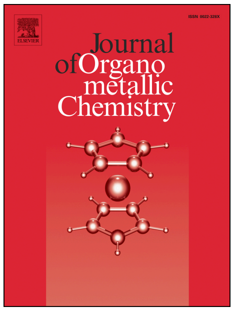

A reliable one-pot synthesis of aryl azides from aryl amines using organotin azides as effective and recoverable reagents

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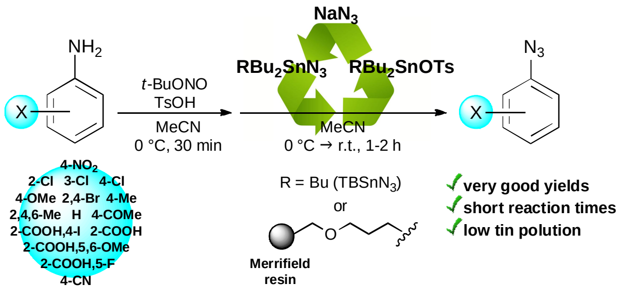
NaN$_3$
RBu$_2$SnN$_3$
RBu$_2$SnOTs
NH$_2$
N$_3$
X
t-BuONO
TsOH
MeCN
0 °C, 30 min
MeCN
0 °C → r.t., 1-2 h
4-NO$_2$
2-Cl 3-Cl 4-Cl
4-OMe 2,4-Br 4-Me
2,4,6-Me H 4-COMe
2-COOH,4-I 2-COOH
2-COOH,5,6-OMe
2-COOH,5-F
4-CN
R = Bu (TBSnN$_3$)
or
O
Merrifield resin
✓ very good yields
✓ short reaction times
✓ low tin polution

A reliable one-pot synthesis of aryl azides from aryl amines using organotin azides as effective and recoverable reagents

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Abstract

A mild and mass-efficient procedure based on the one-pot diazotization-azidodediazoniation of aromatic amines is described. A wide range of aryl azides are obtained in moderate to high yields by using tributyltin azide as an effective and reusable azide source in the presence of *p*-toluenesulfonic acid at room temperature. The method was also successfully applied employing an insoluble polymer-supported organotin azide.

Aryl azides; Tributyltin azide; Azidodeamination; Diazotization-azidodediazoniation; Polymer-supported organotin azide; Recoverable reagent

1. Introduction

Among organic azides, and due to their relatively high stability, aryl azides have found an extensive range of applications in diverse fields. In organic chemistry, as valuable intermediates for the synthesis of aza-derivatives, isocyanates, peptides and heterocycles with a currently increasing interest within the concept of "Click Chemistry" [1], in biochemistry, acting either as selective fluorescent probes [2] or photoreactive crosslinking-labeling groups, and also, in materials chemistry, for the synthesis of conducting polymers [3] or for light-induced activation of polymer surfaces [4]. Consequently, developments for new reliable and efficient methods for introducing this key functionality are always welcome.

Although a large and growing number of synthetic approaches towards the preparation of aryl azides can be found in the literature, the arenediazonium-based azidations are advantageous and attractive alternatives because they start from inexpensive and broadly available anilines and are hence usually orthogonal to halide-based reactions. Therefore, several protocols have been developed with the aim to improve both the efficiency and usefulness of the classical diazotization-azidodediazoniation route. Among these, neutral conditions [5], neutral and mild conditions with non-hazardous reagents [6], reusable ionic liquids as solvents [7], water media [8], stable diazonium salts intermediates [9], continuous flow processes [10] and polymer-supported diazotizing [11] or azidating [12] reagents, are a few of the implemented strategies.

Especially attractive is the method proposed by Moses and coworkers [6] for the one-pot azidation of diverse aromatic amines, using *tert*-butylnitrite (*t*-BuONO) in combination with trimethylsilyl azide ($TMSN_3$), which they also found to be suitable for building triazole linkages by CuAAC, through a microwave-assisted tandem methodology [13]. It is interesting to note that $TMSN_3$ plays a key role on the success of the azidation process. Indeed, due to its covalent features, it allows avoiding the use of large excesses of sodium azide which are needed in non-aqueous solvents [5]; moreover, because it reacts with the in situ generated diazonium salts, as soon as they formed, neither excesses of *t*-BuONO or additives are required. Nevertheless, despite above-mentioned advantages, the use of $TMSN_3$ has some downsides; it is a highly expensive reagent which is also both difficult and hazardous to prepare [14] and, due to its extremely high sensitivity to hydrolysis, decomposes slowly upon storage. In addition, only 36.5% of its molar mass can be used for the azidation reaction and the volatile trimethylsilyl byproducts are inevitably lost during solvent evaporation.

Like $TMSN_3$, tributyltin azide ($TBSnN_3$) is also a covalently linked azide that allows reactions in relatively homopolar solvents; it is less sensitive to hydrolysis, very stable to storage and readily accessible from the corresponding tributyltin chloride in very good yield [15]. In fact currently, organotin azides are among the reagents of choice for the last-stage generation of tetrazole linkages in pharmaceutical synthesis of losartan AT1-receptor antagonist and its analogues [16].

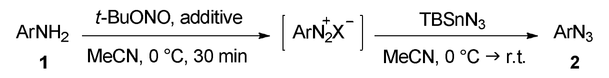
In connection with our continuing effort to explore the synthetic potential of organotin compounds [17], and given that many of these reagents have become invaluable tools in organic chemistry, we envisioned that the use of $TBSnN_3$, in place of $TMSN_3$, on Moses's methodology, would also achieve the in-situ azidodediazoniation pathway and then, after an appropriate workup, it could be recovered and recycled from the low volatile and highly stable tributyltin byproducts.

We report here the results obtained from a selection of anilines together with the specific protocols developed to allow the removal of most of the tin residues from the aryl azide products, and the recycling of $TBSnN_3$. Moreover, encouraged by the proven effectiveness of $TBSnN_3$ and, given the growing concern about the toxicity of organotin residues, which makes necessary to remove them down to ppm levels, we set out to study these reactions employing a polymer-supported organotin azide. Some selected preliminary results are also reported.

2. Results and discussion

We began by applying the standard conditions of Moses's methodology to the reaction of aniline (**1a**). When $TBSnN_3$, instead of $TMSN_3$, was added dropwise to a stirred solution of **1a** and *t*-BuONO in MeCN at 0 °C, only traces of azidobenzene (**2a**) were detected together with **1a** in almost quantitative yield (GC-MS), even after 19 h at room temperature. An identical result was obtained from a reaction conducted at 40 °C, over the same extended time period. In both cases, any possible side product (benzene, phenol, azobenzene or biphenyl) which are often observed in diazonium reactions [18], was not detected in the reaction mixtures (Table 1, entries 1 and 2).

Table 1. Optimization of the reaction conditions

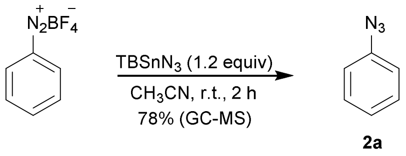


Entry	**1a** [M]	Additive	Molecular ratio (**1a**/*t*-BuONO/$TBSnN_3$/additive)	Yield (%)[a]
1[b]	0.625	none	1.0/1.5/1.2/0.0	Traces[c]
2[b,d]	0.625	none	1.0/1.5/1.2/0.0	Traces[c]
3	0.312	$BF_3{\cdot}OEt_2$	1.0/1.5/1.2/1.2	68
4	0.312	$BF_3{\cdot}OEt_2$	1.0/1.5/1.8/1.2	75
5	0.143	$TsOH.H_2O$	1.0/1.5/1.2/1.2	85
6	0.143	$TsOH.H_2O$	1.0/1.5/1.8/1.2	96
7	0.143	$TsOH.H_2O$	1.0/2.0/1.2/1.2	88
8	**0.143**	**$TsOH.H_2O$**	**1.0/1.2/1.2/1.2**	**88**
9[e]	0.143	$TsOH.H_2O$	1.0/1.2/1.32/1.2	24

[a] Determined by GC-MS (0.5 mmol scale) using *o*-dichlorobenzene (*o*-DCB) as internal standard. [b] By applying Moses´s methodology. [c] High percentages of **1a** were observed after 19 h of reaction. [d] Reaction temperature was raise to 40 °C (oil bath). [e] By using NaN_3 instead of $TBSnN_3$.

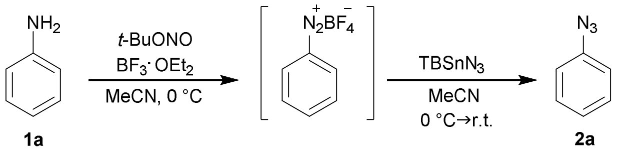
These disappointing results clearly revealed that diazotization step failed and makes it evident that, in contrast to $TBSnN_3$, its silyl analogue is able to exert some synergistic interaction that promotes the generation of transient arenediazonium ions and drives the reaction to completion. Probably, such interactions could be attributed to the stronger oxophilicity of the silicon atom which result, *via* a pentacoordinate complex, in an increased of its Lewis acidity and a more nucleophilic azide group [19].

In order to probe the effectiveness of $TBSnN_3$ in the azidodediazoniation step, we investigated its reaction with the pre-formed benzenediazonium tetrafluoroborate [20] and, fortunately, a good yield of **2a** (78%) was accomplished within 2 h.



Based on the above findings, we took into consideration the use of additives, such Brønsted or Lewis acids, which could promote the in situ generation of the required diazonium salt acting as the anion source.

Initially, we explored the use of boron trifluoride diethyl etherate ($BF_3{\cdot}OEt_2$) in the stepwise one-pot procedure from **1a**, sketched in Scheme 1.



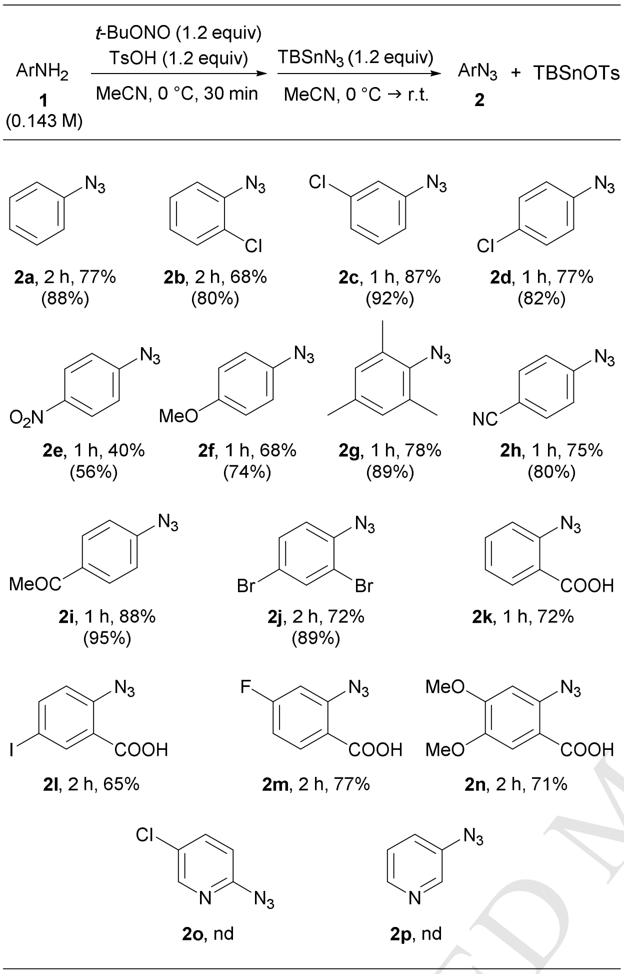
Scheme 1. Stepwise one-pot azidodeamination of **1a**

A promising yield of **2a** was obtained within 2 h at room temperature when the $TBSnN_3$ (1.2 equiv) was added to the reaction mixture at 0 °C, than after **1a** was treated with *t*-BuONO (1.5 equiv) in the presence of $BF_3{\cdot}OEt_2$ (1.2 equiv) during 30 min in MeCN. A slight improvement in yield was observed by increasing the **1a**/$TBSnN_3$ molar ratio (Table 1, entries 3 and 4). Even better results were achieved employing a Brønsted acid as additive; hence, tested at different reactant molar ratios, **2a** was formed in up to 85% yield in the presence of *p*-toluenesulfonic acid monohydrate (Table 1, entries 5-8).

We chose the conditions of the experiment performed at lower molar excess of reagents (Table 1, entry 8) as optimal to explore the scope of this azidodeamination protocol, with focus on establishing the appropriate procedures for the removal of tin byproducts as well as for their recovery and recycling back to $TBSnN_3$. It is worth mentioning that, taking into account the actual amount of NaN_3 consumed for the overall process, we carried out a control experiment by the reaction of **1a** with 1.32 equiv of NaN_3 (Table 1, entry 9). The poor yield observed of **2a** (24%) after 2 h at room temperature, can be attributed to the lower solubility of NaN_3 in comparison with $TBSnN_3$ in MeCN.

It should be noted that, in optimized reaction of **1a**, the tributyltin ester of *p*-toluenesulfonic acid (TBSnOTs) was the only organotin compound detected and identified from crude ^{119}Sn NMR by comparison with an authentic sample [21]. Therefore, we envisioned that TBSnOTs could be easily converted into TBSnN$_3$ by treating with NaN$_3$. In a first attempt, the crude mixture obtained from the reaction of **1a** was subjected to silica gel column chromatography. Although pure **2a** was isolated in good yield from hexane fractions, it was not possible to recover the TBSnOTs, even by using highly polar eluents and silica gel pre-treated with Et$_3$N 10% v/v. Assuming that this issue could be due to a strong affinity of the organotin ester with the silanol sites of silica, we decided to try the conversion of TBSnOTs by adding NaN$_3$ to the reaction mixture upon completion of the azidodediazoniation. Thus, a stoichiometric amount of NaN$_3$ (with respect to initial TBSnN$_3$) was added to the MeCN-Et$_2$O solutions coming from quantitative GC-MS analysis and left overnight under stirring at room temperature. After solid NaOTs was filtered off; the ^{119}Sn NMR spectrum of filtrate showed only one signal at 111.09 ppm which agreed well with that observed for commercial TBSnN$_3$. By silica gel column chromatography, the aryl azide **2a** was isolated in 77% yield (hexane fractions) and the TBSnN$_3$ was recovered in 80% yield eluting with ethyl acetate. This protocol was also successfully applied in the synthesis of aryl azides **2b-g** (Scheme 2).

Scheme 2. Scope of the one-pot azidodeamination by TBSnN$_3$^{a}



[a] Yields of isolated products (2.0 mmol scale), yields in parentheses refers to those determined by GC-MS using *o*-DCB as internal standard.

A more simple procedure was possible for the isolation of azides **2h-j** and recovery of $TBSnN_3$. After conversion of TBSnOTs, these azides were precipitated by dropwise addition of cold hexane to the previously concentrated resulting filtrates, and the $TBSnN_3$ was then recovered from the supernatants in near-quantitative yield. Further purification by recrystallization from hexane afforded the aryl azides **2h-j** in an isolated yield range of 72-88%.

Due to their acidic properties, the above-described procedure for the conversion of TBSnOTs to $TBSnN_3$ must be ruled out for the azidobenzoic acids **2k-n**, considering the risks associated with any possible release of dangerous hydrazoic acid. In this regard, these compounds were precipitated by gradual addition of an aqueous hydrochloric acid solution; after filtration and washing with water and hexanes, the organotin by product, as TBSnCl, was almost quantitatively recovered from the organic/aqueous mixtures by extraction with diethyl ether. Good yields of target azides **2k-n**, ranging from 65% to 77%, were obtained without needing further purification.

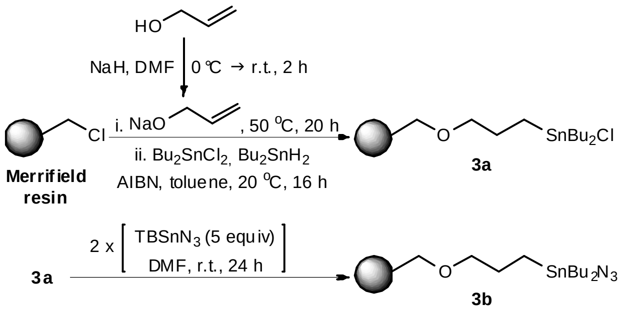
As can be seen from Scheme 2, this method proved to be applicable to various aromatic amines. In general, no significant correlations were found between electronic and steric effects of substituents on the aromatic ring and the outcome of reactions. Thus, good isolated yields of aryl azides **2** were obtained in the presence of both electron-withdrawing and electron-donating groups with a high tolerance to various common functionalities, owing to the mild conditions employed. Among them, several aminobenzoic acid derivatives gave good yields of corresponding azides which did not require purification. Unfortunately, from the reaction of 2-amino-5-chloropyridine (**1o**) and 3-aminopyridine (**1p**), the expected products (**2o** and **2p**) were not obtained. In the first case, the complete disappearance of the starting amine could not be observed on monitoring of the diazotization stage by TLC, and not even traces of **2o** were detected by GC-MS analysis of the reaction mixtures. In the second case, despite of the complete consumption of the starting amine, the reaction failed to give the desired product **2p** and N-(3-pyridinyl)acetamide (GC-MS data) was formed as major product when the temperature was increased to 60 °C in the second stage of the reaction [22].

It is worth to highlight that, in the evaluation on scope and limitations of the proposed method, yields and reaction times were taken from at least two independent experiments for each parameter; by means of the use of recycled TBSnN$_3$ it was possible to accomplish this task consuming somewhat less than 20% of the amount which would have been stoichiometrically required of the parent TBSnCl.

Within this concept of recovery and reuse of chemicals, that contributes to improve processes in terms of both cost reduction and waste minimization, the employment of solid-immobilized reagents is often one of the most convenient approaches. Indeed, this strategy has been extensively applied in reactions involving organotins to facilitate the above-mentioned aspects, the workup procedures, and to minimize the presence of tin at trace level in the products. In such a context, a helpful and motivating review article, about methodologies developed to limiting or avoiding contamination by organotin residues in organic synthesis, has been recently published [23].

Taking into consideration that pollution and safety issues related to the toxicity of the organotin compounds should be circumvented, our findings regarding the efficiency of TBSnN$_3$ as an azide-transfer reagent led us to explore the employment of a polymer-supported azidostannane on the previously described method.

In order to establish the feasibility of this approach, we chose the polystyrene resin-bound dibutyltin chloride **3a**, previously described and characterized [24], which appeared to be a suitable starting material for the syntheses of the corresponding tin azide **3b** as depicted in Scheme 3.



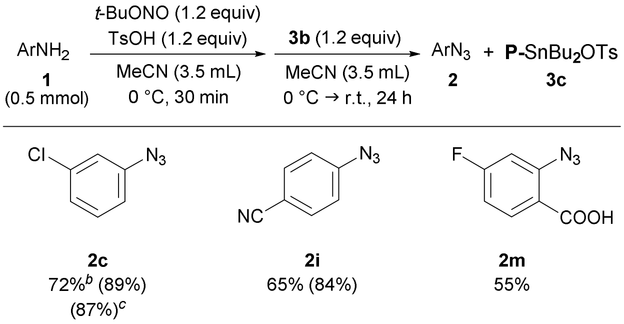
Scheme 3. Synthesis of the polymer-supported dibutyltin azide **3b**

The supported organotin chloride **3a** was prepared in two steps from a Merrifield resin (2.0 mmol Cl/g, 1% DVB), according to previously reported procedures [24], monitoring the progress of the reactions by gel-phase ^{13}C NMR [25]. For the hydrostannylation step, the disappearance of the well-defined vinylic carbon signals (117.1 and 135.0 ppm) of the starting allyl ether, was taken as indicative that this reaction proceeded to completion. Gel-phase ^{119}Sn NMR of the polymer **3a** revealed a single signal at 65.2 ppm. The NMR data were consistent with those previously reported [24].

Taking into account the high hydrophobicity of the crosslinked polystyrene backbone, which may disfavour reactions involving ionic species, and that it is necessary to use low to medium polar solvents for the swelling of microporous resins, we considered that $TBSnN_3$ rather than NaN_3, could be a more suitable reagent to achieve the synthesis of the supported dibutyltin azide **3b** from the chlorostannane **3a**. Hence, **3a** was swelled in DMF and reacted with a 5-fold excess of $TBSnN_3$, with respect to its theoretical loading (1.26 mmol Cl/g), at room temperature. After 24 h, the gel-phase ^{119}Sn NMR spectrum of resulting resin showed a new signal at 25.4 ppm [26]; nonetheless, the presence of a minor peak at 65.2 ppm revealed incomplete reaction as compared with starting resin. By repeating subsequently the same process, a complete conversion was confirmed by gel-phase ^{119}Sn NMR in the limits of this measurement. The azide loading on **3b** (0.84 mmol/g) was determined from elemental analysis indicating a 67 % yield relative to the initial loading of the Merrifield resin. Afterwards, the excesses of $TBSnN_3$ could be recovered and reused by adding an equivalent amount of NaN_3, based on the experimental loading, to the combined filtrates and washing solutions resulting of the usual treatments of **3b**.

Next, we selected the aryl amines 1-azido-3-chlorobenzene (**1c**), 4-azidobenzonitrile (**1i**) and 2-azido-4-fluorobenzoic acid (**1m**) to assess if the polymer-supported dibutyltin azide **3b** might also be effective on our azidodeamination protocol (Scheme 4).

Scheme 4. One-pot azidodeamination of aryl amines **1c**, **1i** and **1m** by polymer-supported dibutyltin azide **3b**[a]



[a] Yields of crude products, yields in parentheses refers to those determined by GC-MS using *o*-DCB as internal standard. [b] Residual tin content: 47 ppm (ICP). [c] By using recovered **3b**

By applying the same stepwise procedure **3b** was added, instead of TBSnN$_3$, prior dilution with MeCN (to allow its swelling) and the suspensions were kept under stirring at room temperature for 24 h before vacuum filtration. After the usual treatments, the filtrates obtained from the reactions of **1c** and **1i** were submitted to quantitative GC-MS analyses. As shown in Scheme 4, very good yields of the corresponding aryl azides **2c** and **2i** were observed, only slightly below of those achieved in solution (Scheme 2). However, there was a major decrease in the crude yields of these products, as well as in the azidobenzoic acid **2m**, after complete removal of solvents. Indeed, this issue should not be considered as unexpected since it is known that organic azides with an unfavourable (C + O)/N relationship (≤ 3) are more prone to decomposition in neat form [27]. Although the resulting losses could be minor, they became more significant on yields because we have worked on a 0.5 mmol scale (less than 90 mg of aryl azides) in this preliminary study. Regardless, it is interesting to highlight that, ^{1}H and ^{13}C NMR analysis of all crude samples showed fairly pure aryl azides. Moreover, without further purification, **2c** exhibited a very low tin contamination of 47 ppm (ICP) [28] whereas, in the same compound obtained in solution, it was about 10,000 ppm (1%) after chromatographic isolation; it should be noted that by a subsequent column chromatography on KF-silica gel (1:9) [29], its residual tin was reduced to less than 50 ppm, but the yield was dropped from 87% to 70%.

So far, these results showed that the effectiveness of **3b**, as azide-transfer reagent, is comparable to that of its soluble counterpart TBSnN$_3$ in the proposed method. As expected, the use of the resin-bound tin azide meant a great improvement as regards to isolation of the aryl azides when compared with those implemented in solution for the same compounds. By a simple filtration and solvent elimination, the products were obtained with very low levels of residual tin and did not required further purification.

Then, we focused on the recyclability of **3b** from the polymer-supported dibutyltin sulfonate **3c** recovered by filtration at the end of the reactions (**P**-$SnBu_2OTs$ in Scheme 4) [30]. Bearing in mind the advantageous good leaving group ability of tosylate ion, the same initial procedure carried out in the synthesis of **3b** (by chloride displacement of **3a** with $TBSnN_3$) was applied on the resin **3c** taking into account its theoretical loading (1.04 mmol/g). At the end of the first treatment, a complete conversion to azide **3b** was observed by gel-phase ^{119}Sn NMR analysis and the azide loading was evaluated to be 0.76 mmol N_3/g [31]. The recycled resin was then utilized in the azidodeamination of **1c** and the corresponding azide **2c** was obtained in 87% yield (GC–MS) showing that no significant loss in reactivity took place (Scheme 4).

3. Conclusions

We have shown that tributyltin azide is an effective reagent for the synthesis of diverse aryl azides in good to excellent yields, *via* diazotization of anilines in a one-pot stepwise procedure under mild conditions. Beside its easier access and relative stability, one of the main attractiveness of this covalent azide-transfer reagent lies in that it is readily recoverable from the corresponding stable and low volatile byproducts. The very good yields of these reactions are appropriate to perform tandem strategies and, in regards with the concern about tin pollution, also allow to accomplish further thorough purifications to reduce their tin content at trace levels, if the aryl azides must be isolated. It is in this connection that we sought to explore the alternative use of an insoluble polymer-supported organotin azide and encouraging results were obtained, for a selected group of anilines, in terms of yields, easier workup, low tin pollution of products and recyclability of the reagent. In addition, all resin-bound organotin reagents are very stable and can be stored at 2-4 °C, for an extended period of time, without loss of reactivity. Further explorations on the scope of this approach, as well as on other applications of the supported tin azide, are still ongoing in our laboratory.

4. Experimental Section

4.1. General

All the reactions were carried out in open air glassware. Unless otherwise stated, analytical grade reagents and solvents were purchased and used as received. $TBSnN_3$ was obtained from freshly distilled TBSnCl as described below. Resin-bound dibutyltin chloride (**3a**) was prepared according to the known literature procedure [24] from a Merrifield resin (100-200 mesh, 2 mmol Cl/g, 1% cross-linked) purchased from Sigma-Aldrich. NMR spectra were recorded at room temperature on a 300 MHz spectrometer operating at 300.1 MHz for ^{1}H, 75.5 MHz for ^{13}C and 111.9 MHz for ^{119}Sn. Chemical shifts (δ) are given in ppm referenced to external Me_4Sn (^{119}Sn) and Me_4Si (^{1}H and ^{13}C)

with the residual solvent resonance signal: δ H/C 7.27/77.2 for $CDCl_3$ and δ H/C 2.54/39.5 for DMSO-d_6. All coupling constants (*J* values) are quoted in hertz (Hz). Gel-phase ^{13}C NMR ($CDCl_3$) were recorded with optimized set parameters [25] and gel-phase ^{119}Sn NMR ($CDCl_3$) were performed as the routine experiments. The acquisition of mass spectra and analytical determinations were performed using a GC–MS instrument (HP5–MS capillary column, 30 m × 0.25 mm × 0.25 μm) equipped with a HP-5972 selective mass detector operating at 70 eV in electron-ionization (EI) mode. Program: 50 °C for 2 min with increase 10°C/min to 280°C; injection port temperature: 200 ºC. Microanalytical data were obtained using an Exeter Analytical CE-440 CHN/O instrument. The tin content was determined by inductively coupled plasma-atomic emission spectroscopy (ICP-AES) analysis at LANAQUI laboratories (CERZOS-CONICET-UNS-Bahía Blanca, Argentina).

CAUTIONS: Because azides are potentially explosive compounds, all azidation reactions and subsequent workups should be operated carefully and conducted in a fume hood with the sash positioned as low as possible. For safety instructions on lab-scale synthesis of azido compounds see ref [1a], pp 5-6.

4.2. Synthesis of tributyltin azide (TBSnN$_3$)

A round bottom flask was charged with TBSnCl (1.63 g, 1.36 mL, 10 mmol) and NaN_3 (0.72 g, 11 mmol). After being stirred for 4 h at room temperature, the reaction mixture was diluted with Et_2O (100 mL) and washed successively with H_2O (3 × 50 mL) and brine. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure to give 2.96 g (89 % yield) of $TBSnN_3$, as a colorless liquid, whose NMR spectral data were identical to those of commercial (Sigma-Aldrich) sample.

*4.3. General procedure for azidodeamination of aryl amines **1***

In a 25 mL round bottom flask, a solution of aryl amine **1** (2 mmol) and $TsOH{\cdot}H_2O$ (0.456 g, 2.4 mmol) in MeCN (14 mL) was cooled to 0°C in an ice bath and stirred for 15 min. *t*-BuONO (0.247 g, 0.285 mL, 2.4 mmol) was added dropwise and the solution was kept under stirring for further 15 min at the same temperature. After dropwise addition of $TBSnN_3$ (0.797 g, 0.657 mL, 2.4 mmol) the reaction mixture was allowed to attain room temperature and stirred for the time indicated in Scheme 2.

All synthesized aryl azides are known compounds whose physical and spectroscopic properties are in agreement with those previously reported: **2a**, **2e-f**, **2h-I**, **2k-m** [6]; **2c** [32], **2d** [33], **2g** [34], **2j** [35]. The characterization data for **2b** matched that of an authentic commercial sample (Sigma-Aldrich, CAS# 3296-05-7).

*4.3.1. General procedure for isolation of aryl azides **2a-j** and recovery of TBSnN$_3$*

After the above-described procedure, 20 µL of *o*-DCB (internal standard) was added to the reaction mixture followed by appropriate dilution with Et_2O (to 50 mL) for quantitative GC–MS analysis. Thereafter, NaN_3 (0.156 g, 2.4 mmol) was added to the MeCN–Et_2O resulting solution and the suspension was left overnight under stirring at room temperature. The precipitated NaOTs was filtered off under vacuum, rinsed with Et_2O (3 × 5 mL) and the filtrate solution was washed successively with distilled water (5 × 15 mL) and brine. The organic layer was dried over $MgSO_4$, filtered and concentrated under reduced pressure.

For aryl azides **2a-g**, the residue obtained after complete removal of solvent, was subjected to flash chromatography on silica gel pre-treated with Et_3N (10% v/v) giving the corresponding product in fractions eluted with hexanes. Then, after a fast increasing of eluting power, the TBSnN$_3$ was recovered from AcOEt fractions in around 80 % yield.

Instead, the aryl azides **2h-j** were precipitated from the concentrated filtrates by dropwise addition of cold hexane, and pure products were obtained by recrystallization from the same solvent. The TBSnN$_3$ was then recovered from the supernatants, in near quantitative yield, after solvent removal and vacuum drying.

*Azidobenzene (**2a**).* Following the general procedures within 2 hours of reaction, 77 % yield of the title compound was obtained as yellow oil ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50–7.41, (m, 2H), 7.26 (t, J = 7.4 Hz, 1H), 7.14 (dd, J = 8.6, 1.1 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 140.0, 129.7, 124.8, 119.0; MS m/z (% rel. intensity, ion) 119 (25, $M^{+\cdot}$), 91 [100, ($M^{+\cdot}$– N_2)], 64 (61).

*1-Azido-2-chlorobenzene (**2b**).* Following the general procedures within 2 hours of reaction, 68 % yield of the title compound was obtained as yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 (dd, J = 8.0, 1.5 Hz, 1H), 7.25–7.17 (td, J = 8.1, 1.5 Hz, 1H), 7.10 (dd, J = 8.0, 1.5 Hz, 1H), 7.00 (td, J = 7.7, 1.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.3, 130.9, 128.0, 125.8, 125.2, 119.8; MS m/z (% rel. intensity, ion) 153 (22, $M^{+\cdot}$), 125 [100, ($M^{+\cdot}$-N_2)], 90 (69), 63 (48).

*1-Azido-3-chlorobenzene (**2c**).* Following the general procedures within 2 hours of reaction, 87 % yield of the title compound was obtained as pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (t, J = 8.0 Hz, 1H), 7.06 (ddd, J = 8.0, 1.9, 1.0 Hz, 1H), 7.03 (d, J = Hz, 1H), 6.96 (t, J = 2.1 Hz, 1H), 6.86 (ddd, J = 8.1, 2.2, 1.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.6, 135.6, 130.8, 125.2, 119.5, 117.4; MS *m/z* (% rel. intensity, ion) 153 (22, $M^{+\cdot}$), 125 [100, ($M^{+\cdot}$ - N_2)], 90 (69), 63 (48).

*1-Azido-4-chlorobenzene (**2d**).* Following the general procedures within 1 hour of reaction, 77 % yield of the title compound was obtained as yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (d, J = 8.7 Hz, 2H), 6.85 (d, J = 8.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.8, 130.3, 129.9, 120.3; MS *m/z* (% rel. intensity, ion) 153 (22, $M^{+\cdot}$), 125 [100, ($M^{+\cdot}$ - N_2)], 90 (69), 63 (48).

*1-Azido-4-nitrobenzene (**2e**).* Following the general procedures within 1 hour of reaction, 40 % yield of the title compound was obtained as orange oil; ^{1}H NMR (300 MHz, CDCl$_3$) δ (ppm) 7.06 (d, J = 9.0 Hz, 2H), 8.18 (d, J = 9.0 Hz, 2H). ^{13}C NMR (75 MHz, CDCl$_3$) δ (ppm) 147.0, 144.8, 125.7, 119.5. MS *m/z* (% rel. intensity, ion) 164 (20, $M^{+\cdot}$), 136 [56, ($M^{+\cdot}$- N$_2$)], 90 (71), 63 (100).

*1-Azido-4-methoxybenzene (**2f**).* Following the general procedures within 1 hour of reaction, 68 % yield of the title compound was obtained as yellow oil; ^{1}H NMR (300 MHz, CDCl$_3$) δ 6.87 (d, J = 9.1 Hz, 2H), 6.80 (d, J = 9.1 Hz, 2H), 3.70 (s, 1H); ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 157.1, 132.5, 120.1, 115.3, 55.7; MS *m/z* (% rel. intensity, ion) 149 (20, $M^{+\cdot}$), 121 [100, ($M^{+\cdot}$- N$_2$)], 107 (42, *p*-An$^+$), 78 (54), 52 (38).

*1-Azido-2,4,6-trimethylbenzene (**2g**)*. Following the general procedures within 1 hour of reaction, 78 % yield of the title compound was obtained as pale brown oil; ^{1}H NMR (300 MHz, CDCl$_3$) δ 6.75 (s, 2H), 2.24 (s, 6H), 2.17 (s, 3H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 135.5, 134.5, 132.0, 129.6, 20.8, 18.1; MS *m/z* (% rel. intensity, ion) 161 (18, $M^{+\cdot}$), 133 [100, ($M^{+\cdot}$- N$_2$)], 119 (61).

*4-Azido-benzonitrile (**2h**).* Following the general procedures within 1 hour of reaction, 75 % yield of the title compound was obtained as orange crystals; ^{1}H NMR (300 MHz, CDCl$_3$) δ (ppm) 7.64 (d, J = 8.2 Hz, 2H), 7.45 (d, J = 8.2 Hz, 2 H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 144.9, 133.8, 119.7, 118.3, 108.3; MS m/z (% rel. intensity, ion) 144 (33, $M^{+\cdot}$), 116 [100, ($M^{+\cdot}$ – N$_2$)], 89 (73), 62 (45).

*1-(4-Azidophenyl)ethan-1-one (**2i**).* Following the general procedures within 1 hour of reaction, 88 % yield of the title compound was obtained as orange crystals; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.99 (d, J = 8.8 Hz, 2H), 7.09 (d, J = 8.8 Hz, 2H), 2.60 (s, 3H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 196.5, 144.9, 133.9, 130.3, 119.0, 26.4; MS *m/z* (% rel. intensity, ion) 161 (42, $M^{+\cdot}$), 133 [100, ($M^{+\cdot}$ - N$_2$)], 90 (54), 63 (63).

*1-azido-2,4-dibromobenzene (**2j**)*. Following the general procedures within 2 hours of reaction, 72 % yield of the title compound was obtained as yellow solid; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.62 (d, J = 2.2 Hz, 1H), 7.38 (dt, J = 10.0, 2.8 Hz, 1H), 6.97 (d, J = 8.6, 1.8 Hz, 1H); ^{13}C NMR (75 MHz, CDCl$_3$) δ (ppm) 138.2, 136.3, 131.7, 120.6, 117.9; MS *m/z* (% rel. intensity, ion) 277 (20, $M^{+\cdot}$), 249 [60, ($M^{+\cdot}$- N$_2$)], 170 (100).

*4.3.2. General procedure for isolation of azidobenzoic acids **2k-n** and recovery of TBSnCl*

Once azidodeamination is completed, the reaction mixture was cooled to 0 °C, and 5.4 N aqueous HCl was added dropwise until no further precipitation is observed. The solid was collected by vacuum filtration, rinsing it sequentially with distilled water (3 × 10 mL) and cold hexane (3 × 5 mL), providing the title compound in fairly pure form after drying under vacuum. Thereafter, the organic layer was separated from the resulting filtrate and the aqueous layer was neutralized and extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with distilled water (3 × 10 mL) and brine, dried over $MgSO_4$ and concentrated under reduced pressure recovering the TBSnCl in about 95 % yield.

*2-Azidobenzoic acid (**2k**).* Following the general procedures within 1 hour of reaction, 72 % yield of the title compound was obtained as beige solid; ^{1}H NMR (300 MHz, DMSO) δ 7.76 (dd, J = 7.8, 1.7 Hz, 1H), 7.59 (tt, J = 7.5, 1.7 Hz, 1H), 7.21–7.39 (m, 2H), 3.43 (br s, 1H). ^{13}C NMR (75 MHz, DMSO) δ 166.5, 138.7, 133.0, 131.1, 124.9, 124.0, 120.9, 39.5.

*2-Azido-5-iodobenzoic acid (**2l**).* Following the general procedures within 2 hours of reaction, 65 % yield of the title compound was obtained as brown solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.38 (d, J = 2.1 Hz, 1H), 7.87 (dd, J = 8.5 and 2.1 Hz, 1H), 7.02 (d, J = 8.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.7, 143.1, 141.9, 140.2, 122.6, 121.5, 88.0.

*2-Azido-4-fluorobenzoic acid (**2m**).* Following the general procedures within 2 hours of reaction, 77 % yield of the title compound was obtained as white solid; ^{1}H NMR (300 MHz, DMSO) δ 13.17 (br s, 1H), 7.86 (dd, J = 8.7, 6.4 Hz, 1H), 7.28 (dd, J = 9.9, 2.5 Hz, 1H), 7.11 (td, J = 8.4, 2.5 Hz, 1H); ^{13}C NMR (75 MHz, DMSO) δ 165.5 (d, J_{CF} = 25.8 Hz), 162.5, 141.5 (d, J_{CF} = 10.2 Hz), 133.6 (d, J_{CF} = 10.4 Hz), 120.3 (d, J_{CF} = 3.2 Hz), 111.9 (d, J_{CF} = 21.9 Hz), 108.3 (d, J_{CF} = 25.2 Hz).

*2-Azido-4,5-dimethoxybenzoic acid (**2n**).* Following the general procedures within 2 hours of reaction, 71 % yield of the title compound was obtained as grey solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 (s, 1H), 7.28 (s, 1H), 6.67 (s, 1H), 3.99 (s, 3H), 3.92 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.8, 154.2, 146.5, 134.1, 114.7, 112.7, 102.4, 56.5, 56.4.

*4.4. Synthesis of [3-(azidodibutylstannyl)propoxy]methyl Polystyrene (**3b**)*

To a suspension of resin-bound dibutyltin chloride **3a** (2.25 g, 2.83 mmol, theoretical loading: 1.26 mmol Cl/g) in DMF (25 mL), $TBSnN_3$ (4.7 g, 14.17 mmol, 5 equiv) was added dropwise and the mixture was left under gentle stirring 24 h at room temperature. The resin was washed with DMF (3 × 20 mL) and the same reaction process was repeated once. After vacuum filtration, the resin was washed successively with DMF, EtOH, DCM and Et_2O (3 × 20 mL each) and then dried under high vacuum (ca. 3 h) to give **3b** as a pale yellowish resin (2.03 g, 60 %, 0.84 mmol N_3/g, theoretical loading: 1.25 mmol N_3/g); ^{13}C NMR (gel-phase in $CDCl_3$, 75 MHz) δ 45.3, 40.4, 28.0, 26.9, 25.7, 16.1, 13.8, 10.5; ^{119}Sn NMR (gel-phase in $CDCl_3$, 112 MHz) δ 25.4; Elemental Analysis found: C, 61.49; H. 6.48; N 3.54. All combined filtrates and washing solutions were concentrated and then left overnight under stirring following addition of NaN_3 (0.156 g, 2.4 mmol). After the usual workup and routine controls, this recovered $TBSnN_3$ (4 g, 12 mmol, 80 %) was used for another reactions.

*4.4.1 General procedure for azidodeamination of aryl amines **1c**, **1i** and **1m** by using **3b**, and its later recovery*

After the above-described diazotization step of aryl amine (0.5 mmol), MeCN (3.5 mL) and resin **3b** (0.5 g, 0.6 mmol, 0.84 mmol N_3/g) were added, the suspension was gently stirred for 24 h at room temperature and the polymeric material was removed by vacuum filtration, washing it successively with MeCN and Et_2O (3 × 5 mL each). Whether it is appropriate, the combined filtrates and washing solutions were subjected to quantitative GC–MS analysis and thereafter, solvent removal and vacuum drying afforded the corresponding pure aryl azide **2**. The collected resin **3c** was further washed successively with EtOH, DCM and Et_2O (3 × 5 mL each), dried under high vacuum to constant weight, and stored at 2-4 °C; opportunely, after several experiments, it was reacted with a 5-fold excess of $TBSnN_3$ in accordance with its theoretical loading (1.04 mmol/g). After the first reaction process and subsequent workup, applying the same above-described procedures for its synthesis, **3b** was recovered as a yellowish resin (in around 60 % yield) and was found to contain 0.76 mmol of N_3/gr. Elemental Analysis: C, 67.19; H, 6.93; N, 3.19.

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Supporting Information available

Experimental procedures, characterization data, and copies of gel phase ^{13}C and ^{119}Sn NMR spectra of resin **3b**.

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Highlights

- One-pot stepwise diazotization-azidodediazoniation of aromatic amines.
- Mild and efficient procedure with no risk of release of hydrazoic acid.
- Tributyltin azide as hydrolytically stable, easily available and recoverable azide-transfer reagent.
- A novel and recyclable polymer-supported organotin azide enables down tin residues to ppm levels in aryl azide products.
- Long-term storable reagents.