the basis of peroxide decomposition is supported by the results of peroxide tests performed at the end of runs in the light. Thus, after 141 hours methyldioxolane had acquired a greater rate and gave a stronger peroxide test than did dioxolane, even though the latter had absorbed a total of approximately 25% more oxygen. In conclusion, it must be emphasized that these considerations are tentative and that further work is required before a clear understanding of the ether peroxidation reaction can be acquired. However, it is believed that our results prove the importance of oxygen absorption measurements in a study of the peroxides of compounds containing ether linkages.

Summary

The use of the Barcroft–Warburg apparatus for the measurement of oxygen absorption by dioxolane and methyldioxolane has been described. The rates of oxygen absorption by the dioxolanes in the dark and in the light have been reported. The accelerative action of the peroxides and the inhibitory action of ethanol and water have been discussed. The inhibitory action of hydroquinone has been reported. Some factors that may account for the complexities of the dioxolane and methyldioxolane–oxygen reactions have been suggested.

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Hydrogen Fluoride as a Condensing Agent. XVI. Reactions of Carbon Monoxide

BY J. H. SIMONS AND A. C. WERNER[1]

Carbon monoxide is known to react with numerous organic substances in the presence of catalysts. It has, for instance, been known for a long time that carbon monoxide reacts with aromatic hydrocarbons in the presence of aluminum chloride to produce aromatic aldehydes.[2] More recently it has been shown to react with chlorobenzene using active carbon and cuprous chloride to form a small amount of benzoic acid.[3] Its reactions have also been studied with the higher alcohols, olefins, and methyl alcohol, using active carbon impregnated with phosphoric acid as a catalyst.[4,5]

In this situation it has seemed worth while to study the possible reaction of carbon monoxide in the presence of hydrogen fluoride with various organic compounds.

It was found that alcohols reacted to form aliphatic acids, and that alkyl halides reacted in the presence of water or methanol to form acids. Attempts to prepare an ester from diethyl ether, benzoic acid from phenol, and an aldehyde from toluene all resulted in the formation of tarry products. The last mentioned indicates that the Gattermann and Koch reaction occurred but that the aldehyde product polymerized under the influence of the catalyst. Benzaldehyde has been

(1) For the previous paper of this series see THIS JOURNAL, **63**, 1921 (1941).

(2) Gattermann and Koch, *Ber.*, **30**, 1622 (1897).

(3) Marecek, *Chem. Obzor.*, **7**, 171 (1932).

(4) Krase and Singh, *Ind. Eng. Chem.*, **27**, 909 (1935).

(5) Hardy, *J. Chem. Soc.*, 358 (1936).

found in this Laboratory to polymerize under the conditions used, and toluene to be unaffected.

First Procedure.—To a mixture of 1 to 2.5 moles of anhydrous hydrogen fluoride and 0.5 to 0.67 mole of an organic material in a cold copper bomb of 150-cc. capacity, 0.5 to 1 mole of 90% formic acid was added, the bomb then sealed and heated to 100–160° for one to two days. Carbon monoxide was generated in the mixture and at the end of the reaction period was vented through a small hole in the cap of the cold bomb. The product formed was poured over ice, made alkaline with sodium carbonate, filtered, extracted with ether to remove non-acidic material, and the aqueous layer acidified with hydrochloric acid. The resulting solution was then extracted with ether, the ethereal solution dried over calcium chloride, and the ether evaporated.

Isopropyl alcohol thus treated gave rise to a tar, but no acidic product. *n*-Propyl alcohol gave 16 g. (28%) of isobutyric acid identified by its b. p. 148–149° and its anilide, m. p. 105–106°. *n*-Amyl bromide gave some high-boiling material, some tar, and 14 g. (19%) of recovered amyl bromide, a very small amount of alkali-soluble material being obtained which with difficulty yielded an anilide in amount insufficient to purify. *s*-Amyl bromide gave 6 g. (11%) of acidic material, b. p. 185–187°, identified as a six-carbon acid by its neutralization equivalent 121 (calcd. 116).

In a variation of this procedure, nickel carbonyl (42 g.) was used in place of the formic acid. Six moles of hydrogen fluoride (120 g.), 40 g. of isopropyl chloride and 20 g. of water were used. No reaction resulted after one day of heating at 109°, but 8 g. (20%) of isobutyric acid was obtained after one and one-half days of heating at 150°.

Second Procedure.—Instead of using formic acid, carbon monoxide was added under pressure to the mixture of hydrogen fluoride and organic material in a copper pressure

vessel fitted with a reflux condenser and placed in a furnace in a shaking machine. Upon cooling the vessel, the excess pressure was exhausted by means of a valve and the reaction products examined in the same manner as in the First Procedure.

When one mole of isopropyl chloride was treated in this manner with 125 g. of hydrogen fluoride at 43 atm. (650 lb. per sq. in.) pressure and 160° for one day, only a very small amount of residue was obtained. Neither isobutyric acid nor the expected product, the fluoride of this acid, was obtained. In other similar experiments, a method of treating the products was used in which water was not added but still the acid fluoride was not found. In an experiment in which one-half mole of the same chloride was added to 20 g. of water and 90 g. of hydrogen fluoride and treated at 150° and the same pressure for two days, 24.6 g. (56%) of isobutyric acid was obtained. This was identified by its b. p. 150–153°, its neutralization equivalent 90, and its p-toluidide, m. p. 104–106°. In another experiment one mole of isopropyl chloride was mixed with 40 g. of methanol and 70 g. of hydrogen fluoride and treated at 150° with carbon monoxide at 53 atm. (800 lb. per sq. in.). After one day, 5.5 g. (7%) of isobutyric acid was found.

Discussion

As the preliminary experiments were done with the formic acid technique in which water is always present, it was thought that the use of carbon monoxide under pressure would result in higher yields of acids. It was surprising to find that under the anhydrous conditions isopropyl chloride did not yield appreciable quantities of isobutyric acid. This cannot be explained as caused by the formation of isopropyl alcohol as an intermediate from a reaction of the halide and the water for two reasons. First: experiments using isopropyl alcohol resulted in only tarry products; and second, the addition of methyl alcohol had a similar effect to the addition of water; and methyl alcohol is not dehydrated under the conditions of the experiments as has been found in this laboratory. An explanation could be offered on the assumption that an intermediate of the fluoride of isobutyric acid is formed in the absence of water or methanol and that the active halogen atom reacts with active hydrogen atoms on adjacent molecules to form chain polymers and tars. In the presence of water, the acid is formed from the acid halide. To test this an experiment was tried using t-butyl chloride. The acid halide that would be formed would have no α hydrogen atoms; and, if the above assumption were correct, the acid halide or the acid resulting from its hydrolysis (if water is added) should be formed as a product. This experiment produced only a trace of aliphatic acid. The mechanism of these reactions should probably follow the hypotheses outlined by Sprauer and Simons.[6]

Summary

Carbon monoxide has been found to react with certain alcohols and alkyl halides in the presence of hydrogen fluoride. Isobutyric acid has been obtained from isopropyl chloride and from normal propyl alcohol. Isopropyl chloride in the absence of water or methanol and isopropyl alcohol under similar conditions did not yield the acid.

(6) Sprauer and Simons, This Journal, 64, 648 (1942).

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Syntheses in the Quinoline Series. IV. 2,4-Disubstituted Quinoline Derivatives

By Fred J. Buchmann[1] and Cliff S. Hamilton

The use of dialkylaminoalkylaminoquinoline derivatives, especially plasmoquin and atebrin, in the treatment of malaria has become well established. Quinoline derivatives with the aliphatic amino side chains in either the two or the four position have been reported[2] but possessed little or no antimalarial activity. The introduction of an hydroxyl group in the 2-position of certain derivatives of pyridine and quinoline has been shown to greatly alter the chemotherapeutic properties of these compounds.[3] Thus, it seemed advisable to attempt the preparation of 2- and 4-dialkylaminoalkylaminoquinoline derivatives with hydroxyl or alkoxyl groups in the 4- or 2-positions as the case might be.

Friedlaender and Weinberg[4] have reported that 2,4-dichloroquinoline reacts with alcoholic potassium hydroxide to produce a chloroethoxyquinoline melting at 43° and they have shown it

(1) Parke, Davis and Company Fellow.

(2) Magidson and Rubtsov, J. Gen. Chem. (U. S. S. R.), 7, 1896 (1937); Chem. Abs., 32, 564 (1938).

(3) Binz and Rath, Biochem. Z., 203, 218 (1928).

(4) Friedlaender and Weinberg, Ber., 15, 2679 (1882).