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Synthesis of 4,5-Dihydroisoxazoles from *N*-Nitroso-4,5-dihydropyrazoles

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Abstract—*N*-Nitroso-4,5-dihydropyrazoles obtained from ethyl(methyl) 5-aryl-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrazole-3-carboxylates and ethyl(methyl) 7-aryl-6,8-dioxo-1,2,7-triazaspiro[4.4]non-2-ene-3-carboxylates eliminate nitrogen molecule on heating to afford the corresponding 4,5-dihydroisoxazole derivatives.

We previously showed that 4,5-dihydropyrazoles incorporated into a bicyclic or spirocyclic system react with electrophilic halogenating agents to give the corresponding halodihydropyrazoles which eliminate nitrogen molecule on heating with formation of substituted halocyclopropanes [1].

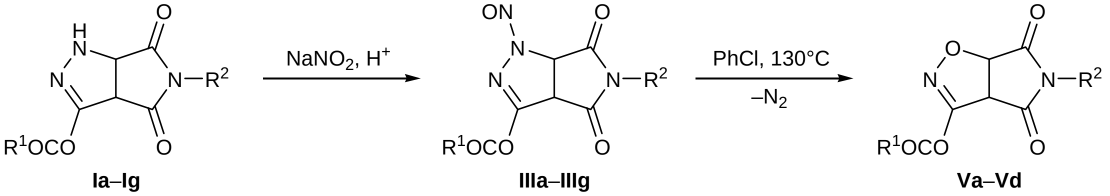
We now report that nitrosation of dihydropyrazole derivatives **Ia**–**Ig** using the system $NaNO_2$–H_2SO_4–CH_2Cl_2 with addition of ethanol or $NaNO_2$–CH_3COOH [2] as a source of nitrosonium cation leads to formation of ethyl 5-aryl-1-nitroso-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrazole-3-carboxylates **IIIa**–**IIIg** (Scheme 1) in up to 90% yield. The structure of compounds **IIIa**–**IIIg** was confirmed by spectral data and elemental analyses. Their IR spectra contained absorption bands at 1460 (N=O) and 1720 cm^{-1} (C=O). In the ^1H NMR spectra of **IIIa**–**IIIg**, we observed doublet signals from the 3a-H and 6a-H protons at δ 4.8 and 5.9 ppm, respectively (*J* = 10 Hz), as well as signals from aromatic protons and protons of the ester group. The 6a-H signal in the spectra of **IIIa**–**IIIg** is located in a considerably weaker field than the corresponding signal of initial esters **Ia**–**Ig** (δ ~5.1 ppm) due to deshielding effect of the nitroso group.

Nitrosation of spiro dihydropyrazoles **IIa**–**IIe** under analogous conditions afforded up to 80% of ethyl 7-aryl-1-nitroso-6,8-dioxo-1,2,7-triazaspiro[4.4]non-2-ene-3-carboxylates **IVa**–**IVe** (Scheme 2) which showed in the IR spectra absorption bands at 1470 (N=O) and 1720 cm^{-1} (C=O). In the ^1H NMR spectra of esters **IVa**–**IVe**, signals from the methylene protons in the dihydropyrazole ring appeared as doublets at δ 3.4 and 3.9 ppm (*J* = 19 Hz), and methylene protons in the pyrrolidine ring gave rise to doublets at δ 3.0 and 3.3 ppm (*J* = 19 Hz). The ^{13}C NMR spectra of **IVa** and **IVc** contained a signal at δ_C 68 ppm from the spiro carbon atom.

There are almost no published data on thermolysis of *N*-nitrosodihydropyrazoles. Nagarajan and Rajagopalan reported [3] that heating of *N*-nitrosodihydropyrazole obtained by cycloaddition of diazomethane to benzonitrile oxide leads to its transformation into the corresponding dihydroisoxazole in 10 to 35% yield, depending on the reaction conditions.

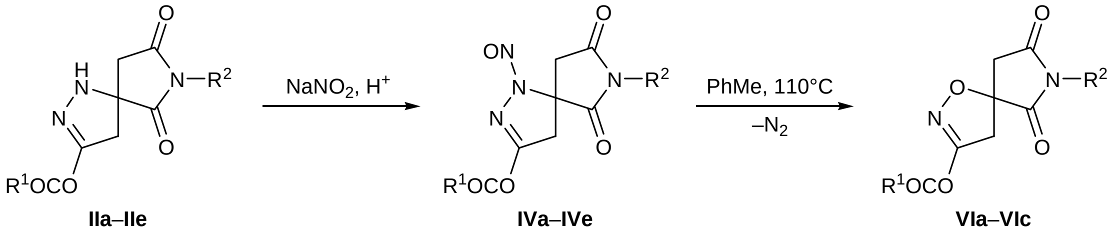
We performed thermolysis of *N*-nitrosodihydropyrazoles **IIIa**, **IIIb**, **IIId**, **IIIf**, and **IVb**–**IVd** by heating under reduced pressure at a temperature

Scheme 1.



I, **III**, R^1 = Et, R^2 = C_6H_5 (**a**), 3-$MeOC_6H_4$ (**b**), 4-$MeOC_6H_4$ (**c**), 4-BrC_6H_4 (**d**), 2,4,6-$Me_3C_6H_2$ (**e**), 4-EtC_6H_4 (**f**); R^1 = Me, R^2 = 4-MeC_6H_4 (**g**); **V**, R^1 = Et, R^2 = C_6H_5 (**a**), 4-$MeOC_6H_4$ (**b**), 4-BrC_6H_4 (**c**), 4-EtC_6H_4 (**d**).

Scheme 2.



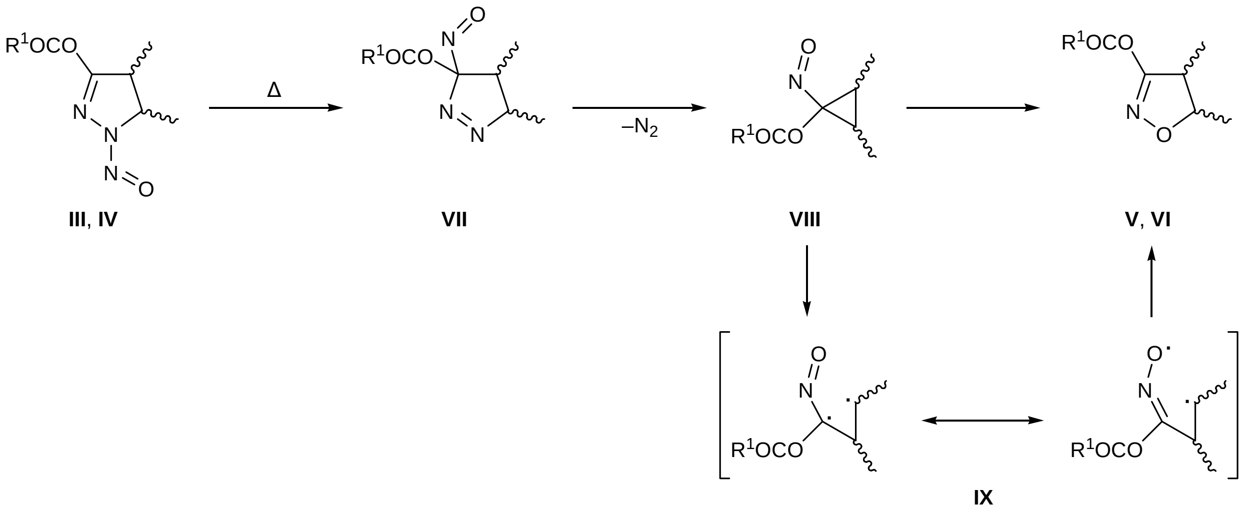
II, **IV**, R^1 = Et, R^2 = 3-MeOC$_6$H$_4$ (**a**), 3-BrC$_6$H$_4$ (**b**), 3,4-Cl$_2$C$_6$H$_3$ (**c**); R^1 = Me, R^2 = 4-ClC$_6$H$_4$ (**d**), 3,4-Me$_2$C$_6$H$_3$ (**e**);
VI, R^1 = Et, R^2 = 3,4-Cl$_2$C$_6$H$_3$ (**a**); R^1 = Me, R^2 = 4-ClC$_6$H$_4$ (**b**), 3,4-Me$_2$C$_6$H$_3$ (**c**).

approaching the melting point or by heating in boiling chlorobenzene or toluene. In all cases, the yield of the target product was greater when the thermolysis was carried out in a solvent. From compounds **IIIa**, **IIIc**, **IIId**, and **IIIf** we obtained ethyl 5-aryl-4,6-dioxo-4,5,6,6a-tetrahydro-3a*H*-pyrrolo[3,4-*d*]isoxazole-3-carboxylates **Va**–**Vd** (Scheme 1) in up to 70% yield. Analysis of the reaction mixtures by ^{1}H NMR spectroscopy showed that they contained about 90% of dihydroisoxazoles **Va**–**Vd**; however, the subsequent purification by recrystallization was accompanied by an appreciable loss of the target product. We failed to improve the yield by chromatographic isolation due to partial decomposition of compounds **Va**–**Vd**. The IR spectra of **Va**–**Vd** contained a carbonyl stretching vibration band at 1720 cm^{-1}. The 3a-H and 6a-H signals appeared in the ^{1}H NMR spectra as doublets at δ 4.9 and 5.7 ppm, respectively (J = 10 Hz). The signals from C^{3a} and C^{6a} in the ^{13}C NMR spectrum of **Vd** were observed at δ_C 54 and 83 ppm, respectively.

Thermolysis of esters **IVc**–**IVe** gave ethyl(methyl) 7-aryl-6,8-dioxo-1-oxa-2,7-diazaspiro[4.4]non-2-ene-3-carboxylates **VIa**–**VIc** (Scheme 2) which were isolated in up to 60% yield. According to spectral data, initial nitrosodihydropyrazoles **IVc**–**IVe** were converted into dihydroisoxazole derivatives **VIa**–**VIc** almost completely (85–90%); however, as in the previous case, the target product was partially lost during chromatographic isolation. The ^{1}H NMR spectra of **VIa**–**VIc** contained doublet signals from the methylene protons in the dihydroisoxazole (δ 3.4, 4.0 ppm; J = 19 Hz) and pyrrolidine rings (δ 3.1, 3.4 ppm; J = 19 Hz). In the ^{13}C NMR spectrum of ester **VIa**, the C^5 signal was located at δ_C 86 ppm.

Two alternative mechanisms for the formation of dihydroisoxazoles from *N*-nitrosodihydropyrazoles were proposed in [3]. The first of these involves intermediate formation of dihydrooxatriazepine, followed by ring contraction via elimination of nitrogen. The second mechanism is based on homolytic cleavage of the N–N bond with formation of nitrosyl radical which then adds at the C=N bond to give 1-nitroso-4,5-dihydro-3*H*-pyrazole; elimination of nitrogen molecule from the latter leads to the final product. On the other

Scheme 3.



hand, it is known that nitrosyl chloride adds to R,R-disubstituted cyclopropenecarboxylates, yielding nitrosocyclopropane dimer (R = *n*-Pr) or substituted 4,5-dihydroisoxazole (R = Ph). In the latter case, the reaction is likely to involve formation of unstable nitrosocyclopropane [4]. We believe that the reaction under study also occurs through the corresponding intermediate nitrosocyclopropane **VIII** which undergoes rearrangement in a way similar to the azacyclopropane–dihydropyrazole rearrangement [5] (Scheme 3).

EXPERIMENTAL

The IR spectra were obtained on a UR-20 spectrometer from 2% solutions in chloroform. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX-300 instrument at 300.13 and 75.47 MHz, respectively, using $CDCl_3$, DMCO-d_6, or acetone-d_6 as solvent. The purity of the products was checked, and the reaction mixtures were analyzed, by thin-layer chromatography on Silufol UV-254 plates.

Ethyl(methyl) 5-aryl-1-nitroso-4,6-dioxo-1,3a,-4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrazole-3-carboxylates IIIa–IIIg and ethyl(methyl) 7-aryl-1-nitroso-6,8-dioxo-1,2,7-triazaspiro[4.4]non-2-ene-3-carboxylates IVa–IVe. *a.* Concentrated sulfuric acid was added dropwise under vigorous stirring at room temperature to a mixture of 1 g of ester **Ia**–**Ig** or **IIa**–**IIe**, 15–20 drops of ethanol, and 1 g of sodium nitrite in 40–60 ml of methylene chloride until the solution turned light green (TLC). The mixture was washed with two portions of a 10% solution of sodium carbonate, the organic phase was separated and dried over $MgSO_4$, the solvent was evaporated, and the residue was recrystallized from methanol.

b. Sodium nitrite, 1 g, was added in small portions over a period of 20 min to a solution of 1 g of ester **Ia**–**Ig** or **IIa**–**IIe** in glacial acetic acid under stirring at room temperature. The mixture was stirred for an additional 20 min and poured into cold water. The precipitate was filtered off, washed with a 10% solution of sodium carbonate and with water, and recrystallized from methanol.

Ethyl 1-nitroso-4,6-dioxo-5-phenyl-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrazole-3-carboxylate (IIIa) was synthesized as described above in *a* from 1 g (3.5 mmol) of ester **Ia**. Yield 0.90 g (82%), mp 142–144°C (decomp.). IR spectrum, ν, cm^{-1}: 970, 1060, 1080, 1130, 1180 s, 1230, 1370, 1450, 1610, 1730 v.s, 3050. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 1.33 t (3H, CH_3), 4.32–4.42 m (2H, CH_2O), 4.82 d (1H, CH, *J* = 10), 5.91 d (1H, CH, *J* = 10), 7.29–7.51 m (5H, C_6H_5). Found, %: C 53.28; H 3.98; N 17.59. $C_{14}H_{12}N_4O_5$. Calculated, %: C 53.17; H 3.82; N 17.71.

Ethyl 5-(3-methoxyphenyl)-1-nitroso-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrazole-3-carboxylate (IIIb) was synthesized as described above in *b* from 1 g (3.1 mmol) of ester **Ib**. Yield 0.76 g (69%), mp 133–135°C (decomp.). IR spectrum, ν, cm^{-1}: 970, 1060, 1080, 1130, 1170 s, 1370, 1460, 1730 v.s, 3050. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 1.34 t (3H, CH_3), 3.74 s (3H, CH_3O), 4.33–4.41 m (2H, CH_2O), 4.85 d (1H, CH, *J* = 10), 5.91 d (1H, CH, *J* = 10), 6.86 d (1H, H_{arom}, *J* 8), 6.92 t (1H, H_{arom}, *J* = 2), 7.03 d.d (1H, H_{arom}, *J* = 8, 2), 7.38 t (1H, H_{arom}, *J* = 8). Found, %: C 52.05; H 4.09; N 16.12. $C_{15}H_{14}N_4O_6$. Calculated, %: C 52.03; H 4.07; N 16.18.

Ethyl 5-(4-methoxyphenyl)-1-nitroso-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrazole-3-carboxylate (IIIc) was synthesized as described above in *a* from 1.1 g (3.5 mmol) of ester **Ic**. Yield 1.09 g (90%), mp 148–150°C (decomp.). IR spectrum, ν, cm^{-1}: 950, 1050, 1080, 1120, 1170 s, 1370, 1460, 1730 v.s, 3050. ^{1}H NMR spectrum (acetone-d_6), δ, ppm (*J*, Hz): 0.88 t (3H, CH_3), 3.28 s (3H, CH_3O), 3.87–3.96 m (2H, CH_2O), 4.54 d (1H, CH, *J* = 10), 5.52 d (1H, CH, *J* = 10), 6.42 d (2H, C_6H_4, *J* = 8), 6.65 d (2H, C_6H_4, *J* = 8). Found, %: C 51.97; H 4.14; N 16.21. $C_{15}H_{14}N_4O_6$. Calculated, %: C 52.03; H 4.07; N 16.18.

Ethyl 5-(4-bromophenyl)-1-nitroso-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrazole-3-carboxylate (IIId) was synthesized as described above in *a* from 1 g (2.7 mmol) of ester **Id**. Yield 0.96 g (89%), mp 155–157°C (decomp.). IR spectrum, ν, cm^{-1}: 960, 1050, 1090, 1120, 1170 s, 1390, 1460, 1720 v.s, 3050. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 1.34 t (3H, CH_3), 4.33–4.42 m (2H, CH_2O), 4.84 d (1H, CH, *J* = 10), 5.89 d (1H, CH, *J* = 10), 7.28 d (2H, C_6H_4, *J* = 10), 7.70 d (2H, C_6H_4, *J* = 10). Found, %: C 42.65; H 3.01; N 14.05. $C_{14}H_{11}BrN_4O_5$. Calculated, %: C 42.55; H 2.81; N 14.18.

Ethyl 1-nitroso-4,6-dioxo-5-(2,4,6-trimethylphenyl)-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrazole-3-carboxylate (IIIe) was synthesized as described above in *a* from 1 g (3 mmol) of ester **IIIe**. Yield 0.77 g (71%), mp 107–108°C (decomp.). IR spectrum, ν, cm^{-1}: 950, 1040, 1080, 1100, 1130, 1180 s, 1240, 1390, 1470, 1610, 1730 v.s, 3050. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 1.33 t (3H, CH_3, *J* = 7), 1.72 s (3H, CH_3), 2.07 s (3H, CH_3), 2.25 s (3H, CH_3), 4.37–4.43 m (2H, CH_2O), 5.07 d (1H, CH, J = 10), 6.05 d (1H, CH, J = 10), 6.95 s (1H, H_{arom}), 6.99 s (1H, H_{arom}). Found, %: C 56.81; H 4.99; N 15.64. $C_{17}H_{18}N_4O_5$. Calculated, %: C 56.98; H 5.06; N 15.63.

Ethyl 5-(4-ethylphenyl)-1-nitroso-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrazole-3-carboxylate (IIIf) was synthesized as described above in *b* from 1 g (3.2 mmol) of ester **IIIf**. Yield 0.95 g (87%), mp 135–137°C (decomp.). IR spectrum, ν, cm^{-1}: 960, 1060, 1080, 1110, 1130, 1180 s, 1230, 1370, 1460, 1610, 1730 v.s, 3050. ^1H NMR spectrum (DMSO-d_6), δ, ppm (J, Hz): 1.19 t (3H, CH_3), 1.34 t (3H, CH_3), 2.64 q (2H, $C\mathbf{H}_2CH_3$, J = 7), 4.36–4.42 m (2H, $CH_3C\mathbf{H}_2O$), 4.84 d (1H, CH, J = 10), 5.89 d (1H, CH, J = 10), 7.19 d (2H, C_6H_4, J = 8), 7.30 d (2H, C_6H_4, J = 8). Found, %: C 55.78; H 4.52; N 16.11. $C_{16}H_{16}N_4O_5$. Calculated, %: C 55.81; H 4.68; N 16.27.

Methyl 5-(4-methylphenyl)-1-nitroso-4,6-dioxo-1,3a,4,5,6,6a-hexahydropyrrolo[3,4-*c*]pyrazole-3-carboxylate (IIIg) was synthesized as described above in *b* from 1 g (3.5 mmol) of ester **Ig**. Yield 0.84 g (77%), mp 148–150°C (decomp.). IR spectrum, ν, cm^{-1}: 950, 1050, 1080, 1110, 1130, 1180 s, 1230, 1390, 1460, 1610, 1730 v.s, 3050. ^1H NMR spectrum (DMSO-d_6), δ, ppm (J, Hz): 2.33 s (3H, CH_3), 3.93 s (3H, CH_3O), 4.83 d (1H, CH, J = 10), 5.89 d (1H, CH, J = 10), 7.17 d (2H, C_6H_4, J = 8), 7.27 d (2H, C_6H_4, J = 8). Found, %: C 53.18; H 3.71; N 17.83. $C_{14}H_{12}N_4O_5$. Calculated, %: C 53.17; H 3.82; N 17.71.

Ethyl 7-(3-methoxyphenyl)-1-nitroso-6,8-dioxo-1,2,7-triazaspiro[4.4]non-2-ene-3-carboxylate (IVa) was synthesized as described above in *a* from 0.96 g (2.9 mmol) of ester **IIa**. Yield 0.64 g (61%), mp 119–120°C (decomp.). IR spectrum, ν, cm^{-1}: 890, 950, 1050, 1080, 1110, 1120, 1170 s, 1390, 1470, 1720 v.s, 3050. ^1H NMR spectrum ($CDCl_3$), δ, ppm (J, Hz): 1.45 t (3H, CH_3, J = 7), 2.93 d (1H, CH_2, J = 19), 3.24 d (1H, CH_2, J = 19), 3.38 d (1H, CH_2, J = 19), 3.83 d (1H, CH_2, J = 19), 3.85 s (3H, CH_3O), 4.49 q (2H, $CH_3C\mathbf{H}_2O$, J = 7), 6.89 t (1H, H_{arom}, J = 2), 6.95 d (1H, H_{arom}, J 8), 7.01 d.d (1H, H_{arom}, J = 8, 2), 7.43 t (1H, H_{arom}, J = 8). ^{13}C NMR spectrum, δ_C, ppm: 14.5 (CH_3); 40.59 (C^4); 45.1 (C^9); 55.9 (CH_3O); 63.7 ($CH_3\mathbf{C}H_2O$); 68.0 (C^5); 112.6, 115.7, 119.0, 130.6, 132.6, 160.4 (C_{arom}); 153.0 (C=N); 160.7, 171.2, 171.3 (C=O). Found, %: C 53.19; H 4.43; N 15.61. $C_{16}H_{16}N_4O_6$. Calculated, %: C 53.33; H 4.48; N 15.55.

Ethyl 7-(3-bromophenyl)-1-nitroso-6,8-dioxo-1,2,7-triazaspiro[4.4]non-2-ene-3-carboxylate (IVb) was synthesized as described above in *b* from 0.72 g (1.9 mmol) of ester **IIb**. Yield 0.56 g (72%), mp 106–107°C (decomp.). IR spectrum, ν, cm^{-1}: 970, 1050, 1110, 1120, 1180 s, 1400, 1470, 1720 v.s, 3050. ^1H NMR spectrum ($CDCl_3$), δ, ppm (J, Hz): 1.46 t (3H, CH_3, J = 7), 2.97 d (1H, CH_2, J = 19), 3.27 d (1H, CH_2, J = 19), 3.41 d (1H, CH_2, J = 19), 3.86 d (1H, CH_2, J = 19), 4.49 q (2H, $CH_3C\mathbf{H}_2O$, J = 7), 7.34–7.56 m (4H, C_6H_4). Found, %: C 44.09; H 3.14; N 13.52. $C_{15}H_{13}BrN_4O_5$. Calculated, %: C 44.03; H 3.20; N 13.69.

Ethyl 7-(3,4-dichlorophenyl)-1-nitroso-6,8-dioxo-1,2,7-triazaspiro[4.4]non-2-ene-3-carboxylate (IVc) was synthesized as described above in *a* from 1 g (2.7 mmol) of ester **IIc**. Yield 0.80 g (74%), mp 141–143°C (decomp.). IR spectrum, ν, cm^{-1}: 950, 1040, 1100, 1120, 1180 s, 1390, 1470, 1730 v.s, 3050. ^1H NMR spectrum ($CDCl_3$), δ, ppm (J, Hz): 1.45 t (3H, CH_3, J = 7), 2.97 d (1H, CH_2, J = 19), 3.26 d (1H, CH_2, J = 19), 3.41 d (1H, CH_2, J = 19), 3.85 d (1H, CH_2, J = 19), 4.50 q (2H, $CH_3C\mathbf{H}_2O$, J = 7), 7.27 d.d (1H, H_{arom}, J = 8, 2), 7.53 d (1H, H_{arom}, J = 2), 7.61 d (1H, H_{arom}, J = 8). ^{13}C NMR spectrum, δ_C, ppm: 14.5 (CH_3); 40.57 (C^4); 45.1 (C^9); 63.8 ($CH_3\mathbf{C}H_2O$); 67.8 (C^5); 126.0, 128.7, 130.7, 131.5, 133.8, 134.2 (C_{arom}); 153.1 (C=N); 160.3, 170.5, 170.8 (C=O). Found, %: C 44.99; H 3.04; N 13.92. $C_{15}H_{12}Cl_2N_4O_5$. Calculated, %: C 45.13; H 3.03; N 14.04.

Methyl 7-(4-chlorophenyl)-1-nitroso-6,8-dioxo-1,2,7-triazaspiro[4.4]non-2-ene-3-carboxylate (IVd) was synthesized as described above in *a* from 1 g (3.1 mmol) of ester **IId**. Yield 0.87 g (80%), mp 168–170°C (decomp.). IR spectrum, ν, cm^{-1}: 1100, 1120, 1180 s, 1390, 1470, 1500, 1730 v.s, 3050. ^1H NMR spectrum (acetone-d_6), δ, ppm (J, Hz): 3.86 d (1H, CH_2, J = 19), 3.94 d (1H, CH_2, J = 19), 4.34 d (1H, CH_2, J = 19), 4.47 d (1H, CH_2, J = 19), 4.56 s (3H, CH_3O), 7.97 d (2H, C_6H_4, J = 8), 8.12 d (2H, C_6H_4, J = 8). Found, %: C 47.81; H 3.05; N 15.79. $C_{14}H_{11}ClN_4O_5$. Calculated, %: C 47.95; H 3.16; N 15.97.

Methyl 7-(3,4-dimethoxyphenyl)-1-nitroso-6,8-dioxo-1,2,7-triazaspiro[4.4]non-2-ene-3-carboxylate (IVe) was synthesized as described above in *b* from 1 g (3.2 mmol) of ester **IIe**. Yield 0.68 g (62%), mp 144–146°C (decomp.). IR spectrum, ν, cm^{-1}: 890, 950, 1050, 1100, 1120, 1180 s, 1390, 1470, 1720 v.s, 3050. ^1H NMR spectrum ($CDCl_3$), δ, ppm (J, Hz): 2.32 s (3H, CH_3), 2.33 s (3H, CH_3), 2.93 d (1H, CH_2, J = 19), 3.23 d (1H, CH_2, J = 19), 3.38 d (1H, CH_2, J = 19), 3.85 d (1H, CH_2, *J* = 19), 4.02 s (3H, CH_3O), 7.09 d.d (1H, H_{arom}, *J* = 8, 2), 7.12 d (1H, H_{arom}, *J* = 2), 7.28 d (1H, H_{arom}, *J* = 8). Found, %: C 55.68; H 4.71; N 16.12. $C_{16}H_{16}N_4O_5$. Calculated, %: C 55.81; H 4.68; N 16.27.

Ethyl 5-aryl-4,6-dioxo-4,5,6,6a-tetrahydro-3a*H*-pyrrolo[3,4-*d*]isoxazole-3-carboxylates Va–Vd. *N*-Nitroso derivative **IIIa**, **IIIc**, **IIId**, or **IIIf** was heated in dry chlorobenzene for 30 min at 130°C under argon (the mixture turned dark). The solvent was distilled off under reduced pressure, the residue was crystallized from ethanol–ethyl acetate, and the precipitate was filtered off and recrystallized from ethanol–acetone.

Ethyl 4,6-dioxo-5-phenyl-4,5,6,6a-tetrahydro-3a*H*-pyrrolo[3,4-*d*]isoxazole-3-carboxylate (Va) was obtained from 2 g (6.3 mmol) of compound **IIIa** in 20 ml of chlorobenzene. Yield 1.1 g (63%), mp 187–188°C. IR spectrum, ν, cm^{-1}: 1050, 1110, 1200, 1370, 1480, 1720 v.s, 3050. ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.42 t (3H, CH_3), 4.41–4.48 m (2H, $CH_3C\mathbf{H}_2O$), 4.90 d (1H, CH, *J* = 10), 5.72 d (1H, CH, *J* = 10), 7.30–7.44 (5H, C_6H_5). Found, %: C 58.43; H 4.37; N 9.79. $C_{14}H_{12}N_2O_5$. Calculated, %: C 58.33; H 4.20; N 9.72.

Ethyl 5-(4-methoxyphenyl)-4,6-dioxo-4,5,6,6a-tetrahydro-3a*H*-pyrrolo[3,4-*d*]isoxazole-3-carboxylate (Vb) was obtained from 2 g (5.8 mmol) of compound **IIIc** in 20 ml of chlorobenzene. Yield 1.1 g (62%), mp 190–191°C. IR spectrum, ν, cm^{-1}: 1050, 1120, 1210, 1370, 1490, 1720 v.s, 3050. ^1H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 1.29 t (3H, CH_3), 3.79 s (3H, CH_3O), 4.29–3.35 m (2H, $CH_3C\mathbf{H}_2O$), 4.91 d (1H, CH, *J* = 10), 5.78 d (1H, CH, *J* = 10), 7.03 d (2H, C_6H_4, *J* = 8), 7.23 d (2H, C_6H_4, *J* = 8). Found, %: C 56.47; H 4.19; N 8.71. $C_{15}H_{14}N_2O_6$. Calculated, %: C 56.61; H 4.33; N 8.80.

Ethyl 5-(4-bromophenyl)-4,6-dioxo-4,5,6,6a-tetrahydro-3a*H*-pyrrolo[3,4-*d*]isoxazole-3-carboxylate (Vc) was obtained from 2 g (5.1 mmol) of compound **IIId** in 25 ml of chlorobenzene. Yield 1.2 g (66%), mp 167–169°C. IR spectrum, ν, cm^{-1}: 1050, 1100, 1210, 1380, 1490, 1720 v.s, 3050. ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.41 t (3H, CH_3), 4.35–4.48 m (2H, $CH_3C\mathbf{H}_2O$), 4.90 d (1H, CH, *J* = 10), 5.73 d (1H, CH, *J* = 10), 7.19 d (2H, C_6H_4, *J* = 8), 7.62 d (2H, C_6H_4, *J* = 8). Found, %: C 45.68; H 2.89; N 7.56. $C_{14}H_{11}BrN_2O_5$. Calculated, %: C 45.80; H 3.02; N 7.63.

Ethyl 5-(4-ethylphenyl)-4,6-dioxo-4,5,6,6a-tetrahydro-3a*H*-pyrrolo[3,4-*d*]isoxazole-3-carboxylate (Vd) was obtained from 1.5 g (4.3 mmol) of compound **IIIf** in 15 ml of chlorobenzene. Yield 0.96 g (70%), mp 146–147°C. IR spectrum, ν, cm^{-1}: 1040, 1100, 1200, 1380, 1480, 1720 v.s, 3050. ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.25 t (3H, CH_3), 1.40 t (3H, CH_3), 2.69 q (2H, $C\mathbf{H}_2CH_3$, *J* = 7), 4.35–4.44 m (2H, $CH_3C\mathbf{H}_2O$), 4.88 d (1H, CH, *J* = 10), 5.69 d (1H, CH, *J* = 10), 7.16 d (2H, C_6H_4, *J* = 8), 7.30 d (2H, C_6H_4, *J* = 8). ^{13}C NMR spectrum, δ_C, ppm: 14.4 (CH_3); 15.7 (CH_3); 29.0 ($CH_3\mathbf{C}H_2$); 54.2 (C^5); 63.5 ($CH_3\mathbf{C}H_2O$); 82.6 (C^1); 126.4, 128.5, 129.2, 146.1 (C_{arom}); 148.2 (C=N); 158.8, 169.0, 170.3 (C=O). Found, %: C 60.59; H 4.18; N 8.71. $C_{16}H_{16}N_2O_5$. Calculated, %: C 60.76; H 5.10; N 8.86.

Ethyl(methyl) 7-aryl-6,8-dioxo-1-oxa-2,7-diazaspiro[4.4]non-2-ene-3-carboxylates VIa–VIc. *N*-Nitroso derivative **IVc**–**IVe** was heated in 10 ml of anhydrous toluene for 40 min at 110°C under argon (the mixture turned dark). The solvent was distilled off under reduced pressure, and the residue was purified by column chromatography on silica gel using hexane–ethyl acetate (2:1, by volume) as eluent or by recrystallization from diethyl ether.

Ethyl 7-(3,4-dichlorophenyl)-6,8-dioxo-1-oxa-2,7-diazaspiro[4.4]non-2-ene-3-carboxylate (VIa) was obtained from 1 g (2.5 mmol) of compound **IVc** in 10 ml of toluene; the product was recrystallized from diethyl ether. Yield 0.51 g (55%), mp 105–106°C. IR spectrum, ν, cm^{-1}: 920, 1040, 1130, 1270, 1380, 1480, 1730 v.s, 3050. ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.40 t (3H, CH_3, *J* = 7), 3.11 d (1H, CH_2, *J* = 19), 3.35 d (1H, CH_2, *J* = 19), 3.42 d (1H, CH_2, *J* = 19), 3.95 d (1H, CH_2, *J* = 19), 4.40 q (2H, $CH_3C\mathbf{H}_2O$, *J* = 7), 7.25 d.d (1H, H_{arom}, *J* = 8, 2), 7.52 d (1H, H_{arom}, *J* = 2), 7.59 d (1H, H_{arom}, *J* = 8). ^{13}C NMR spectrum, δ_C, ppm: 14.5 (CH_3); 42.4 (C^4); 42.5 (C^9); 63.2 (CH_3CH_2O); 86.4 (C^5); 125.7, 128.4, 130.6, 131.3, 133.7, 133.9 (C_{arom}); 151.3 (C=N); 159.7, 171.2, 172.8 (C=O). Found, %: C 48.66; H 3.38; N 6.41. $C_{15}H_{12}Cl_2N_2O_5$. Calculated, %: C 48.54; H 3.38; N 6.82.

Methyl 7-(4-chlorophenyl)-6,8-dioxo-1-oxa-2,7-diazaspiro[4.4]non-2-ene-3-carboxylate (VIb) was obtained from 1 g (2.8 mmol) of compound **IVd** in 10 ml of toluene; the product was recrystallized from diethyl ether. Yield 0.57 g (63%), mp 157–158°C. IR spectrum, ν, cm^{-1}: 920, 1040, 1130, 1170, 1270, 1380, 1480, 1730 v.s, 3050. ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 3.12 d (1H, CH_2, *J* = 19), 3.37 d (1H, CH_2, *J* = 19), 3.42 d (1H, CH_2, *J* = 19), 3.95 s (3H, CH_3O), 3.97 d (1H, CH_2, *J* = 19), 7.32 d (2H, C_6H_4, *J* = 8), 7.49 d (2H, C_6H_4, *J* = 8). Found, %: C 52.27; H 3.67; N 8.45. $C_{14}H_{11}ClN_2O_5$. Calculated, %: C 52.11; H 3.44; N 8.68.

Methyl 7-(3,4-dimethylphenyl)-6,8-dioxo-1-oxa-2,7-diazaspiro[4.4]non-2-ene-3-carboxylate (VIc) was obtained from 1 g (2.9 mmol) of compound **IVe** in 10 ml of toluene; the product was isolated by column chromatography. Yield 0.50 g (54%), mp 138–139°C. IR spectrum, ν, cm^{-1}: 940, 1050, 1130, 1190, 1270, 1390, 1480, 1730 v.s, 3050. ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 2.31 s (6H, CH_3), 3.05 d (1H, CH_2, *J* = 19), 3.33 d (1H, CH_2, *J* = 19), 3.40 d (1H, CH_2, *J* = 19), 3.91 d (1H, CH_2, *J* = 19), 3.95 s (3H, CH_3O), 7.08 d.d (1H, H_{arom}, *J* = 8, 2), 7.12 d (1H, H_{arom}, *J* = 2), 7.24 d (1H, H_{arom}, *J* = 8). Found, %: C 60.71; H 4.97; N 8.82. $C_{16}H_{16}N_2O_5$. Calculated, %: C 60.76; H 5.10; N 8.86.

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