washed with water, and dried to give 3.24 g (88%) of XVIII with mp 183-184°C (from acetic acid). IR spectrum: 1690 cm^{-1} (C=O). UV spectrum, λ_{max} (log ε): 210 (4.49), 264 (4.69), 310 (4.49), 385 (3.96), and 430 nm (3.90). Found: C 74.8; H 5.0; N 11.4%; M^+ 369. $C_{23}H_{19}N_3O_2$. Calculated: C 74.8; H 5.2; N 11.4%; M 369.

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SYNTHESIS AND TRANSFORMATIONS OF 1-METHYL-4-ARYL-7-R-ISOQUINOLINES

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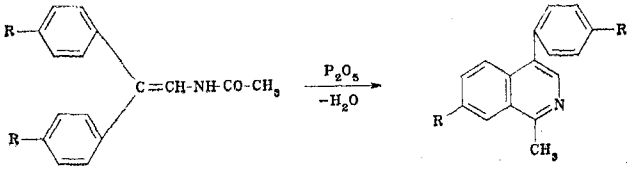
1-Methyl-4-aryl-7-R-isoquinolines were obtained by cyclization of 1,1-diaryl-2-acetamidoethylenes in the presence of phosphorus pentoxide. The condensation of the products with diethyl oxalate leads to the formation of ethyl 1-(4-aryl-7-R-isoquinolyl)pyruvates, which react with o-phenylenediamine to give 1-(4-aryl-7-R-isoquinolyl)-2-[3-(4H)-oxo-2-quinoxalyl]methanes.

We have previously obtained a number of aminoethanols that contain diarylmethylol and primary amino groups, and we also studied the acetylation of the products and synthesized 1,1-diaryl-2-acetamidoethylenes from the acetyl derivatives [1]. Continuing our synthetic studies to obtain physiologically active substances, we attempted to cyclize ethylenes I under the conditions of the Bischler–Napieralski reaction [2] with vinylamides Ia-d as the starting compounds. This made it possible to synthesize not only isoquinolines that contain electron-donor substituents in the aromatic ring but also isoquinolines that contain halogen atoms. Halo derivatives of isoquinoline of this type have previously been obtained only indirectly [3].



Ia-d IIa-d

The most characteristic absorption bands in the IR spectra of isoquinolines II are the bands at ∿1640 and 2980-2990 cm^{-1}, which were assigned, respectively, to the azomethine bond of the isoquinoline ring and to the C–H bond of a methyl group in the 1 position.

Signals of protons of a CH_3 group are found at 2.85-2.95 ppm in the PMR spectra of solutions of these compounds in $CDCl_3$. The PMR spectrum of isoquinoline IIb in this region also contains another two singlet signals (2.35 and 2.47 ppm), which are related, respectively, to the p-CH_3 and 7-CH_3 groups. Of the signals of the aromatic protons (7.15-8.1 ppm), the most distinguishable is the signal of the proton in the 3 position of the isoquinoline ring (8.2-8.3 ppm). On passing to the hydrochlorides the corresponding signals are shifted 0.2-0.3 ppm to weak field (in d_6-DMSO).

It is known that a methyl group in the ortho position relative to the ring nitrogen atom in aromatic nitrogen-containing heterocycles is characterized by increased reactivity [4]. Taking this into account, we carried out the condensation of isoquinolines II with diethyl oxalate (III) in the presence of potassium ethoxide, as a result of which we obtained ethyl isoquinolylpyruvates (IV), which, according to the IR and PMR spectral data, exist primarily in the enol form.

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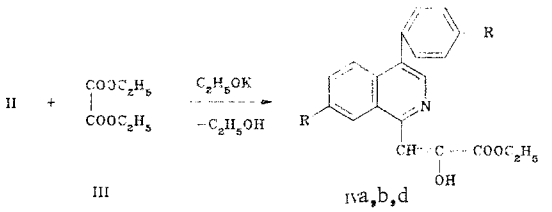
TABLE 1. Characteristics of the Synthesized Compounds

Compound	R	mp, (hydrochloride), °C	N found, %	Empirical formula	N calc., %	Yield, %
IIa	H	78—79 (233—234)	6,4	$C_{16}H_{13}N$	6,4	65
IIb	CH_3	59—60 (214—215)	5,9	$C_{18}H_{17}N$	5,7	69
IIc	Cl	169—170	4,9	$C_{16}H_{11}Cl_2N$	4,9	35
IId	F	130—131	6,1	$C_{16}H_{11}F_2N$	5,9	40
IVa	H	191—192	4,7	$C_{20}H_{17}NO_3$	4,4	69
IVb	CH_3	177—178	4,3	$C_{22}H_{21}NO_3$	4,0	97
IVd	F	234—235	4,2	$C_{20}H_{15}F_2NO_3$	3,9	14
VIa	H	299—300	11,5	$C_{24}H_{17}N_3O$	11,6	55
VIb	CH_3	315—316	10,4	$C_{26}H_{21}N_3O$	10,7	53
VId	F	324—325	10,2	$C_{24}H_{15}F_2N_3O$	10,5	51

Strong bands of an ester carbonyl group (1720-1730 cm^{-1}) conjugated with an aromatic ring, a C=C bond (1600-1605 cm^{-1}), and an enol hydroxy group (3425 cm^{-1}) are present in the IR spectra of esters IV.

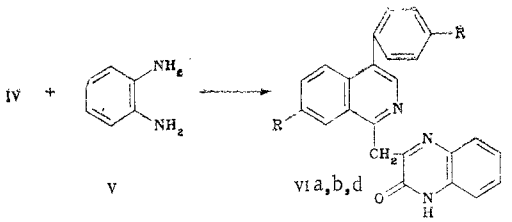


III IVa,b,d

The PMR spectra of solutions of esters IV in $CDCl_3$ are characterized by the presence of a triplet of CH_3 groups and a quartet of CH_2 groups (1.35 and 4.30 ppm), a singlet of an olefin proton (7.00-7.05 ppm), and signals of aromatic protons centered at 7.45 ppm. The signal of the 3-H proton of the isoquinoline ring has a chemical shift of ∿8.1 ppm. In addition to the indicated signals, the PMR spectrum of ester IVb contains two singlets with chemical shifts of 2.44 and 2.50 ppm, which are related to the p-CH_3 and 7-CH_3 groups. Replacement of $CDCl_3$ by CF_3COOH as the solvent affects only the position of the olefin proton, for which a shift to weak field to 7.40 ppm is observed.

It is known that pyruvic acid esters $RCH_2COCOOCH_3$ (R = 2-quinolyl, 2-quinoxalyl, 2-pyrimidyl, 4-pyrimidyl, 3-pyridazinyl, and 2-pyrazyl) are more than 90% enolized [5].

We carried out the condensation of esters IV with o-phenylenediamine (V), inasmuch as this reaction made it possible to obtain derivatives that contain a quinoxaline system with potential pharmacological activity [6-9].



V VIa,b,d

In the IR spectra of methanes VI the amide-1 band is found at ∿1690 cm^{-1}, whereas the band of the NH bond is located at ∿3200 cm^{-1}. Absorption of an azomethine group is present at 1630 cm^{-1}.

The signals of methylene protons have a chemical shift of 5.00 ppm in the PMR spectra of solutions of methanes VI in CF_3COOH. Signals of aromatic ring protons are found at 6.6-8.0 ppm. As in the case of esters IVa-d, the signal of the proton attached to the C_3 atom of the isoquinoline ring is found at weaker field and has a chemical shift of ∿7.8 ppm.

EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-20 spectrometer. The PMR spectra were recorded with a Tesla BS-487c spectrometer (80 MHz).

1-Methyl-4-arylisoquinolines (II, Table 1). A mixture of 0.3 g of I, 3 g of P_2O_5, and 10 ml of absolute toluene was refluxed on a metal bath for 3 h, after which it was cooled, made alkaline with 30% NaOH, and extracted thoroughly with ether. The ether layer was treated repeatedly with 10% HCl, and the acidic layer was made alkaline and extracted repeatedly with ether. The ether layer was dried with KOH, and the ether was removed by successive distillation and evaporation.

Ethyl (4-Arylisoquinolyl)pyruvates (IV, Table 1). A 4-g (0.1 mole) sample of potassium was dissolved in a mixture of 25 ml of absolute ether and 18 ml (0.3 mole) of absolute ethanol, after which a solution of 7.5 g (0.05 mole) of freshly distilled diethyl oxalate in 50 ml of absolute ether was added dropwise. After 15 min, a solution of 0.05 mole of isoquinoline II in ether was added dropwise, and the mixture was allowed to stand for 4 days. The crystalline precipitate was removed by vacuum filtration, and 200 ml of 50% acetic acid was added to the precipitate. After a few hours, the completely liberated ester IV was removed by filtration and recrystallized from ethanol.

(4-Arylisoquinolyl)[3-(4H)-oxoquinoxalyl]methanes (VI, Table 1). A mixture of 0.15 mmole of ester IV, 0.15 mmole of o-phenylenediamine (V), and 10 ml of amyl alcohol was refluxed for 45 min, after which it was cooled, and the resulting precipitate was removed by filtration and recrystallized from xylene.

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AZAHETEROCYCLES BASED ON 1,5-DIKETONES, CYCLIC β-KETOLS, AND ETHANOLAMINE

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The peculiarities of the hydroxyethylamination of 1,5-diketones and three-ring β-ketols under heterogeneous-catalysis conditions as a function of the type of carbonyl compound were ascertained. Catalytic hydroxyethylamination is a convenient preparative method for the production of N-β-hydroxyethyl derivatives of 2,3,5,6-dicycloalkanopiperidines and 9-substituted perhydroacridines.

The synthesis of saturated six-membered nitrogen-containing heterocycles by means of catalytic hydroxyalkyl(aryl)amination of 1,5-diketones was reported in [1].

The present communication is devoted to a study of the catalytic reductive amination of dioxo compounds of the indicated type and three-ring β-ketones in the presence of a binucleophilic reagent, viz., ethanolamine. The substrates were 2,2'-methylenedicyanones (I-III), 2-hydroxy-2,3-tetramethylene-4-alkyl(furyl)bicyclo[3.3.1]nonan-9-ones (IV-VII),

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