A Practical Method for the Disposal of Organotin Residues from Reaction Mixtures

Claudio J. Salomon, Gerardo O. Danelon, and Oreste A. Mascaretti*

Instituto de Química Orgánica de Síntesis (CONICET-UNR) Facultad de Ciencias Bioquímicas y Farmacéuticas. Casilla de Correo 991, 2000 Rosario, Argentina

masca@citynet.net.ar

Received April 7, 2000

Introduction

Organotin compounds are used as versatile reagents for organic synthesis,[1] and an increasing number of academic and industrial groups are using organotin reagents. One of the practical difficulties encountered is the removal and disposal of excess toxic reagent and organotin side products from the reaction mixture. Most of these organotin compounds are highly soluble in nonpolar solvents and very insoluble in water. Several approaches have been adopted for the removal of organotin compounds from reaction mixtures. Corey[2] has recently proposed a useful practical method for the removal of excess of tri-*n*-butyltin hydride from reaction mixtures by conversion to tri-*n*-butyltin halides followed by precipitation as the insoluble tri-*n*-butyltin fluoride by the utilization of a fused mixture of CsF:CsOH. This method is a variant of the standard treatment with KF in MeOH developed by Leibner and Jacob.[3] The method developed by Berge and Roberts[4] is based on the very high solubility of organotin halides and unreacted organotin hydride in hexane and the preferential partitioning of other organic compounds into acetonitrile in the acetonitrile−hexane two-phase system. Crich[5] proposed a method for the removal of organotin residues by reduction with $NaBH_3CN$. Renaud[6] has recently reported a procedure for the removal of organotin residues from reaction mixtures by treatment of tri-*n*-butyltin halide-containing reaction mixtures with Me_3Al.

Farina[7] developed a chromatographic technique that allows the purification of organotin derivatives by reversed-phase flash chromatography on C-18 silica gel. We have found that filtration through a short plug (2 cm) of C-18 reverse-phase silica gel and elution with mixtures of acetonitrile−water is one of the most useful ways to remove organotin derivatives.[8] To limit the residual tin contamination, organotin hydrides have been anchored to an insoluble polymer so that the byproducts can be separated by simple filtration.[9] Enholm has recently reported a new allyltri-*n*-butyltin reagent on non-cross-linked polystyrene.[10] This support differs from the standard cross-linked polymer because it is completely soluble in organic solvents, and tin byproducts can be easily recovered from cold methanol as white crystalline solids. Breslow[11] developed a new water-soluble tri-(methoxyethoxypropyl)tin hydride to perform tin radical chemistry in water. The trialkyltin 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 the tri(methoxyethoxypropyl)tin hydride. In a different approach Curran introduced tris[2-(perfluorohexyl)ethyl]tin hydride as a versatile reducing agent which behaves like tri-*n*-butyltin hydride in radical reduction but offers the practical advantage of allowing easy separation of the tin byproducts from the reduced compound by liquid extraction.[12]

There is a need to search for new methodologies for the disposal of organotin wastes, because of the environmental problems caused by the well-known toxicity of triorganotin residues.[13] These compounds are recognized to be a very serious marine pollutant that induces a major harmful response in a number of marine organisms.[14]

Results and Discussion

In connection with our studies on the cleavage of carboxylic esters by organotin oxides and hydroxides,[15] we were interested in developing an improved method for the disposal of toxic organotin wastes. Our approach has been to convert the triorganotin compounds into inorganic tin compounds of low toxicity. The degradation of bis-tri-*n*-butyltin oxide (BBTO) **1**, trimethyltin hydroxide (TMTOH) **2** (which is very water soluble), allyl-tri-*n*-butyltin **3**, tin tetrachloride **4**, and tri-*n*-butyltin hydride **5** are carried out in aqueous solution with a mixture of HCl and HNO_3 for 1 h at 85 °C. The ^{119}Sn NMR spectrum then shows one predominant singlet signal at -654 ± 4 ppm.[16] We believe that the species present is

(1) (a) Pereyre, M.; Quintard, J. P.; Rahm, A. *Tin in Organic Synthesis*; Butterworth: London, 1987. (b) Harrison, P. G. *Chemistry of Tin*; Blackie: Glasgow, Scotland, 1989. (c) Davies, A. G. *Organotin Chemistry*; Verlag Chemie: Weinheim (Germany), 1997. (d) Smith, P. J. *Chemistry of Tin*, 2nd ed.; International Thomson Publishing: London, 1998.

(2) Edelson, B. S.; Stoltz, B. M.; Corey, E. J. *Tetrahedron Lett.* **1999**, *40*, 6729.

(3) Leibner, J. E.; Jacobus, J. *J. Org. Chem.* **1979**, *44*, 449.

(4) Berge, J. M.; Roberts, S. M. *Synthesis* **1979**, 471.

(5) Crich, D.; Sun, S. *J. Org. Chem.* **1996**, *61*, 7200.

(6) Renaud, P.; Lacote, E.; Quaranta, L. *Tetrahedron Lett.* **1998**, *39*, 2123.

(7) Farina, V. *J. Org. Chem.* **1991**, *56*, 4985.

(8) Salomon, C. J.; Mata, E. G.; Mascaretti, O. A. *J. Org. Chem.* **1994**, *59*, 7259.

(9) (a) Gerigk, U.; Gerlach, M.; Neumann, W. P.; Vieler, R.; Weintritt, V. *Synthesis* **1990**, 448. (b) Gerlach, M.; Jördens, F.; Kuhn, H.; Neumann, W. P.; Peterseim, M. *J. Org. Chem.* **1991**, *56*, 5971. (c) Kuhn, H.; Neumann, W. P. *Synlett* **1994**, 123. (d) Nicolaou, K. C.; Winssinger, N.; Pastor, J.; Murphy, F. *Angew. Chem. Int. Ed.* **1998**, *37*, 2534. (e) Dumartin, G.; Pourcel, M.; Delmond, B.; Donard, O.; Pereyre, M. *Tetrahedron Lett.* **1998**, *39*, 4663.

(10) Enholm, E. J.; Gallagher, M. E.; Moran, K. M.; Lombardi, J. S.; Schulte, J. P., II. *Org. Lett.* **1999**, *1*, 689.

(11) Light, J.; Breslow, R. *Tetrahedron Lett.* **1990**, *31*, 2957.

(12) Curran, D. P.; Hadida, S. *J. Am. Chem. Soc.* **1996**, *118*, 2531 and references cited therein.

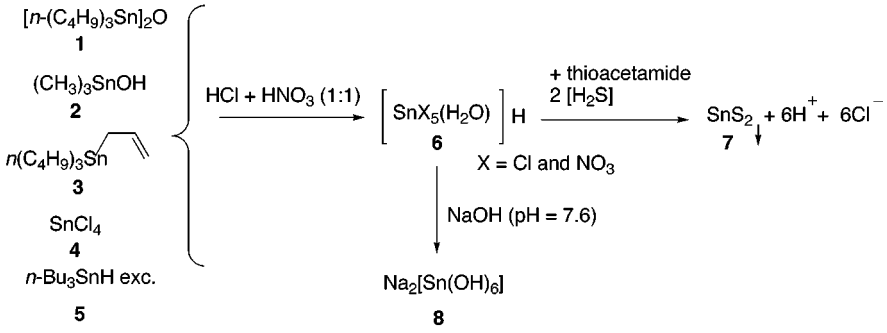
(13) (a) Saxena, A. K. *Appl. Organomet. Chem.* **1987**, *1*, 39. (b) Nicklin, S.; Robson, M. W. *Ibid* **1988**, *2*, 487. (c) Luijten, J. G. A.; Klimmer, O. R. *A Toxicological Assessment of Organotin Compounds*; International Tin Research Institute (ITRI): Middlesex Publication No. 501D, 1978; p 11. (d) Miller, D. P.; Craig, P. J. The analysis of organotin compounds from the natural environment in ref 1d, p 541.

(14) Preston, M. R.; Chester, R. Chemistry and Pollution of the Marine Environment. In *Pollution: Causes, Effects and Control*, 3rd ed.; Harrison, R. M., Ed.; The Royal Society of Chemistry: London, 1996; p 26.

(15) For a review, see: Mascaretti, O. A.; Furlán, R. L. E. *Aldrichimica Acta* **1997**, *30*, 55. See, also: (a) Furlán, R. L. E.; Mata, E. G.; Mascaretti, O. A. *Tetrahedron* **1998**, *54*, 13023. (b) Furlán, R. L. E.; Mata, E. G.; Mascaretti, O. A. *J. Chem. Soc., Perkin Trans. 1* **1998**, 355.

10.1021/jo000525+ CCC: $19.00
Published on Web 11/29/2000

Scheme 1. Transformation of Organotin Compounds into Inorganic Tin Complexes and Then into Insoluble Tin Sulfide

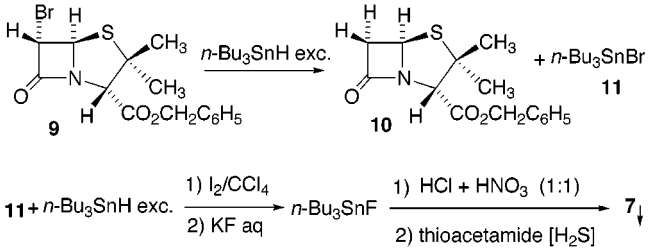


the complex of tin(IV) $[SnX_5(H_2O)]H$ **6**[17] (Scheme 1). However, the formation of some mixed chloro−nitrate complexes of tin(IV) is also possible. Certain very closed signals might correspond to isomeric cis and trans tin(IV)−mixed-ligand species.[18] We have failed to obtain evidence of the structure of complexes of tin(IV) from FAB or electrospray mass spectrometry,[1c] because the mass spectra did not show any molecular ion, and no useful ions were detected. To gain further evidence of formation of water complexes of tin(IV) and chloro−nitrate complexes of tin(IV), the solution of BBTO, after treatment with strong acid ($HCl + NO_3H$, 1:1), was made alkaline with an excess of sodium hydroxide solution (pH = 7.6), and then the ^{119}Sn NMR,which shows at least two singlet signals at pH about 1.0, showed a collapse into only one singlet signal at −587 ± 4 ppm, agreeing with the reported[19] $\delta = -590$ ppm value for the species $Na_2[Sn(OH)_6]$ **8**.

The acidic solutions were neutralized with ammonium hydroxide to pH 6.8 and stirred at room temperature with thioacetamide [H_2S] which acts as a hydrogen sulfide equivalent,[20] and insoluble SnS_2 **7** (which is yellow) was precipitated. The concentration of the tin(IV) compound that remains in solution was ca. 2 mg/L (2 ppm) as determined by atomic absorption spectroscopy. This concentration is equivalent to the solubility of tin(IV) sulfide, 0.0002 g/100 mL, in water solution at 18 °C.[21]

The organotin byproducts and excess reactants can be first separated from the required reaction products as the insoluble organotin fluorides as illustrated in the following example (Scheme 2). Free radical reductive chemo- and diastereoselective dehalogenation of benzyl 6α-bromopenicillinate **9** by tri-*n*-butyltin hydride yielded the corresponding benzyl penicillinate **10**[22] and tri-*n*-butyltin bromide **11**. The crude mixture containing *n*-Bu_3SnBr and an excess of *n*-Bu_3SnH was titrated with iodine in carbon tetrachloride at room temperature for 30 min to oxidize the tri-*n*-butyltin hydride into tri-*n*-butyltin iodide and then treated with aqueous potassium fluoride for 45 min to convert it into the tri-*n*-butyltin fluoride as described by Corey.[2] The tri-*n*-butyltin fluoride was then treated with $HCl + HNO_3$ (1:1), followed by thioacetamide as described above.

Scheme 2



Conclusions

In conclusion, we have presented here a new way for the elimination of toxic organotin waste under oxidizing conditions. We feel that this can be of utility to other chemists who make use of organotin reagents in their synthetic work, with obvious economic and environmental implications for large-scale work. Efforts are currently underway to apply this procedure to other organotin reagents.

Experimental Section

General Procedure for the Transformation of Organotin Compounds into Inorganic Tin Complex and Then into Insoluble Tin Sulfide. A 2 mL volume of a mixture (1:1) of hydrochloric acid (37%) and nitric acid (70%) was added to 0.196 mmol (117 mg) of bis-tri-*n*-butyltin oxide (BBTO) **1** and heated to 85 °C for 1 h. The solution was cooled to room temperature, the pH adjusted to ca. 6.8 with ammonium hydroxide, and then ca. 1.5 mL of saturated aqueous thioacetamide was added. After that, the solution was heated (85 °C) to induce the precipitation of tin sulfide (SnS_2). The yellow solid was filtered off and the solution treated again with thioacetamide and heated to ensure the complete elimination of the Sn^{4+} from the reaction mixture.

Specific Example of This Practical Method for the Disposal of Organotin Compounds. Reduction of Benzyl 6α-Bromopenicillanate by Tri-*n*-butyltin Hydride. Tri-*n*-butyltin hydride **5** (1.98 g, 6.8 mmol) was added to a solution of benzyl 6α-bromopenicillinate **9** (1.259 g, 3.4 mmol) and azobisisobutyronitrile (AIBN) (catalytic amount) in dry toluene (50 mL), under an atmosphere of nitrogen. The mixture was heated to 90−95 °C for 30 min. The organotin bromide and unreacted organotin hydride were then removed by the following procedure.

The reaction mixture was cooled to room temperature and stirred for 30 min with 0.5 mL of carbon tetrachloride. Then

(16) The ^{119}Sn FT NMR spectra were determined with complete proton noise decoupling. Field-frequency control was made with a deuterium-labeled solvent ($CDCl_3$, D_2O, or $(CD_3)_2CO$) lock. The chemical shifts were determined relative to internal Me_4Sn; negative signs indicates highfield shifts from the reference. The formation of more than one water−chloro(and nitrate)−tin(IV) complex were found to be dependent upon the concentration of the acidic solutions of hydrochloric and nitric acids and also dependent on the amount of D_2O in the case of using this solvent as internal lock.

(17) Mao, Xu-An; You, Xiao-Zeng; Dau, A.-B. *Inorg. Chim. Acta* **1989**, *156*, 177.

(18) Dillon, K. B.; Marshall, A. *J. Chem. Soc., Dalton Trans.* **1984**, 1245.

(19) Burke, J. J.; Lauterbur, P. C. *J. Am. Chem. Soc.* **1961**, *83*, 326.

(20) King, E. J. *Qualitative Analysis and Electrolytic Solutions*; Harcourt, Brace & World Inc.: New York, 1959; pp 141 and 180.

(21) CRC *Handbook of Chemistry and Physics*, 58th ed.; CRC Press: Cleveland, OH.

(22) Mata, E. G.; Mascaretti, O. A. *Tetrahedron Lett.* **1989**, *30*, 3905.

the solution was titrated with iodine solution (0.1 M in ether) until the iodine color persisted. Thus, the solvent (toluene) was evaporated in vacuo and the oily residue taken up in ethyl acetate (40 mL) and treated with potassium fluoride (saturated water solution) (2 × 20 mL) to give a white solid (Bu_3SnF) that was filtered off. The organic layer was separated and dried over Na_2SO_4, and the solution was evaporated in vacuo to dryness. The residue was purified by column chromatography on silica gel (hexanes−ethyl acetate, 80:20) to give 635 mg (64%) of pure benzyl penicillinate **10** as a colorless oil.

The white solid Bu_3SnF was converted into the inorganic tin complex by the experimental procedure described above.

Acknowledgment. This work was supported by a research grant from Consejo Nacional de Investigaciones (CONICET). We thank Dr. Eduardo Rubio, Instituto de Química Organometálica, Universidad de Oviedo, Oviedo (Spain), for recording the ^{119}Sn NMR spectra, Professor Heinz G. Floss, Department of Chemistry, Washington University, for obtaining FAB and electrospray mass spectra, and Professor Alwyn G. Davies, Department of Chemistry, University College London, London (U.K.), for valuable discussion.

Supporting Information Available: Copies of the ^{119}Sn NMR spectra for the complex of water−chloro(and nitrate)−tin(IV) complexes and sodium hexahydroxytin(IV) complex **8** are available free of charge via the Internet at http://pubs.acs.org.

JO000525+