DOI: 10.1002/adsc.201000844

Gold(I)-Catalyzed Intramolecular Hydroamination of *N*-Allylic *N*′-Arylureas to form Imidazolidin-2-ones

Hao Li,[a] Feijie Song,[a] and Ross A. Widenhoefer[a,*]

[a] Duke University, French Family Science Center, 124 Science Drive, Durham, North Carolina 27708, USA
Fax: (+1)-919-660-1605; phone: (+1)-919-660-1533; e-mail: rwidenho@chem.duke.edu

Received: November 10, 2010; Revised: December 12, 2010; Published online: April 13, 2011

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201000844.

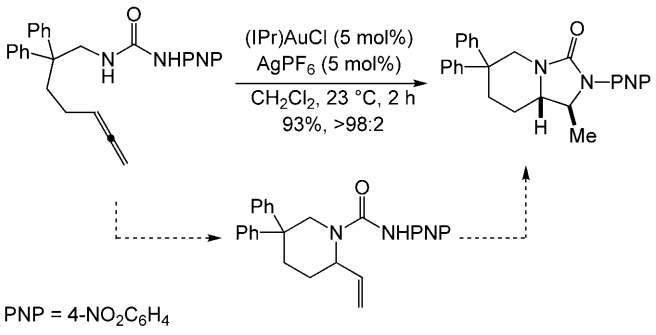
Abstract: Treatment of *N*-allylic *N*′-arylureas with a catalytic 1:1 mixture of di-*tert*-butyl-*o*-biphenylphoshphine gold(I) chloride and silver hexafluorophosphate (1 mol%) in chloroform at room temperature led to 5-*exo*-hydroamination to form the corresponding imidazolidin-2-ones in excellent yield. In the case of *N*-allylic ureas that possessed an allylic alkyl, benzyloxymethyl, or acetoxymethyl substituent, gold(I)-catalyzed 5-*exo*-hydroamination leads to formation of the corresponding *trans*-3,4-disubstituted imidazolidin-2-ones in excellent yield with $\geq$50:1 diastereoselectivity.

Keywords: alkenes; gold; intramolecular hydroamination; nitrogen heterocycles

Introduction

Substituted imidazolidin-2-ones are components of a number of biologically active compounds[1] including NK_1 and muscarinic M3 antagonists,[2,3] HIV protease and human enterovirus 71 inhibitors,[4,5] and antiparasitic[6] and immunosuppressive agents.[7] Furthermore, chiral, non-racemic imidazolidin-2-ones have been employed as chiral auxiliaries[8,9] and as scaffolds for bis(phosphine) ligands[10,11] for use in enantioselective synthesis. A number of approaches to construction of the imidazolidin-2-one ring have been developed[12–20] including carbonylation of vicinal diamines,[13] oxidative diamination of alkenes with ureas,[14,15] and electrophilic cyclization[16] or transition metal-catalyzed carboamination of *N*-allylic ureas.[17,18] In contrast, transition metal-catalyzed alkene hydroamination, which represents perhaps the most conceptually simple and atom-economical approach to the cyclization of readily available *N*-allylic ureas, has gone largely unexplored as a route to the imidazolidin-2-one ring.

In the course of our continuing investigation of the gold(I)-catalyzed intramolecular hydroamination of allenes,[21] we recently found that treatment of *N*-δ-allenylureas with a catalytic 1:1 mixture of the gold(I) N-heterocyclic carbene complex (IPr)AuCl [IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidine] and $AgPF_6$ (5 mol%) led to formation of bicyclic imidazolidin-2-ones in high yield and high diastereoselectivity (Scheme 1).[22] These transformations occurred *via* two discrete steps; initial 6-*exo*-hydroamination of the *N*-δ-allenylurea followed by 5-*exo*-hydroamination of the resulting 1-vinylpiperidine (Scheme 1). Whereas the former step is unremarkable, the latter step represents a rare example of imidazolidin-2-one ring formation *via* intramolecular alkene hydroamination under remarkably mild conditions.[23–25] We therefore considered that gold(I)-catalyzed intramolecular hydroamination of acyclic *N*-allylic ureas might serve as an expedient route to the synthesis of substituted, monocyclic imidazolidin-2-ones. Herein we report the results of this investigation.



Scheme 1. Gold(I)-catalyzed dihydroamination of an *N*-δ-allenylurea.

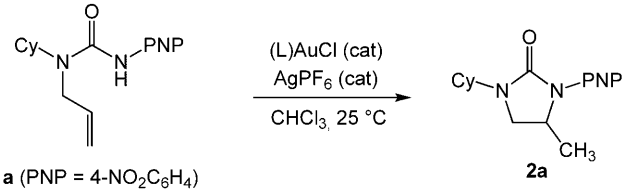
Results and Discussion

Optimization and Scope

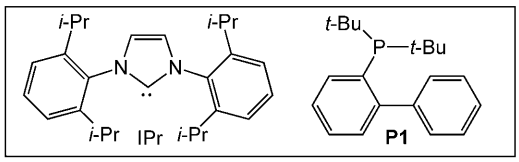
Our starting point for the gold(I)-catalyzed intramolecular hydroamination of acyclic *N*-allylic ureas employed the catalyst system used for the catalytic dihydroamination of *N*-δ-allenylureas with the substitution of chloroform for CH_2Cl_2 owing to the greater solubility of simple *N*-allylic ureas in the former solvent. In an initial experiment, treatment of *N*-allylurea **1a** with a catalytic 1:1 mixture of (IPr)AuCl (5 mol%) and $AgPF_6$ (5 mol%) in chloroform at room temperature for 12 h led to isolation of imidazolidin-2-one **2a** in 97% yield (Table 1, entry 1). The catalyst loading was lowered to 1 mol% without diminished yield, but with the anticipated increase in reaction time (Table 1, entries 2 and 3). Substitution of the sterically hindered phosphine ligand *o*-biphenyl-P(*t*-Bu)$_2$ (**P1**) for IPr led to a ~two-fold increase in reaction rate with no diminishment of product yield (Table 1, entry 4). The effectiveness of ligand **P1** in the conversion of **1a** to **2a** is surprising, given the marked superiority of IPr relative to **P1** in the gold-catalyzed dihydroamination of *N*-δ-allenylureas.[22] The possibility that intramolecular hydroamination of *N*-allylic ureas is catalyzed by Ag^+ or a Brønsted acid generated under the reaction conditions was rigorously ruled out in our investigation of allene dihydroamination.[22]

Acyclic *N*-allyl-*N*′-aryl ureas **1b–1f** that possessed either an electron-rich or electron-deficient *N*′-aryl group in combination with an *N*-alkyl or *N*-aryl substituent underwent gold(I)-catalyzed intramolecular hydroamination to form the corresponding imidazolidin-2-ones **2b–2f** in excellent yield (Table 2, entries 1–5). However, whereas the nature of the *N*′-aryl group had little effect on the rate of cyclization, *N*-methylureas **1b** and **1d** underwent intramolecular hydroamination at lower rates than those bearing an *N*-Cy (**1a** and **1f**) or *N*-Ph (**1c** and **1e**) group (Table 2). Acyclic *N*-allylic ureas that possessed an allylic methyl (**3a**), isopropyl (**3b**), benzyloxymethyl (**3c**), or acetoxymethyl (**3d**) substituent underwent gold(I)-catalyzed intramolecular hydroamination to form the corresponding *trans*-3,4-disubstituted imidazolidin-2-ones **4a–4d** in excellent yield with ≥50:1 diastereoselectivity (Table 2, entries 6–9). In comparison, gold(I)-catalyzed intramolecular hydroamination of *N*-allylic urea **5** that possessed an allylic hydroxymethyl group led to

Table 1. Effect of ligand and catalyst loading on the gold(I)-catalyzed conversion of **1a** to **2a**.



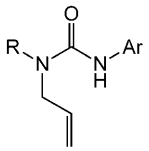
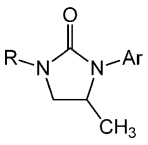
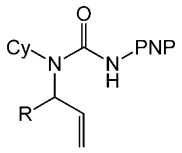
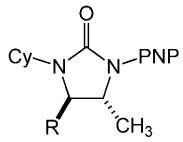
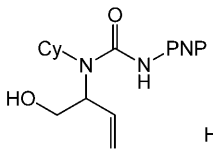
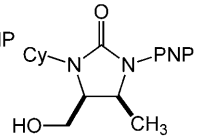
1a (PNP = 4-$NO_2C_6H_4$) **2a**



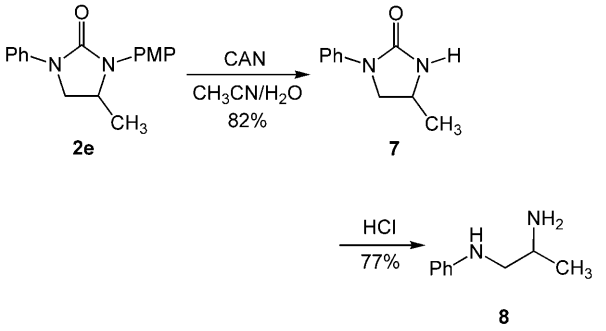
Entry	L	Cat. load [mol %]	Time [h]	Yield []%[a]
1	IPr	5	12	97
2	IPr	2	15	97
3	IPr	1	30	97
4	**P1**	1	15	100

[a] Isolated yields of >95% purity.

Table 2. Substrate scope of the intramolecular hydroamination of *N*-allylic ureas catalyzed by a 1:1 mixture of (**P1**)AuCl and $AgPF_6$ (1 mol%) in $CHCl_3$ at room temperature (PNP = 4-$NO_2C_6H_4$, PMP = 4-$MeOC_6H_4$).

Entry	Substrate	Product	Time [h]	Yield [%][a]	*dr*[b]
					
1[c]	**1b** (R = Me; Ar = PNP)	**2b**	48	92	–
2[d]	**1c** (R = Ph; Ar = PNP)	**2c**	15	93	–
3[e]	**1d** (R = Me; Ar = Ph)	**2d**	72	86	–
4	**1e** (R = Ph; Ar = PMP)	**2e**	16	97	–
5	**1f** (R = Cy; Ar = Ph)	**2f**	30	92	–
					
6	**3a** (R = Me)	**4a**	15	100	50:1
7	**3b** (R = *i*-Pr)	**4b**	16	93	50:1
8	**3c** (R = CH_2OBn)	**4c**	16	98	50:1
9	**3d** (R = CH_2OAc)	**4d**	16	98	50:1
					
10			16	97	3.7:1
	5	**6**			

[a] Isolated yields of >95% purity.
[b] Determined by ^{1}H NMR analysis of the crude reaction mixture.
[c] Catalyst loading = 5 mol%.
[d] Reaction temperature = 60 °C.
[e] Catalyst loading = 10 mol%.



Scheme 2. Dearylation and hydrolysis of imidazolidin-2-one **2e**.

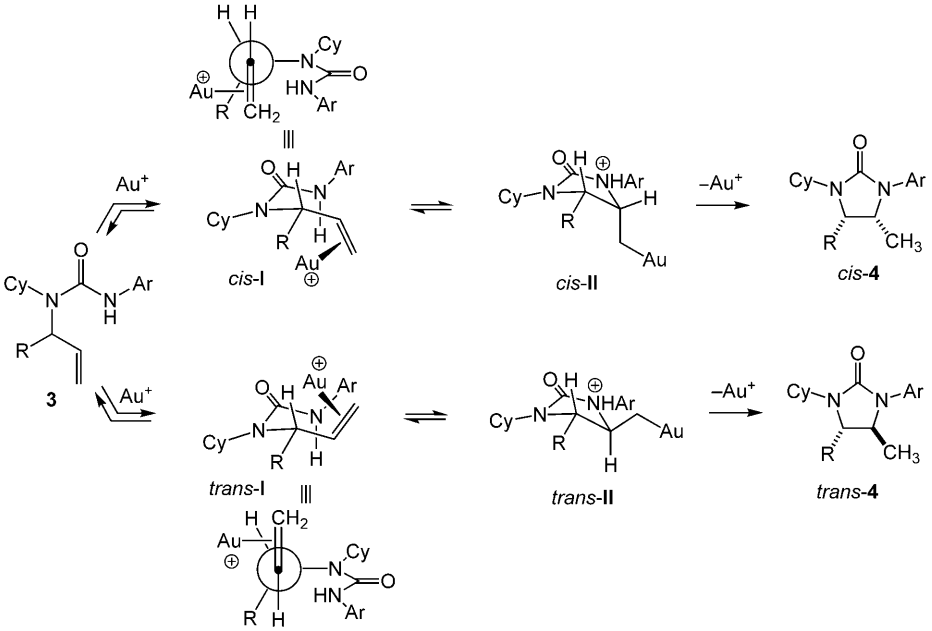
predominant ($dr = 3.7:1$) formation of the *cis*-imidazolidin-2-one **6** in 97% yield (Table 2, entry 10).

Imidazolidin-2-ones also serve as precursors to vicinal diamines and utilization of the *p*-methoxyphenyl (PMP) group allows for efficient dearylation to form primary amines. For example, oxidative removal of the PMP group of **2e** with ceric ammonium nitrate (CAN)[26] followed by acid-catalyzed hydrolysis[20,27] of N–H imidazolidine-2-one **7** led to isolation of the differentially substituted vicinal diamine **8** in 63% yield over two steps (Scheme 2).

Proposed Mechanism and Stereochemical Model

We have previously proposed a mechanism for the gold(I)-catalyzed intramolecular hydroamination of alkenes with carbamates that involves outer-sphere addition of the nucleophile on a cationic gold(I) π-alkene complex followed by protodeauration,[23] although little direct evidence supported this contention.[28] Since that time, we[29] and others[30] have synthesized and characterized cationic gold(I) π-alkene complexes and Toste has recently demonstrated the stoichiometric intramolecular aminoauration of *N*-γ-alkenylureas with $(PPh_3)AuNTf_2$ in the presenece of triethylamine.[31] Toste also demonstrated that treatment of these (β-amino)alkyl gold complexes with TsOH led to rapid reversion to regenerate the *N*-γ-alkenylureas, which was followed by slow protodeauration to form the 1-methylpyrrolidine.[31] Although protodeauration was slow, it appears reasonable that more electron-rich supporting ligands such as **P1** might facilitate protodemetallation.[32] In any event, these results both establish the outer-sphere aminoauration of alkenes with urea nucleophiles and also point to the potential reversibility of C–N bond formation.

From this discussion, it follows that the *trans*-configuration of 3,4-disubstituted imidazolidin-2-ones **4a**–**4d** may be determined either by C–N bond formation in the case of irreversible aminoauration or by protodeauration in the case of reversible aminoauration. In the case of irreversible C–N bond formation, aminoauration of gold (π-alkene) intermediate *trans*-**I** should be favored relative to aminoauration of *cis*-**I** owing to unfavorable interaction of both the alkenyl $=CH_2$ group ($A^{1,3}$ strain) and the coordinated gold atom with the allylic substituent that is absent in the case of *trans*-**I** (Scheme 3). In the case of reversible C–N bond formation, protodeauration from inter-



Scheme 3. Proposed mechanism and stereochemical model for the gold(I)-catalyzed cyclization of *N*-allylic ureas **3**.

mediate *trans*-**II** should be favored relative to protodeauration of *cis*-**II** owing to the unfavorable steric interaction between the exocyclic $-CH_2Au$(**P1**) group and the vicinal R group of *cis*-**II** that should be felt in the transition state for protodeauration from *cis*-**II** to form *cis*-**4** (Scheme 3).

Preferential formation of *cis*-**6** in the gold(I)-catalyzed cyclization of *N*-allylic urea **5** is enigmatic but may result from stabilizing ligation of the allylic hydroxy group to gold in the transition states for conversion of *cis*-**I** to *cis*-**II** and/or the conversion of *cis*-**II** to *cis*-**4** that overrides the inherent steric destabilization of these transition states. Alternatively, recent computational analyses have pointed to the potential role of solvent, and/or counterion in the transfer of proton from the protonated nucleophile to the α-carbon atom of the gold σ-complex generated *via* nucleophilic addition to a gold(I) π-complex.[33] As such, it also appears feasible that the pendant hydroxy group of **5**, either in protonated form or as part of hydrogen-bonded species, may function as an intramolecular proton source for the protodeauration of *cis*-**II** leading to preferential formation of *cis*-**6**.[34]

Conclusions

We have shown that a 1:1 mixture of (**P1**)AuCl [**P1**= *o*-biphenylP(*t*-Bu)$_2$] and $AgPF_6$ catalyzes the 5-*exo*-hydroamination of *N*-allylic *N*′-aryl ureas to form monocyclic imidazolidin-2-ones in excellent yield under mild conditions and with low catalyst loading. Furthermore, in the case of *N*-allylic ureas that possessed an allylic alkyl, benzyloxymethyl, or acetoxymethyl substituent, gold(I)-catalyzed 5-*exo*-hydroamination leads to formation of the corresponding *trans*-3,4-disubstituted imidazolidin-2-ones in $\geq$93% yield with $\geq$50:1 diastereoselectivity.

Experimental Section

General Remarks

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). *N*-Allylic ureas were synthesized employing standard procedures (see Supporting Information).

Typical Procedure for the Synthesis of 1-Cyclohexyl-4-methyl-3-(4-nitrophenyl)imidazolidin-2-one (2a)

A suspension of **1a** (30 mg, 0.10 mmol), (**P1**)AuCl (0.53 mg, 1.0×10^{-3} mmol), and $AgPF_6$ (0.25 mg, 1.0×10^{-3} mmol) in $CHCl_3$ (0.5 mL) was stirred for 15 h at room temperature. The crude reaction mixture was loaded directly onto a silica gel column and chromatographed (hexanes-EtOAc=6:1) to give **2a** as a yellow solid; yield: 30 mg (100%). TLC (hexanes-EtOAc=2:1): R_f=0.4; ^{1}H NMR: δ=8.14 (d, J=9.6 Hz, 2H), 7.66 (d, J=9.6 Hz, 2H), 4.36 (m, 1H), 3.79 (m, 1H), 3.63 (t, J=8.8 Hz, 1H), 3.04 (dd, J=4.0, 8.8 Hz, 1H), 1.80–1.64 (m, 5H), 1.42–1.22 (m, 4H), 1.32 (d, J=6.0 Hz, 3H), 1.08 (m, 1H); ^{13}C{^{1}H} NMR: δ=155.5, 145.3, 141.5, 124.8, 117.4, 51.4, 48.8, 45.1, 30.4, 29.8, 25.4, 25.3, 18.8; IR (neat): ν=2938, 1684, 1503, 1323, 1252, 1111, 851, 751, 690 cm^{-1}; anal. calcd (found) for $C_{16}H_{21}N_3O_3$: H 6.98 (6.83), C 63.35 (63.30).

Imidazolidin-2-ones **2b–2f**, **4a–4d**, and **6** were synthesized employing procedures similar to that used to synthesize **2a**.

1,4-Dimethyl-3-(4-nitrophenyl)imidazolidin-2-one (2b): Yellow solid; yield: 92%. TLC (hexanes-EtOAc=2:1): R_f=0.2; ^{1}H NMR: δ=8.11 (d, J=9.2 Hz, 2H), 7.62 (d, J=9.2 Hz, 2H), 4.34 (m, 1H), 3.61 (t, J=8.8 Hz, 1H), 3.06 (dd, J=3.6, 8.8 Hz, 1H), 2.85 (s, 3H), 1.31 (d, J=6.4 Hz, 3H); ^{13}C{^{1}H} NMR: δ=156.6, 145.1, 141.7, 124.8, 117.6, 51.5, 48.5, 30.8, 18.9; IR (neat): ν=2927, 1697, 1496, 1312, 1267, 1111, 845, 749, 690 cm^{-1}; anal. calcd. (found) for $C_{11}H_{13}N_3O_3$: H, 5.57 (5.47); C, 56.16 (56.22).

4-Methyl-3-(4-nitrophenyl)-1-phenylimidazolidin-2-one (2c): Yellow solid; yield: 93%. TLC (hexanes-EtOAc=3:1): R_f=0.4; ^{1}H NMR: δ=8.26 (d, J=9.0 Hz, 2H), 7.77 (d, J=9.5 Hz, 2H), 7.60 (br d, J=7.5 Hz, 2H), 7.42 (br t, J=7.5 Hz, 2H), 7.17 (br t, J=7.5 Hz, 1H), 4.59 (m, 1H), 4.21 (t, J=9.0 Hz, 1H), 3.61 (dd, J=4.5, 9.0 Hz, 1H), 1.50 (d, J=6.5 Hz, 3H). ^{13}C{^{1}H} NMR:=δ 153.9, 144.5, 142.5, 139.2, 129.0, 124.8, 123.8, 118.8, 118.5, 49.7, 48.3, 19.2; IR (neat): ν=2924, 1701, 1505, 1405, 1282, 1108, 754, 688 cm^{-1}; anal. calcd. (found) for $C_{16}H_{15}N_3O_3$: H 5.09 (4.98), C 64.64 (64.57).

1,4-Dimethyl-3-phenylimidazolidin-2-one (2d): Colorless oil; yield: 86%. TLC (hexanes-EtOAc=3:1): R_f=0.4; ^{1}H NMR: δ=7.40 (m, 2H), 7.31 (br d, J=7.6 Hz, 2H), 7.04 (br t, J=7.2 Hz, 1H), 4.28 (quintet of doublets, J=6.4 m 8.2 Hz, 1H), 3.56 (t, J=8.4 Hz, 1H), 3.01 (dd, J=6.0, 8.4 Hz, 1H), 2.84 (s, 3H), 1.25 (d, J=6.4 Hz, 3H); ^{13}C{^{1}H} NMR: δ=158.3, 138.8, 128.7, 123.3, 120.9, 52.2, 49.0, 31.0, 18.8; IR (neat): ν=2927, 1694, 1494, 1431, 1367, 1261, 756, 694 cm^{-1}; anal. calcd. (found) for $C_{11}H_{14}N_2O$: H 7.42 (7.29), C 69.45 (69.28).

3-(4-Methoxyphenyl)-4-methyl-1-phenylimidazolidin-2-one (2e): White solid; yield: 97%. TLC (hexanes-EtOAc=3:1): R_f=0.4; ^{1}H NMR: δ=7.58 (d, J=8.0 Hz, 2H), 7.34 (d, J=7.2 Hz, 2H), 7.30 (d, J=8.8 Hz, 2H), 7.04 (t, J=7.2 Hz, 1H), 6.91 (d, J=7.2 Hz, 2H), 4.27 (m, 1H), 4.00 (t, J=8.8 Hz, 1H), 3.78 (s, 3H), 3.46 (t, J=7.6 Hz, 1H), 1.28 (d, J=5.6 Hz, 3H); ^{13}C{^{1}H} NMR: δ=156.9, 155.8, 140.3, 130.9, 128.8, 124.8, 122.5, 117.7, 114.3, 55.5, 50.0, 19.3; IR (neat):

ν = 2979, 1688, 1501, 1401, 1241, 754, 688 cm^{-1}; anal. calcd. (found) for $C_{17}H_{18}N_2O_2$: H 6.43 (6.33), C 72.32 (72.15).

1-Cyclohexyl-4-methyl-3-phenylimidazolidin-2-one (2f): Colorless oil; yield: 92%. TLC (hexanes-EtOAc = 2:1): R_f = 0.4; ^{1}H NMR: δ = 7.42 (d, J = 8.0 Hz, 2H), 7.30 (t, J = 8.0 Hz, 2H), 7.02 (br t, J = 7.2 Hz, 1H), 4.27 (quintet of doublets, J = 6.0, 8.8 Hz, 1H), 3.78 (m, 1H), 3.56 (t, J = 8.8 Hz, 1H), 2.98 (dd, J = 5.6, 8.4 Hz, 1H), 1.80–1.64 (m, 5H), 1.43–1.21 (m, 4H), 1.25 (d, J = 6.0 Hz, 3H), 1.08 (m, 1H); ^{13}C{^{1}H} NMR: δ = 157.2, 139.1, 128.7, 123.0, 120.1, 51.2, 49.3, 45.5, 30.3, 30.1, 25.6, 18.9; IR (neat): ν = 2930, 1691, 1419, 1255, 755, 694 cm^{-1}; anal. calcd. (found) for $C_{16}H_{22}N_2O$: H 8.58 (8.60), C 74.38 (74.43).

***trans*-1-Cyclohexyl-4,5-dimethyl-3-(4-nitrophenyl)imidazolidin-2-one (4a):** Yellow solid; yield: 100%. TLC (hexanes-EtOAc = 3:1): R_f = 0.6; ^{1}H NMR: δ = 8.14 (d, J = 9.6 Hz, 2H), 7.67 (d, J = 9.2 Hz, 2H), 3.82 (dq, J = 2.8, 6.0 Hz, 1H), 3.62 (tt, J = 3.6, 12.0 Hz, 1H), 3.35 (dq, J = 2.4, 6.0 Hz, 1H), 1.92–1.05 (m, 10H), 1.29 (d, J = 6.0 Hz, 3H), 1.28 (d, J = 6.0 Hz, 3H); ^{13}C{^{1}H} NMR: δ = 154.9, 145.7, 141.4, 124.8, 117.0, 57.4, 54.5, 53.2, 32.2, 30.6, 25.9, 25.8, 25.4, 21.8, 18.2; IR (neat): ν = 2932, 1645, 1491, 1328, 1302, 1238, 1110, 750, 702, 639 cm^{-1}; anal. calcd. (found) for $C_{17}H_{23}N_3O_3$: H 7.30 (7.41), C 64.33 (64.32).

***trans*-1-Cyclohexyl-5-isopropyl-4-methyl-3-(4-nitrophenyl)imidazolidin-2-one (4b):** Yellow solid; yield: 93%. TLC (hexanes-EtOAc = 3:1): R_f = 0.6; ^{1}H NMR: δ = 8.14 (d, J = 9.2 Hz, 2H), 7.72 (d, J = 9.2 Hz, 2H), 3.96 (br q, J = 6.0 Hz, 1H), 3.55 (m, 1H), 3.16 (m, 1H), 2.03–1.08 (m, 10H), 1.28 (d, J = 6.0 Hz, 3H), 0.95 (d, J = 6.8 Hz, 3H), 0.75 (d, J = 6.4 Hz, 3H); ^{13}C{^{1}H} NMR: δ = 155.2, 145.4, 141.2, 125.1, 116.2, 64.2, 54.0, 49.7, 31.9, 30.7, 30.4, 26.0, 25.4, 20.2, 17.9, 14.3; IR (neat): ν = 2935, 1698, 1495, 1297, 1246, 1107, 854, 754, 692 cm^{-1}; anal. calcd- (found) for $C_{19}H_{27}N_3O_3$: H 7.88 (7.95), C 66.06 (65.98).

***trans*-4-(Benzyloxymethyl)-3-cyclohexyl-5-methyl-1-(4-nitrophenyl)imidazolidin-2-one (4c):** Yellow oil; yield: 98%. TLC (hexanes-EtOAc = 3:1): R_f = 0.5; ^{1}H NMR: δ = 8.08 (d, J = 9.2 Hz, 2H), 7.62 (d, J = 9.2 Hz, 2H), 7.28–7.19 (m, 5H), 4.45 (s, 2H), 4.13 (dq, J = 0.8, 6.0 Hz, 1H), 3.58 (tt, J = 3.6, 12.0 Hz, 1H), 3.50 (m, 1H), 3.33 (m, 1H), 1.82–1.47 (m, 6H), 1.35–1.18 (m, 3H), 1.23 (d, J = 6.4 Hz, 3H), 1.03 (tq, J = 3.2, 12.8 Hz, 1H); ^{13}C{^{1}H} NMR: δ = 155.2, 145.5, 141.3, 137.3, 128.4, 127.9, 127.7, 124.9, 116.6, 73.4, 70.8, 57.9, 53.3, 53.2, 32.1, 30.5, 25.8, 25.7, 25.3, 18.7; IR (neat): ν = 2931, 1701, 1503, 1321, 1234, 849, 751, 697 cm^{-1}; anal. calcd. (found) for $C_{24}H_{29}N_3O_4$: H 6.90 (6.92), C 68.06 (67.95).

***trans*-(3-Cyclohexyl-5-methyl-1-(4-nitrophenyl)-2-oxoimidazolidin-4-yl)methyl acetate (4d):** Yellow solid; yield: 98%. TLC (hexanes-EtOAc = 3:1): R_f = 0.4; ^{1}H NMR: δ = 8.14 (d, J = 9.2 Hz, 2H), 7.69 (d, J = 9.2 Hz, 2H), 4.26 (dd, J = 3.6, 11.6 Hz, 1H), 4.16 (dq, J = 1.6, 6.0 Hz, 1H), 3.91 (dd, J = 7.2, 11.6 Hz, 1H), 3.67 (tt, J = 3.6, 12.0 Hz, 1H), 3.45 (ddd, J = 1.6, 3.6, 7.2 Hz, 1H), 2.00 (s, 3H), 1.93–1.54 (m, 6H), 1.47–1.26 (m, 3H), 1.31 (d, J = 6.0 Hz, 3H), 1.11 (tq, J = 3.6, 12.8 Hz, 1H); ^{13}C{^{1}H} NMR: δ = 170.6, 155.1, 145.2, 141.6, 125.0, 116.7, 64.4, 56.8, 53.4, 53.3, 32.2, 30.6, 25.8, 25.7, 25.3, 20.7, 18.8. IR (neat, cm^{-1}): 2930, 1706, 1503, 1324, 1219, 1040, 858, 752, 693 cm^{-1}; Anal. calcd (found) for $C_{19}H_{25}N_3O_5$: H, 6.71 (6.62); C, 60.79 (60.64).

***cis*-1-Cyclohexyl-5-(hydroxymethyl)-4-methyl-3-(4-nitrophenyl)imidazolidin-2-one (6):** Yellow oil; yield: 97% (*cis*:-*trans* = 3.7:1). TLC (hexanes-EtOAc = 1:1): R_f = 0.45. ^{1}H NMR: δ = [8.15 (d, J = 9.2 Hz), 8.12 (d, J = 9.6 Hz), (3.7:1), 2H], [7.70 (d, J = 9.2 Hz), 7.56 (d, J = 9.2 Hz), (1:3.7), 2H)], [4.45 (quintet, J = 6.9), 4.31 (dq J = 2.0, 6.4 Hz), (3.7:1), 1H)], [3.97 (m), 3.34 (m), (3.7:1), 1 H], [3.90–3.80 (m), 3.73 (m), (3.7:1), 2H] 3.61 (tt, J = 4.0, 12 Hz, 1H), [2.35 (t, J = 4.5 Hz), 2.18 (t, J = 4.8 Hz), (1:3.7), 1H], 1.87–1.46 (m, 6H), 1.41–1.20 (m, 3H), [1.33 (d, J = 6.4 Hz), 1.31 (d, J = 6.4 Hz), (3.7:1), 3H], 1.11 (tq, J = 3.6, 12.8 Hz, 1H); ^{13}C{^{1}H} NMR: δ = [157.1, 155.7, (3.7:1)], [145.4, 144.8, (1:3.7)], [142.1, 141.4, (3.7:1)], [124.9, 124.6 (1:3.7)], [119.3, 117.0, (3.7:1)] [63.1, 60.3, (1:3.7)], [59.6, 56.3, (1:3.7)], [53.9, 53.3 (3.7:1)], [52.6, 52.0 (1:3.7)], [32.4, 31.6 (1:3.7)], [30.6, 29.9 (1:3.7)], [26.0, 25.3 (3.7:1)], [18.9, 12.3 (1:3.7)]; IR (neat): ν = 2932, 1684, 1503, 1320, 1248, 1112, 850, 729, 694 cm^{-1}; HR-MS: m/z = 333.1676, calcd. for $C_{17}H_{23}N_3O_4$ (M^+): 333.1689.

Relative Configurations of 4,5-Disubstituted Imidazolidin-2-ones

The *trans* configuration of 4,5-disubstituted imidazolidin-2-ones **4a**–**4d** was assigned on the basis of the vicinal H-4/H-5 coupling constants, which ranged from $^3J_{H,H} \approx 1$ Hz for **4b** and **4c** to $^3J_{H,H}$ = 2.4 Hz for **4a**. Published values for the vicinal H-4/H-5 coupling constant of *trans*-4,5-disubstituted imidazolidin-2-ones range from 0–3 Hz,[9] while the the vicinal H-4/H-5 coupling constant of *cis*-4,5-disubstituted imidazolidin-2-ones range from 7–9 Hz.[11,15,18] In the same way, the *cis* and *trans* configurations of the major and minor diastereomers of **6** were assigned on the basis of the vicinal H-4/H-5 coupling constants of $^3J_{H,H} \approx 7$ Hz (major) and $^3J_{H,H} \approx 2$ Hz (minor).

N-(2-Aminopropyl)benzenamine (8)[34]

A solution of **2e** (50 mg, 0.18 mmol) in CH_3CN (2 mL) at 0 °C was treated with a solution of ceric ammonium nitrate (CAN, 0.29 g, 0.53 mmol) in water (2.5 mL) over 3 min. The solution was stirred for 25 min at 0 °C, diluted with water (10 mL), and extracted with EtOAc (3 × 10 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated under vacuum to give an oily residue that was chromatographed (EtOAc-hexanes = 2:1) to give 4-methyl-1-phenylimidazolidin-2-one (**7**)[19] as white solid; yield: 26 mg (82%).

A solution of **7** (26 mg, 0.15 mmol) in concentrated HCl (4 mL) was refluxed for 30 h and then extracted with CH_2Cl_2 (3 × 10 mL). The aqueous layer was made basic ($_pH \geq 12$) with 15% NaOH and then extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated under vacuum to give pure **8** as a colorless oil; yield: 16 mg (77%). The ^{1}H and ^{13}C NMR spectra of **7** and **8** were identical with published data.[19,34]

Acknowledgements

Acknowledgements is made to the NIH (GM-080422) for support of this research and to the NCBC (2008-IDG-1010) for support of the Duke University NMR facility.

References

[1] a) C. W. Lee, D. H. Hong, S. B. Han, S.-H. Jung, H. C. Kim, R. L. Fine, S.-H. Lee, H. M. Kim, *Biochem. Pharmacol.* **2002**, *64*, 473–480; b) N. J. Thomas, J. A. Carcillo, W. A. Herzer, Z. Mi, S. P. Tofovic, E. K. Jackson, *Eur. J. Pharmacol.* **2003**, *465*, 133–139; c) D. M. Rotstein, S. D. Gabriel, N. Manser, L. Filonova, F. Padilla, S. Sankuratri, C. Ji, A. deRosier, M. Dioszegi, G. Heilek, A. Jekle, P. Weller, P. Berry, *Bioorg. Med. Chem. Lett.* **2010**, *20*, 3219–3222; d) B. Jiang, J.-F. Liu, S.-Y. Zhao *J. Org. Chem.* **2003**, *68*, 2376–2384; e) F. Heidempergher, A. Pillan, V. Pinciroli, F. Vaghi, C. Arrigoni, G. Bolis, C. Caccia, L. Dho, R. McArthur, M. Varasi, *J. Med. Chem.* **1997**, *40*, 3369–3380; f) H. Eum, Y. Lee, S. Kim, A. Baek, M. Son, K. W. Lee, S. W. Ko, S. Kim, S. Y. Yun, W. K. Lee, H.-J. Ha, *Bull. Korean Chem. Soc.* **2010**, *31*, 611–614.

[2] a) H.-J. Shue, X. Chen, J. H. Schwerdt, S. Paliwal, D. J. Blythin, L. Lin, D. Gu, C. Wang, G. A. Reichard, H. Wang, J. J. Piwinski, R. A. Duffy, J. E. Lachowicz, V. L. Coffin, A. A. Nomeir, C. A. Morgan, G. B. Varty, N.-Y. Shih, *Bioorg. Med. Chem. Lett.* **2006**, *16*, 1065–1069; b) H.-J. Shue, X. Chen, N.-Y. Shih, D. J. Blythin, S. Paliwal, L. Lin, D. Gu, J. H. Schwerdt, S. Shah, G. A. Reichard, J. J. Piwinski, R. A. Duffy, J. E. Lachowicz, V. L. Coffin, F. Liu, A. A. Nomeir, C. A. Morgan, G. B. Varty, *Bioorg. Med. Chem. Lett.* **2005**, *15*, 3896–3899; c) G. A. Reichard, C. Stengone, S. Paliwal, I. Mergelsberg, S. Majmundar, C. Wang, R. Tiberi, A. T. McPhail, J. J. Piwinkski, N.-Y. Shih, *Org. Lett.* **2003**, *5*, 4249–4251.

[3] a) I. Peretto, C. Fossati, G. A. M. Giardina, A. Giardini, M. Guala, E. La Porta, P. Petrillo, S. Radaelli, L. Radice, L. F. Raveglia, E. Santoro, R. Scudellaro, F. Scarpitta, A. Cerri, S. Menegon, G. M. Dondio, A. Rizzi, E. Armani, G. Amari, M. Civelli, G. Villetti, R. Patacchini, M. Bergamaschi, F. Bassani, M. Delcanale, B. P. Imbimbo, *J. Med. Chem.* **2007**, *50*, 1693–1697; b) I. Peretto, R. Forlani, C. Fossati, G. A. M. Giardina, A. Giardini, M. Guala, E. La Porta, P. Petrillo, S. Radaelli, L. Radice, L. F. Raveglia, E. Santoro, R. Scudellaro, F. Scarpitta, C. Bigogno, P. Misiano, G. M. Dondio, A. Rizzi, E. Armani, G. Amari, M. Civelli, G. Villetti, R. Patacchini, M. Bergamaschi, M. Delcanale, C. Salcedo, A. G. Fernández, B. P. Imbimbo, *J. Med. Chem.* **2007**, *50*, 1571–1583; c) I. Peretto, P. Petrillo, B. P. Imbimbo, *Med. Res. Rev.* **2009**, *29*, 867–902.

[4] a) W. M. Kazmierski, E. Furfine, Y. Gray-Nunez, A. Spaltenstein, L. Wright, *Bioorg. Med. Chem. Lett.* **2004**, *14*, 5685–5687; b) E. De Clerq, *Biochim. Biophys. Acta* **2002**, *1587*, 258–275; c) W. M. Kazmierski, F. G. Salituro, R. D. Tung, L. L. Wright, *Bioorg. Med. Chem. Lett.* **2000**, *10*, 1159–1162; d) A. Spaltenstein, M. R. Almond, W. J. Bock, D. G. Cleary, E. S. Furfine, R. J. Hazen, W. M. Kazmierski, F. G. Salituro, R. D. Tung, L. L. Wright, *Bioorg. Med. Chem. Lett.* **2000**, *10*, 1159–1162; e) F. G. Salituro, C. T. Baker, J. J. Court, D. D. Deininger, E. E. Kim, B. Li, P. M. Novak, B. G. Rao, S. Pazhanisamy, M. D. Porter, W. C. Schairer, R. D. Tung, *Bioorg. Med. Chem. Lett.* **1998**, *8*, 3637–3642; f) G. V. De Lucca, P. Y. S. Lam, *Drugs Future* **1998**, *23*, 987–994.

[5] a) J.-H. Chern, C.-S. Chang, C.-L. Tai, Y.-C. Lee, C.-C. Lee, I.-J. Kang, C.-Y. Lee, S.-R. Shih, *Bioorg. Med. Chem. Lett.* **2005**, *15*, 4206–4211; b) K.-S. Shia, W.-T. Li, C.-M. Chang, M.-C. Hsu, J.-H. Chern, M. K. Leong, S.-N. Tseng, C.-C. Lee, Y.-C. Lee, S.-J. Chen, K.-C. Peng, H.-Y. Tseng, Y.-L. Chang, C.-L. Tai, S.-R. Shih, *J. Med. Chem.* **2002**, *45*, 1644–1655.

[6] a) J. K. de A. L. Neves, S. P. S. Botelho, C. M. L. de Melo, V. R. A. Pereira, M. do C. A. de Lima, I. da R. Pitta, M. C. P. de A. Albuquerque, S. L. Galdino, *Parasitol. Res.* **2010**, *107*, 531–538; b) J.-M. H. Robert, C. Sabourin, N. Alvarez, S. Robert-Piessard, G. Le Baut, P. Le Pape, *Eur. J. Med. Chem.* **2003**, *38*, 711–718; c) N. Alvarez, S. Robledo, I. D. Velez, J. M. Robert, G. Le Baut, P. Le Pape, *J. Enzyme Inhib. Med. Chem.* **2002**, *17*, 443–447.

[7] a) C. Sabourin, J.-M. H. Robert, *J. Enzyme Inhib. Med. Chem.* **2008**, *23*, 659–667; b) C. Sabourin, J.-M. H. Robert, S. Robert-Piessard, D. Carbonnelle, F. Lang, *J. Enzyme Inhib. Med. Chem.* **2004**, *19*, 459–465.

[8] a) D. Lucet, T. Le Gall, C. Mioskowski *Angew. Chem.* **1998**, *110*, 2724–2772; *Angew. Chem. Int. Ed.* **1998**, *37*, 2580–2627; b) G. Guillena, C. Nájera, *Tetrahedron: Asymmetry* **1998**, *9*, 1125–1129; c) M. Parisi, A. Solo, W. D. Wulff, I. A. Guzei, A. L. Rheingold, *Organometallics* **1998**, *17*, 3696–3700; d) W. D. Wulff *Organometallics* **1998**, *17*, 3116–3134; e) C. Palomo, M. Oiarbide, A. González, J. M. García, F. Berrée *Tetrahedron Lett.* **1996**, *37*, 4565–4568; f) H. Kubota, A. Kubo, M. Takahashi, R. Shimizu, T. Da-te, K. Okamura, K.-i. Nunami, *J. Org. Chem.* **1995**, *60*, 6776–6784; g) S. C. Davies, G. B. Evans, A. A. Mortlock *Tetrahedron: Asymmetry* **1994**, *5*, 585–606; h) T. Taguchi, A. Shibuya, H. Sasaki J.-i. Endo, T. Morikawa, M. Shirob, *Tetrahedron: Asymmetry* **1994**, *5*, 1423–1426; i) W. Sankhavasi, M. Yamamoto, S. Kohmoto, K. Yamada, *Bull. Chem. Soc. Jpn.* **1991**, *64*, 1425–1427; j) G. Cardillo, M. Orena, M. Penna, S. Sandri, C. Tomasini. *Tetrahedron* **1991**, *47*, 2263–2272; k) S. G. Davies, A. A. Mortlock, *Tetrahedron Lett.* **1991**, *32*, 4191–4194.

[9] a) S. X. Candeias, K. Jenkins, A. S. C. Ribeiro, C. A. M. Afonso, S. Caddick, *Synth. Commun.* **2001**, *31*, 3241–3254; b) G. Guillena, C. Nájera *J. Org. Chem.* **2000**, *65*, 7310–7322; c) G. Cardillo, A. D′Amico, M. Orena, S. Sandri *J. Org. Chem.* **1988**, *53*, 2354–2356.

[10] a) Y. J. Zhang, K. Y. Kim J. H. Park, C. E. Song, K. Lee, M. S. Lah, S.-g. Lee, *Adv. Synth. Catal.* **2005**, *347*, 563–570; b) Y. J. Zhang, J. H. Park, S.-g. Lee, *Tetrahedron: Asymmetry* **2004**, *15*, 2209–2212; c) S.-g. Lee, Y. J. Zhang, *Org. Lett.* **2002**, *4*, 2429–2431; d) S.-g. Lee, Y. J. Zhang, *Tetrahedron: Asymmetry* **2002**, *13*, 1039–1042.

[11] S.-g. Lee, Y. J. Zhang, C. E. Song, J. K. Lee, J. H. Choi, *Angew. Chem.* **2002**, *114*, 875–877; *Angew. Chem. Int. Ed.* **2002**, *41*, 847–849.

[12] a) M. Kim, J. V. Mulcahy, C. G. Espino, J. Du Bois, *Org. Lett.* **2006**, *8*, 1073–1076; b) M. McLaughlin, M. Palucki, I. W. Davies, *Org. Lett.* **2006**, *8*, 3311–3314; c) M. S. Kim, Y.-W. Kim, H. S. Hahm, J. W. Jang, W. K. Lee, H.-J. Ha, *Chem. Commun.* **2005**, 3062–3064;

d) H.-B. Zhou, H. Alper, *J. Org. Chem.* **2003**, *68*, 3439–3445; e) C. Benedí, F. Bravo, P. Uriz, E. Fernandez, C. Claver, S. Castillon, *Tetrahedron Lett.* **2003**, *44*, 6073–6077; f) L. E. Overman, T. P. Remarchuk, *J. Am. Chem. Soc.* **2002**, *124*, 12–13; g) K. E. Bell, M. P. Coogan, M. B. Gravestock, D. W. Knight, S. R. Thornton, *Tetrahedron Lett.* **1997**, *38*, 8545–8548; h) N. Kise, K. Kashiwagi, M. Watanabe, J. Yoshida, *J. Org. Chem.* **1996**, *61*, 428–429; i) Y. S. Park, M. L. Boys, P. Beak, *J. Am. Chem. Soc.* **1996**, *118*, 3757–3758; j) S. Shatzmiller, S. Bercovici, *Liebigs Ann. Chem.* **1992**, 1005–1009; k) S. Ghomi, D. E. Orr, *Chem. Ind.* **1983**, 928–928; l) R. J. Parry, M. G. Kunitani, O. I. Viele, *J. Chem. Soc. Chem. Commun.* **1975**, 321–322.

[13] a) G. Sartori, R. Maggi, *Science of Synthesis: Houben-Weyl Methods of Molecular Transformations*, (Eds.: S. V. Ley, J. G. Knight), Georg Thieme Verlag, Stuttgart, **2005**, Vol. 18, pp 665–758; b) B. Gabriele, G. Salerno, R. Mancuso, M. Costa, *J. Org. Chem.* **2004**, *69*, 4741–4750; c) F. Qian, J. E. McCusker, Y. Zhang, A. D. Main, M. Chlebowski, M. Kokka, L. McElwee-White, *J. Org. Chem.* **2002**, *67*, 4086–4092; d) J.-M. Kim, T. E. Wilson, T. H. Norman, P. G. Schultz, *Tetrahedron Lett.* **1996**, *37*, 5309–5312; e) C. M. Shimizu, M. Kamei, T. Fujisawa, *Tetrahedron Lett.* **1995**, *36*, 8607–8610.

[14] a) H. Li, R. A. Widenhoefer, *Tetrahedron* **2010**, *66*, 4827–4831; b) K. Muñiz, C. H. Hövelmann, J. Streuff, *J. Am. Chem. Soc.* **2008**, *130*, 763–773; c) K. Muñiz, J. Streuff, P. Chávez, C. H. Hövelmann, *Chem. Asian J.* **2008**, *3*, 1248–1255; d) C. H. Hövelmann, J. Streuff, L. Brelot, K. Muñiz, *Chem. Commun.* **2008**, 2334–2336; e) K. Muñiz, C. H. Hövelmann, E. Campos-Gómez, J. Barluenga, J. González, J. Streuff, M. Nieger, *Chem. Asian J.* **2008**, *3*, 776–788; f) K. Muñiz, *J. Am. Chem. Soc.* **2007**, *129*, 14542–14543; g) K. Muñiz, J. Streuff, C. H. Hövelmann, A. Núñez, *Angew. Chem.* **2007**, *119*, 7255–7258; *Angew. Chem. Int. Ed.* **2007**, *46*, 7125–7127; h) J. Streuff, C. H. Hövelmann, M. Nieger, K. Muñiz, *J. Am. Chem. Soc.* **2005**, *127*, 14586–14587; i) G. L. J. Bar, G. C. Lloyd-Jones, K. I. Booker-Milburn, *J. Am. Chem. Soc.* **2005**, *127*, 7308–7309.

[15] X. Hu, Z. Cao, Z. Liu, Y. Wang, H. Du, *Adv. Synth. Catal.* **2010**, *352*, 651–655.

[16] a) M. Fujita, O. Kitagawa, T. Suzuki, T. Taguchi, *J. Org. Chem.* **1997**, *62*, 7330–7335; b) T. W. Balko, R. S. Brinkmeyer, N. H. Terando, *Tetrahedron Lett.* **1989**, *30*, 2045–2048; c) P. A. Hunt, C. May, C. J. Moody, *Tetrahedron Lett.* **1988**, *29*, 3001–3002; d) S. Danishefsky, E. Taniyama, R. R. Webb, *Tetrahedron Lett.* **1983**, *24*, 11–14.

[17] a) H. Harayama, A. Abe, T. Sakado, M. Kimura, K. Fugami, S. Tanaka, Y. Tamaru, *J. Org. Chem.* **1997**, *62*, 2113–2122; b) Y. Tamaru, M. Hojo, H. Higashimura, Z.-i. Yoshida, *J. Am. Chem. Soc.* **1988**, *110*, 3994–4002.

[18] a) J. A. Fritz, J. P. Wolfe, *Tetrahedron* **2008**, *64*, 6838–6852; b) J. A. Fritz, J. S. Nakhla, J. P. Wolfe, *Org. Lett.* **2006**, *8*, 2531–2534.

[19] T. H. Kim, G. J. Lee, *J. Org. Chem.* **1999**, *64*, 2941–2943.

[20] N. G. v. Keyserlingk, J. Martens, *Eur. J. Org. Chem.* **2002**, 301–308.

[21] a) R. E. Kinder, Z. Zhang, R. A. Widenhoefer, *Org. Lett.* **2008**, *10*, 3157–3159; b) Z. Zhang, C. F. Bender, R. A. Widenhoefer, *J. Am. Chem. Soc.* **2007**, *129*, 14148–14149; c) Z. Zhang, C. F. Bender, R. A. Widenhoefer, *Org. Lett.* **2007**, *9*, 2887–2889; d) Z. Zhang, C. Liu, R. E. Kinder, X. Han, H. Qian, R. A. Widenhoefer, *J. Am. Chem. Soc.* **2006**, *128*, 9066–9073.

[22] H. Li, R. A. Widenhoefer, *Org. Lett.* **2009**, *11*, 2671–2674.

[23] We have previously documented the utility of ureas and carbamates as nucleophiles for the gold(I)-catalyzed inter- and intramolecular hydroamination of alkenes: a) X. Han, R. A. Widenhoefer, *Angew. Chem.* **2006**, *118*, 1779–1781; *Angew. Chem. Int. Ed.* **2006**, *45*, 1747–1749; b) C. F. Bender, R. A. Widenhoefer, *Org. Lett.* **2006**, *8*, 5303–5305; c) Z. Zhang, S. D. Lee, R. A. Widenhoefer, *J. Am. Chem. Soc.* **2009**, *131*, 5372–5373.

[24] For examples of the gold(I)-catalyzed hydroamination of alkenes with sulfonamides see: a) X. Giner, C. Najera, *Org. Lett.* **2008**, *10*, 2919–2922; b) X.-Y. Liu, C.-H. Li, C.-M. Che, *Org. Lett.* **2006**, *8*, 2707–2710; c) J. Zhang, C.-G. Yang, C. He, *J. Am. Chem. Soc.* **2006**, *128*, 1798–1799; d) C. Brouwer, C. He, *Angew. Chem.* **2006**, *118*, 1776–1779; *Angew. Chem. Int. Ed.* **2006**, *45*, 1744–1747.

[25] For some recent examples of the hydroamination of electronically unactivated C=C bonds catalyzed by late transition metal complexes see: a) K. D. Hesp, S. Tobisch, M. Stradiotto, *J. Am. Chem. Soc.* **2010**, *132*, 413–426; b) Y. Kashiwame, S. Kuwata, T. Ikariya, *Chem. Eur. J.* **2010**, *16*, 766–770; c) X. Shen, S. L. Buchwald, *Angew. Chem.* **2010**, *122*, 574–577; *Angew. Chem. Int. Ed.* **2010**, *49*, 564–567; d) L. D. Julian, J. F. Hartwig, *J. Am. Chem. Soc.* **2010**, *132*, 13813–13822; e) K. D. Hesp, M. Stradiotto, *Org. Lett.* **2009**, *11*, 1449–1452; f) H. Ohmiya, T. Moriya, M. Sawamura, *Org. Lett.* **2009**, *11*, 2145–2147; g) B. M. Cochran, F. E. Michael, *J. Am. Chem. Soc.* **2008**, *130*, 2786–2792; h) Z. Liu, J. F. Hartwig, *J. Am. Chem. Soc.* **2008**, *130*, 1570–1571; i) C. F. Bender, W. B. Hudson, R. A. Widenhoefer, *Organometallics* **2008**, *27*, 2356–2358.

[26] a) C. Palomo, F. P. Cossio, A. Arrieta, J. M. Odriozola, M. Giarbide, J. M. Ontoria, *J. Org. Chem.* **1989**, *54*, 5736–5745; b) W. Sankhavasi, M. Yamamoto, S. Kohmoto, K. Yamada, *Bull. Chem. Soc. Jpn.* **1991**, *64*, 1425–1427.

[27] O. F. Williams, J. C. Bailar, *J. Am. Chem. Soc.* **1959**, *81*, 4464–4469.

[28] For a recent review on the mechanisms of gold(I)-catalyzed transformations see: A. S. K. Hashmi, *Angew. Chem.* **2010**, *122*, 5360–5369; *Angew. Chem. Int. Ed.* **2010**, *49*, 5232–5241.

[29] a) T. J. Brown, M. G. Dickens, R. A. Widenhoefer, *J. Am. Chem. Soc.* **2009**, *131*, 6350–6351; b) T. J. Brown, M. G. Dickens, R. A. Widenhoefer, *Chem. Commun.* **2009**, 6451–6453.

[30] a) D. Zuccaccia, L. Belpassi, F. Tarantelli, A. Macchioni, *J. Am. Chem. Soc.* **2009**, *131*, 3170–3171; b) P. de Frémont, N. Marion, S. P. Nolan, *J. Organomet. Chem.* **2009**, *694*, 551–560; c) T. N. Hooper, M. Green, J. E. Mcgrady, J. R. Patel, C. A. Russell, *Chem. Commun.*

2009, 3877–3879; d) N. D. Shapiro, F. D. Toste, *Proc. Natl. Acad. Sci. USA* **2008**, *105*, 2779–2782.
[31] R. L. LaLonde, W. E. Brenzovich, D. Benitez, E. Tkatchouk, K. Kelley, W. A. Goddard, F. D. Toste, *Chem. Sci.* **2010**, 226–233.
[32] a) C. M. Krauter, A. S. K. Hashmi, M. Pernointner, *ChemCatChem* **2010**, *2*, 1226–1230; b) J. Zhang, W. Shen, L. Li, M. Li, *Organometallics* **2009**, *28*, 3129–3139; c) G. Kovács, G. Ujaque, A. Lledós, *J. Am. Chem. Soc.* **2008**, *130*, 853–864.
[33] We thank a reviewer for suggesting this pathway.
[34] L. Crombie, K. C. Hooper, *J. Chem. Soc.* **1955**, 3010–3016.

