ISSN 1070-3632, Russian Journal of General Chemistry, 2009, Vol. 79, No. 12, pp. 2655–2657. © Pleiades Publishing, Ltd., 2009.
Original Russian Text © E.A. Dikusar, V.I. Potkin, N.G. Kozlov, 2009, published in Zhurnal Obshchei Khimii, 2009, Vol. 79, No. 12, pp. 2029–2031.

Synthesis of Water-Soluble Azomethines Based on the Substituted Benzaldehydes of Vanillin Series and D-(+)-Glucosamine Hydrochloride

E. A. Dikusar, V. I. Potkin, and N. G. Kozlov

Institute of Physical Organic Chemistry, National Academy of Sciences of Belarus,
ul. Surganova 13, Minsk, 220072 Belarus
e-mail: evgen_58@mail.ru

Received June 8, 2009

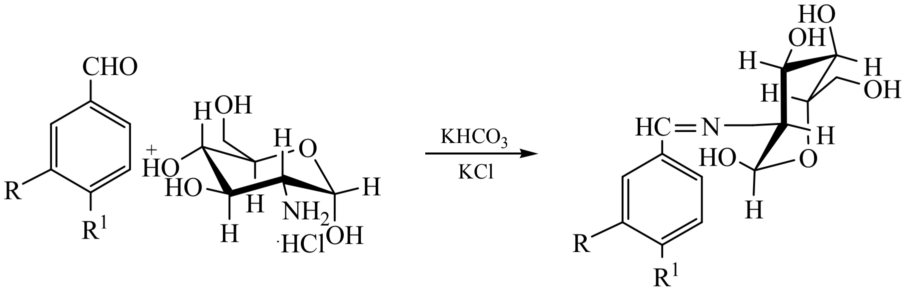
Abstract—A preparative method for the synthesis of water-soluble azomethines by the reaction of substituted benzaldehydes of vanillin series with D-(+)-glucosamine hydrochloride in the presence of potassium hydrogen carbonate in methanol was developed.

DOI: 10.1134/S1070363209120160

Natural aldehydophenols of plant origin, vanillin and vanillal (4-hydroxy-3-methoxy- and -ethoxybenzaldehyde) and their derivatives (**I**) are widely used in food and perfume industry as flavorings, fragrant and odoriferous substances. They may serve as accessible and cheap basic substances for biologically active compounds. D-(+)-Glucosamine [(2*R*,3*R*,4*R*,5*S*,6*R*)-3-amino-6-hydroxymehyltetrahydropyran-2,4,5-triol] is of great importance for the formation and maintaining integrity of tendons, skin, eyes, cerebrospinal fluid, nails, bones, ligaments and heart valves. D-(+)-glucosamine is produced from chitin, the only natural polysaccharide containing nitrogen, which serves as the main organic component of the backbone in invertebrates and of the cell wall of the lower plants (fungi and green algae). Since D-(+)-glucosamine rapidly decomposes on storage, it is usually used as hydrochloride (**II**) [1].

The condensation of substituted benzaldehydes of vanillin series (**I**) with D-(+)-glucosamine hydrochloride (**II**) in the presence of potassium hydrogen carbonate (at a stoichiometric ratio of reagents, 1:1:1) yielded new water-soluble azomethines (Schiff bases) containing hydroxy, ether, and ester groups (**IIIa–IIIx, IVa–IVn**). The condensation was carried out by

---



I **II** **IIIa–IIIx, IVa–IVn**

III, R = R^1 = H (**a**), R^1 = MeO (**b**); R = MeO, R^1 = HO (**c**), MeO (**d**), MeC(O)O (**e**), EtC(O)O (**f**), PrC(O)O (**g**), $Me_2CHC(O)O$ (**h**), BuC(O)O (**i**), $Me_2CHCH_2C(O)O$ (**j**), $Me(CH_2)_6C(O)O$ (**k**), $Me(CH_2)_8C(O)O$ (**l**), $Me(CH_2)_{16}C(O)O$ (**m**), $H_2C{=}C(Me)C(O)O$ (**n**), $C_6H_5CH(Me)CH_2C(O)O$ (**o**), $C_6H_5C(O)O$ (**p**), 2,4-$Cl_2C_6H_3C(O)O$ (**q**), 4-$BrC_6H_4C(O)O$ (**r**), 3-$O_2NC_6H_4C(O)O$ (**s**), MeOC(O)O (**t**), EtOC(O)O (**u**), 1-AdC(O)O (**v**), *o*-$HCB_{10}H_{10}C(O)O$ (**w**), *m*-$HCB_{10}H_{10}C(O)O$ (**x**); **IV**, R = EtO, R^1 = HO (**a**), MeO (**b**), MeC(O)O (**c**), EtC(O)O (**d**), PrC(O)O (**e**), $Me_2CHC(O)O$ (**f**), BuC(O)O (**g**), $Me_2CHCH_2C(O)O$ (**h**), 4-$MeC_6H_4C(O)O$ (**i**), MeOC(O)O (**j**), EtOC(O)O (**k**), 1-AdC(O)O (**l**), *o*-$HCB_{10}H_{10}C(O)O$ (**m**), *m*-$HCB_{10}H_{10}C(O)O$ (**n**).

Yields, melting points, and elemental analysis data of azomethines **IIIa–IIIx, IVa–IVn**

Comp. no.	Yield, %	mp, °C	Found, %			Formula	Calculated, %		
			C	H	N		C	H	N
IIIa	75	174–175	58.87	6.70	4.82	$C_{13}H_{17}NO_5$	58.42	6.41	5.24
IIIb	78	153–154	56.94	6.72	4.26	$C_{14}H_{19}NO_6$	56.56	6.44	4.71
IIIc	72	194–195	54.02	6.37	4.09	$C_{14}H_{19}NO_7$	53.67	6.11	4.47
IIId	74	130–131	55.51	6.10	4.35	$C_{15}H_{21}NO_7$	55.04	6.47	4.28
IIIe	70	71–72	53.65	6.19	4.08	$C_{16}H_{21}NO_8$	54.08	5.96	3.94
IIIf	72	68–69	54.90	6.47	3.44	$C_{17}H_{23}NO_8$	55.28	6.28	3.79
IIIg	73	67–68	56.83	6.12	3.18	$C_{18}H_{25}NO_8$	56.39	6.57	3.65
IIIh	75	65–66	56.13	6.43	3.35	$C_{18}H_{25}NO_8$	56.39	6.57	3.65
IIIi	75	63–64	57.08	6.49	3.72	$C_{19}H_{27}NO_8$	57.42	6.85	3.52
IIIj	70	64–65	57.81	7.23	3.15	$C_{19}H_{27}NO_8$	57.42	6.85	3.52
IIIk	72	60–61	60.53	7.84	2.81	$C_{22}H_{33}NO_8$	60.12	7.57	3.19
IIIl	80	57–58	62.03	8.24	2.53	$C_{24}H_{37}NO_8$	61.65	7.98	3.00
IIIm	82	42–43	66.80	9.22	2.12	$C_{32}H_{53}NO_8$	66.29	9.21	2.42
IIIn	80	73–74	57.06	6.27	3.22	$C_{18}H_{23}NO_8$	56.69	6.08	3.67
IIIo	79	101–102	63.15	6.05	2.67	$C_{24}H_{29}NO_8$	62.73	6.36	3.05
IIIp	77	165–166	60.09	5.78	3.04	$C_{21}H_{23}NO_8$	60.43	5.55	3.36
IIIq[a]	81	202–203	52.17	4.09	2.45	$C_{21}H_{21}Cl_2NO_8$	51.87	4.35	2.88
IIIr[b]	79	208–209	50.46	4.80	2.49	$C_{21}H_{22}BrNO_8$	50.82	4.47	2.82
IIIs	77	232–233	54.07	4.33	5.62	$C_{21}H_{22}N_2O_{10}$	54.55	4.80	6.06
IIIt	70	68–69	51.98	5.36	3.29	$C_{16}H_{21}NO_9$	51.75	5.70	3.77
IIIu	73	65–66	53.35	5.78	3.28	$C_{17}H_{23}NO_9$	52.98	6.02	3.63
IIIv	82	170–171	63.51	7.34	2.63	$C_{25}H_{33}NO_8$	63.14	6.99	2.95
IIIw[c]	76	198–199	42.66	5.82	2.48	$C_{17}H_{29}B_{10}NO_8$	42.23	6.05	2.90
IIIx[d]	74	203–204	41.95	6.13	3.11	$C_{17}H_{29}B_{10}NO_8$	42.23	6.05	2.90
IVa	74	133–134	55.37	6.19	4.42	$C_{15}H_{21}NO_7$	55.04	6.47	4.28
IVb	71	112–113	56.62	6.35	3.81	$C_{16}H_{23}NO_7$	56.30	6.79	4.10
IVc	72	62–63	55.73	6.51	3.33	$C_{17}H_{23}NO_8$	55.28	6.28	3.79
IVd	71	60–61	56.90	6.38	3.24	$C_{18}H_{25}NO_8$	56.39	6.57	3.65
IVe	71	58–59	57.84	6.40	3.83	$C_{19}H_{27}NO_8$	57.42	6.85	3.52
IVf	70	56–57	57.81	7.12	3.80	$C_{19}H_{27}NO_8$	57.42	6.85	3.52
IVg	74	52–53	57.90	6.89	2.97	$C_{20}H_{29}NO_8$	58.38	7.10	3.40
IVh	74	54–55	58.19	7.25	3.48	$C_{20}H_{29}NO_8$	58.38	7.10	3.40
IVi	78	170–171	62.45	6.28	2.74	$C_{23}H_{27}NO_8$	62.01	6.11	3.14
IVj	75	67–68	53.39	6.32	3.16	$C_{17}H_{23}NO_9$	52.98	6.02	3.63
IVk	77	60–61	54.36	6.32	3.19	$C_{18}H_{25}NO_9$	54.13	6.31	3.51
IVl	80	163–164	64.05	7.44	2.43	$C_{26}H_{35}NO_8$	63.79	7.21	2.86
IVm[e]	78	193–194	43.86	6.19	2.60	$C_{18}H_{31}B_{10}NO_8$	43.45	6.28	2.82
IVn[f]	82	197–198	43.17	6.47	2.35	$C_{18}H_{31}B_{10}NO_8$	43.45	6.28	2.82

[a] Found Cl, %: 14.61. Calculated Cl, %: 14.58. [b] Found Br, %: 15.72. Calculated Br, %: 16.10. [c] Found B, %: 21.87. Calculated B, %: 22.36. [d] Found B, %: 22.03. Calculated B, %: 22.36. [e] Found B, %: 21.38. Calculated B, %: 21.73. [f] Found B, %: 22.06. Calculated B, %: 21.73.

boiling a mixture of initial reagents in anhydrous methanol for 3–4 h in an argon atmosphere. The water-soluble azomethines (**IIIa–IIIx, IVa–IVn**) were obtained in preparative yield of 70–82%.

The azomethines **IIIa–IIIx, IVa–IVn** are colorless or slightly colored unstable hygroscopic crystalline substances, well soluble in methanol, ethanol, and water and insoluble in diethyl ether, chloroform, and hydrocarbons. The structure of azomethines **IIIa–IIIx, IVa–IVn** was proved by IR, UV, and ^{1}H NMR spectra and by the elemental analysis (see the table). The purity of the compounds, according to the ^{1}H NMR spectroscopy, was 90±2% (because of their high water absorption and the propensity to tarring in contact with atmospheric oxygen we were not able to obtain these compounds in a pure form).

In the IR spectra of azomethines **IIIa–IIIx, IVa–IVn** the following characteristic absorption bands were observed (ν, cm^{-1}): OH 3550–3050; CH_{arom} 3080–3005, 870–620; CH_{aliph} 2990 – 2830; C=O ester 1770–1740 (**IIIe–IIIx, IVc–IVn, VIa, VIb**); C=N 1640–1637; $C{=}C_{arom}$ 1607–1420; CO 1270–1030. The presence of the NO_2 group in compound **IIIs** was confirmed by the characteristic absorption bands at 1531 and 1348 cm^{-1}. In the IR spectra of the carborane-containing azomethines **IIIw, IIIx, IVm,** and **IVn** there are absorption bands CH_{carbor} 3070 (**IIIw, IVo**) and 3033 (**IIIx, IVn**) and BH 2680–2655 cm^{-1}.

In the UV spectra of compounds **IIIe–IIIx, IVc–IVn** there are the characteristic absorption maxima, λ_{max}, nm (ε): 208 (14000), 220 (13000), 255 (10000), 300 (400), due to the presence in the molecules of 4-acyloxy-3-alkoxybenzylidenamine fragments.

In the ^1H NMR spectra of azomethines **IIIa–IIIx, IVa–IVn** the signals of the protons of glucosamine fragment are multiplets at 3.10–3.80 ppm. In the ^1H NMR spectra of azomethines **IIIb–IIIx, IVb, VIa** the signals of MeO group protons appear as singlets in the region of 3.75–3.85 ppm. In the spectra of compound **IVa–IVn, VIb** the signals of EtO group protons appear in the form of a triplet at 0.90–1.30 ppm (Me) and a quartet at 3.80–4.20 ppm (CH_2). The signals of aromatic protons in compounds **IIIa–IIIx, IVa–IVn, V, VIa, VIb** are in the range of 6.80–8.00 ppm, the signals of the protons of azomethine group (HC=N) appear as a singlet at 8.10–8.20 ppm, which is typical for azomethines of (*E*)-configuration [2].

In the IR, UV and ^1H NMR spectra of azomethines **IIIa–IIIx, IVa–IVn** there are the absorption bands and signals of protons confirming existence of the structural fragments of ester groups [3].

EXPERIMENTAL

The IR spectra of compounds were recorded on a Fourier-transform IR spectrophotometer Protege-460 of Nicolet from thin layers or KBr pellets, UV spectra were taken on a Specord UV Vis instrument from 1×10^{-4} M solutions of compounds in methanol, ^1H NMR spectra were registered on a spectrometer Tesla BS-587A (100 MHz) from 5% solutions in water-d_2 or dimethylsulfoxide-d_6, chemical shifts were determined relative to the internal reference TMS. Elemental analysis was made on the a Vario EL-**III** Elementar C,H,N,O,S-analyzer, error of determination was 0.1%.

Esters of vanillin and vanillal (**I**) were obtained along the methods [4–9].

The initial D-(+)-glucosamine hydrochloride (**II**) was of “chemically pure” grade, purity 99%, mp 190°C (decomp.), $[\alpha]_D^{20} = +72°$.

Water-soluble azomethines (IIIa–IIIx, IVa–IVn). A mixture of 5 mmol of a benzaldehyde derivative of vanillin series **I**, D-(+)-glucosamine hydrochloride **II**, and 5 mmol of potassium hydrogen carbonate in 40 ml of anhydrous methanol was refluxed for 3–4 h under an argon atmosphere. A hot solution was filtered through a plaited paper filter to remove KCl, the solvent was then removed in a vacuum. Azomethines **IIIa–IIIx, IVa–IVn** were purified by dissolving in 10 ml of anhydrous methanol and precipitating by adding 20 ml of ether, the precipitated azomethine was rapidly filtered through a porous glass filter and dried in a vacuum.

REFERENCES

1. Sharnina, F.F., Ivashina, T.N., and Ivashin, V.P., *Struktura i dinamika molekulyarnykh sistem* (Structure and Dynamics of Molecular Systems), Ioshkar-Ola, Ufa, Kazan, Moscow, 2003, no. 10, part 2, p. 274.
2. Daier, D.R., *Prilozheniya absorbtsionnoi spektroskopii organicheskikh soedinenii* (Applications of Absorption Spectroscopy of Organic Compounds), Moscow: Khimiya, 1970, p. 92.
3. Dikusar, E.A., Kozlov, N.G., Tlegenov, R.T., and Uteniyazov, K.U., *Azometiny na osnove vanilina i vanilalya* (Azomethines Based on Vanillin and Vanillal), Nukus: Karakalpakstan, 2007.
4. Dikusar, E.A., Vyglazov, O.G., Moiseichuk, K.L., Zhukovskaya, N.A., and Kozlov, N.G., *Zh. Prikl. Khim.,* 2005, vol. 78, no. 1, p. 122.
5. Dikusar, E.A. and Kozlov, N.G., *Khim. Prirod. Soedin*., 2005, no. 1, p. 74.
6. Dikusar, E.A. and Kozlov, N.G., *Zh. Org. Khim*., 2005, vol. 41, no. 7, p. 1015.
7. Dikusar, E.A., *Zh. Prikl. Khim*., 2006, vol. 79, no. 6, p. 1043.
8. Dikusar, E.A., Kozlov, N.G., Potkin, V.I., Zvereva, T.D., Yuvchenko, A.P., Bei, M.P., and Kovganko, N.V., *Khim. Prirod. Soedim.,* 2006, no. 5, p. 434.
9. Dikusar, E.A., Potkin, V.I., Kozlov, N.G., Yuvchenko, A.P., Bei, M.P., and Kovganko, N.V., *Zh. Org. Khim*., 2008, vol. 44, no. 9, p. 1321.