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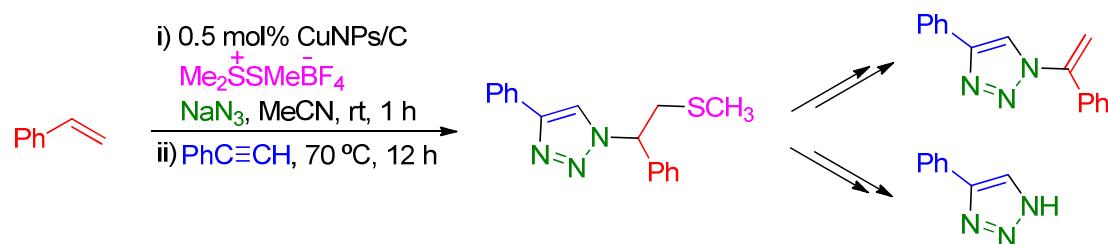
Alkenes as Azido Precursors for the One-Pot Synthesis of 1,2,3-Triazoles Catalyzed by Copper Nanoparticles on Activated Carbon

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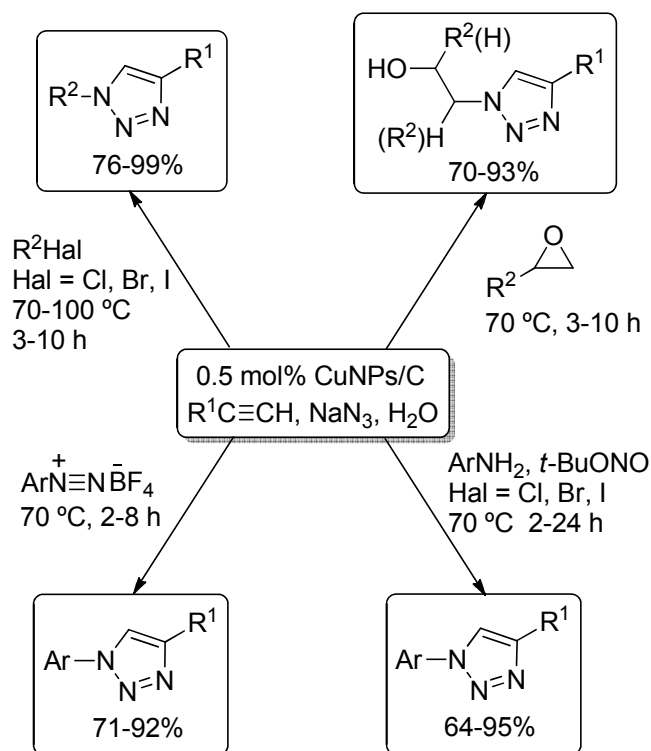
Abstract: A one-pot protocol for the synthesis of 1,2,3-triazoles has been developed starting from inactivated alkenes and based on two click reactions: the azidosulfonylation of the carbon-carbon double bond and the copper-catalyzed azide-alkyne cycloaddition (CuAAC). High yields of the β -methylsulfanyl triazoles have been attained using CuNPs/C as catalyst, with other commercial copper catalysts being completely inactive. The versatility of the methylsulfanyl group has been demonstrated through a series of synthetic transformations, including the direct access to 1-vinyl and 4-monosubstituted triazoles.

Click chemistry has become one of the most important concepts in modern chemistry.¹ It represents certain highly efficient and reliable reactions which are modular, wide in scope, high yielding, stereospecific, and proceed under simple and benign conditions with straightforward procedures for product isolation. Recently, the click's chemistry first decade has been celebrated,² with an endless list of disciplines having been benefited along this time from the unique advantages offered by this type of reactions. The copper-catalyzed azide-alkyne cycloaddition (CuAAC)³ fulfils the aforementioned series of rigorous criteria, as defined by Sharpless et al., turning this reaction into the click reaction by antonomasia.⁴ The nucleophilic opening of spring-loaded rings (i.e., epoxides, aziridines, cyclic sulfates, cyclic sulfamidates, aziridinium ions, and episulfonium ions) also belongs to the privileged list of click reactions because they are reliable, stereospecific, often highly regioselective, and nearly quantitative.¹

The CuAAC has been traditionally implemented with pre-formed organic azides. More advantageous are, however, the methodologies in which the organic azides are generated *in situ* from organic halides⁵ (three-component azide-alkyne cycloaddition) because (a) hazards derived from their isolation and handling are minimized, (b) the time consuming and waste generating additional synthetic step are avoided, and (c) the common organic solvents utilized (e.g., dioxane, toluene, DMF, dichloromethane, hexane) can be replaced by neat water. In this vain, efforts have been recently devoted to develop new catalytic systems which allow the CuAAC from other different azide precursors, namely: amines,⁶ tosylates,⁷ diarylidodonium salts,⁸ epoxides,⁹ alcohols,¹⁰ and boronic acids.¹¹ Favi et al. reported the one-pot copper(II)-catalyzed aza-Michael addition of trimethylsilyl azide to 1,2-diaza-1,3-dienes and copper(I)-catalyzed 1,3-dipolar cycloaddition of the *in situ*-generated α -azidohydrazones with alkynes.¹² However, alkenes are the most commonly available starting materials which can provide a carbon framework. To the best of our knowledge, the synthesis of 1,2,3-triazoles from inactivated alkenes has never been described.

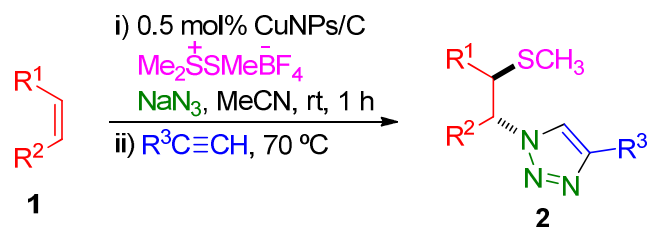
On the other hand, there is an upsurge of interest in the use of nanostructured copper catalysts for the CuAAC because of their large surface-to-volume ratio, varied morphology, and sustainable catalytic applications.¹³ Owing to our dedication to study and understand the reactivity of metal colloids,¹⁴ we found out that active copper [obtained from $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, lithium metal, and a catalytic amount of 4,4'-di-*tert*-butylbiphenyl (DTBB) in THF at room temperature] was able to reduce different organic functionalities under very mild conditions.¹⁵ We also discovered that copper nanoparticles (CuNPs) are formed when the active copper is generated from anhydrous CuCl_2 under the above mentioned conditions. These unsupported copper nanoparticles (10 mol%) effectively catalysed the CuAAC in the presence of triethylamine at 65 °C in THF.¹⁶ Remarkably short reaction times (10–120 min), comparable to those previously reported under microwave heating, were recorded in the absence of any stabilising additive or ligand. Unfortunately, the CuNPs underwent dissolution under the reaction conditions which precluded their reuse. More recently, we introduced a catalyst consisting of oxidized copper nanoparticles on activated carbon (CuNPs/C), readily prepared under mild conditions, which exhibited a high versatility in the multicomponent click synthesis of 1,2,3-triazoles in water.¹⁷ Not only organic halides but diazonium salts, anilines, and epoxides were successfully used as azide precursors in the CuAAC (Scheme 1). We want to present herein the first one-pot transformation of inactivated olefins into 1,2,3-triazoles by taking advantage of two consecutive click reactions: (a) the ring opening of in-situ generated episulfonium ions by the azide anion and (b) the reaction of the in-situ generated azides with alkynes catalyzed by CuNPs/C.

SCHEME 1. Multicomponent Synthesis of 1,2,3-Triazoles from Different Azide Precursors Catalyzed by CuNPs/C in Water.




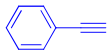
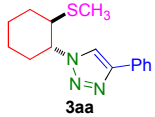
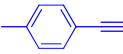
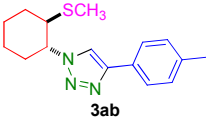
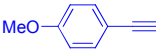
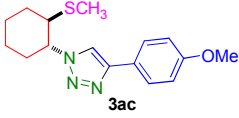
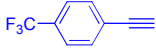
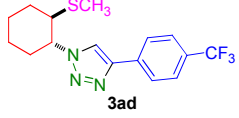
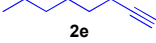
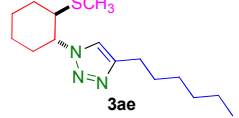

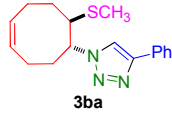

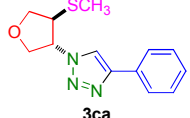
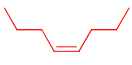
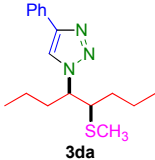
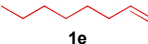
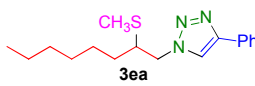
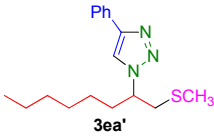

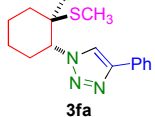
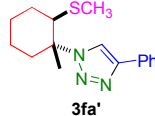

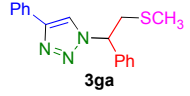
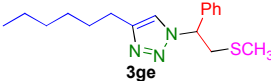
We envisaged the potential transformation of alkenes into triazoles inspired by the azasulfenylation of alkenes developed by Trost et al.¹⁸ In this methodology, an alkene was treated with dimethyl(methylthio)sulfonium tetrafluoroborate (DMTSF)¹⁹ at 0 °C to room temperature, followed by the addition of a nitrogen nucleophile at room temperature and stirring for 1–4 days. After an optimization of the reaction conditions (i.e, solvent, catalyst, temperature, and reaction time) we discovered a more convenient variation of this method in which the alkene was directly mixed with CuNPs/C, DMTSF, and NaN_3 in MeCN to produce the corresponding methylsulfanyl azide in only 1 h at room temperature; apparently, the CuNPs accelerate this process. The subsequent reaction with the alkyne represents, to the best of our knowledge, the first example of triazole synthesis from an inactivated alkene in one pot (Scheme 2).

SCHEME 2. Optimized Conditions for the One-Pot Synthesis of Triazoles from Alkenes Catalyzed by CuNPs/C.



With this methodology in hand, a series of representative alkenes and different alkynes were subjected to this one-pot consecutive double-click protocol (Table 1). We first studied the reaction of cyclohexene with various electronically different alkynes (Table 1, entries 1–5). Good yields were recorded for the electronically neutral alkynes phenylacetylene (**2a**) and *p*-tolylacetylene (**2b**) as well as for the electronically rich and poor 4-methoxyphenylacetylene (**2c**) and 4-(trifluoromethyl)phenylacetylene (**2d**), respectively (Table 1, entries 1–4). The aliphatic alkyne oct-1-yne was found to be more reluctant to react and needed prolonged heating in order to reach a yield similar to those of the aromatic alkynes (Table 1, entry 5). Interestingly, a high control was achieved in the mono-azidosulfenylation of cycloocta-1,5-diene (**1b**). The subsequent reaction with phenylacetylene (**2a**) gave rise to the product **3ba** in excellent yield, which possesses a carbon-carbon double bond available for further functionalization (Table 1, entry 6). Very similar yield and reaction time as those in entry 6 were noted when starting from the oxacyclic olefin 2,5-dihydrofuran (**1c**) (Table 1, entry 7). It is noteworthy that the cyclic olefins **1a–1c** provided exclusively the *trans* methylsulfanyl triazol-1-yl products. These results are in agreement with the reaction taking place through an episulfonium ion intermediate, which undergoes *trans*-diaxial ring opening through an $\text{S}_{\text{N}}2$ process. This is the same trend we observed in the synthesis of 1,2,3-triazoles from cycloalkene oxides.^{17c}

Table 1. One-Pot Click Synthesis of 1,2,3-Triazoles from Alkenes Catalyzed by CuNPs/C.^a

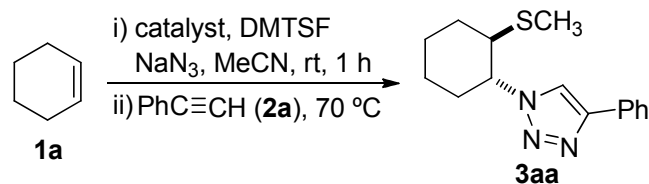
Entry	Alkene	Alkyne	t (h)	Product	Yield (%) ^b
1	 1a	 2a	16	 3aa	81
2	1a	 2b	16	 3ab	79
3	1a	 2c	16	 3ac	85
4	1a	 2d	16	 3ad	83
5	1a	 2e	24	 3ae	77
6	 1b	2a	14	 3ba	91
7	 1c	2a	14	 3ca	89
8	 1d	2a	16	 3da	75
9	 1e	2a	16	 3ea	57
				 3ea'	19
10	 1f	2a	24	 3fa	37
				 3fa'	42
11	 1g	2a	12	 3ga	89
12	1g	2e	12	 3ge	77

^a Reagents and conditions: **1** (0.5 mmol), NaN₃ (0.6 mmol), DMTSF (0.6 mmol), CuNPs/C (0.5 mol%), MeCN (2 mL), r.t., 1 h; **2** (0.5 mmol), 70 °C, t (h). ^b Isolated yield.

We next studied the behavior of acyclic olefins in the title reaction. The symmetrical internal alkene (*Z*)-oct-4-ene (**1d**), when combined with phenylacetylene (**2a**), furnished **3da** with a 4*R**,5*R** relative configuration proposed in view of the aforementioned trend (Table 1, entry 8). The azidosulfenylation of the terminal olefin oct-1-ene (**1e**) was found to be less regioselective when compared with the azidolysis of oct-1-ene oxide.^{17c} In this case, the CuAAC with phenylacetylene (**2a**) yielded a *ca.* 3:1 mixture of regioisomers, the major one derived from the attack of the azide ion to the less hindered position of the intermediate episulfonium ion (Table 1, entry 9). The stabilization of the partially developed positive charge on the internal carbon atom of the episulfonium ion in the transition state could account for the formation of the minor regioisomer **3ea'**. Fortunately, the two regioisomers could be easily separated by column chromatography. Triazoles **3fa** and **3fa'**, derived from the unsymmetric cyclic olefin 1-methylcyclohex-1-ene, were produced in a near 1:1 regioisomeric ratio and could be also separated (Table 1, entry 10). Finally, when styrene was subjected to the standard procedure, either with phenylacetylene (**2a**) or oct-1-yne (**2e**), the expected triazoles **3ga** and **3ge** were obtained, respectively, in good yields as single regioisomers (Table 1, entries 11 and 12). In both cases, attack of the azide ion to the internal carbon atom of the intermediate episulfonium ion was preferred as it was also previously observed in the domino azidolysis-CuAAC of styrene oxide and phenylacetylene.^{17c} These results can be explained by the partially developed positive charge during the nucleophilic azide attack in the unsymmetrical ring-opening transition state, which is more stabilized at the benzylic position of the episulfonium ion. Recently, 1,2,3-triazoles have been successfully applied in organic synthesis as ligands,²⁰ with compounds in Table 3 representing a new family of potential N,S-triazolyl ligands.

Contrary to the good recycling behaviour observed for CuNPs/C in other multicomponent click reactions,¹⁷ in the present case reutilization was inefficient, very probably due to catalyst poisoning by sulfur. Nevertheless, this fact is not so important if we take into account the low copper loading deployed in the experiments (0.5 mol%). On the other hand, it is our premise that any laboratory-made catalyst should be more efficient than commercially available catalysts used for the same purpose; otherwise, it is difficult to economically justify the time, materials and human resources employed during its preparation. With this principle in mind, we undertook a comparative study on the reactivity of CuNPs/C with some commercially available copper sources. The standard conditions were applied to the reaction of cyclohexene (**1a**) with DMTSF, NaN₃, and phenylacetylene (**2a**) leading to **3aa** (Table 2). We were delighted to check that none of the commercial catalysts was active in this transformation, where even the initial azidosulfonylation step failed (Table 2, entries 1–5). In contrast, the copper-nanoparticle supported catalyst produced the desired product in good isolated yield (Table 2, entry 6). These results are in agreement with the fact that CuNPs/C could also catalyze the first synthetic step. This catalytic role was clearly demonstrated by carrying out two experiments: (a) the reaction of cyclohexene with DMTSF and NaN₃ in MeCN at rt (1–24 h) gave a complex mixture of products, with the expected azide representing only 5–24%; (b) the same reaction in the presence of 0.5 mol% CuNPs/C provided that azide quantitatively in only 1 h (see the Supporting Information).

TABLE 2. One-Pot Click Synthesis of 1,2,3-Triazoles from Alkenes Catalyzed by Different Copper Catalysts.^a

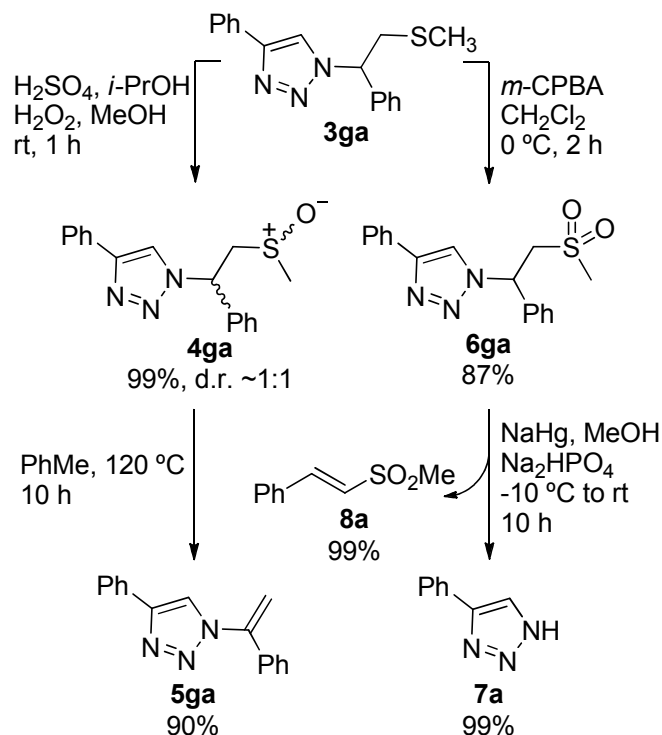


entry	catalyst (mol% Cu)	yield (%) ^b
1	Cu (1)	- ^c
2	CuCl (1)	- ^c
3	CuCl ₂ (1)	- ^c
4	CuO (1)	- ^c
5	Cu ₂ O (1)	- ^c
6	CuNPs/C (0.5)	81

^a **1a** (0.5 mmol), NaN_3 (0.6 mmol), DMTSF (0.6 mmol), MeCN (2 mL). ^b Isolated yield. ^c Not detected.

Finally, we sought to capitalize on the presence of the methylsulfanyl group to structurally modify the triazoles **3** (Scheme 3). A variety of conditions were tested in order to achieve maximum selectivity, with the best results being shown in Scheme 3. Oxidation of the parent triazole **3ga** with hydrogen peroxide was mild and fast giving a *ca.* 1:1 diastereomeric mixture of sulfoxide **4ga**. Sulfoxide elimination under thermal conditions led to the vinyl triazole **5ga** in an overall quantitative conversion. We must point out that the synthesis of 1-vinyl-1,2,3-triazoles has been scarcely studied,²¹ with this method representing an effectual approach. Oxidation of the parent triazole **3ga** to the corresponding sulfone **6ga** was easily accomplished with *m*-CPBA. Treatment of **6ga** with sodium amalgam in methanol afforded the 4-monosubstituted triazole **7a** together with methyl (*E*)- β -styryl sulfone (**8a**). These experiments prove the versatility of the β -(methylsulfanyl)ethyl-substituted 1,2,3-triazoles **3**.

SCHEME 3. Synthetic Transformations of Triazole 3ga.



In conclusion, we have described the first one-pot synthesis of 1,2,3-triazoles from inactivated alkenes through a sequence including two click steps catalyzed by CuNPs/C: the azidosulfenylation of the olefin and the reaction of the in-situ generated organic azide with the terminal alkyne. The β -methylsulfanyl triazoles, potential interesting ligands, are obtained regio- and diastereoselectively in 75–91% isolated yields. In addition, the nanostructured catalyst displayed much higher catalytic activity than the commercial bulk copper catalysts which failed in the first step. Furthermore, simple and quantitative oxidation-elimination procedures allow the transformation of the products into 1-vinyl-4-substituted or 4-monosubstituted 1,2,3-triazoles.

EXPERIMENTAL SECTION

General: Anhydrous copper(II) chloride (97%), lithium powder (MEDALCHEMY S. L.), DTBB (4,4'-di-*tert*-butylbiphenyl), activated charcoal (Norit CA1), and sodium azide were commercially available.

All the starting materials and other reagents were commercially available of the best grade and were used without further purification. THF was dried in a solvent purification system using an alumina column. Melting points are uncorrected. Infrared analysis was performed with a FT-IR spectrophotometer equipped with an ATR component; wavenumbers are given in cm^{-1} . NMR spectra were recorded at 300 or 400 MHz for ^1H NMR and 75 and 101 MHz for ^{13}C NMR; chemical shifts are given in (δ) parts per million and coupling constants (J) in Hertz. Mass spectra (EI) were obtained at 70 eV with a GC-MS apparatus; fragment ions in m/z with relative intensities (%) in parenthesis. HRMS analyses were also carried out in the electron impact mode (EI) at 70 eV using a quadrupole analyzer. The purity of volatile compounds and the chromatographic analyses (GLC) were determined with a gas chromatograph equipped with a flame ionization detector and a 30 m capillary column (0.32 mm diameter, 0.25 μm film thickness), using nitrogen (2 mL/min) as carrier gas, $T_{\text{injector}} = 270\text{ }^\circ\text{C}$, $T_{\text{column}} = 60\text{ }^\circ\text{C}$ (3 min) and 60–270 $^\circ\text{C}$ (15 $^\circ\text{C}/\text{min}$); retention times (t_r) are given in min. Thin layer chromatography was carried out on TLC plastic sheets with silica gel. Column chromatography was performed using silica gel of 40–60 microns (hexane-EtOAc as eluent).

Typical Procedure for the Preparation of CuNPs/C:^{17a,b} Anhydrous copper(II) chloride (135 mg, 1 mmol) was added to a suspension of lithium (14 mg, 2 mmol) and 4,4'-di-*tert*-butylbiphenyl (DTBB, 27 mg, 0.1 mmol) in THF (2 mL) at room temperature under an argon atmosphere. The reaction mixture, which was initially dark blue, rapidly changed to black, indicating that the suspension of copper nanoparticles was formed. This suspension was diluted with THF (18 mL) followed by the addition of the activated carbon (1.28 g). The resulting mixture was stirred for 1 h at room temperature, filtered, and the solid successively washed with water (20 mL), THF (20 mL), and dried under vacuum.

Typical Procedure for the CuNPs/C-Catalyzed Synthesis of 1,2,3-Triazoles from Alkenes: NaN_3 (39 mg, 0.6 mmol), freshly prepared dimethyl(methylthio)sulfonium tetrafluoroborate (DMTSF,¹⁹ 118

mg, 0.6 mmol), and cyclohexene (**1a**, 51 μ L, 0.5 mmol) were added to a suspension of CuNPs/C (10 mg, 0.5 mol% Cu) in MeCN (2 mL) at room temperature under an argon atmosphere.²² After stirring for 1 h, phenylacetylene (**2a**, 55 μ L, 0.5 mmol) was added. The reaction mixture was warmed to 70 °C and monitored by TLC until total or steady conversion of the starting materials. Water (20 mL) was added to the resulting mixture followed by extraction with EtOAc (3 \times 10 mL). The collected organic phases were dried with MgSO₄ and the solvent was removed *in vacuo* to give the corresponding triazole **3aa**, which was purified by column chromatography (hexane-EtOAc, 8:2).

1-[(1*R,2*R**)-2-(Methylthio)cyclohexyl]-4-phenyl-1*H*-1,2,3-triazole (3aa):** Pale yellow solid (110.6 mg, 81%); m.p. 128.0–130.1 °C; *t_r* 18.53 min; *R_f* 0.61 (hexane-EtOAc, 7:3); IR (KBr) ν 3119, 3082, 2935, 2923, 2850, 1480, 1460, 1435, 1211, 1178, 1076, 1048, 974, 762, 697 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.88–7.84 (m, 2H), 7.81 (s, 1H), 7.46–7.35 (m, 2H), 7.34–7.29 (m, 1H), 4.24 (td, *J* = 11.2, 4.2 Hz, 1H), 3.00 (td, *J* = 11.2, 4.2 Hz, 1H), 2.36–2.09 (m, 3H), 1.99–1.86 (m, 2H), 1.71 (s, 3H), 1.56–1.42 (m, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 147.0, 130.8, 128.7, 128.0, 125.7, 119.5, 65.8, 50.4, 33.9, 33.3, 25.9, 25.1, 13.8; GC-MS (EI) *m/z* (%) 273 (26) [*M*⁺], 230 (27), 196 (12), 162 (14), 129 (46), 128 (68), 117 (14), 116 (22), 102 (16), 89 (15), 81 (100), 79 (20), 61 (19); HRMS (EI) *m/z* calcd. for C₁₅H₁₉N₃S 273.1300, found 273.1293.

1-[(1*R,2*R**)-2-(Methylthio)cyclohexyl]-4-(*p*-tolyl)-1*H*-1,2,3-triazole (3ab):** White solid (113.4 mg, 79%); m.p. 135.9–138.1 °C; *t_r* 19.79 min; *R_f* 0.54 (hexane-EtOAc, 7:3); IR (neat) ν 3103, 2942, 2920, 2856, 1498, 1445, 1422, 1214, 1049, 977, 816 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.78 (s, 1H), 7.75 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 4.23 (td, *J* = 11.3, 4.4 Hz, 1H), 3.00 (td, *J* = 11.3, 4.0 Hz, 1H), 2.38 (s, 3H), 2.33–2.25 (m, 1H), 2.24–2.11 (m, 2H), 1.99–1.85 (m, 2H), 1.70 (s, 3H), 1.56–1.39 (m, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 147.3, 137.9, 129.6, 128.1, 125.7, 119.3, 65.9, 50.5, 34.1, 33.4, 26.0, 25.3, 21.4, 14.0; GC-MS (EI) *m/z* (%) 287 (22) [*M*⁺], 244 (14), 131 (10), 130 (19), 129 (51),

128 (15), 115 (18), 81 (100), 79 (15), 77 (10), 61 (19); HRMS (EI) m/z calcd. for $C_{16}H_{21}N_3S$ 287.1456, found 287.1461.

4-(4-Methoxyphenyl)-1- $\{(1R^*,2R^*)$ [2-(methylthio)cyclohexyl]-1*H*-1,2,3-triazole (3ac): Pale yellow solid (128.8 mg, 85%); m.p. 132.8–135.5 °C; t_r 21.95 min; R_f 0.53 (hexane-EtOAc, 6:4); IR (neat) ν 3102, 2937, 2925, 2857, 1497, 1245, 1175, 1030, 828, 815 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 8.8 Hz, 2H), 7.74 (s, 1H), 6.96 (d, J = 8.8 Hz, 2H), 4.23 (td, J = 11.3, 4.4 Hz, 1H), 3.84 (s, 3H), 3.00 (td, J = 11.3, 4.1 Hz, 1H), 2.33–2.06 (m, 3H), 1.98–1.84 (m, 2H), 1.72 (s, 3H), 1.55–1.41 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.7, 147.0, 127.1, 123.6, 118.9, 114.3, 65.9, 55.5, 50.4, 34.1, 33.4, 26.0, 25.3, 13.9; GC-MS (EI) m/z (%) 303 (35) [M^+], 260 (29), 146 (16), 132 (21), 129 (59), 121 (10), 89 (13), 81 (100), 79 (20), 61 (20); HRMS (EI) m/z calcd. for $C_{16}H_{21}N_3OS$ 303.1405, found 303.1411.

1- $\{(1R^*,2R^*)$ -[2-(Methylthio)cyclohexyl]-4-[4-(trifluoromethyl)phenyl]-1*H*-1,2,3-triazole (3ad): Pale yellow solid (141.6 mg, 83%); m.p. 118.4–120.6 °C; t_r 18.18 min; R_f 0.53 (hexane-EtOAc, 7:3); IR (neat) ν 3099, 2943, 2924, 2856, 1620, 1329, 1158, 1123, 1105, 1065, 978, 839 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 8.5 Hz, 2H), 7.91 (s, 1H), 7.68 (d, J = 8.5 Hz, 2H), 4.23 (td, J = 11.5, 4.2 Hz, 1H), 3.01 (td, J = 11.5, 4.2 Hz, 1H), 2.36–2.11 (m, 3H), 2.01–1.87 (m, 2H), 1.74 (s, 3H), 1.58–1.43 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.8, 134.3, 130.0 (q, J = 32.8 Hz, CF_3), 125.9, 125.6, 120.5, 65.9, 50.4, 34.1, 33.4, 25.9, 25.2, 13.8; GC-MS (EI) m/z (%) 341 (4) [M^+], 129 (20), 128 (100), 81 (95), 79 (20), 61 (22); HRMS (EI) m/z calcd. for $C_{16}H_{18}F_3N_3S$ 341.1174, found 341.1180.

4-Hexyl-1- $\{(1R^*,2R^*)$ -[2-(methylthio)cyclohexyl]-1*H*-1,2,3-triazole (3ae): Pale orange solid (108.3, 77%); m.p. 61.0–64.0 °C; t_r 17.12 min; R_f 0.62 (hexane-EtOAc, 6:4); IR (neat) ν 3121, 3069, 2924, 2855, 1445, 1215, 1152, 1056, 847, 724 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.33 (s, 1H), 4.16 (td, J = 11.3, 4.2 Hz, 1H), 2.94 (td, J = 11.3, 4.2 Hz, 1H), 2.73 (t, J = 7.7 Hz, 2H), 2.32–2.24 (m, 1H), 2.19–2.05 (m, 2H), 1.96–1.84 (m, 2H), 1.74–1.63 (m, 2H), 1.66 (s, 3H), 1.52–1.25 (m, 9H), 0.88 (t, J = 6.4

Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 147.8, 120.7, 65.7, 50.5, 34.1, 33.4, 31.7, 29.6, 29.0, 26.0, 25.8, 25.3, 22.7, 14.2, 13.9; GC-MS (EI) m/z (%) 281 (2) [M^+], 129 (21), 128 (82), 80 (14), 79 (18), 61 (22), 55 (10), 53 (10); HRMS (EI) m/z calcd. for $\text{C}_{15}\text{H}_{27}\text{N}_3\text{S}$ 281.1926, found 281.1936.

1-[(1*R,8*R**,*Z*)-8-(Methylthio)cyclooct-4-en-1-yl]-4-phenyl-1*H*-1,2,3-triazole (3ba):** White solid (136.1 mg, 91%); m.p. 111.2–113.8 °C; t_r 21.25 min; R_f 0.60 (hexane-EtOAc, 6:4); IR (neat) ν 3120, 2948, 2919, 1436, 1083, 1051, 764, 712, 704, 692 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.92–7.86 (m, 2H), 7.83 (s, 1H), 7.47–7.39 (m, 2H), 7.38–7.33 (m, 1H), 5.83–5.67 (m, 2H), 4.86 (td, J = 9.7, 3.4 Hz, 1H), 3.46–3.36 (m, 1H), 2.79–2.22 (m, 4H), 2.19–1.98 (m, 4H), 1.77 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 146.8, 130.7, 130.5, 128.9, 128.2, 127.7, 125.9, 120.5, 65.0, 51.3, 33.8, 31.7, 25.7, 24.3, 14.8; GC-MS (EI) m/z (%) 299 (9) [M^+], 285 (11), 284 (54), 253 (14), 252 (71), 156 (5), 154 (24), 148 (20), 143 (16), 117 (28), 116 (35), 115 (12), 113 (10), 107 (38), 106 (15), 105 (17), 104 (31), 103 (14), 102 (26), 91 (37), 90 (11), 89 (24), 81 (19), 80 (15), 79 (100), 78 (12), 77 (29), 74 (10), 67 (27), 65 (13), 63 (11), 61 (21), 54 (10), 53 (18); HRMS (EI) m/z calcd. for $\text{C}_{17}\text{H}_{21}\text{N}_3\text{S}$ 299.1456, found 299.1448.

1-[(1*R,2*R**)-4-(Methylthio)tetrahydrofuran-3-yl]-4-phenyl-1*H*-1,2,3-triazole (3ca):** Yellow semisolid (116.2 mg, 89%); t_r 17.52 min; R_f 0.49 (hexane-EtOAc, 6:4); IR (neat) ν 3079, 2958, 2930, 1459, 1419, 1219, 1077, 1049, 971, 760, 699 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.90 (s, 1H), 7.87–7.81 (m, 2H), 7.47–7.39 (m, 2H), 7.34–7.31 (m, 1H), 5.22 (dd, J = 7.0, 3.8 Hz, 1H), 4.51 (dd, J = 9.8, 7.7 Hz, 1H), 4.27 (d, J = 4.1 Hz, 2H), 3.66 (dd, J = 9.8, 6.4 Hz, 1H), 3.52 (ddd, J = 7.6, 6.5, 2.9 Hz, 1H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 148.6, 130.4, 128.9, 128.5, 125.8, 117.9, 72.8, 71.9, 67.5, 51.9, 15.5; GC-MS (EI) m/z (%) 261 (20) [M^+], 188 (26), 156 (16), 146 (23), 145 (27), 143 (12), 130 (14), 128 (17), 118 (20), 117 (87), 116 (94), 115 (21), 103 (20), 102 (43), 91 (20), 90 (25), 89 (100), 77 (19), 76 (21), 75 (21), 74 (25), 71 (11), 69 (43), 68 (13), 64 (10), 63 (29), 62 (10), 61 (38), 54 (11), 51 (13); HRMS (EI) m/z calcd. for $\text{C}_{13}\text{H}_{15}\text{N}_3\text{OS}$ 261.0936, found 261.0939.

1-[(1*R,2*R**)-5-(Methylthio)octan-4-yl]-4-phenyl-1*H*-1,2,3-triazole (3da):** Pale yellow solid (113.7 mg, 75%); m.p. 52.5–55.3 °C; *t_r* 17.26 min; *R_f* 0.43 (hexane-EtOAc, 9:1); IR (neat) ν 3081, 2955, 2926, 2868, 1460, 1429, 1221, 1081, 976, 765, 725 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.97 (s, 1H), 7.91–7.84 (m, 2H), 7.46–7.39 (m, 2H), 7.36–7.29 (m, 1H), 4.16 (td, *J* = 9.4, 4.6 Hz, 1H), 2.88 (td, *J* = 9.4, 4.6 Hz, 1H), 2.24–2.11 (m, 1H), 2.05–1.95 (m, 1H), 1.99 (s, 3H), 1.64–1.54 (m, 2H), 1.53–1.45 (m, 1H), 1.44–1.35 (m, 1H), 1.29–1.19 (m, 2H), 0.93 (t, *J* = 7.2 Hz, 3H), 0.91 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 147.4, 130.1, 128.9, 128.1, 125.7, 119.0, 65.2, 52.4, 34.5, 34.3, 20.4, 19.5, 15.6, 13.9, 13.8; GC-MS (EI) *m/z* (%) 303 (28) [M⁺], 260 (14), 228 (14), 201 (64), 200 (12), 186 (12), 173 (15), 172 (100), 143 (21), 130 (33), 129 (16), 121 (11), 118 (14), 117 (45), 116 (54), 115 (17), 111 (10), 110 (20), 104 (42), 103 (73), 102 (38), 91 (62), 90 (18), 89 (42), 86 (10), 81 (10), 77 (19), 76 (11), 69 (75), 63 (19), 61 (96), 55 (54); HRMS (EI) *m/z* calcd. for C₁₇H₂₅N₃S 303.1769, found 303.1759.

1-[2-(Methylthio)octyl]-4-phenyl-1*H*-1,2,3-triazole (3ea): Pale yellow solid (86.4 mg, 57%); m.p. 39.8–44.4 °C; *t_r* 19.41 min; *R_f* 0.66 (hexane-EtOAc, 7:3); IR (neat) ν 3081, 2953, 2926, 2855, 1461, 1435, 1224, 1084, 977, 766, 727, 694 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.90 (s, 1H), 7.88–7.81 (m, 2H), 7.47–7.39 (m, 2H), 7.37–7.29 (m, 1H), 4.55 (dd, *J* = 14.0, 6.2 Hz, 1H), 4.45 (dd, *J* = 14.0, 7.2 Hz, 1H), 3.07–2.95 (m, 1H), 1.90 (s, 3H), 1.64–1.38 (m, 4H), 1.33–1.20 (m, 6H), 0.87 (t, *J* = 6.7 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 147.6, 130.6, 128.9, 128.3, 125.9, 120.8, 54.5, 47.6, 32.0, 31.8, 29.1, 26.8, 22.7, 14.2, 13.8; GC-MS (EI) *m/z* (%) 303 (15) [M⁺], 260 (26), 176 (20), 163 (10), 162 (13), 159 (67), 158 (11), 148 (18), 145 (19), 144 (24), 143 (37), 130 (26), 117 (25), 116 (32), 111 (20), 110 (12), 104 (31), 103 (26), 102 (29), 91 (14), 89 (26), 88 (18), 77 (18), 75 (14), 69 (93), 67 (13), 63 (14), 61 (100), 55 (79); HRMS (EI) *m/z* calcd. for C₁₇H₂₅N₃S 303.1769, found 303.1760.

1-[1-(Methylthio)octan-2-yl]-4-phenyl-1*H*-1,2,3-triazole (3ea'): Yellow oil (28.8 mg, 19%); *t_r* 19.01 min; *R_f* 0.69 (hexane-EtOAc, 7:3); IR (neat) ν 2953, 2923, 2856, 1459, 1433, 1224, 762, 694 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.91–7.84 (m, 2H), 7.83 (s, 1H), 7.48–7.39 (m, 2H), 7.37–7.29 (m, 1H),

4.63 (ddt, $J = 8.9, 7.6, 5.7$ Hz, 1H), 3.11–2.93 (m, 2H), 2.13–2.00 (m, 2H), 1.95 (s, 3H), 1.34–1.17 (m, 8H), 0.85 (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 147.5, 130.7, 128.9, 128.3, 125.9, 119.2, 62.4, 39.9, 34.5, 31.6, 28.9, 26.0, 22.6, 16.4, 14.1; GC-MS (EI) m/z (%) 303 (17) [M^+], 260 (28), 228 (12), 215 (10), 214 (63), 163 (23), 159 (36), 158 (71), 148 (36), 144 (24), 143 (21), 130 (26), 117 (50), 116 (52), 104 (43), 103 (31), 102 (30), 91 (35), 90 (16), 89 (32), 77 (12), 75 (10), 69 (86), 67 (13), 63 (15), 61 (100), 55 (60); HRMS (EI) m/z calcd. for $\text{C}_{17}\text{H}_{25}\text{N}_3\text{S}$ 303.1769, found 303.1779.

1-[(1*R,2*R**)-2-Methyl-2-(methylthio)cyclohexyl]-4-phenyl-1*H*-1,2,3-triazole (3fa):** Pale yellow solid (53.1 mg, 37%); m.p. 78.9–81.9 °C; t_r 19.89 min; R_f 0.53 (hexane-EtOAc, 7:3); IR (KBr) ν 3117, 2934, 2858, 1481, 1458, 1434, 1387, 1228, 1077, 979, 764, 697 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.87–7.84 (m, 2H), 7.83 (s, 1H), 7.45–7.40 (m, 2H), 7.35–7.30 (m, 1H), 4.54 (dd, $J = 12.0, 3.9$ Hz, 1H), 2.39–2.29 (m, 1H), 2.09–2.03 (m, 1H), 2.01–1.95 (m, 2H), 1.86 (s, 3H), 1.81–1.73 (m, 2H), 1.72–1.66 (m, 2H), 1.35 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 146.7, 130.9, 128.9, 128.1, 125.8, 120.6, 67.0, 48.1, 38.7, 29.0, 25.4, 21.9, 19.2, 10.8; GC-MS (EI) m/z (%) 287 (56) [M^+], 288 (10) [$\text{M}^+ + 1$], 244 (18), 212 (21), 146 (22), 145 (14), 143 (49), 117 (17), 116 (25), 102 (18), 99 (14), 96 (13), 95 (100), 93 (10), 91 (13), 77 (11), 75 (11), 67 (23), 55 (16); HRMS (EI) m/z calcd. for $\text{C}_{16}\text{H}_{21}\text{N}_3\text{S}$ 287.1456, found 287.1462.

1-[(1*R,2*R**)-1-Methyl-2-(methylthio)cyclohexyl]-4-phenyl-1*H*-1,2,3-triazole (3fa'):** Yellow oil (60.3 mg, 42%); t_r 18.88 min; R_f 0.59 (hexane-EtOAc, 7:3); IR (neat) ν 3130, 2928, 2862, 1458, 1448, 1234, 1025, 765, 699 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.93 (s, 1H), 7.89–7.84 (m, 2H), 7.45–7.39 (m, 2H), 7.35–7.29 (m, 2H), 3.42 (dd, $J = 11.9, 4.0$ Hz, 1H), 2.64–2.54 (m, 1H), 2.16–2.12 (m, 2H), 2.01–1.94 (m, 1H), 1.87–1.77 (m, 2H), 1.75 (s, 3H), 1.69 (s, 1H), 1.66–1.53 (m, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 146.6, 131.0, 128.9, 128.0, 125.7, 118.4, 66.3, 55.9, 39.4, 31.3, 25.9, 22.4, 19.1, 15.9; GC-MS (EI) m/z (%) 287 (9) [M^+], 244 (11), 212 (12), 144 (10), 143 (35), 142 (98), 117 (16), 116 (14),

102 (11), 96 (10), 95 (100), 67 (20), 61 (10), 55 (11); HRMS (EI) m/z calcd. for $C_{16}H_{21}N_3S$ 287.1456, found 287.1460.

1-[2-(Methylthio)-1-phenylethyl]-4-phenyl-1H-1,2,3-triazole (3ga): White solid (131.3 mg, 89%); m.p. 115.5–118.2 °C; t_r 19.24 min; R_f 0.62 (hexane-EtOAc, 6:4); IR (neat) ν 3083, 2921, 2909, 1456, 1436, 1219, 1077, 763, 708, 700, 689 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$) δ 7.87–7.79 (m, 2H), 7.75 (s, 1H), 7.49–7.29 (m, 8H), 5.74 (dd, J = 8.2, 6.7 Hz, 1H), 3.68 (dd, J = 14.0, 8.2 Hz, 1H), 3.37 (dd, J = 14.0, 6.7 Hz, 1H), 2.03 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.8, 137.8, 130.6, 129.3, 129.2, 128.9, 128.3, 127.3, 125.8, 119.6, 66.6, 39.3, 16.5; GC-MS (EI) m/z (%) 295 (7) [M^+], 234 (26), 207 (14), 206 (74), 204 (14), 179 (10), 178 (31), 163 (15), 152 (13), 151 (60), 150 (100), 148 (15), 145 (28), 137 (12), 136 (30), 135 (47), 134 (16), 128 (12), 118 (10), 117 (20), 116 (51), 105 (11), 104 (59), 103 (45), 102 (27), 91 (45), 90 (13), 89 (37), 78 (15), 77 (42), 76 (13), 63 (21), 61 (14), 51 (18); HRMS (EI) m/z calcd. for $C_{17}H_{17}N_3S$ 295.1143, found 295.1137.

4-Hexyl-1-[2-(methylthio)-1-phenylethyl]-1H-1,2,3-triazole (3ge): White solid (116.7 mg, 77%); m.p. 61.2–62.4 °C; t_r 17.91 min; R_f 0.69 (hexane-EtOAc, 6:4); IR (neat) ν 3113, 3064, 2954, 2919, 2854, 1457, 1429, 1058, 851, 747, 704 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$) δ 7.39–7.33 (m, 5H), 7.28 (s, 1H), 5.66 (dd, J = 8.2, 6.7 Hz, 1H), 3.60 (dd, J = 14.0, 8.2 Hz, 1H), 3.31 (dd, J = 14.0, 6.7 Hz, 1H), 2.70 (t, J = 7.7 Hz, 2H), 1.99 (s, 3H), 1.70–1.56 (m, 2H), 1.38–1.24 (m, 6H), 0.86 (t, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.4, 138.1, 129.2, 129.0, 127.3, 120.7, 65.3, 39.4, 31.6, 29.4, 29.0, 25.8, 22.7, 16.3, 14.2; GC-MS (EI) m/z (%) 303 (1) [M^+], 214 (24), 151 (49), 150 (100), 144 (12), 136 (21), 135 (35), 134 (13), 104 (40), 103 (25), 96 (10), 91 (43), 83 (13), 77 (15); HRMS (EI) m/z calcd. for $C_{17}H_{25}N_3S$ 303.1769, found 303.1767.

1-[(Methylsulfinyl)(phenyl)methyl]-4-phenyl-1H-1,2,3-triazole (4ga): In a typical procedure,²³ a round-bottom flask was charged with sulfide **3ga** (50.7 mg, 0.17 mmol), MeOH (1 mL) and the catalyst

[0.1 mL of a solution prepared by mixing 96% H₂SO₄ (1.38 g) and 2-propanol (38 mL)]. H₂O₂ (0.05 mL, 0.50 mmol) was added at once to the stirred mixture and the progress of the oxidation was followed by TLC (1–2 h). Water (10 mL) was added to the mixture after completion of the reaction. The aqueous phase was saturated with NaCl and extracted with EtOAc (3 × 10 mL). The organic phase was dried with MgSO₄ and evaporated to give the pure sulfoxide **4ga** (53.0 mg, 99%) as a *ca.* 1:1 diastereomeric mixture: white solid; m.p. 133.9–135.4 °C; *R_f* 0.34 (EtOAc); IR (KBr) ν 3080, 2926, 1457, 1432, 1032, 1023, 975, 763, 714, 690 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.91 (s, 1H), 7.85 (s, 1H), 7.84–7.87 (m, 16H), 6.20–6.11 (m, 2H), 4.30 (t, *J* = 12.6 Hz, 2H), 4.03 (dd, *J* = 13.2, 5.8 Hz, 2H), 3.79 (dd, *J* = 13.2, 8.7 Hz, 2H), 3.34 (dd, *J* = 13.2, 2.9 Hz, 2H), 2.70 (s, 3H), 2.55 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 148.2, 137.6, 136.9, 130.0, 129.9, 129.8, 129.7, 129.6, 129.5, 129.4, 129.0, 128.6, 128.6, 127.3, 126.9, 126.8, 125.9, 121.2, 120.5, 60.2, 59.5, 58.8, 58.0, 39.2, 38.5; GC-MS (EI) *m/z* (%) 311 (2) [M⁺], 249 (10), 248 (57), 219 (10), 167 (10), 151 (22), 117 (13), 116 (100), 105 (13), 104 (77), 103 (23), 91 (13), 89 (21), 77 (14); HRMS (EI) *m/z* calcd. for C₁₇H₁₇N₃OS 311.1092, found 311.1095.

4-Phenyl-1-(1-phenylvinyl)-1*H*-1,2,3-triazole (5ga): In a typical procedure, the sulfoxide **4ga** (29.5 mg, 0.1 mmol) was heated in toluene at 120° C for 10 h in a pressure tube with a Teflon cap. Evaporation of the solvent gave the pure triazole **5ga** (22.0 mg, 90%) as a yellow oil. The physical and spectroscopic data of **5ga** were compared with those reported in the literature:^{21c} ¹H NMR (300 MHz, CDCl₃) δ 7.88–7.83 (m, 2H), 7.80 (s, 1H), 7.48–7.34 (m, 8H), 5.88 (d, *J* = 1.0 Hz, 1H), 5.57 (d, *J* = 1.0 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 147.7, 143.1, 134.8, 130.3, 130.1, 129.0, 128.5, 127.5, 125.9, 119.9, 109.6.

1-[(Methylsulfonyl)(phenyl)methyl]-4-phenyl-1*H*-1,2,3-triazole (6ga): In a typical procedure,²⁴ a solution of *m*-chloroperbenzoic acid (86.3 mg, 0.50 mmol) in CH₂Cl₂ (2 mL) was added to a solution of triazole **3ga** (29.5 mg, 0.1 mmol) in CH₂Cl₂ (2 mL) at 0 °C; the reaction was stirred at 0 °C for 2 h. Then, it was quenched with saturated aqueous sodium bicarbonate (10 mL) and diluted with CH₂Cl₂

(10 mL). The organic layer was removed and the aqueous layer was extracted with CH₂Cl₂ (10 mL). The combined organic layers were dried with MgSO₄, the solvent was evaporated, and the crude mixture was purified by column chromatography (silica gel, hexane-EtOAc, 3:7)] to give the sulfone **6ga** (28.4 mg, 87%) as a white solid; m.p. 164.7–167.7 °C; *t_r* 21.85 min; *R_f* 0.52 (hexane-EtOAc, 1:1); IR (KBr) ν 3093, 2923, 1335, 1302, 1149, 1129, 1051, 1088, 1051, 976, 747, 696, 669 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.88 (s, 1H), 7.84–7.71 (m, 2H), 7.46–7.32 (m, 8H), 6.14 (dd, *J* = 9.7, 4.0 Hz, 1H), 4.78 (dd, *J* = 15.2, 9.7 Hz, 1H), 3.74 (dd, *J* = 15.2, 4.0 Hz, 1H), 2.56 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 148.6, 136.7, 129.8, 129.8, 129.7, 129.1, 128.8, 126.9, 125.9, 120.8, 60.8, 59.5, 42.4; GC-MS (EI) *m/z* (%) 327 (5) [*M*⁺], 207 (23), 206 (12), 183 (13), 117 (15), 116 (100), 105 (11), 104 (54), 103 (16), 102 (10), 91 (16), 89 (17), 77 (11); HRMS (EI) *m/z* calcd. for C₁₇H₁₇N₃O₂S 327.1041, found 327.1042.

4-Phenyl-1*H*-1,2,3-triazole (7a) and (*E*)-[2-(methylsulfonyl)vinyl]benzene (8a): In a typical procedure,²⁵ a solution of compound **6ga** (50.0 mg, 0.15 mmol) in dry MeOH (1 mL) and THF (0.5 mL) was added to a stirred suspension of Na/Hg [freshly prepared from Na (70.0 mg, 3.0 mmol) and Hg (1.163 g, 5.8 mmol)] and Na₂HPO₄ (428 mg, 3.0 mmol) in MeOH (2 mL) under argon. The reaction progress was monitored by TLC and GLC. The mixture was then filtered and the filter cake was washed with Et₂O. The combined filtrate was evaporated under vacuum and purified by preparative TLC (hexane-EtOAc, 1:1) to give triazole **7a** (21.7 mg, 99%) and vinyl sulfone **8a** (27.3 mg, 99%) as colorless solids in quantitative yields. The physical and spectroscopic data of **7a**²⁶ and **8a**²⁷ were in agreement with those reported in the literature.

ASSOCIATED CONTENT

Supporting information

^1H and ^{13}C NMR spectra and some GLC-MS analyses. This material is free of charge via the Internet at <http://pubs.acs.org>.

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