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$Cu(OAc)_2$-Catalysed Oxidative Dual C–H/N–H Activation of Terminal Alkynes and *N*-Deprotected Sulfonimidamides: An Easy Access to *N*-Alkynylated Sulfonimidamides

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We report a mild and efficient $Cu(OAc)_2$-catalysed protocol for the oxidative C–N cross-coupling of terminal alkynes and *N*-deprotected sulfonimidamides. The reaction leads to hitherto unknown *N*-alkynylated sulfonimidamides. Furthermore, we found that the synthesised *N*-alkynylated sulfonimidamides could undergo silica-gel-mediated hydrolysis to give the corresponding *N*-acyl-sulfonimidamides, as well as borane–dimethyl sulfide-mediated reduction to give the corresponding *N*-alkylated sulfonimidamides.

Introduction

Metal-catalysed C–N cross-coupling reactions have emerged as an extremely powerful methodology in organic synthesis, offering versatile structural modifications of nitrogen-containing substrates.[1] Despite significant advances in this field, the construction of C–N bonds is still a major challenge for organic chemists, not least since new nitrogen-containing moieties emerge, and their reactivity towards coupling partners often need to be validated. Among the many methods reported for C–N coupling, the dual C–H/N–H activation technique has received tremendous attraction, as it directly installs the nitrogen-containing molecule onto simple hydrocarbon substrates. By avoiding the prefunctionalisation of the hydrocarbon into a more reactive substrate, e.g., the corresponding organic halide, the approach becomes straightforward, environment-friendly, and atom-economic. In this context, the last decade has observed the development of several metal-catalysed dual activation protocols for the oxidative amination of alkenes/(hetero)arenes.[2,3] Most recently, Cu-catalysed C–H/N–H functionalisation has transpired as a promising alternative to methods catalysed by costly and toxic metals such as Pd and Rh.[3,4]

Alkynes are important and versatile building blocks in organic synthesis. Heteroatom-substituted alkynes, particularly *N*-alkynylated compounds, are synthetically useful products as the electron-donating ability of the nitrogen lone pair allows the alkyne triple bond to react regioselectively with nucleophilic reagents.[5]

Despite being reported as early as 1960 by Levchenko et al.,[6] the chemistry of sulfonimidamides, i.e., nitrogen analogues of sulfonamides with a hexavalent chiral sulfur centre, has not been explored to a great extent.[7] Nevertheless, in the past decade, the Malacria and Dodd groups have separately investigated the reactivity and applications of sulfonimidamides in organic synthesis, mainly as a nitrogen source for metal-catalysed nitrene-transfer reactions for the imination of sulfides, the aziridination of olefins, and the C–H amination of hydrocarbons.[8] Additionally, Bolm et al. have used sulfonimidamides as ligands for transition-metal-catalysed asymmetric synthesis and as chiral organocatalysts.[9] Also, a few reports, including patent applications, have revealed the utility of the sulfonimidamide functional group in biologically active molecules;[10] our group recently explored sulfonimidamides as potential bioisosteres of sulfonamides in medicinal chemistry.[11]

To date, very few methods have been developed for the *N*-functionalisation of sulfonimidamides. The reported procedures are limited to arylation, acylation, and alkylation.[12] In view of the rich chemistry of *N*-alkynylated compounds, the increasing biological applicability of sulfonimidamides, and the ongoing research[12d–12f] into the applicability of sulfonimidamides in organic synthesis, in this paper we report a $Cu(OAc)_2$-catalysed dual C–H/N–H activation protocol for the synthesis of *N*-alkynylated

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sulfonimidamides through the cross-coupling of terminal alkynes with sulfonimidamides using stoichiometric molecular oxygen as the oxidant.[3f,3g] In addition, a small modification in the purification technique provided the corresponding *N*-acyl-sulfonimidamides as alternative products, albeit in lower yields.

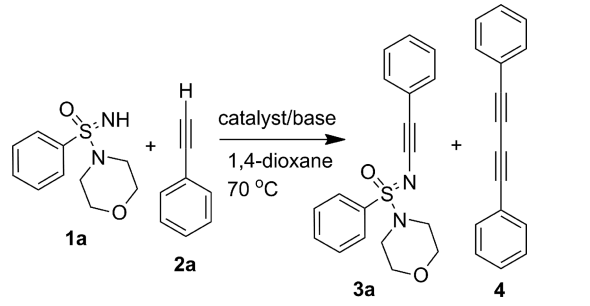
Results and Discussion

The sulfonimidamides (i.e., **1**), which are not commercially available, were prepared according to literature procedures.[12f,13] Our studies began with the reaction of sulfonimidamide **1a** (3.0 equiv.) and phenylacetylene (**2a**; 1.0 equiv.) in the presence of anhydrous $CuCl_2$ as catalyst (0.2 equiv.) and the bases pyridine (2.0 equiv.) and Na_2CO_3 (2.0 equiv.) under a pressurised air balloon in dioxane as the solvent (Table 1, entry 1). Under these conditions, Glaser–Hay dimer **4** was obtained as the major product instead of the expected *N*-alkynylated product (i.e., **3a**). Stahl's group has reported a method[3a] for the oxidative amidation of terminal alkynes using molecular oxygen as the external oxidant. Evano[3b] and Bolm[3e] have also used Stahl's protocol for the alkynylation of diaryl imines and sulfoximines, respectively. Based on these seminal reports, we introduced molecular oxygen as an external oxidant; this modification improved the yield of the expected product (i.e., **3a**) to 76%, and limited dimer **4** to trace amounts. The model reaction was also carried out with the other Cu catalysts, such as $CuBr_2$ and $Cu(OAc)_2$. $Cu(OAc)_2$ gave the highest yield of 78%, whereas $CuBr_2$ yielded a moderate amount of the product (45%) along with Glaser–Hay dimer **4** (Table 1, entries 4 and 5). To establish the optimum amounts of $Cu(OAc)_2$ and sulfonimidamide required for this transformation, a number of test reactions were carried out (Table 1, entries 5–9). The best reaction conditions (based on yield and use of reagents) were determined to be as follows: 2.5 equiv. of sulfonimidamide was treated with 1.0 equiv. of phenylacetylene in the presence of 20 mol-% of $Cu(OAc)_2$, 2.0 equiv. of Na_2CO_3, and 2.0 equiv. of pyridine under a pressurised oxygen balloon at 70 °C using dioxane as the solvent (Table 1, entry 9).

Attempts to use 4-dimethylaminopyridine (DMAP) as the base instead of pyridine were unsuccessful; this gave only 47% of the product, along with Glaser–Hay diyne **4** (Table 1, entry 10). The need for two bases (Na_2CO_3 and pyridine) was established by running two reactions, each with only one of the bases. Surprisingly, Na_2CO_3 did not yield even a trace amount of **3a**, while the pyridine gave only 23% of the expected product (i.e., **3a**) together with **4** (Table 1, entries 11 and 12).

Having optimised the reaction conditions, we went on to investigate the substrate scope of the reaction. Substrates with electron-donating or electron-withdrawing substituents on the aryl ring of the aryl acetylene worked well to give good to high yields. Changes in the position of substitution on the aryl group were also well tolerated, as seen for *N*-alkynylated products **3b**–**3m**. Also, an alkyl-substituted terminal alkyne (1-octyne) gave the corresponding *N*-alkynylated products (i.e., **3o**, **3p**) in good yields. Interestingly, 1-octyne did not react with the anhydrous $CuCl_2$. A further-functionalised alkyl-substituted alkyne, i.e., a silyl-substituted alkyne, was also well tolerated in this transformation, and gave 58% of the respective product (i.e., **3n**). Attempts to modify the structure of the sulfonimidamide partner were successful, as shown by replacing the phenyl group with a *p*-tolyl (**3g**–**3k**) or a *p*-nitrophenyl (**3l**, **3m**, **3o**) group. NO_2-substituted sulfonimidamides in particular gave better yields of the corresponding products (i.e., **3l**, **3m**). Replacement of the morpholine moiety with a piperidine also yielded the corresponding product, albeit in moderate yield (cf. **3f**, 53% and **3a**, 78%).

Table 1. Optimisation of the oxidative C–N cross-coupling reaction conditions.[a]

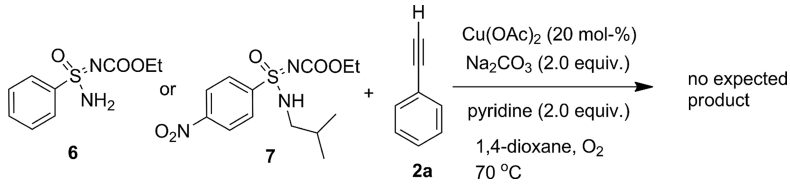


Entry	Catalyst (mol-%)	**1a** [equiv.][b]	Base[c]	Yield [%][d]
1	$CuCl_2$ (20)	3	Na_2CO_3/pyridine	3[e]
2	$CuCl_2$ (20)	3	Na_2CO_3/pyridine	76
3	$CuCl_2$ (10)	3	Na_2CO_3/pyridine	73
4	$CuBr_2$ (20)	3	Na_2CO_3/pyridine	45
5	$Cu(OAc)_2$ (20)	3	Na_2CO_3/pyridine	78
6	$Cu(OAc)_2$ (10)	3	Na_2CO_3/pyridine	76
7	$Cu(OAc)_2$ (30)	3	Na_2CO_3/pyridine	77
8	$Cu(OAc)_2$ (20)	2	Na_2CO_3/pyridine	70
9	$Cu(OAc)_2$ (20)	2.5	Na_2CO_3/pyridine	78
10	$Cu(OAc)_2$ (20)	2.5	Na_2CO_3/pyridine	47
11	$Cu(OAc)_2$ (20)	2.5	Na_2CO_3	–
12	$Cu(OAc)_2$ (20)	2.5	pyridine	23

[a] All the reactions (except entry 1) were carried out in dioxane and under an oxygen atmosphere. [b] Equiv. **1a** relative to **2a**. [c] 2.0 equiv. of all bases was used. [d] Isolated yield. [e] The reaction was carried out under air.

Encouraged by the successful *N*-alkynylation of the imine nitrogen of *N*-deprotected sulfonimidamides **1**, we next attempted the alkynylation of the primary *N*-amino group of *N*-protected sulfonimidamides **6** or **7** with phenylacetylene. Unfortunately, our efforts to use *N*-protected sulfonimidamides **6** or **7** in this transformation were unsuccessful (Scheme 1) under the optimised reaction conditions, and only homocoupled Glaser–Hay diyne was formed.

The *N*-alkynylated sulfonimidamides **3** obtained in Figure 1 above were ideally purified by chromatography on neutral alumina. Purification by silica gel chromatography was accompanied by hydrolysis to the corresponding *N*-acyl-sulfonimidamides (i.e., **5**); similar conversions have been reported in the literature.[3e,14] Prolonged exposure of



Scheme 1. Attempted alkynylation of the primary amino functionality of *N*-protected sulfonimidamides.

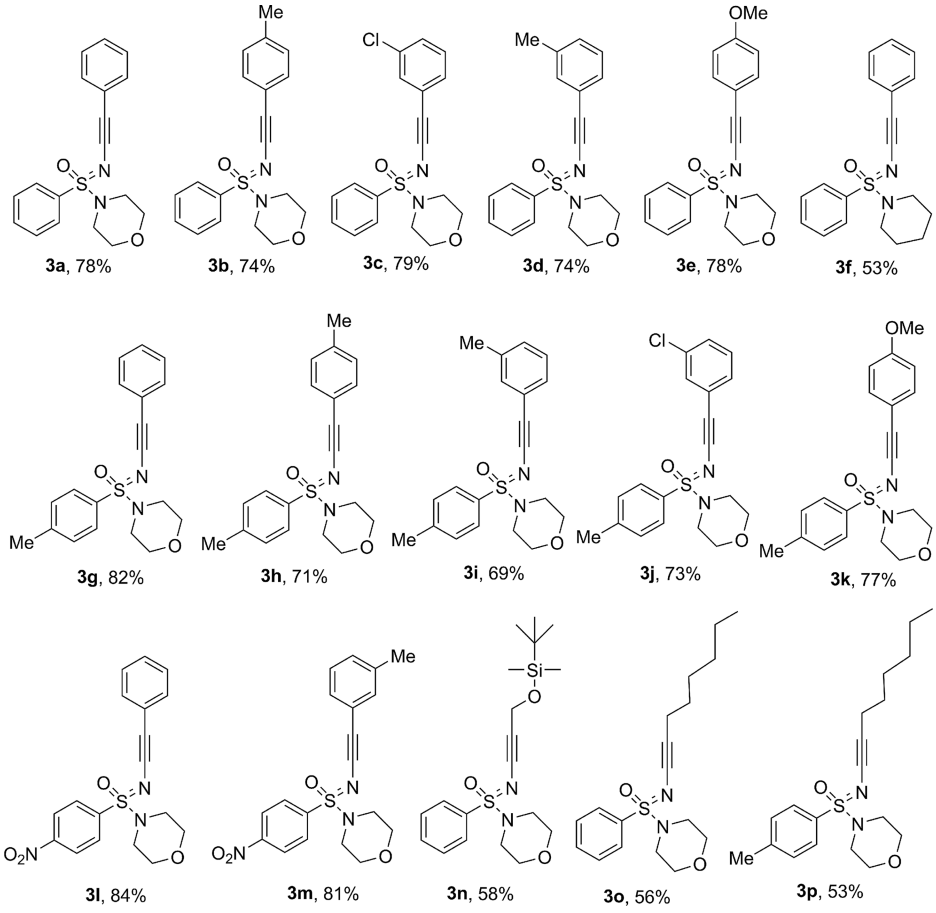
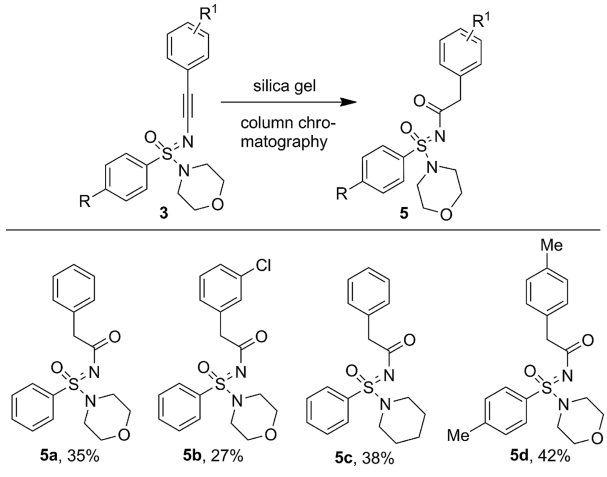


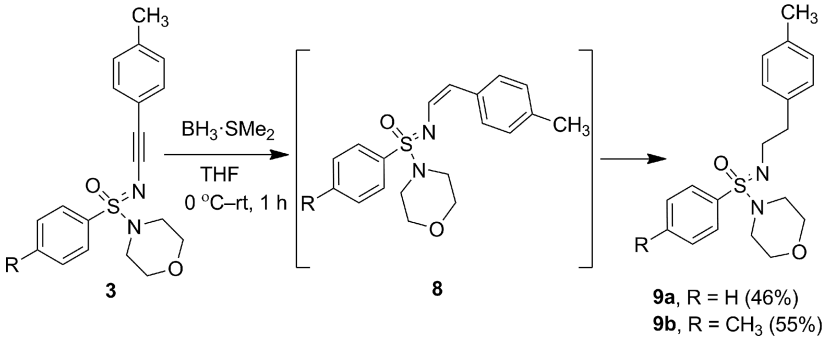
Figure 1. Substrate scope for the oxidative C–N cross-coupling reaction between alkynes and sulfonimidamides to give *N*-alkynylated sulfonimidamides.

N-alkynylated products **3** to silica gel led to decomposition rather than hydrolysis; however, by quickly passing the *N*-alkynylated sulfonimidamide products (i.e., **3**) through a silica gel column, we could reproducibly prepare *N*-acylsulfonimidamide products **5** (Scheme 2).

The alkyne moieties of the *N*-alkynylated sulfonimidamides show unusual reactivity. The triple bond in **3** did not react through common procedures such as, e.g., nucleophilic addition (thiols and Grignard reagents), halogenation (Br_2), [2+2] cycloaddition (isocyanate and isothiocyanate), or hydrogenation ($Pd/C/H_2$). However, attempted reactions of the alkynes in *N*-alkynylated sulfonimidamides **3a** and **3b** with $BH_3{\cdot}SMe_2$ (3.0 equiv.) were successful. To our surprise, the reduction did not lead to the expected *cis*-alkene product (i.e., **8**) as reported in the literature,[15] but directly gave alkane **9a** or **9b**, Scheme 3. To the best of our knowledge, no prior report on the direct reduction of alkynes to



Scheme 2. Hydrolysis of *N*-alkynylated sulfonimidamides on a silica gel column.



Scheme 3. Reduction of *N*-alkynylated sulfonimidamides to *N*-alkyl-sulfonimidamides by $BH_3{\cdot}SMe_2$.

alkanes by $BH_3{\cdot}SMe_2$ has been reported in the literature. We could detect *cis*-alkene **8** as an intermediate by ^1H NMR spectroscopy, but all attempts to prepare alkene **8** on a useful scale, i.e. by using a lower amount of $BH_3{\cdot}SMe_2$ (0.5 equiv.) or a lower temperature, led to poor conversion of the starting material.

Conclusions

In summary, we have developed an efficient and practical protocol for the synthesis of hitherto unknown *N*-alkynylated sulfonimidamides. The protocol is based on an oxidative C–N cross-coupling reaction of terminal alkynes and *N*-deprotected sulfonimidamides. We have used anhydrous $Cu(OAc)_2$, a very cheap catalyst, which was effective for both terminal aryl and alkyl alkynes ($CuCl_2$ was ineffective with terminal aliphatic alkynes). *N*-Alkynyl-substituted sulfonimidamides **3** could be further transformed into *N*-acyl-sulfonimidamides **5** by passing through a silica gel column. Furthermore, we discovered a hitherto unprecedented borane–dimethyl sulfide reduction of the triple bond of *N*-alkynyl-sulfonimidamides directly to the corresponding *N*-alkyl analogues. Further studies directed towards extending the synthetic applications sulfonimidamides and *N*-alkynylated sulfonimidamides are currently underway in our laboratory.

Experimental Section

General Remarks: The starting sulfonimidamides were synthesised in our laboratory by the reported method. The terminal alkynes, anhydrous $Cu(OAc)_2$, $CuBr_2$, pyridine, and 4-(dimethylamino)pyridine (DMAP) were purchased from Sigma–Aldrich, and were used as received. Anhydrous $CuCl_2$ was prepared by freeze drying $CuCl_2{\cdot}H_2O$. ^1H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively, with a Bruker AVANCE III spectrometer. Chemical shifts are expressed in ppm downfield from tetramethylsilane, which was used as an internal standard, and coupling constants are reported in Hz. For IR spectra, attenuated total reflection infrared (ATR-IR) was used for analysis. Mass spectrometric data were recorded with a Bruker Micro TOF-Q II instrument with direct injection of samples in acetonitrile. Crude compounds were purified by column chromatography using neutral alumina.

General Procedure for the Reaction of Sulfonimidamides and Terminal Alkynes to Give *N*-Alkynyl-Sulfonimidamides 3a–3p and *N*-Acyl-Sulfonimidamides 5a–5d: A Schlenk tube (10 mL) containing 1,4-dioxane (1.0 mL) was purged with oxygen for 15 min. Then the sulfonimidamide (2.5 equiv.), $Cu(OAc)_2$ (20 mol-%), Na_2CO_3 (2.0 equiv.), and pyridine (2.0 equiv.) were added. A balloon filled with oxygen was connected to the Schlenk tube. The Schlenk tube was then placed in a preheated oil bath at 70 °C. The terminal alkyne (1.0 equiv.) was dissolved in 1,4-dioxane (2.0 mL), and this solution was added to the reaction mixture dropwise by syringe over 3.5 h. After the addition of the terminal alkyne solution was complete, the reaction mixture was stirred at 70 °C for an additional 2 h. The mixture was then evaporated to dryness, and the residue was purified by neutral alumina column chromatography (5–7% EtOAc in hexane) to give the *N*-alkynylated sulfonimidamide **3a**–**3p**.

Purification of the crude product by column chromatography on silica gel instead of alumina provided the corresponding *N*-acyl-sulfonimidamides **5a**–**5d** as a result of silica-gel-catalysed hydrolysis.

General Procedure for the Reduction of *N*-Alkynyl-Sulfonimidamides (3) to Give *N*-Alkyl-Sulfonimidamides (9): Borane–dimethyl sulfide (3.0 equiv.) was added to a stirred solution of *N*-alkynyl-substituted sulfonimidamides **3a–3b** (0.05 mmol) in anhydrous THF (0.5 mL) at 0 °C. The reaction mixture was stirred at room temperature for 1 h. When the reaction was complete, water was added (2 mL), and the mixture was extracted with EtOAc (2× 10 mL). The organic layer was dried with $MgSO_4$, evaporated, and purified by neutral alumina column chromatography (3–5% EtOAc in hexane) to give the reduced products **9a**–**9b**.

4-[*S*-Phenyl-*N*′-(phenylethynyl)sulfonimidoyl]morpholine (3a): Pale yellow sticky liquid (20 mg, 78%; from 0.07843 mmol of terminal alkyne). IR (ATR): $\tilde{\nu}$ = 3069, 2966, 2201, 1648, 1248 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, J = 7.52 Hz, 2 H), 7.68 (t, J = 7.56 Hz, 1 H), 7.60 (t, J = 7.58 Hz, 2 H), 7.37 (d, J = 6.96 Hz, 2 H), 7.25 (t, J = 7.84 Hz, 2 H), 7.19 (t, J = 7.28 Hz, 1 H), 3.83–3.80 (m, 4 H), 3.18–3.14 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 133.7, 133.5, 131.4, 129.4, 128.2, 128.1, 126.2, 125.6, 85.8, 66.3, 59.4, 46.4 ppm. HRMS (ESI): calcd. for $C_{18}H_{18}N_2O_2S$ $[M + H]^+$ 327.1161; found 327.1173.

4-[*S*-Phenyl-*N*′-(*p*-tolylethynyl)sulfonimidoyl]morpholine (3b): White solid (17.4 mg, 74%; from 0.06897 mmol of terminal alkyne); m.p. 101–102 °C. IR (ATR): $\tilde{\nu}$ = 2960, 2919, 2198, 1352, 1240 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.92 (d, J = 8.84 Hz, 2 H), 7.66 (t, J = 7.4 Hz, 1 H), 7.58 (t, J = 7.88 Hz, 2 H), 7.25 (d, J = 7.96 Hz, 2 H), 7.04 (d, J = 7.96 Hz, 2 H), 3.81–3.78 (m, 4 H), 3.16–3.12 (m, 4 H), 2.31 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.1, 133.7, 133.6, 131.3, 129.4, 128.9, 128.2, 122.5, 84.9, 66.3, 59.3, 46.5, 21.4 ppm. HRMS (ESI): calcd. for $C_{19}H_{20}N_2O_2S$ $[M + H]^+$ 341.1318; found 341.1313.

4-[*S*-Phenyl-*N*′-(3-chlorophenylethynyl)sulfonimidoyl]morpholine (3c): Pale yellow sticky liquid (16.7 mg, 79%; from 0.05882 mmol of terminal alkyne). IR (ATR): ṽ = 2958, 2924, 2856, 2207, 1446, 1112 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92 (d, J = 7.40 Hz, 2 H), 7.68 (t, J = 7.32 Hz, 1 H), 7.59 (t, J = 7.96 Hz, 2 H), 7.31 (s, 1 H), 7.23–7.20 (m, 1 H), 7.15–7.14 (m, 2 H), 3.81–3.79 (m, 4 H), 3.15–3.13 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 133.9, 133.3, 131.2, 129.5, 129.4, 129.3, 128.2, 127.5, 126.4, 87.3, 66.3, 58.3, 46.5 ppm. HRMS (ESI): calcd. for $C_{18}H_{17}ClN_2O_2S$ [M + H]$^+$ 361.0772; found 361.0764.

4-[*S*-Phenyl-*N*′-(3-methylphenylethynyl)sulfonimidoyl]morpholine (3d): Pale yellow sticky liquid (17.7 mg, 74%; from 0.06897 mmol of terminal alkyne). IR (ATR): ṽ = 3069, 2963, 2866, 2213, 1446, 1251, 1112 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92 (d, J = 7.32 Hz, 2 H), 7.67 (t, J = 7.32 Hz, 1 H), 7.58 (t, J = 7.32 Hz, 2 H), 7.18–7.11 (m, 3 H), 6.99 (d, J = 6.96 Hz, 1 H), 3.81–3.78 (m, 4 H), 3.16–3.13 (m, 4 H), 2.29 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.7, 133.7, 133.6, 132.1, 129.4, 128.5, 128.2, 128.0, 127.1, 125.4, 85.4, 66.3, 59.5, 46.5, 21.3 ppm. HRMS (ESI): calcd. for $C_{19}H_{20}N_2O_2S$ [M + H]$^+$ 341.1318; found 341.1300.

4-[*S*-Phenyl-*N*′-(4-methoxyphenylethynyl)sulfonimidoyl]morpholine (3e): White solid (16.8 mg, 78%; from 0.06061 mmol of terminal alkyne); m.p. 125–127 °C. IR (ATR): ṽ = 2957, 2860, 2205, 1448, 1236, 1107 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92 (d, J = 7.72 Hz, 2 H), 7.66 (t, J = 7.32 Hz, 1 H), 7.58 (t, J = 7.92 Hz, 2 H), 7.29 (d, J = 8.68 Hz, 2 H), 6.79 (d, J = 8.68 Hz, 2 H), 3.81–3.78 (m, 7 H), 3.16–3.12 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.3, 133.8, 133.7, 132.8, 129.4, 128.3, 117.9, 113.9, 84.1, 66.4, 59.0, 55.4, 46.6 ppm. HRMS (ESI): calcd. for $C_{19}H_{20}N_2O_3S$ [M + H_2O + H]$^+$ 375.1373; found 375.1383.

1-[*S*-Phenyl-*N*′-(3-phenylethynyl)sulfonimidoyl]piperidine (3f): Brown sticky liquid (13.4 mg, 53%; from 0.07843 mmol of terminal alkyne). IR (ATR): ṽ = 3060, 2925, 2852, 2200, 1446, 1243, 1117 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92 (d, J = 7.32 Hz, 2 H), 7.63 (t, J = 7.40 Hz, 1 H), 7.55 (t, J = 7.80 Hz, 2 H), 7.34 (d, J = 7.00 Hz, 2 H), 7.22 (t, J = 7.08 Hz, 2 H), 7.15 (t, J = 7.36 Hz, 1 H), 3.18–3.14 (m, 4 H), 1.73–1.68 (m, 4 H), 1.49–1.46 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.0, 133.2, 131.4, 129.2, 128.1, 128.0, 126.1, 125.9, 86.7, 59.0, 47.4, 25.5, 23.7 ppm. HRMS (ESI): calcd. for $C_{19}H_{20}N_2OS$ [M + H]$^+$ 325.1369; found 325.1385.

4-[*S*-*p*-Tolyl-*N*′-(phenylethynyl)sulfonimidoyl]morpholine (3g): White solid (21.9 mg, 82%; from 0.07843 mmol of terminal alkyne); m.p. 120–121 °C. IR (ATR): ṽ = 2963, 2856, 2206, 1349, 1249 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78 (d, J = 8.32 Hz, 2 H), 7.36–7.32 (m, 4 H), 7.22 (t, J = 7.2 Hz, 2 H), 7.15 (t, J = 7.2 Hz, 1 H), 3.79–3.76 (m, 4 H), 3.13–3.09 (m, 4 H), 2.44 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.8, 131.4, 130.4, 130.0, 128.3, 128.1, 126.1, 125.7, 86.1, 66.3, 59.2, 46.4, 21.7 ppm. HRMS (ESI): calcd. for $C_{19}H_{20}N_2O_2S$ [M + H]$^+$ 341.1318; found 341.1324.

4-[*S*-*p*-Tolyl-*N*′-(*p*-tolylethynyl)sulfonimidoyl]morpholine (3h): White solid (17.3 mg, 71%; from 0.06897 mmol of terminal alkyne); m.p. 115–117 °C. IR (ATR): ṽ = 2960, 2918, 2201, 1347, 1244, 1109 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79 (d, J = 8.28 Hz, 2 H), 7.36 (d, J = 8.2 Hz, 2 H), 7.25 (d, J = 7.88 Hz, 2 H), 7.04 (d, J = 7.88 Hz, 2 H), 3.80–3.77 (m, 4 H), 3.14–3.10 (m, 4 H), 2.45 (s, 3 H), 2.31 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.8, 136.0, 131.3, 130.5, 130.0, 128.9, 128.3, 122.6, 85.1, 66.4, 59.2, 46.5, 21.7, 21.4 ppm. HRMS (ESI): calcd. for $C_{20}H_{22}N_2O_2S$ [M + H]$^+$ 355.1474; found 355.1458.

4-[*S*-*p*-Tolyl-*N*′-(3-methylphenylethynyl)sulfonimidoyl]morpholine (3i): White solid (16.8 mg, 69%; from 0.06897 mmol of terminal alkyne); m.p. 101–103 °C. IR (ATR): ṽ = 2965, 2910, 2204, 1342, 1250, 1103 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79 (d, J = 8.32 Hz, 2 H), 7.36 (d, J = 8.20 Hz, 2 H), 7.18–7.10 (m, 3 H), 7.99 (d, J = 7.20 Hz, 1 H), 3.80–3.77 (m, 4 H), 3.13–3.10 (m, 4 H), 2.44 (s, 3 H), 2.29 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.7, 137.6, 132.0, 130.3, 129.9, 128.4, 128.2, 128.0, 127.0, 125.5, 85.7, 66.2, 59.2, 46.4, 21.6, 21.3 ppm. HRMS (ESI): calcd. for $C_{20}H_{22}N_2O_2S$ [M + H]$^+$ 355.1474; found 355.1464.

4-[*S*-*p*-Tolyl-*N*′-(3-chlorophenylethynyl)sulfonimidoyl]morpholine (3j): White solid (16.0 mg, 73%; from 0.05882 mmol of terminal alkyne); m.p. 110–112 °C. IR (ATR): ṽ = 2963, 2855, 2203, 1451, 1243, 1111 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79 (d, J = 8.36 Hz, 2 H), 7.38 (d, J = 8.16 Hz, 2 H), 7.30 (s, 1 H), 7.21–7.19 (m, 1 H), 7.15–7.13 (m, 2 H), 3.80–3.78 (m, 4 H), 3.13–3.10 (m, 4 H), 2.46 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.0, 133.8, 131.2, 130.2, 130.1, 129.5, 129.3, 128.3, 127.6, 126.3, 87.6, 66.3, 58.1, 46.4, 21.7 ppm. HRMS (ESI): calcd. for $C_{19}H_{19}ClN_2O_2S$ [M + H]$^+$ 375.0928; found 375.0921.

4-[*S*-*p*-Tolyl-*N*′-(4-methoxyphenylethynyl)sulfonimidoyl]morpholine (3k): White solid (17.2 mg, 77%; from 0.06061 mmol of terminal alkyne); m.p. 166–168 °C. IR (ATR): ṽ = 2959, 2856, 2202, 1457, 1336, 1240, 1111 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79 (d, J = 8.08 Hz, 2 H), 7.36 (d, J = 8.20 Hz, 2 H), 7.28 (d, J = 8.68 Hz, 2 H), 6.78 (d, J = 8.68 Hz, 2 H), 3.80–3.77 (m, 7 H), 3.13–3.10 (m, 4 H), 2.45 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.2, 144.7, 132.7, 130.5, 130.0, 128.3, 117.9, 113.8, 84.2, 66.4, 58.8, 55.4, 46.5. 21.7 ppm. HRMS (ESI): calcd. for $C_{20}H_{22}N_2O_3S$ [M + H_2O + H]$^+$ 389.1529; found 389.1536.

4-[*S*-*p*-Nitrophenyl-*N*′-(4-methoxyphenylethynyl)sulfonimidoyl]-morpholine (3l): Yellow solid (24.4 mg, 84%; from 0.07843 mmol of terminal alkyne); m.p. 162–163 °C. IR (ATR): ṽ = 3102, 2905, 2851, 2207, 1349, 1247, 1111 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.42 (d, J = 8.76 Hz, 2 H), 8.12 (d, J = 8.76 Hz, 2 H), 7.36–7.34 (m, 2 H), 7.27–7.20 (m, 3 H), 3.84–3.80 (m, 4 H), 3.22–3.19 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.8, 140.1, 131.5, 129.4, 128.3, 126.7, 125.0, 124.6, 84.3, 66.3, 60.3, 46.5 ppm. HRMS (ESI): calcd. for $C_{18}H_{17}N_3O_4S$ [M + H]$^+$ 372.1012; found 372.1005.

4-[*S*-*p*-Nitrophenyl-*N*′-(3-methylphenylethynyl)sulfonimidoyl]-morpholine (3m): Brown sticky liquid (21.5 mg, 81%; from 0.06897 mmol of terminal alkyne). IR (ATR): ṽ = 3102, 2919, 2857, 2216, 1529, 1346, 1255, 1112 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.43 (d, J = 8.84 Hz, 2 H), 8.14 (d, J = 8.80 Hz, 2 H), 7.19–7.16 (m, 3 H), 7.05–7.03 (m, 1 H), 3.85–3.82 (m, 4 H), 3.24–3.21 (m, 4 H), 2.32 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.7, 140.1, 137.9, 132.1, 129.4, 128.6, 128.2, 127.6, 124.8, 124.6, 83.9, 66.3, 60.4, 46.5, 21.4 ppm. HRMS (ESI): calcd. for $C_{19}H_{19}N_3O_4S$ [M + H]$^+$ 386.1169; found 386.1153.

4-{*S*-Phenyl-*N*′-[*tert*-butyldimethyl(prop-2-ynyloxy)silane]sulfonimidoyl}morpholine (3n): Pale yellow sticky liquid (10.8 mg, 58%; from 0.04734 mmol of terminal alkyne). IR (ATR): ṽ = 2955, 2895, 2228, 1461, 1236, 1113 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86 (d, J = 7.56 Hz, 2 H), 7.64 (t, J = 7.48 Hz, 1 H), 7.55 (t, J = 7.92 Hz, 2 H), 4.42 (s, 2 H), 3.78–3.75 (m, 4 H), 3.08–3.06 (m, 4 H), 0.98 (s, 9 H), 0.12 (s, 3 H), 0.11 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 133.6, 133.4, 129.3, 128.2, 80.3, 66.2, 56.9, 52.6, 46.4, 26.0, 18.4, –4.77 ppm. HRMS (ESI): calcd. for $C_{19}H_{30}N_2O_3SSi$ [M + H]$^+$ 395.1819; found 395.1821.

4-[*S*-Phenyl-*N*′-(oct-1-ynyl)sulfonimidoyl]morpholine (3o): Pale yellow sticky liquid (13.7 mg, 56%; from 0.07339 mmol of terminal alkyne). IR (ATR): ṽ = 3102, 2919, 2857, 2216, 1529, 1346, 1255,

1112 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (d, J = 7.84 Hz, 2 H), 7.63 (t, J = 7.28 Hz, 1 H), 7.54 (t, J = 7.92 Hz, 2 H), 3.78–3.75 (m, 4 H), 3.09–3.06 (m, 4 H), 2.23 (t, J = 6.80 Hz, 2 H), 1.49–1.45 (m, 2 H), 1.39–1.34 (m, 2 H), 1.29–1.25 (m, 4 H), 0.88 (t, J = 6.72 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 133.7, 133.4, 129.2, 128.2, 74.9, 66.3, 58.2, 46.4, 31.6, 29.9, 28.7, 22.8, 18.9, 14.2 ppm. HRMS (ESI): calcd. for $C_{18}H_{26}N_2O_2S$ [M + H]$^+$ 335.1787; found 335.1796.

4-[*S*-Phenyl-*N*′-(oct-1-ynyl)sulfonimidoyl]morpholine (3p): Pale yellow sticky liquid (13.5 mg, 53%; from 0.07339 mmol of terminal alkyne). IR (ATR): $\tilde{\nu}$ = 2956, 2855, 2235, 1452, 1258, 1229, 1113 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.74 (d, J = 8.32 Hz, 2 H), 7.33 (d, J = 8.16 Hz, 2 H), 3.77–3.75 (m, 4 H), 3.07–3.04 (m, 4 H), 2.43 (s, 3 H), 2.22 (t, J = 6.84 Hz, 2 H), 1.49–1.43 (m, 2 H), 1.39–1.35 (m, 2 H), 1.28–1.25 (m, 4 H), 0.88 (t, J = 6.76 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.4, 130.5, 129.8, 128.3, 75.1, 66.3, 58.0, 46.4, 31.6, 30.0, 28.7, 22.8, 21.6, 18.9, 14.2 ppm. HRMS (ESI): calcd. for $C_{19}H_{28}N_2O_2S$ [M + H]$^+$ 349.1944; found 349.1958.

4-[*S*-Phenyl-*N*′-(phenylacetyl)sulfonimidoyl]morpholine (5a): White solid (9.4 mg, 35%; from 0.07843 mmol of terminal alkyne); m.p. 120–121 °C. IR (ATR): $\tilde{\nu}$ = 2924, 2849, 1655, 1445, 1172 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64 (d, J = 7.68 Hz, 2 H), 7.59 (t, J = 7.40 Hz, 1 H), 7.48 (t, J = 7.80 Hz, 2 H), 7.35–7.30 (m, 4 H), 7.26–7.23 (m, 1 H), 3.69–3.64 (m, 6 H), 3.00–2.86 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.7, 136.3, 135.0, 133.4, 129.7, 129.3, 128.5, 127.8, 126.8, 66.1, 47.6, 45.6 ppm. HRMS (ESI): calcd. for $C_{18}H_{20}N_2O_3S$ [M + H]$^+$ 345.1267; found 345.1263.

1-[*S*-Phenyl-*N*′-(phenylacetyl)sulfonimidoyl]piperidine (5b): White solid (6.0 mg, 27%; from 0.05882 mmol of terminal alkyne); m.p. 85–86 °C. IR (ATR): $\tilde{\nu}$ = 2925, 2854, 1651, 1445, 1176 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.66 (d, J = 7.32 Hz, 2 H), 7.55 (t, J = 7.44 Hz, 1 H), 7.45 (t, J = 7.88 Hz, 2 H), 7.35–7.29 (m, 4 H), 7.26–7.23 (m, 1 H), 3.72–3.64 (m, 2 H), 2.98–2.95 (m, 4 H), 1.56 (br., 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.7, 141.5, 136.5, 133.0, 129.7, 129.1, 128.4, 127.7, 126.6, 47.5, 46.4, 25.3, 23.7 ppm. HRMS (ESI): calcd. for $C_{19}H_{22}N_2O_2S$ [M + H]$^+$ 343.1474; found 343.1463.

4-[*S*-Phenyl-*N*′-(3-chlorophenylacetyl)sulfonimidoyl]morpholine (5c): White solid (10.2 mg, 38%; from 0.07843 mmol of terminal alkyne); m.p. 105–107 °C. IR (ATR): $\tilde{\nu}$ = 2929, 2855, 1650, 1444, 1173 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67 (d, J = 7.44 Hz, 2 H), 7.61 (t, J = 7.28 Hz, 1 H), 7.51 (t, J = 7.84 Hz, 2 H), 7.36 (s, 1 H), 7.26–7.22 (m, 3 H), 3.69–3.65 (m, 6 H), 3.04–2.90 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.8, 138.2, 134.9, 134.2, 133.6, 129.9, 129.7, 129.4, 127.8, 127.8, 126.9, 66.1, 47.0, 45.6 ppm. HRMS (ESI): calcd. for $C_{18}H_{19}ClN_2O_3S$ [M + H]$^+$ 379.0877; found 379.0876.

4-[*S*-*p*-Tolyl-*N*′-(*p*-tolylacetyl)sulfonimidoyl]morpholine (5d): White solid (10.8 mg, 42%; from 0.06897 mmol of terminal alkyne); m.p. 96–98 °C. IR (ATR): $\tilde{\nu}$ = 2930, 2851, 1658, 1446, 1177 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53 (d, J = 8.24 Hz, 2 H), 7.27 (d, J = 8.36 Hz, 2 H), 7.22 (d, J = 7.88 Hz, 2 H), 7.11 (d, J = 7.76 Hz, 2 H), 3.66–3.63 (m, 6 H), 2.99–2.86 (m, 4 H), 2.41 (s, 3 H), 2.35 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.9, 144.4, 136.2, 133.2, 131.8, 130.0, 129.5, 129.1, 127.9, 66.2, 47.1, 45.6, 21.6, 21.2 ppm. HRMS (ESI): calcd. for $C_{20}H_{24}N_2O_3S$ [M + H]$^+$ 373.1580; found 373.1586.

4-[*S*-*p*-Tolyl-*N*′-(*p*-tolylethenyl)sulfonimidoyl]morpholine (8): This intermediate was only isolated in small quantities as a yellow liquid to allow characterization by ^{1}H NMR spectroscopy. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.83 (d, J = 8.2 Hz, 2 H), 7.74 (d, J = 8.23 Hz, 2 H), 7.37 (d, J = 8.14 Hz, 2 H), 7.12 (d, J = 8.14 Hz, 2 H), 6.66 (d, J = 8.77 Hz, 1 H), 5.64 (d, J = 8.77 Hz, 1 H), 3.71–3.68 (m, 4 H), 3.01–2.96 (m, 2 H), 2.93–2.87 (m, 2 H), 2.46 (s, 3 H), 2.33 (s, 3 H) ppm.

4-[*S*-Phenyl-*N*′-(*p*-tolylethyl)sulfonimidoyl]morpholine (9a): Pale yellow syrup (9.3 mg, 46%). IR (ATR): $\tilde{\nu}$ = 2954, 2924, 2852, 1459, 1281, 1256, 930 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80 (d, J = 7.30 Hz, 2 H), 7.57–7.47 (m, 3 H), 7.18 (d, J = 7.84 Hz, 2 H), 7.10 (d, J = 7.84 Hz, 2 H), 3.62–3.55 (m, 4 H), 3.54–3.48 (m, 1 H), 3.32–3.25 (m, 1 H), 2.96–2.86 (m, 2 H), 2.84–2.80 (m, 2 H), 2.64–2.59 (m, 2 H), 2.31 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.8, 135.6, 135.1, 132.4, 129.1, 129.0, 128.8, 128.0, 66.5, 46.8, 44.2, 38.8, 21.1 ppm. HRMS (ESI): calcd. for $C_{19}H_{25}N_2O_2S$ [M + H]$^+$ 345.1637; found 345.1619.

4-[*S*-*p*-Tolyl-*N*′-(*p*-tolylethyl)sulfonimidoyl]morpholine (9b): Yellow syrup (11.0 mg, 55%). IR (ATR): $\tilde{\nu}$ = 2954, 2922, 2853, 1454, 1256, 932 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67 (d, J = 8.4 Hz, 2 H), 7.28 (d, J = 8.4 Hz, 2 H), 7.17 (d, J = 8.4 Hz, 2 H), 7.09 (d, J = 8.4 Hz, 2 H), 3.61–3.53 (m, 4 H), 3.52–3.47 (m, 1 H), 3.30–3.23 (m, 1 H), 2.95–2.85 (m, 2 H), 2.82–2.77 (m, 2 H), 2.63–2.57 (m, 2 H), 2.41 (s, 3 H), 2.31 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.0, 137.9, 135.5, 132.0, 129.4, 129.1, 129.0, 128.1, 66.5, 46.8, 44.2, 38.8, 21.5, 21.1 ppm. HRMS (ESI): calcd. for $C_{20}H_{27}N_2O_2S$ [M + H]$^+$ 359.1793; found 359.1775.

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