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SYNTHESIS AND REDOX PROPERTIES OF PYRROLEDITHIOCARBOXYLIC ACID ESTERS

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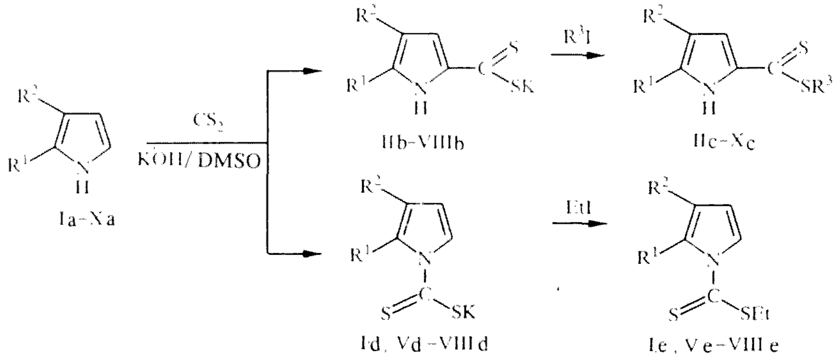
Pyrrole-2-dithiocarboxylates were obtained by reacting alkylpyrroles with carbon disulfide in the presence of alkyl halides in the KOH–DMSO system. The pyrrole and its aryl derivatives were primarily converted into pyrrole-1-dithiocarboxylates in these conditions. The electronic structure and redox properties of the synthesized compounds were investigated by polarography and cyclic voltammetry.

The heightened interest in compounds containing a dithiocarboxylate function, including pyrroledithiocarboxylic acids and their derivatives, is due to the high chemical potential of this series of compounds, their biological activity, and other practically useful properties [1-4].

Pyrroledithiocarboxylates are synthesized from pyrroles and carbon disulfide, and both 2- and 3- and 1-dithiocarboxylates can be products as a function of the conditions of the reaction [3, 4]. In the last case, the reaction is usually conducted in aprotic solvents in the presence of bases [3].

We recently communicated [5, 6] that substituted pyrroles in the KOH–DMSO system easily react with carbon disulfide and alkyl halides, forming either selectively [for example, in the case of 4,5,6,7-tetrahydroindole (IIa)] pyrrole-2-dithiocarboxylate IIc with a yield greater than 70% [5], or a mixture of 1- and 2-isomeric dithiocarboxylates (for example, 2-phenylpyrrole (Va) in analogous conditions yields both expected structural isomers Vc and Ve in the ratio of 2:1) [6].

To obtain a deeper understanding of this reaction and establish the limits of its applicability and the factors affecting its selectivity, we investigated the reaction of a series of substituted pyrroles with carbon disulfide and alkyl halides in the KOH–DMSO system (room temperature, 4-6 h).



R^3 = Et: R^1 = R^2 = H (I), R^1–R^2 = $(CH_2)_4$ (II); R^1 = *n*-Pr, R^2 = Et (III); R^1 = *n*-Bu, R^2 = *n*-Pr (IV); R^1 = Ph, R^2 = H (V); R^1 = Ph, R^2 = *n*-Pr (VI); R^1 = *p*-ClC_6H_4, R^2 = H (VII); R^1 = 2-naphthyl, R^2 = H (VIII); R^3 = R^1 = *n*-Pr, R^2 = Et (IX); R^1 = *n*-Bu, R^2 = *n*-Pr (X)

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TABLE 1. Characteristics of Synthesized Compounds IIc-Xc, Ie, VIe-VIIIe*

Compound	Empirical formula	mp, °C	d_4^{20}	PMR spectrum, δ, ppm (CDCl$_3$)					Yield, %
				R^1	R^2	R^3	R^4	H-3	
IIIc	$C_{12}H_{19}NS_2$	–	1,1009	1,21 (Me); 1,62 (CH$_2$); 2,50 (CH$_2$)	0,90 (Me), 2,40 (CH$_2$)	1,32 (Me); 3,35 (CH$_2$S)		6,9	69
IVc	$C_{14}H_{23}NS_2$	–	1,1006	0,92 (Me); 1,50 (CH$_2$), 2,58 (CH$_2$)	0,92 (Me); 1,51 (CH$_2$), 2,33 (CH$_2$)	1,32 (Me); 3,38 (CH$_2$S)		6,88	71
VIc	$C_{16}H_{19}NS_2$	32...33	–	7,43 (Ph)	0,98 (Me), 1,65 (CH$_2$); 2,60 (CH$_2$)	1,40 (Me); 3,38 (CH$_2$S)	-	7,03	30
VIIc	$C_{13}H_{12}ClNS_2$	60...61	–	7,34 (Ph)	6,59 (H-4)	1,36 (Me), 3,38 (CH$_2$S)		7,16	38
VIIIc	$C_{17}H_{15}NS_2$	62...63	–	7,69...8,01 (naphthyl)	6,72 (H-4)	1,39 (Me), 3,41 (CH$_2$S)		7,16	30
IXc	$C_{13}H_{21}NS_2$	–	1,1132	1,10 (Me); 1,69 (CH$_2$), 2,52 (CH$_2$)	0,98 (Me), 2,41 (CH$_2$)	1,21 (Me); 1,69 (CH$_2$); 3,35 (CH$_2$S)		6,90	75
Xc	$C_{15}H_{25}NS_2$	–	1,0374	0,80 (Me); 1,45 (CH$_2$)	0,80 (Me); 1,45 (CH$_2$)	1,19 (Me), 3,21 (CH$_2$S)		6,78	69
Ie	$C_7H_9NS_2$	–	1,1625	6,27 (H-5)	7,68 (H-4)	1,36 (Me), 3,32 (CH$_2$S)	7,68	6,27	63
VIe	$C_{16}H_{19}NS_2$	–	Oil	7,28 (Ph)	0,84 (Me), 1,48 (CH$_2$); 2,30 (CH$_2$)	1,34 (Me), 3,15 (CH$_2$S)	7,50	6,19	44
VIIe	$C_{13}H_{12}ClNS_2$	29...30	–	7,25 (Ph)	6,35 (H-4)	1,30 (Me), 3,21 (CH$_2$S)	7,42	6,25	37
VIIIe	$C_{17}H_{15}NS_2$	50...51	–	7,35...7,80 (naphthyl)	6,26 (H-4)	1,19 (Me); 3,14 (CH$_2$S)	7,29	6,43	36

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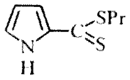
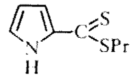
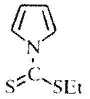
*The characteristics of compounds IIc, Vc, and Ve are reported in [6].

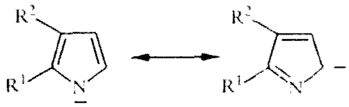
TABLE 2. Dipole Moments of Pyrroledithiocarboxylates (benzene, 25°C)

Compound	R^1	R^2	R^3	μ, D
IIc	$(CH_2)_4$		Et	2,32
IIIc	Pr	Et	Et	2,48
IXc	Pr	Et	Pr	2,42
Xc	Bu	Pr	Pr	2,43
Vc	Ph	H	Et	1,72
Ie	H	H	Et	2,04

TABLE 3. Calculated Dipole Moments of Pyrroles as a Function of the Orientation of the Alkyl Group Relative to the C=S Bond

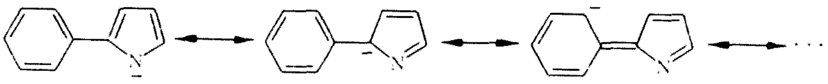
Compound		Configuration		
		cis	*trans*	*gauche*
XII		1,4	2,2	1,8
XIII		2,0	4,0	3,1
Ie		0,5	1,8	2,1

It was found that this reaction is general in character and pyrroles with different substituents, including alkyl and aryl substituents, participate in it. The effect of the substituents on the ratio of pyrrole-1- and pyrrole-2-dithiocarboxylates (Ve-VIIIe):(Vc-VIIIc) formed (Table 1) confirms the conclusion in [6] concerning the change in the nature of ambident pyrrole anions XI as a function of the structure of radicals R^1 and R^2.



XI

Electron-donor alkyl substituents (compounds IIa-IVa) probably concentrate the negative charge in the pyrrole ring and shift the electron density to the $C_{(2)}$ atom, thus facilitating formation of C-adducts IIc-VIIIc, while electron-acceptor aryl substituents on the contrary redistribute the charge from the pyrrole ring to the substituent.



Since the anionic center in position 5 of the pyrrole ring is sterically inaccessible in this case, the carbon disulfide is primarily attacked by the nitrogen atom, and for this reason, the probability of formation of N-dithiocarbamates Ve-VIIIe increases.

The reaction of the unsubstituted pyrrole with carbon disulfide in this system, as in the cases described in the review in [3], exclusively leads to formation of the N-substituted adduct with a yield of 63%.

TABLE 4. Values of $E_{1/2}$ (*V*) and *i*/C (mA/mmole) for Compounds Ie, IIc-VIIIc, VIe-VIIIe

Compound	Anode wave		Cathode waves					
			I		II		III	
	$E_{1/2}$	i/C	$E_{1/2}$	i/C	$E_{1/2}$	i/C	$E_{1/2}$	i/C
IIc	+0,29	3,77	-1,65	3,86	-2,67	7,78		
IIIc	+0,33	3,25	-1,63	3,10	-2,66	6,25		
IVc	+0,28	2,98	-1,83	2,45	-2,66	7,12		
Vc	+0,29	3,30	-1,45	3,60	-2,34	9,88		
VIc			-1,44	2,81	-2,24	4,00		
VIIc	+0,24	2,55	-1,38	3,00	-2,15	7,82	-2,81	2,88
VIIIc	+0,23	3,29	-1,99	3,40	-2,11	10,0	-2,62	4,85
Ie			-1,56	4,60	-2,65	4,60		
VIe			-1,53	2,47	-2,63	2,46		
VIIe			-1,44	3,72	-2,47	3,26		
VIIIe			-1,46	3,45	-2,54	12,00		

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*In the presence of compound VIc, the value of the anode current was greater than the background current, and a maximum was observed in the background anode discharge.

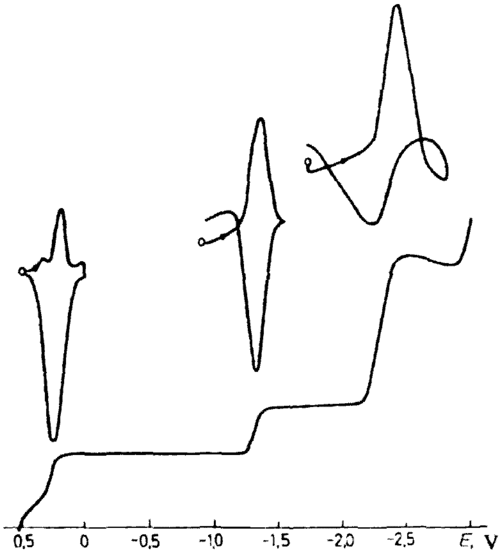


Fig. 1. Polarogram and cyclic voltamperogram (1 V/sec potential scanning rate) of electrochemical processes of 5-phenyl-2-pyrroledithiocarboxylic acid ethyl ester (Vc).

Pyrrole-2- and pyrrole-1-dithiocarboxylates IIc-Xc, Ie, Ve-VIIIe (Table 1), purified by column chromatography (Al_2O_3, hexane), are yellow or orange crystals with low melting points. Pyrrole-1-dithiocarboxylate Ie is a yellow liquid (due to the color, it was not possible to determine the refractive index), and compound VIe is an oil.

The structure of the synthesized compounds was confirmed by IR and PMR spectroscopy. The IR spectra of all of the pyrroles contain absorption bands of a C=S group in the 1200-1270 cm^{-1} region. The bands characteristic of a NH group (3300-3390 cm^{-1}) disappear, and a broad, intense band in the region of 1300 cm^{-1}, which can be assigned to C−N bond stretching vibrations, appears in the IR spectra of all of the pyrroles [7].

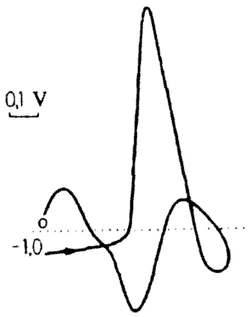


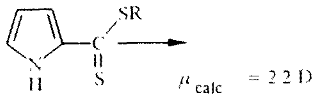
Fig. 2. Cyclic voltamperogram of the first cathode wave of pyrrole-1-dithiocarboxylic acid ethyl ester (Ie) (1 V/sec potential scanning rate).

The signals from pyrrole ring α-protons which exist for pyrrole-1-dithiocarboxylates Ie, Ve-VIIIe are not present in the PMR spectra (Table 1) of pyrrole-2-dithiocarboxylates IIc-Xc. The position, multiplicity, and integral intensities of the signals totally correspond to the structure of compounds IIc-Xc, Ie, Ve-VIIIe.

Their dielectric constants were measured to establish the geometric structure of these pyrroles.

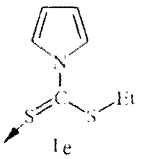
It was found that the dipole moments μ of pyrrole-2-dithiocarboxylates IIc, IIIc, IXc, and Xc containing alkyl substituents in the pyrrole ring are virtually not a function of their structure (Table 2). Introduction of a phenyl group in position 5 of the pyrrole ring (compound Vc) decreases the value of μ, as in the case of NH-pyrroles [8].

The dipole moments of the two possible planar isomers of pyrrole-2-dithiocarboxylic acid propyl esters were calculated with a vector-additive scheme (Table 3, compounds XII, XIII). The best agreement with the experimental value of μ was obtained for isomer XII with *trans*-orientation of the C═S and S−R bonds.



The calculated dipole moment μ_{calc} is directed along the C−C bond joining the dithiocarbonyl group with the pyrrole ring.

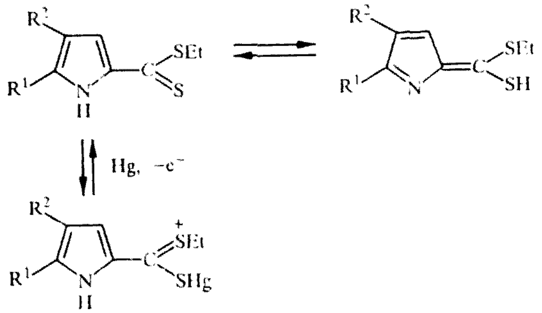
The dipole moment of N-substituted pyrrole Ie is 2.04 D and corresponds to the ethyl group going out of the plane (Table 2, *gauche*-conformer).



Ie

Electrochemical methods were used for studying the electronic structure and redox properties of pyrrole-2- IIc-Xc and pyrrole-1-dithiocarboxylates Ie, Ve-VIIIe: polarography and cyclic voltammetry on a dropping mercury electrode in a solution of 0.1-0.05 M Bu_4NClO_4 in DMF. Both anode and cathode waves are observed in the polarogram of pyrrole-2-dithiocarboxylates (IIc-Vc, VIIc, VIIIc) (Table 4). The anode waves are single-electron, reversible [$\Delta E/\Delta \log i/(i_s - I)$ of 60 mV, the reduction peak corresponds to the oxidation peak on the cyclic voltammetric curve, and the difference between them is 60 mV] and is complicated by adsorption phenomena (Fig. 1).

The ability of thioketones, whose thiocarbonyl group is stabilized by electron-donor substituents, to participate in anode processes has been correlated with enthiolization [9, 10], and if this is not possible, with dual reactivity [10] or a tendency toward complexation with the electrode material [11].



The anode process of pyrrole-2-dithiocarboxylates is due to the reactivity of the dithiocarboxylate group, as the values of the oxidation potential and the whole number of electrons in the anode and cathode processes indicate.

The anode processes in the case of pyrrole-2-dithiocarboxylates indicate a significant negative discharge on the sulfur atom of the thiocarbonyl group.

The dependence of $E_{1/2}$ on the concentration of depolarizer, the shape of the cyclic voltammetric curve (Fig. 1), and the region of potentials in which anode processes are observed for the C(=S)SR group indicate formation of mercaptides [11-15].

Anode processes were not observed for pyrrole-1-dithiocarboxylate derivatives (Ie, VIe-VIIIe).

The number and position of the cathode waves and the magnitude of the current are a function of the position of the C(=S)SR group and substituent in the ring.

The first cathode wave for all compounds was observed in the range of −1.3 to −1.6 V and corresponds to reversible transfer of one electron, but the oxidation peak is significantly smaller than the reduction peak on the cyclic voltammetric curve for compound Ie, although the difference in their potentials is greater than 60 mV (Fig. 2).

For pyrrole-1- and pyrrole-2-dithiocarboxylates, the cathode processes are caused by reduction of the thiocarbonyl group in the dithiocarboxylate fragment. In the case of pyrrole-1-dithiocarboxylates, the potential of the first cathode wave is less dependent on the substituent in the pyrrole ring, and the second cathode wave corresponds to one-electron reduction of a radical anion if R = naphthyl (compound VIIIe), and the current of the second wave corresponds to a three-electron process.

For pyrrole-2-dithiocarboxylates IIc-VIIIc, incorporation of substituents which increase the conjugation in the molecule such as Ph, 4-ClC_6H_4, and naphthyl, shifts $E_{1/2}$ to less negative potentials, i.e., facilitates reduction and increases the number of electrons that participate in the process (Table 4, compounds VIIc, VIIIc).

The region of the potentials of both anode and cathode processes and the whole number of electrons participating in them indicate that compounds IIc-Xc, Ie, Ve-VIIe are in the form of a thiocarbonyl tautomer in a basic aprotic solvent (DMF).

EXPERIMENTAL

The IR spectra of the pyrroles were recorded on a Specord IR-75 in a microlayer (compounds IIIc, IVc, IXc, Xc, Ie) or in KBr pellets (compounds VIc, VIIc, VIIIc, VIIe, VIIIe). The ^1H NMR spectra were recorded on a Tesla BS-567A spectrometer (100 MHz), $CDCl_3$ solvent. The polarographic measurements were performed on a LP-7 polarograph with a dropping mercury electrode (m = 1.43 mg/sec, t = 4.47 sec without electrode polarization in MeOH:H_2O, 1:1). The cyclic voltammetric curves were recorded with a PO-5122 model 0-3 oscillographic polarograph. The half-wave potentials referred to a saturated Calomel electrode. A 0.05-0.1 M solution of Bu_4NClO_4 prepared by neutralization of perchloric acid with tetrabutylammonium hydroxide, Bu_4NOH, with subsequent recrystallization, was used as the base electrolyte. The necessary degree of purity was monitored by polarography. DMF was purified with the method described in [16]. The concentration of depolarizer in the solution was 0.2-1.5 mM.

The dielectric constant (ε) of benzene solutions of these pyrroles were measured on an Epsilon instrument from Angarsk Experimental Design Office for Automation at a frequency of 1 MHz in a platinum cell with constant capacitance. The measurements were performed at 298 K, and the dipole moments were calculated with the Higashi equation.

The course of the reaction and purity of the compounds obtained were monitored by thin-layer chromatography on Silufol UV-254 in hexane–ether system, 1:1.

Pyrrole-1-dithiocarboxylic Acid Ethyl Ester (Ie). A mixture of 1.68 g (25 mmole) of pyrrole Ia and 2.8 g (50 mmole) of KOH in 40 ml of DMSO was stirred for 30 min, and 3.9 g (50 mmole) of carbon disulfide was added and held at room temperature for 2 h. Then 3.9 g (25 mmole) of ethyl iodide was added and stirred for 2 h. The reaction mixture was diluted with water (80 ml) and extracted with ether. After elimination of the ether, the residue was passed through a column packed with aluminum oxide with hexane as eluent. Then 0.3 g of diethyl disulfide and 2.6 g (63%) of pyrrole Ie were separated.

Pyrrole-2-dithiocarboxylic acid esters IIc-Vc were prepared analogously from the corresponding pyrroles, carbon disulfide, and ethyl iodide, and pyrroles IXc, Xc were obtained from pyrroles, carbon disulfide, and propyl iodide.

Reaction of 5-Naphthylpyrrole with Carbon Disulfide and Ethyl Iodide. A mixture of 1.93 g (10 mmole) of 5-naphthylpyrrole and 1.12 g (20 mmole) of KOH in 20 ml of DMSO was stirred for 30 min, and 1.52 g (20 mmole) of carbon disulfide was added and held for 4 h. Then 1.56 g (10 mmole) of ethyl iodide was added and stirred for 2 h. The reaction mixture was diluted with water (40 ml) and extracted with ether. After elimination of 'the ether, the residue was chromatographed on aluminum oxide with hexane as eluent. Then 0.2 g of diethyl disulfide, 0.88 g (30%) of 5-naphthylpyrrole-1-dithiocarboxylic acid ethyl ester (VIIIe), and 1.078 g (36%) of 5-naphthyl-2-dithiocarboxylic acid (VIIIc) were separated.

Pyrroles Vc and Ve, VIc and VIe, and VIIc and VIIe were obtained similarly from the corresponding pyrroles, carbon disulfide, and ethyl iodide.

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