of 10% hydrogen peroxide. Fractional crystallization of 1 g of the oxidation product from alcohol–ether yielded 0.9 g of N-oxide XXVI with mp 200-202° and R_f 0.82. A 0.45-sample of the crude reaction product was converted to the picrate, and the latter was crystallized from ethanol to give 0.7 g of the picrate, with mp 179-180° and R_f 0.82, in conformity with the value for N-oxide XXVI. Found: C 51.4; H 6.2; N 12.0%. $C_{14}H_{25}NO_2 \cdot C_6H_3N_3O_7$. Calculated: C 51.3; H 6.0; N 11.9%. The mother liquor of the picrates gave two products with R_f 0.82 and 0.60, the latter in the form of an impurity.

1,2,9-Trimethyl-4-(1,2-epoxyethyl)decahydro-4-quinolol N-Oxide (XXX). A 0.95 g-sample of crude reaction product was obtained by oxidation of 0.9 g (4.5 mmole) of N-oxide XXVI by means of 1.3 g (4.5 mmole) of 70% peracetic acid in chloroform–methanol. The crude product was converted to the picrate, and the picrate was crystallized to give 0.5 g of the picrate, with mp 192-193° and R_f 0.76, corresponding to N-oxide XXX. Found: C 49.5; H 5.9; N 11.5%. $C_{14}H_{25}NO_3 \cdot C_6H_3N_3O_7$. Calculated: C 49.6; H 5.8; N 11.6%. Workup of the mother liquor yielded 0.1 g of starting N-oxide XXVI.

Oxidation of 2 g (10 mmole) of alcohol XI with 2.2 g (20 mmole) of 70% peracetic acid in 20 ml of $CHCl_3$ gave 2.3 g of a viscous substance. Crystallization of the mixture of picrates yielded 1.27 g of a picrate with mp 192-193° and R_f 0.75 that did not depress the melting point of the picrate of N-oxide XXX, as well as 0.43 g of a picrate with mp 178-179° and R_f 0.82, identical to the picrate of N-oxide XXVI.

N-oxide XXX was also obtained by oxidation of glycidic alcohol XIV (mp 145-146° and R_f 0.84) with 10% hydrogen peroxide in methanol. Glycidic alcohol XIV was synthesized by oxidation of vinyl alcohol XI with performic acid. Found: C 70.4; H 10.6%. $C_{14}H_{16}NO_2$. Calculated: C 70.3; H 10.5%.

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INVESTIGATION OF NAPHTHYRIDINES

VIII.* SYNTHESIS AND PROPERTIES OF 2-ACETYL-10-ARYL-1,2,3,4-TETRAHYDROBENZO[b]-1,6-NAPHTHYRIDINES

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UDC 547.836.3'822.1

2-Acetyl-10-aryl-1,2,3,4-tetrahydrobenzo[b]-1,6-naphthyridines were obtained by reaction of 4'-(2')-R-2-aminobenzophenones with 1-acetyl-4-piperidone, and their pK_a values were determined. It was found that they are oxidized by hydrogen peroxide to give the corresponding N-oxides in good yields. The N-oxides are converted to the 4-acetoxy derivatives by the action of acetic anhydride.

Having in view a comparison of the properties of derivatives of benzo-1,6-naphthyridine and the corresponding quinolines, we showed that 2-acetyl-10-aryl-1,2,3,4-tetrahydrobenzo[b]-1,6-naphthyridines I-VI (Table 1) are formed in 34-80% yields when 4'(2')-R-2-aminobenzophenones are refluxed with 1-acetyl-4-piperidone in glacial acetic acid in the presence of catalytic amounts of concentrated sulfuric acid. In connection with

*See [1] for communication VII.

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TABLE 1. 2-Acetyl-10-aryl-1,2,3,4-tetrahydrobenzo[b]-1,6-naphthyridines (I-VI)

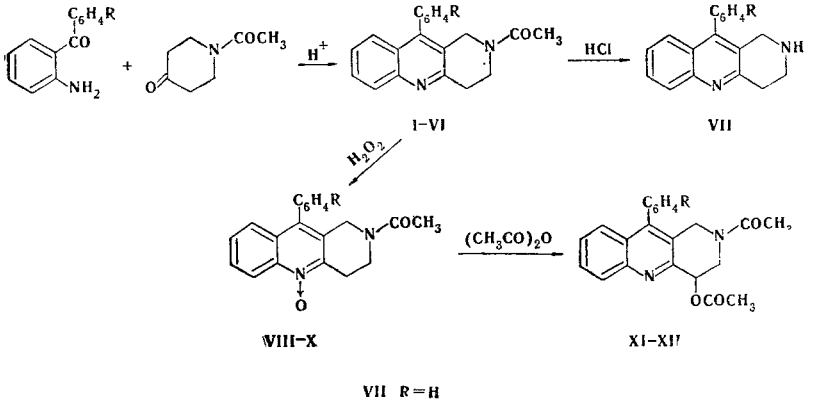
Compound	R	mp, °C	mp of the hydrochloride, °C	Empirical formula	Found, %			Calc., %			pK_a*	Yield, %
					C	H	N	C	H	N		
I	H	166—167	276—278	$C_{20}H_{18}N_2O$	79,2	6,2	9,2	79,4	6,0	9,3	2,48±0,02	80
II	*p*-CH_3	175—176	261—262	$C_{21}H_{20}N_2O$	79,7	6,6	8,9	79,6	6,3	8,9	2,66±0,01	57
III	*p*-Cl	163—164	252—256	$C_{20}H_{17}ClN_2O$	—	—	8,2	—	—	8,3	2,22±0,03	59
IV	*p*-Br	176—178	256—258	$C_{20}H_{17}BrN_2O$	—	—	7,1	—	—	7,3	2,24±0,02	77
V	*p*-CH_3O	182—183	259—260	$C_{21}H_{20}N_2O_2$	—	—	8,6	—	—	8,4	2,80±0,04	62
VI	*o*-CH_3	162—163	266—268	$C_{21}H_{20}N_2O$	—	—	8,8	—	—	8,9	—	34

* The following $pK_a - \sigma$ correlation parameters were obtained: r = 0.997, $\rho = -1.124$, pK_a° calculated = 2.49, and s = 0.018.

TABLE 2. 2-Acetyl-10-aryl-1,2,3,4-tetrahydrobenzo[b]-1,6-naphthyridine N-Oxides (VIII-X)

Compound	R	mp, °C	Empirical formula	N, %		Yield, %
				found	calc.	
VIII	H	199—200	$C_{20}H_{18}N_2O_2$	9.0	8.8	89
IX	*p*-CH_3	187—188	$C_{21}H_{20}N_2O_2$	8,6	8,4	76
X	*p*-Cl	177—178	$C_{20}H_{17}ClN_2O_2$	7,6	7,9	95

the fact that the reaction products are usually contaminated by the starting 2-aminobenzophenones, they are heated with acetic anhydride for separation from the latter prior to purification.



VII R = H

10-Phenyl-1,2,3,4-tetrahydrobenzo[b]-1,6-naphthyridine (VII) was obtained by acid hydrolysis of acetyl derivative I.

The ionization constants of I-V and VII in 96° ethanol was determined by potentiometric titration. The pK_a values of these compounds ranged from 2.2 to 2.8 units, changed only slightly under the influence of substituents in the aryl grouping attached to the $C_{(10)}$ atom, and were linearly dependent on the Hammett σ constants. The $pK_a - \sigma$ correlation for the series of benzonaphthyridines I-V is satisfied with a slope of −1.124, which is considerably lower than the reaction constant of the series of substituted quinolines (5.6) [2]. This provides evidence that transmission of the electronic effects of the substituents in the aryl grouping to the nitrogen atom of the quinoline ring of the benzonaphthyridine system of I-V is hindered, probably because of the noncoplanar orientation of the aryl and benzonaphthyridine rings. The pK_{a2} value of VII is 0.2 unit lower than the pK_a value of I; this is associated with the higher electronegativity of the ammonium cation (the 2 position) in protonated VII as compared with the acetamido group in I.

It was shown in the case of I-III that the naphthyridines are smoothly converted to the corresponding N-oxides (VII-X, Table 2) on reaction with hydrogen peroxide in glacial acetic acid. The UV spectra of N-oxides VIII-X contain maxima at 244 and 344 nm and are shifted bathochromically as compared with the spectra of naphthyridines I-VI. This shift is expressed most strongly in the case of the long-wave band (by 40 nm), which is of high intensity.

As in the case of the simpler analogs [3], N-oxides VIII and X undergo rearrangement to 2-acetyl-4-acetoxy-10-aryl-1,2,3,4-tetrahydrobenzo[b]-1,6-naphthyridines XI and XII on heating with acetic anhydride.

EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-20 spectrometer. The UV spectra of ethanol solutions of the compounds were obtained with a SpectroMoM-202 spectrophotometer. The ionization constants of I-V and VII were determined by potentiometric titration of 0.01 M solutions in 96° ethanol with a 0.1 M solution of perchloric acid in ethanol with a pH-340 pH-meter. The pH-meter had glass and silver chloride electrodes. The pK_a values were calculated by the usual method [4].

4'(2')-R-2-Aminobenzophenone. These compounds were obtained by reaction of 2-methylbenzo[d]-1,3-oxazin-4-one with arylmagnesium halides and subsequent cleavage of the acetyl group [5].

2-Acetyl-10-aryl-1,2,3,4-tetrahydrobenzo[b]-1,6-naphthyridines (I-VI). A solution of 0.01 mole of 4'(2')-R-2-aminobenzophenone and 0.01 mole of 1-acetyl-4-piperidone in 10 ml of glacial acetic acid was refluxed in the presence of 0.1 ml of concentrated H_2SO_4 for 20 h, after which it was cooled and poured carefully into a mixture of 15 ml of ammonia, 50 ml of water, and 50 g of ice. The liberated substance was dissolved in benzene, and the solution was dried by removal of the water by azeotropic distillation with benzene. Acetic anhydride (20 ml) was added to the dry residue, and the mixture was heated on a water bath for 1 h. It was then cooled and poured into 200 ml of water, the excess acetic anhydride was decomposed, and the solution was made alkaline with ammonia. The liberated product was removed by filtration, dried, and dissolved in ethanol. A saturated ethanol solution of hydrogen chloride was added, and hydrochlorides I-VI were isolated and crystallized from alcohol-ether. The hydrochlorides were treated with dilute ammonium hydroxide (with cooling) to yield bases I-VI, which were crystallized from acetone. An amide carbonyl band was observed at 1640-1650 cm^{-1} (CO) in the IR spectra of I-VI. UV spectrum, λ_{max} (log ε): 234, 296, 308 (4.64, 3.81, 3.78) nm.

10-Phenyl-1,2,3,4-tetrahydrobenzo[b]-1,6-naphthyridine (VII). A 0.25-g sample of naphthyridine I was heated in 10 ml of 10% HCl for 2 h, after which the mixture was cooled and made alkaline, and the product was removed by filtration to give 0.2 g (93%) of VII with mp 117-118° (from hexane). IR spectrum: 3320 cm^{-1} (NH). Found: N 11.1%. $C_{18}H_{16}N_2$. Calculated: N 10.8%. pK_{a1} 6.64, pK_{a2} 2.28. (The pH at the half-neutralization point).

2-Acetyl-10-aryl-1,2,3,4-tetrahydrobenzo[b]-1,6-naphthyridine N-Oxides (VIII-X). A solution of 0.5 g of I-III and 0.5 ml of 30% H_2O_2 in 5 ml of glacial acetic acid was heated on a water bath for 5 h, after which the acetic acid was removed by vacuum distillation, and the residue was made alkaline with 10% sodium carbonate solution. The reaction product was extracted with chloroform, and the extract was dried with anhydrous magnesium sulfate and chromatographed on Al_2O_3. The product was crystallized from ethyl acetate. IR spectrum: 1315-1320 cm^{-1} (N→O)[6]. UV spectrum of VIII, λ_{max} (log ε): 244, 334 (4.69, 4.04) nm.

2-Acetyl-4-acetoxy-10-phenyl-1,2,3,4-tetrahydrobenzo[b]-1,6-naphthyridine (XI). A 1-g sample of N-oxide VIII was heated in 10 ml of acetic anhydride on a water bath for 2 h, after which it was cooled and made alkaline with 10% sodium carbonate solution. The XI was extracted with chloroform, the chloroform extract was dried with anhydrous magnesium sulfate, and the solvent was removed by distillation. The residue was triturated with hexane to give 0.9 g (79%) of a product with mp 184-185° (from ethyl acetate). IR spectrum of XI, cm^{-1}: 1735 (COOR), 1640 (CONH). Found: C 73.2; H 5.6; N 7.8%. $C_{22}H_{20}N_2O_3$. Calculated: C 73.5; H 5.7; N 7.9%.

2-Acetyl-4-acetoxy-10-(p-chlorophenyl)-1,2,3,4-tetrahydrobenzo[b]-1,6-naphthyridine (XII). This compound, with mp 218-219° (from ethyl acetate), was similarly obtained in 67% yield. Found: N 7.1%. $C_{22}H_{19}ClN_2O_3$. Calculated: N 7.4%.

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