Synthesis and structure of aryl(hetaryl)spiropyrrolidones

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Hydrogenation of the diastereouniform 3-[1-aryl(hetaryl)-2-nitroethyl]-3-methoxycarbonyl-4-phenyl(3-pyridyl)-2-pyrrolidones is accompanied by intramolecular acylation of the formed amino group to afford the diastereomerically pure 4,4´-aryl(hetaryl)-3,3´-spirobi-[2-pyrrolidones]. The structures of these diastereomers were characterized by IR, ^{1}H and ^{13}C NMR spectroscopy using heteronuclear correlation experiments, and X-ray diffraction study.

Key words: 2-pyrrolidones, 3,3´-spiropyrrolidones, diastereomers, catalytic hydrogenation.

Spiroconjugated heterocycles are the part of natural compounds and synthetic medicaments. In particular, the substances containing spiroheterocyclic systems are structural components of the antibiotics griseofulvin and rifabutin, the synthetic steroidal spironolacton, and the antihypertensive agent irbesartan.[1] Of great importance are compounds containing the pharmacophore heterocycle, *viz.*, 2-pyrrolidone. They include commonly used medicaments, such as pyracetam,[1] its phenyl analog phenotropyl (carfedone)[2—4], polyvinylpyrrolidones (hemodez, enterodez, and polydez), the 2-pyrrolidone—pyroglutamic acid composition[5] and others.

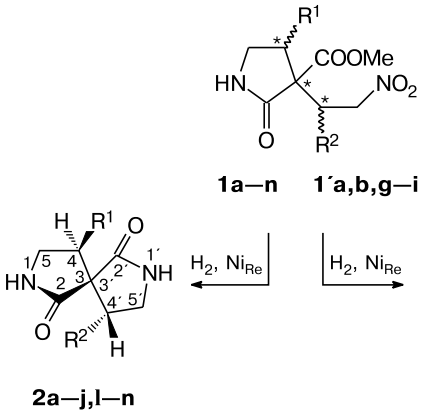
In this regard, the 3,3´-spiropyrrolidone derivatives are interesting by themselves as potential bioactive compounds, as well as precursors of the previously unknown representatives of γ-amino butyric acid and α-pyrrolidone whose molecules contain several heterocycles.

The reduction of the corresponding nitroethylpyrrolidone carboxylates in the presence of a catalyst can be a convenient method for the preparation of aryl(hetaryl)-spiropyrrolidones, which was first shown in Ref. 6 by two examples.

Compounds **1a**—**n** and **1´a**,**b**,**g**—**i** are obtained readily by the reaction of 4-aryl(hetaryl)-3-methoxycarbonyl-2-pyrrolidones with 2-aryl(hetaryl)-1-nitroethenes and isolated as one or two diastereomers **1** and **1´**, which are well-separable by recrystallization.[7,8]

We carried out hydrogenation of the diastereouniform nitroethylpyrrolidone carboxylates **1a**—**n** and **1´a**,**b**,**g**—**i** with electrolytic hydrogen in the presence of the nickel catalyst under atmospheric pressure at 18—20 °C. The reduction was accompanied by intramolecular acylation of the initially formed amino group to afford spiropyrrolidones isolated as the diastereouniform compounds **2a**—**j**,**l**—**n** and **2´a**,**b**,**g**—**i** (Scheme 1).

Scheme 1



R^1 = Ph, R^2 = Ph (**1a**, **1´a**, **2a**, **2´a**), 4-MeC_6H_4 (**1b**, **1´b**, **2b**, **2´b**), 4-$MeOC_6H_4$ (**1c**, **2c**), 4-$Me_2NC_6H_4$ (**1d**, **2d**), 4-ClC_6H_4 (**1e**, **2e**), 4-$O_2NC_6H_4$ (**1f**), 4-$H_2NC_6H_4$ (**2f**), 3-py (**1g**, **1´g**, **2g**, **2´g**), 2-furyl (**1h**, **1´h**, **2h**, **2´h**), 1-methylbenzimidazol-2-yl (**1i**, **1´i**, **2i**, **2´i**), indol-3-yl (**1j**, **2j**);
R^1= 3-py, R^2 = Ph (**1k**, **2g**), 4-$MeOC_6H_4$ (**1l**, **2l**), 4-ClC_6H_4 (**1m**, **2m**), 3-py (**1n**, **2n**)

The resulted spiropyrrolidones are stable high-melting-point crystalline substances. Their structures were confirmed by IR, ^{1}H and ^{13}C NMR spectroscopy using heteronuclear correlation experiments (^{1}H—^{13}C HMQC, ^{1}H—^{13}C HMBC) for particular compounds, and X-ray

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diffraction analysis. Note that the IR spectral and elemental analysis data have been described earlier[6] for diastereomers **2a** and **2´a** obtained by hydrogenation of the corresponding nitroethylpyrrolidone carboxylates. However, the melting points given in Ref. 6 (281 and 275 °C) do not agree with those for compounds **2a** and **2´a** that were prepared and completely characterized by us (228—230 and 210—212 °C, respectively).

In the IR spectra of spiropyrrolidones **2a—j,l—n** and **2´a,b,g—i**, the stretching vibration bands of nitro groups typical of nitroethylpyrrolidone carboxylates disappear as a natural result and there are broadened absorption bands of the NH groups in the high-frequency region (3400—3150 cm^{-1}) (Table 1).

The ^{1}H NMR spectra of compounds **2a—j,l—n** and **2´a,b,g—i** (see Table 1) contain each one signal set for the

Table 1. Melting points, yields, and IR and ^{1}H NMR spectral data for aryl(hetaryl)-3,3´-spiropyrrolidones **2a—j,l—n** and **2´a,b,g—i**

Compound	M.p. /°C	Yield (%)	IR, ν/cm^{-1}		^{1}H NMR (DMSO-d_6), δ (*J*/Hz)						
			NH	C=O	R^1 (m)	R^2	H(1), H(1´) (s)	H(4)	H(4´)	H´(5), H″(5)	H´(5´), H″(5´)
2a	228—230	70	3400, 3274	1711, 1675	7.24, 7.31, 7.55 (all m)		7.88	3.39 (d, 1 H, *J* = 6.5)	3.39 (d, 1 H, *J* = 6.5)	3.24 (d, 1 H, *J* = 9.0); 3.80 (dd, 1 H, *J* = 6.5, *J* = 9.0)	3.24 (d, 1 H, *J* = 9.0); 3.80 (dd, 1 H, *J* = 6.5, *J* = 9.0)
2´a	210—212	85	3393, 3230	1712, 1682	7.03, 7.33, 7.54 (all m)		7.97, 8.34	3.08 (dd, 1 H, *J* = 8.7, *J* = 9.5)	4.16 (dd, 1 H, *J* = 8.7, *J* = 9.5)	3.18 (dd, 1 H, *J* = 9.0, *J* = 9.5); 3.49 (dd, 1 H, *J* = 8.7, *J* = 9.0)	2.92 (dd, 1 H, *J* = 9.0, *J* = 9.5); 3.28 (dd, 1 H, *J* = 8.7, *J* = 9.0)
2b	248—250	68	3394, 3286	1713, 1680	7.25, 7.32, 7.53	7.00, 7.42 (both m); 3.25 (s, Me)	7.85	3.35 (d, 1 H, *J* = 6.3)	3.32 (d, 1 H, *J* = 6.3)	3.22 (d, 1 H, *J* = 9.3); 3.80 (dd, 1 H, *J* = 6.3, *J* = 9.3)	3.18 (d, 1 H, *J* = 9.3); 3.77 (dd, 1 H, *J* = 6.3, *J* = 9.3)
2´b	289—291	72	3393, 3253	1712, 1680	7.19	6.98, 7.05 (both m); 3.39 (s, Me)	7.94, 8.31	3.08 (dd, 1 H, *J* = 8.7, *J* = 9.4)	4.11 (dd, 1 H, *J* = 8.7, *J* = 9.4)	3.19 (dd, 1 H, *J* = 8.9, *J* = 9.4); 3.44 (dd, 1 H, *J* = 8.7, *J* = 8.9)	2.89 (dd, 1 H, *J* = 8.9, *J* = 9.4); 3.24 (dd, 1 H, *J* = 8.7, *J* = 8.9)
2c	241—243	86	3395, 3270	1710, 1678	7.25, 7.32 7.55	6.88, 7.47 (both m); 3.71 (s, Me)	7.92	3.37 (d, 1 H, *J* = 6.4)	3.34 (d, 1 H, *J* = 6.4)	3.23 (d, 1 H, *J* = 9.2); 3.72 (dd, 1 H, *J* = 6.4, *J* = 9.2)	3.18 (d, 1 H, *J* = 9.2); 3.72 (dd, 1 H, *J* = 6.4, *J* = 9.2)
2d	252—253	50	3220, 3165	1713, 1675	7.25, 7.55, 7.64	7.33, 7.55 (both m); 3.00 (s, Me)	8.00	3.40 (d, 1 H, *J* = 6.4)	3.37 (d, 1 H, *J* = 6.4)	3.24 (d, 1 H, *J* = 9.3); 3.72 (dd, 1 H, *J* = 6.4, *J* = 9.3)	3.27 (d, 1 H, *J* = 9.3); 3.75 (dd, 1 H, *J* = 6.4, *J* = 9.3)
2e	264—265	73	3230	1725, 1675	6.55, 7.00	6.57, 6.90 (both m)	8.14	3.47 (d, 1 H, *J* = 6.3)	3.43 (d, 1 H, *J* = 6.3)	2.86 (d, 1 H, *J* = 9.4); 3.94 (dd, 1 H, *J* = 6.3, *J* = 9.4)	2.90 (d, 1 H, *J* = 9.4); 3.94 (dd, 1 H, *J* = 6.3, *J* = 9.4)
2f	289—291	71	3385, 3200	1731, 1700	7.83, 8.05	7.00, 7.21 (both m)	8.00, 7.67[a]	3.45 (d, 1 H, *J* = 6.5)	3.45 (d, 1 H, *J* = 6.5)	3.17 (d, 1 H, *J* = 9.4); 3.85 (dd, 1 H, *J* = 6.5, *J* = 9.4)	3.17 (d, 1 H, *J* = 9.4); 3.85 (dd, 1 H, *J* = 6.5, *J* = 9.4)
2g	272—274	60	3395, 3267	1711, 1680	6.60, 6.97, 7.56	7.33, 7.64, 8.01, 8.14, 8.24 (all m)	8.47, 8.69	3.45 (d, 1 H, *J* = 6.6)	3.73 (d, 1 H, *J* = 6.6)	2.85 (d, 1 H, *J* = 9.1); 3.93 (dd, 1 H, *J* = 6.6, *J* = 9.1)	2.84 (d, 1 H, *J* = 9.1); 3.93 (dd, 1 H, *J* = 6.6, *J* = 9.1)
2´g	205—207	65	3395, 3213	1700, 1676	7.25	7.10—8.51 (m)	8.05	3.05 (dd, 1 H, *J* = 8.8, *J* = 9.6)	4.25 (dd, 1 H, *J* = 8.8, *J* = 9.6)	3.25 (dd, 1 H, *J* = 8.9, *J* = 9.6); 3.55 (dd, 1 H, *J* = 8.8, *J* = 8.9)	3.05 (dd, 1 H, *J* = 8.9, *J* = 9.6); 3.25 (dd, 1 H, *J* = 8.8, *J* = 8.9)

(*to be continued*)

Table 1 (*continued*)

Compound	M.p. /°C	Yield (%)	IR, ν/cm^{-1}		^{1}H NMR (DMSO-d$_6$), δ (*J*/Hz)						
			NH	C=O	R^1 (m)	R^2	H(1), H(1′) (s)	H(4)	H(4′)	H′(5), H″(5)	H′(5′), H″(5′)
2h	235—236	72	3356, 3202	1707, 1675	7.25, 7.31, 7.47	6.33, 6.40, 7.59 (all m)	7.92, 8.01	3.65 (d, 1 H, *J* = 6.4)	3.60 (d, 1 H, *J* = 6.4)	3.37 (d, 1 H, *J* = 9.0); 3.82 (dd, 1 H, *J* = 6.4, *J* = 9.0)	3.28 (d, 1 H, *J* = 9.0); 3.65 (dd, 1 H, *J* = 6.4, *J* = 9.0)
2′h	215—217	72	3395, 3282	1723, 1684	7.14, 7.22	6.25, 6.49, 7.70 (all m)	7.91, 8.26	3.05 (dd, 1 H, *J* = 8.6, *J* = 9.5)	4.16 (dd, 1 H, *J* = 8.6, *J* = 9.5)	3.22 (dd, 1 H, *J* = 9.0, *J* = 9.5); 3.50 (dd, 1 H, *J* = 8.6, *J* = 9.0)	2.80 (dd, 1 H, *J* = 9.0, *J* = 9.5); 3.30 (dd, 1 H, *J* = 8.6, *J* = 9.0)
2i	285—287	60	3292, 3230	1720, 1667	6.52, 6.71, 6.91	7.05, 7.52 (both m); 2.85 (s, Me)	7.93, 8.12	3.70 (d, 1 H, *J* = 6.7)	3.67 (d, 1 H, *J* = 6.7)	2.95 (d, 1 H, *J* = 9.1); 4.00 (dd, 1 H, *J* = 6.7, *J* = 9.1)	2.95 (d, 1 H, *J* = 9.1); 3.97 (dd, 1 H, *J* = 6.7, *J* = 9.1)
2′i	310—312	68	3230, 3150	1727, 1694	7.23, 7.47	7.23, 7.53, 7.70 (all m); 3.75 (s, Me)	7.98, 8.41	3.15 (dd, 1 H, *J* = 8.7, *J* = 9.4)	4.52 (dd, 1 H, *J* = 8.7, *J* = 9.4)	3.23 (dd, 1 H, *J* = 9.1, *J* = 9.4); 3.58 (dd, 1 H, *J* = 8.7, *J* = 9.1)	3.27 (dd, 1 H, *J* = 9.1, *J* = 9.4); 3.54 (dd, 1 H, *J* = 8.7, *J* = 9.1)
2j	170—172	68	3307, 3231	1706, 1684	7.26, 7.35, 7.51	7.05, 7.35, 7.48, 7.57 (all m)	7.95, 8.00, 11.10[b]	3.36 (d, 1 H, *J* = 6.2)	3.85 (d, 1 H, *J* = 6.2)	3.25 (d, 1 H, *J* = 9.6); 3.68 (dd, 1 H, *J* = 6.2, *J* = 9.6)	3.36 (d, 1 H, *J* = 9.6); 3.64 (dd, 1 H, *J* = 6.2, *J* = 9.6)
2l	243—245	63	3225	1703, 1680	7.33, 8.00, 8.45, 8.64	6.86, 7.48, (both m); 3.69 (s, Me)	8.00	3.42 (d, 1 H, *J* = 6.6)	3.32 (d, 1 H, *J* = 6.6)	3.21 (d, 1 H, *J* = 9.0); 3.75 (dd, 1 H, *J* = 6.6, *J* = 9.0)	3.27 (d, 1 H, *J* = 9.0); 3.75 (dd, 1 H, *J* = 6.6, *J* = 9.0)
2m	176—178	61	3260, 3120	1705, 1682	7.34, 8.00, 8.45, 8.66	7.35, 7.58 (both m)	8.03	3.44 (d, 1 H, *J* = 6.7)	3.42 (d, 1 H, *J* = 6.7)	3.22 (d, 1 H, *J* = 9.0); 3.78 (dd, 1 H, *J* = 6.7, *J* = 9.0)	3.25 (d, 1 H, *J* = 9.0); 3.75 (dd, 1 H, *J* = 6.7, *J* = 9.0)
2n	333—335	45	3395, 3270	1710, 1680	7.34, 8.00, 8.45, 8.69 (all m)		8.06	3.47 (d, 1 H, *J* = 6.5)	3.30 (d, 1 H, *J* = 6.5)	3.30 (d, 1 H, *J* = 9.1); 3.77 (dd, 1 H, *J* = 6.5, *J* = 9.1)	3.42 (d, 1 H, *J* = 9.1); 3.77 (dd, 1 H, *J* = 6.5, *J* = 9.1)

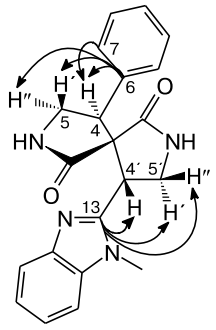
[a] The signal relates to the NH_2 protons of the *p*-aminophenyl group. [b] The signal relates to the NH proton of the indole ring.

protons of all structural fragments, which evidences their diastereo uniformities, the methylene and methyne protons of both rings form two three-spin systems in the region of δ 2.85—3.95. For this reason, to interpret correctly the positions of the signals for the methylene and methyne protons of spiropyrrolidones **2a**—**j**,**l**—**n** and **2′a**,**b**,**g**—**i**, we applied the techniques of two-dimensional heteronuclear correlation spectroscopy ^{1}H—^{13}C HMQC and ^{1}H—^{13}C HMBC performed for isomers **2a**,**e**,**g**—**j**,**l**—**n** and **2′a**,**h**,**i**. For example, the ^{1}H—^{13}C HMQC spectrum of compound **2i** (Fig. 1) displays the correlations between H(4) (δ 3.70) and C(4) atoms (δ 45.22), H(4′) (δ 3.67) and C(4′) (δ 36.40); H′(5) (δ 2.95) and C(5) (δ 48.75), H″(5) (δ 4.00) and C(5) (δ 48.75); H′(5′) (δ 2.95) and C(5′) (δ 46.40), H″(5′) (δ 3.97) and C(5′) (δ 46.40). The analogous correlation is observed in the spectrum of isomer **2′i** (Fig. 2).

Consequently, the analysis of the ^{1}H—^{13}C HMQC spectra of diastereomers **2i** and **2′i** allowed distinguishing the signals for the methyne (H(4) and H(4′)) and methylene (H′(5), H″(5), H′(5′), and H″(5′)) protons of the pyrrolidone rings in the multispin systems, as well as determining the chemical shifts for the *ipso*-C atom of the phenyl group ($\delta_{C(6)}$ 142.66 and 142.36, respectively) and the C(13) atom of the benzimidazole ring ($\delta_{C(13)}$ 155.74 and 151.53, respectively) (see Figs 1 and 2; Table 2).

The correctness of the signal assignment for the methyne and methylene protons belonging to a certain pyrroli-

done ring in the molecules of spiropyrrolidones **2i** and **2´i** was confirmed by $^1H—^{13}C$ HMBC. For example, the $^1H—^{13}C$ HMBC spectrum of compound **2i** (Fig. 3) displays the correlation between the H(4) proton (δ 3.70) and the *ipso*-C atom of the phenyl ring ($\delta_{C(6)}$ 142.66), the H´(5) (δ 2.95), H″(5) protons (δ 4.00) and the C(6) atom of the phenyl ring (δ 142.66); between the H(4´) proton (δ 3.67) and the C(13) atom of the benzimidazole ring (δ 155.74); between the H´(5´) (δ 2.95), H″(5´) protons (δ 3.97) and the C(13) atom (δ 155.74), as well as between the H(4) proton (δ 3.70) and the *ortho*-C atom of the phenyl group ($\delta_{C(7)}$ 128.59). The analogous correlation is observed in the $^1H—^{13}C$ HMBC spectrum of diastereomer **2´i** (Fig. 4).



The correlation spectra showed the difference in the appearance of the H(4) and H(4´) methyne protons of the pyrrolidone rings: in isomer **2´i**, the signals for H(4) and H(4´) are shifted upfield (δ 3.15) and downfield (δ 4.52), respectively, compared to the analogous signals for isomer **2i** ($\delta_{H(4)}$ 3.70 and $\delta_{H(4´)}$ 3.67). Such pattern is typical of all compounds synthesized (see Table 1).

The analysis of the $^1H—^{13}C$ HMQC and $^1H—^{13}C$ HMBC spectra of compounds **2a**,**e**,**g—j**,**l—n** and **2´a**,**h**,**i** allows correct high-probability interpretation of the ^1H and ^{13}C NMR spectra of all obtained spiropyrrolidones **2a—j**,**l—n** and **2´a**,**b**,**g—i**.

We received an important information on the structures of compounds **2a—j**,**l—n** and **2´a**,**b**,**g—i** from the X-ray diffraction study of diastereomers **2i** and **2´i** (Figs 5—8 and Table 3).

Compounds **2i** and **2´i** crystallize as racemates and have the following relative configuration of two asymmetric carbon atoms (C(4) and C(4´)): *rel*-(4*S*,4´*S*) (*R*,*R*) and *rel*-(4*S*,4´*R*) (*R*,*S*), respectively. In both molecules, the lactam rings of spiropyrrolidone are arranged almost perpendicularly to each other: the dihedral angles between the ring planes C(5)N(1)C(2)C(3)C(4) and C(5´)N(1´)C(2´)C(3)C(4´) are 87.5(2) and 86.8(1)° in the molecules of **2i** and **2´i**, respectively. The five-membered rings in both molecules have the envelope conformation. In the molecule of **2i**, the fragments C(5)N(1)C(2)C(3) and C(5´)N(1´)C(2´)C(3) are planar

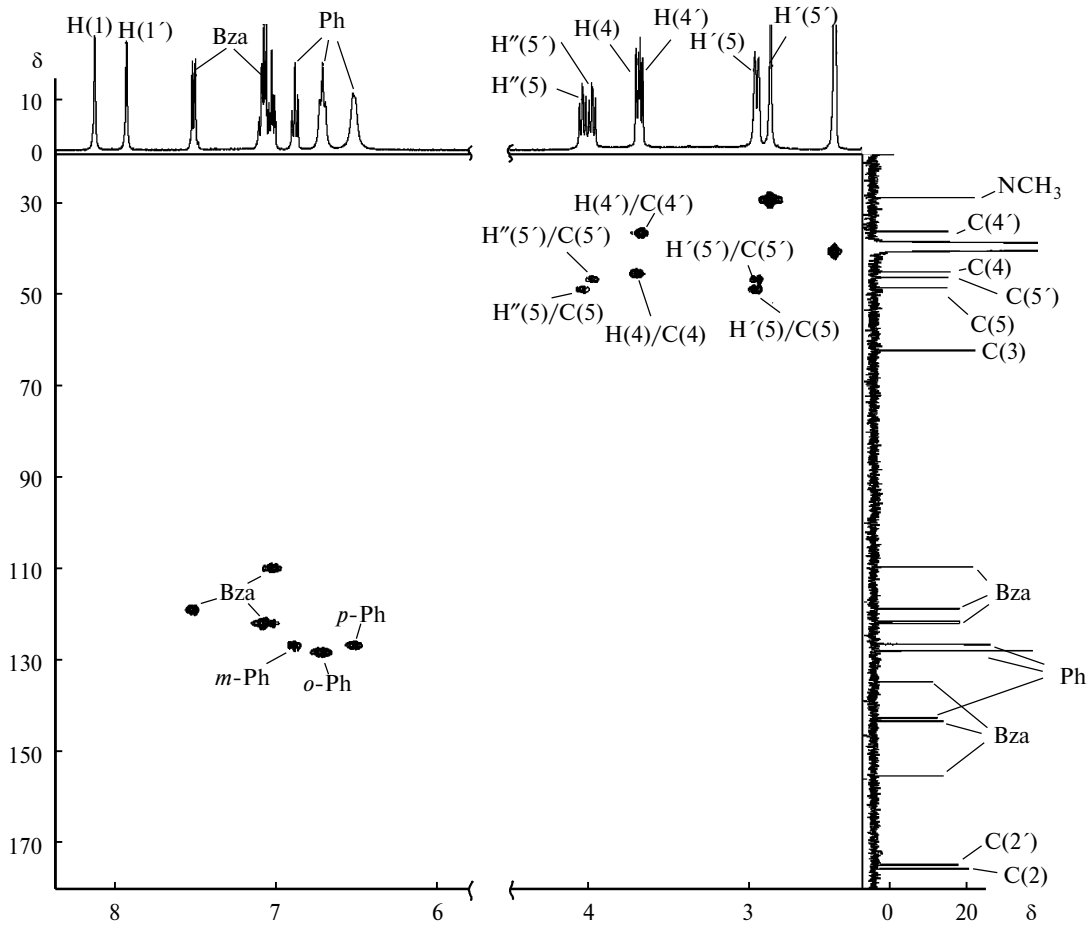


Fig. 1. $^1H—^{13}C$ HMQC spectrum of compound **2i** in DMSO-d_6 (here and in Figs 2—4 Bza designates the benzimidazole fragment).

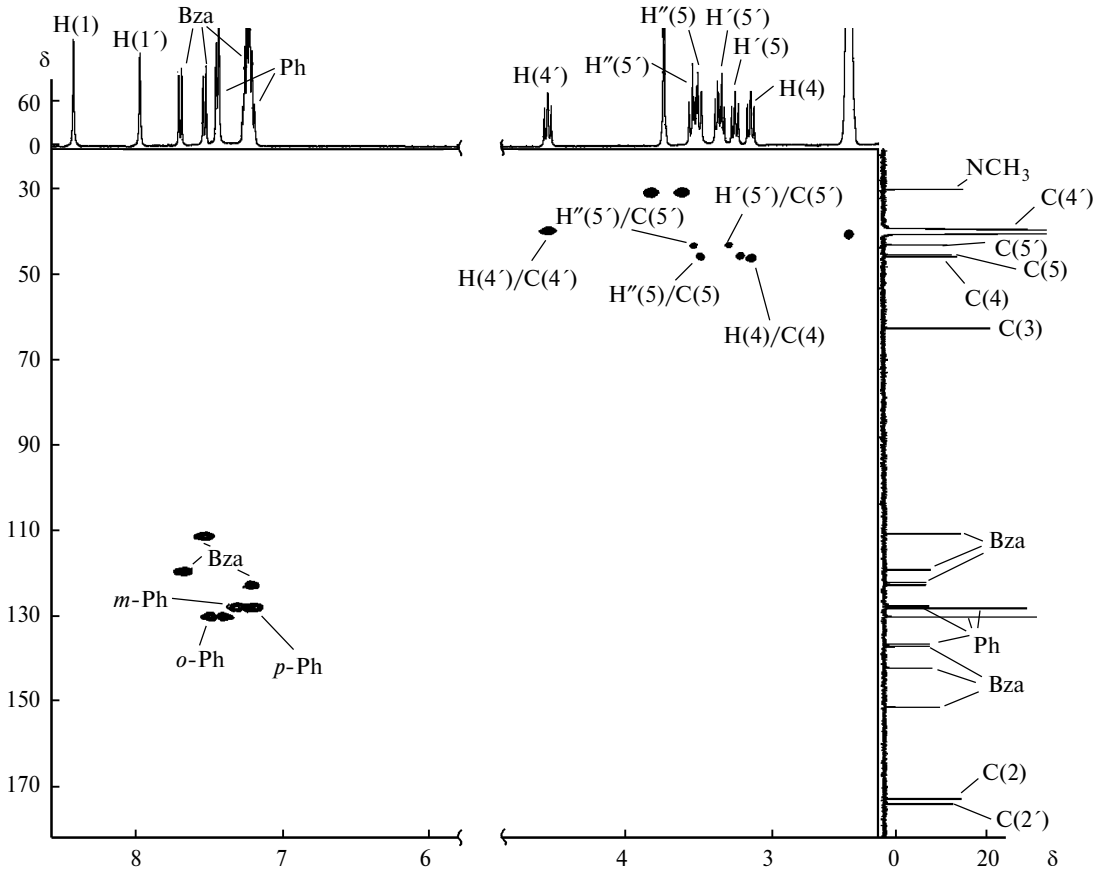


Fig. 2. $^{1}H—^{13}C$ HMQC spectrum of compound **2´i** in DMSO-d_6.

within 0.020(2) and 0.016(2) Å and the deviations of the C(4) and C(4´) from these planes are 0.480(2) and 0.446(3) Å, respectively. In the molecule of **2´i**, the fragments C(5)N(1)C(2)C(3) and C(5´)N(1´)C(2´)C(3)

Table 2. ^{13}C NMR spectra of compounds **2a,e,g—j,l—n** and **2´a,h,i** in DMSO-d_6

Compound	δ							
	C(2)	C(2´)	C(3)	C(4)	C(4´)	C(5)	C(5´)	R^1, R^2
2a	173.51	173.51	62.94	46.58	46.58	45.43	45.43	127.70, 128.50, 130.71, 136.72
2´a	174.04	174.53	63.09	45.37	44.87	45.60	42.16	127.71, 128.00, 128.27, 128.77, 129.59, 130.80, 137.23, 137.32
2e	175.85	175.85	62.45	45.67	45.05	48.55	48.45	126.32, 126.75, 128.23, 128.31, 128.64, 131.17, 141.73, 142.67
2g	173.27	173.20	62.76	46.86	43.86	45.40	45.00	123.59, 127.81, 128.50, 130.73, 136.43, 138.10, 148.94, 151.50
2h	173.40	173.07	61.38	47.60	39.30	44.66	43.46	108.07, 111.08, 127.90, 128.68, 130.43, 136.50, 142.52, 152.17
2´h	173.76	173.50	62.12	46.25	39.80	45.33	41.92	108.83, 110.98, 128.00, 128.68, 129.68, 137.19, 143.44, 151.69
2i	175.02	175.75	62.28	45.22	36.40	48.75	46.40	110.14, 118.78, 121.82, 122.01, 126.59, 128.32, 134.85, 142.66, 143.32, 155.74, 29.10 (Me)
2´i	173.01	174.25	62.64	45.84	40.00	45.43	43.12	110.86, 119.37, 122.28, 122.89, 127.80, 128.33, 130.34, 137.29, 136.75, 142.36, 151.53, 30.09 (Me)
2j	174.31	174.69	63.00	46.69	37.89	45.41	47.18	109.55, 112.16, 118.23, 119.28, 121.49, 125.63, 127.76, 128.68, 128.76, 130.41, 136.03, 137.39
2l	172.98	172.70	62.51	47.67	43.56	45.36	44.74	126.83, 127.55, 131.44, 138.02, 140.67, 142.94, 147.88, 159.34, 55.11 (Me)
2m	173.10	173.10	62.71	46.12	43.90	45.26	44.93	123.65, 128.55, 132.33, 132.55, 132.89, 135.35, 138.14, 149.02, 151.51
2n	173.14	173.14	62.52	44.71	44.71	44.05	44.05	123.76, 132.37, 138.28, 149.11, 151.57

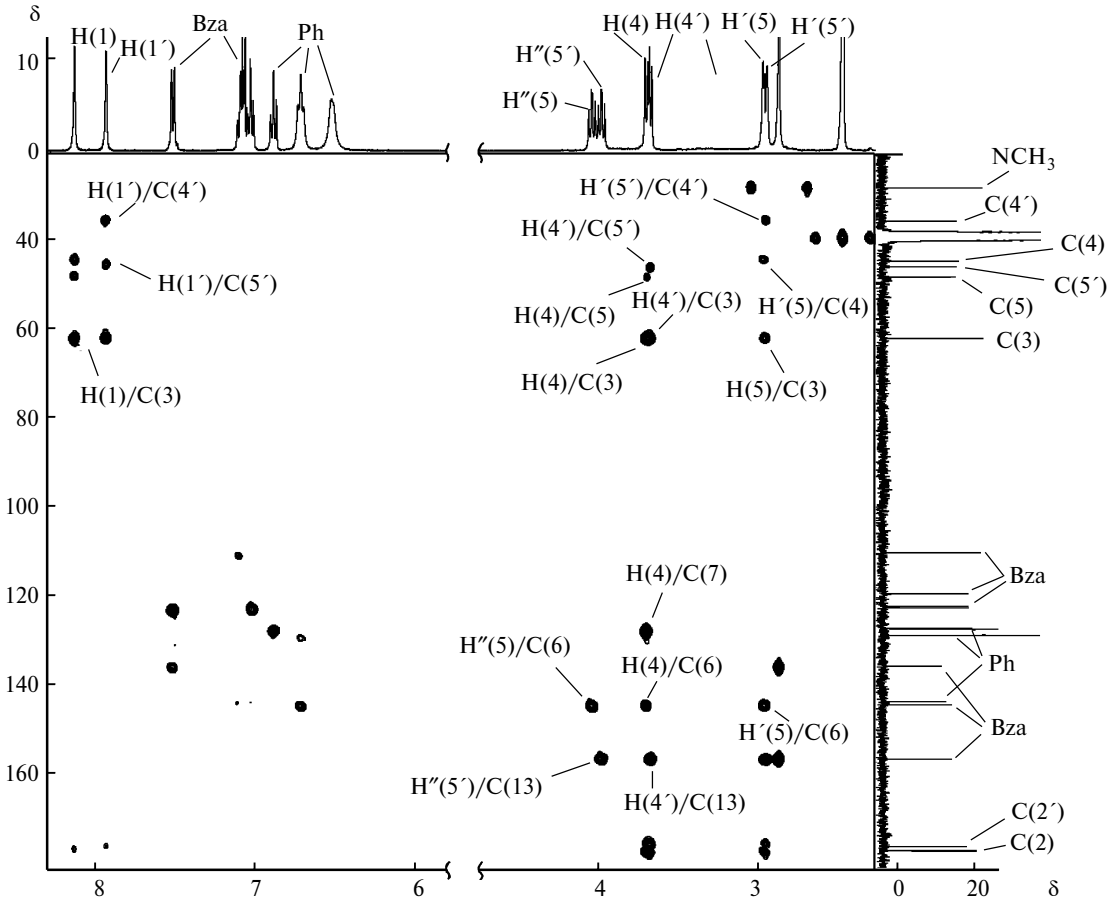


Fig. 3. $^{1}H—^{13}C$ HMBC spectrum of compound **2i** in DMSO-d_6.

are planar within 0.014(3) and 0.010(2) Å and the deviations of the C(4) and C(4´) atoms are 0.378(3) and 0.446(3) Å, respectively.

The crystals of compounds **2i** and **2´i** are stabilized by the N—H...O- and O—H...O hydrogen bonds. In the crystal of **2i**, there are only the N—H...O hydrogen bonds and

Table 3. Crystallographic parameters and X-ray diffraction data for compounds **2i** and **2´i**

Parameter	**2i**	**2´i**
Color, habit	Colorless prysmatic	
Molecular formula	$C_{21}H_{20}N_4O_2$	$C_{21}H_{20}N_4O_2 \cdot C_2H_6O$
Molecular weight	360.41	406.48
Crystal system	Monoclinic	
Space group	$P2_1/n$	$P2_1/c$
a/Å	10.775(1)	9.836(3)
b/Å	10.017(1)	24.132(6)
c/Å	16.718(2)	9.463(2)
β/deg	91.018(2)	108.683(3)
V/Å^3	1804.2(3)	2128(1)
Z	4	4
d_{calc}/g cm^{-3}	1.327	1.269
μ(Mo)/cm^{-1}	0.88	0.86
F(000)	760	864
θ range/deg	$2.2 \le \theta \le 26.0$	$2.2 \le \theta \le 27.0$
R_{int}	0.061	0.069

Parameter	**2i**	**2´i**
h, k, and l indice measurement interval	$-12 \le h \le 13$, $-12 \le k \le 12$, $-20 \le l \le 20$	$-12 \le h \le 12$, $-30 \le k \le 30$, $-12 \le l \le 12$
Number of measured/ independent reflections	13322/ /3543	22731/ /4640
Number of observed reflections with $I > 2\sigma(I)$	2149	2657
R	0.0544	0.0630
R_w	0.1254	0.1526
R_{all}	0.0955	0.1164
$R_{w,all}$	0.1440	0.1847
Stiffness parameter	1.04	1.05
Number of refined parameters	324	355

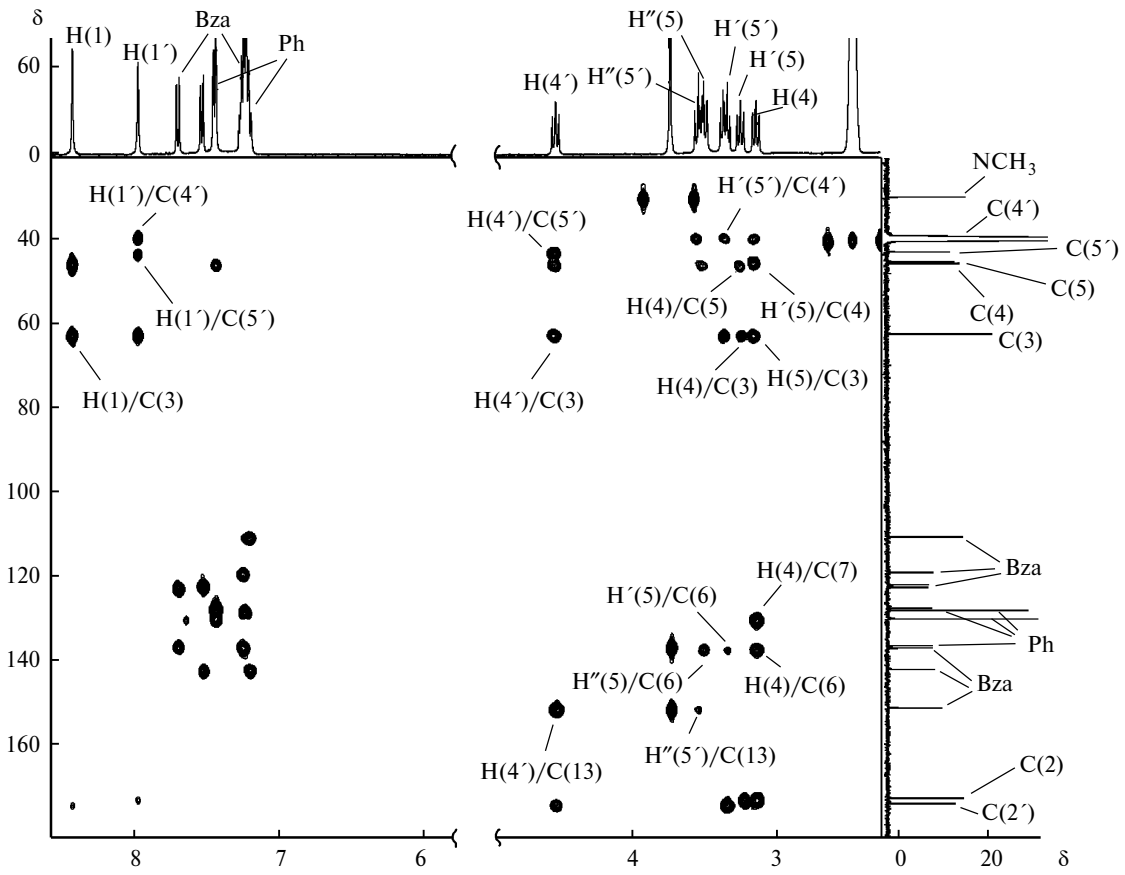


Fig. 4. $^{1}H—^{13}C$ HMBC spectrum of compound **2′i** in DMSO-d_6.

two-dimensional grid of hydrogen bonds (see Fig. 7). In the crystal of **2′i**, there are both N—H...O and O—H...O hydrogen bonds and the hydrogen bonding motif is a tape (see Fig. 8). The parameters for the hydrogen bonds are given in Table 4.

Since the ^{1}H NMR spectral data of diastereomers **2i** and **2′i** agree good with the spectra of all obtained

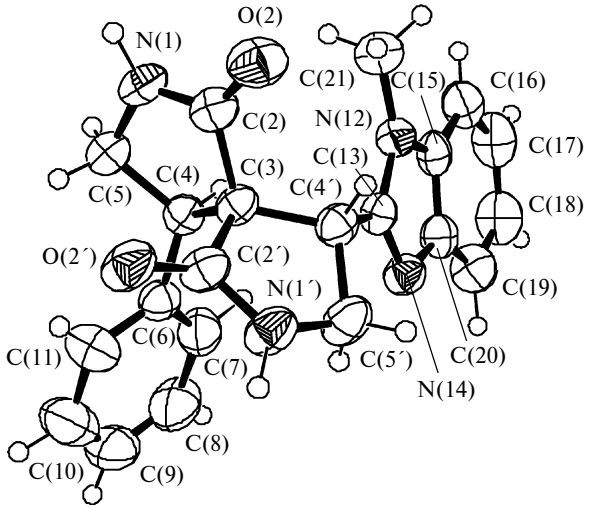


Fig. 5. Molecular geometry of compound **2i** in the crystal. Anisotropic thermal vibrations are given with 50% probability.

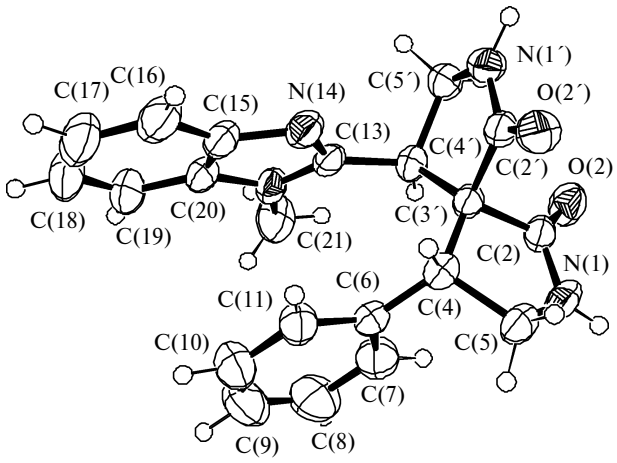


Fig. 6. Molecular geometry of compound **2′i** in the crystal (the solvate molecule of ethanol is not shown). Anisotropic thermal vibrations are shown with 50% probability.

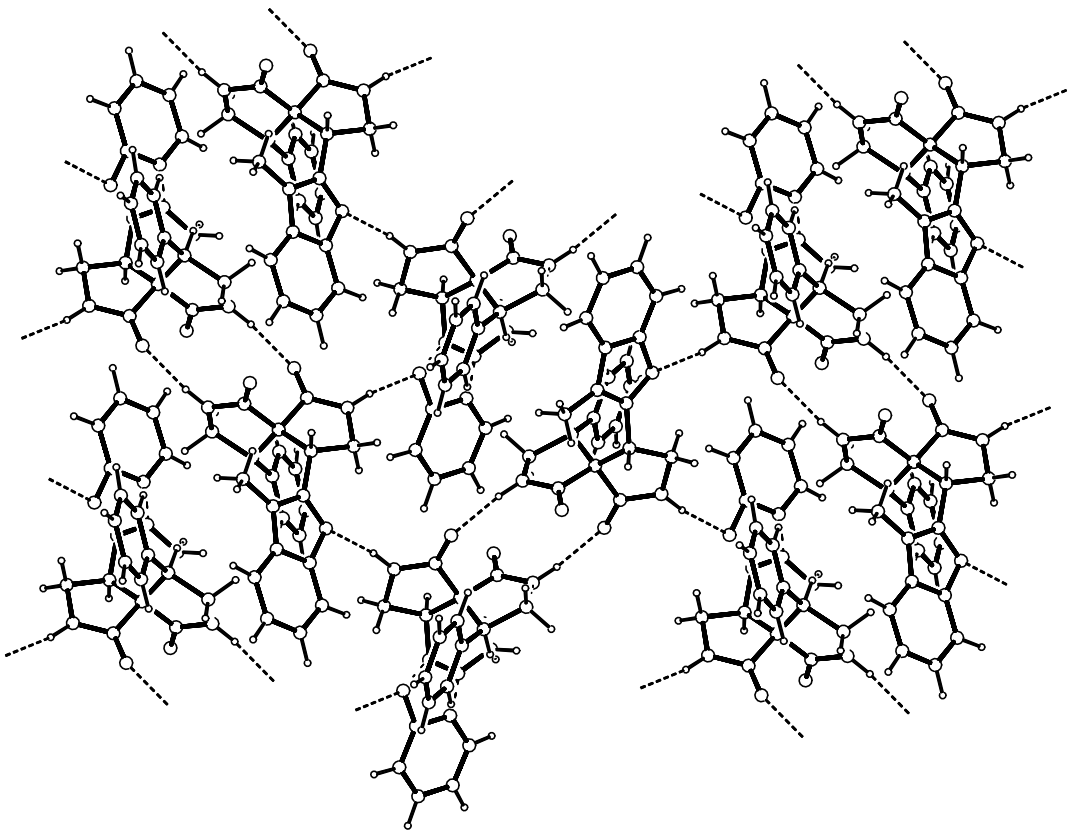


Fig. 7. Hydrogen bonding system in the crystal of compound **2i**.

spiropyrrolidones **2a**—**j**,**l**—**n** and **2′a**,**b**,**g**—**i**, one can assume that all diastereomers of the type **2** have the configuration of two chiral centers analogous to that in the molecule of **2i** and all diastereomers of the type **2′** have the configuration analogous to that in the molecule of **2′i**.

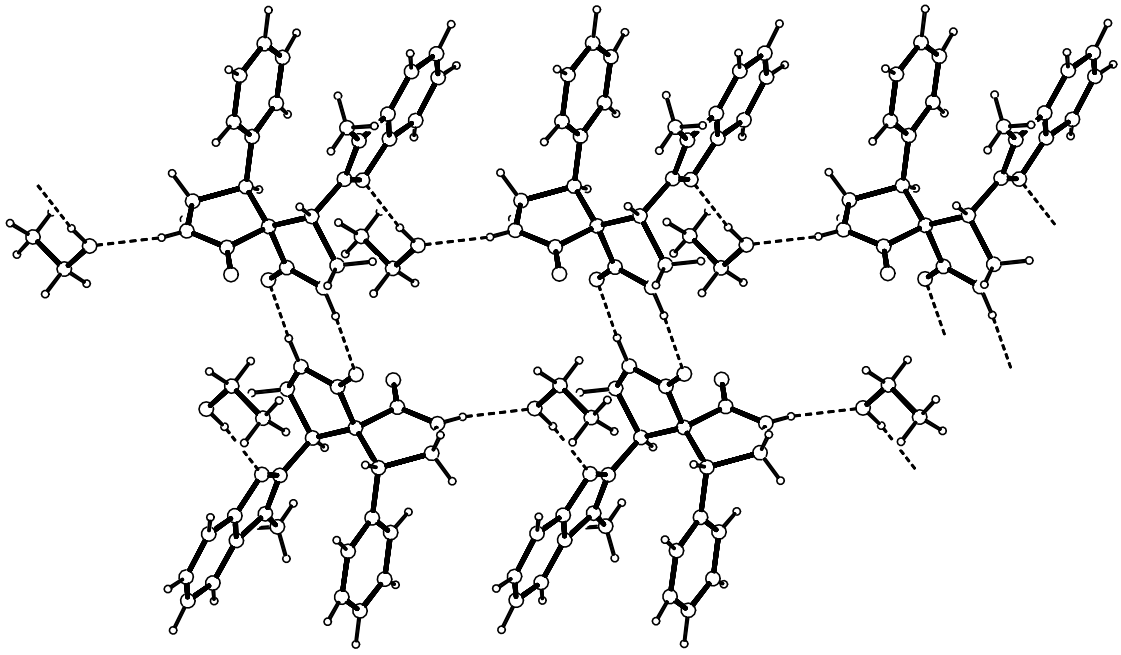


Fig. 8. Hydrogen bonding system in the crystal of compound **2′i**.

Table 4. Parameters of the intermolecular hydrogen bonds in the crystals of compounds **2i** and **2´i** (D is a donor and A is an acceptor)

Bond D—H...A	*d*/Å			DHA angle /deg	Symmetry operation
	D—H	H...A	D...A		
Crystal of compound **2i**					
N(1)—H(1)...O(2´)	0.92(3)	1.95(3)	2.857(3)	169(3)	$1-x, -y, 1-z$
N(1´)—H(1´)...N(14)″	0.98(3)	2.06(3)	3.031(3)	171.1(19)	$3/2-x, -1/2+y, 1/2-z$
Crystal of compound **2´i**					
N(1)—H(1)...O(50)	0.79(4)	2.08(4)	2.862(4)	169(3)	—
N(1´)—H(1´)...O(2´)´	0.92(4)	2.01(4)	2.919(3)	170(3)	$-x, -y, 1-z$
O(50)—H(50)...N(14)´	0.88(4)	2.00(4)	2.865(4)	173(4)	$1+x, y, z$

Thus, we obtained a series of novel aryl(hetaryl)-containing spiropyrrolidones **2a—j,l—n** and **2´a,b,g—i** whose structures were characterized and proved reliably by IR, ^{1}H and ^{13}C NMR spectroscopy (using ^{1}H—^{13}C HMQC and ^{1}H—^{13}C HMBC experiments) and X-ray diffraction study. The ^{1}H NMR spectral analysis showed that the comparative values of chemical shifts of the H(4) and H(4´) protons can be used as the analytic signs upon determination of the stereomerism of compounds **2a—j,l—n** and **2´a,b,g—i**.

The obtained compounds **2a—j,l—n** and **2´a,b,g—i** can be used for the synthesis of novel derivatives of γ-amino butyric acid and spiropyracetam and are of interest as promising bioactive compounds.

Experimental

^{1}H, ^{13}C{^{1}H}, ^{1}H—^{13}C HMQC, and ^{1}H—^{13}C HMBC spectra were recorded on Jeol ECX400A spectrometer (399.782 MHz (^{1}H) and 100. 525 MHz (^{13}C)) in DMSO-d_6 using the residual signal for the non-deuterated solvent as the internal standard. Vibrational spectra were recorded on IR Prestige-21 (Shimadzu) Fourier spectrometer in KBr pellets.

Single-crystal X-ray diffraction studies of compounds **2i** and **2´i** were performed in the Joint Spectroanalysis Center of the A. E. Arbuzov Institute of Organic and Physical Chemistry.

The single crystals of compounds **2i** and **2´i** were obtained by crystallizaion from ethanol. The X-ray diffraction experiment was performed on a Bruker Smart APEX II CCD autodiffractometer (graphite monochromator, λ(Mo-Kα) = 0.71073 Å, 293 K, ω-scan range). The semiempirical account of absorption was performed according to the SADABS program.[9] The crystallographic data and main refinement parameters for compounds **2i** and **2´i** are given in Table 3. The structures were solved by the direct method using the SIR program.[10] A solvate molecule of ethanol was found in the crystal of **2´i**. Hydrogen atoms were revealed from difference Fourier series and refined in the isotropic approximation. The hydrogen atoms of the ethanol molecule in the structure of **2´i** were placed in the geometrically calculated positions and refined in the riding model. All calculations were performed using the SHELXL-97[11] and WinGX programs.[12]

Data collection and editing and refinement of the unit cell parameters were performed by the APEX2 program.[13] The analysis of intermolecular interactions and imaging were performed using the PLATON program.[14]

The atomic coordinates of structures and their thermal parameters were deposited at the Cambridge Crystallographic Data Centre (http://www.ccdc.cam.ac.uk) under Nos 883002 and 883003, respectively.

Melting points were measured on a PTP(M) instrument.

3-Aryl(hetaryl)-3-methoxycarbonyl-2-nitroethyl-4-phenyl-2-pyrrolidones **1a—j** and **1´a,b,g—i** and 3-aryl(hetaryl)-3-methoxycarbonyl-2-nitroethyl-4-(3-pyridyl)-2-pyrrolidones **1k—n** were synthesized according to the published procedures.[7,8]

***rel*-(4*S*,4´*R*)-4,4´-Diphenyl-3,3´-spirobi[2-pyrrolidone] (2a).** A suspension of skeletal nickel catalyst (2.4 g) in ethanol (15 mL) was saturated with electrolytic hydrogen. 3-Methoxycarbonyl-3-(1-phenyl-2-nitroethyl)-4-phenyl-2-pyrrolidone (**1a**) (2.5 g, 6.7 mmol) in ethanol (80 mL) was added in the hydrogen stream and the mixture was hydrogenized until complete absorption of the calculated amount of hydrogen (0.460 L, 0.02 mol). The catalyst was separated on a filter and washed by portionwise decantation with boiling ethanol (3×100 mL). The filtrate was concentrated by 2/3 of the initial volume under reduced pressure (15—20 Torr). The crystalline product was separated on a filter to yield pyrrolidone **2a** (1.52 g, 5 mmol, 70%), m.p. 228—230 °C (from ethanol) (*cf.* Ref. 6: m.p. 281 °C (from methanol)). Found (%): C, 74.41; H, 5.61; N, 8.98. $C_{19}H_{18}N_2O_2$. Calculated (%): C, 74.49; H, 5.92; N, 9.14.

Compounds **2b—n** and **2´a,b,g—i** were prepared according to the procedure for compound **2a** using the same molar ratios of reagents.

***rel*-(4*S*,4´*S*)-4,4´-Diphenyl-3,3´-spirobi[2-pyrrolidone] (2´a)** was obtained from compound **1´a**. The yield was 85%, m.p. 210—212 °C (from ethanol) (*cf.* Ref. 6: m.p. 275 °C (from methanol)). Found (%): C, 74.58; H, 6.08; N, 8.99. $C_{19}H_{18}N_2O_2$. Calculated (%): C, 74.49; H, 5.92; N, 9.14.

***rel*-(4*S*,4´*R*)-4´-(4-Methylphenyl)-4-phenyl-3,3´-spirobi[2-pyrrolidone] (2b)** was obtained from compound **1b**. The yield was 68%, m.p. 248—250 °C (from ethanol). Found (%): C, 75.12; H, 6.29; N, 8.82. $C_{20}H_{20}N_2O_2$. Calculated (%): C, 74.98; H, 6.29; N, 8.74.

***rel*-(4*S*,4´*S*)-4´-(4-Methylphenyl)-4-phenyl-3,3´-spirobi-[2-pyrrolidone] (2´b)** was obtained from compound **1´b**. The yield was 72%, m.p. 289—291 °C (from ethanol). Found (%):

C, 74.04; H, 6.24; N, 8.44. $C_{20}H_{20}N_2O_2$. Calculated (%): C, 74.98; H, 6.29; N, 8.74.

***rel*-(4*S*,4´*R*)-4´-(4-Methoxyphenyl)-4-phenyl-3,3´-spirobi[2-pyrrolidone] (2c)** was obtained from compound **1c**. The yield was 86%, m.p. 241—243 °C (from ethanol). Found (%): C, 71.46; H, 5.84; N, 7.94. $C_{20}H_{20}N_2O_3$. Calculated (%): C, 71.41; H, 5.99; N, 8.33.

***rel*-(4*S*,4´*R*)-4´-(4-*N*,*N*-Dimethylaminophenyl)-4-phenyl-3,3´-spirobi[2-pyrrolidone] (2d)** was obtained from compound **1d**. The yield was 50%, m.p. 252—253 °C (from ethanol). Found (%): C, 72.08; H, 6.67; N, 11.72. $C_{21}H_{23}N_3O_2$. Calculated (%): C, 72.18; H, 6.63; N, 12.03.

***rel*-(4*S*,4´*R*)-4´-(4-Chlorophenyl)-4-phenyl-3,3´-spirobi[2-pyrrolidone] (2e)** was obtained from compound **1e**. The yield was 73%, m.p. 264—265 °C (from ethanol). Found (%): C, 66.85; H, 5.25; N, 8.98. $C_{19}H_{17}ClN_2O_2$. Calculated (%): C, 66.96; H, 5.03; N, 8.88.

***rel*-(4*S*,4´*R*)-4´-(4-Aminophenyl)-4-phenyl-3,3´-spirobi[2-pyrrolidone] (2f)** was obtained from compound **1f**. The yield was 71%, m.p. 289—291 °C (from ethanol). Found (%): C, 70.91; H, 5.85; N, 13.93. $C_{19}H_{19}N_3O_2$. Calculated (%): C, 71.01; H, 5.96; N, 13.08.

***rel*-(4*S*,4´*R*)-4-Phenyl-4´-(3-pyridyl)-3,3´-spirobi[2-pyrrolidone] (2g)**. The yield was 60% and m.p. 272—274 °C (from ethanol) upon the synthesis from **1g**; the yield was 55%, m.p. 270—272 °C (from ethanol) upon the synthesis from **1k**. The sample mixture of the compound obtained by reduction of compound **1g** with the sample obtained by reduction of compound **1k** showed no temperature depression. Found (%): C, 70.13; H, 5.64; N, 13.23. $C_{18}H_{17}N_3O_2$. Calculated (%): C, 70.34; H, 5.58; N, 13.67.

***rel*-(4*S*,4´*S*)-4-Phenyl-4´-(3-pyridyl)-3,3´-spirobi[2-pyrrolidone] (2´g)** was obtained from compound **1´g**. The yield was 65%, m.p. 205—207 °C (from ethanol). Found (%): C, 70.05; H, 5.68; N, 13.28. $C_{18}H_{17}N_3O_2$. Calculated (%): C, 70.34; H, 5.58; N, 13.67.

***rel*-(4*S*,4´*S*)-4´-(2-Furyl)-4-phenyl-3,3´-spirobi[2-pyrrolidone] (2h)** was obtained from compound **1h**. The yield was 72%, m.p. 235—236 °C (from ethanol). Found (%): C, 68.46; H, 5.98; N, 9.47. $C_{17}H_{16}N_2O_3$. Calculated (%): C, 68.91; H, 5.44; N, 9.45.

***rel*-(4*S*,4´*R*)-4´-(2-Furyl)-4-phenyl-3,3´-spirobi[2-pyrrolidone] (2´h)** was obtained from compound **1´h**. The yield was 72%, m.p. 215—217 °C (from ethanol). Found (%): C, 68.42; H, 5.97; N, 9.57. $C_{17}H_{16}N_2O_3$. Calculated (%): C, 68.91; H, 5.44; N, 9.45.

***rel*-(4*S*,4´*S*)-4´-(1-Methylbenzimidazol-2-yl)-4-phenyl-3,3´-spirobi[2-pyrrolidone] (2i)** was obtained from compound **1i**. The yield was 60%, m.p. 285—287 °C (from ethanol). Found (%): C, 69.52; H, 5.94; N, 15.99. $C_{21}H_{20}N_4O_2$. Calculated (%): C, 69.98; H, 5.59; N, 15.55.

***rel*-(4*S*,4´*R*)-4´-(1-Methylbenzimidazol-2-yl)-4-phenyl-3,3´-spirobi[2-pyrrolidone] (2´i)** was obtained from compound **1´i**. The yield was 68%, m.p. 310—312 °C (from ethanol). Found (%): C, 70.02; H, 5.90; N, 15.34. $C_{21}H_{20}N_4O_2$. Calculated (%): C, 69.98; H, 5.59; N, 15.55.

***rel*-(4*S*,4´*R*)-4´-(Indol-3-yl)-4-phenyl-3,3´-spirobi[2-pyrrolidone] (2j)** was obtained from compound **1j**. The yield was 68%, m.p. 170—172 °C (from ethanol). Found (%): C, 73.45; H, 5.54; N, 12.33. $C_{21}H_{18}N_3O_2$. Calculated (%): C, 73.24; H, 5.27; N, 12.20.

***rel*-(4*S*,4´*R*)-4´-(4-Methoxyphenyl)-4-(3-pyridyl)-3,3´-spirobi[2-pyrrolidone] (2l)** was obtained from compound **1l**. The yield was 63%, m.p. 243—245 °C (from ethanol). Found (%): C, 67.36; H, 5.78; N, 12.47. $C_{19}H_{19}N_3O_3$. Calculated (%): C, 67.64; H, 5.68; N, 12.46.

***rel*-(4*S*,4´*R*)-4´-(4-Chlorophenyl)-4-(3-pyridyl)-3,3´-spirobi[2-pyrrolidone] (2m)** was obtained from compound **1m**. The yield was 61%, m.p. 176—178 °C (from ethanol). Found (%): C, 63.45; H, 4.88; N, 12.05. $C_{18}H_{16}ClN_3O_2$. Calculated (%): C, 63.25; H, 4.72; N, 12.29.

***rel*-(4*S*,4´*R*)-4,4´-Di(3-pyridyl)-3,3´-spirobi[2-pyrrolidone] (2n)** was obtained from compound **1n**. The yield was 45%, m.p. 333—335 °C (from ethanol). Found (%): C, 66.57; H, 5.32; N, 18.15. $C_{17}H_{16}N_4O_2$.Calculated (%): C, 66.23; H, 5.19; N, 18.18.

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