progeny, but in the other twenty vials twelve days after the parents had been transferred to them the new generation began to emerge and was removed daily. The parent flies were placed in fresh vials after eight days in order to keep them separate from the offspring. Parent females lived up to twenty-three days, males up to twenty-four days. The number of progeny from the twenty fertile females ranged from seven to 393, average 146.5 ± 14.7, with a ratio of 116 males to 100 females, the total count being 1,573 males to 1,356 females. Apparently virgin females produce no progeny, following the usual rule among the Muscidae.

It seems to us possible that *Leptocera* spp. as representatives of a fly family, the Borboridae, which are widespread if not cosmopolitan in nature upon the dung of mammalia,[3] with their small convenient size, short life cycle, easily satisfied food conditions, capability of continuing their life histories in the now familiar laboratory milk bottle, and apparent hardihood in withstanding repeated etherization, combine a group of characteristics which might well make them utilizable material for investigations in insect physiology, genetics, etc. It may be mentioned in addition that members of the Borboridae, both larvae and adults, are reported as hosts of herpetomonads.[4]

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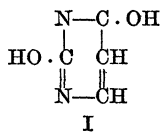
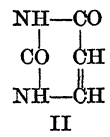
## SPECIAL ARTICLES

### THE SYNTHESIS OF PYRIMIDINE-NUCLEOSIDES

THE pyrimidine "uracil" can be expressed structurally either by a *lactim* or a *lactam* construction as represented by formulas I and II, respectively. The *lactam* form II



I

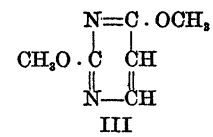


II

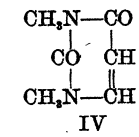
is the stable configuration. Corresponding to these two constructions we have also the alkyl derivatives of uracil, of which the methyl compounds expressed by formulas III and IV are the simplest dialkylated representatives. Both forms can be obtained without difficulty.

[3] Howard, "A Contribution to the Study of the Insect Fauna of Human Excrement," *Proc.* Wash. Acad. Sciences, 1900, 2: 541–604.

[4] Patton and Cragg, "A Text-book of Medical Entomology," 1913, p. 311.

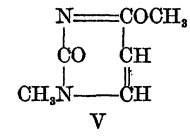


III

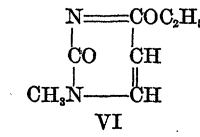


IV

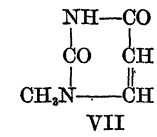
We now find—(1) that the *lactim-ethers* represented by formula III can easily be transformed by molecular rearrangement into their isomeric *lactam-isomers* IV, and (2) that this change is a progressive one and is subject to experimental control. Complete transformation of the dimethyl ether III to the pyrimidine IV is accomplished by heating the lactim-form slightly above its boiling point. A partial and selective rearrangement is brought about at ordinary temperature by treatment with methyl iodide, and under such conditions only one *lactim* grouping is destroyed leading to the formation of a 3-nitrogen derivative. The pyrimidine III interacts, for example, with methyl-iodide to form 2-oxy-3-methyl-6-methoxypyrimidine V. The same type of change can also be brought about by interaction of 2, 6-diethoxypyrimidine with methyl-iodide giving 2-oxy-3-methyl-6-ethoxy-pyrimidine VI. Hydrolysis of the compounds V and VI with acids leads to the formation of 3-methyluracil VII. The corresponding rearrangements in the purine series are now under investigation.



V

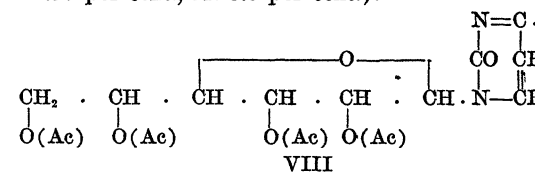


VI



VII

The ease of molecular rearrangement of *lactim* constructions in the pyrimidine series, the quantitative nature of these transformations, and finally the definiteness of change leading always to the formation of 3-nitrogen compounds, led us to a study of the behavior of the dimethoxypyrimidine III towards bromotetraacetyl-glucose. We now wish to report in this preliminary paper that this bromide interacts normally as an alkyl halide with the *lactim* compound III, at a temperature of 50°, giving an excellent yield of the pyrimidine-nucleoside derivative $C_{19}H_{24}O_{11}N_2$ represented structurally by the formula VHI (C, 50.50 per cent., H. 5.8 per cent.).



VIII

This compound is easily obtained in a pure condition crystallizing as colorless needles, and melting without decomposition at 221°. No reducing substance is formed by mild hydrolysis with hydrochloric acid. The compound is converted by intense hydrolysis into soluble products which easily reduce Fehling's solution. We are now engaged in the study of this interesting compound and are planning to utilize our new reaction for the synthesis of other sugar-pyrimidine and sugar-purine constructions (nucleosides), several of which are known to be formed by degradation of the nucleic acid molecule. A study of the pentose sugar-ribose will be incorporated into this research. We hope to be able to obtain data by synthetic methods, which will enable us to determine conclusively the nature of the sugar linkage in nucleosides, and also the position of attachment of the sugar in the pyrimidine and purine rings. The final results of our research will be published in the *Journal* of the American Chemical Society.[1]

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MAY 20, 1929

## CRYSTALLINE PEPSIN

A CRYSTALLINE material has been obtained which has the properties of the enzyme pepsin, in that it hydrolyzes gelatin, casein, egg albumin and edestin in acid solution and is rapidly inactivated by alkali or heat. The composition and activity remain constant through at least seven successive crystallizations and the crystals have constant solubility on repeated washings in dilute hydrochloric acid. There is evidence, therefore, that the material is a pure substance. It crystallizes in small hexagonal prisms from 0.01 to 0.10 mm long, sometimes separate and sometimes in clusters. It is insoluble in 0.001 M HCl (pH 3.0) and soluble in acid or alkali. It is precipitated by half saturation with ammonium sulfate, by copper salts, uranium acetate, lead acetate, trichloracetic acid and safranin and coagulates on boiling. It contains 14.5 per cent. nitrogen and has a diffusion coefficient in water at 8° C. of 0.085 cm² per day corresponding to a molecular weight of about ten thousand.

The activity is about 1: 20,000 U. S. P. and is therefore less than some amorphous preparations.

[1] The authors have been able to make this preliminary report at this early date as a result of the kindly cooperation of Dr. P. A. Levene, of the Rockefeller Institute for Medical Research in New York City, who arranged for the microchemical analysis of our compound, and also that of Dr. C. H. Hudson, of the Hygienic Laboratory in Washington, D. C., who kindly furnished pure bromotetraacetyl-glucose for our preliminary work. (T. B. Johnson.)

The crystals were prepared from commercial[1] 1: 10,000 pepsin by dialysis of a concentrated solution under pressure at pH 3.0 and 5° C. until a heavy precipitate forms. The suspension is then stirred at 37° C. for an hour, filtered, and the filtrate allowed to cool slowly. The crystals separate after about 24 hours and continue to form for several days. The yield amounts to one or two per cent. of the original material. Recrystallization is carried out by dissolving in dilute sodium bicarbonate at 37° C. and precipitating with dilute sulfuric acid.

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## CONCERNING RETINAL PRESSURE IMAGES AND THEIR BROWNIAN-LIKE MOVEMENT

IF the writer's own experience is any criterion, many persons in their youth discovered by chance that slight pressure continued for a short time on the eyeballs would elicit luminous manifestations in the subjective optical foreground which resolved themselves into flickering or vibrating mosaic-like designs of great intricacy and beauty. Kaleidoscopic in their variety, and in their symmetry, delicacy and intangibility more fascinating than snow crystals, they have perhaps served many of us as a pastime.

Upon closing the eyelids and pressing gently on the front of the eyes with the tips of the fingers, there begins, after a pause of a few seconds, a fantastic play of light and dark geometrical figures, the vividness of which is dependent among other factors upon the state of rest or fatigue of the visual elements. That is, in one experiment the bright divisions of the optical field may appear brighter and the dark divisions darker than in a second trial performed soon after when their dimness or the lack of contrast between them is such that the observer is unable to analyze or even to distinguish the pattern they compose. The sequence, however, in which the different kaleidoscopic designs follow one another relatively quickly is remarkably constant. But their individual units are never stationary; they oscillate or quiver with the rapidity and degree of excursion of Brownian motion.

I may be permitted to indicate a few of the conspicuous phases of the phenomenon. After the initial latent period, the dominating impression, as the light tracery crystallizes, so to speak, upon the shadowy foreground, is an involved checkerboard design consisting of thousands and thousands of facets. Indeed the regularity and symmetry with which these are arranged remains the basic plan despite the successive modifications in their form. From zone to zone the

[1] Parke Davis pepsin, U. S. P. 1: 10,000.