was no extensive shift of the center of the band with different organic solvents, although such a shift was shown to occur with benzene-azophenol.[4b] On this same graph is also given the curve for eight times the original concentration in ligroin (Curve 3), showing the exact position and strength of the first weak band. In the absorption curve of the entire band, this first band appears so weak that some observers have missed it entirely.

Summary

1. The absorption spectra of benzene-azobenzene have been determined in a number of solvents, and there has been shown to be no extensive shift of the band with a change of typical organic solvents as was the case with benzene-azophenol.

2. It has been shown that the absorption band of benzene-azobenzene is not simple but consists of a smaller band on the lower frequency side of the principal band which adds to the principal band to produce the observed absorption curve.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF LOUISVILLE]

THE SYNTHESIS OF ACRIDINE-9-ETHYLAMINE

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Introduction

Among the alkaloids, strychnine and brucine,[2] as well as among the valuable pharmaceutical products, acriflavine and rivanol[3] are found acridine derivatives, and therefore this group of substances, about which only little is known, has gained new interest for the chemist.

For this reason one of the authors has undertaken a series of investigations on acridine derivatives. In this paper we shall report about the preparation of acridine-9-ethylamine.

Acridine itself has antiseptic properties, and it was thought that by introducing an ethylamine side chain the optimum effect would be obtained. In the pharmaceutical investigations of the amino-alkyl bases of the phenols and of the iminazoles it has been found that the carbon skeleton giving optimum sympathomimetic activity consists of a benzene-iminazole

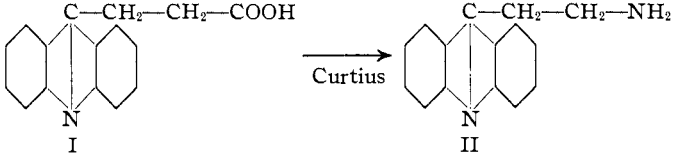
[1] This paper is an abstract of a part of a thesis presented by Louis Howland in partial fulfilment of the requirements for the degree of Master of Science in Chemistry at the University of Louisville.

[2] Perkin and Robinson, *J. Chem. Soc.*, **97**, 305 (1910).

[3] For the physiological effect of these compounds, see E. Laqueur, "Die neueren chemotherapeutischen Praeparate aus der Chinin- und aus der Akridinreihe," Julius Springer, Berlin, **1923.**

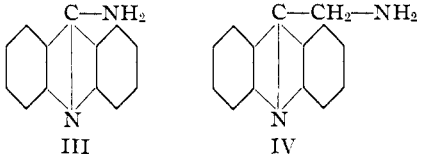
ring with a side chain of two carbon atoms, the terminal one bearing the amino group.[4]

For this reason we have chosen bases of this type in the acridine series also and first of all acridine-9-ethylamine. For the preparation of this compound acridine-9-propionic acid I, which is already known, was converted by successive steps into the ester, hydrazide, azide and the urethan and the latter by boiling with concd. hydrochloric acid into the desired acridine-9-ethylamine II.



I II

Further experiments in the preparation of 9-amino-acridine III and acridine-9-methylamine IV are in progress in order that their physiological effects may be compared with that of acridine-9-ethylamine.



III IV

Experimental Part

Preparation of Acridine-9-propionic Acid.[5]—The method of Volpi has been changed to some extent; 36 g. of succinic acid, 80 g. of diphenylamine and 90 g. of zinc chloride are heated together for eight hours at 190–200°. The melt is extracted first with a 50% sodium carbonate solution in order to decompose the zinc chloride and then with a 10% solution of sodium carbonate. By acidifying the different filtrates faintly with acetic acid, the acridine propionic acid precipitates as a fine, yellow powder. The acid is purified by re-dissolving in sodium carbonate solution and precipitating with acetic acid.

Methyl Acridine-9-propionate.[6]—Ten g. of acridine-9-propionic acid is refluxed for five hours with 150 g. of a 6% solution of hydrogen chloride in methyl alcohol. The main part of the alcohol is distilled, the remaining alcoholic solution is diluted with water, made alkaline with sodium carbonate and the ester shaken out with ether. The ether solution is dried with sodium sulfate and the ether distilled; the ester remains as an oil and is purified from petroleum ether; m. p., 95°.

Hydrazide of the Acridine-9-propionic Acid.—Ten g. of methyl acridine-9-propionate is heated with 2.5 g. of hydrazine hydrate during ten hours on the water-bath under a reflux condenser; the excess of hydrazine is then driven off and the hydrazide

[4] Pyman, *J. Chem. Soc.*, **111**, 1124 (1917).

[5] Volpi, *Ber.*, **25**, R. 940 (1892).

[6] Schenck, *Ber.*, **39**, 2425 (1906).

remains as a solid, crystalline cake. The hydrazide is purified from ethyl alcohol, separating in stout, white needles; m. p., 205–206°. It is insoluble in water and ether and difficultly soluble in alcohol and benzene.

Anal. Calcd. for $C_{16}H_{15}N_3O$: C, 72.45; H, 5.66. Found: C, 72.64; H, 5.87.

HYDROCHLORIDE.—This precipitates from absolute alcohol in yellow needles, which decompose at 270°.

Anal. Calcd. for $C_{16}H_{15}N_3O.2HCl$: Cl, 21.00. Found: 20.80.

Acridine-urethan.—To a solution of 5.3 g. of hydrazide in 50 cc. of absolute alcohol is added 2.6 g. of amyl nitrite dissolved in 15 cc. of absolute alcohol and then a solution of 0.8 g. of hydrogen chloride in 10 cc. of absolute alcohol is gradually added, with cooling. The solution is set aside for 12 hours and then boiled for eight hours under a reflux condenser, when a lively evolution of nitrogen takes place. The main part of the alcohol is distilled and the rest diluted with water and made alkaline with sodium carbonate. The urethan separates and is purified by crystallization from carbon tetrachloride. It then forms fine, faintly yellow needles; m. p., 144–145°. It is insoluble in water, difficultly soluble in carbon tetrachloride and petroleum ether and soluble in alcohol and ether.

Anal. Calcd. for $C_{18}H_{18}N_2O_2$: C, 73.47; H, 6.12. Found: C, 73.4; H, 6.53.

HYDROCHLORIDE.—This separates from alcohol in yellow needles which decompose at 217–218°.

Anal. Calcd. for $C_{18}H_{18}N_2O_2.HCl$: Cl, 10.71. Found: 10.65.

PICRATE.—This is prepared in alcoholic solution and purified by crystallization from alcohol, forming needles; m. p., 195°.

Anal. Calcd. for $C_{18}H_{18}N_2O_2.C_6H_3N_3O_7$: C, 55.07; H, 4.02. Found: C, 54.88; H, 4.29.

Acridine-9-ethylamine.—Five g. of urethan is heated with 150 cc. of concd. hydrochloric acid for seven hours under a reflux condenser. The main part of the acid is then evaporated on the water-bath. By cooling the solution the greater part of the dihydrochloride precipitates. The salt is purified by crystallization from absolute alcohol; it precipitates in fine, yellow needles which contain one molecule of water of crystallization and decompose between 225° and 230°. It is very easily soluble in water and difficultly soluble in absolute alcohol and ether.

Anal. Calcd. for $C_{15}H_{14}N_2.2HCl.H_2O$: Cl, 22.80. Found: 22.73, 22.70.

BENZOYL DERIVATIVE.—By shaking the acridyl-ethylamine dihydrochloride with benzoyl chloride in 10% sodium hydroxide solution the benzoyl derivative is formed; it separates from alcohol in white needles; m. p., 213°.

Anal. Calcd. for $C_{22}H_{18}N_2O$: C, 81.00; H, 5.52. Found: C, 81.33; H, 5.87.

PICRATE.—This is prepared in alcoholic solution, then forming short, yellow needles; m. p., 225°.

In order to obtain the free base, the dihydrochloride is dissolved in water and aqueous ammonia is added. The free base precipitates in silky leaves; m. p., 145°.

In the air or in the vacuum desiccator the substance turns red.

Summary

Acridine-9-ethyl amine has been prepared from acridine-9-propionic acid by successive formation of the ester, the hydrazide, the azide, the urethan and finally the ethylamine.

LOUISVILLE, KENTUCKY