a greater degree, and the sensitivity of the reaction center to the electronic effect of the substituent is consequently lower. The data set forth above make it possible to assume the mechanism (shown above) for the first step in the electrical reduction.

The subsequent steps in the electrode process are not indicated in this scheme, but if R is an electron acceptor, they lead to cleavage of the heteroring (cleavage of the >N-N< bond and reduction of the azomethine bond).

EXPERIMENTAL

The purity of the recrystallized I-VI was monitored by means of thin-layer chromatography; solutions with depolarizer concentrations of $2 \cdot 10^{-4}$ M were prepared for the polarographic studies, and the working solutions were prepared from Britton-Robinson buffer solutions containing 10% dimethylformamide (DMF). The ionic strength of the investigated solutions was held constant (0.25). The polarograms were recorded with LP-60 and OH-102 polarographs equipped with a thermostatted cell at 25.0 ± 0.2 deg. The cathode was a dropping mercury electrode with forced drop detachment with the characteristics m = 2.75 mg/sec and t = 0.2 sec (open circuit), and the anode was a saturated calomel electrode. The correlation equations were calculated by the method of least squares with a computer.

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PYRIMIDINES.

LIX.* HYDROXYTETRAHYDROPYRIMIDINES — INTERMEDIATES IN THE SYNTHESIS OF PYRIMIDINES FROM α,β-UNSATURATED CARBONYL COMPOUNDS AND AMIDINES

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UDC 547.853.5.07

It is shown in the case of condensation of benzamidine with cinnamaldehyde and benzalacetophenone that the synthesis of pyrimidines from α,β-unsaturated carbonyl compounds and amidines proceeds through a step involving the formation of hydroxytetrahydropyrimidines.

*See [1] for communication LVIII.

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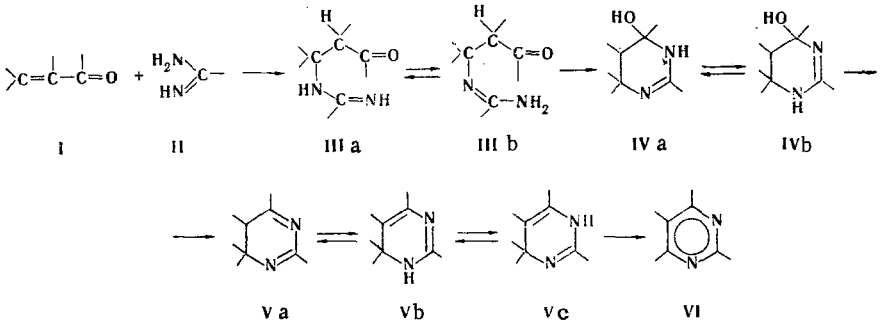
It has previously been shown [2, 3] that the corresponding pyrimidines are formed in the condensation of amidines and guanidines with α,β-unsaturated carbonyl compounds under conditions that promote dehydration and dehydrogenation.

The choice of experimental conditions was due to the proposed scheme of the complex processes of condensation of α,β-unsaturated carbonyl compounds with amidines and guanidines. One of the ways to confirm the proposed reaction scheme may be the isolation of the intermediates (III, IV, or V) and subsequent conversion of them to pyrimidines under the previously described conditions.



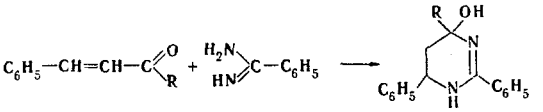
I II IIIa IIIb IVa IVb

Va Vb Vc VI

The present research was devoted to the synthesis of the primary products of the reaction of amidine compounds with α,β-unsaturated carbonyl compounds.

Only a few papers that contain information regarding the primary products of the reaction of amidines and guanidines with α,β-unsaturated carbonyl compounds are known [4-6], but hydroxytetrahydropyrimidines were obtained in good yields only by Le Berre and Renault [6] during a study of the reaction of cyclic amidines with α,β-unsaturated carbonyl compounds when the reactions were carried out in the cold in dry acetone.

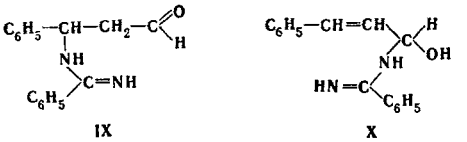
We assume that by using the conditions employed in [6] we would be able to obtain products of addition of other amidines also to α,β-unsaturated carbonyl compounds and in this way synthesize addition products III or cyclization products IV via the scheme proposed above. In fact, we obtained 4-hydroxy-2,6-diphenyl-1,4,5,6-tetrahydropyrimidine (VII), which corresponds to cyclization products IV in the scheme (disregarding the amidine tautomerism), by a somewhat modified method [6] by reaction of equimolar amounts of benzamidine and cinnamaldehyde in dry acetone.



VII, VIII

VII R=H; VIII R=C_6H_5

The results of elementary analysis and the molecular weight and empirical formula (determined by mass spectrometry) were in agreement with structure VII. The IR spectrum of the product contains an absorption band at 1620 cm^{-1} (C=N) and 3420 cm^{-1} (NH), and the absorption band of C=O stretching vibrations is absent; this indicates the cyclic structure of VII. The cyclic structure also follows from the chemical behavior of VII: it does not decolorize bromine water and does not give a qualitative reaction for the aldehyde group. Compound VII therefore cannot be either benzamidinohydrocinnamaladehyde (IX) or benzamidinocinnamyl alcohol (X):



IX X

In the examination of the structures of the cyclic N,O-hemiacetals obtained from nitrogen-unsubstituted amidines one should take into consideration the possibility of amidine tautomer-

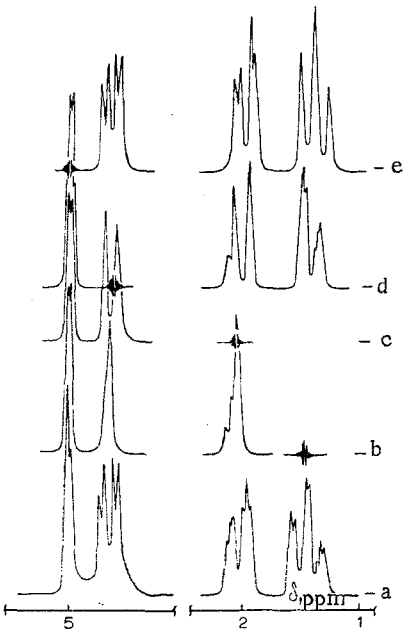
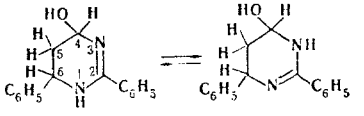


Fig. 1. PMR spectra of tetrahydropyrimidine VII (without the signals of the aromatic protons): a) monoresonance spectrum; b,c,d,e) NMDR spectra obtained by perturbation of the signals at 1.44, 2.03, 4.66, and 5.02 ppm, respectively.

ism and, for example, two tautomeric forms (VIIa and VIIb) can, in principle, be written for VII.

The NMR spectral data are in good agreement with structure VII. The PMR spectrum of a solution of tetrahydropyrimidine VII in d_6-DMSO contains signals at 7.13-8.13, 5.02, 4.66, 2.03, and 1.44 ppm with an intensity ratio of 12:1:1:1:1; we assigned these signals, to, respectively, H_{arom}, H^4, H^6, H^{5e}, and H^{5a}, during which the signals of the OH and NH groups are included in the multiplet of aromatic protons. The correctness of this assignment was demonstrated by means of double nuclear magnetic resonance (^1H—^1H NMDR, see Fig. 1). Thus when a strong radiofrequency field is superimposed on the H^6 resonance frequency, the H^{5a} and H^{5e} signals represent an AB system with $J_{H^{5a}-H^{5e}} = 11$ Hz. It is known from the literature data that coupling between nonequivalent geminal protons leads to splitting of the signal of each of them into a doublet, as a result of which the spectrum consists of a pair of doublets. The spin—spin coupling constant (SSCC) of these protons is on the order of 11 Hz [7]. In the spectra of most cyclic compounds the signals of the axial protons develop at higher field than the corresponding equatorial protons [8].



VII a VII b

The signals of the H^6 proton in the monoresonance spectrum represent a doublet of doublets with $J_{H^6-H^{5a}} = 12$ Hz and $J_{H^6-H^{5e}} = 4$ Hz. Thus decoupling of the spin—spin coupling with H^{5a} leads to the "disappearance" of the doublet with a constant of 12 Hz in the H^6 signal and of the doublet with a constant of 4 Hz in the H^{5e} signal.

The hydrogen atom in the 4 position (H^4) shows up in the spectrum in the form of a broad singlet ($\Delta\gamma_{1/2}$ = 8 Hz), which indicates small values of spin—spin coupling with H^{5a} and H^{5e}; in fact, as seen from the ^1H—^1H NMDR spectrum, the superimposition of a strong saturating radiofrequency field on the frequency of the H^4 signal leads to "disappearance" of the spin—spin coupling with H^{5a} (4 Hz) and with H^{5e} (2.3 Hz). On the basis of the SSCC, in agreement with the literature data [8], it may be concluded that the hydrogen atom in the 6 position (H^6) is axially oriented and that the hydrogen atom in the 4 position (H^4) is equatorially oriented.

The signals of the NH and OH protons were superimposed on the multiplet of aromatic protons, since the H_{arom}:H^4:H^6:H^{5a}:H^{5e} intensity ratio became 10:1:1:1:1 when CD_3OD was added.

Our data are in agreement with the PMR data presented by Wendelin [4] for 2-amino-4-hydroxy-6-phenyl-1,4,5,6-tetrahydropyrimidine hydrochloride. Under the previously found conditions (DMSO, molecular sieves, air), VII is converted to 2,4-diphenylpyrimidine in 80% yield. Under the same conditions, 4-hydroxy-2,4,6-triphenyl-1,4,5,6-tetrahydropyrimidine (VIII), obtained by reaction of chalcone with benzamidine, underwent 90% conversion to 2,4,6-triphenylpyridine. The structure of tetrahydropyrimidine VIII was established by NMR spectroscopy as described above for VII. The spectral characteristics of VIII are similar to the characteristics obtained for tetrahydropyrimidine VII.

The corresponding dihydropyrimidines are formed in 80-90% yields when VII and VIII are refluxed in benzene with removal of the water by azeotropic distillation; the products are oxidized quantitatively to pyrimidines when they are allowed to stand in DMSO. It is interesting to note that tetrahydropyrimidines VII and VIII, respectively, the amounts of which gradually decreased, were detected in the reaction mixture by thin-layer chromatography (TLC) on Al_2O_3 when the reaction of benzamidine with chalcone and cinnamaldehyde was carried out in DMSO–toluene [2].

Thus it can be considered to be an established fact that the condensation of α,β-unsaturated carbonyl compounds with amidines proceeds through a step involving the formation of hydroxytetrahydropyrimidines (cyclization products IV in the reaction scheme proposed above).

EXPERIMENTAL

The molecular weights were determined by mass spectrometry with an MS-3301 spectrometer at an ionizing voltage of 19 eV. The IR spectra of the compounds were recorded with a Perkin–Elmer 180 spectrometer. The NMR spectra were recorded with Varian A 56/60 and HA-100 spectrometers; the chemical shifts are presented on the δ scale in parts per million, and the internal standard was tetramethylsilane.

4-Hydroxy-2,6-diphenyl-1,4,5,6(?)-tetrahydropyrimidine (VII). A solution of 8.58 g (0.065 mole) of cinnamaldehyde in 20 ml of absolute acetone was added slowly dropwise with vigorous magnetic stirring at 5° to a solution of 7.8 g (0.06 mole) of benzamidine in 30 ml of absolute acetone. At the end of the addition (30 min), the mixture was stirred for another 30 min, after which the cooling bath was removed and the mixture was stirred at room temperature. After 2 h, a copious precipitate began to form. Stirring was continued for another 3 h, and the precipitate was then removed by filtration and washed with small portions of cold methyl ethyl ketone and absolute ether. The yield of tetrahydropyrimidine VII, with mp 140-141°, was 14 g (93%). Found, %: C 76.1; H 6.4; N 11.1; M 252. $C_{16}H_{16}N_2O$. Calculated, %: C 76.2; H 6.4; N 11.1; M 252.

2,4-Diphenylpyrimidine was formed when 5.04 g (0.02 mole) of tetrahydropyrimidine VII was heated in 30 ml of DMSO at 135° for 8 h in the presence of molecular sieves of the 4A type with passage of a stream of dry air through the reaction mixture. The product was isolated by vacuum distillation. The yield of 2,4-diphenylpyrimidine, with bp 190-196° (3 mm), was 3.11 g (67%).

4-Hydroxy-2,4,6-triphenyl-1,4,5,6(?)-tetrahydropyrimidine (VIII). This compound was obtained as in the previous experiment from 2.88 g (0.024 mole) of benzamidine and 5.45 g (0.026 mole) of benzalacetophenone in 25 ml of dry acetone. The yield of tetrahydropyrimidine VIII, with mp 123-124°, was 7.1 g (90%). IR spectrum: 3420 (NH), 3100-3250 (OH), and 1620 cm^{-1} (C=N); a band of C=O vibrations was absent. Found,%: C 80.4; H 6.2; N 8.5; M 328. $C_{22}H_{20}N_2O$. Calculated, %: C 80.5; H 6.1; N 8.6; M 328. PMR spectrum, δ: 1.43 (1H, H^{5a}), 2.15 (1H, H^{5e}), 4.87 (1H, H^6), and 7.15-8.28 ppm (17H, aromatic protons on which the protons of the NH and OH groups are superimposed). An AB spectrum was obtained for the CH_2 group in the 5 position of the pyrimidine ring. The SSCC ($J_{H5a\text{-}H5e}$ =11 Hz, $J_{H5a\text{-}H6}$ =12 Hz, and $J_{H5e\text{-}H6}$ =4 Hz) were found by the double-resonance method.

2,4,6-Triphenylpyrimidine [2.8 g (90%)], with mp 185-186° (from acetic acid), was formed when 3.28 g (0.01 mole) of tetrahydropyrimidine VIII was heated in 15 ml of DMSO at 130° for 8 h in the presence of molecular sieves of the 4A type with passage of a stream of dry air through the reaction mixture.

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PYRIMIDINES.

LXI.* SYNTHESIS OF N-PYRIMIDINYLANTHRANILIC ACIDS AND 2,4-DIARYLPYRIMIDO[2,1-b]QUINAZOL-6-ONES

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V. A. Samsonov, and V. P. Mamaev

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N-(4,6-Diarylpyrimidinyl)anthranilic acids, obtained by condensation of the appropriate 2-chloropyrimidines with anthranilic acid, are converted to 2,4-diarylpyrimido[2,1-b]quinazol-6-ones when they are treated with acetic anhydride.

The number of studies devoted to the synthesis of physiologically active anthranilic acid derivatives has increased in recent years [2-4]. A great deal of attention is being paid to the synthesis of N-heteroaryl-substituted anthranilic acids, including pyrimidine derivatives [4-6]. On the other hand, it is known that the introduction of aryl substituents in pyrimidine and quinazoline derivatives in some cases leads to new physiologically active compounds, the action of which differs from that of their unsubstituted or alkyl-substituted analogs [7, 8]. We therefore undertook the synthesis of pyrimidinylanthranilic acids with aryl substituents in the 4 and 6 positions of the pyrimidine ring by means of the readily accessible 2-oxo-4,6-diarylpyrimidines as the starting compounds [9].

2-(o-Carboxyphenylamino)-4,6-diarylpyrimidines (IIIa-f) were obtained in good yields when 2-chloro-4,6-diarylpyrimidines (IIa-f), obtained by the usual method from 2-oxo derivatives of pyrimidine (Ia-f), were fused with anthranilic acid or when the starting components were refluxed in alcohol for a long time. Similarly, 2-(o-carboxyphenylamino)-4-phenyl-5,6-dihydrobenzo[h]quinazoline (IV) was isolated from 2-chloro-4-phenyl-5,6-dihydrobenzo[h]quinazoline.

Compounds III are stable crystalline substances. However, intramolecular cyclization with splitting out of a water molecule to give 2,4-diarylpyrimido[2,1-b]quinazol-6-ones (Va-d) occurs when they are heated briefly in acetic anhydride. Similar behavior has also been previously noted for other N-pyrimidinylanthranilic acids [10, 11].

*See [1] for communication LX.

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