Pergamon

Tetrahedron Letters 43 (2002) 4309–4311

TETRAHEDRON
LETTERS

PAH-supported tin hydride: a new tin reagent easily removable from reaction mixtures

Stéphane Gastaldi[a,]* and Didier Stien[b,]*

[a]LCMO-UMR 6517, Université d'Aix-Marseille III, Avenue Escadrille Normandie-Niemen, 13397 Marseille cedex 20, France
[b]LAPP-UMR 5810, Université de Montpellier 2, CC19, 34095 Montpellier cedex 5, France

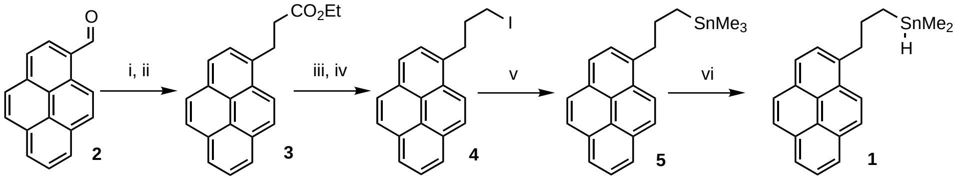
Received 20 March 2002; revised 23 April 2002; accepted 24 April 2002

Abstract—We demonstrate here that a new pyrene-supported tin hydride can be used in radical chemistry. Final products were easily purified by adsorption of the PAH-supported tin side product with activated carbon. © 2002 Elsevier Science Ltd. All rights reserved.

Tributyltin hydride is an important reagent in preparative free radical chemistry, but product isolation is quite often complicated by the presence of non-polar tin-containing materials formed as side products in these reactions. The usefulness of tin reagents in chemistry is broadly acknowledged and tin hydrides privileged role in radical chemistry persists despite the problems of separation and tin disposal. Indeed, radical chemists community has been addressing the problem of purification of radical reaction mixtures for nearly ten years now.

The fashionable technique to overcome difficulties associated with the removal of reagent-derived side products in general is to use a polymer supported reagent.[1] Although such tin reagent have been synthesized and used with some success,[1] some of them have also been reported to release tin slowly.[2] For that reason, the reaction mixtures were often still contaminated with tin residues. We therefore prospected for alternative modified tin reagents that might allow easy removal of tin residues from reaction mixtures. A few of these reagents designed with modified alkyl chains have been reported before. These include fluorous tin hydrides,[3] water-soluble,[4] base-soluble[5] and acid-soluble tin hydrides,[6] and more recently a tin hydride unstable under basic and acidic conditions.[7] This publication from Clive appeared when our article was in the process of being written. The authors reported very accurately the literature related to tin removal from reaction mixtures, covering both direct methods of removal of tributyltin derivatives and synthesis and use of modified tin hydrides. We therefore wish to refer the reader to this article rather than to duplicate their excellent literature review.

We report in this communication the preparation and use of stannane **1**, a compound whose 3-pyrenylpropyl side chain simplifies tin removal and product isolation. We designed **1** assuming that tin side-products would be easily removable by adsorption on activated carbon. In fact, the use of polyaromatic hydrocarbons (PAHs) as soluble supports in organic synthesis was first described by Ramage for peptide purification.[8] The



Scheme 1. *Reagents and conditions*: (i) $(EtO)_2(O)PCH_2CO_2Et/NaH$ (88%); (ii) $NaBH_4/CoCl_2$ (94%); (iii) $LiAlH_4$ (96%); (iv) PPh_3/I_2/imidazole (77%); (v) Me_6Sn_2/MeLi (86%); (vi) $I_2/CHCl_3$, then $NaBH_4$/MeOH (67%).

---

* Corresponding authors. Tel.: +4 91 28 85 96; fax: +4 91 67 09 44 (S.G.); tel.: +4 67 14 48 65; fax: +4 67 14 48 66 (D.S.); e-mail: stephane.gastaldi@univ.u-3mrs.fr; stien@univ-montp2.fr

PII: S0040-4039(02)00801-8

desired *N*-tetrabenzofluorenylmethyloxycarbonyl (Tbfmoc) peptides were separated from truncated *N*-acetyl ones by affinity purification on porous graphitized carbon. Later on, the affinity of the tetrabenzofluorenyl group (Tbf) for activated carbon has been utilized in the purification of oligonucleotides and proteins, and Tbf was successfully used as liquid-phase support for parallel organic synthesis.[9] More recently, a PAH, namely pyrene, has been used as an anchor for scavenging functionality.[10] We tested pyrene against Tbf toward adsorption on charcoal and we found that pyrene is retained more efficiently, presumably because Tbf is non planar. For this reason, and because it is commercially available and inexpensive, we opted for pyrene, following the example of Warmus and da Silva.[10]

Stannane **1** can be prepared straightforwardly from commercially available 1-pyrenecarboxaldehyde **2** following the route summarized in Scheme 1.

Wittig–Horner olefination followed by reduction of the double bond with $NaBH_4/CoCl_2$[11] gave ester **3**. Iodide **4** was obtained in two steps from **3** by reduction with $LiAlH_4$ and transformation of the resulting primary alcohol with I_2/PPh_3. Substitution of the primary iodide in **4** with trimethylstannyllithium[12] afforded tetraalkylstannane **5** in very good yield. Treatment with exactly 1 equiv. of I_2 substituted one methyl group in **5** selectively. The desired tin hydride was finally obtained as a white solid after reduction with $NaBH_4$ and chromatography over neutral alumina. Compound **1** is stable since it was found unchanged after several months at −15°C (freezer).

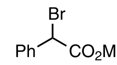
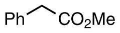
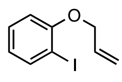
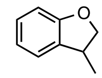
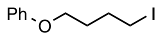
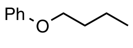
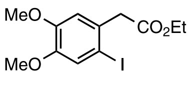
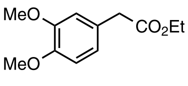
Adsorption potential of various commercially available activated carbons were evaluated. Experiments were conducted on tetraalkylstannane **5** along with Ph-CHBr-CO_2Me. This second compound was chosen to evaluate whether or not we will be able to separate PAHs from typical substrates or reaction products, including monoaromatic ones. According to Ramage's recommendation, we used $MeOH/CH_2Cl_2$ (3/2) for purification. In fact, we experimented various solvents and we agree that this system is well suited to selective adsorption of substituted PAHs on charcoal. All activated carbon adsorbed nearly quantitatively the pyrene derivative **5**, the difference laying in the unwanted loss of a part of the other product hold by the charcoal. In our hands, Darco® KB-B[13] gave the best results. After 30 min, the desired product may be collected by filtration of the activated carbon and evaporation. ^1H NMR with internal standard indicates quantitative recovery of Ph-CHBr-CO_2Me with purity above 98%.

Compound **1** may be used for tin hydride mediated radical reactions in the same way as tributyl tin hydride. We have evaluated its performance by using it for reduction of different alkyl halides, as exemplified in Table 1.[14] Reduction yields are comparable to tributyltin hydride mediated reactions, and purities were satisfactory for most purposes. We were pleased to discover that the use of a catalytic amount of **1** is also possible following the procedure described by Stork (entry 1).[15] In addition, an attempt of classical cyclization of an aryl radical led to the expected benzodihydrofuran in 84% yield (entry 2).

Radical reactions were performed in dry deoxygenated benzene with 1.2 equiv. of **1**. After one hour, the solvent was evaporated and the residue was dissolved in $MeOH/CH_2Cl_2$ (3/2) for purification.[14] Work-up with activated carbon afforded essentially pure products. Integration of the ^1H NMR spectra allowed us to evaluate the amount of residual supported tin derivative which was found to be below 1 mol% is all cases, and even not detectable in some samples (Table 1, entries 1, 2 and 5). Therefore, the method gives satisfying results for organic chemistry purposes. However, further purification may be compulsory if the radical reaction product is meant for biological assays.

We envisioned the possibility that the adsorbed tin–PAH derivative might be recoverable. In fact, we wish to point out that recovery after radical reaction is low-yielding and somewhat awkward. Solid–liquid extraction of the activated carbon ($CHCl_3$, 48 h) followed by reduction of the crude residue ($NaBH_4$) and purification (Al_2O_3) led only to 20% the amount of the initial tin hydride. This low recovery rate is most certainly the consequence of very strong π-stacking associations between the pyrene moiety and the polyaromatic foils of activated carbon. While we have here an inconvenience, it is worth noting that the same supramolecular interactions allow quantitative removal of tin from crude reaction mixtures, the key challenge to our venture.

Table 1. Reduction of various aryl- and alkyl-halides using **1**

Entry	Substrate	Product[a]	Isolated Yield (%)
1			89% (84%)[b]
2		 [c]	84%
3	1-bromododecane	dodecane	86%
4			94%
5			96%

[a] Standard procedure.[14]

[b] Catalytic method: $NaBH_3CN/\mathbf{1}/t$BuOH.[15]

[c] A trace of allylphenyl ether was detected in the ^1H NMR spectrum of the crude reaction mixture (<2%).

In conclusion, this work with a tin hydride provides a prototype for rendering a reagent PAH-supported. Our dimethyl-3-pyrenypropyl tin hydride represents a useful alternative to tin hydrides extensively used in radical chemistry. However, its six-step synthesis is to be improved (35% overall yield), especially because the tin hydride was only prepared on small scale (500 mg) and was therefore purified by chromatography with neutral alumina. Larger scale preparations should allow purification by crystallization thanks to the pyrene moiety. Indeed, this reagent is crystalline and odorless, and tin hydride weighing and addition into reaction vessels is very convenient. Other PAH-supported tin reagents are under investigation and progress will be reported in due course.

References

1. Ley, S. V.; Baxendale, I. R.; Bream, R. N.; Jackson, P. S.; Leach, A. G.; Longbottom, D. A.; Nesi, M.; Scott, J. S.; Storer, R. I.; Taylor, S. J. *J. Chem. Soc.*, *Perkin Trans. 1* **2000**, 3815–4195. See pp. 3896–3897 for a list of known polymer-supported tin hydrides.
2. Dumartin, G.; Pourcel, M.; Delmond, B.; Donard, O.; Pereyre, M. *Tetrahedron Lett.* **1998**, *39*, 4663–4666.
3. Curran, D. P.; Hadida, S.; Kim, S.-Y.; Luo, Z. *J. Am. Chem. Soc.* **1999**, *121*, 6607–6615 and references cited therein. See also: http://fluorous.com/tin.html.
4. (a) Light, J.; Breslow, R. *Tetrahedron Lett.* **1990**, *31*, 2957–2958; (b) Han, X.; Hartmann, G. A.; Brazzale, A.; Gaston, R. D. *Tetrahedron Lett.* **2001**, *42*, 5837–5839.
5. Collum, D. B.; Rai, R. *Tetrahedron Lett.* **1994**, *35*, 6221–6224.
6. (a) Vedejs, E.; Duncan, S. M.; Haight, A. R. *J. Org. Chem.* **1993**, *58*, 3046–3050; (b) Clive, D. L. J.; Yang, W. *J. Org. Chem.* **1995**, *60*, 2607–2609.
7. Clive, D. L. J.; Wang, J. *J. Org. Chem.* **2002**, *67*, 1192–1198.
8. Ramage, R.; Raphy, G. *Tetrahedron Lett.* **1992**, *33*, 385–388.
9. Hay, A. M.; Hobbs-Dewitt, S.; MacDonald, A. A.; Ramage, R. *Synthesis* **1999**, 1979–1985 and references cited therein.
10. Warmus, J. S.; da Silva, M. I. *Org. Lett.* **2000**, *2*, 1807–1809.
11. Leutenegger, U.; Madin, A.; Pfaltz, A. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 60–61.
12. Still, J. C. *J. Am. Chem. Soc.* **1977**, *99*, 4836–4838.
13. Commercially available from Aldrich (ref 26,810-6).
14. General procedure: Under an inert atmosphere, a solution of substrate (0.2 mmol), **1** (1.2 equiv.) and AIBN (0.1 equiv.) in dry degassed benzene (1–2 mL) was stirred under reflux for 1 h (TLC monitoring). The mixture was cooled and evaporated. Methanol/dichloromethane 3/2 (4 mL) was added to the residue immediately followed by activated carbon (800 mg). The suspension was stirred for 30 min (the adsorption of the pyrene core was monitored by UV). After filtration, the activated carbon was washed with MeOH and the combined filtrates were evaporated, allowing isolation of the radical reaction product in pure form.
15. Stork, G.; Sher, P. M. *J. Am. Chem. Soc.* **1986**, *108*, 303–304.