ISSN 1070-4280, Russian Journal of Organic Chemistry, 2009, Vol. 45, No. 5, pp. 705–711. © Pleiades Publishing, Ltd., 2009.
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Synthesis and Reactions of 1-Benzyl-3-haloalkyl-5-chloropyrazoles

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Received July 28, 2008

Abstract—Synthesized 1-benzyl-3-chloroalkyl-5-chloropyrazoles reacted with indole and pyrrole in DMSO in the presence of alkali to give 3-(heter-1-yl)alkyl-substituted 1-benzyl-5-chloropyrazoles. 1-[(1-Benzyl-5-chloropyrazol-3-yl)methyl]indole reacted regiospecifically with chloroal trifluoromethylsulfonyl- and 4-chlorophenylsulfonylimines providing the products of C-amidotrichloroethylation into the position 3 of the indole ring. {1-[(1-Benzyl-5-chloropyrazol-3-yl)methyl]indol-3-yl}sulfanylacetic acid was obtained by the reaction of 1-[(1-benzyl-5-chloropyrazol-3-yl)methyl]-indole with iodine, thiourea, and chloroacetic acid.

DOI: 10.1134/S1070428009050108

The synthesis and chemical transformations of pyrazoles attract a wide interest for they are extensively employed in pharmaceutical industry, agriculture, and in new materials production. In particular, the halopyrazoles are key intermediates in the production of light-sensitive materials, dyes, insecticides, fungicides, herbicides, and drugs of a wide range of action, including antiphlogistic, anti-fever, antibacterial etc. activity [1–9].

In extension of our systematic research aimed at the purposeful synthesis and the study of chemical properties of halopyrazoles [10] we synthesized a series of 1-benzyl-3-haloalkyl-5-chloropyrazoles and established that these pyrazoles enter into reactions with indole and pyrrole affording products of N-alkylation of the said heterocycles in good yields.

The synthesis of previously unknown 1-benzyl-3-haloalkyl-5-chloropyrazoles was carried out by treating haloalkyl 2,2-dichlorovinyl ketones with benzylhydrazine similarly to the preparation of 5-chloro-3-chloro-methyl-1-ethylpyrazole [11].

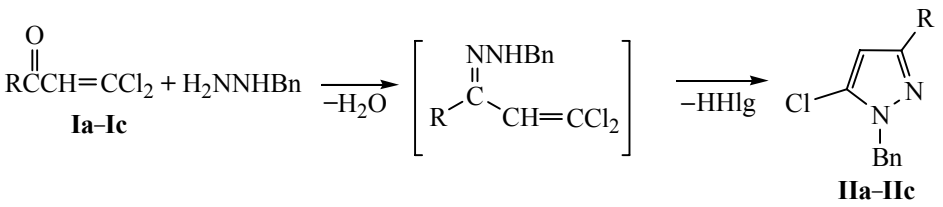
The corresponding ketones **Ia–Ic**, among them previously unknown **Ib** and **Ic**, were obtained from the chlorides of haloalkanecarboxylic acids and vinylidene chloride in the presence of aluminum chloride by procedure [12].

The structure of haloalkyl 2,2-dichlorovinyl ketones **Ia–Ic** and pyrazoles **IIa–IIc** obtained therefrom was confirmed by IR and NMR spectra, and their composition, by elemental analysis (Scheme 1).

The obtained ketones **Ia–Ic** are light-yellow fluids distillable in a vacuum and possessing a lacrimator action.

The IR spectra of ketones **Ia–Ic** contained the characteristic absorption bands of carbonyl groups, C=C and =C–H bonds, and also absorption bands of alkyl CH bonds.

Scheme 1.



R = CH_2Cl (**a**), CH_3CHCl (**b**), CH_3CH_2CHBr (**c**).

^{1}H NMR spectrum of compounds **Ia–Ic** contained the proton signals from haloalkyl moieties and the signals of vinyl protons. In the ^{13}C NMR spectra signals were observed belonging to carbon atoms of methyl and methylene fragments, of CH=, $=CCl_2$, and C=O groups. The carbon signal from the CHCl fragment appeared downfield compared to the analogous signal from CHBr group.

The IR spectra of pyrazoles **IIa–IIc** contained absorption bands of C=C, C=N bonds, of CH bonds from the alkyl fragments, and of C^4H in the pyrazole ring.

The ^{1}H NMR spectra of pyrazoles **IIa–IIc** are characterised by the presence of the proton signals from the chloroalkyl and benzyl fragments, and of H^4 in the pyrazole ring. The integral intensity of the signals was consistent with the assumed structures. In ^{13}C NMR spectra signals were present of atoms C^3, C^4, and C^5 of the pyrazole ring, and also of groups CH_2Ph and RCHHlg.

Aiming at preparation of new polyheterocyclic ensembles we studied the reactions of 3-(haloalkyl)-substituted pyrazoles with indole and pyrrole.

1-Benzyl-5-chloro-3-chloromethylpyrazole reacted with indole and pyrrole in the presence of alkali in DMSO solution at room temperature under the conditions of the N-alkylation of indoles [13] resulting in the corresponding heterocyclic compounds, 1-[(1-benzyl-5-chloropyrazol-3-yl)methyl]indole (**III**) and 1-[(1-benzyl-5-chloropyrazol-3-yl)-methyl]pyrrole (**IV**) in 75 and 63% yield respectively (Scheme 2).

The structure of compounds **III** and **IV** was proved by IR and NMR spectroscopy, their composition was confirmed by elemental analysis.

In the IR spectra of compounds **III** and **IV** the absorption bands were observed originating from the aromatic and heterocyclic fragments and of alkyl CH bonds. The ^{1}H NMR spectrum of substituted indole **III** contained the proton signals of two methylene groups and H^4 proton of the pyrazole ring, doublets of indole protons H^2 and H^3, and also the signals of the phenyl protons.

In the ^{1}H NMR spectrum of compound **IV** also the signals were observed from the protons of two methylene groups, of H^4 proton of the pyrazole ring, two signals from the protons of the pyrrole ring, and also the signals of the phenyl protons.

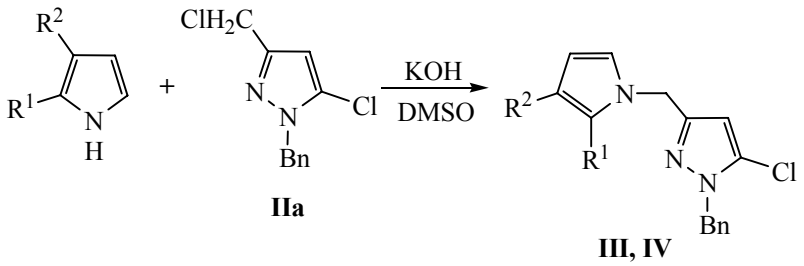
The presence in the pyrazole molecule of chloroethyl or bromopropyl group complicated the reaction of 3-(haloalkyl)-substituted pyrazoles with indole.

For instance, in the reaction of 1-benzyl-5-chloro-3-(1-chloroethyl)pyrazole (**IIb**) with indole under the conditions analogous to used in the synthesis of compound **III** formed a mixture of 1-[1-(1-benzyl-5-chloropyrazol-3-yl)ethyl]indole (**V**) with the initial indole in the ratio 4:1 (^{1}H NMR data). The increased reaction time and the use of excess pyrazole **IIb** (up to twofold excess) did not lead to the enhance yield of target product **V**. We failed to separate the mixture of the alkylated and initial indoles, but the formed pyrazoloindole **V** was characterized by the ^{1}H NMR spectrum.

Yet 1-benzyl-3-(1-bromopropyl)-5-chloropyrazole (**IIc**) under the similar conditions did not effect the *N*-alkylation of indole, but underwent the dehydrobromination yielding 1-benzyl-3-(1-propenyl)-5-chloropyrazole (**VI**). Under the studied conditions propenylpyrazole **VI** formed with a difficultly separable admixture of the initial pyrazole **IIc** in a ratio 4:1.

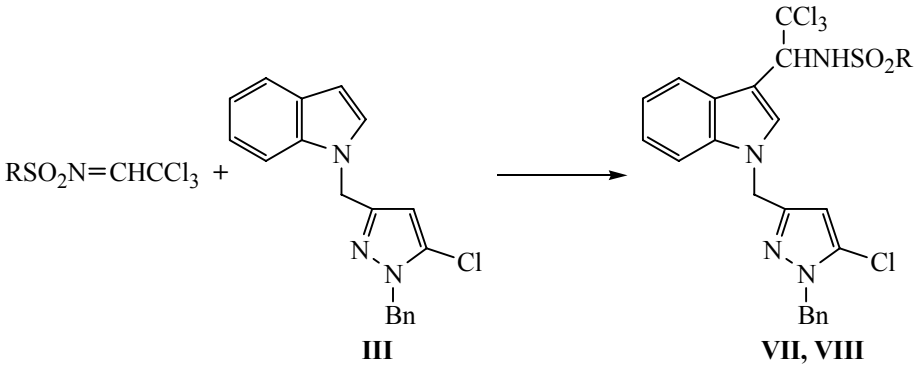
We studied the properties of the synthesized indolomethylpyrazole **III** and established that it entered into reactions with highly electrophilic chloral trifluoromethylsulfonyl- and 4-chlorobenzenesulfonylimines without catalyst or heating providing in good yields products of C-amidotrichloroethylation of indole into the position *3* **VII** and **VIII** (Scheme 3).

Scheme 2.



$R^1, R^2 = (CH)_4$ (**III**), $R^1 = R^2 = H$ (**IV**).

Scheme 3.



R = CF_3 (**VII**), 4-ClC_6H_4 (**VIII**).

Chloral sulfonylimines prepared from the corresponding *N,N*-dichloroamides and trichloroethylene [14,15] were brought into the reaction with indolomethylpyrazole **III** without isolation of the imines from the reaction mixture under the conditions previously developed for the C-amidoalkylation of indoles [16].

We did not find any products of C-amidoalkylation into the position *4* of the pyrazole ring. This is due to the lower nucleophilicity of the position *4* of the pyrazole ring compared to the position *3* of the indole ring, and evidently also to the steric effect of the bulky methylindole substituent.

The synthesized compounds **VII** and **VIII** are light-pink and light-brown powders.

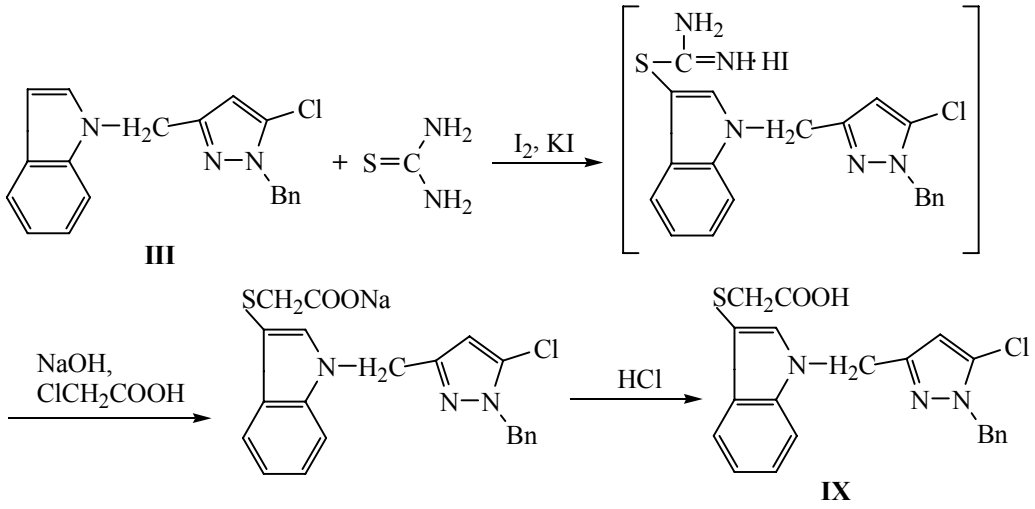
The ^1H NMR spectra of compounds **VII** and **VIII** contain a singlet from the proton in the position *4* of the pyrazole ring and no proton signal from the position *3* of the indole ring unambiguously indicating the direction of the C-amidoalkylation. Besides in the spectra of compounds **VII** and **VIII** signals are observed of the coupled protons of the fragment CH–NH, of protons from CH_2 groups, of the indole and aromatic rings.

Indolomethylpyrazole **III** can be used in the synthesis of {1-[(1-benzyl-5-chloropyrazol-3-yl)-methyl]indol-3-yl}sulfanylacetic acid (**IX**), interesting as a promising biologically active substance [17–20] or a precursor for the preparation of such substances (Scheme 4).

We planned both to introduce the pyrazole ring into the structure of indolylsulfanylacetic acids and to investigate the effect of the pyrazole fragment on the direction of the reaction of compound **III** with thiourea and iodine.

The molecule of indolomethylpyrazole **III** contains several reaction sites where a halogen atom can be

Scheme 4.



introduced: the positions *2* and *3* of the indole ring and the position *4* of the pyrazole ring. Besides, it is not possible to exclude a priori the substitution of a chlorine in the pyrazole ring of compound **III** for an isothiuronium fragment under the action of the thiourea.

The reaction of indolomethylpyrazole **III** with thiourea and iodine was carried out by the one-pot method we had developed before without isolation of the isothiuronium salt from the reaction mixture [21] It was established that no substitution products in the pyrazole ring formed, and that the reaction occurred only at the position *3* of the indole ring.

The structure of compound **IX** was proved by IR and NMR spectroscopy, its composition was confirmed by elemental analysis. The IR spectrum contained the absorption bands of COOH group, of C=N, C=C, =C–H, and C–H bonds.

In the ^{1}H NMR spectra signals appeared from the protons in the position *2* of the indole ring and in the position *4* of the pyrazole ring.

Therefore as a result of the performed research we carried out the synthesis of 1-benzyl-3-halo-alkyl-5-chloropyrazoles that were brought into the reactions with indole and pyrrole; a high reactivity was demonstrated of the obtained 1-[(1-benzyl-5-chloropyrazol-3-yl)-methyl]indole in reactions with chloral trifluoromethyl- and 4-chlorophenylsulfonylimines, and by its reaction with iodine, thiourea, and monochloroacetic acid a pyrazoloindol-3-ylsulfanylacetic acid was obtained.

EXPERIMENTAL

IR spectra were recorded on a spectrophotometer Specord 75IR from pellets with KBr. ^{1}H and ^{13}C NMR spectra were registered on a spectrometer Bruker DPX-400 (at 400.13 and 100.61 MHz respectively), internal reference HMDS, chemical shifts values were given relative to TMS, measurements accuracy was 0.01 and 0.02 ppm for ^{1}H and ^{13}C respectively, coupling constants were determined with the accuracy of 0.1 Hz.

Chloromethyl 2,2-dichlorovinyl ketone (**Ia**) and previously unknown 2,2-dichlorovinyl 1-chloroethyl ketone (**Ib**), 1-bromopropyl 2,2-dichlorovinyl ketone (**Ic**) were prepared by procedure [12]. Physicochemical constants of ketone **Ia** were consistent with the published data [12].

2,2-Dichlorovinyl 1-chloroethyl ketone (Ib) was obtained from 12.69 (0.1 mol) of α-chloropropionyl chloride and 11.63 g (0.12 mol) of vinylidene chloride. Yield 15.0 g (80%), bp 104–106°C (20 mm Hg). IR spectrum, ν, cm^{-1}: 3056 (=C–H), 2986, 2935, 2867 (CH_{alk}), 1704 (C=O), 1580 (C=C). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.61 d (3H, CH_3, *J* 6.6 Hz), 4.37 q (1H, CHCl, *J* 6.6 Hz), 7.01 s (1H, $CH=CCl_2$). ^{13}C NMR spectrum, δ, ppm: 19.56 (CH_3), 58.49 (CHCl), 122.13 (CH=), 138.96 (CCl_2), 189.10 (C=O). Found, %: C 32.44; H 2.68; Cl 56.79. $C_5H_5Cl_3O$. Calculated, %: C 32.04; H 2.69; Cl 56.74.

1-Bromopropyl 2,2-dichlorovinyl ketone (Ic) was obtained from 18.55 g (0.1 mol) α-bromobutyryl chloride and 11.63 g (0.12 mol) of vinylidene chloride. Yield 21.0 g (85%), bp 124–126°C (20 mm Hg). IR spectrum, ν, cm^{-1}: 3054 (=CH), 2973 2937, 2882 (CH_{alk}), 1697 (C=O), 1572 (C=C). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.03 t (3H, CH_3, *J* 7.3 Hz), 2.01 m (2H, CH_2, *J* 6.4, 7.3 Hz), 4.21 t (1H, CHBr, *J* 6.4 Hz), 6.92 s (1H, $CH=CCl_2$). ^{13}C NMR spectrum, δ, ppm: 11.95 (CH_3), 26.67 (CH_2), 55.91 (CHBr), 123.00 (CH=), 138.70 ($=CCl_2$), 188.27 (C=O). Found, %: C 29.38; H 2.88; Br 32.55; Cl 28.71. $C_6H_7BrCl_2O$. Calculated, %: C 29.30; H 2.87; Br 32.49; Cl 28.83.

1-Benzyl-5-chloro-3-chloromethylpyrazole (IIa). To a solution of 8.67 g (0.05 mol) of ketone **Ia** in 30 ml of ethanol was added dropwise 6.10 g (0.05 mol) of benzylhydrazine and 5.06 g (0.05 mol) of triethylamine. The reaction mixture was boiled for 3 h, cooled, and poured into water, extracted with ethyl ether, the extract was dried with $CaCl_2$, the ether was removed in a vacuum. Yield 9.05 g (75%), mp 28–30°C. IR spectrum, ν, cm^{-1}: 3120, 3050, 3030 (=C–H), 2945 (CH_{alk}), 1590, 1500 (C=N, C=C). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 4.52 s (2H, CH_2Cl), 5.28 s (2H, CH_2), 6.30 s (1H, H^4), 7.19 d, 7.29 m (5H, C_6H_5). ^{13}C NMR spectrum, δ, ppm: 38.98 (CH_2Cl), 52.91 (CH_2), 104.70 (C^4), 127.39, 128.05, 128.78 (C_6H_5), 135.00 (C^5), 149.00 (C^3). Found, %: C 54.85; H 4.28; Cl 29.39; N 11.60. $C_{11}H_{10}Cl_2N_2$. Calculated, %: C 54.79; H 4.18; Cl 29.41; N 11.62.

1-Benzyl-5-chloro-3-(1-chloroethyl)pyrazole (IIb) was obtained similarly from 9.37 g (0.05 mol) of ketone **Ib**, 6.10 g (0.05 mol) of benzylhydrazine, and 5.06 g (0.05 mol) of triethylamine. Yield 10.87 g (86%), bp 130°C (15 mm Hg). IR spectrum, ν, cm^{-1}: 3141 (CH_{Ht}), 3089, 3064, 3032 (=CH), 2981, 2931, 2875 (CH_{alk}), 1514 1496 (C=N, C=C). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.79 d (3H, CH_3, *J* 6.8 Hz), 5.06 q (1H, CHCl, *J* 6.8 Hz), 5.23 s (2H, CH_2), 6.27 s (1H, C^4H), 7.21 m (5H, C_6H_5). ^{13}C NMR spectrum, δ, ppm: 24.59 (CH_3), 51.77 (CHCl), 52.70 (CH_2), 102.80 (C^4_{Ht}), 127.18 ($C^{3,5}_{Ph}$), 127.56

(C^5_{Ht}), 127.81 (C^4_{Ph}), 128.57 ($C^{2,6}_{Ph}$), 135.60 (C^1_{Ph}), 153.70 (C^4_{Ht}). Found, %: C 56.65; H 4.38; Cl 27.80; N 11.08. $C_{12}H_{12}Cl_2N_2$. Calculated %: C 56.71; H 4.36; Cl 27.90; N 11.02.

1-Benzyl-3-(1-bromopropyl)-5-chloropyrazole (IIc) was obtained similarly from 12.29 g (0.05 mol) of ketone **Ic**, 6.10 g (0.05 mol) of benzylhydrazine, and 5.06 g (0.05 mol) of triethylamine. Yield 12.2 g (78%), bp 146–148°C (5 mm Hg). IR spectrum, ν, cm^{-1}: 3134 (=CH_{Ht}), 3089, 3065, 3032 (=CH), 2971, 2934, 2875 (CH_{alk}), 1511, 1497 (C=N), (C=C). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.00 t (3H, CH_3, *J* 7.3 Hz), 2.17 m (2H, CH_2, *J* 7.3, 7.4 Hz), 4.90 t (1H, CHBr, *J* 7.4 Hz), 5.26 s (2H, CH_2), 6.27 s (1H, C^4H), 7.24 m (5H, C_6H_5). ^{13}C NMR spectrum, δ, ppm: 12.62 (CH_3), 32.05 (CH_2CH_3), 49.12 (CHBr), 52.82 (CH_2Ph), 103.50 (C^4_{Ht}), 127.19 ($C^{3,5}_{Ph}$), 127.78 (C^5_{Ht}), 127.89 (C^4_{Ph}), 128.67 ($C^{2,6}_{Ph}$), 135.74 (C^1_{Ph}), 153.38 (C^3_{Ht}). Found, %: C 49.85; H 4.21; Br 25.39; Cl 11.39; N 8.88. $C_{13}H_{14}BrClN_2$. Calculated %: C 49.95; H 4.19; Br 25.56; Cl 11.34; N 8.96.

1-[(1-Benzyl-5-chloropyrazol-3-yl)methyl]indole (III). A mixture of 1.2 g (0.03 mol) of NaOH and 5 ml of DMSO was stirred for 10–20 min, and 1.17 g (0.01 mol) of indole was added. The mixture was stirred additionally for 20–30 min, then at cooling to 18–20°C was slowly added dropwise a solution of 2.65 g (0.011 mol) of pyrazole **IIa** in 2 ml of DMSO, and the reaction mixture was stirred for 8 h at 20–22°C. Then the reaction mixture was poured into 50 ml of ice water, extracted with ethyl ether, the extract was dried with $MgSO_4$. The ether was removed in a vacuum, the residue was recrystallized from a mixture of ethyl ether and hexane. Yield 2.41 g (75%), mp 68–71°C. IR spectrum, ν, cm^{-1}: 2850, 2920, 2950 (CH_{alk}), 3130 (=C–H). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 5.27 s (2H, CH_2), 5.30 s (2H, CH_2), 5.94 s (1H, $H^4_{pyrazole}$), 6.54 d (1H, H^3_{indole}, *J* 3.1 Hz), 7.18 d (1H, H^2_{indole}, *J* 3.1 Hz), 7.22 m, 7.32 m (7H, $H^{4,7}_{indole}$, C_6H_5), 7.40 d (1H, H^5_{indole}, *J* 7.8 Hz), 7.65 d (1H, H^6_{indole}, *J* 7.8 Hz). Found, %: C 69.00; H 5.19; Cl 13.06; N 10.86. $C_{19}H_{16}ClN_3$. Calculated, %: C 71.01; H 5.02; Cl 13.08; N 10.89.

1-[(1-Benzyl-5-chloropyrazole-3-yl)methyl]-pyrrole (IV) was obtained from 2.65 g (0.011 mol) of pyrazole **IIa** and 0.68 g (0.01 mol) of pyrrole in 1.71 g (63%) yield, mp 80–85°C. IR spectrum, ν, cm^{-1}: 2850, 2920, 2950 (CH_{alk}), 3130 (=C–H). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 4.92 s (2H, CH_2), 5.27 s (2H, CH_2), 6.00 s (1H, $H^4_{pyrazole}$), 6.14 s (2H, $H^{3,4}_{pyrrole}$), 6.69 C (2H, $H^{2,5}_{pyrrole}$), 7.23 m (5H, Ph). Found, %: C 67.01; H 5.29; Cl 13.06; N 15.06. $C_{15}H_{14}ClN_3$. Calculated, %: C 66.30; H 5.19; Cl 13.05; N 15.46.

Reaction of 1-benzyl-5-chloro-3-(1-chloroethyl)-pyrazole (IIb) with indole. The reaction was carried out as described above for compound **III** using 2.80 g (0.011 mol) of pyrazole **IIb** and 1.17 g (0.01 mol) of indole. We obtained 2.4 g of a mixture containing according to ^{1}H NMR data **1-[1-(1-benzyl-5-chloropyrazol-3-yl)ethyl]indole (V)** and initial indole in a ratio 4:1.

Compound **V**. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.87 d (3H, CH_3, *J* 7.1 Hz), 5.26 s (2H, CH_2), 5.63 q (1H, CH, *J* 7.1 Hz), 5.84 s (1H, $H^4_{pyrazole}$), 6.54 d (1H, H^3_{indole}, *J* 3.1 Hz), 7.18 d (1H, H^2_{indole}, *J* 3.1 Hz), 7.22 m, 7.32 m, 7.61 m (9H, $H^{4_i-_n7}_{dole}$, C_6H_5).

Reaction of 1-benzyl-3-(1-bromopropyl)-5-chloropyrazole (IIc) with indole. The reaction was carried out as described above for compound **III** using 3.44 g (0.011 mol) of pyrazole **IIc**, 1.17 g (0.01 mol) of indole and applying 1.12 g (0.02 mol) of KOH. We obtained 2.5 g of a mixture containing according to ^{1}H NMR data compoundя **VI** and initial pyrazole **IIc** in a ratio 4:1.

1-Benzyl-3-(1-propenyl)-5-chloropyrazole (VI). IR spectrum, ν, cm^{-1}: 1664 (C=C), 2851, 2913, 2935, 2962 (CH_{alk}), 3032, 3065, 3088, 3134 (=C–H). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.82 d (3H, CH_3, *J* 6.5 Hz), 5.24 s (2H, CH_2), 6.15 m (1H, =CHMe), 6.23 s (1H, $H^4_{pyrazole}$), 6.29 m (1H, =CH), 7.23 m (5H, Ph).

***N*-(1-{1-[(1-Benzyl-5-chloropyrazol-3-yl)methyl]-indol-3-yl}-2,2,2-trichloroethyl)trifluoromethanesulfonamide (VII).** To a solution of chloral trifluoromethylsulfonylimine obtained from 2.18 g (0.01 mol) of trifluoromethanesulfonic acid *N,N*-dichloroamide and 7 ml of trichloroethylene as described in [15] was added by small portions at stirring 3.22 g of indolomethylpyrazole **III**. After 6 h the solvent was removed in a vacuum. The residue was washed with hot water, dried, twice recrystallized from hexane, and was dried in a vacuum. Yield 4.18 g (78%), mp 63°C. IR spectrum, ν, cm^{-1}: 1550, 1610 (C=N, C=C), 2950 (CH_{alk}), 3035 (=CH), 3280 (NH). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 5.22 s (2H, CH_2), 5.25 s (2H, CH_2), 5.59 s (1H, CH–CCl_3), 5.85 s (1H, $H^4_{pyrazole}$), 6.95 br.s (1H, NH), 7.12–7.38 m (8H, C_6H_5, $3H_{indole}$), 7.41 C (1H, H^2_{indole}), 7.67 d (1H, H^7_{indole}). ^{13}C NMR spectrum, δ, ppm: 44.71 (CH_2), 52.84 (CH_2), 66.53 (CH–NH), 101.47 (CCl_3), 103.78 ($C^4_{pyrazole}$), 109.06 (C^3_{indole}), 110.25 (C^4_{indole}), 119.08 (C^7_{indole}), 119.25 q (CF_3, $^1J_{C-F}$ 321.4 Hz), 120.92 (C^5_{indole}), 122.86 (C^6_{indole}), 127.34

($C^{2,6}_{Ph}$), 127.41 (C^{4a}_{indole}), 127.74 (C^{2}_{indole}), 128.21 (C^{4}_{Ph}), 128.54 ($C^{5}_{pyrazole}$), 128.89 ($C^{3,5}_{Ph}$), 135.63 (C^{1}_{Ph}), 135.71 (C^{7a}_{indole}), 148.43 ($C^{3}_{pyrazole}$). Found, %: C 44.10; H 2.80; Cl 23.58; N 9.30; S 5.30. $C_{22}H_{17}Cl_4F_3N_4O_2S$. Calculated, %: C 44.02; H 2.85; Cl 23.62; N 9.33; S 5.34.

***N*-(1-{1-[(1-Benzyl-5-chloropyrazol-3-yl)methyl]-indol-3-yl}-2,2,2-trichloroethyl)-4-chlorobenzene-sulfonamide (VIII)** was obtained from 3.22 g (0.01 mol) of indolomethylpyrazole **III** and chloral 4-chlorophenylsulfonylimine obtained from 2.61 g (0.01 mol) of *N,N*-dichloro-4-chlorobenzenesulfonamide and 7 ml of trichloroethylene as described in [14]. Yield 4.76 g (75%), mp 197–199°C. IR spectrum, ν, cm^{-1}: 1545, 1590 (C=N, C=C), 2850, 2915, 2950 (CH_{alk}), 3020, 3050, 3125 (=CH) 3255 (NH). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 5.50 d (2H, CH_2), 5.62 s (1H, CH–CCl_3), 5.66 s (2H, CH_2), 6.50 s (1H, $H^{4}_{pyrazole}$), 7.17–7.78 m (13H, C_6H_5, C_6H_4, $4H_{indole}$), 7.90 s (1H, H^{2}_{indole}), 9.36 s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 44.07 (CH_2), 52.57 (CH_2), 65.74 (CH), 103.09 (CCl_3), 104.52 ($C^{4}_{pyrazole}$), 108.88 (C^{3}_{indole}), 110.37 (C^{4}_{indole}), 118.87 (C^{7}_{indole}), 120.24 (C^{5}_{indole}), 122.02 (C^{6}_{indole}), 127.32 (C^{4a}_{indole}), 127.58, 127.92 ($C^{5}_{pyrazole}$), 128.29, 128.48, 128.56, 129.14, 129.38, 135.04, 136.72, 137.25, 139.24, 148.88 ($C^{3}_{pyrazole}$). Found, %: C 50.50; H 3.35; Cl 27.73; N 8.78; S 4.90. $C_{27}H_{21}Cl_5N_4O_2S$. Calculated, %: C 50.45; H 3.29; Cl 27.58; N 8.72; S 4.99.

{1-[(1-Benzyl-5-chloropyrazol-3-yl)methyl]indol-3-yl}sulfanylacetic acid (IX). To a solution of 3.22 g (0.01 mol) of indolomethylpyrazole **III** and 1.52 g (0.02 mol) of thiourea in 30 ml of ethanol was added dropwise in an argon flow within 30 min a solution of 2.53 g (0.01 mol) of iodine and 1.66 g (0.01 mol) of potassium iodide in 20 ml of 50% C_2H_5OH. The reaction mixture was heated at 30–40°C for 3 h, then was added dropwise 0.50 g (0.01 mol) of hydrazine hydrate and slowly was added a solution of 2.00 g (0.05 mol) of NaOH in 5 ml of water and 1.42 g (0.015 mol) of monochloroacetic acid in 5 ml of water. The reaction mixture was heated on a boiling water bath for 2 h at pH no less than 9. On completion of the reaction the ethanol was evaporated, the separated precipitate was dissolved at heating in water with activated carbon added, the solution was kept for 30–60 min, then it was filtered, and the filtrate was acidified with 10% HCl to pH 2–4, then it was maintained at 5°C at least 12 h till the product completely settled and crystallized. The precipitate was filtered off and dried in air. Yield 2.80 g (80%), mp 106–110°C. IR spectrum, ν, cm^{-1}: 1580, 1610 (C=N, C=C), 1700 (C=O), 2950 (CH_2), 3050, 3120 (=CH), 3400 (OH). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.18 s (2H, CH_2), 5.08 s (2H, CH_2), 5.11 s (2H, CH_2), 6.04 s (1H, $H^{4}_{pyrazole}$), 6.92 m, 7.07 m (9H, $4H_{indole}$, C_6H_5), 7.43 (1H, H^{2}_{indole}). Found, %: C 58.95; H 4.43; Cl 8.11; N 9.78; S 14.71. $C_{21}H_{19}ClN_3O_2S$. Calculated, %: C 58.87; H 4.47; Cl 8.17; N 9.81; S 14.94.

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