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Synthesis and Properties of Substituted Benzaldehyde Phenylhydrazones

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Abstract—Phenylhydrazones containing hydroxy, alkoxy and acyloxy groups are synthesized from aromatic aldehydes of vanillin series by reaction with phenylhydrazine.

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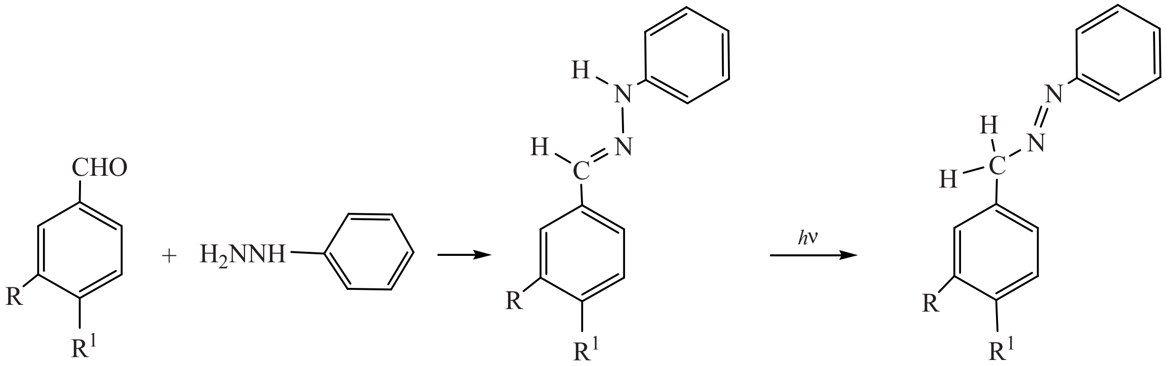
We reported earlier on the syntheses of thiosemicarbazides and *E*-3-alkoxy-4-hydroxy(alkoxy, acyloxy)phenylmethylenephenylamines (azomethines) by reaction of substituted aromatic aldehydes of vanillin series with hydrazinothiocarboxylic acid amide (thiosemicarbazone) or aniline [1, 2]. These compounds turned out to be promising objects for preparation of nanofilms and nanomaterials [3].

The aim of this work was the synthesis and study of properties of phenylhydrazones of substituted aromatic aldehydes from the vanillin series, containing hydroxy, alkoxy and acyloxy groups. By a reaction of substituted aromatic aldehydes (**I**) with phenylhydrazine (**II**) in anhydrous diethyl ether we prepared in 80–90% yield the corresponding phenylhydrazones (**IIIa–IIIt, IVa–IVm**), possessing hydroxy, alkoxy and acyloxy groups. The reaction was completed in 8–30 h, proceeded under mild conditions (ratio of reagents 1:1, temperature –5°C, protection against light) without catalysts. According to the data of ^{1}H NMR spectroscopy the purity of obtained compounds was 92±2 %.

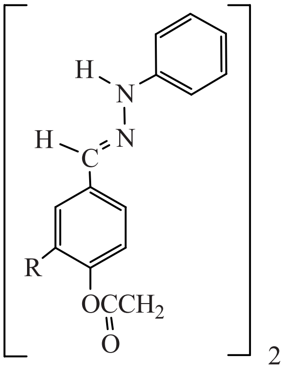
Freshly synthesized phenylhydrazones **IIIa–IIIt**, **IVa–IVk** are colorless or slightly colored crystalline substances with distinct melting points (Table 1). Unlike semicarbazides [1] and azomethines [2] the substituted aromatic aldehyde phenylhydrazones **IIIa–IIIt**, **IVa–IVk** are unstable compounds rapidly darkening when exposed to light and at the contact with air oxygen. The phenylhydrazones **IIIa–IIIt**, **IVa–IVk** transform readily via free radical isomerization into thermodynamically more stable azo compounds **V** [4]. The substituted aromatic aldehyde phenylhydrazones **IIIa–IIIt**, **IVa–IVk** can be stored for a long period when sealed in glass ampoules under argon atmosphere, in the dark at the temperature below –5°C . Structures of phenylhydrazones **IIIa–IIIt**, **IVa–IVk** were proved by elemental analysis, cryoscopic determination of molecular weight (Table 1), data of IR and ^{1}H NMR spectroscopy.

In the IR spectra of phenylhydrazones **IIIa–IIIt**, **IVa–IVk**) absorption bands were observed of groups NH in the region of 3313±2; C–H$_{ar}$ at 3100–3000, 880–610; C–H$_{alk}$ at 2980–2840; C=N at 1600±2; C–C$_{ar}$ at 1600–1390; C–O at 1270–1025 cm^{-1}. The presence of OH group in phenols **IIIb** and **IVa** is confirmed by the absorption band at 3495±5 cm^{-1} in their IR spectra. The IR spectra of esters **IIId–IIIt, IVc–IVk** contain bands of C=O group in the region of 1770–1740 cm^{-1}. The presence of nitro group in the nitro derivative **IIIq** is confirmed by characteristic absorption bands at 1539 and 1352 cm^{-1}.

In the ^{1}H NMR spectra of phenylhydrazones **IIIa–IIIt**, **IVa–IVk** the signals of protons C–H$_{ar}$ (C_6H_5 and C_6H_3) and of the NH group proton appear as a multiplet in the region of 6.75–7.40 ppm. The proton of HC=N group is observed as a singlet at 7.50–7.75 ppm. The presence of OH group in phenols **IIIb**, **IVa** is confirmed by a broad singlet in the region of 5.80–5.85 ppm. Groups MeO of phenylhydrazones **IIIa–IIIt**, **IVb**, **IVi** give in ^{1}H NMR spectra singlets in the range 3.85–4.00 ppm, in the spectra of compounds **IIIs**, **IVa–IVk** the EtO group gives rise to a triplet in the range 1.20–1.70 ppm (Me) and a quadruplet at 4.00–4.50 ppm (CH_2). In the spectra of acetates (**IIId**,



I **II** **IIIa–IIIs, IVa–IVj** **V**



IIIt, IVk

III, R = H, R^1 = MeO (**a**); R = MeO, R^1 = HO (**b**), MeO (**c**), MeC(O)O (**d**), EtC(O)O (**e**), PrC(O)O (**f**), $Me_2CHC(O)O$ (**g**), $Me(CH_2)_6C(O)O$ (**h**), $Me(CH_2)_8C(O)O$ (**i**), $Me(CH_2)_{16}C(O)O$ (**j**), $H_2C{=}C(Me)C(O)O$ (**k**), $C_6H_5CH_2C(O)O$ (**l**), $C_6H_5CH(Me)CH_2C(O)O$ (**m**), $C_6H_5C(O)O$ (**n**), 2,4-$Cl_2C_6H_3C(O)O$ (**o**), 4-$BrC_6H_4C(O)O$ (**p**), 3-$O_2NC_6H_4C(O)O$ (**q**), MeOC(O)O (**r**), EtOC(O)O (**s**); R = MeO (**t**); **IV**, R^1 = EtO, R^1 = HO (**a**), MeO (**b**), MeC(O)O (**c**), EtC(O)O (**d**), PrC(O)O (**e**), $Me_2CHC(O)O$ (**f**), $Me_2CHCH_2C(O)O$ (**g**), 4-$MeC_6H_4C(O)O$ (**h**), MeOC(O)O (**i**), EtOC(O)O (**j**); R = EtO (**k**).

IVc) the protons of MeC(O)O group give singlets at 2.35 ppm.

The IR and ^{1}H NMR spectra of phenylhydrazones **IIIa**–**IIIt**, **IVa**–**IVk** contain absorption bands and proton signals confirming the presence of respective structural fragments of ester groups.

In the IR spectra of the samples of phenylhydrazones **IIIa**–**IIId**, **IVa**, **IVd** that have darkened or strongly colored to red-brown due to the action of light and air oxygen occurred a decrease in the intensity of the absorption bands of groups NH and C=N. In the ^{1}H NMR spectra of these samples a decrease was registered in the intensity of the signal of HC=N proton and a gradual increase in the intensity of the singlet at 4.40 ppm corresponding to CH_2 group of the formed azo compounds **V**, that confirmed the proposed scheme of isomerization [5].

To analyse the observed isomerization of phenylhydrazones **IIIa**–**IIIt**, **IVa**–**IVk** into azo compounds **V** we carried out quantum-chemical calculations of heat of formation (H_f, kcal mol^{-1}) of *E*–*Z* configuration isomers of phenylhydrazones **IIIa**–**IIId**, **IVa** and **IVd** and related isomeric *trans* and *cis* azo compounds **V** (Table 2).

The quantum-chemical calculations were performed in the framework of semiempirical approximation MNDO PM3 [6, 7] using GAMESS program [8]. We completely optimized all bond lengths, bond angles and dihedral angles. From the calculations follows that *E*-configuration of phenylhydrazones **IIIa**–**IIId**, **IVa** and **IVd** is by 0.1–0.7 kcal mol^{-1} more stable thermodynamically that *Z*-configuration ($\Delta H_{E/Z}$), and *trans*-configuration of azo compounds **V** is by 2.3–6.0 kcal mol^{-1} more advantageous than the *cis*-configuration ($\Delta H_{trans/cis}$). From the consideration of the data for the most stable configurations of the studied compounds *E*-(**IIIa**–**IIId**, **IVa**, **IVd**) and *trans*-**V** follows that at the isomerization of phenylhydrazones **IIIa**–**IIIt** and **IVa**–**IVk** into azo compounds **V** the energy gain is 2.3–5.3 kcal mol^{-1} ($\Delta H_{E/trans}$) (Table 2).

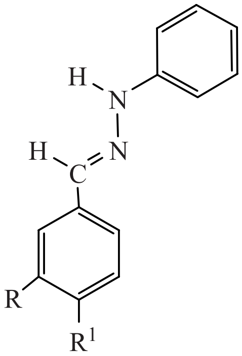
Table 1. Yields, melting points, and data of elemental analyses and molecular weight measurements of phenylhydrazones (**IIIa**–**IIIt**, **IVa**–**IVk**)

Comp. no.	Yield, %	mp °C	Found, %			Formula	Calculated, %			*M*	
			C	H	N		C	H	N	found	calculated
IIIa	86	114–115	74.86	6.28	12.07	$C_{14}H_{14}N_2O$	74.31	6.24	12.38	218.0	226.3
IIIb	80	64–65	69.90	6.03	11.19	$C_{14}H_{14}N_2O_2$	69.41	5.82	11.56	234.3	242.3
IIIc	82	94–95	70.45	6.34	10.58	$C_{15}H_{16}N_2O_2$	70.29	6.29	10.93	241.8	256.3
IIId	88	93–94	67.92	5.70	9.49	$C_{16}H_{16}N_2O_3$	67.59	5.67	9.85	268.5	284.3
IIIe	90	114–115	68.84	6.19	9.07	$C_{17}H_{18}N_2O_3$	68.44	6.08	9.39	290.2	298.3
IIIf	86	104–105	69.53	6.48	8.65	$C_{18}H_{20}N_2O_3$	69.21	6.45	8.97	304.1	312.4
IIIg	84	98–99	69.37	6.52	8.60	$C_{18}H_{20}N_2O_3$	69.21	6.45	8.97	301.2	312.4
IIIh	85	84–85	71.84	7.73	7.32	$C_{22}H_{28}N_2O_3$	71.71	7.66	7.60	352.4	368.5
IIIi	87	67–68	73.02	8.26	6.84	$C_{24}H_{32}N_2O_3$	72.70	8.13	7.06	388.4	396.5
IIIj	88	62–63	75.91	9.67	5.23	$C_{32}H_{48}N_2O_3$	75.55	9.51	5.51	480.7	508.7
IIIk	83	53–54	69.96	5.89	8.65	$C_{18}H_{18}N_2O_3$	69.96	5.85	9.03	298.6	310.4
IIIl	86	97–98	73.67	5.67	7.48	$C_{22}H_{20}N_2O_3$	73.32	5.59	7.77	350.1	360.4
IIIm	85	47–48	74.60	6.33	7.04	$C_{24}H_{24}N_2O_3$	74.21	6.23	7.21	374.3	388.5
IIIn	87	209–210	73.06	5.25	7.82	$C_{21}H_{18}N_2O_3$	72.82	5.24	8.09	333.8	346.4
IIIo[a]	88	128–129	60.97	3.95	6.47	$C_{21}H_{16}Cl_2N_2O_3$	60.74	3.88	6.75	405.7	415.3
IIIp[b]	90	153–154	59.64	4.18	6.20	$C_{21}H_{17}BrN_2O_3$	59.31	4.03	6.59	434.5	452.3
IIIq	89	152–153	64.83	4.54	10.28	$C_{21}H_{17}N_3O_5$	64.45	4.38	10.74	380.4	391.4
IIIr	85	113–114	64.25	5.46	8.99	$C_{16}H_{16}N_2O_4$	63.99	5.37	9.33	289.6	300.3
IIIs	86	132–133	65.12	5.81	8.58	$C_{17}H_{18}N_2O_4$	64.96	5.77	8.91	303.2	314.3
IIIt	85	203–204	68.06	5.48	9.60	$C_{32}H_{30}N_4O_6$	67.83	5.34	9.89	541.9	566.6
IVa	82	132–133	70.56	6.43	10.54	$C_{15}H_{16}N_2O_2$	70.29	6.29	10.93	243.3	256.3
IVb	80	115–116	71.45	6.85	10.00	$C_{16}H_{18}N_2O_2$	71.09	6.71	10.36	259.0	270.3
IVc	84	108–109	68.73	6.09	8.98	$C_{17}H_{18}N_2O_3$	68.44	6.08	9.39	291.4	298.3
IVd	84	107–108	69.50	6.50	8.62	$C_{18}H_{20}N_2O_3$	69.21	6.45	8.97	301.5	312.4
IVe	86	110–111	70.14	6.88	8.63	$C_{19}H_{22}N_2O_3$	69.92	6.79	8.58	317.7	326.4
IVf	88	111–112	70.19	6.92	8.34	$C_{19}H_{22}N_2O_3$	69.92	6.79	8.58	314.8	326.4
IVg	85	106–107	70.65	7.23	7.88	$C_{20}H_{24}N_2O_3$	70.57	7.11	8.23	328.5	340.4
IVh	88	137–138	73.98	6.02	7.12	$C_{23}H_{22}N_2O_3$	73.78	5.92	7.48	362.6	374.4
IVi	86	110–111	65.20	5.85	8.73	$C_{17}H_{18}N_2O_4$	64.96	5.77	8.91	301.8	314.3
IVj	84	53–54	66.03	6.28	8.18	$C_{18}H_{20}N_2O_4$	65.84	6.14	8.53	319.2	328.4
IVk	88	196–197	68.92	5.93	9.22	$C_{34}H_{34}N_4O_6$	68.67	5.76	9.42	583.0	594.7

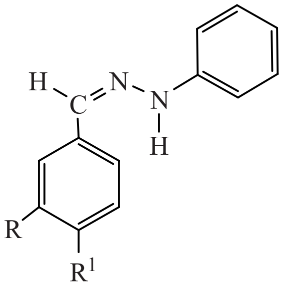
[a] Found Cl, %: 16.81. Calculated Cl, %: 17.07. [b] Found Br, %: 18.43. Calculated Br, %: 18.79.

Table 2. Results of quantum-chemical calculations of heat of formation (H_f, kcal mol^{-1}) of phenylhydrazones **IIIa**–**IIId**, **IVa**, **IVd** *E*- and *Z*-isomers and related isomeric *trans* and *cis* azo compounds **V**

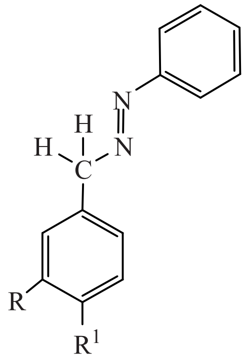
Comp. no.	*E*	*Z*	$\Delta H_{E/Z}$	*trans*-**V**	*cis*-**V**	$\Delta H_{trans/cis}$	$\Delta H_{E/trans}$
IIIa	50.6	50.7	0.1	48.3	50.6	2.3	2.3
IIIb	9.0	9.3	0.3	5.3	9.7	4.4	3.7
IIIc	16.3	17.0	0.7	13.9	17.1	3.2	2.4
IIId	–27.7	–27.0	0.7	–30.5	–25.5	5.0	2.8
IVa	4.5	5.0	0.5	–0.8	5.2	6.0	5.3
IVd	–37.1	–36.7	0.4	–40.5	–35.2	5.3	3.4



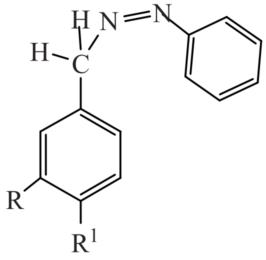
E



Z



trans



cis

Phenylhydrazones of the substituted aromatic aldehydes **IIIa–IIIt** and **IVa–IVk** owing to their high light sensitivity can be used for thermal vacuum spraying of nano films for formation on the films of a relief with submicro elements by the methods of laser ablation lithography [3].

EXPERIMENTAL

The IR spectra were registered on an IR Fourier spectrophotometer Protege-460 Nicolet in KBr pellets, ^{1}H NMR spectra were obtained on a BS-587A 100 MHz Tesla instrument from 5% solutions in $CDCl_3$, chemical shifts were measured from internal TMS. Elemental analysis was carried out on a C, H, N, O, S-analyzer Vario EL-III Elementar, the measurements error 0.1%. Molecular weight was determined by cryoscopy in benzene.

Vanillin and vanillal esters **I** were obtained along the procedures in [9–12]. Phenylhydrazine **II** of “analytically pure” grade, purity 99%, mp 19–20°C was used in the syntheses.

Substituted aromatic aldehydes phenylhydrazones (IIIa–IIIt and IVa–IVk). A 5 mmol portion of a substituted aromatic aldehyde **I** and 5 mmol of phenylhydrazine **II** were dissolved in 10 ml of anhydrous diethyl ether at –5°C at protection against light, under argon atmosphere (in the synthesis of succinates **IIIt** and **IVk** was taken 10 mmol of phenylhydrazine **II** per 5 mmol of the corresponding aldehyde **I**). The formed homogenous solution or suspension was kept under the above conditions for 8–30 h. Excess of ether was carefully (without heating) removed in a vacuum and the formed crystals of compounds **IIIa–IIIt, IVa–IVk** were separated by filtration on a porous glass filter and dried in a vacuum.

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