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Improved Synthesis of Tributyltin tritide (TBTT)

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In our recent publication on the tritium labelling of RAD001 [1] we described the synthesis of tributyltin tritide from lithium tritide. In order to avoid significant formation of tritium gas, fast addition of tri-n-butyltin chloride to a mixture of lithium tritide and triethylborane in THF appeared to be essential. Optimization of this procedure, however, revealed that this is not the case. Careful distillative purification under high vacuum of the tri-n-butyltin chloride resulted in reproducible yields independent of the speed of addition. Hence it is evident that a proton-bearing impurity of tri-n-butyltin chloride was the reason for the original result. Our actual procedure for the synthesis of tributyltin-tritide reads now as follows:

Synthesis of tributyltin tritide (TBBT)
Lithium tritide was prepared from n-BuLi (1.5 mmol) as described in our recent paper[1]. After cessation of the tritium-uptake the mixture was cooled to -195°C and unconsumed tritium was reabsorbed on the uranium-trap. The solvent and TMEDA were lyophilized off and the remaining Li^3H was dried at room temperature and high vacuum for 30 minutes. Protection gas (H_2, He or Ar) was admitted to a pressure of 500 hPa. Subsequently 1.5 ml of dry THF was injected via a syringe (in case of BEt_3-catalyzed radical reactions 200 µl of BEt_3 was added) followed by 360 µl of tri-n-butyltin chloride (freshly distilled under high vacuum) under intensive stirring. After a short dissolution the formed lithium chloride precipitated. The solvent was lyophilized off and replaced by 2 ml of n-hexane or n-heptane. The resulting slurry was filtered over 2 g of silica gel with 10 x 2 ml of n-hexane or n-heptane. The filtrate was evaporated on a rotary evaporator and the residue dried at room temperature under high vacuum to obtain 365 mg (83 %) of pure and base-free tri n-butyltin tritide.

Reference:

[1] Th. Moenius, H. Andres, M. Acemoglu, B. Kohler, P. Schnelli, C. Zueger, Journal of Radiolabelled Compounds and Pharmaceuticals **43**, 113 (2000).

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