EVOLUTION OF HYDROGEN IN THE REACTION OF HYDROHETEROAROMATIC COMPOUNDS WITH DEHYDROGENATING AGENTS

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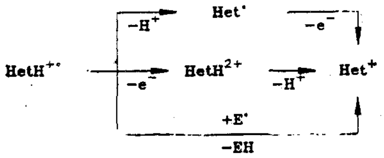
The yields of molecular hydrogen in the reactions of benzimidazolines 1,2-dihydropyrimidines with a number of dehydrogenating agents have been determined. The formation of hydrogen is due to breakdown of the cation-radicals of the hydrohetarenes formed in the first stage of the reactions. The EPR spectrum of the cation-radical from 1,3-dimethyl-2-phenylbenzimidazoline has been obtained.

The dehydrogenation of hydroaromatic compounds, formerly regarded as involving hydride transfer, is now more frequently considered to be a stepwise reaction commencing with one-electron oxidation of the substrate [1, 2]. The principal mode of breakdown of the hydrohetarene cation-radical formed in the first stage of the reaction is deprotonation to the neutral free radical [1-3]. Much less frequently, deprotonation precedes oxidation of the cation-radical to the dication [4]. If electron transfer leads to the formation of another reactive radical in addition to the cation radical, it has been suggested [5] that aromatization of the cation-radical may occur by loss of a hydrogen atom in the solvent cell, i.e., in the region of space in which repeated collisions of the two species occur [6].

$$HetH + E^{+} \longrightarrow HetH^{+\cdot} + E^{\cdot}$$



Finally, another route is possible, in which the cation-radical undergoes breakdown with loss of an atom of hydrogen, as in the fragmentation of the cation-radicals of organotin [7] and organosilicon hydrides [8]:

$$HetH^{+\cdot} \longrightarrow Het^{+} + H^{\cdot}$$

$$2\,H^{\cdot} \longrightarrow H_2$$

In the present investigation, we set ourselves the task of detecting loss of free hydrogen in HetH—oxidant systems. The subjects chosen for study were benzimidazolines and 1,2-dihydropyrimidines. Both chemical and electrochemical oxidation was studied.

On examining the electrochemical oxidation of 1,3-dimethyl-2-phenylbenzimidazoline (I) in dimethylformamide at a rotating disk electrode and ring, it was found to occur in a single wave of approximately two electrons (n = 1.75) at a potential E_p of 0.28 V. The final oxidation product is the 1,3-dimethyl-2-phenylbenzimidazolium cation (cf. [9]), confirmed by the presence in the electrooxidation products of a reduction wave for this cation with E_p 1.6 V, the same as in authentic solutions containing 1,3-dimethyl-2-phenylbenzimidazolium perchlorate. Reduction waves are recorded on the ring at potentials similar to those corresponding to the oxidation wave on the disk. They correspond to the reverse reduction of the imidazoline cation-radical of (I) ($I^{+\cdot}$) to the starting material.

The absence of a relationship between the coefficient N_H, which is a measure of the ratio of the current at the ring to that at the disk, and the concentration of the depolarizer shows

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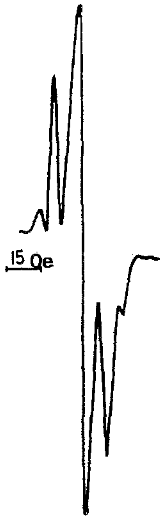


Fig. 1. EPR spectrum of the adduct of 1,3-dimethyl-2-phenylbenzimidazolium cation with atomic hydrogen.

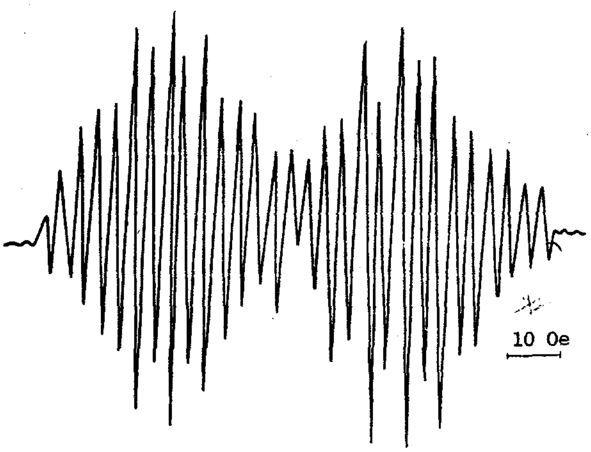
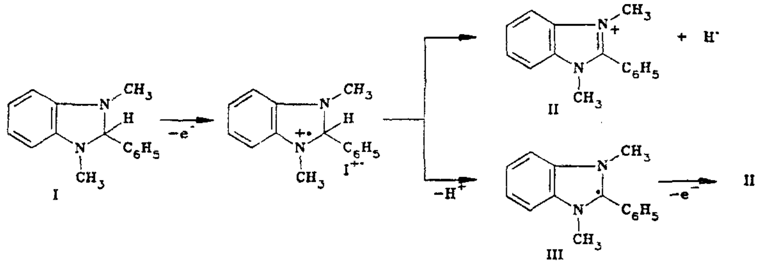


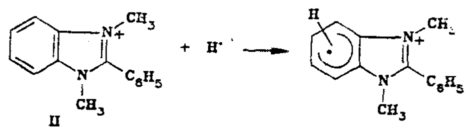
Fig. 2. EPR spectrum of 1,3-dimethyl-2-phenylbenzimidazolium cation.

that the breakdown of the cation-radical is first or pseudo-first order [10], as would be the case if either a proton or a hydrogen atom were eliminated. The rate constant for the breakdown of the cation-radical, found from N_H, is around 6 sec^{-1}, in accordance with a half-breakdown time of the order of 0.1 sec.

Breakdown of the cation-radical ($I^{+\cdot}$) with loss of an atom of hydrogen is thermodynamically favored, since it is then converted directly into the fully aromatic benzimidazolium cation. The same conclusion is reached from a comparison of the potential $E^{H+/H^\cdot}$ and $E_p^{II/III}$ (0.1 and −1.6 V respectively):



Nevertheless, electrolysis of the imidazoline (I) in DMF results in the evolution of only trace amounts of free hydrogen. Possible reasons for this are the high reactivity of the hydrogen atoms, and parallel deprotonation of the cation-radical. The reactivity of atomic hydrogen is so great that even the reaction product (cation (II)) can capture it with the formation of a paramagnetic adduct. This has been confirmed by control experiments, during which atomic hydrogen was generated photochemically in a sulfuric acid matrix [11] in the presence of 1,3-dimethyl-2-phenylbenzimidazolium perchlorate. The EPR spectrum of the adduct is shown in Fig. 1. The nature of this spectrum shows that addition of hydrogen takes place at the benzene ring of the cation:



Electrochemical oxidation of the imidazoline (I) in acetonitrile also takes place without evolution of hydrogen, clearly as a result of the high reactivity of atomic hydrogen towards this solvent.

In spite of the low stability of the cation-radical ($I^{+\cdot}$), we have been able to record it by EPR in the oxidation of the imidazoline (I) with silver cation in acetonitrile at −30°C. The EPR spectrum of the cation-radical, which consists of a doublet of multiplets (Fig. 2), is due to interaction of the unpaired electron with the 2-H, 5-H, and 6-H protons and those

TABLE 1. Yield of Molecular Hydrogen in the Reactions of Hydroheteroaromatic Compounds with Oxidants*

Compound	Amt. of comp., g	Oxidant	Amt. of oxidant, g	Reaction temp., °C	Yield of hydrogen, % †
I	0,1	$AgNO_3$	0,5	100—120	0,2
I	0,1	$Fe(ClO_4)_3 \cdot 9H_2O$	1,5	150—170	0
IV	0,1	$AgNO_3$	0,7	100—120	0,4
V	0,14	$AgNO_3$	0,6	120—140	15
V	0,14	$Fe(ClO_4)_3 \cdot 9H_2O$	1,5	140—160	0,1
V	0,14	$Cu(BF_4)_2 \cdot 6H_2O$	1,0	170—190	0
V	0,14	Phenothiazine cation-radical perchlorate	0,6	140—160	4
—		Phenothiazine cation-radical perchlorate	0,6	150—170	0
Phenothiazine	0,15	$AgNO_3$	0,6	150—170	0
VI	0,2	$AgNO_3$	0,6	150—160	0

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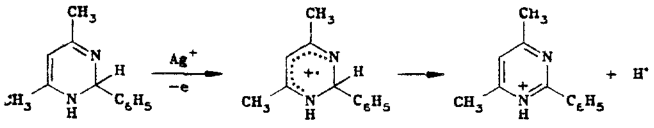
*The starting material was heated with the oxidant in 10 ml of dodecane under nitrogen, until no more gas was evolved (0.2-0.5 h).

†Calculated for the reaction HetH → $HetH^{+\cdot}$ → Het^+ + 0.5 H_2.

of the methyl groups with the two equivalent nitrogen atoms. The hyperfine splitting constants (HSC) are 40, 3.4, 6.8, and 6.8 Oe respectively. Noteworthy is the unusually high HSC with the proton in the 2-position, indicating the quite high density of the unpaired electron in this ring. This factor clearly facilitates the elimination of hydrogen in the atomic form.

The cation-radical ($I^{+\cdot}$) can also be generated by oxidizing (I) in the system $AlCl_3$–CH_2Cl_2 (see preliminary communication [12]). Here, it shows unusual stability as a result of adsorption on to the aluminum chloride, and can be recorded by EPR even at +20°C. Although adsorbed radicals normally give anisotropic EPR spectra, that of the radical-ion ($I^{+\cdot}$) in the system (I)–$AlCl_3$–CH_2Cl_2 is isotropic. This interesting observation is doubtless due to the retention of the ability of the cation-radical to rotate rapidly, while its diffusion is at the same time restricted (cf. [13]).

Chemical oxidation of the imidazoline (I) and of 1,3-dimethylbenzimidazoline (IV) with silver nitrate [14] in dodecane results in the formation of small amounts of molecular hydrogen (Table 1). Much greater yields of hydrogen are obtained when 2-phenyl-4,6-dimethyl-1,2-dihydropyrimidine (V) is oxidized by silver nitrate. However, when 2,2-diphenyl-4,6-dimethyl-1,2-dihydropyrimidine (VI) is used instead of the dihydro-compound (V), no hydrogen is formed. This shows that the source of the hydrogen in the oxidation of (V) with silver nitrate is the hydrogen atom in the 2-position of the dihydro-compound:



V

The yield of hydrogen in the system (V)–oxidant falls sharply, or is even zero when more energetic oxidizing agents than silver nitrate are used, for example iron(III) perchlorate or copper(II) fluoroborate (Table 1), which are clearly able to oxidize atomic hydrogen to a proton.

The possible formation of hydrogen in the dehydrogenation of benzimidazolines and other hydroaromatic compounds by the silver cation has been assumed previously [14, 15], although it was not confirmed experimentally. The source of the hydrogen in such reactions was assumed to be the unstable silver hydride, the product of the transfer of a hydride ion from the hydrogenated heterocycle to Ag^+. This postulate is, however, not supported by the observed formation of the cation-radical ($I^{+\cdot}$) in the system (I)–Ag^+, or by the fact that evolution of hydrogen also occurs in the electrochemical oxidation of hydrohetarenes, or when oxidants are used which do not contain a metal cation. It has been found that on heating the dihydropyrimidine (V) with the phenothiazine cation-radical perchlorate, a typical one-electron acceptor, hydrogen is evolved (Table 1), while control experiments have shown that the cation-radical itself does not liberate hydrogen under the reaction conditions.

When the one-electron oxidation of the benzimidazoline is carried out with an organic cation, in addition to the benzimidazole cation-radical, a neutral radical is formed, which is obviously able to take up an atom of hydrogen. This fact makes it possible to hydrogenate the neutral radical with the hydrogen of the cation-radical, thereby dehydrogenating the substrate by the $-e^-$, $-H^\bullet$ route, for instance:

$$\mathrm{I} + \mathrm{R}^+ \longrightarrow \mathrm{I}^{+\bullet} + \mathrm{R}^\bullet \longrightarrow \mathrm{II} + \mathrm{RH}$$

R^+ is an organic cation

When the second step is rapid, the reaction kinetics will be indistinguishable from the kinetics proposed for bimolecular hydrogen transfer. An argument in favor of the ion-radical mechanism for dehydrogenation under these conditions is the detection of free-radical electron-transfer products.

On examining the dehydrogenation of the benzimidazoline (I) with the 2,4,6-triphenylpyrilium cation in acetonitrile, we found that the reaction is second order overall (first order in each reactant). The rate constant is 1.26 liter/mole·sec. EPR has shown that the system (I) – 2,4,6-triphenylpyrilium perchlorate contains the known [16] 2,4,6-triphenylpyranyl free radical, this being the product of the one-electron reduction of the pyrilium cation. These observations are best interpreted as resulting from an $-e^-$, $-H^+$ mechanism of dehydrogenation.

EXPERIMENTAL

EPR spectra were obtained on a Varian E-12 spectrometer.

Electrochemical dehydrogenation of (I) was carried out at a rotating ring electrode with a ring constructed similarly to the electrode, as described in [17]. Immediately before recording the voltamperogram, the electrodes were cleaned with abrasive paper, and washed with chromic acid mixture, water, and chemically pure grade acetone. The reproducibility of the experiments was ±20 mV. The volt-amperograms at the disk were recorded by the three-electrode method on a P-5848 potentiostat, and at the ring, by an LP-7 polarograph with a symmetrical input [18]. The constant potential of the ring corresponded to the foot of the wave at the disk.

The electrode efficiency coefficient N_{eff}, which depends solely on the electrode geometry [19], was measured using as standard cation 2,4,6-triphenylpyrilium and NNN'N'-tetramethyl-p-phenylenediamine, for which the electrochemical reactions (reduction and oxidation respectively) are fully reversible [20]. The value found for N_{eff} was 0.1.

The rate constant for the breakdown of the ion-radical ($I^{+\bullet}$) was determined with a correction for the non-monoelectron character of the oxidation wave of the benzimidazoline, using the formula given in [10].

Kinetic measurements were carried out by the electrochemical method, using a rotating platinum disk and ring electrode, under pseudo-first order conditions in one of the reactants. The rate constant for the dehydrogenation of the benzimidazoline by the 2,4,6-triphenylpyrilium cation was found from the equation (cf. [21]):

$$k = \frac{I_0[(I_2 - I_1) - (I_3 - I_2)]^2}{2c_0\Delta(I_3 - I_1)(I_2 - I_1)(I_3 - I_2)},$$

where I_0, I_1, I_2, and I_3 are the currents observed at times t_0, t_1, t_2, and t_3 from the commencement of the reaction, on condition that $t_1 - t_0 = t_2 - t_1 = t_3 - t_2 = \Delta$. The value of Δ was 600 sec. The initial concentration c_0 of the depolarizer (the benzimidazoline (I) of the 2,4,6-triphenylpyrilium cation) ranged from $1 \cdot 10^{-4}$ to $5 \cdot 10^{-3}$ M.

In all the electrochemical experiments, the base electrolyte was a 0.2 mole/liter solution of lithium perchlorate. The reference electrode was saturated calomel with a water-impermeable diaphragm.

The concentration of hydrogen in the products of the reactions of the hydrohetarenes with oxidants were measured by GC on a Khrom-5 chromatograph, sorbent molecular sieve 13 X, carrier gas helium, column temperature 25°C, and a catharometer detector. As a result of the high thermal conductivity of hydrogen (greater than that of helium), its peaks on the chromatograms were recorded with negative polarity.

1,3-Dimethyl-2-phenylbenzimidazoline [22], 1,3-dimethylbenzimidazoline [23], 2-phenyl- and 2,2-diphenyl-4,6-dimethyl-1,2-dihydropyrimidines [24], and the phenothiazine cation-radical perchlorate [25] were obtained as described in these literature citations.

The reaction of 1,3-dimethyl-2-phenylbenzimidazolium perchlorate [26] with atomic hydrogen was carried out by irradiating a mixture of 1.5 volumes of concentrated sulfuric acid and 3.5 volumes of an aqueous solution containing $7 \cdot 10^{-2}$ M of iron(II) sulfate and 10^{-2} M of the benzimidazolium salt at 77°K with ultraviolet light, $\lambda_{max} > 260$ nm from a DPSh-1000 lamp. In the absence of the benzimidazolium salt, only the EPR spectrum of atomic hydrogen was observed (a doublet with splitting of approximately 500 Oe).

The ability of the silver cation to dehydrogenate 2-phenyl-4,6-dimethyl-1,2-dihydropyrimidine was confirmed by the preparative isolation of 2-phenyl-4,6-dimethylpyrimidine when the reaction was carried out with silver nitrate in propanol, in which this reaction proceeds most smoothly.

2-Phenyl-4,6-dimethylpyrimidine. A mixture of 0.5 g (2.7 mmole) of (V), 1.7 g (10 mmole) of silver nitrate, and 4 ml of propanol was boiled under reflux for 2 h. The solid which separated, consisting of a mixture of metallic silver and the reaction product, was separated from the solvent, extracted with 25 ml of water, treated with 20 ml of 15% aqueous ammonia, and extracted repeatedly with ether. Removal of the ether gave 0.23 g (47%) of 2-phenyl-4,6-dimethylpyrimidine, mp 83-84°C (from aqueous ethanol). A mixed melting point with an authentic sample [27] gave no depression.

LITERATURE CITED

1. A. S. Morkovnik and O. Yu. Okhlobystin, Khim. Geterotsikl. Soedin., No. 8, 1011 (1980).
2. N. T. Berberova and O. Yu. Okhlobystin, Khim. Geterotsikl. Soedin., No. 8, 1011 (1984).
3. V. D. Pokhodenko, L. S. Legtyarev, V. G. Koshechko, and V. S. Kuts, Topics in the Chemistry of Free Radicals [in Russian], Nauk. Dumka, Kiev (1984), p. 90.
4. O. N. Chupakhin, I. M. Sosonkin, A. I. Matern, and G. N. Strogov, Dokl. Akad. Nauk SSSR, 250, 879 (1980).
5. M. Ballester, J. Riera-Figueras, J. Castafier, and A. Rodriquez-Siurana, Tetrahedron, Lett., 2079 (1971).
6. A. L. Buchachenko, R. Z. Sagdeev, and K. M. Salikhov, Magnetic and Spin Effects in Chemical Reactions [in Russian], Nauka, Novosibirsk. Sib. Section (1978), p. 8.
7. R. J. Klingler, K. Machida, and J. K. Kochi, J. Am. Chem. Soc., 101, 6626 (1979).
8. N. T. Berberova and O. Yu. Okhlobystin, Zh. Obshch. Khim., 51, 244 (1981).
9. S. F. Nelsen, E. L. Clennan, L. Echegoyan, and L. A. Grezzo, J. Org. Chem., 43, 2621 (1978).
10. W. J. Albery and S. Bruckenstein, Trans. Faraday Soc., 62, 1946 (1966).
11. N. T. Berberova, N. N. Bubnov, E. P. Ivakhnenko, and O. Yu. Okhlobystin, Khim. Gerosikl. Soedin., No. 11, 1568 (1980).
12. N. T. Berberova, I. P. Ivakhnenko, A. S. Morkovnik, and O. Yu. Okhlobystin, Khim. Geterotsikl. Soedin., No. 12, 1696 (1979).
13. D. W. Pratt, J. J. Dillon, R. N. Lloyd, and D. E. Wood, J. Phys. Chem., 75, 3486 (1971).
14. A. V. El'tsov and Kh. L. Muravich-Aleksandr, Zh. Org. Khim., 1, 1673 (1965).
15. A. F. Blinokhvatov, Z. N. Parnes, V. G. Kharchenko, and D. N. Kursanov, Izv. Akad. Nauk SSSR, Ser. Khim., No. 8, 1831 (1974).
16. L. A. Polyakova, K. A. Bilevich, N. N. Bubnov, G. N. Dorofeenko, and O. Yu. Okhlobystin, Dokl. Akad. Nauk SSSR, 212, 370 (1973).
17. A. N. Frumkin and L. N. Nekrasov, Dokl. Akad. Nauk SSSR, 129, 115 (1959).
18. V. A. Subbotin, I. M. Sosonkin, N. G. Fedyainov, and V. N. Kumantsov, Khim. Geterotsikl. Soedin., No. 4, 516 (1978).
19. Yu. V. Pleskov and V. Yu. Filinovksii, The Rotating Disk Electrode [in Russian], Nauka, Moscow (1972), p. 344.
20. J. Margarit, G. Dubosi, and M. Levy, Bull. Soc. Chim. France, No. 5, 2096 (1972).
21. E. T. Denisov, The Kinetics of Homogeneous Chemical Reactions [in Russian], Vyssh. Shkola, Moscow (1978), p. 25.
22. A. V. El'tsov and Kh. L. Muravich-Aleksandr, Zh. Org. Khim., 1, 1307 (1965).
23. A. A. Konstantinchenko, A. S. Morkovnik, A. F. Pozharskii, and V. A. Tertov, Khim. Geterotsikl. Soedin., No. 12, 1694 (1985).
24. Yu. G. Bogachev and B. A. Tertov, Author's Cert. (USSR) No. 833 964; Publ. in Byull. Isobret., No. 20, p. 103 (1981).

25. A. S. Morkovnik, N. M. Dobaeva, and O. Yu. Okhlobystin, Khim. Geterotsikl. Soedin., No. 9, 1214 (1981).
26. A. V. El'tsov and M. Z. Girshovich, Zh. Org. Khim., 3, 1332 (1967).
27. B. A. Tertov and Yu. G. Bogachev, Khim. Geterotsikl. Soedin., No. 1, 119 (1981).

CYCLOCONDENSATION OF 3-ARYL-2-CYANO-2-BUTENOIC ACID ESTERS WITH SCHIFF BASES

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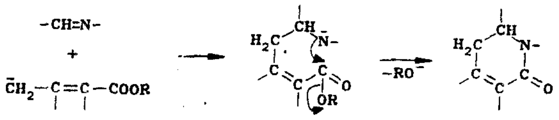
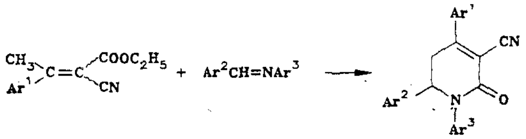
The condensation of ethyl 3-aryl-2-cyano-2-butenoates with benzylideneanilines in the presence of aluminum chloride affords 1,4,6-triaryl-2-oxo-1,2,5,6-tetrahydropyridine-2-carbonitriles; the reaction with hydrobenzamide gives N-unsubstituted tetrahydropyridine.

The first attempts to use the reaction of Schiff bases with CH-acid compounds in the synthesis of six-membered nitrogen-containing heterocycles showed that it is possible to obtain compounds of the tetrahydropyridine [1] and dihydroisoquinolinone [2, 3] series. This simple reaction was the basis of the synthesis of several alkaloids and their analogs [4]. At the same time, the formation of cyclic compounds from γ-carbanions of 2-butenoic acid esters [5, 6] suggested that it is possible to obtain pyridine derivatives according to the scheme



As far as we know, cyclocondensation of this type has not been described in the literature.

Attempts to carry out such cyclocondensation with a basic catalyst (sodium hydride in tetrahydrofuran or lithium amide in liquid ammonia) were unsuccessful. Therefore, we decided to use anhydrous aluminum chloride, catalyzing the reaction of Schiff bases with arylacetic acid esters to β-anilinopropionic acids [7].



Ia,f,g IIa-e IIIa-g

I—III a $Ar^1=Ar^2=Ar^3=C_6H_5$, b $Ar^1=Ar^3=C_6H_5$, $Ar^2=4\text{-}CH_3OC_6H_4$, c $Ar^1=Ar^3=C_6H_5$, $Ar^2=4\text{-}ClC_6H_4$, d $Ar^1=Ar^2=C_6H_5$, $Ar^3=4\text{-}CH_3OC_6H_4$, e $Ar^1=Ar^2=C_6H_5$, $Ar^3=4\text{-}ClC_6H_4$, f $Ar^1=4\text{-}CH_3C_6H_4$, $Ar^2=Ar^3=C_6H_5$, g $Ar^1=4\text{-}ClC_6H_4$, $Ar^2=Ar^3=C_6H_5$

It was found that in the presence of aluminum chloride at 20°C, ethyl 3-aryl-2-cyanobutenoates I reacted with benzylideneaniline and substituted benzylideneanilines II, forming in comparatively good yields (48-62%) the expected 1,4,6-triaryl-2-oxo-1,2,5,6-tetrahydropyridine-3-carbonitriles (III). Ethyl 3-aryl-2-butenoates not containing a cyano group in the α-position did not react with Schiff bases under these conditions, but the reaction of ethyl 3-phenyl-2-cyano-2-butenoate (Ia) with hydrobenzamide IV occurred in 20% yield only with heating.

The composition and structure of all the synthesized compounds were confirmed by data of elemental analysis and spectroscopy (Tables 1 and 2). For compound V, it was determined that during preparation it was partially dehydrogenated to nitrile VI, identical to the one described in [8] with respect to melting point and spectral data. The two substances were separated by preparative thin-layer chromatography.

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