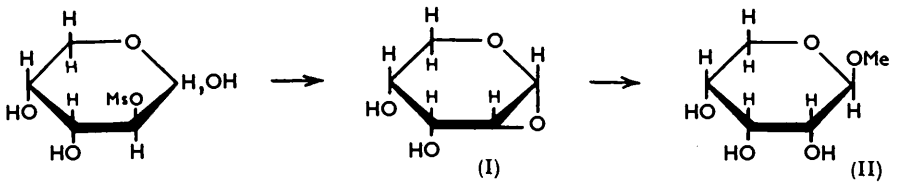
520. *The Action of Base on Methanesulphonyl Esters of Reducing Sugars.*

By D. C. C. Smith.

Reaction of 4-*O*-formyl-2-*O*-methanesulphonyl-D-arabinose with sodium methoxide gives rise to a mixture of methyl pentosides. 3 : 5-*O*-Benzylidene-4-*O*-formyl-2-*O*-methanesulphonyl-*aldehydo*-D-arabinose hydrate, 1 : 4 : 6-tri-*O*-acetyl-3-*O*-methanesulphonyl-2-*O*-methyl-α-D-glucose, 3-*O*-methanesulphonyl-D-xylose, and 4 : 6-*O*-benzylidene-3-*O*-methanesulphonyl-D-glucose have been synthesised. Alkaline hydrolysis of each of these substances conforms to the patterns already described for 4-*O*-formyl-2-*O*-methanesulphonyl-D-arabinose and 3-*O*-methanesulphonyl-D-glucose.[1]

ALKALINE hydrolysis of 2-*O*-methanesulphonyl-D-arabinose is reported to give D-ribose in high yield, accompanied by a small amount of D-arabinose.[2] Hydrolysis of 4-*O*-formyl-2-*O*-methanesulphonyl-D-arabinose[3] with precautions against exposure of the products unnecessarily to alkali, gives D-ribose containing no D-arabinose.[1] Alkaline hydrolysis of 2-*O*-methanesulphonyl-D-arabinose has been followed titrimetrically and found to be sixteen times faster than that of methyl 2-*O*-methanesulphonyl-(αβ)-D-arabinopyranoside under the same conditions, suggesting that the free reducing group plays an important part in the reaction. Anhydro-ring formation involving the reducing group (cf. I), followed by opening of the anhydro-ring by attack of hydroxyl ion at the anomeric carbon, has been suggested.[2]

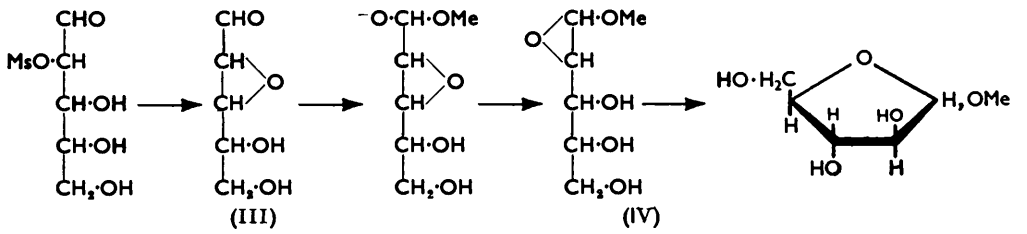


In order to test this mechanism, sodium methoxide has been substituted for sodium hydroxide. The reaction was followed titrimetrically and found to be twenty times slower than that with aqueous sodium hydroxide of equivalent concentration. The main product was a mixture of methyl pentosides with free arabinose and ribose. The last two products were probably produced by traces of the more reactive sodium hydroxide. Using 4-*O*-formyl-2-*O*-methanesulphonyl-D-arabinose in place of 2-*O*-methanesulphonyl-D-arabinose gave a 97% yield of methyl pentosides uncontaminated with reducing sugars; this is probably because saponification of the formyl ester grouping removes traces of hydroxyl ions that are present and so prevents them from reacting at the anomeric position. Methyl β-D-ribopyranoside was isolated from the mixture and the combined results of periodate oxidation, hydrolysis, measurements of optical rotation, and paper chromatography indicate the presence in the reaction product of 62% of this substance accompanied by both anomeric methyl D-arabinofuranosides. The presence of only methyl pentosides in the product indicates that methanol or methoxide ions must attack the anomeric position at some stage. Such a reaction has already been described in the conversion of 2 : 3-*O*-*iso*propylidene-5-*O*-toluene-*p*-sulphonyl-L-rhamnose into methyl 2 : 3-*O*-*iso*propylidene-β-D-allomethyloside,[4] and, since this work was completed, in the conversion of

[1] D. C. C. Smith, *Chem. and Ind.*, 1955, 92.
[2] Jones and Nicholson, *J.*, 1955, 3050.
[3] Barker and D. C. C. Smith, *Chem. and Ind.*, 1952, 1035.
[4] Levene and Compton, *J. Biol. Chem.*, 1936, **116**, 169.

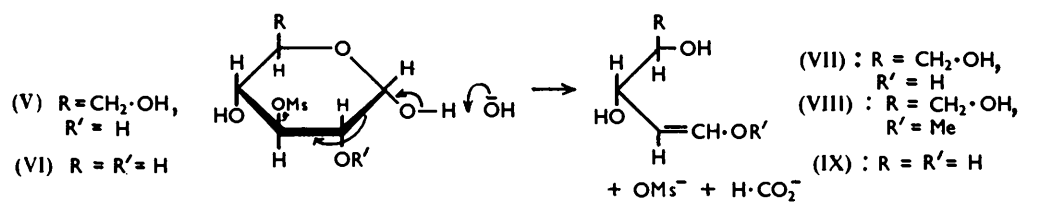
1 : 3 : 5-tri-*O*-benzoyl-2-*O*-methanesulphonyl-α-D-ribose into methyl α-D-arabinopyranoside.[5]

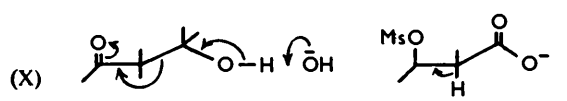
In the present case, the intermediate formation of 1 : 2-anhydro-D-ribopyranose (I) would enable attack of methoxide ion to occur at the anomeric position, and can account for the predominance of β-anomers, and particularly of methyl β-D-ribopyranoside (II), in the product. The formation of methyl D-arabinosides from 2-*O*-methanesulphonyl-D-arabinose involves retention of configuration at position 2. In view of the mild reaction conditions and since inversion of configuration with intramolecular nucleophilic assistance always accompanies such mild alkaline hydrolysis of sulphonyl esters, it seems probable that the formation of methyl arabinosides in this reaction involves two successive inversions at position 2. This can occur by the intermediate formation of 2 : 3-anhydro-D-ribose (III), subsequent addition of methoxide ion in two possible stereo-configurations to



the 1-carbonyl group, and migration of the epoxide ring to give two anomeric methyl epoxyethers (IV). Such substances would be expected [6] to react with alcoholic sodium alkoxide at room temperature. The oxygen on position 4 is in a favourable situation to act as the attacking alkoxide ion and in so doing would give rise to an anomeric mixture of methyl D-arabinofuranosides.

The reaction of 3-*O*-methanesulphonyl-D-glucose with sodium hydroxide, described in a preliminary communication, has been found to yield 2-deoxy-D-ribose and formate. The mechanism proposed [1] (V) involves the enol of 2-deoxy-D-ribose (VII) as an intermediate. This elimination has an analogy in the reverse aldol reaction (X), the two





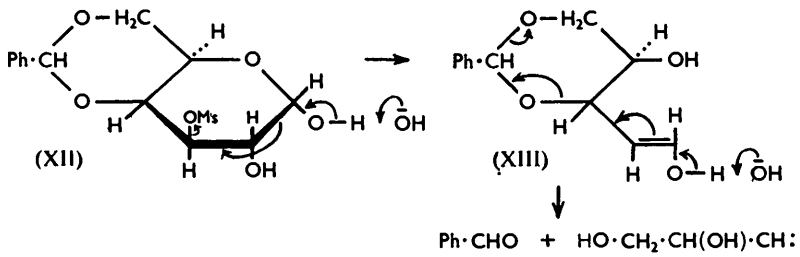
having the relation proposed by Hughes [7] as existing between a removable group X in C—X and the —*M* effect of oxygen in C=O. The related system (XI) has been found by Linstead, Owen, and Webb [8] to undergo a different type of elimination, leaving an unsaturated acid as the main product. This reaction is slower than the eliminations reported in the present work and probably takes place instead because of the —*M* effect of the

[5] Ness and Fletcher, *J. Amer. Chem. Soc.*, 1956, **78**, 4710.
[6] Stevens and Dykstra, *ibid.*, 1954, **76**, 4402.
[7] Hughes, *Nature*, 1941, **147**, 812.
[8] Linstead, Owen, and Webb, *J.*, 1953, 1211.

potential carbonyl group of the carboxylic acid group diverts any tendency for the carboxylate anion to supply electrons in assisting elimination of the methanesulphonyloxy-group. The elimination of the phosphate group employed in stepwise degradation of oligonucleotides [9] is more likely to be analogous to (V), yielding formic acid: this would explain its rapidity and also the neutralisation of two equivalents of alkali per nucleotide residue.[9]

Evidence for the intermediate formation of the enol (VII) in the reaction of 3-*O*-methanesulphonyl-D-glucose with sodium hydroxide has been obtained from the reaction of 1 : 4 : 6-tri-*O*-acetyl-3-*O*-methanesulphonyl-2-*O*-methyl-α-D-glucopyranose with sodium hydroxide. The tri-*O*-acetyl derivative was used for this reaction rather than free 3-*O*-methanesulphonyl-2-*O*-methyl-D-glucose because the glycosidic grouping in methyl 4 : 6-benzylidene-3-*O*-methanesulphonyl-2-*O*-methyl-β-D-glucopyranoside was found to be resistant to acid hydrolysis, an effect frequently reported for various toluene-*p*-sulphonyl esters of methyl glycosides.[2] However, acetolysis of our methyl glycoside occurred smoothly at room temperature. Quantitative saponification of the resulting 1 : 4 : 6-tri-*O*-acetyl-3-*O*-methanesulphonyl-2-*O*-methyl-α-D-glucopyranose consumed 4·8 equivalents of alkali, yielding formate (detected chromatographically) and substances stable to excess of alkali and giving a strong Dische reaction.[10] These were isolated as a syrup showing a strong absorption band at 1685 cm.$^{-1}$, consistently with the double-bond stretching vibration of an enol ether [11] but whose methoxyl content was too low for the expected 5-methoxypent-4-ene-1 : 2 : 3-triol (VIII), and which on drying was transformed into a glass with loss of methanol. This behaviour resembles that of the polymer formed from methyl 2-deoxy-D-ribofuranoside by loss of methanol,[12] and it seems likely that, though it could not be isolated, the triol (VIII) is the initial product of saponification.

3-*O*-Methanesulphonyl-D-xylose (VI) was synthesised from 3-*O*-methanesulphonyl-1 : 2-5 : 6-di-*O*-*iso*propylidene-D-glucose and found to react with sodium hydroxide in an analogous manner. When precautions were taken to avoid excess of alkali, formate (detected chromatographically) and D(−)-βγ-dihydroxybutyraldehyde (keto-form of IX) were obtained.



4 : 6-*O*-Benzylidene-3-*O*-methanesulphonyl-D-glucose (XII) neutralised 3 equivalents of 0·01N-sodium hydroxide in 20 min. at room temperature. The product gave no Dische reaction, confirming that 2-deoxy-D-ribose and its derivatives are absent, and benzoic acid was recovered after acidification. Presumably the benzylidene group is eliminated from the enol (XIII) initially formed giving benzaldehyde which becomes oxidised in dilute aqueous solution to benzoic acid with neutralisation of a further equivalent of alkali. This accords with the mechanism for elimination of alkoxy-groups from β-alkoxycarbonyl compounds involving initial enolisation suggested by Corbett and Kenner.[13] Formation of the requisite enol by elimination of the methanesulphonyl group occurs much more rapidly than formation of a similar enol by keto–enol tautomeric change.

[9] Brown, Fried, and Todd, *J.*, 1955, 2206.
[10] Deriaz, Stacey, Teece, and Wiggins, *J.*, 1949, 1222.
[11] Meakins, *J.*, 1953, 4170.
[12] Overend, Shafizadeh, and Stacey, *J.*, 1951, 994.
[13] Corbett and Kenner, *J.*, 1953, 2245.

Hence the elimination of the benzylidene group in 4 : 6-*O*-benzylidene-3-*O*-methanesulphonyl-D-glucose occurs more rapidly than the reported [14] elimination of the *iso*propylidene group and benzylidene group from 2 : 3-5 : 6-di-*O*-*iso*propylidene-D-mannose and 4 : 6-*O*-benzylidene-D-glucose respectively.

Oxidation of 4:6-*O*-benzylidene-3-*O*-methanesulphonyl-D-glucose with sodium periodate yielded 3 : 5-*O*-benzylidene-4-*O*-formyl-2-*O*-methanesulphonyl-*aldehydo*-D-arabinose hydrate, which neutralised 3 equivalents of 0·01N-alkali within 5 minutes and a further equivalent during the next hour. With N-sodium hydroxide for 10 minutes the above compound gave benzaldehyde which was isolated as its 2 : 4-dinitrophenylhydrazone in 71% yield. The release of benzaldehyde is only slightly slower than from 4 : 6-*O*-benzylidene-3-*O*-methanesulphonyl-D-glucose, and the 3 : 5-*O*-benzylidene-D-ribose which is presumably initially formed apparently eliminates the benzylidene group to yield saccharinic acids, four of which were detected as their lactones by paper chromatography. The rapidity of the elimination of the benzylidene grouping as compared with previous examples of this reaction may be due to the *aldehydo*-structure of 3 : 5-*O*-benzylidene-D-ribose.

In the preparation of 4 : 6-*O*-benzylidene-3-*O*-methanesulphonyl-D-glucose by condensation of 3-*O*-methanesulphonyl-D-glucose with benzaldehyde, a di-*O*-benzylidene-3-*O*-methanesulphonyl-D-glucose was obtained as a by-product. Since 4 : 6-*O*-benzylidene-3-*O*-methanesulphonyl-D-glucose shows no tendency to condense further with benzaldehyde, this is probably 1 : 2-5 : 6-di-*O*-benzylidene-3-*O*-methanesulphonyl-D-glucofuranose; it was reduced with lithium aluminium hydride to a hitherto unknown di-*O*-benzylidene-glucose.

Experimental

Paper chromatograms were in the system butan-1-ol–water unless otherwise stated.

Reaction of 4-O-*Formyl*-2-O-*methanesulphonyl*-D-*arabinose with Sodium Methoxide.*—This compound (1·0 g.) was added to a solution prepared by dissolving sodium (0·5 g.) in dried methanol (100 c.c.). After 24 hr. at room temperature the colourless solution was diluted with chloroform (100 c.c.), neutralised with carbon dioxide, filtered, and evaporated. Extraction of the residue with chloroform gave methyl pentosides as a viscous syrup (0·36 g., 97%), subliming at 95° (bath-temp.)/10^{-5} mm., $[\alpha]_D^{18}$ −79·1° (*c* 1·2 in H_2O) (Found : C, 43·85; H, 7·35; OMe, 18·65. Calc. for $C_6H_{12}O_5$: C, 43·9; H, 7·4; OMe, 18·9%). It migrated as one main spot of R_F 0·41, and one or more unresolved and indistinct spots of R_F 0·22—0·41, detected with ammoniacal silver nitrate. No free pentoses were present. A portion was hydrolysed with 0·5N-hydrochloric acid at 95° for 1 hr., neutralised with silver carbonate, and examined by paper chromatography in butan-1-ol–water and in ethyl methyl ketone–water. Ribose and arabinose were both present, possibly a trace of xylose, and no lyxose. Spraying with acid naphtharesorcinol reagent failed to reveal ketoses. R_F values of the various methyl glycosides of ribose and arabinose in butanol–water were determined for comparison :

α-D-Ribopyranoside	0·29	α-D-Ribofuranoside	0·26
β-D-Ribopyranoside	0·41	β-D-Ribofuranoside	0·41
α-L-Arabopyranoside	0·22		
β-L-Arabopyranoside	0·26	(αβ)-L-Arabofuranosides	0·30

Only the methyl β-D-ribosides correspond in R_F to the main spot, R_F 0·41, of the mixture. The identity of this spot was shown by chromatographing the mixture (70 mg.) on a sheet of No. 1 Whatman paper 21″ wide, extracting the section at the leading edge of the component of R_F 0·41, and recrystallising the product from ethyl acetate; methyl β-D-ribopyranoside (15 mg.) obtained had m. p. and mixed m. p. 80—83°.

The product of the above vacuum-sublimation (79·26 mg.) and 0·1928M-sodium metaperiodate (7 c.c.) were made up to 25 c.c. and kept at room temperature. Excess of periodate was determined by Barnebey's method.[15] Free acid was determined after reduction of excess

[14] Corbett, Kenner, and Richards, *J.*, 1955, 1709.
[15] Barnebey, *J. Amer. Chem. Soc.*, 1916, **38**, 330.

of periodate with ethylene glycol, by titrating aliquot parts with 0·01N-sodium hydroxide to the end-point of phenol-red :

Time (min.)	4	12	30	60	90	130	180	1200
Periodate consumed (mols.)	0·96	1·06	1·27	1·35	1·49	1·57	1·64	1·64
Time (min.)	6	14	45	90	130	180	1200	
Acid released (equiv.)	0·41	0·41	0·46	0·46	0·51	0·55	0·62	

If the release of 0·62 equiv. of acid is due to the oxidation of 0·62 mol. of methyl pentopyranoside then 2 × 0·62 = 1·24 mols. of periodate will be consumed in this. The remaining slow consumption of periodate (1·64—1·24 = 0·40 mol.) agrees closely with the unaccounted methyl pentoside (1·00—0·62 = 0·38 mol.), suggesting that this consists mostly of slowly oxidised methyl arabinofuranoside. The observed rotation of the methyl pentoside is consistent with the composition : methyl β-D-ribopyranoside ($[\alpha]_D$ −106·5°) (61%), α-D-arabinofuranoside ($[\alpha]_D$ +123°) (9%), and β-D-arabinofuranoside ($[\alpha]_D$ −86°, calculated by applying Hudson's isorotation rules to the foregoing value) (30%).

The specific rotation of the products after completion of the oxidation was $[\alpha]_D^{18}$ −81·4° (calc. as $C_6H_{12}O_5$; *c* 0·317) when compared with the values given by Jackson and Hudson,[16] for the optical rotations of the periodate oxidation products of methyl pentosides of the D-series, recalculated as referring to the specific rotations of $C_6H_{12}O_5$: α-furanoside, +119° ; α-pyranoside, +99° ; β-furanoside, −149° ; β-pyranoside, −99°. This indicates a predominance of β-anomers in the glycosidic mixture. The observed rotation of the oxidation products (−81·4°) is consistent with the composition : methyl β-D-ribopyranoside (61%), α-D-arabinofuranoside (14%), and β-D-arabinofuranoside (25%).

Methyl 4 : 6-O-*Benzylidene*-3-O-*methanesulphonyl*-2-O-*methyl*-β-D-*glucopyranoside and its Anomer.*—3-*O*-Methanesulphonyl-D-glucose[17] (10 g.) in 2% methanolic hydrogen chloride (300 c.c.) was refluxed for 20 hr., neutralised with silver oxide (30 g.), filtered through active charcoal, and evaporated to a syrup (10·8 g.). This was shaken with benzaldehyde (150 c.c.) and powdered anhydrous zinc chloride (30 g.) for 12 hr. Shaking the clear solution with light petroleum and water precipitated a gum which solidified. This was powdered, washed with light petroleum and water, and dried (product A) (10·5 g.). This was methylated with silver oxide and methyl iodide (nine treatments), isolated with chloroform, and chromatographed on neutral alumina. Benzene eluted *methyl* 4 : 6-O-*benzylidene*-3-O-*methanesulphonyl*-2-O-*methyl*-β-D-*glucopyranoside*, prisms (from ethyl acetate–light petroleum) (3·4 g.), m. p. 109—110°, $[\alpha]_D^{20}$ −66° (*c* 1·7 in $CHCl_3$) (Found : C, 51·5; H, 5·7. $C_{16}H_{22}O_8S$ requires C, 51·4; H, 5·9%). Ether eluted *methyl* 4 : 6-O-*benzylidene*-3-O-*methanesulphonyl*-α-D-*glucopyranoside*, prisms (from chloroform–ether) (2·7 g.), m. p. 146—147°, $[\alpha]_D^{20}$ +94·4° (*c* 1·0 in $CHCl_3$) (Found : C, 49·7; H, 5·6. $C_{15}H_{20}O_8S$ requires C, 50·0; H, 5·6%).

In a separate experiment the product (A) was extracted exhaustively with ether to remove the α-glycoside, and the residue crystallised from chloroform–methanol to yield *methyl* 4 : 6-O-*benzylidene*-3-O-*methanesulphonyl*-β-D-*glucopyranoside* (1·65 g.), prisms (from chloroform–methanol), m. p. 187—188°, $[\alpha]_D^{20}$ −52·5° (*c* 2·9 in $CHCl_3$) (Found : C, 49·7; H, 5·7%).

Methylation of methyl 4 : 6-*O*-benzylidene-3-*O*-methanesulphonyl-α-D-glucopyranoside (1·85 g.) with methyl iodide, methanol, and silver oxide (nine treatments), followed by chromatography on neutral alumina in benzene, yielded *methyl* 4 : 6-O-*benzylidene*-3-O-*methanesulphonyl*-2-O-*methyl*-α-D-*glucopyranoside* (1·26 g.) as plates (from ethyl acetate–light petroleum, m. p. 163—164°, $[\alpha]_D^{20}$ +71·8° (*c* 2·1 in $CHCl_3$) (Found : C, 51·4; H, 5·8%).

1 : 4 : 6-*Tri*-O-*acetyl*-3-O-*methanesulphonyl*-2-O-*methyl*-α-D-*glucopyranose.*—Methyl 4 : 6-*O*-benzylidene-3-*O*-methanesulphonyl-2-*O*-methyl-β-D-glucopyranoside (2·9 g.) was dissolved in a cooled mixture of acetic anhydride (70 c.c.), acetic acid (30 c.c.) and concentrated sulphuric acid (2 c.c.). The reaction, followed polarimetrically, was completed in 2 hr. at room temperature. The mixture was poured into a solution of sodium acetate trihydrate (150 g.) in the minimum volume of water, and after 45 min. the milky suspension was extracted with ether. The extract was dried (Na_2SO_4), and ether and acetic acid distilled off to leave a colourless syrup (3·9 g.) containing, besides the product, benzylidene acetate. Dissolution in ethyl acetate–light petroleum, followed by intense cooling, initiated crystallisation. Repeated

[16] Jackson and Hudson, *J. Amer. Chem. Soc.*, 1937, **59**, 994.
[17] Helferich, Dressler, and Griebel, *J. prakt. Chem.*, 1939, **153**, 285.

recrystallisation from these solvents yielded 1 : 4 : 6-*tri*-O-*acetyl*-3-O-*methanesulphonyl*-2-O-*methyl*-α-D-*glucopyranose* (0·60 g.), m. p. 114—115°, $[\alpha]_D^{20}$ +104·2° (*c* 1·6 in $CHCl_3$) (Found : C, 42·5; H, 6·0. $C_{12}H_{22}O_{11}S$ requires C, 42·2; H, 5·6%).

Reaction of 1 : 4 : 6-*Tri*-O-*acetyl*-3-O-*methanesulphonyl*-2-O-*methyl*-α-D-*glucopyranose with Sodium Hydroxide.*—This substance (0·0420 g.) in methanol (1 c.c.) was treated with 0·00924N-sodium hydroxide (80 c.c.) and made up to 100 c.c. with water. The amount of sodium hydroxide neutralised was determined by titration of aliquot parts with 0·01N-sulphuric acid to the end-point of phenol-red :

Time (min.)	5	15	40	95	180	1200
Alkali neutralised (equiv./mol.)	1·7	2·8	3·7	4·3	4·5	4·8

Paper chromatography of the solution showed sodium formate (R_F 0·04; strongly reducing to ammoniacal silver nitrate) and a substance described below (R_F 0·45).

A mixture of 1 : 4 : 6-tri-*O*-acetyl-3-*O*-methanesulphonyl-2-*O*-methyl-α-D-glucopyranose with benzylidene acetate (2·96 g., estimated to contain 1·8 g. of the sugar derivative) in methanol (10 c.c.) was mixed with N-sodium hydroxide (60 c.c.) and immediately evaporated *in vacuo*. The residue in methanol (30 c.c.) and chloroform (200 c.c.) was neutralised with carbon dioxide, filtered to remove insoluble salts, evaporated *in vacuo*, extracted with chloroform, filtered, and again evaporated to a clear syrup (0·73 g.). It showed a strong absorption band at 1685 $cm.^{-1}$, attributable to an enol ether,[11] but paper chromatography revealed three components, with R_F's zero (tailing forward), 0·45, and 0·54 respectively, all giving a mauve colour when sprayed with Dische reagent (diphenylamine sulphate) (0·1 g.) and sulphuric acid (one drop) in glacial acetic acid (50 c.c.) and then heated at 80°. Chromatograms of freshly saponified 1 : 4 : 6-tri-*O*-acetyl-3-*O*-methanesulphonyl-2-*O*-methyl-α-D-glucopyranose occasionally showed only the component of R_F 0·45, making it probable that this is the initial product, but the other components appeared spontaneously on storage. The syrup as isolated had $[\alpha]_D^{20}$ −18·3° (*c* 3·5 in MeOH) (Found : C, 46·1; H, 7·6; OMe, 7·2%). When dried to constant weight *in vacuo* at 25° it set to a hard glass, $[\alpha]_D^{20}$ zero (*c* 2·0 in MeOH), showing only the component of R_F zero (Found : C, 52·6, 52·6, 50·8; H, 6·7, 6·2, 6·0; OMe, 1·9. Calc. for $C_5H_8O_3$: C, 51·7; H, 6·9; OMe, 0%).

1 : 2-O-iso*Propylidene*-3-O-*methanesulphonyl*-α-D-*xylofuranose.*—1 : 2-5 : 6-Di-*O*-*iso*propylidene-3-*O*-methanesulphonyl-D-glucose (38 g.) in acetic acid (60 c.c.) and water (20 c.c.) was heated at 50—60° for 3 hr., evaporated *in vacuo*, diluted with water (200 c.c.), made alkaline (40 c.c. of N-sodium hydroxide), kept for 2 hr., then brought to pH 5 (20 c.c. of N-sulphuric acid). This solution, stirred in ice, was treated with powdered sodium metaperiodate (52 g.) at such a rate as to keep the temperature below 20°. The pasty suspension was kept for 1 hr. at room temperature, and the solids were filtered off and washed with methanol (100 c.c.). The aqueous filtrate and the methanol washings were combined and run slowly into a vigorously stirred suspension of anhydrous magnesium sulphate (500 g.) in ether (3 l.). The magnesium sulphate was filtered off and washed with ether. The combined filtrate and washings were evaporated to a syrup (30·7 g.) smelling of formaldehyde. This was taken up in methanol (180 c.c.) and water (60 c.c.) and treated with potassium borohydride (9·0 g.). The reaction was marked by a vigorous effervescence and was moderated by cooling. After 15 min. acetic acid was added to decompose excess of reducing agent, and methanol was distilled off *in vacuo*. The residue was diluted with water (250 c.c.) and extracted several times with chloroform. Evaporation of the chloroform extracts yielded a syrup (29·6 g.) which crystallised. This was taken up in ethyl acetate (100 c.c.), diluted with light petroleum (100 c.c.), and on being seeded deposited crystals of 1 : 2-O-iso*propylidene*-3-O-*methanesulphonyl*-α-D-*xylofuranose* (22·4 g.), m. p. 81—83°, $[\alpha]_D^{18}$ −26·1° (*c* 3·0 in $CHCl_3$) (Found : C, 40·25; H, 5·9. $C_9H_{16}O_7S$ requires C, 40·3; H, 6·0%).

3-O-*Methanesulphonyl*-D-*xylose.*—1 : 2-*O*-*iso*Propylidene-3-*O*-methanesulphonyl-α-D-xylofuranose (21·9 g.) in ethanol (50 c.c.) and water (50 c.c.) was heated with N-sulphuric acid (2 c.c.) for 3 hr. Ethanol and acetone were distilled off, water (50 c.c.) added, and the solution heated on a water-bath for 1 hr. The brown solution was filtered through Norit and passed successively through columns of Amberlite IR-120 (H^+) (100 g.) and Amberlite IR-4B (basic form) (100 g.). Evaporation of the eluate *in vacuo* was accompanied by spontaneous crystallisation. The residue was taken up in methanol (180 c.c.), seeded, and allowed to evaporate. 3-O-*Methanesulphonyl*-D-*xylose* was obtained (13·0 g.), having m. p. 140—141°, $[\alpha]_D^{24}$ +37·6° (15

min.), +24·5° (33 min.), +20·5° (61 min.), +19·6° (114 min. and equil.) (*c* 3·7 in H_2O) (Found: C, 31·3; H, 5·2. $C_6H_{12}O_7S$ requires C, 31·5; H, 5·3%).

Reaction of 3-O-*Methanesulphonyl*-D-*xylose with Sodium Hydroxide*.—3-*O*-Methanesulphonyl-D-xylose (5·0 g.) in water (1 l.) was stirred, and N-sodium hydroxide (33 c.c., 75% of the theoretical amount) was run in continuously during 1·5 hr. The solution was passed through Amberlite IR-120 (H^+) (100 g.) and then through Amberlite IR-4B (basic form) (100 g.) and evaporated *in vacuo* to a syrup (2·3 g.). Paper chromatograms developed in water-saturated butan-1-ol and sprayed with ammoniacal silver nitrate showed the presence of 3-*O*-methanesulphonyl-D-xylose (R_F 0·31), D(−)-βγ-dihydroxybutyraldehyde (R_F 0·49), and unknown substances B (R_F 0·13) and C (R_F 0·10). The mixture was taken up in butan-1-ol (20 c.c.), saturated with water and run on a hydrocellulose column (5·5 cm. diam., 23 cm. long) and eluted with water-saturated butan-1-ol. The effluent from the column yielded successively D(−)-βγ-*dihydroxybutyraldehyde* (0·79 g.), mixture (0·21 g.), 3-*O*-methanesulphonyl-D-xylose (0·66 g.), B (0·30 g.), and C (0·04 g.). D(−)-βγ-Dihydroxybutyraldehyde was a colourless syrup, $[\alpha]_D^{20}$ −6·4° (immediate and equil. value) (*c* 1·2 in H_2O) (Found: C, 46·3; H, 7·4. $C_4H_8O_3$ requires: C, 46·1; H, 7·7%). B and C remain unidentified but they may be products of aldol self-condensation of D(−)-βγ-dihydroxybutyraldehyde.

Condensation of 3-O-*Methanesulphonyl*-D-*glucose with Benzaldehyde*.—3-*O*-Methanesulphonyl-D-glucose (5 g.) was shaken with benzaldehyde (70 c.c.) and powdered anhydrous zinc chloride (20 g.) for 12 hr. Shaking the product with light petroleum and water precipitated a gum which solidified. This was powdered, washed with light petroleum and water, and dried (product D) (5·6 g.). Recrystallisation from chloroform containing a few drops of methanol yielded 4 : 6-*O*-benzylidene-3-*O*-methanesulphonyl-D-glucose as its chloroform-adduct, plates, m. p. 126—128°, $[\alpha]_D^{19}$ +27·1° (*c* 1·88 in 1 : 1 $CHCl_3$–MeOH). This gave variable analyses (Found: C, 43·75, 39·8, 43·2; H, 4·7, 4·35, 4·9; Cl, 9·45, 6·95, 5·95%), illustrating that chloroform is partly removed on drying. Mother-liquor from this crystallisation when concentrated and diluted with methanol deposited *di*-O-*benzylidene*-3-O-*methanesulphonyl*-D-*glucose* (1·1 g.) as needles, m. p. 179—181°, $[\alpha]_D^{17}$ +84·2° (*c* 2·28 in $CHCl_3$) (Found: C, 57·8; H, 5·4. $C_{21}H_{22}O_8S$ requires C, 58·1; H, 5·1%).

A similar experiment using less zinc chloride (2·5 g.) yielded the chloroform adduct of the monobenzylidene compound (2·9 g.) and the di-*O*-benzylidene compound (0·5 g.).

Product D (1·23 g.) was chromatographed on neutral alumina: ethyl acetate (1 part) and chloroform (2 parts) eluted the di-*O*-benzylidene compound (0·49 g.); methanol eluted 4 : 6-O-*benzylidene*-3-O-*methanesulphonyl*-D-*glucose* (0·52 g.), needles (from ethyl acetate–light petroleum), m. p. 144—146°, $[\alpha]_D^{18}$ +32·8° (*c* 1·05 in 1 : 1 $CHCl_3$–MeOH) (Found: C, 48·5; H, 5·2. $C_{14}H_{18}O_8S$ requires C, 48·6; H, 5·2%).

Di-O-*benzylidene*-D-*glucose*.—Di-*O*-benzylidene-3-*O*-methanesulphonyl-D-glucose (0·3 g.) and lithium aluminium hydride (1·0 g.) were stirred in ether under reflux for 12 hr. Ethyl acetate, methanol, and water were added in this order, and the product was taken up in ether, washed with sodium hydroxide solution and water, dried, and evaporated to a residue (0·12 g.) which, recrystallised from ethyl acetate–light petroleum (yield, 0·09 g.), had m. p. 162—163°, $[\alpha]_D^{18}$ +123° (*c* 0·64 in $CHCl_3$) (Found: C, 67·15; H, 5·65. $C_{20}H_{20}O_6$ requires C, 67·4; H, 5·7%).

3 : 5-O-*Benzylidene*-4-O-*formyl*-2-O-*methanesulphonyl*-aldehydo-D-*arabinose Hydrate*.—The chloroform adduct of 4 : 6-*O*-benzylidene-3-*O*-methanesulphonyl-D-glucose (1·6 g.) was dissolved in water (30 c.c.) with warming. The resulting solution was cooled, stirred with powdered sodium metaperiodate (1·6 g.), and kept in darkness at 0° for 2 days. The needles which had separated were washed with cold water and air-dried (0·44 g.); they had m. p. 164—166°, $[\alpha]_D^{20}$ −4·22° (initial and equil.) (*c* 2·47 in 1 : 1 $CHCl_3$–MeOH) (Found: C, 46·35; H, 5·15. $C_{14}H_{16}O_8S,H_2O$ requires C, 46·4; H, 5·0%).

Methyl 2-O-*Methanesulphonyl*-(αβ)-D-*arabinopyranoside*.—4-*O*-Formyl-2-*O*-methanesulphonyl-D-arabinose[3] (0·75 g.) in 4% dry methanolic hydrogen chloride (80 c.c.) was heated under reflux for 6 hr., cooled, neutralised with silver carbonate, filtered through Norit, and evaporated to a colourless syrup (0·54 g.) (Found: C, 35·1; H, 6·05. Calc. for $C_7H_{14}O_7S$: C, 34·7; H, 5·8%).

Measurement of the Approximate Comparative Rates of Alkaline Hydrolysis (see Tables).—Each sugar or glucoside (0·25 millimol.) was dissolved in 0·01N-sodium hydroxide (50 c.c.) at room temperature; aliquot parts withdrawn at the stated times were titrated with 0·01N-sulphuric acid to the end-point of phenol-red.

2-*O*-Methanesulphonyl-D-arabinose :

Time (min.)	3	6	10	23	39
Alkali neutralised (equiv./mol.)	0·26	0·48	0·62	0·84	0·86

4-*O*-Formyl-2-*O*-methanesulphonyl-D-arabinose :

Time (min.)	5	9	20	32	97
Alkali neutralised (equiv./mol.)	1·32	1·52	1·66	1·74	1·78

Methyl 2-*O*-methanesulphonyl-(αβ)-D-arabinopyranoside :

Time (min.)	2	19	100	255	720
Alkali neutralised (equiv./mol.)	0·02	0·21	0·52	0·70	0·91

3-*O*-Methanesulphonyl-D-glucose :

Time (min.)	3	11	20	38	96
Alkali neutralised (equiv./mol.)	0·38	0·88	1·26	1·50	1·70

3-*O*-Methanesulphonyl-D-xylose :

Time (min.)	2·5	10·5	17·5	29	45
Alkali neutralised (equiv./mol.)	0·97	1·48	1·58	1·67	1·71

Methyl-3-*O*-methanesulphonyl-(αβ)-D-glucopyranoside :

Time (min.)	5	27	95	237	450
Alkali neutralised (equiv./mol.)	0·05	0·23	0·58	0·77	0·85

Each benzylidene compound (0·03 millimol.) was dissolved in dioxan (10 c.c.) and 0·02N-sodium hydroxide (10 c.c.), and made up to 25 c.c. with water at room temperature; aliquot parts were titrated as above.

3 : 5-*O*-Benzylidene-4-*O*-formyl-2-*O*-methanesulphonyl-*aldehydo*-D-arabinose hydrate :

Time (min.)	2·5	5·5	16	58	107
Alkali neutralised (equiv./mol.)	2·73	3·04	3·44	3·79	3·97

4 : 6-*O*-Benzylidene-3-*O*-methanesulphonyl-D-glucose :

Time (min.)	1·7	8	20	50	115
Alkali neutralised (equiv./mol.)	1·66	2·65	3·05	3·24	3·49

Rate of Reaction of 2-O-*Methanesulphonyl-*D-*arabinose with Methanolic Sodium Methoxide.*—2-*O*-Methanesulphonyl-D-arabinose (0·20 millimol.) was dissolved in 0·01N-sodium methoxide in methanol (50 c.c.) at room temperature. Aliquot parts were withdrawn at the stated times, treated with a measured excess of standard acid, and back-titrated with 0·01N-sodium hydroxide to the end-point of phenol-red.

Time (min.)	60	120	164	420
Alkali neutralised (equiv./mol.)	0·32	0·48	0·59	0·72

Reaction of 4 : 6-O-*Benzylidene*-3-O-*methanesulphonyl*-D-*glucose with Sodium Hydroxide.*—This substance (0·00867 g.) was dissolved in dioxan (1 c.c.) and water (2 c.c.) and treated with 1 c.c. of 0·1N-sodium hydroxide (4 equiv./mol.). After 1 hr. samples removed for paper chromatography showed no Dische reaction, and the only detectable constituents were sodium formate (R_F 0·04) and a spot (R_F 0·82) giving a yellow colour with 2 : 4-dinitrophenylhydrazine hydrochloride. Extraction by ether yielded impure benzoic acid, m. p. 115—120°.

Reaction of 3 : 5-O-*Benzylidene*-4-O-*formyl*-2-O-*methanesulphonyl*-aldehydo-D-*arabinose Hydrate with Sodium Hydroxide.*—This substance (0·48 g.) was dissolved in methanol (30 c.c.) and diluted with water (150 c.c.), and N-sodium hydroxide (8 c.c.) was run in with stirring during 10 min. Liberated benzaldehyde was immediately extracted with ether and yielded the 2 : 4-dinitrophenylhydrazone (0·27 g.), m. p. 237—238°. The aqueous layer was acidified by passing it through a column of Amberlite IR-120 (H^+) (100 g.), then extracted continuously by ether. Evaporation of the extract yielded a syrupy mixture (0·04 g.). Paper chromatography showed the presence of at least four substances (R_F 0·33, 0·40, 0·50, and 0·80), all giving a pink colour with the hydroxylamine–ferric chloride spray reagent,[18] and hence probably all lactones of saccharinic acids.

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[18] Smith and Abdel-Akher, *J. Amer. Chem. Soc.*, 1951, **73**, 5859.