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Polymer-Supported Dibutylstannyl Azide: An Efficient and Recoverable Reagent in the One-Pot Synthesis of Aryl Azides and 5-Aryl 1*H*-tetrazoles

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Herein, a very stable and highly reactive insoluble polymer-supported organotin azide was prepared from a Merrifield resin and its azide loading was determined by elemental analysis. This immobilized azide was employed in one-pot diazotization-azidodediazoniation of aromatic amines to provide a wide range of aryl azides in very good yields under mild conditions. On the other hand, this supported reagent was successfully applied in the 1,3-dipolar cycloaddition reaction with aromatic nitriles to provide 5-aryl 1*H*-tetrazoles in good yields. In addition, the recyclability of tin azide from the supported dibutyltin sulfonate recovered in the synthesis processes was reported. The developed methods allow the recycling and reuse of the supported tin azide, without significant loss of reactivity after four cycles in our reaction scale and less than 20 ppm of residual tin concentration in final products without additional purification.

Keywords: polymer-supported organotin azide, aryl azides, azidodeamination, 5-aryl 1*H*-tetrazoles, 1,3-dipolar cycloaddition

Introduction

Organotin compounds play a major role in decisive steps for the development of many organic synthesis methodologies involved in the production of natural products,[1] catalysts,[2] radiopharmaceuticals,[3] and molecules of biological interest.[4] Indeed, some organotin complexes are fungicides,[5] antifoulants,[6] pesticides,[7] bactericides,[8] and antitumor agents.[9] However, the valuable potential of this chemical tool is currently confronted with the controversy surrounding the toxicity of their byproducts, the stoichiometric proportion in which they are generated and the difficulties associated with their complete elimination in the final products.[10] Over the last years, different procedures that facilitate the separation of tin residues from the desired products have been developed. Among these, a few of the implemented strategies are: conversion of tin byproducts to insoluble polymeric tin fluorides, methodologies involving a catalytic amount of an organotin reagent with *in situ* recycling by means of a metal hydride reagent and reactions carried out in ionic liquids or polar solvents.[11]

The most convenient approaches to reduce contamination and facilitate the purification of products have been the design of organotin reagents anchored on different matrices.[11] The high increase in the number of papers describing the use of polymeric supports in organic chemistry, over the past decade, is a demonstration of its impact on scientific community. There are several main factors which contribute to the popularity of the technique, such as the elimination or simplification of purification steps, the easy recovery and regeneration of the reactants or catalysts supported without considerable loss of reactivity, the tin contents in the reaction crude reduced to levels below 50 ppm, among others.[11] Considering these remarkable advantages, we have recently reported a preliminary study focused on the synthesis of aryl azides, via diazotization-azidodediazoniation of anilines in a one-pot stepwise procedure by using an immobilized organotin azide.[12] Herein, we report the expansion of the substrate scope to several aniline derivatives.

It is well known that tetrazoles are important and versatile heterocycles with a wide range of chemical applications.[13] In medicinal and pharmaceutical chemistry, this interest is due to its ability as a carboxylic acid

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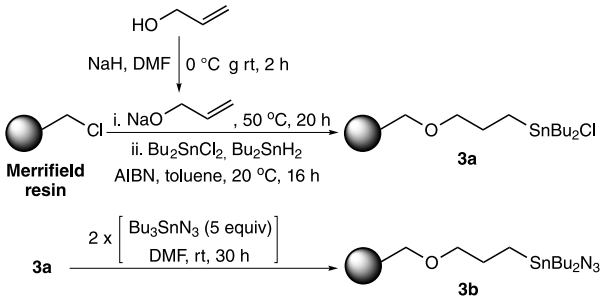
bioisostere for the design of active pharmaceutical targets.[14] These compounds together with their derivatives act as analgesics,[15] antivirals,[16] antibacterials,[17] antifungals,[18] anti-HIV drug candidates,[19] and anticancer agents.[20] Several procedures have been reported for their synthesis by reaction between organic nitriles and different azides such as silyl, tin and sodium azide under the influence of different Lewis acid catalysts.[21] Among them, the use of tributyltin azide is the most preferable and practicable one in terms of its availability, safety, stability and solubility in organic solvents, as it is exemplified on the first synthesis of valsartan,[22] and in the numerous efforts for its improvement.[23] Recently, Chrétien *et al.*,[24] developed a method for synthesizing 5-substituted 1*H*-tetrazoles via polymer-supported organotin alkoxide which is used for the *in situ* formation of tributylstannyl azide by reaction with trimethylsilyl azide. This heterogeneous synthesis afforded a residual tin concentration in the products compatible to pharmaceutical applications. Furthermore, the use in a catalytic amount of the organotin reagent allows an alternative type of recyclability. However, this protocol used an excess of $TMSN_3$, a hazardous reagent,[25] not reusable or recoverable. Furthermore, it does not allow the subsequent functionalization of the stannylated tetrazole restricting the scope of this procedure. Notably, we have not found precedents for the use of immobilized organotin azides. Therefore, in connection with our continuing effort to study the synthetic potential of organotin compounds,[26] and considering the relevance of tetrazoles in organic synthesis, we were encouraged to explore the 1,3-dipolar cycloaddition reaction between a polymer-supported organotin azide and various nitriles with a special focus on the recovery and reuse of this reagent.

Results and Discussion

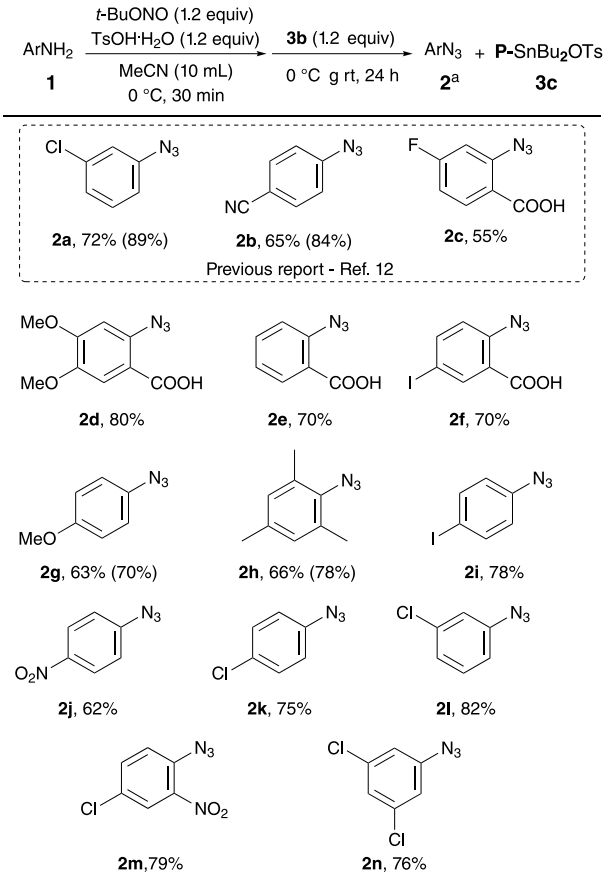
To further expand the substrate scope of our previously reported azidodeamination method,[12] we carried out the reactions of a representative series of anilines and polymer-supported organotin azide **3b** prepared from the resin-bound dibutyltin chloride **3a** by means of two consecutive treatments with tributylstannyl azide ($TBSnN_3$) in dimethylformamide (DMF) at room temperature for 30 h each (Scheme 1). The azide loading on **3b** (0.84 mmol N_3 g^{-1}) was determined by elemental analysis and afterwards, the excess of $TBSnN_3$ were recovered from the filtrates and the washing solutions by adding an equivalent amount of NaN_3 with respect to the experimental azide loading of **3b**.

The optimal reaction conditions, established with azides **2a-2c**, for *in situ* generation of the aryldiazonium



Scheme 1. Synthesis of the polymer-supported dibutyltin azide **3b**.

tosylates, followed by its azidodediazoniation by means of the addition of **3b** swollen in MeCN, were applied to a series of aromatic amines (Scheme 2). Finally, 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. These results confirmed that the employment of the resin-bound tin azide meant a great improvement as regards to isolation of aryl azides and removal of tin byproducts from the crude reaction.



Scheme 2. Scope of the one-pot azidodeamination of aryl amines by polymer-supported dibutyltin azide **3b**. (a) Yields of isolated products (0.5 mmol scale), yields in parentheses refers to those determined by GC-MS using *ortho*-dichlorobenzene as internal standard.

The reusability of **3b**, obtained from recovered **3c** by treatment with $TBSnN_3$,[12] was evaluated in four-run recycling tests for the azidodeamination of 2-amino-4,5-dimethoxybenzoic acid (**1d**). As shown in Table 1, the successively yields obtained from the corresponding aryl azide (**2d**) showed that no significant loss in reactivity took place. It is important to highlight that in our test conditions the number of runs was limited by the available mass of **3b** after the workup of each reaction.

Table 1. Reusability testing of recycled **3b** in the synthesis of **2d**

Run	Azide loading[a] / (mmol N_3 g^{-1})	Yield[b] / %
1	0.84	80
2	0.83	78
3	0.79	75
4	0.79	73

[a]Determined by elemental analysis of recycled **3b**.[b]Yields of isolated products after usual workup.

Afterwards, we set out to explore the synthetic potential of the resin-bound tin azide **3b** as dipolar partner in the synthesis of 5-aryl 1*H*-tetrazoles through the Huisgen 1,3-dipolar cycloaddition with nitriles. We started by testing the reported conditions for reactions of tributyltin azide in solution phase,[27] employing benzonitrile (**4a**) as model substrate, in an equimolar ratio with respect to **3b**. After heating the mixture of **3b** and benzonitrile in xylenes at reflux during 24 h, subsequent filtration and washing, we carried out the solvolysis of the polymer-supported stannyl tetrazole with a solution of concentrated hydrochloric acid in MeOH [HCl_{aq}/MeOH 10% v/v]. After 30 min, an impure 5-phenyl 1*H*-tetrazole (**5a**) was obtained from the crude filtrates as confirmed by ^1H and ^{13}C nuclear magnetic resonance (NMR). Despite we were not able to determine the identity of the additional signals in the NMR spectra, we could observe, by thin layer chromatography (TLC) analysis, the presence of tin residues in the sowing point. Considering that such residues could be form due to the C–O bonds breaking off the spacer to the Merrifield resin [Sn–$(CH_2)_3$–O–], promoted by the applied solvolysis conditions, we decided to investigate the proton-mediated cleavage step in order to avoid this drawback.

At first, we set out to explore the solvolysis on a previously swollen resin. After the 24 h cycloaddition step, we swelled the resin-bound stannyl tetrazole in dichloromethane (DCM) and carried out the solvolysis with HCl_{aq}/MeOH 10% v/v. In these conditions, **5a** was obtained in 52% yield but we found evidence of tin residues by TLC analysis. Taking these results into account, we decided to evaluate the effect of the concentration from the hydrochloric acid solutions at different reaction times. We carried out the respective solvolysis steps by using HCl_{aq}/MeOH 5 and 2% v/v at 10 and 30 min each. After performing the corresponding washes, by TLC analysis of the collected filtrates, we were able to determine that the use of HCl_{aq}/MeOH, regardless of its concentration or reaction time, promotes the release of tin residues from the solid support. Based on these results, we carried out a new reaction using $TsOH{\cdot}H_2O$ as an alternative source of proton to perform the cleavage of the Sn-tetrazole bond. The new solvolysis procedure was carried out by swelling the polymeric material in DCM and stirring with a 0.15 M solution of $TsOH{\cdot}H_2O$ in MeOH during 30 min at room temperature. Thereby, the corresponding spectroscopically pure **5a** could be obtained by simple filtration and washing in 72% yield.

Taking into account that the efficiency in the solvolysis step depends on the nature of the Merrifield resin spacer, we carried out the synthesis of 5-(2-methylphenyl)-1*H*-tetrazole (**5b**) using $TsOH{\cdot}H_2O$ (Table 2, entry 1). Despite that a cycloaddition step of 24 h provided a 66% yield and taking into account a certain degree of steric hindrance of the substrate, we decided to evaluate whether a longer reaction time would improve this result or not. In order to accomplish this, we performed the synthesis of **5b**, keeping the heating mixture of 2-methylbenzonitrile (**4b**) with **3b** at reflux for 48 h (Table 2, entry 2). After usual workup, this product was obtained in 60% yield. By TLC analysis of the supernatant before the solvolysis step, we could observe the presence of the corresponding tetrazole together with tin residues, which had not been detected in the previous reaction. We realized that the longer reaction time caused the protodestannylation of the supported stannyl tetrazole.

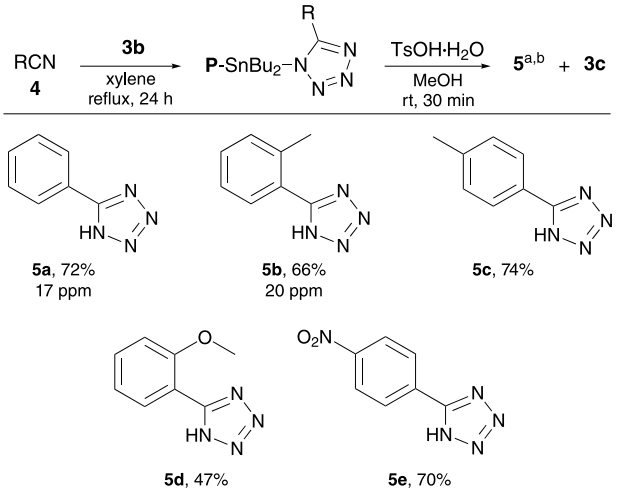
One of the many advantages to employ a solid-supported reactant is the possibility to work with an excess of reagents that allow driving reactions to completion and the easy recovery of the unused reagents. Consequently, we decided to carry out the same reaction using 2 equivalents of benzonitrile **4b**. In this opportunity, spectroscopically pure **5b** was obtained without significant yield improvement (Table 2, entry 3).

Table 2. Optimization of the cycloaddition step in the synthesis of **5b**

entry	**4b**:**3b**	Condition	Yield[a] / %
1	1:1	reflux, 24 h	66
2	1:1	reflux, 48 h	60
3	2:1	reflux, 24 h	69
4	1:1	MW, 150 °C, 250 W, 2 × 20 min	35
5	1:1	MW, 150 °C, 150 W, 2 × 20 min	38

[a]Yields of isolated products (0.5 mmol scale). MW: microwave.

On the other hand, we envisioned that the accelerating effect of microwaves could potentially reduce the reaction time. In such context, during the last years, several procedures have been developed to obtained tetrazoles from nitriles and silyl or sodium azide promoted by microwaves.[28] To analyze the effect of microwaves in this cycloaddition reaction, we carried out the synthesis of **5b** under microwave heating, using a power of 250 W and a temperature of 150 °C, for two cycles of 20 min (Table 2, entry 4). Unfortunately, it was only obtained in 35% yield and, by TLC analysis, we once again observed the corresponding product in the supernatant before doing the solvolysis step. Next, we decided to carry out the cycloaddition by using a lower power (150 W) and a temperature of 150 °C for two cycles of 20 min (Table 2, entry 5). Once more, we only obtained **5b** in 38% yield. After these discouraging results, we tried to perform the synthesis of tetrazoles within 24 h under thermal conventional heating. This time, we obtained various 5-aryl 1*H*-tetrazoles in good yields (Scheme 3). Moreover, after work-up and isolation of **5a** and **5b**, without further purification, several analyses by inductively coupled plasma (ICP) were carried out and exhibited a very low tin contamination (under 20 ppm).



Scheme 3. Synthesis of 5-aryl 1*H*-tetrazoles. (a) Yields of isolated products (0.5 mmol scale). (b) Tin residues concentration by ICP (ppm).

At this point, we decided to examine the recyclability of **3b**. To accomplish this, the polymer-supported dibutyltin sulfonate **3c**, recovered by filtration at the end of the reactions, was treated with $TBSnN_3$ according to our protocol previously reported. The recycled polymer-supported dibutyltin azide **3b** was reused in the synthesis of **5a**, as a model reaction. The corresponding tetrazole **5a** was obtained in three consecutive runs of 67, 60, 48% yield, respectively. In this case, the number of times **3b** was reused is not only limited by its available mass after the workup of the reaction. Furthermore, a high degradation of the resin is evident due to the temperature used in the cycloaddition step, as we detected when the reaction was carried out for 48 h.

Conclusions

In this report, it was demonstrated the efficiency of a polymer-supported dibutyltin azide in the one-pot synthesis of aryl azides via diazotization of anilines under mild conditions. Furthermore, to the best of our knowledge, this is the first report concerning the cycloaddition reaction with nitriles using a supported organotin azide, in order to provide 5-aryl 1*H*-tetrazoles in good yields without need of further purification. The developed methods are very advantageous in terms of yields, easier and efficient workup, and low tin pollution of products in comparison with conventional protocols. The most important advantage lies on the recyclability and reuse of the supported tin azide being reused up to four times in our reaction scale. However, on a larger scale it can be reused multiple times. Furthermore, the supported tin reagent was found to be very stable and can be stored at 2-4 °C, for an extended period of time, without losing reactivity. Finally, it is noteworthy that tin contamination of the products was limited to less than 20 ppm even using equimolar amounts of supported tin azide.

Experimental

Materials and/or methods

Unless otherwise stated, analytical grade reagents and solvents were purchased from Sigma-Aldrich (St. Louis, United States) and Anedra (Buenos Aires, Argentina) and used as received. $TBSnN_3$ was obtained from TBSnCl as described in our previous report.[12] Resin-bound dibutyltin chloride (**3a**) was prepared according to the known literature procedure,[29] from a Merrifield resin (100-200 mesh, 2 mmol Cl g^{-1}, 1% cross-linked) purchased from Sigma-Aldrich (St. Louis, United States). NMR spectra were recorded at room temperature on a Bruker Advance 300 spectrometer (Zürich, Switzerland) 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 7.26/77.2 for $CDCl_3$ and δ H/C 2.50/39.5 for deuterated dimethyl sulfoxide (DMSO-d_6). Gel-phase ^{13}C NMR ($CDCl_3$) were recorded with optimized set parameters,[30] 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 gas chromatography-mass spectrometry (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 (Agilent Technologies, Santa Clara, USA). Program: 50 °C for 2 min with increase 10 °C min^{-1} to 280 °C; injection port temperature: 200 °C. Melting points were determined on a Reichert-Kofler (Vienna, Austria) hot-stage microscope and were uncorrected. Microanalytical data were obtained using an Exeter Analytical CE-440 CHN/O instrument (Coventry, England). The tin content was determined by inductively coupled plasma-atomic emission spectroscopy (ICP-AES) analysis at LANAQUI laboratories (CERZOS-CONICET-UNS, Bahía Blanca, Argentina).

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 the literature.[31]

Aryl azides **2d-2n** and tetrazoles **5a-5e** are known compounds whose physical and spectroscopic properties are either in agreement with those previously reported.

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^{-1}) 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 procedure 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^{-1}, theoretical loading: 1.25 mmol N_3 g^{-1}); ^{13}C NMR (75 MHz, gel-phase in $CDCl_3$) δ 128.0, 73.3, 71.0, 45.3, 40.4, 28.0, 26.9, 25.7, 16.1, 13.8, 10.5 (Figure S1, Supplementary Information (SI) section); ^{119}Sn NMR (gel-phase in $CDCl_3$, 112 MHz) δ 25.5 (Figure S2, SI section); 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.

General procedure for azidodeamination of aryl amines by using **3b**, and its later recovery

In a 25 mL round bottom flask, a solution of aryl amine **1** (0.5 mmol) and $TsOH{\cdot}H_2O$ (0.114 g, 0.6 mmol) in MeCN (10 mL) was cooled to 0 °C in an ice bath and stirred for 15 min, *tert*-butyl nitrite (0.061 g, 70 μL, 0.6 mmol) was added dropwise and the solution was kept under stirring for further 15 min at the same temperature. After the addition of the resin **3b** (0.73 g, 0.6 mmol, 0.82 mmol N_3 g^{-1}) swollen in MeCN the suspension was allowed to attain room temperature and was gently stirred for 24 h. Then, the polymeric material was removed by vacuum filtration, washed successively with MeCN and Et_2O (3 × 5 mL each). Thereafter, the combined filtrates and washing solutions were concentrated in vacuum to give the corresponding pure aryl azide **2**. For the aryl azides **2g** and **2h** the combined organic layers were subjected to quantitative GC-MS analysis prior to vacuum concentration. The collected resin **3c** was further washed successively with EtOH, DCM and Et_2O (3 × 5 mL each), dried under reduced pressure 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^{-1}). 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 g^{-1}. elemental analysis: C, 67.19; H, 6.93; N, 3.19.

2-Azido-4,5-dimethoxybenzoic acid (**2d**)[32]

Beige solid; 80% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (s, 1H), 6.65 (s, 1H), 3.97 (s, 3H), 3.91 (s, 3H) (Figure S3, SI section); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.5, 154.2, 146.5, 134.1, 114.7, 112.7, 102.7, 56.5, 56.4 (Figure S4, SI section).

2-Azidobenzoic acid (**2e**)[32]

Beige solid; 70% yield; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.77 (dd, 1H, *J* 7.8, 1.7 Hz), 7.59 (m, 1H), 7.35 (br d, 1H, *J* 8.1 Hz), 7.26 (t, 1H, *J* 7.6 Hz) (Figure S5, SI section); ^{13}C NMR (75 MHz, DMSO-d_6) δ 166.5, 138.7, 133.0, 131.1, 124.9, 124.0, 120.8 (Figure S6, SI section).

2-Azido-5-iodobenzoic acid (**2f**)[32]

Brown solid; 70% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.38 (d, 1H, *J* 2.2 Hz), 7.87 (dd, 1H, *J* 8.5, 2.2 Hz), 7.02 (d, 1H, *J* 8.5 Hz) (Figure S7, SI section); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.7, 143.1, 141.9, 140.2, 122.6, 121.5, 88.0 (Figure S8, SI section).

1-Azido-4-methoxybenzene (**2g**)[32]

Yellow oil; 63% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.96 (d, 2H, *J* 9.1 Hz), 6.89 (d, 2H, *J* 9.1 Hz), 3.80 (s, 3H) (Figure S9, SI section); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 157.1, 132.4, 120.0, 115.2, 55.6 (Figure S10, SI section).

1-Azido-2,4,6-trimethylbenzene (**2h**)[33]

Pale brown oil; 66% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.84 (s, 2H), 2.33 (s, 6H), 2.26 (s, 3H) (Figure S11, SI section); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.5, 134.5, 132.0, 129.6, 20.8, 18.2 (Figure S12, SI section).

1-Azido-4-iodobenzene (**2i**)[32]

Brown solid; 78% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (dd, 2H, *J* 8.8, 2.0), 6.78 (dd, 2H, *J* 8.8, 2.0) (Figure S13, SI section); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.1, 138.8, 121.1, 88.3 (Figure S14, SI section).

1-Azido-4-nitrobenzene (**2j**)[33]

Orange oil; 62% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.24 (d, 2H, *J* 9.0 Hz), 7.13 (d, 2H, *J* 9.0 Hz) (Figure S15, SI section); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.0, 144.8, 125.7, 119.5 (Figure S16, SI section).

1-Azido-4-chlorobenzene (**2k**)[33]

Yellow oil; 78% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (d, 2H, *J* 8.8 Hz), 6.84 (d, 2H, *J* 8.8 Hz) (Figure S17, SI section); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.8, 130.3, 129.9, 120.3 (Figure S18, SI section).

1-Azido-3-chlorobenzene (**2l**)[34]

Pale yellow oil; 82% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 (t, 1H, *J* 8.0 Hz), 7.12 (ddd, 1H, *J* 8.0, 2.0, 1.0), 7.03 (1H, t, *J* 2.1 Hz), 6.92 (1H, ddd, *J* 8.1, 2.2, 1.0) (Figure S19, SI section); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.6, 135.6, 130.8, 125.2, 119.5, 117.4 (Figure S20, SI section).

1-Azido-4-chloro-2-nitrobenzene (**2m**)[35]

Yellow solid; 79% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (d, 1H, *J* 2.4 Hz), 7.55 (dd, 1H, *J* 8.7, 2.4 Hz), 7.23 (d, 1H, *J* 1.9 Hz) (Figure S21, SI section); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.2, 133.7, 130.4, 126.2, 122.1 (Figure S22, SI section).

1-Azido-3,5-dichlorobenzene (**2n**)[36]

Brown solid; 76% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.13 (t, 1H, *J* 1.8 Hz), 6.92 (d, 2H, *J* 1.8 Hz) (Figure S23, SI section); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.6, 136.2, 125.3, 117.9 (Figure S24, SI section).

General procedure for 1,3-dipolar cycloaddition between nitriles and **3b**

In a 25 mL Schlenk tube under nitrogen atmosphere, nitrile **4** (0.5 mmol), **3b** (0.60 g, 0.50 mmol, 0.84 mmol N_3 g^{-1}) and xylenes (6 mL) were heated under reflux for 24 h. Then, the polymeric material was removed by vacuum filtration, and washed successively with xylenes and acetone (3 × 5 mL each). Next, it was carried out the cleavage of Sn–N bond by stirring the polymeric material in DCM (4 mL) with a 0.15 M solution of $TsOH{\cdot}H_2O$ in MeOH (4 mL) at room temperature for 30 min. The resultant resin was removed by vacuum filtration and, washed successively with DCM and Et_2O (3 × 5 mL each). The organic layer was washed with water, dried over $MgSO_4$ and concentrated under reduced pressure giving the corresponding pure tetrazole **5**.

5-Phenyl-1*H*-tetrazole (**5a**)[37]

White solid; 72% yield; mp 215-216 °C (lit. 215-216 °C); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.02-7.99 (m, 2H), 7.59-7.55 (m, 3H) (Figure S25, SI section); ^{13}C NMR (75 MHz, DMSO-d_6) δ 155.4, 131.1, 129.4, 126.9, 124.3 (Figure S26, SI section).

5-(2-Methylphenyl)-1*H*-tetrazole (**5b**)[37]

White solid; 66% yield; mp 152-153 °C (lit. 150-151 °C); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.65 (d, 1H, *J* 7.5 Hz), 7.45-7.32 (m, 3H), 2.45 (s, 3H, below DMSO-d_6 signal); ^{13}C NMR (75 MHz, DMSO-d_6) δ 155.3, 137.1, 131.3, 130.7, 129.4, 126.3, 123.9, 20.5 (Figure S27, SI section).

5-(4-Methylphenyl)-1*H*-tetrazole (**5c**)[38]

White solid; 74% yield; mp 250-251 °C (lit. 248-249 °C); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.89 (d, 2H, *J* 7.8 Hz), 7.38 (d, 2H, *J* 7.8 Hz), 2.39 (s, 3H, below DMSO-d_6 signal); ^{13}C NMR (75 MHz, DMSO-d_6) δ 155.2, 141.1, 129.9, 126.8, 121.4, 21.0 (Figure S28, SI section).

5-(2-Methoxyphenyl)-1*H*-tetrazole (**5d**)[39]

White solid; 47% yield; mp 157-159 °C (lit. 159-160 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 (d, 1H, *J* 8.2 Hz), 7.52 (m, 1H), 7.20-7.12 (m, 2H), 3.82 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.6, 152.1, 133.4, 130.1, 122.2, 111.8, 111.6, 56.4 (Figure S29, SI section).

5-(4-Nitrophenyl)-1*H*-tetrazole (**5e**)[37]

White solid; 70% yield; mp 218-220 °C (lit. 219-221 °C); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.42 (m, 2H), 8.28 (m, 2H) (Figure S30, SI section); ^{13}C NMR (75 MHz, DMSO-d_6) δ 155.3, 148.7, 130.7, 128.2, 124.6 (Figure S31, SI section).

Supplementary Information

Supplementary information (^{1}H, ^{13}C and ^{119}Sn NMR spectra) is available free of charge at http://jbcs.sbq.org.br as PDF file.

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Author Contributions

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References

1. Mitchell, T. N. In *Metal-Catalyzed Cross-Coupling Reactions*; de Meijere, A.; Diederich F., eds.; 2nd ed.; Wiley-VCH: Weinheim, Germany, 2004, ch. 2; Grindley, T. B. In *Tin Chemistry: Fundamentals, Frontiers, and Applications*; Davies, A. G.; Gielen, M.; Pannell, K. H.; Tiekink E. R. T., eds.; John Wiley & Sons: Chichester, UK, 2008, ch. 5, p. 497-514.
2. Otera, J.; Biesemans, M.; Pinoie, V.; Poelmans, K.; Willem, R.; Blank, W. J.; Hessell, E. T.; Kinart, W. J.; Kinart, C. M. In *Tin Chemistry: Fundamentals, Frontiers, and Applications*; Davies, A. G.; Gielen, M.; Pannell, K. H.; Tiekink E. R. T., eds.; John Wiley & Sons: Chichester, UK, 2008, ch. 6, p. 667-720; Zubair, M.; Sirajuddin, M.; Haider, A.; Hussain, I.; Tahir, M. N.; Ali, S.; *Appl. Organomet. Chem.* **2019**, *34*, e5305 [Crossref]; Devendra, R.; Edmonds, N. R.; Sohnel, T.; *Heliyon* **2020**, *6*, e040744. [Crossref]
3. Chaturvedi, S.; Mishra, A. K.; *Front. Med.* **2016**, *3*, 5 [Crossref]; Zarrad, F.; Zlatopolskiy, B. D.; Krapf, P.; Zischler, J.; Neumaier, B.; *Molecules* **2017**, *22*, 2231. [Crossref]
4. Nicolaou, K. C.; Bulger, P. G.; Sarlah, D.; *Angew. Chem., Int. Ed.* **2005**, *44*, 4442 [Crossref]; Nicolaou, K. C.; Rigol, S.; *Nat. Prod. Rep.* **2020**, *37*, 1404 [Crossref]; Sirajuddin, M.; Ali, S.; McKee, V.; Wadood, A.; Ghufran, M.; *J. Mol. Struct.* **2019**, *1181*, 93. [Crossref]
5. García-López, M. C.; Muñoz-Flores, M. B.; Jiménez-Perez, V. M.; Moggio, I.; Arias, E.; Chan-Navarro, R.; Santillan, R.; *Dyes Pigm.* **2014**, *106*, 188 [Crossref]; Adeyemi, J. O.; Onwudiwe, D. C.; *Molecules* **2018**, *23*, 2571. [Crossref]
6. Qian, P.-Y.; Xu, Y.; Fusetani, N.; *Biofouling* **2019**, *26*, 223. [Crossref]
7. Gui, W.; Tian C.; Sun, Q.; Li, S.; Zhang, W.; Tang, J.; Zhu, G.; *Water Res.* **2016**, *95*, 185 [Crossref]; Ma, Y.-M.; Cao, C.-Y.; Wang, Q.-W.; Gui, W.-J.; Zhu, G.-N.; *Aquat. Toxicol.* **2016**, *179*, 55. [Crossref]
8. Butt, A. F.; Bhatti, M. H.; Aamir, M.; Ch, M. A.; Tahir, M. N.; Sher, M.; Ahmed, M. J.; Akhtar, J.; *ChemistrySelect* **2018**, *3*, 10325 [Crossref]; da Silva Santos, A. F.; da Silveira Maia, J. R.; *J. Eng. Exact Sci.* **2019**, *5*, 0452. [Crossref]
9. Devi, J.; Yadav, J.; *Anticancer Agents Med. Chem.* **2018**, *18*, 335 [Crossref]; Pantelić, N. Đ.; Zmejkovski, B. B.; Žižak, Ž.; Banjac, N. R.; Božić, B. Đ.; Stanojković, T. P.; Kaluderović, G. N.; *J. Chem.* **2019**, *2019*, ID 2905840. [Crossref]
10. Sunday, A. O.; Alafara, B. A.; Oladele, O. G.; *Chem. Speciation Bioavailability* **2012**, *24*, 216 [Crossref]; Barbosa, C. M. L.; Ferrão, F, M.; Graceli, J. B.; *Front. Endocrinol.* **2018**, *9*, 256 [Crossref]; Zhang, S.; Li, P.; Li, Z.-H.; *Comp. Biochem. Physiol. C Toxicol. Pharmacol.* **2021**, *246*, 109054. [Crossref]
11. Chrétien, J.-M.; Kilburn, J. D.; Zammattio, F.; Le Grognec, E.; Quintard, J.-P. In *Tin Chemistry: Fundamentals, Frontiers, and Applications*; Davies, A. G.; Gielen, M.; Pannell, K. H.; Tiekink E. R. T., eds.; John Wiley & Sons: Chichester, UK, 2008, ch. 5, p. 607-621; Le Grognec, E.; Chrétien, J.-M.; Zammattio, F.; Quintard, J.-P.; *Chem. Rev.* **2015**, *115*, 10207 [Crossref]; Cordovilla, C.; Bartolomé, C.; Martínez-Ilarduya, J. M.; Espinet, P.; *ACS Catal.* **2015**, *5*, 3040. [Crossref]
12. Godoy Prieto, L.; Lo Fiego, M. J.; Chopa, A. B.; Lockhart, M. T.; *J. Organomet. Chem.* **2017**, *830*, 26. [Crossref]
13. Selected reviews: Lamberth, C. *Pest. Manage. Sci.* **2013**, *69*, 1106 [Crossref]; Nasrollahzadeh, M.; Nezafat, Z.; Bidgoli, N. S. S.; Shafiei, N.; *Mol. Catal.* **2021**, *513*, 111788. [Crossref]
14. Zou, Y.; Liu, L.; Liu, J.; Liu, G.; *Future Med. Chem.* **2020**, *12*, 91 [Crossref]; Myznikov, L. V.; Hrabalek, A.; Koldobskii, G. I.; *Chem. Heterocycl. Compd.* **2007**, *43*, 1. [Crossref]
15. Lamie, P. F.; Philoppes, J. N.; Azouz, A. A.; Safwat, N. M.; *J. Enzyme Inhib. Med. Chem.* **2017**, *32*, 805. [Crossref]
16. Yogesh, R.; Srivastava, N.; *Asian J. Chem.* **2021**, *33*, 2599. [Crossref]
17. Gao, F.; Xiao, J.; Huang, G.; *Eur. J. Med. Chem.* **2019**, *184*, 111744 [Crossref]; DiPuma Jr., T.; Thabthimthong, T.; Kelley, E. H.; Konczak, K.; Beulke, M.; Herbert, C.; Mohammad, T. S. H.; Starus, A.; Nocek, B.; Olsen, K. W.; Holz, R. C.; Becker, D. P.; *Bioorg. Med. Chem. Lett.* **2023**, *83*, 129177. [Crossref]
18. Łukowska-Chojnacka, E.; Mierzejewska, J.; Milner-Krawczyk, M.; Bondaryk, M.; Staniszewska, M.; *Bioorg. Med. Chem.* **2016**, *24*, 6058. [Crossref]
19. Zhan, P.; Li, Z.; Liu, X.; De Clercq, E.; *Mini Rev. Med. Chem.* **2009**, *9*, 1014. [Crossref]
20. Dhiman, N.; Kaur, K.; Jaitak, V.; *Bioorg. Med. Chem.* **2020**, *28*, 115599. [Crossref]

21. Roh, J.; Vávrová, K.; Hrabálek, A.; *Eur. J. Org. Chem.* **2012**, *2012*, 6101 [Crossref]; Sarvary, A.; Maleki, A.; *Mol. Diversity* **2015**, *19*, 189 [Crossref]; Neochoritis, C. G.; Zhao, T.; Dömling, A.; *Chem. Rev.* **2019**, *119*, 1970 [Crossref]; Sagmeister, P.; Kaldre, D.; Sedelmeier, J.; Moessner, C.; Püntener, K.; Kummli, D.; Williams, J. D.; Kappe, C. O.; *Org. Process Res. Dev.* **2021**, *25*, 1206. [Crossref]
22. Bühlmayer, P.; Furet, P.; Criscione, L.; de Gasparo, M.; Whitebread, S.; Schmidlin, T.; Lattman, R.; Wood, J.; *J. Bioorg. Med. Chem. Lett.* **1994**, *4*, 29. [Crossref]
23. Wang, G.; Sun, B.; Peng, C.; *Org. Process Res. Dev.* **2011**, *15*, 986 [Crossref]; Aalla, S.; Gilla, G.; Bojja, Y.; Anumula, R. R.; Vummenthala, P. R.; Padi, P. R.; *Org. Process Res. Dev.* **2012**, *16*, 682 [Crossref]; Hiebler, K.; Soritz, S.; Gavric, K.; Birrer, S.; Maier, M. C.; Grabner, B.; Gruber-Woelfler, H.; *J. Flow Chem.* **2020**, *10*, 283 [Crossref]; Carpentier, F.; Felpin, F.-X.; Zammattio, F.; Le Grognec, E.; *Org. Process Res. Dev.* **2020**, *24*, 752. [Crossref]
24. Chrétien, J. M.; Kerric, G.; Zammattio, F.; Galland, N.; Paris, M.; Quintard, J.-P.; Le Grognec, E.; *Adv. Synth. Catal.* **2018**, *361*, 747. [Crossref]
25. Jafarzadeh, M.; *Synlett* **2007**, *13*, 2144 [Crossref]; Langerman, N; *Chemical Safety: Explosion Hazard in Synthesis of Azidotrimethylsilane*; Chemical & Engineering News, 2014, p. 92. [Link] accessed in May 2023
26. Lo Fiego, M. J.; Dorn, V. B.; Badajoz, M. A.; Lockhart, M. T.; Chopa, A. B.; *RCS Adv.* **2014**, *4*, 49079 and references cited herein. [Crossref]
27. Penthala, N. R.; Bommagani, S.; Yadlapalli, J.; Crooks, P. A.; *Tetrahedron Lett.* **2016**, *57*, 1807. [Crossref]
28. Myznikov, L. V.; Vorona, S. V.; Artamonova, T. V.; Zevatskii, Y. E.; *Chem. Heterocycl. Compd.* **2016**, *52*, 887. [Crossref]
29. Zhu, X.; Blough, B. E.; Carroll, F. I.; *Tetrahedron Lett.* **2000**, *41*, 9219 [Crossref]; Hernán, A. G.; Guillot, V.; Kuvshinov, A.; Kilburn, J. D.; *Tetrahedron Lett.* **2003**, *44*, 8601. [Crossref]
30. Lorgé, F.; Wagner, A.; Mioskowski, C.; *J. Comb. Chem.* **1999**, *1*, 25. [Crossref]
31. Keicher, T.; Löebbecke, S. In *Organic Azides: Syntheses and Applications*; Bräse, S.; Banert, K., eds.; John Wiley & Sons, Ltd.: Chichester, UK, 2010, ch. 1.
32. Barral, K.; Moorhouse, A. D.; Moses, J. E.; *Org. Lett.* **2007**, *9*, 1809. [Crossref]
33. Li, Y.; Gao, L.-X.; Ham, F.-S.; *Chem. Eur. J.* **2010**, *16*, 7969. [Crossref]
34. Gribanov, P. S.; Topchiy, M. A.; Golenko, Y. D.; Lichtenstein, Y. I.; Eshtukov, A. V.; Terekhov, V. E.; Asachenko, A. F.; Nechaeva, M. S.; *Green Chem.* **2016**, *18*, 5984. [Crossref]
35. Dyall, L. K.; *Aust. J. Chem.* **1986**, *39*, 89. [Crossref]
36. Meguro, T.; Terashima, N.; Ito, H.; Koike, Y.; Kii, I.; Yoshida, S.; Hosoya, T.; *Chem. Commun.* **2018**, *54*, 7904. [Crossref]
37. Wang, Z.; Liu, Z.; Cheon, S. H.; *Bull. Korean Chem. Soc.* **2015**, *36*, 198. [Crossref]
38. Jin, T.; Kitahara, F.; Kamijo, S.; Yamamoto, Y.; *Chem. Asian J.* **2008**, *3*, 1575. [Crossref]
39. Zhu, Y.; Ren, Y.; Cai, C.; *Helv. Chim. Acta* **2009**, *9*, 171. [Crossref]

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