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Azomethines on the Basis of Sodium Salts of Valine and Leucine

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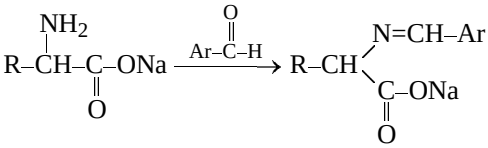
Abstract — Sodium salts of valine and leucine [$RCH(NH_2)COONa$, R = $(CH_3)_2CH$, $(CH_3)_2CHCH_2$] were reacted with benzaldehyde and its derivatives to obtain azomethines $RCH(COONa)N{=}CHAr$ (Ar = C_6H_5, 2-ClC_6H_4, 4-ClC_6H_4, 2-HOC_6H_4, 4-HOC_6H_4). The structure of the products was proved by IR and ^1H NMR spectroscopy, mass spectrometry, and elemental analysis.

Amino acids and their derivatives exhibit a well-pronounced physiological activity and enter in the composition of a series of medicinal drugs and biostimulants [1–3]. Therefore, we considered it topical to synthesize novel organic derivatives of amino acids and to study their biological activity. Schiff bases are widely used in organic synthesis [4, 5]. However, azomethines derived from amino acids and their synthetic applications have poorly been explored. In the present work we report on the synthesis of azomethines on the basis of sodium salts of valine and leucine.

It was found that both valine and leucine fail to react with benzaldehyde in absolute methanol at room temperature. Stirring of the reaction mixtures for 5 days, too, gave no Schiff bases. At the same time, azomethines readily formed in mild conditions on addition to solutions of sodium salts of valine or leucine in absolute methanol of benzaldehyde or its derivatives.



Ia, Ib **II–XI**

R = $(CH_3)_2CH$ (**Ia**); Ar = C_6H_5 (**II**), 2-ClC_6H_4 (**III**), 4-ClC_6H_4 (**IV**), 2-HOC_6H_4 (**V**), 4-HOC_6H_4 (**VI**); R = $(CH_3)_2CHCH_2$ (**Ib**); Ar = C_6H_5 (**VII**), 2-ClC_6H_4 (**VIII**), 4-ClC_6H_4 (**IX**), 2-HOC_6H_4 (**X**), 4-HOC_6H_4 (**XI**).

The synthesized compounds are solids soluble in methanol, ethanol, and water and poorly soluble in ordinary organic solvents. Their physicochemical characteristics are listed in Table 1.

Table 1. Physicochemical and spectral characteristics of Schiff bases

Comp. no.	Yield, %	mp, °C	IR spectrum, ν, cm^{-1}		Found, %			Formula	Calculated, %		
			C=O	C=N	C	H	N		C	H	N
II	89	278–280	1597	1642	63.69	6.41	5.93	$C_{12}H_{14}NNaO_2$	63.43	6.21	6.16
III	91	260–262	1592	1633	55.24	5.28	5.14	$C_{12}H_{13}ClNNaO_2$	55.08	5.01	5.35
IV	90	268–270	1596	1639	55.27	5.31	5.06	$C_{12}H_{13}ClNNaO_2$	55.08	5.01	5.35
V	85	230–233	1604	1635	59.50	6.01	5.55	$C_{12}H_{14}NNaO_3$	59.26	5.80	5.76
VI	83	[a]	1577	1642	59.43	6.07	5.48	$C_{12}H_{14}NNaO_3$	59.26	5.80	5.76
VII	90	276–278	1592	1642	65.01	6.93	5.66	$C_{13}H_{16}NNaO_2$	64.72	6.68	5.81
VIII	90	253–255	1592	1633	56.98	5.71	4.87	$C_{13}H_{15}ClNNaO_2$	56.63	5.48	5.08
IX	92	264–266	1594	1643	56.81	5.52	4.76	$C_{13}H_{15}ClNNaO_2$	56.63	5.48	5.08
X	87	166–168	1609	1636	60.87	6.38	5.31	$C_{13}H_{16}NNaO_3$	60.69	6.29	5.45
XI	84	[a]	1581	1643	60.75	6.44	5.52	$C_{13}H_{16}NNaO_3$	60.69	6.29	5.45

[a] Decomposes.

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Table 2. ^{1}H NMR spectra of valine derivatives, δ, ppm

Comp. no.	CH_3	$(CH_3)_2CH$	NaOOCCH	ArC*H*	Ar
Ia	0.85 d (3H, *J* 7 Hz), 0.96 d (3H, *J* 7 Hz)	1.92–2.03 m (1H)	3.04 d (1H, *J* 4.8 Hz)	–	–
II	0.88 d (3H, *J* 6.7 Hz), 0.99 d (3H, *J* 6.7 Hz)	2.11–2.49 m (1H)	3.46 d (1H, *J* 8 Hz)	8.26 s (1H)	7.37–7.44 m (3H), 7.75–7.84 m (2H)
III	0.89 d (3H, *J* 6.8 Hz), 0.99 d (3H, *J* 6.7 Hz)	2.15–2.50 m (1H)	3.53 d (1H, *J* 7.6 Hz)	8.65 s (1H)	7.27–7.41 m (3H), 8.03–8.13 m (1H)
IV	0.87 d (3H, *J* 6.7 Hz), 1.03 d (3H, *J* 6.4 Hz)	2.11–2.50 m (1H)	3.47 d (1H, *J* 7.7 Hz)	8.23 s (1H)	7.40 d (2H, *J* 8.4 Hz), 7.79 d (2H, *J* 8.5 Hz)
V	0.97 d (3H, *J* 6.7 Hz), 0.99 d (3H, *J* 6.9 Hz)	2.12–2.50 m (1H)	3.69 d (1H, *J* 5.9 Hz)	8.31 s (1H)	6.69–6.83 m (2H), 7.21–7.35 m (2H)
VI	0.89 d (3H, *J* 6.7 Hz), 0.99 d (3H, *J* 6.7 Hz)	2.14–2.48 m (1H)	3.49 d (1H, *J* 7.7 Hz)	8.10 s (1H)	6.72 d (2H, *J* 8.7 Hz), 7.66 d (2H, *J* 8.8 Hz)

Table 3. ^{1}H NMR spectra of leucine derivatives, δ, ppm

Comp. no.	CH_3	$(CH_3)_2CHCH_2$	NaOOCC*H*	C*H*Ar	Ar
Ib	0.92 d (3H, *J* 6.2 Hz), 0.94 d (3H, *J* 6.3 Hz)	1.25–1.90 m (3H)	3.21 t (1H, *J* 5.2 Hz)	–	–
VII	0.91 d (3H, *J* 6.1 Hz), 0.94 d (3H, *J* 6.3 Hz)	1.25–1.93 m (3H)	3.95 t (1H, *J* 7.1 Hz)	8.30 s (1H)	7.38–7.44 m (3H), 7.75–7.84 m (2H)
VIII	0.92 d (3H, *J* 6.2 Hz), 0.94 d (3H, *J* 6.3 Hz)	1.47–1.91 m (3H)	4.00 t (1H, *J* 7 Hz)	8.70 s (1H)	7.28–7.42 m (3H), 8.03–8.13 m (1H)
IX	0.90 d (3H, *J* 6.2 Hz), 0.93 d (3H, *J* 6.3 Hz)	1.25–1.90 m (3H)	3.95 t (1H, *J* 7 Hz)	8.28 s (1H)	7.40 d (2H, *J* 8.8 Hz), 7.78 d (2H, *J* 8.6 Hz)
X	0.92 d (3H, *J* 6.2 Hz), 0.96 d (3H, *J* 6.1 Hz)	1.45–1.91 m (3H)	4.02 t (1H, *J* 7 Hz)	8.37 s (1H)	6.71–6.83 m (2H), 7.21–7.35 m (2H)
XI	0.92 d (3H, *J* 6.0 Hz), 0.94 d (3H, *J* 6.1 Hz)	1.35–1.90 m (3H)	3.95 t (1H, *J* 7 Hz)	8.12 s (1H)	6.72 d (2H, *J* 8.7 Hz), 7.64 d (2H, *J* 8.7 Hz)

The structure of the products was proved by ^{1}H NMR (Tables 2 and 3) and IR spectroscopy, mass spectrometry, and elemental analysis. The IR spectra contain, along with absorption bands typical of alkyl, aryl, and carboxy groups, absorption bands at 1630–1645 cm^{-1}, characteristic of C=N vibrations [6, 7].

The mass spectra all lack molecular ion peaks. The most abundant peaks in all the spectra belong to $RCH(CO)CN^+$, $RCHCO^+$, $NCHAr^+$, $CHAr^+$, and Ar^+ ions, where R = $(CH_3)_2CH$, $(CH_3)_2CHCH_2$ and Ar = C_6H_5, 2(4)-ClC_6H_4, 2(4)-HOC_6H_4.

EXPERIMENTAL

The IR spectra were recorded on a Protege-460 Fourier spectrophotometer in KBr. The ^{1}H NMR spectra were obtained on a Tesla BS-567A spectra for deuterometanol solutions, reference TMS. The mass spectra were measured on an MKh-1320 instrument, ionizing energy 35 eV.

Sodium salt of valine (Ia). Metallic sodium, 0.23 g, was added to 50 ml of anhydrous methanol. After all sodium had dissolved, the solution was cooled to room temperature, and a solution of 1.17 g of valine in 50 ml of methanol was added to it. The reaction mixture was stirred for 6 h, filtered, and concentrated in a vacuum. Ether, 100 ml, was added, and the precipitate that formed was filtered off, washed with ether, and dried in a vacuum. Reprecipitation from methanol gave 1.25 g (90%) of compound **Ia**, mp 228–230°C. Found, %: C 43.31; H 7.45; N 9.98. $C_5H_{10}NNaO_2$. Calculated,%: C 43.17; H 7.24; N 10.07.

Sodium salt of leucine (**Ib**) was prepared similarly from 1.31 g of leucine and 0.23 g of metallic sodium. Yield 1.36 g (89%), mp 172–174°C. Found, %: C 47.17; H 8.01; N 9.03. $C_6H_{12}NNaO_2$. Calculated, %: C 47.05; H 7.90; N 9.15.

Synthesis of azomethines *(general procedure).* A solution of 2.2 mmol of aldehyde to 20 ml of methanol was added to a solution of 2 mmol of salt **Ia** or **Ib** in 30 ml of absolute methanol. The reaction mixture was stirred at room temperature for 48 h, filtered, concentrated in a vacuum until precipitation began, and treated with 100 ml of anhydrous ether. The precipitate that formed was filtered off, washed with ether, dried in a vacuum, and purified by reprecipitation from methanol.

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