ACS Combinatorial Science

LETTER

pubs.acs.org/acscombsci

Synthesis of Pyrrolo[1,2-*a*]quinoxalines via Gold(I)-Mediated Cascade Reactions

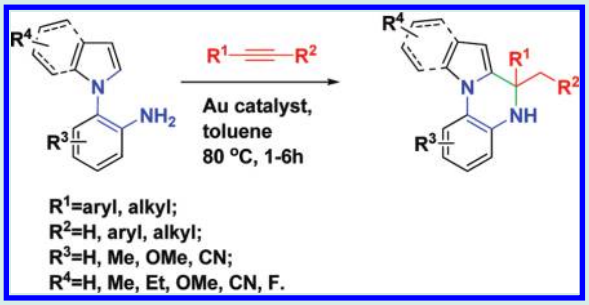
Guannan Liu,[†,‡] Yu Zhou,[†] Daizong Lin,[†] Jinfang Wang,[†] Lei Zhang,[†] Hualiang Jiang,[†] and Hong Liu[†,*]

[†]The Center for Drug Discovery and Design, State Key Laboratory of Drug Research, Shanghai Institute of Materia Medica, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, 555 Zuchongzhi Road, Shanghai 201203, P. R. China

[‡]Department of Pharmacy, College of Life Sciences, China Jiliang University, Hangzhou 310018, P. R. China.

Supporting Information

ABSTRACT: In this study, we developed an efficient tandem process of hydroamination and hydroarylation using a gold catalyst to enable and study the reactions between pyrrole-substituted anilines and alkynes. The gold(I)-catalyzed reactions were achieved in toluene at 80 °C over a reaction time of 1−6 h. These reactions are applicable to a variety of aromatic amino compounds and both the terminal and internal alkynes. Substituted pyrrolo[1,2-*a*]quinoxalines were obtained in moderate to excellent yields. A presumed mechanism involving intermolecular C−N bond formation and intramolecular nucleophilic reaction via a cationic gold complex has been proposed on the basis of the deuterium labeling studies.



KEYWORDS: gold-catalyst, cascade reaction, hydroamination, hydroarylation

Efficiency is an important characteristic for the design and development of innovative strategies in chemical synthesis. One of the most effective methods of achieving synthetic efficiency is to implement a cascade reaction to enable multiple bond-forming and bond-cleaving events to occur in a single synthetic operation.[1] Among these are transition metal-catalyzed domino reactions for the synthesis of various fused polycyclic heterocyclic compounds.[2] Gold-catalyzed reaction cascades have attracted much interest as a result of the ability of gold ions to activate alkyne, alkene, and allene functionality under mild conditions and at low catalyst loadings.[3]

Although pyrrolo[1,2-*a*]quinoxalines and their 4,5-dihydro derivatives play important roles in drug discovery as biologically active compounds and valuable synthetic intermediates,[4] the available strategies for the synthesis of these compounds are limited. So far, only a few methods have been described for the assembly of 4,5-dihydropyrrolo[1,2-*a*]quinoxalines, which normally require additional additives, long reaction times, limited reaction tolerance, and low reaction selectivity.[5] Recently, Patil et al developed the $PtBr_2$- and Au(I)-catalyzed hydroamination-hydroarylation cascade reactions of 2-(1*H*-pyrrol-1-yl)anilines with alkynes to form 4,5-dihydropyrrolo-[1,2-*a*]quinoxalines.[6] Although these transformations are encouraging, they are limited to the terminal alkynes and require long reaction times.

On the basis of our previous experience with gold catalysts in the preparation of heterocycles,[7] we describe here the scope and mechanism of an improved version of the gold-catalyzed intermolecular C—N bond formation and intramolecular nucleophilic reaction. Both terminal and internal alkynes can be used, increasing the range of structural diversity accessible in the products. Furthermore, only a small quantity of gold catalyst (1 mol %) is needed, without other additives, and short reaction times (1−6 h) are required.

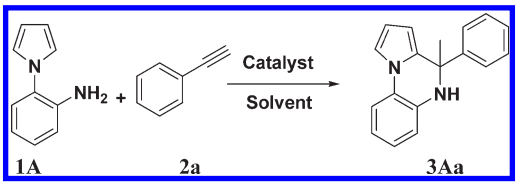
Preliminary experiments directed toward optimizing the reaction conditions of the transformation were carried out using commercially available 2-(1*H*-pyrrol-1-yl)aniline (**1A**) and phenylacetylene (**2a**) in the presence of gold catalysts in toluene. The results are shown in Table 1.

No reaction occurred in the absence of catalysts (Table 1, entry 1), and $AuCl_3$ provided the target product in only 25% yield (Table 1, entry 2). However, certain cationic gold(I) complexes were found to be exhibit significantly better activity in this reaction (Table 1, entries 3 to 7). Among these species, catalyst 4 ($[Au\{P(t\text{-}Bu)_2(o\text{-biphenyl})\}\{CH_3CN\}]SbF_6$) was found to be superior, with the target product being obtained in 95% yield (Table 1, entry 7). Doubling the amount of Au catalyst (to 2 mol %) provided no faster or higher yielding reaction (Table 1, entry 8), and Ag(I) salts were found to be ineffective as cocatalysts (Table 1, entries 9 and 10).

The nature of the solvent plays an important role in this transformation. Toluene, acetonitrile, and ethanol provided significantly better yields than dichloromethane, THF, acetone, *N*,*N*-dimethylformamide, and water (Table 1, entries 7, 11−17). Changing the reaction temperature to 25 °C, 60 °C, or 100 °C adjusted the reaction times as one would expect but did not improve yields (Table 1, entries 18−20). Thus, optimal results

Received: December 6, 2010
Revised: February 22, 2011
Published: April 13, 2011

Table 1. Optimization of the Reaction Conditions[a]



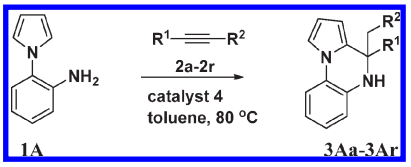
entry	catalyst[b]	solvent	temp (°C)	time (h)	yield (%)[c]
1		toluene	80	1	0
2	$AuCl_3$	toluene	80	1	25
3	$Au(PPh_3)Cl$	toluene	80	1	42
4	catalyst 1	toluene	80	1	85
5	catalyst 2	toluene	80	1	82
6	catalyst 3	toluene	80	1	76
7	catalyst 4	toluene	80	1	95
8[d]	catalyst 4	toluene	80	1	93
9[e]	catalyst 4	toluene	80	1	88
10[f]	catalyst 4	toluene	80	1	86
11	catalyst 4	CH_3CN	80	1	84
12	catalyst 4	CH_2Cl_2	80	1	63
13	catalyst 4	EtOH	80	1	90
14	catalyst 4	H_2O	80	1	trace
15	catalyst 4	THF	80	1	trace
16	catalyst 4	DMF	80	1	0
17	catalyst 4	acetone	80	1	trace
18	catalyst 4	toluene	r.t.	36	91
19	catalyst 4	toluene	60	3	89
20	catalyst 4	toluene	100	1	92

[a] **1A** (0.40 mmol), **2a** (0.44 mmol), catalyst (1 mol %), Ar protection. [b] Catalyst 1 = [Au{P(*t*-Bu)$_2$(*o*-biphenyl)}]Cl; catalyst 2 = [Au{1,3-bis(2,6-di-*iso*-propylphenyl)imidazol-2-yli-dene}]Cl; catalyst 3 = [Au{P-(2,4-di-*tert*-butylphenoxy)$_3$}]Cl; catalyst 4 = [Au{P(*t*-Bu)$_2$(*o*-biphenyl)}-{CH_3CN}]SbF_6. [c] Isolated yields based on **1A**. [d] 2 mol % catalyst 4 used. [e] $AgSbF_6$ (5 mol %) used as cocatalyst. [f] AgOTf (5 mol %) used as cocatalyst.

were obtained when 2-(1*H*-pyrrol-1-yl)aniline (0.40 mmol, **1A**) and phenylacetylene (0.44 mmol, **2a**) in toluene were treated with 1 mol % of catalyst 4 in a sealed tube under Ar at 80 °C for 1 h.

To evaluate the scope of the catalytic method, we investigated the reaction of 2-(1*H*-pyrrol-1-yl)aniline (**1A**) and a variety of alkynes (**2**) under the above optimized conditions. As shown in Table 2, a series of aromatic and aliphatic terminal alkynes gave the desired products **3Aa**−**3Ak** in moderate to good yields (53−98%) (Table 2, entries 1−11). Yields with ortho-substituted phenylacetylene derivatives were significantly lower than for substrates with meta- and para-substituents (**2b**−**2d**), presumably because of steric effects (Table 2, entries 2−4). Substrate **2e**, which possesses a 4-*tert*-butylphenyl group, was incorporated with no difficulty (Table 2, entry 5). Electronic effects were also indicated by the slight reduction in yield of substrate **2f** having an electron-donating *p*-methoxyphenyl group (Table 2, entry 6). Excellent yields were obtained irrespective of the presence of electron-withdrawing or halide groups at the R^1 position (Table 2, entries 7−9). However, the 2-pyridyl group of 2-ethynylpyridine (**2l**) was not tolerated; the desired product **3Al** was not formed and the starting materials were completely recovered (Table 2, entry 12).

Table 2. Gold(I)-Catalyzed Reaction of 2-(1*H*-pyrrol-1-yl)aniline 1A and Alkynes 2[a]



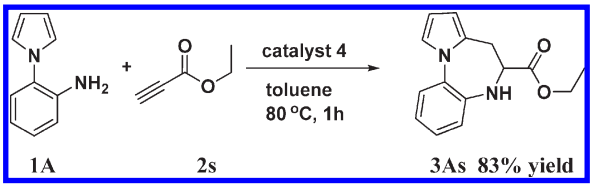
entry	product	yield (%)[b]	entry	product	yield (%)[b]
1	**3Aa**	95	10	**3Aj**	80[c]
2	**3Ab**	53	11	**3Ak**	77[c]
3	**3Ac**	94	12	**3Al**	0[c]
4	**3Ad**	98	13	**3Am**	98
5	**3Ae**	95	14	**3An**	96
6	**3Af**	82	15	**3Ao**	94[d]
7	**3Ag**	90	16	**3Ap**	63[d]
8	**3Ah**	93	17	**3Aq**	26[d]
9	**3Ai**	87	18	**3Ar**	20[d]

[a] Reaction conditions: **1A** (0.40 mmol), **2** (0.44 mmol), catalyst 4 (1 mol %), Ar protection. [b] Isolated yield based on **1A**. [c] The reaction was carried out for 2 h. [d] The reaction was carried out for 6 h.

We were also pleased to find that the reaction was not limited to substrates with aryl groups at the R^1 position. Compounds possessing alkyl groups were transformed smoothly into the products **3Aj** and **3Ak** in good yield (Table 2, entries 10 and 11). Furthermore, certain internal alkynes were also found to be compatible (Table 2, entries 13−18). The methoxycarbonyl substituents of compounds **2m**−**2o** facilitated efficient transformation, and the desired products were obtained in excellent

dx.doi.org/10.1021/co1000844 |*ACS Comb. Sci.* 2011, 13, 209–213

Scheme 1. Gold(I)-Catalyzed Reaction of 2-(1*H*-pyrrol-1-yl)aniline 1A and Ethyl Propiolate 2s



yields, up to 98% (Table 2, entries 13−15). In contrast, internal alkyne substrates bearing more electron-rich (or noncoordinating) R^2 groups, such as ethyl and phenyl, reacted more slowly. For example, **3Ap** was obtained in 63% yield after 6 h (Table 2, entry 16), and phenyl-containing alkynes gave lower yields of the desired products **3Aq** and **3Ar** (26% and 20% yield, respectively; Table 2, entries 17 and 18). Unexpectedly, the 7-member ring-closure product ethyl 6,7-dihydro-5*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]diazepine-6-carboxylate (**3As**) was formed in excellent yield from the reaction of the starting material (**1A**) with ethyl propiolate (**2s**).[8]

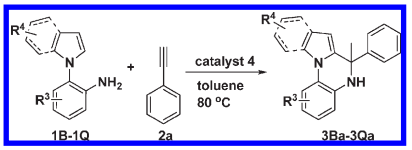
To further expand the scope of this transformation, gold-catalyzed cyclizations of phenylacetylene **2a** with various pyrrole- and indole-substituted anilines **1** were investigated (Table 3). These results demonstrated that the proposed reaction could be extended to generate substituted-4-methyl-4-phenyl-4,5-dihydropyrrolo[1,2-*a*]quinoxalines (**3Ba**−**3Fa**). However, the reaction was significantly effected by the nature of the R^3 substituent on the aniline ring. Thus, while 3-, 4-, and 5-methyl-substituted substrates gave similar results (Table 3, entries 1−3), a much lower yield was obtained for the electron-rich 4-methoxy analogue (Table 3, entry 4). In contrast, the electron-withdrawing 4-cyano group led to smooth conversion to the desired product (Table 3, entry 5). Good yields were also obtained for a pyrrole-substituted heterocyclic amine (Table 3, entry 6) and for the *N*-methylated aniline **1H** (Table 3, entry 7). Use of a benzylic amine (**1I**) instead of aniline did not give the desired product (Table 3, entry 8).

Substitution on the pyrrole ring of 2-(substituted-1*H*-pyrrol-1-yl)anilines was also found to be important. Ethyl and methyl groups provided good yields (Table 3, entries 9, 10), but a 2-cyano-pyrrol-1-yl group and a 1*H*-pyrazol-1-yl group each gave no conversion (Table 3, entries 11, 12). The latter result presumably derives from the significantly decreased nucleophilicity of the C5 atoms of the 2-cyanopyrrole and pyrazole, respectively. Gratifyingly, indole-substituted aniline bearing a variety of substituents gave cyclized products **3Na**−**3Qa** in good to excellent yields (71−92%, Table 3, entries 13−16).

All the pyrrolo[1,2-*a*]quinoxalines synthesized were characterized by spectral and analytical data. As shown in Figure 1, the absolute configuration of the product was determined by X-ray analysis of **3Ai**.[9]

To gain insights into the mechanism of the reaction, we performed labeling studies with deuterated starting materials.[10] The reaction of 2-(1*H*-pyrrol-1-yl)aniline **1A** with DC≡CPh ***d*-2a** under our gold catalysis conditions yielded the product ***d*-3Aa-1,** with deuterium incorporation on the 4-methyl group (26%) as confirmed by ^{1}H NMR (Scheme 2, eq 1). Conversely, 28% of the 4-methyl hydrogen of ***d*-3Aa-2** was found to contain deuterium when *N*-deuterated 2-(1*H*-pyrrol-1-yl)aniline ***d*-1A** was reacted with HC≡CPh **2a** (Scheme 2, eq 2). A similar result was obtained when the internal alkyne was used in the reaction. The treatment of ***d*-1A** with methyl 3-phenylpropiolate **2n** resulted in synthesis of the product ***d*-3An,** with deuterium incorporation at

Table 3. Gold(I)-Catalyzed Reaction of Pyrrole- and Indole-Substituted Anilines 1 and Phenylacetylene 2a[a]



entry	product	yield (%)[b]	entry	product	yield (%)[b]
1	**3Ba**	89	9	**3Ja**	76
2	**3Ca**	85	10	**3Ka**	93
3	**3Da**	78	11	**3La**	0[d]
4	**3Ea**	28[d]	12	**3Ma**	0[d]
5	**3Fa**	86[c]	13	**3Na**	91[c]
6	**3Ga**	79[c]	14	**3Oa**	90[c]
7	**3Ha**	76[c]	15	**3Pa**	92[c]
8	**3Ia**	0[d]	16	**3Qa**	71[c]

[a] Reaction conditions: **1** (0.40 mmol), **2a** (0.44 mmol), catalyst 4 (1 mol %), Ar protection. [b] Isolated yield based on **1**. [c] The reaction was carried out for 3 h. [d] The reaction was carried out for 6 h.

the α-position of the carbonyl group (44%) without significant exchange to other positions (Scheme 2, eq 3). In addition, a deuterium-incorporation pattern was also observed for the reaction of *N*-deuterated 2-(1*H*-pyrrol-1-yl)aniline ***d*-1A** with methyl propiolate **2s** (Scheme 2, eq 4); in this case, the deuterium was selectively incorporated into the methylene group (42%) of ***d*-3As**.

The reaction mechanism shown in Figure 2 is proposed to account for these observations, consistent with previous investigations of gold-catalyzed reactions.[3,11] First, the carbon−carbon triple bond of **2** is activated by coordination with the gold catalyst to form the gold-alkyne π-complex **I**. Intermolecular hydroamination of 2-(1*H*-pyrrol-1-yl)aniline **1A** gives the enamine intermediate **II**, which is followed by proton transfer to produce the cationic

dx.doi.org/10.1021/co1000844 |*ACS Comb. Sci.* 2011, 13, 209–213

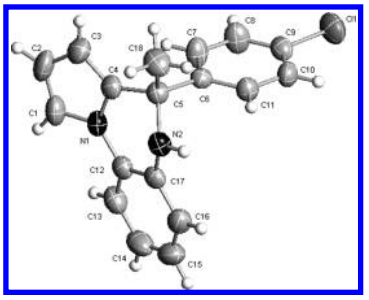
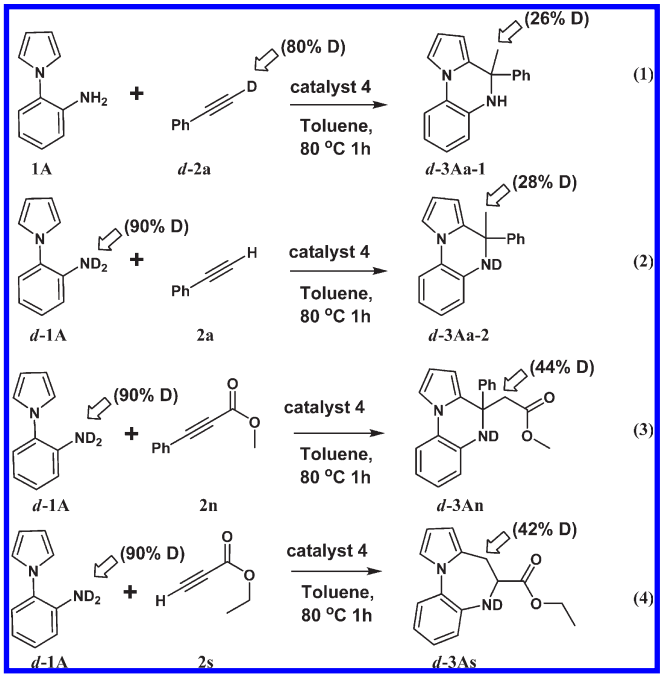


Figure 1. X-ray Crystal Structure of **3Ai**.[9]

Scheme 2. Deuterium-Labeling Study



intermediate **III**. The intramolecular nucleophilic reaction can then proceed *via* either path 1 or path 2 to form the imine intermediates **IV** and **IV′**, respectively. Most of the reactions proceed though path 1 to give the 6-membered intermediate **IV**. However, presumably owing to the electron-withdrawing nature of the carbonyl group, the use of ethyl propiolate **3s** as a starting material affords the 7-member ring-closure intermediate **IV′** via path 2. Finally, protonation of the resulting organogold complexes **IV** and **IV′** provides the final products **3** and **3As**, respectively, with regeneration of the gold catalyst.

In summary, we have described a versatile and efficient synthetic method in which a gold catalyst is used under mild reaction conditions to produce a broad range of functionalized 4,5-dihydropyrrolo[1,2-*a*]quinoxalines and 5,6-dihydroindolo[1,2-*a*]quinoxalines, which are useful as versatile synthetic intermediates and potentially as biologically active compounds. Deuterium labeling studies support a mechanism featuring a sequence of intermolecular hydroamination and nucleophilic pyrrole cyclization steps. We expect that the resulting biologically intriguing structures will have broad applications in our related medicinal chemistry program.

EXPERIMENTAL PROCEDURES

General Procedure for the Preparation of 4-Methyl-4-phenyl-4,5-dihydropyrrolo[1,2-*a*]quinoxaline 3Aa. To a 10 mL reaction flask containing toluene (5 mL) under argon was added 2-(1*H*-pyrrol-1-yl)aniline (63.2 mg, 0.40 mmol), phenylacetylene (48 μL, 0.44 mmol), and [Au{P(*t*-Bu)$_2$(*o*-biphenyl)}{CH$_3$CN}]SbF$_6$ (3 mg, 1 mol %). The resulting mixture was heated at 80 °C for 1 h, and then diluted with 20 mL of EtOAc, washed with water and brine, and dried by anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure, and the product was isolated by column chromatography with Petro Ether (PE)/EtOAc (25/1, v/v) as eluent to yield the desired product: (78 mg, 95%) as white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.32−7.22 (m, 5H), 7.19−7.16 (m, 2H), 6.97−6.91 (m, 1H), 6.81−6.76 (m, 2H), 6.36−6.34 (t, J = 3.3 Hz, 1H), 6.07−6.06 (m, 1H), 1.90 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 146.3, 135.1, 132.9, 128.2, 126.9, 125.7, 124.7, 119.3, 115.8, 114.6, 114.3, 109.9, 104.5, 56.9, 29.3 ppm; MS (ESI, 70 eV) m/z (%) 261 (100) $[M + H]^+$; HRMS (ESI) calcd for $C_{18}H_{17}N_2$ $[M + H]^+$ 261.1392, found 261.1407.

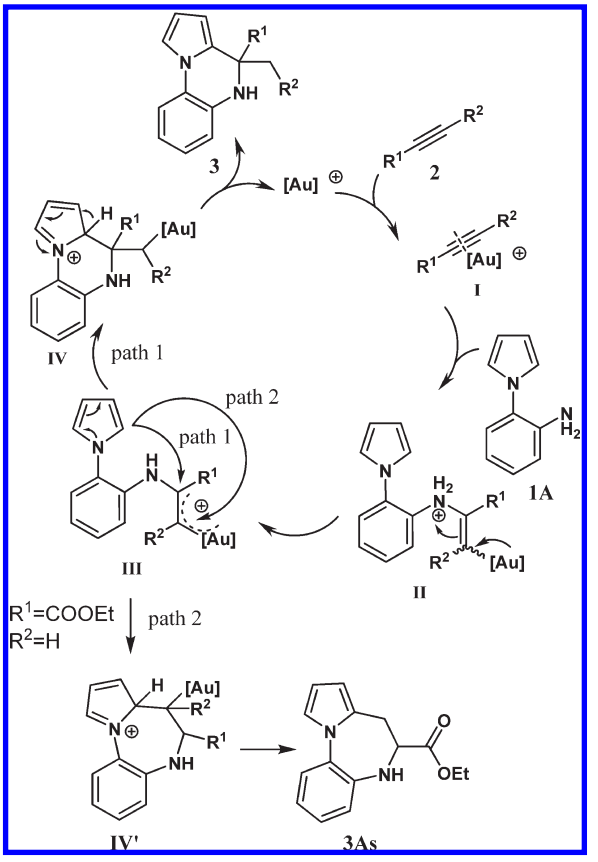


Figure 2. Possible mechanism for Au(I)-catalyzed reaction.

ASSOCIATED CONTENT

Supporting Information. Additional experimental details, general information, and ^{1}H and ^{13}C NMR spectra for all products. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

*Phone: +86-21-50807042. Fax: +86-21-50807042. E-mail: hliu@mail.shcnc.ac.cn.

Funding Sources

We gratefully acknowledge financial support from the National Natural Science Foundation of China (Grants 20872153, 21021063 and 81025017).

REFERENCES

(1) (a) Nicolaou, K. C.; Edmonds, D. J.; Bulger, P. G. Cascade Reactions in Total Synthesis. *Angew. Chem., Int. Ed.* **2006**, *45*, 7134–7186. (b) Park, S.; Lee, D. Gold-Catalyzed Intramolecular Allylation of Silyl Alkynes Induced by Silane Alcoholysis. *J. Am. Chem. Soc.* **2006**, *128*, 10664–10665. (c) Tietze, L. F. Domino Reactions in Organic Synthesis. *Chem. Rev.* **1996**, *96*, 115–136.

(2) (a) McReynolds, M. D.; Dougherty, J. M.; Hanson, P. R. Synthesis of Phosphorus and Sulfur Heterocycles via Ring-Closing Olefin Metathesis. *Chem. Rev.* **2004**, *104*, 2239–2258. (b) Alonso, F.; Beletskaya, I. P.; Yus, M. Transition-Metal-Catalyzed Addition of Heteroatom-Hydrogen Bonds to Alkynes. *Chem. Rev.* **2004**, *104*, 3079–3160. (c) Deiters, A.; Martin, S. F. Synthesis of Oxygen- and Nitrogen-Containing Heterocycles by Ring-Closing Metathesis. *Chem. Rev.* **2004**, *104*, 2199–2238. (d) Nakamura, I.; Yamamoto, Y. Transition-Metal-Catalyzed Reactions in Heterocyclic Synthesis. *Chem. Rev.* **2004**, *104*, 2127–2198. (e) Zeni, G.; Larock, R. C. Synthesis of Heterocycles via Palladium π-Olefin and π-Alkyne Chemistry. *Chem. Rev.* **2004**, *104*, 2285–2310. (f) Yet, L. Metal-Mediated Synthesis of Medium-Sized Rings. *Chem. Rev.* **2000**, *100*, 2963–3008.

(3) For selected reviews on gold catalysis, see: (a) Bongers, N.; Krause, N. Golden Opportunities in Stereoselective Catalysis. *Angew. Chem., Int. Ed.* **2008**, *47*, 2178–2181. (b) Gorin, D. J.; Sherry, B. D.; Toste, F. D. Ligand Effects in Homogeneous Au Catalysis. *Chem. Rev.* **2008**, *108*, 3351–3378. (c) Jiménez-Núñez, E.; Echavarren, A. M. Gold-Catalyzed Cycloisomerizations of Enynes: A Mechanistic Perspective. *Chem. Rev.* **2008**, *108*, 3326–3350. (d) Li, Z.; Brouwer, C.; He, C. Gold-Catalyzed Organic Transformations. *Chem. Rev.* **2008**, *108*, 3239–3265. (e) Skouta, R.; Li, C. J. Gold-Catalyzed Reactions of C−H bonds. *Tetrahedron* **2008**, *64*, 4917–4938. (f) Muzart, J. Gold-Catalysed Reactions of Alcohols: Isomerisation, Inter- and Intramolecular Reactions Leading to C−C and C−Heteroatom Bonds. *Tetrahedron* **2008**, *64*, 5815–5849. (g) Shen, H. C. Recent Advances in Syntheses of Heterocycles and Carbocycles via Homogeneous Gold Catalysis. Part 1: Heteroatom Addition and Hydroarylation Reactions of Alkynes, Allenes, and Alkenes. *Tetrahedron* **2008**, *64*, 3885–3903. (h) Gorin, D. J.; Toste, D. Relativistic Effects in Homogeneous Gold Catalysis. *Nature* **2007**, *446*, 395–403. (i) Fürstner, A.; Davies, P. W. Catalytic Carbophilic Activation: Catalysis by Platinum and Gold π Acids. *Angew. Chem., Int. Ed.* **2007**, *46*, 3410–3449. (j) Jiménez-Núñez, E.; Echavarren, A. M. Molecular Diversity through Gold Catalysis with Alkynes. *Chem. Commun.* **2007**, 333–346. (k) Hashmi, A. S. K. Gold-Catalyzed Organic Reactions. *Chem. Rev.* **2007**, *107*, 3180–3211.

(4) For recent examples of synthesis and SAR, see: (a) Tradtrantip, L.; Sonawane, N. D.; Namkung, W.; Verkman, A. S. Nanomolar Potency Pyrimido-pyrrolo-quinoxalinedione CFTR Inhibitor Reduces Cyst Size in a Polycystic Kidney Disease Model. *J. Med. Chem.* **2009**, *52*, 6447–6455. (b) Szabó, G.; Kiss, R.; Páyer-Lengyel, D.; Vukics, K.; Szikra, J.; Baki, A.; Molnár, L.; Fischer, J.; Keserű, G. M. Hit-to-Lead Optimization of Pyrrolo[1,2-*a*]quinoxalines as Novel Cannabinoid Type 1 Receptor Antagonists. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 3471–3475. (c) Guillon, J.; Moreau, S.; Mouray, E.; Sinou, V.; Forfar, I.; Fabre, S. B.; Desplat, V.; Millet, P.; Parzy, D.; Jarry, C.; Grellier, P. New Ferrocenic Pyrrolo[1,2-*a*]quinoxaline Derivatives: Synthesis, and in Vitro Antimalarial Activity. *Bioorg. Med. Chem.* **2008**, *16*, 9133–9144. (d) Guillon, J.; Forfar, I.; Mamani-Matsuda, M.; Desplat, V.; Saliège, M.; Thiolat, D.; Massip, S.; Tabourier, A.; Léger, J.-M.; Dufaure, B.; Haumont, G.; Jarry, C.; Mossalayi, D. Synthesis, Analytical Behaviour and Biological Evaluation of New 4-Substituted Pyrrolo[1,2-*a*]quinoxalines as Antileishmanial Agents. *Bioorg. Med. Chem.* **2007**, *15*, 194–210. (e) Guillon, J.; Grellier, P.; Labaied, M.; Sonnet, P.; Léger, J.-M.; Déprez-Poulain, R.; Forfar-Bares, I.; Dallemagne, P.; Lemaître, N.; Péhourcq, F.; Rochette, J.; Sergheraert, C.; Jarry, C. Synthesis, Antimalarial Activity, and Molecular Modeling of New Pyrrolo[1,2-*a*]quinoxalines, Bispyrrolo[1,2-*a*]quinoxalines, Bispyrido[3,2-*e*]pyrrolo[1,2-*a*]pyrazines, and Bispyrrolo-[1,2-*a*]thieno[3,2-*e*]pyrazines. *J. Med. Chem.* **2004**, *47*, 1997–2009. (f) Kobayashi, K.; Irisawa, S.; Matoba, T.; Matsumoto, T.; Yoneda, K.; Morikawa, O.; Konishi, H. Synthesis of Pyrrolo[1,2-*a*]quinoxaline Derivatives by Lewis Acid-Catalyzed Reactions of 1-(2-Isocyanophenyl)pyrroles. *Bull. Chem. Soc. Jpn.* **2001**, *74*, 1109–1114. (g) Armengol, M.; Joule, J. A. Synthesis of Thieno[2,3-*b*]quinoxalines and Pyrrolo[1,2-*a*]-quinoxalines from 2-Haloquinoxalines. *J. Chem. Soc., Perkin Trans. 1* **2001**, 978–984. (h) Guillon, J.; Boulouard, M.; Lisowski, V.; Stiebing, S.; Lelong, V.; Dallemagne, P.; Rault, S. Synthesis of New 2-(Aminomethyl)-4-phenylpyrrolo[1,2-*a*]-quinoxalines and their Preliminary In-Vivo Central Dopamine Antagonist Activity Evaluation in Mice. *J. Pharm. Pharmacol.* **2000**, *52*, 1369–1375.

(5) (a) Yi, C. S.; Yun, S. Y. Scope and Mechanistic Study of the Ruthenium-Catalyzed *ortho*-C−H Bond Activation and Cyclization Reactions of Arylamines with Terminal Alkynes. *J. Am. Chem. Soc.* **2005**, *127*, 17000–17006. (b) Abonia, R.; Insuasty, B.; Quiroga, J.; Kolshorn, H.; Meier, H. A Versatile Synthesis of 4,5-Dihydropyrrolo-[1,2-*a*]quinoxalines. *J. Heterocyclic Chem.* **2001**, *38*, 671–674.

(6) (a) Patil, N. T.; Kavthe, R. D.; Raut, V. S.; Reddy, V. V. N. Platinum-Catalyzed Formal Markownikoff's Hydroamination/Hydroarylation Cascade of Terminal Alkynes Assisted by Tethered Hydroxyl Groups. *J. Org. Chem.* **2009**, *74*, 6315–6318. (b) Patil, N. T.; Lakshmi, P. G. V. V.; Singh, V. Au^{I}-Catalyzed Direct Hydroamination/Hydroarylation and Double Hydroamination of Terminal Alkynes. *Eur. J. Org. Chem.* **2010**, No. 24, 4719–4731.

(7) (a) Ye, D.; Wang, J.; Zhang, X.; Zhou, Y.; Ding, X.; Feng, E.; Sun, H.; Liu, G.; Jiang, H.; Liu, H. Gold-Catalyzed Intramolecular Hydroamination of Terminal Alkynes in Aqueous Media: Efficient and Regioselective Synthesis of Indole-1-carboxamides. *Green Chem.* **2009**, *11*, 1201–1208. (b) Ye, D.; Zhang, X.; Zhou, Y.; Zhang, D.; Zhang, L.; Wang, H.; Jiang, H.; Liu, H. Gold- and Silver-Catalyzed Intramolecular Hydroamination of Terminal Alkynes: Water-Triggered Chemo- and Regioselective Synthesis of Fused Tricyclic Xanthines. *Adv. Synth. Catal.* **2009**, *351*, 2770–2778. (c) Zhou, Y.; Zhai, Y.; Ji, X.; Liu, G.; Feng, E.; Ye, D.; Zhao, L.; Jiang, H.; Liu, H. Gold(I)-Catalyzed One-Pot Tandem Coupling/Cyclization: An Efficient Synthesis of Pyrrolo-/Pyrido[2,1-*b*]benzo[*d*] [1,3]oxazin-1-ones. *Adv. Synth. Catal.* **2010**, *352*, 373–378. (d) Zhou, Y.; Feng, E.; Liu, G.; Ye, D.; Li, J.; Jiang, H.; Liu, H. Gold-Catalyzed One-Pot Cascade Construction of Highly Functionalized Pyrrolo[1,2-*a*]quinolin-1(2*H*)-ones. *J. Org. Chem.* **2009**, *74*, 7344–7348.

(8) The seven-membered ring product **3As** was unstable in the air at room temperature, which could be oxidized to its dehydrogenated product ethyl 5*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]diazepine-6-carboxylate.

(9) Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 771175 for **3Ai**.

(10) The synthetic methods of the deuterated starting materials were provided in the Supporting Information.

(11) (a) Shi, X.; Gorin, D. J.; Toste, F. D. Synthesis of 2-Cyclopentenones by Gold(I)-Catalyzed Rautenstrauch Rearrangement. *J. Am. Chem. Soc.* **2005**, *127*, 5802–5803. (b) Liu, X. -Y.; Ding, P.; Huang, J. -S.; Che, C. -M. Synthesis of Substituted 1,2-Dihydroquinolines and Quinolines from Aromatic Amines and Alkynes by Gold(I)-Catalyzed Tandem Hydroamination-Hydroarylation under Microwave-Assisted Conditions. *Org. Lett.* **2007**, *9*, 2645–2648. (c) Benitez, D.; Shapiro, N. D.; Tkatchouk, E.; Wang, Y.; Goddard, W. A., III; Toste, F. D. A Bonding Model for Gold(I) Carbene Complexes. *Nature Chem.* **2009**, *1*, 482–486.