HYDROACRIDINES AND RELATED COMPOUNDS

X.* 4-BENZOYLHYDROACRIDINES

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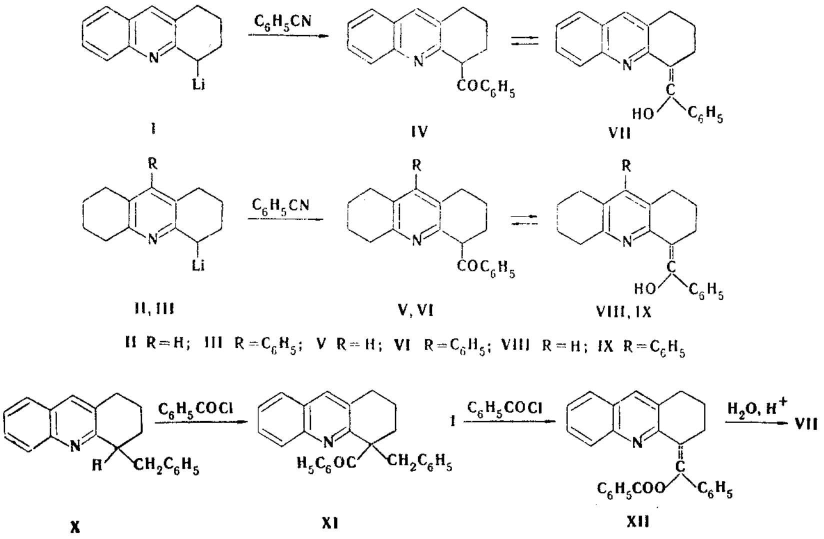
UDC 547.835.07

4-Benzoylhydroacridines were synthesized by the reaction of 4-lithiohydroacridines with benzonitrile or benzoyl chloride. Their capacity for keto–enol tautomerism was noted.

In a continuation of our research [1-3], we have synthesized 4-benzoylhydroacridines. 4-Benzoyl-1,2,3,4-tetrahydroacridine (IV), 4-benzoyl-sym-octahydroacridine (V), and 4-benzoyl-9-phenyl-sym-octahydroacridine (VI), respectively, were obtained by the reaction of 4-lithio-1,2,3,4-tetrahydroacridine (I), 4-lithio-sym-octahydroacridine (II), and 4-lithio-9-phenyl-sym-octahydroacridine (III) with benzonitrile. Under similar conditions, 4-lithio-4-benzyl-1,2,3,4-tetrahydroacridine (X) does not react with benzonitrile; we were able to obtain 4-benzoyl-4-benzyl-1,2,3,4-tetrahydroacridine (XI) by the reaction of X with benzoyl chloride. This can apparently be explained by the lower reactivity of I as compared, for example, with that of I [1].



The compounds obtained are analogs of 2-phenacylpyridine, for which a capacity for keto–enol tautomerism has been noted [4]. It seemed of interest to examine how IV-VI behave in this respect.

Absorption bands of carbonyl and hydroxyl groups are absent in the IR spectra of solid IV or its solutions. A similar pattern was observed for the enol forms of substituted 2-phenacylpyridines [4]; the latter spectral peculiarity was explained by the formation of a hydrogen bond with the nitrogen atom. Compound IV gives a positive reaction for an enol with ferric chloride and forms a complex salt on treatment with cupric acetate, but does not react with phenylhydrazine. Thus the base exists in enol form VII. On the other hand, there is a distinct absorption band at 1690 cm^{-1} in the spectrum of the hydrochloride. Conse-

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*See [1] for communication IX.

Far-Eastern State University, Vladivostok. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 984-986, July, 1972. Original article submitted June 8, 1971.

TABLE 1. 4-R-Hydroacridines

Compound	mp, °C	Empirical formula	Found, %			Calc., %			Yield, %
			C	H	N	C	H	N	
IV[a]	82—84	$C_{20}H_{17}NO$	83,7	6,4	4,7	83,6	6,0	4,9	62
IV · HCl	213—214	$C_{20}H_{17}NO \cdot HCl$	—	—	4,1	—	—	4,3	—
V[b]	81,5—83	$C_{20}H_{21}NO$	81,9	7,4	5,1	82,4	7,3	4,8	36
V · HCl	215—217	$C_{20}H_{21}NO \cdot HCl$	—	—	4,1	—	—	4,3	—
Phenylhydrazone of V	128—129	$C_{26}H_{27}N_3$	—	—	11,2	—	—	11,0	26
VI	130—132	$C_{26}H_{25}NO$	85,2	7,1	3,9	85,0	6,9	3,8	38
VI · $C_6H_3O_7N_3$	175—178	$C_{26}H_{25}NO \cdot C_6H_3O_7N_3$	—	—	9,0	—	—	9,4	—
XI	137—138	$C_{27}H_{23}NO$	86,1	6,6	—	85,9	6,2	—	62
XI · $C_6H_3O_7N_3$	176—178	$C_{27}H_{23}NO \cdot C_6H_3O_7N_3$	—	—	10,1	—	—	9,6	—
XII	153,5—154	$C_{27}H_{21}NO_2$	83,0	5,6	—	82,8	5,4	—	55

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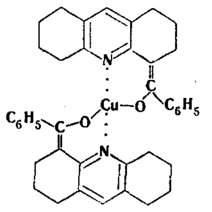
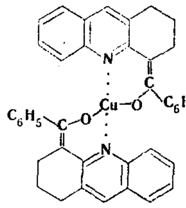
[a] The copper salt was obtained by mixing alcohol solutions of the base and cupric acetate and decomposed above 200° Found: Cu 10.7%. $C_{40}H_{32}CuN_2O_2$. Calculated: Cu 10.6%. [b] The copper salt decomposed above 250°. Found: Cu 10.2%. $C_{40}H_{40}CuN_2O_2$. Calculated: Cu 10.5%. The proposed structures of the complexes are:





quently, the salt is formed by ketone form IV. The VII structure is also confirmed by the reaction of I with benzoyl chloride. The reaction product is the benzoate of enol XII, as follows from the IR spectrum of this compound (ester carbonyl absorption at 1740 cm^{-1}) and its hydrolysis to VII.

Compounds V and VI are inclined to undergo enolization to an apparently lesser degree than IV. Solid V does not display carbonyl absorption in the IR spectrum and apparently exists in enol form VIII. The equilibrium V $\rightleftharpoons$ VIII is apparently established in solution, since, on the one hand, an absorption band appears at 1690 cm^{-1} in the IR spectrum, and the substance forms a phenylhydrazone (although in low yield), while, on the other hand, it gives a positive reaction for an enol with ferric chloride and forms a copper salt. A similar pattern is also observed for VI.

Ketone XI, the structure of which excludes the possibility of the formation of an enol form, displays carbonyl group absorption in its IR spectrum at 1690 cm^{-1}, does not give coloration with ferric chloride, and does not form a complex salt on reaction with cupric acetate. In contrast to yellow IV-VI, ketone XI is colorless.

Of the VII, VIII, and IX structures, the first has the most developed conjugation system. This apparently also leads to the fact that IV exists primarily in enol form VII, which is additionally stabilized by a hydrogen bond of the chelate type between the hydroxyl hydrogen atom and the ring nitrogen atom. In the hydrochloride of IV, this sort of additional stabilization becomes impossible, and, as a result, the ketone form, which is also recorded by the IR spectrum, develops. The conjugation chain is shorter in VIII and IX than in VII, and the shift to favor the formation of an enol is not so great for the corresponding ketones.

EXPERIMENTAL

The IR spectra of CCl_4 solutions and KBr pellets of the compounds were recorded.

4-Benzylhydroacridines. A solution of 5.2 g (0.05 mole) of benzonitrile in 10 ml of absolute ether was added dropwise in the course of 15 min to a suspension of 4-lithiohydroacridine, prepared from 0.05 mole of the appropriate hydroacridine and an equimolar amount of an ether solution of phenyllithium. In the synthesis of XI and XII, 0.1 mole of benzoyl chloride was added in place of benzonitrile. The mixtures were stirred for 1-2 h.

A. Compounds IV-VI. Water (40 ml) was added to the reaction mixture, the organic layer was separated, and 30 ml of 20% hydrochloric acid was added to it. The hydrochloride was separated, washed with ether, and treated with warm sodium hydroxide solution. The base was then crystallized from alcohol.

B. Compound XI. The reaction mixture was diluted with water, the ether layer was separated and dried with magnesium sulfate, and the ether was evaporated. The residue was triturated with 120 ml of petroleum ether, and the reaction product was removed by filtration. An analytically pure sample was obtained by crystallization from alcohol.

C. Compound XII. The reaction mixture was cooled to 0° to precipitate the reaction product.

Data on the substances are presented in Table 1.

Hydrolysis of the Benzoate of the Enol Form of 4-Benzoyl-1,2,3,4-tetrahydroacridine (XII). A mixture of 1 g of XII and 20 ml of 30% sulfuric acid was refluxed for 6 h, and the resulting solution was poured carefully with ice cooling into 200 ml of 20% potassium hydroxide solution. The base was extracted with ether, and the ether extract was evaporated to 20 ml and treated with 20 ml of 20% hydrochloric acid to precipitate 0.78 g (94%) of the hydrochloride of IV with mp 213-215° (from water), which did not depress the melting point of a sample obtained via organometallic synthesis.

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