Use of Mesitylenesulphonyl ('Mesisyl') Chloride as a Selective Sulphonylating Reagent

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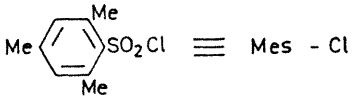
Summary Mesitylenesulphonyl ('mesisyl') chloride has been shown to react with *vic*-hydroxy-systems to give the mono-ester as the major or sole product, and an improved procedure for the synthesis of methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-mannoside is given; *vic*-di-*O*-mesisyl esters are not cleaved by alkali to give epoxides.

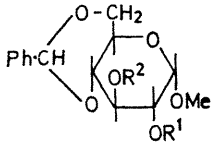
CONTROLLED selective sulphonylation of secondary poly-hydroxy-systems to give mono- and di-esters would be useful for the preparation of important synthetic intermediates, in that it would avoid blocking–unblocking sequences. However selective esterification by tosyl and mesyl chloride, the two most used sulphonylating reagents

has *not* been widely studied, and it is still difficult to predict the results of such reactions.[1] In an effort to seek greater control of selectivity in sulphonylation we have begun to explore the use of mesitylenesulphonyl chloride (**1**) (mesisyl chloride), a bulky sulphonylating agent. This reagent has been used by Khorana[2] as a condensing reagent in nucleotide synthesis, but there is only one report[3] on its use for esterification, namely for selectively sulphonylating a primary hydroxy-group in the presence of a secondary one, for which it was found to have no advantage over tosyl chloride.

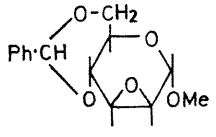


≡ Mes - Cl

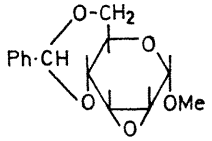
(1)



	R^1	R^2
(2)	H	H
(3)	Ts	H
(4)	Mes	H
(5)	Mes	Mes
(6)	Ts	Ts



(7)



(8)

One useful selective tosylation much used in carbohydrate chemistry is the formation of the 2-*O*-tosyl derivative (**3**) of methyl 4,6-*O*-benzylidene-α-D-glucoside (**2**), a precursor of the *manno*-epoxide (**7**). The best conditions for the selective tosylation involve cooling to −40° and careful addition of reagents.† We have now found that mono-mesisylation of (**2**) in pyridine occurred at room temperature during 6 days when 1 equiv. of (**1**) was used, the product being the expected 2-ester (**4**)[4] as shown by its ready conversion into the epoxide (**7**). Crude (**4**) (85%) prepared using 1·5 equiv. of (**1**) could be converted into (**7**) to give an overall yield of 63% from (**2**), compared with *ca.* 35% when prepared§ via the 2-*O*-tosylate (**3**). Reaction of the diol (**2**) with 3 mol. equiv. (**1**) for 1 month at room temperature still gave (**4**) as the major product plus the 2,3-di-*O*-mesisyl compound (**5**) (25%). The latter could also be prepared (22% yield) by treatment of (**4**) with (**1**) for 4 days at 40°.

Treatment of the corresponding di-*O*-tosyl compound (**6**) with NaOMe gives the anhydro-alloside (**8**)[5], presumably *via* O–S fission of the sulphonate group on C-2 (S_N2S cleavage).[6] Similar treatment of (**5**) either at room temperature or under reflux gave unchanged starting material plus a slight trace (t.l.c.) of (**8**). This unreactivity compared to the di-*O*-tosyl derivative (**6**) is presumably caused by steric hindrance to attack at sulphur in the C-2 mesisyl group.

Similar treatment of the β-anomer of (**2**) with 1·5 equiv. of (**1**) gave, after chromatography, the parent diol (12%), and the 2-*O*-mesisyl (27%), 3-*O*-mesisyl (33%), and 2,3-di-*O*-mesisyl (11%) esters. The mono-*O*-mesisyl esters were characterised by conversion into epoxides. These results follow the pattern shown by tosylation.[7] Again the 2,3-di-*O*-mesisyl compound failed to react with NaOMe solution, although the di-*O*-tosyl derivative has been reported to yield the β-anomer of (**7**).[8]

The difficulty of forming mesisyl esters on neighbouring secondary hydroxy-groups was further emphasised when it was found that *trans*-cyclohexane-1,2-diol with 2 equiv. of (**1**) for 42 h at room temperature gave 66% of mono-ester and 18% of di-ester, whereas under the same conditions, tosylation gave 44% and 40% respectively. However, normal reagents can approach a vicinal monohydroxy–monomesisyl system as shown by the ready acetylation of all of the monomesisyl compounds described herein.

In other work we have found that in some cases mesisyl chloride (**1**) may have advantages over tosyl chloride for selective sulphonylation of primary hydroxy-groups in the presence of secondary ones.[9] A comparison of the reactions of tosylates and mesisylates is currently in progress.

Although expensive if bought commercially mesisyl chloride (**1**) can be made easily in a one-step reaction between the readily available mesitylene and chlorosulphonic acid.[10]

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† The method generally used in our Laboratory is that described in ref. 4 but with cooling to −40° rather than in an ice-bath.
‡ All new compounds were crystalline and had satisfactory elemental analyses.
§ The overall yield given for (2) to (7) in ref. 4 is 24%. For the modification mentioned in footnote† we find the yield increased to 34—40%.

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