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Selective sulfonylation of 1,2-diols and derivatives catalyzed by a recoverable fluorous tin oxide[†]

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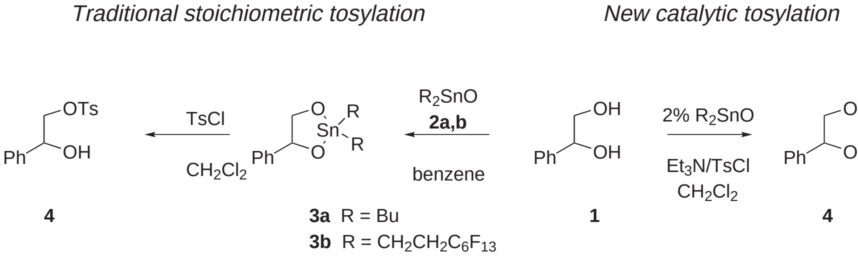
Abstract

Fluorous tin oxide $(C_6F_{13}CH_2CH_2)_2SnO$ is readily synthesized, exhibits spectra that are generally similar to dibutyltin oxide and appears to exist as an oligomer or polymer. The fluorous tin oxide can be used catalytically to effect the selective monotosylation of 1,2-diols with $TsCl/Et_3N$, and it can be readily recovered and reused. © 2000 Published by Elsevier Science Ltd.

The selective reaction of 1,2-diols with electrophiles mediated by dialkyltin oxides has proven value both within and beyond carbohydrate chemistry.[1] In general, a 1,2-diol like **1** is reacted first with an equivalent amount of dibutyltin oxide **2a** (R = Bu)[2,3] under dehydrating conditions to provide an intermediate stannoxane **3a** (Eq. (1)). This is then reacted in a separate step with an electrophile to provide a monofunctionalized product **4**, often with high regioselectivity. Tosylation is shown in Eq. (1), but acylation and a number of other transformations can be accomplished by this procedure. Recently, Martinelli and co-workers described an important advance in selective sulfonylation of 1,2-diols by introducing a one-step procedure that requires only 2% of the tin oxidfle along with triethylamine (Eq. (1)).[4] This procedure is attractive because only a small amount of tin must be removed from the final product; however, chromatography is still required, and the tin is not recovered for reuse. Even when catalytic amounts of tin are used, environmental concerns dictate that it be recovered rather than discarded whenever possible.



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[†] Dedicated to Professor Harry Wasserman on the occasion of his 80th birthday.

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We have recently introduced a family of fluorous tin reagents exemplified by tin hydrides that bear either one [$Rf(CH_2)_nSn(Me)_2H$] or three [$(Rf(CH_2)_n)_3SnH$] fluorous chains.[5] If suitable alkylene spacers are used, these reagents mimic their organic parents in reactivity but are readily separated from crude products by fluorous-organic liquid–liquid or solid–liquid extractions.[6] Recovery and reuse of the tin reagents is often possible. The long range goal of this work is to understand the reaction and separation features of a complete family of fluorous reagents. To further advance this goal, we decided to make a fluorous analog **2b** ($R=CH_2CH_2C_6F_{13}$) of dibutyltin oxide **2a** and to test its use in selective diol functionalization with a focus on the Martinelli catalytic sulfonylation procedure. We summarize herein the results of this study.

Bis-perfluorohexylethyltin oxide **2b** was synthesized as shown in Eq. (2).[7] The Grignard reagent derived from **5** was coupled with diphenyltin dichloride **6** to give about a 7:1 mixture of fluorous tin reagent **7** and the Wurtz coupled dimer ($C_6F_{13}(CH_2)_4C_6F_{13}$). These were not easily separable, so the mixture was treated with chloroacetic acid following the procedure of Kong.[8] Recrystallization of the crude product from hexane gave pure bis-chloroacetate **8**. This was then stirred in ether with 2.5 M sodium hydroxide. The ether phase was washed, dried and evaporated to provide tin oxide **2b** as a free-flowing white powder. This product was used without further purification.

$$\underset{\mathbf{5}\ Rf = C_6F_{13}}{ICH_2CH_2Rf} \xrightarrow[\text{2) } Ph_2SnCl_2\ \mathbf{6}]{\text{1) Mg/THF}} \underset{\mathbf{7}}{Ph_2Sn(CH_2CH_2Rf)_2} \xrightarrow{ClCH_2CO_2H} \underset{\mathbf{8}}{(ClCH_2CO_2)_2Sn(CH_2CH_2Rf)_2} \xrightarrow[\text{ether}]{\text{NaOH}} \underset{\mathbf{2b}}{[OSn(CH_2CH_2Rf)_2]_n} \qquad (2)$$

Dibutyltin oxide **2a** is not monomeric and is thought to exist as a polymer.[1–3] Fluorous tin oxide **2b** generally resembles dibutyltin oxide in its spectroscopic behavior. For example, **2b** exhibits broad resonances in the ^1H NMR spectrum, but resonances in its ^{13}C and ^{19}F spectra are sharp and interpretations are straightforward.[9] Based on these similarities, we suspect that **2b** is oligomeric or polymeric. The following partition coefficients (FC-72/organic solvent) were measured for **2b**: CH_2Cl_2, 1.7; CH_3CN, 0.28; toluene, 1.9.

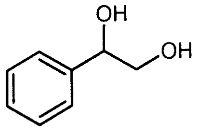
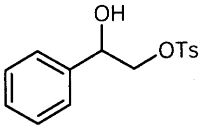
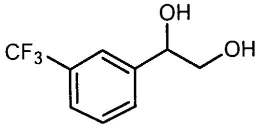
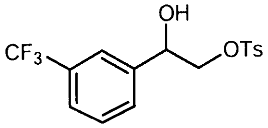
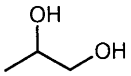
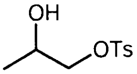
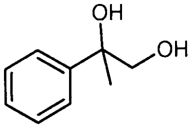
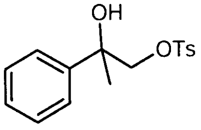
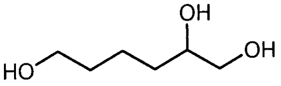
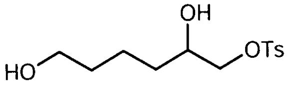
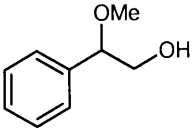
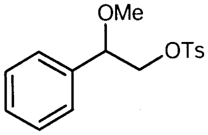
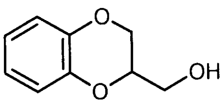
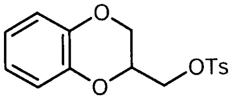
We first probed the usefulness of tin oxide **2b** in a standard two-step procedure (Eq. (1)).[7] A benzene solution of 1-phenyl-1,2-ethanediol **1** and **2b** was refluxed for 24 h in the presence of 4 Å molecular sieves. Evaporation of the benzene then gave stannylidene **3b** in 83% yield. Reaction of this crude product with tosyl chloride in dichloromethane gave tosylate **4** in 80% yield after aqueous workup and eight washings with FC-72 to remove the tin.[10] No resonances could be detected in the ^{19}F NMR spectrum of **4**. The results of this preliminary experiment were very encouraging. The yields and rates of reactions of the fluorous tin reagent **2b** were roughly comparable to dibutyltin oxide. The reaction succeeded in a standard organic solvent; fluorinated cosolvents were not required.

Fluorous tin oxide **2b** served equally well in Martinelli's catalytic procedure.[4] In two identical reactions, diol **1** (1 mmol, 1 equiv.), tosyl chloride (1 equiv.), triethylamine (1 equiv.) and fluorous tin oxide **2b** were stirred in dichloromethane for 1 h.[11] After acidic workup, one crude product was taken up in dichloromethane and washed with FC-72 (eight times) to provide the tosylate **4** in 80% yield. The other product was charged to a column of fluorous reverse phase silica gel, which was eluted with 9:1 $MeOH/H_2O$ to give the tosylate **4** in 80% yield. Like Martinelli, we observed only the monotosylate in these catalyzed reactions, and this tosylate was free of fluorous tin products as assessed by ^{19}F NMR spectroscopy.

The generality of the method was tested by reacting the substrates (1 mmol) shown in Table 1 under the catalytic procedure with fluorous tin oxide **2b**. These reaction products were purified by liquid–liquid extraction and the tin oxide was recovered. Only monotosylate products of the 1-alcohol were observed in each case. The reaction in Entry 1 was conducted three times with the recovered tin oxide. Yields of all reactions were comparable and an average of 92% of the initial fluorous tin oxide was recovered each time. This reaction was also run on 10 mmol (~1 g) scale with comparable results. For the triol (Entry 5), only the 1°-alcohol of the 1,2-diol was tosylated. Reaction times were roughly of the order observed by Martinelli when using dibutyltin oxide.[4a] 1,2-Diols reacted very quickly (about 1 h), while alkoxyalcohols (Entries 6 and 7) reacted considerably more slowly (about 1 day).

Since only a small amount of tin is added to the reaction (2 mol%), it is difficult to assess the effectiveness of the workup in removing the tin. To clearly show that the workup did remove the

Table 1
Monotosylation of alcohols with 2% fluorous tin oxide

Entry	Substrate	Reaction time[a] (h)	Yield of monotosylate[b] (%)	Structure of monotosylate
1[c]		1–2	75–80	
2		1	77	
3		1	72	
4		1	70	
5		1	74	
6		23	84	
7		23	94	

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[a] Reactions were followed by TLC.

[b] Isolated yields of purified product.

[c] Reaction time and yield ranges for multiple runs with recovered tin oxide.

tin, we carefully assessed the product of Entry 2 by using ^{19}F NMR spectroscopy with the CF_3 group of the monotosylated product as an internal standard. The ^{19}F NMR spectrum of the crude product prior to any purification showed seven peaks: one for the CF_3 group of the tosylate and six for the CF_2 groups (5) and CF_3 (1) of **2b** in the expected 50:1 ratio. The mixture was then divided into two equal parts, one of which was purified by liquid–liquid extraction and the other of which was purified by solid–liquid extraction. Each of these final products showed only one peak in its ^{19}F NMR spectrum, which corresponded to the CF_3 group of the tosylate; the resonances of **2b** were no longer detectable.

Fluorous tin oxide **2b** is easy to make and handle, and the preliminary results suggest that it will be a valuable alternative to the standard dibutyltin oxide **2a** in both catalytic and stoichiometric procedures. Accordingly, we recommend that the fluorous tin oxide be used in the catalytic sulfonylation procedure of Martinelli and be tried on other procedures where dibutyltin oxide is usually the reagent of choice.

Acknowledgements

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9. ^{1}H NMR (300 MHz, acetone-d_6): δ 2.50–2.61 (broad band, 4H), 2.77–2.84 (t, 4H); ^{13}C NMR (75 MHz, acetone-d_6) δ 123.56–108.52 (m, 12C), 27.13 (m, 2C), 20.48 (t, 2C); ^{19}F NMR (282 MHz, acetone-d_6 with $CFCl_3$) δ −125.69, −122.84, −122.35, −121.37, −115.17, −80.56; ^{119}Sn NMR (111.8 MHz, $CDCl_3$ with $(CH_3)_4Sn$) δ −59.1.

10. Based on the partition coefficient, this should remove about 99% of the tin. Since only 2 mol% tin is used in the catalytic procedure, fewer washings may suffice.
11. 1-Phenyl-1,2-ethane diol (1 mmol) was dissolved in CH_2Cl_2 (5 mL). Triethylamine (1 mmol) and tin oxide **2b** (0.02 mmol) were added. Tosyl chloride was added and the solution was stirred at room temperature for 50 min. Water (1 mL) was added and the aqueous layer was washed with dichloromethane (2×10 mL). The combined organic layers were washed with H_2O (2×25 mL) and brine (2×25 mL). The organic layer was dried over $MgSO_4$. Removal of the solvent yielded a mixture of **4** and tin oxide. One part of the resulting mixture was washed with FC-72 (8×25 mL). The dichloromethane was evaporated to yield **4** and the FC-72 was evaporated to yield **2b**. The other part was transferred to a column containing fluorous reverse phase silica gel (bonded phase $–OSi(Me)_2CH_2CH_2C_6F_{13}$) (100 mg). The column was then washed with a mixture of 9:1 methanol:water (3 mL), followed by THF (3 mL). Evaporation of the methanol:water mixture yielded **4**.