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The Synthesis of Carrabiose*¹Susumu HIRASE and Choji ARAKI*²*Department of Chemistry, Faculty of Industrial Arts, Kyoto Technical University, Matsugasaki, Kyoto*

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Carrabiose (3,6-anhydro-4-*O*- β -D-galactopyranosyl-D-galactose) was synthesized by a series of reactions involving the condensation of methyl 2-*O*-*p*-tosyl-3,6-anhydro- α -D-galactopyranoside with tetra-*O*-acetyl- α -D-galactopyranosyl bromide, followed by deacetylation, detosylation, and removal of the glycosidic methoxyl group. From the resulting disaccharide, several crystalline derivatives were prepared. All of these derivatives were identical in every respect with the corresponding compounds, which had been obtained from natural sources.

Carrabiose is a name of the disaccharide, whose structure is 3,6-anhydro-4-*O*- β -D-galactopyranosyl-D-galactose (V).¹⁾ The structure was assigned on the basis of chemical evidence.¹⁻³⁾ The disaccharide was isolated from κ -carrageenan²⁾ and other similar polysaccharides.^{1,4,5)} In the present paper, the synthesis of the disaccharide will be reported.

The starting compound, methyl 2-*O*-*p*-toluenesulfonyl-3,6-anhydro- α -D-galactopyranoside (II),

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1) C. Araki and S. Hirase, *This Bulletin*, **29**, 770 (1956).

2) A. N. O'Neill, *J. Am. Chem. Soc.*, **77**, 6324 (1955).

3) T. J. Painter, *J. Chem. Soc.*, **1964**, 1396.

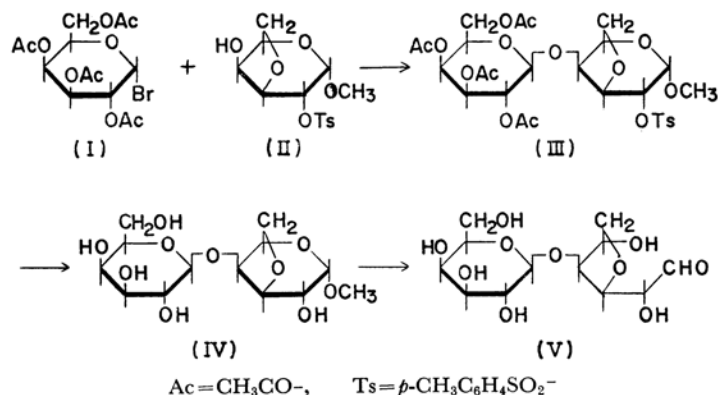
4) T. J. Painter, *Can. J. Chem.*, **38**, 112 (1960).

5) A. L. Clingmann and J. R. Nunn, *J. Chem. Soc.*, **1959**, 493.

prepared according to Rao and Smith,⁶⁾ was allowed to condense with tetra-*O*-acetyl- α -D-galactopyranosyl bromide (I) in chloroform in the presence of silver oxide and anhydrous calcium sulfate. The resulting syrup (III) was treated with dilute sodium methoxide solution to remove the acetyl groups, and then with 12% sodium hydroxide solution to remove the *p*-toluenesulfonyl (*p*-tosyl) group. In the latter reaction, no inversion of the configuration would have taken place on the carbon atoms concerned, as was proved by Rao and Smith⁶⁾ in the detosylation of the compound (II). Chromatographic purification of the detosylated product on a cellulose powder column gave methyl 3,6-anhydro-4-*O*- β -D-galactopyranosyl- α -D-galactopyranoside (methyl α -carrabiose) (IV) in a crystalline form.

When IV was hydrolyzed with very dilute sulfuric

6) P. A. Rao and F. Smith, *ibid.*, **1944**, 229.



acid, carrabiose (V) was obtained in an amorphous form. The disaccharide was then converted into the crystalline phenyllosazone and crystalline hepta-*O*-acetyl-carrabi-itol. On the other hand, the treatment of IV with dilute methanolic hydrogen chloride produced carrabiose dimethyl acetal, which gave the crystalline hexaacetate. All of these crystalline derivatives were identical with the corresponding compounds, obtained from natural sources.

Experimental

General Procedure. Solutions were evaporated under reduced pressure at about 40°C. Paper chromatography was performed on Toyo Filter Paper No. 51 with 1-butanol-acetic acid-water (4:1:2 v/v). The chromatographic spray reagent used was *o*-aminophenol in ethanol acidified with phosphoric acid.⁷⁾

Methyl α -Carrabioside (IV). A mixture of II⁶⁾ (19.8 g), silver oxide (30 g), Drierite[®] (50 g) and some pieces of glass bead was shaken in chloroform (150 ml) at room temperature for 1 hr to ensure the dryness. Tetra-*O*-acetyl- α -D-galactopyranosyl bromide⁹⁾ (24.6 g) was then added, and the resulting mixture was shaken at room temperature for 24 hr, at which time a test for ionizable bromide was negative. The mixture was filtered, and the filtrate was evaporated to dryness.

The residual syrup (37 g) obtained was dissolved in a mixture of absolute methanol (300 ml) and 0.1 *N* sodium methoxide solution (20 ml) in methanol, and left at room temperature for 12 hr. The solution was then evaporated to a syrup (31 g). When this syrup was dissolved in water (150 ml) under ice-cooling, the unchanged II (8 g) was crystallized and filtered off. The filtrate was then neutralized with carbon dioxide, and concentrated to a syrup (23 g).

The detosylation⁶⁾ was carried out by dissolving the above syrup in methanol (60 ml), adding 12% aqueous sodium hydroxide solution (34 ml), and heating the mixture at 60°C for 30 hr. The resulting dark solution,

after being diluted with water and evaporated to remove most of the methanol, was passed through the columns of Amberlite IR-120 (400 ml) and Amberlite IR-45 (400 ml). Evaporation of the deionized solution gave a syrup (10 g), which showed, on a paper chromatogram, several spots, of which the spot with R_f 0.32 was the most intense one. The syrup was chromatographed on a cellulose powder column (4.5 \times 30 cm), using 1-butanol-water (6:1 v/v). Fractions of 14 ml were collected and monitored by paper chromatography. The compound with R_f 0.32 was obtained as a syrup (5.0 g). Crystallization was effected by dissolving the syrup in methanol (25 ml) and adding ethanol (25 ml); yield 3.8 g (31% of the theoretical amounts, when the recovered material was subtracted); mp 201–203°C. Two recrystallizations of the crystals from methanol-ethanol (1:1 v/v) gave the pure glycoside (IV); mp 203–204°C, $[\alpha]_D^{25} +36.0^\circ$ (c 1.0, water), $[\alpha]_D^{25} +44.0^\circ$ (c 1.0, methanol). This compound is a new crystalline derivative of carrabiose, the β -anomer being reported previously.¹⁾

Found: C, 46.32; H, 6.35; OCH₃, 9.33%. Calcd for C₁₃H₂₂O₁₀: C, 46.15; H, 6.56; OCH₃, 9.16%.

Carrabiose (V). A solution of IV (1.5 g) in 0.02 *N* sulfuric acid (30 ml) was heated at 100°C. The optical rotation of the solution changed from $[\alpha]_D +36.0^\circ$ to a constant value $[\alpha]_D +18.8^\circ$ during 45 min. The solution was then neutralized with barium carbonate, filtered, and evaporated to dryness. The residue was purified by dissolution in methanol, filtration, and re-evaporation to dryness. Carrabiose was obtained as a colorless amorphous solid; yield 1.4 g, $[\alpha]_D^{25} +15.2^\circ$ (c 1.25, water). The reported value is $[\alpha]_D^{25} +15.6^\circ$ (water).¹⁾

Phenyllosazone: Recrystallized from 80% ethanol; mp 214–215°C, $[\alpha]_D^{25} +68.2^\circ$ (5 min) \rightarrow $+45.0^\circ$ (48 hr, c 0.60, pyridine-ethanol (2:3)). The reported values are mp 216°C and $[\alpha]_D^{25} +46.0^\circ$ (pyridine-ethanol (2:3)).¹⁾ The melting point was not depressed on admixture with an authentic sample of natural origin.¹⁾

Found: C, 57.90; H, 6.20; N, 11.09%. Calcd for C₂₄H₃₀O₈N₄: C, 57.36; H, 6.02; N, 11.15%.

Carrabi-itol. Carrabiose (0.50 g), obtained above, was reduced with sodium borohydride (0.06 g) in water (10 ml) for 15 hr. The solution was then neutralized with dilute sulfuric acid, and deionized with Amberlite IR-120 and Amberlite IR-45. Evaporation of the solution gave a syrup (0.50 g).

7) S. Hirase, C. Araki and S. Nakanishi, This Bulletin, **26**, 183 (1953).

8) Anhydrous calcium sulfate of the W. A. Hammond Drierite Co., Ohio, U. S. A.

9) W. T. Haskins, R. M. Hann and C. S. Hudson, *J. Am. Chem. Soc.*, **64**, 1852 (1942).

Heptaacetate. Recrystallized twice from 90% ethanol; mp 143–145°C, $[\alpha]_D^{25} -6.4^\circ$ (c 0.78, chloroform). The reported values are mp 144–145°C and $[\alpha]_D^{25} -7.6^\circ$ (chloroform).⁵⁾

Found: C, 50.52; H, 5.98%. Calcd for $C_{26}H_{36}O_{17}$: C, 50.32; H, 5.85%.

Carrabiose Dimethyl Acetal. A solution of IV (0.18 g) in 0.5% methanolic hydrogen chloride (15 ml) was refluxed for 30 min. The solution was then neutralized with silver carbonate, filtered, and evaporated to a syrup (0.17 g); $[\alpha]_D^{20} +24.6^\circ$ (c 0.61, water). The reported value is $[\alpha]_D^{15} +25.0^\circ$ (water).

Hexaacetate. Recrystallized from methanol-water (1 : 2 v/v); mp 146–147°C; $[\alpha]_D^{18} -16.2^\circ$ (c 0.93, benzene). The reported values are mp 147–149°C and $[\alpha]_D^{18} -16.3^\circ$ (benzene),¹⁾ and mp 154.5°C and $[\alpha]_D^{20} -8.5^\circ$ (benzene).³⁾ The melting point was not depressed on admixture with an authentic sample¹⁾ of natural origin.

Found: C, 50.43; H, 6.10; OCH_3 , 9.81%. Calcd for $C_{26}H_{38}O_{17}$: C, 50.16; H, 6.15; OCH_3 , 9.96%.

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