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SYNTHESIS AND HYDROSILYLATION OF FURAN AND THIOPHENE N-METHYLENEFLUOROANILINES IN THE PRESENCE OF Pd(I) COMPLEX

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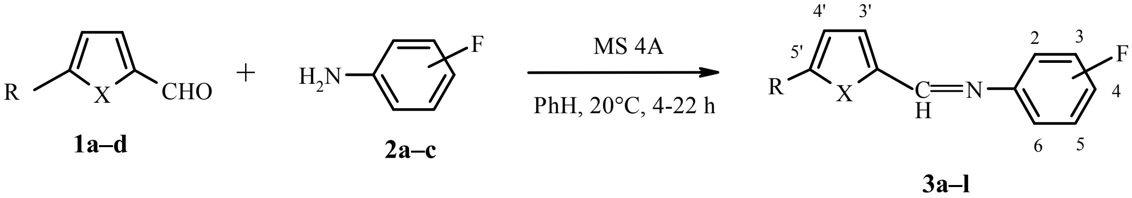
A series of new N-hetarylaldimines were synthesized by the reactions of furan and thiophene aldehydes with 2-, 3-, and 4-fluoroanilines in the presence of molecular sieves. The reaction of some of the synthesized azomethines with triethoxysilane in the presence of the [Pd(allyl)Cl]$_2$ complex was studied. It was found that the structure of the initial aldimines has an effect on the direction of hydrosilylation. All the studied substrates are transformed into the corresponding amines. The products of N- and C-silylation were also detected in the reaction mixtures. In certain cases reduction of the furan and thiophene rings occurs.

Keywords: Pd complexes, Schiff bases, thiophene, fluoroaniline, furan, hydrosilylation, catalysis.

Earlier we developed an effective method for the synthesis of a wide range of azomethines by the condensation of heterocyclic aldehydes with various amines in the presence of molecular sieves [1-5]. The latter act in these processes not only as a dehydrating agent but also as an optimum acidic catalyst that does not lead (unlike most homogeneous systems) to resinification of the acidophobic heterocyclic substrates. In the present work a series of syntheses (Scheme 1) were realized by this method, and the corresponding furan and thiophene aldimines – N-hetarylmethylene-substituted 2-, 3-, and 4-fluoroanilines **3a-l** – substituted with fluorine in the aza part of the molecule were obtained. The characteristics of the synthesized compounds and their ^{1}H NMR and mass spectra are given in Tables 1-3.

Scheme 1



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* Dedicated to Prof. N. S. Zefirov as a sign of respect in connection with his birthday

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TABLE 1. The Characteristics of the Synthesized Compounds **3a-i**

Imine*	X	R	Position of F	Reaction time, h	Empirical formula	Found, % Calculated, %				mp, °C*^{2}	Yield, %
						C	H	N	S		
3a	O	H	2-	19	$C_{11}H_8FNO$	69.82 69.84	4.26 4.26	7.30 7.40	—	76-77	87
3b	O	Me	2-	19	$C_{12}H_{10}FNO$	70.58 70.93	4.86 4.96	6.76 6.89	—	39-40	76
3c	S	H	2-	22	$C_{11}H_8FNS$	64.27 64.37	3.77 3.93	6.67 6.82	15.55 15.62	65-66	70
3d	S	Me	2-	22	$C_{12}H_{10}FNS$	65.58 65.73	4.48 4.59	6.22 6.39	14.47 14.62	40-41	75
3e	O	H	3-	20	$C_{11}H_8FNO$	—	—	—	—	—	83
3f	O	Me	3-	20	$C_{12}H_{10}FNO$	—	—	—	—		82
3g	S	H	3-	22	$C_{11}H_8FNS$	—	—	—	—	—	78
3h	S	Me	3-	22	$C_{12}H_{10}FNS$	65.70 65.73	4.65 4.59	6.35 6.39	14.59 14.62	43-44	71
3i	O	H	4-	4	$C_{11}H_8FNO$	—	—	—	—	—	70
3j	O	Me	4-	4	$C_{12}H_{10}FNO$	—	—	—	—	—	78
3k	S	H	4-	20	$C_{11}H_8FNS$	63.41 64.37	3.87 3.93	6.55 6.82	15.05 15.62	38-39	78
3l	S	Me	4-	20	$C_{12}H_{10}FNS$	65.46 65.73	4.68 4.59	6.28 6.39	14.54 14.62	77-78	75

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* The imines **3e-g**,**i**,**j** are oily substances.

*^{2} Solvent for recrystallization: 1:1 hexane–ethyl acetate for **3a**,**c** or hexane for **3b**,**d**,**h**,**k**,**l**.

It is necessary to mention certain relationships observed in the ^{1}H NMR spectra of the series of synthesized aldimines (Table 2). The presence of the methyl group in the heteroaromatic ring leads to an upfield shift of the signal for CH=N compared with the unsubstituted molecules. All the thiophene imines are characterized by larger chemical shifts of the signals for the protons of the CH=N and CH_3 groups than in the corresponding furan compounds.

In numerous investigations (see the reviews [6-9] and also the papers [10-13]) it was shown that silylation of the CH=N double bond leads mainly to the formation of N-silylated products. Recently we found for the first time [14] that addition of the silyl group to the carbon atom of the imine bond CH=N also occurs in addition to N-silylation in the reaction of alkylhydrosilanes with furan, thiophene, and pyridine methylene-*ortho*-trifluoromethylanilines. In this connection it seemed of interest to investigate the hydrosilylation of the newly synthesized azomethines **3a-d** containing a fluoro group at the *ortho* position of the aza part of the molecules.

Earlier [11, 14] we found that one of the most active catalysts for the hydrosilylation of heterocyclic imines is the dimeric complex of monovalent palladium bis{[μ-chloroallyl]palladium} $[Pd(allyl)Cl]_2$. The reaction of the new furan and thiophene aldimines **3a-d** with triethylsilane in the presence of this complex was studied. The reactions were conducted in benzene at 65°C with the optimum substrate–silane ratio 1:1.2 mol and a catalyst concentration of 2 mol %. The reaction was monitored by TLC and GLC-MS. On completion of silylation (the reaction times are given in Table 4) the reaction mixture was treated (as indicated in the experimental section) and analyzed by ^{1}H NMR.

In the ^{1}H NMR spectra of the reaction mixtures there are sets of signals that indicate the formation of several types of products containing central CH_2–HN, CH_2–$NSiEt_3$, Et_3SiCH–NH, and CH=N groups. These compounds are characterized by a signal for CH_2 and a broad singlet for NH (2H and 1H), a singlet for CH_2 (2H), two broad singlets for the protons of the CH–NH group (1H–1H), and a singlet in the region of CH=N respectively (Table 4). The signals for the protons of the (hetero)aromatic rings of all the obtained compounds are in the characteristic regions of the spectra. The $SiEt_3$ group appears in the ^{1}H NMR spectra of the synthesized silyl compounds in the form of two groups of signals for the protons of the CH_2 (6H, q) and CH_3

TABLE 2. The ^{1}H NMR Spectra of the Imines **3a-l**

Compound	Chemical shifts, δ, ppm (SSCC, *J*, Hz)		
	CH=N, s	CH_3, s	Ring protons
3a	8.40	—	6.60 (1H, dd, *J* = 2.0, *J* = 3.6, H-4); 7.0-7.5 (5H, m, H-3,3',H-4',5',6'); 7.68 (1H, m, H-5)
3b	8.26	2.44	6.21 (1H, d, *J* = 3.2, H-4); 7.0-7.4 (5H, m, H-3,3',4',5',6')
3c	8.63	—	7.0-7.2 (5H, m, H-4,3',4',5',6'); 7.5 (1H, m, H-3,5)
3d	8.53	2.56	6.83 (1H, d, *J* = 3.0, H-4); 7.0-7.2 (3H, m, H-3,4',5'); 7.3 (1H, m, H-3'); 7.46 (1H, m, H-6')
3e	8.28	—	6.59 (1H, dd, *J* = 1.8, *J* = 3.4, H-4); 6.8-7.2 (4H, m, H-3, 2',4',5'); 7.35 (1H, m, H-6'); 7.65 (1H, s, H-5)
3f	8.18	2.45	6.23 (1H, d, *J* = 2.0, H-4), 6.8-7.2 (4H, m, H-3,2',4',5'); 7.35 (1H, m, H-6')
3g	8.54	—	6.8-7.1 (3H, m, H-2',4',5'); 7.15 (1H, m, *J* = 4.6, H-4); 7.35 (1H, m, H-6'); 7.56 (2H, m, H-3,5)
3h	8.43	2.55	6.7-7.1 (4H, m, H-4,2',4',5'); 7.2-7.5 (2H, m, H-3,6')
3i	8.25	—	6.55 (1H, dd, *J* = 2.0, *J* = 3.6, H-4); 6.93 (1H, d, *J* = 3.6, H-3); 6.9-7.1 (2H, m, H-2',6'); 7.1-7.3 (2H, m, H-3',5'); 7.60 (1H, m, H-5)
3j	8.14	2.42	6.16 (1H, d, *J* = 2.8, H-4); 6.82 (1H, d, *J* = 2.8, H-3); 7.0-7.1 (2H, m, H-2',6'); 7.1-7.3 (2H, m, H-3',5')
3k	8.54	—	7.0-7.3 (5H, m, H-3,4,5,2',6'); 7.5-7.6 (2H, m, H-3',5')
3l	8.48	2.57	6.87 (1H, br. s, H-4); 7.0-7.2 (2H, m, H-2',6'); 7.2-7.5 (2H, m, H-3',5'); 7.6 (1H, br. s, H-3)

TABLE 3. The Mass Spectra of the Imines Het–CH=N–Ar **3a-l***

Com-pound	m/z (I_{rel}, %)									
	M^+	$[M-H]^+$	$[M–Me]^+$	$[M–HCO]^+$	$[M–Me–HCO]^+$	$[M–HCO–HCN]^+$	$[M–MeCO–HCN]^+$	$[M–Het]^+$	Ar^+	$[Ar–HF]^+$
3a	189 (100)	188 (78)	—	160 (12)	—	133 (19)	—	122 (12)	95 (35)	75 (31)
3b	203 (100)	202 (52)	188 (22)	—	160 (17)	—	133 (12)	122 (14)	95 (30)	75 (33)
3c	205 (77)	204 (100)	—	—	—	133 (3)	—	122 (8)	95 (32)	75 (28)
3d	219 (84)	218 (100)	204 (4)	—	—	—	133 (1)	122 (13)	95 (27)	75 (23)
3e	189 (100)	188 (50)	—	160 (48)	—	133 (40)	—	122 (7)	95 (87)	75 (55)
3f	203 (100)	202 (34)	188 (40)	—	160 (74)	—	133 (32)	122 (8)	95 (68)	75 (42)
3g	205 (97)	204 (100)	—	—	—	133 (7)	—	122 (8)	95 (60)	75 (33)
3h	219 (89)	218 (100)	204 (9)	—	—	—	133 (1)	122 (11)	95 (42)	75 (23)
3i	189 (100)	188 (60)	—	160 (24)	—	133 (32)	—	122 (11)	95 (61)	75 (41)
3j	203 (100)	202 (41)	188 (32)	–	160 (47)	—	133 (24)	122 (13)	95 (57)	75 (38)
3k	205 (92)	204 (100)	—	—	—	133 (7)	—	122 (6)	95 (58)	75 (35)
3l	219 (88)	218 (100)	204 (6)	—	—	—	133 (1)	122 (12)	95 (52)	75 (29)

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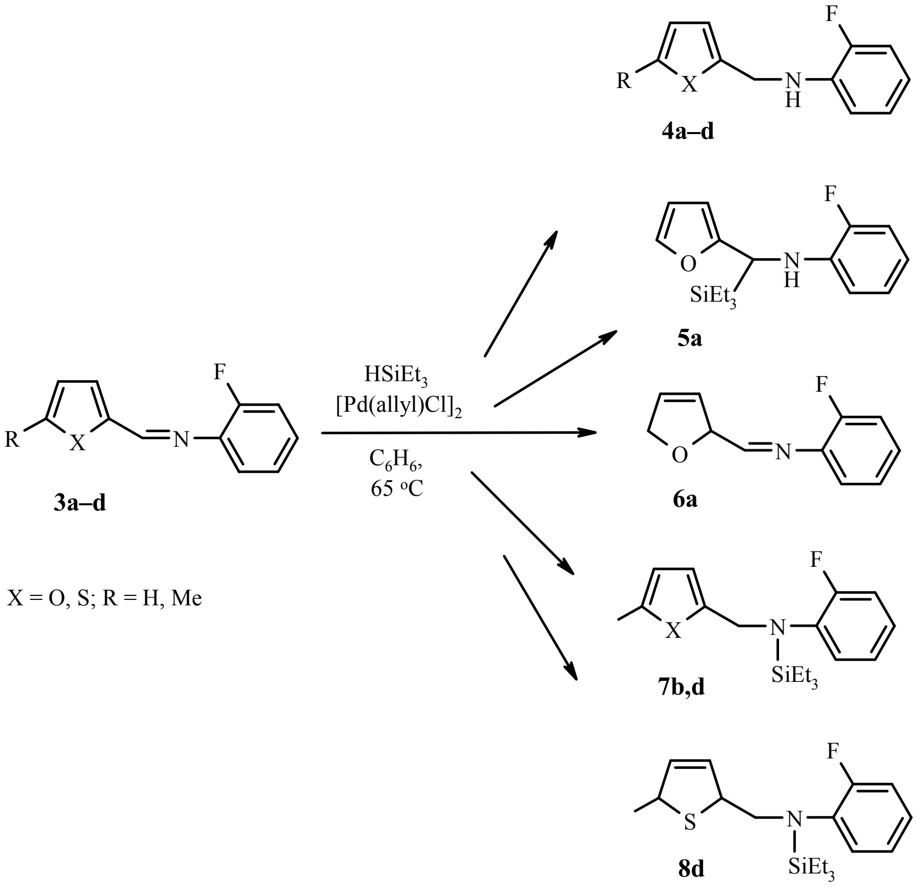
* The signals of the characteristic ions are indicated. Peaks with m/z < 75 are not shown.

(9H, t) in the region of δ 0.5-1.6 ppm. By preparative column chromatography it was possible to isolate nearly all the synthesized compounds (Table 4), which are yellow oily substances. The mass spectra of the obtained compounds (Table 5) correspond to the indicated types of products.

According to the obtained data, it can be concluded that the corresponding amines – (2-hetarylmethyl)(2-fluorophenyl)amines **4a-d** (in the case of the thiophene imine **3c**, with 99% selectivity) – are formed during the hydrosilylation of all the investigated imines **3a-d**. The C-silylated amine **5a** is only formed from the aldimine **3a**. In addition this imine is reduced to the dihydrofuran derivative **6a**. N-Silylamines with the expected structure **7b**,**d** are formed (in a mixture with other products) during the transformation of both methyl derivatives of imines **3b**,**d**, while the latter also gives a small amount of the N-silylated derivative **8d** with a dihydrothiophene ring in the structure of the molecule (Scheme 2).

It is interesting to compare the obtained results with our data [15] on the hydrosilylation of an aromatic analog of the heterocyclic aldimines studied in the present work, i.e., N-benzylidene-2-fluoroaniline. The latter is converted completely under identical conditions into the corresponding amine in 8 h, i.e., has higher reactivity than the substrates **3a-d** and according to the direction of reaction is an analog of the thiophene imine **3c**.

Scheme 2



In addition, it can be seen that the presence of the bulky CF$_3$ group at the *ortho* position of the aza part of the reacting molecules favors the unusual reaction path, i.e., C-silylation, to a greater degree than the F group. This indicates that steric factors have the effect proposed in [15].

TABLE 4. The Characteristics of the Hydrosilylation Reactions and their Products

Initial imine	Reaction time, h	Conversion of imine, % (GLC)	Product		^{1}H NMR spectrum, δ, ppm			
			in reaction mixture* (yield, %, GLC)	after isolation*^{2}	CH_3 (3H, s)	CH_2–N (2H, s)	CH–N (1H, s)	CH=N (1H, s)
3a	15	80	**4a** (55)	**4a**	—	4.33	—	—
			5a (20)	**5a**	—	—	4.11	—
			6a (25)	—	—	—	—	7.18
3b	15	70	**4b** (25)	**4b**	2.22	4.22	—	—
			7b (75)	**7b**	2.15	4.20	—	—
3c	16	70	**4c** (99)	**4c**	–	4.49	—	—
3d	16	80	**4d** (30)	**4d**	2.40	4.22	—	—
			7d (40)	**7d**	2.53	4.44	—	—
			8d (10)	—	2.35	4.10	—	—

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* According to data from the ^{1}H NMR spectra and GLC-MS of the mixture of products.

*^{2} The products were isolated by column chromatography; eluent 3:1 hexane–ethyl acetate (compounds **4a** and **5a**) and 10:0.05 benzene–ethyl acetate (compounds **4b-d** and **7b**).

TABLE 5. The Mass Spectra* of the Hydrosilylation Products

Compound	*m/z* (I_{rel}, %)					
	M^+	$[M – H]^+$	$[M – Et]^+$	$[M–HSiEt_3]^+$	$[SiEt_3]^+$	$[HetCH_2]^+$
4a	191 (32)	190 (15)	—	—	—	81 (100)
5a	305 (25)	304 (100)	—	189 (11)	115 (29)	—
6a	191 (12)	190 (100)	—	—	—	—
4b	205 (14)	—	—	—	—	95 (100)
7b	319 (8)	—	290 (7)	—	—	95 (100)
4c	207 (21)	—	—	—	—	97 (100)
4d	221 (14)	—	—	—	—	111 (100)
7d	335 (10)	—	306 (8)	—	—	111 (100)
8d	337 (100)	—	—	—	115 (35)	—

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* The signals of the characteristic ions are given.

EXPERIMENTAL

The ^{1}H NMR spectra were investigated on Varian Mercury (200 MHz) and Bruker WH-90/DS (90 MHz) spectrometers in deuterochloroform with TMS as internal standard. The mass spectra were obtained on an HP 6890 GC/MS chromato-mass spectrometer with an HP-5 MS capillary column (30.0 m × 250 μ × 0.25 μ) with programmed temperature from 70 to 260°C (10 deg/min). Before use the benzene was distilled over CaH_2. The aldehydes, amines, hydrosilane, and Pd complex were supplied by Acros, Aldrich, and Fluka. Molecular sieves 4A from VEB Laborchemie Apolda were used.

Synthesis of Aldimines (General Procedure). We placed dry benzene (10 ml), each of the initial aldehyde and amine (5 mmol), and then freshly calcined molecular sieves (5 g) in a flask. The reaction was conducted at room temperature in an atmosphere of argon, and samples were taken periodically and analyzed by TLC and GLC-MS. After a certain time, depending on the substrate (Table 1), they were completely transformed into the respective products. At the end of the reaction the sieves were filtered off and washed with benzene. The filtrate was evaporated at reduced pressure (40°C, 15 mm Hg), and the small residues of the initial substances were removed under vacuum (45-50°C, 0.1 mm Hg). The products were oily or crystalline yellow substances. The solids were purified by recrystallization from hexane or its mixture with ethyl acetate, and the ^{1}H NMR spectra were recorded.

Hydrosilylation (General Procedure). A 5-cm^3 Pierce reaction tube was blown with argon, and dry benzene (2 ml), the catalyst (0.01 mmol), and the initial imine (0.5 mmol) were placed in it, and the mixture was then stirred at room temperature for 30 min. The solution was then cooled with ice to 0°C, and hydrosilane (0.6 mmol) was added with a syringe. The reaction was conducted at 65°C, and samples were taken periodically and analyzed by TLC and GLC-MS. At the end of silylation the reaction mixture was evaporated at reduced pressure (30°C, 15 mm Hg), and the ^{1}H NMR spectra were recorded. The mixture was separated by liquid chromatography on a column of silica gel (Kieselgel 60, 0.063-0.200 mesh, Merck) with various eluants. All the obtained products were yellow oily substances.

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