DIRECT SUBSTITUTION OF 2-BENZENESULPHONYL CYCLIC ETHERS USING ORGANOZINC REAGENTS

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Summary: 2-Benzenesulphonyl cyclic ethers are converted in good yield at room temperature to the 2-aryl-, 2-alkenyl- or 2-alkynyl product by treatment with the corresponding organozinc species.

There is a continued interest in being able to form carbon-carbon bonds at the 2-position of cyclic ethers from lactol derivatives¹, especially for natural product synthesis. We² and others³ have recently described the use of 2-benzenesulphonyl stabilised cyclic ether carbanions as one solution to this problem. Here we show how the versatile benzenesulphonyl group can be directly replaced by reaction with organozinc reagents (Scheme).



Although some sulphones are commercially available, they can be readily obtained from lactols, lactol ethers or dihydropyrans and furans by treatment with benzenesulphinic acid.^{2a,b} Alternatively they can be prepared by oxidation of the corresponding sulphides.^{3a,4,5}. These sulphones are shelf stable starting materials, and they are often crystalline and readily purified.

In a typical experiment the Grignard reagent (2 equiv.) formed from the bromide, was reacted with anhydrous zinc bromide⁶ (1.2 equiv.) in dry tetrahydrofuran at room temperature for 30 minutes under argon to afford the organozinc species. The sulphone (1 equiv.) was added to this suspension as a solution in dry tetrahydrofuran and the reaction mixture stirred at room temperature for 3-24 hours. Acidic workup and purification by silica chromatography (Et₂O: 40-60 petrol) gave the product in good yield (Table 1).



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Table 2



The reaction works for both aryl and vinyl bromides but not alkyl bromides. Tetrahydrofuran is the solvent of choice as none of the desired product is observed with diethyl ether. 6-Substituted tetrahydropyrans give exclusively the *trans*-product irrespective of sulphone stereochemistry (Table 1. Entries 5-9). The product of entries 8 and 9 is interesting in that the 2-methoxyl substituent is readily converted to the corresponding benzenesulphonyl group i.e. the sulphone used in experiments 5 and 6. In this way it is possible to use the method to afford *trans*-2,6-bis-substituted cyclic ethers. 2-Alkynyl cyclic ethers are also readily prepared by the above method (Table 2). The alkynyl Grignard reagent is prepared by stirring a mixture of the alkyne (2 equiv.) and *iso*-propyl magnesium bromide (2 equiv.) in dry tetrahydrofuran at room temperature for 2 hours then adding the zinc bromide and sulphone as above.

Although we have not yet explored the scope of the above reaction we believe the method offers a new way to controlling substituents at both the 2 and 6 positions of cyclic ethers.

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- 4. J.F. Cassidy and J.M. Williams, Tetrahedron Lett., 1986, 27, 4355.
- 5. All new compounds gave satisfactory micro analyses and/or accurate mass spectroscopic data.
- 6. Anhydrous zinc bromide was prepared as a 1M solution in dry tetrahydrofuran by heating at reflux for two hours a 1M solution of 1,2-dibromoethane containing excess zinc.

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