tracted with chloroform, and the chloroform extracts subjected to preparative TLC using benzene – EtOAc 1:1; yield 5 %. ^{1}H NMR ($CDCl_3$): δ 3.35 (CH_2-S), 4.46 (CH_2-N), 6.20 (H-6), 7.22 [(H-7), $J_{6,7}$ 8.5 Hz].

1. Lærum, T. and Undheim, K. *Acta Chem. Scand. B 32* (1978) 68. Part XLVIII.
2. Hagen, S., Ulsaker, G. A. and Undheim, K. *Acta Chem. Scand. B 28* (1974) 523.
3. Lewis, E. S. and Johnson, M. D. *J. Am. Chem. Soc. 81* (1959) 2070.
4. Davies, L. S. and Jones, G. *J. Chem. Soc. C* (1970) 688.
5. Kønig, W., Coenen, M., Lorenz, W., Bahr, F. and Bassl, A. *J. Prakt. Chem. 30* (1965) 96.
6. Kønig, W., Coenen, M., Bahr, F., May, B. and Bassl, A. *J. Prakt. Chem. 33* (1966) 54.
7. Kühn, R. and Drawert, R. *Justus Liebigs Ann. Chem. 590* (1954) 55.
8. Abramovitch, R. A. and Vinutha, A. R. *J. Chem. Soc. B* (1971) 131.
9. Den Hertog, H. J. and van der Plas, H. C. In Viehe, H. G., Ed., *Chemistry of Acetylenes*, Decker, New York 1969, p. 1149.
10. Lærum, T. and Undheim, K. *Unpublished work.*
11. Undheim, K., Nordal, V. and Tjønneland, K. *Acta Chem. Scand. 23* (1969) 1704.

Received October 31, 1977.

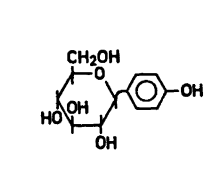
Reaction of D-Glucose with Phenol and with Pyrogallol under Acidic Conditions

PER-ÅKE PERNEMALM

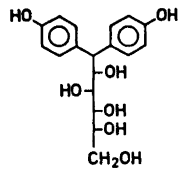
Department of Chemistry, Swedish University of Agricultural Sciences, S-750 07 Uppsala 7, Sweden

Phenols are formed when carbohydrates are degraded in aqueous weak acid [1,2] or in alkali,[3] and phenolic compounds have also been isolated from the reaction of glucose with methylamine [4] or glycine [5] (the Maillard reaction). As the phenols are isolated in lower yields in the presence of amines, it is reasonable to assume that amines, besides favouring the formation of other reaction products, catalyze the further reactions of the phenols. The phenols may react to some extent with the large excess of unreacted carbohydrates present in the reaction mixture.

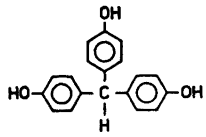
In acidic media, glucose may attack phenol at oxygen or carbon. The former reaction yields phenyl glucosides,[6] while the latter (Friedel-Crafts) reaction yields phenylglucitol derivatives. Thus, *2* has been isolated from the reaction mixture of phenol and glucose in hydrogen fluoride.[7] In an early investigation of the reaction between glucose and phenol in hydrogen chloride-acetic acid or in concentrated hydrochloric acid, one water-soluble (A), one water- and benzene-insoluble (B) and one benzene-soluble (C) reaction product were isolated.[8] This investigation has now been repeated, using chromatographic and spectroscopic techniques.



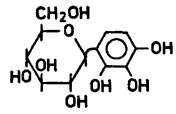
1



2



3



4

Product A was a complex mixture, while B seemed to be a polymeric material. Product C was pure leucoaurin (*3*). Product A was fractionated on silica gel columns and phenyl α- and β-D-glucopyranoside and *1* and *2* were isolated. The molecular formula of *1* was

established by high-resolution mass spectrometry, and the initial fragmentation of the glucose moiety indicated a *C*-glucoside.[9] This was confirmed by the ^{1}H NMR spectrum, which showed the presence of a *para*-disubstituted phenyl group. The pyranose structure followed from the uniquely high field position (δ 3.72–3.94) of the H-5 multiplet and the *S* configuration from the large splitting ($J_{1,2}$ 9.5 Hz) of the H-1 doublet in the well-resolved ^{1}H NMR spectrum of the pentaacetate. Compound *2* was identified by spectral means and previously published data.[12] Compounds *1*–*3* are analogues of reaction products from anisole and glucose in hydrogen fluoride,[10] and the original tentative structures suggested for A, B and C [8] are inconsistent with the present results.

Pyrogallol was one of the phenols isolated from the reaction of glucose in water at pH 4–5 with [5] and without [2] the presence of glycine. In order to investigate aromatic substitution reactions under similar conditions, glucose was treated with an equimolar amount of pyrogallol in acetate buffer (pH 4.6) at reflux temperature. In a parallel run an equimolar amount of glycine was added. From the latter experiment the new compound *4* was isolated by column chromatography and identified analogously to *1*. Small portions were removed during the reaction and analyzed by GLC [11] (Fig. 1). It was found that glycine

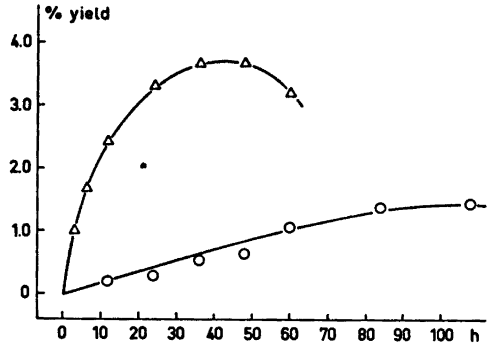


Fig. 1. The formation of 1,5-anhydro-1-*C*-(2,3,4-trihydroxyphenyl)-(*S*)-D-glucitol (*4*) from pyrogallol and D-glucose in acetate buffer at 100 °C. △, with glycine; ○, without glycine.

catalyzes the formation of *4*, probably owing to the formation of immonium ions with glucose.

The formation of aryl *C*-glycosides and related compounds in weakly acidic solutions may be important when brown polymeric substances are formed in carbohydrate degradations as well as in reactions between lignins and carbohydrates, for example in humification and in pulping processes.

Experimental. Evaporations were performed under reduced pressure below 40 °C. TLC was effected with silica gel (Merck, HF_{254}). Ethanolic *p*-anisaldehyde–sulfuric acid and aq. iron(III) chloride were used as spray reagents. CC was carried out on silica gel (Merck, 230-400 mesh). Compound *4* was analyzed by GLC [11] as its per(trimethylsilyl) ether on a Varian 1840 instrument, using inositol as internal standard, and a column containing 3 % OV-1 on Varaport 30 (100–120 mesh). The temperature was programmed from 200 to 300 °C at 6 °C/min. IR spectra were recorded on a Perkin-Elmer 337 and ^{1}H NMR spectra on a Varian HA-100 D instrument. Low- and high-resolution mass spectra were recorded on Varian MAT CH 7 and AEI MS 902 instruments respectively, the latter spectra at the Institute of Medical Biochemistry, University of Gothenburg.

Reaction of D-*glucose and phenol.* Products A, B and C were prepared from D-glucose (90.0 g) and phenol (47.0 g) and isolated as previously described (slow process).[8] A (9.1 g) was charged on a silica gel column and eluted with ethyl acetate–ethanol–water, 83:11:6 (v/v/v). The mixture of slower moving compounds were rechromatographed on a silica gel column with aqueous 2-butanone. The separation was monitored by TLC, using the same eluent. Two fractions were collected: 1. A mixture of phenyl α,β-D-glucopyranoside (identified by TLC) and *2*, from which *2* crystallized on standing. 2. Compound *1*.

*1,5-Anhydro-1-C-(4-hydroxyphenyl)-(S)-*D-*glucitol* (1). Colourless syrup, 62 mg. $[\alpha]_{5780}^{20}$ +19° (*c* 1.5, ethanol). MS [IP 70 eV; *m/e* (% rel. int.)]: 256 (0.7, *M*), 238 (6), 166 (7), 165 (32), 136 (7), 124 (9), 123 (*100*), 121 (13), 107 (40), 95 (21), 77 (17), 60 (20), 57 (10), 43 (8). Mol. wt., obs. 256.096, calc. for $C_{12}H_{16}O_6$ 256.095. ^{1}H NMR (100 MHz, CD_3OD): δ 3.25–3.95 (6 H, m), 4.05 (1 H, d, $J_{1,2}$ 8.5 Hz, H-1), 6.76 (2 H, d, *J* 9.0 Hz), 7.23 (2 H, d, *J* 9.0 Hz). IR (film): 3340 (s), 1610 (m), 1600 (m), 1510 (m), 1425 (m), 1250 (m), 1230 (m), 1085 (s), 1045 (s), 905 (w), 880 (w), 835 (s), 805 (w) cm^{-1}. Acetylation (Ac_2O/pyridine) yielded the *pentaacetate*, recrystallized from isopropyl ether, m.p. 163–164 °C. Anal. $C_{22}H_{26}O_{11}$: C, H. ^{1}H NMR (100 MHz, $CDCl_3$): δ 1.80 (3 H, s), 1.98 (3 H, s), 2.04 (3 H, s), 2.07 (3 H, s), 2.26 (3 H, s), 3.72–3.94 (1 H, m, H-5), 4.15 (1 H, dd, $J_{5,6}$ 2.1 Hz, $J_{6,6'}$ −12.5 Hz, H-6), 4.27 (1 H, dd, $J_{5,6'}$ 4.9 Hz, H-6'), 4.40 (1 H, d, $J_{1,2}$ 9.5 Hz, H-1), 5.00–5.46 (3 H, m, H-2, H-3 and H-4), 7.08 (2 H, d, *J* 8.5 Hz), 7.35 (2 H, d, *J* 8.5 Hz).

*1-Deoxy-1,1-bis(4-hydroxyphenyl)-*D-*glucitol* (*2*) was recrystallized from ethyl acetate, 125 mg, m.p. 177–178 °C. (lit.[12] 176–177 °C). MS [IP 70 eV; *m/e* (% rel. int.)]: 201 (12), 200

(49), 199 (*100*), 181 (10), 153 (6), 152 (6), 107 (16), 55 (9), 44 (21), 43 (17). ^{1}H NMR (100 MHz, CD_3OD): δ 3.55–3.75, (5 H, m, H-3, H-4, H-5, H-6 and H-6'), 4.11 (1 H, d, $J_{1,2}$ 10.0 Hz, H-1), 4.41 (1-H, dd, $J_{2,3}$ 1.5 Hz, H-2), 6.66 (2 H, d, J 8.5 Hz), 6.70 (2 H, d, J 8.5 Hz), 7.12 (2 H, d, J 8.5 Hz), 7.20 (2 H, d, J 8.5 Hz).

Product B (46 g) seemed to be polymeric material (TLC) and was not further investigated.

Tris(4-hydroxyphenyl)methane (Product C, leucoaurin) (*3*), 33 mg, m.p. 235–237 °C (lit. 240 °C). MS [IP 70 eV; *m/e* (% rel.int.)]: 293 (20), 292 (*100*, *M*), 291 (34), 275 (32), 199 (62), 198 (35), 197 (28), 181 (18), 115 (11), 65 (11).

^{1}H NMR (100 MHz, CD_3OD): δ 5.25 (1 H, s), 6.66 (6 H, d, J 8.5 Hz), 6.86 (6 H, d, J 8.5 Hz).

Reaction of D-*glucose and pyrogallol.* A solution of D-glucose (18.0 g), pyrogallol (12.6 g) and glycine (7.5 g) in acetate buffer (200 ml, 0.5 M, pH 4.6) was refluxed for 60 h. During the reaction, small portions were removed for GLC analysis. The water was evaporated and the residue treated with abs. ethanol in an ultrasonic bath for 2 h. The supernatant was evaporated and charged on a silica gel column, which was eluted with aq. 2-butanone. The separation was monitored by TLC and *4* was isolated.

*1,5-Anhydro-1-*C*-(2,3,4-trihydroxyphenyl)-*(S)*-*D*-glucitol (4).* Amorphous, 135 mg. $[\alpha]_{5780}^{20}$ +30° (*c* 1.6, ethanol). MS [IP 70 eV; *m/e* (% rel.int.)]: 288 (3, *M*), 270 (9), 252 (2), 234 (3), 198 (5), 179 (9), 178 (10), 168 (27), 155 (10), 140 (12), 139 (*100*), 138 (18), 126 (24) 65 (12), 43 (21). Mol. wt., obs. 288.086, calc., for $C_{12}H_{16}O_8$ 288.085. ^{1}H NMR (100 MHz, CD_3OD): δ 3.25–3.95 (6H, m), 4.44 (1H, d, $J_{1,2}$ 9.0 Hz, H-1), 6.37 (1H, d, J 8.5 Hz), 6.68 (1H, d, J 8.5 Hz). IR (KBr): 3360 (s), 1740 (w), 1630 (m), 1510 (m), 1480 (m), 1370 (m), 1310 (m), 1240 (m), 1075 (s), 1015 (s), 885 (w), 800 (w) cm^{-1}. Acetylation (Ac_2O/pyridine) yielded the *heptaacetate*, recrystallized from isopropyl ether, m.p. 148–150 °C. Anal. $C_{26}H_{30}O_{15}$: C, H. ^{1}H NMR (100 MHz, $CDCl_3$): δ 1.83 (3 H, s), 2.01 (3 H, s), 2.06 (3 H, s), 2.10 (3 H, s), 2.26 (6 H, s), 2.35 (3 H, s), 3.69–3.92 (1 H, m, H-5), 4.10 (1 H, dd, $J_{5,6}$ 2.1 Hz, $J_{6,6'}$ −12.5 Hz, H-6), 4.27 (1H, dd, $J_{5,6'}$ 5.4 Hz, H-6'), 4.60 (1 H, d, $J_{1,2}$ 9.0 Hz, H-1), 5.06–5.46 (3 H, m, H-2, H-3 and H-4), 7.19 (1 H, d, J 9.0 Hz), 7.38 (1 H, d, J 9.0 Hz).

The same reaction was also carried out without glycine, but was only used for GLC analysis of *4* (Fig. 1).

Acknowledgements. The author thanks Professor Olof Theander and Docent Kjell Olsson for valuable discussions, Mr. Rolf Andersson and Mr. Suresh Gohil for recording and help in interpreting the NMR and mass spectra, and Mr. Tomas Nyhammar for skilled technical assistance.

1. Popoff, T. and Theander, O. *Carbohydr. Res. 22* (1972) 135.
2. Popoff, T. and Theander, O. *Acta Chem. Scand. B 30* (1976) 397.
3. Forsskåhl, I., Popoff, T. and Theander, O. *Carbohydr. Res. 48* (1976) 13.
4. Olsson, K., Pernemalm, P.-Å., Popoff, T. and Theander, O. *Acta Chem. Scand. B 31* (1977) 469.
5. Olsson, K., Pernemalm, P.-Å. and Theander, O. *Acta Chem. Scand. In press.*
6. Conchie, J., Levvy, G. A. and March, C. A. *Adv. Carbohydr. Chem. 12* (1957) 157.
7. Linn, C. B. *Am. Chem. Soc. Div. Petrol. Chem. Prepr. 2* (1957) 173.
8. Niederl, J. B. and Mauermeyer, R. K. *J. Am. Chem. Soc. 61* (1939) 1005.
9. Prox, A. *Tetrahedron 24* (1968) 3697.
10. Micheel, F. and Stanek, Jr., J. *Justus Liebigs Ann. Chem. 759* (1972) 37.
11. Sweeley, C. C., Bentley, R., Makita, M. and Wells, W. W. *J. Am. Chem. Soc. 85* (1963) 2497.
12. Heerema, J., Bollenback, G. N. and Linn, C. B. *Am. Chem. Soc. Div. Petrol. Chem. Prepr. 2* (1957) 185.

Received September 26, 1977.