1-hydroxypropane (II) reported in the above reference.

The formation of the symmetrical isomer probably arises from the intermediate ethylene oxide.

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The Uronic Acid Component of Heparin

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Sulfuric acid and D-glucosamine[1] have been the only identified hydrolytic products of heparin, the blood anticoagulant isolable from animal tissues. Qualitative[2] and quantitative data[3] indicating the presence of a uronic acid in heparin have been obtained. It has been demonstrated[4] that the hydrolytic conditions which will liberate the uronic acid can also readily destroy it since it is decomposed by acidity. We have accordingly subjected crystalline barium acid heparinate to oxidative hydrolysis, considering that any uronic acid liberated might be stabilized as the acid-resistant dibasic acid. From the reaction mixture there was isolated D-glucosaccharic acid (as the crystalline potassium acid salt) and crystalline D-glucosaminic acid. Under similar non-oxidative hydrolytic conditions, no D-glucosaccharic acid was isolable. These results therefore establish the uronic acid component of heparin as D-glucuronic acid. We wish to remark that the optical rotation of our isolated D-glucosaccharic acid was ascertained, a significant point generally overlooked in most isolations of this substance.

Experimental

An amount of 200 mg. of crystalline barium acid heparinate was dissolved in 2 cc. of water and cooled to near 0°. Five drops of bromine were added, followed by the gradual addition, over a period of ten minutes, of a total of 5 cc. of concentrated sulfuric acid. The mixture was allowed to stand at *ca.* 3° for one week. From time to time, as the solution became less colored, a few drops more of bromine were added. The solution was finally kept at room temperature for *ca.* five hours, aerated to effect bromine removal, and poured into 75 cc. of cold (near 0°) water. The sulfuric acid was neutralized in the cold with barium carbonate and the mixture filtered. Concentration (30–40°) of the filtrate under reduced pressure yielded a thick sirup.

The sirup was acidified with a drop of concentrated hydrochloric acid and extracted at room temperature with 95% ethanol. The extract was neutralized to *ca.* *p*H 6 with 10% aqueous potassium hydroxide, filtered and concentrated under reduced pressure to a thick sirup. The sirup was treated with 10 cc. of absolute ethanol, filtered and again concentrated under reduced pressure to a sirup. This sirup was dissolved in 1 cc. of water, neutralized with solid potassium carbonate and 1 cc. of glacial acetic acid added. Crystals formed overnight that had the appearance of potassium acid saccharate when viewed under the microscope. A further quantity of like crystals were obtained by extracting the barium sulfate (formed above in the neutralization of the sulfuric acid) at room temperature with 10 cc. of 1% aqueous potassium hydroxide. The neutralized (with acetic acid) extract was concentrated (30–40°) under reduced pressure to a volume of 1 cc. and acidified with an equal volume of glacial acetic acid. Crystals formed on standing overnight; total yield 29.9 mg., $[\alpha]^{20}D$ +10° (*c* 2.5 as dipotassium salt, water). The polarization was effected by solution in an equivalent (to phenolphthalein) amount of aqueous potassium carbonate solution. A known sample of potassium acid D-glucosaccharate gave the same value, $[\alpha]^{20}D$ +10°, under the same conditions. The solutions were colored slightly yellow by the neutralization procedure.

Anal. Calcd. for $C_6H_9O_8K$: K, 15.72. Found: K, 15.82.

The crystalline product was therefore identified as potassium acid D-glucosaccharate.

The insoluble material remaining after the ethanol extraction described above was treated with a small amount of silver carbonate and extracted at room temperature with 25 cc. of 95% ethanol. The extract was concentrated to 5 cc., filtered and ether added to incipient opalescence. Crystals (long needles) separated on standing; yield 26 mg., dec. 250–260°, $[\alpha]^{21}D$ −19 ±2° (*c* (as weighed) 1.0, 2.5% hydrochloric acid, twelve hours). The crystals were acid toward litmus and contained amino nitrogen (by soda-lime fusion). A crystalline copper salt (bluish-green crystals) was formed with cupric carbonate. These data identify the substance as D-glucosaminic acid,[5] for which Fischer and Leuchs[6] cite the constants: dec. 250°, $[\alpha]^{18}D$ −17° → −15° (*c* 10, 2.5% hydrochloric acid, thirty hours).

On repeating the above described hydrolysis of crystalline barium acid heparinate but omitting the bromine, no potassium acid D-glucosaccharate was formed.

(1) E. Jorpes and S. Bergström, *Z. physiol. Chem.*, **244**, 253 (1936).
(2) W. H. Howell, *Bull. Johns Hopkins Hosp.*, **42**, 199 (1928).
(3) M. L. Wolfrom, D. I. Weisblat, J. V. Karabinos, W. H. McNeely and J. McLean, THIS JOURNAL, **65**, 2077 (1943).
(4) M. L. Wolfrom and J. V. Karabinos, *ibid.*, **67**, 679 (1945).
(5) E. Fischer and F. Tiemann, *Ber.*, **27**, 138 (1894).
(6) E. Fischer and H. Leuchs, *ibid.*, **35**, 3787 (1902); **36**, 24 (1903).

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NEW COMPOUNDS

3-Trichloromethyl-6-hydroxy-7-chlorophthalide and its Acetyl Derivative

The hydroxyphthalide was prepared by Chattaway and Calvet's method.[1] Three grams of 2-chloro-3-hydoxybenzoic acid and 4 g. of U. S. P. chloral hydrate were dissolved in 30 g. of concentrated sulfuric acid. After standing twenty-four hours, the solution was poured into cracked ice and water, and the precipitate, which formed, when washed with water and dried weighed 5.2 g. and melted at 190–192°. One crystallization from benzene and two from ethanol–water raised the melting point to 195.5–196°. The compound forms a precipitate when warmed with alcoholic silver nitrate, is readily soluble in 5% aqueous sodium hydroxide solution, and produces a green fluorescence with resorcinol and sulfuric acid.

Anal. Calcd. for $C_9H_4Cl_4O_3$: Cl, 46.97. Found: Cl, 46.91, 46.94.

The acetyl derivative was prepared by the method of Pratt and Robinson.[2] Five-tenths gram of the hydroxyphthalide gave 0.48 g. of a product melting at 175–177°.

(1) Chattaway and Calvet, *J. Chem. Soc.*, 1092 (1928).
(2) Pratt and Robinson, *ibid.*, **127**, 1184 (1925).

One crystallization from benzene and several from methanol elevated the melting point to 181.5–182°.

Anal. Calcd. for $C_{11}H_6Cl_4O_4$: Cl, 41.23. Found: 41.02, 41.18.

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Derivatives of *sym*-Trialkylbenzenes

2,4,6-Triethylbenzonitrile.—A mixture of 60 g. of 2,4,6-ethylbromobenzene,[1] 5.0 g. of cuprous cyanide and 60 ml. of pyridine was heated under reflux for eleven hours, allowed to cool somewhat and poured into 400 ml. of dilute ammonium hydroxide solution. The nitrile was extracted with a mixture of benzene and ether. The solution was washed with water and with dilute ammonium hydroxide solution, dried over calcium chloride and distilled. The nitrile boiled at 150–151° (24 mm.); $n^{20}D$ 1.5201; d^{25}_4 0.9366; yield 64%.

Anal. Calcd. for $C_{13}H_{17}N$: C, 83.37; H, 9.15. Found: C, 83.23; H, 9.12.

Dillingham and Reid[2] made this compound by another method; they reported the boiling point as 108.5° (2 mm.) and the density as d^{25}_4 0.9356, but did not include an analysis.

3,5-Dinitro-2,4,6-triethylbenzonitrile.—Two grams of 2,4,6-triethylbenzonitrile was added slowly to 20 ml. of fuming nitric acid which had been cooled to 0°. The mixture was allowed to stand for thirty minutes in an ice-bath and was then poured into 200 ml. of water. The product was recrystallized from methanol; m. p. 69–70.5°; yield 1.5 g.

Anal. Calcd. for $C_{13}H_{15}O_4N_3$: C, 56.30; H, 5.41. Found: C, 56.21; H, 5.57.

1-Ethyl-2,4,6-triisopropylbenzene.—2,4,6-Triisopropylbenzyl chloride was coupled with methylmagnesium iodide according to the method described for 4-*t*-butyl-2,6-dimethylbenzyl chloride.[3] 1,2-Di-(2,4,6-triisopropylphenyl)-ethane[4] was obtained in 63% yield. The alkylation product, 2,4,6-triisopropylethylbenzene, boiled at 101–103° (5 mm.); $n^{20}D$ 1.4927.

Anal. Calcd. for $C_{17}H_{28}$: C, 87.85; H, 12.15. Found: C, 88.21; H, 12.04.

Ethyl 4-*t*-Butyl-2,6-dimethylbenzyl Ether.—This compound was produced in an attempt to reduce 4-*t*-butyl-2,6-dimethylbenzyl chloride. To a solution of 15 g. of sodium hydroxide pellets in 220 ml. of 95% ethanol was added 25 g. of the chloride. Three grams of aluminum powder was added slowly, with stirring, and the mixture heated under reflux for three hours. The ether, isolated in the usual way, boiled at 126–126.5° (7 mm.); $n^{20}D$ 1.5008; yield 78%.

Anal. Calcd. for $C_{15}H_{24}O$: C, 81.75; H, 10.98. Found: C, 82.02; H, 11.03.

Ethyl 2,4,6-Triisopropylbenzyl Ether.—This compound was produced in an attempt to reduce 2,4,6-triisopropylbenzyl chloride by a procedure similar to that used with 4-*t*-butyl-2,6-dimethylbenzyl chloride. The product, isolated in the usual manner, boiled at 132–134° (6 mm.); $n^{20}D$ 1.4928.

Anal. Calcd. for $C_{18}H_{30}O$: C, 82.38; H, 11.52. Found: C, 82.05; H, 11.50.

An attempt to brominate this ether converted it to bromomesitylene.

2,4,6-Triisopropylbenzyl Acetate.—A mixture of 10 g. of silver acetate, 15 g. of 2,4,6-triisopropylbenzyl chloride and 30 ml. of glacial acetic acid was heated for six hours on a steam-bath. The silver chloride was removed by filtration and the solvent evaporated under diminished pressure. The acetate boiled at 161–162° (13 mm.); $n^{15}D$ 1.5033; d^{20}_4 0.9536.

Anal. Calcd. for $C_{18}H_{28}O_2$: C, 78.19; H, 10.21. Found: C, 78.15; H, 10.44.

Hydrolysis of the acetate yielded 2,4,6-triisopropylbenzyl alcohol, m. p. 83–84°.[4]

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(1) Fuson and Corse, THIS JOURNAL, **60**, 2063 (1938).

(2) Dillingham and Reid, *ibid.*, **60**, 2606 (1938).

(3) Fuson, Denton and Kneisley, *ibid.*, **63**, 2652 (1941).

(4) Fuson, Horning, Ward, Rowland and Marsh, *ibid.*, **64**, 30 (1942).

Derivatives of 8-Chloroquinoline[1]

8-Chloroquinoline Picrate.—A 7.0-g. portion of picric acid (containing 10% water) was dissolved in 90 ml. of benzene. The solution was dried over anhydrous sodium sulfate, filtered, and added to a solution of 4.5 g. of 8-chloroquinoline[2] in 25 ml. of benzene. The yellow precipitate was collected, washed with benzene, and dried. The yield was 10.5 g. (97%); m. p. 178–180°. A sample was recrystallized from ethanol (70 ml./g.) for analysis, m. p. 178–180°.

Anal. Calcd. for $C_{15}H_9O_7N_4Cl$ (392.7): C, 45.88; H, 2.31. Found: C, 45.50; H, 2.11.

Thiourea Addition Compound of 8-Chloroquinoline.—This compound was obtained during an attempted preparation of 8-quinolinethiol from 8-chloroquinoline via the isothiuronium salt. A solution of 1.64 g. of 8-chloroquinoline in 15 ml. of absolute ethanol was boiled under reflux with 0.76 g. of thiourea for fifteen minutes; the thiourea gradually dissolved. On cooling, the clear solution deposited 1.0 g. (38%) of colorless needles, m. p. 131–132°. (The same result was obtained when the reaction mixture was boiled five hours.) The addition compound (0.8 g.) was recrystallized from ethanol for analysis; recovery 0.6 g., colorless needles, m. p. 132–133°. The compound gave positive sodium-fusion tests for nitrogen, halogen and sulfur, but was completely inert to hot alcoholic silver nitrate. This showed that it was not the desired 8-quinolineisothiuronium chloride, but an isomeric addition-compound of 8-chloroquinoline and thiourea.

Anal. Calcd. for $C_{10}H_{10}N_3SCl$ (239.7): C, 50.08; H 4.21. Found: C, 49.78; H, 4.34.

(1) This work was done under a contract recommended by the Committee on Medical Research between the Office of Scientific Research and Development and the University of Rochester.

(2) Claus and Scholler, *J. prakt. Chem.*, (2) **48**, 140 (1893).

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SOME HYDROXYPEROXIDES

The peroxides shown in Table I have been synthesized[1] in an anhydrous ethereal solution. Hydroxy dicarbethoxymethyl hydroperoxide and di-[hydroxy-dicarbethoxymethyl]-peroxide were prepared from ethyl oxomalonate,[2] while α,α'-dihydroxydiisoamyl peroxide and α,α'-dihydroxy-di-*n*-hexyl peroxide were prepared from isovaleric aldehyde and *n*-hexaldehyde, respectively. α,α'-Dihydroxy-di-*n*-hexyl peroxide was also prepared in good

(1) Milas, Harris and Panagiotakos, THIS JOURNAL, **61**, 2430 (1939).

(2) Dox, "Organic Syntheses," Coll. Vol. 1, John Wiley and Sons, Inc., New York, 1941, p. 266.