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Dedicated to the Full Member of the Russian Academy of Sciences G.A. Tolstikov on occasion of his 75th anniversary

Incomparably Easy Migration of Functionalized Enol Substituent in Pyrrole Ring

L. N. Sobenina, V. N. Drichkov, O. V. Petrova, I. A. Ushakov, T. V. Kashik, L. B. Krivdin, Yu. Yu. Rusakov, E. V. Zykova, A. I. Mikhaleva, and B. A. Trofimov

Faworsky Irkutsk Institute of Chemistry, Siberian Division, Russian Academy of Sciences, Irkutsk, 664033 Russia
e-mail: boris_trofimov@irioch.irk.ru

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Abstract—Functionalized pyrroleьvьe enols, 2-(1-hydroxy-2,2-dicyanoethenyl)-1-methylpyrroles, at heating (75–135°C) unexpectedly readily rearranged in high yield into 3-isomers. Evidently the migration of the enol fragment involves a mesomeric zwitterion formed as a result of an intra- and intermolecular autoprotonation of the pyrrole ring by the acidic enol hydroxy group. Under similar conditions no migration of the ethenyl moiety occurred in 2-(1-hydroxy-2-carbamoyl-2-cyanoethenyl)-1-methylpyrroles. The quantum-chemical calculations (MP2/6-311G**) show a clear-cut distinction in the relative stability of 2- and 3-isomers of 1H- and 1-methylhydroxyethenylpyrroles: in the former case the 2-isomer is more stable, whereas in the 1-methyl-substituted compound, the 3-isomer.

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C-Ethenylpyrroles are extensively studied building blocks for the synthesis of versatile members of the pyrrole series, especially of fused heterocycles related to pyrrole [1]. Their structure is present in the molecules of many life-supporting systems (porphyrins, vitamin B_{12}, bile pigments, prodigiosins, myoglobin and hemoglobin performing oxygen transport in live bodies of mammals, and chlorophyll playing the key role in photosynthesis processes, i.e., in the photocatalytic transformation of the solar energy [2]).

Taking in consideration the unique role of C-ethenylpyrroles in the living matter the development of their syntheses is an important task (especially procedures for preparation of C-ethenylpyrroles with functional groups attached to the double bond).

Among the functional vinyl compounds enols and their reactive cationic intermediates are now the most intensively investigated [3, 4]; therewith a great attention is focused on heterocyclic enols [4].

The combination of an enol and a pyrrole moieties in one molecule may result in a synergic effect of these important chemical functions and can significally extend the application limits of polyfunctional C-ethenylpyrrole compounds.

Our research in the field of the chemistry of functionally-substituted C-ethenylpyrroles led to the development of a simple and efficient preparation method for stable enols of the pyrrole series, 2-(1-hydroxy-2-cyanoethenyl)pyrroles [5], important intermediates and models of transformations in DNA and enzymes [6]. However their regioisomers, 3-(1-hydroxy-2-cyanoethenyl)-pyrroles, up till now were virtually inaccessible. The development of synthetic method for these compounds is an urgent target, the more so because it is far more difficult to synthesize 3-substituted pyrroles than their 2-isomers for the majority of electrophilic substitution reactions and the metallation of N- substituted pyrroles occurs mainly at the α-position in the pyrrole ring.

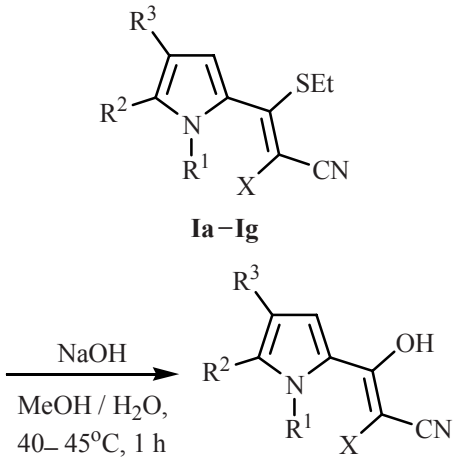
We discovered recently an unexpected easy migration of an enol function from the α- into the β-position of the pyrrole ring on an example of 2-(1-hydroxy-2,2-dicyanoethenyl)-1-methyl-4,5,6,7-tetrahydroindole [7]. This rearrangement in event of its general character might open the route to highly functionalized ethenylpyrroles with an enol substituent in the position *3*.

The target of the present study was establishing the application limits of this rearrangement, acquiring new information on its rules and specific features, and also extending the series of functionally substituted 3-(1-

hydroxy-2-cyanoethenyl)pyrroles, important key synthetic intermediates for preparation of potential pharmacophores and materials for optronics.

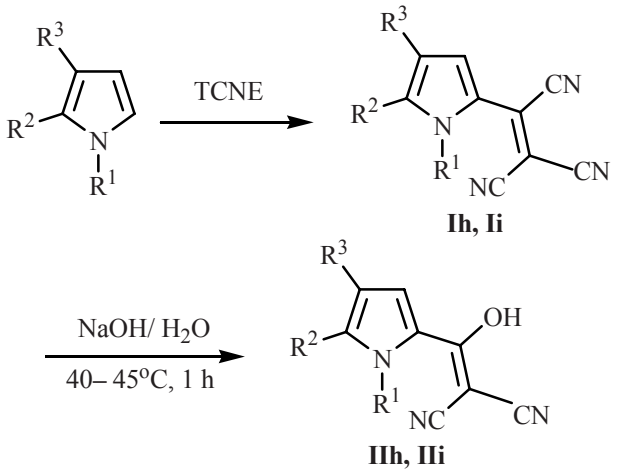
To this end we synthesized and tested under the conditions of the rearrangement [7] NH- (**IIa–IId**) and NMe- (**IIe–IIi**) -2-(1-hydroxy-2-cyanoethenyl)pyrroles, measured their acidity, and carried out a quantum-chemical evaluation of the relative stability of the corresponding 2- and 3-isomers.

Scheme 1.



R^1 = H, R^2 = Pr, R^3 = Et, X = CN (**a**); R^1 = H, R^2 = Bu, R^3 = Pr, X = CN (**b**); R^1 = R^3 = H, R^2 = Ph, X = CN (**c**); R^1 = R^3 = H, R^2 = Ph, X = $CONH_2$ (**d**); R^1 = Me, R^2,R^3 = $(CH_2)_4$, X = CN (**e**); R^1 = Me, R^2 = R^3 = H, X = $CONH_2$ (**f**); R^1 = Me, R^2,R^3 = $(CH_2)_4$, X = $CONH_2$ (**g**).

Scheme 2.



R^1 = Me, R^2 = R^3 = H (**h**); R^1 = Me, R^2 = Pr, R^3 = Et (**i**).

Two approaches were used in the synthesis of enols **IIa–IIi**: the exchange of EtS group in 2-(2-cyano-1-ethylsulfanylethenyl)pyrroles **Ia–Ig** (Scheme 1) and substitution of cyano by hydroxy group in 2-(1,2,2-tricyanoethenyl)-pyrroles **Ih** and **Ii**, (Scheme 2) by procedures [5] and [8] respectively.

It was considered formerly that tricyanoethenylation of 1-methylpyrrole with tetracyanoethylene (TCNE) in acetone selectively provided 2-tricyanoethenylpyrrole [8]. However we found that not only in acetone but also in THF and DMSO this reaction resulted in a mixture of 2- and 3-tricyanoethenylpyrroles [the ratio **Ih:Ij** = 30:70 (acetone), 15:85 (THF), 75:25 (DMSO)] (Scheme 3).

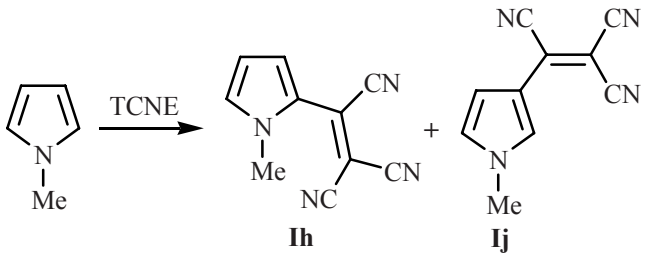
Further in the synthesis of enols **IIh** and **IIIh** we used the mixture prepared in acetone. After its hydrolysis (40–45°C, 1 h) and workup the ratio of enols **IIh:IIIh** = 8:92.

The tricyanoethenylation of 1-methyl-2-propyl-3-ethylpyrrole in DMSO proceeded selectively and provided tricyanoethenylpyrrole (**Ii**) in 51% yield.

As mentioned above, 2-(1-hydroxy-2,2-dicyanoethenyl)-1-methyl-4,5,6,7-tetrahydroindole (**IIe**) uncommonly easily rearranged into 3-(1-hydroxy-2,2-dicyanoethenyl)-1-methyl-4,5,6,7-tetrahydroindole (**IIIe**) (Scheme 4). At boiling pyrrole **IIh** unsubstituted in positions *4* and *5* in benzene, toluene, and *o*-xylene for 5 min was convertied into 3-isomer to 3, 4, and 8% respectively (^{1}H NMR data). At longer heating (1 h) in toluene (105°C) and *m*-xylene (135°C) the conversion of reagent **IIh** was respectively 60 and 95%. However in the last case the rearrangement was accompanied with tarring hampering the isolation of 3-isomer **IIIh**. The latter was prepared by boiling in toluene for 1 h of the mixture of 2- and 3-(1-hydroxy-2,2-dicyanoethenyl)-1-methylpyrroles (**IIh** and **IIIh**), hydrolysis products of the corresponding tricyanoethenylpyrroles **Ih** and **Ij**.

The findings obtained suggest that the alkyl substituents in the pyrrole ring accelerate the isomerization.

Scheme 3.

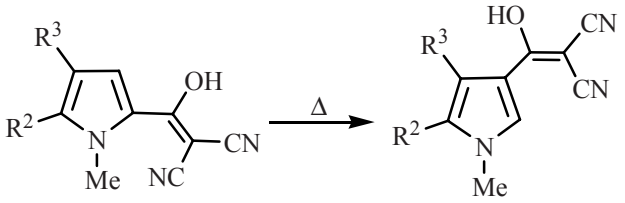


This is confirmed by the high yield (90%) of 3-(1-hydroxy-2,2-dicyanoethenyl)-1-methylpyrrole (**IIIi**), obtained by heating in toluene (105°C, 1 h) its 2-isomer **IIi**.

The observed rearrangement is unique for pyrrole chemistry since the thermal migration of substituents occurs at considerably higher temperature and as a rule led to the prevailing formation of α-isomers [9]. The migration from the α- into the β-position of the pyrrole ring proceeded relatively easily only in the presence of acids and was characteristic of mainly electron-acceptor moieties [10]. We showed that acid addition did not increase the conversion of α- into β-isomer. For instance, pyrrole **IIh** isomerization on boiling in benzene in the presence of a catalytic quantity of HCl proceeded similarly to the reaction without acid, approximately to 3–5%. At the same time in the presence of HCl degradation process of the pyrrole ring intensified (^{1}H NMR data).

Apparently the ready migration of the enol fragment from the α- into the β-position originated from the sensitivity of the pyrrol ring to protonation combined with the enhanced acidity of the hydroxy group of the

Scheme 4.

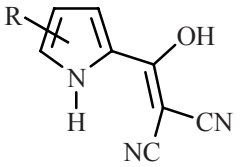


IIe, IIh, IIi **IIIe, IIIh, IIIi**

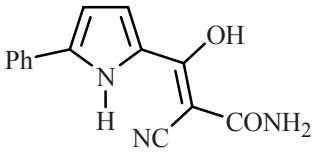
functionalized enol substituent (due to the effect of two strong electron-acceptor groups). Actually, as showed our measurements (see the table), enols **IIa–IIc**, **IIe, IIh**, and **IIi** proved to be strong acids (pK_a 5–6) comparable in the acidity with the picric acid (pK_a in methanol 4.8 [11]).

Therefore the rearrangement mechanism may be represented by Scheme 5: An intramolecular autoprotonation of the α-position of the pyrrole ring leads to the formation of a zwitterion **A** that through the isomer form **B** transforms into zwitterion **C**. The process is completed by a proton transfer in the zwitterion **C** from position *3* of the pyrrole ring to the oxygen atom.

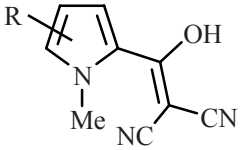
Acidity constants of enols in methanol



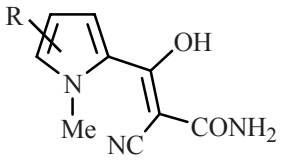
IIa–IIc



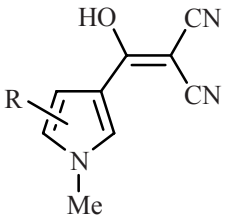
IId



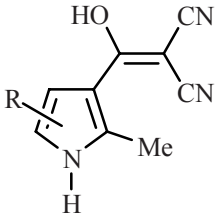
IIe, IIh, IIi



IIe, IIg



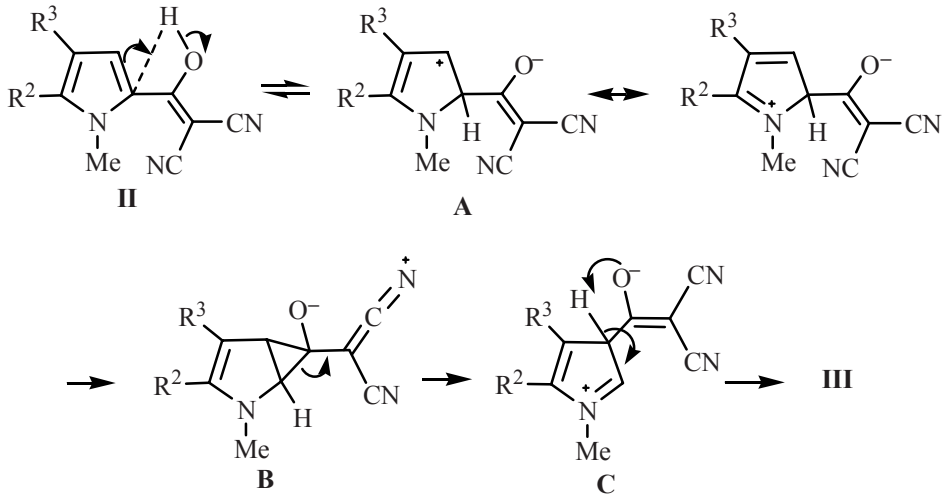
IIIe, IIIh, IIIi



IIIk, IIIl

Compd. no.	pK_a	Compd. no.	pK_a
IIa	5.37	**IIh**	5.25
IIb	5.50	**IIi**	5.72
IIc	5.28	**IIIe**	6.09
IId	8.76	**IIIh**	5.79
IIe	5.67	**IIIi**	6.69
IIf	8.35	**IIIk**	6.77
IIg	9.04	**IIIl**	6.35

Scheme 5.



An intermolecular protonation of a pyrrole ring of one molecule by the enol hydroxyl of another molecule also cannot be excluded.

The importance of the hydroxy proton in the course of the rearrangement was proved by no isomerization at heating ethylsulfanyl- (**Ia–Ig**) or cyano (**Ih** and **Ii**) analogs.

The relative stability of 2- and 3-isomers was estimated by quantum-chemical calculation of relative energies of pyrrole **IIh** and **IIIh** in four possible conformations (Fig. 1).

It should be mentioned first of all that 3-(1-hydroxy-2,2-dicyanoethenyl)-1-methylpyrrole (**IIIh**) is by 2.2 kcal mol^{-1} more stable than the corresponding 2-isomer **IIh**

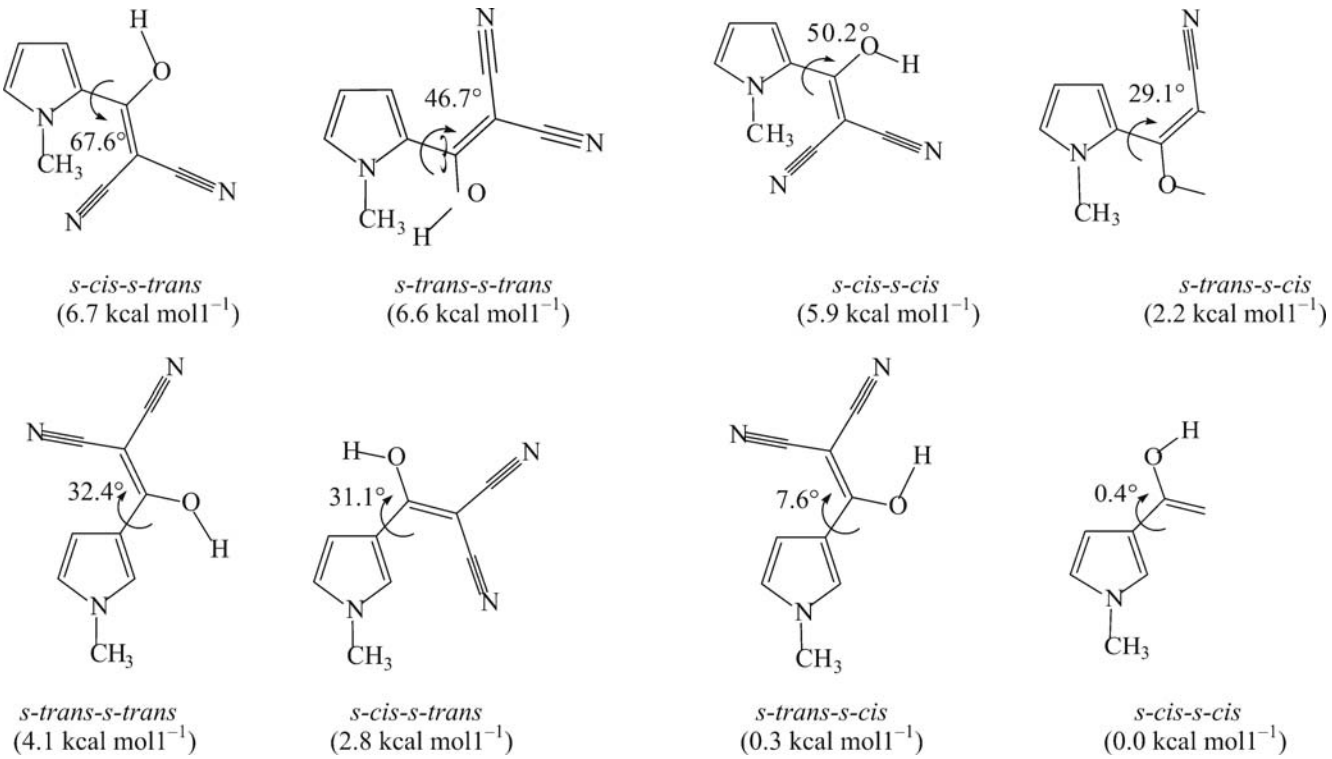


Fig. 1. Relative energies and deviation from planar structire of rotation conformations of 2- and 3-(1-hydroxy-2,2-dicyanoethenyl)-1-methylpyrroles **IIh** and **IIIh** optimized by method MP2/6-311G**.

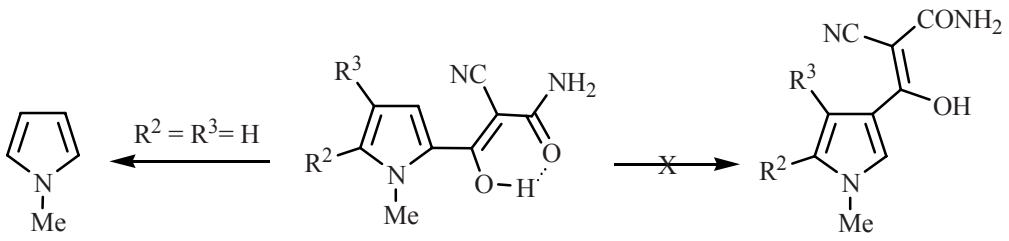
(if both isomers are taken in their preferred conformations: *s-trans-s-cis* for **IIh** and *s-cis-s-cis* for **IIIh**) leading to the equilibrium isomers ratio in the reaction mixture ~5:95 (*T* 350 K). The observed equilibrium ratio of the isomers is comparable with the calculated one. For instance, at heating reagent **IIe** in benzene-d_6 (75°C, 1.5 h) whose intermolecular interaction with the enol was insignificant the ratio **IIe:IIIe** reached 6:94 (^{1}H NMR data). At heating under the similar conditions isomer **IIIe** a mixture of compounds **IIe** and **IIIe** formed in a ratio 4:96. Thus the α,β-migration of the enol function in the pyrrol ring under consideration is thermodynamically favorable and according to the experimental findings it is governed by the thermodynamical control. A higher thermodynamic stability of 3-(1-hydroxy-2,2-dicyanoethenyl)-1-methylpyrrole compared to its 2-isomer apparently, in particular, originates from the destabilization of the 2-isomer by a spatial interaction of the N-methyl group with the ethenyl fragment. This is revealed by a considerable deviation of the ethenyl fragment from the plane of the pyrrole ring in all possible conformations of 2-(1-hydroxy-2,2-dicyanoethenyl)-1-methylpyrrole, from ~30 deg in the preferable *s-trans-s-cis*-conformation to nearly 70 deg in the *s-cis-s-trans*-conformation possessing the highest energy (Fig. 1). On the other hand, these steric interactions in the 3-isomer are virtually lacking in the preferable *s-cis-s-cis*-conformation that is virtually planar (0.4 deg) and to notably lesser extent appear in the conformations of higher energy, *s-trans-s-cis*-, *s-cis-s-trans*- , and *s-trans-s-trans*-conformations (~10–30 deg) (Fig. 1).

Besides the higher stability of isomers with the enol substituent in the position *3* is in agreement with the reduction in the acidity of their hydroxy group [about 0.5 log unit (compounds **IIIe, IIIi, IIIh, IIIk**, and **IIIl**) compared with the α-isomer (see the table)]. The latter fact means also that the 3-pyrrolyl fragment is a more strong donor with respect to enol substituent than the corresponding 2-pyrrolyl, namely, the conjugation (with a charge transfer) of the pyrrole part of the molecule (strond π-donor) with strongly electron-deficient enol part of the molecule is stronger in the 3-isomers than in the 2-isomers. Thus the higher thermodynamic stability of the 3-isomers can be ascribed to the stronger conjugation of the pyrrole ring with the enol substituent.

The variation of enols pK_a in the series **IIe, IIh, IIi** is well consistent with the electronic effects of the substituents in the pyrrole ring. Actually, the introduction of electron-donor substituents in the molecule of 2-(1-hydroxy-2,2-dicyanoethenyl)-1-methylpyrrole in positions *4* and *5* of the pyrrole ring results in the decrease in the acidity of the hydroxy function in the series **IIh** > **IIe** > **IIi**; seemingly, the rate of the rearrangement should have decelerate in this sequence. However taking into account that the ease of the migration of the enol substituent is affected also by the proton affinity of the pyrrole ring that grows in this enol series **IIh**, **IIe**, **IIi** the competition of the two influences should be expected. The experimental results suggest that the growing proton affinity of the pyrrole ring is the prevailing factor governing the capability of α-enols to rearrange into β-enols. Actually, as was already shown above and also according to NMR data [the relative fraction of 3-isomer after 1 h of heating (DMSO-d_6, 110°C) was 57, 39, and 12% for **IIIe, IIIi**, and **IIIh** respectively] the rearrangement rate increased in the series **IIh < IIi < IIe**. Note that the rearrangement in DMSO-d_6 proceeded slower than in benzene due apparently to the concurrent bonding of the hydroxy group by the solvent.

At heating (in benzene-d_6, toluene-d_8, DMSO-d_6, *m*-xylene-d_{10}, 75–135°C) pyrroles **IIf** and **IIg** having at the double bond instead of one cyano group a less electron-acceptor carbamoyl substituent no migration of the ethenyl fragment occurred. At heating pyrrole **IIf** in *m*-xylene (130–135°C, 1 h) in the ^{1}H NMR spectrum signals appeared belonging to the product of its destruction, 1-methyl-pyrrole (Scheme 6).

Scheme 6.



IIf, IIg

According to X-ray diffraction analysis [5] in enols **IIf** and **IIg** the hydroxy group formed a stromg intramolecular hydrogen bond with the carbonyl group. This hydrogen bond was conserved also in solutions of enols **IId**, **IIf** and **IIg**, in particular, in methanol, as seen from the abnormal low acidity of these compounds compared with enols containing two cyano groups **IIa–IIc**, **IIe**, **IIh**, and **IIi**. The electron-acceptor ability of CN and $CONH_2$ groups expressed through the nucleophilic constants σ^- (σ^-_{CN} 1.0, $\sigma^-_{CONH_2}$ 0.627 [12]) is not strongly different (0.37 log unit). At the same time the variation of pK_a in pairs **IIf–IIh, IIg–IIe, IId–IIc** amounts to a large value, 3.3 log unit, that cannot be ascribed only to the decreased electron-acceptor effect of the $CONH_2$ group compared with CN.

In keeping with Hammett's equation $pK_a = pK_O + \rho\sigma$ the difference in the pK_a values for two members of the reaction series (ΔpK_a) divided by the difference in the values of polar effects of the substituents in the mentioned members $\Delta\sigma$ can characterize the value of the reaction constant c that is known to have definite values. For instance, in the series of substituted phenols which may be regarded as models of the enols under study the value ρ in question is in methanol 2.8.

The approximate estimate of the ρ parameter for enols dissociation in methanol considering the above given values ΔpK_a 3.3 and $\Delta\sigma^-$ 0.37 ($\rho = \Delta pK_a/\Delta\sigma^-$) equals 8.92. As far as we know this value has no analogs in the series of acids with the oxygen-centered anion. This fact indicates that in methanol solution in the molecules of carbamoyl-containing enols alongside the electronic effect operates an additional structural factor considerably reducing the acidity of these compounds. This factor is evidently just the mentioned stong intramolecular hydrogen bond that is conserved also in methanol. Solving the reverse problem, namely, $\Delta pK_a = \rho\Delta\sigma^-$ where ρ 2.8, $\Delta\sigma^-$ 0.37 we get a value ΔpK_a 1.04 that shows to what extent the carbamoyl-containing enols (in keeping only with their electronic effects) would be less strong acids than their CN-substituted analogs. For instance, the expected for compound **IIg** pK_a value would be 6.29, whereas the experiment gives 8.35.

N-Unsubstituted tricyanoethenylpyrrole **IIa** was stable under the rearrangement conditions: at heating in *m*-xylene (135°C, 4 h) no migration of the enol substituent was observed, and in DMSO (110°C, 4 h) the rearrangement occurred only to 6% (^{1}H NMR data).

In this connection it is interesting to compare the relative thermodynamic stability of 2- and 3-(1-hydroxy-2-cyanoethenyl)-1*H*-pyrroles (**IV**) and (**V**) (Fig. 2) with the previously considered 2- and 3-(1-hydroxy-2-cyanoethenyl)-1-methylpyrroles (**IIh**) and (**IIIh**) (Fig. 1). First of all our attention is arrested by the fundamental difference in the stability of 2- and 3-isomers in 1*H*- and 1-methyl-substituted pyrrole of this series: in the former pair the more stable is 2-isomer **IV**, whereas in the latter case of 1-methyl-substituted pyrroles **IIh** and **IIIh** the pattern is reversed, namely, the more stable is 3-isomer **IIIh**. The reason of this difference we presume to be in additional stabilization of 2-isomer **IV** owing to the formation of a weak intramolecular hydrogen bond involving the NH proton of the pyrrole ring and the nitrogen of the cyano group located in the *cis*-position with respect to the pyrrole fragment. This suggestion is supported by the short distance C≡N···H–N ($d_{N\cdots H}$ ≈ 2.3 E) and by the significant deviation from the linear structure of the C–C≡N fragment located in the *cis*-position with respect to the pyrrole ring (bond angle CCN ≈ 3.0 deg), but to the greater extent just by the fact of *s-cis-s-cis*-conformation of isomer (**IV**) being the preferable one, where the presence of the hydrogen bond C≡N···H–N is expectable. Note for comparison that in the 2-isomer of 1-methyl-substituted pyrrole **IIh** where the formation of such intramolecular hydrogen bond is impossible the preferable conformation is *s-trans-s-cis* (Fig. 1). The preferred low-energy conformations of both isomers of 1-hydroxy-2,2-dicyanoethenyl-1*H*-pyrrole in contrast to 1-hydroxy-2,2-dicyanoethenyl-1-methyl-pyrrole are nearly ideally planar (Fig. 2) evidencing the absence of sterical interactions of the pyrrole and ethenyl fragments in the former case whereas the presence of N-methyl group in 2- and 3-isomers of 1-hydroxy-2,2-dicyanoethenyl-1-methyl-pyrrole results in strong deviation of the structure of both its isomers from planarity (see above).

The energy difference of 2- and 3-isomers of 1-hydroxy-2-cyanoethenyl-1*H*-pyrroles (**IV**) and (**V**) taken in their preferable conformations (Fig. 2) amounts to 0.9 kcal mol^{-1} that would correspond to their ratio in the reaction mixture ~77:23 (*T* 380 K). Thus the fundamental difference in the occurrence of the rearrangement for 1*H*- and 1-methyl-substituted pyrroles of this series can be attributed to thermodynamic reasons; hence the α,β-migration of the enol function in the pyrrole ring is thermodynamically controlled.

Besides the π-donor properties of the N-unsubstituted ring with respect to the π-acceptor enol system (in

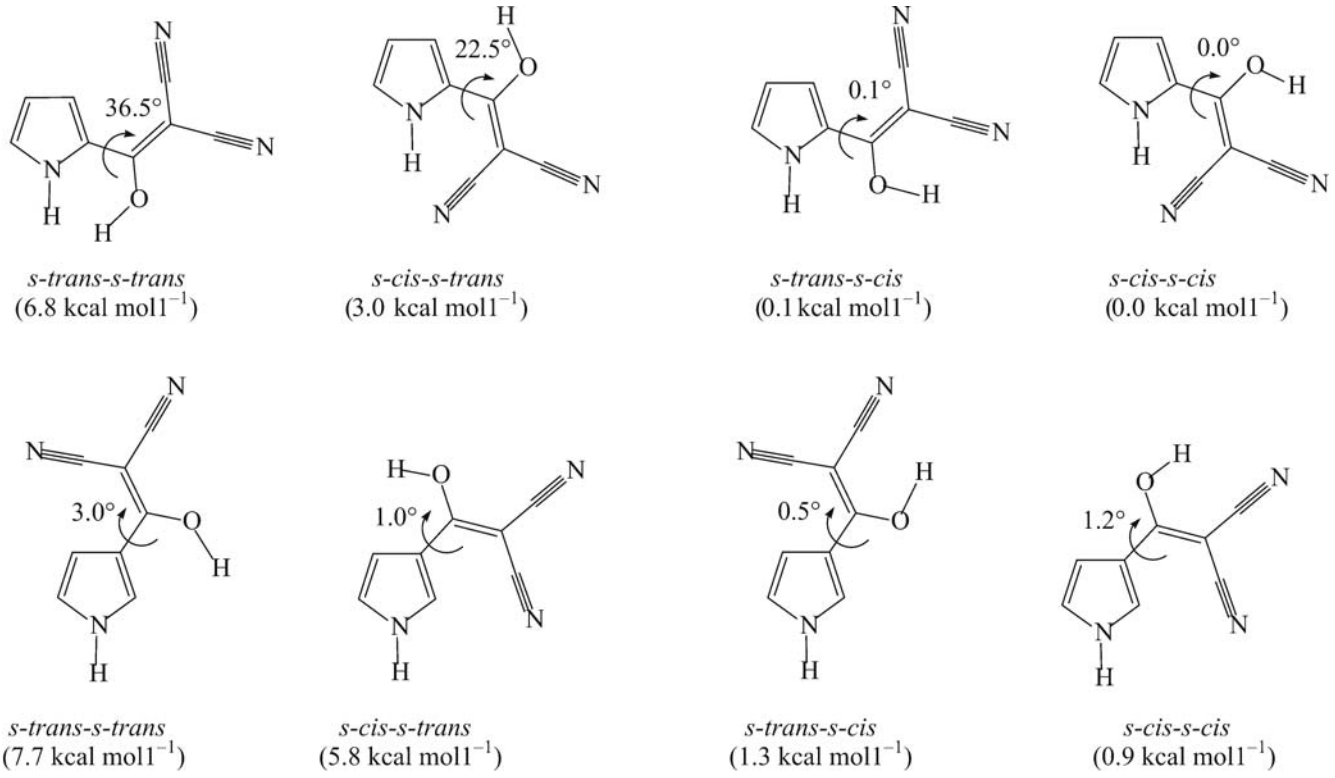


Fig. 2. Relative energies and deviation from planar structire of rotation conformations of model 2- and 3-(1-hydroxy-2,2-dicyanoethenyl)-1*H*-pyrroles (**IV**) and (**V**), optimized by method MP2/6-311G**.

compound **IV**) are weaker in the N-methyl-substituted analog **IIh** leading to the decrease in the energy of the intramolecular donor-acceptor interaction (charge transfer) in the former molecule. Probably just this is the principal reason of the difficulty for the enol substituent migration from the position *2* into position *3*.

The investigation of enol substituents migration in the pyrrole ring is a fundamental supplement to the existing concepts on the rearrangement processes involving pyrrolium cations, and it significantly extends the synthetic prospects of functionalized C-ethenylpyrroles.

EXPERIMENTAL

IR spectra of synthesized compounds in the region 400–4000 cm^{-1} were recorded on a spectrophotometer Bruker IFS-25 from KBr pellets. ^{1}H and ^{13}C NMR spectra were registered on a spectrometer Bruker DPX 400 [400.13 (^{1}H) and 100. 6 (^{13}C) MHz]; solvent $CDCl_3$, DMSO-d_6, *m*-xylene-d_{10}, internal reference HMDS. The assignment of signals in ^{1}H NMR spectra was performed with the help of 2D homonuclear correlation procedures COSY and NOESY. The resonance signals of carbon atoms were assigned based on the analysis of 2D spectra HSQC and HMBC.

Dissociation constants of enols in anhydrous methanol were established by the potentiometric titration [12] using universal ion meter EV-74 equipped with glass-calomel electrodes system. The calomel reference electrode was filled with a saturated methanol solution of KCl. As titrant 0.1N solution of NaOH in methanol was used. The measurements were performed at enols concentrations enolOβ 0.005–0.01 mol l^{-1}. Benzoic acid was applied as reference whose dissociation constant was measured in methanol by several methods and equaled pK_a 9.4 [11].

The quantum-chemical calculations were carried out using GAMESS software [13]. The optimization of geometric parameters and calculation of relative energies of rotation conformations of compounds **IIh, IIIh**, **IV**, and **V** were performed in the framework of the Møller – Plesset second order perturbation theory MP2 [14] using correlation-consistent Pople basis sets expanded with the polarization *d*-functions for the atoms of the second period and polarization *p*-functions for hydrogen atoms, 6-311G** [15].

2-(1-Methyl-1*H*-pyrrol-2-yl)- (Ih) and 2-(1-methyl-1*H*-pyrrol-3-yl)ethylene-1,1,2-tricarbonitrile (Ij). A mixture of 0.406 g (5 mmol) of 1-methylpyrrole and 0.640 g (5 mmol) of tetracyanoethylene in 20 ml of acetone was stirred at room temperature for 1 h, then diluted with water (100 ml), extracted with ether, and the extracts were dried with potassium carbonate. On removing the solvent we obtained 0.650 g (71%) of a mixture of pyrroles **Ih** and **Ij** in a ratio 30:70 (^{1}H NMR data). Pyrrole **Ih.** ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.96 s (3H, Me), 6.46 d.d (1H, H^4, *J* 4.65, 2.45 Hz), 7.40 d.d (1H, H^3, *J* 4.65, 1.70 Hz), 7.60 d.d (1H, H^5, *J* 2.45, 1.70 Hz). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 36.6, 50.3, 112.6, 112.7, 113.6, 113.8, 122.6, 124.5, 138.4, 180.8. Pyrrole **Ij**. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.77 s (3H, Me), 6.90 d.d (1H, H^4, *J* 3.18, 1.60 Hz), 7.15 d.d (1H, H^5, *J* 3.18, 1.60 Hz), 8.20 d.d (1H, H^2, *J* 1.60, 1.60 Hz). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 36.7, 78.3, 108.3, 113.3, 113.4, 114.2, 117.1, 128.5, 133.6, 133.7.

2-(1-Methyl-5-propyl-4-ethyl-1*H*-pyrrol-2-yl)-1,1,2-ethylenetricarbonitrile (Ii). A mixture of 0.220 g (1.72 mmol) of 1-methyl-2-propyl-3-ethylpyrrole and 0.260 g (1.72 mmol) of tetracyanoethylene in 4 ml of DMSO was stirred at room temperature for 1 h, then diluted with water (40 ml), extracted with ether, and the extracts were dried with $MgSO_4$. On removing the solvent the residue was dried in a vacuum and recrystallized from methanol. Yield 0.221 g (51%), mp 109^{o}C. IR spectrum, ν, cm^{-1}: 2972, 2928, 2877, 2228, 2195, 1544, 1513, 1494, 1475, 1464, 1456, 1430, 1421, 1374, 1314, 1169, 1160, 1091, 1023, 969, 836, 745, 724, 675, 555, 541. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 0.93 t (3H, Me), 1.12 t (3H, Me), 1.52 m (2H, CH_2), 2.44 m (2H, CH_2), 2.70 m (2H, CH_2), 3.81 C (3H, NMe), 7.36 s (1H, H^3). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 13.7, 14.3, 18.4, 21.6, 26.4, 33.5, 73.7, 113.7, 114.6, 114.9, 121.5, 125.3, 128.9, 150.3, 165.5. Found, %: C 71.05; H 6.29; N 22.55. $C_{15}H_{16}N_4$. Calculated, %: C 71.40; H 6.39; N 22.21.

2-(2-Methyl-4,5,6,7-tetrahydro-1*H*-indol-3-yl)-1,1,2-ethylenetricarbonitrile and 2-(2-methyl-5-phenyl-1*H*-pyrrol-3-yl)-1,1,2-ethylenetricarbonitrile were similarly prepared, their spectral and physicochemial characteristics were reported in [16].

2-[Hydroxy(5-phenyl-1*H*-pyrrol-2-yl)methylene]-malononitrile (IIc). To a solution of 0.280 g (1 mmol) of 2-(2,2-dicyano-1-ethylsulfanylethenyl)-5-phenylpyrrole in 2 ml of MeOH heated to 60°C was added a solution of 0.080 g (2 mmol) of NaOH in 1 ml of H_2O, the mixture was stirred for 3 h at the mentioned temperature. The methanol was removed in a vacuum, the residue was acidified with 10% HCl till pH 3. The separated precipitate was filtered off, washed with water, and dried. Yield 0.110 g (53%), mp 183°C (from benzene). IR spectrum, ν, cm^{-1}: 3293, 3158, 2930, 2850, 2222, 2205, 1637, 1589, 1541, 1506, 1480, 1457, 1406, 1374, 1299, 1277, 1235, 1204, 1083, 1063, 1003, 851, 797, 760, 718, 688, 668, 611. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 6.59 d.d (1H, H^4, *J* 2.9, 1.8 Hz), 6.98 d.d (1H, H^3, *J* 2.9, 2.0 Hz), 7.22 m (1H^n), 7.36 m (2H^O), 7.79 m (2H^m), 11.46 br.s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 53.3, 109.4, 117.5, 119.3, 121.5, 124.2, 127.7, 128.8, 131.2, 137.8, 178.5. Found, %: C 71.27; H 3.90; N 17.40. $C_{14}H_9N_3O$. Calculated, %: C 71.48; H 3.86; N 17.86.

Enols **IIa, IIb, IId–IIg** were obtained by the same procedure. Their spectral and physicochemial characteristics were reported in [5].

2-[Hydroxy(1-methyl-1*H*-pyrrol-3-yl)methylene]-malononitrile (IIIh). To a mixture of 0.150 g (0.82 mmol) of 2-(1-methyl-1*H*-pyrrol-2-yl)- (**Ih**) and 2-(1-methyl-1*H*-pyrrol-3-yl)ethylene-1,1,2-tricarbonitrile (**Ij**) was added 1.3 ml (3.7 mmol) of 10% NaOH solution, and the reaction mixture was stirred for 15 min at 40–45°C. On cooling to room temperature 1.5 ml of 10% HCl was added to the reaction mixture. The formed loose precipitate was filtered off, washed with water, and dried. We obtained 0.073 g (51%) of a mixture of 2- and 3-isomers **IIh** and **IIIh** in a ratio 8:92. The mixture was heated for 1 h in 3 ml of toluene at 103–105°C. On cooling the separated crystals were filtered off and dried in a vacuum to obtain 0.070 g (96%) of pyrrole **IIIh**, mp 166–167°C. IR spectrum, ν, cm^{-1}: 3437, 3127, 2961, 2923, 2851, 2226, 2212, 1569, 1633, 1453, 1415, 1364, 1343, 1291, 1236, 1163, 1090, 1075, 993, 970, 856, 846, 819, 720, 646, 547. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.70 s (3H, Me), 6.63 d.d (1H, H^4, *J* 2.9, 1.8 Hz), 6.90 d.d (1H, H^5, *J* 2.9, 2.0 Hz), 7.60 d.d (1H, H^2, *J* 2.0, 1.8 Hz). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 13.7, 16.2, 17.9, 22.9, 25.1, 33.8, 54.3, 113.7, 116.3, 118.1, 121.8, 125.5, 131.2, 181.1. Found, %: C 62.40; H 4.02; N 24.20. $C_9H_7N_3O$. Calculated, %: C 62.42; H 4.07; N 24.26.

2-[Hydroxy(1-methyl-5-propyl-4-ethylpyrrol-2-yl)methylene]malononitrile (IIi). A dispersion of 0.100 g (0.40 mmol) of reagent **Ii** in 0.65 ml of 10% solution of NaOH was stirred for 70 min at 40–45°C. The reaction mixture was diluted with water (2 ml), and carbon dioxide was passed through till the solution get

turbid (pH 4). Then it was extracted with benzene (4 × 3 ml), the extracts were dried with $MgSO_4$, the solvent was removed, the residue was dried in a vacuum. Yield 0.083 g (86%), dark red crystals, mp 204°C. IR spectrum, ν, cm^{-1}: 3437, 2960, 2931, 2870, 2205, 2167, 1627, 1570, 1526, 1446, 1426, 1401, 1331, 1310, 1184, 913, 744, 559. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 0.90 t (3H, Me), 1.05 t (3H, Me), 1.43 m (2H, CH_2), 2.32 m (2H, CH_2), 2.47 m (2H, CH_2), 3.57 s (3H, NMe), 6.50 s (1H, H^3). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 13.9, 15.8, 18.6, 22.7, 25.6, 31.9, 45.4, 112.0, 119.9, 122.6, 123.8, 128.8, 132.8, 179.4. Found, %: C 68.95; H 6.99; N 17.38. $C_{14}H_{17}N_3O$. Calculated, %: C 69.11; H 7.04; N 17.27.

Pyrroles **IIIk** and **IIIl** were similarly prepared.

2-[Hydroxy(2-methyl-4,5,6,7-tetrahydro-1*H*-indol-3-yl)methylene]malononitrile (IIIk). Yield 79%, mp 170–171°C (from benzene). IR spectrum, ν, cm^{-1}: 3330, 3214, 2931, 2851, 2222, 1610, 1561, 1465, 1441, 1377, 1355, 1310, 1288, 1219, 1172, 1112, 1032, 1006, 963, 949, 896, 798, 724, 668, 563. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.59 m (2H, CH_2), 1.65 m (2H, CH_2), 2.22 s (3H, Me), 2.37 m (2H, CH_2), 2.40 m (2H, CH_2), 10.98 br.s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 12.7, 21.7, 21.8, 22.5, 23.0, 56.7, 112.5, 115.7 (2CN), 116.0, 126.3, 130.0, 182.3. Found, %: C 68.50; H 5.70; N 18.20. $C_{13}H_{13}N_3O$. Calculated, %: C 68.71; H 5.77; N 18.49.

2-[Hydroxy(2-methyl-5-phenyl-1*H*-pyrrol-3-yl)methylene]malononitrile (IIIl). Yield 79%, mp 204–206°C (from benzene). IR spectrum, ν, cm^{-1}: 3261, 3199, 3069, 2930, 2865, 2228, 2209, 1683, 1593, 1575, 1540, 1501, 1445, 1383, 1220, 1181, 1140, 1075, 1029, 998, 937, 877, 804, 759, 694, 653. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 2.39 s (3H, Me), 6.81 s (1H, H^4), 7.20 m (1H, Ph-*p*), 7.38 m (2H, Ph-*m*), 7.60 m (2H, Ph-*O*), 11.69 br.s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 13.2, 54.3, 106.2, 115.8, 116.9, 118.3, 123.6, 126.3, 128.8, 130.1, 131.6, 134.3, 181.3. Found, %: C 72.50, H 4.56, N 16.20. $C_{15}H_{11}N_3O$. Calculated, %: C 72.28; H 4.45; N 16.86.

Study of isomerization of 2-(1-hydroxy-2-cyanoethenyl)pyrroles (II). A solution of 5 mg of reagent **II** in 0.6 ml of xylene-d_{10} or DMSO-d_6 was heated in an NMR test tube at 130–135 and 110–112°C respectively with intermittent registering of NMR spectra.

3-[Hydroxy(1-methyl-5-propyl-4-ethylpyrrol-2-yl)methylene]malononitrile (IIIi). In 3 ml of toluene 0.050 g (0.21 mmol) of reagent **IIi** was heated for 1 h at 103–105°C. On removing the solvent the separated crystals were washed with hexane and dried in a vacuum. Yield 0.045 g (90%), dark red crystals, mp 147°C. IR spectrum, ν, cm^{-1}: 3139, 2960, 2932, 2872, 2223, 2206, 1574, 1538, 1470, 1453, 1417, 1242, 1212, 1176, 1137, 1113, 1077, 1063, 1034, 909, 849, 807, 797, 752, 712, 694, 620. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.98 t (3H, Me), 1.07 t (3H, Me), 1.51 m (2H, CH_2), 2.48 m (2H, CH_2), 2.57 m (2H, CH_2), 3.60 C (3H, NMe), 7.66 s (1H, H^2). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 13.70, 16.19, 17.90, 22.91, 25.13, 33.83, 54.23, 113.68, 116.30, 118.10, 121.80, 125.49, 131.17, 181.58. Found, %: C 68.90; H 7.08; N 17.40. $C_{14}H_{17}N_3O$. Calculated, %: C 69.11; H 7.04; N 17.27.

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