Russian Journal of Organic Chemistry, Vol. 41, No. 7, 2005, pp. 1036–1042. Translated from Zhurnal Organicheskoi Khimii, Vol. 41, No. 7, 2005, pp. 1058–1063.

Reactions of Substituted Ethyl 1,2,3,4,4',5'-Hexahydrospiro-[naphthalene-2,5'-pyrazole]-3'-carboxylates with Halogens

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Received November 3, 2004

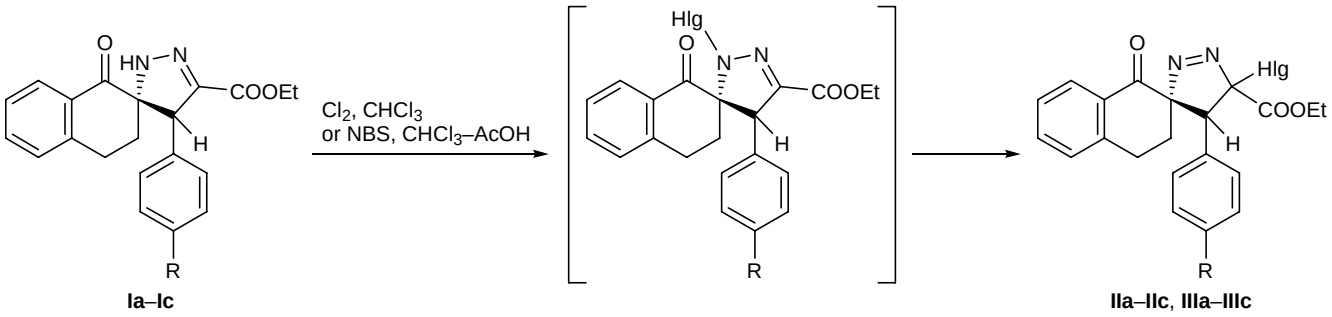
Abstract—Substituted ethyl 1,2,3,4,4',5'-hexahydrospiro[naphthalene-2,5'-pyrazole]-3'-carboxylates react with chlorine or *N*-bromosuccinimide to give spirocyclic substituted 3-halo-4,5-dihydro-3*H*-pyrazoles which lose nitrogen molecule on heating with formation of substituted spirocyclic 1-halocyclopropane-1-carboxylates. Heating of the title compounds with bromine in acetic acid results in opening of the spiro-fused six-membered ring to afford ethyl 4-aryl-5-[2-(2-carboxyphenyl)ethyl]pyrazole-3-carboxylates.

We previously showed that reactions of bi- and spirocyclic 4,5-dihydropyrazoles with halogenating agents lead to formation of substituted 3-halo-4,5-dihydro-3*H*-pyrazoles. Thermolysis of the latter is accompanied by loss of nitrogen molecule to afford substituted 1-halocyclopropanecarboxylates [1–6]. In the present work we examined reactions of ethyl 4'-aryl-1-oxo-1,2,3,4,4',5'-hexahydro-1'*H*-spiro[naphthalene-2,5'-pyrazole]-3'-carboxylates **Ia**–**Ic** with chlorine and *N*-bromosuccinimide and isolated ethyl 4'-aryl-3'-chloro-1-oxo-1,2,3,4,4',5'-hexahydro-3'*H*-spiro[naphthalene-2,5'-pyrazole]-3'-carboxylates **IIa**–**IIc** in 44–72% yield and their 3'-bromo-substituted analogs **IIIa**–**IIIc** in 45–61% yield (Scheme 1). Initial esters **Ia**–**Ic** were synthesized by reaction of ethyl diazoacetate with (*E*)-2-arylmethylidene-1,2,3,4-tetrahydronaphthalen-1-ones [7]

The structure of compounds **IIa**–**IIc** and **IIIa**–**IIIc** was determined on the basis of their spectral parameters, and satisfactory elemental analyses were also obtained for compounds **IIb** and **IIIc**. It should be noted that spirocyclic pyrazoles **IIa**–**IIc** and **IIIa**–**IIIc** slowly decompose even at room temperature. Their ^{1}H NMR spectra contained singlets from the 4'-H proton at δ 4.3–4.6 ppm, signals from aromatic protons, and signals from the ethyl and ethylene (CH_2CH_2) moieties. In the ^{13}C NMR spectrum of **IIb** we observed the following signals, δ_C, ppm: 14.1 (CH_3), 20.1 (CH_2), 31.1 (CH_2), 53.6 (CH), 64.1 (CH_2), 103.2 (C), 104.8 (C), 164.9 (CO), 190.1 (CO); also, signals from aromatic carbon atoms were present in the spectrum.

On heating to 80°C, dihydropyrazoles **IIa**–**IIc** and **IIIa**–**IIIc** lose nitrogen molecule, thus being converted into ethyl 3'-aryl-2'-halo-1-oxo-1,2,3,4-tetrahydrospiro-[naphthalene-2,1'-cyclopropane]-2'-carboxylates **IVa**–**IVc** and **Va**–**Vc** in 59–74 and 37–44% yield, respectively (Scheme 2). The structure of compounds **IVa**–

Scheme 1.



Ia–Ic **IIa–IIc**, **IIIa–IIIc**

II, Hlg = Cl; **III**, Hlg = Br; R = H (**a**), Cl (**b**), Me (**c**).

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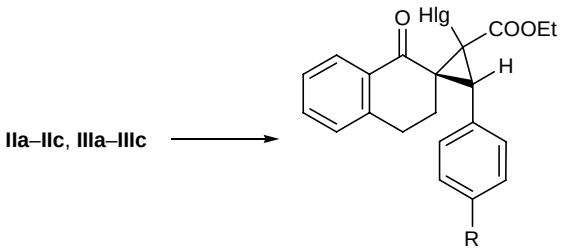
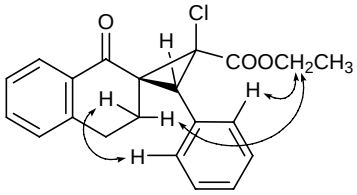
Scheme 2.



IV, Hlg = Cl; **V**, Hlg = Br; R = H (**a**), Cl (**b**), Me (**c**).

IVc and **Va**–**Vc** was confirmed by spectral methods and elemental analysis. The ^{1}H NMR spectra of **IVa**–**IVc** and **Va**–**Vc** contained singlets from the cyclopropane ring proton at δ 3.87–3.93 ppm, as well as signals from aromatic protons and those in the ethyl and ethylene groups. Compound **IVc** displayed the following signals in the ^{13}C NMR spectrum, δ_C, ppm: 14.5 (CH_3), 21.5 (CH_3), 25.0 (CH_2), 28.3 (CH_2), 39.2 (CH), 45.6 (C), 48.8 (C), 63.2 (CH_2), 166.0 (CO), 191.0 (CO); in addition, signals from aromatic carbon atoms were present. Signals from carbon atoms in the cyclopropane ring appeared in a stronger field relative to those belonging to the pyrazole ring carbon atoms in the spectra of the initial compounds. The IR spectra of the products contained absorption bands in the region 1690–1740 cm^{-1} due to stretching vibrations of the carbonyl groups.

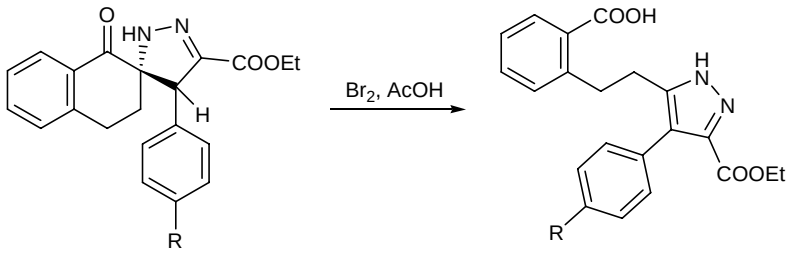
The ^{1}H–^{1}H NOESY spectrum of **IVa** revealed cross peaks originating from interaction between protons of the ester methylene group and proton in the *ortho* position of the phenyl substituent and between the former and methylene protons in the tetrahydronaphthalene ring. In addition, we observed a cross peak corresponding to interaction between *ortho*-proton in the benzene ring and methylene protons in the tetrahydronaphthalene ring. No cross peak between the proton in the cyclopropane ring and methylene protons in the ester fragment was present. These data unambiguously indicate *trans* arrangement of the chlorine atom with respect to the phenyl group and *cis* orientation of the former relative to the carbonyl group in the tetrahydronaphthalene ring.



The spectra of the reaction mixtures obtained by heating dihydropyrazoles **IIa**–**IIc** and **IIIa**–**IIIc** contained a set of signals corresponding to a single cyclopropane diastereoisomer. On the other hand, by heating compounds **Ib** and **Id** with bromine in acetic acid at 70°C we isolated 33–60% of ethyl 4-aryl-5-[2-(2-carboxyphenyl)ethyl]pyrazolecarboxylates **VIa** and **VIb** (Scheme 3). The structure of products **VIa** and **VIb** was proved by the spectral and analytical data. The ^{1}H NMR spectra of **VIa** and **VIb** contained triplets from the methylene protons at δ 2.83–3.19 ppm, signals from protons in the ethyl group and aromatic protons, and a broadened signal at δ 13.2–13.5 ppm from the acid and NH protons. The carbonyl absorption band appears in the IR spectra at 1730–1740 cm^{-1}, and stretching vibrations of the O–H bond in the carboxy group gives rise to absorption at 3340 cm^{-1}. The structure of compound **VIa** was unambiguously proved by the X-ray diffraction data (see figure).

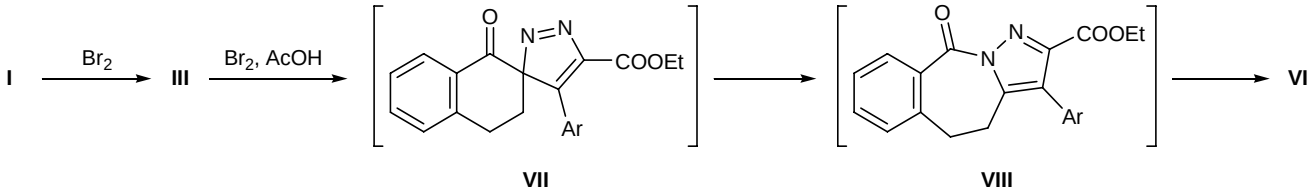
Presumably, as in the reaction with *N*-bromosuccinimide, 4,5-dihydropyrazoles **I** are initially converted into 3-bromodihydropyrazoles **III**. Heating of compounds **III** with bromine in acetic acid gives 3*H*-pyrazole **VII** which undergoes acyl shift by analogy with the van Alfen–Hüttel rearrangement. Acid hydrolysis of tricyclic intermediate **VIII** leads to formation of final product **VI** (Scheme 4).

Scheme 3.



Id, R = NO_2; **VIa**, R = Cl; **VIb**, R = NO_2.

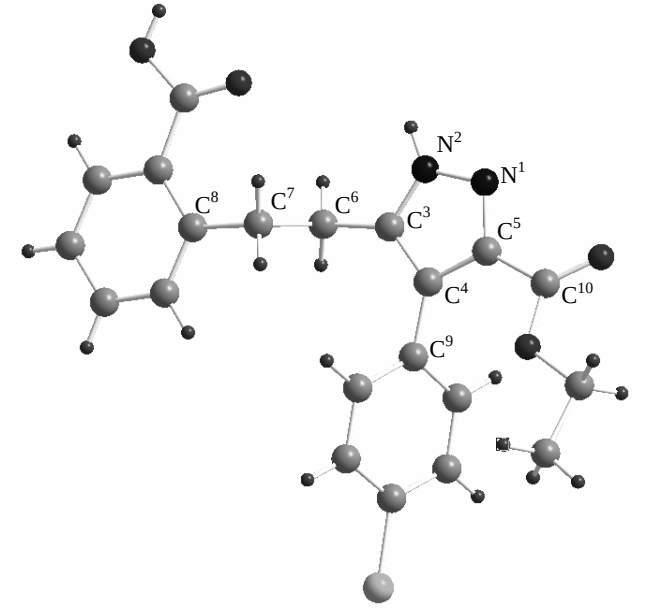
Scheme 4.



Dehydrobromination of esters **IIIa**–**IIIc** with sodium ethoxide in ethanol gave 30–36% of diesters **IXa**–**IXc** (Scheme 5), and hydrolysis of diester **IXb** and monoester **VIb** in ethanol in the presence of sodium ethoxide afforded dicarboxylic acid **X** (Scheme 6). The structure of compounds **IXa**–**IXc** was confirmed by spectral methods and elemental analysis. The ^{1}H NMR spectra of **IXa**–**IXc** contained triplets from protons in the ethylene bridge (δ 2.82–3.27 ppm), signals from aromatic protons, and signals from protons in the two ester fragments.

EXPERIMENTAL

The IR spectra were obtained on Specord 75IR and UR-20 spectrometers 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 DMSO-d_6 as solvent. The products and reaction mixtures were analyzed by TLC on Silufol UV-254 plates.



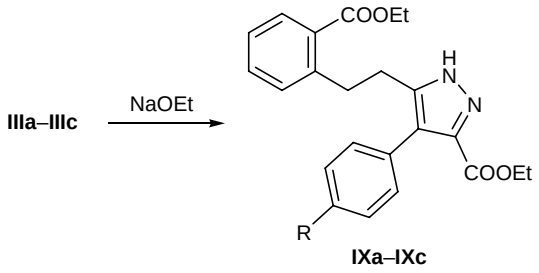
Structure of ethyl 5-[2-(2-carboxyphenyl)ethyl]-4-(4-chlorophenyl)pyrazole-3-carboxylate (**VIa**) according to the X-ray diffraction data.

Ethyl 4'-aryl-3'-chloro-1-oxo-1,2,3,4,4',5'-hexahydro-3'*H*-spiro[naphthalene-2,5'-pyrazole]-3'-carboxylates IIa–IIc (*general procedure***).** Dry gaseous chlorine was passed through a solution of 3 mmol of ester **Ia**–**Ic** in 30 ml of anhydrous chloroform at room temperature until the reaction was complete (TLC). The solution was evaporated to a volume of 5 ml, diluted with 10 ml of ethanol, and evaporated again, and the precipitate was filtered off.

Ethyl 3'-chloro-1-oxo-4'-phenyl-1,2,3,4,4',5'-hexahydro-3'*H*-spiro[naphthalene-2,5'-pyrazole]-3'-carboxylate (IIa). Yield 44%, mp 79–80°C (decomp.). ^{1}H NMR spectrum, δ, ppm: 0.90 t (3H, *J* = 7 Hz), 2.10 m (1H), 2.74 m (2H), 3.24 m (1H), 4.00 m (2H), 4.41 s (1H), 7.02 m (2H), 7.33–7.36 m (3H), 7.41 d (1H, *J* = 7 Hz), 7.44 d (1H, *J* = 7 Hz), 7.67 t.d (1H, *J* = 8, 2 Hz), 7.94 d (1H, *J* = 8 Hz).

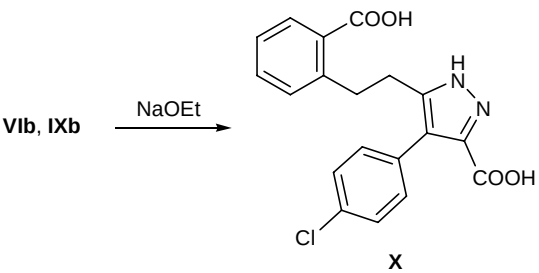
Ethyl 3'-chloro-4'-(4-chlorophenyl)-1-oxo-1,2,3,-4,4',5'-hexahydro-3'*H*-spiro[naphthalene-2,5'-pyrazole]-3'-carboxylate (IIb). Yield 55%, mp 110°C (decomp.). ^{1}H NMR spectrum, δ, ppm: 0.92 t (3H, *J* =

Scheme 5.



R = H (**a**), Cl (**b**), Me (**c**).

Scheme 6.



7 Hz), 2.11 m (1H), 2.66 d.t (1H, *J* = 14, 5 Hz), 2.80 d.t (1H, *J* = 17, 5 Hz), 3.27 m (1H), 4.03 m (2H), 4.47 s (1H), 7.07 d (2H, *J* = 9 Hz), 7.44 m (4H), 7.67 t (1H, *J* = 7 Hz), 7.93 d (1H, *J* = 7 Hz). ^{13}C NMR spectrum, δ_C, ppm: 14.1 (CH_3), 20.1 (CH_2), 31.1 (CH_2), 53.6 (CH), 64.1 (CH_2), 103.2 (C), 104.8 (C), 128.0 (CH), 128.8 (CH), 129.5 (CH), 130.1 (C), 131.4 (C), 132.0 (CH), 132.5 (CH), 134.2 (C), 135.7 (CH), 144.7 (C), 164.9 (CO), 190.1 (CO). Found, %: C 60.36; H 4.44; N 6.88. $C_{21}H_{18}Cl_2N_2O_3$. Calculated, %: C 60.45; H 4.35; N 6.71.

Ethyl 3'-chloro-4'-(4-methylphenyl)-1-oxo-1,2,3,-4,4',5'-hexahydro-3'*H*-spiro[naphthalene-2,5'-pyrazole]-3'-carboxylate (IIc). Yield 72%, mp 87–88°C (decomp.). ^{1}H NMR spectrum, δ, ppm: 0.94 t (3H, *J* = 7 Hz), 2.09 m (1H), 2.27 s (3H), 2.68 m (1H), 2.79 m (1H), 3.25 m (1H), 4.01 m (2H), 4.36 s (1H), 6.90 d (2H, *J* = 8 Hz), 7.15 d (2H, *J* = 8 Hz), 7.40 d (1H, *J* = 7 Hz), 7.44 t (1H, *J* = 7 Hz), 7.67 t (1H, *J* = 7 Hz), 7.93 d (1H, *J* = 8 Hz).

Ethyl 4'-aryl-3'-bromo-1-oxo-1,2,3,4,4',5'-hexahydro-3'*H*-spiro[naphthalene-2,5'-pyrazole]-3'-carboxylates IIIa–IIIc (*general procedure***).** *N*-Bromosuccinimide, 0.6 g (3.3 mmol), was added at room temperature to a solution of 3 mmol of ester **Ia–Ic** in a mixture of 20 ml of anhydrous chloroform and 10 ml of acetic acid. When the reaction was complete (TLC), the mixture was stirred for an additional 40 min and washed with water, a 5% solution of sodium hydrogen carbonate, and water again. The organic phase was dried over $MgSO_4$, evaporated to a volume of 5 ml, diluted with 10 ml of ethanol, and evaporated again, and the precipitate was filtered off.

Ethyl 3'-bromo-1-oxo-4'-phenyl-1,2,3,4,4',5'-hexahydro-3'*H*-spiro[naphthalene-2,5'-pyrazole]-3'-carboxylate (IIIa). Yield 45%, mp 101–102°C (decomp.). ^{1}H NMR spectrum, δ, ppm: 0.80 t (3H, *J* = 7 Hz), 2.01 m (1H), 2.68 m (2H), 3.23 m (1H), 3.87 m (2H), 4.48 s (1H), 6.96 m (2H), 7.33 m (3H), 7.42 m (2H), 7.66 t (1H, *J* = 7 Hz), 7.91 d (1H, *J* = 8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 14.0 (CH_3), 26.1 (CH_2), 31.2 (CH_2), 54.3 (CH), 63.4 (CH_2), 94.9 (C), 102.7 (C), 127.9 (CH), 128.7 (CH), 129.2 (CH), 129.5 (CH), 130.0 (CH), 130.2 (CH), 131.6 (C), 134.3 (CH), 135.6 (C), 144.5 (C), 165.7 (CO), 190.5 (CO).

Ethyl 3'-bromo-4'-(4-chlorophenyl)-1-oxo-1,2,3,-4,4',5'-hexahydro-3'*H*-spiro[naphthalene-2,5'-pyrazole]-3'-carboxylate (IIIb). Yield 61%, mp 125°C (decomp.). ^{1}H NMR spectrum, δ, ppm: 0.85 t (3H, *J* = 7 Hz), 2.01 m (1H), 2.67 m (2H), 3.25 m (1H), 3.92 m (2H), 4.55 s (1H), 7.0 d (2H, *J* = 9 Hz), 7.40 d (1H, *J* = 7 Hz), 7.41 d (2H, *J* = 9 Hz), 7.43 t (1H, *J* = 7 Hz), 7.65 t (1H, *J* = 7 Hz), 7.90 d (1H, *J* = 7 Hz).

Ethyl 3'-bromo-4'-(4-methylphenyl)-1-oxo-1,2,3,-4,4',5'-hexahydro-3'*H*-spiro[naphthalene-2,5'-pyrazole]-3'-carboxylate (IIIc). Yield 57%, mp 111–112°C. ^{1}H NMR spectrum, δ, ppm: 0.83 t (3H, *J* = 7 Hz), 2.03 m (1H), 2.26 s (3H), 2.68 m (2H), 3.22 m (1H), 3.90 m (2H), 4.42 s (1H), 6.83 d (2H, *J* = 7 Hz), 7.13 d (2H, *J* = 7 Hz), 7.39 d (1H, *J* = 8 Hz), 7.43 t (1H, *J* = 8 Hz), 7.66 t (1H, *J* = 7 Hz), 7.90 d (1H, *J* = 8 Hz). Found, %: C 59.79; H 5.08; N 6.29. $C_{22}H_{21}BrN_2O_3$. Calculated, %: C 59.87; H 4.80; N 6.35.

Ethyl 3'-aryl-2'-chloro-1-oxo-1,2,3,4-tetrahydrospiro[naphthalene-2,1'-cyclopropane]-2'-carboxylates IVa–IVc (*general procedure***).** A solution of 0.3 mmol of ester **IIa–IIc** in 4 ml of toluene was heated for 40 min at 80°C (TLC). Gas evolution was observed. The solvent was distilled off under reduced pressure, 2 ml of ethanol was added to the residue, and the precipitate was filtered off and recrystallized from ethanol.

Ethyl 2'-chloro-1-oxo-3'-phenyl-1,2,3,4-tetrahydrospiro[naphthalene-2,1'-cyclopropane]-2'-carboxylate (IVa). Yield 59%, mp 102–103°C. IR spectrum, ν, cm^{-1}: 820, 1030, 1140, 1280 s, 1700 v.s, 1730 v.s, 2980. ^{1}H NMR spectrum, δ, ppm: 1.08 t (3H, *J* = 7 Hz), 2.31 d.t (1H, *J* = 14, 3 Hz), 2.68 t.d (1H, *J* = 14, 5 Hz), 3.00 m (2H), 3.93 s (1H), 4.10 m (2H), 7.23 d (2H, *J* = 7 Hz), 7.32 m (3H), 7.42 d (1H, *J* = 7 Hz), 7.43 t (1H, *J* 8 Hz), 7.64 t.d (1H, *J* = 7, 1 Hz), 8.01 d (1H, *J* = 8 Hz). Found, %: C 71.72; H 5.95. $C_{21}H_{19}ClO_3$. Calculated, %: C 71.64; H 5.74.

Ethyl 2'-chloro-3'-(4-chlorophenyl)-1-oxo-1,2,3,4-tetrahydrospiro[naphthalene-2,1'-cyclopropane]-2'-carboxylate (IVb). Yield 74%, mp 126–127°C. IR spectrum, ν, cm^{-1}: 810, 1010, 1150, 1250, 1280 s, 1490, 1700 v.s, 1740 v.s, 3030. ^{1}H NMR spectrum, δ, ppm: 1.10 t (3H, *J* = 7 Hz), 2.23 m (1H), 2.70 m (1H), 2.91 m (1H), 3.04 m (1H), 3.91 s (1H), 4.12 q (2H, *J* = 7 Hz), 7.27 d (2H, *J* = 8 Hz), 7.39 d (2H, *J* = 8 Hz), 7.42 d (1H, *J* = 8 Hz), 7.43 t (1H, *J* = 8 Hz), 7.64 t (1H, *J* = 7 Hz), 8.01 d (1H, *J* = 8 Hz). Found, %: C 64.57; H 4.72. $C_{21}H_{18}Cl_2O_3$. Calculated, %: C 64.80; H 4.66.

Ethyl 2'-chloro-3'-(4-methylphenyl)-1-oxo-1,2,3,4-tetrahydrospiro[naphthalene-2,1'-cyclo-

propane]-2'-carboxylate (IVc). Yield 62%, mp 100–101°C. IR spectrum, ν, cm^{-1}: 820, 1030, 1120, 1150 s, 1260, 1290 v.s, 1600, 1690 v.s, 1740 v.s, 2930, 3040. ^1H NMR spectrum, δ, ppm: 1.10 t (3H, *J* = 7 Hz), 2.29 s (3H), 2.33 m (1H), 2.64 m (1H), 2.99 m (2H), 3.87 s (1H), 4.10 m (2H), 7.10 d (2H, *J* = 8 Hz), 7.15 (2H, *J* = 8 Hz), 7.41 d (1H, *J* = 8 Hz), 7.43 t (1H, *J* = 8 Hz), 7.64 t (1H, *J* = 7 Hz), 8.00 d (1H, *J* = 7 Hz). ^{13}C NMR spectrum, δ_C, ppm: 14.5 (CH_3), 21.5 (CH_3), 25.0 (CH_2), 28.3 (CH_2), 39.2 (CH), 45.6 (C), 48.8 (C), 63.2 (CH_2), 127.8 (CH), 128.3 (CH), 129.7 (CH), 129.8 (CH), 130.0 (C), 130.2 (CH), 132.4 (C), 135.1 (CH), 137.2 (C), 144.9 (C), 166.0 (CO), 191.0 (CO). Found, %: C 70.85; H 5.74. $C_{22}H_{21}ClO_3$. Calculated, %: C 71.64; H 5.74.

Ethyl 3'-aryl-2'-bromo-1-oxo-1,2,3,4-tetrahydrospiro[naphthalene-2,1'-cyclopropane]-2'-carboxylates Va–Vc (*general procedure***).** A solution of 0.3 mmol of compound **IIIa**–**IIIc** in 4 ml of toluene was heated for 40 min at 80°C (TLC). Gas evolution was observed. The solvent was distilled off under reduced pressure, 2 ml of ethanol was added to the residue, and the precipitate was filtered off and recrystallized from ethanol.

Ethyl 2'-bromo-1-oxo-3'-phenyl-1,2,3,4-tetrahydrospiro[naphthalene-2,1'-cyclopropane]-2'-carboxylate (Va). Yield 44%, mp 81–82°C. IR spectrum, ν, cm^{-1}: 800, 1040, 1150, 1300, 1610, 1700 s, 1750 v.s, 3040 s. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.23 t (3H, *J* = 7 Hz), 2.42 d.d.d (1H, *J* = 14, 4, 3 Hz), 2.54 m (1H), 2.98 d.t (1H, *J* = 17, 3 Hz), 3.33 m (1H), 4.07 s (1H), 4.19 q (2H, *J* = 7 Hz), 7.31 m (6H), 7.39 t (1H, *J* = 7 Hz), 7.55 t. d (1H, *J* = 8, 1 Hz) 8.19 d (1H, *J* = 8 Hz). Found, %: C 63.01; H 4.76. $C_{21}H_{19}BrO_3$. Calculated %: C 63.17; H 4.80.

Ethyl 2'-bromo-3'-(4-chlorophenyl)-1-oxo-1,2,3,4-tetrahydrospiro[naphthalene-2,1'-cyclopropane]-2'-carboxylate (Vb). Yield 38%, mp 96–97°C. IR spectrum, ν, cm^{-1}: 800, 1010, 1150, 1300, 1690, 1740, 3030. ^1H NMR spectrum, δ, ppm: 1.11 t (3H, *J* = 7 Hz), 2.11 m (1H), 2.69 m (1H), 3.04 m (2H), 3.83 s (1H), 4.12 q (2H, *J* = 7 Hz), 7.29 d (2H, *J* = 8 Hz), 7.40 d (2H, *J* = 8 Hz), 7.43 d (1H, *J* = 7 Hz), 7.44 t (1H, *J* = 7 Hz), 7.65 t (1H, *J* = 7 Hz), 8.01 d (1H, *J* = 7 Hz). Found, %: C 58.22; H 4.36. $C_{21}H_{18}BrClO_3$. Calculated, %: C 58.15; H 4.18.

Ethyl 2'-chloro-3'-(4-methylphenyl)-1-oxo-1,2,3,4-tetrahydrospiro[naphthalene-2,1'-cyclopropane]-2'-carboxylate (Vc). Yield 37%, mp 77–78°C. IR spectrum, ν, cm^{-1}: 820, 1030, 1150 s, 1260 s, 1290 v.s, 1320, 1460, 1610, 1690 v.s, 1740 v.s, 2930, 3040. ^1H NMR spectrum, δ, ppm: 1.11 t (3H, *J* = 7 Hz), 2.17 m (1H), 2.29 s (3H), 2.61 m (1H), 3.07 m (2H), 3.79 s (1H), 4.11 q (2H, *J* = 7 Hz), 7.15 s (4H), 7.42 d (1H, *J* = 7 Hz), 7.43 t (1H, *J* = 7 Hz), 7.64 t (1H, *J* = 8 Hz), 8.00 d (1H, *J* = 8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 14.4 (CH_3), 21.5 (CH_3), 25.3 (CH_2), 28.1 (CH_2), 38.3 (C), 38.7 (CH), 43.4 (C), 63.2 (CH_2), 127.7 (CH), 128.4 (CH), 129.7 (CH), 129.9 (CH), 130.2 (CH), 132.0 (C), 135.1 (CH), 137.3 (C), 145.0 (C), 166.1 (CO), 191.6 (CO). Found, %: C 63.97; H 4.94. $C_{22}H_{21}BrO_3$. Calculated, %: C 63.93; H 5.12.

Ethyl 4-aryl-5-[2-(2-carboxyphenyl)ethyl]pyrazole-3-carboxylates VIa and VIb (*general procedure***).** A mixture of 1.5 mmol of ester **Ib** or **Id** and 0.5 g (3 mmol) of bromine in 20 ml of acetic acid was heated for 5 h at 70°C (TLC). The mixture was then poured into water, and the precipitate was filtered off and recrystallized from ethanol.

Ethyl 5-[2-(2-carboxyphenyl)ethyl]-4-(4-chlorophenyl)pyrazole-3-carboxylate (VIa). Yield 60%, mp 211–212°C. IR spectrum, ν, cm^{-1}: 810, 1010, 1040, 1100, 1280, 1300 s, 1450, 1680 s, 1740 v.s, 2600 br, 3040 br, 3360. ^1H NMR spectrum, δ, ppm: 1.12 t (3H, *J* = 7 Hz), 2.83 t (2H, *J* = 7 Hz), 3.19 t (2H, *J* = 7 Hz), 4.12 q (2H, *J* = 7 Hz), 7.08 m (3H), 7.28 t (1H, *J* = 7 Hz), 7.36 m (3H), 7.78 d (1H, *J* = 7 Hz), 13.17 br.s (2H). Found, %: C 63.57; H 4.91; N 6.83. $C_{21}H_{19}ClN_2O_4$. Calculated, %: C 63.24; H 4.77; N 7.03.

Ethyl 5-[2-(2-carboxyphenyl)ethyl]-4-(4-nitrophenyl)pyrazole-3-carboxylate (VIb). Yield 33%, mp 219–220°C. IR spectrum, ν, cm^{-1}: 810, 870, 1010, 1030, 1050, 1090, 1110, 1230, 1300, 1350 v.s, 1450, 1600, 1690, 1730 v.s, 3040 br, 3330. ^1H NMR spectrum, δ, ppm: 1.12 t (3H, *J* = 7 Hz), 2.89 m (2H), 3.19 t (2H, *J* = 7 Hz), 4.14 q (2H, *J* = 7 Hz), 7.07 d (1H, *J* = 7 Hz), 7.27 t (1H, *J* = 7 Hz), 7.38 m (3H), 7.76 d (1H, *J* = 7 Hz), 8.16 d (2H, *J* = 8 Hz), 13.00 br.s (1H), 13.51 br.s (1H). Found, %: C 61.55; H 4.71; N 10.13. $C_{21}H_{19}N_3O_6$. Calculated, %: C 61.61; H 4.68; N 10.26.

Reaction of ethyl 3'-bromo-4'-(4-chlorophenyl)-1-oxo-1,2,3,4,4',5'-hexahydro-1'*H*-spiro[naphthalene-2,5'-pyrazole]-3'-carboxylate (IIIb) with bromine in acetic acid. A mixture of 2 mmol of ester **IIIb** and 4 mmol of bromine in 20 ml of acetic acid was heated for 1.5 h at 70–75°C (TLC). The mixture was

poured into water, and the precipitate was filtered off and recrystallized from ethanol. Yield of **VIa** 80%.

Ethyl 4-aryl-5-[2-(2-ethoxycarbonylphenyl) ethyl]pyrazole-3-carboxylates IXa–IXc (*general procedure***).** Ester **IIIa–IIIc**, 2 mmol, was added in portions under stirring at room temperature to a solution of sodium ethoxide prepared from 0.15 g (6 mmol) of sodium and 5 ml of anhydrous ethanol. The solution turned yellow, and the reaction was complete in 10 min (TLC). The mixture was passed through a column charged with silica gel using ethyl acetate as eluent, the eluate was evaporated, and the precipitate was filtered off.

Ethyl 5-[2-(2-ethoxycarbonylphenyl)ethyl]-4-phenylpyrazole-3-carboxylate (IXa). Yield 36%, mp 131–132°C. IR spectrum, ν, cm^{-1}: 810, 1050, 1090, 1120 s, 1150, 1190, 1270 v.s, 1360, 1380, 1440, 1710 v.s, 3010 br, 3410. ^{1}H NMR spectrum, δ, ppm: 1.10 t (3H, *J* = 7 Hz), 1.22 t (3H, *J* = 7 Hz), 2.83 t (2H, *J* = 7 Hz), 3.15 t (2H, *J* = 7 Hz), 4.13 m (4H), 7.08 m (3H), 7.30 m (4H), 7.43 t (1H, *J* = 8 Hz), 7.73 d (1H, *J* = 8 Hz), 13.44 br.s (1H). Found, %: C 70.38; H 6.15; N 7.03. $C_{23}H_{24}N_2O_4$. Calculated, %: C 70.39; H 6.16; N 7.14.

Ethyl 4-(4-chlorophenyl)-5-[2-(2-ethoxycarbonylphenyl)ethyl]pyrazole-3-carboxylate (IXb). Yield 33%, mp 115–116°C. IR spectrum, ν, cm^{-1}: 810, 1020, 1040, 1090, 1110, 1150, 1200, 1270 v.s, 1300, 1450, 1720 v.s, 3030 s, 3420. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.27 t (3H, *J* = 7 Hz), 1.40 t (3H, *J* = 7 Hz), 2.95 t (2H, *J* = 8 Hz), 3.27 (2H, *J* = 8 Hz), 4.28 q (2H, *J* = 7 Hz), 4.36 q (2H, *J* = 7 Hz), 7.11 d (1H, *J* = 8 Hz), 7.16 d (2H, *J* = 8 Hz), 7.28 m (2H), 7.37 m (3H), 7.92 d (1H, *J* = 8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 14.5 (CH_3), 14.6 (CH_3), 26.9 (CH_2), 34.1 (CH_2), 61.2 (CH_2), 61.5 (CH_2), 122.2 (C), 126.9 (CH), 128.4 (CH), 129.7 (C), 131.0 (CH), 131.4 (CH), 132.0 (CH), 132.6 (CH), 133.6 (C), 143.0 (C), 162.0 (CO), 168.0 (CO). Found, %: C 64.96; H 5.58; N 6.63. $C_{23}H_{23}ClN_2O_4$. Calculated, %: C 64.71; H 5.43; N 6.56.

Ethyl 5-[2-(2-ethoxycarbonylphenyl)ethyl]-4-(4-methylphenyl)pyrazole-3-carboxylate (IXc). Yield 30%, mp 118–119°C. IR spectrum, ν, cm^{-1}: 810, 1030, 1090, 1120, 1160, 1190, 1260 v.s, 1440, 1710 v.s, 3000 br, 3430. ^{1}H NMR spectrum, δ, ppm: 1.12 t (3H, *J* = 7 Hz), 1.22 t (3H, *J* = 7 Hz), 2.31 s (3H), 2.82 br.s (2H), 3.14 t (2H, *J* = 8 Hz), 4.16 m (4H), 6.94 br.m (2H), 7.11 br.m (3H), 7.30 t (1H, *J* = 8 Hz), 7.43 t (1H, *J* = 8 Hz), 7.73 d (1H, *J* = 8 Hz), 13.35 br.s (1H). Found, %: C 70.89; H 6.50; N 6.89. $C_{24}H_{26}N_2O_4$. Calculated, %: C 70.92; H 6.45; N 6.89.

5-[2-(2-Carboxyphenyl)ethyl]-4-(4-chlorophenyl)pyrazole-3-carboxylic acid (X). *a*. Ester **IXb**, 0.15 g (0.35 mmol), was added to a solution prepared from 0.1 g (4.3 mmol) of sodium and 10 ml of ethanol. The mixture was heated for 2.5 h at 90°C. The solvent was evaporated, 20 ml of water was added to the residue, and the mixture was extracted with chloroform. The aqueous phase was acidified with concentrated hydrochloric acid, and the precipitate was filtered off. Yield of acid **X** 55%, mp 256°C.

b. Ester **VIa**, 0.5 g (1.20 mmol), was added to a solution prepared from 0.1 g (4.3 mmol) of sodium and 10 ml of ethanol. The mixture was heated for 2 h at 90°C, the solvent was distilled off, 20 ml of water was added to the residue, and the mixture was extracted with chloroform. The aqueous phase was acidified with concentrated hydrochloric acid, and the precipitate was filtered off. Yield 25%. IR spectrum (KBr), ν, cm^{-1}: 870, 1010, 1100, 1205, 1265, 1285, 1310, 1410, 1700 v.s, 2400–3600. ^{1}H NMR spectrum, δ, ppm: 2.80 t (2H, *J* = 8 Hz), 3.19 t (2H, *J* = 8 Hz), 7.08 d (1H, *J* = 7 Hz), 7.14 d (2H, *J* = 8 Hz), 7.28 t (1H, *J* = 8 Hz), 7.36 d (2H, *J* = 8 Hz), 7.40 m (1H), 7.78 d (1H, *J* = 8 Hz), 12.80 br.s (2H). Found, %: C 61.35; H 4.21; N 7.28. $C_{19}H_{15}ClN_2O_4$. Calculated, %: C 61.55; H 4.08; N 7.56.

X-Ray diffraction data for compound (VIa). $C_{21}H_{19}ClN_2O_4$. *M* 398.83. Triclinic crystals, space group *P*-1 (no. 2); unit cell parameters: *a* = 7.0326(7), *b* = 7.3013(7), *c* = 20.636(2) Å; α = 99.25(0), β = 91.58(0), γ = 110.26(0)°; *V* = 997.15(16) $Å^3$; *Z* = 2; *d* = 1.355 g/cm^3; μ = 0.078 mm^{-1}; *F*(000) = 912; irradiation source MoK_α, λ = 0.71073 Å, graphite monochromator. Below are given the bond lengths (Å) and bond angles (deg): N^1–N^2 1.342(3), N^1–C^5 1.336(3), N^2–C^3 1.350(3), C^3–C^4 1.383(3), C^3–C^6 1.494(3), C^4–C^5 1.410(3), C^4–C^9 1.481(3), C^5–C^{10} 1.480(3), C^6–C^7 1.538(3), C^7–C^8 1.511(3), $N^1N^2C^3$ 113.55(15), $C^5N^1N^2$ 104.31(16), $N^1C^5C^4$ 111.39(18), $N^2C^3C^4$ 105.97(16), $C^3C^4C^5$ 104.78(18), $N^1C^5C^{10}$ 118.50(18), $C^4C^3C^6$ 131.65(19), $C^5C^4C^9$ 127.41(15). The complete set of crystallographic data was deposited to the Cambridge Crystallographic Data Center (entry no. 255055).

The authors are grateful to the Foundation of Prof. A. de Meijere (Georg-August Universität, Göttingen, Germany) for providing a personal research grant to V.S. Korotkov.

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