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SYNTHESIS OF VINYLIC AND CYCLIC SULFONES VIA A RADICAL ADDITION-ELIMINATION SEQUENCE

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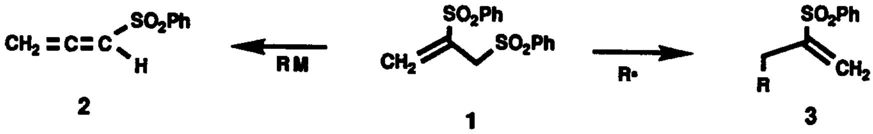
Abstract: Radical attack on the double bond of 2,3-*bis*(phenylsulfonyl)-1-propene leads to an intermediate sulfonyl stabilized radical. This species readily fragments to produce a new vinyl sulfone which can undergo further radical cyclization to give a six ring sulfone.

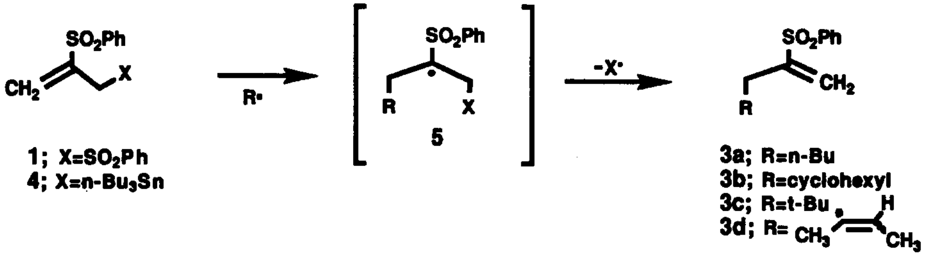
The development of synthetic methodology permitting the radical construction of organic substrates remains an active area of research.[1] An attractive feature of this process is that in certain cases it may serve as a surrogate for synthetically inaccessible ionic reactions. For example, the SN_2' reaction of 2,3-bis(phenylsulfonyl)-1-propene (1)[2] with carbanions suffers an unavoidable problem. Thus, treatment of 1 with various organometallic reagents results primarily in β-elimination of the phenylsulfonyl group, producing allene 2. In this letter, we communicate a new stratagem for preparing vinyl sulfones (3) which involves a radical addition-elimination sequence using *bis*-sulfone 1 as well as the structurally related stannane 4.[3]



Free radical addition reactions are recognized as a powerful method for inter and intramolecular carbon-carbon bond formation.[1] The rate and regioselectivity of the reaction are affected by substituents on both the attacking radical and pi-bond.[4] The exothermic addition of alkyl radical to alkenes involves an early transition state and molecular orbital calculations have suggested a dipolar complex.[5] This charge distribution is in accord with the concept that alkyl radicals behave as nucleophiles and will readily add to electron deficient olefins. Indeed, addition to electronically activated pi-bonds dominates even when unhindered, unactivated alkenes are available.[6] Methods utilized for free-radical generation are usually tin hydride mediated, and halides, selenides and sulfur containing compounds have been used as radical precursors in most studies.[7-9] More recently, Barton and coworkers have shown that the thermal or photochemical decomposition of thiohydroxamic esters represents an excellent method for generating alkyl radicals.[10] The synthetic utility of this procedure using various radical traps has been elegantly exploited to yield a variety of functional groups.[11]

Our initial impetus to study such radical additions stemmed from the compact and useful arrangement of functionality found in compounds 1 and 4. Both contain the α,β-unsaturated sulfonyl group, which has previously been shown to act as an efficient radical acceptor.[12] In addition, compounds 1 and 4 contain functionality in the allylic position which are known to promote SH_2' displacement reactions.[13] Consequently, radical attack on the double bond of 1 or 4 leads to an intermediate sulfonyl stabilized radical 5 (Scheme I) which can undergo facile fragmentation to form a new vinyl sulfone.

Scheme I

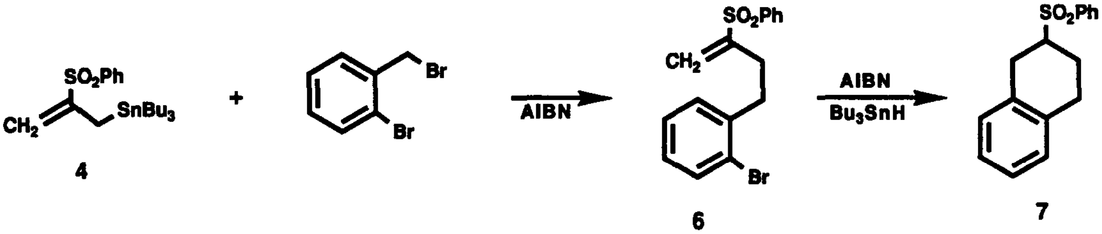


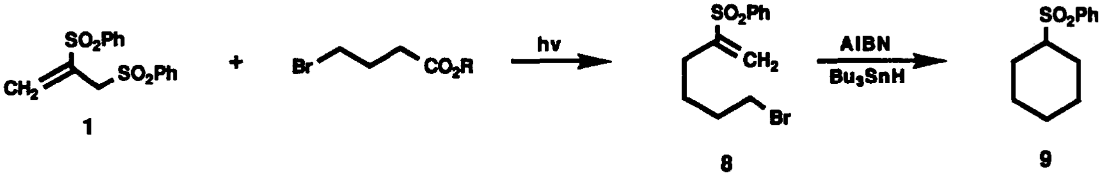
Using Barton's method of generating alkyl radicals *via* hydroxamic acid esters[11], we were able to add primary, secondary and tertiary alkyl radicals to *bis*-sulfone 1. In a typical procedure, a solution of 1 and a 3-fold excess of a thiohydroxamic acid ester was irradiated with a 250 W tungsten lamp for 30 min to produce adducts 3 as sole products in 80-95% yield. An sp^2 center could also be added using conventional tributyltin hydride conditions. The slow addition of 1.2 equiv of tributyltin hydride to a refluxing toluene solution of *bis*-sulfone 1, 2-bromo-2-butene (1 equiv) and a catalytic amount of AIBN resulted in the formation of diene 3d in 83% yield.

One would expect substrate 4[14] to exhibit similar chemistry, with one notable exception. Whereas the phenylsulfonyl radical is a poor atom abstracter,[15] the tributyltin radical ejected from intermediate 5 can sustain a radical chain, obviating the need for the external addition of tributyltin hydride. This sequence was demonstrated by the addition of primary, secondary and tertiary radicals to 4 by heating with various alkyl halides in the presence of AIBN. In a typical procedure, a solution containing 200 mg of 4, 23 μL of n-butyl bromide and 5 mg of AIBN in 0.4 mL of benzene was heated at reflux for 24 h. Workup and isolation via silica gel chromatography gave 2-(phenylsulfonyl)-1-heptene (3a) in 85% yield.

With the viability of the initial radical addition thus established, we turned out attention toward ring formation, taking advantage of the newly formed vinyl sulfone functionality as a second radical acceptor. Toward this end, treatment of 4 with 2-bromobenzyl bromide in refluxing benzene in the presence of AIBN produced vinyl sulfone 6 which could then be closed in a subsequent step with tributyltin hydride to produce the known tetrahydronaphthalene 7 in 88% yield.[16] Similarly, irradiation of *bis*-sulfone **1** and the thiohydroxamic ester derived from ω-bromobutyric acid yielded the unsaturated sulfone **8**, which could be cyclized to cyclohexyl phenyl sulfone **9**[17] in 82% yield. Alternatively, treatment of an equimolar mixture of **1** and 1,3-dibromopropane with a 3-fold excess of tributyltin hydride affords **9** directly.

Ring closure reactions of 5-hexenyl radicals have received much synthetic attention in recent years.[18] In fact, sequential radical cyclizations have been used to construct multiple rings in one step,[19] and guidelines for understanding the stereochemical influence of ring substituents have been published.[18] A marked preference for *exo* ring closure generally exists giving rise to cycloalkylcarbinyl radicals. It should be noted, however, that in the above cases, cyclization gave only the six-membered ring. This result is in accord with earlier observations made in the literature where substitution at the 5-position causes a distinct preference for *endo* closure.[20]





The simple and direct synthesis of vinyl and cyclic sulfones via the radical addition-elimination reaction to 2,3-*bis*(phenylsulfonyl)-1-propene indicates the potential of this sequence as a synthetic method. The scope of the process is under further investigation and we will report additional findings at a later date.

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