Reduction of substituted spiro[cyclopropane-3-(1-pyrazolines)] to spiro[cyclopropane-3-pyrazolidines] and 1-(2-aminoethyl)cyclopropylamine derivatives

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Raney nickel-catalyzed hydrogenation of 5-substituted spiro[cyclopropane-3-(1-pyrazoline)]-5-carboxylates occurs with N—N bond cleavage with simultaneous cyclocondensation to give 3-aminopyrrolidin-2-ones containing a spirocyclopropane fragment. The presence of the second ester group in the pyrazoline side chain, in the position ensuring the formation of a five-membered ring results in 6,11-diazadispiro[2.1.4.2]undecane-7,10-dione, the product of double cyclocondensation of the intermediate diamine. Hydrogenation of the aryl-substituted spiro[cyclopropane-3-(1-pyrazolines)] in the presence of acetone affords hexahydrospiro[cyclopropane-4-pyrimidines], which can be converted into the cyclopropane-containing 1,3-diamines in the individual state or as salts.

Key words: spiro[cyclopropane-3-(1-pyrazolines)], spiro[[cyclopropane-3-pyrrolidin-5-ones], hexahydrospiro[cyclopropane-4-pyrimidines], 1,3-diamines, reduction, cyclocondensation.

Hydrogenolysis of 1- or 2-pyrazolines gives either pyrazolidines[1—3] or 1,3-diamines,[3—8] depending on the nature of reducing reagents and reaction conditions; stabilization of the pyrazolidines normally requires the introduction of a protecting group to a nitrogen atom. Transformation of pyrazolines into diamines is mainly carried out by catalytic hydrogenation of 1- or 2-pyrazolines under a hydrogen pressure in the presence of Raney nickel. The reduction of pyrazolines that contain an ester or amide group in the γ-position to the amino group formed deserves special consideration. In this case, the 1,3-diamines formed initially undergo intramolecular condensation to give 3-amino-2-pyrrolidone derivatives.[9,10] These are of interest as potential biologically active substances and structural fragments of complex polycyclic systems present in natural products.

This communication reports the first study of the reduction, under various conditions, of spirocyclopropane-containing pyrazolines prepared either previously[11—13] or in this study.

Results and Discussion

The presence of the cyclopropane fragment as a reaction site in spiro[cyclopropane-3-(1-pyrazoline)] molecules creates certain difficulties for the selective reduction of the heterocyclic N=N bond. Indeed, in none of the experiments were we able to eliminate completely the formation of by-products resulting from hydrogenolysis (or isomerization) of the cyclopropane ring. However, under certain conditions, it is possible to direct the reduction toward the predominant formation of pyrazolidines or 1,3-diamines, which retain the cyclopropane fragment in the molecule. Thus, the catalytic reduction of spiro[cyclopropane-3-(1-pyrazoline)] **1**, obtained by addition of diazocyclopropane to methyl methacrylate,[11] was found to proceed most efficiently in an ethanol solution when catalyzed by the Raney nickel (p_{H_2} = 80—90 bar, 70 °C, 4 h). Under these conditions, spiro[cyclopropane-3-(1-pyrrolidin-5-one)] **2** is formed as the major reaction product in 52—55% yield upon complete reduction of pyrazoline **1** to diamino ester **3**, which then undergoes intramolecular condensation (Scheme 1). As the temperature is decreased to 50 °C, a substantial portion of the starting pyrazoline remains unchanged, while temperature rise above 90 °C decreases the yield of pyrrolidinone **2** due to the formation of heavier products, apparently upon various intermoecular transformations.

It is noteworthy that the reaction mixture formed after hydrogenation of pyrazoline **1** with hydrogen in the pres-

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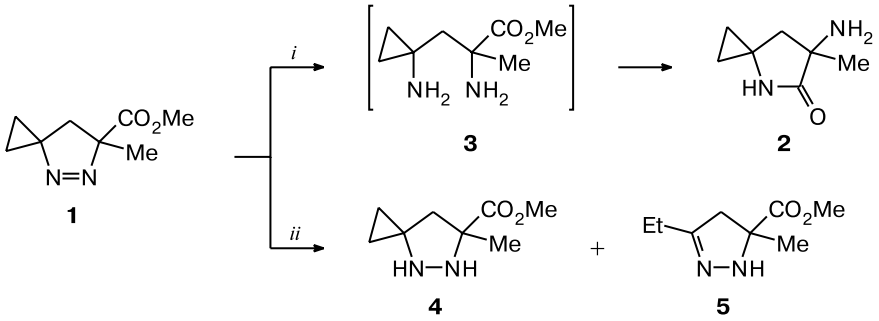
Scheme 1



Reagents and conditions: *i*. H_2, Ni, 80 bar, 70 °C, 4 ч; *ii*. Zn, NH_4Cl, THF/H_2O.

ence of Raney nickel almost does not contain spiro[cyclopropane-3-(1-pyrazolidine)] **4** (according to ^1H NMR), which is either unstable under these conditions or is easily reduced to diamine, which is then converted into pyrrolidinone **2**.

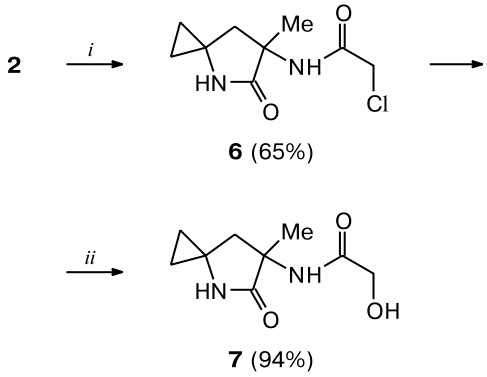
Unlike catalytic hydrogenation, the reduction of pyrazoline **1** with zinc in aqueous THF in the presence of NH_4Cl yields mainly a mixture of two structural isomers, spiro[cyclopropane-3-pyrazolidine] (**4**) and ethylpyrazoline **5** (see Scheme 1). Unfortunately, we were unable to isolate these compounds in a pure state, but their presence in the reaction mixture is indicated by the full set of non-overlapping signals of the corresponding protons in the ^1H NMR spectrum (see Experimental). According to the integral intensity, the overall yield of compounds **4** and **5** is ~85%, while their ratio is ~1.8 : 1. The substantial formation of pyrazoline **5** containing no cyclopropane fragment is apparently due to isomerization of pyrazolidine **4** induced by the arising zinc salt, which acts as a Lewis acid. The catalytic reduction of pyrazoline **1** in the presence of Raney nickel gives almost no ethylpyrazoline **5**.

Acylation of 3-aminopyrrolidin-2-one **2** with chloroacetyl chloride in the presence of Et_3N involves the amino group (Scheme 2) and gives chloroacetamide derivative **6** in ~65% yield. Refluxing of this product with KOH in MeOH does not affect the overall structure of the molecule, being accompanied only by hydrolysis of the C—Cl bond to give 2-hydroxyacetamide **7**.

Raney nickel-catalyzed hydrogenation of spiro[cyclopropane-3-(1-pyrazoline)] (**8**), synthesized in 68% yield by cyanoethylation of pyrazoline **9** under the action of MeONa/MeOH at −10 °C (see Ref. 12), proceeds in the same way as the reduction of pyrazoline **1**, giving rise to 3-aminospiro[cyclopropane-2-pyrrolidin-5-one] **10** in 38% yield (for the recrystallized product) (Scheme 3).

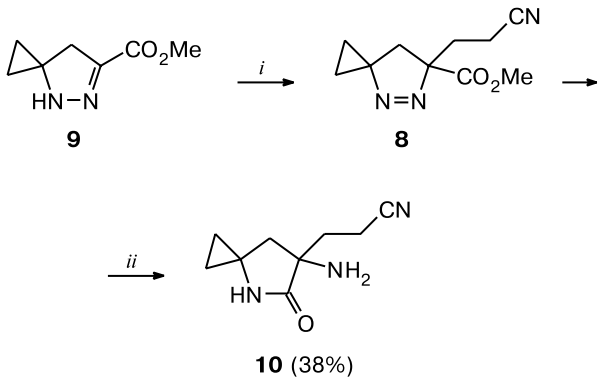
The reduction of pyrazoline **11**, containing two ester groups in the molecule,[12] is accompanied by two intramolecular condensations of the intermediate diamine, giving rise to 6,11-diazadispiro[2.1.4.2]undeca-7,10-dione (**12**) (Scheme 4) in 43% yield. The ^{13}C NMR spectrum of this

Scheme 2



Reagents and conditions: *i*. $ClCH_2COCl$, Et_3N, CH_2Cl_2, 20 °C; *ii*. KOH/MeOH, 64 °C, 2 h.

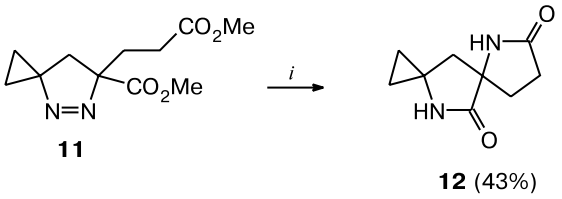
Scheme 3



Reagents and conditions: *i*. CH_2=CHCN, MeONa/MeOH, −10 °C; *ii*. H_2, Ni, 90 bar, 80 °C, 5 h.

compound shows, apart from the five CH_2 groups, four signals from the quaternary C atoms, two of these being spiro atoms (δ_C 36.7 and 66.6), and the other two being parts of carbonyl groups (δ_C 178.9 and 180.9).

Scheme 4



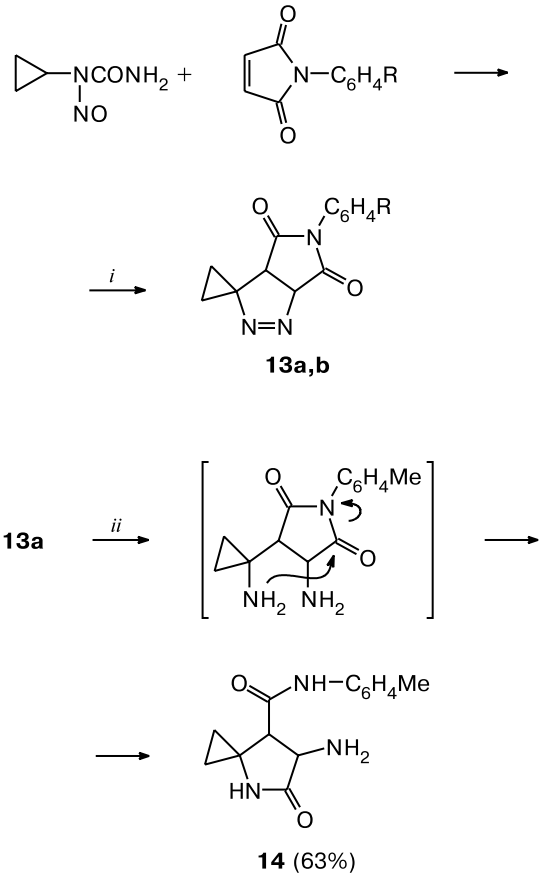
i. H_2, Ni, 100 bar, 80 °C, 5 h.

Dilactam **12** is a spirocyclopropane analog of 1,7-diazaspiro[4,4]nonane-2,6-dione synthesized previously in several step from pyroglutamic acid, in particular, as the chiral (5*R*)-isomer.[14,15] Previously, the 1,7-diazaspiro[4,4]nonane-2,6-dione fragment has been widely used for the design of conformationally rigid peptidomimetics, including analogs of the hormone thyrotropin (TRH).[15—19] The catalytic hydrogenation of pyrazolines, containing two ester groups in definite sites of the molecule can serve as yet another method for the preparation of spiro-bislactams.

We studied hydrogenation of fused spiro[cyclopropanepyrazolines] **13a,b**, prepared by 1,3-dipolar cycloaddition of diazocyclopropane generated *in situ* to *N*-(*p*-tolyl)- and *N*-(4-bromophenyl)maleimides. It was found that even minor changes in the nature of the aryl substituent have a pronounced effect on the pattern of transformations. Thus the reduction of pyrazoline **13a** with hydrogen in the presence of thoroughly washed Raney nickel containing no traces of alkali gives, as the major product (63%), *N*-(*p*-tolyl)amide of 6-amino-5-oxo-4-azaspiro[2.4]heptane-7-carboxylic acid (**14**), whose formation is preceded by selective reduction of the N=N bond to the corresponding diamino derivative (Scheme 5). The subsequent cyclocondensation involves the amino group located most closely to the cyclopropane ring, which furnishes the most stable five-membered heterocycle. In addition to the proton signals from the aryl and cyclopropane fragments, the ^{1}H NMR spectrum of compound **14** in $(CD_3)_2SO$ exhibits two doublets with δ 3.14 and 3.88 with coupling constants J = 8.5 Hz, due to the methine protons, and three broadened singlets with δ 9.8, 7.8, and 3.3, corresponding to the protons of two amide and one amino groups. The ^{13}C NMR spectrum has two low-field signals of equal intensity (Δδ 5—7), due to the C atoms of two different amide groups (see Experimental).

Attempts at reducing pyrazoline **13b** into 3-aminopyrrolidin-2-one under the same conditions failed due to the easy alcoholysis of the imide ring. Indeed, even mere refluxing of bromophenyl derivative **13b** for 2 h or treatment of **13b** with 2 mol.% NaOH in EtOH at 25 °C gives 2-pyrazoline **15** (85—90% yields), which is not reduced under the above-described conditions.

Scheme 5



R = Me (**a**), Br (**b**)

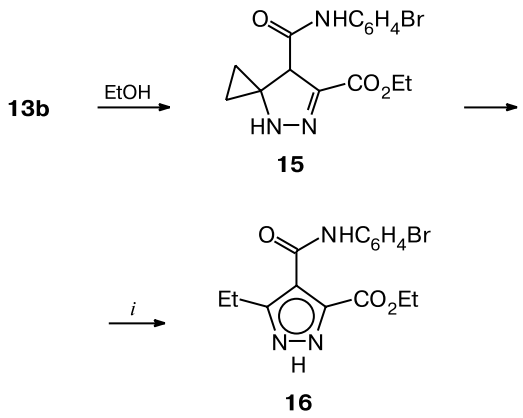
Reagents and conditions: *i*. K_2CO_3, CH_2Cl_2, 5—8 °C; *ii*. H_2, Ni, 100 bar, 80 °C, 6 h.

Treatment of pyrazoline **13b** or **15** with an equivalent amount of a base induces a more extensive transformation, resulting in trisubstituted pyrazole **16** in 80—95% yield (Scheme 6).

Unlike hydrogenation of the above-discussed spiro[cyclopropanepyrazolines] containing electron-withdrawing substituents in position 3 of the heterocycle, which ensure further transformations of the diamines formed, hydrogenation of 5-phenylspiro[cyclopropane-3-(1-pyrazoline)] (**17a**)[13] was expected to stop after the formation of amines. However, no pyrazolidine **18a** or diamine **19a** could be isolated in a pure state upon the reduction of pyrazoline **17a** with H_2 in the presence of Raney nickel (80 °C, 100 bar), despite the virtually complete conversion of the starting pyrazoline.

In order to trap the amines, we carried out hydrogenation of pyrazoline **17a** under the same conditions but with preliminary addition of a 10-fold molar excess of acetone. In this case, hexahydropyrimidine **20a** was isolated in

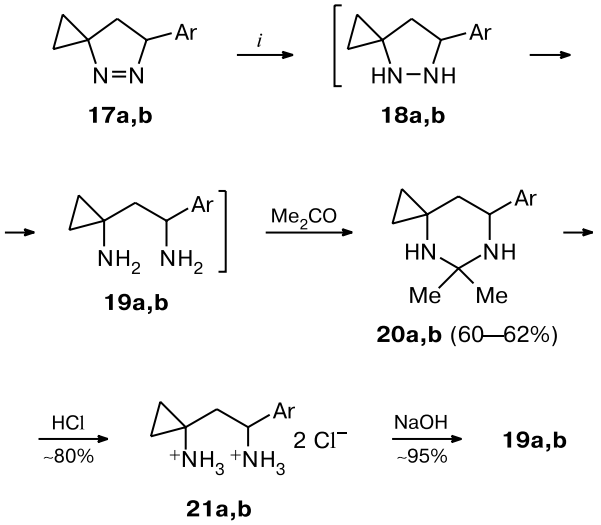
Scheme 6



i. NaOH (1 equiv.), EtOH.

~60% yield, indicating that hydrogenation of pyrazoline **17a** actually involves the N=N bond with the intermediate formation of diamine **19a** (Scheme 7). Despite the fact that we did not succeed in isolating diamine **19a** upon direct catalytic hydrogenation of pyrazoline **17a**, this compound was obtained in a pure state upon decomposition of compound **20a**. Indeed, treatment of hexahydropyrimidine **20a** with two equivalents of HCl in dioxane results in elimination of the acetone molecule to give diamine dihydrochloride **21a**, which is converted into free diamine **19a** upon neutralization with aqueous NaOH. On refluxing in acetone, this product is converted again into hexahydropyrimidine **20a** in ~90% yield.

Scheme 7



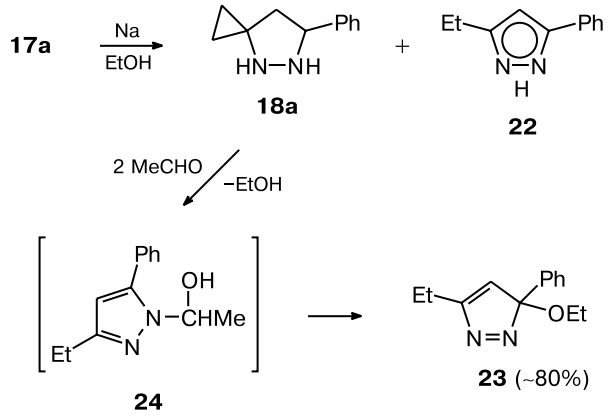
Ar = Ph (**a**), 4-C_6H_4F (**b**)

i. H_2, Ni, 100 bar, 80 °C, 6 h.

A similar strategy was used to prepare diamine **19b**, containing a *p*-fluorophenyl substituent in the molecule. The initial 1-pyrazoline **17b** was prepared in ~65% yield by 1,3-dipolar cycloaddition of *in situ* generated diazocyclopropane to *p*-fluorostyrene. Hydrogenation of pyrazoline **17b** with hydrogen over Raney nickel in the presence of acetone affords hexahydropyrimidine **20b** (yield 62%), which was converted into diamine **19b** in 91% yield *via* the dihydrochloride **21b**.

In order to estimate the feasibility of preparing pyrazolidine derivative **18a**, we studied the action of other reducing agents on pyrazoline **17a**. Alkyl- and aryl-substituted pyrazolines can be reduced to pyrazolidines on treatment with $LiAlH_4$ in THF[20] or to diamines with Na in refluxing EtOH.[21] It was found that spirocyclopropanepyrazoline **17a** does not change under the action of $LiAlH_4$ in THF, whereas treatment with Na in ethanol (Scheme 8) gives a mixture of pyrazolidine **18a** and 3(5)-phenyl-5(3)-ethylpyrazole (**22**)[13] in ~4 : 1 ratio rather than diamine **19a**. Pyrazole **22** results apparently from isomerization of the starting pyrazoline **17a** taken place at at 78 °C and induced by the EtONa formed.

Scheme 8



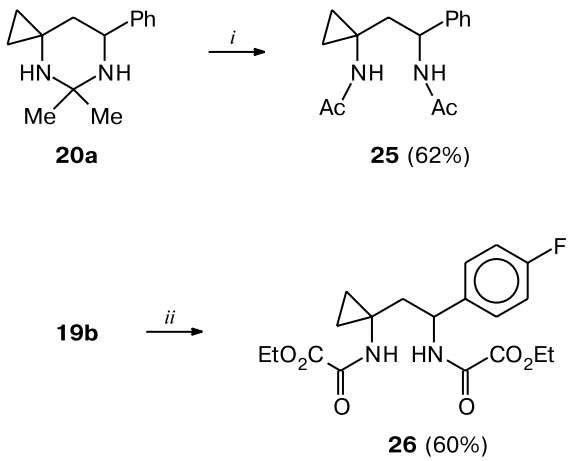
Pyrazolidine **18a**, which is readily oxidized in air to give pyrazoline **17a**, was identified by the ^1H NMR spectrum of the reaction mixture. Its spectrum closely resembles the spectrum of the starting pyrazoline **17a**, but the signals for the cyclopropane-ring protons and three interrelated heterocycle protons are somewhat shifted upfield (see Experimental). Chromatography on SiO_2 gave only pyrazole **22**.

Acyclic 1,2-disubstituted hydrazines are known[22] to react with two moles of aldehydes to give 1,3,4-oxadiazolidine derivatives. However, if the freshly obtained reaction mixture containing ~60% pyrazolidine **18a** is made to react with acetaldehyde, 3-ethoxy-3-phenyl-5-ethylpyrazole **23** is formed in ~50% yield instead of oxadiazoline. The product structure was proved by ^1H and

^{13}C NMR spectra and NOESY experiments (coupling of the OCH_2 group with the phenyl *ortho*-protons is observed). Pyrazole **23** is probably formed through oxidation and condensation of pyrazolidine **18a** with two acetaldehyde molecules accompanied by cyclopropane ring opening and yielding intermediate **24**, which then isomerizes (see Scheme 8).

Finally, we demonstrated that acyl derivatives of diamines **19** of the cyclopropane series can be obtained directly from hexahydropyrimidines **20** or diamine salts **21**. The reaction of compound **20a** with acetic anhydride, as in the case of hexahydropyrimidines containing no spirocyclopropane fragment,[23] leads to 1,2′-bis(acetylamino)-1-(2′-phenylethyl)cyclopropane (**25**) in 62% yield (Scheme 9). It is noteworthy that the reaction of dihydrochloride **21b** with diethyl oxalate in the presence of Et_3N as the base gives bis-ethyloxalylamide **26** rather than cyclic oxamide. A change in the reactant ratio and the order of addition does not give the cyclization product either, although the reaction of usual 1,3-diamines with diethyl oxalate or oxalyl chloride is a known method for the synthesis of cyclic oxamides.[24]

Scheme 9



Reagents and conditions: *i*. Ac_2O/Et_2O, 18 °C, 48 h; *ii*. $(CO_2Et)_2/Et_3N$, Et_2O, 18 °C, 72 h.

Thus, catalytic hydrogenation of substituted spiro[cyclopropane(1-pyrazolines)] with hydrogen in the presence of Raney nickel provides the route to diamines; when the molecule contains ester groups, they are immediately converted into pyrrolidin-2-ones or, in the presence of acetone, into the corresponding hexahydropyrimidines containing a spirocyclopropane fragment. The latter products are convenient synthons for the preparation of new promising cyclopropane-containing 1,3-diamines both free and as salts.

Experimental

^1H and ^{13}C NMR spectra were recorded on Bruker AC-200 (200 and 50.3 MHz) and Bruker AM-300 (300 and 75.5 MHz, respectively) spectrometers for solutions in $CDCl_3$, CD_3OD, or $(CD_3)_2SO$ containing 0.05% Me_4Si as the internal standard. Mass spectra were run on a Finnigan MAT INCOS-50 (EI, 70 eV, direct injection). Spiro[cyclopropanepyrazolines] **1**, **9**, **11**, and **17a,c** were synthesized by known procedures.[11—13,20] Thin layer chromatography was performed using silica gel 60 (0.040—0.063 mm) produced by Merck.

6-Amino-6-methyl-4-azaspiro[2.4]heptan-5-one (2). Pyrazoline **1** (0.55 g, 3.3 mmol), EtOH (10 mL), and Raney nickel (0.05 g) were placed in a 100-mL steel autoclave and hydrogenated at 70 °C and at a 80 bar H_2 pressure for 4 h. The reaction mixture was filtered, the solvent was evaporated, and the residue was treated with ether. The resulting precipitate was filtered off and dried *in vacuo* to give 0.26 g (55%) of pyrrolidin-2-one **2** as a colorless finely crystalline compound, m.p. 283—284 °C. Found (%): C, 60.15; H, 8.68; N, 19.77. $C_7H_{12}N_2O$. Calculated (%): C, 59.98; H, 8.63; N, 19.98. ^1H NMR ($CDCl_3$), δ: 0.70, 0.84 (both m, 2 H each, CH_2CH_2); 1.38 (s, 3 H, Me); 1.80 (br.s, 2 H, NH_2); 1.94, 2.22 (both d, 1 H each, $H_2C(7)$, ^2J = 12.1 Hz); 6.42 (br.s, 1 H, NH). ^{13}C NMR (DMSO-d_6), δ: 6.6, 10.8 (CH_2CH_2); 20.9 (Me); 35.1 (C(3)); 40.2 (C(7)); 57.1 (C(6)); 172.6 (CO). MS, *m/z* (I_{rel} (%)): 140 $[M]^+$ (14), 123 $[M - NH_3]^+$ (4), 112 (20), 111 (38), 97 (21), 70 (31); 57 (60), 42 (100).

Reduction of pyrazoline 1 in a Zn—NH_4Cl system. Ammonium chloride (4.28 g, 0.08 mol) in water (10 mL) and Zn (5.20 g, 0.08 g-at) were added to a solution of pyrazoline **1** (0.15 g, 0.9 mmol) in THF (10 mL), and the suspension was stirred for 24 h at 20 °C. The mixture was filtered, and water (30 mL) and CH_2Cl_2 (30 mL) were added to the filtrate. The organic layer was separated and dried with anhydrous Na_2SO_4, and the solvent was evaporated *in vacuo* at 20 °C. According to ^1H NMR data, the residue (0.13 g) was mainly a mixture of 6-methoxycarbonyl-6-methyl-4,5-diazaspiro[2.4]heptane (**4**) and 5-ethyl-3-methyl-3-methoxycarbonyl-3,4-dihydro-2*H*-pyrazole (**5**) (ratio ~(1.8 : 1), overall yield ~85%). **Compound 4.** ^1H NMR ($CDCl_3$), δ: 0.61, 0.89 (both m, 2 H each, CH_2CH_2); 1.54 (s, 3 H, Me); 1.93, 2.44 (both d, 1 H each, $H_2C(7)$, ^2J = 12.6 Hz); 3.78 (s, 3 H, OMe). **Compound 5.** ^1H NMR ($CDCl_3$), δ: 1.12 (t, 3 H, Me, J = 7.5 Hz); 1.50 (s, 3 H, Me); 2.29 (q, 2 H, CH_2, J = 7.5 Hz); 2.58, 3.19 (both d, 1 H each, $H_2C(4)$, ^2J = 16.7 Hz); 3.74 (s, 3 H, OMe).

2-Chloro-*N*-{6-methyl-5-oxo-4-azaspiro[2.4]hept-6-yl}acetamide (6). Triethylamine (0.15 g, 1.5 mmol) was added at 5 °C to a solution of amide **2** (0.10 g, 0.73 mmol) in CH_2Cl_2 (3 mL); then a solution of chloroacetyl chloride (0.082 g, 0.73 mmol) in CH_2Cl_2 (1 mL) was added. After keeping for 12 h, the reaction mixture was treated with water (20 mL), the organic layer was separated and dried with anhydrous Na_2SO_4, the solvent was removed *in vacuo*, and the residue was treated with ether to give 0.102 g (65%) of acetamide **6** as colorless crystals, m.p. 167—169 °C. Found (%): C, 50.03; H, 6.16; Cl, 16.18; N, 12.79. $C_9H_{13}ClN_2O_2$. Calculated (%): C, 49.89; H, 6.05; Cl, 16.36; N, 12.93. ^1H NMR ($CDCl_3$), δ: 0.60—1.02 (m, 4 H, CH_2CH_2); 1.59 (s, 3 H, Me); 2.18, 2.81 (both d, 1 H each, $H_2C(7)$, ^2J = 12.5 Hz); 4.02 (s, 2 H, CH_2Cl), 7.12,

7.20 (both br.s, 1 H each, 2 NH). ^{13}C NMR ($CDCl_3$), δ: 8.0, 12.5 (CH_2CH_2); 22.5 (Me); 36.6 (C(3)); 42.5 (CH_2Cl); 43.2 (C(7)); 59.3 (C(6)); 165.7 (NHCO); 176.9 (C(5)). Partial MS, *m/z* (I_{rel} (%)): 218 (0.1) and 216 (0.3) $[M]^+$, 181 $[M - Cl]^+$ (0.5), 123 (100).

2-Hydroxy-*N*-(6-methyl-5-oxo-4-azaspiro[2.4]hept-6-yl)acetamide (7). A mixture of acetamide **6** (0.016 g, 0.07 mmol) and KOH (0.05 g, 0.1 mmol) in MeOH (1 mL) was refluxed for 4 h. The solvent was evaporated to 2/3 of the initial volume, the precipitate was filtered off, and the filtrate was evaporated *in vacuo* to give 0.013 g (94%) of hydroxyacetamide **7** as a colorless finely crystalline compound, m.p. 301—302 °C. Found (%): C, 54.32; H, 7.19; N, 14.01. $C_9H_{14}N_2O_3$. Calculated (%): C, 54.53; H, 7.12; N, 14.13. ^{1}H NMR (CD_3OD), δ: 0.55—0.90 (m, 4 H, CH_2CH_2); 1.51 (s, 3 H, Me); 1.89, 2.81 (both d, 1 H each, $H_2C(7)$, ^2J = 12.4 Hz); 3.42 (br.s, 2 NH, OH); 3.91 (s, 2 H, OCH_2). ^{13}C NMR (CD_3OD), δ: 8.6, 12.9 (CH_2CH_2); 23.3 (Me); 37.0 (C(3)); 43.3 (C(7)); 60.0 (C(6)); 72.5 (OCH_2); 171.6 (NHCO); 178.8 (C(5)). Partial MS, *m/z* (I_{rel} (%)): 198 $[M]^+$ (0.6), 149 (11), 139 (1.5), 123 (100).

6-(2-Cyanoethyl)-6-methoxycarbonyl-4,5-diazaspiro[2.4]hept-4-ene (8). Sodium methoxide (0.07 g, 1.2 mmol) in MeOH (0.2 mL) was added at −10 °C to a vigorously stirred mixture of 6-methoxycarbonyl-4,5-diazaspiro[2.4]hept-5-ene (**9**) (1.80 g, 12 mmol) and acrylonitrile (0.60 g, 12 mmol) in CH_2Cl_2 (7 mL), and the mixture was stirred for 20 min. The reaction mixture was treated with 10 mL of water, the organic layer was separated, the aqueous layer was extracted with CH_2Cl_2 (10 mL), and the organic solution was dried with anhydrous Na_2SO_4. The solvent was removed *in vacuo* and the residue was recrystallized from hexane to give 1.69 g (68%) of pyrazoline **8** as yellowish crystals, m.p. 53—54 °C. ^{1}H NMR ($CDCl_3$), δ: 1.21 (m, 2 H, CHCH, directed away from the heterocycle N atoms); 1.78, 2.29 (both d, 1 H each, $H_2C(7)$, ^2J = 13.0 Hz); 1.86 (m, 2 H, CHCH, directed toward the heterocycle N atom); 2.49 (m, 4 H, CH_2CH_2); 3.82 (s, 3 H, OMe). ^{13}C NMR ($CDCl_3$), δ: 12.7, 14.9 (CH_2CH_2); 14.7 ($\underline{C}H_2CN$); 31.6 (C(7)); 33.5 ($\underline{C}H_2CH_2CN$); 53.1 (OMe); 70.4 (C(3)); 94.9 (C(6)); 118.8 (CN); 170.0 (CO). Partial MS, *m/z* (I_{rel} (%)): 139 $[C_7H_9NO_2]^+$ (35), 79 $[C_5H_5N]^+$ (100).

6-Amino-6-(2-cyanoethyl)-4-azaspiro[2.4]heptan-5-one (10). Spiro[cyclopropanepyrazoline] **8** (1.28 g, 6.2 mmol), ethanol (40 mL), and Raney nickel (0.05 g) were placed in a 100-cm^3 steel autoclave and hydrogenated at 80 °C and at a hydrogen pressure of 90 bar for 5 h. Then the reaction mixture was filtered and the solvent was evaporated *in vacuo*. The residue (~1.2 g) was treated with ethyl acetate at −20 °C, the precipitate was filtered off, washed with chloroform, and dried *in vacuo* to give 0.42 g (38%) of compound **10** as a colorless powder, m.p. 166—168 °C. ^{1}H NMR (CD_3OD), δ: 0.72—0.91 (m, 4 H, CH_2CH_2); 1.98 (m, 2 H, CH_2CN); 2.10, 2.19 (both d, 1 H each, $H_2C(7)$, ^2J = 13.5 Hz); 2.60 (m, 2 H, CH_2). ^{13}C NMR (CD_3OD), δ: 8.3, 10.4 (*cyclo*-CCH_2CH_2); 10.9 ($\underline{C}H_2CN$); 32.4 (CH_2); 34.6 (C(3)); 41.3 (C(7)); 58.6 (C(6)); 120.6 (CN); 177.8 (CO). Partial MS, *m/z* (I_{rel} (%)): 179 $[M]^+$ (8), 162 $[M - NH_3]^+$ (18), 151 (19), 150 (59), 122 (46), 111 (100), 97 (82).

6,11-Diazadispiro[2.1.4.2]undecane-7,10-dione (12). Pyrazoline **11** (0.105 g, 0.44 mmol), ethanol (6 mL), and Raney nickel (0.02 g) were placed in a 100-cm^3 autoclave and hydrogenated at 80 °C and a hydrogen pressure of 100 bar for 5 h. The reaction mixture was filtered, the solvent was evaporated, and the residue (0.073 g) was treated with ether. The precipitate was filtered off. After drying, 0.032 g (40%) of compound **12** was formed as a colorless finely crystalline compound, m.p. 302—303 °C. Found (%): C, 59.67; H, 6.48; N, 15.32. $C_9H_{14}N_2O_2$. Calculated (%): C, 59.99; H, 6.71; N, 15.55. ^{1}H NMR (DMSO-d_6), δ: 0.51—0.92 (m, 4 H, CH_2CH_2); 1.96, 2.36 (both d, 1 H each, $H_2C(7)$, ^2J = 12.5 Hz); 2.02—2.29 (m, 4 H, CH_2CH_2); 7.89, 7.98 (both br.s, 1 H each, 2 NH). ^{1}H NMR (CD_3OD), δ: 0.61—1.02 (m, 4 H, CH_2CH_2); 2.02, 2.51 (both d, 1 H each, $H_2C(7)$, ^2J = 13.0 Hz); 2.30—2.48 (m, 4 H, CH_2CH_2). ^{13}C NMR (CD_3OD), δ: 9.0, 12.1 (CH_2CH_2); 31.0, 32.8 (C(8), C(9)); 36.7 (C(3)); 43.7 (C(4)); 66.6 (C(5)); 178.9, 180.9 (2 CO). Partial MS, *m/z* (I_{rel} (%)): 180 $[M]^+$ (59), 152 (56), 97 (52), 54 (100).

Synthesis of 7-arylspiro[cyclopropane-2,3,7-triazabicyclo[3.3.0]oct-2-ene-6,8-diones] (13a,b) (general procedure). Potassium carbonate (2.61 g, ~15 mmol) containing ~20% H_2O was added at 5—7 °C to a mixture of *N*-arylmaleimide (2.8 mmol) and *N*-nitroso-*N*-cyclopropylurea (0.71 g, 5.5 mmol) in CH_2Cl_2 (20 mL), and the mixture was vigorously stirred for 3 h at the same temperature. Then the reaction mixture was filtered, the solvent was evaporated *in vacuo*, and the residue was recrystallized from benzene. **Compound 13a**, yield 63%, m.p. 145—147 °C. Found (%): C, 65.68; H, 5.08; N, 16.32. $C_{14}H_{13}N_3O_2$. Calculated (%): C, 65.87; H, 5.13; N, 16.46. ^{1}H NMR ($CDCl_3$), δ: 1.44, 1.92 (both m, 2H each, CH_2CH_2); 2.37 (s, 3 H, Me); 3.13 (d, 1 H, H(5), ^3J = 8.5 Hz); 6.02 (d, 1 H, H(1), ^3J = 8.5 Hz); 7.12, 7.28 (both d, 2H each, C_6H_4, J = 8.7 Hz). ^{13}C NMR ($CDCl_3$), δ: 11.2, 16.8 (CH_2CH_2); 21.2 (Me); 41.6 (C(5)); 73.6 (C(4)); 91.7 (C(1)); 126.1 (C_m); 128.4 (C_p); 130.0 (C_o); 139.2 (C_{ipso}); 168.8 and 173.7 (2 CO). Partial MS, *m/z* (I_{rel} (%)): 255 $[M]^+$ (51), 227 (10), 133 (13), 66 (100). **Compound 13b**, yield 74%, m.p. 195—197 °C. Found (%): C, 48.58; H, 3.08; Br, 24.62. $C_{13}H_{10}BrN_3O_2$. Calculated (%): C, 48.77; H, 3.15; Br, 24.96. ^{1}H NMR ($CDCl_3$), δ: 1.48, 1.95 (both m, 2H each, CH_2CH_2); 3.15 (d, 1 H, H(5), ^3J = 8.4 Hz); 6.02 (d, 1 H, H(1), ^3J = 8.4 Hz); 7.16, 7.58 (both d, 2H each, C_6H_4, J = 8.7 Hz). ^{13}C NMR ($CDCl_3$), δ: 11.3, 16.9 (CH_2CH_2); 41.6 (C(5)); 73.5 (C(4)); 91.8 (C(1)); 122.9 (C_p); 127.8 (C_m); 129.9 (C_{ipso}); 132.4 (C_o); 168.3, 173.2 (2 CO). Partial MS, *m/z* (I_{rel} (%)): 321 (0.5) and 319 (0.5) $[M]^+$, 184 (20), 94 (35), 66 (100%).

***N*-(*p*-Tolyl)-6-amino-5-oxo-4-azaspiro[2.4]heptan-7-carboxamide (14).** Pyrazoline **13a** (0.38 g, 1.5 mmol), ethanol (50 mL), and Raney nickel (0.05 g) were placed in a 100-cm^3 steel autoclave and hydrogenated at 80 °C and at a hydrogen pressure of 100 bar for 6 h. Then the reaction mixture was filtered, the solvent was evaporated, the residue was treated with ethyl acetate, and the precipitate was filtered off and dried *in vacuo* to give 0.25 g (64%) of compound **14** as colorless crystals, m.p. 199—201 °C. ^{1}H NMR (DMSO-d_6), δ: 0.82, 1.54 (both m, 2 H each, CH_2CH_2); 2.24 (s, 3 H, Me); 3.14 (d, 1 H, J = 8.5 Hz); 3.32 (br.s, 2 H, NH_2); 3.88 (d, 1 H, J = 8.5 Hz); 7.11, 7.48 (both d, 2 H each, C_6H_4, J = 8.7 Hz); 7.82, 9.80 (both br.s, 1 H each, 2 NH). ^{13}C NMR (DMSO-d_6), δ: 7.9, 8.7 (CH_2CH_2); 19.9 (Me); 37.2 (C(3)); 54.6 (C(7)); 55.3 (C(6)); 118.9 (C_m); 128.6 (C_o); 132.0 (C_p); 135.7 (C_{ipso}); 167.6, 175.2 (2 CO). Partial MS, *m/z* (I_{rel} (%)): 259 $[M]^+$ (7), 203 (4), 163 (18), 126 (64), 107 (100).

***N*-(4-Bromophenyl)-6-ethoxycarbonyl-4,5-diazaspiro[2.4]hept-5-ene-7-carboxamide (15).** Sodium hydroxide (1.6 mg, 0.04 mmol) in ethanol (1 mL) was added to a suspen-

sion of pyrazoline **13b** (0.65 g, 2 mmol) in ethanol (5 mL), and the mixture was stirred for 10 h. Then the solvent was removed *in vacuo*, the residue was treated with $CHCl_3$, and the insoluble part, representing product **15**, was filtered off and dried in air to give 0.55 g (85%) of compound **15** as slightly yellowish crystals, m.p. 217—219 °C. ^{1}H NMR (DMSO-d_6), δ: 0.88 (m, 4 H, CH_2CH_2); 1.16 (t, 3 H, Me, J = 7.0 Hz); 3.92 (s, 1 H, CH); 4.11 (q, 2 H, OCH_2, J = 7.0 Hz); 7.50 (m, 4 H, C_6H_4); 8.60 (br.s, 1 H, NH); 10.05 (br.s, 1 H, CONH). ^{13}C NMR (DMSO-d_6), δ: 7.9, 13.8 (CH_2CH_2); 13.6 (Me); 48.5 (C(3)); 54.0 (OCH_2); 59.2 (C(7)); 114.5 (C_p); 120.7 (C_m); 131.0 (C_o); 134.3 (C_{ipso}); 137.5 (C(6)); 161.6, 167.2 (2 CO). Partial MS, m/z (I_{rel} (%)): 367 (0.5) and 365 (0.5) $[M]^+$, 168 (38), 122 (100).

***N*-Bromophenyl-5-ethyl-3-ethoxycarbonylpyrazole-4-carboxamide (16).** Sodium hydroxide (80 mg, 2.0 mmol) in ethanol (1 mL) was added to a suspension of pyrazoline **13b** (0.64 g, 2.0 mmol) in ethanol (5 mL) and the mixture was stirred for 10 h. The homogeneous reaction mixture was concentrated, and the residue was dissolved in CH_2Cl_2 (5 mL) and washed with water (10 mL). The organic layer was dried with anhydrous Na_2SO_4. Removal of the solvent gave 0.51 g (80%) of pyrazole **16**, m.p. 205—207 °C. ^{1}H NMR ($CDCl_3$), δ: 1.27 (t, 3 H, Me, J = 7.3 Hz); 1.49 (t, 3 H, Me, J = 7.5 Hz); 2.93 (q, 2 H, CH_2, J = 7.5 Hz); 4.48 (q, 2 H, OCH_2, J = 7.3 Hz); 5.29 (br.s, 1 H, NH); 7.29, 7.52 (both d, 2H each, C_6H_4, J = 9.0 Hz); 12.49 (br.s, 1 H, CONH). ^{13}C NMR (DMSO-d_6), δ: 13.5, 13.6 (2 Me); 19.9 (CH_2); 59.2 (OCH_2); 106.1 (C(4)); 114.4 (C_p); 120.8 (C_m); 131.2 (C_o); 138.2 (C_{ipso}); 146.9, 153.0 (C(3), C(5)); 161.1, 164.6 (2 CO). Partial MS, m/z (I_{rel} (%)): 367 (22) and 365 (24) $[M]^+$, 321 (25) and 319 (25) $[M - EtOH]^+$, 195 (48), 173 (90), 171 (100).

A similar procedure starting from 2-pyrazoline **15** (0.27 g, 0.73 mmol) and NaOH (0.033 g, 0.8 mmol) in ethanol (5 mL) with a 10-h stirring at room temperature gave 0.25 g (95%) of pyrazole **16**.

6-(4-Fluorophenyl)-4,5-diazaspiro[2.4]hept-4-ene (17b). *N*-Nitroso-*N*-cyclopropylurea (2.56 g, 20 mmol) was added at −20 °C over a period of 15 min to a vigorously stirred mixture of 4-fluorostyrene (3.15 g, 26 mmol) and MeONa (1.40 g, 26 mmol) in MeOH (4 mL) and CH_2Cl_2 (20 mL), and the mixture was stirred for additional 15 min. Then the temperature was increased to 5 °C and water (~0.5 mL) was added. The organic layer was separated, and the solid residue was washed with CH_2Cl_2 (10 mL), dried with anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was recrystallized from an ether—hexane mixture (1 : 3) to give 3.20 g (65%) of pyrazoline **17b** as yellow crystals, m.p. 38—39 °C. ^{1}H NMR ($CDCl_3$), δ: 1.18 (m, 2 H, CHCH, directed away from the heterocycle N atoms); 1.88 (m, 2 H, CHCH, directed toward the heterocycle N atom); 1.74 (dd, 1 H, $H_aC(7)$, ^2J = 9.9 Hz, ^3J = 7.1 Hz); 2.27 (dd, 1 H, $H_bC(7)$, ^2J = 9.9 Hz, ^3J = 12.9 Hz); 5.62 (dd, 1 H, H(6), ^3J = 7.1 and 12.9 Hz); 7.05, 7.22 (both m, 2H each, C_6H_4F). ^{13}C NMR ($CDCl_3$), δ: 14.2 (CH_2CH_2); 33.4 (C(7)); 69.6 (C(3)); 89.2 (C(6)); 115.8 (d, C_m, J = 21.5 Hz); 128.9 (d, C_o, J = 7.6 Hz); 135.4 (C_{ipso}); 162.3 (d, C_p, J = 246 Hz). Partial MS, m/z (I_{rel} (%)): 190 $[M]^+$ (6), 161 (18), 147 (100).

Catalytic reduction of pyrazolines 17 in the presence of acetone (general procedure). Pyrazoline **17** (3.3 mmol), acetone (0.38 g, 6.6 mmol), ethanol (10 mL), and Raney nickel (0.05 g) were placed in a 100-cm^3 autoclave. Hydrogenation was carried out at 80 °C and at a hydrogen pressure of 100 bar for 6 h. The reaction mixture was filtered, the solvent was evaporated *in vacuo*, and the residue was recrystallized from ether.

5,5-Dimethyl-7-phenyl-4,6-diazaspiro[2.5]octane (20a) was prepared from pyrazoline **17a** (0.57 g), yield 0.43 g (60%), colorless crystals, m.p. 71—73 °C. Found (%): C, 77.51; H, 9.18; N, 13.02. $C_{14}H_{20}N_2$. Calculated (%): C, 77.73; H, 9.32; N, 12.95. ^{1}H NMR ($CDCl_3$), δ: 0.36—0.78 (m, 4 H, CH_2CH_2); 1.18 (dd, 1 H, $H_aC(8)$, ^2J = 13.4 Hz, ^3J = 11.9 Hz); 1.34, 1.53 (both s, 3 H each, 2 Me); 1.89 (dd, 1 H, $H_bC(8)$, ^2J = 13.4, ^3J = 3.0 Hz); 2.07 (br.s, 2 H, 2 NH); 4.28 (dd, 1 H, H(7), ^3J = 3.0 and 11.9 Hz); 7.28 (m, 5 H, Ph). ^{13}C NMR ($CDCl_3$), δ: 11.2, 16.4 (CH_2CH_2); 24.3, 32.6 (2 Me); 33.2 (C(3)); 42.4 (C(8)); 54.0 (C(7)); 67.7 (C(5)); 126.6 (C_m); 127.2 (C_p); 128.5 (C_o); 144.4 (C_{ipso}). Partial MS, m/z (I_{rel} (%)): 215 $[M - H]^+$ (4), 187 (42), 158 (61), 106 (100).

5,5-Dimethyl-7-(4-fluorophenyl)-4.6-diazaspiro[2.5]octane (20b) was prepared from pyrazoline **17b** (0.63 g), yield 0.48 g (62%), colorless crystals, m.p. 74—75 °C. ^{1}H NMR ($CDCl_3$), δ: 0.35—0.74 (m, 4 H, CH_2CH_2); 1.26 (dd, 1 H, $H_aC(8)$, ^2J = 13.2 Hz, ^3J = 11.7 Hz); 1.32, 1.51 (both s, 3 H each, 2 Me); 1.57 (br.s, 2 H, 2 NH); 1.82 (dd, 1 H, $H_bC(8)$, ^2J = 13.2 Hz, ^3J = 3.0 Hz); 4.23 (dd, 1 H, H(7), ^3J = 3.0 and 11.7 Hz); 7.02, 7.32 (both m, 2 H each, C_6H_4F). ^{13}C NMR ($CDCl_3$), δ: 11.2, 16.4 (CH_2CH_2); 24.3, 33.1 (2 Me); 32.6 (C(3)); 42.5 (C(8)); 53.4 (C(7)); 67.7 (C(5)); 115.2 (d, C_m, J = 21.2 Hz); 128.2 (d, C_o, J = 7.9 Hz); 140.2 (C_{ipso}); 161.9 (d, C_p, J = 241 Hz). Partial MS, m/z (I_{rel} (%)): 234 $[M]^+$ (4), 221 (23), 177 (28), 165 (100).

Reduction of phenylpyrazoline 17a with sodium in ethanol. Sodium (1.8 g, 80 mmol) was added in small portions over a period of 20 min to a boiling solution of pyrazoline **17a** (0.34 g, 2 mmol) in ethanol (50 mL). After completion of the reaction, the mixture was cooled to 20 °C, water (50 mL) was added, and the mixture was extracted with CH_2Cl_2 (50 mL). The solution was dried with anhydrous Na_2SO_4 and the solvent was evaporated *in vacuo*. According to ^{1}H NMR data, the residue (0.34 g) contained 6-phenyl-4,5-diazaspiro[2.4]heptane (**18a**) and 3(5)-phenyl-5(3)-ethylpyrazole (**22**) in ~(4 : 1) ratio as the major identified products (overall content ~80%). Compound **22** was identified by comparison with an authentic sample.[13] **Compound 18a.** ^{1}H NMR ($CDCl_3$), δ: 0.72, 0.91 (both m, 2H each, CH_2CH_2); 2.12 (dd, 1 H, $H_aC(7)$, ^2J = 12.5 Hz, ^3J = 6.5 Hz); 2.48 (dd, 1 H, $H_bC(7)$, ^2J = 12.5 Hz, ^3J = 8.7 Hz); 3.90 (br.s, 2 H, NH—NH); 4.52 (dd, 1 H, H(6), ^3J = 6.5 and 8.7 Hz); 7.22—7.52 (m, 5 H, Ph). ^{13}C NMR ($CDCl_3$), δ: 10.7, 12.7 (CH_2CH_2); 43.9 (C(7)); 45.9 (C(3)); 66.5 (C(6)); 126.8 (C_m); 127.3 (C_p); 128.7 (C_o); 142.7 (C_{ipso}).

3-Phenyl-3-ethoxy-5-ethyl-3*H*-pyrazole (23). Petroleum ether (b.p. 40—70 °C) (5 mL) and freshly distilled acetaldehyde (0.075 g, 1.7 mmol) were added to the reaction mixture (0.24 g) obtained in the previous experiment and containing ~60% pyrazolidine **18a**, and the mixture was refluxed until the starting pyrazoline disappeared (TLC, Silufol, $CHCl_3$—MeOH, 4 : 1, as the eluent). After 2 h, the reaction mixture was cooled and the solvent was evaporated *in vacuo* at 20 °C. Vacuum microdistillation of the residue (bath temperature 140 °C, 0.15 Torr) gave 0.065 g of a yellowish liquid, containing, according to ^{1}H NMR data, ~90% pyrazole **23** (yield ~50%). ^{1}H NMR ($CDCl_3$), δ: 1.29 (t, 3 H, Me, J = 7.6 Hz); 1.38 (t, 3 H, Me, J = 7.3 Hz); 2.69 (q, 2 H, CH_2, J = 7.6 Hz); 4.09 (q, 2 H, OCH_2, J = 7.3 Hz); 6.08 (s, H(4)); 7.32—7.48 (m, 5 H, Ph). ^{13}C NMR ($CDCl_3$), δ: 14.0, 15.9 (2 Me); 21.5 (CH_2); 44.1 (OCH_2); 104.1

(C(4)); 128.2, 128.6, 128.7, 131.3 (Ph); 143.7 (C(3)); 153.8 (C(5)). Partial MS, m/z (I_{rel} (%)): 216 $[M]^+$ (3), 200 (68), 172 (74), 77 (100).

Preparation of diammonium salts 21a,b. A 4 *M* solution of HCl in dioxane (1 mL) was added in one portion to a solution of hexahydropyrimidine **20a** or **20b** (1.6 mmol) in dioxane (1 mL), and, after 15 min, the solvent was evaporated *in vacuo*. The residue was dissolved in water, the solution was washed with CH_2Cl_2, and water was evaporated *in vacuo*.

1-(2-Amino-2-phenylethyl)cyclopropylamine dihydrochloride (21a). Yield 73%, m.p. 267—268 °C. Found (%): C, 52.73; H, 7.49; Cl, 11.46; N, 28.30. $C_{11}H_{18}Cl_2N_2$. Calculated (%): C, 53.07; H, 7.28; Cl, 11.24; N, 28.46. ^{1}H NMR (DMSO-d_6), δ: 0.19, 0.89, 1.16 (all m, 1 + 2 + 1 H, CH_2CH_2); 2.07 (dd, 1 H, ^2J = 15.5 Hz, ^3J = 8.9 Hz) and 2.31 (dd, 1 H, CH_2, ^2J = 15.5 Hz, ^3J = 6.1 Hz); 4.80 (dd, 1 H, HC, ^3J = 6.1 and 8.9 Hz); 7.41, 7.69 (both m, 2 + 3 H, Ph); 8.84 (br.s, 6 H, 2 H_3N^+). ^{13}C NMR (DMSO-d_6), δ: 8.4, 9.6 (CH_2CH_2); 23.4 (C); 30.0 (CH_2); 50.6 (CH); 127.0 (C_o); 128.1 (C_p); 128.2 (C_m); 161.6 (C_{ipso}).

1-[2-Amino-2-(4-fluorophenyl)ethyl]cyclopropylamine dihydrochloride (21b). Yield 93%, colorless crystal, m.p. 141—142 °C. Found (%): C, 49.31; H, 6.32; Cl, 26.37; N, 10.30. $C_{11}H_{17}Cl_2FN_2$. Calculated (%): C, 49.45; H, 6.41; Cl, 26.54; N, 10.49. ^{1}H NMR (DMSO-d_6), δ: 0.19, 0.89, 1.04 (all m, 1 + 2 + 1 H, CH_2CH_2); 2.21 (m, 2 H, CH_2); 4.81 (m, 1 H, HC); 7.71, 7.39 (both m, 2H each, C_6H_4F); 8.71 (br.s, 6 H, 2 H_3N^+). ^{13}C NMR (DMSO-d_6), δ: 8.4, 9.5 (CH_2CH_2); 25.0 (C); 30.0 (CH_2); 49.8 (CH); 115.1 (d, C_m, J = 21.5 Hz); 129.3 (d, C_o, J = 8.4 Hz); 134.0 (C_{ipso}); 161.6 (d, C_p, J = 245 Hz).

1-(2-Amino-2-phenylethyl)cyclopropylamine (19a). A 10% aqueous solution of NaOH (1.5 mL) was added to a solution of salt **21a** (0.30 g, 1.2 mmol) in water (1 mL), and the mixture was stirred for 5 min and extracted with CH_2Cl_2 (3 mL). The organic layer was separated and dried with anhydrous Na_2SO_4, and the solvent was evaporated *in vacuo* to give 0.21 g (98%) of diamine **19a** as a slightly yellowish thick liquid. Found (%): C, 74.71; H, 9.03; N, 15.62. $C_{11}H_{16}N_2$. Calculated (%): C, 74.96; H, 9.15; N, 15.89. ^{1}H NMR ($CDCl_3$), δ: 0.27, 0.52 (both m, 1 + 3 H, CH_2CH_2); 1.79 (br.d, 2 H, CH_2, $J \approx$ 7.0 Hz); 2.20 (br.s, 4 H, 2 NH_2); 4.23 (br.t, 1 H, CH, $J \approx$ 7.0 Hz); 7.28 (m, 5 H, Ph). ^{13}C NMR ($CDCl_3$), δ: 14.2, 15.3 (CH_2CH_2); 33.0 (C); 49.4 (CH_2); 55.1 (CH); 126.3 (C_o); 127.1 (C_p); 128.6 (C_m); 147.0 (C_{ipso}).

1-[2-Amino-2-(4-fluorophenyl)ethyl]cyclopropylamine (19b). A similar procedure starting from salt **21b** (55 mg, 0.21 mmol) gave diamine **19b** (38 mg, 98%) as a yellowish thick liquid. ^{1}H NMR ($CDCl_3$), δ: 0.26, 0.52 (both m, 1 + 3 H, CH_2CH_2); 1.70 (dd, 1 H, CH_2, ^2J = 14.0 Hz, ^3J = 8.1 Hz); 1.74 (dd, 1 H, CH_2, ^2J = 14.0 Hz, ^3J = 5.9 Hz); 1.82 (br.s, 4 H, 2 NH_2); 4.26 (dd, 1 H, CH, ^3J = 5.9 and 8.1 Hz); 7.01, 7.34 (both m, 2 H each, C_6H_4F). ^{13}C NMR ($CDCl_3$), δ: 14.1, 15.2 (CH_2CH_2); 32.7 (C), 49.4 (CH_2); 54.3 (CH); 115.2 (d, C_m, J = 21.1 Hz); 127.8 (d, C_o, J = 7.9 Hz); 142.5 (C_{ipso}); 161.8 (d, C_p, J = 245).

***N*-[1-(2-Acetylamino-2-phenylethyl)cyclopropyl]acetamide (25).** Acetic anhydride (0.054 g, 0.5 mmol) was added to a solution of hexahydropyrimidine **20a** (0.055 g, 0.25 mmol) in anhydrous ether (4 mL). The reaction mixture was kept for 72 h at 20 °C. The precipitate was filtered off and washed with cooled ether (1 mL) to give 0.040 g (62%) of bisacetamide **25**, m.p. 208—209 °C. Found (%): C, 69.41; H, 7.83; N, 10.60. $C_{15}H_{20}N_2O_2$. Calculated (%): C, 69.20; H, 7.74; N, 10.76. ^{1}H NMR ($CDCl_3$), δ: 0.65, 0.79 (both m, 2H each, CH_2CH_2); 1.53 (dd, 1 H, H_a from CH_2, ^2J = 14.4 Hz, ^3J = 10.5 Hz); 1.82, 2.04 (both s, 3 H each, 2 Me); 2.40 (dd, 1 H, H_b from CH_2, ^2J = 14.4 Hz, ^3J = 4.3 Hz); 5.20 (ddd, 1 H, CH, ^3J = 4.3 and 10.5 Hz, $^3J_{HCNH}$ = 9.0 Hz); 6.21 (br.d, 1 H, NH, ^3J = 9.0 Hz); 6.62 (br.s, 1 H, NH); 7.28 (m, 5 H, Ph). ^{13}C NMR ($CDCl_3$), δ: 13.0, 13.4 (CH_2CH_2); 23.5, 23.6 (2 Me); 30.4 (C); 41.5 (CH_2); 51.3 (CH); 126.6 (C_m); 127.6 (C_o); 128.8 (C_p); 141.6 (C_{ipso}); 170.3, 177.0 (2 CO). Partial MS, m/z (I_{rel} (%)): 260 $[M]^+$ (0.4), 217 $[M - Ac]^+$ (12), 106 (100).

1,2′-Bis(ethoxyoxalylamino)-1-[2′-(4″-fluorophenyl)ethyl]cyclopropane (26). Triethylamine (0.10 g, 1.0 mmol) and diethyl oxalate (0.13 g, 1.3 mmol) were added successively to a suspension of salt **19b** (0.115 g, 0.43 mmol) in CH_2Cl_2 (5 mL), and the reaction mixture was kept for 72 h at 20 °C. The solvent and excess diethyl oxalate was removed *in vacuo* and the residue was chromatographed on a column with SiO_2 (ether—AcOEt, 1 : 1, as the eluent) to give 0.094 g (59%) of compound **26** as a resinous beige-colored liquid. Found (%): C, 57.54; H, 5.59; N, 6.93. $C_{17}H_{23}FN_2O_6$. Calculated (%): C, 57.86; H, 5.88; N, 7.10. ^{1}H NMR ($CDCl_3$), δ: 0.81, 0.92 (both m, 2H each, CH_2CH_2); 1.38 (q, 6 H, 2 Me, ^3J = 7.0 Hz); 1.71 (dd, 1 H, H_a from CH_2, ^2J = 14.3 Hz, ^3J = 9.6 Hz); 2.50 (dd, 1 H, H_b from CH_2, ^2J = 14.3 Hz, ^3J = 4.9 Hz); 4.32 (m, 4 H, 2 OCH_2); 5.18 (ddd, 1 H, CH, ^3J = 4.9 and 9.6 Hz, $^3J_{HCNH}$ = 8.6 Hz); 7.02, 7.29 (both m, 2H each, Ph); 7.52 (br.d, 1 H, NH, ^3J = 8.6 Hz); 7.79 (br.s, 1 H, NH). ^{13}C NMR ($CDCl_3$), δ: 12.9, 13.4 (2 Me); 14.0 (CH_2CH_2); 30.8 (C); 40.7 (CH_2); 51.5 (CH); 63.2, 63.5 (2 OCH_2); 115.8 (d, C_m, J = 21.6 Hz); 128.5 (d, C_o, J = 8.2 Hz); 135.8 (C_{ipso}); 159.9 (d, C_p, J = 246 Hz); 160.4, 164.3 (2 CO). Partial MS, m/z (I_{rel} (%)): 394 $[M]^+$ (0.2), 321 $[M - CO_2Et]^+$ (7), 224 (100).

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