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

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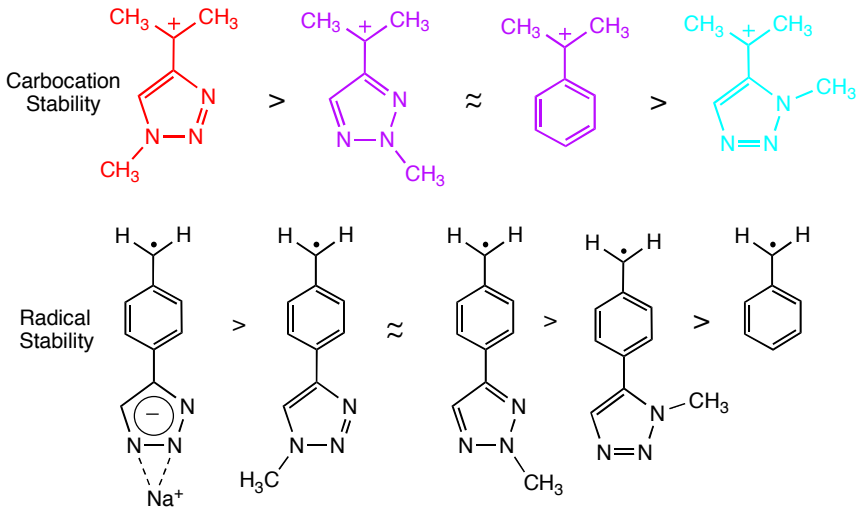
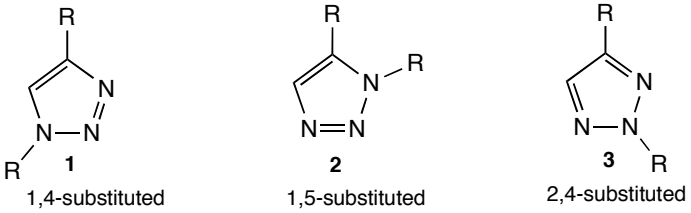
Abstract



Three fluorobenzenes substituted with *meta*-triazole groups have been prepared and ^{19}F 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, while the 1,5-triazole is carbocation destabilizing. γ^+ values indicate that the 1,4 triazole group is cation stabilizing relative to the phenyl group, while 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]

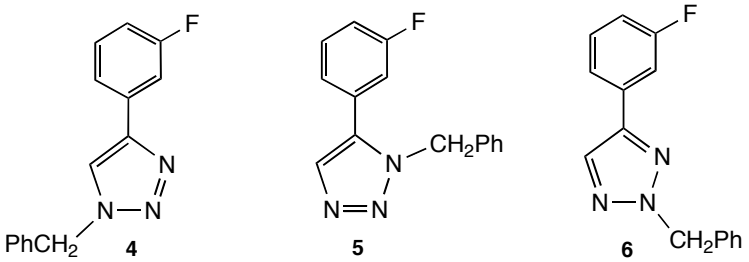


Despite the thousands of papers dealing with triazoles of structure **1**-**3**, the simple electronic properties of these substrates have not been thoroughly studied. Are they electron donor or electron acceptor groups? Are triazoles carbocation stabilizing groups? Are they radical stabilizing groups, and if so, how stabilizing? We sought to answer these questions by determining classical σ_I, σ^+ and $\sigma^{\cdot}$ 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_I Values. Inductive effects of substituents, σ_I values, are measured by a variety of methods. These include the original Taft σ_I 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 ions[7] and from

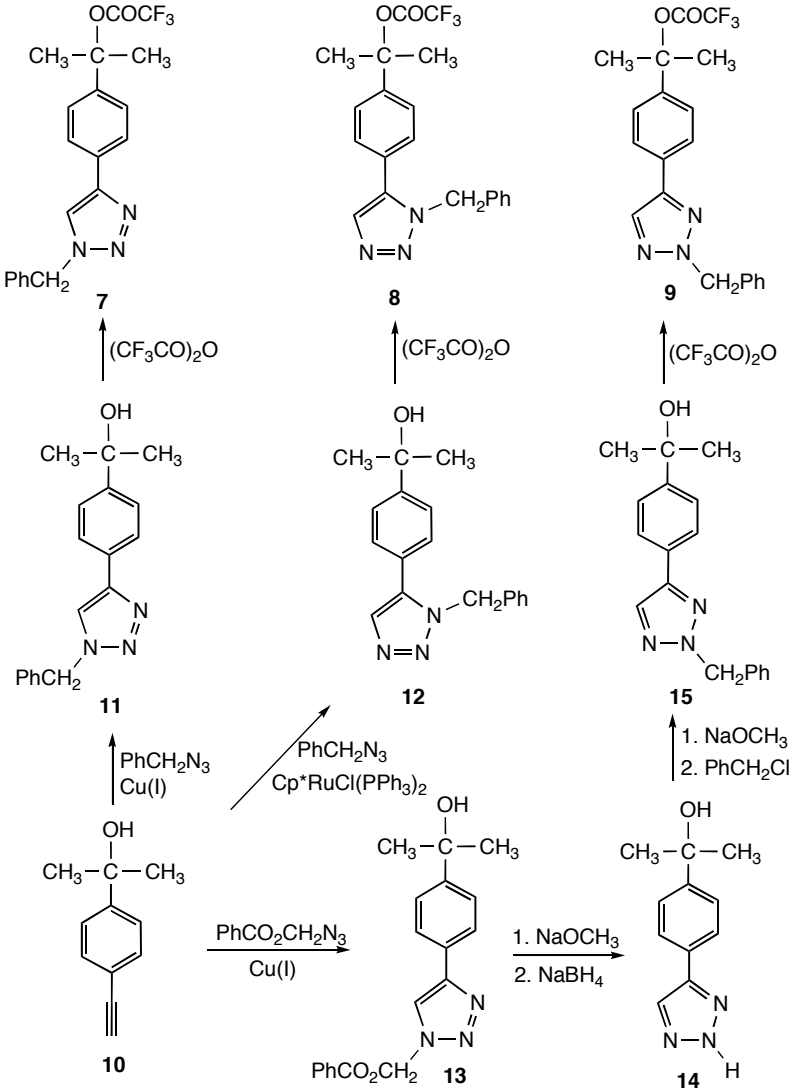
dissociation constants of 4-substituted quinuclidines.[8] Dissociation constants of 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids,[9] 4-substituted cubane-1-carboxylic acids,[10] and 3-substituted adamantane carboxylic acids[11] have also been used to evaluate σ_I values. These methods of determining various $\boldsymbol{\sigma_I}$ 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 ^{19}F chemical shifts of a series of *m*-substituted fluorobenzenenes correlated well with σ_I values.[12] Hence the fluorobenzenes **4**-**6**, where the fluorine is *meta* to the triazole 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_I values are shown. By comparison, the σ_I value for the moderately electron-withdrawing CH_3CO (acetyl) group is 0.30.



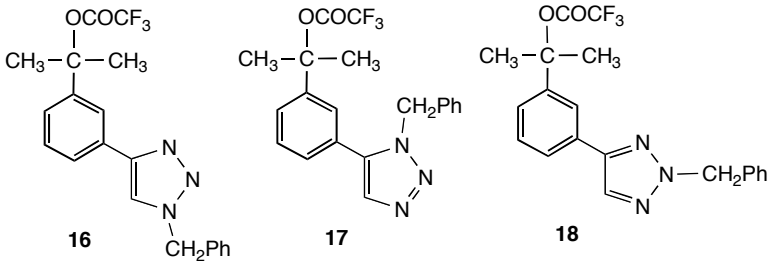
Carbocation Effects. Determination of σ^+ and γ^+ Values. Attention was next turned to σ^+ values,[13] which are a measure of carbocation stabilizing effects on cumyl carbocations. Cumyl trifluoroacetates **7**, **8**, and **9** were prepared, where the effects of the *para*-triazole groups on rates of solvolyses of these substrates could be measured, and the corresponding σ^+ values could be calculated. Also prepared were the *meta*-analogs **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*-analog of **10**.

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

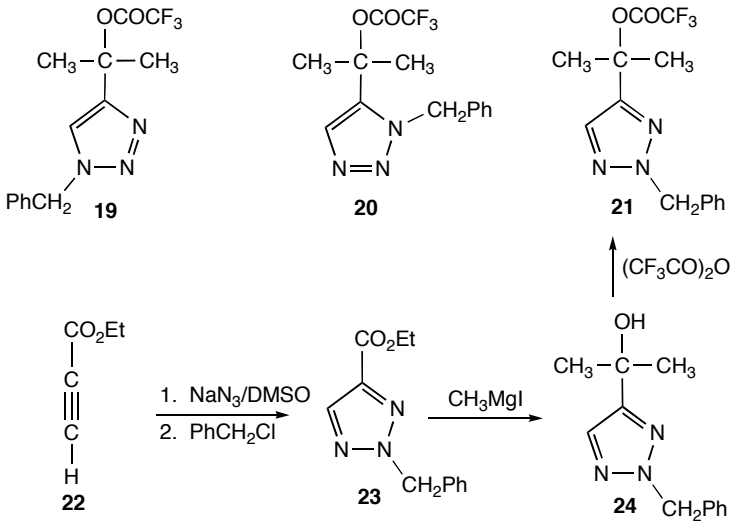


Scheme 2. Substrates for Determination of σ^{+}_{meta}.



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.

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



The solvent chosen for most kinetic studies was CD_3CO_2D, while EtOH was used for reactions that were too fast to measure in CD_3CO_2D. 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 CD_3CO_2D, 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. By way of contrast, the triazole group in **8** considerably slows the acetolysis rate and is therefore destabilizing with respect to the cumyl cation ($\sigma^+ = +0.23$). The rate enhancing effects in **7** and **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 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_I 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** level[16] (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 $PhCH_2$ group has been replaced by CH_3).

Scheme 4. Resonance Stabilization of Cations 26 and 27.

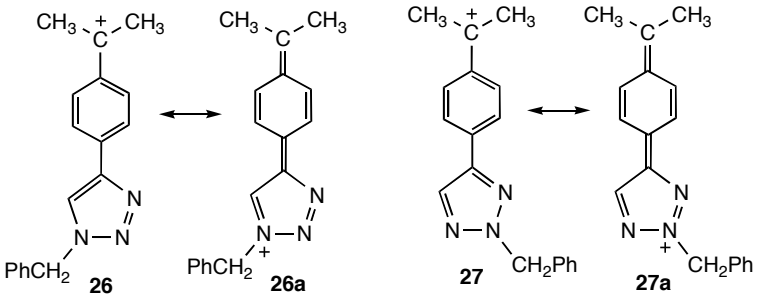
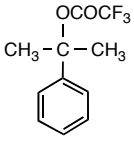
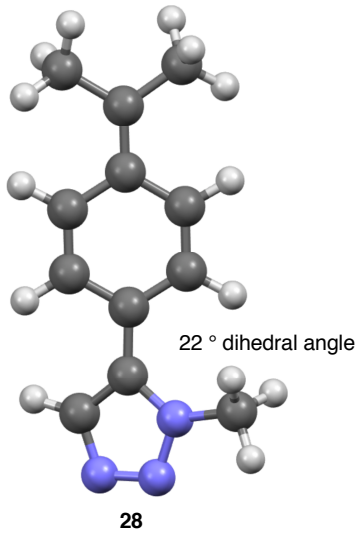


TABLE 1. Solvolysis Rates for Substrates in CD_3CO_2D and EtOH.

Compound	Solvent	T (°C)	k (s^{-1})	k_{rel}
7	EtOH	20.0	6.60×10^{-4}	8.54
8	CD_3CO_2D	25.0	3.56×10^{-5}	0.075
9	CD_3CO_2D	25.0	1.27×10^{-3}	2.67
16	CD_3CO_2D	25.0	1.43×10^{-4}	0.30
17	CD_3CO_2D	25.0	1.65×10^{-5}	0.035
18	CD_3CO_2D	25.0	8.61×10^{-5}	0.18
19	EtOH	20.0	5.66×10^{-3}	73.3
20	CD_3CO_2D	25.0	2.37×10^{-6}	0.005
21	CD_3CO_2D	25.0	2.73×10^{-4}	0.575
 **25**	EtOH	20.0	7.72×10^{-5}	1.00
	CD_3CO_2D	25.0	4.74×10^{-4}	1.00



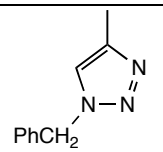
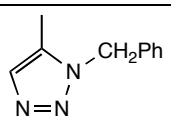
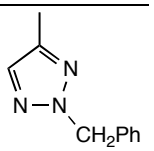
28

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

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 (σ^+_{meta} = 0.32) suggests that this 1,5-triazole is about as electron-withdrawing as a *m*-chloro substituent.

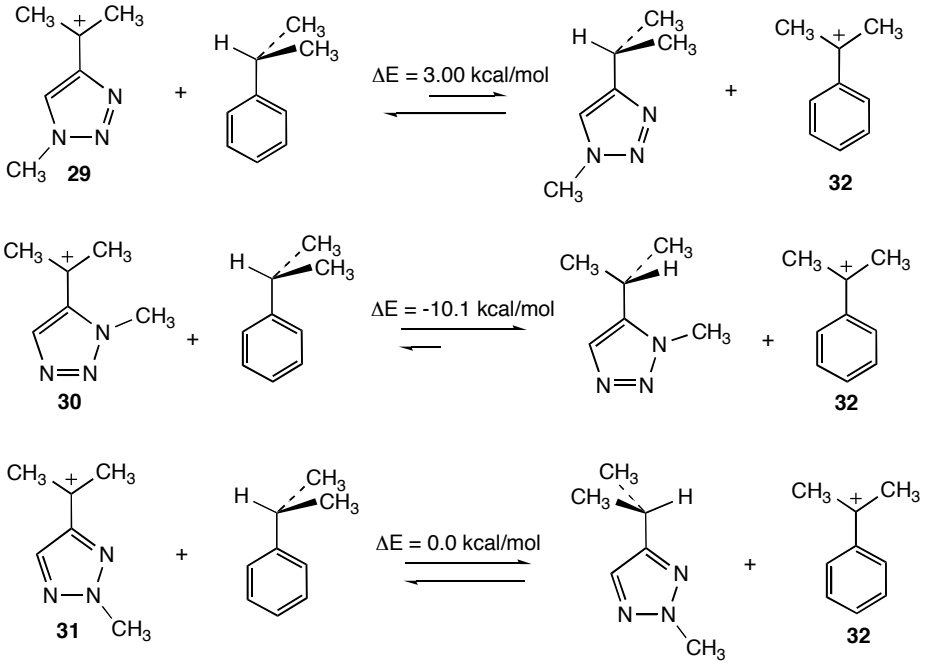
Attention was next turned to the trifluoroacetates **19-21**, where direct comparison of the triazole groups with the phenyl group allows calculation of γ^+ values (group σ^+ values).[17] The trifluoroacetate **19** is a very reactive compound that was isolated with difficulty. It is so reactive that it decomposed in solvents such as $CDCl_3$ and C_6D_6 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 CD_3CO_2D, and a relatively fast NMR kinetic method could be used to monitor rates. Trifluoroacetate **19** solvolyzed with a half-life of only two minutes 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 CD_3CO_2D. In other words, trifluoroacetate **19** is 1.47 x 10^4 times more reactive than **20**. This dramatic rate spread is indicative of a large difference in 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 since, 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)

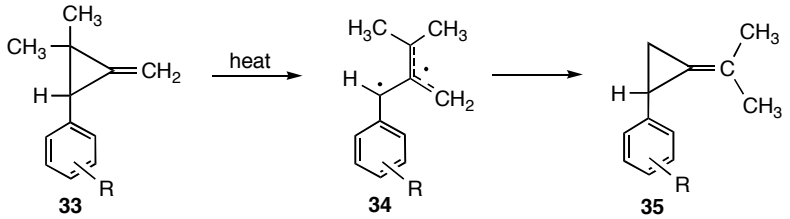
Scheme 5. Isodesmic Reactions of Triazole Substituted Cations with Cumene.



were therefore used to evaluate carbocation stabilities. Cation **29** is more stable than cumyl cation **32**, while cation **30** is 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 is 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 · Values. Attention was next turned to the effect of triazole groups on radicals, i.e., free radical substituent constants, σ ·.[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 via a radical mechanism.[18] Substituents R can stabilize or destabilize the radical intermediate **34** and

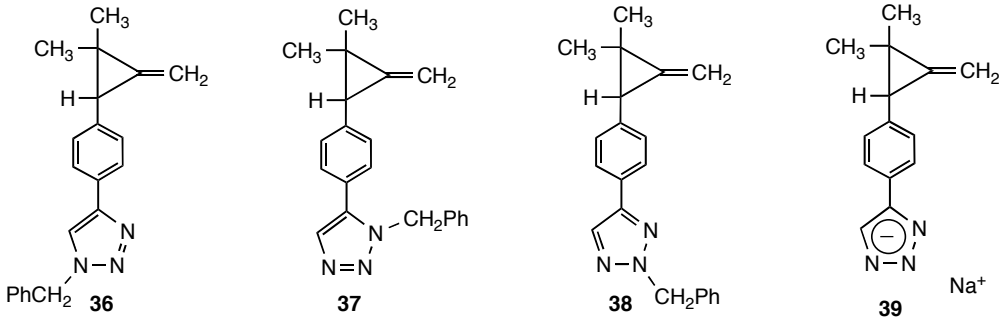
Scheme 6. Methylenecyclopropane Rearrangement Used for Determination of σ · Values.



33 **34** **35**

affect the rearrangement rate. The substrates **36**-**39** (Scheme 7) have now been 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.

Scheme 7. Triazoles Used for Determination of σ ·.



36 **37** **38** **39**

TABLE 3. Rearrangement Rates for Substrates **33**, and **36-39**.

Compound	Solvent	T (°C)	k (s^{-1})	k_{rel}
33 R = H	C_6D_6	80.0	5.57×10^{-5}	1.00
	C_6D_6	70.0	1.72×10^{-5}	
	C_6D_6	60.0	5.05×10^{-6}	
36	C_6D_6	80.0	1.66×10^{-4}	2.98
	C_6D_6	70.0	5.55×10^{-5}	
	C_6D_6	60.0	1.64×10^{-5}	
37	C_6D_6	80.0	1.10×10^{-4}	1.98
	C_6D_6	70.0	3.50×10^{-5}	
	C_6D_6	60.0	1.05×10^{-5}	
38	C_6D_6	80.0	1.68×10^{-4}	3.02
	C_6D_6	70.0	5.51×10^{-5}	
	C_6D_6	60.0	1.66×10^{-5}	
39	DMSO-d_6	80.0	4.69×10^{-4}	5.93
	DMSO-d_6	60.0	9.42×10^{-5}	
	DMSO-d_6	50.0	1.44×10^{-5}	
	DMSO-d_6	40.0	3.88×10^{-6}	

The first thing that is apparent 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. 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 studies[19] have shown a very good correlation between the rearrangement rate of

methylenecyclopropanes **33** and the B3LYP/6-31G* calculated radical stabilization energy[20] 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 shown in Scheme 8 are a very good measure of

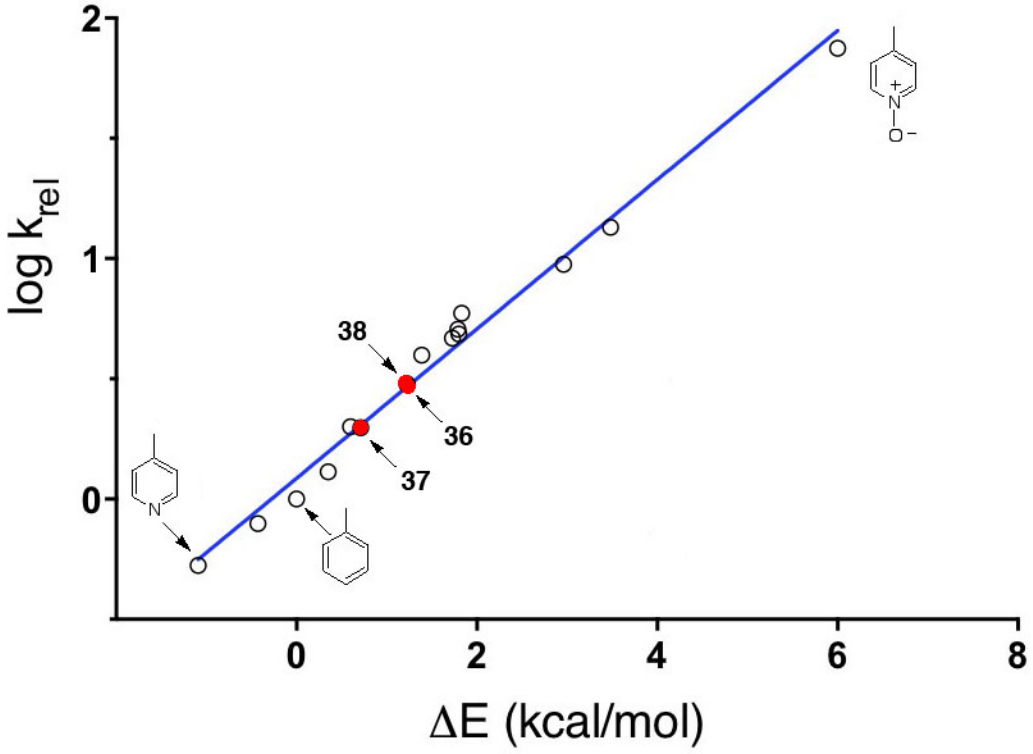
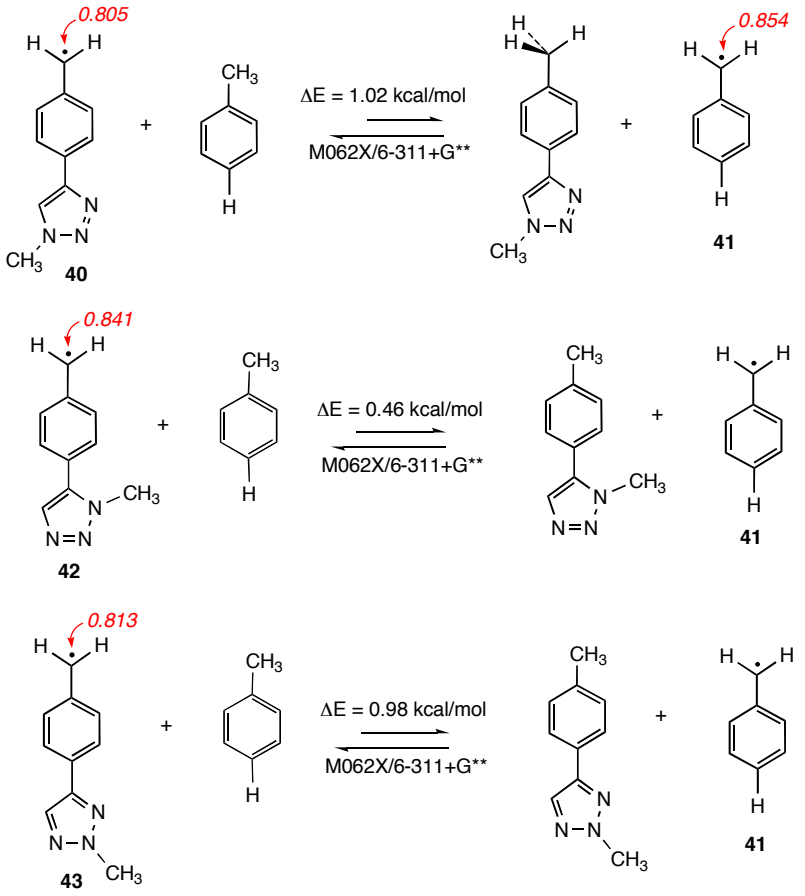


Figure 2. A plot of log k_{rel} for the rearrangement of **33** vs. the radical stabilization energy of the analogous benzylic radical.

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 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.

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



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). 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**.

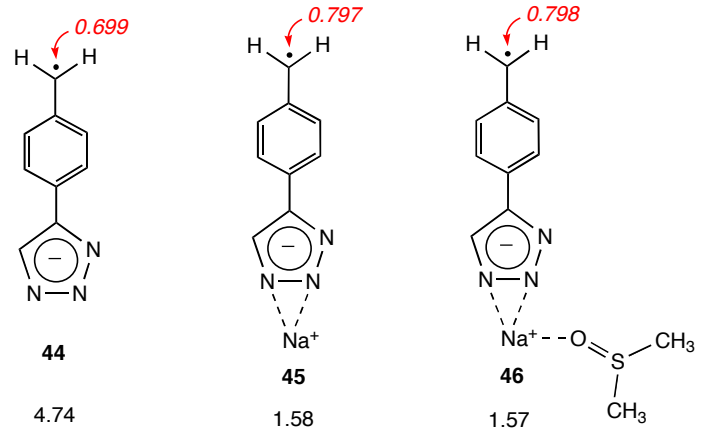


Figure 3. M062X/6-311+G** calculated radical stabilization energies.

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 Nuclear 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

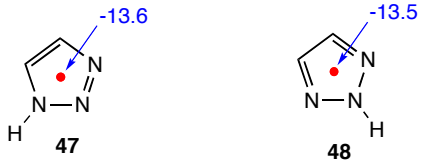


Figure 4. Calculated NICS values for triazoles **47** and **48**.[22]

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 5 shows the relative energies of these six molecules. The nonaromatic analogs are all significantly higher in energy than the aromatic triazoles. Of interest is the magnitude of the energy differences between the aromatic triazoles and their nonaromatic analogs. The 37.1 kcal/mole 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**.

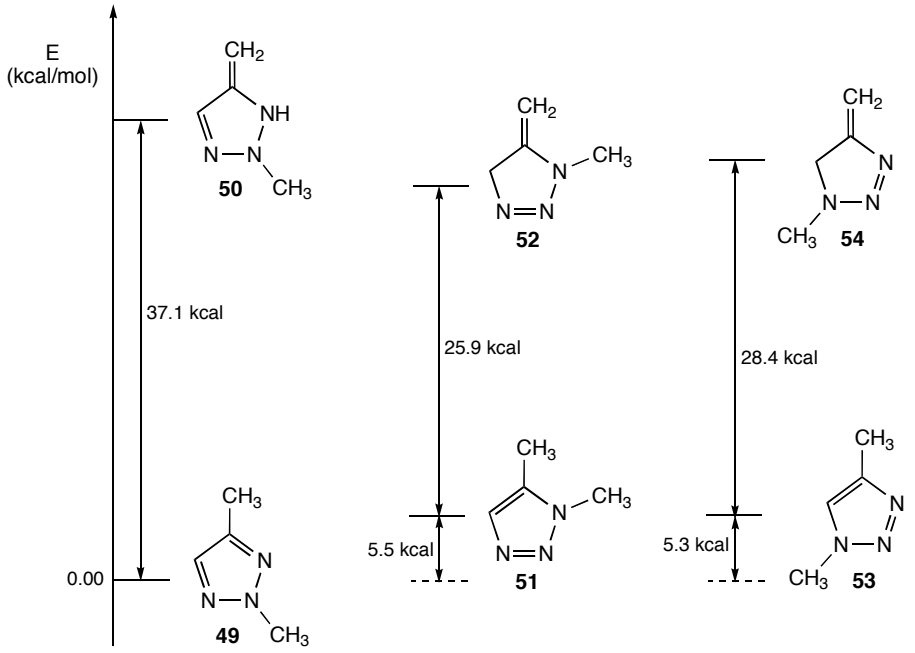


Figure 5. B3LYP/6-311+G** calculated relative energies of triazoles and nonaromatic analogs.

Conclusions. 1,2,3-triazoles are inductively electron-withdrawing groups as revealed by σ_I 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 due to a stronger inductive effect that is not offset by resonance. All three of the isomeric triazoles, as well as the anionic triazole analog, 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 Brucker 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 130 mg of $PhCH_2N_3$ (0.977 mmol) in 2 mL of methylene chloride and 2 mL of water was stirred and 18 mg of copper sulfate pentahydrate was added. After the copper sulfate dissolved, 40 mg of sodium ascorbate was then added in small portions and stirring was continued for 24 h. The mixture was then taken up into ether, washed with water, 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. ^{1}H 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_{C-F} = 246 Hz), 147.1 (d, J_{C-F} = 2.7 Hz), 134.5, 132.7 (d, J_{C-F} = 8.7 Hz), 130.4 (d, J_{C-F} = 8.4 Hz), 129.2, 128.9, 128.1, 121.3 (d, J_{C-F} = 3.0 Hz), 119.9, 115.0 (d, J_{C-F} = 21.3 Hz), 112.6 (d, J_{C-F} = 22.9 Hz), 54.3. HRMS (ESI) (MH^+) calculated for $C_{15}H_{13}FN_3$ 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 Cp*RuCl(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 as 10 mg of Cp*RuCl(PPh_3)$_2$ was added. The solution was heated to reflux 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. ^{1}H 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_{C-F} = 248 Hz), 136.9, 135.1, 133.4, 130.7 (d, J_{C-F} = 8.6 Hz), 128.9, 128.8 (d, J_{C-F} = 7.9 Hz), 128.3, 127.1, 124.6 (d, J_{C-F} = 3.1 Hz), 116.6 (d, J_{C-F} = 21 Hz), 116.0 (d, J_{C-F} = 23 Hz), 52.0. HRMS (ESI) (MH^+) calculated for $C_{15}H_{13}FN_3$ 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 $PhCO_2CH_2Cl$[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, saturated NaCl solution, and then dried over Na_2SO_4. After filtration, the solvent was removed using a rotary evaporator. NMR analysis showed $PhCO_2CH_2N_3$ 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 $PhCO_2CH_2N_3$ (181 mg; 58% yield) eluted with 1-2% ether in pentane as a solid, mp 47-48 °C. ^{1}H 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) ($M+Na^+$) calculated for $C_8H_7N_3NaO_2$ 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 $PhCO_2CH_2N_3$ 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, 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. ^{1}H 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_{C-F} = 246 Hz), 147.3, 134.2, 132.1 (d, J_{C-F} = 8.5 Hz), 130.5 (d, J_{C-F} = 8.4 Hz), 130.1, 128.7, 128.0, 121.8, 121.5 (d, J_{C-F} = 3.0 Hz), 115.3 (d, J_{C-F} = 21 Hz), 112.8 (d, J_{C-F} = 23. Hz), 70.0. HRMS (ESI) (MH^+) calculated for $C_{16}H_{13}FN_3O_2$ 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 CH_3OH and 2.8 mL of 0.510 M $NaOCH_3$ (1.428 mmol) in CH_3OH was then added. After 15 min, 32 mg (0.847 mmol) of $NaBH_4$ was added, the mixture was stirred for 3 h, and the CH_3OH 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 $NaHCO_3$ with stirring. The aqueous component of the mixture was carefully decanted from the solid precipitate using a pipet. The solid was then 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 $PhCO_2CH_3$.

The crude NH triazole above was partially dissolved in 2 mL of methanol and 2.1 mL of 0.510 M $NaOCH_3$ (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 150 mg (1.186 mmol) of $PhCH_2Cl$ was then 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, saturated NaCl solution, dried over a mixture of Na_2SO_4 and $MgSO_4$, 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. ^{1}H NMR of **6** ($CDCl_3$) 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). ^{13}C NMR of **6** ($CDCl_3$) δ 163.1 (d, $J_{C\text{-}F}$ = 246 Hz), 147.0 (d, $J_{C\text{-}F}$ = 2.8 Hz), 135.1, 132.5 (d, $J_{C\text{-}F}$

= 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^+) calculated for $C_{15}H_{13}FN_3$ 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 CH_2Cl_2 and 2 mL of water was stirred and 36 mg of $CuSO_4$ pentahydrate was added. After the $CuSO_4$ dissolved, 73 mg of sodium ascorbate was then 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 $MgSO_4$, 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. ^{1}H NMR of **11** ($CDCl_3$) 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). ^{13}C NMR of **11** ($CDCl_3$) 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^+) calculated for $C_{18}H_{20}N_3O$ 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*$RuCl(PPh_3)_2$ was added. The mixture was then gently refluxed for 2 h. The entire mixture was then 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. ^{1}H NMR of **12** ($CDCl_3$) 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). ^{13}C NMR of **12** ($CDCl_3$) 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^+) calculated for $C_{18}H_{20}N_3O$ 294.1601, found 294.1604.

Preparation of 2,4-Substituted Triazoles. 2,4-Substituted triazoles were prepared by reaction of the appropriate alkyne with $PhCO_2CH_2N_3$ catalyzed by $CuSO_4$/sodium ascorbate. This initial triazole was reacted sequentially with $NaOCH_3$ in CH_3OH followed by $NaBH_4$. The resultant NH triazole was then deprotonated with $NaOCH_3$ 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 CH_2Cl_2 was added followed by 200 mg (1.250 mmol) of the alcohol **10**. Water (2 mL) was added followed by 18 mg of $CuSO_4$ pentahydrate. The mixture was stirred to dissolve the $CuSO_4$. 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 Na_2SO_4, 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. ^{1}H NMR ($CDCl_3$) 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). ^{13}C NMR ($CDCl_3$) 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^+) calculated for $C_{19}H_{20}N_3O_3$ 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 and 2.7 mL of 0.51 M $NaOCH_3$ in CH_3OH (1.377 mmol) was then added while stirring. The triazole completely dissolved. After 1 h, 40 mg of $NaBH_4$ was added and the mixture was stirred for an additional 1 h. The CH_3OH 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 $NaHCO_3$. The aqueous phase was then carefully decanted from the precipitated triazole **14** using a pipet. The precipitate was then washed with about 2 mL of water and the water was again decanted from the solid. The flask containing the triazole **14** was then 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 $NaOCH_3$ (1.02 mmol) in CH_3OH. The CH_3OH was then removed using a rotary evaporator and the residue was dissolved in 5 mL of DMSO. Benzyl chloride (133 mg; 1.051 mmol) was then added and the mixture was stirred at room temperature for 20 h. The mixture was then transferred to a separatory funnel using ether and water. The ether extract was washed with water, 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 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. ^{1}H NMR of **15** ($CDCl_3$) 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). ^{13}C NMR of **15** ($CDCl_3$) 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^+) calculated for $C_{18}H_{20}N_3O$ 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 and 56 mg of trifluoroacetic anhydride (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. ^{1}H 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. ^{1}H 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. ^{1}H 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-1*H*-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 then 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. ^{1}H 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^+) calculated for $C_{18}H_{20}N_3O$ 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. ^{1}H 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-1*H*-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 $Cp^*RuCl(PPh_3)_2$ 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. ^{1}H 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^+) calculated for $C_{18}H_{20}N_3O$ 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. ^{1}H 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-2*H*-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 then 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 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 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)-1*H*-1,2,3-triazol-1-yl)methyl benzoate, **59**, eluted with 80-100% ether as an oil. ^{1}H 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^+) calculated for $C_{19}H_{20}N_3O_3$ 338.1499, found 338.1505.

The triazole **59** prepared above was dissolved in 1.5 mL of methanol and 2.7 mL of 0.51 M $NaOCH_3$ in CH_3OH (1.377 mmol) was then 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 then 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 then 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, 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-2*H*-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. ^{1}H 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^+) calculated for $C_{18}H_{20}N_3O$ 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. ^{1}H 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-ol[14] 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. ^{1}H 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-ol[14] 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. ^{1}H 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. ^{1}H 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 then 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 then added. The mixture was stirred at room temperature for 3 hr 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, 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. ^{1}H 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^+) calculated for $C_{12}H_{14}N_3O_2$ 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 re-cooled in ice. The solution was then quenched with aqueous NH_4Cl solution. The ether extract was separated and washed with water, 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. ^{1}H 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) ($M+Na^+$) calculated for $C_{12}H_{15}N_3NaO$ 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** (R = *p*-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). ^{1}H 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^+) calculated for $C_{14}H_{14}$ 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 then 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). ^{1}H 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^+) calculated for $C_{21}H_{22}N_3$ 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 $Cp^*RuCl(PPh_3)_2$ 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. ^{1}H 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^+) calculated for $C_{21}H_{22}N_3$ 316.1808, found 316.1819.

Preparation of (4-(4-(2,2-dimethyl-3-methylenecyclopropyl)phenyl)-1*H*-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 CH_2Cl_2 and 1.5 mL of water was stirred and 12 mg of $CuSO_4$ pentahydrate was added. After the $CuSO_4$ dissolved, 30 mg of sodium ascorbate was then 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 Na_2SO_4, 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. ^{1}H NMR of **64** ($CDCl_3$) 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). ^{13}C NMR of **64** ($CDCl_3$) 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^+) calculated for $C_{22}H_{22}N_3O_2$ 360.1707, found 360.1689.

Preparation of Triazole 38. The triazole **64** prepared above (143 mg) was partially dissolved in 3 mL of CH_3OH and 1.20 mL of 0.51 M in $NaOCH_3$ in CH_3OH was then added with stirring. The triazole immediately dissolved. After 20 min 16 mg of $NaBH_4$ was added. The mixture was stirred for 1 h and the CH_3OH 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 then brought to pH of ~5 by adding small portions of $NaHCO_3$ 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 then 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 $PhCO_2CH_3$ and gave 80 mg of 4-(4-(2,2-dimethyl-3-methylenecyclopropyl)phenyl)-2*H*-1,2,3-triazole, **65**.

The NH triazole **65** prepared above (80 mg) was dissolved in 2 mL of CH_3OH and 1.00 mL of 0.510 M $NaOCH_3$ was added. After 15 min the CH_3OH was removed using a rotary evaporator and the solid residue was dissolved in 2 mL of DMSO. Benzyl chloride (70 mg) was then 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, saturated NaCl solution, and dried over Na_2SO_4. 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. ^{1}H NMR of **38** ($CDCl_3$) 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). ^{13}C NMR of **38** ($CDCl_3$) 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^+) calculated for $C_{21}H_{22}N_3$ 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 CH_3OH and 0.11 mL of 0.510 M $NaOCH_3$ in CH_3OH (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 ^{1}H NMR spectroscopy. Approximately 5 mg of the appropriate trifluoroacetate was dissolved in 450 mg of CD_3CO_2D containing approximately 1.5 equivalents of 2,6-lutidine. The same bottle of CD_3CO_2D was used for all studies since rates depend somewhat on small amounts of water present in CD_3CO_2D 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 ^{1}H NMR to determine amounts of starting trifluoroacetate. The signal at δ 2.75 due to 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 method[28] 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 C_6D_6 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: xxx.

Complete reference 16.

Computational details

^{1}H and ^{13}C NMR spectra of new compounds

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Notes

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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. *P. 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. *Helvetica Chim. Acta* **1980**, *63*, 57.

(9) Holtz, H. D.; Stock, L. M. *J. Am. Chem. Soc*. **1964**, *86*, 5188.

(10) Cole, Jr., T. W.; 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.

(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.