Allylic Sulfones as Allyl Anion Equivalents: Homoallylic Alcohols from Metal Catalysed Reactions of Sulfones with Aldehydes and Ketones

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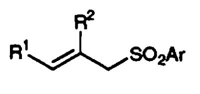
Reduction of allylic sulfones with diethylzinc, catalysed by palladium(0), gives nucleophilic organometallic species, which react *in situ* with carbonyl compounds to give homoallylic alcohols in high yield.

Sulfonyl groups are easy to introduce into organic molecules, and their anion-stabilising properties make it easy to build up complex structures in a few steps. For these reasons, among others, sulfones are very widely used in organic synthesis.[1] Removal of the sulfonyl group is usually achieved by reduction (for example, with alkali metals[2] and their amalgams,[3] or with Raney nickel[4]), which simply replaces the sulfonyl group with a hydrogen atom, or by base-catalysed[5] or reductive[6] eliminations, which leave behind a double bond. More constructive desulfonylations rely on transition metal catalysed transformation of a (usually allylic[7,8] or vinylic[9]) sulfone into an organometallic electrophile, such as a π-allyl palladium species,[8] which can react with nucleophiles with overall nucleophilic substitution of the sulfonyl group. We have recently described[10] the nucleophilic substitution of *tert*-butylsulfonyl groups from aromatic nuclei by Grignard reagents under nickel catalysis. Trost[11] has represented allyl sulfones **1** as the triionic synthons **2** because of the dual nucleophilic and electrophilic character of the carbon atom bearing the sulfonyl group.

Here we report that the sulfonyl group of allylic sulfones can also be removed by overall *electrophilic* substitution, with the allylic sulfones being transformed, by reduction, into organometallic *nucleophiles*, which react *in situ* and in high yield with carbonyl compounds. With this new reaction, allylic sulfones can be represented as the trianionic synthon **3**, opening up possible new synthetic uses for them.

Our early (only partly successful) trials[12] involved reduction of the allylic sulfones with chromium(II) salts, in the manner of the Nozaki–Hiyama reaction.[13] During these studies, it became evident that the presence of nickel or palladium was important for activation of the sulfone towards the reducing agent. A π-allyl metal intermediate was probably involved.[14,15] A number of methods have been described for inverting the usually electrophilic character of π-allyl palladium(II).[16] Tamaru and coworkers[16a] for example, has made use of a ligand-exchange reaction with diethylzinc to convert allylic acetates, *via* π-allyl palladium species, to nucleophilic allyl zinc species. Application of his method to our allylic sulfones allowed us to convert them very efficiently into allyl anion equivalents which reacted with aldehydes and ketones.

Allyl phenyl sulfone **4** (1 mmol) was treated with a catalytic amount of $Pd(PPh_3)_4$, benzaldehyde (1.2 mmol) and diethylzinc (2 mmol). After refluxing in THF for 2 h, the sulfone had all been consumed, and the homoallylic alcohol **5** could be isolated in 86% yield (Scheme 1). The reaction was general for a variety of aldehydes and ketones, and gave high yields of homoallylic alcohols from allylic sulfones with a range of substitution patterns, as shown in Table 1.†



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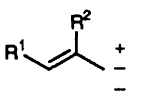

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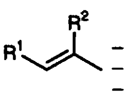


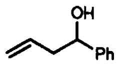
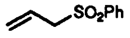
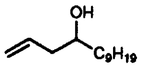
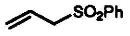
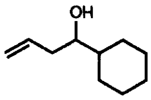
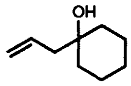
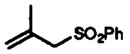
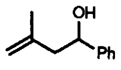
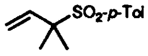
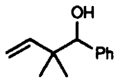
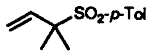
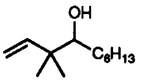
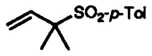
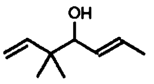
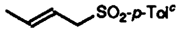
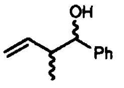
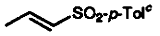
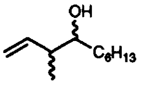
3

4 **5** 86%

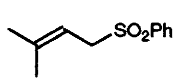
Scheme 1 *Reagents and conditions*: $Pd(PPh_3)_4$ (× 0.05), Et_2Zn(×2), PhCHO (× 1.2), THF, reflux, 2 h

Unsymmetrical allylic sulfones reacted with complete regioselectivity at their more-substituted termini (entries 6–10), in accordance with the expected behaviour of allylzinc species.[17] However, crotyl *p*-tolyl sulfone exhibited almost no diastereoselectivity in its reactions (entries 9 and 10), giving more or less equal amounts of *syn* and *anti* alcohols, probably because of the zinc salts' Lewis acidity.[18] Crotyl *p*-tolyl sulfone sulfone, substituted in the γ position, also reacted more slowly than sulfones unsubstituted in this position, and the γ,γ-disubstituted sulfone **6** was completely unreactive under these conditions. In any case, the products from reaction of **6** would be the same as those in entries 6 and 7. Allyl *tert*-butyl sulfone

Table 1 Reactions of allylic sulfones with aldehydes and ketones

Entry	Sulfone	Aldehyde or ketone	Product	Yield (%)[a]
1		PhCHO		86
2		n-$C_9H_{19}CHO$		97
3		$C_6H_{10}CHO$[b]		63
4		Cyclohexanone		82
5		PhCHO		88
6		PhCHO		86
7		n-$C_6H_{13}CHO$		81
8		$Me_2C=CH$-CHO		67
9		PhCHO		64[d]
10		n-$C_6H_{13}CHO$		76[e]

[a] Isolated yield of pure homoallylic alcohol. [b] Cyclohexanecarbaldehyde. [c] 3:1 *E*:*Z*. [d] 50:50 *anti*:*syn*. [e] 60:40 *anti*:*syn*.



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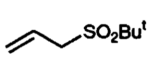

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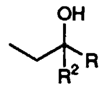

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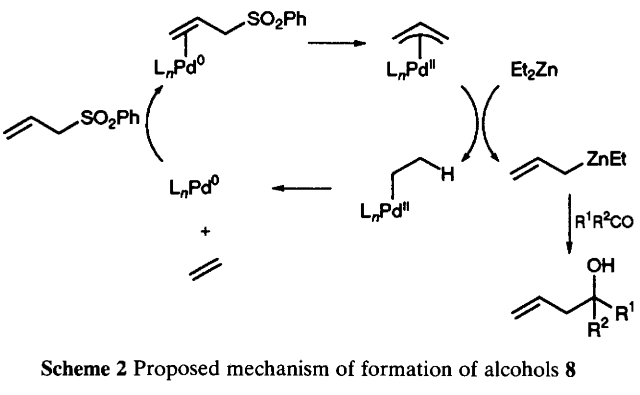

Scheme 2 Proposed mechanism of formation of alcohols **8**

7 reacted with benzaldehyde to give the expected homoallylic alcohol **5** in 70% yield.

In some cases, small amounts (less than 10%) of alcohols **8** were also formed in these reactions by transfer of an ethyl group from the diethylzinc to the carbonyl compound. These quantities increased when the sulfone itself was slow to react, or if the reaction was carried out at a lower temperature. Reducing the quantity of aldehyde from 1.2 to 1.0 equiv. led to a slight fall in the yield, but a higher yield was obtained when the sulfone was present in excess.

We assume that the mechanism of this reaction (Scheme 2) is similar to that proposed by Tamaru[16a] for the palladium catalysed, zinc mediated addition of allylic acetates to aldehydes and ketones. The palladium(0) catalyst complexes with the double bond and inserts into the allylic C–S bond to give a π-allyl palladium(II) complex. Metal exchange with the diethylzinc creates a nucleophilic allylzinc, which reacts with the carbonyl compound, and an ethylpalladium(II) species, which undergoes reductive β-elimination to regenerate the palladium(0) catalyst. $Pd(PPh_3)_2Cl_2$ also catalysed the reaction successfully, though $Ni(PPh_3)_2Cl_2$ did not.

In these reactions, the sulfonyl group is acting as a latent metal atom which can in principle be carried through several stages of a synthesis before being 'revealed'. The transformations they represent were previously possible only in two-step addition–desulfonylation procedures.[14,19]

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Footnote

[†] The aldehyde or ketone (1.2 mmol) and diethylzinc (2.0 ml of a 1 mol dm^{-3} solution in hexane, 2.0 mmol) were added to a solution of allylic sulfone (1.0 mmol) and $Pd(PPh_3)_4$ (0.05 mmol) in dry THF (3 ml), and the mixture was refluxed under nitrogen for 2–5 h or overnight. On completion of the reaction (total consumption of the sulfone by TLC or by GC), diethyl ether and 1% aq. HCl were added. The layers were separated and the aqueous layer was extracted with diethyl ether (× 2). The combined organic fractions were washed with saturated aq. $NaHCO_3$, dried (Na_2SO_4), evaporated, and purified by chromatography on silica to yield the homoallylic alcohol.

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