

SHORT
COMMUNICATIONS

Synthesis of Indole-containing Hexahydrobenzofuranes

V. M. Berestovitskaya, O. S. Vasil'eva, and S. M. Aleksandrova

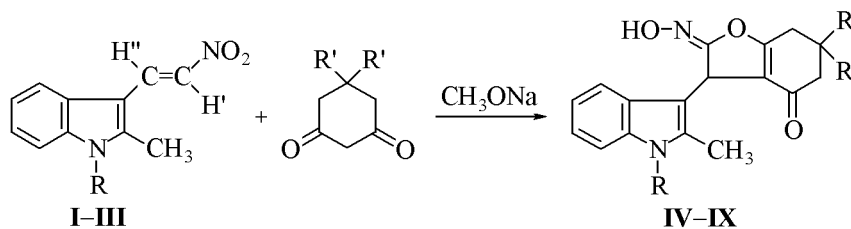
Herzen Russian State Pedagogical University, St. Petersburg, 191186 Russia

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Indole-containing heterocyclic compounds are interesting as potential biologically active substances. Just this group of compounds contains the widely used pharmaceuticals, e.g., diazoline, cavinton, ondasetrone [1–3] etc.

We were first to demonstrate that 2-methylindolyl-nitroalkenes in contrast to analogs unsubstituted in the indole ring formed with 1,3-cyclohexanediones

not open-chain addition products [4] but oximes of hexahydrobenzofuranons. Reactions of 2-methyl-3-(2-nitrovinyl)indoles (**I–III**) with dimedone and dihydroresorcinol proceed in the presence of sodium methylate and the primary Michael adduct undergoes heterocyclization into new heterocyclic systems **IV–IX**. Note that the synthesis of similar compounds was formerly described by an example of dimedone condensation with 1-methyl(phenyl)-2-nitroethenes [5, 6].



R = H (**I**), CH₃ (**II**), CH₂C₆H₅ (**III**); R = H, R' = H (**IV**), CH₃ (**V**); R = CH₃, R' = H (**VI**), CH₃ (**VII**); R = CH₂C₆H₅, R' = H (**VIII**), CH₃ (**IX**).

The indole-containing hexahydrobenzofuranes obtained **IV–IX** are colored crystalline compounds with sharp melting points. Their structure is unambiguously proved by ¹H NMR, IR, and mass spectra. For instance, in the mass spectrum of compound **V** is present a molecular ion peak of *m/z* 324 corresponding to the molecular weight of the assumed structure.

The ¹H NMR spectrum of compound **V** alongside the signals from the protons of the indole moiety [7.02 (indole), 2.40 (CH₃), 10.20 ppm (NH)] and also from methylene (2.12–2.66 ppm) and methyl (1.08 ppm) groups of the cyclohexenone fragment contains a singlet from methine proton in the dihydrofuran ring (5.08 ppm) and a broadened peak from the proton of NOH group (11.0 ppm).

In the IR spectra of hexahydrobenzofuranes **VI–IX** appears a strong absorption band from stretching

vibrations of the conjugated C=O and C=N bonds at 1600–1700 cm⁻¹; in the high-frequency region is present a weak broadened band at 3100–3700 cm⁻¹ that should be assigned to the stretching vibrations of NO–H bond.

Compounds **I–III** were prepared along procedure [7]; we failed to find characteristics of compound **II** in the literature; compound **III** was obtained for the first time.

1,2-Dimethyl-3-(2-nitrovinyl)indole (II). Yield 72%. mp 170°C (from methanol). ¹H NMR spectrum, δ, ppm: 2.57 s (3H, CH₃), 3.77 s (3H, N–CH₃), 7.50 m (4H, indole), 7.80 d (1H, H'), 8.34 d (1H, H'). Found, %: C 66.76, 66.75; H 5.68, 5.64; N 12.93, 12.95. C₁₂H₁₂N₂O₂. Calculated, %: C 66.67; H 5.56; N 12.96.

1-Benzyl-2-methyl-3-(2-nitrovinyl)indole (III). Yield 72%. mp 114–116°C (from methanol).

^1H NMR spectrum, δ , ppm: 2.60 s (3H, CH_3), 5.39 s (2H, N- CH_2), 7.30 m (5H, C_6H_5), 7.50 m (4H, indole), 7.80 d (1H, H'), 8.40 d (1H, H'(-5h)'). Found, %: C 74.09, 74.02; H 5.53, 5.53; N 9.62, 9.61. $\text{C}_{18}\text{H}_{16}\text{N}_2\text{O}_2$. Calculated, %: C 73.97; H 5.48; N 9.59.

2-Hydroxyimino-3-(2-methylindol-3-yl)-2,3,4,5,6,7-hexahydrobenzofuran-4-one (IV). Yield 57%. mp 190–191°C (from methanol). IR spectrum, ν , cm^{-1} : 1600–1700 (C=O, C=N), 3350 br.s (NH, NOH). ^1H NMR spectrum, δ , ppm: 2.06–2.75 m (6H, 3 CH_2), 2.42 s (3H, CH_3), 5.01 s (1H, CH), 7.03 m (4H, indole), 10.00 s (1H, NH), 10.70 s (1H, NOH). Found, %: C 69.31, 69.37; H 6.17, 6.16; N 9.78, 9.77. $\text{C}_{17}\text{H}_{16}\text{N}_2\text{O}_3$. Calculated, %: C 68.90; H 5.40; N 9.46.

2-Hydroxyimino-6,6-dimethyl-3-(2-methylindol-3-yl)-2,3,4,5,6,7-hexahydrobenzofuran-4-one (V). Yield 67%. mp 220–221°C (from methanol). IR spectrum, ν , cm^{-1} : 1640–1710 (C=O, C=N), 3370 br (NH, NOH). ^1H NMR spectrum, δ , ppm: 1.08 s (6H, 2 CH_3), 2.12–2.66 m (4H, 2 CH_2), 2.40 s (3H, CH_3), 5.08 s (1H, CH), 7.02 m (4H, indole), 10.20 s (1H, NH), 11.00 s (1H, NOH). Mass spectrum, m/z 324 M^+ : Found, %: C 70.52, 70.51; H 6.29, 6.27; N 8.60, 8.61. $\text{C}_{19}\text{H}_{20}\text{N}_2\text{O}_3$. Calculated, %: C 70.40; H 6.17; N 8.64. M 324.

2-Hydroxyimino-3-(1,2-dimethylindol-3-yl)-2,3,4,5,6,7-hexahydrobenzofuran-4-one (VI). Yield 67%. mp 175–177°C (from methanol). IR spectrum, ν , cm^{-1} : 1630–1710 (C=O, C=N), 3400 br (NOH). ^1H NMR spectrum, δ , ppm: 2.06–2.74 m (6H, 3 CH_2), 2.44 s (3H, CH_3), 3.70 s (3H, N- CH_3), 5.16 s (1H, CH), 7.10 m (4H, indole), 10.00 s (1H, NOH). Found, %: C 69.34, 69.35; H 5.90, 5.91; N 9.45, 9.41. $\text{C}_{18}\text{H}_{18}\text{N}_2\text{O}_3$. Calculated, %: C 69.70; H 5.81; N 9.03.

2-Hydroxyimino-6,6-dimethyl-3-(1,2-dimethylindol-3-yl)-2,3,4,5,6,7-hexahydrobenzofuran-4-one (VII). Yield 50%. mp 180–182°C (from methanol). IR spectrum, ν , cm^{-1} : 1640–1705 (C=O, C=N), 3410 br (NOH). ^1H NMR spectrum, δ , ppm: 1.06 s (6H, 2 CH_3), 2.12–2.66 m (4H, 2 CH_2), 2.42 s (3H, CH_3), 3.64 s (3H, N- CH_3), 5.10 s (1H, CH), 7.01 m (4H, indole), 10.00 s (1H, NOH). Found, %: C 71.15, 71.13; H 6.59, 6.54; N 8.33, 8.34. $\text{C}_{20}\text{H}_{22}\text{N}_2\text{O}_3$. Calculated, %: C 71.00; H 6.50; N 8.28.

3-(1-Benzyl-2-methylindol-3-yl)-2-hydroxyimino-2,3,4,5,6,7-hexahydrobenzofuran-4-one (VIII). Yield 60%. mp 120–122°C (from methanol). IR spectrum, ν , cm^{-1} : 1620–1700 (C=O, C=N),

3400 br (NOH). ^1H NMR spectrum, δ , ppm: 2.07–2.78 m (6H, 3 CH_2), 2.42 s (3H, CH_3), 5.20 s (1H, CH), 5.34 s (2H, N- CH_2), 7.08 m (4H, indole), 7.26 m (5H, C_6H_5), 10.14 s (1H, NOH). Found, %: C 74.57, 74.63; H 5.82, 5.83; N 7.31, 7.31. $\text{C}_{24}\text{H}_{22}\text{N}_2\text{O}_3$. Calculated, %: C 74.61; H 5.70; N 7.25.

3-(1-Benzyl-2-methylindol-3-yl)-2-hydroxyimino-6,6-dimethyl-2,3,4,5,6,7-hexahydrobenzofuran-4-one (IX). Yield 62%. mp 128–130°C (from methanol). IR spectrum, ν , cm^{-1} : 1620–1700 (C=O, C=N), 3400 br (NOH). ^1H NMR spectrum, δ , ppm: 1.09 s (6H, 2 CH_3), 2.11–2.68 m (4H, 2 CH_2), 5.11 s (1H, CH), 5.37 s (2H, N- CH_2), 7.05 m (4H, indole), 7.24 m (5H, C_6H_5), 10.17 s (1H, NOH). Found, %: C 75.59, 76.00; H 6.92, 6.91; N 6.88, 6.88. $\text{C}_{26}\text{H}_{26}\text{N}_2\text{O}_3$. Calculated, %: C 75.36; H 6.28; N 6.76.

IR spectra were recorded on spectrophotometer Specord 75IR from KBr pellets (compounds **I–VII**) and from mulls in mineral oil (compounds **VIII, IX**). ^1H NMR spectra were registered on spectrometer Bruker AC-200 (200 MHz) in $\text{DMSO}-d_6$, internal reference HMDS. Mass spectrum was measured on MKh-1321 instrument, ionizing voltage 70 eV, ionizing chamber temperature 180°C.

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