Exploring Pd-Catalyzed Enantioselective Hydroalkynylation of Cyclopropenes

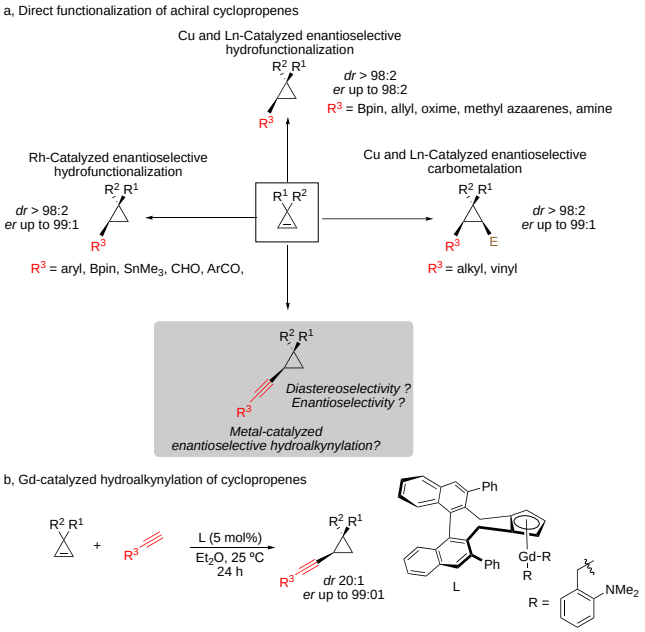
Nkosi T. Mthembu & Zanele P. Khumalo*

Faculty of Chemistry, University of Cape Town, Cape Town, 7701, South Africa

ABSTRACT: We are reporting herein an easy, mild and robust Pd-catalyzed enantioselective hydroalkynylation reaction of achiral cyclopropenes. Commercially available Pd(acac)2 and (*R*)-DM-BINAP proved to be the best combination to reach high diastereo- and enantioselectivities.

KEYWORDS: *enantioselective, hydroalkynylation, cyclopropenes, cyclopropanes, palladium*

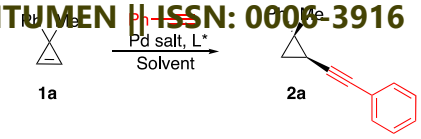
The diastereo- and enantioselective addition of organometallic species across unactivated 1,2-disubstituted double bonds (carbometalation) still stands nowadays as one of the most challenging transformations in organic synthesis.[1] Due to the release of ring-strain, the addition on cyclopropenes represents a particular but successful case providing a new entry to a large variety of polysubstituted enantioenriched cyclopropanes.[2] In this context, and since the pioneering work of Lautens,[3] Fox[4] and Nakamura,[5] the direct functionalization of achiral unsaturated[6] three-membered carbocycles have attracted a lot of attention.[7] We and others have reported the catalytic enantioselective copper-, rhodium- and lanthanides-catalyzed addition of sp^3 and sp^2-hydridized alkyl groups[8-10] as well as the addition of heteroelements[10a,11] in excellent diastereo- and enantioselectivities (Scheme 1a). However, an important but still missing transformation in this arsenal of direct functionalization of achiral unsaturated three-membered carbocycles was the introduction of alkynyl groups[12] until the very recent report of Hou describing the highly diastereo- and enantioselective half-sandwich gadolinium-catalyzed enantioselective hydroalkynylation of cyclopropenes (Scheme 1b).[13] As diastereo- and enantiomerically pure alkynyl cyclopropanes are motifs present in several natural products[14] and are considered as important building blocks in the construction of more complex skeletons,[15] we wanted to develop an alternative, more efficient and easiest approach to reach these scaffolds with high selectivities. The availability of palladium complexes combined with their robustness, ease of preparation and manipulation, high functional group tolerance were key factors to investigate the Pd-catalyzed alkynylation reaction of cyclopropenes.[16] Additionally, and at the opposite of gadolinium complexes, most palladium (pre)catalysts can easily be handled outside a glove-box advocating for their user-friendliness.



Scheme 1. Direct functionalization of achiral unsaturated cyclopropenes.

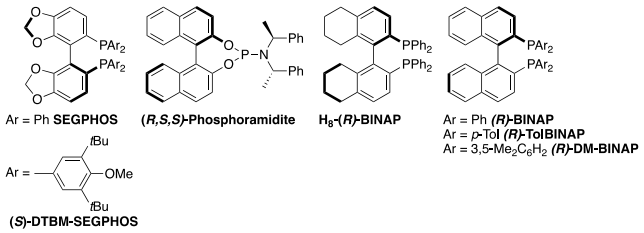
Cyclopropene **1a** and commercially available phenylacetylene were used as model substrates to explore the diastereo- and enantioselective Pd-catalyzed hydroalkynylation reaction. Various parameters such as nature of the (i) catalyst, (ii) chiral ligand, (iii) solvent were screened as shown in Table 1 (See supporting information for full details). Our preliminary experiment was performed with $Pd(OAc)_2$ as catalyst and (*S*)-DTBM-SEGPHOS as ligand in $(CH_2Cl)_2$ for 16 h. Under this experimental condition, we were pleased to observe that alkynylated cyclopropane **2a** was formed with a moderate enantiomeric ratio (Table 1, entry 1, *er* 64:36).

Table 1 Optimization of the Pd-catalyzed asymmetric hydroalkynylation of cyclopropene 1a.



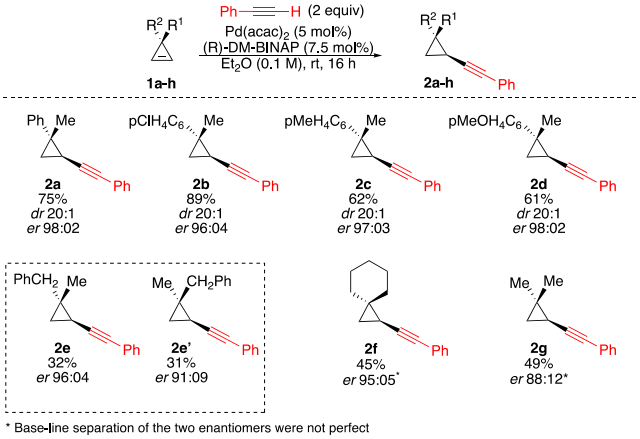
Entry	Pd salt	L*	Solvent	*er*[b]
1	$Pd(OAc)_2$	(*S*)-DTBM-SEGPHOS	DCE	36:64
2	$Pd(OAc)_2$	(*R,S,S*)-phosphoramidite	DCE	57:43
3	$Pd(OAc)_2$	H_8-(*R*)-BINAP	DCE	85:15
4	$Pd(OAc)_2$	(*R*)-BINAP	DCE	70:30
5	$Pd(OAc)_2$	(*R*)-Tol-BINAP	DCE	71:29
6	$Pd(OAc)_2$	(*R*)-DM-BINAP	DCE	86:14
7	$Pd(OAc)_2$	(*R*)-DM-BINAP	DCM	94:06
8[c]	$Pd(OAc)_2$	(*R*)-DM-BINAP	MeCN	ND
9[c]	$Pd(OAc)_2$	(*R*)-DM-BINAP	toluene	ND
10	$Pd(OAc)_2$	(*R*)-DM-BINAP	Et_2O	93:07
11	$Pd(OAc)_2$	(*R*)-DM-BINAP	THF	94:06
12	$Pd(OAc)_2$	(*R*)-DM-BINAP	DCM	90:10
13	$Pd(acac)_2$	(*R*)-DM-BINAP	DCM	95:05
14	$Pd(dpa)_2$	(*R*)-DM-BINAP	DCM	93:07
15	$(PdAllylCl)_2$	(*R*)-DM-BINAP	DCM	60:40
16	**$Pd(acac)_2$**	**(*R*)-DM-BINAP**	**Et_2O**	**98:02**[a]
17	$Pd(acac)_2$	(*R*)-DM-BINAP	THF	96:04
18[c]	$Pd(acac)_2$	(*R*)-DM-BINAP	DMF	ND
19[c]	$Pd(acac)_2$	(*R*)-DM-BINAP	DMSO	ND
20	$Pd(acac)_2$	(*R*)-DM-BINAP	acetone	93:07

[a] The reactions were run on a 0.05 mmol scale using 2 equivalent of the alkyne, Pd salt (5 mol%), L* (7.5 mol%) in the corresponding solvent (0.1 M) and the reaction mixture was stirred at room temperature for 16 h. In all cases, conversion was higher than 70%. [b] Determined by chiral HPLC. [c] No detection of the desired product **2a**, cyclopropene **1a** was recovered.



Based on this initial finding, different chiral ligands were evaluated (Table 1, entries 2 to 6) and the commercially available (*R*)-DM-BINAP was found to be the best ligand (Table 1, entry 6, *er* 86:14). Using (*R*)-DM-BINAP as the most effective ligand, different solvents were tested (Table 1, entries 7-11) and DCM, THF or Et_2O provided similar selectivities. Further additional screening of palladium salts and solvents (Table 1, entries 12-20) revealed that the ideal combination was $Pd(acac)_2$ with (*R*)-DM-BINAP in Et_2O (Table 1, entry 16). The desired alkynylcyclopropane **2a** was obtained in excellent enantio- and diastereoselectivity (er 98:02, dr 20:1). Having established the best experimental conditions for a mild Pd-catalyzed diastereo- and enantioselective hydroalkynylation reaction of achiral cyclopropenes **1a**, we then explored the nature of the substituents of the three-membered rings on the selectivity of the reaction.

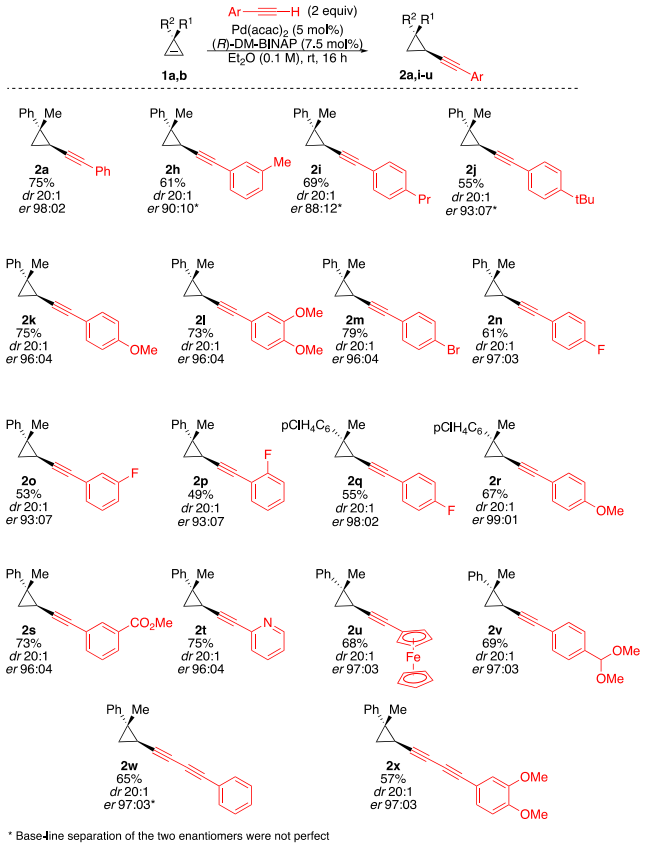
As shown in Scheme 2, cyclopropenes bearing electron-withdrawing or donating groups gave the corresponding hydroalkynylated cyclopropanes **2b-d** in good yields with constantly excellent diastereo- and enantioselectivity. When the cyclopropene possessing a benzyl group was treated in our experimental condition (**1e**, R^1 = Me, R^2 = CH_2Ph), the desired alkynyl cyclopropanes **2e** and **2e′** were isolated with good to excellent enantiomeric ratios but as an equimolar diastereoisomeric mixture of products, easily obtained independently by purification by column chromatography. Furthermore, cyclopropenes possessing identical groups on C_3 could easily be transformed into the expected products in high enantioselectivity (**2f**, Scheme 2), underlining that the aromatic ring present on the cyclopropenyl ring is not mandatory to reach good enantioselectivity.



Scheme 2. Pd-catalyzed enantioselective hydroalkynylation of cyclopropenes.

Encouraged by this result, the simplest dimethyl cyclopropene was prepared and submitted to our catalytic Pd-catalyzed enantioselective alkynylation reaction. We were pleased to find that the desired alkynylated cyclopropane **2g** could be isolated in moderate yield with a promising enantiomeric ratio of 88:12. In the last two cases, a substitution on C1 of the cyclopropenyl ring would lead to the creation of two quaternary stereocenters. Unfortunately, in this case, our catalytic procedure doesn't work anymore. Stimulated by these positive results, we then turned our attention to the nature of the nucleophilic alkynyl groups that could be introduced. A series of different substituted aromatic acetylenes were added to cyclopropane **1a** and in all cases, excellent selectivities were observed. Alkyl substituents could either be in a *meta* or *para* position of the aromatic ring without drastically altering the diastereo- and enantioselectivity (Scheme 3, compare 2h with **2i** and **2j**). Electron-donating groups provided the expected alkynylated cyclopropanes (**2k** and **2l**) with identical enantiomeric ratios. It is worth mentioning that electron-deficient para-bromo- phenyl acetylene could also be tolerated in this transformation and afford the desired cyclopropane **2m** in 79% yield with

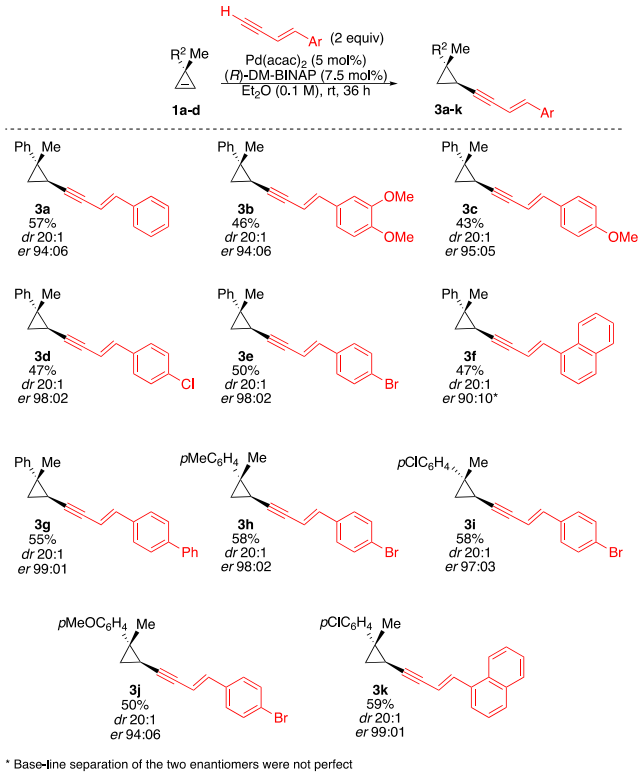
excellent diastereo- and enantioselective control (dr 20:1, er 96:04). Interestingly, ortho, meta and para-fluoro phenyl acetylene gave the desired fluoro-containing enantiomerically enriched alkynyl cyclopropanes (Scheme 3, **2n-2p**) also with excellent stereocontrol. To establish the absolute configuration of the alkynyl cyclopropanes, product **2r** has been prepared and the configuration was determined by X-ray diffraction analysis.[17] All other absolute configurations of products have been assigned by analogy.[18]



Scheme 3. Pd-catalyzed enantioselective hydroalkynylation reaction of cyclopropenes with different terminal alkynes.

Various functional groups present on the alkynyl part can be also tolerated such as ester, ferrocene, pyridine and acetal, (Scheme 3, **2s-v**). An important extension of this approach is the catalytic enantioselective addition of 1,3-butadiyn-1-ylbenzene. In the two examined cases (Scheme 3, **2w** and **2x**), the diynyl cyclopropanes were obtained in excellent diastereo- and enantioselectivities. It should be noted that TMS-substituted alkynes led to nearly racemic products with (*R*)-DM-BINAP whereas alkyl-substituted alkynes didn't lead to the expected products.

Encouraged by the excellent selectivity of the last two examples in Scheme 3, we were then wondering if this approach could be extended to more challenging systems and we were particularly interested in the catalytic enantioselective addition of conjugated enynes. Thus, a series of enynes were synthesized and tested in our standard condition (Scheme 4). To our delight, the cyclopropanes **3a-k** were isolated in moderate yields but in excellent diastereo- and enantioselectivity (*dr* 20:1, *er* up to 99:01). For instance, the Pd-catalyzed enantioselective addition of (*E*)-4-phenyl-3-buten-1-yne to **1a** provided the product **3a** in 57% with 94:06 enantiomeric ratio. Variously substituted aromatic ring can be used without altering the diastereo- and enantioselectivities.



Scheme 4. Pd-catalyzed enantioselective hydroalkynylation reaction of cyclopropenes with terminal enynes.

In conclusion, we have developed a friendly and easy to use Pd-catalyzed enantioselective hydroalkynylation reaction of achiral cyclopropenes by addition of different terminal alkynes, diynes and enynes with $Pd(acac)_2$ and commercially available (*R*)-DM-BINAP as chiral ligand with excellent diastereo- and enantioselectivity. This hydroalkynylation reaction provides a simple, mild and atom-economy approach towards a large variety of enantiomerically enriched alkynylated cyclopropanes.

AUTHOR INFORMATION

Corresponding Author

*E-mail: chilanm@technion.ac.il

ORCID

Ilan Marek: 0000-0001-9154-2320

Notes

The authors declare no competing financial interest.

■ ASSOCIATED CONTENT

● Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acscatal.xxxx.
Experimental procedures, instrumentation used, conditional screening, ligands used, ^{1}H and ^{13}NMR spectra of all new compounds, HPLC traces of racemic and enantiomerically pure compounds (PDF)
Crystallographic data of **2r** (CIF)

■ ACKNOWLEDGMENT

I.M. is holder of the Sir Michael and Lady Sobell Academic Chair. This project has received funding from the European Union's Horizon 2020 research and innovation program under grant agreement no. 786976 and by the Ministry of Science and Technology (grant No 330/17).

■ REFERENCES

(1) For selected reviews, see: (a) Marek I. Enantioselective Carbometallation of Unactivated Olefins. *J. Chem. Soc. Perkin Trans. 1*, **1999**, 535-544. (b) Müller D. S.; Marek I. Copper Mediated Carbometalation Reactions. *Chem. Soc. Rev*. **2016**, *45*, 4552-4566. (c) Shimizu Y.; Kanai M. Recent Progress in Copper-Catalyzed Difunctionalization of Unactivated Carbon-Carbon Multiple Bonds. *Tetrahedron Lett*. **2014**, *55*, 3727-3737.

(2) (a) Simaan S.; Marek I. Stereodivergent Carbometalation Reactions of Cyclopropenylcarbinol Derivatives. *Org. Lett*. **2007**, *9*, 2569-2571. (b) Unger R.; Cohen T.; Marek I. Diastero- and Enantioselective Intramolecular Carbometalation Reaction. *Tetrahedron* **2010**, *66*, 4874-4881. (c) Didier D.; Delaye P.-O.; Simaan M.; Island B.; Eppe G.; Eijsberg H.; Kleiner A.; Knochel P.; Marek I. Modulable and Highly Diastereoselective Carbometalations of Cyclopropenes. *Chem. Eur. J*. **2014**, *20*, 1038-1048.

(3) Kramer K.; Leong P.; Lautens M. Enantioselective Palladium-Catalyzed Carbozincation of Cyclopropenes. *Org. Lett*. **2011**, *13*, 819-821.

(4) Liu X.; Fox J. M. Enantioselective, Facially Selective Carbomagnesation of Cyclopropenes. *J. Am. Chem. Soc*. **2006**, *128*, 5600-5601.

(5) (a) Nakamura M.; Arai M.; Nakamura E. Carbometalation of Cyclopropene. Ligand-Induced Enantioselective Allylzincation. *J. Am. Chem. Soc*. **1995**, *117*, 1179-1180. (b) Nakamura M.; Inoue T.; Sato A.; Nakamura E. Asymmetric Construction of Quaternary Carbon Centers by Regio- and Enantiocontrolled Allylzincation. *Org. Lett*. **2000**, *2*, 2193-2196.

(6) Binger P.; Cetinkaya M.; Doyle M. J.; Germer A.; Schuchardt U. (1985) Reaction-Modes of Unsaturated Three-Membered Carbocycles at Transition-Metal-Catalysts. In: Tsutsui M., Ed.; Fundamental Research in Homogeneous Catalysis. Springer, Boston, MA **1985**, p. 271.

(7) Dian L.; Marek I. Asymmetric Preparation of Polysubstituted Cyclopropanes Based on Direct Functionalization of Achiral Three-Membered Carbocycles. *Chem. Rev*. **2018**, *118*, 8415-8434.

(8) (a) Müller D. S.; Marek I. Asymmetric Copper-Catalyzed Carbozincation of Cyclopropenes En Route to the Formation of Diastereo- and Enantiomerically Enriched Polysubstituted Cyclopropanes. *J. Am. Chem. Soc*. **2015**, *137*, 15414-15417. (b) Dian L.; Müller D. S.; Marek I. Asymmetric Copper-Catalyzed Carbomagnesiation of Cyclopropenes. *Angew. Chem. Int. Ed*. **2017**, *56*, 6783-6787. (c) Simaan M.; Marek I. Asymmetric Catalytic Preparation of Polysubstituted Cyclopropanes and Cyclopropylamine Derivatives. *Angew. Chem. Int. Ed*. **2018**, *57*, 1543-1546. (d) Sommer H.; Marek I. Diastereo- and Enantioselective Copper Catalyzed Hydroallylation of Disubstituted Cyclopropenes. *Chem. Sci.* **2018**, *9*, 6503-6508.

(9) (a) Müller D. S.; Werner V.; Akyol, S.; Schmalz H.-G.; Marek I. Tandem Hydroalumination/Cu-Catalyzed Asymmetric Vinyl metalation as a New Access to Enantioenriched Vinylcyclopropane Derivatives. *Org. Lett*. **2017**, *19*, 3970-3973. (b) Dian L.; Marek I. Rhodium-Catalyzed Arylation of Cyclopropenes Based on Asymmetric Direct Functionalization of Three-Membered Carbocycles. *Angew. Chem. Int. Ed.* **2018**, *57*, 3682-3686. (c) Phan D. H. T.; Kou, K. G. M.; Dong V. M. Enantioselective Desymmetrization of Cyclopropenes by Hydroacylation. *J. Am. Chem. Soc*. **2010**, *132*, 16354-16355. (d) Sherrill W. M.; Rubin M. Rhodium-Catalyzed Hydroformylation of Cyclopropenes. *J. Am. Chem. Soc*. **2008**, *130*, 13804-13809. (e) Liu F.; Bugaut, X.; Schedler, M.; Fróhlich, R.; Glorius, F. Designing *N*–Heterocyclic Carbenes: Simultaneous Enhancement of Reactivity and Enantioselectivity in the Asymmetric Hydroacylation of Cyclopropenes. *Angew. Chem. Int. Ed*. **2011**, *50*, 12626-12630. (f) Zhang H.; Huang W.; Wang T.; Meng F. Cobalt-Catalyzed Diastereo- and Enantioselective Hydroalkenylation of Cyclopropenes with Alkenylboronic Acids. *Angew. Chem. Int. Ed*. **2019**, *58*, 11049-11053. (i) Li Z.; Zhang M.; Zhang Y.; Liu S.; Zhao J.; Zhang Q. Multicomponent Cyclopropane Synthesis Enabled by Cu-Catalyzed Cyclopropene Carbometalation with Organoboron Reagent: Enantioselective Modular Access to Polysubstituted 2-Arylcyclopropylamines. *Org. Lett.* **2019**, *21*, 5432-5437.

(10) (a) Teng, H.-L.; Luo, Y.; Wang, B.; Zhang, L.; Nishiura, M.; Hou, Z. Synthesis of Chiral Aminocyclopropanes by Rare-Earth-Metal-Catalyzed Cyclopropene Hydroamination. Angew. Chem., Int. Ed. 2016, 55, 15406-15410. (b) Teng, H.-L.; Luo, Y.; Nishiura, M.; Hou, Z. Diastereodivergent Asymmetric Carboamination/Annulation of Cyclopropenes with Aminoalkenes by Chiral Lanthanum Catalysts. J. Am. Chem. Soc. 2017, 139, 16506-16509. (c) Luo, Y.; Teng, H.-L.; Nishiura, M.; Hou, Z. Asymmetric Yttrium-Catalyzed C(sp3)–H Addition of 2-Methyl Azaarenes to Cyclopropenes. Angew. Chem., Int. Ed. 2017, 56, 9207-9210.

(11) (a) Parra, A.; Amenós, L.; Guisan-Ceinos, M.; López, A.; Garció Ruano, J. L.; Tortosa, M. Copper-Catalyzed Diastereo-and Enantioselective Desymmetrization of Cyclopropenes: Synthesis of Cyclopropylboronates. *J. Am. Chem. Soc*. **2014**, *136*, 15833-15836. (b) Tian, B.; Liu, Q.; Tong, X.; Tian, P.; Lin, G. Q. Copper (I)-Catalyzed Enantioselective Hydroboration of Cyclopropenes: Facile Synthesis of Optically Active Cyclopropylboronates. *Org. Chem. Front*. **2014**, *1*, 1116-1122. (c) Rubina, M.; Rubin, M.; Gevorgyan, V. Catalytic Enantioselective Hydroboration of Cyclopropenes. *J. Am. Chem. Soc*. **2003**, *125*, 7198-7199. (d) Edwards, A. Rubina, M. Rubin, M. Directed Rh^{I}-Catalyzed Asymmetric Hydroboration of Prochiral 1-Arylcycloprop-2-Ene-1-Carboxylic Acid Derivatives. *Chem. Eur. J*. **2018**, 24, 1394-1403. (e) Rubina, M. Rubin, M. Gevorgyan, V. Catalytic Enantioselective Hydrostannation of Cyclopropenes. *J. Am. Chem. Soc*. **2004**, *126*, 3688-3689. (f) Li, Z.; Zhao, J.; Sun, B.; Zhou, T.; Liu, M.; Liu, S.; Zhang, M.; Zhang, Q. Asymmetric Nitrone Synthesis via Ligand-Enabled Copper-Catalyzed Cope-Type Hydroamination of Cyclopropene with Oxime. *J. Am. Chem. Soc*. **2017**, *139*, 11702-11705.

(12) For asymmetric cyclopropanation strategies to prepare chiral alkynyl cyclopropanes, see: a) Davies, H. M. L.; Boebel, T. A. Asymmetric Synthesis of 1-Alkynylcyclopropane-1-Carboxylates. *Tetrahedron Lett*. **2000**, *41*, 8189-8192. (b) Du, H. F.; Long, J.; Shi, Y. A. Catalytic Asymmetric Simmons–Smith Cyclopropanation of Silyl Enol Ethers. Efficient Synthesis of Optically Active Cyclopropanol Derivatives. *Org. Lett*. **2006**, *8*, 2827-2829. For enantioselective hydroalkynylation of olefins or

allenes catalyzed by different transition metals, see (c) Shirakura, M.; Suginome, M. Nickel-Catalyzed Asymmetric Addition of Alkyne C–H Bonds across 1,3-Dienes Using Taddol-Based Chiral Phosphoramidite Ligands. *Angew. Chem. Int. Ed*. **2010**, *49*, 3827-3829. (d) Fan, B.-M.; Yang, Q.-J.; Hu, J.; Fan, C.-L.; Li, S.-F.; Yu, L.; Huang, C.; Tsang, W. W.; Kwong F. Y. Asymmetric Hydroalkynylation of Norbornadienes Promoted by Chiral Iridium Catalysts. *Angew. Chem. Int. Ed.* **2012**, *51*, 7821–7824. (e) Meng, F.; Jang, H.; Jung, B.; A. H. Hoveyda. Cu-Catalyzed Chemoselective Preparation of 2-(Pinacolato)boron-Substituted Allylcopper Complexes and their In Situ Site-, Diastereo-, and Enantioselective Additions to Aldehydes and Ketones. *Angew. Chem. Int. Ed.* **2013**, 52, 5046-5051.

(13) Teng, H.-L.; Ma, Y.; Zhan, G.; Nishiura, M.; Hou, Z. Asymmetric C(sp)–H Addition of Terminal Alkynes to Cyclopropenes by a Chiral Gadolinium Catalyst. *ACS Catal*. **2018**, *8*, 4705-4709.

(14) (a) Zampella, A.; D'Auria, M. V.; Minale, L.; Debitus, C.; Roussakis, C. Callipeltoside A: A Cytotoxic Aminodeoxy Sugar-Containing Macrolide of a New Type from the Marine Lithistida Sponge Callipelta sp. *J. Am. Chem. Soc*. **1996**, *118*, 11085-11088. (b) Zampella, A.; D'Auria, V.; Minale, L. Callipeltosides B and C, Two Novel Cytotoxic Glycoside Macrolides from a Marine Lithistida Sponge Callipelta sp. *Tetrahedron* **1997**, *53*, 3243-3248. (c) Trost, B. M.; Dirat, O.; Gunzner, J. L. Callipeltoside A: Assignment of Absolute and Relative Configuration by Total Synthesis. *Angew. Chem. Int. Ed*. **2002**, *41*, 841-843.

(15) (a) Zhang, J.; Schmalz, H.-G. Gold (I)-Catalyzed Reaction of 1-(1-Alkynyl)-cyclopropyl Ketones with Nucleophiles: A Modular Entry to Highly Substituted Furans. *Angew. Chem. Int. Ed*. **2006**, 45, 6704-6707. (b) Chen, A.; Lin, R.; Liu, Q.; Jiao, N. Fe-Catalyzed Highly Selective Ring Expansion of Alkynylcyclopropyl Alkanols to Cyclobutanols. *Chem. Commun*. **2009**, 6842-6844. (c) Yang, X.-H.; Song, R.-J.; Li, J.-H. Metal - Free [4+ 2] Annulation of Arylalkynes with *tert*-Butyl Nitrite through C(sp2)-H Oxidation to Assemble Benzo[e][1, 2]oxazin-4-ones. *Adv. Synth. Catal*. **2015**, *357*, 3849-3856. (d) Pan, D.; Wei, Y.; Shi, M. Rh(II)-Catalyzed Chemoselective Oxidative Amination and Cyclization Cascade of 1-(Arylethynyl)cycloalkyl)methyl Sulfamates. *Org. Lett*. **2017**, *19*, 3584-3587. (e) Li, J.-H.; Huang, Q.; Wang, S.-Y.; Ji, S.-J. Trisulfur Radical Anion ($S_3^{\bullet-}$) Involved [1 + 2 + 2] and [1 + 3 + 1] Cycloaddition with Aromatic Alkynes: Synthesis of Tetraphenylthiophene and 2-Benzylidenetetrahydrothiophene Derivatives. *Org. Lett*. **2018**, *20*, 4704-4708.

(16) For the racemic Pd-catalyzed hydroalkynylation of cyclopropenes, see: (a) Yin, J.; Chisholm, J. D. Palladium-Catalyzed Addition of Alkynes to Cyclopropenes. *Chem. Commun*. **2006**, 632-634. (b) Tenaglia, A.; Jeune, K. L.; Giordano, L.; Buono, G. Palladium-Catalyzed Addition of Alkynes to Cyclopropenes: an Entry to Stereodefined Alkynylcyclopropanes. *Org. Lett*. **2011**, *13*, 636-639. The only report of Pd-catalyzed enantioselective hydroalkynylation reaction on a double bond was reported on norbornadiene in 24-36% enantiomeric excess, see: (c) Gatineau, D.; Giordano, L.; Buono, G. *J. Am. Chem. Soc*. **2011**, *133*, 10728-10731.

(17) Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre, accession number **2r**:1897640.

(18) All compounds have very high positive values of optical rotation

TOC