Journal of Labelled Compounds — October-December — Vol. II, No. 4

Synthesis of tributyltin-113 benzoate

P.Ph.H.L. OTTO
Centraal Laboratorium T.N.O., Delft, Holland
H.M.J.C. CREEMERS and J.G.A. LUIJTEN
Organisch Chemisch Instituut T.N.O., Utrecht, Holland

Received on 1st January 1966

SUMMARY

Tributyltin-113 benzoate was prepared from tin metal labelled with tin-113, by a three step synthesis, with a chemical yield of 37%. The radio-chemical yield was 22%.

The amount of tributyltin-113 benzoate prepared was 1.3 g, the specific activity 0.7 mC/gram, and the radiochemical purity 98.9%.

Apart from Sn-113 no other gamma-emitting tin isotopes were present, neither did antimony radio-isotopes occur.

1. INTRODUCTION

The aim of this investigation was the synthesis of the antimicrobial agent tributyltin benzoate, labelled with radio-isotope Sn-113. Its intended use was in toxicological experiments. A total activity of 1 mC and a specific activity of 1 mC per gram were desired. Preparations of higher specific activities are, however, feasible by the procedure developed. The synthetic route is represented by the following reaction equations :

a) $Sn^* + 2\ Cl_2 \rightarrow Sn^*Cl_4$

b) $Sn^*Cl_4 + 3\ Bu_4Sn \rightarrow 4\ Bu_3Sn^*Cl$

c) $Bu_3Sn^*Cl + C_6H_5C(O)ONa \rightarrow Bu_3Sn^*\ OC(O).\ C_6H_5 + NaCl$

These reactions, which are mentioned in the literature (see for example the review on organotin compounds by Ingham *et al* (1)), were modified and adapted to a small scale.

For the synthesis of tin-113 tetrachloride (reaction a) a measured amount of chlorine was allowed to react with tin powder in a closed vessel. An excess of chlorine was employed and the chlorine gas was condensed upon the tin powder by cooling with liquid air. The excess could easily be removed afterwards by fractional distillation. The purity of the tin powder proved of decisive importance. A partially oxidized sample reacted with the formation of a non-volatile residue, which presumably consisted of a mixture of stannic oxide and oxychloride. Unfortunately, the labelled tin used showed the same adverse behaviour. The synthesis of labelled tin tetrachloride had already been described by Herok and Götte (2), and by Frye and Horst (3). In these preparations, a stream of chlorine is passed over labelled tin powder.

The labelled tin used was obtained from highly enriched tin-112 by neutron irradiation. It contained virtually no antimony radio-isotopes. Therefore the purification procedure with antimony carrier, described by Herok and Götte (2), could be omitted.

The redistribution reaction between tin tetrachloride and tetrabutyltin (reaction b), when carried out on a small scale, was accompanied by severe decomposition. This could be diminished considerably by coating the walls of the reaction tube with an organosilicon compound.

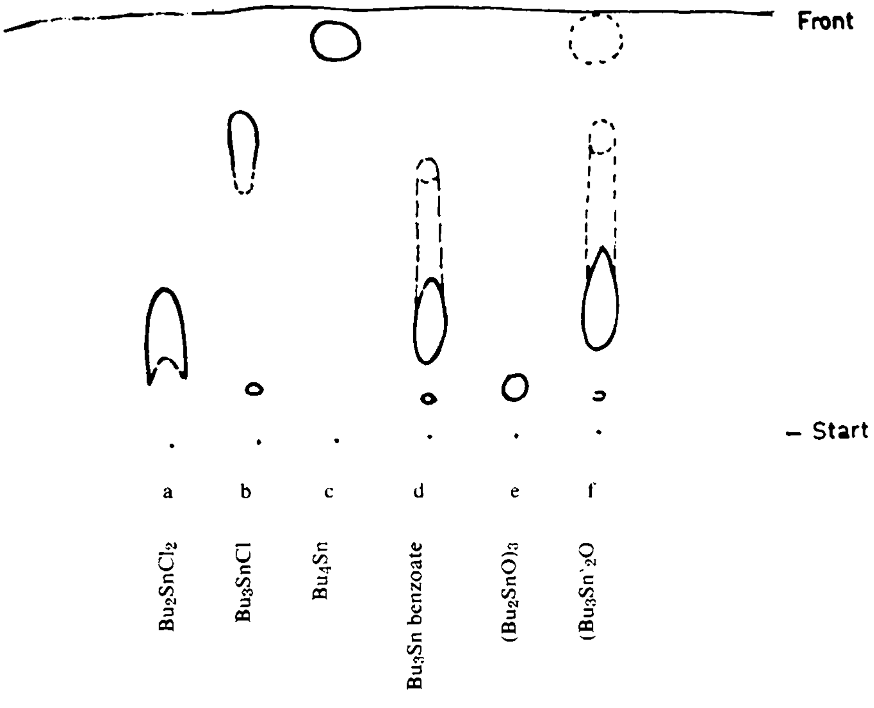

FIG. 1. — Thin-layer chromatograms of butyltin derivatives

Sorbent : silicagel G, 0.25 mm
Solvent : hexane/acetic acid 12 : 2
Detection : Br_2 ; pyrocatechol violet

In one of the preliminary experiments, the reaction mixture was analyzed chromatographically after various reaction times (fig. 2; compare with fig. 1). Of several methods described in the literature (4, 5, 6), the method by Van der Heide (6) gave the best results in our case. In this method, silicagel G and a mixture of hexane and glacial acetic acid (12 : 1) are used.

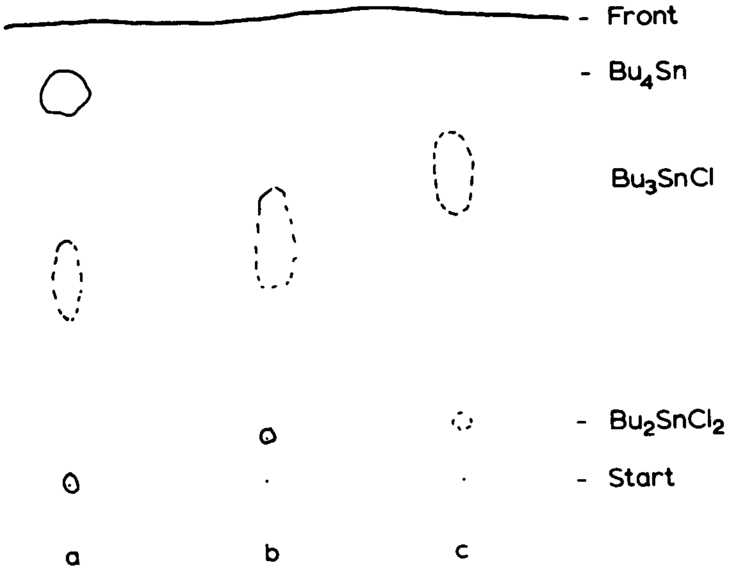

FIG. 2. — Thin-layer chromatograms of redistribution reaction mixtures ($SnCl_4 + 3\,Bu_4Sn$)

a) Before heating.
b) After heating at 230°C for 90 min.
c) After heating at 230°C for 3 hours :
sorbent : silicagel G. 0.25 mm ;
solvent : hexane/acetic acid 12 : 1 ;
detection : Br_2, pyrocatechol violet.

The conversion of tributyltin chloride into tributyltin benzoate (reaction c) was carried out in ethanol. Absolute ethanol is not suited, because the solubility of sodium benzoate in this solvent is too low. In 96% ethanol, solubility is sufficient to give a smooth reaction. The reaction mixture was eventually evaporated, and the residue was extracted with benzene to remove the sodium chloride formed.

Chemical and radio-chemical purity of the obtained tributyltin-113 benzoate were investigated by means of thin-layer chromatography and auto-radiography (figs 3 and 4).

The γ-ray spectrum of the tributyltin-113 benzoate was determined in order to enable accurate determination of specific activity, and to investigate radioisotopic purity.

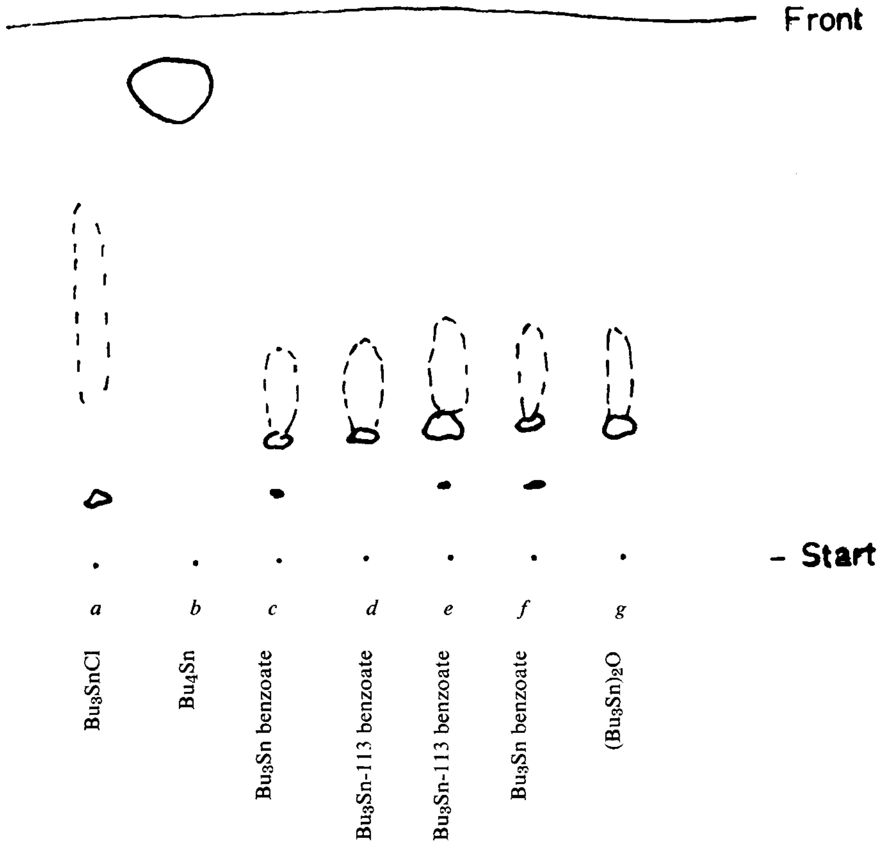

FIG. 3. — Thin-layer chromatograms of tributyltin-113 benzoate and reference compounds

Sorbent : silicagel G, 0.25 mm.
Solvent : hexane/acetic acid 12 : 1.
Detection : Br_2 ; pyrocatechol violet

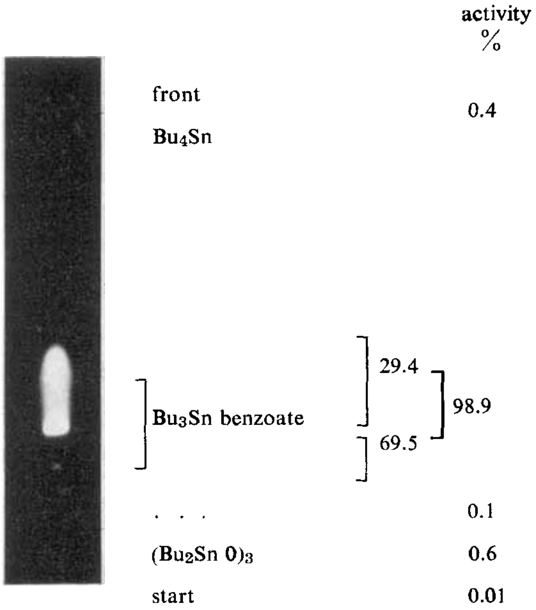

FIG. 4. — Auto-radiogram on Kodak no screen medical X-ray film (exposure time 18 hours) of a thin-layer chromatogram of tributyltin benzoate-Sn-113 (50 μg) on silicagel (0.25 mm; silicagel G, Merck) in hexane-acetic acid (12 : 1).

In order to determine the distribution of the activity over the several components, the spots were scratched off and measured in a Well-scintillation counter.

EXPERIMENTAL PART *

2.1. PREPARATION OF TIN-113 TETRACHLORIDE

In reaction flask A (fig. 6), pure tin powder ** (51 mg, 0.43 milligram atom) was degassed and dried under vacuum by heating for 45 minutes. Then the radio-active tin powder (10.5 mg, 0.09 milligram atom; 4 mC, obtained by neutron irradiation of Sn-112 enriched tin) was added, and the system re-evacuated. Flask A was cooled with liquid nitrogen, and the chlorine (100 ml, 8 milligram atom, i.e. a four-fold excess) from storage flask D, allowed to condense in A. While warming up to room temperature, a violent reaction suddenly occurred in A.

---

* The experiments were carried out with the assistance of Miss E. Blok and Mr. D. Oudijn.

** Sample supplied by N.V. Hollandse Metallurgische Industrie Billiton, Arnhem.

Not all of the labelled tin had reacted, however. Therefore the formed volatile products were condensed in B, an excess of chlorine redistilled into A (B at −80 °C and A at −190 °C), stopcock F closed and flask A heated, first to 130 °C for 5 minutes, and finally to 230 °C for 15 minutes. These efforts met with little success. A rough estimate by means of a G.M.-tube showed that about 30% of the radio-activity was still present in the form of non-volatile pale yellow products, probably tin oxychlorides.

Stopcock F was opened and all the products condensed in A. Subsequently the excess chlorine was distilled from A into B (A at −80 °C, B at −190 °C).

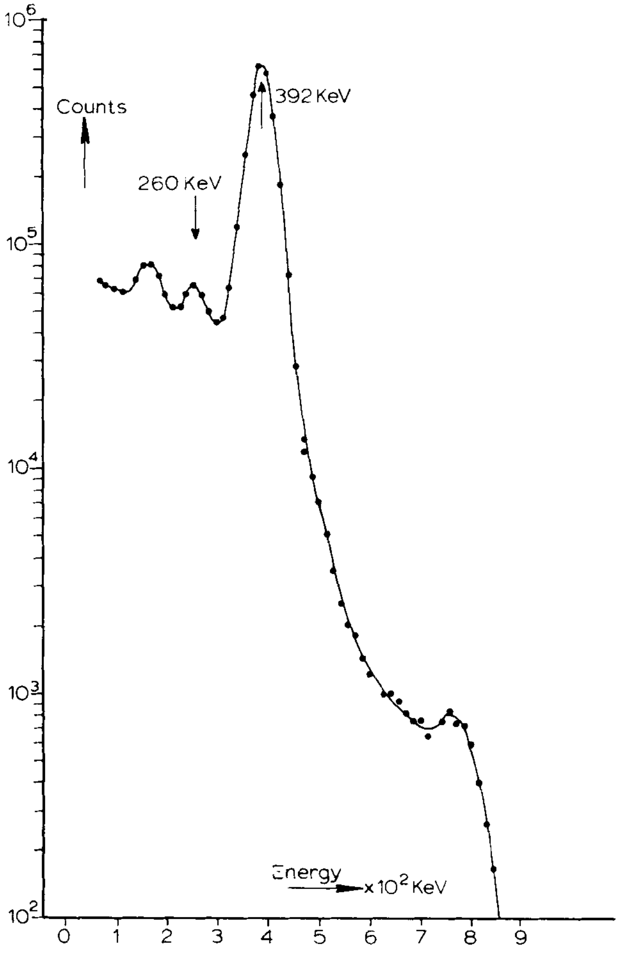

Fig. 5. — Gamma ray spectrum of tributyltin-113 benzoate.

After three minutes, the chlorine had distilled off. The remaining tin-113 tetrachloride was slightly pale yellow.

2.2. PREPARATION OF TRIBUTYLTIN-113 CHLORIDE

Stopcock F (fig. 6) was closed again. Tube C was provided with carrier tin tetrachloride (0.44 g, 1.68 mM). Tube B was replaced by a tube containing tetrabutyltin (1.94 g, 5.6 mM, short measure). This tube was coated with Desicote 18772, Beckman Instrument Inc., California. The system was evacuated, stopcock F opened, and the tin-113 chloride in A diluted by distilling the tin tetrachloride from C into A. Finally, all tin tetrachloride was collected in B, the system filled with nitrogen, and flask B heated to 220-240 °C for 1½ hours. After intermediate cooling to room temperature (7), B was heated to 220-240 °C for another 1½ hours.

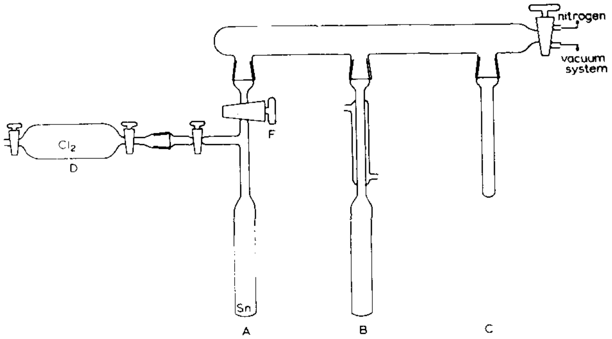

FIG. 6. — Apparatus used for preparation of tributyltin-113 chloride.

2.3. PREPARATION OF TRIBUTYLTIN-113 BENZOATE

By means of a pipet, the tributyltin-113 chloride was brought into a 50 ml reaction flask with sealed-on reflux condensor. The flask contained sodium benzoate (0.964 g = 6.7 mM). Flask B was washed with 96% ethanol (25 ml in total), and the ethanol added to the mixture of tributyltin-113 chloride and sodium benzoate. This mixture was refluxed for 30 minutes. Then all volatile components were evaporated under vacuum. The remaining tributyltin-113 benzoate was dissolved in benzene, and separated from insoluble material. From a 15 ml pear-shaped Claisen flask, the benzene was distilled off at normal pressure. The tributyltin-113 benzoate was distilled under vacuum, and the fraction b.p. 137-138 °C/0.16 mm collected. The yield was 1.3 g = 3.16 mM, corresponding to 37% based on total amount of tin tetrachloride.

2.4. THIN-LAYER CHROMATOGRAPHIC ANALYSIS

Chloroform solutions, containing 50 μg organotin compounds each, were applied to a silicagel layer of 0.25 mm thickness (silicagel G. Merck; activation by heating at 110 °C for one hour). The chromatograms were developed with a mixture of hexane-acetic acid (12 : 1), dried at 80 °C for 30 minutes, exposed to bromine vapours for half an hour, and sprayed with an 0.1% solution of pyrocatechol violet in ethanol. R_F values are summarized in table I. Chromatograms are shown in figures 1, 2 and 3.

From a chromatogram of the labelled compound, an auto-radiogram was obtained on Kodak no screen X-ray film (fig. 4).

TABLE I. R_F values of butyltin derivatives. Thin-layer chromatograms on silicagel G, 0.25 mm.

Compound	Solvent :	
	Hexane-acetic acid 12 : 1	Hexane-acetic acid 12 : 2
	R_F	R_F
$BuSnCl_3$	0-0.15	
Bu_2SnCl_2	0.20-0.30	0.27-0.28
Bu_3SnCl	0.60-0.80	0.75-0.85
Bu_4Sn	0.80-0.98	
Bu_3Sn benzoate	0.25-0.30 .... (0.50)	0.40-0.50 .... (0.70)
$(Bu_3Sn)_2O$		0.40-0.50 .... (0.70)
$[Bu_2SnO]_3$	0.10-0.20	0.20-0.30

2.5. PURITY OF THE RADIO-ISOTOPE AND DETERMINATION OF SPECIFIC ACTIVITY

The γ-ray spectrum * of the tributyltin-113 benzoate was determined with a Well-type NaI(Tl)-crystal 3 × 3 inch connected with a photomultiplier tube and RCLiac 128 multi scaler analyzer. The obtained γ-ray spectrum is shown in figure 5. The absence of a peak at 600 KeV indicates absence of antimony isotopes Sb-124 and Sb-125.

The specific activity of the tributyltin-113 benzoate was determined on both the 0.392 MeV γ-band and the 0.024MeV röntgen-band (table II). The results of both measurements agree within the limits of experimental error. From this follows the absence of Sn-119 m isotope.

---

* The spectrum was analyzed by Ir. A.C. Meijer and Drs. A. Kemper.

TABLE II. Specific activity of Bu_3Sn-113 benzoate

Sample weight	Measured activity of 0.392 MeV γ-rays	Specific activity *	Measured activity of 0.024 MeV röntgen rays	Specific activity *
mg	counts per 49.2 sec.	mC/gram	counts per 49.2 sec.	mC/gram
0.49	184502	0.703	177442	0.717
0.54	193429	0.668	187320	0.687
0.57	202315	0.662	195433	0.679
		Mean : 0.678		Mean : 0.694

* Defined as spec. act. (mC/g) $= A/\alpha.\varepsilon.g.\ 3.7 \times 10^7$

A is the measured activity (counts per second)

α is a decay scheme correction ($\alpha = 0.64$ for the Sn-113 γ-rays of 0.392 MeV and $\alpha = 1.11$ for the Sn-113 röntgen rays of 0.024 MeV)

ε is the counter yield, determined at 0.46 ± 0.005 for γ-rays with an energy of 0.392 MeV and 0.25 ± 0.01 for röntgen rays of 0.024 MeV.

g is sample weight (gram).

3. DISCUSSION

The thin-layer chromatography of the butyltin derivatives has been a point of much concern. Some questions are left unanswered, however, and not all the difficulties were solved in satisfactory way.

In the course of the redistribution reaction, samples were taken, and progress of the reaction was followed chromatographically. The chromatograms are shown in figure 2. There is an interesting shift of the spots, but it is not clear what causes a shift to higher R_F-values for the spot corresponding to Bu_3SnCl.

In all the chromatograms, the spots corresponding to the tributyltin derivatives investigated show a « tail ». If the main spot is eluated and the solution re-chromatographed, a spot with a « tail » is reproduced. If the « tail » is eluated and the solution re-chomatographed, the main spot with a much longer « tail » is obtained.

The auto-radiogram of tributyltin-113 benzoate (fig. 4) has exactly the same appearance as a thin-layer chromatogram of inactive tributyltin benzoate (fig. 3). If it is accepted that both the main spot and the tail together are representative for tributyltin benzoate, then it may be concluded that the butyltin-113 benzoate has a *radio-chemical purity* of 98.9% (see fig. 4 for a determination of the distribution of the activity over the several components).

Efforts to obtain a purification by preparative thin-layer chromatography of an impure forerun of tributyltin-113 benzoate have not yet been successful. Elution of the band corresponding to the main spot and analysis of this solution resulted in chromatograms showing the solution to contain many by-products.

The *purity of the radio-isotope* is good. No indication was found that other γ-emitting tin isotopes or antimony radio-isotopes are present.

The *radio-chemical yield* was 22%. Loss of radio-isotope could be attributed to the presence of oxides in the labelled tin, giving rise to the formation of unreactive tin oxychlorides in the reaction with chlorine. The radio-isotope was obtained by neutron irradiation of Sn-112 enriched tin. The supplier (Philips-Duphar) stated that no special precautions had been taken in order to avoid oxidation during irradiation. Irradiation in an inert atmosphere is feasible. It will, therefore, be interesting to attempt improvement of radiochemical yield by using labelled tin obtained under conditions which exclude the formation of tin oxides.

REFERENCES

1. R.K. Ingham, S.D. Rosenberg and H. Gilman — *Chem. Reviews*, **60** (1960), 459-539. Organotin compounds.
2. J. Herok, and H. Götte, — *Int. Journ. Appl. Rad. and Isotopes*, **14** (1963), 461-479. Radiometrische Untersuchungen über das Verhalten von Triphenylzinnacetat in Pflanze und Tier.
3. A.H. Frye, and R.W. Horst,— *Int. Journ. Appl. Rad. and Isotopes*, **15** (1964), 169-174. The preparation of certain radioactively tagged organotin compounds.
4. M. Türler, and O. Högl, — *Mitt. Gebiete Lebensm. Hyg.*, **52** (1961) 123-130. Identifizierung von Organozinnstabilisatoren in Polyvinylchlorid durch Dünnschichtchromatographie.
5. K. Bürger, — *Z. Anal. Chem.*, **192** (1963), 280-286. Dünnschichtchromatographische Arbeitsweisen zum Nachweis, zur Kennzeichnung und zur Trennung von Spuren mono-, di-, tri- und nullvalenter Organozinnverbindungen.
6. R.F. van der Heide, — *Z. Lebensm. Untersuch. u. -Forsch.*, **124** (1964) 348-350. Identifizierung von schwefelhaltigen Organozinnstabilisatoren durch Dünnschichtchromatographie.
7. G.J.M. van der Kerk, and J.G.A. Luijten, — *J. Appl. Chem.*, **6** (1956) 49-55. Investigations on organotin compounds IV. The preparation of a number of trialkyl- and triaryltin compounds.