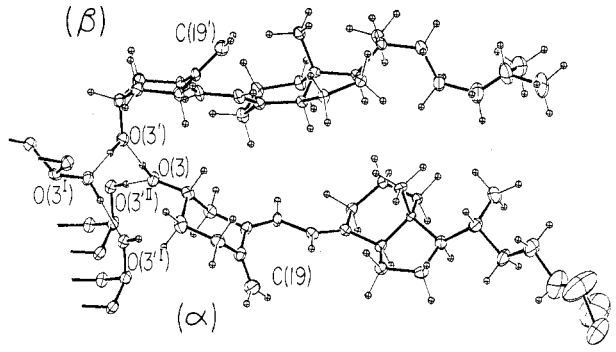

Figure 3. Hydrogen bonding scheme showing the α and β conformers connected in the crystalline state by their single hydroxyl groups to form an infinite spirallike hydrogen-bonded oxygen chain. Each helical chain is constrained about a 2_1 axis in the b direction, with the two conformers occupying alternating positions. O(3^I) and O(3'^{I}) are related to O(3) and O(3'), respectively, by the screw axis, while O(3'^{II}) is related to O(3'^{I}) by a whole lattice translation along the b axis. The unusually large thermal ellipsoids for the isopropyl carbon atoms at the end of the side chain of the α conformer relative to those for the other nonhydrogen atoms are attributed at least in part to these atoms possessing more than one crystal orientation.

by the steric constraints imposed by the infinite helical hydrogen-bonded oxygen chain.

Experimental Section

Vitamin D_3, $C_{27}H_{44}O$, crystallizes with eight molecules in an orthorombic unit cell of dimensions a = 19.730 (4), b = 7.340 (2), and c = 35.716 (6) Å, and of symmetry $P2_12_12_1$ such that the two conformers comprise the crystallographically independent unit.

Intensity data were collected on a Datex-controlled, General Electric diffractometer with an E&A full circle to $2\theta \leq 120°$ with Cu Kα (1.5418 Å) radiation. The data processing included an intensity correction for crystal decay (i.e., ca. 20% over the entire data collection). Of the 4366 measured crystallographically independent reflections, the 2585 reflections for which $I \geq 2\sigma(I)$ were used in the structural analysis.

The structure was solved by the application of MULTAN.[12,13] An E map revealed 34 of the 56 independent nonhydrogen atoms. Subsequent Fourier syntheses yielded unambiguous locations for all nonhydrogen atoms except for the three end carbon atoms [viz., C(25), C(26), and C(27)] on the side chain in one of the two independent molecules. Fourier and difference Fourier maps consistently showed a cluster of small electron-density peaks which from stereochemical considerations was completely compatible with a crystal disorder for this isopropyl carbon fragment. The results reported here are based upon a refinement in which the three strongest peaks in the cluster were taken as whole-weighted occupancies for these carbon atoms. Idealized positions for the hydrogen atoms (except for those attached to the three crystal-disordered carbon atoms) were calculated and then included in the structure factor calculations as fixed-position atom contributors in the final anisotropic full-matrix least-squares refinement which yielded an unweighted $R_1(F)$ index of 8.7% and a weighted $R_2(F)$ index of 10.0%. Bond distances and angles are within their expected ranges[13] except for those corresponding to the three carbon atoms at the end of the side chain of one of the two independent molecules (due to a crystal disorder of this isopropyl carbon fragment).

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Supplementary Material Available. Tables of atomic parameters, bond distances, and bond angles along with their estimated standard deviations (11 pages). Ordering information is given on any current masthead page.

Registry No.—Vitamin D_3, 67-97-0.

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3-*O*-α-L-Rhamnopyranosyl-D-glucose, a New Disaccharide Synthesized by the Koenigs–Knorr Reaction

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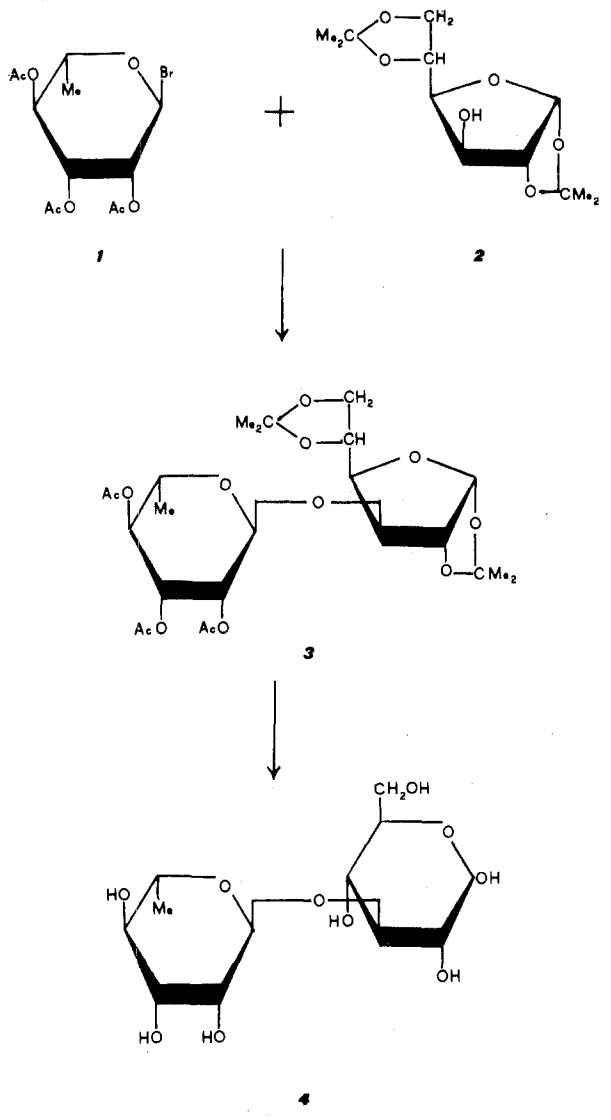
The Koenigs–Knorr reaction is probably the most widely applicable and important method for the condensation of two monosaccharide units; by using this reaction, 2-*O*-β-D-glucopyranosyl-D-xylose,[1] rutinose[2] (6-*O*-α-L-rhamnopyranosyl-D-glucose), robinobiose[3] (6-*O*-α-L-rhamnopyranosyl-D-galactose), and other disaccharides have been synthesized. The present work deals with the synthesis of 3-*O*-α-L-rhamnopyranosyl-D-glucose, a new disaccharide prepared by the Koenigs–Knorr reaction. This preparation was carried out as follows (Scheme I): α-acetobromorhamnose (1) was condensed with 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (2) in the presence of mercuric acetate to form the compound **3** which on deacetylation with sodium methoxide and hydrolysis with oxalic acid gave 3-*O*-α-L-rhamnopyranosyl-D-glucose (**4**) in a overall yield of 10%. The structure of this disaccharide was

Scheme I



determined as follows: acid hydrolysis (10% acetic acid, 3.5 h under reflux) gave rhamnose and glucose identified by paper chromatography; methylation of disaccharide with methyl iodide in dimethylformamide in the presence of silver oxide followed by acid hydrolysis (0.3 N HCl; 4 h under reflux) gave 2,3,4-tri-*O*-methyl-L-rhamnose and 2,4,6-tri-*O*-methyl-D-glucose identified by paper chromatography and thin layer chromatography. The configuration of the glycosidic linkage of this disaccharide was indicated by the similarity of the optical rotation ($[\alpha]_D$ +4) to that ($[\alpha]_D$ −0.1) of isomeric disaccharide rutinose for whose configuration independent evidence was obtained by Gorin and Perlin.[4]

The α-L-glycosidic linkage was confirmed by ^1H NMR spectroscopy (D_2O). Table I shows the chemical shifts of H-1 proton signals of the rhamnose moiety in some compounds. From the above data it appears that the configuration of the glycosidic linkage in the synthesized disaccharide is α since the chemical shifts of the H-1 proton signal of the rhamnose moiety would be expected at a higher value of τ for the β configuration.[5]

Table I. Chemical Shifts of H-1 Proton Signals of the Rhamnose Moiety in Some Compounds

Compd	Chemical shift, $\tau(D_2O)$
Rutinose	4.91
4-*O*-α-L-Rhamnopyranosyl-D-glucose	4.90
3-*O*-α-L-Rhamnopyranosyl-D-glucose	4.92
α-Methyl-L-rhamnopyranoside	4.88
β-Methyl-L-rhamnopyranoside	5.24

Experimental Section

^1H NMR spectra were taken at 100 MHz on a Varian HA-100 in D_2O (DSS as internal reference, τ 10). Rutinose was prepared from rutin by controlled acid hydrolysis; an authentic sample of 4-*O*-α-L-rhamnopyranosyl-D-glucose was supplied by Dr. G. O. Aspinall (York University, Ontario). α- and β-methyl-L-rhamnopyranoside were prepared according to Hough et al.[6]

3-*O*-α-L-Rhamnopyranosyl-D-glucose. A mixture of 0.68 g of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose, mercuric acetate (0.25 g), and α-acetobromorhamnose (0.66 g) was shaken in dry benzene (10 ml) for 4 days protected from atmospheric moisture in the dark at room temperature. The reaction mixture was washed twice with water, dried (Na_2SO_4), and filtered; removal of the solvent gave 0.55 g of residue (A). The acetyl groups were removed by shaking a solution of A in methanol (4 ml) with 0.1 N sodium methoxide (0.5 ml) at room temperature for 6 h, followed by neutralization with aqueous oxalic acid. Removal of most of the methanol at 40 °C (15 mm) was followed by the removal of isopropylidene groups by treatment of the residue with oxalic acid (0.01 N, 10 ml) at 100 °C for 3 h. After neutralization with barium carbonate and filtration, the remaining ions were removed by Amberlite IR-100H and IR-4B ion-exchange resins. Evaporation of the water left a colorless syrup (B). Examination on a paper chromatogram (solvent mixture: 1-butanol–acetic acid–water, 12:3:5) showed the presence of rhamnose (R_G 2.04), glucose (R_G 1), and a substance with R_G value 0.92 (3-*O*-α-L-rhamnopyranosyl-D-glucose). The syrup (B) was dissolved in water and from this solution the disaccharide was isolated by preparative chromatography on Whatman 3MM paper (solvent mixture: 1-butanol–acetic acid–water, 12:3:5). The bands (R_G 0.92) located by a test strip with aniline phosphate were excised and extracted with water. The aqueous extracts on evaporation to dryness in vacuo gave 62 mg of 3-*O*-α-L-rhamnopyranosyl-D-glucose ($[\alpha]_D$ +4 in water).

Acid Hydrolysis of Disaccharide. A solution of disaccharide (50 mg) in 10% acetic acid (50 ml) was refluxed for 3.5 h. The hydrolysate was evaporated to dryness in vacuo and excess acetic acid was removed by adding a small amount of water to the residue and evaporating to dryness. Examination on a paper chromatogram (solvent mixture: 1-butanol–acetic acid–water, 12:3:5) showed the presence of rhamnose and glucose.

Methylation of Disaccharide. 3-*O*-α-L-Rhamnopyranosyl-D-glucose (50 mg) was dissolved in dimethylformamide (20 ml); methyl iodide (20 ml) and silver oxide (5 g) were added. The mixture was stirred at room temperature in the dark for 18 h and filtered. The solution was evaporated to dryness and the residue dissolved in 0.3 N HCl (50 ml) and refluxed for 4 h; after cooling, the solution was taken to dryness in vacuo. The residue, dissolved in water, was analyzed for methylated sugars by paper chromatography according to Petek[7] and thin layer chromatography on silica gel (solvent mixture: ethyl acetate–chloroform, 1:1). 2,3,4-Tri-*O*-methyl-L-rhamnose and 2,4,6-tri-*O*-methyl-D-glucose were identified.

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Registry No.—1, 5158-64-5; 2, 582-52-5; 4, 36506-90-8; 2,3,4-tri-*O*-methyl-L-rhamnose, 7439-05-6; 2,4,6-tri-*O*-methyl-D-glucose, 4578-22-7.

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