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LETTERS

Synthesis of Alcohols via Mild Oxidation of Perfluoroethylstannanes

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Abstract: Alkaline H_2O_2 oxidizes perfluoroethyl-substituted stannanes to the corresponding alcohols with retention of configuration.

Keywords: tin; oxidation; alcohols; stereospecificity

The trialkylstannane moiety participates in a variety of useful synthetic transformations[1] including chemoselective oxidation to carbonyls[2] or their equivalent.[3] Their direct conversion to alcohols, in contrast, has proven more elusive in all but a few structurally restricted cases[4] and generally requires comparatively strong oxidants such as lead tetraacetate[5] or 3-chloroperbenzoic acid (*m*-CPBA).[6] Some alternative, 2-step procedures are also available, e.g., (i) cleavage of an alkyl substituent from the tin using molecular bromine followed by ammoniacal *m*-CPBA[7] or (ii) initial hydroboration of the stannane and oxidation of the resultant borane.[8] Herein, we describe the preparation of perfluoroethyl-substituted[9] stannanes and their direct, stereospecific oxidative transformation to the corresponding alcohols under mild conditions.

The scope of the tin-to-alcohol conversion was explored with a panel of representative perfluoroethyl-substituted stannanes and the results are summarized in Table 1. Since the oxidation of aryltins is often difficult,[8] dibutyl(perfluoroethyl)phenylstannane (**1**) was used as a model system to evaluate reaction parameters. The best yield of phenol (**2**) was obtained with slightly alkaline 30% H_2O_2 in methanol/THF at room temperature (Entry 1). Notably, the trialkyl analog of **1**, i.e., tributylphenylstannane, completely resisted these conditions and could be recovered quantitatively after 2 days. Reactions of **1** with H_2O_2 were significantly

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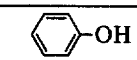
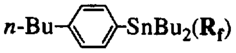
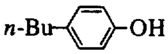
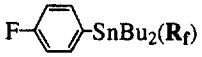
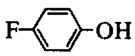
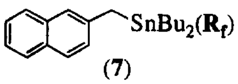
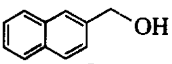
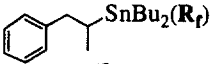
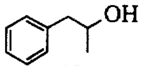
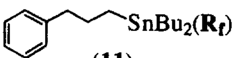
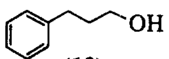
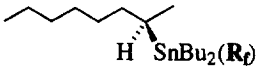
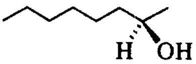
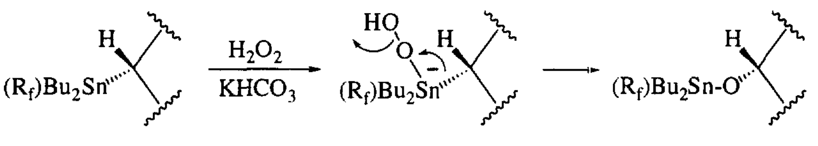
Table 1. Oxidation of Perfluoroethyl-Substituted Stannanes

Entry	Stannane	Solvent	Time (h)	Oxidant/Base	Product	Yield (%)
1	 (1)	MeOH/THF	14	H_2O_2/$KHCO_3$	 (2)	94
2	1	THF	72	H_2O_2/$KHCO_3$	2	50[a]
3	1	THF	2	KO_2	2	85
4	1	THF/H_2O	24	$NaBO_3$	2	87
5	1	MeOH/THF	15	Oxone	2	0
6	 (3)	MeOH/THF	14	H_2O_2/$KHCO_3$	 (4)	90
7	 (5)	MeOH/THF	14	H_2O_2/$KHCO_3$	 (6)	86
8	 (7)	MeOH/THF	16	H_2O_2/$KHCO_3$	 (8)	85
9	 (9)	MeOH/THF	14	H_2O_2/$KHCO_3$	 (10)	68
10	 (11)	MeOH/THF	30	H_2O_2/$KHCO_3$	 (12)	38
11	 (13)	MeOH/THF	14	H_2O_2/$KHCO_3$	 (14)	73

[a] Balance is unreacted starting material. $R_f = CF_3CF_2$-

slower in the absence of base or in non-hydroxylic solvents such as THF (Entry 2). Synthetically useful yields were also achieved utilizing powdered potassium superoxide (Entry 3) or sodium perborate (Entry 4), but not Oxone® (Entry 5). Moderate electron donating (Entry 6) and withdrawing groups (Entry 7), represented by 4-butylphenylstannane (**3**) and 4-fluorophenylstannane (**5**), respectively, had little influence on the course of the oxidation and gave rise to the corresponding phenols **4** and **6** in good to excellent yields.

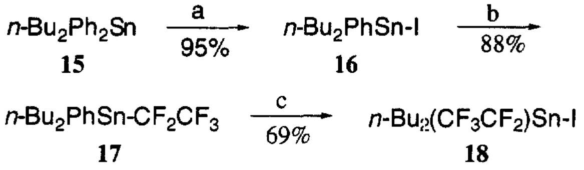
Likewise, benzylstannane **7** and secondary alkylstannane **9** were smoothly converted to alcohols **8** and **10**, respectively, by the combined actions of H_2O_2/$KHCO_3$. On the other hand, the oxidation of primary alkylstannane **11** to alcohol **12** was sluggish. This is consistent with nucleophilic attack of the peroxide anion at tin (eq. 1) followed by migration of a stannyl-substituent to the electrophilic oxygen center. Aqueous quench and hydrolysis of the newly generated stannyl ether liberates the corresponding alcohol. The poor migratory aptitude[10] of unactivated, primary alkyl groups, together with competition from the other *n*-alkyl substituents on tin, account for the low yield of **12**. Additional evidence in support of the mechanistic hypothesis in equation 1 comes from the observation that chiral (R)-stannane **13** was stereospecifically transformed to (R)-2-octanol (**14**) with virtually complete retention of configuration as determined by chiral phase HPLC[11] and NMR comparisons of the derived Mosher ester versus a standard.



(eq 1)

The perfluoroethylstannanes in Table 1 were prepared in good to excellent yields via addition of the appropriate Grignard or lithium reagent to iodide **18** under standard conditions. The latter reagent was conveniently secured (Scheme 1) from commercial (Strem Chem., Inc.) di-*n*-butyldiphenyltin (**15**) by selective phenyl cleavage utilizing molecular iodine to give **16** which was then subjected to nucleophilic displacement with *in situ* generated perfluoroethyllithium.[12] Controlled iodine exchange of the resultant stannane **17** and chromatographic purification provided ready access to **18**.

Scheme 1



[a] I$_2$ (1 equiv), Et$_2$O, 0° to 23°C, 12 h.[b] CF$_3$CF$_2$-I, MeLi, Et$_2$O, -78°C, 10 min; **16**, 6 h.[c] I$_2$, Et$_2$O/hexane (5:1), 23°C, 3 h.

General Oxidation Procedure: Hydrogen peroxide (aqueous 30%, 5 mmol) was added to a room temperature solution of perfluoroethylstannane (1 mmol) and $KHCO_3$ (3 mmol) in MeOH/THF (1:1, 8 mL). After stirring for the designated time (Table 1), the reaction mixture was neutralized with 5% HCl, concentrated under reduced pressure, and the residue partitioned between Et_2O and H_2O. The combined ethereal extracts were evaporated *in vacuo* and the product purified via SiO_2 chromatography.

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