

Synthesis of (*E*)-*N*-(3-Alkoxy-4-acyloxyphenylmethylene)-*N*-(*e*-cyclohexyl)amines

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Abstract—Previously unknown *E* isomers of azomethines (Schiff bases) were synthesized from vanillal and vanillin esters by their reaction with cyclohexylamine.

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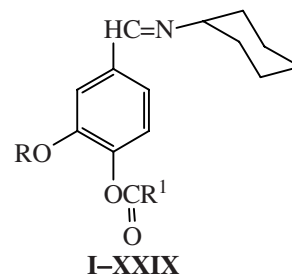
Azomethines derived from natural aldehydophenols, such as vanillin and vanillal, exhibit a high biologic activity and reveal film-forming properties and are thermo- and light-sensitive [1, 2].

The aim of this work was to obtain new azomethines on the basis of previously synthesized vanillin and vanillal esters [3–6]. Condensation of the vanillin and vanillal esters with cyclohexylamine in absolute methanol (method *a*) gave corresponding (*E*)-*N*-(3-alkoxy-4-acyloxyphenylmethylene)-*N*-(*e*-cyclohexyl)amines **I–XXIX** containing ester and ether groups (yield 83–93%). According to ¹H NMR data, the purity of the compounds was 97 ± 1%.

Liquid and low-melting vanillin and vanillal esters also readily react with cyclohexylamine without a solvent. By simply mixing stoichiometric amounts of corresponding aldehyde and cyclohexylamine and subsequently carefully heating the resulting mixture at 60–80°C (method *b*) we obtained azomethines **I–IX**, **XV–XXIV**, **XXVIII**, and **XXIX** in quantitative (99 ± 1%) yields. The purity of the products was 92 ± 2%.

Compounds **I–XXIX** are colorless or slightly colored crystalline compounds with well-defined melting points. The azomethines do not need additional purification and contain no admixtures of the starting compounds. The structure of azomethines **I–XXIX** was established by the elemental analyses and cryoscopic molecular weights (see table), as well as IR, UV, and ¹H NMR spectra.

The IR spectra of azomethines **I–XXIX** show absorption bands (ν, cm^{−1}) of C–H_{Ar} (3100–3000, 890–



R = Me, R¹ = Et (**I**), Pr (**II**), Me₂CH (**III**), Me(CH₂)₆ (**IV**), Me(CH₂)₈ (**V**), Me(CH₂)₁₆ (**VI**), H₂C=CMe (**VII**), C₆H₅CH₂ (**VIII**), C₆H₅C(Me)HCH₂ (**IX**), C₆H₅ (**X**), 4-ClC₆H₄ (**XI**), 2,4-Cl₂C₆H₃ (**XII**), 4-BrC₆H₄ (**XIII**), 3-O₂NC₆H₄ (**XIV**), MeO (**XV**), EtO (**XVI**); R = Et, R¹ = Me (**XVII**), Et (**XVIII**), Pr (**XIX**), Me₂CH (**XX**), Me₂CHCH₂ (**XXI**), Me(CH₂)₈ (**XXII**), Me(CH₂)₁₁ (**XXIII**), Me(CH₂)₁₆ (**XXIV**), Z-C₆H₅C(H)=C(C≡N) (**XXV**), 4-MeC₆H₄ (**XXVI**), 3,5-(O₂N)₂C₆H₃ (**XXVII**), MeO (**XXVIII**), EtO (**XXIX**).

770), C–H_{Alk} (2980–2800), C=O (1770–1730), C=N (1647–1641), C–C_{arom} (1600–1350), and C–O (1300–1000) bonds. The presence of NO₂ groups in compounds **XIV**, **XXVII** is confirmed by characteristic bands at 1540–1525 and 1349–1345 cm^{−1}. The C≡N group in compound **XXV** absorbs at 2225 cm^{−1}.

The UV spectra of compounds **I–XXIX** contain the following absorption bands [λ_{max}, nm (ε · 10^{−3})]: 209 (13), 220 (13), 253 (9), 300 (4). They are characteristic of the (*E*)-*N*-(3-alkoxy-4-acyloxyphenylmethylene)-*N*-(*e*-cyclohexyl)amine chromophore.

Yields, melting points, elemental analyses, and molecular weights of azomethines **I–XXIX**

Comp. no.	Yield, %	mp, °C	Found, %			Formula	Calculated, %			<i>M</i>	
			C	H	N		C	H	N	found	calculated
I	87	52–53	70.74	8.22	4.30	C ₁₇ H ₂₃ NO ₃	70.56	8.01	4.48	281.3	289.4
II	88	44–45	71.57	8.43	4.41	C ₁₈ H ₂₅ NO ₃	71.26	8.31	4.62	290.5	303.4
III	84	51–52	71.49	8.38	4.37	C ₁₈ H ₂₅ NO ₃	71.26	8.31	4.62	292.7	303.4
IV	83	32–33	73.72	9.37	3.65	C ₂₂ H ₃₃ NO ₃	73.50	9.25	3.90	348.0	359.5
V	89	36–37	74.50	9.86	3.48	C ₂₄ H ₃₇ NO ₃	74.38	9.62	3.61	377.1	387.6
VI	90	65–66	77.08	10.89	2.54	C ₃₂ H ₅₃ NO ₃	76.90	10.69	2.80	481.8	499.8
VII	83	44–45	71.94	7.80	4.33	C ₁₈ H ₂₅ NO ₃	71.73	7.69	4.65	290.2	301.4
VIII	93	33–34	75.35	7.28	3.81	C ₂₂ H ₂₅ NO ₃	75.19	7.17	3.99	337.4	351.4
IX	90	27–28	76.19	7.83	3.52	C ₂₄ H ₂₉ NO ₃	75.96	7.70	3.69	364.0	379.5
X	92	84–85	74.92	6.94	3.92	C ₂₁ H ₂₃ NO ₃	74.75	6.87	4.15	321.6	339.4
XI^a	93	117–118	68.02	6.04	3.50	C ₂₁ H ₂₂ ClNO ₃	67.83	5.96	3.77	358.5	371.9
XII^b	89	96–97	62.31	5.37	3.19	C ₂₁ H ₂₁ Cl ₂ NO ₃	62.08	5.21	3.45	390.9	406.3
XIII^c	93	127–128	60.78	5.40	2.97	C ₂₁ H ₂₂ BrNO ₃	60.59	5.33	3.36	404.4	416.3
XIV	90	73–74	66.14	5.82	7.04	C ₂₁ H ₂₂ N ₂ O ₅	65.96	5.80	7.33	362.7	382.4
XV	85	27–28	66.25	7.37	4.58	C ₁₆ H ₂₁ NO ₄	65.96	7.26	4.81	282.3	291.3
XVI	86	55–56	67.02	7.69	4.23	C ₁₇ H ₂₃ NO ₄	66.86	7.59	4.59	297.1	305.4
XVII	88	47–48	70.68	8.12	4.22	C ₁₇ H ₂₃ NO ₃	70.56	8.01	4.48	282.0	289.4
XVIII	90	61–62	71.66	8.45	4.47	C ₁₈ H ₂₅ NO ₃	71.26	8.31	4.62	292.2	303.4
XIX	91	42–43	72.04	8.59	4.14	C ₁₉ H ₂₇ NO ₃	71.89	8.57	4.41	308.3	317.4
XX	92	53–54	72.06	8.64	4.20	C ₁₉ H ₂₇ NO ₃	71.89	8.57	4.41	305.8	317.4
XXI	93	42–43	72.73	8.96	4.01	C ₂₀ H ₂₉ NO ₃	72.47	8.82	4.23	321.8	331.5
XXII	90	46–47	75.05	9.93	3.08	C ₂₅ H ₃₉ NO ₃	74.77	9.79	3.49	387.2	401.6
XXIII	88	47–48	75.91	10.29	2.87	C ₂₈ H ₄₅ NO ₃	75.80	10.22	3.16	429.7	443.7
XXIV	85	30–31	77.34	10.93	2.50	C ₃₃ H ₅₅ NO ₃	77.14	10.79	2.73	492.6	513.8
XXV	93	48–49	74.83	6.55	6.42	C ₂₅ H ₂₆ N ₂ O ₃	74.60	6.51	6.96	388.4	402.5
XXVI	93	108–109	75.72	7.54	3.55	C ₂₃ H ₂₇ NO ₃	75.59	7.45	3.83	354.9	365.5
XXVII	90	92–93	60.03	5.32	9.18	C ₂₂ H ₂₃ N ₃ O ₇	59.86	5.25	9.52	421.0	441.4
XXVIII	86	32–33	66.99	7.75	4.46	C ₁₇ H ₂₃ NO ₄	66.86	7.59	4.59	292.5	305.4
XXIX	88	24–25	67.94	8.03	4.10	C ₁₈ H ₂₅ NO ₄	67.69	7.89	4.39	308.7	319.4

^a Found Cl, %: 9.28, calculated Cl, %: 9.53. ^b Found Cl, %: 17.11, calculated Cl, %: 17.45. ^c Found Br, %: 18.89, calculated Br, %: 19.19

The ¹H NMR spectra of azomethines **I–XVI** display signals of the methoxy group as singlets at 3.85–3.92 ppm. The ethoxy protons in the ¹H NMR spectra of compounds **XVII–XXIX** give a triplet at 1.40–1.70 ppm (Me) and a quartet at 4.00–4.50 ppm (CH₂O). The cyclohexyl protons (C₆H₁₁) appear as a multiplet at 1.10–2.10 ppm. The aromatic proton (C₆H₃) signals of azomethines **I–XXIX** resonate at

7.00–7.50 ppm. The HC=N proton signals are singlets at 8.20–8.30 ppm, what is characteristic of *E* isomers [1–9].

The IR, UV, and ¹H NMR spectra of azomethines **I–XXIX** contain absorption bands and proton signals confirming the presence of corresponding structural fragments of ester groups [1–9].

To confirm the *E* configuration assigned to the synthesized azomethines, we performed quantum-chemical calculations of heats of formation (H_f) for the *E* and *Z* isomers of azomethines **I**, **VIII**, **XVII**, and **XXVI** (equatorial conformations). The calculations were made by the semiempirical MNDO PM3 method with full geometry optimization, using the GAMESS program [10]. The following H_f values (kcal mol⁻¹) were obtained for the *E* and *Z* (in brackets) isomers: **I** -101.3 (-100.5); **VIII** -67.7 (-66.8); **XVII** -102.9 (-102.5); **XXVI** -76.7 (-75.9). According to the quantum-chemical results, the *E* configuration is 0.4–0.9 kcal mol⁻¹ more favored by energy than *Z*, which agrees well with data for related compounds [7–9].

Heats of formation were also calculated for the equatorial and axial conformers of the more stable *E* isomers of azomethines **I**, **VIII**, **XVII**, and **XXVI**. The following values (kcal mol⁻¹) were obtained (values in brackets relate to the axial conformers): **I** -101.3 (-100.9); **VIII** -67.7 (-66.5); **XVII** -102.9 (-100.9); **XXVI** -76.7 (-75.2). These results show that the equatorial conformation is 0.4–2.2 kcal mol⁻¹ more favored by energy than the axial one. Hence, quantum-chemical calculations gave evidence for our assignment to azomethines **I–XXIX** of the (*E*)-*N*-(3-alkoxy-4-acyloxyphenylmethylene)-*N*-(*e*-cyclohexyl)-amine structure.

EXPERIMENTAL

The IR spectra were recorded on a Nicolet Protege-460 IR Fourier spectrometer in KBr pellets. The UV spectra were obtained on a Varian UV-Vis Cary-300 spectrophotometer for 1×10^{-4} M solutions in methanol. The ¹H NMR spectra were taken on a Tesla BS-587A (100 MHz) spectrometer for 5% CDCl₃ solutions against TMS. The elemental analyses were obtained on an Elementar Vario EL-II C,H,N,O,S-analyzer (uncertainty 0.1%). The molecular weights were determined cryoscopically in benzene.

Vanillin and vanillal esters were synthesized according to [3–6].

(*E*)-*N*-(3-Alkoxy-4-acyloxyphenylmethylene)-*N*-(*e*-cyclohexyl)amines **I–XXIX.** Method *a*. A solution of 5 mmol of vanillin or vanillal ester and 5 mmol of

cyclohexylamine in 30 ml of absolute methanol was refluxed for 15 min and then filtered while hot through a folded paper filter, cooled, and left for 10–15 h at 5°C. Crystals of compounds **I–XXIX** formed and were filtered off on a glass frit, washed with a little methanol, and dried in air (see table).

(*E*)-*N*-(3-Alkoxy-4-acyloxyphenylmethylene)-*N*-(*e*-cyclohexyl)amines **I–IX, **XV–XXIV**, **XXVIII**, and **XXIX**.** Method *b*. A mixture of 5 mmol of vanillin or vanillal ester and 5 mmol of cyclohexylamine was carefully heated at 60–80°C for 10–15 min in a ceramic crucible. The homogeneous melt that formed crystallized after cooling, and the product was dried in air.

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