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SUBSTITUTION REACTIONS OF 2-BENZENESULPHONYL CYCLIC ETHERS WITH SILYL ENOL ETHERS PROMOTED BY ALUMINIUM TRICHLORIDE[§]

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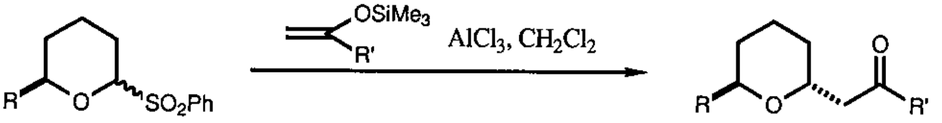
Abstract- Several cyclic ether 2-benzenesulphones were shown to react with silyl enol ethers in the presence of $AlCl_3$ to give the corresponding alkylated products in good yield. Where substitution occurred to give 2,6-disubstituted products there was a marked preference for the formation of the trans- isomer.

There are now a large number of reports concerning the substitution of cyclic ethers by exchange of substituents at the anomeric position with nucleophilic reagents. Popular groups for this displacement include halides[2], carboxylates[2a,b,3], and sulphides[4,2g] while the typical carbon nucleophiles are allyl silanes[2c-f,3a-j,u], alkanes[2h-j,4a,5], alkenes[2c,i,k,6], alkynes[2i,l,5a], arenes[2h,i,m,4b,c,5a-c,7], cyanide[2c,3j,q,r,8], and especially silyl enol ethers[2b,c,m-r,3j-p,4b,c,7a,9].

We have been developing the use of 2-benzenesulphonyl substituted cyclic ethers as interesting entities since these permit both reaction with electrophiles[10] following initial deprotonation, or reaction with nucleophilic species[5a,11]. This bifunctional reactivity greatly enhances the utility of these compounds. Furthermore the 2-benzenesulphonyl derivatives are readily prepared from dihydropyrans, or furans and also from the corresponding lactols or lactol ethers by treatment with benzenesulphinic acid[10a,b]. Alternatively they may be obtained by oxidation of the corresponding sulphide[10d,12]. The sulphones are often stable crystalline compounds and in some cases are now commercially available.

Here we report further reactions of these sulphones with various carbon nucleophiles and in particular with silyl enol ethers (Scheme).

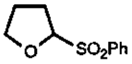
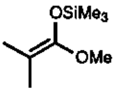
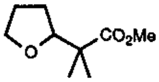
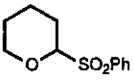
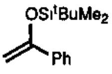
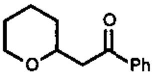
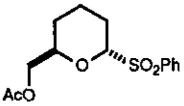
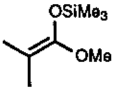
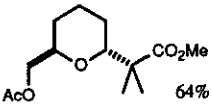
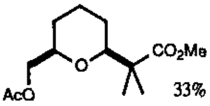
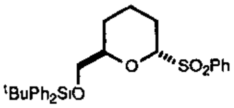
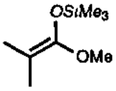
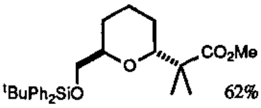
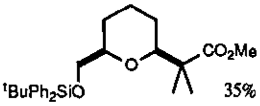
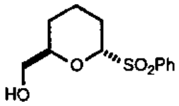
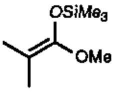
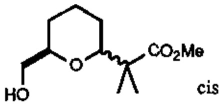
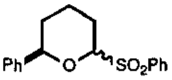
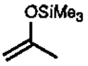
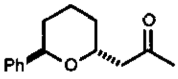
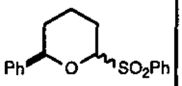
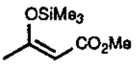
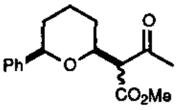
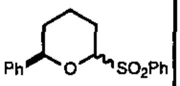
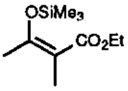
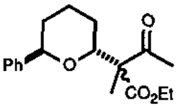
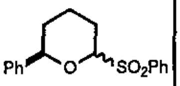
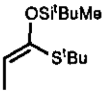
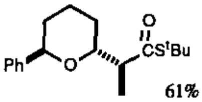
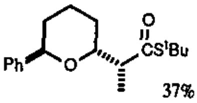


Scheme

Typical reaction conditions are reminiscent of related Mukaiyama reactions[13]. The cyclic ether sulphones were added to a cooled (-78°C) dichloromethane solution of the silyl enol ether (2 equiv.) containing anhydrous aluminium chloride (2 equiv.). Slow warming to -35°C (over 1h) and subsequent reaction for 1-5 hours at this temperature gave the corresponding addition products in good yields (Table 1)[14].

[§] Dedicated to Professor Sir Derek Barton F.R.S. on the occasion of his 70th Birthday.

Table 1. Reaction of Sulphones with Silyl Enol Ethers

	Sulphone	Enol Ether	Product(s)	Yield
1				87%
2				90%
3			 64%  33%	
4			 62%  35%	
5		[†]	 cis:trans, 1:1	[††] 79%
6				84%
7				70%
8				77%
9			 61%  37%	

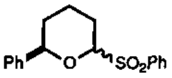
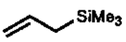
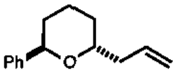
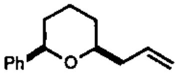
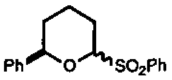
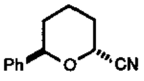
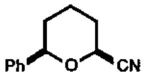
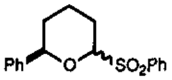
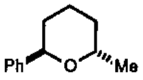
† 3 Equiv. of silyl enol ether and 1.05 equiv. of $AlCl_3$ were used. †† 10% Recovered starting material was also obtained

Interesting general conclusions can be drawn from these results. For example both 5 and 6 membered ring ethers may be used as substrates and a range of other functional groups are also tolerated. In examples where there is a stereochemical consequence in the reaction we find that 2,6-trans- orientated groupings are preferred. One apparent anomaly to this is entry 7 where a cis-product was obtained from the silyl enol ether of methyl acetoacetate. We believe this is most reasonably explained as involving initial trans-product formation which undergoes rapid equilibration through ring opening and subsequent recyclisation to the more thermodynamically stable diequatorial cis-product. In favour of this process it should be noticed that in entry 8 where the ring opening is blocked by replacement of the acidic proton by an angular methyl group the only product formed is the trans-isomer.

The overall reaction often affords sterically demanding products and in some cases where diastereoisomeric products may be formed there is a preference for one isomer (entry 9). The proof of structure in this last example follows the x-ray single crystal structure analysis[15]. The initial geometry of the starting sulphone, whether cis- or trans-, has little effect in determining the final stereochemical outcome indicating the possibility of a common oxonium ion intermediate during the reaction.

In a brief study of other carbon nucleophiles which may participate in the displacement of the benzenesulphonyl group, and hence lead to formation of carbon bonds at the 2-position of cyclic ethers, we have examined alternative reagents as indicated in Table 2. The above procedure for silyl enol ethers was used in the reaction of the sulphone with allyltrimethylsilane or trimethylsilyl cyanide whereas the conditions reported by Nicolaou were used for the reaction with trimethylaluminium[5d]. Also in these last examples the major products are once again 2,6-trans-substituted isomers. The above reactions clearly demonstrate the further utility of 2-benzenesulphonyl ethers for organic synthesis.

Table 2. Reactions of Sulphones with other Carbon Nucleophiles.

	Sulphone	**Reagent**	**Product(s)**	**Yield**
1			 	80% 11%
2		Me_3SiCN	 	60% 36%
3		$AlMe_3$		98%

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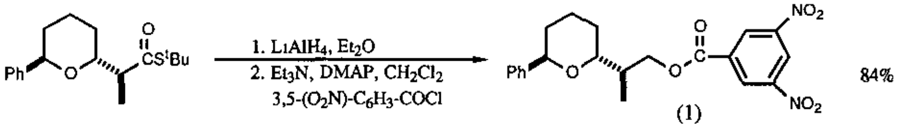
14. All new compounds gave satisfactory microanalyses and/or accurate mass spectroscopic data.
15. Single crystal structure analysis was performed on the dinitrobenzoyl derivative (1). We thank Dr. D.J. Williams (Imperial College) for this result.



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