ՀԱՅԱՍՏԱՆԻ ՀԱՆՐԱՊԵՏՈՒԹՅԱՆ ԳԻՏՈՒԹՅՈՒՆՆԵՐԻ
ԱԶԳԱՅԻՆ ԱԿԱԴԵՄԻԱ
НАЦИОНАЛЬНАЯ АКАДЕМИЯ НАУК РЕСПУБЛИКИ АРМЕНИЯ
NATIONAL ACADEMY OF SCIENCES OF THE REPUBLIC OF ARMENIA

Հայաստանի քիմիական հանդես
Химический журнал Армении **72, №4, 2019** Chemical Journal of Armenia

SYNTHESIS AND ANTIBACTERIAL ACTIVITY OF 4-AMINO-1,3,5-TRIARYL-1H-PYRROL-2(5H)-ONES

M. V. ALEXANYAN, G. K. HARUTYUNYAN, S. P. GASPARYAN, H. M. STEPANYAN and R. E. MURADYAN

The Scientific Technological Centre of Organic and Pharmaceutical Chemistry NAS RA
26, Azatutyan Str., Yerevan, 0014, Armenia
E-mail: g_sahak@yahoo.com

By acylation of α-aminonitriles with phenylacetyl chloride and subsequent intramolecular cyclization in the presence of caustic potassium, the synthesis of 4-amino-1,3,5-triaryl-1H-pyrrol-2(5H)-ones was carried out. The antibacterial activity of synthesized compounds was studied, among which 4-amino-5-(4-isopropoxyphenyl)-3-phenyl-1-o-tolyl-1H-pyrrol-2(5H)-one is the most active, inhibiting the growth of gram-positive microorganisms in the zone with diameter d = 17-18 mm. Other derivatives are inactive or completely devoid of antibacterial activity.

Table 1, references 13.

Pyrrolones are well known compounds due to their presence in natural products. They have various biological properties and are potential compounds in the development of new drugs [1].

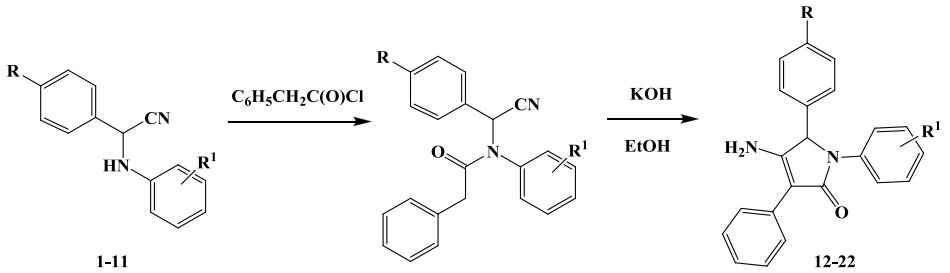
Several approaches to the synthesis of pyrrolones are known in the literature, particularly, the reaction of *α,β*-diketones with various acetamides possessing a strong electron-withdrawing group in the *α*-position, the cycloisomerization reaction of alkylidenecarbene derivative of amides, the condensation reaction of benzoylformanilide with acetophenones to yield aldol-type products and the subsequent treatment with HCl, the ruthenium-catalyzed reaction of *α,β*-unsaturated imines with carbon monoxide and ethylene [2-5].

4-Aminosubstituted pyrrolones are little known compounds, and there are few reports about their synthesis in the literature. These include reactions of pyrrolidine-2,4-diones with primary amines and reactions of secondary amines with phenylacetyl chloride and further cyclization of amides in the presence of caustic potassium [1,6].

We have previously developed an effective method for the synthesis of substituted *β*- and *γ*-lactams based on acylation reactions of corresponding *α*-aminonitriles (obtained by the Strecker reaction) with monochloroacetyl or 3-

chloropropionyl chlorides and subsequent intramolecular cyclization under phase transfer catalysis condition.

In continuation of research in this direction, by acylation of *α*-aminonitriles **1-11** with phenylacetyl chloride and subsequent intramolecular cyclization in the presence of caustic potassium, 4-amino-1,3,5-triaryl-1*H*-pyrrol-2(5*H*)-ones **12-22** were synthesized.



R = R^1 = H (**1**,**12**); R = H, R^1 = 4-CH_3 (**2**,**13**); R = H, R^1 = 2-CH_3 (**3**,**14**); R = H, R^1 = 3,5-$(CH_3)_2$ (**4**,**15**); R = H, R^1 = 4-CH_3O (**5**,**16**); R = H, R^1 = 2-CH_3O (**6**,**17**); R = 4-*iso*-C_3H_7O, R^1 = H (**7**,**18**); R = 4-*iso*-C_3H_7O, R^1 = 4-CH_3 (**8**,**19**); R = 4-*iso*-C_3H_7O, R^1 = 2-CH_3 (**9**,**20**); R = 4-*iso*-C_3H_7O, R^1 = 3,5-$(CH_3)_2$ (**10**,**21**); R = 4-*iso*-C_3H_7O, R^1 = 2-CH_3O (**11**,**22**).

The structure of the synthesized compounds was confirmed by elemental analysis, IR, ^1H and ^{13}C NMR spectra.

The antibacterial activity of synthesized compounds **12-22** was studied using the "diffusion in agar" method [7], with a bacterial load of 20 *mln* microbial cells per 1 *ml* of medium. Gram-positive staphylococci (*St. aureus 209p, Bac. subtilis*) and gram-negative rods (*Sh. flexneri* 6858, *E. coli* 055) were used in experiments. Solutions of tested compounds and the control preparation were prepared in DMSO at a dilution of 1:20. On Petri dishes with crops of the above strains, solutions of compounds were applied in a volume of 0.1 *ml*. The results were recorded by the diameter (d, *mm*) of the zone of no microbial growth at the site of application of the compounds after daily growth of the test cultures in a thermostat at 37°C. Furazolidone was used as a positive control [8].

Among synthesized compounds, 4-amino-5-(4-isopropoxyphenyl)-3-phenyl-1-*o*-tolyl-1*H*-pyrrol-2(5*H*)-one **(20)** was found to be the most active, inhibiting the growth of gram-positive microorganisms in the zone with diameter d = 17-18 *mm*, the remaining derivatives were inactive or completely devoid of antibacterial activity (Table).

Table

Antibacterial activity of 4-amino-1,3,5-triaryl-1H-pyrrol-2(5H)-ones

Comp. №	The diameter of the zone of absence of microbial growth (d, *mm*)			
	St. aureus 209p	*Bac. subtilis*	*Sh. flexneri 6858*	*E. coli 055*
12	0	0	0	0
13	0	0	0	0
14	0	0	0	0
15	13	12	12	12
16	12	11	15	15
17	13	13	12	10
18	10	10	12	10
19	0	0	0	0
20	17	17	13	13
21	0	0	0	0
22	0	0	0	0
Furazolidone	25	24	24	24

Experimental part

IR spectra were recorded on a "Nicolet Avatar 330" spectrometer from samples dispersed in mineral oil. The ^{1}H and ^{13}C NMR spectra were recorded on a Varian "Mercury-300VX" instrument at 303 *K* with a frequency of 300.078 and 75.46 *MHz*, respectively. In the assignment of signals, the methods of double resonance, DEPT and HMQC were used. Chemical shifts are given in ppm relative to the internal TMS for DMSO-d_6/CCl_4 1/3 solutions. The course of the reactions and the purity of the substances were controlled using thin-layer chromatography on Silufol UV-254 plates, in eluent systems: acetone–nonane, 2:1 (a), acetone–nonane, 3:2 (b) and acetone–nonane, 1:1 (c), spots were visualized by treatment with iodine vapor.

Syntheses of α-aminonitriles 1-3**,** 5-11 **are described in [9-13].**

2-(3,5-Dimethylphenylamino)-2-phenylacetonitrile (4). To a solution of 1.06 *g* (10 *mmol*) of benzaldehyde in 20 *ml* of EtOH with stirring at room temperature, a solution of 0.5 *g* (10 *mmol*) of NaCN in 10 *ml* of water is added, stirred for 10 *min*, then 0.6 *g* (10 *mmol*) of AcOH is added, stirred for another 10 *min* and a solution of 1.2 *g* (10 *mmol*) of 3,5-dimethylaniline in 10 *ml* of EtOH is added. Stirring is continued for 2 *h*, 10 *ml* of cold water is added and left overnight. The precipitate formed is filtered, washed with water, dried and recrystallized from EtOH. Yield 2.0 *g* (85%) of compound 4, mp 103-104°C, R_f 0.60 (a). ^{1}H NMR spectrum, δ, ppm, *Hz*: 2.24 (s, 6H, 2×CH_3); 5.65 (d, 1H, *J* = 9.4, CH); 6.18 (d, 1H, *J* = 9.4, NH); 6.36 (br., 1H, 4-H C_6H_3); 6.39 (br., 2H, 2,2'-H C_6H_3); 7.34-7.46 (m, 3H, *m*,*p*-C_6H_5); 7.57-7.62 (m, 2H, *o*- C_6H_5). ^{13}C

NMR spectrum δ_c, ppm: 21.0 (2×CH_3); 48.4 (CH); 111.6 (2,2'-CH C_6H_3); 118.4 (CN); 120.1 (4-H C_6H_3); 126.8 (2×CH C_6H_5); 128.0 (*p*- C_6H_5); 128.2 (2×CH C_6H_5); 135.0; 137.4 (3,3'-CH C_6H_3); 145.4 (1-C C_6H_3). Found, %: C 81.17; H 6.91; N 12.03. $C_{16}H_{16}N_2$. Calculated, %: C 81.32; H 6.82; N 11.85.

General procedure for the preparation of 4-amino-1,3,5-triaryl-1H-pyrrol-2(5H)-ones (12-22). To a mixture of 10 *mmol* of the corresponding 2-arylacetonitrile **1-11** in 20 *ml* of 1,2-dichloroethane and 1.4 *g* (10 *mmol*) of dry K_2CO_3, 1.6 *g* (10 *mmol*) of phenylacetyl chloride is added dropwise at 10-15°C, the reaction mixture is stirred at room temperature for 30 *min* and then 2 *h* at 40-45°C. Upon completion, the whole is cooled, 20 *ml* of 1,2-dichloroethane is added, washed several times with water and dried with $CaCl_2$. The solvent is removed, the residue is dissolved in 30 *ml* of EtOH, 2.8 *g* (50 *mmol*) of KOH in 10 *ml* of water is added, and stirred at 60–65 °C for 1 *h*. After cooling, 20 *ml* of water is added, the precipitate formed is filtered and recrystallized from EtOH.

4-Amino-1,3,5-triphenyl-1*H*-pyrrol-2(5*H*)-one (12). Yield 78%, mp 246-248°C, R_f 0.60 (b). IR spectrum, ν, cm^{-1}: 1632 (C=O), 3306 (NH_2). ^{1}H NMR spectrum, δ, ppm: 5.58 (s, 1H, CH); 6.08 (br., 2H, NH_2); 6.80-6.83 (m, 1H, *p*-C_6H_5); 7.11-7.19 (m, 3H, Ar); 7.21-7.38 (m, 5H, Ar); 7.42-7.46 (m, 2H, *o*-C_6H_5); 7.51-7.56 (m, 2H, *o*- C_6H_5); 7.58-7.63 (m, 2H, *o*-C_6H_5). ^{13}C NMR spectrum δ_c, ppm: 62.4 (CH); 98.5; 119.3 (2×CH); 121.5 (CH); 124.8 (CH); 126.9 (2×CH); 127.4 (2×CH); 127.5 (CH); 127.66 (2×CH); 127.71 (2×CH); 128.2 (2×CH); 132.5; 137.5; 138.5; 159.0; 169.0. Found, %: C 80.78; H 5.45; N 8.64. $C_{22}H_{18}N_2O$. Calculated, %: C 80.96; H 5.56; N 8.58.

4-Amino-3,5-diphenyl-1-*p*-tolyl-1*H*-pyrrol-2(5*H*)-one (13) is described in [1].

4-Amino-3,5-diphenyl-1-*o*-tolyl-1*H*-pyrrol-2(5*H*)-one (14). Yield 65%, mp 213-215°C, R_f 0.57 (c). IR spectrum, ν, cm^{-1}: 1638 (C=O), 3297 (NH_2). ^{1}H NMR spectrum, δ, ppm: 2.11 (s, 3H, CH_3); 5.36 (s, 1H, CH); 5.95 (br., 2H, NH_2); 6.97-7.12 (m, 4H, Ar); 7.13-7.19 (m, 1H, *p*- C_6H_5); 7.25-7.32 (m, 5H, Ar); 7.33-7.39 (m, 2H, *m*-C_6H_5); 7.65-7.69 (m, 2H, *o*-C_6H_5). ^{13}C NMR spectrum δ_c, ppm: 18.2 (CH_3); 64.8 (CH); 98.9; 124.6 (CH); 125.3 (CH); 125.9 (CH); 127.4 (2×CH); 127.4 (CH); 127.5 (2×CH); 127.7 (CH); 127.8 (2×CH); 128.0 (2×CH); 130.0 (CH). Found, %: C 81.30; H 5.78; N 8.32. $C_{23}H_{20}N_2O$. Calculated, %: C 81.15; H 5.92; N 8.23.

4-Amino-1-(3,5-dimethylphenyl)-3,5-diphenyl-1*H*-pyrrol-2(5*H*)-one (15). Yield 82%, mp 205-206 °C, R_f 0.46 (a). IR spectrum, ν, cm^{-1}: 1638 (C=O), 3333 (NH_2). ^{1}H NMR spectrum, δ, ppm: 2.21 (s, 6H, 2×CH_3); 5.53 (s, 1H, CH); 6.03 (br., 2H, NH_2); 6.51 (m, 1H, 4H C_6H_3); 7.12 (br., 2H, 2,2'-H C_6H_3); 7.13-7.18 (m, 1H, 4-CH C_6H_5); 7.21-7.27 (m, 1H, 4-CH C_6H_5); 7.28-7.37 (m, 4H, 2 *m*- C_6H_5); 7.39-7.43 (m, 2H, *o*-C_6H_5); 7.58-7.62 (m, 2H, *o*-C_6H_5). ^{13}C NMR spectrum δ_c, ppm: 21.0 (2×CH_3); 62.6 (CH); 98.5; 117.7 (2×CH); 123.6 (CH); 124.7 (CH); 127.0 (2×CH); 127.4 (2×CH); 127.5 (CH); 127.6 (2×CH); 128.1

(2×CH); 132.6; 136.5 (2 C CH_3); 137.6; 138.2; 158.8. Found, %: C 81.30; H 5.78; N 8.32. $C_{24}H_{22}N_2O$. Calculated, %: C 81.33; H 6.26; N 7.90.

4-Amino-1-(4-methoxyphenyl)-3,5-diphenyl-1*H*-pyrrol-2(5*H*)-one (16). Yield 73%, mp 225-226°C, R_f 0.40 (a). IR spectrum, ν, cm^{-1}: 1634 (C=O), 3302 (NH_2). ^{1}H NMR spectrum, δ, ppm: 3.70 (s, 3H, OCH_3); 5.52 (s, 1H, CH); 6.00 (br., 2H, NH_2); 6.68-6.73 (m, 2H, C_6H_4); 7.13-7.19 (m, 1H, *p*-C_6H_5); 7.21-7.43 (m, 9H, Ar); 7.60-7.64 (m, 2H, Ar). ^{13}C NMR spectrum δ_c, ppm: 54.4 (OCH_3); 63.0 (CH); 98.6; 113.1 (2×CH C_6H_4); 121.8 (2×CH C_6H_4); 124.7 (CH); 127.2 (CH Ph); 127.5 (2×CH Ph); 127.5 (CH Ph); 127.6 (2×CH Ph); 128.1 (2×CH Ph); 131.5; 132.7; 137.5; 154.6; 158.6; 169.6. Found, %: C 77.63; H 5.41; N 7.60. $C_{23}H_{20}N_2O_2$. Calculated, %: C 77.51; H 5.66; N 7.86.

4-Amino-1-(2-methoxyphenyl)-3,5-diphenyl-1*H*-pyrrol-2(5*H*)-one (17). Yield 71%, mp 154-156°C, R_f 0.42 (a). IR spectrum, ν, cm^{-1}: 1627 (C=O), 3297 (NH_2). ^{1}H NMR spectrum, δ, ppm, *Hz*: 3.86 (s, 3H, OCH_3); 5.60 (s, 1H, CH); 5.95 (br., 2H, NH_2); 6.78 (td, 1H, J = 7.6, J = 1.4, C_6H_4); 6.89 (dd, 1H, J = 8.2, J = 1.3, C_6H_4); 7.05-7.12 (m, 2H, Ar); 7.13-7.19 (m, 1H, Ar); 7.21-7.31 (m, 5H, Ar); 7.33-7.39 (m, 2H, Ar); 7.64-7.68 (m, 2H, Ar). ^{13}C NMR spectrum δ_c, ppm: 55.0 (OCH_3); 63.7 (CH); 99.6; 111.3 (CH); 119.6 (CH); 124.5 (CH); 126.0; 126.3 (CH); 127.4 (2×CH); 127.4 (CH); 127.5 (2×CH); 127.7 (2×CH); 127.8 (2×CH); 129.6 (CH); 133.0; 137.2; 154.4; 159.0; 170.0. Found, %: C 77.33; H 5.52; N 7.71. $C_{23}H_{20}N_2O_2$. Calculated, %: C 77.51; H 5.66; N 7.86.

4-Amino-5-(4-isopropoxyphenyl)-1,3-diphenyl-1*H*-pyrrol-2(5*H*)-one (18). Yield 68%, mp 207-209°C, R_f 0.46 (a). IR spectrum, ν, cm^{-1}: 1610 (C=O), 3307 (NH_2). ^{1}H NMR spectrum, δ, ppm, *Hz*: 1.30 (d, 6H, J = 6.0, 2×CH_3); 4.52 (sp, 1H, J = 6.0, OCH); 5.51 (s, 1H, CH); 6.03 (br., 2H, NH_2); 6.76-6.81 (m, 2H, C_6H_4); 6.85-6.90 (m, 1H, *p*- C_6H_5); 7.13-7.20 (m, 3H, *m*-C_6H_5); 7.29-7.38 (m, 4H, Ar); 7.52-7.56 (m, 2H, *o*-C_6H_5); 7.53-7.63 (m, 2H, *o*-C_6H_5). ^{13}C NMR spectrum δ_c, ppm: 21.61 (CH_3); 21.65 (CH_3); 61.9 (NCH); 68.7 (OCH); 98.4; 115.2 (2×CH C_6H_4); 119.5 (2×CH C_6H_4); 121.5 (CH); 124.7 (CH); 127.5 (2×CH Ph); 127.65 (2×CH Ph); 127.7 (2×CH Ph); 128.1 (2×CH Ph); 128.7; 132.6; 138.5; 157.1; 159.2; 169.7. Found, %: C 78.22; H 6.41; N 7.04. $C_{25}H_{24}N_2O_2$. Calculated, %: C 78.10; H 6.29; N 7.29.

4-Amino-5-(4-isopropoxyphenyl)-3-phenyl-1-*p*-tolyl-1*H*-pyrrol-2(5*H*)-one (19). Yield 72%, mp 194-196°C, R_f 0.46 (a). IR spectrum, ν, cm^{-1}: 1627 (C=O), 3321 (NH_2). ^{1}H NMR spectrum, δ, ppm, *Hz*: 1.29 (d, 6H, J = 6.0, 2×CH_3); 2.23 (s, 3H, CH_3-Ar); 4.51 (sp, 1H, J = 6.0, OCH); 5.46 (s, 1H, CH); 5.96 (br., 2H, NH_2); 6.74-6.79 (m, 2H, $C_6H_4OC_3H_7$); 6.93-6.98 (m, 2H, *p*-C_6H_5); 7.11-7.17 (m, 1H, *p*-C_6H_5); 7.25-7.30 (m, 2H, $C_6H_4OC_3H_7$); 7.31-7.40 (m, 4H, $C_6H_4CH_3$ и *m*-C_6H_5); 7.58-7.62 (m, 2H, *o*-C_6H_5). ^{13C} NMR spectrum δ_c, ppm: 20.2 (CH_3); 21.6 and 21.6 (2×CH_3); 62.0 (NCH); 68.6 (OCH); 98.4; 115.1 (2×CH); 119.8 (2×CH); 124.6 (CH); 127.4 (2×CH); 127.6 (2×CH); 128.1 (2×CH); 128.3 (2×CH). Found, %: C 78.51; H 6.39; N 7.19. $C_{26}H_{26}N_2O_2$. Calculated, %: C 78.36; H 6.58; N 7.03.

4-Amino-5-(4-isopropoxyphenyl)-3-phenyl-1-*o*-tolyl-1*H*-pyrrol-2(5*H*)-one (20). Yield 68%, mp 198-200°C, R_f 0.45 (a). IR spectrum, ν, cm^{-1}: 1632 (C=O), 3297 (NH_2). ^{1}H NMR spectrum, δ, ppm, *Hz*: 1.30 (d, 6H, *J* = 6.0, 2×CH_3); 2.13 (s, 3H, CH_3-Ar); 4.53 (sp, 1H, *J* = 6.0, OCH); 5.29 (s, 1H, CH); 5.90 (br., 2H, NH_2); 6.73-6.78 (m, 2H, $C_6H_4OC_3H_7$); 6.97-7.20 (m, 7H, Ar); 7.33-7.39 (m, 2H, Ar); 7.65-7.70 (m, 2H, Ar). ^{13}C NMR spectrum δ_c, ppm: 18.2 (CH_3); 21.6 (2×CH_3); 64.4 (NCH); 68.7 (OCH); 98.9; 114.9 (2×CH); 124.6 (CH); 125.3 (CH); 125.9 (CH); 127.4 (2×CH); 127.5 (2×CH); 128.3; 129.2 (2×CH); 130.0 (CH); 133.0; 136.6; 136.7; 157.3; 158.8; 169.4. Found, %: C 78.18; H 6.46; N 6.82. $C_{26}H_{26}N_2O_2$. Calculated, %: C 78.36; H 6.58; N 7.03.

4-Amino-1-(3,5-dimethylphenyl)-5-(4-isopropoxyphenyl)-3-phenyl-1*H*-pyrrol-2(5*H*)--one (21). Yield 87%, mp 198-200°C, R_f 0.64 (a). IR spectrum, ν, cm^{-1}: 1639 (C=O), 3302 (NH_2). ^{1}H NMR spectrum, δ, ppm, *Hz*: 1.29 (d, 6H, *J* = 6.0, 2×CH_3); 2.21 (t, 6H, *J* = 0.5, CH_3-Ar); 4.51 (sp, 1H, *J* = 6.0, OCH); 5.45 (s, 1H, CH); 5.96 (br., 2H, NH_2); 6.51 (m, 1H, 4-H $C_6H_3(CH_3)_2$); 6.75-6.80 (m, 2H, C_6H_4); 7.11 (br., 2H, 2,2′-H $C_6H_3(CH_3)_2$); 7.12-7.17 (m, 1H, 4-H C_6H_4); 7.25-7.30 (m, 2H, C_6H_4); 7.30-7.37 (m, 2H, *m*- C_6H_5); 7.57-7.62 (m, 2H, *o*- C_6H_5). ^{13}C NMR spectrum δ_c, ppm: 21.1 (2×CH_3); 21.66 (CH_3); 21.71 (CH_3); 62.1 (NCH); 68.7 (OCH); 98.5; 115.2 (2×CH); 117.9 (2×CH); 123.6; 124.7; 127.5 (2×CH); 127.7 (2×CH); 128.2 (2×CH); 128.8; 132.8; 136.6; 138.2; 157.2; 159.1; 169.7. Found, %: C 78.44; H 6.93; N 6.70. $C_{27}H_{28}N_2O_2$. Calculated, %: C 78.61; H 6.84; N 6.79.

4-amino-5-(4-isopropoxyphenyl)-1-(2-methoxyphenyl)-3-phenyl-1*H*-pyrrol-2(5*H*)- -one (22). Yield 64%, mp 210-212°C, R_f 0.64 (b). IR spectrum, ν, cm^{-1}: 1640 (C=O), 3268 (NH_2). ^{1}H NMR spectrum, δ, ppm, *Hz*: 1.28 (d, 3H, *J* = 6.0, CH_3); 1.29 (d, 3H, *J* = 6.0, CH_3); 3.86 (s, 3H, OCH_3); 4.50 (sp, 1H, *J* = 6.0, OCH); 5.52 (s, 1H, CH); 5.87 (br., 2H, NH_2); 6.71-6.76 (m, 2H, $C_6H_4OC_3H_7$); 6.80 (ddd, 1H, *J* = 7.9, *J* = 7.2, *J* = 1.3, $C_6H_4OCH_3$); 6.88-6.92 (m, 1H, $C_6H_4OCH_3$); 7.06-7.18 (m, 5H, Ar); 7.32-7.38 (m, 2H, *m*- C_6H_5); 7.63-7.67 (m, 2H, *o*-C_6H_5). ^{13}C NMR spectrum δ_c, ppm: 21.59 (CH_3); 21.62 (2×CH_3); 55.0 (OCH_3); 63.2 (NCH); 68.6 (OCH); 98.5; 111.3; 114.8 (2×CH); 119.6; 124.5; 126.1; 126.3; 127.4 (2×CH); 128.5; 128.8; 129.6; 133.1; 154.5; 157.1; 159.1; 169.9. Found, %: C 75.21; H 6.13; N 6.58. $C_{26}H_{26}N_2O_3$. Calculated, %: C 75.34; H 6.32; N 6.76.

4-ԱՄԻՆՈ-1,3,5-ՏՐԻԱՐԻԼ-1Հ-ՊԻՐՐՈԼ-2(5Հ)-ՈՆՆԵՐԻ ՍԻՆԹԵԶԸ ԵՎ ՆՐԱՆՑ ՀԱԿԱՄԱՆՐԷԱՅԻՆ ԱԿՏԻՎՈՒԹՅՈՒՆԸ

Մ. Վ. ԱԼԵՔՍԱՆՅԱՆ, Գ. Կ. ՀԱՐՈՒԹՅՈՒՆՅԱՆ, Ս. Պ. ԳԱՍՊԱՐՅԱՆ, Ն. Մ. ՍՏԵՓԱՆՅԱՆ և Ռ. Ե. ՄՈՒՐԱԴՅԱՆ

Ֆենիլքացախաթթվի քլորանհիդրիդով α-ամինոնիտրիլների ացիլմամբ և կալիումի հիդրօքսիդի առկայությամբ հետագա ներմոլեկուլային ցիկլման արդյունքում իրակա-նացվել է 4-ամինո-1,3,5-տրիարիլ-1Հ-պիրրոլ-2(5Հ)-ոննների սինթեզ և հետազոտվել են

սինթեզված միացությունների հակամանրէային հատկությունները: Ըստ կենսաբանական արդյունքների, ամենաբարձր ակտիվություն ցուցաբերել է 4-ամինո-5-(4-իզոպրոպօքսիֆենիլ)-3-ֆենիլ-1-օ-տոլիլ-1H-պիրրոլ-2(5H)-ոնը, ճնշելով գրամդրական միկրոօրգանիզմների աճը d = 17-18 մմ տրամագծով գոտում, մնացած ածանցյալներն օժտված են թույլ հակամանրէային ակտիվությամբ կամ ընդհանրապես զուրկ են ակտիվությունից:

СИНТЕЗ И АНТИБАКТЕРИАЛЬНАЯ АКТИВНОСТЬ 4-АМИНО-1,3,5-ТРИАРИЛ-1Н-ПИРРОЛ-2(5Н)-ОНОВ

М. В. АЛЕКСАНЯН, Г. К. АРУТЮНЯН, С. П. ГАСПАРЯН, Г. М. СТЕПАНЯН и Р. Е. МУРАДЯН

Научно-технологический центр органической и фармацевтической химии
НАН Республики Армения
Армения, 0014, Ереван, пр. Азатутян, 26
E-mail: g_sahak@yahoo.com

Ацилированием α-аминонитрилов хлорангидридом фенилуксусной кислоты и последующей внутримолекулярной циклизацией в присутствии едкого калия осуществлен синтез 4-амино-1,3,5-триарил-1*H*-пиррол-2(5*H*)-онов. Изучена антибактериальная активность синтезированных соединений, среди которых наиболее активным является 4-амино--5-(4-изопропоксифенил)-3-фенил-1-*о*-толил-1*H*-пиррол-2(5*H*)-он, подавляющий рост грамположительных микроорганизмов в зоне диаметром d = 17-18 *мм*. Остальные производные малоактивны или вовсе лишены антибактериальной активности.

REFERENCES

[1] *Zali-Boeini H., Mobin M., Hajibabaei K., Ghani M.* // *J. Org. Chem.*, 2012, v. 77, №13, p. 5808.
[2] *Howard E.G., Lindsey R.V., Teobald C.W.* // *J. Am. Chem. Soc.*, 1959, v. 81, №16, p. 4355.
[3] *Gilbert J.C., Blackburn B.K.* // *J. Org. Chem.*, 1986, v. 51, №19, p. 3656.
[4] *Huisgen R., Mloston G., Langhals E.* // *J. Org. Chem.*, 1986, v. 51, №21, p. 4087.
[5] *Hill L., Hunter G.A., Haider S. I., McNab H., O'Neill W.J.* // *Synthesis*, 2009, p. 2531.
[6] *Soliman F.S.G., Kappe T.* // *Monatsh. Chem.* 1982, v. 113, №4, p. 475.
[7] Guidelines for conducting preclinical studies of drugs / by ed. Mironova A.N., M., Medicine, 2012, p. 509.
[8] *Mashkovsky M.D.* // Medicinal products. M., New Wave, 2010, p. 851.
[9] *Gasparyan S.P., Alexanyan M.V., Harutyunyan G.K., Hovhanesyan V.Ye., Martirosyan V.V., Paronikyan R.V., Stepanyan H.M., Martirosyan A.H.* // *Pharm. Chem. J.*, 2012, v. 46, №6, p. 331.
[10] *Gasparyan S.P.* // *Chem. J. of Armenia*, 2014, v. 67, №1, p. 111.
[11] *Gasparyan S.P., Alexanyan M.V., Harutyunyan G.K., Hovhanesyan V.Ye., Martirosyan A.H., Panosyan H.A.* // *Chem. J. of Armenia*, 2014, v. 67, №2-3, p. 239.
[12] *Gasparyan S.P.* // *Chem. J. of Armenia*, 2016, v. 69, №3, p. 333.
[13] *Martirosyan A.H., Gasparyan S.P., Alexanyan M.V., Harutyunyan G.K., Panosyan H.A., Schinazi R.F.* // *Med. Chem. Res.*, 2017, v. 26, №1, p. 101.