp 116°C, $C_{15}H_{20}N_2O$.

B. Deoxyvasicinone (0.93 g, 5 mmol) was dissolved in anhydrous ether (100 mL), cooled to 0°C, and treated dropwise under N_2 with *n*-BuLi in hexane at a rate such that the temperature remained below 5°C. The addition took 30 min. After the *n*-BuLi was added, the mixture was again cooled to 0°C, treated dropwise with MeOH (10 mL) from a dropping funnel, held at this temperature for 8 h, left overnight, and treated with water (50 mL). The resulting crystals were filtered off, washed with water until neutral, and recrystallized from hexane to afford a product (0.4 g, 33%) with mp 116°C, R_f 0.09 (acetone:$CHCl_3$, 2:1). A mixed melting point with the sample obtained by method A was not depressed.

IR spectrum (cm^{-1}): 3669, 3506, 3395, 3336, 3103. PMR spectrum (400 MHz, $CDCl_3$, δ, ppm): 0.8 (3H, t), 1.45–1.57 (2H, m), 1.76 (1H, br.s, OH), 2.13 (2H, t), 2.34–2.47 (2H, m), 2.79 (2H, t), 3.48–3.59 (2H, m), 4.39 (2H, t), 7.1 (1H, d), 7.27 (2H, t), 7.6 (1H, d); HR-ES-MS, (*m*/*z*): 226 $[M - 18]^+$, 171 $[M - 73]^+$.

Reduction of Deoxyvasicinone by $LiAlH_4$. Deoxyvasicinone (1.86 g, 0.01 mol) in THF (25 mL) under N_2 was treated with $LiAlH_4$ (1.52 g, 0.04 mol), refluxed for 8 h, treated with NaCl solution to destroy the remaining $LiAlH_4$, filtered, and extracted with $CHCl_3$ (3×). The organic layer was dried over anhydrous $MgSO_4$. The solvent was distilled off. The solid was separated over a column (petroleum ether:EtOAc, 1:1) to afford **4** (0.612 g, 35.6%), mp 86–87°C (lit. mp 86–87°C) [6]. We also isolated **5** (0.929 g, 53.4%), mp 69–70°C (lit. mp 69–70°C) [7].

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