

Fig. 13.—Totaquine U.S.P. XII: 1, pH 6.0; 2, pH 5.0; 3, pH 4.0.

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TABLE II

MELTING POINTS AND CRYSTAL HABIT		
Compound	M. p., °C. ^a	Crystal habit
Quinine	174.5	Soft rosetts
Quinidine	173	Monoclinic crystals, 2 mm. on major axis
Cinchonidine	205.5	Hexagonal plates, 2–3 mm. along major axis
Cinchonine	263 ^b	Very fine rhombohedra or spherulites
Dihydroquinine	171.5
Dihydroquinidine	168.4
Dihydrocinchonine	273
Dihydrocinchonidine	235 ^c

^a All melting points corrected. ^b To avoid decomposition the bath was preheated to 255°. ^c 229°, uncor.; the literature gives 229° for m. p.

Chemical Works for the sample of totaquine. It is a pleasure to acknowledge the discussions with Dr. E. S. Cook of Institutum Divi Thomae and Dr. J. M. Vandenberg of Parke, Davis & Company.

Summary

The spectra of a number of cinchona alkaloids have been reported together with a method for spectrophotometrically estimating the amount of the methoxy-alkaloids in crude materials with special reference to quinine–quinidine in totaquine.

ADRIAN, MICHIGAN

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Allylic Chlorides. II. Catalytic Hydrolysis and Characterization of 1,3-Dichloropropene¹

BY LEWIS F. HATCH AND GEORGE B. ROBERTS

Although 1,3-dichloropropene has become readily available through the development of the high temperature substitutive chlorination of propylene,^{2,3} the two geometrical isomers (*cis* and *trans*) have not as yet been characterized as to their geometrical configuration. The present investigation was undertaken to effect this characterization.

A reaction mechanism has recently been proposed for the cuprous chloride catalyzed hydrochloric acid hydrolysis of allyl chloride which postulates that the ionization step of the hydrolysis is accelerated by the cuprous chloride–chloride ion complex forming an intermediate association complex or transition state with the double bond.⁴ If this hypothesis were valid, the actual

rate determining step would be the involvement of the cuprous chloride complex with the double bond, and any difference in the relative reaction rates of the two isomers of 1,3-dichloropropene in a similar hydrolysis would be related to geometrical configuration. The relationship between relative reactivity and geometrical configuration in reactions involving the double bond is well established. For example, Wright⁵ has reported that *cis*-methyl cinnamate mercurated about three times as fast as the *trans* isomer and *cis*-stilbene mercurated readily while the *trans* form did not mercurate. Thomas and Wetmore⁶ mercurated the isomeric 2-butenes and on the basis of reaction rates assigned the *trans* configuration to the isomer which reacted more slowly.

The results of a number of hydrolyses of 1,3-dichloropropene using a hydrochloric acid solution of cuprous chloride are given in Fig. 1.

(1) Presented in part at the Texas Regional Meeting of the American Chemical Society, Austin, Texas, December 8, 1945.

(2) Williams, *Trans. Am. Inst. Engrs.*, **37**, 157 (1941); *Chem. Met. Engr.*, **47**, 834 (1940).

(3) Groll and Hearne, *Ind. Eng. Chem.*, **31**, 1530 (1939).

(4) Hatch and Estes, *THIS JOURNAL*, **67**, 1730 (1945).

(5) Wright, *ibid.*, **57**, 1993 (1935).

(6) Thomas and Wetmore, *ibid.*, **63**, 136 (1941).

From these data it is concluded that the effect of the cuprous chloride-chloride ion complex is through the double bond, that the action of the complex is the rate controlling step, that the configuration of the isomer directly affects this rate of reaction. Therefore, the *trans* structure has been assigned to the low boiling (alpha) isomer of 1,3-dichloropropene and the *cis* structure assigned to the high boiling (beta) isomer. This assignment of configuration is substantiated by the work of Hatch and Moore⁷ who have reported that the low boiling (alpha) chloroalcohol, derived from the corresponding 1,3-dichloropropene, dehydrochlorinates readily to give propargyl alcohol while the higher boiling (beta) isomer does not. Michael⁸ has noted that chlorofumaric acid (*trans*) dehydrochlorinates forty-eight times as readily as chloromaleic acid (*cis*).

Because the course of the reaction was followed by the formation of chloride ion, it was necessary to determine if the vinyl chlorine as well as the allylic chlorine of 1,3-dichloropropene was hydrolyzed under the conditions of the reaction. Table I gives the results of treating the two isomeric basic hydrolysis products (3-chloro-2-propen-1-ol) of the dichlorides with an acid solution of cuprous chloride. Apparently a small amount of the vinyl chlorine can be removed but as the quantity is essentially the same for each isomer this does not affect the conclusions drawn from the hydrolysis of the dichlorides.

TABLE I
HYDROLYSIS OF 1,3-DICHLOROPROPENE

Compound hydrolyzed	Hydrolyzing agent	Reaction time, min.	Hydrolyzed, %
α 1,3-Dichloropropene	0.2% CuCl, 1.5% HCl	30	30
β 1,3-Dichloropropene	0.2% CuCl, 1.5% HCl	30	73
α 1,3-Dichloropropene	1.0% aq. NaOH	30	39
β 1,3-Dichloropropene	1.0% aq. NaOH	30	32
α 1,3-Dichloropropene	1.5% HCl	30	3
β 1,3-Dichloropropene	1.5% HCl	30	4
α 3-Chloro-2-propen-1-ol	0.2% CuCl, 1.5% HCl	60	5
β 3-Chloro-2-propen-1-ol	0.2% CuCl, 1.5% HCl	60	3

Table I also contains some comparative data on the relative catalytic activity of cuprous chloride compared to acid and basic hydrolysis.

Experimental

1,3-Dichloropropene.—Crude material from the high temperature dichlorination of propylene^{2,3} served as the source of 1,3-dichloropropene. This material contained approximately 60% 1,3-dichloropropene and 30% dichloropropane and the unsaturated dichlorides were ob-

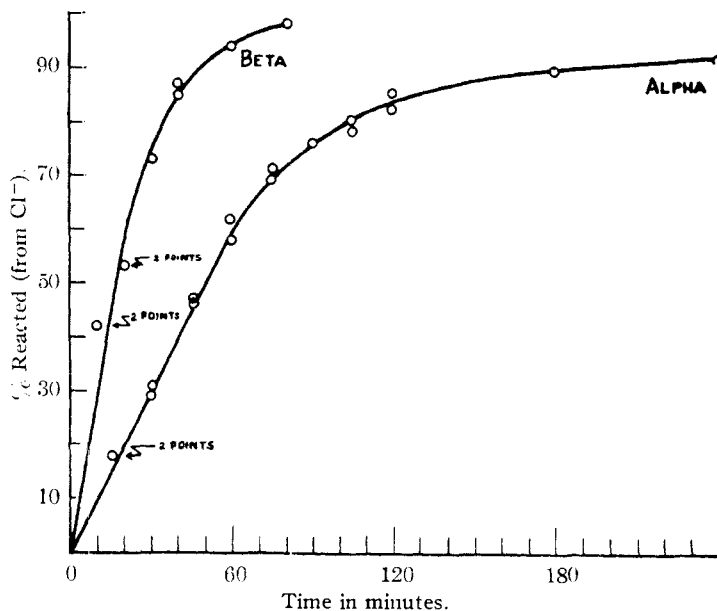


Fig. 1.—Catalytic hydrolysis of 1,3-dichloropropene.

tained by distillation through a 5-ft. glass helix-packed column. Fractions with a boiling range of 102.5–105.5° and 109.5–112.5° were taken and then refractionated at 150 mm. pressure to obtain constant boiling fractions at 57.5° (low boiling or alpha isomer) and 64.8° (high boiling or beta isomer). The densities and indices of refraction corresponded to those previously given in the literature.⁷

3-Chloro-2-propen-1-ol.—The two isomers of 3-chloro-2-propen-1-ol were prepared by sodium carbonate hydrolysis of the corresponding 1,3-dichloropropenes.⁷ Fractions boiling at 101° (alpha) and 108° (beta) under 150 mm. pressure were taken and had physical constants corresponding to those given in the literature.

Cuprous Chloride.—Merck "Reagent Grade" cuprous chloride was purified by the usual method.⁹ Electrodeposition analysis indicated a cuprous chloride content of 99.8% assuming the impurity to be cupric chloride.

Catalytic Hydrolysis of 1,3-Dichloropropene.—The apparatus for the hydrolysis of 1,3-dichloropropene consisted of a 250-ml. three-necked flask fitted with an efficient high-speed mercury sealed stirrer, thermometer, and reflux condenser. The catalyst solution was prepared by adding a solution of 0.5 g. of cuprous chloride in 8.25 ml. of concd. hydrochloric acid to a volumetric flask and diluting the mixture to 250 ml. Using a pipet, 100 ml. of the catalyst solution was transferred to a 500-ml. volumetric flask for dilution and analysis for chloride ion. One hundred ml. was also transferred to the reaction flask. The flask was swept with carbon dioxide before and during the addition of the catalyst solution as well as during the reaction to minimize air oxidation of the cuprous ion. Five ml. of the desired isomer of 1,3-dichloropropene was then introduced by pipet directly into the catalyst solution through a side neck of the flask and the neck then closed with a stopper containing the thermometer. Rapid stirring was begun and the mixture heated to 80° within one minute and that temperature was held within 2° for the reaction time. At the end of the desired time a water solution of sodium hydroxide containing sufficient base to make the reaction mixture slightly alkaline was added and the catalyst precipitated. The mixture was immediately cooled to room temperature with an ice-bath and then transferred quantitatively to a 500-ml. volumetric flask, diluted and analyzed for chloride ion. The increase

(7) Hatch and Moore, THIS JOURNAL, **66**, 285 (1944).

(8) Michael, *J. prakt. Chem.*, **52**, 308 (1895).

(9) Henderson and Fernelius, "Inorganic Preparations," McGraw-Hill and Company, New York, N. Y., 1935, p. 24.

in chloride ion was taken as an indication of the extent of reaction. The results were reproducible to within 2%. The data thus obtained are plotted in Fig. 1.

One mole each of the two isomers was hydrolyzed for two hours under conditions similar to those for the smaller runs. The low boiling dichloride gave the low boiling chloroalcohol (α -3-chloro-2-propen-1-ol) and the high boiling dichloride gave the high boiling (beta) chloroalcohol.

Catalytic Hydrolysis of 3-Chloro-2-propen-1-ol.—The low and high boiling isomers of 3-chloro-2-propen-1-ol were subjected to a sixty-minute regular catalytic hydrolysis to ascertain the extent of hydrolysis of the vinyl chlorine. The results are in Table I.

Acid and Basic Hydrolysis of 1,3-Dichloropropene.—The two dichlorides were also hydrolyzed using a 1% sodium hydroxide solution and a 1.5% hydrochloric acid solution to give a comparison of the extent of reaction in thirty minutes with cuprous chloride catalyzed acid hydrolysis. All conditions were similar to those for the catalytic hydrolysis except for the hydrolyzing medium. The results are in Table I.

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Summary

1. 1,3-Dichloropropene has been hydrolyzed by the use of a hydrochloric acid solution of cuprous chloride; the low boiling (alpha) isomer hydrolyzed more slowly than the high boiling (beta) isomer.

2. From this fact it was concluded that the effect of the cuprous chloride-chloride ion complex is through the double bond, that the action of the complex is the rate controlling step, and that the configuration of the isomer directly affects this rate of reaction.

3. The *trans* structure has been assigned to the low boiling (alpha) isomer of 1,3-dichloropropene and the *cis* structure assigned to the high boiling (beta) isomer.

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The Reaction of 2-Methylfuran with Formaldehyde and Substituted Ammonium Chlorides¹

BY R. F. HOLDREN AND R. M. HIXON

Recent work in this Laboratory had made 2-methylfuran readily available.² It was observed that this compound undergoes the Mannich reaction when treated with formaldehyde and substituted ammonium chlorides. Preparation of several substituted furfuryl amines by this reaction is reported herein.

Materials.—The ethyl and dimethylamine hydrochlorides were of Eastman Kodak Co. White Label grade and were used without further purification. Isopropylamine was prepared by catalytic hydrogenation of 2-nitropropane, Eastman practical grade. The octyl-, dodecyl- and octadecylamines were supplied through the courtesy of the Chemical Division of Armour and Company. The morpholine and piperidine were of Eastman practical, the other amines were of Eastman white label grade. All the amines were converted into hydrochlorides by adding the calculated amount of hydrochloric acid, evaporating to dryness and recrystallizing from ether-ethanol.

Procedure.—The details of the reaction of 2-methylfuran with formaldehyde and ethylamine hydrochloride will illustrate the general procedure followed.

(A) To a solution of 163 g. (2 moles) of ethylamine hydrochloride in 162 g. of 37% formaldehyde (2 moles) at 30° in a flask equipped with a dropping funnel, stirrer and reflux condenser, 82 g. (1 mole) of 2-methylfuran was added dropwise during one hour. Stirring was continued until heat evolution ceased. The mixture was cooled to room temperature and neutralized with 81 g. of sodium hydroxide dissolved in 160 cc. of water. The top, organic layer was separated and the water solution extracted once

with 100 cc. of ether. The combined ether and amine layer was washed with two 50-cc. portions of water and dried over sodium sulfate.

The ether was removed and the residue distilled under reduced pressure, giving a colorless oil, b. p. 71° (17 mm.), yield, 36.9 g. or 25.9%.

(B) An alternate procedure, which was used only in the case of the ethyl derivative, was to keep the reaction mixture cooled to 30–35° while adding the 2-methylfuran. The yield of secondary amine was increased to 44.6% by this method.

The hydrochlorides of the amines were prepared by adding the calculated quantity of cold, concentrated hydrochloric acid to a solution of 3–5 cc. of the amine in 20 cc. of anhydrous ether cooled to 0°. Crystallization could be induced, if the hydrochloride separated as an oil, by evaporating a solution of it in 100 cc. of acetone to 25 cc. and pouring this slowly into 100 cc. of boiling ether. In some cases recrystallization from acetone-alcohol mixtures is practical.

After the secondary amines had been removed from the reaction mixture, *n*-alkyldi-(5-methylfurfuryl)-amines were isolated by distillation. In the direct preparation of the compound derived from ethylamine a yield of 74% was realized if the temperature was controlled at 30–40°. If the reaction was allowed to heat to reflux the yield was only 43%.

Results.—The data regarding the compounds thus prepared are collected in the tables. Little attempt was made to find optimum conditions for the reactions. In one or two cases it was observed that higher yields were obtained by cooling the reaction mixture instead of allowing reflux temperatures to be reached. The acid-labile furan nucleus was polymerized by the hydrochlorides at the higher temperatures with resulting decrease in yield.

(1) From a thesis submitted by R. F. Holdren to the Graduate Faculty of Iowa State College in partial fulfillment of the requirements for the degree of Doctor of Philosophy. Supported in part by a grant from Quaker Oats Company to the Industrial Science Research Institute of Iowa State College.

(2) Burnette, *Iowa State Coll. J. Sci.*, **19**, 9 (1944).