Azide-Benzyne Cycloaddition and Olefination to Vinyl Benzotriazoles

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Azide-Benzyne Cycloaddition and Olefination to Vinyl Benzotriazoles

A Master’s Thesis Presented to Faculty of Science of The City College of New York In Candidacy for the Degree of Master of Science (MS)

By
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Thesis Advisor: Professor Barbara Zajc

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I would really like to take this chance to thank all of those individuals that have helped me along this journey. First and foremost I would like to thank my father, who unfortunately is no longer here, and my mother for their love and support. They have made me the man I am today.

A special thanks to Prof. Barbara Zajc for all of her mentoring, encouragement, and knowledge she has shared with me as well as the opportunity to work in her lab. Next, I would like to thank Prof. Lakshman for his guidance and role as a mentor through my time in the lab. I would also like to thank Prof. Boson for taking the time out to serve as a committee member during my thesis committee.

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INTRODUCTION

Heterocycles are an important class of compounds, that are widely spread in nature. Examples of naturally occurring heterocycles are pigments, vitamins, and antibiotics. Further, innumerable synthetic heterocycles are used in everyday life, such as drugs, pesticides, dyes, and plastics.$^1$ Benzotriazoles are one class of heterocycles, containing three nitrogen atoms (Figure 1).

![Figure 1. Structure of benzotriazole](image)

Benzotriazoles have been the focus of recent research because of their possible uses as pharmaceuticals as well as because of their versatility as important synthetic intermediates. In various benzotriazole derivatives, the benzotriazole unit can serve as a good leaving group leading to further substitution.$^2$ The benzotriazole core has also been found in many biologically important molecules, that were shown to induce growth inhibition in cancer cells (Figure 2).$^3,4$

![Figure 2. Benzotriazoles as potential anti cancer agents](image)
The presence of the benzotriazole unit in many compounds is therefore of great importance in the pharmaceutical industry, where such derivatives are also showing antiviral/antifungal properties. Some of these structures are shown below in Figure 3.

\[ \text{Figure 3. Potential antiviral/antimicrobial benzotriazoles} \]

Studies of a series of benzotriazolyl acrylonitriles have shown that several members are potent tubulin inhibitors. The most active such compounds are shown below in Figure 4.

\[ \text{Figure 4. Benzotriazoles as potential tubulin inhibitors} \]
There are two approaches to the synthesis of benzotriazole and benzotriazole derivatives that have been classically used. One is by intramolecular amination by metal catalysis, shown in Scheme 1.\textsuperscript{8}

\textit{Scheme 1. Benzotriazole via metal catalysis}

![Scheme 1](image1)

The second approach is the reaction of an ortho-diamine benzene with sodium nitrite and acetic acid. The first step of the reaction is diazotization of one of the amine groups and then generation of the triazole ring.\textsuperscript{9}

\textit{Scheme 2. Benzotriazole via diazotization}

![Scheme 2](image2)

A more modern approach to the synthesis of the benzotriazole ring is by a dipolar cycloaddition. This method is a very powerful tool in the synthesis of five-membered heterocycles. This is a pericyclic reaction between an enediyne and an azide to give the corresponding benzotriazole.\textsuperscript{10}

\textit{Scheme 3. Benzotriazole via cycloaddition}

![Scheme 3](image3)

Another recent approach to the synthesis of benzotriazoles is by a benzyne-azide cycloaddition reaction, also known as benzyne “click chemistry”. Benzyne “click chemistry” provides a quick and efficient method to produce substituted and
functionalized benzotriazoles. Scheme 4 shows an example of this powerful synthetic method.

**Scheme 4. Benzotriazole via benzyne**

\[
\begin{align*}
\text{Ts} & \quad + \\
\text{R}^1 - \text{N}_3 
& \quad \xrightarrow{\text{CsF}, \text{MeCN, rt. 18-24h}} \\
\end{align*}
\]

\[N\text{-vinyl derived benzotriazoles can serve as useful synthetic intermediates. Vinyl compounds occupy central position as intermediates in organic synthesis. There are numerous synthetic methods for the preparation of vinyl derivatives. One modular synthesis of vinyl compounds is by the Wittig reaction, shown in Scheme 5.} \]

In this reaction an aldehyde or ketone reacts with a triphenyl phosphonium ylide, called a Wittig reagent, to give an alkene and triphenylphosphine oxide.

**Scheme 5. Wittig olefination**

Another modular approach is Horner-Wadsworth-Emmons, shown in Scheme 6 below. Similarly, in this Wittig-like reaction a ketone or aldehyde reacts in the presence of base, but instead of ylide a phosphonate is used to create the desired alkene.

**Scheme 6. Horner-Wadsworth-Emmons olefination**

In Peterson olefination, \(\alpha\)-silylcarbanion adds to the carbonyl compound and rearranges to form a betainE-like intermediate. Anti-elimination occurs in the acidic hydrolysis workup (Scheme 7).
One other possible route for the synthesis of alkenes is classical Julia olefination reaction, which converts a phenyl sulfone to a vinyl compound, in the reaction with an aldehyde or a ketone. The classical Julia reaction is multistep and cumbersome. The one-pot or modified Julia-Kocienski olefination, on the other hand, utilizes a heteroaryl sulfone and proceeds in one step as shown in Scheme 8. It is widely used in synthesis, including synthesis of natural products.\textsuperscript{16, 17, 18}

**Scheme 8. Modified Julia-Kocienski olefination**

In this context, vinyl benzotriazoles have been used as synthetic intermediates in the synthesis of indoles.\textsuperscript{19} Further, their thermal and photochemical conversions have been reported as well.\textsuperscript{20} Synthesis of vinyl benzotriazoles has been reported. Scheme 9
shows the use of a 2-step addition, and subsequent elimination reaction to create the vinyl benzotriazole from benzotriazole chloride and an alkene.\textsuperscript{21, 22}

**Scheme 9. Synthesis of vinyl benzotriazoles via addition-elimination sequence**

\[
\text{Cl} \quad \text{Me} \
\text{N} \quad \text{N} \
\text{N} \quad \text{Me} \
\text{N} \quad \text{N} \quad \text{Me} \
\text{N} \quad \text{N} \
\text{Cl} \
\]

1. Cold Benzene
2. DMF, Potassium Butoxide, 0 °C

Among modular approaches, Wittig (Scheme 10) and Peterson olefination (Scheme 11) have also been used for the synthesis of vinyl benzotriazoles.\textsuperscript{23} Among the two, Peterson olefination gave higher yields than the Wittig. However, the stereochemical outcome of these two olefination has not been reported.

**Scheme 10. Wittig approach to vinyl benzotriazoles**

\[
\text{N} \quad \text{N} \
\text{PPh}_3\text{Cl} \quad \text{O} \quad \text{O} \
\text{N} \quad \text{PPh}_3\text{Cl} \
\text{N} \quad \text{N} \quad \text{R}_1 \quad \text{R}_2 \
\text{N} \quad \text{N} \quad \text{R}_1 \quad \text{R}_2 \
\text{N} \quad \text{N} \
\text{PPh}_3\text{Cl} \
\]

n-BuLi, DMSO

**Scheme 11. Peterson approach to vinyl benzotriazoles**

\[
\text{N} \quad \text{N} \
\text{SiMe}_3 \quad \text{O} \quad \text{O} \
\text{N} \quad \text{SiMe}_3 \
\text{N} \quad \text{N} \quad \text{R}_1 \quad \text{R}_2 \
\text{N} \quad \text{N} \quad \text{R}_1 \quad \text{R}_2 \
\text{N} \quad \text{N} \
\text{SiMe}_3 \
\]

TBAF, THF

One other recently reported method for obtaining the vinyl benzotriazoles was through a Cu-catalyzed coupling reaction of a vinyl bromide and a benzotriazole. A mixture of $N_1$- and $N_2$-substituted vinyl derivatives was obtained. This is shown below in Scheme 12.\textsuperscript{24}
Our research group has been involved in the use of Julia-Kocienski olefination for the synthesis of variously functionalized alkenes and fluoroalkenes. We became interested in the use of Julia-Kocienski olefination for the synthesis of vinyl benzotriazoles.

There are in principle two general approaches to the synthesis of N-vinyl benzotriazoles. The first is a stepwise approach, where the vinyl benzotriazole is assembled from the appropriate benzotriazole precursor. Alternatively, the benzotriazole core can be assembled via a modular approach, using a dipolar cycloaddition reaction of an azide and a benzyne, with concomitant introduction of olefination handle.

We decided to pursue a synthetic strategy, where the benzotriazole core would be assembled via “click chemistry”. A benzotriazole core with an appropriate handle for Julia-Kocienski olefination would then offer an easy access to vinyl benzotriazole derivatives.

Scheme 13 shows the retrosynthetic approach. Reaction between an azidomethyl heteroaryl sulfide with in situ formed benzyne would generate the desired benzotriazole core. Oxidation of sulfide to sulfone, followed by Julia-Kocienski olefination would furnish the desired vinyl benzotriazole.
Scheme 13. Retrosynthetic scheme

\[
\begin{align*}
R_1\equiv N\equiv N & \quad \Downarrow \\
N\equiv N & \quad \Downarrow \\
N\equiv N \quad + \quad R_1\equiv O & \\
N\equiv N \quad + \quad \cyclic{6} &
\end{align*}
\]}
RESULTS AND DISCUSSION

Our synthesis started with the preparation of an azidomethyl heteroaryl sulfide. Initially, benzothiazole-derived Julia reagents were targeted, but cycloaddition proved unsuccessful and resulted in complex reaction mixture. Therefore, we chose to synthesize phenyltetrazolyl derivative, due to its higher stability, compared to benzothiazole. Phenyltetrazole thiol was reacted with bromochloromethane in an S_N_2 type mechanism to give the desired 5-[(chloromethyl)thio]-1-phenyl-1H-tetrazole 1 (Scheme 14).

Scheme 14. Synthesis of 5-[(chloromethyl)thio]-1-phenyl-1H-tetrazole 1

With the “Julia-Kocienski handle” in place, we proceeded to the assembly of the benzotriazole unit in a three-step procedure. Due to poorer leaving group ability of chloride, 1 was converted to 5-[(iodomethyl)thio]-1-phenyl-1H-tetrazole 2 via a Finkelstein reaction (Scheme 15, step 1). The azide was introduced under relatively mild conditions, using sodium azide at 50 °C in DMF (Scheme 15, step 2). Finally, in the third step the benzotriazole core was assembled in a dipolar cycloaddition of the 5-[(azidomethyl)thio]-1-phenyl-1H-tetrazole 3 and benzyne. As a benzyne precursor, anthrinilic acid was first used to create the benzyne in situ but only complex reaction mixture was isolated upon reaction with azide 3. Synthesis of benzotriazoles was reported via [3+2] cycloaddition of azides to benzyne, generated in situ from o-(trimethylsilyl)phenyl triflate. This method was therefore utilized to create the
benzotriazole moiety. Reactions shown in Scheme 2 were successful and were repeated on large scales of up to 3 grams, yielding products 2, 3, and 4 in 81, 82, and 86% yield, respectively.

**Scheme 15. A three-step synthetic sequence for assembly of N-substituted benzotriazole, precursor to Julia-Kocienski reagent**

**Step 1**

\[
\begin{align*}
\text{N} & \equiv \text{N} \quad \text{Cl} \quad + \quad \text{N} & \equiv \text{N} \quad \text{I} \\
\text{N} & \equiv \text{N} \quad \text{S} \quad \text{Cl} \quad + \quad \text{N} & \equiv \text{N} \quad \text{S} \quad \text{I} \\
\text{Acetone} & \quad \text{Reflux} \quad 81\% \\
\text{N} & \equiv \text{N} \quad \text{S} \quad \text{I} \\
\end{align*}
\]

**Step 2**

\[
\begin{align*}
\text{N} & \equiv \text{N} \quad \text{S} \quad \text{I} \quad + \quad \text{NaN}_3 \quad \text{DMF} \quad 50 \, ^\circ\text{C} \quad 82\% \\
\text{N} & \equiv \text{N} \quad \text{S} \quad \text{N}_3 \\
\end{align*}
\]

**Step 3**

\[
\begin{align*}
\text{N} & \equiv \text{N} \quad \text{S} \quad \text{N}_3 \quad + \quad \text{N} & \equiv \text{N} \quad \text{S} \quad \text{TMS} \\
\text{OTf} & \quad + \quad \text{KF} \quad + \quad 18\text{-Crown-6} \quad \text{MeCN} \quad \text{rt} \quad 86\% \\
\text{N} & \equiv \text{N} \quad \text{S} \quad \text{N}_3 \\
\end{align*}
\]

Once the benzotriazole core was constructed, compound 4 was further oxidized to Julia-Kocienski reagent. Reaction of 4 with chromium trioxide and periodic acid yielded the desired 1-\{(1-phenyl-1H-tetrazol-5-yl)sulfonyl\}methyl]-1H-benzo[d][1,2,3]triazole (5, Scheme 16) in 69% yield.
Scheme 16. Oxidation of 4 to Julia-Kocienski reagent for synthesis of vinyl benzotriazoles

With the desired benzotriazole-derived Julia-Kocienski reagent in hand, various conditions were screened for the condensation reactions (Undergraduate Honors Research, Jorge Swett, Unpublished).

Table 1. Optimization of reaction conditions

<table>
<thead>
<tr>
<th>Entry</th>
<th>Conditions</th>
<th>Yield&lt;sup&gt;a&lt;/sup&gt;</th>
<th>E/Z Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NaOH, rt</td>
<td>--&lt;sup&gt;b&lt;/sup&gt;</td>
<td>50:50</td>
</tr>
<tr>
<td>2</td>
<td>KHMDS, 0 °C</td>
<td>66%</td>
<td>60/40</td>
</tr>
<tr>
<td>3</td>
<td>LHMDS, 0 °C</td>
<td>59%</td>
<td>73/27</td>
</tr>
<tr>
<td>4</td>
<td>NaHMDS, 0 °C</td>
<td>45%</td>
<td>60/40</td>
</tr>
</tbody>
</table>

<sup>a</sup>Isolated yield. <sup>b</sup>Product not isolated.
All reactions were performed under Barbier conditions, i.e. base was added to a mixture of sulfone 5 and carbonyl compound. Although the yield was highest when KHMDS was used as base, higher selectivity was achieved with LHMDS as base. Once the optimal conditions were identified, the effect of substrate structure on yield/stereoselectivity was studied. In a typical experiment, 1 molar equiv of sulfone, 1.2-1.5 molar equiv of carbonyl compound and 2.4 molar equiv of LHMDS was used. The only exception was reaction with acetophenone (entry 13), where no desired product was detected in reaction mixture under these conditions. In this case, 2 molar equiv of sulfone, 1 molar equiv of acetophenone and 3 molar equiv of LHMDS were used. Table 2 shows results of the condensation reactions.

Table 2. Condensation reactions of Julia-Kocienski reagent 5 with aldehydes and ketones

<table>
<thead>
<tr>
<th>Entry</th>
<th>Aldehyde</th>
<th>Time</th>
<th>Product: Yield, $^a$ E/Z Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1$^b$</td>
<td><img src="image1.png" alt="Image of aldehyde 1" /></td>
<td>30 min</td>
<td>6: 59%, 73/27</td>
</tr>
<tr>
<td>2$^b$</td>
<td><img src="image2.png" alt="Image of aldehyde 2" /></td>
<td>30 min</td>
<td>7: 84%, 93/7</td>
</tr>
<tr>
<td>3$^b$</td>
<td><img src="image3.png" alt="Image of aldehyde 3" /></td>
<td>30 min</td>
<td>8: 82%, 41/59</td>
</tr>
<tr>
<td>No.</td>
<td>Compound</td>
<td>Reaction Time</td>
<td>Isolated Yield</td>
</tr>
<tr>
<td>-----</td>
<td>----------</td>
<td>---------------</td>
<td>----------------</td>
</tr>
<tr>
<td>4</td>
<td><img src="image" alt="F3C phenyl ketone" /></td>
<td>2 h</td>
<td>62%, 29/71</td>
</tr>
<tr>
<td>5&lt;sup&gt;b&lt;/sup&gt;</td>
<td><img src="image" alt="Thiophene" /></td>
<td>30 min</td>
<td>90%, 40/60</td>
</tr>
<tr>
<td>6</td>
<td><img src="image" alt="Benzofuran" /></td>
<td>1 h</td>
<td>65%, 64/36</td>
</tr>
<tr>
<td>7</td>
<td><img src="image" alt="Benzotriazole" /></td>
<td>3 h</td>
<td>72%, 71/29</td>
</tr>
<tr>
<td>8</td>
<td><img src="image" alt="Imidazole" /></td>
<td>2 h</td>
<td>71%, 29/71</td>
</tr>
<tr>
<td>9&lt;sup&gt;b&lt;/sup&gt;</td>
<td><img src="image" alt="Butanoic acid" /></td>
<td>30 min</td>
<td>67%, 4/96</td>
</tr>
<tr>
<td>10&lt;sup&gt;b&lt;/sup&gt;</td>
<td><img src="image" alt="Hexanoic acid" /></td>
<td>30 min</td>
<td>73%, 22/78</td>
</tr>
<tr>
<td>11</td>
<td><img src="image" alt="Octanoic acid" /></td>
<td>2 h</td>
<td>52%, 20/80</td>
</tr>
<tr>
<td>12</td>
<td><img src="image" alt="Nonanal" /></td>
<td>1 h</td>
<td>80%, 16/84</td>
</tr>
<tr>
<td>13</td>
<td><img src="image" alt="Acetophenone" /></td>
<td>3 h</td>
<td>31%</td>
</tr>
<tr>
<td>14</td>
<td><img src="image" alt="quinolinone" /></td>
<td>3 h</td>
<td>77%</td>
</tr>
</tbody>
</table>

<sup>a</sup>Isolated yield. <sup>b</sup>Undergraduate Honors Research, Jorge Swett, unpublished.

The condensation reactions gave moderate to good yields of vinyl benzotriazoles with a wide range of aldehydes. Stereoselectivity depended on the structure of the
aldehyde. Electron-rich aromatic aldehydes reacted to give E-isomer as the major one (entries 1, 2, 6, 7). This is consistent with the mechanism proposed by Julia, where formation of zwitterionic intermediates was suggested in the case of electron-rich aldehydes, leading to E-stereoselectivity.\textsuperscript{12} Exception in our case were 5-membered heterocycles with carboxaldehyde substituent in the ortho position to the heteroatom, i.e. thiophene and N-protected imidazole derivative (entries 5 and 8). In the case of electron-deficient aromatic aldehydes, where formation of zwitterionic intermediates is disfavored, condensations proceeded with Z-stereoselectivity (entries 3 and 4). Condensations with alkanals were Z-selective. Selectivity was highest with n-octanal (entry 9), whereas branching at the alpha (entries 10, 11) or beta position (entry 12) decreased the selectivity. Condensation proceeded also with ketones (entries 13, 14). Whereas acetophenone gave product in a low 31\% yield, N-benzyl piperdone yielded vinyl benzotriazole 19 in a good 77\% yield.

In order to test the methodology for the synthesis of substituted vinyl benzotriazoles, azidomethyl (phenyl)tetrazolyl sulfide 4 was reacted with substituted benzenes (Table 3). As aryne precursors, symmetrical naphtho derivative (entry 1) and 4,5-dimethoxyphenyl derivative (entry 2) were chosen. The unsymmetrical aryne precursors, that can give two regioisomeric products, were 3-methoxy (entry 3), 4-methoxy (entry 4), 4-methyl (entry 5) and 3-methyl (entry 6) phenyl derivatives. Results of cycloaddition reactions are displayed in Table 3. In all cases tested, reactions proceeded in 80-88\% yield to give substituted benzotriazoles. In the reaction of 3-methoxy benzyne precursor the yield was lower (68\%, entry 3), but only one regioisomer was formed. Formation of a single regioisomer in the case of 3-methoxy benzyne precursor has been reported in reaction with benzyl azide.\textsuperscript{9} In the present case, the
structure of the regioisomer 22 (entry 3) was determined by NOESY experiment and is consistent with the regioselectivity reported. Other unsymmetrical benzyne precursors, i.e. 4-methoxy (entry 4), 4-methyl (entry 5), and 3-methyl (entry 6) gave both possible regioisomers. The structures of regioisomers were determined by NOESY experiment and are shown in Table 3, along with their ratios (entries 4-6).

Table 3. Cycloaddition of azide 3 with naphthyne and substituted benzenes

<table>
<thead>
<tr>
<th>Entry</th>
<th>Benzyne Precursor</th>
<th>Product Structuresa</th>
<th>Product: Yield, % Isomer Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$\text{OTf}$</td>
<td>![Structure 20]</td>
<td>20: 83%</td>
</tr>
<tr>
<td>2</td>
<td>$\text{OE}$</td>
<td>![Structure 21]</td>
<td>21: 80%</td>
</tr>
<tr>
<td>3</td>
<td>$\text{OTf}$</td>
<td>![Structure 22]</td>
<td>22: 68%</td>
</tr>
</tbody>
</table>

\[ \text{N}=\text{N}-\text{S}\text{N}_3 + \text{R}-\text{TMS} + \text{KF} + 18\text{-Crown-6} \rightarrow \text{MeCN} \quad \text{rt} \quad 68-85\% \]
For unsymmetrical benzyne precursors, structures of regioisomers were determined by a NOESY experiment. \(^b\) Isolated yield.

The methodology proved successful, and we proceeded to oxidize the symmetrical naphthotropic 

20 and symmetrically substituted benzotriazole 21, in order
to test them in the Julia-Kocienski condensation reactions. First, the oxidation of naphthotriazole derivative 20 (Scheme 17) was performed, using H₅IO₆/CrO₃. However, instead of the expected sulfide to sulfone conversion, oxidation of the central ring of the naphthotriazole to the corresponding quinone occurred, resulting in product 26.

Scheme 17. Oxidation of naphthotriazole 20 to quinone derivative 26

After initial attempts to oxidize napthotriazole derivative 20 to sulfone resulted in the undesired quinone derivative 26, various oxidation conditions were screened to obtain the desired sulfone (Table 4). The use of MCPBA (3 molar equiv) over 24 h gave a mixture of sulfoxide and sulfone in a ratio of 73/27, respectively (entry 1). The use of KMnO₄ with BTEAC gave the desired sulfone with a side product, but the side product was major (entry 2). Oxidation reactions with RuCl₃ and NaIO₄, as well as ammonium molybdate with hydrogen peroxide gave a mixture of sulfide and sulfone (entries 3, 4).

Table 4. Screening of conditions for oxidation of naphthotriazole derivative 20 to Julia-Kocienski reagent
<table>
<thead>
<tr>
<th>Entry</th>
<th>Conditions</th>
<th>Products: NMR ratio, Yield&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MCPBA (3 molar equiv), rt, 24 h</td>
<td>Sulfoxide/Sulfone: 73/27&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>2</td>
<td>KMnO&lt;sub&gt;4&lt;/sub&gt;/BTEAC, rt, 20 h</td>
<td>Sulfone + Side product&lt;sup&gt;c&lt;/sup&gt;: Side product major&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>3</td>
<td>RuCl&lt;sub&gt;3&lt;/sub&gt;/NaIO&lt;sub&gt;4&lt;/sub&gt;, rt, 24 h</td>
<td>Sulfide/Sulfone: 74/26&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>4</td>
<td>Mo&lt;sub&gt;7&lt;/sub&gt;O&lt;sub&gt;24&lt;/sub&gt;(NH&lt;sub&gt;4&lt;/sub&gt;)&lt;sub&gt;6&lt;/sub&gt;·4H&lt;sub&gt;2&lt;/sub&gt;O (0.27 molar equiv)/ H&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt;–EtOH, rt 30 h</td>
<td>Sulfide/Sulfone: 11/89&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>5</td>
<td>Mo&lt;sub&gt;7&lt;/sub&gt;O&lt;sub&gt;24&lt;/sub&gt;(NH&lt;sub&gt;4&lt;/sub&gt;)·4H&lt;sub&gt;2&lt;/sub&gt;O (1 molar equiv)/ H&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt;–CH&lt;sub&gt;3&lt;/sub&gt;CN, rt, 24 h</td>
<td>Sulfone + Minor impurity: 69%&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>Yield of purified sulfone. <sup>b</sup>Sulfone not isolated. <sup>c</sup>Structure not determined.

Upon the use of stoichiometric amount of ammonium molybdate and hydrogen peroxide in acetonitrile, formation of only sulfone 27 and minor impurity was observed (entry 5). The desired naphthotriazole sulfone 27 was isolated in 69% yield (Scheme 18).

Scheme 18. Successful oxidation of naphthotriazole derivative 20 to Julia-Kocienski reagent 27

Oxidation of monomethoxy benzotriazole derivative 22 was also performed with stoichiometric amount of ammonium molybdate and hydrogen peroxide in acetonitrile, and sulfone 28 was isolated in 51% yield (Scheme 19).
Next, oxidation conditions for conversion of dimethoxy benzotriazole derivative 21 to sulfone were screened (Table 5). Oxidation reactions with KMnO₄ with BTEAC and RuCl₃ with sodium periodate proved unsuccessful, giving no desired product (entries 1, 2). Reactions with ammonium molybdate/hydrogen peroxide and chromium trioxide/periodic acid were also unsuccessful, and only starting sulfide was observed (entries 3, 4). Oxidation was then performed with MCPBA (6 molar equiv, 24 h) and formation of sulfoxide was observed. Analysis of reaction mixture showed presence of sulfide and sulfoxide in a ratio of 60/40 (entry 5). Increasing the amount of MCPBA (10 molar equiv) and heating to 50 °C gave sulfone in a modest 41% yield.

**Table 5. Screening of conditions for oxidation of dimethoxybenzotriazole 21 to sulfone**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Conditions</th>
<th>Products: NMR ratio, Yield¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>KMnO₄/BTEAC, rt, 24 h</td>
<td>No desired product, --</td>
</tr>
</tbody>
</table>
Several attempts at oxidation of the pure sulfide 21 were unsuccessful. The crude sulfide 21, on the other hand, reacted with MCPBA (8 molar equiv) at room temperature, to give the desired sulfone 29 in 58% yield (Table 5, entry 7 and Scheme 20).

**Scheme 20. Successful oxidation of dimethoxy benzotriazole derivative 21 to Julia-Kocienski reagent 29**

```
\[
\begin{align*}
\text{21} & \quad + \quad \text{MCPBA} \\
\text{CHCl}_3 & \quad -10^\circ C \quad \rightarrow \quad 0^\circ C
\end{align*}
\]
```

With the desired sulfone 29 in hand, Julia-Kocienski olefinations were performed with two aldehydes. Results of the condensation reactions are shown in Table 6. In both cases, dimethoxy-substituted N-vinyl benzotriazole derivatives were isolated. The structure of the benzotriazole moiety had an effect on olefination, since both the yield and
stereoselectivity of olefination with tosyl-protected imidazole differed from those, obtained in the reaction with the unsubstituted benzotriazole reagent 5 (compare Table 2, entry 8 and Table 6, entry 1). The yield was somewhat higher with the 4,5-dimethoxy substituted benzotriazole sulfone 29, and the selectivity was reversed. However, in the case of citronellal, the yield was higher with benzotriazole reagent 5; whereas in the condensation reaction with benzotriazole sulfone 5 the selectivity was high E/Z 16/84, reaction with 29 was nonselective (compare Table 2, entry 12 and Table 6, entry 2).

Table 6. Olefination reactions with dimethoxy benzotriazole reagent 30

<table>
<thead>
<tr>
<th>Entry</th>
<th>Aldehyde</th>
<th>Time</th>
<th>Product: Yield(^a), E/Z Ratio</th>
</tr>
</thead>
</table>
| 1     | \[
\begin{array}{c}
\text{Ts} \\
\text{N} \\
\text{N} \\
\text{S} \\
\text{O} \\
\text{O} \\
\text{N} \\
\text{N}
\end{array}
\] | 25 min | 30: 80%, 60/40 |
| 2     | \[
\begin{array}{c}
\text{R} \\
\text{O} \\
\text{O} \\
\text{N} \\
\text{N}
\end{array}
\] | 25 min | 31: 68%, 41/59 |

\(^a\) Yield of purified product.

Next, condensations with naphthotriazole derivative 28 were performed. Due to the poor solubility of the pure sulfone 28 in THF, the crude reaction mixture, obtained in the oxidation of 21 to sulfone 28, was used in the olefinations. Results of the condensation reactions are shown in Table 7. In all three cases tested, reactions resulted
in naphthotriazole vinyl derivatives. The yield of olefination with p-
trifluoromethylbenzaldehyde was comparable to reaction with unsubstituted
benzotriazole sulfone 5. Although the selectivity dropped, the E/Z trend was maintained
(compare Table 2, entry 4 and Table 7, entry 5). However, in the case of 2-ethyl
butyraldehyde, the yield was much higher in the condensation reaction with benzotriazole
sulfone 5 and the selectivity was unchanged (compare Table 2, entry 10 and Table 7,
entry 7). Reaction of 3, 4, 5 trimethoxy benzaldehyde proceeded with naphthotriazole
sulfone 28 with E selectivity, and in a good 75% yield (Table 7, entry 1). Due to poor
solubility of reagent 28 in THF, reaction could be performed with crude 28 only, since
purification of 28 decreased its solubility. The use of other, more polar solvents was
tested for the condensations. Pure sulfone 28 was soluble in a mixture of THF/DMF (3/1
1ml/333µL, entry 2) and the reversal of selectivity was observed, whereas the yield was
comparable (compare entry 1 and entry 2). The use of DMF as solvent gave product 32
with slightly better Z-selectivity than in the case of THF/DMF, but the yield increased
significantly (compare entry 2 and entry 3). Reaction was also performed in DMPU,
however both Z-selectivity as well as the yield were lower than those obtained in DMF
(compare entry 3 and entry 4). Condensation of 28 with p-trifluoromethyl benzaldehyde
gave a slightly lower Z-selectivity and yield in THF, compared to DMF as solvent
(compare entry 5 and entry 6). Reaction with 2-ethyl butanal, on the other hand, gave
higher Z-selectivity in THF than in DMF (compare entry 7, and entry 8), whereas the
yield was lower in DMF.
Table 7. Olefination reaction with naphthotriazole reagent 28

![Chemical structure of reagents 27 and products 32-34](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Aldehyde</th>
<th>Solvent/Time</th>
<th>Product: Yield, E/Z Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>THF/ 20 min</td>
<td>32: 75%, 65/35&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>2</td>
<td><img src="image" alt="Aldehyde structure" /></td>
<td>THF-DMF (3:1) / 30 min</td>
<td>74%, 42/58</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>DMF/ 40 min</td>
<td>93%, 37/63</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>DMPU/ 40 min</td>
<td>82%, 43/57</td>
</tr>
<tr>
<td>5</td>
<td><img src="image" alt="Aldehyde structure" /></td>
<td>THF/ 20 min</td>
<td>33: 57%, 44/56&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>DMF/ 40 min</td>
<td>62%, 41:59</td>
</tr>
<tr>
<td>7</td>
<td><img src="image" alt="Aldehyde structure" /></td>
<td>THF/ 25 min</td>
<td>34: 54%, 22/78&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>8</td>
<td></td>
<td>DMF/ 40 min</td>
<td>70%, 33/67</td>
</tr>
</tbody>
</table>

<sup>a</sup>Crude sulfone 27 was used in olefinations.
CONCLUSION

We have developed an efficient methodology for modular synthesis of vinyl benzotriazoles. The benzotriazole core with a handle containing heteroaryl sulfonyl moiety was synthesized in a four-step procedure. Final oxidation of sulfide to sulfone gave the Julia-Kocienski reagent. The Julia-Kocienski reagent was reacted with various aldehydes and ketones to give vinyl benzotriazoles in moderate to good yields. Olefinations were E-selective for electron-rich aromatic aldehydes, except in the case of two heteroaromatic carboxaldehydes with substituent in the ortho position to the heteroatom, where, Z-isomer formed as the major one. Electron-deficient aromatic aldehydes reacted with Z-stereoselectivity, and condensations with alkanals were Z-selective. The methodology was applied also to substituted benzotriazoles by reacting our azidomethyl heteroaryl sulfide with various substituted benzyne precursors. In all cases tested, the corresponding substituted benzotriazole derivatives were formed in good yields (68%-88%). Aryltriazoles derived from 2, 3-naphthyne and 4, 5-dimethoxybenzyne precursors were oxidized to Julia-Kocienski reagents and subjected to olefinations, to give the corresponding vinyl-substituted aryltriazoles.
EXPERIMENTAL SECTION

General Methods and Techniques: THF was distilled over LiAlH₄ first and then over sodium. MeCN was distilled over CaCl₂. All other solvents and reagents were obtained commercially. All glassware for reactions that were performed under a nitrogen atmosphere, was flame dried under vacuum. Thin layer chromatography was performed on 200 μm Analtech silica plates. Visualization of developed TLC plates was accomplished by UV light and in some instances they were stained using an iodine or permanganate chamber to make the spots more visible. Column chromatographic purifications were performed on 200-300 mesh silica gel. ¹H NMR spectra were recorded at 500 MHz in CDCl₃, and are referenced to residual CHCl₃. ¹⁹F NMR spectra were recorded at 282 MHz using CFCl₃ as internal standard. ¹³C NMR spectra were recorded at 125 MHz and are referenced to the carbon resonance of the deuterated solvent. Chemical shifts (δ) are reported in parts per million and coupling constants (J) are in Hertz (Hz). HRMS data were gathered using a TOF analyzer.

Synthesis of 5-[(chloromethyl)thio]-1-phenyl-1H-tetrazole (1)

Potassium carbonate (19.4 g, 141 mmol, 5.00 molar equiv) was added to a solution of phenyl-1H-tetrazol-5-thiol (5.00 g, 28.1 mmol, 1.00 molar equiv) and chlorobromomethane (4.36 g, 33.7 mmol, 1.20 molar equiv) in 75.0 mL of acetone. A
stirring bar was placed inside the flask, and a condenser was attached. The reaction mixture was then allowed to reflux for 3 hours and monitored by TLC (SiO₂, 20% EtOAc in hexanes). After 3 hours, TLC indicated total consumption of the starting material, the solvent was concentrated and water was added to the mixture. The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was then washed with water, followed by brine. Anhydrous Na₂SO₄ was added to the organic layer to remove traces of water, and the solvent was evaporated under reduced pressure. The product was purified by column chromatography (SiO₂, eluted with 10% EtOAc in hexanes, with a stepwise increase to 20% EtOAc in hexanes) to yield 1.94 g (51%, white solid) of 5-[(chloromethyl)thio]-1-phenyl-1H-tetrazole (1). R<sub>f</sub>(20% EtOAc in hexanes) = 0.44 ¹H NMR (500 MHz, CDCl₃): δ 7.60-7.54 (m, 5H, Ar-H), 5.37 (s, 2H, CH₂). ¹³C NMR (125 MHz, CDCl₃): δ 151.51, 132.98, 130.59, 129.97, 123.887, 45.67. HRMS (ESI) calcld for C₇N₄H₆S [M+H]⁺ 227.0153, found 227.0172.

Synthesis of 5-[(iodomethyl)thio]-1-phenyl-1H-tetrazole (2)

![Diagram of synthesis](image)

A solution of 5-[(chloromethyl)thio]-1-phenyl-1H-tetrazole (1, 0.950 g, 4.19 mmol, 1.00 molar equiv) and sodium iodide (2.51 g, 16.8 mmol, 4.00 molar equiv) was refluxed in 100 mL of acetone. After 4 hours the TLC (SiO₂, 30% EtOAc in hexanes) showed total consumption of the starting 1. The solvent was evaporated under reduced pressure, followed by work up. Water was added to the reaction mixture and extraction was performed with ethyl acetate (3 x 10 mL). The combined organic layer was then washed
with water, followed by brine. Organic layer was dried over anhydrous Na$_2$SO$_4$, the solvent was evaporated under reduced pressure and 1.08 g (82%, yellow solid) crude product 2 was isolated. R$_f$(30% EtOAc in hexanes) = 0.46. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.60-7.53 (m, 5H, Ar-H), 4.81 (s, 2H, CH$_2$). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 152.92, 133.31, 130.67, 130.14, 123.97, -6.81. HRMS (ESI) calcd for C$_7$N$_4$H$_6$S [M+H]$^+$ 318.9509, found 318.9512.

**Synthesis of 5-[(azidomethyl)thio]-1-phenyl-1$H$-tetrazole (3)**

A solution of 5-[(iodomethyl)thio]-1-phenyl-1$H$-tetrazole (2, 2.60 g, 8.17 mmol, 1.00 molar equiv) and sodium azide (1.06 g, 16.3 mmol, 2.00 molar equiv) in 80.0 mL of DMF was allowed to stir at 50 °C using a sand bath. The reaction was monitored by TLC (SiO$_2$, 20% EtOAc in hexanes) that showed complete consumption of starting material after 45 min. The reaction was quenched by pouring into water. The aqueous layer was extracted with ethyl acetate (3 x 10 mL), the combined organic layer was washed with water, followed by brine. Anhydrous Na$_2$SO$_4$ was added to the organic layer to remove any trace of water, and the organic solvent was evaporated under reduced pressure to yield 1.70 g (89%, brown solid) of 5-[(azidomethyl)thio]-1-phenyl-1$H$-tetrazole (3). No purification was required and crude azide 3 was used in the subsequent step. R$_f$ (30% EtOAc in hexanes) = 0.36. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.62-7.56 (m, 5H, Ar-H), 5.14 (s, 2H, CH$_2$). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 152.35, 133.19, 130.50, 129.95, 123.81, 53.87. HRMS (ESI) calcd for C$_7$N$_4$H$_6$S [M+H]$^+$ 234.0556, found 234.0564.
**Synthesis of 1-\{[(1-phenyl-1H-tetrazol-5-yl)thio]methyl\}-1H-benzo[d][1,2,3]triazole (4)**

To a mixture of 5-\{(azidomethyl)thio\}-1-phenyl-1H-tetrazole (3, 0.870 g, 3.73 mmol, 1.00 molar equiv), 2-(trimethylsilyl)phenyltrifluoromethanesulfonate (1.67 g, 5.50 mmol, 1.50 molar equiv), 18-crown-6-ether (2.96 g, 11.2 mmol, 3.00 molar equiv) and potassium fluoride (0.867 g, 14.9 mmol, 4.00 molar equiv) under nitrogen, dry acetonitrile (70.0mL) was added. The reaction was allowed to stir at room temperature, and after 1 hour TLC (SiO₂, 40% EtOAc : hexanes) showed consumption of the starting azide 3. The reaction was quenched with water and the aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was washed with water, followed by brine. Anhydrous Na₂SO₄ was added to the organic layer to remove any trace of water, and the organic solvent was evaporated under reduced pressure. The pure compound was isolated by column chromatography (SiO₂, 20% EtOAc in hexanes, with a stepwise increase to 30% EtOAc in hexanes) to yield 0.979g (85%, white solid) of 1-\{[(1-phenyl-1H-tetrazol-5-yl)thio]methyl\}-1H-benzo[d][1,2,3]triazole (4). $R_f$ (40% EtOAc in hexanes) = 0.54. $^1$H NMR (500 MHz, CDCl₃): $\delta$ 8.06 (d, 1H, Ar-H, $J = 8.3$ Hz), 7.93 (d, 1H, Ar-H, $J = 8.3$ Hz), 7.56 (t, 1H, Ar-H, $J = 7.3$ Hz), 7.53-7.51 (m, 4H, Ar-H), 7.42-7.39 (m, 2H, Ar-H), 6.65 (s, 2H, CH₂). $^{13}$C NMR (125 MHz, CDCl₃): $\delta$ 152.18, 146.33, 133.13, 132.68, 130.78, 130.13, 128.68, 124.84, 123.97, 120.32, 110.76, 49.32. HRMS (ESI) calcd for C₇N₄H₆S [M+H]$^+$ 310.0869, found 310.0880.
Synthesis of 1-{{(1-phenyl-1H-tetrazol-5-yl)sulfonyl}methyl}-1H-benzo[d][1,2,3]triazole (5)

Periodic acid (2.86 g, 12.5 mmol, 4.00 molar equiv) in 26.0 mL of dry acetonitrile was stirred at room temperature for 30 min. Chromium trioxide (0.016 g, 0.159 mmol, 0.050 molar equiv) was added and the mixture was allowed to stir for another 5 min. After 5 min, periodic acid/CrO₃ suspension was added to a solution of 1-{{(1-phenyl-1H-tetrazol-5-yl)thio}methyl}-1H-benzo[d][1,2,3]triazole (4, 0.970 g, 3.14 mmol, 1.00 molar equiv) under a N₂ ballon. The reaction was monitored by TLC (SiO₂, 40% EtOAc in hexanes). After 3 hours, TLC showed complete consumption of starting material. The reaction mixture was cooled on ice and quenched with aqueous solution of NaHCO₃ and sodium bisulfate. The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was then washed with water, followed by brine. Anhydrous Na₂SO₄ was added to the organic layer to remove any trace of water, and the organic solvent was evaporated under reduced pressure. The product was purified by column chromatography (10% acetone in hexanes) to yield 0.730 g (69%, yellow solid) of the 1-{{(1-phenyl-1H-tetrazol-5-yl)sulfonyl}methyl}-1H-benzo[d][1,2,3]triazole (5). Rₚ (40% acetone in hexanes) = 0.47. ¹H NMR (500 MHz, CDCl₃): δ 8.09 (d, 1H, Ar-H, J = 8.3 Hz), 7.66 (d, 1H, Ar-H, J = 8.3 Hz), 7.58 (t, 1H, Ar-H, J = 7.6 Hz), 7.53 (t, 1H, Ar-H, J = 7.4 Hz), 7.45 (t, 3H, Ar-H, J = 7.8 Hz), 7.37 (d, 2H, Ar-H, J = 7.8 Hz), 6.46 (s, 2H, CH₂). ¹³C NMR (125 MHz, CDCl₃): δ 152.07, 146.18, 133.19, 132.43, 131.87, 129.73, 129.56,

32
125.42, 125.38, 120.79, 109.74, 67.60. HRMS (ESI) calcd for C\textsubscript{7}N\textsubscript{4}H\textsubscript{6}S [M+H]\textsuperscript{+} 342.0768, found 342.0764.

**Synthesis of (E,Z)-1-[4-(trifluoromethyl)styryl]-1\textit{H}-benzo[\textit{d}][1,2,3]triazole (E/Z-9)**

A solution of 1-[[1-phenyl-1\textit{H}-tetrazol-5-yl]sulfonyl]methyl]-1\textit{H}-benzo[\textit{d}][1,2,3]triazole (5, 0.102 g, 0.300 mmol, 1.00 molar equiv) and 4-(trifluoromethyl)benzaldehyde (0.078 g, 0.450 mmol, 1.50 molar equiv.), in THF (5.10 mL) under nitrogen, was cooled to 0 °C. LHMDS (0.113 g, 0.720 mmol, 2.40 molar equiv) was added. The reaction was allowed to stir at 0 °C. After 2h, the reaction was checked by TLC (SiO\textsubscript{2}, 40% EtOAc in hexanes), that showed complete consumption of the starting sulfone 5. The reaction was quenched with saturated aqueous ammonium chloride. The aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layer was then washed with water, followed by brine. Anhydrous Na\textsubscript{2}SO\textsubscript{4} was added to the organic layer to remove any trace of water, and the organic solvent was evaporated under reduced pressure. The crude compound was purified by column chromatography (SiO\textsubscript{2}, 10% EtOAc in hexanes with a stepwise increase to 20% EtOAc in hexanes) to yield 0.054g of (E,Z)-1-[4-(trifluoromethyl)styryl]-1\textit{H}-benzo[\textit{d}][1,2,3]triazole (E/Z- 9, 62%, yellow solid). \textit{Rf}(20% EtOAc in hexanes) = 0.41. \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}): \(\delta\) 8.13 (d, 1H, \textit{E} - isomer, \(J = 8.3\) Hz), 8.10-8.06 (m, \textit{E} + \textit{Z} isomer), 8.02 (d, 1H, \textit{E}-isomer, \(J = 14.7\) Hz), 7.78 (d, 1H, \textit{E}-isomer, \(J = 8.3\) Hz), 7.68-7.64 (m, \textit{E} + \textit{Z} isomer), 7.61 (t, 1H, \textit{E} - isomer, \(J = 8.3\) Hz),
7.51 (d, 1H, E - isomer, J = 15.1Hz), 7.46 (t, 1H, E - isomer, J = 8.3Hz), 7.43 (d, 2H, Z - isomer, J = 8.3Hz), 7.38-7.35 (m, E + Z - isomer), 7.17 (d, 2H, Z - isomer, J = 8.3Hz), 7.08-7.04 (m, E + Z - isomer), 6.77 (d, 1H, Z - isomer, J = 9.3Hz). $^{19}$F NMR (282MHz): δ -63.10 (s, E – isomer), -63.39 (s, Z-isomer). HRMS (ESI) calcd for C$_7$N$_4$H$_6$S [M+H]$^+$ 290.0900, found 290.0913.

**Synthesis of (E,Z)-1-[2-(benzofuran-5-yl)vinyl]-1H-benzo[d][1,2,3]triazole (E/Z-11)**

A solution of 1-{{[1-phenyl-1H-tetrazol-5-yl)sulfonyl]methyl}-1H-benzo[d][1,2,3] triazole (5, 0.102 g, 0.300 mmol, 1.00 molar equiv) and benzofuran-5-carbaldehyde (0.066 g, 0.450 mmol, 1.50 molar equiv), in THF (5.10 mL) under nitrogen, was cooled to 0 °C. LHMDS (0.113 g, 0.720 mmol, 2.40 molar equiv) was added. The reaction was allowed to stir at 0 °C. After 2h, the reaction was checked by TLC (SiO$_2$, 40% EtOAc in hexanes), that showed complete consumption of the starting sulfone 5. The reaction was quenched with saturated aqueous ammonium chloride. The aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layer was then washed with water, followed by brine. Anhydrous Na$_2$SO$_4$ was added to the organic layer to remove any trace of water, and the organic solvent was evaporated under reduced pressure. The crude compound was purified by column chromatography (10% EtOAc in hexanes with a stepwise increase to 15% EtOAc in hexanes) to yield 0.051g of (E,Z)-1-[2-(benzofuran-5-yl)vinyl]-1H-benzo[d][1,2,3] triazole (E/Z-11, 65%, white solid). R$_f$ (20% EtOAc in
hexanes) = 0.38. \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 8.14 (d, 1H, \(E\) - isomer, \(J = 8.3\) Hz), 8.09 (d, 1H, \(Z\) - isomer, \(J = 7.8\) Hz), 7.94 (d, 1H, \(E\) - isomer, \(J = 14.7\) Hz), 7.80-7.78 (m, \(E + Z\) - isomer), 7.68 (d, 1H, \(E\) - isomer, \(J = 2.0\)Hz), 7.60 (d, 1H, \(E\) - isomer, \(J = 14.7\) Hz), 7.60-7.52 (m, \(E + Z\) isomer), 7.46 (t, 1H, \(E\) - isomer, \(J = 7.6\) Hz), 7.33 (t, 1H, \(Z\) - isomer, \(J = 7.8\) Hz), 7.31-7.27 (m, \(E + Z\) - isomer), 7.03 (d, 1H, \(Z\) - isomer, \(J = 8.3\) Hz), 6.93-6.89 (m, \(E + Z\) - isomer), 6.82 (d, 1H, \(E\) - isomer, \(J = 2.0\) Hz), 6.60 (d, 1H, \(Z\) - isomer, \(J = 2.0\) Hz). HRMS (ESI) calcd for C\(_7\)N\(_4\)H\(_6\)S [M+H]\(^+\) 262.0975, found 262.0980.

**Synthesis of \((E,Z)\)-1-[2-(1-tosyl-1H-indol-3-yl)vinyl]-1H-benzo[d][1,2,3]triazole \((E/Z-12)\)**

A solution of 1-\{[(1-phenyl-1H-tetrazol-5-yl)sulfonyl]methyl\}-1H-benzo[d][1,2,3]triazole (5, 0.102 g, 0.300 mmol, 1.00 molar equiv) and 1-tosyl-1H-indole-3-carbaldehyde (0.070 g, 0.450 mmol, 1.50 molar equiv), in THF (5.10 mL) under nitrogen, was cooled to 0 °C. LHMDS (0.113 g, 0.720 mmol, 2.40 molar equiv) was added. The reaction was allowed to stir at 0 °C. After 2h, the reaction was checked by TLC (SiO\(_2\), 40% EtOAc in hexanes), that showed complete consumption of the starting sulfone 5. The reaction was quenched with saturated aqueous ammonium chloride. The aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layer was then washed with water, followed by brine. Anhydrous Na\(_2\)SO\(_4\) was added to the organic layer
to remove any trace of water, and the organic solvent was evaporated under reduced pressure. The crude compound was purified by column chromatography (10% EtOAc in hexanes with a stepwise increase to 40% EtOAc in hexanes) to yield 0.089g of (E,Z)-1-[2-(1-tosyl-1H-indol-3-yl)vinyl]-1H-benzo[d][1,2,3]triazole (E/Z-12, 72%, pale pinkish colored solid). Rf (40% EtOAc in hexanes) = 0.45. 1H NMR (500 MHz, CDCl3): δ 8.06 (d, 2H, Z - isomer, J = 8.3 Hz), 8.00 (d, 1H, E - isomer, J = 8.3 Hz), 7.95 (d, 1H, E - isomer, J = 14.7 Hz), 7.88 (d, 1H, Z - isomer, J = 8.3 Hz), 7.77-7.70 (m, E + Z - isomer), 7.56-7.52 (m, E + Z - isomer), 7.49 (d, 1H, E - isomer, J = 14.7 Hz), 7.43 (s, 1H, Z - isomer), 7.40-7.18 (m, E + Z - isomer), 7.15-7.11 (m, E + Z - isomer), 6.76 (d, 1H, Z - isomer, J = 9.3 Hz), 2.35 (s, 3H, CH3, E – isomer), 2.33 (s, 3H, CH3, Z – isomer). HRMS (ESI) calcd for C7N4H6S [M+H]+ 415.1223, found 415.1224.

**Synthesis of (E,Z)-1-[2-(1-tosyl-1H-imidazol-4-yl)vinyl]-1H-benzo[d][1,2,3]triazole (E/Z-13)**

A solution of 1-[(1-phenyl-1H-tetrazol-5-yl)sulfonyl]methyl]-1H-benzo[d][1,2,3]triazole (5, 0.102 g, 0.300 mmol, 1.00 molar equiv) and 1-tosyl-1H-imidazol-4-carbaldehyde (0.113 g, 0.450 mmol, 1.50 molar equiv), in THF (5.10 mL) under nitrogen, was cooled to 0 °C. LHMDS (0.113 g, 0.720 mmol, 2.40 molar equiv) was added. The reaction was allowed to stir at 0 °C. After 2h, the reaction was checked by TLC (SiO2, 40% EtOAc in hexanes), that showed complete consumption of the starting sulfone 5.
The reaction was quenched with saturated aqueous ammonium chloride. The aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layer was then washed with water, followed by brine. Anhydrous Na₂SO₄ was added to the organic layer to remove any trace of water, and the organic solvent was evaporated under reduced pressure. The crude compound was purified by column chromatography (50% DCM in hexanes with a stepwise increase to 70% DCM in hexanes) to yield 0.078 g of (E,Z)-1-[2-(1-tosyl-1H-imidazol-4-yl)vinyl]-1H-benzo[d][1,2,3]triazole (E/Z-13, 71%, white solid). Rₐ (40% EtOAc in hexanes) = 0.37. \(^1\)H NMR (500 MHz, CDCl₃): δ 8.16 (d, 1H, E – isomer, J = 14.2 Hz), 8.10 (d, 1H, J = 8.3 Hz, E – isomer), 8.04 (s, 1H, E - isomer), 7.87 (d, 2H, J = 8.3 Hz, E - isomer), 7.70 (d, 1H, E – isomer, J = 8.3 Hz), 7.56 (t, 1H, J = 7.6 Hz, E - isomer), 7.44-7.38 (m, 3H, E - isomer), 7.33 (s, 1H, E - isomer), 7.33 (d, 1H, J = 13.7 Hz, E – isomer), 2.46 (s, 3H, CH₃, E - isomer). 8.13 (d, 1H, J = 7.3 Hz, Z - isomer), 7.93 (dd, 2H, J = 3.0 Hz; 3.9 Hz, Z -isomer), 7.75 (d, 2H, J = 8.8 Hz, Z - isomer), 7.60 (s, 1H, Z - isomer), 7.52 (t, 1H, J = 8.3 Hz, Z - isomer), 7.45-7.32 (m, 3H, Z – isomer), 7.15 (d, 1H, J = 9.8 Hz, Z - isomer), 6.66 (d, 1H, J = 9.8 Hz, Z - isomer), 2.43 (s, 3H, CH₃, Z - isomer). HRMS (ESI) calcd for C₇N₄H₆S [M+H]⁺ 366.1019, found 366.1005.

**Synthesis of (E,Z)-1-(2-cyclohexylvinyl)-1H-benzo[d][1,2,3]triazole (E/Z-16)**

\[ \text{LiHMDS, THF} \quad 0 \degree C \]

A solution of 1-[[1-phenyl-1H-tetrazol-5-yl)sulfonyl]methyl]-1H-benzo[d][1,2,3] triazole (5, 0.102 g, 0.300 mmol, 1.00 molar equiv) and cyclohexane carboxaldehyde
(0.051 g, 0.450 mmol, 1.50 molar equiv), in THF (5.10 mL) under nitrogen, was cooled to 0 °C. LHMDS (0.113 g, 0.720 mmol, 2.40 molar equiv) was added. The reaction was allowed to stir at 0 °C. After 2h, the reaction was checked by TLC (SiO₂, 40% EtOAc in hexanes), that showed complete consumption of the starting sulfone 5. The reaction was quenched with saturated aqueous ammonium chloride. The aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layer was then washed with water, followed by brine. Anhydrous Na₂SO₄ was added to the organic layer to remove any trace of water, and the organic solvent was evaporated under reduced pressure. The crude compound was purified by column chromatography (10% EtOAc in hexanes with a stepwise increase to 20% EtOAc in hexanes) to yield 0.036 g of (E,Z)-1-(2-cyclohexylvinyl)-1H-benzo[d][1,2,3]triazole (E/Z-16, 52%, white solid). Rf (20% EtOAc in hexanes) = 0.5. ¹H NMR (500 MHz, CDCl₃): δ 8.07 (d, 1H, Z - isomer, J = 8.3 Hz), 8.06 (d, 1H, Z - isomer, J = 7.3 Hz), 7.63 (d, 1H, Z - isomer, J = 8.3 Hz), 7.52-7.49 (m, E + Z - isomer), 7.41-7.39 (m, E + Z - isomer) 7.27 (dd, 1H, J = 1.8 Hz; 14.2 Hz, E - isomer), 6.86 (d, 1H, Z – isomer, J = 8.8 Hz) 6.47 (dd, 2H, E – isomer, J = 7.3 Hz; 14.6 Hz) 5.67 (dd, 2H, E – isomer, J = 8.7 Hz; 9.8 Hz), 2.80–2.72 (m, 1H, Z – isomer), 2.31-2.24 (m, 1H, E - isomer), 1.93-1.63 (m, E + Z – isomer), 1.40-1.16 (m, E + Z – isomer). HRMS (ESI) calcd for C₇N₄H₆S [M+H]⁺ 228.1495, found 228.1495.
Synthesis of (S, E/Z)-1-(4,8-dimethylnona-1,7-dien-1-yl)-1H-benzo[d][1,2,3]triazole

\((E/Z-17)\)

\[
\begin{align*}
\text{LiHMDS, THF} & \quad 0^\circ C \\
5 & \\
\rightarrow & \\
Z\text{-isomer Z-17} & \\
E\text{-isomer E-17} & \\
\end{align*}
\]

A solution of 1-{[(1-phenyl-1H-tetrazol-5-yl)sulfonyl]methyl}-1H-benzo[d][1,2,3]triazole (5, 0.102 g, 0.300 mmol, 1.00 molar equiv) and (R)-3,7-dimethyloct-6-enal (0.069 g, 0.450 mmol, 1.50 molar equiv), in THF (5.10 mL) under nitrogen, was cooled to 0 °C. LHMDS (0.113 g, 0.720 mmol, 2.40 molar equiv) was added. The reaction was allowed to stir at 0 °C. After 2 h, the reaction was checked by TLC (SiO\(_2\), 40% EtOAc in hexanes), that showed complete consumption of the starting sulfone 5. The reaction was quenched with saturated aqueous ammonium chloride. The aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layer was then washed with water, followed by brine. Anhydrous Na\(_2\)SO\(_4\) was added to the organic layer to remove any trace of water, and the organic solvent was evaporated under reduced pressure. The crude compound was purified by column chromatography (50% DCM in hexanes with a stepwise increase to 70% DCM in hexanes) to yield 0.065 g of (S, E/Z)-1-(4,8-dimethylnona-1,7-dien-1-yl)-1H-benzo[d][1,2,3]triazole \((E/Z-17, 80\%, \text{ yellow oil})\). \(R_f\) (20% EtOAc in hexanes) = 0.61. \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 8.08 (d, 1H, Z – isomer, \(J = 8.8\) Hz) 7.65 (d, 1H, E – isomer, \(J = 8.3\) Hz), 7.54-7.48 (m, \(E + Z\) isomer), 7.39 (td, 1H, Z – isomer, \(J = 1.0\) Hz; 7.8 Hz; 14.7 Hz), 7.30 (d, 1H, E – isomer, \(J = 14.6\) Hz), 7.05
(d, 1H, Z – isomer, J = 8.8 Hz), 5.93 (dt, 1H, E – isomer, J = 7.2 Hz; 15.1 Hz), 5.88 (q, 1H, Z – isomer, J = 7.2 Hz) 5.13-5.03 (m, E + Z – isomer) 2.40-1.80 (m, E + Z –isomer), 1.64-0.74 (m, E + Z –isomer). HRMS (ESI) calcd for C_{7}N_{4}H_{6}S [M+H]\(^{+}\) 270.1965, found 270.1985.

**Synthesis of (E,Z)-1-(2-phenylprop-1-en-1-yl)-1H-benzo[d][1,2,3]triazole (E/Z-18)**

A solution of 1-\{[(1-phenyl-1H-tetrazol-5-yl)sulfonyl]methyl\}-1H-benzo[d][1,2,3]triazole (5, 0.102 g, 0.300 mmol, 2.00 molar equiv), acetophenone (0.018 g, 0.150 mmol, 1.00 molar equiv), in THF (5.10 mL) under nitrogen, was cooled to 0 °C. LHMDS (0.113 g, 0.720 mmol, 2.40 molar equiv) was added. The reaction was allowed to stir at 0 °C. After 2 h, the reaction was checked by TLC (SiO\(_2\), 40% EtOAc in hexanes), that showed complete consumption of the starting sulfone 5. The reaction was quenched with saturated aqueous ammonium chloride. The aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layer was then washed with water, followed by brine. Anhydrous Na\(_2\)SO\(_4\) was added to the organic layer to remove any trace of water, and the organic solvent was evaporated under reduced pressure. The crude compound was purified by column chromatography (10% EtOAc in hexanes with a stepwise increase to 20% EtOAc in hexanes) to yield 0.011 g of (E,Z)-1-(2-phenylprop-1-en-1-yl)-1H-benzo[d][1,2,3]triazole (E/Z-18, 31%, white solid). R\(_f\) (40% EtOAc in hexanes) = 0.65. \(^{1}\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 8.12 (d, 1H, J = 8.3 Hz, minor isomer), 8.08 (d, 1H, J = 8.3
Hz, minor isomer), 7.95 (d, 1H, J = 6.8 Hz, major isomer), 7.72 (d, 1H, J = 8.3 Hz), minor isomer), 7.60 (d, 2H, J = 7.3 Hz, minor isomer), 7.54-7.33 (m, major + minor isomer), 7.25-7.11 (m, 2H, major isomer), 7.10 (t, 3H, J = 3.4 Hz, major isomer), 7.03-7.01 (m, 2H, major isomer), 6.98 (d, 1H, J = 6.8 Hz, major isomer), 6.86 (s, 1H, small isomer), 2.39 (d, 3H, CH₃, J = 1.0 Hz, major isomer), 2.29 (d, 3H, CH₃, J = 1.0 Hz, minor isomer). HRMS (ESI) calcd for C₇N₄H₆S [M+H]+ 236.1182, found 236.1206.

**Synthesis of 1-[(1-benzylpiperidin-4-ylidene)methyl]-1H-benzo[d][1,2,3]triazole (19)**

![Chemical structure](image)

A solution of 1-[(1-phenyl-1H-tetrazol-5-yl)sulfonyl]methyl]-1H-benzo[d][1,2,3] triazole (5, 0.102 g, 0.300 mmol, 1.00 molar equiv) and n-benzyl piperdone (0.085 g, 0.450 mmol, 1.50 molar equiv), in THF (5.10 mL) under nitrogen, was cooled to 0 °C. LiHMDS (0.113 g, 0.720 mmol, 2.40 molar equiv) was added. The reaction was allowed to stir at 0 °C. After 2 h, the reaction was checked by TLC (SiO₂, 40% EtOAc in hexanes), that showed complete consumption of the starting sulfone 5. The reaction was quenched with saturated aqueous ammonium chloride. The aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layer was then washed with water, followed by brine. Anhydrous Na₂SO₄ was added to the organic layer to remove any trace of water, and the organic solvent was evaporated under reduced pressure. The crude compound was purified by column chromatography (10% EtOAc in hexanes with a stepwise increase to 40% EtOAc in hexanes) to yield 0.070 g of 1-[(1-benzylpiperidin-4-ylidene)methyl]-1H-benzo[d][1,2,3] triazole (19, 77%, brown solid). Rₛ (40% EtOAc in...
hexanes) = 0.34. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.07 (d, 1H, $J$ = 8.5 Hz), 7.50 (td, 1H, $J$ = 0.9 Hz; 6.9 Hz; 8.2 Hz), 7.45 (d, 1H, $J$ = 8.2 Hz), 7.38 (td, 1H, $J$ = 1.2 Hz; 6.7 Hz; 7.9 Hz), 7.35-7.25 (m, 5H, Ar-H), 6.89 (s, 1H), 3.58 (s, 2H), 2.66-2.43 (m, 8H). HRMS (ESI) calcd for C$_7$N$_4$H$_6$S [M+H]$^+$ 305.1761, found 305.1773.

**Synthesis of 1-[[1-phenyl-1H-tetrazol-5-yl]thio]methyl]-1H-naphtho[2,3-d][1,2,3]triazole (20)**

To a mixture of 5-[(azidomethyl)thio]-1-phenyl-1H-tetrazole (3, 0.070 g, 0.300 mmol, 1.00 molar equiv), 3-(trimethylsilyl)-2-naphthyl trifluoromethanesulfonate (0.269 g, 0.750 mmol, 2.50 molar equiv), 18-crown-6-ether (0.317g, 1.20 mmol, 4.00 molar equiv) and potassium fluoride (0.070 g, 1.20 mmol, 4.00 molar equiv) under nitrogen, dry acetonitrile (14.0 mL) was added. The reaction was allowed to stir at room temperature, and after 1 hour TLC (SiO$_2$, 40% EtOAc : hexanes) showed consumption of starting azide 3. The reaction was quenched with water and the aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was washed with water, followed by brine. Anhydrous Na$_2$SO$_4$ was added to the organic layer to remove any trace of water, and the organic solvent was evaporated under reduced pressure. The pure compound was isolated by column chromatography (20% EtOAc in hexanes with a stepwise increase to 30% EtOAc in hexanes) to yield 0.108g of 1-[[1-phenyl-1H-tetrazol-5-yl]thio]methyl]-1H-naphtho[2,3-d][1,2,3]triazole (20) (85%, white solid). $R_f$ (30% EtOAc in hexanes) = 0.23. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.61 (s, 1H, Ar-H), 8.28 (s, 1H, Ar-H), 8.05-8.04 (d,
1H, Ar-H, J = 8.8 Hz), 8.03-8.01 (d, 1H, Ar-H, J = 8.3 Hz), 7.55 (t, 1H, Ar-H, J = 6.8 Hz), 6.78 (s, 2H, CH2). 13C NMR (125 MHz, CDCl3): δ 152.37, 145.51, 133.62, 133.17, 131.03, 130.79, 130.73, 130.08, 129.50, 128.52, 127.45, 125.45, 124.00, 118.68, 106.73, 49.86. HRMS (ESI) calcd for C7N4H6S [M+H]+ 360.1026, found 360.1025.

**Synthesis of 5,6-dimethoxy-1-[[1-phenyl-1H-tetrazol-5-yl]thio)methyl]-1H benzo[d][1,2,3]triazole (21)**

To a mixture of 5-[(azidomethyl)thio]-1-phenyl-1H-tetrazole (3, 0.116 g, 0.500 mmol, 1.00 molar equiv), 4,5-dimethoxy-3-(trimethylsilyl)phenyl trifluoromethanesulfonate (0.269 g, 0.750 mmol, 1.5 molar equiv), 18-crown-6-ether (0.528 g, 2.00 mmol, 4.00 molar equiv) and potassium fluoride (0.116 g, 2.00 mmol, 4.00 molar equiv) under nitrogen, dry acetonitrile (24.0 mL) was added. The reaction was allowed to stir at room temperature, and after 1 hour TLC (SiO2, 40% EtOAc : hexanes) showed consumption of starting azide 3. The reaction was quenched with water and the aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was washed with water, followed by brine. Anhydrous Na2SO4 was added to the organic layer to remove any trace of water, and the organic solvent was evaporated under reduced pressure. The pure compound was isolated by column chromatography (20% EtOAc in hexanes with a stepwise increase to 30% EtOAc in hexanes) to yield 0.157g of 5,6-dimethoxy-1-[[1-phenyl-1H-tetrazol-5-yl]thio)methyl]-1H-benzo[d][1,2,3]triazole (21) (85%, white solid).
R_f (30% EtOAc in hexanes) = 0.15. \(^{1}\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 7.52-7.51 (m, 3H, Ar-H), 7.42-7.39 (m, 3H, Ar-H), 7.32 (s, 1H, Ar-H), 6.59 (s, 2H, CH\(_2\)), 4.01 (s, 3H, OCH\(_3\)), 3.95 (s, 3H, OCH\(_3\)). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \(\delta\) 152.61, 152.39, 149.22, 140.81, 133.12, 130.83, 130.14, 128.08, 123.98, 99.01, 91.51, 56.80, 56.47, 49.48. HRMS (ESI) calcd for C\(_7\)N\(_4\)H\(_6\)S [M+H]\(^+\) 370.1081, found 370.1060.

**Synthesis of 4-methoxy-1-\{[(1-phenyl-1H-tetrazol-5-yl)thio]methyl\}-1H-benzo[d]**

![Diagram of reaction](image)

To a mixture of 5-\{[azidomethyl]thio\}-1-phenyl-1H-tetrazole (3, 0.070 g, 0.600 mmol, 1.00 molar equiv), 3-methoxy-2-(trimethylsilyl)phenyl trifluoromethanesulfonate (0.197 g, 0.600 mmol, 2.00 molar equiv), 18-crown-6-ether (0.317 g, 1.20 mmol, 4.00 molar equiv) and potassium fluoride (0.070 g, 2.00 mmol, 4.00 molar equiv) under nitrogen, dry acetonitrile (14.0 mL) was added. The reaction was allowed to stir at room temperature, and after 1 hour TLC (SiO\(_2\), 40% EtOAc : hexanes) showed consumption of starting azide 3. The reaction was quenched with water and the aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was washed with water, followed by brine. Anhydrous Na\(_2\)SO\(_4\) was added to the organic layer to remove any trace of water, and the organic solvent was evaporated under reduced pressure. The pure compound was isolated by column chromatography (20% EtOAc in hexanes with a stepwise increase to 30% EtOAc in hexanes) to yield 0.069 g of 4-methoxy-1-\{[(1-phenyl-1H-tetrazol-5-yl)thio]methyl\}-1H-benzo[d] [1,2,3]triazole (22) (68%, yellow oil). R_f (30% EtOAc in hexanes) = 0.24. \(^{1}\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 7.51-7.50 (m, 3H, Ar-H), 7.44 (t, 1H, H-
6, Ar-H, J = 7.8 Hz), 7.41-7.38 (m, 3H, Ar-H), 6.72 (d, H-5, 1H, Ar-H, J = 7.8 Hz), 6.60 (s, 2H, CH₂), 4.09 (s, 3H, OCH₃). Assignment of protons based on 2D NOESY spectrum.


**Synthesis of 6-methoxy-1-{
[(1-phenyl-1H-tetrazol-5-yl)thio]methyl}-1H benzo[d]
[1,2,3]triazole (23a & 23b)**

To a mixture of 5-[(azidomethyl)thio]-1-phenyl-1H-tetrazole (3, 0.070 g, 0.300 mmol, 1.00 molar equiv), 4-methoxy-2-(trimethylsilyl)phenyltrifluoromethanesulfonate (0.197 g, 0.600 mmol, 2.00 molar equiv), 18-crown-6-ether (0.317 g, 1.20 mmol, 4.00 molar equiv) and potassium fluoride (0.070 g, 1.20 mmol, 4.00 molar equiv) under nitrogen, dry acetonitrile (14.0 mL) was added. The reaction was allowed to stir at room temperature, and after 1 hour TLC (SiO₂, 40% EtOAc : hexanes) showed consumption of starting azide 3. The reaction was quenched with water and the aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was washed with water, followed by brine. Anhydrous Na₂SO₄ was added to the organic layer to remove any trace of water, and the organic solvent was evaporated under reduced pressure. The pure compound was isolated by column chromatography (20% EtOAc in hexanes with a stepwise increase to 30% EtOAc in hexanes) to yield 0.086 g of 6-methoxy-1-{
[(1-phenyl-1H-tetrazol-5-}
yl)thio)methyl]-1H benzo[d] [1,2,3]triazole (23a & 23b) (85%, white solid). 

**Synthesis of 6-methyl-1-[(1-phenyl-1H-tetrazol-5-yl)thio]methyl]-1H-benzo[d]**

To a mixture of 5-[(azidomethyl)thio]-1-phenyl-1H-tetrazole (3, 0.070 g, 0.300 mmol, 1.00 molar equiv), 4-methyl-2-(trimethylsilyl)phenyltrifluoromethanesulfonate (0.187 g, 0.600 mmol, 2.00 molar equiv), 18-crown-6-ether (0.316 g, 1.20 mmol, 4.00 molar equiv) and potassium fluoride (0.070 g, 1.20 mmol, 4.00 molar equiv) under nitrogen, dry acetonitrile (14.0 mL) was added. The reaction was allowed to stir at room temperature,
and after 1 hour TLC (SiO$_2$, 40% EtOAc : hexanes) showed consumption of starting azide 3. The reaction was quenched with water and the aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was washed with water, followed by brine. Anhydrous Na$_2$SO$_4$ was added to the organic layer to remove any trace of water, and the organic solvent was evaporated under reduced pressure. The pure compound was isolated by column chromatography (20% EtOAc in hexanes with a stepwise increase to 30% EtOAc in hexanes) to yield 0.078 g of 6-methyl-1-[[1(phenyl-1H-tetrazol-5-yl)thio]methyl]-1H-benzo[d][1,2,3]triazole (24a & 24b) (80%, brown solid). $R_f$(20% EtOAc in hexanes) = 0.09. Some resonances in $^1$H NMR were assigned to isomer 24a, or 24b using 2D NOESY spectroscopy. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.92-7.89 (d, 1H, $J = 8.8$ Hz, 24b), 7.79 (s, 1H, Ar-H, 24a) 7.78 (d, 1H, $J = 9.3$ Hz, 24a), 7.60 (s, 1H, 24b), 7.52-7.50 (m, 24a + 24b), 7.41-7.38 (m, 24a + 24b), 7.35 (s, 1H, Ar-H, 24a), 7.22 (d, 1H, $J = 8.3$ Hz, 24b), 6.61 (s, 2H, CH$_2$, 24a), 6.58 (s, 2H, CH$_2$, 24b), 2.53 (s, 3H, CH$_3$, 24b), 2.50 (s, 3H, CH$_3$, 24a). HRMS (ESI) calcd for C$_7$N$_4$H$_6$S [M+H]$^+$ 324.1026, found 324.1029.
Synthesis of 7-methyl-1-{{(1-phenyl-1H-tetrazol-5-yl)thio}methyl}-1H-benzo[d]

[1,2,3]triazole (25a & 25b)

To a mixture of 5-[(azidomethyl)thio]-1-phenyl-1H-tetrazole (0.070 g, 0.300 mmol, 1.00 molar equiv), 2-methyl-6-(trimethylsilyl)phenyl trifluoromethanesulfonate (0.187 g, 0.600 mmol, 2.00 molar equiv), 18-crown-6-ether (0.316 g, 1.20 mmol, 4.00 molar equiv) and potassium fluoride (0.070 g, 1.20 mmol, 4.00 molar equiv) under nitrogen, dry acetonitrile (14.0 mL) was added. The reaction was allowed to stir at room temperature, and after 1 hour TLC (SiO₂, 40% EtOAc : hexanes) showed consumption of starting azide 3. The reaction was quenched with water and the aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was washed with water, followed by brine. Anhydrous Na₂SO₄ was added to the organic layer to remove any trace of water, and the organic solvent was evaporated under reduced pressure. The pure compound was isolated by column chromatography (20% EtOAc in hexanes with a stepwise increase to 30% EtOAc in hexanes) to yield 0.079 g of 7-methyl-1-{{(1-phenyl-1H-tetrazol-5-yl)thio}methyl}-1H-benzo[d] [1,2,3]triazole (25a & 25b) (82%, brown solid). Rf (20% EtOAc in hexanes) = 0.10. Ratio of regioisomers in a mixture of 25a and 25b is nearly 1:1. (49:51, based on integration of CH₂ signals). Some resonances in ¹H NMR were
assigned to isomer 25a, or 25b using 2D NOESY spectroscopy. \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 7.88-7.87 (d, 1H, \(J = 7.7\) Hz, 25b), 7.67-7.65 (d, 1H, \(J = 7.3\) Hz, 25a) 7.51-7.48 (m, 25a + 25b), 7.45-7.37 (m, 25a + 25b), 7.30-7.22 (m, 25a + 25b overlapping with CDCl\(_3\)), 7.15 (d, 1H, \(J = 6.8\) Hz, 25a), 6.68 (s, 2H, CH\(_2\), 25b), 6.61 (s, 2H, CH\(_2\), 25a), 2.80 (s, 3H, CH\(_3\), 25b), 2.77 (s, 3H, CH\(_3\), 25a). HRMS (ESI) calcd for C\(_7\)N\(_4\)H\(_6\)S [M+H]\(^+\) 324.1032, found 324.1026.

**Synthesis of 1-[[[1-phenyl-1H-tetrazol-5-yl]thio)methyl]-1H-naphtho[2,3-d][1,2,3]triazole-4,9-(4aH,8aH)-dione (26)**

\[
\begin{align*}
\text{N} & \text{N} \\
\text{N} & \text{N} \\
\text{N} & \text{N}
\end{align*}
\]

\[+ \text{H}_3\text{IO}_6 + \text{CrO}_3 \xrightarrow{\text{MeCN}}\]

\[
\begin{align*}
\text{N} & \text{N} \\
\text{N} & \text{N} \\
\text{N} & \text{N}
\end{align*}
\]

Periodic acid (0.123 g, 0.542 mmol, 4.00 molar equiv) in 2.50 mL of dry acetonitrile was stirred at room temperature for 30 min. Chromium trioxide (0.007 g, 0.007 mmol, 0.050 molar equiv) was added and the mixture was allowed to stir for another 5 min. After 5 min, periodic acid/CrO\(_3\) suspension was added to a solution of 1-[[[1-phenyl-1H-tetrazol-5-yl]thio]methyl]-1H-naphtho[2,3-d][1,2,3]triazole (20, 0.050 g, 0.136 mmol, 1.00 molar equiv) under a N\(_2\) ballon. The reaction was monitored by TLC (SiO\(_2\), 40% EtOAc in hexanes). After 3 hours, TLC showed complete consumption of starting material. The reaction mixture was cooled on ice and quenched with aqueous solution of NaHCO\(_3\) and sodium bisulfate. The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was then washed with water, followed by brine. Anhydrous Na\(_2\)SO\(_4\) was added to the organic layer to remove any trace of water, and the organic
The pure compound was isolated by column chromatography (20% EtOAc in hexanes with a stepwise increase to 30% EtOAc in hexanes) to yield 1-([(1-phenyl-1H-tetrazol-5-yl)thio]methyl]-1H-naphtho[2,3-d][1,2,3] triazole-4,9-(4aH,8aH)-dione (26). Rf (20% EtOAc in hexanes) = 0.29. ¹H NMR (500 MHz, CDCl₃): δ 8.35 (d, 1H, Ar-H, J = 7.3 Hz), 8.24 (d, 1H, Ar-H, J = 7.8 Hz), 7.89 (t, 1H, Ar-H, J = 7.8 Hz), 7.84 (t, 1H, Ar-H, J = 7.3 Hz), 7.52-7.47 (m, 5H, Ar-H), 6.58 (s, 2H, Ar-H). HRMS (ESI) calcd for C₇N₄H₆S [M+H]⁺ 412.0587, found 412.0562.

**Synthesis of 1-([(1-phenyl-1H-tetrazol-5-yl)sulfonyl]methyl]-1H-naphtho[2,3-d]

[1,2,3]triazole (27)**

To a solution of 1-([(1-phenyl-1H-tetrazol-5-yl)thio]methyl]-1H-naphtho[2,3-d][1,2,3] triazole (0.300 g, 0.831 mmol, 1.00 molar equiv) in 30 mL acetonitrile, a solution of ammonium molybdate (0.822 g, 0.665 mmol, 1.00 molar equiv) and hydrogen peroxide (2.95 mL, 104 mmol, 125 molar equiv) was added. The reaction was monitored by TLC (SiO₂, 40% EtOAc in hexanes). After 24 hours, TLC showed complete consumption of starting material. The reaction mixture was quenched with the addition of water. The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was then washed with water, followed by brine. Anhydrous Na₂SO₄ was added to the organic layer to remove any trace of water, and the organic solvent was evaporated under reduced pressure. The pure compound was isolated by column chromatography (20% EtOAc in hexanes with a stepwise increase to 30% EtOAc in hexanes) to yield 1-([(1-phenyl-1H-tetrazol-5-yl)sulfonyl]methyl]-1H-naphtho[2,3-d][1,2,3] triazole-4,9-(4aH,8aH)-dione (27).
EtOAc in hexanes with a stepwise increase to 40% EtOAc in hexanes) to yield 1-\{[(1-phenyl-1H-tetrazol-5-yl)sulfonyl]methyl\}-1H-naphtho[2,3-d][1,2,3]triazole (27). R_{f}(30\% EtOAc in hexanes) = 0.49. \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}): \textsuperscript{\delta} 8.66 (s, 1H, Ar-H), 8.09-8.08 (m, 2H, Ar-H), 7.99 (d, 1H, Ar-H, J = 8.3 Hz), 7.58 (t, 1H, Ar-H, J = 7.1 Hz), 7.52 (t, 1H, Ar-H, J = 7.3 Hz), 7.48 (t, 2H, Ar-H, J = 6.8Hz), 7.37 (d, 2H, Ar-H, J = 9.3 Hz), 6.59 (s, 2H, CH\textsubscript{2}). HRMS (ESI) calcd for C\textsubscript{7}N\textsubscript{4}H\textsubscript{6}S [M+H]\textsuperscript{+} 392.0924, found 392.0912.

**Synthesis of 7-methoxy-1-\{[(1-phenyl-1H-tetrazol-5-yl)sulfonyl]methyl\}-1H-benzo[d][1,2,3]triazole (28)**

To a solution of 4-methoxy-1-\{[(1-phenyl-1H-tetrazol-5-yl)thio]methyl\}-1H-benzo[d][1,2,3]triazole (0.123 g, 0.542 mmol, 4.00 molar equiv) in acetonitrile, a solution of the ammonium molybdate (0.123 g, 0.542 mmol, 4.00 molar equiv) and hydrogen peroxide (0.123 g, 0.542 mmol, 4.00 molar equiv) was added. The reaction was monitored by TLC (SiO\textsubscript{2}, 40\% EtOAc in hexanes). After 24 hours, TLC showed complete consumption of starting material. The reaction mixture was quenched with the addition of water. The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was then washed with water, followed by brine. Anhydrous Na\textsubscript{2}SO\textsubscript{4} was added to the organic layer to remove any trace of water, and the organic solvent was evaporated under reduced pressure. The pure compound was isolated by column chromatography (10\% EtOAc in hexanes with a stepwise increase to 40\% EtOAc in hexanes) to yield 7-methoxy-1-\{[(1-phenyl-1H-tetrazol-5-yl)sulfonyl]methyl\}-1H-benzo[d][1,2,3]triazole.
(28). \( R_f \) (30% EtOAc in hexanes) = 0.26. \(^1\)H NMR (500 MHz, CDCl\(_3\)): \( \delta \) 7.53-7.38 (m, 6H, Ar-H), 7.16 (d, 1H, Ar-H, \( J = 8.3 \) Hz), 6.75 (d, 1H, Ar-H, \( J = 8.0 \) Hz), 6.409 (s, 2H, CH\(_2\)), 4.11 (s, 3H, OCH\(_3\)). HRMS (ESI) calcd for C\(_7\)N\(_4\)H\(_6\)S [M+H]\(^+\) 372.0879, found 372.0895.

**Synthesis of 5,6-dimethoxy-1-\{[(1-phenyl-1H-tetrazol-5-yl)sulfonyl]methyl\}-1H-benzo[d][1,2,3]triazole (29)**

A solution of MCPBA (0.690 g, 4.00 mmol, 8.00 molar equiv) in 40 mL chloroform was added to 5,6-dimethoxy-1-\{[(1-phenyl-1H-tetrazol-5-yl)thio]methyl\}-1Hbenzo[d][1,2,3]triazole in 20 mL chloroform at -10°C (ice and salt bath). The reaction mixture was left to stir overnight and allowed to warm to room temperature. The reaction was monitored by TLC (SiO\(_2\), 40% EtOAc in hexanes). After 3 hours, TLC showed complete consumption of starting material. The reaction was quenched with aqueous solution of NaHCO\(_3\) and sodium bisulfate. The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was then washed with water, followed by brine. Anhydrous Na\(_2\)SO\(_4\) was added to the organic layer to remove any trace of water, and the organic solvent was evaporated under reduced pressure. The pure compound was isolated by column chromatography (20% EtOAc in hexanes with a stepwise increase to 50% EtOAc in hexanes) to yield 0.115 g of 5, 6-dimethoxy-1-\{[(1-phenyl-1H-tetrazol-5-yl)sulfonyl]methyl\}-1H-benzo[d][1,2,3]triazole (29) (58%, white solid). \( R_f \) (40% EtOAc
in hexanes) = 0.41.  

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.53 (t, 1H, Ar-H, $J$ = 7.8 Hz), 7.47 (t, 2H, Ar-H, $J$ = 8.3 Hz), 7.38-7.36 (m, 3H, Ar-H), 7.01 (s, 1H, Ar-H), 6.38 (s, 2H, CH$_2$), 3.99 (s, 3H, OCH$_3$), 3.97 (s, 3H, OCH$_3$).  

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 153.05, 152.28, 149.53, 140.62, 132.49, 131.91, 129.76, 128.59, 125.51, 99.49, 90.27, 67.77, 56.79, 56.58. HRMS (ESI) calcd for C$_7$N$_4$H$_6$S [M+H]$^+$ 402.0979, found 402.0973.

**Synthesis of (E, Z)-5,6-dimethoxy-1-(2-(1-tosyl-1H-imidazol-4-yl)vinyl)-1H-benzo[d][1,2,3]triazole (E/Z-30)**

A solution of 5,6-dimethoxy-1-[(1-phenyl-1H-tetrazol-5-yl)sulfonyl]methyl]-1H-benzo[d][1,2,3]triazole (29, 0.060 g, 0.150 mmol, 1.00 molar equiv) and 1-Tosyl-1H-imidazole-4-carbaldehyde (0.045 g, 0.18 mmol, 1.20 molar equiv), in THF (6.00 mL) under nitrogen, was cooled to 0 °C. LHMDS (360 µL, 0.360 mmol, 2.40 molar equiv) was added. After 25 min the reaction was checked by TLC (SiO$_2$, 40% EtOAc in hexanes), that showed complete consumption of the starting sulfone 29. The reaction was quenched with saturated aqueous ammonium chloride. The aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layer was then washed with water, followed by brine. Anhydrous Na$_2$SO$_4$ was added to the organic layer to remove any trace of water, and the organic solvent was evaporated under reduced pressure. The crude compound was purified by column chromatography (10% ethyl acetate in hexanes with a
stepwise increase to 40% ethyl acetate in hexanes) to yield 0.036g of E/Z-30, (80%, white solid). Rf(40% EtOAc in hexanes) = 0.16. 1H NMR (500 MHz, CDCl3): δ 8.04 (s, 1H, E-isomer), 8.02 (d, 1H, J = 14.2 Hz, E–isomer), 7.87 (d, 2H, J = 7.8 Hz, E-isomer), 7.39 (d, 2H, J = 8.8 Hz, E-isomer), 7.38 (s, 1H, E-isomer), 7.32 (s, 1H, E-isomer), 7.31(d, 1H, J = 13.2 Hz, E-isomer), 6.98 (s, 1H, E-isomer), 4.00 (s, 3H, OCH3, E-isomer), 3.98 (s, 3H, OCH3, E-isomer) 2.46 (s, 3H, CH3, E-isomer). 7.93 (s, 1H, Z-isomer), 7.70 (d, 2H, J = 8.3 Hz, Z-isomer), 7.43 (s, 2H, Z-isomer), 7.31 (d, 2H, J = 7.8 Hz, Z-isomer), 7.10 (d, 1H, J = 9.3 Hz, Z-isomer), 6.62 (d, 1H, J = 9.8 Hz, Z-isomer), 6.53 (s, 1H, Z-isomer), 3.97 (s, 3H, OCH3, Z-isomer), 3.74 (s, 3H, OCH3, Z-isomer), 2.44 (s, 3H, CH3, Z-isomer). HRMS (ESI) calcd for C7N4H6S [M+H]+ 426.1231, found 426.1217.

**Synthesis of (S/E,Z)-1-(4,8-dimethylnona-1,7-dien-1-yl)-5,6-dimethoxy-1H-benzo[d][1,2,3]triazole (E/Z-31)**

![Diagram of synthesis](attachment:image.png)

A solution of 5,6-dimethoxy-1-\{[(1-phenyl-1H-tetrazol-5-yl)sulfonyl]methyl\}-1H-benzo[d][1,2,3]triazole (29, 0.060 g, 0.15 mmol, 1.00 molar equiv) and (S)-citronellal (0.028 g, 0.223 mmol, 1.50 molar equiv.), in THF (6.00 mL) under nitrogen, was cooled to 0 °C. LHMDS (360μL, 0.360 mmol, 2.40 molar equiv) was added and the reaction was
checked by TLC (SiO₂, 40% EtOAc in hexanes), that showed complete consumption of the starting sulfone 29. The reaction was quenched with saturated aqueous ammonium chloride. The aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layer was then washed with water, followed by brine. Anhydrous Na₂SO₄ was added to the organic layer to remove any trace of water, and the organic solvent was evaporated under reduced pressure. The crude compound was purified by column chromatography (5% ethyl acetate in hexanes to 10% ethyl acetate in hexanes) to yield 0.034g of (S/E/Z-31, 68%, yellow oil). Rₛ(40% EtOAc in hexanes) = 0.65. ¹H NMR (500 MHz, CDCl₃): δ 7.39 (s, 1H, Z - isomer), 7.38 (s, 1H, E - isomer), 7.18 (d, 1H, E - isomer, J = 14.2 Hz), 6.97 (d, 1H, Z - isomer, J = 8.8 Hz), 6.92 (s, 1H, Z - isomer), 6.78 (s, 1H, E - isomer), 6.45 (dt, 1H, E - isomer, J = 7.8 Hz; 14.2 Hz), 5.85 (q, 1H, Z - isomer, J = 7.8 Hz), 5.11 (t, 1H, E - isomer, J = 7.3 Hz), 5.04 (t, 1H, Z - isomer, J = 7.3 Hz), 4.00 (s, 3H, OCH₃), 3.98 (s, 3H, OCH₃), 2.46-1.87 (m, E + Z-isomer), 1.69 (s, CH₃, E - isomer), 1.65 (s, CH₃, Z - isomer), 1.61 (s, CH₃, Z - isomer), 1.55 (s, CH₃, E - isomer), 1.00 (d, CH₃, E - isomer, J = 6.4 Hz), 0.95 (d, CH₃, Z - isomer, J = 6.8 Hz). HRMS (ESI) calcd for C₇N₄H₆S [M+H]⁺ 330.2176, found 330.2169.
Synthesis of (E,Z)-1-(3,4,5-trimethoxystyryl)-1H-naptho[2,3-d][1,2,3]triazole (E/Z-32) – Method 1

A solution of 1-[(1-phenyl-1H-tetrazol-5-yl)sulfonyl]methyl]-1H-naptho[2,3-d][1,2,3]triazole (27, 0.060 g, 0.15 mmol, 1.00 molar equiv) and 3,4,5-trimethoxybenzaldehyde (0.045 g, 0.223 mmol, 1.50 molar equiv.), in THF (1.00 mL) under nitrogen, was cooled to 0 °C. LHMDS (360 µL, 0.360 mmol, 2.40 molar equiv) was added and the reaction was checked by TLC (SiO₂, 40% EtOAc in hexanes), that showed complete consumption of the starting sulfone 27. The reaction was quenched with saturated aqueous ammonium chloride. The aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layer was then washed with water, followed by brine. Anhydrous Na₂SO₄ was added to the organic layer to remove any trace of water, and the organic solvent was evaporated under reduced pressure. The crude compound was purified by column chromatography (5% ethyl acetate in hexanes with a stepwise increase to 30% ethyl acetate in hexanes) to yield 0.031g of (E/Z-32, 75%, yellow oil). Rᵥ (30% EtOAc in hexanes) = 0.30. ¹H NMR (500 MHz, CDCl₃): δ 8.70 (s, 1H, E - isomer), 8.65 (s, 1H, Z - isomer), 8.24 (s, 1H, Z - isomer), 8.10 (d, 1H, Z - isomer, J = 8.3 Hz), 8.08-8.05 (m, E + Z isomer), 7.76 (d, 1H, Z - isomer, J = 7.8 Hz), 7.58 (t, 1H, E - isomer, J = 7.6 Hz), 7.53 (t, 1H, E - isomer, J = 7.3 Hz), 7.47-7.42 (m, E + Z-isomer), 7.38 (d,
1H, Z - isomer, $J = 8.7$ Hz), 6.82 (s, 2H, $E$ - isomer), 6.74 (d, 1H, $Z$ - isomer, 9.3 Hz), 6.28 (s, 2H, $Z$ - isomer), 3.97 (s, 3H, OCH$_3$), 3.91 (s, 3H, OCH$_3$), 3.74 (s, 3H, OCH$_3$), 3.44 (s, 3H, OCH$_3$). HRMS (ESI) calcd for C$_7$N$_4$H$_6$S [M+H]$^+$ 362.1499, found 362.1490.

**Synthesis of (E,Z)-1-(3,4,5-trimethoxystyryl)-1H-naphtho[2,3-d][1,2,3]triazole (E/Z-32) – Method 2**

![Chemical Reaction Diagram]

A solution of 1-{{[(1-phenyl-1H-tetrazol-5-yl)sulfonyl]methyl}-1H-naphtho[2,3-d][1,2,3]triazole (27, 0.060 g, 0.15 mmol, 1.00 molar equiv) and 3,4,5-trimethoxybenzaldehyde (0.0075 g, 0.030 mmol, 1.50 molar equiv.), in THF/DMF (1.00 mL/300µL) under nitrogen, was cooled to 0 °C. LHMDS (60µL, 0.060 mmol, 2.40 molar equiv) was added and the reaction was checked by TLC (SiO$_2$, 40% EtOAc in hexanes), that showed complete consumption of the starting sulfone 27. The reaction was quenched with saturated aqueous ammonium chloride. The aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layer was then washed with water, followed by brine. Anhydrous Na$_2$SO$_4$ was added to the organic layer to remove any trace of water, and the organic solvent was evaporated under reduced pressure. The crude compound was purified by column chromatography (5% ethyl acetate in hexanes with a stepwise increase to 30% ethyl acetate in hexanes) to yield 0.0067g of E/Z-32, (74%, yellow oil).
Synthesis of (E,Z)-1-(3,4,5-trimethoxystyryl)-1H-naphtho[2,3-d][1,2,3]triazole (E/Z-32) – Method 3

A solution of 1-[(1-phenyl-1H-tetrazol-5-yl)sulfonyl]methyl]-1H-naphtho[2,3-d][1,2,3]triazole (27, 0.010 g, 0.025 mmol, 1.00 molar equiv) and 3,4,5-trimethoxybenzaldehyde (0.0075 g, 0.030 mmol, 1.50 molar equiv.), in DMF (1.00 mL) under nitrogen, was cooled to 0 °C. LHMDS (60 µL, 0.060 mmol, 2.40 molar equiv) was added and the reaction was checked by TLC (SiO₂, 40% EtOAc in hexanes), that showed complete consumption of the starting sulfone 27. The reaction was quenched with saturated aqueous ammonium chloride. The aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layer was then washed with water, followed by brine. Anhydrous Na₂SO₄ was added to the organic layer to remove any trace of water, and the organic solvent was evaporated under reduced pressure. The crude compound was purified by column chromatography (5% ethyl acetate in hexanes with a stepwise increase to 30% ethyl acetate in hexanes) to yield 0.0084g of E/Z-32 (93%, yellow oil).
Synthesis of \((E,Z)-1-(3,4,5\text{-trimethoxystyryl})-1H\text{-naphtho}[2,3-d][1,2,3]\text{triazole } (E/Z-32) – \text{Method 4}

\[ \text{N} \equiv \text{N} \quad \text{S} \quad \text{N} \equiv \text{N} \quad \text{N} \equiv \text{N} \]

\begin{align*}
\text{LiHMDS, DMPU} & & 0^\circ \text{C} \\
\text{Z-isomer} & & \text{E-isomer}
\end{align*}

A solution of 1-[(1-phenyl-1H-tetrazol-5-yl)sulfonyl]methyl]-1H-naphtho[2,3-d][1,2,3]triazole (27, 0.010 g, 0.025 mmol, 1.00 molar equiv) and trimethoxy benzaldehyde (0.0075 g, 0.030 mmol, 1.50 molar equiv.), in DMPU (1.00 mL) under nitrogen, was cooled to 0 °C. LHMDS (60 µL, 0.060 mmol, 2.40 molar equiv) was added and the reaction was checked by TLC (SiO\(_2\), 40% EtOAc in hexanes), that showed complete consumption of the starting sulfone 27. The reaction was quenched with saturated aqueous ammonium chloride. The aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layer was then washed with water, followed by brine. Anhydrous Na\(_2\)SO\(_4\) was added to the organic layer to remove any trace of water, and the organic solvent was evaporated under reduced pressure. The crude compound was purified by column chromatography (5% ethyl acetate in hexanes with a stepwise increase to 30% ethyl acetate in hexanes) to yield 0.0074 g of \(E/Z-32\) (82%, yellow oil).
Synthesis of \((E,Z)-1-(4-\text{[(trifluoromethyl)styryl]}-1H\text{-naphtho}[2,3-d][1,2,3]\text{triazole})\)

\((E/Z\text{-33})\)-Method 1

A solution of 1-\{[(1-phenyl-1H-tetrazol-5-yl)sulfonyl]methyl\}-1H-naphtho[2,3-d][1,2,3]\text{triazole} \(27\), 0.010 g, 0.025 mmol, 1.00 molar equiv) and 4-(trifluoromethyl)benzaldehyde (0.0066 g, 0.030 mmol, 1.50 molar equiv.), in THF (1.00 mL) under nitrogen, was cooled to 0 °C. LHMDS (60 µL, 0.060 mmol, 2.40 molar equiv) was added and the reaction was checked by TLC (SiO\textsubscript{2}, 40% EtOAc in hexanes), that showed complete consumption of the starting sulfone 27. The reaction was quenched with saturated aqueous ammonium chloride. The aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layer was then washed with water, followed by brine. Anhydrous Na\textsubscript{2}SO\textsubscript{4} was added to the organic layer to remove any trace of water, and the organic solvent was evaporated under reduced pressure. The crude compound was purified by column chromatography (5% ethyl acetate in hexanes with a stepwise increase to 20% ethyl acetate in hexanes) to yield 0.0034g of \((E/Z\text{-33}, 56\%, \text{yellow solid})\). \(R_f\) (40% EtOAc in hexanes) = 0.68. \(^1\)H NMR (500 MHz, CDCl\textsubscript{3}): \(\delta\) 8.67 (s, 1H, \(Z\) - isomer), 8.07 (d, 1H, \(Z\) - isomer, \(J = 7.8\) Hz), 7.74 (d, 1H, \(Z\) - isomer, \(J = 7.8\)Hz), 7.52-7.45 (m, 6H, \(Z\) - isomer), 7.41 (s, 1H, \(Z\) - isomer), 7.27 (d overlapping with CDCl\textsubscript{3}, 2H, \(Z\) - isomer, \(J = 8.3\) Hz), 6.78 (d, 1H, \(Z\) - isomer, \(J = 9.3\) Hz). 8.71 (s, 1H, \(E\) -
A solution of 1-[[1-phenyl-1H-tetrazol-5-yl]sulfonyl]methyl]-1H-naphtho[2,3-d][1,2,3]triazole (27, 0.030 g, 0.075 mmol, 1.00 molar equiv) and 4-(trifluoromethyl)benzaldehyde (0.020 g, 0.090 mmol, 1.50 molar equiv.), in DMF (1.00 mL) under nitrogen, was cooled to 0 °C. LHMDS (180µL, 0.180 mmol, 2.40 molar equiv) was added and the reaction was checked by TLC (SiO₂, 40% EtOAc in hexanes), that showed complete consumption of the starting sulfone 27. The reaction was quenched with saturated aqueous ammonium chloride. The aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layer was then washed with water, followed by brine. Anhydrous Na₂SO₄ was added to the organic layer to remove any trace of water, and the organic solvent was evaporated under reduced pressure. The crude compound was purified by column chromatography (5% ethyl acetate in hexanes with a
stepwise increase to 20% ethyl acetate in hexanes) to yield 0.016g of \((E/Z-33, 62\%,\) yellow solid).

**Synthesis of \((E,Z)-1-(3\text{-ethylpent-1-en-1-yl})\text{-1H-naphtho}[2,3-d][1,2,3]\text{triazole} \((E/Z-\text{34})\)**

\[
\begin{align*}
&\text{27} \\
&\text{LiHMDS,THF} \\
&0^\circ C \\
&\text{Z-isomer} \quad \text{Z-34} \\
&\text{E-isomer} \quad \text{E-34}
\end{align*}
\]

A solution of 1-\{[(1-phenyl-1H-tetrazol-5-yl)sulfonyl]methyl\}-1H-naphtho[2,3-d][1,2,3]triazole (27, 0.010 g, 0.025 mmol, 1.00 molar equiv) and 2-ethylbutanal (0.0038 g, 0.030 mmol, 1.50 molar equiv.), in THF (1.00 mL) under nitrogen, was cooled to 0 °C. LHMDS (60µL, 0.060 mmol, 2.40 molar equiv) was added and the reaction was checked by TLC (SiO\(_2\), 40% EtOAc in hexanes), that showed complete consumption of the starting sulfone 27. The reaction was quenched with saturated aqueous ammonium chloride. The aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layer was then washed with water, followed by brine. Anhydrous Na\(_2\)SO\(_4\) was added to the organic layer to remove any trace of water, and the organic solvent was evaporated under reduced pressure. The crude compound was purified by column chromatography (5% ethyl acetate in hexanes to 10% ethyl acetate in hexanes) to yield 0.0025g of \((E/Z-\text{34}, 54\%,\) yellow oil). \(R_f\) (30% EtOAc in hexanes) = 0.74. \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 8.65 (s, 1H, Z - isomer), 8.08 (d, 1H, Z - isomer, 8.8 Hz), 8.02-7.96 (m, \(E + Z\) - isomer), 7.56-7.42 (m, \(E + Z\)-isomer), 7.15 (d, 1H, Z - isomer, \(J = 8.8\) Hz), 6.31
(dd, 1H, E - isomer, \( J = 9.6 \) Hz; 14.6 Hz), 5.63 (dd, 1H, Z – isomer, \( J = 9.0 \) Hz; 10.4 Hz), 2.89-2.81 (m, 1H, Z - isomer), 2.17-2.12 (m, 1H, E - isomer), 1.70-1.23 (m, E + Z - isomer), 1.01 (t, 3H, E - isomer, \( J = 7.8 \) Hz), 0.89 (t, 3H, Z - isomer, \( J = 7.8 \) Hz). HRMS (ESI) calcd for C\(_7\)N\(_4\)H\(_6\)S \([M+H]^+\) 266.152, found 266.1664.

**Synthesis of \((E,Z)-1-(3\text{-ethylpent-1-en-1-yl})-1H\text{-naphtho}[2,3-d][1,2,3]\text{triazole (E/Z-34)-Method 2}**

A solution of 1-[[1-phenyl-1H-tetrazol-5-yl]sulfonyl]methyl]-1H-naphtho[2,3-d][1,2,3]triazole (27, 0.030 g, 0.075 mmol, 1.00 molar equiv) and 2-ethylbutanal (0.011 g, 0.090 mmol, 1.50 molar equiv.), in DMF (1.00 mL) under nitrogen, was cooled to 0 °C. LHMDS (180µL, 0.180 mmol, 2.40 molar equiv) was added and the reaction was checked by TLC (SiO\(_2\), 40% EtOAc in hexanes), that showed complete consumption of the starting sulfone 27. The reaction was quenched with saturated aqueous ammonium chloride. The aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layer was then washed with water, followed by brine. Anhydrous Na\(_2\)SO\(_4\) was added to the organic layer to remove any trace of water, and the organic solvent was evaporated under reduced pressure. The crude compound was purified by column chromatography (5% ethyl acetate in hexanes to 10% ethyl acetate in hexanes) to yield 0.015g of \((E/Z-34, 70\%, \text{yellow oil})\).
REFERENCES


GS-1231-01-51-PureTS

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Operator: barbara
File: GS-1231-01-51-PureTS
INOVA-500 “capella500”

Pulse 57.9 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
100 repetitions
OBSEERVE H1, 499.7707226 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 3 min, 10 sec

500MHz, CDCl3

APPENDIX: 1H AND 13C NMR SPECTRA
1231-GS-01-51-Cloride-13C-CDCL3

Pulse Sequence: s2pul
Solvent: dcl3
Temp. 25.0 C / 298.1 K
Operator: barbara
File: 1231-GS-01-51-Cloride-13C-CDCL3
INOVA-500 "riga"

Relax. delay 4.000 sec
Pulse 52.1 degrees
Acq. time 1.300 sec
Width 29996.3 Hz
32 repetitions
OBSERVE C13, 125.6674530 MHz
DECOUPLE R1, 499.7732084 MHz
Power 42 dB
on during acquisition
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 2 hr, 57 min, 20 sec
GS-1231-01-72-PTSulfide-I

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
Operator: barbara
File: GS-1231-01-72-PTSulfide-I
INOVA-500 "riga"

Pulse 57.9 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
44 repetitions
OBSERVE H1, 499.7707217 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 3 min, 10 sec

500MHz, CDCl3
1231-GS-01-72-PT-iodide-13C-CDCl3

Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: barbara
File: 1231-GS-01-72-PT-iodide-13C-CDCl3
INOVA-500 "riga"

Relax. delay 4.000 sec
Pulse 52.1 degrees
Acq. time 1.300 sec
Width 29996.3 Hz
44 repetitions
OBSERVE C13, 125.6674296 MHz
DECOUPLE R1, 499.7732084 MHz
Power 42 dB
on during acquisition
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 131072
Total time 18 min, 3 sec
GS-1231-01-90-Azide

Archive directory: /export/home/mlnl/vnmrsys/data
Sample directory: auto_13Dec2004

Pulse Sequence: s2pul
Solvent: dcl3
Temp. 24.0 C / 297.1 K
Operator: barbara
File: GS-1231-01-90-Azide
INOVA-500 "riga"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.892 sec
Width 10000.0 Hz
56 repetitions
OBSERVE H1, 499.7707215 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 4 min, 50 sec
1231-GS-01-90-PT-azole-13C-CDCl3

Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: barbara
File: 1231-GS-01-90-PT-azole-13C-CDCl3
INOVA-500 "riga"

Relax. delay 4.000 sec
Pulse 52.1 degrees
Acq. time 1.300 sec
Width 29996.3 Hz
20 repetitions
OBSERVE C13, 125.6674525 MHz
DECOUPLE R1, 499.7732084 MHz
Power 42 dB
on during acquisition
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 131072
Total time 18 min, 3 sec

125MHz, CDCl3
GS-1231-01-54-PureCompound

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Operator: barbara
File: GS-1231-01-54-PureCompound
INOVA-500 "riga"

Pulse 57.9 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
68 repetitions
OBSERVE H1, 499.7707217 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 3 min, 10 sec

500MHz, CDCl3
1231-GS-01-90-PTBT-sulfide-13C-CDCl3

Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: barbara
File: 1231-GS-01-92-PTBT-sulfide-13C-CDCl3
INOVA-500 "riga"

Relax. delay 4.000 sec
Pulse 52.1 degrees
Acq. time 1.300 sec
Width 29996.3 Hz
96 repetitions
OBSERVE C13, 125.6674228 MHz
DECOUPLE R1, 499.7732084 MHz
Power 42 dB
on during acquisition
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 18 min, 3 sec

125MHz, CDCl3
GS-1231-01-70-pure

Archive directory: /export/home/mkl/vnmrsys/data
Sample directory: auto_13Dec2004

Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 24.0 C / 297.1 K
Operator: barbara
File: GS-1231-01-70-pure
INOVA-500 "riga"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.892 sec
Width 7544.3 Hz
36 repetitions

OBSERVE H1, 499.7707216 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 9 min, 40 sec

500MHz, CDCl3
GS-1231-01-57-PTBT-Sulfone-13C-CDCL3

Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: barbara
File: GS-1231-01-57-PTBT-Sulfone-13C-CDCL3
INova-500 "riga"

Relax. delay 4.000 sec
Pulse 52.1 degrees
Acq. time 1.300 sec
Width 29996.3 Hz
380 repetitions
OBSERVE C13, 125.6674228 MHz
DECOUPLE H1, 499.7732084 MHz
Power 42 dB
on during acquisition
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 131072
Total time 2 hr, 57 min, 20 sec
GS-1231-01-79-pure

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0°C / 297.1 K
Operator: barbara
File: GS-1231-01-79-pure
INOVA-500 "riga"

Pulse 57.9 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
100 repetitions
OBSERVE H1, 499.7707212 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 3 min, 10 sec

E/Z-9
500MHz, CDCl3
GS-1231-01-85-pure

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Operator: barbara
File: GS-1231-01-85-pure
INOVA-500 "riga"

Pulse 57.9 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
92 repetitions
OBSERVE 1H, 499.7707111 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 3 min, 10 sec

E/Z-11
500MHz, CDCl3
GS-1231-01-80-pureIndol

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
Operator: barbara
File: GS-1231-01-80-pureIndol
INova-500 "riga"

Pulse 57.9 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
100 repetitions
OBSERVE H1, 499.7707500 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 3 min, 10 sec

E/Z-12
500MHz, CDCl3
GS-1231-01-68-mixpure

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
Operator: barbara
File: GS-1231-01-68-mixpure
INOVA-500 "riga"

Pulse 57.9 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
64 repetitions
OBSERVE H1, 499.7707202 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 3 min, 10 sec

E/Z-13
500MHz, CDCl₃
GS-1231-01-68-pureBS

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
Operator: barbara
File: GS-1231-01-68-pureBS
INOVA-500 "riga"

Pulse 57.9 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
100 repetitions
OBSERVE H1, 499.7707207 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 3 min, 10 sec

Z-13
500MHz, CDCl3
Pulse Sequence: s2pul
Solvent: CDCl3
Temperature: 24.0 °C / 297.1 K
Operator: Barbara
Date: 01-01-68-pure-TP

500 MHz, CDCl3

Pulse 5.9 degrees
At 90 GHz
Width 8000.0 Hz sec
84 repetitions
H1, 499.7707207 MHz
LINE BROADENING 0.1 Hz
TR size 32768
Total time 3 min, 10 sec

5.9 Hz

PPm

82
GS-1231-01-78-pure

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 °C / 297.1 K
Operator: barbara
File: GS-1231-01-78-pure

INNOVA-500 "riga"

Pulse 57.9 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
100 repetitions

OBSERVE R1, 499.7707222 MHz

DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 3 min, 10 sec

E/Z-16
500MHz, CDCl3
GS-1231-01-64-Cond4-Citrunellal-Pure

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 24.0 C / 297.1 K
Operator: barbara
File: GS-1231-01-64-Cond4-Citrunellal-Pure
INNOVA-500 "riga"

Pulse 57.9 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
48 repetitions
OBSERVE 81, 499.7707222 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 3 min, 10 sec

E/Z-17
500MHz, CDCl3
GS-1231-03-195-pureMixture

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Operator: barbara
File: GS-1231-03-195-pureMixture
INOVA-500 "riga"

Pulse 57.9 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
56 repetitions
OBSERVE H1, 499.7707207 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 3 min, 10 sec
GS-1231-01-piperidonecondensation-7

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 °C / 298.1 K
Operator: barbara
File: GS-1231-01-piperidonecondensation-7
INova-500 "riga"

Pulse 57.9 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
36 repetitions
OBSERVE Hz, 499.7707212 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 6 min, 20 sec

E/Z-19
500MHz, CDCl3
GS-1231-03-179-PureNapthyl

Pulse Sequence: s2pul
Solvent: CDCl$_3$
Temp. 25.0 °C / 298.1 K
Operator: barbara
File: GS-1231-03-179-PureNapthyl
INova-500 "riga"

Pulse 57.9 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
56 repetitions
OBSERVE #1, 499.7707197 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 3 min, 10 sec

500MHz, CDCl$_3$

![Napthyl Molecule Diagram]
GS-1231-03-179-Naphthyl-CDCl3-C13

Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: barbara
File: GS-1231-03-179-Naphthyl-CDCl3-C13
INOVA-500 "riga"

Relax. delay 2.500 sec
Pulse 52.1 degrees
Acq. time 1.300 sec
Width 29996.3 Hz
1956 repetitions
OBSERVE C13, 125.6674209 MHz
DECOUPLE R1, 499.7732084 MHz
Power 42 dB
on during acquisition
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 131072
Total time 2 hr, 7 min, 14 sec

125MHz, CDCl3
GS-1231-02-147-pure

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Operator: barbara
File: GS-1231-02-147-pure
INOVA-500 “riga”

Pulse 57.9 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
100 repetitions
Observe H1 499.770202 MHz
Data Processing
Line broadening 0.1 Hz
FT Size 32768
Total time 3 min, 10 sec

500MHz, CDCl3
GS-1231-02-147-C13-CDCl3

Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: barbara
File: GS-1231-02-147-C13-CDCl3
INOVA-500 "riga"

Relax. delay 2.500 sec
Pulse 52.1 degrees
Acq. time 1.300 sec
Width 29996.3 Hz
8804 repetitions
OBSERVE C13, 125.6674223 MHz
DECOPUPLE R1, 499.7732084 MHz
Power 42 dB
on during acquisition
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 131072
Total time 9 hr, 31 min, 39 sec
GS-1231-02-105-pure

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Operator: barbara
File: GS-1231-02-105-pure
INOVA-500 "riga"

Pulse 57.9 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
76 repetitions
OBSERVE H1, 499.7707212 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 3 min, 10 sec
GS-1231-01-94-clickMethoxy-TS

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Operator: barbara
File: GS-1231-01-94-clickMethoxy-TS
INOVA-500 "riga"

Pulse 57.9 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
100 repetitions
OBSEVE H1, 499.7707222 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 3 min, 10 sec
GS-1231-01-94-ClickMethoxy-LS

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Operator: barbara
File: GS-1231-01-94-ClickMethoxy-LS
INOVA-500 "riga"

Pulse 57.9 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
48 repetitions
OBSEIVE H1, 499.7707222 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 3 min, 10 sec

500MHz, CDCl3

23a

8 7 6 5 4 3 2 1 ppm
GS-1231-02-117-pure

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Operator: barbara
File: GS-1231-02-117-pure
INNOVA-500 "riga"

Pulse 57.9 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
56 repetitions
CREASE H1, 499.7707212 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 3 min, 10 sec

24a and 24b
500MHz, CDCl3

\[
\text{\chem{N-N-S-N-N}}_{-} \text{phenyl} \quad + \quad \text{\chem{N-N-S-N-N}}_{-} \text{phenyl}
\]
GS-1231-02-116-pure

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Operator: barbara
File: GS-1231-02-116-pure
INOVA-500 "riga"

Pulse 57.9 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
56 repetitions
OBSERVE H1, 499.7707212 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 3 min, 10 sec

25a and 25b
500MHz, CDCl3
GS-1231-02-146-pure-f2

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Operator: barbara
File: GS-1231-02-146-pure-f2
INOVA-500 "riga"

Pulse 57.9 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
100 repetitions
OBSERVE H1, 499.7707212 MHz

DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 3 min, 10 sec
GS-1231-02-161-pure

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Operator: barbara
File: GS-1231-02-161-pure
INOVA-500 "riga"

Pulse 57.9 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
68 repetitions
OBSERVE H1, 499.7707217 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 3 min, 10 sec

500MHz, CDCl3
GS-1231-196-monomethoxySulfone

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Operator: barbara
File: GS-1231-196-monomethoxySulfone

INOVA-500 "riga"

Pulse 57.9 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
100 repetitions
OBSERVE H1, 499.7707207 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 3 min, 10 sec
GS-1231-02-169-pure

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Operator: barbara
File: GS-1231-02-169-pure
INOVA-500 “riga”

Pulse 57.9 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
92 repetitions

OBSERVE H1, 499.7707212 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 3 min, 10 sec

500MHz, CDCl3
GS-1231-03-185-pureTS

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 °C / 298.1 K
Operator: barbara
File: GS-1231-03-185-pureTS
INOVA-500 "riga"

Pulse 57.9 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
44 repetitions
Observe H1, 499.7707236 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 3 min, 10 sec

E/Z-30
500MHz, CDCl3
GS-1231-03-194-pureMixture

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Operator: barbara
File: GS-1231-03-194-pureMixture
INOVA-500 "riga"

Pulse 57.9 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
48 repetitions
OBSERVE H1, 499.7707212 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 3 min, 10 sec

E/Z-32
500MHz, CDCl3
GS-1231-03-188-pure

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 °C / 298.1 K
Operator: barbara
File: GS-1231-03-188-pure
INOVA-500 "riga"

Pulse 57.9 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
100 repetitions
OBSERVE H1, 499.7707207 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 3 min, 10 sec

E/Z-33
500MHz, CDCl3
GS-1231-03-207-pureTs

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Operator: barbara
File: GS-1231-03-207-pureTs
INOVA-500 "riga"

Pulse 57.9 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
100 repetitions
OBSERVE H1, 499.7707217 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 3 min, 10 sec

Z-33
500MHz, CDCl3
GS-1231-03-207-pureBs

Pulse Sequence: s2pul
溶剂: CDCl3
温度: 25.0 °C / 298.1 K
操作员: barbara
文件: GS-1231-03-207-pureBs
INOVA-500 "riga"

脉冲角度 57.9 度
采集时间 1.892 秒
宽度 8000.0 Hz
52 次重复
观察 H1, 499.7707222 MHz
数据处理
线宽 0.1 Hz
FT 尺寸 32768
总时间为 3 分钟，10 秒

500MHz, CDCl3

Z-33
GS-1231-03-190-pure

Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Operator: barbara

File: GS-1231-03-190-pure
INOVA-500 "riga"

Pulse 57.9 degrees
Acq. time 1.892 sec
Width 8000.0 Hz
156 repetitions

OBSEVE H1, 499.7707212 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 6 min, 20 sec

E/Z-34
500MHz, CDCl3