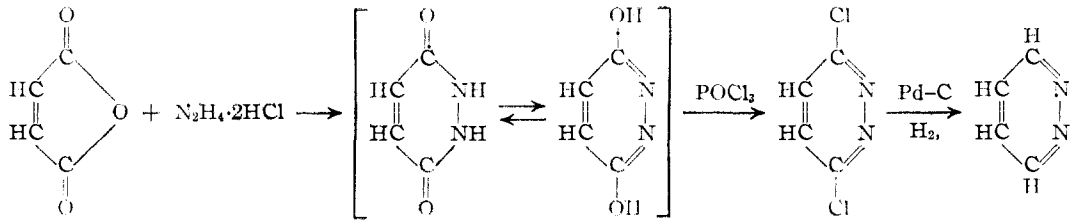

Fig. 1.

thesis is that of Tauber[1] involving oxidation of 3,4,5,6-dibenzopyridazine and decarboxylation of the resultant pyridazinetetracarboxylic acid. Gabriel and Colman[2] started with 2-(*p*-ethoxybenzoyl)-propionic acid and obtained the parent 1,2-diazine in low yield. In more recent times the lengthy procedure of Gabriel,[3] a six-step synthesis from α-ketoglutaric acid, was the preferred method.[4] Evans and Wiselogle[4] modified this procedure with a resultant increase in yield.

The object of the present work was to seek a less elaborate procedure which would give good yields of pyridazine. The process investigated, which employs the readily available maleic anhydride, is shown schematically in Fig. 1.

Maleic hydrazide, a tautomer of 3,6-pyridazine diol, has been prepared by interaction of hydrazine hydrate and maleic anhydride in alcoholic solution.[5] Considerable amounts of the monohydrazone of maleic anhydride are formed as a side product. A significant improvement in yield results by allowing maleic anhydride and a mineral acid salt of hydrazine to react in boiling aqueous solution. Substitution of maleic acid for the anhydride is almost as effective in the preparation of the cyclic hydrazide.

The chlorination of 3,6-pyridazine diol is accomplished by boiling with phosphorus oxychloride. 3,6-Dichloropyridazine is a stable crystalline solid which is purified readily by sublimation or distillation. Hydrogenolysis of this substance with palladium–charcoal catalyst in the presence of sodium hydroxide at atmospheric pressure results in low yields of pyridazine. Similar results are encountered in the absence of alkali with pyridazine monohydrochloride being isolated. The use of palladium–charcoal, hydrogen at three atmospheres pressure, and aqueous alcoholic ammonia was found to improve the yield to 60%.

Acknowledgment.—The authors wish to thank Ciba Pharmaceutical Products, Inc., Summit, N. J., for their kindness in providing laboratory facilities for this work, and Mr. Louis Dorfman for the microanalyses.

Experimental[6]

3,6-Pyridazinediol.—To a boiling solution of 75.6 g. (0.7 mole) of hydrazine dihydrochloride in 500 cc. of water there was added in one lot 68.6 g. (0.7 mole) of maleic anhydride, with stirring. The mixture was maintained at the boiling point for 3 hours. During this period the solution was reduced to a small volume, and water was added from time to time to prevent evaporation to dryness. After dilution to *ca.* 500 cc., crystallization was allowed to proceed in the cold. A white solid (66.8 g., 85.4%) melting at 299.5–300° was obtained and identified as 3,6-pyridazine diol. Recrystallization from hot water did not alter the melting point.

Anal. Calcd. for $C_4H_4N_2O_2$: C, 42.86; H, 3.60; N, 25.00. Found: C, 43.01; H, 3.50; N, 25.62.

3,6-Dichloropyridazine.—Twenty-five grams of 3,6-pyridazine diol was refluxed with 300 cc. of phosphorus oxychloride for 5 hours. Excess reagent was distilled *in vacuo* and the cooled residue poured onto ice. Ammonium hydroxide (28%) was added until the suspension was slightly alkaline to litmus. The light tan solid was filtered off and dried *in vacuo*. The combined filtrates were extracted once with chloroform and the extract was dried over anhydrous magnesium sulfate. The solid obtained after filtration of this solution and removal of the solvent was combined with that obtained first. After thorough drying this substance melted at 59–63° (29 g., 87%). Purification was effected by sublimation. The m.p. of this material was 68–69° (27 g., 81%).

Anal. Calcd. for $C_4H_2Cl_2N_2$: C, 32.24; H, 1.35; N, 18.81; Cl, 47.60. Found: C, 32.42; H, 1.59; N, 18.72; Cl, 47.35.

Hydrogenolysis of 3,6-Dichloropyridazine. (**A**).—A mixture of 12 g. of 3,6-dichloropyridazine, 6 g. of palladium–charcoal (10%) and 50 cc. of absolute alcohol was hydrogenated at atmospheric pressure over a 4-hour period. The suspension was filtered and the residue was washed with alcohol. The combined filtrate and washings were treated with *ca.* one volume of ether which was added slowly. The hygroscopic yellow solid was dried over phosphorus pentoxide and then purified by sublimation. A yield of 2.6 g. (27.8%) of pyridazine monohydrochloride was obtained, m.p. 161–163° (sealed tube).

Anal. Calcd. for $C_4H_5ClN_2$: N, 24.04; Cl, 30.42. Found: N, 23.85; Cl, 30.11.

(**B**).—A mixture of 29.6 g. of 3,6-dichloropyridazine, 40 cc. of ammonium hydroxide (28%), 2 g. of palladium–charcoal (5%) and 70 cc. of alcohol was hydrogenated at 3 atmospheres pressure. Uptake of hydrogen was rapid, and the reaction was complete in 45 minutes. Two such runs were combined and filtered. The filtrate was made strongly alkaline by the addition of sodium hydroxide pellets, with cooling after each addition. The solution was extracted continuously with ether. The extract was dried with anhydrous potassium carbonate. Solvent was removed *in vacuo* and the residue distilled *in vacuo*, b.p. 86–87° at 14 mm. (19.4 g., 60.7%).

Anal. Calcd. for $C_4H_4N_2$: C, 59.98; H, 5.03; N, 34.99. Found: C, 59.87; H, 5.13; N, 34.99.

DEPARTMENT OF CHEMISTRY
POLYTECHNIC INSTITUTE OF BROOKLYN
BROOKLYN, N. Y. RECEIVED NOVEMBER 6, 1950

(1) E. Tauber, *Ber.*, **28**, 45 (1895).
(2) S. Gabriel and J. Colman, *ibid.*, **32**, 395 (1899).
(3) S. Gabriel, *ibid.*, **42**, 654 (1909).
(4) R. C. Evans and F. Y. Wiselogle, THIS JOURNAL, **67**, 60 (1945).
(5) T. Curtius and H. A. Foersterling, *J. prakt. Chem.*, [2] **51**, 391 (1895).
(6) Melting points are uncorrected.

The Action of Formaldehyde on L-Ascorbic Acid-1-C^{14}

BY E. H. MOSBACH, J. J. BURNS AND C. G. KING

The reaction of ascorbic acid with formaldehyde results in a complex mixture of compounds which have not been identified.[1,2] Reithel and West

(1) Reithel and West, THIS JOURNAL, **70**, 898 (1948).
(2) Snow and Zilva, *Biochem. J.*, **37**, 630 (1943).

have shown that under suitable conditions, however, one mole of carbon dioxide is liberated per mole of ascorbic acid reacting with formaldehyde. Recently, Reithel and Wither[3] have presented data suggesting that ascorbic acid is oxidized by formaldehyde to dehydroascorbic acid, which slowly undergoes decarboxylation. Conclusive evidence concerning the origin of the carbon dioxide evolved during the reaction has not been presented. The availability[4] of L-ascorbic acid-1-C^{14}, however, has enabled us to show definitely that the carbon dioxide is derived entirely from the carboxyl carbon of L-ascorbic acid.

Experimental

Thirty milligrams of L-ascorbic acid-1-C^{14} (specific activity 130 counts per minute per milligram under our conditions of measurement[5]) was dissolved in 1 ml. of carbon dioxide-free distilled water in a test-tube (25 × 150 mm.) fitted with a dropping funnel and two side-arms so that any gases evolved could be swept with nitrogen into a saturated barium hydroxide solution. The test-tube was cooled to 0° in an ice-bath and 2 ml. of carbon dioxide-free distilled water was added, followed by 0.3 ml. of a 37% formaldehyde solution. The *p*H was adjusted to 7.5 by addition of 0.5 *N* carbon dioxide-free sodium hydroxide. The reaction was then carried out at 60° for a period of four hours. At the end of this time the reaction mixture was cooled to 0° in an ice-bath, acidified with 10 ml. of 1.8 *M* sulfuric acid, and the evolved carbon dioxide collected in the saturated barium hydroxide solution. The precipitated barium carbonate was prepared for counting as described previously.[5]

In preliminary experiments it had been shown that the yields of carbon dioxide corresponded closely to those obtained by Reithel and West.[1] When the experiment was carried out under the same conditions without adding formaldehyde, less than 0.3 mg. of barium carbonate was recovered.

The experimental data obtained with labeled ascorbic acid are summarized in Table I.

TABLE I

SPECIFIC ACTIVITIES OF ASCORBIC ACID AND BARIUM CARBONATE, IN THE ASCORBIC ACID–FORMALDEHYDE REACTION

Expt. number	Specific activity of carboxyl carbon of ascorbic acid (counts/min./mg. C)	Specific activity of barium carbonate (counts/min./mg. C)
1	1910	2070
2	1910	1950

Thus, within the over-all precision of measurement (±6%), the radioactivity of the carbon dioxide evolved was derived exclusively from the carboxyl carbon of L-ascorbic acid.

Acknowledgment.—The authors are indebted to the Nutrition Foundation, Inc., and to the National Institutes of Health, U. S. Public Health Service, for grants in support of the present investigation.

(3) Reithel and Wither, THIS JOURNAL, **71**, 1879 (1949).
(4) Burns and King, *Science*, **111**, 257 (1950).
(5) Burns, Ph.D. Dissertation, Columbia University, 1950.

DEPARTMENT OF CHEMISTRY
COLUMBIA UNIVERSITY
NEW YORK, NEW YORK RECEIVED OCTOBER 14, 1950

Some 7-Substituted Derivatives of 8-Quinolinol

BY J. P. PHILLIPS AND STANLEY PRICE

A substituent in the 2-position of 8-quinolinol has been shown to create enough steric hindrance to prevent the molecule from forming a chelate with aluminum.[1,2] Since it seemed possible that large substituents in the 7-position would also produce steric hindrance to chelate formation, the following investigation was carried out.

The compounds studied were 7-phenylazo-8-quinolinol-5-sulfonic acid (I), 7-*o*-tolylazo-8-quinolinol-5-sulfonic acid (II), 7-*m*-tolylazo-8-quinolinol-5-sulfonic acid (III), 7-*o*-tolylazo-8-hydroxyquinaldine-5-sulfonic acid (IV) and 7-*m*-tolylazo-8-hydroxyquinaldine-5-sulfonic acid (V). Since the complexes formed by these compounds with metal ions were water soluble, a spectrophotometric investigation of whether or not the compounds formed chelates with aluminum was employed. The compounds with a 2-substituent, IV and V, did not react; those having only the 7-substituent did react under the same conditions, as shown by a marked decrease in extinction from the value calculated for no reaction (Table I). Evidently the 7-substituents used in this study do not produce steric hindrance to chelate formation.

TABLE I

REACTION WITH ALUMINUM AT *p*H 3.5 (WAVE LENGTH 530 mμ)

Compound	Calcd. extinction for no reaction	Obs. extinction
I	0.73	0.302
II	1.12	0.895
III	0.80	0.470
IV	1.10	1.13
V	0.9	1.0

Similar qualitative tests were run with magnesium, copper and ferric iron in both 0.1 *N* hydrochloric acid and a buffer of *p*H 3.5. No positive

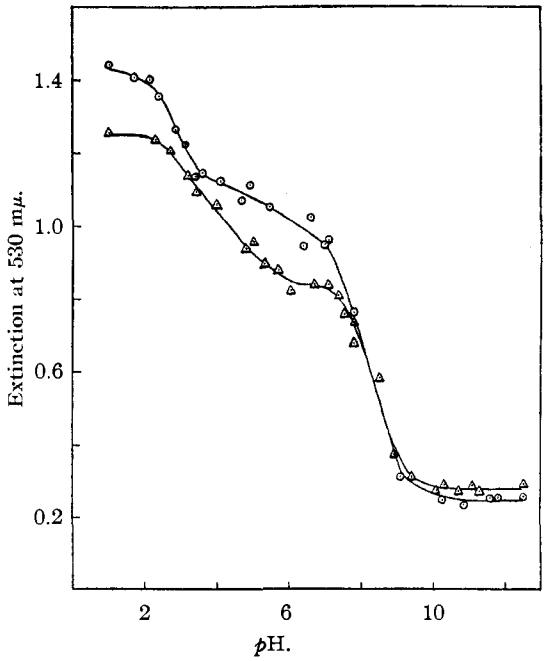

Fig. 1.—Structure changes with changing *p*H: ⊙, 7-*o*-tolylazo-8-quinolinol-5-sulfonic acid; △, 7-*o*-tolylazo-8-hydroxyquinaldine-5-sulfonic acid.

(1) J. P. Phillips and L. L. Merritt, THIS JOURNAL, **71**, 3984 (1949).
(2) H. Irving, E. J. Butler and M. F. Ring, *J. Chem. Soc.*, 1489 (1949).