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VINYL SULPHONES DERIVED FROM THIOGLYCOSIDES: SYNTHESIS AND ALKYLATION

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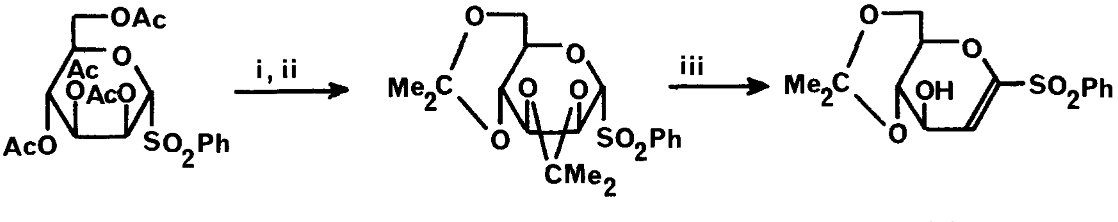
Summary. Vinyl sulphones (1-sulphonyl glycals) are formed in good yield by elimination of propanone from 2,3-O-isopropylidene derivatives of D-mannopyranosyl and L-rhamnopyranosyl sulphones. Attempted conjugate addition of carbon nucleophiles to these vinyl sulphones, which are deactivated towards nucleophiles by the ring oxygen atom, was unsuccessful but lithiation followed by methylation yielded the 2-methyl vinyl sulphone derivatives when t-butyl sulphones rather than phenyl sulphones were used.

In the increasingly common use of monosaccharides as chiral starting materials for the synthesis of chiral natural products[1] it is frequently necessary to introduce alkyl groups in a regiospecific manner. This paper reports a study of the synthesis and alkylation of vinyl sulphones (1-sulphonyl glycals) derived from thioglycosides.

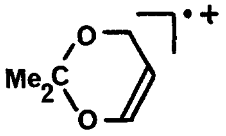
Attempts to synthesise glycosyl sulphones by reaction of glycosyl halides with sodium benzenesulphinate under a variety of conditions were unsuccessful, but such sulphones are readily prepared by oxidation of thioglycosides.[2] Thus the D-mannosyl sulphone (1) was prepared from D-mannose penta-O-acetate via phenyl 2,3,4,6-tetra-O-acetyl-1-thio-α-D-mannopyranoside. The sulphone tetra-O-acetate[3] (1) was deacetylated and reaction of the resulting tetraol with 2,2-dimethoxypropane in the presence of p-toluenesulphonic acid or tin (II) chloride[4] gave the bis-acetal (2) which was found to undergo base-promoted elimination[5] of propanone to form the vinyl sulphone (3) in good yield.



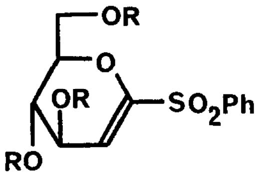
(1) (2) (3)

Key: i) NaOMe/MeOH, ii) Ref 4, iii) Ref 5

This was readily characterised by proton n.m.r. (δ 6.0, 1H d, vinylic H) and mass spectra [m/z 326 (0.4%) M; 114, (31%) ion (4) resulting from a retro-Diels Alder fragmentation]. A vinyl sulphone of this type was first reported[6] by Ferrier and coworkers when (5) was isolated as the product of a reaction in which an attempt was made to displace the phenylsulphonyl group from 2,3,4,6-tetra-O-benzyl β-D-glucopyranosyl phenylsulphone. The synthetic utility of such compounds has not been investigated.

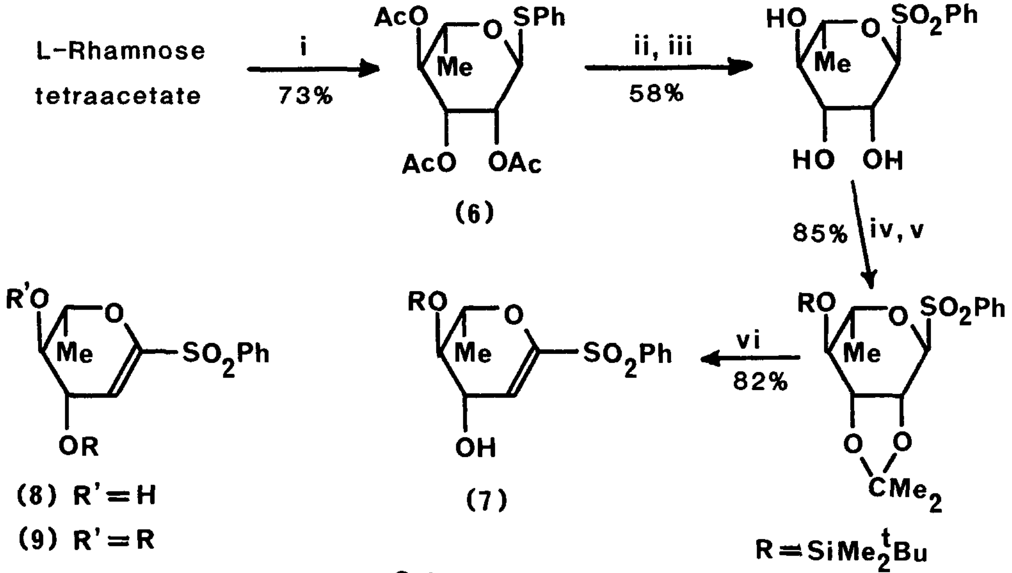


(4)



(5) $R = CH_2Ph$

L-Rhamnopyranose tetra-O-acetate was similarly converted via the phenyl thioglycoside (6) into the vinyl sulphone (7) (see scheme 1). When solutions of (7) were kept for



Scheme 1

Key: i) PhSH, CH_2Cl_2, $BF_3.Et_2O$ ii) $KMnO_4$, HOAc iii) NaOMe,MeOH iv) Ref 4 v) RCl, imidazole

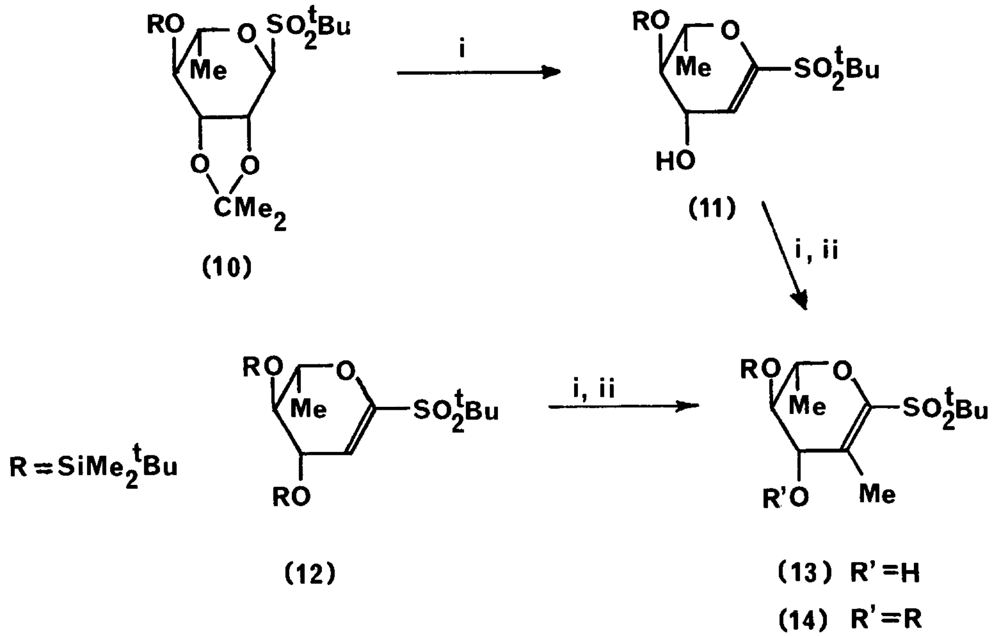
prolonged periods migration of the silyl ether occurred to give a mixture of (7) and its 3-O-t-butyldimethylsilyl isomer (8), especially in the presence of base.

Vinyl sulphones such as (4) and (7), 1-sulphonylglycals, are potential substrates for Michael additions, and it was hoped that methyl lithium could be used both to generate the vinyl sulphone and to effect nucleophilic addition to the alkene in sequential reactions. If the resulting anion at C-1 could be alkylated[7] then a tandem alkylation would be possible leading to 2-deoxy-C-glycosides with a methyl (or other alkyl) group at C-2 in a one-pot process. Addition of methyl lithium to vinyl sulphones possessing a γ-hydroxyl group was reported by Barton, Conrad and Fuchs[8] who claimed that the reactions involved co-ordination of methyl lithium to the alkoxide and, hence, intramolecular assisted delivery of the methyl nucleophile. However, the vinyl sulphone (7) underwent no Michael addition on reaction with two equivalents of methyl lithium in tetrahydrofuran, a mixture of starting material and the product (8) of silyl migration being recovered. Repetition of the reaction using tetra-N-methylethanediamine to co-ordinate the lithium and increase the nucleophilicity of the methyl lithium gave the same result. The bis-silyl ether (9), prepared from (7), was also found to be unreactive towards methyl lithium.

Other nucleophilic reagents have been studied. Eisch and Galle[9] reported that although conjugate addition of methyl lithium to some γ-hydroxyphenylvinylsulphones did not occur addition was achieved using Grignard reagents. Both the mono- and bis-silyl ether derivatives (7) and (9) did not add methylmagnesium iodide in either diethyl ether or tetrahydrofuran as solvent. Lithium dimethyl cuprate also did not add to (7).

An important feature of the structure of the vinyl sulphones (7) and (9) is the presence of the (ring) oxygen substituent α to the sulphone. This deactivates the alkene towards nucleophilic addition by mesomeric release of electrons. Although no precedent could be found for Michael addition to an α-alkoxyvinylsulphone examples of the addition of lithium dimethylcuprate to an enone possessing an α-alkoxy substituent are known[10]. Since the electrong demand of the sulphone group in (7) and (9) could be partly met by delocalisation of π-electrons of the phenyl ring, the corresponding t-butylsulphones were synthesised in the hope that they would be more reactive. Elimination of propanone occurred in high yield (80%) when the sulphone acetal (10), prepared by a route that parallelled the synthesis of (7), was treated with methyl lithium in THF.

When the t-butylvinylsulphone (11)[11] was reacted with methyl lithium (2.5 equivalents, -66° to 25°C) the reaction was quenched with D_2O in order to identify the anion formed. No Michael addition occurred and the proton n.m.r. spectrum of the recovered starting material showed that metallation at C-2 had occurred to give the 2-deuterio derivative. Barton et al reported that conjugate additions of organolithium reagents to cyclic vinyl sulphones were more efficient for t-butyl sulphones than for the phenyl sulphones when complex aryllithium compounds were used and they argued that the more bulky t-butyl group retarded removal of the vinylic proton. In such cases γ-silyloxy-αβ-unsaturated t-butylsulphones were found to be most suitable for conjugate additions. However, in the reaction of the bis-silyl ether (12) with the small methyl lithium reagent no conjugate addition occurred; instead lithiation at C-2 occurred and subsequent reaction with iodomethane gave the 2-methyl vinyl sulphone (13) in 69% yield. The monosilyl ether (11) could similarly be methylated at C-2 to give (14)[12] as the major product together with a small amount of the O-methylated 2-methyl compound. Thus



(10) (11) (12)

(13) R'=H

(14) R'=R

Key: i) MeLi, THF, -66 to 25 C ii) MeI

although the vinyl sulphones derived from thioglycosides are too unreactive to undergo Michael additions substitution of the vinylic hydrogen is possible to give the alkylated vinyl sulphone[13,14].

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11. δ_H 5.85 (d, H-2); δ_C 113.0 (C-2), 149.6 (C-1)
12. δ_H 2.08 (s, Me-2); δ_C 13.6 (Me-2) 123.11, 143.8 (quaternary, C-2, C-1)
13. We are indebted to Mr. Clive James for the first prepartion of the sulphone derivatives (1), (2) and (3).
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