A One-Pot β-Chloro-N′-tosylamidination of Olefins with Chloramine-T

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Abstract: A new method for the direct synthesis of β-chloro-*N*′-tosylamidines from olefins using chloramine-T and trifluoromethanesulfonic acid is described.

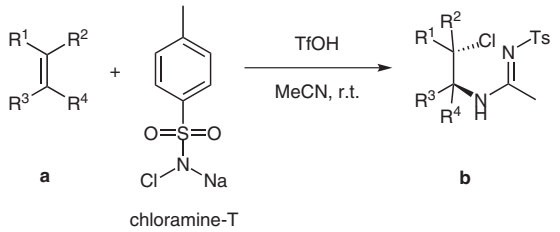
Key words: olefins, chloramine-T, amidination, amidines, amines

The amidine group is an important functional group present in several biologically active and pharmaceutically important molecules.[1] Amidine derivatives are also excellent precursors in the synthesis of nitrogen-containing heterocycles such as imidazole, pyrimidine and pyrrole derivatives.[2] Moreover, they are valuable intermediates in the synthesis of 1,2-diamines and amidinium carbamates (ionic liquids).[3] In addition, chiral amidine derivatives have been used as novel bidentate ligands in metal-mediated asymmetric transformations.[4]

Amidines are usually prepared starting from nitriles, isonitriles, amides, ynamides, ortho esters, thioesters or imidoylbenzotriazoles.[5] Recently, a number of transition metal catalyzed multicomponent reactions have been developed for the synthesis of cyclic and acyclic amidines.[6] A 'click chemistry' based strategy has also been explored in the synthesis of *N*′-sulfonylamidines.[7]

Interestingly, diamination of olefins using *N*-chlorosaccharin as a nitrogen source has been reported.[8] Very recently, copper(II) acetate catalyzed conversion of olefins into β-chloroamidines has been realized using dichloramine-T as a nitrogen source.[9]

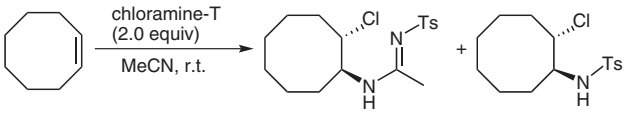
Herein, we report a simple and efficient method for the direct synthesis of β-chloro-*N*′-tosylamidines from olefins under mild reaction conditions using chloramine-T as an inexpensive nitrogen source (Scheme 1).[10]



Scheme 1 β-Chloro-*N*′-tosylamidination of olefins with chloramine-T

During the course of our investigations on the direct amination of olefins with chloramine-T in the presence of formic acid in acetonitrile medium, we observed an unusual formation of synthetically useful β-chloro-*N*′-tosylamidines in low yield. In order to improve the efficiency of this new method, a detailed investigation with different Brønsted acids was carried out, and the results are summarized in Table 1. Among the acids screened, trifluoromethanesulfonic acid was found to be the most efficient catalyst to bring about the required transformation. Thus, treatment of cyclooctene (**1a**, 1.0 equiv) with chloramine-T (2.0 equiv) and trifluoromethanesulfonic acid (2.0 equiv) in anhydrous acetonitrile (4 mL/mmol of olefin) at room temperature for two hours resulted in a mixture (6:1) of β-chloro-*N*′-tosylamidine **1b** and β-chloro-*N*-tosylamine **1c** in 69% yield (Table 1, entry 5).

Table 1 Reaction of Cyclooctene Using Different Brønsted Acids



1a 1b 1c

Entry	Acid	Temp (°C)	Time (h)	Ratio (**1b**/**1c**)	Yield[a,b] (%)
1	HCO_2H	r.t.	3	1:0	27
2	MsOH	r.t.	3	–	no reaction
3	MsOH	reflux	2	1:0	20
4	TFA	r.t.	3	1:0	31
5	**TfOH**	**r.t.**	**2**	**6:1**	**69**

[a] Yield based on cyclooctene.
[b] Combined yield of **1b** and **1c**.

To generalize the scope of this *N*′-tosylamidination reaction, several substituted olefins were examined, and the results are summarized in Table 2. Cyclohexene (**2a**) reacted readily at room temperature to give the corresponding β-chloro-*N*′-tosylamidine **2b** in excellent yield (Table 2, entry 2). The structure of amidine **2b** was confirmed by single crystal X-ray analysis (Figure 1).

Similarly, cyclopentene (**3a**) reacted readily to give the corresponding β-chloro-*N*′-tosylamidine **3b** in excellent yield (Table 2, entry 3). Under similar reaction conditions, electron-rich olefins such as 3,4-dihydro-2*H*-pyran (**4a**) and 3,4,6-tri-*O*-benzylglucal (**5a**) gave the corresponding β-chloro-*N*′-tosylamidines as a mixture of the

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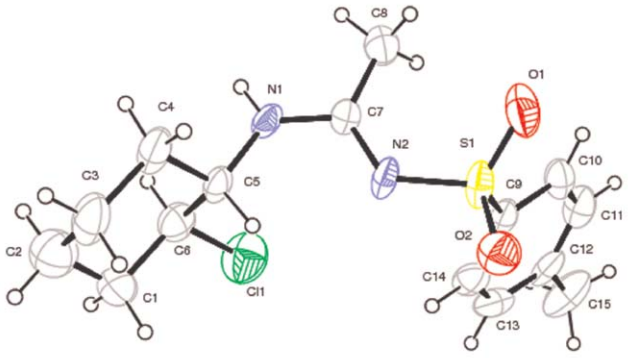


Figure 1 ORTEP diagram of compound **2b**

cis- and *trans*-isomers with the chloro group at C-2 and the *N*′-tosylamidine group at C-1 (Table 2, entries 4 and 5). The observed regio- and stereoselectivity signifies the formation of an oxonium ion[11] after the initial reaction of the enol ether double bond with chloronium ion and a subsequent nucleophilic attack by acetonitrile at C-1. For the first time, electron-rich olefins have been directly converted into the corresponding β-chloro-*N*′-tosylamidines in good yields.

Table 2 Reaction of Various Olefins with Chloramine-T[a]

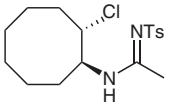
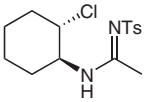
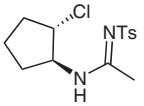
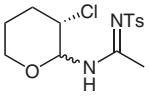
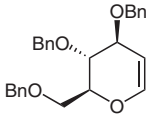
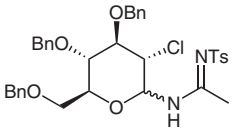
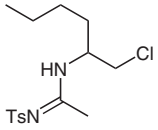
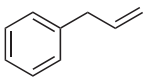
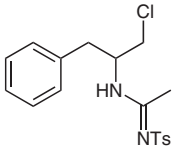
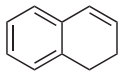
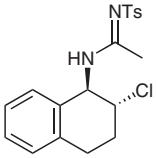
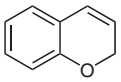
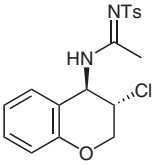
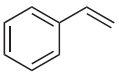
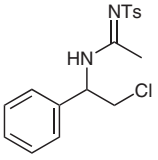
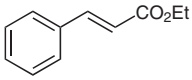
Entry	Olefin **a**	Amidine **b**	Yield[b] (%)
1	 **1a**	 **1b**	60
2	 **2a**	 **2b**	89[c]
3	 **3a**	 **3b**	95[c]
4	 **4a**	 *cis*/*trans* = 1:4 **4b**	73[d]
5	 **5a**	 *cis*/*trans* = 4.5:1 **5b**	55[d]

Table 2 Reaction of Various Olefins with Chloramine-T[a] (continued)

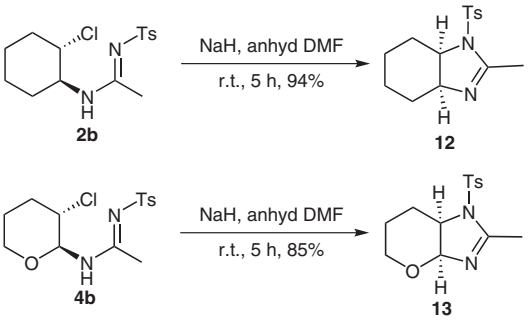
Entry	Olefin **a**	Amidine **b**	Yield[b] (%)
6	 **6a**	 **6b**	54[c]
7	 **7a**	 **7b**	52
8	 **8a**	 **8b**	14[e]
9	 **9a**	 **9b**	15[f]
10	 **10a**	 **10b**	0[g]
11	 **11a**	–	no reaction

[a] Reaction conditions: olefin/TfOH/chloramine-T = 1.0:2.0:2.0 (molar ratio), MeCN, r.t., 2 h.
[b] Isolated yield of β-chloro-*N*′-tosylamidine.
[c] Yield based on chloramine-T. Reaction conditions: olefin/TfOH/chloramine-T = 2.0:2.0:1.0 (molar ratio), MeCN (4 mL/mmol of CT), r.t., 2 h.
[d] Yield refers to a mixture of the *cis*- and *trans*-isomers.
[e] The corresponding β-chloro-*N*-tosylamine **8c** was isolated in 55% yield.
[f] The corresponding β-chloro-*N*-tosylamine **9c** was isolated in 60% yield.
[g] Under reflux conditions, the corresponding β-chloro-*N*-tosylamine **10c** was isolated in 84% yield.

Similarly, terminal olefins such as 1-hexene (**6a**) and allylbenzene (**7a**) underwent regioselective reaction to give the corresponding β-chloro-*N*′-tosylamidines in good yields (Table 2, entries 6 and 7); however, under similar reaction conditions, conjugated aromatic olefins such as 1,2-dihydronaphthalene (**8a**) and 2*H*-chromene (**9a**) favored the formation of the 2-chloro-1-(*N*-tosylamino) derivatives as the major products with the corresponding 2-chlorinated 1-(*N*′-tosylamidines) being isolated as the mi-

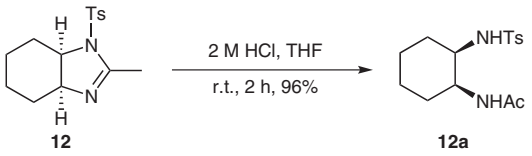
nor products (Table 2, entries 8 and 9). Moreover, styrene (**10a**) was reacted under reflux conditions to afford the 2-chloro-1-(*N*-tosylamino)ethyl derivative **10c** as the only product (Table 2, entry 10). An electron-deficient olefin was found to be inert under the reaction conditions (Table 2, entry 11).

The synthetic potential of the β-chloro-*N*′-tosylamidine derivatives was further explored in the stereoselective synthesis of *N*-tosylimidazolines. Thus, on exposure to sodium hydride in *N*,*N*-dimethylformamide, β-chloro-*N*′-tosylamidines **2b** and **4b** underwent smooth cyclization to give the corresponding imidazoline derivatives **12** and **13**, respectively, in excellent yields (Scheme 2).



Scheme 2 Synthesis of imidazoline derivatives from amidines

The imidazoline derivative **12** was hydrolysed using 2 M hydrochloric acid in tetrahydrofuran to afford the cyclohexane-1,2-diamine derivative **12a** in quantitative yield (Scheme 3).



Scheme 3 Synthesis of *cis*-cyclohexane-1,2-diamine derivative **12a** from imidazoline **12**

The relative configuration of compound **12a** was unambiguously confirmed by single crystal X-ray analysis (Figure 2).

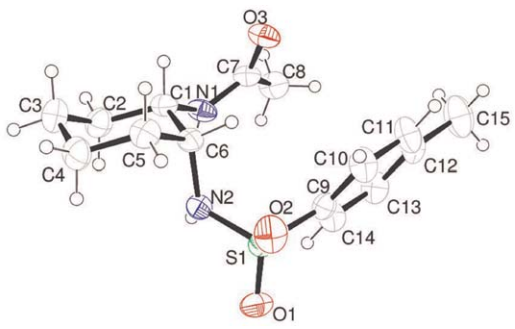
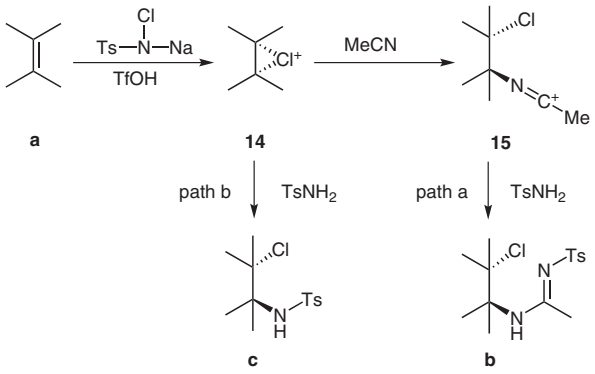


Figure 2 ORTEP diagram of compound **12a**

A tentative mechanism for the formation of β-chloro-*N*′-tosylamidine **b** from olefin **a** is shown in Scheme 4.[12] It is likely that the olefin forms a cyclic chloronium ion intermediate **14** on exposure to chloramine-T and the Brønsted acid. Nucleophilic ring opening of the cyclic chloronium ion **14** by acetonitrile would lead to iminium ion **15** (Ritter reaction) and subsequent reaction with *p*-toluenesulfonamide, present in the reaction medium, would lead to the corresponding β-chloro-*N*′-tosylamidine **b** (Scheme 4, path a); however, direct ring opening of the cyclic chloronium ion **14** by *p*-toluenesulfonamide would result in the β-chloro-*N*-tosylamine **c** (Scheme 4, path b).



Scheme 4 Plausible mechanism for the β-chloro-*N*′-tosylamidination reaction

In conclusion, we have developed a simple and efficient method for the one-pot synthesis of β-chloro-*N*′-tosylamidines from olefins using chloramine-T as an inexpensive nitrogen source. This reaction takes place readily at room temperature and, for the first time, 3,4-dihydro-2*H*-pyran and a glucal derivative have been successfully used as substrates. This new methodology provides an easy access to synthetically useful *N*-tosylimidazoline derivatives.

IR spectra were run as KBr disks or neat on a Nicolet 4700 spectrophotometer. ^{1}H and ^{13}C NMR spectra were determined for solutions in $CDCl_3$ with TMS as internal standard on a Bruker 400-MHz instrument. HRMS data were measured on a Micromass Q-TOF mass spectrometer.

β-Chloro-*N*′-tosylamidines; General Procedure

To a stirred suspension of chloramine-T (2.0 mmol) in MeCN (4 mL/mmol of olefin) at r.t. was added an olefin (1.0 mmol), followed by TfOH (2.0 mmol) dropwise over a period of 10 min. After 2 h, the reaction mixture was quenched with sat. $NaHCO_3$ soln and extracted with EtOAc (2 × 10 mL). The combined organic layer was washed with H_2O (2 × 5 mL) and brine soln (1 × 5 mL), and dried (anhyd Na_2SO_4). The organic layer was concentrated under reduced pressure and the crude product was purified by column chromatography over silica gel (EtOAc–hexanes gradient) to furnish the desired compound.

***N*-(2-Chlorocyclooctyl)-*N*′-tosylacetimidamide (1b)**

Yield: 189 mg (60%); R_f = 0.4 (EtOAc–hexanes, 3:7).

IR (KBr): 3286, 2937, 1576, 1554, 1438, 1276, 1141, 1090 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.74 (d, *J* = 8.1 Hz, 2 H), 7.24 (d, *J* = 8.1 Hz, 2 H), 6.52 (d, *J* = 7.4 Hz, 1 H), 4.15–4.13 (m, 1 H), 3.99–3.91 (m, 1 H), 2.41 (s, 3 H), 2.32 (s, 3 H), 2.08–1.95 (m, 4 H), 1.77–1.49 (m, 6 H), 1.48–1.43 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.5, 142.3, 140.7, 129.2, 126.2, 62.5, 51.7, 34.1, 32.3, 29.5, 27.7, 23.3, 22.9, 21.4, 21.1.

HRMS (ESI): *m*/*z* $[M]^+$ calcd for $C_{17}H_{25}ClN_2O_2S$: 357.1404; found: 357.1415.

***N*-(2-Chlorocyclooctyl)-4-methylbenzenesulfonamide (1c)**
Yield: 28 mg (9%); R_f = 0.6 (EtOAc–hexanes, 3:7).

IR (KBr): 3434, 3256, 3064, 3040, 2925, 2870, 1469, 1448, 1321, 1157, 1095 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 7.8 Hz, 2 H), 7.29 (d, *J* = 7.6 Hz, 2 H), 4.93 (s, 1 H), 3.96–3.92 (m, 1 H), 3.33 (s, 1 H), 2.44 (s, 3 H), 2.13–1.34 (m, 12 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.4, 136.9, 129.5, 127.5, 65.6, 60.5, 32.0, 31.2, 25.7, 25.4, 25.3, 23.9, 21.5.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{15}H_{23}ClNO_2S$: 316.1138; found: 316.1135.

***N*-(2-Chlorocyclohexyl)-*N*′-tosylacetimidamide (2b)**
Yield: 1.07 g [89%, based on chloramine-T; Reaction conditions: olefin/TfOH/chloramine-T = 2.0:2.0:1.0 (molar ratio), MeCN (4 mL/mmol of CT), r.t., 2 h]; R_f = 0.3 (EtOAc–hexanes, 3:7).

IR (neat): 3288, 3123, 2942, 2868, 1549, 1440, 1303, 1270, 1139, 1087, 810, 754, 700, 667 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 8.0 Hz, 2 H), 7.23 (d, *J* = 8.0 Hz, 2 H), 6.99 (d, *J* = 8.4 Hz, 1 H), 4.09–4.01 (m, 1 H), 3.77 (dt, *J* = 10.4, 4.4 Hz, 1 H), 2.38 (s, 3 H), 2.26 (s, 3 H), 2.19–2.03 (m, 2 H), 1.72–1.62 (m, 3 H), 1.33–1.20 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.2, 142.2, 140.6, 129.2, 126.3, 61.4, 56.9, 35.9, 31.5, 25.2, 24.1, 21.5, 20.9.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{15}H_{22}ClN_2O_2S$: 329.1091; found: 329.1090.

***N*-(2-Chlorocyclopentyl)-*N*′-tosylacetimidamide (3b)**
Yield: 1.1 g [95%, based on chloramine-T; Reaction conditions: olefin/TfOH/chloramine-T = 2.0:2.0:1.0 (molar ratio), MeCN (4 mL/mmol of CT), r.t., 2 h]; R_f = 0.3 (EtOAc–hexanes, 3:7).

IR (neat): 2971, 1541, 1494, 1417, 1382, 1266, 1190, 1175, 1144, 1089, 1040, 906, 813, 724, 656 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (mixture of tautomers) = 8.07 (d, *J* = 6.0 Hz, 0.8 H), 7.74 (dd, *J* = 6.8, 6.0 Hz, 3.7 H), 7.40 (d, *J* = 7.6 Hz, 2 H), 7.20 (d, *J* = 7.6 Hz, 1.9 H), 4.72 (d, *J* = 8.0 Hz, 1 H), 4.55 (d, *J* = 7.2 Hz, 1 H), 4.35–4.28 (m, 0.8 H), 4.23–4.18 (m, 0.8 H), 2.56 (s, 3 H), 2.44 (s, 3 H), 2.35 (s, 3 H), 2.30 (d, *J* = 0.8 Hz, 2.4 H), 2.27–2.04 (m, 5 H), 1.97–1.72 (m, 7 H), 1.60–1.44 (m, 2.6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.2, 165.4, 147.2, 141.9, 140.7, 133.9, 130.9, 129.1, 127.6, 126.2, 67.3, 64.1, 62.7, 61.2, 35.0, 34.2, 32.9, 29.0, 22.3, 21.8, 21.4, 21.2, 20.6, 14.9.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{14}H_{20}ClN_2O_2S$: 315.0934; found: 315.0933.

***N*-(*cis*-3-Chlorotetrahydro-2*H*-pyran-2-yl)-*N*′-tosylacetimidamide (*cis*-4b)**
Yield (*cis*-**4b** + *trans*-**4b**): 1.2 g (73%); R_f = 0.5 (EtOAc–hexanes, 4:6).

IR (neat): 3298, 2927, 2857, 1586, 1534, 1438, 1374, 1274, 1144, 1081, 1039, 932, 896, 810, 762, 698, 670 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (mixture of tautomers) = 7.76–7.70 (m, 2 H), 7.21–7.19 (m, 2 H), 6.30 (br s, 1 H), 5.31 (d, *J* = 7.2 Hz, 1 H), 4.81 (d, *J* = 7.6 Hz, 0.5 H), 4.17 (br s, 1 H), 3.93–3.83 (m, 3 H), 3.52 (t, *J* = 11.6 Hz, 2 H), 2.33 (s, 6 H), 2.11–1.94 (m, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.4, 142.5, 139.9, 129.3, 126.5, 79.0, 67.6, 60.4, 58.3, 30.7, 21.5, 21.0, 19.1, 14.2.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{14}H_{20}ClN_2O_3S$: 331.0883; found: 331.0883.

***N*-(*trans*-3-Chlorotetrahydro-2*H*-pyran-2-yl)-*N*′-tosylacetimidamide (*trans*-4b)**
R_f = 0.4 (EtOAc–hexanes, 4:6).

IR (neat): 3298, 2927, 2857, 1586, 1534, 1438, 1374, 1274, 1144, 1081, 1039, 932, 896, 810, 762, 698, 670 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (mixture of tautomers) = 7.83–7.80 (m, 2 H), 7.28–7.25 (m, 2 H), 5.85 (d, *J* = 7.2 Hz, 1 H), 5.19 (t, *J* = 6.8 Hz, 0.4 H), 4.53 (dd, *J* = 8.1, 8.4 Hz, 0.6 H), 4.02–3.92 (m, 1 H), 3.76–3.74 (m, 1 H), 3.62–3.51 (m, 2 H), 2.42 (s, 3 H), 2.40 (s, 3 H), 1.89–1.69 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.9, 143.2, 142.3, 140.1, 136.8, 129.3, 129.1, 126.5, 126.3, 85.9, 82.6, 67.1, 66.7, 56.9, 56.7, 33.8, 33.6, 26.1, 25.6, 21.4, 20.9.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{14}H_{20}ClN_2O_3S$: 331.0883; found: 331.0882.

***N*-[4,5-Bis(benzyloxy)-6-(benzyloxymethyl)-3-chlorotetrahydro-2*H*-pyran-2-yl]-*N*′-tosylacetimidamide (*cis*-5b)**
Yield (*cis*-**5b** + *trans*-**5b**): 102 mg (55%); R_f = 0.4 (EtOAc–hexanes, 1:1).

IR (neat): 3299, 2922, 1592, 1534, 1450, 1271, 1143, 1063, 911, 809, 736, 694, 546 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (mixture of tautomers) = 7.76 (d, *J* = 8.0 Hz, 0.4 H), 7.71 (d, *J* = 8.4 Hz, 1.3 H), 7.28–7.02 (m, 17 H), 5.97 (d, *J* = 8.8 Hz, 0.7 H), 5.26 (t, *J* = 8.4 Hz, 0.7 H), 4.91–4.84 (m, 1.2 H), 4.78–4.67 (m, 2.4 H), 4.56 (t, *J* = 8.4 Hz, 0.8 H), 4.51–4.44 (m, 2 H), 4.41–4.35 (m, 2.2 H), 3.79–3.70 (m, 0.8 H), 3.63–3.53 (m, 5.8 H), 3.49–3.41 (m, 1.3 H), 2.34 (s, 3 H), 2.32 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.9, 165.9, 143.3, 143.2, 142.4, 142.3, 140.0, 139.9, 137.7, 137.6, 137.2, 137.1, 129.8, 129.6, 129.4, 128.4, 128.4, 128.4, 128.3, 128.3, 128.0, 128.0, 127.9, 127.9, 127.9, 127.8, 127.8, 127.7, 127.6, 126.8, 126.6, 126.5, 126.3, 126.3, 80.7, 79.8, 78.5, 78.0, 76.5, 76.2, 75.0, 74.9, 73.9, 73.6, 73.5, 73.4, 73.4, 72.1, 68.4, 67.7, 57.6, 56.9, 21.4, 21.4, 21.3, 20.8.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{36}H_{40}ClN_2O_6S$: 663.2296; found: 663.2302.

***N*-[4,5-Bis(benzyloxy)-6-(benzyloxymethyl)-3-chlorotetrahydro-2*H*-pyran-2-yl]-*N*′-tosylacetimidamide (*trans*-5b)**
R_f = 0.3 (EtOAc–hexanes, 5:5).

IR (neat): 3296, 3035, 2869, 1592, 1535, 1449, 1275, 1214, 1144, 1062, 910, 809, 735, 694 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (mixture of tautomers) = 7.72–7.65 (m, 2 H), 7.33–7.11 (m, 17 H), 6.45 (d, *J* = 7.6 Hz, 0.4 H), 5.54 (t, *J* = 6.8 Hz, 0.6 H), 5.20 (dd, *J* = 7.6, 4.0 Hz, 0.6 H), 4.76–4.36 (m, 6 H), 4.29 (dd, *J* = 6.4, 3.2 Hz, 0.7 H), 4.07 (t, *J* = 4.4 Hz, 0.5 H), 3.92–3.80 (m, 2 H), 3.70–3.59 (m, 2 H), 3.54–3.51 (m, 0.6 H), 3.42 (t, *J* = 5.2 Hz, 0.8 H), 2.34 (s, 3 H), 2.32 (s, 3 H).

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{36}H_{39}ClN_2O_6SNa$: 685.2115; found: 685.2103.

***N*-(1-Chlorohexan-2-yl)-*N*′-tosylacetimidamide (6b)**
Yield: 213 mg (54%, based on chloramine-T; Reaction conditions: olefin/TfOH/chloramine-T = 2.0:2.0:1.0 (molar ratio), MeCN (4 mL/mmol of CT), r.t., 2 h]); R_f = 0.3 (EtOAc–hexanes, 3:7).

IR (neat): 3354, 2930, 2860, 1543, 1445, 1371, 1155, 665 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.65 (d, *J* = 8.4 Hz, 2 H), 7.22 (d, *J* = 8.0 Hz, 2 H), 6.02 (d, *J* = 8.4 Hz, 1 H), 3.90–3.82 (m, 1 H), 2.97–2.93 (m, 1 H), 2.89–2.82 (m, 1 H), 2.34 (s, 3 H), 1.88 (s, 3 H), 1.37–1.31 (m, 2 H), 1.22–1.12 (m, 4 H), 0.77 (t, *J* = 6.4 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.9, 143.4, 136.9, 129.7, 126.9, 49.0, 46.9, 31.7, 27.9, 23.3, 22.4, 21.5, 13.9.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{15}H_{24}ClN_2O_2S$: 331.1247; found: 331.1239.

***N*-(1-Chloro-3-phenylpropan-2-yl)-*N*′-tosylacetimidamide (7b)**
Yield: 323 mg (52%); R_f = 0.4 (EtOAc–hexanes, 4:6).

IR (neat): 3305, 3063, 2925, 1545, 1495, 1431, 1367, 1265, 1140, 1090, 1031, 1016, 831, 734, 697, 662 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ (mixture of tautomers) = 7.66 (d, *J* = 8.4 Hz, 2 H), 7.26–7.14 (m, 9 H), 7.04–7.02 (m, 2 H), 4.20–4.18 (m, 1 H), 3.75–3.69 (m, 1 H), 3.55 (dd, *J* = 11.4, 4.0 Hz, 0.5 H), 3.41 (dd, *J* = 11.2, 3.2 Hz, 2 H), 3.32–3.25 (m, 1 H), 2.95–2.81 (m, 3 H), 2.33 (s, 3 H), 2.31 (s, 3 H), 1.85 (s, 1.5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.0, 142.4, 140.3, 136.5, 129.3, 129.2, 128.9, 128.7, 128.6, 128.6, 127.1, 126.9, 126.3, 60.8, 50.6, 47.6, 46.7, 42.2, 37.4, 23.3, 21.5, 21.1.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{22}ClN_2O_2S$: 365.1091; found: 365.1091.

***N*-(2-Chloro-1,2,3,4-tetrahydronaphthalen-1-yl)-*N*′-tosylacetimidamide (8b)**
Yield: 40 mg (14%); R_f = 0.2 (EtOAc–hexanes, 3:7).

IR (neat): 3287, 3119, 2918, 2848, 1540, 1439, 1379, 1350, 1274, 1207, 1141, 1089, 1036, 909, 801, 749 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.79 (d, *J* = 8.4 Hz, 2 H), 7.28–7.12 (m, 6 H), 6.05 (d, *J* = 7.2 Hz, 1 H), 5.25 (dd, *J* = 7.0, 4.8 Hz, 1 H), 4.52 (q, *J* = 2.8 Hz, 1 H), 3.05–3.01 (m, 1 H), 2.85–2.76 (m, 1 H), 2.43 (s, 6 H), 2.25–2.15 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.5, 142.3, 140.3, 135.9, 131.8, 129.7, 129.2, 129.0, 128.4, 126.9, 126.3, 56.7, 56.2, 27.6, 25.1, 21.5, 21.3.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{19}H_{22}ClN_2O_2S$: 377.1091; found: 377.1095.

***N*-(2-Chloro-1,2,3,4-tetrahydronaphthalen-1-yl)-4-methylbenzenesulfonamide (8c)**
Yield: 151 mg (55%); R_f = 0.5 (EtOAc–hexanes, 3:7).

IR (neat): 3287, 3119, 2918, 2848, 1540, 1439, 1379, 1350, 1274, 1207, 1141, 1089, 1036, 909, 801, 749 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 8.0 Hz, 2 H), 7.32 (d, *J* = 8.0 Hz, 2 H), 7.10 (dt, *J* = 7.2, 0.8 Hz, 1 H), 7.01 (d, *J* = 7.6 Hz, 1 H), 6.95 (t, *J* = 7.6 Hz, 1 H), 6.44 (d, *J* = 7.6 Hz, 1 H), 4.66 (d, *J* = 5.6 Hz, 1 H), 4.50 (q, *J* = 2.8 Hz, 1 H), 4.30 (dd, *J* = 5.2, 3.2 Hz, 1 H), 2.98–2.93 (m, 1 H), 2.70–2.64 (m, 1 H), 2.42 (s, 3 H), 2.32–2.25 (m, 1 H), 2.04–2.00 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.1, 136.9, 135.9, 131.5, 129.9, 129.7, 129.2, 128.4, 127.4, 126.9, 58.4, 56.9, 24.7, 23.6, 21.6.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{17}H_{18}ClNNaO_2S$: 358.0644; found: 358.0646.

***N*-(3-Chlorochroman-4-yl)-*N*′-tosylacetimidamide (9b)**
Yield: 21 mg (15%); R_f = 0.2 (EtOAc–hexanes, 4:6).

IR (neat): 3292, 2922, 2857, 1655, 1535, 1482, 1452, 1377, 1266, 1148, 1090, 1034, 908, 813, 768 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.80 (d, *J* = 8.4 Hz, 2 H), 7.23–7.18 (m, 3 H), 7.12–7.09 (m, 1 H), 6.91 (dt, *J* = 7.6, 1.2 Hz, 1 H), 6.85 (d, *J* = 8.4 Hz, 1 H), 5.65 (d, *J* = 6.0 Hz, 1 H), 5.05 (dd, *J* = 6.4, 4.0 Hz, 1 H), 4.39 (dd, *J* = 6.4, 3.6 Hz, 1 H), 4.19–4.18 (m, 1 H), 2.43 (s, 3 H), 2.35 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.2, 153.6, 142.6, 139.9, 134.3, 130.3, 129.7, 129.3, 129.3, 126.5, 126.3, 121.9, 118.2, 117.3, 117.2, 68.7, 66.5, 66.0, 52.6, 52.3, 29.7, 21.5, 21.2.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{20}ClN_2O_3S$: 379.0883; found: 379.0879.

***N*-(3-Chlorochroman-4-yl)-4-methylbenzenesulfonamide (9c)**
Yield: 71 mg (60%); R_f = 0.4 (EtOAc–hexanes, 4:6).

IR (neat): 3268, 2923, 1590, 1487, 1457, 1409, 1336, 1260, 1225, 1208, 1156, 1091, 909, 866, 814, 730, 663 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 8.4 Hz, 2 H), 7.32 (d, *J* = 8.0 Hz, 2 H), 7.08 (dt, *J* = 7.8, 1.2 Hz, 1 H), 6.77 (d, *J* = 8.0 Hz, 1 H), 6.71 (t, *J* = 7.6 Hz, 1 H), 6.42 (dd, *J* = 8.0, 1.6 Hz, 1 H), 4.38–4.31 (m, 2 H), 4.22–4.17 (m, 2 H), 2.41 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.9, 143.9, 136.0, 129.9, 129.7, 129.5, 126.9, 121.3, 116.9, 116.6, 64.4, 54.1, 53.1, 21.2.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{16}H_{16}ClNNaO_3S$: 360.0437; found: 360.0444.

***N*-(2-Chloro-1-phenylethyl)-4-methylbenzenesulfonamide (10c)**
Yield: 226 mg (84%); R_f = 0.3 (EtOAc–hexanes, 3:7).

IR (neat): 3259, 1455, 1427, 1327, 1156 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.55 (d, *J* = 8.2 Hz, 2 H), 7.12–7.04 (m, 7 H), 5.34 (d, *J* = 6.6 Hz, 1 H), 4.50 (dd, *J* = 12.4, 6.1 Hz, 1 H), 3.64 (dd, *J* = 6.0, 2.3 Hz, 2 H), 2.31 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.6, 137.2, 136.9, 129.5, 128.7, 128.3, 127.2, 126.9, 58.4, 47.9, 21.5.

HRMS (ESI): *m*/*z* $[M + H + Na]^+$ calcd for $C_{15}H_{17}ClNNaO_2S$: 333.0566; found: 333.0566.

2-Methyl-1-tosyl-3a,4,5,6,7,7a-hexahydro-1*H*-benzimidazole (12)
To a stirred suspension of NaH (6 mg, 0.136 mmol) in anhyd DMF (2 mL) was added amidine **2b** (30 mg, 0.091 mmol) in anhyd DMF (2 × 1 mL) and the resultant mixture was stirred at r.t. for 5 h. The reaction mixture was quenched with ice-cold H_2O and extracted with EtOAc (2 × 10 mL). The combined organic layer was washed with H_2O (2 × 5 mL), brine (1 × 5 mL) and dried (Na_2SO_4). The organic layer was concentrated under reduced pressure and the crude product was purified by column chromatography over silica gel (EtOAc–hexanes gradient) to furnish the imidazoline derivative **12**.

Yield: 25 mg (94%); R_f = 0.4 (EtOAc–hexanes, 3:7).

IR (neat): 2934, 2861, 1647, 1597, 1443, 1349, 1257, 1161, 1096, 994, 940 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.66 (d, *J* = 8.4 Hz, 2 H), 7.25 (d, *J* = 8.0 Hz, 2 H), 3.98–3.95 (m, 1 H), 3.63–3.61 (m, 1 H), 2.36 (s, 3 H), 2.20 (d, *J* = 1.6 Hz, 3 H), 1.93–1.81 (m, 2 H), 1.62–1.44 (m, 3 H), 1.42–1.23 (m, 2 H), 1.19–1.13 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.0, 144.2, 137.3, 129.9, 126.9, 63.0, 60.8, 27.8, 26.8, 21.5, 19.9, 19.6, 17.4.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{15}H_{21}N_2O_2S$: 293.1324; found: 293.1322.

***N*-[*cis*-2-(Tosylamino)cyclohexyl]acetamide (12a)**

To a stirred solution of imidazoline derivative **12** (20 mg, 0.068 mmol) in THF (3 mL) was added 2 M HCl (1.5 mL) and the resultant mixture was stirred at r.t. for 2 h. The reaction mixture was extracted with EtOAc (2 × 5 mL). The combined organic layer was washed with H_2O (2 × 5 mL), brine (1 × 5 mL) and dried (Na_2SO_4). The organic layer was concentrated under reduced pressure and the crude product was purified by column chromatography over silica gel (EtOAc–hexanes gradient) to furnish the diamine derivative **12a**.

Yield: 19 mg (96%); R_f = 0.2 (EtOAc–hexanes, 4:6).

IR (neat): 3280, 2932, 1657, 1438, 1328, 1275, 1153 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.71 (d, *J* = 8.0 Hz, 2 H), 7.24 (d, *J* = 8.0 Hz, 2 H), 6.08 (br s, 1 H), 5.35 (br s, 1 H), 3.77 (br s, 1 H), 3.80–3.60 (m, 1 H), 2.36 (s, 3 H), 1.84 (s, 3 H), 1.70–1.50 (m, 2 H), 1.41–1.24 (m, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.1, 143.7, 136.9, 129.8, 127.1, 52.8, 49.4, 29.7, 27.6, 23.4, 23.3, 21.5, 19.9.

2-Methyl-1-tosyl-1,3a,5,6,7,7a-hexahydropyrano[2,3-*d*]imidazole (13)

To a stirred suspension of NaH (87 mg, 1.815 mmol) in anhyd DMF (7.5 mL) was added amidine **4b** (500 mg, 1.512 mmol) in anhyd DMF (6 mL) dropwise over a period of 10 min and the resultant mixture was stirred at r.t. for 5 h. The reaction mixture was quenched with ice-cold H_2O and extracted with EtOAc (2 × 20 mL). The combined organic layer was washed with H_2O (2 × 10 mL), brine solution (10 mL) and then dried (Na_2SO_4). The organic layer was concentrated under reduced pressure and the crude product was purified by column chromatography over silica gel (EtOAc–hexanes gradient) to furnish the imidazoline derivative **13**.

Yield: 379 mg (85%); R_f = 0.5 (EtOAc–hexanes, 4:6).

IR (neat): 3280, 2932, 1526, 1438, 1328, 1275, 1153 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.73 (d, *J* = 8.4 Hz, 2 H), 7.36 (d, *J* = 8.4 Hz, 2 H), 5.34 (dd, *J* = 7.6, 0.8 Hz, 1 H), 3.95–3.91 (m, 1 H), 3.72–3.68 (m, 2 H), 2.46 (s, 3 H), 2.37 (d, *J* = 1.2 Hz, 3 H), 2.09–2.02 (m, 2 H), 1.69–1.60 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.6, 144.8, 136.1, 130.2, 127.1, 91.3, 60.1, 58.1, 22.6, 21.6, 19.4, 18.6.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{14}H_{19}N_2O_3S$: 295.1116; found: 295.1126.

Supporting Information

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

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