4. Stereoisomeric forms of 1,3-dimethyl-2-*n*-propylpyrrolidine were isolated depending on the method of preparation. The form giving the higher-melting picrate was converted to the other by dehydrogenation followed by hydrogenation.

URBANA, ILLINOIS RECEIVED OCTOBER 21, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF BARNARD COLLEGE]

Addition Reactions of *alpha*-Ketonic Acids. VII

BY MARIE REIMER AND ANNE L. MORRISON

In former papers of this series[1] it has been shown that the reactions of the side-chain of benzalpyruvic acid are strongly influenced by the nature and position of groups substituted in the benzene ring. A conspicuous effect is that of the *p*-methoxyl group which inhibits the sunlight reactions characteristic of the unsubstituted acid and to a less extent of its ortho- and meta-methoxy substitution products. This fact gave rise to the question as to whether the blocking of the light reaction were due to para substitution, in general, or to the *p*-methoxyl group, as such. In an attempt to answer this question *p*-methyl[2] and *p*-bromo[1]-benzalpyruvic acid were studied. Of these compounds, the *p*-methyl substituted acid is slightly, the *p*-bromo acid very markedly, light sensitive: the *p*-methoxyl is then the only group so far encountered in this series to completely block the light reaction. That the inhibiting effect is that of a *p*-alkoxyl, and not of the *p*-methoxyl group, specifically, is shown in the present paper which deals with the behavior of the *p*-ethoxy compound.

p-Ethoxybenzalpyruvic acid and its esters are found to be entirely unaffected by light. In other respects, too, the influence of the *p*-ethoxyl parallels that of the *p*-methoxyl group. The *p*-ethoxy acid and its derivatives give brilliantly colored compounds when dissolved in concentrated sulfuric acid. The acid forms no hydrate. It combines with bromine to form an unstable dibromide.

With all the benzalpyruvic acid dibromides of this series, treatment with boiling water has eliminated one molecular proportion of hydrogen bromide to form a colorless bromo compound with properties not to be expected of an unsaturated α-ketonic acid, a fact emphasized in the preceding paper on *p*-bromobenzalpyruvic acid.[1] In that case it was found possible to prepare an isomeric unsaturated bromo acid of more usual properties and evidence was obtained to show that the marked differences in behavior of the isomers could be accounted for on the assumption that the colorless isomer was a chelated, the other, an open chain compound. In the present case also, isomeric unsaturated bromo acids have been obtained and the evidence again indicates a chelated structure for the colorless acid. This pure white bromo acid, obtained by boiling aqueous suspensions of *p*-ethoxybenzalpyruvic acid dibromide, forms colorless methyl and ethyl derivatives with diazomethane and diazoethane, respectively. It does not react in the cold with alcohol saturated with hydrogen chloride, as is the case with all other analogous colorless acids of the series. On long heating in methanol–hydrogen chloride mixture the solution gradually becomes yellow and, on cooling, deposits brilliantly yellow crystals of a methyl ester isomeric with the one prepared by the diazomethane reaction. A yellow ethyl ester can be prepared by a similar procedure. A yellow, isomeric acid, corresponding to these two yellow esters, can be obtained from the colorless acid by prolonged treatment with sodium carbonate solution.

This yellow acid has the properties to be expected of a β,γ-unsaturated α-ketonic acid: it is brilliantly colored; it is fairly soluble in water, less so in benzene; it is esterified rapidly in the cold by alcohol saturated with hydrogen chloride; it forms a stable yellow sodium salt, very slightly soluble in alcohols, very readily soluble in water, this aqueous solution being oxidized rapidly by hydrogen peroxide to the corresponding cinnamic acid. The isomeric bromo acid is white; it is very slightly soluble in water, readily soluble in benzene; it is not esterified by alcohols and hydrogen chloride, isomerization to the yellow acid preceding esterification; it forms a colorless sodium salt, readily soluble in alcohols, very slightly soluble in water, transformed, in alkaline solution, into the isomeric yellow salt. From aqueous

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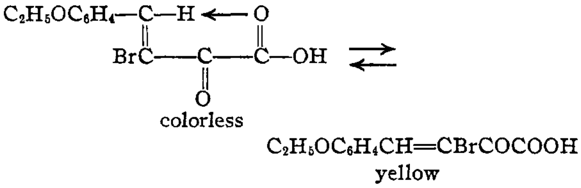
[1] No. VI, Reimer and Tobin, THIS JOURNAL, 62, 2515 (1940).

[2] Reimer and Chase, *ibid.*, 60, 2469 (1938).

solutions of the colorless sodium derivative hydrogen peroxide precipitates the colorless pyruvic acid corresponding to the original salt. There is no further action with hydrogen peroxide showing no tendency of the colorless acid to oxidation by this reagent although such oxidation is a distinguishing characteristic of α-ketonic acids.

Transformation of either acid to the other is rapid and quantitative, the white to the yellow by standing in alkaline solution, the yellow to the white rapidly on warming alone or in solution in water or benzene and, more slowly, by standing at room temperature. Such a quantitative change from one isomer to another in either direction, at will, is not a characteristic of *cis–trans* isomers nor are the properties of the colorless acid those to be expected of either geometrical form of an α-ketonic acid. They can be explained however on the assumption that the colorless acid is chelated



colorless

$C_2H_5OC_6H_4CH{=}CBrCOCOOH$

yellow

thereby losing its conjugation and consequently its color. Because the carbonyl oxygen of the carboxyl group takes part in the hydrogen bridge it is not available for reaction with alcohol and hydrogen chloride to form an ester. The solubilities of this acid and of its sodium derivative and the complete blocking of the oxidation reaction with hydrogen peroxide are in agreement with the chelate structure.

Color reactions with sulfuric acid described in the experimental part show differences between the isomers to be expected on the basis of the structures given; red changing to brown with the colorless compound, red changing finally to green with the yellow acid. This final persistent green color was that found by Kuhn and Winterstein[3] for solutions in concentrated sulfuric acid of highly conjugated unsaturated hydrocarbons. The shorter chain hydrocarbons with fewer conjugated linkages gave yellow or red-brown solutions.

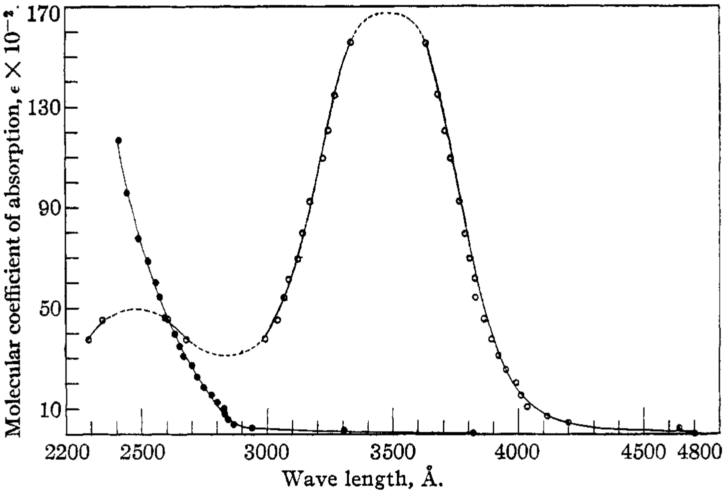


Fig. 1.—O-O-O-O-, Yellow ester (75–76°) in methyl alcohol; ●-●-●-●-, colorless ester (85–86°) in methyl alcohol.

Finally, perhaps the most convincing evidence for this interpretation of the differences between the two isomers is found in the ultraviolet absorption spectra[4] of their stable methyl esters. These show selective absorption for the yellow ester, indicating an unsaturated compound with a high degree of conjugation, but none for the colorless ester, a closed chain with the conjugation broken.

Experimental

p-Ethoxybenzalpyruvic Acid, 4-$C_2H_5OC_6H_4CH{=}CHCOCOOH$ (I) was prepared in good yield by alkaline condensation of pyruvic acid with p-ethoxybenzaldehyde which was obtained in 70% yield by treatment of p-hydroxybenzaldehyde with ethyl bromide in alcoholic potassium hydroxide solution.[5] A well cooled mixture of 8.7 g. (0.1 mole) of pyruvic acid and 15 g. (0.1 mole) of p-ethoxybenzaldehyde was treated with 42 ml. (1.8 moles) of 25% potassium hydroxide in methyl alcohol. The deep red solution began to deposit a yellow salt within a few minutes and, in an hour, a nearly solid mass of the salt had separated. By washing the filtered crystals with cooled methyl alcohol, nearly pure potassium p-ethoxybenzalpyruvate was obtained. The yields in different preparations were from 85 to 93%. The corresponding acid was obtained in quantitative yield by acidification of the cooled saturated aqueous solution of the salt. The acid separates as an oil which rapidly solidifies to hard yellow crystals. To avoid contamination of the acid by potassium salt it was found advisable to let the acid solution stand for eight to ten hours before filtering. The acid separates from a large volume of boiling water in gleaming yellow, elongated plates, melting at 89–90°. It is most conveniently purified by solution in a small volume of boiling benzene from which it separates, slowly, in stout yellow rods, melting at 47°.

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[3] Kuhn and Winterstein, *Ann.*, **461**, 132 (1928); *cf.* Reimer and Howard, THIS JOURNAL, **50**, 2506 (1928).

[4] We are indebted to Mr. R. H. Hay of the Physics Department of Columbia University for these determinations.

[5] Kostanecki and Schneider, *Ber.*, **29**, 1892 (1896).

These solvated crystals readily become opaque and then melt at 89-90°.

Anal. Calcd. for $C_{12}H_{12}O_4$: C, 65.46; H, 5.45. Found: C, 65.07; H, 5.64.

The acid is not readily soluble in water but dissolves easily in the usual organic solvents.

The methyl ester (II) was obtained in quantitative yield by action of methanol saturated with hydrogen chloride. Crystals of the acid stirred into approximately twice the volume of this solution dissolved rapidly and immediately the liquid was filled with the pale yellow ester. It crystallizes from methanol in rosets of pale yellow blades, melting at 79°.

Anal. Calcd. for $C_{13}H_{14}O_4$: C, 66.66; H, 5.98. Found: C, 66.20; H, 6.09.

This same ester was obtained from the acid by action of diazomethane.

The ethyl ester (III) was prepared by action of ethyl alcohol saturated with hydrogen chloride. It separates slowly requiring vigorous stirring and cooling to induce crystallization. It crystallizes from ethyl alcohol in pale yellow needles, melting at 41-42°.

Anal. Calcd. for $C_{14}H_{16}O_4$: C, 67.74; H, 6.44. Found: C, 67.62; H, 6.46.

The acid and its esters were not affected by several months of exposure to the light.

Oxidation of *p*-ethoxybenzalpyruvic acid with hydrogen peroxide in alkaline solution gave *p*-ethoxycinnamic acid in good yield. After two crystallizations from methanol the acid was pure, separating in gleaming colorless plates which melted to a cloudy liquid at 190°, to a clear liquid at 194°. The methyl ester, readily prepared by treatment with methanol saturated with hydrogen chloride, crystallized from methanol in large flat plates, melting to a cloudy liquid at 69-70°, to a clear liquid at 70-71°. These two substances are identical in crystalline form and behavior on melting with those prepared by Stoermer[6] by the Perkin synthesis.

***p*-Ethoxybenzalpyruvic Acid Dibromide, 4-$C_2H_5OC_6H_4$-CHBrCHBrCOCOOH (IV).**—The substance was obtained in 86% yield, when the ethoxy acid I was treated with bromine in cold chloroform solution. Fifteen grams of the unsaturated acid was dissolved in 150 ml. of chloroform and 10.8 g. of bromine added slowly with shaking. The decolorization of the bromine was rapid at first, less so as the reaction proceeded. When about one-half the bromine had been added a white granular solid began to separate. On completion of the reaction this was filtered and washed with cold chloroform. This dibromide is unstable, losing hydrogen bromide rapidly on warming and on exposure to moist air so that it was not found possible to purify it further. The crude product, melting at 140-143° with previous softening and with decomposition, was analyzed.

Anal. Calcd. for $C_{12}H_{12}O_4Br_2$: C, 37.89; H, 3.16. Found: C, 37.79; H, 4.07.

The methyl ester (V) of this dibromide could not be prepared from the unstable acid but was obtained in good yield by bromination of methyl *p*-ethoxypyruvate II. A well chilled solution of 1.5 g. of the ester II in 5 ml. of dried chloroform rapidly absorbed the calculated quantity of bromine. The clear, faintly colored solution was concentrated to an oil by aspirating at room temperature with a stream of dry air. When the oil was dissolved in the least quantity of anhydrous ether and petroleum ether added to faint turbidity, a solid separated. By repetition of this procedure, large, clear, colorless, diamond-shaped crystals, melting at 101-102°, were obtained.

Anal. Calcd. for $C_{13}H_{14}O_4Br_2$: C, 39.61; H, 3.58. Found: C, 39.32; H, 3.63.

This ester is more stable than the acid, undergoing no decomposition during several months in a desiccator. It is rapidly decomposed by warm water yielding a mixture of the unsaturated bromo ester VIII and the acid VI.

Colorless β-Bromo-*p*-ethoxybenzalpyruvic Acid (VI).—This acid was obtained by boiling the dibromo acid IV in water. When 10 g. of the acid was mixed with a liter of boiling water a bright yellow oil was formed at once. Within a few minutes the oil solidified in the boiling solution and after about ten minutes had dissolved to form a clear yellow solution[7] which, on cooling, deposited an 80% yield of gleaming white needles. The acid can be readily purified by crystallization from benzene or methyl alcohol from which it separates in shining white needles melting at 148-149° to a yellow liquid.

Anal. Calcd. for $C_{12}H_{11}O_4Br$: C, 48.16; H, 3.68. Found: C, 47.91; H, 3.77.

One gram of the acid dissolves in 200 ml. of boiling water, in 3 ml. of boiling benzene or methyl alcohol.

Two isomeric methyl esters were obtained from this acid.

The colorless methyl ester (VII) was prepared in quantitative yield by treatment of the acid VI with an ethereal solution of diazomethane. After three recrystallizations from methanol the slight yellow color of the product was eliminated, the ester separating in pure white, shining, hexagonal plates, resembling mica, melting at 85-86°.

Anal. Calcd. for $C_{13}H_{13}O_4Br$: C, 49.84; H, 4.15. Found: C, 49.93; H, 4.09.

The yellow methyl ester (VIII) was prepared from the acid VI by prolonged action of methanol saturated with hydrogen chloride. One gram of the acid dissolved, on warming, in 3 ml. of the alcoholic solution to form a pale yellow solution. When this solution was cooled immediately the stiff colorless needles of the original acid crystallized. When refluxed for forty-five minutes the original color changed to deep yellow and, on cooling, the solution was filled with soft, yellow needles. This ester is more soluble in alcohol than its colorless isomer but may be crystallized from small volumes of methanol from which it separates in rosets of long, yellow, fibrous needles, m. p. 75-76°. A mixture with the colorless isomer melted at 60-72°.

Anal. Calcd. for $C_{13}H_{13}O_4Br$: C, 49.84; H, 4.15. Found: C, 49.84; H, 4.51.

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(6) Stoermer, *Ber.*, **61**, 2323 (1928).

(7) The behavior of the dibromide on being brought into boiling water and the yellow color of the solution indicated the presence of the yellow *isomeric acid XI to be described later.* This was proved by extracting the yellow filtrates with ether which removed all the color. The ether extracts, thoroughly dried, were treated with an excess of diazomethane. On spontaneous evaporation of the solution, crystals of the yellow ester *VIII of the yellow isomeric* acid XI were obtained.

This ester was also obtained from the yellow acid XI by action of diazomethane and by treatment in the cold with methanol saturated with hydrogen chloride, from the dibromoester V by action of anhydrous sodium acetate in boiling methyl alcohol solution and from the colorless ester VII by refluxing with methyl alcohol saturated with hydrogen chloride.

The colorless ethyl ester (IX) was prepared from the acid VI by reaction with diazoethane. It separates from ethyl alcohol in large, colorless rhombic crystals, melting point 80–81°.

Anal. Calcd. for $C_{14}H_{15}O_4Br$: C, 51.38; H, 4.59. Found: C, 51.58; H, 4.54.

The yellow ethyl ester (X) was obtained when the acid VI was refluxed in a solution of ethyl alcohol saturated with hydrogen chloride. The deep yellow solution deposited, on cooling, a yellow oil which solidified slowly when cooled in a freezing mixture. This ester is more soluble in ethyl alcohol than its colorless isomer but it can be crystallized from a small volume of ethyl alcohol from which it separates in fine, yellow needles, m. p. 55–56°.

Anal. Calcd. for $C_{14}H_{15}O_4Br$: C, 51.38; H, 4.59. Found: C, 50.94; H, 4.60.

β-Bromo-*p*-ethoxybenzalpyruvic acid (XI), a yellow, relatively unstable isomer of the colorless acid VI, was obtained by acidifying aged sodium carbonate solutions of the latter. When 1 g. of the colorless acid VI was treated with 20 ml. of a 1% aqueous solution of sodium carbonate, a heavy white precipitate of a sodium derivative was formed almost at once. After the mixture had been shaken vigorously for one hour the solid had dissolved forming a clear, pale yellow solution. Immediate treatment with dilute hydrochloric acid precipitated a mixture of white needles and a yellow solid. If, however, the alkaline solution was allowed to stand for three days, acidification produced exclusively a yellow product which separated as an oil rapidly solidifying to a granular yellow solid. In a melting point tube this substance became white at about 60°, yellow at 145°, melting to a yellow liquid at 148–149°, the melting point of the colorless acid VI. The yellow acid evidently changed to the white at 60° as a mixed melting point with the pure colorless acid gave no depression. This same conversion to the acid VI occurs when the yellow acid is warmed in water or benzene solution and, even in the dry state, it slowly loses color till the change to the white acid is complete. This conversion in the dry condition could be followed by esterification with diazomethane. A portion of the yellow acid dried overnight in a desiccator, on treatment with an ether solution of diazomethane, yielded the characteristic fibrous needles of the yellow ester VIII, m. p. 75–76°. After three days of standing the rest of the acid had changed from deep yellow to a pale cream color. Treatment with diazomethane then yielded the mica-like plates of the white ester VII, m. p. 85–86°. The behavior toward dilute sodium carbonate solution also characterizes the yellow isomeric acid. It dissolves at once to a clear solution with no separation of an insoluble sodium derivative as is the case of the colorless isomer. This difference in solubilities in sodium carbonate solution makes possible a quick separation of mixtures of the acids.

The conversion of the yellow acid XI to the white acid VI and to the yellow ester VIII prove its composition. In addition, a stable sodium salt XII has been prepared and analyzed.

Yellow sodium β-bromo-*p*-ethoxybenzalpyruvate (XII) was prepared from the yellow acid XI by suspending a small quantity of the acid in cold water and adding slowly the calculated quantity of sodium carbonate. The acid dissolved rapidly, forming a pale yellow solution. This was allowed to evaporate spontaneously at room temperature. The pale yellow solid remaining was dissolved in warm methyl alcohol and ether added to the cooled solution to faint turbidity. The sodium salt separated in pale yellow microscopic needles.

Anal. Calcd. for $C_{12}H_{10}O_4BrNa$: Na, 7.17. Found: Na, 7.08.

This salt is very soluble in cold water, much less so in methyl alcohol. It is extremely stable, showing no conversion to the colorless salt over a period of many months. Its solution on acidification gives the yellow acid XI.

Colorless sodium β-bromo-*p*-ethoxybenzalpyruvate XIII was obtained as the first product whenever the colorless acid VI was brought into contact with sodium carbonate solution. When 1 g. of the acid VI was treated with 20 ml. of 1% sodium carbonate solution, rapid solution of the acid was followed immediately by precipitation of this white sodium derivative in shining, colorless plates. After filtering and washing thoroughly with cold water the dry compound was analyzed.

Anal. Calcd. for $C_{12}H_{10}O_4BrNa$: Na, 7.17. Found: Na, 7.11.

The substance is readily soluble in alcohols, very slightly soluble in cold water. In hot water conversion to the yellow salt occurs.

Reactions with Hydrogen Peroxide. The yellow sodium salt XII (50 mg.) was dissolved in water (15 ml.) and 10 ml. of hydrogen peroxide (30 vols.) added. The pale yellow color of the solution faded rapidly and within a few minutes a fine, colorless precipitate began to separate. This solid proved to be α-bromo-*p*-ethoxycinnamic acid XIV. A further amount was obtained by acidification of the filtrates.

The colorless sodium derivative XIII suspended in water and treated with hydrogen peroxide under the same conditions went into solution slowly with simultaneous separation of fine white needles which proved to be the original β-bromo-*p*-ethoxybenzalpyruvic acid VI. This acid had then been precipitated from its sodium salt by hydrogen peroxide but was not oxidized by it.

The isomeric bromo acids show the same differences in behavior. A freshly prepared solution of the yellow acid XI was treated with hydrogen peroxide. The yellow color faded rapidly and, within a few minutes, crystals of α-bromo-*p*-ethoxycinnamic acid began to separate. Under the same conditions a suspension of the colorless acid VI remained unchanged even after many days in contact with hydrogen peroxide.

α-Bromo-*p*-ethoxycinnamic acid (XIV) was prepared in excellent yields by hydrogen peroxide oxidation of the yellow acid XI in alkaline solution or from the colorless acid VI after it had been standing many hours in a solution of sodium carbonate. The yellow, alkaline solutions, on treatment with hydrogen peroxide, rapidly lost their color and on acidification of the clear, colorless solutions deposited a colorless acid, which, after two crystallizations from benzene, separated in opaque rods melting at 180–181°.

Anal. Calcd. for $C_{11}H_{11}O_3Br$: C, 48.71; H, 4.06. Found: C, 48.60; H, 4.10.

The methyl ester (XV) of this acid was prepared by the diazomethane reaction and by methanol saturated with hydrogen chloride. It separates from methanol in rosets of soft fibrous needles, melting at 51–52°.

Anal. Calcd. for $C_{12}H_{13}O_3Br$: C, 50.53; H, 4.56. Found: C, 50.64; H, 4.74.

Reactions with Sulfuric Acid.—Approximately 1 mg. of substance was stirred into two to three drops of pure concentrated sulfuric acid on a porcelain plate. *p*-Ethoxycinnamic acid and its derivatives gave a pale yellow color, which faded rapidly. The ketonic acids and their esters dissolved with brilliant red color followed rapidly by a series of changes to a final solution the color of which persisted for hours. With *p*-ethoxybenzalpyruvic acid, its esters and its dibromo addition product the colors were red ⟶ red orange ⟶ reddish yellow. In the case of the isomeric bromo acids the color differences are striking: with the colorless, apparently chelated acid VI, cherry-red ⟶ deep red ⟶ violet ⟶ deep brown and its esters the same. With the yellow, isomeric acid XI and its esters, brilliant red ⟶ purple ⟶ purple-blue ⟶ green.

Summary

The influence of the *p*-ethoxyl group on the behavior of the side chain of benzalpyruvic acid has been shown to be similar to that of the *p*-methoxyl group. Isomeric *β*-bromo-*p*-ethoxybenzalpyruvic acids have been prepared, the differences in physical and chemical properties of these isomers indicating a chelated form for the colorless acid, an open chain form for the yellow isomer.

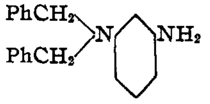
NEW YORK, N. Y. RECEIVED OCTOBER 21, 1940

[CONTRIBUTION FROM THE ORGANIC CHEMICAL LABORATORY OF THE UNIVERSITY OF FLORIDA]

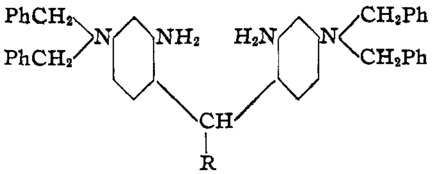
Reactions of Aldehydes with Amines. II. A New Aldehyde Reagent[1]

BY F. G. SINGLETON[2] AND C. B. POLLARD

Preliminary attempts to condense N,N-dibenzyl-*m*-phenylenediamine (I) with aromatic aldehydes to form substituted tetraminotriphenylmethanes (II) were unsuccessful. However, it was noticed that the addition of an aldehyde to an alcoholic solution of (I) containing a small amount of mineral acid caused the immediate formation of a red color which was followed by a strong green fluorescence. This paper deals with the color and fluorescence and describes a new test for aldehydes based upon these properties.

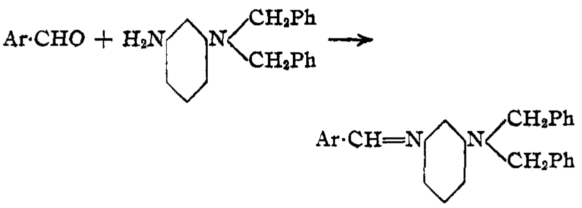


(I)



(II)

The Color.—When (I) was heated with aromatic aldehydes in neutral alcohol solution, yellow oils separated which were shown to be Schiff bases



Purification gave yellow, amorphous solids which could not be crystallized. Treatment with dry hydrogen chloride in anhydrous ether gave blood-red, resinous monohydrochlorides. Further treatment gave almost colorless dihydrochlorides which lost hydrogen chloride slowly in air, forming the red mono- salts. The di- salts were hydrolyzed by water in the cold to (I) and the original aldehydes. The six derivatives prepared are described in Table I. All of these compounds softened gradually on heating and became liquids below 100°.

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(1) This paper is abstracted from a portion of a dissertation submitted by F. G. Singleton to the Graduate Council of the University of Florida in partial fulfillment of the requirements for the degree of Doctor of Philosophy, August, 1940.

(2) Present address: Kansas State College, Manhattan, Kansas. Part of this work was done in the laboratory of Mme. Ramart-Lucas, Professor at the Sorbonne while Mr. Singleton was Research Fellow (1938–39) of the Société des Amis de l'Université de Paris.