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# $SmI_2$ Mediated Reductive Addition of Bis-Phenylsulfones to Ketones

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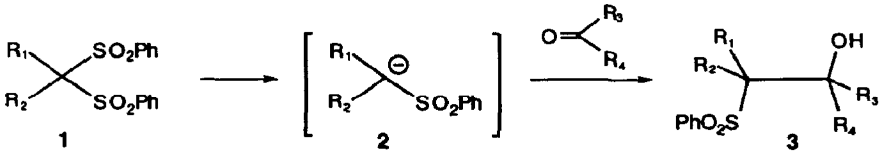
**Key Words:** β-hydroxyphenylsulfone, desulfonylation, alkylation, diiodosamarium.

**Abstract:** $SmI_2$ mediates the *in situ* reductive addition of geminal bis-phenylsulfones to unhindered ketones at room temperature affording β-hydroxyphenylsulfones in good to excellent yields.

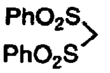
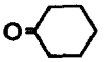
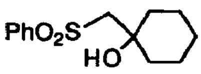
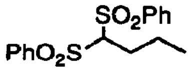
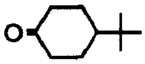
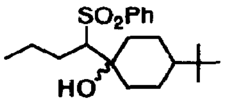
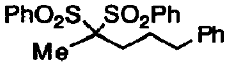
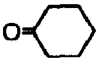
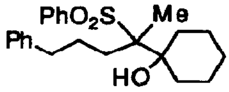
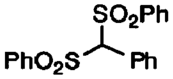
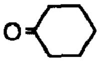
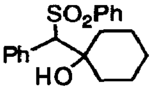
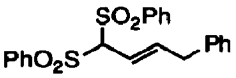
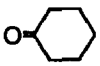
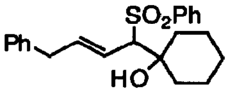
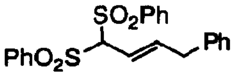
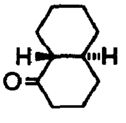
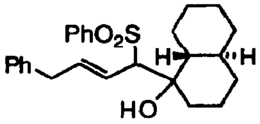
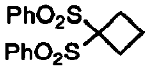
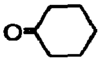
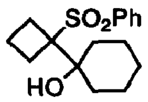
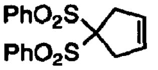
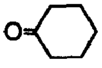
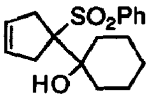
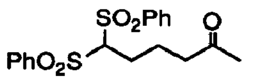
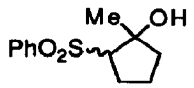
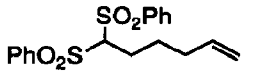
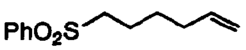
In the preceding report,[1] we describe a mild and efficient procedure for the stepwise reductive cleavage of geminal bis-phenylsulfones **1**[2] using lithium naphthalenide in THF at -78°C. The resultant α-sulfonyl carbanions **2** readily participate in a wide range of nucleophilic reactions including alkylations to create new carbon-carbon bonds.[3] However, in common with α-metalated sulfones generated by more conventional methods, addition of **2** to ketones is often unsatisfactory.[4] This important limitation has been attributed to facile reversion of the initial adduct to starting materials and has been obviated in only a few cases by transposing the reaction components, adding $BF_3 \cdot Et_2O$, or *in situ* trapping.[5] Herein, we disclose that $SmI_2$ mediates the reductive addition of geminal bis-phenylsulfones to ketones affording tri- and tetrasubstituted β-hydroxyphenylsulfones **3** in good to excellent yields (eq 1).[6,7]



(eq 1)

The results obtained with a cross-section of typical geminal bis-phenylsulfones are compiled in Table I.[8] Ketone additions using the parent bis-sulfone (entry 1), i.e., bis(phenylsulfonyl)methane (Aldrich Chem. Co.), as well as mono- and di-substituted examples (entries 2 and 3, respectively) proceeded smoothly in less than 15 min at ambient temperature in THF. Optimum yields require 3 equivalents of $SmI_2$; more $SmI_2$ does not improve the yield and less leads to incomplete reactions. Significantly, addition to the carbonyl, but not desulfonylation, is completely suppressed in the presence of HMPA (10 equiv).[6,7a] A moderate preference for equatorial attack (4:1 ax/eq alcohols,[9] entry 2) is consistent with the stereochemical outcome between other organometallics and unbiased cyclic ketones.[10]

**Table I.** SmI$_2$ Mediated Reductive Addition of Bis-Phenylsulfones

| Entry | Bis-Sulfone | Electrophile | Product | Yield[a],% |
|---|---|---|---|---|
| 1 |  |  |  | 71 |
| 2 |  |  |  | 77$^b$ |
| 3 |  |  |  | 85 |
| 4 |  |  |  | 80 |
| 5 |  |  |  | 81 |
| 6 |  |  |  | 62$^c$ |
| 7 |  |  |  | 92 |
| 8 |  |  |  | 86 |
| 9 |  | |  | 71$^d$ |
| 10 |  | |  | 72 |

[a] Based on isolated, chromatographically homogeneous material. [b] 4:1 mixture of ax/eq alcohols. [c] Single diastereomer as determined by $^{13}$C NMR and chromatographic analysis. [d] 10:1 diastereomeric mixture.

Benzylic (entry 4) and allylic (entries 5 and 6) bis-sulfones are also suitable substrates and show no tendency towards over-reduction under the reaction conditions. In the latter conjugated examples, neither $\gamma$-addition nor olefin migration are observed.[11] Despite steric hindrance, the synthetically useful bicyclic adducts in entries 7 and 8 are isolated in good yield. The intramolecular version of this reaction, is illustrated in entry 9 by preparation of a cyclopentanol as a 10:1 diastereomeric mixture.[12]

The exact nature of the intermediates involved in the above reactions are unknown, but it is worth noting that introduction of $SmI_2$ to a preformed solution of **2** in its lithium salt form will not suffice for ketone addition. Furthermore, the exact sequence of reagent addition is critical. Even though bis-sulfones are cleaved rapidly and in good yield by $SmI_2$, subsequent addition of ketone generates little, if any, adduct. It is likely that some samarium species[13] with Lewis acid character is generated *in situ* or that the reaction does not involve a discrete anion but rather a radical or radical anion.[14] With respect to the latter, such an intermediate could not be intercepted with a terminal olefin (Table I, entry 10).

**General Procedure**: Bis-phenylsulfone (1 mmol) in 4 ml of THF is added dropwise to a room temperature, dark blue mixture of $SmI_2$[15] (3 mmol) and ketone (1 mmol) in 30 ml of THF under argon. A color change to yellow, usually within 5-15 min, heralds complete consumption of the reactants. The mixture is diluted with $Et_2O$ and sequentially washed with 5% hydrochloric acid, saturated sodium thiosulfate solution, water, and brine. After drying over $Na_2SO_4$, the solvent is evaporated *in vacuo* and the residue chromatographed on $SiO_2$ to afford the $\beta$-hydroxyphenylsulfone in the yields summarized in Table 1.

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8. Satisfactory spectral data ($^1H$ and $^{13}C$ NMR, MS) were obtained for all new compounds using chromatographically homogeneous samples.
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