theoretically required for complete esterification. Heating of the reaction mixture often occurred at this point. The mixture was allowed to stand at room temperature for twenty-four hours after all of the sugar was in solution. Stirring was helpful in accelerating the rate of solution of the sugar in certain cases, as with sucrose, in which an exothermic reaction does not occur. The reaction mixture was then concentrated *in vacuo* with a bath temperature of 50–80°. If the derivative was known to be crystalline, the sirupy residue was induced to crystallize by scratching or seeding. The crystals were then dried in a vacuum desiccator over solid sodium hydroxide and concentrated sulfuric acid and finally in a vacuum oven. When the ester was a sirupy liquid it was either purified directly by distillation or freed of traces of pyridine by drying in thin layers in a vacuum oven.

Acyl analyses, with the exception of those on the esters of D-glucose, were carried out by saponification at room temperature in acetone solution with either aqueous or alcoholic potassium hydroxide. The glucose esters were analyzed by a slight modification of the method of Elek and Harte.[4]

Acknowledgment.—Mr. C. H. Van Etten performed several of the acyl analyses listed in the table.

STARCH AND DEXTROSE DIVISION
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PEORIA, ILLINOIS[5] RECEIVED JULY 7, 1945

(4) Elek and Harte, *Ind. Eng. Chem., Anal. Ed.*, **8**, 267–269 (1936).

(5) One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, U. S. Department of Agriculture. Article not copyrighted.

The Species Specificity of Heparin

BY M. L. WOLFROM,[1] J. V. KARABINOS,[1] C. S. SMITH,[2] P. H. OHLIGER,[2] J. LEE[3] AND O. KELLER[3]

Charles and Scott[4] demonstrated that a blood anticoagulant, presumably heparin, was widely distributed in various tissues of beef. It was found in greatest quantities in muscle, liver and lung; smaller quantities were obtained from heart, thymus, spleen and blood. Charles and Todd[5] proved the chemical and biological identity of the crystalline barium acid heparinate isolated from beef lung and beef liver. Jaques, Waters and Charles[6] isolated crystalline barium acid heparinate from the lungs of pork and sheep and from the liver of dogs. These workers found no significant chemical differences in the product from these sources and from beef but they claimed a wide variation in biological activity, the blood anticoagulant potencies being in the order 10:5:2:1 = dog:beef:pork:sheep.

Species specificity is the rule with protein material but is unusual for carbohydrate principles. The heparin from dog liver, being reputedly of the highest activity, was of greatest interest and was accordingly prepared. The crude heparin (sodium heparinate) was isolated from the excised dog livers according to the general procedure of Charles and Scott.[7] The crude product was purified through the benzidine salt and converted into the amorphous sodium salt. This substance showed an anticoagulant potency[8] of 577 Roche anticoagulant units (ACU) per mg. (dry basis). The sodium salt was transformed into the crystalline barium acid heparinate which showed a potency of 600 Roche ACU per mg. (dry basis). These potencies are entirely within the normal range for beef heparin prepared by the same procedures. Had the potencies of the dog heparin been twice that of beef, values in the range of 1200 Roche ACU per mg. should have been found.

Our results therefore do not support the claim of Jaques and co-workers that a species variation exists between dog and beef heparin. It is possible that the variation in potencies found by these workers is to be ascribed to the sensitivity of the crystalline barium acid salt and the ease with which it is inactivated by mild acidity.[9]

(1) Department of Chemistry, The Ohio State University.

(2) Department of Physiological Chemistry, The Ohio State University.

(3) Scientific Department, Hoffmann-La Roche, Inc.

(4) A. F. Charles and D. A. Scott, *J. Biol. Chem.*, **103**, 431 (1933).

(5) A. F. Charles and A. R. Todd, *Biochem. J.*, **34**, 112 (1940).

(6) L. B. Jaques and E. T. Waters, *J. Physiol.*, **99**, 454 (1941); L. B. Jaques, *Science*, **92**, 488 (1941); L. B. Jaques, E. T. Waters and A. F. Charles, *J. Biol. Chem.*, **144**, 229 (1942).

(7) A. F. Charles and D. A. Scott, *Biochem. J.*, **30**, 1927 (1936).

(8) The bioassays were performed according to the procedure described by R. H. K. Foster, *J. Lab. Clin. Med.*, **27**, 820 (1942). We are indebted to Dr. R. H. K. Foster for the bioassays.

(9) M. L. Wolfrom and W. H. McNeely, THIS JOURNAL, **67**, 748 (1945).

NUTLEY, NEW JERSEY
COLUMBUS, OHIO RECEIVED JULY 7, 1945

NEW COMPOUNDS

p-Acetamino-(β-chloro-*t*-butyl)-benzene

The monoacetamino derivative of neophyl chloride was prepared by means of the general procedure previously described.[1] Recrystallization from dilute alcohol yielded nacreous flakes, m. p. 155–156°.

Anal. Calcd. for $C_{12}H_{16}ONCl$: Cl, 15.72. Found: Cl, 15.59.

No diacetamino derivative was isolated, presumably because of hindrance by the chlorobutyl group of nitration in the ortho position.

(1) V. N. Ipatieff and L. Schmerling, THIS JOURNAL, **59**, 1056 (1937); **60**, 1476 (1938).

RESEARCH LABORATORIES
UNIVERSAL OIL PRODUCTS COMPANY V. N. IPATIEFF
RIVERSIDE, ILLINOIS LOUIS SCHMERLING
RECEIVED JULY 19, 1945

N,N-Dimethylphthalamidic Acid

The reaction of phthalic anhydride with dimethylamine gave a 71–75% yield of N,N-dimethylphthalamidic acid. In a 3-liter, two-necked, round-bottomed flask fitted with a reflux condenser and an inlet tube were placed 296.2 g. (2.0 moles) of phthalic anhydride and 1000 ml. of *dry* benzene. The mixture was heated to boiling and 90 g. (2.0 moles) of liquid dimethylamine was allowed to evaporate in a separate flask and bubble slowly through the inlet tube. (The dry amine was previously obtained by the

addition of solid potassium hydroxide to a commercial (Rohm and Haas) 25% aqueous solution of dimethylamine. The gas evolved was passed through two drying towers containing solid potassium hydroxide and was then condensed in a receiver cooled by a Dry Ice–acetone bath.) The mixture was refluxed for fifteen minutes after the introduction of all the amine. The condenser was then placed downward for distillation and two-thirds of the benzene was distilled. The residue on cooling deposited 298–316 g. of crude product, m. p. 122–124°. One recrystallization from dry benzene gave 274–291 g. (71–75%) of white microcrystals, m. p. 124–125°.

Anal.[1] Calcd. for $C_{10}H_{11}O_3N$: C, 62.16; H, 5.74; N, 7.25. Found: C, 62.20; H, 5.53; N, 7.14.

(1) Microanalyses were carried out by Miss Theta Spoor.

NOYES CHEMICAL LABORATORY
UNIVERSITY OF ILLINOIS ROBERT L. FRANK
URBANA, ILLINOIS FRED E. BOETTNER

RECEIVED JULY 9, 1945

2-Keto-7-*n*-propylhexamethyleneimine and 6-Aminononanoic Acid

2-Keto-7-*n*-propylhexamethyleneimine.—2-*n*-Propylcyclohexanone oxime, m. p. 65–66° (uncor.),[1] 1.7 g., was rearranged in 92% sulfuric acid essentially according to the procedure of Marvel and Eck.[2]

(1) Vavon and Anziani, *Bull. soc. chim.*, **41** (4), 1638 (1927).
(2) Marvel and Eck, "Organic Syntheses," **17**, 60 (1937).

The relatively high acid concentration has been reported to be conducive to higher yields.[3] The product, 2-keto-7-*n*-propylhexamethyleneimine, after being vacuum distilled as the residue from a chloroform extraction of the neutralized reaction mixture, melted at 97–98° (uncor.).

Attempted fractional crystallization of the product from chloroform–petroleum ether resulted in a 97% yield of the lactam, m. p. 100.5–101.5° (uncor.). Only a trace of partially crystalline residue remained.

Anal. Calcd. for $C_9H_{17}ON$: C, 69.68; H, 10.97. Found: C, 69.84; H, 11.13.

6-Aminononanoic Acid.—By hydrolysis of the lactam there was obtained the corresponding amino acid hydrochloride; it did not crystallize. After treating the hydrochloride with silver oxide, 6-aminononanoic acid was isolated, m. p. 198.5–199° (temperature rise of 4°/min.).

Anal. Calcd. for $C_9H_{19}O_2N$: C, 62.39; H, 11.05. Found: C, 62.34; H, 11.01.

The formation of but one isomer during the Beckmann rearrangement of a 2-alkylcyclohexanone oxime is in accordance with previous results.[3,4,5]

(3) Hildebrand and Bogert, THIS JOURNAL, **58**, 650 (1936).
(4) Wallach, *Ann.*, **389**, 169 (1912).
(5) Ungnade and McLaren, *J. Org. Chem.*, **10**, 29 (1945).

DEPARTMENT OF CHEMISTRY
CANISIUS COLLEGE A. D. MCLAREN
BUFFALO, N. Y. G. PITZL

RECEIVED MAY 17, 1945

COMMUNICATIONS TO THE EDITOR

SMALL-ANGLE X-RAY DIFFRACTION STUDIES ON MUSCLE

Sir:

A type of protein fibril (I), distinguished by a certain large structural pattern, has been described for molluscan muscles.[1,2] Recently another variety of fibril (II) has been identified in the same and other muscles by means of small-angle X-ray diffraction. The relatively widespread occurrence of the type II fibrils is presumptive, although purely circumstantial, evidence that they are related to the fibrous protein, myosin.

Diffractions characterizing both types of fibril have been observed in the following muscles: the adductor muscles of the molluscs *Venus*, *Anodonta*, *Pecten*, *Mya* and *Mytilus*, and the retractor muscle of the sipunculid annelid, *Phascolosoma*. The first three muscles possess both white and tinted portions, the colorless components being more purely type I, the colored ones showing relatively more type II. While these muscles have been variously classified histologically,[3] the colored Pecten component alone seems definitely cross-striated and not to possess the type I fibrils. The striated frog sartorius and the smooth dog retractor penis muscles also exhibit only the type II diffractions.

The new diffraction system (II) is generally faint, diffuse and susceptible of damage by physical and chemical manipulation of the muscle. The best patterns have been obtained from *Venus* (pink component) and *Mya* muscles, in which type II fibrils are plentiful and are also undoubtedly stabilized by the accompanying type I component. As with other protein fibers,[1] the small-angle diffractions of system II are almost exclusively exhibited near or on the pattern meridian. The diffraction positions correspond to the following calculated spacings[4]: 58, 51, 27.2, 18.7, 13.8, 11.2, 9.2 and 6.9 Å. From such pattern details as sharpness and concentration of intensity with respect to the meridian, it seems probable that the structure involved is similar to that found for system I,[2] except that the repeating units are much smaller. The following tentative comparisons can be made: Fiber axis periods are 725 (I) and possibly 350 to 420 Å. (II); meridionally accentuated diffractions are orders of 145 (I) in contrast to about 27 Å. (II); and the

(1) R. S. Bear, THIS JOURNAL, **66**, 2043 (1944).
(2) C. E. Hall, M. A. Jakus, and F. O. Schmitt, *J. Applied Phys.*, **16**, 459 (1945).
(3) See H. Plenk, *Z. wiss. Zool.*, **122**, 20 (1924).
(4) I. MacArthur, *Nature*, **152**, 38 (1943), quotes measurements of W. T. Astbury, on frog sartorius muscle, which include all but the first two of the spacings given here.