CATALYTIC *N*-ARYLATION OF TRIAZOLES AND C–H ACTIVATION LEADING TO AROMATIC HETEROCYCLES

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2016

Submitted to the Faculty of the
Graduate College of the
Oklahoma State University
in partial fulfillment of
the requirements for
the Degree of
DOCTOR OF PHILOSOPHY
May 2021

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ACKNOWLEDGEMENTS

I would like to acknowledge all who have helped me on my quest to acquire my doctorate. Each one of you has helped me along the way, and I wouldn't have made it here without you. First, I would like to thank my wife, Katey, for being there when I needed her most. I would also like to thank my mother, father, and sisters for their support from afar, keeping me grounded in the beginning years. I would like to thank all my undergraduate mentors for giving me a solid foundation of the material so that I could excel in the future, including Dr. Vincent Sichula, Dr. Mallory Cortez, and Dr. Chadwick Young. Finally, I would also like to thank my Graduate Mentor, Dr. Jeanne L. Bolliger, for teaching me, guiding me, and allowing me to develop my skills during my time as a graduate student at Oklahoma State University.

Name: SCOTT MICHAEL HUTCHINSON

Date of Degree: MAY, 2021

Title of Study: CATALYTIC *N*-ARYLATION OF TRIAZOLES AND C–H ACTIVATION LEADING TO AROMATIC HETEROCYCLES

Major Field: CHEMISTRY

Abstract: 5-Membered *N*-heterocycles have become valuable structural motives in organometallic chemistry, organic synthesis, and medicinal chemistry. Such compounds can act as ligands for organometallic complexes and catalysts, as organocatalysts, and are structural components of many FDA-approved pharmaceuticals. We developed a new method for the synthesis of 1-aryl-4-substituted-triazolium salts, employing copper catalysis and diaryliodonium salts. Previously, 1-aryl-4-substituted-triazolium salts were synthesized by a multistep, low-yielding, synthetic pathway. Our arylation procedure progressed in two short steps, first, starting from cheap primary amines converting to the corresponding 4-substituted-1,2,4-triazoles, followed by the copper-catalyzed *N*-arylation. The arylation of the 4-substituted-triazoles progressed under mild conditions, was tolerant of water and oxygen, and permitted a wide variety of functional groups in moderate to high yields. Further functionalization of our triazolium salts with amine substituents led to the discovery of an alternative approach to fused azoles. Bicyclic azoles were previously synthesized starting from a combination of hydrazonyl halide and thioether substituted azoles or starting from amino or hydrazinyl azoles. Our iodine-promoted cyclization began from 4-(2-nitrophenyl)-1-substituted-4*H*-1,2,4-triazol-1-ium salts, which were all synthesized from 4-(2-nitrophenyl)-1,2,4-triazole using our arylation procedure and substitution reactions with high yields. Our nitro-containing triazolium salts were reduced and isolated as 4-(2-ammoniophenyl)-1-substituted-4*H*-1,2,4-triazol-1-ium chlorides in high yields. Finally, subjecting the 4-(2-ammoniophenyl)-1-substituted-4*H*-1,2,4-triazol-1-ium chlorides to iodine-promoted intramolecular cyclization allowed the synthesis of 9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium salts in low to moderate yields. Our method allowed for a mild sequential synthesis of imidazo[2,1-*c*][1,2,4]triazol-1-ium salts from primary amines. Overall, we are confident that our procedure will allow access to novel organocatalysts and organometallic ligands, as well as compounds that exhibit biological activity.

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CHAPTER I

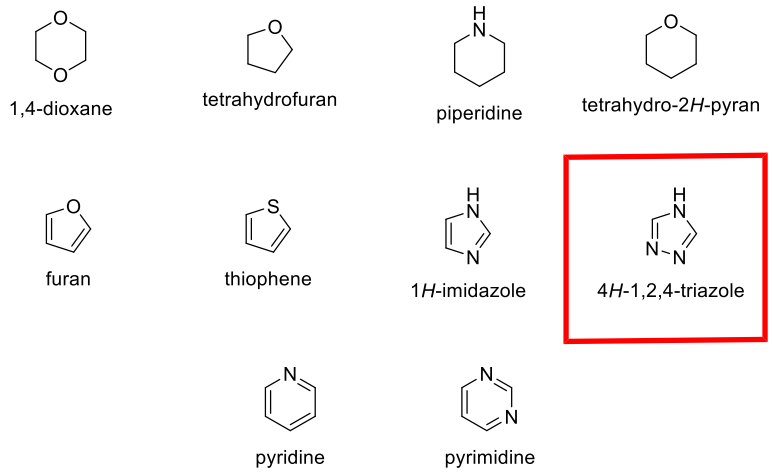
INTRODUCTION

Section 1.0 Heterocycles in Chemistry

Heterocycles were first discovered in the early to mid-1800s.[1,2] With few substantial discoveries in over 100 years, heterocycles have recently gained prominence in medicinal chemistry,[3–5] organic synthesis,[6–11] and organometallic chemistry.[9,11–14] A heterocycle is defined as a cycle consisting of at least two different elements.[1] In organic chemistry, these generally consist of one or more carbocycles with one or more oxygen, sulfur, or nitrogens in the cyclic structure. Examples of common aliphatic heterocycles are 1,4-dioxanes, tetrahydrofuran, tetrahydropyran, and piperidine; common aromatic heterocycles are furan, pyridine, thiophene, pyrimidine, 1,2,4-triazole, and imidazole (Figure 1). When comparing cycles of like ring size and double bond substitution, heterocycles are very similar to carbocycles in their geometry and stabilities. However, heterocycles use their unshared pairs of electrons to coordinate, hydrogen bond, or act nucleophilicly. These interactions are essential for applications as catalysts, ligands, and pharmaceuticals.

Many heterocycles are known as common solvents and bases, but their application expands to an astounding scale when incorporated into larger organic frameworks.

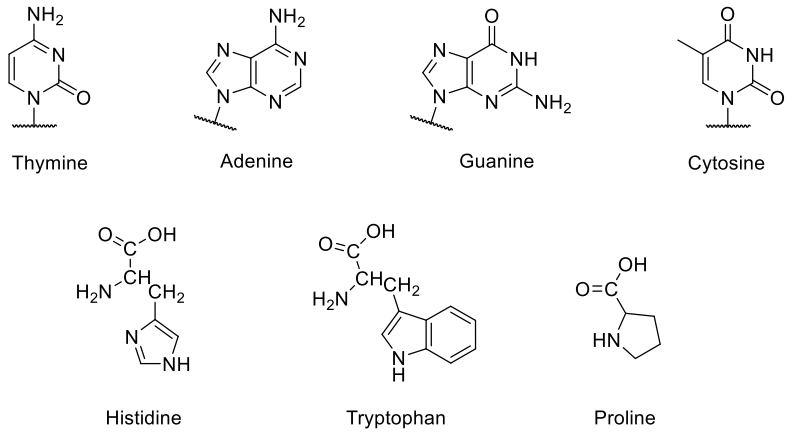
Figure 1. Examples of 5-Membered and 6-Membered Heterocycles



Section 1.1. Heterocycles in Medicinal Chemistry

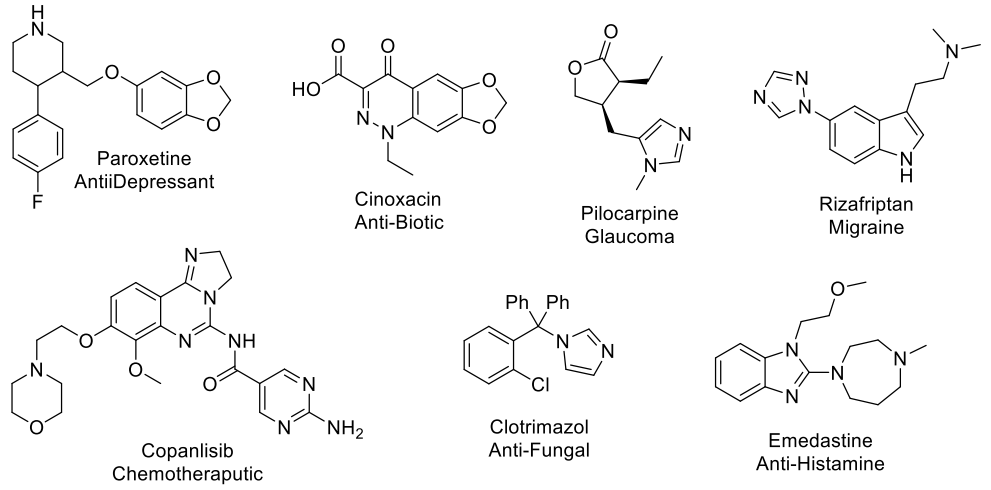
In medicinal chemistry, heterocycles have essential functions both within our body and as components of drug molecules.[1,15] Within humans, DNA and RNA's function is dependent on the sequence of the nucleic acids adenine, thymine, guanine, and cytosine (Figure 2), which are all aromatic heterocycles.[1] The ribose sugar linker, as it appears in our RNA, is an oxygen-containing aliphatic heterocycle. The three amino acids proline, tryptophan, and histidine are *N*-heterocycles necessary for many biological processes.[1] Heterocycles are essential pharmacophores in various commercial drugs capable of eliciting a biological response when interacting with our proteins and DNA.

Figure 2. Heterocycles in Nucleic Bases and Amino Acid



Some heterocycles are found throughout FDA-approved pharmaceuticals and are considered potent pharmacophores and useful structural motives.[16] The Njardarson group analyzed the FDA's pharmaceutical database for the proportion of heterocycles containing oxygen,[3] nitrogen,[5], and sulfur.[4] Their analysis revealed that the 2012 FDA database contained 1086 unique small-molecule drugs, of which 640 (59%) contained at least one *N*-heterocycle,[5] and 208 (19%) contained at one or more sulfurs in the structure.[4] Their review of the 2017 database for O-heterocycles found 311 (27%) unique O-heterocycles from the list of approximately 1152 unique small drug molecules approved by the FDA.[3]

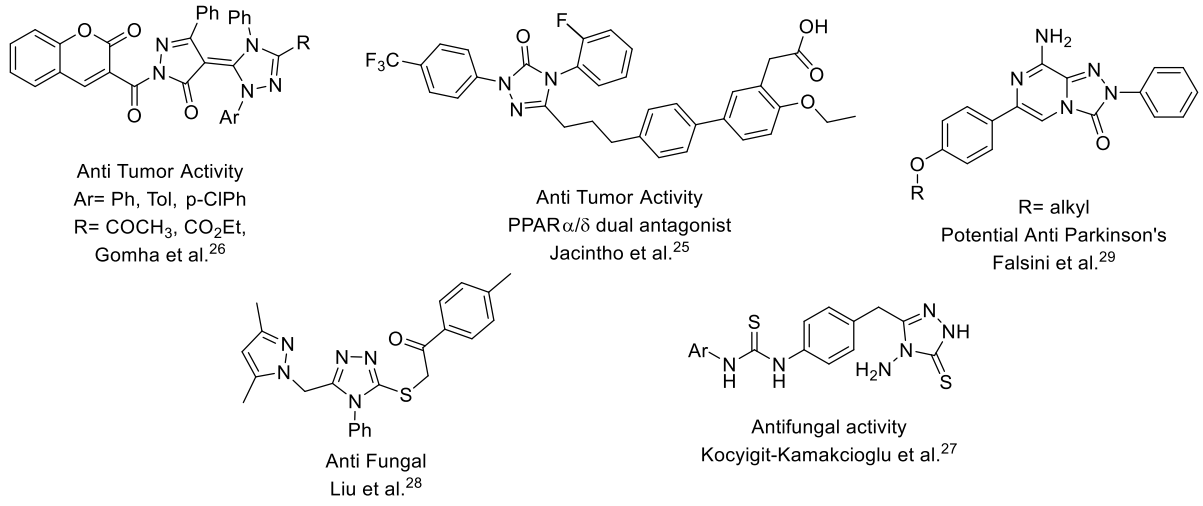
Figure 3. Examples of Heterocycle Containing FDA Approved Pharmaceuticals



A sample of FDA-approved pharmaceuticals is depicted in Figure 3, displaying the potential range of applications from antihistamines to antidepressants and even chemotherapeutics.[3,5] Reviewing the 2012 and 2017 FDA pharmaceutical databases revealed that many pharmaceuticals contain multiple heterocycles, with the most common being 5- and 6-membered heterocycles.[3,5] The bioactivity of heterocycle-containing small molecules sparked several research groups to investigate the isolation, synthesis, and biological activity of potential drug candidates along with previously established pharmaceuticals.[17–20] Recently, there has been significant advances in the synthesis of various substitutions of azoles. 1,2,4-Triazoles (highlighted structure in Figure 1) will be the primary focus of this dissertation. Though not as abundant, research into the small molecules containing 5-membered azoles has revealed potential drug candidates containing 1,2,4-triazoles and imidazole displaying similar biological potencies as shown by several FDA-approved pharmaceuticals.[21–24] Figure 4 depicts a sample of recently investigated 1,2,4-triazole-containing bioactive molecules displaying biological activity as anti-tumor agents,[25,26] anti-fungal agents,[27,28] as well as promising activities that could lead to an anti-Parkinson's agent.[29] 1,2,4-Triazoles and

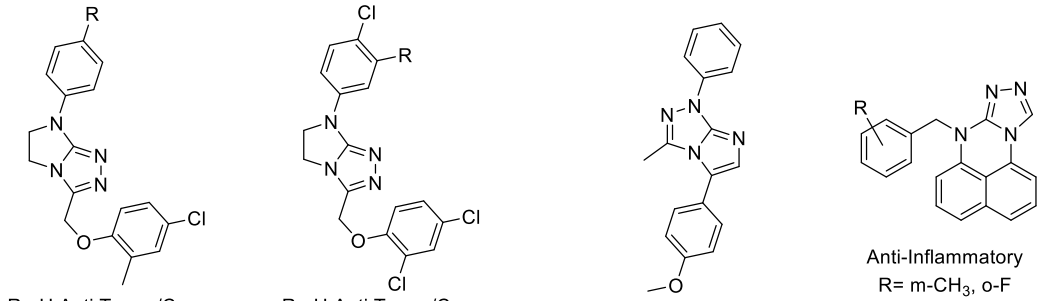
derivatives have shown a wide range of biological applications, including anti-inflammatory, analgesic, anti-convulsant, antioxidant, anti-migraine, diuretic, and muscle relaxants, displaying the broad applicability of 1,2,4-triazoles and *N*-heterocycles in general.[2]

Figure 4. Examples of Triazole-Containing Bioactive Molecules in Literature



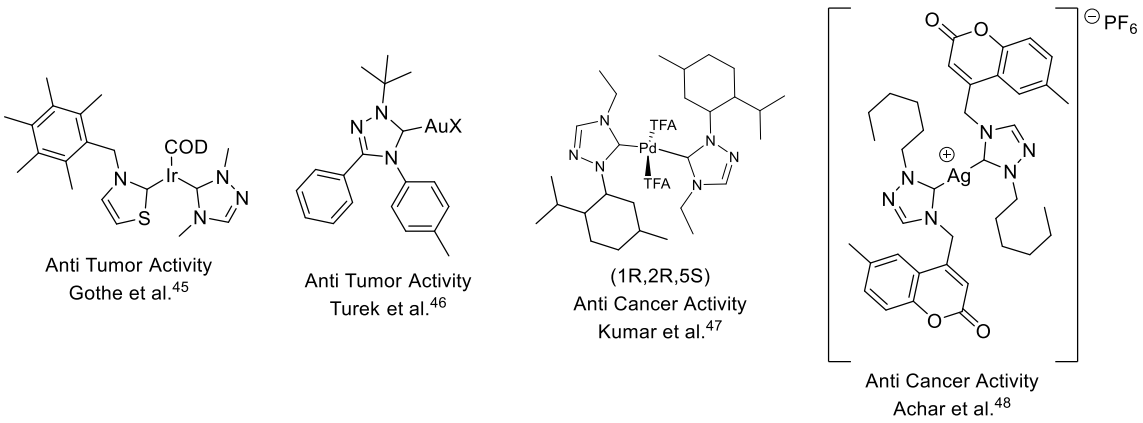
In pharmaceuticals, fused polycyclic systems are abundant. The Njardarson group stated that in the 2012 FDA pharmaceutical database, 14% of unique nitrogen-containing small drug molecules contained fused rings.[5] The medicinal chemistry field has echoed this notion with a recent increase in research on the synthesis and biological activity of fused nitrogen-containing aromatic heterocycles.[30–36] Shown in Figure 5 are samples of biologically active agents containing 1,2,4-triazoles in a fused heterocyclic system displaying anti-fungal,[37] anti-inflammatory activities [38] and anti-tumor/cancer agents.[39] Research into the biological applications of 1,2,4-triazole-containing fused heterocyclic systems revealed compounds exhibiting antibacterial,[40,41] anti-viral,[42] analgesic, and antioxidant activity.[43,44]

Figure 5. Examples of Biologically Active Fused Bicyclic Azoles



The biological activity of transition metal complexes containing 1,2,4-triazole ligands has also been measured. Figure 6 shows some examples of these complexes that display anti-cancer/tumor activities.[45–48]

Figure 6. 1,2,4-Triazole Containing Transition Metal Complexes as Anti-Cancer/Tumor Agents

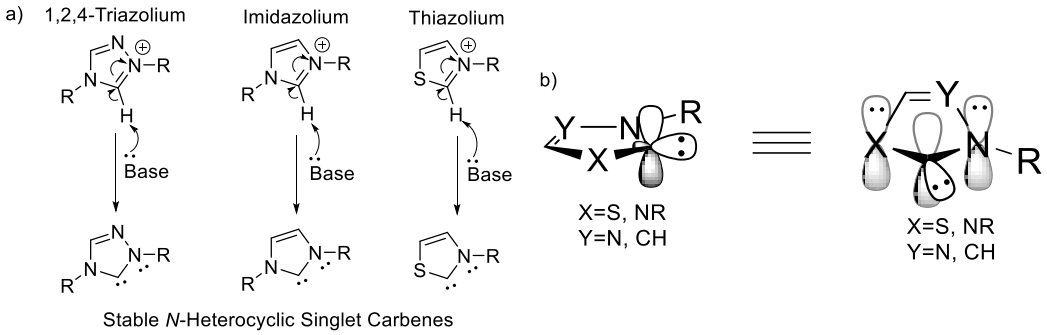


The deprotonation of the 1,2,4-triazolium salts precursors results in *N*-heterocyclic carbene (NHC) ligands which coordinate to form complexes with iridium,[45] gold,[46] palladium,[47] and silver,[48] as depicted in Figure 6. 1,2,4-Triazolium, imidazolium, and thiazolium salts form *N*-

heterocyclic carbenes (Figure 7a),[9,11] which have applications as organocatalysts beside their uses as ligands for transition metal catalysts/complexes.[8,12,13,38]

Section 1.2: *N*-Heterocyclic Carbenes

Figure 7. Stable *N*-Heterocyclic Singlet Carbenes from Substituted Azoles

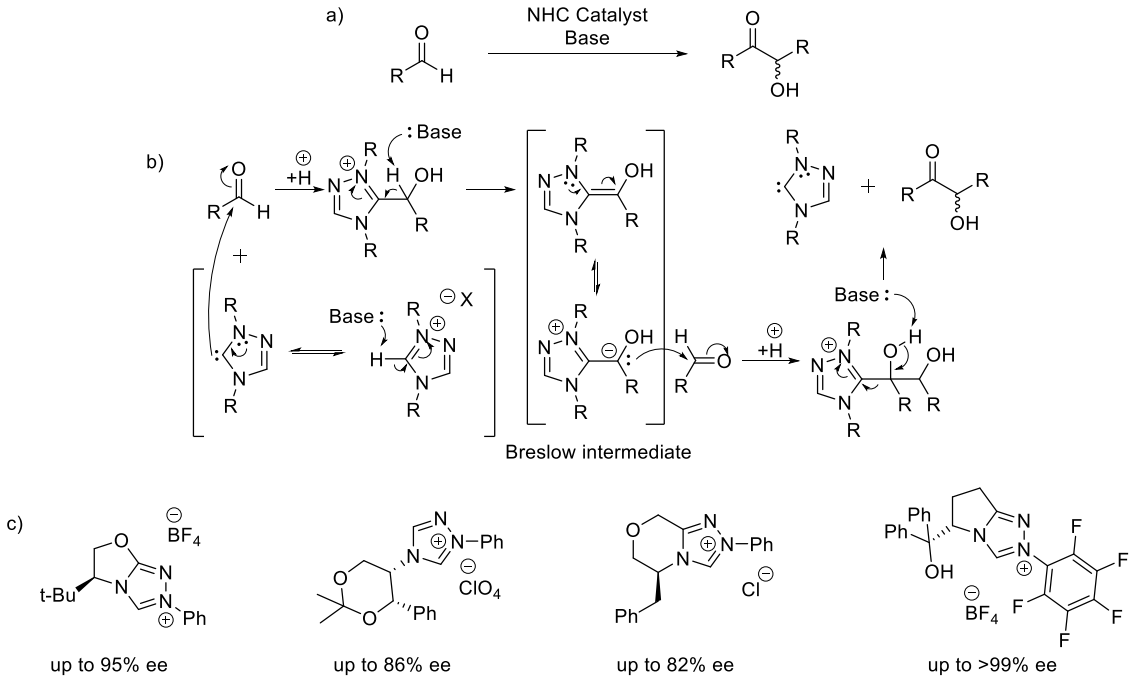


Carbenes are reactive intermediates characterized by an uncharged carbon atom with two non-bonded electrons. Carbenes can exist in either the singlet or triplet form. Singlet carbenes are characterized by a lone pair of electrons occupying an sp^2 hybridized orbital on an uncharged carbon atom with an empty p orbital (Figure 7b), allowing singlet carbenes to potentially act either nucleophilicly or electrophilicly. In contrast, triplet carbenes are characterized by two unpaired electrons, one occupying the sp^2 hybridized orbital and one in the unhybridized p orbital, displaying reactivity similar to di-radicals. The deprotonation of substituted azolium salts results in a stable singlet carbene (Figure 7a).[11] One reason for this reactivity is the stabilization of the empty p-orbital by overlapping with the filled p-orbitals of adjacent heteroatoms (Figure 7b).[11] This understanding allows for a better-educated design of potential organocatalysts and transition metal complexes/catalysts.

Section 1.3: Application of 1,2,4-Triazolium Salts as Organocatalysts

A well-known reaction catalyzed by *N*-heterocyclic carbenes is the benzoin condensation (Scheme 1a).[7] The NHC catalyzed benzoin condensation progresses through the umpolung of an aldehyde, forming a "Breslow intermediate", which is nucleophilic and can attack an electrophile, such as an aldehyde, and form the product after deprotonation and subsequent dissociation of the catalyst (Scheme 1b).

Scheme 1. *N*-Heterocyclic Carbenes as Organocatalysts for the Benzoin Condensation

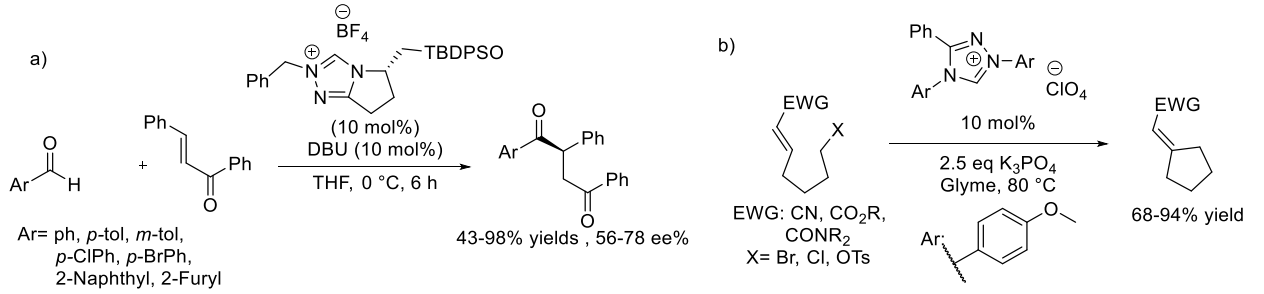


F. Glorius et al., *Chem. Soc. Rev*., 2012, **41**, 3511-3522.[7]

Scheme 1c depicts samples of chiral catalysts which were found to catalyze the benzoin condensation with good to excellent enantioselectivity (>82% ee).[7] Another NHC catalyzed reaction is the Stetter reaction which involves a Michael acceptor as the electrophile for the Breslow intermediate, resulting in a 1,4-dioxo species (Scheme 2a). The Enders group

showed that their novel catalyst was capable of catalyzing the Stetter reaction in moderate to high yields (43-98%) with moderate to good enantioselectivity (56-87%).[49] NHCs can also be used to umpolung a Michael acceptor; Fischer and coworkers proved that with a variation of the Enders triazole it is possible to promote an intramolecular β-alkylation of Michael acceptors in good to high yield (64-94%). Moreover, a variety of leaving groups and electron-withdrawing groups were tolerated (Scheme 2b).[50]

Scheme 2. NHC Catalyzed Stetter Reaction and Umpolung of Michael Acceptor



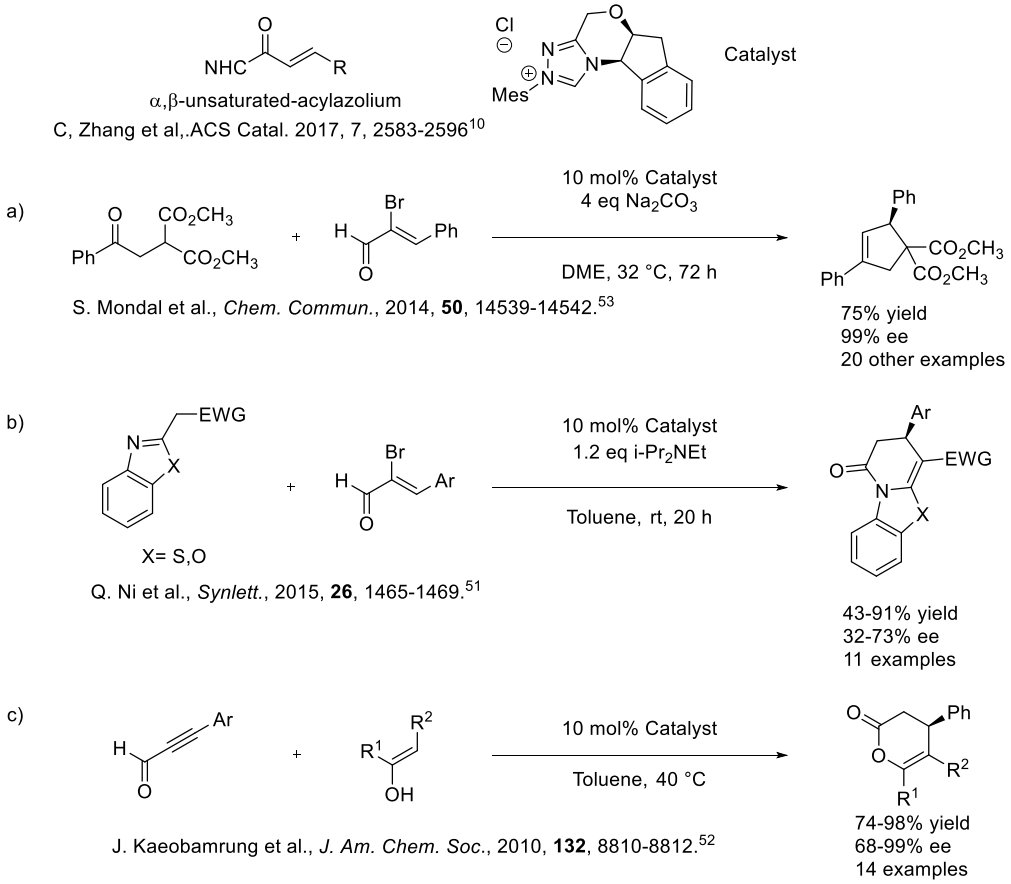
D. Enders et al., *Chem. Commun*., 2008, 3989-3991.[49]

C. Fischer et al., *J. Am. Chem. Soc*., 2006, **128**, 1472-1473.[50]

Another organocatalytic application of NHCs is the functionalization of α,β-unsaturated aldehydes via the α,β-unsaturated acyl azolium intermediate.[10] This intermediate accentuates the electrophilic properties of the β-position and the carbonyl carbon (Scheme 3b,c),[51,52] while also allowing the α-position to act as a nucleophile (Scheme 3a).[53] The examples depicted in Scheme 3 describe research by Biju, Enders, and Bode using the same chiral catalyst to perform different reactions through the α,β-unsaturated acyl azolium intermediate. The Biju group outlined the synthesis of different cyclopentenes in low to moderate yields (40-85%) with excellent enantioselectivity (>90% ee). They proposed that the β-position of the α,β-unsaturated acyl azolium intermediate was attacked first by the enolate formed between the 1,3-ester groups. This was followed by an attack on the aryl ketone by the

enolate formed at the α-position from the attack at the β-position, with an elimination to form the final product (Scheme 3a).[53] Research by Enders and coworkers described a 1,3-addition to α,β-unsaturated aldehydes by a substituted benzothiazole in moderate to high yields (43-91%) with low to moderate enantioselectivity (32-73% ee) (Scheme 3b).[51] Finally, the Bode group published an alternative 1,3-addition of the α,β-unsaturated aldehyde using a substituted enol as the nucleophile. This reaction proceeded with good to high yields (74-98%) and moderate to high enantioselectivity (68-99% ee) (Scheme 3c).[52] These examples are not an exhaustive list of the potential organocatalytic applications for *N*-heterocyclic carbenes, as there are many others described in the literature.[8,54]

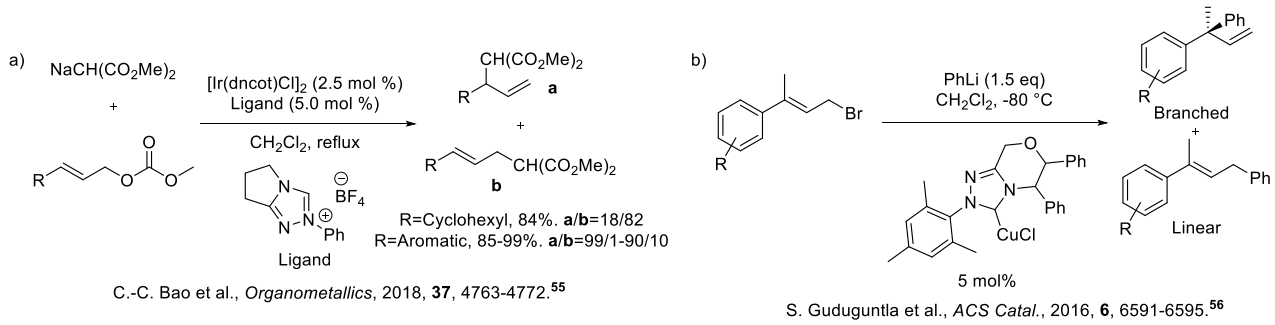
Scheme 3. NHC Catalysis via the α,β-Unsaturated Acyl Azolium Intermediate



Section 1.4. 1,2,4-Triazolium Salts as Ligand Precursors for Transition Metal Catalysts

N-Heterocyclic carbenes are well-known as ligands for transition metal complexes.[12–14] An *N*-heterocyclic carbene is considered a strong σ-donor with the potential to act as a π-acceptor.[9,11] The substituents on the *N*-heterocyclic carbene have a steric effect on the metal complex and an electronic effect on the metal center, allowing for tunable alteration to the selectivity and efficiency of transition metal catalysts.[12,14] Bao and coworkers catalyzed the substitution of an allylic carbonate ester employing an iridium complex formed *in situ* from a bicyclic achiral 1,2,4-triazolium salt pre-catalyst and an iridium salt.[55] Through variation of the R-substituent on the allylic carbonate ester, they found that aromatic substituents favored **Product a** (85-99 % yield), and alkyl substituents favored **Product b** (84% yield) (Scheme 4a).[55] The Feringa group performed a catalytic arylation of an allylic bromide with aryl lithium reagents, for which they used a chiral bicyclic 1,2,4-triazole copper(I) catalyst.[56] They observed a preference for the branched regioisomer (35-88%), obtained with over 90% ee (Scheme 4b).[56]

Scheme 4. Bicyclic 1,2,4-Triazolium Salts as Ligands for Transition Metal Catalysts



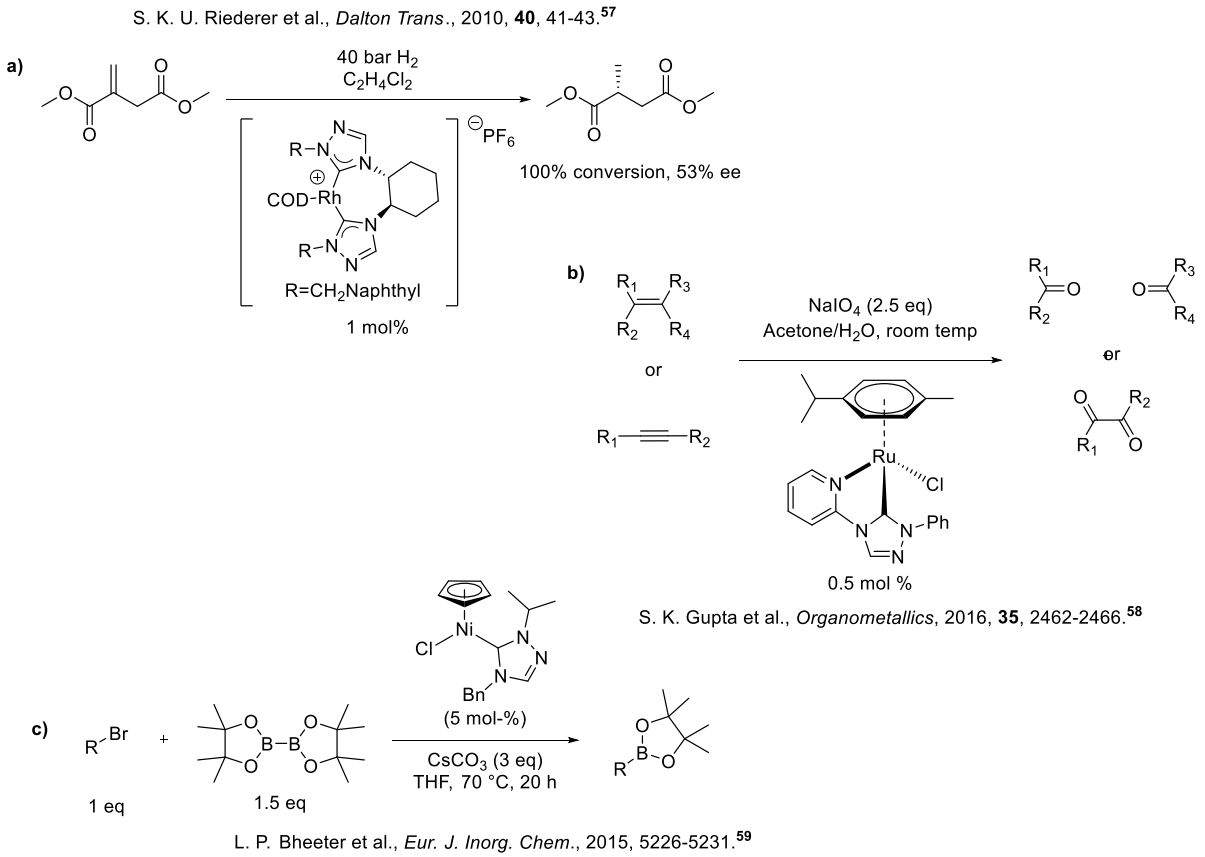
C.-C. Bao et al., *Organometallics*, 2018, **37**, 4763-4772.[55]

S. Guduguntla et al., *ACS Catal.*, 2016, **6**, 6591-6595.[56]

Scheme 5 depicts three examples of the application of 1,4-substituted-1,2,4-triazole complexes. The Kuhn group demonstrated that their bidentate rhodium(I) complex could

promote the hydrogenation of α,β-unsaturated esters with a high *ee*, up to 61% (Scheme 5a).[57] The Choudhury group demonstrated their ruthenium(I) complex containing a bidentate triazole ligand caused olefins and alkynes to oxidize to ketones/aldehydes and 1,2-diones, respectively.[58] A comparison between related imidazole and 1,2,4-triazole catalysts indicated that the 1,2,4-triazole catalyst was superior (52-92% yields) to the analogous imidazole complex (2-58% yields).[58] Finally, the Darcel group reported a borylation reaction catalyzed by a nickel(I) complex (Scheme 5c), for which high conversions (71-98%) but low isolated yields were reported (8-40%).[59] In summary, transition metal complexes bearing carbene ligands are effective catalysts for a large range of reactions. Further examples include aryl-aryl cross-coupling reactions, aryl C–H activations, olefin metathesis, chiral conjugate additions, carbonyl reductions, polymerizations, and cycloadditions.[9,12,13,60]

Scheme 5. 1,4-Disubstituted-1,2,4-triazoles as Ligands for Transition Metal Catalysts

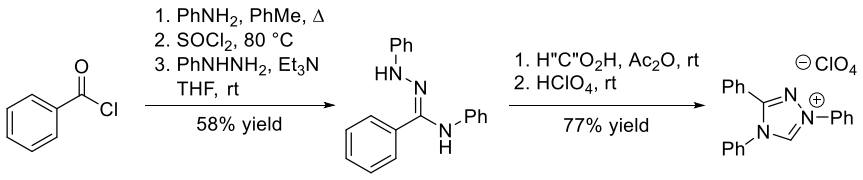


Section 1.5. Synthesis of 1,3,4-Trisubstituted-1,2,4-triazolium Salts

The broad application of the 1,2,4-triazole motif in catalysts, ligand, and bioactive molecules is a strong motivation to develop new pathways for their synthesis. 1,3,4- and 1,4-substituted-triazolium salts (Scheme 6-11) are common substitution patterns for catalyst or ligand precursors. The triazole ring is formed in the last step in the standard synthesis of 1-aryl-3,4-substituted-1,2,4-triazolium salts. The desired compounds can be made from an aryl hydrazine, a single carbon electrophilic species (HCO_2H, $HC(OEt)_3$), and a precursor capable of a nucleophilic acyl substitution followed by an imine condensation.[61–63] A well-known

1,2,4-triazolium salt used in organocatalysis is the Enders catalyst. The Enders group synthesized this catalyst precursor from benzoyl chloride by first forming the *N*-phenyl benzamide followed by a thionyl chloride activated imine condensation to form *N,N'*-diphenylbenzohydrazonamide in 58% yield.[61] The cyclization is initiated using formic acid as a single carbon electrophile and acetic anhydride as a dehydrating agent, with a strong acid such as perchloric acid necessary to form the 1,3,4-triphenyl-1,2,4-triazolium perchlorate in 77% yield (Scheme 6).[61] By substituting either the amine or the aryl hydrazine in the first step, it is possible to tune the resulting carbene catalyst's reactivity and selectivity. For example, when the Fisher group utilized 4-methoxyphenyl substituents as replacements for the phenyl substituents at the N^1 and N^4 position, higher yields were observed in the umpolung of a Michael acceptor when compared to the original Enders catalyst (Scheme 2b).[50]

Scheme 6. Synthesis of Enders Triazoles

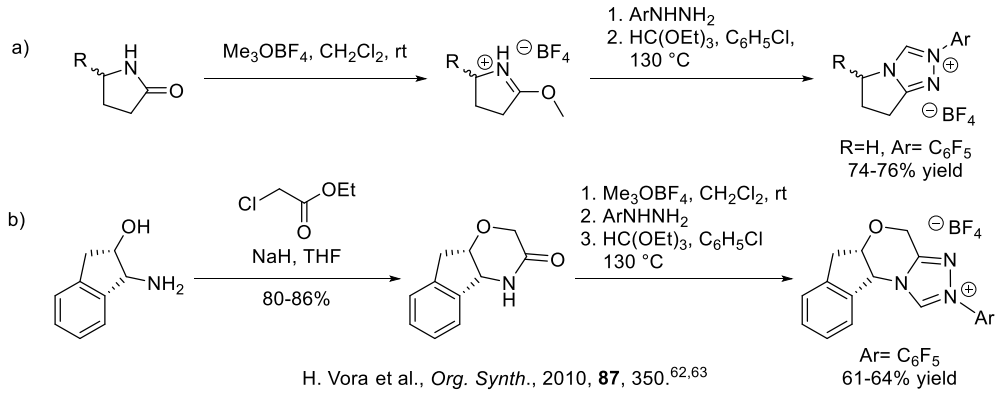


D. Enders et al., *Synthesis*, 2003, 1292-1295.[61]

The synthesis of bicyclic 1-aryl-3,4-substituted-1,2,4-triazolium salts begins with a cyclic amide starting material, first undergoing an alkylation using trimethyloxonium tetrafluoroborate to form the protonated imine ester *in situ* (Scheme 7).[62] This undergoes a nucleophilic acyl substitution by aryl hydrazine which is then cyclized using triethoxymethane as the single carbon electrophile to form the desired 1,2,4-triazolium salts. The yields obtained by this approach vary significantly and depend on the exact aryl

hydrazine and the original amide chosen for this reaction. The Rovis group synthesized examples of chiral and achiral bicyclic 1,2,4-triazolium salts (Scheme 7). For their synthesis of the achiral bicyclic 1,2,4-triazolium salts, good yields were observed (74-76%) (Scheme 7a),[62,63] while the chiral bicyclic 1,2,4-triazolium salts were obtained in slightly lower yields (61-64%) (Scheme 7b).[62,63]

Scheme 7. Synthesis of Bicyclic 1,3,4-Trisubstituted-1,2,4-triazolium Salts



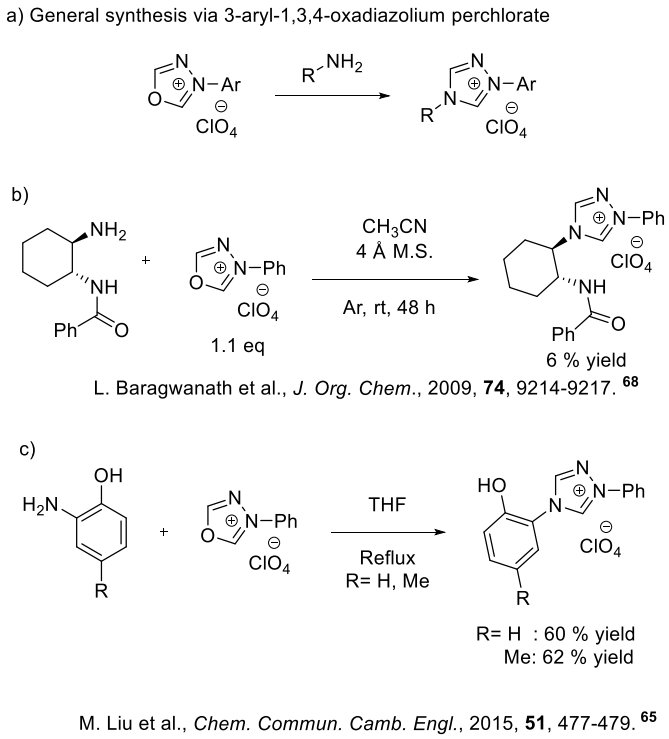
H. Vora et al., *Org. Synth.*, 2010, **87**, 350.[62,63]

Section 1.6. Synthesis of 1,4-Disubstituted-1,2,4-triazolium Salts

1,4-Disubstituted-1,2,4-triazolium salts are synthesized by different methods depending on the nature of the *N*-substituents. The synthesis of 1-alkyl-4-substituted-1,2,4-triazolium salts, where the substituent can be aryl or alkyl, only required a substitution reaction of a 4-substituted-1,2,4-triazole or 4*H*-1,2,4-triazoles with an alkyl halide to access the 1-alkyl-4-substituted-1,2,4-triazolium halide or 1,4-dialkyl-1,2,4-triazolium halide, respectively.[64] The synthesis of 1-aryl-4-substituted-1,2,4-triazolium salts is more difficult, requiring the exchange of oxygen in 3-aryl-1,3,4-oxadiazolium salts for the nitrogen of a primary amine (Scheme 8a).[65–70] Depending on the aryl group, the synthesis and use of these 3-aryl-1,3,4-oxadiazolium salts can be problematic as yields vary significantly depending on the aryl

substitution. The use of perchloric acid in this synthesis poses a safety hazard that should not be neglected. Scheme 8b and Scheme 8c describe two examples of the synthesis of 1-phenyl-4-substituted-1,2,4-triazolium salts using 3-phenyl-1,3,4-oxadiazolium perchlorate. The Connon group attempted to form a chiral 1-aryl-4-alkyl-1,2,4-triazolium salt under anhydrous conditions but could not isolate the product with yields greater than 6%.[68]

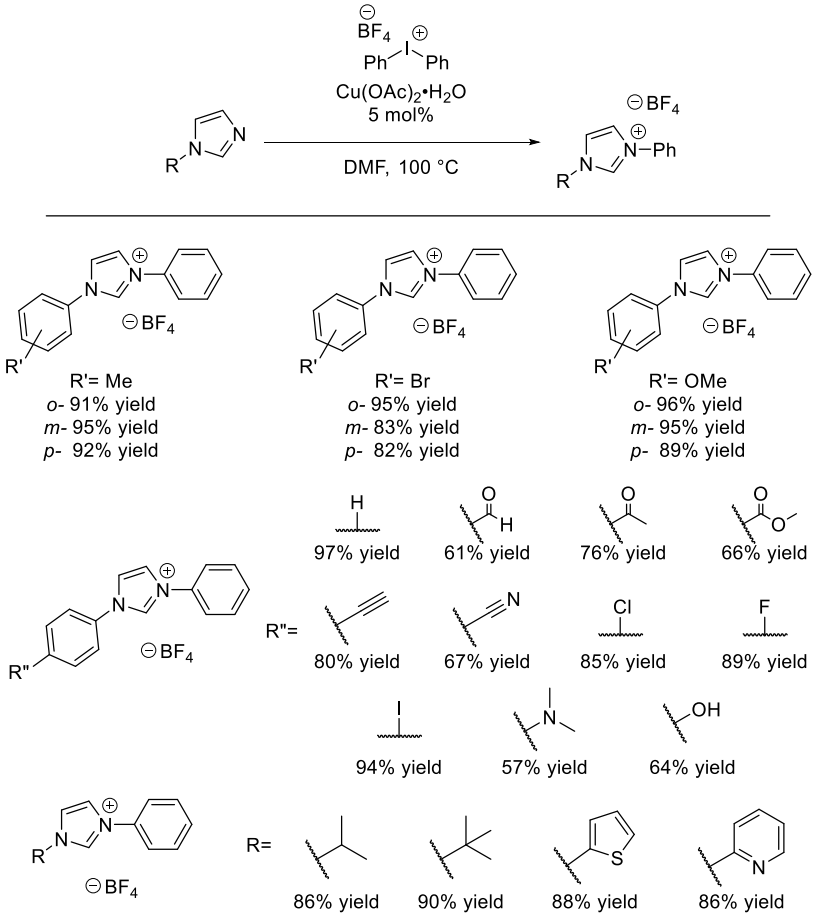
Scheme 8. Synthesis of 1-Aryl-4-substituted-1,2,4-triazolium Salts via 3-Aryl-1,3,4-oxadiazolium Salts



However, Connon and coworkers showed that this catalyst had excellent enantioselectivity (99% ee) for the benzoin condensation but were unable to isolate the product in yields above 33%.[68] The Schmidt group successfully formed their 1-phenyl-4-substituted-1,2,4-triazolium salts in higher yields (60-62%) (Scheme 8c). They prepared various sulfur, selenium, borate mono-dentate, and bidentate adducts incorporating this triazolium unit in moderate yields.[65] A completely different pathway to these compounds could procced via the arylation of a

1,2,4-triazole precursor. The copper-catalyzed *N*-arylation of 4*H*-1,2,4-triazoles was first reported using aryl iodides in the presence of CuO nanoparticles.[71] Recently, an alternative copper-catalyzed arylation method was reported using a soluble copper salt catalyst with diaryliodonium salts as an arene source.[72–75] Lv and coworkers were the first to use symmetrical diaryliodonium salts to synthesize diaryl *N*-heterocyclic carbene precursors from 1-substituted-imidazoles.[72] They were able to arylate imidazoles containing aliphatic groups, heterocycles, and various functionalized phenyl groups, in moderate to high yields (57-97%) (Scheme 9).[72]

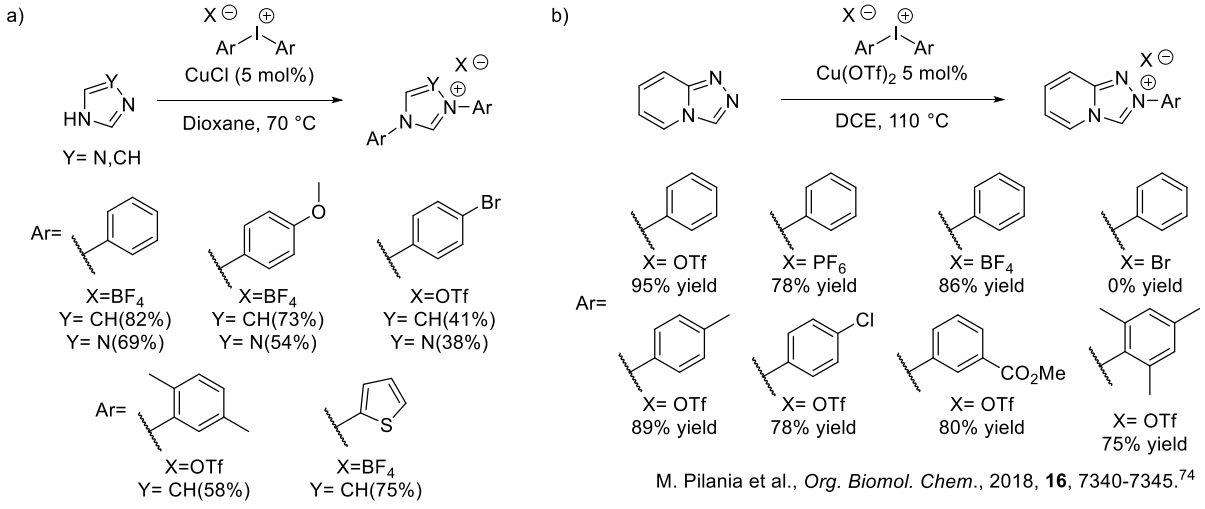
Scheme 9. Copper-Catalyzed Arylation of 1-Substituted-Imidazoles using Diaryliodonium Salts



T. Lv et al., *J. Org. Chem.*, 2013, **78**, 5723-5730.[72]

The same group also reported a direct *N*-arylation of unsubstituted imidazoles and 1,2,4-triazoles to give the *N*,*N*-diarylimidazolium salts in 41-82% yield and the corresponding 1,2,4-triazolium salts in 38-69% yields (Scheme 10a).[73] The Kumar group arylated the N^1 position of [1,2,4]triazolo[4,3-*a*]pyridine using symmetrical diaryliodonium salts in good to excellent yields (75-95%) (Scheme 10b).[74] These developments offer the potential for rapid catalyst optimization since it is known that the N^4 substituent will dominate the electronics of organocatalysts. These methods allow for late-stage *N*-arylation of *N*-heterocycles, which previously had yet to be conducted on 4-substituted-1,2,4-triazoles until in 2019 when the Bolliger group reported the copper-catalyzed arylation of various 4-substituted-1,2,4-triazoles with simple diaryliodonium salts (Chapter 2).[75]

Scheme 10. Catalytic *N*-Arylation of 1,2,4-Triazoles with Diaryliodonium Salts



T.-Y. Lv et al., *Chin. Chem. Lett.*, 2013, **24**, 773-776.[73]

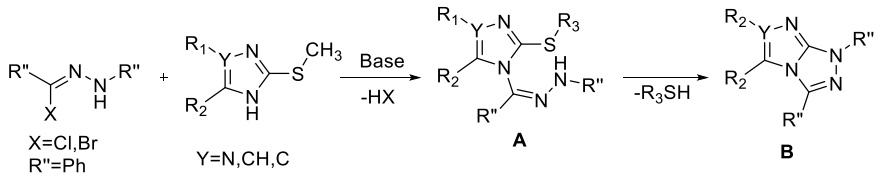
M. Pilania et al., *Org. Biomol. Chem.*, 2018, **16**, 7340-7345.[74]

Section 1.7. Synthesis of Bicyclic Azoles

To reiterate from Section 1.1, several FDA-approved pharmaceuticals contain fused heterocycles, such as 1*H*-imidazo[2,1-*c*][1,2,4]triazoles and 1*H*-[1,2,4]triazolo[3,4-

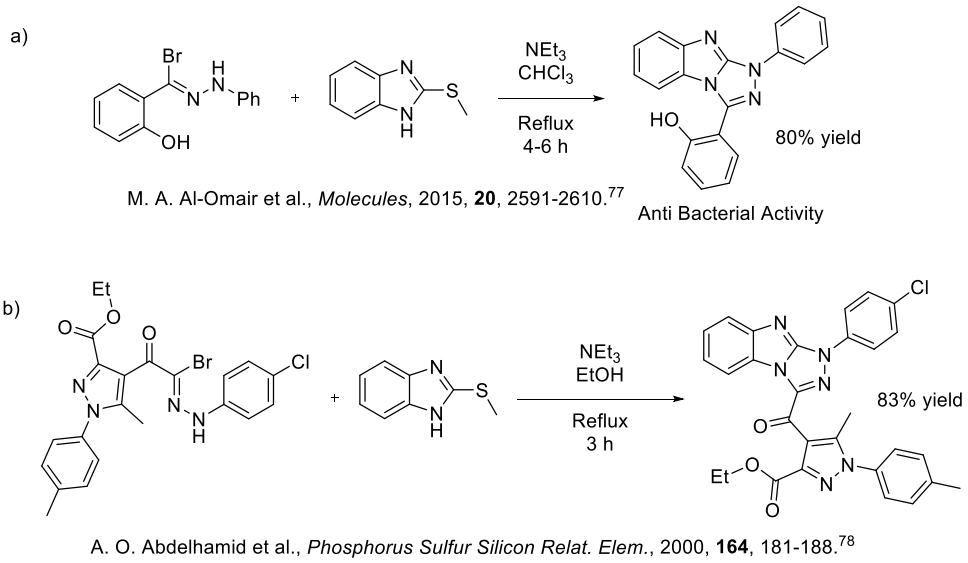
c][1,2,4]triazoles. These fused aromatic heterocycles have been synthesized over the years in various ways.[76] Currently a common method for the synthesis of 1*H*-imidazo[2,1-*c*][1,2,4]triazoles and 1*H*-[1,2,4]triazolo[3,4-*c*][1,2,4]triazoles employs hydrazonyl halides and methylthio-substituted azoles initially forming the amidrazone intermediate **A**, which cyclizes *in situ* with concurrent elimination of CH_3SH to form the desired product **B** (Scheme 11).[77] Depicted in Scheme 12 and Scheme 13 are three related examples of the synthesis of a 1,2,4-triazole ring in fused bicyclic systems utilizing substituted hydrazonyl halides.

Scheme 11. General Synthesis of Bicyclic Azoles via Aryl Hydrazonyl Halides



Al-Omair and coworkers used 2-(methylthio)-1*H*-benzo[*d*]imidazole and a simple hydrazonyl bromide to form their imidazo[2,1-*c*][1,2,4]triazole in a yield of 80% (Scheme 12a).[77] Testing its biological activity revealed strong activity against a variety of Gram-positive and Gram-negative bacteria.[77] Abdelhamid and coworkers synthesized their respective imidazo[2,1-*c*][1,2,4]triazole using 2-(methylthio)-1*H*-benzo[*d*]imidazole and a more functionalized hydrazonyl bromide in 83% yield (Scheme 12b).[78]

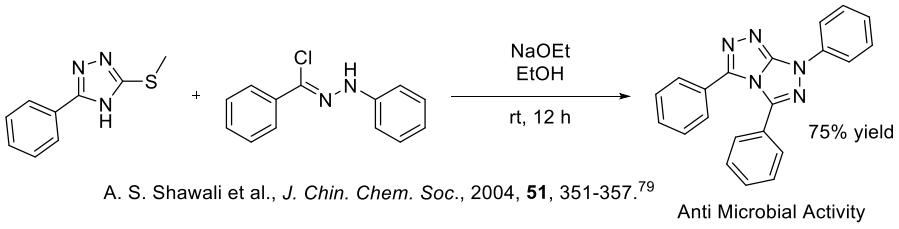
Scheme 12. Synthesis of 1,3-Disubstituted-1*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazole



A. O. Abdelhamid et al., *Phosphorus Sulfur Silicon Relat. Elem.*, 2000, **164**, 181-188.[78]

The Shawali group elected to use a 3-thiomethyl-5-phenyl-1,2,4-triazole and a (*Z*)-*N*-phenylbenzohydrazonoyl chloride to synthesize 1*H*-[1,2,4]triazolo[3,4-*c*][1,2,4]triazole, formed in 75% yield (Scheme 13). Upon testing the biological activity of this compound, they discovered that it was effective as an anti-microbial agent.[79]

Scheme 13. Synthesis of Triazolo[3,4-*c*][1,2,4]triazole

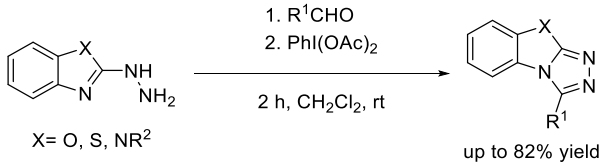


A. S. Shawali et al., *J. Chin. Chem. Soc.*, 2004, **51**, 351-357.[79]

Imidazo[2,1-*c*][1,2,4]triazole can be synthesized from amino or hydrazinyl substituted azoles. The Demmer group started from hydrazinyl azoles, first forming the imine and then cyclizing using $PhI(OAc)_2$ as an oxidant. Utilizing this method, it was possible to prepare

various examples of thiazolo[2,3-*c*][1,2,4]triazoles, oxazolo[2,3-*c*][1,2,4]triazoles, and imidazo[2,1-*c*][1,2,4]triazoles in up to 82% yields (Scheme 14).[80]

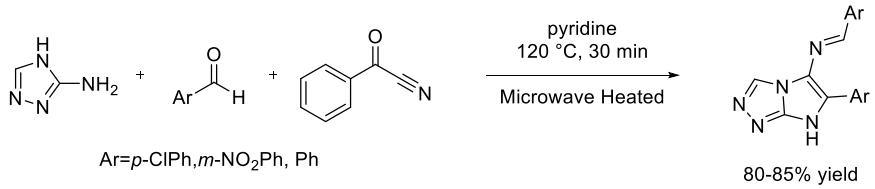
Scheme 14. Synthesis of 1,2,4-Triazole Containing Bicyclic Azoles via Oxidative Cyclization



C. S. Demmer et al., *Synlett,* 2014, **25**, 1279-1282.[80]

More recently, Sadek and coworkers used a microwave-assisted Strecker reaction to form their variation of imidazo[2,1-*c*][1,2,4]triazole from 3-amino-1,2,4-triazole, an aldehyde, and benzoyl cyanide (Scheme 15). Using high temperatures and short reaction times, they isolated the products in 80-85% yields.[81]

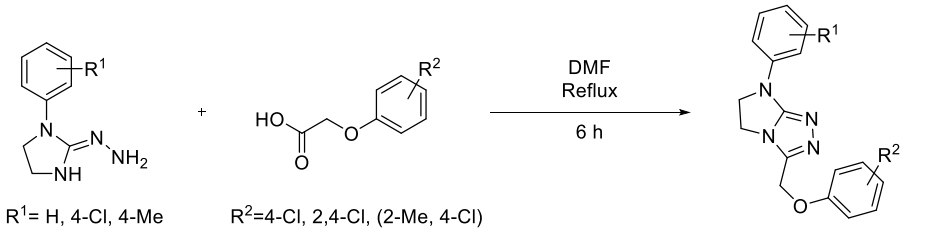
Scheme 15. Synthesis of Imidazo[2,1-*c*][1,2,4]triazoles via the Strecker Reaction



K. U. Sadek et al., *Green Process. Synth*., 2019, **8**, 297-301.

The Sztanke group synthesized dihydroimidazo[2,1-*c*][1,2,4]triazoles using 2-hydrazineylidene-1-methylimidazolidine and carboxylic acid as starting materials (Scheme 16). The amide forms first followed by an intramolecular imine condensation, generating their desired product in 43-70% yields.[39] Testing the biological activity of their substrates, they discovered that a few exhibited both anti-tumor and anti-microbial activity.

Scheme 16. Synthesis of Dihydroimidazo[2,1-*c*][1,2,4]triazoles



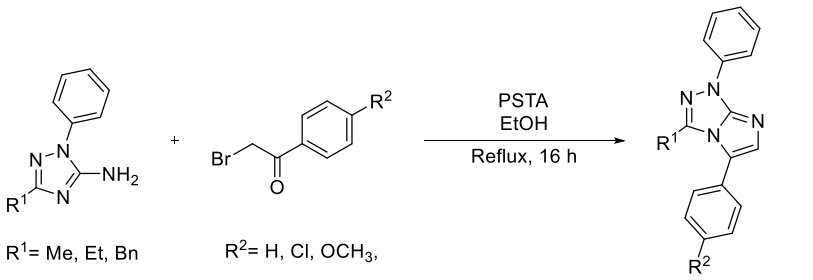
R^1= H, 4-Cl, 4-Me R^2=4-Cl, 2,4-Cl, (2-Me, 4-Cl)

43.5-69.7% yield
Anti-tumor, Anti-Microbrial

K. Sztanke et al., *Eur. J. Med. Chem*., 2008, **43**, 404-419.[37]

Aouali and coworkers used two different methods to synthesize their imidazo[2,1-*c*][1,2,4]triazole substrates. Starting from 5-amino-substituted triazoles and α-bromoketones, they synthesized several 1-phenyl-3,5-substituted-imidazo[2,1-*c*][1,2,4]triazole in moderate to high yields (53-83%) and proved that they possessed anti-microbial activity (Scheme 17).[37]

Scheme 17. Synthesis of Imidazo[2,1-c][1,2,4]triazoles Via Acid-Promoted Cycilization



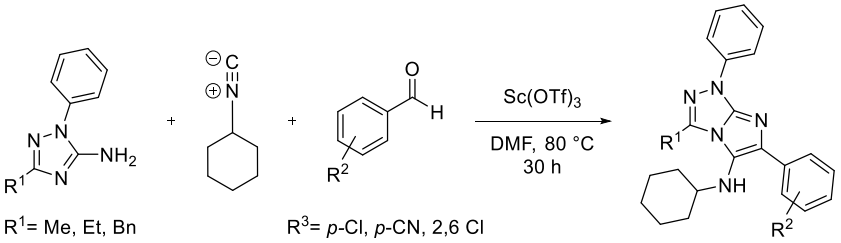
R^1= Me, Et, Bn R^2= H, Cl, OCH_3,

53-83% yield
Anti Microbrial Activity

M. Aouali et al., *Synth. Commun.*, 2014, **44**, 748-756.[38]

In their second approach, Aouali and coworkers used scandium triflate as the Lewis acid to promote the multicomponent cyclization to access *N*-substituted-1-phenyl-3,6-substituted-1H-imidazo[2,1-*c*][1,2,4]triazol-5-amine in 54-70% yields (Scheme 18).[82]

Scheme 18. Multicomponent Cyclization for the Synthesis of Imidazo[2,1-c][1,2,4]triazoles



M. Aouali et al., *Med. Chem. Res*., 2015, **24**, 2732-2741.[82] 54-70% yield

Section 1.8. Overview

For years, 1,2,4-triazoles have been less common in medicinal chemistry, organic synthesis, and organometallic chemistry, with imidazoles and thiazoles having a higher abundance in all three fields. Advances in the synthesis of 1,2,4-triazole-containing systems are likely to make 1,2,4-triazole based structural motifs more attractive. When attempting to prepare specific 1,4-disubstituted-1,2,4-triazolium salts for a different project, the Bolliger group discovered that some of the desired substitution patterns were impossible to obtain via traditional synthetic routes. We predicted that a copper-catalyzed arylation could be used to arylate 4-substituted-1,2,4-triazoles utilizing diaryliodonium salts as an aryl source and that this alternative method would allow us to access various 1,4-disubstituted-1,2,4-triazolium salts quickly. We determined that this would be a valuable tool for the synthesis of potential organocatalysts and ligands. During the synthesis of an amine-containing triazolium salt via reduction of a nitro group, we discovered the formation of a benzo[4,5]imidazo[2,1-*c*][1,2,4]triazolium salt byproduct. While these reductive conditions resulted in a mixture of products, we hypothesized that oxidative conditions would allow us better control over the reaction and lead to the exclusive formation of benzo[4,5]imidazo[2,1-*c*][1,2,4]triazolium

salts. We believe this method provides an alternative synthetic route to a potentially biologically active motif. Our work can bridge gaps in this highly competitive field and, additionally, allows rapid diversification, modification, and tuning of potential aryl-substituted triazolium salts for organocatalytic applications or as ligands in transition metal complexes/catalysts.

CHAPTER II

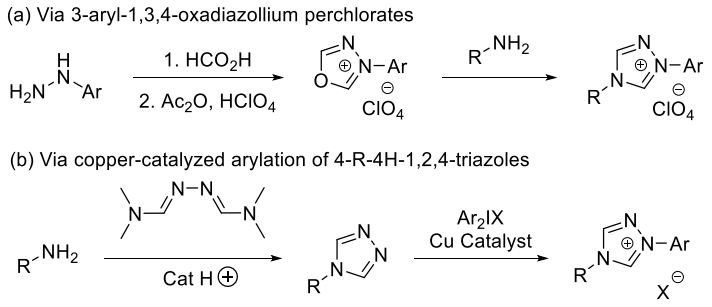
CATALYTIC PREPARATION OF 1-ARYL-SUBSTITUTED-1,2,4-TRIAZOLIUM SALTS

Section 2.0 Introduction

In the literature, 1,2,4-triazolium salts are well established as precursors to *N*-heterocyclic carbenes (NHC's), with applications as organocatalysts (Schemes 1-3)[8,83–88] and ligands for transition metal catalysts/complexes (Schemes 4,5).[55–58,88,89] Furthermore, phosphorescent cyclometalated complexes have been synthesized containing 1,2,4-triazole based ligands, where varied substitution allowed for tunable emission wavelengths.[90–92] In medicinal chemistry, 1,2,4-triazoles are proven pharmacophores in natural products and are present in several FDA-approved pharmaceuticals.[16] When incorporated into organic frameworks, 1,2,4-triazoles have shown potential as antimicrobial,[27,28,93–98] anti-inflammatory,[99,100] anti-viral agents,[101] and also shows activity against cancer (Figure 4).[101–104] When incorporated into late transition metal complexes, 1,2,4-triazole ligands have shown *in vitro* anticancer activity against breast, cervical, colon, liver, lung, and skin cancers and have displayed anticancer activity against leukemia (Figure 6).[45–48,105] Some 1,2,4 triazolium salts have exhibited applications as ionic liquids capable of successfully dissolving cellulose.[106]

Previously, the syntheses of 1-aryl-substituted-1,2,4-triazolium salts were carried out via a three-step process, forming an oxadiazolium intermediate from an aryl hydrazine in two steps, then using a primary amine to form the 1,2,4-triazole ring (Schemes 8,19).[65,67–69]

Scheme 19. Preparation of 1-Aryl-4-substituted-4*H*-1,2,4-triazolium Salts



This synthetic method has a limited functional group tolerance and is potentially hazardous to synthesize on large scales. The oxadiazolium perchlorate intermediate is extremely water-sensitive and utilizes perchloric acid in its synthesis. Second, apart from phenylhydrazine, aryl hydrazines are expensive when purchased and can decompose and release nitrogen gas rapidly under certain conditions. Third, while the synthesis of the phenyl oxadiazolium intermediate was not problematic and formed in nearly quantitative yield, the 3-mesityl-1,3,4-oxadiazolium intermediate synthesized from the mesityl hydrazine proved troublesome (8% yield). An alternative route to form 1,4-diaryl- and 1-aryl-4-alkyl-1,2,4-triazolium salts had to be investigated to expand our research. We decided to begin with primary amines, which are readily available and relatively straightforward to synthesize. The amines are first converted to the 4-substituted-4*H*-1,2,4-triazoles, followed by an *N*-arylation using diaryliodonium salts and a copper catalyst to obtain the 1,4-disubstituted triazolium salts. Diaryliodonium salts are well established in the literature as arylation reagents for oxygen and nitrogen nucleophiles,

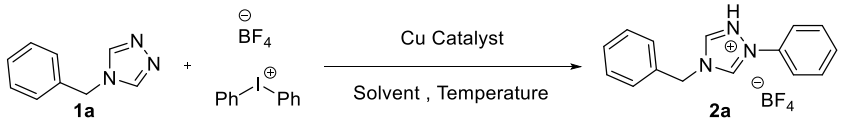
which can be catalyzed by various copper salt/complexes.[107–109] Chen and coworkers described a copper-free route to *N*-aryl pyridinium species from pyridinium *N*-oxides or sulfonamidates and diaryliodonium salts.[110,111] However, a copper catalyst was required for the *N*-arylation of pyridines.[112,113] Kumar and coworkers investigated fused triazolium salts utilizing a copper-catalyzed *N*-arylation of [1,2,4]triazolo-[4,3-*a*]pyridines (Scheme 10b).[74] The preparation of 4-aryltriazolium or 3-arylimidazolium salts via similar methods has been reported previously (Schemes 9,10a).[72,73,114–122] To our knowledge, examples of the copper-catalyzed 1-arylation of monocyclic triazoles with diaryliodonium salts have not been described in the literature.

Section 2.1: Optimization and Substrate Scope of the Copper Catalyzed Arylation

Mild conditions and shorter reaction times were driving factors for optimizing the copper-catalyzed arylation. Initially, on a 0.5 mmol scale, we began optimizing the copper-catalyzed 1-arylation of 4-substituted-4*H*-1,2,4-triazoles utilizing the substrates 4-benzyl-4*H*-1,2,4-triazole (**1a**) and diphenyliodonium tetrafluoroborate, which was conducted in sealed microwave tubes, monitored by LCMS (Table 1). In the presence of all copper(I) and copper(II) catalysts, except CuI, we found that >95% conversion to **2a** was achieved after 4 h at 100 °C in DMF and acetonitrile while reactions in water required longer reaction times (**entries 1−13**). Varying copper(I) versus copper (II) salts in acetonitrile at 80 °C, we observed that after 4 h, CuOAc achieved 100% conversion and that anhydrous $Cu(OAc)_2$ and $Cu(OAc)_2 \cdot H_2O$ achieved 87% and 88% yields, respectively (**entries 14−16**). These results suggest that copper(I) is superior under these conditions. We also observed that this reaction proceeded with no unexpected byproducts

when monitored by LCMS or NMR. Without a copper catalyst, a conversion of 17% (**entry 17**) was observed after 4 h.

Table 1. Optimization of the Copper Catalyzed Arylation [a)]



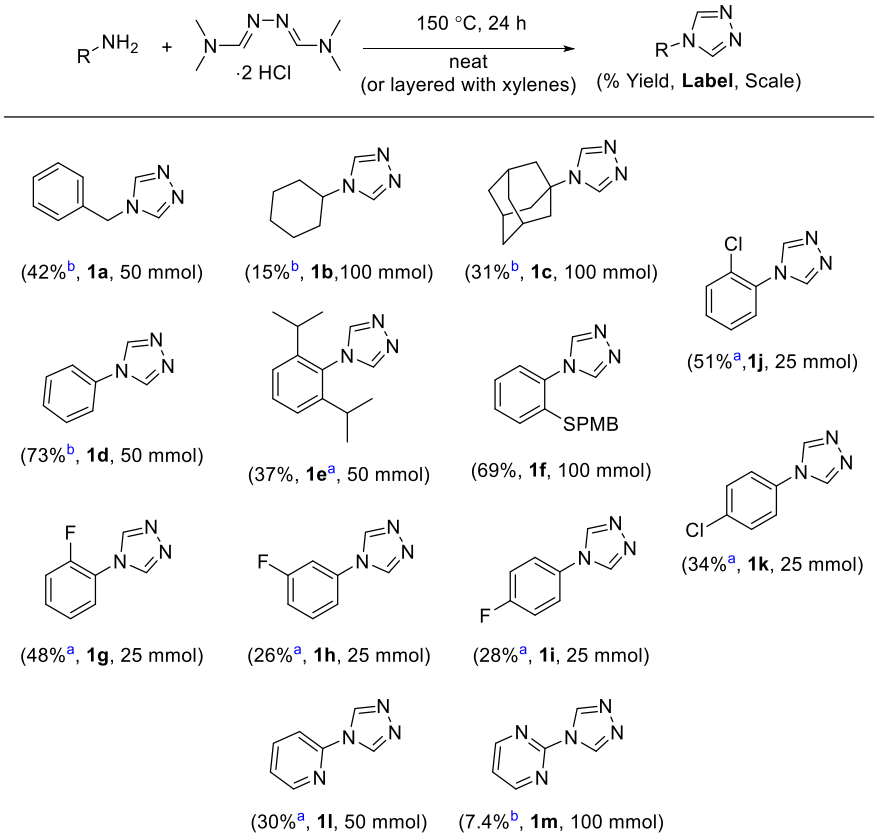
Entry	Cu Catalyst	Catalyst Loading	Solvent	Temperature	Time	Conversion [c)]
1	$Cu(OAc)_2.H_2O$	5 mol%	DMF	100 °C	4h	>95%
2	$Cu(OAc)_2$	5 mol%	DMF	100 °C	4h	>95%
3	Cu(OAc)	5 mol%	DMF	100 °C	4h	>95%
4 [d)]	$Cu(OAc)_2$	5 mol%	H_2O	100 °C	4h	>80%
5 [d)]	Cu(OAc)	5 mol%	H_2O	100 °C	4h	>80%
6	$Cu(OAc)_2.H_2O$	5 mol%	MeCN	100 °C	4h	>95%
7	$Cu(OAc)_2$	5 mol%	MeCN	100 °C	4h	>95%
8	Cu(OAc)	5 mol%	MeCN	100 °C	4h	>95%
9	$Cu(OTf)_{0.5}$ Tol	5 mol%	MeCN	100 °C	4h	>95%
10	Cu(TC)	5 mol%	MeCN	100 °C	4h	>95%
11	$Cu(OTf)_2$	5 mol%	MeCN	100 °C	4h	>95%
12	$Cu(acac)_2$	5 mol%	MeCN	100 °C	4h	>95%
13	CuI	5 mol%	MeCN	100 °C	4h	<30%
14	$Cu(OAc)_2.H_2O$	5 mol%	MeCN	80 °C	4h	88%
15	$Cu(OAc)_2$	5 mol%	MeCN	80 °C	4h	87%
16	Cu(OAc)	5 mol%	MeCN	80 °C	4h	~100%
17	None		MeCN	80 °C	4h	17%
18	$Cu(OAc)_2.H_2O$	5 mol%	MeCN	80 °C	1h	80%
19	$Cu(OAc)_2$	5 mol%	MeCN	80 °C	1h	79%
20	Cu(OAc)	5 mol%	MeCN	80 °C	1h	97%

[a)] Reaction conditions: triazole **1a** (0.5 mmol), Ph_2IBF_4 (1.5 equiv.), Cu catalyst (relative to 1**a**), solvent (2 mL), and reaction time. [b)] Relative to 1**a**. [c)] Conversion based on LCMS analysis. [d)] After 18 h, >95% conversion.

A shortened reaction time of 1 hour resulted in 97% conversion when CuOAc was used as the catalyst. However, using anhydrous $Cu(OAc)_2$ and $Cu(OAc)_2 \cdot H_2O$ as catalysts resulted in significantly lower conversions when subjected to these shorter reaction times (**entries 18–20**). We decided that CuOAc was the most efficient and least expensive

catalyst for the arylation reaction at 80 °C in acetonitrile. Investigation of the scope of the copper-catalyzed *N*-arylation began with 4-substituted-4*H*-1,2,4-triazoles (**1a−1m**), which were synthesized from their corresponding 1° amines with yields ranging from 7.4% to 74% (Table 2).[64,123–128]

Table 2: Synthesis of 4-Substituted-1,2,4-triazoles

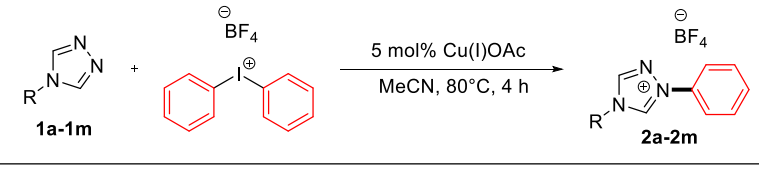


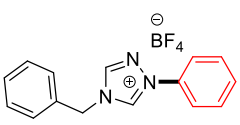
[a)] Reaction conditions: primary amine (1.0 equiv), *N*,*N*-dimethylformylamide azine 2·HCl (1.5 equiv), neat, 24 h, 150 °C. [b)] Reaction conditions: primary amine (1.0 equiv), *N*,*N*-dimethylformylamide azine 2·HCl (1.5 equiv), layered with xylenes, 24 h, 150 °C.

We subjected **1a-1m** to our previously optimized arylation conditions using diphenyliodonium tetrafluoroborate as the aryl source. Our findings are summarized in Table 3. Using NMR analysis, we found that 100% conversion was observed for all 4-substituted-4*H*-1,2,4-triazoles (**1a−1m**), and the arylation products (1-phenyl-4-

substituted-4*H*-1,2,4-triazolium salts **2a−2m**) were all obtained in good to excellent yields (Appendix D, Figures D001−D014) with no other arylation products. Simple alkyl (**2a−2c**), aryl (**2d** and **2e**), and haloaryl substituents (**2g−2k**) were arylated in good yields. The copper-catalyzed arylation of **1f** yielded **2f** without any arylation of the *para*-methoxy-substituted sulfide. Similarly, **1l** and **1m** formed **2l** and **2m** preferentially despite containing several heteroaryl nitrogen atoms that could have been arylated. No other possible arylation products were observed under the optimized reaction conditions. Generally, the isolated yields were within 5−10% of the predicted NMR yields. However, we observed significantly lower isolated yields for the heteroaryl-substituted-triazolium salts (**2l, 2m**). Interestingly **2l** appeared to be strongly retained on silica, while **2m** decomposed on silica and required recrystallization. Aryl substitution at the N^1-position of 1,2,4-triazolium salts affected the ring's electronics when used for organocatalytic transformation, making easy late-stage arylation which is of general interest for the organic community. Varying the diaryliodonium salts (Table 4), we began investigating the scope of the copper-catalyzed quaternization using triazole **1d** as the control. Testing diaryliodonium tetrafluoroborates and triflates, we observed 100% conversion of starting material after 4 hours of reaction time forming 1-aryl-4-phenyl-triazolium salts preferentially (**2d−9d**). Electron-poor (e.g., **7d**) and unhindered electron-rich (e.g., **6d**) aryl groups were examined and gave high yields. However, the introduction of ortho-substituted aryl groups (**3d−5d**) resulted in decreased isolated yields. Interestingly, product **9d** could not be isolated with LCMS, but indicated complete consumption of starting material, through ^{1}H NMR and ^{19}F NMR data were inconclusive when searching for the presence of the perfluoro arylated product.

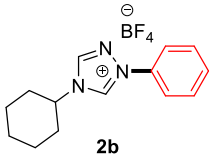
Table 3. Scope of 1,2,4-Triazoles[a)]





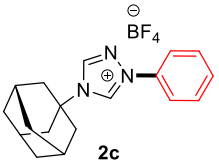
2a

100%[b] (91%[c], 99%[d])



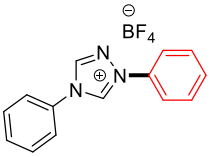
2b

100%b (98%[c], 90%d)



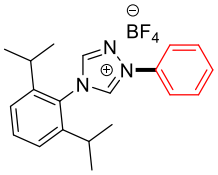
2c

100%[b] (73%[c], 70%[d])



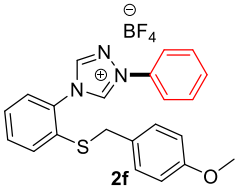
2d

100%[b] (95%[c], 96%[d])



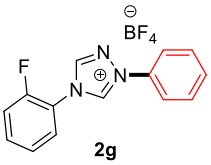
2e

100%[b] (93%[c], 96%[d])



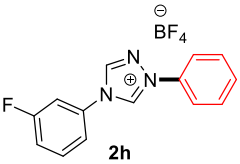
2f

100%[b] (84%[c], 79%[d])



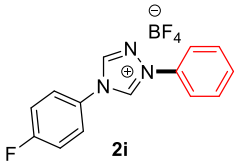
2g

100%[b] (87%[c], 95%[d])



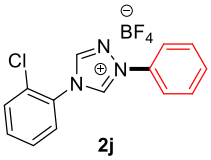
2h

100%[b] (97%[c], 96%[d])



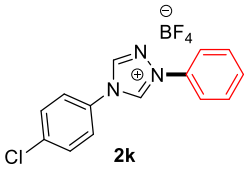
2i

100%[b] (88%[c], 94%[d])



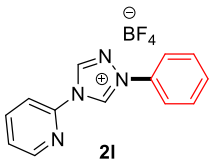
2j

100%[b] (96%[c], 95%[d])



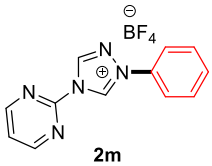
2k

100%[b] (92%[c], 90%[d])



2l

100%[b] (94%c, 82%[d])

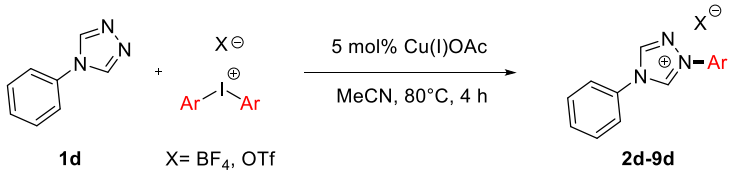


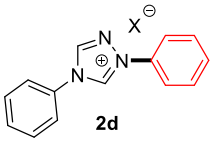
2m

100%[b] (85%[c], 58%[d])

[a)] Reaction conditions: triazoles **1a−1m** (1.0 mmol), Ph_2IBF_4 (1.5 mmol), CuOAc (0.05 mmol, 5 mol%), MeCN (4 mL), 80 °C, and 4 h. [b)] Conversion based on NMR analysis. [c)] NMR yield as determined by ^1H NMR analysis relative to mesitylene as the internal standard. [d)] Isolated yield.

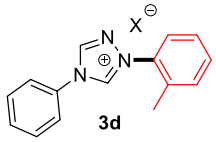
Table 4. Scope of Diaryliodonium Salts [a)]





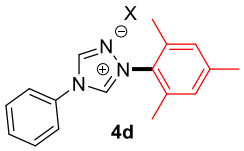
2d

X= BF_4: 100%[b] (95%[c], 96%[d])
X= OTf: 100%[b] (93%[c], 95%[d])



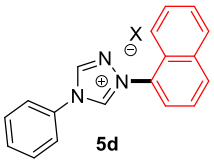
3d

X= OTf: 100%[b] (77%[c], 81%[d])



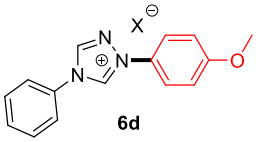
4d

X= BF_4: 100%[b] (80%[c], 52%[d])
X= OTf: 100%[b] (83%[c], 74%[d])



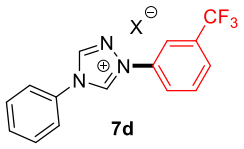
5d

X= BF_4: 100%[b] (85%[c], 81%[d])



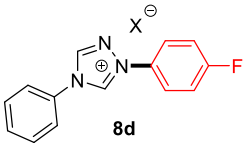
6d

X= BF_4: 100%[b] (93%[c], 91%[d])



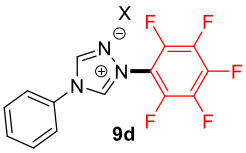
7d

X= BF_4: 100%[b] (98%[c], 95%[d])



8d

X= OTf: 100%[b] (96%[c], 74%[d])

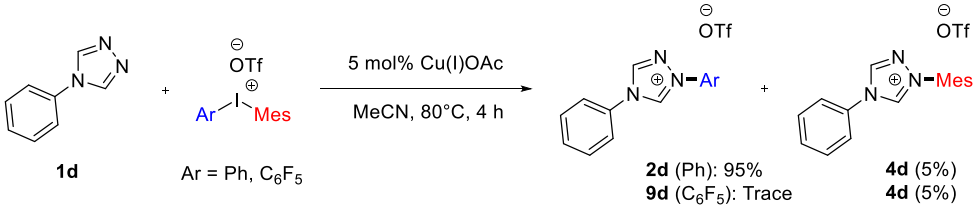


9d

not observed

[a)] Reaction conditions: triazole **1d** (1.0 mmol), Ar_2IBF_4 or Ar_2IOTf (1.5 mmol), CuOAc (0.05 mmol, 5 mol%), MeCN (4 mL), 80 °C, and 4 h. [b)] Conversion based on NMR analysis. [c)] NMR yield as determined by ^{1}H NMR analysis relative to mesitylene as the internal standard. [d)] Isolated yield. [e)] Conversion determined by LCMS.

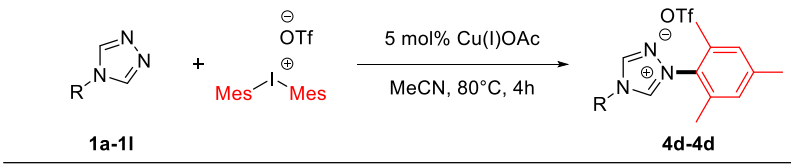
Scheme 20. *N*-Arylation with Unsymmetrical Diaryliodonium Triflates

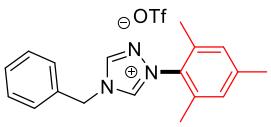


As an alternative method to obtain and isolate **9d**, it was questioned whether unsymmetrical diaryliodonium salts could be used for the arylation of triazole **1d**

(Scheme 20).[109] Unfortunately, we found that only traces of the desired compound **9d** were detected while 5% of the side product **4d** was isolated. The remaining components consisted of unreacted starting materials, including the unreacted mesityl(perfluorophenyl)iodonium triflate. When using mesityl(phenyl)iodonium triflate, instead of mesityl(perfluorophenyl)iodonium triflate for the *N*-arylation, we found the more electron-deficient aryl group was transferred preferentially, giving **2d** with 95% selectivity.[107] Unsymmetrical diaryliodonium salts have the potential to form two different arylation products. In our case, we found with the formation of **2d** came in tandem with the formation of **4d**, and separation by column chromatography was only possible on a small scale (Scheme 20). Preparing symmetrical diaryliodonium salts avoids the problematic separation, making them the preferable iodonium salts to perform the *N*-arylation of triazoles. We were interested in applying our *N*-arylation method to synthesize 1-mesityl-substituted-1,2,4-triazolium salts **4a**−**4l** (Table 5), due to our low yields observed via the traditional route (Scheme 19a). We observed that for all reactions, complete conversion was obtained, but isolated yields were generally lower for each substrate compared to the corresponding phenyl derivatives (Table 3). A possible explanation could be the difficulty of separating the desired product from the remaining Mes_2IOTf starting material via column chromatography.

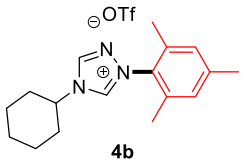
Table 5. Synthesis of 1-Mesityl-1,2,4-triazolium Salts [a)]





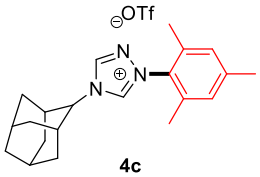
4a

100%[b] (76%[c], 58%[d])



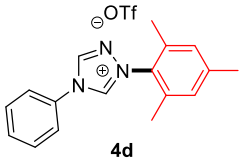
4b

100%[b] (89%[c], 86%[d])



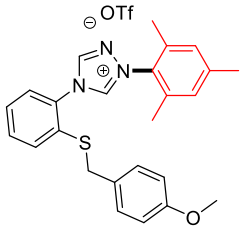
4c

100%[b] (66%[c], 75%[d],77%[e])



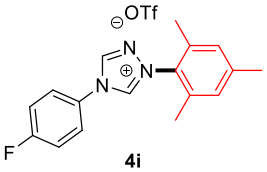
4d

100%[b] (83%[c], 74%[d])



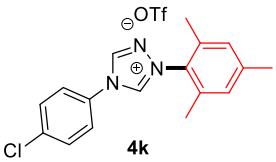
4f

100%[b] (73%[c], 59%[d])



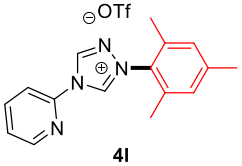
4i

100%[b] (80%[c], 54%[d])



4k

100%[b] (86%[c], 58%[d])



4l

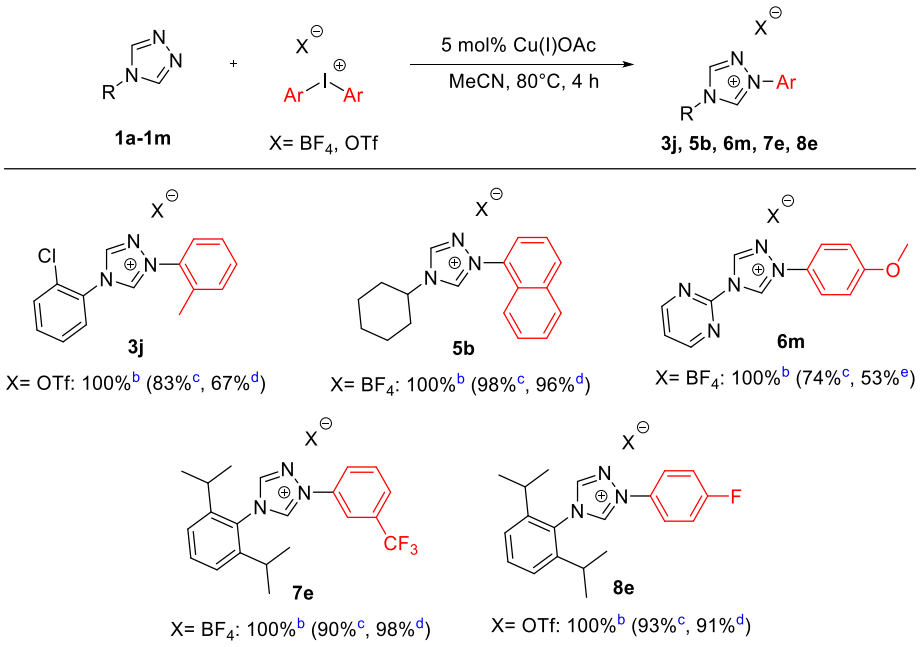
100%[b] (62%[c], 54%[d])

[a)] Reaction conditions: triazoles **1a−1l** (1.0 mmol), Mes_2IOTf (1.5 mmol), CuOAc (0.05 mmol, 5 mol%), MeCN (4 mL), 80 °C, and 4 h. [b)] Conversion based on NMR analysis. [c)] NMR yield as determined by ^1H NMR analysis relative to mesitylene as the internal standard. [d)] Isolated yield; 1 mmol scale. [e)] Isolated yield; 8 mmol scale.

Upon scaling up the catalytic reaction for various substrates (e.g., with **4c**), we observed increased yields for challenging substrates, as recrystallization became a potential alternative purification method. The copper-catalyzed quaternization of 4-substituted-4*H*-1,2,4-triazoles **1a−1m** allows for varying electronic and steric parameters in an efficient and systematic route. The preparation of unsymmetrically substituted electron-rich carbene precursors (**3j** and **5b**) and sterically hindered electron-poor 1,2,4-triazolium salts (**7e** and **8e**) gave high yields (Table 6). The electron-rich pyrimidine derivative **6m**

formed cleanly, but required recrystallization to purify. Our reaction conditions proved to be an ideal method for the *N*-arylation of 4-substituted-4*H*-1,2,4-triazoles within short reaction times. To gain deeper insight into this reaction's limitations, parameters such as temperature, catalyst loading, and stoichiometry of the diaryliodonium salt were varied (Figures 8-10).

Table 6. Variation of Steric and Electronic Parameters [a)]



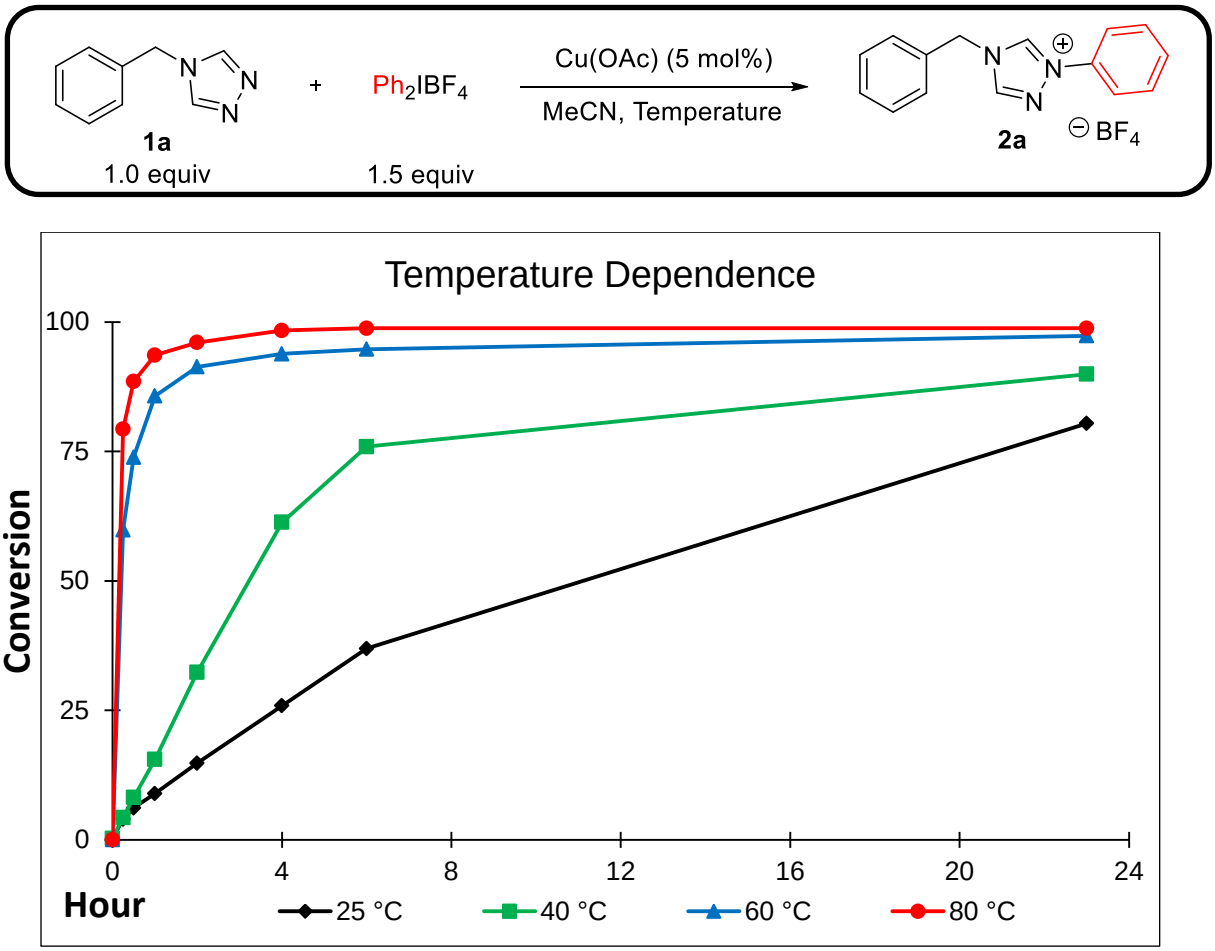
[a)] Reaction conditions: triazoles **1a−1m** (1.0 mmol), Ar_2IBF_4 or Ar_2IOTf (1.5 mmol), CuOAc (0.05 mmol, 5 mol%), MeCN (4 mL), 80 °C, and 4 h. [b)] Conversion based on NMR analysis. [c)] NMR yield as determined by ^1H NMR analysis relative to mesitylene as the internal standard. [d)] Isolated yield; 1 mmol scale. [e)] Isolated yield; 3 mmol scale.

Section 2.2. Effects of Varying Reaction Parameters on Rate of Conversion

To better understand the *N*-arylation's temperature dependence, we ran four 0.5 mmol scale reactions using **1a** as our triazole and diphenyliodonium tetrafluoroborate as our aryl source. Keeping a consistent reaction temperature at 25 °C, 40 °C, 60 °C, and/or 80 °C for the four reactions and taking LCMS samples at varying time intervals, we

monitored the conversion of the starting material **1a.** We found that lowering the reaction temperature below 60 °C decreased the rate of conversion significantly, with prolonged reaction times necessary to achieve complete conversion (Figure 8).

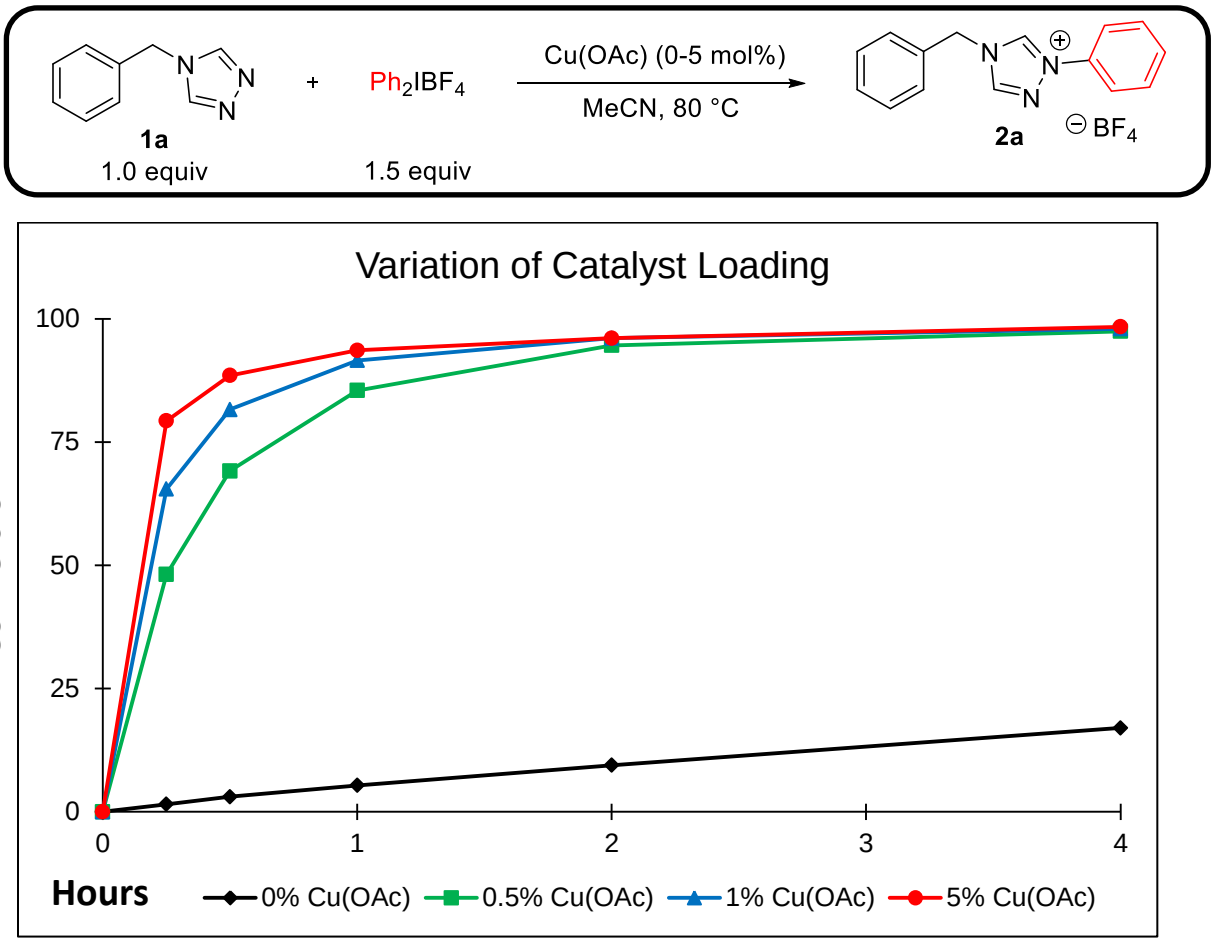
Figure 8. Temperature Dependence of the Rate of Conversion of 1a



Similar to the temperature variation experiments, four reactions were completed keeping the temperature constant at 80 °C and lowering the catalyst loading from 5 mol% to 0.5 mol% and without catalyst. We monitored the reaction at the same time intervals. As expected, we found that lower rates of conversion occurred with lower catalyst loading in the first hour. However, reaction progress was not altered, with complete conversion achieved when a copper catalyst was present within 4 hours of reaction time. Without the

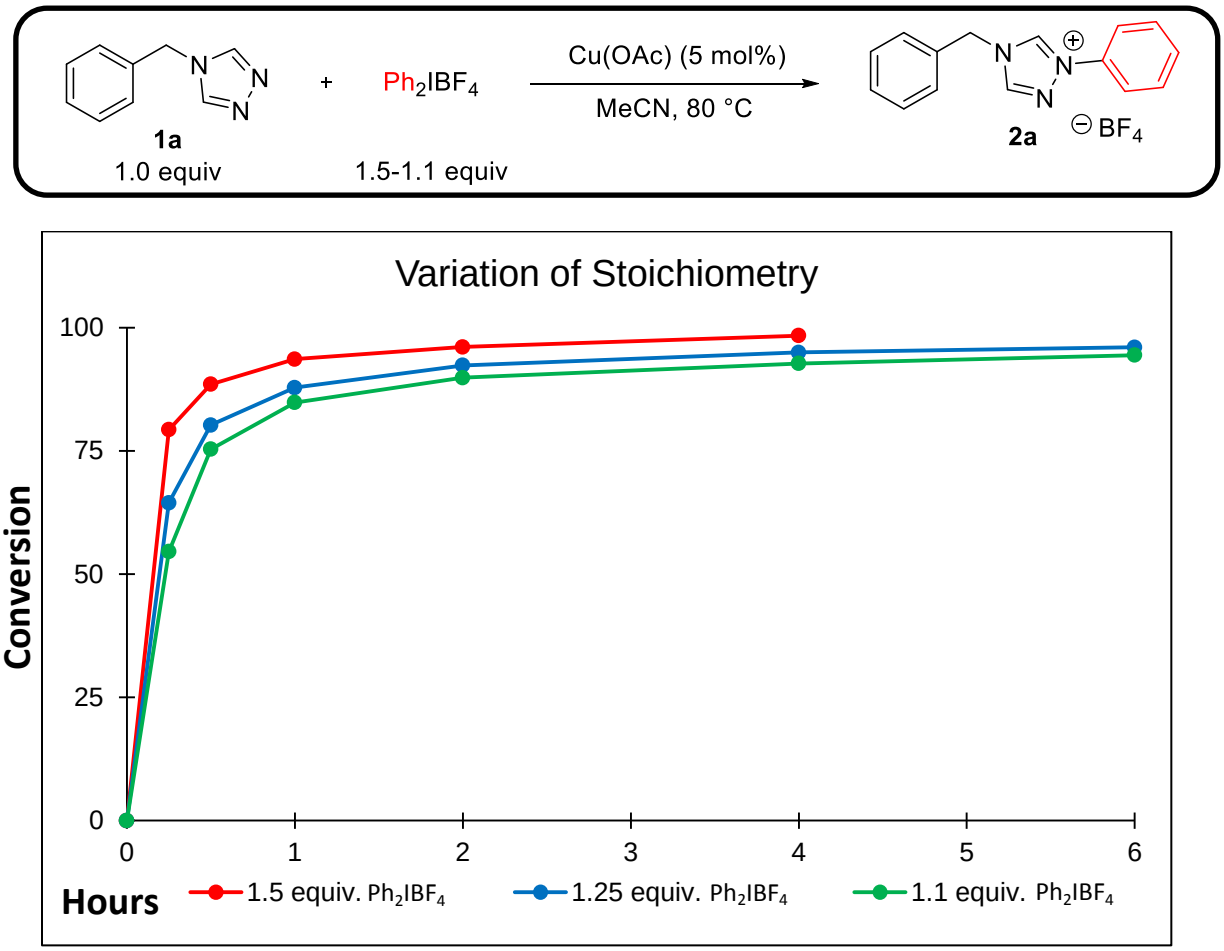
addition of a copper catalyst, quaternization still occurred at 80 °C, but at a significantly lower rate with 82% conversion obtained after 23 h (Figure 9).

Figure 9. Effects of Catalyst Loading on the Rate of Conversion of 1a



To determine the optimal stoichiometric ratio of the diaryliodonium salt, we ran four reactions decreasing the loading of diphenyliodonium tetrafluoroborate from 1.5 equivalents to 1.0 equivalent. Complete conversion of the starting material was obtained after 4 hours when the reaction contained 1.5 equivalents of the iodonium salt, but 1.25 and 1.1 equivalents required six-hour reaction times to achieve complete conversion (Figure 10). When 1.0 equivalent of iodonium salt was added, 24 h was necessary to achieve complete conversion.

Figure 10. Effects of Varied Stoichiometry on the Rate of Conversion of 1a



We propose a Cu(I)/Cu(III) mechanism for the *N*-arylation of 1,2,4-triazoles in analogy to the related literature.[74,107,129] Our findings that the copper(I) salt proved to be more efficient than the corresponding copper(II) salt at promoting the *N*-arylation was in agreement with this mechanism.

Section 2.3. Conclusions

In summary, we have developed an efficient and selective method for the synthesis of 1-aryl-4-substituted-4*H*-1,2,4-triazolium salt via a copper-catalyzed arylation of 4-substituted-4*H*-1,2,4-triazoles using diaryliodonium salts. Our method allows for late-

stage arylation of 1,2,4-triazoles in high yields using cheap and safe reagents under mild reaction conditions and without the need for oxadiazolium perchlorate intermediates. We now have access to novel 1-aryl-4-substituted-4*H*-1,2,4-triazolium salts that were previously difficult to obtain, thus opening new avenues of research for applications of 1,2,4-triazoles in transition metal complexes, as organocatalysts, and in medicinal chemistry.

Section 2.4: General Procedures and Characterization Data for 1,2,4-Triazoles (1a-1m)

General Procedure Ia for the Synthesis of Triazoles 1a−1m.

The amine (1 equiv) and the dihydrochloride of *N*,*N*-dimethylformylamide azine (1.5 equiv) were ground together in a mortar until the mixture liquefied or became a homogeneous solid. It was then transferred to a round-bottom flask equipped with a stir bar. The flask was fitted with a reflux condenser, the atmosphere of the system was exchanged for argon, and the reaction was heated in an oil bath to 150 °C for 16 h. After cooling to room temperature, the reaction mixture was basified with 1 M NaOH and then was extracted with DCM (3 × 100 mL). The combined organic phase was washed with water (2 × 50 mL), dried ($MgSO_4$), filtered, and concentrated. The crude product was purified by column chromatography (5% methanol in DCM) or by precipitation from a DCM solution using hexanes or diethyl ether.

General Procedure Ib for the Synthesis of Triazoles 1a−1m.

The amine (1 equiv), the dihydrochloride of *N*,*N*-dimethylformylamide azine (1.5 equiv), and *para*-toluenesulfonic acid (0.05 equiv) were ground together in a mortar until the mixture liquefied or became a homogeneous solid and then was transferred to a round-bottomed flask equipped with a stir bar. The reaction mixture was suspended in xylenes, a reflux condenser was placed on the round-bottomed flask, and the mixture was heated under argon in an oil bath to 150 °C for 16 h. After cooling to room temperature, the crude product was purified as described in procedure Ia.

Reaction/Structural Data of Formed 1,2,4 Triazoles.

4-Benzyl-4*H*-1,2,4-triazole (1a).

The title compound was prepared on a 50 mmol scale according to general procedure Ib. Purification by column chromatography (silica, 5% methanol in DCM) yielded the product as a colorless solid in 42% yield (3.31 g, 20.8 mmol). The measured analytical data were in agreement with the literature values.[127]

4-Cyclohexyl-4*H*-1,2,4-triazole (1b).

The title compound was prepared on a 100 mmol scale according to general procedure Ib. The product was precipitated with hexanes from a concentrated DCM solution which gave the pure pale-yellow solid in 15% yield (2.19 g, 14.5 mmol). The measured analytical data were in agreement with the literature values.[123]

4-((3*s*,5*s*,7*s*)-Adamantan-1-yl)-4*H*-1,2,4-triazole (1c).

The title compound was prepared on a 100 mmol scale according to general procedure Ib. The crude product was dissolved in a minimal amount of 5% methanol in DCM and precipitated with toluene which gave the pure product as a colorless solid in 31% yield (6.38 g, 31.4 mmol). The measured analytical data were in agreement with the literature values.[125]

4-Phenyl-4*H*-1,2,4-triazole (1d).

The title compound was prepared according to general procedure Ib on a 50 mmol scale. The pure light brown solid was obtained by precipitation with hexanes from a concentrated solution of DCM. Yield: 73% (5.29 g, 36.5 mmol). The measured analytical data were in agreement with the literature values.[123,127]

4-(2,6-Diisopropylphenyl)-4*H*-1,2,4-triazole (1e).

The title compound was prepared according to general procedure Ia on a 50 mmol scale. Purification by column chromatography (silica, 5% methanol in DCM) yielded the product as an off-white solid in 37% yield (4.20 g, 18.3 mmol). The measured analytical data were in agreement with the literature values.[73]

4-(2-((4-Methoxybenzyl)thio)phenyl)-4*H*-1,2,4-triazole (1f).

The title compound was prepared in 69% yield according to a literature procedure on a 100 mmol scale.[64] The measured analytical data were in agreement with the literature values.[64]

4-(2-Fluorophenyl)-4*H*-1,2,4-triazole (1g).

The title compound was prepared on a 25 mmol scale according to general procedure Ia. Purification by column chromatography (silica, 5% methanol in DCM) yielded the product as an off-white solid in 48% yield (1.96 g, 12.0 mmol). ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): 8.49 (s, 2H), 7.55-7.50 (m, 1H), 7.23-7.14 (m, 3H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$, 298 K): δ = 163.3 (d, $J_{C\text{-}F}$ = 250.7 Hz), 141.3, 135.1 (d, $J_{C\text{-}F}$ = 9.7 Hz), 132.0 (d, $J_{C\text{-}F}$ = 9.1 Hz), 117.9 (d, $J_{C\text{-}F}$ = 3.5 Hz), 116.2 (d, $J_{C\text{-}F}$ = 21.0 Hz), 110.1 (d, $J_{C\text{-}F}$ = 25.2 Hz); ^{19}F{1H} NMR (376 MHz, $CDCl_3$, 298 K, referenced to C_6H_5F): δ = -110.21.

4-(3-Fluorophenyl)-4*H*-1,2,4-triazole (1h).

The title compound was prepared on a 25 mmol scale according to general procedure Ia. Purification by column chromatography (silica, 5% methanol in DCM) yielded the product as a pale-yellow solid in 26% yield (1.04 g, 6.38 mmol). ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 8.35 (d, $J_{C\text{-}F}$ = 1.5 Hz, 2H), 7.50-7.43 (m, 2H), 7.34-7.30 (m, 2H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$, 298 K): δ = 154.3 (d, $J_{C\text{-}F}$ = 250.1 Hz), 142.3 (d, $J_{C\text{-}F}$ = 2.3 Hz), 130.8 (d, $J_{C\text{-}F}$ = 7.7 Hz), 125.2, 122.0 (d, $J_{C\text{-}F}$ = 12.3 Hz), 117.6 (d, $J_{C\text{-}F}$ = 19.3 Hz); ^{19}F{1H} NMR (376 MHz, $CDCl_3$, 298 K, referenced to C_6H_5F): δ = -123.56.

4-(4-Fluorophenyl)-4*H*-1,2,4-triazole (1i).

The title compound was prepared on a 25 mmol scale according to general procedure Ia. Purification by column chromatography (silica, 5% methanol in DCM) yielded the product as an off-white solid in 28% yield (1.16 g, 7.1 mmol). ^{1}H NMR (400 MHz,

$CDCl_3$, 298 K): δ = 8.45 (s, 2H), 7.43-7.38 (m, 2H), 7.28-7.22 (m, 2H); $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$, 298 K): δ = 162.6 (d, J_{C-F} = 250.1 Hz), 141.8, 130.0 (d, J_{C-F} = 11.0 Hz), 132.4 (d, J_{C-F} = 3.6 Hz), 124.5 (d, J_{C-F} = 8.8 Hz), 117.4 (d, J_{C-F} = 23.4 Hz); $^{19}F\{1H\}$ NMR (376 MHz, $CDCl_3$, 298 K, referenced to C_6H_5F): δ = -110.10.

4-(2-Chlorophenyl)-4*H*-1,2,4-triazole (1j).

The title compound was prepared on a 25 mmol scale according to general procedure Ia. Purification by column chromatography (silica, 5% methanol in DCM) yielded the product as an off-white solid in 51% yield (2.31 g, 12.9 mmol). ^1H NMR (400 MHz, $CDCl_3$, 298 K): δ = 8.46 (s, 2H), 7.62-7.60 (m, 1H), 7.51-7.39 (m, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 298 K): δ = 142.9, 131.5, 131.3, 131.2, 129.9, 128.5, 127.6.

4-(4-Chlorophenyl)-4*H*-1,2,4-triazole (1k).

The title compound was prepared on a 25 mmol scale according to general procedure Ia. Purification by column chromatography (silica, 5% methanol in DCM) yielded the product as an off-white solid in 34% yield (1.51 g, 12.0 mmol). ^1H NMR (400 MHz, $CDCl_3$, 298 K): δ = 8.47 (s, 2H), 7.51 (d, J = 8.8 Hz, 2H), 7.36 (d, J = 8.8 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 298 K): δ = 141.5, 135.2, 132.4, 130.6, 123.7.

2-(4*H*-1,2,4-Triazol-4-yl)pyridine (1l).

The title compound was prepared on a 50 mmol scale according to general procedure Ia. Purification by column chromatography (silica, 5% methanol in DCM) yielded the

product as a pale-yellow solid in 30% yield (2.22 g, 15.2 mmol). The measured analytical data were in agreement with the literature values.[126,127]

2-(4*H*-1,2,4-Triazol-4-yl)pyrimidine (1m).

The title compound was prepared on a 100 mmol scale according to general procedure Ib. Purification by column chromatography (silica, 5% methanol in DCM) yielded the product as a pale-yellow solid in 7.4% yield (1.09 g, 7.4 mmol). The measured analytical data were in agreement with the literature values.[130]

Section 2.5: General Procedures and Characterization Data for 1,4-Substituted-1,2,4-triazolium Salts

General Procedure IIa for the Catalytic Arylation of Triazoles 1a−1m.

A 10 mL Schlenk flask equipped with a stir bar was loaded with the triazole (1 mmol, 1.0 equiv), diaryliodonium salt (1.5 mmol, 1.5 equiv), and copper(I) acetate (0.05 mmol, 5 mol%) and sealed with a PTFE screwcap and filled with argon through septa on sidearm. Dry acetonitrile (4 mL) was added under a stream of argon, and the flask was resealed, then placed into an oil bath where the solution was stirred for 4 h at 80 °C. After the reaction mixture was cooled to room temperature, the solvent was evaporated. Calculated yields and conversions from NMR analysis were determined by the addition of mesitylene (1 mmol, 1 equiv) in DMSO-d_6 to the crude reaction mixture. The pure triazolium salts were obtained either by recrystallization or column chromatography (DCM/acetone, 4:1).

General Procedure IIb for the Catalytic Arylation of Triazoles 1a−1m.

A 5 mL microwave tube equipped with a stir bar was loaded inside a glovebox with the triazole (0.5 mmol, 1.0 equiv) and the diaryliodonium salt (0.75 mmol, 1.5 equiv). After sealing the microwave tube and removing it from the glovebox, the catalyst (copper(I) acetate (0.025 mmol 0.05 equiv, 5 mol%) in 2 mL of acetonitrile) was added via syringe to the reaction mixture. The mixture was then stirred for 4 h in an oil bath at 80 °C, cooled to room temperature, and concentrated. Calculated yields and conversions from NMR analysis were determined by the addition of mesitylene (0.5 mmol, 1 equiv) in DMSO-d_6 to the crude reaction mixture. The pure triazolium salts were obtained either by recrystallization or column chromatography (DCM/acetone, 4:1) as described below.

4-Benzyl-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([2a]BF_4).

The title compound was prepared according to general procedure IIb. Purification by column chromatography (silica, 1. DCM 2. DCM/acetone 4:1, $R_f = 0.28$) yielded the product as an off-white solid in >99% yield (161 mg, 0.498 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 10.98 (s, 1H), 9.52 (s, 1H), 7.92 (d, *J* = 7.7 Hz, 2H), 7.72-7.68 (m, 2H), 7.64 (t, *J* = 7.3 Hz, 1H), 7.56 (d, *J* = 7.6 Hz, 2H), 7.50-7.44 (m, 3H), 5.59 (s, 2H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 145.0, 141.8, 135.0, 133.2, 130.6, 130.2, 129.1, 129.0, 128.8, 120.8, 51.0. HRMS (ESI) calcd, $[C_{15}H_{14}N_3]^+$ 236.1182; observed, 236.1171.

4-Cyclohexyl-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([2b]BF_4).

The title compound was prepared according to general procedure IIb. Purification by column chromatography (silica, 1. DCM, 2. DCM/acetone 4:1, $R_f = 0.33$) yielded the

product as an off-white solid in 90% yield (141 mg, 0.449 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 10.86 (s, 1H), 9.54 (s, 1H), 7.95 (d, *J* = 7.7 Hz, 2H), 7.73-7.69 (m, 2H), 7.63 (t, *J* = 7.3 Hz, 1H), 4.45 (tt, *J* = 11.7 Hz, *J* = 4.0 Hz, 1H), 2.28-2.24 (m, 2H), 1.91-1.69 (m, 5H), 1.49-1.38 (m, 2H), 1.28-1.19 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 143.9, 140.5, 135.1, 130.5, 130.1, 120.7, 58.4, 32.0, 24.4, 24.2. HRMS (ESI) calcd, $[C_{14}H_{18}N_3]^+$ 228.1495; observed, 228.1487.

4-((3*s*,5*s*,7*s*)-Adamantan-1-yl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([2c]BF$_4$).

The title compound was prepared according to general procedure IIb. Purification by column chromatography (silica, 1. DCM, 2. DCM/acetone 4:1, R_f = 0.36) yielded the product as a white solid in 70% yield (128 mg, 0.348 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 10.83 (s, 1H), 9.71 (s, 1H), 7.99 (d, *J* = 7.7 Hz, 2H), 7.73-7.69 (m, 2H), 7.63 (t, *J* = 7.3 Hz, 1H), 2.26 (bs, 9H), 7.99 (d, *J* = 7.7 Hz, 2H), 7.99 (d, *J* = 7.7 Hz, 2H), 1.78 (d, *J* = 12.4 Hz, 3H), 1.72 (d, *J* = 12.4 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 142.6, 139.7, 135.2, 130.4, 130.1, 120.8, 60.6, 41.4, 34.9, 28.8. HRMS (ESI) calcd, $[C_{18}H_{22}N_3]^+$ 280.1808; observed, 280.1797.

1,4-Diphenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([2d]BF$_4$).

The title compound was prepared according to general procedure IIb. Purification by column chromatography (silica, 1. DCM, 2. DCM/acetone 4:1, R_f = 0.22) yielded the product as an off-white solid in 96% yield (148 mg, 0.479 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.43 (s, 1H), 10.01 (s, 1H), 8.04 (d, *J* = 7.7 Hz, 2H), 7.94 (d, *J* =

7.7 Hz, 2H), 7.79-7.75 (m, 4H), 7.72-7.67 (m, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6, 298 K): δ = 143.3, 140.5, 134.9, 132.1, 130.8, 130.3, 122.6, 120.8. HRMS (ESI) calcd, $[C_{14}H_{12}N_3]^+$ 222.1026; observed, 222.1019.

1,4-Diphenyl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate ([2d]OTf).

The title compound was prepared according to general procedure IIb. Purification by column chromatography (silica, 1. DCM, 2. DCM/acetone 4:1, $R_f = 0.17$) yielded the product as a white solid in 95% yield (176 mg, 0.473 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.43 (s, 1H), 10.01 (s, 1H), 8.04 (d, *J* = 7.7 Hz, 2H), 7.94 (d, *J* = 7.7 Hz, 2H), 7.79-7.75 (m, 4H), 7.72-7.67 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 143.3, 140.5, 134.9, 132.1, 130.8, 130.3, 122.6, 120.7. HRMS (ESI) calcd, $[C_{14}H_{12}N_3]^+$ 222.1026; observed, 222.1022.

4-(2,6-Diisopropylphenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([2e]BF_4).

The title compound was prepared according to general procedure IIb. Purification by column chromatography (silica, 1. DCM, 2. DCM/acetone 4:1, $R_f = 0.56$) yielded the product as an off-white solid in 96% yield (189 mg, 0.480 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.38 (s, 1H), 9.93 (s, 1H), 8.05 (d, *J* = 7.7 Hz, 2H), 7.78-7.67 (m, 4H), 7.54 (d, *J* = 7.7 Hz, 2H), 2.57 (sept, *J* = 6.7 Hz,12H'), 1.19 (d, *J* = 6.7 Hz, 6H') 1.14 (d, *J* = 6.7 Hz, 6H'); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 146.0, 145.5, 142.1, 135.1, 132.4, 130.8, 130.0, 127.2, 124.8, 120.9, 27.7, 24.2, 23.5. HRMS (ESI) calcd, $[C_{20}H_{24}N_3]^+$ 306.1965; observed, 306.1958.

1-Phenyl-4-(2-((4-methoxybenzyl)thio)phenyl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([2f]BF_4).

The title compound was prepared according to general procedure IIb. Purification by column chromatography (silica, 1. DCM, 2. DCM/acetone 4:1, R_f = 0.35) yielded the product as an off-white solid in 79% yield (181 mg, 0.394 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.13 (s, 1H), 9.73 (s, 1H), 7.97 (d, *J* = 7.7 Hz, 2H), 7.89 (dd, *J* = 7.9 Hz, *J* = 1.4 Hz, 1H), 7.79-7.64 (m, 6H), 7.06 (d, *J* = 8.6 Hz, 2H), 6.76 (d, *J* = 8.6 Hz, 2H), 4.15 (s, 2H'), 3.64 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 158.5, 145.5, 141.8, 134.7, 133.8, 132.2, 132.1, 132.0, 130.9, 130.3, 129.9, 128.9, 128.3, 127.2, 120.6, 113.9, 54.9, 38.4. HRMS (ESI) calcd, $[C_{22}H_{20}N_3OS]^+$ 374.1322; observed, 274.1305.

4-(2-Fluorophenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([2g]BF_4).

The title compound was prepared according to general procedure IIb. Purification by column chromatography (silica, 1. DCM, 2. DCM/acetone 4:1, R_f = 0.17) yielded the product as an off-white solid in 95% yield (155 mg, 0473 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.47 (s, 1H), 10.03 (s, 1H), 8.03 (d, *J* = 7.7 Hz, 2H), 7.97-7.93 (m, 1H), 7.87-7.81 (m, 2H), 7.79-7.75 (m, 2H), 7.69 (t, *J* = 7.3 Hz, 1H) 7.62-7.57 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 162.2 (d, J_{C-F} = 245.1 Hz), 143.3, 140.7, 134.8, 133.2 (d, J_{C-F} = 11.0 Hz), 132.4 (d, J_{C-F} = 8.8 Hz), 130.9, 130.4, 120.7, 118.7 (d, J_{C-F} = 3.3 Hz), 117.7 (d, J_{C-F} = 20.7 Hz), 110.4 (d, J_{C-F} = 27.1 Hz); ^{19}F{^{1}H} NMR (376 MHz, DMSO-d_6, 298 K, referenced to C_6H_5F): δ = -109.97, -148.42. HRMS (ESI) calcd, $[C_{14}H_{11}FN_3]^+$ 240.0932; observed, 204.0922.

4-(3-Fluorophenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([2h]BF_4).

The title compound was prepared according to general procedure IIb. Purification by column chromatography (silica, 1. DCM, 2. DCM/acetone 4:1, R_f = 0.17) yielded the product as a pale-yellow solid in 96% yield (158 mg, 0.482 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.42 (s, 1H), 9.93 (d, J = 1.7 Hz, 1H), 8.03 (d, J = 7.7 Hz, 2H), 7.96 (dt, J = 7.8 Hz, J = 1.6 Hz, 1H), 7.82-7.67 (m, 5H), 7.61 (dt, J = 7.5 Hz, J = 1.6 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 154.3 (d, J_{C-F} = 252.7 Hz), 144.6 (d, J_{C-F} = 3.8 Hz), 142.0, 134.8, 133.3 (d, J_{C-F} = 8.0 Hz), 130.9, 130.3, 126.7, 126.0 (d, J_{C-F} = 4.0 Hz), 121.0, 120.0 (d, J_{C-F} = 11.3 Hz), 117.5 (d, J_{C-F} = 18.4 Hz); ^{19}F{^{1}H} NMR (376 MHz, DMSO-*d*6, 298 K, referenced to C_6H_5F): δ = -123.16, -148.41. HRMS (ESI) calcd, $[C_{14}H_{11}FN_3]^+$ 240.0932; observed, 240.0921.

4-(4-Fluorophenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([2i]BF_4).

The title compound was prepared according to general procedure IIb. Purification by column chromatography (silica, 1. DCM, 2. DCM/acetone 4:1, R_f = 0.19) yielded the product as an off-white solid in 94% yield (154 mg, 0.470 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.42 (s, 1H), 9.96 (s, 1H), 8.04-7.98 (m, 4H), 7.78-7.75 (m, 2H), 7.71-7.64 (m, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 162.9 (d, J_{C-F} = 249.9 Hz), 143.5, 140.7, 134.9, 130.8, 130.4, 128.5 (d, J_{C-F} = 2.9 Hz), 125.4 (d, J_{C-F} = 9.6 Hz), 120.7, 117.4 (d, J_{C-F} = 23.6 Hz); ^{19}F{^{1}H} NMR (376 MHz, DMSO-d_6, 298 K, referenced to C_6H_5F): δ = -109.92, -148.41. HRMS (ESI) calcd, $[C_{14}H_{11}FN_3]^+$ 240.0932; observed, 240.0921.

4-(2-Chlorophenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([2j]BF_4).

The title compound was prepared according to general procedure IIb. Purification by column chromatography (silica, 1. DCM, 2. DCM/acetone 4:1, R_f = 0.19) yielded the product as an off-white solid in 95% yield (136 mg, 0.474 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.41 (s, 1H), 9.95 (s, 1H), 8.04 (d, *J* = 7.7 Hz, 2H), 7.97-7.92 (m, 2H), 7.81-7.68 (m, 5H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 153.9, 145.2, 142.4, 134.8, 133.3, 131.0, 130.3, 129.4, 129.0, 128.7, 128.5, 120.9. HRMS (ESI) calcd, $[C_{14}H_{11}ClN_3]^+$ 256.0636; observed, 256.0627.

4-(4-Chlorophenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([2k]BF_4).

The title compound was prepared according to general procedure IIb. Purification by column chromatography (silica, 1. DCM, 2. DCM/acetone 4:1, R_f = 0.37) yielded the product as an off-white solid in 90% yield (155 mg, 0.491 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.45 (s, 1H), 10.00 (s, 1H), 8.03 (d, *J* = 7.7 Hz, 2H), 7.98 (d, *J* = 9.0 Hz, 2H), 7.89 (d, *J* = 9.0 Hz, 2H), 7.79-7.75 (m, 2H), 7.69 (t, *J* = 7.3 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 143.3, 140.6, 135.4, 134.8, 131.0, 130.9, 130.4, 130.3, 124.5, 120.7. HRMS (ESI) calcd, $[C_{14}H_{11}ClN_3]^+$ 256.0636; observed, 256.0627.

1-Phenyl-4-(pyridin-2-yl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([2l]BF_4).

The title compound was prepared according to general procedure IIb. Purification by column chromatography (silica, 1. DCM, 2. DCM/acetone 4:1, R_f = 0.22) yielded the

product as a white solid in 82% yield (127 mg, 0.410 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.68 (s, 1H), 10.24 (s, 1H), 8.77-8.75 (m, 1H), 8.37-8.32 (m, 1H), 8.15 (d, *J* = 8.1 Hz, 1H), 8.05 (d, *J* = 7.7 Hz, 2H), 7.78 (m, 3H), 7.69 (t, *J* = 7.3 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 149.5, 144.7, 142.0, 140.9, 139.7, 134.9, 130.9, 130.28, 126.2, 120.9, 115.4. HRMS (ESI) calcd, $[C_{13}H_{11}N_4]^+$ 223.0978; observed, 223.0973.

1-Phenyl-4-(pyrimidin-2-yl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([2m]BF_4).

The title compound was prepared according to general procedure IIb. After evaporation of the reaction solvent, the crude residue was washed with diethyl ether (5 mL), THF (3 X 5 mL), acetone (3 times 2 mL). Recrystallization from methanol yielded the pure product as pale yellow solid in 58% yield (89.9 mg, 0.288 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.83 (s, 1H), 10.33 (s, 1H), 9.19 (d, *J* = 4.9 Hz, 2H), 8.14 (d, *J* = 7.7 Hz, 2H), 7.91 (t, *J* = 4.9 Hz, 1H), 7.77-7.68 (m, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 160.4, 151.0, 142.2, 140.1, 134.8, 131.0, 130.2, 123.4, 121.2. HRMS (ESI) calcd, $[C_{12}H_{10}N_5]^+$ 224.0931; observed, 224.0929.

4-Phenyl-1-(o-tolyl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate ([3d]OTf).

The title compound was prepared according to general procedure IIb. Purification by column chromatography (silica, 1. DCM, 2. DCM/acetone 4:1, $R_f = 0.17$) yielded the product as an off-white solid in 81% yield (155 mg, 0.404 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.17 (s, 1H), 10.03 (s, 1H), 7.94 (d, *J* = 7.7 Hz, 2H), 7.79-7.53 (m, 7H), 2.40 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 143.0, 142.8, 134.1, 133.8, 132.1, 132.0, 131.6, 130.7, 130.2, 127.3, 126.3, 122.6, 17.3. HRMS (ESI) calcd, $[C_{15}H_{14}N_3]^+$ 236.1182; observed, 236.1174.

4-(2-Chlorophenyl)-1-(o-tolyl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate ([3j]OTf).

The title compound was prepared according to general procedure IIb. Purification by column chromatography (silica, 1. DCM, 2. DCM/acetone 4:1, $R_f = 0.24$) yielded the product as a white solid in 67% yield (140 mg, 0.333 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.2 (s, 1H), 9.97 (s, 1H), 7.79 (dd, *J* = 7.5 Hz, *J* = 2.2 Hz, 1H), 7.94 (dd, *J* = 7.5 Hz, *J* = 2.0 Hz, 1H), 7.82-7.73 (m, 3H), 7.68-7.55 (m, 3H), 2.39 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 175.4, 164.8, 158.8, 156.3, 146.9, 144.2, 140.4, 131.5, 130.1, 127.0, 125.3, 122.9, 121.0, 38.3, 26.3. HRMS (ESI) calcd, $[C_{15}H_{13}ClN_3]^+$ 270.0793; observed, 270.0785.

4-Benzyl-1-mesityl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate ([4a]OTf).

The title compound was prepared according to general procedure IIb. Purification by column chromatography (silica, 1. DCM, 2. DCM/acetone 4:1, $R_f = 0.18$) yielded the product as an off-white solid in 58% yield (123 mg, 0.287 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 10.60 (s, 1H), 9.59 (s, 1H), 7.53-7.45 (m, 5H), 7.16 (s, 2H), 5.63 (s, 2H), 2.34 (s, 3H), 2.01 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 146.2, 145.4, 141.9, 135.1, 133.9, 131.6, 129.9, 129.7, 129.6, 129.1, 51.6, 21.1, 17.3. HRMS (ESI) calcd, $[C_{18}H_{20}N_3]^+$ 278.1652; observed, 278.1642.

4-Cyclohexyl-1-mesityl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate ([4b]OTf).

The title compound was prepared according to general procedure IIb. Purification by column chromatography (silica, 1. DCM, 2. DCM/acetone 4:1, $R_f = 0.54$) yielded the product as an off-white solid in 86% yield (181 mg, 0.431 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 10.55 (s, 1H), 9.56 (s, 1H), 7.17 (s, 2H), 4.48 (tt, J = 11.5 Hz, J = 3.8 Hz, 1H), 2.35 (s, 3H), 2.32-2.28 (m, 2H), 2.04 (s, 6H), 1.91-1.68 (m, 5H), 1.50-1.38 (m, 2H), 1.29-1.18 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 144.4, 143.5, 141.4, 134.8, 132.2, 129.4, 58.4, 31.8, 24.3, 24.2, 20.7, 16.8. HRMS (ESI) calcd, $[C_{17}H_{24}N_3]^+$ 270.1965; observed, 270.1959.

4-((3*s*,5*s*,7*s*)-Adamantan-1-yl)-1-mesityl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate ([4c]OTf).

On a 0.5 mmol scale, The title compound was prepared according to general procedure IIb Purification by column chromatography (silica, 1. DCM, 2. DCM/acetone 4:1, R_f = 0.56) yielded the product as an off-white solid in 75% yield (176 mg, 0.374 mmol). Purification of 8 mmol scale: After evaporation of the reaction solvent, the crude product was dissolved in DCM (50 mL), filtered and crashed out with hexanes (70 mL) which yielded the pure product as a colorless powder in 77% yield (2.89 g, 6.13 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 10.65 (s, 1H), 9.81 (s, 1H), 7.18 (s, 1H), 2.35 (s, 3H), 2.28 (bs, 9H), 2.05 (s, 6H), 1.79-1.71 (m, 6H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 143.3, 142.7, 141.4, 134.8, 131.3, 129.4, 60.9, 41.3, 34.7, 28.9, 20.7, 16.9. HRMS (ESI) calcd, $[C_{21}H_{28}N_3]^+$ 322.2278; observed, 322.2273.

1-Mesityl-4-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([4d]BF_4).

The title compound was prepared according to general procedure IIb. Purification by column chromatography (silica, 1. DCM, 2. DCM/acetone 4:1, R_f = 0.36) yielded the product as an off-white solid in 52% yield (91 mg, 0.266 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.10 (s, 1H), 10.11 (s, 1H), 7.97 (d, *J* = 8.0 Hz, 2H), 7.78-7.74 (m, 2H), 7.69 (t, *J* = 7.4 Hz, 1H), 7.21 (s, 2H), 2.37 (s, 3H), 2.16 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 143.8, 143.2, 141.6, 134.9, 132.2, 131.0, 130.7, 130.2, 129.5, 122.5, 20.7, 17.0. HRMS (ESI) calcd, $[C_{17}H_{18}N_3]^+$ 264.1495; observed, 264.1490.

1-Mesityl-4-phenyl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate ([4d]OTf).

The title compound was prepared according to general procedure IIb. Purification by column chromatography (silica, 1. DCM, 2. DCM/acetone 4:1, $R_f = 0.19$) yielded the product as an off-white powder in 74% yield (153 mg, 0.372 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.10 (s, 1H), 10.11 (s, 1H), 7.96 (d, *J* = 8.0 Hz, 2H), 7.78-7.74 (m, 2H), 7.69 (t, *J* = 7.4 Hz, 1H), 7.21 (s, 2H), 2.37 (s, 3H), 2.16 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 143.8, 143.2, 141.6, 134.9, 132.2, 131.0, 130.6, 130.1, 129.5, 122.5, 20.7, 17.0. HRMS (ESI) calcd, $[C_{17}H_{18}N_3]^+$ 264.1495; observed, 264.1485.

1-Mesityl-4-(2-((4-methoxybenzyl)thio)phenyl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate ([4f]OTf).

The title compound was prepared according to general procedure IIb. Purification by column chromatography (silica, 1. DCM, 2. DCM/acetone 4:1, $R_f = 0.48$) yielded the product as a light brown oil (which solidified upon standing) in 59% yield (166 mg, 0.229 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 10.95 (s, 1H), 9.68 (s, 1H), 7.91 (dd, *J* = 7.9 Hz, *J* = 1.3 Hz, 1H), 7.88 (dd, *J* = 7.9 Hz, *J* = 1.3 Hz, 1H), 7.74 (td, *J* = 7.7 Hz, *J* = 1.3 Hz, 1H), 7.66 (td, *J* = 7.7 Hz, *J* = 1.3 Hz, 1H), 7.22 (s, 2H), 7.10 (d, *J* = 8.7 Hz, 2H), 6.83 (d, *J* = 8.7 Hz, 2H), 4.20 (s, 2H), 3.72 (s, 3H), 2.37 (s, 3H'), 2.13 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 158.6, 146.0, 145.6, 141.7, 134.8, 133.1, 132.7, 132.2, 131.8, 130.8, 129.9, 129.5, 128.5, 128.2, 127.7, 55.1, 38.3, 20.7, 17.0. HRMS (ESI) calcd, $[C_{25}H_{26}N_3OS]^+$ 416.1791; observed, 416.1766.

4-(4-Fluorophenyl)-1-mesityl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate ([4i]OTf).

The title compound was prepared according to general procedure IIb. Purification by column chromatography (silica, 1. DCM, 2. DCM/acetone 4:1, $R_f = 0.47$) yielded the product as a white powder in 54% yield (117 mg, 0.277 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.05 (s, 1H), 10.06 (s, 1H), 8.04-8.01 (m, 2H), 7.68-7.63 (m, 2H), 7.20 (s, 1H), 2.37 (s, 3H'), 2.15 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 162.7 (d, J_{C-F} = 248.6 Hz), 144.0, 143.3, 141.6, 134.9, 131.0, 129.5, 128.7 (d, J_{C-F} = 3.0 Hz), 125.3 (d, J_{C-F} = 9.3 Hz), 117.1 (d, J_{C-F} = 23.8 Hz), 20.7, 17.0; ^{19}F{^{1}H} NMR (376 MHz, DMSO-d_6, 298 K, referenced to C_6H_5F): δ = -77.85, -110.18. HRMS (ESI) calcd, $[C_{17}H_{17}FN_3]^+$ 282.1401; observed, 282.1393.

4-(4-Chlorophenyl)-1-mesityl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate ([4k]OTf).

The title compound was prepared according to general procedure IIb. Purification by column chromatography (silica, 1. DCM, 2. DCM/acetone 4:1, $R_f = 0.43$) yielded the product as an off-white powder in 58% yield (130 mg, 0.291 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.10 (s, 1H), 10.10 (s, 1H), 8.00 (d, J = 8.9 Hz, 2H), 7.88 (d, J = 8.9 Hz, 2H), 7.20 (s, 2H), 2.37 (s, 3H), 2.15 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 143.9, 143.3, 241.6, 135.2, 134.9, 131.2, 131.0, 130.1, 129.5, 124.5, 20.7, 17.0. HRMS (ESI) calcd, $[C_{17}H_{17}ClN_3]^+$ 298.1106; observed, 298.1101.

1-Mesityl-4-(pyridin-2-yl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate ([4l]OTf).

The title compound was prepared according to general procedure IIb. Purification by washing with hexanes (2 times, 10 mL) and diethyl ether (2 times, 10 mL, followed by recrystallization from 1,4-dioxane, yielded the product as a colorless powder in 54% yield (112 mg, 0.271 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.37 (s, 1H), 10.30 (s, 1H), 8.74-8.73 (m, 1H), 8.34-8.30 (m, 1H), 8.12 (d, *J* = 8.2 Hz, 1H), 7.77-7.74 (m, 1H), 7.20 (s, 2H), 2.37 (s, 3H), 2.14 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 149.3, 145.0, 142.8, 142.6, 141.6, 140.6, 134.9, 131.1, 129.4, 126.0, 115.5, 20.7, 17.0. HRMS (ESI) calcd, $[C_{16}H_{17}N_4]^+$ 265.1448; observed, 265.1444.

4-Cyclohexyl-1-(naphthalen-1-yl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([5b]BF_4).

The title compound was prepared according to general procedure IIb. Purification by column chromatography (silica, 1. DCM, 2. DCM/acetone 4:1, R_f = 0.41) yielded the product as an off-white powder in 96% yield (175 mg, 0.478 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 10.78 (s, 1H), 9.69 (s, 1H), 8.32 (d, *J* = 8.3 Hz, 1H), 8.20-8.18 (m, 1H), 7.97-7.95 (m, 1H), 7.86-7.69 (m, 4H), 4.52 (tt, *J* = 11.6 Hz, *J* = 3.9 Hz, 1H), 2.37-2.33 (m, 2H), 1.94-1.70 (m, 5H), 1.51-1.44 (m, 2H), 1.30-1.20 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 144.0, 143.7, 133.7, 132.0, 131.2, 128.5, 128.3, 127.6, 127.1, 125.3, 125.1, 122.1, 58.4, 31.9, 24.4, 24.2. HRMS (ESI) calcd, $[C_{18}H_{14}N_3]^+$ 278.1652; observed, 278.1647.

1-(Naphthalen-1-yl)-4-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([5d]BF_4).

The title compound was prepared according to general procedure IIb. Purification by column chromatography (silica, 1. DCM, 2. DCM/acetone 4:1, $R_f = 0.19$) yielded the product as a brown powder in 81% yield (145 mg, 0.406 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.36 (s, 1H), 10.15 (s, 1H), 8.37 (d, *J* = 8.4 Hz, 1H), 8.24-8.20 (m, 1H), 8.06-8.02 (m, 2H), 7.98 (d, *J* = 8.0 Hz, 2H), 7.85-7.70 (m, 6H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 143.7, 143.4, 133.7, 132.2 (2 signals), 131.0, 130.7, 130.3, 128.5, 128.4, 127.7, 127.1, 125.4, 125.2, 122.6, 122.3. HRMS (ESI) calcd, $[C_{18}H_{14}N_3]^+$ 272.1182; observed, 272.1173.

1-(4-Methoxyphenyl)-4-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([6d]BF_4).

The title compound was prepared according to general procedure IIb. Purification by column chromatography (silica, 1. DCM, 2. DCM/acetone 4:1, $R_f = 0.19$) yielded the product as a pale brown powder in 91% yield (155 mg, 0.456 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.30 (s, 1H), 9.97 (s, 1H), 7.96-7.91 (m, 4H), 7.86-7.74 (m, 2H), 7.68 (t, *J* = 7.3 Hz, 1H), 7.29 (d, *J* = 9.1 Hz, 2H), 3.88 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 160.7, 143.1, 139.7, 132.1, 130.7, 130.3, 128.0, 122.5, 115.28, 55.8. HRMS (ESI) calcd, $[C_{15}H_{14}N_3O]^+$ 252.1131; observed, 252.1124.

1-(4-Methoxyphenyl)-4-(pyrimidin-2-yl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([6m]BF_4).

The title compound was prepared according to general procedure IIb on a 3 mmol scale. After evaporation of the reaction solvent, the crude product was washed with hexanes (2 times, 10 ml), diethyl ether (2 times, 10 mL), and THF (3 times, 5 mL). Extraction of

the resulting solid with acetone (2 times 10 mL) yielded the desired product upon evaporation as a pale brown powder in 53% yield (273 mg, 0.798 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.69 (s, 1H), 10.27 (s, 1H), 9.16 (d, *J* = 4.5 Hz, 2H), 8.04 (d, *J* = 8.5 Hz, 2H), 7.89 (t, *J* = 4.5 Hz, 1H), 7.26 (d, *J* = 8.5 Hz, 2H), 3.88 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 160.9, 160.4, 151.0, 142.1, 139.2, 127.8, 123.3, 122.9, 115.2, 55.9. HRMS (ESI) calcd, $[C_{15}H_{14}N_3O]^+$ 254.1036; observed, 254.1035.

4-Phenyl-1-(3-(trifluoromethyl)phenyl)-4*H*-1,2,4-tri-azol-1-ium tetrafluoroborate ([7d]BF_4).

The title compound was prepared according to general procedure IIb. Purification by column chromatography (silica, 1. DCM, 2. DCM/acetone 4:1, R_f = 0.37) yielded the product as an off-white solid in 95% yield (178 mg, 0.473 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.59 (s, 1H), 10.08 (s, 1H), 8.45 (s, 1H), 8.37 (d, *J* = 8.0 Hz, 1H), 8.10 (d, *J* = 8.0 Hz, 1H), 8.03 (t, *J* = 8.0 Hz, 1H), 7.94 (d, *J* = 7.7 Hz, 2H), 7.81-7.77 (m, 2H), 7.73-7.70 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 143.2, 142.3, 135.3, 131.8, 130.6, 130.5 (q, *J* = 32.8 Hz), 130.2, 127.2 (q, *J* = 3.8 Hz), 124.8, 123.2 (q, *J* = 272.2 Hz), 122.3, 117.7 (q, *J* = 3.8 Hz); ^{19}F{^{1}H} NMR (376 MHz, DMSO-d_6, 298 K, referenced to C_6H_5F): δ = -61.42, -148.42. HRMS (ESI) calcd, $[C_{15}H_{14}N_3O]^+$ 290.0900; observed, 290.0891.

4-(2,6-Diisopropylphenyl)-1-(3-(trifluoromethyl)phenyl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([7e]BF_4).

The title compound was prepared according to general procedure IIb. Purification by column chromatography (silica, 1. DCM, 2. DCM/acetone 4:1, $R_f = 0.50$) yielded the product as a pale yellow-green oil in 98% yield (226 mg, 0.489 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.48 (s, 1H), 9.98 (s, 1H), 8.43 (s, 1H), 8.39 (d, *J* = 8.0 Hz, 1H), 8.10 (d, *J* = 8.0 Hz, 1H), 8.02 (t, *J* = 8.0 Hz, 1H), 7.73 (t, *J* = 7.8 Hz, 1H), 7.55 (d, *J* = 7.8 Hz, 2H), 2.60 (sept, *J* = 6.7 Hz, 2H), 1.20 (d, *J* = 6.7 Hz, 6H), 1.15 (d, *J* = 8.0 Hz, 6H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 146.0, 145.5, 143.1, 135.8, 132.5, 131.5, 130.4 (q, *J* = 32.9 Hz), 127.2 (q, *J* = 3.7 Hz), 127.1, 125.1, 124.9, 123.4 (q, *J* = 272.6 Hz), 118.1 (q, *J* = 4.0 Hz); ^{19}F{^{1}H} NMR (376 MHz, DMSO-d_6, 298 K, referenced to C_6H_5F): δ = -61.37, -148.41. HRMS (ESI) calcd, $[C_{15}H_{14}N_3O]^+$ 374.1839; observed, 374.1827.

1-(4-Fluorophenyl)-4-phenyl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate ([8d]OTf).

The title compound was prepared according to general procedure IIb. Purification by column chromatography (silica, 1. DCM, 2. DCM/acetone 4:1, $R_f = 0.11$) yielded the product as off-white powder in 74% yield (144 mg, 0.369 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.41 (s, 1H), 10.02 (s, 1H), 8.11-8.06 (m, 2H), 7.94 -7.92 (m, 2H), 7.93 (d, *J* = 7.7 Hz, 2H), 7.79-7.75 (m, 2H), 7.70 (t, *J* = 7.3 Hz, 1H), 7.66-7.62 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 162.8 (d, *J* = 247.9 Hz), 143.3, 140.7, 132.0, 131.4 (d, *J* = 3.0 Hz), 130.8, 130.3, 123.5 (d, *J* = 9.3 Hz), 122.5, 117.4 (d, *J* = 24.0 Hz); ^{19}F{^{1}H} NMR (376 MHz, DMSO-d_6, 298 K, referenced to

C_6H_5F): δ = -77.85, -109.86. HRMS (ESI) calcd, $[C_{15}H_{14}N_3O]^+$ 240.0932; observed, 240.0925.

4-(2,6-Diisopropylphenyl)-1-(4-fluorophenyl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate ([8e]OTf).

The title compound was prepared according to general procedure IIb. Purification by column chromatography (silica, 1. DCM, 2. DCM/acetone 4:1, R_f = 0.44) yielded the product as an off-white solid in 91% yield (216 mg, 0.456 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.34 (s, 1H), 9.93 (s, 1H), 8.13-8.10 (m, 2H), 7.72 (t, *J* = 7.8 Hz, 1H), 7.66-7.62 (m, 2H), 7.55 (t, *J* = 7.8 Hz, 2H), 2.58 (sept, *J* = 6.7 Hz, 2H), 1.20 (d, *J* = 6.7 Hz, 6H), 1.15 (d, *J* = 6.7 Hz, 6H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 298 K): δ = 162.8 (d, *J* = 248.9 Hz), 146.0, 145.5, 142,2, 132.4, 131.7 (d, *J* = 3.0 Hz), 127.1, 124.9, 123.7 (d, *J* = 9.0 Hz), 122.3, 119.1, 117.0 (d, *J* = 24.0 Hz); ^{19}F{^{1}H} NMR (376 MHz, DMSO-d_6, 298 K, referenced to C_6H_5F): δ = -77.85, -109.94. HRMS (ESI) calcd, $[C_{15}H_{14}N_3O]^+$ 324.1871; observed, 324.1864.

CHAPTER III

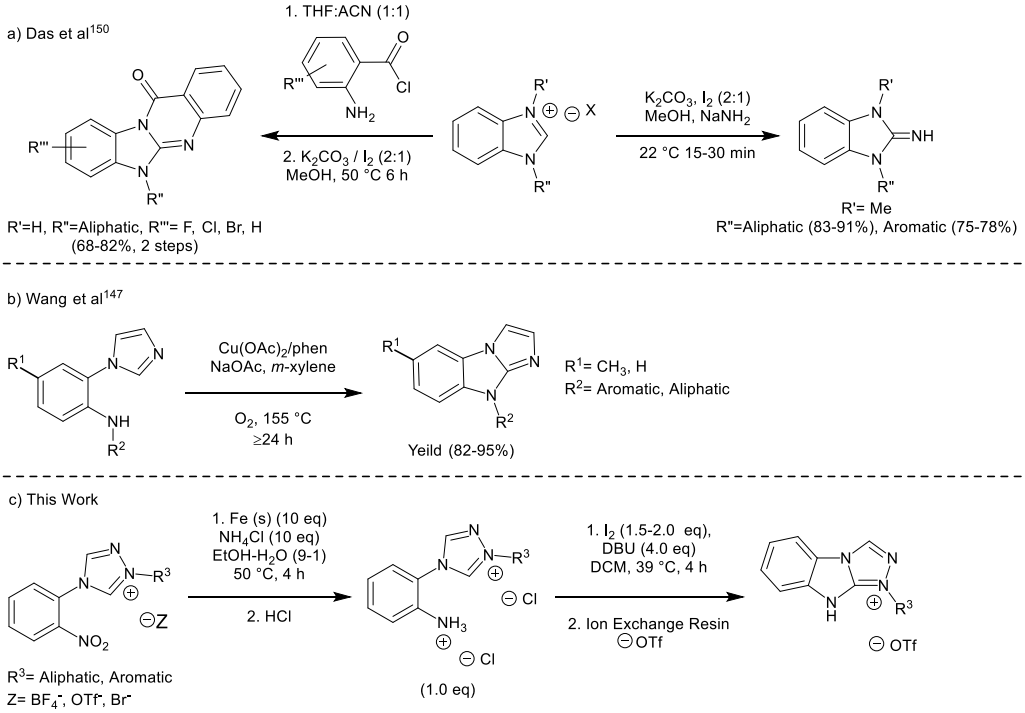
IODINE MEDIATED C–H ACTIVATION LEADING TO BENZO[4,5]IMIDAZO-[2,1-*c*][1,2,4]TRIAZOL-1-IUM SALTS

Section 3.0: Introduction

Fused bicyclic azoles containing 1,2,4-triazole and imidazole units have shown biological activities as anti-microbial,[31,32,35,40,131] anti-viral,[132] anti-inflammatory,[133,134] and anti-cancer agents.[30,32,33,39,135,136] Fused bicyclic azoles containing a 1,2,4-triazole unit are primarily synthesized via two methods. One method employs substituted hydrazonyl halides which are coupled with thioether substituted azoles by two sequential nucleophilic acyl substitutions. (Schemes 11-13).[76,78,137–145] Alternatively, amino or hydrazinyl azoles are used as the structural template to synthesize 1,2,4-triazole-containing bicyclic azoles (Schemes 14-18).[2,39,80,146] Both of these approaches employ complex starting materials in a convergent synthesis to access highly functionalized imidazo[1,2-a]imidazoles. More recent methods involve C(sp^2)-H activation, allowing for post functionalization of a preexisting azole in the presence of an amine nucleophile.[147–150] The Roy group previously explored the C(sp^2)-H activation of imidazolium, thiazolium, and a few triazolium salts using I_2 as the oxidant under basic conditions.

Roy and coworkers showed that the C(sp^2)-H activation results in imination and amination of the C^2 position in the presence of an amine nucleophile with yields ranging from 66-91% (Scheme 21a).[150] The Fu group synthesized 9*H*-benzo[*d*]imidazo[1,2-*a*]imidazole using Cu(I) catalysis in the presence of oxygen at high temperatures to carry out the C(sp^2)-H activation and subsequent intramolecular cyclization of *ortho*-substituted secondary anilines to form a guanidine moiety in 82-97% yields (Scheme 21b).[147] Similar Cu(I) catalyzed C(sp^2)-H activation was employed by Gautier[148] and Subramanian[151] employing different amine sources and a multi-step one-pot synthesis, respectively, to obtain imidazo[1,2-*a*]imidazole and imidazo[2,1-*c*][1,2,4]-triazoles. We developed an alternative method for the synthesis of 9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]-triazol-1-ium salts employing iodine-promoted C(sp^2)-H activation, leading to an intramolecular amination of 4-(2-ammoniophenyl)-1-substituted-4*H*-1,2,4-triazol-1-ium chlorides (Scheme 21c).

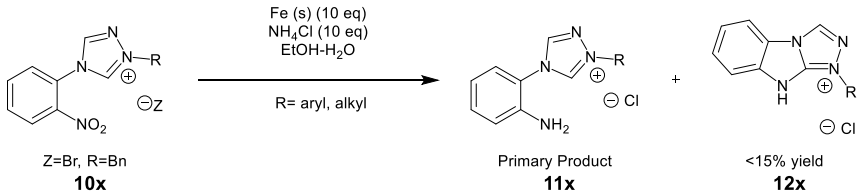
Scheme 21. Previous Research on the C–H Activation of Azoles



Section 3.1 Initial Formation of Benzo[4,5]imidazo[2,1-*c*][1,2,4}triazol-1-ium Salts

Initially, we detected an unexpected byproduct **12x** during the synthesis of 4-(2-aminophenyl)-1-substituted-4*H*-1,2,4-triazol-1-ium salts **11x** during iron-catalyzed reduction of 1-substituted-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium salts **10x** (Scheme 22).

Scheme 22. Discovery of an Unexpected Cyclized Product

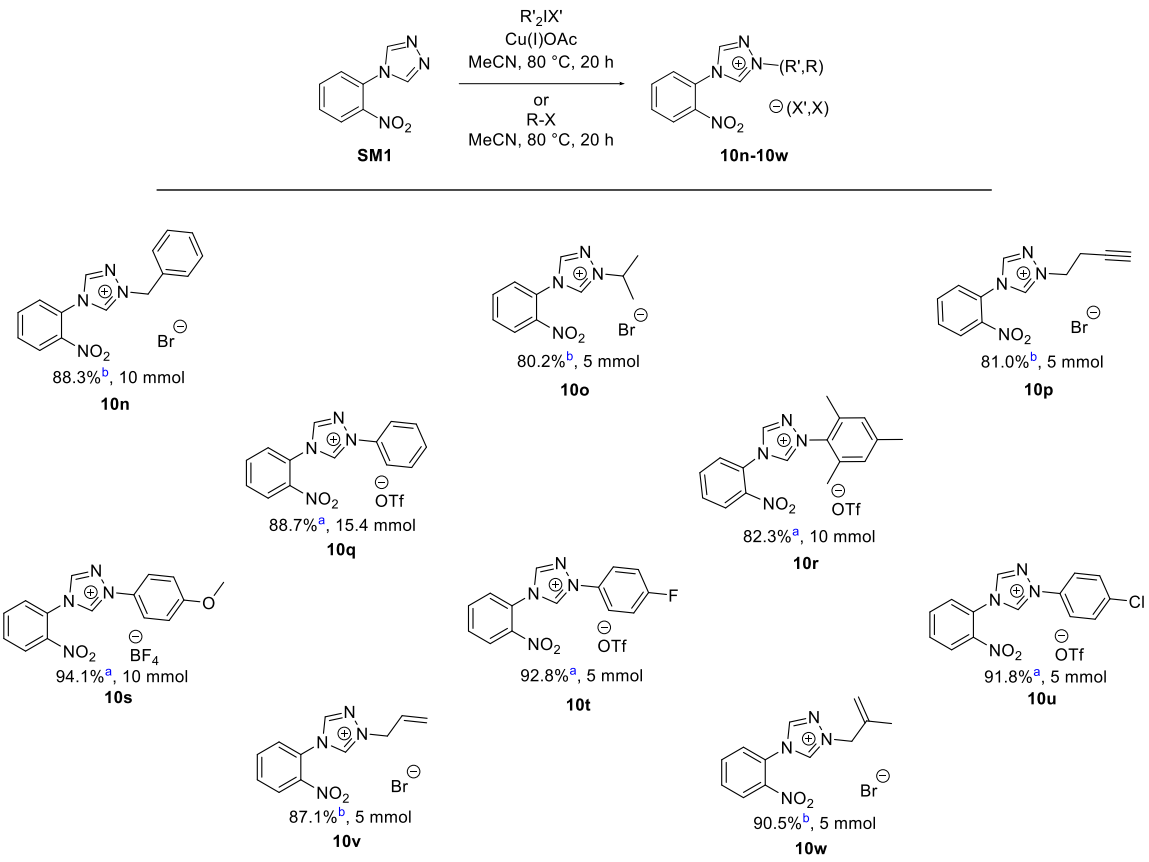


Attempts to optimize this method for the synthesis of 9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium chlorides under iron-promoted reductive conditions failed. We were unable to discover conditions that exclusively formed the cyclized product for both aryl and alkyl substituents. Testing optimized methods on phenyl and benzyl-containing substrates, we discovered that the phenyl substrate more readily cyclized, while the benzyl substrate failed to undergo the cyclization. After 4 h, complete conversion was obtained for all substrates. Allowing the reaction to continue for 20 h resulted in no appreciable increase in the formation of the respective cyclized products. We discovered methods that formed the amine product exclusively during this optimization, which was used to form the precursors for the final step. Searching the literature for proposed mechanisms of the iron-catalyzed reduction of an aromatic nitro, we hypothesized that the nitroso or hydroxylamine intermediates thought to form during the reduction were essential for this cyclization. Since the reduction failed, we attempted to obtain the heterocycle **12x** under oxidative conditions from 4-(2-aminophenyl)-1-substituted-4*H*-1,2,4-triazol-1-ium salts.

Section 3.2: Synthesis of Starting Material for the Iodine-Promoted Intramolecular Cyclization

We began by synthesizing 1-substituted-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium salts (**10n-10w**), starting from 4-(2-nitrophenyl)-4*H*-1,2,4-triazole. We arylated 4-(2-nitrophenyl)-4*H*-1,2,4-triazole using our copper-catalyzed *N*-arylation method to acquire substrates **10q-10u** in high yields (82-94%). We also alkylated 4-(2-nitrophenyl)-4*H*-1,2,4-triazole in high yields (80-91%), introducing the alkyl substituents benzyl (**10n**), isopropyl (**10o**), allyl **(10v**), 2-methylallyl (**10w**), and 3-butynyl (**10p**) (Table 7).

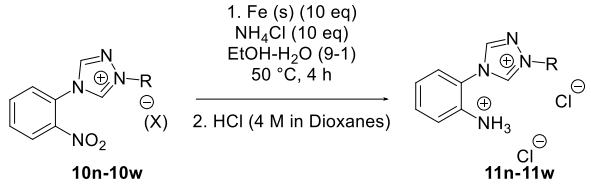
Table 7. Synthesis of 1-Substituted-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium Salts

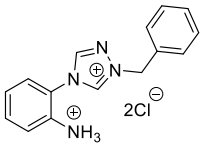


[a)] Reaction conditions: 4-(2-nitrophenyl)-4*H*-1,2,4-triazole (1.0 equiv), diaryl iodonium salt (1.5 equiv), Cu(I)OAc, MeCN, 80 °C, 20 h. [b)] Reaction conditions: 4-(2-nitrophenyl)-4*H*-1,2,4-triazole (1.0 equiv), alkyl bromide (1.0-4.0 equiv), MeCN, 80 °C, 20 h.

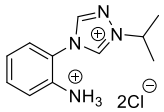
One problem encountered while converting the 1-substituted-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium salts (**10n-10w**) to the amine using iron as the reducing agent under acidic conditions, was that the free base form of 4-(2-aminophenyl)-1-substituted-4*H*-1,2,4-triazol-1-ium salts rapidly decomposed. Therefore we isolated all of these compounds as the hydrochloride salts (Table 8).

Table 8. Synthesis of 4-(2-Ammoniophenyl)-1-substituted-4*H*-1,2,4-triazol-1-ium Chlorides [a]

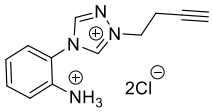




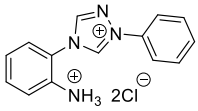
94.9%, 5.7 mmol
11n



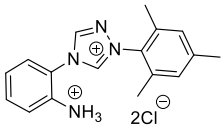
99.8%,3.39 mmol
11o



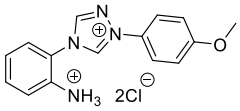
99.8%, 3.31 mmol
11p



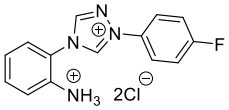
77.5%, 2.0 mmol
11q



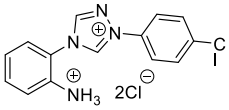
42.8%, 2.5 mmol
11r



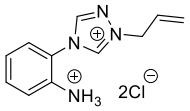
80.5%, 5 mmol
11s



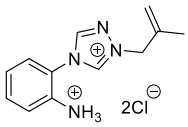
77.3%, 2.0 mmol
11t



54.0%, 2.0 mmol
11u



76.0%, 2.0 mmol
11v



98.5%, 2.1 mmol
11w

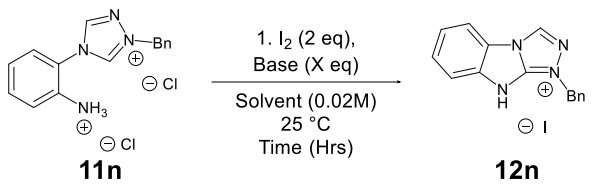
[a)] Reaction conditions: 1) 4-nitrophenyl-1,2,4-triazolium salt (1.0 equiv), NH_4Cl (10 equiv) Fe(0) (10 equiv), EtOH/H_2O 9/1, 50 °C, 4 h. 2) 4 equiv of HCl (4 M in dioxanes)

Section 3.3: Optimization of Iodine-Promoted Intramolecular Cyclization

To optimize the cyclization reaction under oxidative conditions, we charged a microwave vial with **11n** and the chosen oxidant and tested different reaction conditions shown in Table 9. We subjected **11n** to different oxidants, such as *m*-CPBA, H_2O_2, DMSO, and DMSO/ I_2. Among the oxidants attempted, only DMSO/I_2 resulted in conversion of the

starting material to the product. All other oxidants failed to give **12n**, either reforming the 1-substituted-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium salts **11n (**H_2O_2), decomposing the starting material (*m*-CPBA), or achieved incomplete conversion (DMSO anhy). We refined the reaction using iodine as the oxidant in DMSO and an excess of the base (Table 9). Initially, we screened six different bases; $NaHCO_3$ (1.1 equiv), K_2CO_3 (1.1 equiv), NEt_3 (4.0 equiv), *t*-BuOK (4.0 equiv), imidazole (4.0 equiv), DBU (4.0 equiv), and with no base in DMSO at room temperature (Table 9, **Entries 1-7**). We found that *t*-BuOK and DBU were the best bases with DMSO solvent. It was decided that DBU was an easier base with which to work and provided slightly higher yields. Given the yields with the basic salts $NaHCO_3$ and K_2CO_3, no repetition of the reaction with 4 equiv of base was performed. We then varied the ratio of base to oxidant and found that an excess of DBU to I_2 yielded the best results (Table 9, **Entries 8-9**). Testing the solvents MECN, EtOH, EtOAc, and DCM and allowing overnight reaction, it was found that DCM and MECN achieved similar but slightly lower yields compared to the DMSO reactions (Table 9. **Entries 10-13**). We decided that using DCM and MECN would result in easier purification via column chromatography. To validate this hypothesis, we obtained isolated yields from reaction in DCM, MECN, and DMSO, confirming that DCM provided greater ease of purification resulting in higher isolated yields.

Table 9. Optimization of Iodine-Promoted Intramolecular Cyclization [a]



11n **12n**

Entry	Scale (mmol)	Base (X equiv)[b]	Solvent	Time (H)	% Consumption [c] **11n**	% Yield [c] **12n**
1	0.1	None	DMSO	4	46 [b]	~0 [b]
2	0.1	$NaHCO_3$ (1.1)	DMSO	4	100 [b]	~0 [b]
3	0.1	K_2CO_3 (1.1)	DMSO	4	95 [b]	~10 [b]
4	0.1	NEt_3 (4)	DMSO	6	95 [b]	~18 [b]
5	0.1	*t*-BuOK (4)	DMSO	6	87 [b]	~58 [b]
6	0.1	Imidazole (4)[a]	DMSO	6	100 [b]	~11 [b]
7	0.1	DBU (4)	DMSO	6	100 [b]	~76 [b]
8	0.1	DBU (2)	DMSO	2.5	72 [b]	~61 [b]
9	0.1	DBU (4)	DMSO	2.5	100 [b]	~88 [b]
10	0.1	DBU (4)	MECN	20	90 [b]	~60 [b]
11	0.1	DBU (4)	EtOH	20	100 [b]	~34 [b]
12	0.1	DBU (4)	EtOAc	20	100 [b]	~42 [b]
13	0.1	DBU (4)	DCM	20	100 [b]	~74 [b]

[a)] Reaction conditions: triazolium salt **11n** (0.1 mmol), Base, Oxidant: I_2 (2eq), solvent (5 mL, 0.02M), and reaction time. [b)] Relative to **11n**. [c)] Conversion based on LCMS analysis.

Section 3.4: Substrate Scope for the Iodine-Promoted Intramolecular Cyclization

The substrate scope was tested by subjecting our substrates to our optimized reaction conditions. We found that the cyclization was higher yielding with aliphatic substituents (**12n**: 46%, **12o**: 63%), also allowing for alkyne (**12p**: 52%) and alkenes (**12v**: 42%, **12w**: 34%). Aryl substituents are also tolerated but progressed with lower yield; electron-rich and weakly electron-withdrawing aryl substrates displayed similar yields (**12r**: 39%, **12s**: 23%, **12t**: 32%), with the *para*-chlorophenyl and unsubstituted phenyl having noticeably lower yields (**12q**: 19%, **12u**: 12%). Strongly electron-withdrawing groups such as *para*-trifluoromethylphenyl were not tolerated well with product formation not observed.

Table 10. Substrate Scope for the Iodine-Promoted Intramolecular Cyclization

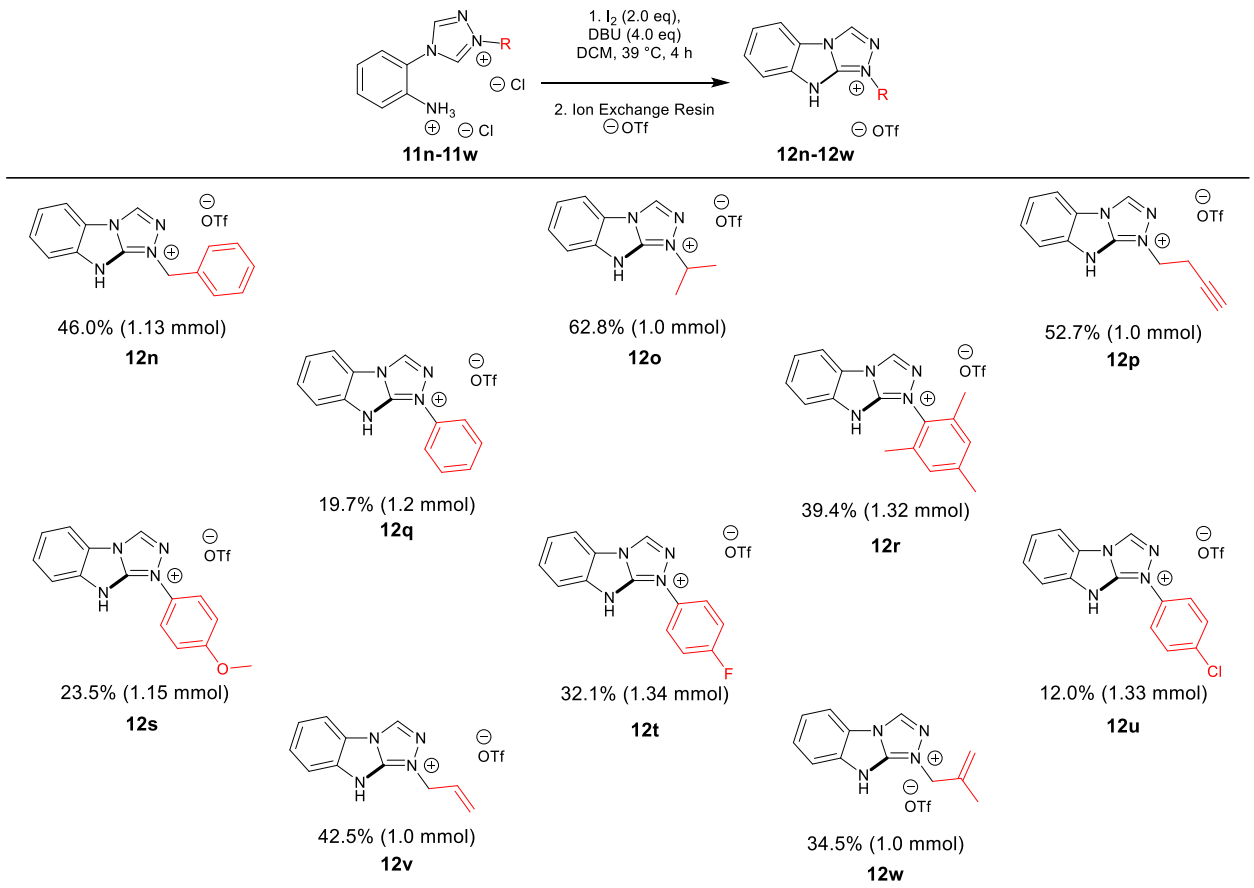


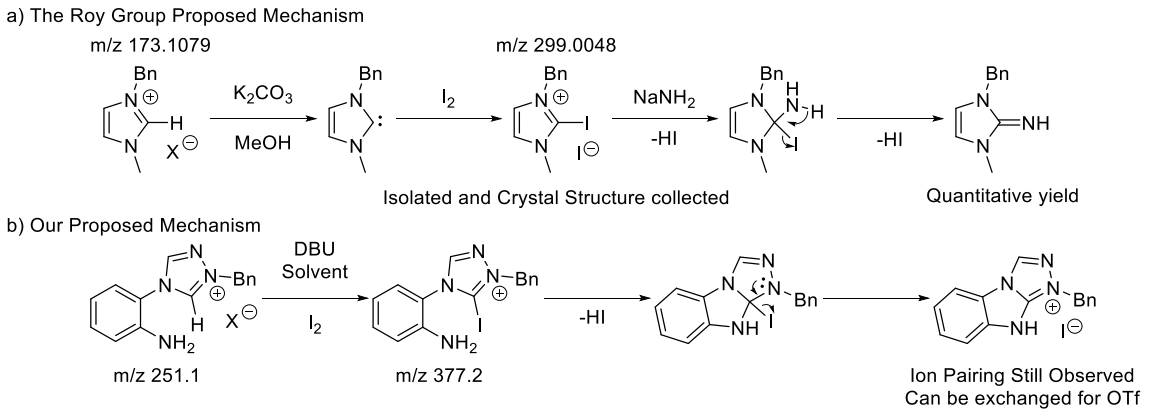
Table 10. Reaction conditions: 4-(2-ammoniophenyl)-[1,2,4]-triazol-1-ium chlorides (1.0 equiv) I_2 (2.0 equiv), DBU (4.0 equiv), DCM (0.02 M), 37 °C, 4 hours

Section 3.5: Potential Mechanism for the Iodine-Promoted Intramolecular Cyclization

The Roy group previously theorized that their iodine-promoted imination progressed through an iodoimidazolium intermediate (Scheme 23a). They observed, isolated, and characterized the iodoimidazolium salt, and when subjecting the iodoimidazolium salt to their optimized reaction conditions obtained near quantitative yields (Scheme 23a).[150] Likewise, we have observed the formation of a similar iodotriazolium intermediate by LCMS (Scheme 23b). Upon addition of iodine, the triazolium salt was observed to be converted to the iodotriazolium amines via LCMS, indicating complete conversion after 1

hour. Conducting the reaction in hygroscopic solvents, we observed the formation of the oxo-triazole species. The Roy Group also studied the formation of the oxo-imidazole when water was used as the nucleophile.[150] We observed that ion pairing was still present in the product. We hypothesized that the second deprotonation proposed by the Roy group for their imidazolium salts did not occur in the case of 1,2,4 triazolium salts.

Scheme 23. Plausible Mechanism for Iodine-Promoted Intramolecular Cyclization



Scheme 23. a) Mechanism proposed by the Roy group. b) Similar mechanism proposed by the Bolliger group.

Section 3.6: Conclusion

In this work, we have developed an alternative synthesis of 9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium salts under relatively mild conditions utilizing inexpensive starting materials. Despite yields being lower than desired, we believe that the substrate specific optimization could significantly increase yields for particular substrates. This research revealed a new synthetic pathway for fused 1,2,4-triazole containing bicyclic azoles, which could potential allow for the development of novel drug molecules.

Section 3.7: Procedure and Characterization data for 4-(2-Nitrophenyl)-[1,2,4]triazole

Synthesis of 4-(2-Nitrophenyl)-[1,2,4]triazole (SMI) (General Procedure III)

A mortar was loaded with 2-nitroaniline (1 equiv), *N*,*N*-dimethylformylamide azine (DMAZ, 1.5 equiv), and *para*-toluenesulfonic acid (TsOH, 0.05 equiv). This mixture was ground together until the mixture became a homogeneous solid. The mixture was then transferred to a round-bottomed flask equipped with a stir bar which was then fitted with a reflux condenser. The mixture was heated (neat) to 150 °C for 16 hours with constant stirring.

Workup: After 16 hours, the mixture was cooled to 23 °C and completely dissolved using 1 M NaOH (aq), and the mixture was then extracted with DCM (3 x 100 mL). The organic layer was washed with H_2O (2 x 50 mL), dried ($MgSO_4$), filtered, and concentrated on a vacuum rotary evaporator. The crude product was purified by precipitating from DCM (~20 mL) using excess diethyl ether. Alternatively, purification was carried out by column chromatography eluted with DCM/methanol (95:5) or DCM/acetone (7:3) if precipitation resulted in an impure mixture.

Observations: The reaction mixture liquefied during heating, and efficient stirring did not occur until liquefaction had occurred.

4-(2-Nitrophenyl)-4*H*-1,2,4-triazole (sm1)

The title compound was prepared on a 98 mmol scale according to the general procedure III. Purification by DCM-ether precipitation yielded the product as brown-orange powder in 51% yield (9.48 g, 49.9 mmol). Purification by column chromatography (silica, DCM/acetone 7:3, R_f = 0.22) also resulted in a pure product. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 8.30 (s, 2H), 8.13 (dd, *J* = 8.1 Hz, *J* = 1.3 Hz, 1H), 7.81 (td, *J* = 7.7 Hz, *J* = 1.4 Hz, 1H), 7.72 (td, *J* = 8.0 Hz, *J* = 1.3 Hz, 1H), 7.49 (dd, *J* = 7.8 Hz , *J* = 1.2 Hz, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCL_3$, 298 K): δ = 144.8, 142.9, 134.7, 131.3, 129.3, 127.1, 126.1. NMR Data is in accordance with literature.[64] HRMS (ESI) calcd, $[C_8H_6N_4O_2]H^+$ 191.0564; observed, 191.0559.

Section 3.8: General Procedure and Characterization Data for 1-Substituted-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium Salts

Catalytic Arylation of 4-(2-Nitrophenyl)-4*H*-1,2,4-triazole (sm1) General Procedure IV

4-(2-Nitrophenyl)-4*H*-1,2,4-triazole (1.0 equiv), diaryliodonium salt (1.0-1.1 equiv), copper(I) acetate (0.05 equiv), was also added to a round-bottomed flask and dissolved in acetonitrile (0.25 M). The flask was fitte with a reflux condenser, and the atmosphere was exchanged for argon. The solution was heated to reflux (82 °C) for 16 h with constant stirring.

Workup: The solvent was removed under vacuum, and the product was dissolved in a minimum amount of 9:1 DCM/acetone. This mixture was then stirred with slow addition

of diethyl ether until no more solid precipitated out. If further purification was needed, a silica column eluted with a DCM/acetone gradient (8:2 then 7:3) results in a pure product.

Observations: Overnight reaction times were necessary for the nitro-containing systems due to the deactivating effects of the nitro. Precipitation of product utilizing diethyl ether removed only small proportions of the 4-(2-nitrophenyl)-4*H*-1,2,4-triazole starting material. Column chromatography was required if considerable amounts of residual starting material were present.

Alkylation of 4-(2-Nitrophenyl)-4*H*-1,2,4-triazole (sm1) General Procedure V

4-(2-Nitrophenyl)-4*H*-1,2,4-triazole (1.0 equiv) and an alkyl bromide (equivalents varied) were loaded in a round-bottomed flask. Acetonitrile (2 M) was added and the flask was fitted with a reflux condenser, and heated to reflux (82 °C) with constant stirring overnight (16 h).

Workup: The product was concentrated under vacuum. The product was loaded onto a silica column using DCM and eluted initially with DCM/methanol (8:2). An alternative purification method involved precipitating the product from DCM by dropwise addition of diethyl ether.

Observations: Complete conversion of the 4-(2-nitrophenyl)-4*H*-1,2,4-triazole starting material was necessary if precipitation was to be considered a potential purification method.

1-Substituted-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium Salts

1-Benzyl-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium bromide (10n)

The title compound was prepared on a 10 mmol scale according to general procedure V using 1.1 equiv of benzyl bromide. Purification by precipitation from DCM using diethyl ether followed by column chromatography (silica, DCM/methanol 8:2, R_f = 0.42), yielded the product as a light yellow powder in 88% yield (3.19 g, 8.8 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 10.80 (s, 1H), 9.64 (s, 1H), 8.49 (dd, *J* = 8.2 Hz, *J* = 1.3 Hz, 1H), 8.13 (td, *J* = 8.0 Hz, *J* = 1.3 Hz, 1H), 8.09 (dd, *J* = 8.0 Hz, *J* = 2.0 Hz, 1H), 8.02 (td, *J* = 8.3 Hz, *J* = 2.0 Hz, 1H), 7.53 (dd, *J* = 8.0 Hz, *J* = 1.8 Hz, 2H), 7.51 – 7.43 (m, 3H), 5.84 (s, 2H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6, 298 K): δ =145.8, 144.0, 143.2, 135.7, 133.13, 132.9, 130.4, 129.1, 128.9, 128.9, 126.5, 125.3, 55.1. HRMS (ESI) calcd, $[C_{15}H_{13}N_4O_2]^+$ 281.1033; observed, 281.1026.

1-Isopropyl-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium bromide (10o)

The title compound was prepared on a 5 mmol scale according to general procedure V using 4 equiv of 2-bromopropane. Purification by precipitation from DCM using diethyl ether followed by column chromatography (silica, DCM/methanol 8:2, R_f = 0.30), yielded the product as a light yellow powder in 80% yield (1.26 g, 4.0 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 10.75 (s, 1H), 9.65 (s, 1H), 8.50 (dd, *J* = 8.2 Hz, *J* = 1.3 Hz, 1H), 8.14 (td, *J* = 7.9 Hz, *J* = 1.3 Hz, 1H), 8.09 (dd, *J* = 7.9 Hz, *J* = 1.9 Hz, 1H), 8.02 (td, *J* = 8.2 Hz, *J* = 1.9 Hz, 1H), 4.97 (hept, *J* = 6.6 Hz, 1H), 1.61 (d, *J* = 6.6 Hz, 6H); ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6, 298 K): δ = 145.3, 143.2, 142.6, 135.7, 133.1, 130.4, 126.5, 125.2, 55.8, 21.2. HRMS (ESI) calcd, $[C_{11}H_{13}N_4O_2]^+$ 233.1033; observed, 233.1027.

1-(But-3-yn-1-yl)-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium bromide (10p)

The title compound was prepared on a 5 mmol scale according to general procedure V using 1.5 equiv of 4-bromobut-1-yne. Purification by precipitation from DCM using diethyl ether followed by column chromatography (silica, DCM/methanol 8:2, R_f = 0.33), yielded the product as a light yellow powder in 81% yield (1.31 g, 4.1 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 10.80 (s, 1H), 9.69 (s, 1H), 8.50 (dd, *J* = 8.2 Hz, *J* = 1.4 Hz, 1H), 8.13 (td, *J* = 7.8 Hz, *J* = 1.4 Hz, 1H), 8.08-7.99 (dd, *J* = 8.0 Hz, *J* = 1.5 Hz), (td, *J* = 7.7 Hz, *J* = 1.5 Hz) 2H), 4.70 (t, *J* = 6.6 Hz, 2H), 3.06 (t, *J* = 2.6 Hz, 1H), 2.95 (td, *J* = 6.6 Hz, *J* = 2.6 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6, 298 K): δ = 145.5, 144.1, 143.2, 135.8, 133.2, 130.3, 126.6, 125.2, 79.1, 74.4, 50.6, 18.4. HRMS (ESI) calcd, $[C_{12}H_{11}N_4O_2]^+$ 243.0877; observed, 243.0870.

4-(2-Nitrophenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (10q)

The title compound was prepared on a 15.4 mmol scale according to general procedure IV using 1.5 equiv of diphenyliodonium trifluoromethanesulfonate. Purification by precipitation from DCM using diethyl ether followed by column chromatography (silica, DCM/acetone 7:3, R_f = 0.11), yielded the product as an off-white powder in 89% yield (5.70 g, 9.6 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.37 (s, 1H), 9.90 (s, 1H), 8.54 (dd, *J* = 8.2 Hz, *J* = 1.3 Hz, 1H), 8.18 (td, *J* = 7.7 Hz, *J* = 1.3 Hz, 1H), 8.13-8.04 (unresolved m, 2H), 8.02 (d, *J* = 7.6 Hz, 2H), 7.77 (t, *J* = 7.6 Hz, 2H), 7.70 (t, *J* = 7.4 Hz, 1H), ; ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6, 298 K): δ =146.0, 143.2, 142.8, 135.9, 134.6, 133.4, 131.0, 130.5, 130.3, 126.7, 125.0, 120.7. HRMS (ESI) calcd, $[C_{14}H_{11}N_4O_2]^+$ 267.0877; observed, 267.0870.

1-Mesityl-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (10r)

The title compound was prepared on a 10 mmol scale according to general procedure IV using 1.2 equiv of dimesityliodonium trifluoromethanesulfonate. Purification by precipitation from DCM using diethyl ether followed by column chromatography (silica, DCM/acetone 7:3, R_f = 0.2), yielded the product as an off-white powder in 82% yield (3.78 g, 8.2 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 10.95 (s, 1H), 9.90 (s, 1H), 8.56 (dd, *J* = 7.3 Hz, *J* = 1.3 Hz, 1H), 8.23 (dd, *J* = 7.9 Hz, *J* = 1.7 Hz, 1H), 8.18 (td, *J* = 7.9 Hz, *J* = 1.3 Hz, 1H), 8.07 (td, *J* = 7.3 Hz, *J* = 1.7 Hz, 1H) 7.23 (s, 2H), 2.37 (s, 3H), 2.16 (s, 6H); ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6, 298 K): δ =146.3, 145.9, 143.2, 141.8, 135.8, 134.8, 133.5, 130.8, 130.7, 129.5, 126.7, 125.1, 20.7, 16.9. HRMS (ESI) calcd, $[C_{17}H_{17}N_4O_2]^+$ 309.1346; observed, 309.1339.

1-(4-Methoxyphenyl)-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate(10s)

The title compound was prepared on a 10 mmol scale according to general procedure IV using 1.01 equiv of bis(4-methoxyphenyl)iodonium tetrafluoroborate. Purification by precipitation from DCM using diethyl ether followed by column chromatography (silica, DCM/acetone 7:3, R_f = 0.17), yielded the product as a light brown powder in 94% yield (3.615 g, 9.4 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.24 (s, 1H), 9.85 (s, 1H), 8.54 (dd, *J* = 8.2 Hz, *J* = 1.4 Hz, 1H), 8.18 (dd, *J* = 7.7 Hz, *J* = 1.4 Hz, 1H), 8.09 (td, *J* = 7.7 Hz, *J* = 1.5 Hz, 1H), 8.06 (td, *J* = 8.2 Hz, *J* = 1.5 Hz, 1H), 7.94 (d, *J* = 9.1 Hz, 2H), 7.30 (d, *J* = 9.1 Hz, 2H), 3.89 (s, 3H): ^{13}C{^{1}H} NMR (101 MHz,

DMSO-d_6, 298 K): δ = 160.9, 145.8, 143.2, 142.0, 135.9, 133.4, 130.3, 127.6, 126.7, 125.0, 122.5, 115.4, 55.9. HRMS (ESI) calcd, $[C_{15}H_{13}N_4O_3]^+$ 297.0982; observed, 297.0976.

1-(4-Fluorophenyl)-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (10t)

The title compound was prepared on a 5 mmol scale according to general procedure IV using 1.1 equiv of bis(4-fluorophenyl)iodonium trifluoromethanesulfonate. Purification by precipitation from DCM using diethyl ether followed by column chromatography (silica, DCM/acetone 7:3, R_f = 0.11), yielded the product as tan powder in 93% yield (2.02 g, 4.6 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.37 (s, 1H), 9.90 (s, 1H), 8.54 (d, J = 8.0 Hz, 1H), 8.18 (td, J = 7.6 Hz, J = 1.3 Hz, 1H), 8.13-8.03 (unresolved m, 4H), 7.65 (t, J = 8.6 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6, 298 K): δ = 163.3 (d, J_{C-F} = 248.5 Hz), 146.4, 143.7, 136.4, 133.9, 131.5 (d, J_{C-F} = 3.0 Hz), 130.7, 127.2, 125.4, 123.9 (d, J_{C-F} = 9.3 Hz), 117.9 (d, J_{C-F} = 23.7 Hz); ^{19}F NMR (376 MHz, DMSO-d_6) δ = -77.85, -109.51 . HRMS (ESI) calcd, $[C_{14}H_{10}FN_4O_2]^+$ 285.0782; observed, 285.0777

1-(4-Chlorophenyl)-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (10u)

The title compound was prepared on a 5 mmol scale according to general procedure IV using 1.1 equiv of bis(4-chlorophenyl)iodonium trifluoromethanesulfonate. Purification

by precipitation from DCM using diethyl ether followed by column chromatography (silica, DCM/acetone 7:3, R_f = 0.11), yielded the product as an off-white powder in 92% yield (2.07 g, 4.6 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.40 (s, 1H), 9.91 (s, 1H), 8.54 (d, *J* = 8.1 Hz, *J* = 1.3 Hz, 1H), 8.18 (t, *J* = 7.9 Hz, 1H), 8.10-8.02 (unresolved d, *J* = 9.0 Hz , 4H), 7.87 (d, *J* = 9.0 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6, 298 K): δ = 146.0, 143.2, 143.2, 135.9, 135.8, 133.5, 133.4, 130.5, 130.3, 126.8, 124.9, 122.6. HRMS (ESI) calcd, $[C_{14}H_{10}ClN_4O_2]^+$ 301.0487; observed, 301.0481.

1-Allyl-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium bromide (10v)

The title compound was prepared on a 5 mmol scale according to general procedure V using 1.1 equiv of allyl bromide. Purification by precipitation from DCM using diethyl ether followed by column chromatography (silica, DCM/methanol 4:1, R_f = 0.31), yielded the product as yellow powder in 87% yield (1.4 g, 4.4 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 10.69 (s, 1H), 9.66 (s, 1H), 8.50 (dd, *J* = 8.2 Hz, *J* = 1.4 Hz, 1H), 8.13 (td, *J* = 7.7 Hz, *J* = 1.4 Hz, 1H), 8.07 (dd, *J* = 7.9, *J* = 1.6 Hz, 1H), 8.02 (td, *J* = 7.7, *J* = 1.6 Hz, 1H), 6.14 (ddt, *J* = 16.5 Hz, *J* = 10.4 Hz, *J* = 6.0 Hz, 1H), 5.51-5.43 ((dd, *J* = 10.4 Hz, *J* = 1.2 Hz), (dd, *J* = 16.5 Hz, *J* = 1.2 Hz), 2H), 5.24 (d, *J* = 6.0 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6, 298 K): δ =146.0, 144.4, 143.7, 136.2, 133.6, 130.9, 130.4, 127.0, 125.7, 121.9, 54.5. HRMS (ESI) calcd, $[C_{11}H_{11}N_4O_2]^+$ 231.0877; observed, 231.0875.

1-(2-Methylallyl)-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium bromide (10w)

The title compound was prepared on a 5 mmol scale according to general procedure V using 1.1 equiv of 2-methyl-3-bromoprop-1-ene. Purification by precipitation from DCM

using diethyl ether followed by column chromatography (silica, DCM/methanol 4:1, R_f = 0.28), yielded the product as yellow powder in 91% yield (1.472 g, 4.5 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 10.71 (s, 1H), 9.66 (s, 1H), 8.51 (dd, *J* = 8.2 Hz, *J* = 1.4 Hz, 1H), 8.13 (td, *J* = 7.6 Hz, *J* = 1.5 Hz, 1H), 8.08 (dd, *J* = 7.9 Hz, *J* = 1.7 Hz, 1H), 8.02 (td, *J* = 7.4 Hz, *J* = 1.6 Hz, 12H), 5.20 (s, 2H), 5.17 (s, 1H), 5.05 (s, 1H), 1.78 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6, 298 K): δ = 145.7, 144.3, 143.3, 137.7, 135.8, 133.2, 130.4 126.5, 125.2, 116.4, 57.2, 19.4. HRMS (ESI) calcd, $[C_{12}H_{13}N_4O_2]^+$ 245.1033; observed, 245.1032.

Section 3.9. General Procedure, Analysis, and Characterization Data for 1-Substituted-(2-ammoniophenyl)-4*H*-1,2,4-triazol-1-ium Salts

Compounds in this section readily decompose when not existing as ammonium salts and must be acidified within the day to minimize decomposition. Amines were found to decompose on a silica column, although the ammonium salts were never tried. Reduction of the nitro group by H_2 and Pd/C worked successfully for benzyl substituted triazolium with an isolated yield of 63 % on a 2.5 mmol scale, but the palladium-*c*atalyzed reduction of aryl-substituted triazolium salts result in ~0% conversion.

Reduction of Aryl NO_2 Triazolium salts (VI)

2-Nitrophenyl-1,2,4-triazolium salts (1.0 equiv) were mixed with Fe(s) (10 equiv) and NH_4Cl (10 equiv) in a round-bottomed flask, followed by EtOH/H_2O (9:1, 0.02 M). the flask was fitted with a condenser and sealed with a septum. The atmosphere was

exchanged for argon, and the mixture was stirred at 50 °C for 4 hours with constant stirring.

Workup: Immediately after the reaction was complete, the mixture was diluted with 3x the volume of brine and extracted with DCM (3 x 50 mL). The aqueous layer was further diluted with 1x the volume of saturated $NaHCO_3$, and the mixture was further extracted with DCM (3 x 50 mL). The aqueous layer was further diluted with 1x the volume of 1 M NaOH, and the mixture was extracted a third and final time with DCM (3 x 50mL). The organic layers were combined, dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to yield a crude product. The product was dissolved in a DCM/acetone mixture (1:1), and a stir bar was added to the flask. With stirring, 4 M HCl in dioxane was added dropwise until 4 equiv of HCl had been added. Diethyl ether was added dropwise until no more solid precipitated. The system was allowed to cool to 0 °C overnight. The solution was decanted, leaving the ammonium salt to be dried under high vacuum.

Further purification of this salt was carried out by precipitating it from 6 mL of methanol/acetone 1:1 with excess diethyl ether or by washing with a 5:1 mixture of DCM/acetone.

Observations: 4-(2-aminophenyl)-4*H*-1,2,4-triazol-1-ium salts were discovered to be unstable if not converted into ammonium salts. The ammonium salt was potentially challenging to purify by column chromatography and by solvent extraction. Thus all 1-substituted-4-(2-aminophenyl)-4*H*-1,2,4-triazol-1-ium salts were precipitated as ammonium salts. If left open to the air, the ammonium salts absorb water and decompose.

Testing of Ammonium Salt Ion Composition

Exact amounts of the benzyl (55.29 mg), *para*-fluorophenyl (43.31 mg), *para*-methoxyphenyl (56.97 mg), and *para*-chlorophenyl (25.77 mg) 4-(2-ammoniophenyl)-4*H*-1,2,4-triazol-1-ium salts were mixed with an exact amount of a fluorine-*c*ontaining standard. Sodium trifluoromethylsulfonate was chosen for the benzyl and *para*-methoxyphenyl salts (22.67 mg and 25.50 mg), respectively. Sodium tetrafluoroborate was chosen for *para*-fluorophenyl and *para*-chlorophenyl salts (106.31 mg and 49.08 mg), respectively. The samples were dissolved in enough DMSO-d_6 to create a homogeneous solution. The ^{19}F NMR analyses indicated no or only trace amounts of the fluorine ions other than the standard for each 4-(2-ammoniophenyl)-4*H*-1,2,4-triazol-1-ium salts. The solutions were then diluted in 20 mL of H_2O/methanol (1:1). Silver nitrate 2 g was dissolved in 40 mL of H_2O/methanol (1:1), and 10 mL of this solution was added to each sample, causing the silver halide to precipitate. Approximately 10 mL of methanol was added to assist in dissolving the organic portion of the molecules. The solutions were centrifuged in vials, and the supernatant was decanted from the pellet. The pellet was washed with methanol and centrifuged again. The supernatant was decanted from the pellet again and was then dried under high vacuum. The following isolated yields of silver chloride were obtained (with theoretical yields calculated for the reaction of dichloride anion with silver nitrate) benzyl (98.0%), *para*-fluorophenyl (101.42%), *para*-methoxyphenyl (93.64%), and *para*-chlorophenyl (95.71%). These results were within experimental error and implied that each of the 1-substituted-4-(2-ammoniophenyl)-4*H*-1,2,4-triazol-1-ium salts exist as the dichloride anion.

Characterization data for the 4-(2-ammoniophenyl)-4*H*-1,2,4-triazol-1-ium chlorides

4-(2-Ammoniophenyl)-1-benzyl-4*H*-1,2,4-triazol-1-ium chloride (11n)

The title compound was prepared on a 5.70 mmol scale according to general procedure VI. Purification by precipitating as the ammonium salt from DCM/ether (1:5) then washing the solid with DCM/acetone (5:1) yielded the product as a beige solid (95%, 5.4 mmol, 1.75 g). (DCM/acetone (4:1), R_f = 0.36), ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.00 (s, 1H), 9.52 (s, 1H), 7.59 (dd, *J* = 7.6 Hz, *J* = 1.8 Hz, 2H), 7.46 – 7.39 (m, 4H), 7.34 (td, *J* = 7.6 Hz, *J* = 1.5 Hz, 1H) 7.07 (dd, *J* = 8.3 Hz, *J* = 1.2 Hz, 1H), 6.81 (td, *J* = 7.6 Hz, *J* = 1.2 Hz, 1H), 5.71 (s, 2H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6, 298 K): δ = 145.4, 143.9, 142.2, 133.0, 131.9, 129.4, 128.9, 128.8, 127.8, 117.9, 117.8, 117.6, 54.9. HRMS (ESI) calcd, $[C_{15}H_{15}N_4]^+$ 251.1291; observed, 251.1285.

4-(2-Ammoniophenyl)-1-isopropyl-4*H*-1,2,4-triazol-1-ium chloride (11o)

The title compound was prepared on a 3.39 mmol scale according to general procedure VI. Purification by precipitating as the ammonium salt from DCM/ether (1:5) then washing the solid with DCM/acetone (5:1) yielded the product as an off-white solid (99.8%, 3.3 mmol, 932 mg). (DCM/acetone (4:1), R_f = 0. 18), ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 10.63 (s, 1H), 9.47 (s, 1H), 7.36 (dd, *J* = 8.0 Hz, *J* = 1.4 Hz, 1H), 7.33 (td, *J* = 7.7 Hz, *J* = 1.4 Hz, 1H), 6.99 (dd, *J* = 8.0 Hz, *J* = 1.3 Hz, 1H), 6.77 (td, *J* = 7.7 Hz, *J* =1.3 Hz, 1H), 4.84 (hept, *J* = 6.6 Hz, 1H), 1.59 (d, *J* = 6.6 Hz, 6H); ^{13}C{^{1}H}

NMR (101 MHz, DMSO-d_6, 298 K): δ = 144.9, 143.9, 142.4, 141.6, 131.9, 127.9, 118.2, 118.1, 55.4, 21.2. HRMS (ESI) calcd, $[C_{11}H_{15}N_4]^+$ 203.1291; observed, 203.1288.

4-(2-Ammoniophenyl)-1-(but-3-yn-1-yl)-4*H*-1,2,4-triazol-1-ium chloride (11p)

The title compound was prepared on a 3.31 mmol scale according to general procedure VI. Purification by precipitating as the ammonium salt from DCM/ether (1:5) then washing the solid with DCM/acetone (5:1) yielded the product as off-white solid (99.8% yield, 3.3 mmol, 943 mg). (DCM/acetone 4:1, R_f = 0.15), ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 10.77 (s, 1H), 9.52 (s, 1H), 7.35-7.28 (m, 2H), 6.98 (dd, *J* = 8.2 Hz, *J* =1.3 Hz, 1H), 6.74 (td, *J* = 7.5 Hz, *J* = 1.3 Hz, 1H), 4.59 (t, *J* = 7.2 Hz, 2H), 3.10 (t, *J* = 2.7 Hz, 1H), 2.94 (td, *J* = 7.2 Hz, *J* = 2.7 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6, 298 K): δ = 145.2, 144.0, 143.5, 131.9, 127.4, 117.1, 116.8, 116.6, 79.7, 74.2, 50.2, 18.3. HRMS (ESI) calcd, $[C_{12}H_{13}N_4]^+$ 213.1135; observed, 213.1130.

4-(2-Ammoniophenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium chloride (11q)

The title compound was prepared on a 2.0 mmol scale according to general procedure VI. Purification by precipitating as the ammonium salt from DCM/ether (1:5) then washing the solid with DCM/acetone (5:1) yielded the product as an off-white solid (78%, 1.5 mmol, 479 mg). (DCM/acetone (4:1), R_f = 0.28), ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.51 (s, 1H), 9.76 (s, 1H), 8.06 (d, *J* = 7.1 Hz, 2H), 7.72 (t, *J* = 7.6 Hz, 2H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.49 (dd, *J* = 7.9 Hz, *J* = 1.5 Hz, 1H), 7.38 (td, *J* = 7.7 Hz, *J* = 1.5 Hz, 1H), 7.09 (dd, *J* = 7.9 Hz, *J* = 1.0 Hz, 1H), 6.84 (td, *J* = 7.7 Hz, *J* = 1.0 Hz, 1H); ^{13}C{^{1}H} NMR (101

MHz, DMSO-d_6, 298 K): δ = 145.9, 143.1, 142.9, 135.6, 132.5, 131.0, 130.6, 128.3, 121.3, 118.2, 118.0, 117.9. HRMS (ESI) calcd, $[C_{14}H_{13}N_4]^+$ 237.1135; observed, 237.1130.

4-(2-Ammoniophenyl)-1-mesityl-4*H*-1,2,4-triazol-1-ium chloride (11r)

The title compound was prepared on a 2.55 mmol scale according to general procedure VI. Purification by precipitating as the ammonium salt from DCM/ether (1:5) then washing the solid with DCM/acetone (5:1) yielded the product as an off-white solid (43%, 1.09 mmol, 383 mg). (DCM/acetone (4:1), R_f = 0.34), ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.01 (s, 1H), 9.84 (s, 1H), 7.51 (dd, *J* = 7.9 Hz, *J* = 1.5 Hz, 1H), 7.37 (td, *J* = 7.8 Hz, *J* = 1.5 Hz, 1H), 7.18 (s, 2H), 7.05 (d, *J* = 8.2 Hz, 1H), 6.82 (td, *J* = 7.6 Hz, *J* = 1.0 Hz, 1H), 2.35 (s, 3H), 2.22 (s, 6H); ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6, 298 K): δ = 146.04, 145.25, 142.40, 141.22, 134.80, 132.05, 131.09, 129.61, 128.06, 118.26, 117.92, 117.72, 20.71, 17.43. HRMS (ESI) calcd, $[C_{17}H_{19}N_4]^+$ 279.1604; observed, 279.1598.

4-(2-Ammoniophenyl)-1-(4-methoxyphenyl)-4*H*-1,2,4-triazol-1-ium chloride (11s)

The title compound was prepared on a 5 mmol scale according to general procedure VI. Purification by precipitating as the ammonium salt from DCM/ether (1:5) then washing the solid with DCM/acetone (5:1) yielded the product as tan powder (81%, 4.03 mmol, 1.37 g). (DCM/acetone (4:1), R_f = 0.31), ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.28 (s, 1H), 9.68 (s, 1H), 7.95 (d, *J* = 9.1 Hz, 2H), 7.45 (dd, *J* = 8.1 Hz, *J* = 1.5 Hz, 1H), 7.36 (td, *J* = 7.7 Hz, *J* = 1.5 Hz, 1H), 7.26 (d, *J* = 9.1 Hz, 2H), 7.03 (dd, *J* = 8.1 Hz, *J* = 1.1 Hz, 1H), 6.80 (td,

J = 7.7 Hz, *J* = 1.1 Hz, 1H), 3.87 (s, 3H); $^{13}C\{^{1}H\}$ NMR (101 MHz, DMSO-d_6, 298 K): δ = 160.6, 145.4, 143.2, 141.8, 132.1, 128.2, 127.8, 122.6, 117.3, 117.1, 116.8, 115.2, 55.9. HRMS (ESI) calcd, $[C_{15}H_{15}N_4O]^+$ 267.1240; observed, 267.1234.

4-(2-Ammoniophenyl)-1-(4-fluorophenyl)-4*H*-1,2,4-triazol-1-ium chloride (11t)

The title compound was prepared on a 2 mmol scale according to general procedure VI. Purification by precipitating as the ammonium salt from DCM/ether (1:5) then washing the solid with DCM/acetone (5:1) yielded the product as an off-white powder (77%, 1.55 mmol, 506 mg). (DCM/acetone (4:1), R_f = 0.31), ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 11.42 (s, 1H), 9.73 (s, 1H), 8.10 (dd, *J* = 9.1 Hz, *J* = 4.6 Hz, 2H), 7.61 (t, *J* = 8.7 Hz, 2H), 7.45 (dd, *J* = 7.8 Hz, *J* = 1.2 Hz, 1H), 7.37 (ddd, *J* = 8.7 Hz, *J* = 7.3 Hz, *J* = 1.5 Hz, 1H), 7.03 (d, *J* = 8.3 Hz, *J* = 0.8 Hz, 1H), 6.81 (t, *J* = 7.6 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (101 MHz, DMSO-d_6, 298 K): δ = 162.6 (d, $J_{C\text{-}F}$ = 248.0 Hz), 145.5, 143.2, 142.8, 132.1, 131.6 (d, $J_{C\text{-}F}$ = 3.0 Hz), 127.8, 127.7, 123.5 (d, $J_{C\text{-}F}$ = 9.3 Hz), 117.3, 117.1, 116.9 (d, $J_{C\text{-}F}$ = 14.3 Hz); ^{19}F NMR (376 MHz, DMSO-d_6) δ = -110.23. HRMS (ESI) calcd, $[C_{14}H_{12}FN_4]^+$ 255.1041; observed, 255.1036.

4-(2-Ammoniophenyl)-1-(4-*c*hlorophenyl)-4*H*-1,2,4-triazol-1-ium chloride (11u)

The title compound was prepared on a 2.0 mmol scale according to general procedure VI. Purification by precipitating as the ammonium salt from DCM/ether (1:5) then washing the solid with DCM/ acetone (5:1) yielded the product as an off-white powder (54%, 1.07 mmol, 371 mg). (DCM/acetone (4:1), R_f = 0.31), ^{1}H NMR (400 MHz, DMSO-d_6, 298 K):

δ = 11.53 (s, 1H), 9.76 (s, 1H), 8.09 (d, *J* = 8.9 Hz, 2H), 7.83 (d, *J* = 8.9 Hz, 2H), 7.48 (dd, *J* = 8.0 Hz, *J* = 0.8 Hz, 1H), 7.38 (ddd, *J* = 7.8 Hz, *J* = 1.3 Hz, *J* = 1.0 Hz, 1H), 7.07 (d, *J* = 8.2 Hz, 1H), 6.84 (t, *J* = 7.6 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (101 MHz, DMSO-d_6, 298 K): δ =145.6, 143.1, 142.6, 135.0, 133.9, 132.2, 130.2, 127.9, 127.8, 122.7, 117.7, 117.4. HRMS (ESI) calcd, $[C_{14}H_{12}ClN_4]^+$ 271.0745; observed, 271.0741.

1-Allyl-4-(2-ammoniophenyl)-4*H*-1,2,4-triazol-1-ium chloride (11v)

The title compound was prepared on a 2.0 mmol scale according to general procedure VI. Purification by precipitating as the ammonium salt from DCM/ether (1:5) then washing the solid with DCM/acetone (5:1) yielded the product as an off-white powder (76%, 1.52 mmol, 415 mg). (DCM/acetone (4:1), R_f = 0.20), ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 10.77 (s, 1H), 9.52 (s, 1H), 7.41 – 7.33 ((dd, *J* = 7.9 Hz, *J* = 1.3 Hz), (dd, *J* = 7.4 Hz, *J* = 1.5 Hz), 2H), 7.07 (dd, *J* = 8.2 Hz, *J* = 1.2 Hz, 1H), 6.83 (td, *J* = 7.6 Hz, *J* = 1.2 Hz, 1H), 6.13 (ddt, *J* = 17.1 Hz, *J* = 10.3 Hz, *J* = 6.2 Hz, 1H), 5.56 (dd, *J* = 17.1 Hz, *J* = 1.2 Hz, 1H), 5.45 (dd, *J* = 10.3 Hz, *J* = 1.2 Hz, 1H), 5.12 (d, *J* = 6.2 Hz, 2H); $^{13}C\{^{1}H\}$ NMR (101 MHz, DMSO-d_6, 298 K): δ = 145.2, 143.8, 141.9, 131.9, 130.0, 127.8, 121.6, 118.0, 117.9, 117.8, 53.9. HRMS (ESI) calcd, $[C_{11}H_{13}N_4]^+$ 201.1135; observed, 201.1134.

4-(2-Ammoniophenyl)-1-(2-methylallyl)-4*H*-1,2,4-triazol-1-ium chloride (11w)

The title compound was prepared on a 2.05 mmol scale according to general procedure VI. Purification by precipitating as the ammonium salt from DCM/ether (1:5) then washing the solid with DCM/acetone (5:1) yielded the product as an off-white powder

(99%, 2.01 mmol, 580 mg). (DCM/acetone (4:1), R_f = 0.26), ^{1}H NMR (400 MHz, DMSO-d_6, 298 K): δ = 10.87 (s, 1H), 9.59 (s, 1H), 7.46 (dd, *J* = 8.0 Hz, *J* = 1.4 Hz, 1H), 7.39 (td, *J* = 7.8 Hz, *J* = 1.4 Hz, 1H), 7.14 (dd, *J* = 8.0 Hz, *J* = 1.1 Hz, 1H), 6.89 (td, *J* = 7.8 Hz, *J* = 1.1 Hz, 1H), 5.16 (s, 1H), 5.13 (s, 1H), 5.05 (s, 2H), 1.80 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6, 298 K): δ = 145.3, 144.1, 141.0, 137.6, 132.0, 127.9, 126.0, 118.6, 118.5, 117.0, 57.2, 19.9. HRMS (ESI) calcd, $[C_{12}H_{15}N_4]^+$ 215.1291; observed, 215.1290.

Section 3.10: General Procedure and Characterization Data for 9*H*-Benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium Salts

2.5 Synthesis of benzoimidazole triazolium salts (General Procedure VII)

Iodine (1.5-2.0 equiv) and freshly washed 1-substituted-4-(2-ammoniophenyl)-4*H*-1,2,4-triazol-1-ium chloride (1.0 equiv) were added to a round-bottomed flask, which was then equipped with a condenser. The solids were suspended in DCM (0.02 M), and then DBU (4.0 equiv) was injected. The atmosphere was exchanged for argon, and the reaction mixture was allowed to stir at reflux for 4 h.

Workup: The mixture was concentrated by rotary evaporation. The product was loaded onto a silica column and eluted using hexane-acetone (4:1) with an incremental 5% increase in acetone until the compound eluted, which was usually around 20-25% acetone. A 1:1 mixture of hexanes/acetone was used to force any remaining compound from the silica column. TLC was used to determine pure fractions, which were then collected and concentrated by rotary evaporation. The purified fractions were then eluted through a 30 cm x 2 cm column loaded with the ion exchange resin, amberlyst 15 (eluted

50 mL MeOH, 50 mL H_2O, 50 mL 1M(aq) $NH_4^+OTf^-$, 50 mL H_2O) Silver nitrate test was carried out on test samples to ensure complete conversion to triflate.

Observations: LCMS analysis of test reaction at 1 h, 2 h, 4 h, and 8 h, indicated that complete consumption of the starting material had been reached at 1 h. However, reactions were allowed to react for 4 hours to ensure complete conversion for deactivated systems.

Characterization data for 9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium salts

1-Benzyl-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (12n)

The title compound was prepared on a 1.13 mmol scale according to general procedure VII. Purification by column chromatography (silica, hexane/acetone (4:1), R_f = 0.14), followed by elution through an ion exchange column, yielded the product as an off-white powder (46%, 0.52 mmol, 208 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ = 8.32 (s, 1H), 7.72 (d, *J* = 8.2 Hz, 1H), 7.66 (d, *J* = 8.0 Hz, 1H), 7.46 (dd, *J* = 8.0 Hz, *J* = 1.6 Hz, 2H), 7.41 (td, *J* = 7.8 Hz, *J* = 1.1 Hz, 1H), 7.38 – 7.30 (unresolved m, 3H), 7.21 (td, *J* = 7.8 Hz, *J* = 0.8 Hz, 1H), 5.44 (s, 2H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$, 298 K) δ = 153.3, 149.3, 135.20, 129.0, 128.5, 128.4, 127.3, 125.3, 125.1, 119.8, 118.7, 111.3, 52.1. HRMS (ESI) calcd, $[C_{15}H_{14}N_4]^+$ 249.1135; observed, 249.1134.

1-Isopropyl-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (12o)

The title compound was prepared on a 1.0 mmol scale according to general procedure VII. Purification by column chromatography (silica, hexane/acetone (4:1), R_f = 0.18), followed by elution through an ion exchange column, yielded the product as an off-white powder (63%, 0.63 mmol, 220 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ = 8.79 (s, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.81 (d, *J* = 8.3 Hz, 1H), 7.57 (td, *J* = 7.9 Hz, *J* = 1.1 Hz, 1H), 7.46 (td, *J* = 7.7 Hz, *J* = 1.1 Hz, 1H), 5.07 (hept, *J* = 6.6 , 1H), 1.66 (d, *J* = 6.6 Hz, 6H); ^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$, 298 K) δ = 145.2, 136.9, 130.0, 128.5, 124.5, 121.9, 115.8, 113.3, 54.3, 21.4. HRMS (ESI) calcd, $[C_{11}H_{13}N_4]^+$ 201.1135; observed, 201.1134.

1-(But-3-yn-1-yl)-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (12p)

The title compound was prepared on a 1.0 mmol scale according to general procedure VII. Purification by column chromatography (silica, hexane/acetone (7:3), R_f = 0.33), followed by elution through an ion exchange column, yielded the product as tan powder (53%, 0.53 mmol, 190 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ = 8.80z (s, 1H), 7.92 (d, *J* = 8.2 Hz, 1H), 7.79 (d, *J* = 8.3 Hz, 1H), 7.60 (t, *J* = 7.6 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 1H), 4.67 (t, *J* = 6.3 Hz, 2H), 2.92 (td, *J* = 6.3 Hz, *J* = 2.6 Hz, 2H), 1.97 (t, *J* = 2.6 Hz, 1H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$, 298 K) δ = 146.6, 137.0, 130.4, 128.7, 124.7, 122.1, 115.9, 113.3, 78.4, 72.3, 49.2, 19.1. HRMS (ESI) calcd, $[C_{12}H_{11}N_4]^+$ 211.0978; observed, 211.0979.

1-Phenyl-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (12q)

The title compound was prepared on a 1.2 mmol scale according to general procedure VII. Purification by column chromatography (silica, hexane/acetone (4:1), R_f = 0.35), followed by elution through a ion exchange column, yielded the product as off-white powder (20%, 0.24 mmol, 90 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ = 8.43 (s, 1H), 8.25 (d, *J* = 8.0 Hz, 2H), 7.81 (d, *J* = 8.2 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.54 (t, *J* = 8.0 Hz, 2H), 7.44 (td, *J* = 7.8 Hz, *J* = 1.1 Hz, 1H), 7.31 – 7.22 (Unresolved t, 1H), 7.31-7.22 (Unresolved t, 1H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$, 298 K) δ = 151.0, 149.2, 137.5, 129.6, 127.9, 125.8, 125.5, 124.4, 120.6, 119.2, 117.5, 111.3. HRMS (ESI) calcd, $[C_{14}H_{11}N_4]^+$ 235.0978; observed, 235.0978

1-Mesityl-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (12r)

The title compound was prepared on a 1.32 mmol scale according to general procedure VII. Purification by column chromatography (silica, hexane/acetone (4:1), R_f = 0.32), followed by elution through an ion exchange column, yielded the product as an off-white powder (39%, 0.52 mmol, 221 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ = 8.47 (s, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.67 (d, *J* = 8.2 Hz, 1H), 7.39 (td, *J* = 7.7 Hz, *J* = 1.2 Hz, 1H), 7.21 (td, *J* = 7.7 Hz, *J* = 1.1 Hz, 1H), 7.00 (s, 2H), 2.34 (s, 3H), 2.10 (s, 6H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$, 298 K) δ = 153.5, 150.7, 140.1, 136.8, 131.5, 129.5, 127.7, 125.5, 125.1, 119.5, 119.3, 111.2, 21.3, 17.9. HRMS (ESI) calcd, $[C_{17}H_{17}N_4]^+$ 277.1448; observed, 277.1447.

1-(4-Methoxyphenyl)-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (12s)

The title compound was prepared on a 1.15 mmol scale according to general procedure VII. Purification by column chromatography (silica, hexane/acetone (4:1), R_f = 0.27), followed by elution through an ion exchange column, yielded the product as a white powder (24%, 0.27 mmol, 112 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ = 8.40 (s, 1H), 8.12 (d, *J* = 9.1 Hz, 2H), 7.78 (d, *J* = 8.2 Hz, 1H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.42 (ddd, *J* = 8.2 Hz, *J* = 7.5 Hz, *J* = 1.1 Hz, 1H), 7.23 (ddd, , *J* = 8.0 Hz, *J* = 7.8 Hz, *J* = 1.0 Hz, 1H), 7.05 (d, *J* = 9.1 Hz, 2H), 3.86 (s, 3H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$, 298 K) δ = 157.6, 151.6, 150.3, 131.3, 127.2, 125.3, 124.8, 120.1, 119.5, 119.1, 114.8, 111.1, 55.8. HRMS (ESI) calcd, $[C_{15}H_{13}N_4O]^+$ 265.1084; observed, 265.1083.

1-(4-Fluorophenyl)-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (12t)

The title compound was prepared on a 1.34 mmol scale according to general procedure VII. Purification by column chromatography (silica, hexane/acetone (4:1), R_f = 0.36), followed by elution through an ion exchange column, yielded the product as a white powder (32%, 0.43 mmol, 172 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ = 8.43 (s, 1H), 8.23 – 8.17 (m, *J* = 9.1 Hz, *J* = 7.0 Hz, *J* = 6.8 Hz, 2H), 7.79 (d, *J* = 8.2 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.44 (td, *J* = 8.2 Hz, *J* = 1.0 Hz, 1H), 7.29 – 7.18 (m, 3H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$, 298 K) δ = 160.4 (d, $J_{C\text{-}F}$ = 245.5 Hz), 151.3, 149.9, 133.9 (d, $J_{C\text{-}F}$ = 2.9 Hz), 127.8, 125.5, 124.7, 120.5, 119.5, 119.2 (d, $J_{C\text{-}F}$ = 8.2 Hz), 116.4 (d, $J_{C\text{-}F}$ = 23.2 Hz), 111.2; ^{19}F NMR (376

MHz, CDCl) δ = -78.52, -116.51. HRMS (ESI) calcd, $[C_{14}H_{10}FN_4]^+$ 253.0884; observed, 253.0884.

1-(4-Chlorophenyl)-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (12u)

The title compound was prepared on a 1.33 mmol scale according to general procedure VII. Purification by column chromatography (silica, hexane/acetone (4:1), R_f = 0.43), followed by elution through an ion exchange column, yielded the product as a tan powder 12% yield, 0.16 mmol, 68 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ =8.43 (s, 1H), 8.18 (d, *J* = 8.9 Hz, 2H), 7.79 (d, *J* = 8.3 Hz, 1H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.49 (d, *J* = 8.9 Hz, 2H), 7.44 (t, *J* = 7.9 Hz, 2H), 7.26 (t, *J* = 7.9 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$, 298 K) δ = 151.1, 149.6, 136.2, 131.1, 129.7, 128.0, 125.7, 124.6, 120.8, 119.5, 118.7, 111.3. HRMS (ESI) calcd, $[C_{14}H_{10}ClN_4]^+$ 269.0589; observed, 269.0590.

1-Allyl-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (12v)

The title compound was prepared on a 1.0 mmol scale according to general procedure VII. Purification by column chromatography (silica, hexane/acetone (4:1), R_f = 0.14), followed by elution through an ion exchange column, yielded the product as an off-white powder (43%, 0.43 mmol, 148 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ = 8.54 (s, 1H), 7.77 (d, *J* = 8.1 Hz, 1H), 7.71 (d, *J* = 8.3 Hz, 1H), 7.46 (td, *J* = 7.5 Hz, *J* = 1.0 Hz, 1H), 7.30 (td, *J* = 7.4 Hz, *J* =1.0 Hz, 1H), 6.05 (ddt, *J* = 17.0 Hz, *J* = 10.1 Hz, *J* = 6.1 Hz, 2H), 5.47 (dd, *J* = 17.0 Hz, *J* = 1.1 Hz, 1H), 5.40 (dd, *J* = 10.1 Hz, *J* = 1.1 Hz, 1H), 4.95 (d, *J* = 6.1 Hz, 2H);

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$, 298 K) δ = 148.7, 141.7, 129.3, 129.3, 127.3, 123.3, 122.7, 121.8, 116.8, 112.7, 52.0. HRMS (ESI) calcd, $[C_{11}H_{11}N_4]^+$ 199.0978; observed, 199.0978.

1-(2-Methylallyl)-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (12w)

The title compound was prepared on a 1.0 mmol scale according to general procedure VII. Purification by column chromatography (silica, hexane/acetone (4:1), R_f = 0.21), followed by elution through ion exchange column, yielded the product as an off-white powder (35%, 0.35 mmol, 125 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ = 8.83 (s, 1H), 7.93 (d, *J* = 8.2 Hz, 1H), 7.79 (d, *J* = 8.2 Hz, 1H), 7.57 (t, *J* = 8.2 Hz, 1H), 7.47 (t, *J* = 8.2 Hz, 1H), 5.13 (s, 1H), 5.11 (s, 1H), 5.00 (s, 2H), 1.80 (s, 3H); ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$, 298 K) δ = 146.3, 137.1, 136.7, 130.2, 128.7, 124.6, 122.1, 117.6, 116.0, 113.3, 56.1, 20.0. HRMS (ESI) calcd, $[C_{12}H_{13}N_4]^+$ 213.1135; observed, 213.1135.

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CHAPTER IV

CONCLUSION

We have developed novel methods for synthesizing triazole-containing heterocycles. Beginning from amines, we were able to access novel 1,4-disubstituted-1,2,4-triazolium salts rapidly through a two-step synthesis, first progressing through the 4-substituted-1,2,4-triazoles, and finally using a copper-catalyzed *N*-arylation to access the final product. The 1,2,4-triazole formation progressed in low to moderate yields (7.4-73%), but was considered acceptable due to the low cost of the starting materials. The copper-catalyzed arylation progressed in higher yields; triazoles containing heterocycles, aliphatic groups, sterically hindered aryl groups, and haloaryl groups were all arylated with moderate to excellent yields (58-99%). We were also able to introduce various aryl groups at this late stage, including electron-withdrawing, electron-donating, sterically hindered, fluorine-containing, and non-functionalized aryl groups. All resulted in moderate to high yields (52-96%). Arylating various triazoles with a mesityl group resulted in the formation of the desired products in moderate yields (54-86%). These yields were acceptable compared to the 8% yield we obtained when the compounds were synthesized via the traditional method.

The preparation of unsymmetrically substituted electron-rich carbene precursors, sterically hindered electron-poor 1,2,4-triazolium salts, and electron-rich pyrimidine derivatives were realized cleanly in moderate to high yields (53-98%). 1,4-Substituted-1,2,4-triazolium salts containing a mesityl group were challenging to separate from the starting materials via column chromatography, and incorporation of heterocycles such as pyridine and pyrimidine caused the resulting 1,4-substituted-1,2,4-triazolium salt to decompose on or strongly bond to the silica gel. Despite occasional difficulties in purification, our copper-catalyzed arylation allows access to previously unobtainable, unsymmetrically substituted triazolium precatalysts and ligands, with the potential to easily vary the steric and electronic parameters of the resulting NHCs. In the future, we plan to synthesize 1,2,4-triazole containing transition metal complexes, varying the steric and electronic effects around the metal center; we hope to discover an efficient catalyst for the Suzuki, Heck, or Sonogashira coupling reaction. We also plan to determine the organocatalytic efficiency of our synthesized 1,4-disubstitued-1,2,4-triazolium salts for the benzoin condensation or the Stetter reaction. Our method also allows for 1,2,4-triazolium salts to become more abundant in research, potentially elucidating new reactions and more efficient methods.

We set out to synthesize various 9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium triflates via iodine promoted C–H activation. Starting from 4-(2-nitrophenyl)-1,2,4-triazole, we synthesized several 4-(2-nitrophenyl)-1-(aryl)-1,2,4-triazolium salts in moderate to high yields (82-94%) and 4-(2-nitrophenyl)-1-(alkyl)-1,2,4-triazolium bromides also in moderate to high yields (80-91%). The 4-(2-nitrophenyl)-1-substituted-1,2,4-triazolium salts were first reduced by iron(0) under acidic conditions and then

isolated and stored as the HCl derivative. We were able to isolate various 4-(2-ammoniophenyl)-[1,2,4]-triazol-1-ium chlorides in moderate to high yields (42-99%). By subjecting these substrates to our optimized conditions, we found that the C–H activation progressed in low to moderate yields (12-63%). Aliphatic substituted triazoles cyclized with higher yields (34-63%), with groups including alkenes and alkynes being tollerated.. Aryl-substituted triazoles had much lower yields (12-39%), with the *para*-chlorophenyl and unsubstituted phenyl systems giving the lowest yields: 12% and 19%, respectively. *Para*-trifluoromethyl phenyl substituted triazolium salts failed to cyclize and resulted in decomposition instead, implying that strongly electron-withdrawing substituents are not tolerated. We observed that the 4-(2-nitrophenyl)-1-phenyl-[1,2,4]-triazol-1-ium triflate underwent reductive cyclization more readily. Despite the lower than desired yields, this method allows for a relatively efficient and straightforward method for the acquisition of novel substituted 9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium salts. Further development of the method would be necessary to derive a more generalized reaction. However, optimization for specialized substrates, better solvent-substrate pairing, and additives to stabilize the amine could increase isolated yields. Testing the biological activity of our 9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium salts against various bacteria, fungus, viruses, and tumors/ cancers would be the most logical next course of action. We could also further functionalize our structural motif and determine these substrates' biological activity. Structure-activity relationship studies could be undertaken if we find that our imidazo triazolium salts display potent biological activity against certain classes of microbes or tumors. We are confident that we have developed novel methods for the arylation of 4-substituted-1,2,4-triazoles and incorporating 1,2,4-triazolium salts into poly

heterocyclic systems. These advancements will allow for easier development of novel 1,2,4-triazole containing organocatalysts, ligands, and potentially biological active molecules.

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APPENDICES

APPENDIX A: GENERAL INFORMATION

Most reagents and solvents were obtained from commercial sources and used as supplied unless otherwise noted. Acetonitrile used for catalytic reactions was dried under an inert atmosphere over CaH_2 and distilled before use. DMSO-d_6 was dried over molecular sieves. Analysis. ^{1}H NMR, $^{13}C\{^{1}H\}$ NMR spectra, and $^{19}F\{^{1}H\}$ NMR spectra were all recorded on a 400 MHz Bruker Avance III spectrometer with a 5 mm liquid-state Smart Probe. Chemical shifts (δH and δC) are expressed in parts per million (ppm) and reported relative to the resonance of the residual protons of the DMSO-d_6 (δH = 2.50 ppm) or $CDCl_3$ (δH = 7.26 ppm) or in $^{13}C\{^{1}H\}$ NMR spectra relative to the resonance of the deuterated solvent DMSO-d_6 (δC = 39.52 ppm) or $CDCl_3$ (δC = 77.16 ppm). Chemical shifts in $^{19}F\{1H\}$ NMR spectra are reported relative to the internal standard fluorobenzene (δF = −113.15). Coupling constants (*J*) are given in Hz. All measurements were carried out at 298 K. Abbreviations used in the description of NMR data are as follows: s, singlet; d, doublet; t, triplet; q, quartet; sept, septet; and m, multiplet. High-Resolution Mass Spectrometry (HRMS) data were obtained on an LTQ Orbitrap XL in FT Orbitrap mode at a resolution of 100,000.

APPENDIX B: COMMON ABBREVIATIONS

DMF – Dimethylformamide
DCM – Dichloromethane, methylene chloride
DCE – 1,2-Dichloroethane
$CDCl_3$ – Deuterated chloroform
DMSO-d_6 – Deuterated dimethylsulfoxide
FDA – Food and drug Administration
DNA– Deoxyribose nucleic acid
RNA– Ribose nucleic acid
PPAR α/β– Peroxisome Proliferator Activated Receptor Alpha / Beta
NHC– *N*-Heterocyclic Carbene
ee– Enantiomeric Excess
DBU– 1,8-Diazabicyclo[5.4.0]undec-7-ene
THF– Tetrahydrofuran
EWG– Electron Withdrawing Group
m-CPBA– meta-Chloroperoxybenzoic acid
DMSO– Dimethylsulfoxide
phen– Phenanthroline
equiv. – Equivalents
HRMS– High Resolution Mass Spectroscopy
LCMS– Liquid Chromatography–Mass Spectrometry
NMR– Nuclear Magnetic Resonance Spectroscopy
M.S. – Molecular Sieves
rt– Room Temperature
DME– Dimethoxyethane
NEt_3– Triethylamine
Ac_2O– Acetic Anhydride
i-PrOH– Isopropanol
MeOH– Methanol
OTf– Trifluoromethanesulfonyloxy (Triflate)
BF_4– Tetrafluoroborate
Pd/C– Palladium on Carbon
Cu(OAc) – Cupric Acetate / Copper (I) Acetate
$Cu(OAc)_2$– Cuprous Acetate / Copper (II) Acetate
$Cu(OTf)_2$– Cuprous triflate / Copper (II) Triflate
DMAZ– *N*,*N*-Dimethylformamide Azine Dihydrochloride
HCO_2H– Formic Acid
PTSA, TsOH– p-Toluenesulfonic Acid
$CHCl_3$– Chloroform
MECN, MeCN– Acetonitrile
$HClO_4$– Perchloric acid
$NaIO_4$– Sodium Periodate
$[Ir(dncot)Cl]_2$– Iridium (I) Dinaphthocyclooctatetraene chloride Dimer
$PhI(OAc)_2$– (Diacetoxyiodo)benzene / Phenyliodine(III) Diacetate
$Sc(OTf)_3$– Scandium Trifluoromethanesulfonate/ Scandium (III) Triflate
$HC(OEt)_3$– Triethyl Orthoformate
Me_3OBF_4– Trimethyloxonium Tetrafluoroborate
NaOEt– Sodium Ethoxide
EtOH – Ethanol

APPENDIX C: INDEX OF MOLECULES AND STRUCTURES

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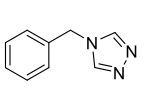
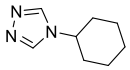


1a



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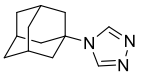

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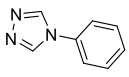

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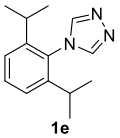

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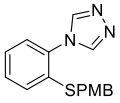

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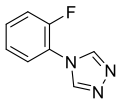

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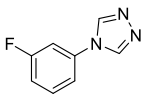

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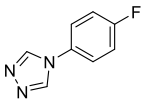

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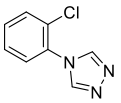

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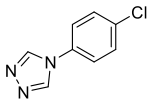

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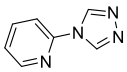

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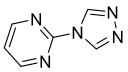

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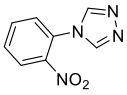

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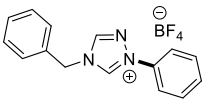

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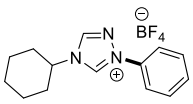

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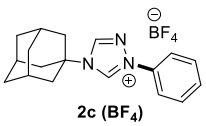

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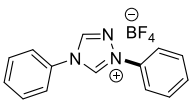

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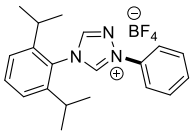

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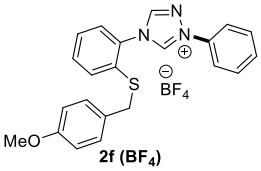

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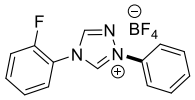

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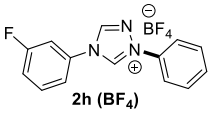

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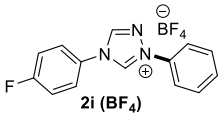

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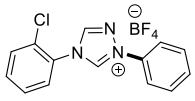

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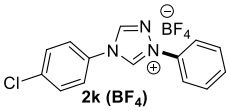

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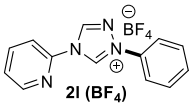

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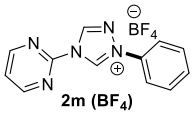

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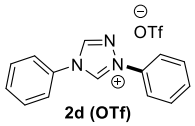

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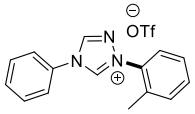

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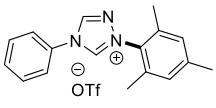

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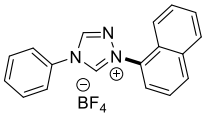

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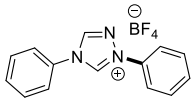

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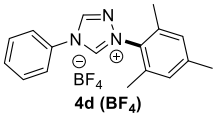

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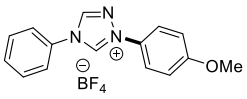

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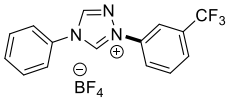

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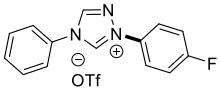

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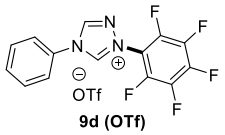

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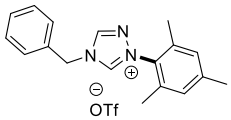
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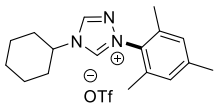
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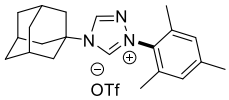
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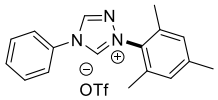
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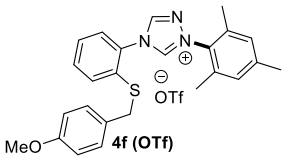
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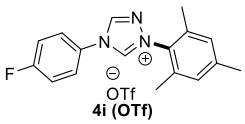
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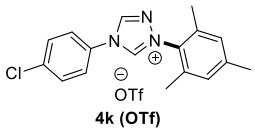
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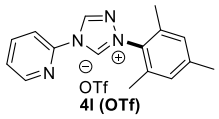
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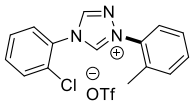
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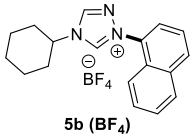
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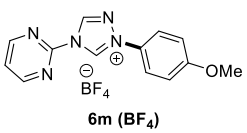
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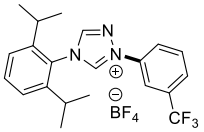
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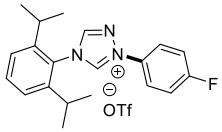
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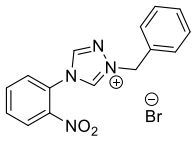
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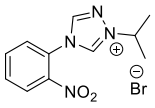
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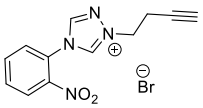
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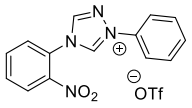
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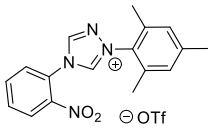
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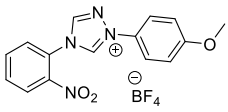
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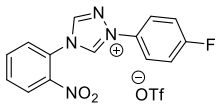
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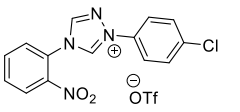
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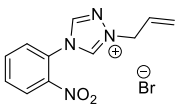
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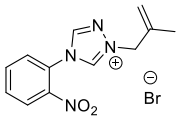
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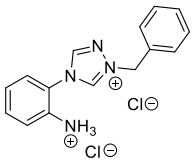
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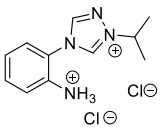
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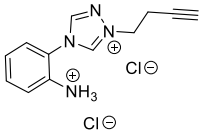
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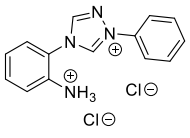
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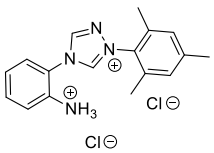
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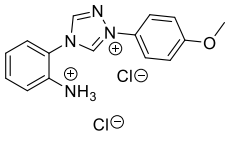
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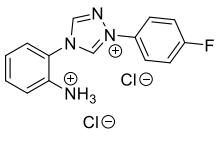
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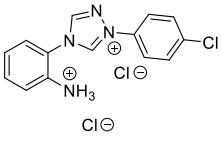
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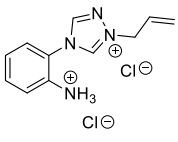
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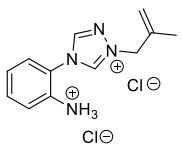
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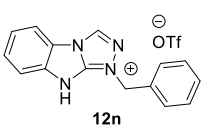
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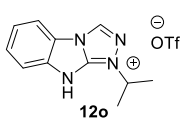
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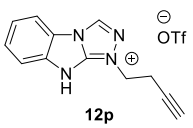
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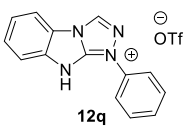
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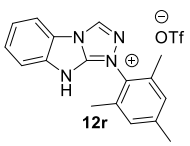
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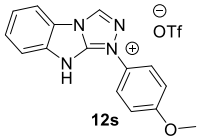
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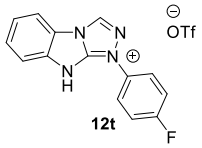
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APPENDIX D: SPECTRA FOR CHAPTER 2

Section D.1: NMR Yields for 1,4-Disubstituted-1,2,4-triazolium Salts (D001-D033)

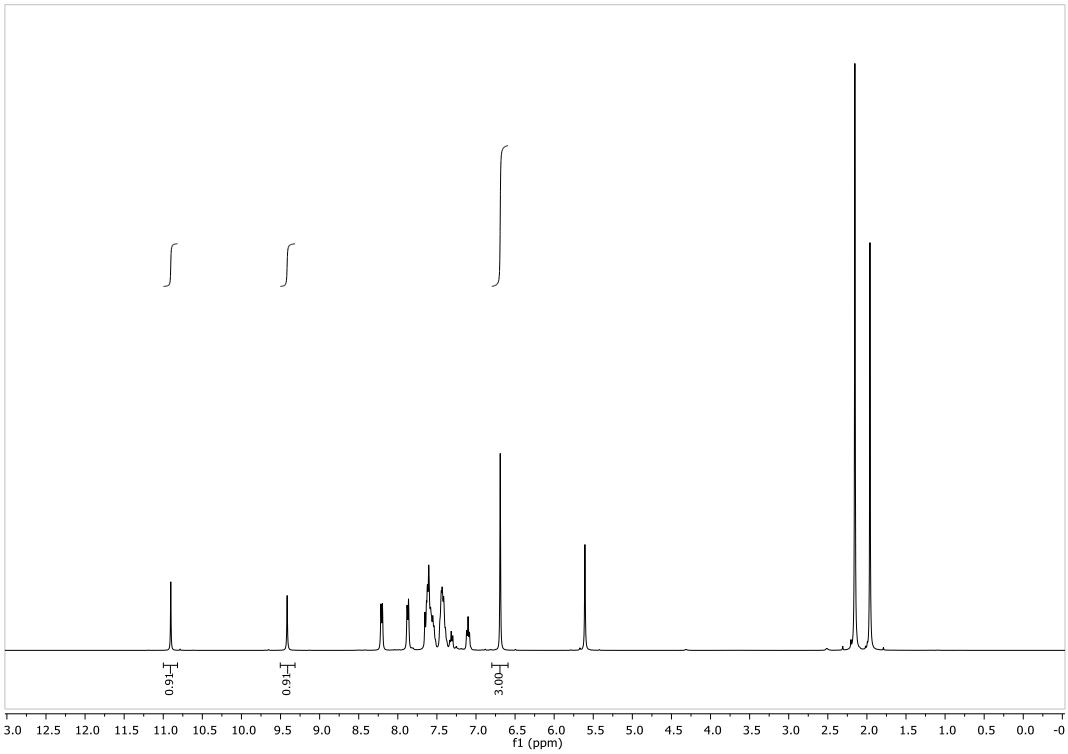

Figure D001: NMR yield of crude 4-benzyl-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([2a]BF_4)

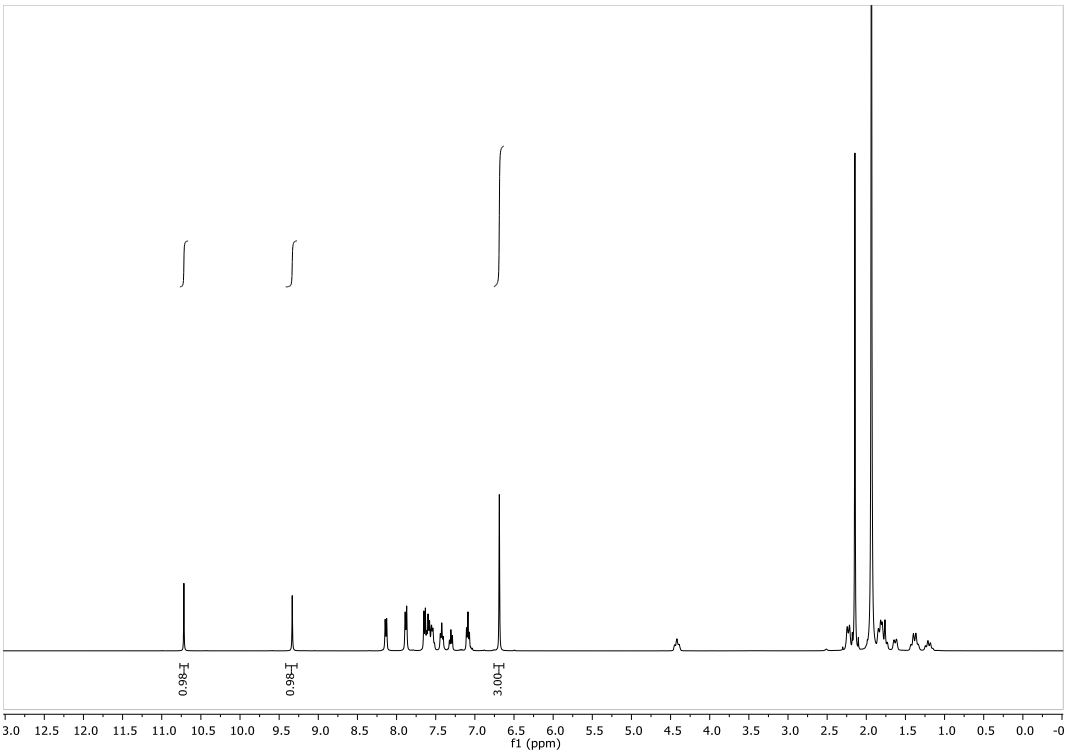

Figure D002: NMR yield of crude 4-*c*yclohexyl-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([2b]BF_4)

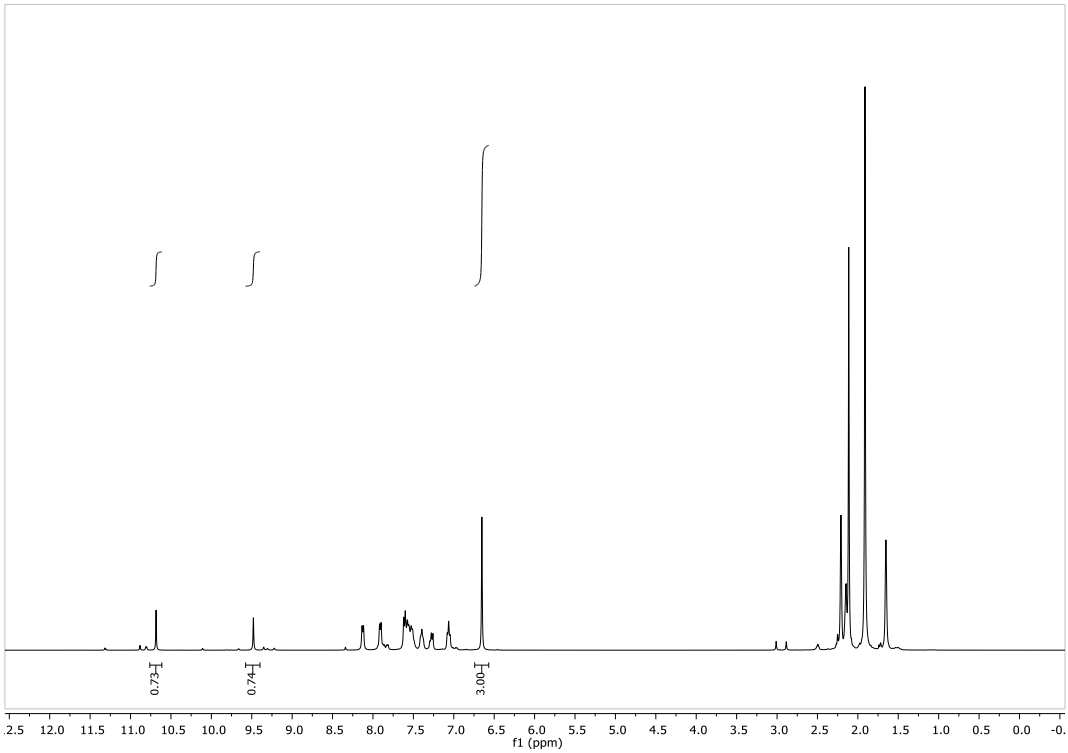

Figure D003: NMR yield of crude 4-((3*s*,5*s*,7*s*)-adamantan-1-yl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([2c]BF_4)

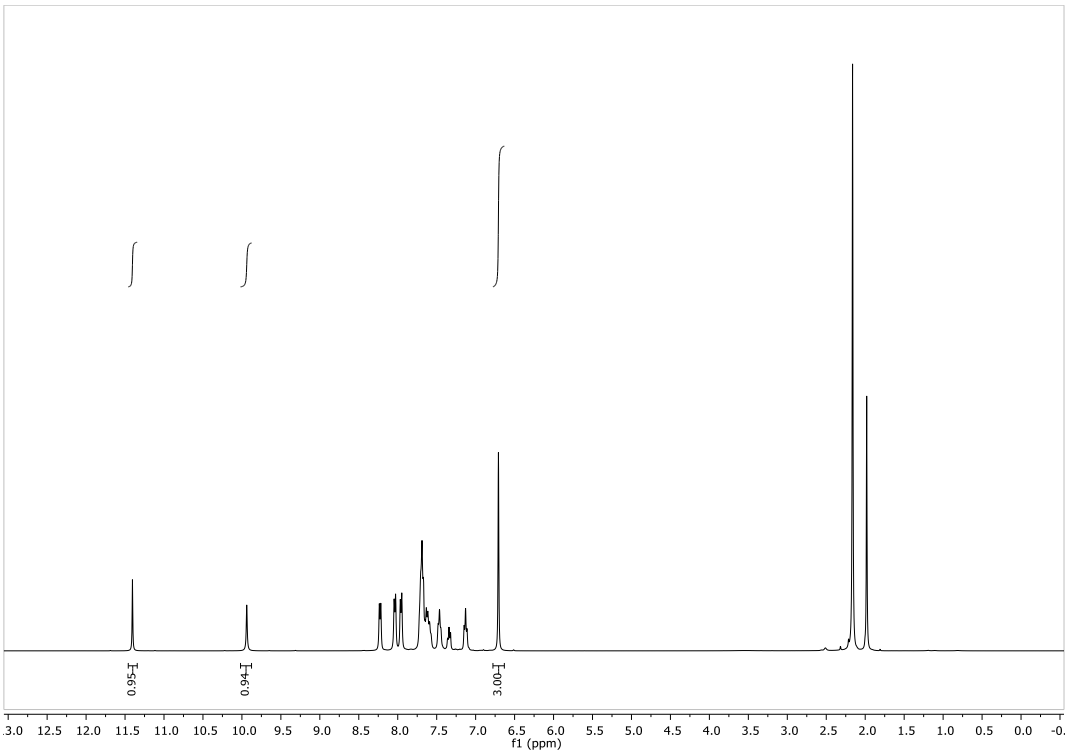

Figure D004: NMR yield of crude 1,4-diphenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([2d]BF_4)

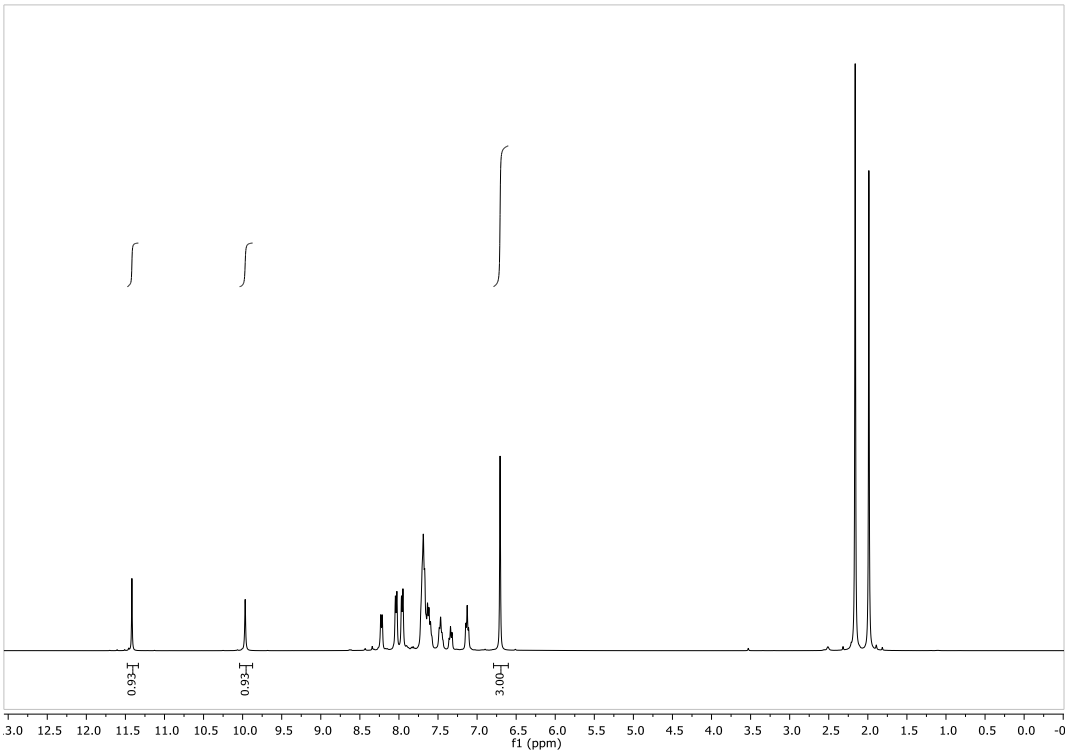

Figure D005: NMR yield of crude 1,4-diphenyl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate ([2d]OTf)

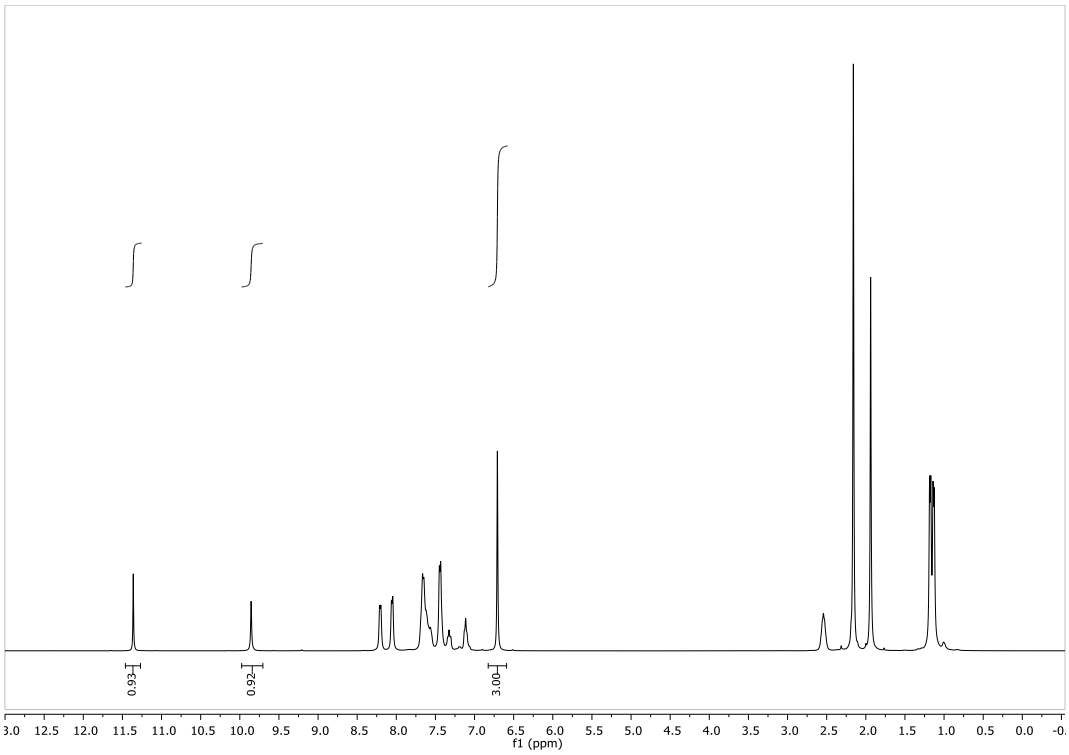

Figure D006: NMR yield of crude 4-(2,6-diisopropylphenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([2e]BF_4)

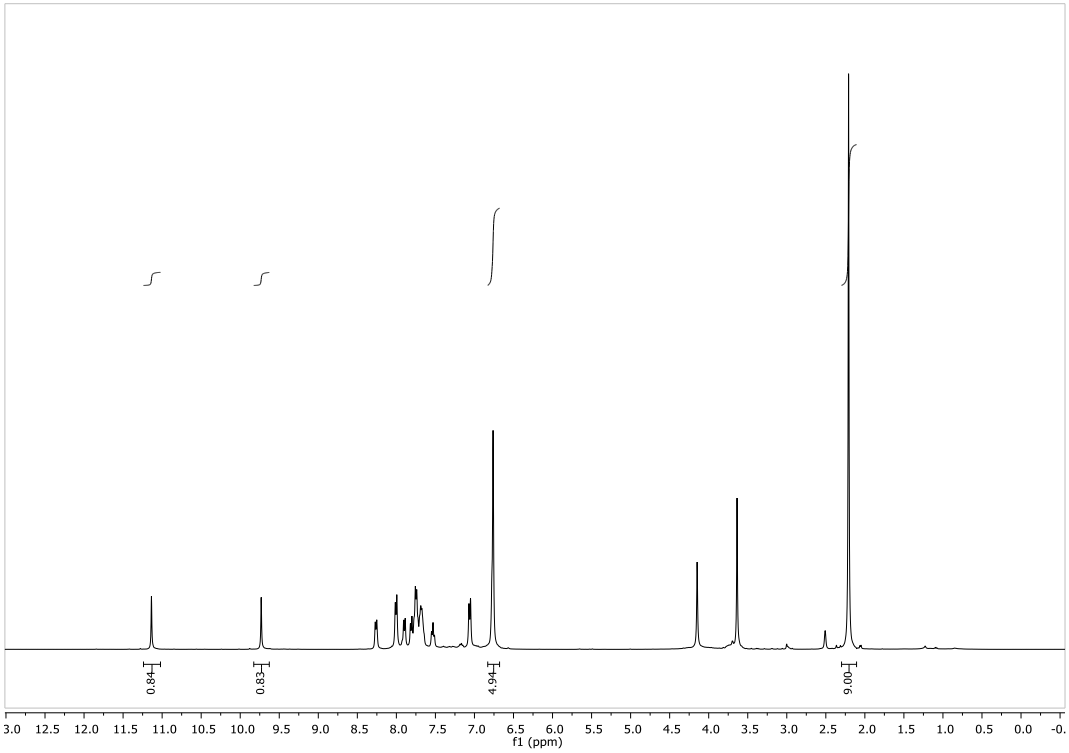

Figure D007: NMR yield of crude 1-phenyl-4-(2-((4-methoxybenzyl)thio)phenyl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([2f]BF_4)

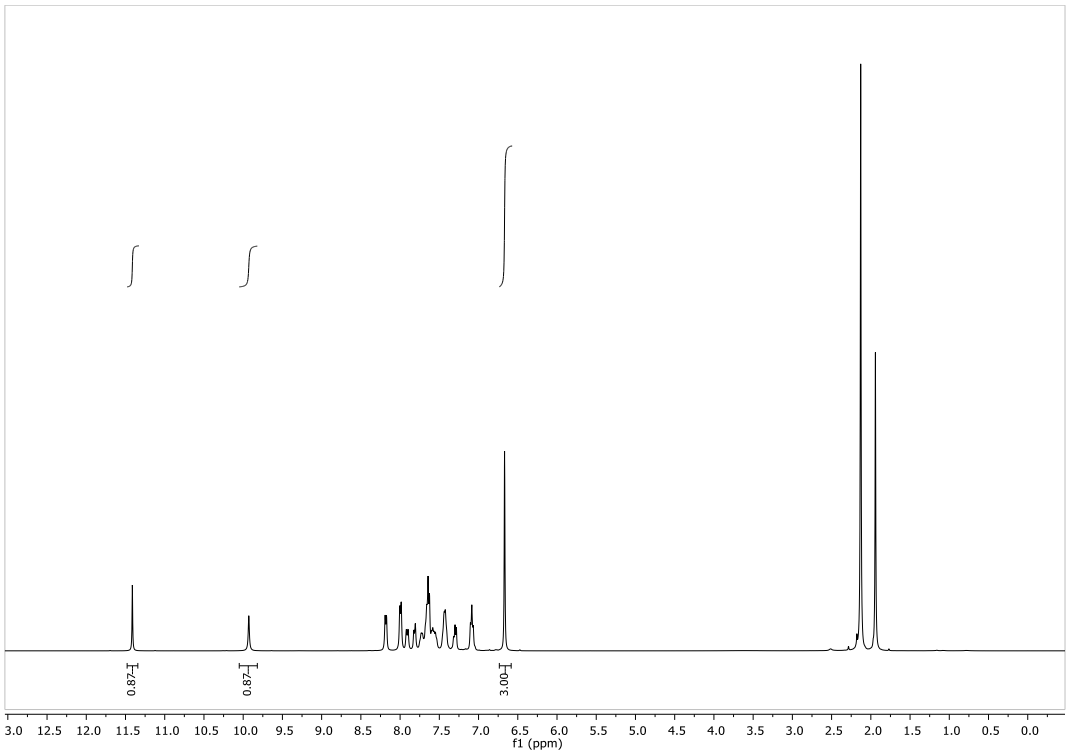

Figure D008: NMR yield of crude 4-(2-fluorophenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([2g]BF_4)

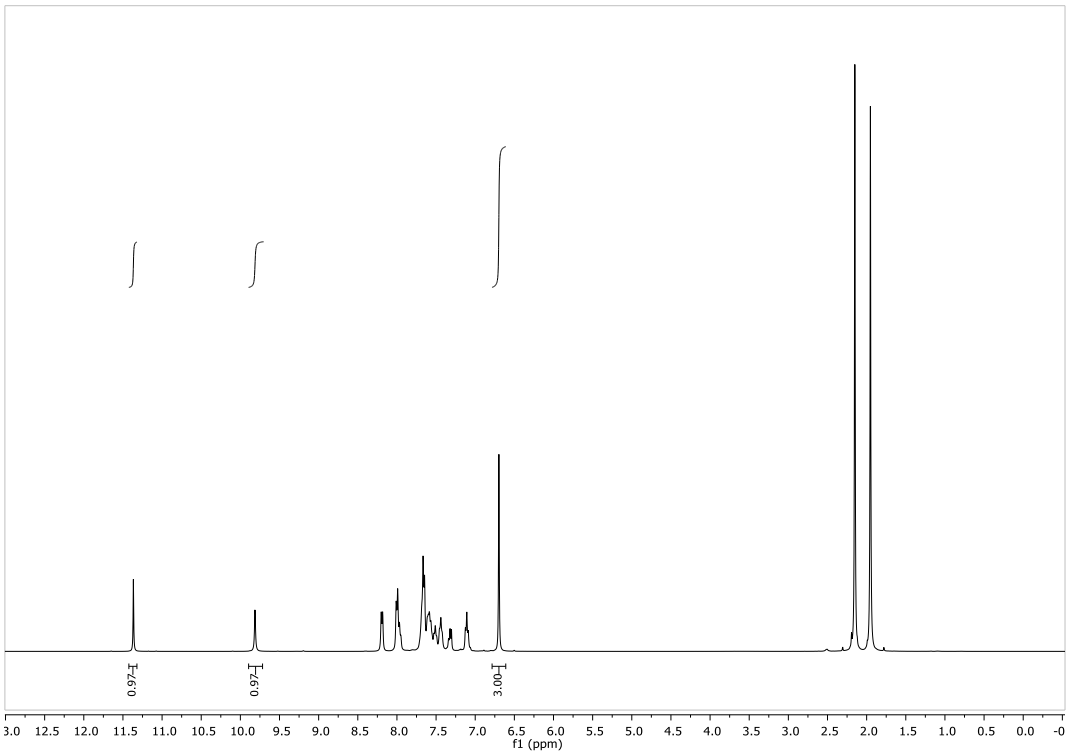

Figure D009: NMR yield of crude 4-(3-fluorophenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([2h]BF_4)

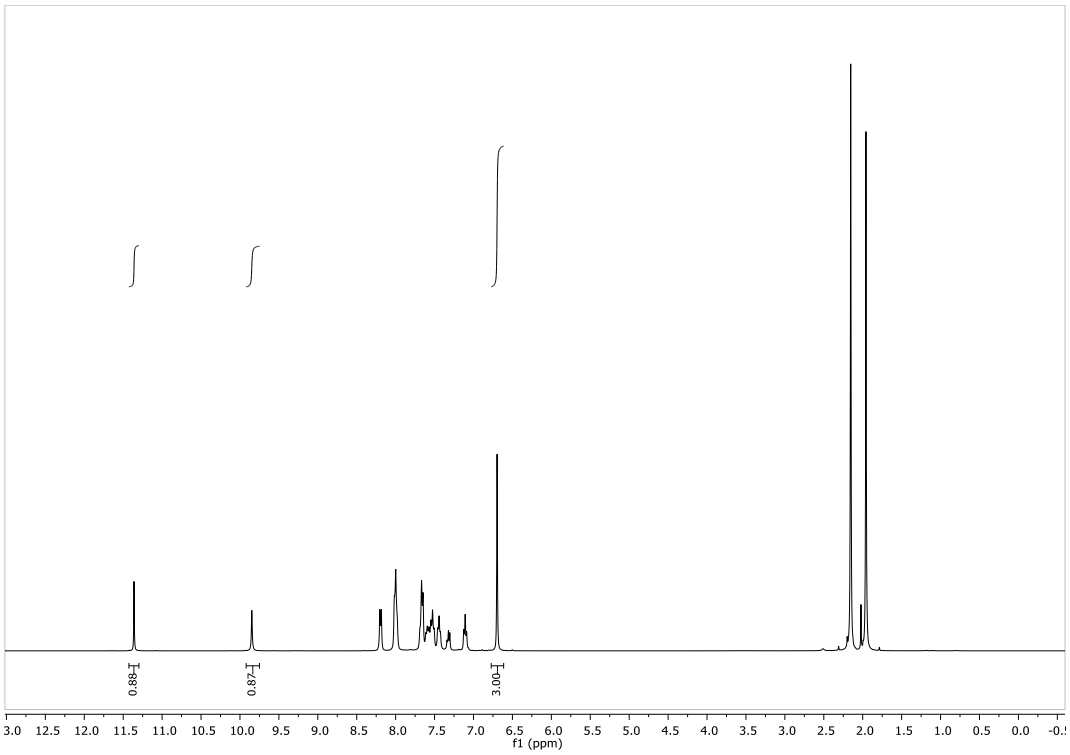

Figure D010: NMR yield of crude 4-(4-fluorophenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([2i]BF_4)

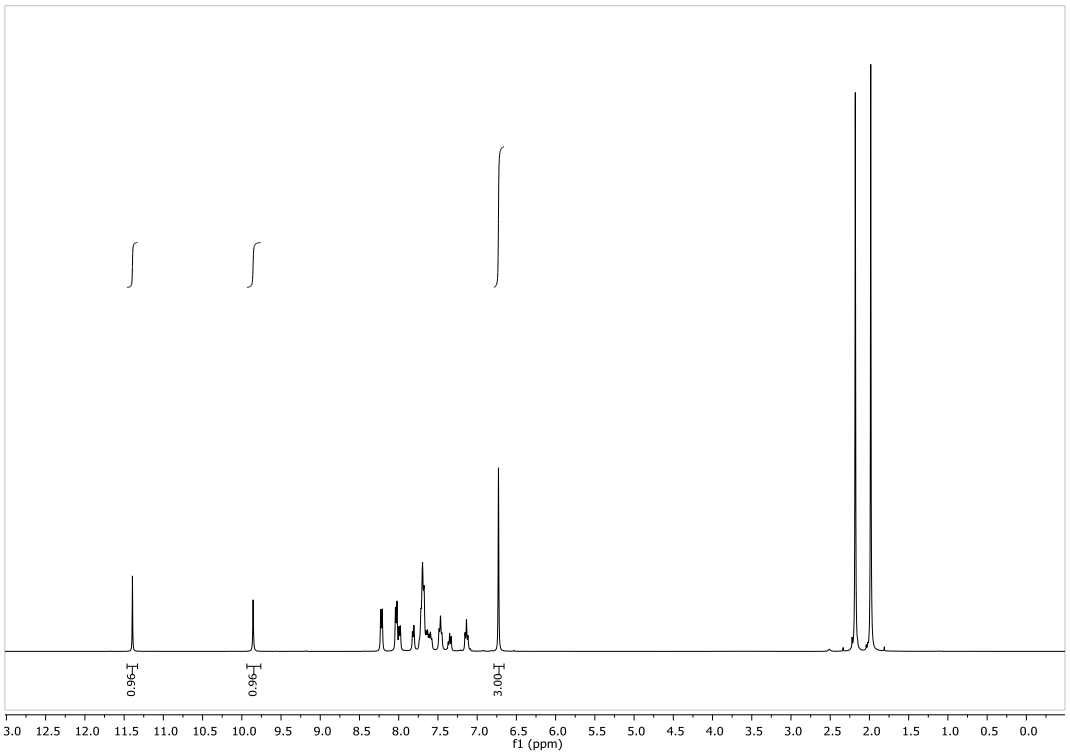

Figure D011: NMR yield of crude 4-(2-*c*hlorophenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([2j]BF_4)

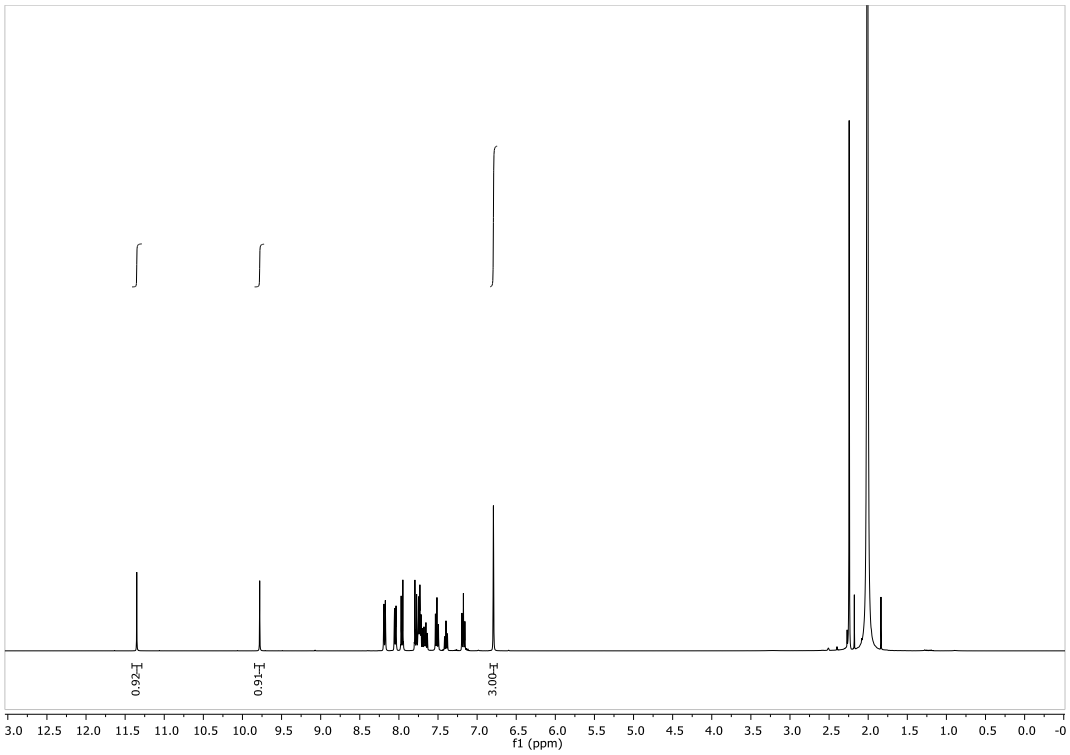

Figure D012: NMR yield of crude 4-(4-*c*hlorophenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([2k]BF_4)

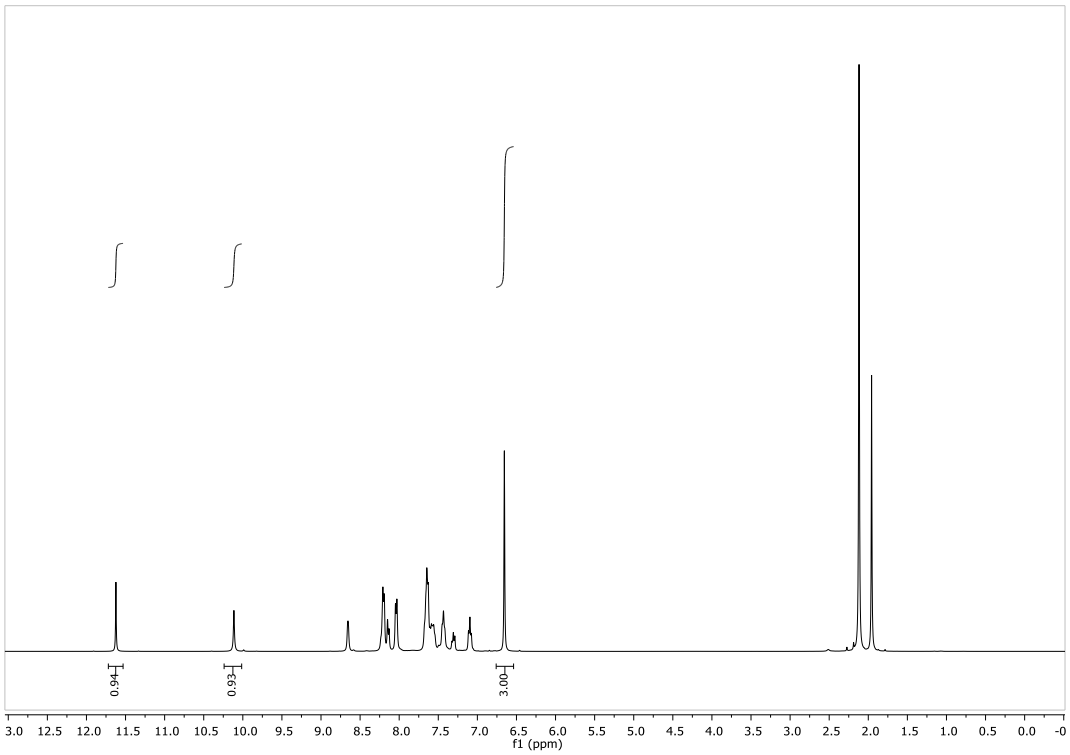

Figure D013: NMR yield of crude 1-phenyl-4-(pyridin-2-yl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([2l]BF_4)

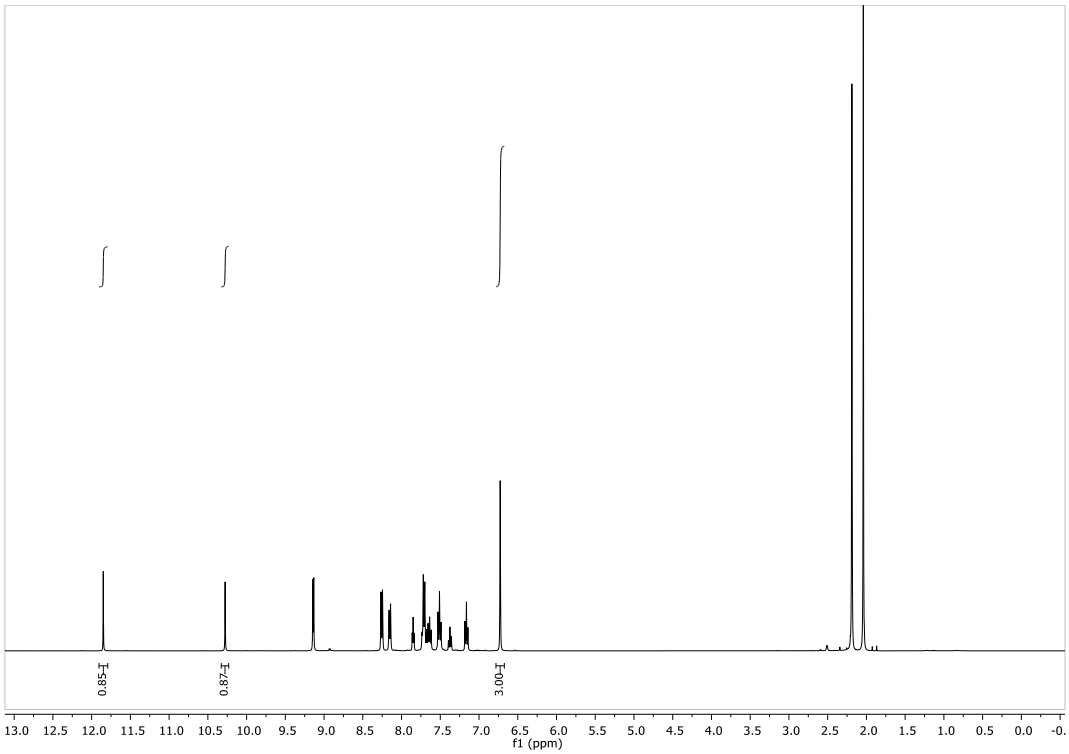

Figure D014: NMR yield of crude 1-phenyl-4-(pyrimidin-2-yl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([2m]BF_4)

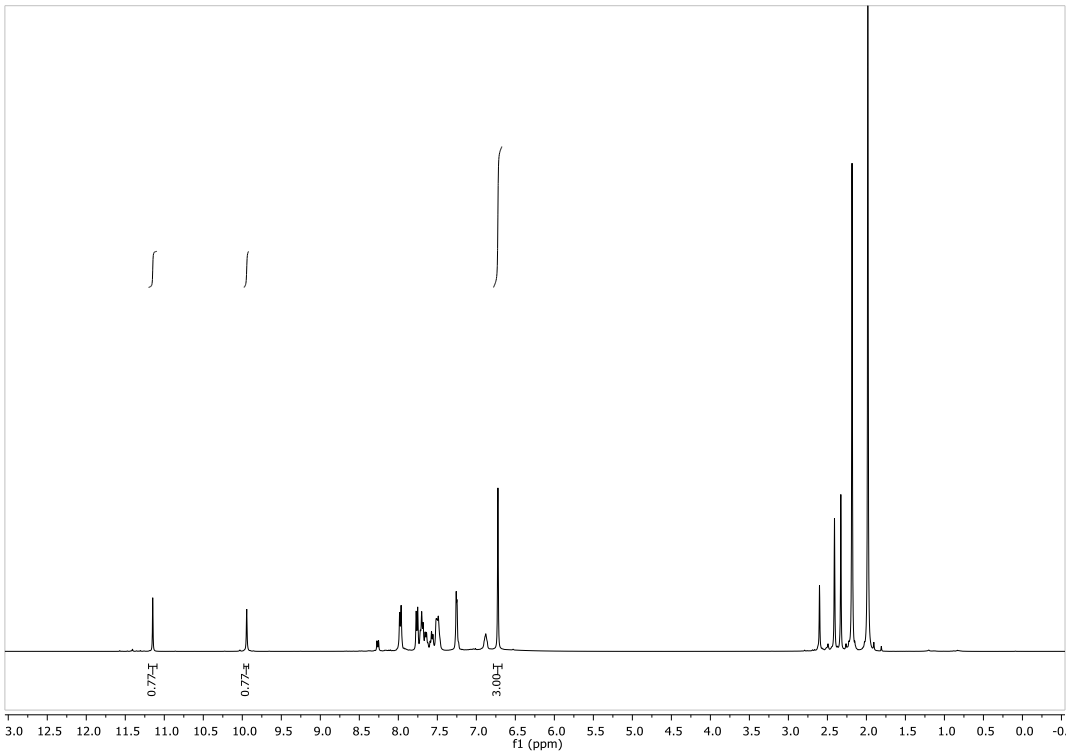

Figure D015: NMR yield of crude 4-phenyl-1-(o-tolyl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate ([3d]OTf)

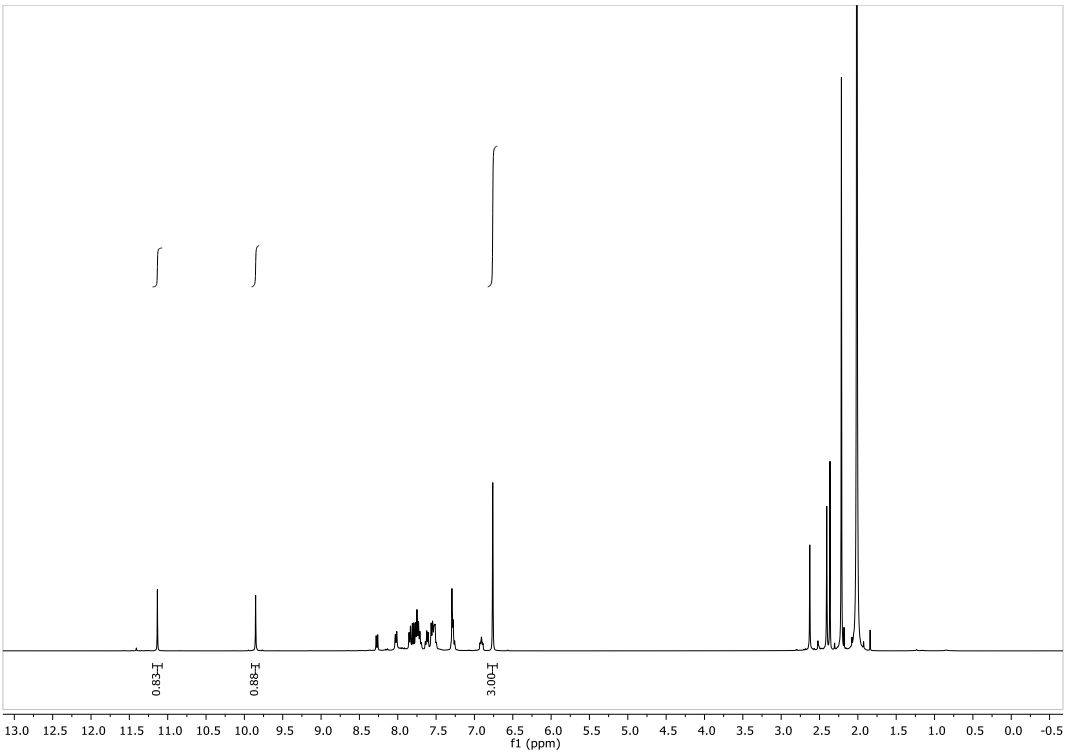

Figure D016: NMR yield of crude 4-(2-*c*hlorophenyl)-1-(o-tolyl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate ([3j]OTf)

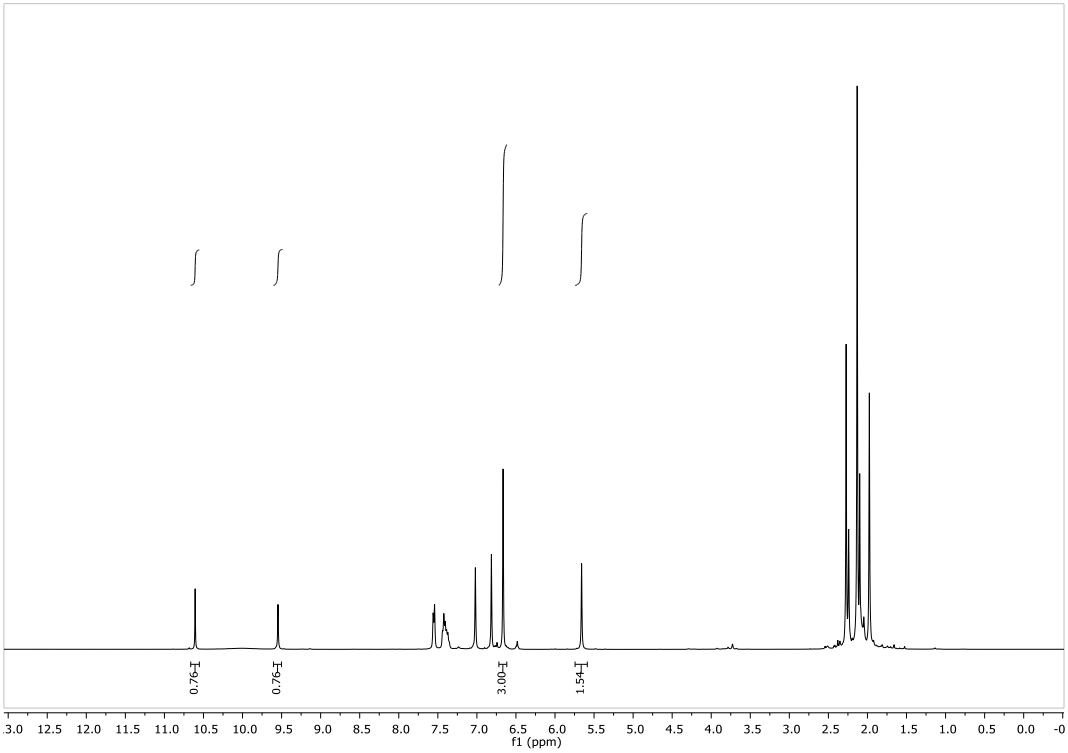

Figure D017: NMR yield of crude 4-benzyl-1-mesityl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate ([4a]OTf)

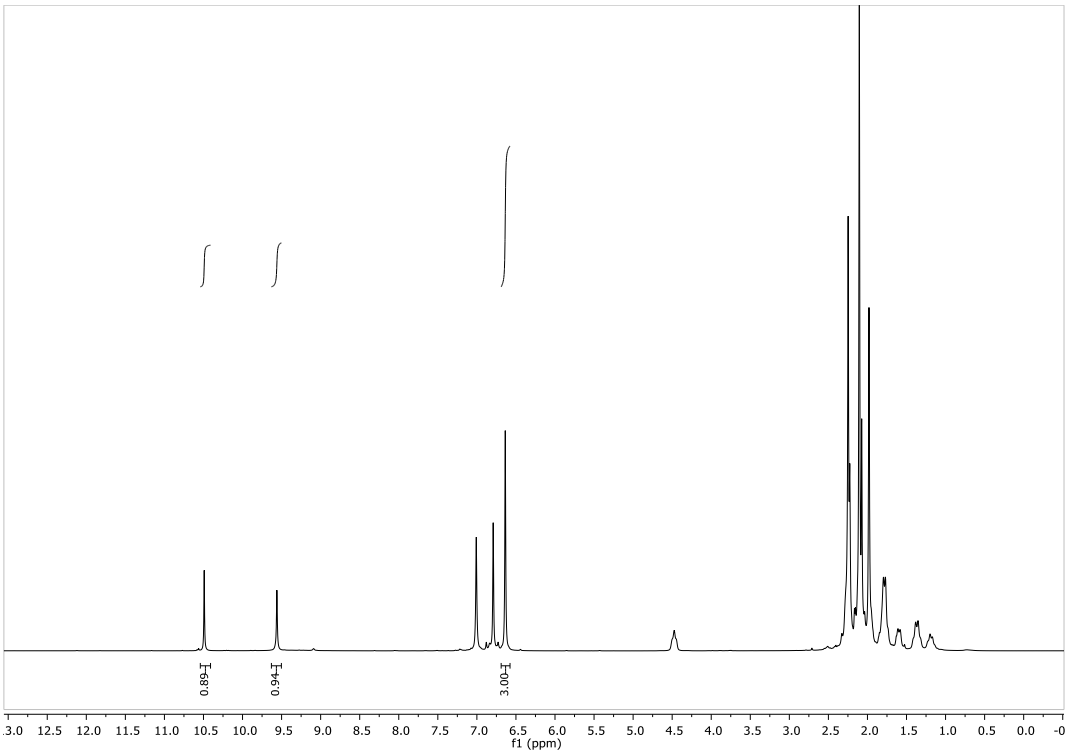

Figure D018: NMR yield of crude 4-*c*yclohexyl-1-mesityl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate ([4b]OTf)

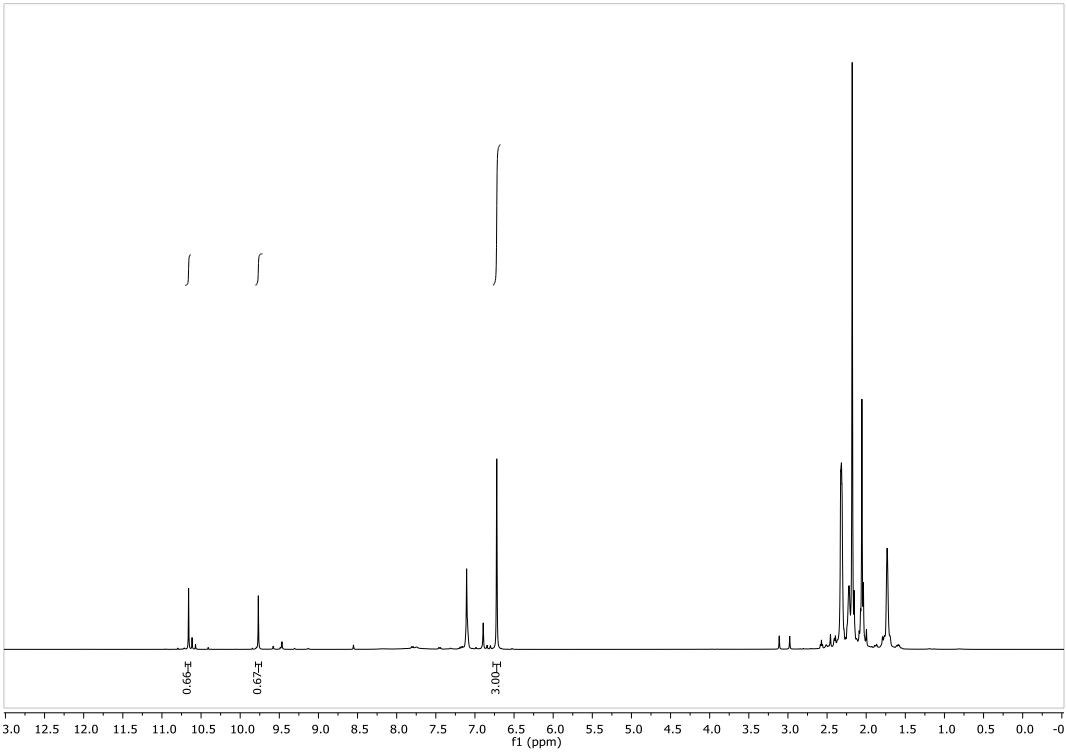

Figure D019: NMR yield of crude 4-((3*s*,5*s*,7*s*)-adamantan-1-yl)-1-mesityl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate ([4c]OTf)

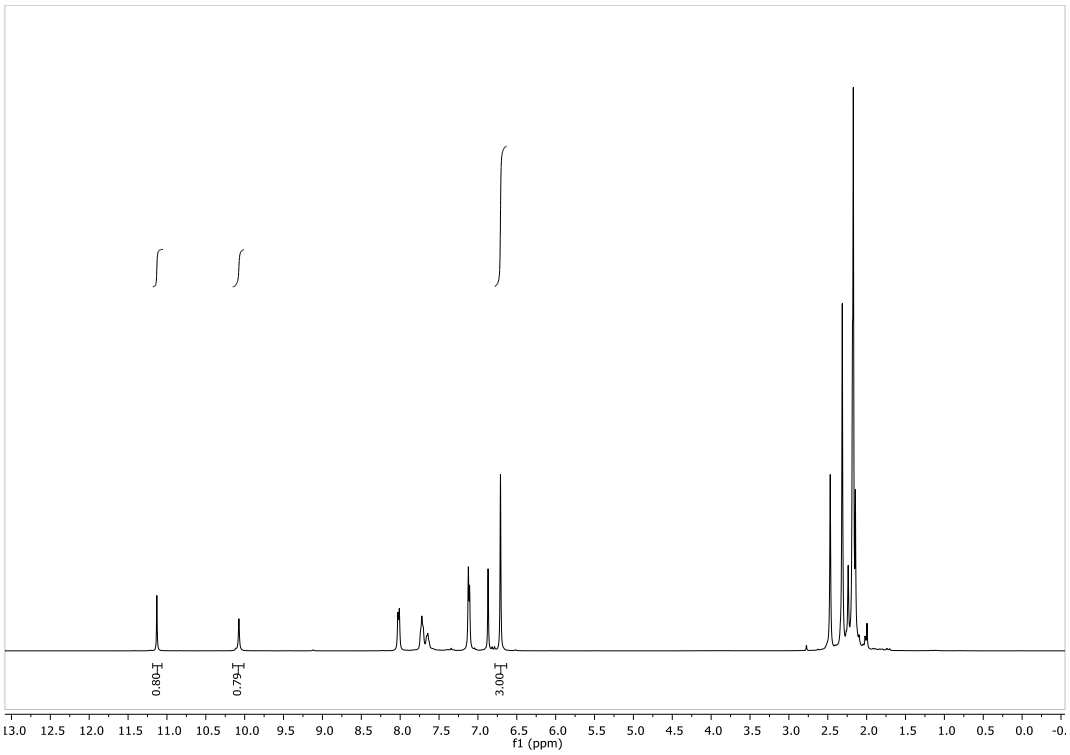

Figure D020: NMR yield of crude 1-mesityl-4-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([4d]BF_4)

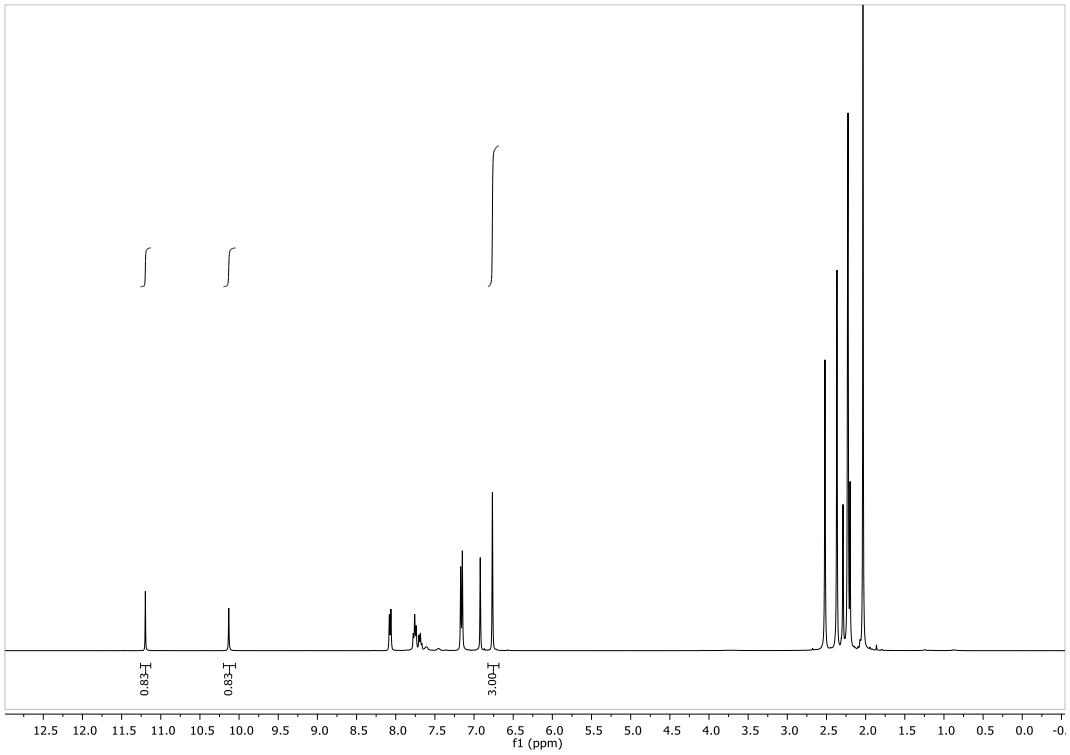

Figure D021: NMR yield of crude 1-mesityl-4-phenyl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate ([4d]OTf)

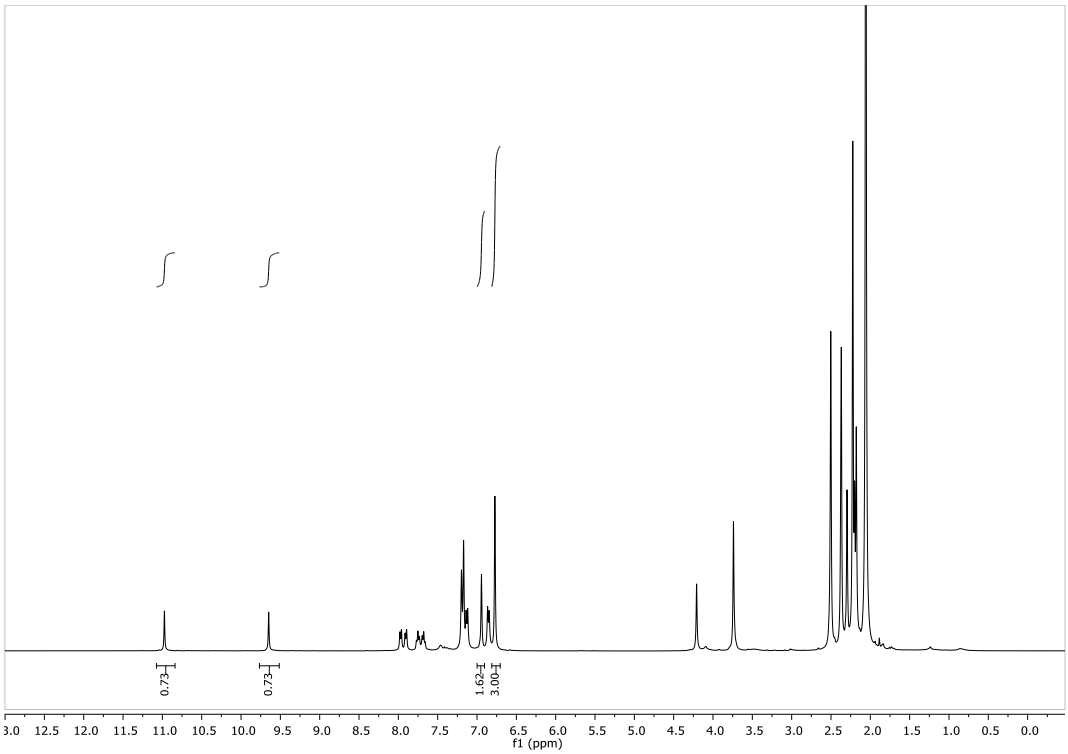

Figure D022: NMR yield of crude 1-mesityl-4-(2-((4-methoxybenzyl)thio)phenyl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate ([4f]OTf)

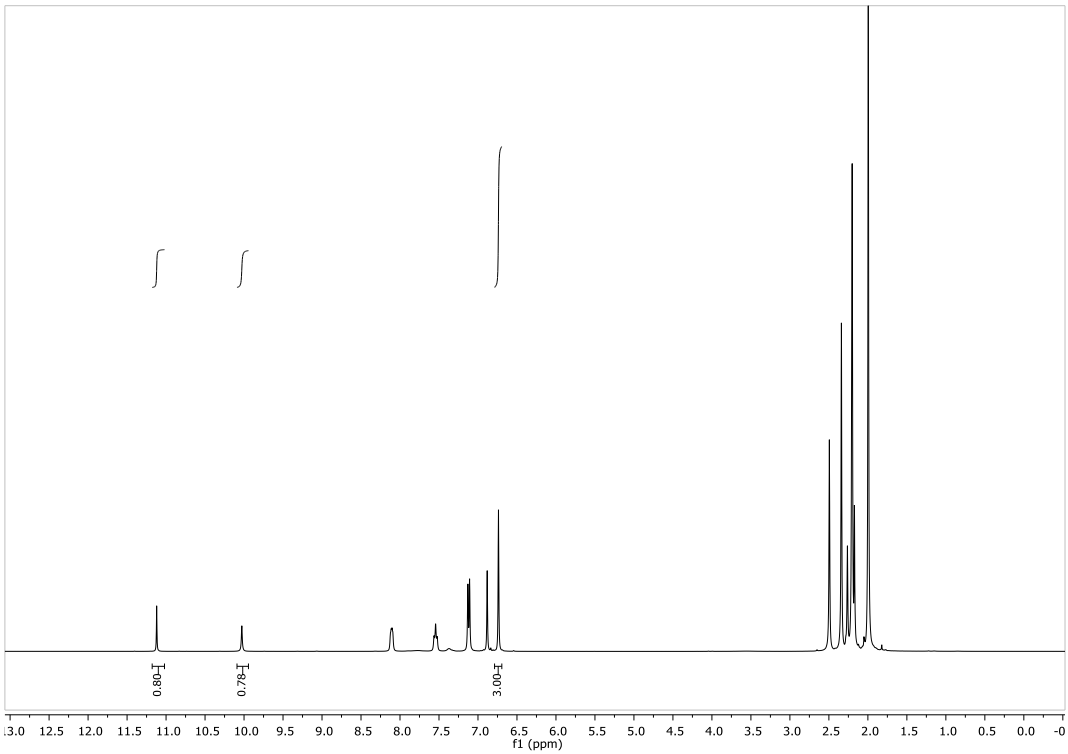

Figure D023: NMR yield of crude 4-(4-fluorophenyl)-1-mesityl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate ([4i]OTf)

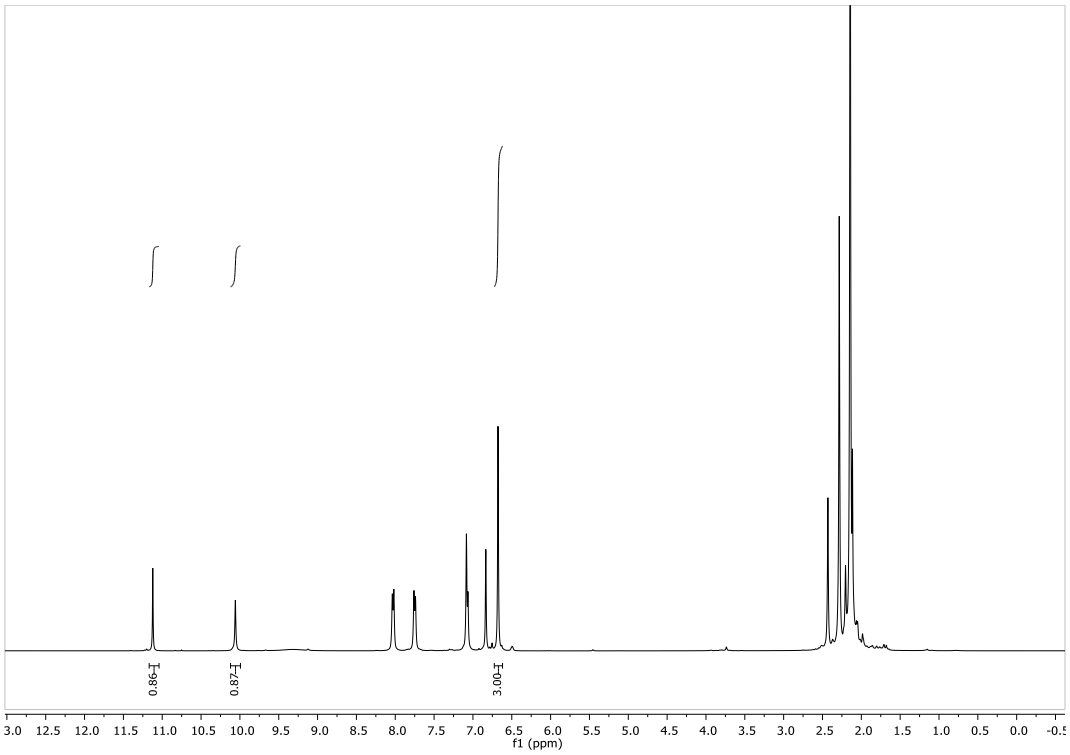

Figure D024: NMR yield of crude 4-(4-*c*hlorophenyl)-1-mesityl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate ([4k]OTf)

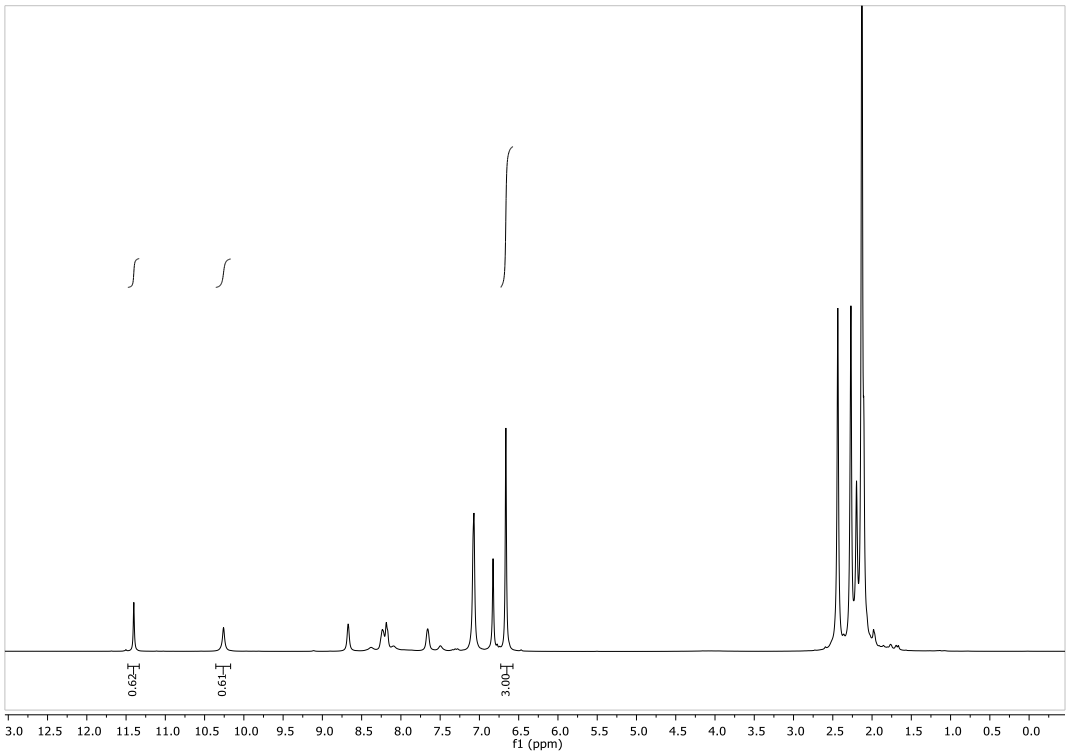

Figure D025: NMR yield of crude 1-mesityl-4-(pyridin-2-yl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate ([4l]OTf)

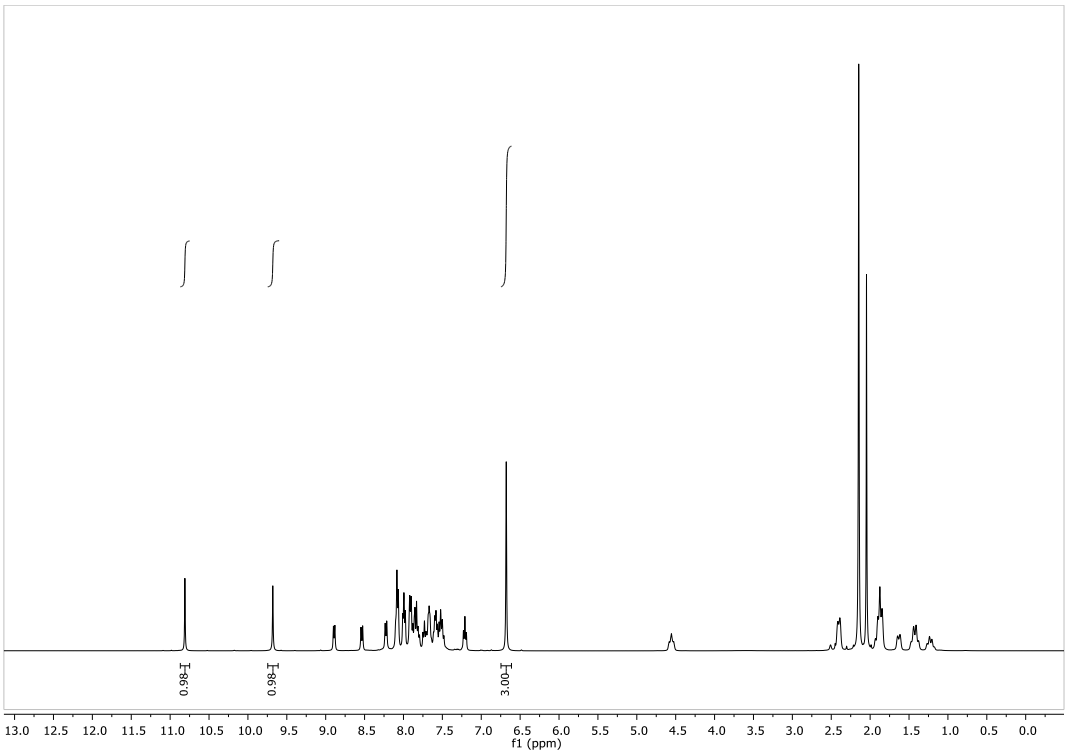

Figure D026: NMR yield of crude 4-*c*yclohexyl-1-(naphthalen-1-yl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([5b]BF_4)

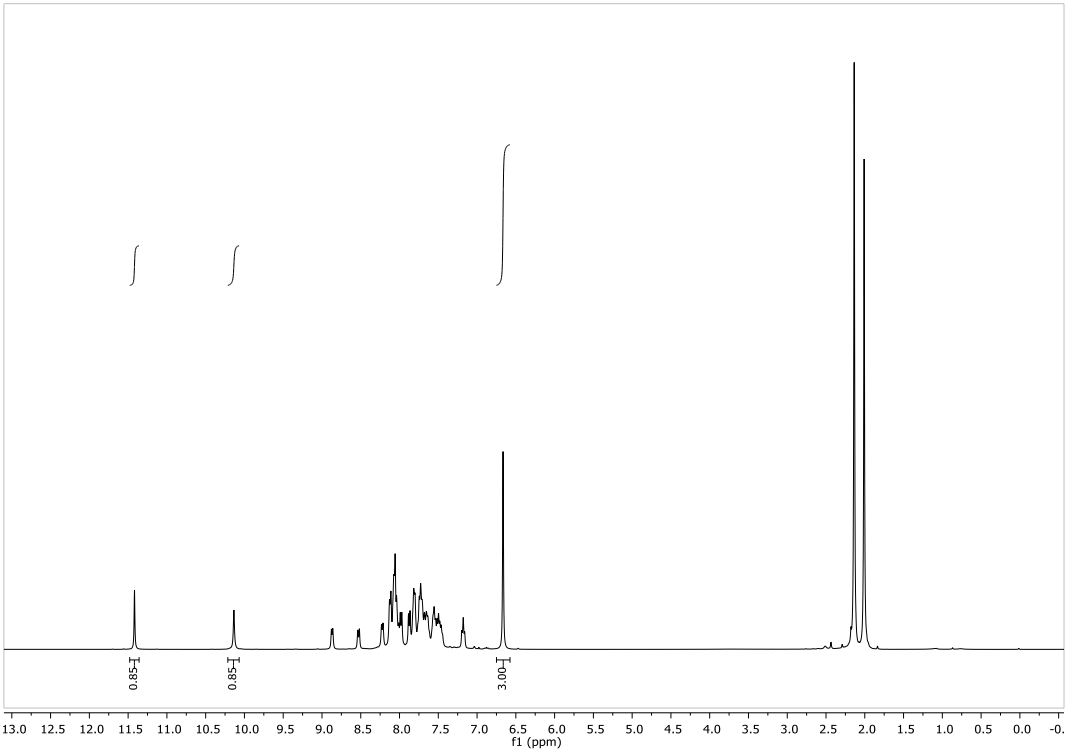

Figure D027: NMR yield of crude 1-(naphthalen-1-yl)-4-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([5d]BF_4)

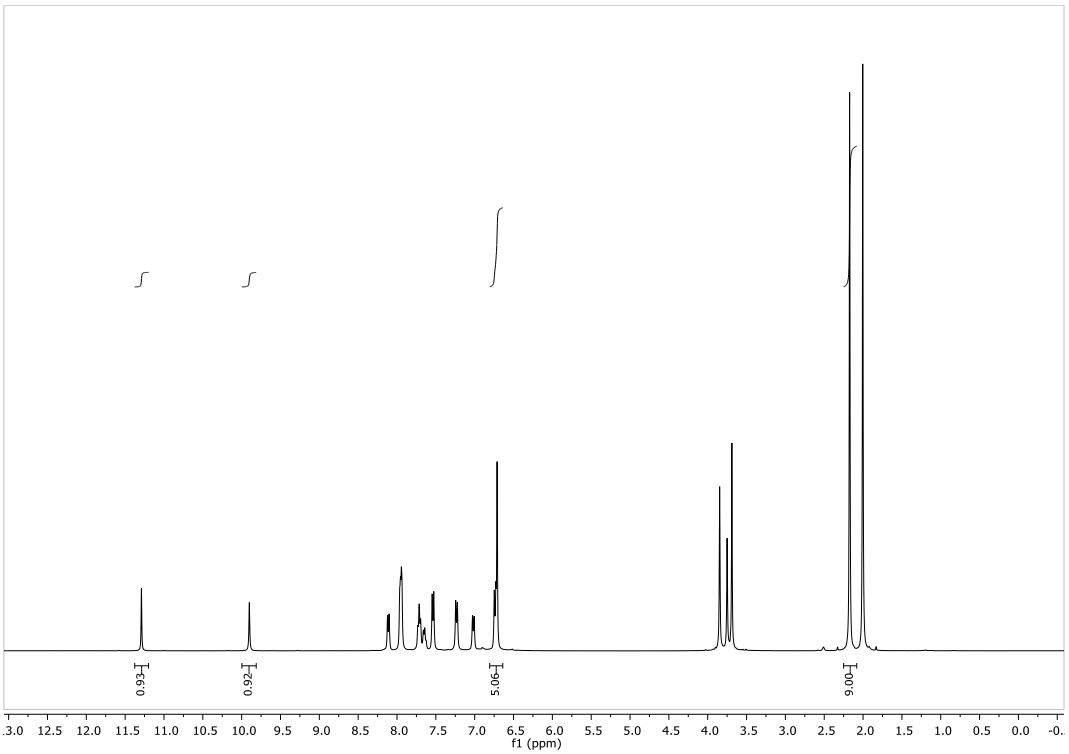

Figure D028: NMR yield of crude 1-(4-methoxyphenyl)-4-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([6d]BF_4)

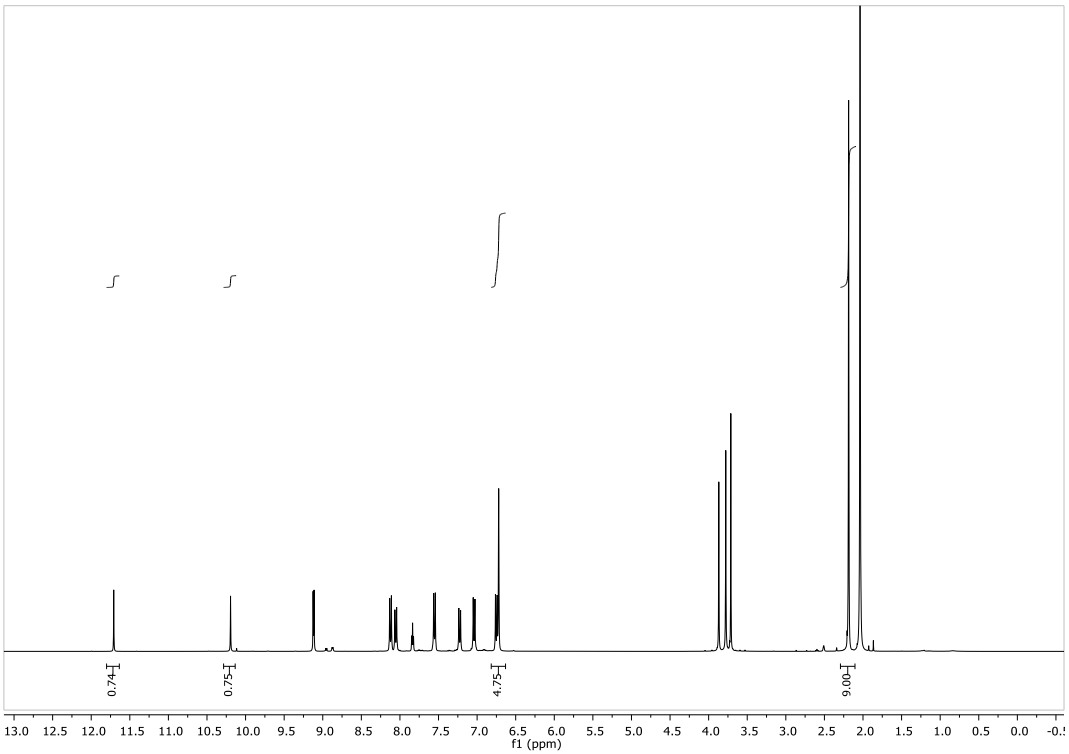

Figure D029: NMR yield of crude 1-(4-methoxyphenyl)-4-(pyrimidin-2-yl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([6m]BF_4)

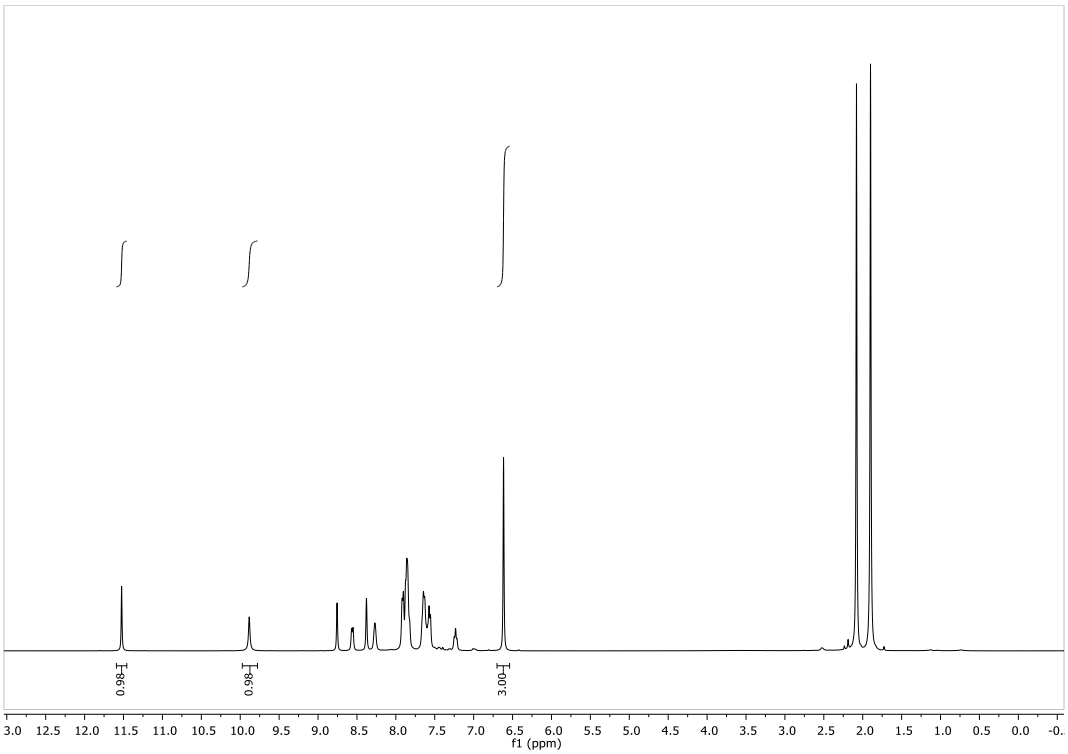

Figure D030: NMR yield of crude 4-phenyl-1-(3-(trifluoromethyl)phenyl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([7d]BF_4)

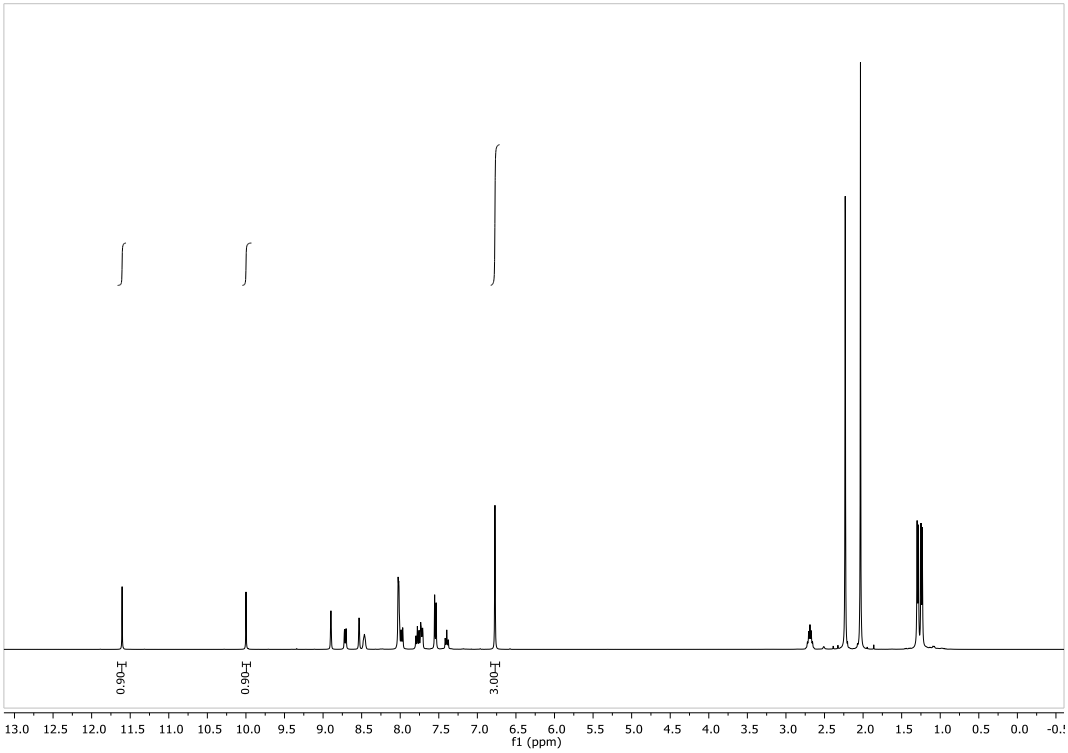

Figure D031: NMR yield of crude 4-(2,6-diisopropylphenyl)-1-(3-(trifluoromethyl)phenyl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([7e]BF_4)

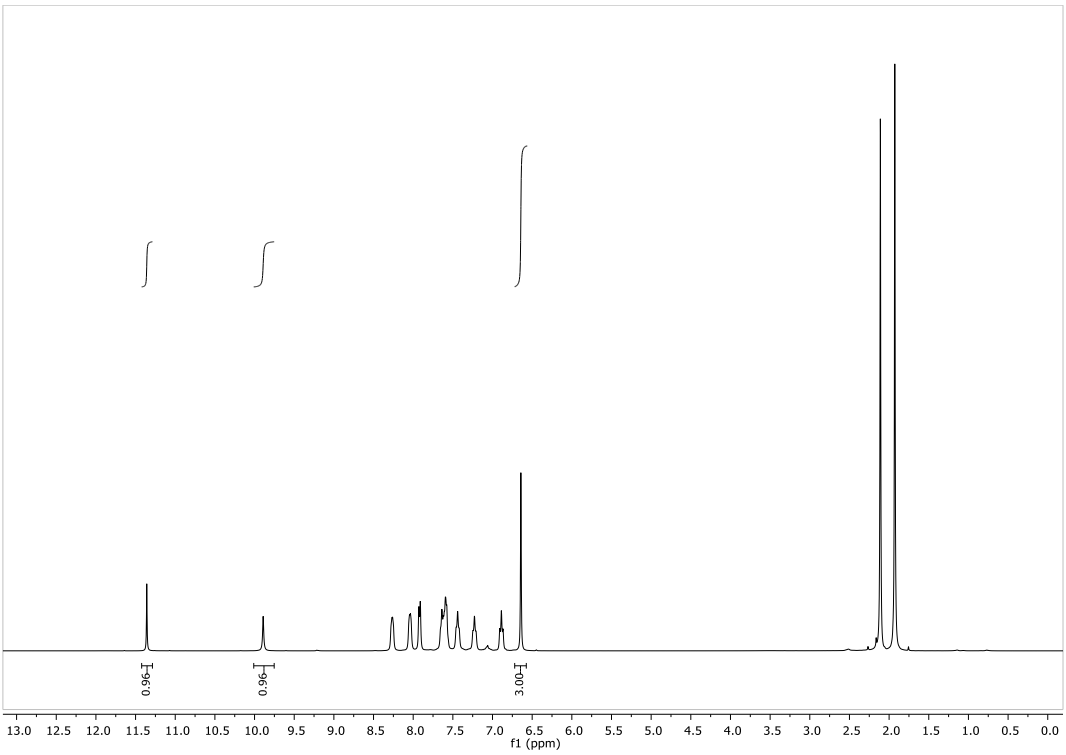

Figure D032: NMR yield of crude 1-(4-fluorophenyl)-4-phenyl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate ([8d]OTf)

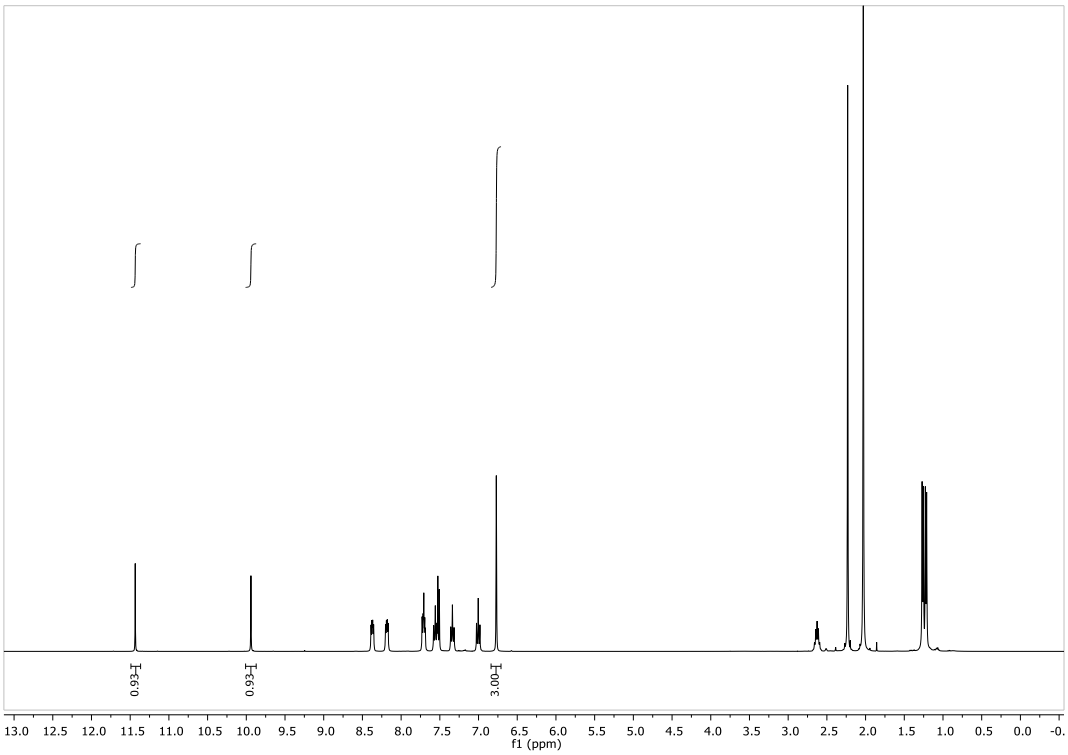

Figure D033: NMR yield of crude 4-(2,6-diisopropylphenyl)-1-(4-fluorophenyl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate ([8e]OTf)

Section D.2: Spectra of 1,4-Disubstituted-1,2,4-triazolium Salts (D034-D107)

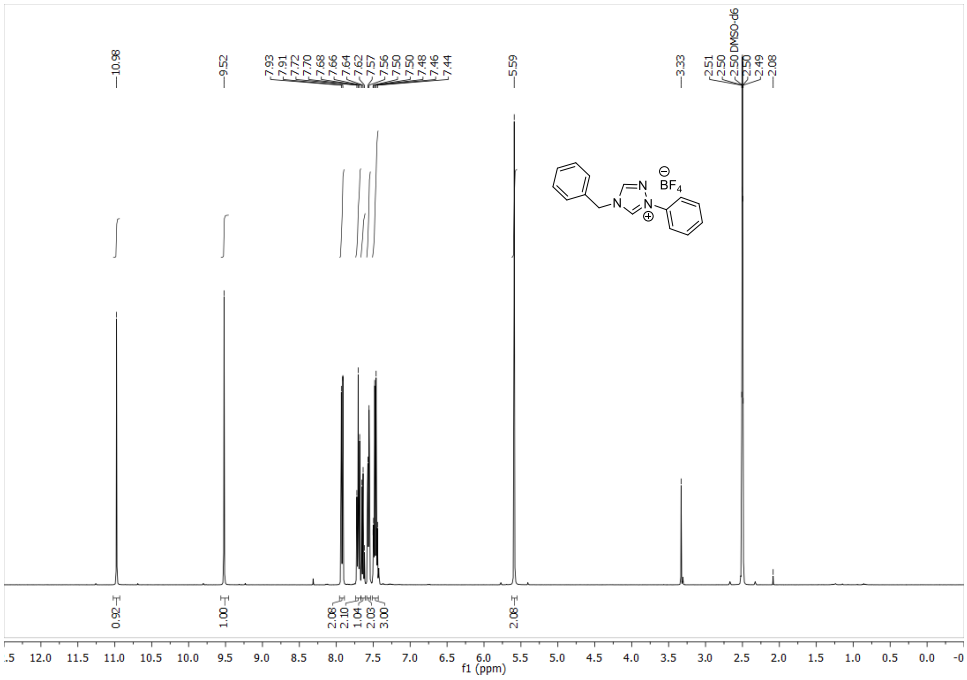

Figure D034: ^{1}H NMR spectrum of 4-benzyl-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[2a]BF$_4$**) (400 MHz, DMSO-d_6, 298 K).

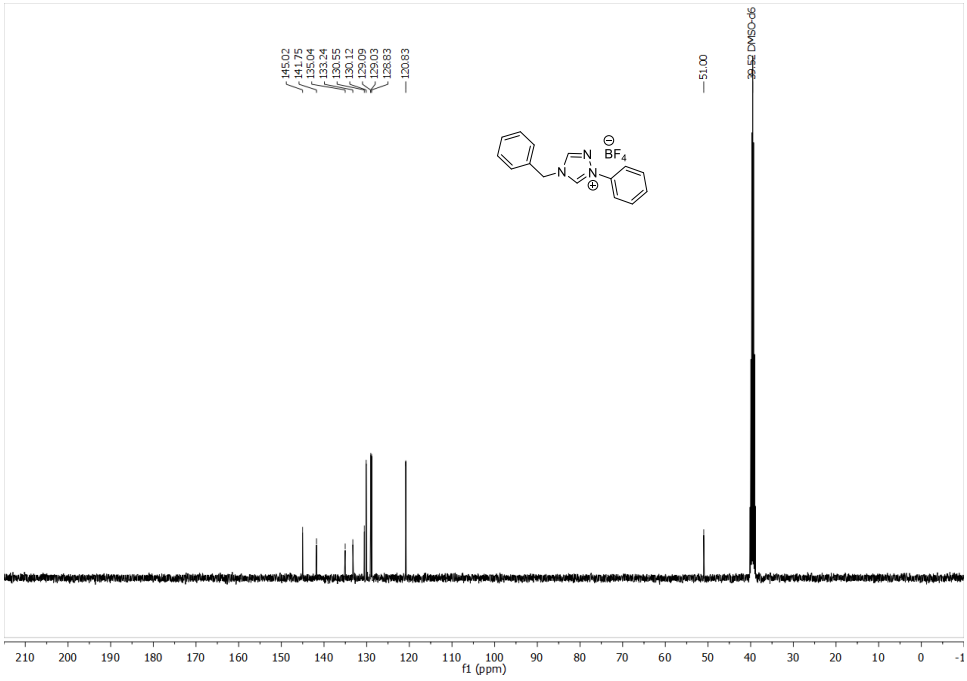

Figure D035: ^{13}C NMR spectrum of 4-benzyl-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[2a]BF$_4$**) (100 MHz, DMSO-d_6, 298 K).

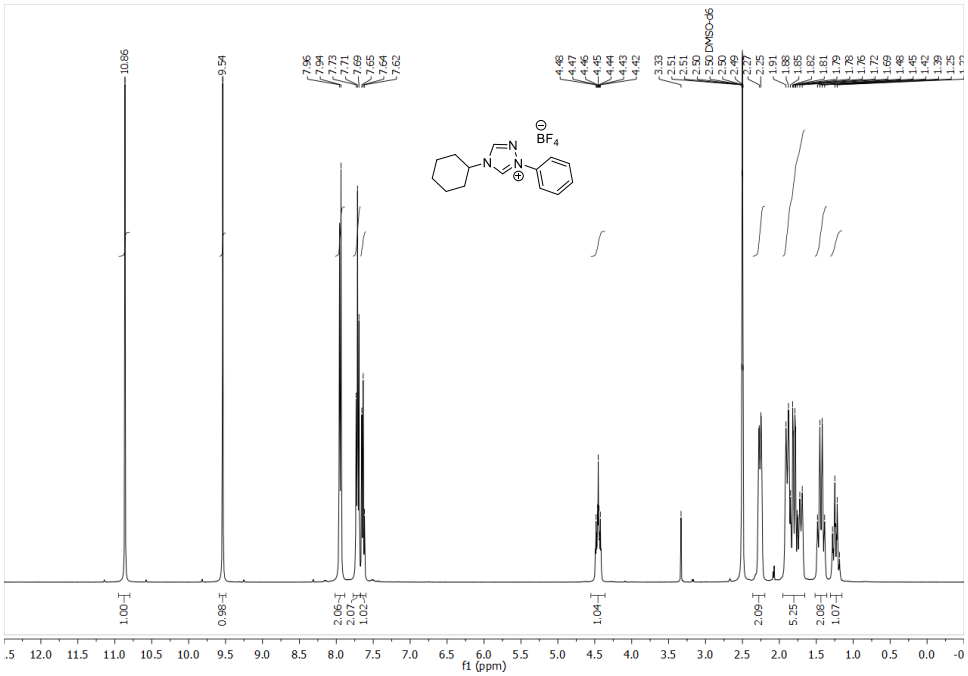

Figure D036: ^{1}H NMR spectrum of 4-*c*yclohexyl-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[2b]BF$_4$**) (400 MHz, DMSO-d_6, 298 K).

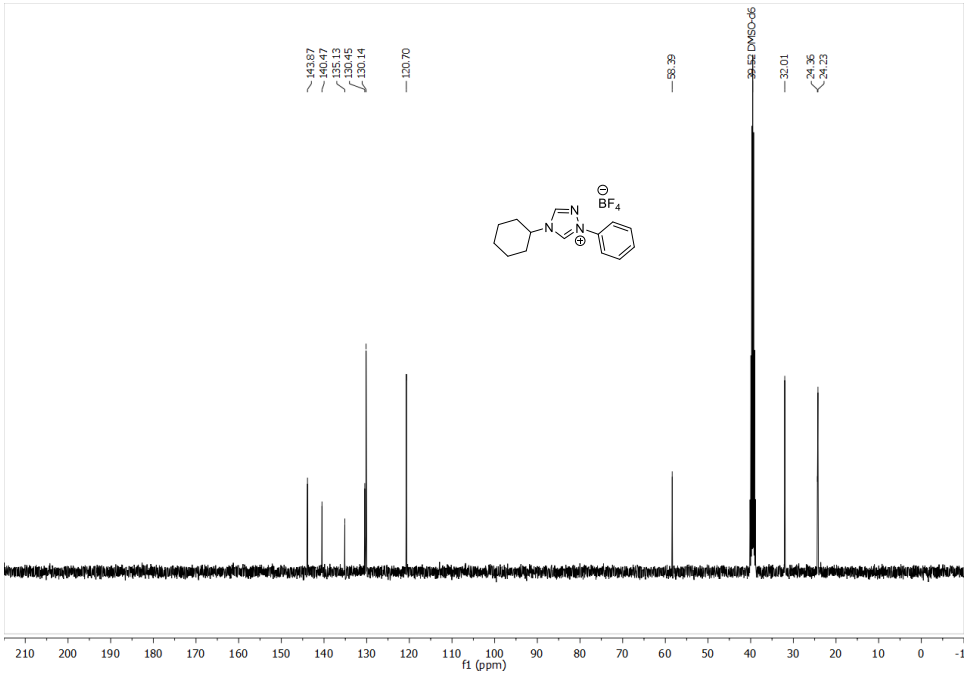

Figure D037: ^{13}C NMR spectrum of 4-*c*yclohexyl-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[2b]BF$_4$**) (100 MHz, DMSO-d_6, 298 K).

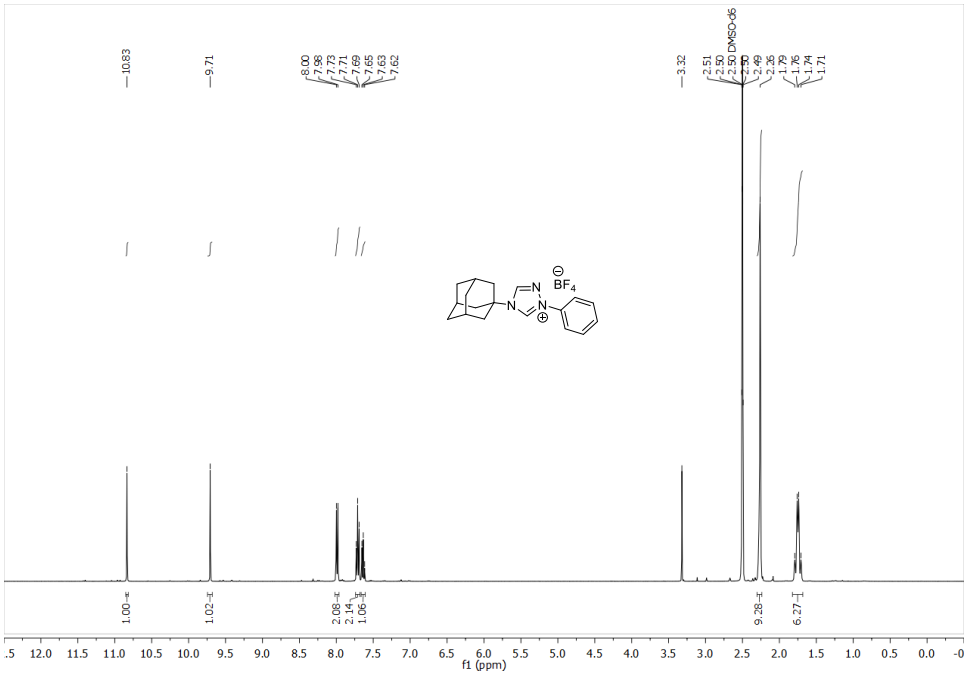

Figure D038: ^{1}H NMR spectrum of 4-((3*s*,5*s*,7*s*)-adamantan-1-yl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[2c]BF$_4$**) (400 MHz, DMSO-d_6, 298 K).

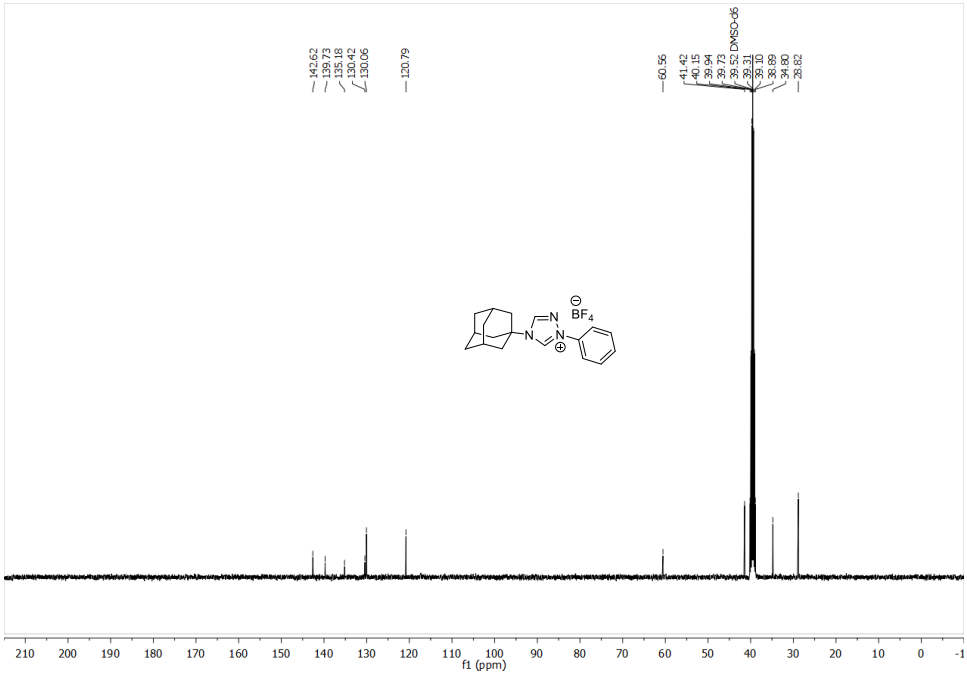

Figure D039: ^{13}C NMR spectrum of 4-((3*s*,5*s*,7*s*)-adamantan-1-yl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[2c]BF$_4$**) (100 MHz, DMSO-d_6, 298 K).

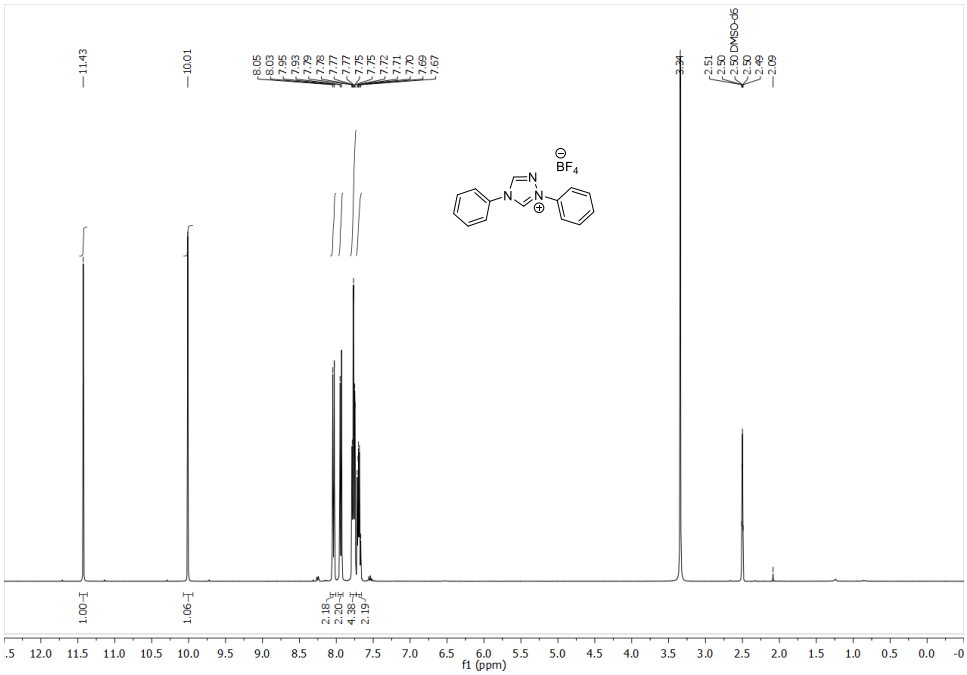

Figure D040: ^{1}H NMR spectrum of 1,4-diphenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[2d]BF$_4$**) (400 MHz, DMSO-d_6, 298 K).

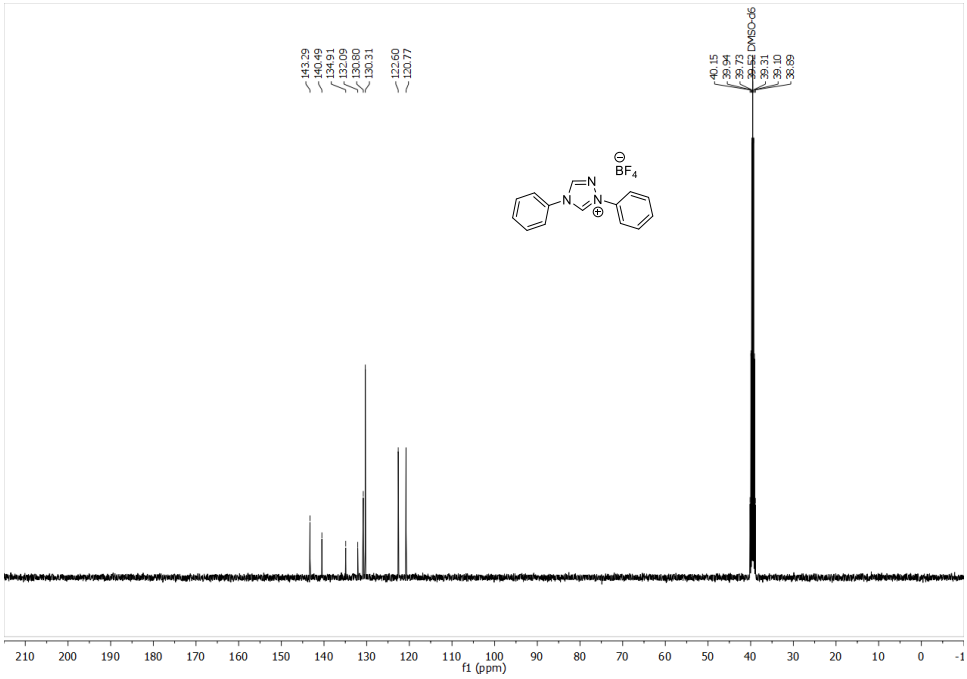

Figure D041: ^{13}C NMR spectrum of 1,4-diphenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[2d]BF$_4$**) (100 MHz, DMSO-d_6, 298 K).

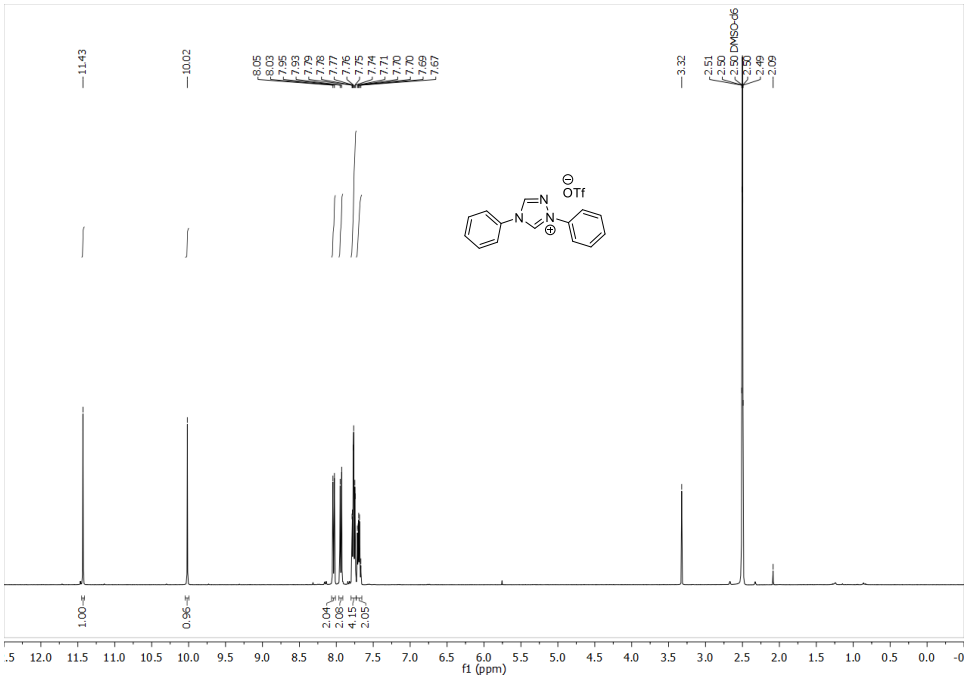

Figure D042: ^{1}H NMR spectrum of 1,4-diphenyl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**[2d]OTf**) (400 MHz, DMSO-d_6, 298 K).

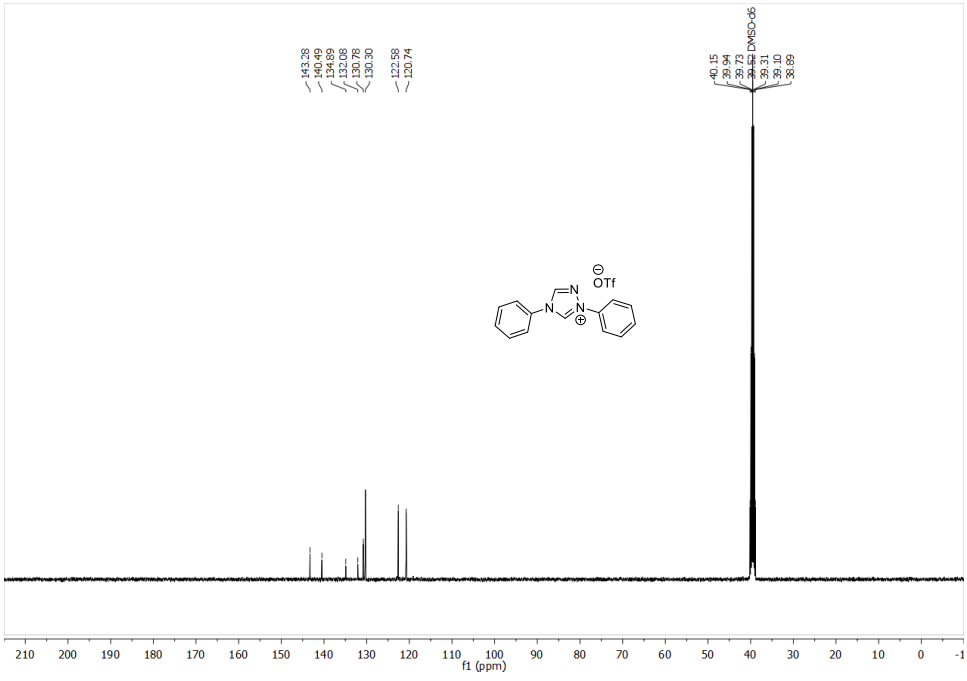

Figure D043: ^{13}C NMR spectrum of 1,4-diphenyl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**[2d]OTf**) (100 MHz, DMSO-d_6, 298 K).

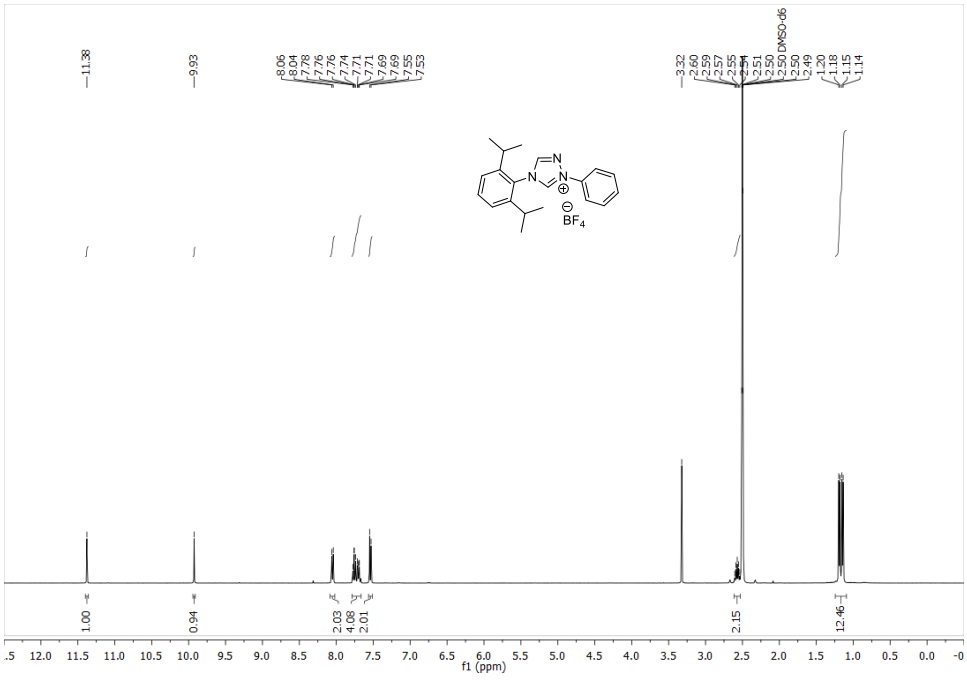

Figure D044: ^{1}H NMR spectrum of 4-(2,6-diisopropylphenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[2e]BF$_4$**) (400 MHz, DMSO-d_6, 298 K).

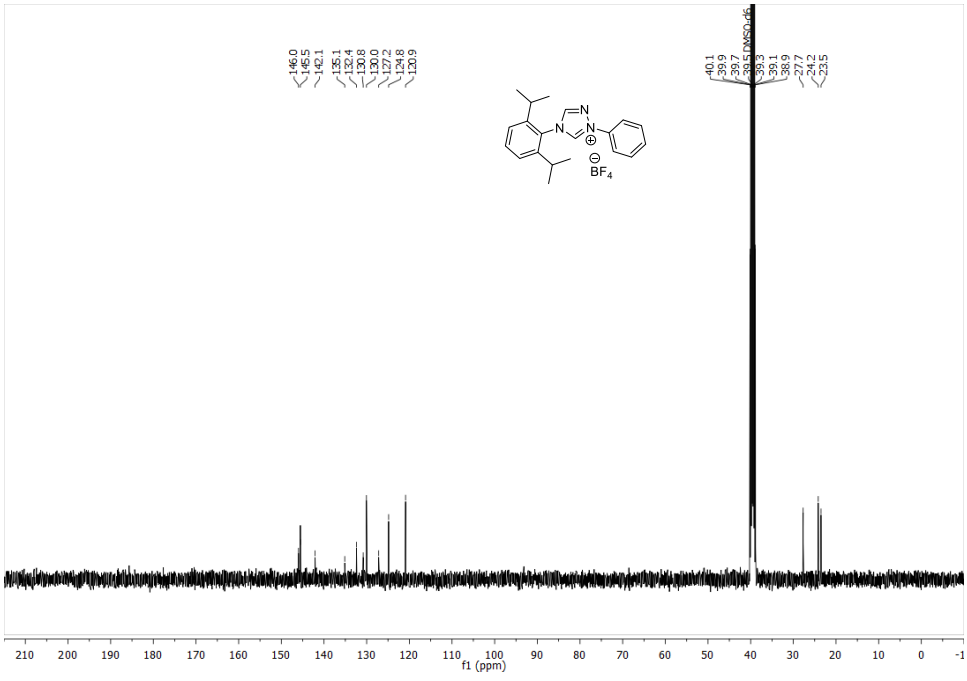

Figure D045: ^{13}C NMR spectrum of 4-(2,6-diisopropylphenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[2e]BF$_4$**) (100 MHz, DMSO-d_6, 298 K).

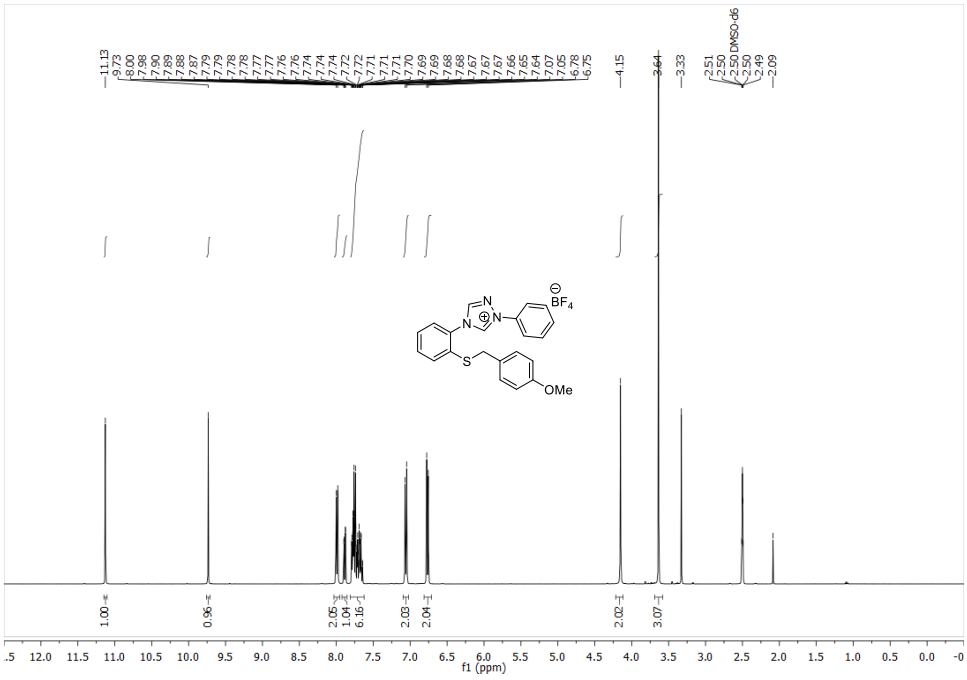

Figure D046: ^{1}H NMR spectrum of 1-phenyl-4-(2-((4-methoxybenzyl)thio)phenyl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[2f]BF$_4$**) (400 MHz, DMSO-d_6, 298 K).

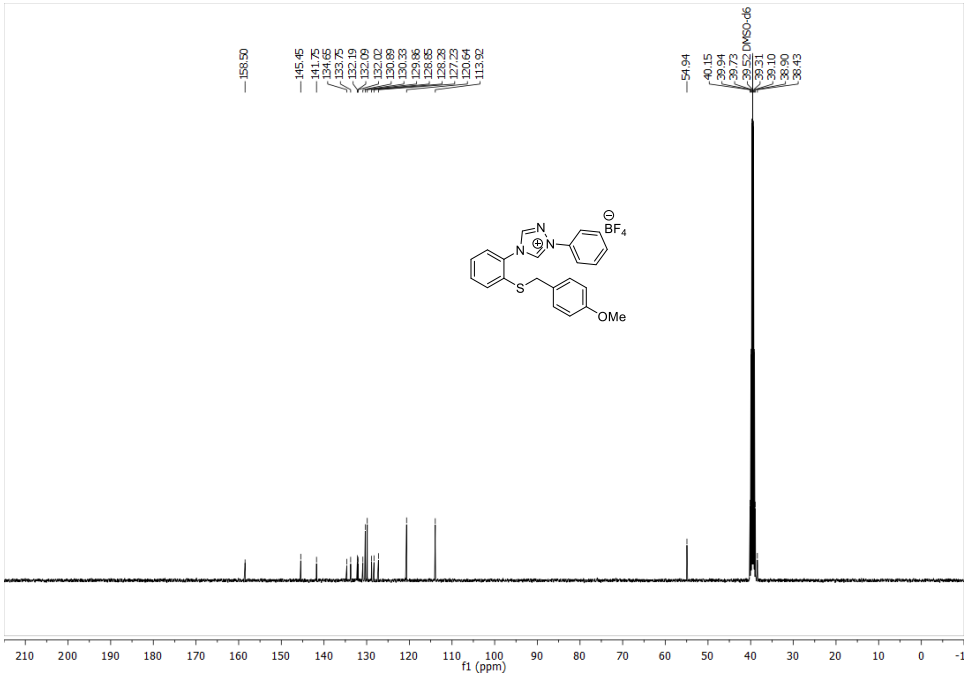

Figure D047: ^{13}C NMR spectrum of 1-phenyl-4-(2-((4-methoxybenzyl)thio)phenyl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[2f]BF$_4$**) (100 MHz, DMSO-d_6, 298 K).

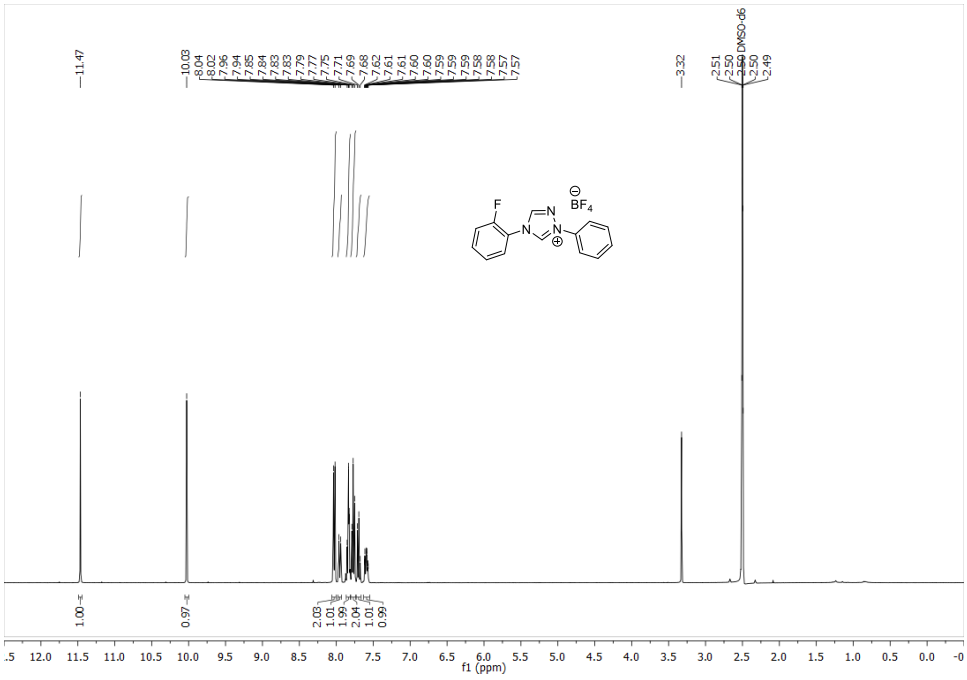

Figure D048: [1]H NMR spectrum of 4-(2-fluorophenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[2g]BF$_4$**) (400 MHz, DMSO-d_6, 298 K).

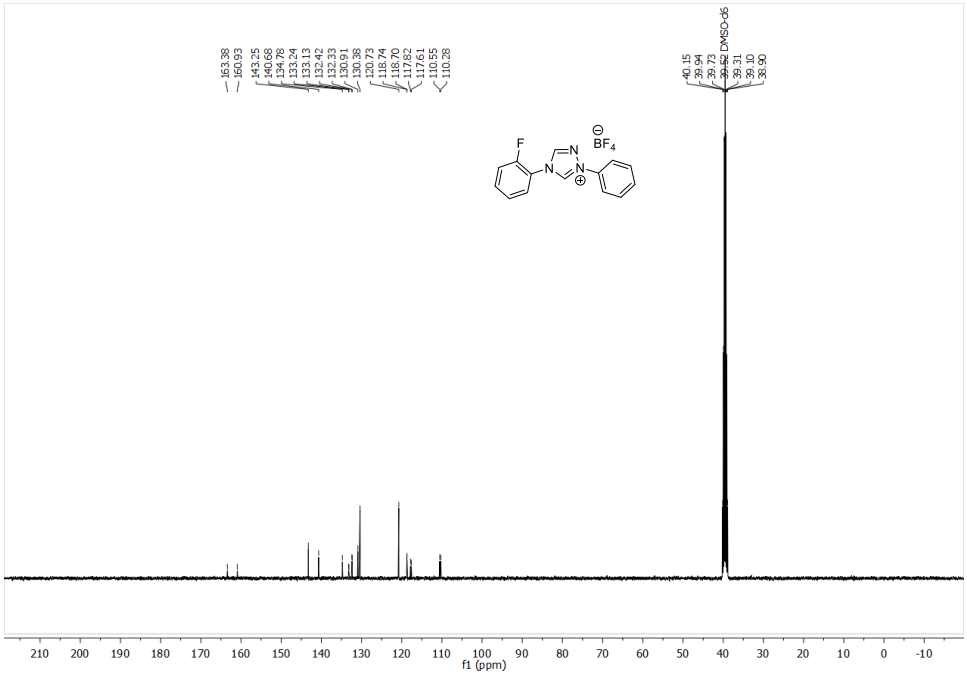

Figure D049: [13]C NMR spectrum of 4-(2-fluorophenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[2g]BF$_4$**) (100 MHz, DMSO-d_6, 298 K).

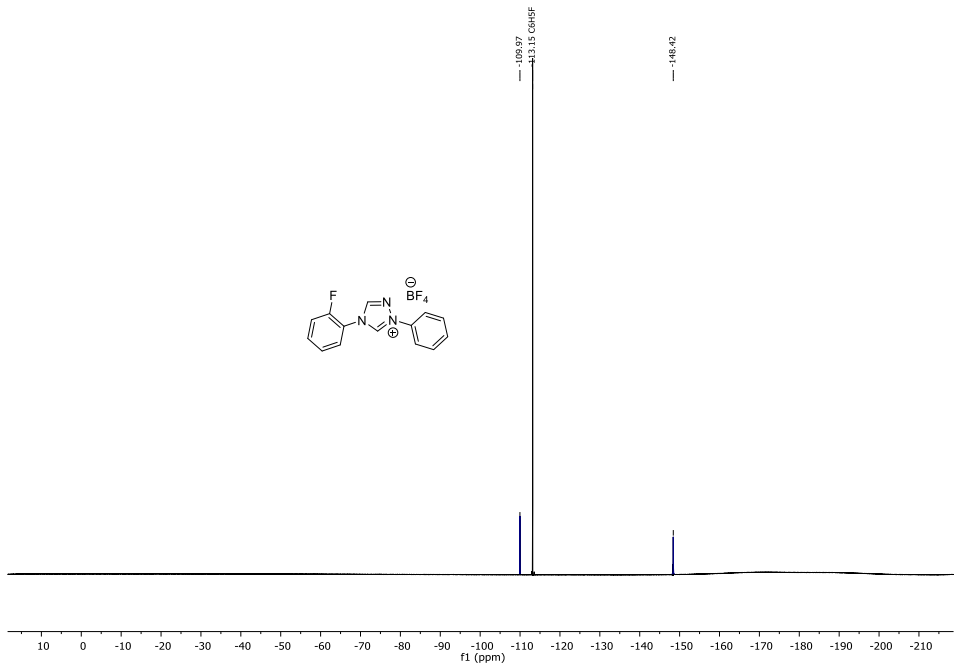

Figure D050: ^{19}F NMR spectrum of 4-(2-fluorophenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[2g]BF$_4$**) (376 MHz, DMSO-d_6, 298 K, referenced to fluorobenzene).

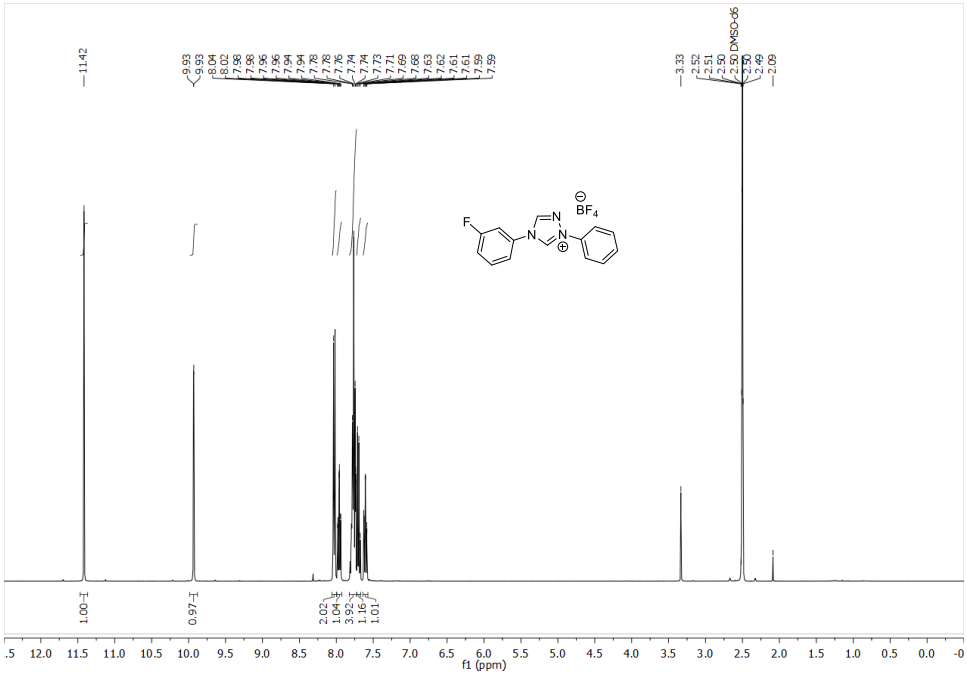

Figure D051: ^{1}H NMR spectrum of 4-(3-fluorophenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[2h]BF$_4$**) (400 MHz, DMSO-d_6, 298 K).

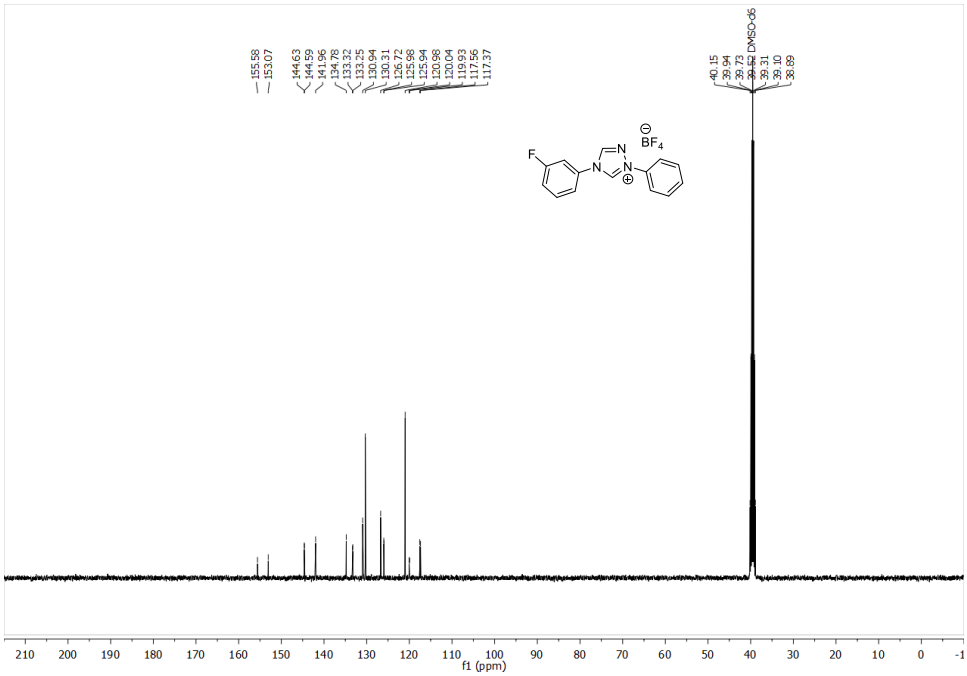

Figure D052: ^{13}C NMR spectrum of 4-(3-fluorophenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[2h]BF$_4$**) (100 MHz, DMSO-d_6, 298 K).

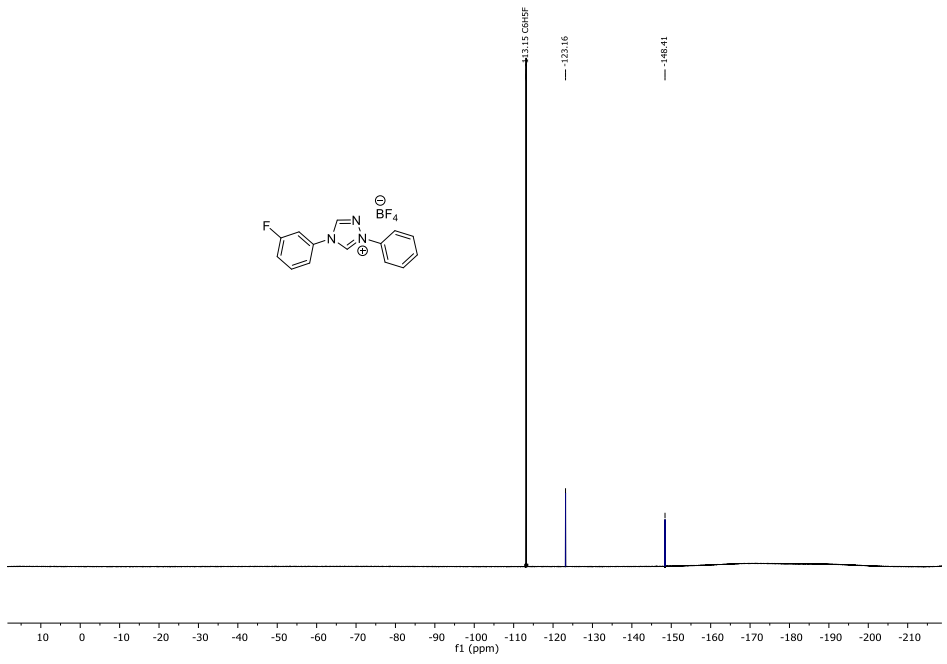

Figure D053: ^{19}F NMR spectrum of 4-(3-fluorophenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[2h]BF$_4$**) (376 MHz, DMSO-d_6, 298 K, referenced to fluorobenzene).

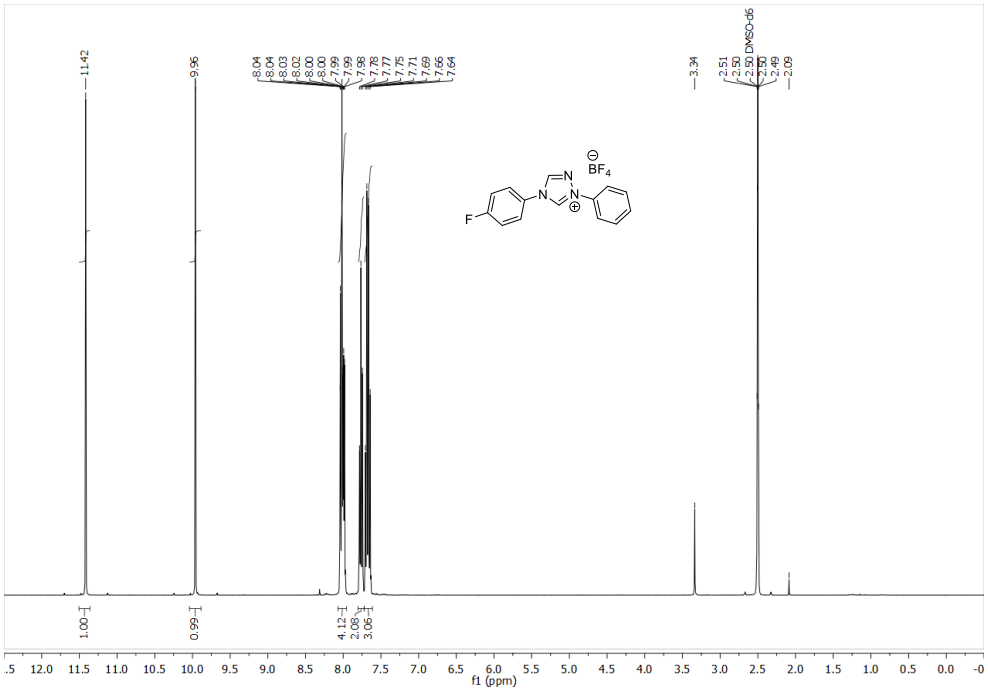

Figure D054: ^{1}H NMR spectrum of 4-(4-fluorophenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[2i]BF$_4$**) (400 MHz, DMSO-d_6, 298 K).

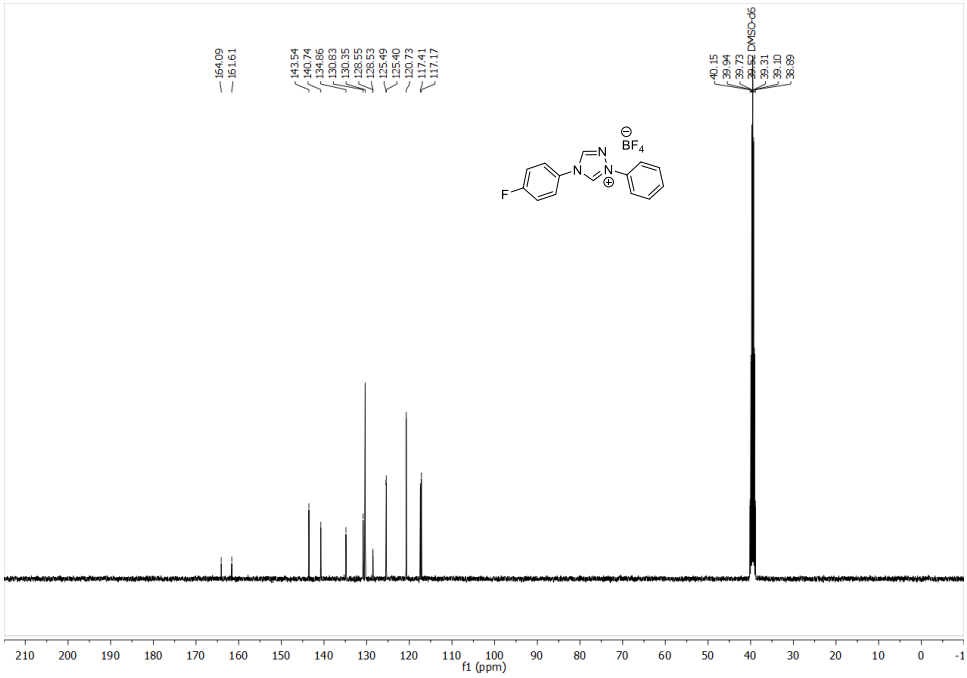

Figure D055: ^{13}C NMR spectrum of 4-(4-fluorophenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[2i]BF$_4$**) (100 MHz, DMSO-d_6, 298 K).

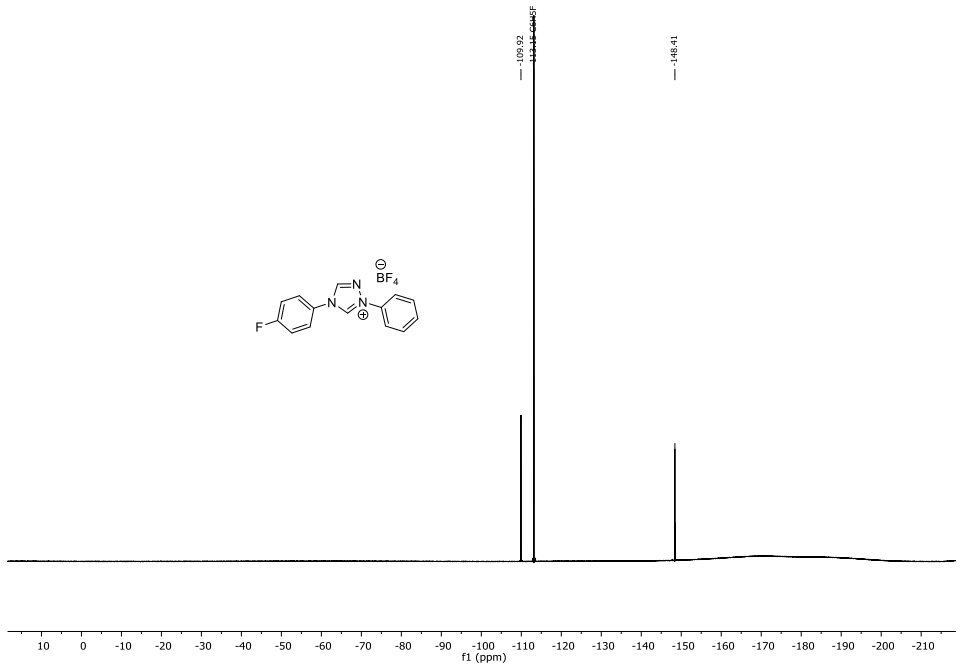

Figure D056: ^{19}F NMR spectrum of 4-(4-fluorophenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[2i]BF$_4$**) (376 MHz, DMSO-d_6, 298 K, referenced to fluorobenzene).

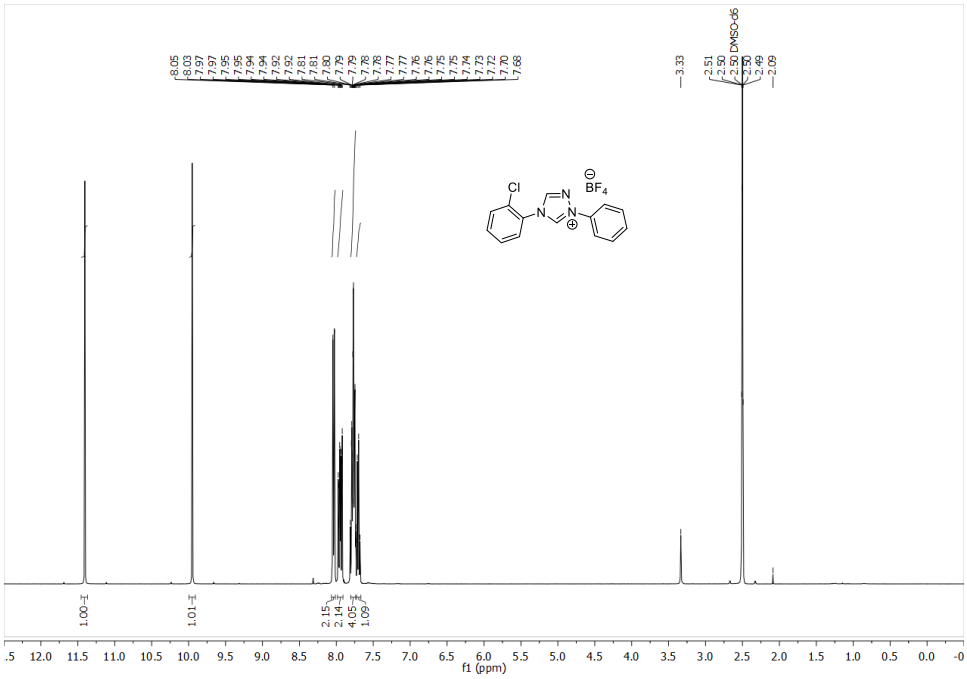

Figure D057: ^{1}H NMR spectrum of 4-(2-*c*hlorophenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[2j]BF$_4$**) (400 MHz, DMSO-d_6, 298 K).

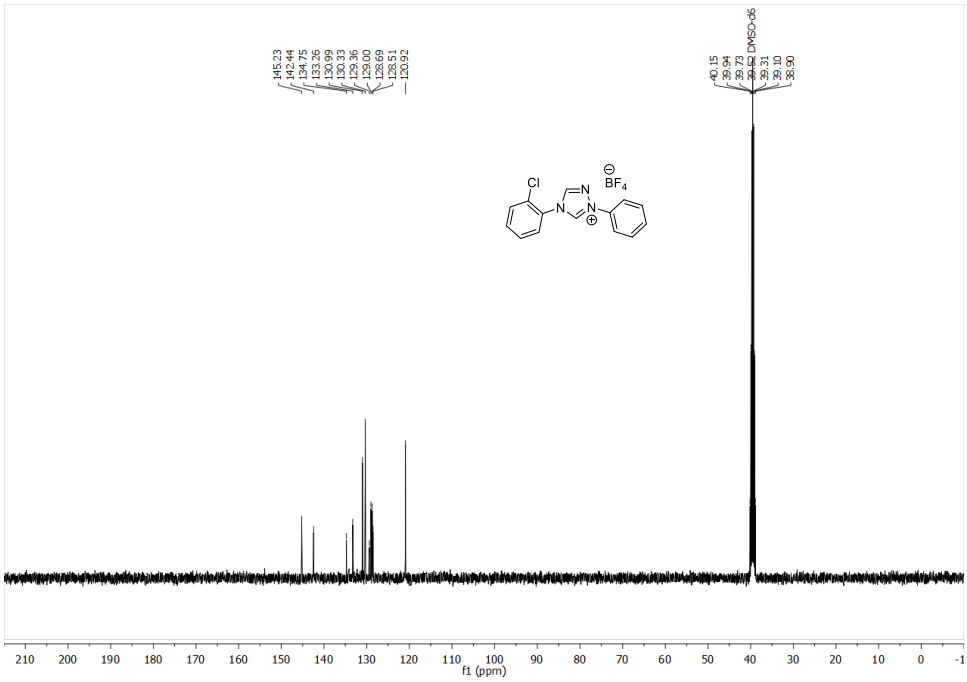

Figure D058: ^{13}C NMR spectrum of 4-(2-*c*hlorophenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[2j]BF$_4$**) (100 MHz, DMSO-d_6, 298 K).

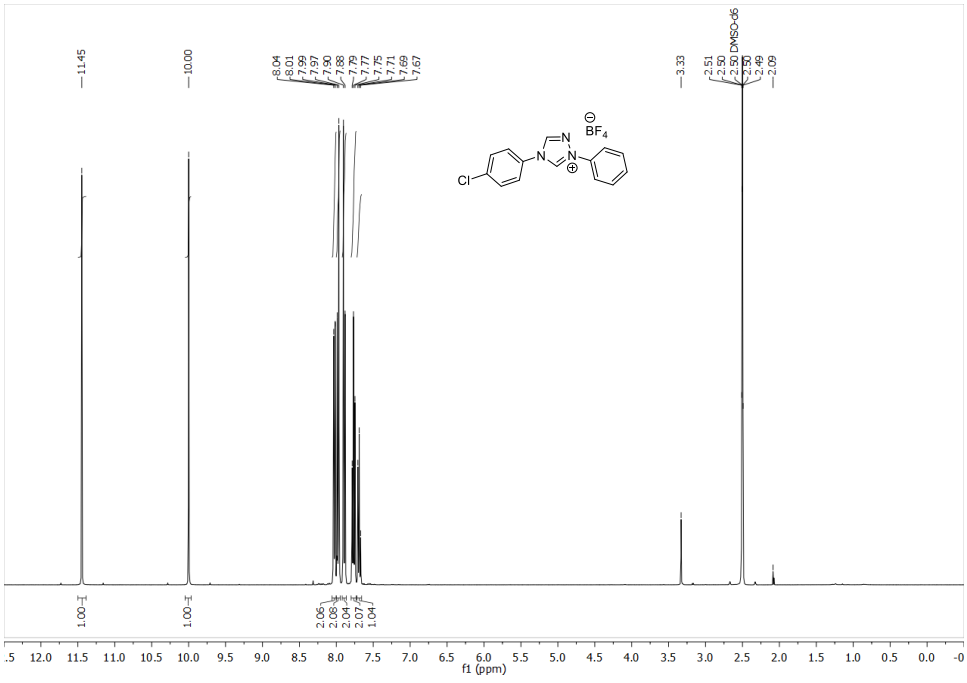

Figure D059: ^{1}H NMR spectrum of 4-(4-*c*hlorophenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[2k]BF$_4$**) (400 MHz, DMSO-d_6, 298 K).

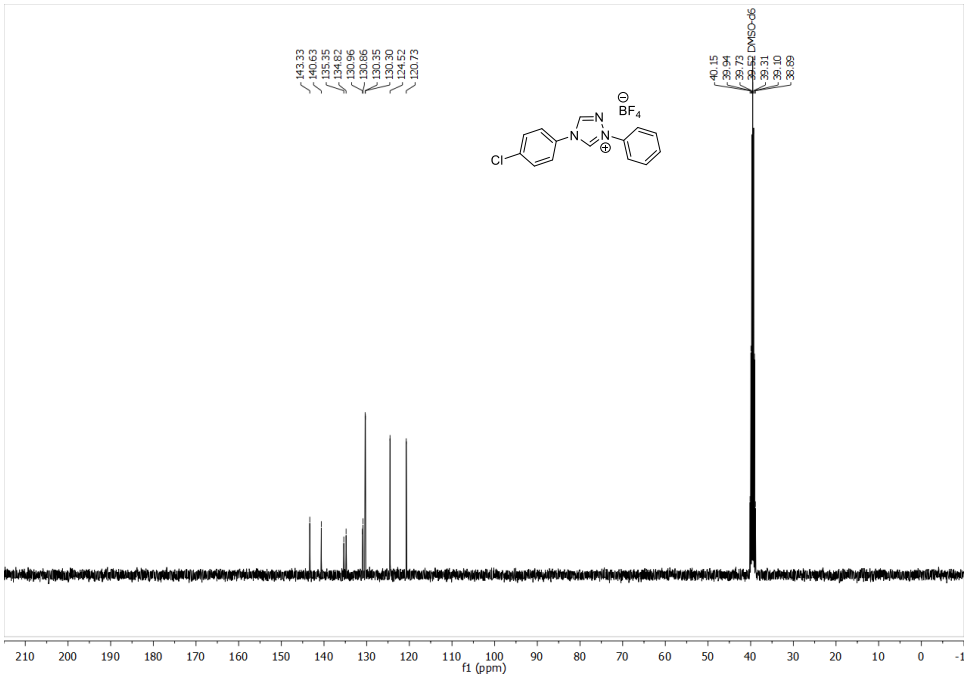

Figure D060: ^{13}C NMR spectrum of 4-(4-*c*hlorophenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[2k]BF$_4$**) (100 MHz, DMSO-d_6, 298 K).

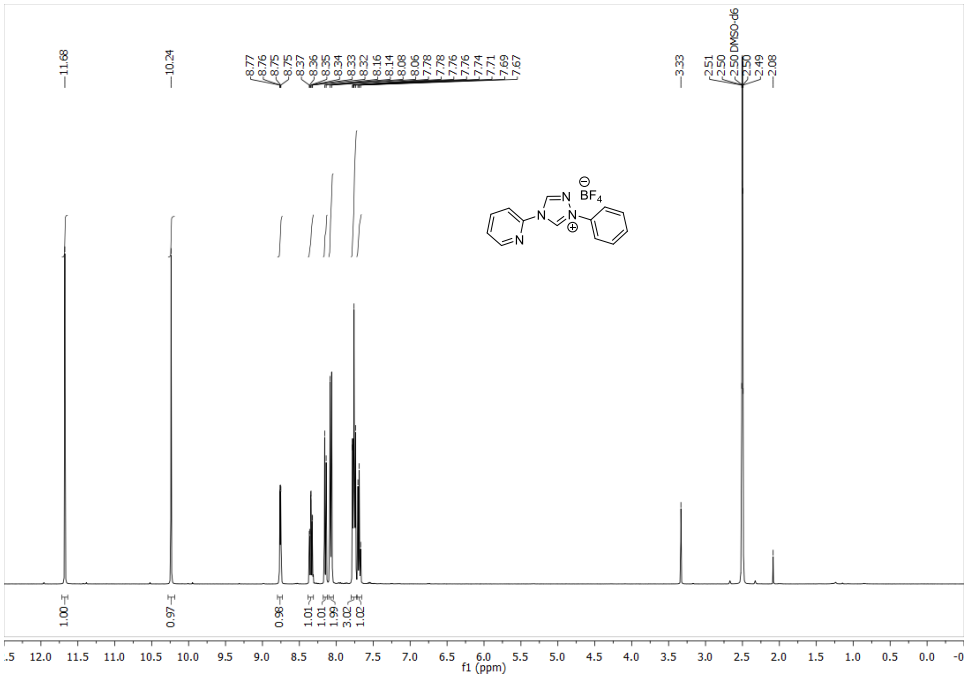

Figure D061: ^{1}H NMR spectrum of 1-phenyl-4-(pyridin-2-yl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[2l]BF$_4$**) (400 MHz, DMSO-d_6, 298 K).

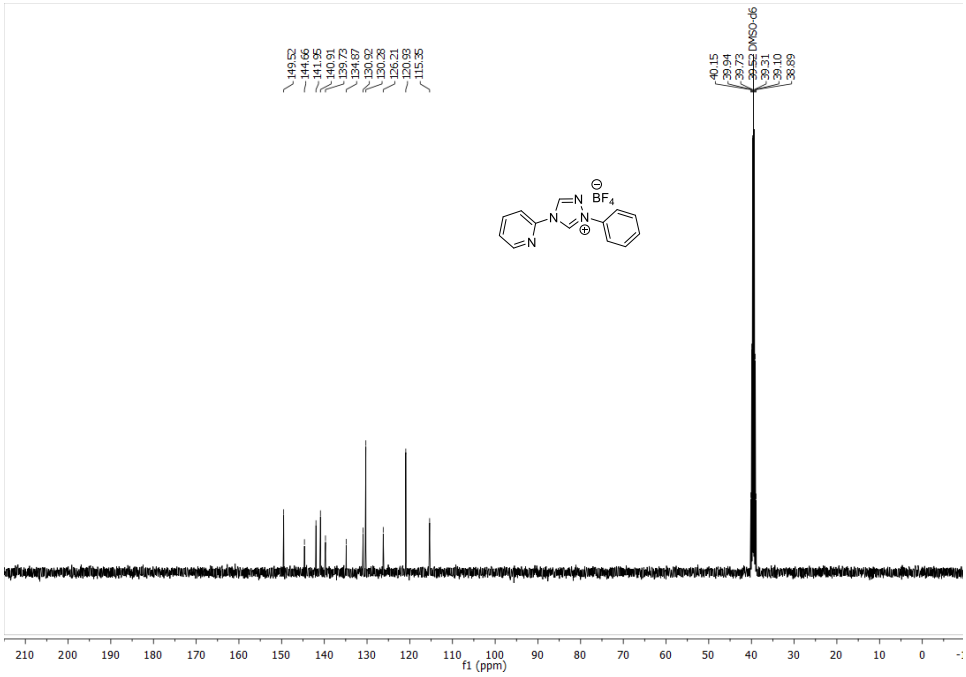

Figure D062: ^{13}C NMR spectrum of 1-phenyl-4-(pyridin-2-yl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[2l]BF$_4$**) (100 MHz, DMSO-d_6, 298 K).

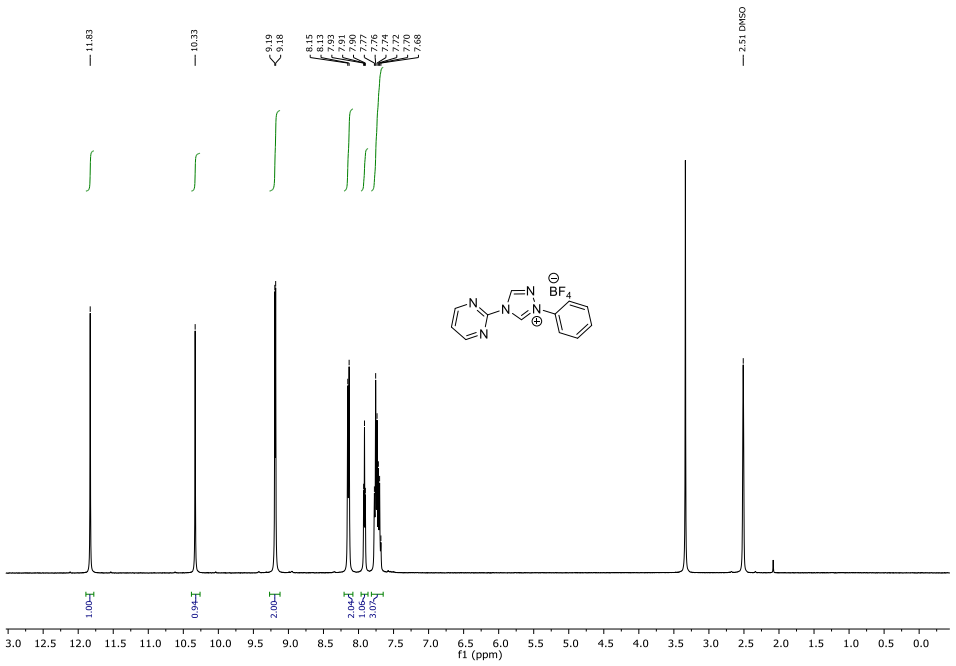

Figure D063: ^{1}H NMR spectrum of 1-phenyl-4-(pyrimidin-2-yl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[2m]BF$_4$**) (400 MHz, DMSO-d_6, 298 K).

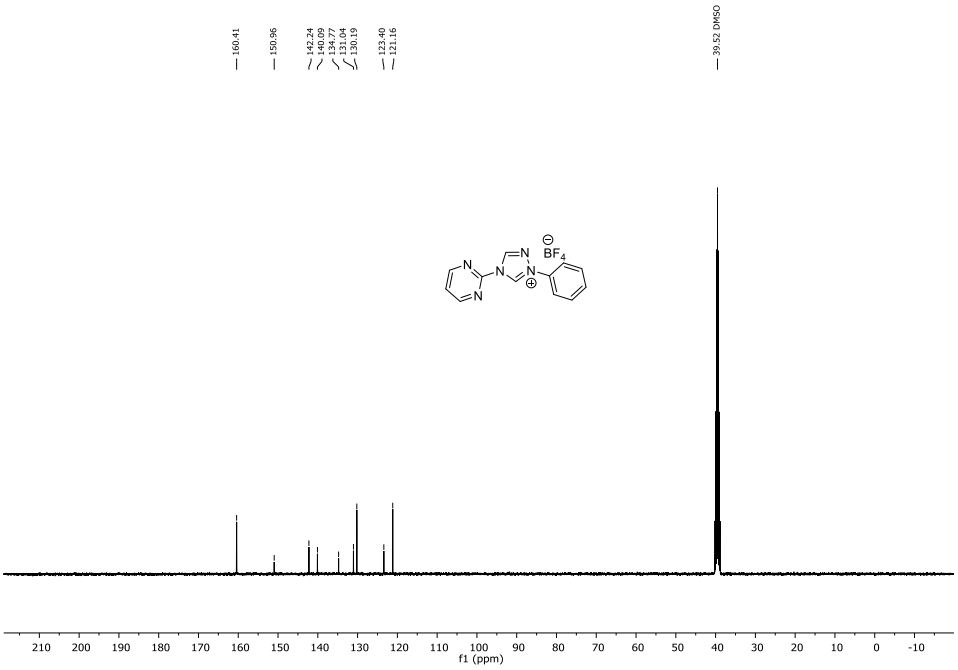

Figure D064: ^{13}C NMR spectrum of 1-phenyl-4-(pyrimidin-2-yl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[2m]BF$_4$**) (100 MHz, DMSO-d_6, 298 K).

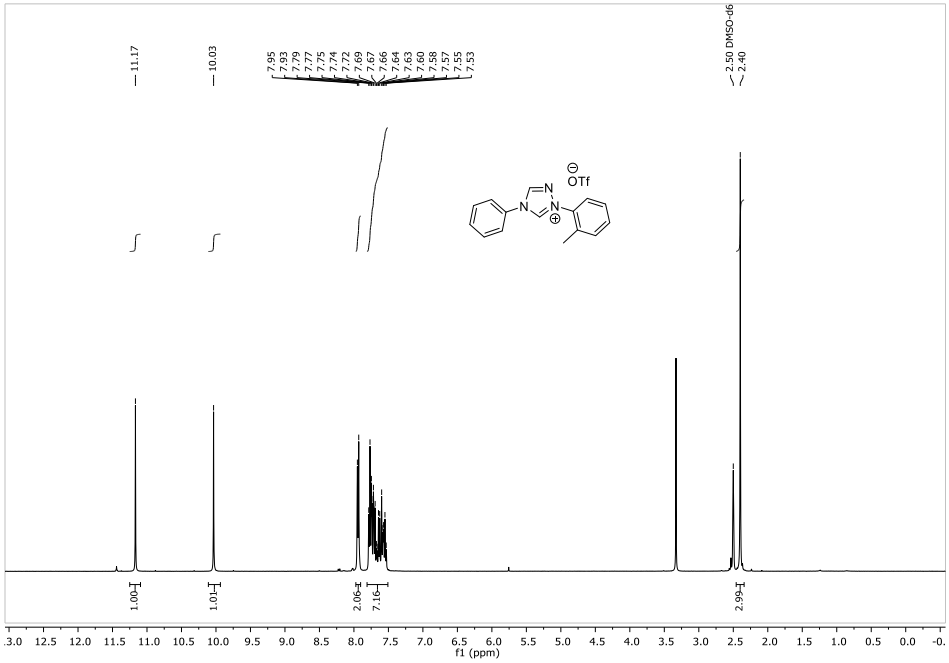

Figure D065: ^{1}H NMR spectrum of 4-phenyl-1-(o-tolyl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**[3d]OTf**) (400 MHz, DMSO-d_6, 298 K).

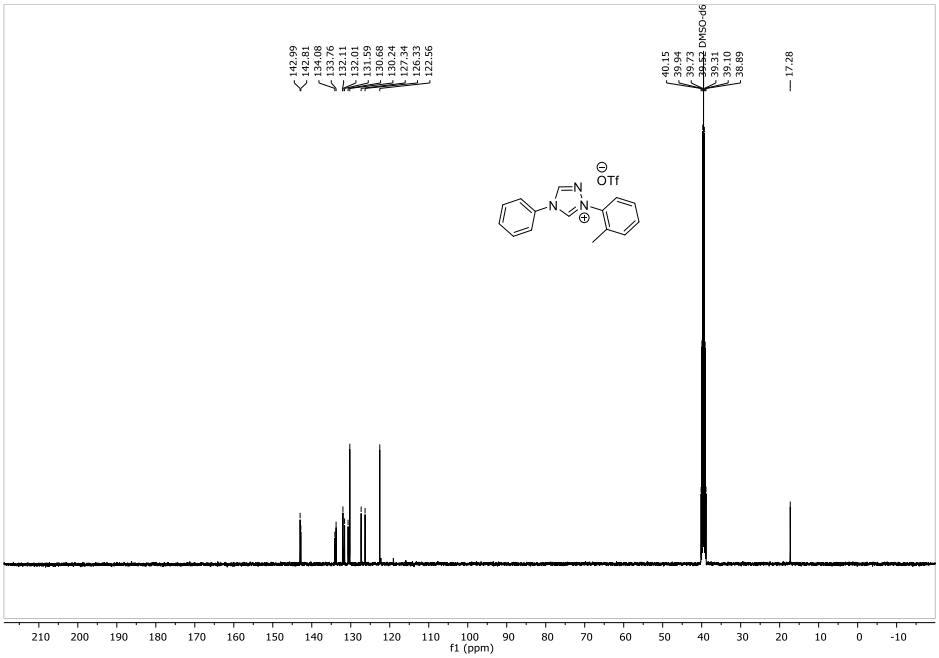

Figure D066: ^{13}C NMR spectrum of 4-phenyl-1-(o-tolyl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**[3d]OTf**) (100 MHz, DMSO-d_6, 298 K).

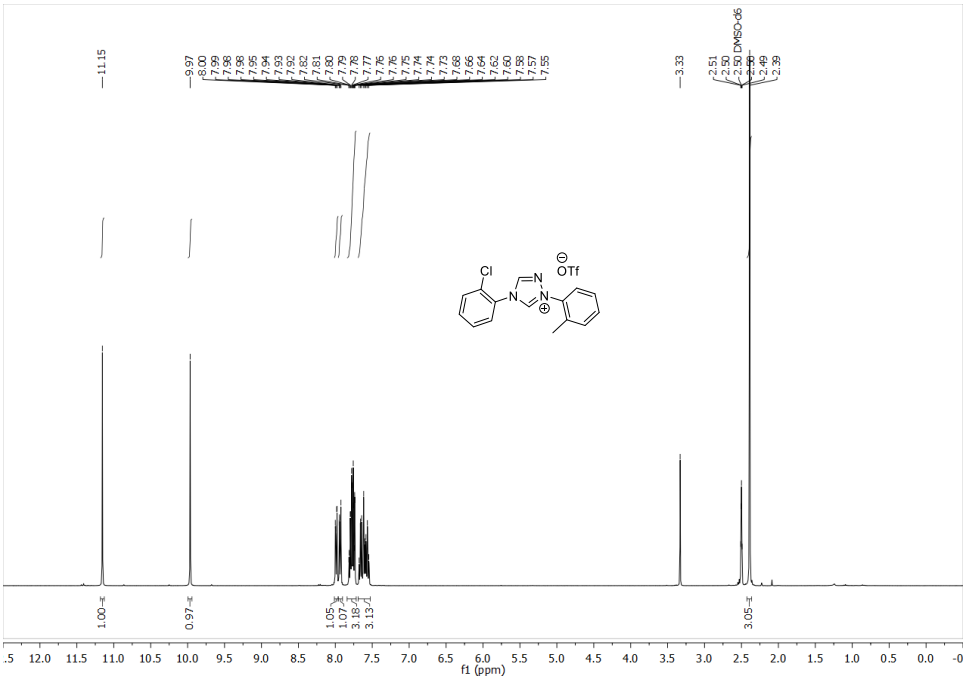

Figure D067: ^{1}H NMR spectrum of 4-(2-*c*hlorophenyl)-1-(o-tolyl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**[3j]OTf**) (400 MHz, DMSO-d_6, 298 K).

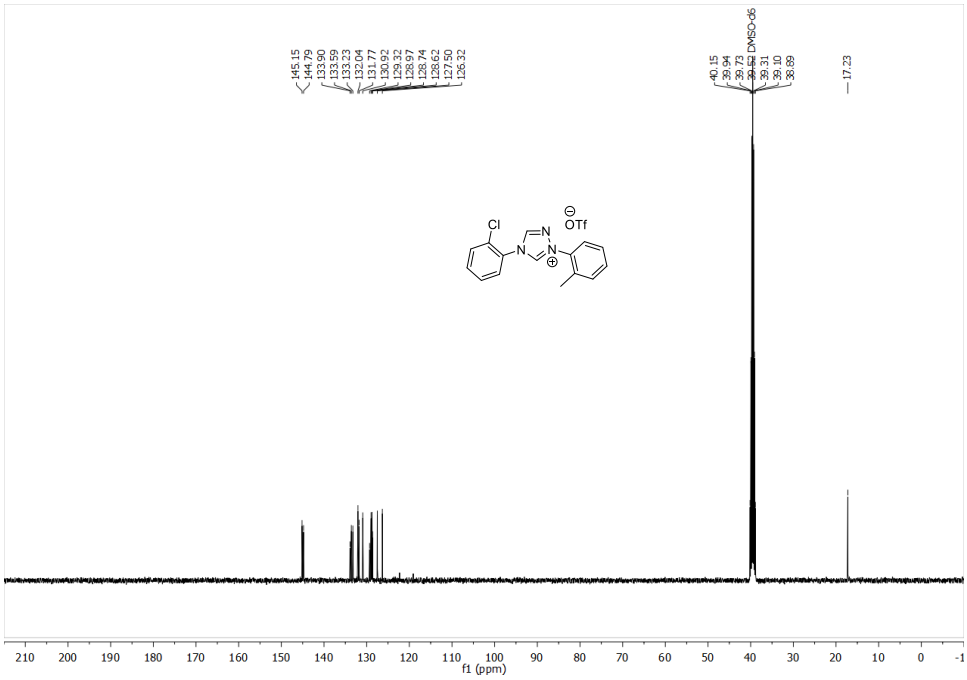

Figure D068: ^{13}C NMR spectrum of 4-(2-*c*hlorophenyl)-1-(o-tolyl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**[3j]OTf**) (100 MHz, DMSO-d_6, 298 K).

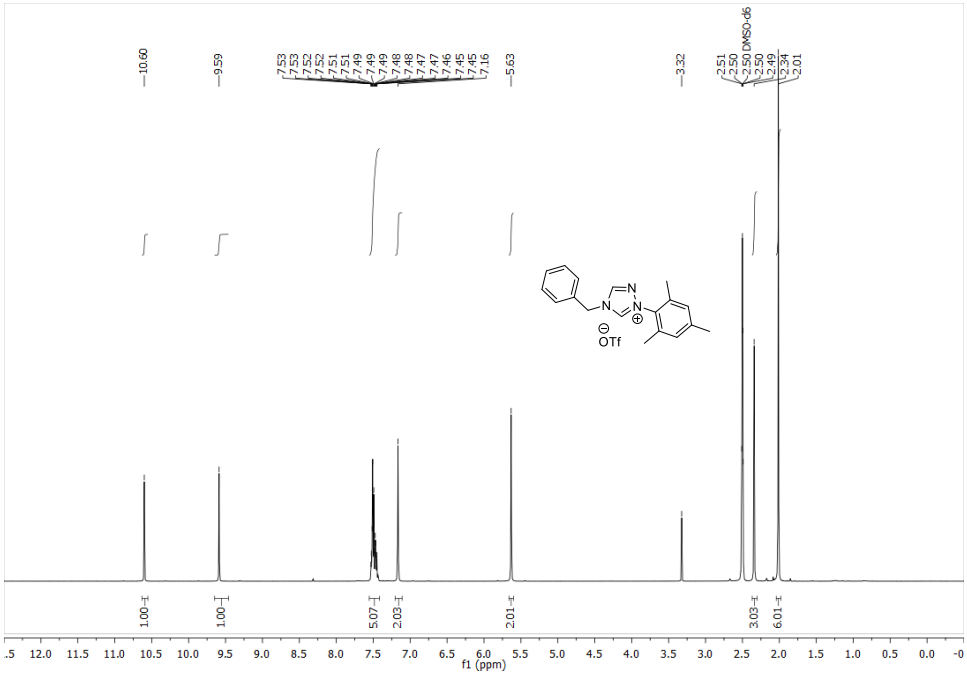

Figure D069: ^{1}H NMR spectrum of 4-benzyl-1-mesityl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**[4a]OTf**) (400 MHz, DMSO-d_6, 298 K).

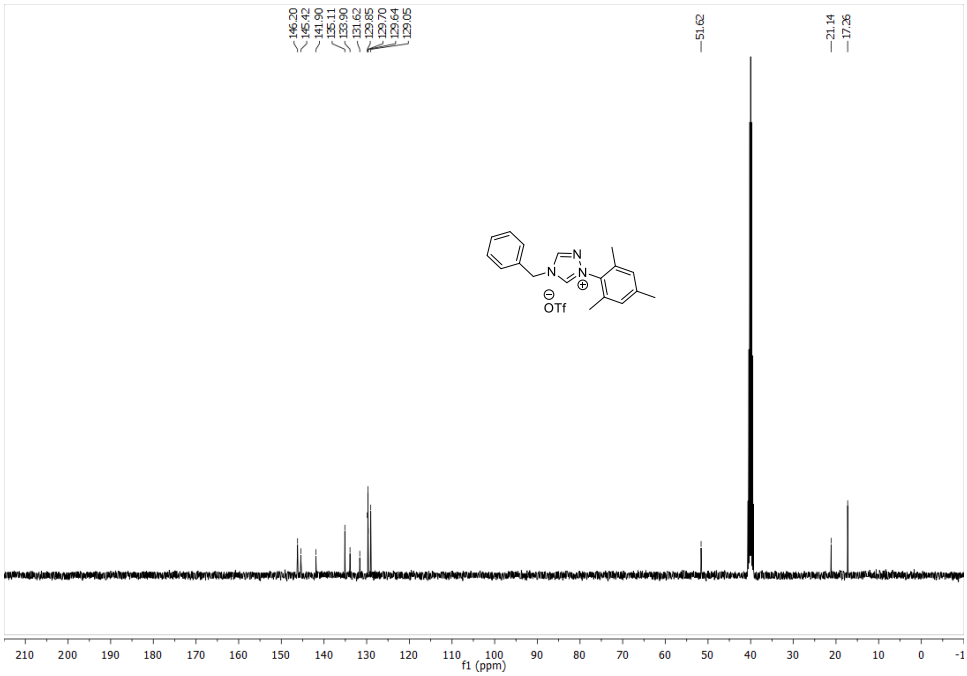

Figure D070: ^{13}C NMR spectrum of 4-benzyl-1-mesityl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**[4a]OTf**) (100 MHz, DMSO-d_6, 298 K).

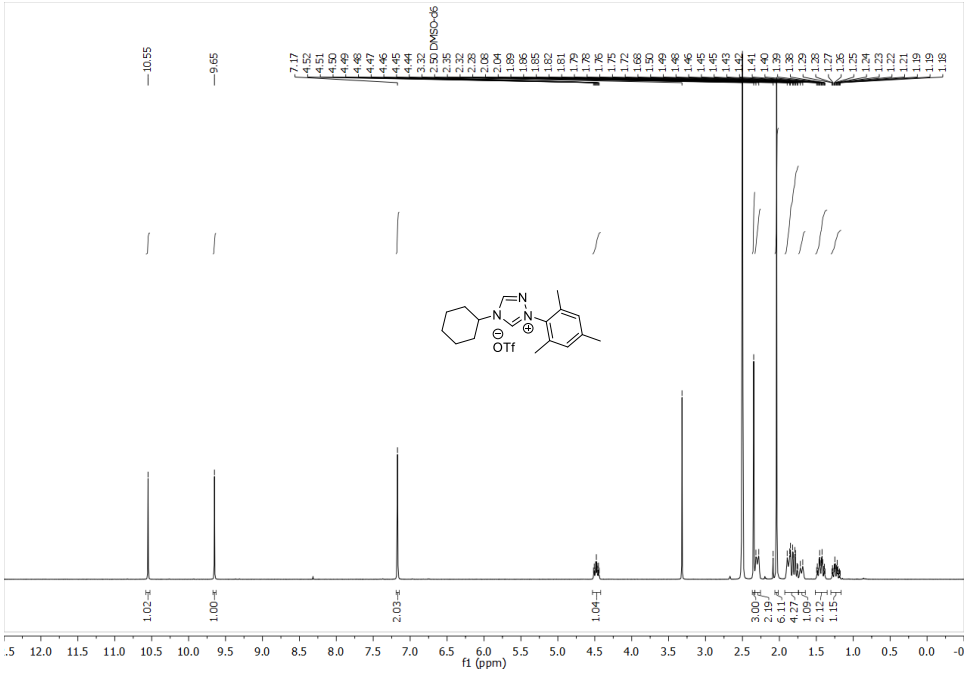

Figure D071: ^{1}H NMR spectrum of4-*c*yclohexyl-1-mesityl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**[4b]OTf**) (400 MHz, DMSO-d_6, 298 K).

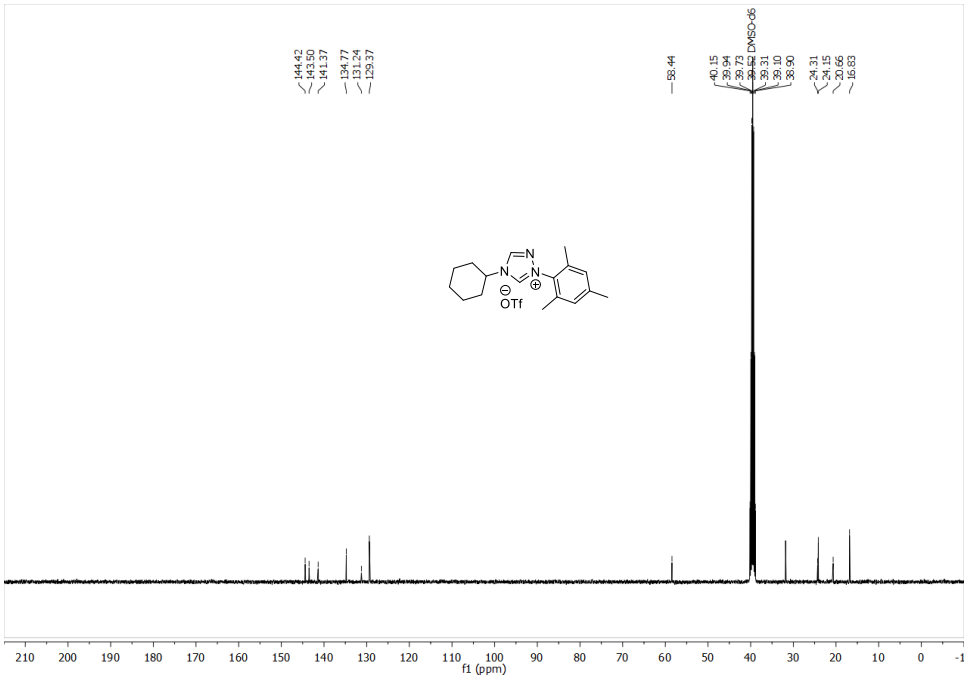

Figure D072: ^{13}C NMR spectrum of 4-*c*yclohexyl-1-mesityl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**[4b]OTf**) (100 MHz, DMSO-d_6, 298 K).

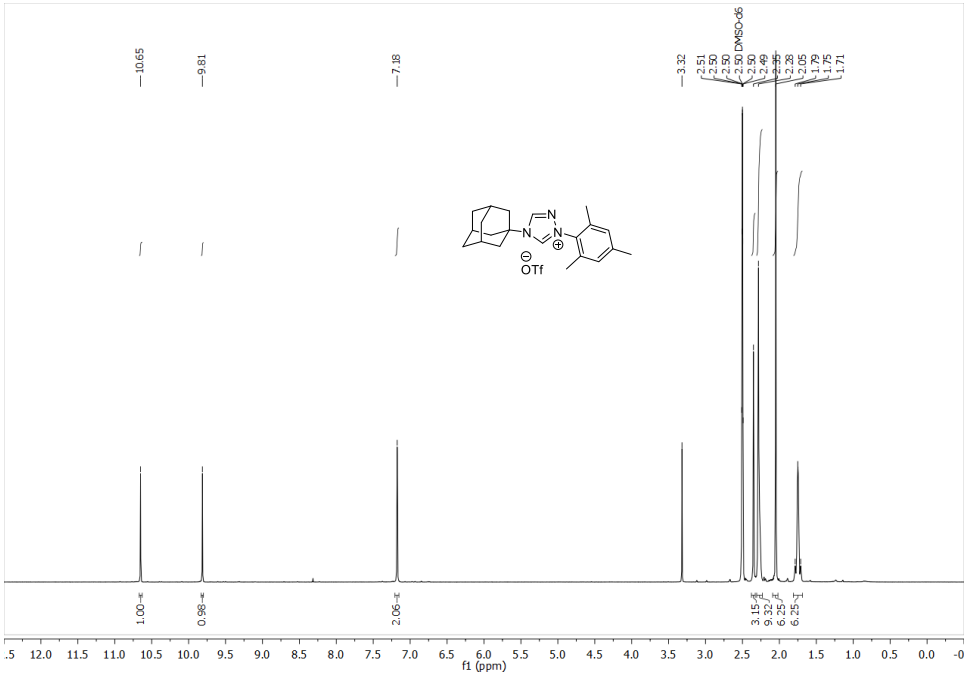

Figure D073: ^{1}H NMR spectrum of 4-((3*s*,5*s*,7*s*)-adamantan-1-yl)-1-mesityl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**[4c]OTf**) (400 MHz, DMSO-d_6, 298 K).

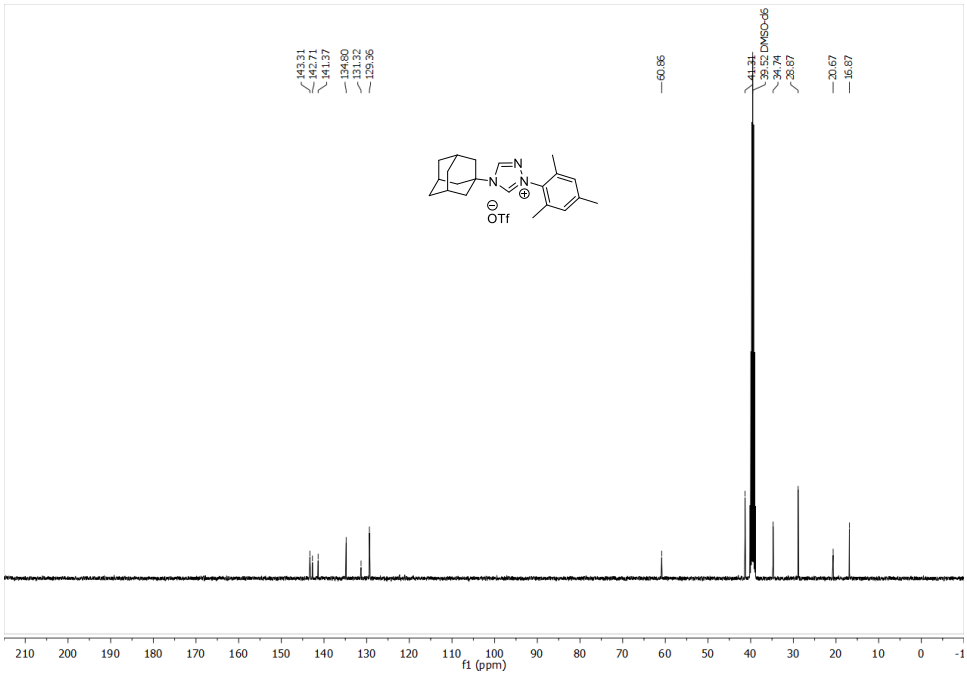

Figure D074: ^{13}C NMR spectrum of 4-((3*s*,5*s*,7*s*)-adamantan-1-yl)-1-mesityl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**[4c]OTf**) (100 MHz, DMSO-d_6, 298 K).

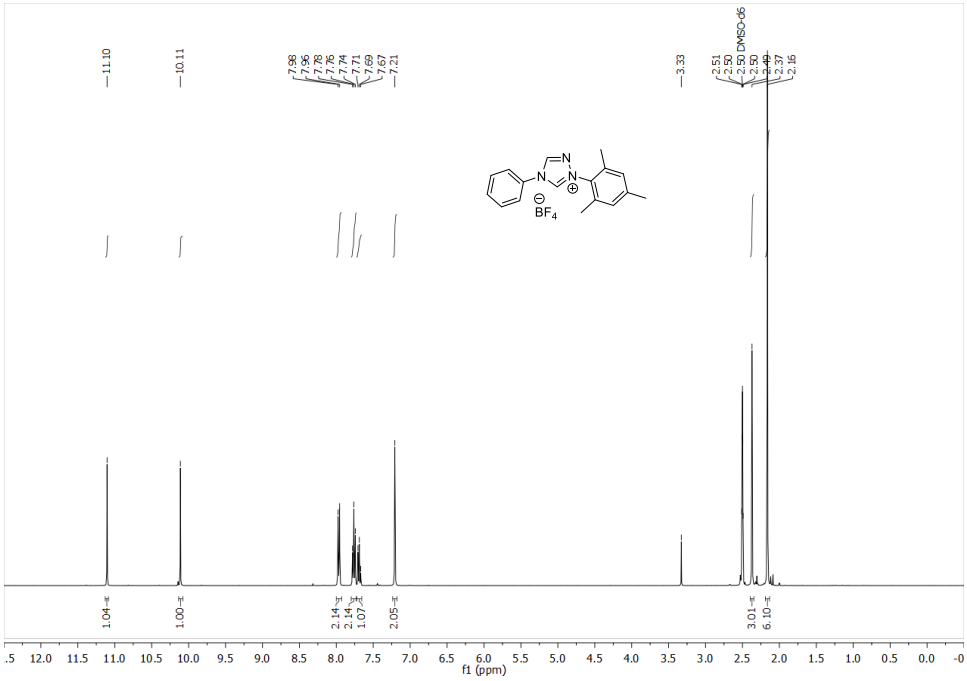

Figure D075: ^{1}H NMR spectrum of 1-mesityl-4-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[4d]BF$_4$**) (400 MHz, DMSO-d_6, 298 K).

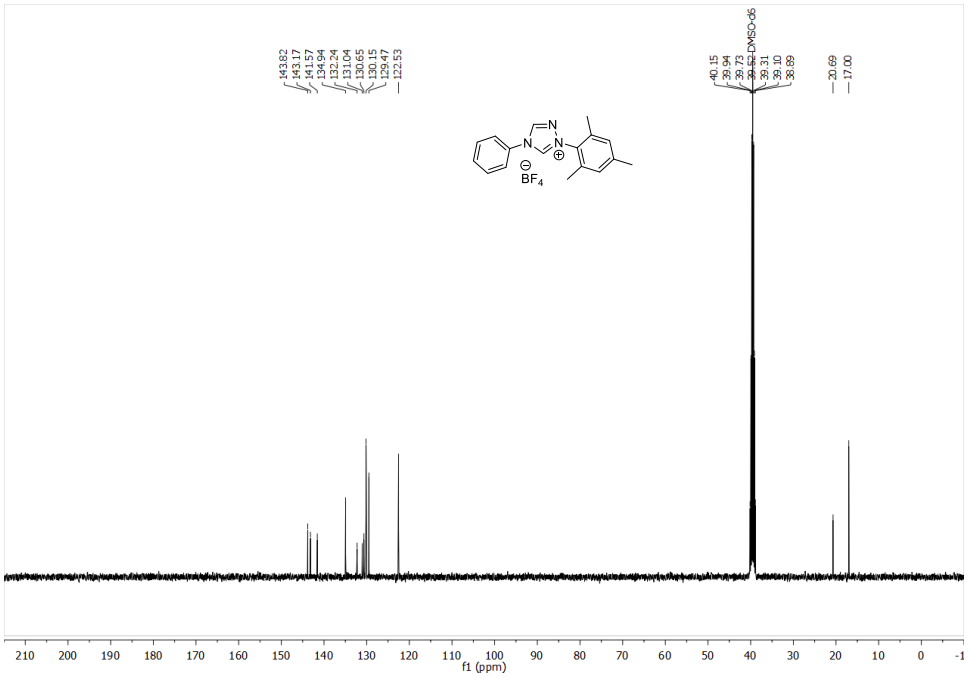

Figure D076: ^{13}C NMR spectrum of 1-mesityl-4-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[4d]BF$_4$**) (100 MHz, DMSO-d_6, 298 K).

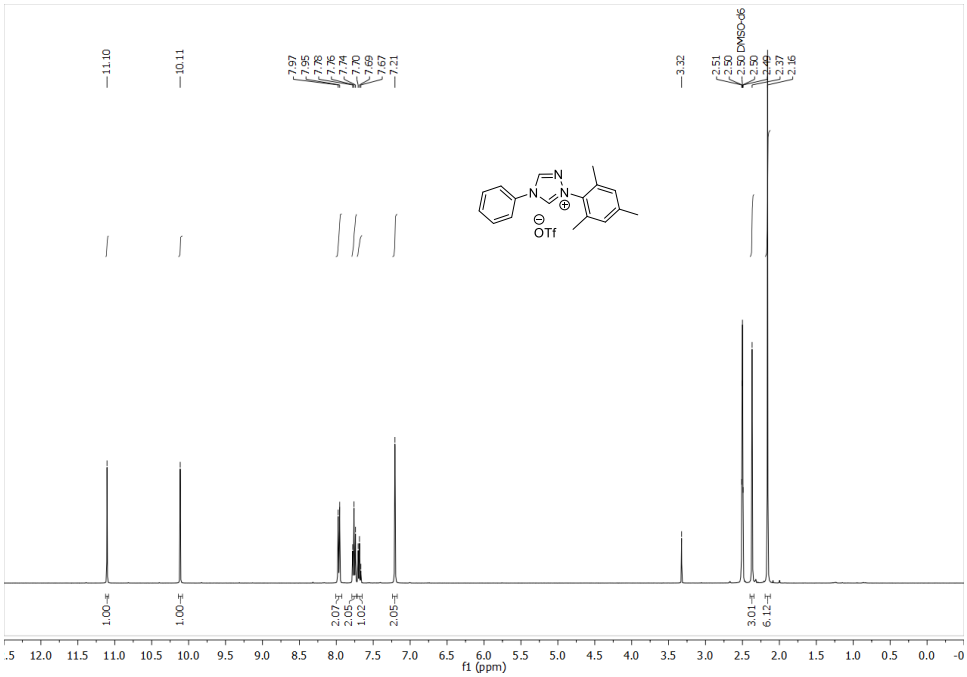

Figure D077: ^{1}H NMR spectrum of 1-mesityl-4-phenyl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**[4d]OTf**) (400 MHz, DMSO-d_6, 298 K).

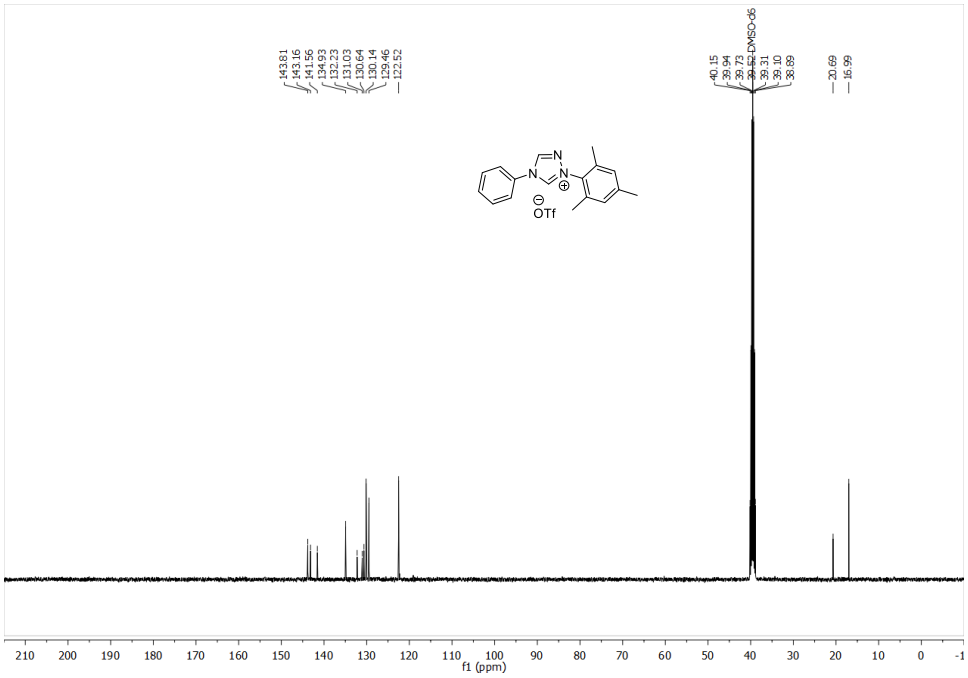

Figure D078: ^{13}C NMR spectrum of 1-mesityl-4-phenyl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**[4d]OTf**) (100 MHz, DMSO-d_6, 298 K).

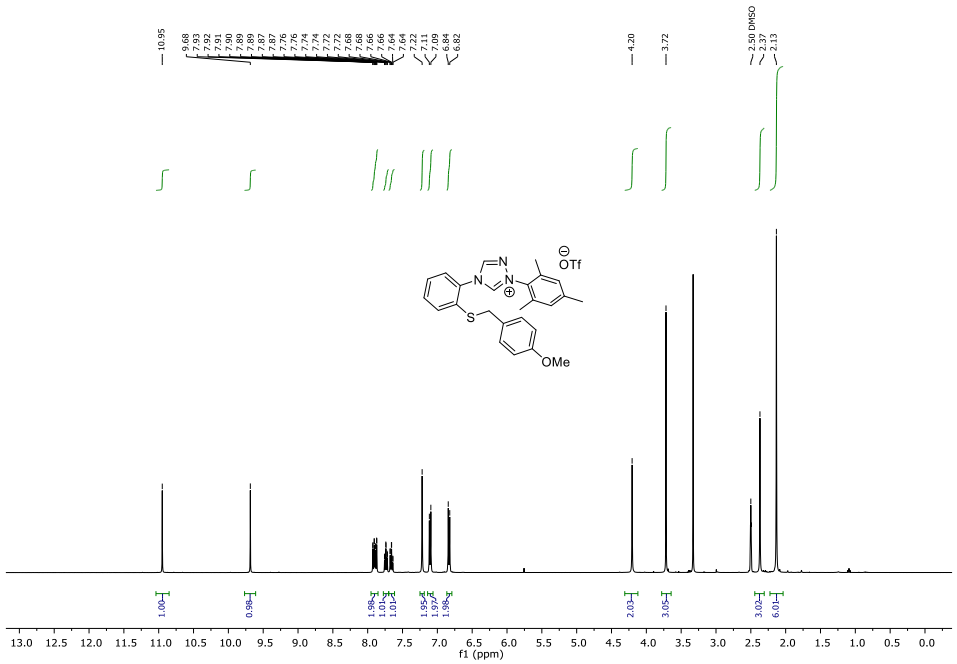

Figure D079: ^{1}H NMR spectrum of 1-mesityl-4-(2-((4-methoxybenzyl)thio)phenyl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**[4f]OTf**) (400 MHz, DMSO-d_6, 298 K).

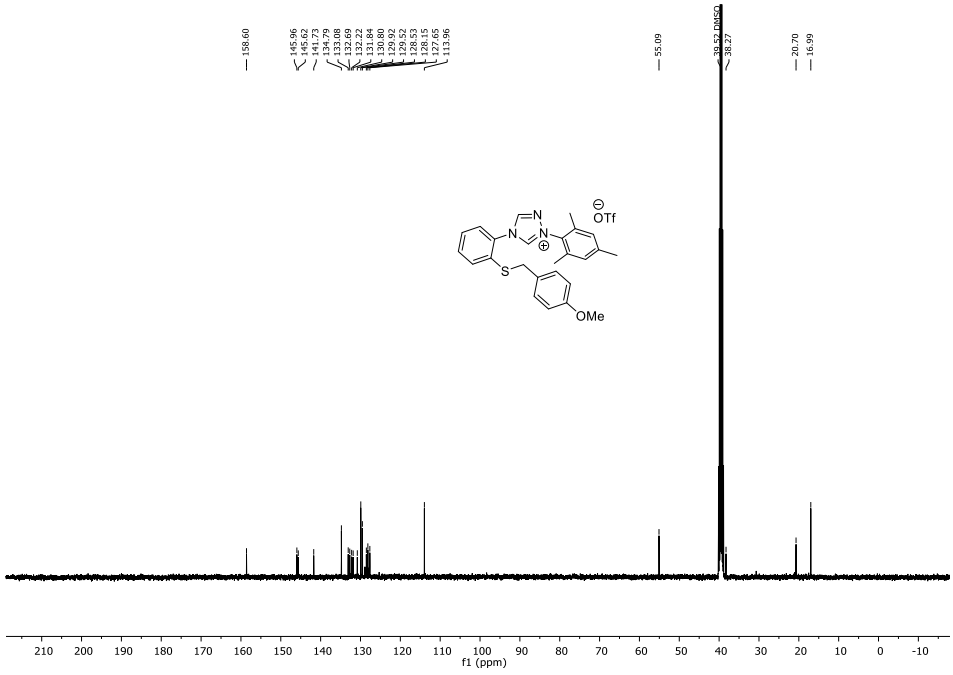

Figure D080: ^{13}C NMR spectrum of 1-mesityl-4-(2-((4-methoxybenzyl)thio)phenyl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**[4f]OTf**) (100 MHz, DMSO-d_6, 298 K).

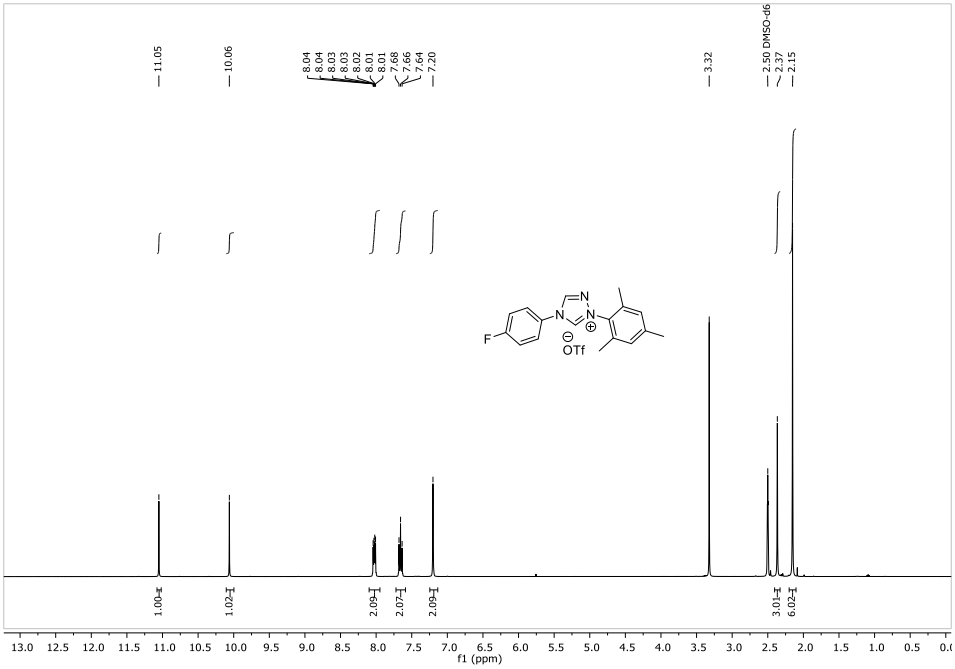

Figure D081: ^{1}H NMR spectrum of 4-(4-fluorophenyl)-1-mesityl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**[4i]OTf**) (400 MHz, DMSO-d_6, 298 K).

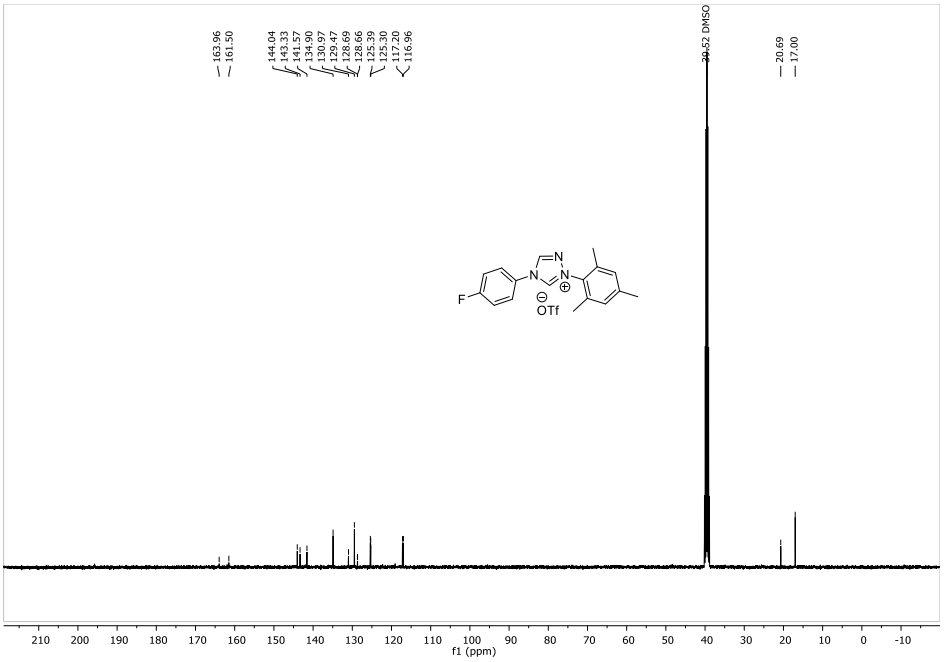

Figure D082: ^{13}C NMR spectrum of 4-(4-fluorophenyl)-1-mesityl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**[4i]OTf**) (100 MHz, DMSO-d_6, 298 K).

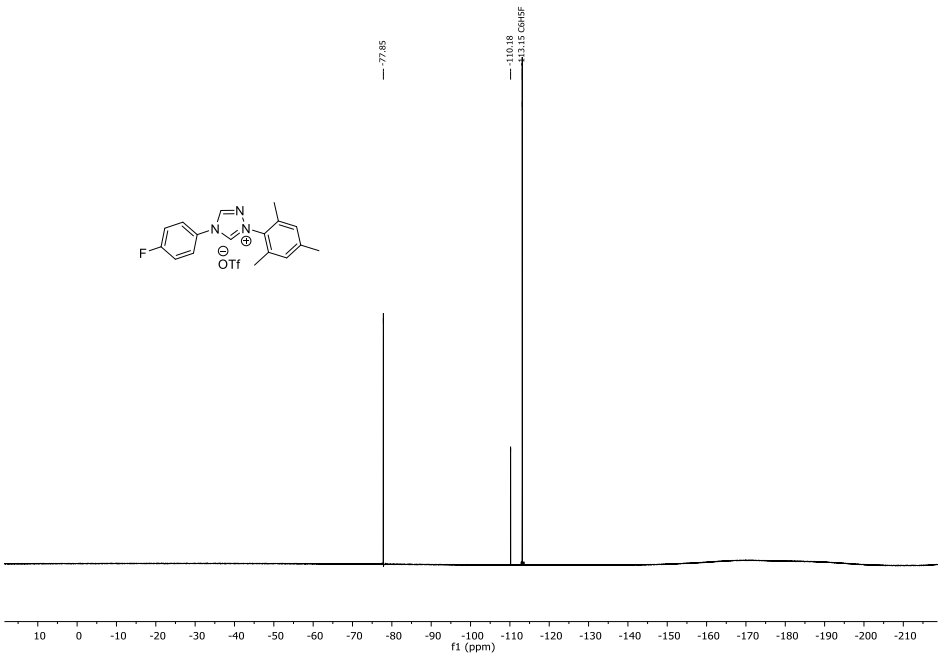

Figure D083: ^{19}F NMR spectrum of 4-(4-fluorophenyl)-1-mesityl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**[4i]OTf**) (376 MHz, DMSO-d_6, 298 K).

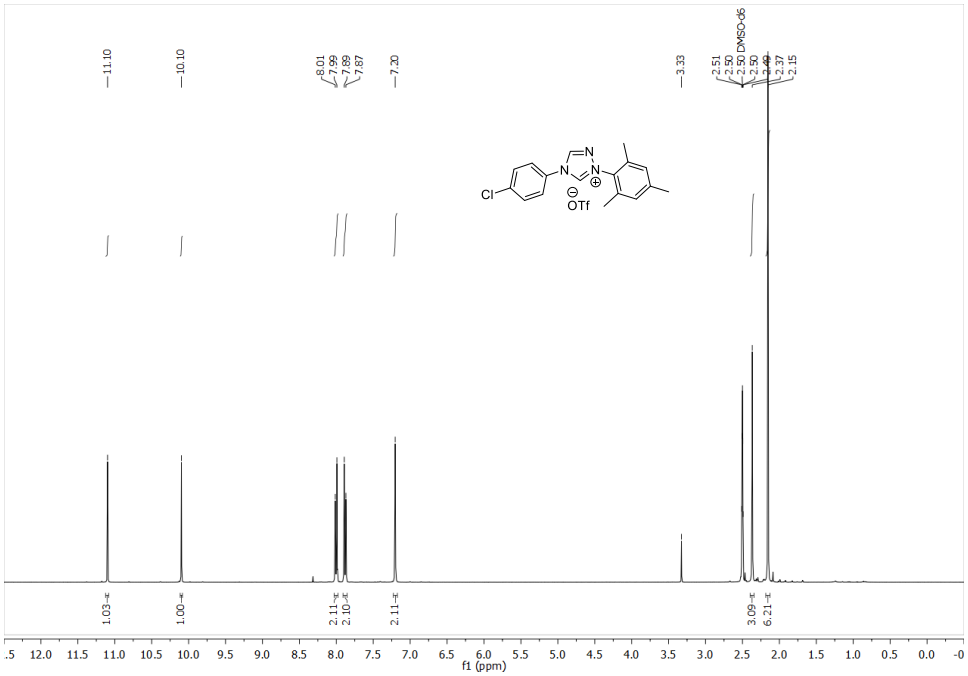

Figure D084: ^{1}H NMR spectrum of 4-(4-*c*hlorophenyl)-1-mesityl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**[4k]OTf**) (400 MHz, DMSO-d_6, 298 K).

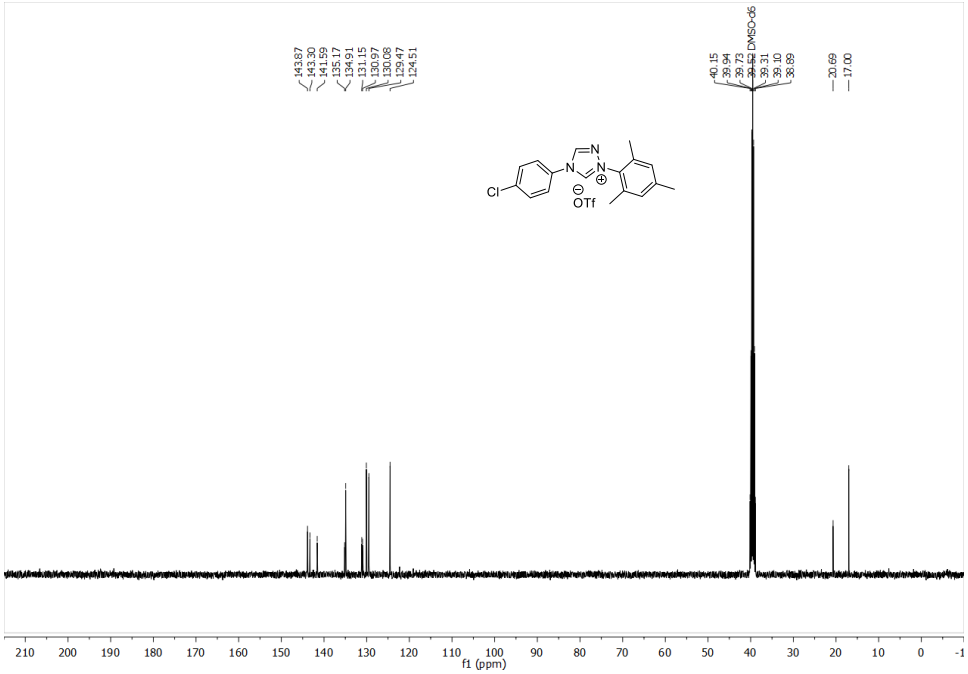

Figure D085: ^{13}C NMR spectrum of 4-(4-*c*hlorophenyl)-1-mesityl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate ([**4k]OTf**) (100 MHz, DMSO-d_6, 298 K).

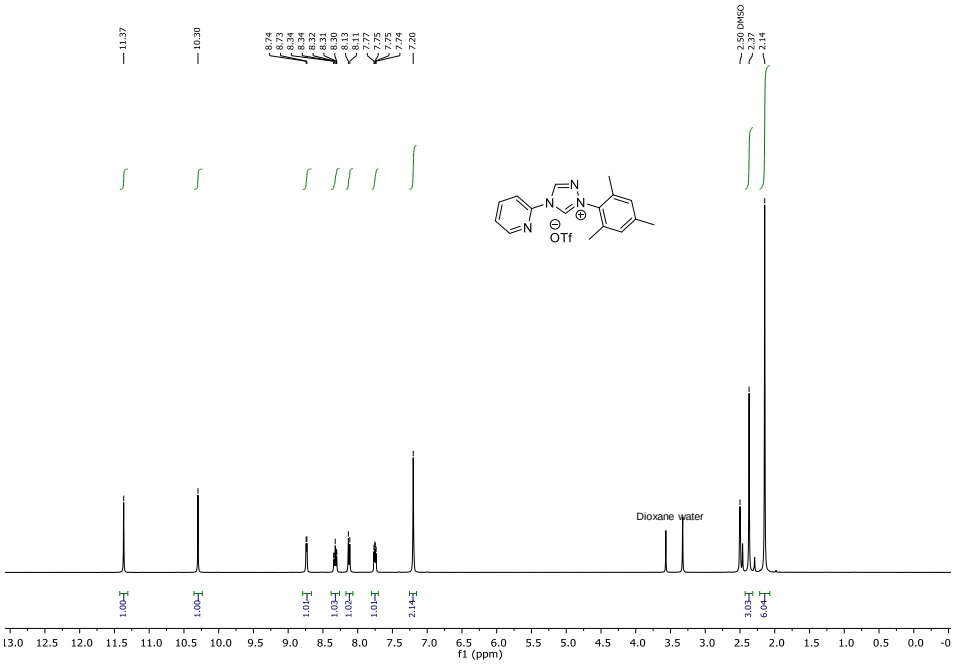

Figure D086: ^{1}H NMR spectrum of 1-mesityl-4-(pyridin-2-yl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**[4l]OTf**) (400 MHz, DMSO-d_6, 298 K).

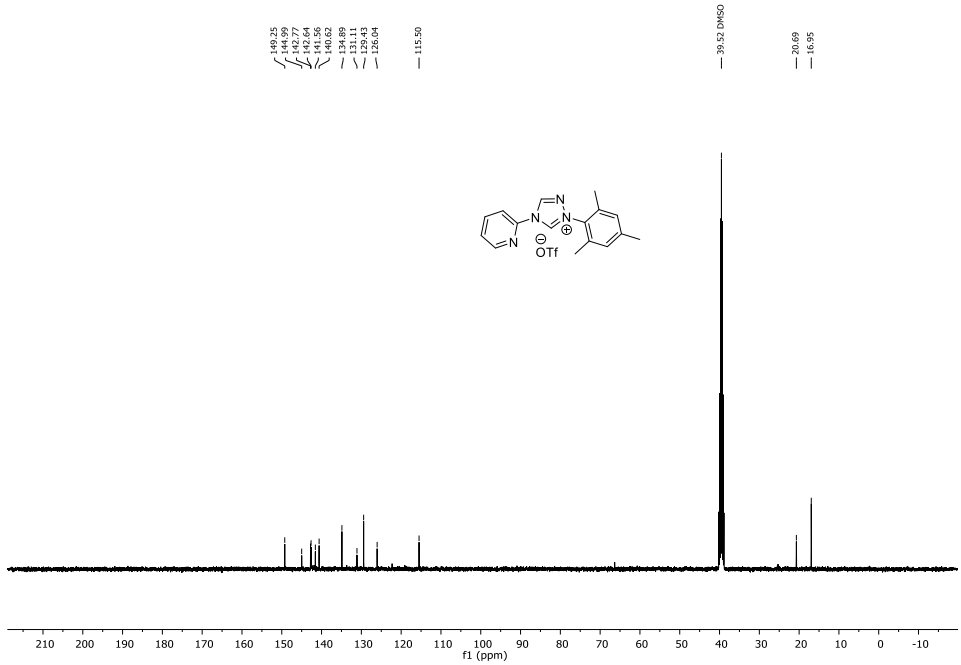

Figure D087: ^{13}C NMR spectrum of 1-mesityl-4-(pyridin-2-yl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**[4l]OTf**) (100 MHz, DMSO-d_6, 298 K).

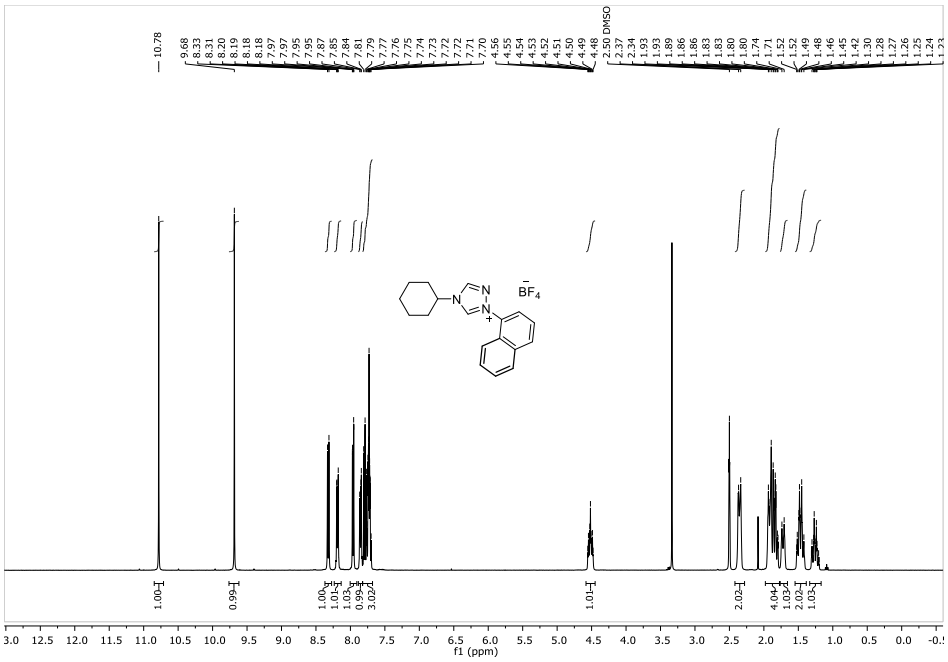

Figure D088: ^{1}H NMR spectrum of 4-*c*yclohexyl-1-(naphthalen-1-yl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[5b]BF$_4$**) (400 MHz, DMSO-d_6, 298 K).

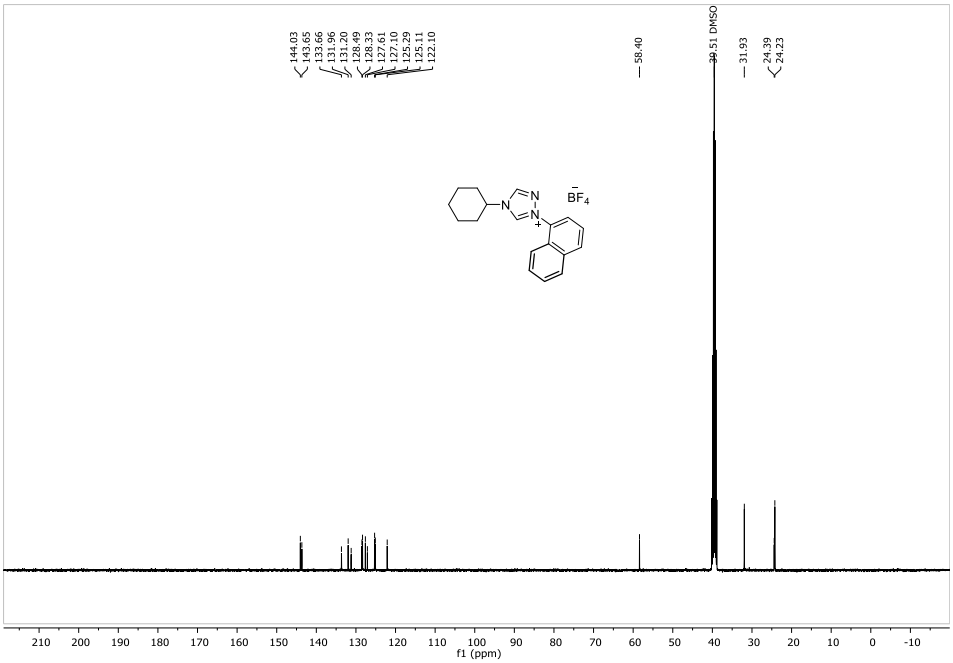

Figure D089: ^{13}C NMR spectrum of 4-*c*yclohexyl-1-(naphthalen-1-yl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[5b]BF$_4$**) (100 MHz, DMSO-d_6, 298 K).

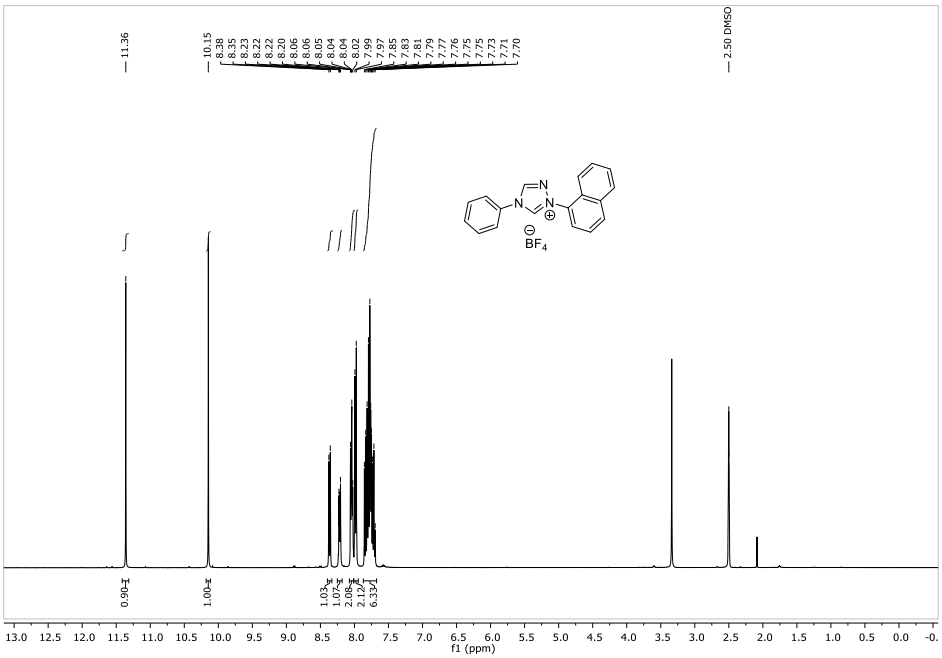

Figure D090: ^{1}H NMR spectrum of 1-(naphthalen-1-yl)-4-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[5d]BF$_4$**) (400 MHz, DMSO-d_6, 298 K).

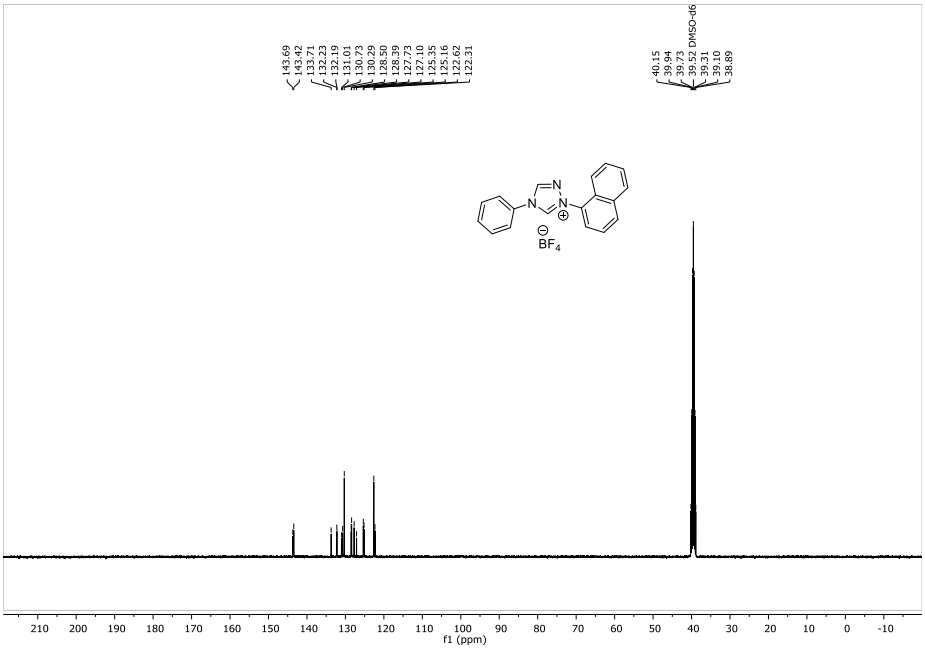

Figure D091: ^{13}C NMR spectrum of 1-(naphthalen-1-yl)-4-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[5d]BF$_4$**) (100 MHz, DMSO-d_6, 298 K).

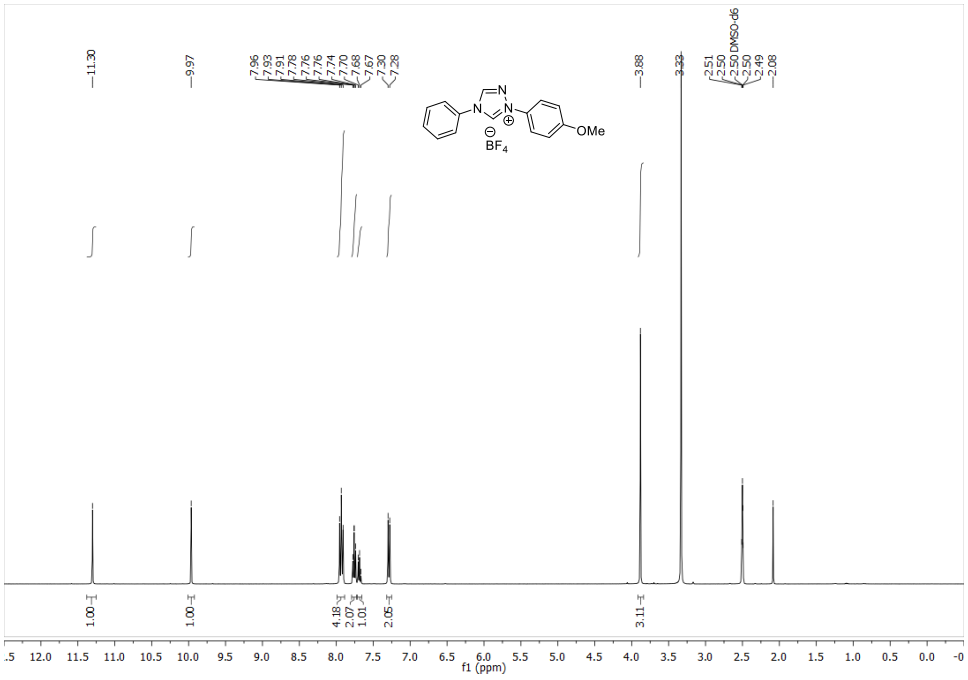

Figure D092: ^{1}H NMR spectrum of 1-(4-methoxyphenyl)-4-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[6d]BF$_4$**) (400 MHz, DMSO-d_6, 298 K).

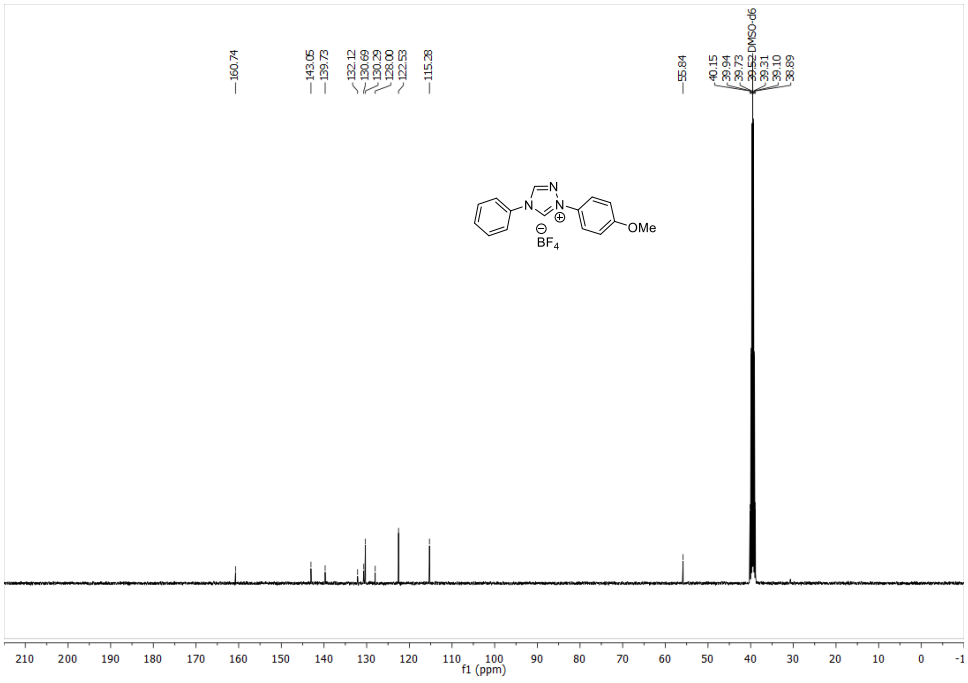

Figure D093: ^{13}C NMR spectrum of 1-(4-methoxyphenyl)-4-phenyl-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[6d]BF$_4$**) (100 MHz, DMSO-d_6, 298 K).

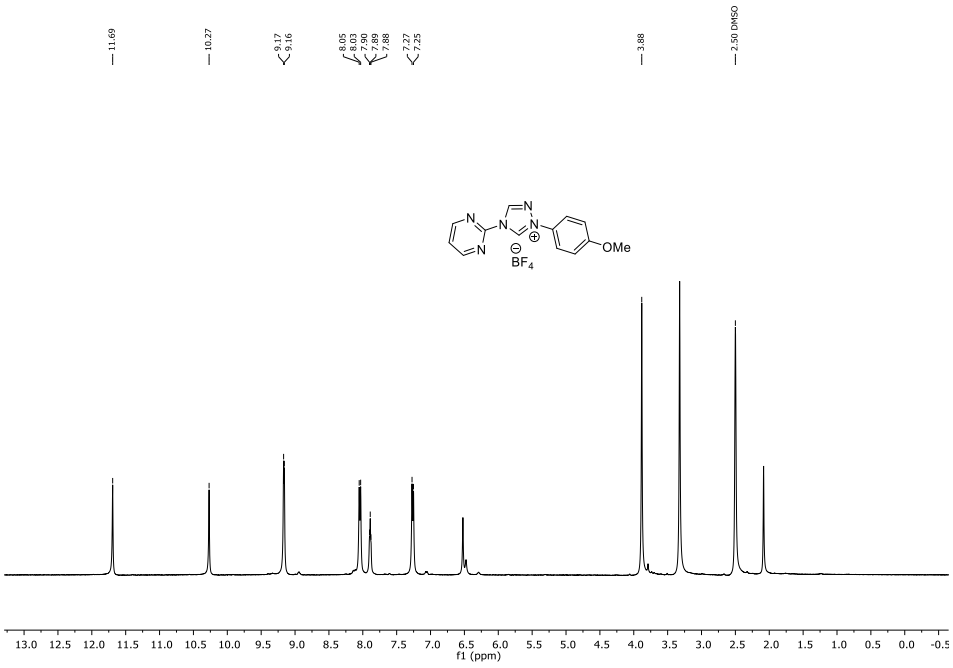

Figure D094: ^{1}H NMR spectrum of 1-(4-methoxyphenyl)-4-(pyrimidin-2-yl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[6m]BF$_4$**) (400 MHz, DMSO-d_6, 298 K). The impurities around 6.6 ppm were introduced during the extraction with (impure) acetone and could not be removed by recrystallization.

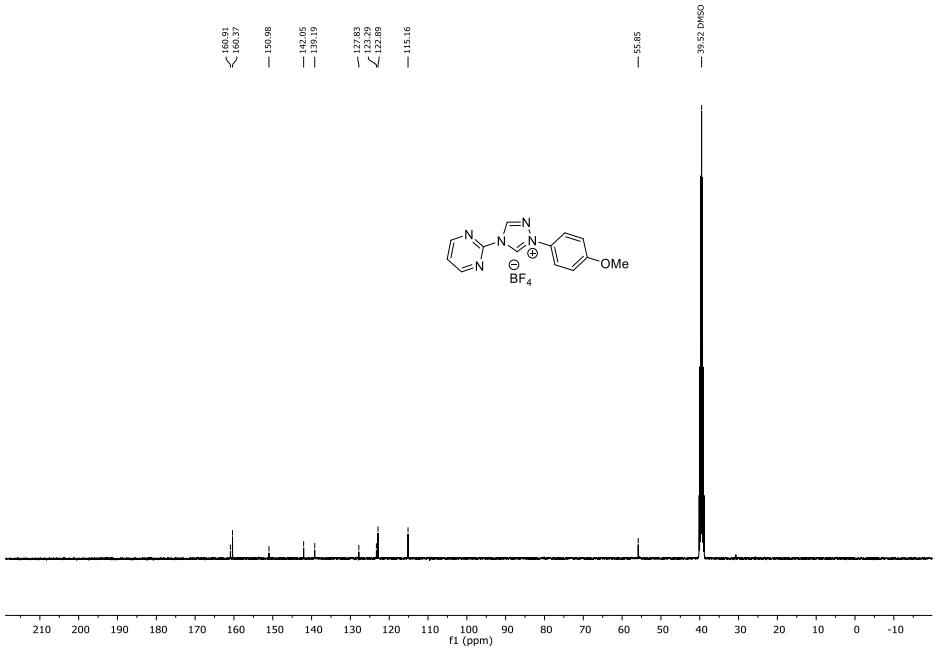

Figure D095: ^{13}C NMR spectrum of 1-(4-methoxyphenyl)-4-(pyrimidin-2-yl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[6m]BF$_4$**) (100 MHz, DMSO-d_6, 298 K).

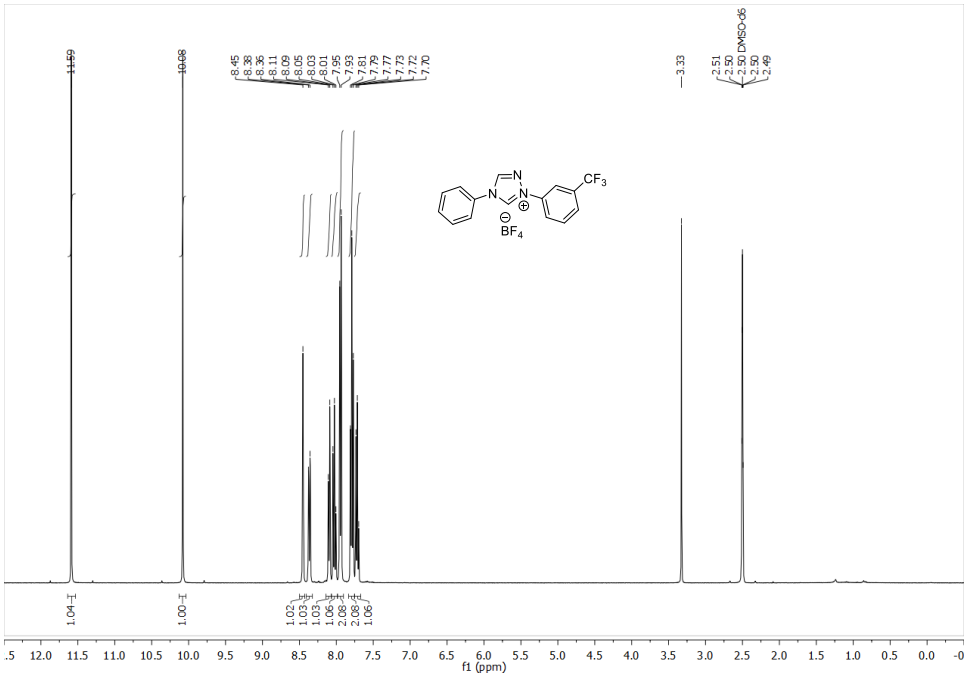

Figure D096: [1]H NMR spectrum of 4-phenyl-1-(3-(trifluoromethyl)phenyl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[7d]BF$_4$**) (400 MHz, DMSO-d_6, 298 K).

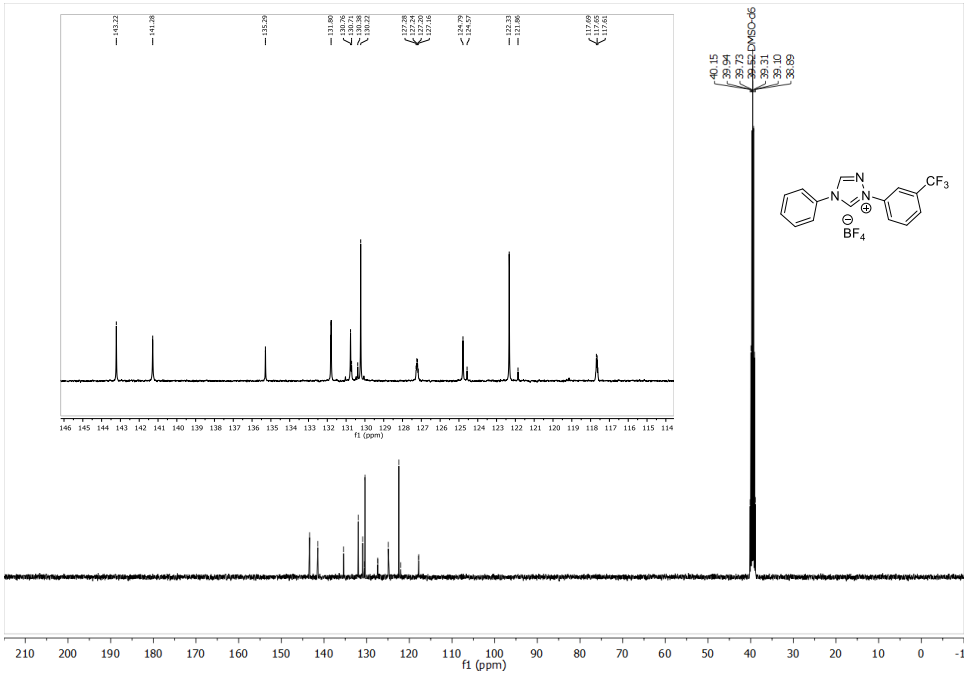

Figure D097: [13]C NMR spectrum of 4-phenyl-1-(3-(trifluoromethyl)phenyl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([**7d]BF$_4$**) (100 MHz, DMSO-d_6, 298 K).

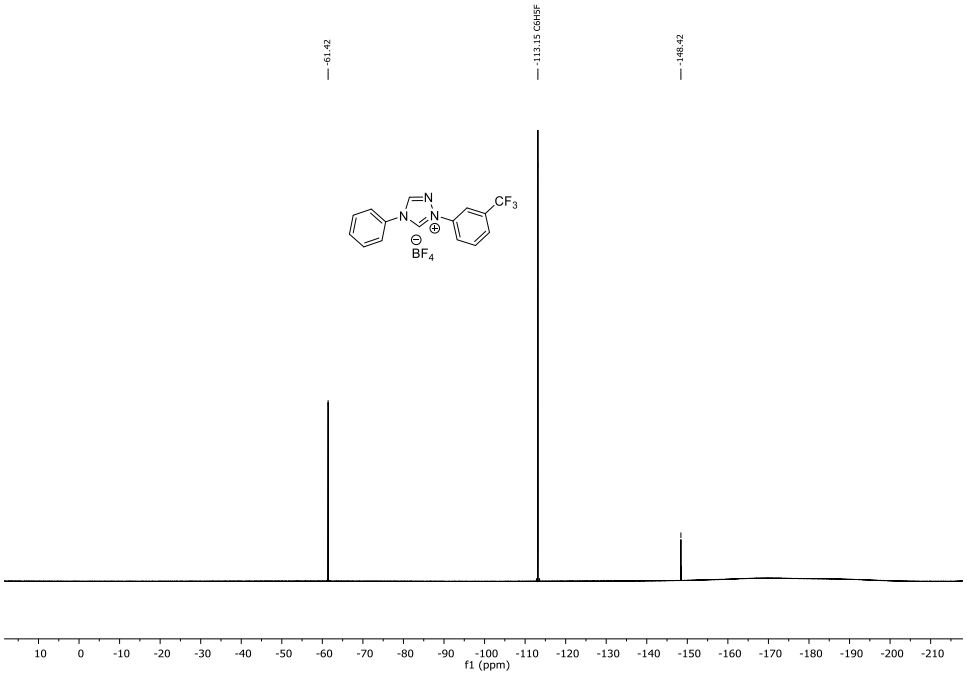

Figure D098: ^{19}F NMR spectrum of 4-phenyl-1-(3-(trifluoromethyl)phenyl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[7d]BF$_4$**) (376 MHz, DMSO-d_6, 298 K, referenced to fluorobenzene).

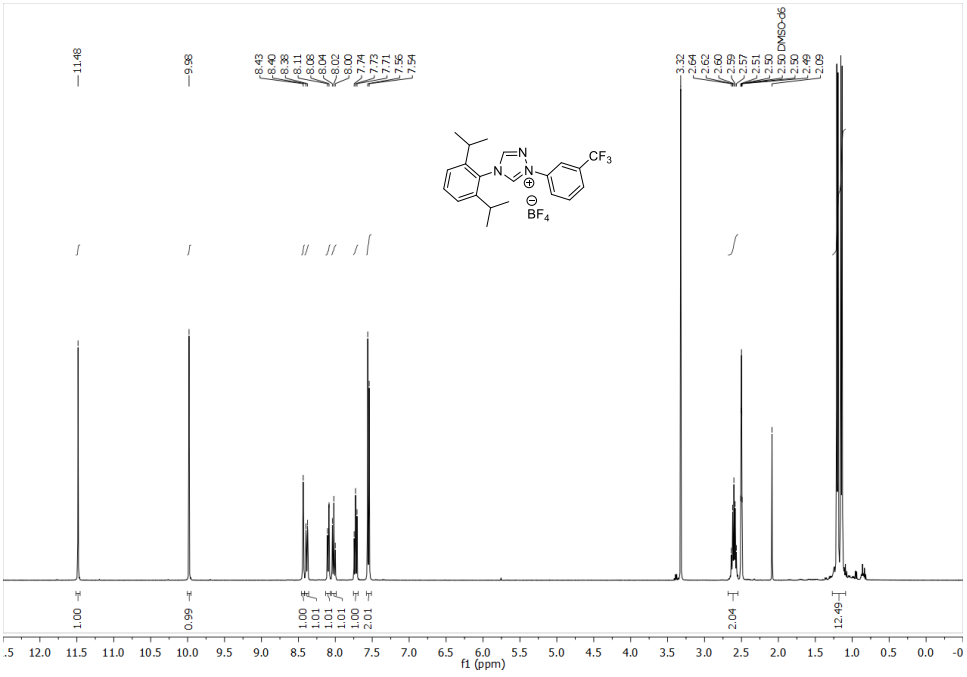

Figure D099: ^{1}H NMR spectrum of 4-(2,6-diisopropylphenyl)-1-(3-(trifluoromethyl)phenyl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[7e]BF$_4$**) (400 MHz, DMSO-d_6, 298 K).

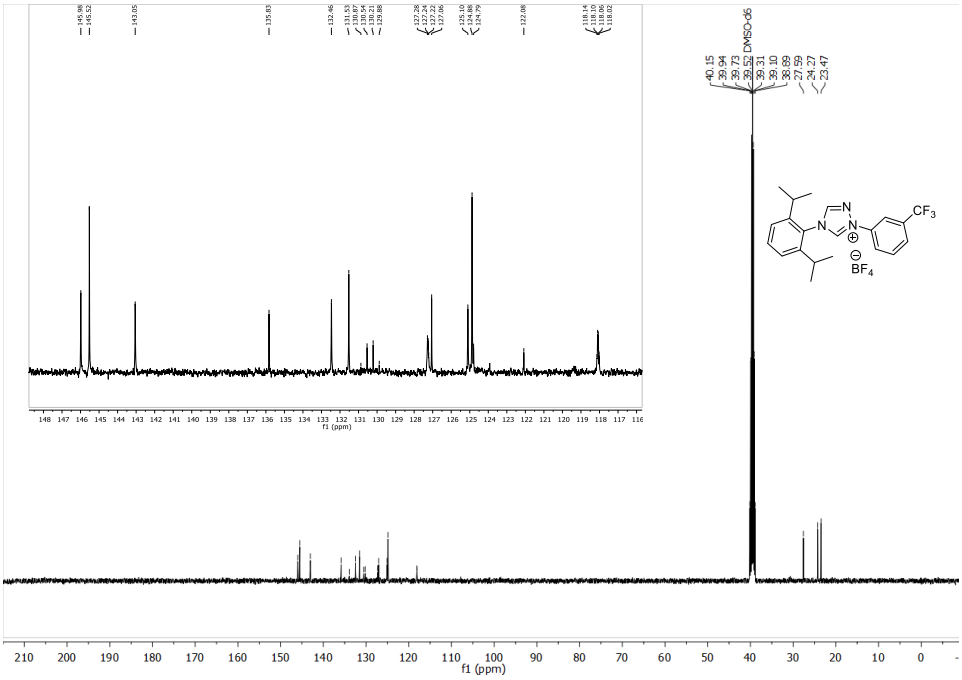

Figure D100: ^{13}C NMR spectrum of 4-(2,6-diisopropylphenyl)-1-(3-(trifluoromethyl)phenyl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**[7e]BF$_4$**) (100 MHz, DMSO-d_6, 298 K).

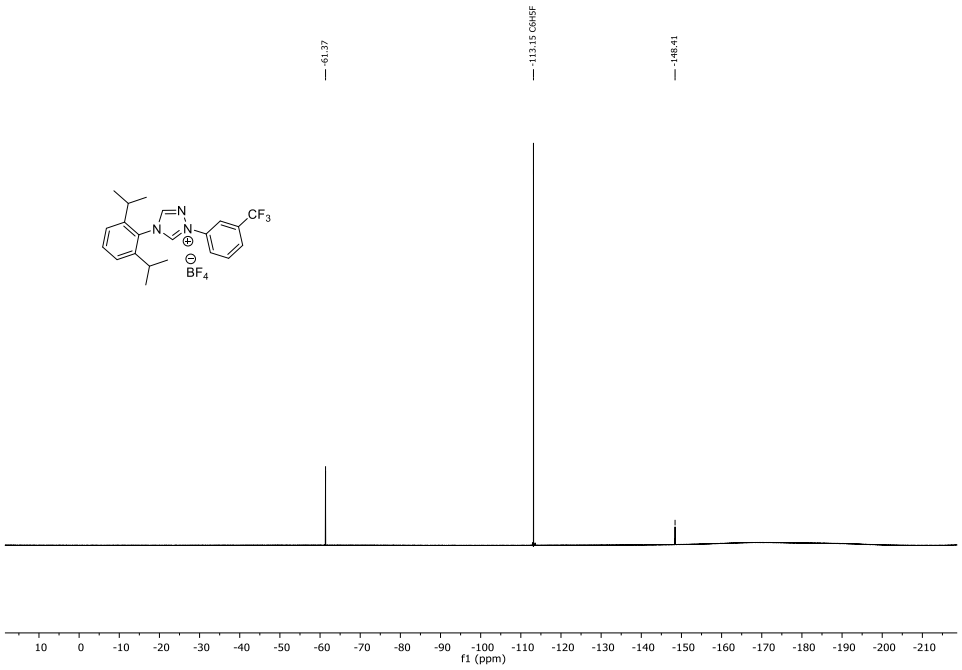

Figure D101: ^{19}F NMR spectrum of 4-(2,6-diisopropylphenyl)-1-(3-(trifluoromethyl)phenyl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate ([**7e]BF$_4$**) (376 MHz, DMSO-d_6, 298 K, referenced to fluorobenzene).

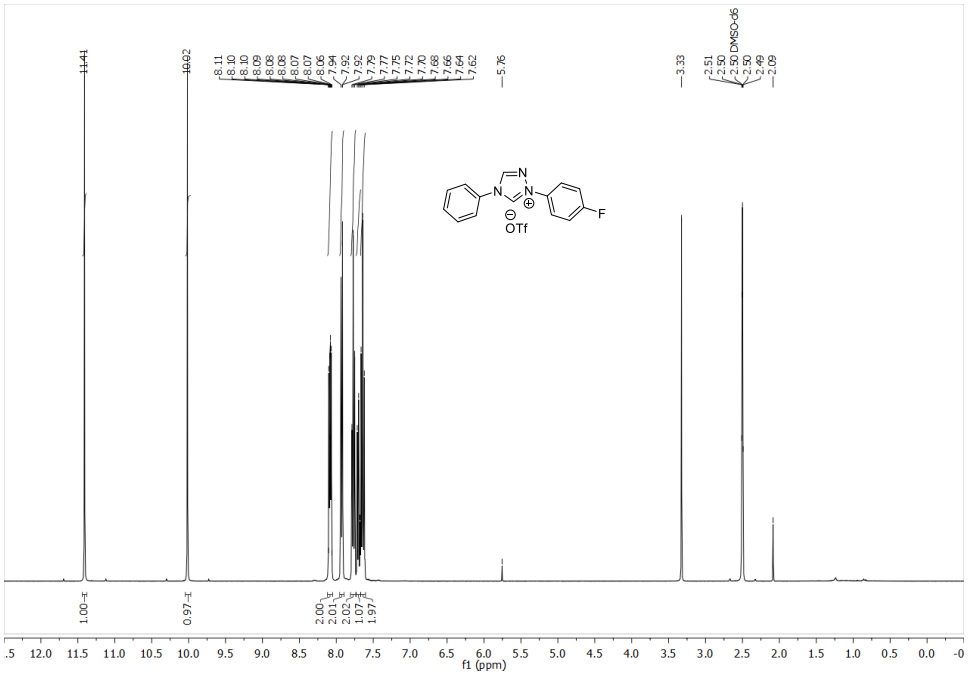

Figure D102: ^{1}H NMR spectrum of 1-(4-fluorophenyl)-4-phenyl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**[8d]OTf**) (400 MHz, DMSO-d_6, 298 K).

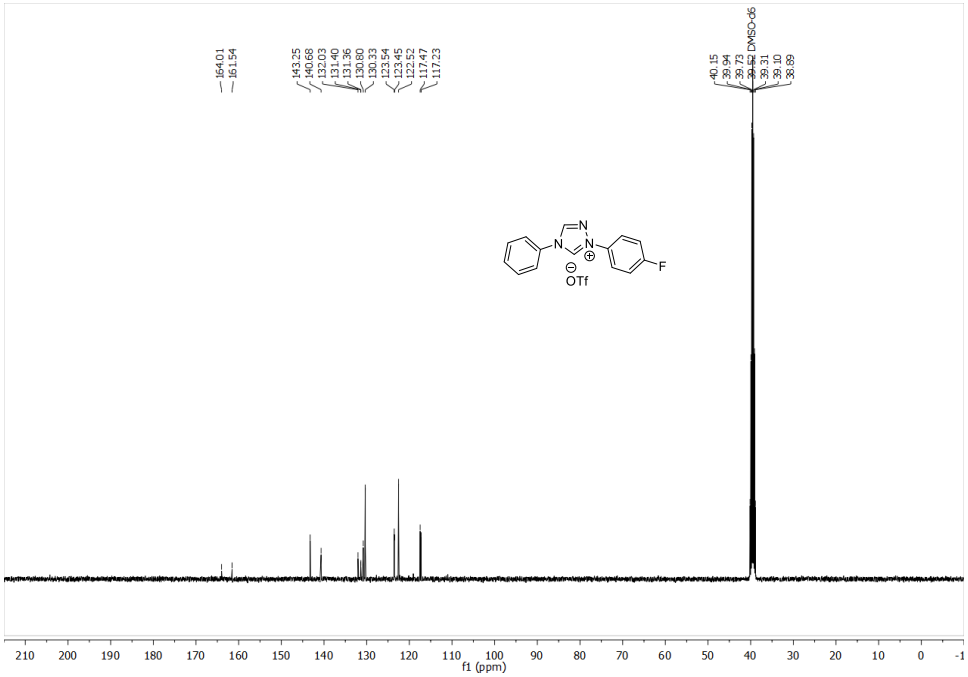

Figure D103: ^{13}C NMR spectrum of 1-(4-fluorophenyl)-4-phenyl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**[8d]OTf**) (100 MHz, DMSO-d_6, 298 K).

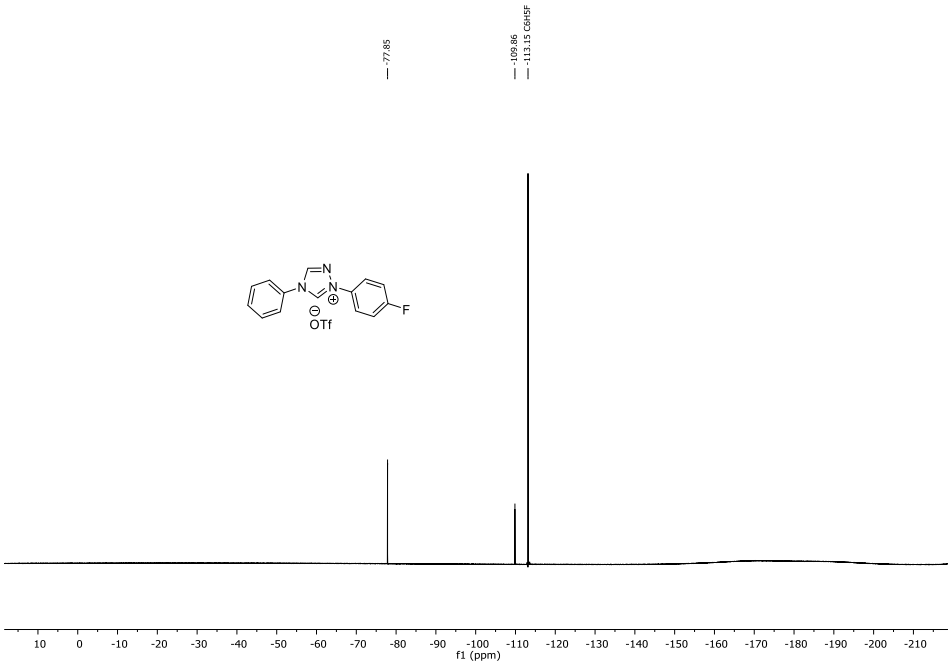

Figure D104: ^{19}F NMR spectrum of 1-(4-fluorophenyl)-4-phenyl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**[8d]OTf**) (376 MHz, DMSO-d_6, 298 K, referenced to fluorobenzene).

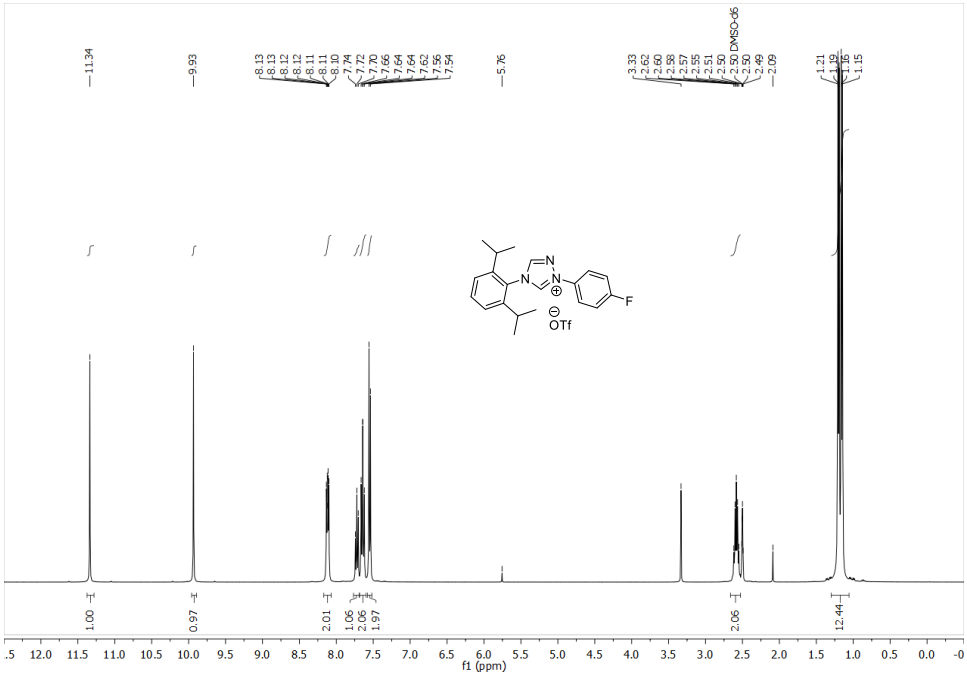

Figure D105: ^{1}H NMR spectrum of 4-(2,6-diisopropylphenyl)-1-(4-fluorophenyl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**[8e]OTf**) (400 MHz, DMSO-d_6, 298 K).

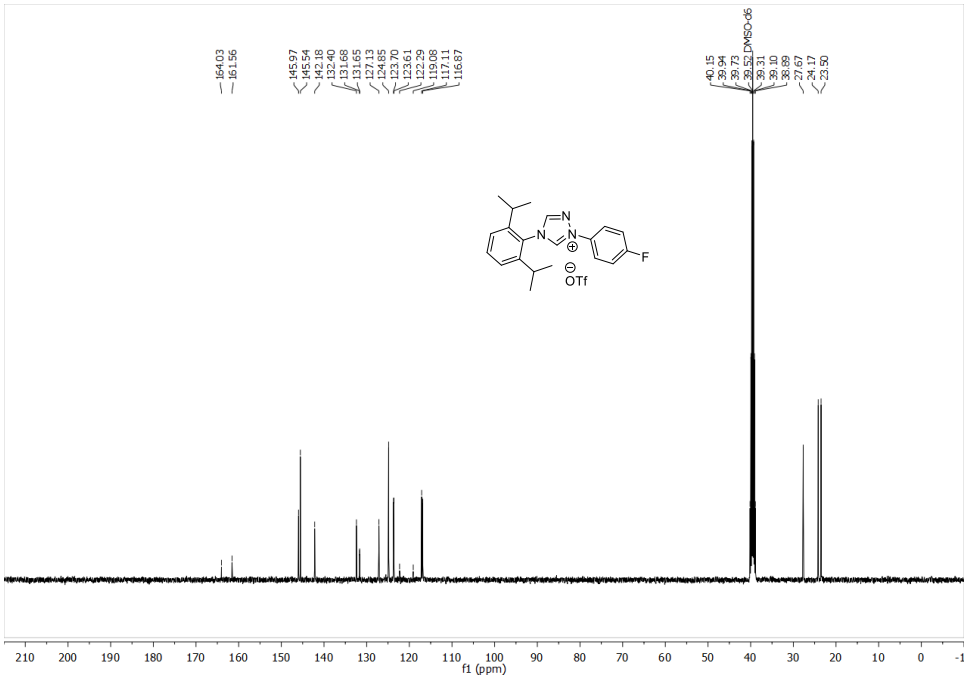

Figure D106: ^{13}C NMR spectrum of 4-(2,6-diisopropylphenyl)-1-(4-fluorophenyl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**[8e]OTf**) (100 MHz, DMSO-d_6, 298 K).

Figure D107: ^{19}F NMR spectrum of 4-(2,6-diisopropylphenyl)-1-(4-fluorophenyl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**[8e]OTf**) (376 MHz, DMSO-d_6, 298 K, referenced to fluorobenzene).

APPENDIX E: SPECTRA FOR CHAPTER 3

Section E.1: Spectra for 4-(2-Nitrophenyl)-4*H*-1,2,4-triazole (E001-E002)

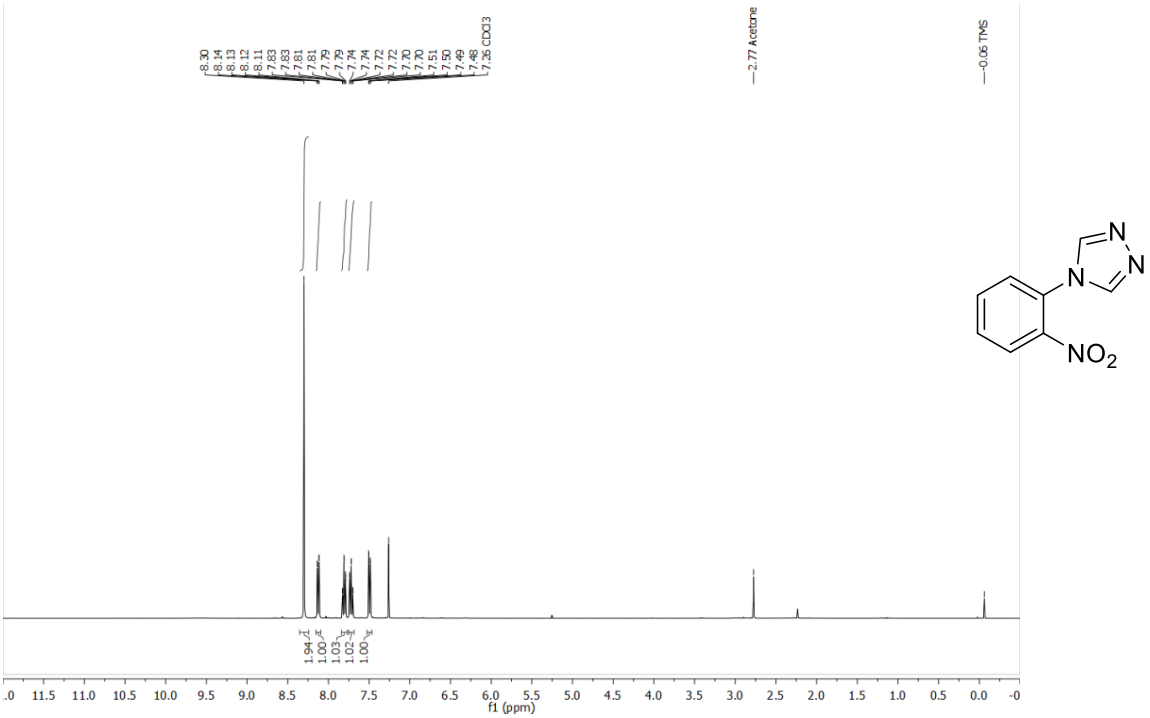

Figure E01: ^{1}H NMR spectrum of 4-(2-nitrophenyl)-4*H*-1,2,4-triazole (sm1) (400 MHz, DMSO-d_6, 298 K).

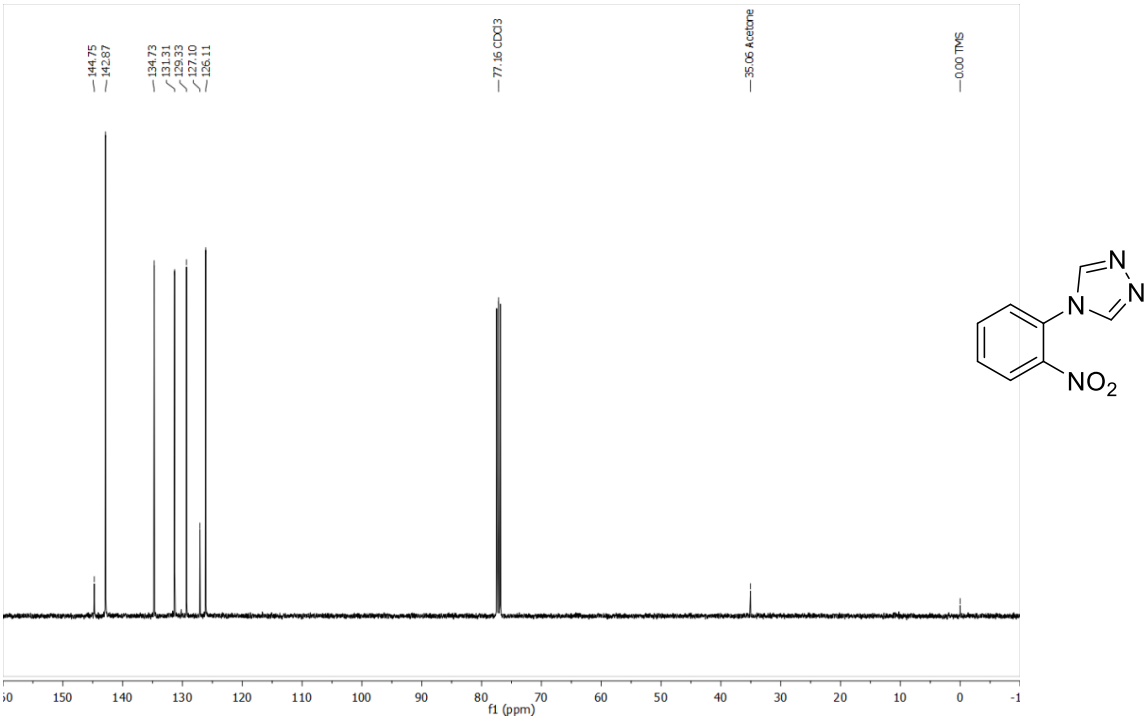

Figure E002: ^{13}C NMR spectrum of 4-(2-nitrophenyl)-4*H*-1,2,4-triazole (sm1) (101 MHz, DMSO-d_6, 298 K).

Section E.2: Spectra for 1-Substituted-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium Salts (E003-E023)

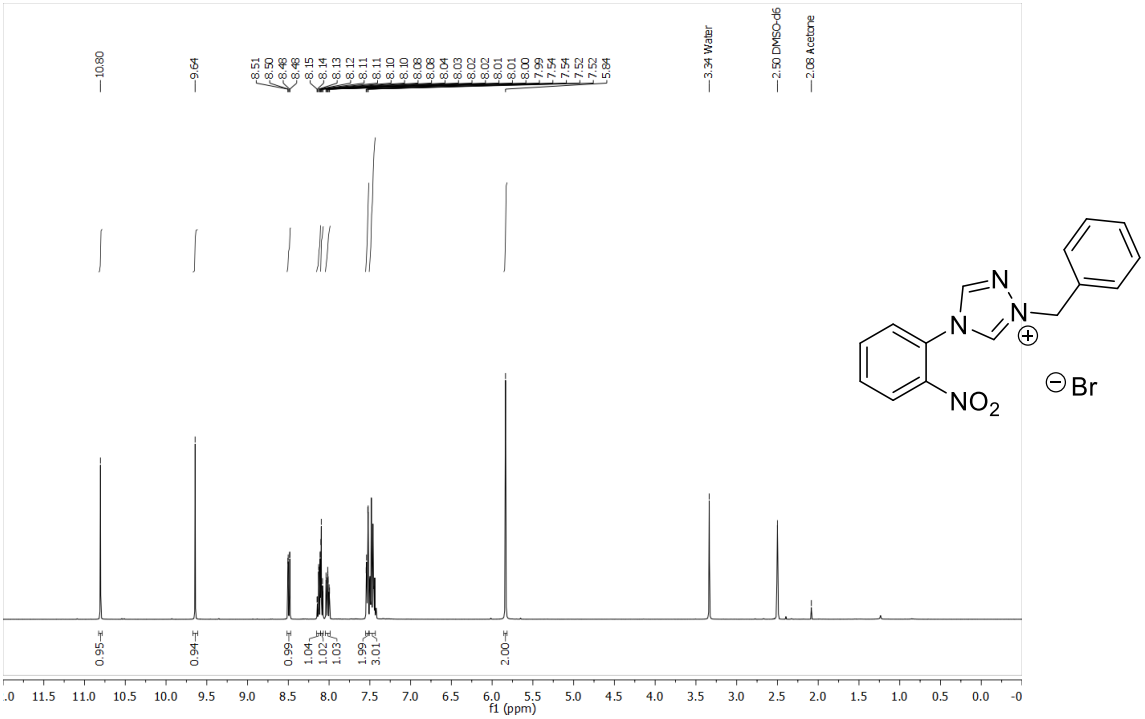

Figure E003: ^{1}H NMR spectrum of 1-benzyl-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium bromide (**10n**) (400 MHz, DMSO-d_6, 298 K).

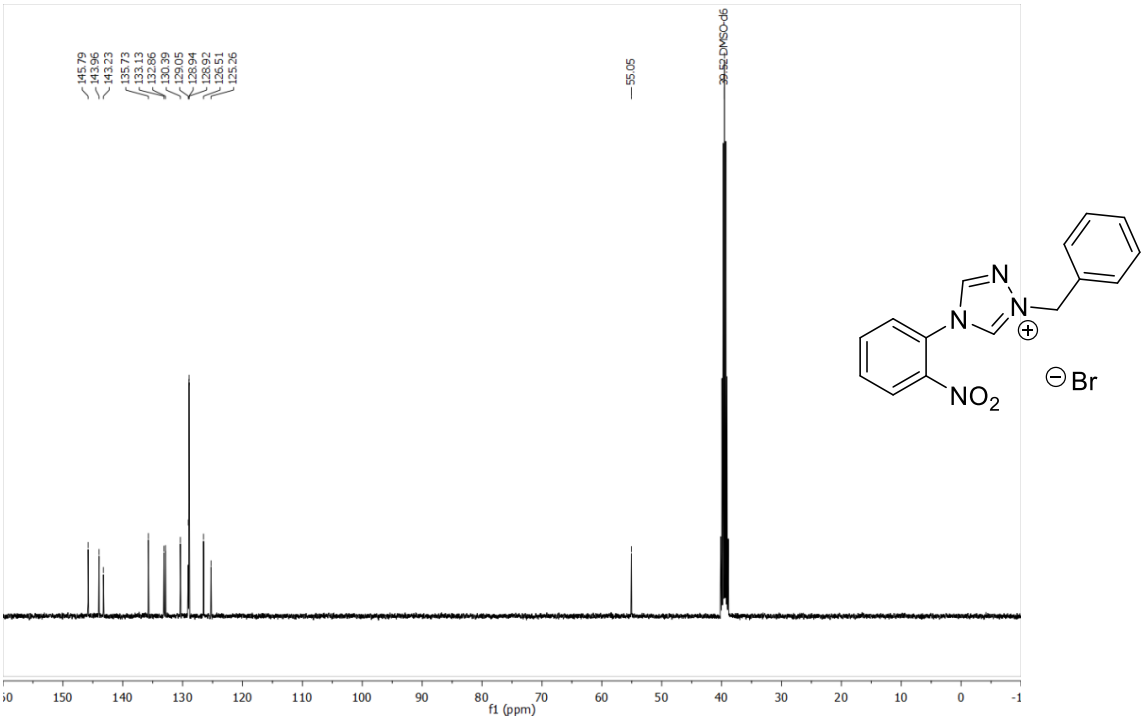

Figure E004: ^{13}C NMR spectrum of 1-benzyl-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium bromide (**10n**) (101 MHz, DMSO-d_6, 298 K).

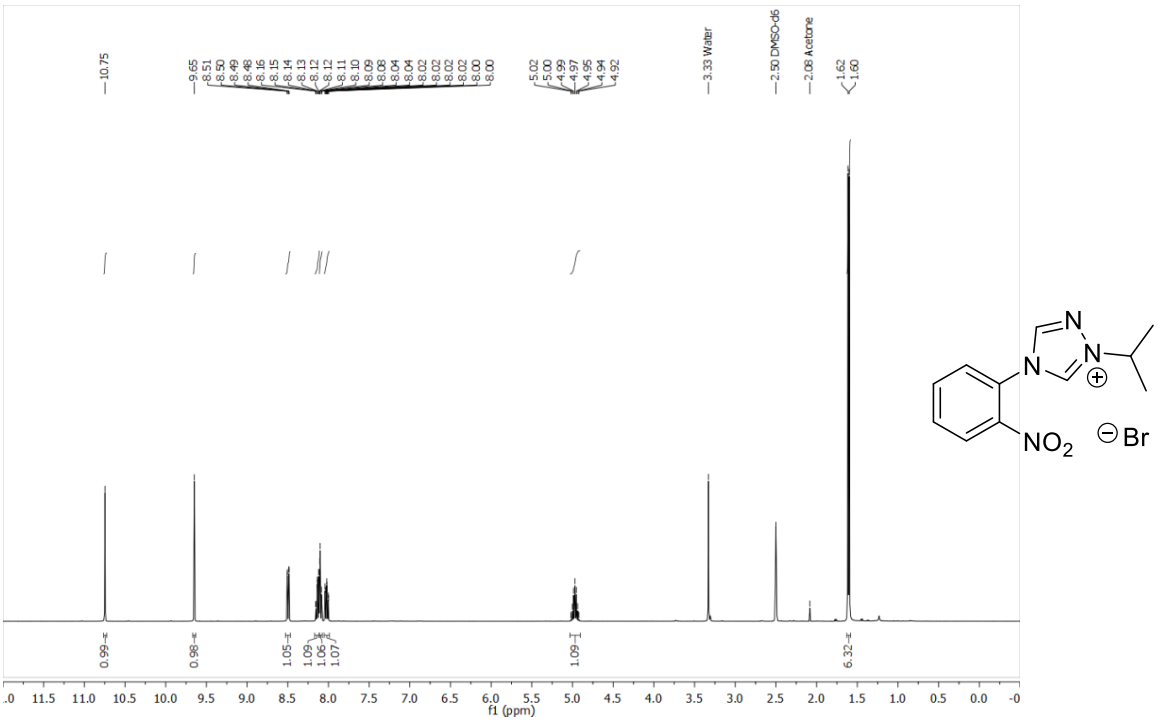

Figure E005: ^{1}H NMR spectrum of 1-isopropyl-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium bromide (**10o**) (400 MHz, DMSO-d_6, 298 K).

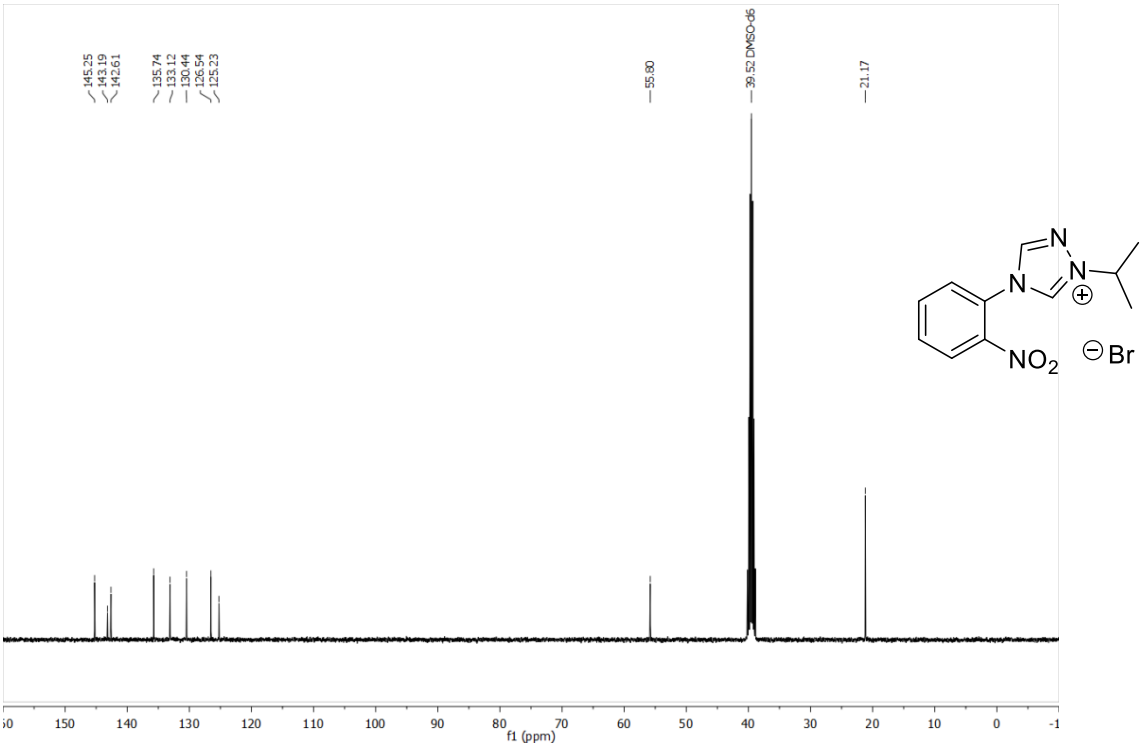

Figure E006: ^{13}C NMR spectrum of 1-isopropyl-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium bromide (**10o**) (101 MHz, DMSO-d_6, 298 K).

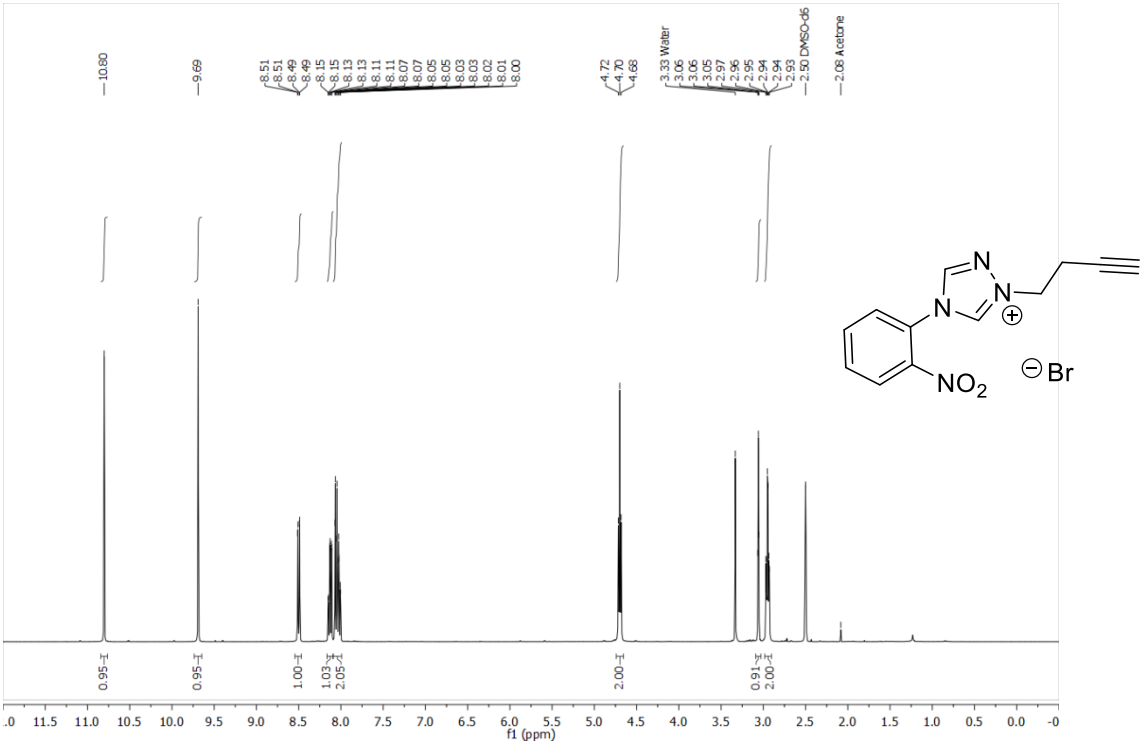

Figure E007: ^{1}H NMR spectrum of 1-(but-3-yn-1-yl)-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium bromide (**10p**) (400 MHz, DMSO-d_6, 298 K).

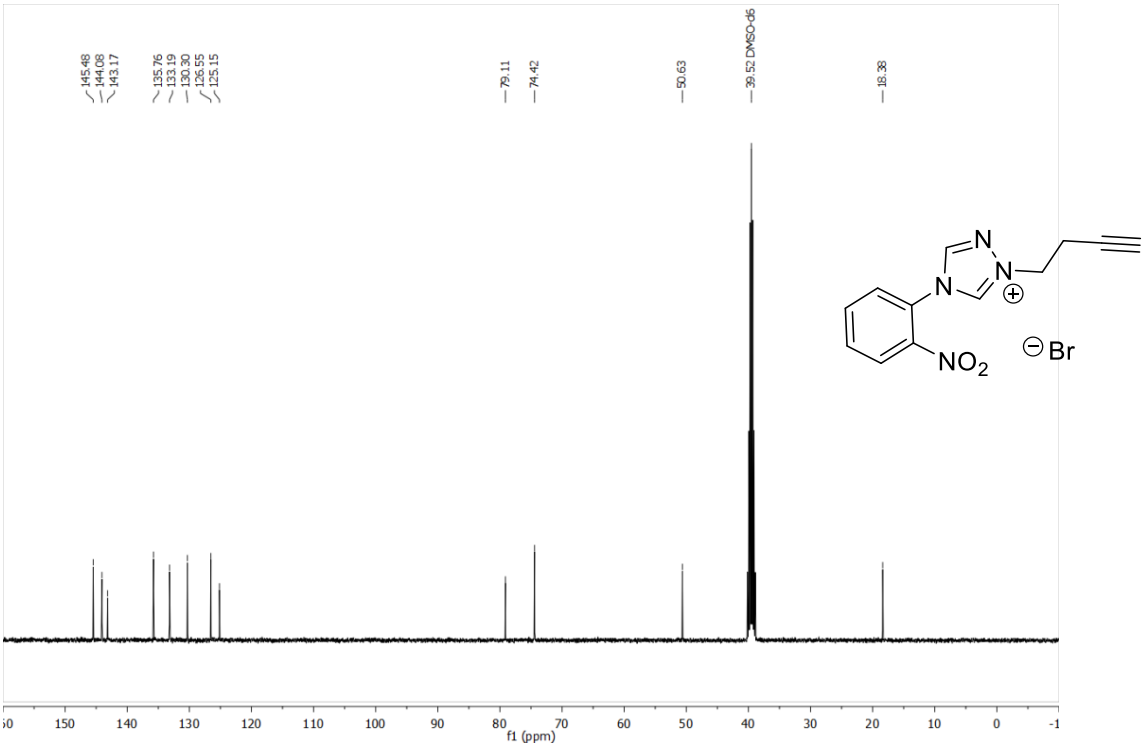

Figure E008: ^{13}C NMR spectrum of 1-(but-3-yn-1-yl)-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium bromide (**10p**) (101 MHz, DMSO-d_6, 298 K).

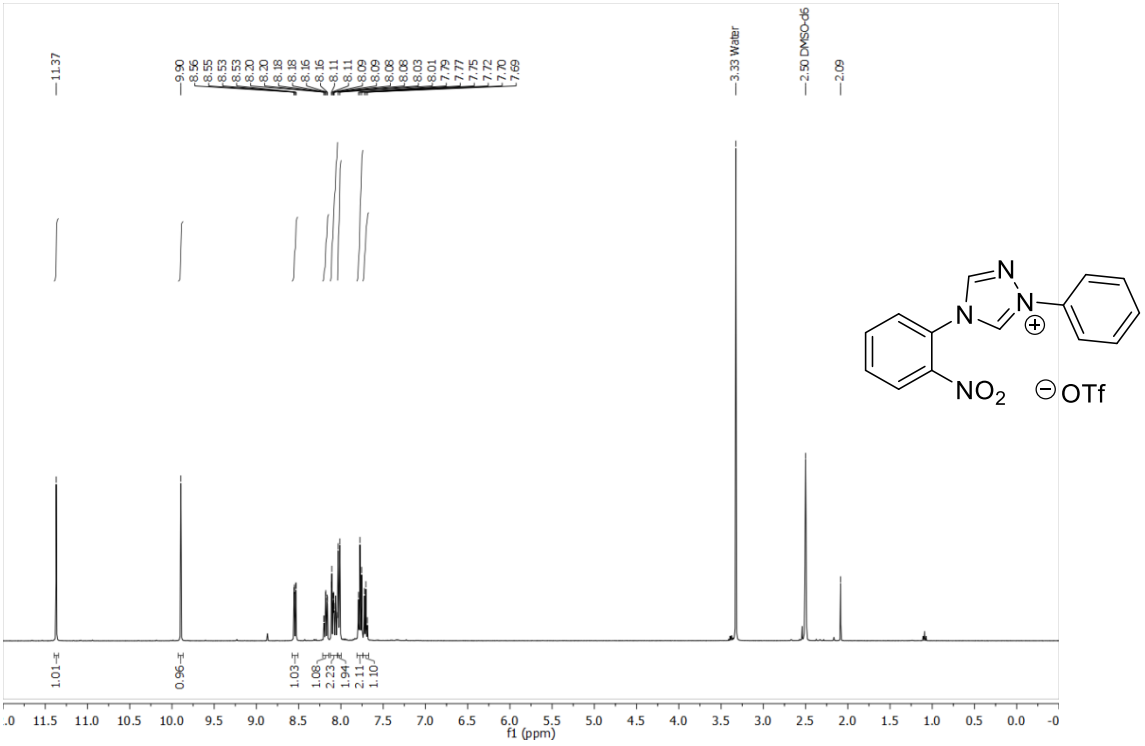

Figure E009: ^{1}H NMR spectrum of 4-(2-nitrophenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**10q**) (400 MHz, DMSO-d_6, 298 K).

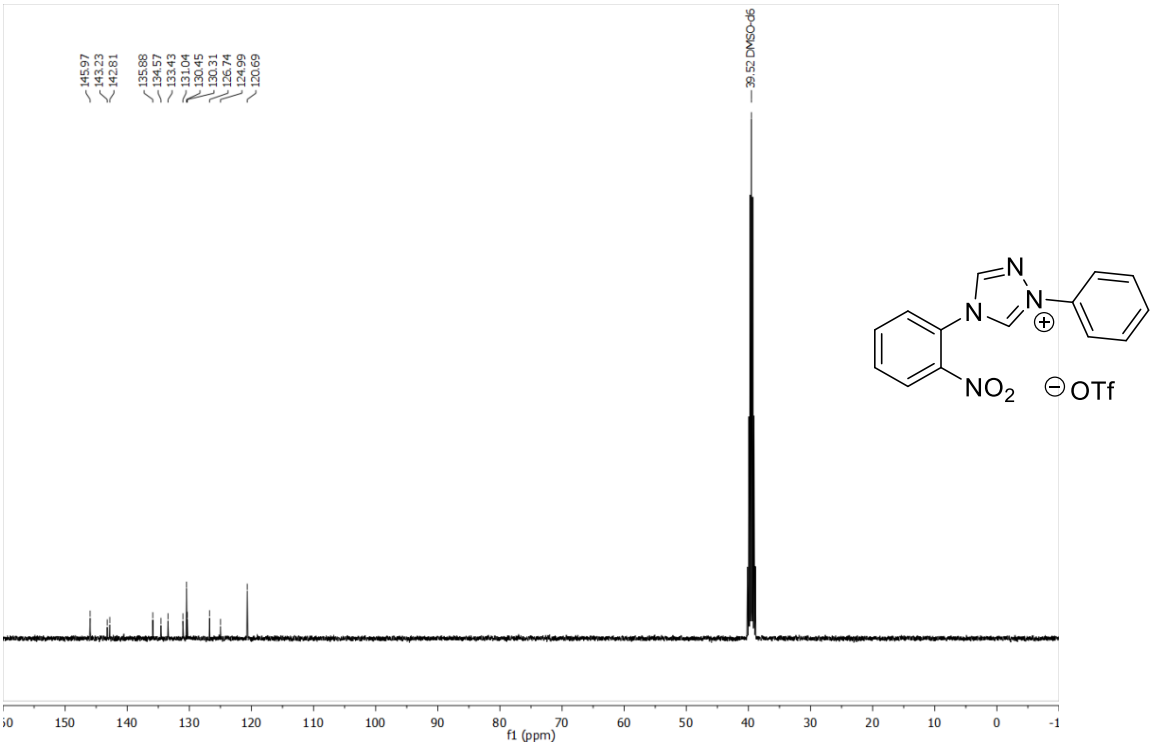

Figure E010: ^{13}C NMR spectrum of 4-(2-nitrophenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**10q**) (101 MHz, DMSO-d_6, 298 K).

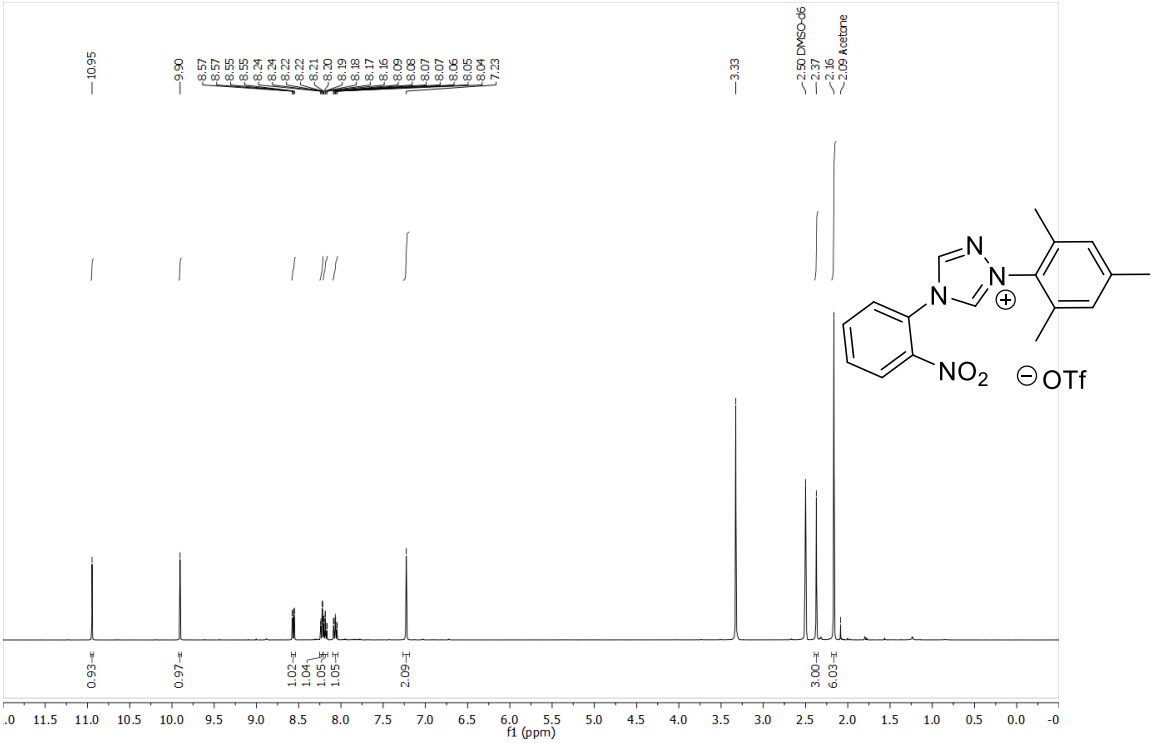

Figure E011: ^{1}H NMR spectrum of 1-mesityl-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**10r**) (400 MHz, DMSO-d_6, 298 K).

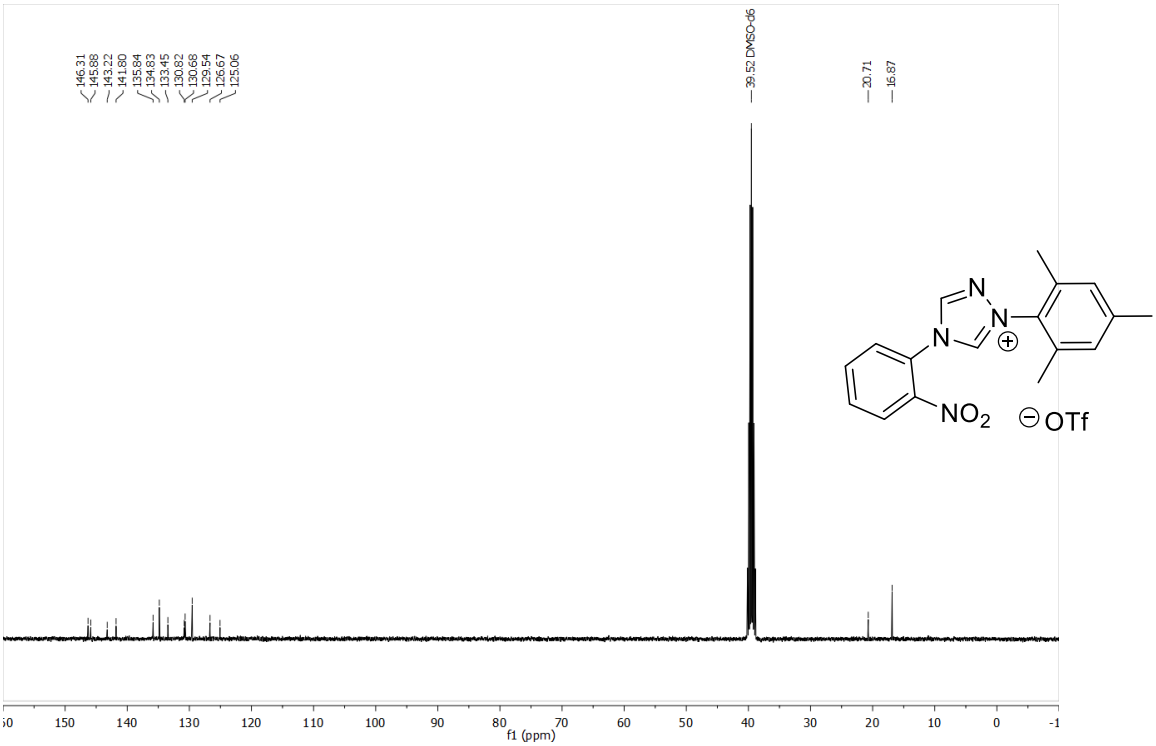

Figure E012: ^{13}C NMR spectrum of 1-mesityl-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**10r**) (101 MHz, DMSO-d_6, 298 K).

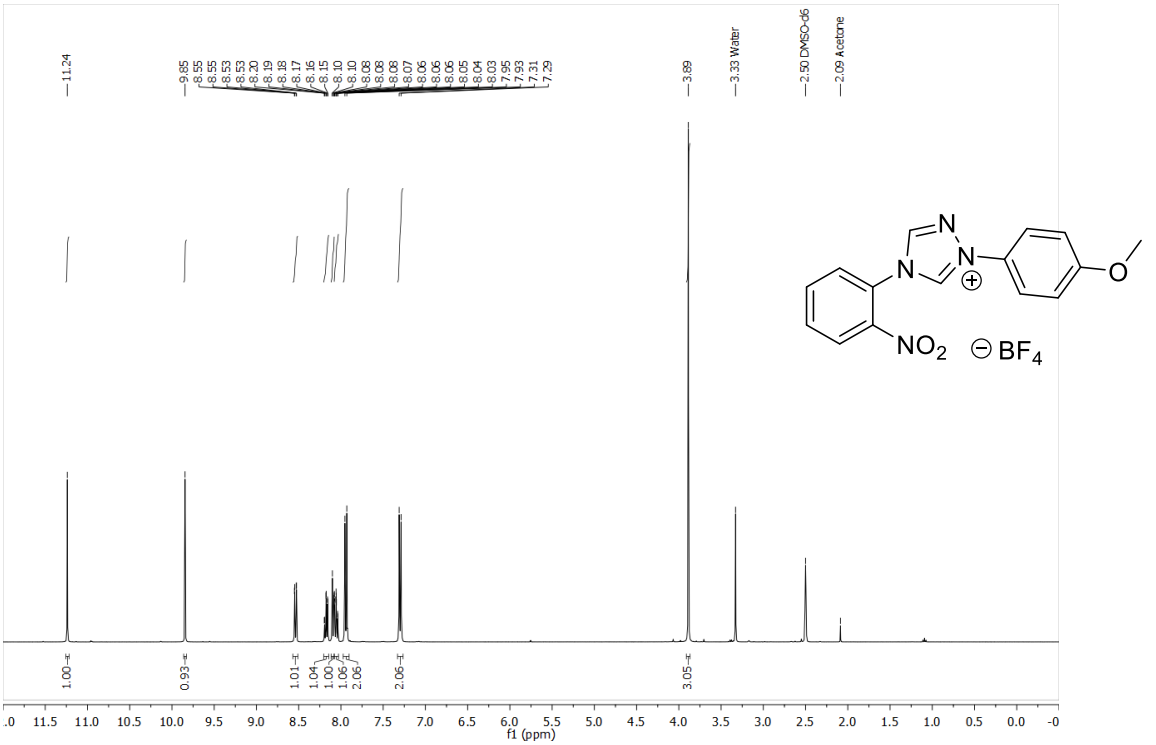

Figure E013: ^{1}H NMR spectrum of 1-(4-methoxyphenyl)-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**10s**) (400 MHz, DMSO-d_6, 298 K).

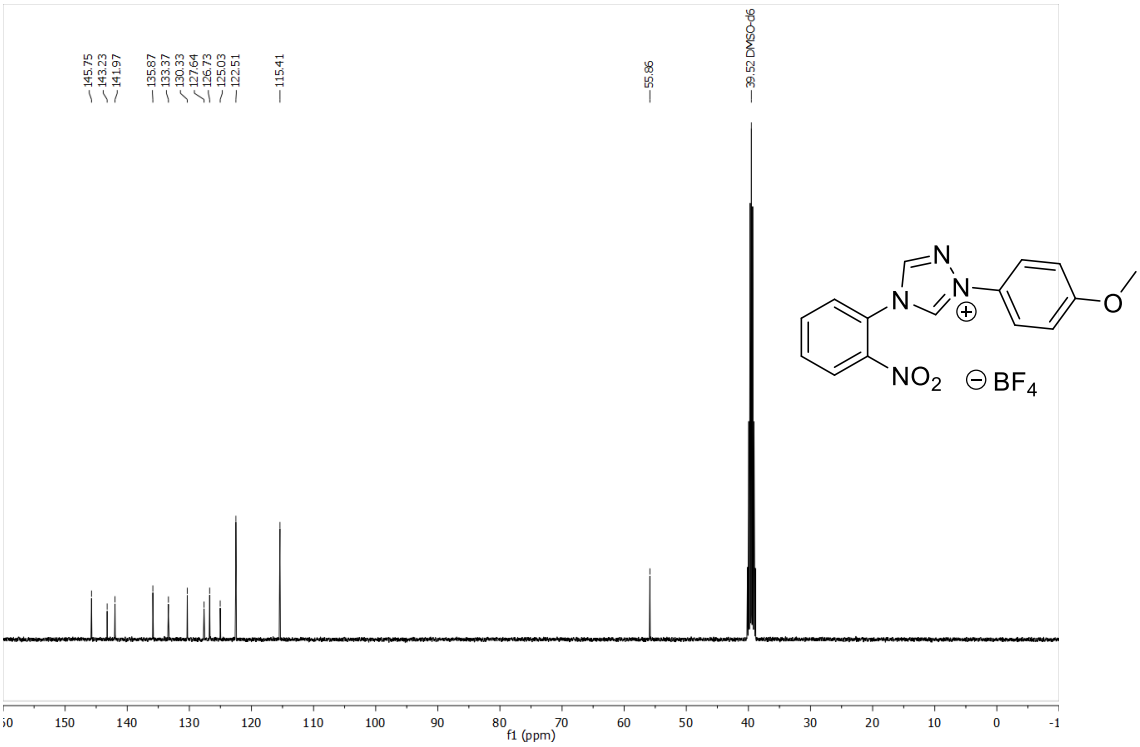

Figure E014: ^{13}C NMR spectrum of 1-(4-methoxyphenyl)-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium tetrafluoroborate (**10s**) (101 MHz, DMSO-d_6, 298 K).

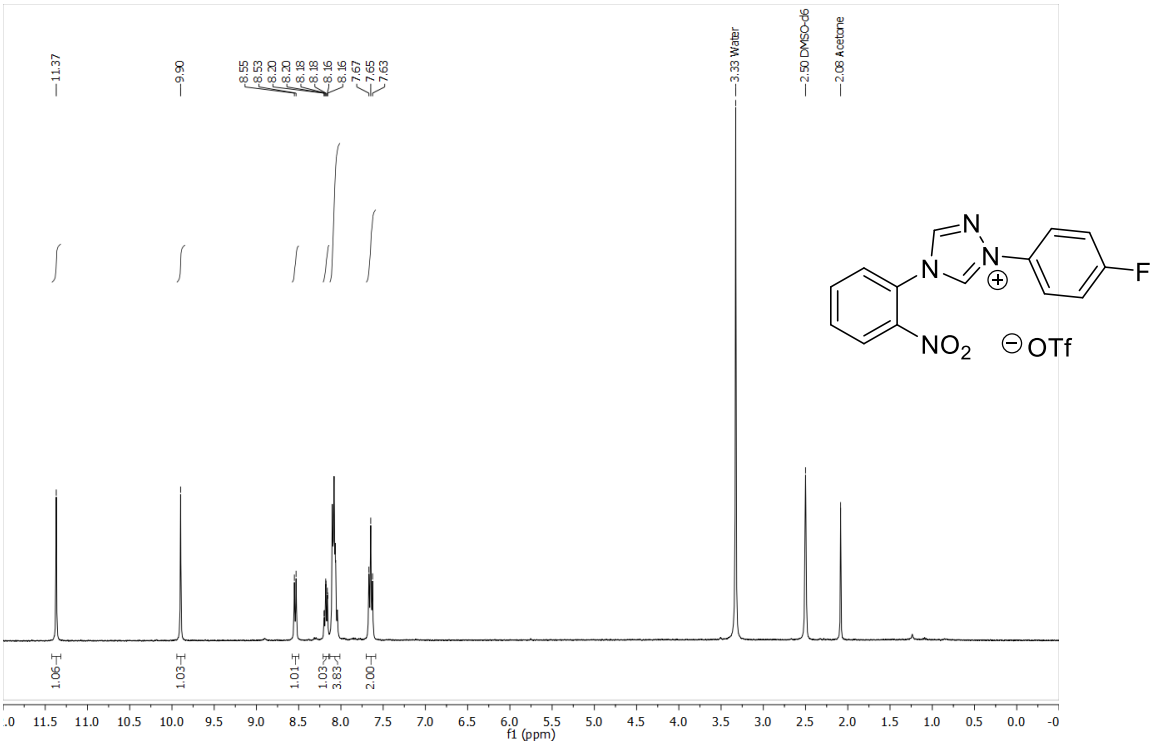

Figure E015: ^{1}H NMR spectrum of 1-(4-fluorophenyl)-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**10t**) (400 MHz, DMSO-d_6, 298 K).

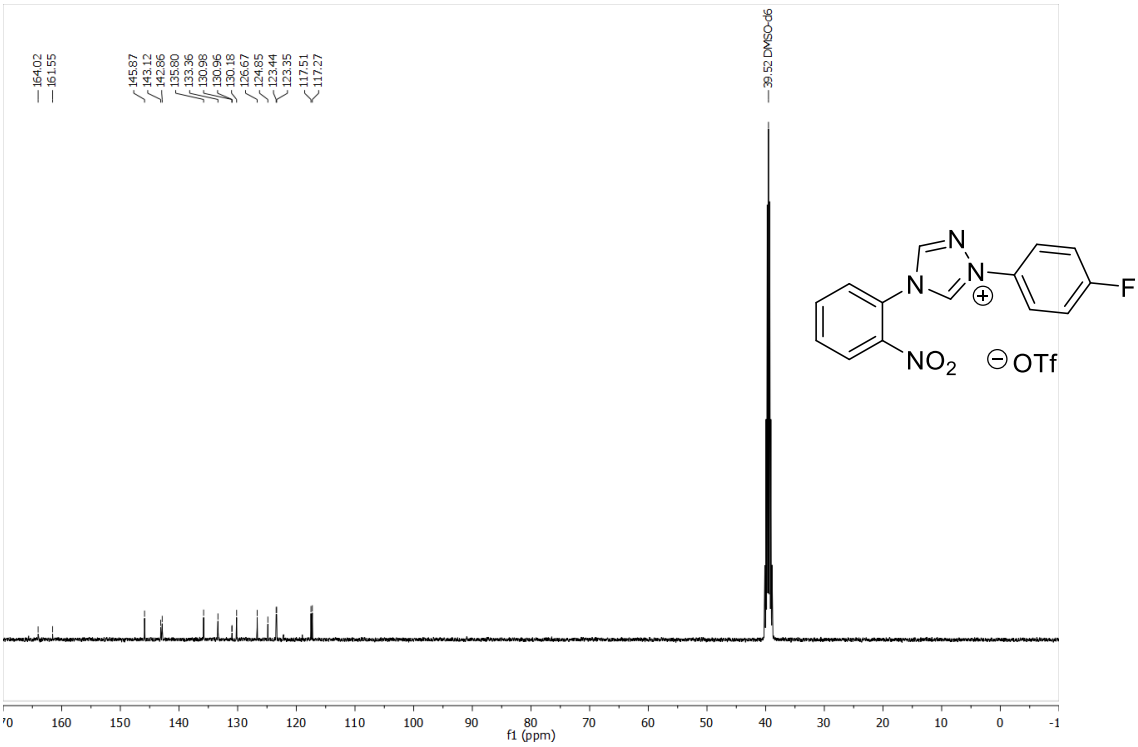

Figure E016: ^{13}C NMR spectrum of 1-(4-fluorophenyl)-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**10t**) (101 MHz, DMSO-d_6, 298 K).

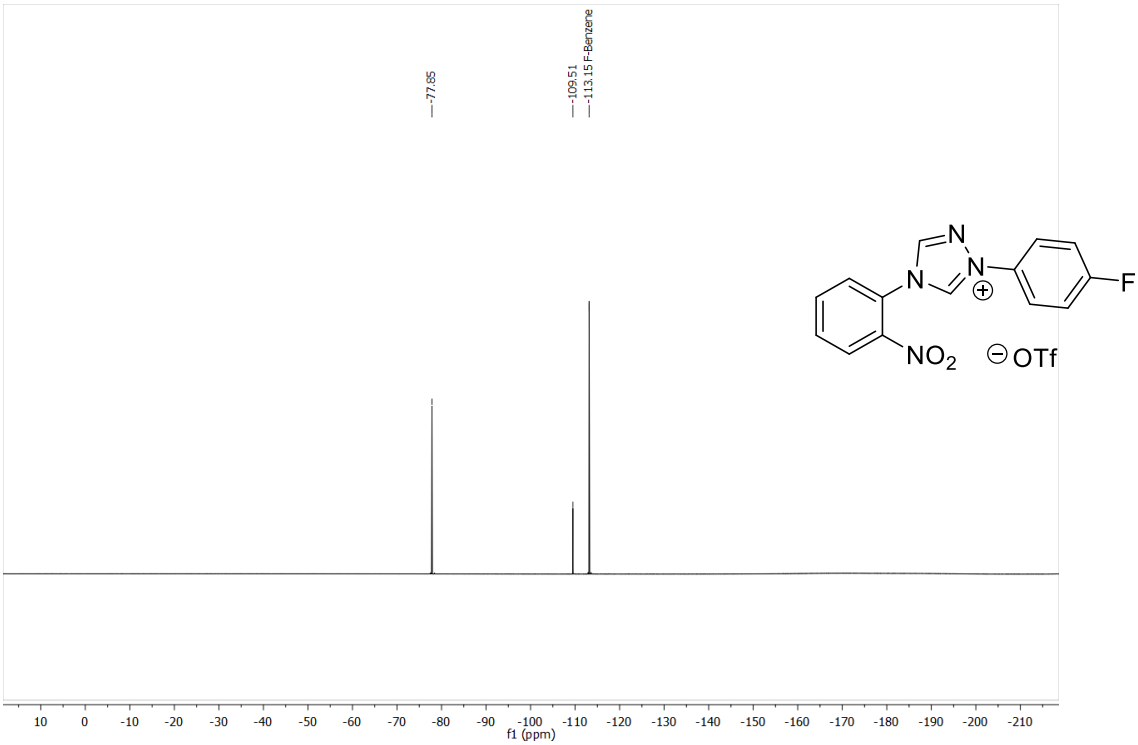

Figure E017: ^{19}F NMR spectrum of 1-(4-fluorophenyl)-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**10t**) (376 MHz, DMSO-d_6, 298 K).

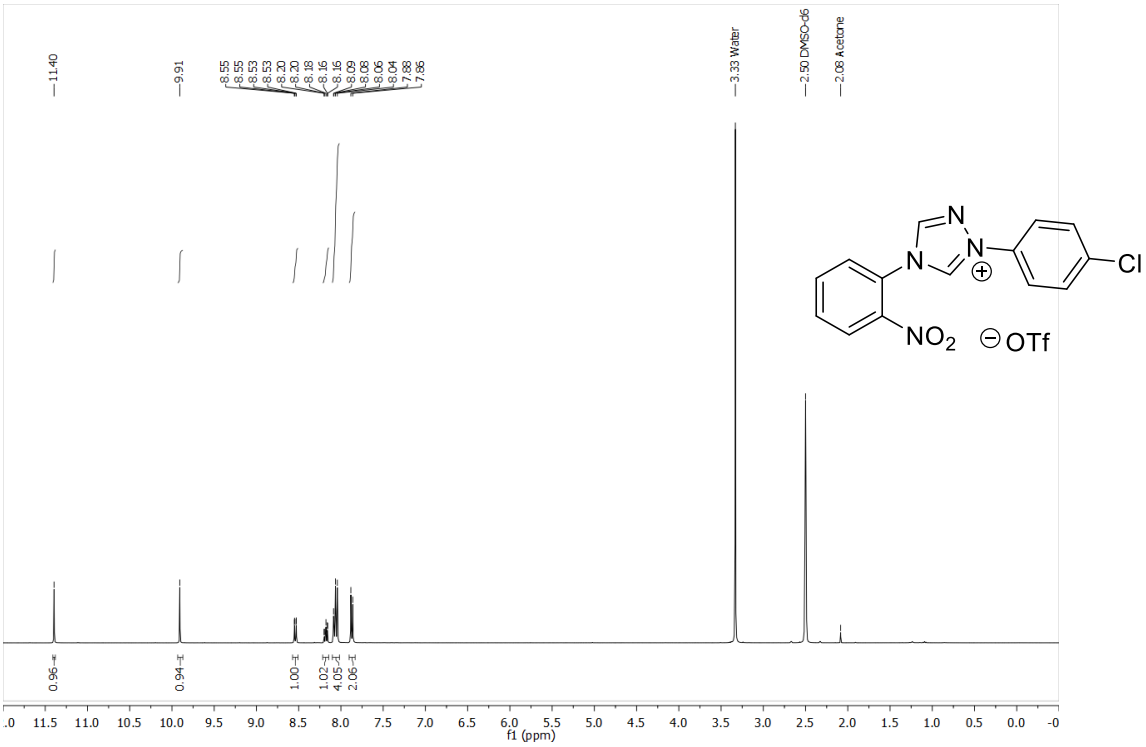

Figure E018: [1]H NMR spectrum of 1-(4-*c*hlorophenyl)-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**10u**) (400 MHz, DMSO-d_6, 298 K).

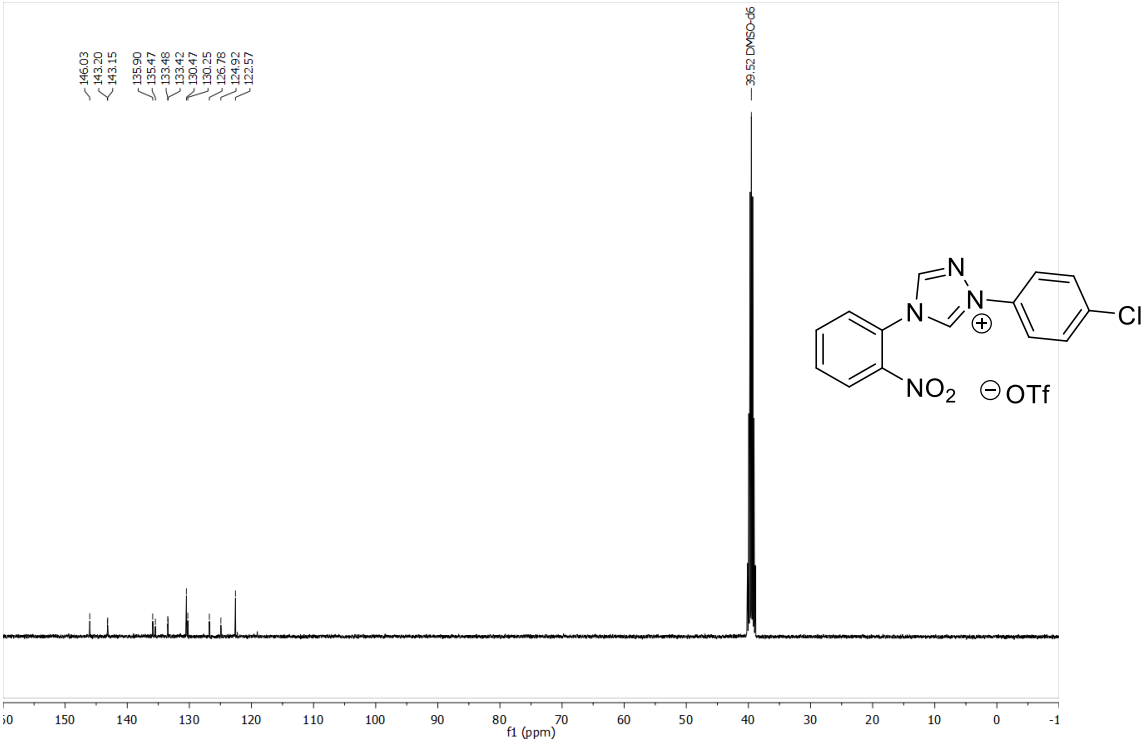

Figure E019: [13]C NMR spectrum of 1-(4-*c*hlorophenyl)-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium trifluoromethanesulfonate (**10u**) (101 MHz, DMSO-d_6, 298 K).

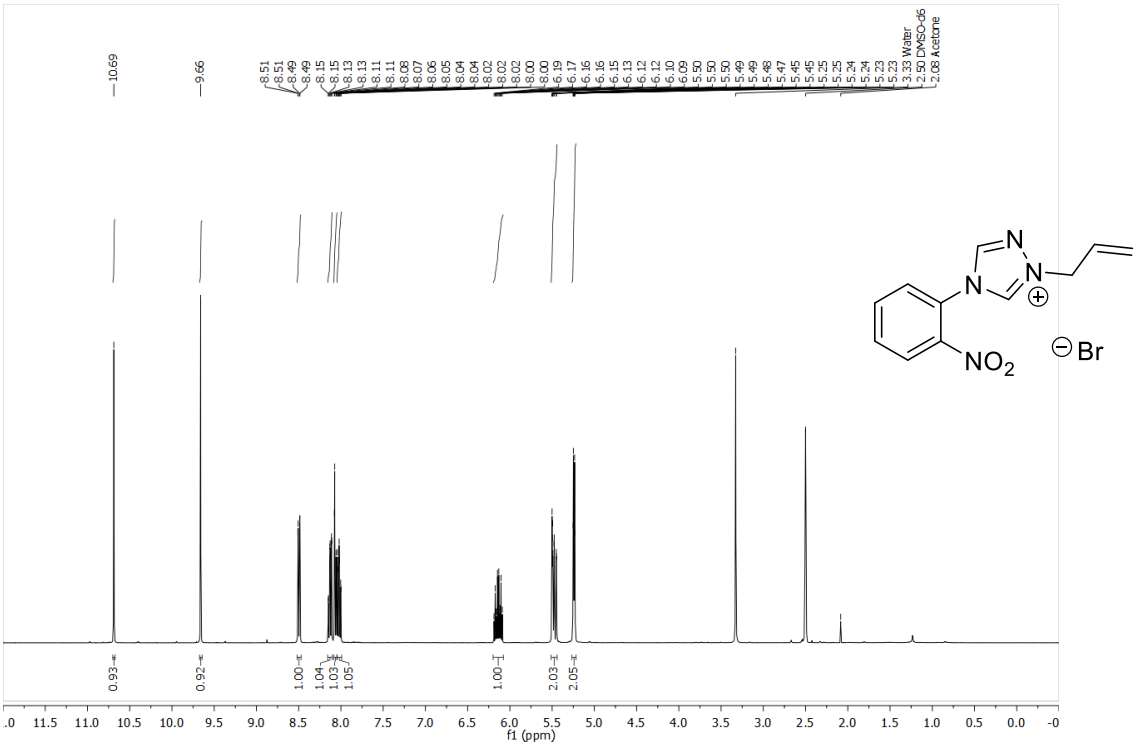

Figure E020: ^{1}H NMR spectrum of 1-allyl-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium bromide (**10v**) (400 MHz, DMSO-d_6, 298 K).

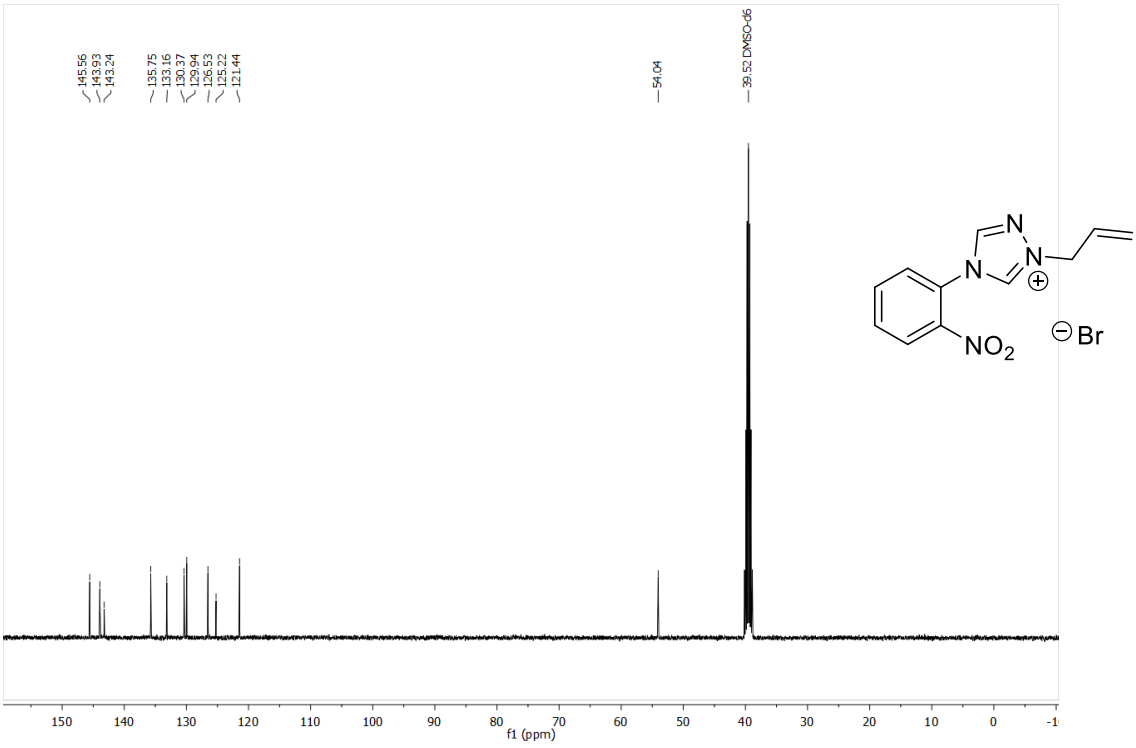

Figure E021: ^{13}C NMR spectrum of 1-allyl-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium bromide (**10v**) (101 MHz, DMSO-d_6, 298 K).

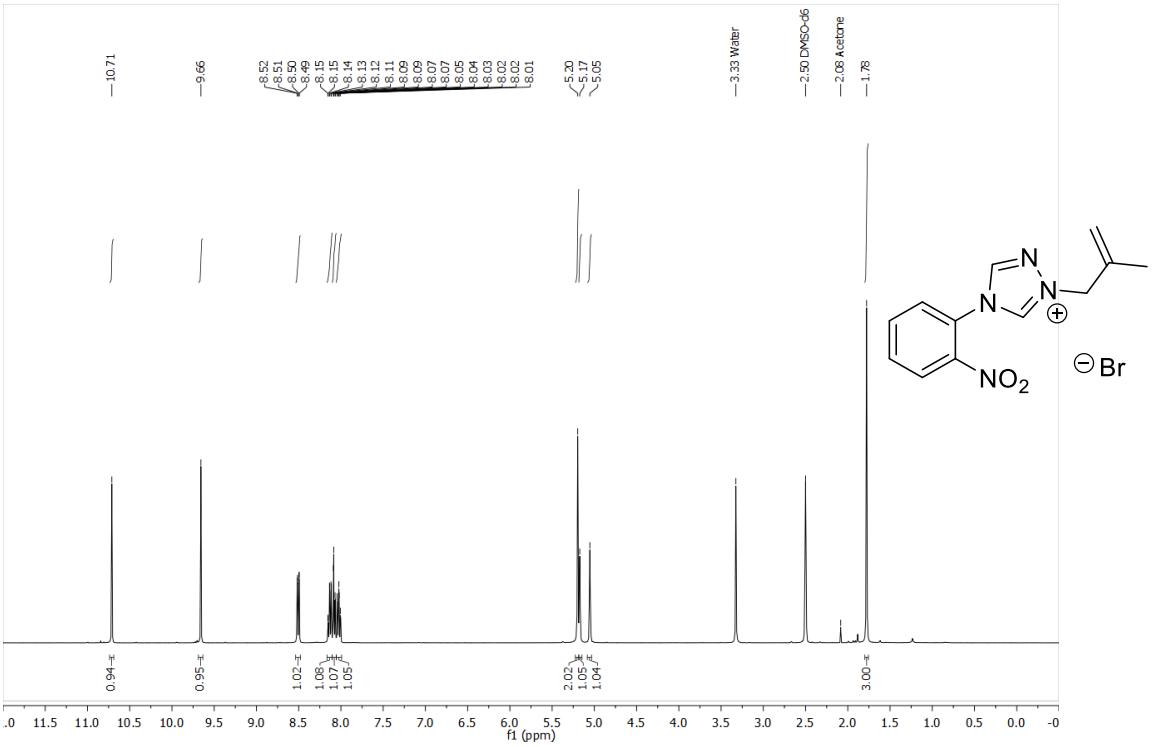

Figure E022: ^{1}H NMR spectrum of 1-(2-methylallyl)-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium bromide (**10w**) (400 MHz, DMSO-d_6, 298 K).

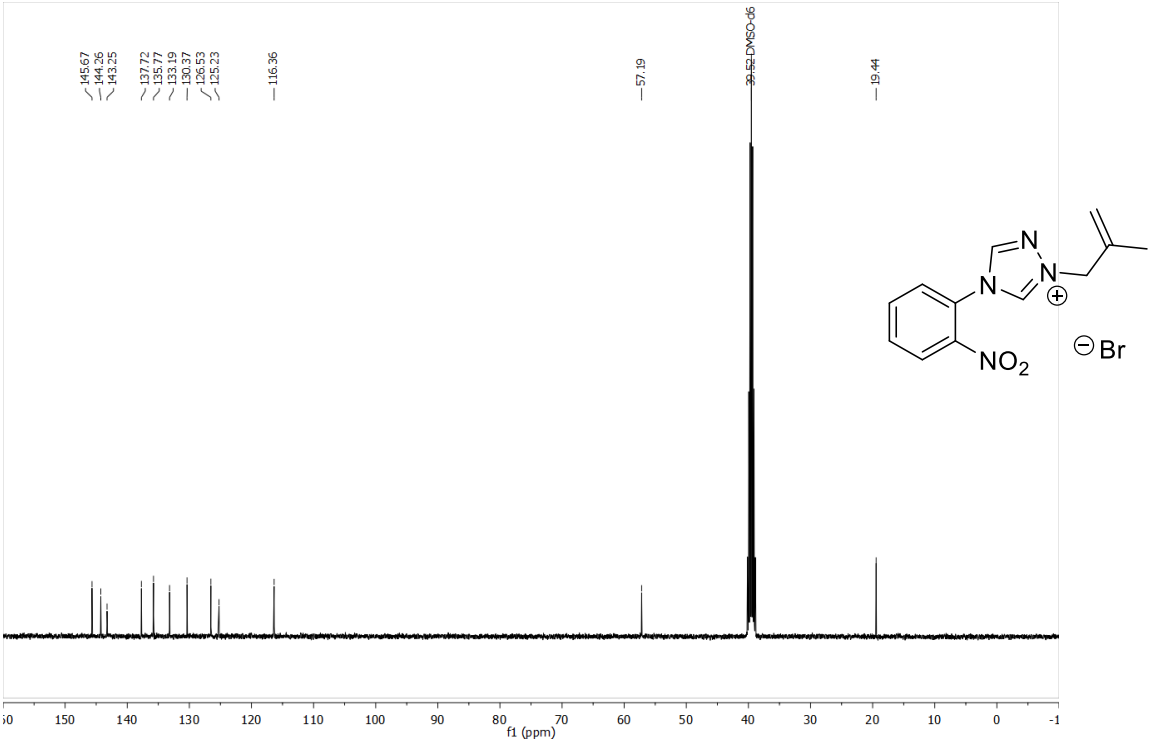

Figure E023: ^{13}C NMR spectrum of 1-(2-methylallyl)-4-(2-nitrophenyl)-4*H*-1,2,4-triazol-1-ium bromide (**10w**) (101 MHz, DMSO-d_6, 298 K).

Section E.3: Spectra for 1-Substituted-(2-ammoniophenyl)-4*H*-1,2,4-triazol-1-ium Salts (E024-E044)

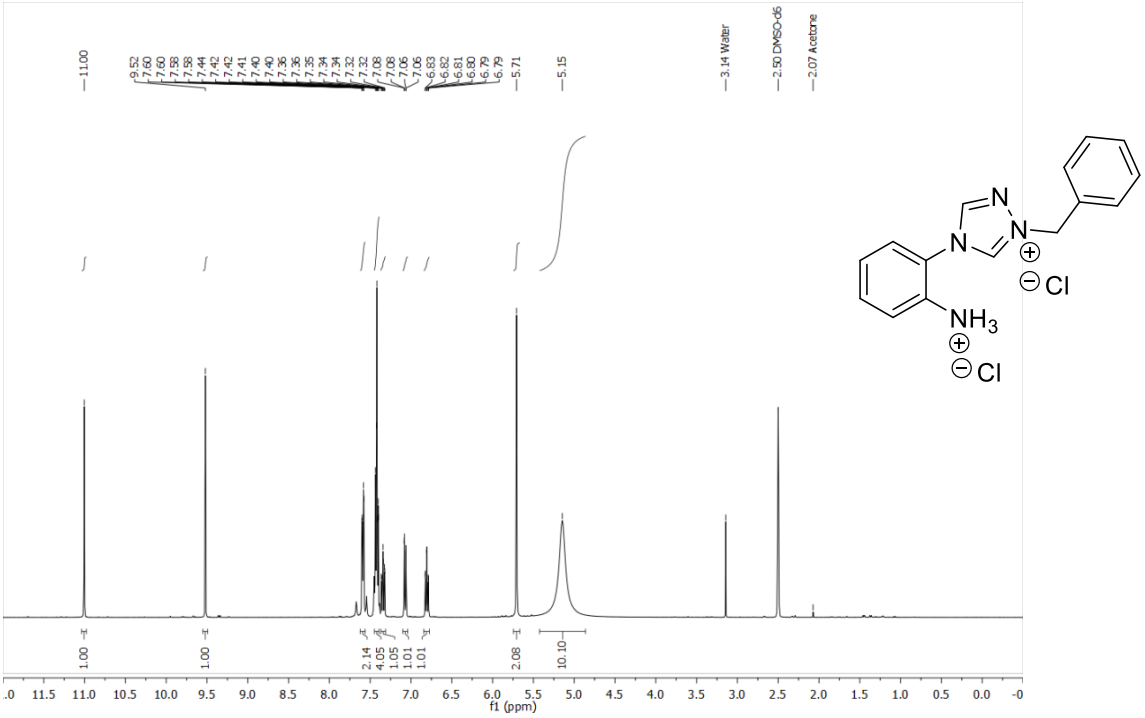

Figure E024: ^{1}H NMR spectrum of 4-(2-ammoniophenyl)-1-benzyl-4*H*-1,2,4-triazol-1-ium chloride (**11n**) (400 MHz, DMSO-d_6, 298 K).

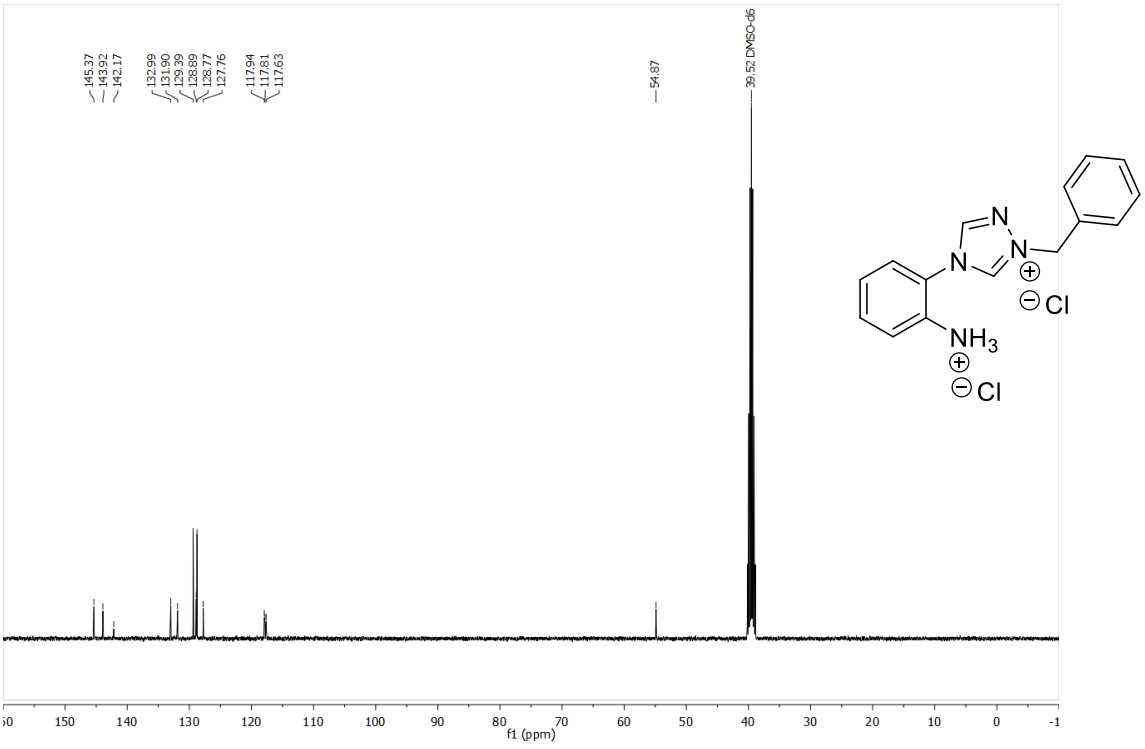

Figure E025: ^{13}C NMR spectrum of 4-(2-ammoniophenyl)-1-benzyl-4*H*-1,2,4-triazol-1-ium chloride (**11n**) (101 MHz, DMSO-d_6, 298 K).

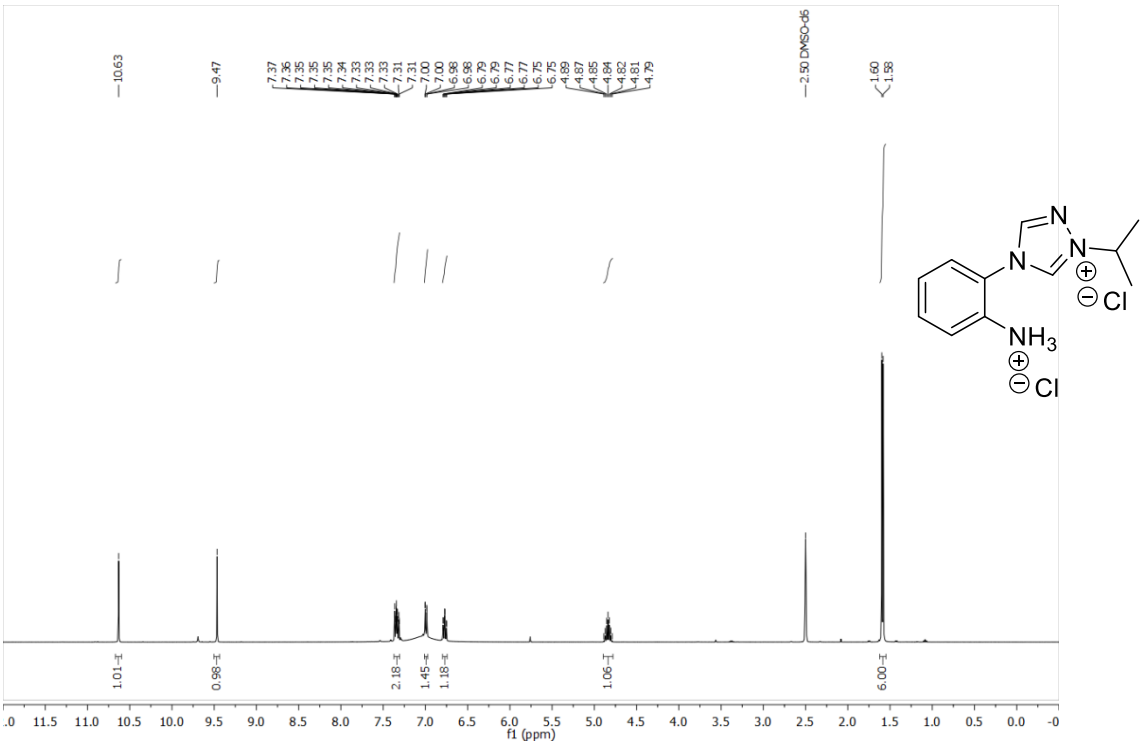

Figure E026: [1]H NMR spectrum of 4-(2-ammoniophenyl)-1-isopropyl-4*H*-1,2,4-triazol-1-ium chloride (**11o**) (400 MHz, DMSO-d_6, 298 K).

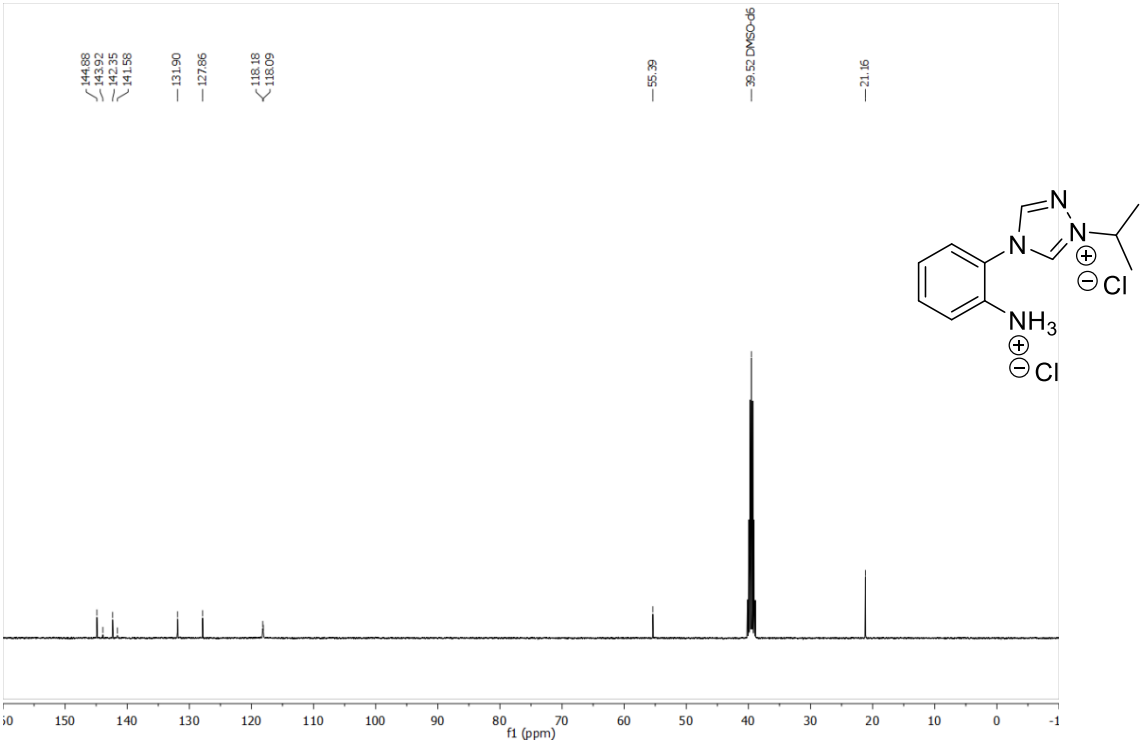

Figure E027: [13]C NMR spectrum of 4-(2-ammoniophenyl)-1-isopropyl-4*H*-1,2,4-triazol-1-ium chloride (**11o**) (101 MHz, DMSO-d_6, 298 K).

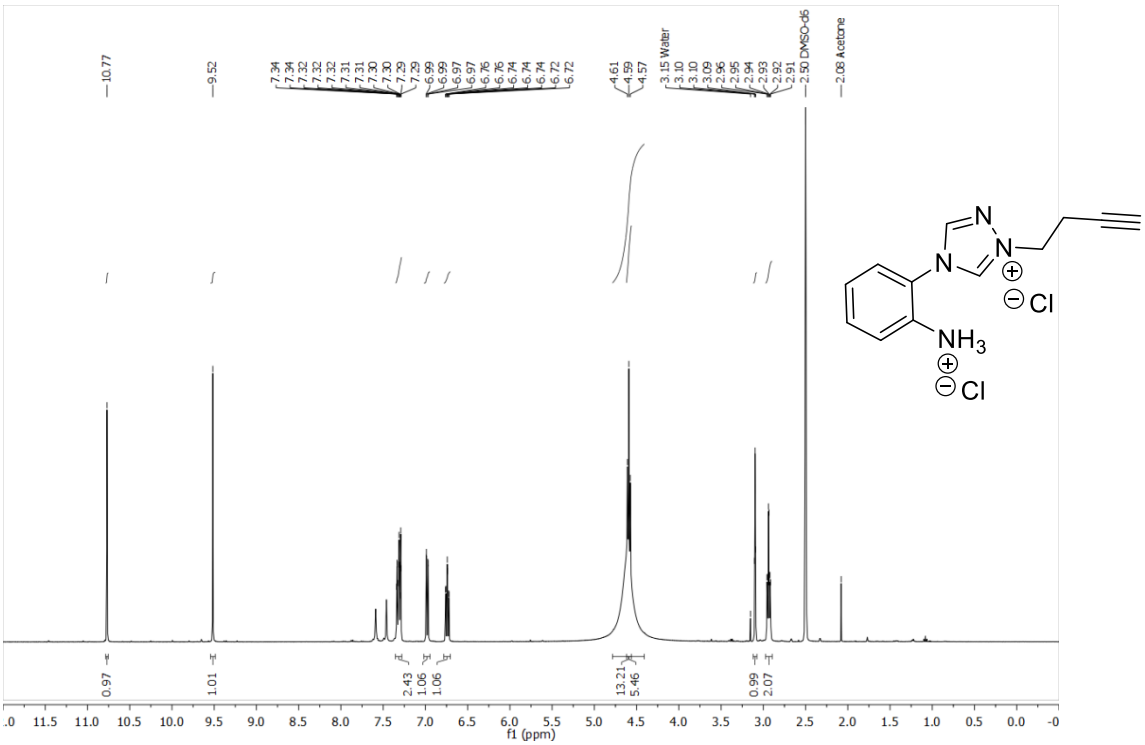

Figure E028: ^{1}H NMR spectrum of 4-(2-ammoniophenyl) -1-(but-3-yn-1-yl)-4*H*-1,2,4-triazol-1-ium chloride (**11p**) (400 MHz, DMSO-d_6, 298 K).

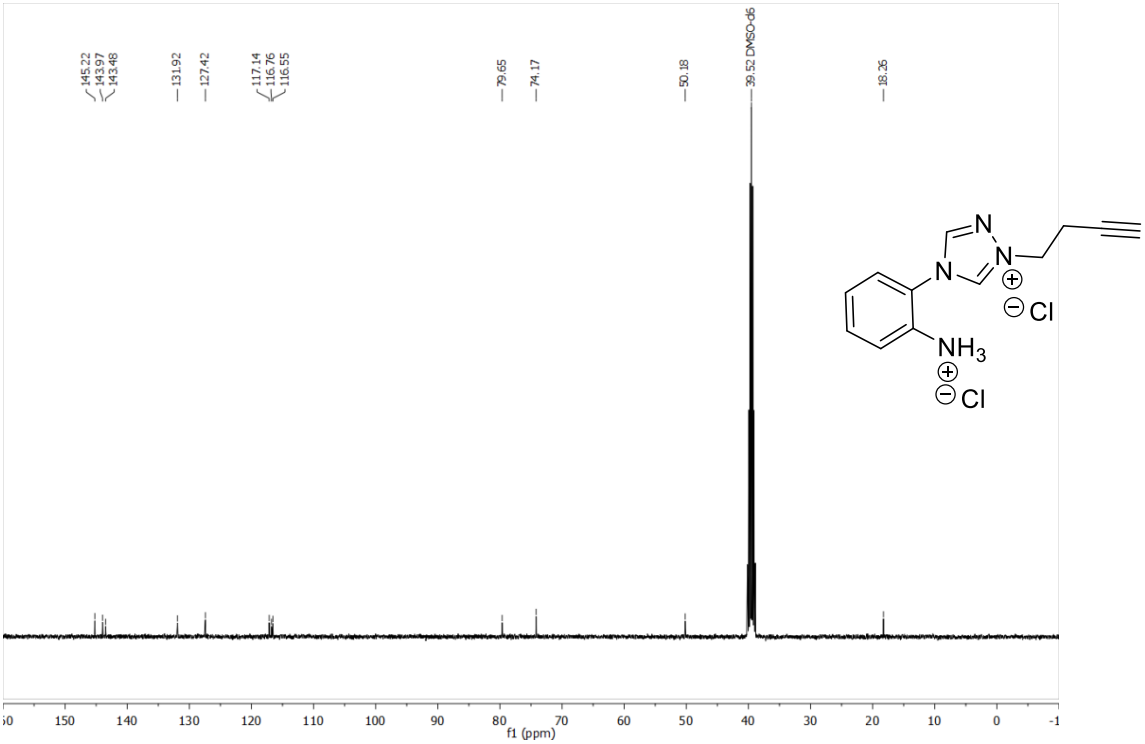

Figure E029: ^{13}C NMR spectrum of 4-(2-ammoniophenyl)-1-(but-3-yn-1-yl)-4*H*-1,2,4-triazol-1-ium chloride (**11p**) (101 MHz, DMSO-d_6, 298 K).

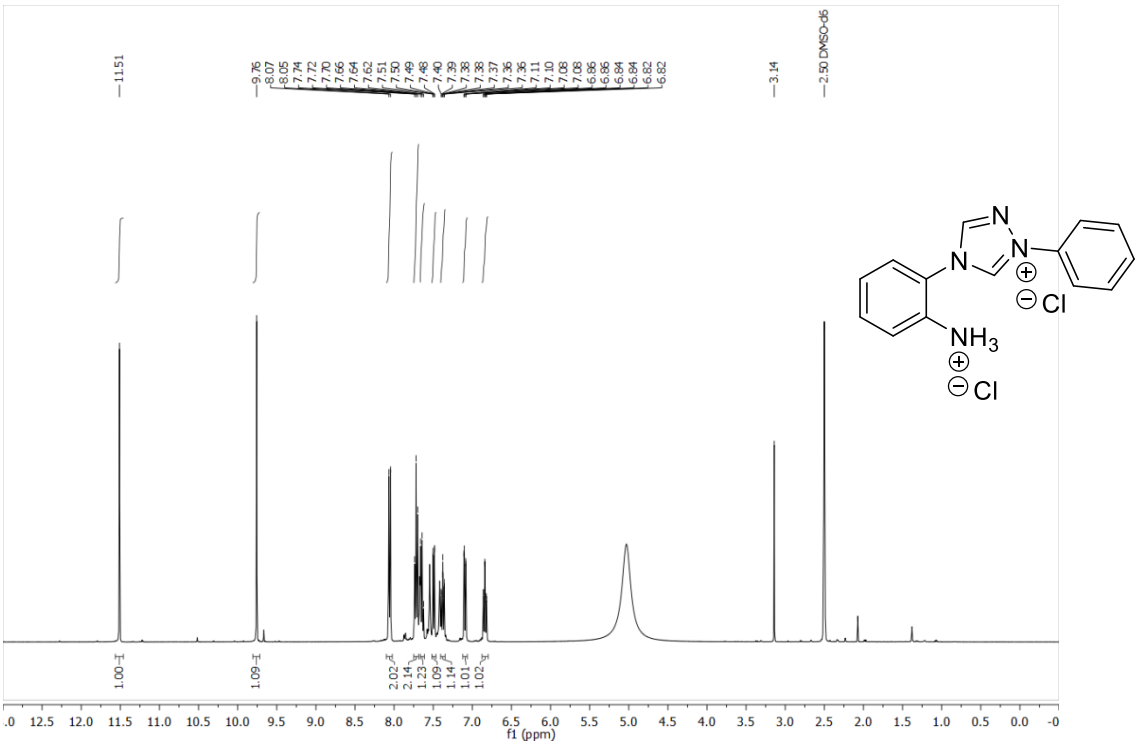

Figure E030: ^{1}H NMR spectrum of 4-(2-ammoniophenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium chloride (**11q**) (400 MHz, DMSO-d_6, 298 K).

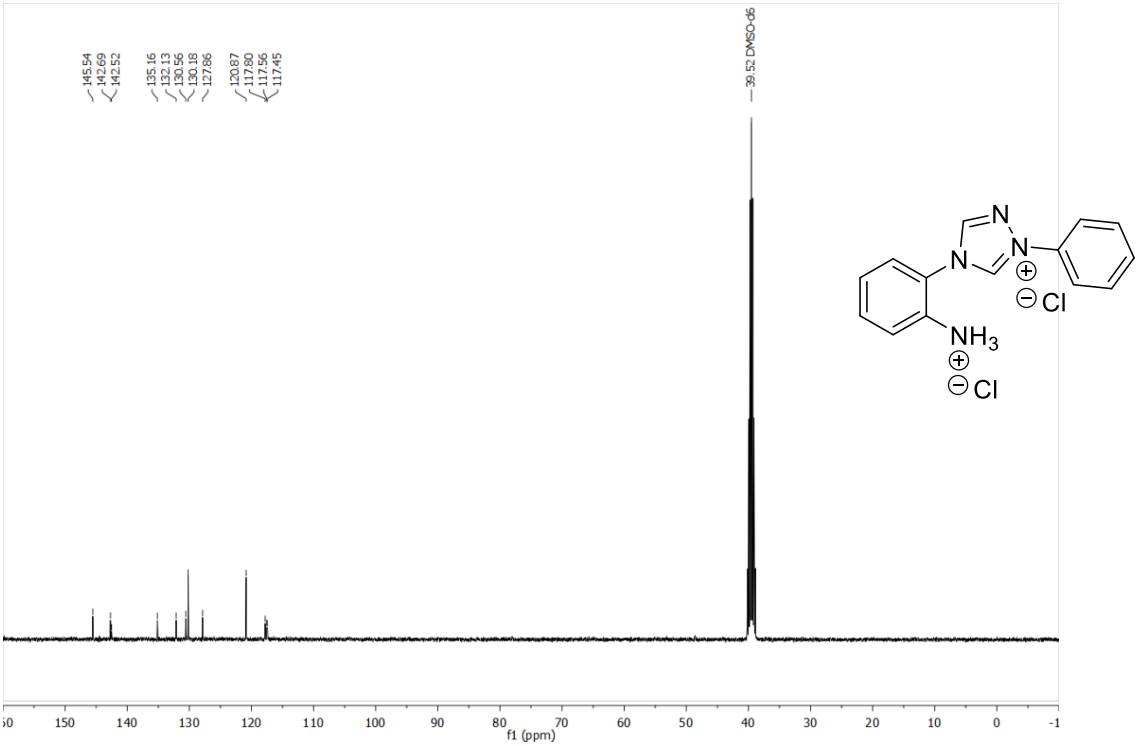

Figure E031: ^{13}C NMR spectrum of 4-(2-ammoniophenyl)-1-phenyl-4*H*-1,2,4-triazol-1-ium chloride (**11q**) (101 MHz, DMSO-d_6, 298 K).

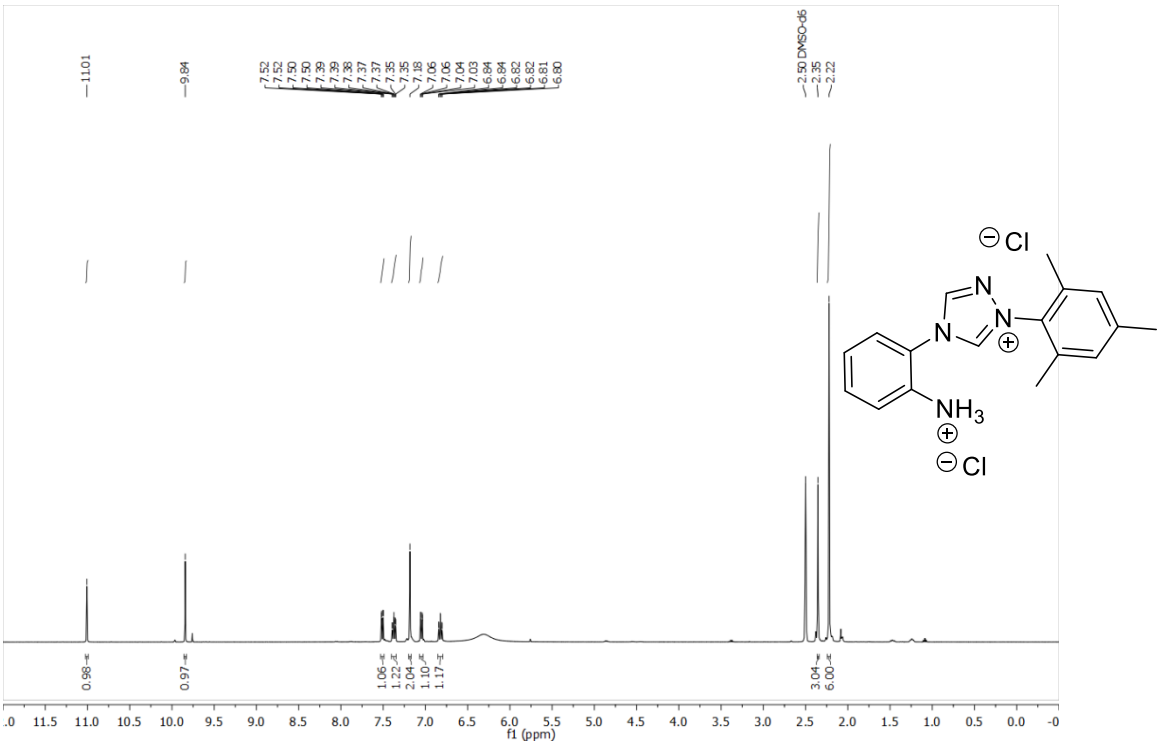

Figure E032: ^{1}H NMR spectrum of 4-(2-ammoniophenyl)-1-mesityl-4*H*-1,2,4-triazol-1-ium chloride (**11r**) (400 MHz, DMSO-d_6, 298 K).

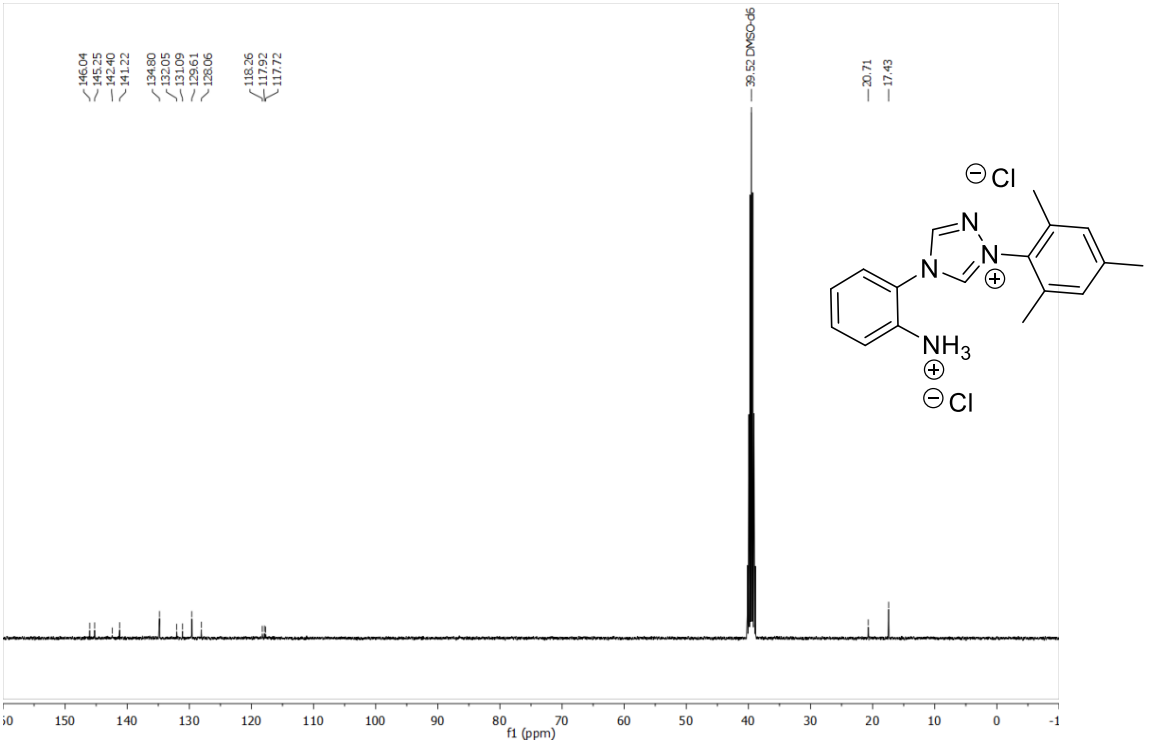

Figure E033: ^{13}C NMR spectrum of 4-(2-ammoniophenyl)-1-mesityl-4*H*-1,2,4-triazol-1-ium chloride (**11r**) (101 MHz, DMSO-d_6, 298 K).

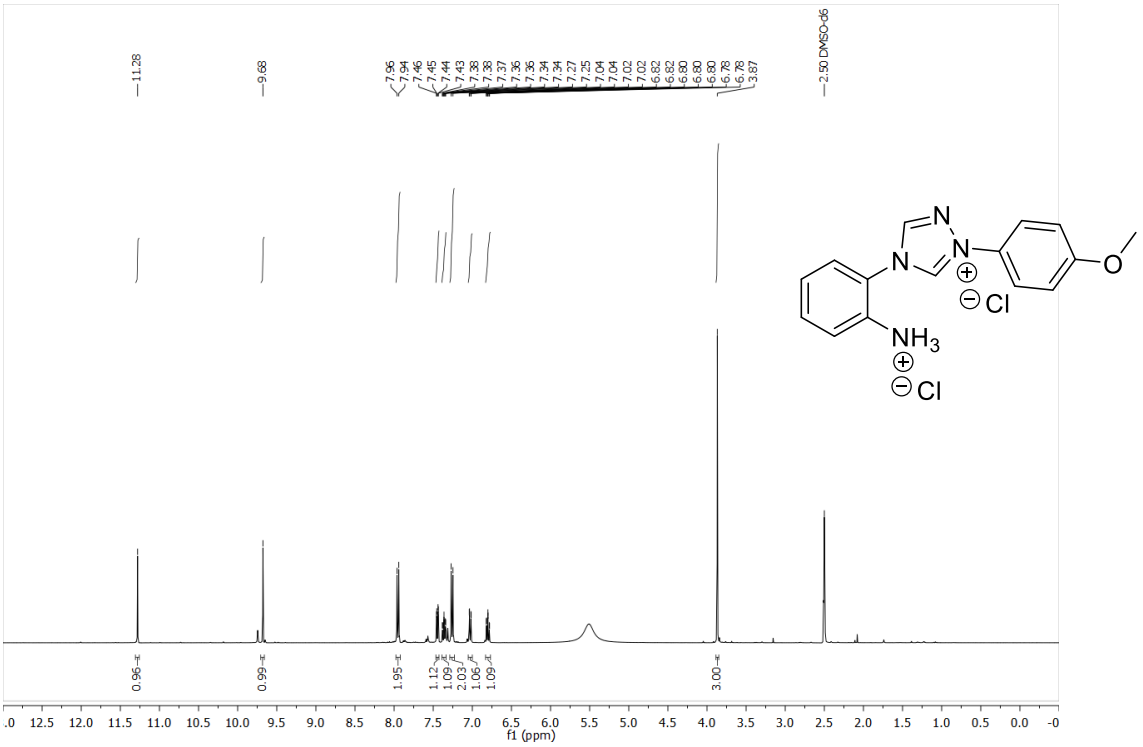

Figure E034: [1]H NMR spectrum of 4-(2-ammoniophenyl)-1-(4-methoxyphenyl)-4*H*-1,2,4-triazol-1-ium chloride (**11s**) (400 MHz, DMSO-d_6, 298 K).

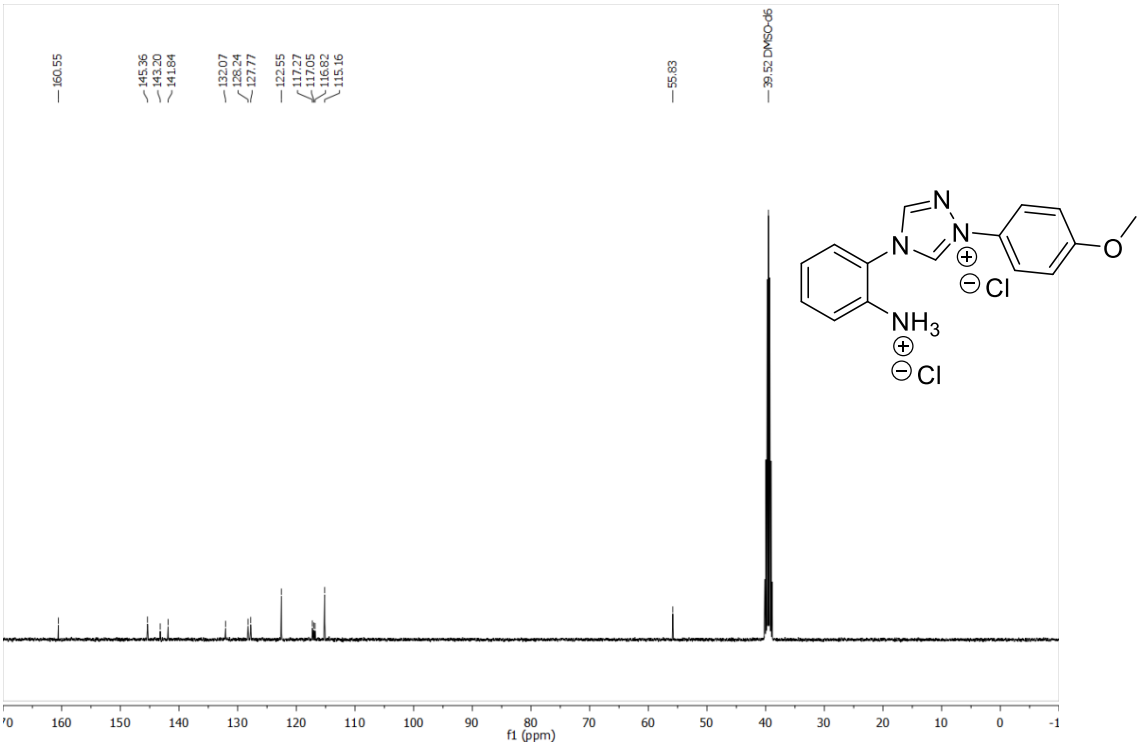

Figure E035: [13]C NMR spectrum of 4-(2-ammoniophenyl)-1-(4-methoxyphenyl)-4*H*-1,2,4-triazol-1-ium chloride (**11s**) (101 MHz, DMSO-d_6, 298 K).

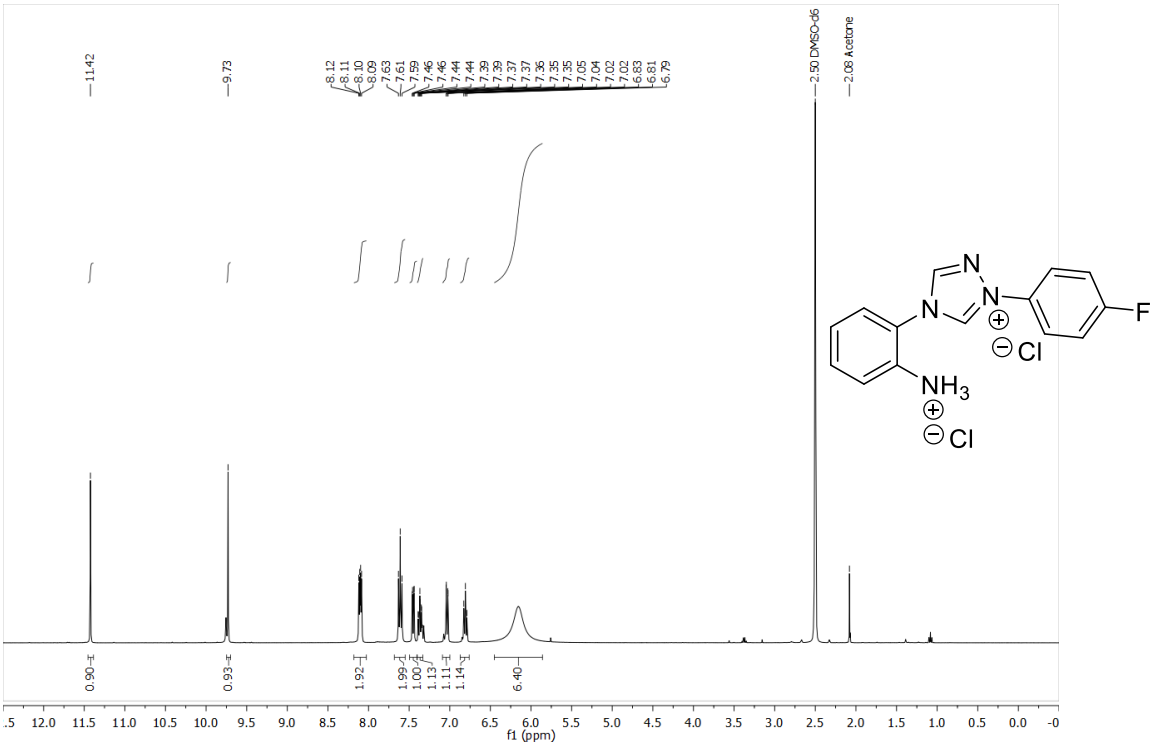

Figure E036: [1]H NMR spectrum of 4-(2-ammoniophenyl)-1-(4-fluorophenyl)-4*H*-1,2,4-triazol-1-ium chloride (**11t**) (400 MHz, DMSO-d_6, 298 K).

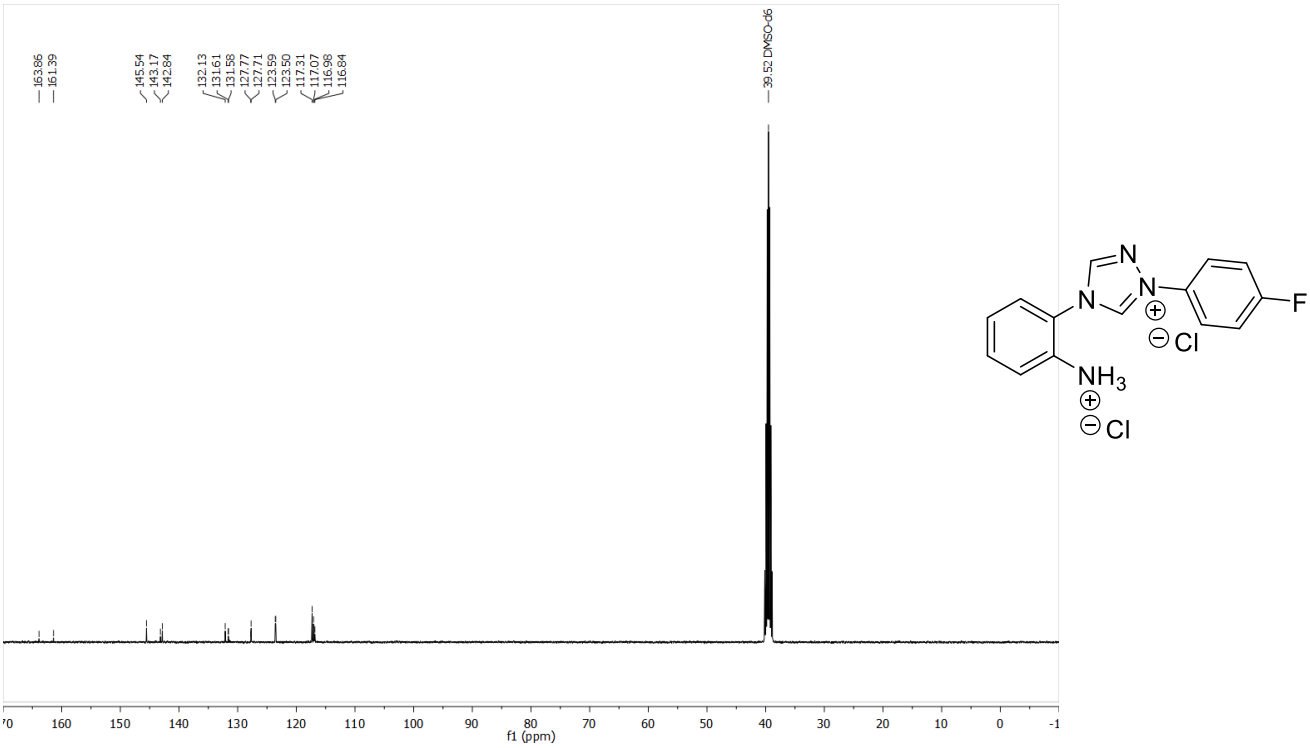

Figure E037: [13]C NMR spectrum of 4-(2-ammoniophenyl)-1-(4-fluorophenyl)-4*H*-1,2,4-triazol-1-ium chloride (**11t**) (101 MHz, DMSO-d_6, 298 K).

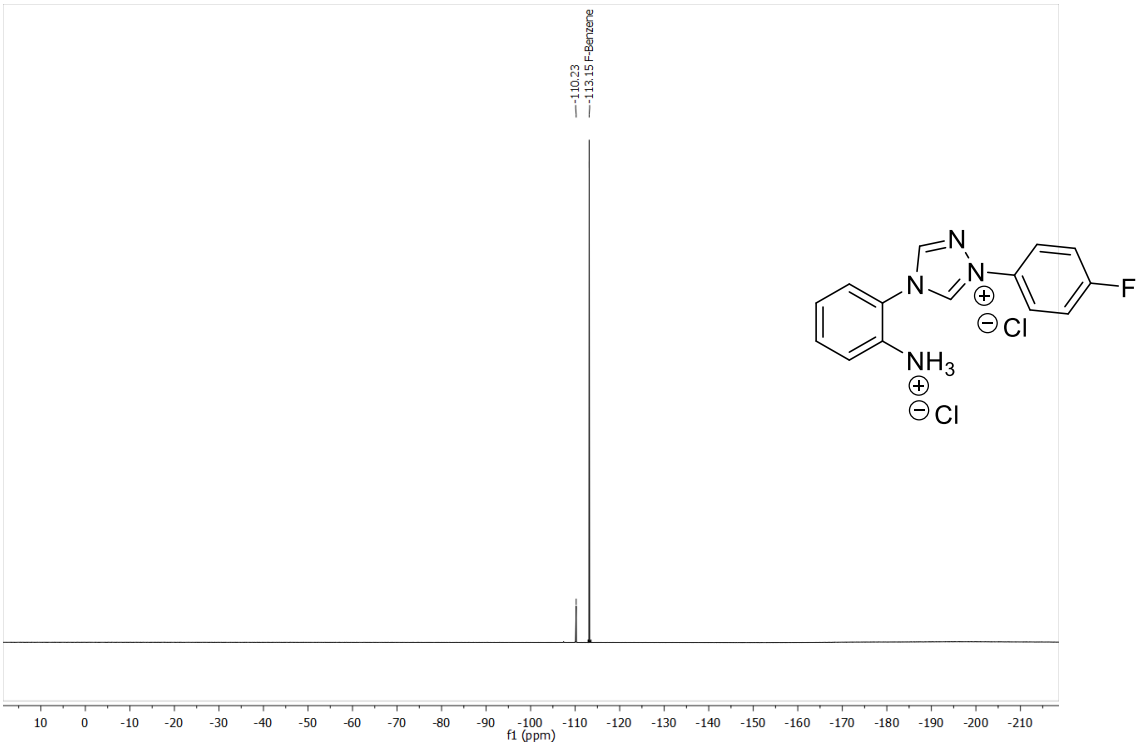

Figure E038: ^{19}F NMR spectrum of 4-(2-ammoniophenyl)-1-(4-fluorophenyl)-4*H*-1,2,4-triazol-1-ium chloride (**11t**) (376 MHz, DMSO-d_6, 298 K).

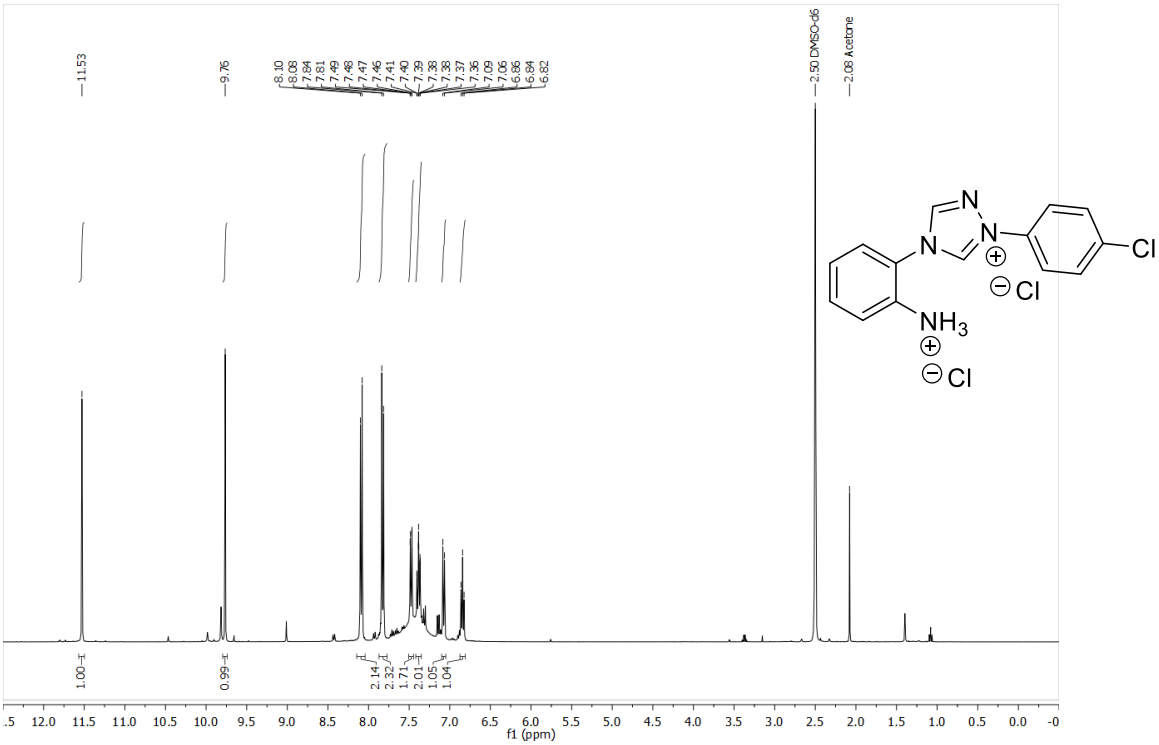

Figure E039: ^{1}H NMR spectrum of 4-(2-ammoniophenyl)-1-(4-*c*hlorophenyl)-4*H*-1,2,4-triazol-1-ium chloride (**11u**) (400 MHz, DMSO-d_6, 298 K).

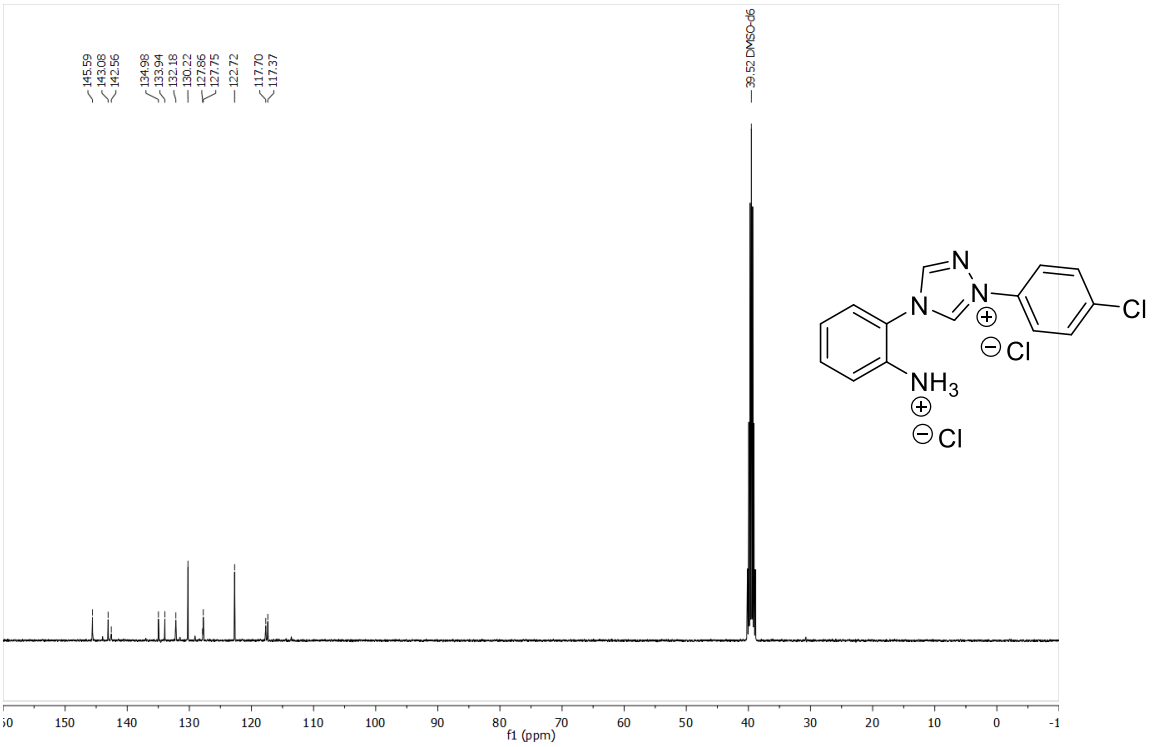

Figure E040: ^{13}C NMR spectrum of 4-(2-ammoniophenyl)-1-(4-*c*hlorophenyl)-4*H*-1,2,4-triazol-1-ium chloride (**11u**) (101 MHz, DMSO-d_6, 298 K).

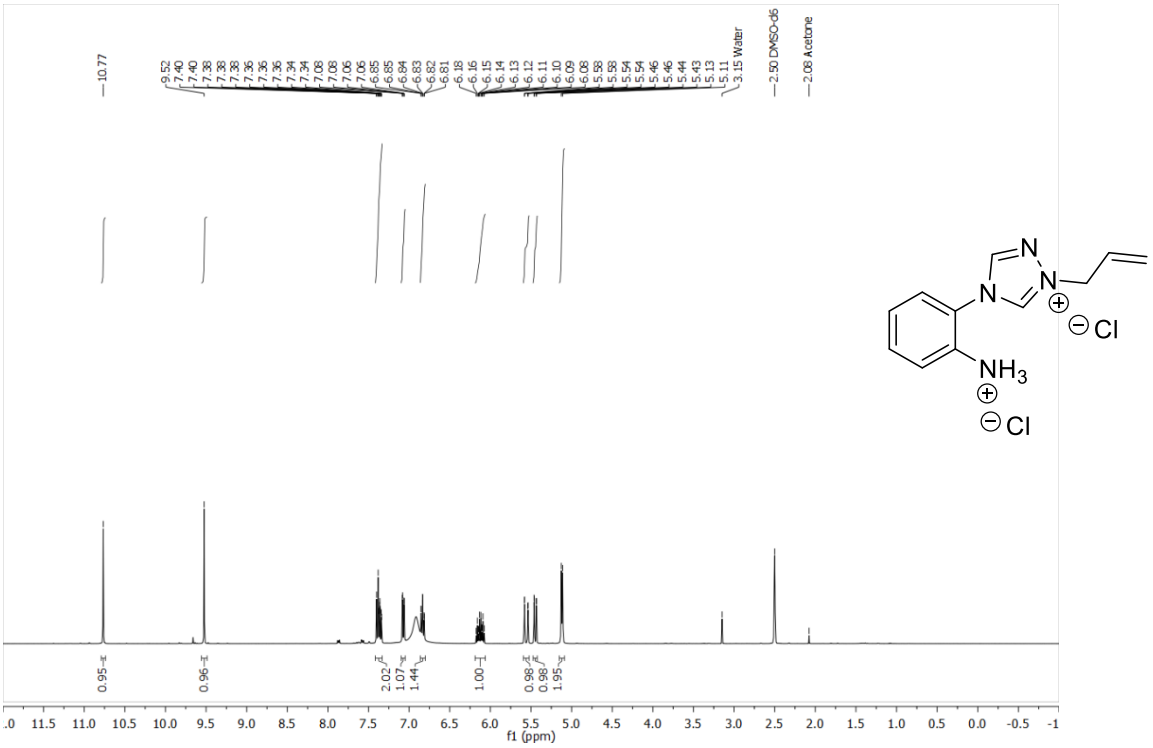

Figure E041: ^{1}H NMR spectrum of 1-allyl-4-(2-ammoniophenyl)-4*H*-1,2,4-triazol-1-ium chloride (**11v**) (400 MHz, DMSO-d_6, 298 K).

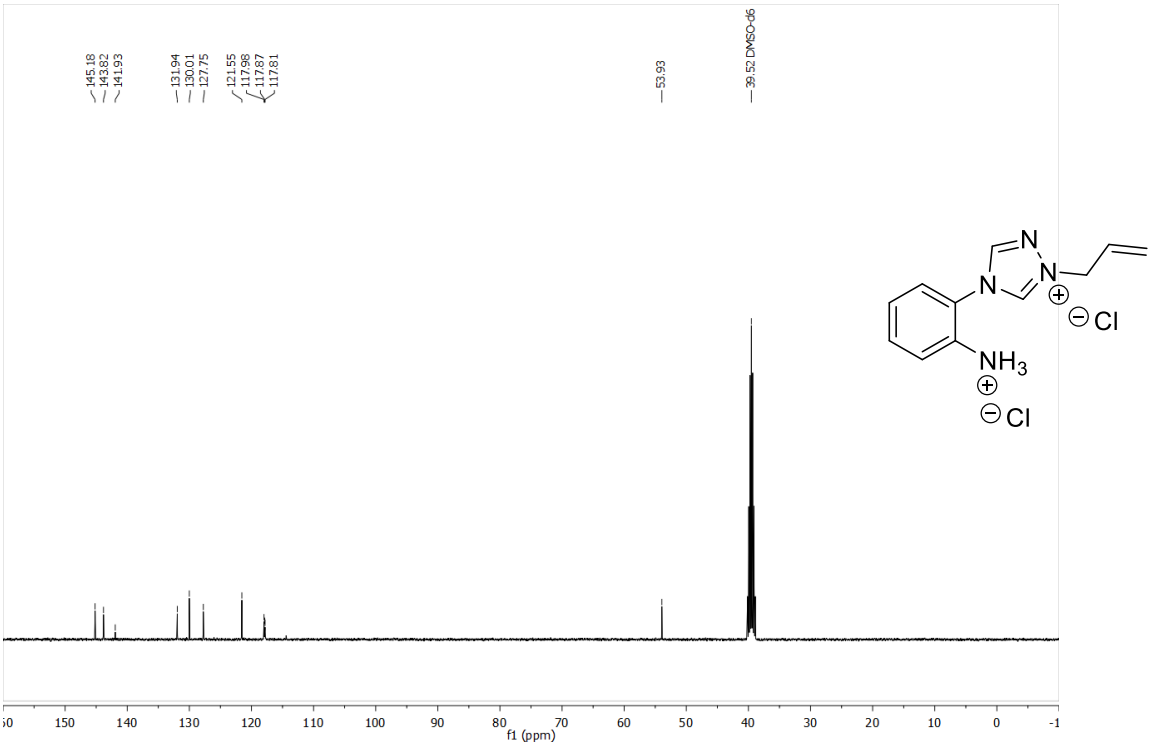

Figure E042: ^{13}C NMR spectrum of 1-allyl-4-(2-ammoniophenyl)-4*H*-1,2,4-triazol-1-ium chloride (**11v**) (101 MHz, DMSO-d_6, 298 K).

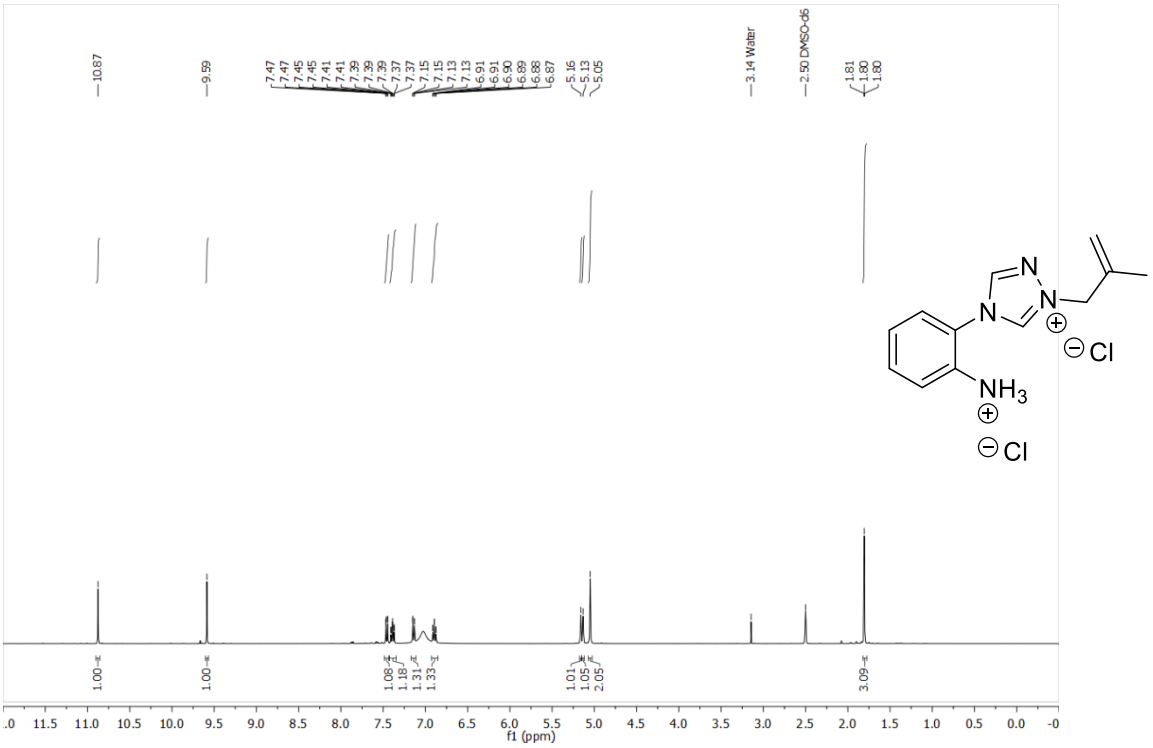

Figure E043: ^{1}H NMR spectrum of 4-(2-ammoniophenyl)-1-(2-methylallyl)-4*H*-1,2,4-triazol-1-ium chloride (**11w**) (400 MHz, DMSO-d_6, 298 K).

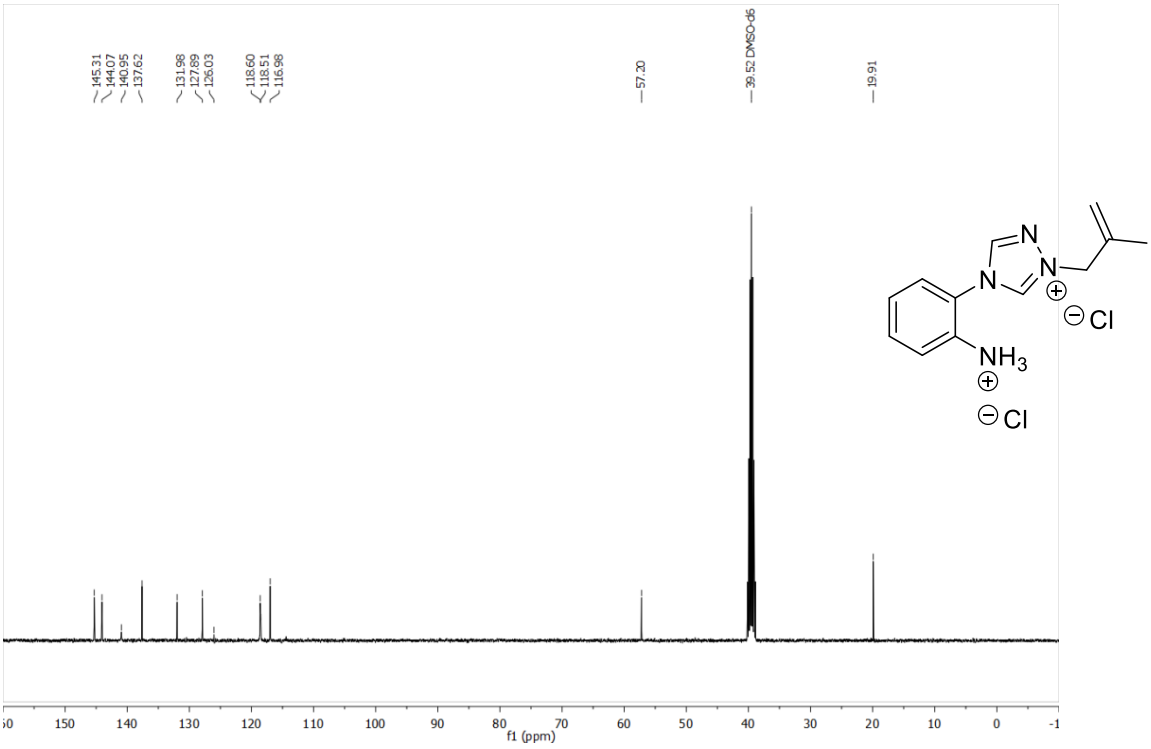

Figure E044: ^{13}C NMR spectrum of 4-(2-ammoniophenyl)-1-(2-methylallyl)-4*H*-1,2,4-triazol-1-ium chloride (**11w**) (101 MHz, DMSO-d_6, 298 K).

Section E.4: Spectra of 9*H*-Benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium Salts (E045-E065)

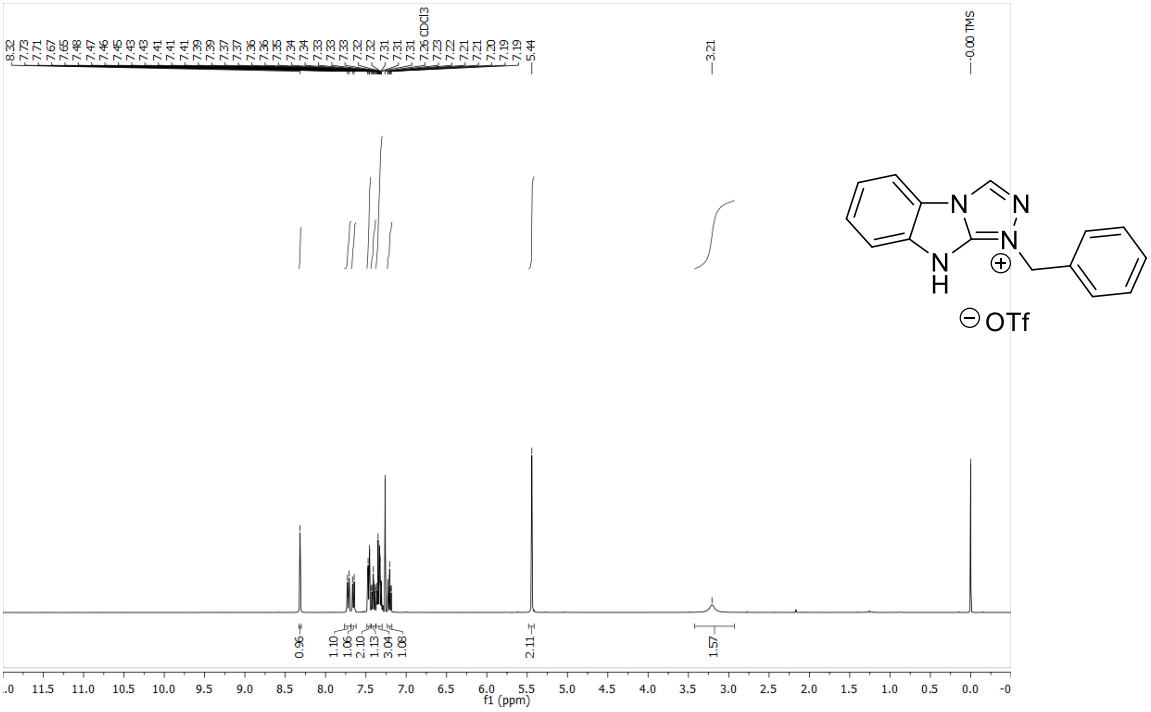

Figure E045: ^{1}H NMR spectrum of 1-benzyl-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (**12n**) (400 MHz, $CDCl_3$, 298 K).

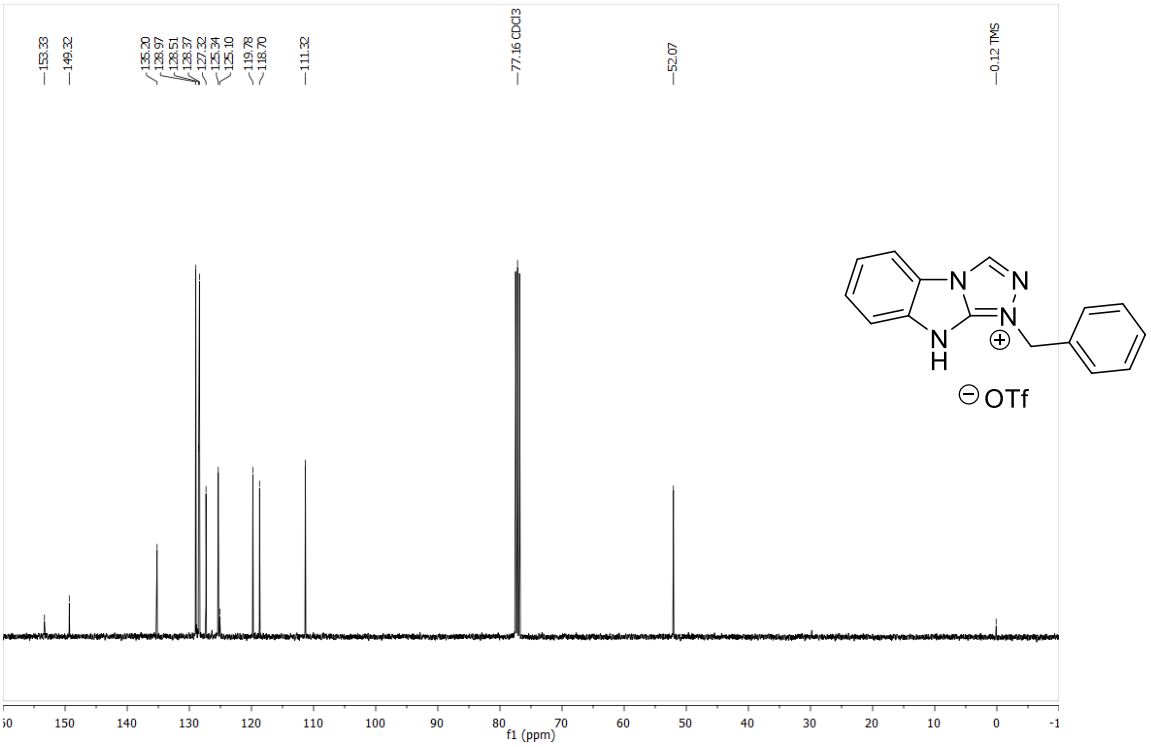

Figure E046: ^{13}C NMR spectrum of 1-benzyl-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (**12n**) (101 MHz, $CDCl_3$, 298 K).

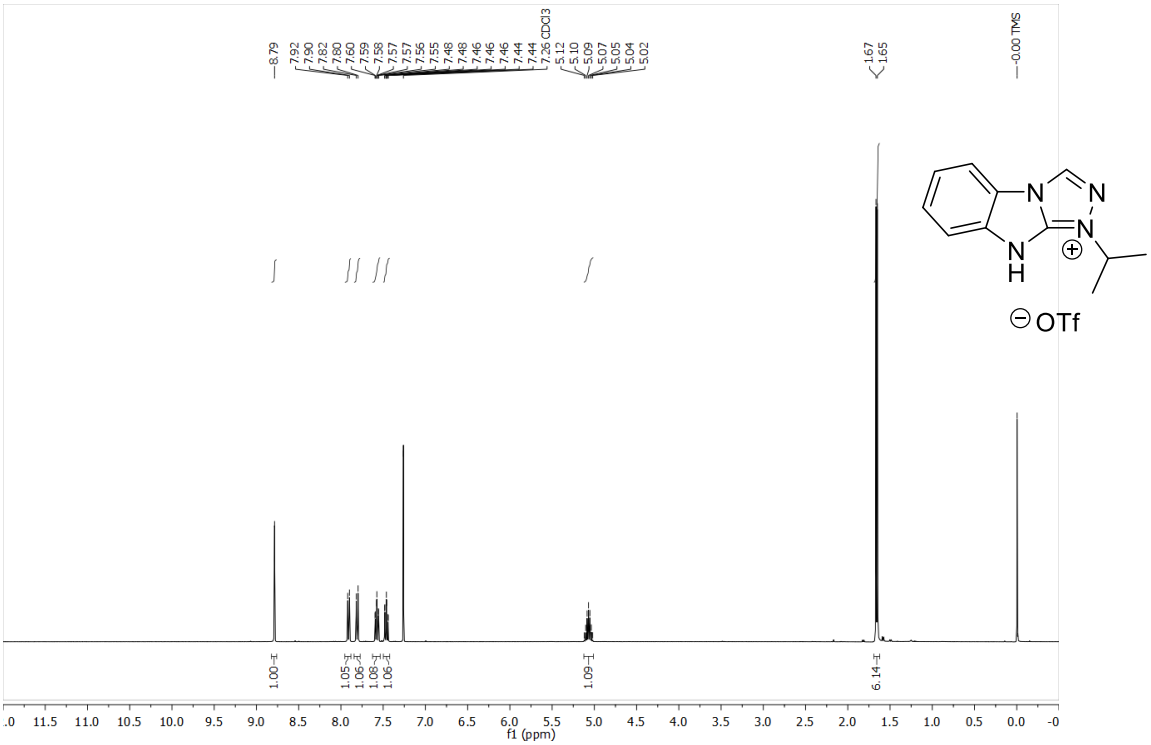

Figure E047: ^{1}H NMR spectrum of 1-isopropyl-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (**12o**) (400 MHz, $CDCl_3$, 298 K).

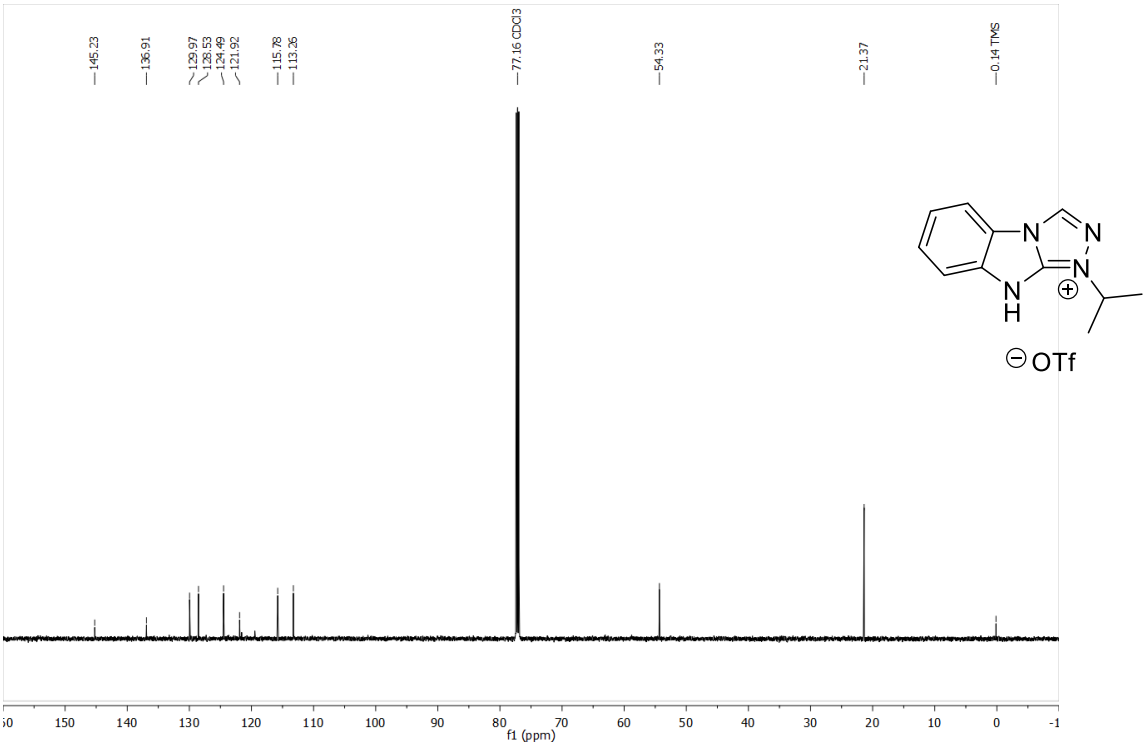

Figure E048: ^{13}C NMR spectrum of 1-isopropyl-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (**12o**) (101 MHz, $CDCl_3$, 298 K).

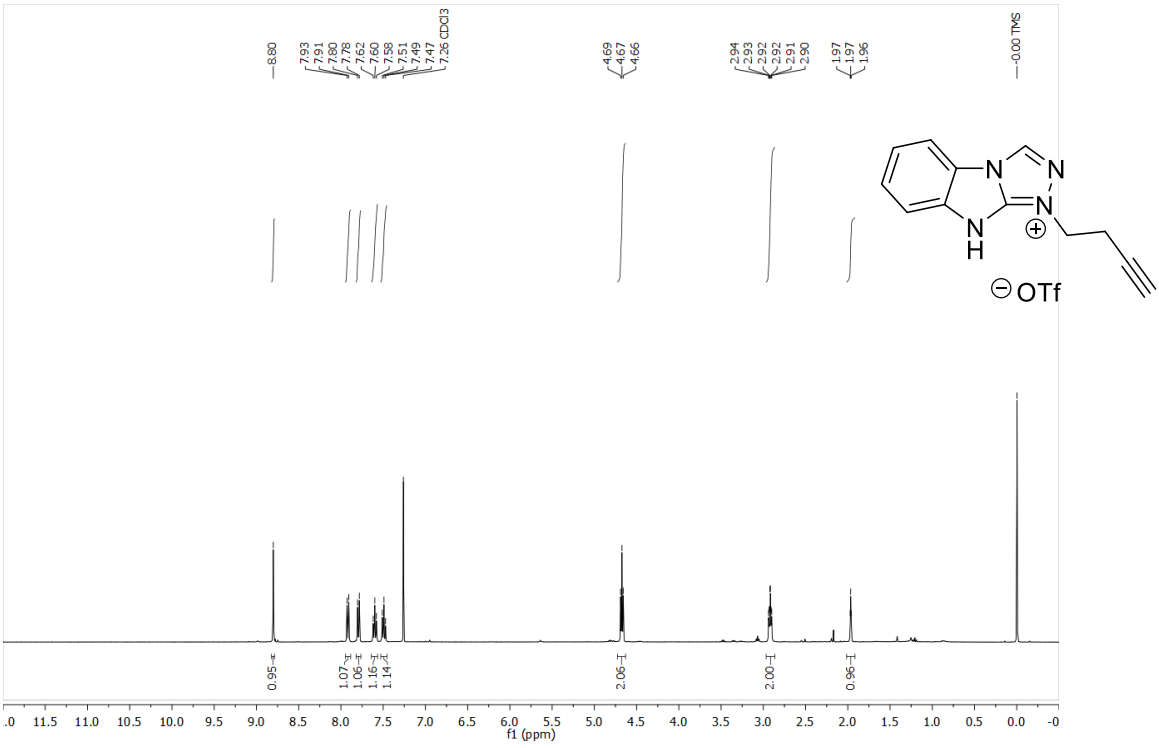

Figure E049: ^{1}H NMR spectrum of 1-(but-3-yn-1-yl)-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (**12p**) (400 MHz, $CDCl_3$, 298 K).

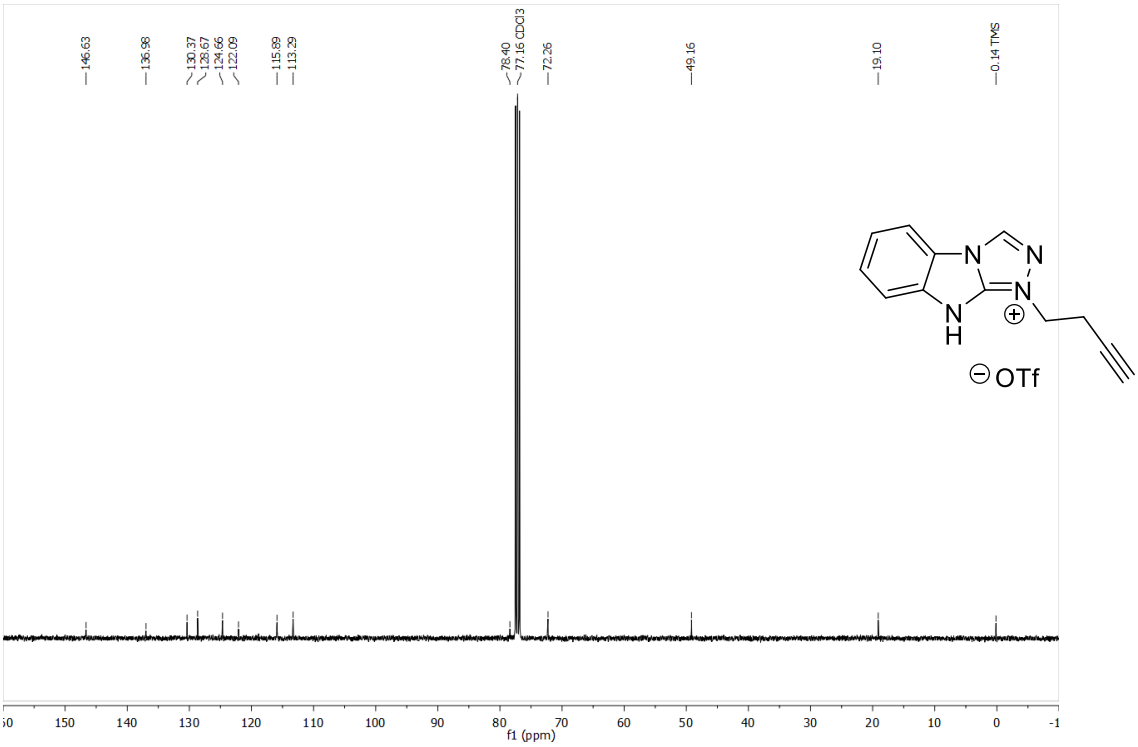

Figure E050: ^{13}C NMR spectrum of 1-(but-3-yn-1-yl)-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (**12p**) (101 MHz, $CDCl_3$, 298 K).

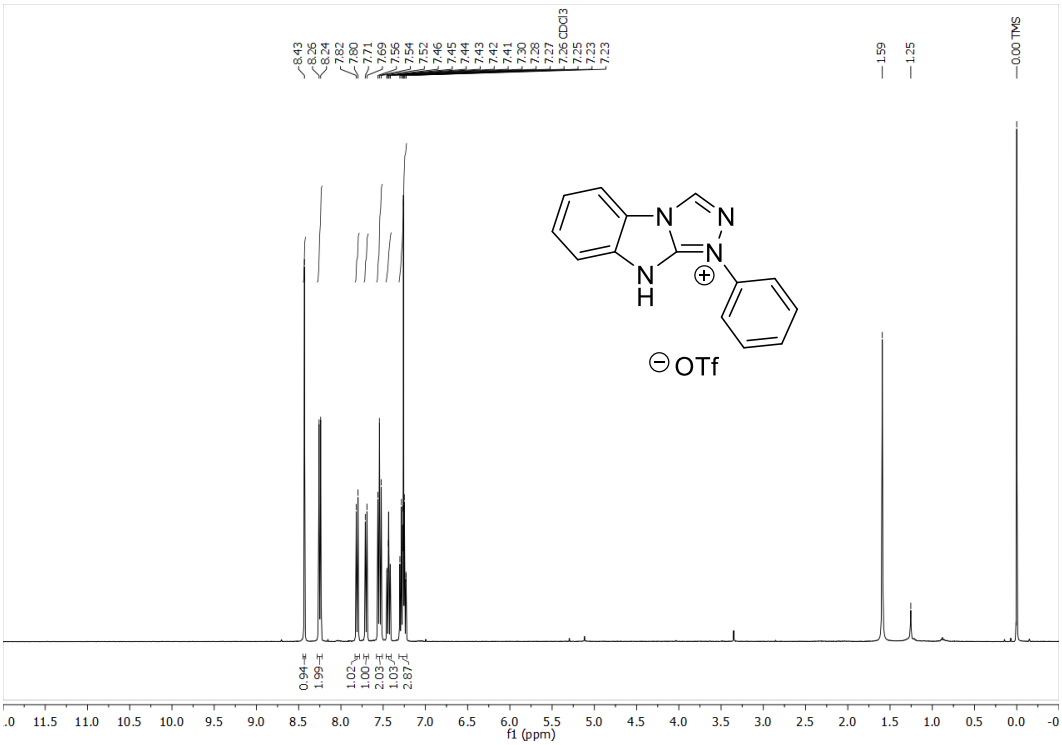

Figure E051: ^{1}H NMR spectrum of 1-phenyl-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (**12q**) (400 MHz, $CDCl_3$, 298 K).

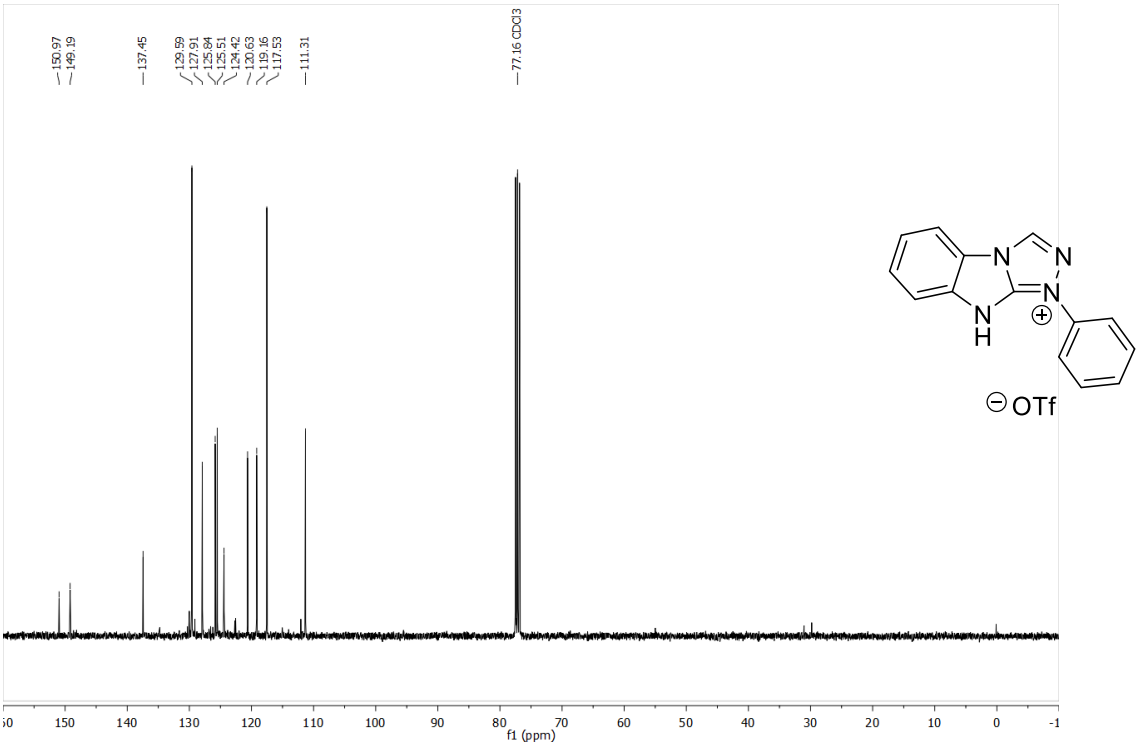

Figure E052: ^{13}C NMR spectrum of 1-phenyl-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (**12q**) (101 MHz, $CDCl_3$, 298 K).

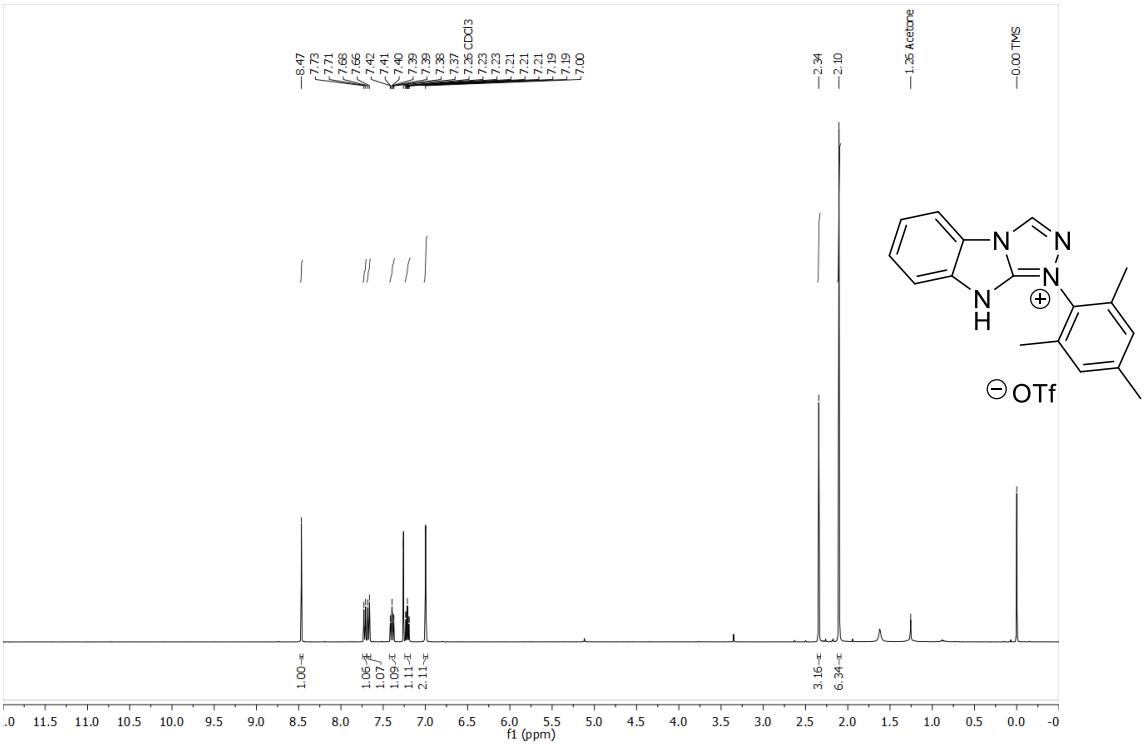

Figure E053: ^{1}H NMR spectrum of 1-mesityl-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (**12r**) (400 MHz, $CDCl_3$, 298 K).

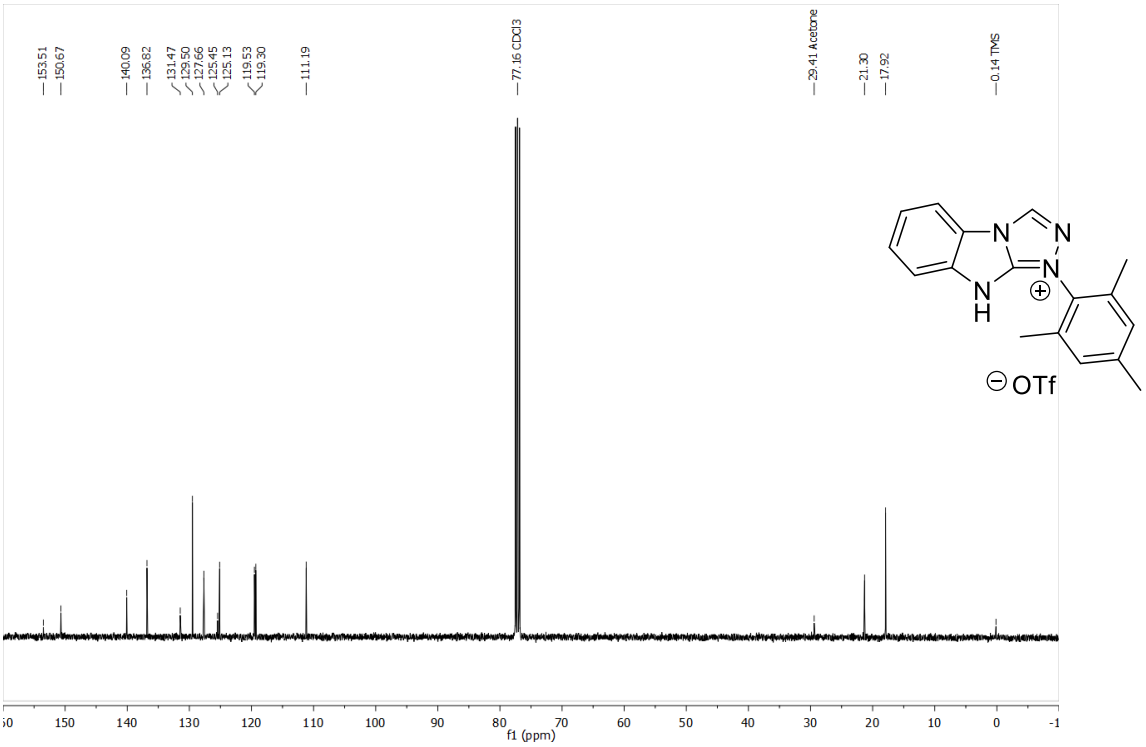

Figure E054: ^{13}C NMR spectrum of 1-mesityl-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (**12r**) (101 MHz, $CDCl_3$, 298 K).

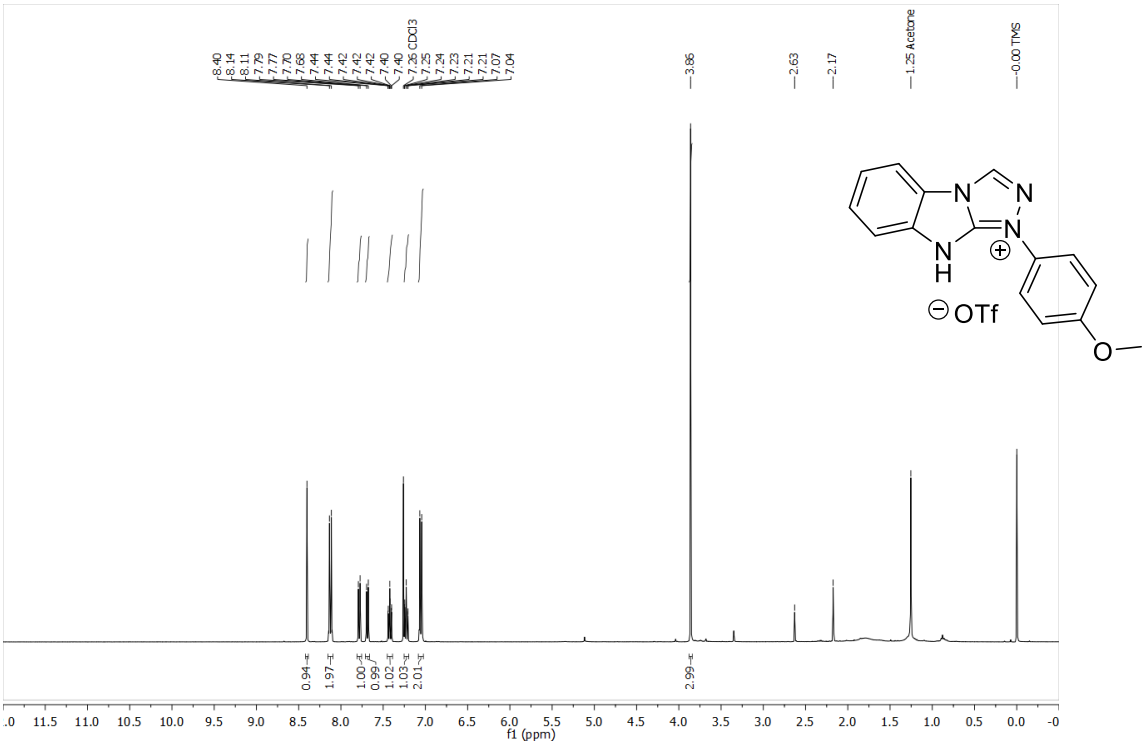

Figure E055: ^{1}H NMR spectrum of 1-(4-methoxyphenyl)-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (**12s**) (400 MHz, $CDCl_3$, 298 K).

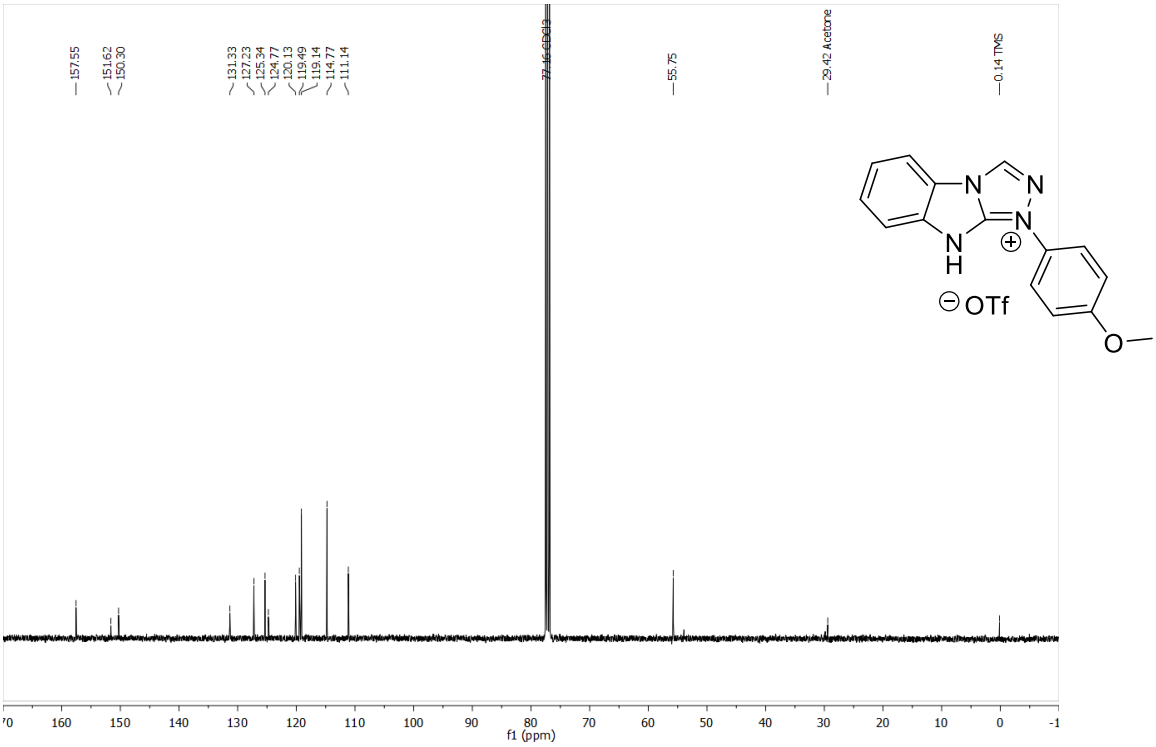

Figure E056: ^{13}C NMR spectrum of 1-(4-methoxyphenyl)-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (**12s**) (101 MHz, $CDCl_3$, 298 K).

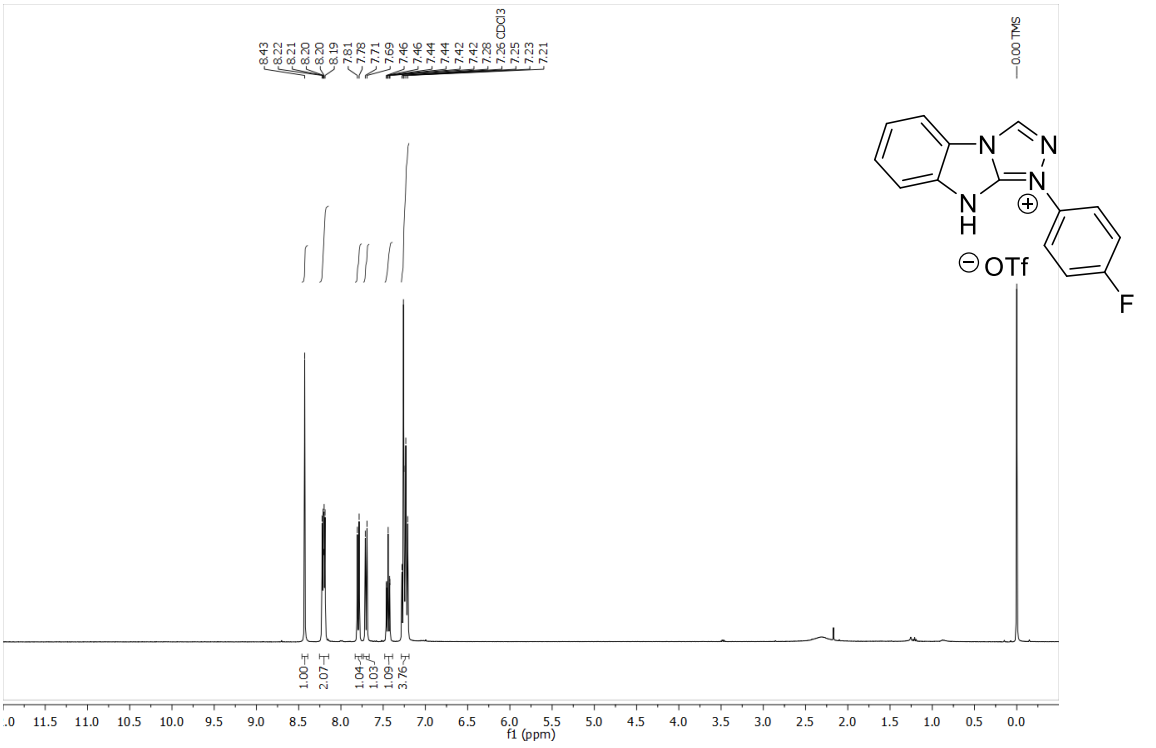

Figure E057: ^{1}H NMR spectrum of 1-(4-fluorophenyl)-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (**12t**) (400 MHz, $CDCl_3$, 298 K).

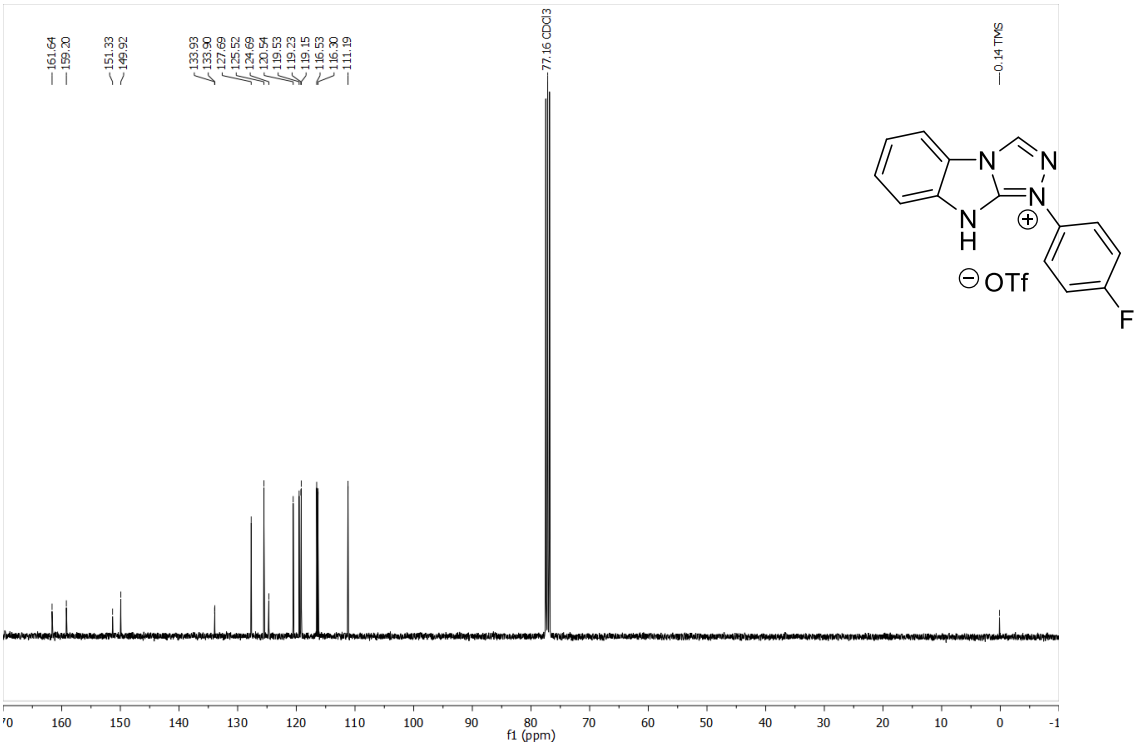

Figure E058: ^{13}C NMR spectrum of 1-(4-fluorophenyl)-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (**12t**) (101 MHz, $CDCl_3$, 298 K).

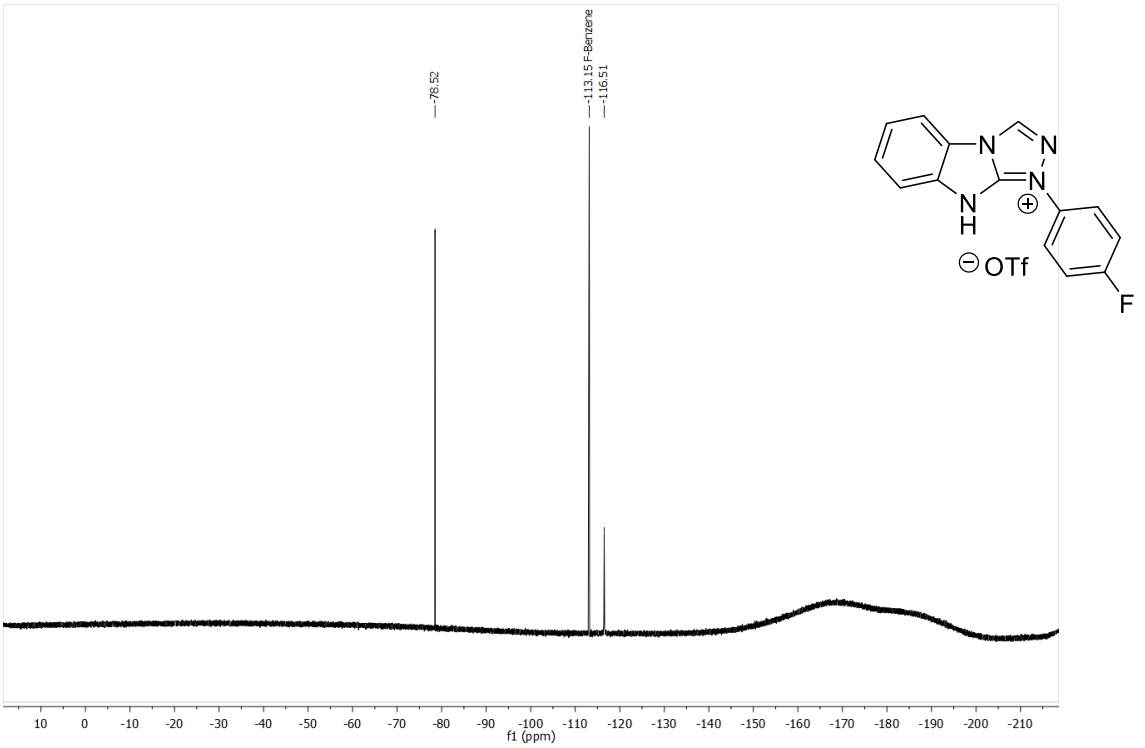

Figure E059: ^{19}F NMR spectrum of 1-(4-fluorophenyl)-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (**12t**) (376 MHz, $CDCl_3$, 298 K).

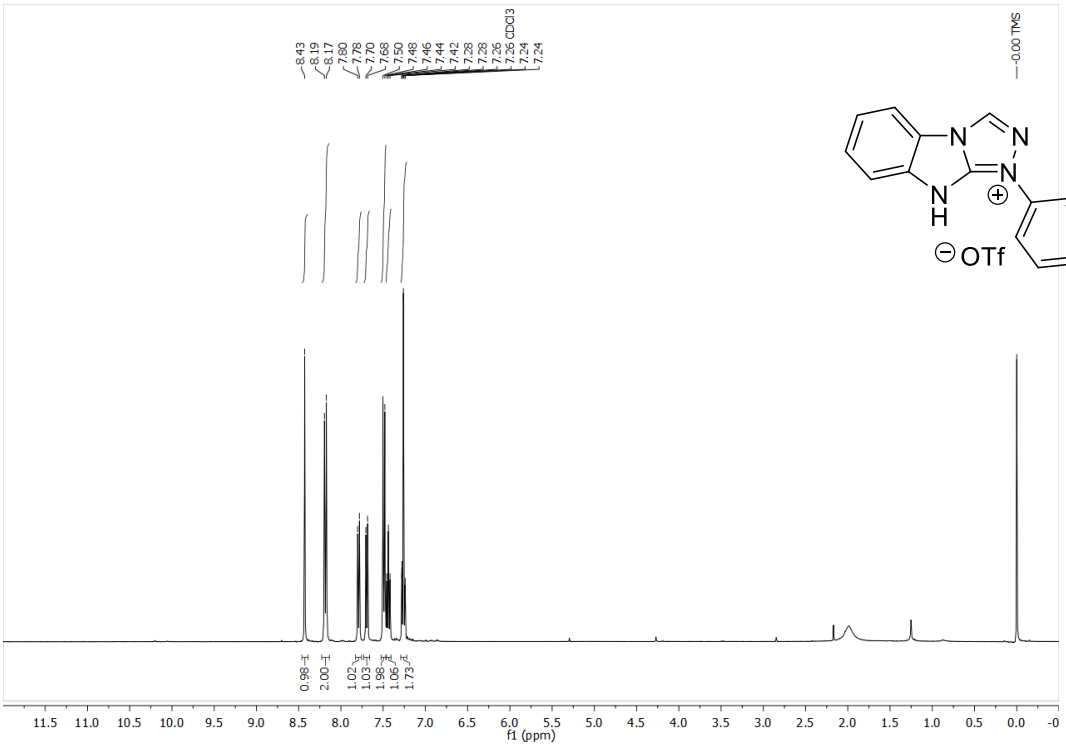

Figure E060: ^{1}H NMR spectrum of 1-(4-*c*hlorophenyl)-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (**12u**) (400 MHz, $CDCl_3$, 298 K).

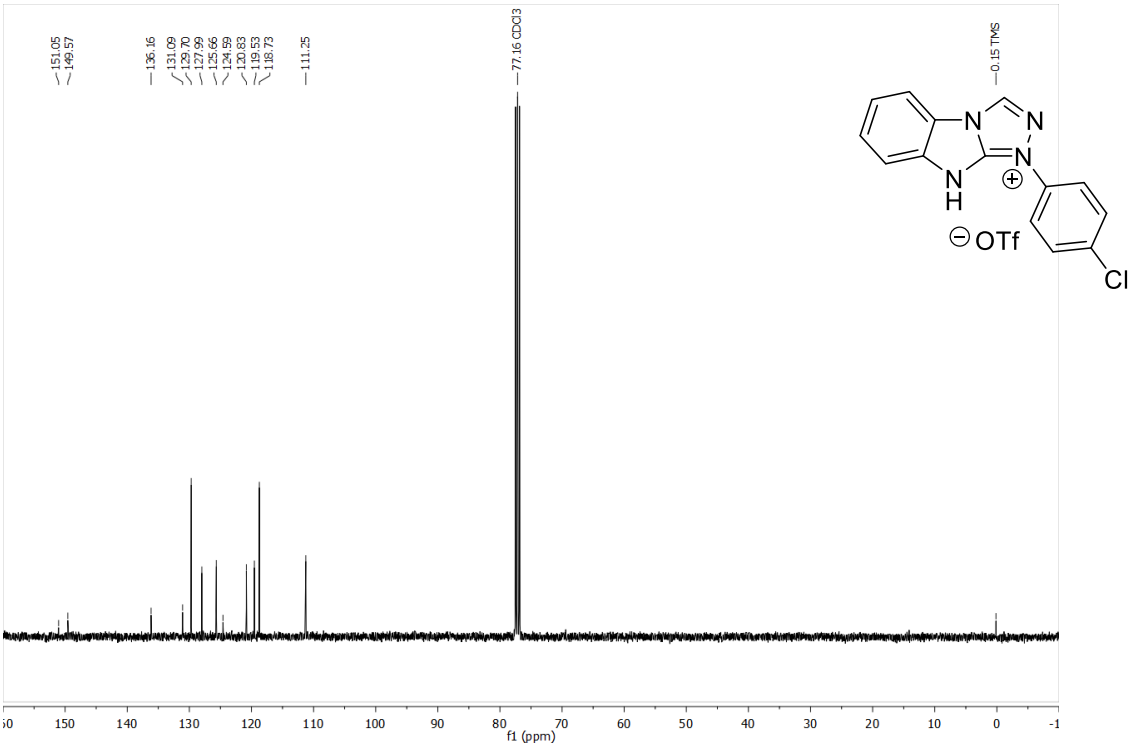

Figure E061: ^{13}C NMR spectrum of 1-(4-*c*hlorophenyl)-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (**12u**) (101 MHz, $CDCl_3$, 298 K).

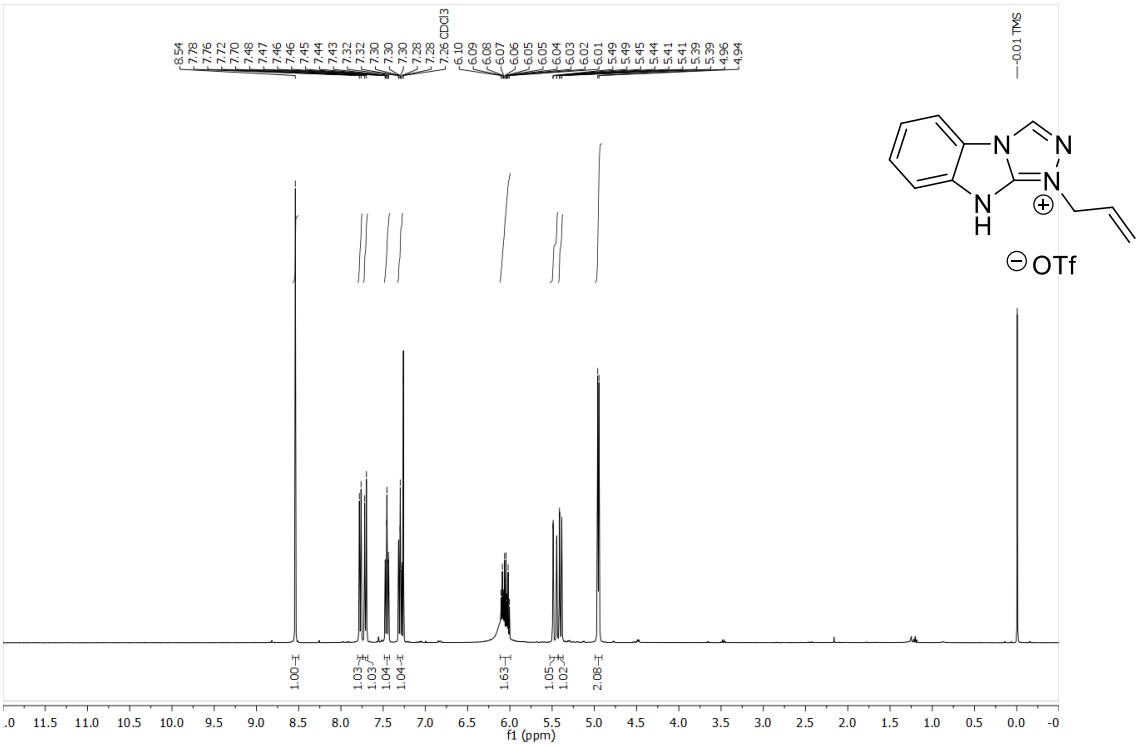

Figure S62: ^{1}H NMR spectrum of 1-allyl-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (**12v**) (400 MHz, $CDCl_3$, 298 K).

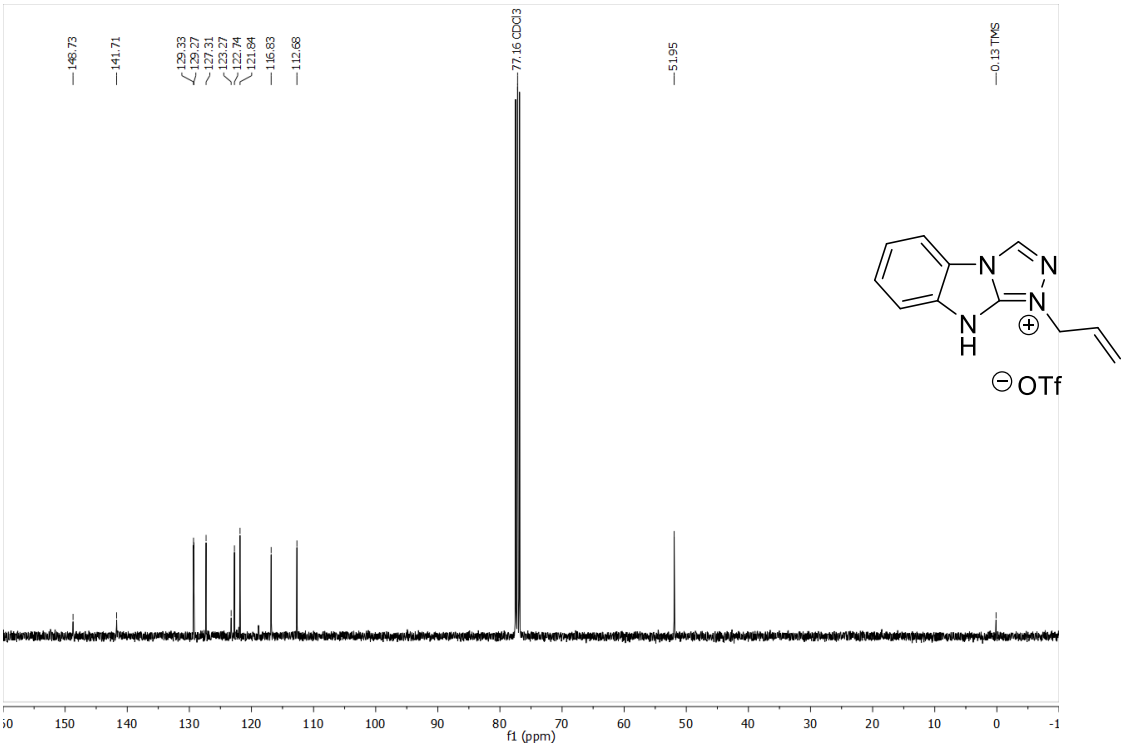

Figure E063: ^{13}C NMR spectrum of 1-allyl-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (**12v**) (101 MHz, $CDCl_3$, 298 K).

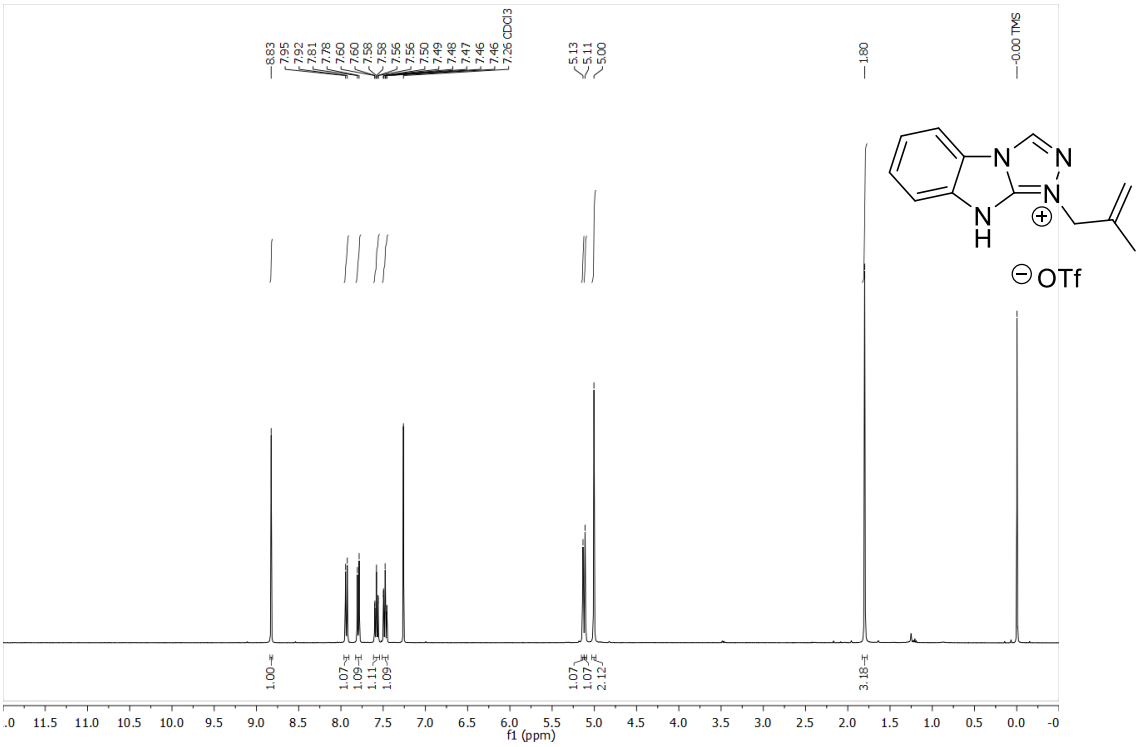

Figure E064: ^{1}H NMR spectrum of 1-(2-methylallyl)-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (**12w**) (400 MHz, $CDCl_3$, 298 K).

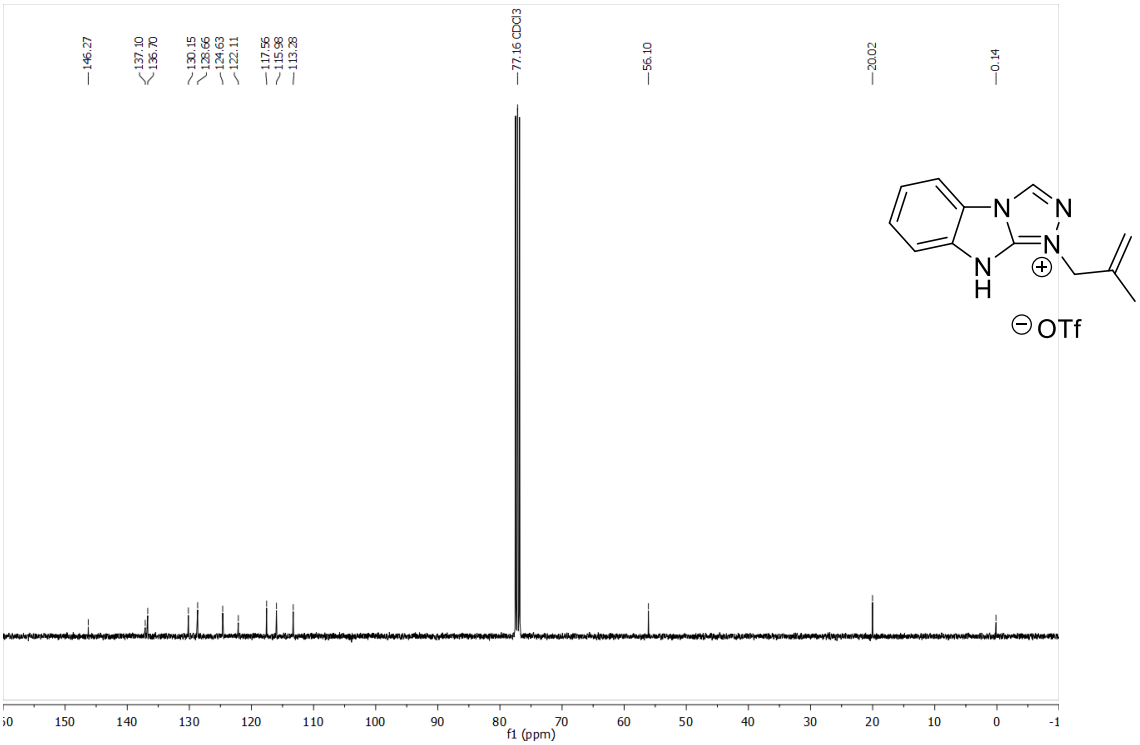

Figure E065: ^{13}C NMR spectrum of 1-(2-methylallyl)-9*H*-benzo[4,5]imidazo[2,1-*c*][1,2,4]triazol-1-ium trifluoromethanesulfonate (**12w**) (101 MHz, $CDCl_3$, 298 K).

VITA

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Doctor of Philosophy

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Biographical:

Education:

Completed the requirements for the Doctor of Philosophy/Education in Chemistry at Oklahoma State University, Stillwater, Oklahoma, in May 2021.

Completed the requirements for the Bachelor of Science/Arts in Chemistry at Nicholls State University, Thibodaux, Louisiana, in 2016.

Experience:

Developed synthetic methodologies for the synthesis of 1,2,4-triazoles within larger organic frameworks for synthetic and biological applications.
Skills: NMR, GCMS, LCMS, UV-Vis, FT-IR, organic purification.

Graduate Teaching Assistant - Oklahoma State University: 2016-2021

Professional Memberships:

American Chemical Society, Alpha Lambda Delta, Phi Eta Sigma, Phi Kappa Phi