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A WATER SOLUBLE TIN HYDRIDE REAGENT

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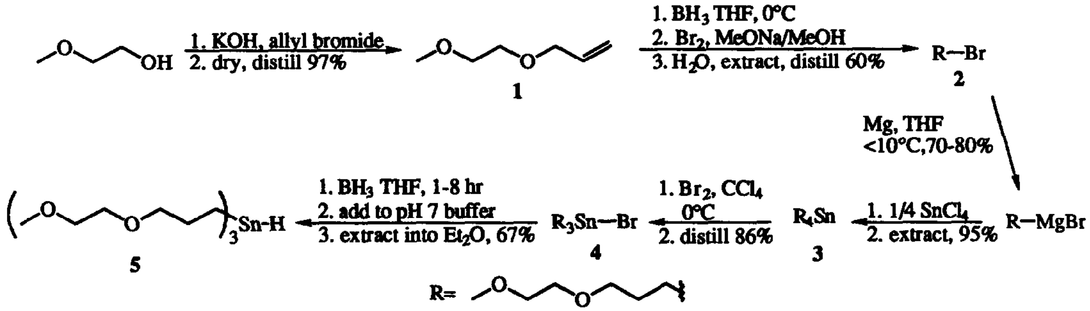
Abstract: A water soluble tin hydride has been synthesized carrying three methoxyethoxypropyl groups. It reduces various alkyl halides in water, or in organic solvents.

Tin hydride radical chemistry is widely used,[1] but the solubility of tri-*n*-butyl tin hydride limits it to organic solvents. In order to perform tin radical chemistry in water, we designed and synthesized tin hydride **5**. This is sufficiently soluble in water (ca. 30 mM at r.t., more on warming) to reduce alkyl halides under free radical conditions. It is also nonvolatile and odorless.



Hydroboration then bromination[2] of **1** gave **2**, isolated by continuous hexane extraction and vacuum distillation at 50°C, 0.8 torr.[3] The Grignard was titrated,[4] and added via cannula to 1/4 eq. $SnCl_4$ at -78°C. The solution was allowed to warm to room temperature overnight, then refluxed for two hours. An aqueous workup and extraction into hexanes gave **3**, which could be vacuum distilled, bp 210-215°C at 0.005 torr.[5] Treatment of **3** with one eq. Br_2 gave **4**, bp 190-195°C at 0.005 torr;[6] 1 eq. of **2** was also recovered. Reduction of **4** by the usual methods[7] failed, but 1.0M BH_3 in THF was effective. Pure tin hydride **5** could be isolated by dripping the reaction mixture into 0.5 M pH 7 phosphate buffer, and extracting into ether. Hydride **5** could be further purified by kugelrohr distillation, fraction 100-120°C at 0.01 torr: found (calc.) %C 45.88 (45.74), %H 8.56 (8.71), %Sn 25.19 (25.08). It was additionally characterized by IR, ^{1}H, ^{13}C, and ^{119}Sn spectroscopy.[8]

Tin hydride **5** can reduce alkyl bromides and iodides in water, with 4,4'-azobis(4-cyanovaleric acid) [ACVA (Aldrich)] or sunlamp initiation. Reactions were generally performed with solutions 10-25 mM, or with up to 100 mM **5** partly in suspension but in solution on warming. Phosphate buffers kept the reactions non-acidic. For example mono-6-iodo-β-cyclodextrin was reduced in water to 6-deoxy-β-cyclodextrin in 76% yield, using 10% ACVA and 80-90°C for 2 hr. *m*-Bromobenzoic acid was also reduced to benzoic acid in 88% yield in 5% $NaHCO_3$ $_{aq}$ at r.t. with 1.2 eq. of **5**, using a sunlamp for 40 min. 6-Bromo-6-deoxy-α-methylglucopyranoside was reduced in water in 84% yield, and 2-bromopentanoic acid in 37% yield. In benzene solution, 1.2 eq. of **5** reduced 1-bromooctane to octane with AIBN initiation in 99% yield.

The trialkyl tin species is easily recovered. Acidifying the water to pH <2 with HCl regenerates the trialkyltin chloride, which is extracted into $CHCl_3$, distilled, and reduced with BH_3 in THF, regenerating tin hydride **5**. Its easy synthesis and useful water solubility make it attractive for bioorganic studies.

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Notes and references

1 Neumann, W. P. *Synthesis* **1987**, 665-683. Tin chemistry review: Omae, I. 'Organotin Chemistry' Elsevier, NY, 1989.

2 Brown, H. C.; Lane, C. F. *J. Am. Chem. Soc.* **1970**, *92*, 6660-6661.

3 Compound **2:** ^1H NMR 300 MHz, $CDCl_3$ δ 3.68-3.54 (m, 8H), 3.42 (s, 3H), 2.18 (quintet, 2H). ^{13}C NMR 75.4 MHz, $CDCl_3$ δ 71.92, 69.40, 68.76, 59.14, 32.88, 30.75.

4 Watson, S. C.; Eastman, J. F. *J. Organomet. Chem.* **1967**, *9*, 165-168.

5 Compound **3:** ^1H NMR 300MHz, $CDCl_3$ δ 3.55 (AA'BB' m, 16H), 3.39 (s, 12H), 3.39 (t, 8H), 1.78 (m, 8H), 0.77 (m, 8H, apparent t within a doublet). In D_2O, TSP ref. δ 3.64 (m, 16H), 3.53 (t, 8H), 3.40 (s, 12H), 1.84 (m, 8H), 0.89 (m, 8H). ^{13}C NMR 75.4 MHz, $CDCl_3$ δ 74.28, 71.42, 69.58, 58.43, 26.24, 4.08 (apparent ^{13}C-^{119}Sn ^1J=322, ^2J=19, ^3J=66). ^{119}Sn NMR 111.86 MHz (200mg/ml) $CDCl_3$, Me_4Sn ref. δ -3.8 ppm (inverse gated decoupled).

6 Compound **4**: 1H NMR 200MHz, C6D6 d 3.35 (m, 6H), 3.25 (m, 12H), 3.14 (s, 9H), 1.95 (bquintet, 6H), 1.38 (bt, 6H). ^{13}C NMR 75.4 MHz $CDCl_3$ δ 73.2, 71.5, 69.9, 58.7, 25.9, 14.9 ppm (apparent ^{13}C-^{119}Sn ^1J=413, ^3J=64). ^{119}Sn NMR 111.86 MHz (200mg/ml); Me_4Sn ref. δ +60.0 ppm (inverse gated decoupled).

7 $LiAlH_4$ byproducts could not be separated from the polyether ligands on the product **5**. The "H-siloxane" method, Hayahi, K.; Iyoda, J.; Shiihara, I. *J. Organomet. Chem.* **1967**, *10*, 81-94, gave no reaction.

8 Compound **5:** IR (film) $\nu_{Sn\text{-}H}$ 1810 cm^{-1}. ^1H NMR 200MHz, C_6D_6 δ 4.13 (AA'BB', 12H), 3.36 (t,J =6.4, 6H), 3.15 (s, 9H), 1.85 (quintet, J_{avg}≈7 Hz), 0.94 (td, J=8, J_{HSnCH}=1.8 Hz). ^{13}C NMR 75.4 MHz, C_6D_6 δ 74.45, 72.39, 70.49, 58.70, 27.95, 5.31 (apparent ^{13}C-^{119}Sn ^1J=354, ^2J=22, ^3J=52 Hz). ^{119}Sn NMR 111.86 MHz (200mg/ml), C_6D_6, Me_4Sn stnd. δ -82.4 ppm (d of septets, $^1J_{Sn\text{-}H}$=1612, $^2J_{Sn\text{-}H}$≈55 Hz).

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