Synthesis and Reactions of Schiff Bases Containing an *m*-Phenoxyphenyl Group: I. *N*-Aryl-*m*-phenoxybenzylideneamines and *N*-Aryl-*N'*-(*m*-phenoxybenzylidene)hydrazines

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Abstract—Condensation of *m*-phenoxybenzaldehyde with aromatic amines and hydrazines gave the corresponding Schiff bases and *m*-phenoxybenzaldehyde arylhydrazones. The products are promising as biologically active substances, polyfunctional additives to rubber compounds, and inhibitors of acid corrosion.

Schiff bases, i.e., compounds having a double C=N bond, are used as starting materials in the synthesis of important drugs, such as antibiotics and antiallergic, antiphlogistic, and antitumor substances [1, 2, 3]. They are also used as components of rubber compounds [4]. Hydrazones have found application in synthetic and analytical chemistry, but their most valuable property is high physiological activity [5].

The goal of the present study was to develop procedures for synthesizing a series of new Schiff bases and hydrazones containing an *m*-phenoxyphenyl group and to find ways for their practical utilization. m-Phenoxybenzaldehyde (I) readily reacted with aromatic amines IIa-IIp to afford the corresponding *N*-aryl-*m*-phenoxybenzylideneamines **IIIa**–**IIIp**. The reactions started even at room temperature and were accompanied by appreciable heat evolution: the mixtures warmed up by 10-15°C. However, the rate of the condensation was low, and in 1.5–2 h the products were formed in 60-80% yield (Scheme 1). The reactant molar ratio I:II was 1:1. Raising the temperature to 60-80°C strongly accelerated the process, and the reaction was complete in 10-15 min, but the yields of products II did not change. Analysis of the reaction

mixtures by GLC did not reveal appreciable amounts of by-products. By the end of the process the mixture contained Schiff base **II**, water, and small amounts of the initial reactants.

A possible reason for relatively low yields of the condensation products in reactions of aldehyde I with aromatic amines is equilibrium character of the process. It is known that condensation of aldehydes with amines is reversible [2]. We performed a series of experiments with continuous removal of water as azeotropic mixture with benzene. In the reactions of I with aniline, *p*-anisidine, and *p*-bromoaniline the theoretical amount of water separated in 50 min, but the yields of the products slightly differed from those obtained in the previous experiments. The yield of *N*-phenyl-*m*-phenoxybenzylideneamine increased by 1.5%, of N-p-methoxyphenyl-m-phenoxybenzylideneamine, by 2%, and of N-p-bromophenyl-m-phenoxybenzylideneamine, by 3%. Therefore, we can conclude that reactions of aldehyde I with aromatic amines are almost irreversible.

Aromatic hydrazines turned out to be more reactive toward aldehyde **I**, as compared with aromatic amines [6]. The reactions readily occurred at room tempera-



 $\mathbf{R} = C_{6}H_{5}(\mathbf{a}), o - O_{2}NC_{6}H_{4}(\mathbf{b}), m - O_{2}NC_{6}H_{4}(\mathbf{c}), p - O_{2}NC_{6}H_{4}(\mathbf{d}), o - CH_{3}OC_{6}H_{4}(\mathbf{e}), p - CH_{3}OC_{6}H_{4}(\mathbf{f}), o - HOC_{6}H_{4}(\mathbf{g}), p - HOC_{6}H_{4}(\mathbf{h}), o - CH_{3}C_{6}H_{4}(\mathbf{i}), p - CH_{3}C_{6}H_{4}(\mathbf{j}), p - CIC_{6}H_{4}(\mathbf{k}), p - BrC_{6}H_{4}(\mathbf{l}), 2,5 - (CH_{3})_{2}C_{6}H_{3}(\mathbf{m}), C_{6}H_{5}CH_{2}(\mathbf{n}), \alpha - naphthyl (\mathbf{o}), 2 - thiazolyl (\mathbf{p}).$

Comp.	Yield,	mp, °C, or bp, °C (<i>p</i> , mm)	Found, %			Eormula	Calculated, %		
no.	%		С	Н	Ν	гоппина	С	Н	N
IIIa	91	57–60	83.10	5.85	5.70	C ₁₉ H ₁₅ NO	83.50	5.49	5,13
IIIb	60	75–78	70.23	4.42	8.66	$C_{19}H_{14}N_2O_3$	71.69	4.40	8.81
IIIc	66	55–57	71.32	4.54	9.08	$C_{19}H_{14}N_2O_3$	71.69	4.40	8.81
IIId	88	138–140	71.09	4.34	8.40	$C_{19}H_{14}N_2O_3$	71.69	4.40	8.81
IIIe	68	275–277 (2)	79.44	6.57	4.53	$C_{20}H_{15}NO_2$	79.26	5.61	4.62
IIIf	67	52–55	79.69	5.28	4.75	$C_{20}H_{17}NO_2$	79.26	5.61	4.62
IIIg	68	80-82	78.61	5.14	5.50	$C_{19}H_{15}NO_2$	79.89	5.19	4.84
IIIh	62	131–133	80.69	6.01	5.11	$C_{19}H_{15}NO_2$	79.89	5.19	4.84
IIIi	65	225–228 (2)	82.68	5.94	4.75	C ₂₀ H ₁₇ NO	83.62	5.92	4.87
IIIj	66	41-42	82.53	5.94	5.11	$C_{20}H_{17}NO$	83.62	5.92	4.87
IIIk	78	47–49	73.48	4.30	4.40	C ₁₉ H ₁₄ NOCl	74.15	4.55	4.55
IIII	82	53–55	64.72	4.02	3.91	C ₁₉ H ₁₄ NOBr	64.58	3.96	3.96
IIIm	71	265–267 (2)	82.72	6.37	4.24	$C_{21}H_{19}NO$	83.72	6.31	4.65
IIIn	85	49–51	82.97	5.02	4.43	C ₂₀ H ₁₇ NO	83.62	5.92	4.88
IIIo	77	27-30	82.60	4.90	4.30	$C_{22}H_{17}NO$	83.45	5.26	4.33
IIIp	79	127-129	67.52	5.32	4.34	$C_{16}H_{12}N_2OS$	68.57	4.28	10.0
Va	90	57–59	78.89	5.04	9.42	$C_{19}H_{16}N_2O$	79.20	5.50	9.72
Vb	96	158–160	75.49	5.41	7.84	$C_{20}H_{16}N_2O_2$	75.90	5.05	8.86
Vc	80	202-204	59.71	4.08	15.6	C ₁₉ H ₁₄ N ₄ O ₅	60.32	3.70	14.8
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Yields, melting or boiling points, and elemental analyses of Schiff bases IIIa-IIIp and hydrazones Va-Vc

ture and were exothermic: the mixtures warmed up by $30-35^{\circ}$ C. To complete the reaction, the mixtures were heated for 40-60 min at $60-70^{\circ}$ C. The reactant ratio aldehyde I:hydrazine IV was 1:1, and chloroform was used as solvent (Scheme 2).



The reaction of aldehyde **I** with aromatic hydrazines is selective, and hydrazones Va-Vc are formed in high yields (90–96%); the process can be regarded as irreversible.

N-Aryl-*m*-phenoxybenzylideneamines **IIIa**–**IIIp** and arylhydrazones **Va**–**Vc** are as a rule colored viscous liquids or crystalline substances which were purified by vacuum distillation or recrystallization. Their structure was confirmed by the IR and ¹H NMR spectra and elemental analyses (see table).

The IR spectra of **III** and **V** contain a characteristic absorption band in the region $1630-1633 \text{ cm}^{-1}$, which belongs to the C=N double bond. The lack of absorption in the regions of 1720 and 3300 cm⁻¹ indicates the absence of carbonyl and amino groups.

In the ¹H NMR spectra of *N*-aryl-*m*-phenoxybenzylideneamines **IIIa–IIIp** we observed an upfield singlet at δ 7.90–8.20 ppm due to the CH proton. Aromatic protons give rise to a multiplet at δ 6.94– 7.44 ppm whose intensity corresponds to 14 protons.

The results of simulation of biological activity of Schiff bases III and hydrazones V showed that the potential pharmacophoric fragment in *m*-phenoxybenzaldehyde derivatives is $C_6H_5OC_6H_4CH=N$ which includes the diphenyl ether moiety and CH=N double bond. Compounds possessing such a fragment could exhibit pronounced fungicide activity. It should be noted that a series of Schiff bases having an *m*-phenoxyphenyl group, were registered at the Russian Research Center for Safety of Biologically Active Substances. In addition, *N*-aryl-*m*-phenoxybenzylideneamines can be used as polyfunctional components of resin mixtures, as well as inhibitors of acid corrosion [7–10].

EXPERIMENTAL

The IR spectra were recorded on a Specord M82 instrument (NaCl or KBr prism) from samples prepared as thin films (liquid products) or dispersions in mineral oil (crystalline products). The ¹H NMR spectra were obtained on a Tesla BS-487 spectrometer (100 MHz) relative to hexamethyldisiloxane as internal reference; the solvents were CCl₄, CDCl₃, and acetone- d_{6} .

N-Phenyl-*m*-phenoxybenzylideneamine (IIIa). A four-necked reactor equipped with a stirrer, reflux condenser, and thermometer was charged with 15 g (0.076 mol) of *m*-phenoxybenzaldehyde (I), and 7.05 g (0.076 mol) of aniline was added under vigorous stirring and cooling with water. The mixture was then heated for 1.5–2 h at 100–110°C. It crystallized on cooling. The product was recrystallized from ethanol. Yield 88%, mp 58–60°C. Found, %: C 82.97; H 5.73; N 5.80. $C_{13}H_{15}NO$. Calculated, %: C 83.50; H 5.49; N 5.13.

Compounds **IIIb–IIIp** were synthesized following a similar procedure (see table).

N-Benzoyl-*N'*-(*m*-phenoxybenzylidene)hydrazine (Vb). A four-necked reactor equipped with a stirrer, reflux condenser, and thermometer was charged with 15 g (0.076 mol) of *m*-phenoxybenzaldehyde and 50 ml of chloroform. Benzoylhydrazine, 10.3 g (0.076 mol), was added under vigorous stirring and cooling with water, the mixture was heated for 1 h at 60–65°C, and the solvent was removed. The product was recrystallized from ethanol. Yield 23 g (96%), mp 158–160°C. Found, %: C 75.49; H 5.91; N 7.84. $C_{19}H_{16}N_2O$. Calculated, %: C 75.90; H 5.86; N 8.46.

Hydrazones **Va** and **Vc** were synthesized in a similar way (see table).

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