THE OXIDATION OF ISOBARBITURIC ACID.
A NEW CLASS OF INDIGOIDS.

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In studying the oxidation of natural occurring pyrimidines, Baudisch (1) observed that uracil (I) and cytosine (II) yielded solutions which were brilliant yellow in color. The coloring agent, or agents, were, however, not isolated. Since isobarbituric acid (III) could be demonstrated to be an intermediate product in the oxidation of these pyrimidines, it was anticipated that an investigation of this substance might give an insight into the nature of the colored derivatives.

The subject appeared especially promising because of the possible analogy between isobarbituric acid (III) and indoxyl (IV). It was to be expected that just as the latter yields indigo (V) on oxidation, so isobarbituric acid might give rise to a highly colored bicyclic molecule (VI).

Previous investigators have shown that on oxidation isobarbituric acid is readily attacked at the double bond. Thus, by bromine water\(^1\) it is converted into isodialuric acid (VII), while

\(^1\) Behrend and Rooseen (2), p. 242.
Oxidation of Isobarbituric Acid

with permanganate the cycle is ruptured and formyl-oxalylurea (VIII) is produced (3).

\[
\begin{align*}
\text{VII.} & \quad \text{VIII.} \\
\text{NH} \cdot \text{CO} & \quad \text{NH} \cdot \text{CO} \\
\text{CO} & \quad \text{CO} \\
\text{CO} & \quad \text{COOH} \\
\text{NH} \cdot \text{CHOH} & \quad \text{NH} \cdot \text{CHO}
\end{align*}
\]

By utilizing ferricyanide as the oxidant, it has now been found possible to control the oxidation so that, in a portion of the oxidized material at least, the double bond remains intact, the reaction proceeding with the loss of 1 hydrogen atom from the molecule and the subsequent coupling of two cycles (formula (IX)).

\[
\begin{align*}
\text{III.} & \quad \text{IX.} \\
\text{NH} \cdot \text{CO} & \quad \text{NH} \cdot \text{CO} \\
\text{CO} & \quad \text{CO} \\
\text{CO} & \quad \text{CO} \\
\text{NH} \cdot \text{CHOH} & \quad \text{NH} \cdot \text{CHOH} \\
\end{align*}
\]

For this product the name 4,4'-di-isobarbituric acid is proposed. The compound is of a bright lemon-yellow color, is exceedingly insoluble, forms red alkali metal salts, and dissolves in excess of alkali to give solutions possessing a beautiful green fluorescence. Since, unlike isobarbituric acid, and other 5-hydroxypyrimidines, it does not yield a blue salt with ferric chloride, it probably exists in the keto form (formula (X)).

**Urindigo.**

Thus far the expected analogy between isobarbituric acid and indoxyl had not been realized, the behavior of isobarbituric acid resembling much more that of aromatic phenols which, on oxidation, yield ortho-diphenols,

\[
\begin{align*}
\text{OH} & \quad \text{OH} \quad \text{OH}
\end{align*}
\]

with this difference, however, that di-isobarbituric acid no longer retained the enol form (IX), but appeared rather in the keto form (X). It seemed probable, therefore, that further oxidation
of di-isobarbituric acid might lead to the unsaturated derivative (VI) originally anticipated. This was found to be the case, for with nitric acid or bromine water di-isobarbituric acid is converted into a scarlet-colored compound with the loss of 2 hydrogen atoms.

\[
\begin{align*}
\text{NH} & \cdot \text{CO} \hspace{0.5cm} \text{CO} \hspace{0.5cm} \text{NH} \\
\text{CO} & \hspace{0.5cm} \text{CO} \hspace{0.5cm} \text{CO} \hspace{0.5cm} \text{CO} \\
\text{NH} & \cdot \text{CH} \cdot \text{CH} \cdot \text{NH}
\end{align*}
\rightarrow
\begin{align*}
\text{NH} & \cdot \text{CO} \hspace{0.5cm} \text{CO} \hspace{0.5cm} \text{CO} \\
\text{CO} & \hspace{0.5cm} \text{CO} \hspace{0.5cm} \text{CO} \hspace{0.5cm} \text{CO} \\
\text{NH} & \cdot \text{C} = \text{C} \hspace{0.5cm} \text{NH}
\end{align*}
\]

This substance contains the indigoid grouping \(-\text{CO} - \text{C} = \text{C} - \text{CO}\), hence its systematic name (4) is di-uracil-4,4'-indigo. It is the first colored representative of the pyrimidine indigoïds.\(^2\) Because of its close similarity to indigo (V) and its derivation from uracil, the convenient name “urindigo” is proposed for it.

**EXPERIMENTAL PART.**

**Isobarbituric Acid.**—A modification of the method of Behrend and Roosen\(^3\) was employed. 50 gm. of 5-nitro-uracil (5) and 100 gm. of tin were heated on the steam bath with 550 cc. of water and 550 cc. of concentrated hydrochloric acid until all the nitro compound had gone into solution and hydrogen was being evolved. The reaction mixture was then quickly filtered by suction. The filtrate, on cooling, yielded 26 gm. of pure, colorless isobarbituric acid (63 per cent of theory). About 5 gm. of 5-amino-uracil may be recovered from the mother liquor.

**Di-Isobarbituric Acid.**—A chilled \((5^\circ)\) filtered solution of 51.2 gm. (2 mols) of potassium ferricyanide in 200 cc. of water is

\(^2\) The isomeric colorless dehydro-hydurilic acid

\[
\begin{align*}
\text{NH} & \cdot \text{CO} \hspace{0.5cm} \text{CO} \hspace{0.5cm} \text{NH} \\
\text{CO} & \hspace{0.5cm} \text{C} = \text{C} \\
\text{NH} & \cdot \text{CO} \hspace{0.5cm} \text{CO} \hspace{0.5cm} \text{NH}
\end{align*}
\]


\(^3\) Behrend and Roosen (2), p. 230.
added at once to a chilled, filtered solution of 10 gm. (1 mol) of isobarbituric acid, and 13.2 gm. (3 mols) of potassium hydroxide in 200 cc. of water. The reaction mixture is at first dark brown and opaque, but after being stirred a few moments, it becomes bright red and transparent, whereupon the red dipotassium salt of di-isobarbituric acid begins to precipitate. The separation of the product is facilitated by shaking the reaction mixture for a few minutes. After centrifugating, the salt is suspended in water, filtered, and washed with water. Yield 1.5 gm.\(^4\)

**Analysis.**  
\[ C_4H_4O_6N_4K_2 \]

Calculated.  \( \text{N} \) 19.97.  
Found.  \( \text{N} \) 17.12.

That the filtrate contains isodialuric acid (or dialuric acid) is shown by the precipitation of a purple salt on adding barium hydroxide.

To obtain the free di-isobarbituric acid the salt was suspended in water and poured into 200 cc. of boiling water containing an excess of acetic acid. The very insoluble lemon-yellow product separated immediately in microscopic rhombic plates, was filtered hot, and washed with hot water.

**Analysis.**  
\[ C_4H_4O_6N_4 \]

Calculated.  \( C \) 37.78, \( H \) 2.38, \( N \) 22.06.  
Found.  \( C \) 38.06, \( H \) 2.64, \( N \) 22.17.

Di-isobarbituric acid is very insoluble in all common solvents. It dissolves in concentrated sulfuric acid, and is precipitated on dilution. When treated with dilute alkali, it is converted into its red alkali salts, which dissolve in excess of alkali to give solutions possessing a strong green fluorescence. The red alkali salts may be reprecipitated from these solutions by passing in carbon dioxide. Di-isobarbituric acid reduces silver nitrate solution in the cold. With concentrated nitric acid it gives a brilliant scarlet solution (urindigo), the color of which gradually fades. On evaporation of the solution and moistening the residue with ammonia, a deep purple-red color is obtained (murexide

\(^4\) It is to be noted that a small quantity of the red sodium salt of di-isobarbituric acid is obtained on evaporating a solution of isobarbituric acid in sodium bicarbonate in an open dish on the water bath, or by passing oxygen into a warm solution of sodium isobarbiturate.
test). With diazobenzenesulfonic acid and sodium bicarbonate it gives no immediate color, but gradually develops a deep wine color on standing. It does not melt below 310°.

**Urindigo.**—1 gm. (1 mol) of finely pulverized di-isobarbituric acid was suspended in about 50 cc. of cold water and 0.2 cc. (1 mol) of bromine added, and the mixture vigorously shaken. The yellow acid was immediately transformed into the scarlet indigoïd, which was filtered off and washed with water. Yield 0.7 gm. The product was bromine-free.

**Analysis.**

\[
\text{C}_4\text{H}_6\text{O}_6\text{N}_4. \quad \text{Calculated. C } 38.08, \text{ H } 1.60, \text{ N } 22.23.
\]

\[
\text{Found. } " 38.09, " 1.87, " 21.95.
\]

Urindigo is insoluble in the common organic solvents. It dissolves in concentrated sulfuric acid, from which it is reprecipitated on dilution. It dissolves in concentrated nitric acid, but is gradually oxidized. It slowly dissolves in bromine water; if the solution is now treated with excess of barium hydroxide, a purple precipitate (barium dialurate) is obtained. It is immediately decomposed by alkali; on neutralizing the solution and adding ferric chloride, the deep blue ferric salt characteristic of 5-hydroxy derivatives of uracil is obtained. The solution probably contains 5-hydroxyuracil-4-aldehyde, the urindigo presumably having undergone a type of hydrolysis peculiar to indigoids (6).

\[
\text{NH} \cdot \text{CO} \quad \text{CO} \quad \text{NH} \quad \text{CO} \quad \text{H}_2\text{O} \quad \text{CO} \quad \text{COH} \quad + \quad \text{CO} \quad \text{NH} \quad \text{C} \cdot \text{CHO} \quad \text{NH}_2\text{COOH}
\]

Urindigo does not melt below 310°.

**BIBLIOGRAPHY.**