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Intramolecular diamination and alkoxyamination of alkenes with *N*-sulfonyl ureas employing *N*-iodosuccinimide

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ABSTRACT

Reaction of *N*-δ-alkenyl-*N*′-sulfonyl urea **1** with *N*-iodosuccinimde (NIS; 2 equiv) and a catalytic amount of AgOTf (20 mol %) at room temperature led to intramolecular alkoxyamination to form bicyclic isourea **2a** in 95% isolated yield. In comparison, reaction of **1** with NIS and sodium bicarbonate (1 equiv) at room temperature led to isolation of bicyclic imidazolidin-2-one **2b** in 91% yield. These NIS-mediated alkoxyamination and diamination protocols were effective for a range of *N*-δ-alkenyl-*N*′-sulfonyl ureas to form the corresponding heterobicyclic compounds in good yield with high chemoselectivity and good to excellent diastereoselectivity.

1. Introduction

Vicinal diamines,[1] vicinal amino alcohols,[2] and related derivatives are component of a number of naturally occurring and biologically active molecules and find employment as synthetic intermediates, chiral ligands, and chiral auxiliaries. A particularly attractive route to the synthesis of vicinal diamines and amino alcohols is through the direct difunctionalization of alkenes. Early approaches to alkene difunctionalization by Backväll,[3] Barluenga,[4] Sharpless,[5] and others[6] employed stoichiometric amounts of a heavy metal complex or salt. The hydroxyamination of alkenes was subsequently rendered catalytic in osmium[7] and eventually, both catalytic and enantioselective.[8] There has been renewed interest in the direct difunctionalization of alkenes[9] and recent efforts in this area have led to the development of effective processes for the copper-mediated diamination of alkenes with sulfamides,[10,11] the Pd(II)-[12,13] or Ni(II)-catalyzed[14] diamination of alkenes with ureas, sulfamides, or guanidines in the presence of a stoichiometric oxidant, the palladium-catalyzed oxidative aminoacetoxylation of alkenes,[15] and the Pd(0)- or Cu(I)-catalyzed diamination of alkenes with di-*tert*-butyldiaziridinone and related reagents.[16]

A pair of recent reports have demonstrated that the difunctionalization of alkenes with *N*-sulfonyl ureas can be realized with hypervalent iodine or iodonium reagents in the absence of transition metal catalysts. Michael has reported the intramolecular alkoxyamination of alkenes with *N*-sulfonyl ureas mediated by PhI=O in the presence of a strong Lewis or Brønsted acid.[17] Similarly, Muñiz has reported the IPy_2BF_4-mediated diamination of alkenes with *N*-sulfonyl ureas to form bicyclic imidazolidin-2-one derivatives, although high reaction temperature (120 °C) was required to achieve optimal yield.[18] In the course of our investigation of a potential gold(I)-catalyzed route to the difunctionalization of alkenes with *N*-sulfonyl ureas, we instead discovered a pair of complementary procedures for the selective, room temperature intramolecular diamination and alkoxyamination of alkenes with *N*-sulfonyl ureas mediated by *N*-iodosuccinimide (NIS). Herein we provide an account of our results in this area.

2. Results and discussion

As part of our ongoing interest in the development of gold(I)-catalyzed processes for the hydroamination of unactivated alkenes,[19] we recently reported the room temperature intramolecular hydroamination of *N*-δ- and *N*-ε-alkenyl ureas catalyzed by a gold(I) *N*-heterocyclic carbene complex.[20] We noted with interest recent reports that described the utilization of *N*-iodosuccinimide (NIS) in conjunction with gold(I)-catalysis for the iodofunctionalization of alkynes and allenes.[21] On the basis of these precedents, we envisioned a gold(I)-catalyzed, NIS-mediated pathway for the oxidative difunctionalization of an *N*-δ-alkenyl urea involving electrophilic trapping of the initially formed gold alkyl species **I** with NIS to form the alkyl iodide **II** followed by intramolecular halide displacement by the pendant urea (Scheme 1).[22]

In apparent support of the pathway outlined in Scheme 1, reaction of 1-(2,2-diphenylpent-4-enyl)-3-tosylurea (**1**) with NIS (2 equiv) and a catalytic 1:1 mixture of (IPr)AuCl [IPr=1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidine] and AgOTf (5 mol %) in toluene for 24 h at room temperature led to isolation of isourea **2a** in

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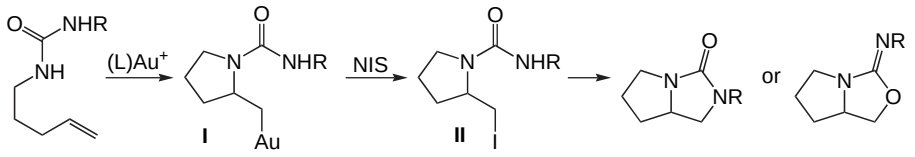
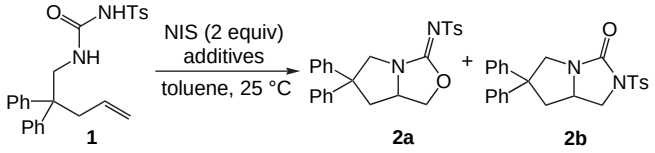


Scheme 1.

82% yield (Table 1, entry 1). However, subsequent control experiments revealed that silver, but not gold, was required for the efficient conversion of **1** to **2a**. In the absence of metal catalyst, reaction of **1** with NIS (2 equiv) at room temperature was sluggish (~30% conversion in 24 h) and formed bicyclic imidazolidin-2-one **2b** as the exclusive product (Table 1, entry 2). In contrast, treatment of **1** with NIS (2 equiv) and a catalytic amount of AgOTf (5 mol %) in toluene at room temperature for 14 h led to complete consumption of **1** with isolation of isourea **2a** in 95% yield as the exclusive (>98% of the crude reaction mixture) product (Table 1, entry 3). Silver presumably facilitates the initial C–N formation through activation of NIS[23] and facilitates C–O bond formation in preference to C–N bond formation in the second ring-closing step by enhancing the electrophilicity of an alkyl iodide intermediate analogous to **II**, leading to preferential attack by the hard oxygen nucleophile.[24]

Table 1
Effect of metal and additives on the reaction of **1** with NIS



Entry	Additive	Time (h)	**2a** (%)[a]	**2b** (%)[a]
1	(IPr)AuCl/AgOTf (5 mol %)	24	82	—
2	None	24	—	30
3	AgOTf (20 mol %)	14	95	—[b]
4	$NaHCO_3$ (1 equiv)	2	—[c]	91

[a] Isolated yield of >95% purity.
[b] Compound **2b** constituted <5% of the crude reaction mixture.
[c] Compound **2a** constituted <5% of the crude reaction mixture

The presence of a metal-free reaction pathway for the conversion of **1** to imidazolidin-2-one **2b** was, in retrospect, not surprising as C–N bond formation in the electrophilic cyclization of unsaturated carboxamide derivatives has been demonstrated.[25] One approach to the realization of selective C–N bond formation in these transformations is through employment of base in conjunction with an acidic carboxamide derivative such as an *N*-sulfonyl carboxamide.[26] We therefore considered that employment of a base in the reaction of **1** with NIS might facilitate the C–N bond forming processes in the conversion of **1** to **2b**. This was indeed found to be the case, and reaction of **1** with NIS in the presence of sodium bicarbonate (1 equiv) at room temperature for 2 h led to formation of a >95:5 mixture of **2b** and **2a**, from which **2b** was isolated in 91% yield (Table 1, entry 4).

Having identified efficient routes to the selective conversion of **1** to either **2a** or **2b**, we probed the scope and generality of the NIS-mediated intramolecular alkoxyamination and diamination of alkenes with *N*-tosylureas (Table 2). *N*-δ-Alkenyl ureas **3** and **4** that possessed *gem*-dialkyl substitution at the β-position of the alkenyl chain and the unsubstituted *N*-δ-alkenyl urea **5** underwent efficient intramolecular alkoxyamination and diamination to form the corresponding heterocycles **6**–**8** in >85% isolated yield (Table 2, entries 1–6). *N*-δ Alkenyl ureas **9**-**11** that possessed a single alkyl or phenyl group at the β-position of the alkenyl chain also underwent intramolecular alkoxyamination and diamination to form the corresponding heterocycles **12**–**14** in >70% isolated yield with up to 9:1 dr with predominant formation of the diastereomer possessing a trans arrangement of the exocyclic hydrocarbyl group and bridgehead hydrogen atom (Table 2, entries 7–12). *N*-δ-Alkenyl urea **15** that possessed a methyl substituent at the internal olefinic carbon atom underwent intramolecular alkoxyamination and diamination to form heterocycles **16** in good yield (Table 2, entries 13 and 14). *N*-δ-Alkenyl ureas **17** and **18** that possessed a methyl or phenyl substituent at the terminal olefinic carbon atom underwent intramolecular alkoxyamination to form heterocycles **19a** and **20a**, respectively in >70% yield with selective formation of the diastereomer possessing a cis arrangement of the exocyclic alkyl group and bridgehead hydrogen atom (Table 2, entries 15 and 16). *N*-δ-Alkenyl ureas **17** and **18** also underwent NIS-mediated diamination to form bicyclic imidazolidin-2-ones **19b** and **20b**, respectively, albeit with diminished yield and/or diastereoselectivity relative to alkoxyamination (Table 2, entries 17 and 18). The *N*-ω-alkenyl urea **21** underwent efficient NIS-mediated alkoxyamination to form isourea **22a** in 83% yield (Table 2, entry 19), but failed to undergo efficient diamination. In contrast, the *N*-allylaniline derived urea **23** underwent effective diamination to form imidazolidin-2-one **24b** in 82% yield (Table 2, entry 20), but failed to undergo effective alkoxyamination.

3. Summary

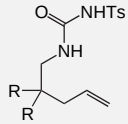
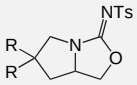
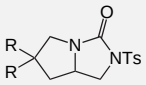
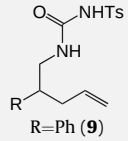
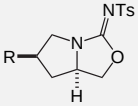
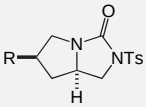
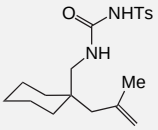
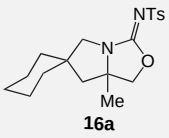
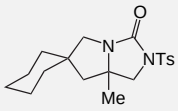
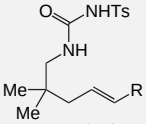
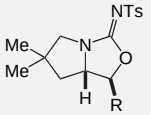
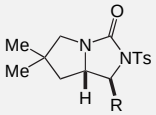
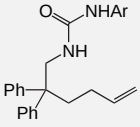
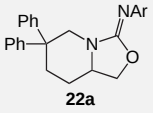
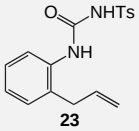
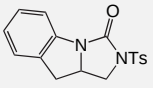
We have developed an effective method for the intramolecular diamination of *N*-alkenyl ureas with NIS catalyzed by AgOTf to form bicyclic imidazolidin-2-ones and for the intramolecular alkoxyamination of *N*-alkenyl urea with NIS in the presence of a sodium bicarbonate or triethylamine. These processes are characterized by high chemoselectivity, good yield and in many cases, excellent diastereoselectivity.

4. Experimental

4.1. General methods

Catalytic reactions were performed in sealed glass tubes under an atmosphere of dry nitrogen unless noted otherwise. NMR spectra were obtained on a Varian spectrometer operating at 400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR in $CDCl_3$ unless noted otherwise. IR spectra were obtained on a Bomen MB-100 FT IR spectrometer. Gas chromatography was performed on a Hewlett-Packard 5890 gas chromatograph equipped with a 25 m polydimethylsiloxane capillary column. Flash column chromatography was performed employing 200–400 mesh silica gel (EM). Thin layer chromatography (TLC) was performed on silica gel 60 F254. Elemental analyses were performed by Complete Analysis Laboratories (Parsippany, NJ). *p*-Toluenesulfonyl isocyanate (Acros) was used as received. Tosylureas **1**,[18] **3**–**5**,[18] **9**,[16] **15**,[18] **17**,[18] **18**,[18] and **23**[11] and *p*-nitrophenylurea **21**[27] were synthesized employing published procedures.

Table 2
Intramolecular alkoxyamination and diamination of γ- and δ-alkenyl ureas mediated by NIS (2 equiv) in toluene at 25 °C

Entry	Substrate	Additive[a]	Time (h)	Isourea product	Yield[b]	Urea product	Yield[b]
							
1	R=Me (**3**)	**A**	2	**6a**	94%		
2	R=–$(CH_2)_5$– (**4**)	**A**	2	**7a**	93%		
3	R=H (**5**)	**A**	3	**8a**	86%		
4	R=Me (**3**)	**B**	1			**4b**	97%
5	R=–$(CH_2)_5$– (**4**)	**C**	1			**7b**	85%
6	R=H (**5**)	**B**	3			**8b**	93%
							
7	R=Ph (**9**)	**A**	2	**12a**	72% (5:1)		
8	R=*i*-Pr (**10**)	**B**	3	**13a**	94% (9:1)		
9	R=Et (**11**)	**A**	2	**14a**	82% (4:1)		
10	R=Ph (**9**)	**B**	1			**12b**	92% (8:1)
11	R=*i*-Pr (**10**)	**A**	1			**13b**	88% (9:1)
12	R=Et (**11**)	**B**	2			**14b**	82% (5:1)
	 **15**			 **16a**			
13		**A**	1		95%		
14		**B**	1			**16b**	88%
							
15	R=Me (**17**)	**A**	24	**19a**	72% (>20:1)		
16	R=Ph (**18**)	**A**	3	**20a**	83% (>20:1)		
17	R=Me (**17**)	**B**	2			**19b**	84% (4.5:1)
18	R=Ph (**18**)	**B**	3			**20b**	69% (>20:1)
							
19	**21** (Ar = 4-$C_6H_4NO_2$)	**A**	24	**22a**	83%		
							
20	**23**	**B**	16			**24b**	82%

[a] Additives: **A**=AgOTf (20 mol %); **B**=$NaHCO_3$ (1 equiv); **C**=NEt_3 (1 equiv).
[b] Isolated yields of >95% purity. Diastereomeric purity shown in parentheses.

4.2. Synthesis of *N*-alkenyl ureas

*4.2.1. 1-(2-Isopropyl-4-pentenyl)-3-tosylurea (**10**).* *p*-Toluenesulfonyl isocyanate (0.21 mL, 1.4 mmol) was added to a solution of 2-isopropyl-4-pentenylamine[11] (0.3 g, 1.4 mmol) in CH_2Cl_2 (10 mL) at 0 °C and the resulting mixture was stirred overnight at room temperature. The solvent was evaporated under vacuum and the resulting oily residue was chromatographed to give **10** in 87% yield. TLC (hexanes–EtOAc=1:1): R_f=0.4. ^{1}H NMR: δ 9.57 (s, 1H), 7.75 (d, J=8.0 Hz, 2H), 7.27 (d, J=8.0 Hz, 2H), 6.53 (t, J=6.0 Hz, 1H), 5.69 (tdd, J=6.5, 10.5, 17 Hz, 1H), 5.03–4.98 (m, 2H), 3.17 (m, 2H), 2.41 (s, 3H), 2.08 (td, J=5.5, 14 Hz, 1H), 1.84 (td, J=8.0, 14 Hz, 1H), 1.59 (m, 1H), 1.38 (m, 1H), 0.845 (d, J=7.0 Hz, 3H), 0.843 (d, J=7.0 Hz, 3H). ^{13}C{^{1}H} NMR: δ 152.4, 144.6, 136.95, 136.92, 129.8, 126.9, 116.5, 44.0, 41.1, 33.4, 28.3, 21.6, 19.5, 19.1. IR (neat, cm^{-1}): 3343, 2958, 1656, 1553, 1464, 1346, 1163, 891, 664. Anal. calcd (found) for $C_{27}H_{28}N_2O$: H, 7.46 (7.43); C, 59.23 (59.25).

*4.2.2. 1-(2-Ethyl-4-pentenyl)-3-tosylurea (**11**).* Reaction of 2-ethyl-4-pentenylamine[28] with *p*-toluenesulfonyl isocyanate employing a procedure similar to that used to synthesize **10** gave **11** in 82% yield. TLC (hexanes–EtOAc=3:1): R_f=0.7. ^{1}H NMR: δ 9.54 (s, 1H), 7.76 (d, J=8.0 Hz, 2H), 7.24 (d, J=8.0 Hz, 2H), 6.51 (t, J=5.6 Hz, 1H), 5.66 (m, 1H), 4.98 (d, J=5.2 Hz, 1H), 4.95 (s, 1H), 3.12 (t, J=5.2 Hz,

1H), 2.38 (s, 3H), 1.94 (m, 2H), 1.48 (septet, J=6.8 Hz, 1H), 1.20 (pentet, J=6.8 Hz, 2H), 0.82 (t, J=7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR: δ 152.4, 144.4, 136.7, 135.9, 129.6, 126.9, 116.5, 42.6, 39.1, 35.5, 23.7, 21.4, 10.8. IR (neat, cm^{-1}): 3336, 3100, 1654, 1547, 1347, 1162, 1089, 893, 813, 664. Anal. calcd (found) for $C_{27}H_{28}N_2O$: H, 7.14 (7.21); C, 58.04 (58.05).

4.3. Synthesis of bicyclic isoureas

4.3.1. Compound ***2a***[17]. A suspension of **1** (43 mg, 0.10 mmol), NIS (45 mg, 0.20 mmol), and AgOTf (1.3 mg, 4.7×10^{-3} mmol) in toluene (1.0 mL) was stirred for 14 h at room temperature. The crude reaction mixture was loaded directly onto a silica gel column and chromatographed (hexanes–EtOAc=1:1) to give **2** (42 mg, 95%). TLC (hexanes–EtOAc=1:1): R_f=0.3. ^1H NMR: δ 7.85 (d, J=8.5 Hz, 2H), 7.32–7.14 (m, 12H), 4.70 (t, J=9.0 Hz, 1H), 4.35 (dd, J=7.0, 9.0 Hz, 1H), 4.31 (d, J=11.0 Hz, 1H), 4.16 (m, 1H), 3.90 (d, J=11.0 Hz, 1H), 2.59 (dd, J=5.0, 11.5 Hz, 1H), 2.41 (dd, J=10.0, 11.0 Hz, 1H), 2.40 (s, 3H). $^{13}C\{^1H\}$ NMR: δ 160.5, 144.9, 144.6, 142.5, 139.4, 129.2, 128.7, 128.6, 127.2, 127.1, 126.9, 126.7, 126.4, 73.3, 58.7, 58.2, 57.2, 43.1, 21.6.

Remaining bicyclic isoureas were synthesized employing procedures similar to that used to synthesize **2a**. The ^1H and ^{13}C NMR spectra of known compounds **6a**–**8a**,[17] **12a**,[18] **19a**,[18] and **20a**[18] were identical to reported spectra.

4.3.2. Compound ***13a***. TLC (hexanes–EtOAc=1:1): R_f=0.2. ^1H NMR: δ 7.77 (d, J=8.4 Hz, 2H), 7.17 (d, J=8.4 Hz, 2H), 4.58 (dd, J=8.0, 9.2 Hz, 1H), 4.26 (dd, J=5.2, 9.2 Hz, 1H), 4.01 (tdd, J=5.6, 8.0. 10.8 Hz, 1H), 3.33 (dd, J=8.8, 11.2 Hz, 1H), 3.18 (dd, J=8.8, 11.2 Hz, 1H), 2.33 (s, 3H), 2.12–2.02 (m, 2H), 1.48 (septet of doublets, J=6.4, 8.8 Hz, 1H), 1.12 (q, J=10.8 Hz, 1H), 0.82 (d, J=6.8 Hz, 3H). $^{13}C\{^1H\}$ NMR: δ 160.4, 142.4, 139.9, 129.1, 129.0, 127.03, 126.99, 72.9, 60.9, 60.8, 50.6, 49.4, 36.1, 32.4, 21.5, 21.2. IR (neat, cm^{-1}): 2956, 1596, 1426, 1277, 1147, 857, 682, 614. Anal. Calcd (found) for $C_{20}H_{22}N_4O_5S$: H, 6.88 (6.86); C, 59.60 (59.50).

4.3.3. Compound ***14a***. TLC (hexanes–EtOAc=1:1): R_f=0.3. ^1H NMR: δ 7.79 (d, J=8.0 Hz, 2H), 7.20 (d, J=8.0 Hz, 2H), 4.62 (t, J=9.2, 1H), 4.28 (dd, J=6.0, 9.2 Hz, 1H), 4.06 (m, 1H), 3.37 (dd, J=8.8, 10.8 Hz, 1H), 3.16 (dd, J=8.8, 10.8 Hz, 1H), 2.36 (s, 3H), 2.30 (m, 1H), 2.13 (td, J=5.6, 11.6 Hz, 1H), 1.38 (pentet, J=7.2 Hz, 2H), 1.11 (q, J=10.8 Hz, 1H), 0.86 (t, J=7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR: δ 160.5, 142.3, 139.8, 129.0, 126.9, 73.1, 60.6, 51.6, 43.4, 37.4, 26.8, 21.4, 12.5. IR (neat, cm^{-1}): 2961, 1585, 1440, 1284, 1152, 1080, 859, 823, 666, 613. Anal. Calcd (found) for $C_{20}H_{22}N_4O_5S$: H, 5.15 (4.96); C, 55.80 (55.67).

4.3.4. Compound ***16a***. TLC (hexanes–EtOAc=1:1): R_f=0.3. ^1H NMR: δ 7.79 (d, J=8.4 Hz, 2H), 7.20 (d, J=8.4 Hz, 2H), [4.29, 4.25, ABq, J=8.8 Hz, 2H], 3.77 (d, J=12.4 Hz, 1H), 2.81 (d, J=12.4 Hz, 1H), 2.36 (s, 3H), [1.67, 1.58, ABq, J=13.2 Hz, 2H], 1.47–1.27 (m, 8H), 1.32 (s, 3H), 1.15–1.03 (m, 2H). $^{13}C\{^1H\}$ NMR: δ 161.5, 142.2, 139.8, 128.9, 126.9, 81.1, 66.2, 56.4, 50.2, 45.9, 37.5, 36.5, 26.8, 25.3, 23.8, 22.9, 21.5. IR (neat, cm^{-1}): 2925, 1595, 1311, 1156, 816, 663. Anal. Calcd (found) for $C_{20}H_{22}N_4O_5S$: H, 5.15 (4.96); C, 55.80 (55.67).

4.3.5. Compound ***22a***. TLC (hexanes–EtOAc=3:1): R_f=0.6. ^1H NMR: δ 8.13 (d, J=8.0 Hz, 2H), 7.38 (d, J=8.0 Hz, 2H), 7.31–7.18 (m, 10H), 4.90 (br d, J=14.0, 1H), 4.56 (m, 1H), 3.79 (m, 2H), 3.05 (dd, J=1.2, 14.0 Hz, 1H), 2.75 (br d, J=13.6 Hz, 1H), 2.37 (dt, J=2.8, 13.6 Hz, 1H), 1.91 (qd, J=2.8, 13.2 Hz, 1H), 1.25 (br q, J=13 Hz, 1H). $^{13}C\{^1H\}$ NMR: δ 155.0, 152.6, 146.5, 143.8, 142.0, 128.6, 128.5, 127.7, 126.7, 126.5, 126.3, 124.7, 123.8, 71.5, 55.1, 50.0, 46.0, 33.8, 26.1. IR (neat, cm^{-1}): 1648, 1567, 1495, 1316, 1265, 1002, 859, 697. HRMS calcd (found) for $C_{25}H_{23}N_3O_3$ (M^+): 413.1739 (413.1756).

4.4. Syntheses of bicyclic ureas

4.4.1. Synthesis of compound ***2b***. A suspension of **1** (43 mg, 0.10 mmol), NIS (45 mg, 0.20 mmol), and $NaHCO_3$ (8.4 mg, 0.10 mmol) in toluene (1.0 mL) was stirred at room temperature for 2 h. The crude reaction mixture was loaded directly onto a silica gel column and chromatographed (SiO_2; hexanes–EtOAc=3:1) to give **2b** (40 mg, 91%). TLC (hexanes–EtOAc=3:1): R_f=0.4. ^1H NMR: δ 7.92 (d, J=8.0 Hz, 2H), 7.34 (d, J=8.0 Hz, 2H), 7.31–7.12 (m, 10H), 4.10–4.07 (m, 2H), 3.93 (tt, J=5.5, 10 Hz, 1H), 3.88 (d, J=11.5 Hz, 1H), 3.65 (dd, J=5.5, 9.5 Hz, 1H), 2.57 (dd, J=5.0, 11.5 Hz, 1H), 2.47 (s, 3H), 2.26 (dd, J=9.5, 12.0 Hz, 1H). $^{13}C\{^1H\}$ NMR: δ 156.3, 145.5, 145.3, 144.8, 135.0, 129.7, 128.6, 128.1, 126.8, 126.78, 126.5, 56.9, 56.2, 54.1, 48.0, 43.7, 21.7.

Remaining imidizolidin-2-ones were synthesized employing procedures similar to that used to synthesize **2b**. The ^1H and ^{13}C NMR spectra of known compounds **6b**–**8b**,[18] **16b**,[18] **19b**,[17] **20b**,[18] and **24b**[12] were identical to reported spectra.

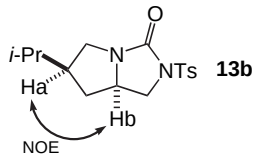
4.4.2. Compound ***12b***. TLC (hexanes–EtOAc=3:1): R_f=0.3. ^1H NMR: δ 7.92 (d, J=10.0 Hz, 2H), 7.32 (d, J=10.0 Hz, 2H), .26–7.17 (m, 3H), 7.06 (d, J=8.5 Hz, 1H), 4.02 (dd, J=10.0, 12.0 Hz, 1H), 3.90–3.81 (m, 2H), 3.53–3.44 (m, 3H), 2.42 (s, 3H), 2.34 (m, 1H), 1.47 (dd, J=13.0, 28.5 Hz, 1H). $^{13}C\{^1H\}$ NMR: δ 156.4, 144.9, 141.0, 135.1, 129.7, 128.7, 128.0, 127.0, 126.9, 56.4, 52.0, 46.9, 45.5, 40.1, 21.7. IR (neat, cm^{-1}): 2963, 1725, 1359, 1166, 1091, 759, 702, 662. Anal. Calcd (found) for $C_{20}H_{22}N_4O_5S$: H, 5.15 (4.96); C, 55.80 (55.67).

4.4.3. Compound ***13b***. TLC (hexanes–EtOAc=1:1): R_f=0.7. ^1H NMR: δ 7.84 (d, J=8.5 Hz, 2H), 7.25 (d, J=8.5 Hz, 2H), 3.90 (dd, J=9.0, 11.0 Hz, 1H), 3.66 (m, 2H), 3.10 (dd, J=3.0, 9.0 Hz, 2H), 2.36 (s, 3H), 1.92 (m, 2H), 1.36 (tdd, J=6.5, 9.0, 13.5 Hz, 1H), 0.95 (q, J=11.5 Hz, 1H), 0.78 (d, J=7.0 Hz, 6H). $^{13}C\{^1H\}$ NMR: δ 156.2, 144.7, 135.1, 129.6, 127.9, 56.1, 49.3, 47.9, 47.1, 36.2, 32.5, 21.6, 21.2, 21.1. IR (neat, cm^{-1}): 2964, 1726, 1387, 1356, 1168, 1095, 821, 662. Anal. Calcd (found) for $C_{13}H_{15}N_3O_3$: H, 6.88 (6.92); C, 59.60 (59.51).

4.4.4. Compound ***14b***. TLC (hexanes–EtOAc=3:1): R_f=0.7. ^1H NMR: δ 7.89 (d, J=8.0 Hz, 2H), 7.30 (d, J=8.0 Hz, 2H), 3.95 (dd, J=8.5, 9.5 Hz, 1H), 3.70 (m, 1H), 3.18 (dd, J=8.5, 11.5 Hz, 1H), 3.08 (dd, J=8.0, 11.5 Hz, 1H), 2.41 (s, 3H), 2.22–2.14 (m, 1H), 2.11–2.06 (m, 1H), 1.33 (m, 2H), 0.98 (q, J=10.5, 1H), 0.84 (t, J=8.0 Hz, 3H). $^{13}C\{^1H\}$ NMR: δ 156.4, 144.8, 135.1, 129.7, 128.0, 55.9, 50.4, 47.3, 42.1, 37.6, 27.1, 21.7, 12.6. IR (neat, cm^{-1}): 2962, 1726, 1358, 1165, 1092, 757, 662. Anal. Calcd (found) for $C_{20}H_{22}N_4O_5S$: H, 5.15 (4.96); C, 55.80 (55.67).

4.5. Assignment of product relative configuration

The relative configuration of **13b** was established by the presence of a strong cross peak relating tertiary proton H_a to bridgehead proton H_b in the ^1H–^1H NOESY spectrum. The relative configurations of compounds **12b**, **14b**, and **12a**–**14a** were assigned based on analogy to **13b**. The relative configurations of compounds **19a**, **19b**, **20a**, and **20b** were assigned from the published spectra.[17,18]



13b

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References and notes

1. Lucet, D.; Gall, T. L.; Mioskowski, C. *Angew. Chem.* **1998**, *110*, 2724; *Angew. Chem., Int. Ed.* **1998**, *37*, 2580.
2. Bergmeier, S. C. *Tetrahedron* **2000**, *56*, 2561.
3. Backväll, J.-E. *Tetrahedron Lett.* **1978**, *19*, 163.
4. (a) Aranda, V. G.; Barluenga, J.; Aznar, F. *Synthesis* **1974**, 504; (b) Barluenga, J.; Aznar, F.; de Mattos, M. C. S.; Kover, W. B.; Garcia-Granda, S.; Pérez-Carreño, E. *J. Org. Chem.* **1991**, *56*, 2930.
5. (a) Chong, A. O.; Oshima, K.; Sharpless, K. B. *J. Am. Chem. Soc.* **1977**, *99*, 3420; (b) Sharpless, K. B.; Patrick, D. W.; Truesdale, L. K.; Biller, S. A. *J. Am. Chem. Soc.* **1975**, *97*, 2305; (c) Patrick, D. W.; Truesdale, L. K.; Biller, S. A.; Sharpless, K. B. *J. Org. Chem.* **1978**, *43*, 2628.
6. Becker, P. N.; White, M. A.; Bergman, R. G. *J. Am. Chem. Soc.* **1980**, *102*, 5676.
7. Sharpless, K. B.; Chong, A. O.; Oshima, K. *J. Org. Chem.* **1976**, *41*, 177; (b) Herranz, E.; Biller, S. A.; Sharpless, K. B. *J. Am. Chem. Soc.* **1978**, *100*, 3596; (c) Herranz, E.; Sharpless, K. B. *J. Org. Chem.* **1978**, *43*, 2544.
8. (a) Li, G.; Chang, H.-T.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 451; (b) Li, G.; Angert, H. H.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2813; (c) Bodkin, J. A.; McLeod, M. D. *J. Chem. Soc., Perkin Trans. 1* **2002**, 2733; (d) Donohoe, T. J.; Johnson, P. D.; Pye, R. J. *Org. Biomol. Chem.* **2003**, *1*, 2025.
9. de Figueiredo, R. M. *Angew. Chem., Int. Ed.* **2009**, *48*, 1190.
10. Zabawa, T. P.; Kasi, D.; Chemler, S. R. *J. Am. Chem. Soc.* **2005**, *127*, 11250.
11. Zawaba, T. P.; Chelmer, S. R. *Org. Lett.* **2007**, *9*, 2035.
12. Streuff, J.; Hövelmann, C. H.; Nieger, M.; Muñiz, K. *J. Am. Chem. Soc.* **2005**, *127*, 14586.
13. (a) Bar, G. L. J.; Lloyd-Jones, G. C.; Booker-Milburn, K. I. *J. Am. Chem. Soc.* **2005**, *127*, 7308; (b) Muñiz, K.; Hövelmann, C. H.; Streuff, J. *J. Am. Chem. Soc.* **2008**, *130*, 763; (c) Muñiz, K.; Streuff, J.; Chávez, P.; Hövelmann, C. H. *Chem. Asian J.* **2008**, *3*, 1248; (d) Muñiz, K. *J. Am. Chem. Soc.* **2007**, *129*, 14542; (e) Hövelmann, C. H.; Streuff, J.; Brelot, L.; Muñiz, K. *Chem. Commun.* **2008**, 2334.
14. Muñiz, K.; Streuff, J.; Hövelmann, C. H.; Núñez, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 7125.
15. (a) Liu, G.; Stahl, S. S. *J. Am. Chem. Soc.* **2006**, *128*, 7179; (b) Alexanian, E. J.; Sorensen, E. J. *J. Am. Chem. Soc.* **2005**, *127*, 7690; (c) Desai, L. V.; Sanford, M. S. *Angew. Chem., Int. Ed.* **2007**, *46*, 5737.
16. (a) Du, H.; Zhao, B.; Shi, Y. *J. Am. Chem. Soc.* **2007**, *129*, 762; (b) Du, H.; Yuan, W.; Zhao, B.; Shi, Y. *J. Am. Chem. Soc.* **2007**, *129*, 11688; (c) Xu, L.; Du, H.; Shi, Y. *J. Org. Chem.* **2007**, *72*, 7038; (d) Xu, L.; Shi, Y. *J. Org. Chem.* **2008**, *73*, 749; (e) Zhao, B.; Du, H.; Shi, Y. *Org. Lett.* **2008**, *10*, 1087.
17. Cochran, B. M.; Michael, F. E. *Org. Lett.* **2008**, *10*, 5039.
18. Muñiz, K.; Hövelmann, C. H.; Campos-Gómez, E.; Barluenga, J.; González, J. M.; Streuff, J.; Nieger, M. *Chem. Asian J.* **2008**, *3*, 776–788.
19. (a) Han, X.; Widenhoefer, R. A. *Angew. Chem., Int. Ed.* **2006**, *45*, 1747; (b) Bender, C. F.; Widenhoefer, R. A. *Chem. Commun.* **2006**, 4143; (c) Bender, C. F.; Widenhoefer, R. A. *Chem. Commun* **2008**, 2741; (d) Zhang, Z.; Lee, S. D.; Widenhoefer, R. A. *J. Am. Chem. Soc.* **2009**, *131*, 5372.
20. Bender, C. F.; Widenhoefer, R. A. *Org. Lett.* **2006**, *8*, 5303.
21. (a) Buzas, A.; Gagosz, F. *Org. Lett.* **2006**, *8*, 515; (b) Buzas, A.; Istrate, F.; Gagosz, F. *Org. Lett.* **2006**, *8*, 1957; (c) Buzas, A.; Gagosz, F. *Synlett* **2006**, 2727; (d) Crone, B.; Kirsch, S. F. *J. Org. Chem.* **2007**, *72*, 5435; (e) Kirsch, S. F.; Binder, J. T.; Crone, B.; Duschek, A.; Haug, T. T.; Liébert, C.; Menz, H. *Angew. Chem., Int. Ed.* **2007**, *46*, 2310; (f) Yu, M.; Zhang, G.; Zhang, L. *Org. Lett.* **2007**, *9*, 2147; (g) Yu, M.; Zhang, G.; Zhang, L. *Tetrahedron* **2009**, *65*, 1846; (h) Menz, H.; Binder, J. T.; Crone, B.; Duschek, A.; Haug, T. T.; Kirsch, S. F.; Klahn, P.; Liébert, C. *Tetrahedron* **2009**, *65*, 1880; (i) Buzas, A.; Istrate, F.; Gagosz, F. *Tetrahedron* **2009**, *65*, 1889; (j) Poonoth, M.; Krause, N. *Adv. Synth. Catal.* **2009**, *351*, 117; (k) Gockel, B.; Krause, N. *Eur. J. Org. Chem.* **2010**, 311.
22. Muñiz has recently demonstrated the validity of such an approach employing iodosobenzene diacetate as the stoichiometric oxidant: Iglesias, A.; Muñiz, K. *Chem.—Eur. J.* **2009**, *15*, 10563.
23. (a) Komadsson, P.; Udodong, W. E.; Fraser-Reid, B. *Tetrahedron Lett.* **1990**, *31*, 4313; (b) Chang, G. X.; Lowary, T. L. *Org. Lett.* **2000**, *2*, 1505; (c) Ercegovic, T.; Meijer, A.; Magnusson, G.; Ellervik, U. *Org. Lett.* **2001**, *3*, 913; (d) Gadikota, R. R.; Callam, C. S.; Appelmelk, B. J.; Lowary, T. L. *J. Carbohyd. Chem.* **2003**, *22*, 149; (e) Han, J.; Gadikota, R. R.; McCarren, P. R.; Lowary, T. L. *Carbohydr. Res.* **2003**, *338*, 581.
24. Rudakov, E. S.; Kozhevnikov, I. V.; Zamashchikov, V. V. *Russ. Chem. Rev.* **1974**, *43*, 305.
25. Robin, S.; Rousseau, G. *Tetrahedron* **1998**, *54*, 13681.
26. (a) Fujita, M.; Kitagawa, O.; Suzuki, T.; Taguchi, T. *J. Org. Chem.* **1997**, *62*, 7330; (b) Kitagawa, O.; Fujita, M.; Li, M.; Taguchi, T. *Tetrahedron Lett.* **1997**, *38*, 615; (c) Biloski, A. J.; Wood, R. D.; Ganem, B. *J. Am. Chem. Soc.* **1982**, *104*, 3233; (d) Rajendra, G.; Miller, M. J. *Tetrahedron Lett.* **1985**, *26*, 5385; (e) Rajendra, G.; Miller, M. J. *J. Org. Chem.* **1987**, *52*, 4471; (f) Rajendra, G.; Miller, M. J. *Tetrahedron Lett.* **1987**, *28*, 6257; (g) Bertele, E.; Boos, H.; Dunitz, J. D.; Elsinger, F.; Eschenmoser, A.; Felner, I.; Gribi, H. P.; Gschwend, H.; Meyer, E. F.; Pesaro, M.; Scheffold, R. *Angew. Chem.* **1964**, *76*, 393; (h) Boeckman, R. K.; Connell, B. T. *J. Am. Chem. Soc.* **1995**, *117*, 12368.
27. Li, H.; Widenhoefer, R. A. *Org. Lett.* **2009**, *11*, 2671.
28. Keiji, T.; Akio, T.; Sakae, U. *J. Chem. Soc., Perkin Trans. 1* **1986**, *10*, 1837.