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ONE-POT SELECTIVE SYNTHESIS OF N-VINYL-4,5-DIHYDROBENZO[*g*]INDOLE FROM 1-TETRALONE AND ACETYLENE IN THE SYSTEM $NH_2OH·HCL$–KOH–DMSO

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The chemistry of benzoindoles has been intensively developed in connection with the discovery of the indole antibiotics CC-1065 and duocarmycin [1, 2]. Benzo[*g*]indole derivatives show antiarrhythmic, anti-inflammatory, and hypotensive activity and also act as central nervous system depressants [3]. 4,5-Dihydrobenzo[*g*]indole and its methoxy derivative have been used to create novel, highly active fluorophores of the boradiazaindacene family, emitting in the long wave region (λ_{max} 673 nm) with a quantum yield of 0.38 and proposed as high efficiency fluorescence labels [4]. Benzo[*g*]indole is prepared by the oxidation of hydroxynaphthopiperidine in 27% yield [5] or by cyclization of pyruvic acid with naphthylhydrazine and subsequent decarboxylation in 55% yield [6].

4,5-Dihydrobenzo[*g*]indoles are of particular interest in a synthetic sense because they opens up new possibilities for functionalizing the benzo[*g*]indole skeleton. This is because, in contrast to other members of this series, the position 2 in the 4,5-dihydro isomers shows a high and selective sensitivity to electrophilic attack, being pyrroles in a chemical sense. Hence a route to the hard to obtain 2-functionalized benzo[*g*]indoles is opened up. At the same time, methods for the synthesis of 4,5-dihydrobenzo[*g*]indoles are limited and, so far as we are aware, exclusively based on the reaction of 1-tetralone oxime with acetylene in the systems KOH-DMSO [7] or LiOH–DMSO [4] (the Trofimov reaction [8-10]).

Recently, 4,5-dihydrobenzo[g]indole and its N-vinyl derivative have been prepared as a mixture from 1-tetralone by treatment consecutively with $NH_2OH·HCl$–$NaHCO_3$ in DMSO and then reaction of the oxime formed with acetylene (after blowing away the carbon dioxide gas evolved) using the system KOH–DMSO (100ºC, 5 h, 1 atm, yield of nonvinyl product 72%) [11]. Using these reagent, we were able to obtain N-vinyl-4,5-dihydrobenzo[*g*]indole selectively, carrying out the final stage under acetylene pressure (100-105ºC, 3 h, 14 atm, yield 79%) [12]. The obvious advantage of this method is that it eliminates the need to separate and purify the oxime. At the same time, the synthesis involves the use of an additional base ($NaHCO_3$) and preliminary total removal of carbon dioxide gas from the reaction mixture (CO_2 residues lower the catalytic activity of the KOH–DMSO system).

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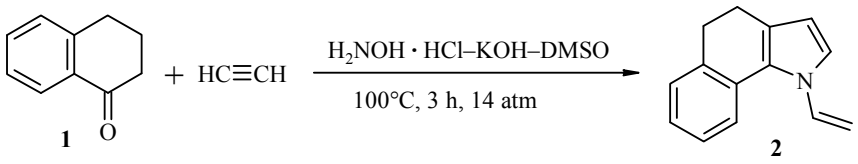
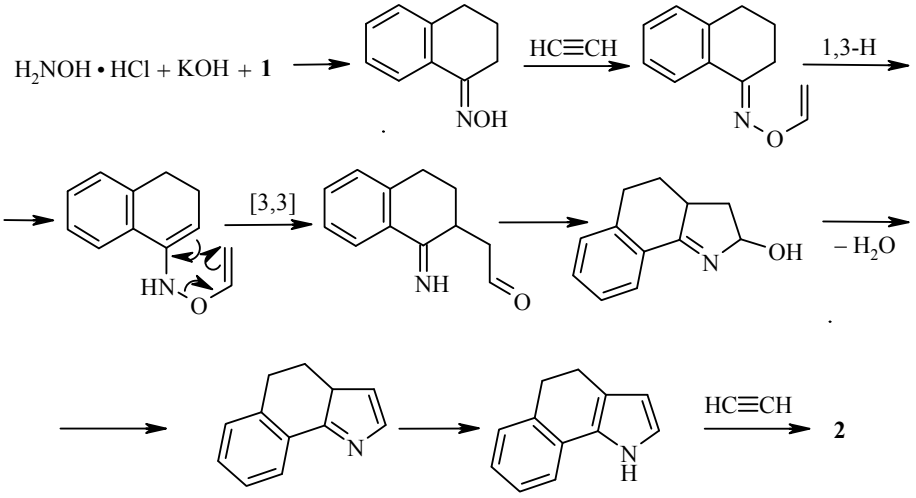
We now report a novel, selective, one-pot synthesis of N-vinyl-4,5-dihydrobenzo[*g*]indole (**2**) from 1-tetralone (**1**) and acetylene in the system $NH_2OH·HCl$–KOH–DMSO (molar ratio of **1**:$NH_2OH·HCl$: KOH = 1:1:2.5). The synthesis does not need the use of an additional base or the removal of carbon dioxide gas from the reaction mixture. The yield of chromatographically pure indole **2** is 71%.



This synthesis occurs in one pot as a typical multicomponent process including a series of consecutive and parallel reactions which are: reaction of hydroxylamine hydrochloride with KOH, oximation of ketone **1**, vinylation of the oxime formed using acetylene followed by a domino reaction of the O-vinyloxime to the intermediate 4,5-dihydro-1H-benzo[*g*]indole, and finally its further vinylation.



The novel, simple, and selective method for synthesis of compound **2** broadens the horizons of its use as a precursor of medicines and as a monomer in the design of optoelectronic materials.

^1H and ^{13}C NMR spectra were recorded on a Bruker 400DPX spectrometer (400 and 100 MHz respectively) using $CDCl_3$ and with HMDS as internal standard at 0.05 ppm.

N-Vinyl-4,5-dihydrobenzo[*g*]indole (2). A mixture of 1-tetralone (**1**) (5.00 g, 34 mmol), $NH_2OH·HCl$ (2.34 g, 34 mmol), and $KOH·0.5H_2O$ (5.52 g, 85 mmol) in DMSO (50 ml) was placed in a steel, rotating autoclave (V = 0.5 l). It was heated for 0.5 h at 100ºC after which it was treated with acetylene at the same temperature. The initial pressure in the autoclave was 14 atm. At reaction temperature, it reached a maximum of 28 atm. and began to fall rapidly. After discharge from the autoclave the reaction mixture was diluted with water (150 ml), extracted with diethyl ether (5×30 ml), and the ether extracts were washed with water and dried over K_2CO_3. Removal of ether gave a residue which was purified by flash-chromatography on alumina (eluent benzene–ether with a gradient from 1:0 to 1:0.5). The yield of compound **2** as a bright-red, viscous liquid was 4.74 g (71%) and its physicochemical characteristics agreed with those in the literature [13]. ^1H NMR spectrum, δ, ppm (J, Hz): 7.48 (1H, m, H Ar); 7.39 (2H, m, H Ar); 7.36 (1H, dd, $^3J_{B\text{-}X}$ = 15.6, $^3J_{A\text{-}X}$ = 8.9, H_X); 7.19 (1H, m, H Ar); 7.02 (1H, m, H-2); 6.25 (1H, m, H-3); 5.35 (1H, d, $^3J_{B\text{-}X}$ = 15.6, H_B); 4.94 (1H, d, $^3J_{A\text{-}X}$ = 8.9, H_A); 2.97

(2H, m, H-5); 2.76 (2H, m, H-4). ^{13}C NMR spectrum, δ, ppm: 137.7 (C-5a); 136.2 (C-9b); 133.3 (C-α); 128.2 (C-7); 127.9 (C-9a); 127.9 (C-6); 125.4 (C-8); 125.1 (C-3a); 122.0 (C-9); 120.6 (C-2); 110.0 (C-3); 100.7 (C-β); 30.8 (C-5); 22.3 (C-4). Found, %: C 86.21; H 6.68; N 7.22. $C_{14}H_{13}N$. Calculated, %: C 86.12; H 6.71; N 7.17.

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