Mesitylenesulphonyl Chloride: a Selective Sulphonylating Reagent for Carbohydrates [1]

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Mesitylenesulphonyl chloride (trimsyl chloride) has been shown to react more selectively with one hydroxy-group of a vicinal diol than does toluene-*p*-sulphonyl chloride. Vicinal *trans*-bistrimsyloxy-systems do not form oxirans on treatment with methanolic sodium methoxide, in contrast to the analogous bistosyloxy-systems.

SELECTIVE sulphonylation of secondary polyhydroxy-systems is known, but the results of such reactions may be difficult to predict. The most widely used sulphonylating reagents are tosyl (toluene-*p*-sulphonyl) and mesyl (methanesulphonyl) chlorides. Of these the former is generally slightly more selective than the latter, but the effect is not usually marked.

It was decided therefore to explore the use of a bulky sulphonylating agent in the hope that for a vicinal diol, the presence of one bulky group would effectively prevent reaction at the second site. Mesitylene-sulphonyl chloride ‡ (1) (trimsyl chloride; 'TmCl') was selected as a potential reagent of this class.

In connection with their work on the synthesis of internucleotide bonds using arenesulphonyl chlorides as reagents,[2] Khorana and his co-workers studied the rates of sulphonylation with tosyl and trimsyl chlorides of the primary 5'-hydroxy-group of 2',3'-di-*O*-benzoyl-uridine in dry pyridine.[3] The rates were not very different, but tri-isopropylbenzenesulphonyl chloride

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‡ In the preliminary publication [1] it was proposed that the abbreviated trivial name 'mesisyl chloride' should be used with the symbol MES. Experience has shown that this name causes confusion with mesyl chloride and so it is now proposed that the abbreviation 'trimsyl' (Tm) should be used instead.

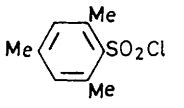
[1] Preliminary communication, S. E. Creasey and R. D. Guthrie, *Chem. Comm.*, 1971, 801.

[2] T. M. Jacob and H. G. Khorana, *J. Amer. Chem. Soc.*, 1964, **86**, 1630.

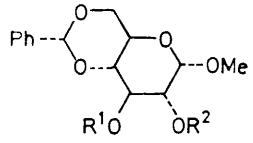
[3] R. Lohrmann and H. G. Khorana, *J. Amer. Chem. Soc.*, 1966, **88**, 829.

(tripsyl chloride; TpCl) had a much slower rate of reaction. This reagent is considerably more bulky than trimsyl chloride. Other workers [4] showed, as would be expected, that the use of trimsyl chloride offered no significant advantage over the use of tosyl chloride for the selective esterification of a primary hydroxy-group in the presence of a secondary one.

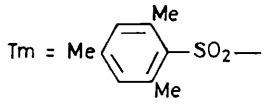
No work on selective esterification amongst secondary hydroxy-groups by trimsyl chloride is recorded. Trimsyl chloride is expensive if bought commercially, but it can be made easily in a one-step reaction between mesitylene and chlorosulphonic acid.[5,6]



(1)



(2) $R^1 = H = R^2$
(3) $R^1 = H$, $R^2 = Ts$
(4) $R^1 = H$, $R^2 = Tm$
(5) $R^1 = Tm = R^2$
(6) $R^1 = R^2 = Ts$
(7) $R^1 = Ms$, $R^2 = Tm$



Tosylation and mesylation of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (2) have been found [7,8] to proceed selectively at O-2. The 2-tosylate (3) is much used in carbohydrate chemistry as a synthetic precursor, particularly of methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-mannopyranoside. Compound (3) is formed by selective tosylation, which involves cooling to about −40° and careful addition of reagents. The use of a bulkier reagent than tosyl chloride might be expected to increase the selectivity. Methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (2) was treated with 1 equiv. of trimsyl chloride at room temperature for 6 days, the product being the expected 2-ester (4), obtained in high yield. The location of the trimsyl group at O-2 was confirmed by the ready conversion of the product into methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-mannopyranoside. The overall yield from the starting diol of epoxide prepared *via* crude (4) was 63%, as compared with about 35% when the epoxide was prepared *via* the 2-tosylate (3).[9] Hence the substitution of trimsyl chloride for tosyl chloride in the preparation of the oxiran is extremely advantageous. The large size and hindered nature of the trimsyl group are reflected by the longer reaction time required for trimsylation (*cf.* Khorana's finding [3] that rates of tosylation and trimsylation were similar for a primary hydroxy-group); relief of hindrance on removal of the group is shown by the shorter time required for formation of the epoxide from (4) than from (3).

Various attempts to make the 2,3-di-*O*-trimsyl derivative (5) gave only low yields. However, acetylation of the 2-ester (4) under normal conditions gave 77% of the 3-acetate, demonstrating that normal reagents can approach a vicinal monohydroxy-monotrimsyl system, whereas approach of bulky reagents is hindered.

Methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside is formed when the ditosylate (6) is treated with methanolic sodium methoxide.[10] One of the ester groups must undergo O–S cleavage (S_N2S displacement), facilitated by the inductive effect of the other sulphonyloxy-group.[11,12] Similar treatment of (5) either at room temperature or under reflux gave unchanged starting material, along with a trace (t.l.c.) of the anhydro-alloside. This lack of reactivity in comparison with the ditosylate (6) is probably caused by steric hindrance to attack at sulphur in the C-2 trimsyl group. This is in contrast to the findings of Bunnett and Bassett,[13] who studied the reactions of mono- and di-nitrophenyl esters of toluene-*p*-sulphonic and mesitylenesulphonic acids with nucleophilic reagents. The esters were found to undergo both C–O and S–O fission, methyl groups introduced *ortho* to the sulphonate group having relatively little effect on the proportions of these processes. Bunnett and Bassett concluded that such methyl groups provided little steric hindrance to nucleophilic attack at the sulphur atom.

The 3-mesyl compound (7) was prepared by mesylation of (4), the reaction being slower than a normal mesylation. If this compound, on treatment with sodium methoxide, were to form an oxiran, it would first have to undergo one O–S fission.[14] Since the results for the ditrimsylate (5) indicate that this can only happen at a trimsyl group with great difficulty, the mesyl group offered an alternative site for such cleavage: from this, methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-mannopyranoside would be formed. However, prolonged treatment of (7) with sodium methoxide, either at room temperature or under reflux, gave a high yield of starting material, with traces of other compounds including the *manno*-oxiran and the 2-*O*-trimsyl compound (4). That little reaction occurred shows that the formation of anhydro-sugars from disulphonates must involve initial attack at the 2-ester group, which is probably the more accessible, as has been noted before.

Monotrimsylation of methyl 4,6-*O*-benzylidene-β-D-

[4] W. S. Johnson, J. C. Collins, jun., R. Pappo, M. B. Rubin, P. J. Kropp, W. F. Johns, J. E. Pike, and W. Bartmann, *J. Amer. Chem. Soc.*, 1963, **85**, 1409.
[5] C. H. Wang and S. G. Cohen, *J. Amer. Chem. Soc.*, 1957, **79**, 1924.
[6] C. S. Gibson, *J. Chem. Soc.*, 1920, **117**, 948.
[7] G. J. Robertson and C. F. Griffith, *J. Chem. Soc.*, 1935, 1193.
[8] H. R. Bolliger and D. A. Prins, *Helv. Chim. Acta*. 1945, **28**, 465.
[9] L. F. Wiggins, *Methods Carbohydrate Chem.*, 1963, **2**, 189.
[10] N. K. Richtmyer, *Methods Carbohydrate Chem.*, 1962, **1**, 109.
[11] S. J. Angyal and P. T. Gilham, *J. Chem. Soc.*, 1957, 3691.
[12] A. C. Cope and T. Y. Shen, *J. Amer. Chem. Soc.*, 1956, **78**, 5912.
[13] J. F. Bunnett and J. Y. Bassett, jun., *J. Amer. Chem. Soc.*, 1959, **81**, 2104.
[14] F. H. Newth, *Quart. Rev.*, 1959, **13**, 30.

glucopyranoside gave, after chromatography, the parent diol (12%), and the 2-trimsyl (27%), 3-trimsyl (33%), and ditrimsyl (11%) esters. These results follow the pattern shown by tosylation,[15,16] although the amount of diester formed on trimsylation is less than the amount formed on tosylation, and the amount of 2-ester is greater. This is a consequence of the large size of the trimsyl group, since it was postulated [16] for tosylation that on formation of the 2-ester the 3-position was activated, leading to diester formation; this is less likely for steric reasons in the case of the trimsylates. The 2- and 3-trimsylates of methyl 4,6-*O*-benzylidene-β-D-glucopyranoside were characterized by conversion into β-anhydromannoside and β-anhydroalloside, respectively, and both monoesters were readily acetylated. Methyl 4,6-*O*-benzylidene-2,3-di-*O*-trimsyl-β-D-glucopyranoside did not react with sodium methoxide.

To confirm the behaviour described in the previous section, the reactions of a simpler system were studied. *trans*-Cyclohexane-1,2-diol was chosen since its hydroxy-groups are arranged similarly to those in methyl 4,6-*O*-benzylidene-D-glucopyranosides. The compound was treated with 2 equiv. of trimsyl chloride in pyridine for 42 h at room temperature, chromatography of the resulting mixture giving 66% of monoester and 18% of diester. In a similar reaction with tosyl chloride, the yields were: monoester, 44; diester 40%. These results emphasize the difficulty of *O*-trimsylation of neighbouring secondary hydroxy-groups as compared with formation of *vic*-ditosylates. However, the monotrimsylate formed an acetate under normal conditions, showing that the approach of a small molecule to a vicinal monohydroxy-monotrimsyl system is not hindered.

Tripsyl chloride is an even more bulky reagent than trimsyl chloride. Reaction of this compound with *trans*-cyclohexane-1,2-diol showed (t.l.c.) no sign of diester formation, even after 7 days.[17]

Several workers have studied the selective esterification of methyl α-D-glucopyranoside to give benzoates,[18,19] mesylates,[20,21] tosylates,[22] laurates,[23,24] palmitates,[25] and oleates.[24] It has emerged that, of the secondary hydroxy-groups, that at C-2 is the most reactive, followed by the 3- and then by the 4-hydroxy-group. Less work has been carried out on the β-anomer, but Chalk, Ball, and Long [20] found that the order of reactivity found for mesylation of the α-anomer did not hold for the β-anomer. We decided therefore to investigate the reactions of methyl D-glucopyranosides with trimsyl chloride.

Reaction of methyl α-D-glucopyranoside at room temperature overnight with 4 mol. equiv. of trimsyl chloride gave 97% of a syrupy diester and a minor fraction which consisted of a mixture of compounds. Periodate oxidation of the diester could not be carried out because the compound was extremely insoluble in aqueous solvents, even in 1 : 1 water–dimethylformamide. The compound formed a crystalline acetate and consideration of various shifts in the n.m.r. spectra of the acetate and of the parent diol (see later) indicated that the diol was methyl 2,6-di-*O*-trimsyl-α-D-glucopyranoside (we assume that one trimsyl group was situated at C-6). This same diester was obtained in 38% yield on treatment of methyl α-D-glucopyranoside with 4 mol. equiv. of trimsyl chloride in pyridine for 17 days at room temperature. The other products were obtained as a mixture of higher mobility on t.l.c. It was thought that the components of the mixtures might become separable after acetylation, but the acetates ran as closely together on t.l.c. as did the hydroxy-compounds.

Since no other product of similar R_F to the 2,6-di-trimsylate was separable by chromatography, it is reasonable to suppose that no other ditrimsylate was formed in the reactions, the only other products being higher esters. Hence, as has been found for other esterifying agents, the 2-hydroxy-group is the most reactive secondary hydroxy-group in methyl α-D-glucopyranoside.

In the case of methyl β-D-glucopyranoside, treatment at room temperature for 4 days with 1 mol. equiv. of trimsyl chloride in pyridine gave a slow reaction, the product of which was a monoester, obtained in low yield. The compound formed a triacetate, and periodate oxidation showed it to be the expected 6-ester, since it consumed almost 3 mol. equiv. of periodate during 6 days, the theoretical amount being 2 mol. equiv.*

On treatment with 4 mol. equiv. of trimsyl chloride in pyridine at room temperature overnight, methyl β-D-glucopyranoside gave 64% of a monoester, 9% of a diester, and a mixture containing two components, of R_F values intermediate between those of the other products. The diester was a syrup but gave a crystalline diacetate, and consumed no periodate on attempted oxidation, indicating that it was the 3,6-di-*O*-trimsyl derivative. This assignment was further substantiated by the lack of shifts in the n.m.r. spectrum (see later). When methyl β-D-glucopyranoside was treated with 4 mol. equiv. of trimsyl chloride at room temperature from 17 days, no monoester was obtained. At least seven products were seen on t.l.c., only one of which, the 3,6-diester, was separable (21% yield). The other products were obtained as a two-component mixture of lower R_F than that of the ditrimsylate, which appeared

* Methyl 6-*O*-tosyl-α-D-glucopyranoside consumed 2·5 mol. equiv. of periodate in 4 days under the same conditions.

[15] S. Stirm, O. Luderitz, and O. Westphal, *Annalen*, 1966, **696**, 180.
[16] A. M. Prior, D.Phil. Thesis, University of Sussex, 1968.
[17] J. Cléophax, personal communication.
[18] T. Lieser and R. Schweitzer, *Annalen*, 1935, **519**, 271; *Naturwiss.*, 1935, **23**, 131.
[19] J. M. Williams and A. C. Richardson, *Tetrahedron*, 1967, **23**, 1369.
[20] R. C. Chalk, D. H. Ball, and L. Long, jun., *J. Org. Chem.*, 1966, **31**, 1509.
[21] A. K. Mitra, D. H. Ball, and L. Long, jun., *J. Org. Chem.*, 1962, **27**, 160.
[22] J. Jary, K. Čapek, and J. Kovář, *Coll. Czech. Chem. Comm.*, 1964, **29**, 930.
[23] E. Reinefeld and D. Ahrens, *Annalen*, 1971, **747**, 39.
[24] Z. Jedlinski, *Bull. Acad. polon. Sci., Ser. Sci. chim.*, 1961, **9**, 103.
[25] J. Asselineau, *Bull. Soc. chim. France*, 1955, 937.

from its spectra and t.l.c. behaviour to have the same composition as the mixture obtained in the overnight reaction. A three-component mixture of higher R_F than that of the ditrimsylate was also obtained. None of the mixtures could be separated after acetylation.

Since the 3,6-diester was obtained in higher yield than either of the components of the low-R_F mixture, the 3-hydroxy-group is the most reactive secondary hydroxy-group with respect to reaction of trimsyl chloride with methyl β-D-glucopyranoside.

Spectroscopic Properties of Mesitylenesulphonyl Esters.—A general feature of the i.r. spectra of tosylates [26] is the peak at 1595—1605 cm^{-1}, of medium intensity, given by the aromatic ring. This signal was also present in the i.r. spectra of trimsyl esters; it was broader than and of the same intensity as the tosylate absorption. In the spectra of all the esters prepared in this study, another, weaker absorption was present at 1565 cm^{-1}; this was usually broad.

The n.m.r. spectra of trimsyl esters also showed some similarities to those of the corresponding tosylates. The Table contains most of the n.m.r. data for the compounds studied. The trimsyl aromatic protons resonated at about τ 3·0 for the 2-ester groups in methyl 4,6-*O*-benzylidene-D-glucopyranosides and for all the trimsyl groups in methyl D-glucopyranosides, and at about τ 3·3 for the 3-ester groups in methyl 4,6-*O*-benzylidene-D-glucopyranosides. The shift of the 3-ester group signal only in the benzylidene compounds indicated that the aromatic ring of the benzylidene group may shield the 3-trimsyl aromatic protons.

All compounds containing a 2-ester group showed an upfield shift in the position of the methoxy-signal with respect to its position in the spectra of compounds not containing a 2-ester group, as was found for tosylates.[27]

Conclusions.—Our results demonstrate that mesitylenesulphonyl chloride can be used as a blocking reagent for both primary and secondary hydroxy-groups. It can also participate in selective reactions, its effectiveness in such situations being due to its large size. It remains to be seen whether trimsylates undergo the whole range of reactions of tosylates. They might become useful as synthetic intermediates if they are found to be easily transformed; their one disadvantage is the length of time required for their formation.

A similar study of the reactions of tripsyl chloride would be useful; because of the much larger size of this molecule, it might show even more selectivity than trimsyl chloride, but its reactions might prove too slow to be of use.

N.m.r. spectra of trimsylates (τ values *; 60 MHz; solvent $CDCl_3$)

Compound	Aromatic	Ph*CH*	H-1	OCH_3	ArCH_3(*o*)	ArCH_3(*p*)	Other
(a) Methyl 4,6-*O*-benzylidene-D-glucopyranosides							
2-Tm-α	3·00br	4·50	5·28 (d)	6·73	7·33	7·70	
3-Ac-2-Tm-α	3·00br	4·53		6·69	7·36	7·70	8·11 (Ac)
2-Tm-3-Ms-α	3·10br	4·50	5·35	6·82	7·33	7·69	7·02 ($MeSO_2$)
2,3-Tm_2-α	3·04br (C-2)	4·78		6·80	7·39 (C-2)	7·72 (C-2)	
	3·39br (C-3)				7·57 (C-3)	7·88 (C-3)	
2-Tm-β	3·00br	4·49		6·79	7·33	7·71	
3-Ac-2-Tm-β	3·02br	4·53		6·79	7·36	7·72	8·08 (Ac)
3-Tm-β	3·32br	4·70		6·46	7·50	7·87	
2-Ac-3-Tm-β	3·26br	4·67		6·52	7·50	7·83	8·03 (Ac)
2,3-Tm_2-β	3·04br (C-2)	4·77		6·94	7·37 (C-2)	7·72 (C-2)	
	3·33br (C-3)				7·51 (C-3)	7·87 (C-3)	
(b) Methyl D-glucopyranosides							
2,6-Tm_2-α	3·00br		5·52 (d)	6·84	7·37	7·70	
					7·39		
6-Tm-β [a]	3·04br			6·52	7·37	7·70	
2,3,4-Ac_3-6-Tm-β	3·00br			6·57	7·39	7·70	8·0 (3 × Ac)
3,6-Tm_2-β	2·99br			6·52	7·35	7·68	
2,4-Ac_2-3,6-Tm_2-β	3·01 (d)			6·56	7·3	7·69	8·11, 8·25 (2 × Ac)
					7·41	7·71	

* Singlets unless otherwise specified.
[a] 100 MHz.

EXPERIMENTAL

Optical rotations are quoted for solutions in chloroform unless otherwise stated.

Methyl 4,6-Benzylidene-2-O-trimsyl-α-D-glucopyranoside (4).—Solutions of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (2 g) and trimsyl chloride (2·3 g, 1·5 mol. equiv.) in dry pyridine (8 and 6 ml, respectively) were cooled in ice and mixed. After 6 days at room temperature the mixture was poured into ice–water (140 ml) and the resulting precipitate was collected and recrystallized from aqueous ethanol to give *compound* (4) (1·9 g, 58%), m.p. 174—174·5°, $[M]_D$ +255·2° (*c* 0·14) (Found: C, 59·3; H, 6·1%; M^+, 464. $C_{23}H_{28}O_8S$ requires C, 59·5; H, 6·0%; *M*, 464).

Methyl 4,6-O-Benzylidene-2,3-di-O-trimsyl-α-D-glucopyranoside (5).—(a) *From methyl 4,6-O-benzylidene-α-D-glucopyranoside.* A solution of the title diol (500 mg) in dry pyridine (10 ml) was cooled to 0° and treated with trimsyl chloride (700 mg, 3 mol. equiv.). The mixture was kept at room temperature for 4 days and was then poured into ice–water (75 ml). The resulting solid was extracted with chloroform, and the extract was then evaporated. P.l.c. [chloroform–petroleum (9 : 1)] of the residue gave, as the most mobile band, *methyl 4,6-O-benzylidene-2,3-di-O-trimsyl-α-D-glucopyranoside* (45 mg, 7%), m.p. 227—229° (from chloroform–petroleum), $[M]_D$ +174·4° (*c* 0·30) (Found: C,

[26] R. D. Guthrie and H. Spedding, *J. Chem. Soc.*, 1960, 953.
[27] S. E. Creasey, R. D. Guthrie, and A. M. Prior, *J. Chem. Soc.* (*C*), 1970, 1961.

59·5; H, 6·0%; M^+, 646. $C_{32}H_{38}O_{10}S_2$ requires C, 59·4; H, 5·9; *M*, 646). Repetition of this reaction for 30 days at room temperature also gave the trimsylate (170 mg, 25%).

(b) *From methyl* 4,6-O-*benzylidene*-2-O-*trimsyl*-α-D-*glucopyranoside* (4). A mixture of the compound (4) (500 mg) and trimsyl chloride (350 mg, 1·5 mol. equiv.) was dissolved in dry pyridine (5 ml); the solution was kept at 40° for 4 days, then poured into ice–water (50 ml) and was extracted with chloroform. The extracts were washed with saturated aqueous sodium hydrogen carbonate and evaporated to give a solid. P.l.c. (chloroform) gave the ditrimsylate (150 mg, 22%) as the more mobile component.

Methyl 3-O-*Acetyl*-4,6-O-*benzylidene*-2-O-*trimsyl*-α-D-*glucopyranoside*.—Methyl 4,6-*O*-benzylidene-2-*O*-trimsyl-α-D-glucopyranoside (500 mg) was acetylated with acetic anhydride in pyridine for 24 h at room temperature to give the *acetate* (420 mg, 77%), m.p. 144—146° (from aqueous ethanol), $[M]_D$ +298° (*c* 2·47) (Found: C, 59·0; H, 6·2. $C_{25}H_{30}O_9S$ requires C, 59·3; H, 6·4%).

Methyl 4,6-O-*Benzylidene*-3-O-*mesyl*-2-O-*trimsyl*-α-D-*glucopyranoside* (7).—Methyl 4,6-*O*-benzylidene-2-O-trimsyl-α-D-glucopyranoside (4) (1·6 g) was dissolved in dry pyridine (16 ml), cooled to 0°, and treated slowly with a cold solution of mesyl chloride (0·95 ml, 4 mol. equiv.) in dry pyridine (10 ml). The mixture was kept at 0° overnight and then at room temperature for 2 days, before being diluted with ice–water (200 ml). The resulting precipitate was collected and recrystallized from chloroform–petroleum to give the *mesylate* (1·2 g, 64%), m.p. 178—179°, $[M]_D$ +406° (*c* 0·06) (Found: C, 52·7; H, 5·7. $C_{24}H_{30}O_{10}S_2$ requires C, 52·95; H, 5·5%).

Trimsylation of Methyl 4,6-O-*Benzylidene*-β-D-*glucopyranoside*.—Solutions of the title compound (2 g) and trimsyl chloride (2·3 g, 1·5 mol. equiv.) in dry pyridine (8 and 10 ml, respectively) were cooled to 0° and mixed. After 6 days at room temperature the solution was poured into ice–water (180 ml) and the mixture was extracted with chloroform. The extracts were washed with saturated aqueous sodium hydrogen carbonate and evaporated to give a pale brown solid, which showed five bands on p.l.c. [chloroform–petroleum (9 : 1), 2 passes; chloroform, 1 pass]: (i) *methyl* 4,6-O-*benzylidene*-2,3-*di*-O-*trimsyl*-β-D-*glucopyranoside* (490 mg, 11%), m.p. 200—201° (from chloroform–petroleum), $[M]_D$ −254° (*c* 0·31) (Found: C, 59·8; H, 6·0. $C_{32}H_{38}O_{10}S_2$ requires C, 59·4; H, 5·9%); (ii) *methyl* 4,6-O-*benzylidene*-2-O-*trimsyl*-β-D-*glucopyranoside* (900 mg, 23%), m.p. 131·5—132·5° (from aqueous ethanol), $[M]_D$ −310° (*c* 0·12) (Found: C, 59·3; H, 6·1. $C_{23}H_{28}O_8S$ requires C, 59·5; H, 6·0%); (iii) *methyl* 4,6-O-*benzylidene*-3-O-*trimsyl*-β-D-*glucopyranoside* (1·1 g, 33%), m.p. 79—80° (from aqueous ethanol), $[M]_D$ −496° (*c* 0·88) (Found: C, 59·0; H, 6·2. $C_{23}H_{28}O_8S$ requires C, 59·5; H, 6·0%); (iv) 60 mg of syrup, unidentified; and (v) starting material (230 mg, 11·5%).

Formation of Acetates from Methyl 4,6-O-*Benzylidene*-β-D-*glucopyranoside Monotrimsylates*.—Each monotrimsylate (200 mg) was treated for 22 h at room temperature with acetic anhydride in pyridine to give: *methyl* 2-O-*acetyl*-4,6-O-*benzylidene*-3-O-*trimsyl*-β-D-*glucopyranoside* (60 mg, 28%), m.p. 216—217·5° (from aqueous ethanol), $[M]_D$ −325° (*c* 0·2) (Found: C, 59·3; H, 6·2. $C_{25}H_{30}O_9S$ requires C, 59·3; H, 6·4%); *methyl* 3-O-*acetyl*-4,6-O-*benzylidene*-2-O-*trimsyl*-β-D-*glucopyranoside* (150 mg, 69%), m.p. 194—195·5° (from aqueous ethanol), $[M]_D$ −188° (*c* 0·80) (Found: C, 59·45; H, 6·4. $C_{25}H_{30}O_9S$ requires C, 59·3; H, 6·4%).

Attempted Formation of Oxirans.—(a) *From methyl* 4,6-O-*benzylidene*-2-O-*trimsyl*-α-D-*glucopyranoside* (4). The sulphonate (500 mg) was added to a solution of sodium methoxide (33 mg of sodium in 3 ml of dry methanol) and the suspension was refluxed for 3 h; solid was present at all times. The product which separated on cooling was collected and recrystallized from ethanol to give methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-mannopyranoside (170 mg, 50%), m.p. 139—141° (lit.,[28] 145—147°), identified by comparison [t.l.c. (chloroform)] with an authentic sample. In another experiment, the title trimsylate was prepared from methyl 4,6-*O*-benzylidene-α-D-glucopyranoside according to the foregoing procedure and the crude product (85%; m.p. 160°) was converted into the anhydromannoside, m.p. 140—143° (lit.,[28] 145—147°) [yield 75% from the 2-trimsylate; 63% from the starting diol].

(b) *From methyl* 4,6-O-*benzylidene*-2,3-*di*-O-*trimsyl*-α-D-*glucopyranoside* (5). Compound (5) (100 mg) was dissolved in chloroform (1 ml) and treated with a solution of sodium (14 mg) in dry methanol (0·4 ml). After 4 days at room temperature the mixture was diluted with water and the chloroform layer was removed, washed twice with water, and evaporated to yield a solid. Extraction of the main band from p.l.c. [chloroform–petroleum (1 : 1)] gave a solid (75 mg) shown by the t.l.c. (same solvent) to be mainly starting material, containing traces of methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside. A solution of this material (75 mg) and sodium (14 mg) in dry methanol (4 ml) was refluxed for 3·5 h and then kept at room temperature for 2·5 days and evaporated to dryness. The resulting solid was partitioned between chloroform and water. Evaporation of the chloroform layer gave a white solid (70 mg) which was shown by t.l.c. (chloroform) to be mainly the ditrimsylate, containing traces of anhydroalloside and 2-trimsylate.

(c) *From methyl* 4,6-O-*benzylidene*-2-O-*trimsyl*-3-O-*mesyl*-α-D-*glucopyranoside* (7). Compound (7) (500 mg) was dissolved in chloroform (7 ml) and treated with a solution of sodium (90 mg) in dry methanol (2·5 ml). After 8 days at room temperature t.l.c. [chloroform–petroleum (1 : 1)] showed that no reaction had occurred. Solvents were evaporated off and the residue was dissolved in dry methanol (20 ml) containing sodium (50 mg). The mixture was refluxed for 5 h and the resulting solution cooled. The precipitate which formed was filtered off and shown by t.l.c. (chloroform) to be starting material (360 mg). T.l.c. (chloroform) of the mother liquor showed the presence of starting material and another, unidentified product. The precipitate (300 mg) was re-treated with sodium methoxide solution (30 mg of sodium in 30 ml of dry methanol) for 17 h under reflux. Solvent was evaporated off; the resulting white solid was only partially soluble in chloroform. T.l.c. (chloroform) of the resulting suspension showed that it consisted largely of starting material. There were also traces of anhydromannoside and of the 2-trimsylate.

(d) *From methyl* 4,6-O-*benzylidene*-2-O-*trimsyl*-β-D-*glucopyranoside*. The title compound (200 mg) was dissolved in dry methanolic sodium methoxide (3 ml) [from sodium (10 mg)]. The solution was refluxed for 3 h, then evaporated to dryness, and the residue was extracted with hot ethanol. On cooling, the extract deposited crystals which were filtered off to give methyl 2,3-anhydro-4,6-*O*-benzyl-

[28] L. F. Wiggins, *Methods Carbohydrate Chem.*, 1963, **2**, 189.

idene-β-D-mannopyranoside (65 mg, 58%), m.p. 185—187° (lit.,[29] 182°), identified by t.l.c. comparison [chloroform–methanol (95 : 5)] with an authentic sample.

(e) *From methyl* 4,6-O-*benzylidene*-3-O-*trimsyl*-β-D-*glucopyranoside*. The procedure was as in (a); methyl 2,3-anhydro-4,6-*O*-benzylidene-β-D-allopyranoside (60 mg, 53%) had m.p. 136—137° (lit.,[29] 138°), identified by t.l.c. comparison [chloroform–methanol (95 : 5)] with an authentic sample.

(f) *From methyl* 4,6-O-*benzylidene*-2,3-*di*-O-*trimsyl*-β-D-*glucopyranoside*. The ditrimsylate (100 mg) was dissolved in chloroform (1·1 ml) and treated with a solution of sodium (14 mg) in dry methanol (0·4 ml). The mixture was kept at room temperature for 10 days and then diluted with water. The chloroform layer was removed, washed with water, and evaporated to give a white solid, which was shown to be starting material by t.l.c. [chloroform–petroleum (1 : 1)] and by mixed m.p.

Trimsylation of trans-*Cyclohexane*-1,2-*diol*.—Solutions of the diol (0·5 g) and trimsyl chloride (1·9 g, 2 mol. equiv.) in dry pyridine (7 and 8 ml, respectively) were cooled to 0° and mixed. The mixture was kept at room temperature for 42 h and then poured into ice–water (130 ml). The resulting mixture was extracted with chloroform and the extracts were evaporated to give a brown syrup, which contained three components [p.l.c. in chloroform–petroleum (b.p. 40—60°) (9 : 1)]. Extraction of the two most mobile bands gave the *ditrimsylate* (380 mg, 18%), m.p. 166—167° (from chloroform–petroleum) (Found: C, 59·9; H, 6·7. $C_{24}H_{32}O_6S_2$ requires C, 60·0; H, 6·7%), and the *monotrimsylate* (850 mg, 66%), m.p. 86—87° (from aqueous ethanol) (Found: C, 60·1; H, 7·6. $C_{15}H_{22}O_4S$ requires C, 60·4; H, 7·4%). The latter was treated with acetic anhydride in pyridine for 2 h at room temperature to give the *acetate* (48 mg, 22%), m.p. 43—45° (from aqueous ethanol) (Found: C, 60·1; H, 7·0. $C_{17}H_{24}O_3S$ requires C, 60·0; H, 6·9%).

Tosylation of trans-*Cyclohexane*-1,2-*diol*.—This was carried out exactly as for trimsylation. The products were the ditosylate (735 mg, 40%), m.p. 106—107·5° (from chloroform–petroleum), τ (60 MHz; $CDCl_3$) 2·10—2·80 (8H, aromatic), 5·40—5·70 (2H, broad, H-1 and H-2), 7·51 (6H, s, $ArCH_3$), and 7·80—8·80 (8H, broad, ring protons) (Found: C, 56·8; H, 5·95%; M^+, 424. $C_{20}H_{24}O_6S_2$ requires C, 56·5; H, 5·7%; *M*, 424) (lit.,[30] m.p. 128·5—129·5°); and the *monotosylate* (515 mg, 44%), m.p. 93·5—95° (from aqueous ethanol) (lit.,[30] m.p. 96°).

Trimsylation of Methyl α-D-*Glucopyranoside*.—The sugar (1 g) in dry pyridine (20 ml) was treated with trimsyl chloride (4·5 g, 4 mol. equiv.). The solution was kept at room temperature overnight and then poured into ice–water (200 ml). The mixture was extracted with chloroform and the extracts were washed with saturated aqueous sodium hydrogen carbonate and evaporated to give material (3·03 g) which on p.l.c. [chloroform–petroleum (1 : 1)] gave three bands. These bands were extracted to give: (i) 10 mg, unidentified; (ii) 400 mg, one spot on t.l.c. [chloroform; chloroform–petroleum (1 : 1); chloroform–methanol (95 : 5)], but not identifiable as one compound from n.m.r. (100 MHz; $CDCl_3$); (iii) *methyl* 2,6-*di*-O-*trimsyl*-α-D-*glucopyranoside* (2·8 g, 97%) as a syrup, characterized as its *diacetate* (67%), m.p. 136—137° (from methanol), $[M]_D$ +893° (*c* 0·13) (Found: C, 54·1; H, 6·2. $C_{29}H_{38}O_{12}S_2$ requires C, 54·2; H, 5·9%). When the experiment was repeated for 17 days at room temperature, the products after p.l.c. [chloroform–petroleum (1 : 1)] were: (i) 130 mg, unidentified; (ii) 2·38 g, unidentified mixture; and (iii) 2,6-ditrimsylate (1·02 g, 38%).

Trimsylation of Methyl β-D-*Glucopyranoside*.—A solution of methyl β-D-glucopyranoside (1 g) in dry pyridine (20 ml) was treated with trimsyl chloride (4·5 g, 4 mol. equiv.) and kept at room temperature overnight. Ice–water (200 ml) was added and the solution extracted with chloroform. The extracts were washed with saturated aqueous sodium hydrogen carbonate and evaporated to give a mixture of products which was separated by p.l.c. [chloroform–petroleum (1 : 1)]. The bands were: (i) and (ii) total 10 mg, unidentified; (iii) 50 mg, for which t.l.c. [chloroform–petroleum (1 : 1)] showed three components; (iv) *methyl* 3,6-*di*-O-*trimsyl*-β-D-*glucopyranoside* (270 mg, 9%), a syrup, characterized as its *diacetate*, m.p. 118·5—119·5° (from ethanol), $[M]_D$ +18·0° (*c* 0·25) (Found: C, 54·3; H, 6·15. $C_{29}H_{38}O_{12}S_2$ requires C, 54·2; H, 5·9%); (v) 1·15 g, syrup, for which t.l.c. [chloroform–petroleum (1 : 1)] showed two components, one charring black, the other brown, both unidentified; (vi) *methyl* 6-O-*trimsyl*-β-D-*glucopyranoside* (1·24 g, 64%), m.p. 172—173° (from water), $[M]_D$ −48·7° (*c* 0·34 in H_2O) (Found: C, 51·0; H, 6·45. $C_{16}H_{24}O_8S$ requires C, 51·1; H, 6·4%). Treatment with acetic anhydride in pyridine at room temperature for 17 h gave the *triacetate*, m.p. 151—152° (from methanol), $[M]_D$ −500° (*c* 0·04) (Found: C, 52·4; H, 6·2. $C_{22}H_{30}O_{11}S$ requires C, 52·6; H, 6·0%).

The reaction was repeated with methyl β-D-glucopyranoside (500 mg) at room temperature for 17 days. The following products were obtained after p.l.c. [chloroform–petroleum (1 : 1)]: (i) 130 mg, for which t.l.c. [chloroform–petroleum (1 : 1)] showed at least two components; (ii) 650 mg, for which t.l.c. [chloroform–petroleum (1 : 1)] showed three components; (iii) the 3,6-ditrimsylate (300 mg, 21%), identified by comparison [t.l.c. in chloroform–petroleum (1 : 1) and n.m.r. spectrum] with authentic material; (iv) 210 mg, for which t.l.c. [chloroform; chloroform–methanol (95 : 5)] showed two components.

Periodate Oxidation of Methyl 6-O-*Trimsyl*-β-D-*glucopyranoside*.—The trimsylate [(i) 18·45 mg or (ii) 6·53 mg] was dissolved in water (25·0 ml) and sodium periodate solution (0·02002M; 25·0 ml) was added. Samples (2 ml) of the solutions were analysed for periodate content by the Müller–Friedberger method.[31] The results (mol. equiv. uptake) were as follows:

Time (min):	2790	8520
(i)	2·57	2·64
(ii)	2·66	3·16

Periodate Oxidation of Methyl 3,6-*Di*-O-*trimsyl*-β-D-*glucopyranoside*.—The trimsylate [(i) 41·88 mg or (ii) 20·98 mg] was dissolved in dimethylformamide–water (1 : 1; 10·0 ml) and sodium periodate solution (10·0 ml) was added. A blank solution was also prepared. Samples (2 ml) of the solutions were analysed for periodate content by the Müller–Friedberger method.[31] No periodate was consumed during 2680 min.

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