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ONE-POT SYNTHESIS OF SPIRO-N-METHYLHEXAHYDROBENZO[*f*]ISOQUINOLINE-1,2'-(TETRAHYDRO-1'-NAPHTHALENONE) BY THE CONDENSATION OF α-TETRALONE WITH FORMALDEHYDE AND METHYLAMINE

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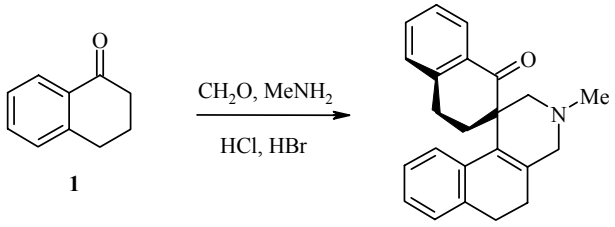
The condensation of a three-component mixture consisting of acetophenone, formaldehyde, and methylamine under conditions of the Mannich reaction gives a Mannich double base, which may then be converted by the action of alkali into 3-benzoyl-4-hydroxy-4-phenylpyridine [1]. Upon heating at reflux in hydrobromic acid, this pyridine product undergoes dehydration and cyclization to give tetrahydroindeno-[2,1-*c*]pyridine, which has antihistaminic activity [2]. In the present work, we have found that the use of α-tetralone (**1**), a cyclic acetophenone analog, in an analogous mixture permits a one-pot condensation, leading in one step to spiro compound **2**. This pentacyclic compound is, to the best of our knowledge, the first example of a new heterocyclic system.



1 **2**

In accord with the prediction by the PASS Internet system [3], ketone **2** may have antineurotoxic and psychotropic (antiepileptic) activity with probability 71 and 75%, respectively. Furthermore, this product may be an inhibitor of the reverse capture of neuromediators and display antiparkinsonian action (75%).

The ^{1}H NMR spectra were taken on a Bruker WP-400 spectrometer at 400 MHz in $CDCl_3$ with the residual protons of the deuterated solvent as the internal standard. The electron impact mass spectra were taken on a Finnigan MAT Incos 50 mass spectrometer at 70 eV. The IR spectra were taken on an IR-75 spectrometer in KBr pellets.

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Spiro-N-methyl-1,2,3,4,5,6-hexahydrobenzo[*f*]isoquinoline-1,2'-(1',2',3',4'-tetrahydro-1'-naphthalenone) (2). A mixture of α-tetralone (**1**) (23.4 g, 0.16 mol), formalin (12 ml, 38%), methylamine hydrochloride (5.4 g, 0.08 mol), and hydrochloric acid (10 ml, 10%) was heated for 1 h at 90°C with stirring until a homogeneous solution was formed. Then, hydrobromic acid (50 ml, 48%) was added to the reaction mixture, which was heated at reflux for 2 h and maintained for 20 h at 20°C. The mixture formed was diluted by adding 50 ml water, brought to pH 9 by adding alkali, and extracted with ether. The extract was dried and the solvent was distilled off in vacuum. The residue was subjected to chromatography on an alumina column using ether–hexane as the eluent to give compound **2** (1.9 g, 18%) as light-beige crystals; mp 159-161°C. IR spectrum, ν, cm^{-1}: 1673 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.16-2.27 (3H, m, C–CH_2); 2.36 (3H, s, CH_3); 2.72-2.94 (4H, m, C–CH_2); 2.86 (2H, s, NCH_2); 3.07-3.28 (3H, m, NCH_2 and C–CH_2); 6.74, 6.93, 7.01, and 7.10 (1H each, ABCD system, ^3J = 7.4, ^3J = 7.2 and ^3J = 7.1, H_{arom}); 7.29, 7.36, 7.53, and 8.16 (1H each, ABCD system, ^3J = 7.7, ^3J = 7.6 and ^3J = 7.1, H_{arom}). Mass spectrum, *m/z* (I_{rel}, %): 329 (97), 328 (14), 286 (21), 285 (40), 184 (19), 183 (22), 182 (18), 170 (100), 165 (22), 141 (38), 128 (23), 115 (31), 91 (20), 90 (21), 57 (95). Found %: C 83.92; H 7.21; N 4.36. $C_{23}H_{23}NO$. Calculated, %: C 83.85; H 7.04; N 4.25.

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3. http://195.178.207.233/PASS/