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Electrophilic Intramolecular Cyclization of Functional Derivatives of Unsaturated Compounds: V.* Cyclization of Anilides of Styrylacetic Acids in Polyphosphoric Acid

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Abstract— Anilides of styrylacetic acids at heating in polyphosphoric acid undergo an intramolecular cyclization giving 1,5-diarylpyrrolidin-2-ones, 5-aryl-1,3,4,5-tetrahydro-2*H*-benzazepin-2-ones, and 5-(3-fluorophenyl) dihydrofuran-2(3*H*)-one, where the ratio of the products depends on the character of the aromatic substituents in the amide and styrene fragments of the substrate.

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In the series of styrylacetic acids an important place belongs to amides whose biologic properties are governed as a rule by the chemical versatility of the amide fragment. The efforts of researchers directed to its structural modification made it possible to develop the methods of the synthesis of inhibitors of histone deacetylase [2], monoamine oxidase [3], and also substances stimulating the cardiovascular system [4] and exhibiting antitumor [5] activity. However the styrylacetamides as original polyfunctional systems containing several nucleophilic sites remain poorly studied. In particular, the literature contains only information on the reaction of *N*-arylamides of styrylacetic acids with sulfenyl chlorides that depending on the conditions proceeds either as addition [6] or as electrophilic cyclization [7]. In the latter case along with the intramolecular transformation involving the oxygen atom of the amide group a cyclization reaction also occurs with the participation of the *ortho*-carbon atom of *N*-arylamide.

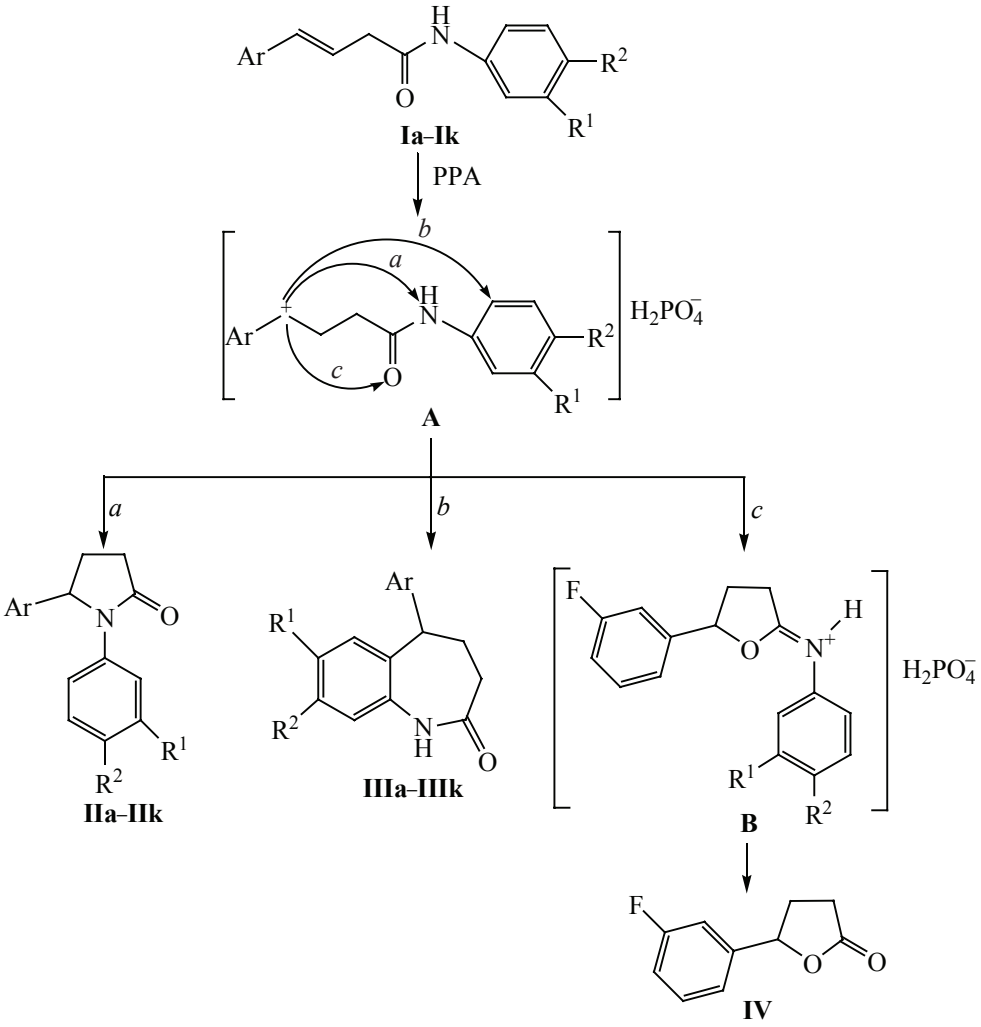
With the goal to extend the synthetic potential of the styrylacetic acid anilides and to search for convenient paths to synthesize on their basis important heterocyclic systems we investigated in this study their proton-initialed cyclization under the action of polyphosphoric acid (PPA). PPA is an efficient cyclizing reagent and simultaneously a good polar solvent and proton donor [8]. Formerly PPA was successfully applied to lactonization [9] and lactamization [10] of amides of unsaturated carboxylic acids.

As the principal objects of the study we selected amides **Ia–Ik** containing diverse by the nature aryl substituents in the styrene and the amide fragments. It was established experimentally that their virtually 100% conversion in the reaction products occurred within 1 h at heating in PPA at 105–110°C. Analysis of the reaction products by the GC-MS method after the treatment of the reaction mixture with water and extraction with dichloromethane (see the table) showed that from amides **Ia, Ib, Id–Ig, Ii, Ij** a mixture formed containing pyrrolidin-2-ones **IIa, IIb, IId–IIg, IIi, IIj** and benzazepin-2-ones **IIIa, IIIb, IIId–IIIg, IIIi, IIIj**. Amides **Ic, Ih** along with pyrrolidin-2-ones **IIc, IIh** and benzazepin-2-ones **IIIc, IIIh** furnished also furan-2-one **IV** (see the scheme).

The versatility of the transformation products originates from operation of three possible cyclization routes of the carbocation **A** primary formed by the

* For Communication IV, see [1].

Scheme.



$R^1 = R^2 = H$, Ar = Ph (a), 2-FC_6H_4 (b), 3-FC_6H_4 (c), 4-FC_6H_4 (d), 4-MeC_6H_4 (e); $R^1 = R^2 = MeO$, Ar = Ph (f), 2-FC_6H_4 (g), 3-FC_6H_4 (h), 4-FC_6H_4 (i), 4-MeC_6H_4 (j); $R^1 = H$, $R^2 = EtOC(O)$, Ar = Ph (k).

Composition (%) of products of amides **Ia–Ik** cyclization in PPA according to GC-MS data

Initial amide	Pyrrolidin-2-ones **IIa–IIk**	Benzazepin-2-ones **IIIa–IIIk**	Furan-2-ones **IV**
Ia	37	60	–
Ib	18	80	–
Ic	53	29	17
Id	53	44	–
Ie	92	7	–
If	15	83	–
Ig	13	75	–
Ih	23	55	21
Ii	33	66	–
Ij	56	42	–
Ik	90	5	–

protonation of the multiple bond. The dominant among these paths is the attack of C^+ on the amide nitrogen atom (path *a*) or on the *ortho*-position of the *N*-aryl substituent (path *b*). The attack on the amide oxygen atom (path *c*) is less favorable probably because of its additional protonation, and it leads to the formation of an easily hydrolysable iminium salt **B** (see the scheme).

As seen from the table, the ratio of the reaction products depends on the character of the aryl substituents in the amide and styrene fragments of compounds **I**. From the unsubstituted anilide **Ia** pyrrolidinone **IIa** and benzazepinone **IIIa** formed in the ratio 37:60. The increased electron density in the *ortho*-position of the *N*-aryl substituent in compound **If** originating from the donor effect of the methoxy groups results in the growth

of the fraction of benzazepine **IIIf** in the reaction mixture to 83%, and *vice versa*, in the presence of the electron-acceptor ethoxycarbonyl substituent in compound **Ik** the fraction of pyrrolidinone **IIk** reaches 90%. The comparison of compounds **Ia** and **Ie**, and also **If** and **Ik** shows that at the same *N*-aryl substituent the growth of the donor effect of the styrene substituent of the amides **Ie, Ik** (Ar = 4-MeC_6H_4) also results in the increased yield of pyrrolidinones **IIe, IIk** by 55 and 41% respectively.

In its turn the introduction of a fluorine atom in the *ortho*-position of the aryl fragment in the styrene part of the molecule of compound **Ib** results in the increased by 20% yield of benzazepine **IIIb** as compared to a benzazepine **IIIa**. However in the case of compound **Ig** with more electron-donor *N*-aryl substituent the fraction of benzazepine **IIIg** is by 8% less than that of benzazepine **IIIf**. The presence of the fluorine atom in the *para*-position (compounds **Id, Ii**) independent of the character of the *N*-aryl substituent leads to the increased fraction of pyrrolidines **IId, IIi** by 16–17% and to the analogous decrease in the fraction of benzazepines **IIId, IIIi**. *meta*-Fluoroaryl substituents of compounds **Ic, Ih** direct the cyclization both to the increase in the fraction of pyrrolidines **IIc, IIh** and to the formation of a considerable amount of furanone **IV**.

The column chromatography proved to be an efficient method of preparative separation of the reaction mixture, and it was sufficient for isolation and identification of all cyclization products except for benzazepine **IIIk** whose amount reached 5% (according to GC-MS data).

The structure of pyrrolidin-2-ones **IIa–IIk**, benzazepin-2-ones **IIIa–IIIj**, and furan-2-one (**IV**) was proved by their spectral evaluation as well as by the agreement of the physicochemical characteristics of formerly known compounds **IIa** and **IIIa** to the published data [11] and [12, 13] respectively. In the ^{1}H NMR spectra of compounds **IIa–IIk** alongside the typical signals of aromatic substituents multiplets of the protons of the methylene (1.79–2.79 ppm) and methine (5.08–5.72 ppm) groups are observed, and in the ^{13}C NMR spectra the signals appear belonging to the pyrrolidinone ring, δ, ppm: 27–29 (C^4), 30–32 (C^3), 57–63 (C^5), 174–175 (C^2). The ^{1}H NMR spectra of diazepinones **IIIa–IIIj** are characterized by the multiplets of methylene (2.18–2.57 ppm) and methine (4.09–4.50 ppm) protons, and the ^{13}C NMR spectra contain characteristic carbon atoms of the azepine ring, δ, ppm: 30–33 (C^3), 33–34 (C^4), 37–45 (C^5), 173–175 (C^2).

Therefore the cyclization of anilides of styrylacetic acids under the action of PPA can be regarded as a convenient one-stage method of the synthesis of 1,5-diaryl-substituted pyrrolidin-2-ones and of derivatives of 5-arylbenzazepin-2-one. It has significant advantage compared to the methods of preparation of 1,5-disubstituted lactams [11, 14–17] as well as of 5-arylbenzazepinones [12, 13, 18, 19].

EXPERIMENTAL

IR spectra were recorded on a spectrophotometer UR-20 from pellets with KBr. ^{1}H and ^{13}C NMR spectra were registered on a spectrometer Varian VXR-400 (399.97 and 125.74 MHz respectively), internal reference TMS. GC-MS measurements were carried out on an instrument Agilent110\DAD\HSD\VLG 119562.

Cyclization of anilides Ia–Ik. In 45 g of PPA 5 mmol of anilide **Ia–Ik** was heated for 1 h on an oil bath at 105–110°C. The reaction mixture was slowly cooled and poured on ice. The formed solid reaction product was extracted with dichloromethane, the solvent was distilled off, and the residue was chromatographed on silica gel, eluent chloroform–methanol, 25:1.

1,5-Diphenylpyrrolidin-2-one (IIa). Yield 0.43 g (36%), mp 108–110 °C (110–112°C [11]). IR spectrum, cm^{-1}: 1720, 1600, 1510, 1360, 1330, 1240, 1160. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.82–1.88 m (1H, CH), 2.51–2.67 m (3H, CH, CH_2), 5.45–5.48 m (1H, C^5H), 7.04 t ($1H_{arom}$, *J* 7.0 Hz), 7.20–7.30 m ($7H_{arom}$), 7.46 d ($2H_{arom}$, *J* 9.0 Hz). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 29.02 (C^4), 31.33 (C^3), 62.85 (C^5), 122.80 ($2C_{arom}$), 124.89 (C_{arom}), 126.66 ($2C_{arom}$), 127.86 (C_{arom}), 128.87 ($2C_{arom}$), 129.19 ($2C_{arom}$), 138.76 (C_{arom}), 142.41 (C_{arom}), 174.58 (C^2). Mass spectrum: *m/z* 238 $[M + 1]^+$. Found, %: C 80.76; H 6.25; N 5.67. $C_{16}H_{15}NO$. Calculated, %: C 80.98; H 6.37; N 5.90. *M* 237.296.

5-(2-Fluorophenyl)-1-phenylpyrrolidin-2-one (IIb). Yield 0.20 g (16%), mp 95–97 °C. IR spectrum, cm^{-1}: 1690, 1590, 1490, 1460, 1390, 1350, 1300, 1240, 1230, 1180, 1100, 1050. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.89–1.97 m (1H, CH), 2.53–2.69 m (3H, CH, CH_2), 5.67–5.72 m (1H, C^5H), 7.05–7.12 m ($2H_{arom}$), 7.15–7.20 m ($1H_{arom}$), 7.23–7.30 m ($4H_{arom}$), 7.43 d ($2H_{arom}$, *J* 8.4 Hz). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 27.18 (C^4), 31.26 (C^3), 57.33 (C^5), 116.23 d (C_{arom}–F, *J* 21.25 Hz), 122.67 ($2C_{arom}$), 125.16 (C_{arom}), 125.20 (C_{arom}), 128.49 d (C_{arom}–F, *J* 3.75 Hz), 128.79 d (C_{arom}–F, *J* 12.50 Hz), 129.00 ($2C_{arom}$), 130.01 d (C_{arom}–F, *J* 8.75 Hz), 138.49 (C_{arom}), 160.32 d (C_{arom}–F, *J* 243.75 Hz), 174.40

(C^2). Mass spectrum: *m/z* 256 $[M + 1]^+$. Found, %: C 75.14; H 5.48; N 5.41. $C_{16}H_{14}FNO$. Calculated, %: C 75.28; H 5.53; N 5.49. *M* 255.287.

5-(3-Fluorophenyl)-1-phenylpyrrolidin-2-one (IIc). Yield 0.54 g (42%), mp 78–80 °C. IR spectrum, cm^{-1}: 3080, 2970, 1710, 1600, 1500, 1450, 1360, 1320, 1290, 1250, 1220, 1150, 1120, 1060, 960. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.94–2.01 m (1H, CH), 2.56–2.66 m (2H, CH_2), 2.71–2.79 m (1H, CH), 5.21–5.25 m (1H, C^5H), 6.89–6.91 m ($2H_{arom}$), 6.99 d ($2H_{arom}$, *J* 7.6 Hz), 7.06 t ($1H_{arom}$, *J* 7.6 Hz), 7.23–7.26 m ($3H_{arom}$), 7.39 d ($2H_{arom}$, *J* 7.6 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 29.00 (C^4), 31.09 (C^3), 63.33 (C^5), 113.01 d (C_{arom}–F, *J* 21.25 Hz), 114.77 d (C_{arom}–F, *J* 21.25 Hz), 121.59 d (C_{arom}–F, *J* 2.50 Hz), 122.12 ($2C_{arom}$), 125.07 (C_{arom}), 128.78 ($2C_{arom}$), 130.66 d (C_{arom}–F, *J* 8.75 Hz), 138.04 (C_{arom}), 144.18 d (C_{arom}–F, *J* 6.25 Hz), 163.20 d (C_{arom}–F, *J* 246.25 Hz), 174.65 (C^2). Mass spectrum: *m/z* 256 $[M + 1]^+$. Found, %: C 75.11; H 5.46; N 5.44. $C_{16}H_{14}FNO$. Calculated, %: C 75.28; H 5.53; N 5.49. *M* 255.287.

5-(4-Fluorophenyl)-1-phenylpyrrolidin-2-one (IId). Yield 0.61 g (48%), mp 67–69 °C. IR spectrum, cm^{-1}: 1700, 1610, 1520, 1430, 1380, 1240, 1150. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.80–1.89 m (1H, CH), 2.51–2.69 m (3H, CH, CH_2), 5.44–5.52 m (1H, C^5H), 7.03–7.07 m ($1H_{arom}$), 7.11 t ($2H_{arom}$, *J* 8.0 Hz), 7.26 t ($2H_{arom}$, *J* 8.0 Hz), 7.31–7.34 m ($2H_{arom}$), 7.41 d ($2H_{arom}$, *J* 8.4 Hz). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 28.99 (C^4), 31.30 (C^3), 62.16 (C^5), 115.95 d ($2C_{arom}$–F, *J* 21.25 Hz), 123.00 ($2C_{arom}$), 125.0 (C_{arom}), 128.81 d ($2C_{arom}$–F, *J* 8.70 Hz), 128.88 ($2C_{arom}$), 138.50 (C_{arom}), 138.57 (C_{arom}), 161.81 d (C_{arom}–F, *J* 242.50 Hz), 174.48 (C^2). Mass spectrum: *m/z* 256 $[M + 1]^+$. Found, %: C 75.17; H 5.49; N 5.48. $C_{16}H_{14}FNO$. Calculated, %: C 75.28; H 5.53; N 5.49. *M* 255.287.

5-(4-Methylphenyl)-1-phenylpyrrolidin-2-one (IIe). Yield 0.89 g (71%), mp 119–120 °C. IR spectrum, cm^{-1}: 1690, 1600, 1510, 1390, 1360, 1240, 1160, 1120. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.80–1.86 m (1H, CH), 2.23 c (3H, CH_3), 2.53–2.66 m (3H, CH, CH_2), 5.39–5.43 m (1H, C^5H), 7.04 t ($1H_{arom}$, *J* 7.6 Hz), 7.09 d ($2H_{arom}$, *J* 7.6 Hz), 7.15 d ($2H_{arom}$, *J* 8.0 Hz), 7.25 t ($2H_{arom}$, *J* 8.0 Hz), 7.42 d ($2H_{arom}$, *J* 8.0 Hz). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 21.09 (CH_3), 29.08 (C^4), 31.35 (C^3), 62.66 (C^5), 122.78 ($2C_{arom}$), 124.83 (C_{arom}), 126.58 ($2C_{arom}$), 128.84 ($2C_{arom}$), 129.76 ($2C_{arom}$), 137.02 (C_{arom}), 138.79 (C_{arom}), 139.36 (C_{arom}), 174.53 (C^2). Mass spectrum: *m/z* 252 $[M + 1]^+$. Found, %: C 81.16; H 6.74; N 5.48. $C_{17}H_{17}NO$. Calculated, %: C 81.24; H 6.82; N 5.57. *M* 251.323.

1-(3,4-Dimethoxyphenyl)-5-phenylpyrrolidin-2-one (IIf). Yield 0.19 g (13%), oily substance. IR spectrum, cm^{-1}: 2950, 1700, 1610, 1520, 1460, 1400, 1320, 1250, 1180, 1150, 1110, 1080, 1030. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.96–2.04 m (1H, CH), 2.55–2.61 m (2H, CH_2), 2.71–2.78 m (1H, CH), 3.74 s, 3.76 s (6H, $2OCH_3$), 5.12–5.17 m (1H, C^5H), 6.65–6.72 m ($2H_{arom}$), 7.13–7.29 m ($6H_{arom}$). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 28.98 (C^4), 31.20 (C^3), 55.84 (OCH_3), 55.91 (OCH_3), 64.55 (C^5), 107.26 (C_{arom}), 110.93 (C_{arom}), 114.75 (C_{arom}), 126.08 ($2C_{arom}$), 127.82 (C_{arom}), 128.95 ($2C_{arom}$), 131.63 (C_{arom}), 141.51 (C_{arom}), 146.37 (C_{arom}), 148.72 (C_{arom}), 174.77 (C^2). Mass spectrum: *m/z* 298 $[M + 1]^+$. Found, %: C 72.67; H 6.33; N 4.66. $C_{18}H_{19}NO_3$. Calculated, %: C 72.71; H 6.44; N 4.71. *M* 297.348.

1-(3,4-Dimethoxyphenyl)-5-(2-fluorophenyl)-pyrrolidin-2-one (IIg). Yield 0.17 g (11%), mp 75–77 °C. IR spectrum, cm^{-1}: 1690, 1530, 1460, 1410, 1320, 1230, 1180, 1120, 1040. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.00–2.08 m (1H, CH), 2.58–2.63 m (2H, CH_2), 2.71–2.77 m (1H, CH), 3.76 s, 3.78 s (6H, $2OCH_3$), 5.49–5.54 m (1H, C^5H), 6.67–6.77 m ($2H_{arom}$), 7.00–7.06 m ($2H_{arom}$), 7.12–7.16 m ($1H_{arom}$), 7.19–7.23 m ($2H_{arom}$). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 27.31 (C^4), 31.15 (C^3), 55.82 (OCH_3), 55.90 (OCH_3), 57.99 d (C^5–F, *J* 5.00 Hz), 106.83 (C_{arom}), 111.00 (C_{arom}), 114.34 (C_{arom}), 115.80 d (C_{arom}–F, *J* 21.25 Hz), 124.53 d (C_{arom}–F, *J* 3.75 Hz), 127.39 d (C_{arom}–F, *J* 3.75 Hz), 128.19 d (C_{arom}–F, *J* 13.75 Hz), 129.44 d (C_{arom}–F, *J* 7.50 Hz), 131.37 (C_{arom}), 146.44 (C_{arom}), 148.81 (C_{arom}), 160.20 d (C_{arom}–F, *J* 245.00 Hz), 174.57 (C^2). Mass spectrum: *m/z* 316 $[M + 1]^+$. Found, %: C 68.52; H 5.63; N 4.36. $C_{18}H_{18}FNO_3$. Calculated, %: C 68.56; H 5.75; N 4.44. *M* 315.339.

1-(3,4-Dimethoxyphenyl)-5-(3-fluorophenyl)-pyrrolidin-2-one (IIh). Yield 0.33 g (21%), oily substance. IR spectrum, cm^{-1}: 2950, 1700, 1590, 1520, 1450, 1390, 1320, 1260, 1220, 1140, 1120, 1030. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.96–2.00 m (1H, CH), 2.56–2.65 m (2H, CH_2), 2.70–2.77 m (1H, CH), 3.76 s (6H, $2OCH_3$), 5.14–5.17 m (1H, C^5H), 6.68–6.71 m ($2H_{arom}$), 6.91–6.92 m ($2H_{arom}$), 6.99–7.00 m ($1H_{arom}$), 7.15–7.17 m ($1H_{arom}$), 7.23–7.26 m ($1H_{arom}$). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 28.66 (C^4), 30.93 (C^3), 55.85 (OCH_3), 55.90 (OCH_3), 63.94 (C^5), 107.20 (C_{arom}), 110.98 (C_{arom}), 113.07 d (C_{arom}–F, *J* 22.50 Hz), 114.64 (C_{arom}), 114.80 d (C_{arom}–F, *J* 21.25 Hz), 121.70 d (C_{arom}–F, *J* 2.50 Hz), 130.61 d (C_{arom}–F, *J* 8.75 Hz), 131.34 (C_{arom}),

144.27 d (C_{arom}–F, *J* 7.50 Hz), 146.51 (C_{arom}), 148.80 (C_{arom}), 163.14 d (C_{arom}–F, *J* 246.25 Hz), 174.61 (C^2). Mass spectrum: *m/z* 316 $[M + 1]^+$. Found, %: C 68.53; H 5.69; N 4.37. $C_{18}H_{18}FNO_3$. Calculated, %: C 68.56; H 5.75; N 4.44. *M* 315.339.

1-(3,4-Dimethoxyphenyl)-5-(4-fluorophenyl)-pyrrolidin-2-one (IIi). Yield 0.30 g (19%), oily substance. IR spectrum, cm^{-1}: 2980, 1710, 1610, 1520, 1450, 1330, 1270, 1240, 1180, 1120, 1040, 920. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.84–1.92 m (1H, CH), 2.48–2.56 m (2H, CH_2), 2.60–2.68 m (1H, CH), 3.68 s, 3.69 s (6H, $2OCH_3$), 5.08–5.11 m (1H, C^5H), 6.61–6.65 m ($1H_{arom}$), 6.90 t ($2H_{arom}$, *J* 8.5 Hz), 7.04–7.06 m ($1H_{arom}$), 7.11–7.13 m ($2H_{arom}$). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 28.92 (C^4), 31.05 (C^3), 55.79 (OCH_3), 55.82 (OCH_3), 63.94 (C^5), 107.46 (C_{arom}), 110.98 (C_{arom}), 114.95 (C_{arom}), 115.77 d ($2C_{arom}$–F, *J* 21.25 Hz), 127.79 d ($2C_{arom}$–F, *J* 8.75 Hz), 131.33 (C_{arom}), 137.23 d (C_{arom}–F, *J* 2.50 Hz), 146.47 (C_{arom}), 148.74 (C_{arom}), 162.07 d (C_{arom}–F, *J* 245.00 Hz), 174.57 (C^2). Mass spectrum: *m/z* 316 $[M + 1]^+$. Found, %: C 68.51; H 5.66; N 4.33. $C_{18}H_{18}FNO_3$. Calculated, %: C 68.56; H 5.75; N 4.44. *M* 315.339.

1-(3,4-Dimethoxyphenyl)-5-(4-methylphenyl)-pyrrolidin-2-one (IIj). Yield 0.83 g (53%), mp 109–111 °C. IR spectrum, cm^{-1}: 2950, 1690, 1610, 1530, 1450, 1390, 1360, 1250, 1180, 1140, 1110, 1030, 990. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.79–1.86 m (1H, CH), 2.23 s (3H, CH_3), 2.51–2.67 m (3H, CH, CH_2), 3.65 s, 3.66 s (6H, $2OCH_3$), 5.33–5.36 m (1H, C^5H), 6.80 s ($2H_{arom}$), 7.09–7.17 m ($5H_{arom}$). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 21.09 (CH_3), 28.90 (C^4), 31.33 (C^3), 55.98 ($2OCH_3$), 63.17 (C^5), 108.29 (C_{arom}), 111.87 (C_{arom}), 115.58 (C_{arom}), 126.75 ($2C_{arom}$), 129.68 ($2C_{arom}$), 132.04 (C_{arom}), 137.00 (C_{arom}), 139.58 (C_{arom}), 146.29 (C_{arom}), 148.68 (C_{arom}), 174.24 (C^2). Mass spectrum: *m/z* 312 $[M + 1]^+$. Found, %: C 73.14; H 6.75; N 4.47. $C_{19}H_{21}NO_3$. Calculated, %: C 73.29; H 6.80; N 4.50. *M* 311.375.

Ethyl 4-(2-oxo-5-phenylpyrrolidin-1-yl)-benzoate (IIk). Yield 1.26 g (83%), mp 108–110 °C. IR spectrum, cm^{-1}: 1720, 1690, 1610, 1520, 1460, 1390, 1360, 1280, 1240, 1180, 1110, 1030. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.26 t (3H, CH_3, *J* 6.9 Hz), 1.83–1.91 m (1H, CH), 2.53–2.73 m (3H, CH, CH_2), 4.24 q (2H, CH_2, *J* 6.9 Hz), 5.51–5.55 m (1H, C^5H), 7.19–7.32 m ($5H_{arom}$), 7.60 d ($2H_{arom}$, *J* 9.3 Hz), 7.82 d ($2H_{arom}$, *J* 9.3 Hz). ^{13}C NMR spectrum, δ, ppm: 14.61 (CH_3), 28.89 (C^4), 31.41 (C^3), 60.98 (CH_2), 62.58 (C^5), 121.71 ($2C_{arom}$), 125.68 (C_{arom}), 126.52 ($2C_{arom}$), 127.95 (C_{arom}), 129.26 ($2C_{arom}$), 130.03 ($2C_{arom}$), 141.92 C_{arom}), 142.93 (C_{arom}), 165.64 ($C_{эфирн.}$=O), 175.13 (C^2). Mass spectrum: *m/z* 310 $[M + 1]^+$. Found, %: C 73.66; H 6.09; N 4.47. $C_{19}H_{19}NO_3$. Calculated, %: C 73.77; H 6.19; N 4.53. *M* 309.359.

5-Phenyl-1,3,4,5-tetrahydro-2*H*-1-benzazepin-2-one (IIIa). Yield 0.69 g (58%), mp 179–181 °C (179–180 °C [13]). IR spectrum, cm^{-1}: 3200, 3090, 1690, 1490, 1390, 1250, 1170. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 2.18–2.44 m (4H, $2CH_2$), 4.22–4.28 m (1H, C^5H), 6.67 d ($1H_{arom}$, *J* 7.8 Hz), 6.97–7.03 m ($2H_{arom}$), 7.19 t ($1H_{arom}$, *J* 7.8 Hz), 7.30–7.41 m ($5H_{arom}$), 9.65 s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 30.30 (C^3), 33.78 (C^4), 45.35 (C^5), 122.26 (C^9), 124.93 (C^7), 127.32 (C^8), 127.39 (C_{arom}), 128.59 (C^6), 128.97 ($2C_{arom}$), 129.30 ($2C_{arom}$), 136.50 (C^{5a}), 138.84 (C^{9a}), 141.87 (C_{arom}), 173.58 (C^2). Mass spectrum: *m/z* 238 $[M + 1]^+$. Found, %: C 80.87; H 6.34; N 5.86. $C_{16}H_{15}NO$. Calculated, %: C 80.98; H 6.37; N 5.90. *M* 237.296.

5-(2-Fluorophenyl)-1,3,4,5-tetrahydro-2*H*-1-benzazepin-2-one (IIIb). Yield 0.96 g (75%), mp 203–205 °C. IR spectrum, cm^{-1}: 3210, 3080, 2980, 1690, 1590, 1490, 1390, 1330, 1230, 1210, 1110, 1040, 960. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 2.20–2.48 m (4H, $2CH_2$), 4.46–4.50 m (1H, C^5H), 6.61 d ($2H_{arom}$, *J* 7.6 Hz), 6.99–7.05 m ($2H_{arom}$), 7.19–7.28 m ($2H_{arom}$), 7.30 t ($2H_{arom}$, *J* 7.6 Hz), 7.37–7.42 m ($1H_{arom}$), 7.58 t ($2H_{arom}$, *J* 7.6 Hz), 9.70 s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 32.74 (C^3), 33.21 (C^4), 38.28 d (C^5F, *J* 2.50 Hz), 116.07 d (C_{arom}–F, *J* 21.25 Hz), 122.38 (C^9), 125.00 d (C_{arom}–F, *J* 3.75 Hz), 125.15 (C^7), 127.51 (C^8), 127.64 (C^6), 128.55 d (C_{arom}–F, *J* 15.00 Hz), 129.48 d (C_{arom}–F, *J* 8.75 Hz), 130.43 d (C_{arom}–F, *J* 3.75 Hz), 135.21 (C^{5a}), 138.78 (C^{9a}), 160.73 d (C_{arom}–F, *J* 243.75 Hz), 173.44 (C^2). Mass spectrum: *m/z* 256 $[M + 1]^+$. Found, %: C 75.22; H 5.45; N 5.39. $C_{16}H_{14}FNO$. Calculated, %: C 75.28; H 5.53; N 5.49. *M* 255.287.

5-(3-Fluorophenyl)-1,3,4,5-tetrahydro-2*H*-1-benzazepin-2-one (IIIc). Yield 0.34 g (27%), mp 191–192 °C. IR spectrum, cm^{-1}: 3200, 3120, 2970, 1690, 1590, 1490, 1460, 1400, 1270, 1220, 1150, 970. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 2.20–2.48 m (4H, $2CH_2$), 4.28–4.33 m (1H, C^5H), 6.69 d ($1H_{arom}$, *J* 8.0 Hz), 7.01–7.04 m ($2H_{arom}$), 7.12–7.24 m ($4H_{arom}$), 7.40–7.45 m ($1H_{arom}$), 9.64 s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 33.21 (C^3), 33.49 (C^4), 45.01 (C^5), 114.10 d (C_{arom}–F, *J* 21.25 Hz), 116.08 d (C_{arom}–F, *J* 21.25 Hz), 122.35 (C^9), 125.02 (C^7), 125.44 d (C_{arom}–F,

J 2.50 Hz), 127.58 (C^8), 128.52 (C^6), 130.78 d (C_{arom}–F, *J* 8.75 Hz), 135.95 (C^{5a}), 138.82 (C^{9a}), 144.96 d (C_{arom}–F, *J* 7.50 Hz), 162.81 d (C_{arom}–F, *J* 241.25 Hz), 173.46 (C^2). Mass spectrum: *m/z* 256 $[M + 1]^+$. Found, %: C 75.23; H 5.51; N 5.47. $C_{16}H_{14}FNO$. Calculated, %: C 75.28; H 5.53; N 5.49. *M* 255.287.

5-(4-Fluorophenyl)-1,3,4,5-tetrahydro-2*H*-1-benzazepin-2-one (IIId). Yield 0.46 g (36%), mp 203–205 °C. IR spectrum, cm^{-1}: 3210, 3080, 1700, 1610, 1520, 1490, 1400, 1310, 1240, 1170, 1110, 1030. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 2.19–2.49 m (4H, $2CH_2$), 4.22–4.36 m (1H, C^5H), 6.66 d ($1H_{arom}$, *J* 7.2 Hz), 7.02 t ($2H_{arom}$, *J* 7.8 Hz), 7.19–7.24 m ($3H_{arom}$), 7.38 t ($2H_{arom}$, *J* 7.8 Hz), 9.66 s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 33.23 (C^3), 33.92 (C^4), 44.53 (C^5), 115.64 d ($2C_{arom}$–F, *J* 21.25 Hz), 122.32 (C^9), 125.03 (C^7), 127.48 (C^8), 128.46 (C^6), 131.09 d ($2C_{arom}$–F, *J* 7.50 Hz), 136.38 (C^{5a}), 137.94 (C_{arom}), 138.75 (C^{9a}), 161.55 d (C_{arom}–F, *J* 241.25 Hz), 173.66 (C^2). Mass spectrum: *m/z* 256 $[M + 1]^+$. Found, %: C 75.26; H 5.44; N 5.48. $C_{16}H_{14}FNO$. Calculated, %: C 75.28; H 5.53; N 5.49. *M* 255.287.

5-(4-Methylphenyl)-1,3,4,5-tetrahydro-2*H*-1-benzazepin-2-one (IIId). Yield 0.08 g (6%), mp 189–190 °C. IR spectrum, cm^{-1}: 3180, 2970, 1685, 1520, 1490, 1400, 1330, 1240, 1210, 1170, 1030, 930. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.37 s (3H, CH_3), 2.43–2.57 m (4H, $2CH_2$), 4.33–4.41 m (1H, C^5H), 6.81 d ($1H_{arom}$, *J* 6.9 Hz), 6.98–7.06 m ($2H_{arom}$), 7.15–7.23 m ($5H_{arom}$), 7.61 br.s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 21.09 (CH_3), 32.85 (C^3), 33.88 (C^4), 44.72 (C^5), 121.85 (C^9), 125.61 (C^7), 127.23 (C^8), 128.75 (C^6), 128.80 ($2C_{arom}$), 129.32 ($2C_{arom}$), 136.66 (C^{5a}), 137.06 (C_{arom}), 137.32 (C_{arom}), 137.96 (C^{9a}), 175.22 (C^2). Mass spectrum: *m/z* 252 $[M + 1]^+$. Found, %: C 81.17; H 6.78; N 5.56. $C_{17}H_{17}NO$. Calculated, %: C 81.24; H 6.82; N 5.57. *M* 251.323.

7,8-Dimethoxy-5-phenyl-1,3,4,5-tetrahydro-2*H*-1-benzazepin-2-one (IIIf). Yield 0.94 g (63%), mp 155–158 °C. IR spectrum, cm^{-1}: 3270, 2950, 1680, 1530, 1460, 1390, 1270, 1230, 1130, 1020. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 2.18–2.43 m (4H, $2CH_2$), 3.48 s, 3.72 s (6H, $2OCH_3$), 4.17–4.21 m (1H, C^5H), 6.26 s (1H, C^6H), 6.66 s (1H, C^9H), 7.28–7.40 m ($5H_{arom}$), 9.35 s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 33.32 (C^3), 33.95 (C^4), 45.08 (C^5), 56.10 (OCH_3), 56.14 (OCH_3), 107.26 (C^9), 113.04 (C^6), 127.23 (C_{arom}), 128.28 (C^{5a}), 128.92 ($2C_{arom}$), 129.09 ($2C_{arom}$), 131.79 (C^{9a}), 142.29 (C_{arom}), 145.93 (C^7), 148.04 (C^8), 173.72 (C^2). Mass spectrum: *m/z* 298 $[M + 1]^+$. Found, %: C 72.68; H 6.37; N 4.76. $C_{18}H_{19}NO_3$. Calculated, %: C 72.71; H 6.44; N 4.71. *M* 297.348.

7,8-Dimethoxy-5-(2-fluorophenyl)-1,3,4,5-tetrahydro-2*H*-1-benzazepin-2-one (IIIg). Yield 1.06 g (67%), mp 179–181 °C. IR spectrum, cm^{-1}: 3290, 2950, 1690, 1530, 1380, 1270, 1230, 1190, 1020. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 2.19–2.50 m (4H, $2CH_2$), 3.46 s, 3.73 s (6H, $2OCH_3$), 4.40–4.45 m (1H, C^5H), 6.16 s (1H, C^6H), 6.68 s (1H, C^9H), 7.21 t ($1H_{arom}$, *J* 8.4 Hz), 7.29 t ($1H_{arom}$, *J* 8.0 Hz), 7.37–7.42 m ($1H_{arom}$), 7.55 t ($1H_{arom}$, *J* 8.0 Hz), 9.44 s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 33.01 (C^3), 33.23 (C^4), 37.99 (C^5), 56.09 (OCH_3), 56.13 (OCH_3), 107.33 (C^9), 111.92 (C^6), 116.01 d (C_{arom}–F, *J* 22.50 Hz), 124.96 d (C_{arom}–F, *J* 1.25 Hz), 126.92 (C^{5a}), 128.92 d (C_{arom}–F, *J* 7.50 Hz), 129.42 d (C_{arom}–F, *J* 7.50 Hz), 130.22 d (C_{arom}–F, *J* 3.75 Hz), 131.82 (C^{9a}), 146.08 (C^7), 148.22 (C^8), 160.71 d (C_{arom}–F, *J* 242.50 Hz), 173.56 (C^2). Mass spectrum: *m/z* 316 $[M + 1]^+$. Found, %: C 68.51; H 5.69; N 4.40. $C_{18}H_{18}FNO_3$. Calculated, %: C 68.56; H 5.75; N 4.44. *M* 315.339.

7,8-Dimethoxy-5-(3-fluorophenyl)-1,3,4,5-tetrahydro-2*H*-1-benzazepin-2-one (IIIh). Yield 0.76 g (48%), mp 139–141 °C. IR spectrum, cm^{-1}: 3210, 3100, 2980, 1685, 1620, 1590, 1530, 1450, 1390, 1270, 1230, 1130, 1040, 1020, 920. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 2.20–2.48 m (4H, $2CH_2$), 3.52 s, 3.72 s (6H, $2OCH_3$), 4.22–4.26 m (1H, C^5H), 6.30 s (1H, C^6H), 6.66 s (1H, C^9H), 7.10–7.19 m ($3H_{arom}$), 7.39–7.44 m ($1H_{arom}$), 9.36 s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 32.66 (C^3), 33.84 (C^4), 44.44 (C^5), 56.05 (OCH_3), 56.17 (OCH_3), 106.38 (C^9), 111.75 (C^6), 113.97 d (C_{arom}–F, *J* 21.25 Hz), 115.65 d (C_{arom}–F, *J* 21.25 Hz), 124.46 d (C_{arom}–F, *J* 2.50 Hz), 128.25 (C^{5a}), 130.05 d (C_{arom}–F, *J* 8.75 Hz), 130.15 (C^{9a}), 143.98 d (C_{arom}–F, *J* 7.50 Hz), 146.73 (C^7), 148.15 (C^8), 162.99 d (C_{arom}–F, *J* 245.00 Hz), 175.34 (C^2). Mass spectrum: *m/z* 316 $[M + 1]^+$. Found, %: C 68.50; H 5.74; N 4.43. $C_{18}H_{18}FNO_3$. Calculated, %: C 68.56; H 5.75; N 4.44. *M* 315.339.

7,8-Dimethoxy-5-(4-fluorophenyl)-1,3,4,5-tetrahydro-2*H*-1-benzazepin-2-one (IIIi). Yield 0.96 g (61%), mp 151–153 °C. IR spectrum, cm^{-1}: 3210, 3110, 1680, 1520, 1390, 1270, 1230, 1170, 1130, 1020. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 2.18–2.43 m (4H, $2CH_2$), 3.50 s, 3.72 s (6H, $2OCH_3$), 4.18–4.24 m (1H, C^5H), 6.24 s (1H, C^6H), 6.66 s (1H, C^9H), 7.20 t ($2H_{arom}$, *J* 8.8 Hz), 7.37 t ($2H_{arom}$, *J* 6.8 Hz), 9.36 s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 33.24 (C^3),

34.06 (C^4), 44.27 (C^5), 56.10 (OCH_3), 56.11 (OCH_3), 107.25 (C^9), 112.79 (C^6), 115.60 d ($2C_{arom}$–F, *J* 21.25 Hz), 128.10 (C^{5a}), 130.90 d ($2C_{arom}$–F, *J* 7.50 Hz), 131.68 (C^{9a}), 138.43 (C_{arom}), 145.95 (C^7), 148.03 (C^8), 161.45 d (C_{arom}–F, *J* 241.25 Hz), 173.71 (C^2). Mass spectrum: *m/z* 316 $[M + 1]^+$. Found, %: C 68.52; H 5.71; N 4.44. $C_{18}H_{18}FNO_3$. Calculated, %: C 68.56; H 5.75; N 4.44. *M* 315.339.

7,8-Dimethoxy-5-(4-methylphenyl)-1,3,4,5-tetrahydro-2*H*-1-benzazepin-2-one (IIIj). Yield 0.53 g (34%), mp 167–169 °C. IR spectrum, cm^{-1}: 3200, 3090, 2980, 1680, 1520, 1460, 1390, 1350, 1270, 1230, 1160, 1120, 1040, 1020, 920. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 2.20–2.42 m (7H, CH_3, $2CH_2$), 3.48 s, 3.72 s (6H, $2OCH_3$), 4.09–4.19 m (1H, C^5H), 6.29 s (1H, C^6H), 6.66 s (1H, C^9H), 7.18 m ($4H_{arom}$), 9.35 s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 21.11 (CH_3), 33.33 (C^3), 34.13 (C^4), 44.69 (C^5), 56.09 (OCH_3), 56.23 (OCH_3), 107.24 (C^9), 113.08 (C^6), 128.44 (C^{5a}), 128.95 ($2C_{arom}$), 129.50 ($2C_{arom}$), 131.77 (C^{9a}), 136.19 (C_{arom}), 139.18 (C_{arom}), 145.91 (C^7), 148.02 (C^8), 173.72 (C^2). Mass spectrum: *m/z* 312 $[M + 1]^+$. Found, %: C 73.16; H 6.79; N 4.47. $C_{19}H_{21}NO_3$. Calculated, %: C 73.29; H 6.80; N 4.50. *M* 311.375.

5-(3-Fluorophenyl)dihydrofuran-2(3*H*)-one (IV). Yield 0.14 g (16%) from compound (**Ic**), 0.17 g (19%) from compound (**Ih**), oily substance. IR spectrum, cm^{-1}: 1790, 1610, 1500, 1450, 1330, 1230, 1190, 1090, 1040, 990, 920. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.13–2.19 m (1H, CH), 2.61–2.71 m (3H, CH, $2CH_2$), 5.46–5.50 m (1H, C^5H), 6.99–7.04 m ($2H_{arom}$), 7.09 d ($1H_{arom}$, *J* 7.2 Hz), 7.31–7.37 m ($1H_{arom}$). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 28.75 (C^4), 30.84 (C^3), 80.30 (C^5), 112.34 d (C_{arom}–F, *J* 22.50 Hz), 115.29 d (C_{arom}–F, *J* 21.25 Hz), 120.87 d (C_{arom}–F, *J* 3.75 Hz), 130.50 d (C_{arom}–F, *J* 8.75 Hz), 142.12 d (C_{arom}–F, *J* 7.50 Hz), 162.95 d (C_{arom}–F, *J* 245.00 Hz), 176.58 (C^2). Mass spectrum: *m/z* 181 $[M + 1]^+$. Found, %: C 66.63; H 5.01. $C_{10}H_9FO_2$. Calculated, %: C 66.66; H 5.03. *M* 180.176.

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