Russian Journal of Organic Chemistry, Vol. 38, No. 11, 2002, pp. 1641–1646. Translated from Zhurnal Organicheskoi Khimii, Vol. 38, No. 11, 2002, pp. 1697–1703.

Synthesis of (3-Indolylsulfanyl)alkanecarboxylic Acids

G. G. Levkovskaya, E. V. Rudyakova, and A. N. Mirskova

Faworsky Irkutsk Institute of Chemistry, Siberian Division, Russian Academy of Sciences, Irkutsk, 664033 Russia

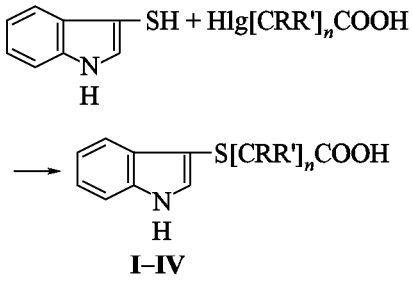
Received June 27, 2001

Abstract—A method was developed for preparation of (3-indolylsulfanyl)alkanecarboxylic acids from 1*H*-, 1-methyl(benzyl)-, 2-methylindoles, thiourea, iodine, and halocarboxylic acids.

(3-Indolylsulfanyl)alkanecarboxylic acids attract interest as biologically active substances [1], semiproducts in pharmaceutical syntheses [2–4], and as technically valuable products [5]. In extension of our systematic studies aimed at preparation of biologically active substances based on organylsulfanylalkanecarboxylic acids [6], in particular, indolylsulfanylacetic acid [7], we developed a preparative synthesis of 1*H*-, 1- and 2-methyl(benzyl)-substituted (3-indolylsulfanyl)alkanecarboxylic acids.

Previously some representatives of this class compounds were obtained by a traditional method utilizing reaction of indolethiols with halocarboxylic acids or derivatives thereof [1–3]. Therewith this method became widespread after development of 3-indolethiol preparation from equimolar amounts of indole, thiourea, and iodine [2]. But this method was unsuitable for preparative synthesis of 2-methylindole-3-thiol for in the course of reaction between 2-methylindole, thiourea, iodine, and potassium iodide formed a complex mixture of products [8].

By heating under inert atmosphere 3-indolethiol obtained by the known method [2] with equimolar amounts of bromo- or chloroalkanecarboxylic acids in the presence of alcoholic alkalis we also prepared a series of acids, both known and previously not described, (**I**–**VI**) (Tables 1, 2).



I–**IV**

Hlg = Cl, Br; *n* = 1, R = H, R' = H (**I**), CH_3 (**II**), C_2H_5 (**III**), R = R'= CH_3 (**IV**); *n* = 2, R = R'= H (**V**), *n*= 3, R = R'= H (**VI**).

However the acids **I**–**VI** were isolated in yields no more than 40–50% (Table 1). Note that indolethiol is very unstable and is easily oxidized with air oxygen to di(3-indolyl) disulfide. Therefore the (3-indolylsulfanyl)alkanecarboxylic acids obtained by condensation of indolethiol with halocarboxylic acids contained this disulfide as impurity. The additional purification both of indolethiol under inert atmosphere and of target products reduced the yield of the latter and provided complications for the process as a whole.

Aiming at developing a preparative procedure for (3-indolylsulfanyl)alkanecarboxylic acids we studied a reaction of monohalocarboxylic acids with S-(3-indolyl)isothiuronium iodide [9, 10] used instead of indolethiol. In a saturated alcoholic solution of alkali this reaction afforded acids **I**–**VI**. It should be mentioned however that here the yield of acids **I**–**VI** also was unstable and did not exceed 50%, and the products obtained also required additional purification.

To improve the yield and purity of the target products **I**–**VI** we investigated how these parameter were affected by the ratio of the initial reagents and by the order of their introducing into the reaction.

It was established that S-(3-indolyl)isothiuronium iodide could be obtained only at simultaneous bringing into reaction of thiourea and indole, and the stable yield of the product is attainted at the reagents ratio indole–thiourea–iodine of 1 : 2 : 1. This fact disagrees with the previously assumed formation mechanism of S-(3-indolyl)- and S-(2-pyrrolyl)isothiuronium salts [9, 10]. According to this mechanism first thiourea is oxidized by halogen to disulfide that again reacts with halogen furnishing the corresponding sulfenyl halide. The latter effects an electrophilic substitution of a hydrogen atom in the heterocycle to form isothiuronium salt. Basing on this scheme Harris [9, 10] recommended to use the reagents in equimolar amounts. The reaction between indoles, thiourea, and iodine was formerly studied at the reagents ratio 1 : 2 : 1 respectively. In this case with 95% yield were isolated

1070-4280/02/3811-1641$27.00 © 2002 MAIK "Nauka/Interperiodica"

Table 1. Yields, melting points, and elemental analyses of 3-indolylsulfanylalkanecarboxylic acids (**I**–**IX**)

Compd. no.	Yield, %[a]	mp, °C	Found, %				Formula	Calcd., %			
			C	H	N	S		C	H	N	S
I	84 (50)	110 [2]	57.54	4.47	6.72	15.38	$C_{10}H_9NO_2S$	57.96	4.38	6.76	15.47
II	62 (50)	95–98	59.74	4.79	6.53	14.32	$C_{11}H_{11}NO_2S$	59.73	4.98	6.33	14.48
III	69 (40)	78–80	61.97	5.38	5.90	13.30	$C_{12}H_{13}NO_2S$	61.25	5.57	5.95	13.62
IV	62 (50)	101–103	60.74	7.79	5.53	13.22	$C_{12}H_{13}NO_2S$	61.25	5.57	5.95	13.62
V	53 (50)	130–132 [3]	59.81	4.88	6.23	14.52	$C_{11}H_{11}NO_2S$	59.73	4.98	6.33	14.48
VI	60 (50)	65–68	61.44	5.38	5.83	13.51	$C_{12}H_{13}NO_2S$	61.25	5.57	5.95	13.62
VII	89	98–100	59.84	4.87	6.46	14.41	$C_{11}H_{11}NO_2S$	59.73	4.98	6.33	14.48
VIII	84	103–106	68.71	5.06	4.74	10.71	$C_{17}H_{15}NO_2S$	68.67	5.09	4.71	10.76
IX	69	150–155	59.70	5.03	6.41	14.53	$C_{11}H_{11}NO_2S$	59.73	4.98	6.33	14.48

[a] Yields obtained by method *a* is given in parentheses.

Table 2. IR and ^{1}H NMR spectra of 3-indolylsulfanylalkanecarboxylic acids (**I**–**IX**)

Compd. no.	IR spectra, ν, cm^{-1}				^{1}H NMR spectra, δ, ppm (*J*, Hz)				
	NH	Alk	COOH	C=C	Het	CH_2	CH_3	SCH_2 (SCH)	NH (COOH)
I	3350	2900	1690	1500, 1540, 1600	7.18 m, 7.48 m, 7.57 s	–	–	3.41 s	11.44[a]
II	3420	2920, 2960	1680	1440, 1485, 1600	6.90 m, 7.28 m, 7.42 s	–	1.05 d (6.6)	(3.27 q)	11.39[a]
III	3360	2900, 2940	1680	1550, 1590	7.18 m, 7.53 m, 7.69 s	1.70 m	0.96 t (7.1)	(3.29)	11.35[a]
IV	3410	2890, 2920 2970	1670	1450, 1485, 1600	7.12 m, 7.42 d, 7.46 s, 7.63 d	–	1.42 s 1.36 s	–	11.52[a]
V	3350	2920,	1660	1440, 1485	7.11 m, 7.44 d (7.8), 7.52 d (2.5), 7.64 d	2.44 t (7.1)	–	2.82 t	11.39 (12.23)
VI	3350	2890, 2910	1670	1485, 1600	7.10 m, 7.34 d, 7.55 s, 7.65 d	2.39 m 1.17 s	–	2.69 t	11.41[a]
VII[b]	–	2900, 2980	1690	1500	6.69 d (7.6), 7.11 t, 7.19 t, 7.38 d, 7.39 s	–	3.77	3.39 t	–[a]
VIII[c]	–	2900, 2940	1690	1460, 1500	7.15 m, 7.47 d (7.6), 7.75 s	5.43 m	–	3.43 s	–[a]
IX	3375	2900, 2950	1700	1630	7.06 m, 7.27 d (7.8), 7.50 d	–	2.47	3.25 s	11.25 (12.20)

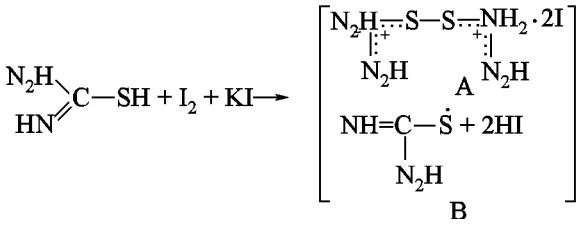
[a] Proton signal of COOH group not observed due to fast exchange with protons of water present in the solvent.
[b] ^{1}H NMR spectrum registered in acetone-d_6.
[c] Proton signals of C_6H_5, δ, ppm: 7.22 m, 7.29 m.

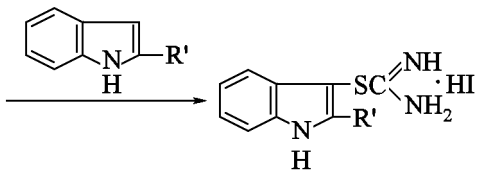
the corresponding bis(3-indolyl) disulfides. It was presumed that the disulfides arose from a succession of reactions: indole halogenation, conversion of 3-iodoindoles under the action of thiourea into isothiuronium salts that provided thiols by decomposition in alkaline medium. Finally the thiols were oxidized by iodine excess or oxygen yieldingthe disulfides. The route to isothiuronium salts presumed in [11] was found to be wrong for it was demonstrated in [10] that iodopyrrol prepared by independent procedure did not react with thiourea under similar conditions.

We established that carrying out the reaction between indole, thiourea, and iodine taken in the ratio

1 : 2 : 1 respectively under inert atmosphere furnished not a disulfide but isothiuronium iodide in a quantitative yield. Therewith the reaction time was shorter and in the reaction mixture lacked excessive iodine that could have decreased the yield of the target product by oxidizing the heterocycle and the isothiuronium salt.

The published data [9–11] and our own experiments suggest two possible routes of indolylisothiuronium salt formation. Firstly, it may be presumed that arising disulfide cation (A) reacts with indole *in statu nascendi*. It should be reminded that the preliminary prepared disulfide (A) is incapable of electrophilic substitution in the indole ring. Secondly, the substitution in the indole ring may be effected by the primarily formed thiyl radical (B).

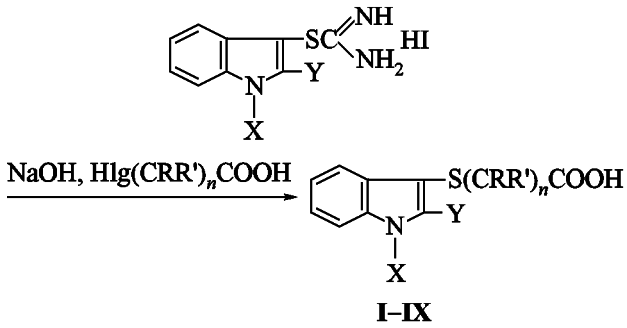




$+ NH_2C(S)NH_2 + HI + KI$

Thus the lower yield of target products at the equimolar reagents ratio is due to the mechanism of indolylthiuronium salt formation involving successive bringing into reaction of the original and recovered thiourea.

We demonstrated that the (3-indolyl)isothiuronium iodides treated without preliminary isolation with monohalocarboxylic acids in the presence of alkali afforded in high and reproducible yields indolylsulfanylalkanecarboxylic acids **I**–**X** of high purity. It was especially feasible that this process allowed preparation both derivatives of 1-methyl(benzyl)indolethiols and 2-methylindolethiol. This is obviously a very attractive possibility taking into account that the 2-methylindole-3-thiol is excessively unstable and has not been previously isolated [8].



I–IX

Hlg = Cl, Br; n = 1, R = R' = H, X = CH_3, Y = H (**VII**), X = $C_6H_5CH_2$, Y = H (**VIII**), X = H, Y = CH_3 (**IX**).

We also established that addition of hydrazine hydrate from 20 mol% with respect to indole up to an equimolar amount at the stage of reaction between isothiuronium salts and halocarboxylic acids increased the yield and purity of the target products apparently due to suppression of the side oxidation processes occurring with indolethiol and isothiuronium salts.

The reactions were carried out in methanol, ethanol, or 2-propanol. The purity of acids obtained by the developed procedure without additional purification was estimated by potentiometric titration of their methanol solutions with a solution of sodium methylate; the determined purity was ~99%.

The acids **I**–**IX** synthesized are crystalline compounds with a specific odor, of cream color, well soluble in alcohol, DMSO, insoluble in water, stable at storage. The structure of compounds synthesized was proved by IR and ^{1}H NMR spectroscopy, the composition was confirmed by elemental analysis and potentiometric titration (Tables 1, 2).

IR spectra of acids **I**–**IX** contain weak absorption bands at 1400–1600 cm^{-1} corresponding to vibrations of the heterocycle, strong bands at 1670–1700 cm^{-1} of C=O vibrations. In the spectra of compounds **I**–**VI, IX** appear the absorption bands of the NH bonds vibrations at 3350–1420 cm^{-1}.

In the ^{1}H NMR spectra of acids **I**–**IX** alongside the proton signals from the indole moiety (6.90–7.69 ppm) appear singlets from NH protons (in compounds **I**–**VI, IX**), and the signals with the characteristic splitting from the protons attached to carbon chains (Table 2). For instance, in the ^{1}H NMR spectrum of acid **II** is present a doublet from the protons of a methyl group and a quartet from the methine proton. In the spectrum of compound **III** the

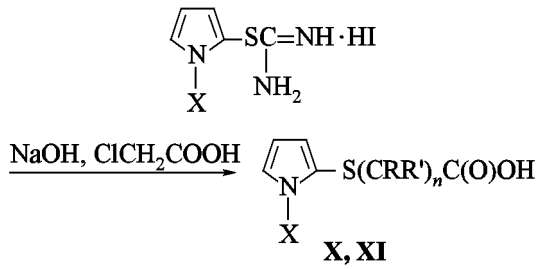
methyl group signal appears as a triplet, and the ethyl group of this compound gives rise to a triplet of the methyl group and a multiplet from the methylene group. The ^{1}H NMR spectra of acids **VI** and **VII** contain multiplets belonging to CH_2 and CH_3 groups. Note that the ^{1}H NMR spectrum of acid **IV** contains two singlets from methyl groups evidencing that the rotation is hindered in the fragment $SC(CH_3)_2COOH$ of the molecule.

The signal from protons in the groups $SCH_2C(O)$ and SCHRC(O) in the spectra of acids **I–III, VII–IX** is shifted downfield by 0.4–0.7 ppm as compared with that of the protons in the SCH_2 group in the spectra of acids **V, VI**.

It should also be noted that in the ^{1}H NMR spectra of compounds **I–III** is present a signal from the proton in the *2* position of the indole ring, and it is sometimes split with a coupling constant of ~2 Hz. In the ^{1}H NMR spectrum of compound **IX** this signal is lacking; only signals from the benzene part of the indole moiety are observed with the characteristic splittings (Table 2), and also appear the proton resonances from the alkyl part of the molecule.

The procedure described in this paper was also applied to preparation of (2-pyrrolylsulfanyl)acetic acid. It was already mentioned in [10] that 3,5-dimethyl-4-ethoxycarbonylpyrrole also afforded the corresponding (2-pyrrolyl)isothiuronium salt when reacted with thiourea and iodine.

The reaction of 1*H*- and 1-methylpyrrole with thiourea and iodine at the respective reagents ratio 1:2:1 under conditions we developed followed by treatment with monochloroacetic acid in the presence or absence of hydrazine hydrate furnished (2-pyrrolylsulfanyl)acetic acids that however contained unidentified impurity as shown by IR and ^{1}H NMR spectra.



X, XI

X = CH_3 (**X**), H (**XI**).

In the IR spectra of acids **X, XI** are present the absorption bands corresponding to vibrations of C=O bonds, pyrrole ring, and alkyl groups. In the ^{1}H NMR spectra of the compounds appear the signals of protons from pyrrole rings, OH groups, and SCH_2 of the expected intensity. At the same time in the spectra was observed unidentified singlet at 1.5 ppm.

Thus we developed preparative procedures for synthesis of a number of (3-indolylsulfanyl)alkanecarboxylic acids. It was shown that addition to the reaction mixture of hydrazine hydrate in equimolar to indole amount improved the yield and purity of the final products apparently by excluding the side oxidation processes involving indole, indolethiol, and isothiuronium salts.

EXPERIMENTAL

IR spectra were recorded on spectrophotometer Specord IR 75 from samples pelletized with KBr. ^{1}H NMR spectra were recorded on spectrometers Bruker DPX-400 (400 MHz) and Jeol FX-90 Q (90 MHz) from solutions in DMSO-d_6, internal reference HMDS.

The potentiometric titration was performed on ionomer EA-74. Initial monohalocarboxylic acids used in the study were purified by distillation. Ethanol was dried with calcium oxide. Isothiuronium disulfide diiodide (A) and 3-indolethiol were obtained by published methods [2, 9. 10]. Initial 1-methyl and 1-benzylindoles were prepared by known procedures [12, 13].

(3-Indolylsulfanyl)acetic acid (I). (a) To a dispersion of 14.9 g of 3-indolethiol in 25 ml of anhydrous ethanol at stirring was added under nitrogen or argon atmosphere a solution of 13 g of KOH in 100 ml of ethanol and a solution of 11.3 g (20% excess) of monochloroacetic acid in 50 ml of ethanol. The reaction mixture was boiled on a water bath while stirring under inert atmosphere for 3 h, then it was cooled, the alcohol was distilled off. The separated precipitate was dissolved in 150 ml of water, the solution was acidified with HCl till pH 2–4 and maintained at 5°C for 12 h for total precipitation of the product. Then the precipitate was filtered off and dried. We obtained 10.3 g (50%) of acid **I**.

(b) To a solution of 11.7 g (0.1 mol) of indole and 7.6 g (0.1 mol) of thiourea in 200 ml of methanol at stirring and bubbling nitrogen or argon was added by portions a solution of 25 g (0.1 mol) of iodine and 17 g (0.1 mol) of KI in 50 ml of water maintaining the temperature of the reaction mixture below 40°C. Then 20% solution of NaOH was added to pH 9 and a solution of 11.28 g (0.12 mol) of monochloroacetic acid. The pH of the reaction mixture was maintained

no lower than 9 by adding 20% solution of NaOH. The reaction mixture was heated to boiling for 2–4 h. Then the alcohol was distilled off, the residue was dissolved in water at heating, activated carbon was added, and the mixture was left standing for 0.5–1 h. The solution was filtered and acidified with HCl to pH 2–4 and then was kept at 20–25°C no less than 12 h to wait for complete precipitation and crystallization of the product. The precipitated acid was filtered off and dried. We obtained 10.4 g (51%) of acid **I**.

(c) To a solution of 11.7 g (0.1 mol) of indole and 15.2 g (0.2 mol) of thiourea in 200 ml of methanol at stirring and bubbling nitrogen or argon was added by portions a solution of 25 g (0.1 mol) of iodine and 17 g (0.1 mol) of KI in 50 ml of water maintaining the temperature of the reaction mixture below 40°C. Then 20% solution of NaOH was added to pH 9 and a solution of 11.3 g (0.12 mol) of monochloroacetic acid. The further procedure was the same as described under (b). We obtained 17.41 g (84%) of compound **I** of 99.1% purity as estimated by potentiometric titration of the acid methanol solution with sodium methylate.

2-(3-Indolylsulfanyl)propanoic acid (II). (a) According to procedure (a) described for acid **I** from 1.49 g of 3-indolethiol and 1.30 g (0.012 mol) of 2-chloropropanoic acid or 1.83 g (0.012 mol) of 2-bromopropanoic acid was obtained 1.11 g of acid **II**. (b) According to procedure (c) used for acid **I** from 11.7 g (0.1 mol) of indole, 15.2 g (0.2 mol) of thiourea, 25 g (0.1 mol) of iodine, 17 g (0.1 mol) of potassium iodide, and 18.3 g (0.12 mol) of 2-bromopropanoic acid was obtained 13.77 g of acid **II**.

2-(3-Indolylsulfanyl)butanoic acid (III). (a) According to procedure (a) described for acid **I** from 1.49 g of 3-indolethiol and 2.0 g (0.012 mol) of 2-bromobutanoic acid was obtained 0.94 g of acid **III**. (b) According to procedure (c) used for acid **I** from 11.7 g (0.1 mol) of indole, 15.2 g (0.2 mol) of thiourea, 25 g (0.1 mol) of iodine, 17 g (0.1 mol) of potassium iodide, and 20.4 g (0.12 mol) of 2-bromobutanoic acid was obtained 16.23 g of acid **III**.

2-(3-Indolylsulfanyl)-2-methylpropanoic acid (IV). (a) According to procedure (a) described for acid **I** from 14.9 g of 3-indolethiol and 20.4 g (0.12 mol) of 2-bromo-2-methylpropanoic acid was obtained 11.75 g of acid **IV**. (b) According to procedure (c) used for acid I from 11.7 g (0.1 mol) of indole, 15.2 g (0.2 mol) of thiourea, 25 g (0.1 mol) of iodine, 17 g (0.1 mol) of potassium iodide, and 20.4 g (0.12 mol) of 2-bromo-2-methylpropanoic acid was obtained 15.29 g of acid **IV**.

3-(3-Indolylsulfanyl)propanoic acid (V). (a) According to procedure (a) described for acid **I** from 14.9 g of 3-indolethiol and 18.3 g (0.12 mol) of 3-bromopropanoic acid was obtained 11.05 g of acid **V**. (b) According to procedure (c) used for acid **I** from 11.7 g (0.1 mol) of indole, 15.2 g (0.2 mol) of thiourea, 25 g (0.1 mol) of iodine, 17 g (0.1 mol) of potassium iodide, and 18.3 g (0.12 mol) of 3-bromopropanoic acid was obtained 11.71 g of acid **V**.

4-(3-Indolylsulfanyl)butanoic acid (VI). (a) According to procedure (a) described for acid I from 14.9 g of 3-indolethiol and 16.7 g (0.12 mol of 4-chlorobutanoic acid or 20.04 g (0.12 mol) of 4-bromobutanoic acid was obtained 12.23 g of acid **VI**. (b) According to procedure (c) used for acid **I** from 11.7 g (0.1 mol) of indole, 15.2 g (0.2 mol) of thiourea, 25 g (0.1 mol) of iodine, 17 g (0.1 mol) of potassium iodide, and 20.04 g (0.12 mol) of 4-bromobutanoic acid was obtained 14.12 g of acid **VI**.

(1-Methylindol-3-ylsulfanyl)acetic acid (VII) was prepared in the same way as compound **IX** from 13.1 g (0.1 mol) of 1-methylindole, 15.2 g (0.2 mol) of thiourea, 25 g (0.1 mol) of iodine, 17 g (0.1 mol) of potassium iodide, and 11.34 g (0.12 mol) of monochloroacetic acid. Yield of acid **VII** 19.7 g.

(1-Benzylindol-3-ylsulfanyl)acetic acid (VIII) was prepared in the same way as compound **IX** from 20.7 g (0.1 mol) of 1-benzylindole, 15.2 g (0.2 mol) of thiourea, 25 g (0.1 mol) of iodine, 17 g (0.1 mol) of potassium iodide, and 11.34 g (0.12 mol) of monochloroacetic acid. Yield of acid **VIII** 25 g.

(2-Methylindol-3-ylsulfanyl)acetic acid (IX). To a solution of 3.93 g (0.03 mol) of 2-methylindole and 4.57 g (0.06 mol) of thiourea in 30 ml of methanol at stirring under argon was added dropwise a solution of 7.62 g (0.03 mol) of iodine and 4.98 g (0.03 mol) of potassium iodide in 25 ml of water maintaining the temperature of the reaction mixture below 30°C. The reaction mixture was kept at 30–40°C for 3 h, then was added dropwise 1.5 g (0.03 mol) of hydrazine hydrate and then slowly was added a solution of 6 g of sodium hydroxide in 30 ml of water and 2.97 g of monochloroacetic acid in 5 ml of alcohol. The mixture was heated on boiling water bath for 2 h, then cooled, and the solvent was distilled off in a vacuum. The separated precipitate was dissolved in 50 ml of 1% solution of NaOH, the solution was heated with activated carbon to 60°C for 30 min, filtered, and acidified with concn. HCl till it no more get turbid at addition of the next portion of the acid. The mixture was maintained at 5°C for 12 h. We obtained 4.5 g of acid **IX**.

(1-Methylpyrrol-2-ylsulfanyl)acetic acid (X) was prepared in the same way as compound **IX** from 4.05 g (0.05 mol) of 1-methylpyrrole, 7.6 g (0.1 mol) of thiourea, 12.5 g (0.05 mol) of iodine, 8.5 g (0.05 mol) of potassium iodide, and 5.7 g (0.06 mol) of monochloroacetic acid. We obtained 6.35 g of acid **X** with an impurity of unestablished structure, mp 67°C. IR spectrum, ν, cm^{-1}: 1700 (COOH), 1520 (C=C). ^1H NMR spectrum, δ, ppm: 3.02 s (3H, NCH_3), 3.25 s (2H, SCH_2), 6.08 d (1H, pyrrole, *J* 3.4 Hz), 6.31 d (1H, pyrrole, *J* 3.4 Hz), 7.33 br (1H, pyrrole) (in the spectrum is present a signal at 1.56 ppm corresponding to 3H). Found, %: C 48.50; H 5.91; N 7.11; S 14.89. $C_7H_9NO_2S$. Calculated, %: C 49.11; H 5.30; N 8.18; S 18.73.

(2-Pyrrolylsulfanyl)acetic acid (XI) was prepared in the same way as compound **IX** from 6.7 g (0.1 mol) of pyrrole, 15.2 g (0.2 mol) of thiourea, 25 g (0.1 mol) of iodine, 17 g (0.1 mol) of potassium iodide, and 11.5 g (0.12 mol) of monochloroacetic acid. Yield of acid XI 2.85 g with an impurity of unestablished structure, mp 140–142°C. IR spectrum, ν, cm^{-1}: 3350 (NH), 1690 (COOH), 1620, 1550 (C=C). ^1H NMR, δ, ppm: 3.48 br (2H, SCH_2), 6.11 br (2H, pyrrole), 6.75 br (1H, pyrrole), 10.64 br.s. (1H, NH), 11.22 br.s (1H, OH) ((in the spectrum is present a signal at 1.52 ppm corresponding to 3H) Found, %: C 44.45; H 4.89; N 7.81; S 19.00. $C_6H_7NO_2S$. Calculated, %: C 45.85; H 4.49; N 8.91; S 20.40.

Similar results were obtained at addition in the course of the process of hydrazine hydrate in amount equimolar to pyrrole.

REFERENCES

1. Nagargjan, K., Aryav, P., Partasarathy, T.N., Shenou, S., Shah, R.K., and Kulkarni, J.S., *Ind. J. Chem. Sect. B*, 1981, vol. 20, pp. 672–679; *Chem. Abstr.*, vol. 96, 142615k.
2. Bourdais, J. and Lorre, A., *Eur. J. Med. Chem.-Chim. Ther.*, 1974, vol. 9, no. 3, pp. 269–273; Chem. Abstr., 1975, vol. 82, 31199.
3. Harris, R.L.N. and Geissler, A.E., *Austral. J. Plant. Physiol.*, 1977, vol. 4, no. 2, p. 235; *Chem. Abstr.*, 1977, vol. 87, 79499.
4. US Patent 4059583, 1977; *Ref. Zh. Khim.*, 1978, 14O 115P.
5. Levkovskaya, G.G., Mirskova, A.N., and Bel'kova, O.N., *Zh. Prikl. Khim.*, 1996, vol. 69, no. 12, pp. 2034–2037.
6. Levkovskaya, G.G., Mirskova, A.N., Kalikhman, I.D., and Voronkov, M.G., *Zh. Org. Khim.*, 1984, vol. 20, no. 3, pp. 634–638; Nefedova, T.V., Kazimirovskaya, V.B., Levkovskaya, G.G., Bryuzgin, A.A., Guseva, S.A., Mirskova, A.N., and Voronkov, M.G., *Khim.-Farm. Zh.*, 1986, no. 3, pp. 291–295; Nefedova, T.V., Kubatiev, A.L., Kazimirovskaya, V.B., Chernyakhovskaya, B.I., Mirskova, A.N., Guseva, S.A., Levkovskaya, G.G., and Voronkov, M.G., *Khim.-Farm. Zh.*, 1988, no. 10, pp. 1197–1203.
7. RF Patent 2086239, 1997; *Byull. Izobr.*, 1997, no. 22; RF Patent 2080861, 1997; *Byull. Izobr.*, 1997, no. 16; RF Patent 2108100, 1998; *Byull. Izobr.*, 1998, no. 10, p. 153.
8. Hino, T., Endo, M., and Nakagava, M., *Chem. Pharm. Bull.*, 1974, vol. 22, no. 11, p. 2728.
9. Harris, R.L.N., *Tetrahedron Lett.*, 1969, no. 51, pp. 4465–4467.
10. Harris, R.L.N., *Tetrahedron Lett.*, 1968, no. 37, pp. 4045–4047.
11. Woodbridge, R.G. and Dougherty, G., *J. Am. Chem. Soc.*, 1950, vol. 72, no. 9, pp. 4320–4321.
12. Suvorov, N.N., Smushkevich, Yu.I., Velezheva, V.S., Rozhkov, V.S., and Simakov, S.V., *Khim. Geterotsikl. Soed.*, 1976, no. 2, pp. 191–193.
13. Pozharskii, A.F., Anisimova, V.A., and Tsupak, E.B., *Prakticheskie raboty po khimii geterotsiklov* (Practicum on Chemistry of Heterocycles), Rostov: PGU, 1988, p. 22.