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COPPER-MEDIATED N1-ARYLATION OF BENZOTRIAZOLES

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COPPER-MEDIATED N1-ARYLATION OF BENZOTRIAZOLES

By

Magdalena R. Andrzejewska

A Thesis Presented to
The Faculty of the Chemistry and Biochemistry Program
The City College of New York

In (Partial) Fulfilment of the Requirements for the Degree
Master of Science

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Barbara Zajc, Committee Member and Masters Advisor
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ABSTRACT

Benzotriazoles are a group of bicyclic heterocyclic compounds that contain three nitrogen atoms fused to a benzene ring. Along with their derivatives, they possess a wide range of properties. They are used in medical field, as they exhibit such properties as antibacterial, antiplasmodial, antiprotozoal, antifungal and anti-inflammatory activities, among others. They are also used in various industries as herbicides, UV absorbers, deicing and antiicing agents and corrosion inhibitors, to list a few. Because of their wide range of applications, we designed a new two-step synthesis for the formation of N-1-aryl benzotriazoles. 1-Hydroxy-1H-benzotriazole N-oxides were synthesized using phenylboronic acid (PhB(OH)₂), pyridine in CH₂Cl₂ as the solvent. A wide range of aryl boronic acids showed good reactivity with 1-hydroxy-1H-benzotriazole as well as 6-chloro-1-hydroxy-1H-benzotriazole under established conditions and moderate to high yields of products were isolated. Obtained N-oxides were then deoxygenated using tetrahydroxydiboron (B₂(OH)₄) in MeCN, following previously established conditions. N-Oxides resulting from the reactions of 5,6-dichloro-1H-hydroxybenzotriazole were difficult to purify and prone to degradation. To alleviate the problem, a two-step one-pot reaction was designed. After N-arylation was complete and without any further purification, the reduction step was performed using B₂(OH)₄ in MeCN. The method proved beneficial for the reaction with phenylboronic acid, and no significant improvement was observed in others. A reaction using 2-methoxypyrimidine-4-boronic acid showed that using established conditions, compounds with potential biological activity can be synthesized.
INTRODUCTION

Benzotriazoles are bicyclic heterocyclic compounds that contain three nitrogen atoms fused to a benzene ring. They can contain substituents on the aromatic ring or on the nitrogen ring. They are one of the most important groups of heterocyclic compounds in medicinal and pharmaceutical chemistry. Along with their derivatives, benzotriazoles possess a wide range of applications such as antibacterial, antiplasmoidal, antiprotozoal, antifungal and anti-inflammatory activities.

In the context of the biological applications of benzotriazoles, Szyszka and coworkers reported that 4,5,6,7-tetrabromo-1H-benzotriazole (TBBt) successfully inhibited animal and plant protein kinase 2 (CK2). Against the two types of casein kinases, CK1 and CK2, TBBt exhibited low activity versus the CK1 enzymes, but it showed good inhibition of CK2. In recent years, CK2 has been a research target with potential in cancer treatment because of its high activity in cancer cells. Since the discovery of the inhibition properties of TBBt other more potent inhibitors have been synthesized, many of which are TBBt analogues.

Severe acute respiratory syndrome (SARS) is a relatively new coronavirus that was first observed in patients in 2002. Using the main protease (M$^{\text{pro}}$), also known as chymotrypsin-like protease (3CL$^{\text{pro}}$), among other enzymes, the SARS virus encodes two of the positive-strand RNA polyproteins. So far, there is no known cure for SARS and only a few 3CL$^{\text{pro}}$ inhibitors have been discovered. Benzotriazole esters derivatives have been identified as strong inhibitors of severe acute respiratory syndrome 3CL$^{\text{pro}}$.

Respiratory syncytial virus (RSV) is an infectious virus occurring worldwide and, in the United States, it has been identified as the most common cause of death in children under 5 years of age by a virus. To date, no vaccines are approved to prevent RSV and the treatment
In recent years, benzotriazole derivatives, containing a benzimidazole moiety, have shown RSV inhibition. It appears that these molecules block the fusion of virus with host membranes.\textsuperscript{11}

Vorozole is a benzotriazole derivative that underwent clinical trials as a potential drug for treatment of postmenopausal breast cancer. It causes reversible inhibition of cytochrome P450 aromatase and is selective, meaning that it does not effect other cytochrome P450-dependent reactions under certain conditions.\textsuperscript{12} In 1999 Vorozole was ultimately withdrawn from the clinical trial when no difference was detected compared to progestational agent, megasterol acetate.\textsuperscript{13}

In addition to the examples above, a berberine derivative containing a benzotriazole moiety inhibits the growth of Gram-positive bacteria, Gram-negative bacteria, and fungi, with results superior when compared to the synthesized precursors.\textsuperscript{14} $\text{N}^1$-alkylated benzotriazoles are also known to have a high bonding affinity to a wide range of proteins such as tyrosine kinase.\textsuperscript{15} Examples of other benzotriazole derivatives with medicinal applications are shown in Figure 1.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{benzotriazole derivatives.png}
\caption{Examples of benzotriazole derivatives with medicinal properties.}
\end{figure}

Apart from their biological activities, benzotriazolyl derivatives have also found applications in other industries. In agriculture, they are used as herbicides,\textsuperscript{16-a} insecticides,\textsuperscript{16-b} and acaricides.\textsuperscript{16-c} They are also used as ultraviolet stabilizers in many
consumer products. They are known to be efficient corrosion inhibitors for metals, such as copper alloys and other transition metals. In the aircraft industry, 1H-benzotriazole and tolyl benzotriazole are found to be the primary agents in most types of aircraft deicing/antiicing fluid (ADAFs). Additional applications include, but are not limited to lubricant additive, stabilizers for plastic materials, photographic papers, automotive break fluids, antifreeze agents, organic solar cells, and surface coating. Examples of benzotriazole derivatives with activities described above are shown in Figure 2.

Figure 2. Examples of benzotriazole derivatives with applications in various industries.

Benzotriazoles are commonly used reagents in organic chemistry, because of their low cost, low toxicity, high stability and wide range of synthetic applications. They serve as synthetic auxiliaries and synthetic precursors in many organic transformations and also as a ligand in cross-coupling reactions.
Scheme 1. Examples of applications of benzotriazoles in organic synthesis.

Historically, the first published reports of benzotriazoles appeared in 1934 and 1935, when Fries\textsuperscript{27} and Fieser\textsuperscript{28} independently reported the synthesis of 1\textit{H}-benzotriazole via multi-step synthesis, in relatively low yields. It was not until 1940 that a successful one-step synthesis of 1\textit{H}-benzotriazole was reported in the literature.\textsuperscript{29} Damschrodner and Peterson were able to synthesize the 1\textit{H}-benzotriazole in a high yield (80\%) by nitrosation of \textit{o}-phenylenediamine with sodium nitrite in glacial acetic acid and water (Scheme 2). Since then, multiple pathways for the synthesis of benzotriazoles and their derivatives have been reported.\textsuperscript{30}

Scheme 2. Synthesis of 1\textit{H}-benzotriazole via diazotization of \textit{o}-phenylenediamine.
Among benzotriazole derivatives, N-aryl benzotriazoles are also quite important because of their medicinal and biological activities. Singh et al., reported that N-acridinyl benzotriazoles displayed antibacterial activity. Since both acridine and benzotriazole themselves exhibit medicinal properties in multiple contexts, the authors hypothesized that when the structural elements were combined, the resulting N-acridinylbenzotriazole derivatives should also possess biological properties. Several compounds were synthesized and tested against the S. aureus and B. subtilis (gram positive) and E. coli (gram negative) bacteria. The results showed that the new molecules showed good antibacterial activity. An increased activity was observed when the C-2 position of acridine was substituted with either an –OCH3 or –CH3 (Figure 3, second from the left).

For centuries malaria has been a major health problem in tropical countries. To this day it remains dangerous, causing over a million deaths each year. For many years, chloroquine has been used as the only synthetic drug against malaria. However, the Plasmodium falciparum parasite that causes malaria has become resistant to the drug, causing the need for discovery of new, potent antimalarial drug. This problem was alleviated to some extent with the use of 4-chlorochalcone and 2,4-dichlorochalcone substituted benzotriazole derivatives, which showed antiplasmoidal activity against P. falciparum and caused parasitic death. Substituting the chlorine atom in these chalcone substituted benzotriazole derivatives with an -OMe group (Figure 3, left), resulted in compounds with antifilarial activities.

In recent years, Ohsawa and coworkers published results where tetrahydronaphthalene derivative of benzotriazole showed an activity as a ligand for the retinoid X receptor (RXR)
and therefore, can be considered an agonist against type 2 diabetes and autoimmune disease (Figure 3, right).\textsuperscript{35} This is an important discovery, as according to a study, over 100 million Americans have either diabetes or prediabetes, and it is one of the major causes of death in adults.\textsuperscript{36} With results showing activity against RXR, they modified the molecule by altering the nitrogen atoms of the triazole ring and found that compound containing trifluoromethyl group at the benzimidazole 2 position showed similar activity to the benzotriazole derivative, therefore both compounds were considered to be RXR partial agonists.

Recently, Palmer and co-workers prepared a series of amino pyrimidine derivatives of benzotriazole and evaluated them for their possible c-Jun N-terminal kinase (JNK) inhibition properties (Figure 3, second from the right).\textsuperscript{37} The JNKs are protein kinases that play an important role in the T cell immune response and regulate the expression or function of a multiple pro-inflammatory cytokines, crucial to many human inflammatory disorders.\textsuperscript{38} For this reason, the inhibition of JNK potentially has therapeutic application. Multiple synthesized molecules showed good inhibition of JNK1, with superior results when compared to the inhibition of JNK2. Also, the 1,2,3-benzotriazole derivative showed significantly higher potency when compared to other heterocyclic systems, such as imidazopyridine, 1,2,4-triazolopyridine or benzimidazole.

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure3.png}
\caption{\textit{N}-aryl benzotriazoles with medicinal applications.}
\end{figure}
N-Arylated benzotriazoles have also found applications in areas outside of the medical/biological field. For example, thiophene-2-aryl-2H-benzotriazole-thiophene oligomers show optical and electrochemical properties with possible applications in organic electronics and aryloxyphenyl N-arylbenzotriazoles possess herbicidal activity. Similar to other benzotriazole derivatives, octrizeole, an N-2 arylated benzotriazole, can serve as a UV-screen. Structures of the aforementioned benzotriazoles are shown in Figure 4.

![Figure 4. Examples of N-aryl benzotriazole derivatives with applications in various industries.](image)

**SYNTHESIS OF N-ARYL BENZOTRIAZOLES**

Several metal-mediated and metal-free methods have been reported for the synthesis of N-arylated benzotriazoles. These processes are summarized below.

**Metal-Mediated Approaches**

In 1995, Lopez-Alvarado and Avendaño reported Cu(OAc)₂ mediated synthesis of N-aryl benzotriazoles. The authors coupled 1,2,3-benzotriazole with p-tolyllead triacetate using NaH, Cu(OAc)₂ in DMF at 140 °C (equation 1 in Scheme 3). Despite the harsh conditions, the reaction resulted in a mixture of N-1 and N-2 arylated products in 25:1 ratio, in a relatively low 23% yield. A direct arylation approach has been developed for N-arylation of benzotriazoles via C–H bond activation at the C2 position of pyrroles, furans, and thiophenes.
These reactions were mediated by Cu(OAc)$_2$ in combination with Selectfluor in nitromethane at 120 °C. Antilla et al. reported a selective $N$-1 arylation of benzotriazoles with aryl iodides using CuI, $N,N'$-dimethyl-1,2-cyclohexyldiamine, and K$_3$PO$_4$ in toluene at 110 °C (equation 3 in Scheme 3). However, when the $N$-arylation of benzotriazoles with aryl halides was carried out using CuBr$_2$, TBAF at 145 °C, the regioselectivity was lost and both $N$-1 and $N$-2 arylated products were observed (equation 4 in Scheme 3). In addition to the copper-mediated $N$-arylation of benzotriazoles, palladium-catalyzed synthesis of $N$-arylated benzotriazoles were also investigated. One such study showed that $N$-arylated benzotriazoles could be synthesized by Pd(OAc)$_2$-catalyzed C–H bond activation of aryl triazenes in presence of Cs$_2$CO$_3$ under O$_2$ atmosphere (equation 5 in Scheme 3). Although, C–H bond activation was preferred on unsubstituted aryl groups, in the case of unsymmetrical triazenes, under these conditions, significant amounts of regioisomeric products were also observed. An alternative approach for the synthesis of regioselective $N$-arylated benzotriazoles was reported by Zhou et al. where $N$-methyl-$N$-aryl-$N'$-bromoaryl triazenes were cyclized using Pd(OAc)$_2$, dppp, and KOAc in DMF at 110 °C (equation 6 in Scheme 3). The cyclization takes place via a 1,7-palladium migration by the C–H bond activation followed by dealkylative cyclization. Despite the successful methodologies for the synthesis of $N$-arylated benzotriazoles, some methods require harsh conditions, multiple steps for the synthesis of starting materials, expensive reagents, and some result in regioisomeric products.
Scheme 3. Metal-catalyzed Synthesis of N-aryl benzotriazoles.

Metal-Free Approaches

In 2014, Lukasik and Wrobel reported a metal-free synthesis of N1-aryl-1H-benzotriazoles. This was accomplished by treating 2-(arylamino)aryliminophosphoranes with NaNO₂ in AcOH at 0 °C and this resulted in formation of N-aryl-1H-benzotriazoles in high yields (Scheme 4). However, 2-(arylamino)aryliminophosphoranes require multiple step synthesis from 2-halonitroarenes and anilines.
**Scheme 4. Synthesis of N-aryl benzotriazoles by diazotization of 2-aryl(arylamino)aryliminophosphoranes**

Wang et al. designed a two-step process for the synthesis of N-aryl benzotriazoles using diaryliodonium salts and hydroxybenzotriazoles.\(^{48}\) The first step involves O-arylation of N-hydroxybenzotriazoles with diaryliodonium salts, in the presence of KO\(t\)Bu in MeCN at 60 °C (Scheme 5). Heating the O-arylated benzotriazoles in MeCN at 60 °C for extended periods of time allows the N–O bond cleavage via a [3,3]-sigmatropic rearrangement resulting in the formation of N-arylated benzotriazoles (Scheme 4). In the cases where unsymmetrical benzotriazoles were used under these conditions, both isomeric [3,3] and [1,3]-product were also observed at various ratios.

**Scheme 5. Synthesis of N-aryl benzotriazoles.**

In the more recent examples diazotization has been utilized in multi-step synthesis of N-aryl benzotriazoles.\(^{35,49}\) Within this category Chen and Buchwald designed a three-step reaction for the synthesis of N-arylated benzotriazoles from 2-chloronitrobenzenes and aromatic amines.\(^{50}\) Formation of the C–N bond using iPr\(_2\)NEt at 160–180 °C was followed by the hydrogenation step with Pd/C under \(H_2\) conditions at 45 °C. In the third step, diazotization/cyclization reaction was performed using aqueous HCl and aqueous NaNO\(_2\).
Scheme 6. Synthesis of N-aryl benzotriazoles via diazotization reaction.

In 2008, Shi et al. reported a general method for synthesis of substituted N-arylated benzotriazoles via a 1,3-dipolar cycloaddition of benzyynes with azides, under mild conditions (equation 1 in Scheme 7).

They were able to obtain high yields with a wide range of azides and o-(trimethylsilyl)phenyl triflate, using CsF to generate the aryne, in acetonitrile as the solvent. Zhang and Moses used a similar strategy and synthesized N-aryl benzotriazoles, but in a one-pot approach by generating aryl azides in situ from anilines, followed by the 1,3-dipolar cycloaddition with benzyynes (equation 2 in Scheme 7). Another approach utilizes 1,3-dipolar cycloaddition using 1,5-diynes and NaN₃. Although high yields were obtained, the designed method required multiple steps to synthesize the starting materials, and resulted in the formation of two different N-aryl benzotriazoles (equation 3 in Scheme 7).

Scheme 7. Synthesis of N-aryl benzotriazoles via 1,3-dipolar cycloaddition of azides and benzyynes.
As mentioned earlier, despite the availability of various methods for the synthesis of N-aryl benzotriazoles, many suffer from drawbacks, such as the requirement for harsh conditions, need for multiple steps, utilization of highly reactive intermediates or starting materials and, in some cases, the lack of regioselectivity let alone the issue of regiospecificity. Given these considerations, we were interested in developing an easy and regiospecific synthesis of N-aryl benzotriazoles from easily accessible starting materials such as N-hydroxybenzotriazoles and arylboronic acids. Our idea was based upon an earlier disclosure, where we had shown that N-hydroxybenzotriazoles could be “deoxygenated” (reduced) to benzotriazoles with tetrahydroxydiboron.\(^5\) In that work we had proposed a plausible O to N prototropy as being operational, which reveals an intermediate N-oxide. This intermediate could then undergo reduction to the 1H-benzotriazole. If indeed tautomerization to an intermediate N-oxide can occur, we hypothesized that this could be captured via a Chan-Lam-Evans type of reaction with aryl boronic acids.\(^5\) This forms the basis of the currently reported results.

**Scheme 8.** *Reduction of N-hydroxybenzotriazoles to benzotriazoles using B\(_2\)(OH)\(_4\).*
RESULTS AND DISCUSSION

We began our initial evaluation of our hypothesis with the arylation of 1-hydroxy-1H-benzotriazole using phenylboronic acid (PhB(OH)₂), in presence of 1 equiv. of Cu(OAc)₂ and 4 equiv. of pyridine. Reactions were typically run in a 10 mL round bottom flask with stirring, for 24 hours at room temperature (data shown in Table 1). We screened three solvents for this reaction, CH₂Cl₂, ClCH₂CH₂Cl and DMSO. Between the three tested solvents comparable results were obtained with CH₂Cl₂ and ClCH₂CH₂Cl (entries 1 and 2). No reactivity observed when DMSO was used (entry 3). CH₂Cl₂ was chosen as the solvent for further reactions because of its low boiling point and the higher product yield obtained in comparison to ClCH₂CH₂Cl (42% versus 27% in the two solvents). The yields in the first two reactions were relatively modest and since all of the starting material was consumed, we suspected that this might be the result of water solubility of the reaction product during the aqueous work-up conducted after completion of the reaction and before purification. To verify this, in the next reaction the solvent from the reaction mixture was evaporated and the reaction mixture was loaded directly onto the silica gel column, skipping the aqueous wash (entry 4). After purification by column chromatography, the yield from this reaction was a significantly improved 77% as compared to the previous 42%. Then, we attempted to substitute pyridine with Et₃N and 2,2’-dipyridine. The results of these reactions showed relatively low product yields, 30% and 10%, respectively (entries 5 and 6). We also found that stoichiometric amount of Cu(OAc)₂ was necessary for the reaction. When 0.5 equiv. and 0.25 equiv. of Cu(OAc)₂ were used low product yields were observed (entries 7 and 8). Similarly, low yields were recorded when Cu(OAc)₂ was substituted with Cul and CuCl (entries 9 and 10).
Table 1. Optimization of reaction conditions for the N-arylation of hydroxy-1H-
benzotriazoles with PhB(OH)₂.¹

<table>
<thead>
<tr>
<th>Entry</th>
<th>Conditions</th>
<th>Solvent</th>
<th>Yield (%)ᵇ</th>
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<tr>
<td>1</td>
<td>pyridine (4 equiv.), Cu(OAc)₂ (1 equiv.)</td>
<td>ClCH₂CH₂Cl</td>
<td>27 c</td>
</tr>
<tr>
<td>2</td>
<td>pyridine (4 equiv.), Cu(OAc)₂ (1 equiv.)</td>
<td>CH₂Cl₂</td>
<td>42 c</td>
</tr>
<tr>
<td>3</td>
<td>pyridine (4 equiv.), Cu(OAc)₂ (1 equiv.)</td>
<td>DMSO</td>
<td>NRd</td>
</tr>
<tr>
<td>4</td>
<td>pyridine (4 equiv.), Cu(OAc)₂ (1 equiv.)</td>
<td>CH₂Cl₂</td>
<td>77 e</td>
</tr>
<tr>
<td>5</td>
<td>Et₃N (4 equiv.), Cu(OAc)₂ (1 equiv.)</td>
<td>CH₂Cl₂</td>
<td>30 e</td>
</tr>
<tr>
<td>6</td>
<td>2,2'-dipyridine (2 equiv.), Cu(OAc)₂ (1 equiv.)</td>
<td>CH₂Cl₂</td>
<td>10 e</td>
</tr>
<tr>
<td>7</td>
<td>pyridine (4 equiv.), Cu(OAc)₂ (0.5 equiv.)</td>
<td>CH₂Cl₂</td>
<td>26 e</td>
</tr>
<tr>
<td>8</td>
<td>pyridine (4 equiv.), Cu(OAc)₂ (0.25 equiv.)</td>
<td>CH₂Cl₂</td>
<td>14 e</td>
</tr>
<tr>
<td>9</td>
<td>pyridine (4 equiv.), CuI (1 equiv.)</td>
<td>CH₂Cl₂</td>
<td>11 e</td>
</tr>
<tr>
<td>10</td>
<td>pyridine (4 equiv.), CuCl (1 equiv.)</td>
<td>CH₂Cl₂</td>
<td>14 e</td>
</tr>
</tbody>
</table>

¹Reactions were conducted with 100 mg of BtOH in 2 mL of solvent, under a balloon filled with O₂ gas. ᵇYield is of isolated and chromatographically purified product. ᶜReaction using aqueous workup. ᵈNR = no reaction. ᵉNo aqueous workup, reaction mixture was chromatographed directly.

With optimization of the reaction conditions completed, it was necessary to assess if the product of the reaction was either the benzotriazole phenyl ether or 1-phenyl-1H-benzotriazole-3-oxide. It has previously been reported by Lam et al. that the reaction of 1-hydroxy-1H-benzotriazole with PhB(OH)₂ using Cu(OAc)₂, pyridine and CH₂Cl₂ under air conditions resulted in formation of benzotriazole phenyl ether. To establish if the reaction in fact leads to the formation of ether and not 1-phenyl-1H-benzotriazole-3-oxide, the product was crystallized using a mixture of CH₂Cl₂ and hexanes. Crystallographic data confirmed that the obtained compound was in fact an N-oxide and not the benzotriazole phenyl ether as previously reported.⁵⁵
Figure 5. X-ray structure of 1-phenyl-1H-benzotriazole-3-oxide.

With reaction conditions established and the product structure confirmed, reactions of various aryl boronic acids with BtOH were analyzed. The reaction scope summarized in Figure 6. Generally, good yields were obtained in most cases. However, lower yields were obtained with ortho-substituted boronic acids. In the reaction of o-methoxyphenylboronic acid the yield was lower as compared to that from p-methoxyphenylboronic acid (compare yields of products 3 and 4). Steric factors became more significant in the case of the o-tolylboronic acid. Here only 14% yield of the desired compound 5 was obtained as compared to the 62% of product 6 obtained with p-tolylboronic acid. Similarly, product 9 from 1-naphthylboronic acid was obtained in a 45% yield as compared to the 73% yield of product 10 obtained from the reaction with 2-naphthylboronic acid.
Figure 6. Products structures and yields of products obtained from the reactions of 1-hydroxy-1H-benzotriazole with various aryl boronic acids (1.1 equiv.). Yields in the parentheses were from reactions with 2 equiv. of the aryl boronic acid.

In some cases where the yields were low, significantly improved yields were obtained when the amount of the boronic acid was doubled. For example, with 1-naphthylboronic acid the initial 24% obtained with 1 equiv. of the boronic acid was almost doubled to 45% when 2 equiv. were used. Low yields were also observed in reactions involving heteroaryl boronic acids. In these cases, the yields for reactions with both 1.1 equiv. and 2.0 equiv. of boronic acids were evaluated. The yield of product 11 from 3-thienylboronic acid improved from 37% to 47% and that of product 13 from benzo[b]thien-2-ylboronic acid increased from 13% to 26%. However, no improvement was observed in the reaction of 4-
(dibenzofuranyl)boronic acid with the increased amount of boronic acid. In certain reactions, dimeric byproducts were observed. Specifically, 4,4′-bi(dibenzofuran), 2,2′-bithiophene, and 2,2′-bi[benzo[b]thiophene, and 4,4′-dinitrophenyl were all obtained in the reactions with the corresponding boronic acids. Increased dimer formation was observed in the reaction where 2.0 equiv. of 4-(dibenzofuranyl)boronic acid was used.

To additionally investigate the scope of the reaction tested two different benzotriazoles, 1-hydroxy-7-azabenzotriazole and 6-chloro-1-hydroxy-1H-benzotriazole (6-Cl BtOH), were also evaluated. The reaction of 1-hydroxy-7-azabenzotriazole with PhB(OH)₂ showed almost no reactivity. Reactions with substituted 6-Cl BtOH resulted in good yields (15–17), comparable to product yields with the unsubstituted 1-hydroxy-1H-benzotriazole (Figure 4). In the case of 15, we also proved that the yield can be further improved, by using 2.0 equiv. of PhB(OH)₂ in the reaction.

![Figure 7](image)

**Figure 7.** Products structures and yields of products obtained from the reactions of 6-chloro-1-hydroxy-1H-benzotriazole with three aryl boronic acids (1.1 equiv.). The yield in the parentheses was from a reaction reaction with 2 equiv. of the PhB(OH)₂.

As a final step in the synthesis venture, the synthesized 1-aryl-1H-benzotriazole 3-oxides were reduced. Prior research from our group has demonstrated that 1-hydroxy-1H-benzotriazoles and pyridine N-oxides can be reduced by B₂(OH)₄ (also see Scheme 8). Because the products prepared via the current synthesis were N-oxides, it was anticipated that B₂(OH)₄ alone, in the absence of Et₃N, should suffice for the reduction. Reaction times
and yields of the reductions are summarized in Figure 8. As expected, all reactions were complete within relatively short reaction times (2–6 h) and the products were isolated in high yields (76–95% yields).

![N-Aryl benzotriazoles](image)

**Figure 8.** *Products obtained from the reduction of 1-aryl-1H-benzotriazole 3-oxides with \( B_2(OH)_4 \).*

The X-ray structure of the \( N \)-oxide 1 (Figure 5) confirmed the structure of the reaction intermediate. However, we wanted to unambiguously prove the regiochemistry for entry of the aryl group. That is, we wanted to provide that the incoming aryl group enters at the
nitrogen atom remote from the hydroxyl group of the $N$-hydroxy benzotriazoles. For this, the $^1H$ NMR data for 5-chloro-1-($p$-tolyl)-1$H$-benzotriazole (34) were compared to the $^1H$ NMR spectrum for the already reported 6-chloro-1-($p$-tolyl)-1$H$-benzotriazole. The spectra show significant differences and dissimilarities in proton shifts indicate that the two compounds in fact differ from each other. Additionally, to prove the location of the aryl group with reference to the chlorine atom on the benzotriazole, compound 34 obtained from $N$-oxide 17, was crystallized using a mixture of hexanes and CH$_2$Cl$_2$ and the X-ray structure was obtained. The crystallographic data confirmed the initial hypothesis that the arylation step is directed by $N$-hydroxyl group, plausibly via an $N^1$-OH $\rightarrow$ $N^3$ tautomerism.

![Figure 9. X-ray structure of 5-chloro-1-($p$-tolyl)-1$H$-benzotriazole (34).](image)

We also used a disubstituted benzotriazole, 5,6-dichloro-1$H$-hydroxybenzotriazole (5,6-dichloro BtOH) for the $N$-arylation under the conditions we developed. While the reactions did proceed and the final products were obtained in satisfactory yields, the purification of the 5,6-dichloro-1-aryl-1$H$-benzotriazole 3-oxides was problematic. They appeared to be somewhat unstable and prone to degradation. In order to resolve this, a two-step, one-pot reaction was attempted. Here, after the $N$-arylation was completed, the solvent was evaporated and without any further purification, the reduction step was performed using B$_2$(OH)$_4$ in MeCN. Originally three reactions were performed using 5,6-dichloro-1-aryl-1$H$-
benzotriazole in the two-step, one-pot strategy with phenyl, 2-naphthyl, and \( p \)-bromophenyl boronic acids. In the reaction with phenylboronic acid, there was a significant improvement in the yield of product 35, while in the reactions of 2-naphthyl and \( p \)-bromophenyl boronic acids, small yield improvements were observed for products 36 and 37 (Table 2, Entries 1-3). After these positive results, we decided to apply the same strategy to additional reactions, to test if higher yields could be obtained. Compounds 25, 28 and 33 were chosen for the resynthesis because the overall yields in the two-step process were low in these cases. For these three reactions, the results showed no significant change in the isolated product yields compared to the original two-step process (Table 2, Entries 4-6). However, it appears that the modified method may be beneficial when the intermediate \( N \)-oxide is prone to degradation. It should be noted that the two-step, one pot approach may not be readily applicable in some cases. For example, in reactions, where the dimeric byproducts were observed (11–14), this approach could potentially cause an issue with purification of the final products, because both the dimeric byproducts and the final deoxygenated products are relatively non-polar and there is a possibility of the two having very similar \( R_f \) values.
Table 2. Yield comparisons for the synthesis of N-aryl-1H-benzotriazoles via the two-step and two-step, one-pot processes.

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<th>Entry</th>
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<th>Product</th>
<th>Two-step</th>
<th>Two-step, one-pot</th>
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<td>62%</td>
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<tr>
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<td>26%</td>
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<tr>
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<td><img src="image" alt="Product 34" /></td>
<td>54%</td>
<td>50%</td>
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<tr>
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<td>X = Y = H</td>
<td></td>
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<td>34%</td>
</tr>
<tr>
<td>6</td>
<td>X = H, Y = Cl</td>
<td></td>
<td><img src="image" alt="Product 43" /></td>
<td>48%</td>
<td>42%</td>
</tr>
</tbody>
</table>

Because benzotriazole derivatives are known to possess biological activity, we synthesized a product containing the privileged pyrimidine motif, by using 2-methoxypyrimidine-4-boronic acid (Scheme 9). Since our previous results showed low yields for the reaction with heteroaryl boronic acid, we conducted two reactions: one with 1.1 equiv. of the boronic acid at room temperature over 24 hours and another with 2.0 equiv. of the boronic acid at room temperature over 48 hours. The extended reaction time of the second setup was necessary due to the low solubility of the 2-methoxypyrimidine-4-boronic acid. The yields were modest but the reaction with 2.0 equiv. of boronic acid gave a higher yield of 31% compared to the 22% obtained with 1.1 equiv. The benzotriazole 3-oxide 38 obtained from this reaction was reduced using B₂(OH)₄ in MeCN at 50 °C, resulting in the N-
arylbenzotriazole derivative 39 in a 91% yield. This compound demonstrates that biologically important molecules can be synthesized via this method.

CONCLUSION

In conclusion, we designed an efficient method for synthesis of \( N^1 \)-arylated benzotriazoles from hydroxybenzotriazols and arylboronic acids. A wide range of arylboronic acids gave satisfactory results. Low yields were recorded for the boronic acids with ortho substituents, where steric factor was significant, and also for those boronic acids that contain a heteroatom within the ring. In most of the low yielding reactions, an improvement was observed when the amount of the boronic acid was doubled. Also investigated were the substituted benzotriazoles, 6-Cl BtOH and 5,6-dichloro BtOH. While the reactions using 6-Cl BtOH resulted in good yields, those with 5,6-dichloro BtOH showed that the formed oxides were difficult to purify and prone to degradation. To alleviate that problem, a two-step one-pot reaction was designed, where the reduction was done without purification of an oxides. This method proved beneficial for reactions with 5,6-dichloro BtOH, however did not show a significant difference as compared to the original two-step reaction. A reaction using 2-methoxypyrimidine-4-boronic acid confirmed that compounds with potential biological activity can be synthesized by this method.
EXPERIMENTAL

General procedure for the N-arylation of 1-hydroxy-1H-benzotriazoles (synthesis of 1-phenyl-1H-benzotriazole 3-oxide 1)

\[ \text{In a clean, dry 10 mL round bottom flask equipped with a stir bar and} \]
\[ \text{containing 20 mg of 4 Å molecular sieves, was placed 1-hydroxy-1H-benzotriazole (125.1 mg, 1.0 mmol). CH}_2\text{Cl}_2 (2.5 mL) \]
\[ \text{and pyridine (324 μL, 4.0 mmol, 4 equiv.) were added, and the mixture was stirred until the solid dissolved. Next, phenylboronic acid (134.1 mg, 1.1 equiv.) and Cu(OAc)}_2 (181.6 mg, 1.0 equiv.) \]
\[ \text{were added, and the mixture was stirred for 24 h at room temperature, under an atmosphere of oxygen gas. The mixture was evaporated under reduced pressure and the residue was directly loaded onto a 100–200 mesh silica column. Gradient elution with 10%, 30%, and 50% EtOAc in hexanes gave 132.8 mg (77% yield) of compound 1 as a white solid. } R_f(\text{SiO}_2 \text{ and 50% EtOAc in hexanes}) = 0.16. \]
\[ ^1\text{H NMR (500 MHz, CDCl}_3\text{): } \delta = 8.09 \text{ (d, } J = 8.5 \text{ Hz, 1H, ArH), 7.78 \text{ (d, } J = 8.6 \text{ Hz, 1H, ArH}) 7.73 \text{ (d, } J = 7.6 \text{ Hz, 2H, ArH}), 7.67 \text{ (dd, } J = 8.0, 7.5 \text{ Hz, 1H, ArH}), 7.60 \text{ (t, } J = 7.9 \text{ Hz, 2H, ArH}), 7.48 \text{ (q, } J = 7.2 \text{ Hz, 2H, ArH}). \]
\[ ^{13}\text{C NMR (125 MHz, CDCl}_3\text{): } \delta = 146.7, 137.2,132.5, 130.0, 128.8, 128.4, 124.6, 123.1, 120.5, 110.5. \]
\[ \text{HRMS (ESI/TOF) } m/z \text{ calculated for C}_{12}\text{H}_{9}\text{N}_3\text{O}_2\text{Na \[M + Na\]^+: 234.0638, found 234.0635.} \]

General procedure for the reduction of 1-aryl-1H-benzotriazole 3-oxides (synthesis of 1-phenyl-1H-benzotriazole 18)

\[ \text{In a clean, dry reaction vial equipped with a stir bar was placed } N\text{-oxide 1 (50 mg, 1.0 equiv.) and MeCN (250 μL) was added followed by the addition of B}_2\text{(OH)}_4 \text{ (23.3 mg, 1.1 equiv.). The vial was flushed with nitrogen gas and heated at 50 °C in a pre-equilibrated sand bath. The reaction was complete in 2 hours. The solvent was} \]
evaporated and the crude material was subjected to flash chromatography on 200-300 mesh silica. Elution with 10% EtOAc in hexanes gave 42.0 mg (91% yield). Rf(SiO2 and 50% EtOAc in hexanes) = 0.68. 1H NMR (500 MHz, CDCl3): δ = 8.15 (d, J = 8.3 Hz, 1H, ArH), 7.79 (d, J = 8.2 Hz, 2H, ArH), 7.76 (d, J = 8.3 Hz, 1H, ArH), 7.62 (t, J = 7.7 Hz, 2H, ArH), 7.53 (dt, J = 20.8, 7.4 Hz, 2H, ArH), 7.44 (t, J = 7.6 Hz, 1H, ArH). 13C NMR (125 MHz, CDCl3): δ = 146.7, 137.2, 132.5, 130.0, 128.8, 128.4, 124.6, 123.0, 120.5, 110.5. HRMS (ESI/TOF) m/z calculated for C12H9N3Na [M + Na]+: 218.0689, found 218.0681.

1-(3-Trifluoromethyl)phenyl)-1H-benzotriazole 3-oxide (2)

Compound 2 (165.8 mg 72%) was prepared from the corresponding 1-hydroxy-1H-benzotriazole precursor (135.1 mg, 1.1 mmol) and was obtained as a white crystalline solid after chromatography on a silica gel column by sequential elution with 10% EtOAc in hexanes to 50% EtOAc in hexanes. Rf (SiO2 and 50% EtOAc in hexanes) = 0.18. 1H NMR (500 MHz, CDCl3): δ = 8.10 (d, J = 8.5 Hz, 1H, ArH), 8.02 (s, 1H, ArH), 7.95 (dd, J = 5.3, 3.4 Hz, 1H, ArH), 7.79 (d, J = 8.6 Hz, 1H, ArH), 7.77-7.71 (m, 3H, ArH), 7.52 (t, J = 7.7 Hz, 1H, ArH). 13C NMR (125 MHz, CDCl3): δ = 136.7, 133.1, 132.9 (q, JCF = 32 Hz), 131.9, 131.1, 125.4, 125.3, 125.2 (q, JCF = 3.6 Hz), 123.4 (q, JCF = 272 Hz), 119.2 (q, JCF = 3.8 Hz) 116.6, 111.3. HRMS (ESI/TOF) m/z calculated for C13H8F3N3ONa [M + Na]+: 302.0512, found 302.0501.

1-(2-Methoxyphenyl)-1H-benzotriazole 3-oxide (3)

Compound 5 (123.6 mg, 51% yield) was prepared from 1-hydroxy-1H-benzotriazole (135.1 mg, 1.1 mmol) and was obtained as a white, crystalline solid after column chromatography on 100-200 mesh silica by sequential elution with 10%, 30%, and 50% EtOAc in hexanes. Rf(SiO2 and 50% EtOAc in hexanes) = 0.21. 1H NMR (500
MHz, CDCl₃): δ = 8.04 (d, J = 8.5 Hz, 1H, ArH), 7.56 (t, J = 7.7 Hz, 1H, ArH), 7.52 (t, J = 7.6 Hz, 2H, ArH), 7.41 (t, J = 7.7 Hz, 1H, ArH), 7.30 (d, J = 8.5 Hz, 1H, ArH), 7.13 (t, J = 8.1 Hz, 2H), 3.82 (s, 3H, CH₃). ¹³C NMR (125 MHz, CDCl₃): δ = 154.0, 135.1, 131.4, 130.8, 130.4, 128.5, 124.4, 124.1, 121.4, 115.6, 112.7, 112.7, 56.0. HRMS (ESI/TOF) m/z calculated for C₁₅H₁₂N₃O₂ [M + H]⁺: 264.0743, found 264.0740.

1-(4-Methoxyphenyl)-1H-benzotriazole 3-oxide (4)

Compound 4 (168.9 mg, 70% yield) was prepared from 1-hydroxy-1H-benzotriazole (135.1 mg, 1.1 mmol) and was obtained as a white, crystalline solid after column chromatography on 100–200 mesh silica by sequential elution with (135.1 mg, 1.1 mmol) and was obtained as a white, crystalline solid after column chromatography on 100–200 mesh silica by sequential elution with 10%, 30%, and 10%, 30%, and 50% EtOAc in hexanes. Rf(SiO₂ and 50% EtOAc in hexanes) = 0.18. ¹H NMR (500 MHz, CDCl₃): δ = 8.07 (d, J = 8.5 Hz, 1H, ArH), 7.68 (d, J = 8.5 Hz, 1H, ArH), 7.65 (d, J = 7.1 Hz, 1H, ArH), 7.61 (d, J = 8.9 Hz, 2H, ArH) 7.46 (t, J = 7.6 Hz, 1H, ArH), 7.09 (d, J = 8.9 Hz, 2H, ArH), 3.30 (s, 3H, CH₃). ¹³C NMR (125 MHz, CDCl₃): δ = 159.9, 133.4, 131.2, 131.0, 128.9, 124.8, 124.6, 116.1, 115.3, 111.5, 55.9. HRMS (ESI/TOF) m/z calculated for C₁₅H₁₁N₃O₂Na [M + Na]⁺: 264.0743, found 264.0740.

1-(o-Tolyl)-1H-benzotriazole 3-oxide (5)

Compound 5 (30.7 mg, 14% yield) was prepared from 1-hydroxy-1H-benzotriazole (135.1 mg, 1.1 mmol) and was obtained as a white solid after column chromatography on 100–200 mesh silica by sequential elution with 10%, 30%, and 50% EtOAc in hexanes. Rf(SiO₂ and 50% EtOAc in hexanes) = 0.17. ¹H NMR (500 MHz, CDCl₃): δ = 8.07 (d, J = 8.5 Hz, 1H, ArH), 7.59 (t, J = 7.7 Hz, 1H, ArH), 7.49–7.43 (br m, 3H, ArH), 7.39
(br s, 2H, ArH), 7.29 (d, J = 8.5 Hz, 1H, ArH), 2.20 (s, 3H, CH3). 13C NMR (125 MHz, CDCl3): δ = 136.1, 133.2, 131.5, 131.3, 130.2, 128.8, 125.1, 123.4, 122.6, 116.2, 111.7, 17.9. HRMS (ESI/TOF) m/z calculated for C13H11N3ONa [M + Na]+: 248.0794, found 248.0798.

1-(p-Tolyl)-1H-benzotriazole 3-oxide (6)

Compound 6 (140.3 mg, 62% yield) was prepared from 1-hydroxy-1H-benzotriazole (135.1 mg, 1.1 mmol) and was obtained as a white solid after column chromatography on 100–200 mesh silica by sequential elution with 10%, 30%, and 50% EtOAc in hexanes. Rf (SiO2 and 50% EtOAc in hexanes) = 0.18. 1H NMR (500 MHz, CDCl3): δ = 8.07 (d, J = 8.5 Hz, 1H, ArH), 7.73 (d, J = 8.6 Hz, 1H, ArH), 7.64 (t, J = 7.7 Hz, 1H, ArH), 7.58 (d, J = 8.2 Hz, 2H, ArH), 7.45 (t, J = 7.7 Hz, 1H, ArH), 7.38 (d, J = 8.1 Hz, 2H, ArH), 2.46 (s, 3H, CH3). 13C NMR (125 MHz, CDCl3): δ = 139.1, 133.5, 133.2, 131.2, 131.1, 130.7, 125.0, 122.6, 116.0, 111.6, 21.3. HRMS (ESI/TOF) m/z calculated for C13H11N3ONa [M + Na]+: 248.0794, found 248.0799.

1-(4-Bromophenyl)-1H-benzotriazole 3-oxide (7)

Compound 7 (207.8 mg, 72% yield) was prepared from 1-hydroxy-1H-benzotriazole (135.1 mg, 1.1 mmol) and was obtained as a white solid after column chromatography on 100–200 mesh silica by sequential elution with 10%, 30%, and 50% EtOAc in hexanes. Rf (SiO2 and 50% EtOAc in hexanes) = 0.19. 1H NMR (500 MHz, CDCl3): δ = 8.09 (d, J = 8.5 Hz, 1H, ArH), 7.74 (t, J = 8.2 Hz, 1H, ArH), 7.73 (d, J = 8.3 Hz, 2H, ArH), 7.68 (t, J = 7.7 Hz, 1H, ArH), 7.62 (d, J = 8.7 Hz 2H, ArH), 7.49 (t, J = 7.7 Hz, 1H, ArH). 13C NMR (125 MHz, CDCl3): δ = 135.2, 133.4, 133.1, 131.7, 131.6, 125.2, 123.9, 122.4, 116.5, 111.4. HRMS (ESI/TOF) m/z calculated for C12H8BrN3ONa [M + Na]+: 311.9743, found 311.9742.

1-(3-(Ethoxycarbonyl)phenyl)-1H-benzotriazole 3-oxide (8)
Compound 8 (168.5 mg, 59% yield) was prepared from 1-hydroxy-1H-benzotriazole (135.1 mg, 1.1 mmol) and was obtained as a white solid after column chromatography on 100–200 mesh silica by sequential elution with 10%, 30%, 50% EtOAc in hexanes. $R_f$ (SiO$_2$/50% EtOAc in hexanes) = 0.19. $^1$H NMR (500 MHz, CDCl$_3$): and 8.41 (s, 1H, ArH), 8.15 (d, $J$ = 7.8 Hz, 1H, ArH), 8.10 (d, $J$ = 8.5 Hz, 1H, ArH), 7.93 (dt, $J$ = 1.0, 8.0 Hz, 1H, ArH), 7.81 (d, $J$ = 8.5 Hz, 1H, ArH), 7.72–7.67 (m, 2H, ArH), 7.50 (t, $J$ = 7.7 Hz, 1H, ArH), 4.44 (q, $J$ = 7.1 Hz, 2H, CH$_2$), 1.43 (t, $J$ = 7.1 Hz, 3H, CH$_3$). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 165.4, 136.4, 133.2, 132.8, 131.8, 130.5, 129.5, 126.5, 125.2, 123.1, 116.4, 111.6, 61.9, 14.5. HRMS (ESI/TOF) $m/z$ calculated for C$_{15}$H$_{13}$N$_3$O$_3$Na [M + Na]+: 306.0849, found 306.0842.

1-(Naphthalen-1-yl)-1H-benzotriazole 3-oxide (9)

Compound 9 (63.1 mg, 24% yield with 1 equiv. of boronic acid and 118 mg, 45% yield with 2 equiv. of boronic acid) was prepared from 1-hydroxy-1H-benzotriazole (135.1 mg, 1.1 mmol) and was obtained as a brown solid after column chromatography on 100–200 mesh silica by sequential elution with 10%, 30%, and 50% EtOAc in hexanes. $R_f$ (SiO$_2$ and 50% EtOAc in hexanes) = 0.22. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 8.17 (d, $J$ = 8.5 Hz, 1H, ArH), 8.11 (d, $J$ = 8.1 Hz, 1H, ArH), 8.04 (d, $J$ = 8.0 Hz, 1H, ArH), 7.70 (dd, $J$ = 1.2, 8.3 Hz, 1H, ArH), 7.68–7.54 (m, 6H, ArH), 7.51 (t, $J$ = 7.7 Hz, 1H, ArH). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 135.7, 134.7, 131.5, 131.1, 131.0 129.2, 128.8, 128.2, 127.5, 125.6, 125.5, 124.9, 122.6, 116.2, 111.8. HRMS (ESI/TOF) $m/z$ calculated for C$_{16}$H$_{11}$N$_3$ONa [M + Na]+: 284.0794, found 284.0793.

1-(Naphthalen-2-yl)-1H-benzotriazole 3-oxide (10)
Compound 10 (190.4 mg, 73% yield) was prepared from 1-hydroxy-1H-benzotriazole (135.1 mg, 1.1 mmol) and was obtained as a brown solid after column chromatography on 100–200 mesh silica by sequential elution with 10%, 30%, and 50% EtOAc in hexanes. Rf (SiO2 and 50% EtOAc in hexanes) = 0.18. 1H NMR (500 MHz, CDCl3): δ = 8.16 (s, 1H, ArH), 8.11 (d, J = 8.4 Hz, 1H, ArH), 8.06 (d, J = 8.7 Hz, 1H, ArH), 7.94 (d, J = 8.0 Hz, 2H, ArH), 7.87 (d, J = 8.6 Hz, 1H, ArH), 7.84 (d, J = 8.8 Hz, 1H, ArH), 7.70 (t, J = 7.8 Hz, 1H, ArH), 7.63–7.58 (br m, 2H, ArH), 7.50 (t, J = 7.7 Hz, 1H, ArH). 13C NMR (125 MHz, CDCl3): δ = 133.5, 133.5, 133.4, 132.8, 131.6, 131.4, 130.6, 128.3, 128.2, 127.8, 127.4, 125.1, 120.8, 120.7, 116.4, 111.8. HRMS (ESI/TOF) m/z calculated for C16H11N3ONa [M + Na]+: 284.0794, found 284.0795.

1-(Thiophen-3-yl)-1H-benzotriazole 3-oxide (11)

Compound 11 (81.0 mg, 37% yield with 1 equiv. of boronic acid and 102.9 mg, 47% yield with 2 equiv. of boronic acid) was prepared from 1-hydroxy-1H-benzotriazole (135.1 mg, 1.1 mmol) and was obtained as a light-brown solid after column chromatography on 100–200 mesh silica by sequential elution with 10%, 30%, and 50% EtOAc in hexanes. Rf (SiO2 and 50% EtOAc in hexanes) = 0.30. 1H NMR (500 MHz, CDCl3): δ = 8.08 (d, J = 8.5 Hz, 1H, ArH), 7.76 (d, J = 8.6 Hz, 1H, ArH), 7.69 (td, J = 0.9, 7.8 Hz, 1H, ArH), 7.59 (dd, J = 1.4, 3.1 Hz, 1H, ArH), 7.55 (dd, J = 3.2, 5.2 Hz, 1H, ArH), 7.51–7.49 (m, 1H, ArH), 7.48–7.46 (m, 1H, ArH). 13C NMR (125 MHz, CDCl3): δ = 134.2, 133.1, 131.4, 131.2, 127.7, 125.0, 121.9, 116.2, 115.5, 111.6. HRMS (ESI/TOF) m/z calculated for C10H7N3OSNa [M + Na]+: 240.0208, found 240.0197.

1-(4-Nitrophenyl)-1H-benzotriazole 3-oxide (12)
Compound 12 (141.0 mg, 55% yield) was prepared from 1-hydroxy-1H-benzotriazole (135.1 mg, 1.1 mmol) and was obtained as a yellow solid after column chromatography on 100–200 mesh silica by sequential elution with 10%, 40%, and 90% EtOAc in hexanes. $R_f$ (SiO$_2$ and 70% EtOAc in hexanes) = 0.23. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 8.49 (d, $J$ = 9.0 Hz, 2H, ArH), 8.14 (d, $J$ = 8.5 Hz, 1H, ArH), 7.97 (d, $J$ = 9.0 Hz, 2H, ArH), 7.89 (d, $J$ = 8.6 Hz, 1H, ArH), 7.78 (t, $J$ = 7.8 Hz, 1H, ArH), 7.56 (t, $J$ = 7.8 Hz, 1H, ArH). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 141.0, 133.0, 132.4, 126.4, 126.0, 125.9, 121.8, 116.9, 111.7. HRMS (ESI/TOF) $m/z$ calculated for C$_{12}$H$_8$N$_4$O$_2$Na [M + Na]+: 279.0489, found 279.0485.

1-(Benzothiophen-2-yl)-1H-benzotriazole 3-oxide (13)

Compound 13 (35.0 mg, 13% yield with 1 equiv. of boronic acid and 70 mg, 26% yield with 2 equiv. of boronic acid) was prepared from 1-hydroxy-1H-benzotriazole (135.1 mg, 1.1 mmol) and was obtained as a light-yellow solid after column chromatography on 100–200 mesh silica by sequential elution with 10%, 30%, and 50% EtOAc in hexanes. $R_f$ (SiO$_2$ and 50% EtOAc in hexanes) = 0.32. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 8.10 (d, $J$ = 8.5 Hz, 1H, ArH), 7.93 (d, $J$ = 8.5 Hz, 1H, ArH), 7.85 (t, $J$ = 7.2 Hz, 2H, ArH), 7.77–7.74 (m, 1H, ArH), 7.57 (s, 1H, ArH), 7.53 (t, $J$ = 7.7 Hz, 1H, ArH), 7.48–7.42 (m, 2H, ArH). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 137.8, 136.5, 136.4, 133.6, 132.0, 131.8, 125.8, 125.7, 125.6, 124.4, 122.5, 116.5, 115.0, 112.0. HRMS (ESI/TOF) $m/z$ calculated for C$_{14}$H$_9$N$_3$OSNa [M + Na]+: 290.0359, found 290.0360.

1-(Dibenzofuran-4-yl)-1H-benzotriazole 3-oxide (14)

Compound 14 (39.6 mg, 26% yield with 1 equiv. of boronic acid and 42.6 mg, 28% yield with 2 equiv. of boronic acid) was prepared from 1-hydroxy-1H-benzotriazole (135.1 mg, 1.1 mmol) and was obtained as a cream-colored solid after
column chromatography on 100–200 mesh silica by sequential elution with 10%, 30%, and 50% EtOAc in hexanes. \( R_f (\text{SiO}_2 \text{ and 50\% EtOAc in hexanes}) = 0.25. \)  \(^1\)H NMR (500 MHz, CDCl\(_3\)):
\[
\delta = 8.14 \text{ (d, } J = 8.5 \text{ Hz, } 1\text{H, ArH}), 8.11 \text{ (d, } J = 7.7 \text{ Hz, } 1\text{H, ArH}), 8.05 \text{ (d, } J = 7.7 \text{ Hz, } 1\text{H, ArH}), 7.76 \text{ (d, } J = 7.8 \text{ Hz, } 1\text{H, ArH}), 7.67 \text{ (t, } J = 7.7 \text{ Hz, } 1\text{H, ArH}), 7.60–7.51 \text{ (m, } 5\text{H, ArH}), 7.45 \text{ (t, } J = 7.4 \text{ Hz, } 1\text{H, ArH}).
\]

\(^1\)C NMR (125 MHz, CDCl\(_3\)):
\[
\delta = 156.5, 148.5, 134.6, 131.5, 131.0, 128.6, 127.3, 125.0, 124.0, 124.0, 123.8, 123.7, 121.8, 121.3, 120.6, 116.0, 112.7, 112.4. \)

HRMS (ESI/TOF) m/z calculated for C\(_{18}\)H\(_{12}\)N\(_3\)O\(_2\) [M + H]+: 302.0924, found 301.0924.

5-Chloro-1-phenyl-1H-benzotriazole 3-oxide (15)

Compound 15 (133.1 mg, 52% yield) was prepared from the corresponding 1- hydroxy-1H-benzotriazole precursor (169.6 mg, 1.1 mmol) and was obtained as a white, crystalline solid after column chromatography on 100–200 mesh silica by sequential elution with 10%, 30%, and 50% EtOAc in hexanes. \( R_f (\text{SiO}_2 \text{ and 50\% EtOAc in hexanes}) = 0.68. \)  \(^1\)H NMR (500 MHz, CDCl\(_3\)):
\[
\delta = 8.07 \text{ (s, } 1\text{H, ArH}), 7.71–7.67 \text{ (m, } 3\text{H, ArH}), 7.62–7.59 \text{ (br m, } 3\text{H, ArH}), 7.51 \text{ (t, } J = 7.4 \text{ Hz, } 1\text{H, ArH}).
\]

\(^1\)C NMR (125 MHz, CDCl\(_3\)):
\[
\delta = 135.7, 132.3, 132.0, 131.8, 131.2, 130.3, 129.2, 122.7, 115.8, 112.8. \)

HRMS (ESI/TOF) m/z calculated for C\(_{12}\)H\(_9\)ClN\(_3\)O [M + H]+: 246.0429, found 246.0435.

1-(4-Bromophenyl)-5-chloro-1H-benzotriazole 3-oxide (16)

Compound 16 (205.4 mg, 63% yield) was prepared from the corresponding 1- hydroxy-1H-benzotriazole precursor (169.6 mg, 1.1 mmol) and was obtained as a white, crystalline solid after column chromatography on 100–200 mesh silica by sequential elution with 10%, 30%, and 50% EtOAc in hexanes. \( R_f (\text{SiO}_2 \text{ and 50\% EtOAc in hexanes}) = 0.60. \)  \(^1\)H NMR (500 MHz, CDCl\(_3\)):
\[
\delta = 8.08 \text{ (s, } 1\text{H, ArH}), 7.74 \text{ (d, } J = 8.2 \text{ Hz, } 2\text{H, ArH}), 7.67 \text{ and 7.63 (ABq, } J = 9.0 \text{ Hz, } 2\text{H, ArH}), 7.57 \text{ (d, } J = 8.2 \text{ Hz, } 2\text{H, ArH}).
\]

\(^1\)C
NMR (125 MHz, CDCl₃): δ = 134.8, 133.6, 132.7, 132.2, 131.7, 131.5, 124.0, 122.8, 116.1, 112.5. HRMS (ESI/TOF) m/z calculated for C₁₂H₈BrClN₃O [M + H]⁺: 323.9534, found 323.9520.

5-Chloro-1-(p-tolyl)-1H-benzotriazole 3-oxide (17)

Compound 17 (203.0 mg, 78% yield) was prepared from the corresponding 1- hydroxy-1H-benzotriazole precursor (169.6 mg, 1.1 mmol) and was obtained as a white, crystalline solid after column chromatography on 100–200 mesh silica by sequential elution with 10%, 30%, and 50% EtOAc in hexanes. Rᵣ(SiO₂ and 50% EtOAc in hexanes) = 0.53. ¹H NMR (500 MHz, CDCl₃): δ = 8.06 (s, 1H, ArH), 7.65 (d, J = 9.0 Hz, 1H, ArH), 7.58 (dd, J = 1.7, 9.0 Hz, 1H, ArH), 7.54 (d, J = 8.2 Hz, 2H, ArH), 7.39 (d, J = 8.0 Hz, 2H, ArH), 2.46 (s, 3H, CH₃). ¹³C NMR (125 MHz, CDCl₃): δ = 139.5, 134.2, 133.2, 132.3, 131.8, 131.1, 130.8, 122.7, 112.7, 21.4. HRMS (ESI/TOF) m/z calculated for C₁₃H₁₀ClN₃ONa [M + Na]⁺: 282.0405, found 282.0406.

1-(3-(Trifluoromethyl)phenyl)-1H-benzotriazole (19)

Compound 19 (46.6 mg, 94% yield) was prepared from the corresponding N-oxide precursor (50.0 mg, 0.18 mmol) and was obtained as a white, crystalline solid after column chromatography on 100–200 mesh silica with 10% EtOAc in hexanes. Rᵣ(SiO₂ and 50% EtOAc in hexanes) = 0.74. ¹H NMR (500 MHz, CDCl₃): δ = 8.19 (d, J = 8.4 Hz, 1H, ArH), 8.11 (s, 1H, ArH), 8.04 (br m, 1H, ArH), 7.77 (m, 3H, ArH), 7.62 (t, J = 7.7 Hz, 1H, ArH), 7.48 (t, J = 7.7 Hz, 1H, ArH). ¹³C NMR (125 MHz, CDCl₃): δ = 146.9, 137.7, 132.75 (q, JCF = 33.0 Hz), 132.2, 130.8, 129.0, 125.9, 125.4 (q, JCF = 3.7 Hz), 125.0, 123.6 (q, JCF = 273.0 Hz), 120.8, 119.7 (q, JCF = 3.8 Hz), 110.2. HRMS (ESI/TOF) m/z calculated for C₁₃H₈F₃N₃Na [M + Na]⁺: 286.0563, found 286.0542.
1-(2-Methoxyphenyl)-1H-benzotriazole (20)

Compound 20 (41.7 mg, 88% yield) was prepared from the corresponding N-oxide precursor (50.0 mg, 0.21 mmol) and was obtained as a white, crystalline solid after column chromatography on 100–200 mesh silica with 10% EtOAc in hexanes. $R_f$ (SiO$_2$ and 50% EtOAc in hexanes) = 0.72. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 8.13 (d, $J$ = 8.3 Hz, 1H, ArH), 7.55–7.52 (m, 2H, ArH), 7.47 (t, $J$ = 7.5 Hz 1H, ArH), 7.41–7.37 (m, 2H, ArH), 7.18–7.14 (m, 2H, ArH), 3.80 (s, 3H, CH$_3$). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 154.1, 146.0, 134.4, 131.2, 128.4, 127.7, 125.8, 124.0, 121.4, 120.1, 112.8, 111.3, 56.1. HRMS (ESI/TOF) $m/z$ calculated for C$_{13}$H$_{11}$N$_3$Na [M + Na]+: 248.0794, found 248.0793.

1-(4-Methoxyphenyl)-1H-benzotriazole (21)

Compound 21 (44.9 mg, 95% yield) was prepared from the corresponding N-oxide precursor (50.0 mg, 0.21 mmol) and was obtained as a white, crystalline solid after column chromatography on 100–200 mesh silica with 10% EtOAc in hexanes. $R_f$ (SiO$_2$ and 50% EtOAc in hexanes) = 0.71. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 8.14 (d, $J$ = 8.3 Hz, 1H, ArH), 7.67 (d, $J$ = 8.8 Hz, 3H, ArH, contains 1 benzotriazolyl d), 7.53 (t, $J$ = 7.6 Hz, 1H, ArH), 7.42 (t, $J$ = 7.6 Hz, 1H, ArH), 7.12 (d, $J$ = 8.9 Hz, 2H, ArH), 3.91 (s, 3H, CH$_3$). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 160.2, 146.6, 133.0, 130.4, 128.1, 124.9, 124.3, 120.5, 115.3, 110.4, 55.9. HRMS (ESI/TOF) $m/z$ calculated for C$_{13}$H$_{11}$N$_3$ONa [M + Na]+: 248.0794, found 248.0791.

1-(o-Tolyl)-1H-benzotriazole (22)

Compound 22 (40.9 mg, 89% yield) was prepared from the corresponding N-oxide precursor (50.0 mg, 0.22 mmol) and was obtained as a white, crystalline solid after column chromatography on 100–200 mesh silica with 10% EtOAc in hexanes. $R_f$
(SiO$_2$ and 50% EtOAc in hexanes) = 0.82. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 8.16 (d, $J$ = 8.3 Hz, 1H, ArH), 7.52–7.39 (m, 6H, ArH), 7.35 (d, $J$ = 8.3 Hz, 1H, ArH), 2.13 (s, 3H, CH$_3$). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 154.1, 146.0, 134.4, 131.2, 128.4, 127.7, 125.8, 124.0, 121.4, 120.1, 112.8, 111.3, 56.1. HRMS (ESI/TOF) $m/z$ calculated for C$_{13}$H$_{11}$N$_3$Na [M + Na]$^+$: 232.0845, found 232.0854.

**1-(p-Tolyl)-1H-benzotriazole (23)**

Compound 23 (36.3 mg, 79% yield) was prepared from the corresponding N-oxide precursor (50.0 mg, 0.22 mmol) and was obtained as a white, crystalline solid after column chromatography on 100–200 mesh silica with 10% EtOAc in hexanes. $R_f$ (SiO$_2$ and 50% EtOAc in hexanes) = 0.79. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 8.14 (d, $J$ = 8.3 Hz, 1H, ArH), 7.72 (d, $J$ = 8.4 Hz, 1H, ArH), 7.66 (d, $J$ = 8.3 Hz, 2H, ArH), 7.54 (t, $J$ = 7.6 Hz, 1H, ArH), 7.45–7.40 (m, 3H, ArH), 2.48 (s, 3H, CH$_3$). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 146.6, 139.0, 134.7, 132.6, 130.6, 128.2, 124.4, 123.0, 120.4, 110.6, 21.4. HRMS (ESI/TOF) $m/z$ calculated for C$_{13}$H$_{11}$N$_3$Na [M + Na]$^+$: 232.0845, found 232.0851.

**1-(4-Bromophenyl)-1H-benzotriazole (24)**

Compound 24 (45.0 mg, 92% yield) was prepared from the corresponding N-oxide precursor (50.0 mg, 0.17 mmol) and was obtained as a white solid after chromatography column chromatography on 100–200 mesh silica with 10% EtOAc in hexanes. $R_f$ (SiO$_2$ and 50% EtOAc in hexanes) = 0.84. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 8.16 (d, $J$ = 8.3 Hz, 1H, ArH), 7.75 (d, $J$ = 8.7 Hz, 2H, ArH), 7.72 (d, $J$ = 8.5 Hz, 1H, ArH), 7.70 (d, $J$ = 8.7 Hz, 2H, ArH), 7.58 (t, $J$ = 7.6 Hz, 1H, ArH), 7.46 (t, $J$ = 7.7 Hz, 1H, ArH). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 146.8, 136.2, 133.3, 132.3, 128.8, 124.8, 124.4, 122.5, 120.7, 110.3. HRMS (ESI/TOF) $m/z$ calculated for C$_{12}$H$_8$BrN$_3$Na [M + Na]$^+$: 295.9794, found 295.9790.
**Ethyl 3-(1H-benzotriazol-1-yl)benzoate (25)**

Compound 25 (43.6 mg, 91% yield) was prepared from the corresponding N-oxide precursor (50.0 mg, 0.19 mmol) and was obtained as a white solid after column chromatography on 100–200 mesh silica with 10% EtOAc in hexanes. \( R_f \) (SiO\(_2\) and 50% EtOAc in hexanes) = 0.84. \(^1\)H NMR (500 MHz, CDCl\(_3\)): \( \delta = 8.48 \) (s, 1H, ArH), 8.19 (t, \( J = 8.6 \) Hz, 2H, ArH), 8.03 (d, \( J = 7.8 \) Hz, 1H, ArH), 7.79 (d, \( J = 8.3 \) Hz, 1H, ArH), 7.71 (t, \( J = 7.8 \) Hz, 1H, ArH), 7.60 (t, \( J = 7.5 \) Hz, 1H, ArH), 7.47 (t, \( J = 7.4 \) Hz, 1H, ArH), 4.45 (q, \( J = 6.8 \) Hz, 2H, CH\(_2\)), 1.43 (t, \( J = 6.8 \) Hz, 3H, CH\(_3\)). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \( \delta = 165.6, 146.8, 137.4, 132.6, 132.4, 130.2, 129.7, 128.8, 127.1, 124.8, 123.6, 120.7, 110.4, 61.8, 14.5\). HRMS (ESI/TOF) m/z calculated for C\(_{15}\)H\(_{13}\)N\(_3\)O\(_2\)Na [M + Na]: 290.0900, found 290.0902.

**1-(Naphthalen-1-yl)-1H-benzotriazole (26)**

Compound 26 (41.9 mg, 89% yield) was prepared from the corresponding N-oxide precursor (50.0 mg, 0.18 mmol) and was obtained as a white solid after column chromatography on 100–200 mesh silica with 10% EtOAc in hexanes. \( R_f \) (SiO\(_2\) and 50% EtOAc in hexanes) = 0.79. \(^1\)H NMR (500 MHz, CDCl\(_3\)): \( \delta = 8.22 \) (d, \( J = 8.3 \) Hz, 1H, ArH), 8.14 (d, \( J = 7.7 \) Hz, 1H, ArH), 8.05 (d, \( J = 7.5 \) Hz, 1H, ArH), 7.82 (d, \( J = 7.8 \) Hz, 1H, ArH), 7.63 (d, \( J = 8.3 \) Hz, 1H, ArH), 7.60–7.55 (m, 3H, ArH), 7.53–7.48 (m, 2H, ArH), 7.44 (t, \( J = 7.4 \) Hz, 1H, ArH). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \( \delta = 145.9, 134.9, 134.6, 132.8, 130.6, 129.3, 128.6, 128.3, 127.8, 127.2, 125.4, 124.8, 124.5, 122.9, 120.3, 110.6\). HRMS (ESI/TOF) m/z calculated for C\(_{16}\)H\(_{11}\)N\(_3\)Na [M + Na]: 268.0845, found 268.0844.

**1-(Naphthalen-2-yl)-1H-benzotriazole (27)**

Compound 27 (46.3 mg, 99% yield) was prepared from the corresponding N-oxide precursor (50.0 mg, 0.19 mmol) and was obtained as a white solid.
after column chromatography on 100–200 mesh silica with 10% EtOAc in hexanes. \( R_f \) (SiO₂ and 50% EtOAc in hexanes) = 0.84. \(^1\)H NMR (500 MHz, CDCl₃): \( \delta = 8.24 \) (s, 1H, ArH), 8.19 (d, \( J = 8.4 \) Hz, 1H, ArH), 8.10 (d, \( J = 8.7 \) Hz, 1H, ArH), 7.98–7.95 (m, 3H, ArH), 7.86 (d, \( J = 8.4 \) Hz, 1H, ArH), 7.63–7.58 (m, 3H, ArH), 7.47 (t, \( J = 7.4 \) Hz, 1H, ArH). \(^{13}\)C NMR (125 MHz, CDCl₃): \( \delta = 146.7, 134.6, 133.5, 132.9, 132.6, 130.2, 128.5, 128.4, 128.1, 127.5, 127.2, 124.6, 121.3, 121.0, 120.5 \) 110.6. HRMS (ESI/TOF) \( m/z \) calculated for C₁₆H₁₁N₃Na [M + Na]⁺: 268.0845, found 268.0827.

**1-(Thiophen-3-yl)-1\textit{H}-benzotriazole (28)**

![Thiophen-3-yl-benzotriazole](image)

Compound 28 (41.2 mg, 89% yield) was prepared from the corresponding N-oxide precursor (50.0 mg, 0.23 mmol) and was obtained as a white solid after column chromatography on 100–200 mesh silica with 10% EtOAc in hexanes. \( R_f \) (SiO₂ and 50% EtOAc in hexanes) = 0.76. \(^1\)H NMR (500 MHz, CDCl₃): \( \delta = 8.16 \) (d, \( J = 8.2 \) Hz, 1H, ArH), 7.77 (d, \( J = 8.1 \) Hz, 1H, ArH), 7.67 (dd, \( J = 1.3, 3.1 \) Hz, 1H, ArH), 7.63 (dd, \( J = 1.3, 5.2 \) Hz, 1H, ArH), 7.59–7.56 (m, 2H, ArH), 7.45 (t, \( J = 7.6 \) Hz, 1H, ArH). \(^{13}\)C NMR (125 MHz, CDCl₃): \( \delta = 146.2, 135.5, 132.3, 128.6, 127.3, 124.7, 122.4, 120.5, 115.6, 110.4 \) 110.4. HRMS (ESI/TOF) \( m/z \) calculated for C₁₀H₇N₃SNa [M + Na]⁺: 224.0253, found 224.0251.

**1-(4-Nitrophenyl)-1\textit{H}-benzotriazole (29)**

![4-Nitrophenyl-benzotriazole](image)

 Compound 29 (42.8 mg, 89% yield) was prepared from the corresponding N-oxide precursor (50.0 mg, 0.20 mmol) and was obtained as a yellow solid after column chromatography on 100–200 mesh silica with 10% EtOAc in hexanes. \( R_f \) (SiO₂ and 50% EtOAc in hexanes) = 0.76. \(^1\)H NMR (500 MHz, CDCl₃): \( \delta = 8.52 \) (d, \( J = 9.0 \) Hz, 2H, ArH), 8.21 (d, \( J = 8.4 \) Hz, 1H, ArH), 8.09 (d, \( J = 9.0 \) Hz, 2H, ArH), 7.85 (d, \( J = 8.4 \) Hz, 1H, ArH), 7.67 (t, \( J = 7.7 \) Hz, 1H, ArH), 7.52 (t, \( J = 7.5 \) Hz, 1H, ArH). \(^{13}\)C NMR (125 MHz, CDCl₃): \( \delta = \)
147.2, 147.1, 142.2, 131.9, 129.4, 125.8, 125.4, 122.5, 121.2, 110.3. HRMS (ESI/TOF) m/z calculated for C_{13}H_{8}N_{4}O_{2}Na [M + Na]: 263.0539, found 263.0554.

1-(Benzothiophen-2-yl)-1H-benzotriazole (30)

Compound 30 (36.3 mg, 76% yield) was prepared from the corresponding N-oxide precursor (50.0 mg, 0.19 mmol) and was obtained as a cream solid after column chromatography on 100–200 mesh silica with 10% EtOAc in hexanes. R_f (SiO_2 and 50% EtOAc in hexanes) = 0.86. ^1H NMR (500 MHz, CDCl_3): δ = 8.18 (d, J = 8.3 Hz, 1H, ArH), 7.93 (d, J = 8.4 Hz, 1H, ArH), 7.88 (t, J = 8.3 Hz, 2H, ArH), 7.66–7.63 (m, 2H, ArH), 7.50–7.41 (m, 3H, ArH). ^13C NMR (125 MHz, CDCl_3): δ = 146.8, 138.2, 137.9, 136.8, 132.6, 129.2, 125.62, 125.57, 125.2, 124.4, 122.6, 120.9, 114.5, 110.7. HRMS (ESI/TOF) m/z calculated for C_{14}H_{11}N_{3}S [M + H]: 352.0590, found 252.0605.

1-(Dibenzofuran-4-yl)-1H-benzotriazole (31)

Compound 31 (31.8 mg, 66% yield) was prepared from the corresponding N-oxide precursor (50.0 mg, 0.17 mmol) and was obtained as a white solid after column chromatography on 100–200 mesh silica with 10% EtOAc in hexanes. R_f (SiO_2 and 50% EtOAc in hexanes) = 0.89. ^1H NMR (500 MHz, CDCl_3): δ = 8.22 (d, J = 8.1 Hz, 1H, ArH), 8.14 (d, J = 7.7 Hz, 1H, ArH), 8.06 (d, J = 7.6 Hz, 1H, ArH), 7.82 (d, J = 7.8 Hz, 1H, ArH), 7.63 (d, J = 8.2 Hz, 1H, ArH), 7.60–7.54 (m, 3H, ArH), 7.53–7.48 (m, 2H, ArH), 7.44 (t, J = 7.4 Hz, 1H, ArH). ^13C NMR (125 MHz, CDCl_3): δ = 156.6, 148.7, 146.3, 133.7, 128.4, 128.3, 127.1, 124.6, 123.8, 123.7, 121.7, 121.2, 120.4, 112.4, 111.2. HRMS (ESI/TOF) m/z calculated for C_{18}H_{11}N_{3}ONa [M + Na]: 308.0794, found 308.0792.

5-Chloro-1-phenyl-1H-benzotriazole (32)
Compound 32 (45.9 mg, 92% yield) was prepared from the corresponding N-oxide precursor (50.0 mg, 0.20 mmol) and was obtained as an off-white solid after column chromatography on 100–200 mesh silica with 10% EtOAc in hexanes. $R_f$ (SiO$_2$ and 50% EtOAc in hexanes) = 0.79. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 8.14 (s, 1H, ArH), 7.76 (d, $J$ = 7.7 Hz, 2H, ArH), 7.69 (d, $J$ = 8.8 Hz, 1H, ArH), 7.63 (t, $J$ = 7.5 Hz, 2H, ArH), 7.55 (d, $J$ = 7.9 Hz, 1H, ArH), 7.52 (d, $J$ = 8.7 Hz, 1H, ArH). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 147.3, 136.8, 131.3, 130.4, 130.2, 129.3, 129.2, 123.1, 119.9, 111.5. HRMS (ESI/TOF) m/z calculated for C$_{12}$H$_8$Cl$_3$N$_3$Na [M + Na$^+$]: 252.0299 found 252.0290.

1-(4-Bromophenyl)-5-chloro-1H-benzotriazole (33)

Compound 33 (46.3 mg, 76% yield) was prepared from the corresponding N-oxide precursor (50.0 mg, 0.15 mmol) and was obtained as an off-white solid after column chromatography on 100–200 mesh silica with 10% EtOAc in hexanes. $R_f$ (SiO$_2$ and 50% EtOAc in hexanes) = 0.80. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 8.14 (s, 1H, ArH), 7.76 (d, $J$ = 8.5 Hz, 2H, ArH), 7.67–7.65 (m, 3H, ArH), 7.54 (d, $J$ = 8.9 Hz, 1H, ArH). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 145.6, 135.5, 134.1, 133.5, 131.3, 129.7, 124.4, 123.3, 121.5, 111.6. HRMS (ESI/TOF) m/z calculated for C$_{12}$H$_8$BrCl$_3$N$_3$ [M + H$^+$]: 307.9585, found 307.9537.

5-Chloro-1-(p-tolyl)-1H-benzotriazole (34)

Compound 34 (46.3 mg, 87% yield) was prepared from the corresponding N-oxide precursor (50.0 mg, 0.94 mmol) and was obtained as an off-white solid after column chromatography on 100–200 mesh silica with 10% EtOAc in hexanes. $R_f$ (SiO$_2$ and 50% EtOAc in hexanes) = 0.75. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 8.12 (s, 1H, ArH), 7.66–7.62 (m, 3H, ArH), 7.50 (d, $J$ = 8.8 Hz, 1H, ArH), 7.42 (d, $J$ = 7.2 Hz,
2H, ArH), 2.48 (s, 3H, CH3). 13C NMR (125 MHz, CDCl3): δ = 147.2, 139.5, 134.3, 131.3, 130.7, 130.3, 129.2, 123.0, 119.8, 111.5, 21.4. HRMS (ESI/TOF) m/z calculated for C13H10ClN3Na [M + Na]+: 266.0455 found 266.0439.

5,6-Dichloro-1-phenyl-1H-benzotriazole (35)

Compound 35 (163.7 mg, 62% yield) was prepared from 5,6-dichloro-1-aryl-1H-benzotriazole (204.0 mg, 1.0 mmol) and was obtained as an off-white solid after column chromatography on 100–200 mesh silica with 10% EtOAc in hexanes. Rf (SiO2 and 50% EtOAc in hexanes) = 0.72. 1H NMR (500 MHz, CDCl3): δ = 8.27 (s, 1H, ArH), 7.89 (s, 1H, ArH), 7.73 (d, J = 7.7 Hz, 2H, ArH), 7.65 (t, J = 7.8 Hz, 2H, ArH), 7.56 (t, J = 7.4 Hz, 1H, ArH). 13C NMR (125 MHz, CDCl3): δ = 145.6, 136.5, 133.7, 131.6, 130.2, 129.5, 129.4, 123.1, 121.4, 111.8. HRMS (ESI/TOF) m/z calculated for C12H7Cl2N3H [M + H]+: 264.0090, found 264.0118.

5,6-Dichloro-1-(naphthalene-2-yl)-1H-benzotriazole (36)

Compound 36 (122.5 mg, 39% yield) was prepared from 5,6-dichloro-1-aryl-1H-benzotriazole (204.0 mg, 1.0 mmol) and was obtained as an off-white solid after column chromatography on 100–200 mesh silica with 10% EtOAc in hexanes. Rf (SiO2 and 50% EtOAc in hexanes) = 0.75. 1H NMR (500 MHz, CDCl3): δ = 8.29 (s, 1H, ArH), 8.17 (s, 1H, ArH), 8.11 (d, J = 8.7 Hz, 1H, ArH), 8.01–7.97 (m, 3H, ArH), 7.86 (dd, J = 1.9, 8.7 Hz, 1H, ArH), 7.64 (m, 2H, ArH). 13C NMR (125 MHz, CDCl3): δ = 145.6, 133.8, 133.8, 133.5, 133.3, 131.7, 130.6, 129.5, 128.5, 128.3, 127.9, 127.6, 121.4, 121.3, 121.0, 111.9. HRMS (ESI/TOF) m/z calculated for C16H9Cl2N3Na [M + Na]+: 336.0066, found 336.0089.

1-(4-Bromophenyl)-5,6-dichloro-1H-benzotriazole (37)
Compound 37 (89.2 mg, 26% yield) was prepared from the corresponding 5,6-dichloro-1-aryl-1H-benzotriazole (204.0 mg, 1.0 mmol) and was obtained as an off-white solid after column chromatography on 100–200 mesh silica with 10% EtOAc in hexanes. $R_f$(SiO$_2$ and 50% EtOAc in hexanes) = 0.80. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 8.26 (s, 1H, ArH), 7.85 (s, 1H, ArH), 7.77 (d, $J$ = 8.3 Hz, 2H, ArH), 7.63 (d, $J$ = 8.4 Hz, 2H, ArH). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 145.7, 135.5, 134.1, 133.5, 131.3, 129.7, 124.4, 123.3, 121.5, 111.6. HRMS (ESI/TOF) $m/z$ calculated for C$_{12}$H$_7$BrCl$_2$N$_3$ [M + H]$^+$: 341.9195, found 341.9209.

1-(2-Methoxypyrimidin-5-yl)-1H-benzotriazole 3-oxide (38)

Compound 38 (54.6 mg, 22% yield with 1 equiv. of boronic acid and 75.9 mg, 31% with 2 equiv. of boronic acid) was prepared from 1-hydroxy-1H-benzotriazole (135.1 mg, 1.0 mmol) and was obtained as white solid after column chromatography on 100-200 mesh silica by sequential elution in 50% EtOAc in hexanes to pure EtOAc. $R_f$(SiO$_2$ and EtOAc) = 0.29. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 8.90 (s, 2H, ArH), 8.11 (d, $J$ = 8.5 Hz, 1H, ArH), 7.73 (t, $J$ = 8.0 Hz, 1H, ArH), 7.63 (d, $J$ = 8.6 Hz, 1H, ArH), 7.52 (t, $J$ = 7.7 Hz, 1H, ArH), 4.13 (s, 3H, Me). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 165.0, 154.0, 133.7, 132.1, 131.6, 126.5, 125.5, 116.6, 110.6, 56.2. HRMS (ESI/TOF) $m/z$ calculated for C$_{11}$H$_3$N$_5$O$_2$ [M + H]$^+$: 244.0829, found 244.0846.

1-(2-Methoxypyrimidin-5-yl)-1H-benzotriazole (39)

Compound 39 (84.9 mg, 91% yield) was prepared from the corresponding N-oxide precursor (100 mg, 0.41 mmol) and was obtained as white solid after column chromatography on 100-200 mesh silica with EtOAc. $R_f$(SiO$_2$ and EtOAc) = 0.77. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 8.95 (s, 2H, ArH), 8.17 (d, $J$ = 8.4 Hz, 1H, ArH), 7.65-7.60 (m,..
2H, ArH), 7.48 (t, J = 7.4 Hz, 1H, ArH), 4.14 (s, 3H, Me). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 165.3, 154.0, 146.5, 132.7, 129.3, 127.4, 125.1, 120.9, 109.4, 56.1. HRMS (ESI/TOF) m/z calculated for C$_{11}$H$_9$N$_5$O [M + H]: 228.0880, found 228.0903.
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\[
\begin{align*}
\text{Formula: } & O^- \overset{\text{N=N}}{\text{N}} \overset{\text{N}}{\text{N}} \overset{\text{N}}{\text{N}} \\
\text{Structure: } & \text{10}
\end{align*}
\]
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![Chemical Structure Diagram](image)
\[ \text{O}^- \text{N}^+ \text{N} \text{Br} \text{Cl} \]