Synthesis of *N*-Sulfonylazetidin-2-imines via the Copper(I) Oxide Catalyzed Multicomponent Reaction of Alkynes, Sulfonyl Azides and Diimines under Solvent-Free Conditions

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Abstract: *N*-Sulfonylazetidin-2-imines are synthesized efficiently via three-component reactions of sulfonyl azides, terminal alkynes, and carbodiimides using copper(I) oxide as an inexpensive and eco-friendly catalyst under solvent-free conditions, without the need for an additional base or ligand. The same method is applied to the preparation of an azetidin-2-ylidene derivative using a 1,2-diimine as the nucleophile.

Key words: *N*-sulfonylazetidin-2-imines, multicomponent reaction, copper(I) oxide, solvent-free, sulfonyl azides

The copper-catalyzed azide–alkyne cycloaddition (CuAAC) reaction has been the focus of significant interest in organic synthesis, materials science, biosciences, and medicinal chemistry.[1] Previous reports showed that the key intermediates generated in situ during the copper-catalyzed reaction of terminal alkynes with sulfonyl azides were ketenimines.[2] On in situ reaction of the ketenimine species with nucleophiles such as amines, alcohols, water, or heteroaromatics, the ensuing copper-catalyzed multicomponent reaction affords the corresponding amidines, imidates, amides, or functionalized heteroaromatics, respectively.[3] As a result of the intrinsic benefits of multicomponent reactions in modern organic synthesis, as well as in the fields of combinatorial chemistry and drug discovery,[4] the copper-catalyzed azide–alkyne cycloaddition multicomponent process has been utilized as a very important synthetic tool leading to satisfactory results.[5] An important example of this procedure is the synthesis of azetidine-2-imine derivatives via the formal [2+2] cycloaddition of in situ generated ketenimine intermediates with a range of imines.[2b,6] The resulting azetidines contain a β-lactam group which is a key structure in a variety of antibiotics including the cephalosporins and penicillins.[7] The interesting biological and antibacterial activities of azetidin-2-imines have rendered them suitable as substrates in the design and development of functionalized antibacterial agents.[8] The groups of Xu[6a] and Fokin[6b] have reported several copper(I) iodide catalyzed multicomponent reactions of sulfonyl azides, alkynes and imines to construct such azetidine-2-imine ring systems. Disadvantageously, however, these reactions either proceeded in organic solvents or in the presence of ligands or bases. Hence, the development of environmentally friendly, simple, general, and synthetically useful methods for the synthesis of azetidin-2-imines is highly desirable.

A large number of copper systems have been utilized successfully for the catalysis of azide–alkyne cycloadditions.[1] Of these copper(0–II) catalytic species, copper(I) oxide (Cu_2O) is the most readily available, and above all, is inexpensive. As part of our interest in the development of non-precious metal catalyzed organic reactions, in particular the synthesis of heterocycles,[9] we previously developed a copper(I) oxide catalyzed azide–alkyne cycloaddition for the synthesis of triazoles.[9a] In continuation of this work, we found that *N*-sulfonylazetidin-2-imines could be prepared via the copper(I) oxide catalyzed three-component reaction of sulfonyl azides, phenylacetylene and carbodiimides under solvent-free conditions. Our results showed that this one-pot transformation proceeded well under neat conditions to afford the desired azetidine derivatives in very short reaction times and in good to high yields. In addition, no undesired side reactions occurred.

An initial investigation of the catalytic species was performed using tosyl azide (**1a**), phenylacetylene (**2a**) and *N*,*N*′-dicyclohexylcarbodiimide (DCC) (**3a**) as model substrates (Table 1). Several copper(I) and copper(II) salts (10 mol%) were examined as candidates. Copper(I) oxide proved to be the best furnishing the desired *N*-sulfonylazetidin-2-imine **4a** in 80% yield after four hours (Table 1, entry 1). Surprisingly, copper(II) bromide ($CuBr_2$) and copper(II) acetate [$Cu(OAc)_2$], both being copper(II) salts, also promoted the reaction to provide the expected imine in yields of 56% and 77% (Table 1, entries 3 and 4). In contrast, the other screened copper salts showed very little catalytic activity (Table 1, entries 2 and 5). In a control experiment, no transformation was observed when the reaction was conducted in the absence of a catalyst, even after an extended reaction time of five hours (Table 1, entry 6). These results corroborated our previous work on triazoles in which copper(I) oxide was used as the catalyst in water.[9a]

Having established an efficient catalytic system [copper(I) oxide (10 mol%), solvent-free conditions, room temperature], the scope of this three-component reaction was explored using various sulfonyl azides, terminal al-

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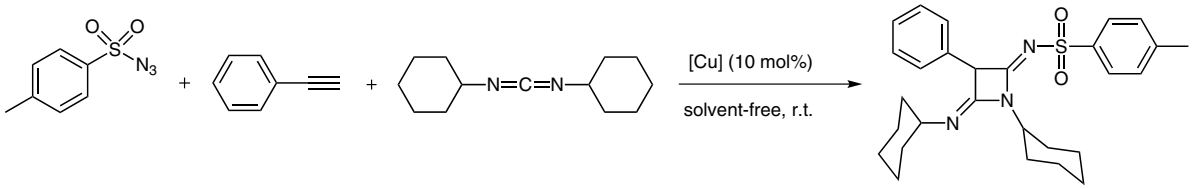
Table 1 Optimization of the Copper Catalyst

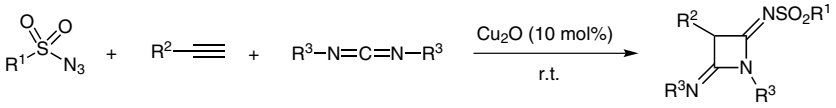


1a **2a** **3a** **4a**

Entry	Catalyst	Time (h)	Yield (%)[a]
1	Cu_2O	4	80
2	CuI	4.5	17
3	$CuBr_2$	3	56
4	$Cu(OAc)_2$	4	77
5	$Cu(OTf)_2$	3	11
6	none	5	0

[a] Yield of isolated product.

Table 2 Copper(I) Oxide Catalyzed Multicomponent Reaction of Sulfonyl Azides, Alkynes and Carbodiimides for the Synthesis of *N*-Sulfonylazetidin-2-imines **4**[a]



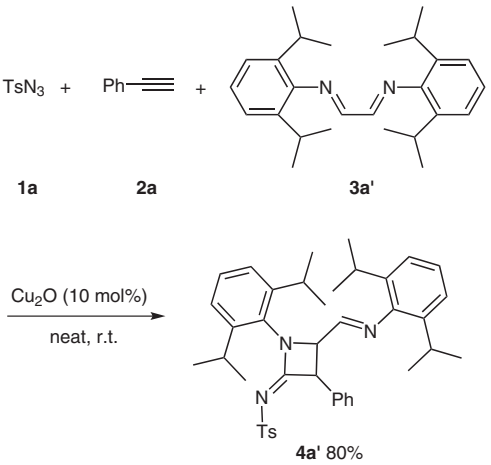
1 **2** **3** **4**

Entry	R^1	R^2	R^3	Time (h)	Product	Yield (%)[b]
1	4-MeC_6H_4 (**1a**)	Ph (**2a**)	*c*-Hex (**3a**)	4	**4a**	80
2	**1a**	4-MeC_6H_4 (**2b**)	**3a**	2	**4b**	72
3	**1a**	2-$F_3CC_6H_4$ (**2c**)	**3a**	2.5	**4c**	76
4	**1a**	$BocNHCH_2$ (**2d**)	**3a**	3	**4d**	85
5	**1a**	4-*t*-BuC_6H_4 (**2e**)	**3a**	4	**4e**	81
6	**1a**	EtO_2C (**2f**)	**3a**	1	**4f**	89
7	**1a**	3-FC_6H_4 (**2g**)	**3a**	1.5	**4g**	94
8	**1a**	*c*-Pr (**2h**)	**3a**	9	**4h**	59
9	Me (**1b**)	**2a**	**3a**	2	**4i**	93
10	**1a**	**2b**	*i*-Pr (**3b**)	5	**4j**	74
11	**1a**	**2a**	**3b**	5	**4k**	78
12	**1a**	4-FC_6H_4 (**2i**)	**3a**	2	**4l**	88
13	**1a**	4-BrC_6H_4 (**2j**)	**3a**	2	**4m**	90
14	**1a**	3-$H_2NC_6H_4$ (**2k**)	**3a**	24	**4n**	0

[a] Reaction conditions: sulfonyl azide (1.0 mmol), alkyne (1.2 mmol), carbodiimide (1.2 mmol), Cu_2O (10 mol%), r.t., solvent-free.
[b] Yield of isolated product.

kynes, and carbodiimides, and the results are summarized in Table 2. Good to excellent yields of the azetidin-2-imines **4a**–**g** were obtained in short reaction times when the aromatic sulfonyl azide **1a**, possessing an electron-donating group (Table 2, entries 1–7), was treated with non-substituted aromatic terminal alkyne **2a** (Table 2, entry 1), or with a range of substituted terminal alkynes bearing either electron-donating (Table 2, entries 2, 4 and 5) or electron-withdrawing (Table 2, entries 3, 6 and 7) substituents. It is noteworthy that although the best yield of 94% was obtained using 1-ethynyl-3-fluorobenzene (**2g**) (Table 2, entry 7), the conversion required a slightly longer reaction time (1.5 hours) compared to the 89% yield afforded by ethynyl propionate (**2f**) in one hour (Table 2, entry 6). As expected, the reaction of tosyl azide (**1a**) with non-aromatic ethynylcyclopropane (**2h**) and *N*,*N*′-dicyclohexylcarbodiimide (**3a**) resulted in a low yield of product (59%) after an extended reaction time of nine hours (Table 2, entry 8). To further investigate the scope of this procedure, we examined the reactions of tosyl azide (**1a**) and various terminal alkynes with either **3a** or *N*,*N*′-diisopropylcarbodiimide (DIC) (**3b**). With the exception of alkyne **2k**, the aromatic sulfonyl azide took part in the reaction to give the corresponding *N*-sulfonylazetidin-2-imines in good to excellent yields (Table 2, entries 10–13). Interestingly, carbodiimide **3b** reacted with phenylacetylene (**2a**) and azide **1a** to give the corresponding *N*-sulfonylazetidin-2-imine **4k** in a comparable yield to that obtained from the analogous reaction using alkyne **2b** (Table 2, entries 10 and 11). With substrates **2i** and **2j**, improved results were obtained when tosyl azide (**1a**) was reacted with carbodiimide **3a** (Table 2, entries 12 and 13). Surprisingly, a very good 93% yield (Table 2, entry 9) was obtained when aliphatic methylsulfonyl azide (**1b**) was treated with phenylacetylene (**2a**) and carbodiimide **3a**. The employed reaction system is thus in agreement with Xu's work in which addition of a base as the promoter was not required;[6a] the carbodiimide is believed to function as both a reactant and weak base. On the other hand, treatment of **1a** with **2k** did not result in any transformation (Table 2, entry 14). From the observed effects of the R^1 and R^2 substituents (Table 2), it was apparent that our reaction was adaptable, and this inspired us to investigate possible diversification of the approach using a diimine as the nucleophile.

Various sulfonyl azides and terminal alkynes were investigated in reactions with the 1,2-diimine nucleophile, **3a′** under the optimized conditions (Scheme 1). To our surprise, only the reaction of tosyl azide (**1a**), phenylacetylene (**2a**) and 1,2-diimine **3a′** gave the expected azetidine **4a′** (80% yield). The structure of **4a′** was established from ^{1}H NMR, ^{13}C NMR and HRMS spectral data. Unambiguous confirmation of the structure was obtained by X-ray diffraction analysis[10] (Figure 1). Our observations reinforce the work of Chang[11] in which an alcohol is used as a carbon nucleophile instead, and by extension, supports the fact that the cycloaddition involved participation of a 1,2-diimine nucleophile.



Scheme 1 Copper(I) oxide catalyzed synthesis of azetidin-2-ylidene **4a′** under neat conditions

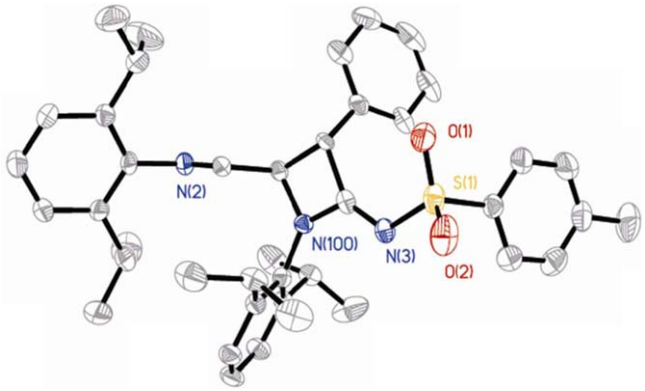


Figure 1 X-ray crystal structure of compound **4a′**

In conclusion, an efficient copper(I) oxide catalyzed, solvent-free, multicomponent reaction of sulfonyl azides, terminal alkynes, and carbodiimides has successfully been established for the synthesis of *N*-sulfonylazetidin-2-imines. In addition, a novel route for the selective synthesis of azetidine-2-ylidene **4a′** using a 1,2-diimine as the nucleophile has been described. This latter approach turned out to be quite specific, with the coupling only proceeding with tosyl azide, phenylacetylene and 1,2-diimine **3a′** as the substrates. Further synthetic modifications applicable to reactions of a variety of substrates with a 1,2-diimine nucleophile are currently under investigation.

All reagents were purchased from commercial sources and were used without further treatment unless otherwise indicated. TLC was performed on Quindao Haiyang plastic silica gel plates. The products were purified by column chromatography over ZCX-II 300–400 mesh silica gel. Petroleum ether (PE) refers to the fraction boiling in the 30–60 °C range. Melting points were obtained using a Yuhua X-4 apparatus and are uncorrected. ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectra were recorded at 25 °C using a Varian Unity 500 spectrometer. TMS was used as the internal standard. Mass spectra were recorded on an AutoflexIII Smartbeam spectrometer. High-resolution mass spectra (ESI) were recorded on a Bruck MicroTof instrument.

Compounds **4a**, **4b**, **4f**, **4i**, and **4k** are known compounds.[6a]

(*Z*)-*N*-[(*E*)-1-Cyclohexyl-4-(cyclohexylimino)-3-phenylazetidin-2-ylidene]-4-methylbenzenesulfonamide (4a); Typical Procedure

Tosyl azide (**1a**) (197 mg, 1.0 mmol), phenylacetylene (**2a**) (122 mg, 1.2 mmol), DCC (**3a**) (247 mg, 1.2 mmol) and Cu_2O (14 mg, 0.1 mmol) were added to a flask containing a stir bar, and the resulting mixture was stirred at r.t. (25 °C) without exclusion of air. After the reaction was complete (monitored by TLC), the mixture was diluted with CH_2Cl_2 (10 mL) and aq NH_4Cl soln (10 mL). The mixture was stirred for an additional 30 min and the two layers were separated. The aq layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layer was dried over $MgSO_4$, filtered and the solvent evaporated. The residue was purified by silica gel column chromatography (PE–EtOAc, 15:1) to afford the title product **4a**.

Yield: 0.38 g (80%); white solid; mp 168–169 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.31–7.27 (m, 3 H), 7.19 (d, *J* = 7.0 Hz, 2 H), 7.09 (d, *J* = 8.0 Hz, 2 H), 6.98 (d, *J* = 8.0 Hz, 2 H), 5.26 (s, 1 H), 3.83–3.79 (m, 1 H), 2.97–2.93 (m, 1 H), 2.32 (s, 3 H), 2.09–0.79 (m, 20 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.7, 151.1, 142.5, 138.1, 132.0, 128.8, 128.7, 128.0, 126.5, 60.4, 58.6, 52.9, 34.3, 33.3, 29.6, 29.5, 25.2, 25.0, 24.7, 24.3, 24.2, 21.3.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{28}H_{35}N_3O_2SNa$: 500.2348; found: 500.2349.

(*Z*)-*N*-[(*E*)-1-Cyclohexyl-4-(cyclohexylimino)-3-(*p*-tolyl)azetidin-2-ylidene]-4-methylbenzenesulfonamide (4b)

Yield: 0.35 g (72%); white solid; mp 171–172 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.11 (d, *J* = 8.0 Hz, 2 H), 7.06 (s, 4 H), 6.97 (d, *J* = 8.0 Hz, 2 H), 5.21 (s, 1 H), 3.83–3.78 (m, 1 H), 2.98–2.94 (m, 1 H), 2.37 (s, 3 H), 2.33 (s, 3 H), 2.08–0.82 (m, 20 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.2, 151.3, 142.3, 138.2, 137.8, 129.3, 128.8, 128.7, 127.8, 126.4, 60.3, 58.5, 52.8, 34.4, 33.3, 29.5, 29.4, 25.2, 25.0, 24.6, 24.3, 24.2, 21.3, 21.1.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{29}H_{37}N_3O_2SNa$: 514.2504; found: 514.2495.

(*Z*)-*N*-{(*E*)-1-Cyclohexyl-4-(cyclohexylimino)-3-[2-(trifluoromethyl)phenyl]azetidin-2-ylidene}-4-methylbenzenesulfonamide (4c)

Yield: 0.42 g (76%); white solid; mp 166–167 °C.

IR (KBr): 2931, 2854, 1765, 1613, 1307, 1611, 811 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 8.0 Hz, 1 H), 7.43–7.40 (m, 1 H), 7.32–7.30 (m, 3 H), 7.08–7.04 (m, 3 H), 5.64 (s, 1 H), 3.88–3.82 (m, 1 H), 3.05–2.99 (m, 1 H), 2.34 (s, 3 H), 2.12–0.74 (m, 20 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.2, 149.3, 142.7, 138.3, 132.0, 131.1, 128.9, 128.7, 128.5, 128.3, 128.1, 127.3, 127.1, 127.0, 126.4, 125.0, 122.8, 57.5, 57.1, 53.0, 34.4, 33.5, 29.5, 25.2, 25.1, 24.7, 24.1, 21.4.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{29}H_{35}F_3N_3O_2S$: 546.2402; found: 546.2427.

***tert*-Butyl {[(2*E*,4*Z*)-1-Cyclohexyl-2-(cyclohexylimino)-4-(tosylimino)azetidin-3-yl]methyl}carbamate (4d)**

Yield: 0.45 g (85%); white solid; mp 158–159 °C.

IR (KBr): 2932, 2856, 1615, 1315, 1161, 1019, 890 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 7.0 Hz, 2 H), 7.31 (d, *J* = 8.0 Hz, 2 H), 4.92 (br s, 1 H), 4.21 (s, 1 H), 3.96–3.86 (m, 2 H), 3.65–3.63 (m, 1 H), 3.38–3.36 (s, 1 H), 2.42 (s, 3 H), 1.39 (s, 9 H), 1.92–1.14 (m, 20 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.6, 155.4, 148.2, 143.2, 138.5, 129.4, 126.6, 79.4, 58.5, 57.3, 52.7, 37.3, 35.0, 33.9, 33.8, 29.6, 29.4, 29.2, 28.2, 25.5, 25.1, 24.9, 24.8, 24.5, 24.4, 21.5.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{28}H_{43}N_4O_4S$: 531.3005; found: 531.3018.

(*Z*)-*N*-[(*E*)-3-(4-*tert*-Butylphenyl)-1-cyclohexyl-4-(cyclohexylimino)azetidin-2-ylidene]-4-methylbenzenesulfonamide (4e)

Yield: 0.43 g (81%); white solid; mp 230–231 °C.

IR (KBr): 2932, 2856, 1623, 1315, 1163, 936, 673 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.27 (d, *J* = 8.5 Hz, 2 H), 7.11–7.08 (m, 4 H), 6.82 (d, *J* = 8.5 Hz, 2 H), 5.25 (s, 1 H), 3.83–3.80 (m, 1 H), 2.96–2.92 (m, 1 H), 2.30 (s, 3 H), 1.33 (s, 9 H), 2.09–0.79 (m, 20 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.3, 151.5, 151.2, 142.4, 138.5, 128.9, 128.8, 127.8, 126.6, 125.6, 60.2, 58.7, 52.9, 34.6, 34.4, 33.4, 31.4, 29.7, 29.6, 25.3, 25.1, 24.8, 24.4, 24.2, 21.5.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{32}H_{44}N_3O_2S$: 534.3154; found: 534.3125.

Ethyl (2*E*,4*Z*)-1-Cyclohexyl-2-(cyclohexylimino)-4-(tosylimino)azetidine-3-carboxylate (4f)

Yield: 0.42 g (89%); white solid; mp 143–145 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.78 (d, *J* = 8.5 Hz, 2 H), 7.29 (d, *J* = 8.5 Hz, 2 H), 4.84 (s, 1 H), 4.29–4.20 (m, 2 H), 3.74–3.68 (m, 1 H), 3.27–3.22 (m, 1 H), 2.42 (s, 3 H), 1.97–1.13 (m, 23 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.8, 161.0, 144.4, 143.2, 138.0, 129.2, 126.7, 62.1, 59.7, 59.3, 53.3, 34.3, 34.2, 29.2, 25.2, 24.9, 24.6, 24.3, 24.2, 21.4, 13.8.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{25}H_{35}N_3O_4SNa$: 496.2246; found: 496.2233.

(*Z*)-*N*-[(*E*)-1-Cyclohexyl-4-(cyclohexylimino)-3-(3-fluorophenyl)azetidin-2-ylidene]-4-methylbenzenesulfonamide (4g)

Yield: 0.46 g (94%); white solid; mp 158–159 °C.

IR (KBr): 2932, 2857, 1760, 1612, 1315, 1160, 854 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.29–7.25 (m, 1 H), 7.19 (d, *J* = 8.0 Hz, 2 H), 7.05–6.99 (m, 4 H), 6.83 (d, *J* = 9.0 Hz, 1 H), 5.26 (s, 1 H), 3.83–3.78 (m, 1 H), 2.96–2.92 (m, 1 H), 2.34 (s, 3 H), 2.10–0.83 (m, 20 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.0, 163.7, 161.8, 150.3, 142.9, 138.1, 134.6, 134.5, 130.5, 130.4, 129.0, 126.4, 124.0, 115.2, 115.0, 114.9, 114.8, 60.1, 58.9, 53.1, 34.4, 33.5, 29.65, 29.58, 25.3, 25.1, 24.8, 24.4, 24.2, 21.4.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{28}H_{35}FN_3O_2S$: 496.2434; found: 496.2459.

(*Z*)-*N*-[(*E*)-1-Cyclohexyl-4-(cyclohexylimino)-3-cyclopropylazetidin-2-ylidene]-4-methylbenzenesulfonamide (4h)

Yield: 0.26 g (59%); white solid; mp 116–117 °C.

IR (KBr): 2932, 2851, 1652, 1585, 1537, 1271, 1136, 1092, 703 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 8.0 Hz, 2 H), 7.29 (d, *J* = 8.0 Hz, 2 H), 3.92 (d, *J* = 9.0 Hz, 1 H), 3.67–3.62 (m, 1 H), 3.28–3.24 (m, 1 H), 2.42 (s, 3 H), 1.98–1.12 (m, 21 H), 0.89–0.84 (m, 1 H), 0.75–0.70 (m, 1 H), 0.65–0.61 (m, 1 H), 0.35–0.30 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.4, 150.5, 142.7, 139.5, 129.2, 126.4, 59.5, 52.5, 34.8, 34.6, 29.4, 29.3, 25.5, 25.1, 24.8, 24.7, 24.5, 21.5, 9.8, 6.2, 4.5.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{36}N_3O_2S$: 442.2528; found: 442.2550.

(*Z*)-*N*-[(*E*)-1-Cyclohexyl-4-(cyclohexylimino)-3-phenylazetidin-2-ylidene]methanesulfonamide (4i)

Yield: 0.37 g (93%); white solid; mp 127–129 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.38–7.35 (m, 2 H), 7.32–7.31 (m, 3 H), 5.21 (s, 1 H), 3.88–3.81 (m, 1 H), 2.98–2.92 (m, 1 H), 2.47 (s, 3 H), 2.14–0.81 (m, 20 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.5, 150.7, 132.0, 129.0, 128.5, 127.9, 60.3, 58.8, 53.0, 41.7, 34.4, 33.4, 29.7, 29.6, 25.3, 25.1, 24.8, 24.4, 24.2.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{22}H_{31}N_3O_2SNa$: 424.2035; found: 424.2023.

(*Z*)-*N*-[(*E*)-1-Isopropyl-4-(isopropylimino)-3-(*p*-tolyl)azetidin-2-ylidene]-4-methylbenzenesulfonamide (4j)
Yield: 0.30 g (74%); white solid; mp 148–149 °C.

IR (KBr): 2968, 2931, 1610, 1316, 1166, 716, 665 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.12 (d, *J* = 8.0 Hz, 2 H), 7.09–7.07 (m, 4 H), 6.98 (d, *J* = 8.5 Hz, 2 H), 5.22 (s, 1 H), 4.21–4.16 (m, 1 H), 3.35–3.30 (m, 1 H), 2.37 (s, 3 H), 2.32 (s, 3 H), 1.47–1.45 (m, 6 H), 1.06 (d, *J* = 6.5 Hz, 3 H), 0.70 (d, *J* = 6.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.1, 151.0, 142.5, 138.3, 138.0, 129.5, 128.8, 128.7, 128.0, 126.5, 60.3, 50.7, 45.6, 24.4, 23.4, 21.4, 21.2, 19.9, 19.8.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{30}N_3O_2S$: 412.2059; found: 412.2085.

(*Z*)-*N*-[(*E*)-1-Isopropyl-4-(isopropylimino)-3-phenylazetidin-2-ylidene]-4-methylbenzenesulfonamide (4k)
Yield: 0.31 g (78%); white solid; mp 141–143 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34–7.29 (m, 3 H), 7.22 (d, *J* = 7.0 Hz, 2 H), 7.09 (d, *J* = 8.0 Hz, 2 H), 6.99 (d, *J* = 8.0 Hz, 2 H), 5.26 (s, 1 H), 4.21–4.18 (m, 1 H), 3.33–3.30 (m, 1 H), 2.31 (s, 3 H), 1.48–1.45 (m, 6 H), 1.07 (d, *J* = 6.0 Hz, 3 H), 0.67 (d, *J* = 6.0 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.5, 150.7, 142.6, 138.0, 131.8, 128.8, 128.2, 128.1, 126.5, 60.5, 50.8, 45.6, 24.4, 23.2, 21.3, 19.87, 19.82.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{22}H_{27}N_3O_2SNa$: 420.1722; found: 420.1703.

(*Z*)-*N*-[(*E*)-1-Cyclohexyl-4-(cyclohexylimino)-3-(4-fluorophenyl)azetidin-2-ylidene]-4-methylbenzenesulfonamide (4l)
Yield: 0.44 g (88%); white solid; mp 192–193 °C.

IR (KBr): 2934, 2857, 1761, 1612, 1316, 1160, 854, 693 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.18–7.15 (m, 4 H), 7.04 (d, *J* = 8.0 Hz, 2 H), 6.96 (t, *J* = 8.5 Hz, 2 H), 5.25 (s, 1 H), 3.83–3.79 (m, 1 H), 2.94–2.90 (m, 1 H), 2.34 (s, 3 H), 2.08–0.82 (m, 20 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.7, 163.4, 161.4, 150.9, 142.8, 138.2, 129.8, 129.7, 128.9, 127.9, 126.4, 115.9, 115.7, 59.7, 58.8, 53.0, 34.4, 33.4, 29.7, 29.6, 25.3, 25.1, 24.7, 24.4, 24.3, 21.4.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{28}H_{35}FN_3O_2S$: 496.2434; found: 496.2412.

(*Z*)-*N*-[(*E*)-3-(4-Bromophenyl)-1-cyclohexyl-4-(cyclohexylimino)azetidin-2-ylidene]-4-methylbenzenesulfonamide (4m)
Yield: 0.50 g (90%); white solid; mp 198–199 °C.

IR (KBr): 2929, 2855, 1764, 1741, 1610, 1317, 1160, 935, 689 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.36 (d, *J* = 8.5 Hz, 2 H), 7.16–7.13 (m, 2 H), 7.05–7.03 (m, 4 H), 5.22 (s, 1 H), 3.81–3.79 (m, 1 H), 2.93–2.89 (m, 1 H), 2.34 (s, 3 H), 2.08–0.84 (m, 20 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.4, 150.3, 142.8, 138.2, 131.9, 131.1, 129.7, 129.0, 126.3, 122.1, 59.8, 58.8, 53.1, 34.4, 33.5, 29.7, 29.6, 25.3, 25.1, 24.8, 24.3, 24.2, 21.5.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{28}H_{35}BrN_3O_2S$: 556.1633; found: 556.1613.

(*E*)-*N*-{1-(2,6-Diisopropylphenyl)-4-[(*E*)-(2,6-diisopropylphenylimino)methyl]-3-phenylazetidin-2-ylidene}-4-methylbenzenesulfonamide (4a′)
Yield: 0.52 g (80%); white solid; mp 126–127 °C.

IR (KBr): 1594, 1388, 1197, 1170, 989, 765, 691, 676, 585, 539 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.70 (d, *J* = 6.5 Hz, 1 H), 7.39–7.38 (m, 3 H), 7.36–7.33 (m, 5 H), 7.20 (d, *J* = 7.5 Hz, 1 H), 7.16 (d, *J* = 7.5 Hz, 1 H), 7.04–7.03 (m, 5 H), 5.09 (s, 1 H), 5.04 (d, *J* = 6.5 Hz, 1 H), 3.30–3.27 (m, 1 H), 3.01–2.99 (m, 1 H), 2.40–2.37 (m, 2 H), 2.35 (s, 3 H), 1.32–1.29 (m, 6 H), 1.14 (d, *J* = 6.5 Hz, 3 H), 0.99–0.98 (m, 9 H), 0.89–0.87 (m, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.0, 160.8, 147.4, 146.9, 145.9, 142.2, 139.1, 136.1, 134.3, 130.0, 129.5, 129.2, 128.8, 128.2, 127.8, 126.6, 124.8, 124.7, 123.8, 122.8, 75.0, 55.8, 29.5, 29.4, 27.7, 24.6, 24.4, 23.8, 23.7, 23.3, 22.3, 21.4.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{41}H_{50}N_3O_2S$: 648.3624; found: 648.3609.

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Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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