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

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Abstract

Treatment of *N*-allylic,*N′*-aryl ureas 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 ≥50:1 diastereoselectivity.

Keywords

Nitrogen heterocycles; Intramolecular hydroamination; Gold; Alkenes

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-allenyl ureas 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-allenyl urea followed by 5-*exo* hydroamination of the resulting 1-vinyl piperidine

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(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.

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-allenyl ureas 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*-allyl urea **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). 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 P(*t*-Bu)$_2$*o*-biphenyl (**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-allenyl ureas.[22] The possibility that intramolecular hydroamination of *N*-allylic ureas is catalyzed by Ag^+ or Brønsted acid generated under 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*-methyl ureas **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 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 with acid released in the C–N bond forming step,[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-alkenyl ureas with $(PPh_3)AuNTf_2$ and 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-alkenyl ureas, which was followed by slow protodeauration to form the 1-methyl pyrrolidine.[31] Although protodeauration was slow, it appears reasonable that more electron-rich supporting ligands such as **P1** might facilitate protodemetallation. 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 intermediate *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 hydroxyl 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.[32] As such, it also appears feasible that the pendant hydroxyl 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**.[33]

Conclusion

We have shown that a 1:1 mixture of (**P1**)AuCl [**P1** = P(*t*-Bu)$_2$*o*-biphenyl] 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 ≥93% yield with ≥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 ^1H 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).

Imidazolidin-2-ones

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** (30 mg, 100%) as a yellow solid. TLC (hexanes–EtOAc = 2:1): R_f = 0.4. ^{1}H NMR: δ = 8.14 (d, *J* = 9.6 Hz, 2 H), 7.66 (d, *J* = 9.6 Hz, 2 H), 4.36 (m, 1 H), 3.79 (m, 1 H), 3.63 (t, *J* = 8.8 Hz, 1 H), 3.04 (dd, *J* = 4.0, 8.8 Hz, 1 H), 1.80-1.64 (m, 5 H), 1.42-1.22 (m, 4 H), 1.32 (d, *J* = 6.0 Hz, 3 H), 1.08 (m, 1 H). ^{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, cm^{-1}): 2938, 1684, 1503, 1323, 1252, 1111, 851, 751, 690. 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, 92%. TLC (hexanes–EtOAc = 2:1): R_f = 0.2. ^{1}H NMR: δ = 8.11 (d, *J* = 9.2 Hz, 2 H), 7.62 (d, *J* = 9.2 Hz, 2 H), 4.34 (m, 1 H), 3.61 (t, *J* = 8.8 Hz, 1 H), 3.06 (dd, *J* = 3.6, 8.8 Hz, 1 H), 2.85 (s, 3 H), 1.31 (d, *J* = 6.4 Hz, 3 H). ^{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, cm−1): 2927, 1697, 1496, 1312, 1267, 1111, 845, 749, 690. 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, 93%. TLC (hexanes–EtOAc = 3:1): R_f = 0.4. ^{1}H NMR: δ = 8.26 (d, *J* = 9.0 Hz, 2 H), 7.77 (d, *J* = 9.5 Hz, 2 H), 7.60 (br d, *J* = 7.5 Hz, 2 H), 7.42 (br t, *J* = 7.5 Hz, 2 H), 7.17 (br t, *J* = 7.5 Hz, 1 H), 4.59 (m, 1 H), 4.21 (t, *J* = 9.0 Hz, 1 H), 3.61 (dd, *J* = 4.5, 9.0 Hz, 1 H), 1.50 (d, *J* = 6.5 Hz, 3 H). ^{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, cm^{-1}): 2924, 1701, 1505, 1405, 1282, 1108, 754, 688. 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, 86%. TLC (hexanes–EtOAc = 3:1): R_f = 0.4. ^{1}H NMR: δ = 7.40 (m, 2 H), 7.31 (br d, *J* = 7.6 Hz, 2 H), 7.04 (br t, *J* = 7.2 Hz, 1 H), 4.28 (quintet of doublets, *J* = 6.4 m 8.2 Hz, 1 H), 3.56 (t, *J* = 8.4 Hz, 1 H), 3.01 (dd, *J* = 6.0, 8.4 Hz, 1 H), 2.84 (s, 3 H), 1.25 (d, *J* = 6.4 Hz, 3 H). ^{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, cm^{-1}): 2927, 1694, 1494, 1431, 1367, 1261, 756, 694. 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, 97%. TLC (hexanes–EtOAc = 3:1): R_f = 0.4. ^{1}H NMR: δ = 7.58 (d, *J* = 8.0 Hz, 2 H), 7.34 (d, *J* = 7.2 Hz, 2 H), 7.30 (d, *J* = 8.8 Hz, 2 H), 7.04 (t, *J* = 7.2 Hz, 1 H), 6.91 (d, *J* = 7.2 Hz, 2 H), 4.27 (m, 1 H), 4.00 (t, *J* = 8.8 Hz, 1 H), 3.78 (s, 3 H), 3.46 (t, *J* = 7.6 Hz, 1 H), 1.28 (d, *J* = 5.6 Hz, 3 H). ^{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, cm^{-1}): 2979, 1688, 1501, 1401, 1241, 754, 688. 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, 92%. TLC (hexanes–EtOAc = 2:1): R_f = 0.4. ^{1}H NMR: δ = 7.42 (d, *J* = 8.0 Hz, 2 H), 7.30 (t, *J* = 8.0 Hz, 2 H), 7.02 (br t, *J* = 7.2 Hz, 1 H), 4.27 (quintet of doublets, *J* = 6.0, 8.8 Hz, 1 H), 3.78 (m, 1 H), 3.56 (t, *J* = 8.8 Hz, 1 H), 2.98 (dd, *J* = 5.6, 8.4 Hz, 1 H), 1.80-1.64 (m, 5 H), 1.43-1.21 (m, 4 H), 1.25 (d, *J* = 6.0 Hz, 3 H), 1.08 (m, 1 H). ^{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, cm^{-1}): 2930, 1691, 1419, 1255, 755, 694. 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, 100%. TLC (hexanes–EtOAc = 3:1): R_f = 0.6. ^{1}H NMR: δ = 8.14 (d, *J* = 9.6 Hz, 2 H), 7.67 (d, *J* = 9.2 Hz, 2 H), 3.82 (dq, *J* = 2.8, 6.0 Hz, 1 H), 3.62 (tt, *J* = 3.6, 12.0 Hz, 1 H), 3.35 (dq, *J* = 2.4, 6.0 Hz, 1 H), 1.92-1.05 (m, 10 H), 1.29 (d, *J* = 6.0 Hz, 3 H), 1.28 (d, *J* = 6.0 Hz, 3 H). ^{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, cm^{-1}): 2932, 1645, 1491, 1328, 1302, 1238, 1110, 750, 702, 639. 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, 93%. TLC (hexanes–EtOAc = 3:1): R_f = 0.6. ^{1}H NMR: δ = 8.14 (d, *J* = 9.2 Hz, 2 H), 7.72 (d, *J* = 9.2 Hz, 2 H), 3.96 (br q, *J* = 6.0 Hz, 1 H), 3.55 (m, 1 H), 3.16 (m, 1 H), 2.03-1.08 (m, 10 H), 1.28 (d, *J* = 6.0 Hz, 3 H), 0.95 (d, *J* = 6.8 Hz, 3 H), 0.75 (d, *J* = 6.4 Hz, 3 H). ^{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, cm^{-1}): 2935, 1698, 1495, 1297, 1246, 1107, 854, 754, 692. 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, 98%. TLC (hexanes–EtOAc = 3:1): R_f = 0.5. ^{1}H NMR: δ = 8.08 (d, *J* = 9.2 Hz, 2 H), 7.62 (d, *J* = 9.2 Hz, 2 H), 7.28-7.19 (m, 5 H), 4.45 (s, 2 H), 4.13 (dq, *J* = 0.8, 6.0 Hz, 1 H), 3.58 (tt, *J* = 3.6, 12.0 Hz, 1 H), 3.50 (m, 1 H), 3.33 (m, 1 H), 1.82-1.47 (m, 6 H), 1.35-1.18 (m, 3 H), 1.23 (d, *J* = 6.4 Hz, 3 H), 1.03 (tq, *J* = 3.2, 12.8 Hz, 1 H). ^{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, cm^{-1}): 2931, 1701, 1503, 1321, 1234, 849, 751, 697. 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, 98%. TLC (hexanes–EtOAc = 3:1): R_f = 0.4. ^{1}H NMR: δ = 8.14 (d, *J* = 9.2 Hz, 2 H), 7.69 (d, *J* = 9.2 Hz, 2 H), 4.26 (dd, *J* = 3.6, 11.6 Hz, 1 H), 4.16 (dq, *J* = 1.6, 6.0 Hz, 1 H), 3.91 (dd, *J* = 7.2, 11.6 Hz, 1 H), 3.67 (tt, *J* = 3.6, 12.0 Hz, 1 H), 3.45 (ddd, *J* = 1.6, 3.6, 7.2 Hz, 1 H), 2.00 (s, 3 H), 1.93-1.54 (m, 6 H), 1.47-1.26 (m, 3 H), 1.31 (d, *J* = 6.0 Hz, 3 H), 1.11 (tq, *J* = 3.6, 12.8 Hz, 1 H). ^{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. 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, 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), 2 H], [7.70 (d, *J* = 9.2 Hz), 7.56 (d, *J* = 9.2 Hz), (1:3.7), 2 H)], [4.45 (quintet, *J* = 6.9), 4.31 (dq *J* = 2.0, 6.4 Hz), (3.7:1), 1 H)], [3.97 (m), 3.34 (m), (3.7:1), 1 H], [3.90-3.80 (m), 3.73 (m), (3.7:1), 2 H] 3.61 (tt, *J* = 4.0, 12 Hz, 1 H), [2.35 (t, *J* = 4.5 Hz), 2.18 (t, *J* = 4.8 Hz), (1:3.7), 1 H], 1.87-1.46 (m, 6 H),

1.41-1.20 (m, 3 H), [1.33 (d, J = 6.4 Hz), 1.31 (d, J = 6.4 Hz), (3.7:1), 3 H], 1.11 (tq, J = 3.6, 12.8 Hz, 1 H). $^{13}C\{^{1}H\}$ 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, cm^{-1}): 2932, 1684, 1503, 1320, 1248, 1112, 850, 729, 694. HRMS calcd (found) for $C_{17}H_{23}N_3O_4$ (M^+): 333.1689 (333.1676).

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 H4-H5 coupling constants, which ranged from $^{3}J_{HH} \approx 1$ Hz for **4b** and **4c** to $^{3}J_{HH} = 2.4$ Hz for **4a**. Published values for the vicinal H4-H5 coupling constant of *trans*-4,5-disubstituted imidazolidin-2-ones range from 0–3 Hz,[9] while the the vicinal H4-H5 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 H4-H5 coupling constants of $^{3}J_{HH} \approx 7$ Hz (major) and $^{3}J_{HH} \approx 2$ 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] (26 mg, 82%) as white solid. 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** (16 mg, 77%) as a colorless oil. The ^{1}H and ^{13}C NMR spectra of **7** and **8** were identical with published data.[19,34]

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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References

1. (a) Lee CW, Hong DH, Han SB, Jung SH, Kim HC, Fine RL, Lee SH, Kim HM. Biochem Pharmacol. 2002; 64:473–480. [PubMed: 12147299] (b) Thomas NJ, Carcillo JA, Herzer WA, Mi Z, Tofovic SP, Jackson EK. Eur J Pharmacol. 2003; 465:133–139. [PubMed: 12650842] (c) Rotstein DM, Gabriel SD, Manser N, Filonova L, Padilla F, Sankuratri S, Ji C, deRosier A, Dioszegi M, Heilek G, Jekle A, Weller P, Berry P. Bioorg Med Chem Lett. 2010; 20:3219–3222. [PubMed: 20457517] (d) Jiang B, Liu JF, Zhao SY. J Org Chem. 2003; 68:2376–2384. [PubMed: 12636405] (e) Heidempergher F, Pillan A, Pinciroli V, Vaghi F, Arrigoni C, Bolis G, Caccia C, Dho L, McArthur R, Varasi M. J Med Chem. 1997; 40:3369–3380. [PubMed: 9341912] (f) Eum H, Lee Y, Kim S, Baek A, Son M, Lee KW, Ko SW, Kim S, Yun SY, Lee WK, Ha HJ. Bull Korean Chem Soc. 2010; 31:611–614.

2. (a) Shue HJ, Chen X, Schwerdt JH, Paliwal S, Blythin DJ, Lin L, Gu D, Wang C, Reichard GA, Wang H, Piwinski JJ, Duffy RA, Lachowicz JE, Coffin VL, Nomeir AA, Morgan CA, Varty GB,

Shih NY. Bioorg Med Chem Lett. 2006; 16:1065–1069. [PubMed: 16290143] (b) Shue HJ, Chen X, Shih NY, Blythin DJ, Paliwal S, Lin L, Gu D, Schwerdt JH, Shah S, Reichard GA, Piwinski JJ, Duffy RA, Lachowicz JE, Coffin VL, Liu F, Nomeir AA, Morgan CA, Varty GB. Bioorg Med Chem Lett. 2005; 15:3896–3899. [PubMed: 16019209] (c) Reichard GA, Stengone C, Paliwal S, Mergelsberg I, Majmundar S, Wang C, Tiberi R, McPhail AT, Piwinkski JJ, Shih NY. Org Lett. 2003; 5:4249–4251. [PubMed: 14601972]

3. (a) Peretto I, Fossati C, Giardina GAM, Giardini A, Guala M, La Porta E, Petrillo P, Radaelli S, Radice L, Raveglia LF, Santoro E, Scudellaro R, Scarpitta F, Cerri A, Menegon S, Dondio GM, Rizzi A, Armani E, Amari G, Civelli M, Villetti G, Patacchini R, Bergamaschi M, Bassani F, Delcanale M, Imbimbo BP. J Med Chem. 2007; 50:1693–1697. [PubMed: 17352463] (b) Peretto I, Forlani R, Fossati C, Giardina GAM, Giardini A, Guala M, La Porta E, Petrillo P, Radaelli S, Radice L, Raveglia LF, Santoro E, Scudellaro R, Scarpitta F, Bigogno C, Misiano P, Dondio GM, Rizzi A, Armani E, Amari G, Civelli M, Villetti G, Patacchini R, Bergamaschi M, Delcanale M, Salcedo C, Fernández AG, Imbimbo BP. J Med Chem. 2007; 50:1571–1583. [PubMed: 17352462] (c) Peretto I, Petrillo P, Imbimbo BP. Med Res Rev. 2009; 29:867–902. [PubMed: 19399831]
4. (a) Kazmierski WM, Furfine E, Gray-Nunez Y, Spaltenstein A, Wright L. Bioorg Med Chem Lett. 2004; 14:5685–5687. [PubMed: 15482948] (b) De Clerq E. Biochim Biophys Acta. 2002; 1587:258–275. [PubMed: 12084468] (c) Kazmierski WM, Salituro FG, Tung RD, Wright LL. Bioorg Med Chem Lett. 2000; 10:1159–1162. [PubMed: 10866371] (d) Spaltenstein A, Almond MR, Bock WJ, Cleary DG, Furfine ES, Hazen RJ, Kazmierski WM, Salituro FG, Tung RD, Wright LL. Bioorg Med Chem Lett. 2000; 10:1159–1162. [PubMed: 10866371] (e) Salituro FG, Baker CT, Court JJ, Deininger DD, Kim EE, Li B, Novak PM, Rao BG, Pazhanisamy S, Porter MD, Schairer WC, Tung RD. Bioorg Med Chem Lett. 1998; 8:3637–3642. [PubMed: 9934485] (f) De Lucca GV, Lam PYS. Drugs Future. 1998; 23:987–994.
5. (a) Chern JH, Chang CS, Tai CL, Lee YC, Lee CC, Kang IJ, Lee CY, Shih SR. Bioorg Med Chem Lett. 2005; 15:4206–4211. [PubMed: 16054357] (b) Shia KS, Li WT, Chang CM, Hsu MC, Chern JH, Leong MK, Tseng SN, Lee CC, Lee YC, Chen SJ, Peng KC, Tseng HY, Chang YL, Tai CL, Shih SR. J Med Chem. 2002; 45:1644–1655. [PubMed: 11931618]
6. (a) Neves, JKdeAL.; Botelho, SPS.; de Melo, CML.; Pereira, VRA.; de Lima, MdoCA.; Pitta, IdaR; Albuquerque, MCPdeA; Galdino, SL. Parasitol Res. 2010; 107:531–538. [PubMed: 20440624] (b) Robert JMH, Sabourin C, Alvarez N, Robert-Piessard S, Le Baut G, Le Pape P. Eur J Med Chem. 2003; 38:711–718. [PubMed: 12932902] (c) Alvarez N, Robledo S, Velez ID, Robert JM, Le Baut G, Le Pape P. J Enz Inhib Med Chem. 2002; 17:443–447.
7. (a) Sabourin C, Robert JMH. J Enz Inhib Med Chem. 2008; 23:659–667.(b) Sabourin C, Robert JMH, Robert-Piessard S, Carbonnelle D, Lang F. J Enz Inhib Med Chem. 2004; 19:459–465.
8. (a) Lucet D, Le Gall T, Mioskowski C. Angew Chem Int Ed. 1998; 37:2580–2627.(b) Guillena G, Nájera C. Tetrahedron: Asymm. 1998; 9:1125–1129.(c) Parisi M, Solo A, Wulff WD, Guzei IA, Rheingold AL. Organometallics. 1998; 17:3696–3700.(d) Wulff WD. Organometallics. 1998; 17:3116–3134.(e) Palomo C, Oiarbide M, González A, García JM, Berrée F. Tetrahedron Lett. 1996; 37:4565–4568.(f) Kubota H, Kubo A, Takahashi M, Shimizu R, Da-te T, Okamura K, Nunami K-i. J Org Chem. 1995; 60:6776–6784.(g) Davies SC, Evans GB, Mortlock AA. Tetrahedron Asymm. 1994; 5:585–606.(h) Taguchi T, Shibuya A, Sasaki H, Endo J-i, Morikawa T, Shirob M. Tetrahedron Asymm. 1994; 5:1423–1426.(i) Sankhavasi W, Yamamoto M, Kohmoto S, Yamada K. Bull Chem Soc Jpn. 1991; 64:1425–1427.(j) Cardillo G, Orena M, Penna M, Sandri S, Tomasini C. Tetrahedron. 1991; 47:2263–2272.(k) Davies SG, Mortlock AA. Tetrahedron Lett. 1991; 32:4191–4194.
9. (a) Candeias SX, Jenkins K, Ribeiro ASC, Afonso CAM, Caddick S. Synth Comm. 2001; 31:3241–3254.(b) Guillena G, Nájera C. J Org Chem. 2000; 65:7310–7322. [PubMed: 11076588] (c) Cardillo G, D'Amico A, Orena M, Sandri S. J Org Chem. 1988; 53:2354–2356.
10. (a) Zhang YJ, Kim KY, Park JH, Song CE, Lee K, Lah MS, Lee S-g. Adv Synth Catal. 2005; 347:563–570.(b) Zhang YJ, Park JH, Lee S-g. Tetrahedron: Asymm. 2004; 15:2209–2212.(c) Lee, S-g; Zhang, YJ. Org Lett. 2002; 4:2429–2431. [PubMed: 12098264] (d) Lee, S-g; Zhang, YJ. Tetrahedron: Asymm. 2002; 13:1039–1042.
11. Lee, S-g; Zhang, YJ.; Song, CE.; Lee, JK.; Choi, JH. Angew Chem Int Ed. 2002; 41:847–849.
12. (a) Kim M, Mulcahy JV, Espino CG, Du Bois J. Org Lett. 2006; 8:1073–1076. [PubMed: 16524271] (b) McLaughlin M, Palucki M, Davies IW. Org Lett. 2006; 8:3311–3314. [PubMed:

16836393] (c) Kim MS, Kim YW, Hahm HS, Jang JW, Lee WK, Ha HJ. Chem Commun. 2005:3062–3064.(d) Zhou HB, Alper H. J Org Chem. 2003; 68:3439–3445. [PubMed: 12713344] (e) Benedí C, Bravo F, Uriz P, Fernandez E, Claver C, Castillon S. Tetrahedron Lett. 2003; 44:6073–6077.(f) Overman LE, Remarchuk TP. J Am Chem Soc. 2002; 124:12–13. [PubMed: 11772049] (g) Bell KE, Coogan MP, Gravestock MB, Knight DW, Thornton SR. Tetrahedron Lett. 1997; 38:8545–8548.(h) Kise N, Kashiwagi K, Watanabe M, Yoshida J. J Org Chem. 1996; 61:428–429. [PubMed: 11666950] (i) Park YS, Boys ML, Beak P. J Am Chem Soc. 1996; 118:3757–3758.(j) Shatzmiller S, Bercovici S. Liebigs Ann Chem. 1992:1005–1009.(k) Ghomi S, Orr DE. Chem Ind. 1983:928–928.(l) Parry RJ, Kunitani MG, Viele OI. J Chem Soc Chem Commun. 1975:321–322.

13. (a) Sartori, G.; Maggi, R. Science of Synthesis: Houben-Weyl Methods of Molecular Transformations. Ley, SV.; Knight, JG., editors. Vol. 18. Thieme; Stuttgart: 2005. p. 665-758.(b) Gabriele B, Salerno G, Mancuso R, Costa M. J Org Chem. 2004; 69:4741–4750. [PubMed: 15230597] (c) Qian F, McCusker JE, Zhang Y, Main AD, Chlebowski M, Kokka M, McElwee-White L. J Org Chem. 2002; 67:4086–4092. [PubMed: 12054942] (d) Kim JM, Wilson TE, Norman TH, Schultz PG. Tetrahedron Lett. 1996; 37:5309–5312.(e) Shimizu CM, Kamei M, Fujisawa T. Tetrahedron Lett. 1995; 36:8607–8610.
14. (a) Li H, Widenhoefer RA. Tetrahedron. 2010; 66:4827–4831. [PubMed: 21566674] (b) Muñiz K, Hövelmann CH, Streuff J. J Am Chem Soc. 2008; 130:763–773. [PubMed: 18081279] (c) Muñiz K, Streuff J, Chávez P, Hövelmann CH. Chem Asian J. 2008; 3:1248–1255. [PubMed: 18655067] (d) Hövelmann CH, Streuff J, Brelot L, Muñiz K. Chem Commun. 2008:2334–2336.(e) Muñiz K, Hövelmann CH, Campos-Gómez E, Barluenga J, González J, Streuff J, Nieger M. Chem Asian J. 2008; 3:776–788. [PubMed: 18357591] (f) Muñiz K. J Am Chem Soc. 2007; 129:14542–14543. [PubMed: 17985900] (g) Muñiz K, Streuff J, Hövelmann CH, Núñez A. Angew Chem Int Ed. 2007; 46:7125–7127.(h) Streuff J, Hövelmann CH, Nieger M, Muñiz K. J Am Chem Soc. 2005; 127:14586–14587. [PubMed: 16231907] (i) Bar GLJ, Lloyd-Jones GC, Booker-Milburn KI. J Am Chem Soc. 2005; 127:7308–7309. [PubMed: 15898768]
15. Hu X, Cao Z, Liu Z, Wang Y, Du H. Adv Synth Catal. 2010; 352:651–655.
16. (a) Fujita M, Kitagawa O, Suzuki T, Taguchi T. J Org Chem. 1997; 62:7330–7335. [PubMed: 11671848] (b) Balko TW, Brinkmeyer RS, Terando NH. Tetrahedron Lett. 1989; 30:2045–2048. (c) Hunt PA, May C, Moody CJ. Tetrahedron Lett. 1988; 29:3001–3002.(d) Danishefsky S, Taniyama E, Webb RR. Tetrahedron Lett. 1983; 24:11–14.
17. (a) Harayama H, Abe A, Sakado T, Kimura M, Fugami K, Tanaka S, Tamaru Y. J Org Chem. 1997; 62:2113–2122. [PubMed: 11671516] (b) Tamaru Y, Hojo M, Higashimura H, Yoshida Z-i. J Am Chem Soc. 1988; 110:3994–4002.
18. (a) Fritz JA, Wolfe JP. Tetrahedron. 2008; 64:6838–6852. [PubMed: 19122758] (b) Fritz JA, Nakhla JS, Wolfe JP. Org Lett. 2006; 8:2531–2534. [PubMed: 16737306]
19. Kim TH, Lee GJ. J Org Chem. 1999; 64:2941–2943. [PubMed: 11674372]
20. Keyserlingk, NGv; Martens, J. Eur J Org Chem. 2002:301–308.
21. (a) Kinder RE, Zhang Z, Widenhoefer RA. Org Lett. 2008; 10:3157–3159. [PubMed: 18570376] (b) Zhang Z, Bender CF, Widenhoefer RA. J Am Chem Soc. 2007; 129:14148–14149. [PubMed: 17967025] (c) Zhang Z, Bender CF, Widenhoefer RA. Org Lett. 2007; 9:2887–2889. [PubMed: 17595096] (d) Zhang Z, Liu C, Kinder RE, Han X, Qian H, Widenhoefer RA. J Am Chem Soc. 2006; 128:9066–9073. [PubMed: 16834380]
22. Li H, Widenhoefer RA. Org Lett. 2009; 11:2671–2674. [PubMed: 19514795]
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) Han X, Widenhoefer RA. Angew Chem Int Ed. 2006; 45:1747–1749.(b) Bender CF, Widenhoefer RA. Org Lett. 2006; 8:5303–5305. [PubMed: 17078703] (c) Zhang Z, Lee SD, Widenhoefer RA. J Am Chem Soc. 2009; 131:5372–5373. [PubMed: 19326908]
24. For examples of the gold (I)-catalyzed hydroamination of alkenes with sulfonamides see: (a) Giner X, Najera C. Org Lett. 2008; 10:2919–2922. [PubMed: 18553970] (b) Liu XY, Li CH, Che CM. Org Lett. 2006; 8:2707–2710. [PubMed: 16774237] (c) Zhang J, Yang CG, He C. J Am Chem Soc. 2006; 128:1798–1799. [PubMed: 16464072] (d) Brouwer C, He C. 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) Hesp KD, Tobisch S, Stradiotto M. J Am Chem Soc. 2010; 132:413–426. [PubMed: 20000354] (b) Kashiwame Y, Kuwata S, Ikariya T. Chem Eur J. 2010; 16:766–770.(c) Shen X, Buchwald SL. Angew Chem Int Ed. 2010; 122:564–567.(d) Julian LD, Hartwig JF. J Am Chem Soc. 2010; 132:13813–13822. [PubMed: 20839807] (e) Hesp KD, Stradiotto M. Org Lett. 2009; 11:1449–1452. [PubMed: 19231849] (f) Ohmiya H, Moriya T, Sawamura M. Org Lett. 2009; 11:2145–2147. [PubMed: 19379007] (g) Cochran BM, Michael FE. J Am Chem Soc. 2008; 130:2786–2792. [PubMed: 18254623] (h) Liu Z, Hartwig JF. J Am Chem Soc. 2008; 130:1570–1571. [PubMed: 18183986] (i) Bender CF, Hudson WB, Widenhoefer RA. Organometallics. 2008; 27:2356–2358.

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

27. Williams OF, Bailar JC. J Am Chem Soc. 1959; 81:4464–4469.

28. For a recent review on the mechanisms of gold(I)-catalyzed transformations see: Hashmi ASK. Angew Chem Int Ed. 2010; 49:5232–5241.

29. (a) Brown TJ, Dickens MG, Widenhoefer RA. J Am Chem Soc. 2009; 131:6350–6351. [PubMed: 19368391] (b) Brown TJ, Dickens MG, Widenhoefer RA. Chem Commun. 2009:6451–6453.

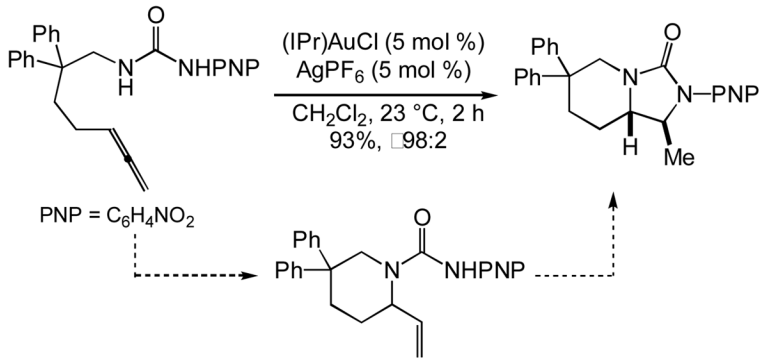
30. (a) Zuccaccia D, Belpassi L, Tarantelli F, Macchioni A. J Am Chem Soc. 2009; 131:3170–3171. [PubMed: 19219980] (b) de Frémont P, Marion N, Nolan SP. J Organomet Chem. 2009; 694:551–560.(c) Hooper TN, Green M, Mcgrady JE, Patel JR, Russell CA. Chem Commun. 2009:3877–3879.(d) Shapiro ND, Toste FD. Proc Natl Acad Sci USA. 2008; 105:2779–2782.

31. LaLonde RL, Brenzovich WE, Benitez D, Tkatchouk E, Kelley K, Goddard WA, Toste FD. Chem Sci. 2010:226–233.

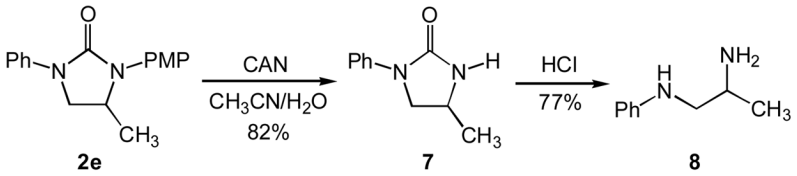
32. (a) Krauter CM, Hashmi ASK, Pernointner M. Chem Cat Chem. 2010; 2:1226–1230.(b) Zhang J, Shen W, Li L, Li M. Organometallics. 2009; 28:3129–3139.(c) Kovács G, Ujaque G, Lledós A. J Am Chem Soc. 2008; 130:853–864. [PubMed: 18166047]

33. We thank a reviewer for suggesting this pathway.

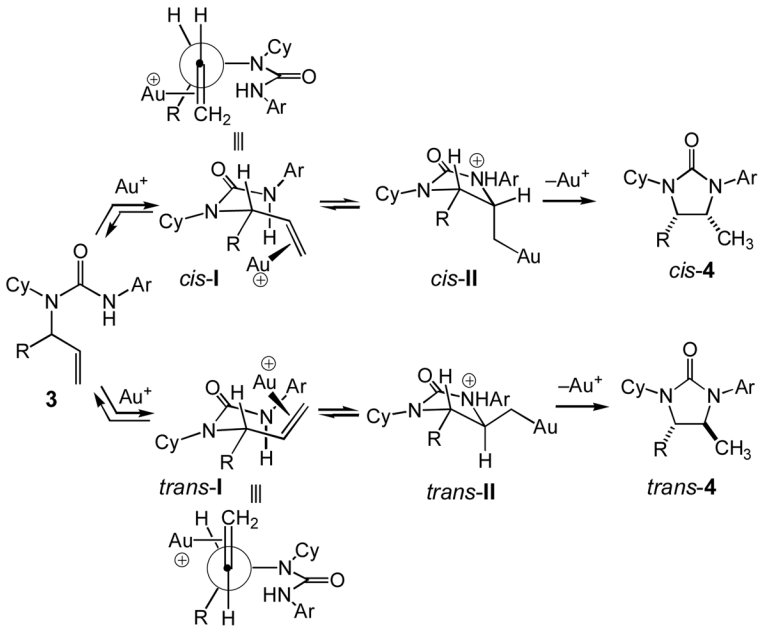
34. Crombie L, Hooper KC. J Chem Soc. 1955:3010–3016.



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



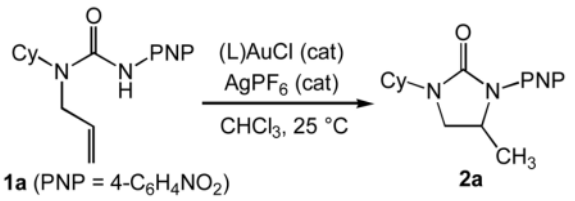
Scheme 2.
Dearylation and hydrolysis of imidazolidin-2-one **2e**.



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

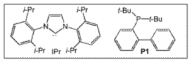
Table 1

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



1a (PNP = 4-$C_6H_4NO_2$) **2a**

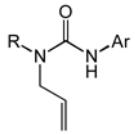
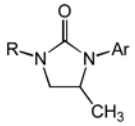
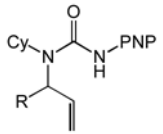
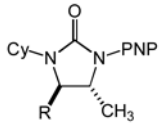
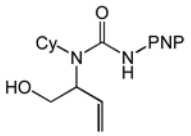
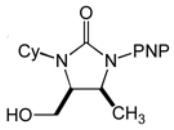
entry	L	cat load (mol %)	time (h)	yield (%)[a]
1	IPr	5	12	97
2	IPr	2	15	97
3	IPr	1	30	97
4	**P1**	1	15	100



[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-$C_6H_4NO_2$, PMP = 4-C_6H_4OMe).

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	 **5**	 **6**	16	97	3.7:1

[a] Isolated yields of >95% purity.

[b] Determined by ^1H NMR analysis of the crude reaction mixture..

[c] Catalyst loading = 5 mol %.

[d] Reaction temperature = 60 °C.

[e] Catalyst loading = 10 mol %.