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Utilization of Borane-Catalyzed Hydrosilylation as a Dearomatizing Tool: Six-Membered Cyclic Amidine Synthesis from Isoquinolines and Pyridines

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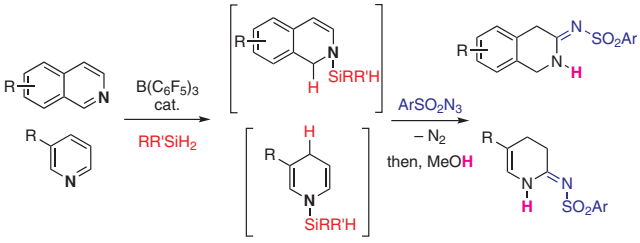

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Abstract In this study, a convenient strategy to synthesize six-membered cyclic amidines from isoquinolines and pyridines has been developed. Borane-catalyzed hydrosilylation of each *N*-heteroarene was utilized as a dearomatizing tool. Substrate scope is broad with respect to both isoquinolines and pyridines, with various reaction pathways depending on the substitution pattern of the *N*-heteroarenes. The reaction mechanism and reactivity of each class of *N*-heteroarenes has been discussed. The resulting six-membered (*Z*)-sulfonyl amidine products are rarely reported and are mostly unprecedented. The scalability of this method and versatility of the cyclic amidine products are also presented.

Key words cyclic amidine, hydrosilylation, *N*-heteroarenes, dearomatization, [3+2] cycloaddition, $B(C_6F_5)_3$

Cyclic amidine is an important structural motif in organic synthesis and medicinal chemistry because of its ubiquitous presence in natural and pharmaceutical molecules.[1] The biological activities of the six-membered cyclic amidines have been widely studied and evaluated as human iNOS inhibitor, mRNA modulator, proapoptotic agent, anti-inflammatory agent, hBGT1 inhibitor, and matriptase inhibitor (Figure 1).[2] As a result, various synthetic strategies toward the six-membered cyclic amidines have been reported.[3] As part of this effort, our group recently reported a new synthetic strategy toward the six-membered cyclic amidines from readily available quinolines and sulfonyl azides (Scheme 1a).[4] We utilized the borane ($B(C_6F_5)_3$, BCF) catalyzed 1,4-hydrosilylation of quinoline **1** as a dearomatizing tool.[5] The resulting *N*-silyl enamine intermediate **2** was then reacted with organic azide via [3+2] cycloaddition to achieve a six-membered sulfonyl amidine **3**.[6] While most of the other strategies had produced (*E*)-sulfonylamidines as a major product,[3a,7] our approach could selectively achieve (*Z*)-sulfonylamidines. This *E*/*Z* selectivity originated from the unique concerted mechanism during the [3+2] cycloaddition step. Moreover, since only a few examples of the synthesis of six-membered (*Z*)-sulfonyl amidines have been reported to date, this approach could enlarge the molecular library for organic and medicinal chemistry society. In the same vein, utilization of this strategy for the construction of new cyclic amidines from other *N*-heteroarenes would also be important. Moreover, during this study, various mode of reaction of each *N*-heteroarene will be discussed. Herein, we report an extensive application of our dearomatization strategy to synthesize cyclic (*Z*)-sulfonyl amidines from isoquinolines and pyridines (Scheme 1b).

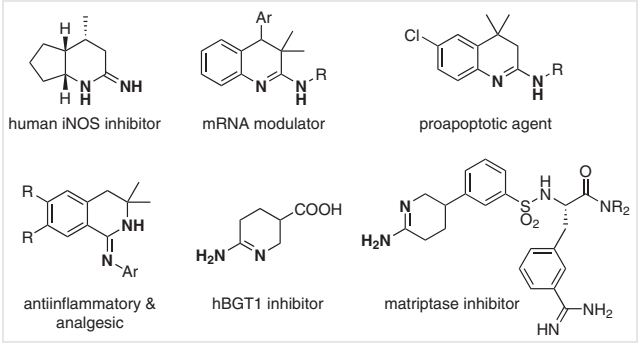

Figure 1 Selected six-membered cyclic amidine compounds with biological activities

Before we commenced our study, we carefully compared the reactivity of each target class of *N*-heteroarenes with quinolines. Isoquinoline was chosen as the initial substrate. Compared to hydrosilylation of quinoline with

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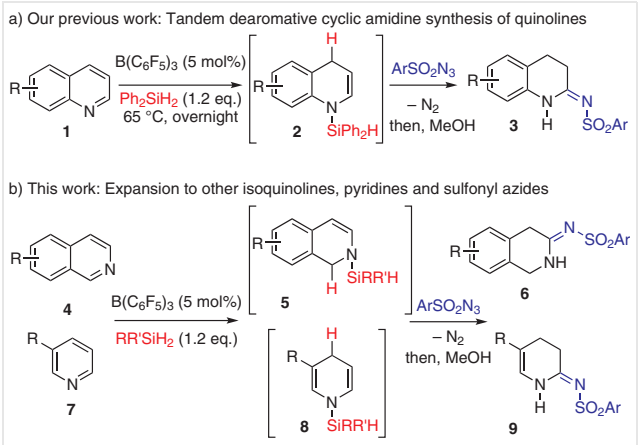
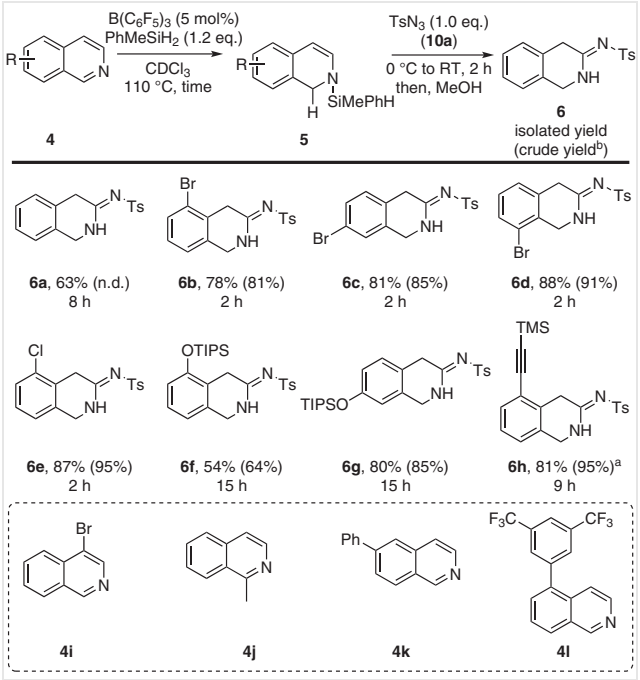


Scheme 1 Six-membered cyclic amidine synthesis by using dearomative hydrosilylation strategy



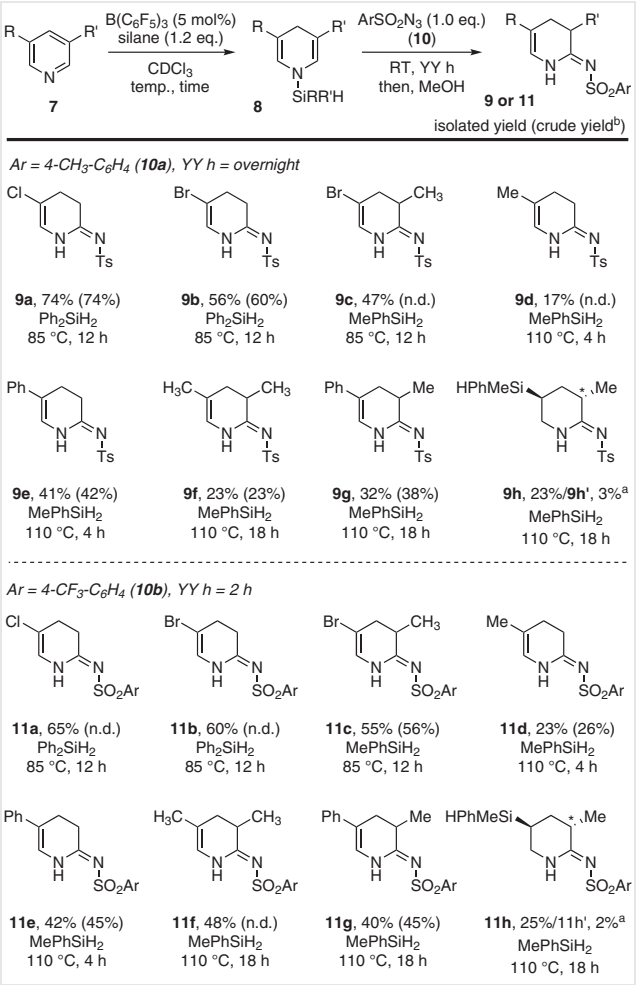
Scheme 2 Substrate scope of the reaction with respect to isoquinolines. *Reagents and conditions*: **4** (0.5 mmol), $B(C_6F_5)_3$ (0.025 mmol), and $MePhSiH_2$ (0.6 mmol) were heated in $CDCl_3$ (0.5 mL) in a screw-capped NMR tube. [a] Required 1.7 equiv of silane for full conversion. [b] Determined by ^1H NMR analysis of the crude mixture (internal standard: tetrachloroethane).

diphenylsilane at 65 °C, hydrosilylation of the isoquinoline required more reactive methylphenylsilane and higher temperature (110 °C) to obtain reasonable conversion.[4] This distinction originated from the reactivity difference between the 1,2-hydrosilylation of isoquinoline and 1,4-hydrosilylation of quinolines.[5a] In situ NMR monitoring of the reaction mixture clearly showed the slower 1,2-hydrosilylation.[8] The structure of the resulting conjugated enamine intermediate **5** from isoquinoline was also contrasted to that of the unconjugated enamine intermediate **2** from the quinolines. To examine the reactivity differences from these aspects, we investigated the substrate scope of the reaction with respect to isoquinolines and tosyl azide **10a** (Scheme 2). Note that all reactions were conducted in chloroform-*d* in the NMR cell so that we could observe the conversion of each step by using in situ ^1H NMR analysis.

Under the optimized conditions for the synthesis of isoquinolines, dearomative hydrosilylation of isoquinoline **4a** produced the conjugated enamine **5a** in 8 h. The subsequent addition of tosyl azide **10a** induced [3+2] cycloaddition, hydride shift, and a nitrogen extrusion process to produce the desired cyclic amidine in excellent conversion from the enamine intermediate. Note that an ice bath was required for the second step due to the vigorous exothermic reaction. Next, the dearomative hydrosilylation of 5-bromoisoquinoline (**4b**) produced the desired enamine intermediate **5b** with excellent conversion in 2 h. Subsequent addition of tosyl azide **10a** resulted in formation of the cyclic amidine in excellent yield. Since the 7-bromo- and 8-bromo-isoquinolines **4c** and **4d** showed similar high reactivity toward the hydrosilylation, the electron-withdrawing effect of the bromides might have increased the reactivity. Similarly, the dearomative hydrosilylation of 5-chloroisoquinoline **4e** also resulted in rapid conversion into the respective enamine intermediate **5e**. The following addition of azide **10a** resulted in formation of the desired cyclic amidine product **6e** in good yield. The reactions of the electron-donating silyloxy-substituted isoquinolines **4f** and **4g** also resulted in good to excellent yields, although longer reaction time was required. Additionally, reaction of substrate **4h**, bearing an alkyne functional group, resulted in formation of the desired product **6h** without undesired hydrosilylation on the alkyne.[9] With respect to these results, 4-bromoisoquinoline **4i** was also tested in our cascade process. The first dearomative hydrosilylation of **4i** led to its conversion into enamine intermediate **5i**, like the other halogen-substituted isoquinolines. However, the ensuing azide addition resulted in a complex mixture. The halogen on the enamine intermediate may participate in other side reactions by acting as a leaving group during the [3+2] cycloaddition, hydride shift, and nitrogen gas extrusion process. After that, the reactivity of the 1-methylisoquinoline **4j** was also tested under the dearomative hydrosilylation conditions. Although **4j** was reactive enough for the dearomatization, the N–Si bond of the enamine intermediate from **5j** was too unstable for this stepwise process and resulted in a complex mixture. Note that this result is similar to the over-reduction of 2-methylquinoline.[10] 6-Phenylisoquinoline (**4k**) was also tested for our process. However, it was not reactive towards the dearomative hydrosilylation. The hydrosilylation of the electron-deficient aryl isoquinoline **4l**

resulted in the same. The extended conjugation from the additional aryl group might stabilize **4k** and **4l** and deactivate it.

We then turned our attention to the pyridines. A borane-catalyzed multiple hydrosilylation of the pyridines had been discussed by Chang and Park.[5b] Dearomative hydrosilylation of simple pyridine and 2-substituted pyridines with 1.0 equiv of the silane resulted in a complex mixture.[11] We believe that the substituent near the nitrogen of the pyridine affected the stability of the *N*-silyl enamine intermediates. In the case of the 4-substituted pyridines, double hydrosilylation was too fast to capture the *N*-silyl enamine intermediate. Therefore, we decided to focus on the 3-substituted pyridines to determine the pyridine substrate scope (Scheme 3, top).

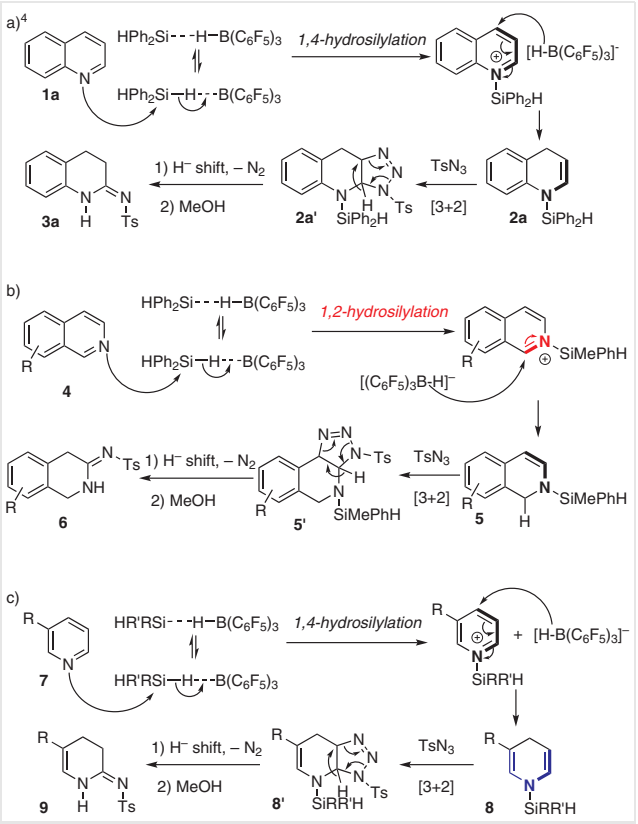


Scheme 3 Substrate scope of the reaction with respect to pyridines. *Reagents and conditions*: **7** (0.5 mmol), $B(C_6F_5)_3$ (0.025 mmol), and silane (0.6 mmol) were heated in $CDCl_3$ (0.5 mL) in a screw-capped NMR tube. [a] 1.25 mmol (2.5 equiv) of silane was added. [b] Determined by ^1H NMR analysis of the crude mixture (internal standard: tetrachloroethane).

As initial reaction conditions, we chose diphenylsilane at 85 °C for the dearomative hydrosilylation of 3-chloropyridine (**7a**) and 3-bromopyridine (**7b**). The resulting enamine intermediates were converted into cyclic amidines **9a** and **9b** via regioselective [3+2] cycloaddition with tosyl azide **10a**. Interestingly, the reaction rate for the cycloaddition step was much slower than for the other *N*-heteroarenes. On the other hand, 3-bromo-5-methylpyridine **7c** had lower reactivity than the 3-halopyridines toward the dearomatization step. Therefore, we changed the silane to more reactive methylphenylsilane so as to achieve moderate yield of cyclic amidine **9c**. Note that the azide preferred to react with 2-methylenamine rather than 2-bromoenamine of **8c**. Eventually, we increased the temperature of the dearomative hydrosilylation to 110 °C to achieve reasonable conversion of the rest of our pyridines (**7d–g**). Both 3-methylpyridine **7d** and 3-phenylpyridine **7e** showed moderate conversion during the dearomative hydrosilylation step, but the additional side reactions during the second step with azide **10a** led to lower yield of **9d**.[12] The reaction of 3,5-dimethylpyridine **7f** produced **9f** in a low yield, but the reaction of 3-methyl-5-phenylpyridine **7g** resulted in a moderate yield of **9g**. Note that the azide preferred to react with the 2-methylenamine over 2-phenylenamine of intermediate **8g**. More interestingly, we could obtain double hydrosilylation intermediate **8d′** from 3-methylpyridine **7d** by adding more silane (2.5 equiv).[5b] Subsequent addition of azide **10a** resulted in silylated cyclic amidine **9h** as the major product along with diastereomer **9h′** as the minor product. The major diastereomer was *trans* since the azide approached from the other side of the methyl substituent.[13]

After exploring the substrate scope of the reaction with pyridines and tosyl azide **10a**, we thought that the longer reaction time during the cycloaddition step could allow side reactions to occur. Therefore, 4-(trifluoromethyl)benzenesulfonyl azide (**10b**) was applied to reduce the reaction time of the second step. This electron-deficient azide exhibited higher reactivity than **10a**.[4] After the dearomative hydrosilylation of **7**, **10b** was added to the reaction mixture instead of **10a**. The dienamine intermediates were quickly converted into cyclic amidines within 2 h (Scheme 3, bottom). The isolated yields of the new cyclic amidines from **10b** (**11a–g**) were similar to or higher than the corresponding amidines from **10a**. The crystal structure of **11g** (CCDC 1987424) was also obtained,[14] which supported the (*Z*)-sulfonyl amidine structure of **9** and **11**. The modified procedure to obtain silylated cyclic amidine **11h** and **11h′** from the doubly hydrosilylated intermediate **8d′** was also applied successfully with **10b**.

After exploring the substrate scope of the isoquinolines and pyridines, we compared the reaction mechanism and reactivity of the *N*-heteroarenes (Scheme 4).[15] The previously reported quinoline is also presented for comparison (Scheme 4a). The quinoline was dearomatized by borane catalyzed 1,4-hydrosilylation. The resulting unconjugated

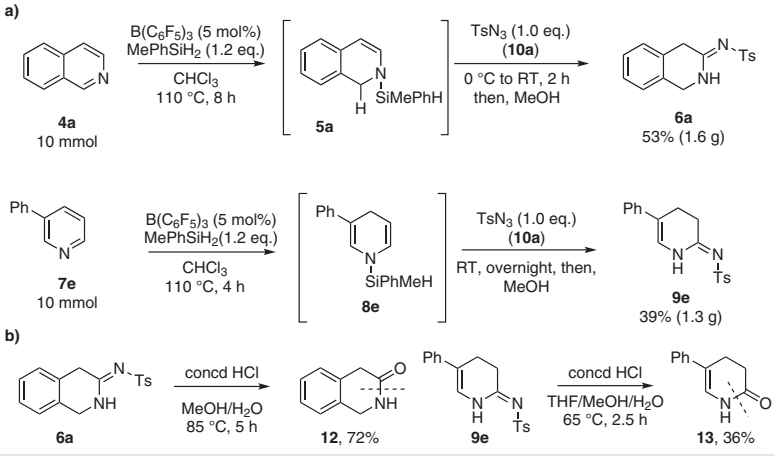


Scheme 4 Comparison of the proposed mechanisms of the cyclic amidine synthesis from *N*-heteroarenes

N-silylenamine **2a** was subjected to [3 + 2] cycloaddition with **10a**, hydride shift, and nitrogen extrusion process to produce cyclic amidine **3a** after methanol quenching. In the case of isoquinoline **4** (Scheme 4b), 1,2-hydrosilylation occurred because C1 is the only electropositive reaction site on **4**. An elevated temperature was required for this 1,2-hydrosilylation. Although the dearomative hydrosilylation was not effective on the aryl isoquinolines, the hydrosilylation of electron-deficient and electron-donating isoquinolines generally resulted in the formation of enamine **5** with good conversion. Note that the hydrosilylation of electron-deficient isoquinolines were faster than of electron-rich isoquinolines. Subsequent addition of the tosyl azide resulted in cyclic amidine **6** with excellent conversion from **5**. Note that the conjugated enamine **5** had higher reactivity toward azide than that of the isolated enamine from quinoline **2**.

In the case of the 3-substituted pyridines **7** (Scheme 4c), 1,4-hydrosilylation dominated. Again, the electron-deficient pyridines were more reactive than the electron-rich pyridines toward the 1,4-hydrosilylation. The reaction of the resulting dihydropyridine **8** with sulfonyl azide showed interesting regioselectivity. The azide preferred to react with sterically less hindered enamine rather than more hindered enamine of the dienamine **8**. Compared to the isoquinolines, the electron density of the reactive enamine nitrogen might be decreased due to the additional conjugation toward the other alkene; this, in turn, may slow the second [3+2] cycloaddition step.

Finally, the synthetic utility of this method was investigated (Scheme 5). To test the scalability of this process, we performed gram-scale reactions of the representative isoquinoline and pyridine (Scheme 5a). Isoquinoline **4a** (10 mmol) was converted into *N*-silyl enamine intermediate **5a**, then subsequent addition of the azide resulted in the formation to 1.6 g of the cyclic amidine **6a**. The 10 mmol scale hydrosilylation of the 3-phenylquinoline **7e** resulted in *N*-silyl-dienamine intermediate **8e** with moderate conversion. Subsequent addition of the tosyl azide resulted in 1.3 g of **9e**. The yield of the 10 mmol scale reactions were similar to those of the 0.5 mmol scale reactions (Scheme 2, Scheme 3) and proved the scalability of this process. The resulting cyclic amidine product **6a** and **9e** could be further functionalized to lactam **12** and **13** in moderate to good yields



Scheme 5 Practical application of the cyclic amidine synthesis from isoquinolines and pyridines

(Scheme 5b).[16] Since the synthetic utility of the lactams have been widely studied, including ring-opening pathways,[17] this suggests the possible application of this strategy for the synthesis of linear structures from the novel *N*-heteroarenes.

In conclusion, we have synthesized various six-membered (*Z*)-sulfonyl amidines by using borane-catalyzed hydrosilylation of *N*-heteroarenes as a dearomatizing tool to access the key *N*-silyl enamine intermediate. The resulting *N*-silyl enamine intermediates were converted into cyclic amidine via a [3+2] cycloaddition with sulfonyl azide, hydride shift, and nitrogen gas extrusion mechanism. This strategy is widely applicable to various *N*-heteroarenes and is scalable. This report expands the molecular library and synthetic utility of (*Z*)-sulfonyl cyclic amidines, which were rarely synthesized by previous methods. The reactivity of each step of this process was examined in detail in an effort to expand the application of the strategy. Further applications of this strategy with other classes of substrates are under investigation in our laboratory.

Unless otherwise stated, all catalytic reactions were carried out under an argon atmosphere. Chloroform-*d* from Eurisotop and dichloromethane-d_2 from Deutero were used as solvent without additional purification for optimization, substrate scope, and mechanistic studies. Tris(pentafluorophenyl)borane was purchased from TCI or Alfa Aesar and stored at –15 °C. All other reagents were directly used as purchased without further purification unless otherwise stated.

Analytical thin-layer chromatography (TLC) was performed on precoated silica gel 60 F254 plates. Visualization on TLC was achieved by the use of UV light (254 nm), and by exposure to acidic *p*-anisaldehyde stain followed by heating. Column chromatography was undertaken on silica gel (400–630 mesh) using a suitable eluent. ^{1}H NMR was recorded with a Jeol ECZ-500R ($CDCl_3$ or CD_2Cl_2 in 500 MHz) for characterization of compounds. ^{13}C{^{1}H} NMR was recorded with a Jeol ECZ-500R ($CDCl_3$ or CD_2Cl_2 in 125 MHz) and was fully decoupled by broad-band proton-decoupling. Chemical shifts are quoted in parts per million (ppm) referenced to tetramethylsilane or to the appropriate solvent peak (^{1}H NMR of $CHCl_3$ in $CDCl_3$: δ = 7.24 ppm (singlet), and CH_2Cl_2 in CD_2Cl_2: δ = 5.32 ppm (triplet); ^{13}C NMR of $CDCl_3$: δ = 77.0 ppm (triplet), and CD_2Cl_2: δ = 53.1 ppm (quin)). Infrared (IR) spectra were recorded with a Perkin Elmer Frontier ATR-FT-IR spectrophotometer, ν_{max} in cm^{-1}. High-resolution mass spectra were obtained by using the EI method from Korea Basic Science Institute (Daegu). X-ray diffraction data were collected with a Bruker D8 QUEST; samples were coated with Parabar oil under a stream of N_2 (g) at 173 K.

Synthesis of Cyclic Amidines 6 from Isoquinolines 4 and Tosyl Azide 10a (Scheme 2); General Procedure

Step 1: Tris(pentafluorophenyl)borane ($B(C_6F_5)_3$) catalyst (0.025 mmol, 5 mol%) in an NMR tube was dissolved in $CDCl_3$ (0.5 mL) under argon atmosphere. $MePhSiH_2$ (0.6 mmol, 1.2 equiv) was added at r.t. (H_2 bubbles were evolved), and TCE (0.3 mmol) was added into the reaction mixture as internal standard. Isoquinoline **4a–k** (0.5 mmol, 1.0 equiv) was subsequently added to the reaction mixture, which was then heated to 110 °C in an oil bath for the indicated time. The resulting mixture was subjected to NMR analysis to monitor the conversion.

Step 2: To the resulting mixture from the first step in an NMR cell was added tosyl azide **10a** (0.5 mmol, 1.0 equiv) at 0 °C and the mixture was warmed to r.t. (N_2 bubbling was observed) with NMR spectra recorded every 2 h. The reaction was quenched with MeOH and the mixture was filtered through silica with CH_2Cl_2 washing. The resulting crude mixture was purified by column chromatography.

N-(1,4-Dihydroisoquinolin-3(2*H*)-ylidene)-4-methylbenzenesulfonamide (6a)

Compound **6a** was prepared from **4a** according to the general procedure for 8 h; eluent: EtOAc/hexane/CH_2Cl_2 = 20:80:20.

Yield: 95.2 mg (63%); yellowish solid; mp 140–142 °C.

IR (neat): 3322, 1606, 1392, 1265, 1145, 1070, 930, 910, 805, 727, 660, 599, 533 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.96 (s, 1 H), 7.82 (d, *J* = 8.3 Hz, 2 H), 7.30–7.21 (m, 4 H), 7.20–7.12 (m, 2 H), 4.49 (s, 2 H), 3.64 (s, 2 H), 2.38 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.1, 142.8, 139.4, 130.7, 130.3, 129.3 (2C), 128.0, 127.5, 127.2, 126.3 (2C), 125.2, 45.5, 36.6, 21.5.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{16}H_{16}N_2O_2S$: 300.0932; found: 300.0930.

N-(5-Bromo-1,4-dihydroisoquinolin-3(2*H*)-ylidene)-4-methylbenzenesulfonamide (6b)

Compound **6b** was prepared from **4b** according to the general procedure for 2 h; eluent: EtOAc/hexane/acetone = 35:65:5.

Yield: 148.7 mg (78%); yellowish solid; mp 161–163 °C.

IR (neat): 3243, 1626, 1296, 1284, 1149, 1136, 920, 662, 593, 551 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.13 (s, 1 H), 7.86 (d, *J* = 8.1 Hz, 2 H), 7.51 (d, *J* = 3.1 Hz, 1 H), 7.29 (d, *J* = 7.8 Hz, 2 H), 7.20–7.05 (m, 2 H), 4.56 (s, 2 H), 3.76 (s, 2 H), 2.41 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.3, 143.1, 139.2, 132.2, 131.9, 129.8, 129.5 (2C), 128.5, 126.5 (2C), 124.5, 123.3, 45.6, 36.2, 21.5.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{16}H_{15}BrN_2O_2S$: 378.0038; found: 378.0035.

N-(7-Bromo-1,4-dihydroisoquinolin-3(2*H*)-ylidene)-4-methylbenzenesulfonamide (6c)

Compound **6c** was prepared from **4c** according to the general procedure for 2 h; eluent: EtOAc/hexane = 35:65.

Yield: 152.7 mg (81%); yellowish solid; mp 180–182 °C.

IR (neat): 3300, 1627, 1601, 1257, 1134, 1070, 899, 813, 703, 676, 552, 535 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.00 (s, 1 H), 7.83 (d, *J* = 8.3 Hz, 2 H), 7.40 (dd, *J* = 8.1, 2.0 Hz, 1 H), 7.34 (d, *J* = 2.0 Hz, 1 H), 7.28 (d, *J* = 7.7 Hz, 2 H), 7.04 (d, *J* = 8.0 Hz, 1 H), 4.47 (s, 2 H), 3.60 (s, 2 H), 2.40 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.5, 143.1, 139.2, 132.9, 131.1, 129.5 (2C), 129.4, 129.1, 128.3, 126.4 (2C), 120.9, 45.0, 36.2, 21.6.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{16}H_{15}BrN_2O_2S$: 378.0038; found: 378.0034.

N-(8-Bromo-1,4-dihydroisoquinolin-3(2*H*)-ylidene)-4-methylbenzenesulfonamide (6d)

Compound **6d** was prepared from **4d** according to the general procedure for 2 h; eluent: EtOAc/hexane = 30:70.

Yield: 167.0 mg (88%); yellowish solid; mp 207–209 °C.

IR (neat): 3336, 1615, 1255, 1139, 1075, 1065, 821, 805, 790, 692, 590, 537, 524 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.95 (s, 1 H), 7.86–7.82 (m, 2 H), 7.48 (dd, *J* = 7.8, 1.3 Hz, 1 H), 7.30–7.25 (m, 2 H), 7.16 (dd, *J* = 7.7, 7.7 Hz, 1 H), 7.11 (dd, *J* = 7.6, 1.2 Hz, 1 H), 4.58 (s, 2 H), 3.69 (s, 2 H), 2.40 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.3, 143.0, 139.2, 132.3, 131.1, 130.3, 129.4 (2C), 129.3, 126.7, 126.4 (2C), 121.1, 45.9, 36.3, 21.5.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{16}H_{15}BrN_2O_2S$: 378.0038; found: 378.0036.

N-(5-Chloro-1,4-dihydroisoquinolin-3(2*H*)-ylidene)-4-methylbenzenesulfonamide (6e)

Compound **6e** was prepared from **4e** according to the general procedure for 2 h; eluent: CH_2Cl_2/acetone = 100:1.

Yield: 145.0 mg (87%); yellowish solid; mp 154–156 °C.

IR (neat): 3244, 1627, 1298, 1286, 1151, 1143, 920, 664, 594, 542 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 9.22 (s, 1 H), 7.90–7.83 (m, 2 H), 7.32–7.25 (m, 3 H), 7.18 (dd, *J* = 7.9, 7.9 Hz, 1 H), 7.06 (dd, *J* = 7.6, 3.0 Hz, 1 H), 4.56 (s, 2 H), 3.76 (s, 2 H), 2.40 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.2, 143.0, 139.2, 133.0, 132.1, 129.5 (2C), 128.5, 128.2, 128.0, 126.5 (2C), 123.8, 45.4, 33.4, 21.5.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{16}H_{15}ClN_2O_2S$: 334.0543; found: 334.0545.

4-Methyl-N-(5-((triisopropylsilyl)oxy)-1,4-dihydroisoquinolin-3(2*H*)-ylidene)benzenesulfonamide (6f)

Compound **6f** was prepared from **4f** according to the general procedure for 15 h; eluent: CH_2Cl_2/EtOAc = 98:2.

Yield: 128.1 mg (54%); yellowish solid; mp 144–146 °C.

IR (neat): 3319, 2944, 2866, 1615, 1268, 1142, 1038, 785, 660, 546 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 9.08 (s, 1 H), 7.84 (d, *J* = 8.0 Hz, 2 H), 7.26 (d, *J* = 7.3 Hz, 2 H), 7.10 (dd, *J* = 8.0, 8.0 Hz, 1 H), 6.85–6.70 (m, 2 H), 4.51 (s, 2 H), 3.67 (s, 2 H), 2.40 (s, 3 H), 1.38–1.25 (m, 3 H), 1.08 (d, *J* = 8.1 Hz, 18 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.4, 153.1, 142.7, 139.7, 131.3, 129.3 (2C), 127.7, 126.4 (2C), 120.4, 117.5, 116.8, 45.4, 30.6, 21.5, 18.0 (6C), 13.0 (3C).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{25}H_{36}N_2O_3SSi$: 472.2216; found: 472.2217.

4-Methyl-N-(7-((triisopropylsilyl)oxy)-1,4-dihydroisoquinolin-3(2*H*)-ylidene)benzenesulfonamide (6g)

Compound **6g** was prepared from **4g** according to the general procedure for 15 h; eluent: EtOAc/hexane = 25:75.

Yield: 189.1 mg (80%); yellowish solid; mp 156–158 °C.

IR (neat): 3296, 2942, 2865, 1611, 1248, 1060, 817, 661 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.89 (s, 1 H), 7.83 (d, *J* = 8.0 Hz, 2 H), 7.27 (d, *J* = 8.3 Hz, 2 H), 7.00 (d, *J* = 8.4 Hz, 1 H), 6.79 (dd, *J* = 8.1, 2.6 Hz, 1 H), 6.70 (d, *J* = 2.5 Hz, 1 H), 4.44 (s, 2 H), 3.58 (s, 2 H), 2.40 (s, 3 H), 1.30–1.19 (m, 3 H), 1.09 (d, *J* = 7.4 Hz, 18 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.4, 155.2, 142.8, 139.4, 131.6, 129.4 (2C), 128.5, 126.4 (2C), 122.4, 119.6, 116.5, 45.6, 36.0, 21.5, 17.9 (6C), 12.6 (3C).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{25}H_{36}N_2O_3SSi$: 472.2216; found: 472.2213.

4-Methyl-N-(5-((trimethylsilyl)ethynyl)-1,4-dihydroisoquinolin-3(2*H*)-ylidene)benzenesulfonamide (6h)

Compound **6h** was prepared from **4h**, $MePhSiH_2$ (0.85 mmol, 1.7 equiv) and **10a** according to the general procedure for 9 h; eluent: EtOAc/hexane = 30:70.

Yield: 159.7 mg (81%); yellowish solid; mp 185–187 °C.

IR (neat): 3252, 2959, 2901, 2150, 1627, 1496, 1417, 1296, 1149, 1080, 919, 837, 658, 588, 553 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 9.18 (s, 1 H), 7.86 (d, *J* = 8.4 Hz, 2 H), 7.40 (d, *J* = 7.3 Hz, 1 H), 7.27 (d, *J* = 8.1 Hz, 2 H), 7.18 (dd, *J* = 7.7, 7.7 Hz, 1 H), 7.10 (d, *J* = 7.8 Hz, 1 H), 4.51 (s, 2 H), 3.84 (s, 2 H), 2.39 (s, 3 H), 0.26 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.8, 142.8, 139.4, 131.8, 131.7, 130.4, 129.3 (2C), 126.7, 126.3 (2C), 125.3, 122.0, 101.4, 100.5, 45.2, 34.3, 21.4, –0.1 (3C).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{21}H_{24}N_2O_2SSi$: 396.1328; found: 396.1330.

Synthesis of Cyclic Amidines 9 from Pyridines 7 and Tosyl Azide 10a (Scheme 3); General Procedure

Step 1: $B(C_6F_5)_3$ catalyst (0.025 mmol, 5 mol%) in an NMR tube was dissolved in $CDCl_3$ (0.5 mL) under argon atmosphere. Silane (0.6 mmol, 1.2 equiv) was added at r.t. (H_2 bubbles were evolved) and TCE (0.3 mmol) was added into the reaction mixture as internal standard. Pyridine **7a–h** (0.5 mmol, 1.0 equiv) was subsequently added and the mixture was heated to the indicated temperature in an oil bath for the indicated time. The resulting mixture was subjected to NMR analysis to monitor the conversion.

Step 2: To the resulting mixture from the first step in an NMR cell was added tosyl azide **10a** (0.5 mmol, 1.0 equiv) at r.t. After standing overnight, an NMR spectrum was recorded, and the reaction was quenched with MeOH. The mixture was filtered through silica with CH_2Cl_2 washing, and the resulting crude mixture was purified by column chromatography.

N-(5-Chloro-3,4-dihydropyridin-2(1*H*)-ylidene)-4-methylbenzenesulfonamide (9a)

Compound **9a** was prepared from **7a**, Ph_2SiH_2 (0.6 mmol, 1.2 equiv) and **10a** according to the general procedure for 12 h at 85 °C; eluent: EtOAc/hexane = 25:75.

Yield: 106.0 mg (74%); yellowish solid; mp 194–196 °C.

IR (neat): 3177, 3088, 2948, 1575, 1409, 1286, 1132, 912, 844, 740, 673, 590, 552 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 9.47 (s br, 1 H), 7.78 (d, *J* = 8.3 Hz, 2 H), 7.27 (d, *J* = 8.0 Hz, 2 H), 6.26 (d, *J* = 4.4 Hz, 1 H), 2.72 (t, *J* = 8.8 Hz, 2 H), 2.53 (dd, *J* = 7.8, 1.4 Hz, 2 H), 2.40 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.0, 143.5, 138.5, 129.5 (2C), 126.5 (2C), 120.7, 116.3, 30.5, 26.7, 21.5.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{12}H_{13}ClN_2O_2S$: 284.0386; found: 284.0388.

N-(5-Bromo-3,4-dihydropyridin-2(1*H*)-ylidene)-4-methylbenzenesulfonamide (9b)

Compound **9b** was prepared from **7b**, Ph_2SiH_2 (0.6 mmol, 1.2 equiv) and **10a** according to the general procedure for 12 h at 85 °C; eluent: CH_2Cl_2.

Yield: 92.1 mg (56%); white solid; mp 166–168 °C.

IR (neat): 3173, 1574, 1286, 1155, 1132, 1084, 910, 735, 666, 641, 551 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.49 (s, 1 H), 7.81 (d, *J* = 8.1 Hz, 2 H), 7.30 (d, *J* = 8.0 Hz, 2 H), 6.39 (s, 1 H), 2.73 (s, 2 H), 2.65 (t, *J* = 7.5 Hz, 2 H), 2.42 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.5, 143.6, 138.5, 129.6 (2C), 126.6 (2C), 123.4, 103.9, 30.6, 28.5, 21.6.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{12}H_{13}BrN_2O_2S$: 327.9881; found: 327.9883.

N-(5-Bromo-3-methyl-3,4-dihydropyridin-2(1*H*)-ylidene)-4-methylbenzenesulfonamide (9c)

Compound **9c** was prepared from **7c**, $MePhSiH_2$ (0.6 mmol, 1.2 equiv) and **10a** according to the general procedure for 12 h at 85 °C; eluent: EtOAc/hexane = 10:90.

Yield: 80.8 mg (47%); white solid; mp 117–119 °C.

IR (neat): 3313, 1584, 1282, 1133, 1081, 817, 701, 578, 547 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.53 (s, 1 H), 7.82 (d, *J* = 8.3 Hz, 2 H), 7.30 (d, *J* = 8.5 Hz, 2 H), 6.39 (s, 1 H), 2.95–2.67 (m, 2 H), 2.56–2.32 (m, 4 H), 1.23 (d, *J* = 6.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.5, 143.4, 138.6, 129.5 (2C), 126.4 (2C), 122.9, 103.1, 36.2, 35.8, 21.6, 16.8.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{13}H_{15}BrN_2O_2S$: 342.0038; found: 342.0040.

4-Methyl-*N*-(5-methyl-3,4-dihydropyridin-2(1*H*)-ylidene)-benzenesulfonamide (9d)

Compound **9d** was prepared from **7d**, $MePhSiH_2$ (0.6 mmol, 1.2 equiv) and **10a** according to the general procedure for 4 h at 110 °C; eluent: EtOAc/hexane = 15:85.

Yield: 22.6 mg (17%); white solid; mp 166–168 °C.

IR (neat): 3311, 1584, 1271, 1072, 893, 732, 670, 592, 553, 525 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.34 (s, 1 H), 7.83 (d, *J* = 7.1 Hz, 2 H), 7.30 (d, *J* = 7.2 Hz, 2 H), 5.89 (d, *J* = 5.2 Hz, 1 H), 2.61 (t, *J* = 7.7 Hz, 2 H), 2.43 (s, 3 H), 2.20 (t, *J* = 7.7 Hz, 2 H), 1.74 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 162.2, 143.1, 139.2, 129.4 (2C), 126.4 (2C), 118.7, 117.9, 29.7, 24.2, 21.6, 19.4.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{13}H_{16}N_2O_2S$: 264.0932; found: 264.0934.

4-Methyl-*N*-(5-phenyl-3,4-dihydropyridin-2(1*H*)-ylidene)-benzenesulfonamide (9e)

Compound **9e** was prepared from **7e**, $MePhSiH_2$ (0.6 mmol, 1.2 equiv) and **10a** according to the general procedure for 4 h at 110 °C; eluent: CH_2Cl_2/EtOAc = 99:1.

Yield: 66.2 mg (41%); white solid; mp 196–198 °C.

IR (neat): 3228, 1557, 1282, 1147, 1131, 1079, 899, 751, 701, 654, 573, 549 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.68 (s, 1 H), 7.85 (d, *J* = 6.8 Hz, 2 H), 7.38–7.23 (m, 7 H), 6.52 (s, 1 H), 2.81–2.72 (m, 2 H), 2.71–2.67 (m, 2 H), 2.42 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 268.2, 143.3, 138.9, 137.3, 129.5 (2C), 128.8 (2C), 127.5, 126.6 (2C), 124.5 (2C), 121.0, 119.7, 29.9, 21.9, 21.6.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{18}H_{18}N_2O_2S$: 326.1089; found: 326.1090.

N-(3,5-Dimethyl-3,4-dihydropyridin-2(1*H*)-ylidene)-4-methylbenzenesulfonamide (9f)

Compound **9f** was prepared from **7f**, $MePhSiH_2$ (0.6 mmol, 1.2 equiv) and **10a** according to the general procedure for 18 h at 110 °C; eluent: EtOAc/hexane = 20:80.

Yield: 31.8 mg (23%); white solid; mp 104–106 °C.

IR (neat): 3328, 1588, 1422, 1270, 1134, 1079, 923, 881, 680, 589, 549 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.33 (s, 1 H), 7.84–7.80 (m, 2 H), 7.29–7.27 (m, 2 H), 5.88–5.82 (m, 1 H), 2.65–2.56 (m, 1 H), 2.41 (s, 3 H), 2.34 (dd, *J* = 17.1, 7.0 Hz, 1 H), 1.91 (dd, *J* = 17.0, 7.6 Hz, 1 H), 1.73 (s, 3 H), 1.17 (d, *J* = 7.1 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.9, 142.9, 139.3, 129.4 (2C), 126.3 (2C), 117.5, 117.2, 34.3, 32.1, 21.5, 19.6, 16.7.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{14}H_{18}N_2O_2S$: 278.1089; found: 278.1092.

4-Methyl-*N*-(3-methyl-5-phenyl-3,4-dihydropyridin-2(1*H*)-ylidene)benzenesulfonamide (9g)

Compound **9g** was prepared from **7g**, $MePhSiH_2$ (0.6 mmol, 1.2 equiv) and **10a** according to the general procedure for 18 h at 110 °C; eluent: EtOAc/hexane = 25:75.

Yield: 55.1 mg (31%); white solid; mp 130–132 °C.

IR (neat): 3316, 1582, 1399, 1264, 1124, 1076, 924, 881, 761, 683, 591, 549 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.68 (s, 1 H), 7.86 (d, *J* = 8.3 Hz, 2 H), 7.47–7.23 (m, 7 H), 6.48 (d, *J* = 4.6 Hz, 1 H), 2.84–2.75 (m, 2 H), 2.49–2.43 (m, 1 H), 2.42 (s, 3 H), 1.25 (d, *J* = 6.7 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.8, 143.2, 139.0, 137.6, 129.4 (2C), 128.8 (2C), 127.4, 126.4 (2C), 124.5 (2C), 119.9, 119.0, 34.5, 29.7, 21.6, 16.7.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{19}H_{20}N_2O_2S$: 340.1245; found: 340.1247.

4-Methyl-*N*-((3*S*,5*S*,*Z*)-3-methyl-5-((*S*)-methyl(phenyl)silyl)piperidin-2-ylidene)benzenesulfonamide (9h)

Compound **9h** was prepared from **7d**, $MePhSiH_2$ (1.25 mmol, 2.5 equiv) and **10a** according to the general procedure for 12 h at 110 °C; eluent: EtOAc/hexane = 25:75.

Yield: 45.1 mg (23%), 1:1 diastereomeric mixture of Si stereogenic center; yellowish liquid.

IR (neat): 3290, 2924, 2116, 1599, 1392, 1253, 1140, 1079, 813, 723, 665, 579 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.56 (d, *J* = 7.5 Hz, 1 H), 7.83–7.74 (m, 2 H), 7.50–7.45 (m, 2 H), 7.44–7.35 (m, 3 H), 7.24 (d, *J* = 8.0 Hz, 2 H), 4.34–4.25 (m, 1 H), 3.44–3.30 (m, 1 H), 3.27–3.16 (m, 1 H), 2.61–2.52

(m, 1 H), 2.39 (s, 3 H), 1.77–1.71 (m, 1 H), 1.63 (dddd, *J* = 18.4, 13.8, 4.8, 2.8 Hz, 1 H), 1.51 (dddd, *J* = 17.8, 12.7, 5.3, 2.8 Hz, 1 H), 1.21 (dd, *J* = 9.2, 7.4 Hz, 3 H), 0.39 (dd, *J* = 5.7, 4.0 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = (169.6, 169.6), 142.4, 139.9, (134.5, 134.4) (2C), 132.7, 130.1, 129.2 (2C), 128.2 (2C), 126.1 (2C), (44.5, 44.3), 34.4, (28.3, 28.2), 21.4, (19.5, 19.5), (14.7, 14.6), (–7.9, –8.0).

IR: 3290, 2924, 2116, 1599, 1392, 1253, 1140, 1079, 813, 723, 665, 579 cm^{-1}.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{20}H_{26}N_2O_2SSi$: 386.1484; found: 386.1484.

4-Methyl-*N*-((3*R*,5*S*,*Z*)-3-methyl-5-((*S*)-methyl(phenyl)silyl)piperidin-2-ylidene)benzenesulfonamide (9h')

Compound **9h'** was prepared from **7d**, $MePhSiH_2$ (1.25 mmol, 2.5 equiv) and **10a** according to the general procedure for 12 h at 110 °C; eluent: EtOAc/hexane = 25:75.

Yield: 5.1 mg (3%), 1:1 diastereomeric mixture of Si stereogenic center; yellowish liquid.

IR (neat): 3290, 2926, 2116, 1598, 1392, 1260, 1127, 1081, 896, 868, 725, 575 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.59 (s, 1 H), 7.78 (d, *J* = 8.0 Hz, 2 H), 7.52–7.46 (m, 2 H), 7.44–7.36 (m, 3 H), 7.24 (d, *J* = 8.1 Hz, 2 H), 4.28 (tt, *J* = 7.4, 3.9 Hz, 1 H), 3.47–3.33 (m, 1 H), 3.22 (td, *J* = 12.9, 4.0 Hz, 1 H), 2.46–2.41 (m, 1 H), 2.39 (s, 3 H), 1.97 (dddt, *J* = 18.2, 13.7, 6.2, 2.3 Hz, 1 H), 1.42 (dddt, *J* = 15.4, 10.8, 5.3, 2.7 Hz, 1 H), 1.35–1.23 (m, 1 H), 1.19 (dd, *J* = 9.1, 6.9 Hz, 3 H), 0.40 (dd, *J* = 4.0 Hz, 4.0 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.0, 142.3, 140.2, (134.6, 134.5) (2C), (132.8, 132.7), 130.2, 129.2 (2C), 128.3 (2C), 126.1 (2C), (44.9, 44.7), 36.8, (30.6, 30.6), 21.5, (20.1, 20.0), (18.3, 18.2), (–7.9, –8.0).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{20}H_{26}N_2O_2SSi$: 386.1484; found: 386.1484.

Synthesis of Cyclic Amidines 11 from Pyridines 7 and 4-(Trifluoromethyl)benzenesulfonyl Azide 10b (Scheme 3); General Procedure

Step 1: $B(C_6F_5)_3$ catalyst (0.025 mmol, 5 mol%) in an NMR tube was dissolved in $CDCl_3$ (0.5 mL) under argon atmosphere. Silane (0.6 mmol, 1.2 equiv) was added at r.t. (H_2 bubbles were evolved) and TCE (0.3 mmol) was added into the reaction mixture as internal standard. Pyridine **7a–h** (0.5 mmol, 1.0 equiv) was subsequently added and the mixture was heated to the indicated temperature in an oil bath for the indicated time. The resulting mixture was subjected to NMR analysis to monitor the conversion.

Step 2: To the resulting mixture from the first step in an NMR cell was added 4-(trifluoromethyl)benzenesulfonyl azide **10b** (0.5 mmol, 1.0 equiv) at r.t. (N_2 bubbling was observed) and an NMR spectrum was recorded after 2 h. The reaction was quenched with MeOH, and the mixture was filtered through silica, and washed with CH_2Cl_2. The resulting crude mixture was purified by column chromatography.

***N*-(5-Chloro-3,4-dihydropyridin-2(1*H*)-ylidene)-4-(trifluoromethyl)benzenesulfonamide (11a)**

Compound **11a** was prepared from **7a**, Ph_2SiH_2 (0.6 mmol, 1.2 equiv) and **10b** according to the general procedure for 12 h at 85 °C; eluent: CH_2Cl_2/hexane/acetone = 60:40:5.

Yield: 109.8 mg (65%); white solid; mp 230–232 °C.

IR (neat): 3183, 3075, 1575, 1406, 1290, 1131, 1060, 918, 843, 710, 598, 573 cm^{-1}.

^{1}H NMR (500 MHz, CD_2Cl_2): δ = 9.39 (s, 1 H), 8.03 (d, *J* = 8.0 Hz, 2 H), 7.78 (d, *J* = 8.1 Hz, 2 H), 6.35–6.28 (m, 1 H), 2.81–2.73 (m, 2 H), 2.65–2.55 (m, 2 H).

^{13}C NMR (125 MHz, CD_2Cl_2): δ = 160.7, 144.2, 133.6 (q, *J* = 32.5 Hz), 126.7 (2C), 125.7 (q, *J* = 3.8 Hz, 2C), 123.1 (q, *J* = 270.0 Hz), 120.1, 116.8, 30.3, 26.3.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{12}H_{10}ClF_3N_2O_2S$: 338.0104; found: 338.0102.

***N*-(5-Bromo-3,4-dihydropyridin-2(1*H*)-ylidene)-4-(trifluoromethyl)benzenesulfonamide (11b)**

Compound **11b** was prepared from **7b**, Ph_2SiH_2 (0.6 mmol, 1.2 equiv) and **10b** according to the general procedure for 12 h at 85 °C; eluent: CH_2Cl_2/hexane/acetone = 40:60:5.

Yield: 114.5 mg (60%); white solid; mp 177–179 °C.

IR (neat): 3177, 3070, 1576, 1406, 1322, 1156, 1130, 1060, 914, 843, 740, 709, 613, 570 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.42 (s, 1 H), 8.03 (d, *J* = 8.3 Hz, 2 H), 7.78 (d, *J* = 8.1 Hz, 2 H), 6.42 (d, *J* = 4.9 Hz, 1 H), 2.82–2.71 (m, 2 H), 2.71–2.66 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 161.7, 144.8, 133.5 (q, *J* = 32.5 Hz), 126.7 (2C), 125.7 (q, *J* = 3.9 Hz, 2C), 123.1 (q, *J* = 270.0 Hz), 122.8, 104.4, 30.7, 28.0.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{12}H_{10}BrF_3N_2O_2S$: 381.9598; found: 381.9595.

***N*-(5-Bromo-3-methyl-3,4-dihydropyridin-2(1*H*)-ylidene)-4-(trifluoromethyl)benzenesulfonamide (11c)**

Compound **11c** was prepared from **7c**, $MePhSiH_2$ (0.6 mmol, 1.2 equiv) and **10b** according to the general procedure for 12 h at 85 °C; eluent: EtOAc/hexane = 20:80.

Yield: 108.8 mg (55%); yellow solid; mp 126–128 °C.

IR (neat): 3305, 1593, 1403, 1321, 1264, 1169, 1122, 930, 822, 717, 622, 550 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.45 (s, 1 H), 8.07 (d, *J* = 8.2 Hz, 2 H), 7.78 (d, *J* = 8.2 Hz, 2 H), 6.40 (dd, *J* = 4.7, 1.4 Hz, 1 H), 2.85–2.75 (m, 2 H), 2.50–2.39 (m, 1 H), 1.25 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.3, 144.9, 134.2 (q, *J* = 32.9 Hz), 127.0 (2C), 126.0 (q, *J* = 3.4 Hz, 2C), 123.30 (q, *J* = 271.8 Hz), 122.73, 104.01, 36.11, 35.82, 16.72.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{13}H_{12}BrF_3N_2O_2S$: 395.9755; found: 395.9753.

***N*-(5-Methyl-3,4-dihydropyridin-2(1*H*)-ylidene)-4-(trifluoromethyl)benzenesulfonamide (11d)**

Compound **11d** was prepared from **7d**, $MePhSiH_2$ (0.6 mmol, 1.2 equiv) and **10b** according to the general procedure for 4 h at 110 °C; eluent: EtOAc/hexane = 15:85.

Yield: 36.6 mg (23%); white solid; mp 155–157 °C.

IR (neat): 3374, 3094, 1576, 1406, 1318, 1156, 1127, 1061, 927, 842, 719, 606, 524 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.33 (s, 1 H), 8.07 (d, *J* = 8.1 Hz, 2 H), 7.76 (d, *J* = 8.0 Hz, 2 H), 5.91 (s, 1 H), 2.63 (t, *J* = 8.3 Hz, 2 H), 2.21 (t, *J* = 8.3 Hz, 2 H), 1.74 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 162.5, 145.5, 134.0 (q, *J* = 32.7 Hz), 127.0 (2C), 126.0 (q, *J* = 3.8 Hz, 2C), 123.4 (q, *J* = 272.8 Hz), 119.50, 117.8, 29.7, 24.1, 19.4.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{13}H_{13}F_3N_2O_2S$: 318.0650; found: 318.0652.

N-(5-Phenyl-3,4-dihydropyridin-2(1*H*)-ylidene)-4-(trifluoromethyl)benzenesulfonamide (11e)

Compound **11e** was prepared from **7e**, $MePhSiH_2$ (0.6 mmol, 1.2 equiv) and **10b** according to the general procedure for 4 h at 110 °C; eluent: EtOAc/hexane = 20:80.

Yield: 80.0 mg (42%); white solid; mp 195–197 °C.

IR (neat): 3189, 1569, 1405, 1321, 1156, 1131, 1061, 991, 909, 751, 715, 612, 566 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 9.61 (s, 1 H), 8.10 (d, *J* = 8.5 Hz, 2 H), 7.78 (d, *J* = 2.9 Hz, 2 H), 7.49–7.12 (m, 5 H), 6.51 (d, *J* = 4.0 Hz, 1 H), 3.20–2.39 (m, 4 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 162.3, 145.2, 137.0, 134.2 (q, *J* = 32.6 Hz), 128.8 (2C), 127.7, 127.1 (2C), 126.0 (q, *J* = 6.3 Hz, 2C), 124.6 (2C), 123.3 (q, *J* = 271.3 Hz), 121.8, 119.3, 30.0, 21.9.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{18}H_{15}F_3N_2O_2S$: 380.0806; found: 380.0804.

N-(3,5-Dimethyl-3,4-dihydropyridin-2(1*H*)-ylidene)-4-(trifluoromethyl)benzenesulfonamide (11f)

Compound **11f** was prepared from **7f**, $MePhSiH_2$ (0.6 mmol, 1.2 equiv) and **10b** according to the general procedure for 18 h at 110 °C; eluent: EtOAc/hexane = 15:85.

Yield: 67.5 mg (48%); white solid; mp 123–125 °C.

IR (neat): 3331, 1590, 1432, 1321, 1267, 1116, 1061, 927, 888, 716, 622, 598 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 9.34 (s, 1 H), 8.07 (d, *J* = 7.9 Hz, 2 H), 7.76 (d, *J* = 8.3 Hz, 2 H), 5.89–5.86 (m, 1 H), 2.71–2.59 (m, 1 H), 2.39–2.30 (m, 1 H), 1.99–1.91 (m, 1 H), 1.75 (s, 3 H), 1.18 (d, *J* = 7.1 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.6, 145.6, 133.9 (q, *J* = 32.9 Hz), 126.9 (2C), 125.9 (q, *J* = 4.0 Hz, 2C), 123.4 (q, *J* = 272.8 Hz), 118.4, 117.1, 34.4, 32.1, 19.6, 16.6.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{14}H_{15}F_3N_2O_2S$: 332.0806; found: 332.0807.

N-(3-Methyl-5-phenyl-3,4-dihydropyridin-2(1*H*)-ylidene)-4-(trifluoromethyl)benzenesulfonamide (11g)

Compound **11g** was prepared from **7g**, $MePhSiH_2$ (0.6 mmol, 1.2 equiv) and **10b** according to the general procedure for 18 h at 110 °C; eluent: EtOAc/hexane = 20:80.

Yield: 78.5 mg (40%); white solid; mp 143–145 °C.

IR (neat): 3312, 1586, 1445, 1399, 1260, 1124, 1083, 1060, 932, 888, 835, 718, 691, 624, 555 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 9.67 (s, 1 H), 8.11 (d, *J* = 8.1 Hz, 2 H), 7.77 (d, *J* = 8.2 Hz, 2 H), 7.42–7.26 (m, 5 H), 6.49 (d, *J* = 5.3 Hz, 1 H), 2.89–2.78 (m, 2 H), 2.55–2.43 (m, 1 H), 1.27 (d, *J* = 6.7 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.5, 145.3, 137.3, 134.04 (q, *J* = 32.5 Hz), 128.8 (2C), 127.63, 127.0 (2C), 126.00 (q, *J* = 4.0 Hz, 2C), 124.6 (2C), 123.3 (q, *J* = 271.3 Hz), 120.8, 118.7, 34.5, 29.7, 16.6.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{19}H_{17}F_3N_2O_2S$: 394.0963; found: 394.0962.

N-((3*S*,5*S*,*Z*)-3-Methyl-5-((*S*)-methyl(phenyl)silyl)piperidin-2-ylidene)-4-(trifluoromethyl)benzenesulfonamide (11h)

Compound **11h** was prepared from **7d**, $MePhSiH_2$ (1.25 mmol, 2.5 equiv) and **10b** according to the general procedure for 12 h at 110 °C; eluent: EtOAc/hexane = 20:80.

Yield: 55.2 mg (25%), 1:1 diastereomeric mixture of Si stereogenic center; white solid; mp 98–100 °C.

IR (neat): 3296, 2924, 2108, 1621, 1394, 1321, 1273, 1154, 1103, 1059, 728, 710, 697, 613, 602 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.67–8.56 (m, 1 H), 8.02 (d, *J* = 8.1 Hz, 2 H), 7.71 (d, *J* = 8.2 Hz, 2 H), 7.50–7.46 (m, 2 H), 7.44–7.35 (m, 3 H), 4.35–4.26 (m, 1 H), 3.48–3.33 (m, 1 H), 3.30–3.18 (m, 1 H), 2.58 (tdd, *J* = 13.5, 6.5, 2.7 Hz, 1 H), 1.85–1.73 (m, 1 H), 1.67–1.60 (m, 1 H), 1.58–1.47 (m, 1 H), 1.22 (dd, *J* = 9.2, 7.4 Hz, 3 H), 0.40 (dd, *J* = 5.9, 3.8 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = (170.4, 170.3), 146.2, (134.5, 134.4), 133.5 (q, *J* = 32.5 Hz), 132.55, 130.14 (2C), 128.23 (2C), 126.61 (2C), 125.7 (q, *J* = 3.8 Hz, 2C), 123.4 (q, *J* = 271.3 Hz), (44.7, 44.5), 34.5, (28.3, 28.1), (19.5, 19.4), (14.8, 14.6), (–7.9, –8.0).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{20}H_{23}F_3N_2O_2SSi$: 440.1202; found: 440.1202.

N-((3*R*,5*S*,*Z*)-3-Methyl-5-((*S*)-methyl(phenyl)silyl)piperidin-2-ylidene)-4-(trifluoromethyl)benzenesulfonamide (11h′)

Compound **11h′** was prepared from **7d**, $MePhSiH_2$ (1.25 mmol, 2.5 equiv) and **10b** according to the general procedure for 12 h at 110 °C; eluent: EtOAc/hexane = 20:80.

Yield: 5.1 mg (2%), 1:1 diastereomeric mixture of Si stereogenic center; white solid; mp 144–146 °C.

IR (neat): 3294, 2929, 2120, 1598, 1391, 1320, 1262, 1126, 1084, 1061, 899, 870, 829, 715, 612 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.63 (s, 1 H), 8.02 (d, *J* = 8.2 Hz, 2 H), 7.71 (d, *J* = 8.3 Hz, 2 H), 7.52–7.47 (m, 2 H), 7.46–7.34 (m, 3 H), 4.34–4.25 (m, 1 H), 3.51–3.36 (m, 1 H), 3.25 (td, *J* = 12.9, 3.9 Hz, 1 H), 2.50–2.38 (m, 1 H), 2.05–1.92 (m, 1 H), 1.49–1.39 (m, 1 H), 1.36–1.24 (m, 1 H), 1.19 (dd, *J* = 9.2, 6.9 Hz, 3 H), 0.41 (t, *J* = 4.1 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.7, 146.4, (134.6, 134.5) (2C), 133.5 (q, *J* = 32.5 Hz), (132.6, 132.5), 130.2, 128.3 (2C), 126.6 (2C), 125.8 (q, *J* = 3.6 Hz, 2C), 123.4 (q, *J* = 272.5 Hz), (45.1, 44.9), 36.9, (30.5, 30.4), (20.1, 20.0), (18.2, 18.1), (–7.9, –8.0).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{20}H_{23}F_3N_2O_2SSi$: 440.1202; found: 440.1202.

Synthesis of 1,4-Dihydroisoquinolin-3(2*H*)-one (12) from Cyclic Amidine 6a (Scheme 5)

A round-bottom flask was charged with amidine **6a** (0.18 mmol, 54 mg), then MeOH (1.6 mL), H_2O (0.4 mL), and conc. HCl (0.1 mL) were added sequentially at r.t. and the reaction mixture was stirred and heated to 85 °C for 5 h (**12**) before sat. $NaHCO_3$ solution was added to neutralize the mixture. After evaporation of MeOH, the resulting aqueous layer was extracted with EtOAc and the organic layer was dried over $MgSO_4$, and evaporated under reduced pressure. The crude mixture was purified by column chromatography on silica gel with EtOAc/hexane.

EtOAc/hexane = 70:30.

Yield: 19.2 mg (72%); white solid; mp 154–156 °C.

IR (neat): 3185, 3029, 1652, 1496, 1429, 1396, 1345, 1327, 833, 742, 550, 457 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34 (s, 1 H), 7.28–7.22 (m, 2 H), 7.20–7.14 (m, 2 H), 4.51 (d, *J* = 2.3 Hz, 2 H), 3.59 (s, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 172.2, 131.8, 131.1, 127.8, 127.5, 126.7, 125.4, 45.3, 36.6.

HRMS (EI): *m*/*z* [M]$^+$ calcd for C_9H_9NO: 147.0684; found: 147.0684.

Synthesis of 5-Phenyl-3,4-dihydropyridin-2(1*H*)-one (13) from Cyclic Amidine 9e (Scheme 5)

A round-bottom flask was charged with amidine **9e** (0.18 mmol, 59 mg), then THF (0.8 mL), MeOH (1.0 mL), H_2O (0.1 mL), and HCl conc. (0.05 mL) were added sequentially at r.t. The reaction mixture was stirred and heated to 65 °C for 2.5 h before sat. $NaHCO_3$ solution was added to neutralize the mixture. After evaporation of THF and MeOH, the resulting aqueous layer was extracted with EtOAc and the organic layer was dried over $MgSO_4$, and evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel with EtOAc/hexane.

EtOAc/hexane = 50:50.

Yield: 11.2 mg (36%); white solid; mp 120–122 °C.

IR (neat): 3196, 3076, 2945, 1682, 1645, 1594, 1388, 1295, 1212, 1144, 752, 693, 577, 514, 499, 460 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.71 (s, 1 H), 7.38–7.28 (m, 4 H), 7.26–7.19 (m, 1 H), 6.50 (d, *J* = 4.6 Hz, 1 H), 2.79 (dd, *J* = 8.6, 7.4 Hz, 2 H), 2.65 (dd, *J* = 8.9, 7.2 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.8, 138.3, 128.7 (2C), 126.7, 124.3 (2C), 121.3, 117.5, 30.3, 23.4.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{11}H_{11}NO$: 173.0841; found: 173.0841.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0040-1707323.

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