Radicals are involved in both the synthesis and the reactions of carbohydrate sulfones. Sulfones produce carbon-centered radicals by group abstraction, dissociative electron-transfer, and photochemical bond homolysis. Sulfone synthesis takes place when a sulfonyl radical adds to an unsaturated carbohydrate.

A. Addition-Elimination Reactions

Addition of a carbohydrate radical to an allylic\(^{41}\) or vinylic\(^{42}\) sulfone is the first step in a reaction that forms a new carbon–carbon bond and expels an arylsulfonyl radical. The reaction shown in eq 7 uses this addition-elimination process to attach a six-carbon-atom chain to a pyranoid ring.\(^{41}\) Addition-elimination reaction also can replace an arylsulfonyl group in an unsaturated sulfone with a tri-n-butyltin group (eq \(8^{43-47}\)). A basic difference in these two reactions is the location of the double bond in the product. When an allylic sulfone reacts (eq 7), the double bond shifts to a new position, but reaction of a vinylic sulfone returns the double bond to its original place (eq 8).

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\text{R} = \text{CH}_2\text{CH}_3
\]

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\text{OTBS}
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B. Electron-Transfer Reactions

1. Samarium(II) Iodide

Electron transfer from SmI\(_2\) to a glycosyl aryl sulfone generates a pyranos-1-yl radical. The options for reactions of this radical are limited either to combination with a second molecule of SmI\(_2\) or to radical reaction that is fast enough to occur before combination can take place. Combination of pyranos-1-yl radicals with SmI\(_2\) produces organosamarium intermediates that undergo typical reactions of organometallic compounds. These reactions include addition to aldehydes and ketones,\(^{48-57}\) proton abstraction,\(^{7,58}\) and \(\beta\)-elimination.\(^{7,56-58}\)

a. Reactions of Organosamarium Compounds
(1). Addition to Carbonyl Compounds

Addition to an aldehyde or ketone is a common reaction for an organosamarium compound generated from a pyranos-1-yl radical. Formation of the organometallic intermediate takes place during the radical phase of such a reaction while addition of this organosamarium compound to an aldehyde or ketone occurs during the nonradical portion of the process (Scheme 14). In most such reactions the addition is to a simple carbonyl compound such as cyclohexanone, but sometimes it is to an aldehydo group in a carbohydrate. Addition reactions of the type shown in Scheme 14 are usually accompanied by β elimination to form glycals. At least in some instances, addition of small amounts of nickel(II) iodide to a reaction mixture can decrease glycal formation in favor of an increase in the yield of addition products.

![Scheme 14](image)

(2). β-Elimination and Proton-Transfer Reactions

Elimination to give a glycal occurs as a side reaction when a glycosyl phenyl sulfone reacts with SmI\(_2\) in the presence of an aldehyde or ketone, but elimination can be the major reaction pathway, when carbonyl compounds are absent. The amount of glycal formed in a reaction depends upon how easily a C-2 substituent can depart as an anion. A carbohydrate with an O-acetyl group at C-2 gives a far higher yield of glycal than does one with an O-benzyl group at this position (Scheme 15). A process competing with elimination is proton abstraction from a donor (presumably water) present in the reaction mixture. The O-acetyl group is so effective as a leaving group that proton transfer from H\(_2\)O to the organosamarium compound is inconsequential, but for the less effective O-benzyl leaving group proton transfer is significant. Proton transfer actually becomes the major reaction pathway when greater than a trace amount of water is present in the reaction mixture. The data given in Scheme 15 show how the balance between β-elimination and proton abstraction changes as reaction conditions and substrate structure change.
b. Radical Cyclization

Cyclization of some radicals is fast enough to prevent combination with SmI\(_2\) from occurring prior to ring formation.\(^{59-63}\) The unsaturated glycosyl phenyl sulfone 14, for example, forms a new ring even though combination of the intermediate radical 15 with SmI\(_2\) potentially could suppress this reaction (Scheme 16).\(^{62}\) HMPA is critical to the reaction shown in Scheme 16 because it promotes electron transfer by reducing the energy required for electron donation from the highest occupied molecular orbital (HOMO) of SmI\(_2\) to the lowest unoccupied molecular orbital (LUMO) of the sulfone (Figure 1).\(^{60}\) The effect of HMPA is so great that in its absence phenyl sulfones do not react with SmI\(_2\).\(^{60}\)
HMPA is not required for reaction of 2-pyridyl sulphones due to the effect of the 2-pyridyl group on sulphone MO energy levels. Because the LUMO energy of a 2-pyridyl sulphone is lower than that of a phenyl sulphone, transfer of an electron to the 2-pyridyl derivative occurs more easily than transfer to the corresponding phenyl sulphone (Figure 2); as a result, ring formation from a 2-pyridyl sulphone can take place without HMPA assisting electron transfer (Scheme 17). ⁶⁰

Figure 1. Effect of HMPA on the HOMO energy of the Sml₂

Figure 2. Difference in LUMO (σ*) energy levels between phenyl and 2-pyridyl sulphones
c. Radical Dimerization

When the 2-pyridylsulfone 16 reacts with SmI$_2$ (no HMPA present), the glycal 18 forms in high yield (Scheme 18).$^{64}$ Adding HMPA slowly to the reaction mixture over a period of two hours has little effect on the glycal yield, but if the same amount of HMPA is present at the beginning of the reaction, glycal yield decreases and the three possible dimers formed from the pyranos-1-yl radical 17 become (in combination) the major product (Scheme 18). Formation of these dimers indicates that HMPA accelerates the production of 17 but not its reaction with SmI$_2$. When HMPA is present at the beginning of the reaction, the concentration of 17 quickly builds to the point that its dimerization takes place more rapidly than its reaction with SmI$_2$.$^{64}$ {Radical formation from glycosyl bromides [Chapter 2, Section III.G.1] and glycosyl phenyl selenides [Chapter 4, Section II.B.6] under the proper conditions gives dimers similar to those shown in Scheme 18.}

Photolysis of glycosyl phenyl sulfones is another way for producing pyranos-1-yl radicals that dimerize.$^{65}$ The product mixture from such a reaction is more complex and the dimer yield lower than that from the reaction with SmI$_2$ shown...
in Scheme 18 (HMPA present at the beginning of the reaction). The ratios of the three stereoisomeric dimers in photochemical and SmI$_2$ reactions are quite similar, a fact considered to be a “stereochemical signature” for pyranos-1-yl radical dimerization.$^{64}$

### 2. Chromium(II) Complexes

Chromium(II) complexes also can function as electron donors in reactions of carbohydrate sulfones,$^{66}$ but such reactions are far less common than those in which SmI$_2$ is the electron donor. The radical produced by electron transfer from [Cr(II)(EDTA)]$^{2-}$ has the same types of options available as a radical generated by electron transfer from SmI$_2$; that is, the radical either can combine with another chromium(II) complex or undergo a radical reaction that is fast enough to compete with the combination process (Scheme 19). One reaction that is sufficiently rapid is radical addition to a compound with an electron-deficient double bond (eq 9).$^{66}$

#### C. Sulfone Synthesis

$p$-Tolylsulfonyl radicals add reversibly to carbon–carbon multiple bonds. If the adduct radical is “captured” before addition is reversed, the resulting product is a sulfone.$^{67-69}$ Radical cyclization, such as that shown in Scheme 20,$^{68}$ is rapid enough to trap the intermediate radical 16. As long as the new ring remains intact, loss of the $p$-tolylsulfonyl group will not take place, insuring completion of sulfone formation.
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