NOTES

Derivatives of Furfuryl and Tetrahydrofurfuryl Alcohols

By Richard D. Kleene and Sherman Fried

As an aid in the identification of furfuryl and tetrahydrofurfuryl alcohols, the following esters have been prepared following the method of Shriner and Fuson.[1] They were obtained as colorless crystals by recrystallization from ethanol. The original alcohols were furnished through the courtesy of the Quaker Oats Company, Chicago.

Furfuryl *p*-Nitrobenzoate.—Needles, m. p. 75–77°. *Anal.* Calcd. for $C_{12}H_9O_5N$: N, 5.67. Found: N, 6.16.

Tetrahydrofurfuryl *p*-Nitrobenzoate.—Glistening white leaflets, m. p. 46–48°. *Anal.* Calcd. for $C_{12}H_{13}O_5N$: N, 5.58. Found: N, 5.70.

Tetrahydrofurfuryl 3,5-Dinitrobenzoate.—Small needles, m. p., 83–84°. *Anal.* Calcd. for $C_{12}H_{12}O_7N_2$: N, 9.46. Found: N, 9.52.

The analyses were performed by Dr. T. S. Ma.

(1) Shriner and Fuson, "Identification of Organic Compounds," John Wiley and Son, New York, N. Y., 1935, p. 142.

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The Decrease in Resistance of Constantan with a Magnetic Field at Temperatures between 1 and 20°K.

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In various magnetic experiments at the temperatures of liquid hydrogen and helium we have employed a coil of no. 40 Constantan wire ("advance" wire, Driver Harris Co., Harrison, N. J.) as a heater to evaporate liquid helium so that liquid hydrogen could be added for work at the higher temperatures. It seemed worth while to take the opportunity to measure the effect of a magnetic field on the resistance of Constantan, especially since the resistance decreases with magnetic field strength. This effect has been measured down to 90°K. by Obata.[1] The observations, which were made with a current of 2.5×10^{-4} ampere, are given in Table I. Although the coil was not placed carefully with respect to field direction, the current was approximately at right angles to the field.

(1) Obata, "I. C. T.," Vol. VI, p. 422.

Table I

Decrease in the Resistance of Constantan in a Magnetic Field

		$(\Delta R/R) \times 10^3$, H in gauss				
T, °K.	$R(H = 0)$ ohms	H = 850	H = 1600	H = 3000	H = 4100	H = 8300
1.47	220.804	−0.72	−1.61	−2.77	−3.47	−5.38
4.22	221.441	− .66	−1.55	−2.78	−3.54	−5.63
10.67	223.412	− .87	−1.88	−3.33	−4.28	−7.05
20.34	226.613	−1.59	−2.94	−4.84	−6.02	−9.51

At the temperatures of this investigation the change of resistance is proportional to somewhat more than the first power of the field strength at the lower fields and decreases to considerably less than the first power at the higher fields. Some very rough observations near the temperature of liquid air indicated a proportionality to the square of the field strength, as was the case in the observations of Obata.

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Polarographic Determination of Certain Natural Products

By E. B. Hershberg, John K. Wolfe and Louis F. Fieser

In a recent report[1] a method was described for the quantitative determination of ketosteroids, consisting in condensation with excess Girard's reagent and polarographic analysis of a suitably buffered aqueous solution of the reaction mixture. The method is well adapted to the determination of the 17-ketosteroids in urinary extracts, for among the saturated compounds those having a single carbonyl group at C_3 are indifferent and those with a lone ketonic group at C_{20} give a somewhat different polarographic response. Δ^4-3-Ketosteroids are determinable by the same method and are distinguishable from the 17-keto compounds because discharge occurs at a significantly lower potential.

We have now found that the method can be extended to the determination of non-ketonic alcohols of the sterol group by oxidation of these substances to the corresponding ketones with aluminum *t*-butoxide according to Oppenauer.[2] Thus 100 mg. of dehydroisoandrosterone was

(1) Wolfe, Hershberg and Fieser, *J. Biol. Chem.*, in press.
(2) Oppenauer, *Rec. trav. chim.*, **56**, 137 (1937).

oxidized by Oppenauer's procedure and a portion of the resulting solution equivalent to 0.5 mg. of hormone was condensed with Girard's reagent by our standard procedure,[1] and one-fourth of the mixture was polarographed in aqueous sodium acetate–acetic acid solution. The automatically recorded current–voltage curve consisted of a double wave, the first discharge occurring at a half-wave potential of about −1.2 v. (±0.05 v.) and the second at about −1.5 v. (uncorrected empirical potentials). Under the same conditions the Girard derivative of dehydroisoandrosterone or other 17-ketosteroid gives a single wave at about −1.44 v., while that of testosterone discharges at −1.23 v. When submitted to Oppenauer oxidation in a parallel experiment, androsterone gave a single wave at about −1.4 v. indistinguishable from that of the original hormone. The Oppenauer reaction was applied to the ketonic fraction of a urinary extract from a female with an adrenal tumor. This was known from isolation experiments of one of us (J. K. W.) and from colorimetric determinations of the 3 α and 3 β steroids[3] carried out by Dr. N. B. Talbot to contain about equal parts of androsterone and dehydroisoandrosterone. The polarogram obtained after conversion of the oxidized material to the Girard derivative exhibited one wave at −1.2 to −1.3 v., corresponding to an α,β-unsaturated 3-sterone, and another at about −1.5 v., characteristic of the 17-ketosteroids and of the upper wave of androstenedione. Only the second wave appeared on analysis of the unoxidized extract, and a comparison of the polarograms made before and after Oppenauer oxidation indicated about the same proportion for the saturated and unsaturated steroids as found by the other methods.

Vitamin K_1 can be determined polarographically in aqueous isopropanol containing potassium chloride. The typical curve reproduced in Fig. 1 shows a sharply defined wave at −0.58 v. The definition was somewhat less satisfactory in a solution of 2.5 cc. of isopropanol containing 10 mg. of lithium chloride, but even in this case 50 γ of the vitamin could be determined accurately in this volume of solution.

Compounds of the heart poison group have been found to fall within the scope of the polarographic method. A satisfactory medium consists in a mixture of 0.5 cc. of isopropanol, 0.5 cc. of 0.2 *N* tetraethylammonium hydroxide, and 1 cc. of water. When examined in this solvent medium, digitoxin, convallatoxin, thevetin and lanatoside C were all found to give characteristic waves at potentials between −1.9 and −2.0 v., and the wave spans[1] were proportional to the concentration. Gitoxin shows a potential about 0.1 v. less negative. Since sodium ion discharges in the same potential range, the reagents must be carefully tested in blank determinations for freedom from this ion. Tetraethylammonium hydroxide which had been freshly prepared and stored in a platinum container proved satisfactory. The waves for gitoxin and digitoxin were found to decrease in extent on standing by about 50% in two hours. The alteration, which is not so rapid as to interfere seriously with the analytical determination, indicates that the observed waves are not due to the presence of sodium in the samples, for a polarogram made with a blank containing added sodium hydroxide remained constant over the same time interval. In a still more rigorous test, 9.521 mg. of the digitoxin preparation was burned in a combustion tube and the slight residue weighing 10 γ was leached with 1 cc. of water and polarographed as above. No sodium was detected.

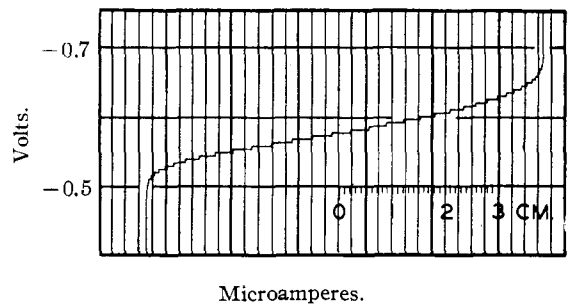

Fig. 1.—Vitamin K_1; 0.5 mg. in a mixture of 1 cc. of isopropanol and 1 cc. of 0.1 *N* aqueous potassium chloride solution, polarographed at sensitivity D.

Both glycosides and aglycones of the cardiac group appear to be determinable. Figure 2 gives a comparison of the polarograms obtained with approximately equal weights of digitoxin (curve 1) and of digitoxigenin (curve 2) under comparable conditions (the portions of other curves appearing in these reproductions of the Micromax charts are purely incidental). The ratio of the wave spans (38 and 75 mm.), as measured by the method previously outlined,[1] is very nearly the same as the inverse ratio of the molecular weights.

(3) Talbot, Butler and MacLaughlan, *J. Biol. Chem.*, **132**, 595 (1940).

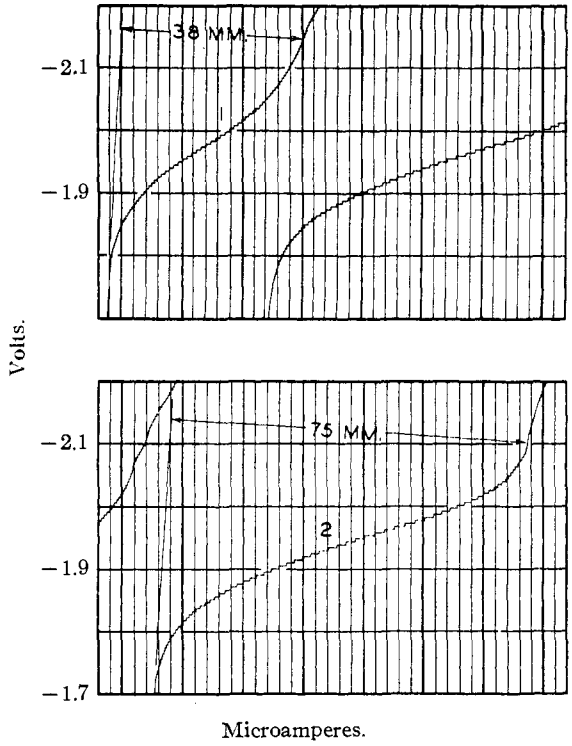

Fig. 2.—Heart poisons polarographed in 0.5 cc. of isopropanol, 0.5 cc. of 0.2 *N* tetraethylammonium hydroxide and 1 cc. of water at sensitivity C. Curve 1: Digitoxin, 0.979 mg., molecular weight 764.95. Curve 2: Digitoxigenin, 0.975 mg., molecular weight 374.50.

For samples of some of the pure cardiotonic principles examined we are indebted to Professor R. P. Linstead, Dr. W. S. Johnson, and Mr. R. C. Jones.

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On the Nature of Haslewood's Hepatols

BY H. B. MACPHILLAMY

Considerable attention has recently been given to investigating the steroids found in various types of animal tissues. One of the most interesting is the report by Haslewood,[1] in which he described the isolation from ox liver of β-7-hydroxycholesterol and of two alcohols of possible steroid nature, the hepatols. I have applied his procedure to hog liver and have also been able to isolate β-7-hydroxycholesterol and the hepatol melting at 277–279°.

However, during the procedure several steps seemed to warrant closer investigation. It appeared unusual that dissolving in pyridine and precipitation with ether according to Schoenheimer[2] should not be sufficient to split the hepatol digitonide, while boiling xylene was effective. The digitonin residue after this xylene extraction showed considerable charring, indicating that possibly the hepatol might be a decomposition product of digitonin.

In Haslewood's procedure the cholesterol present in the digitonide precipitate was removed by the addition of an excess of bromine. A separate experiment carried out with cholesterol digitonide showed that it was not possible to remove all of the cholesterol by this procedure. More important yet, the digitonides treated with bromine showed a positive Beilstein test in spite of several washings with ether, indicating the possible presence of cholesterol dibromide. In order to study the effect of this impurity on digitonin, a mixture of 1 g. of digitonin (Hoffmann–La Roche) and 100 mg. of cholesterol dibromide was heated in boiling xylene. On working up the xylene solution about 200 mg. of a compound melting at 278–279° was obtained. Acetylation with acetic anhydride in pyridine solution yielded a diacetate with a melting point of 227–228°. The substance seemed to be identical with the hepatol obtained from liver and gave the same analysis as that reported by Haslewood for one of his hepatols.

Digitogenin would seem to be the most likely digitonin decomposition product present. The melting point of the pure hepatol given by Haslewood, 284–285°, corresponds quite closely with that given for purified digitogenin, 280–283°. Digitogenin forms a triacetate melting at 190° obtained by acetylation with boiling acetic anhydride and sodium acetate. A sample of digitogenin, prepared by the acid hydrolysis of digitonin, was acetylated by heating with acetic anhydride in pyridine solution. A diacetate with a melting point of 231–233° and identical with "hepatol acetate" was obtained. It is possible to form either a diacetate or a triacetate from digitogenin depending upon the acetylation conditions.

The analytical data given below are quite consistent with those for digitogenin considering that it was obtained from an impure digitonin.

Anal. Calcd. for digitogenin, $C_{27}H_{44}O_6$: C, 72.28; H, 9.89. Found by Haslewood for hepatol: C, 71.8, 71.2; H, 9.7, 9.9. Found in this work for hepatol: C, 71.7, 71.8; H, 9.9, 9.8. Calcd. for digitogenin diacetate,

(1) Haslewood, *Biochem. J.*, **33**, 709 (1933).

(2) Schoenheimer and Dam, *Z. physiol. Chem.*, **215**, 59 (1933).