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REDUCTIVE DESULFONYLATION OF PHENYL SULFONES BY SAMARIUM(II) IODIDE-HEXAMETHYLPHOSPHORIC TRIAMIDE

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Summary. Samarium(II) iodide in tetrahydrofuran reductively desulfonylates phenyl sulfones in the presence of hexamethylphosphoric triamide. This transformation is illustrated here for ten substrates, which include secondary alicyclic, β-hydroxy, vicinal bis-, and α,β-unsaturated sulfones.

The most popular transformations for carbon-carbon bond formation, employing arylsulfonyl bearing synthons, include alkylation of α-arylsulfonyl carbanions,[1] Michael addition of organometallic reagents to α,β-unsaturated sulfones, occasionally followed by an additional alkylation step on the intermediate α-sulfonyl carbanion,[2] and Diels-Alder reactions with electron-deficient dienophiles, e. g., phenyl vinyl sulfone,[3] (*Z*)- and (*E*)-1,2-bis(phenylsulfonyl)ethylene,[4] or ethynyl *p*-tolyl sulfone.[5] Since the ultimate target molecules generally lack the sulfone moiety, the overall efficacy of such protocols is tightly related to reliable methods for the removal of the sulfur substituent. Dissolving-metal reductive desulfonylations, I→II, have emerged as a particular important class of reactions in this context, with amalgams, preferably those of Group IA-IIIA metals, in alcoholic solution ranking as the reagents of choice.[6]

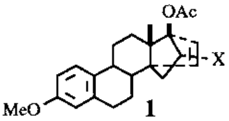
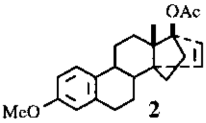
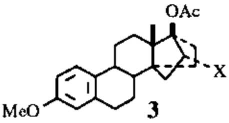
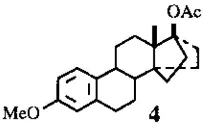
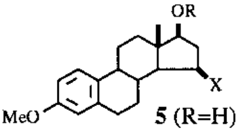
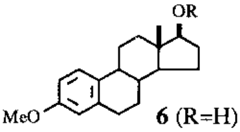
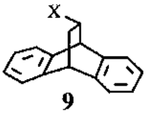
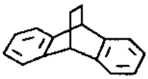
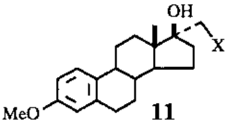
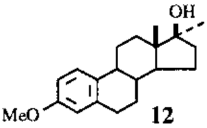
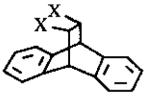
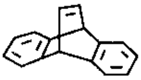
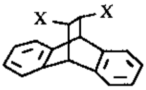
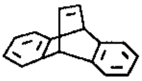
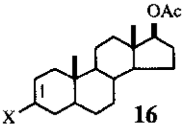
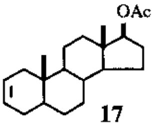
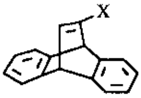
$$\underset{\text{I}}{R^1R^2R^3C\text{-}SO_2Ph} \longrightarrow \underset{\text{II}}{R^1R^2R^3C\text{-}H}$$

Except for the solitary cases of α-phenylsulfonyl ketones[7] and β-hydroxy imidazolyl sulfones,[8] where samarium(II) iodide (SmI_2) in tetrahydrofuran (THF) has been reported to give rise to the parent ketones[7] and to olefinic products,[8] respectively, the lanthanide reagent does not seem to have been successfully applied in reductive desulfonylations of non-activated phenyl sulfones. In fact, Kende and Mendoza noticed in their work on β-hydroxy imidazolyl sulfones that the corresponding β-hydroxy phenyl sulfones fail to be desulfonylated by SmI_2.[8] Interestingly, it has also been demonstrated that SmI_2 promotes deoxygenation of sulfoxides[9] and certain sulfones[10] to the corresponding sulfides.

These reports prompt us to disclose some of our own findings regarding SmI_2-mediated reductive desulfonylations of phenyl sulfones.

In our hands, neither deoxygenation nor desulfonylation occurred upon treatment of a series of sulfones with SmI_2-THF at various temperatures. However, when hexamethylphosphoric triamide (HMPA)[11] was added to a solution of commercially available or, preferably, freshly prepared SmI_2 in THF containing a phenyl sulfone substrate under an atmosphere of argon, a color change from blue-green to purple was observed and thin-layer chromatography of samples withdrawn from the reaction mixture revealed formation of a new, less-polar product, which was devoid of any sulfur functionality. Representative examples for this transformation are compiled in the Table below. Reaction conditions have been optimized to some degree, in order to secure satisfactory yields.

Table. SmI_2/HMPA-Promoted Reductive Desulfonylation Of Phenyl Sulfones, X=SO_2Ph

Entry	Substrate	Product	Reaction Conditions; Yield
1	 **1**	 **2**	-20°C, 70 min; 70%
2	 **3**	 **4**	-20°C, 90 min; 87%
3a	 **5** (R=H)	 **6** (R=H)	+22°C, 90 min; 50%
3b	**7** (R=Ac)	**8** (R=Ac)	-20°C, 90 min; 52%
4	 **9**	 **10**	-20°C, 30 min; 74%
5	 **11**	 **12**	+22°C, 60 min; 53%
6	 **13**	 **14**	-20°C, 30 min; 83%
7	 **15**	 **14**	-20°C, 30 min; 91%
8	 **16**	 **17**	-20°C, 90 min; 68%
9	 **18**	 **14**	-20°C, 30 min; 77%

Thus, the cycloadduct **1**, obtained by Diels-Alder reaction between phenyl vinyl sulfone and 17-acetyloxy-3-methoxyestra-1,3,5(10),14,16-pentaene,[12] was submitted to desulfonylation at -20°C. After 70 minutes, the starting material was almost completely consumed and the product **2**[12] was isolated in 70% yield following aqueous work-up and chromatography on silica gel. Remarkably, both the acetate functionality and the norbornenyl double bond remained largely intact at -20°C, a situation which changed to the worse, when the reaction was performed at 0°C. The superior stability of the hydrogenated steroid **3**[12] versus **1** in the SmI_2/HMPA-promoted desulfonylation process is reflected by a high 87% yield of the product **4**.[12] An additional secondary steroidal sulfone was prepared by Michael reaction between thiophenol and 3-methoxyestra-1,3,5(10),15-tetraen-17-one,[13] $NaBH_4$-reduction of the carbonyl group, and oxidation[14] of the sulfur atom. Acetylation of the γ-hydroxy sulfone **5** led to the protected derivative **7**. From two desulfonylation runs, estradiol methyl ether (**6**) and the acetate **8** were isolated in 50% and 52% yield, respectively. Approximately 30% of each starting material was recovered unchanged in these instances. Reduction of the cycloadduct **9**, readily synthesized from phenyl vinyl sulfone and anthracene,[15] furnished dibenzobicyclo[2.2.2]octadiene (**10**) in 74% yield.[15] As an example for the desulfonylation of β-hydroxy phenyl sulfones, we have listed the reduction of the steroid derivative **11**, which was made available by alkylation of the Li-anion of methyl phenyl sulfone with 3-methoxyestra-1,3,5(10)-trien-17-one. The tertiary alcohol **12** was isolated as the main product, together with 17-methylene-3-methoxyestra-1,3,5(10)-triene (20%), and 20% of educt **11**.

Not unexpectedly, the SmI_2/HMPA reagent combination seems also excellently suited for the conversion of vicinal bis(arylsulfonyl) derivatives into the corresponding olefins by reductive desulfonylation.[16] This useful reaction is realized here in the transformation of cycloadducts **13** and **15**, derived from (*Z*)- and (*E*)-1,2-bis(phenylsulfonyl)ethylene and anthracene, into dibenzobarrelene **14**[16] in 83% and 91% yield, respectively.

Acceptable results may also be achieved with certain α,β-unsaturated phenyl sulfones.[17] The steroid derivative **16** was obtained by thioketalization-elimination,[18] followed by oxidation[14] of the intermediate vinyl sulfide. Again, mild reaction conditions guarantee a satisfactory 68% yield of the acetate **17**. Still another synthesis of dibenzobarrelene (**14**) was accomplished by reduction of the vinyl sulfone **18**. The starting material **18** was generated by elimination of benzenesulfinic acid from **13** in dimethylformamide containing aqueous potassium carbonate.[19]

In conclusion, this novel reductive desulfonylation protocol[20] expands the synthetic utility of the SmI_2-THF reagent to some extent, although the level of chemoselectivity attainable in reactions with highly functionalized molecules will be limited.[11, 21]

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20. A characteristic reductive desulfonylation procedure is as follows.
    Under an atmosphere of argon, 0.494 g (1 mmol) of **3** was dissolved in 50 mL of a freshly prepared solution of SmI_2-THF (approximately 0.1 molar). This mixture was cooled to -20°C under stirring and hexamethylphosphoric triamide (4 mL) was added dropwise by syringe, whereupon the color of the solution changed from blue to purple. After 90 minutes, the reaction was terminated with aqueous ammonium chloride (5 mL). Most of the tetrahydrofuran was removed in vacuo by rotary evaporation. The product was precipitated by addition of cold hydrochloric acid (0.5 molar) and isolated by suction-filtration. The solid residue was dissolved in ethyl acetate, the resulting organic phase was washed with aqueous sodium thiosulfate solution, followed by brine, and then dried over anhydrous sodium sulfate. Chromatography of the crude product on silica gel (hexane-ethyl acetate, 9:1) provided 0.308 g (87%) of **4**, mp 119-120 °C (acetone-hexane).
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