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SYNTHESIS AND PROPERTIES OF 2-(2-FURYL)-1-METHYL-1H-ACENAPHTHO[9,10-*d*]IMIDAZOLE

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2-(2-Furyl)-1-methyl-1H-acenaphtho[9,10-d]imidazole was obtained by the condensation of 9,1-acenaphthenequinone with furfural in the presence of ammonium acetate followed by N-methylation of the obtained 2-(2-furyl)-1H-acenaphtho[9,10-d]imidazole with methyl iodide in N-methylpyrrolid-2-one in the presence of potassium hydroxide. It was established that its electrophilic substitution in an acidic medium only takes place at position 2 of the furan ring while in a neutral medium both position 2 and position 7 of the aromatic part of the molecule undergo electrophilic attack.

Keywords: 9,10-acenaphthenequinone, 2-(2-furyl)-1H-acenaphtho[9,10-*d*]imidazole, methylation, electrophilic substitution.

While continuing investigations in the series of 2-substituted imidazoles [1], we decided to develop methods for the synthesis of 2-(2-furyl)-1H-acenaphtho[9,10-*d*]imidazole (**1**), to study its reactivity, and also to determine the mutual influence of the polynuclear aromatic system of 1H-acenaphtho[9,10-*d*]imidazole and a furan ring linked by a simple bond.

The reaction of acenaphthenequinone with aromatic aldehydes in an ammoniacal medium was studied earlier [2]. According to the data in this paper, various aromatic aldehydes form only oxazoles at low temperature, while at high temperature they form imidazoles or a mixture of both compounds. In ammonia 4-nitro-, 4-hydroxy-, and 4-methoxybenzaldehydes in ammonia give only imidazoles both at low and at higher temperature. However, we were not able to obtain 2-furyl-substituted acenaphtho[9,10]imidazole **1** at either low or high temperatures. We therefore used a method involving the condensation of 9,10-acenaphthenequinone and furfural in the presence of ammonium acetate in acetic acid. The yield of the targeted imidazole **1** did not exceed 50% on account of the formation of a significant amount of tar and a red side product, which was isolated in the pure form. According to the ^{1}H NMR spectrum, it was not furylacenaphtho[9,10-*d*]oxazole but, probably, the product from condensation of the acenaphthenequinone with ammonia.

It was possible to methylate the imidazole **1** with yields close to theoretical in the potassium hydroxide–N-methyl-2-pyrrolidone system with an equivalent amount of methyl iodide and without the appreciable formation of quaternization products. Our choice of such an exotic solvent as N-methyl-2-pyrrolidone was based on the very poor solubility of compound **1**. The N-methylation product **1a** was subjected to the action of electrophilic reagents (carboxylic acids and urotropine in polyphosphoric acid, bromine in dichloroethane and polyphosphoric acid, acetyl nitrate, sulfuric and nitric acids in polyphosphoric acid, etc.).

Earlier we showed [3, 4] that various 2-hetarylimidazoline systems are able to stabilize the five-membered π-excessive heterocycles that enter the composition of the molecules in direct conjugation with the imidazole fragment. The loss of acidophobic characteristics, due to the redistribution of excess electron density

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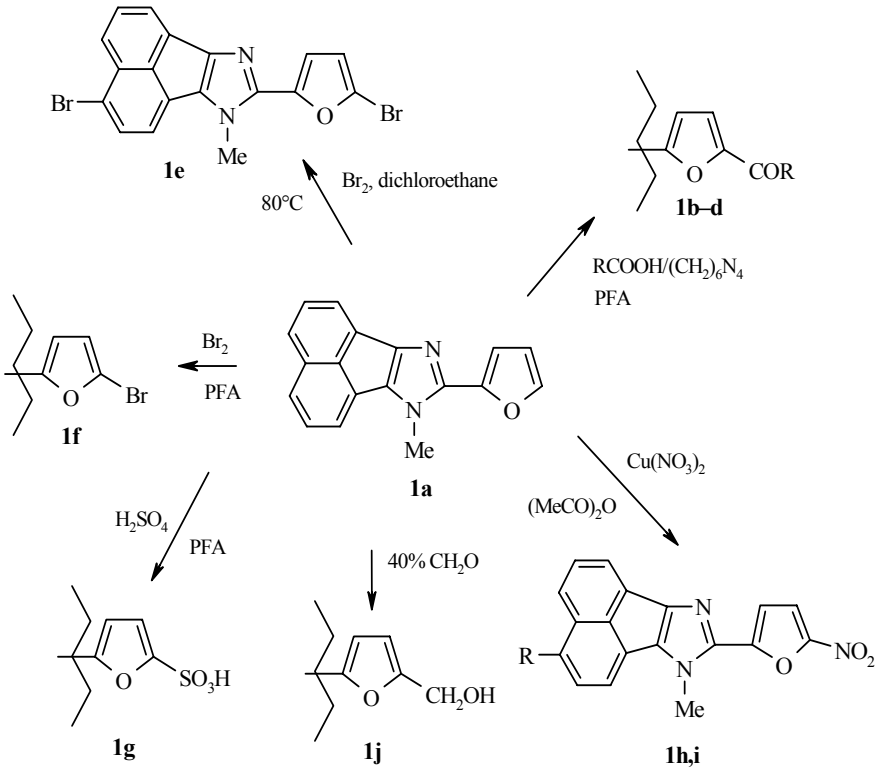
between the hetaryl and imidazole rings, makes it possible to carry out various electrophilic reactions under drastic conditions (temperature up to 200°C, polyphosphoric acid, conc. hydrochloric acid, etc.), and this considerably extends the scope for the study of these compounds. As shown by our investigations, change of the aromatic system in the benzene, naphthalene, and acenaphthene series, condensed with the imidazole ring, does not have a significant effect on the nature of stabilization of the molecules in an acidic medium.

The reaction of compound **1a** with carboxylic acids and urotropine in the presence of polyphosphoric acid leads exclusively to 5'-acyl-2-furyl-1H-acenaphtho[9,10-*d*]imidazoles **1b-d**.



1 b R = H, **c** R = Me, **d** R = Ph, **h** R = H, **i** R = NO_2

However, unlike benzoylation, the acetylation of compound **1a** takes place with the formation of significant amounts (~36%) of a side product. The reaction is probably complicated by substitution in the acetyl group, leading to 2-(5-acetoacetyl-2-furyl)-1-methyl-1H-acenaphtho[9,10-*d*]imidazole (**1k**).

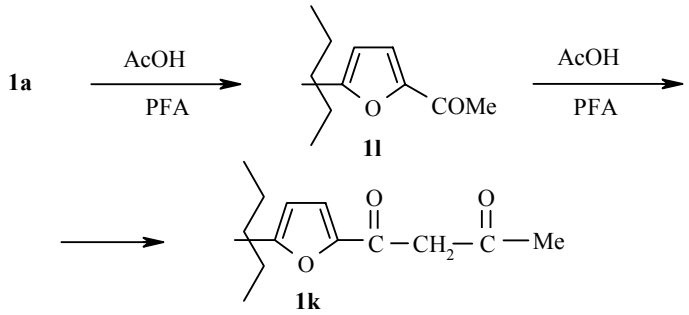


TABLE 1. Physicochemical Characteristics of the Synthesized Compounds **1a-j**

Compound	Empirical formula	Found, % / Calculated, %			mp, °C (*i*-PrOH)	IR spectrum, ν, cm^{-1}	Yield, %
		C	H	N			
1	$C_{17}H_{10}N_2O$	78.77 / 79.07	4.12 / 3.90	—	184-186	—	49
1a	$C_{18}H_{12}N_2O$	79.62 / 79.39	4.18 / 4.44	10.08 / 10.29	87-89	—	90
1b	$C_{19}H_{12}N_2O_2$	76.15 / 75.99	4.21 / 4.03	9.47 / 9.33	111-113	1680	81
1c	$C_{20}H_{14}N_2O_2$	76.18 / 76.42	4.17 / 4.49	9.24 / 8.91	124-126	1660	86
1d	$C_{25}H_{16}N_2O_2$	78.05 / 79.77	4.42 / 4.28	7.28 / 7.44	147-149	1680	92
1e	$C_{18}H_{10}Br_2N_2O$	50.38 / 50.27	2.56 / 2.34	6.27 / 6.51	93-95	—	71
1f	$C_{18}H_{11}BrN_2O$	61.74 / 61.56	3.28 / 3.16	7.69 / 7.98	117-119*	—	78
1g	$C_{18}H_{12}N_2O_4S$	61.49 / 61.36	3.62 / 3.43	7.68 / 7.95	>400	1280	91
1h	$C_{18}H_{11}N_3O_2$	67.93 / 68.14	3.61 / 3.49	13.12 / 13.24	154-156	1350, 1530	83
1i	$C_{18}H_{10}N_4O_5$	59.67 / 59.82	2.78 / 2.63	19.33 / 19.53	236-238*	1370, 1530	74
1j	$C_{19}H_{14}N_2O_2$	75.77 / 75.48	4.34 / 4.67	—	214-216	3240	14

* From ethanol.

During the action of bromine on compound **1a** the reaction takes place in two ways: In dichloroethane the C atoms undergo attack not only in the furan ring but also in the acenaphthene ring, whereas the reaction with bromine in polyphosphoric acid leads to the 5'-bromofuryl derivative. The entry of the substituent into the acenaphthene ring during bromination in dichloroethane results from the π-donor effect of the hetaryl ring, which probably increases the electron density at position 7 of the acenaphthene ring. In a strongly acidic medium (PPA) the "pyridine" N atom is protonated, leading to deactivation of the acenaphthoimidazole fragment, and only the furan ring is attacked.

The sulfonylation of compound **1a** with an equivalent amount of sulfuric acid in polyphosphoric acid at 110-120°C, as also in the case of acylation, leads exclusively to the formation of the 5'-sulfo derivative **1g**, while increase of the temperature and increase of the H_2SO_4 concentration lead to partial formation of the sulfone.

It was possible to nitrate compound **1a** successfully by the action of the complex of $Cu(NO_3)_2$ and acetic anhydride [4]. Here it was found that compound **1a** reacts readily at 20°C with the formation of the 5-nitrofuryl derivative **1b**, whereas at 60°C it gives the dinitro derivative **1i**.

Furoacenaphthoimidazole **1a** reacts with 37% formalin very slowly; after boiling for 12 h the conversion of the initial heterocycle amounted to only ~17%. The carbinol **1j** was isolated with a yield of 14% by column chromatography.

TABLE 2. ^{1}H NMR Spectra of Compounds **1a-j**

Compound	Chemical shifts, δ, ppm. (SSCC, *J*, Hz)*								
	N–CH_3, (3H, s)	H-4' (1H)	H-3' (1H, d)	H-7 arom. (1H, d)	H-6 arom. (1H, d)	H-9 arom. (1H, d)	H-5,8 arom.	H-4 arom. (1H, d)	other signals
1a	4.18	6.56 (br. s)	6.88 (J_{43} = 2.49)	7.44 (J_{78} = 3.51)	7.46 (J_{65} = 3.74)	7.59 (J_{98} = 6.81)	7.69 (2H, t, J = 15.23)	7.83 (J_{45} = 6.81)	7.55 (1H, d, J_{45} = 2.2, H-5')
1b	4.30	7.30 (d, J_{34} = 3.32)	7.12 (J_{43} = 3.28)	7.42 (J_{78} = 3.50)	7.46 (J_{65}=3.72)	7.59 (J_{98} = 6.81)	7.70 (2H, t, J = 15.21)	7.81 (J_{45} = 6.81)	9.76 (1H, s, CHO)
1c	4.28	7.28 (d, J_{34} = 3.30)	7.10 (J_{43} = 3.30)	7.43 (J_{78} = 3.48)	7.46 (J_{65} = 3.70)	7.60 (J_{98} = 6.79)	7.70 (2H, t, J = 15.20)	7.80 (J_{45} = 6.80)	2.52 (3H, s, CH_3)
1d	4.30	7.25 (d, J_{34} = 3.30)	7.07 (J_{43} = 3.30)	7.43 (J_{78} = 3.50)	7.48 (J_{65} = 3.72)	7.59 (J_{98} = 6.80)	7.69 (2H, t, J = 15.20)	7.83 (J_{45} = 6.80)	7.55 (3H, m, 3H arom.); 8.00 (2H, d, 2H arom.)
1e	4.18	6.55 (d, J_{34} = 3.28)	7.08 (J_{43} = 3.30)	—	7.42 (J_{65} = 3.70)	7.55 (J_{98} = 6.70)	7.55 (1H, d, J = 7.22); 7.70 (1H, t, J = 15.20)	7.80 (J_{45} = 6.80)	—
1f	4.16	6.57 (d, J_{34} = 3.28)	7.10 (J_{43} = 3.28)	7.44 (J_{78} = 3.51)	7.42 (J_{65} = 3.70)	7.56 (J_{98} = 6.72)	7.70 (2H, t, J = 15.22)	7.83 (J_{45} = 6.82)	—
1g	4.30	7.32 (d, J_{34} = 3.15)	7.15 (J_{43} = 3.15)	7.42 (J_{78} = 3.48)	7.48 (J_{65} = 3.72)	7.60 (J_{98} = 6.80)	7.68 (2H, t, J = 15.20)	7.82 (J_{45} = 6.80)	—
1h	4.32	7.35 (d, J_{34} = 3.32)	7.10 (J_{43} = 3.30)	7.44 (J_{78} = 3.48)	7.48 (J_{65}=3.70)	7.60 (J_{98} = 6.80)	7.70 (2H, t, J = 15.15)	7.82 (J_{45} = 6.82)	—
1i	4.25	6.45 (d, J_{34} = 3.30)	7.08 (J_{43} = 3.28)	7.40 (J_{78} = 3.50)	7.52 (J_{65} = 3.74)	7.62 (J_{98} = 6.75)	7.72 (2H, t, J = 14.88)	7.86 (J_{45} = 6.80)	3.65 (2H, s, CH_2)
1j	4.32	7.40 (d, J_{34} = 3.30)	7.12 (J_{43} = 3.30)	—	7.56 (J_{65} = 3.70)	7.70 (J_{98} = 6.80)	8.48 (1H, d, J_{89} = 7.20); 7.70 (1H, t, J = 15.20)	7.84 (J_{45} = 6.80)	—

* ^{1}H NMR spectrum registered in $CDCl_3$ (compounds **1a-f,i,j**) and DMSO-d_6 (compounds **1g,h**).

EXPERIMENTAL

The IR spectra of the investigated compounds were obtained in Vaseline oil on a Specord-75 spectrometer. The mass spectra were obtained on a Varian Unity 300 instrument (300 Hz) with HMDS as internal standard (δ 0.05 ppm). The reactions and the individuality of the synthesized compounds were monitored by TLC on plates with Al_2O_3 of II Brockman activity (development with iodine vapor) in CH_2Cl_2 and on Silufol UV-254 plates in CH_2Cl_2. The physicochemical and spectral characteristics of the compounds are given in Tables 1 and 2.

2-(2-Furyl)-1H-acenaphtho[9,10-*d*]imidazole (1). To a boiling solution of acenaphthenequinone (1.82 g, 10 mmol) in acetic acid (50 ml) we quickly added a solution of ammonium acetate (15.4 g, 200 mmol) and furfural (1.34 g, 14 mmol) in acetic acid (10 ml). The mixture was boiled for 1.5-2 h and allowed to stand at room temperature for 2-3 h. The precipitated intermediate product was filtered off and washed with acetic acid (10 ml). The filtrate was diluted with water (100 ml) and neutralized with an aqueous solution of ammonia. The crystals were separated and dried. Yield 1.26 g.

2-(2-Furyl)-1-methyl-1H-acenaphtho[9,10-*d*]imidazole (1a). To a solution of compound **1** (2.58 g, 10 mmol) in N-methyl-2-pyrrolidone (10 ml) we added powdered potassium hydroxide (0.62 g, 11 mmol). To the mixture we added dropwise methyl iodide (1.42 g, 10 mmol). The precipitate was separated and dried. Yield 2.45 g.

2-(5-Formyl-2-furyl)-1-methyl-1H-acenaphtho[9,10-*d*]imidazole (1b). A mixture of compound **1a** (2.72 g, 10 mmol) and urotropine (4.2 g, 30 mmol) in polyphosphoric acid (40 g) was stirred at 80-90°C for 4 h. The reaction mass was diluted with water (200 ml) and neutralized with a solution of ammonia. The product that separated was extracted with methylene chloride. The extract was dried with sodium sulfate and chromatographed on a column of aluminum oxide with methylene chloride as eluent. Yield 2.43 g.

2-(5-Acetyl-2-furyl)-1-methyl-1H-acenaphtho[9,10-*d*]imidazole (1c). A mixture of compound **1a** (2.72 g, 10 mmol) and acetic acid (0.6 g, 20 mmol) in polyphosphoric acid (40 g) was stirred at 120°C for 8 h. The reaction product was separated by analogy with compound **1b**. Yield 2.70 g.

2-(5-Acetoacetyl-2-furyl)-1-methyl-1H-acenaphtho[9,10-*d*]imidazole (1k). After compound **1c** had emerged from the column, by continuing the elution we isolated the side product **1k** in the form of yellow crystals; mp 242-244°C (alcohol). IR spectrum, ν, cm^{-1}: 1620, 1660. ^1H NMR spectrum (deuterochloroform), δ, ppm (*J*, Hz): 2.55 (3H, s, CH_3); 4.28 (3H, s, N-CH_3); 6.15 (1H, d, J = 1.07, CH_2); 6.45 (1H, d, J = 2.15, CH_2); 7.30 (1H, d, J_{34} = 3.30, H-4'); 7.12 (1H, d, J_{43} = 3.30, H-3'); 7.42 (1H, d, J_{78} = 3.48, H-7 arom.); 7.46 (1H, d, J_{65} = 3.70, H-6 arom.); 7.60 (1H, d, J_{98} = 6.79, H-9 arom.); 7.72 (2H, t, J = 15.20, H-5,8 arom.); 7.80 (1H, d, J_{45} = 6.80, H-4 arom.). Found %: C 73.82; H 4.17. $C_{22}H_{16}N_2O_3$. Calculated %: C 74.15; H 4.53. M (mass spectrometry) 356.

2-(5-Benzoyl-2-furyl)-1-methyl-1H-acenaphtho[9,10-*d*]imidazole (1d). A mixture of compound **1a** (2.72 g, 10 mmol) and benzoic acid (6.1 g, 50 mmol) in polyphosphoric acid (40 g) was stirred at 150°C for 6 h. The reaction product was isolated by analogy with compound **1b**. Yield 3.46 g.

2-(5-Bromo-2-furyl)-1-methyl-1H-7-bromoacenaphtho[9,10-*d*]imidazole (1e). To a solution of compound **1a** (2.72 g, 10 mmol) in dichloroethane (40 ml) at room temperature we gradually added a solution of bromine (3.2 g, 20 mmol) in dichloroethane (20 ml). The mixture was boiled for 2 h and was then diluted with water and neutralized with a solution of ammonia. The bottom layer was separated and chromatographed on a column of aluminum oxide with methylene chloride as eluent. Yield 3.05 g.

2-(5-Bromo-2-furyl)-1-methyl-1H-acenaphtho[9,10-*d*]imidazole (1f). A mixture of compound **1a** (2.72 g, 10 mmol), polyphosphoric acid (40 g), and bromine (1.6 g, 10 mmol) was heated at 80-90°C for 4 h. The reaction mass was cooled and diluted with 200 ml of water. The product was separated and recrystallized from alcohol. Yield 2.74 g.

1-Methyl-2-(5-sulfo-2-furyl)-1H-acenaphtho[9,10-*d*]imidazole (1g). A mixture of compound **1a** (2.72 g, 10 mmol), sulfuric acid (*d* 1.84) (1.95 g, 20 mmol), and polyphosphoric acid (40 g) was heated at 100°C for 1 h. The reaction mass was cooled and diluted with water (200 ml), and the precipitated sulfonic acid was filtered off. For purification the product was dissolved in 5% alkali, boiled with active carbon, and neutralized to a weakly acidic reaction with hydrochloric acid. Yield 3.20 g.

1-Methyl-2-(5-nitro-2-furyl)-1H-acenaphtho[9,10-*d*]imidazole (1h). To a solution of compound **1a** (2.72 g, 10 mmol) in freshly distilled acetic anhydride (20 ml) with vigorous stirring we added in small portions nitrating mixture (2.85 ml) [4] at room temperature. The mixture was stirred for 30-40 min. The mixture was diluted with cold water (50 ml) and neutralized with a solution of ammonia. The product was extracted with methylene chloride and chromatographed on a column of aluminum oxide with methylene chloride as eluent. Yield 2.63 g.

1-Methyl-2-(5-nitro-2-furyl)-1H-7-nitroacenaphtho[9,10-*d*]imidazole (1i). To a solution of compound **1a** (2.72 g, 10 mmol) in freshly distilled acetic anhydride (20 ml) with vigorous stirring we added in small portions nitrating mixture (2.85 ml) [4] at room temperature. The mixture was then heated on a water bath at 60°C for 2-3 min. The crystals that separated on cooling were filtered off, washed with a small amount of acetic acid and with water, neutralized with a solution of ammonia, and dried. Yield 2.68 g.

2-(5-Hydroxymethyl-2-furyl)-1-methyl-1H-acenaphtho[9,10-*d*]imidazole (1j). A solution of compound **1a** (2.72 g, 10 mmol) in 37% formalin (25 ml) was heated on a boiling water bath for 16 h. The product was extracted with methylene chloride, chromatographed on a column of aluminum oxide, and eluted with methylene chloride. Yield 0.43 g.

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