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# Divergent Mechanisms of the Banert Cascade with Propargyl Azides

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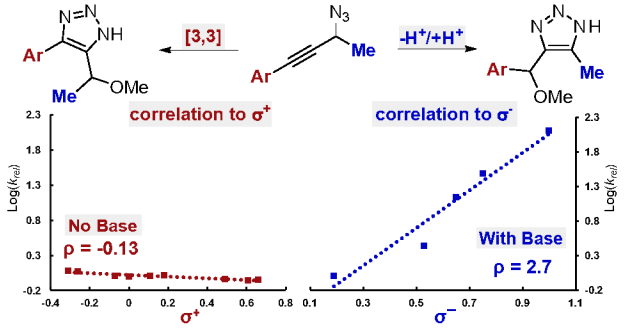
*Supporting Information Placeholder*

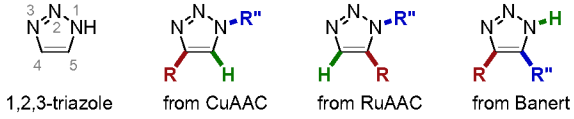



**ABSTRACT:** Triazoles are privileged heterocycles for a variety of applications. The synthesis of 1*H*-triazoles can be accomplished by the Banert cascade from propargylic azides. Depending on the substrate and conditions, the Banert cascade can proceed by either a sigmatropic or prototropic mechanism. This report describes the first detailed kinetic analysis of the Banert cascade proceeding by both pathways including substituent effects and KIE. The analysis identified the inflection point in the divergent pathways, allowing future work to predict which Banert products are accessible.

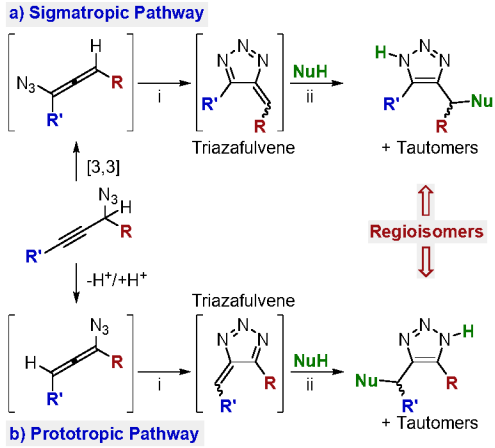
## Introduction

The triazole heterocycle is a common motif found in a wide variety of materials and biologically active molecules.[1–6] The triazole ring is recognized as an amide bond surrogate and an effective peptidomimetic.[7] Alternatively, triazole linked polysaccharides are known to possess a variety of desirable functional properties.[8] The most common synthesis of 1,2,3-triazoles is via the copper-catalyzed alkyne-azide cycloaddition (CuAAC) reaction.[9–12] The major triazole product of a CuAAC reaction is substituted at the 1 and 4 positions (Figure 1). Typically, CuAAC is ineffective at directly affording triazole products with a carbon substituent at the 5 position because the mechanism is proposed to proceed through a copper acetylide complex.[13–15] Although exceptions have been reported with specifically functionalized alkynes.[16–19] Alternatively, the ruthenium-catalyzed alkyne-azide cycloaddition (RuAAC) results in an isomeric 1,5-disubstituted 1,2,3-triazole (Figure 1).[20,21] Therefore, CuAAC and RuAAC reactions are considered complementary. However, the synthesis of 1*H*-triazoles with substituents at the 4 and 5 positions is much less straightforward.[22–28] Conceptually, a 1*H*-triazole may be more analogous to a native peptide due to the presence of both a hydrogen bond donor and acceptor atoms and because it can adopt tautomeric structures.[29] One potentially efficient 1*H*-triazole synthesis is via the Banert cascade (Figure 1 and Scheme 1).[30,31] The Banert cascade has been used for this purpose in several synthetic contexts.[32–43]

**Figure 1.** Isomeric Triazoles and Corresponding Synthesis




**Scheme 1.** Divergent Mechanisms of the Banert Cascade




Banert reported a synthesis of 1*H*-triazoles in 1989 that arose from propargylic azides (Scheme 1).[30] Initially, a sigmatropic cascade was reported that proceeds through an initial [3,3] rearrangement, resulting in an allenyl azide (Scheme 1a).[44,45] Banert found that the rate of electrocyclization (step i, Scheme 1) of allenyl azides could be fit to the Taft equation.[45] This

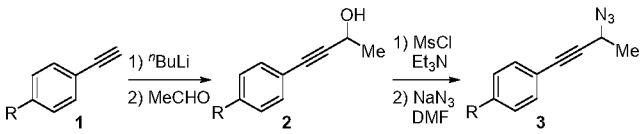
sigmatropic reaction is reminiscent of the Winstein rearrangement, which is known for allylic azides.[46–48] In the Banert cascade, the allenyl azide is thought to undergo a rapid electrocyclization to generate a triazafulvene (step i).[45] The triazafulvene is highly electrophilic, similar to an *o*-quinone methide, and can polymerize, be trapped by solvent, or captured by another nucleophile (step ii).[31,49] Shortly after the initial report, Banert disclosed that a prototropic pathway could be mediated by base (Scheme 1b).[50] Interestingly, this process provides a regioisomeric triazole from the same starting material (Scheme 1a vs 1b).

Due to our ongoing interest in triazole synthesis[51,52] and allylic azides,[53–55] we were interested in investigating the reactivity of propargylic azides in the Banert cascade. We endeavored to quantify how various substituents would affect the rate of rearrangement and to understand the prototropic vs sigmatropic dichotomy. Reported herein is a detailed kinetic study of substituted 1-aryl-3-azido-1-butynes, which identified the break point in the divergent mechanisms.

## Results and Discussion

Our study began with the synthesis of the requisite azide substrates (Scheme 2), which was accomplished from commercially available aryl-acetylenes **1a-i**. Lithiation with $^n$BuLi and subsequent addition to acetaldehyde afforded propargylic alcohols **2a-i**. Derivatization was accomplished with MsCl and $Et_3N$ followed by nucleophilic substitution with $NaN_3$. This afforded propargylic azides **3a-i**, which were stable to silica gel purification and prolonged storage at -20 °C.

**Scheme 2.** Synthesis of Propargylic Azides



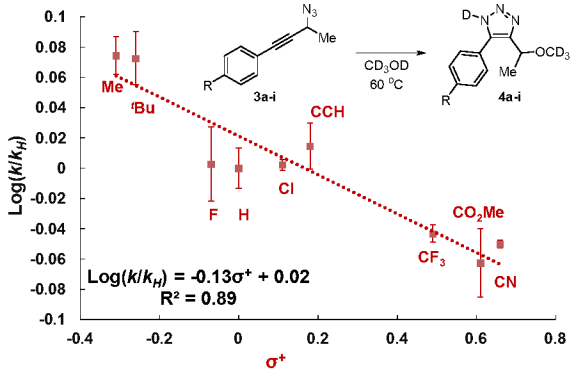

| | | | |
|---|---|---|---|
| R = Me, | **1a** | 74%, **2a** | 88%, **3a** |
| $^t$Bu, | **1b** | 59%, **2b** | 83%, **3b** |
| H, | **1c** | 64%, **2c** | 81%, **3c** |
| F, | **1d** | 59%, **2d** | 85%, **3d** |
| Cl, | **1e** | 80%, **2e** | 87%, **3e** |
| CCH, | **1f** | 56%, **2f** | 61%, **3f** |
| $CF_3$, | **1g** | 96%, **2g** | 79%, **3g** |
| $CO_2Me$, | **1h** | 51%, **2h** | 78%, **3h** |
| CN, | **1i** | 67%, **2i** | 72%, **3i** |

To investigate the Banert cascade under sigmatropic conditions, azides **3a** – **3i** were dissolved in MeOH and heated to 60 °C for 24 h, which resulted in near quantitative formation of triazoles **4a** – **4i** (see supporting information for details). The same reaction was conducted in MeOD and monitored by $^1$H NMR using trimethoxybenzene as an internal standard. The reaction time course was fit using Copasi software[56] for a simple, single step, first order reaction (azide **3** to triazole **4**). This simplified kinetic model for the Banert cascade provided a satisfactory fit. Alternatively the conversion of azides **3a** – **3i** could be fit using the classical linear transform (ln([**3**]/[**3**$_0$]) vs t). Both methods provided similar values for the rate constant (e.g. for **3a** to **4a** the Copasi fit was 1.48 x $10^{-4}$ sec$^{-1}$ and the linear transform was 1.23 x $10^{-4}$ sec$^{-1}$). The ability to use a simplified kinetic model for the complex cascade process is consistent with Banert's observation that there is minimal buildup of allenyl azide during the reaction.[45] For the azides investigated here, neither the allenyl azide nor the triazafulvene intermediate were directly observed as an intermediate by $^1$H NMR. This is consistent with a computational model of this cascade which predicts a rate determining barrier for the initial sigmatropic process (Scheme 1, [3,3]) and a fast electrocyclization (Scheme 1a, step i).[57]

For a series of azides **3a** – **3i**, the rate of the sigmatropic Banert cascade could be correlated to the Hammett values σ ($R^2$ = 0.86, ρ = -0.15), $\sigma^+$ ($R^2$ = 0.89, ρ = -0.13), and $\sigma^-$ ($R^2$ = 0.69, ρ = -0.09).[58] The best correlation was to $\sigma^+$ (Figure 2), which is consistent with prior observations that the rate of the Winstein rearrangement is slightly accelerated with electron donating groups.[46,48,53] It should be noted that the ρ value is quite small (-0.13), which indicates that this process is largely unaffected by substituent effects ($k_{rel}$ for 4-Me vs 4-CN is less than 1.5). This is loosely consistent with the broad substrate scope previously reported for the sigmatropic Banert cascade.[30,31,49]

Having determined parameters for the sigmatropic pathway, the prototropic pathway was investigated. Azides **3a** - **3i** were heated to 60 °C under basic conditions (10 equiv of NaOMe in MeOH). Unlike the sigmatropic reaction, the prototropic reaction showed a striking qualitative dependence on the aryl substituent. For azides **3a** - **3d**, the prototropic product was not observed, likely because the sigmatropic pathway was faster, and only triazoles **4a** - **4d** were isolated. On the other hand, azide **3i** produced only triazole **5i** (R = CN) in high yield via the prototropic pathway.

**Figure 2.** Hammett Correlation for Sigmatropic Cascade



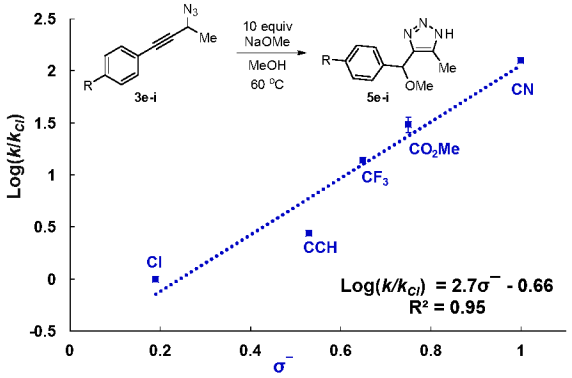

Plot of Log($k/k_H$) vs $\sigma^+$ for substituent effects on the sigmatropic Banert cascade of azides **3a**–**3i** in MeOH at 60 °C. Rates were determined by $^1$H NMR spectroscopy and measured in duplicate. The average of two replicates is shown. The error bar reflects the difference between the two trials.

Given the qualitative differences observed, the reaction was queried by conducting the cascade of azide **3f** at different concentrations. The product ratio of triazoles **5f**:**4f** was determined. The **5f**:**4f** ratio was taken as $k_{rel}$ for the prototropic vs sigmatropic pathways, which demonstrated a first order dependence on the concentration of NaOMe (see supporting information). This prompted a detailed kinetic analysis. A quantitative assay was established by HPLC-UV to monitor the reaction progress. Attempts at using $^1$H NMR analysis, as was done for the sigmatropic reaction, did not afford high quality data. A number of factors complicated the $^1$H NMR analysis including partial triazole ionization under basic conditions (signal broadening) and the presence of adventitious water, which could trap the cascade competitively with methanol. The HPLC assay was therefore found to be more reliable. The rate of the reaction for azide **3g** to triazole **4g** was determined by

both methods and only a minimal difference was observed (See Table S1). The reaction conditions used a ten-fold excess of NaOMe relative to the azide substrate to ensure pseudo-first order reactions at 60 °C. The reaction time course data was fit using Copasi software for a simple kinetic model for parallel first order reactions (azide **3** to triazole **4** and azide **3** to triazole **5**), which provided $k_{obs}$ for the prototropic pathway. The conversion of azide **3** could also be fit using the classical linear transform (ln([**3**]/[**3**$_0$]) vs t), providing the sum of the two rates.

The rate of the prototropic Banert cascade with azides **3e – 3i** could be correlated to the Hammett values σ ($R^2$ = 0.87, ρ = 4.1), $\sigma^+$ ($R^2$ = 0.85, ρ = 3.1), and $\sigma^-$ ($R^2$ = 0.95, ρ = 2.7). The best correlation was to $\sigma^-$ (Figure 3) and the ρ value of 2.7 is consistent with an anionic intermediate, as would be expected for deprotonation by NaOMe. The modest correlation for the formation of triazole **5f** may be due to the competing acidity of the terminal CC-H bond. The difference in Hammett value correlation and ρ value for the sigmatropic and prototropic pathways clearly indicate divergent mechanisms for these competing processes (Figure 2 vs Figure 3).

**Figure 3.** Hammett Correlation for the Prototropic Cascade



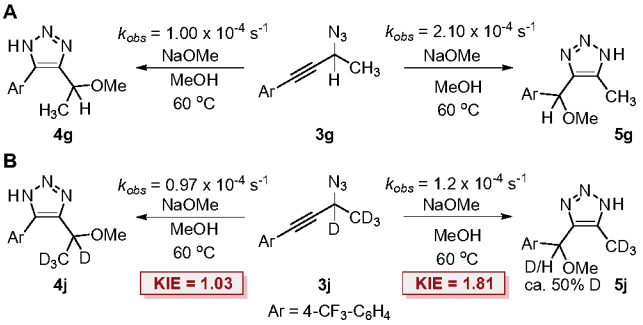

Plot of Log($k/k_{Cl}$) vs $\sigma^-$ for substituent effects on the prototropic Banert cascade of azides **3e** – **3i** in MeOH at 60 °C. Rates were measured by HPLC-UV and measured in duplicate. The average of two replicates is shown. The error bar reflects the difference between the two trials. For error bars not visible, the difference was smaller than the point marker.

To substantiate the observed divergence in mechanism, a deuterated substrate (**3j**) was prepared from tetradeutero-acetaldehyde to measure a kinetic isotope effect (KIE, see experimental section for synthesis). The reaction with azide **3j** could be compared to the cascade with azide **3g** (Scheme 3). The formation of both triazoles was monitored simultaneously in the presence of NaOMe by HPLC-UV. The sigmatropic reaction (azides **3** to triazoles **4**) proceeded with a minimal KIE = 1.03, which is likely within error of unity based on the HPLC assay. The α-azido deuterium label remained intact in the product as well. The observed KIE is consistent with a sigmatropic process for the formation of triazoles **4**, where no C-H bond breaking/making is required. However, a distinct primary KIE = 1.81 was observed for the prototropic cascade (azides **3** to triazoles **5**). Furthermore, ca. 50% of the α-azido deuterium label was washed out during the formation of triazole **5j**. Both of these observations are expected in the prototropic reaction where the α-C-H/D bond is broken.

## Conclusion

This study has provided definitive evidence that the Banert cascade can proceed via two divergent mechanisms. Both processes show distinct correlations to either the Hammett value $\sigma^+$ or $\sigma^-$ and these correlations provide ρ values of opposite sign. Furthermore, the sigmatropic reaction shows a minimal KIE whereas the prototropic reaction shows a primary KIE. Significantly, a 4-Cl-$C_6H_4$ group defines the inflection point in the two mechanisms, which can be used for predictive purposes to identify substrates that should be susceptible to the prototropic mechanism.

**Scheme 3.** Kinetic Isotope Effect for Banert Cascades




## Experimental Section

**Azide Safety.** Azides are known to be high energy materials and explosions have been reported when working with azides.[59] In the course of this work, no issues were encountered. All of the azides synthesized in this report have C/N ratios equal to or above the recommended guideline of 3. Precautionary safety shields were used for all reactions using or producing more than 1 mmol of azide. Safety shields were used both in the fume hood and during rotary evaporation. All waste and aqueous solution which could be contaminated with azide were kept in individually labeled containers and were kept STRICTLY free of acid to avoid the accidental production on $HN_3$ – DO NOT use aqueous HCl during work up of any of the reactions reported herein. Further reading on azide safety is available.[60,61]

**General Methods**. All reactions conducted at elevated temperature used aluminum heating blocks with magnetic stirrings (500 rpm). Reported temperatures were based on an external thermal couple. All commercially available chemicals were used without further purification. Dry tetrahydrofuran anddimethylformamide were obtained from a commercial solvent system utilizing activated alumina columns under a positive pressure of argon. Thin-layer chromatography (TLC) was used for monitoring reaction progress. Visualization was conducted by using UV light, $KMnO_4$, or PMA stains. Organic solutions were concentrated using rotary evaporator under reduced pressure at or below 40 ˚C. Flash chromatography was performed on a Teledyne Isco CombiFlash Rf system utilizing normal phase pre-column load cartridges and gold high performance columns. All proton ($^1$H) nuclear magnetic resonance spectra were recorded at 400 MHz or 500 MHz. All carbon ($^{13}$C) nuclear magnetic resonance spectra were recorded at 100 MHz or 125 MHz. The fluorine ($^{19}$F) nuclear magnetic resonance spectra was recorded at 376 or 470 MHz with proton decoupling. Chemical shifts are expressed in parts per million and are referenced to residual solvent ($CDCl_3$: 7.27 ppm), to the central carbon in the NMR solvent ($CDCl_3$: 77.0 ppm). Data is presented as follows: chemical shift, multiplicity (s = singlet, d

= doublet, ad = apparent doublet – para disubstituted pattern, t = triplet, q = quartet and m = multiplet), integration, and coupling constant in Hertz (Hz). Infrared (IR) spectra were taken in a Nicolet Nexus 670 FT-IR with salt plates. IR spectra were reported in $cm^{-1}$.

*4-(p-tolyl)but-3-yn-2-ol* (**2a**). A procedure was adapted from a known method.[62] To a solution of 4-ethynyltoulene **1a** (1.31 mL, 10.3 mmol) in THF (30 mL) cooled in an ice bath, *n*-butyllithium (5.2 mL, 2.5 M in hexanes, 13 mmol) was added dropwise. After 30 min, acetaldehyde (0.8 mL, 14 mmol) was added dropwise, and the ice bath was removed. After 30 min, the reaction mixture was poured onto $NH_4Cl$ (15 mL, sat. aq.). The resulting mixture was extracted with EtOAc (3 x 15 mL). The combined organic phases were washed with brine, dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Purification by column chromatography (0-40% EtOAc/hexanes) afforded alcohol **2a** (850 mg, 74%) as a yellow oil. Characterization data for this compound has been reported.[63] An image of the $^1H$ NMR spectrum is supplied in the supporting information.

*4-(4-(tert-butyl)phenyl)but-3-yn-2-ol* (**2b**). Following the procedure above for compound **2a** using 4-*tert*-butylethynylbenzene **1b**, the product (252 mg, 59%) was isolated as a colorless solid: $^1H$ NMR (500 MHz; $CDCl_3$) δ 7.38 (d, $J$ = 8.6 Hz, 2H), 7.35 (d, $J$ = 8.6 Hz, 2H), 4.78 (q, $J$ = 6.6 Hz, 1H), 1.93 (br, 1H), 1.57 (d, $J$ = 6.6 Hz, 3H), 1.33 (s, 9H); $^{13}C\{^1H\}$ NMR (125 MHz; $CDCl_3$) δ 151.7, 131.4, 125.3, 119.5, 90.3, 84.1, 58.9, 34.8, 31.2, 24.5; IR (NaCl, thin film, $cm^{-1}$) 3286, 2960, 2902, 2886, 2250, 1505, 1365, 1097; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{14}H_{18}NaO^+$ 225.1250, found 225.1243.

*4-(4-(tert-butyl)phenyl)but-3-yn-2-ol* (**2c**). Following the procedure above for compound **2a** using phenylacetylene **1c**, the product (415 mg, 64%) was isolated as a yellow oil. Characterization data for this compound has been reported.[62] An image of the $^1H$ NMR spectrum is supplied in the supporting information.

*4-(4-fluorophenyl)but-3-yn-2-ol* (**2d**). Following the procedure above for compound **2a** using 4-fluorophenylacetylene **1d**, the product (481 mg, 59%) was isolated as a yellow oil. Characterization data for this compound has been reported.[62] An image of the $^1H$ NMR spectrum is supplied in the supporting information.

*4-(4-chlorophenyl)but-3-yn-2-ol* (**2e**). Following the procedure above for compound **2a** using (4-chlorophenyl)acetylene **1e**, the product (722 mg, 80%) was isolated as a colorless solid. Characterization data for this compound has been reported.[64] An image of the $^1H$ NMR spectrum is supplied in the supporting information.

*4-(4-ethynylphenyl)but-3-yn-2-ol* (**2f**). The procedure above for compound **2a** was modified by cooling a solution of 1,4-diethynylbenzene **1f** (1.26 g, 9.96 mmol) in THF to – 78 °C prior to the addition of $^n$BuLi (4.4 mL, 2.5 M in hexanes, 11 mmol) and acetaldehyde (236 mg, 5.37 mmol). After 2 h at –78 °C, the reaction was quenched. The product (513 mg, 56%) was isolated as a pale yellow solid: $^1H$ NMR (500 MHz; $CDCl_3$) δ 7.43 (d, $J$ = 7.7 Hz, 2H), 7.38 (d, $J$ = 7.7 Hz, 2H), 4.78 (q, $J$ = 6.6 Hz, 1H), 3.19 (s, 1H), 2.38 (br, 1H), 1.57 (d, $J$ = 6.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (125 MHz; $CDCl_3$) δ 132.0, 131.5, 123.1, 122.0, 93.0, 83.4, 83.2, 79.0, 58.7, 24.3; IR (NaCl, thin film, $cm^{-1}$) 3280, 2984, 2934, 2229, 1498, 1265, 1105, 1034; HRMS (EI-TOF) *m/z* $[M]^+$ calcd for $C_{12}H_{10}O^+$ 170.0726, found 170.0709.

*4-(4-(trifluoromethyl)phenyl)but-3-yn-2-ol* (**2g**). Following the procedure above for compound **2a** using 4-trifloromethylphenylacetylene **1g**, the product (987 mg, 96%) was isolated as a yellow oil. Characterization data for this compound has been reported.[65] An image of the $^1H$ NMR spectrum is supplied in the supporting information.

*methyl 4-(3-hydroxybut-1-yn-1-yl)benzoate* (**2h**). The procedure above for compound **2a** was modified by cooling a solution of methyl 4-ethynylbenzoate **1h** (498 mg, 3.1 mmol) in THF to – 78 °C prior to addition of $^n$BuLi (1.4 mL, 2.5 M in hexanes, 3.4 mmol) and acetaldehyde (0.21 mL, 3.7 mmol). After 1.5h at – 78 °C, the reaction was quenched. The product (322 mg, 51%) was isolated as a pale yellow solid. Characterization data for this compound has been reported.[63] An image of the $^1H$ NMR spectrum is supplied in the supporting information.

*4-(3-hydroxybut-1-yn-1-yl)benzonitrile* (**2i**). The procedure above for compound **2a** was modified by cooling a solution of 4-ethynylbenzonitrile **1i** (640 mg, 5.03 mmol) in THF to – 78 °C prior to addition of $^n$BuLi (2.2 mL, 2.5 M in hexanes, 5.5 mmol) and acetaldehyde (0.34 mL, 6.0 mmol). After 2h at – 78 °C, the reaction was quenched. The product (573 mg, 67%) was isolated as a pale yellow solid. Characterization data for this compound has been reported.[63] An image of the $^1H$ NMR spectrum is supplied in the supporting information.

*4-(4-(trifluoromethyl)phenyl)but-3-yn-1,1,1,2-$d_4$-2-ol* (**2j**). Following the procedure above for compound **2a** using 4-trifloromethylphenylacetylene **1g** and $d_4$-acetaldehyde, product (814 mg, 75%) was isolated as a yellow oil. Characterization data for the unlabeled compound has been reported:[65] $^1H$ NMR (500 MHz; $CDCl_3$) δ 7.59 (d, $J$ = 8.6 Hz, 2H), 7.55 (d, $J$ = 8.6 Hz, 2H), 1.89 (br, 1H); $^{13}C\{^1H\}$ NMR (125 MHz; $CDCl_3$) δ 131.8, 130.1 (q, $J_{C\text{-}F}$ = 32.8 Hz), 126.4 (q, $J_{C\text{-}F}$ = 1.8 Hz), 125.2 (q, $J_{C\text{-}F}$ = 3.7 Hz), 123.8 (q, $J_{C\text{-}F}$ = 272.1 Hz), 93.3, 82.7. (Note that no attempt was made to detect multiples featuring a $J_{C\text{-}D}$ coupling, which were too broad to readily identify), $^2H$ NMR (77 MHz; $CDCl_3$) δ 4.74 (s, 1D), 1.52 (s, 3D); $^{19}F\{1H\}$ NMR (376 MHz; $CDCl_3$) δ -62.9; IR (NaCl, thin film, $cm^{-1}$) 3328, 2934, 2239, 1616, 1325, 1170, 1126; HRMS (EI-TOF) *m/z* $[M]^+$ calcd for $C_{11}H_5D_4F_3O^+$ 218.0851, found 218.0853.

*1-(3-azidobut-1-yn-1-yl)-4-methylbenzene* (**3a**). A solution of alcohol **2a** (650 mg, 4.0 mmol) in diethyl ether (8 mL) was cooled in an ice bath. Triethylamine (1.1 mL, 8.0 mmol) was added, followed by dropwise addition of methanesulfonyl chloride (0.40 mL, 4.8 mmol). After 5 min, the mixture was poured onto $NH_4Cl$ (15 mL, sat. aq.). The resulting mixture was extracted with diethyl ether (3 x 15 mL). The combined organic phases were washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The crude mesylate (910 mg) was immediately used without further purification. The residue was dissolved in DMF (4 mL). Sodium azide (310 mg, 4.6 mmol) was added as a solid at room temperature. After 1h, the mixture was poured onto water (20 mL). The resulting mixture was extracted with EtOAc (3 x 15 mL). The combined organic phases were washed with brine, dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Purification by flash chromatography (gradient elution 0 – 20% EtOAc in hexanes) afforded the product as a pale yellow oil (650 mg, 88% over two steps): $^1H$ NMR (500 MHz; $CDCl_3$) δ 7.38 (d, $J$ = 7.9 Hz, 2H), 7.15 (d, $J$ = 7.9 Hz, 2H), 4.42 (q, $J$ = 6.8 Hz, 1H), 2.38

(s, 3H), 1.55 (d, $J$ = 6.8 Hz, 3H); $^{13}C\{^1H\}$ NMR (125 MHz; $CDCl_3$) δ 138.9, 131.8, 129.1, 118.9, 86.3, 84.9, 49.1, 21.6, 21.5; IR (NaCl, thin film, $cm^{-1}$) 3030, 2988, 2935, 2870, 2239, 2095, 1607, 1510, 1222, 1080; HRMS (EI-TOF) *m/z* $[M]^+$ calcd for $C_{11}H_{11}N_3^+$ 185.0947, found 185.0961.

*1-(3-azidobut-1-yn-1-yl)-4-(tert-butyl)benzene* (**3b**). Following the procedure above for compound **3a** using alcohol **2b**, the product (280 mg, 83%) was isolated as a yellow oil over two steps: $^1H$ NMR (500 MHz; $CDCl_3$) δ 7.44 (d, $J$ = 8.1 Hz, 2H), 7.38 (d, $J$ = 8.1 Hz, 2H), 4.43 (q, $J$ = 7.0 Hz, 1H), 1.56 (d, $J$ = 7.0 Hz, 3H), 1.35 (s, 9H); $^{13}C\{^1H\}$ NMR (125 MHz; $CDCl_3$) δ 152.1, 131.6, 125.4, 119.0, 86.3, 84.9, 49.1, 34.8, 31.2, 21.6; IR (NaCl, thin film, $cm^{-1}$) 2964, 2905, 2869, 2101, 1505, 1235, 1080; HRMS (EI-TOF) *m/z* $[M]^+$ calcd for $C_{14}H_{17}N_3^+$ 227.1417, found 227.1409; $[M - N_2]^+$ calcd for $C_{14}H_{17}N^+$ 199.1356, found 199.1349.

*1-(3-azidobut-1-yn-1-yl)-benzene* (**3c**). Following the procedure above for compound **3a** using alcohol **2c**, the product (710 mg, 81%) was isolated as a yellow oil over two steps: $^1H$ NMR (500 MHz; $CDCl_3$) δ 7.52 (d, $J$ = 7.4 Hz, 2H), 7.40-7.34 (m, 3H), 4.45 (q, $J$ = 7.0 Hz, 1H), 1.57 (d, $J$ = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (125 MHz; $CDCl_3$) δ 131.9, 128.8, 128.4, 122.0, 86.2, 85.6, 49.0, 21.6; IR (NaCl, thin film, $cm^{-1}$) 2989, 2936, 2101, 1490, 1321, 1236; HRMS (EI-TOF) *m/z* $[M]^+$ calcd for $C_{10}H_9N_3^+$ 171.0791, found 171.0794.

*1-(3-azidobut-1-yn-1-yl)-4-fluorobenzene* (**3d**). Following the procedure above for compound **3a** using alcohol **2d**, the product (220 mg, 85%) was isolated as a colorless oil over two steps: $^1H$ NMR (500 MHz; $CDCl_3$) δ 7.47 (dd, $J$ = 8.2, 5.7 Hz, 2H), 7.04 (apparent t, $J$ = 8.6 Hz, 2H), 4.42 (q, $J$ = 7.0 Hz, 1H), 1.55 (d, $J$ = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (125 MHz; $CDCl_3$) δ 162.7 (d, $J_{C\text{-}F}$ = 250.3 Hz), 133.8 (d, $J_{C\text{-}F}$ = 8.3 Hz), 118.1 (d, $J_{C\text{-}F}$ = 3.4 Hz), 115.6 (d, $J_{C\text{-}F}$ = 22.0 Hz), 85.3, 85.1, 48.9, 21.5; $^{19}F\{1H\}$ NMR (376 MHz; $CDCl_3$) δ -110.2; IR (NaCl, thin film, $cm^{-1}$) 2990, 2937, 2243, 2099, 1602, 1514, 1222, 835; HRMS (EI-TOF) *m/z* $[M]^+$ calcd for $C_{10}H_8FN_3^+$ 189.0697, found 189.0698.

*1-(3-azidobut-1-yn-1-yl)-4-chlorobenzene* (**3e**). Following the procedure above for compound **3a** using alcohol **2e**, the product (490 mg, 87%) was isolated as a colorless oil over two steps: $^1H$ NMR (500 MHz; $CDCl_3$) δ 7.41 (d, $J$ = 8.2 Hz, 2H), 7.32 (d, $J$ = 8.2 Hz, 2H), 4.42 (q, $J$ = 7.0 Hz, 1H), 1.55 (d, $J$ = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (125 MHz; $CDCl_3$) δ 134.8, 133.1, 128.7, 120.5, 86.6, 85.0, 48.9, 21.4; IR (NaCl, thin film, $cm^{-1}$) 2988, 2936, 2101, 1490, 1232, 1091, 1014, 828; HRMS (EI-TOF) *m/z* $[M]^+$ calcd for $C_{10}H_8{}^{35}ClN_3^+$ 205.0401, found 205.0398, $[M - N_2]^+$ calcd for $C_{10}H_8{}^{37}ClN^+$ 207.0372, found 207.0383.

*1-(3-azidobut-1-yn-1-yl)-4-ethynylbenzene* (**3f**). Following the procedure above for compound **3a** using alcohol **2f**, the product (116 mg, 61%) was isolated as a yellow oil over two steps: $^1H$ NMR (500 MHz; $CDCl_3$) δ 7.44 (d, $J$ = 8.0 Hz, 2H), 7.40 (d, $J$ = 8.0 Hz, 2H), 4.40 (q, $J$ = 6.9 Hz, 1H), 3.17 (s, 1H), 1.52 (d, $J$ = 6.9 Hz, 3H);$^{13}C\{^1H\}$ NMR (125 MHz; $CDCl_3$) δ 132.1, 131.8, 122.5, 122.4, 87.6, 85.5, 83.1, 79.1, 49.0, 21.4; IR (NaCl, thin film, $cm^{-1}$) 3294, 2989, 2936, 2104, 1498, 1325, 1234; HRMS (EI-TOF) *m/z* $[M]^+$ calcd for $C_{12}H_9N_3^+$ 195.0791, found 195.0785.

*1-(3-azidobut-1-yn-1-yl)-4-(trifluoromethyl)benzene* (**3g**). Following the procedure above for compound **3a** using alcohol **2g**, the product (370 mg, 79%) was isolated as a colorless oil over two steps: $^1H$ NMR (500 MHz; $CDCl_3$) δ 7.61 (d, $J$ = 8.4 Hz, 2H), 7.59 (d, $J$ = 8.4 Hz, 2H), 4.44 (q, $J$ = 6.9 Hz, 1H), 1.57 (d, $J$ = 6.9 Hz, 3H); $^{13}C\{^1H\}$ NMR (125 MHz; $CDCl_3$) δ 132.1, 130.5 (q, $J_{C\text{-}F}$ = 32.7 Hz), 125.8 (q, $J_{C\text{-}F}$ = 1.8 Hz), 125.2 (q, $J_{C\text{-}F}$ = 3.6 Hz), 123.8 (q, $J_{C\text{-}F}$ = 272.8 Hz), 88.0, 84.7, 48.8, 21.3; $^{19}F\{1H\}$ NMR (376 MHz; $CDCl_3$) δ -62.9; IR (NaCl, thin film, $cm^{-1}$) 2992, 2939, 2105, 1616, 1326, 1192, 1067; HRMS (EI-TOF) *m/z* $[M]^+$ calcd for $C_{11}H_8F_3N_3^+$ 239.0665, found 239.0668.

*methyl 4-(3-azidobut-1-yn-1-yl)benzoate* (**3h**). Following the procedure above for compound **3a** using alcohol **2h**, the product (164 mg, 78%) was isolated as a yellow oil over two steps: $^1H$ NMR (500 MHz; $CDCl_3$) δ 8.02 (d, $J$ = 8.3 Hz, 2H), 7.54 (d, $J$ = 8.3 Hz, 2H), 4.44 (q, $J$ = 6.9 Hz, 1H), 3.95 (s, 3H), 1.57 (d, $J$ = 6.9 Hz, 3H); $^{13}C\{^1H\}$ NMR (125 MHz; $CDCl_3$) δ 166.4, 131.8, 130.1, 129.5, 126.6, 88.5, 85.3, 52.3, 48.9, 21.4; IR (NaCl, thin film, $cm^{-1}$) 2991, 2952, 2102, 1725, 1276; HRMS (EI-TOF) *m/z* $[M]^+$ calcd for $C_{12}H_{11}N_3O_2^+$ 229.0846, found 229.0848.

*4-(3-azidobut-1-yn-1-yl)benzonitrile* (**3i**). Following the procedure above for compound **3a** using alcohol **2i**, the product (260 mg, 72%) was isolated as a yellow oil over two steps: $^1H$ NMR (500 MHz; $CDCl_3$) δ 7.64 (d, $J$ = 8.0 Hz, 2H), 7.56 (d, $J$ = 8.0 Hz, 2H), 4.44 (q, $J$ = 7.0 Hz, 1H), 1.56 (d, $J$ = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (125 MHz; $CDCl_3$) δ 132.4, 132.1, 126.9, 118.3, 112.2, 90.0, 84.4, 48.8, 21.2; IR (NaCl, thin film, $cm^{-1}$) 2989, 2937, 2229, 2104, 1605, 1501, 1236, 841; HRMS (EI-TOF) *m/z* $[M]^+$ calcd for $C_{11}H_8N_4^+$ 196.0743, found 196.0741.

*1-(3-azidobut-1-yn-1-yl-3,4,4,4-d$_4$)-4-(trifluoromethyl)benzene* (**3j**). Following the procedure above for compound **3a** using alcohol **2j**, the product (320 mg, 82%) was isolated as a colorless oil over two steps. The data provided here is for comparison to the unlabeled compound: $^1H$ NMR (400 MHz; $CDCl_3$) δ 7.61 (d, $J$ = 8.8 Hz, 2H), 7.59 (d, $J$ = 8.8 Hz, 2H); $^{13}C\{1H\}$ NMR (125 MHz; $CDCl_3$) δ 132.1, 130.5 (q, $J_{C\text{-}F}$ = 32.9 Hz), 125.8 (q, $J_{C\text{-}F}$ = 1.8 Hz), 125.3 (q, $J_{C\text{-}F}$ = 8.6 Hz), 123.8 (q, $J_{C\text{-}F}$ = 273.1 Hz), 87.9, 84.7. (Note that no attempt was made to detect multiples featuring a $J_{C\text{-}D}$ coupling, which were too broad to readily identify); $^2H$ NMR (61 MHz; $CDCl_3$) δ 4.38 (s, 1D), 1.50 (s, 3D); $^{19}F\{1H\}$ NMR (376 MHz; $CDCl_3$) δ -62.9; IR (NaCl, thin film, $cm^{-1}$) 2098, 1617, 1325, 1171, 1129; HRMS (EI-TOF) *m/z* $[M]^+$ calcd for $C_{11}H_4D_4F_3N_3^+$ 243.0916, found 243.0913.

**Triazole Representation**

The 1*H*-1,2,3-triazoles or NH-1,2,3-triazoles likely exist as a mixture of tautomeric structures. The structure shown for compound **4a** has been arbitrarily chosen to represent this motif throughout. For a more thorough discussion, please see a detailed study on the tautomerization.[29]

*4-(1-methoxyethyl)-5-(p-tolyl)-1H-1,2,3-triazole* (**4a**). A solution of azide **3a** (38 mg, 0.2 mmol) in MeOH (2 mL) was heated to 60 °C in a sealed 4 mL vial. After 24 h, the solution was cooled to room temperature and concentrated under reduced pressure. Purification by flash chromatography (gradient elution 40 – 100% EtOAc in hexanes) afforded the product **4a** as a colorless solid (39 mg, 91%): $^1H$ NMR (500 MHz; $CDCl_3$) δ 10.95 (br, 1H), 7.68 (d, $J$ = 8.1 Hz, 2H), 7.29 (d, $J$ = 8.1 Hz, 2H), 4.86 (q, $J$ = 6.6 Hz, 1H), 3.33 (s, 3H), 2.42 (s, 3H), 1.60 (d, $J$ = 6.6 Hz, 3H); $^{13}C\{1H\}$ NMR (125 MHz; $CDCl_3$) δ 143.8, 142.7, 138.6, 129.5, 128.1, 126.9, 71.0, 56.1, 21.3, 19.9; IR (NaCl, thin film, $cm^{-1}$) 3162, 2983, 2932, 2825, 1454, 1115, 1094, 832; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{12}H_{15}N_3NaO^+$ 240.1107, found 240.1113.

*5-(4-(tert-butyl)phenyl)-4-(1-methoxyethyl)-1H-1,2,3-triazole* (**4b**). Following the procedure above for compound **4a** using azide **3b**, the product (56 mg, 97%) was isolated as a colorless solid: $^1$H NMR (500 MHz; $CDCl_3$) δ 12.43 (br, 1H), 7.74 (d, $J$ = 8.3 Hz, 2H), 7.50 (d, $J$ = 8.3 Hz, 2H), 4.90 (q, $J$ = 6.6 Hz, 1H), 3.34 (s, 3H), 1.61 (d, $J$ = 6.6 Hz, 3H), 1.37 (s, 9H); $^{13}$C{1H} NMR (125 MHz; $CDCl_3$) δ 151.6, 143.6, 142.7, 127.9, 127.0, 125.7, 71.1, 56.1, 34.7, 31.3, 20.0; IR (NaCl, thin film, cm$^{-1}$) 3162, 2983, 2932, 2825, 1454, 1115, 1093, 823; HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{15}H_{21}N_3NaO^+$ 282.1577, found 282.1578.

*4-(1-methoxyethyl)-5-phenyl-1H-1,2,3-triazole* (**4c**). Following the procedure above for compound **4a** using azide **3c**, the product (65 mg, 99%) was isolated as a colorless solid: $^1$H NMR (500 MHz; $CDCl_3$) δ 10.90 (br, 1H), 7.78 (d, $J$ = 7.8 Hz, 2H), 7.46 (dd, $J$ = 7.8, 7.2 Hz, 2H), 7.40 (t, $J$ = 7.3 Hz, 1H), 4.89 (q, $J$ = 6.6 Hz, 1H), 3.33 (s, 3H), 1.61 (d, $J$ = 6.9 Hz, 3H); $^{13}$C{1H} NMR (125 MHz; $CDCl_3$) δ 143.8, 130.1, 128.7, 128.5, 128.3, 126.7, 71.1, 56.1, 20.0; IR (NaCl, thin film, cm$^{-1}$) 3413, 3161, 2986, 2932, 2823, 1449, 1116, 1097; HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{11}H_{13}N_3NaO^+$ 226.0951, found 226.0957.

*5-(4-fluorophenyl)-4-(1-methoxyethyl)-1H-1,2,3-triazole* (**4d**). Following the procedure above for compound **4a** using azide **3d**, the product (48 mg, 99%) was isolated as a colorless oil: $^1$H NMR (500 MHz; $CDCl_3$) δ 10.64 (br, 1H), 7.77 (dd, $J$ = 8.6, 5.6 Hz, 2H), 7.13 (apparent t, $J$ = 8.6 Hz, 2H), 4.84 (q, $J$ = 6.8 Hz, 1H), 3.32 (s, 3H), 1.58 (d, $J$ = 6.8 Hz, 3H); $^{13}$C{1H} NMR (125 MHz; $CDCl_3$) δ 162.9 (d, $J_{C\text{-}F}$ = 246.6 Hz), 130.1 (d, $J_{C\text{-}F}$ = 8.9 Hz), 128.5 (d, $J_{C\text{-}F}$ = 8.5 Hz), 126.3 (d, $J_{C\text{-}F}$ = 2.6 Hz), 115.7 (d, $J_{C\text{-}F}$ = 21.6 Hz), 115.3 (d, $J_{C\text{-}F}$ = 21.1 Hz), 71.1, 56.0, 19.8; $^{19}$F{1H} NMR (376 MHz; $CDCl_3$) δ -112.9; IR (NaCl, thin film, cm$^{-1}$) 3428, 3162, 2987, 2936, 2826, 1508, 1227, 1115, 1092; HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{11}H_{12}FN_3NaO^+$ 244.0857, found 244.0856.

*5-(4-chlorophenyl)-4-(1-methoxyethyl)-1H-1,2,3-triazole* (**4e**). Following the procedure above for compound **4a** using azide **3e**, the product (65 mg, 93%) was isolated as a pale yellow solid: $^1$H NMR (500 MHz; $CDCl_3$) δ 11.28 (br, 1H), 7.77 (d, $J$ = 8.4 Hz, 2H), 7.45 (d, $J$ = 8.4 Hz, 2H), 4.85 (q, $J$ = 6.7 Hz, 1H), 3.34 (s, 3H), 1.59 (d, $J$ = 6.7 Hz, 3H); $^{13}$C{1H} NMR (125 MHz; $CDCl_3$) δ 143.4, 143.2, 134.7, 129.5, 129.0, 128.6, 71.1, 56.1, 19.7; IR (NaCl, thin film, cm$^{-1}$) 3165, 2984, 2933, 2823, 1466, 1116, 1094, 835; HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{11}H_{12}{}^{35}ClN_3ONa^+$ 260.0561, found 260.0570, [M + Na]$^+$ calcd for $C_{11}H_{12}{}^{37}ClN_3NaO^+$ 262.0532, found 262.0533.

*5-(4-ethynylphenyl)-4-(1-methoxyethyl)-1H-1,2,3-triazole* (**4f**). Following the procedure above for compound **4a** using azide **3f**, the product (48 mg, 99%) was isolated as a pale yellow solid: $^1$H NMR (500 MHz; $CDCl_3$) δ 13.1 (br, 1H), 7.80 (d, $J$ = 7.1 Hz, 2H), 7.60 (d, $J$ = 7.8 Hz, 2H), 4.87 (q, $J$ = 6.6 Hz, 1H), 3.35 (s, 3H), 3.17 (s, 1H), 1.59 (d, $J$ = 6.6 Hz, 3H); $^{13}$C{1H} NMR (125 MHz; $CDCl_3$) δ 143.5, 143.3, 132.5, 130.6, 128.1, 122.2, 83.3, 78.3, 71.2, 56.2, 19.8; IR (NaCl, thin film, cm$^{-1}$) 3285, 2936, 1450, 1376, 1118; HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{13}H_{13}N_3NaO^+$ 250.0951, found 250.0949.

*4-(1-methoxyethyl)-5-(4-(trifluoromethyl)phenyl)-1H-1,2,3-triazole* (**4g**). Following the procedure above for compound **4a** using azide **3g**, the product (62 mg, 98%) was isolated as a colorless solid: $^1$H NMR (500 MHz; $CDCl_3$) δ 11.37 (s, 1H), 7.98 (d, $J$ = 8.0 Hz, 2H), 7.74 (d, $J$ = 8.0 Hz, 2H), 4.89 (q, $J$ = 6.6 Hz, 1H), 3.37 (s, 3H), 1.61 (d, $J$ = 6.6 Hz, 3H); $^{13}$C{1H} NMR (125 MHz; $CDCl_3$) δ 143.7, 143.4, 133.7 (q, $J_{C\text{-}F}$ = 1.6 Hz),, 130.5 (q, $J_{C\text{-}F}$ = 32.6 Hz), 128.5, 125.7 (q, $J_{C\text{-}F}$ = 3.8 Hz), 124.0 (q, $J_{C\text{-}F}$ = 272.4 Hz), 71.2, 56.2, 19.7; $^{19}$F{1H} NMR (376 MHz; $CDCl_3$) δ -62.7; IR (NaCl, thin film, cm$^{-1}$) 3163, 2988, 2934, 1622, 1326, 1120, 1070; HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{12}H_{12}F_3N_3NaO^+$ 294.0825, found 294.0827.

*methyl 4-(4-(1-methoxyethyl)-1H-1,2,3-triazol-5-yl)benzoate* (**4h**). Following the procedure above for compound **4a** using azide **3h**, the product (65 mg, 99%) was isolated as a colorless solid: $^1$H NMR (500 MHz; $CDCl_3$) δ 13.4 (br, 1H), 8.13 (d, $J$ = 7.8 Hz, 2H), 7.91 (d, $J$ = 7.8 Hz, 2H), 4.89 (q, $J$ = 6.7 Hz, 1H), 3.96 (s, 3H), 3.34 (s, 3H), 1.59 (d, $J$ = 6.1 Hz, 3H); $^{13}$C{1H} NMR (125 MHz; $CDCl_3$) δ 167.0, 143.5, 143.3, 134.9, 130.0, 129.8, 128.1, 71.2, 56.2, 52.3, 19.8; IR (NaCl, thin film, cm$^{-1}$) 3193, 2934, 1717, 1614, 1281, 1113; HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{13}H_{15}N_3NaO_3^+$ 284.1006, found 284.1002.

*4-(4-(1-methoxyethyl)-1H-1,2,3-triazol-5-yl)benzonitrile* (**4i**). Following the procedure above for compound **4a** using azide **3i**, the product (23 mg, 99%) was isolated as a colorless solid: $^1$H NMR (500 MHz; $CDCl_3$) δ 10.26 (br, 1H), 8.02 (d, $J$ = 8.4 Hz, 2H), 7.78 (d, $J$ = 8.4 Hz, 2H), 4.88 (q, $J$ = 6.7 Hz, 1H), 3.36 (s, 3H), 1.59 (d, $J$ = 6.7 Hz, 3H); $^{13}$C{1H} NMR (125 MHz; $CDCl_3$) δ 135.0, 132.5, 132.0, 129.6, 128.7, 118.7, 112.0, 71.2, 56.2, 19.6; IR (NaCl, thin film, cm$^{-1}$) 3172, 2985, 2933, 2826, 2228, 1613, 1115, 1092, 846; HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{12}H_{12}N_4NaO^+$ 251.0903, found 251.0908.

*4-(1-methoxyethyl-1,2,2,2-d$_4$)-5-(4-(trifluoromethyl)phenyl)-1H-1,2,3-triazole* (**4j**). Following the procedure above for compound **4a** using azide **3j**, the product (44.0 mg, quant.) was isolated as a colorless solid: $^1$H NMR (500 MHz; $CDCl_3$) δ 13.03 (br, 1H), 7.96 (d, $J$ = 8.0 Hz, 2H), 7.72 (d, $J$ = 8.0 Hz, 2H), 3.36 (s, 3H); $^{13}$C{1H} NMR (125 MHz; $CDCl_3$) δ 143.5, 133.9, 130.4 (q, $J_{C\text{-}F}$ = 32.8 Hz), 128.4, 125.7 (q, $J_{C\text{-}F}$ = 3.72 Hz), 124.0 (q, $J_{C\text{-}F}$ = 273.0 Hz), 56.1. (Note that no attempt was made to detect multiplets featuring a $J_{C\text{-}D}$ coupling, which were too broad to readily identify); $^2$H NMR (77 MHz; $CDCl_3$) δ 4.89 (s, 1D), 1.58 (s, 3D); $^{19}$F{1H} NMR (470 MHz, $CDCl_3$) δ -62.7; IR (NaCl, thin film, cm$^{-1}$) 3165, 3008, 2933, 2825, 2360, 2343, 1623, 1411, 1327, 1166, 1125, 1075, 1001, 849; HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{12}H_8D_4F_3N_3NaO^+$ 298.1076, found 298.1093.

**Triazole Synthesis *via* Prototropic Shift**

Due to the observed break in mechanism, a mixture of both prototropic and sigmatropic triazole products (**4** and **5**) were observed in some cases. This has been noted below where possible. These NH triazoles also demonstrated dynamic behavior by $^1$H NMR and $^{13}$C NMR. In most cases, the $^{13}$C resonances for the triazole carbons were not readily detected (very broad and weak signal). For triazole **5e** and **5i**, a $^{13}$C NMR is provided in the supporting information that was collected at rt in $CDCl_3$ and a second $^{13}$C NMR is provided that was collected at 60 °C in $C_6D_6$, where the remaining carbons are detectable.

*4-((4-chlorophenyl)(methoxy)methyl)-5-methyl-1H-1,2,3-triazole* (**5e**). A solution of azide **3e** (70 mg, 0.34 mmol) and NaOMe (0.77 mL, 25 wt% in MeOH, 3.40 mmol) in MeOH (2.5 mL) was heated to 60 °C in a sealed 4 mL vial. After 24 h, the solution was cooled to room temperature, acidified with AcOH (4 mL, 1 M in $H_2O$, 4 mmol) and extracted with EtOAc (5 x 5 mL). The combined organic layers were dried ($Na_2SO_4$), filtered, and concentrated under reduced pressure. Purification by flash chromatography (gradient elution 40 – 100% EtOAc in

hexanes) afforded the product **5e** (15 mg, 18%) as a colorless oil. Triazole **4e** (53 mg, 70%) was also isolated as a colorless oil: $^1$H NMR (500 MHz; $CDCl_3$) δ 12.26 (br, 1H), 7.33 (m, 4H), 5.51 (s, 1H), 3.39 (s, 3H), 2.21 (s, 3H); $^{13}$C{1H} NMR (125 MHz; $CDCl_3$) 138.0, 133.6, 128.9, 128.6, 128.2, 128.0, 77.1, 56.9, 10.0; $^{13}$C{1H} NMR (125 MHz; $C_6D_6$, 60 °C) 144.9, 140.6, 139.2, 133.8, 128.8, 128.4, 77.8, 56.5, 10.0; IR (NaCl, thin film, cm$^{-1}$) 3155, 2928, 1595, 1408, 1194, 1089, 1014, 970, 835; HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{11}H_{12}ClN_3ONa^+$ 260.0561, found 260.0555.

*4-((4-ethynylphenyl)(methoxy)methyl)-5-methyl-1H-1,2,3-triazole* (**5f**). Following the procedure above for compound **5e** using azide **3f**, triazole **4f** (33 mg, 50%) and triazole **5f** (17 mg, 26%, colorless oil) were isolated: $^1$H NMR (500 MHz; $CDCl_3$) δ 7.49 (d, *J* = 8.1 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 5.54 (s, 1H), 3.40 (s, 3H), 3.07 (s, 1H), 2.19 (s, 3H); $^{13}$C{1H} NMR (125 MHz; $CDCl_3$) 140.2, 132.2, 126.5, 121.6, 83.3, 77.4, 77.4, 57.0, 10.0; IR (NaCl, thin film, cm$^{-1}$) 3287, 2934, 1591, 1501, 1192, 1090, 1018, 969, 847; HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{13}H_{13}N_3ONa^+$ 250.0951, found 250.0948.

*4-(methoxy(4-(trifluoromethyl)phenyl)methyl)-5-methyl-1H-1,2,3-triazole* (**5g**). Following the procedure above for compound **5e** using azide **3g**, triazole **4g** (11 mg, 14%) and triazole **5g** (57 mg, 71%, colorless oil) were isolated: $^1$H NMR (500 MHz; $CDCl_3$) δ 13.17 (br. s, 1H), 7.60 (d, *J* = 8.2 Hz, 2H), 7.52 (d, *J* = 8.2 Hz, 2H), 5.61 (s, 1H), 3.41 (s, 3H), 2.21 (s, 3H); $^{13}$C{1H} NMR (125 MHz; $CDCl_3$) δ 143.6, 133.3 ($J_{C\text{-}F}$ = 1.6 Hz), 130.6, 129.9 ($J_{C\text{-}F}$ = 32.5 Hz), 126.8, 125.3 ($J_{C\text{-}F}$ = 3.6 Hz), 124.0 ($J_{C\text{-}F}$ = 273.5 Hz), 77.2, 57.0, 9.8; $^{19}$F{1H} NMR (470 MHz, $CDCl_3$) δ -62.6; IR (NaCl, thin film, cm$^{-1}$) 3141, 2937, 1620, 1415, 1326, 1163, 1126, 1067, 1018, 971; HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{12}H_{12}F_3N_3ONa^+$ 294.0825, found 294.0825.

*methyl 4-(methoxy(5-methyl-1H-1,2,3-triazol-4-yl)methyl)benzoate* (**5h**). Following the procedure above for compound **5e** using azide **3h**, triazole **5h** (18 mg, 35%) was isolated as a colorless oil: $^1$H NMR (500 MHz; $CDCl_3$) δ 12.12 (brs, 1H), 8.05 – 7.99 (m, 2H), 7.47 (d, *J* = 8.1 Hz, 2H), 5.60 (s, 1H), 3.92 (s, 3H), 3.41 (s, 3H), 2.18 (s, 3H); $^{13}$C{1H} NMR (125 MHz; $CDCl_3$) 166.9, 144.7, 130.0, 129.7, 129.6, 126.5, 77.4, 57.1, 52.1, 10.0; IR (NaCl, thin film, cm$^{-1}$) 3147, 2931, 2359, 1723, 1611, 1436, 1283, 1193, 1096, 1019, 967 752; HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{13}H_{15}N_3O_3Na^+$ 284.1006, found 284.0999.

*4-(methoxy(5-methyl-1H-1,2,3-triazol-4-yl)methyl)benzonitrile* (**5i**). Following the procedure above for compound **5e** using azide **3i**, triazole **5i** (67 mg, 76%) was isolated as a colorless oil: $^1$H NMR (500 MHz; $CDCl_3$) δ 12.56 (brs, 1H), 7.65 (d, *J* = 8.1 Hz, 2H), 7.52 (d, *J* = 8.1 Hz, 2H), 5.60 (s, 1H), 3.41 (s, 3H), 2.20 (s, 3H); $^{13}$C{1H} NMR (125 MHz; $CDCl_3$) 145.0, 132.2, 127.1, 118.6, 111.5, 77.0, 57.1, 9.9; $^1$H NMR (500 MHz, $C_6D_6$) δ 7.14 - 7.10 (m, 2H), 7.06 – 7.02 (m, 2H), 5.33 (s, 1H), 3.03 (s, 3H), 2.00 (s, 3H); $^{13}$C{1H} NMR (126 MHz, $C_6D_6$, 60 °C) δ 145.3, 144.3, 140.4, 132.2, 127.3, 118.7, 112.2, 77.6, 56.7, 9.9; IR (NaCl, thin film, cm$^{-1}$) 3143, 2933, 2359, 2229, 1608, 1503, 1444, 1280, 1190, 1092, 971, 798; HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{12}H_{12}N_4ONa^+$ 251.0903, found 251.0906.

*4-(methoxy(4-(trifluoromethyl)phenyl)methyl)-5-(methyl-d3)-1H-1,2,3-triazole* (**5j**). Following the procedure above for compound **5e** using azide **3j**, triazole **5j** (49 mg, 71%) was isolated as a yellow oil: $^1$H NMR (500 MHz; $CDCl_3$) δ 13.14 (br, 1H), 7.60 (d, *J* = 8.1 Hz, 2H), 7.52 (d, *J* = 8.1 Hz, 2H), 5.62 (s, 0.5H, ~50%H and ~50%D), 3.41 (s, 3H); $^{13}$C{1H} NMR (125 MHz, $CDCl_3$) δ 143.9, 143.6 (apparent d assigned 1 C for $d_4$-5j and 1 C for $d_3$-5j), 139.6, 129.9 (q, $J_{C\text{-}F}$ = 31.8 Hz), 126.8, 125.4, (q, $J_{C\text{-}F}$ = 3.7 Hz), 124.1 (q, $J_{C\text{-}F}$ = 271.7 Hz), 77.3, 57.0 (apparent d assigned 1 C for $d_4$-5j and 1 C for $d_3$-5j); $^2$H NMR (77 MHz; $CDCl_3$) δ 5.61 (s, 0.5D, ~50%H and ~50%D), 2.17 (s, 3D); $^{19}$F{1H} NMR (470 MHz, $CDCl_3$) δ -62.6; IR (NaCl, thin film, cm$^{-1}$) 3136, 3027, 2936, 2828, 1660, 1619, 1588, 1412, 1327, 1166, 1125, 1068, 1018, 821; HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{12}H_8D_4F_3N_3NaO^+$ 298.1076, found 298.1076, [M + Na]$^+$ calcd for $C_{12}H_9D_3F_3N_3NaO^+$ 297.1013, found 297.1020.

## ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: XXXXXXXX.

**Kinetic data, HPLC images, spectral images (PDF)**

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The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

### Notes

The authors declare no competing financial interests.

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