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REACTIONS OF D-XYLOSE AND D-GLUCOSE IN ALKALINE, AQUEOUS SOLUTIONS*

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ABSTRACT

Treatment of D-xylose and D-glucose with 0.63M sodium hydroxide at 96° in an atmosphere of nitrogen yielded, in addition to acidic, aliphatic degradation-products, the following cyclic enols and phenolic compounds: 2-hydroxy-3-methyl-2-cyclopenten-1-one (**1**), 2-hydroxy-3,4-dimethyl-2-cyclopenten-1-one (**2**), pyrocatechol (**3**), 3-methyl-1,2-benzenediol (**4**), 4-methyl-1,2-benzenediol (**5**), 3,4-dimethyl-1,2-benzenediol (**6**), 2-methyl-1,4-benzenediol (**7**), 2,5-dihydroxyacetophenone (**8**), 3-hydroxy-5-methylacetophenone (**9**), 3,4-dihydroxyacetophenone (**10**), 3,4-dihydroxybenzaldehyde (**11**), 2,3,4-trihydroxy-5-methylacetophenone (**12**), and 2,3-dihydroxy-6-methylacetophenone (**13**).

INTRODUCTION

We recently reported the isolation of a series of cyclic degradation products, including catechols and chromones, after the exposure of hexuronic acids and pentoses to slightly acidic conditions[1,2].

The treatment of sugars with alkali has been extensively studied[3–5], interest being mainly focussed on isomerisation and the formation of saccharinic acids and acyclic fragments. Lactic, glycolic, dihydroxybutyric, acetic, and formic acids have been reported in yields of 7–60%, whereas acetol, methylglyoxal (pyruvaldehyde), pyruvic acid, reductone, and biacetyl have been detected only in smaller amounts[4]. Hoppe-Seyler[6] reported indications of the formation of enols and phenols by the treatment of sugars with alkali. Enkvist *et al.*[7,8] reported the formation of aromatic compounds and cyclic enols, and identified small amounts of 2-hydroxy-3-methyl-2-cyclopenten-1-one (**1**), after the degradation of mono- and oligo-saccharides under

*Formation of Aromatic Compounds: Part II. For Part I, see Ref. 1.

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strongly alkaline conditions. Shaw *et al.*[9] reported the formation of a series of compounds from the treatment of D-fructose with a slightly alkaline, aqueous solution, including several furan derivatives, **1**, 2-hydroxy-3,4-dimethyl-2-cyclopenten-1-one (**2**), and the corresponding 3,5-isomer. The last three compounds, having strong caramel-like odours, had, together with two other cyclic diketones, previously been isolated by Gianturco *et al.*[10] from the aroma-complex of roasted coffee.

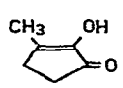
When this work was in progress, the formation of three benzoquinones and the catechols **3–5** was reported as products of the alkaline degradation of sucrose[11]. The benzoquinones were not formed on similar treatment of glucose and fructose.

We now report the isolation of **1**, **2**, and a series of phenols from the treatment of D-xylose and D-glucose with aqueous alkali.

RESULTS AND DISCUSSION

T.l.c. and g.l.c. of the ether extracts of solutions of D-xylose and D-glucose in aqueous sodium hydroxide which had been stored at 96° for 4 h showed an apparent similarity in the pattern of reaction products. The complex mixture of extracted products gave positive reactions with reagents for phenolic and carbonyl compounds. The acidic degradation products present in the aqueous phases were not examined, as such products have been thoroughly studied[3–5,12].

In large-scale experiments, separate 8% solutions of D-xylose and D-glucose in 0.63M sodium hydroxide were stored at 96° for 4 h under nitrogen. The product mixtures then obtained by extraction with ethyl acetate and ether were fractionated on Sephadex LH-20, and the main compounds (**1–13**) were isolated and identified. Some minor phenolic products were also isolated but not further studied.



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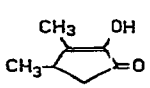

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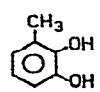

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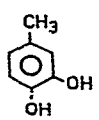

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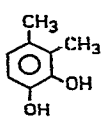

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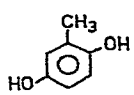

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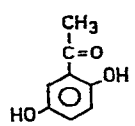

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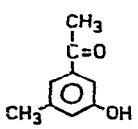

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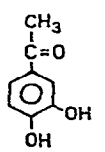

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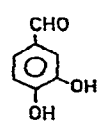

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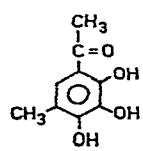

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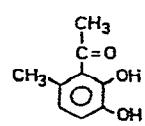

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The yields of the isolated compounds, determined by g.l.c. of the ether extracts, gravimetrically, or by g.l.c. of the Sephadex fractions, are given in Table I, together with chromatographic properties. The proportions of identified compounds were similar in the two experiments; the somewhat higher yield (4%) of the products extracted from the xylose reaction than from the glucose reaction (1.9%) was probably due to the higher solubility of the condensation products of high molecular weight in ethyl acetate than in ether.

Compounds **1**–**8**, **10**, **11**, and **13** were identified, on the basis of spectroscopic data (i.r., m.s., u.v., and n.m.r.) and by comparison with authentic samples (m.p. and mixture m.p.), as 2-hydroxy-3-methyl-2-cyclopenten-1-one (**1**), 2-hydroxy-3,4-dimethyl-2-cyclopenten-1-one (**2**), pyrocatechol (**3**), 3-methyl-1,2-benzenediol (**4**), 4-methyl-1,2-benzenediol (**5**), 3,4-dimethyl-1,2-benzenediol (**6**), 2-methyl-1,4-benzenediol (**7**), 2,5-dihydroxyacetophenone (**8**), 3,4-dihydroxyacetophenone (**10**), 3,4-dihydroxybenzaldehyde (**11**) and 2,3-dihydroxy-6-methylacetophenone (**13**).

The colour reaction of **9** indicated the presence of a carbonyl group, and m.s. gave a molecular weight of 150 and showed a dominating loss of methyl characteristic of an acetophenone. The n.m.r. spectrum indicated a phenol containing a methyl and an acetyl group. The i.r. band at 1660 cm^{-1} indicated the absence of *o*-hydroxyl. The compound was further identified by comparison of the melting point and the i.r. spectrum with the corresponding literature data[13].

Compound **12** gave a characteristic blue colour with *p*-anisidine hydrochloride. M.s. and elemental analysis indicated the formula $C_9H_{10}O_4$. The n.m.r. data of **12** and its acetate indicated an acetophonone derivative containing one methyl and three hydroxyl groups. The downfield position of the signal for the aromatic proton (δ 7.17) in the n.m.r. spectrum of **12** compared with those (δ 6.50 and 6.73) for the corresponding protons in **13**, and the small coupling (J 0.8 Hz) observed between this proton and the methyl group[14] indicated the structure to be 2,3,4-trihydroxy-5-methylacetophenone. An attempt to prepare **12** from 2,3,4-trihydroxyacetophenone using methyl iodide and sodium methoxide, as described by Reidl[15] for the synthesis of 2,4,6-trihydroxy-3-methylacetophenone failed, but acylation of 4-methyl-1,2,3-benzenetriol[16] with acetic anhydride gave a product which was identical with **12**. The formation of only one isomer in the acylation is noteworthy; no trace of 2,3,4-trihydroxy-6-methylacetophenone was observed.

The low yields of the compounds isolated from the alkaline treatment of D-glucose and D-xylose are not surprising because of their instability under the alkaline reaction conditions and the work-up procedure (giving coloured products). In order to obtain information about the rate of degradation of catechols at various pH values, **3** was treated at 96° with acetate buffer (pH 4.5), phosphate buffer (pH 7), and 0.63M sodium hydroxide under nitrogen which may have contained traces of oxygen. Unreacted catechol was determined by quantitative g.l.c. The results are given in Fig. 1. The half-life of **3** in alkaline solution was ~5 h. At pH 4.5 (at which value the earlier studies[1] were performed), degradation was negligible, but at pH 7

TABLE I

COMPOUNDS ISOLATED FROM D-XYLOSE AND D-GLUCOSE

Compound	*M.p.* (*degrees*)	*Yield* (%)		*G.l.c.* (*rel. retention*)	*T.l.c.*[d] (R_F)	*Colour with spray reagents*			
		D-*Xyl*	D-*Glc*			A	B	C	D
1	103–105	0.07[c]	0.08[c,b]	0.68	0.98	white	violet[e]	yellow[e]	yellow
2	68–69.5	0.03[c]	0.04[c]	0.77	0.98	white	violet[e]	yellow[e]	yellow
3	103–105	0.09[c]	0.10[c]	1.00	0.56	grey	bluish-black	brown[e]	brown
4[f]		0.03[c]	0.06[c]	1.20	0.70	reddish-brown	black	brownish-red	brown
5[f]		0.10[c]		1.33	0.59	brownish-grey	greenish-black	brownish-red	reddish-brown
6[f]		[a]	[a]	1.66	0.70	brownish-violet	greenish-black	brownish-red	brown
7	125–126	0.02[b]	0.02[b]	1.46	0.42	white	white	orange	white
8	205–206	0.04[b]	0.04[b]	2.33	0.56	yellow[e]	grey[e]	yellow	yellow[e]
9	122–123	0.02[b]	0.02[b]	2 20	0.58		yellow[e]	red	red
10	114–116	[a]	[a]		0.20	greenish-grey	greenish-black	yellow	brown
11	154–156	0.09[b]	[a]		0.23	orange	greenish-blue	reddish-orange	beige
12	167–168	0.13[b]	0.13[b]	3.77	0.72	blue	black	greenish-yellow	greenish-yellow
13	82–83	[a]	[a]	1.46	0.95	brown	brownish-black	yellow[e]	brown

[a]Detected but not determined. [b]Determined gravimetrically. [c]Determined by g.l.c. [d]Solvent *A*. [e]Weak. [f]Insufficient material available for m.p. determination.

it was significant. The lability of the other catechol derivatives in alkaline solution is probably similar to that of **3**.

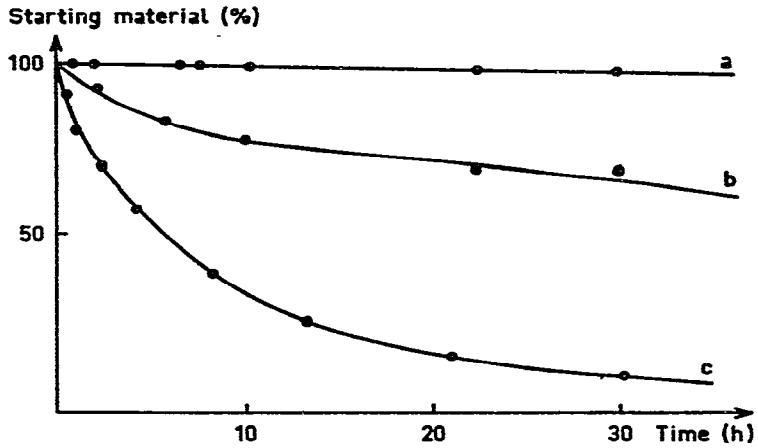

Fig. 1. Degradation of pyrocatechol (**3**) in an atmosphere of nitrogen at 96°: (*a*) acetate buffer (pH 4.5); (*b*) phosphate buffer (pH 7.0); and (*c*) 0.63M NaOH.

Many of the compounds isolated in the present investigation are also likely to be formed in peeling reactions from the reducing ends of polysaccharides during alkaline and kraft (sulphate) pulping processes. Compounds **1** and **3** are present[8] in kraft cooking liquors and, more recently, **9** has been isolated from the kraft cooking liquors of spruce by Nordman[19]. The present results indicate that these compounds are degradation products of carbohydrates rather than of lignin. One would also expect the other compounds isolated here to be formed under alkaline and kraft pulping conditions, and thus to be intermediates in the colour formation under such conditions.

Phenolic units containing α-carbonyl groups, which can be present in wood extractives or in lignin building-units, are considered to be important sensitizers in the photo-induced yellowing of wood and high-yield pulps exposed to light and air[20,21]. Compounds **8**–**13** are structures of this kind. If also formed from polysaccharides under alkaline pulping conditions, these compounds, in addition to being intermediates in the formation of coloured condensation products, may also act as sensitizers in photo-induced yellowing reactions, probably causing modifications of lignin and polysaccharides.

The mechanism of formation of enolic and phenolic compounds from monosaccharides under alkaline conditions is complex, and includes fragmentation and recombination. The similarity in the pattern of products from D-glucose and D-xylose indicates the formation of the same C_2, C_3, or C_4 fragments, with subsequent recombination and probable cyclization, at least partly *via* base-catalyzed aldol condensation. Similar C_4, C_5, and C_6 acids were obtained[12] from pentoses and

D-fructose, indicating fragmentation and recombination. The validity of such a condensation mechanism is supported by early reports[22,23] of the formation of 2,5-dimethyl-*p*-benzoquinone and 2,5-dimethyl-1,4-benzenediol after the alkaline treatment of biacetyl, which is a fragmentation product obtained on alkaline treatment of monosaccharides. The similarity in structure between these compounds and **7**, which could arise from condensation of one mole of biacetyl with one mole of pyruvaldehyde, may be noted.

There was a striking difference in the pattern of reaction products obtained when pentoses were treated in slightly acidic solution[1,2]. Small amounts of **3** and **4** were the only common, identifiable products from the previous and the present alkaline conditions.

EXPERIMENTAL

General. — Concentrations were carried out at diminished pressure below 40°. Sublimations were performed at diminished pressure. Melting points are corrected.

T.l.c. was performed on Silica Gel HF_{254} (Merck), using *A* dichloromethane–acetic acid (9:1) and *B* chloroform–cyclohexane–acetic acid (60:40:5), and detection with u.v. light and then with *A* *p*-anisidine hydrochloride, *B* ferric chloride, *C* 2,4-dinitrophenylhydrazine, *D* diazotized *p*-nitroaniline, or *E* silver nitrate–ammonium hydroxide.

Column chromatography was performed on Sephadex LH-20 (elution with water) and silicic acid [70–235 mesh, Merck, with solvent *D*; or 100-mesh, Mallinckrodt, with dichloromethane–acetonitrile, 9:1 (solvent *C*)].

Preparative and quantitative g.l.c. were carried out on a Varian Aerograph 705 fitted with a flame-ionization detector, with nitrogen as carrier gas and columns (5–8 ft × 0.25 in.) of 10% of SE-30 or QF-1 on Chromosorb DMCS (60/80 mesh). Mass spectra were recorded on a Perkin–Elmer 270 instrument, and g.l.c.–m.s. analyses were performed using a Perkin–Elmer Model 900 gas chromatograph (OV-1 column, programmed 100→200° at 5°/min).

I.r., u.v., and n.m.r. spectra were recorded with Perkin–Elmer 237, Beckman DB, and Varian HA 100D spectrometers, respectively.

Alkaline degradations. — (*a*) A solution of D-xylose (100 g) in 0.63M sodium hydroxide (1.25 litres) was kept at 96° for 4 h under nitrogen. The pH of the dark-brown solution was adjusted to 6 with dilute hydrochloric acid, and the solution was then extracted continuously with ethyl acetate (2 × 24 h). The dried ($MgSO_4$) extract was concentrated and the syrupy residue (3.97 g) was eluted from a column of Sephadex LH-20 with water to give the following fractions: **1** (362 mg), **1+2** (347 mg), **1+13** (317 mg), **3** (372 mg), **4+5** (212 mg), **6–9+11** (289 mg), **10** (127 mg), and **12** (267 mg).

The compounds were purified by elution from columns of silicic acid, using solvents *B* (for **1**, **2** and **13**) and *C* (for **3–12**), and by crystallization (**1**, **3**, **7–10** and **11**), sublimation (**2**, **4**, **5**, **12** and **13**), or preparative g.l.c. at 160° (**6**).

(*b*) A solution of D-glucose (140 g) in 0.63M sodium hydroxide (1.74 litres) was treated as described above, but extracted with ether (8 × 400 ml). Concentration of the dried extract gave a syrup (2.7 g) which was eluted from Sephadex LH-20 with water to give the following fractions: **1**+**2** (269 mg), **1**+**13** (135 mg), **3** (87 mg), **4**+**5** (166 mg), **7**+**8**+**11** (97 mg), **8**+**9**+**10**+**11** (87 mg), and **12** (291 mg).

The compounds were purified as described above.

(*c*) D-Xylose (35 g) and D-glucose (35 g) were treated as described above. Each solution was extracted with ether (8 × 200 ml), and the extract was dried ($MgSO_4$), concentrated to 50 ml, and analysed by g.l.c. The peak height was used as a measure of the amount of each individual compound, and calibration curves were made for **1**–**5**.

Identification of compounds. — Compounds **1**, **3**–**5**, **7**, **8**, and **11** were identical (mixture m.p.) with commercial samples of 2-hydroxy-3-methyl-2-cyclopenten-1-one, pyrocatechol, 3-methyl-1,2-benzenediol, 4-methyl-1,2-benzenediol, 2-methyl-1,4-benzenediol, 2,5-dihydroxyacetophenone, and 3,4-dihydroxybenzaldehyde, respectively.

2-Hydroxy-3,4-dimethyl-2-cyclopenten-1-one (**2**), synthesized according to the procedure of Gianturco and Friedel[24], had m.p. 68–69.5°; lit. m.p. 71–72°. Mass spectrum: *m/e* 41 (46% of base peak), 42 (20), 43 (100), 53 (18), 55 (74), 56 (15), 69 (13), 70 (16), 83 (53), 98 (22), 111 (52), 112 (11), 126 (M^+, 54), 127 (12).

3,4-Dimethyl-1,2-benzenediol (**6**), synthesized according to the procedure of Loudon and Scott[25], had m.p. 82–84°; ν_{max}^{KBr} 1630, 1590, 1500, 1310, 1280, 1250, 1200, 1070, 1010, 970, 880, and 790 cm^{-1}; lit. m.p. 85–86° .Mass spectrum: *m/e* 51 (12% of base peak), 65 (17), 77 (13), 91 (30), 92 (23), 123 (60), 137 (40), 138 (M^+, 100), 139 (10).

3,4-Dihydroxyacetophenone (**10**) was obtained together with 2,3-dihydroxyacetophenone in the synthesis of the latter compound[26]. A mixture of pyrocatechol (1 g), acetic anhydride (0.9 ml), and perchloric acid (0.3 ml) was heated (100°) for 3 h and then neutralized with a 1:1 mixture of aqueous sodium hydroxide (20%) and sodium carbonate (20%). The mixture was extracted with ether, and the ether-soluble fraction was eluted from a column (60 × 2 cm) of silicic acid with chloroform–acetonitrile (9:1) to give 2,3-dihydroxyacetophenone (50 mg), m.p. 96–98°, and 3,4-dihydroxyacetophenone (77 mg), m.p. 118–120°; ν_{max}^{KBr} 1680, 1595, 1530, 1445, 1370, 1295, and 1225 (broad) cm^{-1}; lit.[27] 119–121°. Mass spectrum: *m/e* 43 (34% of base peak), 51 (18), 52 (13), 53 (13), 55 (14), 63 (11), 81 (22), 109 (36), 137 (100), 138 (10), 152 (M^+, 43). N.m.r. data (CD_3OD): δ 2.49 (s, 3 H), 6.82 (d, 1 H, *J* 8.5 Hz), 7.40 (d, 1 H, *J* 2.0 Hz), and 7.74 (dd, *J* 2.0 and 8.5 Hz).

2,3-Dihydroxy-6-methylacetophenone (**13**), which was identical with a sample prepared by Nordman[19], had m.p. 82–83°; ν_{max}^{KBr} 3480, 1610, 1430, and 1260 cm^{-1}. Mass spectrum: *m/e* 43 (29% of base peak), 51 (15), 65 (10), 77 (15), 123 (15), 148 (11), 151 (100), 152 (10), and 166 (M^+, 56). N.m.r. data (CD_3OD): δ 2.18 (d, 3 H, *J* 0.7 Hz), 2.53 (s, 3 H), 6.50 (dd, 1 H, *J* 8.0 and 0.7 Hz), and 6.73 (d, 1 H 8.0 Hz).

2,3,4-Trihydroxy-5-methylacetophenone (**12**). — 4-Methyl-1,2,3-benzenetriol[16]

(0.6 g) and 95% acetic anhydride (0.4 g) were added to a heated (140°) mixture of acetic acid (0.5 ml) and zinc chloride (0.35 g). After 1 h at 140–145°, the mixture was concentrated under reduced pressure and water (3 ml) was added with stirring. The crude product was collected, and crystallized from water saturated with sulphur dioxide to give the acetate **12** (290 mg), m.p. 135–143°. The n.m.r. spectrum revealed the presence of acetyl groups. Deacetylation with boron trifluoride etherate in methanol[28] yielded, after elution of the product from silicic acid (solvent *C*), **12** (195 mg), m.p. 164–167°. Sublimation raised the m.p. to 167–168°. The product had ν_{max}^{KBr} at 3470, 3370, 1630, 1590, and 1500 cm^{-1}. Mass spectrum: *m/e* 43 (26% of base peak), 51 (10), 53 (13), 65 (18), 93 (17), 121 (10), 139 (10), 164 (11), 167 (100), 168 (93), 169 (29), 181 (53), 182 (M^+, 40), 183 (17). N.m.r. data (CD_3OD): δ 2.15 (d, 3 H, *J* 0.8 Hz), 2.51 (s, 3 H), 7.17 (d, 1 H, *J* 0.8 Hz).

Anal. Calc. for $C_9H_{10}O_4$: C, 59.3; H, 5.4. Found: C, 59.1; H, 5.4.

Degradation of pyrocatechol (**3**). — Pyrocatechol (250 mg) was added severally to 0.5M acetate buffer (pH 4.5), 0.3M phosphate buffer (pH 7), and 0.63M sodium hydroxide (250 ml of each). The solutions were kept at 96° under nitrogen. At intervals, portions (20 ml) of each solution were adjusted to pH 4 and extracted with ethyl acetate (3 × 30 ml), the combined extracts were dried ($MgSO_4$) and concentrated to 5 ml, and the amount of **3** was determined by g.l.c.

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