B) This compound was similarly obtained from 1 g (3.43 mmole) of amide I and 0.36 ml (7.0 mmole) of bromine. The yield of salt XII was 0.85 g (50%).

C) A 1.18-ml (23 mmole) sample of bromine was added to a suspension of 2.92 g (10 mmole) of pyridone XIII [1] in 60 ml of chloroform, and the mixture was allowed to stand in a refrigerator for 3 h. The precipitate was removed by filtration and washed with petroleum ether to give 5 g (94%) of salt XII.

Recrystallization of salt XII from benzene gave dihydropyridone XV (Table 3), whereas recrystallization from ethanol gave XVI.

5-Bromo-3-carbamoyl-4,6-diphenyl-2-pyridone (XVIII). This compound was obtained from dihydropyridone XV by a method similar to that used to prepare IXa (Table 3).

α-Bromo-α-(N-methylcarbamoyl)-β-phenyl-γ-benzoyl-γ-butyrolactone (VIa). A 0.17-ml (3.31 mmole) sample of bromine was added to a suspension of 1 g (3.09 mmole) of lactone Va [3] in 20 ml of acetic acid. The next day, the solution was poured into water, and the precipitate was separated (Table 3). IR spectrum: 1665, 1695, 1788, and 3375 cm^{-1}. PMR spectrum (d_6-DMSO): 2.33 (CH_3), 4.34 (β-H), 6.46 (γ-H), and 7.2-8.0 ppm (aromatic protons, NH).

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SYNTHESIS OF HYDROGENATED HETEROCYCLIC COMPOUNDS FROM α-METHYLENE-1,5-DIKETONES.

5.* SYNTHESIS AND STEREOCHEMISTRY OF THE PRODUCTS OF ADDITION OF HYDRAZINES TO 2,4-DIBENZOYL-3-PHENYL-1,4-PENTADIENE

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UDC 547.828.829.07:541.63

The addition of phenyl- and 1,1-dimethylhydrazine to 2,4-dibenzoyl-3-phenyl-1,4-pentadiene leads to the formation of the corresponding 1-substituted 3,5-dibenzoyl-4-phenylpiperidines. 3-Benzoyl-4,6-diphenyl-1,7-diazabicyclo[3.2.1]oct-6-ene was obtained in the reaction with hydrazine.

We have previously reported [2] the addition of primary amines and hydroxylamine to 2,4-dibenzoyl-3-phenyl-1,4-pentadiene (I), which leads to the formation of the corresponding substituted piperidines. In the present paper we present data on the addition of phenylhydrazine, 1,1-dimethylhydrazine, and hydrazine to diketone I.

*See [1] for Communication 4.

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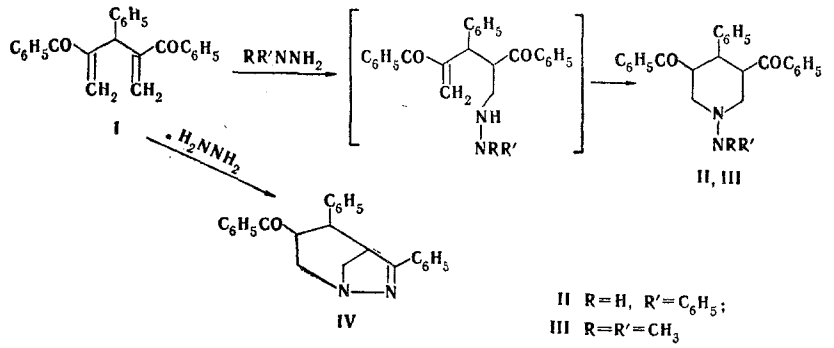
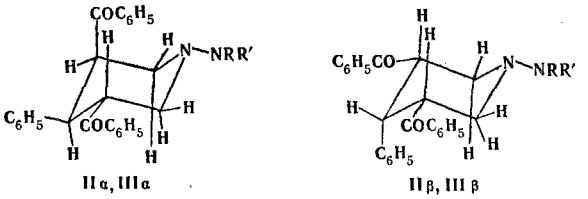


The first two hydrazines add to diketone I to give II and III, as in the reaction with primary amines [2]; however, these reactions proceed at a significantly lower rate. 1,1-Diphenyl- and 1-benzyl-1-phenylhydrazines, semicarbazide, and thiosemicarbazide do not react at all. The rate of addition of hydrazine itself is just as high as the rate of addition of methylamine and hydroxylamine, which are the most active reagents in this reaction [2], but the chief product is bicyclic pyrazoline IV.

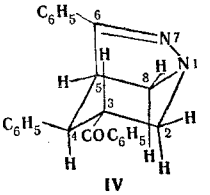
The structures of II and III (see Table 1) follow from a comparison of their IR spectra with the spectrum of diketone I [3], which has absorption bands at 1660 (C=O) and 1630 cm^{-1} ($C=CH_2$). The PMR spectra of II and III are similar to the spectra of the previously obtained piperidines [2] and indicate the formation of mixtures of α and β stereoisomers. Isomers IIα and IIIα are the corresponding 1-amino-3t,5c-dibenzoyl-4r-phenylpiperidines, i.e., the threo form, and IIβ and IIIβ are one of the two possible meso forms, viz., 1-amino-3c,-5c-dibenzoyl-4r-phenylpiperidines.



The action of catalytic amounts of NaOH on an alcohol solution of a mixture of IIα and IIβ leads to complete IIβ→IIα isomerization, whereas similar treatment of a mixture of IIIα and IIIβ does not lead to any changes. The basicity of dimethylhydrazine or III is probably sufficient for the establishment of equilibrium between the isomers in the course of the synthesis.

The IR spectrum of IV (Table 1) does not contain an NH absorption band, whereas a C=O band lies at 1680 cm^{-1}. The absorption of a C=N bond is found at 1550 cm^{-1}, which exceeds the boundaries of the 1580-1627 cm^{-1} range determined [4] for this bond in unsubstituted and 3-aryl-substituted Δ^2-pyrazolines. This is possibly due to the bicyclic structure of the pyrazoline (it is known [5] that the frequency of the vibrations of the C=C bond of cycloalkenes decreases as a result of the fusion of a second ring).

Judging from the PMR spectra (see the experimental section), IV is 3-benzoyl-4r,6-diphenyl-1,7-diazobicyclo[3.2.1]oct-6-ene.



Treatment of the compound with an alcohol solution of NaOH does not alter it.

EXPERIMENTAL

The course of the reactions and the evaluation of the individuality of the substances were monitored by thin-layer chromatography (TLC) on Silufol in a benzene–ethyl acetate mixture (1:1, system B) or in a petroleum ether–ethyl acetate mixture (1:1, system A) with de-

TABLE 1. Substituted Piperidines II-IV

Compound	mp, °C (solvent)	R_f (system)	IR spectrum, cm^{-1}	Found, % C	Found, % H	Found, % N	Empirical formula	Calc., % C	Calc., % H	Calc., % N	Yield, %
IIα, β	203—212° (CH_3OH)	0,62; 0,69 (A)	1500 (C=C, NH), 1605 (C_6H_5—N), 1680 (C=O), 3300 (NH)	81,1	6,1	6,0	$C_{31}H_{28}N_2O_2$	80,8	6,1	6,1	73
IIα	211,5—213,5 (dioxane)	0,62 (A)	1500 (C=C, NH), 1605 (C_6H_5—N), 1680 (C=O), 3300 (NH)	80,5	6,3	6,2					
IIIα, β	156—166 (CH_3OH)	0,65; 0,70 (B)	1680 (C=O)	78,2	7,0	6,8	$C_{27}H_{28}N_2O_2$	78,6	6,8	6,8	85
IV*	191—192 (CH_3OH)	0,39 (B)	1550 (C=N), 1680 (C=O)	81,7	6,0	7,7	$C_{25}H_{22}N_2O$	81,9	6,0	7,6	65

*Found: M^+ 366. $C_{25}H_{22}N_2O$. Calculated: M 366.

velopment of the spots with iodine vapors. The melting points of the substances were determined with a Boetius stage. The IR spectra of mineral oil suspensions and solutions of the substances in $CHCl_3$ were recorded with a UR-20 spectrometer. The PMR spectra of saturated solutions in $CDCl_3$ were recorded with a Bruker HX-90E spectrometer (90 MHz) with tetramethylsilane as the internal standard. The mass spectrum was recorded with an MKh-1303 spectrometer at 30 eV with direct introduction of the sample into the ion source.

Addition of Phenylhydrazine to Diketone I. A 0.03-mole sample of diketone I [3] was added to a solution of 0.06 mole of phenylhydrazine in 100 ml of DMF, and the mixture was stirred at room temperature for 15 h, after which it was allowed to stand for 4 days. It was then diluted with 200 ml of water, and the liberated oil was triturated with water until it crystallized. The crystals were removed by filtration and recrystallized from alcohol to give 10.1 g (73%) of a mixture of IIα and IIβ (Table 1). PMR spectrum: two CH_2 (IIβ), 2e-H, 6e-H, 4a-H (IIα), δ 3.28-3.78 ppm, multiplet; 4e-H (IIβ), δ 3.91 ppm, 1H, triplet, J = 5.6 Hz; 3a-H, 5a-H (IIβ), 5e-H (IIα), δ 4.35 ppm, 2H, quintet; NH, δ 4.88 (IIα), δ 4.92 (IIβ), 1H, singlet; aromatic protons, δ 6.5-8.1 ppm. The ratios of the isomers were 52% IIα and 48% IIβ. A 7.4-g sample of the resulting mixture was refluxed in 250 ml of CH_3OH, after which the hot solution was filtered to remove the undissolved material and cooled to give 3.6 g of crystals with the same melting point as the starting mixture. The CH_3OH-insoluble residue was recrystallized from 30 ml of dioxane to give 1.8 g of IIα. PMR spectrum: 4-H, δ 3.70 ppm, 1H, quartet, J = 10.6 and 4.7 Hz; 3a-H, δ 5.53 ppm, 1H, sextet, J = 10.6, 10.6, and 4.1 Hz; 5e-H, δ 4.23 ppm, 1H, quartet, J = 4.7, 4.4, and 3.5 Hz; 2a-H, δ 2.57 ppm, 1H, triplet, J = 10.6 and —10.8 Hz; 6a-H, δ 2.99 ppm, 1H, quartet, J = 4.4 and —11.7 Hz; NH, δ 4.85 ppm, 1H, singlet, which disappeared when CD_3OD was added.

Addition of 1,1-Dimethylhydrazine to Diketone I. A 0.02-mole sample of 1,1-dimethylhydrazine was added to a solution of 0.01 mole of I in 75 ml of DMF, and the resulting solution was allowed to stand for 7 days. After the addition of 250 ml of water, the mixture was saturated with NaCl, and the resulting precipitate was washed with water and dried to give 3.7 g (90%) of a mixture of IIIα and IIIβ. Recrystallization from 18 ml of CH_3OH gave 3.5 g (85%) of a purified mixture of IIIα and IIIβ (Table 1). Subsequent recrystallization did not lead to a change in the physical constants. PMR spectrum: CH_3 (IIIα), δ 2.19 ppm, 3H, singlet; CH_3 (IIIβ), δ 2.02 ppm, 3H, singlet; 3a-H (IIIα), δ 5.38 ppm, 1H; the remaining protons of the piperidine rings are found at δ 2.3-4.3 ppm; aromatic protons, δ 6.9-8.1 ppm. The composition of the mixture was 43% IIIα and 57% IIIβ.

Addition of Hydrazine to Diketone I. A 10.6-g (96%) sample of crude IV was obtained by the method described above from a solution of 0.06 mole of absolute hydrazine and 0.03 mole of I in 100 ml of DMF after 5 h. The same results were obtained when hydrazine hydrate or a reagent molar ratio of 1:1 was used. Recrystallization from CH_3OH gave 7.1 g (64%) of homogeneous (according to TLC) IV (Table 1). PMR spectrum: 3-H, δ 4.40 ppm, 1H, sextet, J = 10.8, 10.6, and 6.4 Hz; the remaining protons were those of a bicyclic system, δ 2.92-3.94 ppm, 6H. INDOR spectra: 2a-H, δ 3.05 ppm, 1H, quartet, J = 10.8 and —13.5 Hz; 2e-H, δ 3.78 ppm, 1H, quartet, J = 6.4 and —13.5 Hz; 4a-H, δ 3.53 ppm, 1H, quartet, J = 10.6 and 6.4 Hz; 8a-H, 8e-H, δ 3.24-3.44 ppm, 2H, multiplet; 5e-H, δ 3.92 ppm, 1H, narrow multiplet.

Action of Sodium Hydroxide on II-IV. A solution of 0.5 g of a mixture of IIα and IIβ in 25 ml of CH_3OH was refluxed with 1 ml of a saturated solution of NaOH in CH_3OH for several minutes, after which the mixture was cooled, and IIα was removed by filtration. According to TLC data, isomer IIβ was absent in the mother liquor.

Treatment of a mixture of IIIα and IIIβ and IV does not alter them.

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SYNTHESIS AND PROPERTIES OF 4-SUBSTITUTED 1,5-NAPHTHYRIDINES AND THEIR N-OXIDES

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4-Substituted 1,5-naphthyridines and their N-oxides were synthesized, and their structures and properties were studied. The IR and UV spectra of 4-hydroxy- and 4-methoxy-1,5-naphthyridines and their 1-oxides and 1-ethyl-4-oxo-1,4-dihydro-1,5-naphthyridine were examined. It is shown that 4-hydroxy-1,5-naphthyridine and its 1-oxide exist in the crystalline state in the lactam form. A quantitative estimate of the position of the tautomeric equilibrium of 4-hydroxy-1,5-naphthyridine as a function of the polarity of the solvent is given, and the tautomeric equilibrium constants and the percentages of the lactim form are calculated. The basicity constants of 4-chloro-, 4-methoxy-, 4-hydrazino-, 4-methylthio-, 4-acetamido-, and 4-amino-1,5-naphthyridines were measured. A comparison of the calculated and experimental pK_a data provides evidence in favor of the fact that the compounds are protonated at the N_1 atom. A correlation of the basicity constants with the σ substituent constants is examined.

Research on the chemistry of x,y-naphthyridines has expanded considerably in recent years in connection with the fact that biologically active compounds have been detected among derivatives of these heterocycles.

In our previously published papers we have reported the synthesis and structure of 2-substituted 1,5-naphthyridines and their N-oxides, among which substances that have antibacterial activity have been found [1]. Continuing our study of 1,5-naphthyridine derivatives we synthesized 4-substituted 1,5-naphthyridines and their N-oxides and studied their structures and properties.

Compounds II-VII were synthesized from 4-chloro-1,5-naphthyridine (I). By alkylation of III we obtained 4-alkylthio derivatives Va-c of 1,5-naphthyridine and by subsequent oxidation of them we obtained sulfones VIa, c.

Chloro derivative I is readily oxidized with hydrogen peroxide in the presence of Na_2WO_4 to give N-oxide VIII. Under more severe conditions the reaction proceeds ambiguously and is accompanied by partial replacement of chlorine by a hydroxy group. The structure of N-oxide VIII was proved by comparisons of its PMR spectrum with the spectrum of I (see Table 1): The shift of the H_8 signal in the spectrum of the N-oxide to weak field ($\Delta\delta = -0.62$ ppm), which is characteristic for the protons of aromatic heterocycles in the peri position

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