ISSN 1070-3632, Russian Journal of General Chemistry, 2015, Vol. 85, No. 8, pp. 1838–1844. © Pleiades Publishing, Ltd., 2015.
Original Russian Text © E.S. Ostroglyadov, O.S. Vasil'eva, S.M. Aleksandrova, V.V. Pelipko, V.M. Berestovitskaya, I.N. Tyurenkov, V.V. Bagmetova, 2015, published in Zhurnal Obshchei Khimii, 2015, Vol. 85, No. 8, pp. 1280–1287.

# Indole-Containing Derivatives of α-Pyrrolidone: Synthesis and Structure

**E. S. Ostroglyadov[a], O. S. Vasil'eva[a], S. M. Aleksandrova[b], V. V. Pelipko[a], V. M. Berestovitskaya[a], I. N. Tyurenkov[c], and V. V. Bagmetova[c]**

[a] *Herzen State Pedagogical University of Russia, nab. reki Moiki 48, St. Petersburg, 191186 Russia*
*e-mail: kohrgpu@yandex.ru*

[b] *Pskov State University, Pskov, Russia*

[c] *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, $^{1}$H NMR, $^{1}$H–$^{13}$C HMQC, and $^{1}$H–$^{1}$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].

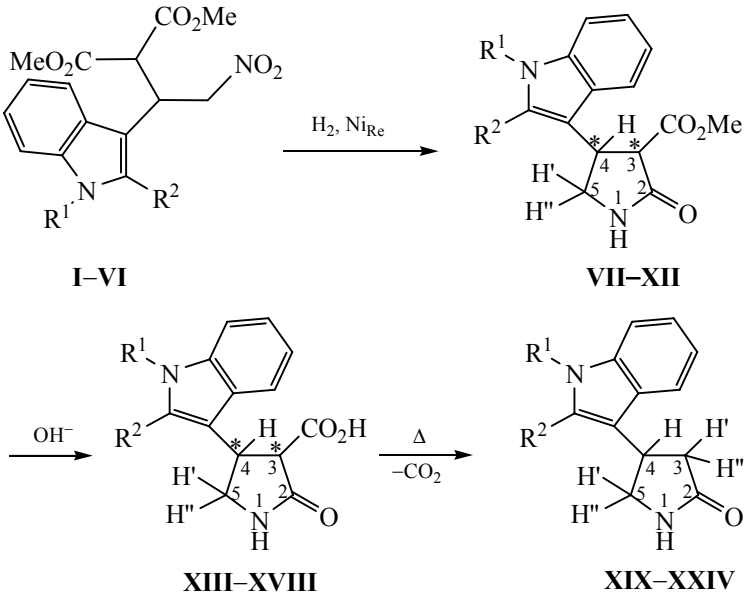
We carried out hydrogenation of nitroesters **I–VI** with electrolytic hydrogen on Raney nickel (atmospheric pressure, 18–20°C) in methanol or a 1 : 1 acetone–methanol mixture. The 4-nitrobutanoates **I–VI** were obtained via condensation of nitroethenes with malonic ester as described earlier [6–8].

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%). Noteworthily, 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, $^{1}$H NMR, and $^{13}$C NMR spectro-

**Scheme 1.**




**I–VI** **VII–XII**

**XIII–XVIII** **XIX–XXIV**

$R^1$ = 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 (1745–1730 $cm^{-1}$) and the lactam (1705–1685 $cm^{-1}$) carbonyl groups; the spectra of pyrrolidone carboxylic acids **XIII**–**XVIII** contained broadened absorption bands (1712–1613 $cm^{-1}$) 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 (1693–1679 $cm^{-1}$) (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 3315–3185 and 3415–3350 $cm^{-1}$, respectively.

$^1$H 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 ($C^4$H)] and a doublet [3.55 ppm ($C^3$H), $^3J_{34}$ 10.7 Hz] in the $^1$H NMR spectrum of pyrrolidone carboxylic acid **XIV**; the methylene protons resonated as triplets [3.42, 3.51 ppm (S5N'H"), ($C^5$H'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 $C^4$H (4.07 ppm) and the $C^4$ atom (36.97 ppm) as well as between the $C^3$H (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 $C^3$H, $C^4$H, and $C^5H_2$ atoms of the pyrrolidone ring and showed that the $C^4$H proton signal appeared in a weaker field region as compared to that of the $C^3$H 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.

$^1$H 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 | ν, $cm^{-1}$ | | $\delta_H$, ppm | | | | | | *J*, Hz | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | NH ($NH_{Ind}$) | $CO_2Me$, C=O | Ind, ($R^1$), [$R^2$] | $C^3H$, $C^3H'$ ($C^3H''$) | $C^4H$ | $C^5H'$ ($C^5H''$) | NH ($NH_{Ind}$) | $CH_3$ (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 |

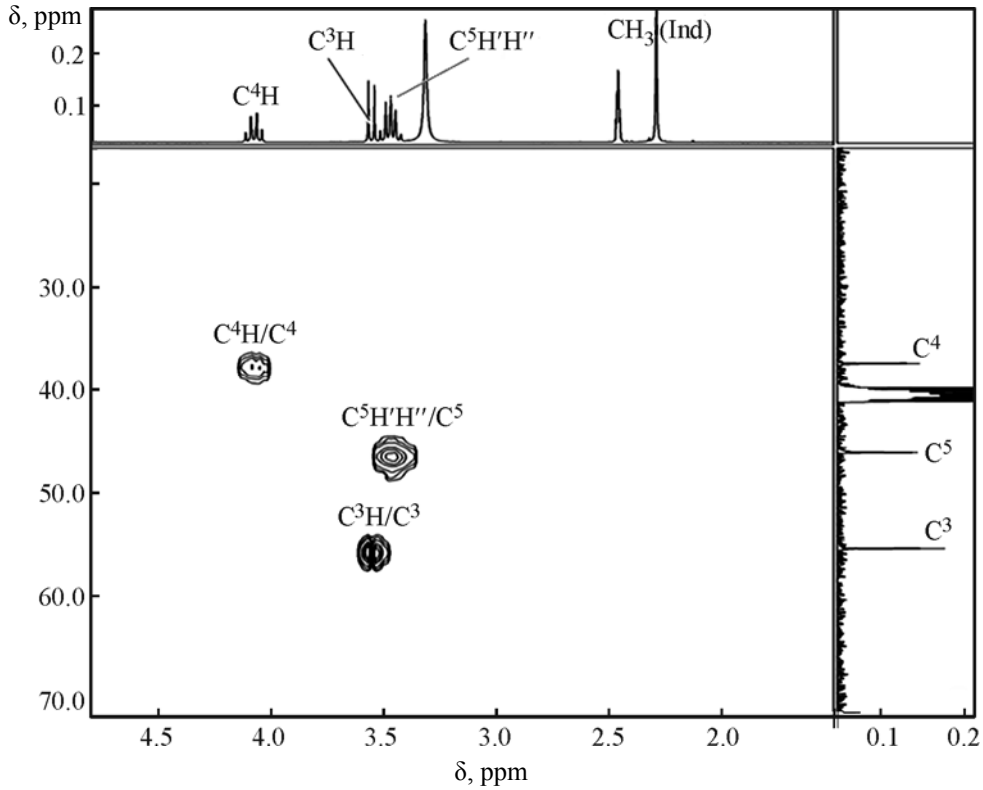
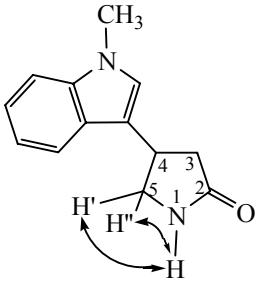



**Fig. 1.** Fragment of $^{1}H–^{13}C$ HMQC spectrum of compound **XIV** in DMSO-$d_6$.

$C^4H$ methine proton (3.95 ppm) of the pyrrolidone ring; the signals of the $C^3H'H''$ 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 $C^5H'H''$ protons resonated as a triplet [3.21 ppm ($C^5H'$), $^3J_{45'}$ 8.8, $^2J_{5'5''}$ 8.8 Hz] and a doublet of doublets [3.64 ppm $C^5H''$), $^3J_{45''}$ 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 $C^3H$ and $C^5H$ methylene protons of pyrrolidone ring was aided by heteronuclear NMR spectroscopy. In particular, the correlations between the signals of the $C^4H$ (3.95 ppm) and $C^4$ (32.82 ppm), $C^3H'H''$ (2.30, 2.55 ppm) and $C^3$ (37.81 ppm), $C^5H'H''$ (3.21, 3.64 ppm) and $C^5$ (48.55 ppm) atoms were found in the HMQC spectrum of compound **XXI** (Fig. 2). Validity of signal assignment of the $C^3$ and $C^5$ 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 $C^5H'H''$ 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 δ 2.30 and 2.55 ppm to the $C^3$ 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 $^1H$ 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 γ-aminobutyric acid and piracetam. Furthermore, they are of interest as potentially biologically active compounds. For example, 4-(indol-

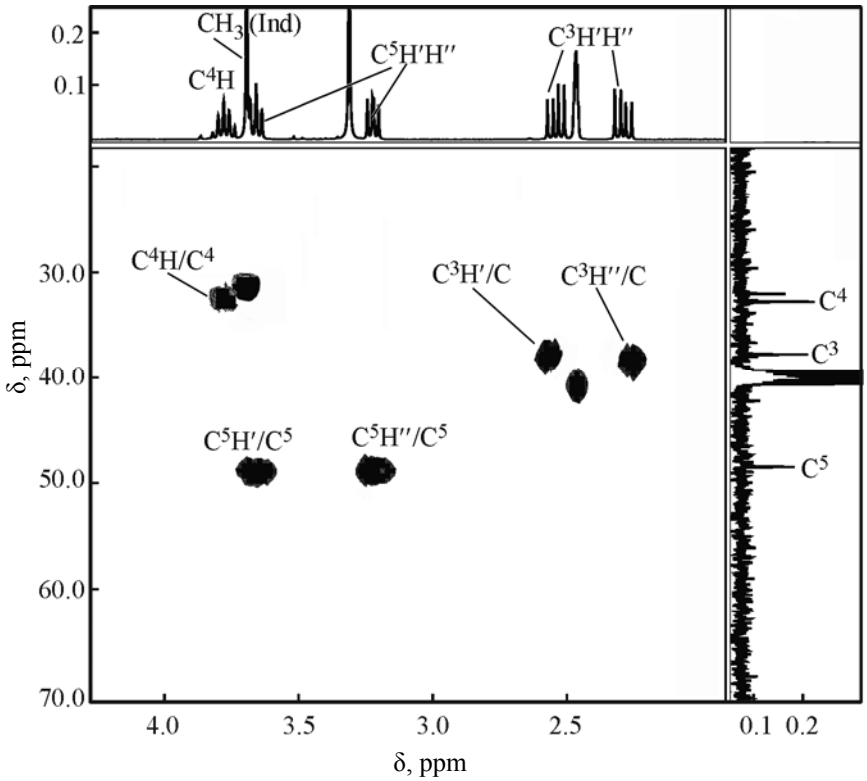



**Fig. 2.** Fragment of $^{1}H–^{13}C$ HMQC spectrum of compound **XXI** in DMSO-$d_6$.

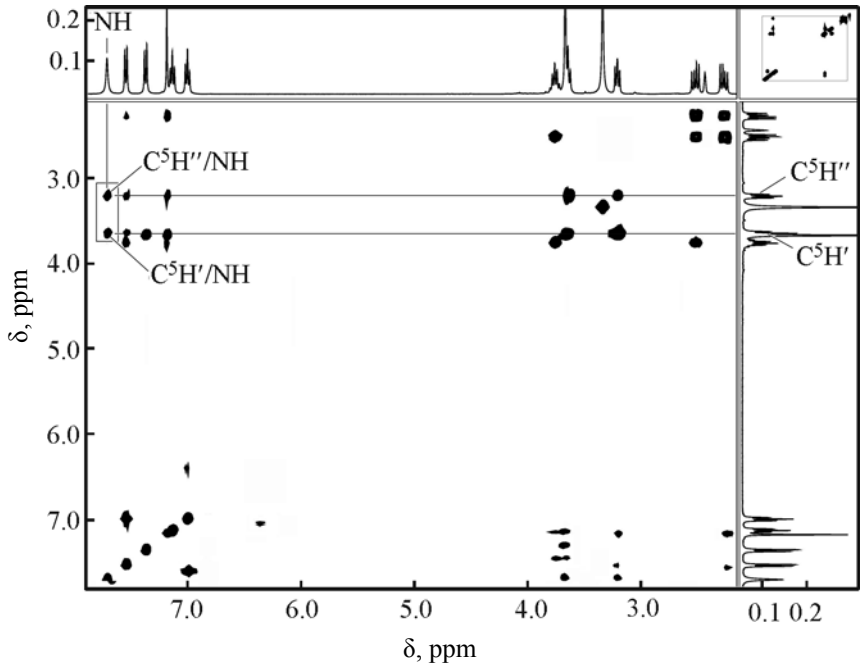



**Fig. 3.** $^{1}H–^{1}H$ NOESY spectrum of compound **XXI** in DMSO-$d_6$.

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.

$^1$H, $^1$H–$^{13}$C HMQC NMR spectra of the solutions in DMSO-$d_6$ were recorded using a Jeol ECX400A spectrometer operating at 399.78 ($^1$H) and 100.525 MHz ($^{13}$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 × 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 $C_{14}H_{14}N_2O_3$. 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. $C_{15}H_{16}N_2O_3$. 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. $C_{15}H_{16}N_2O_3$. 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. $C_{21}H_{20}N_2O_3$. 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 × 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. $C_{16}H_{18}N_2O_3$. 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. $C_{22}H_{22}N_2O_3$. 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 ~ 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 $C_{13}H_{12}N_2O_3$. 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). $^{13}$C NMR spectrum (DMSO-$d_6$), $\delta_C$, ppm: 172.67 ($C^2$), 54.63 ($C^3$), 36.97 ($C^4$), 45.51 ($C^5$), 171.94 (COOH); 108.27, 111.44, 118.45, 119.01, 120.70, 126.69, 133.27, 136.02 (Ind), 11.88 ($CH_3$Ind). Found, %: C 65.00, 64.99; H 5.58, 5.57; N 10.99, 11.01. $C_{14}H_{14}N_2O_3$. 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. $C_{13}H_{18}N_2O$. 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

1. Berestovitskaya, V.M., Vasil'eva, O.S., and Ostroglyadov, E.S., *2-Pirrolidon i ego proizvodnye* (2-Pyrrolidone and Its Derivatives), St. Petersburg: Asterion, 2013, 192 p. ISBN: 978-5-00045-072-7.
2. Mashkovskii, M.D., *Lekarstvennye sredstva* (Drugs), Moscow: RIA "Novaya Volna," 2012.
3. EP Patent 002380, 1999.
4. 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.
5. Perekalin, V.V. and Zobacheva, M.M., *Zh. Obshch. Khim.*, 1959, vol. 29, no. 9, p. 2095.
6. Mamaev, V.P. and Rodina, O.A., *Izv. Sib. Otd. Akad. Nauk SSSR*, 1962, no. 8, p. 72.
7. Kobzareva, V.N., Vasil'eva, O.S., Zobacheva, M.M., Berestovitskaya, V.M., *Zh. Org. Khim.*, 1997, vol. 33, no. 10, p. 1598.
8. *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.
9. Baron, M., Lemaire, M., Metay, E., and Popowycz, F., *Green Chem*., 2013, vol. 15, no. 4, p. 1006. DOI: 10.1039/c3gc37024k.
10. Papayan, G.L., *Arm. Khim. Zh.*, 1970, vol. 23, no. 2, p. 200.
11. 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.
12. 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.
13. 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.
14. Pretch, E., Bühlmann, P., and Affolter, C., *Structure Determination of Organic Compounds: Tables of Spectral Data*, Berlin: Springer, 2000.
15. Nifant'ev, I.E. and Ivchenko, P.V., *Prakticheskii kurs spektroskopii yadernogo magnitnogo resonansa* (Practical Course of Nuclear Magnetic Resonance Spectroscopy), Moscow: MGU, 2006, p. 34.
16. Gunther, H. *NMR-Spectroskopie*, Stuttgart: Georg Thieme Verlag, 1973.