

when a current is passed through previously pressurized acid water, and bubbles form in pre-pressurized 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.

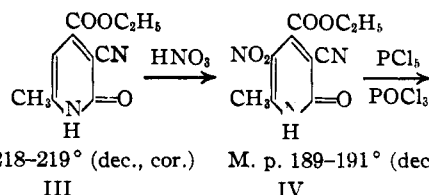
(2) Scott, Norris, Heuser, Bruce, Coover, Bellamy and Gunsalus, *J. Biol. Chem.*, **154**, 713 (1944).

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

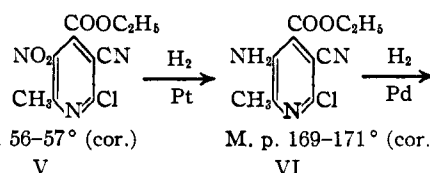
(4) Scott, Norris, Heuser and Bruce, unpublished results.

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

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

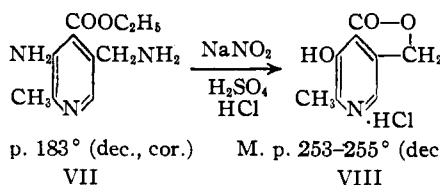


M. p. 218-219° (dec., cor.) M. p. 189-191° (dec., cor.)



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.