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

A Series of Highly Colored Condensation Products from Benzamidine and Glyoxal. I

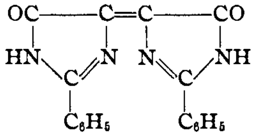
BY JOHN B. EKELEY AND ANTHONY R. RONZIO

In a former paper[1] it was reported that the filtrate from the addition product formed in the reaction of benzamidine with glyoxal changes to a bright red color and gives products among which is one we now know to be identical with "glyoxaline red." The present paper describes a number of highly colored compounds resulting from the action of benzamidine upon glyoxal under varying temperatures, time of reaction, concentrations of reagents and amounts of water present. We have isolated six compounds, $C_{18}H_{12}N_4O_2$, $C_{18}H_{12}N_4O_2 \cdot H_2O$, $C_{20}H_{18}N_4O_4$, $(C_{20}H_{17}N_2O_3)_2O$, $C_{42}H_{30}N_8O_6$ and $C_{22}H_{20}N_4O_3$, the first two, respectively, being identical with Ruhemann and Stapleton's[2] glyoxaline red and its yellow hydrate isolated by them from the reaction product between benzamidine and acetylene dicarboxylic ester. We have repeated R. and S.'s experiments but, since they give no details regarding the quantities and concentrations of the reagents used, had great difficulty in reproducing their results. We finally were successful by using the following procedures.

About 1.5 g. of ester was mixed with 25 cc. of a water solution of 2 equivalents of benzamidine hydrochloride. Enough 95% alcohol was then added to bring the ester into solution. Addition of 2.5 equivalents of potassium hydroxide solution produced a yellow color which gradually changed to red. After standing for twelve hours, neutralization with hydrochloric acid yielded an orange-yellow precipitate. After being filtered and boiled with 95% alcohol, the precipitate was redissolved in potassium hydroxide solution and reprecipitated with hydrochloric acid. Washed with water, cold acetic acid, alcohol and ether, successively, the product was "glyoxaline red," a ruby-red amorphous powder, which did not melt but sublimed between 350–375° (electric bloc Maquenne) with decomposition; soluble in pyridine, so very slightly soluble in the usual organic solvents to a yellow solution that we were unable to obtain one strong enough for molecular weight determinations, but strong enough for absorption spectra purposes; soluble in bases to a ruby-red solution. Boiling acetic acid slowly dissolves it and has the effect of adding one molecule of water to the compound. R. and S. state that their product, on being boiled with acetic acid, took up one molecule of water to form yellow needles and on the addition of potassium hydroxide gave a yellow solution which turned red on standing. Our product from acetic acid was brownish-red and upon the addition of base gave a red solution at once. However, similar treatment with dilute hydrochloric acid yielded microscopic crystals of the same composition and of a metallic bronze sheen. With potassium hydroxide they gave a yellow solution which slowly changed to red on standing.

Anal. Calcd. for glyoxaline red, $C_{18}H_{12}N_4O_2$: C, 68.35; H, 3.80; N, 17.72. Found: C, 68.53; H, 3.93; N, 17.75.

R. and S. regarded the structure of glyoxaline red to be



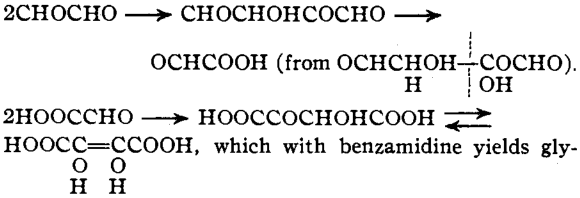
in order to account for the loss of two hydrogen atoms as shown by their ultimate analyses of the compound.

We obtained glyoxaline red and its hydrate from benzamidine and glyoxal by the following methods.

Glyoxaline Red from Benzamidine and Glyoxal.—Exactly 2 g. of benzamidine-glyoxal was added to 100 cc. of absolute alcohol in which 2 g. (8 equivalents) of sodium had been dissolved. The solution turned immediately to a brilliant permanganate color. After being refluxed for two hours and cooled, the resulting precipitate (the sodium salt of glyoxaline red) was filtered off, dissolved in water, filtered again and decomposed with hydrochloric acid, yielding a ruby-red amorphous powder; yield 0.2 g. This was purified exactly as in the preceding case, giving an identical product as to physical and chemical properties and absorption spectrum.

Anal. Calcd. for $C_{18}H_{12}N_4O_2$: C, 68.35; H, 3.80; N, 17.72. Found 1: C, 68.25, 68.63; H, 3.85, 4.08; N, 17.74, 17.51.

The formation of glyoxaline red from benzamidine and glyoxal is explained, as far as we can see, only by the following assumption



$$2CHOCHO \longrightarrow CHOCHOHCOCHO \longrightarrow OCHCOOH\ (\text{from } \underset{H}{OCHCHOH}\,\vdots\,\underset{OH}{COCHO}).$$

$$2HOOCCHO \longrightarrow HOOCCOCHOHCOOH \rightleftarrows HOOC\underset{\underset{H}{O}}{C}{=}\underset{\underset{H}{O}}{C}COOH,$$

which with benzamidine yields glyoxaline red.

Hydration Product of Glyoxaline Red.—About 0.5 g. of glyoxaline red from benzamidine-glyoxal was boiled with 25 cc. of acetic acid for about thirty minutes until

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(1) Ekeley and Ronzio, THIS JOURNAL, **57**, 1353 (1935).

(2) Ruhemann and Stapleton, *J. Chem. Soc.*, **77**, 809 (1900); *Proc. Chem. Soc.*, **16**, 121 (1900).

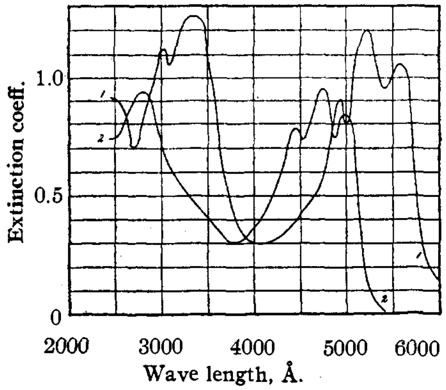


Fig. 1.[*]—Curve 1, Ruhemann and Stapleton's "Glyoxaline Red" 0.00060 g./50 ml. of KOH–H_2O solution; Curve 2, same, 0.00060 g./50 ml. of dioxane.

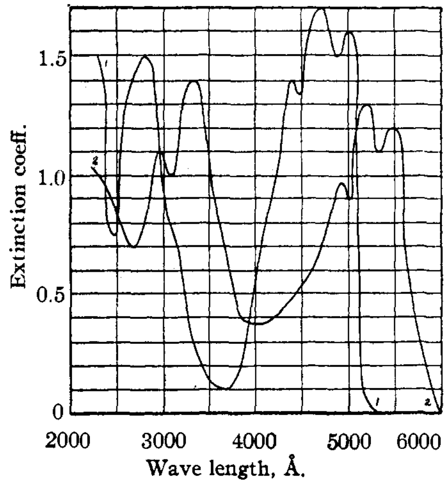


Fig. 2.—Curve 1, Ekeley and Ronzio's "Glyoxaline Red" 0.00168 g./50 ml. dioxane, 1-cm. cell; Curve 2, same, 0.00200 g./50 ml. of KOH–H_2O.

solution was complete to a brownish-red. Concentration by standing in the open air yielded brownish-red needles, which with potassium hydroxide gave a ruby red solution. Soluble in the usual organic solvents to a brownish-yellow color, m. p. 267°, with decomposition.

Anal. Calcd. for $C_{18}H_{12}N_4O_2 \cdot H_2O$: C, 64.67; H, 4.19; N, 16.76. Found: C, 64.54; H, 4.42; N, 16.65.

Compound $C_{20}H_{18}N_4O_4$, from 2 Moles of Amidine and 3 Moles of Glyoxal.—This compound was first obtained using a glyoxal (Polyglyoxal, Schuchardt) which contained only a little glyoxylic acid. The mother liquor remaining after the preparation of benzamidine-glyoxal was allowed to stand for about a week, whereupon it assumed a deep red color. Acidification with hydrochloric acid precipitated a dark red gum which could be collected on a stirring rod and solidified when washed with cold water. The solid was dissolved in potassium hydroxide solution, reprecipitated with hydrochloric acid and washed with water until the washings gave no test for chlorides. The dark red amorphous powder could not be obtained crystalline, m. p. 183° (capillary tube). The same substance giving the same ultimate analysis was produced from two different mother liquors obtained using the same glyoxal; soluble in alcohol, acetic acid and in potassium hydroxide to a deep red solution.

Anal. Calcd. for $(C_{10}H_9N_2O_2)_x$: C, 63.44; H, 4.76; N, 14.81. Found: C, 63.51, 63.60; H, 4.63, 4.64; N, 14.35.

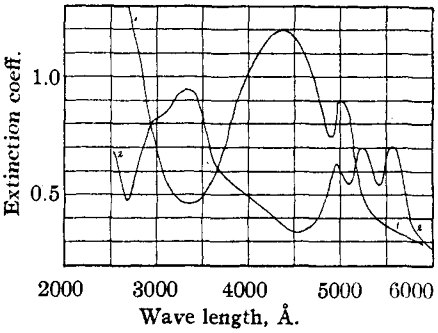
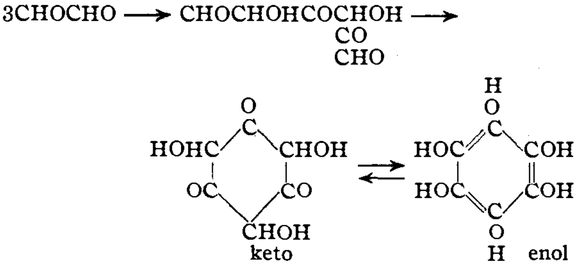


Fig. 3.—Curve 1, Glyoxaline Red + 1 H_2O, 0.00101 g./50 ml. dioxane, 1-cm. cell; Curve 2, same in H_2O, 0.00094 g./50 ml. of H_2O containing 0.01 g. of KOH.

When a new lot of glyoxal (Schuchardt) which contained 78% of acid calculated as glyoxylic was used, a similar red product was obtained by the same method but it was not quite so pure. At the same time a relatively large amount of 1-phenyl-4-oxy-5-pyrimidine carboxylic acid was obtained.

Anal. Less pure product: Found for $(C_{10}H_9N_2O_2)_2$: C, 63.18; H, 5.37; N, 13.30.

Structure of the Compound $C_{20}H_{18}N_4O_4$.—The only explanation we are able to give for the formation of this compound is one that assumes the formation of a triketotrihydroxyhexahydrobenzene from three molecules of glyoxal.



$$3\text{CHOCHO} \longrightarrow \text{CHOCHOHCO}\underset{\substack{\text{CO} \\ \text{CHO}}}{\text{C}}\text{HOH} \longrightarrow$$

That such a polymerization does actually take place under the influence of alkali is shown by Homalka,[3] who prepared tetrahydroxyquinone by this method. The enol form of the above, condensing with benzamidine would yield 1,3-dibenzamidyl-4,6-dihydroxyquinol, $C_{20}H_{18}N_4O_4$.

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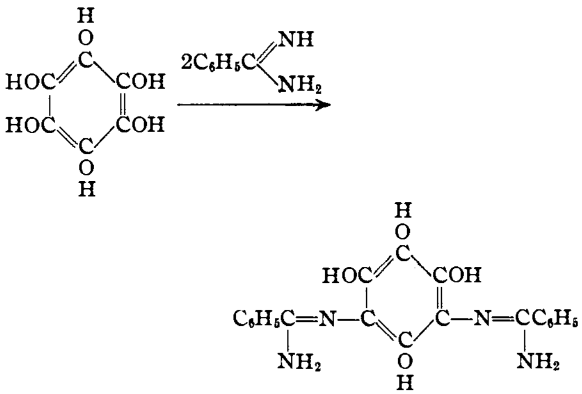
[*] E3 Hilger quartz spectrograph was used in conjunction with a Hilger sectorphotometer. Spectra were photographed on Eastman Panchromatic plates.

(3) Homalka, *Ber.*, **54**, 1393 (1921).



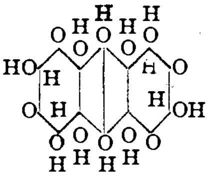
Compound $(C_{20}H_{17}N_4O_3)_2O$.—When the compound just described is heated in boiling alcohol or dissolved in strong bases and allowed to stand or when benzamidine-glyoxal is allowed to stand in strong potassium hydroxide solution, a product is obtained which is only slightly soluble in alcohol and separates in microscopic black needles with a green iridescence; easily soluble in pyridine and somewhat soluble in dioxane. In alkaline solution it has a deep permanganate color, m. p. 326° (electric bloc Maquenne) with decomposition.

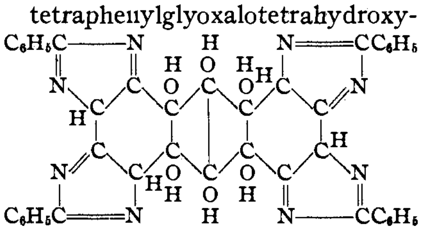
Anal. Calcd. for $(C_{20}H_{17}N_4O_3)_2O$: C, 65.02; H, 4.64; N, 15.17. Found: C, 65.19, 64.91; H, 4.66, 4.72; N, 15.01, 15.31. Since this compound $C_{40}H_{34}N_4O_7$ is obtained from $(C_{10}H_9N_2O_2)_x$ by the loss of one mole of H_2O, the original is evidently $C_{20}H_{18}N_4O_4$.

Compound $C_{42}H_{30}N_8O_6$.—A very small yield (about 1%) of a compound having the above empirical formula was obtained at will when benzamidine-glyoxal was allowed to stand in a stoppered flask in one-half equivalent solution of sodium alcoholate for forty-eight hours. A somewhat better yield was obtained when benzamidine-glyoxal was dissolved in dilute hydrochloric acid and one equivalent of glyoxal bisulfite added. The compound separated out in microscopic green fiber-like crystals of very characteristic appearance under the microscope. Soluble in pyridine, glacial acetic acid and dioxane to an emerald-green solution which soon began to decompose and turn brown. When oxidized with strong nitric acid, a deep red solution was obtained which yielded a small amount of a precipitate when neutralized and redissolved in alkali to a red solution. The amount of this product was too small for analysis. We intend to investigate it further: m. p. green crystals, 264° (elect. bloc Maquenne).

Anal. Calcd. for $(C_{21}H_{15}N_4O_3)_2$: C, 67.90; H, 4.07; N, 15.09. Found: C, 67.82, 67.93; H, 4.16, 4.28; N, 15.00, 14.94. On account of its unstable nature, we were unable to obtain the absorption spectrum. It is evident from its empirical formula that this compound is obtained by the elimination of 8 moles of water from 7 moles of glyoxal and 4 moles of benzamidine.

Possible Structure of Compounds $C_{42}H_{30}N_8O_6$.—From the work of Homalka we know that three molecules of glyoxal under the influence of alkali polymerize to a triketotrihydroxyhexahydrobenzene. The formation of this compound may be explained similarly to that of $C_{20}H_{18}N_4O_4$ by the condensation of four molecules of benzamidine with a ketohydroxyhydroanthracene yielding a tetraphenylglyoxalotetrahydroxyanthraquinol.





Compound $C_{22}H_{20}N_4O_3$.—Benzamidine-glyoxal dissolved in absolute alcohol containing 4 equivalents of sodium and refluxed for forty-eight hours yielded a product which, ruby-red in this solution, separated out upon acidification as a dark orange precipitate. Filtered, washed with hot water until free from chlorides and dried, the yield was from 20 to 25%; soluble in alcohol, acetic acid, and butyl acetate. We were unable to obtain it crystalline from any solvent, yet it always gave a melting point of 249° (bloc Maquenne), and a constant percentage composition.

Anal. Calcd. for $C_{22}H_{20}N_4O_3$: C, 68.02; H, 5.19; N, 14.42. Found: C, 68.25, 67.82; H, 5.01, 5.08; N, 14.51, 14.36.

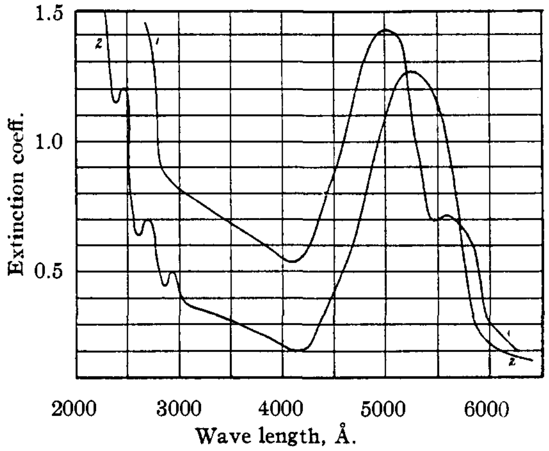
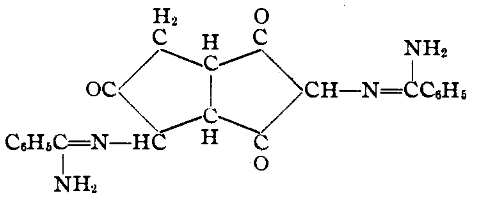
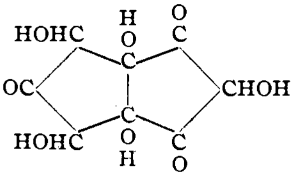


Fig. 4.—Curve 1, compound $(C_{20}H_{17}N_4O_3)_2O$, 0.00158 g./50 ml. dioxane; Curve 2, same, 0.00048 g./50 ml. of 95% alcohol + KOH.

We can only suggest the following possible structural formula for a compound, $C_{22}H_{20}N_4O_3$



which theoretically would be formed from the reduction of three hydroxyl groups to hydrogen in the compound formed by the condensation of two benzamidine molecules with a hypothetical polymerization product of four molecules of glyoxal to the triketopentahydroxy compound



We have isolated several other highly colored reaction products of benzamidine and glyoxal, but have not yet obtained them pure enough to be certain of their empirical formulas.

Summary

A series of highly colored condensation products of benzamidine and glyoxal has been prepared. In two cases their absorption spectra in neutral and basic solution have been determined and a theory has been proposed to explain their formation. Among these are the following:

1. Glyoxaline red, formerly obtained by the condensation of benzamidine and acetylenedicarboxylic ester.
2. A condensation product between 2 g. moles of benzamidine and 3 g. moles of glyoxal.
3. A condensation product between 4 g. moles of benzamidine and 6 g. moles of glyoxal.
4. A condensation product between 4 g. moles of benzamidine and 7 g. moles of glyoxal.
5. A condensation product between 2 g. moles of benzamidine and 4 g. moles of glyoxal.

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Argentic Salts in Acid Solution. IV. The Kinetics of the Reduction by Water and the Formation by Ozone of Argentic Silver in Nitric Acid Solution[1]

BY ARTHUR A. NOYES, CHARLES D. CORYELL, FRED STITT AND ALEXANDER KOSSIAKOFF

In a preceding paper[2] of this series there were discussed preliminary results concerning the rate of oxidation by ozone of acid solutions of argentous nitrate, and of the rate of reduction by water of the argentic solutions thus formed. The present article describes in detail the more extensive kinetic study referred to there, as well as further observations on the behavior of argentic solutions toward some reducing agents.

Methods of Analysis

Considerable effort was spent in search of a rapid, accurate method of analysis for argentic silver in nitric acid solutions in the presence of ozone. A series of qualitative experiments revealed several interesting facts briefly summarized here.

The Action of Argentic Nitrate[3] and of Ozone on Certain Reducing Agents.—The following experiments were made with solutions of argentic nitrate or of ozone either 2 or 4 N in nitric acid and initially at 0°.

The following reducing agents reduce both argentic nitrate and ozone completely in a short time: Fe^{++}, $Fe(CN)_6^{\equiv}$ $HAsO_2$, Hg_2^{++}, Mn^{++}. This was shown by the immediate disappearance of the brown-black argentic nitrate color on adding argentic solution to the reducing agent in a glass-stoppered flask, or by the absence of the odor of ozone after adding to the reducing agent a sample of ozone-saturated nitric acid. Argentic nitrate solutions oxidize Mn^{++} to MnO_4^-, but ozone oxidizes it principally to manganese dioxide even with argentous ion present. Tl^+ also reduces both argentic nitrate and ozone, but the reduction of ozone is not complete within a few minutes (with shaking) unless a rather large excess of reagent is used. A ten-fold excess results in complete reduction of ozone in less than two minutes, and in much less time if argentic silver is also present.

The following reducing agents reduce argentic nitrate immediately, but within an hour with occasional shaking do not reduce ozone completely even in the presence of argentous ion, as is shown by the persistence of the ozone odor:

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[1] This investigation was initiated by Professor Noyes, who directed a large part of the experimental work. After his death in June, 1936, the junior authors brought the work to a close and prepared this article for publication. They assume full responsibility for imperfections and wish to acknowledge their great debt to Professor Noyes.

[2] Noyes, Hoard and Pitzer, THIS JOURNAL, **57**, 1221 (1935).

[3] The term "argentic nitrate" is used in this paper to designate argentic silver in nitric acid solution, although no compound $Ag(NO_3)_2$ has yet been isolated.