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PREPARATION OF CYCLIC ETHER ACETALS FROM 2-BENZENESULPHONYL DERIVATIVES: A NEW MILD GLYCOSIDATION PROCEDURE

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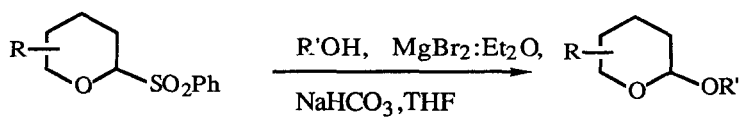
Summary: Several alcohols ranging from hindered to those containing chemically sensitive groups react with 2-benzenesulphonyl cyclic ethers in the presence of magnesium bromide etherate and sodium bicarbonate to give good yields of the corresponding acetals.

The tetrahydropyranyl group is widely accepted as a protecting group for alcohols despite the fact that most methods for its introduction involve acidic catalysts[1]. Also there is great interest in related glycosidation procedures with many new developments being reported.[2] As the demands of modern synthesis constantly require greater functional group compatibility there is a continuing need to study alternative systems.

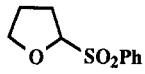
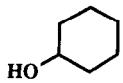
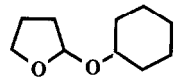
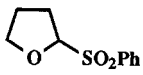
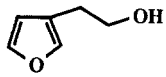
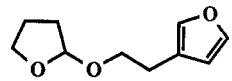
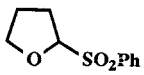
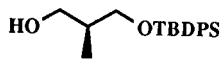
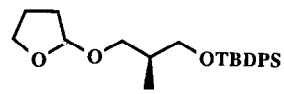
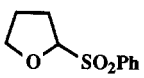
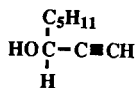
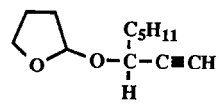
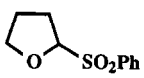
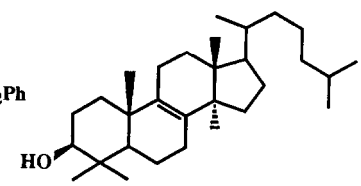
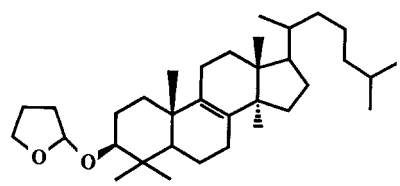
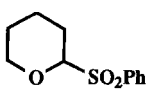
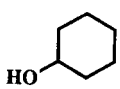
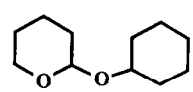
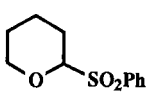
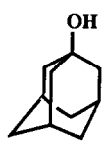
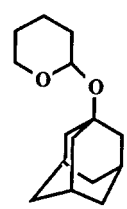
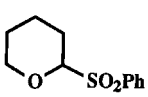
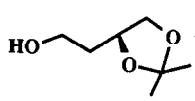
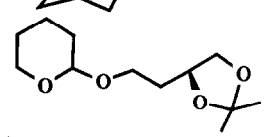
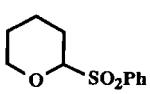
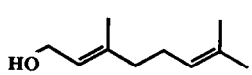
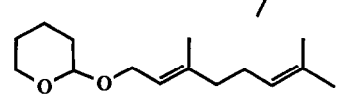
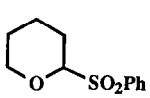
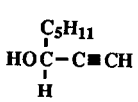
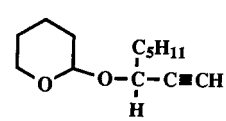
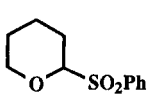
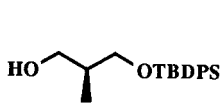
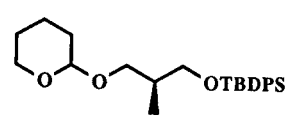
We[3] and others[4] have recently introduced the use of 2-benzenesulphonyl cyclic ethers for the formation of new carbon bonds at the 2-position of the ethers and reasoned that these compounds should also be suitable precursors for the corresponding acetal preparation. Here we describe how this chemistry can be achieved leading to an especially mild procedure for acetal formation.

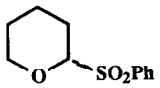
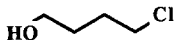
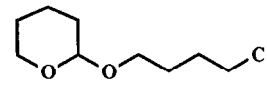
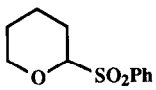
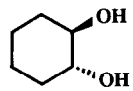
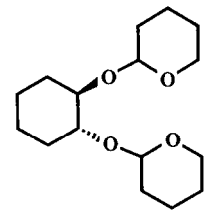
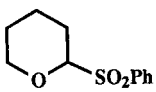
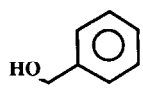
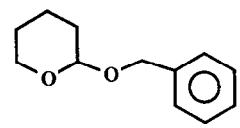
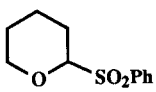
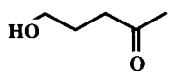
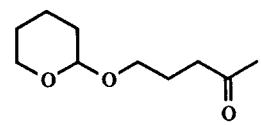
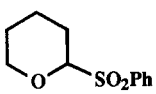
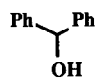
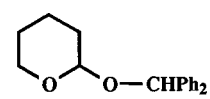
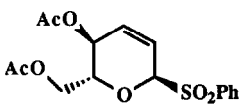
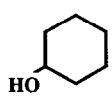
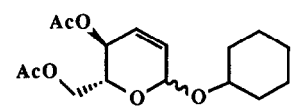
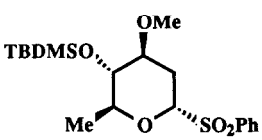
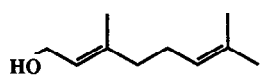
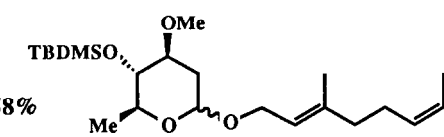
While some of the starting 2-benzenesulphonyl ether derivatives are commercially available, others may be readily prepared either from dihydropyrans, lactols and simple lactol ethers or by oxidation of the corresponding sulphides.[4a,5] The general procedure involves addition of the alcohol (1-2 eq) to a stirred tetrahydrofuran[6] solution of the sulphone (1 eq) containing magnesium bromide etherate (2 eq) and solid sodium bicarbonate[7](1 eq) at room temperature. (Scheme 1) (Table)



Scheme 1

Although most reactions were complete overnight (by tlc analysis), for slow reactions the mixture could be warmed to 50°C or better immersed in a small ultrasonic bath in which case a dramatic rate enhancement was observed.

Sulphone	Alcohol	Conditions	Yield	Product[8]
		a	98%	
		b	92%	
		a	100%	
		a	100%	
		c	89%	
		a b	92% 91%	
		a b	80% 70%	
		a	78%	
		a b	90% 91%	
		a b	97% 87%	
		a c	100% 82%	

Sulphone	Alcohol	Conditions	Yield	Product[8]
		a	97%	
		d	65%	
		b	93%	
		a b	85% 65%	
		b	67%	
		a e	20% 77%	 α:β, 6:1
		f	58%	 α:β, 2:1

Conditions

(a) 1 eq. Sulphone, 2 eq. Alcohol, 2 eq. $MgBr_2.Et_2O$, 1 eq. $NaHCO_3$
(b) 1 eq. Sulphone, 1 eq. Alcohol, 2 eq. $MgBr_2.Et_2O$, 1 eq. $NaHCO_3$
(c) 1.5 eq. Sulphone, 1 eq. Alcohol, 2 eq. $MgBr_2.Et_2O$, 1 eq. $NaHCO_3$
(d) 2.2 eq. Sulphone, 1 eq. Alcohol, 3 eq. $MgBr_2.Et_2O$, 1 eq. $NaHCO_3$
All the above stirred at room temperature overnight (15-24 hrs)
(e) As (a) but in ultrasound bath overnight
(f) 1 eq. Sulphone, 5 eq. Alcohol, 5 eq. $MgBr_2.Et_2O$, 5 eq. $NaHCO_3$ heated at 50°C overnight

The table shows the wide range of alcohols to which this method of acetal formation has been applied for tetrahydrofuranyl and tetrahydropyranyl ethers. High yields were obtained with a wide variety of alcohols and even sterically hindered substrates gave respectable yields. Other functional groups present in the molecules such as a furan ring, silyl protected alcohols, double and triple bonds, acetals and carbonyl groups were unaffected by the method.

We have also briefly investigated the extension of the method to the formation of glycoside bonds as in the last two entries of the table. In both cases these sulphones are less reactive, but adjustment of conditions by either heating or ultrasonication proved successful.

We believe this mild acetalation procedure should find application in natural product synthesis and in examples where sensitive functional groups are present.

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7. We thank Professor Philip Kocienski (University of Southampton) for suggesting the use of sodium bicarbonate in this reaction.
8. All new compounds gave satisfactory micro analysis and/or accurate mass spectroscopic data.

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