phosphate. Moreover, sodium aspartate is not interchangeable with sodium chloride in the activation of purified pancreatic amylase.

The work is being extended to a similar study of the effects of other amino acids.

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REDUCTION OF DIHYDROXY-THYMOQUINONE BY MEANS OF PALLADIUM-HYDROGEN.

BY NELLIE A. WAKEMAN.

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Thymoquinone and its oxidation and reduction products form an interesting series of compounds which have, from time to time, received considerable attention at the hands of organic chemists. The writer's interest in these compounds was aroused by the seemingly important role which they appear to play in the pigmentation of several species of *Monarda,* and it has been held no less by the behavior of the substances themselves than by their biochemical significance.

Two or three years ago, in reviewing the work of Pall[1] and Skita[2] upon the hydrogenation of organic compounds by means of palladium as a catalyst, it was learned that one of them[3] had in this manner reduced quinone to hydroquinone. The question of the action of thymoquinone toward this reagent therefore naturally presented itself, and accordingly the action was tried in alcoholic solution. Thymoquinone reduced very readily. Upon evaporation of the solvent, it yielded hydrothymoquinone which was identified by its melting point, its solubility, and its crystalline form.

The reduction of thymoquinone to hydrothymoquinone ordinarily presents little difficulty. A more interesting reaction promised to be the reduction of dihydroxy-thymoquinone to tetrahydroxy-cymene by the same reagent.

Zincke,[4] in 1881, reduced the mother liquors from which dimethylamino-thymoquinone had crystallized, by the use of sulfurous acid, thus obtaining a solution which, upon oxidation, yielded a mixture of mono- and dihydroxy-thymoquinone. Zincke believed that the reduced liquid

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[1] *Ber.*, **38,** 1401, 2414 (1905); **40,** 1392, 2201 (1907); **41,** 805, 818, 2272, 2287 (1908); **42,** 1572, 2239, 3930 (1909).

[2] *Ibid.*, **41,** 2938 (1908); **42,** 1627 (1909); **43,** 3393 (1910); **44,** 2862 (1911); **45,** 1948 (1912).

[3] *Ibid.*, **43,** 3393 (1910).

[4] *Ibid.*, **14,** 92 (1881).

contained a solution of both tri- and tetrahydroxy-cymene. All attempts of the writer to produce these polyatomic phenols by the reduction of the corresponding quinones had hitherto proved fruitless.

Following the reduction of thymoquinone, a small quantity of dihydroxy-thymoquinone was treated in the same way. The reduction took place very readily, marked by the change in color of the solution from red, or yellow, to water white. Before the solvent could be evaporated, however, the color returned and crystals of the original red compound separated out. Ether was next chosen as a solvent. The reduction took place even more readily than before. The same difficulty, to a less degree, was experienced in obtaining the products of reduction in a solid form, for though flaky, white crystals of the reduced compound were obtained upon evaporation of the solvent, red needle-like crystals of the original substance formed almost simultaneously, the mass took on a pinkish gray color, and finally changed to red dihydroxy-thymoquinone with its characteristic melting point of 226°. By evaporating the ether in an atmosphere of hydrogen an abundance of pure white, flaky crystals was obtained. Upon removal from the reducing atmosphere, however, these became mixed with the red needle-like crystals before even a melting point could be determined. This mixture, upon standing, passed through the process of changing, through pinkish gray, back to red.

The red dihydroxy-thymoquinone was next dissolved in acetic acid anhydride and subjected to the same reducing process, the object being to transform some, or all, of the hydroxy groups to acetyl groups, thus rendering them more stable. This reduction took place more slowly; nevertheless, it was completed in the course of a few hours. Upon the evaporation of the greater portion of the solvent, the reduced product crystallized out in white, prismatic crystals which melted at 180–182° and exhibited a saponification value[1] equal to that required for 4 acetyl groups. The tetraacetyl derivative thus obtained is stable in the air. The yield[2] is almost quantitative. Upon hydrolysis of the acetyl derivative, practically all of the dihydroxy-thymoquinone started with can be recovered.

In carrying out the above reduction another change, which will be further investigated, was noted. Part of the acetic acid anhydride appears to have been reduced and an ester of some sort to have been formed. At any rate, when a portion of the freshly reduced solution was

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[1] Subs., 0.504.
Used 24 cc. KOH solution, factor 0.3936 = 94.46 cc. 0.1 N KOH.
To neutralize required 55.3 cc. 0.1 N HCl.
To saponify required 39.16 cc. 0.1 N KOH.
Calc. for 4 acetyl groups 38.9 cc. 0.1 N KOH.

[2] From 0.5 g. of dihydroxy-thymoquinone a little more than 0.8 g. of the tetraacetyl derivative was obtained.

strongly diluted with cold water a pleasant fruity odor, resembling somewhat both ethyl and amyl acetates, but differing from either, was developed. Upon standing a short time in contact with water this pleasant odor disappeared. Moreover, it could not be obtained from the reduced solution which had stood for some time in the air.

All of the above reductions were carried out in a simple reduction flask, prepared by turning up the ends of an ordinary 250 cc. gas sampling tube with two glass stopcocks. The hydrogen was generated from zinc and hydrochloric acid and passed through first an alkaline and then an acid solution of potassium permanganate. After this it was passed through sulfuric acid and then into the reduction flask. During the first reductions a shaking machine was used for shaking the flask; but the process went on so readily that this was not necessary. At first, also, the palladium chloride used was placed in a little water with a very small quantity of mucilage of acacia added to hold the resulting palladium in suspension. This also, was found unnecessary, even undesirable. In all of the later work a concentrated, warm, solution of the substance to be reduced was placed in the reduction flask. It usually crystallized out upon cooling. About 0.1 g. of palladium chloride was suspended in a little of the same solvent and added to the solution in the flask. Hydrogen was now passed through the flask until most of the air had been replaced, when the exit tube was closed. After this the flask was shaken occasionally until the reduction was complete. In using ether as a solvent, it was found necessary to fill the flask with hydrogen and close both stopcocks, opening the inlet only to pass in more hydrogen, from time to time, as it had been absorbed, otherwise the pressure of the ether was often greater than that of the hydrogen and trouble resulted.

For the greater part of the above work the same charge of palladium chloride, 0.1 g. was used over and over again without any sign of exhaustion of its catalytic property. The reduced solution was poured out through a filter. The palladium remaining in the flask, and that on the filter, was washed with a small portion of the pure solvent, then, repeatedly, with alcohol and ether. The portion of palladium upon the filter was carefully returned to the flask and another reduction was carried out. In this way a large number of reductions were made without the addition of fresh palladium chloride, several different substances, each in two or three different solvents, being reduced. Whether or not the change of substances, and of solvents, had any influence upon the presistent power of the catalyst is not known. It certainly retained this power to a remarkable degree, the only evidence of the catalyst "wearing out" noticed being the small loss incurred by adhesion to the filter.

MADISON, WIS.