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Synthesis of *N*-[3-Alkoxy-4-(hydroxy-, alkoxy-, or acyloxy)-benzylidene- and -phenylmethyl]biphenyl-2-amines

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Abstract—Condensation of aldehydes of the vanillin series (vanillin, vanillal, and ethers and esters derived therefrom) with biphenyl-2-amine in anhydrous methanol gave the corresponding Schiff bases which were reduced with Na[BH(OAc)$_3$] in benzene under mild conditions to obtain *N*-[3-alkoxy-4-(hydroxy-, alkoxy-, or acyloxy)phenylmethyl]biphenyl-2-amines.

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We previously reported on the synthesis of *N*-[(*E*)-3-alkoxy-4-acyloxyphenylmethylidene)biphenyl-4-amines (Schiff bases) by condensation of biphenyl-4-amine with esters derived from vanillin and vanillal [1–3]. Aromatic Schiff bases of the vanillin series attract interest as materials for the preparation of nanofilms and nanomaterials [4].

The goal of the present work was to develop a preparative procedure for the synthesis of new aromatic Schiff bases containing hydroxy groups and ether or ester moieties. By condensation of biphenyl-2-amine with vanillin, vanillal, and their ethers and esters on heating in boiling anhydrous methanol we obtained the corresponding aromatic Schiff bases **IIIa**–**IIIu** and **IVa**–**IVm** which were isolated in 82–91% yield. The reactions were complete in 10–15 min under mild conditions in the absence of a catalyst, so that labile ester groups were conserved.

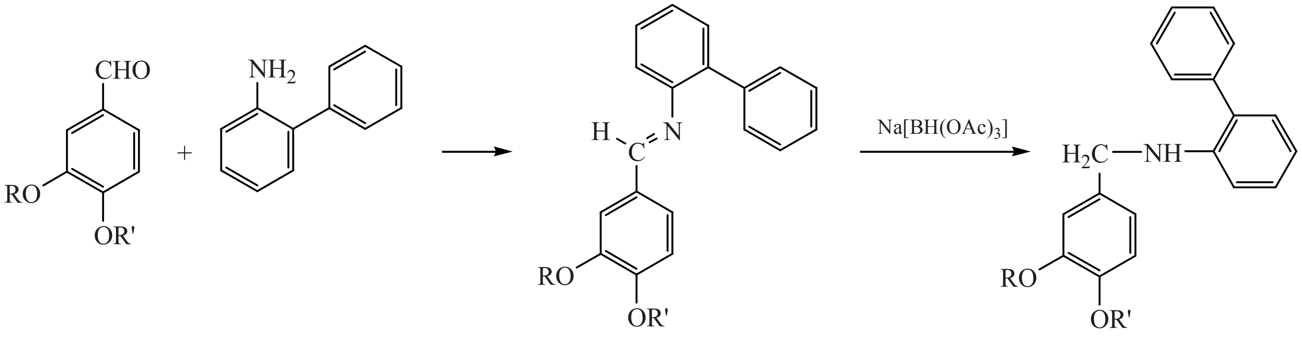
Schiff bases **IIIa**–**IIIu** and **IVa**–**IVm** were subjected to mild reduction with sodium triacetoxyhydridoborate Na[BH(OAc)$_3$] in benzene at 20–23°C. The reactions were complete in 18–20 h, and the products were the corresponding secondary amines **Va**–**Vu** and **VIa**–**VIm**; their yields were almost quantitative (93–96%). The reduction of the azomethine bond [5] was not accompanied by side reduction or hydrolysis of ester groups (Scheme 1).

The structure of Schiff bases **IIIa**–**IIIu** and **IVa**–**IVm** and secondary amines **Va**–**Vu** and **VIa**–**VIm** was confirmed by elemental analysis, cryoscopic determination of molecular weight (see Table 1), and IR and ^{1}H NMR spectroscopy. According to the ^{1}H NMR data, the purity of the isolated compounds was 95±1%.

Compounds **IIIa**–**IIIu**, **IVa**–**IVm**, **Va**–**Vu**, and **VIa**–**VIm** are colored (mostly yellow) viscous glassy or crystalline substances which are soluble in benzene, chloroform, and acetone and insoluble in water and hexane. Secondary amines **Va**–**Vu** and **VIa**–**VIm**, especially those containing hydroxy groups (compounds **Va** and **VIa**), are unstable; they quickly darken on exposure to light and atmospheric oxygen as a result of oxidation with formation of tarry products. These compounds can be stored for a long time in sealed ampules under argon in the dark at reduced temperature.

The IR spectra of compounds **III**–**VI** contained absorption bands due to stretching vibrations of aromatic C–H bonds (3100–3000, δ 880–700 cm^{-1}), aliphatic C–H bonds (3000–2840 cm^{-1}), carbonyl groups (1770–1720 cm^{-1}), aromatic C=C bonds (1600–1370 cm^{-1}), and C–O bonds (1280–1035 cm^{-1}). In the IR spectra of Schiff bases **IIIa**–**IIIu** and **IVa**–**IVm** we observed an absorption band at 1632–1618 cm^{-1}, which is typical of stretching vibrations of azomethine

Scheme 1.



I **II** **IIIa–IIIu, IVa–IVm** **Va–Vu, VIa–VIm**

III, **V**, R = Me, R′ = H (**a**), Me (**b**), MeC(O) (**c**), EtC(O) (**d**), PrC(O) (**e**), $Me_2CHC(O)$ (**f**), $Me(CH_2)_6C(O)$ (**g**), $Me(CH_2)_8C(O)$ (**h**), $Me(CH_2)_{16}C(O)$ (**i**), $H_2C{=}C(Me)C(O)$ (**j**), $PhCH_2C(O)$ (**k**), $PhCH(Me)CH_2C(O)$ (**l**), PhC(O) (**m**), 4-$ClC_6H_4C(O)$ (**n**), 2,4-$Cl_2C_6H_3C(O)$ (**o**), 4-$BrC_6H_4C(O)$ (**p**), 3-$O_2NC_6H_4C(O)$ (**q**), MeOC(O) (**r**), EtOC(O) (**s**), 1/2 $[(O)C(CH_2)_2C(O)]$ (**t**), *m*-$HCB_{10}H_{10}CC(O)$ (**u**); **IV**, **VI**, R = Et, R′ = H (**a**), Me (**b**), MeC(O) (**c**), EtC(O) (**d**), PrC(O) (**e**), $Me_2CHC(O)$ (**f**), $Me_2CHCH_2C(O)$ (**g**), 4-$MeC_6H_4C(O)$ (**h**), 3,5-$(O_2N)_2C_6H_3C(O)$ (**i**), MeOC(O) (**j**), EtOC(O) (**k**), 1/2 $[(O)C(CH_2)_2C(O)]$ (**l**), *m*-$HCB_{10}H_{10}CC(O)$ (**m**).

C=N bond; no such band was present in the spectra of secondary amines **Va**–**Vu** and **VIa**–**VIm**. In contrast, amines **V** and **VI** characteristically displayed absorption in the region 3450–3390 cm^{-1} due to stretching vibrations of the N–H bond. In addition, the IR spectra of nitro-substituted derivatives **IIIq**, **IVi**, **Vq**, and **VIi** contained absorption bands belonging to symmetric and antisymmetric vibrations of the nitro group (1532–1528 and 1350–1344 cm^{-1}), while *m*-carborane derivatives **IIIu**, **IVm**, **Vu**, and **VIm** showed absorption bands at 3065–3063 (C–H) and 2680–2500 cm^{-1} (B–H).

Table 1. Yields, melting points, elemental analyses, and molecular weights of Schiff bases **IIIa**–**IIIu** and **IVa**–**IVm** and secondary amines **Va**–**Vu** and **VIa**–**VIm**

Comp. no.	Yield, %	mp, °C	Found, %			Formula	Calculated, %			*M*	
			C	H	N		C	H	N	found	calculated
IIIa	82	–	79.44	5.67	4.43	$C_{20}H_{17}NO_2$	79.19	5.65	4.62	292.8	303.4
IIIb	88	–	79.63	6.12	4.15	$C_{21}H_{19}NO_2$	79.47	6.03	4.41	310.3	317.4
IIIc	90	–	76.82	5.60	3.86	$C_{22}H_{19}NO_3$	76.50	5.54	4.06	338.1	345.4
IIId	89	82–83	77.09	6.01	3.72	$C_{23}H_{21}NO_3$	76.86	5.89	3.90	352.7	359.4
IIIe	91	–	77.43	6.25	3.58	$C_{24}H_{23}NO_3$	77.19	6.21	3.75	365.0	373.5
IIIf	91	–	77.45	6.19	3.54	$C_{24}H_{23}NO_3$	77.19	6.21	3.75	366.2	373.5
IIIg	90	–	78.83	7.41	2.97	$C_{28}H_{31}NO_3$	78.29	7.27	3.26	421.3	429.6
IIIh	87	55–56	79.04	7.79	2.85	$C_{30}H_{35}NO_3$	78.74	7.71	3.06	448.2	457.6
IIIi	84	76–77	80.35	9.22	2.19	$C_{38}H_{51}NO_3$	80.10	9.02	2.46	557.4	569.8
IIIj	82	–	77.82	5.76	3.54	$C_{24}H_{21}NO_3$	77.61	5.70	3.77	362.4	371.4
IIIk	83	–	80.08	5.53	3.05	$C_{28}H_{23}NO_3$	79.79	5.50	3.32	415.9	421.5
IIIl	85	73–74	80.44	6.16	2.76	$C_{30}H_{27}NO_3$	80.15	6.05	3.12	440.2	449.5
IIIm	88	132–133	79.87	5.34	3.18	$C_{27}H_{21}NO_3$	79.59	5.19	3.44	398.6	407.5
IIIn[a]	90	150–151	73.58	4.73	2.71	$C_{27}H_{20}ClNO_3$	73.38	4.56	3.17	429.0	441.9
IIIo[b]	86	94–95	68.34	4.13	2.63	$C_{27}H_{19}Cl_2NO_3$	68.08	4.02	2.94	465.3	476.4

Table 1. (Contd.)

Comp. no.	Yield, %	mp, °C	Found, %			Formula	Calculated, %			*M*	
			C	H	N		C	H	N	found	calculated
IIIp[c]	89	160–161	66.93	4.26	2.56	$C_{27}H_{20}BrNO_3$	66.68	4.14	2.88	473.1	486.3
IIIq	91	64–65	71.92	4.55	5.84	$C_{27}H_{20}N_2O_5$	71.67	4.46	6.19	438.6	452.5
IIIr	88	47–48	73.36	5.39	3.57	$C_{22}H_{19}NO_4$	73.12	5.30	3.88	354.2	361.4
IIIs	88	101–102	73.83	5.72	3.48	$C_{23}H_{21}NO_4$	73.58	5.64	3.73	368.4	375.4
IIIt	87	183–184	76.99	5.31	3.77	$C_{44}H_{36}N_2O_6$	76.73	5.27	4.07	669.8	688.8
IIIu[d]	83	141–142	58.61	5.84	2.70	$C_{23}H_{27}B_{10}NO_3$	58.33	5.75	2.96	464.5	473.6
IVa	84	102–103	79.64	6.12	4.18	$C_{21}H_{19}NO_2$	79.47	6.03	4.41	312.0	317.4
IVb	85	–	80.09	6.45	4.00	$C_{22}H_{21}NO_2$	79.73	6.39	4.23	325.3	331.4
IVc	86	–	77.01	6.04	3.66	$C_{23}H_{21}NO_3$	76.86	5.89	3.90	350.2	359.4
IVd	87	–	77.35	6.32	3.64	$C_{24}H_{23}NO_3$	77.19	6.21	3.75	362.5	373.5
IVe	88	–	77.82	6.50	3.43	$C_{25}H_{25}NO_3$	77.49	6.50	3.61	374.3	387.5
IVf	86	–	77.73	6.62	3.40	$C_{25}H_{25}NO_3$	77.49	6.50	3.61	378.7	387.5
IVg	88	–	77.98	6.85	3.22	$C_{26}H_{27}NO_3$	77.78	6.78	3.49	388.2	401.5
IVh	91	137–138	80.21	5.93	2.99	$C_{29}H_{25}NO_3$	79.98	5.79	3.22	420.6	435.5
IVi	90	136–137	65.86	4.28	7.94	$C_{28}H_{21}N_3O_7$	65.75	4.14	8.22	496.8	511.5
IVj	86	–	73.67	5.74	3.38	$C_{23}H_{21}NO_4$	73.58	5.64	3.73	366.3	375.4
IVk	83	51–52	74.24	6.10	3.32	$C_{24}H_{23}NO_4$	74.02	5.95	3.60	376.4	389.5
IVl	90	115–116	77.25	5.73	3.55	$C_{46}H_{40}N_2O_6$	77.08	5.62	3.91	698.0	716.8
IVm[e]	89	90–91	59.43	6.17	2.54	$C_{24}H_{29}B_{10}NO_3$	59.12	5.99	2.87	478.5	487.6
Va	93	–	78.87	6.36	4.23	$C_{20}H_{19}NO_2$	78.66	6.27	4.59	292.4	305.4
Vb	95	–	79.18	6.67	4.06	$C_{21}H_{21}NO_2$	78.97	6.63	4.39	307.8	319.4
Vc	94	–	76.35	6.20	3.84	$C_{22}H_{21}NO_3$	76.06	6.09	4.03	336.0	347.4
Vd	94	65–66	76.68	6.62	3.64	$C_{23}H_{23}NO_3$	76.43	6.41	3.88	350.5	361.4
Ve	94	–	77.05	6.78	3.44	$C_{24}H_{25}NO_3$	76.77	6.71	3.73	363.8	375.5
Vf	93	–	76.94	6.70	3.41	$C_{24}H_{25}NO_3$	76.77	6.71	3.73	361.9	375.5
Vg	96	–	78.12	7.79	2.98	$C_{28}H_{33}NO_3$	77.93	7.73	3.25	413.2	431.6
Vh	94	–	78.67	8.24	2.69	$C_{30}H_{37}NO_3$	78.40	8.11	3.05	450.1	459.6
Vi	94	54–55	80.06	9.60	2.42	$C_{38}H_{53}NO_3$	79.82	9.34	2.45	562.2	571.8
Vj	93	–	77.43	6.32	3.62	$C_{24}H_{23}NO_3$	77.19	6.21	3.75	360.0	373.5
Vk	96	–	79.85	6.08	3.03	$C_{28}H_{25}NO_3$	79.41	5.95	3.31	412.3	423.5
Vl	94	52–53	80.05	6.57	2.85	$C_{30}H_{29}NO_3$	79.80	6.47	3.10	435.6	451.6
Vm	93	–	79.50	5.73	3.19	$C_{27}H_{23}NO_3$	79.20	5.66	3.42	398.2	409.5
Vn[f]	93	128–129	73.26	5.12	2.80	$C_{27}H_{22}ClNO_3$	73.05	4.99	7.99	430.4	443.9
Vo[g]	94	77–78	68.12	4.44	2.57	$C_{27}H_{21}Cl_2NO_3$	67.79	4.42	2.93	466.3	478.4
Vp[h]	95	138–139	66.49	4.61	2.53	$C_{27}H_{22}BrNO_3$	66.40	4.54	2.87	467.7	488.4
Vq	96	–	71.58	5.00	5.85	$C_{27}H_{22}N_2O_5$	71.36	4.88	6.16	450.2	454.5
Vr	95	–	72.94	5.98	3.43	$C_{22}H_{21}NO_4$	72.71	5.82	3.85	348.7	363.4
Vs	95	82–83	73.51	6.18	3.50	$C_{23}H_{23}NO_4$	73.19	6.14	3.71	360.1	377.4

Table 1. (Contd.)

Comp. no.	Yield, %	mp, °C	Found, %			Formula	Calculated, %			*M*	
			C	H	N		C	H	N	found	calculated
Vt	96	162–163	76.53	5.97	3.72	$C_{44}H_{40}N_2O_6$	76.28	5.82	4.04	675.8	692.8
Vu[i]	94	124–125	58.38	6.23	2.45	$C_{23}H_{29}B_{10}NO_3$	58.08	6.15	2.95	458.2	475.6
VIa	93	84–85	79.16	6.64	4.04	$C_{21}H_{21}NO_2$	78.97	6.63	4.39	312.3	319.4
VIb	93	–	79.46	7.00	3.98	$C_{22}H_{23}NO_2$	79.25	6.95	4.20	324.4	333.4
VIc	95	–	76.83	6.48	3.49	$C_{23}H_{23}NO_3$	76.43	6.41	3.88	350.2	361.4
VId	95	–	77.01	6.82	3.40	$C_{24}H_{25}NO_3$	76.77	6.71	3.73	363.8	375.5
VIe	94	–	77.34	7.15	3.19	$C_{25}H_{27}NO_3$	77.09	6.99	3.60	380.0	389.5
VIf	94	–	77.42	7.20	3.20	$C_{25}H_{27}NO_3$	77.09	6.99	3.60	378.4	389.5
VIg	93	–	77.90	7.34	3.18	$C_{26}H_{29}NO_3$	77.39	7.24	3.47	391.1	403.5
VIh	96	115–116	79.83	6.32	2.95	$C_{29}H_{27}NO_3$	79.61	6.22	3.20	419.3	437.5
VIi	95	117–118	65.84	4.63	7.86	$C_{28}H_{23}N_3O_7$	65.49	4.51	8.18	489.4	513.5
VIj	94	–	73.45	6.27	3.46	$C_{23}H_{23}NO_4$	73.19	6.14	3.71	364.4	377.4
VIk	93	–	73.84	6.55	3.23	$C_{24}H_{25}NO_4$	73.64	6.44	3.58	381.4	391.5
VIl	94	94–95	76.93	6.19	3.80	$C_{46}H_{44}N_2O_6$	76.65	6.15	3.89	698.3	720.9
VIm[j]	93	82–83	59.11	6.46	2.52	$C_{24}H_{31}B_{10}NO_3$	58.87	6.38	2.86	469.7	489.6

[a] Found Cl, %: 7.86. Calculated Cl, %: 8.02. [b] Found Cl, %: 14.60. Calculated Cl, %: 14.88. [c] Found Br, %: 16.14. Calculated Br, %: 16.43. [d] Found B, %: 22.44. Calculated B, %: 22.83. [e] Found B, %: 21.86. Calculated B, %: 22.17. [f] Found Cl, %: 7.58. Calculated Cl, %: 7.99. [g] Found Cl, %: 14.53. Calculated Cl, %: 14.82. [h] Found Br, %: 16.11. Calculated Br, %: 16.36. [i] Found B, %: 22.28. Calculated B, %: 22.73. [j] Found B, %: 2184. Calculated B, %: 22.08.

In the ^{1}H NMR spectra of **IIIa–IIIu**, **IVb**, **Va**–**Vu**, and **VIb**, protons in the methoxy group resonated as a singlet in the region δ 3.78–3.93 ppm, while protons of the ethoxy group in compounds **IVa–IVm** and **VIa–VIm** gave a triplet at δ 1.15–1.45 ppm (CH_3) and a quartet at δ 3.90–4.20 ppm (CH_2). Signals from aromatic protons were located in the δ range from 6.90 to 7.60 ppm, and the azomethine proton signal appeared in the ^{1}H NMR spectra of Schiff bases **IIIa–IIIu** and **IVa–IVm** as a singlet at δ 8.42–8.50 ppm, which is typical of *E* isomers [6]. Secondary amines **Va–Vu** and **VIa**–**VIm** displayed in the ^{1}H NMR spectra signals from protons in the C**H**$_2$NH group as a broadened singlet at δ 4.36–4.38 ppm. Signals from the carborane CH protons in *m*-carborane derivatives **IIIu**, **IVm**, **Vu**, and **VIm** were located at δ 3.00–3.05 ppm (broadened singlet).

Wide homologous series of Schiff bases and secondary amines **III–VI** based on biphenyl-2-amine (**II**) are necessary for detailed study on the effect of the R and R^1 substituents on the topology of nanofilms prepared from these compounds [7].

EXPERIMENTAL

The IR spectra were recorded in KBr on a Nicolet Protégé-460 spectrometer with Fourier transform. The ^{1}H NMR spectra were measured on a Tesla BS-587A instrument (100 MHz) from 5% solutions in $CDCl_3$; the chemical shifts were determined relative to tetramethylsilane as internal reference. The elemental analyses were obtained on a VarioEL-III CHNOS analyzer with an accuracy of ±0.1%. The molecular weights were determined by cryoscopy in benzene.

The initial vanillin and vanillal esters were synthesized according to the procedures described in [8–11].

***N*-[(*E*)-3-Alkoxy-4-(hydroxy, alkoxy, or acyloxy) benzylidene]biphenyl-2-amines IIIa–IIIu and IVa–IVm** *(general procedure).* A solution of 5 mmol of the corresponding aldehyde **I** and 5 mmol of biphenyl-2-amine (**II**) in 30 ml of anhydrous methanol was heated for 10–15 min. The hot solution was filtered through a folded paper filter, the filtrate was cooled and left to stand for 10–15 h at 5°C, and the precipitate was filtered off through a glass porous filter or separated by decanting, washed with a small amount of methanol, and dried in air.

***N*-[3-Alkoxy-4-(hydroxy, alkoxy, or acyloxy) phenylmethyl]biphenyl-2-amines Va–Vu and VIa–VIm** *(general procedure)*. A mixture of 5 mmol of Schiff base **IIIa–IIIu** or **IVa–IVm**, 10 mmol of $NaBH_4$, 30 mmol of glacial acetic acid, and 50 ml of anhydrous benzene was left to stand for 18–20 h. The solution was washed with water and a 5% solution of $NaHCO_3$, the solvent was removed under reduced pressure, and the residue was purified by recrystallization from benzene–hexane or by column chromatography on silica gel (100–160 µm) using benzene as eluent.

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