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Use of Carbohydrates in the Preparation of Optically Active Sulphoxides

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Summary The diastereomeric sulphinate esters formed from arenesulphinyl chlorides and 1,2:5,6-di-*O*-cyclohexylidene- β -D-glucopyranose afford optically active sulphoxides on treatment with Grignard reagents.

In a common preparation of optically active sulphoxides, the diastereomeric sulphinates from toluene-*p*-sulphinyl chloride and (–)-menthol are separated by crystallisation and the less soluble stereomer is then treated with a Grignard reagent to afford an (*R*)-alkyl *p*-tolyl sulphoxide.¹ The process is restricted to the preparation of sulphoxides with a *p*-tolyl substituent, and has been applied to other aryl sulphinates, optically active alcohols, or amines with limited success.^{2,3}

We were attracted by the possibility of using a suitably protected carbohydrate derivative in the ester moiety on account of the ready availability of, and unique chirality associated with, these compounds. Surprisingly, sulphinate esters of carbohydrates are unknown and we now report their preparation and subsequent conversion into optically active sulphoxides.

Treatment of 1,2:5,6-di-*O*-cyclohexylidene- β -D-glucopyranose (**1**) with 1 equiv. of the arenesulphinyl chloride in ether-pyridine at –78 °C readily afforded the diastereomeric sulphinates (**2**) and (**3**) in high yields (Table). When the reaction was carried out at higher temperatures, the ratio of the diastereomers was closer to unity, whilst alternative bases or solvents resulted in inferior yields of products.

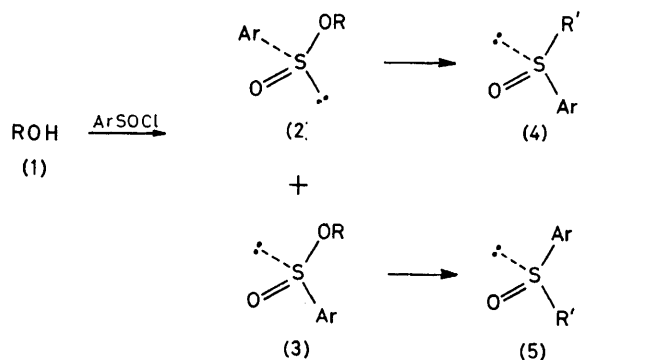
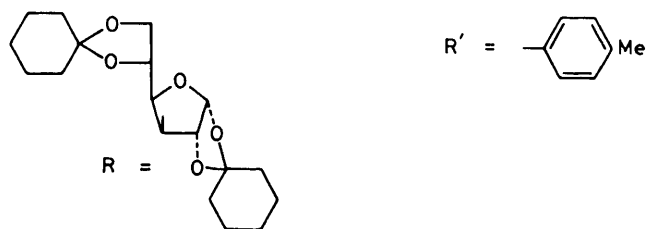


TABLE. Conversion of arenesulphinyl chlorides into aryl *p*-tolyl sulphoxides *via* sulphinates (**2**) and (**3**).

Aryl substituent	Diastereomeric esters		Sulphoxides (4) + (5) % yield
	(2) (major) % yield	(3) (minor) % e.e.	
Phenyl	96	43	88
<i>p</i> -Chlorophenyl	92	52	84
<i>p</i> -Methoxyphenyl	97	50	77
1-Naphthyl	81	42	97
2-Naphthyl	92	48	62
Mesityl	95 ^a	39	71

^a Major diastereomer readily crystallised from this mixture. Yield of pure diastereomer was 26%.



The diastereomeric sulphinates proved difficult to separate, except for the mesityl derivative when a single diastereomer was isolated by fractional recrystallisation. Thus generally the mixed sulphinates (**2**) and (**3**) were treated with excess of *p*-tolylmagnesium bromide and gave the aryl *p*-tolyl sulfoxides (**4**) and (**5**), in ratios which corresponded to the ratio of the sulphinates. By measurement of the optical rotation of the crude sulfoxide mixture and by comparison of these data with literature values, it was shown that in each case the major enantiomer present had the absolute configuration (**4**) [*i.e.* the (*S*)-enantiomer in all cases except for (*R*)-phenyl *p*-tolyl sulfoxide]. Finally, on the assumption that the Grignard displacement proceeded with inversion,⁴ the major sulphinate diastereomer (**2**) had the (*S*)-configuration at sulphur.

It transpired that enantiomerically enriched sulfoxides were obtained in all cases from the crude sulfoxide mixture by recrystallisation. For example, one recrystallisation of the mixed 1-naphthyl phenyl sulfoxides [enantiomeric excess (*e.e.*) *ca.* 40%] from the Grignard reaction afforded (*S*)-1-naphthyl phenyl sulfoxide (*e.e.* 95%) and the overall yield of this product from 1-naphthalenesulphinyl chloride was 29%. Thus the procedure is of use in the preparation of optically active sulfoxides and approaches the efficiency of the Andersen method for the preparation of *p*-tolyl derivatives,¹ whilst having extension to hitherto unknown optically pure sulfoxides particularly those of the 1-naphthyl and mesityl series.

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⁴ K. Mislow, M. M. Green, P. Laur, J. T. Melillo, T. Simmons, and A. L. Ternay, Jr, *J. Am. Chem. Soc.*, 1965, **87**, 1958.