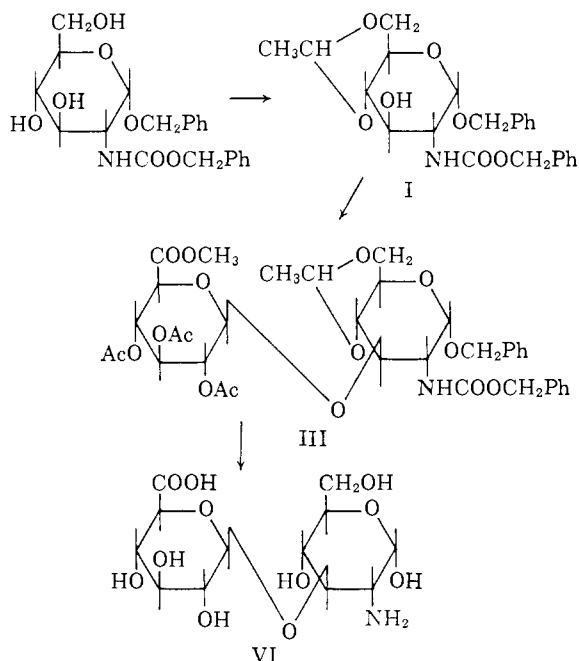


THE SYNTHESIS OF HYALOBIOURONIC ACID AND CHONDROSINE

Sir:

The structures of various mucopolysaccharides are fairly well established and they may be regarded as polymers of varying chain length composed of disaccharide repeating units. However, the structure of the component disaccharides is known only through degradative methods.

Hyalobiuronic acid is the unit disaccharide of hyaluronic acid and chondrosine is that of chondroitin sulfuric acid A or C. The former was characterized as 2-amino-2-deoxy-3-*O*- β -D-glucopyranuronosyl-D-glucose¹ and the latter as 2-amino-2-deoxy-3-*O*- β -D-glucopyranuronosyl-D-galactose². We wish to report here the synthesis of these two disaccharides.



Benzyl 2-amino-*N*-benzyloxycarbonyl-2-deoxy- α -D-glucopyranoside³ was converted to benzyl 2-amino-*N*-benzyloxycarbonyl-2-deoxy-4,6-*O*-ethylidene- α -D-glucopyranoside (I) and benzyl 2-amino-4,6-*O*-benzylidene-*N*-benzyloxycarbonyl-2-deoxy- α -D-glucopyranoside (II). I, m.p. 165°, and II, m.p. 218°, were obtained, respectively, in 67 and 80% yields.

An attempted condensation of methyl (tri-*O*-acetyl- α -D-glucopyranosyl bromide) uronate with I by the Koenigs-Knorr reaction was effected, but not with II. The product from the condensation of I was chromatographed on Florisil column and benzyl 2-amino-*N*-benzyloxycarbonyl-2-deoxy-4,6-*O*-ethylidene-3-*O*-[(methyl tri-*O*-acetyl- β -D-glucopyranosyl)uronate]- α -D-glucopyranoside (III), m.p. 189°, was obtained from the first frac-

tion eluted with a mixture of chloroform and petroleum ether (4:1). The yield was 25%.

Heating of III in 50% acetic acid on a water bath afforded benzyl 2-amino-*N*-benzyloxycarbonyl-2-deoxy-3-*O*-[(methyl tri-*O*-acetyl- β -D-glucopyranosyl)uronate]- α -D-glucopyranoside (IV), and the latter was treated with 0.2 *N* sodium hydroxide at room temperature. Benzyl 2-amino-*N*-benzyloxycarbonyl-2-deoxy-3-*O*- β -D-glucopyranuronosyl- α -D-glucopyranoside (V), m.p. 190° (dec.), was precipitated by acidifying with hydrochloric acid. The yield was 69% based on III.

The *N*-benzyloxycarbonyl and benzyl glycosidic linkages in V were split by catalytic hydrogenation over 10% palladium-carbon in water and resulting 2-amino-2-deoxy-3-*O*- β -D-glucopyranuronosyl-D-glucose (VI) was purified by dissolving in dilute hydrochloric acid followed by neutralization with sodium bicarbonate. The yield was 73%. The compound darkened at 190°, having no characteristic melting or decomposing point. It crystallized with one molecule of water which was lost on heating *in vacuo* over phosphorus pentoxide at 80° for 8 hours: $[\alpha]^{20}_D +34 \rightarrow +30^\circ$ (*c* 1.08, 0.1 *N* hydrochloric acid).

Anal. Calcd. for $C_{12}H_{21}NO_{11} \cdot H_2O$: C, 38.61; H, 6.21; N, 3.75. Found: C, 38.81; H, 6.09; N, 3.75. Calcd. for $C_{12}H_{21}NO_{11}$: N, 3.94. Found: N, 3.92.

Paper chromatography of VI and authentic hyalobiuronic acid gave a single spot on an ascending paper chromatogram developed with butanol-acetic acid-water.

Similarly, 2-amino-2-deoxy-3-*O*- β -D-glucopyranuronosyl-D-galactose was prepared by condensation of benzyl 2-amino-*N*-benzyloxycarbonyl-2-deoxy-4,6-*O*-ethylidene- α -D-galactopyranoside, m.p. 183°, with methyl (tri-*O*-acetyl- α -D-glucopyranosyl bromide) uronate, then removal of protecting groups, and this compound was obtained as a crystalline hydrate which darkened at 185° without melting. It was identified with authentic chondrosine by paper chromatography and infrared absorption spectra: $[\alpha]^{20}_D +39^\circ$ (*c* 1.0, water).

Anal. Calcd. for $C_{12}H_{21}NO_{11} \cdot H_2O$: C, 38.61; H, 6.21; N, 3.75. Found: C, 38.80; H, 6.12; N, 3.64. Calcd. for $C_{12}H_{21}NO_{11}$: N, 3.94. Found: N, 3.98.

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