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Certain Azomethines in the Pyrimidazolone Series

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When 2-aminopyridine is treated with diketene it gives an acetoacetanilide (I, R = CH_3) that is identical with that obtainable from the same amine and ethyl acetoacetate. However, when this amide was treated by the methods used in color photography[1] it gave a magenta solution instead of the yellow that is anticipated of acetoacetanilides.[2] The 3- and 4-isomers gave yellow solutions under the same conditions. These observations suggested that either the 2-amide did not have the structure assigned or that an unexpected reaction was taking place. Since the structure of 2-acetoacetaminopyridine seems to have been well established,[3,4,5] the first possibility was discarded.

Accordingly, the behavior of *p*-nitrosodimethylaniline with the amide was examined. A mixture of 2-acetoacetaminopyridine and *p*-nitrosodimethylaniline in hot alcohol rapidly becomes a deep magenta color, and after an hour the dye has separated. From the analyses, the empirical formula was established as $C_{15}H_{14}ON_4$. By the use of two other nitrosoamines, *p*-nitrosodiethyltoluidine and nitroso-2,4-diphenylpyrrole, two other dyes of similar color were obtained; their empirical formulas differed only by that of the nitrosoamine residue. That is, the remainder of the molecule was the same in each instance.

When 2-(4′-methoxybenzoyl)-acetamidopyridine (I, R = $C_6H_4OCH_3$-4) was similarly treated[1] with oxidized developer, a yellow color was formed at first, but this soon changed to magenta. From the spectrophotometric data, the solution appeared to contain a mixture of a yellow and a red dye. By suitable manipulation of the reaction product of this amide and *p*-nitrosodimethylaniline, a red dye was isolated which was found to be identical with the one obtained from 2-acetoacetaminopyridine. The formation of the same dye from two different starting materials can only come about if the unlike parts of the molecules are eliminated at some stage of the reaction. The only unlike parts are the acyl residues, RCO, that terminate the side chain; hence, these must be cleaved during the dye formation.

The isolation of the yellow dye from the reaction mixture has not yet been accomplished, probably on account of its very reactive nature. However, Vittum and Brown of these Laboratories were successful in preparing the isomeric 2′-methoxy dye in a very pure condition, by a reaction under very mild conditions the details of which they will publish separately. The yellow solutions in organic solvents, even at room temperature, slowly become red; the changes take place more rapidly on heating or in the presence of mineral acid. From the spectrophotometric data, it is evident that the same red dye is formed. Thus it appears that the first action of the nitrosoamine is to form a yellow azomethine II, as would be expected, and that this undergoes a subsequent reaction resulting in the formation of the magenta dye. Other 2-acylacetaminopyridines exhibited a similar behavior, forming mixtures; in each instance, the yellow dyes were unlike but the red substance was the same. There was one exception: the mesitoyl derivative gave only a yellow dye.

The sequence of reactions may, thus, be written as follows

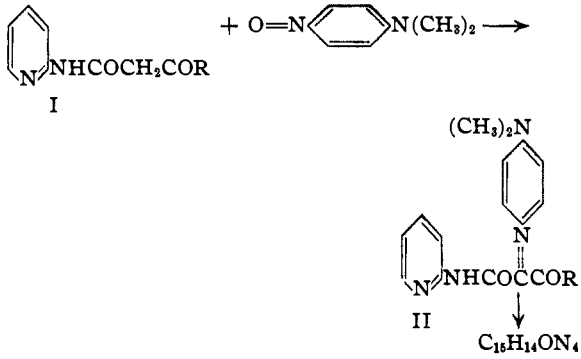
(1) Weissberger and Porter, THIS JOURNAL, **65**, 52, 1502 (1943).

(2) British Patent 458,664 [*C. A.*, **31**, 3803 (1937)]; U. S. Patent 2,108,602.

(3) Palazzo and Tamburini, *Atti. accad. Lincei*, [5] **20**, I, 37 (1911); [*C. A.*, **5**, 1586 (1911)].

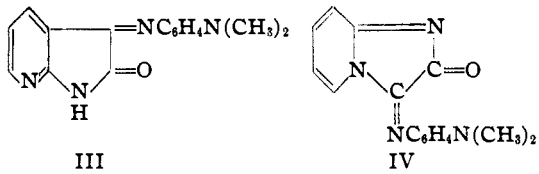
(4) Cripps and Scevola, *Gazz. chim. ital.*, **67**, 327 (1937); [*C. A.*, **32**, 166 (1938)].

(5) Khitrik, *J. Gen. Chem.* (U. S. S. R.), **9**, 1109 (1939); [*C. A.*, **33**, 8615 (1939)]. Khitrik examined the reaction between acetoacetic ester and 2-aminopyridine with great care, and cleared up the previously reported apparent contradictions.



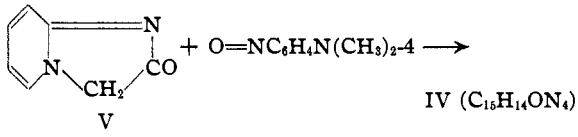
The difference between the azomethine II and the red substance is RCOH. This suggests that a ring closure has taken place.

There are two possible cyclic structures that could be so formed: the pyridinopyrrole III and the pyrimidazolone IV.



The pyridinopyrrole may be excluded because (1) ring closure in 2-aminopyridines has never been observed to take place in the 3-position,[6] (2) the 3- and 4-acetoacetaminopyridines, which could cyclize in similar fashion, fail to exhibit such behavior, (3) acetoacetanilides do not undergo ring closure, but are permanently yellow, and (4) 2-amino-3-picoline gives an acetoacetamide that gives a magenta dye—in this instance the 3-position is blocked by the methyl group. By exclusion, the red substance must be the pyrimidazolone IV.

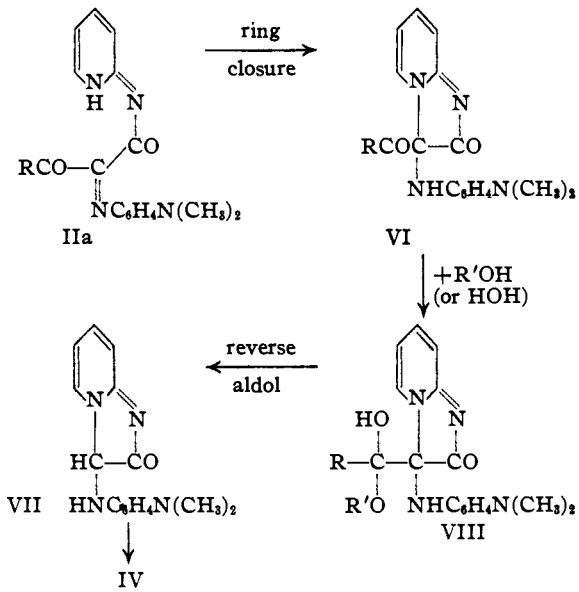
That this conclusion was correct was verified by its synthesis from the known 2-keto-2,3-dihydropyrimidazole V and *p*-nitrosodimethylaniline.



Reindel and Rosendahl[7] undoubtedly had an impure specimen of this pyrimidazolone IV which was secured by a similar series of reactions using the hydrochloride; it was amorphous rather than crystalline, and its structure, though suggested, was left in question.

The mechanism of the formation of the red pyrimidazole from 2-acylacetoaminopyridines is not too obvious. It may be plausibly represented by the following scheme. The yellow dye II is formed by the usual azomethine reaction. An intramolecular ring closure then takes place through the tautomeric imide form IIa to give VI. It is known from Reindel's work[8] that an acetyl group is extraordinarily easily hydrolyzed in the pyrimidazolone series, either by treatment with cold alkaline solutions or in boiling alcohol, thus accounting for the cleavage of the acyl group just described. The dihydro derivative VII is then dehydrogenated to the red dye IV by the excess nitrosoamine.

The cleavage of the acyl group, an apparent hydrolysis, probably proceeds through addition of water or alcohol to the carbonyl group, which would give a hemiacetal VIII as an intermediate. Such an addition cannot take place with the mesitoyl derivative which fails to change from yellow to red; it is well known that in mesityl ketones the *ortho* methyl groups are a hindrance to such addition reactions.[9,10,11] By the reversal of an aldol condensation, this hemiacetal is cleaved to VII and an acid or its ethyl ester, if the reaction takes place in alcohol. In support of this step, ethyl anisate was isolated from the reaction mixture, when 2-(4′-methoxybenzoyl)-acetoacetaminopyridine was used, and ethyl *o*-methoxybenzoate from the yellow 2′-methoxyazomethine previously mentioned.

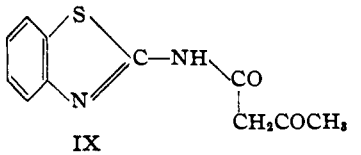


Additional support of this mechanism is afforded by the fact that the rate of dye formation is much slower in benzene and butyl acetate than in alcohol.

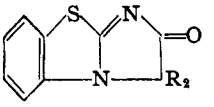
Other similarly constituted acetoacetamides that do not exhibit this behavior are known. For example, 2-acetoacetaminobenzothiazole IX gives a yellow dye[2] which does not change to red. The difference may be attributed to the difficulty inherent in forming the unknown ring system X

(6) Chichibabin, *Ber.*, **57**, 2092 (1924).
(7) Reindel and Rosendahl, *ibid.*, **59**, 1064 (1926).
(8) Reindel and Rauch, *ibid.*, **58**, 393 (1925).
(9) Kohler, Stone and Fuson, THIS JOURNAL, **49**, 3187 (1927).
(10) Fuson and Walker, *ibid.*, **52**, 3269 (1930).
(11) Kohler and Barnes, *ibid.*, **55**, 690 (1933).

composed of two fused five-membered rings, one of which is attached to a benzene nucleus.



IX



X

2-Cyanoacetaminopyridine also fails to cyclize.

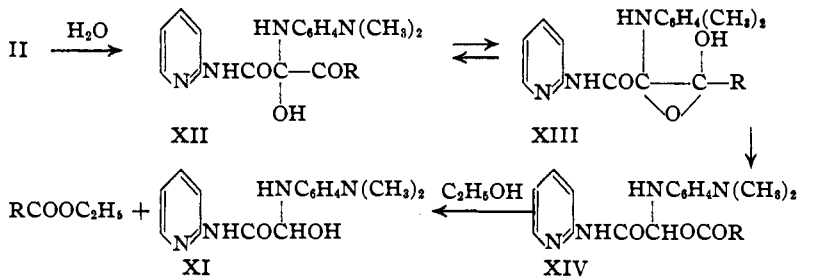
Since the yield of the red dye is by no means quantitative, the nature of the side reactions was investigated. It was found that the yellow azomethine dye II (R = 2′-$CH_3OC_6H_4$) was a very reactive substance, giving other products besides the red dye. In the presence of various catalysts the latter is formed in accordance with the equation

$$C_{23}H_{22}O_3N_4 + ROH = C_{16}H_{14}ON_4 + C_8H_7O_3R + 2H$$

In the absence of a catalyst, boiling an alcoholic solution of the yellow dye gives a new substance; the acyl group is cleaved as in the previous reaction. The new substance is pale yellow, and fails to give a color with alkali, acid, oxidizing agent, or mixtures of these. Thus, it does not appear to be an intermediate in the formation of the red dye. It is tentatively assigned the structure of an aminoalcohol, XI. Its formation from the azomethine II is in accordance with the equation

$$C_{16}H_{16}O_2N_4R\ (II) + H_2O + C_2H_5OH = C_{15}H_{18}O_2N_4 + RCOOC_2H_5$$

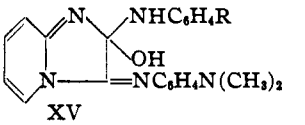
As a first step, the water adds to the azomethine linkage; this addition product XII is in equilibrium with its tautomeric oxanol form XIII. The oxanol yields the ester XIV by the reverse of an aldol condensation, a mechanism already shown to be applicable to similar reactions.[12] The ester is then cleaved by an alcoholysis to the aminoalcohol XI and ethyl *o*-methoxybenzoate (when R = *o*-$CH_3OC_6H_4$).



XII XIII XI XIV

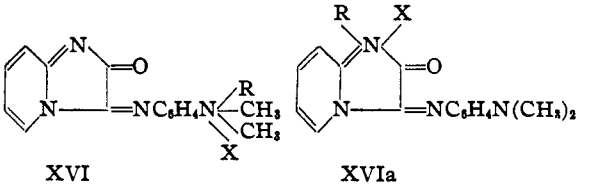
A yellow substance, the analytical results from which correspond to $C_{23}H_{26}ON_6$, was also isolated from the reaction mixture of several of the 2-acylaminopyridines and *p*-nitrosodimethylaniline. It proved to be a 1:1 addition product of the red dye IV and *p*-aminodimethylaniline, probably formed during the dehydrogenation (of VII to form IV). An analog was made using *p*-anisidine. Apparently, the characteristic tendency of pyrimidazolones to form addition products is still present in the dye. Upon gentle warming in alcoholic solution in the presence of a trace of mineral acid, the magenta color is restored, *i. e.*, the components of the addition product are regenerated. A little more acid forms the blue color of the salt (above) which disappears with an excess.

Of the many possible structures that can be written for an addition product of this sort, that of an hydroxyamine XV seems preferable, on account of the ease of its formation and dismutation, and the disappearance of the red color, characteristic of this particular variety of 5-membered ring systems.[1,2] The azomethine linkage remaining is probably responsible for its yellow color.



XV

The red dye IV gives blue salts by the addition of one equivalent of mineral acid or methyl iodide. The methiodide has a maximum absorption at 593 mμ, and dyes wool a pure blue. The structures of these salts are uncertain. According to Brooker's[13] conclusions on color and constitution, the quaternary nitrogen would be the one in the 5-membered ring XVIa. However, since the red dye formed from nitrosodiphenylpyrrole does not show color changes with mineral acid,



XVI XVIa

it seems more likely that it is really the nitrogen of the dimethylamino group that has become "quaternarized" XVI. This would be in agreement with Pummerer's conclusions[14] based on the behavior of isatin-2-*p*-dimethylaminoanil, which forms a blue salt with one equivalent of mineral acid.

With methyl iodide, however, Pummerer reported only a methylation on the heterocyclic nitrogen atom, whereas in our work a salt was formed. Since the methiodide and hydrochloride are both blue, it seems reasonable to assume that they have the same type of structure; formula XVI is, therefore, preferred.

In Fig. 1 are shown some of the spectral absorption characteristics of these azomethine dyes.

(12) Allen and Gates, THIS JOURNAL, 65, 1232 (1943).

(13) Brooker and Sprague, *ibid.*, 63, 3203 (1941).

(14) Pummerer and Goettler, *Ber.*, 42, 4269 (1909).

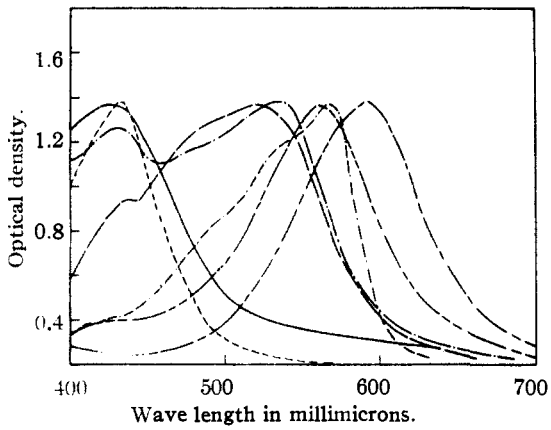


Fig. 1.— ——, mesitoyl dye; -----, acetoacetanilide; — —, red azomethine dye IV; — - - —, red dye from nitrosodiethyltoluidine, -- · --, red dye from the nitrosopyrrole; — - —, the methiodide XV; — · —, mixture of dyes from *p*-methoxy amide.

Experimental

A. The 2-Acylacetamides I.—2-Acetoacetaminopyridine (I, R = CH_3) was prepared by adding 4.1 g. of diketene in 5 cc. of ether to 4.7 g. of 2-aminopyridine in 25 cc. of ether. After two hours, 6.4 g. (68%) of product had separated; it was recrystallized once from alcohol. It was also secured by interaction of 2-aminopyridine and ethyl acetoacetate in a yield of 28% by the usual procedure,[4] or 29% by the use of either a Fenske or a variable take-off column. 2-Acetoacetamino-3-methylpyridine was prepared by the diketene procedure; it melts at 132°.

The aroylacetaminopyridines were obtained by the use of the last-mentioned type column with added xylene, in yields up to 56%. There were prepared 2-methoxy- (m. p. 100°), 4-methoxy- (m. p. 121°), 2-chloro- (m. p. 93°), 3-methyl- (m. p. 87°), and 2,4,6-trimethyl- (m. p. 110°) benzoylacetaminopyridines.

Anal. Calcd. for (*x*-methoxy) $C_{15}H_{14}O_3N_2$: N, 10.3; for (2,4,6-trimethyl) $C_{17}H_{18}O_2N_2$: C, 72.3; H, 6.4. Found: (2-methoxy) N, 10.7; (4-methoxy) N, 10.3; (2,4,6-trimethyl) C, 72.3; H, 6.3.

When 3,5-dibromo-2-acetoacetaminopyridine was expected as the product from 3,5-dibromo-2-aminopyridine and ethyl acetoacetate, the solid that resulted was insoluble in dilute acids and alkalies, the analysis indicated that it was 3-methyl-1',3'-dibromo-1,2-divinylene-uracil (plus alcohol of crystallization).

Anal. Calcd. for $C_9H_6ON_2Br_2 \cdot C_2H_6O$: Br, 42.9. Found: Br, 43.3.

It failed to give a color,[1] in contrast to the behavior of the acetoacetamides. Thus, it appears that ring closure to form a pyrimidine is facilitated by the bromine atoms, for with the unsubstituted amide, drastic treatment is necessary for cyclization.[3,4,5]

The 4-acetoacetaminopyridine was obtained as an oil by both procedures, but the 3-isomer[15] by the second one only.[16] The melting point was 144 instead of 134°; the low-melting material contains some of the Schiff base as an impurity.

2-Acetoacetaminobenzothiazole IX was obtained in a quantitative yield by allowing a mixture of 3.7 g. of 2-aminobenzothiazole and 2.1 cc. of diketene to stand; after about ten minutes, there was a vigorous reaction, the mixture liquefied and then solidified. It was crystallized from alcohol. It was identical with the same amide prepared as directed in the literature[17]; m. p. 219°.

B. Mesitoylacetic ester (ethyl 2,4,6-trimethylbenzoylacetate) could not be prepared by the only published procedure,[18] but it was secured by esterification of ω-cyano-2,4,6-trimethylacetophenone[19] by means of hydrogen chloride and absolute ethanol; since this method of preparation[20] is new, the details are given. The use of sulfuric acid brought about a hydrolysis to acetomesitylene.

A mixture of 15 g. of the nitrile and 150 cc. of absolute methanol at 0–3° was saturated with hydrogen chloride, left overnight at room temperature, and the solvent then removed *in vacuo*. The residue was dissolved in a mixture of 50 cc. of absolute ethanol, 4.4 cc. of water, and 1.5 cc. of concentrated hydrochloric acid, and the whole refluxed for one-half hour. After the mixture cooled, 250 cc. of water was added to dissolve the salt and the oily ester was extracted with ether. The oil was fractionated twice *in vacuo*, and the ester was collected at 121–124° (11 mm.), in a yield of 44%.

C. 2-ω-Cyanoacetaminopyridine.[21]—To 15 g. of ethyl cyanoacetate at 140° was added 9.4 g. of 2-aminopyridine, and the mixture was heated at 180–200° in an oil-bath for one hour; 4.5 cc. of alcohol distilled. Upon the addition of 5 cc. of methanol to the cooled liquid, crystallization took place. It was recrystallized from methanol, using Darco; it melts at 159–160°.

Anal. Calcd. for $C_8H_7ON_3$: N, 26.1. Found: N, 26.3.

The condensation did not take place in boiling xylene, as in the procedure used for the other amides.

D. The Azomethines.—1. The general procedure consisted in refluxing for two to three hours an absolute ethanolic solution of the acylacetamino compound containing two equivalents of *p*-nitrosodimethylaniline. For example, 1.78 g. of 2-acetoacetaminopyridine, 3 g. of the nitrosamine, and 25 cc. of ethanol gave 0.98 g. (36%) of the dye, IV. The same dye was also formed from 2-anisoylacetaminopyridine. Nitrosodiethyl toluidine gave the analogous dye, XVII, while 2-nitroso-3,5-diphenylpyrrole[22] gave the dye XVIII. No dye could be isolated from the intractable mixture formed with 2-mesitoylacetaminopyridine. The azomethines crystallized best from *n*-butanol. Their properties are listed in Table I.

2-Cyanoacetaminopyridine gave an orange-red azomethine dye XX. The yellow azomethine (II, R = 2-$CH_3OC_6H_4$) was prepared by Vittum and Brown by a procedure to be published separately. It gives a red color with mineral acid, which soon turns blue and then becomes colorless, as described below under the red dye.

The isolation of ethyl anisate from one run was accomplished, after the red dye was removed, by evaporating the solution to dryness on the steam-bath and then steam-distilling the ester; the yield, after suitable manipulation, was 1.2 g. (14%). The refractive index was the same as that of an authentic specimen. It was converted into anisamide, which was identical with a sample prepared by a known method. The melting point alone or on admixture was 159–160°.

2 - (4' - Dimethylaminoanilino) - 2 - hydroxy - 3 - (4''-dimethylaminoanil) XIX (XV, R = $(CH_3)_2N$—) was isolated from the reaction mixture. It was also synthesized from the red dye and *p*-aminodimethylaniline by four hours of refluxing in alcoholic solution. A molecular weight determination in carbon tetrachloride solution (calcd. 402; found 300) indicated partial dissociation.

(15) Palazzo and Marogna, *Atti accad. Lincei*, **21**, II, 512 (1912); [*C. A.*, **7**, 992 (1913)].

(16) We are indebted to Dr. C. J. Kibler of these Laboratories for the preparation by the ester procedure.

(17) German Patent 603,623 [*Frdl.*, **21**, 317 (1936)].

(18) Wenzel, *Monatsh.*, **35**, 950 (1914).

(19) Fuson and Beveridge, THIS JOURNAL, **53**, 1987 (1931). After the alcohol was removed under reduced pressure, the residue that remained after extracting with water as specified, was retreated; the yield was thereby increased to 87%.

(20) First done by Mr. E. C. Armstrong in these Laboratories.

(21) We are indebted to Dr. C. J. Kibler of these Laboratories, for this procedure and substance.

(22) Rogers, *J. Chem. Soc.*, 590 (1943). We have confirmed Rogers' observation that the nitrosopyrrole is strongly dermatitic in some subjects.

TABLE I

PROPERTIES OF AZOMETHINE DYES

Number	M. p., °C.	Empirical formula	Analyses, % Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
IV	248	$C_{18}H_4ON_4$	67.7	5.3	21.0	67.7	5.3	21.0
						67.7	5.3	21.1
XV	186	$C_{28}H_{26}ON_6$	68.7	6.5	20.9	69.0	6.2	21.0
XVII	204–205	$C_{18}H_{20}ON_4$	70.3	6.5		70.3	6.1	
XVIII	260	$C_{23}H_{16}ON_4$	75.8	4.4	15.4	75.5	4.2	15.6
						75.8	4.4	15.6
XX	204–205	$C_{16}H_{15}ON_5$	65.4	5.1	23.8	65.7	5.4	24.0
XXI	145	$C_{22}H_{23}O_2N_5$			18.0			18.3

2-(4′-Methoxyanilino)-2-hydroxy-3-(4″-dimethylaminoanil) XXI was prepared by the same procedure.

4,4′-Tetramethyldiaminoazoxybenzene, a common by-product in reactions involving *p*-nitrosodimethylaniline[23] was also separated from the reaction mixture.

From the yellowish-red alcoholic reaction mixture of *p*-nitrosodimethylaniline and 2-mesitoylacetaminopyridine were isolated very small amounts of two yellow solids. One seems to be the substance, m. p. 216°, described below (Section 3). The other, m. p. 202°, appears to have the empirical formula $C_{23}H_{26}O_2N_6$, but a molecular weight determination was unsatisfactory. Its orange-yellow alcoholic solution becomes a greenish-yellow upon addition of mineral acid.

Anal. Calcd. for $C_{23}H_{26}O_2N_6$: C, 66.0; H, 6.7; N, 20.1; mol. wt., 418. Found: C, 66.0; H, 6.4; N, 20.0; mol. wt. (in CCl_4), 246.

An analogous instance, in which the product formed by addition of water to a comparable ring system, was described several years ago.[24]

2. Synthesis of 2-Ketodihydropyrimidazole-3-(4′-dimethylaminoanil) IV.—After three minutes of heating of a mixture of 1.7 g. of 2-ketodihydropyrimidazole hydrochloride,[25] 0.82 g. of sodium acetate and 15 cc. of absolute ethanol, the salt formed was filtered, and 1.5 g. of *p*-nitrosodimethylaniline added; a vigorous reaction ensued. After the solution was refluxed for one-half hour, the black crystals that had separated were filtered, washed with methanol, slurried with water, again washed with methanol, and recrystallized from butanol. The yield was 1.42 g. (53%); it melted at 244°. It gives a blue color with traces of mineral acid, but is decolorized by an excess. The reverse color changes can be observed when the acidic solution is treated with ammonia.

The procedure described by Reindel[7] gave a very impure, dull product, containing very little dye. On repetition, it was found that the hydrochloride appears to be slightly impure, but is largely converted into other products than the desired dye by sodium acetate, as specified.

3. The Yellow Azomethine Dye II.—This was obtained from Dr. Vittum and Mr. Brown of these Laboratories and is a brick-red solid that gives a yellow solution in organic solvents. It is insoluble in water but dissolves to a colorless solution on the addition of mineral acid. The yellow alcoholic solutions are unchanged by a trace of mineral acid, or ammonium and potassium persulfates or potassium ferricyanide, but if both acid and oxidizing agent are present, the solution at once becomes blue, owing to the formation of a salt of IV. The reaction can be carried on so that the transient red color is observable. Addition of ammonia transforms the blue salt to the red dye.

The yellow alcoholic solution of the dye slowly turns red when ammonium hydroxide is added, more rapidly with piperidine, and almost immediately with a trace of sodium hydroxide or methoxide. Excess of the latter reagent causes the color to disappear—it can be partially regenerated by the addition of acetic acid.

When an alcoholic solution of the yellow dye is refluxed in the absence of catalysts for six hours, a pale yellow solid separates; after recrystallization from butanol, it melts at 216°.

Anal. Calcd. for $C_{15}H_{13}O_2N_4$: C, 62.9; H, 5.6; N, 19.6. Found: C, 63.5; H, 5.4; N, 19.7.

On evaporation, the filtrate left a dark-colored oil that reeked of ethyl *o*-methoxybenzoate. It was taken up in ether, extracted with aqueous sodium carbonate (no acid, on acidification), and hydrolyzed by alcoholic potash. Upon acidification, *o*-methoxybenzoic acid was precipitated, and identified by comparison with a specimen at hand. The residual solution turned blue, as do all specimens of the red or yellow dyes, as well as apparatus in which they have been used, in the acidic laboratory atmosphere.

4. Salts.—The monohydrochloride of IV was prepared from the same components but omitting the sodium acetate, being precipitated from the solution by the addition of acetone; purification was accomplished by repeated solution in methanol and reprecipitation by acetone. It forms blue-black crystals, m. p. 210–211° dec., which are very soluble in water and methanol, but insoluble in ether and acetone.

Anal. Calcd. for $C_{15}H_{13}ON_4Cl \cdot H_2O$: N, 17.6. Found: N, 17.7.

The blue solutions turn red on the addition of ammonia but become colorless on addition of hydrochloric acid.

The methiodide XVI.—A mixture of 0.5 g. of the dye IV, 6 cc. of methyl iodide, and 8 cc. of nitrobenzene was shaken occasionally for two hours and then left for two and one-half days; the original magenta color turned blue after a few hours. The solid was filtered, washed with ether, and triturated with (1:3) acetone-ether solution. The greenish crystals give a pure blue aqueous solution.

Anal. Calcd. for $C_{15}H_{14}O_4N \cdot CH_3I$: N, 13.7; I, 31.1. Found: N, 13.7; I, 30.9.

Acknowledgment.—We are pleased to acknowledge the valuable assistance and suggestions of Dr. P. W. Vittum and Mr. G. H. Brown of these Laboratories.

Summary

2-Acylacetaminopyridines react with aromatic nitrosoamines to give a variety of substances. The most characteristic is a magenta dye.

This dye is an azomethine derivative of pyrimidazolone-2 as shown by its synthesis. Its formation from the 2-acylaminopyridine involves a cleavage and a ring closure.

The expected yellow azomethine dye cannot be isolated from the nitrosoamine reaction, but it appears to be present in solutions prepared from the 2-acylaminopyridine and oxidized developers, along with the red dye.

(23) Ehrlich and Sachs, *Ber.*, **32**, 2343 (1899).

(24) Finger and Zeh, *J. prakt. Chem.*, **82**, 53 (1910).

(25) Reindel, *Ber.*, **57**, 1331 (1924).

One yellow dye has been isolated from such a solution. The conditions under which it changes into the red dye have been determined.

A mechanism has been proposed to account for the series of reactions which result in formation of the red dye, and the evidence is discussed.

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o-Phenylenemalonamide

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The reaction between *o*-phenylenediamine and malonic acid has been found to produce a compound with the empirical formula $C_9H_8N_2O_2$. This compound has been obtained by a number of investigators,[2,3,4] but the only data bearing on its structure were the formation of a sparingly soluble sodium salt[2] and hydrolysis to regenerate *o*-phenylenediamine. Both Meyer[2] and Phillips[3] assigned the seven membered ring structure shown by formula I. This compound sublimed at about 360° and was quite insoluble in most solvents. Because of this low solubility and also since the reaction involved two bifunctional molecules[5] a polyamide structure was also suggested as a possibility.[4] The present paper reports experimental evidence that the compound does have the ring structure (I).

Because of the extreme insolubility of compound I in all solvents, its molecular weight could not be directly determined. To surmount this difficulty the dimethyl derivative (II) was prepared by treatment of compound I with methyl iodide and sodium ethoxide in alcoholic solution. Analysis revealed that methyl groups had replaced two hydrogen atoms. Although this dimethyl derivative had a lower melting point (255°) than I and was more soluble, good values for its molecular weight could not be obtained. By using *p*-nitrotoluene as a solvent, approximate values were found which indicated that this compound was not polymeric.

To determine whether the methyl groups were affixed to the nitrogen atoms or to the methylene group, the compound was hydrolyzed with dilute sulfuric acid. The expected products would be either *o*-phenylenediamine or N,N′-dimethyl-*o*-phenylenediamine. Neither of these was obtained but upon addition of an excess of potassium hydroxide, 1,2,3-trimethyl-2-hydroxy-2,3-dihydrobenzimidazole (III) was obtained. It is suggested that the acid hydrolysis opened the ring with subsequent loss of carbon dioxide to form N-acetyl-N,N′-dimethyl-*o*-phenylenediamine, which then cyclized to give III. Compound III has been described previously by Pinnow,[6] Fischer,[7] and Niementowski.[8]

For purposes of comparison compound III was prepared by a series of known reactions. 2-Methylbenzimidazole, prepared from *o*-phenylenediamine and acetic anhydride, was methylated with two moles of methyl iodide in a sealed tube at 100°. This method is similar to that of Fischer,[7] who carried out the methylation in two steps. The product, 1,2,3-trimethylbenzimidazole iodide (IV), was converted to the corresponding chloride (V) by shaking with silver chloride in hot methanol. Treatment of this chloride (V) with hot potassium hydroxide caused the precipitation of compound III.

Although compounds IV and V are quaternary ammonium salts, compound III is not a quaternary type of compound. This is shown by its ready solubility in the non-polar solvents, ether and benzene, but slight solubility in water. It is also stable to heat whereas quaternary ammonium bases decompose when heated.

Samples of compound III obtained by the two methods described above proved identical in every respect and a melting point of a mixture of the two samples showed no depression.

Experimental

***o*-Phenylenemalonamide.**—A mixture of 10.8 g. of *o*-phenylenediamine (0.1 mole) and 5.2 g. (0.05 mole) of malonic acid in 50 ml. of approximately 4 *N* hydrochloric acid was refluxed in an oil-bath at 125–130° for two and one-half hours with vigorous stirring. The mixture was cooled, filtered and insoluble product washed with cold water. The white granular product weighed 5.37 g. (61.8%). As previously reported,[2,3,4] it was insoluble in water, dilute acid, dilute alkalies, and organic solvents. The compound sublimes with partial decomposition near 360°.

Anal. Calcd. for $C_9H_8N_2O_2$: C, 61.34; H, 4.58; N, 15.91. Found: C, 61.39; H, 4.49; N, 15.88.

When equimolecular amounts of *o*-phenylenediamine and malonic acid are used in this same reaction, there forms in addition to the *o*-phenylenemalonamide, 2-amino-malonanilic acid as described by Phillips.[3]

Lower yields of *o*-phenylenemalonamide were obtained when diethylmalonate was used instead of the free acid, and when the ratio of *o*-phenylenediamine to malonic acid

(1) From a thesis submitted to the Faculty of the Graduate School in partial fulfillment of the requirements for the degree, Doctor of Philosophy, in the Department of Chemistry, Indiana University.

(2) Meyer, *Ann.*, **327**, 1 (1903); **347**, 17 (1906); **415**, 29 (1918).

(3) Phillips, *J. Chem. Soc.*, 172, 2393 (1928); THIS JOURNAL, **64**, 187 (1942).

(4) Shriner and Upson, *ibid.*, **63**, 2277 (1941); **64**, 187 (1942).

(5) Carothers, *Trans. Faraday Soc.*, **32**, 41 (1936); *Chem. Rev.*, **8**, 353 (1931).

(6) Pinnow and Sämann, *Ber.*, **32**, 2191 (1899).

(7) Fischer, *ibid.*, **25**, 2826 (1892); *J. prakt. Chem.*, **73**, 427 (1906)

(8) Niementowski, *ibid.*, **20**, 1888 (1899).