UDC 547.835 + 542.95

AMINOMETHYLATING 9-METHYL-3, 4- AND 9-METHYL-1, 2-BENZOACRIDINE

V. S. Tanaseichuk and I. Ya. Postovskii

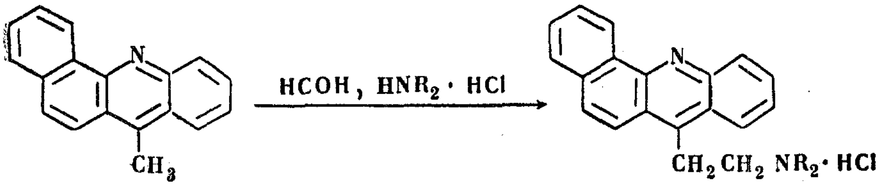
Khimiya Geterotsiklicheskikh Soedinenii, Vol. 1, No. 3, pp. 390-393, 196

Aminomethylating 9-methyl-3, 4-benzoacridine with cycloalkylamine (pyrrolidine, piperidine, and morpholine) hydrochlorides in alcohol is described. The isomeric 9-methyl-1, 2-benzoacridine does not aminomethylate under similar conditions, apparently because the annulated benzene ring at positions 1, 2 in the acridine gives rise to steric hindrance, and the reaction product is 9-β-hydroxyethyl-1, 2-benzoacridine, converted by further heating to 9-vinyl-1, 2-benzoacridine.

The lower reactivity of the methyl group of 9-methyl-1, 2-benzoacridine compared with that of 9-methyl-3, 4-benzoacridine can be ascribed to steric hindrance due to the annulated benzene ring at positions 1, 2 in the acridine.

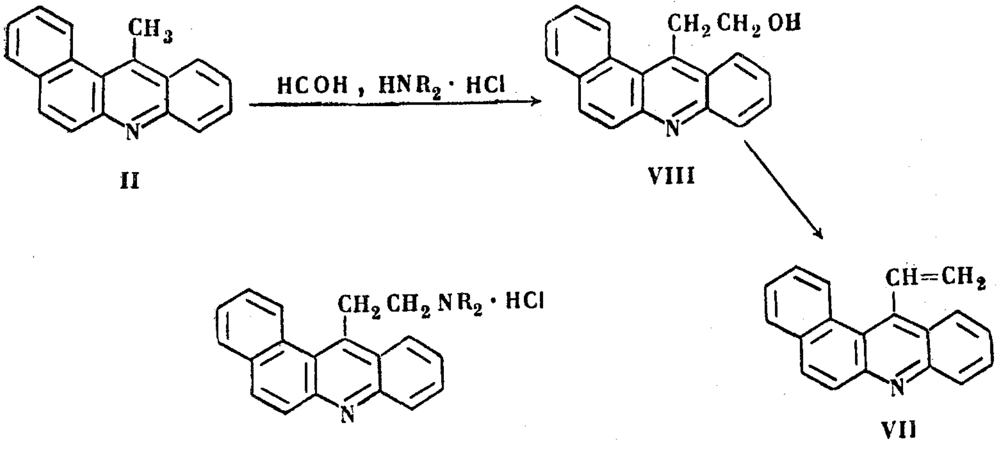
The Mannich reaction was carried out in alcohol, using hydrochlorides of cycloaliphatic amines, pyrrolidine, piperidine, and morpholine. The Mannich reaction proceeds normally* for 9-methyl-3, 4-benzoacridine; as the bases obtained are quite soluble in the usual organic solvents, the pyrrolidine (III) and piperidine (IV) derivatives were isolated as their hydrochlorides, though it proved possible to obtain the morpholine derivative (V) as a stable base.

When an attempt was made to aminomethylate the isomeric 9-methyl-1, 2-benzoacridine (II) with hydrochlorides of cycloalkylamines in alcohol, and reaction carried out with various of the latter, the expected products were not obtained, but instead, the same one every time, viz., 9-vinyl-1, 2-benzoacridine (VII). The same compound was obtained by heating 9-methyl-1, 2-benzoacridine (II) with formaldehyde in alcohol, in the presence of a trace of hydrochloric acid. A precipitate of the vinyl derivative VII started to form after 15-20 hr heating, but if the heating was stopped after 10-12 hr, the precipitate which formed on cooling is a mixture of 9-β-hydroxyethyl-1, 2-benzoacridine (VIII) and 9-vinyl-1, 2-benzoacridine (VII). The more sparingly soluble vinyl compound VII was separated from the β-hydroxy compound VIII by crystallizing from methanol.



I

III—V



II

VIII

VII

VI

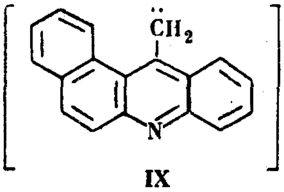
III NR_2 = pyrrolidyl; IV NR_2 = piperidyl; V NR_2 = morpholinyl.

Heating the compound VIII for 3-5 hr with hydrochloric acid in alcohol converts it to 9-vinyl-1, 2-benzoacridine (VII).

---

*As it does with 9-methylacridine [2].

The peculiar behavior of 9-methyl-1, 2-benzoacridine (II) during aminomethylation is probably due to annulation of the benzene ring causing steric hindrance for attack by the bulky carbonium ion (IX) [3]; linked to this is simultaneous reaction with formaldehyde to give a β-hydroxyethyl derivative (VIII).



IX

Noteworthy too is the ease with which 9-β-hydroxyethyl-1, 2-benzoacridine changes into 9-vinyl-1, 2-benzoacridine. Actually steric hindrance due to annulation by the benzene ring also affects the ease of dehydration.

Experimental

9-β-N-Piperidinoethyl-3, 4-benzoacridine (IV) was prepared by heating together on a water bath for 2 hr, 1. 2 g 9-methyl-3, 4-benzoacridine (I), 0. 65 ml formalin (30%), and 0. 6 g piperidine hydrochloride in 5 ml ethanol. The alcohol solution was then poured into water, and the precipitate of hydrochloride (IV) which soon formed, filtered off. Yield 1. 7 g (91. 5%). The crystalline precipitate was slightly yellow, soluble in alcohols, but only slightly soluble in water.

Compounds III and V were prepared similarly. The table gives the property and analytical data, for the compounds prepared.

9-Vinyl-1, 2-benzoacridine (VII).

a) A mixture of 1. 2 g II, 0. 65 ml formalin (30%) and 0. 005 mole cycloalkylamine hydrochloride* in 5 ml ethanol, was heated for 2-4 hr. The precipitate was filtered off, and washed with alcohol. Yield 0. 4 g (31%). Colorless long needles (from benzene), mp 232-233°. Found: C 89. 31; H 5. 54; N 5.10%. Calculated for $C_{19}H_{13}$: C 89. 38; H 5. 13; N 5. 48%.

b) A mixture of 1. 2 g II, 0. 65 ml formalin (30%) in 5 ml ethanol, containing 1 drop of hydrochloric acid, was heated till a precipitate formed (15-20 hr). The precipitate was filtered off, and washed with alcohol, yield 0. 58 g (44%), mp 231-232°.

The same substance was isolated from the filtrate; it had mp 232-233°, and crystallized in a different form (short colorless needles), but the mixed mp of the two forms was undepressed.

9-β-Hydroxy-1, 2-benzoacridine (VIII). A mixture of 9. 72 g 9-methyl-1, 2-benzoacridine, 5. 2 ml formalin (30%), in 40 ml ethanol containing 1 drop of hydrochloric acid, was heated for 10-12 hr. The precipitate which separated on cooling, was filtered off. Yield 4. 7-5. 0 g. The admixed vinyl derivative VII was separated by recrystallizing from methanol, in which the vinyl compound was sparingly soluble. Colorless plates mp 184-186° (from methanol), readily soluble in alcohols. Found: C 83. 39; H 5.53%. Calculated for $C_{19}H_{15}NO$: C 83. 49; H 5. 53%. After further heating for 5-10 hr, the mother liquors gave a precipitate of 9-vinyl-1, 2-benzoacridine.

The IR absorption spectrum of compound VII contained a broad band in the region 3253 cm^{-1}, which is connected with valence vibration of the hydroxyl group involved in intermolecular hydrogen bonding.

9-β-Cycloalkylaminoethyl-3, 4-benzoacridines.

No.	Compound	Mp, °C	Formula	Found, %				Calculated, %				Yield, %
				C	H	Cl	N	C	H	Cl	N	
III	9-β-N-Pyrrolidinoethyl-3, 4-benzoacridine hydrochloride	191—192	$C_{23}H_{22}N_2 \cdot HCl$	76.11	6.53	9.59	7.57	76.12	6.11	9.77	7.71	75
IV	9-β-N-Piperidinoethyl-3, 4-benzoacridine hydrochloride	203—205	$C_{24}H_{24}N_2 \cdot HCl$	76.52	6.64	9.26	7.30	76.47	6.41	9.40	7.43	91
V	9-β-N-Morpholinoethyl-3, 4-benzoacridine hydrochloride	122—123	$C_{23}H_{22}N_2O$	80.67	6.39	—	8.49	80.67	6.48	—	8.18	89

---

*Apparently the cycloalkylamine hydrochloride catalyzed the reaction, triethylamine hydrochloride having the same effect.

REFERENCES

1. B. M. Mikhailov and G. S. Ter-Sarkisyan, Izv. AN SSSR, OKhN, 846, 1954.
2. L. Monti, Gazz., 63, 724, 1933; C. A., 28, 2357, 1934.
3. H. Hellman, Angew. Chem., 65, 473, 1953.

18 April 1964

Kirov Urals Polytechnic Institute,
Sverdlovsk