373. *The Hydrolysis of Sulphonium Nucleosides and Glycosides by Alkali.*

By J. Baddiley, W. Frank, N. A. Hughes, and J. Wieczorkowski.

The 5′-sulphonium salts of nucleosides, *e.g.*, adenosylmethionine, are unstable towards dilute alkali under mild conditions, liberating the pyrimidine or purine bases and 5-sulphonium salts of both D-ribose and L-lyxose. Similarly, in alcoholic solution an alkali-catalysed aglycone exchange occurs, with the formation of glycosides of both sugar series. Nucleoside sulphones are also labile towards alkali.

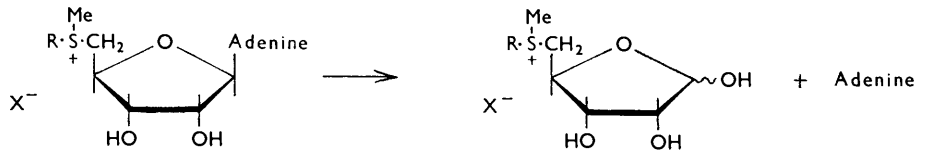
From methyl 5-deoxy-5-methylthio-β-D-ribofuranoside (XV) the corresponding 5-sulphonium iodide (XVIa) was prepared. Periodate oxidation, reduction with sodium borohydride, and acid hydrolysis gave 1-deoxy-1-dimethylsulphonio-L-glycerol (XI). A similar procedure on the sulphonium glycoside after treatment with methanolic sodium methoxide gave an extensively racemised product.

The mechanism of the alkaline hydrolysis of sulphonium glycosides and nucleosides is discussed, and a similarity is suggested between this and a corresponding reaction of vitamin B_{12} coenzyme.

It has long been known that some glycosides, notably *N*-glycosyl quaternary ammonium salts [1,2] and certain aryl glycosides,[3] are sensitive to alkali and that this behaviour is due to the electron-attracting nature of the aglycone. In 1958 Parks and Schlenk [4] reported that the intermediate in many enzymic transmethylations, adenosylmethionine (I), decomposed in cold aqueous alkali to adenine and the sugar (II). The related dimethylsulphonium nucleoside (III) behaved similarly, giving adenine and the sugar (IV). In neither case, however, was the sulphonium sugar positively identified as a derivative of D-ribose. The possibility that transfer of a methyl from the sulphonium group to the purine ring had occurred, giving an alkali-sensitive quaternary nucleoside, was excluded

[1] Karrer and Smirnoff, *Helv. Chim. Acta*, 1921, **4**, 817.
[2] Kaplan, Colowick, and Barnes, *J. Biol. Chem.*, 1951, **191**, 461.
[3] Ballou and Link, *Adv. Carbohydrate Chem.*, 1954, **9**, 59.
[4] Parks and Schlenk, *J. Biol. Chem.*, 1958, **230**, 295.

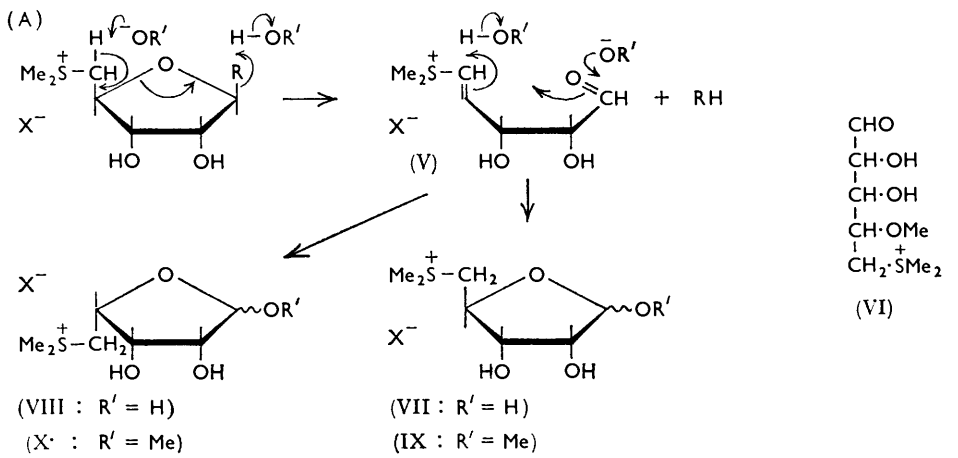
by the absence of any of the methyladenines among the products. This ready alkaline hydrolysis is remarkable in view of the stability of other adenine nucleosides towards alkali.



(I : R = $CH_2 \cdot CH_2 \cdot CH(NH_2) \cdot CO_2^-$)
(III : R = Me , X^- = I^-)

(II : R = $CH_2 \cdot CH_2 \cdot CH(NH_2) \cdot CO_2^-$)
(IV : R = Me , X^- = I^-)

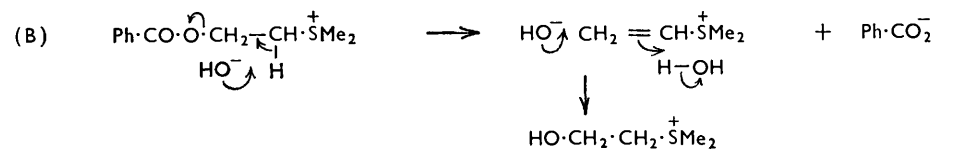
Parks and Schlenk's observations on the nucleoside (III) were confirmed; crude preparations of the corresponding uracil and hypoxanthine nucleosides also decomposed in alkali, yielding uracil and hypoxanthine respectively, together with a sulphonium sugar. When the reaction was carried out with sodium methoxide in methanol rather than aqueous alkali, methanolysis took place, giving the appropriate purine or pyrimidine base and a compound with the properties expected for a methyl glycoside of the sulphonium sugar. This glycoside was itself sensitive towards alkali; with aqueous alkali the sulphonium sugar was formed, and treatment with sodium n-butoxide in butan-1-ol gave a compound with the chromatographic properties expected for the corresponding n-butyl glycoside. Thus, the sensitivity of these compounds towards alkali is independent of the aglycone and is consequent only on the presence of a sulphonium group. The annexed general mechanism (A) is suggested for this type of hydrolysis. The first stage is an alkali-catalysed elimination of the type which has been described [5] for β-substituted ethyldimethylsulphonium compounds. These authors also showed that nucleophilic



(VIII : R′ = H)
(X· : R′ = Me)

(VII : R′ = H)
(IX : R′ = Me)

addition could then occur to the resulting olefin in the manner (B). The second stage of the proposed scheme differs from that for the benzoyl ester shown in (B) that the

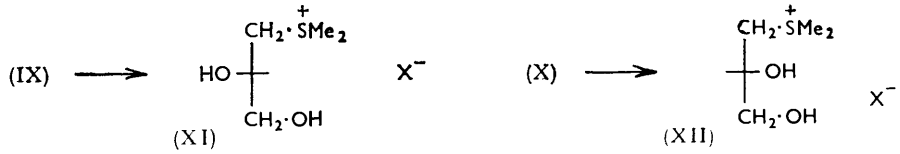


addition of the nucleophilic ion occurs, not at position 4 of the intermediate (V), but at position 1 by reversal of the original elimination process. This is shown by the experiment

[5] Mamalis and Rydon, *J.*, 1955, 1049; Doering and Hoffmann, *J. Amer. Chem. Soc.*, 1955, **77**, 521.

with sodium methoxide in methanol, when addition of methoxide ion at position 4 would have given the acyclic sugar (VI).

The formation of an ethylenic bond at position 4, and thus loss of asymmetry at that position, should permit the formation of the sugars (VII) and (VIII), derivatives of D-ribose and L-lyxose respectively. Unfortunately, no separation of isomeric sugar derivatives was observed by paper chromatography or electrophoresis of alkaline-hydrolysis products from the nucleosides; similarly, isomers obtained by treatment with sodium methoxide in methanol on the nucleosides and then acid hydrolysis could not be separated. This, and the difficulty in obtaining derivatives of L-lyxose for comparison, caused us to adopt an alternative method for establishing the partial inversion of position 4 during these reactions.



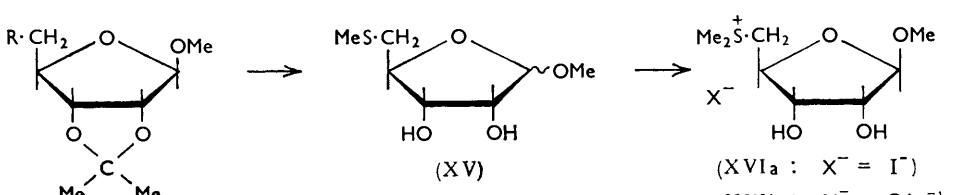
(XIa : X^- = I^-)
(XIb : X^- = OAc^-)
(XIc : X^- = Reineckate$^-$)

(XIIa : X^- = I^-)
(XIIb : X^- = OAc^-)
(XIIc : X^- = Reineckate$^-$)

Degradation of the glycosides (IX) and (X) by periodate oxidation, borohydride reduction, and acid hydrolysis would lead to the enantiomorphic 1-deoxy-1-dimethylsulphonioglycerols (XI) and (XII). The production of both glycosides (IX) and (X) in the methoxide-catalysed methanolysis of the nucleoside (III) could thus be proved by subjecting them to this degradation and isolating a mainly racemic mixture of the glycerol derivatives (XI) and (XII).

The value of this degradative scheme would depend upon the stability, particularly under alkaline conditions, of the enantiomorphs (XI) and (XII); consequently, a synthesis of the D-isomer (XII) was undertaken and its behaviour in alkali was studied. Reaction of 2,3-*O*-isopropylidene-1-*O*-toluene-*p*-sulphonyl-D-glycerol with sodium methyl sulphide in dimethylformamide, followed by removal of the isopropylidene group with dilute acid, gave 1-deoxy-1-methylthio-D-glycerol. With methyl iodide in methanol this gave the pure D-isomer (XII) (acetate, $[\alpha]_D^{20}$ −38°; iodide, $[\alpha]_D^{20}$ −27°). This compound was stable in aqueous alkali and showed no tendency to racemise. Presumably the hydroxyl-protons are removed first and this prevents an elimination of the type envisaged for the sulphonium glycosides.

The nucleoside (III) was not available in large quantities, so the corresponding methyl glycoside (XVI) was chosen for the proposed degradation; it offered the further advantage that a more appropriate control experiment could be performed. The toluene-*p*-sulphonate



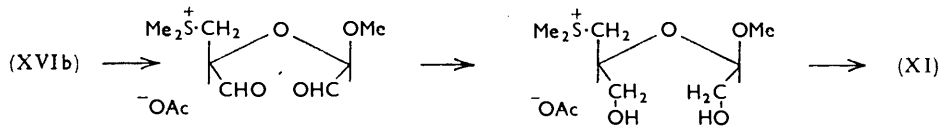
(XIII : R = *p*-Me·C_6H_4·SO_2·O)
(XIV : R = MeS)

(XVIa : X^- = I^-)
(XVIb : X^- = OAc^-)

(XIII) was converted into the thio-ether (XIV) by reaction with sodium methyl sulphide. Hot hydrochloric acid in aqueous methanol was necessary for the removal of the isopropylidene group and, although conditions were chosen which minimised hydrolysis to

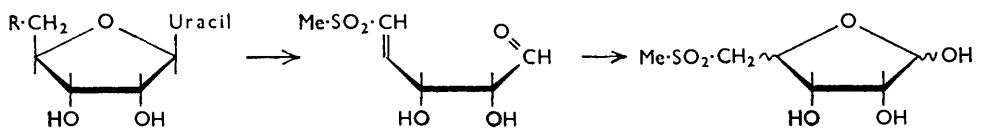
the free sugar, the glycoside (XV) ($[\alpha]_D^{20}$ −3·6°) was probably a mixture of α- and β-forms. However, methylation with methyl iodide in methanol gave the crystalline glycoside (XVIa) ($[\alpha]_D^{20}$ −17°) to which the β-configuration was assigned.

The glycoside (XVIb) consumed one mol. of neutral periodate and showed no tendency to over-oxidation. Reduction of the resulting dialdehyde (XVII) to the alcohol (XVIII) was carried out with sodium borohydride in a borate buffer at pH 9 (ref. 6). This control of alkalinity prevented a possible base-catalysed elimination in the dialdehyde. Hydrolysis of the dialcohol (XVIII) with dilute acid gave the pure L-glycerol sulphonium derivative (XI) (acetate, $[\alpha]_D^{20}$ +38°; iodide, $[\alpha]_D^{20}$ +27°), isolated as its reineckate. The optical purity of this compound indicated that no partial inversion of position 4 had occurred during the degradation. When the glycoside (XVIb) was dissolved in methanol containing sodium methoxide the increase in optical rotation ceased after 90 min. The resulting



glycosides, when subjected to the degradative procedure, gave a mixture of almost equal proportions of the glycerol sulphonium compounds (XI) and (XII) (acetate, $[\alpha]_D^{21}$ +0·5°; iodide, $[\alpha]_D^{20}$ +0·2°). It follows that treatment with methoxide in methanol had converted the riboside sulphonium compound (XVIb) into almost equal amounts of the D-riboside (IX) and the L-lyxoside (X), thereby providing proof of the proposed mechanism. The degradation sequence in each case was performed without isolation of intermediates; the yields of glycerol derivatives were not quantitative but were comparable in the two cases.

Mamalis and Rydon [5] suggested that a trimethylammonium group would not have the same effect as a dimethylsulphonium group in these eliminations. The sulphonium group, being able to invoke the *d*-electrons of the sulphur, behaves as a powerful $-T$ substituent, whereas the ammonium group behaves only as a $-I$ substituent. 5-Deoxy-5-trimethylammonio-D-ribofuranosides are being examined in this connection. Other 5-deoxy-D-ribofuranosides possessing powerful $-T$ substituents at position 5 should behave in a similar manner to the sulphonium D-ribofuranosides. This has been confirmed with the uridine sulphone (XX), obtained from the methylthiouridine (XIX) by oxidation with hydrogen peroxide in acetic acid. This compound was even more sensitive towards alkali than were the sulphonium derivatives. An aqueous solution of the sulphone



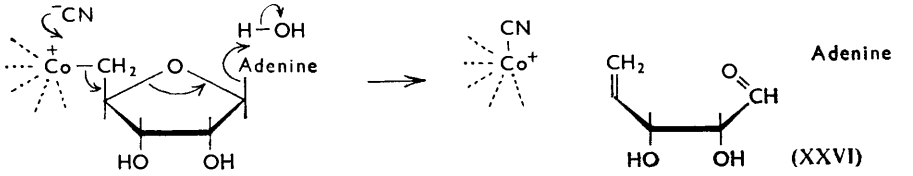
decomposed slowly to uracil and presumably the sugar mixture (XXI) through the intermediate (XXII); alkali accelerated the decomposition. The recently reported [7] replacement of β-substituents in the sulphone (XXIII) is analogous to the behaviour of the nucleoside sulphone. With ethoxide ions in ethanol this gave the sulphone (XXIV), presumably through the olefin (XXV).

[6] Baddiley, Buchanan, and Fawcett, *J.*, 1959, 2192.
[7] Stirling, *Chem. and Ind.*, 1960, 933.

p-Me·C$_6$H$_4$·SO$_2$·CH$_2$·CH$_2$·OR
(XXIII) R = Ph
(XXIV) R = Et

p-Me·C$_6$H$_4$·SO$_2$·CH=CH$_2$
(XXV)

The novel mechanism of alkaline hydrolysis of the adenine nucleosides (I) and (III) provides a remarkably close analogy to the suggested mechanism [8] of decomposition in aqueous potassium cyanide of vitamin B_{12} coenzyme. This compound contains a 5′-deoxy-



(XXVI)

adenosine residue linked to cobalt at the 5′-position in the sugar.[9] In this case the ethylenic bond in the sugar (XXVI) is not activated as was that in the ethylenic intermediates from the sulphonium nucleosides; consequently further addition reactions do not occur.

Experimental

Paper Chromatography.—Whatman No. 1 paper was used with ascending development in the system butan-1-ol–acetic acid–water (4 : 1 : 5, upper layer). Sulphur derivatives were detected with potassium iodoplatinate,[10] sulphides giving white spots and sulphonium compounds purple-blue spots on a pink background. α-Glycols were detected with the periodate–Schiff reagents.[11] Reducing sugars were detected with aniline phthalate [12] or silver nitrate.[13] Wherever possible, sulphonium compounds were applied as their acetates; in some cases iodides and acetates gave different R_F values.

5′-Deoxy-5′-dimethylsulphonioadenosine Iodide (III).—5′-Deoxy-5′-methylthioadenosine [14] (579 mg.) in a 3 : 1 mixture (10 ml.) of formic and acetic acid was treated with methyl iodide (5 ml.) and kept for 5 days in darkness at room temperature. Solvents were removed *in vacuo* and a solution of the residue in water (20 ml.) was continuously extracted with ether until no free iodine remained in the water layer. Removal of water *in vacuo* left a glass which was dissolved in methanol. Addition of ether precipitated the *iodide* (682 mg.) as a hygroscopic amorphous white powder with R_F 0·24 (Found: C, 33·3; H, 5·0. $C_{12}H_{18}IN_5O_3S,2CH_3·OH$ requires C, 33·4; H, 5·2%).

1-Deoxy-1-methylthio-D-glycerol.—Toluene-*p*-sulphonyl chloride (14·0 g.) was added with cooling to a solution of 2,3-*O*-isopropylidene-D-glycerol [15] (9·0 g.) in dry pyridine (40 ml.). After 20 hr. at room temperature the crude toluene-*p*-sulphonate was isolated by extraction with chloroform. The syrupy product was dissolved in dimethylformamide (170 ml.), and sodium methyl sulphide (9·0 g.) was added. The solution was kept at 100° for 2 hr. and at room temperature for a further 14 hr. Solvent (150 ml.) was removed *in vacuo*, water (100 ml.) was added, and the product was extracted with chloroform (2 × 100 ml.). Removal of chloroform from the dried extract left a residue which was heated on a water-bath with N-hydrochloric acid (100 ml.) for 1 hr. The acid was neutralised with sodium hydrogen carbonate, the solution was evaporated to 15 ml., and the product was extracted with chloroform (3 × 25 ml.). After removal of solvent the residual oil was purified by vacuum-distillation. *1-Deoxy-1-methylthio-D-glycerol* (7·4 g.) was a viscous oil with b. p. 65—67°/0·05 mm., R_F 0·70, n_D^{20} 1·4977, and $[\alpha]_D^{20}$ −11·6° (*c* 1·9 in MeOH) (Found: C, 38·9; H, 8·45. $C_4H_{10}O_2S$ requires C, 39·3; H, 8·25%).

[8] Johnson and Shaw, *Proc. Chem. Soc.*, 1961, 447.
[9] Hodgkin and Lenhert, 2nd European Symposium on "Vitamin B_{12} and Intrinsic Factor," see *Nature*, 1961, **191**, 1154.
[10] Winegard, Toennies, and Block, *Science*, 1948, **108**, 506.
[11] Baddiley, Buchanan, Handschumacher, and Prescott, *J.*, 1956, 2818.
[12] Partridge, *Nature*, 1949, **164**, 443.
[13] Trevelyan, Procter, and Harrison, *Nature*, 1950, **166**, 444.
[14] Baddiley, *J.*, 1951, 1348.
[15] Baer and Fischer, *J. Biol. Chem.*, 1939, **128**, 463.

1-*Deoxy*-1-*dimethylsulphonio*-D-*glycerol Iodide* (XIIa).—Freshly distilled methyl iodide (1 ml.) was added to a solution of 1-deoxy-1-methylthio-D-glycerol (235 mg.) in methanol (5 ml.) and the mixture was kept in darkness for 2 days. Solvents were removed *in vacuo* and the brown residue was dissolved in water (5 ml.). The solution was extracted continuously with ether to remove iodine and then evaporated *in vacuo* to constant weight. The *iodide* (469 mg.) was a pale yellow viscous oil with $[\alpha]_D^{20}$ −27·2° (*c* 1·0 in MeOH) (Found: C, 23·05; H, 5·4. $C_5H_{13}IO_2S$ requires C, 22·7; H, 4·9%).

Conversion of the Iodide (XIIa) *into the Reineckate* (XIIc).—A 1% solution of ammonium reineckate (15 ml.) was added to a solution of the iodide (XIIa) (80 mg.) in water (5 ml.) which had been acidified with a drop of perchloric acid. A lustrous pink crystalline precipitate was formed instantly. After being kept at 0° overnight the solution was filtered and the residue was washed and dried. The reineckate (112 mg., 81%) formed pink plates, m. p. 149—151° (decomp.).

Conversion of the Reineckate (XIIc) *into the Acetate* (XIIb).—The reineckate (54·0 mg.) was dissolved in acetone (0·5 ml.), and the solution was diluted with methanol (2 ml.) and passed through a column (2 × 1 cm.) of Dowex-2 (acetate form) resin which had been previously washed with acetone–methanol (1 : 4). Evaporation of the eluate (10 ml.) gave the *acetate* (23·5 mg., 99%) as a viscous oil with R_F 0·33 and $[\alpha]_D^{20}$ −38·4° (*c* 1·2 in MeOH) (Found: C, 42·5; H, 8·7. $C_7H_{16}O_4S$ requires C, 42·8; H, 8·25%).

Conversion of the Reineckate (XIIc) *into the Iodide* (XIIa).—The reineckate (XIIc) (54·4 mg.) in acetone–methanol (1 : 4; 2·5 ml.) was passed slowly in darkness through a column (5 × 1 cm.) of Dowex-2 (iodide form) resin previously washed in darkness with the above solvent mixture. Evaporation of the eluate (20 ml.) gave the iodide (31·5 mg., 100%) with $[\alpha]_D^{20}$ −26·6° (*c* 1·6 in MeOH).

Methyl 5-*Deoxy*-5-*methylthio*-2,3-O-*isopropylidene*-β-D-*ribofuranoside* (XIV).—A solution of sodium methyl sulphide (15·0 g.) and methyl 2,3-*O*-isopropylidene-5-*O*-toluene-*p*-sulphonyl-β-D-ribofuranoside (18·0 g.) in dimethylformamide (250 ml.) was kept at 100° for 2 hr. and at room temperature for a further 48 hr. Solvent (200 ml.) was removed *in vacuo* and water (50 ml.) was added. The solution was extracted with chloroform (4 × 100 ml.), and the extract, after drying and removal of chloroform, was purified by vacuum-distillation. The sulphide (8·0 g.) was a colourless liquid, b. p. 81°/0·4 mm., n_D^{20} 1·4750, $[\alpha]_D^{20}$ −103° (*c* 3·8 in MeOH) (Found: C, 51·4; H, 7·9. Calc. for $C_{10}H_{18}O_4S$: C, 51·3; H, 7·7%). Satoh and Yoshimura [16] report b. p. 55—60°/0·001 mm.

Methyl 5-*Deoxy*-5-*methylthio*-D-*ribofuranoside* (XV).—A solution of the isopropylidene derivative (XIV) (6·05 g.) in methanol (150 ml.) and 0·3N-hydrochloric acid (30 ml.) was refluxed for 4·5 hr., then passed through a column (9 × 2 cm.) of Dowex-3 (OH^- form) resin, and the combined eluate and methanol washings (300 ml.) were evaporated *in vacuo* to a syrup. The *sulphide* (4·4 g.) was distilled at 116°/0·007 mm. and had R_F 0·75, n_D^{20} 1·5080, and $[\alpha]_D^{20}$ −3·6° (*c* 2·5 in MeOH) (Found: C, 43·4; H, 7·6. $C_7H_{14}O_4S$ requires C, 43·3; H, 7·2%).

Methyl 5-*Deoxy*-5-*dimethylsulphonio*-β-D-*ribofuranoside Iodide* (XVIa).—Freshly distilled methyl iodide was added to the sulphide (XV) (6·1 g.) in methanol (150 ml.), and the solution was kept in darkness for 36 hr. Solvents were removed *in vacuo*, the residue was dissolved in water (20 ml.), and iodine was removed by continuous extraction with ether. Evaporation of the aqueous solution yielded a residue which crystallised on addition of acetone. Recrystallisation from acetone–methanol (20 : 1) gave prisms of the *sulphonium iodide* (6·9 g.), m. p. 105—106°, R_F 0·31, $[\alpha]_D^{20}$ −17·2° (*c* 1·7 in MeOH) (Found: C, 28·9; H, 5·2. $C_8H_{17}IO_4S$ requires C, 28·6; H, 5·1%).

Degradation of the Sulphonium Iodide (XVIa).—A solution of the iodide (914 mg.) in water (15 ml.) was passed through a column (15 × 1 cm.) of Dowex-2 (acetate form) resin. The eluate (200 ml. after washing with water) was evaporated *in vacuo* to 100 ml., 50% periodic acid solution (2·2 ml.) was added, and the solution was kept in darkness at room temperature for 5 hr. Periodate and iodate were removed by passing the solution through a column of Dowex-2 (acetate form) resin as before and the eluate and washings were evaporated *in vacuo* to 70 ml. 2M-Boric acid (50 ml.) and 0·05M-sodium borate (35 ml.) were added and the volume was adjusted to 200 ml.; the solution had pH 8·4. Sodium borohydride (0·91 g.) in water (15 ml.) was added slowly during 30 min. After 4 hr. the pH of the solution was 9·2; it was adjusted to pH 7 with 2N-hydrochloric acid and then passed through a column (15 × 2 cm.)

[16] Satoh and Yoshimura, *J. Chem. Soc. Japan*, 1952, **73**, 350.

of Dowex-2 (chloride form) resin. The combined eluate and washings (400 ml.) were evaporated *in vacuo* to 10 ml., and then methanol (20 ml.) was added and the precipitated inorganic salts were removed by filtration. Methanol was removed under reduced pressure, 0·3N-hydrochloric acid (20 ml.) was added, and the solution was kept at 100° for 3·5 hr. The solution was passed successively through columns (15 × 1 cm.) of Dowex-3 (free base form) and Dowex-2 (acetate form) resins, and the eluate and washings were concentrated to 20 ml. Ammonium reineckate (1 g.) in 2% perchloric acid (100 ml.) was added and the solution was kept at 0° overnight. The pink precipitate was filtered off, washed, and dried. The reineckate (XIc) (1·09 g., 86%) formed pink plates, m. p. 149—151° (decomp.) The *acetate* (XIb) had R_F 0·33 and $[\alpha]_D^{20}$ +37·7° (*c* 2·2 in MeOH), +38·0° (*c* 0·8 in MeOH) (Found: C, 43·0; H, 9·0. $C_7H_{16}O_4S$ requires C, 42·8; H, 8·25%). The *iodide* (XIa) had $[\alpha]_D^{20}$ +27·4° (*c* 4·1 in MeOH), +26·7° (*c* 1·5 in MeOH) (Found: C, 22·7; H, 5·5. $C_5H_{13}IO_2S$ requires C, 22·7; H, 4·9%).

Treatment of the Sulphonium Iodide (XVIa) *with Sodium Methoxide and Degradation of the Glycosides Produced.*—The sulphonium iodide (903 mg.) in methanol (20 ml.) was passed through a column (15 × 1 cm.) of Dowex-2 (acetate form) resin previously washed with methanol. The eluate and washings (200 ml.) were concentrated to 2 ml., and 0·1N-sodium methoxide in methanol (30 ml.) was added. After 2 hr. at room temperature the solution was adjusted to pH 6 with acetic acid, methanol was removed *in vacuo*, and the residue was dissolved in water (100 ml.). To this was added 50% periodic acid (2·2 ml.), and subsequent operations were carried out as before. The reineckate (965 mg., 79%) had m. p. 149—151° (decomp.). The *acetate* had R_F 0·33 and $[\alpha]_D^{20}$ +0·5° (*c* 2·1 in MeOH) (Found: C, 43·1; H, 9·0%). The *iodide* had $[\alpha]_D^{20}$ +0·2°: (*c* 4·2 in MeOH) (Found: C, 23·3; H, 5·3%).

5′-Deoxy-5′-methylthiouridine (XIX).—This was synthesised independently by a method similar to that described later by Bannister and Kagan.[17] It had m. p. 192—193° and R_F 0·56 (Found: C, 43·6; H, 5·45. Calc. for $C_{10}H_{14}N_2O_5S$: C, 43·8; H, 5·1%). Bannister and Kagan report m. p. 191—193°.

5′-Deoxy-5′-methylsulphonyluridine (XX).—The methylthiouridine (24 mg.) in acetic acid (5 ml.) was treated with 30% hydrogen peroxide (1 ml.) and was kept at 100° for 1 hr. and then at room temperature for 12 hr. After removal of solvents *in vacuo* the residue recrystallised from a little water, to give the *sulphone* (13 mg.) as needles, m. p. 214—215°, R_F 0·34 (Found: C, 39·0; H, 4·5. $C_{10}H_{14}N_2O_7S$ requires C, 39·2; H, 4·6%).

Experiments with 5′-Deoxy-5′-dimethylsulphonioadenosine Iodide (III).—(*a*) The iodide (5 mg.) in water (0·5 ml.) was treated with 0·2N-sodium hydroxide (0·1 ml.). After 2 hr. at room temperature acetic acid was added to pH 7. Paper chromatography indicated the presence of adenine (R_F 0·49) and a sulphonium sugar (R_F 0·24), but no starting material was detected.

(*b*) The iodide (20 mg.) in methanol (2 ml.) was treated with 0·2N-sodium methoxide in methanol (0·4 ml.). After 2 hr. at room temperature acetic acid was added to pH 7. The products were adenine (R_F 0·49) and a sulphonium glycoside (R_F 0·31), but no starting material was detected. An impure preparation (10 mg.) of the glycoside was isolated by chromatography on Whatman No. 3 paper and used in the following experiments:

(*c*) As for (*a*) above, but with the glycoside in place of the iodide. Only the sulphonium sugar (R_F 0·24) was detected; no glycoside remained.

(*d*) The glycoside (5 mg.) in butan-1-ol (0·5 ml.) was treated with 0·2N-sodium n-butoxide in butan-1-ol (0·1 ml.). After 2 hr. at room temperature acetic acid was added to pH 7. The original glycoside had disappeared and was replaced by a faster-moving glycoside (R_F 0·58).

Experiments with 5′-Deoxy-5′-methylsulphonyluridine (XX).—(*a*) The sulphone (1 mg.) in water (0·1 ml.) was kept for 2 days at room temperature. Paper chromatography showed the presence of uracil (R_F 0·46) and a sugar (R_F 0·36), in addition to the original sulphone (R_F 0·34).

(*b*) The sulphone (2 mg.) in 0·01N-sodium hydroxide (0·2 ml.) was kept for 2 hr. at room temperature and then acetic acid was added to pH 7. Only uracil (R_F 0·46) and a sugar (R_F 0·36) were detected.

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