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Utilizing perhalopyridine-based alkynes as suitable precursors for the synthesis of novel poly(1,2,3-triazolyl)-substituted perhalopyridines†

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A novel series of poly(1,2,3-triazolyl)-substituted perhalopyridines **5a–f** were successfully synthesized from the click reaction of the terminal alkynes (drived from the nucleophilic substitution reactions of PFP **1a** and PCP **1b** with excess amounts of propargyl alcohol) with aryl azides **4a–c** under ultrasonic irradiation. Likewise, the sonication of reaction mixtures containing pyridyl cores **3**, alkyl bromides **6a,b**, and NaN_3 under one-pot conditions afforded their respective aliphatic 1,2,3-triazoles **7a–d** in yields ranging from 71% to 83%. We next developed an effective method for the regioselective preparation of 2,3,4,5-tetrachloro-6-(prop-2-yn-1-yloxy)pyridine **3c** through S_NAr reaction of PCP with propargyl alcohol without the utilization of any catalyst. It was then used to fabricate several ((1,2,3-triazol-4-yl)methoxy)-3,4,5,6-tetrachloropyridines **8a–c** under the reaction conditions. Finally, the $Pd(PPh_3)_4$-catalyzed SMC reaction of tris-triazoles **5b,e** with arylboronic acids **9a–c** offered a practical method for the synthesis of biaryl-embedded poly(1,2,3-triazoles) **10a–f** in good yields.

1. Introduction

Organofluorines (OFs) exhibit a wide range of applications in liquid crystals,[1] agrochemicals,[2] electro-optic devices,[1a,3] and ^{19}F-magnetic resonance imaging (MRI).[4,5a] Proteins and peptides tagged with the fluorine-18 isotope are also applied as radiotracers in positron emission tomography (PET).[5] On the other hand, Organochlorines (OCs) find extensive use as building blocks for chemical research and industrial uses.[6–10] Among these, perhalogenated pyridines offer a high degree of structural diversity and have proven to be useful for searching new materials and therapeutic leads. Using perhalopyridines instead of pyridine itself is a suitable alternative method for the synthesis of substituted-perhalopyridine derivatives. In this regard, the nucleophilic aromatic substitution reactions (S_NAr) of pentafluoropyridne (PFP) and pentachloropyridine (PCP) with different species including oxygen,[11] nitrogen,[12] sulfur,[12e,13] and carbon-centered[12e–14] nucleophiles have been explored. The site-selectivity of reactions is overally determined by several factors including the positioning of halogen atoms on the pyridine core, solvent, the reaction conditions, as well as the strength and nature of nucleophile and base. In general, the replacement of halogen atoms on the pyridine cores takes place in a selective and step-by-step manner.[12e,15] While substitution reaction of PFP with stoichiometric amount of nucleophiles under mildly basic conditions occurs solely at the C-4 position, it can be substituted sequentially at two positions (C-2, C-6) using strong nucleophiles under harshly basic conditions or elevated temperatures. On the basis, Iacono *et al.* succeeded to synthesize 2,3,5,6-tetrafluoro-[*N*-(3-aminopropyl)-ε-caprolactam]-4-pyridine *via* the site-selective reaction of PFP with 1,8-diazabicyclo[5.4.0]undec-7-ene with PFP.[16] The controlled regio-selective S_NAr reaction of PFP with 4-ethynylphenol and phenol has also been led to the formation of 2,6-bis(4-ethynylphenoxy)-3,5-difluoro-4-phenoxypyridine, as a unique polymer precursor suitable for thermal polymerization.[17] Likewise, fluoropyridyl silicone-based oils and network elastomers have been synthesized through hydrosilylation of the derived monomers through regio-controlled functionalization of PFP with alcohols possessing terminal alkenes.[18] Alongside these, semifluorinated trifunctional-ene monomers, which play a crucial role in thiol–ene thermoset materials, are synthesized *via* the site-selective S_NAr reactions of PFP with 4-penten-1-ol or eugenol.[19] PFP has also been assessed as an activator in the synthesis of acyl fluoride from carboxylic acids.[20] Recently, there has been research conducted on the reaction of pentachloropyridine. *o*-Perhalopyridines have been utilized as amination agents under photocatalyst conditions.[21] Among these research, 2′,3′,5′,6′-tetrachloro-4-(dimethylamino)-[1,4′-bipyridin]-1-ium treated with oxygen and nitrogen nucleophile.[11e,22] Our team has previously evaluated the site reactivity of PCP with indoles[12c] and *N*-

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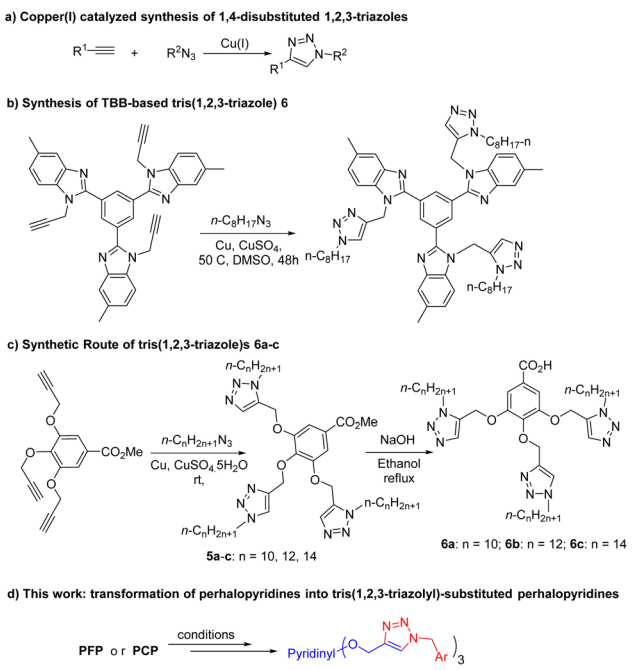
substituted sulfonamides[12d] as potential bioactive candidates. Another report is presented on the intramolecular cyclization of 4-phenylsulfonyl-2,3,5,6-tetrachloropyridine, which results in the rapid formation of a range of novel benzothienopyridine-*S*,*S*-dioxide frameworks under gentle reaction conditions.[23] Ehlers *et al.*[24] investigated the site-selective reaction of pentachloropyridine and aryl boronic acid for the synthesis of mono- and disubstituted pyridine rings. The cross-coupling reaction between cyclobutanone *O*-perchloropyridin-4-yl oxime and nitrostyrene presents an environmentally sustainable approach for the production of cyanoalkylated alkenes.[25]

1,2,3-Triazoles are receiving increasing interest of both academia and industry for their applications in the synthesis of dyes,[26] photographic materials,[27] agrochemicals,[28] photo-stabilizers,[29] and as linkers for binding two biologically potent scaffolds.[30] Although 1,2,3-triazole motifs are not normally found in nature, versatile biological activities have been specified for them.[31–37] Copper(I)-catalyzed 1,3-dipolar cycloaddition (CuAAC) reaction of organic azides with terminal alkynes has become an efficient and rapid method for the regioselective synthesis of 1,4-disubmitted 1,2,3-triazoles (Scheme 1a).[30d,38] On the other hand, the introduction of polytriazole moieties into chemical structures has been proved to be a beneficial strategy in the synthesis of macromolecular 1,2,3-triazole-based functional materials and drug design.[39] For instance, a number of synthesized bistriazoles have been considered as potent antibacterial, antifungal and plasmin inhibitors.[39a,40] Xiong *et al.* have succeeded to synthesize a 1,3,5-tri(1*H*-benzo[*d*]imidazole-2-yl)benzene(TBB)-based tris(1,2,3)triazole as a selective and highly sensitive fluorescent chemosensor for the detection of picric acid (Scheme 1b).[41] Gallic acid-based tris(1,2,3-triazole)s have also been made by a click reaction to form their respective supramolecular columnar liquid crystals (Scheme 1c).[42] likewise, tris-(benzyltriazolylmethyl)amines have been offered as powerful stabilizing ligand for copper(I).[39g] Moreover, various state-of-the-art click chemistry strategies have been developed for the formation of poly(1,2,3-triazole)-based materials with interesting application in molecular recognition, chemical sensing, drug chemistry, biochemistry, and conducting materials.[39c–e,43] Despite all these achievement and progress, there are a few reports on the synthesis of non-polymeric poly(1,2,3-triazole) analogues. Furthermore, the incorporation of perhalopyridine units in 1,2,3-triazole scaffolds opens new avenues for seeking new ploytriazoles with sought after functions in materials science and medicinal chemistry. On the basis and in continuation of our ongoing research on perhalopyridines,[11a,b,44] we were interested to report our findings on the synthesis of a novel series of tris(1,2,3-triazolyl)-substituted perhalopyridines (Scheme 1d).



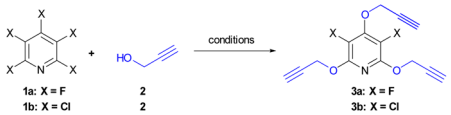
Scheme 1 An overview.

2. Results and discussion

2.1. Synthesis poly(1,2,3-triazolyl)-substituted perhalopyridine derivatives

Our initially efforts were directed towards the synthesis of perhalopyridine-based alkyne precursors. As depicted in Table 1, 3,5-difluoro-2,4,6-tris(prop-2-yn-1-yloxy)pyridine **3a** and 3,5-dichloro-2,4,6-tris(prop-2-yn-1-yloxy)pyridine **3b** were synthesized through the nucleophilic substitution reactions of PFP **1a** and PCP **1b** with propargyl alcohol **2**, respectively. We first aimed to find the best reaction conditions for the preparation of precursor **3a**. In this respect, the reaction of **1a** and propargyl alcohol was carried out under different conditions and the results are shown in Table 1. Stirring a mixture of PFP (1 mmol), **2** (3 mmol), and K_2CO_3 (3.9 mmol) in various solvents including CH_3CN, DMF, DMSO, and THF at room temperature for 48 hours, led to the producing of **3a** in yield ranging from 28% to 60% (entries 1–4). Hence, performing the reaction in DMF solvent using higher molar ratios of reactants was investigated to improve the efficiency of the reaction. While, the treatment of PFP (1 mmol) with **2** (6 mmol) and K_2CO_3 (7.8 mmol) in DMF at r.t for 48 hours afforded product **3a** in the yield of 81% (entry 5), a similar efficacy was also observed when PFP and 2 were used in a 1 : 9 molar ratio (entry 6). However, we succeeded to isolate product **3a** in a yield of 93% by lengthening the reaction time to 72 hours from the r.t reaction of PFP (1 mmol) with **2** (6 mmol) and K_2CO_3 (7.8 mmol) in DMF (entry 7). In continuation, the influence of several factors such as solvent, reactants' molar ratio, and reaction temperature was studied on the reaction of PCP and **2** in the presence of K_2CO_3 as base (Table 1, entries 8–15). Given the corresponding optimal conditions (Table 1, entry 15), a mixture of PCP (1 mmol), **2** (9 mmol), and K_2CO_3 (11.7 mmol) in DMF was heated at 60 °C for 24 hours and product **3b** was obtained in yield of 83%. The validation of chemical structures for **3a** and **3b** was verified through IR and NMR, analyses. The IR spectrum of **3a** and **3b** showed an absorbance bond for the corresponding terminal acetylenic group, respectively in 2127, and 2123 cm^{-1}. The NMR spectrum of these cores was in good agreement with the

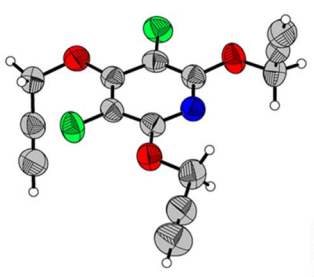
Table 1 Screening on the reaction of perhalopyridine **1** with propargyl alcohol **2**



Entry	**1** (mmol)	**2** (mmol)	K_2CO_3 (mmol)	Solvent	Time (h)	*T* (°C)	Yield[a] (%)
1	**1a** (1)	3	3.9	CH_3CN	48	r.t	50
2	**1a** (1)	3	3.9	DMF	48	r.t	60
3	**1a** (1)	3	3.9	DMSO	48	r.t	56
4	**1a** (1)	3	3.9	THF	48	r.t	28
5	**1a** (1)	6	7.8	DMF	48	r.t	81
6	**1a** (1)	9	11.7	DMF	48	r.t	89
7	**1a (1)**	**6**	**7.8**	**DMF**	**72**	**r.t.**	**93**
8	**1b** (1)	3	3.9	CH_3CN	72	r.t	23
9	**1b** (1)	3	3.9	DMF	72	r.t	28
10	**1b** (1)	3	3.9	DMSO	72	r.t	25
11	**1b** (1)	3	3.9	THF	72	r.t	12
12	**1b** (1)	3	3.9	DMF	24	60	50
13	**1b** (1)	3	3.9	DMF	24	80	35
14	**1b** (1)	6	7.8	DMF	24	60	80
15	**1b (1)**	**9**	**11.7**	**DMF**	**24**	**60**	**83**

[a] Isolated yield.

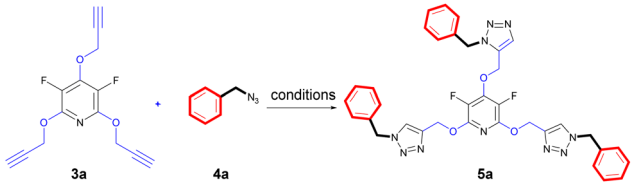
assigned structures. Appearing a single resonance at $\delta = -164.37$ ppm of the ^{19}F-NMR spectrum of **3a** indicates the displacement of the propargyl alcohol in three positions of the PFP ring. The ^{1}H-NMR spectra of **3a** and **3b** exhibit a high degree of resemblance, except for certain variations observed in their chemical shifts. For example, the ^{1}H-NMR spectrum of **3b** shows two triplet peaks at $\delta = 3.67$, and $\delta = 3.56$, with a relative integration ratio of 1 : 2, which are due to the terminal acetylenic hydrogens. Furthermore, the presence of two doublet peaks at $\delta = 4.95$, and $\delta = 5.07$ ppm are attributed to methylenic hydrogens attached to oxygens. The ^{13}C-NMR spectrum of compound **3b** showed 9 distinct signals in agreement with the proposed target molecule. Two appeared signals at $\delta = 55.54$ and $\delta = 61.29$ ppm are related to the methylenic groups, and three signals in the range of 78.05–80.32 ppm were reported due to the presence of the acetylenic carbons. The structure elucidation of the product **3a** was also done by single-crystal X-ray analysis (Scheme 2).



Scheme 2 Crystal structure of **3a**.

The chemical community is interested in preparing polytriazoles for various applications.[39–43] On the other hand, incorporation of halogen atom(s) into organic compounds and polymers have been introduced as a powerful method to change or improve the chemical, physical and/or biological activity of a desired molecule. On the basis, it was objected to produce a novel series of poly(1,2,3-triazolyl)-substituted perhalopyridines. First, the required aryl azides **4a–c** for producing triazolyl scaffolds were prepared using methods described in the literature.[45] Then, the reaction between **3a** and benzyl azide **4a** for the clickable synthesis of compound **5a** was chosen as a model and the effect of parameters such as solvent, copper catalysts, and reaction conditions were investigated on the efficiency of the reaction. The results are summarized in Table 2. The reaction of precursor **3a** (3.5 mmol) with benzyl azide **4a** (11.5 mmol) in the presence of $CuSO_4 \cdot 5H_2O$ (5 mol%) and NaAsc (15 mol%) in CH_3CN at room temperature afforded a trace amount of 2,4,6-tris((1-benzyl-1*H*-1,2,3-triazol-4-yl) methoxy)-3,5 difluoropyridine **5a** after 24 hours. While performing this reaction in DMF solvent led to the production of **5a** in 23% yield, utilizing DMF/H_2O (1 : 1) provided an improvement in the yield of reaction (entries 1 and 2). Accordingly, carrying out the model reaction in several aqueous medium involving THF/H_2O (1 : 1), *t*-BuOH/H_2O (1 : 1), and CH_2Cl_2/H_2O (1 : 1) was done and the product **5a** was obtained in yields ranging from 43% to 90% (entries 4–7). On this basis, CH_2Cl_2/H_2O (1 : 1) was considered as the best solvent of choice (entry 6). Our next experiments showed that the replacement of $CuSO_4 \cdot 5H_2O$ with other copper catalysts including CuI and $Cu(OAc)_2$ reduces the yield of product **5a**. Furthermore, the importance of copper catalyst for the construction of triazole scaffolds was

Table 2 Optimization of the conditions for the reaction of **3a** and **4a** to form 1,2,3-triazole **5a**[a]

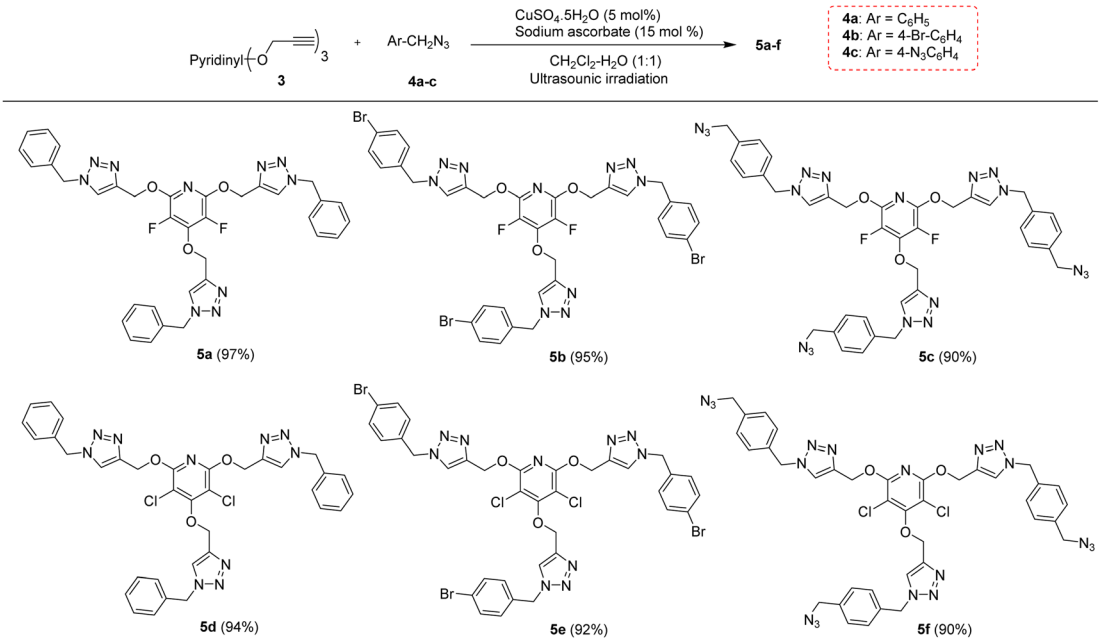


			Ambient conditions	US conditions
Entry	Catalyst (mol%)	Solvent	Time (h)/yield[b] (%)	Time (h)/yield[b] (%)
1	$CuSO_4 \cdot 5H_2O$ (5)	CH_3CN	24/trace	8/trace
2	$CuSO_4 \cdot 5H_2O$ (5)	DMF	24/23	5/23
3	$CuSO_4 \cdot 5H_2O$ (5)	DMF/H_2O (1 : 1)	24/36	5/38
4	$CuSO_4 \cdot 5H_2O$ (5)	THF/H_2O (1 : 1)	24/43	8/48
5	$CuSO_4 \cdot 5H_2O$ (5)	^{t}BuOH/H_2O (1 : 1)	24/80	2/88
6	**$CuSO_4 \cdot 5H_2O$ (5)**	**CH_2Cl_2/H_2O (1 : 1)**	**24/90**	**2/97**
7	$CuSO_4 \cdot 5H_2O$ (9)	CH_2Cl_2/H_2O (1 : 1)	24/90	2/97
8	—	CH_2Cl_2/H_2O (1 : 1)	48/n.r.[c]	8/n.r.
9	CuI (5)	CH_2Cl_2/H_2O (1 : 1)	24/23	2/23
10	$Cu(OAc)_2.H_2O$ (5)	CH_2Cl_2/H_2O (1 : 1)	24/23	24/23

[a] All experiments were run using the reaction of precursor **3a** (3.5 mmol) with benzyl azide **4a** (11.5 mmol) in the presence of NaAsc (15 mol%). [b] Isolated yield. [c] n.r. = no reaction.

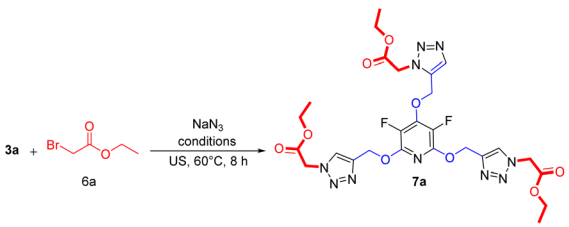
demonstrated when no reaction progress was observed in the treatment of **3a** with **4a** in the absence of copper catalysts (entry 8). As reported in the literature, the necessity of Cu(II) for this reaction is due to its insitu reduction to Cu(I) required for the Copper-Catalyzed Azide–Alkyne Cycloaddition (CuAAC) reactions. Furthermore, the model reaction was carried out under ultrasonic irradiation, and the sonication procedure was identified to be a powerful alternative to the conventional method. In general, the product **5a** was obtained in higher yields and shorter reaction times (entries 1–10). When we increased the amount of copper catalyst, the reaction yield did not change (entry 7). Accordingly, we proceeded to investigate the preparation of tris(1,2,3-triazolyl)-substituted perhalopyridines *via* the reaction of precursors **3** (3.5 mmol) with aryl azides **4a–c** (11.5 mmol) in the presence of $CuSO_4 \cdot 5H_2O$ (5 mol%) and NaAsc (15 mol%) in CH_2Cl_2/H_2O (1 : 1) under ultrasonic irradiation. Lukily, treatment of **3a** with 1-(azidomethyl)-4-bromobenzene **4b** and 1,4-bis(azidomethyl)benzene **4c** under optimal conditions afforded tris(1,2,3-triazolyl)-substituted perfluoropyridines **5b** and **5c** in 95% and 90% yields, respectively. In a similar way, tris(1,2,3-triazolyl)-substituted perchloropyridines **5d–f** were successfully obtained through the reaction of precursor **3b** and aryl azides **4a–c** in yields ranging from 90–94% (Scheme 3). The newly synthesized compounds (**5a–f**) were characterized based on their infrared spectrum as well as ^{1}H, ^{13}C, and ^{19}F-NMR spectra. For example, the structure of tris-triazolyl **5a** was demonstrated by the absence of acetylenic bond in the FT-IR spectrum. The ^{1}H-NMR spectrum of **5a** shows a single sharp peak at $\delta = 8.28$ ppm due to the triazolyl-CH groups, and three singlets at $\delta = 5.40$ (s, 2H, CH_2–N) and $\delta = 5.44$ (s, 4H, CH_2–N), $\delta = 5.59$ (s, 6H, CH_2O) which are related to the three nonequivalent series of methylene bridges. Similarly, the tris-1,2,3-triazole system exhibits a consistent arrangement of aromatic patterns in all instances (refer to the experimental section for more details).

Encouraged by the above results, it was hypothesized that this methodology could be expanded to generate tris(1,2,3-triazoles) containing perhalopyridine moieties using aliphatic triazides **6**. To achieve aliphatic triazoles **7**, the reaction of precursor **3a** and ethyl 2-azidoacetate **6a** was studied to find the optimal reaction conditions. It was found tris(triazole) **7a** does not form a satisfactory yield applying the optimal conditions used for the synthesis of tris(1,2,3-triazoles) **5a–f**. So, we decided to improve the yield of product **7a** through the one-pot reaction of **3a** with a small excess amount of sodium azide and aliphatic bromide in the presence of a copper(II) catalyst with 5 mol% loading under sonication, and the results are shown in Table 3. The corresponding tris(triazole) **7a** was obtained in the highest yield *via* the one-pot click reaction **3a** (1 mmol), sodium azide (3.6 mmol), ethyl 2-bromoacetate **6a** (3 mmol), $CuSO_4 \cdot 5H_2O$ (5 mol%) and sodium ascorbate (15 mol%) in ^{t}BuOH/H_2O (1 : 3) under ultrasonic irradiation for 8 hours at 60 °C (Table 3, entry 5). Under these conditions, precursor **3a** was also reacted with 3-bromoprop-1-ene **6b** for 8 hours and the corresponding aliphatic triazole **7b** was isolated in 83% yield (Scheme 3). Similarly, pyridyl core **3b** was submitted to the reaction with ethyl 2-bromoacetate **6a** and bromoprop-1-ene **6b**, and their respective tris(triazoles) **7c** and **7d** were obtained in yields of 78% and 71%, respectively (Scheme 4). This study highlighted the challenges and outcomes of synthesizing tris(triazoles) with perfluoropyridine moieties, emphasizing the importance of reaction conditions and reactant selection for achieving the desired products, efficiently.



Scheme 3 The chemical structures of synthesized tris(1,2,3-triazolyl)-substituted perhalopyridines **5a–f**.

Table 3 Investigation of the optimal conditions for the reaction of **3a** with ethyl 2-bromoacetate **6a**

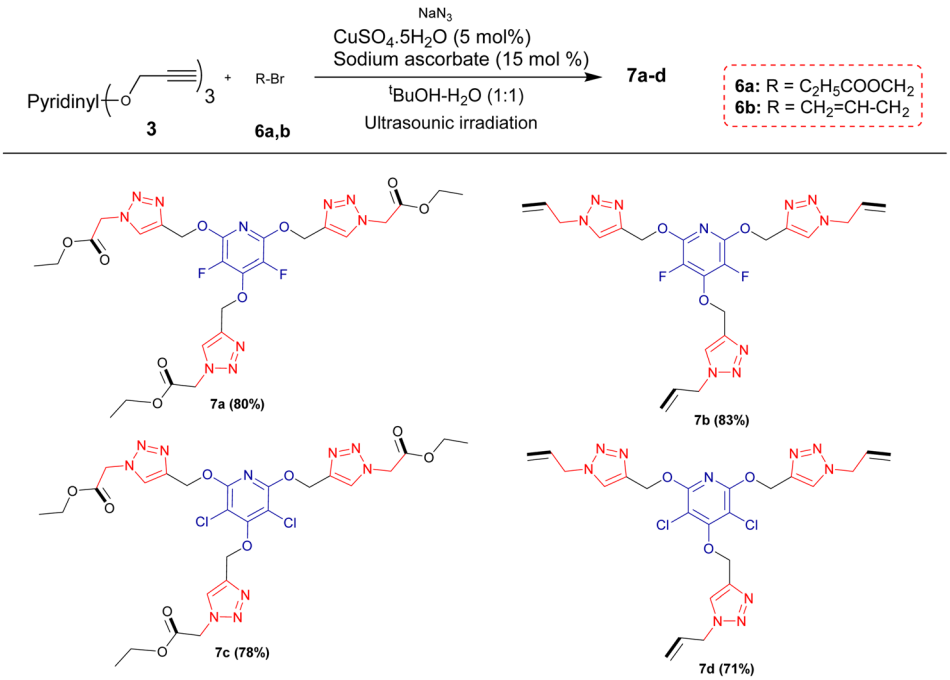


Entry	Solvent (1 : 3)	Catalyst[a]	Yield[b] (%)
1	CH_2Cl_2/H_2O (1 : 3)	$CuSO_4 \cdot 5H_2O$/NaAsc	70
2	CH_2Cl_2/H_2O (1 : 3)	$Cu(OAc)_2 \cdot H_2O$/NaAsc	68
3	CH_2Cl_2/H_2O (1 : 3)	$CuSO_4 \cdot 5H_2O$/NaAsc	73
4	^{t}BuOH/H_2O (1 : 3)	$Cu(OAc)_2 \cdot H_2O$/NaAsc/1,10-Phen.H_2O	78
5	**^{t}BuOH/H_2O (1 : 3)**	**$CuSO_4 \cdot 5H_2O$/NaAsc**	**80**

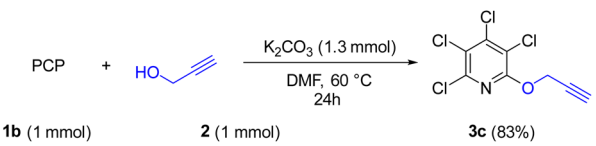
[a] $CuSO_4 \cdot 5H_2O$ and $Cu(OAc)_2.H_2O$ at 5 mol%, along with NaAsc 15 mol%. [b] Isolated yield.

2.2. Synthesis of 2-((1-benzyl-1*H*-1,2,3-triazol-4-yl)methoxy)-3,4,5,6-tetrachloropyridine derivatives

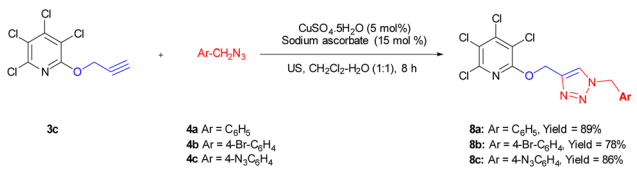
Due to the significance of site-selective nucleophilic substitution reactions involving pentachloropyridine,[44] particularly position 4 as the primary preference against nucleophilic attacks, herein, we describe, for the first time, the direct execution of nucleophilic substitution at the C-2 position of pentachloropyridine without the utilization of any catalyst. In this respect, we were interested in synthesizing 2,3,4,5-tetrachloro-6-(prop-2-yn-1-yloxy)pyridine **3c** through regioselective nucleophilic substitution reaction of pentachloropyridine with propargyl alcohol under those conditions reported in section 2.1 but using PCP and propargyl alcohol in a 1 : 1 molar ratio. Accordingly, the reaction of PCP (1 mmol) with **2** (1 mmol) in the presence of K_2CO_3 (1.3 mmol) in DMF at 60 °C for 24 hours afforded product **3c** in 83% yield (Scheme 5). The derived product **3c** (1 mmol) was, then, submitted to the reactions with aryl azides **4a–c** (1.2 mmol) in the presence of $CuSO_4 \cdot 5H_2O$ (5 mol%) and NaAsc (15 mol%) in CH_2Cl_2/H_2O (1 : 1) under ultrasonic irradiation at 60 °C for 8 hours and their respective ((1,2,3-triazol-4-yl)methoxy)-3,4,5,6-tetrachloropyridines **8a–c** were synthesized in yields of 78–89% (Scheme 6). Furthermore, the structure of **8b** was confirmed by X-ray crystallographic data (Scheme 7). The structure elucidation of **3a** was first performed by infrared and NMR spectroscopy. In the FT-IR spectrum of product **3c**, the absorption band of the acetylenic group is observed at



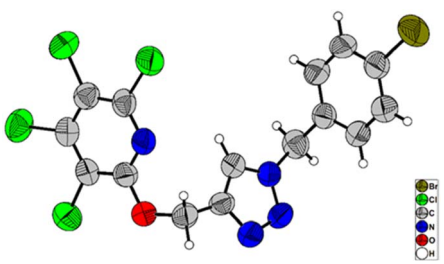
Scheme 4 Synthesis of aliphatic tris(1,2,3-triazoles) bearing perhalopyridine moieties.



Scheme 5 Site-selective synthesis of 2,3,4,5-tetrachloro-6-(prop-2-yn-1-yloxy)pyridine **3c**.



Scheme 6 Synthesis of ((1,2,3-triazol-4-yl)methoxy)-3,4,5,6-tetrachloropyridine **8a–c** derivatives. Reaction conditions: **3c** (1 mmol) was, then, aryl azides **4a–c** (1.2 mmol), $CuSO_4 \cdot 5H_2O$ (5 mol%), NaAsc (15 mol%) in CH_2Cl_2/H_2O (1 : 1) under ultrasonic irradiation at 60 °C for 8 hours.



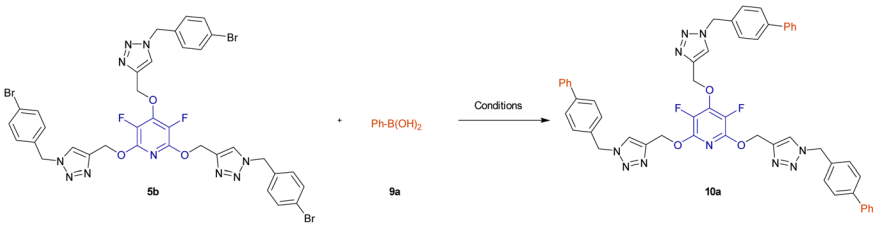
Scheme 7 X-ray crystal structure of **8b**.

2132 cm^{-1}. The ^{1}H-NMR spectrum of **3c** shows two distinct peaks at $\delta = 3.65$, and $\delta = 5.05$ ppm which are attributed to the acetylenic and methylenic hydrogens, respectively. In the ^{13}C-NMR, five signals appearing in the region $\delta = 117.04$–155.94 ppm are related to the fourth type carbons of the pyridine ring, and three distinct signals in the $\delta = 79.19$, $\delta = 78.36$, and $\delta = 56.46$ ppm can be attributed to the presence of acetylenic and methylenic groups, respectively.

2.3. Synthesis of biaryl-embedded perhalopyridine-based poly(1,2,3-triazoles)

Biaryls are an integral part of various natural products[46] and biologically active compounds.[47] They are also fundamental building blocks[46d] in organic synthesis and material chemistry. Biaryl scaffolds are traditionally formed *via* the transition-metal catalyzed Suzuki–Miyaura coupling (SMC) reactions of aryl boronic acids with aryl halides.[48] After the successful synthesis of tris(1,2,3-triazoles) **5b** or **5e**, we aimed to synthesis their respective biaryl-embedded 1,2,3-triazoles. Therefore, the Suzuki–Miyaura cross-coupling (SMC) reaction of tris-triazole **5b** and phenylboronic acid **9a** in the presence of $Pd(PPh_3)_4$ was chosen as a model, and the effect of different variants including solvent, base, molar ratios of substrates and catalyst loading was explored under thermal conditions. The results are listed in Table 4. In the best conditions, the coupling product **10a** was obtained in yield of 72% through stirring a mixture of **5a** (1 mmol), phenylboronic acid **9a** (3.8 mmol), Cs_2CO_3 (4.5 mmol), and $[Pd(PPh_3)_4]$ (0.045 mol%) in DMF/H_2O (1 : 3) at 70 °C for 24 hours. Under these conditions, tris(1,2,3-triazolyl)-substituted perfluoropyridine **5b** was also reacted with 2-naphthylboronic acid **9b** to achieve the corresponding biaryl-embedded perfluoropyridine-based poly(1,2,3-triazoles) **10b** in

Table 4 Screening of the reaction conditions for the SMC reaction of compound **5b** with phenylboronic acid **9a**[a]



Entry	Base	**5b : 9a**: base (mmol)	Solvent (1 : 3)	$Pd(PPh_3)_4$ (mol%)	Time (h)	Yield[b] (%)
1	Et_3N	1 : 3.8 : 4.5	DMF/H_2O	0.018	24	38
2	Et_3N	1 : 3.8 : 4.5	THF/H_2O	0.018	24	25
3	K_3PO_4	1 : 3.8 : 4.5	DMF/H_2O	0.018	24	51
4	K_2CO_3	1 : 3.8 : 4.5	DMF/H_2O	0.018	24	53
5	K_2CO_3	1 : 4.2 : 4.5	DMF/H_2O	0.045	24	65
6	**Cs_2CO_3**	**1 : 3.8 : 4.5**	**DMF/H_2O**	**0.045**	**24**	**72**
7	Cs_2CO_3	1 : 4.2 : 4.5	DMF/H_2O	—	24	—

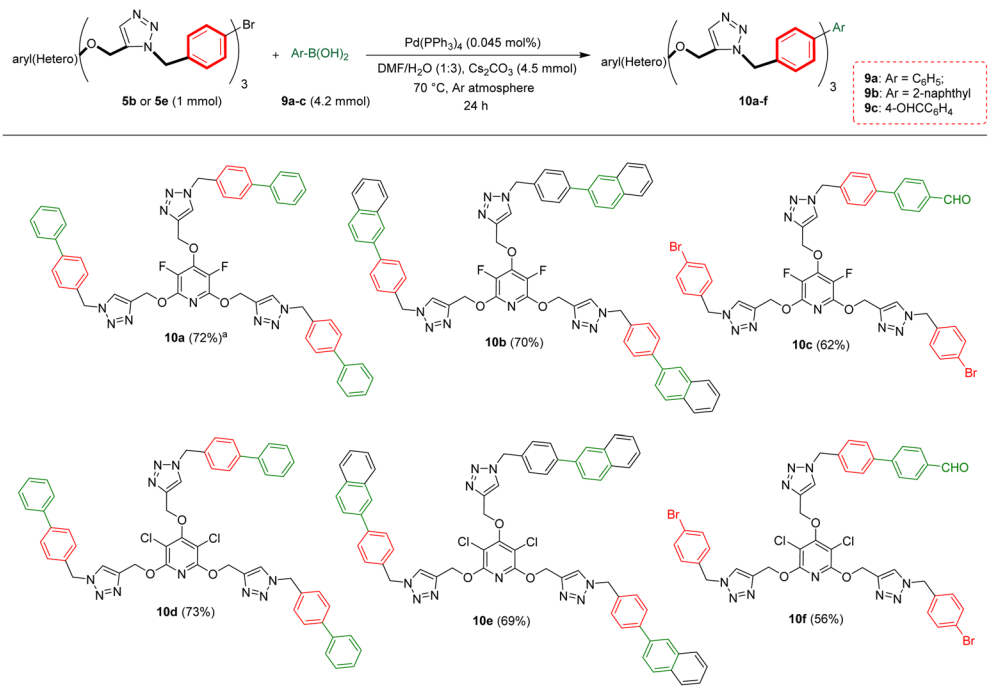
[a] All the reactions were run in 4 mL of solvent at 70 °C. [b] Isolated yield.

70% yield. However, in the treatment of **5b** with 4-formylphenylboronic acid **9c** under optimized conditions, the coupling reaction took place at only one position, and product **10c** gained in yield of 62% (Scheme 7). In a similar way, the reaction of tris(1,2,3-triazolyl)-substituted perchloropyridine **5e** with arylboronic acids **9a–c** afforded their respective biaryl-embedded perchloropyridine-based poly(1,2,3-triazoles) **10d** and **10e** in good yields (Scheme 8). As similar to **5b**, aryl bromide **5e** was coupled with 4-formylphenylboronic acid **9c** at only one position under optimal conditions, and the corresponding product **10f** was isolated in a yield of 56%. The structures of coupling products were confirmed using FT-IR and NMR analyses.

3. Experimental details

3.1. General information

All chemicals purchased from Merck chemical company and used without further purification unless specified. The advancement of the reactions was tracked through TLC analysis



Scheme 8 $Pd(PPh_3)_4$ catalyzed Suzuki–Miyaura coupling reaction of aryl bromides **5b** and **5e** with arylboronic acids **9a–c**. [a]Isolated yield.

on polyester sheets coated with silica gel-60 and fluorescent indicator (F-252) obtained from Merck. Melting points were conducted on a Stuart SMP2 apparatus and left uncorrected. IR spectra were recorded on a Nicolet-Impact 400D spectrophotometer using KBr pellets. ^{1}H-, ^{13}C-, and ^{19}F-NMR spectra were recorded on a Bruker Ultrashield-400 NMR spectrometer using DMSO-d_6 as a solvent, while those for ^{19}F were reported in ppm relative to $CFCl_3$ as the standard. The ultrasonic device used was an UP 400 S instrument from Dr Hielscher GmbH. An S3 immersion horn emitting 24 kHz ultrasound at intensity levels tunable to maximum sonic power density of 460 W cm^2 was used. Sonication was carried out at 100% (maximum amplitude 210 lm). A 3 mm long sonotrode (maximum immerse depth of 90 mm) was immersed directly into the reaction mixture.

3.2. Synthesis of 3,5-difluoro-2,4,6-tris(prop-2-yn-1-yloxy) pyridine 3a

In a 25 mL round-bottomed flask, a mixture of propargyl alcohol (6 mmol), K_2CO_3 (7.8 mmol), and DMF (5 mL) was stirred at room temperature for 30 minutes. Next, PFP (1 mmol) was added and the resulting mixture was stirred at room temperature for 72 hours. Then, the reaction mixture was poured into 10 mL water and extracted with ethyl acetate (2 × 30 mL). The organic phase was dried over $MgSO_4$, and the solvent evaporated. The pure product **3a** was obtained in 93% yield after washing with hexane.

Light yellow solid. Yield 93%. MP 118–120 °C; IR (KBr) $\tilde{\nu}$ 3283, 2943, 2127, 1632 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ 5.08 (d, J = 2.4 Hz, 2H, CH_2–O), 5.02 (d, 4H, J = 2.4 Hz, CH_2–O), 3.72 (t, 1H, J = 4.9 Hz, acetylene-H), 3.54 (t, J = 4.9 Hz, 2H, acetylene-H) ppm. ^{13}C-NMR (126 MHz, DMSO-d_6) δ 144.16 (dm, $^2J_{CF}$ = 10.90 Hz, C2,6-py), 143.45 (d, $^2J_{CF}$ = 10.40 Hz, C4-py), 134.24 (d, $^1J_{CF}$ = 248.9 Hz, C3,5-py), 80.53 (acetylene-CH), 79.20 (acetylene-C), 78.42 (acetylene-CH), 78.13 (acetylene-C), 61.55 (CH_2–O), 54.81 (CH_2–O) ppm. ^{19}F NMR (470 MHz, DMSO-d_6) δ −164.37 (2F, F3,5-py).

3.3. Synthesis of 3,5-dichloro-2,4,6-tris-prop-2-ynyloxy-pyridine 3b

In a 25 mL round-bottomed flask, a mixture of propargyl alcohol (9 mmol), K_2CO_3 (11.7 mmol), and DMF (5 mL) was stirred at room temperature for 30 minutes. Next, PCP (1 mmol) was added and the resulting mixture was stirred at 60 °C for 24 hours. Then, the reaction mixture was poured into 10 mL water and extracted with ethyl acetate (2 × 30 mL). The organic phase was dried over $MgSO_4$, and the solvent evaporated. The pure product **3b** was obtained in 83% yield after washing with hexane.

Light brown solid. Yield 83%. MP 121–124 °C. IR (KBr) $\tilde{\nu}$ 3277, 2513, 2123, 1796 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ 5.07 (d, 4H, J = 2.4 Hz, CH_2–O), 4.95 (d, 2H, J = 2.4 Hz, CH_2–O), 3.67 (t, 1H, J = 5 Hz, acetylene-H), 3.56 (t, 2H, J = 5 Hz, acetylene-H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6) δ 160.30, 155.04, 104.19, 80.32 (acetylene-CH), 79.07 (acetylene-C), 78.53 (acetylene-CH), 78.05 (acetylene-C), 61.29 (CH_2–O), 55.54 (CH_2–O) ppm.

3.4. General procedure for the synthesis of aryl azides 4a–c (ref. 45)

Aryl azides **4a–c** were prepared according to the reported method in the literature.[41] To a stirred solution of NaN_3 (5.5 mmol) in DMSO (5.0 mL) was added benzyl bromide (5.0 mmol). The resulting mixture was stirred at 80 °C overnight. The reaction mixture was then cooled to room temperature and diluted with water (15 mL), it was extracted with diethyl ether (3 × 10 mL) and washed with brine, dried over $MgSO_4$, and concentrated under a vacuum to give the products **4a–c** as colorless liquids in quantitative yields. They were used directly without further purification.

3.5. General procedure for the synthesis of tris(1,2,3-triazoles) 5a–f under ultrasonic irradiation

Precursors **3a,b** (3.5 mmol) was dissolved in CH_2Cl_2/H_2O (5 mL, 1 : 1), aryl azides **4a–c** (11.5 mmol), $CuSO_4 \cdot 5H_2O$ (5 mol%) and NaAsc (15 mol%) were added and the resulting mixture was sonicated at 60 °C for 8 hours. The completion of the reaction was controlled by TLC until the consumption of precursors **3**. Then, H_2O (5 mL) was added to the mixture, and the precipitate was collected by filtration, washed thoroughly with H_2O, and CH_2Cl_2, and dried under vacuum. The crude was purified by column chromatography using CH_2Cl_2/MeOH (95/5) as eluent to obtain products **5a–f**.

2,4,6-Tris((1-benzyl-1*H*-1,2,3-triazol-4-yl)methoxy)-3,5-difluoropyridine 5a. White solid. Yield 97%. MP 165–168 °C. IR (KBr) $\tilde{\nu}$ 3726, 3630, 3448, 3137, 3087, 3032, 2956 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.29 (s, 3H, tetrazole-H), 7.26–7.40 (m, 15H, Ar–H), 5.59 (s, 6H, CH_2O), 5.44 (s, 4H, CH_2–N), 5.40 (s, 2H, CH_2–N). ^{13}C NMR (126 MHz, DMSO-d_6): δ 144.90 (dm, $^2J_{CF}$ = 10.01 Hz, C2,6-py), 143.94 (d, $^2J_{CF}$ = 8.67 Hz, C4-py), 143.03 (triazole-C), 142.38 (triazole-C), 136.42 (Ar–C), 134.0 (d, $^1J_{CF}$ = 247.5 Hz, C3,5-py), 129.21 (Ar–CH), 129.18 (Ar–CH), 128.61 (Ar–CH), 128.56 (Ar–CH), 128.46 (Ar–CH), 128.17 (Ar–CH), 125.9 (alkene-CH), 125.4 (alkene-CH), 66.67 (CH_2–O), 60.03 (CH_2–O), 53.32 (CH_2–N), 53.26 (CH_2–N) ppm. ^{19}F NMR (470 MHz, DMSO-d_6) δ −164.61 (2F, F3,5-py).

2,4,6-Tris((1-(4-bromobenzyl)-1*H*-1,2,3-triazol-4-yl)methoxy)-3,5-difluoropyridine 5b. White solid. Yield 95%. MP 184–186 °C; IR (KBr) $\tilde{\nu}$ 3725, 3431, 1626, 1491 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8–30 (s, 3H, tetrazole-H), 7.55 (d, J = 8.3 Hz, 6H, Ar–H), 7.27 (d, J = 8.4 Hz, 4H), 7.20 (d, J = 8.5 Hz, 2H), 5.58 (s, 6, CH_2O), 5.46 (s, 4H, CH_2–N), 5.40 (s, 2H, CH_2–N) ppm. ^{13}C NMR (125 MHz, DMSO-d_6): 144.91 (m, C2,6-py), 144.01 (m, C4-py), 143.08, 142.43, 135.78, 135.01 (d, $^1J_{CF}$ = 247.5 Hz, C3,5-py), 133.03, 132.12, 130.66, 130.49, 125.84 (alkene-CH), 125.45, 121.90, 121.87 (alkene-CH), 66.65 (CH_2–O), 60.01 (CH_2–O), 52.58 (CH_2–N), 52.55 (CH_2–N) ppm. ^{19}F NMR (470 MHz, DMSO-d_6) δ −164.62 (2F, F3,5-py).

2,4,6-Tris((1-(4-(azidomethyl)benzyl)-1*H*-1,2,3-triazol-4-yl) methoxy)-3,5-difluoropyridine 5c. White solid. Yield 90%. MP 200 °C (dec); IR (KBr) $\tilde{\nu}$ 3726, 3630, 3448, 3137, 2927, 2099, 1626 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8–26 (s, 3H, tetrazole-H), 7.33–7.35 (m, 12H, Ar–H), 5.60 (s, 6, CH_2O), 5.45 (s, 4H, CH_2–N), 5.40 (s, 2H, CH_2–N), 4.46 (s, 2H, CH_2–N_3), 4.41 (s,

4H, CH_2–N_3) ppm. ^{13}C NMR (126 MHz, DMSO-d_6) 162.71, 143.87 (m), 142.99, 142.37 (m), 142.33, 136.28, 136.10, 135.99 134.18 (d, $^1J_{CF}$ = 203.75 Hz, C3,5-py), 129.17, 128.73, 128.50, 125.39 (alkene-CH), 66.61 (CH_2–O), 60.01 (CH_2–O), 53.72 (CH_2–N), 52.92 (CH_2–N), 36.19, 31.20 ppm. ^{19}F NMR (470 MHz, DMSO-d_6) δ −164.62 (2F, F3,5-py).

2,4,6-Tris((1-benzyl-1*H*-1,2,3-triazol-4-yl)methoxy)-3,5-dichloropyridine 5d. White solid. Yield 94%. MP 175–177 °C; IR (KBr) $\tilde{\nu}$ 3726, 3449, 3132, 3066, 3032, 2953, 1576 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.33–8.35 (3H, tetrazole-H), 7.27–7.36 (m, 15H, Ar–H), 5.60 (6, CH_2O), 5.50 (4H, CH_2–N), 5.22 (2H, CH_2–N) ppm. ^{13}C-NMR (126 MHz, DMSO-d_6) δ 160.79, 155.75, 142.89, 136.45, 136.40,129.20 (Ar–CH), 129.15 (Ar–CH), 128.87 (Ar–CH), 128.60 (Ar–CH), 128.52 (Ar–CH), 128.43 (Ar–CH), 128.15 (alkene-CH), 125.99, 125.42, 103.67 (alkene–CH), 66.57 (CH_2–O), 60.77 (CH_2–O), 53.31 (CH_2–N), 53.23 (CH_2–N) ppm.

2,4,6-Tris((1-(4-bromobenzyl)-1*H*-1,2,3-triazol-4-yl)methoxy)-3,5-dichloropyridine 5e. Light brown solid. Yield 92%. MP 200–203 °C; IR (KBr) $\tilde{\nu}$ 3841, 3725, 3448, 3061, 2953 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8–30 (s, 3H, tetrazole-H), 7.51–7.55 (m, 6H, Ar–H), 7.19–7.29 (m, 6H, Ar–H), 5.58 (s, 6, CH_2O), 5.51 (s, 4H, CH_2–N), 5.21 (s, 2H, CH_2–N) ppm. ^{13}C-NMR (126 MHz, DMSO-d_6) δ 155.74, 142.93, 135.76, 132.12 (Ar–CH), 132.07 (Ar–CH), 130.68 (Ar–CH), 130.46 (Ar–CH), 126.01 (Ar–CH), 125.45 (Ar–CH), 121.90 (alkene-CH), 103.69 (alkene-CH), 66.56 (CH_2–O), 60.75 (CH_2–O), 52.58 (CH_2–N), 52.54 (CH_2–N) ppm.

2,4,6-Tris((1-(4-(azidomethyl)benzyl)-1*H*-1,2,3-triazol-4-yl) methoxy)-3,5-dichloropyridine 5f. Light brown solid. Yield 90%. MP 250 °C (dec); IR (KBr) $\tilde{\nu}$ 3726, 3424, 3136, 2949, 2098, 1561. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.33 (s, 3H, tetrazole-H), 7.22–7.43 (m, 12H, Ar–H), 5.61–5.48 (m, 12H, CH_2O, CH_2–N), 5.22 (s, 2H, CH_2N_3), 4.41 (s, 4H, CH_2N_3) ppm. ^{13}C-NMR (126 MHz, DMSO-d_6) δ 135.76, 132.16, 132.11 (Ar–CH), 131.89, 130.60 (Ar–CH), 130.48, 129.07 (Ar–CH), 128.33 (Ar–CH), 127.80 (Ar–CH), 127.55, 125.37, 125.36 (Ar–CH), 121.87 (alkene-CH), 115.68 (alkene-CH), 67.90 (CH_2–O), 60.03 (CH_2–O), 52.56 (CH_2–N), 52.55 (CH_2–N), 38.58, 30.27 ppm.

3.6. General procedure for the synthesis of tris(1,2,3-triazoles) 7a–d under ultrasonic irradiation

To a mixture of precursors **3a,b** (1 mmol), aliphatic bromides **6a,b** (3 mmol), and NaN_3 (3.6 mmol) in ^{t}BuOH/H_2O (8 mL, 1 : 3 v/v), was added $CuSO_4 \cdot 5H_2O$ (5 mol%) and AscNa (15 mol%). The mixture was then sonicated at 60 °C for the appropriate time. Finally, the crude product was purified by column chromatography using CH_2Cl_2/MeOH (95 : 5) as eluent to obtain the pure products **7a–d**.

Triethyl 2,2′,2″-((((3,5-difluoropyridine-2,4,6-triyl)tris(oxy)) tris(methylene))tris(1*H*-1,2,3-triazole-4,1-diyl))triacetate 7a. White solid. Yield 80%. MP 153–155 °C; IR (KBr) $\tilde{\nu}$ 3726, 3146, 2964, 2100, 1743, 1626 cm^{-1}. ^{1}H-NMR (500 MHz, DMSO-d_6): δ 8.26 (s, 3H, tetrazole-H), 5.52 (s, 4H, CH_2O), 5.47 (s, 2H, CH_2–O), 5.39 (s, 6H, CH_2–N), 4.14–4.19 (q, 6H, J = 7.9 Hz, CH_2), 1.20 (t, 9H, J = 7.6 Hz, CH_3) ppm. ^{13}C NMR (126 MHz, DMSO-d_6) δ 167.56, 144.90 (dm, $^2J_{CF}$ = 11.25 Hz, C2,6-py), 144.05, 143.96, 142.76, 142.12, 133.96 (d, $^1J_{CF}$ = 245 Hz, C3,5-py), 126.99, 126.68, 66.57, 61.93, 60.00, 50.86, 14.36 ppm. ^{19}F NMR (470 MHz, DMSO-d_6) δ −164.83 (2F, F3,5-py).

2,4,6-Tris((1-allyl-1*H*-1,2,3-triazol-4-yl)methoxy)-3,5-difluoropyridine 7b. Light brown liquid. Yield 83%. IR (KBr) $\tilde{\nu}$ 3726, 3375, 2926, 2139, 1657, 1625. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.21 (s, 3H, tetrazole-H), 5.95–6.09 (m, 3H, CH), 5.51 (s, 4H, CH_2O), 5.44 (s, 2H, CH_2–O), 5.16–5.25 (ddt, 6H, CH=), 5.01–5.05 (m, 6H, CH_2–N) ppm. ^{13}C-NMR (126 MHz, DMSO-d_6) δ 144.94 (dm, $^2J_{CF}$ = 10 Hz, C2,6-py), 144.53, 144.02 (m), 143.18, 142.89, 142.24, 134.21 (d, $^1J_{CF}$ = 208.5 Hz, C3,5-py), 125.50, 125.11, 119.25, 66.64 (CH_2–O), 60.01 (CH_2–O), 55.20 (CH_2–N), 52.18 (CH_2–N) ppm. ^{19}F NMR (470 MHz, DMSO-d_6) δ −164.80 (2F, F3,5-py).

Triethyl 2,2′,2″-((((3,5-dichloropyridine-2,4,6-triyl)tris(oxy)) tris(methylene))tris(1H-1,2,3-triazole-4,1-diyl))triacetate 7c. White solid. Yield 78%. MP 168–170 °C; IR (KBr) $\tilde{\nu}$ 2923, 2855, 1638, 1420 cm^{-1}. ^{1}H-NMR (500 MHz, DMSO-d_6): δ 8.33 (s, 3H, tetrazole-H), 5.62 (s, 4H, CH_2–O), 5.45 (s, 6H, CH_2–N), 5.30 (s, 2H, CH_2–O), 4.14–4.24 (q, 6H, J = 7.8 Hz, CH_2), 1.23 (t, 9H, J = 6.1 Hz CH_3) ppm. ^{13}C NMR (126 MHz, DMSO-d_6) δ 167.69, 167.57, 160.94, 155.79, 142.66, 142.13, 127.24, 126.84, 103.69, 66.63, 61.99, 60.78, 50.90, 14.41 ppm.

2,4,6-Tris((1-allyl-1*H*-1,2,3-triazol-4-yl)methoxy)-3,5-difluoropyridine 7d. Light brown liquid. Yield 71%. IR (KBr) $\tilde{\nu}$ 3652, 3418, 2923, 1720, 1578. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.21–8.27 (s, 3H, tetrazole-H), 5.98–6.09 (m, 3H, CH), 5.55 (s, 4H, CH_2O), 5.50 (s, 2H, CH_2–O), 5.20–5.26 (ddt, 6H, CH=), 5.00–5.04 (m, 6H, CH_2–N) ppm. ^{13}C-NMR (126 MHz, DMSO-d_6): δ 155.79, 142.73, 142.71, 133.13, 125.74, 125.21 (Ar–C), 124.46, 119.31, 118.94, 103.73, 66.70 (CH_2–O), 60.80 (CH_2–O), 52.17 (CH_2–N), 52.06 (CH_2–N) ppm.

3.7. Synthesis of 2,3,4,5-tetrachloro-6-(prop-2-yn-1-yloxy) pyridine 3c

In a 25 mL round-bottomed flask, a mixture of propargyl alcohol (1 mmol), K_2CO_3 (1.3 mmol), and DMF (2 mL) was stirred at room temperature for 30 minutes. Next, PCP (1 mmol) was added and the resulting mixture was stirred at 60 °C for 24 hours. Then, the reaction mixture was poured into 10 mL water and extracted with ethyl acetate (2 × 30 mL). The organic phase was dried over $MgSO_4$, and the solvent evaporated. The pure product **3c** was obtained in 83% yield after washing with hexane.

Brown solid. Yield 83%. IR (KBr) $\tilde{\nu}$ 3394, 3143, 2919, 2132, 1627. ^{1}H NMR (500 MHz, DMSO-d_6) δ 5.05 (d, 2H, CH_2–O), 3.65 (t, 1H, acetylene-H) ppm. ^{13}C-NMR (125 MHz, DMSO-d_6) δ 155.94, 143.79, 143.54, 117.04, 79.19 (acetylene-C), 78.36 (acetylene-CH), 56.46 (CH_2–O) ppm.

3.8. Synthesis of ((1,2,3-triazol-4-yl)methoxy)-3,4,5,6-tetrachloropyridine 8a–c derivatives

Precursors **3c** (1 mmol) were dissolved in CH_2Cl_2/H_2O (5 mL, 1 : 1). Aryl azides **4a–c** (1.2 mmol), $CuSO_4 \cdot 5H_2O$ (5 mol%), and NaAsc (15 mol%) were added and the resulting mixture was sonicated at 60 °C for 8 hours. The completion of the reaction was controlled by TLC until the consumption of precursors **3c**. Then, H_2O (5 mL) was added to the mixture, and the precipitate was collected by filtration, washed thoroughly with H_2O, and

CH_2Cl_2, and dried under vacuum. The crude was purified by column chromatography using EtOAc/Hexane (50/20) as eluent to obtain products **8a–c**.

2-((1-Benzyl-1*H*-1,2,3-triazol-4-yl)methoxy)-3,4,5,6-tetrachloropyridine 8a. White solid. Yield 89%. MP 135–137 °C; IR (KBr) $\tilde{\nu}$ 3416, 2924, 2853, 1618, 1497 cm^{-1}. ^{1}H-NMR (500 MHz, DMSO-d_6) δ 8.37 (s, 1H, tetrazole-H), 7.28–7.36 (m, 5H, Ar-CH), 5.63 (s, 2H, CH_2–O), 5.33 (s, 2H, CH_2–N) ppm. ^{13}C-NMR (126 MHz, DMSO-d_6) δ 144.43, 143.35, 135.81, 133.21, 132.11, 131.28, 130.62, 125.31, 121.88, 59.68 (CH_2–O), 52.56 (CH_2–N) ppm.

2-((1-(4-Bromobenzyl)-1*H*-1,2,3-triazol-4-yl)methoxy)-3,4,5,6-tetrachloropyridine 8b. White crystal. Yield 78%. MP 146–147 °C; IR (KBr) $\tilde{\nu}$ 3726, 3423, 2929, 2513, 1796, 1721, 1639 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.67 (s, 1H, tetrazole-H), 7.52–7.55 (d, 2H, Ar–H), 7.18–7.20 (d, 2H, Ar–CH), 5.56 (s, 2H, CH_2–N), 5.52 (s, 2H, CH_2–O) ppm. ^{13}C-NMR (125 MHz, $CDCl_3$) δ 156.20, 144.09, 143.75, 142.97, 133.38, 132.35, 129.75, 123.95, 123.07, 122.40, 117.30, 61.43 (CH_2–O), 53.56 (CH_2–N) ppm.

2-((1-(4-Bromobenzyl)-1*H*-1,2,3-triazol-4-yl)methoxy)-3,4,5,6-tetrachloropyridine 8c. Light brown solid. Yield 86%. MP 159–162 °C; IR (KBr) $\tilde{\nu}$ 3726, 3416, 2924, 2853, 1629, 1497 cm^{-1}. ^{1}H-NMR (500 MHz, DMSO-d_6) δ 8.36 (1H, tetrazole-H), 6.90–7.64 (m, 4H, Ar–H), 5.60–5.70 (m, 2H, CH_2–O), 5.31–5.45 (m, 2H, CH_2–N), 3.55 (s, 2H, CH_2–N_3), 5.28–5.48 (m, 2H, CH_2–N) ppm. ^{13}C-NMR (125 MHz, DMSO-d_6): δ 143.57, 141.96, 136.25, 132.17, 132.04, 129.29, 129.16, 128.87, 125.87, 61.83 (CH_2–O), 53.62 (CH_2–N) ppm.

3.9. General procedure for SMC reactions of triazolyl bromides 5b,e with arylboronic acids 9a–c under thermal condition

A mixture of triazolyl bromides **5a,e** (1 mmol), phenylboronic acid **9a** (3.8 mmol), Cs_2CO_3 (4.5 mmol), and $[Pd(PPh_3)_4]$ (0.045 mol%) in DMF/H_2O (1 : 3) was stirred at 70 °C under argon atmosphere for 24 hours. The catalyst was separated by filtration and the crude product was purified by column chromatography on silica gel using CH_2Cl_2–MeOH (9 : 1) as eluent to obtain the pure coupling products **10a–f**.

2,4,6-Tris((1-([1,1′-biphenyl]-4-ylmethyl)-1*H*-1,2,3-triazol-4-yl)methoxy)-3,5-difluoropyridine 10a. White solid. Yield 72%. MP 203–207 °C; IR (KBr) $\tilde{\nu}$ 3062, 2957, 2929, 1723, 1626 cm^{-1}. ^{1}H-NMR (500 MHz, DMSO-d_6) δ 8.17 (s, 3H, tetrazole-H), 7.58–7.66 (m, 12H, Ar–H), 7.33–7.43 (m, 10H), 7.19–7.27 (m, 4H), 5.55–5.64 (m, 6H, CH_2O), 5.40–5.48 (m, 4H, CH_2–N), 5.25 (s, 2H, CH_2–N) ppm. ^{13}C NMR (126 MHz, DMSO-d_6) δ 167.40, 144.00 (m), 143.05, 142.43, 142.36 (m), 140.50, 140.00, 135.77, 135.51, 134.04 (d, $^1J_{CF}$ = 247.5 Hz, C3,5-py) 132.20, 132.11 (d, $^2J_{CF}$ = 8.67 Hz, C4-py), 131.98, 130.65, 130.57 (Ar–C), 130.49, 129.35 (Ar–CH), 129.08 (Ar–CH), 129.03 (Ar–CH), 128.97 (Ar–CH), 128.89 (Ar–CH), 128.02 (Ar–CH), 127.84, 127.49, 127.12 (alkene-CH), 125.81, 125.42, 124.80 (alkene-CH), 67.89 (CH_2–O), 60.03 (CH_2–O), 53.00 (CH_2–N), 52.54 (CH_2–N) ppm. ^{19}F NMR (470 MHz, DMSO-d_6) δ −164.65 (2F, F3,5-py).

3,5-Difluoro-2,4,6-tris((1-(4-(naphthalen-2-yl)benzyl)-1*H*-1,2,3-triazol-4-yl)methoxy)pyridine 10b. White solid. Yield 70%. MP 263–265 °C; IR (KBr) $\tilde{\nu}$ 3424, 3052, 2952, 1626, 1593, 1491 cm^{-1}. ^{1}H-NMR (500 MHz, DMSO-d_6) δ 8.37 (s, 3H, tetrazole-H), 8.29–8.30 (d, J = 6 Hz, 2H), 8.00–8.05 (m, 9H), 7.95 (d, J = 7.8 Hz, 2H), 7.52–7.66 (m, 12H, Ar–H), 7.25 (d, J = 8.1 Hz, 4H), 7.20 (d, J = 8.7 Hz, 2H), 5.57–5.58 (s, 6, CH_2O), 5.45 (s, 4H, CH_2–N), 5.40 (s, 2H, CH_2–N) ppm. ^{13}C NMR (126 MHz, DMSO-d_6) δ 143.46 (m), 143.03, 142.40 (m), 136.74 (d, $^1J_{CF}$ = 245.0 Hz, C3,5-py), 135.63, 133.86, 132.77 (triazole-C), 132.12 (triazole-C), 132.10, 130.65 (Ar–C), 130.49, 128.98 (Ar–CH), 128.67 (Ar–CH), 127.95 (Ar–CH), 126.90, 126.63, 126.03 (alkene-CH), 125.82, 125.70, 125.42 (alkene-CH), 121.86, 66.62 (CH_2–O), 60.01 (CH_2–O), 52.57 (CH_2–N), 52.54 (CH_2–N) ppm. ^{19}F NMR (470 MHz, DMSO-d_6) δ −164.65 (2F, F3,5-py).

4′-((4-(((2,6-Bis((1-(4-bromobenzyl)-1*H*-1,2,3-triazol-4-yl)methoxy)-3,5-difluoropyridin-4-yl)oxy)methyl)-1*H*-1,2,3-triazol-1-yl)methyl)-[1,1′-biphenyl]-4-carbaldehyde 10c. White solid. Yield 62%. MP 285–288 °C; IR (KBr) $\tilde{\nu}$ 3725, 3424, 3136, 3061, 2958, 28.60, 1724. ^{1}H-NMR (500 MHz, DMSO-d_6) δ 10.07 (s, 1H, CHO), 8.21–8.34 (s, 3H, tetrazole-H), 8.03 (d, 2H, J = 8.4 Hz, Ar), 7.99 (d, 2H, J = 8.2 Hz), 7.84–7.87 (d, J = 8.2 Hz, 2H), 7.52–7.55 (m, 6H, Ar–H), 7.25–7.28 (m, 4H), 7.20 (d, 2H, J = 8.4 Hz), 5.58 (s, 6, CH_2O), 5.45 (s, 4H, CH_2–N), 5.40 (s, 2H, CH_2–N). ^{13}C-NMR (126 MHz, DMSO-d_6) δ 193.14, 144.88 (dm, $^2J_{CF}$ = 10.01 Hz, C2,6-py), 144.06 (m), 143.96, 135.74, 134 (d, $^1J_{CF}$ = 242.5 Hz, C3,5-py), 132.18, 132.10, 131.96 (triazole-C), 130.65 (triazole-C), 130.60 (Ar–C), 130.52, 129.10 (Ar–CH), 128.33 (Ar–CH), 127.96 (Ar-CH), 127.80, 127.57, 125.43 (alkene-CH), 121.90, 115.67 (alkene-CH), 67.90 (CH_2–O), 60.01 (CH_2–O), 58.91 (CH_2–N), 52.59 (CH_2–N) ppm. ^{19}F NMR (470 MHz, DMSO-d_6) δ −164.61 (2F, F3,5-py).

2,4,6-Tris((1-([1,1′-biphenyl]-4-ylmethyl)-1*H*-1,2,3-triazol-4-yl)methoxy)-3,5-dichloropyridine 10d. White solid. Yield 73%. MP 232–234 °C; IR (KBr) $\tilde{\nu}$ 3060, 2952, 1578, 1561, 1489 cm^{-1}. ^{1}H-NMR (500 MHz, DMSO-d_6) δ 8.24 (s, 3H, tetrazole-H), 7.60–7.66 (m, 5H, Ar), 7.53–7.56 (m, 5H, Ar), 7.42–7.47 (m, 5H, Ar–H), 7.334–7.40 (m, 6H, Ar), 7.24–7.29 (m, 4H, Ar), 7.20–7.23 (d, 2H, J = 8.2 Hz), 5.55–5.63 (m, 6, CH_2O), 5.45–5.54 (m, 4H, CH_2–N), 5.37–5.44 (m, 2H, CH_2–N) ppm. ^{13}C NMR (126 MHz, DMSO-d_6) δ 146.05, 142.95, 135.88, 135.77, 134.94, 132.13, 132.08, 130.68 (triazole-C), 130.63 (triazole-C), 130.47 (Ar–C), 129.35, 129.06 (Ar–CH), 128.81 (Ar–CH), 128.02 (Ar–CH), 127.84 (Ar–CH), 127.50 (Ar–CH), 127.12 (Ar–CH), 126.26, 125.99, 125.42 (alkene-CH), 125.12, 121.90, 121.83 (alkene-CH), 66.59 (CH_2–O), 60.79 (CH_2–O), 52.58 (CH_2–N), 52.49 (CH_2–N) ppm.

3,5-Dichloro-2,4,6-tris((1-(4-(naphthalen-2-yl)benzyl)-1*H*-1,2,3-triazol-4-yl)methoxy)pyridine 10e. White solid. Yield 69%. MP 274–276 °C; IR (KBr) $\tilde{\nu}$ 3449, 3052, 1580, 1490, 1412 cm^{-1}. ^{1}H-NMR (500 MHz, DMSO-d_6) δ 8.37 (s, 3H, tetrazole-H), 8.29 (d, J = 6 Hz, 3H), 8.00–8.05 (m, 8H), 7.95 (d, J = 7.8 Hz, 4H), 7.53–7.56 (m, 12H, Ar–H), 7.26 (d, J = 8.1 Hz, 4H), 7.20 (d, J = 8.7 Hz,2H), 5.59 (s, 6, CH_2O), 5.51 (s, 4H, CH_2–N), 5.22 (s, 2H, CH_2–N) ppm. ^{13}C NMR (126 MHz, DMSO-d_6) δ 143.91, 143.21, 141.99, 137.72, 135.76, 137.73, 133.86,132.77, 132.74, 132.13 (triazole-C), 132.08 (triazole-C), 130.68 (Ar–C),128.99, 128.67, 127.96 (Ar–CH), 126.91 (Ar–CH), 126.64 (Ar–CH), 126.30, 126.04, 125.71 (alkene-CH), 125.44, 121.90 (alkene-CH), 66.97 (CH_2–O), 60.74 (CH_2–O), 52.59 (CH_2–N), 52.44 (CH_2–N) ppm.

4′-((4-(((2,6-Bis((1-(4-bromobenzyl)-1*H*-1,2,3-triazol-4-yl)methoxy)-3,5-dichloropyridin-4-yl)oxy)methyl)-1*H*-1,2,3-triazol-

1-yl)methyl)-[1,1′-biphenyl]-4-carbaldehyde 10f. White solid. Yield 56%. MP 280 °C (dec); IR (KBr) $\tilde{\nu}$ 3726, 3448, 3138, 2951, 2841, 1694. ^{1}H NMR (500 MHz, DMSO-d_6). δ 10.07 (s, 3H, CHO), 8.30 (s, 3H, tetrazole-H), 8.03 (d, 2H, J = 8.4 Hz), 7.99 (d, 2H, J = 8.2 Hz), 7.49–7.57 (m, 6H), 7.24–7.31 (m, 4H), 7.21 (d, 2H, J = 8.5 Hz), 5.56–5.62 (m, 6, CH_2O), 5.480–5.54 (m, 4H, CH_2–N), 5.24 (s, 2H, CH_2–N) ppm. ^{13}C NMR (126 MHz, DMSO-d_6): δ 193.19, 155.74, 144.83, 142.93, 142.35, 136.25, 135.78, 132.13, 132.08, 130.69 (triazole-C), 130.62 (Ar–C), 130.47, 128.35 (Ar-CH), 127.81 (Ar–CH), 125.47, 121.92, 103.69, 67.56 (CH_2–O), 60.76 (CH_2–O), 52.58 (CH_2–N), 52.51 (CH_2–N) ppm.

4. Conclusions

In summary, perhalopyridine-based alkyne precursors **3a** and **3b** were prepared through the S_NAr reaction of PFP and PCP with excess amounts of propargyl alcohol. We have accordingly developed the click reaction of the derived alkynes with aryl azides **4a–c** under ultrasonic irradiation as an effective method for synthesizing poly(1,2,3-triazolyl)-substituted perhalopyridines **5a–f**. However, aliphatic 1,2,3-triazole analogues **7a–d** were formed *via* the sonication reaction of pyridyl cores **3**, alkyl bromides **6a,b**, and NaN_3 under one-pot conditions. Utilizing 2,3,4,5-tetrachloro-6-(prop-2-yn-1-yloxy)pyridine **3c**, drived from the regioselective S_NAr reaction of PCP with propargyl alcohol, we also succeeded to furnish several ((1,2,3-triazol-4-yl)methoxy)-3,4,5,6-tetrachloropyridines **8a–c** under the reaction conditions. Finally, biaryl-embedded perfluoropyridine-based poly(1,2,3-triazoles) **10a–f** were produced in good yields *via* the SMC reaction of tris-triazole **5b,e** with arylboronic acids **9a–c** under $Pd(PPh_3)_4$ catalysis.

Author contributions

Fereshteh Khorasani: conceptualization, investigation, methodology, data analysis, writing – review & editing; Reza Ranjbar-Karimi and Kazem Mohammadiannejad: investigation, writing – review & editing; Reza Ranjbar-Karimi: supervision.

Conflicts of interest

There are no conflicts to declare.

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