

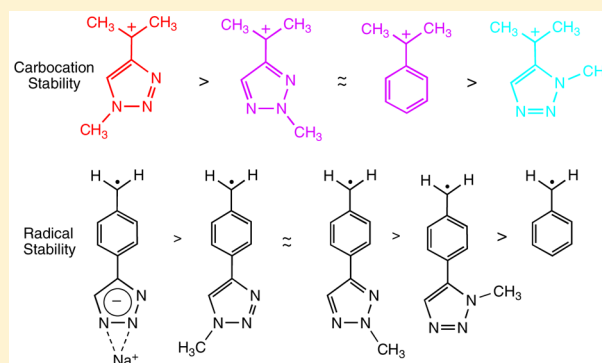
Electronic Properties of Triazoles. Experimental and Computational Determination of Carbocation and Radical-Stabilizing Properties

Xavier Creary,*[✉] Kyle Chormanski, Gabriel Peirats, and Carol Renneburg

Department of Chemistry and Biochemistry, University of Notre Dame, Notre Dame, Indiana 46556, United States

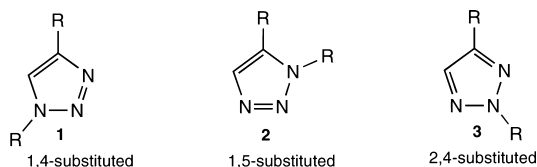
S Supporting Information

ABSTRACT: Three fluorobenzenes substituted with *meta*-triazole groups have been prepared, and ¹⁹F chemical shifts indicate that these triazole groups are all inductively electron-withdrawing in character, with the 1,5-triazole being the most electron-withdrawing. σ^+ values for these three triazoles have also been determined from solvolysis rates of substituted cumyl trifluoroacetates. When substituted in the *para*-position, the 1,4 and the 2,4-triazoles are cation-stabilizing, whereas the 1,5-triazole is carbocation-destabilizing. γ^+ values indicate that the 1,4 triazole group is cation-stabilizing relative to the phenyl group, albeit the 1,5 triazole is significantly destabilizing relative to phenyl. These studies all suggest that the 1,5-triazole group exerts a strong electron-withdrawing effect on carbocations that is not offset by a resonance effect. The three triazole groups all enhance the methylenecyclopropane rearrangement rate and are therefore radical stabilizers. The smallest stabilizing effect is seen for the 1,5-triazole, and this is attributed to the triazole group being twisted out of conjugation in the developing benzylic radical. Finally, the anionic triazole group is the most effective radical-stabilizing group. Computational studies indicate that these triazole groups all stabilize benzylic radicals by a spin delocalization mechanism.



INTRODUCTION

Since Sharpless first introduced the copper-catalyzed reaction of alkynes with organic azides to form 1,4-disubstituted triazoles of type **1**,¹ the so-called “Click Reaction” has become one of the most utilized reactions in chemistry. References for this reaction, which has largely replaced the original Huisgen cycloaddition,² are too numerous to list, and hence some reviews of this reaction are given.³ The isomeric 1,5-disubstituted triazoles **2** are also available via a ruthenium-catalyzed reaction of azides with alkynes, and also from addition of acetylides to organic azides.⁴ Methods for synthesis of 2,4-disubstituted isomers **3** are less general, but these isomers can also be prepared.⁵



Despite the thousands of papers dealing with triazoles of structure **1–3**, the simple electronic properties of these substrates have not been thoroughly studied. Are they electron-donor or electron-acceptor groups? Are triazoles carbocation-stabilizing groups? Are they radical-stabilizing groups, and if so, how stabilizing? We sought to answer these questions by determining classical σ , σ^+ , and σ^- values for these

three triazole groups. We also wanted to determine γ^+ values for these triazole groups to allow a direct comparison of the cation-stabilizing ability of these aromatic triazole groups with the phenyl group. Reported here are the results of these studies.

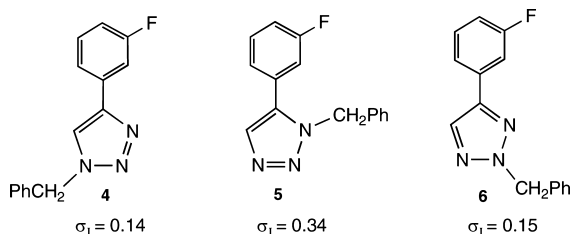
RESULTS AND DISCUSSION

Determination of σ_1 Values. Inductive effects of substituents, σ_1 values, are measured by a variety of methods. These include the original Taft σ_1 values that are derived from a combination of base-catalyzed and acid-catalyzed ester hydrolysis rates.⁶ Inductive substituent constants have also been determined from dissociation constants of substituted 2-methylpyridinium ions⁷ and from dissociation constants of 4-substituted quinuclidines.⁸ Dissociation constants of 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids,⁹ 4-substituted cubane-1-carboxylic acids,¹⁰ and 3-substituted adamantane carboxylic acids¹¹ have also been used to evaluate σ_1 values. These methods of determining various σ_1 values all involve, from our point of view, somewhat tedious syntheses and/or measurements of pK_a values. We therefore chose a simple NMR spectroscopic method based on Taft's observation that ¹⁹F chemical shifts of a series of *m*-substituted fluorobenzenes correlated well with σ_1 values.¹² Hence the fluorobenzenes **4–6**, where the fluorine is *meta* to the triazole

Received: March 7, 2017

Published: May 5, 2017

substituent, were prepared by simple methods. Measured ^{19}F chemical shifts for 4–6 were 0.37, 1.80, and 0.44 ppm, respectively, downfield from fluorobenzene. These shifts therefore indicate that the triazole groups in 4 and 6 are weak inductively electron-withdrawing groups, while the 1,5-triazole in 5 is significantly more electron-withdrawing. Calculated σ_1 values are shown. By comparison, the σ_1 value for the moderately electron-withdrawing CH_3CO (acetyl) group is 0.30.



Carbocation Effects. Determination of σ^+ and γ^+ Values. σ^+ Values,¹³ a measure of carbocation-stabilizing effects on cumyl carbocations, were investigated next. Cumyl trifluoroacetates 7, 8, and 9 were prepared, where the effects of the *para*-triazole groups on rates of solvolyses of these substrates could be measured, and the corresponding σ^+ values could be calculated. Also prepared were the *meta*-analogues 16–18 as well as the related trifluoroacetates 19, 20, and 21. These latter substrates allow for a direct comparison of rates with cumyl trifluoroacetate and for determination of γ^+ values (group σ^+ values).

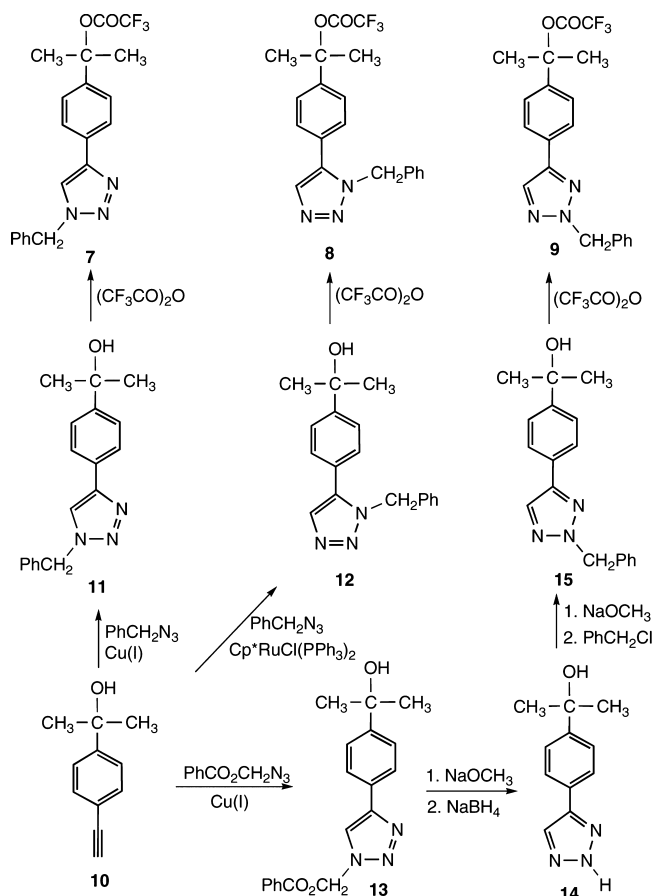
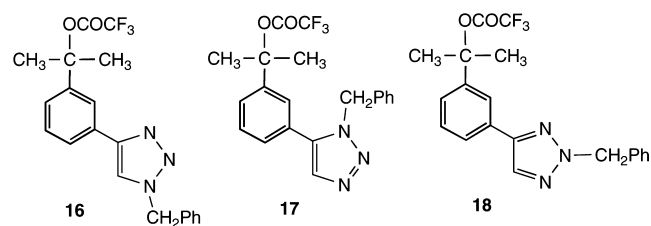
Syntheses of trifluoroacetates 7 and 8 were straightforward (Scheme 1) from the corresponding alcohols 11 and 12, which were available using Cu(I)- and ruthenium-catalyzed protocols starting with alkyne 10. The preparation of trifluoroacetate 9 involved benzylation of NH triazole 14, which was available from the benzoate ester 13. The resultant triazole 15 (precursor to 9) was readily separable via chromatography from the isomeric triazole 11 also formed in this benzylation reaction. The *meta*-substituted trifluoroacetates 16–18 (Scheme 2) were prepared by completely analogous methods starting with the *m*-analogue of 10.

The alcohol precursors to trifluoroacetates 19 and 20 have been previously prepared.¹⁴ The alcohol precursor to trifluoroacetate 21 was prepared by reaction of triazole 23 with CH_3MgI (Scheme 3). The ester 23 was available, in turn, from benzylation of the triazole anion derived from reaction of sodium azide with ethyl propiolate, 22.¹⁵ Separation of 23 from the isomeric triazole products was readily achieved by chromatography.

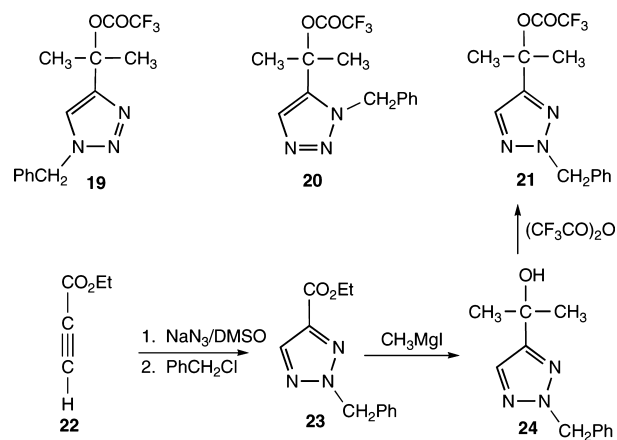
The solvent chosen for most kinetic studies was $\text{CD}_3\text{CO}_2\text{D}$, whereas EtOH was used for reactions that were too fast to measure in $\text{CD}_3\text{CO}_2\text{D}$. Substrates 7–9 and 16–21 all reacted by first-order processes to give mixtures of substitution and elimination products. Table 1 gives kinetic data for these trifluoroacetates, as well as for the parent substrate, cumyl trifluoroacetate, 25.

The trifluoroacetate 7, which is very reactive in $\text{CD}_3\text{CO}_2\text{D}$, is 8.5 times more reactive than cumyl trifluoroacetate in EtOH. This corresponds to a σ^+ value of -0.20 and indicates that the triazole substituent in 7 is therefore cation-stabilizing. The triazole group in 9 also enhances the acetolysis rate of cumyl trifluoroacetate by a smaller factor and is also cation-stabilizing. Contrastively, the triazole group in 8 considerably slows the

Scheme 1. Syntheses of Trifluoroacetates 7, 8, and 9

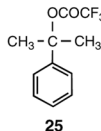
Scheme 2. Substrates for Determination of σ^+ _{meta}

Scheme 3. Syntheses of Trifluoroacetates 19, 20, and 21

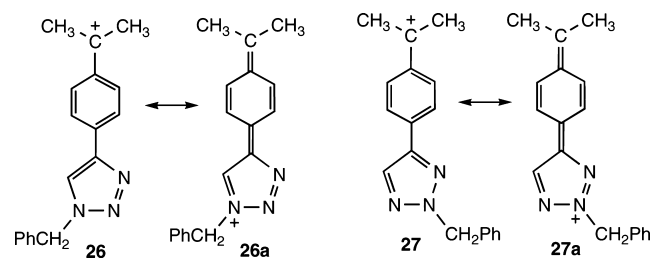


acetolysis rate and is therefore destabilizing with respect to the cumyl cation ($\sigma^+ = +0.23$). The rate-enhancing effects in 7 and

Table 1. Solvolysis Rates for Substrates in CD₃CO₂D and EtOH

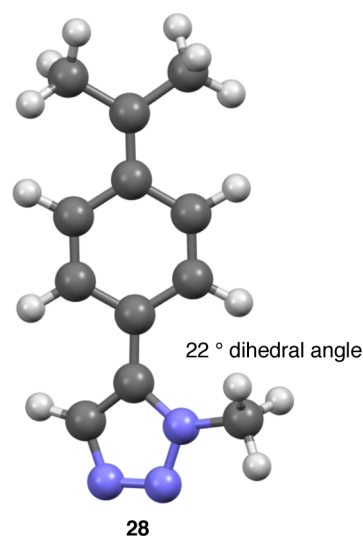
Compound	Solvent	T (°C)	<i>k</i> (s ⁻¹)	<i>k</i> _{rel}
7	EtOH	20.0	6.60 × 10 ⁻⁴	8.54
8	CD ₃ CO ₂ D	25.0	3.56 × 10 ⁻⁵	0.075
9	CD ₃ CO ₂ D	25.0	1.27 × 10 ⁻³	2.67
16	CD ₃ CO ₂ D	25.0	1.43 × 10 ⁻⁴	0.30
17	CD ₃ CO ₂ D	25.0	1.65 × 10 ⁻⁵	0.035
18	CD ₃ CO ₂ D	25.0	8.61 × 10 ⁻⁵	0.18
19	EtOH	20.0	5.66 × 10 ⁻³	73.3
20	CD ₃ CO ₂ D	25.0	2.37 × 10 ⁻⁶	0.005
21	CD ₃ CO ₂ D	25.0	2.73 × 10 ⁻⁴	0.575
 25	EtOH	20.0	7.72 × 10 ⁻⁵	1.00
	CD ₃ CO ₂ D	25.0	4.74 × 10 ⁻⁴	1.00

9 are consistent with resonance stabilization of cations 26 and 27 by the triazole group, as reflected in forms 26a and 27a (Scheme 4). The cation destabilization by the triazole group in

Scheme 4. Resonance Stabilization of Cations 26 and 27

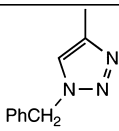
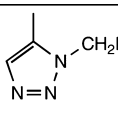
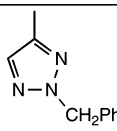
solvolysis of 8 is a reflection of the intrinsic electron-withdrawing nature of the 1,5-triazole group. This isomer 8 contains the most electron-withdrawing of the three triazole isomers, as indicated by the σ_1 value. The inductive destabilizing effect on the carbocation intermediate is not offset by resonance stabilization in solvolysis of 8. A computational study at the M062X/6-311+G** level¹⁶ (Figure 1) suggests that the triazole group in this isomer, due to a steric effect, is twisted 22° out of conjugation with the benzene ring in the carbocation 28 (where, for computational purposes, the PhCH₂ group has been replaced by CH₃).

The series of *meta*-substituted triazoles 16–18 confirms the intrinsic electron-withdrawing nature of all three triazole groups. They all inductively slow the solvolysis rates, with the 1,5-isomer 17 being the slowest-reacting. The rate-retarding factor of 29 ($\sigma_{\text{meta}}^+ = 0.32$) suggests that this 1,5-triazole is about as electron-withdrawing as a *m*-chloro substituent.

**Figure 1.** M06X/6-311+G** calculated structure of cation 28.

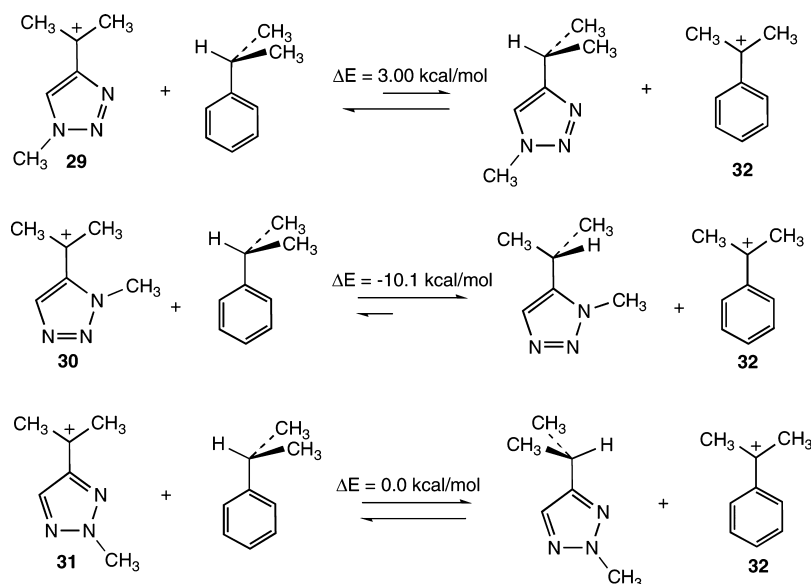
Attention was next turned to the trifluoroacetates 19–21, where direct comparison of the triazole groups with the phenyl group allows the calculation of γ^+ values (group σ^+ values).¹⁷ The trifluoroacetate 19 is a very reactive compound that was isolated with difficulty. It is so reactive that it decomposed in solvents such as CDCl₃ and C₆D₆ during acquisition of NMR spectra at room temperature. Spectra were therefore recorded at 10 °C and kinetic studies were carried out in EtOH, where rates are slower than in CD₃CO₂D, and a relatively fast NMR kinetic method could be used to monitor rates. Trifluoroacetate 19 solvolyzed with a half-life of only 2 min at 20 °C in ethanol. This is 73 times faster than cumyl trifluoroacetate, 25, under the same conditions. On the other hand, trifluoroacetate 20 is 200 times less reactive than 25 in CD₃CO₂D. In other words, trifluoroacetate 19 is 1.47 × 10⁴ times more reactive than 20. This dramatic rate spread is indicative of a large difference in the stability of the triazole-substituted carbocations involved in these reactions. Table 2 summarizes pertinent σ^+ and γ^+ values and emphasizes the differing electronic characteristics of the three triazole groups.

Table 2. σ^+ and γ^+ Values for Triazole Groups

Triazole			
σ_{para}^+	-0.20	+0.24	-0.09
σ_{meta}^+	+0.11	+0.32	+0.16
γ^+	-0.40	+0.50	+0.05

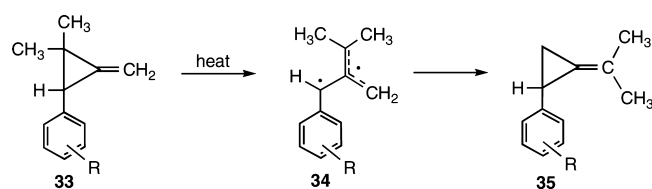
Computational studies at the M062X/6-311+G** level were again used to gain insight into the large rate differences between trifluoroacetate 19, 20, and 21. A direct computational comparison between energies of cationic intermediates was not used because, as will be subsequently shown, the three triazole rings have different aromatic stabilization energies. The isodesmic reactions of the cations 29–31 with isopropylbenzene to generate the cumyl cation, 32 (Scheme 5) were therefore used to evaluate carbocation stabilities. Cation 29 is more stable than cumyl cation 32, while cation 30 is

Scheme 5. Isodesmic Reactions of Triazole-Substituted Cations with Cumene

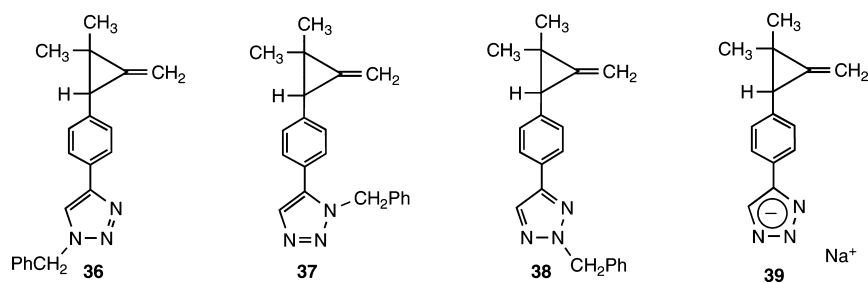


substantially destabilized. Although these gas phase stabilities probably overestimate solution stabilities, they parallel the observed solvolytic reactivities of 19–21. They confirm the electron-withdrawing properties of the 1,5-substituted triazole group on carbocations that are not offset by resonance stabilization. These computational studies are also in agreement with the observed relative reactivity of trifluoroacetate 21, in that cation 31 is comparable in stability to cumyl cation 32.

Radical Effects. Determination of σ^\cdot Values. Attention was next turned to the effect of triazole groups on radicals, i.e., free radical substituent constants, σ^\cdot .¹⁸ We have developed a method for determining the effect of groups on free radical stabilities based on the thermal rearrangement of methylenecyclopropanes of type 33 to 35, (Scheme 6) which proceeds

Scheme 6. Methylenecyclopropane Rearrangement Used for Determination of σ^\cdot Values

via a radical mechanism.¹⁸ Substituents R can stabilize or destabilize the radical intermediate 34 and affect the rearrangement rate. The substrates 36–39 (Scheme 7) have now been

Scheme 7. Triazoles Used for Determination of σ^\cdot 

prepared by methods analogous to those described earlier, and the effect of these *para*-triazole groups on the rate of the thermal methylenecyclopropane rearrangement have been determined. Rate data are summarized in Table 3.

Table 3. Rearrangement Rates for Substrates 33, and 36–39

compound	solvent	T (°C)	k (s ⁻¹)	k _{rel}
33 R = H	C ₆ D ₆	80.0	5.57 × 10 ⁻⁵	1.00
	C ₆ D ₆	70.0	1.72 × 10 ⁻⁵	
	C ₆ D ₆	60.0	5.05 × 10 ⁻⁶	
36	C ₆ D ₆	80.0	1.66 × 10 ⁻⁴	2.98
	C ₆ D ₆	70.0	5.55 × 10 ⁻⁵	
	C ₆ D ₆	60.0	1.64 × 10 ⁻⁵	
37	C ₆ D ₆	80.0	1.10 × 10 ⁻⁴	1.98
	C ₆ D ₆	70.0	3.50 × 10 ⁻⁵	
	C ₆ D ₆	60.0	1.05 × 10 ⁻⁵	
38	C ₆ D ₆	80.0	1.68 × 10 ⁻⁴	3.02
	C ₆ D ₆	70.0	5.51 × 10 ⁻⁵	
	C ₆ D ₆	60.0	1.66 × 10 ⁻⁵	
39	DMSO- <i>d</i> ₆	80.0	4.69 × 10 ⁻⁴	5.93
	DMSO- <i>d</i> ₆	60.0	9.42 × 10 ⁻⁵	
	DMSO- <i>d</i> ₆	50.0	1.44 × 10 ⁻⁵	
	DMSO- <i>d</i> ₆	40.0	3.88 × 10 ⁻⁶	

The first apparent thing is that all three triazole groups enhance the methylenecyclopropane rearrangement rate relative to the parent substrate 33 (R = H). As in our previous

studies, these rate enhancements are real, but small compared to rate enhancements in carbocation reactions. Hence, triazole groups in **36–38** all stabilize the developing benzylic radicals in the rearrangement process. Also of interest is the somewhat smaller stabilizing effect in the 1,5-isomer **37**.

Computational studies again were used to gain insight into these radical-stabilizing effects. Our previous studies¹⁹ have shown a very good correlation between the rearrangement rate of methylenecyclopropanes **33** and the B3LYP/6-31G* calculated radical stabilization energy²⁰ of benzylic radicals. In fact, data for **36–38** (shown in red) fit very nicely on this plot as shown in Figure 2. In other words, the isodesmic reactions

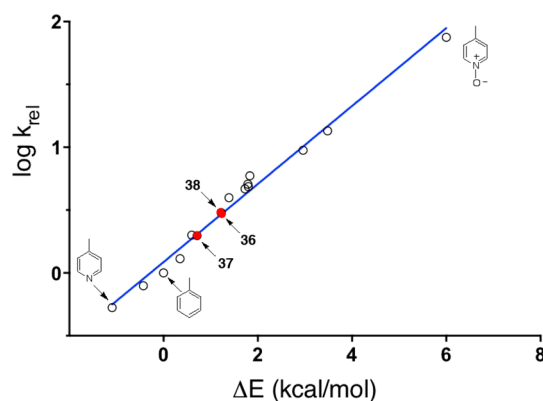
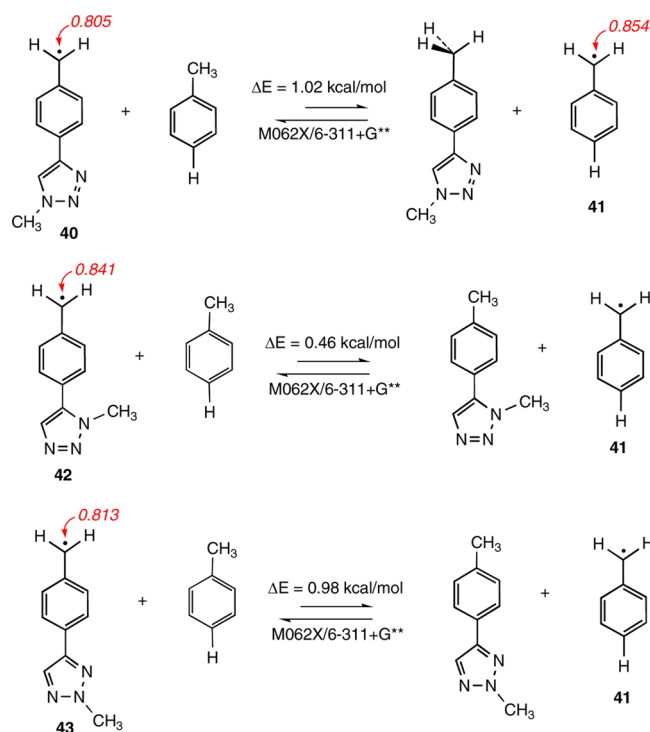


Figure 2. Plot of $\log k_{\text{rel}}$ for the rearrangement of **33** vs the radical stabilization energy of the analogous benzylic radical.

shown in Scheme 8 are a very good measure of the ability of triazole groups to stabilize benzylic radicals. These calculations, which have now been carried out at the M062X/6-311+G** level, also show a corresponding lowering of spin density at the

Scheme 8. Isodesmic Reactions of Triazole-Substituted Radicals with Toluene



benzylic carbon that parallels radical stabilization. The calculated spin density (shown in red) drops from 0.854 in the benzyl radical, **41**, down to 0.805 in radical **40**. In other words, spin delocalization involving the triazole group leads to radical stabilization. Of note is the calculated structure of radical **42**, the least stabilized radical, which shows that the triazole group is twisted 41° out of conjugation with the phenyl group. This would account for the slightly lower radical stabilization by this group.

The anionic triazole group in **39** is of interest. Rearrangement rates were measured in DMSO-*d*₆, where solubility is not an issue. Rate data in Table 3 indicate that this anion is the best triazole radical stabilizer. This finding is in line with our previous observations of enhanced radical stabilization by other anionic groups.¹⁸ However, a computational study on the simple uncoordinated anionic triazole system **44** is misleading. The calculated radical stabilization energy of 4.74 kcal/mol predicts a much larger rate enhancement in rearrangement of **39** than the observed enhancement of 5.9. However, when the calculation is carried out on the anion **45** that is coordinated with a sodium cation,²¹ a much more reasonable radical stabilization energy of 1.58 kcal/mol is calculated (Figure 3).

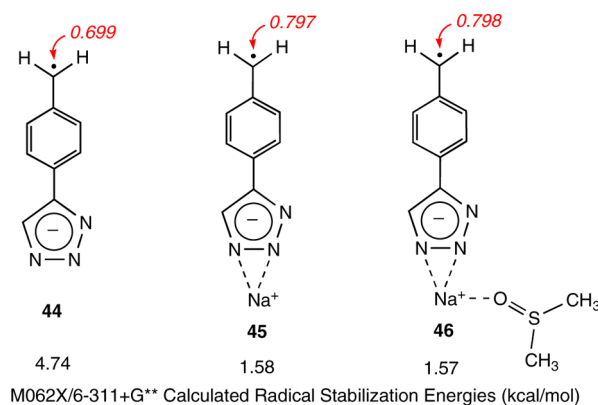


Figure 3. M062X/6-311+G** calculated radical stabilization energies.

Inclusion of a molecule of coordinated DMSO into the calculation in **46** has little effect on the radical stabilization energy or on spin density at the benzylic carbon relative to **45**.

Aromatic Character of Triazoles. A final study addresses the aromatic nature of 1,2,3-triazoles. While the topic of aromaticity is difficult to define,^{22a} these triazoles can all be classified as aromatic using the classic $(4n + 2)$ rule. The unsubstituted 1,2,3-triazoles **47** and **48** have also been classified as aromatic using the nucleus independent chemical shift (NICS) criterion.^{22b} Both triazoles have a large negative NICS value (Figure 4) at the center of the ring, which is indicative of an aromatic ring current.²³ We have now evaluated the aromatic character of triazoles **49**, **51**, and **53** computationally by examining the energy differences between these triazoles and the nonaromatic 1,3-hydrogen shift tautomers **50**, **52**, and **54**.

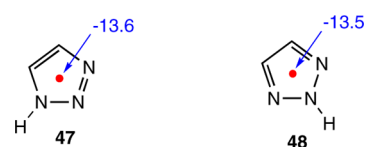


Figure 4. Calculated NICS values for triazoles **47** and **48**.²²

Figure 5 shows the relative energies of these six molecules. The nonaromatic analogues are all significantly higher in energy

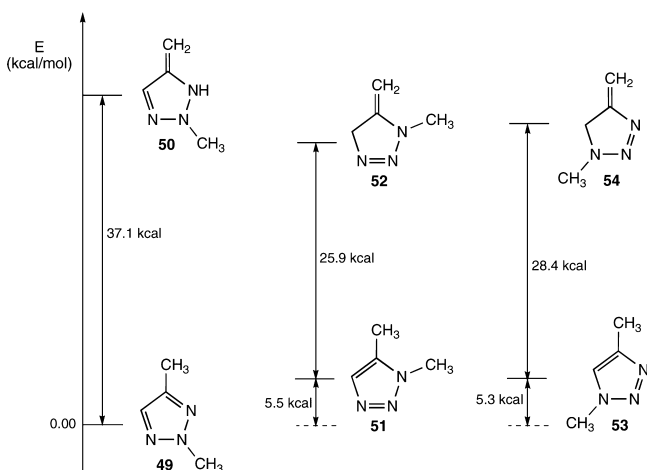


Figure 5. B3LYP/6-311+G** calculated relative energies of triazoles and nonaromatic analogues.

than the aromatic triazoles. Also of interest is the magnitude of the energy differences between the aromatic triazoles and their nonaromatic analogues. The 37.1 kcal/mol energy difference between 49 and 50 suggests that triazole 49 has the largest aromatic stabilization energy. This value is comparable to the aromatic stabilization energies calculated for 2-methylpyridine (34.1 kcal/mol) and for toluene (33.8 kcal/mol) by this method. This computational method suggests that the 2,4-triazole 49 is significantly "more aromatic" than both the 1,5-triazole 51 and the 1,4-triazole 53.

CONCLUSIONS

1,2,3-Triazoles are inductively electron-withdrawing groups as revealed by σ_1 values. However, 1,4- and 2,4-disubstituted triazoles are carbocation stabilizers due to charge delocalizing resonance effects. On the other hand, 1,5-disubstituted triazoles are carbocation destabilizers because of a stronger inductive effect that is not offset by resonance. All three of the isomeric triazoles, as well as the anionic triazole analogue, are benzylic radical-stabilizing groups by a spin delocalization mechanism. The 1,5-disubstituted triazole system is twisted out of conjugation with the benzylic radical, and this results in a smaller radical-stabilizing effect. Finally, the 2,4-disubstituted triazole system is significantly more aromatic than the other two isomeric triazoles, as shown by Computational Studies.

EXPERIMENTAL SECTION

General. NMR spectra were recorded on a Varian DirectDrive 600 MHz spectrometer or on a Varian Inova 500 MHz spectrometer. HRMS measurements were carried out using a Bruker MicroTOF-II spectrometer (electrospray ionization source with time-of-flight mass analyzer).

Preparation of 1,4-Substituted Triazoles. 1,4-Substituted triazoles were prepared by reaction of the appropriate alkyne with benzyl azide, catalyzed by CuSO_4 /sodium ascorbate using methylene chloride/water as solvent.²⁴ The following procedure is illustrative.

1-Benzyl-4-(3-fluorophenyl)-1,2,3-triazole, 4.²⁵ 1-Ethynyl-3-fluorobenzene (58 mg; 0.483 mmol) and PhCH_2N_3 (130 mg; 0.977 mmol) in 2 mL of methylene chloride and 2 mL of water were stirred, and 18 mg of copper sulfate pentahydrate was added. After the copper sulfate dissolved, 40 mg of sodium ascorbate was added in small portions, and stirring was continued for 24 h. The mixture was then

taken up into ether, washed with water followed by saturated NaCl solution, and dried over a mixture of Na_2SO_4 and MgSO_4 . After filtration, about 1.5 g of silica gel was added to the ether extract and the solvents were removed using a rotary evaporator. The residue was added to a column prepared from 10 g of silica gel. The column was eluted with increasing amounts of ether in pentane. The triazole 4 (114 mg; 93% yield), mp 111–112 °C (lit.²⁵ 109–110 °C), eluted with 50% ether in pentane. ^1H NMR of 4 (CDCl_3) δ 7.66 (s, 1 H), 7.56 (m, 1 H), 7.53 (m, 1 H), 7.42–7.30 (m, 6 H), 7.00 (m, 1 H), 5.58 (s, 2 H); ^{13}C NMR of 4 (CDCl_3) δ 163.1 (d, $J_{\text{C-F}} = 246$ Hz), 147.1 (d, $J_{\text{C-F}} = 2.7$ Hz), 134.5, 132.7 (d, $J_{\text{C-F}} = 8.7$ Hz), 130.4 (d, $J_{\text{C-F}} = 8.4$ Hz), 129.2, 128.9, 128.1, 121.3 (d, $J_{\text{C-F}} = 3.0$ Hz), 119.9, 115.0 (d, $J_{\text{C-F}} = 21.3$ Hz), 112.6 (d, $J_{\text{C-F}} = 22.9$ Hz), 54.3; HRMS (ESI) (MH^+) calcd for $\text{C}_{15}\text{H}_{13}\text{FN}_3$ 254.1088, found 254.1085.

Preparation of 1,5-Substituted Triazoles. 1,5-Substituted triazoles were prepared by reaction of the appropriate alkyne with benzyl azide catalyzed by $\text{Cp}^*\text{RuCl}(\text{PPh}_3)_2$.⁴ The following procedure is illustrative.

Preparation of 1-Benzyl-5-(3-fluorophenyl)-1,2,3-triazole, 5. Benzyl azide (103 mg; 0.774 mmol) and 87 mg (0.725 mmol) of 1-ethynyl-3-fluorobenzene in 3 mL of C_6H_6 under argon was stirred for 5 h. About 1 g of silica gel was added to the mixture, and the C_6H_6 was then removed using a rotary evaporator. The residue was added to a chromatography column prepared from 5.5 g of silica gel. The column was eluted with increasing amounts of ether in pentane. The triazole 5 (163 mg, 89% yield), mp 43–44 °C, eluted with 50% ether in pentane. ^1H NMR of 5 (CDCl_3) δ 7.76 (s, 1 H), 7.39 (m, 1 H), 7.33–7.27 (m, 3 H), 7.14 (m, 1 H), 7.08 (m, 2 H), 7.04 (m, 1 H), 6.96 (m, 1 H), 5.57 (s, 2 H); ^{13}C NMR of 5 (CDCl_3) δ 162.6 (d, $J_{\text{C-F}} = 248$ Hz), 136.9, 135.1, 133.4, 130.7 (d, $J_{\text{C-F}} = 8.6$ Hz), 128.9, 128.8 (d, $J_{\text{C-F}} = 7.9$ Hz), 128.3, 127.1, 124.6 (d, $J_{\text{C-F}} = 3.1$ Hz), 116.6 (d, $J_{\text{C-F}} = 21$ Hz), 116.0 (d, $J_{\text{C-F}} = 23$ Hz), 52.0; HRMS (ESI) (MH^+) calcd for $\text{C}_{15}\text{H}_{13}\text{FN}_3$ 254.1088, found 254.1086.

Azidomethyl Benzoate. Sodium azide (142 mg; 2.185 mmol) in 4 mL of DMSO was stirred as 299 mg of $\text{PhCO}_2\text{CH}_2\text{Cl}$ ²⁷ (2.098 mmol) was added. After 15 h, the mixture was transferred to a separatory funnel using water and a mixture of ether and pentane. The organic extract was washed with two portions of cold water followed by saturated NaCl solution, and then dried over Na_2SO_4 . After filtration, the solvent was removed using a rotary evaporator. NMR analysis showed $\text{PhCO}_2\text{CH}_2\text{N}_3$ and PhCON_3 in a 2:1 ratio. The crude product mixture was then chromatographed on a column prepared from 5 g of silica gel and eluted with pentane. The PhCON_3 eluted with pure pentane. The $\text{PhCO}_2\text{CH}_2\text{N}_3$ (181 mg; 58% yield) eluted with 1–2% ether in pentane as a solid, mp 47–48 °C. ^1H NMR (CDCl_3) δ 8.09 (d, $J = 7.6$ Hz, 2 H), 7.461 (t, $J = 7.5$ Hz, 1 H), 7.48 (t, $J = 7.6$ Hz, 2 H), 5.40 (s, 2 H); ^{13}C NMR (CDCl_3) δ 166.1, 133.8, 130.0, 128.9, 128.6, 75.1; HRMS (ESI) (M^+Na^+) calcd for $\text{C}_8\text{H}_7\text{N}_3\text{NaO}_2$ 200.0430, found 200.0415.

Preparation of (4-(3-Fluorophenyl)-1,2,3-triazol-1-yl)methyl benzoate, 55. 1-Ethynyl-3-fluorobenzene (123 mg; 1.025 mmol) and 185 mg (1.045 mmol) of $\text{PhCO}_2\text{CH}_2\text{N}_3$ were dissolved in 3 mL of methylene chloride, and 3 mL of water was added. Copper sulfate pentahydrate (24 mg) was added and the mixture was stirred for 10 min to dissolve. Sodium ascorbate (65 mg) was then added in small portions with stirring. Stirring was continued for 16 h and the mixture was then taken up into ether. The ether extract was washed with water followed by saturated NaCl solution, and dried over a mixture of Na_2SO_4 and MgSO_4 . After filtration, about 1 g of silica gel was added to the solution and the solvents were removed using a rotary evaporator. The residue was added to a column prepared from 6 g of silica gel. The column was eluted with increasing amounts of ether in pentane. The triazole product 55 (252 mg; 83% yield), mp 98–99 °C, eluted with 50–55% ether in pentane. ^1H NMR of 55 (CDCl_3) δ 8.18 (s, 1 H), 8.07 (d, $J = 7.8$ Hz, 2 H), 7.65–7.56 (m, 3 H), 7.47 (t, $J = 7.8$ Hz, 2 H), 7.39 (m, 1 H), 7.04 (m, 1 H), 6.54 (s, 2 H); ^{13}C NMR of 55 (CDCl_3) δ 165.8, 163.1 (d, $J_{\text{C-F}} = 246$ Hz), 147.3, 134.2, 132.1 (d, $J_{\text{C-F}} = 8.5$ Hz), 130.5 (d, $J_{\text{C-F}} = 8.4$ Hz), 130.1, 128.7, 128.0, 121.8, 121.5 (d, $J_{\text{C-F}} = 3.0$ Hz), 115.3 (d, $J_{\text{C-F}} = 21$ Hz), 112.8 (d, $J_{\text{C-F}} = 23$ Hz).

Hz), 70.0; HRMS (ESI) (MH⁺) calcd for C₁₆H₁₃FN₃O₂ 298.0986, found 298.0985.

Preparation of 2-Benzyl-4-(3-fluorophenyl)-1,2,3-triazole, 6. The triazole **55** prepared above (250 mg; 0.842 mmol) was partially dissolved in 1.5 mL of CH₃OH, and then 2.8 mL of 0.510 M NaOCH₃ (1.428 mmol) in CH₃OH was added. After 15 min, 32 mg (0.847 mmol) of NaBH₄ was added, the mixture was stirred for 3 h, and the CH₃OH was then removed using a rotary evaporator. The residue was dissolved in 3 mL of water, and then acidified with 10% HCl. A solid precipitate formed. The acidic mixture was then brought to pH of ~5 by adding small portions of NaHCO₃ with stirring. The aqueous component of the mixture was carefully decanted from the solid precipitate using a pipet. The solid was washed with 3 mL of distilled water and the aqueous component was again decanted. The flask was then placed on a rotary evaporator for 1.5 h to remove much of the residual water. The flask was then evacuated at 0.15 mm for 6 h at room temperature to remove residual water and PhCO₂CH₃.

The crude NH triazole above was partially dissolved in 2 mL of methanol, and 2.1 mL of 0.510 M NaOCH₃ (1.071 mmol) was added. The methanol was then removed using a rotary evaporator. The solid residue was dissolved in 4 mL of DMSO and then 150 mg (1.186 mmol) of PhCH₂Cl was added. The mixture was stirred at room temperature for 24 h and then transferred to a separatory funnel using ether and water. The ether extract was washed with 2 portions of water followed by saturated NaCl solution, dried over a mixture of Na₂SO₄ and MgSO₄, and filtered. NMR analysis of a small sample showed triazoles **4**, **5**, and **6** in a 53:2:45 ratio. About 1 g of silica gel was added to the filtrate, and the ether was removed using a rotary evaporator. The residue was added to a column prepared from 5 g of silica gel. The column was eluted with increasing amounts of ether in pentane. The triazole **6** (72 mg; 40% yield), mp 53–54 °C, eluted with 8–10% ether in pentane. Triazole **4** (87 mg; 48% yield) eluted with 50% ether in pentane. ¹H NMR of **6** (CDCl₃) δ 7.85 (s, 1 H), 7.54 (d, *J* = 7.8 Hz, 1 H), 7.52 (m, 1 H), 7.40–7.30 (m, 6 H), 7.03 (m, 1 H), 5.62 (s, 2 H); ¹³C NMR of **6** (CDCl₃) δ 163.1 (d, *J*_{C-F} = 246 Hz), 147.0 (d, *J*_{C-F} = 2.8 Hz), 135.1, 132.5 (d, *J*_{C-F} = 8.4 Hz), 131.6, 130.4 (d, *J*_{C-F} = 8.4 Hz), 128.8, 128.4, 128.0, 121.5 (d, *J*_{C-F} = 3.0 Hz), 115.2 (d, *J*_{C-F} = 21 Hz), 112.9 (d, *J*_{C-F} = 23 Hz), 58.8; HRMS (ESI) (MH⁺) calcd for C₁₅H₁₃FN₃ 254.1088, found 254.1072.

Preparation of Alcohol 11. A mixture of 224 mg (0.765 mmol) of 2-(4-ethynylphenyl)propan-2-ol, **10** and 223 mg (1.677 mmol) of benzyl azide in 2 mL of CH₂Cl₂ and 2 mL of water was stirred. CuSO₄ pentahydrate (36 mg) was added. After the CuSO₄ dissolved, 73 mg of sodium ascorbate was added in small portions with stirring. Stirring was continued for 24 h, and the mixture was then taken up into ether. After separation of the aqueous phase, the solution was dried over MgSO₄, filtered, and the solvent was removed using a rotary evaporator. The crude product was chromatographed on 12 g of silica gel, and the column was eluted with increasing amounts of ether in pentane. The solid product **11**, mp 103–104 °C, (390 mg; 95% yield) eluted with 100% ether. ¹H NMR of **11** (CDCl₃) δ 7.77 (d, *J* = 8.6 Hz, 2 H), 7.65 (s, 1 H), 7.52 (d, *J* = 8.6 Hz, 2 H), 7.42–7.34 (m, 3 H), 7.33–7.29 (m, 2 H), 5.58 (s, 2 H), 1.73 (bs, 1 H), 1.96 (s, 6 H); ¹³C NMR of **11** (CDCl₃) δ 149.2, 148.0, 134.7, 129.2, 128.9, 128.8, 128.0, 125.6, 124.9, 119.4, 72.5, 54.2, 31.7; HRMS (ESI) (MH⁺) calcd for C₁₈H₂₀N₃O 294.1601, found 294.1602.

Preparation of Alcohol 12. A mixture of 72 mg (0.450 mmol) of 2-(4-ethynylphenyl)propan-2-ol, **10**²⁶ and 64 mg of benzyl azide (0.481 mmol) in 3 mL of benzene under argon was stirred as 6 mg of Cp^{*}RuCl(PPh₃)₂ was added. The mixture was then gently refluxed for 2 h. The entire mixture was chromatographed on 4 g of silica gel, and the column was eluted with increasing amounts of ether in pentane. The solid alcohol **12**, mp 87–88 °C (127 mg; 96% yield) eluted with 80–100% ether in pentane. ¹H NMR of **12** (CDCl₃) δ 7.74 (s, 1 H), 7.55 (d, *J* = 8.5 Hz, 2 H), 7.32–7.26 (m, 3 H), 7.23 (d, *J* = 8.5 Hz, 2 H), 7.12–7.06 (m, 2 H), 5.55 (s, 2 H), 2.65 (bs, 1 H), 1.61 (s, 6 H); ¹³C NMR of **12** (CDCl₃) δ 150.9, 138.1, 135.4, 132.9, 128.8, 128.7, 128.2, 127.0, 125.1, 124.8, 72.3, 51.8, 31.8; HRMS (ESI) (MH⁺) calcd for C₁₈H₂₀N₃O 294.1601, found 294.1604.

Preparation of 2,4-Substituted Triazoles. 2,4-Substituted triazoles were prepared by reaction of the appropriate alkyne with PhCO₂CH₂N₃ catalyzed by CuSO₄/sodium ascorbate. This initial triazole was reacted sequentially with NaOCH₃ in CH₃OH, followed by NaBH₄. The resultant NH triazole was deprotonated with NaOCH₃, and the anion was reacted with benzyl bromide. The 2,4-substituted triazole was easily separable from the isomeric 1,5-triazole by chromatography on silica gel. The following procedure is illustrative.

Preparation of Triazole 13. Azidomethyl benzoate (243 mg; 1.373 mmol) was placed in a flask and 2 mL of CH₂Cl₂ was added, followed by 200 mg (1.250 mmol) of the alcohol **10**. Water (2 mL) was added, followed by 18 mg of CuSO₄ pentahydrate. The mixture was stirred to dissolve the CuSO₄. Sodium ascorbate (39 mg) was then added in small portions with stirring. The mixture was vigorously stirred for 21 h at room temperature and then was diluted with ether. The organic phase was separated, dried over Na₂SO₄, and then filtered. About 1 g of silica gel was added to the ether extract, and the solvent was removed using a rotary evaporator. This solid residue was added to a column prepared from 6 g of silica gel packed with 10% ether in pentane. The column was eluted with increasing amounts of ether in pentane. The solid triazole product **13**, mp 117–118 °C, (374 mg; 89% yield) eluted with pure ether. ¹H NMR (CDCl₃) δ 8.15 (s, 1 H), 8.07 (d, *J* = 8.0 Hz, 2 H), 7.81 (d, *J* = 8.4 Hz, 2 H), 7.61 (t, *J* = 7.5 Hz, 1 H), 7.55 (d, *J* = 8.4 Hz, 2 H), 7.46 (t, *J* = 8.0 Hz, 2H), 6.53 (s, 2 H), 1.87, (bs, 1 H), 1.60 (s, 6 H); ¹³C NMR (CDCl₃) δ 165.9, 149.5, 148.2, 134.2, 130.1, 128.7, 128.4, 128.1, 125.8, 125.0, 121.2, 72.5, 70.0, 31.7; HRMS (ESI) (MH⁺) calcd for C₁₉H₂₀N₃O₃ 338.1499, found 338.1480.

Preparation of Alcohol 15. The triazole **13** prepared above (300 mg; 0.890 mmol) was partially dissolved in 2 mL of methanol. Then, 2.7 mL of 0.51 M NaOCH₃ in CH₃OH (1.377 mmol) was added while stirring. The triazole completely dissolved. After 1 h, 40 mg of NaBH₄ was added and the mixture was stirred for an additional 1 h. The CH₃OH was removed using a rotary evaporator and the residue was dissolved in 2 mL of water. The solution was then carefully acidified with 10% HCl and the mixture was brought to a pH of about 5 by adding small portions of solid NaHCO₃. The aqueous phase was carefully decanted from the precipitated triazole **14** using a pipet. The precipitate was washed with about 2 mL of water, and the water was again decanted from the solid. The flask containing the triazole **14** was placed on a rotary evaporator for 7 h and then evacuated at 0.2 mm for 4 h at room temperature to remove the residual water and methyl benzoate.

The triazole **14** was then dissolved in 2.0 mL of 0.51 M NaOCH₃ (1.02 mmol) in CH₃OH. The CH₃OH was removed using a rotary evaporator and the residue was dissolved in 5 mL of DMSO. Benzyl chloride (133 mg; 1.051 mmol) was added and the mixture was stirred at room temperature for 20 h. The mixture was transferred to a separatory funnel using ether and water. The ether extract was washed with water followed by saturated NaCl, and dried over a mixture of Na₂SO₄ and MgSO₄. After filtration, 1.5 g of silica gel was added to the solution and the solvent was then removed using rotary evaporator. The powder was added to a column prepared from 5 g of silica gel packed with 5% ether in pentane. The column was eluted with increasing amounts of ether in pentane. The solid 2,4-triazole product **15**, mp 91–92 °C, (87 mg; 33% yield) eluted with 40% ether in pentane. The second product, triazole **11** (77 mg; 30% yield), eluted with 80–100% ether in pentane. ¹H NMR of **15** (CDCl₃) δ 7.85 (s, 1 H), 7.76 (d, *J* = 8.5 Hz, 2 H), 7.54 (d, *J* = 8.5 Hz, 2 H), 7.37–7.29 (m, 5 H), 5.62 (s, 2 H), 1.82, (bs, 1 H), 1.60 (s, 6 H); ¹³C NMR of **15** (CDCl₃) δ 149.4, 147.8, 135.3, 131.4, 128.77, 128.76, 128.3, 127.9, 125.8, 124.9, 72.5, 58.7, 31.7; HRMS (ESI) (MH⁺) calcd for C₁₈H₂₀N₃O 294.1601, found 294.1579.

Preparation of Trifluoroacetate Esters. Trifluoroacetates were prepared by reaction of the appropriate alcohol with 2,6-lutidine and trifluoroacetic anhydride in ether solvent at –10 °C. These esters are, in most instances, thermally unstable and also prone to hydrolysis. They were stored in ether/pentane solution at –20 °C. The following procedure is illustrative.

Preparation of Trifluoroacetate 7. A solution of 67 mg of alcohol **11** (0.229 mmol) and 105 mg of 2,6-lutidine (0.523 mmol) in 3 mL of ether was cooled to -10°C . Trifluoroacetic anhydride (56 mg, 0.500 mmol) in a small amount of ether was added dropwise. The mixture was warmed to 0°C for 5 min and then transferred to a separatory funnel using a small amount of ether. Pentane (3 mL) was added, and the mixture was then rapidly washed successively with ice water, cold dilute HCl solution, ice water, NaHCO_3 solution, and saturated NaCl solution. The organic extract was dried over a mixture of Na_2SO_4 and MgSO_4 , filtered, and the solvent was removed using a rotary evaporator to give 86 mg (97% yield) of trifluoroacetate **7** as a solid that decomposed when heated. NMR spectra were recorded at 10°C . ^1H NMR of **7** (CDCl_3) δ 7.80 (d, $J = 8.6$ Hz, 2 H), 7.67 (s, 1 H), 7.44–7.35 (m, 5 H), 7.33–7.28 (m, 2 H), 5.58 (s, 2 H), 1.90 (s, 6 H); ^{13}C NMR of **7** (CDCl_3) δ 155.7 (q, $J = 42$ Hz), 147.5, 142.9, 134.5, 130.1, 129.2, 128.8, 128.0, 125.9, 124.8, 119.8, 114.3 (q, $J = 287$ Hz), 87.2, 54.3, 27.9.

Preparation of Trifluoroacetate 8. Following the general procedure, reaction of 56 mg of alcohol **12** (0.191 mmol) and 48 mg of 2,6-lutidine (0.449 mmol) with 78 mg of trifluoroacetic anhydride (0.371 mmol) gave 67 mg (90% yield) of trifluoroacetate **8** as an oil. The oil was taken up into 1 mL of ether, and 1 mL of pentane was added. Upon cooling to -20°C , crystals of **8** formed, mp 70 – 71°C . ^1H NMR of **8** (CDCl_3) δ 7.76 (s, 1 H), 7.42 (d, $J = 8.4$ Hz, 2 H), 7.32–7.23 (m, 5 H), 7.07–7.02 (m, 2 H), 5.56 (s, 2 H), 1.91 (s, 6 H); ^{13}C NMR of **8** (CDCl_3) δ 155.7 (q, $J = 42$ Hz), 144.6, 137.5, 135.3, 133.4, 129.2, 128.9, 128.2, 127.1, 126.6, 124.9, 114.3 (q, $J = 287$ Hz), 86.8, 52.0, 27.9.

Preparation of Trifluoroacetate 9. Following the general procedure, reaction of 29.4 mg of alcohol **15** (0.100 mmol) and 24 mg of 2,6-lutidine (0.224 mmol) with 78 mg of trifluoroacetic anhydride (0.229 mmol) gave 38.3 mg (97% yield) of trifluoroacetate **9** as an oil. ^1H NMR of **9** (CDCl_3) δ 7.87 (s, 1 H), 7.80 (d, $J = 8.5$ Hz, 2 H), 7.44 (d, $J = 8.5$ Hz, 2 H), 7.38–7.30 (m, 5 H), 5.63 (s, 2 H), 1.91 (s, 6 H); ^{13}C NMR of **9** (CDCl_3) δ 155.7 (q, $J = 42$ Hz), 147.4, 143.2, 135.2, 131.5, 130.1, 128.8, 128.3, 127.9, 126.2, 124.8, 114.4 (q, $J = 287$ Hz), 87.2, 58.7, 27.9.

Preparation of 2-(3-(1-Benzyl-1H-1,2,3-triazol-4-yl)phenyl)propan-2-ol, 56. Benzyl azide (124 mg; 0.932 mmol) was placed in a flask and 1 mL of CH_2Cl_2 was added, followed by 108 mg (0.675 mmol) of 2-(3-ethynylphenyl)propan-2-ol. Water (1 mL) was added followed by 10 mg of CuSO_4 pentahydrate. The mixture was stirred to dissolve the CuSO_4 . Sodium ascorbate (20 mg) was then added in small portions with stirring. The mixture was vigorously stirred for 20 h at room temperature and then diluted with 5 mL of CH_2Cl_2 and 5 mL of water. The CH_2Cl_2 phase was separated, dried over Na_2SO_4 , and filtered. The solvent was removed using a rotary evaporator, and the residue was chromatographed on 5 g of silica gel. The column was eluted with increasing amounts of ether in pentane. The triazole product **56** (184 mg; 93% yield) eluted as a clear oil with pure ether: ^1H NMR of **56** (CDCl_3) δ 7.94 (t, $J = 1.7$ Hz, 1 H), 7.69 (s, 1 H), 7.67 (d of t, $J = 7.7$, 1.4 Hz, 1 H), 7.43 (m, 1 H), 7.41–7.23 (m, 4 H), 7.32–7.27 (m, 2 H), 5.56 (s, 2 H), 2.10 (bs, 1 H), 1.60 (s, 6 H); ^{13}C NMR of **56** (CDCl_3) δ 149.9, 148.3, 134.6, 130.3, 129.1, 128.8, 128.7, 128.0, 124.3, 124.0, 121.8, 119.7, 72.5, 54.2, 31.7; HRMS (ESI) (MH^+) calcd for $\text{C}_{18}\text{H}_{20}\text{N}_3\text{O}$ 294.1601, found 294.1622.

Preparation of Trifluoroacetate 16. Following the general procedure, reaction of 45 mg of alcohol **56** (0.154 mmol) and 39 mg of 2,6-lutidine (0.364 mmol) with 67 mg of trifluoroacetic anhydride (0.319 mmol) gave 55 mg (92% yield) of trifluoroacetate **16** as an oil. ^1H NMR of **16** (CDCl_3) δ 7.88 (t, $J = 1.8$ Hz, 1 H), 7.68 (s, 1 H), 7.67 (d of t, $J = 7.8$, 1.4 Hz, 1 H), 7.72–7.29 (m, 7 H), 5.58 (s, 2 H), 1.92 (s, 6 H); ^{13}C NMR of **16** (CDCl_3) δ 155.7 (q, $J = 42$ Hz), 147.8, 143.9, 134.6, 130.9, 129.18, 129.17, 128.8, 128.0, 125.3, 124.0, 121.6, 119.8, 114.3 (q, $J = 287$ Hz), 87.3, 54.3, 28.0.

Preparation of 2-(3-(1-Benzyl-1H-1,2,3-triazol-5-yl)phenyl)propan-2-ol, 57. A mixture of 101 mg (0.631 mmol) of 2-(3-ethynylphenyl)propan-2-ol and 92 mg (0.692 mmol) of benzyl azide in 4 mL of benzene under argon was stirred as 8 mg of $\text{Cp}^*\text{RuCl}(\text{PPh}_3)_2$ was added. The mixture was then gently refluxed

for 3.5 h. The entire mixture was then chromatographed on 5 g of silica gel, and the column was eluted with increasing amounts of ether in pentane. The solid alcohol product **57**, mp 104 – 105°C (132 mg; 71% yield) eluted with 80–100% ether in pentane. ^1H NMR of **57** (CDCl_3) δ 7.74 (s, 1 H), 7.56 (m, 1 H), 7.39 (t, $J = 7.7$ Hz, 1 H), 7.33 (t, $J = 1.8$ Hz, 1 H), 7.31–7.25 (m, 3 H), 7.14 (m, 1 H), 7.07 (m, 2 H), 5.54 (s, 2 H), 2.38 (bs, 1 H), 1.51 (s, 6 H); ^{13}C NMR of **57** (CDCl_3) δ 150.2, 138.4, 135.5, 133.0, 128.8, 128.2, 127.097, 127.089, 126.5, 125.8, 125.1, 72.2, 52.0, 31.7; HRMS (ESI) (MH^+) calcd for $\text{C}_{18}\text{H}_{20}\text{N}_3\text{O}$ 294.1601, found 294.1620.

Preparation of Trifluoroacetate 17. Following the general procedure, reaction of 45 mg of alcohol **57** (0.154 mmol) and 40 mg of 2,6-lutidine (0.374 mmol) with 70 mg of trifluoroacetic anhydride (0.333 mmol) gave 57 mg (95% yield) of trifluoroacetate **17**, mp 75 – 76°C . ^1H NMR of **17** (CDCl_3) δ 7.76 (s, 1 H), 7.48–7.41 (m, 2 H), 7.31–7.25 (m, 3 H), 7.22 (m, 1 H), 7.18 (m, 1 H), 7.05 (m, 2 H), 5.54 (s, 2 H), 1.78 (s, 6 H); ^{13}C NMR of **17** (CDCl_3) δ 155.6 (q, $J = 42$ Hz), 144.0, 137.7, 135.5, 133.5, 129.4, 128.9, 128.6, 128.2, 127.3, 127.0, 125.5, 125.0, 114.2 (q, $J = 287$ Hz), 86.7, 51.9, 27.8.

Preparation of 2-(3-(2-Benzyl-2H-1,2,3-triazol-4-yl)phenyl)propan-2-ol, 60. Azidomethyl benzoate (170 mg; 0.960 mmol) was placed in a flask, and 2 mL of CH_2Cl_2 was added, followed by 131 mg (0.819 mmol) of the 2-(3-ethynylphenyl)propan-2-ol, **58**. Water (2 mL) was added, followed by 12 mg of CuSO_4 pentahydrate. The mixture was stirred to dissolve the CuSO_4 . Sodium ascorbate (26 mg) was added in small portions with stirring. The mixture was vigorously stirred for 20 h at room temperature and then was diluted with ether. The organic phase was separated, dried over Na_2SO_4 , and filtered. About 1 g of silica gel was added to the ether extract and the solvent was removed using a rotary evaporator. This solid residue was added to a column prepared from 5 g of silica gel packed with 10% ether in pentane. The column was eluted with increasing amounts of ether in pentane. The triazole product (4-(3-(2-hydroxypropan-2-yl)phenyl)-1H-1,2,3-triazol-1-yl)methyl benzoate, **59**, eluted with 80–100% ether as an oil. ^1H NMR of **59** (CDCl_3) δ 8.18 (s, 1 H), 8.07 (d, $J = 8.0$ Hz, 2 H), 7.98 (t, $J = 1.8$ Hz, 1 H), 7.72 (d of t, $J = 7.7$, 1.3 Hz, 1 H), 7.61 (t, $J = 7.5$ Hz, 1 H), 7.50–7.43 (m, 4 H), 7.40 (t, $J = 7.7$ Hz, 1 H), 6.54 (s, 2 H), 1.84 (bs, 1 H), 1.62 (s, 6 H); ^{13}C NMR of **59** (CDCl_3) δ 165.8, 150.0, 148.5, 134.1, 130.1, 129.8, 128.8, 128.6, 128.1, 124.6, 124.2, 122.0, 121.4, 72.5, 70.0, 31.8; HRMS (ESI) (MH^+) calcd for $\text{C}_{19}\text{H}_{20}\text{N}_3\text{O}_3$ 338.1499, found 338.1505.

The triazole **59** prepared above was dissolved in 1.5 mL of methanol, and then 2.7 mL of 0.51 M NaOCH_3 in CH_3OH (1.377 mmol) was added with stirring. After 50 min, 40 mg of NaBH_4 (1.058 mmol) was added and the mixture was stirred for 150 min. The CH_3OH was removed using a rotary evaporator and the residue was dissolved in 3 mL of water. The solution was then carefully acidified with 10% HCl, and the mixture was brought to a pH of about 5 by adding small portions of solid NaHCO_3 . An insoluble oil formed on the surface. The aqueous mixture was extracted with ether and the ether extract was dried over a mixture of Na_2SO_4 and MgSO_4 . After filtration, the ether was removed using a rotary evaporator, and the flask was then evacuated at 0.4 mm for 4 h.

The crude NH-triazole was then dissolved in 3.0 mL of 0.51 M NaOCH_3 (1.530 mmol) in CH_3OH . The CH_3OH was then removed using a rotary evaporator and the residue was dissolved in 4 mL of DMSO. Benzyl chloride (210 mg; 1.660 mmol) was added, and the mixture was stirred at room temperature for 26 h. The mixture was then transferred to a separatory funnel using ether and water. The ether extract was washed with water followed by saturated NaCl, and dried over a mixture of Na_2SO_4 and MgSO_4 . After filtration, 1.5 g of silica gel was added to the solution, and the solvent was then removed using rotary evaporator. The powder was added to a column prepared from 5 g of silica gel packed with 2% ether in pentane. The column was eluted with increasing amounts of ether in pentane. The triazole product 2-(3-(2-benzyl-2H-1,2,3-triazol-4-yl)phenyl)propan-2-ol, **60**, (79 mg; 33% yield) eluted as an oil with 50–55% ether in pentane. A 95:5 mixture of 1,4 and 1,5-triazoles (83 mg; 35% yield), eluted with 100% ether. ^1H NMR of **60** (CDCl_3) δ 7.94 (t, $J = 1.8$ Hz, 1 H), 7.88 (s, 1 H), 7.65 (m, 1 H), 7.46 (m, 1 H), 7.39 (t, $J = 7.7$ Hz, 1 H), 7.37–

7.28 (m, 5 H), 5.62 (s, 2 H), 1.89, (bs, 1 H), 1.62 (s, 6 H); ^{13}C NMR of **60** (CDCl_3) δ 149.9, 148.2, 135.3, 131.5, 130.3, 128.78, 128.77, 128.3, 127.9, 124.6, 124.4, 122.0, 72.6, 58.7, 31.8; HRMS (ESI) (MH^+) calcd for $\text{C}_{18}\text{H}_{20}\text{N}_3\text{O}$ 294.1601, found 294.1577.

Preparation of Trifluoroacetate 18. Following the general procedure, reaction of 48 mg of 2-(3-(2-benzyl-2*H*-1,2,3-triazol-4-yl)phenyl)propan-2-ol, **60**, (0.164 mmol) and 42 mg of 2,6-lutidine (0.374 mmol) with 74 mg of trifluoroacetic anhydride (0.352 mmol) gave 62 mg (97% yield) of trifluoroacetate **18** as an oil. ^1H NMR of **18** (CDCl_3) δ 7.86 (s, 1 H), 7.80 (t, $J = 1.8$ Hz, 1 H), 7.71 (m, 1 H), 7.43 (t, $J = 7.6$ Hz, 1 H), 7.39–7.30 (m, 6 H), 5.64 (s, 2 H), 1.93 (s, 6 H); ^{13}C NMR of **18** (CDCl_3) δ 155.7 (q, $J = 42$ Hz), 147.6, 144.0, 135.2, 131.5, 130.8, 129.3, 128.8, 128.3, 128.0, 125.6, 124.3, 121.8, 114.4 (q, $J = 287$ Hz), 87.3, 58.8, 28.1.

Preparation of Trifluoroacetate 19. Following the general procedure, reaction of 46 mg (0.212 mmol) of 2-(1-benzyl-1,2,3-triazol-4-yl)propan-2-ol¹⁴ and 48 mg of 2,6-lutidine (0.449 mmol) with 101 mg of trifluoroacetic anhydride (0.481 mmol) gave 60.4 mg (91% yield) of trifluoroacetate **19** as an oil. Triazole **19** is a very unstable compound that decomposes in CDCl_3 or C_6D_6 while spectra are being recorded at room temperature. Triazole **19** was stored in ether/pentane solution at -20°C . NMR spectra were recorded at 14°C . ^1H NMR of **19** (CDCl_3) δ 7.50, (s, 1 H), 7.43–7.35 (m, 3 H), 7.30–7.25 (m, 2 H), 5.54 (s, 2 H), 1.95 (s, 6 H); ^{13}C NMR of **19** (CDCl_3) δ 155.9 (q, $J = 42$ Hz), 149.5, 134.2, 129.2, 128.9, 128.1, 121.5, 114.2 (q, $J = 287$ Hz), 82.6, 54.3, 26.7.

Preparation of Trifluoroacetate 20. Following the general procedure, reaction of 40 mg (0.184 mmol) of 2-(1-benzyl-1,2,3-triazol-5-yl)propan-2-ol¹⁴ and 42 mg of 2,6-lutidine (0.393 mmol) with 81 mg of trifluoroacetic anhydride (0.386 mmol) gave 50.5 mg (88% yield) of trifluoroacetate **20** as a solid, mp 51 – 52°C . ^1H NMR of **20** (CDCl_3) δ 7.69, (s, 1 H), 7.37–7.28 (m, 3 H), 7.07 (m, 2 H), 5.69 (s, 2 H), 1.84 (s, 6 H); ^{13}C NMR of **20** (CDCl_3) δ 155.2 (q, $J = 43$ Hz), 138.5, 134.9, 132.6, 129.0, 128.4, 126.6, 114.0 (q, $J = 287$ Hz), 81.1, 52.9, 26.7.

Preparation of Trifluoroacetate 21. Following the general procedure, reaction of 47 mg of alcohol **24** (0.217 mmol) and 51 mg of 2,6-lutidine (0.477 mmol) with 110 mg of trifluoroacetic anhydride (0.524 mmol) gave 64.5 mg (96% yield) of trifluoroacetate **21** as an oil. ^1H NMR of **21** (CDCl_3) δ 7.63, (s, 1 H), 7.38–7.30 (m, 3 H), 7.29–7.25 (m, 2 H), 5.57 (s, 2 H), 1.93 (s, 6 H); ^{13}C NMR of **21** (CDCl_3) δ 155.8 (q, $J = 42$ Hz), 149.7, 134.9, 132.2, 128.8, 128.4, 127.8, 114.2 (q, $J = 287$ Hz), 82.3, 58.7, 26.8.

Preparation of Triazole 23. Sodium azide (669 mg; 10.29 mmol) was partially dissolved by stirring and slight warming in 10 mL of DMSO. The mixture was cooled in an ice bath for a few minutes (the DMSO will begin to solidify if cooled too long), and then 677 mg (6.81 mmol) of ethyl propiolate in 2 mL of DMSO was added dropwise over 5 min. On completion of the addition, the mixture was warmed to room temperature for 1 h. Benzyl chloride (1.33 g; 10.51 mmol) was added. The mixture was stirred at room temperature for 3 h and then warmed to 45°C in an oil bath for 12 h. The mixture was then diluted with about 50 mL of water and extracted with 2 portions of ether. The ether extracts were washed with 2 portions of water followed by saturated salt solution, and dried over a mixture of Na_2SO_4 and MgSO_4 . After filtration, the solvent was removed using a rotary evaporator. The residue was chromatographed on 12 g of silica gel and the column was eluted with increasing amounts of ether in pentane. Some PhCH_2N_3 and a small amount of unreacted PhCH_2Cl eluted with 3% ether in pentane. The ethyl 2-benzyl-1,2,3-triazole-4-carboxylate, **23**^{5b} (257 mg) eluted as an oil with 12% ether in pentane, followed by 300 mg of a mixture of **23** and ethyl 1-benzyl-1*H*-1,2,3-triazole-5-carboxylate. Finally, ethyl 1-benzyl-1,2,3-triazole-4-carboxylate (467 mg) eluted with 70% to 100% ether in pentane. ^1H NMR of **23** (CDCl_3) δ 8.06 (s, 1 H), 7.38–7.31 (m, 5 H), 5.65 (s, 2 H), 4.42 (q, $J = 7.2$ Hz, 2 H), 1.40, (t, $J = 7.2$ Hz, 3 H); ^{13}C NMR of **23** (CDCl_3) δ 160.6, 140.3, 137.3, 134.2, 128.9, 128.7, 128.2, 61.4, 59.4, 14.3; HRMS (ESI) (MH^+) calcd for $\text{C}_{12}\text{H}_{14}\text{N}_3\text{O}_2$ 232.1081, found 232.1100.

Preparation of Alcohol 24. Methylmagnesium iodide (4 mL of 0.77 M solution in ether; 3.08 mmol) under argon was cooled in an ice bath as a solution of 234 mg (1.013 mmol) of the ester **23** in 6 mL of ether was added dropwise. The mixture was then warmed to room temperature for 30 min and then recooled in ice. The solution was then quenched with aqueous NH_4Cl solution. The ether extract was separated and washed with water followed by saturated salt solution, and then dried over a mixture of Na_2SO_4 and MgSO_4 . After filtration, the solvent was removed using a rotary evaporator. The residue was chromatographed on 5 g of silica gel, and the column was eluted with increasing amounts of ether in pentane. The alcohol **24** (170 mg; 77% yield) eluted as an oil with 40–50% ether in pentane. ^1H NMR of **24** (CDCl_3) δ 7.53 (s, 1 H), 7.36–7.27 (m, 5 H), 5.53 (s, 2 H), 2.25, (bs, 1 H), 1.60 (s, 6 H); ^{13}C NMR of **24** (CDCl_3) δ 155.8, 135.3, 130.8, 128.7, 128.2, 127.9, 68.6, 58.5, 30.5; HRMS (ESI) ($\text{M}+\text{Na}^+$) calcd for $\text{C}_{12}\text{H}_{15}\text{N}_3\text{NaO}$ 240.1107, found 240.1119.

Preparation of 1-(2,2-Dimethyl-3-methylenecyclopropyl)-4-ethynylbenzene, 63. 1-(Diazomethyl)-4-ethynylbenzene, **62**, was prepared from 4-ethynylbenzaldehyde, **61**, using the general procedure for the preparation of diazomethylbenzenes from aldehydes.²⁹ 1-(Diazomethyl)-4-ethynylbenzene **62** (273 mg) was dissolved in 12 mL of 1,1-dimethylallene, and the solution was sealed under argon in a pyrex tube. The tube was irradiated for 135 min using a Hanovia 450 W lamp. On completion of the irradiation, the solution was transferred to a distillation flask, and the excess allene was removed by distillation at 15 mm pressure. The remaining residue contained 1-(2,2-dimethyl-3-methylenecyclopropyl)-4-ethynylbenzene, **63**, and the isomer **35** ($\text{R} = p\text{-CCH}$) in a 7:3 ratio. This residue was chromatographed on 12 g of silica gel, and the column was eluted with hexanes. Product **63** and the isomeric product **35** both eluted with this solvent, with the earlier fractions being enriched with product **63**. A total of 181 mg of products were isolated from the chromatography (52% yield). ^1H NMR of **63** (CDCl_3) δ 7.39 (d, $J = 8.3$ Hz, 2 H), 7.13 (d, $J = 7.9$ Hz, 2 H), 5.58 (m, 1 H), 5.54 (m, 1 H), 3.05 (s, 1 H), 2.45 (t, $J = 2.1$ Hz, 1 H), 1.34 (s, 3 H), 0.84 (s, 3 H); ^{13}C NMR of **63** (CDCl_3) δ 145.1, 139.6, 131.8, 128.9, 119.4, 103.7, 83.9, 76.8, 32.2, 26.1, 24.3, 18.3; HRMS (EI) (M^+) calcd for $\text{C}_{14}\text{H}_{14}$ 182.1095, found 182.1125.

Preparation of Triazole 36. A mixture of 31 mg of 1-(2,2-dimethyl-3-methylenecyclopropyl)-4-ethynylbenzene, **63**, and 25 mg of benzyl azide in 0.8 mL of CH_2Cl_2 and 0.8 mL of water was stirred, and 4 mg of CuSO_4 pentahydrate was added. After the CuSO_4 dissolved, 6 mg of sodium ascorbate was added in portions with stirring. Stirring was continued for 24 h, and the mixture was then taken up into CH_2Cl_2 . After separation of the aqueous phase, the solution was dried over MgSO_4 , filtered, and the solvent was removed using a rotary evaporator to give 51 mg (95% yield) of crude **36**, m.p. 99 – 101°C (partially rearranges to 1-benzyl-4-(4-(2,2-dimethyl-3-methylenecyclopropyl)phenyl)-1,2,3-triazole on heating). ^1H NMR of **36** (CDCl_3) δ 7.69 (d, $J = 8.2$ Hz, 2 H), 7.63 (s, 1 H), 7.41–7.34 (m, 3 H), 7.30 (m, 2 H), 7.21 (d, $J = 8.1$ Hz, 2 H), 5.59 (m, 1H), 5.57 (s, 2 H), 5.55 (m, 1 H), 2.47 (t, $J = 2.1$ Hz, 1 H), 1.35 (s, 3 H), 0.85 (s, 3 H); ^{13}C NMR of **36** (CDCl_3) δ 148.3, 145.4, 138.6, 134.7, 129.3, 129.1, 128.8, 128.05, 128.02, 125.3, 119.2, 103.5, 54.2, 32.0, 26.1, 24.0, 18.4; HRMS (ESI) (MH^+) calcd for $\text{C}_{21}\text{H}_{22}\text{N}_3$ 316.1808, found 316.1798.

Preparation of Triazole 37. A solution of 20 mg of 1-(2,2-dimethyl-3-methylenecyclopropyl)-4-ethynylbenzene, **63**, and 17 mg of PhCH_2N_3 in 1.5 mL of benzene was stirred as 4 mg of $\text{Cp}^*\text{RuCl}(\text{PPh}_3)_2$ was added. The mixture was heated at 35°C for 9 h and then kept at room temperature for 12 h. The benzene solvent was removed using a rotary evaporator, and the residue was chromatographed on 4 g of silica gel. The column was eluted with increasing amounts of ether in pentane. Unreacted methylenecyclopropane and PhCH_2N_3 eluted with pentane. The product **37** (23 mg; 66% yield) eluted as an oil with 45–50% ether in pentane. ^1H NMR of **37** (CDCl_3) δ 7.73 (s, 1 H), 7.30–7.25 (m, 3 H), 7.22 (d, $J = 7.8$ Hz, 2 H), 7.124 (d, $J = 7.8$ Hz, 2 H), 7.06, (m, 2 H), 5.61 (m, 1 H), 5.56 (m, 1 H), 5.55 (s, 2 H), 2.49 (t, $J = 2.1$ Hz, 1 H), 1.36 (s, 3 H), 0.87 (s, 3 H); ^{13}C NMR of **37** (CDCl_3) δ 144.9, 140.3, 138.2, 135.6, 133.2, 129.5, 128.8, 128.4, 128.1, 127.2, 124.3, 103.9, 51.8, 31.9, 26.1, 24.3,

18.4; HRMS (ESI) (MH⁺) calcd for C₂₁H₂₂N₃ 316.1808, found 316.1819.

Preparation of (4-(4-(2,2-Dimethyl-3-methylenecyclopropyl)phenyl)-1H-1,2,3-triazol-1-yl)methyl benzoate, 64. A mixture of 40 mg of 1-(2,2-dimethyl-3-methylenecyclopropyl)-4-ethynylbenzene, 63, and 41 mg of azidomethyl benzoate in 1.5 mL of CH₂Cl₂ and 1.5 mL of water was stirred, and 12 mg of CuSO₄ pentahydrate was added. After the CuSO₄ dissolved, 30 mg of sodium ascorbate was added in small portions with stirring. Stirring was continued for 20 h and the mixture was then taken up into ether. After separation of the aqueous phase, the solution was dried over Na₂SO₄, filtered, and 0.5 g of silica gel was added to the solution. The solvent was removed using a rotary evaporator, and the residue was added to a column prepared from 3 g of silica gel. The column was eluted with increasing amounts of ether in pentane. The triazole 64 (62 mg; 79% yield) eluted with 40–50% ether in pentane. ¹H NMR of 64 (CDCl₃) δ 8.12 (s, 1 H), 8.06 (d, J = 8.2 Hz, 2 H), 7.74 (d, J = 8.3 Hz, 2 H), 7.61 (m, 1 H), 7.46 (t, J = 7.9 Hz, 2 H), 7.24 (d, J = 8.0 Hz, 2 H), 6.53 (s, 2 H), 5.59 (m, 1 H), 5.56 (m, 1 H), 2.48 (t, J = 2.1 Hz, 1 H), 1.35 (s, 3 H), 0.85 (s, 3 H); ¹³C NMR of 64 (CDCl₃) δ 165.8, 148.5, 145.4, 138.9, 134.1, 130.1, 129.4, 128.6, 128.1, 127.5, 125.5, 121.0, 103.5, 70.0, 32.0, 26.1, 24.0, 18.4; HRMS (ESI) (MH⁺) calcd for C₂₂H₂₂N₃O₂ 360.1707, found 360.1689.

Preparation of Triazole 38. The triazole 64 prepared above (143 mg) was partially dissolved in 3 mL of CH₃OH, and then 1.20 mL of 0.51 M in NaOCH₃ in CH₃OH was added with stirring. The triazole immediately dissolved. After 20 min 16 mg of NaBH₄ was added. The mixture was stirred for 1 h, and the CH₃OH was then removed using a rotary evaporator. The residue was dissolved in 3 mL of water and then acidified with a few drops of 10% HCl. A solid precipitate formed. The acidic mixture was brought to pH of ~5 by adding small portions of NaHCO₃ with stirring. The aqueous component of the mixture was then carefully decanted, the solid was washed with 3 mL of distilled water, and the aqueous component was again carefully decanted. The solid was evacuated at 15 mm to remove much of the residual water. Further evacuation at 0.2 mm for 4 h at room temperature removed the last traces of water and PhCO₂CH₃ and gave 80 mg of 4-(4-(2,2-dimethyl-3-methylenecyclopropyl)phenyl)-2H-1,2,3-triazole, 65.

The NH triazole 65 prepared above (80 mg) was dissolved in 2 mL of CH₃OH, and then 1.00 mL of 0.510 M NaOCH₃ was added. After 15 min, the CH₃OH was removed using a rotary evaporator and the solid residue was dissolved in 2 mL of DMSO. Benzyl chloride (70 mg) was added, and the mixture was stirred at room temperature for 6 h. The mixture was then diluted with water and extracted with ether. The ether extract was washed with 3 portions of water, followed by saturated NaCl solution, and dried over Na₂SO₄. After filtration, about 0.5 g of silica gel was added, and the ether solvent was removed using a rotary evaporator. The residue was added to a column prepared from 7 g of silica. The column was eluted with increasing amounts of ether in pentane. The triazole 38 (46 mg; 37% yield) eluted as an oil with 10% ether in pentane. The triazole 36 (53 mg; 42% yield) eluted with 40–50% ether in pentane. ¹H NMR of 38 (CDCl₃) δ 7.83 (s, 1 H), 7.68 (d, J = 7.8 Hz, 2 H), 7.38–7.280 (m, 5 H), 7.23 (d, J = 7.8 Hz, 2 H), 5.62 (s, 2 H), 5.60 (m, 1 H), 5.56 (m, 1 H), 2.49 (t, J = 2.1 Hz, 1 H), 1.36 (s, 3 H), 0.86 (s, 3 H); ¹³C NMR of 38 (CDCl₃) δ 148.1, 145.4, 138.9, 135.4, 131.3, 129.4, 128.8, 128.3, 127.94, 127.92, 125.5, 103.6, 58.7, 32.1, 26.1, 24.0, 18.4; HRMS (ESI) (MH⁺) calcd for C₂₁H₂₂N₃ 316.1808, found 316.1791.

Preparation of Triazole 39. The NH triazole 65 prepared as described above (8.1 mg; 0.036 mmol) was dissolved in 0.2 mL of CH₃OH, and then 0.11 mL of 0.510 M NaOCH₃ in CH₃OH (0.056 mmol) was added via syringe. The methanol was removed using a rotary evaporator, and the solid residue was dissolved in 1.2 mL of DMSO-*d*₆. This DMSO-*d*₆ solution of 39 was sealed in three NMR tubes and used directly for kinetic studies.

Solvolyses of Trifluoroacetates. Kinetics Procedures. Rate data reported in Table 1 were all determined using ¹H NMR spectroscopy. Approximately 5 mg of the appropriate trifluoroacetate was dissolved in 450 mg of CD₃CO₂D containing approximately 1.5 equiv of 2,6-lutidine. The same bottle of CD₃CO₂D was used for all

studies because rates depend somewhat on small amounts of water present in CD₃CO₂D from different sources. The sample was then placed in a 3 mm NMR tube, and the tube was placed in a temperature-controlled NMR probe at 25.0 °C. At appropriate time intervals, the tube was analyzed by ¹H NMR to determine amounts of starting trifluoroacetate. The signal at δ 2.75 from the 2,6-lutidine was used as an internal standard. For trifluoroacetates 8 and 17, readings were carried out with the NMR probe temperature of 25.0 °C, and the sample was placed in a constant temperature bath at 25.0 °C between readings. For trifluoroacetate 20, rates were measured at 40, 50, and 60 °C, and the rate given at 25.0 °C is an extrapolated rate. Studies on trifluoroacetates 7, 19, and 25 in ethanol (0.05 M in 2,6-lutidine) were carried out using our previously described method²⁸ where the chemical shift of the added 2,6-lutidine was monitored as a function of time.

Thermal Rearrangements of Methylenecyclopropanes. Kinetics Procedures. Rates of rearrangement of 36–38 in C₆D₆ and 39 in DMSO-*d*₆ were measured using our previously described method.^{18,19}

Computational Studies. Ab initio molecular orbital calculations were performed using the Gaussian 09 series of programs.¹⁶ Structures were characterized as energy minima via frequency calculations that showed no negative frequencies.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b00548.

Complete ref 16. Computational details ¹H and ¹³C NMR spectra of new compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail:creary.1@nd.edu

ORCID

Xavier Creary: 0000-0002-1274-5769

Notes

The authors declare no competing financial interest.

■ REFERENCES

- (1) Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 2596.
- (2) (a) Huisgen, R. *Proc. Chem. Soc. (London)* **1961**, 357. (b) Huisgen, R. *Pure Appl. Chem.* **1989**, *61*, 613.
- (3) (a) Evans, R. A. *Aust. J. Chem.* **2007**, *60*, 384. (b) Moses, J. E.; Moorhouse, A. D. *Chem. Soc. Rev.* **2007**, *36*, 1249. (c) Kempe, K.; Krieg, A.; Becer, C. R.; Schubert, U. S. *Chem. Soc. Rev.* **2012**, *41*, 176.
- (4) (a) Zhang, L.; Chen, X.; Xue, P.; Sun, H. Y.; Williams, I. D.; Sharpless, K. B.; Fokin, V. V.; Jia, G. *J. Am. Chem. Soc.* **2005**, *127*, 15998. (b) Rasmussen, L. K.; Boren, B. C.; Fokin, V. V. *Org. Lett.* **2007**, *9*, 5337. (c) Johansson, J. R.; Lincoln, P.; Nordén, B.; Kann, N. J. *Org. Chem.* **2011**, *76*, 2355.
- (5) (a) Yan, W.; Liao, T.; Tuguldur, O.; Zhong, C.; Petersen, J. L.; Shi, X. *Chem. - Asian J.* **2011**, *6*, 2720. (b) Holzer, W. *Tetrahedron* **1991**, *47*, 9783. (c) Mashraqui, S. H.; Kumar, S.; Mudaliar, C. D. *Bull. Chem. Soc. Jpn.* **2001**, *74*, 2133.
- (6) (a) Ehrenson, S.; Brownlee, R. T. C.; Taft, R. W. *Prog. Phys. Org. Chem.* **1973**, *10*, 1. See also (b) Charton, M. *Prog. Phys. Org. Chem.* **1981**, *13*, 119.
- (7) Fischer, A.; King, J. M.; Robinson, F. P. *Can. J. Chem.* **1978**, *56*, 3059.
- (8) Grob, C. A.; Schaub, B.; Schlageter, M. G. *Helv. Chim. Acta* **1980**, *63*, 57.
- (9) Holtz, H. D.; Stock, L. M. *J. Am. Chem. Soc.* **1964**, *86*, 5188.
- (10) Cole, T. W., Jr.; Mayers, C. J.; Stock, L. M. *J. Am. Chem. Soc.* **1974**, *96*, 4555.

- (11) Stetter, H.; Mayer, J. *Chem. Ber.* **1962**, *95*, 667.
- (12) Taft, R. W.; Price, E.; Fox, I. R.; Lewis, I. C.; Andersen, K. K.; Davis, G. T. *J. Am. Chem. Soc.* **1963**, *85*, 709.
- (13) (a) Brown, H. C.; Okamoto, Y. *J. Am. Chem. Soc.* **1957**, *79*, 1913. (b) Stock, L. M.; Brown, H. C. *Adv. Phys. Org. Chem.* **1963**, *1*, 35.
- (14) Creary, X.; Anderson, A.; Brophy, C.; Crowell, F.; Funk, Z. *J. Org. Chem.* **2012**, *77*, 8756.
- (15) Woerner, F. P.; Reimlinger, H. *Chem. Ber.* **1970**, *103*, 1908.
- (16) Frisch, M. J. et al. *Gaussian 09*, Revision A.02; Gaussian, Inc., Wallingford, CT, 2009. See Supporting Information for the entire reference.
- (17) (a) Peters, E. N. *J. Am. Chem. Soc.* **1976**, *98*, 5627. (b) Peters, E. N. *J. Org. Chem.* **1977**, *42*, 1419.
- (18) For a review and leading references, see Creary, X. *Acc. Chem. Res.* **2006**, *39*, 761.
- (19) Creary, X.; Engel, P. S.; Kavaluskas, N.; Pan, L.; Wolf, A. *J. Org. Chem.* **1999**, *64*, 5634.
- (20) Radical stabilization energies of benzylic radicals are determined from the value of ΔE in [Scheme 8](#).
- (21) The N_1-N_2 sodium complex **45** is lower energy than the cation with Na^+ bonded to N_2 and N_3 .
- (22) (a) Stanger, A. *Chem. Commun.* **2009**, 1939. (b) Ramsden, C. A. *Tetrahedron* **2010**, *66*, 2695.
- (23) Schleyer, P. v. R.; Maerker, C.; Dransfeld, A.; Jiao, H.; Hommes, N. J. R. v. E. *J. Am. Chem. Soc.* **1996**, *118*, 6317.
- (24) Lee, B.-Y.; Park, S. R.; Jeon, H. B.; Kim, K. S. *Tetrahedron Lett.* **2006**, *47*, 5105.
- (25) Shao, C.; Wang, X.; Xu, J.; Zhao, J.; Zhang, Q.; Hu, Y. *J. Org. Chem.* **2010**, *75*, 7002.
- (26) Bobrich, M.; Schwarz, H.; Levsen, K.; Schmitz, P. *Org. Mass Spectrom.* **1977**, *12*, 549.
- (27) Ulich, L. H.; Adams, R. *J. Am. Chem. Soc.* **1921**, *43*, 660.
- (28) Creary, X.; Jiang, Z. *J. Org. Chem.* **1994**, *59*, 5106.
- (29) For the general procedure on preparation of diazocompounds, see Creary, X. *Org. Synth.* **1986**, *64*, 207.