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2-(2-Furyl)-5,6-dihydro-1(3)*H*-acenaphtho[4,5-*d*]imidazole. Synthesis and Electrophilic Substitution Reactions

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Abstract—2-(2-Furyl)-5,6-dihydro-1(3)*H*-acenaphtho[4,5-*d*]imidazole was synthesized by the Weidenhagen reaction of acenaphthene-4,5-diamine with furfural. Alkylation of the title compound with methyl iodide in KOH–DMSO gave isomeric 1- and 3-methyl derivative, the latter being the major product. 2-(2-Furyl)-3-methyl-5,6-dihydro-3*H*-acenaphtho[4,5-*d*]imidazole was subjected to electrophilic substitution reactions (bromination, nitration, formylation, acylation, and sulfonation. Depending on the conditions, electrophilic attack was directed at the furan ring or acenaphthene fragment or both these.

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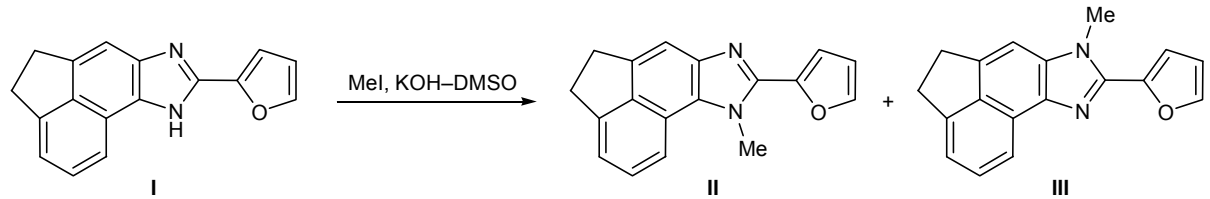
There are almost no published data on the synthesis and properties of acenaphtho[4,5-*d*]imidazole having a furyl substituent. On the other hand, such heterocyclic compounds attract interest as potential biologically active substances and organic luminophores [1]. The synthesis and chemical behavior of 2-(2-furyl)-1*H*-acenaphtho[9,10-*d*]imidazole were reported in [2].

The goal of the present work was to develop a convenient procedure for the synthesis of 2-(2-furyl)-5,6-dihydro-1(3)*H*-acenaphtho[4,5-*d*]imidazole (**I**) and study its transformations in reactions with electrophilic and radical reagents. Compound **I** was synthesized by us for the first time by reaction of acenaphthene-4,5-diamine with furfural according to Weidenhagen [3] (yield 64%). Alkylation of **I** with an equimolar amount of methyl iodide was performed in the system KOH–DMSO, and the yield was nearly quantitative. As unsymmetrical heterocyclic systems studied previously [4], the reaction gave a mixture of two *N*-methyl derivatives, 2-(2-furyl)-1-methyl-5,6-dihydro-1*H*-acenaphtho[4,5-*d*]imidazole (**II**) and 2-(2-furyl)-3-methyl-5,6-dihydro-3*H*-acenaphtho[4,5-*d*]imidazole (**III**) (Scheme 1), due to fast annular tautomerism. According to the ^{1}H NMR data, the major product was isomer **III**; its fraction was about 79%. The NCH_3 group in **III** gave rise to a singlet at δ 4.06 ppm, whereas the corresponding signal of **II** was located at δ 4.44 ppm. Obviously, the downfield position of the NCH_3 signal of **II** is determined by diamagnetic constituent of the ring current in the acenaphthene system.

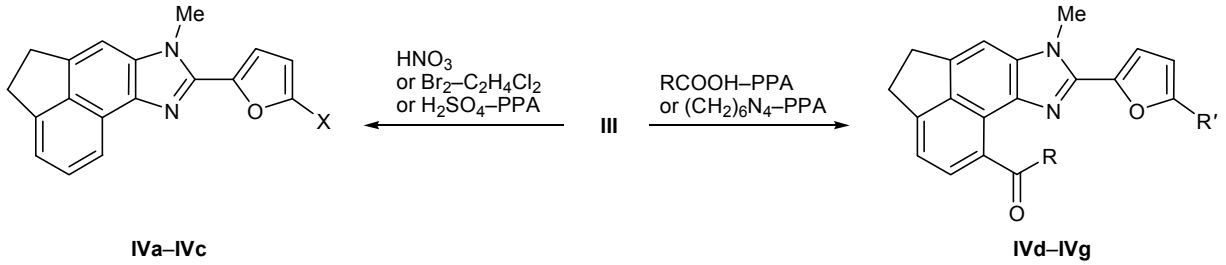
Pure 3-methyl isomer **III** was isolated by column chromatography and was brought into reactions with some electrophilic reagents, in particular with bromine in 1,2-dichloroethane, acetyl nitrate, hexamethylenetetramine in polyphosphoric acid (PPA), and sulfuric and carboxylic acids in PPA, In addition, compound **III** was nitrated with dilute nitric acid (d = 1.42 g/cm^3) (Scheme 2). As we showed previously [4], various 2-hetarylimidazole systems stabilize π-excessive five-membered heterocycles directly conjugated with the imidazole fragment. It was found that the character of stabilization in acid medium does not change appreci-

Scheme 1.



I II III

Scheme 2.



IVa–IVc **IVd–IVg**

X = O_2N (**a**), Br (**b**), $HOSO_2$ (**c**); R = H, R′ = H (**d**), CHO (**e**); R = Me, R′ = H (**f**); R = Ph, R′ = H (**g**).

ably in going from quinoline to naphthalene and then to acenaphthene.

The nitration of **III** was performed using the complex of copper(II) nitrate and acetic anhydride at 20°C [5]. The reaction involved the furan ring, and the yield of 2-(5-nitrofuran-2-yl) derivative **IVa** was ~67%. Radical nitration of **III** with dilute nitric acid on heating was not selective, and we failed to isolate or identify nitration product. Unlike acenaphtho[9,10-*d*]-imidazole analog [2], the bromination of **III** in dichloroethane, as well as in PPA, afforded exclusively 2-(5-bromofuran-2-yl) derivative **IVb** in 63% yield. 5-Sulfo derivative **IVc** was obtained by sulfonation of **III** with 2 equiv of sulfuric acid in PPA at 110–120°C.

Unlike 2-(2-furyl)-1-methyl-1*H*-acenaphtho-[9,10-*d*]imidazole studied previously, Vilsmeier formylation of 2-(2-furyl)-3-methyl-5,6-dihydro-3*H*-acenaphtho[4,5-*d*]imidazole (**III**) occurred at 60–70°C; however, according to the ^{1}H NMR data, the aldehyde group entered position *9* in the acenaphthene fragment (compound **IVd**). By heating compound **III** with hexamethylenetetramine in PPA at 70–80°C we obtained 5,9-dialdehyde **IVe** as a result of formylation at both furan and acenaphthene fragments.

Despite deactivating effect of the imidazoacenaphthene fragment, compound **III** underwent acetylation with acetic acid in PPA at 110–120°C much more readily as compared to acenaphtho[9,10-*d*]imidazole analog. The product was 9-acetyl derivative **IVf**. In the ^{1}H NMR spectrum of **IVf**, methyl protons in the acetyl group resonated as a singlet at δ 2.98 ppm, whereas the corresponding signal of furylacenaphtho[9,10-*d*]imidazole was observed at δ 2.52 ppm; the downfield position of the former is determined by the effect of the pyridine-type nitrogen atom. Benzoylation of **III** with benzoic acid in PPA was carried out at higher temperature (140–150°C); likewise, 9-benzoyl derivative **IVg** was formed in ~56% yield.

Our results may be rationalized in terms of leveling of the reactivities of the acenaphtho[4,5-*d*]imidazole system and deactivated furan ring toward medium-strength electrophiles in polyphosphoric acid.

EXPERIMENTAL

The IR spectra were recorded on a Specord IR-75 spectrometer from compounds dissolved in chloroform or dispersed in mineral oil. The ^{1}H NMR spectra were recorded on a Varian Unity-300 instrument (300 MHz) using the residual proton signals of the deuterated solvents as reference ($CHCl_3$, δ 7.26 ppm; DMSO-d_5, δ 2.50 ppm). The elemental compositions were determined on a Perkin Elmer 2400 analyzer. The melting points were measured in capillaries using a PTP melting point apparatus. The progress of reactions was monitored, and the purity of products was checked, by TLC on Al_2O_3 plates (Brockmann activity grade II; development with iodine vapor) or Silufol UV-254 plates (eluent methylene chloride).

2-(2-Furyl)-5,6-dihydro-1(3)*H*-acenaphtho-[4,5-*d*]imidazole (I). A mixture of 7.37 g (40 mmol) of acenaphthene-4,5-diamine in 75 ml of isopropyl alcohol, 16 g of copper acetate in 200 ml of water, and 3.85 g (40 mmol) of furfural was heated for 2 h at 80–90°C. The mixture was cooled, the precipitate of copper salt was filtered off and dispersed in 100 ml of isopropyl alcohol, and gaseous hydrogen sulfide was passed through the suspension over a period of 1 h. The precipitate of copper sulfide was filtered off, the filtrate was evaporated by half and diluted with 100 ml of water, and the precipitate was filtered off and recrystallized from ethanol. Yield 6.66 g (64%), mp 188–189°C. ^{1}H NMR spectrum, δ, ppm: 3.43 s (4H, CH_2), 6.60–6.62 m (1H, 4′-H), 7.10 d (1H, 3′-H, J = 3.6 Hz), 7.23 s (1H, 4-H), 7.33 d (1H, 7-H, J = 6.5 Hz), 7.55 t (1H, 8-H, J = 7.5 Hz), 7.65 d (1H, 5′-H, J = 1.8 Hz), 8.30 d (1H, 9-H, J = 8.0 Hz), 12.73 br.s (1H, NH).

Found, %: C 78.69; H 4.52; N 10.39. $C_{17}H_{12}N_2O$. Calculated, %: C 78.44; H 4.65; N 10.76.

2-(2-Furyl)-1-methyl-5,6-dihydro-1*H*-acenaphtho[4,5-*d*]imidazole (II) and 2-(2-furyl)-3-methyl-5,6-dihydro-3*H*-acenaphtho[4,5-*d*]imidazole (III). Methyl iodide, 3.12 g (22 mmol), was added dropwise under vigorous stirring at 15–20°C to a solution of 5.21 g (20 mmol) of compound **I** in 20 ml of DMSO containing 1.24 g (22 mmol) of powdered potassium hydroxide. The mixture was stirred for 2 h, poured into 200 ml of water, and extracted with chloroform (2× 50 ml). The combined extracts were evaporated to a volume of 20 ml, dried over sodium sulfate, filtered, and evaporated to isolate 4.00 g (73%) of isomer mixture **II**/**III**. Pure compounds **II** and **III** were isolated by column chromatography on Al_2O_3 (70×3.5 cm) using chloroform as eluent.

Isomer **II**. Yield 0.56 g (14%), mp 137–138°C (from benzene). ^{1}H NMR spectrum, δ, ppm: 3.45 s (4H, CH_2), 4.44 s (3H, NCH_3), 6.58–6.60 m (1H, 4′-H), 7.08 d (1H, 3′-H, J = 3.6 Hz), 7.25 d (1H, 7-H, J = 6.3 Hz), 7.50 t (1H, 8-H, J = 7.2 Hz), 7.61 d (1H, 5′-H, J = 1.8 Hz), 7.62 s (1H, 4-H), 8.03 d (1H, 9-H, J = 8.1 Hz). Found, %: C 78.66; H 5.22. $C_{18}H_{14}N_2O$. Calculated, %: C 78.81; H 5.14.

Isomer **III**. Yield 2.88 g (72%), mp 168–169°C (from ethanol). ^{1}H NMR spectrum, δ, ppm: 3.45 s (4H, CH_2), 4.06 s (3H, NCH_3), 6.58–6.60 m (1H, 4′-H), 7.08 d (1H, 3′-H, J = 3.6 Hz), 7.25 s (1H, 4-H), 7.30 d (1H, 7-H, J = 6.3 Hz), 7.56 t (1H, 8-H, J = 7.2 Hz), 7.61 d (1H, 5′-H, J = 1.8 Hz), 8.27 d (1H, 9-H, J = 8.1 Hz). Found, %: C 79.12; H 4.87; N 10.44. $C_{18}H_{14}N_2O$. Calculated, %: C 78.81; H 5.14; N 10.21.

3-Methyl-2-(5-nitrofuran-2-yl)-5,6-dihydro-3*H*-acenaphtho[4,5-*d*]imidazole (IVa). Acetic anhydride, 15 ml, was added in small portions on cooling to 4.48 g (20 mmol) of copper nitrate, maintaining the temperature below 30–40°C. When the exothermic reaction was over, the mixture was kept for 24 h at room temperature, the precipitate of copper(II) nitrate was filtered off, and the filtrate was used in the nitration of compound **III**.

a. Compound **III**, 0.27 g (1 mmol), was dissolved in 2 ml of freshly prepared acetic anhydride, and 0.28 ml of the nitrating mixture (see above) was added under stirring at room temperature. The reaction time was 30–40 min. The mixture was then treated with 10 ml of cold water and neutralized with 25% aqueous ammonia. The precipitate was filtered off, thoroughly washed with water, and subjected to column chromatography on aluminum oxide (15×2.5 cm) using methylene chloride as eluent. Yield 0.21 g (67%).

b. Sodium nitrite, 0.21 g (3 mmol), was added in portions to a solution of 0.35 g (1 mmol) of compound **IVb** in 5 ml of acetic acid, and the mixture was heated for 1 h under reflux, cooled, poured into 20 ml of water, and treated as described above in *a*. The products obtained by the two methods were identical in the melting point (no depression was observed on mixing). Yield 0.17 g (53%), mp 222–223°C (from ethanol). IR spectrum, ν, cm^{-1}: 1560 (NO_2, asym.), 1380 (NO_2, sym.). ^{1}H NMR spectrum, δ, ppm: 3.44 s (4H, CH_2), 4.12 s (3H, NCH_3), 7.25 s (1H, 4-H), 7.28 d (1H, 3′-H, J = 3.6 Hz), 7.30 d (1H, 7-H, J 7.0 Hz), 7.48 d (1H, 4′-H, J = 3.6 Hz), 7.57 t (1H, 8-H, J = 7.8 Hz), 8.25 d (1H, 9-H, J = 8.1 Hz). Found, %: C 67.87; H 3.89; N 12.93. $C_{18}H_{13}N_3O_3$. Calculated, %: C 67.71; H 4.10; N 13.16.

2-(5-Bromofuran-2-yl)-3-methyl-5,6-dihydro-3*H*-acenaphtho[4,5-*d*]imidazole (IVb). Bromine, 0.21 ml (4 mmol), was added to a solution of 0.55 g (2 mmol) of compound **III** in 10 ml of 1,2-dichloroethane, and the mixture was heated for 2 h under reflux. The mixture was treated with water and neutralized with a solution of ammonia, and the bottom layer was separated and subjected to chromatography in a column charged with Al_2O_3 using methylene chloride as eluent. Yield 0.44 g (63%), mp 127–128°C. ^{1}H NMR spectrum, δ, ppm: 3.45 s (4H, CH_2), 4.06 s (3H, NCH_3), 6.51 d (1H, 4′-H, J = 3.6 Hz), 7.09 d (1H, 3′-H, J = 3.6 Hz), 7.25 s (1H, 4-H), 7.30 d (1H, 7-H, J = 7.2 Hz), 7.56 t (1H, 8-H, J = 7.8 Hz), 8.24 d (1H, 9-H, J = 8.1 Hz). Found, %: C 60.93; H 3.58; Br 23.00. $C_{18}H_{13}BrN_2O$. Calculated, %: C 61.21; H 3.71; Br 22.62.

5-(3-Methyl-5,6-dihydro-3*H*-acenaphtho[4,5-*d*]-imidazol-2-yl)furan-2-sulfonic acid (IVc). A mixture of 0.55 g (2 mmol) of compound **III**, 0.39 g (4 mmol) of sulfuric acid (d = 1.84 g/cm^3), and 8 g of PPA was heated for 1 h at 100°C. The mixture was cooled and diluted with 50 ml of water, and the precipitate was filtered off. The product was dissolved in 5% aqueous sodium hydroxide, and the solution was treated with activated charcoal on heating at the boiling point, filtered, and neutralized with hydrochloric acid until weakly acidic reaction. Yield 0.40 g (57%), mp 302–303°C (from water). IR spectrum: ν 1280 cm^{-1} (SO_2). ^{1}H NMR spectrum, δ, ppm: 3.50 s (4H, CH_2), 4.12 s (3H, NCH_3), 7.10 d (1H, 4′-H, J = 3.3 Hz), 7.27 s (1H, 4-H), 7.29 d (1H, 3′-H, J = 3.3 Hz), 7.32 d (1H, 7-H, J = 7.5 Hz), 7.58 t (1H, 8-H, J = 8.0 Hz), 8.26 d (1H,

9-H, J = 8.2 Hz). Found, %: C 60.73; H 4.17; N 8.22. $C_{18}H_{14}N_2O_4S$. Calculated, %: C 61.01; H 3.98; N 7.90.

2-(2-Furyl)-3-methyl-5,6-dihydro-3*H*-acenaphtho[4,5-*d*]imidazole-9-carbaldehyde (IVd). A solution of 0.55 g (2 mmol) of compound **III** in 4.75 g (65 mmol) of dimethylformamide was cooled to 0–5°C, 4.6 g (30 mmol) of phosphoryl chloride was added dropwise under stirring, and the mixture was stirred for 10 min at 0–5°C and for 1 h at 60°C. The mixture was cooled, neutralized with a concentrated solution of ammonia to pH 7, and extracted with 25 ml of chloroform. The extract was dried over anhydrous sodium sulfate and subjected to chromatography on a column charged with Al_2O_3 using chloroform as eluent. Yield 0.26 (43%), mp 180–181°C (from heptane). IR spectrum: ν 1690 cm^{-1} (C=O). ^1H NMR spectrum, δ, ppm: 3.48 s (4H, CH_2), 4.12 s (3H, NCH_3), 6.59–6.61 m (1H, 4′-H), 7.12 d (1H, 3′-H, J = 3.4 Hz), 7.30 d (1H, 7-H, J = 6.9 Hz), 7.35 s (1H, 4-H), 7.60 d (1H, 8-H, J = 7.5 Hz), 7.62 d (1H, 5′-H, J = 1.8 Hz), 10.29 s (1H, CHO). Found, %: C 75.67; H 4.92; N 8.98. $C_{19}H_{14}N_2O_2$. Calculated, %: C 75.48; H 4.67; N 9.27.

2-(5-Formylfuran-2-yl)-3-methyl-5,6-dihydro-3*H*-acenaphtho[4,5-*d*]imidazole-9-carbaldehyde (IVe). A mixture of 0.55 g (2 mmol) of compound **III** and 0.84 g (6 mmol) of hexamethylenetetramine in 8 g of PPA was stirred for 4 h on heating at 80–90°C. The mixture was diluted with 50 ml of water and neutralized with a solution of ammonia, and the product was extracted into methylene chloride and isolated as described above for **IVd**. Yield 0.48 g (73%), mp 192–193°C (from ethanol). IR spectrum, ν, cm^{-1}: 1690, 1670 (C=O). ^1H NMR spectrum, δ, ppm: 3.48 s (4H, CH_2), 4.10 s (3H, NCH_3), 7.30 d (1H, 7-H, J = 7.0 Hz), 7.32 d (1H, 3′-H, J = 3.6 Hz), 7.35 s (1H, 4-H), 7.40 d (1H, 4′-H, J = 3.6 Hz), 7.62 d (1H, 8-H, J = 7.5 Hz), 9.73 s (1H, CHO), 10.30 s (1H, CHO). Found, %: C 73.09; H 4.43; N 8.57. $C_{20}H_{14}N_2O_3$. Calculated, %: C 72.72; H 4.27; N 8.48.

1-[2-(2-Furyl)-3-methyl-5,6-dihydro-3*H*-acenaphtho[4,5-*d*]imidazol-9-yl]ethanone (IVf). A mixture of 0.55 g (2 mmol) of compound **III** and 0.36 g (6 mmol) of acetic acid in 8 g of PPA was stirred for 6 h at 110–120°C. The mixture was diluted with 25 ml of water, carefully neutralized with a solution of ammonia, and extracted with methylene chloride. The product was isolated by column chromatography using CH_2Cl_2 as eluent. Yield 0.30 g (30%), mp 163–164°C (from ethanol). IR spectrum: ν 1680 cm^{-1} (C=O). ^1H NMR spectrum, δ, ppm: 2.98 s (3H, CH_3), 3.47 s (4H, CH_2), 4.11 s (3H, NCH_3), 6.59–6.61 m (1H, 4′-H), 7.14 d (1H, 3′-H, J = 3.3 Hz), 7.29 d (1H, 7-H, J = 6.9 Hz), 7.34 s (1H, 4-H), 7.58 d (1H, 8-H, J = 7.5 Hz), 7.60 d (1H, 5′-H, J = 1.8 Hz). Found, %: C 76.24; H 4.87; N 9.13. $C_{20}H_{16}N_2O_2$. Calculated, %: C 75.93; H 5.10; N 8.85.

[2-(2-Furyl)-3-methyl-5,6-dihydro-3*H*-acenaphtho[4,5-*d*]imidazol-9-yl]phenylmethanone (IVg). A mixture of 0.55 g (2 mmol) of compound **III** and 1.22 g (10 mmol) of benzoic acid in 8 g of PPA was stirred for 6 h at 140–150°C. The product was isolated as described above for **IVf**. Yield 0.42 g (56%), mp 155–156°C (from ethanol). IR spectrum: ν 1660 cm^{-1} (C=O). ^1H NMR spectrum, δ, ppm: 3.49 s (4H, CH_2), 4.10 s (3H, NCH_3), 6.59–6.62 m (1H, 4′-H), 7.14 d (1H, 3′-H, J = 3.5 Hz), 7.28 d (1H, 7-H, J = 7.0 Hz), 7.34 s (1H, 4-H), 7.51–7.54 m (3H, *m*-H, *p*-H), 7.58 d (1H, 5′-H, J = 1.8 Hz), 7.62 d (1H, 8-H, J = 7.5 Hz), 8.00 d (2H, *o*-H, J = 8.2 Hz). Found, %: C 79.57; H 5.03; N 7.69. $C_{25}H_{18}N_2O_2$. Calculated, %: C 79.35; H 4.79; N 7.40.

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