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).