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Reactions of 5-Nitrospiro[benzimidazole-2,1′-cyclohexane] 1,3-Dioxide with Nucleophiles

V. A. Samsonov, Yu. V. Gatilov, V. A. Savel'ev, and S. S. Baranova

Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Division, Russian Academy of Sciences, pr. Akademika Lavrent'eva 9, Novosibirsk, 630090 Russia
e-mail: Samson@nioch.nsc.ru

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Abstract—Reactions of 5-nitrospiro[benzimidazole-2,1′-cyclohexane] 1,3-dioxide with aliphatic amines and sodium hydroxide resulted in removal of one *N*-oxide oxygen atom and formation of 4-alkylamino- or 4-hydroxy-substituted 5-nitrospiro[benzimidazole-2,1′-cyclohexane] 1-oxides, respectively. The title compound reacted with ammonia and methylamine in the presence of MnO_2 with conservation of both *N*-oxide moieties, and the products were 4-amino- and 4-methylamino-5-nitrospiro[benzimidazole-2,1′-cyclohexane] 1,3-dioxides. The reactions with aromatic amines were accompanied by removal of both *N*-oxide oxygen atoms with formation of *N*-aryl-5-nitrospiro[benzimidazole-2,1′-cyclohexane]-4-amines. In the reactions of 5-nitrospiro[benzimidazole-2,1′-cyclohexane] 1,3-dioxide with sodium azide and aromatic amine hydrochlorides nucleophilic replacement of the 5-nitro group by azido or arylamino occurred, in the first case both *N*-oxide fragments being conserved. The reactions with aromatic amine hydrochlorides afforded *N*-aryl-5-nitrospiro[benzimidazole-2,1′-cyclohexan]-4-amine 1-oxides. Treatment of 5-nitrospiro[benzimidazole-2,1′-cyclohexane] 1,3-dioxide with sodium cyanide led to the formation of 5-oxo-3,5-dihydrospiro[benzimidazole-2,1′-cyclohexane]-4-carbonitrile 1-oxide.

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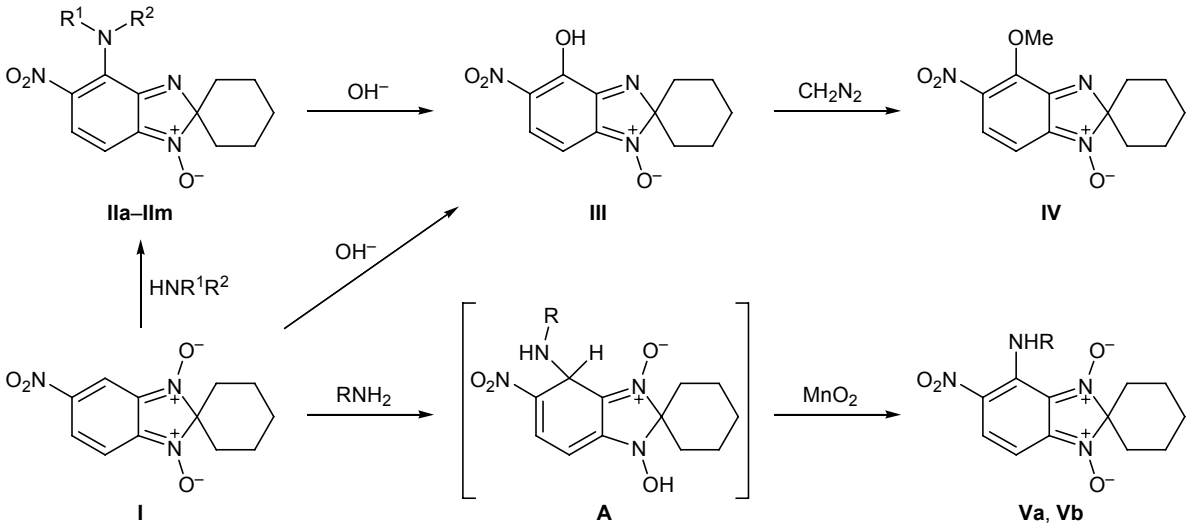
2*H*-Benzimidazoles and their derivatives attract researchers' attention as starting compounds for the synthesis of a number of heterocyclic compounds [1, 2]. 2*H*-Benzimidazole 1,3-dioxides have been studied to a considerably lesser extent despite their unusual reactivity [3]. Some 2*H*-benzimidazole 1,3-dioxides showed high biological activity against *Tripanosoma cruzi* and *Leishmania spp*. According to the World Health Organization data, these trypanosomatids alone are responsible for an infected population of nearly 30 million and more than 400 million are at risk [4–6]. Therefore, studies on the properties and development of methods of synthesis of 2*H*-benzimidazole-1,3-dioxides and preparation of their new derivatives constitute an important problem.

The main procedure for the synthesis of 2*H*-benzimidazole 1,3-dioxides is based on reaction of benzofuroxans with secondary nitroalkanes in the presence of a base. Nitro derivatives of benzofuroxan failed to react in such a way [3]. We have developed a procedure for the synthesis of 2*H*-benzimidazole 1,3-dioxides via reaction of benzofuroxans with alcohols or haloalkanes in sulfuric or perchloric acid [7]. The procedure ensured preparation of a large series of 2*H*-benzimidazole 1,3-dioxides, including those inaccessible by other methods.

The *ortho*-quinone diimine structure of 2*H*-benzimidazole 1,3-dioxides implies that such compounds should be capable of reacting with nucleophiles to give the corresponding addition products, which is typical of quinoid systems. We previously showed that 4,7-dibromo-2,2-dimethyl-2*H*-benzimidazole 1,3-dioxide takes up amine molecule with simultaneous removal of one *N*-oxide oxygen atom and two hydrogen atoms, the *ortho*-quinone diimine system being retained [8].

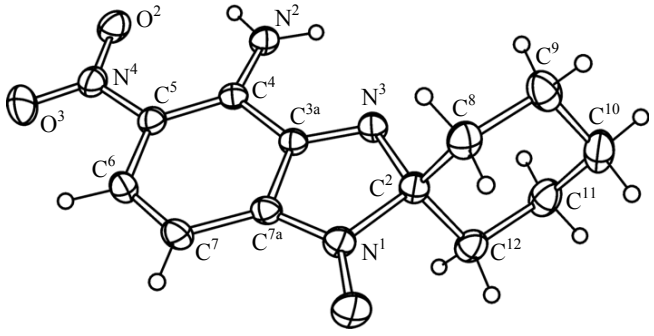
In continuation of these studies in the present work we examined reactions of 5-nitrospiro[benzimidazole-2,1′-cyclohexane] 1,3-dioxide (**I**) prepared by us previously [7] with some nucleophilic reagents. Compound **I** reacted with ammonia in chloroform to produce amine **IIa** (Scheme 1). According to the analytical and spectral data, nucleophilic replacement in molecule **I** was accompanied by elimination of one *N*-oxide oxygen atom and two hydrogen atoms. With a view to

Scheme 1.



II, $R^1 = R^2 = H$ (**a**); $R^1 = H$, $R^2 = Me$ (**b**), $HOCH_2CH_2$ (**c**), $Me(CH_2)_2$ (**d**), $Me(CH_2)_3$ (**e**), *t*-Bu (**f**), cyclohexyl (**g**), 2,2,6,6-tetramethylpiperidin-4-yl (**h**), $PhCH_2$ (**i**), $PhCH_2CH_2$ (**j**); R^1R^2N = piperidino (**k**), morpholino (**l**), pyrrolidin-1-yl (**m**); **V**, R = H (**a**), Me (**b**).

elucidate which *N*-oxide oxygen atom was lost in this reaction, we obtained a single crystal of **IIa**, and the structure of this compound was unambiguously determined by X-ray analysis (see figure). The benzimidazole fragment in molecule **IIa** is planar within ±0.015 Å. The nitro and amino groups reside in the benzimidazole ring plane, the corresponding dihedral angles being equal to 3.19(4) and 1.7(4)°, respectively. The bond lengths in molecule **IIa** are similar to those found for dispiro[benzimidazole-2,1′-cyclohexane-4′,2″-benzimidazole] 1-oxide and dispiro[benzimidazole-2,1′-cyclohexane-4′,2″-benzimidazole] 1,1″-dioxide [9]. Intramolecular hydrogen bonds N^2–H···O^2 [N–H 0.86(2), H···O 2.08(2) Å, ∠NHO 123(2)°] and N^2–H···N^3 [0.89(2), 2.40(2) Å, 105(1)°], as well as intermolecular hydrogen bond N^2–H···O^1 [0.86(2), 2.23(2) Å, 121(2)°], were detected in the crystalline



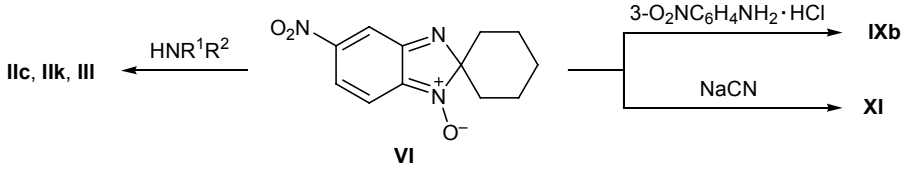
Structure of the molecule of 5-nitrospiro[benzimidazole-2,1′-cyclohexan]-4-amine 1-oxide (**IIa**) according to the X-ray diffraction data.

structure of compound **IIa**; the latter bond is responsible for the formation of chains along the *c* axis. Also, intermolecular N^4–O^2···π interactions were found with the following parameters: O···centroid (C_g) 3.387(1) (benzo), 3.362(1) Å (imidazole), ∠NOC_g 100.81(9), 100.30(9)°.

Treatment of *N*-oxide **IIa** in alcohol with aqueous sodium hydroxide gave compound **III** which was assigned the structure of 5-nitrospiro[benzimidazole-2,1′-cyclohexan]-4-ol 1-oxide on the basis of its spectral parameters and elemental analysis. The ^{1}H NMR spectrum of **III** contained signals from five CH_2 groups in the cyclohexane ring (δ 1.23–1.98 ppm, m), signals from aromatic protons as two doublets at δ 6.58 and 7.40 ppm, and a singlet at δ 9.45 ppm belonging to the hydroxy proton. In the ^{13}C NMR spectrum of **III**, signals from methylene carbon atoms appeared at δ_C 22.83, 24.21, and 34.34 ppm, two aromatic CH carbon atoms resonated at δ_C 103.90 and 125.52 ppm, and five quaternary carbon atoms gave signals at δ_C 105.80, 133.18, 135.75, 153.24, and 160.21 ppm. Presumably, the position of the *N*-oxide moiety in molecule **III** is the same as in **IIa**. By reaction of compound **III** with diazomethane we obtained 4-methoxy-5-nitrospiro[benzimidazole-2,1′-cyclohexane] 1-oxide (**IV**). Compound **III** was also formed directly from 1,3-dioxide **I** by the action of aqueous alkali.

Primary and secondary amines readily reacted with compound **I** to produce mono-*N*-oxides **IIb**–**IIm**. The position of the *N*-oxide moiety in the products was the same as in compound **IIa**. This follows from the

Scheme 2.



formation of *N*-oxide **III** in the reaction of nitro amines **IIc**, **IIk**, and **III** with aqueous alkali as a result of replacement of the amino group by hydroxy. Compound **III** thus obtained was identified by comparing the IR spectra and melting points. Amines **IIc**, **IIk**, and **III** were also synthesized by reaction of 5-nitrospiro-[benzimidazole-2,1′-cyclohexane] 1-oxide (**VI**) reported by us previously [11] with 2-aminoethanol, piperidine, and morpholine, respectively (Scheme 2). Alkylation of **IIa** with methyl iodide gave compound **IIb**. The above findings allowed us to presume the same position of the *N*-oxide oxygen atom in all compounds **IIa**–**IIm**.

5-Nitrospiro[benzimidazole-2,1′-cyclohexan]-4-amine 1,3-dioxide (**Va**) was synthesized by reaction of compound **I** with ammonia in the presence of MnO_2 as oxidant. Presumably, the reaction involves initial nucleophilic 1,6-addition of ammonia to molecule **I** with formation of adduct **A** which is oxidized with MnO_2 to give **Va**. The structure of 5-nitrospiro[benzimidazole-2,1′-cyclohexan]-4-amine 1,3-dioxide (**Va**) was determined on the basis of its spectral parameters and elemental composition (see Experimental). Protons in the amino group resonated in the ^{1}H NMR spectrum of **Va** as two singlets at δ 8.75 and 9.22 ppm, presumably due to formation of intramolecular hydrogen bond between the *N*-oxide oxygen atom and hydrogen atom in the amino group, as well as between the nitro group and the other amino hydrogen atom. Likewise, in the reaction of **I** with $MeNH_2$ in the presence of MnO_2 both *N*-oxide groups were conserved, and the product was *N*-methyl-5-nitrospiro[benzimidazole-2,1′-cyclohexan]-4-amine 1,3-dioxide (**Vb**) (Scheme 1).

The reactions of compound **I** with aromatic amines were accompanied by loss of both *N*-oxide oxygen atoms with formation of *N*-arylspiro[benzimidazole-2,1′-cyclohexan]-4-amines **VIIa**–**VIIf** (Scheme 3). These reactions were carried out by prolonged heating of a mixture of **I** and aromatic amine in boiling benzene or alcohol. Presumably, initial elimination of *N*-oxide oxygen atoms from molecule **I** gives the corresponding 2*H*-benzimidazole which then reacts with aromatic amine. As shown by us previously [10], compound **I** is a strong oxidant, and it loses *N*-oxide oxygen atoms on heating. This is likely to be responsible for the formation of a considerable amount of tars in the reaction of **I** with aromatic amines.

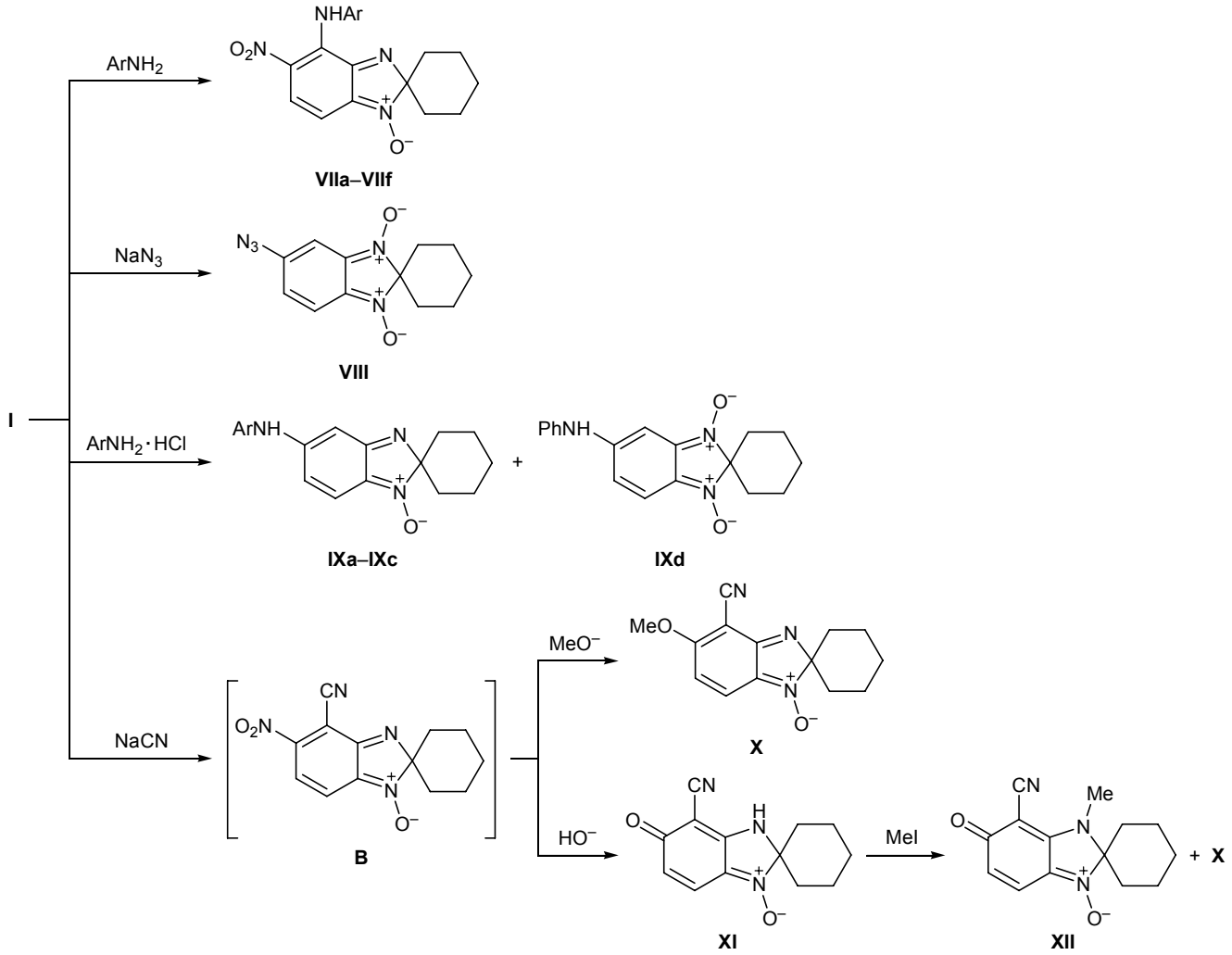
The reaction of **I** with sodium azide occurred as nucleophilic replacement of the nitro group by azido with conservation of the *N*-oxide groups and formation of 5-azidospiro[benzimidazole-2,1′-cyclohexane] 1,3-dioxide (**VIII**) (Scheme 3). The IR spectrum of **VIII** contained an absorption band at 2117 cm^{-1}, which is typical of stretching vibrations of azido group. The other analytical and spectral parameters of **VIII** were also consistent with the assumed structure (see Experimental).

Compound **I** reacted with aromatic amine hydrochlorides (aniline, 4-methoxyaniline, and 3-nitroaniline hydrochlorides) to give the corresponding *N*-arylspiro-[benzimidazole-2,1′-cyclohexan]-5-amine 1-oxides **IXa**–**IXc** whose structure was confirmed by spectral and analytical data. The position of the *N*-oxide group was determined taking into account the formation of compound **IXb** in the reaction of **VI** with 3-nitroaniline hydrochloride. It should be noted that the reaction of *N*,*N*′-dioxide **I** with aniline hydrochloride was accompanied by formation of a small amount of *N*-phenylspiro[benzimidazole-2,1′-cyclohexan]-5-amine 1,3-dioxide (**IXd**).

The reaction of **I** with sodium cyanide in methanol afforded 5-methoxyspiro[benzimidazole-2,1′-cyclohexane]-4-carbonitrile 1-oxide (**X**) and 5-oxo-3,5-dihydrospiro[benzimidazole-2,1′-cyclohexane]-4-carbonitrile 1-oxide (**XI**). Initially, cyanide ion is likely to react with **I** to give intermediate **B**, and next follows nucleophilic replacement of the nitro group by methoxy or hydroxy, as described in [11] for 5-nitrospiro-[benzimidazole-2,1′-cyclohexane]. Compound **XI** was formed as the only product when the reaction was carried out in a two-phase system (chloroform–water).

The structure of 5-methoxyspiro[benzimidazole-2,1′-cyclohexane]-4-carbonitrile 1-oxide (**X**) was determined on the basis of analytical and spectral data. The IR spectrum of **X** contained an absorption band at 2228 cm^{-1}, which is typical of stretching vibrations of

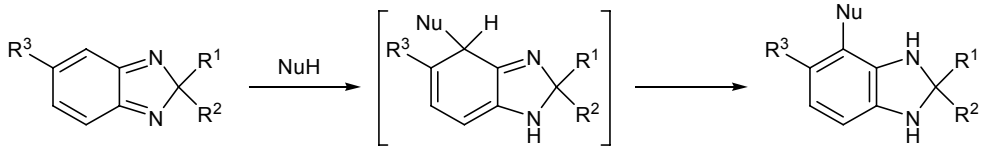
Scheme 3.



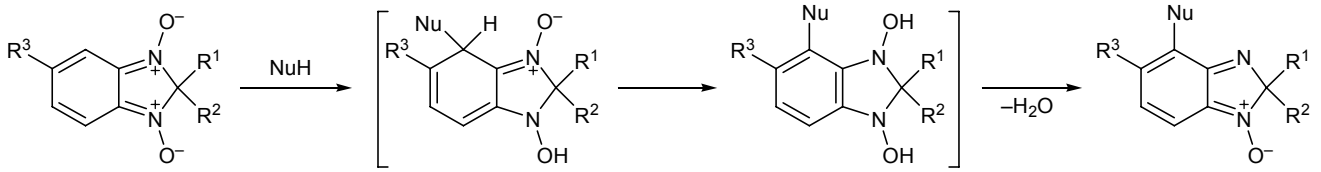
VII, Ar = Ph (**a**), 2-$MeOC_6H_4$ (**b**), 4-$MeOC_6H_4$ (**c**), 4-$O_2NC_6H_4$ (**d**), 4-H_2NSO_2 (**e**), 2-ClC_6H_4 (**f**); **IX**, Ar = Ph (**a**), 3-$O_2NC_6H_4$ (**b**), 4-$MeOC_6H_4$ (**c**).

cyano group. The other spectral parameters of **X** also confirmed the assumed structure. The structure of compound **XI** is likely to be similar to the structure of its known [11] analog having no *N*-oxide group. Compound **XI** displayed in the ^{13}C NMR spectrum a signal at δ_C 181.61 ppm, which is characteristic of quinoid carbonyl carbon atom. The position of the *N*-oxide group in **XI** was confirmed by its synthesis via reaction of **VI** with sodium cyanide (Scheme 2). The alkylation of **XI** with methyl iodide involved nitrogen atom in the imidazole ring with formation of compound **XII**. The IR spectrum of **XII** contained absorption bands at 2205 (C≡N), 1541 (C=N), and 1616 cm^{-1} (C=O). In the ^1H NMR spectrum of this compound, 10 protons in the cyclohexane ring resonated in the region δ 1.32–2.97 ppm, the *N*-methyl group gave a three-proton singlet at δ 3.47 ppm, and two doublets at δ 6.40 and 7.44 ppm were assigned to 6-H and 7-H. In the ^{13}C NMR spectrum of **XII** we observed three signals from methylene carbon atoms in the cyclohexane ring, and a signal at δ_C 31.43 ppm due to methyl carbon atom attached to nitrogen. The cyano group gave a signal at δ_C 78.4 ppm, and two CH signals appeared at δ_C 120.35 and 131.01 ppm. The signal at δ_C 95.35 ppm was assigned to the spiro carbon atom (C^2), and the other quaternary carbon atoms resonated at 116.37, 131.84, and 154.12 ppm; the signal at δ_C 181.75 ppm was typical of carbonyl carbon atom. These data in combination with the mass spectrum and elemental analysis allowed us to identify compound **XII** as 3-methyl-5-oxo-3,5-dihydrospiro[benzimidazole-2,1′-cyclohexane]-4-carbonitrile 1-oxide. In addi-

Scheme 4.



Scheme 5.



C

tion, a small amount of O-alkylation product **X** was isolated (Scheme 3).

The results of addition of nucleophilic reagents to 5-nitrospiro[benzimidazole-2,1′-cyclohexane] 1,3-dioxide (**I**) were compared with the results of analogous reactions with 2*H*-benzimidazoles which are known to produce the corresponding 2,3-dihydro-1*H*-benzimidazoles [11–13] (Scheme 4). It may be presumed that addition of nucleophiles to 2*H*-benzimidazole 1,3-dioxide could give rise to 1,3-dihydroxy-2,3-dihydro-1*H*-benzimidazoles like **C** (Scheme 5). In fact, intermediate **C** loses water molecule, and the *ortho*-quinoid structure is retained. We believe that this is the main difference between 2*H*-benzimidazole 1,3-dioxides and 2*H*-benzimidazoles in reactions with nucleophiles.

EXPERIMENTAL

The IR spectra were recorded in KBr (sample concentration 0.25%) on a Bruker Vector-22 spectrometer; given are the most intense absorption bands. The UV spectra were measured on a Hewlett–Packard 4853 spectrophotometer from solutions in ethanol. The ^{1}H and ^{13}C NMR spectra were obtained on a Bruker AV-300 instrument at 25°C from 10% solutions in $CDCl_3$ or DMSO-d_6; the chemical shifts were determined relative to the residual proton and carbon signals of the solvent ($CHCl_3$, δ 7.24, δ_C 76.90 ppm; DMSO-d_5, δ 2.50, δ_C 39.50 ppm). Signal multiplicities in the ^{13}C NMR spectra were determined using *J*-modulation (JMOD) technique. The mass spectra (electron impact, 70 eV) were recorded on a Thermo Scientific DFS mass spectrometer with direct sample admission into the ion source (ion source temperature 180°C); ion peaks with a relative intensity higher than 10% are given. The progress of reactions and the purity of products were monitored by TLC on Sorbfil UV-254 plates (*Sorbpolimer*, Krasnodar, Russia); the chromatograms were developed under UV light and by treatment with iodine vapor. The melting points were measured on a Kofler hot stage. The elemental compositions were determined at the Microanalysis Laboratory, Novosibirsk Institute of Organic Chemistry, Siberian Division of the Russian Academy of Sciences. Compounds **I** [7] and **VI** [10] were synthesized by known methods.

Single crystals of compound **IIa** for X-ray analysis were obtained by recrystallization from ethyl acetate–hexane (1 : 1). The X-ray diffraction data were acquired at 296 K on a Bruker KAPPA APEX II CCD diffractometer; λ(MoK_α) 0.71073 Å, graphite monochromator, ω,φ-scanning, 2θ <50°. Crystallographic data for compound **IIa**: monoclinic crystal system, space group $P2_1/c$; unit cell parameters: a = 6.5118(3), b = 22.2201(8), c = 8.4692(3) Å; β = 101.814(2)°; V = 1199.47(8) Å^3; $C_{12}H_{14}N_4O_3$; Z = 4, d_{calc} = 1.452 g/cm^3; μ = 0.108 cm^{-1}; crystal dimensions 0.06×0.38×0.40 mm. Absorption by the crystal was taken into account empirically using SADABS program (T_{min}/T_{max} = 0.84/0.97). Intensities of 9846 reflections were measured, 2613 of which were independent (R_{int} = 0.0483). The structure was solved by the direct method. The positions and temperature factors of nonhydrogen atoms were refined in anisotropic approximation by the full-matrix least-squares procedure. Hydrogen atoms in the amino group were localized by difference synthesis, while the other hydrogen atoms were placed into positions calculated on the basis of geometry considerations. The final divergence factors were wR_2 = 0.1156 (all reflections; S = 1.050), R_1 = 0.0405 [2049 reflections with $I \geq 2\sigma(I)$]. All calculations were performed using SHELX and PLATON.

The crystallographic data for compound **IIa** were deposited to the Cambridge Crystallographic Data Centre (entry no. CCDC 827016).

5-Nitrospiro[benzimidazole-2,1′-cyclohexan]-4-amine 1-oxide (IIa). Compound **I**, 1.32 g (0.005 mol), was dissolved in 60 ml of chloroform, 5 ml of a 25% solution of ammonia was added, and the mixture was stirred for 1 h at room temperature. The mixture was treated with 20 ml of water, the organic phase was separated, washed with water (3×20 ml), and dried over $MgSO_4$, the drying agent was filtered off, the filtrate was evaporated, the residue was dispersed in hexane, and the precipitate was filtered off. Yield 1.15 g (87%), mp 251–253°C. IR spectrum, ν, cm^{-1}: 3451, 3331 (NH_2), 1632 (C=N). UV spectrum, λ_{max}, nm (logε): 350 (4.34), 500 (3.65). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.25–2.04 m (10H, CH_2), 6.38 d (1H, CH, J = 10.0 Hz), 7.49 d (1H, CH, J = 10.0 Hz), 8.87 br.s (2H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 22.88, 24.21, 34.28 (CH_2); 101.50, 125.17 (CH); 106.23, 124.82, 134.13, 143.48, 159.07. Mass spectrum, m/z (I_{rel}, %): 262 (100) $[M]^+$, 245 (48), 219 (80), 208 (61), 191 (42), 189 (46). Found, %: C 54.60; H 5.24; N 21.10. m/z 262.1068 $[M]^+$. $C_{12}H_{14}N_4O_3$. Calculated, %: C 54.95; H 5.38; N 21.37. M 262.1060.

***N*-Methyl-5-nitrospiro[benzimidazole-2,1′-cyclohexan]-4-amine 1-oxide (IIb).** *a*. Compound **IIb** was synthesized as described above for **IIa**. Yield 76%, mp 228–230°C. IR spectrum, ν, cm^{-1}: 3205 (NH), 1616 (C=N). UV spectrum, λ_{max}, nm (logε): 229 (4.21), 363 (4.22), 401 (3.94), 527 (3.60). ^{1}H NMR spectrum, δ, ppm ($CDCl_3$): 1.23–2.18 m (10H, CH_2), 3.81 d (3H, CH_3, J = 6.0 Hz), 6.42 d (1H, CH, J = 10.1 Hz), 7.63 d (1H, CH, J = 10.1 Hz), 10.55 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 23.30, 24.46, 34.90 (CH_2); 34.69 (CH_3); 101.89, 125.86 (CH); 105.83, 126.31, 135.66, 145.03, 160.04. Mass spectrum, m/z (I_{rel}, %): 276 (100) $[M]^+$, 259 (41), 233 (80), 203 (56). Found, %: C 56.40; H 5.62; N 20.36. m/z 276.1220 $[M]^+$. $C_{13}H_{16}N_4O_3$. Calculated, %: C 56.51; H 5.84; N 20.28. M 276.1217.

b. Compound **IIa**, 0.3 g (0.0011 mol), was dissolved in 20 ml of acetonitrile, 0.5 g (0.0036 mol) of finely powdered calcined potassium carbonate and 2 ml (0.032 mol) of methyl iodide were added, and the mixture was stirred for 24 h at room temperature. The precipitate was filtered off, the solvent was removed, the residue was treated with 10 ml of water, and the precipitate was filtered off, washed with water, and dried. Yield 0.25 g (79%), mp 228–230°C.

2-[(5-Nitro-1-oxidospiro[benzimidazole-2,1′-cyclohexan]-4-yl)amino]ethanol (IIc). 2-Aminoethanol, 1.5 g (0.025 mol), was added to a solution of 5.26 g (0.02 mol) of compound **I** in 50 ml of chloroform, and the mixture was stirred for 1 h at room temperature. The solvent was distilled off under reduced pressure, and the residue was purified by chromatography on silica gel using chloroform–methanol (10:1) as eluent. Yield 86%, mp 195–197°C. IR spectrum, ν, cm^{-1}: 3400 (NH), 1616 (C=N), 1450, 1329 (NO_2). UV spectrum, λ_{max}, nm (logε): 230 (4.19), 360 (4.25), 520 (3.64). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.20–2.17 m (10H, CH_2), 2.24 br.s (1H, OH), 3.98– 4.02 m (2H, CH_2), 4.46–4.51 m (2H, CH_2), 6.43 d (1H, CH, J = 10.1 Hz), 7.63 d (1H, CH, J = 10.1 Hz), 10.67 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 23.50, 24.45, 35.02, 48.54, 61.61 (CH_2); 102.05, 126.08 (CH); 105.72, 126.96, 135,98, 144.38, 160.12. Mass spectrum, m/z (I_{rel}, %): 306 (97) $[M]^+$, 289 (15), 275 (100), 259 (58), 247 (56), 229 (37), 216 (39), 213 (34), 199 (32). Found, %: C 55.18; H 5.91; N 18.20. m/z 306.1328 $[M]^+$. $C_{14}H_{18}N_4O_4$. Calculated, %: C 54.89; H 5.92; N 18.29. M 306.1323.

Compounds **IId**–**IIm** were synthesized in a similar way.

5-Nitro-*N*-propylspiro[benzimidazole-2,1′-cyclohexan]-4-amine 1-oxide (IId). Yield 76%, mp 198–201°C. IR spectrum, ν, cm^{-1}: 2967 (NH), 1609 (C=N). UV spectrum, λ_{max}, nm (logε): 229 (4.17), 364 (4.16), 401 (3.83), 529 (3.57). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.04 t (3H, CH_3, J = 7.4 Hz), 1.23–2.17 m (12H, CH_2), 4.18–4.28 m (2H, CH_2), 6.41 d (1H, CH, J = 10.0 Hz), 7.63 d (1H, CH, J = 10.0 Hz), 10.61 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 23.20, 23.34, 24.27, 34.70, 48.28 (CH_2); 10.94 (CH_3); 101.59, 125.75 (CH); 105.40, 126.08, 135.50, 144.29, 159.45. Mass spectrum, m/z (I_{rel}, %): 304 (100) $[M]^+$, 287 (59), 275 (68), 247 (36), 241 (29). Found, %: C 58.95; H 6.60; N 18.46. m/z 304.1541 $[M]^+$. $C_{15}H_{20}N_4O_3$. Calculated, %: C 59.19; H 6.62; N 18.41. M 304.1530

***N*-Butyl-5-nitrospiro[benzimidazole-2,1′-cyclohexan]-4-amine 1-oxide (IIe).** Yield 78%, mp 162–164°C. IR spectrum, ν, cm^{-1}: 3236 (NH), 1604 (C=N). UV spectrum, λ_{max}, nm (logε): 231 (4.23), 364 (4.26), 401 (3.94), 529 (3.70). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.90 t (3H, CH_3, J = 7.6 Hz), 1.20–2.17 m (14H, CH_2), 4.20–4.32 m (2H, CH_2), 6.37 d (1H, CH, J = 10.0 Hz), 7.59 d (1H, CH, J = 10.0 Hz), 10.60 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 19.63, 23.12, 24.20, 31.94, 34.63, 46.40 (CH_2); 13.29 (CH_3); 101.47,

125.67 (CH); 105.32, 125.94, 135.44, 144.23, 159.39. Mass spectrum, *m*/*z* (I_{rel}, %): 318 (97) $[M]^+$, 301 (62), 275 (100), 255 (29), 247 (41). Found, %: C 60.30; H 6.76; N 17.58. *m*/*z* 318.1688 $[M]^+$. $C_{16}H_{22}N_4O_3$. Calculated, %: C 60.36; H 6.97; N 17.60. *M* 318.1686.

***N*-*tert*-Butyl-5-nitrospiro[benzimidazole-2,1′-cyclohexan]-4-amine 1-oxide (IIf).** Yield 74%, mp 211–213°C. IR spectrum, ν, cm^{-1}: 2970 (NH), 1612 (C=N), 1427 (NO_2), 1226. UV spectrum, λ_{max}, nm (logε): 231 (4.22), 368 (4.27), 536 (3.72). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.20–2.18 m (10H, CH_2), 1.67 s (9H, CH_3), 6.41 d (1H, CH, *J* = 10.0 Hz), 7.65 d (1H, CH, *J* = 10.0 Hz), 11.23 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 23.38, 24.24, 34.66 (CH_2); 29.61 (CH_3); 101.75, 136.02 (CH); 56.89, 105.00, 127.45, 135.94, 145.70, 157.92. Mass spectrum, *m*/*z* (I_{rel}, %): 318 (66) $[M]^+$, 301 (5), 262 (81), 245 (62), 219 (100), 208 (93), 191 (39). Found, %: C 60.85; H 7.05; N 17.52. *m*/*z* 318.1685 $[M]^+$. $C_{16}H_{22}N_4O_3$. Calculated, %: C 60.36; H 6.97; N 17.60. *M* 318.1686.

***N*-Cyclohexyl-5-nitrospiro[benzimidazole-2,1′-cyclohexan]-4-amine 1-oxide (IIg).** Yield 64%, mp 163–165°C. IR spectrum, ν, cm^{-1}: 2928 (NH), 1605 (C=N), 1513, 1231 (NO_2). UV spectrum, λ_{max}, nm (logε): 230 (4.14), 366 (4.20), 401 (3.87), 530 (3.66). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.20–2.18 m (20H, CH_2), 5.10 m (1H, CH), 6.37 d (1H, CH, *J* = 10.0 Hz), 7.61 d (1H, CH, *J* = 10.0 Hz), 10.54 d (1H, NH, *J* = 7.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 23.68, 24.51, 25.06, 33.59, 34.90 (CH_2); 54.77, 101.61, 126.07 (CH); 105.38, 126.01, 137.76, 143.53, 159.26. Mass spectrum, *m*/*z* (I_{rel}, %): 344 (66) $[M]^+$, 327 (100), 309 (40), 301 (29). Found, %: C 63.0; H 6.96; N 16.54. *m*/*z* 344.1844 $[M]^+$. $C_{18}H_{24}N_4O_3$. Calculated, %: C 62.77; H 7.02; N 16.27. *M* 344.18.43.

5-Nitro-*N*-(2,2,6,6-tetramethylpiperidin-4-yl)-spiro[benzimidazole-2,1′-cyclohexan]-4-amine 1-oxide (IIh). Yield 72%, mp 217–220°C. IR spectrum: ν 1607 cm^{-1} (C=N). UV spectrum, λ_{max}, nm (logε): 231 (4.29), 366 (4.33), 528 (3.83). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.20–2.27 m (14H, CH_2), 1.15 s (6H, CH_3), 1.26 s (6H, CH_3), 5.28 m (1H, CH), 6.38 d (1H, CH, *J* = 10.0 Hz), 7.61 d (1H, CH, *J* = 10.0 Hz), 10.49 d (1H, NH, *J* = 8.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 23.15, 24.26, 34.88, 45.81 (CH_2); 28.73, 34.60 (CH_3); 49.15, 101.69, 126.05 (CH); 50.53, 105.40, 126.32, 135.83, 143.40, 159.59. Mass spectrum, *m*/*z* (I_{rel}, %): 401 (13) $[M]^+$, 138 (9), 124 (100). Found, %: C 63.0; H 7.70; N 17.30. *m*/*z* 401.2422 $[M]^+$. $C_{21}H_{31}N_5O_3$. Calculated, %: C 62.83; H 7.78; N 17.44. *M* 401.2421.

***N*-Benzyl-5-nitrospiro[benzimidazole-2,1′-cyclohexan]-4-amine 1-oxide (IIi).** Yield 68%, mp 172–174°C. IR spectrum, ν, cm^{-1}: 3247 (NH), 1609 (C=N). UV spectrum, λ_{max}, nm (logε): 228 (4.21), 363 (4.22), 526 (3.64). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.22–2.18 m (10H, CH_2), 5.55 d (2H, CH_2, *J* = 6.3 Hz), 7.38 s (5H, H_{arom}), 6.48 d (1H, CH, *J* = 10.0 Hz), 7.67 d (1H, CH, *J* = 10.0 Hz), 10.70 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 23.02, 24.14, 34.66, 50.29 (CH_2); 102.05, 125.48, 127.04, 127.66, 128.57 (CH); 105.58, 127.03, 135.48, 136.65, 143.50, 159.45. Mass spectrum, *m*/*z* (I_{rel}, %): 352 (29) $[M]^+$, 335 (63), 317 (65), 307 (28), 287 (45), 105 (100). Found, %: C 64.73; H 5.69; N 16.08. *m*/*z* 352.1533 $[M]^+$. $C_{19}H_{20}N_4O_3$. Calculated, %: C 64.76; H 5.72; N 15.90. *M* 352.1533.

5-Nitro-*N*-(2-phenylethyl)spiro[benzimidazole-2,1′-cyclohexan]-4-amine 1-oxide (IIj). Yield 66%, mp 206–210°C. IR spectrum, ν, cm^{-1}: 3199 (NH), 1615 (C=N). UV spectrum, λ_{max}, nm (logε): 229 (4.13), 365 (4.15), 401 (3.79), 529 (3.60). ^1H NMR spectrum, δ, ppm ($CDCl_3$): 1.18–2.12 m (10H, CH_2), 3.03 t (2H, CH_2, *J* = 7.0 Hz), 4.54 q (2H, CH_2, *J* = 6.6, 14.6 Hz), 7.15– 7.31 m (5H, H_{arom}), 6.35 d (1H, CH, *J* = 10.3 Hz), 7.56 d (1H, CH, *J* = 10.3 Hz), 10.49 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 23.13, 24.17, 34.66, 36.24, 47.66 (CH_2); 101.78, 125.63, 126.72, 128.34, 128.42 (CH); 105.39, 126.29, 134.46, 137.22, 143.98, 159.48. Mass spectrum, *m*/*z* (I_{rel}, %): 366 (46) $[M]^+$, 349 (60), 316 (25), 275 (95), 259 (54), 247 (38). *m*/*z* 366.1684 $[M]^+$. $C_{20}H_{22}N_4O_3$. Calculated, %: C 65.57; H 6.01; N 15.30. *M* 366.1686.

5-Nitro-4-piperidinospiro[benzimidazole-2,1′-cyclohexane] 1-oxide (IIk). Yield 48%, mp 159–162°C. IR spectrum: ν 1596 cm^{-1} (C=N). UV spectrum, λ_{max}, nm (logε): 242 (4.11), 287 (3.75), 378 (3.91), 531 (3.70). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.23–2.20 m (16H, CH_2), 3.51–3.70 m (4H, CH_2), 6.53 d (1H, CH, *J* = 9.8 Hz), 7.37 d (1H, CH, *J* = 9.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 23.34, 23.25, 24.34, 25.94, 34.70, 52.80 (CH_2); 103.20, 126.87 (CH); 104.60, 132.68, 135.91, 142.38, 161.18. Mass spectrum, *m*/*z* (I_{rel}, %): 330 (54) $[M]^+$, 313 (100), 287 (17), 274 (18), 257 (35). Found, %: C 61.68; H 6.66; N 16.87. *m*/*z* 330.1686 $[M]^+$. $C_{17}H_{22}N_4O_3$. Calculated, %: C 61.80; H 6.75; N 16.96. *M* 330.1685

4-Morpholino-5-nitrospiro[benzimidazole-2,1′-cyclohexane] 1-oxide (III). Yield 43%, mp 180–182°C. IR spectrum: ν 1591 cm^{-1} (C=N). UV spectrum, λ_{max}, nm (logε): 293 (3.64), 375 (3.79), 521

(3.62). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.15–2.20 m (10H, CH_2), 3.55–3.70 m (4H, CH_2), 3.75–3.90 m (4H, CH_2), 6.51 d (1H, CH, J = 10.0 Hz), 7.25 d (1H, CH, J = 10.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 23.58, 24.52, 35.03, 51.70, 66.63 (CH_2); 104.80, 126.40 (CH); 105.25, 134.06, 136.08, 141.16, 161.43. Found, %: C 57.78; H 5.94; N 16.62. $C_{16}H_{20}N_4O_4$. Calculated, %: C 57.82; H 6.07; N 16.86.

5-Nitro-4-(pyrrolidin-1-yl)spiro[benzimidazole-2,1′-cyclohexane] 1-oxide (IIm). Yield 56%, mp 183–188°C. IR spectrum: ν 1594 cm^{-1} (C=N). UV spectrum, λ_{max}, nm (logε): 237 (4.24), 371 (4.01), 533 (3.76). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.10–2.20 m (14H, CH_2), 3.79 s (4H, CH_2), 6.37 d (1H, CH, J = 10.0 Hz), 7.42 d (1H, CH, J = 10.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 23.36, 24.59, 25.48, 34.88, 55.31 (CH_2); 100.99, 128.74 (CH); 104.66, 129.85, 136.16, 141.37, 160.66. Mass spectrum, m/z (I_{rel}, %): 316 (40) $[M]^+$, 299 (100), 266 (48), 265 (58), 253 (47), 243 (80), 225 (47). Found, %: C 60.32; H 6.37; N 17.66. m/z 316.1523 $[M]^+$. $C_{16}H_{20}N_4O_4$. Calculated, %: C 60.76; H 6.33; N 17.72. M 316.1530.

5-Nitrospiro[benzimidazole-2,1′-cyclohexan]-4-ol 1-oxide (III). *a*. Compound **I**, 2.63 g (0.01 mol), was added to a solution of 0.7 g (0.017 mol) of sodium hydroxide in 100 ml of water, and the mixture was vigorously stirred for 6 h at room temperature. The solvent was distilled off to a volume of 20 ml, 5% hydrochloric acid was added until pH 3, and the precipitate was filtered off, washed with water, and dried. The crude product, 2.25 g, was dissolved in alcohol and subjected to chromatography on silica gel using ethyl acetate–hexane (3:1 + 1% of methanol) as eluent. Yield 1.99 g (76%).

b. A solution of 0.5 g (0.0125 mol) of sodium hydroxide in 5 ml of water was added to a solution of 1.0 g (0.00386 mol) of compound **IIa** in 50 ml of methanol, and the mixture was heated for 30 min under reflux. The solvent was distilled off under reduced pressure (water-jet pump), 10 ml of water was added to the residue, and the mixture was acidified to pH 3 with 5% hydrochloric acid. The precipitate was filtered off, washed with water, and dried. Yield 0.83 g (82%), mp 165°C (decomp.). IR spectrum: ν 1606 cm^{-1} (C=N). UV spectrum, λ_{max}, nm (logε): 227 (4.11), 282 (3.45), 349 (3.98), 403 (4.02), 509 (3.34). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.23–1.98 m (10H, CH_2), 6.58 d (1H, CH, J = 10.0 Hz), 7.40 d (1H, CH, J = 10.0 Hz), 9.43 br.s (1H, OH). ^{13}C NMR spectrum, δ_C, ppm: 22.83, 24.21, 34.34 (CH_2); 103.90, 125.52 (CH); 105.80, 133.18, 135.75, 153.24, 160.21. Mass spectrum: m/z (I_{rel}, %): 263 (45) $[M]^+$, 247 (100), 229 (23), 212 (46). Found, %: C 54.62; H 4.96, N 16.10. m/z 263.0902 $[M]^+$. $C_{12}H_{13}N_3O_4$. Calculated, %: C 54.75; H 4.98; N 15.96. M 263.0901.

Following a similar procedure, compound **III** was obtained from compounds **IIc**, **IIk**, and **III** in 95, 72, and 84% yield, respectively.

4-Methoxy-5-nitrospiro[benzimidazole-2,1′-cyclohexane] 1-oxide (IV). A solution of diazomethane prepared from 1 g of nitrosomethylurea in 50 ml of ether was added dropwise at room temperature to a solution of 1.0 g (0.038 mol) of compound **III** in 25 ml of methanol. The mixture was stirred for 2 h at 20°C, the solvent was distilled off under reduced pressure, and the residue was purified by chromatography on silica gel using ethyl acetate–hexane (1:3) as eluent. Yield 0.38 g (36%), mp 75–78°C. IR spectrum: ν 1600 cm^{-1} (C=N). UV spectrum, λ_{max}, nm (logε): 281 (3.78), 322 (3.76), 447 (3.64). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.19–1.98 m (10H, CH_2), 4.48 s (3H, OCH_3), 6.86 d (1H, CH, J = 9.2 Hz), 7.06 d (1H, CH, J = 9.2 Hz). ^{13}C NMR spectrum, δ_C, ppm: 23.06, 24.18, 34.88 (CH_2); 62.08 (OCH_3); 109.44, 123.36 (CH); 106.70, 135.83, 140.02, 148.21, 158.16. Mass spectrum: m/z (I_{rel}, %): 277 (100) $[M]^+$, 260 (55), 247 (43), 223 (36), 213 (31), 206 (86). Found, %: C 56.82; H 5.60; N 15.05. m/z 277.1051 $[M]^+$. $C_{13}H_{15}N_3O_4$. Calculated, %: C 56.31; H 5.45; N 15.16. M 277.1057.

5-Nitrospiro[benzimidazole-2,1′-cyclohexan]-4-amine 1,3-dioxide (Va). Manganese(IV) oxide, 10 g, was added to a solution of 2.63 g (0.01 mol) of compound **I** in 100 ml of chloroform, and dry ammonia was passed through the mixture over a period of 2 h under vigorous stirring at room temperature. The precipitate was filtered off, the solvent was distilled off under reduced pressure, and the residue was subjected to chromatography on silica gel using chloroform as eluent to isolate 0.45 g (17%) of *N*-oxide **IIa** and 1.20 g (44%) of *N*,*N*-dioxide **Va**. mp 215–217°C. IR spectrum, ν, cm^{-1}: 3362, 3252 (NH_2); 1617 (C=N). UV spectrum, λ_{max}, nm (logε): 265 (4.03), 335 (3.98), 621 (3.38). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.53–2.09 m (10H, CH_2), 6.47 d (1H, CH, J = 10.1 Hz), 7.58 d (1H, CH, J = 10.1 Hz), 8.75 br.s (1H, NH), 9.22 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 18.62, 22.86, 33.70 (CH_2); 101.06, 126.76 (CH); 99.82, 123.64, 130.35, 134.61, 140.16. Mass spectrum, m/z (I_{rel}, %): 278 (100) $[M]^+$, 262 (52), 207 (47), 180 (44). Found, %: C 52.11; H 5.12; N 20.20.

m/*z* 278.1008 $[M]^+$. $C_{12}H_{14}N_4O_4$. Calculated, %: C 51.80; H 5.04; N 20.14. *M* 278.1010.

***N*-Methyl-5-nitrospiro[benzimidazole-2,1′-cyclohexan]-4-amine 1,3-dioxide (Vb)** was synthesized in a similar way. Yield 61%, mp 135–137°C. IR spectrum: ν 1592 cm^{-1} (C=N). UV spectrum, λ_{max}, nm (log ε): 267 (4.18), 366 (4.00), 589 (3.48). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.28–2.04 m (10H, CH_2), 2.95 d (3H, CH_3, *J* = 5.8 Hz), 6.39 d (1H, CH, *J* = 10.0 Hz), 7.38 d (1H, CH, *J* = 10.0 Hz), 9.50 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 18.64, 23.04, 33.45 (CH_2); 33.78 (CH_3); 101.65, 129.37 (CH); 100.04, 125.80, 131.63, 134.91, 139.90. Mass spectrum, *m*/*z* (I_{rel}, %): 292 (4) $[M]^+$, 276 (17), 183 (100), 153 (63). Found, %: C 53.38; H 5.35; N 18.85. *m*/*z* 292.1172 $[M]^+$. $C_{13}H_{16}N_4O_4$. Calculated, %: C 53.42; H 5.52; N 19.17. *M* 292.1166.

5-Nitro-*N*-phenylspiro[benzimidazole-2,1′-cyclohexan]-4-amine (VIIa). Aniline, 2.0 g (0.02 mol), was added to a solution of 2.63 g (0.01 mol) of compound **I** in 80 ml of benzene, and the mixture was heated for 6 h under reflux. The solvent was distilled off, and the residue was purified by chromatography on silica gel using ethyl acetate–hexane (1:3) as eluent. Yield 1.70 g (55%), mp 187–190°C. IR spectrum, ν, cm^{-1}: 3194 (NH), 1631 (C=N). UV spectrum, λ_{max}, nm (log ε): 248 (4.13), 360 (4.06), 500 (3.75). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.95–1.94 m (10H, CH_2), 6.60 d (1H, CH, *J* = 10.1 Hz), 7.91 d (1H, CH, *J* = 10.1 Hz), 7.17–7.24 m (2H, H_{arom}), 7.29–7.39 m (3H, H_{arom}), 11.49 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 23.77, 24.95, 32.76 (CH_2); 112.05, 131.69, 125.43, 127.10, 128.33 (CH); 109.45, 129.89, 137.85, 142.39, 154.35, 161.05. Mass spectrum, *m*/*z* (I_{rel}, %): 322 (100) $[M]^+$, 305 (27), 287 (30), 275 (32). Found, %: C 67.37; H 5.51; N 17.11. *m*/*z* 322.1347 $[M]^+$. $C_{18}H_{17}N_4O_2$. Calculated, %: C 67.20; H 5.60; N 17.30. *M* 322.1424.

Compounds **VIIb**–**VIIf** were synthesized in a similar way.

***N*-(2-Methoxyphenyl)-5-nitrospiro[benzimidazole-2,1′-cyclohexan]-4-amine (VIIb).** Yield 41%, mp 172–174°C. IR spectrum, ν, cm^{-1}: 3425 (NH), 1633 (C=N). UV spectrum, λ_{max}, nm (log ε): 252 (4.03), 272 (4.06), 361 (4.00), 500 (3.68). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.78–1.90 m (10H, CH_2), 3.68 s (3H, OCH_3), 6.55 d (1H, CH, *J* = 10.2 Hz), 7.90 d (1H, CH, *J* = 10.2 Hz), 6.88–6.96 m (2H, CH), 7.16–7.30 m (2H, CH), 11.30 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 23.78, 24.91, 32.74 (CH_2); 54.86 (OCH_3); 110.49, 111.54, 119.84, 125.90, 128.24, 131.98 (CH); 109.08, 125.48, 126.80, 143.08, 153,40, 154.68, 158.13. Mass spectrum, *m*/*z* (I_{rel}, %): 352 (21) $[M]^+$, 337 (25), 321 (100), 304 (12). Found, %: C 64.70; H 5.68; N 15.85. *m*/*z* 352.1531 $[M]^+$. $C_{19}H_{20}N_4O_3$. Calculated, %: C 64.76; H 5.72; N 15.90. *M* 352.1530.

***N*-(4-Methoxyphenyl)-5-nitrospiro[benzimidazole-2,1′-cyclohexan]-4-amine (VIIc).** Yield 35%, mp 153–155°C. IR spectrum, ν, cm^{-1}: 3204 (NH), 1631 (C=N). UV spectrum, λ_{max}, nm (log ε): 225 (4.25), 361 (4.04), 502 (3.70). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.09–1.88 m (10H, CH_2), 3.84 s (3H, OCH_3), 6.59 d (1H, CH, *J* = 10.3 Hz), 7.94 d (1H, CH, *J* = 10.3 Hz), 6.88 d (2H, H_{arom}, *J* = 8.9 Hz), 7.14 d (2H, H_{arom}, *J* = 8.9 Hz), 11.56 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 24.06, 25.25, 33.05 (CH_2); 55.48 (OCH_3); 111.92, 113.85, 126.90, 132.22 (CH); 109.63, 125.80, 130.98, 143.24, 154,73, 158.52, 158.86. Mass spectrum, *m*/*z* (I_{rel}, %): 352 (100) $[M]^+$, 337 (67), 318 (24), 290 (17). Found, %: C 64.85; H 5.65; N 16.10. *m*/*z* 352.1527 $[M]^+$. $C_{19}H_{20}N_4O_3$. Calculated, %: C 64.76; H 5.72; N 15.90. *M* 352.1530.

5-Nitro-*N*-(4-nitrophenyl)spiro[benzimidazole-2,1′-cyclohexan]-4-amine (VIId). Yield 70%, mp 108–110°C. IR spectrum: ν 1636 cm^{-1} (C=N). UV spectrum, λ_{max}, nm (log ε): 268 (4.15), 344 (4.13), 494 (3.88). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.20–1.85 m (10H, CH_2), 6.76 d (1H, CH, *J* = 10.1 Hz), 7.32 d (2H, H_{arom}, *J* = 9.0 Hz), 7.87 d (1H, CH, *J* = 10.1 Hz), 8.19 d (2H, H_{arom}, *J* = 9.0 Hz), 11.07 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 23.90, 24.77, 32.46 (CH_2); 114.43, 123.72, 125.00, 130.84 (CH); 110.11, 128.84, 139.50, 143.78, 145.28, 154.11, 157.94. Mass spectrum, *m*/*z* (I_{rel}, %): 367 (61) $[M]^+$, 350 (100), 332 (22), 320 (47). Found, %: C 58.92; H 5.09; N 19.21. *m*/*z* 367.1267 $[M]^+$. $C_{18}H_{17}N_5O_4$. Calculated, %: C 58.85; H 4.66; N 19.07. *M* 367.1275.

4-[(5-Nitro-1-oxidospiro[benzimidazole-2,1′-cyclohexan]-4-yl)amino]benzenesulfonamide (VIIe). Yield 36%, mp 182–185°C. IR spectrum: ν 1634 cm^{-1} (C=N). UV spectrum, λ_{max}, nm (log ε): 268 (3.98), 358 (3.74), 500 (3.56). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.30–1.87 m (10H, CH_2), 6.77 d (1H, CH, *J* = 9.9 Hz), 7.35–7.42 m (4H, H_{arom}, NH_2), 7.69–7.81 m (3H, H_{arom}), 11.05 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 23.96, 24.92, 32.46 (CH_2); 113.48, 123.52, 125.84, 132.34 (CH); 109.01, 128.39, 138.89, 140.67, 142.53, 155.99, 158.34. Mass spectrum, *m*/*z* (I_{rel}, %): 401 (68) $[M]^+$, 366 (77), 338 (17), 303 (20), 274 (100). Found, %: C 54.05; H 4.70; N 17.20; S 8.10.

m/*z* 401.1158 $[M]^+$. $C_{18}H_{19}N_5O_4S$. Calculated, %: C 53.87; H 4.74; N 17.46; S 7.98. *M* 401.1152.

***N*-(2-Chlorophenyl)-5-nitrospiro[benzimidazole-2,1′-cyclohexan]-4-amine (VIIf).** Yield 52%, mp 192–195°C. IR spectrum: ν 1633 cm^{-1} (C=N). UV spectrum, λ_{max}, nm (logε): 255 (4.13), 352 (4.06), 488 (3.73). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.93–1.97 m (10H, CH_2), 6.62 d (1H, CH, *J* = 10.1 Hz), 7.23–7.33 m (3H, H_{arom}), 7.38–7.44 m (1H, H_{arom}), 7.91 d (1H, CH, *J* = 10.1 Hz), 11.22 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 23.76, 24.87, 32.63 (CH_2); 112.51, 126.77, 127.56, 128.40, 129.33, 131.46 (CH); 109.58, 125.98, 131.00, 135.75, 142.32, 154.36, 157.88. Mass spectrum, *m*/*z* (I_{rel}, %): 356 (33) $[M]^+$, 321 (100), 304 (32), 274 (29). Found, %: C 61.1; H 4.70; Cl 10.4; N 20.11. *m*/*z* 356.1036 $[M]^+$. $C_{18}H_{17}ClN_4O_2$. Calculated, %: C 60.67; H 4.78; Cl 9.97; N 19.93. *M* 356.1035.

5-Azidospiro[benzimidazole-2,1′-cyclohexane]-1,3-dioxide (VIII). Sodium azide, 0.80 g (0.012 mol), was added to a solution of 2.63 g (0.01 mol) of compound **I** in 80 ml of methanol, and the mixture was stirred for 24 h at room temperature. The solvent was distilled off under reduced pressure, the residue was extracted with chloroform, the extract was dried over $MgSO_4$, the drying agent was filtered off, the solvent was distilled off, and the residue was purified by chromatography on silica gel using chloroform as eluent. Yield 1.0 g (38%), mp 83°C (decomp.) IR spectrum, ν, cm^{-1}: 2117 (N_3), 1589 (C=N). UV spectrum, λ_{max}, nm (logε): 266 (4.37), 292 (4.36), 543 (3.66). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.39–2.04 m (10H, CH_2), 6.48 d.d (1H, CH, *J* = 9.8, 1.8 Hz), 6.80 d (1H, CH, *J* = 1.8 Hz), 7.19 d (1H, CH, *J* = 9.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 18.65, 23.06, 33.27 (CH_2); 101.25, 116.80, 123.43 (CH); 97.75, 134.33, 135.40, 142.55. Found, %: C 55.10; H 4.90; N 26.88. $C_{12}H_{13}N_5O_2$. Calculated, %: C 55.59; H 5.05; N 27.02.

***N*-Phenylspiro[benzimidazole-2,1′-cyclohexan]-5-amine 1-oxide (IXa).** Aniline hydrochloride, 1.3 g (0.01 mol), was added to a solution of 2.63 g (0.01 mol) of compound **I** in 80 ml of methanol, and the mixture was heated for 4 h under reflux. The solvent was distilled off, 30 ml of water was added to the residue, and the mixture was adjusted to pH 8 by adding a 10% solution of sodium hydroxide and extracted with chloroform (3×20 ml), The extract was dried over $MgSO_4$, the drying agent was filtered off, the solvent was distilled off, and the residue was subjected to chromatography on aluminum oxide using chloroform as eluent to isolate compounds **IXa** (first fraction) and **IXd** (second fraction). Compound **IXa**: Yield 1.65 g (56%), mp 168–170°C. IR spectrum: ν 1623 cm^{-1} (C=N). UV spectrum, λ_{max}, nm (logε): 249 (4.31), 369 (4.46), 511 (3.63). ^1H NMR spectrum, δ, ppm: in $CDCl_3$: 1.20–2.10 m (10H, CH_2), 6.43 d (1H, CH, *J* = 0.8 Hz), 6.57 d.d (1H, CH, *J* = 9.6, 1.5 Hz), 7.08–7.20 m (4H, H_{arom}), 7.28–7.35 m (2H, H_{arom}); in DMSO-d_6: 0.81–2.14 m (10H, CH_2), 6.28 s (1H, 4-H), 6.77 d.d (1H, 6-H, *J* = 9.8, *J* = 1.4 Hz), 7.17 d (1H, 7-H, *J* = 9.8 Hz, 7.06–7.17 m (1H, H_{arom}), 7.24–7.31 m (2H, H_{arom}), 7.35–7.44 m (2H, H_{arom}), 8.96 br.s (1H, NH). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 23.52, 24.78, 35.05 (CH_2); 94.87, 117.52, 122.48, 124.62, 127.52, 129.34 (CH); 104.74, 132.64, 139.07, 148.88, 161.82. Mass spectrum: *m*/*z* (I_{rel}, %): 293 (88) $[M]^+$, 277 (100), 264 (45), 250 (52). Found, %: C 73.49; H 6.48; N 14.34. *m*/*z* 293.1521 $[M]^+$. $C_{18}H_{19}N_3O$. Calculated, %: C 73.69; H 6.53; N 14.33. *M* 293.1523.

***N*-Phenylspiro[benzimidazole-2,1′-cyclohexan]-5-amine 1,3-dioxide (IXd).** Yield 0.15 g (5%), dark green crystals, mp 142–145°C. IR spectrum, ν, cm^{-1}: 3268 (NH), 1595 (C=N). UV spectrum, λ_{max}, nm (logε): 257 (4.48), 279 (4.72), 413 (4.38), 620 (3.5). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.48–2.06 m (10H, CH_2), 6.43 d (1H, CH, *J* = 1.6 Hz), 6.74 d.d (1H, CH, *J* = 9.9, 1.6 Hz), 7.04–7.13 m (4H, H_{arom}), 7.22–7.28 m (2H, H_{arom}), 7.34 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 19.45, 23.63, 33.62 (CH_2); 87.25, 116.24, 122.30, 124.67, 129.05, 129.44 (CH); 96.83, 134.09, 136.95, 138.98, 146.18. Mass spectrum, *m*/*z* (I_{rel}, %): 309 (37) $[M]^+$, 293 (63), 277 (100), 276 (65), 264 (23), 250 (22), 222 (55), 213 (35), 181 (20), 167 (35), 154 (42). Found, %: C 70.49; H 6.48; N 13.34. *m*/*z* 309.1472 $[M]^+$. $C_{18}H_{19}N_3O_2$. Calculated, %: C 69.90; H 6.14; N 13.59. *M* 309.1471.

***N*-(3-Nitrophenyl)spiro[benzimidazole-2,1′-cyclohexan]-5-amine 1-oxide (IXb)** was synthesized in a similar way. Yield 51%, mp 186–189°C. IR spectrum, ν, cm^{-1}: 3327 (NH), 1598 (C=N). UV spectrum, λ_{max}, nm (logε): 368 (4.18), 486 (3.78). ^1H NMR spectrum, δ, ppm: in $CDCl_3$: 1.24–2.13 m (10H, CH_2), 6.56 s (1H, 4-H), 6.62 d.d (1H, CH, *J* = 10.0, 1.5 Hz), 7.22 d (1H, 7-H, *J* = 10.0 Hz), 7.50 t (1H, H_{arom}, *J* = 8.0 Hz), 7.57 d (1H, H_{arom}, *J* = 8.0 Hz), 7.93 d (1H, H_{arom}, *J* = 8.0 Hz), 8.01 s (1H, H_{arom}); in DMSO-d_6: 1.10–1.90 m (10H, CH_2), 6.53 br.s (1H, 4-H), 6.77 d.d (1H, 6-H, *J* = 10.0, 2.0 Hz), 7.22 d (1H, 7-H, *J* = 10.0 Hz), 7.63 t (1H, H_{arom}, *J* = 8.0 Hz), 7.70 d (1H, H_{arom}, *J* = 8.0 Hz), 7.87 d (1H, H_{arom}, *J* = 8.0 Hz), 8.01 br.s (1H, H_{arom}), 9.37 br.s (1H, NH). ^{13}C NMR

spectrum ($CDCl_3$), δ_C, ppm: 23.46, 24.58, 35.08 (CH_2); 97.11, 116.04, 118.08, 118.56, 126.96, 130.21 (CH); 105.02, 132.73, 140.96, 147.89, 148. 96, 161.36. Mass spectrum, *m*/*z* (I_{rel}, %): 338 (40) $[M]^+$, 322 (100), 320 (42), 309 (16), 295 (19), 276 (27), 275 (22), 274 (18), 255 (13) 221 (25). Found, %: C 63.25; H 5.10; N 16.34. *m*/*z* 338.1369 $[M]^+$. $C_{18}H_{18}N_4O_3$. Calculated, %: C 63.90; H 5.32; N 16.57. *M* 338.1373.

***N*-(4-Methoxyphenyl)spiro[benzimidazole-2,1′-cyclohexan]-5-amine 1-oxide (IXc).** Yield 41%, mp 193–195°C. IR spectrum: ν 1619 cm^{-1} (C=N). UV spectrum, λ_{max}, nm (logε): 251 (4.12), 369 (4.02), 507 (3.38). ^1H NMR spectrum, δ, ppm: in $CDCl_3$: 1.17–2.08 m (10H, CH_2), 3.77 s (3H, OCH_3), 6.18 d (1H, 4-H, *J* = 1.5 Hz), 6.51 d.d (1H, 6-H, *J* = 9.8, 1.5 Hz), 6.84 d (2H, H_{arom}, *J* = 8.9 Hz), 7.11 d (2H, H_{arom}, *J* = 8.9 Hz), 7.12 d (1H, 7-H, *J* = 9.8 Hz); in DMSO-d_6: 0.92–1.95 m (10H, CH_2), 3.76 s (3H, OCH_3), 6.01 s (1H, 4-H), 6.73 d.d (1H, 6-H, *J* = 9.6, 1.8 Hz), 6.97 d (2H, H_{arom}, *J* = 9.0 Hz), 7.14 d (1H, H_{arom}, *J* = 9.6 Hz), 7.20 d (2H, H_{arom}, *J* = 9.0 Hz), 8.77 br.s (1H, NH). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 23.49, 24.66, 35.07 (CH_2); 93.57, 114.56, 117.53, 125.44, 127.22 (CH); 65.42 (OCH_3); 104.46, 131.54, 132.60, 150.29, 157.25, 161.63. Mass spectrum, *m*/*z* (I_{rel}, %): 323 (100) $[M - 32]^+$, 307 (98), 292 (97), 290 (16), 280 (56), 265 (15). Found, %: C 64.00; H 6.12; N 11.34. *m*/*z* 323.1682 $[M - 32]^+$. $C_{19}H_{21}N_3O_4$. Calculated, %: C 64.22; H 5.91; N 11.83. *M* 355.1629.

5-Methoxyspiro[benzimidazole-2,1′-cyclohexane]-4-carbonitrile 1-oxide (X) and 5-oxo-3,5-dihydrospiro[benzimidazole-2,1′-cyclohexane]-4-carbonitrile 1-oxide (XI). *a*. Sodium cyanide, 0.70 g (0.014 mol), was added to a solution of 2.63 g (0.01 mol) of compound **I** in 40 ml of methanol, and the mixture was stirred for 4 h at room temperature. The solvent was distilled off under reduced pressure, 40 ml of water was added to the residue, and the mixture was acidified to pH 3 with 5% hydrochloric acid and extracted with ethyl acetate. The extract was washed with a saturated solution of sodium chloride and dried over $MgSO_4$, the drying agent was filtered off, the solvent was distilled off, and the residue was subjected to chromatography on silica gel using chloroform–methanol (10:1) as eluent to isolate compounds **X** (first fraction) and **XI**. Compound **X**: Yield 0.60 g (23%), mp 193–196°C. IR spectrum, ν, cm^{-1}: 2228 (CN), 1600 (C=N). UV spectrum, λ_{max}, nm (logε): 224 (4.44), 352 (4.00), 465 (3.45). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.17–2.00 m (10H, CH_2), 4.15 s (3H, OCH_3), 6.72 d (1H, CH, *J* = 9.0 Hz), 7.39 d (1H, CH, *J* = 9.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 22.94, 24.28, 34.93 (CH_2); 57.76 (OCH_3); 119.24, 122.07 (CH); 92.44, 104.44, 112.71, 131.55, 158.27, 169.23. Mass spectrum, *m*/*z* (I_{rel}, %): 257 (100) $[M]^+$, 240 (58), 228 (49), 212 (20). Found, %: C 65.66; H 5.77; N 16.31. *m*/*z* 257.1161 $[M]^+$. $C_{14}H_{15}N_3O_2$. Calculated, %: C 65.35; H 5.88; N 16.33. *M* 257.1159.

Compound **XI**. Yield 0.50 g (20%), mp 241–242°C. IR spectrum, ν, cm^{-1}: 2226, 2213 (CN); 1630, 1615, 1538 (C=O, C=N). UV spectrum, λ_{max}, nm (logε): 249 (3.88), 345 (4.20), 438 (3.41). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 0.96–1.98 m (10H, CH_2), 6.35 d (1H, CH, *J* = 9.8 Hz), 7.41 d (1H, CH, *J* = 9.8 Hz), 11.18 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 21.39, 23.90, 35.02 (CH_2); 120.67, 131.82 (CH); 79.35, 96.32, 115.73, 131.52, 156.91, 181.61. Mass spectrum, *m*/*z* (I_{rel}, %): 243 (100) $[M]^+$, 226 (70), 214 (23), 200 (32). Found, %: C 63.93; H 5.23; N 16.85. *m*/*z* 243.1002 $[M]^+$. $C_{13}H_{13}N_3O_2$. Calculated, %: C 64.18; H 5.39; N 17.28. *M* 243.1006.

b. A solution of 0.70 g (0.014 mol) of sodium cyanide in 10 ml of water was added to a solution of 2.63 g (0.01 mol) of compound **I** in 80 ml of chloroform. The mixture was vigorously stirred for 4 h at room temperature, 20 ml of water was added, and the organic phase was separated and washed with water (2×10 ml). The aqueous phase was acidified to pH 3 with 5% hydrochloric acid and extracted with chloroform (3×50 ml), the extract was dried over $MgSO_4$, the drying agent was filtered off, the solvent was distilled off, and the residue was purified by chromatography on silica gel using chloroform–methanol (10:1) as eluent. Yield of **XI** 1.84 g (71%).

3-Methyl-5-oxo-3,5-dihydrospiro[benzimidazole-2,1′-cyclohexane]-4-carbonitrile 1-oxide (XII). Compound **XI**, 1.0 g (0.0041 mol), was dissolved in 80 ml of acetone, 11.35 g (0.008 mol) of methyl iodide and 3.0 g (0.02 mol) of calcined potassium carbonate were added, and the mixture was stirred for 16 h at room temperature. The precipitate was filtered off, the solvent was distilled off from the filtrate, and the residue was subjected to chromatography on silica gel using chloroform as eluent to isolate 0.08 g (8%) of methoxy derivative **X** and 0.87 g (82%) of compound **XII**, mp 256°C (decomp.). IR spectrum, ν, cm^{-1}: 2204 (CN), 1616 (C=N). UV spectrum, λ_{max}, nm (logε): 234 (3.30), 259 (3.18), 270 (3.10), 351 (3.70), 447 (3.00). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.20–2.17 m (10H, CH_2), 3.47 s (3H, CH_3), 6.40 d (1H, CH, *J* = 10.0 Hz), 7.44 d (1H, CH, *J* = 10.0 Hz). ^{13}C NMR

spectrum, δ_C, ppm: 19.30, 22.64, 31.43 (CH_2); 30.04 (CH_3); 120.35, 131.01 (CH); 78.40, 95.53, 116.37, 131.84, 154.12, 181.75. Mass spectrum, *m*/*z* (I_{rel}, %): 257 (65.6) $[M]^+$, 241 (82.3), 240 (40.6), 198 (82), 186 (100). Found, %: C 64.97; H 5.60; N 16.30. *m*/*z* 257.1162 $[M]^+$. $C_{14}H_{15}N_3O_2$. Calculated, %: C 65.35; H 5.88; N 16.33. *M* 257.1159.

Reactions of 5-nitrospiro[benzimidazole-2,1′-cyclohexane] 1-oxide (VI) with nucleophilic reagents. The conditions for the reactions of compound **VI** with 2-aminoethanol, morpholine, piperidine, 3-nitroaniline hydrochloride, and sodium cyanide were the same as in the corresponding reactions with compound **I**. The yields of **IIc**, **IIk**, **IIl**, **IXb**, and **XI** were 48, 18, 49, 15, and 17%, respectively.

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