Homoallylic Alcohols from Samarium Diiodide-mediated Coupling of Allylic Sulfones with Carbonyl Compounds

Jonathan Clayden†,* and Marc Julia

École Normalc Supérieure: Laboratoire de Chimie, 24 rue Lhomond, 75231 Paris, Cédex 05, France

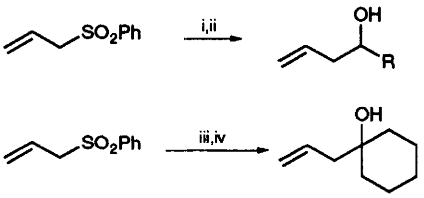
Reduction of allylic sulfones with samarium diiodide gives allylsamarium species which react *in situ* with carbonyl compounds, yielding homoallylic alcohols.

Samarium diiodide is finding ever wider use in organic synthetic reactions as a reagent for promoting a wide range of reductions and coupling reactions.[1] Recently, it has also been shown to effect the desulfonylation of imidazolyl and phenyl sulfones.[2] We are currently developing new methods for the reductive desulfonylation of sulfones to give nucleophilic organometallic species, and have recently reported[3] the coupling of allylic sulfones with aldehydes and ketones using a palladium-catalysed, zinc-mediated reaction (Scheme 1). We therefore decided to investigate the use of samarium(II) as a reagent for mediating this same reaction of allylic sulfones, encouraged by Sinaÿ's report of the samarium(II)-mediated coupling of α-alkoxy sulfones with ketones.[4]

Allyl phenyl sulfone **1** was mixed with an excess of cyclohexanone and then treated with samarium(II) iodide (4 equiv.) in a 20 : 1 mixture of THF and HMPA (hexamethylphosphoramide), in the hope of promoting a Barbier-type coupling reaction. After 5 h, the initial purple colour had faded, and an 87% yield of the homoallylic alcohol **2** could be isolated. The reaction was general for a wide range of sulfones, and worked with aldehydes as well as with ketones, as indicated in Table 1.‡

Allyl phenyl sulfone itself reacted in high yield with aliphatic ketones and aldehydes (entries 1–4), but failed to react with benzaldehyde or acetophenone. Aromatic aldehydes undergo rapid pinacol coupling in the presence of samarium(II) iodide,[5] and GCMS indicated the presence of pinacol coupling products in these crude reaction mixtures. Allyl *tert*-butyl sulfone also reacted well with cyclohexanone (entry 5).

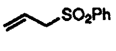
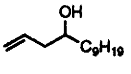
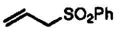
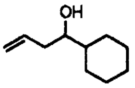
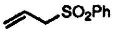
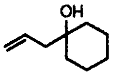
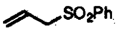
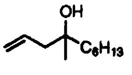
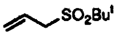
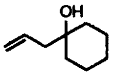
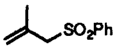
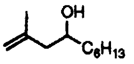
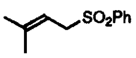
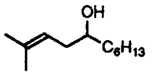
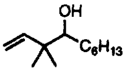
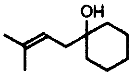
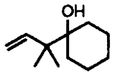
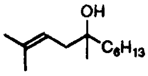
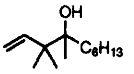
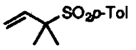
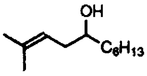
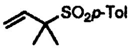
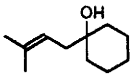
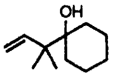
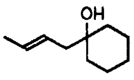
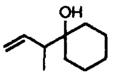
Unsymmetrical sulfones reacted to give, in most cases, mixtures of regioisomers of homoallylic alcohols. Interestingly, the major product in each case arose from inversion of the allylic system. In contrast with our palladium–zinc method[3] for the coupling of allylic sulfones with aldehydes and ketones, γ,γ-disubstituted allylic sulfones (entries 7–9) can give good yields of homoallylic alcohols with samarium(II) iodide. However, the palladium–zinc method has the advantage of promoting regioselective reactions at the more substituted ends of other unsymmetrical allylic sulfones. Allylic halides[6] and phosphates[7] also undergo unregioselective Barbier-type reactions with samarium(II) iodide and aldehydes or ketones, but allylic acetates react regioselectively at their less substituted end under palladium catalysis.[8] Addition of $PdCl_2(PPh_3)_2$ to our reactions had no effect on the regioselectivity.



1 **2** 87%

Scheme 1 *Reagents and conditions*: i, $Pd(PPh_3)_4$ (0.05 equiv.); ii, Et_2Zn (2 equiv.), and RCHO (1.2 equiv.), THF, reflux, 2 h; iii, cyclohexanone (2 equiv.); iv, SmI_2 (4 equiv.); THF–HMPA, 5 h, 20 °C

Table 1 Reactions of allylic sulfones with aldehydes and ketones

Entry	Sulfone	Aldehyde or ketone	Product	Yield (%)[a]
1		n-$C_9H_{19}CHO$		77
2		$C_6H_{10}CHO$[b]		90
3		Cyclohexanone		87
4		Octan-2-one		84
5		Cyclohexanone		91
6		n-$C_6H_{13}CHO$		83
7		n-$C_6H_{13}CHO$		28
				34
8		Cyclohexanone		28
				42
9		Octan-2-one		33
				63
10		n-$C_6H_{13}CHO$		48
11		Cyclohexanone		53
				26
12		Cyclohexanone		62[d]
				14

[a] Isolated yield of pure homoallylic alcohol. [b] Cyclohexanecarbaldehyde. [c] 3 : 1 *E* : *Z*. [d] *E* isomer only.

Much lower yields were obtained if the reagents were not thoroughly degassed, and in the absence of HMPA (which accelerates electron transfer from samarium diiodide[9]), the sulfones did not react. In no case was a product resulting from deoxygenation of the sulfone detected.[10]

The lower temperature, the absence of a transition metal catalyst, and the different substrate-dependency of this samarium(II) based method mean that it complements our palladium–zinc method.[3] The method also demonstrates further the value of samarium diiodide as a synthetic reagent. Allylic sulfones are already well established as useful synthetic intermediates,[11] and here we have demonstrated a new way of inverting their usual electrophilic character,[12] using them as nucleophilic allylating agents.[13]

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Footnotes

† Current address: Department of Chemistry, University of Manchester, Oxford Road, Manchester, UK M13 9PL.

‡ *Typical procedure*: A solution of the allylic sulfone (0.5 mmol) and the aldehyde or ketone (1.0 mmol) in HMPA (1 ml) was degassed by repeated freezing and thawing under vacuum. Samarium diiodide (20 ml of a commercial 0.1 mol dm^{-3} solution in THF) was added and the resulting purple solution was stirred at room temperature under nitrogen for 2 to 18 h, during which time the purple colour disappeared and a cream precipitate formed. Diethyl ether and 1% HCl (aq.) were added. The layers were separated and the aqueous layer was extracted with diethyl ether (×2). The combined organic fractions were washed with saturated aqueous sodium hydrogen carbonate solution, dried (Na_2SO_4), evaporated, and purified by chromatography on silica to yield the homoallylic alcohol.

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