ISSN 1070-3632, Russian Journal of General Chemistry, 2017, Vol. 87, No. 2, pp. 342–346. © Pleiades Publishing, Ltd., 2017.
Original Russian Text © G.A. Gevorgyan, G.Yu. Khachvankyan, A.G. Agababyan, N.Z. Akopyan, G.A. Panosyan, M.G. Malakyan, 2017, published in Zhurnal Obshchei Khimii, 2017, Vol. 87, No. 2, pp. 328–332.

LETTERS TO THE EDITOR

Synthesis of β-Amino Ketones Derived from Aminobenzoic Acids

G. A. Gevorgyan[a]*, G. Yu. Khachvankyan[a], A. G. Agababyan[a], N. Z. Akopyan[a], G. A. Panosyan[b], and M. G. Malakyan[c]

[a] *Mndzhoyan Institute of Fine Organic Chemistry, Scientific Technological Center of Organic and Pharmaceutical Chemistry, National Academy of Sciences of Armenia, ave. Azatutyan 26, Yerevan, 0014 Armenia*
**e-mail: gyulgev@gmail.com*

[b] *Molecular Structure Research Center, Scientific Technological Center of Organic and Pharmaceutical Chemistry, National Academy of Sciences of Armenia, ave. Azatutyan 26, Yerevan, 0014 Armenia*

[c] *Research Center of Radiation Medicine and Burns, Ministry of Health Protection of Armenia, Davtashen 25a, Yerevan, 0054 Armenia*

Received April 7, 2016

Abstract—Alkylation of aminobenzoic acids and their derivatives with 3-diethylamino-1-arylpropan-1-one hydrochlorides gave the corresponding β-aminopropiophenones some of which were tested for antioxidant activity.

Keywords: aminobenzoic acid, 3-(4-aminophenylcarboxamido)propanoic acid, β-aminopropiophenone, alkylation

DOI: 10.1134/S1070363217020311

p-Aminobenzoic acid and its derivatives attract particular interest due to broad spectrum of their biological activity and low toxicity. Compound based thereon occupy an important place among medicinal agents, specifically among local anesthetics; they enhance resistance to radiation sickness, protect from UV radiation, exhibit anticoagulant and antioxidant activity, and inhibit peroxide oxidation of retinal lipids [1–4]. The synthesis and biological activity of new functional derivatives of *p*-aminobenzoic acid have recently been reported [1, 4]. A large series of β-amino ketones with pronounced antidiabetic activity have been synthesized on the basis of the non-steroidal anti-inflammatory drug nabumetone and *p*-aminobenzoic acid [4]. Molecules of these compounds contained two aromatic rings and carboxy and amino groups. It is also known that derivatives 2-aminobenzoic (anthranilic) acid possess anti-inflammatory properties [3, 5, 6].

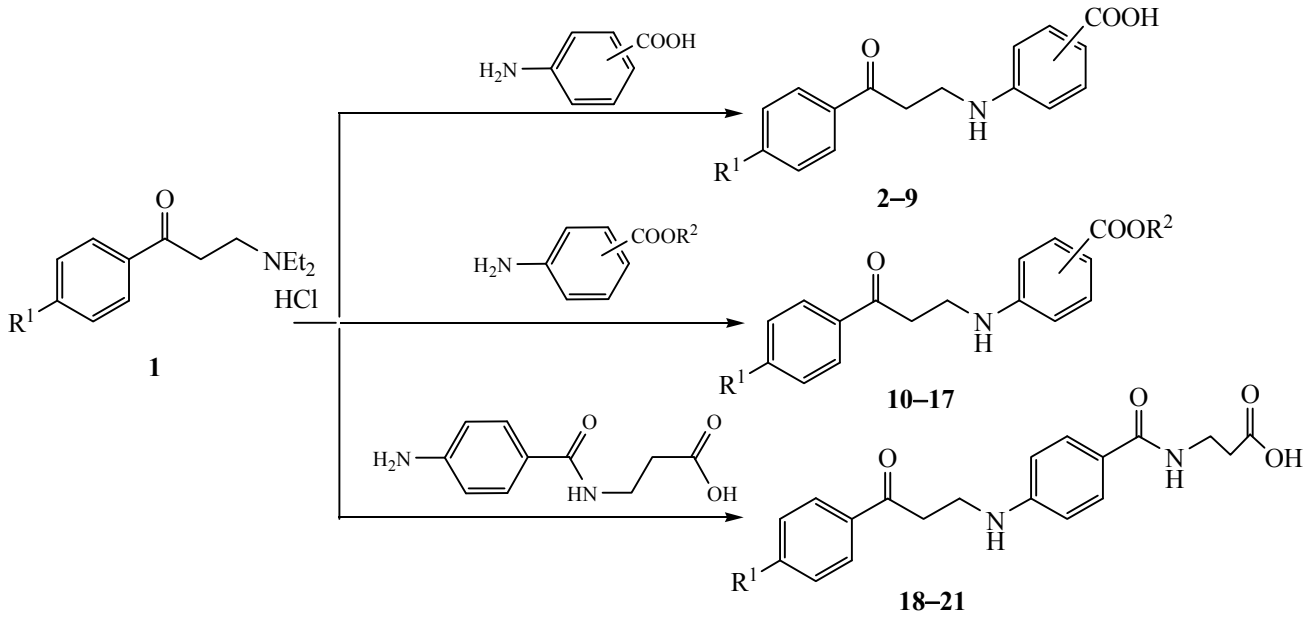
On the basis of published data and results of our studies [7, 8], in this work we propose a synthetic approach to β-aminopropiophenones containing aminobenzoic acid or *N*-(4-aminobenzoyl)-β-alanine [3-(4-aminophenylcarboxamido)propanoic acid] fragment. The alkylation of 2-, 3-, and 4-aminobenzoic acids, ethyl 4-aminobenzoate (benzocaine), 2-diethylaminoethyl 4-aminobenzoate (novocaine), and *N*-(4-aminobenzoyl)-β-alanine with 1-aryl-3-diethylaminopropan-1-one hydrochlorides **1** according to the procedure described in [7] afforded β-amino ketones **2**–**21** in 34–98% yield. The structure of compounds **2**–**21** was confirmed by elemental analyses and IR and ^{1}H spectra (Scheme 1).

The antioxidant activity of some of the synthesized β-amino ketones was studied by the photoinduced chemiluminescence method. Compounds **2** and **7**–**9** showed antioxidant activity at a concentration of 40 nmol, i.e., their activity was four times lower than that of 2,6-di-*tert*-butyl-4-methylphenol (butylated hydroxytoluene) taken as reference drug and considerably lower than the activity of Trolox (6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid).

Initial 1-aryl-3-diethylaminopropan-1-ones hydrochlorides **1** were synthesized as described in [8].

General procedure for the synthesis of compounds 2–9. A mixture of 1.37 g (0.01 mol) of the corresponding aminobenzoic acid and 0.01 mol of amino ketone **1** in 20 mL of water was heated for 1.5–2 h on a boiling water bath. The mixture was cooled, and the precipitate was filtered off and washed on a filter with

Scheme 1.



2-COOH, R^1 = H (**2**); 3-COOH, R^1 = H, (**3**), 4-Cl (**4**), 4-EtO (**5**), 4-*i*-PrO (**6**); 4-COOH, R^1 = H (**7**), 4-EtO (**8**), 4-PrO (**9**); R^1 = H, R^2 = Et (**10**); R^1 = 4-Cl, R^2 = Et (**11**); R^1 = 4-MeO, R^2 = Et (**12**); R^1 = 4-*i*-PrO, R^2 = Et (**13**); R^1 = H, R^2 = $Et_2NCH_2CH_2$ (**14**); R^1 = 4-HO, R^2 = $Et_2NCH_2CH_2$ (**15**); R^1 = 4-Me, R^2 = $Et_2NCH_2CH_2$ (**16**); R^1 = 4-MeO, R^2 = $Et_2NCH_2CH_2$ (**17**); R^1 = H (**18**), 4-Cl (**19**), 4-EtO (**20**), 4-*i*-PrO (**21**).

cold water and ethanol. An additional amount of the product was isolated by evaporation of the mother liquor by half. The product was purified by recrystallization from ethanol or aqueous ethanol (1 : 1).

2-(3-Oxo-3-phenylpropylamino)benzoic acid (2). Yield 58%, mp 145–147°C, R_f 0.67. IR spectrum, ν, cm^{-1}: 3370 (NH), 1675 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.34 t (2H, CH_2, *J* = 6.7), 3.63 t (2H, NCH_2, *J* = 6.7), 6.50 d.d.d (1H, 5-H, *J* = 8.0, 7.1, 1.0), 6.72 d.d (1H, 3-H, *J* = 8.4, 1.0), 7.29 d.d.d (1H, 4-H, *J* = 8.4, 7.1, 1.7), 7.43–7.49 m (2H, *m*-H), 7.53–7.59 m (1H, *p*-H), 7.81 d.d (1H, 6-H, *J* = 8.0, 1.7), 7.95–8.00 m (2H, *o*-H), 7.98 br.s (1H, NH), 12.04 br.s (1H, COOH). Found, %: C 71.52; H 5.31; N 4.95. $C_{16}H_{15}NO_3$. Calculated, %: C 71.36; H 5.61; N 5.20.

3-(3-Oxo-3-phenylpropylamino)benzoic acid (3). Yield 42%, mp 170–171°C, R_f 0.67. IR spectrum, ν, cm^{-1}: 1764 (COOH), 1680 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.30 t (2H, CH_2, *J* = 6.6), 3.51 t (2H, NCH_2, *J* = 6.6), 3.52 br.s (1H, NH), 6.81 m (1H, 6-H), 7.14 t (1H, 5-H, *J* = 7.7), 7.19–7.26 m (2H, 2-H, 4-H), 7.43–7.50 m (2H, *m*-H), 7.52–7.58 m (1H, *p*-H), 7.92–7.97 m (2H, *o*-H). Found, %: C 71.64; H 5.35; N 5.36. $C_{16}H_{15}NO_3$. Calculated, %: C 71.36; H 5.61; N 5.20.

3-[3-(4-Chlorophenyl)-3-oxopropylamino)]benzoic acid (4). Yield 83%, mp 168–170°C, R_f 0.66. IR spectrum, ν, cm^{-1}: 3383 (NH), 1695 (COOH), 1670 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.28 t (2H, CH_2, *J* = 6.6), 3.50 t (2H, NCH_2, *J* = 6.6), 3.87 br.s (1H, NH), 6.76–6.81 m (1H, 6-H), 7.13 d.d (1H, 5-H, *J* = 8.0, 7.5), 7.18–7.24 m (2H, 2-H, 4-H), 7.43–7.48 m (2H, 3′-H, 5′-H), 7.93–7.98 m (2H, 2′-H, 6′-H), 11.95 br.s (1H, COOH). Found, %: C 63.50; H 4.31; Cl 11.40; N 4.35. $C_{16}H_{14}ClNO_3$. Calculated, %: C 63.27; H 4.65; Cl 11.67; N 4.61.

3-[3-(4-Ethoxyphenyl)-3-oxopropylamino)]benzoic acid (5). Yield 93%, mp 165–168°C, R_f 0.67. IR spectrum, ν, cm^{-1}: 3407 (NH), 1669 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.42 t (3H, CH_3, *J* = 7.0), 3.20 t (2H, CH_2, *J* = 6.6), 3.48 t (2H, NCH_2, *J* = 6.6), 4.09 q (2H, OCH_2, *J* = 7.0), 5.17 br.s (1H, NH), 6.74–6.79 m (1H, 6-H), 6.86–6.92 m (2H, 3′-H, 5′-H), 7.12 t (1H, 5-H, *J* = 7.7), 7.16–7.23 m (2H, 2-H, 4-H), 7.87–93 m (2H, 2′-H, 6′-H), 12.00 br.s (1H, COOH). Found, %: C 69.25; H 6.30; N 4.25. $C_{18}H_{19}NO_4$. Calculated, %: C 69.00; H 6.11; N 4.47.

3-{3-Oxo-3-[4-(propan-2-yloxy)phenyl]propylamino}benzoic acid (6). Yield 57%, mp 161–162°C, R_f 0.68. IR spectrum, ν, cm^{-1}: 3363 (NH), 1694 (COOH), 1670 (C=O). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.34 d (6H, CH_3, *J* = 6.1), 3.20 t (2H, CH_2, *J* = 6.6), 3.46 t (2H, NCH_2, *J* = 6.6), 4.68 sept (1H, CH, *J* = 6.1), 5.45 br.s (1H, NH), 6,75 d.d.d (1H, 6-H, *J* = 7.6, 2.3, 1.4), 6.86–6.91 m (2H, 3′-H, 5′-H), 7.09–7.20 m (3H, 2-H, 4-H, 5-H), 7.87–7.92 m (2H, 2′-H, 6′-H), 12.07 br.s (1H, COOH). Found, %: C 69.50; H 6.58; N 4.50. $C_{19}H_{21}NO_4$. Calculated, %: C 69.71; H 6.47; N 4.28.

4-(3-Oxo-3-phenylpropylamino)benzoic acid (7). Yield 59%, mp 145–147°C, R_f 0.67. IR spectrum, ν, cm^{-1}: 3350 (NH), 1680 (C=O). ^1H NMR spectrum, δ, ppm (*J*, Hz): 3.60 t (2H, CH_2, *J* = 5.5), 3.95 t (2H, NCH_2, *J* = 5.5), 7.51–7.58 m (2H, C_6H_5), 7.67–7.75 m (3H, C_6H_5), 7.94–7.99 m (2H, C_6H_4), 8.27–8.33 m (2H, C_6H_4). Found, %: C 71.91; H 5.40; N 5.30. $C_{16}H_{15}NO_3$. Calculated, %: C 71.36; H 5.61; N 5.20.

4-[3-(4-Ethoxyphenyl)-3-oxopropylamino]benzoic acid (8). Yield 59%, mp 145–147°C, R_f 0.72. IR spectrum, ν, cm^{-1}: 3350 (NH), 1680 (C=O). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.35 t (3H, CH_3, *J* = 6.9), 3.25 t (2H, CH_2, *J* = 6.6), 3.44 t.d (2H, NCH_2, *J* = 6.6, 5.5), 4.12 q (2H, OCH_2, *J* = 6.9), 6.42 t (1H, NH, *J* = 5.5), 6.56–6.61 m (2H, 2-H, 6-H), 6.99–7.05 m (2H, 3′-H, 5′-H), 7.64–7.69 m (2H, 2′-H, 6′-H), 7.90–7.95 m (2H, 3-H, 5-H), 11.95 br.s (1H, COOH). Found, %: C 69.29; H 6.30; N 4.60. $C_{18}H_{19}NO_4$. Calculated, %: C 69.00; H 6.11; N 4.47.

4-{3-Oxo-3-[4-(propan-2-yloxy)phenyl]propylamino}benzoic acid (9). Yield 80%, mp 229–231°C, R_f 0.67. IR spectrum, ν, cm^{-1}: 3360 (NH), 1665 (C=O). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.06 t (3H, CH_3, *J* = 7.4), 1.82 t (2H, $CH_3C\underline{H}_2$), 3.21 t (2H, $C\underline{H}_2CH_2N$, *J* = 6.6), 3.49 t. d (2H, $NHC\underline{H}_2$, *J* = 6.6, 5.7), 3.99 t (2H, OCH_2, *J* = 6.5), 5.96 s (1H, NH), 6.04 t (1H, NH, *J* = 5.7), 6.55 m (2H, 2-H, 6-H), 6.91 m (2H, 3′-H, 5′-H), 7.68 m (2H, 3-H, 5-H), 7.90 m (2H, 2′-H, 6′-H), 11.51 br.s (1H, COOH). Found, %: C 69.47; H 6.58; N 4.14. $C_{19}H_{21}NO_4$. Calculated, %: C 69.71; H 6.47; N 4.28.

Compounds **10–17** were synthesized in a similar way from benzocaine or novocaine.

Ethyl 4-(3-oxo-3-phenylpropylamino)benzoate (10). Yield 34%, mp 163–164°C, R_f 0.67. IR spectrum, ν, cm^{-1}: 3379 (NH), 1677 (C=O). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.34 t (3H, CH_3, *J* = 7.1), 3.29 t (2H, CH_2, *J* = 6.6), 3.53 t (2H, NCH_2, *J* = 6.6), 3.74 br.s (1H, NH), 4.22 q (2H, OCH_2, *J* = 7.1), 6.54–6.59 m (2H, 2-H, 6-H), 7.44–7.50 m (2H, *m*-H), 7.53–7.60 m (1H, *p*-H), 7.67–7.72 m (2H, 3-H, 5-H), 7.93–7.98 m (2H, *o*-H). Found, %: C 72.84; H 6.13; N 4.85. $C_{18}H_{19}NO_3$. Calculated, %: C 72.71; H 6.44; N 4.71.

Ethyl-4-[3-(4-chlorophenyl)-3-oxopropylamino]benzoate (11). Yield 98%, mp 207–208°C, R_f 0.67. IR spectrum, ν, cm^{-1}: 3367 (NH), 1694 (COOEt), 1680 (C=O). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.34 t (3H, CH_3, *J* = 7.1), 3.28 t (2H, CH_2, *J* = 6.6), 3.51 t (2H, NCH_2, *J* = 6.6), 4.22 q (2H, OCH_2, *J* = 7.1), 6.16 br.s (1H, NH), 6.52–6.57 m (2H, 2-H, 6-H), 7.45–7.50 m (2H, 3′-H, 5′-H), 7.67–7.72 m (2H, 3-H, 5-H), 7.92–7.97 m (2H, 2′-H, 6′-H). Found, %: C 65.37; H 5.50; Cl 10.42; N 4.10. $C_{18}H_{18}ClNO_3$. Calculated, %: C 65.16; H 5.47; Cl 10.68; N 4.22.

Ethyl 4-[3-(4-methoxyphenyl)-3-oxopropylamino]benzoate (12). Yield 88%, mp 243–245°C, R_f 0.70. IR spectrum, ν, cm^{-1}: 3387 (NH), 1694 (COOEt), 1680 (C=O). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.34 t (3H, CH_3, *J* = 7.1), 3.22 t (2H, CH_2, *J* = 6.6), 3.50 t (2H, NCH_2, *J* = 6.6), 3.87 s (3H, OCH_3), 4.22 q (2H, OCH_2, *J* = 7.1), 6.13 br.s (1H, NH), 6.52–6.57 m (2H, 2-H, 6-H), 6.91–6.96 m (2H, 3′-H, 5′-H), 7.66–7.71 m (2H, 3-H, 5-H), 7.90–7.95 m (2H, 2′-H, 6′-H). Found, %: C 69.55; H 6.26; N 4.55. $C_{19}H_{21}NO_4$. Calculated, %: C 69.71; H 6.47; N 4.28.

Ethyl 4-{3-oxo-3-[4-(propan-2-yloxy)phenyl]propylamino}benzoate (13). Yield 68%, mp 155–156°C, R_f 0.71. IR spectrum, ν, cm^{-1}: 3391, 3363 (NH), 1698 (COOEt), 1675 (C=O). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.34 t (3H, $C\underline{H}_3CH_2O$, *J* = 7.0), 1.35 d (6H, CH_3, *J* = 6.0), 3.21 t (2H, CH_2, *J* = 6.6), 3.50 t (2H, NCH_2, *J* = 6.6), 4.22 q (2H, OCH_2, *J* = 7.0), 4.68 sept (1H, OCH, *J* = 6.0), 6.12 br.s (1H, NH), 6.52–6.57 m (2H, 2-H, 6-H), 6.86–6.91 m (2H, 3′-H, 5′-H), 7.66–7.71 m (2H, 3-H, 5-H), 7.86–7.91 m (2H, 2′-H, 6′-H). Found, %: C 70.75; H 7.26; N 4.11. $C_{21}H_{25}NO_4$. Calculated, %: C 70.96; H 7.09; N 3.94.

2-(Diethylamino)ethyl 4-(3-oxo-3-phenylpropylamino)benzoate (14). Yield 67%, mp 201–204°C, R_f 0.67. IR spectrum, ν, cm^{-1}: 3372 (NH), 1676 (C=O). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.04 t (6H, CH_3, *J* = 7.1), 2.56 q (4H, $NC\underline{H}_2CH_3$, *J* = 7.1), 2.73 t (2H, $NC\underline{H}_2CH_2O$, *J* = 6.3), 3.29 t [2H, $C(O)CH_2$, *J* = 6.6], 3.52 t. d (2H, $NHC\underline{H}_2$, *J* = 6.6, 5.7), 4.19 t (2H, OCH_2, *J* = 6.4), 6.17 br.t (1H, NH, *J* = 5.7), 6.53–6.58 m (2H, 2-H, 6-H), 7.44–7.50 m (2H, *m*-H), 7.53–7.59 m (1H, *p*-H), 7.66–7.71 m (2H, 3-H, 5-H), 7.94–7.98 m (2H,

o-H). Found, %: C 71.85; H 7.90; N 7.40. $C_{22}H_{28}N_2O_3$. Calculated, %: C 71.71; H 7.66; N 7.60.

2-Diethylaminoethyl 4-[3(4-hydroxyphenyl)-3-oxopropylamino]benzoate hydrochloride (15). Yield 69%, mp 211–213°C, R_f 0.65. IR spectrum, ν, cm^{-1}: 3354 (NH), 1662 (C=O). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.37 t (6H, CH_3, *J* = 7.2), 3.13–3.26 m [6H, NCH_2CH_2, $C(O)CH_2$], 3.40–3.53 m (4H, NCH_2), 4.63 br.t (2H, OCH_2, *J* = 5.0), 6.35 br.s (1H, NH), 6.55–6.60 m and 6.78–6.83 m (2H each, C_6H_4N), 7.71–7.82 m (4H, C_6H_4O), 9.97 br.s (1H, OH), 12.06 br.s (1H, HCl). Found, %: N 6.52; Cl 8.50. $C_{22}H_{28}N_2O_4 \cdot HCl$. Calculated, %: N 6.67; Cl 8.42.

2-Diethylaminoethyl 4-[3(4-methylphenyl)-3-oxopropylamino]benzoate hydrochloride (16). Yield 65%, mp 174–175°C, R_f 0.68. IR spectrum, ν, cm^{-1}: 3373 (NH), 1674 (C=O). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.37 t (6H, CH_3, *J* = 7.2), 2.42 s (3H, $C\underline{H}_3C_6H_4$), 3.16–3.26 m [4H, $N(C\underline{H}_2CH_3)_2$], 3.26 t [2H, $C(O)CH_2$, *J* = 6.5], 3.40–3.46 m (2H, NCH_2), 3.52 t (2H, $C\underline{H}_2NH$, *J* = 6.5), 4.61–4.66 m (2H, OCH_2), 6.56–6.62 m (2H, C_6H_4N), 7.24–7.29 m and 7.71–7.76 m (2H each, $CH_3C_6\underline{H}_4$), 7.82–7.87 m (2H, C_6H_4N), 12.17 br.s (2H, NH, HCl). Found, %: N 6.73; Cl 8.51. $C_{23}H_{30}N_2O_3 \cdot HCl$. Calculated, %: N 6.70; Cl 8.46.

2-Diethylaminoethyl 4-[3-(4-methoxyphenyl)-3-oxopropylamino]benzoate hydrochloride (17). Yield 70%, mp 144–146°C, R_f 0.67. IR spectrum, ν, cm^{-1}: 3384 (NH), 1707.7 (COO), 1660 (C=O). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.37 t (6H, CH_3, *J* = 7.1), 3.17–3.26 m (6H, CH_2N), 3.41–3.45 br.q (2H, $NHC\underline{H}_2$, *J* = 5.1), 3.51 t [2H, $C(O)CH_2$, *J* = 6.6], 3.87 s (3H, OCH_3), 4.63 t (2H, OCH_2, *J* = 5.1), 6.28 br.s (1H, NH), 6.56–6.61 m (2H, 2-H, 6-H), 6.92–6.97 m (2H, C_6H_4O), 7.71–7.76 m (2H, 3-H, 5-H), 7.89–7.94 m (2H, C_6H_4O), 6.28 br.s (1H, NH), 12.16 br.s (1H, HCl). Found, %: N 6.31; Cl 8.09. $C_{23}H_{30}N_2O_4 \cdot HCl$. Calculated, %: N 6.45; Cl 8.16.

Compounds **18**–**21** were synthesized in a similar way from *N*-(4-aminobenzoyl)-β-alanine.

3-[4-(3-Oxo-3-phenylpropylamino)benzamido]propanoic acid (18). Yield 87%, mp 111–113°C, R_f 0.65. IR spectrum, ν, cm^{-1}: 3380 (NH_{Ar}), 3352 (NH_{amide}), 1692 (COOH), 1675 (C=O). ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.48 t (2H, $C\underline{H}_2COOH$, *J* = 7.0), 3.29 t [2H, $C(O)CH_2$, *J* = 6.7], 3.42–3.49 m (2H, $NHC\underline{H}_2CH_2 \cdot COOH$), 3.50 t [2H, $C(O)CH_2C\underline{H}_2$, *J* = 6.7], 6.54–6.59 m and 7.57–7.62 m (2H each, C_6H_4); 7.44–7.50 m (2H), 7.53–7.59 m (1H), and 7.94–7.98 m (2H) (C_6H_5); 7.77 br.t (1H, CONH, *J* = 5.7), 11.8 br.s (1H, COOH); the NH signal is strongly broadened due to exchange with water present in the solvent and is observed at δ ~5.8 ppm. Found, %: C 67.24; H 6.26; N 8.05. $C_{19}H_{20}N_2O_4$. Calculated, %: C 67.05; H 5.92; N 8.23.

3-{4-[3-(4-Chlorophenyl)-3-oxopropylamino]benzamido}propanoic acid (19). Yield 36%, mp 199–200°C, R_f 0.67. IR spectrum, ν, cm^{-1}: 3368 (NH_{Ar}), 3349 (NH_{amide}), 1734 (COOH), 1670 (C=O). ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.48 t (2H, $C\underline{H}_2COOH$, *J* = 7.0), 3.28 t [2H, $C(O)CH_2$, *J* = 6.6], 3.42–3.53 m [4H, $NHC\underline{H}_2CH_2COOH$, $C(O)CH_2C\underline{H}_2$], 6.56–6.61 m and 7.57–7.62 m (2H each, C_6H_4N), 7.43–7.48 m and 7.93–7.98 m (2H each, C_6H_4Cl), 7.73 br.t (1H, CONH, *J* = 5.7), 11.9 br.s (1H, COOH); the NH signal is strongly broadened due to exchange with water present in the solvent and is observed at δ ~4.4 ppm. Found, %: C 60.64; H 5.26; Cl 9.85; N 7.75. $C_{19}H_{19}ClN_2O_4$. Calculated, %: C 60.88; H 5.11; Cl 9.46; N 7.47.

3-{4-[3-(4-Ethoxyphenyl)-3-oxopropylamino]benzamido}propanoic acid (20). Yield 79%, mp 212–214°C, R_f 0.69. IR spectrum, ν, cm^{-1}: 3380 (NH_{Ar}), 3340–3320 (NH_{amide}), 1715 (COOH), 1670 (C=O). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.43 t (3H, CH_3, *J* = 7.0), 2.48 t (2H, $C\underline{H}_2COOH$, *J* = 6.9), 3.22 t [2H, $C(O)CH_2$, *J* = 6.6], 3.43–3.51 m [4H, $C(O)CH_2C\underline{H}_2$, $NHC\underline{H}_2CH_2COOH$), 4.10 q (2H, $OC\underline{H}_2CH_3$, *J* = 7.0), 4.6 br.s (1H, $N\underline{H}C_6H_4$), 6.56–6.63 m and 7.57–7.62 m (2H each, C_6H_4N), 6.87–6.92 m and 7.88–7.93 m (2H each, C_6H_4O), 7.73 t (1H, CONH, *J* = 5.5), 11.8 br.s (1H, COOH); the NH signal is strongly broadened due to exchange with water present in the solvent and is observed at δ ~4.6 ppm. Found, %: C 65.74; H 6.06; N 7.06. $C_{21}H_{24}N_2O_5$. Calculated, %: C 65.61; H 6.29; N 7.29.

3-{4-[3-Oxo-3-(4-propan-2-yloxy)propylamino]benzamido}propanoic acid (21). Yield 68%, mp 213–214°C, R_f 0.66. IR spectrum, ν, cm^{-1}: 3390 (NH_{Ar}), 3350 (NH_{amide}), 1720 (COOH), 1685 (C=O), 1650 ($C=O_{amide}$). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.35 d (6H, CH_3, *J* = 6.0), 2.48 t (2H, $C\underline{H}_2COOH$, *J* = 6.9), 3.20 t [2H, $C(O)CH_2$, *J* = 6.6], 3.42–3.51 m [4H, $C(O)CH_2C\underline{H}_2$, $NHC\underline{H}_2CH_2COOH$], 4.68 sept [1H, $OC\underline{H}(CH_3)_2$, *J* = 6.0], 5.5 br.s (1H, $N\underline{H}C_6H_4$), 6.53–6.58 m and 7.56–7.61 m (2H each, C_6H_4N), 6.87–6.92 m and 7.86–7.91 m (2H each, C_6H_4O), 7.75 t (1H, CONH, *J* = 5.5), 11.8 br.s (1H, COOH). Found, %: C 66.21; H 6.77; N 6.89. $C_{22}H_{26}N_2O_5$. Calculated, %: C 66.32; H 6.58; N 7.03.

The IR spectra were recorded on a NEXUS FT-IR spectrometer. The ^{1}H NMR spectra were measured on a Varian Mercury 300 spectrometer at 300 MHz using DMSO–d_6–CCl_4 (1 : 3) as solvent and tetramethylsilane as internal standard. Analytical thin-layer chromatography was performed on Silufol UV-254 plates (eluent butan-1-ol–ethanol–acetic acid–water 8 : 2 : 1 : 3; development with iodine vapor). The melting points were determined on a Boetius melting point apparatus.

The antioxidant activity of aminobenzoic acid derivatives was studied by the photoinduced chemiluminescence method [9] on a PHOTOCHEM apparatus (Analytic Jena, Germany) using a commercial ACL kit for the determination of integral activity of lipid-soluble substances, which was assessed relative to Trolox (water-soluble analog of vitamin E) as standard drug and was expressed in units equivalent to the amount of the standard in nanomoles showing the same activity.

REFERENCES

1. Zhakina, A.Kh., *Izv. Nats. Akad. Nauk Resp. Kazakhstan*, 2010, no. 3, p. 25.
2. Gal'binur, T.P., *Mol. Med*., 2012, no. 5, p. 11.
3. Mashkovskii, M.D., *Lekarstvennye sredstva* (Drugs), Moscow: Novaya Volna, 2010, 16th ed.
4. Tang Guang Xia, Yan Ju Fang, Fan Li, Xu Jin, Song Xiao Li, Jiang Li, Luo Ling Fei, and Yang Da Cheng, *Sci. China: Chem*., 2013, vol. 56, no. 4, p. 490. doi 10.1007/s11426-012-4816-2
5. Kopal, Niranjan kaushik, Pankaj kumar, Hashim R., and Pradeep kumar, *Orient. J. Chem*., 2008, vol. 24, no. 2, p. 641.
6. Shakirova, A.B., *Cand. Sci. (Pharm.) Dissertation*, Perm, 2009.
7. Agababyan, A.G., Gevorgyan, G.A., Avakyan, A.P., Tumadzhyan, A.E., Paronikyan, R.G., and Panosyan, G.A., *Pharm. Chem. J*., 2013, vol. 47, no. 7, p. 361. doi 10.1007/s11094-013-0959-5
8. Agababyan, A.G., Isakhanyan, A.Y., Papoyan, O.A., Tumadzhyan, A.E., Balasanyan, A.S., and Gevorgyan, G.A., *Pharm. Chem. J*., 2005, vol. 39, no. 7, p. 364. doi 10.1007/s11094-005-0156-2
9. Popov, I.N. and Lewin, G.J., *J. Biochem. Biophys. Methods*, 1996, vol. 31, nos. 1–2, p. 1. doi 10.1016/0165-022X(95)00021-I