series), its structure may be further specified by the designation alpha 4-*β*-*d*-galactosido (1,4)-*α*-*d*-fructose, the 1,4-ring being assigned to the galactose portion because of the ring structure of lactose shown in article XXVI. The ring of the fructose component remains unknown, but it obviously cannot be of the 2,4-type. The isolation of *d*-galactose and *d*-fructose by the acid hydrolysis of lactulose agrees with the assigned composition.

Summary

As an experimental introduction to the extension of the Lobry de Bruyn rearrangement for the synthesis of new ketoses, conditions for the conversion of lactose to a disaccharide ketose have been studied and a new ketose named lactulose has been isolated in pure crystalline condition. Lactulose is shown to be 4-*β*-*d*-galactosido(1,4)-*d*-fructose and the crystalline sugar is an alpha form.

WASHINGTON, D. C.

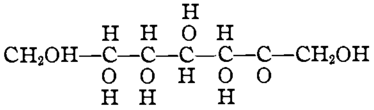
[CONTRIBUTION FROM THE POLARIMETRY SECTION, U. S. BUREAU OF STANDARDS]

RELATIONS BETWEEN ROTATORY POWER AND STRUCTURE IN THE SUGAR GROUP. XXVIII. THE CONVERSION OF *d*-ALPHA-GLUCOHEPTOSE TO A NEW KETOSE, *d*-GLUCOHEPTULOSE[1]

BY W. C. AUSTIN

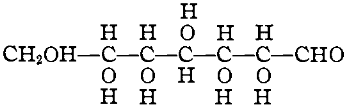
RECEIVED FEBRUARY 3, 1930 PUBLISHED MAY 8, 1930

It is to be expected on structural grounds that a new ketose of configuration (A) may be prepared in some suitable way from the known *d*-*α*-glucoheptose, of configuration[2] (B). The osazone of this hypothetical



$$CH_2OH-\underset{\substack{O\\H}}{\overset{H}{C}}-\underset{\substack{O\\H}}{\overset{H}{C}}-\underset{H}{\overset{\substack{H\\O}}{C}}-\underset{\substack{O\\H}}{\overset{H}{C}}-\underset{O}{C}-CH_2OH$$

A



$$CH_2OH-\underset{\substack{O\\H}}{\overset{H}{C}}-\underset{\substack{O\\H}}{\overset{H}{C}}-\underset{H}{\overset{\substack{H\\O}}{C}}-\underset{\substack{O\\H}}{\overset{H}{C}}-\underset{\substack{O\\H}}{\overset{H}{C}}-CHO$$

B

ketose should be identical with *d*-glucoheptose osazone, which has been prepared by Fischer[2] through the action of phenylhydrazine on either *d*-*α*-glucoheptose or *d*-*β*-glucoheptose. This ketose, to which the name *d-glucoheptulose* might well be given, should bear the same configurational relationship to the epimeric aldoses, *d*-*α*- and *d*-*β*-glucoheptose, as does *d*-fructose to *d*-glucose and *d*-mannose. The properties of *d*-glucoheptulose should apparently be of considerable interest because all the asymmetric

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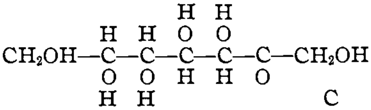
[1] Publication approved by the Director of the U. S. Bureau of Standards. The author was a National Research Fellow in Medicine, 1927–1928. He has arranged with Dr. C. S. Hudson, under whose direction the research was carried out, that it will be included as No. XXVIII in the series entitled "Relations between Rotatory Power and Structure in the Sugar Group." No. XXVII was published in THIS JOURNAL, **52,** 2101 (1930).

[2] Fischer, *Ann.*, **270,** 64 (1892).

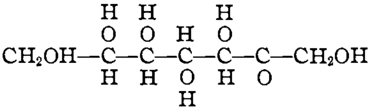
carbon atoms (Nos. 3, 4, 5 and 6) of the sugar have precisely the configurations of the corresponding asymmetric carbon atoms (Nos. 2, 3, 4 and 5) of the *d*-glucose molecule. Also, since *d*-mannoketoheptose, of configuration[3] C shows no mutarotation, it may be expected that its epimeric[4] ketose,



$$\begin{array}{ccccccc} & & & \mathrm{H} & \mathrm{H} & & \\ & \mathrm{H} & \mathrm{H} & \mathrm{O} & \mathrm{O} & & \\ \mathrm{CH_2OH}— & \mathrm{C}— & \mathrm{C}— & \mathrm{C}— & \mathrm{C}— & \mathrm{C}— & \mathrm{CH_2OH} \\ & \mathrm{O} & \mathrm{O} & \mathrm{H} & \mathrm{H} & \mathrm{O} & \\ & \mathrm{H} & \mathrm{H} & & & & \end{array}$$

C

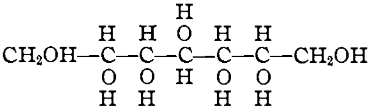
d-glucoheptulose, will not mutarotate. The value of the specific rotation of *d*-glucoheptulose may indeed be calculated in first approximation by adding the "epimeric difference of molecular rotation" (6700)[5] to the molecular rotation of *d*-mannoketoheptose ($[\alpha]_D + 29.2$) and dividing by the mol. wt. (210) of glucoheptulose, with the result that $[\alpha]_D = ((29.2)(210) + 6700)/210 = +61$. From these arguments it obviously follows that the antipodal sugar, *l*-glucoheptulose, of configuration



$$\begin{array}{ccccccc} & \mathrm{H} & \mathrm{H} & & \mathrm{H} & & \\ & \mathrm{O} & \mathrm{O} & \mathrm{H} & \mathrm{O} & & \\ \mathrm{CH_2OH}— & \mathrm{C}— & \mathrm{C}— & \mathrm{C}— & \mathrm{C}— & \mathrm{C}— & \mathrm{CH_2OH} \\ & \mathrm{H} & \mathrm{H} & \mathrm{O} & \mathrm{H} & \mathrm{O} & \\ & & & \mathrm{H} & & & \end{array}$$

may be expected to show $[\alpha]_D\ -61$, approximately, with no mutarotation.

These deductions from structural theory and rotatory relations appear to have an important bearing upon the results of some recent synthetic work in the sugar group. Bertrand and Nitzberg[6] have obtained a pure crystalline ketose, to which they give the name α-glucoheptulose, by the action of the sorbose bacterium upon a solution containing α-glucoheptitol, of configuration



$$\begin{array}{ccccccc} & & & \mathrm{H} & & & \\ & \mathrm{H} & \mathrm{H} & \mathrm{O} & \mathrm{H} & \mathrm{H} & \\ \mathrm{CH_2OH}— & \mathrm{C}— & \mathrm{C}— & \mathrm{C}— & \mathrm{C}— & \mathrm{C}— & \mathrm{CH_2OH} \\ & \mathrm{O} & \mathrm{O} & \mathrm{H} & \mathrm{O} & \mathrm{O} & \\ & \mathrm{H} & \mathrm{H} & & \mathrm{H} & \mathrm{H} & \end{array}$$

Since Bertrand has shown during his extended researches with this bacterium that the ketose which it produces in a given case results from the oxidation of the secondary alcohol group on the carbon atom that is adjacent to a terminal primary alcoholic carbon atom, he and Nitzberg consider that the bacterium probably oxidizes α-glucoheptitol either at its Carbon 2 or 6 and that the configuration of α-glucoheptulose is thus probably either

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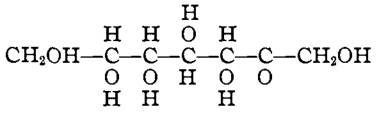
[3] La Forge, *J. Biol. Chem.*, **28**, 511 (1917).

[4] The concept of "epimeric" has been developed for aldoses (Votoček) but it is apparent that it can be extended to ketoses; see Hudson, THIS JOURNAL, **52**, 1680 (1930). Epimeric aldoses (*e. g.*, *d*-glucose and *d*-mannose) differ only in the configuration of their carbon atom 2; epimeric 2-ketoses (*e. g.*, *d*-glucoheptulose and *d*-mannoketoheptose) differ only in the configuration of their carbon atom 3.

[5] Hudson, *ibid.*, **48**, 1434 (1926).

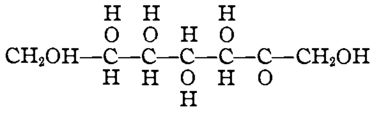
[6] Bertrand and Nitzberg, *Compt. rend.*, **186**, 925, 1172, 1774 (1928).



$CH_2OH-\underset{\underset{H}{O}}{\overset{H}{C}}-\underset{\underset{H}{O}}{\overset{H}{C}}-\underset{H}{\overset{\overset{H}{O}}{C}}-\underset{\underset{H}{O}}{\overset{H}{C}}-\underset{O}{C}-CH_2OH$

d-Glucoheptulose

or



$CH_2OH-\underset{H}{\overset{\overset{H}{O}}{C}}-\underset{H}{\overset{\overset{H}{O}}{C}}-\underset{\underset{H}{O}}{\overset{H}{C}}-\underset{H}{\overset{\overset{H}{O}}{C}}-\underset{O}{C}-CH_2OH$

l-Glucoheptulose

These configurations represent antipodal forms of one sugar and the designations *d* and *l* are used in the sense of the dextro and levo series of Fischer, without regard to the actual directions of rotations of the two enantiomorphs. The researches of Bertrand and Nitzberg have not as yet given a decision between these configurations for their α-glucoheptulose and they use this designation of the ketose in the purely empiric sense that the sugar is derived from α-glucoheptitol. Bertrand and Nitzberg report that α-glucoheptulose shows no mutarotation and that it is levorotatory, $[\alpha]_D$ -67.1. From the agreement of these data with the present deductions from rotatory relations, it seems highly probable that their ketose is *l*-glucoheptulose.

The rotation which has been calculated for *d*-glucoheptulose ($+61$) is of interest also in another respect, since it has now become probable from the data of the preceding paragraph that these calculations are substantially correct. The known alpha form of *d*-mannose (mol. wt. 180) shows[7] $[\alpha]_D$ $+30$ and the 1,A = 1,4-ring has been assigned to it by Hudson.[8] By use of the epimeric difference of rotation Hudson[9] calculated from this value the rotation of the epimeric alpha *d*-glucose, of 1,A = 1,4-ring structure, to be $[\alpha]_D = ((30)(180) + 6700)/180 = +67$. Neither of the two known crystalline forms of *d*-glucose (of $[\alpha]_D$ $+113$ and $+19$, respectively), can be this substance and Hudson concluded that the calculated value must refer to a form of *d*-glucose which has not yet been isolated. If it should now prove possible to isolate a crystalline form of *d*-glucoheptulose having an $[\alpha]_D$ value of approximately $+61$, strong evidence would be at hand for the belief that alpha *d*-glucose of 1,A = 1,4-ring structure rotates near $+67$, because the calculated rotation of *d*-glucoheptulose is obtained from that of *d*-mannoketoheptose by the same method that the rotation of α-*d*-glucose (1,A = 1,4) is obtained from that of α-*d*-mannose (1,A = 1,4). Moreover, the close agreement between the values of $[\alpha]_D$ for α-*d*-mannose (1,A = 1,4) ($+30$) and *d*-mannoketoheptose ($+29.2$) has its counterpart in the agreeing calculated rotations of α-*d*-glucose (1,A = 1,4) ($+67$) and *d*-glucoheptulose ($+61$), which may be correlated with the like configurations of the asymmetric carbon atoms in the members of each of these pairs, as has been indicated.

These various considerations and correlations, which were disclosed to me by Dr. Hudson shortly after the appearance of Bertrand and Nitzberg's

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[7] Levene, *J. Biol. Chem.*, **57**, 329 (1923).

[8] Hudson, This Journal, **48**, 1424 (1926); **52**, 1680 (1930).

[9] Hudson, *ibid.*, **48**, 1434 (1926).

first paper, made the synthesis of *d*-glucoheptulose from *d*-α-glucoheptose by some chemical method which would leave no uncertainty regarding the configuration of the resulting ketose appear very desirable and the work was accordingly undertaken. It was noticed that Philippe[10] had sought to accomplish this synthesis through the reactions *d*-α-glucoheptose ⟶ *d*-α-glucoheptose osazone ⟶ *d*-glucoheptulose, which would be analogous to the methods by which Fischer[11] converted *d*-glucose to *d*-fructose, but that he was unable to carry out the second stage. Repetition of Philippe's work by the writer led likewise to failure. Success came, however, through the use of Lobry de Bruyn's method of conversion of an aldose to a ketose in weakly alkaline solution. It has been possible in this way to synthesize *d*-glucoheptulose with a yield of about 30% by applying to *d*-α-glucoheptose the procedure through which Montgomery and Hudson[12] have recently synthesized lactulose from lactose in this Laboratory. Proof that the new heptose is a ketose was readily obtained from the observation that it is not oxidized by bromine water. Since its osazone proved to be identical with that of *d*-α-glucoheptose in analysis, melting point and mixed melting point, solubility and mixed solubility,[12] rotation and mutarotation, it seems certain that the ketose has the indicated configuration of *d*-glucoheptulose. The sugar crystallizes in prisms of m. p. 171–174°, shows no mutarotation and is dextrorotatory, $[\alpha]_D^{20}$ +67 in dilute aqueous solution. These results, which have been very carefully established, agree in every respect with the theoretical deductions from rotatory relations. They show that the α-glucoheptulose of Bertrand and Nitzberg is *l*-glucoheptulose (m. p. 173.5°, $[\alpha]_D$ −67), the optical antipode of the synthetic *d*-glucoheptulose. The existence of this *d*-glucoheptulose, of $[\alpha]_D$ +67, is strong experimental evidence that Hudson's calculation of +67 for the rotation of the now unknown α-*d*-glucose, of the 1,A = 1,4-ring structure, is substantially correct.

Preparation of *d*-Glucoheptulose.—Following the directions of Wolfrom and Lewis[13] for the enolization of aldoses in alkaline solution, a saturated solution of calcium hydroxide in water at 35° was prepared and some *d*-α-glucoheptose was dissolved in it to make a 10% solution. At 35° the $[\alpha]_D$ value changed from an initial rotation of about −20, the equilibrium rotation of *d*-α-glucoheptose, to −17 after one hour, 0 after ten hours, +30 after forty-six hours, and became constant after about seven days at +40. An iodine estimation of aldoses in this equilibrated solution showed about 40% aldose and 60% ketose. In a second experiment the end rotation was $[\alpha]_D$ +35. These two solutions, representing 55 g. of *d*-α-glucoheptose, were united and concentrated under reduced pressure to about 75 cc. and an equal volume of methyl alcohol was mixed with the sirup. A crop of 4.5 g. of crystalline *d*-α-glucoheptose separated from the solution when it was kept overnight in the ice box. A second crop of 5 g. of the original aldose

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[10] Philippe, *Ann. chim. phys.*, **26**, 324 (1912).

[11] Fischer, *Ber.*, **22**, 87 (1889); Fischer and Tafel, *ibid.*, **20**, 2566 (1887).

[12] Montgomery and Hudson, THIS JOURNAL, **52**, 2101 (1930).

[13] Wolfrom and Lewis, *ibid.*, **50**, 837 (1928).

was obtained from the mother liquor by concentration and like treatment. The second mother liquor was concentrated to a thick sirup which was dissolved in about 600 cc. of methyl alcohol. An amorphous residue was filtered off, 200 cc. of absolute ether was added to the filtrate and more amorphous material was filtered off with the aid of decolorizing carbon. The clear and nearly colorless filtrate was concentrated to a sirup, taken up in about 45 cc. of alcohol and the solution was kept in a vacuum desiccator. After several days crystal foci appeared and on stirring with 80% ethyl alcohol the mass quickly solidified and yielded 27 g. of a new sugar, *d*-glucoheptulose, showing $[\alpha]_D$ +66, without mutarotation. The sugar was recrystallized several times, to constant rotation, by dissolving it in a small amount of water and adding alcohol or glacial acetic acid. It tastes quite sweet. It crystallizes very readily as well-formed prisms of m. p. 171–174°, after softening at 167°. It is anhydrous, does not lose weight on heating at 100° under reduced pressure in the presence of phosphorus pentoxide, and its analysis corresponds to the formula for a heptose, $C_7H_{14}O_7$. The combustion of 0.2-g. samples gave C, 39.81 and 39.72; H, 6.75 and 6.86; calcd.: C, 40.00; H, 6.67. The pure sugar showed $[\alpha]_D^{20}$ +67.46 in 2.5% aqueous solution and 67.66 in 10% solution; hence $[\alpha]_D^{20} = 67.4 + 0.027\ C$ (where C is concentration) in this range. Decrease of temperature increases the rotation and the formula $[\alpha]_D^t = +67.4 + 0.027p - 0.027\ (t-20)$ applies over the range t = 15–30°. Since *d*-glucoheptulose and *d*-sorbose are similar in configuration for carbons 3, 4 and 5, it is interesting to note that they are much alike in the ease of crystallization, absence of mutarotation, and the influence of concentration and temperature on their rotations. The dextrorotation of *d*-sorbose ($[\alpha]_D$ +43) increases with concentration and decreases with rise of temperature.[14] For the mercury yellow line the $[\alpha]_{578}^{20}$ value of *d*-glucoheptulose is +70.28 in 2.5% solution and for the mercury green line $[\alpha]_{546.1}^{20}$ +79.5 and $[\alpha]_{546.1}^{29.3}$ 79.11 in 2.5% solution.

In the first experiment it was possible to obtain the ketose in pure form, unmixed with *d*-α-glucoheptose, but in subsequent preparations the two sugars were obtained as a crystalline mixture, due probably to the existence of crystal nuclei of the ketose in the laboratory. The separation of the ketose from this mixture is best accomplished by the oxidation of the aldose with bromine water containing barium benzoate,[15] which leaves the ketose largely unaffected. The precise directions may be omitted, as they have been published for the similar separation of lactose and lactulose by Montgomery and Hudson.[12] The yield of purified ketose when the bromine oxidation step was included in the procedure was about 30% of the weight of the original *d*-α-glucoheptose.

d-Glucoheptulose is not fermented by baker's yeast. It reduces Fehling's solution on heating and yields 87.6% of the weight of cuprous oxide that is produced by an equal quantity of anhydrous *d*-glucose. It is not oxidized by the hypoiodite reagent and is therefore a ketose. It gives a blue color in the orcin test, stronger than that produced by *d*-xylose and weaker than that shown by *d*-α-glucoheptose. With phloroglucin the same order of color development was found. The ketose also gives positive Seliwanoff and Pinoff tests, as does fructose, while the aldoses do not develop color in these tests; the intensity of the color was much greater for fructose than for *d*-α-glucoheptulose.

Identity of the Osazones of *d*-Glucoheptulose and *d*-α-Glucoheptose.—The osazone of the ketose was prepared by heating a solution of 5 g. of sugar, 15 cc. of phenylhydrazine, 10 cc. of glacial acetic acid and 50 cc. of water for five hours on the steam-bath. After twenty-four hours' standing in the ice box, a good crop of yellow needle crystals was

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[14] Tollens and Smith, *Ber.*, **33**, 1289 (1900). Their measurements were upon the levorotatory *l*-sorbose. Bertrand and Nitzberg (Ref. 6, first article) have called attention to the marked resemblance of their α-glucoheptulose (which may now be designated *l*-glucoheptulose) to *l*-sorbose.

[15] Hudson and Isbell, This Journal, **51**, 2225 (1929).

obtained, weighing 5.5 g. after washing with warm water, 95% alcohol and ether and drying. It was purified by dissolving it in 500 cc. of hot absolute alcohol, treating the solution with decolorizing carbon and keeping it in the ice chest for several days. *Anal.* Combustions of samples weighing 0.2 to 0.3 g. showed C, 58.40 and 58.63; H, 6.32 and 6.36; N (Dumas), 14.43 and 14.25. Calcd. for $C_{19}H_{24}O_5N_4$: C, 58.76; H, 6.19; N, 14.43. The melting point was 194–195° with decomposition after darkening at 185–189°. A solution of 0.4 g. of osazone in 10 cc. of pyridine and 15 cc. of absolute alcohol showed $[\alpha]_D^{20}$ -5.3 two minutes after preparation, $+9.6$ after two and three-fourths hours and $+35.0$ final (ninety-six hours).

The osazone of *d*-α-glucoheptose was prepared similarly and recrystallized twice. *Anal.* N (Dumas), 14.64; calcd. 14.43. The melting point was 194–195° with decomposition after darkening at 189–190°. A solution of 0.4 g. of osazone in the usual pyridine–alcohol mixture showed $[\alpha]_D^{20}$ -1 two minutes after preparation, $+9$ after 2.9 hours and $+35.6$ final (ninety-six hours). A mixture of the two osazones melted at 194–195° with decomposition after darkening in the usual manner. These data show that the two osazones are the same chemical compound, namely, *d*-glucoheptose osazone, according to the usual tests that are applied to osazones.[16]

These tests have been supplemented by one which Montgomery and Hudson[12] have lately suggested in connection with the proof of the identity of the anhydro-osazone from lactose and lactulose, namely, the thermodynamic criterion that the solubility of a mixture of two pure samples of the same chemical substance has the same value as the solubility of either sample alone. This test, which is analogous to the mixed melting point test of substances which do not decompose on melting, is rigorous for osazones because there is no decomposition at the temperature of the solubility measurement, whereas the decomposition that occurs on melting invalidates, from the standpoint of thermodynamic theory, the strict applicability of the mixed melting point test for most osazones. The solubility of *d*-α-glucoheptose osazone in acetone at 20° from undersaturation was 0.0806 g. per 25 cc. of acetone, from supersaturation 0.0814 g.; that of *d*-glucoheptulose osazone was 0.0796 g. from undersaturation and 0.0793 g. from supersaturation, and the solubility of a mixture of the two osazones was 0.0794 g. from undersaturation and 0.0792 g. from supersaturation. Equilibrium was attained in twenty-four to forty-eight hours. This is decisive proof that the two osazones are identical because if such were not the case the mixed solubility would be of the order $0.081 + 0.079 = 0.160$ g. This method is highly recommended in the case of substances for which the mixed melting point test is not theoretically sound because of decomposition on melting or other complications.

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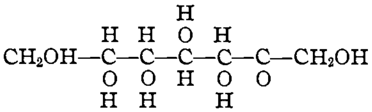
[16] Bertrand and Nitzberg (Ref. 6, first article) state that the osazone of their ketose is identical with *d*-α-glucoheptose osazone but they make no mention of the rotations of the two substances. It seems quite unlikely from the results of the present investigation that the two osazones can be identical. It is to be expected that they are enantiomorphous substances and that the osazone of Bertrand and Nitzberg's ketose, *l*-glucoheptulose, will show a rotation equal to that of *d*-glucoheptose osazone but of opposite sign.

The author wishes to thank the Medical Fellowship Board of the National Research Council for the award of a fellowship which made possible the carrying out of this research. He also expresses his deep indebtedness to Dr. C. S. Hudson for many valuable suggestions.

Summary

A new crystalline ketose, *d*-glucoheptulose, of configuration



$$\begin{array}{rcccccccccl} & & & & & \mathrm{H} & & & & & \\ & \mathrm{H} & & \mathrm{H} & & \mathrm{O} & & \mathrm{H} & & & \\ \mathrm{CH_2OH}— & \mathrm{C} & — & \mathrm{C} & — & \mathrm{C} & — & \mathrm{C} & — & \mathrm{C} & —\mathrm{CH_2OH} \\ & \mathrm{O} & & \mathrm{O} & & \mathrm{H} & & \mathrm{O} & & \mathrm{O} & \\ & \mathrm{H} & & \mathrm{H} & & & & \mathrm{H} & & & \end{array}$$

has been synthesized from *d*-α-glucoheptose by use of the procedure which Montgomery and Hudson have recently developed for the synthesis of ketoses from aldoses through the Lobry de Bruyn rearrangement. It proves to be the optical enantiomorph of the ketose which Bertrand and Nitzberg recently made through the action of the sorbose bacterium upon a solution of α-glucoheptitol and their ketose is accordingly *l*-glucoheptulose. The rotation of *d*-glucoheptulose, which does not exhibit mutarotation, is near the value that was predicted by the rotatory relations developed by Hudson. The existence of this ketose, of the calculated rotation, is strong evidence that Hudson's calculation of +67 for the $[\alpha]_D$ value of an unknown α-*d*-glucose, of the 1,A = 1,4-ring type, is substantially correct.

WASHINGTON, D. C.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF WEST VIRGINIA UNIVERSITY]

ESTERS OF CYCLOHEXYLRESORCINOL AND PARA-CYCLOHEXYLPHENOL[1]

BY VIRGIL GREENE LILLY AND C. E. GARLAND

RECEIVED FEBRUARY 6, 1930 PUBLISHED MAY 8, 1930

In view of the excellent germicidal properties of some of the alkyl and aryl substituted hydroxy derivatives of benzene[2] and their general low toxicity, some esters, of the salol type, have been prepared using cyclohexylresorcinol[2,3] and *p*-cyclohexylphenol, with a hope that they may prove of therapeutic value.[4]

In general, esters of cyclohexylresorcinol are rather difficult to prepare, while those of *p*-cyclohexylphenol are less so. Cyclohexylresorcinol does

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[1] This communication is an abstract of part of a thesis submitted by Virgil Greene Lilly in partial fulfilment of the requirements for the degree Master of Arts in Chemistry at West Virginia University.

[2] For a list of important contributions see Bartlett and Garland, THIS JOURNAL, **49**, 2098 (1927).

[3] Philips, U. S. Patent 1,650,036.

[4] Kursanoff, *Ann.*, **318**, 309 (1901); Wuyts, *Bull. soc. chim. Belg.*, **26**, 304 (1912); Schrauth and Görig, *Ber.*, **56**, 1900 (1923); v. Braun, *Ann.*, **472**, 61 (1929).