

avoiding the development of aldehydes and peroxides on aging.

EXPERIMENTAL

Preliminary work included the preparation of ether made slightly alkaline with ammonia, and of ether mildly acidulated with glacial acetic acid and also sulfuric acid; and the packaging of these ethers in glass bottles, copper-lined cans and tin-lined cans. These samples were examined after three months, eleven months and forty-one months. The acidified ether in all three types of containers showed the presence of aldehydes each time the ethers were tested, while the ammoniated ether did not. These experiments indicated that a condition of mild acidity is unfavorable and one of mild alkalinity favorable for the protection of ether.

In extending this work ethers containing 0.00176, 0.00088, 0.00044, 0.00022 and 0.00011 Gm. of ammonium hydroxide per 100 cc. of ether were prepared and packaged in copper-lined and tin-lined containers. These were stored at room temperature and also at elevated temperature for thirty-three months. Tests showed that 0.00022 Gm. of ammonium hydroxide per 100 cc. was the optimum amount and that, with the other concentrations, the results were not as good.

Subsequently, an ether containing this optimum concentration of ammonia was packaged in copper-lined containers and tin-lined containers. At the same time a normal anesthetic ether was packaged in the same types of containers. These ethers were stored both at room temperature and at elevated temperatures for thirty-three months. They were subjected to the U. S. P. XI tests and also to other still more sensitive tests for aldehydes and peroxides (2). No practical difference was found between the ammoniated ether and the normal ether when packaged in copper-lined containers, but in the tin-lined containers the ammoniated ether showed less development of aldehydes.

At the same time that we studied ethers made alkaline with ammonia, we also studied the effect of other alkalinizing agents, such as monoethanolamine, triethanolamine, alcoholic potassium hydroxide and alcoholic sodium hydroxide. These likewise were packaged in both types of containers and stored for thirty-three months at both room temperature and elevated temperatures. Of this group, monoethanolamine was found to be superior to the other members in the preservation of ether, but was not as good as ammonia.

SUMMARY

From the work carried out, it has been found that faintly alkaline ethers when stored in copper-free containers are superior in stability to regular U. S. P. XI ether and to those which have been faintly acidified.

The ethers faintly alkalized with ammonia are superior in keeping qualities to ether made faintly alkaline with other agents. Faintly ammoniated ethers are slightly more stable in copper-lined containers under adverse storage condition than in the other types of containers studied. The protective effect of tinned iron containers is more readily demonstrated than that of copper-lined containers, because of the difficulty of causing any appreciable aldehyde development, even under severely adverse storage conditions, when ether is stored in copper.

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Color Reactions of Some Aliphatic Acids

By George Roeder*

In the course of some other research work, I made the unexpected observation that alkali citrates, heated in acetic anhydride, give deep red colored solutions. In using acetic acid instead of the anhydride the solutions remained colorless.

The first phase of this reaction probably is the formation of alkali acetate and a mixed anhydride of acetylated citric and acetic acid. Since citric acid dissolved in hot acetic anhydride gives a colorless solution, it is clear that the alkali acetate formed in the first phase of the above reaction brings about the condensation of the mentioned mixed anhydride into the colored compound. Therefore, a solution of citric acid in hot acetic anhydride, with the addition of alkali acetate, should give the coloration. This

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is actually what happens. Furthermore, the same color reaction is observed when alkali salts of any organic acid are added instead of alkali acetate, because in every case alkali acetate is formed from the acetic anhydride and the salt of the organic acid. Citric acid dissolved in hot acetic anhydride gives a deep red solution on adding a few grains of alkali acetate, alkali formate, alkali benzoate, alkali succinate, etc., also when boiled with powdered flint glass.

In principle, the above reaction has been known for several years, since Fuerth and Herrmann (1) and later Casares-Lopez (2) described color reactions of citric, tartaric, aconitic, tricarballic and agaricic acids with a mixture of 35 parts of pyridine and 15 parts of acetic anhydride. Under these conditions tartaric acid gave an emerald-green, citric acid a carmine, aconitic acid a purplish red and agaricic acid a purplish brown coloration.

Color reactions of aconitic acid and of malonic acid with acetic anhydride alone, without addition of basic compounds, have been described before by Taylor (3) and by Kleemann (4).

According to Fuerth and Herrmann, when pyridine is replaced by quinoline or other organic bases, only yellow or brown colors are obtained. This is an error probably caused by the large excess of bases employed by the authors. In fact, the color reactions of all the acids mentioned take place with practically every tertiary base, with trialkylamines and diethylaminoethanol, with quinoline, nicotine, cinchona alkaloids, strychnine, dimethylaniline, etc., when some drops or grains of these compounds are added to the solutions of the acids in acetic anhydride.

Now, the fact that the color reactions occur with alkali acetates and with trialkylamines excludes the assumption of the previous authors that the colors are produced by condensation of the acids with pyridine. Apparently, the basic compounds serve only as a means of condensation and perhaps to form salts or some other kind of addition products.

Among the various transformation products of citric acid, acetonedicarbonic acid

has not been tested by the previous authors. Filling this gap, I have found that this acid, under the described conditions, also gives a splendid color.

In addition, I have succeeded in extending these reactions to a new class of compounds, *e. g.*, to lactones of sugar acids. Ascorbic acid and *d*-iso-ascorbic acid, glucono-*d*-lactone and glucoheptonic lactone have also been found to give coloration.

The chemical constitution of the colors is unknown. They are said to be of very high molecular weight (3000) (1). Their formation from common natural products by a simple condensation process seems to be of biological interest.

EXPERIMENTAL

The shade of the colors depends upon temperature, heating time, quantity of added base and upon the presence of other solvents mixed with the acetic anhydride. Therefore it is understandable that previous statements are partly incomplete and sometimes contradictory. For this reason, in addition to the description of the new color reactions, I give in the following a more complete report of the reactions previously known.

The tests were made each with 50 mg. of acid in 10 cc. of acetic anhydride (95%) adding a few grains of solids or about three drops of liquid bases.

Malonic Acid.—The solution in acetic anhydride when carefully heated first becomes yellow, then orange colored with green fluorescence, as described by Kleemann (4). On adding sodium acetate, pyridine, triethylamine or dimethylaniline and with further heating the color changes into a beautiful ruby-red with increased fluorescence.

Under the above conditions ethylmalonic acid does not give any color reaction.

Aconitic Acid.—The hot solution in acetic anhydride shows first an amethyst and later a green coloration (Taylor) (3). The addition of potassium acetate, pyridine, dimethylaniline, strychnine or triethylamine transforms the color into a deep purple.

Citric Acid.—A deep red color results when a few grains or drops of the following compounds are added to the hot solution of the acid in acetic anhydride: alkali acetates or alkali salts of other carboxylic acids, trialkylamines, pyridine, quinoline, strychnine, nicotine, cinchonine, diethylaminoethanol, triethanolamine, etc. When the acid is dissolved in a mixture of equal parts of acetic acid and acetic anhydride, a beautiful transparent red solution with a bluish shine is obtained after the bases have been added.

Acetyl citric anhydride reacts in the same manner. Alkali citrates give the coloration when heated with acetic anhydride alone.

Agaricin (Cetyl Citric Acid).—Commercial samples of different origin were of different purity. Some left an insoluble residue when dissolved in ethyl acetate, some gave colorations without addition of bases. The best available compound of foreign origin (Eimer & Amend) gave the following colors in boiling acetic anhydride: with alkali acetates and with triethylamine ponceau red, green fluorescence; with pyridine, light amethyst color; with nicotine or strychnine, deep purple; with dimethylaniline, yellow or yellowish green. The intensity of the colors produced by the alkali acetates increased progressively from lithium to caesium.

Tartaric Acid.—Alkali acetates, triethylamine, quinoline, nicotine, strychnine, dimethylaniline, pyridine boiled with the solution of the acid in acetic anhydride give successively a yellow, orange and finally a brown-red color. Increasing the quantity of pyridine changes the color into a deep green.¹

Incidentally, this green color has been previously observed as an inconvenient side result in the preparation of hydroxy-maleinanhydride from diacetyl tartaric anhydride with pyridine (5).

Acetonedicarbonic Acid.—The freshly prepared acid in acetic anhydride gives successively yellow, orange, red and finally brown solutions when alkali acetates or organic bases are added.

Ascorbic Acid.—When the solution in hot acetic anhydride is boiled with a few grains of sodium acetate or potassium acetate, with triethylamine or nicotine, a deep red color with a bluish shine and slightly fluorescent results. When boiled with some drops of pyridine, the solution remains colorless. Dissolving the vitamin in one or two cc. of pyridine, adding acetic anhydride and boiling gives an orange color which deepens with prolonged heating into reddish brown.

d-Iso-ascorbic Acid acts like vitamin C.

Glucono-d-lactone.—The addition of some grains of potassium acetate or caesium carbonate, nicotine or triethylamine to the boiling solution in acetic anhydride produces a bright brown color. When the quantity of the base is increased and heating continued, a deep brown color is obtained. The reaction is much less intense with sodium acetate and nearly zero with the lithium salt.

Glucoheptonic Lactone.—Because of its insolubility in acetic anhydride the lactone is first covered with some pyridine and after warming slightly acetic anhydride is added. This solution remains colorless upon boiling. When caesium carbonate is added and boiling continued, a wine-red color first appears which gradually darkens into reddish brown and dark brown.

¹ The described color reactions of citric and tartaric acid are very suitable for the detection of these acids in aspirin preparations to which they are sometimes added (especially in hot countries) to disguise the ferric chloride reaction of a more or less decomposed aspirin.

Hydroxy-dimethylbutyrolactone.—This constituent of pantothenic acid did not give any visible reaction when boiled with acetic anhydride and basic compounds.

SUMMARY

1. The color reactions of some aliphatic polycarboxylic acids with acetic anhydride and basic compounds, described in the literature, are produced by a modified method.

2. The new method permits the correction of several errors made by earlier authors and complements the picture of these color reactions.

3. New color reactions are described for acetonedicarbonic acid and for a new type of compounds, of lactones of sugar acids, *e. g.*, gluconolactone, vitamin C, iso-ascorbic acid and glucoheptonic lactone.

My thanks are due Dr. E. Fernholz, former Director of the Chemical Laboratory of the Squibb Institute for Medical Research for a sample of hydroxy-dimethylbutyrolactone and to Chas. Pfizer & Co. who generously provided me with vitamin C, iso-ascorbic acid, gluconolactone, aconitic and tricarballic acid.

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“The doorstep to the temple of wisdom is a knowledge of our ignorance”—Spurgeon

Jacob Hendrick van't Hoff (1852–1911), the founder of stereo-chemistry, was awarded the first Nobel Prize for Chemistry in 1901 for his discovery of the laws of chemical dynamics and osmotic pressure in solutions.