

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF LOUISVILLE]

The Reaction of Aldehydes and Aromatic Amines with 8-Quinolinol

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Eleven substituted 7- α -anilinomethyl-8-quinolinols have been prepared by a Mannich type reaction of aldehydes, primary aromatic amines and 8-quinolinol. The absorption spectra and some characteristic spot reactions of these compounds were determined.


A Mannich type reaction of aniline, benzaldehyde and 8-quinolinol yields 7-(α -anilinobenzyl)-8-quinolinol.¹ The unusual simplicity of this reaction and the possible application of the products as analytical reagents led to a further study of the method using a variety of substituted amines and aldehydes.

ucts were obtained with *N*-methylaniline or diphenylamine.

The time required for the first indication of precipitation was recorded (Table II); usually precipitation continued slowly for many days after this time. The most active amine tried was *p*-nitroaniline which usually reacted in a few hours.

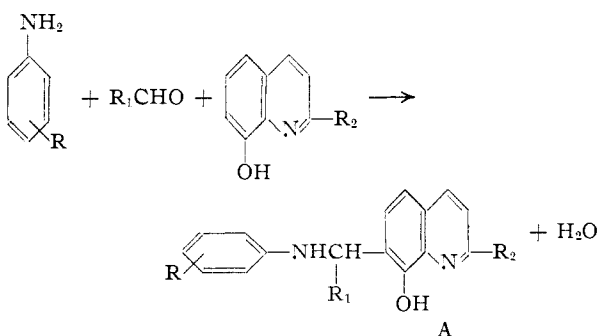
TABLE I

SUBSTITUTED 7- α -ANILINOMETHYL-8-QUINOLINOLS

I	R	Substituents in A		M.p., °C.	Yield, %	Formula	Nitrogen, %	
		R ₁	R ₂				Calcd.	Found
I	H	C ₆ H ₅	H	146 ^a	78	C ₂₂ H ₁₈ N ₂ O
II	H	<i>p</i> -CH ₃ OC ₆ H ₄	H	132	12	C ₂₃ N ₂ O ₂	7.9	7.8
III	<i>o</i> -CH ₃	C ₆ H ₅	H	142	50	C ₂₃ H ₂₀ N ₂ O	8.2	8.2
IV	<i>p</i> -CH ₃	C ₆ H ₅	H	151	25	C ₂₃ H ₂₀ N ₂ O	8.2	8.4
V	<i>o</i> -OCH ₃	C ₆ H ₅	H	133	89	C ₂₃ H ₂₀ N ₂ O ₂	7.9	8.2
VI	<i>m</i> -Cl	C ₆ H ₅	H	95	74	C ₂₂ H ₁₇ N ₂ OC1	7.8	7.5
VII	<i>o</i> -NO ₂	C ₆ H ₅	H	156	3	C ₂₂ H ₁₇ N ₃ O ₃	11.3	11.2
VIII	<i>p</i> -NO ₂	C ₆ H ₅	H	238 ^{a, b}	96	C ₂₂ H ₁₇ N ₃ O ₃
IX	<i>p</i> -NO ₂	C ₆ H ₅	CH ₃	222	93	C ₂₃ H ₁₉ N ₃ O ₃	10.9	11.2
X	<i>p</i> -NO ₂	CH ₃ CH ₂ CH ₂	H	189	90	C ₁₉ H ₁₉ N ₃ O ₃	12.5	12.4
XI	<i>p</i> -NO ₂		H	175	27	C ₂₀ H ₁₃ N ₃ O ₄	11.6	11.5

^a Previously prepared by this reaction. ^b Literature gives 231°.

The reaction was best performed by mixing equimolar amounts of amine and aldehyde in sufficient ethanol to dissolve the Schiff base that usually formed and adding 8-quinolinol. In times ranging from two hours to sixty days the following precipitation reaction occurred



Refluxing did not hasten the reaction and seemed to decrease the yield.

The reaction products (Table I) were filtered off and recrystallized after 45 days in most cases. Nine are new compounds. Products were not obtained, at least not in 45 days, from aniline with *p*-dimethylaminobenzaldehyde, *o*- and *p*-hydroxybenzaldehydes, *p*-nitrobenzaldehyde and 3,4-dichlorobenzaldehyde; using benzaldehyde no prod-

It is probable that the reaction is the addition of 8-quinolinol to a Schiff base. In order to avoid the possibility of confusing the new compounds with Schiff bases a series of three spot reactions were developed which seem to be fairly characteristic. All the compounds except IX gave a green color with ferric chloride and characteristic colors with concentrated sulfuric acid and nitric acid (Table II). All three tests were not given by the reagents alone or by the Schiff bases.

TABLE II

COLOR TESTS AND ABSORPTION SPECTRA OF SUBSTITUTED 7- α -ANILINOMETHYL 8-QUINOLINOLS

Compound	Time, ^a days	H ₂ SO ₄	HNO ₃	Absorption maxima, m μ
I	20	Red	Yellow	248(45000) ^b
II	60	Red	Red	247(49000)
III	30	Red	Red	248(49000)
IV	35	Red	Yellow	248(46000)
V	7	Red	Violet	248(48000)
VI	14	Red	Yellow	248(53000), 298(5300)
VII	35	Red	Yellow	247(46000), 420(6100)
VIII	0.08	Red	Yellow	247(26000), 385(9500)
IX	1	Red	Yellow	249(38000), 385(16000)
X	0.3	Colorless	Yellow	231(14000), 375(32000)
XI	1	Purple	Green	246(37000), 380(18000)

^a Time required for precipitation to begin. ^b Molar absorptivity index in parentheses.

(1) F. Pirrone, *Gazz. chim. ital.*, **71**, 320 (1941); **70**, 520 (1940).

Absorption spectra of the compounds in ethanol all had maxima between 246 and 249 $m\mu$ except for X. The spectrum of X was expected to be somewhat different since this compound was derived from an aliphatic rather than aromatic aldehyde. Compounds containing a nitro group were yellow, as indicated by the spectra as well as observation; all others were colorless.

Experimental

Preparation of Compounds.—To 50 ml. of ethanol were added 0.02 mole of the aldehyde and 0.02 mole of amine. 8-Quinololinol (2.9 g., 0.02 mole) was then added and the mixture stoppered and left to stand at room temperature for 45 days. The compound was removed by filtration and re-

crystallized twice from ethanol or ethanol-acetone mixtures. Further standing of the filtrate sometimes deposited additional product; this was not considered in calculating the yields.

Spot Tests.—The ferric chloride test was performed by adding a drop of an ethanol solution of the compound to 1% ferric chloride. Tests with concentrated sulfuric and nitric acids were performed by adding 1–5 mg. of compound to 2 ml. of concentrated acid. The colors recorded with nitric acid are the initial ones, since fading occurred after a time.

Absorption Spectra.—All measurements were made with a Beckman DU spectrophotometer with 1.00-cm. silica cells. The solvent was 95% ethanol.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF DARTMOUTH COLLEGE]

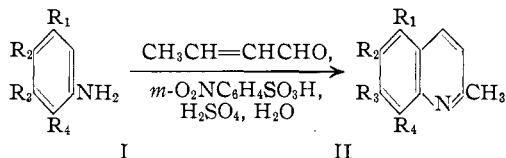
The Synthesis and Nitration of 2,6- and 2,7-Dimethylquinoline and of 2,5,8-Trimethylquinoline

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Several derivatives of quinaldine have been synthesized from aromatic amines and crotonaldehyde by Utermohlen's modification of the Skraup and Doebner-v. Miller syntheses²; the yield of the substituted quinoline is considerably improved by the use of a large excess of crotonaldehyde. The identity of 2,7-dimethylquinoline has been firmly established. The structures of the mononitro derivatives formed from 2,6- and 2,7-dimethylquinoline and from 2,5,8-trimethylquinoline have been determined.

Utermohlen has described a valuable modification of the Skraup and Doebner-v. Miller syntheses; an aromatic amine is treated with a suitable aldehyde or aldehyde diacetate in the presence of *m*-nitrobenzenesulfonic acid.² Although the reaction, as described, is quite general, the reported percentage yields, which vary in several reactions with crotonaldehyde or the corresponding diacetate from 43 to 63, are not so high as might be desired. One of the purposes of this investigation was the search, in the case of crotonaldehyde only, for reaction conditions that would lead to higher yields. A study of the course of the mononitration of 2,6- and 2,7-dimethylquinoline and of 2,5,8-trimethylquinoline was also made.



All R groups = H except as otherwise specified

- | | |
|----------------------------------------------------------------------------|----------------------------------------------------------------------------|
| a, R ₂ = CH ₃ | e, R ₃ = CH ₃ , R ₄ = Cl |
| b, R ₂ = CH ₃ , R ₃ = Cl | f, R ₃ = CH ₃ , R ₁ = R ₄ = Cl |
| c, R ₂ = CH ₃ , R ₁ = R ₄ = Cl | g, R ₁ = R ₄ = CH ₃ |
| d, R ₃ = CH ₃ | h, R ₁ = R ₄ = CH ₃ , R ₃ = Cl |
| d', R ₁ = CH ₃ | i, R ₁ = R ₄ = CH ₃ , R ₂ = Cl |

In the original procedure of Utermohlen equimolar amounts of amine and aldehyde were employed. At the start of the present research, *p*-toluidine (Ia) and crotonaldehyde were condensed in equimolar proportions according to the direc-

tions given previously.² 2,6-Dimethylquinoline (IIa) was easily isolated, but in only 48% yield, while a considerable amount of *p*-toluidine was recovered. Since a good deal of tarry matter was formed during the cyclization reaction, it appeared that much of the crotonaldehyde was destroyed before it could condense with the amine. Accordingly, the ratio of aldehyde to amine was increased to 1.67:1; no unchanged *p*-toluidine was then obtained and the yield of nearly pure 2,6-dimethylquinoline rose to 80% (based on the amine). Since further increase in the amount of aldehyde made isolation of the product more difficult without perceptibly augmenting the yield, this ratio of 1.67:1 was retained in all later applications of the synthesis. In reactions conducted with large quantities (one mole of amine) of starting materials the yields varied from 80 to 86%, while in cyclizations on a greatly reduced scale the quinoline derivative was isolated in yields of from 54 to 74%.

The behavior on nitration of derivatives of quinoline has been discussed in detail by Elderfield.³ Since quinaldine is attacked approximately equally at the 5- and 8-positions, it is to be expected that 2,6-dimethylquinoline (IIa) will undergo substitution at the 5-position, while the 2,7 isomer (IId) will react preferably at the 8-position. After the initiation, but before the completion of this investigation, Price and co-workers reported the nitration of 2,6-dimethylquinoline.⁴ A nitro compound, differing from the known 8-nitro derivative

(1) Abstracted in part from the theses presented by Robert W. Belfit, Jr. (1951) and Rodney A. Walsler (1948) in partial fulfillment of the requirements for the degree of Master of Arts.

(2) W. P. Utermohlen, *J. Org. Chem.*, **8**, 544 (1943).

(3) R. C. Elderfield in "Heterocyclic Compounds," edited by R. C. Elderfield, Vol. 4, John Wiley and Sons, Inc., New York, N. Y., 1952, pp. 264–271.

(4) C. C. Price, B. H. Velzen and D. B. Guthrie, *J. Org. Chem.*, **12**, 208 (1947).