

from 10–20 cc. of absolute ethanol gave 1.6 g. melting 91–92°; 70% of the theoretical yield. No depression was observed in a mixed m. p. with the product obtained before.

Despite the presence of a tertiary chlorine atom in the 1,1-di-(*p*-chlorophenyl)-1,2,2,2-tetrachloroethane, it does not react with 5% alcoholic silver nitrate at room temperature and only slightly with water on refluxing for fifteen minutes. With 5% sodium hydroxide at reflux for fifteen minutes appreciable hydrolysis occurs. It is readily dechlorinated by heating a mixture of 1.0 g. (0.0026 mole), 15 cc. of absolute ethanol, and 1.0 g. of zinc powder at reflux for eight hours. The hot solution was filtered, the zinc washed with hot alcohol, the filtrate poured into 75 cc. of water, and the resulting solid removed by filtration and crystallized from 8–10 cc. of absolute ethanol. The yield of 1,1-di-(*p*-chlorophenyl)-2,2-dichloroethylene was 0.6 g., 66% of the theoretical, melting 86–87° and showing no depression in a mixed m. p. with the same product prepared before.

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Di-(*p*-chlorophenyl)-acetic Acid

This compound was prepared by saponification of 1,1-di-(*p*-chlorophenyl)-2,2-dichloroethylene in an analogous manner to the preparation of diphenylacetic acid.^{1,2} A mixture of 1.0 g. of 1,1-di-(*p*-chlorophenyl)-2,2-dichloroethylene,³ 3 g. of potassium hydroxide, and 20 cc. of 95% alcohol was heated in a sealed Carius tube at 150–160° for twenty hours. The product was poured into 100 cc. of water, about 0.1 g. of Norit was added, and the mixture boiled for a few minutes. After filtering the acid was precipitated by acidifying the filtrate with 10% sulfuric acid and collected by suction filtration. The crude acid weighed 0.6 g., melting 161–164°; one crystallization from absolute ethanol gave 0.5 g. melting 163–164°; 57% of the theoretical yield.

Anal. Calcd. for C₁₄H₁₀Cl₂O₂: Cl, 25.22; neut. eq., 281.1. Found: Cl, 25.09; neut. eq., 281.4.

- (1) Fritzsche and Feldmann, *Ann.*, **306**, 79 (1899).
- (2) Sheibley and Prutton, *THIS JOURNAL*, **62**, 840 (1940).
- (3) Grummitt, Buck and Jenkins, *THIS JOURNAL*, **67**, 155 (1945).

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COMMUNICATIONS TO THE EDITOR

REMOVAL OF GAS NUCLEI FROM LIQUIDS AND SURFACES¹

Sir:

During a study of bubble formation in blood of animals subjected to simulated high altitudes in a low pressure chamber, it became necessary to develop methods that prevent the bubbling of liquids supersaturated with gas. If water at rest in a clean glass vessel is exhausted with an air pump, bubbles usually appear due to the growth of gas nuclei, *i. e.*, small gas masses adhering to walls of the container or particles in the water.

Experiments indicate that there is a population of gas nuclei in every liquid and container (unless special precautions have been taken to remove them) of such a character that a certain group will become unstable and grow into bubbles for each successive increase in ΔP , where ΔP = dissolved gas tension minus total hydrostatic pressure. The conditions for stability and growth of gas nuclei have been described in a previous paper.²

The conventional method of removing gas nuclei is prolonged boiling or evacuation, procedures which have the disadvantage of removing dissolved gas in addition to the gas nuclei. Two new methods, which do not change the gas concentration, proved satisfactory.

(1) The work described in this note was done under a contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Princeton University.

(2) E. N. Harvey, D. K. Barnes, W. D. McElroy, A. H. Whiteley, D. C. Pease and K. W. Cooper, *J. Cell. and Comp. Physiol.*, **24**, 1 (1944).

One method, strong centrifuging of liquid and container, will remove all gas nuclei which grow to bubbles at the vapor pressure of water at 22°, *i. e.*, at a ΔP of 740 mm. Such nuclei are designated gas macronuclei. However, when the tube of centrifuged water, resting at the vapor pressure without forming bubbles, is given a light tap or blow, or is placed in a high frequency sound field, bubbles appear, due to the growth of gas *micronuclei* that have not been removed by the centrifuge treatment. The tap or blow and the supersonic waves increase ΔP above 740 mm. as a result of the negative pressure component of the pulse or sound waves.

The second method, subjecting water and glass container to high hydrostatic pressures (1000 atmospheres), removes gas micronuclei by forcing them into solution. Water so treated has remarkable properties. It can be heated above 200° without bursting into vapor. When intense high frequency sound waves are passed through, no cavitation occurs and no bubbles arise. Finally, if exhausted to the vapor pressure of water, moderate knocks have no effect and only a very severe blow will cause bubbles to form.

The severe blow is believed to develop a sufficiently negative pressure locally to tear cavities in water free of gas nuclei. A similar procedure, which presumably also develops large local negative pressures, is to scratch the glass wall in contact with the prepressurized water at its vapor pressure, when copious bubbles form. Electrolytic gas bubbles will also appear at electrodes

when a current is passed through previously pressurized acid water, and bubbles form in prepressurized water when it is quickly frozen. In both cases so much dissolved gas is concentrated locally at electrode or ice surfaces that spontaneous bubble formation occurs in the absence of gas nuclei.

High pressure treatment of a liquid and container should prove of great value in experimental studies of tensile strength and cavitation of water.

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A SYNTHESIS OF THE LACTONE OF 2-METHYL-3-HYDROXY-4-CARBOXY-5-HYDROXYMETHYL-PYRIDINE¹

Sir:

Scott and associates² have reported that the lactone of 2-methyl-3-hydroxy-4-hydroxymethyl-5-carboxypyridine (I)³ is active in promoting growth and preventing anemia in chicks. The present communication deals with the synthesis of the lactone of 2-methyl-3-hydroxy-4-carboxy-5-hydroxymethylpyridine (II) which is isomeric with (I). The results of repeated experiments⁴ have shown that (II) is as effective as (I), if not more so, in promoting growth and preventing anemia in chicks fed a purified diet containing adequate quantities of all the known vitamins and the "L. casei factor." The isolation of (II) from urine has been announced by Huff and Perlzweig.⁵

In conducting the synthesis of (II), we began with 6-methyl-4-carbomethoxy-3-cyano-2-pyridone (III), which was produced by the condensation of cyanacetamide with ethyl acetylpyruvate. The synthesis of (III) has been described by Bardhan.⁶ This substance was subjected to transformations:

(1) This work was supported in part by the establishment of a fellowship at Cornell University by the Western Condensing Company, San Francisco, California.

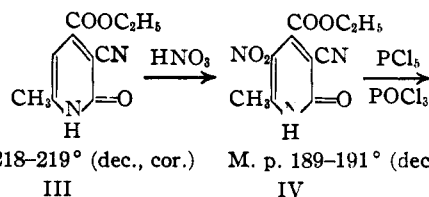
(2) Scott, Norris, Heuser, Bruce, Coover, Bellamy and Gunsalus, *J. Biol. Chem.*, **154**, 713 (1944).

(3) Harris, Stiller and Folkers, *THIS JOURNAL* **61**, 1242 (1939).

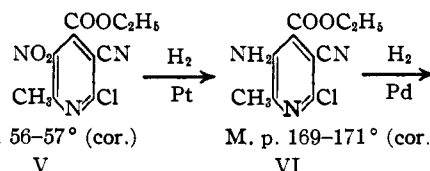
(4) Scott, Norris, Heuser and Bruce, unpublished results.

(5) Huff and Perlzweig, *Science*, **100**, 15 (1944).

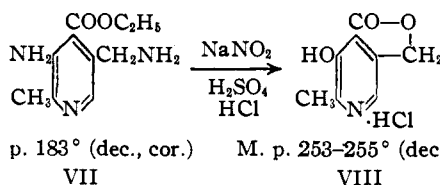
(6) Bardhan, *J. Chem. Soc.*, 2223 (1929).



M. p. 218-219° (dec., cor.) M. p. 189-191° (dec., cor.)



M. p. 56-57° (cor.) M. p. 169-171° (cor.)



M. p. 183° (dec., cor.) M. p. 253-255° (dec., cor.)

Compounds (IV), (V) and (VI) have been described by Itiba and Emoto.⁷ The melting points reported here for these compounds agree closely with those obtained by Itiba and Emoto.

It was shown by a determination of amino nitrogen that the reduction of (VI) resulted in the compound designated (VII). Calculated for (VII): amino N, 13.47. Found: amino N, 15.4.

Diazotization of (VII), followed by hydrolysis with hydrochloric acid gave a substance (VIII) which was isolated as the hydrochloride. Analysis for chlorine supports the structure assigned to (VIII). Calculated for (VIII): Cl, 17.65. Found: Cl, 17.75.

While the growth-promoting and antianemic properties of (II) were being studied, a supply synthesized by another procedure⁸ was received from Merck and Company. The results of an initial study showed that it possessed growth-promoting and antianemic activity.

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(7) Itiba and Emoto, *Sci. Papers. Inst. Phys. Chem. Research (Tokyo)* **38**, 347 (1941) (*C. A.*, **35**, 6960 (1941)).

(8) Personal communication to authors.