[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF KITASATO INSTITUTE]

SKRAUP'S REACTION WITH PARA-AMINORESORCIN DIMETHYL ETHER

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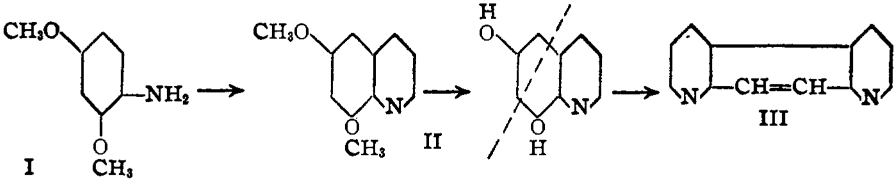
In the course of the study upon the physiological action of certain quinoline compounds, I attempted the synthesis of 6,8-dimethoxyquinoline.[1] For this purpose, *p*-aminoresorcin dimethyl ether was submitted to the Skraup reaction for quinoline synthesis, and a small amount of crystals was isolated by means of benzene. It, however, could neither be a derivative of 6-methoxyquinoline nor any compound having any phenolic hydroxyl substituent. After a further purification, it formed colorless needles, m. p. 173°, being in coincidence with that of *p*-phenanthroline (6,8-dimethoxyquinoline has been reported to melt at 56°).[1]

From the analytical figures and the determination of molecular weight, the molecule formula $C_{12}H_8N_2$ could be assigned to it, and the characteristic constants of several derivatives of this compound were found to be generally in close agreement with the descriptions for those of *p*-phenanthroline given by the previous investigators.[2] Finally, the identification was fairly established by a mixed melting point with an authentic specimen of *p*-phenanthroline which had been prepared by a known method.

Experiments under a variety of conditions to obtain 6,8-dimethoxyquinoline or 6,8-dihydroxyquinoline failed to reveal any of these compounds; moreover, the formation of *p*-phenanthroline also resulted when *p*-benzene-azo-resorcin dimethyl ether or *p*-benzene-azo-resorcin was subjected to the Skraup reaction, which will be reported in a subsequent paper.

This reaction might be explained on the assumption that quinoline compound (II) might have been formed at an intermediate stage and that it might, at the instant of its formation, undergo ring rupture at the indicated place, followed by the condensation of two moles of such a compound, giving *p*-phenanthroline (III) in accordance with the equation



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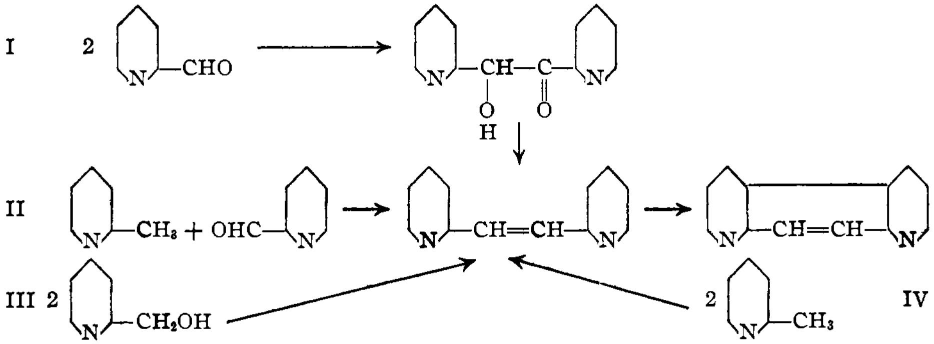
[1] During the investigation, the preparation of 6,8-dimethoxyquinoline through another course of synthesis has been reported by I. G. Farben Industry [*Chem. Zentr.*, I, 2109 (1929); English Patent 301,947].

[2] Skraup, *Monatsh.*, **5**, 569 (1884); Kaufmann, *Ber.*, **42**, 2612 (1909).

If the suggested mechanism be admitted, concerning the final condensation, the following four possible courses which might be taken would be conceivable.



On subjecting benzoin to the Skraup reaction, benzil was formed in a good yield and a mixture of α-picoline and benzaldehyde, or α-picoline only, was also subjected to the Skraup reaction and in these cases α-picoline could be recovered without any notable loss. The possibility of the condensation through the course I, II or IV seems to be excluded by these experiments. On the other hand, the Skraup reaction with benzyl alcohol led to the formation of much resinous matter and neither stilbene nor phenanthrene could be isolated. This last failure appears also to rule out the course III, but recalling the fact that in case of α-methanol-pyridine the hydrogen atom in the side chain would be far more reactive than that of benzyl alcohol, in the case of pyridine series, therefore, such a condensation as through the course III might not be altogether impossible.

Experimental

Skraup's Reaction with *p*-Aminoresorcin Dimethyl Ether.—A mixture of *p*-aminoresorcin dimethyl ether (6 g.), glycerin (18 g.), arsenic acid (9 g.) and concd. sulfuric acid (18 g.) was refluxed on an oil-bath (bath temperature, 170–180°) for nine hours. The reaction mixture was digested with hot water and the filtered liquid, after being made alkaline, was shaken with benzene. On evaporating the solvent, 0.5 g. of colorless needles was obtained. It was best purified through a recrystallization of its sulfate from alcohol and a subsequent recrystallization of the free base regenerated from benzene in the presence of animal charcoal. It formed colorless needles melting at 173°. It is easily soluble in alcohol and hot water, moderately in benzene and chloroform and rather difficultly in ether. The alcoholic solution, in case of only a concentrated solution, gives a reddish-brown color with ferric chloride. The absorption spectra of its 1/10,000 molar alcoholic solution shows the maximum absorption at 2696 Å. The mixed melting point of this substance and *p*-phenanthroline showed no depression.

Anal. (Water of crystallization). Subs., 0.0930: H_2O, 0.0213. Calcd. for $C_{12}H_8N_2 \cdot 3H_2O$: H_2O, 23.08. Found: H_2O, 22.90. Mol. wt. Subs., 0.0542, in 12.6100 g. of C_6H_6: Δt, 0.130°. Subs., 0.374 mg., in 3.189 mg. of camphor: Δt, 25.1°. Calcd. for $C_{12}H_8N_2$: mol. wt. 180. Found: mol. wt. 165, 187.

Anal. Subs., 3.718 mg.: CO_2, 10.933; H_2O, 1.556. Subs., 4.656: CO_2, 13.634; H_2O, 1.983. Subs., 2.350: N_2, 0.336 cc. (32°, 761.5 mm.). Subs., 0.0462: N_2, 6.1 cc. (13.5°, 760 mm.). Calcd. for $C_{12}H_8N_2$: C, 80.00; H, 4.44; N, 15.56. Found: C, 80.02, 79.86; H, 4.65, 4.73; N, 15.36; 15.55.

TABLE I

CHARACTERISTIC CONSTANTS OF THE DERIVATIVES OF THE COMPOUND $C_{12}H_8N_2$

Derivative	Crystal form	M. p., °C.
Picrate	Yellow needles from acetone	255–256
Chloroplatinate	Orange-yellow needles	> 310
Hydrochloride	Colorless prisms from alcohol	> 315
Sulfate	Colorless prisms from alcohol	233–234
Chromate	Orange-yellow needles. Black tar at	225–230
Monomethyl iodide	Light yellow needles from water	268–269
Dimethyl iodide	Garnet colored prisms from water	271
β,β′-Dipyridyl-α,α′-dicarboxylic acid	Short columns	215 (dec.)
Sulfate	Colorless prisms from alcohol	218

Formula		Analytical data, %					
		Calcd.	Found		Calcd.	Found	
$C_{12}H_8N_2 \cdot C_6H_3N_3O_7$	C,	52.81	52.59	H,	2.69	2.85	
				N,	17.11	17.18	17.07
$C_{12}H_8N_2 \cdot 2HCl \cdot PtCl_4$				Pt,	33.10	33.34	
$C_{12}H_8N_2 \cdot 2HCl$				HCl,	28.83	29.09	
$C_{12}H_2N_2 \cdot H_2SO_4 \cdot H_2O$	H_2O,	6.08	6.17	H_2SO_4,	35.25	35.96	
$C_{12}H_8N_2 \cdot H_2Cr_2O_7 \cdot 2 \cdot 5H_2O$				Cr_2O_3,	34.31	34.41	
$C_{13}H_{14}N_2I \cdot H_2O$	H_2O,	5.30	5.45	I,	39.42	39.01	
$C_{14}H_{14}N_2I_2 \cdot H_2O$	H_2O,	3.73	4.22	I,	54.77	54.62	
$C_{12}H_8O_4N_2$	C,	59.02	59.04	H,	3.28	3.56	
				N,	11.48	11.76	
$C_{12}H_8N_2O_4 \cdot H_2SO_4 \cdot 2H_2O$	H_2O,	9.52	9.61	H_2SO_4	28.66	29.24	

I hereby desire to express my hearty thanks to Professor Hata for the interest which he has kindly taken in this work.

Summary

In the Skraup reaction with *p*-aminoresorcin dimethyl ether, the formation of *p*-phenanthroline has been established.

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