

## Indole-Containing Derivatives of $\alpha$ -Pyrrolidone: Synthesis and Structure

E. S. Ostroglyadov<sup>a</sup>, O. S. Vasil'eva<sup>a</sup>, S. M. Aleksandrova<sup>b</sup>, V. V. Pelipko<sup>a</sup>,  
V. M. Berestovitskaya<sup>a</sup>, I. N. Tyurenkov<sup>c</sup>, and V. V. Bagmetova<sup>c</sup>

<sup>a</sup> Herzen State Pedagogical University of Russia, nab. reki Moiki 48, St. Petersburg, 191186 Russia  
e-mail: kohrgpu@yandex.ru

<sup>b</sup> Pskov State University, Pskov, Russia

<sup>c</sup> Volgograd State Medical University, Volgograd, Russia

Received April 30, 2015

**Abstract**—4-(Indol-3-yl)-2-pyrrolidone and its derivatives have been synthesized via sequential hydrogenation of indole-containing esters of 4-nitrobutanoic acid, alkaline hydrolysis of the resulting 3-methoxycarbonyl-2-pyrrolidones, and decarboxylation of the isolated 2-pyrrolidone-3-carboxylic acids. Structures of the products have been confirmed by IR, <sup>1</sup>H NMR, <sup>1</sup>H–<sup>13</sup>C HMQC, and <sup>1</sup>H–<sup>1</sup>H NOESY spectroscopy methods.

**Keywords:** 2-pyrrolidone, pyrrolidone carboxylate, catalytic hydrogenation, heterocyclization, alkaline hydrolysis, decarboxylation

**DOI:** 10.1134/S1070363215080095

2-Pyrrolidone and indole have been recognized as important pharmacophore fragments of many biologically active natural compounds and synthetic drugs. For example, nootropics piracetam [2] and fenotropil (Carphedon) [1, 3, 4] as well as entero-sorbents based on polyvinylpyrrolidone (Enterodez) [2] contain pyrrolidone rings. Widely used indopan (antidepressant), diazolin (antihistamine), indomethacin (anti-inflammatory drug), and bopindalol (used for treatment of angina and hypertension) are examples of indole-containing synthetic drugs [2]. Therefore, the indole-containing 2-pyrrolidones are among the key structures in targeted synthesis of various pharmacologically active substances.

The indole-containing 2-pyrrolidones can be obtained via a general procedure of 4-aminobutyric acid and 2-pyrrolidones synthesis based on preparation of the corresponding 4-nitrobutanoates followed by their hydrogenation in neutral or alkaline media to yield the substituted 2-pyrrolidones [1, 4, 5].

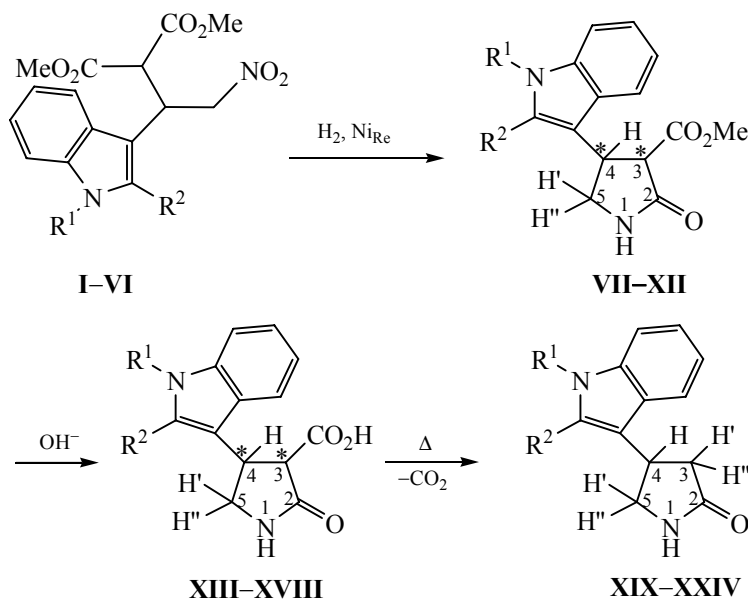
We carried out hydrogenation of nitroesters **I–VI** with electrolytic hydrogen on Raney nickel (atmospheric pressure, 18–20°C) in methanol or a 1 : 1 acetone–methanol mixture. The 4-nitrobutanoates **I–VI** were obtained via condensation of nitroethenes with malonic ester as described earlier [6–8].

Reduction of compounds **I–VI** was accompanied by intramolecular acylation of the initially formed amino group to give 4-(indol-3-yl)-3-methoxycarbonyl-2-pyrrolidone **VII** and its analogs **VIII–XII** in high yields (70%). Noteworthy, synthesis of compound **VII** has been described earlier [6]; however, the product melting point reported in [6] significantly deviated from that determined in this work.

The indole-containing pyrrolidone carboxylates **VII–XII** were stable colorless crystalline solids; they are valuable precursors in preparation of the corresponding 4-aminobutyric acids, pyrrolidone carboxylic acids, and 2-pyrrolidones. In particular, boiling of compounds **VII–XII** in 10% sodium hydroxide aqueous methanol (1 : 10) solution during 10 min resulted in hydrolysis of the ester group to give 4-(indol-3-yl)-3-hydroxycarbonyl-2-pyrrolidone **XIII** and its derivatives **XIV–XVIII** in good yields (see table). Importantly, under the reaction conditions the pyrrolidone ring was not opened. Subsequent heating of compounds **XIII–XVIII** above their melting point under reduced pressure yielded the target indole-containing 2-pyrrolidones **XIX–XXIV** (Scheme 1).

Structures of the 2-pyrrolidones **VII–XXIV** were confirmed by IR, <sup>1</sup>H NMR, and <sup>13</sup>C NMR spectro-

Scheme 1.



$R^1 = H$ :  $R^2 = H$  (**I**, **VII**, **XIII**, **XIX**),  $CH_3$  (**II**, **VIII**, **XIV**, **XX**);  $R^1 = CH_3$ :  $R^2 = H$  (**III**, **IX**, **XV**, **XXI**),  $CH_3$  (**IV**, **X**, **XVI**, **XXII**);  $R^1 = CH_2Ph$ :  $R^2 = H$  (**V**, **XI**, **XVII**, **XXIII**),  $CH_3$  (**VI**, **XII**, **XVIII**, **XXIV**).

scopy methods (see table). The obtained parameters were in good agreement with those for compound **VII** [9], and compounds **XIII** and **XIX** produced via different methods [10–13]. For example, IR spectra of pyrrolidone carboxylates **VII–XII** contained absorption bands assigned to the ester ( $1745\text{--}1730\text{ cm}^{-1}$ ) and the lactam ( $1705\text{--}1685\text{ cm}^{-1}$ ) carbonyl groups; the spectra of pyrrolidone carboxylic acids **XIII–XVIII** contained broadened absorption bands ( $1712\text{--}1613\text{ cm}^{-1}$ ) due to overlapping stretching bands of lactam and carboxyl groups. In the case of 4-aryl(hetaryl)-2-pyrrolidones **XIX–XXIV**, that band was shifted to lower frequency ( $1693\text{--}1679\text{ cm}^{-1}$ ) (see table), characteristic of the lactam carbonyl group stretching [14]. NH-Pyrrolidone groups (compounds **VII–XXIV**) and indole moieties (compounds **VII**, **VIII**, **XIII**, **XIX**, **XIX**, and **XX**) gave rise to absorption bands at  $3315\text{--}3185$  and  $3415\text{--}3350\text{ cm}^{-1}$ , respectively.

$^1H$  NMR spectra of compounds **VII–XVIII** (see table) containing two chiral centers confirmed their diastereo homogeneity. For example, the methine proton signals of pyrrolidone ring appeared as a doublet of triplets [4.07 ppm ( $C^4H$ )] and a doublet [3.55 ppm ( $C^3H$ ),  $^3J_{34}$  10.7 Hz] in the  $^1H$  NMR spectrum of pyrrolidone carboxylic acid **XIV**; the methylene protons resonated as triplets [3.42, 3.51 ppm ( $S5N'H''$ ), ( $C^5H'H''$ ),  $^3J_{45}$  9.1,  $^3J_{45''}$  9.1,  $^2J_{5'5''}$  9.1 Hz]. Magnetic nonequivalence of the methylene protons

could be apparently explained by the presence of adjacent asymmetric carbon atoms [15]. The signals of carboxyl OH groups (12.52 ppm), pyrrolidone NH (8.12 ppm) and indole NH (10.84 ppm) moieties appeared as weak-field singlets. The indole ring protons were assigned to a multiplet at 6.89–7.42 ppm. The singlet at 2.29 ppm corresponded to the methyl group at the  $C^2$  atom of the indole ring.

Assignments of the signals of methine and methylene protons of pyrrolidone rings in the spectra of 2-pyrrolidones were verified taking advantage of 2D NMR spectroscopy technique. In particular, the correlations were revealed between the protons  $C^4H$  (4.07 ppm) and the  $C^4$  atom (36.97 ppm) as well as between the  $C^3H$  (3.55 ppm) and  $C^3$  (54.63 ppm) as well as  $C^5H_2$  (3.42, 3.51 ppm) and  $C^5$  (45.51 ppm) atoms in the HMQC spectrum of **XIV** (Fig. 1). The HMQC spectrum allowed distinguishing the proton signals of  $C^3H$ ,  $C^4H$ , and  $C^5H_2$  atoms of the pyrrolidone ring and showed that the  $C^4H$  proton signal appeared in a weaker field region as compared to that of the  $C^3H$  proton signal (Fig. 1); that coincided with the earlier published data [16] and was apparently explained by the presence of indole ring at the  $C^4$  atom.

$^1H$  NMR spectrum of 4-(1-methylindol-3-yl)-2-pyrrolidone **XXI** contained a multiplet assigned to the

Yields, melting points, and spectral parameters of compounds VII–XXIV

Comp. no.	Yield, %	mp, °C	$\nu$ , $\text{cm}^{-1}$		$\delta_{\text{H}}$ , ppm						$J$ , Hz			
			NH (NH <sub>Ind</sub> )	CO <sub>2</sub> Me, C=O	Ind, (R <sup>1</sup> ), [R <sup>2</sup> ]	C <sup>3</sup> H, C <sup>3</sup> H' (C <sup>3</sup> H <sup>''</sup> )	C <sup>4</sup> H	C <sup>5</sup> H' (C <sup>5</sup> H <sup>''</sup> )	NH (NH <sub>Ind</sub> )	CH <sub>3</sub> (OH)	$J_{3'3''}$	$J_{34}$ ( $J_{3'4}$ , $J_{3''4}$ )	$J_{45'}$ ( $J_{45''}$ )	$J_{5'5''}$
VII	74	185–186	3215 (3395)	1745, 1703	6.94–7.48	3.60	4.12	3.31 (3.67)	8.14 (10.95)	3.59	–	10.2	9.2 (9.2)	9.2
VIII	70	190–192	3258 (3415)	1737, 1685	6.87–7.41, [2.31]	3.65	4.12	3.46 (3.55)	8.12 (10.74)	3.58	–	11.0	9.2 (9.2)	9.2
IX	65	191–193	3213	1742, 1700	6.99–7.51, (3.69)	3.58	4.11	3.31 (3.68)	8.17	3.60	–	10.0	9.0 (9.0)	9.0
X	70	217–219	3199	1740, 1705	6.95–7.51, (3.55), [2.31]	3.71	4.14	3.45 (3.52)	8.22	3.59	–	10.9	9.2 (9.2)	9.2
XI	60	110–112	3205	1734, 1694	6.98–7.46, (6.98–7.46, 5.31)	3.53	4.11	3.36 (3.67)	8.10	3.62	–	10.3	8.9 (8.9)	8.9
XII	70	201–203	3218	1730, 1695	6.92–7.56, (6.92–7.56, 5.35), [2.27]	3.72	4.16	3.50 (3.59)	8.22	3.55	–	10.9	9.3 (9.3)	9.3
XIII	91	152–153	3314 (3409)	1710–1675	6.94–7.51	3.44	4.08	3.28 (3.65)	8.06 (10.95)	(12.62)	–	10.4	8.8 (8.8)	8.8
XIV	87	177–179	3283 (3397)	1710–1665	6.89–7.42, [2.29]	3.55	4.07	3.42 (3.51)	8.12 (10.84)	(12.52)	–	10.7	9.1 (9.1)	9.1
XV	85	165–166	3293	1712–1645	6.98–7.52 (3.70)	3.41	4.08	3.28 (3.65)	8.08	(12.65)	–	10.3	9.0 (9.0)	9.0
XVI	82	193–195	3205	1710–1658	6.95–7.47 (3.60), [2.31]	3.57	4.12	3.47 (3.57)	8.14	(12.53)	–	10.7	9.2 (9.2)	9.2
XVII	88	100–102	3227	1700–1677	6.97–7.50, (6.97–7.50, 5.32)	3.44	4.10	3.30 (3.68)	8.09	(12.67)	–	10.3	8.9 (8.9)	8.9
XVIII	83	168–170	3231	1700–1660	6.93–7.52 (6.93–7.52, 5.34, 5.39), [2.28]	3.59	4.15	3.49 (3.58)	8.15	(12.56)	–	10.6	9.2 (9.2)	9.2
XIX	74	179–180	3315 (3350)	1679	6.94–7.49	2.33 (2.54)	3.78	3.24 (3.65)	7.67 (10.86)	–	16.3	9.0 (8.7)	8.8 (7.8)	8.8
XX	62	182–184	3270 (3390)	1679	6.87–7.38, [2.30]	(2.42)	3.79	3.37 (3.49)	7.75 (10.74)	–	–	–	9.0 (7.9)	9.0
XXI	85	170–172	3185	1685	7.03–7.48, (3.67)	2.30 (2.55)	3.95	3.21 (3.64)	7.67	–	16.3	8.8 (8.7)	8.8 (7.5)	8.8
XXII	79	193–195	3209	1693	6.92–7.41, (3.59), [2.32]	(2.41)	3.85	3.38 (3.49)	7.78	–	–	–	9.1 (7.9)	9.1
XXIII	83	165–167	3214	1686	6.97–7.52, (6.97–7.52, 5.31)	2.32 (2.56)	3.80	3.25 (3.68)	7.67	–	16.3	8.9 (8.7)	8.8 (7.5)	8.8
XXIV	72	88–90	3245	1692	6.93–7.46, (6.93–7.46, 5.34), [2.28]	(2.45)	3.88	3.42 (3.52)	7.80	–	–	–	9.2 (7.8)	9.2

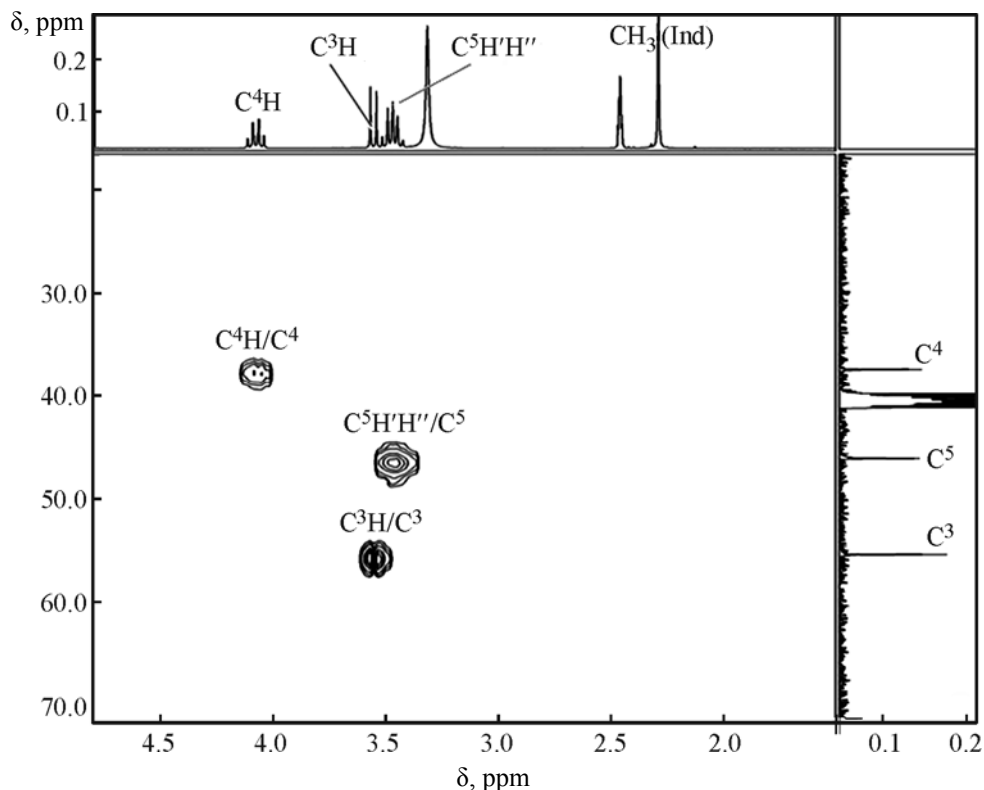
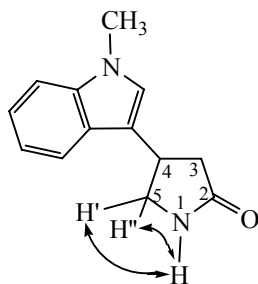


Fig. 1. Fragment of  $^1\text{H}$ – $^{13}\text{C}$  HMQC spectrum of compound **XIV** in  $\text{DMSO-}d_6$ .

$\text{C}^4\text{H}$  methine proton (3.95 ppm) of the pyrrolidone ring; the signals of the  $\text{C}^3\text{H}'\text{H}''$  methylene group protons (2.30, 2.55 ppm,  $^2J_{3'3''}$  16.3,  $^3J_{3'4}$  8.8,  $^3J_{3''4}$  8.7 Hz) appeared as doublets of doublets. The  $\text{C}^5\text{H}'\text{H}''$  protons resonated as a triplet [3.21 ppm ( $\text{C}^5\text{H}'$ ),  $^3J_{45'}$  8.8,  $^2J_{5'5''}$  8.8 Hz] and a doublet of doublets [3.64 ppm ( $\text{C}^5\text{H}''$ ),  $^3J_{45''}$  7.5,  $^2J_{5'5''}$  8.8 Hz]. The singlet at 7.67 ppm was assigned to the NH-proton of lactam group. The signals of the indole fragment protons were detected at 7.03–7.48 ppm. The protons of the N-methyl group of the indole ring gave rise to a strong-field singlet (3.67 ppm).



Assignment of the signals of  $\text{C}^3\text{H}$  and  $\text{C}^5\text{H}$  methylene protons of pyrrolidone ring was aided by heteronuclear NMR spectroscopy. In particular, the correlations

between the signals of the  $\text{C}^4\text{H}$  (3.95 ppm) and  $\text{C}^4$  (32.82 ppm),  $\text{C}^3\text{H}'\text{H}''$  (2.30, 2.55 ppm) and  $\text{C}^3$  (37.81 ppm),  $\text{C}^5\text{H}'\text{H}''$  (3.21, 3.64 ppm) and  $\text{C}^5$  (48.55 ppm) atoms were found in the HMQC spectrum of compound **XXI** (Fig. 2). Validity of signal assignment of the  $\text{C}^3$  and  $\text{C}^5$  methylene groups of the pyrrolidone ring was confirmed by NOESY spectroscopy. In detail, the correlation between the signals of the lactam NH proton (7.67 ppm) and the  $\text{C}^5\text{H}'\text{H}''$  methylene protons (3.21 ppm) was revealed in the spectrum of compound **XXI** (Fig. 3), indicating the spatial proximity of those protons. Consequently, assignment of the signals at  $\delta$  2.30 and 2.55 ppm to the  $\text{C}^3$  methylene protons of the pyrrolidone ring was correct. Hence, taking the NMR spectrum of compound **VII** as a model one and analyzing the 2D NMR spectra of compounds **XIV** and **XXI**, we could assign  $^1\text{H}$  NMR spectra of all the prepared compounds **VII–XXIV** (see table).

The synthesized 2-pyrrolidones are valuable starting materials for preparation of indole-containing derivatives of  $\gamma$ -aminobutyric acid and piracetam. Furthermore, they are of interest as potentially biologically active compounds. For example, 4-(indol-

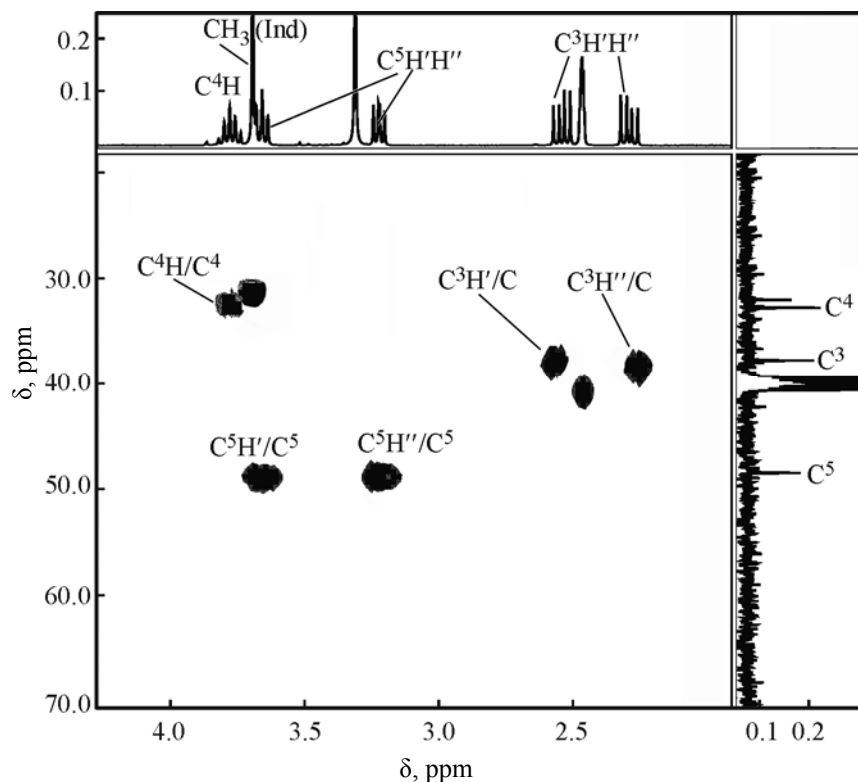


Fig. 2. Fragment of  $^1\text{H}$ - $^{13}\text{C}$  HMQC spectrum of compound XXI in  $\text{DMSO}-d_6$ .

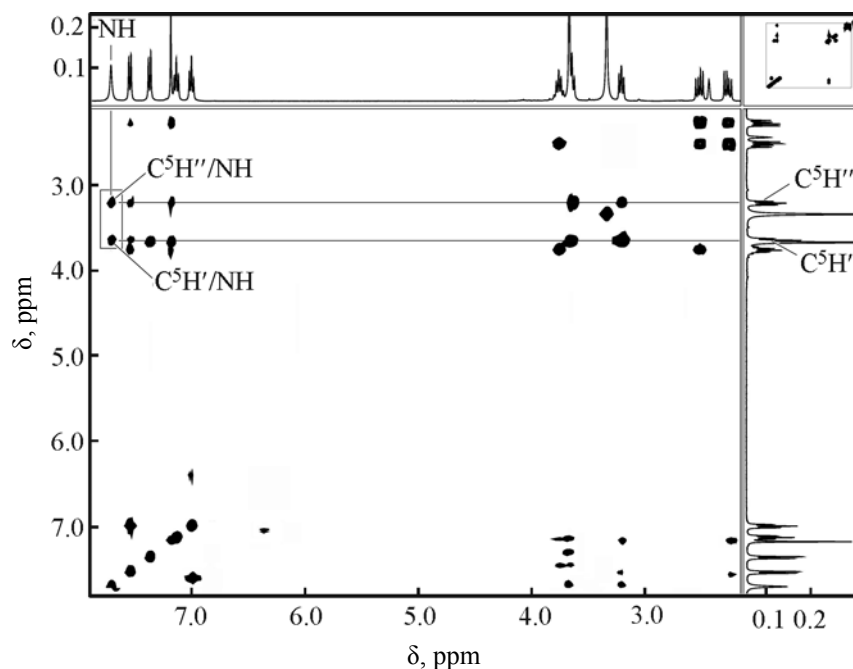


Fig. 3.  $^1\text{H}$ - $^1\text{H}$  NOESY spectrum of compound XXI in  $\text{DMSO}-d_6$ .

3-yl)-2-pyrrolidone XIX exhibited pronounced hypotensive action in experiments with anaesthetized rats, however, inhibiting breathing when applied in the effective dose. The same compound caused a dose-

dependent decrease in blood pressure in the experiments with anesthetized cats, and anti-hypertensive effect during the oral administration was much weaker than in the case of the intravenous administration.

## EXPERIMENTAL

Spectral and elemental analysis data were obtained at the Center for Collective Use, Herzen State Pedagogical University of Russia.

$^1\text{H}$ ,  $^1\text{H}$ - $^{13}\text{C}$  HMQC NMR spectra of the solutions in  $\text{DMSO}-d_6$  were recorded using a Jeol ECX400A spectrometer operating at 399.78 ( $^1\text{H}$ ) and 100.525 MHz ( $^{13}\text{C}$ ) relative to the signal of the residual solvent protons. IR spectra of the pellets with KBr were obtained using a Shimadzu IR Prestige-21 Fourier spectrometer. Elemental analysis was performed with a EuroVector EA 3000 analyzer (CHN Dual mode). Melting points were determined with a PTP (M) instrument.

The starting 3-(indol-3-yl)-4-nitrobutanoates **I–VI** were prepared via the known methods [6–8].

**4-(Indol-3-yl)-3-methoxycarbonyl-2-pyrrolidone (VII).** A suspension of 3.20 g of Raney nickel catalyst in 32 mL of methanol was saturated with hydrogen via electrolysis. A suspension of 2.88 g (0.009 mol) of methyl 3-(indol-3-yl)-2-methoxycarbonyl-4-nitrobutanoate **I** in 60 mL of methanol was then added under a hydrogen stream, and hydrogenation was carried out until uptake of the calculated amount of hydrogen [0.605 L (0.027 mol)]. The catalyst was filtered off and washed with boiling methanol via decantation ( $3 \times 100$  mL). The filtrate was evaporated under reduced pressure (15–20 mmHg) to three-quarters of the original volume. The precipitated crystalline product was filtered off and dried. Yield 1.72 g (74%), mp 185–186°C (methanol) (mp 172.5–173°C [6]). Found, %: C 65.05, 65.03; H 5.73, 5.70; N 10.98, 11.01  $\text{C}_{14}\text{H}_{14}\text{N}_2\text{O}_3$ . Calculated, %: C 65.12; H 5.43; N 10.85.

Compounds **VIII**, **IX**, and **XI** were prepared similarly.

**4-(2-Methylindol-3-yl)-3-methoxycarbonyl-2-pyrrolidinone (VIII).** Yield 70%, mp 190–192°C (methanol). Found, %: C 66.27, 66.28; H 6.05, 6.05; N 10.25, 10.28.  $\text{C}_{15}\text{H}_{16}\text{N}_2\text{O}_3$ . Calculated, %: C 66.18; H 5.88; N 10.29.

**4-(1-Methylindol-3-yl)-3-methoxycarbonyl-2-pyrrolidone (IX).** Yield 62%, mp 191–193°C (methanol). Found, %: C 66.23, 66.25; H 5.92, 5.91; N 10.29, 10.29.  $\text{C}_{15}\text{H}_{16}\text{N}_2\text{O}_3$ . Calculated, %: C 66.18; H 5.88; N 10.29.

**4-(1-Benzylindol-3-yl)-3-methoxycarbonyl-2-pyrrolidone (XI).** Yield 60%, mp 110–112°C (methanol). Found, %: C 72.24, 72.30; H 5.58, 5.67; N 8.25, 8.05.  $\text{C}_{21}\text{H}_{20}\text{N}_2\text{O}_3$ . Calculated, %: C 72.41; H 5.75; N 8.05.

**4-(1,2-Dimethylindol-3-yl)-3-methoxycarbonyl-2-pyrrolidone (X).** A suspension of 3.70 g of Raney nickel in 37 mL of methanol was saturated with hydrogen via electrolysis. A suspension of 3.55 g of (0.01 mol) of methyl 3-(1,2-dimethylindole-3-yl)-2-methoxycarbonyl-4-nitrobutanoate **IV** in 35 mL of a 1 : 1 methanol–acetone mixture was then added under hydrogen stream. The mixture was hydrogenated until uptake of the calculated amount of hydrogen [0.672 L (0.03 mol)]. The catalyst was filtered off and washed with a boiling 1 : 1 mixture of methanol and acetone via decantation ( $3 \times 100$  mL). The filtrate was evaporated under reduced pressure (15–20 mmHg) to three-quarters of the original volume. The precipitated crystalline product was filtered off and dried. Yield 1.80 g (70%), mp 217–219°C (methanol). Found, %: C 67.10, 67.15; H 6.38, 6.36; N 9.84, 9.85.  $\text{C}_{16}\text{H}_{18}\text{N}_2\text{O}_3$ . Calculated, %: C 67.13; H 6.29; N 9.79.

Compound **XII** was prepared similarly.

**4-(1-Benzyl-2-methylindol-3-yl)-3-methoxycarbonyl-2-pyrrolidone (XII).** Yield 70%, mp 201–203°C (methanol). Found, %: C 72.19, 72.15; H 6.22, 6.23; N 7.98, 7.97.  $\text{C}_{22}\text{H}_{22}\text{N}_2\text{O}_3$ . Calculated, %: C 72.93; H 6.08; N 7.73.

**4-(Indol-3-yl)-3-hydroxycarbonyl-2-pyrrolidone (XIII).** A mixture of 14.30 mL of methanol, 1.45 mL of water, 2.00 g (0.05 mol) of sodium hydroxide, and 1.68 g (0.0065 mol) of 4-(indol-3-yl)-3-methoxycarbonyl-2-pyrrolidone **VII** was refluxed during 10 min. After cooling, the precipitate was filtered off and dissolved in 40 mL of water. The resulting solution was carefully acidified upon cooling at 0–5°C with diluted hydrochloric acid (1 : 1) to pH  $\sim$  3–4. The precipitate was filtered off and dried. Yield 1.44 g (91%), mp 152–153°C (methanol) (mp 152.5–153°C [6]). Found, %: C 63.85, 63.80; H 5.11, 5.09; N 11.33, 11.35  $\text{C}_{13}\text{H}_{12}\text{N}_2\text{O}_3$ . Calculated, %: C 63.93; H 4.95; N 11.47.

Compounds **XIV–XVIII** were obtained similarly.

**4-(2-Methylindol-3-yl)-3-hydroxycarbonyl-2-pyrrolidone (XIV).** Yield 87%, mp 177–179°C (methanol).  $^{13}\text{C}$  NMR spectrum ( $\text{DMSO}-d_6$ ),  $\delta_{\text{C}}$ , ppm: 172.67 ( $\text{C}^2$ ), 54.63 ( $\text{C}^3$ ), 36.97 ( $\text{C}^4$ ), 45.51 ( $\text{C}^5$ ), 171.94 (COOH); 108.27, 111.44, 118.45, 119.01, 120.70, 126.69, 133.27, 136.02 (Ind), 11.88 ( $\text{CH}_3\text{Ind}$ ). Found, %: C 65.00, 64.99; H 5.58, 5.57; N 10.99, 11.01.  $\text{C}_{14}\text{H}_{14}\text{N}_2\text{O}_3$ . Calculated, %: C 65.12; H 5.43; N 10.85.

**4-(1-Methylindol-3-yl)-3-hydroxycarbonyl-2-pyrrolidone (XV).** Yield 85%, mp 165–166°C (methanol).

Found, %: C 65.10, 65.09; H 5.40, 5.41; N 10.79, 10.80.  $C_{14}H_{14}N_2O_3$ . Calculated, %: C 65.12; H 5.43; N 10.85.

**4-(1,2-Dimethylindol-3-yl)-3-hydroxycarbonyl-2-pyrrolidone (XVI).** Yield 82%, mp 193–195°C (methanol). Found, %: C 66.09, 66.11; H 6.03, 6.03; N 10.48, 10.49.  $C_{15}H_{16}N_2O_3$ . Calculated, %: C 66.18; H 5.88; N 10.29.

**4-(1-Benzylindol-3-yl)-3-hydroxycarbonyl-2-pyrrolidone (XVII).** Yield 88%, mp 100–102°C (methanol). Found, %: C 71.70, 71.72; H 5.35, 5.36; N 8.34, 8.35.  $C_{20}H_{18}N_2O_3$ . Calculated, %: C 71.86; H 5.39; N 8.38.

**4-(1-Benzyl-2-methylindol-3-yl)-3-hydroxycarbonyl-2-pyrrolidone (XVIII).** Yield 83%, mp 168–170°C (methanol–acetone, 1 : 1). Found, %: C 72.50, 72.45; H 5.81, 5.80; N 8.13, 8.12.  $C_{21}H_{20}N_2O_3$ . Calculated, %: C 72.41; H 5.75; N 8.05.

**4-(Indol-3-yl)-2-pyrrolidone (XIX).** 4-(1-Indol-3-yl)-3-hydroxycarbonyl-2-pyrrolidone **XIII** (1.7 g, 0.007 mol) was heated on a glycerol bath (170–180°C) under reduced pressure (15–20 mmHg) until the evolution of carbon dioxide had ceased. The melt was cooled down and recrystallized. Yield 1.04 g (74%), mp 179–180°C (methanol) {mp 179–180°C (methanol) [6], 181–182°C (water) [10], 163°C (after column chromatography) [11], 170°C (diethyl ether) [13]}. Found, %: C 72.20, 72.23; H 6.14, 6.16; N 14.50, 14.55.  $C_{12}H_{12}N_2O$ . Calculated, %: C 71.98; H 6.04; N 13.99.

Compounds **XX–XXIV** were obtained similarly.

**4-(2-Methylindol-3-yl)-2-pyrrolidone (XX).** Yield 62%, mp 182–184°C (methanol). Found, %: C 72.87, 72.91; H 6.73, 6.70; N 12.94, 12.96.  $C_{13}H_{14}N_2O$ . Calculated, %: C 72.90; H 6.54; N 13.08.

**4-(1-Methylindol-3-yl)-2-pyrrolidone (XXI).** Yield 85%, mp 170–172°C (methanol).  $^{13}C$  NMR spectrum (DMSO- $d_6$ ),  $\delta_C$ , ppm: 176.81 ( $C^2$ ), 37.81 ( $C^3$ ), 32.82 ( $C^4$ ), 48.55 ( $C^5$ ); 110.30, 115.79, 119.05, 119.34, 121.83, 126.45, 127.04, 137.47 (Ind), 32.07 ( $CH_3$ Ind). Found, %: C 72.85, 72.86; H 6.49, 6.50; N 13.00, 13.02.  $C_{13}H_{14}N_2O$ . Calculated, %: C 72.90; H 6.54; N 13.08.

**4-(1,2-Dimethylindol-3-yl)-2-pyrrolidone (XXII).** Yield 79%, mp 193–195°C (methanol). Found, %: C 73.60, 73.61; H 7.07, 7.08; N 12.09, 12.10.  $C_{14}H_{16}N_2O$ . Calculated, %: C 73.68; H 7.02; N 12.28.

**4-(1-Benzylindol-3-yl)-2-pyrrolidone (XXIII).** Yield 83%, mp 165–167°C (methanol). Found, %: C 78.59, 78.60; H 6.18, 6.19; N 9.64, 9.64.  $C_{19}H_{18}N_2O$ . Calculated, %: C 78.62; H 6.21; N 9.66.

**4-(1-Benzyl-2-methylindol-3-yl)-2-pyrrolidone (XXIV).** Yield 72%, mp 88–90°C (diethyl ether). Found, %: C 79.02, 79.04; H 6.64, 6.62; N 9.31, 9.30.  $C_{20}H_{20}N_2O$ . Calculated, %: C 78.95; H 6.58; N 9.21.

## ACKNOWLEDGMENTS

This work was financially supported by the Ministry of Education and Science of Russia in the frame of the basic part of the governmental task.

## REFERENCES

- Berestovitskaya, V.M., Vasil'eva, O.S., and Ostrogl'yadov, E.S., *2-Pyrrolidone i ego proizvodnye* (2-Pyrrolidone and Its Derivatives), St. Petersburg: Asterion, 2013, 192 p. ISBN: 978-5-00045-072-7.
- Mashkovskii, M.D., *Lekarstvennye sredstva* (Drugs), Moscow: RIA "Novaya Volna," 2012.
- EP Patent 002380, 1999.
- Berestovitskaya, V.M., Zobacheva, M.M., and Vasil'eva, O.S., *Izv. RGPU im. A.I. Gertsena, Estestv. i Tochnye Nauki*, 2002, no. 2 (4), p. 133.
- Perekalin, V.V. and Zobacheva, M.M., *Zh. Obshch. Khim.*, 1959, vol. 29, no. 9, p. 2095.
- Mamaev, V.P. and Rodina, O.A., *Izv. Sib. Otd. Akad. Nauk SSSR*, 1962, no. 8, p. 72.
- Kobzareva, V.N., Vasil'eva, O.S., Zobacheva, M.M., Berestovitskaya, V.M., *Zh. Org. Khim.*, 1997, vol. 33, no. 10, p. 1598.
- The Chemistry and Biological Activity of Nitrogen-Containing Heterocycles and Alkaloids*, Kartsev, V.G. and Tolstikov, G.A., Eds., Moscow: Iridium Press, 2001, vol. 2, p. 16.
- Baron, M., Lemaire, M., Metay, E., and Popowycz, F., *Green Chem.*, 2013, vol. 15, no. 4, p. 1006. DOI: 10.1039/c3gc37024k.
- Papayan, G.L., *Arm. Khim. Zh.*, 1970, vol. 23, no. 2, p. 200.
- Boisbrun, M., Jeannin, L., Laronze, J.-Y., and Toupet, L., *Eur. J. Org. Chem.*, 2000, no. 17, p. 3051. DOI: 10.1002/1099-0690(200009)2000:17<3051::AID-EJOC3051>3.0.CO;2-3.
- Boisbrun, M., Kovacs-Kulyassa, A., Jeannin, L., Sapi, J., Toupet, L., and Laronze, J.-Y., *Tetrahedron Lett.*, 2000, vol. 41, p. 9771. DOI: 10.1016/S0040-4039(00)01719-6.
- Boisbrun, M., Vassileva, E., Raoul, M., Laronze, J.-Y., and Sapi, J., *Monatsh. Chem.*, 2003, vol. 134, no. 12, p. 1641. DOI: 10.1007/s0076-003-0068-3.
- Pretch, E., Bühlmann, P., and Affolter, C., *Structure Determination of Organic Compounds: Tables of Spectral Data*, Berlin: Springer, 2000.
- Nifant'ev, I.E. and Ivchenko, P.V., *Prakticheskii kurs spektroskopii yadernogo magnitnogo rezonansa* (Practical Course of Nuclear Magnetic Resonance Spectroscopy), Moscow: MGU, 2006, p. 34.
- Gunther, H. *NMR-Spektroskopie*, Stuttgart: Georg Thieme Verlag, 1973.