JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
pubs.acs.org/JACS
Communication

Catalytic Enantioselective Protonation of Gold Enolates Enabled by Cooperative Gold(I) Catalysis

Kaylaa L. Gutman, Carlos D. Quintanilla, and Liming Zhang*

Cite This: J. Am. Chem. Soc. 2024, 146, 3598−3602
Read Online
ACCESS | Metrics & More | Article Recommendations | Supporting Information

ABSTRACT: Enantioselective protonation is a versatile approach to the construction of tertiary α-stereocenters, which are common structural motifs in various natural products and biologically relevant compounds. Herein we report a mild access to these chiral centers using cooperative gold(I) catalysis. From cyclic ketone enol carbonates, this asymmetric catalysis provides highly enantioselective access to cyclic ketones featuring an α tertiary chiral center, including challenging 2-methylsuberone. In combination with the gold-catalyzed formation of cyclopentadienyl carbonates in a one-pot, two-step process, this chemistry enables expedient access to synthetically versatile α'-chiral cyclopentenones with excellent enantiomeric excesses from easily accessible enynyl carbonate substrates.

Gold(I) enolates were isolated and characterized in the *C*-enolate forms as early as 1969.[1] Their reactivities were studied by Ito in 1988,[2] revealing the lack of nucleophilicity in aldol reactions in the absence of a Lewis acid. This is likely due to the electronegative nature of the metal. With the dramatic advances in homogeneous gold catalysis in the past 20 years, their manifestations in catalysis have been documented.[3] In some reports, the tautomerization between a gold(I) *O*-enolate and its *C*-enolated counterpart[3b−f] is invoked and *O*-enolates are proposed as reacting nucleophilic species.

We surmised that the low nucleophilicity of gold(I) enolates might lend it to enantioselective α-protonation, which has not been documented. In this context, as shown in Scheme 1A, the *C*-enolate form can be protonated to form an enol, which would necessitate challenging asymmetric tautomerization. Direct protonation[4] of gold *C*-enolates to ketones is unlikely due to the aforementioned lack of nucleophilicity. On the other hand, protonation of a gold *O*-enolate would directly deliver the ketone product and might be amenable to chiral induction. Catalytic enantioselective protonation has emerged as a versatile method to construct chiral tertiary carbon centers α to carbonyl groups.[5] The development of a gold-catalyzed version under mild conditions could introduce new strategies to this versatile approach and broaden its scope.

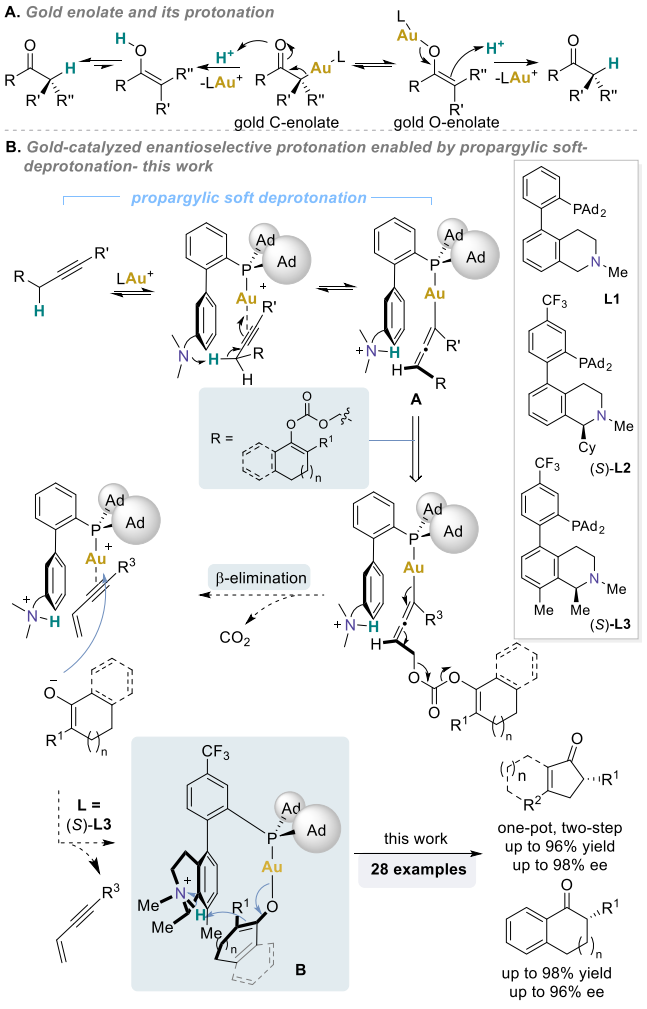
Over the past several years, our laboratory has developed various bifunctional phosphine ligands[6] to enable gold-ligand cooperation[7] in homogeneous gold catalysis. With ligands such as **L1**−**L3** featuring a remote amino group, soft propargylic deprotonation[8] is realized under gold catalysis and leads to the formation of an allenylgold intermediate (e.g., **A**, Scheme 1B), which can undergo *ipso*-protonation to deliver the corresponding allene reversibly[9] or propargylation of aldehydes.[10] With **L2** and **L3** featuring a chiral tetrahydroisoquinoline moiety, high levels of chiral induction with these transformations[9b,10b] were realized. It is plausible that the nucleophilicity of **A** would permit an $E1_{cb}$-type elimination provided the presence of a good leaving group at the homopropargylic position, delivering an anionic leaving group and an enyne byproduct. To this end, as shown in Scheme 1B, we envisioned that an enol carbonate could serve as a leaving group. Upon spontaneous decarboxylation, the enolate generated might recombine with the protonated gold catalyst to generate the gold *O*-enolate **B**. With (*S*)-**L3** as the chiral ligand, the intramolecular proton migration in **B** may be highly stereoselective, offering access to cyclic ketones with excellent enantiomeric excesses.

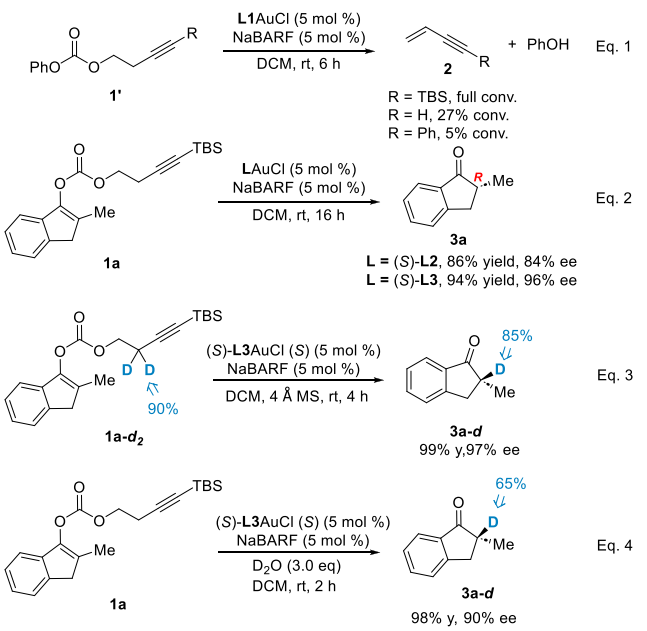
At the outset, we conducted a proof-of-concept study of the intended β-elimination by subjecting 4-(*tert*-butyldimethylsilyl)but-3-yn-1-yl phenyl carbonate (**1′**) to the gold catalysis using the achiral tetrahydroisoquinoline ligand **L1** (eq 1). To our delight, the reaction proceeded smoothly to afford the silylated enyne **2** (R = TBS) and phenol cleanly within 6 h. The use of a TBS-terminated C−C triple bond was inspired by our success in propargylation chemistry.[10] In contrast, removing TBS or replacing it with a phenyl group led to much slower elimination, reaching only 27% and 5% conversion, respectively, after 6 h reaction.

Received: October 25, 2023
Revised: January 16, 2024
Accepted: January 22, 2024
Published: January 31, 2024

https://doi.org/10.1021/jacs.3c11919
J. Am. Chem. Soc. 2024, 146, 3598−3602

Scheme 1. Gold Enolate and Asymmetric Protonation



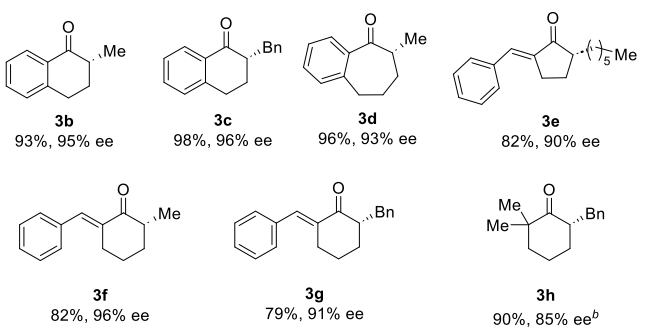


With the feasibility of the β-elimination established, we prepared the carbonate **1a** from 2-methylindanone. As shown in eq 2, by using (*S*)-**L2** as the ligand, the gold catalysis led to 2-methylindanone (**3a**) with 84% ee and in 86% yield. The trimethylated chiral ligand (*S*)-**L3** performed substantially better, leading to 96% ee and 94% yield. The (*R*)-configuration of **3a** was assigned based on the reported HPLC data[11] and is consistent with the model depicted in structure **B** (Scheme 1B). The ee value reflects excellent levels of facial selectivity in ligand-assisted proton delivery. Other documented enantioselective protonation methods leading to this product, including Pd-catalyzed decarboxylative protonation,[12] catalysis by a chiral tin complex,[13] and organocatalysis[14] resulted in <85% ee. The exception is Toste's enantioselective protonation of silyl enol ethers using a chiral Brønsted acid formed from a chiral cationic gold complex, in which a comparable 94% ee was achieved.[15]

To confirm the internal proton migration, we subjected **1a**-d_2 with 90% deuterium incorporation at the propargylic position to the reaction. As shown in eq 3, **3a**-*d* was isolated with 85% deuterium incorporation at the stereogenic center. On the other hand, when the reaction of **1a** was run in the presence of D_2O (3 equiv) and without 4 Å MS, 65% deuterium incorporation was observed (eq 4), and the ee value was notably lower. This result suggests that the internal enolate protonation (as in **B**) is relatively slow in comparison to the H−D exchange with D_2O.

The scope of this enantioselective protonation with homopropargyl carbonate substrates generated from various cyclic ketones was then explored. As shown in Table 1, this

Table 1. Scope with Substrates Derived from Cyclic Ketones[a]



[a]Reaction conditions: (*S*)-**L3**AuCl (5 mol %), NaBARF (5 mol %), 4 Å MS, DCM, rt, 16 h. [b]10 mol % **L3**AuCl and NaBARF used.

enantioselective protonation works well with α-tetralones **3b** and **3c** as well as 2-methylbenzosuberone (**3d**), resulting in ≥93% ee in each case. It is notable that the synthesis of chiral benzosuberones is challenging. The documented enantioselective protonation approach resulted in 44% ee.[16] Alternative synthesis of chiral 2-substituted benzosuberones generally leads to <90% ee[17] except the work by Trost.[18] For monocyclic ketones, α'-substitution is required for effective asymmetric induction. With benzylidene as the substituent, cyclopentanone **3e** and cyclohexanones **3f** and **3g** were formed with excellent ee values and good yields. With *gem*-dimethyl groups at the α'-position, the reaction forming **3h** was sluggish, requiring doubling the amount of the gold catalyst, and 85% ee was realized.

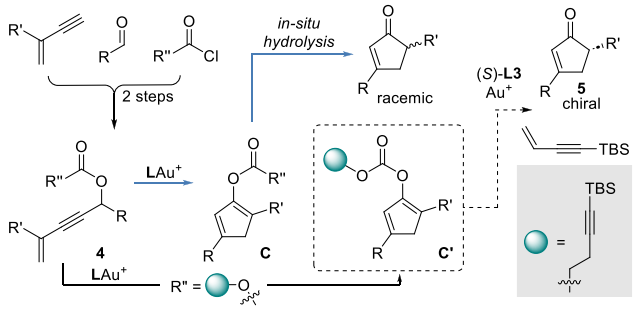
To further explore the synthetic utility of this asymmetric protonation, we considered the combination of this chemistry with a preceding catalysis that delivers enol carbonate substrates for the former. As such, a one-pot access to chiral ketones from potentially non-ketone substrates could be achieved.

We previously reported a gold-catalyzed synthesis of cyclopentenones from enynyl esters via tandem [3,3]-sigmatropic

https://doi.org/10.1021/jacs.3c11919
J. Am. Chem. Soc. 2024, 146, 3598−3602

rearrangement and the Nazarov cyclization (Scheme 2).[19] The cyclopentadienyl ester **C** is generated as an intermediate before

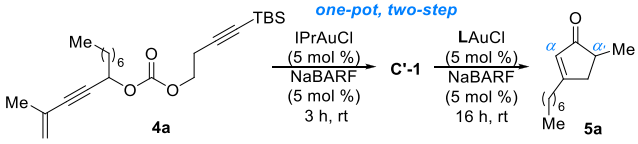
Scheme 2. Access to Chiral Cyclopentenones via In Situ Generated Cyclopentadienyl Carbonates



in situ hydrolysis to deliver the final product. It is anticipated that if the acyl group of **C** is 4-(*tert*-butyldimethylsilyl)but-3-yn-1-yloxycarbonyl, the intermediate, i.e., **C′**, could become a suitable substrate for our gold-catalyzed enantioselective protonation chemistry, thereby offering an efficient access to chiral α'-substituted cyclopentenones (**5**).[20] These structures can be synthetically versatile, but their asymmetric synthesis is lacking and in one instance entails a six-step sequence.[21] On the other hand, the enynyl carbonate substrates of type **4** can be readily prepared in two steps from the corresponding aldehyde.

We chose the enynyl carbonate **4a** as the substrate for reaction development. Our initial attempts to use (*S*)-**L3Au**$^+$ to catalyze both the cyclopentadienyl carbonate formation and the subsequent asymmetric protonation were not successful as the premature fragmentation of the 4-(*tert*-butyldimethylsilyl)but-3-yn-1-yloxycarbonyl moiety of **4a** interfered with the intended [3,3]-sigmatropic rearrangement and Nazarov cyclization. As such, IPrAuCl/NaBARF (5 mol %) was employed to catalyze the first step. To our delight, the reaction proceeded smoothly at ambient temperature to afford dienyl carbonate **C′-1** in nearly quantitative yield in 3 h. We then focused on optimizing conditions for the second step in a one-pot process. As shown in Table 2, the trimethyl ligand (*S*)-**L3** performed markedly better

Table 2. Reaction Optimization[a]



entry	L	solvent	conversion[b] (%)	yield (%)	ee[c] (%)
1	(*S*)-**L2**	DCM	74	37	71
2	(*S*)-**L3**	DCM	100	89	89
3	(*S*)-**L3**	toluene	100	98	87
4	(*S*)-**L3**	$PhCF_3$	100	97	85
5[d]	(*S*)-**L3**	DCM	100	96	91
6[e]	(*S*)-**L3**	DCM	100	94	92
7[f]	(*S*)-**L3**	DCM	100	96	88

[a]Reaction was performed at 0.05 mmol scale and in 0.25 M concentration. [b]Determined by NMR analysis using diethyl phthalate as the internal standard. [c]Detected by HPLC equipped with a column containing chiral stationary phase. [d]4 Å MS used. [e]**C′-1** was used as the substrate. [f]1 mol % IPrAuCl and 1 mol % NaBARF was used and required 8 h for step one to reach completion.

than (*S*)-**L2** in both conversion and enantioselectivity (comparing entry 2 to entry 1). With (*S*)-**L3** as the optimal ligand, toluene and trifluorotoluene led to excellent yields but slightly lower ee values (entries 3−4). The addition of 4 Å MS improved both the yield to 96% and the enantioselectivity to 91% (entry 5). With the isolated **C′-1** as the substrate, the ee value was marginally improved to 92% (entry 6). This suggests that IPrAu$^+$ employed in the first step had little impact on the subsequent asymmetric protonation step. The high level of enantioselectivity in this case is noteworthy considering that there is no substitution at the ketone α-C(sp^2) position. The loading of IPrAuCl/NaBARF was lowered to 1 mol % (entry 7). In addition to a slower conversion of **4a**, **5a** was isolated with a lower 88% ee, which is attributed to increased hydrolysis of **C′-1**. The full mechanistic picture of this one-pot transformation is shown in the SI. Of note is that the configuration of **5a** is stable under the reaction conditions, as no ee erosion was observed upon treating its enantioenriched form for 48 h.

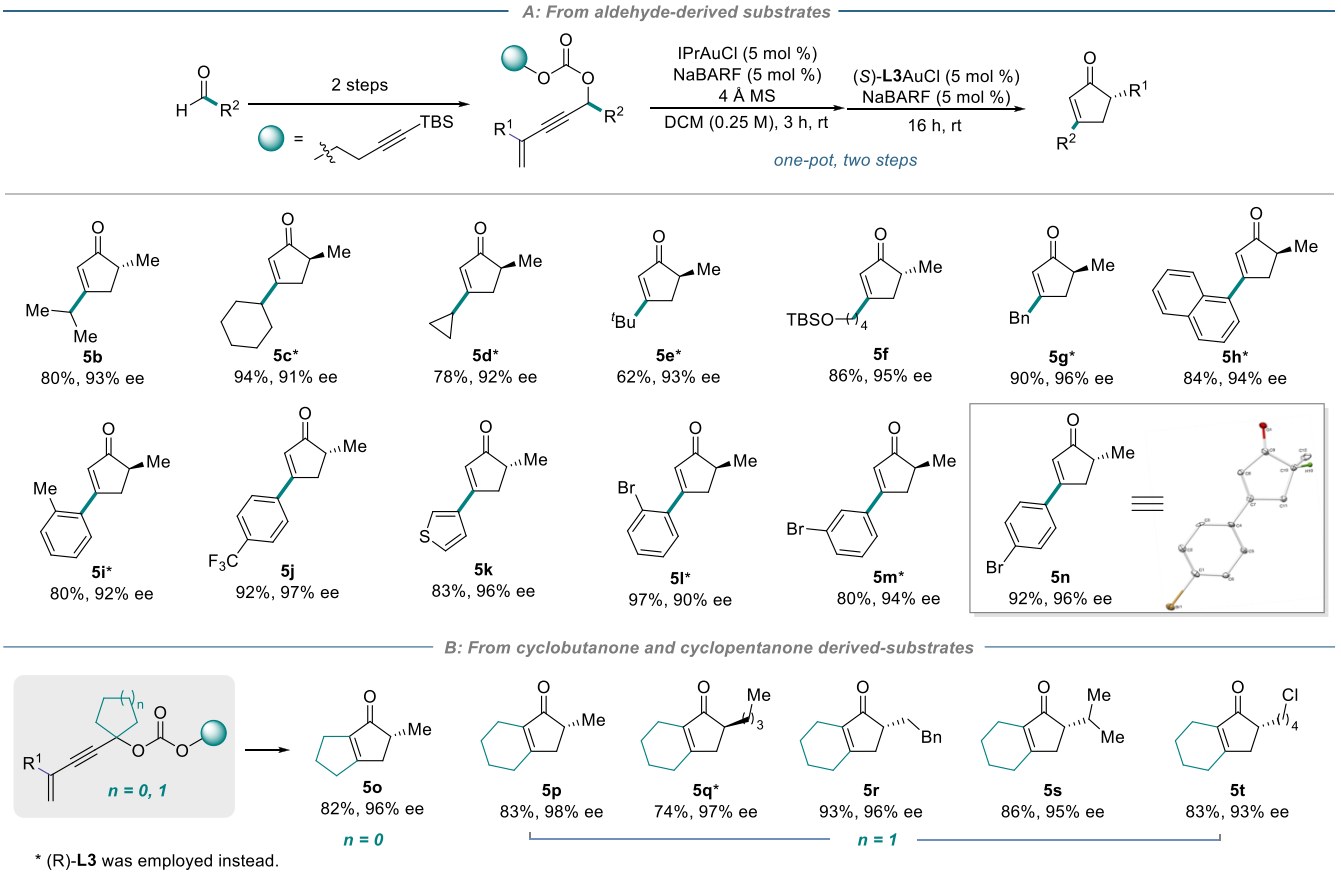
With the optimized conditions in hand, we explored the scope of this expedient access to chiral cyclopentenones. As shown in Table 3A, a variety of substituents at the cyclopentenone β-position were tolerated and afforded the desired chiral cyclopentenones **5b**−**5n** in moderate to excellent yields and with mostly excellent enantioselectivities. Primary, secondary, and tertiary alkyl groups in **5a** −**5e** were all well tolerated. The chemistry readily accommodated a TBS-protected hydroxyl group and a benzyl group to afford the cyclopentanones **5f** and **5g** in high yields and with 95% ee and 96% ee, respectively. Various aryl substituents were allowed (**5h**−**5n**). The electronic characteristics of the benzene ring had no significant effect on the reaction efficiency or selectivity, and **5h**−**5j** were isolated in high optical purity. In addition, the thiophene of **5k** did not affect the reaction. With the substrates bearing a bromo group at the *ortho-*, *meta-*, and *para*-positions of a benzene ring, the desired products **5l**−**5n** were formed smoothly in good yields and with 90%, 94%, and 96% ee, respectively. The comparably lower ee of **5l** (90%) is attributed to steric hindrance. In some cases, (*R*)-**L3** was employed as the ligand. The absolute configuration of **5n** possessing a *para*-bromophenyl group is established as (*R*) by single crystal XRD studies (CCDC 2285067). This stereochemical outcome again supports the stereoinduction model in **B** shown in Scheme 1C. The configurations of other cyclopentenones **5** were similarly assigned.

One limitation of the scope in Table 3A is that the α'-substituent is a methyl group. Replacing it with a bigger primary alkyl group led to <85% ee. We attribute this to the lack of a substituent at the α-C(sp^2) position, which makes facial control challenging. To expand the reaction scope, we probed the synthesis of ring-fused cyclopentenones. It is known that enynyl esters bearing cyclic quaternary centers at the propargyl position can undergo ring expansion through bond migration into a gold carbene center if the ring size is 4 or 5.[22] To this end, a cyclobutane-based substrate was smoothly converted to the 5,5-fused product **5o** in 82% yield with 96% ee (Table 3B). Similarly, cyclopentane-based substrates also performed well in this reaction, affording the 6,5-fused cyclopentenones **5p**−**5s** with excellent enantioselectivity. Remarkably, due to the presence of an α-C(sp^2) substitution, α'-substituents other than methyl including phenethyl (**5r**), isopropyl (**5s**), and 4-chlorobut-1-yl were readily accommodated.

We also screened a range of additives against the chemistry shown in Table 2.[23] It revealed that the reaction tolerated ester,

https://doi.org/10.1021/jacs.3c11919
J. Am. Chem. Soc. 2024, 146, 3598−3602

Table 3. Scope of Forming Chiral Cyclopentenones



tertiary amide, nitrile, *N*-acetylindole, nitrobenzene, and alcohol but not carboxylic acid nor base. The detailed results can be found in the SI.

In conclusion, we developed a gold-catalyzed highly enantioselective enolate protonation. Enabled by enantioselective gold–ligand cooperation, this catalysis converts cyclic ketone enol carbonates to enantiomerically enriched ketone products via internal proton shuttling. It permits the synthesis of challenging 2-methyl benzosuberone with excellent enantioselectivity. By preceding this chemistry with a one-pot gold-catalyzed formation of cyclopentadienyl carbonates, an expedient access to synthetically versatile chiral cyclopentenones from readily available enynyl carbonates was achieved. α'-Methylcyclopentenones featuring a range of β-substituents were formed with up to 97% ee, and 5- and 6-membered ring-fused cyclopentenones accommodating various α'-substituents were also formed with excellent enantioselectivities.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/jacs.3c11919.

Experimental details, compound characterization, and spectra (PDF)

Accession Codes

CCDC 2285067 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

■ AUTHOR INFORMATION

Corresponding Author

Liming Zhang − *Department of Chemistry & Biochemistry, University of California, Santa Barbara, Santa Barbara, California 93106, United States;* orcid.org/0000-0002-5306-1515; Email: zhang@chem.ucsb.edu

Authors

Kaylaa L. Gutman − *Department of Chemistry & Biochemistry, University of California, Santa Barbara, Santa Barbara, California 93106, United States*

Carlos D. Quintanilla − *Department of Chemistry & Biochemistry, University of California, Santa Barbara, Santa Barbara, California 93106, United States*

Complete contact information is available at: https://pubs.acs.org/10.1021/jacs.3c11919

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The authors thank NIGMS (R35GM139640) and NSF (CHE-2247934) for financial support and NSF (MRI-1920299) for the acquisition of Bruker 500 and 400 MHz NMR instruments.

REFERENCES

(1) Puddephatt, R. J. Gold. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon: Oxford, 1982; Chapter 15, pp 765−821.

(2) Murakami, M.; Inouye, M.; Suginome, M.; Ito, Y. Reactions of (Triphenylphosphine)Gold(I) Enolates and Homoenolates *Bull. Chem. Soc. Jpn.* **1988**, *61*, 3649−3652.

(3) (a) Noey, E. L.; Luo, Y.; Zhang, L.; Houk, K. N. Mechanism of Gold(I)-Catalyzed Rearrangements of Acetylenic Amine-N-Oxides: Computational Investigations Lead to a New Mechanism Confirmed by Experiment. *J. Am. Chem. Soc.* **2012**, *134*, 1078−1084. (b) Zhang, L. A Non-Diazo Approach to A-Oxo Gold Carbenes Via Gold-Catalyzed Alkyne Oxidation *Acc. Chem. Res.* **2014**, *47*, 877−888. (c) Sahani, R. L.; Patil, M. D.; Wagh, S. B.; Liu, R.-S. Catalytic Transformations of Alkynes into Either A-Alkoxy or A-Aryl Enolates: Mannich Reactions by Cooperative Catalysis and Evidence for Nucleophile-Directed Chemoselectivity. *Angew. Chem., Int. Ed.* **2018**, *57*, 14878−14882. (d) Wei, H.; Bao, M.; Dong, K.; Qiu, L.; Wu, B.; Hu, W.; Xu, X. Enantioselective Oxidative Cyclization/Mannich Addition Enabled by Gold(I)/Chiral Phosphoric Acid Cooperative Catalysis. *Angew. Chem., Int. Ed.* **2018**, *57*, 17200−17204. (e) Cai, J.; Wang, X.; Qian, Y.; Qiu, L.; Hu, W.; Xu, X. Gold-Catalyzed Oxidative Cyclization/Aldol Addition of Homopropargyl Alcohols with Isatins. *Org. Lett.* **2019**, *21*, 369−372. (f) Zhou, S.; Li, Y.; Liu, X.; Hu, W.; Ke, Z.; Xu, X. Enantioselective Oxidative Multi-Functionalization of Terminal Alkynes with Nitrones and Alcohols for Expeditious Assembly of Chiral α-Alkoxy-β-Amino-Ketones. *J. Am. Chem. Soc.* **2021**, *143*, 14703−14711.

(4) Roth, K. E.; Blum, S. A. Relative Kinetic Basicities of Organogold Compounds. *Organometallics* **2010**, *29*, 1712−1716.

(5) (a) Fehr, C. Enantioselective Protonation of Enolates and Enols. *Angew. Chem., Int. Ed.* **1996**, *35*, 2566−2587. (b) Mohr, J. T.; Hong, A. Y.; Stoltz, B. M. Enantioselective Protonation. *Nat. Chem.* **2009**, *1*, 359−369. (c) Poisson, T.; Oudeyer, S.; Brière, J.-F.; Levacher, V. Organocatalyzed Enantioselective Protonation. In *Enantioselective Organocatalyzed Reactions I: Enantioselective Oxidation, Reduction, Functionalization and Desymmetrization*; Mahrwald, R., Ed.; Springer: Dordrecht, the Netherlands, 2011; pp 67−106. (d) Oudeyer, S.; Brière, J.-F.; Levacher, V. Progress in Catalytic Asymmetric Protonation. *Eur. J. Org. Chem.* **2014**, *2014*, 6103−6119. (e) Min, C.; Seidel, D. Asymmetric Brønsted Acid Catalysis with Chiral Carboxylic Acids. *Chem. Soc. Rev.* **2017**, *46*, 5889−5902.

(6) (a) Zhang, Z.; Smal, V.; Retailleau, P.; Voituriez, A.; Frison, G.; Marinetti, A.; Guinchard, X. Tethered Counterion-Directed Catalysis: Merging the Chiral Ion-Pairing and Bifunctional Ligand Strategies in Enantioselective Gold (I) Catalysis. *J. Am. Chem. Soc.* **2020**, *142*, 3797−3805. (b) Franchino, A.; Martí, À.; Nejrotti, S.; Echavarren, A. M. Silver-Free Au(I) Catalysis Enabled by Bifunctional Urea- and Squaramide-Phosphine Ligands Via H-Bonding. *Chem. - Eur. J.* **2021**, *27*, 11989−11996. (c) Franchino, A.; Martí, À.; Echavarren, A. M. H-Bonded Counterion-Directed Enantioselective Au(I) Catalysis. *J. Am. Chem. Soc.* **2022**, *144*, 3497−3509.

(7) Cheng, X.; Zhang, L. Designed Bifunctional Ligands in Cooperative Homogeneous Gold Catalysis. *CCS Chem.* **2021**, *3*, 1989−2002.

(8) Wang, Y.; Zhu, J.; Durham, A. C.; Lindberg, H.; Wang, Y.-M. A-C−H Functionalization of Π-Bonds Using Iron Complexes: Catalytic Hydroxyalkylation of Alkynes and Alkenes. *J. Am. Chem. Soc.* **2019**, *141*, 19594−19599.

(9) (a) Wang, Z.; Wang, Y.; Zhang, L. Soft Propargylic Deprotonation: Designed Ligand Enables Au-Catalyzed Isomerization of Alkynes to 1,3-Dienes. *J. Am. Chem. Soc.* **2014**, *136*, 8887−8890. (b) Cheng, X.; Wang, Z.; Quintanilla, C. D.; Zhang, L. Chiral Bifunctional Phosphine Ligand Enabling Gold-Catalyzed Asymmetric Isomerization of Alkyne to Allene and Asymmetric Synthesis of 2,5-Dihydrofuran. *J. Am. Chem. Soc.* **2019**, *141*, 3787−3791.

(10) (a) Li, T.; Zhang, L. Bifunctional Biphenyl-2-Ylphosphine Ligand Enables Tandem Gold-Catalyzed Propargylation of Aldehyde and Unexpected Cycloisomerization. *J. Am. Chem. Soc.* **2018**, *140*, 17439−17443. (b) Li, T.; Cheng, X.; Qian, P.; Zhang, L. Gold-Catalysed Asymmetric Net Addition of Unactivated Propargylic C−H Bonds to Tethered Aldehydes. *Nat. Catal.* **2021**, *4*, 164−171.

(11) Claraz, A.; Leroy, J.; Oudeyer, S.; Levacher, V. Catalytic Enantioselective Protonation of Enol Trifluoroacetates by Means of Hydrogenocarbonates and Cinchona Alkaloids. *J. Org. Chem.* **2011**, *76*, 6457−6463.

(12) (a) Mohr, J. T.; Nishimata, T.; Behenna, D. C.; Stoltz, B. M. Catalytic Enantioselective Decarboxylative Protonation. *J. Am. Chem. Soc.* **2006**, *128*, 11348−11349. (b) Kingston, C.; Guiry, P. J. Enantiodivergent Synthesis of Tertiary A-Aryl 1-Indanones: Evidence toward Disparate Mechanisms in the Palladium-Catalyzed Decarboxylative Asymmetric Protonation. *J. Org. Chem.* **2017**, *82*, 3806−3819.

(13) Yanagisawa, A.; Sugita, T.; Yoshida, K. Enantioselective Protonation of Alkenyl Trifluoroacetates Catalyzed by Chiral Tin Methoxide. *chem. - Eur. J.* **2013**, *19*, 16200−16203.

(14) Poisson, T.; Dalla, V.; Marsais, F.; Dupas, G.; Oudeyer, S.; Levacher, V. Organocatalytic Enantioselective Protonation of Silyl Enolates Mediated by Cinchona Alkaloids and a Latent Source of Hf. *Angew. Chem., Int. Ed.* **2007**, *46*, 7090−7093.

(15) Cheon, C. H.; Kanno, O.; Toste, F. D. Chiral Brønsted Acid from a Cationic Gold(I) Complex: Catalytic Enantioselective Protonation of Silyl Enol Ethers of Ketones. *J. Am. Chem. Soc.* **2011**, *133*, 13248−13251.

(16) Claraz, A.; Landelle, G.; Oudeyer, S.; Levacher, V. Asymmetric Organocatalytic Protonation of Silyl Enolates Catalyzed by Simple and Original Betaines Derived from Cinchona Alkaloids *Eur. J. Org. Chem.* **2013**, *2013*, 7693−7696.

(17) (a) Fogassy, G.; Tungler, A.; Lévai, A. Enantioselective Hydrogenation of Exocyclic α,β-Unsaturated Ketones: Part Iii. Hydrogenation with Pd in the Presence of Cinchonidine. *J. Molecul. Catal. A: Chem.* **2003**, *192*, 189−194. (b) Sípos, É.; Fogassy, G.; Tungler, A.; Samant, P. V.; Figueiredo, J. L. Enantioselective Hydrogenations with Highly Mesoporous Carbon Supported Pd Catalysts. *J. Molecul. Catal. A: Chem.* **2004**, *212*, 245−250. (c) Hou, M.; Lin, L.; Chai, X.; Zhao, X.; Qiao, B.; Jiang, Z. Enantioselective Photoredox Dehalogenative Protonation. *Chem. Sci.* **2019**, *10*, 6629−6634. (d) Kong, M.; Tan, Y.; Zhao, X.; Qiao, B.; Tan, C.-H.; Cao, S.; Jiang, Z. Catalytic Reductive Cross Coupling and Enantioselective Protonation of Olefins to Construct Remote Stereocenters for Azaarenes. *J. Am. Chem. Soc.* **2021**, *143*, 4024−4031.

(18) Trost, B. M.; Xu, J.; Schmidt, T. Palladium-Catalyzed Decarboxylative Asymmetric Allylic Alkylation of Enol Carbonates. *J. Am. Chem. Soc.* **2009**, *131*, 18343−18357.

(19) Zhang, L.; Wang, S. Efficient Synthesis of Cyclopentenones from Enynyl Acetates Via Tandem Au(I)-Catalyzed 3,3-Rearrangement and the Nazarov Reaction. *J. Am. Chem. Soc.* **2006**, *128*, 1442−1443.

(20) (a) Spencer, W. T., III; Vaidya, T.; Frontier, A. J. Beyond the Divinyl Ketone: Innovations in the Generation and Nazarov Cyclization of Pentadienyl Cation Intermediates. *Eur. J. Org. Chem.* **2013**, *2013*, 3621−3633. (b) Simeonov, S. P.; Nunes, J. P. M.; Guerra, K.; Kurteva, V. B.; Afonso, C. A. M. Synthesis of Chiral Cyclopentenones. *Chem. Rev.* **2016**, *116*, 5744−5893.

(21) Yan, B.; Spilling, C. D. Synthesis of Cyclopentenones Via Intramolecular Hwe and the Palladium-Catalyzed Reactions of Allylic Hydroxy Phosphonate Derivatives. *J. Org. Chem.* **2008**, *73*, 5385−5396.

(22) Lemiere, G.; Gandon, V.; Cariou, K.; Hours, A.; Fukuyama, T.; Dhimane, A. L.; Fensterbank, L.; Malacria, M. Generation and Trapping of Cyclopentenylidene Gold Species: Four Pathways to Polycyclic Compounds. *J. Am. Chem. Soc.* **2009**, *131*, 2993−3006.

(23) Collins, K. D.; Glorius, F. A Robustness Screen for the Rapid Assessment of Chemical Reactions. *Nat. Chem.* **2013**, *5*, 597−601.

https://doi.org/10.1021/jacs.3c11919
J. Am. Chem. Soc. 2024, 146, 3598−3602