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INTERACTION OF AMINOQUINOLINES WITH UNSATURATED CARBOXYLIC ACIDS

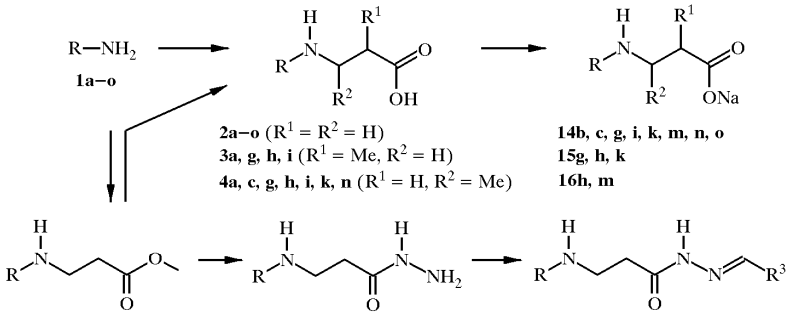
1. SYNTHESIS OF N-QUINOLYL-β-ALANINES AND THEIR BIOLOGICAL ACTIVITY

N-Quinolyl-β-alanines, α-methyl- and β-methyl-N-quinolyl-β-alanines were prepared by reaction of aminoquinolines and acrylic, methacrylic and crotonic acids. The corresponding hydrazides and benzylidenehydrazides were obtained. 4-Aminoquinoline with unsaturated acids in water gave betaines. Biological activity of sodium salts of β-alanines were investigated.

Keywords: aminoquinolines, N-quinolyl-β–alanines, hydrazides, biological activity.

For the first time N-quinolyl-β-aminopropionic acid was synthesized by heating 4,7-dichloroquinoline with β-alanine [1]. In search for the potential anti-cancer agents N-(6-methoxy-8-quinolyl)-β-alanine [2] was obtained by interaction of 6-methoxy-8-aminoquinolines with 3-propanolide. All possible non-substituted N-quinolyl-β-alanines were obtained [3] by hydrolysis of the corresponding esters, which were synthesized from 3-, 4-, 5-, 6-, 7-, or 8-amino-quinolines and methyl acrylate. Interaction of aminoquinolines with acrylic acid and its homologues has not been investigated so far to the best of our knowledge.

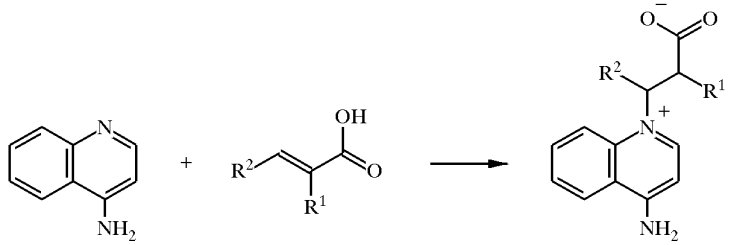
Starting from aminoquinolines **1** and acrylic, methacrylic and crotonic acids in refluxing toluene, N-quinolyl-β-alanines **2** and their methyl homologues **3** and **4** were prepared. Compounds **2–4** were extracted from the reaction mixtures with 10% aqueous solution of NaOH and isolated after acidification of the extracts with acetic acid. It should be noted that the yields of β-alanines **2** were much higher (~80%) than those of their methyl homologues **3** and **4**.



a R = 3-C_9H_6N; **b** R = 4-C_9H_6N; **c** R = 5-C_9H_6N; **d** R = 2-Me-5-C_9H_5N; **e** R = 4,6-Me_2-5-C_9H_4N; **f** R = 8-Cl-5-C_9H_5N; **g** R = 6-C_9H_6N; **h** R = 2-Me-6-C_9H_5N; **i** R = 8-C_9H_6N; **k** R = 2-Me-8-C_9H_5N; **l** R = 4-Me-8-C_9H_5N; **m** R = 5-MeO-8-C_9H_5N; **n** R = 5-Br-8-C_9H_5N; **o** R = 5-Cl-8-C_9H_5N

N-Quinolyl-β-alanines **2f,h,k,n,o** were obtained by hydrolysis of the corresponding methyl esters of N-quinolyl-β-alanines **5**, which were synthesized from aminoquinolines **1** and methyl acrylate in refluxing acetic acid. Esters **5** were extracted from the reaction mixture.

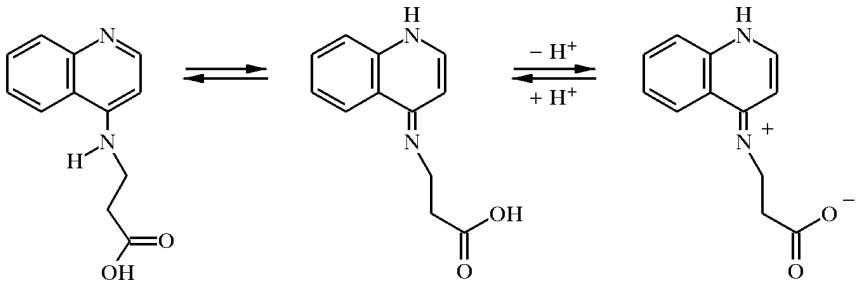
On the contrary to the other aminoquinolines, 4-aminoquinoline with acrylic, methacrylic, and crotonic acids in water gave 4-amino-1-(2-carboxylatoethyl)quinolinium betaine **6** and its homologues **7** and **8**. Reaction of 4-aminoquinoline **1b** with methyl acrylate afforded ester **5** [3].



6b $R^1 = R^2 = H$
7b $R^1 = Me$, $R^2 = H$
8b $R^1 = H$, $R^2 = Me$

The structures of the synthesized N-quinolyl-β-alanines **2–4** were confirmed using H^1 NMR spectroscopy. The characteristic triplets due to the α- and β-CH_2 groups of β-alanines **2** were located at 2.56–2.72 and 3.42–3.80 ppm. Signals of the methyl groups of β-alanines **3** and **4** were observed as doublets at 1.03–1.25 ppm, and the multiplets of the methyne groups were at 2.65–3.05 and 3.50–4.30 ppm respectively. The characteristic signals of methyne and methylene groups in ^1H NMR spectra of betaines **6–8** were shifted to the lower field in comparison with the signals of the corresponding groups of β-alanines **2–4**.

The IR absorptions at 1400 and 1000 cm^{-1} in betaines **6–8** correspond to carboxylate ion. The same absorption observed in the spectrum of β-alanine **2b** could be explained by dissociation with the formation of carboxylate ion.



The maxima at 216, 232, 329 and 340 nm were observed in the UV spectrum of N-(4-quinolyl)-β-alanine (**2b**) and the ones at 217, 240 and 330 nm were seen for betaines **6–8**. The UV spectra of 4-aminoquinoline derivatives **2b**, **5b**, as well as that of 4-aminoquinoline differed from the spectra of the other aminoquinoline derivatives due to the absence of maxima with longer wavelengths.

The characteristic IR absorptions of NH group of β-alanines **2a-i** were observed at 3450–3150 cm^{-1}, and valence =C–H vibrations of quinoline gave signals at 3100–3000 cm^{-1}. Absorption signals at 3020–2800 cm^{-1} were due to C-H and CH_2 groups valence and deformation vibrations. Absorption peaks at 1730–1680 cm^{-1} could be ascribed to C=O group and they overlap the signals of C=C valence vibrations at 1600 cm^{-1} of quinoline.

Under the mild conditions in refluxing ethanol methyl esters **5** as well as β-alanines **2–4** gave hydrazides **9**. Some of them were transformed to benzylidenehydrazides **10–13** on the treatment with benzaldehyde or its derivatives. The ^{1}H NMR spectra of hydrazides **9–11** showed the signals of the hydrazine group protons consisting of amino group signal at 3.92–4.63 ppm and that of imino group at 8.93–9.19 ppm. The absence of amino group signals of hydrazine fragment and the presence of methyne group signals seen at 2.93–3.12 ppm proved the structure of benzylidenehydrazides. Imine group signals were shifted to the lower field and were situated at 10.90–11.72 ppm.

The sodium salts **14**–**16** of the synthesized β-alanines, which are insoluble in water, were prepared for the investigation of their biological activity. The sodium salts of β-alanines added to the nutrient medium of simian kidney cells stimulated cells proliferation (Table 1). Biological activity of these compounds was stipulated by their heterocyclic structure and substituents in aliphatic side chain. The 8-aminoquinoline derivatives were more active in low concentrations than 6-aminoquinoline derivatives [4]. N-(2-Methyl-8-quinolyl)-β-alanine hydrochloride distinguished itself as the most effective compound in $1\cdot10^{-4}$ % concentration. The sodium salt of N-(4-quinolyl)-β-alanine **14b** in $1\cdot10^{-3}$% concentration stimulated proliferation of transplantable diploidic cells of skin and muscular tissues of human embrio by 125%, whereas hydrazide **9b** inhibited their proliferation.

Table 1

The influence of the sodium salts 14–16 on proliferation of isolated simian kidney cells, 4647 line, in Igla MEM nutrient medium with 5% of cattle blood serum

Com-pound	Relative medium yield of cells in comparison with the control (concentration, %)						
	$1\cdot10^{-1}$	$1\cdot10^{-2}$	$1\cdot10^{-3}$	$1\cdot10^{-4}$	$1\cdot10^{-5}$	$1\cdot10^{-6}$	$1\cdot10^{-7}$
14g	1.0	1.7	1.7	1.3	1.0	1.0	1.0
15g	0.8	1.0	2.2	1.6	1.2	1.2	1.0
14h	1.0	1.0	0.9	1.0	1.0	1.0	1.0
15h	1.3	1.0	1.1	0.8	1.0	1.0	1.0
16h	1.2	1.8	2.4	2.1	2.0	1.8	1.7
14i	0.8	1.0	1.0	1.4	1.6	1.8	2.2
14k	1.3	1.9	2.0	3.4	2.1	1.6	1.4
16k		0.8	1.2	1.0	1.0	1.0	
14m	1.0	1.3	1.3	1.4	1.5	1.5	1.3
14n	0.2	1.2	1.8	1.8	1.2	1.0	1.0
14o	0.2	1.0	1.4	1.7	1.3	1.0	1.0

Table 2

Characteristics of compounds 2–12

Compound	Molecular formula	M.p., °C solvent	^{1}H NMR spectra, chemical shifts, δ/ppm*, *J*, Hz	Yield, %
1	2	3	4	5
2a	$C_{12}H_{12}N_2O_2$	190 ethanol	2.65 (t ,CH_2CO); 3.46 (t, NCH_2); 6.50–8.71 (m, 6H, arom.)	50
2b	$C_{12}H_{12}N_2O_2$	260–260.5 ethanol	2.63 (t , CH_2CO); 3.60 (t, NCH_2); 6.25–8.65 (m ,6H, arom.)	74
2c	$C_{12}H_{12}N_2O_2$	194.5–195 ethanol	2.64 (t, CH_2CO); 3.46 (t , NCH_2); 6.50–8.88 (m, 6H, arom.)	39
2d	$C_{13}H_{14}N_2O_2$	144–145 2-propanol	2.60 (s, CH_3); 2.69 (t , CH_2CO); 3.48 (t, NCH_2); 6.38–8.38 (m ,5H, arom.)	43
2e	$C_{14}H_{16}N_2O_2$	199.5–200.5 2-propanol	2.56 (s, 4-CH_3); 2.96–3.29 (m, 6-CH_3, CH_2CO); 3.64 (m, NCH_2); 7.54–8.75 (m, 4H, arom.)	21
2f	$C_{12}H_{11}N_2O_2Cl$	209.5–210.5 ethanol	2.74 (t, CH_2CO); 3.51 (t, NCH_2); 6.38–9.08 (m, 5H, arom.)	48
2g	$C_{12}H_{12}N_2O_2$	210.5–211 1,4-dioxane	2.44 (t, CH_2CO); 3.88 (t, NCH_2); 7.68–9.00 (m, 5H, arom.)	77
2h	$C_{13}H_{14}N_2O_2$	184–185 ethanol	2.74 (s, CH_3); 2.57–3.25 (m, CH_2CO); 3.74 (t, NCH_2); 7.53–8.85 (m, 5H, arom.)	74
2i	$C_{12}H_{12}N_2O_2$	147.2–148 benzene	2.68 (t, CH_2CO); 3.54 (t, NCH_2); 6.60–8.72 (m, 6H, arom.); 10.30 (s, NH)	67
2k	$C_{13}H_{14}N_2O_2$ ·HCl	207.5–209 ethanol–ether	2.62–3.00 (m, CH_2CO); 2.78 (s, 2-CH_3); 3.50–3.75 (m, NH_2); 7.36–8.58(m, 5H, arom.)	27
2l	$C_{13}H_{14}N_2O_2$	158–159 2-propanol	2.58 (s, CH_3); 2.62 (t, CH_2CO); 3.50 (t, NCH_2); 6.63–8.63 (m, 5H, arom.); 9.33 (s, NH)	78
2m	$C_{13}H_{14}N_2O_3$	166–167 ethanol	2.89 (t, CH_2CO); 3.79 (t, NCH_2); 3.94 (s, CH_3O); 6.94–9.38 (m, 5H, arom.)	78
2n	$C_{12}H_{11}N_2O_2Br$	225 (dec) ethanol	2.65 (t, CH_2CO); 3.42 (t, NCH_2); 7.12–9.14 (m, 5H, arom.)	85
2o	$C_{12}H_{11}N_2O_2Cl$	124.5–125.5 2-propanol	2.68 (t, CH_2CO); 3.46 (t, NCH_2); 7.25–9.14 (m, 5H, arom.)	68
3a	$C_{13}H_{14}N_2O_2$	212–213 ethanol	1.01 (d, J = 7, CH_3); 2.55–2.97 (m, CH); 3.13–3.53 (m, CH_2); 7.05–8.53 (m, 6H, arom.)	14
3g	$C_{13}H_{14}N_2O_2$	148.5–150 ethanol	1.03 (d, J = 6, CH_3); 2.70–3.05 (m, CH); 3.43–3.60 (m, CH_2); 7.63–9.00 (m, 6H, arom.)	32
3h	$C_{14}H_{16}N_2O_2$	180–181 ethanol	1.08 (d, J = 6, CH_3); 2.75 (s, 2-CH_3); 2.88–3.18 (m, CH); 3.50–3.78 (m, CH_2); 7.59–8.78 (m, 5H, arom.)	53
3i	$C_{13}H_{14}N_2O_2$	110–111 2-propanol	1.14 (d, J = 7, CH_3); 2.65–2.98 (m, CH); 3.28–3.58 (m, CH_2); 6.45–6.63 (m, NH); 6.65–8.75 (m, 6H, arom.)	16

T a b l e 2 (continued)

1	2	3	4	5
4a	$C_{13}H_{14}N_2O_2$	193–194 ethanol	1.25 (d, J = 7, CH_3); 2.57 (d, J = 6, CH_3); 3.75–4.15 (m, CH); 6.85–8.07 (m, 6H, arom.); 8.45 (s, 1H, NH)	32
4c	$C_{13}H_{14}N_2O_2$	201–202 1,4-dioxane	1.12 (d, J = 5, CH_3); 2.90 (d, J = 6, CH_2CO); 3.80–4.25 (m, CH); 7.65–9.45 (m, 5H, arom.)	26
4g	$C_{13}H_{14}N_2O_2$	160–161 ethanol	1.25 (d, J = 6, CH_3); 2.83 (d, J = 5, CH_3); 3.93–4.35 (m, CH); 7.71–9.14 (m, 6H, arom.)	42
4h	$C_{14}H_{16}N_2O_2$	183–184 ethanol	1.18 (d, J = 6, CH_3); 2.55–3.12 (m, CH_2); 2.75 (s, 2-CH_3); 3.88–4.25 (m, CH); 7.59–8.85 (m, 5H, arom.)	73
4i	$C_{13}H_{14}N_2O_2$	113–114 ethanol	1.15 (d, J = 7, CH_3); 2.80 (m, CH_2); 3.22–3.55 (m, CH); 6.43–8.70 (m, 7H, NH, arom.)	11
4l	$C_{14}H_{16}N_2O_2$	107–108 ethanol	1.34 (d, J = 6.2, CH_3); 2.41 and 2.83 (J_{AB} =15, J_{AX} = 6, J_{BX} = 5, CH_2); 2.53 (s, 4-CH_3); 3.90–4.30 (m, CH); 6.60–8.55 (m, 5H, arom.), 8.55–9.18 (m, NH)	29
4o	$C_{13}H_{13}N_2O_2Cl$	122–123 2-propanol	1.04 (d, J = 6, CH_3); 2.61 (d, CH_2); 3.49–3.91 (m, CH); 7.24–9.20 (m, 5H, NH, arom.)	36
5d	$C_{14}H_{16}N_2O_2$	84–85 ether–hexane	2.64 (s, CH_3); 2.72 (t, J = 6, CH_2CO), 3.65 (s, CH_3); 4.59–4.93 (m, NH); 6.40–8.03 (m, 5H, arom.)	30
5f	$C_{13}H_{13}N_2O_2Cl$	113–113.5 hexane	2.65 (t, J = 6, CH_2CO), 3.45 (t, J = 6, NCH_2); 3.65 (s, CH_3); 5.30 (s, NH); 6.35–8.91 (m, 5H, arom.)	30
5h	$C_{14}H_{16}N_2O_2$	95–96 ether	2.25–2.80 (m, CH_2CO); 2.51 (s, CH_3); 3.55 (s, CH_3O); 3.82–4.66 (m, NCH_2); 6.50–7.90 (m, 5H, arom.)	67
5i	$C_{14}H_{16}N_2O_2$	56–56.5 petrolether	2.50 (s, 2-CH_3); 2.53 (t, J = 7, CH_2CO); 3.46 (t, J = 7, CH_2); 3.50 (s, CH_3O); 6.35–7.78 (m, 5H, arom.)	40
5n	$C_{13}H_{13}N_2O_2Br$	45–46 ether–hexane	2.61(t, J = 6, CH_2CO), 3.50 (t, J = 6, CH_2); 3.63 (s, CH_3O); 6.34–8.60 (m, 5H, arom.)	37
5o	$C_{13}H_{13}N_2O_2Cl$	99.5–101 hexane	2.13 (s, CH_3O); 3.05 (t, J = 5, CH_2CO); 3.58 (t, J = 6, CH_2); 7.33–9.35 (m, 5H, arom.)	21
6b	$C_{12}H_{12}N_2O_2$	233–234 ethanol	2.89 (s, CH_2CO), 4.63 (s, NCH_2); 6.45–8.19 (m, 6H, arom.)	62
7b	$C_{13}H_{14}N_2O_2$	190–191 ethanol	1.06 (d, J = 6, CH_3); 2.80–3.23 (m, CH); 4.10–4.80 (m, CH_2); 6.43–8.18 (m, 6H, arom.)	26
8b	$C_{13}H_{14}N_2O_2$	173.5–174 ethanol	1.39 (d, J = 7, CH_3), 2.84 (d, J = 6, CH_2); 5.19–5.54 (m, CH); 6.50–8.05 (m, 6H, arom.)	55
9b	$C_{12}H_{14}N_4O$	180–181 ethanol–ether	2.70–3.00 (m, CH_2CO); 3.10–3.38 (s, NH_2); 3.46–3.78 (m, NCH_2); 6.43–8.53 (m, 7H, NH, arom.); 9.50–9.98 (s, CONH)	45
9d	$C_{13}H_{16}N_4O$	99.5–101 ethanol–ether	2.46 (t, J = 7, CH_2CO), 2.58 (s, CH_3); 3.20–3.60 (m, NCH_2); 3.92 (s, NH_2); 6.34 (t, J = 7, NH); 6.40–8.48 (m, 5H, arom.); 9.06 (s, CONH)	87

T a b l e 2 (continued)

1	2	3	4	5
9f	$C_{12}H_{14}N_4OCl$	189–189.5 ethanol–ether	2.43 (t, *J* = 7.5, CH_2CO), 3.25–3.59 (m, NCH_2); 4.00–4.42 (m, NH_2); 6.48–8.99 (m, 6H, NH, arom.); 9.07 (s, CONH)	69
9g	$C_{12}H_{14}N_4O$	177–178 ethanol	2.38 (t, *J* = 7.2, CH_2CO), 3.18–3.58 (m, NCH_2); 4.22 (s, NH_2); 6.14 (t, *J* = 6, NH); 6.62–8.50 (m, 6H, arom.); 9.03 (s, CONH)	90
9h	$C_{13}H_{16}N_4O$	171–172 2-propanol	2.40 (t, *J* = 7, CH_2CO); 2.51 (s, CH_3); 3.18–3.52 (m, CH_2); 4.00–4.63 (s, NH_2); 5.82–6.15 (s, NH); 6.58–7.95 (m, 5H, arom.); 8.93–9.10 (s, CONH)	79
9k	$C_{13}H_{16}N_4O$	103–104 ethanol	2.40 (t, *J* = 6.8, CH_2CO); 2.58 (s, CH_3); 3.25–3.63 (m, NCH_2); 3.93–4.38 (s, NH_2); 6.33–6.53 (s, NH); 6.58–8.13 (m, 5H, arom.); 9. 07 (s, CONH)	72
10a	$C_{21}H_{23}N_5O$	198–199 ethanol	2.58–2.78 (m, CH_2CO), 2.94 (s, $N(CH_3)_2$); 3.10–3.25 (m, CH); 3.48–3.75 (m, NCH_2); 6.45–8.52 (m, 11H, NH, arom.); 11.30 (d, *J* = 6, CONH)	88
11d	$C_{22}H_{25}N_5O$	162–163 ethanol	2.50–2.75 (m, CH_2CO), 2.55 (s, CH_3); 2.93 (d, *J* = 2, $N(CH_3)_2$); 3.02–3.20 (m, CH); 3.41–3.78 (m, CH_2); 6.38–8.18 (m, H, arom.); 11.05 (d, *J* = 6, CONH)	98
12g	$C_{19}H_{17}N_5O_3$	238–239 ethanol	2.62 (t, *J* = 7.8, CH_2CO); 3.09 (d, *J* = 6, CH); 3.28–3.68 (m, NCH_2); 6.28 (t, *J* = 6, NH); 6.68–8.58 (m, H, arom.); 11.61 (d, *J* = 5.5, CONH)	96
13g	$C_{19}H_{18}N_4O_2$	254.5–256 ethanol	2.55 (t, *J* = 6, CH_2CO); 2.92–3.12 (m, CH); 3.28–3.67 (m, NCH_2); 6.29 (t, *J* = 6, NH); 6.73–8.60 (m, 10H, arom.); 9.86 (s, OH); 11.20 (q, *J* = 4.2, CONH)	77

∗ DMSO-d_6 was used as a solvent for **2 a-d, f, i, l**, **4 a, i**, **9 a, d, f, g, h**, **10–13**, $CDCl_3$ for **4l, 5** and TFA for **2e, g, h, m, n, o**, **3a, g, h**, **4c, g, h, o** ^{1}H NMR spectra.

T a b l e 3

Melting points of the sodium salts of N-quinolyl-β-alanines 14–16

Com-pounds	Molecular formula	M.p., °C	Solvent
1	2	3	4
14b	$C_{12}H_{11}N_2O_2Na$	340 dec	Ethanol–ether
14c	$C_{12}H_{11}N_2O_2Na$	245 dec	Ethanol
14g	$C_{12}H_{11}N_2O_2Na$	302–303	Ethanol
14i	$C_{12}H_{11}N_2O_2Na$	198–200	Ethanol
14k	$C_{13}H_{13}N_2O_2Na·H_2O$	187.5–189	Ethanol
14m	$C_{13}H_{13}N_2O_3Na$	200.5–202	Ethanol

T a b l e 3 (continued)

1	2	3	4
14n	$C_{12}H_{10}N_2O_2BrNa$	228–229	Ethanol
14o	$C_{12}H_{10}N_2O_2ClNa$	220–221	2-Propanol–ether
15g	$C_{13}H_{13}N_2O_2Na$	271–272	Ethanol
15h	$C_{14}H_{15}N_2O_2Na$	277–278	Ethanol
15k	$C_{14}H_{15}N_2O_2Na$	206–207	Ethanol–ether
16h	$C_{14}H_{15}N_2O_2Na·H_2O$	162–164	Ethanol
16m	$C_{14}H_{15}N_2O_2Na·H_2O$	150.5–152	Ethanol

EXPERIMENTAL

The ^{1}H NMR spectra were recorded at 80 MHz on a Tesla BS 487 C spectrometer using tetramethylsilane (δ_H 0.0) as reference. UV spectra were recorded on a Specord UV-Vis in water. Concentration of the samples was about $4·10^{-5}$ mol/l. IR spectra were recorded on a spectrometer UR-20. Melting points were determined in open capillaries and are uncorrected. Elemental analysis data are in accordance with the calculated values. The data for the synthesized compounds are summarized in tables 2 and 3.

N-Quinolyl-β-alanines (2). The mixture of aminoquinoline **1** (0.1 mol), acrylic acid (7.9 g, 0.11 mol) and 40 ml of toluene was refluxed for 20 h. Aqueous solution of sodium hydroxide (50 ml, 10%) was added to the reaction mass and the mixture was heated for 20 min. After cooling the mixture was filtered. Toluene layer was separated and the aqueous solution was extracted with chloroform. Alkaline solution was acidified with acetic acid up to pH 5–6. The precipitated crystals of **1** were filtered off and washed with water (characteristics are given in Table 2).

α-Methyl-N-quinolyl-β-alanines (3a, g, h, i). The mixture of aminoquinoline **1** (40 mmol), methacrylic acid (4 ml, 46 mmol) and 10 ml of toluene was refluxed for 40 h. Solution of NaOH (20 ml, 10%) was added to the mixture and heated for 20 min. The isolation of the products **3a, g, h, i** was similar to that described above (see Table 2).

β-Methyl-N-quinolyl-β-alanines (4a, c, g, h, i, l, o) were synthesized as α-methyl-N-quinolyl-β-alanines **3a, g, h, j** from the corresponding aminoquinoline **1** and crotonic acid (Table 2).

N-Quinolyl-β-alanine methyl esters (5d, f, h, i, n, o). The mixture of aminoquinoline **1** (0.1 mol), 9.9 ml (0.11 mol) methyl acrylate (9.9 ml, 0.11 mol) and 0.5 ml of acetic acid was refluxed for 10–30 h. Liquid fraction was concentrated *in vacuo*. The residue was extracted with hexane or benzene, the product was isolated on evaporation of the extract.

4-Amino-1-(2-carboxylatoethyl)quinolinium betaine (6b). The mixture of 1.44 g (10 mmol) of aminoquinoline **1b** spectrum, c, acrylic acid (1 ml, 0.11 mmol) and 10 ml of water was refluxed for 2 h. After cooling the reaction mixture the formed crystals **6b** (1.33 g) were filtered off. IR cm^{-1}: 3200 (NH); 3020 (quinoline C–H); 1660 (C=O); 1400, 1050 (COO^-). UV spectrum, nm: λ_{max} = 217 (lgε = 5.49); 240 (lgε = 5.53); 331 (lgε = 5.39).

4-Amino-1-(2-carboxylatoethyl)quinolinium betaine hydrochloride (6b·HCl). M. p. 230 °C, methanol–ether. $C_{12}H_{12}N_2O_2·HCl$.

N-Quinolyl-β-alanine hydrazides (9b, d, f, g). β-Alanine methyl ester **5** (25 mmol) was dissolved in ethanol (20 ml), then 20 ml of hydrazine (50%) was added and the reaction mixture was left at 18–20 °C for a day. The precipitated crystals were filtered off and washed with ether.

N-(4-Quinolyl)-β-alanine 4-dimethylaminobenzylidenehydrazide (10b). Hydrazide **9b** (1.15 g, 5 mmol) was dissolved in ethanol (20 ml), then 4-dimethylaminobenzaldehyde (0.77 g, 5.5 mmol) was added and heated for 6 h at 80 °C. The reaction mixture was left for a day at 5 °C. The precipitated crystals were filtered off and washed with ether. Yield 1.9 g.

N-(2-Methyl-5-quinolyl)-β-alanine 4-dimethylaminobenzylidenehydrazide (11d). Hydrazide **11d** was synthesized as hydrazide **10b** from 0.73 g (3 mmol) of hydrazide **11d**. Yield 1.1 g.

N-(6-Quinolyl)-β-alanine 4-nitrobenzylidenehydrazide (12g) was synthesized as hydrazide **10b** by heating hydrazide **9g** (1.15 g, 5 mmol) with 4-nitrobenzaldehyde (0.79 g, 5.2 mmol) for 1 h. Yield 1.75 g.

N-(6-Quinolyl)-β-alanine 4-hydroxybenzylidenehydrazide (13g) was synthesized as hydrazide **9g** (1.15 g, 5 mmol) with 4-hydroxybenzaldehyde (0,64 g, 5,2 mmol) for 2h. Yield 1,28 g.

Sodium salts of N-quinolyl-β-alanine, α-methyl-N-quinolyl-β-alanine and β-methyl-N-quinolyl-β-alanine (14b, c, g, i, k, m, n, o, 15g, h, k, and 16h, m) were prepared from the corresponding β-alanines and equivalent amount of sodium hydroxyde in quantitative yield (Table 3).

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