OL | Organic Letters

Letter

Cite This: Org. Lett. XXXX, XXX, XXX−XXX

pubs.acs.org/OrgLett

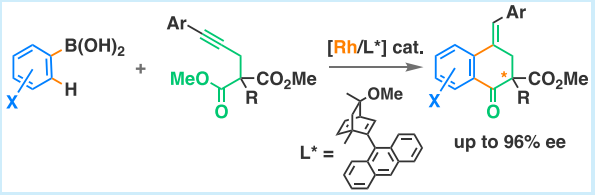
Enantioenriched 1-Tetralones via Rhodium-Catalyzed Arylative Cascade Desymmetrization/Acylation of Alkynylmalonates

Aymane Selmani and Sylvain Darses*

PSL Université Paris, Chimie ParisTech-CNRS, Institute of Chemistry for Life and Health Sciences (i-CLeHS), 11 rue Pierre et Marie Curie, 75005, Paris, France

Supporting Information

ABSTRACT: An efficient atom-economic rhodium-catalyzed asymmetric arylative cyclization to access enantioenriched 1-tetralones, bearing a quaternary carbon stereocenter, is described, involving a highly regioselective alkyne insertion, a 1,4-Rh shift, and an acylation step via the desymmetrization of the malonate moiety thanks to an appropriate chiral diene ligand.

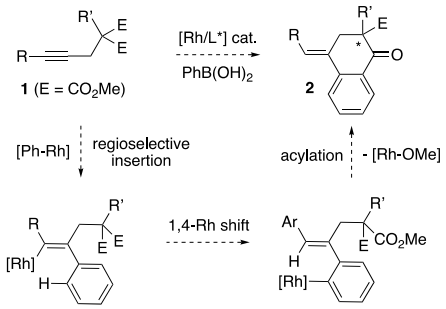


Enantioenriched 1-tetralones are useful building blocks in organic synthesis[1] and represent important scaffolds in a wide range of natural products and in molecules of medicinal and agrochemical interest.[2] While a variety of methodologies have been described to prepare racemic 1-tetralones,[3] the access routes to enantiomerically enriched 1-tetralones by asymmetric catalysis are more rare and consist mainly in the functionalization of the 2-position of already formed tetralones.[4] Given the importance of such substrates, more direct asymmetric and catalytic pathways for synthesizing the chiral 1-tetralone backbone in a single step, via the formation of multiple C−C bonds (cascade reaction) from simple substrates, would be highly desirable but are still in an early stage. Some approaches for the catalytic formation of chiral tetralones by intramolecular asymmetric cyclization reactions have been described, but require multiple steps and tedious preparation of the starting materials.[5] To our knowledge, the only catalytic and enantioselective approach involving the formation of multiple C−C bonds from simple substrates consists of Tamura cycloadditions between homophthalic anhydrides and nitroolefins[6] or α,β-unsaturated *N*-trityl imines.[7]

In our continuous work in rhodium-catalyzed arylative cyclization,[8] we sought to develop an enantioselective synthesis of chiral 1-tetralones from easily available propynylmalonates and arylboronic acids (Scheme 1). This strategy relies on a regioselective control of alkyne insertion, rhodium 1,4-shift[8c,d,9] to generate a new arylrhodium intermediate, and finally desymmetrization by reaction of the arylrhodium with one ester function, generating the ketone functionality and creating a valuable quaternary stereogenic center. Such an approach has been described by Murakami for the formation of racemic 1-tetralones using symmetrical alkynes, but a mixture of products, issued from nonregioselective insertion, was observed starting from unsymmetrical alkynes.[10]

Palladium- or rhodium-catalyzed arylative cyclizations of bifunctionalized substrates, initiated by organoboron reagents, constitute a versatile approach to construct complex chiral molecules,[8,11] but catalytic arylative cyclizations involving desymmetrization have been scarcely explored.[12]

Scheme 1. Proposed Approach to Chiral 1-Tetralones via Arylative Desymmetrization



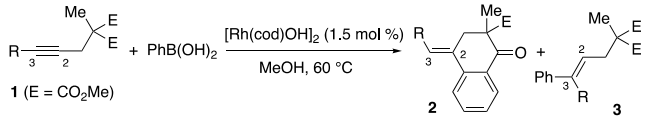
In order to access tetralones via the previously proposed approach (Scheme 1), it is essential to control the regioselectivity of the alkyne insertion. This regioselectivity can be modulated by tuning the steric and electronic properties of the R substituent.[13] We had previously shown that, in the presence of a 2-methylphenyl substituent, the aromatic ring of the boronic acid was introduced selectively into position 2 in the arylative cyclization of *N*-bridged yne-enoate derivatives.[8c] However, under conventional conditions, the cyclization of substrate **1**, where R is 2-methylphenyl, in the presence of phenylboronic acid leads to the formation of the expected tetralone **2** accompanied by uncyclized compound **3**, resulting from the reverse insertion, in a ratio of 2:1 (Table 1, entry 1).

In order to promote the selective formation of **2** over **3**, other R substituents have been evaluated (Table 1), an aliphatic substituent giving the opposite insertion.[8c] In the presence of a 4-trifluomethylphenyl substituent (entry 2), no cyclization occurred, and only regioisomers issued from the insertion/protonation process were observed. In order to force

Received: September 5, 2019

DOI: 10.1021/acs.orglett.9b03153
Org. Lett. XXXX, XXX, XXX−XXX

Table 1. Formation of 1-Tetralones by Forcing the Regioselectivity of Alkyne Insertion[a]



entry	R	yield[b]	2:3 ratio[c]
1	2-MeC_6H_4	90	2:1
2	4-$CF_3C_6H_4$	63	*d*
3	CO_2Me	*e*	–
4	2-Me-4-$CF_3C_6H_3$	72	2:1
5	2-*i*PrC_6H_4	56	2:1
6	1-Np	nd[f]	2:1
7	2-MeOC_6H_4	nd[f]	2:1
8	2,6-$Me_2C_6H_3$	nd[f]	2:1
9	2-$CF_3C_6H_4$	61	>99:1
10	2,4-$(CF_3)_2C_6H_3$	68	>99:1
11[g]	2,4-$(CF_3)_2C_6H_3$	75	>99:1

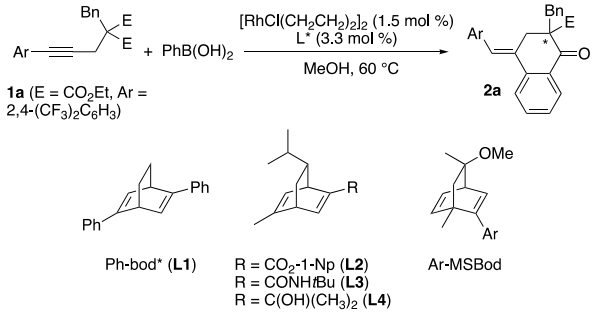
[a]The reaction was conducted with **1** (0.3 mmol), phenylboronic acid (0.6 mmol), and $[Rh(cod)OH]_2$ (1.5 mol %), in degassed methanol at 60 °C for 14 h. [b]Isolated yield. [c]Ratio determined by ^{1}H NMR. [d]1:2.5 ratio of **3** and its regioisomer. [e]Untractable mixture of products. [f]Not determined. [g]Benzyl substituent in place of methyl and E = CO_2Et.

the expected insertion through 1,4-addition, an ester substituent was tested (entry 3), but an untractable mixture of products was obtained. For most of the R substituents evaluated, the **2**:**3** ratio was not modified and remained desperately equal to 2:1 (entries 4–8). We were pleased to find that an aromatic substituent, bearing at least a trifluoromethyl group in the ortho position, afforded exclusively the expected tetralone **2** with a good yield (entries 9 and 10), cleaner reactions being observed in the case of 2,4-bis(trifluoromethyl)phenyl (entry 10). This observation seems general, as total regioselectivity, favoring the formation of tetralone **2**, is also observed when the methyl substituent on the malonate is replaced by a benzyl group (entry 11).

After this successful switch in the regioselective insertion of the alkyne moiety allowing selective formation of 1-tetralones from alkynylmalonates, we envisioned the development of an asymmetric version to access enantioenriched 1-tetralones (Table 2). Among the chiral ligands evaluated, only dienes led to acceptable enantiomeric excesses.[14] The disubstituted chiral dienes **L1**–**L4**, developed by Hayashi,[15] did not lead to satisfactory results in term of enantioselectivity, the ee being less than 50% (entries 1–4). It is only by the use of the C_1-symmetric chiral Ar-MSBod dienes[16] that significant enantioselectivities have been observed, in particular those bearing an aromatic disubstituted in both ortho positions (entries 5–11). We were pleased to find that the use of the chiral diene having an anthracen-9-yl substituent, a very bulky group, allowed not only an excellent yield but also a 85% enantiomeric excess in the arylative cyclization of alkynylmalonate **1a** (entry 11). It should be noted that the substituent on the ester function of the malonate has an influence on the enantioselectivity of the reaction: with dimethyl or diethyl malonates **1a** identical ee's were observed (85% ee) while, with a diisopropyl malonate, the enantiomeric excess is only 68%.

With these reaction conditions in hand, we examined the reactivity of diversely substituted alkynylmalonates **1** with arylboronic acids (Scheme 2). Alkynylmalonates bearing

Table 2. Chiral Dienes in the Desymmetrization of Alkynylmalonates[a]



entry	Ln or Ar-MSBod (Ar =)	yield[b] (%)	ee[c] (%)
1	**L1**	79	2
2	**L2**	77	42
3	**L3**	83	47
4	**L4**	80	46
5	1-Np	90	38
6	2-Me-4-MeOC_6H_3	78	45
7	2-*i*PrOC_6H_4	58	35
8	2,6-(*i*PrO)$_2C_6H_3$	67	13
9	2,6-$(Me)_2C_6H_3$	54	54
10	2,6-$(MeO)_2C_6H_3$	75	73
11	Anthracen-9-yl	94	85

[a]The reaction was conducted with **1a** (0.3 mmol) and phenylboronic acid (0.6 mmol), in the presence of in situ generated chiral L*–rhodium complex (3 mol % Rh) in degassed methanol at 60 °C. [b]Isolated yields. [c]Ee were determined by HPLC analysis using a chiral stationary phase (see Supporting Information).

aliphatic (Me, *n*Bu, or CH_2CH_2Ph) or benzyl substituents reacted smoothly to afford the expected chiral 1-tetralones with high yields and enantioselectivities ranging from 84% to 90%, depending on the arylboronic acid used. Even if tetralone **2d**, having a OBn substituent at the malonate junction, is obtained with a good yield, the enantiomeric excess is meanwhile moderate (64%). On the other hand, very good enantioselectivities have been obtained with NHAc or NHBoc substituents (85 to 96% ee), allowing an easy access to enantiomerically enriched cyclic exotic amino acids bearing a tetralone moiety. Compound **2f** was also obtained on a larger scale, starting from 1.2 mmol of starting material, with a 90% yield and no erosion of the enantioselectivity.

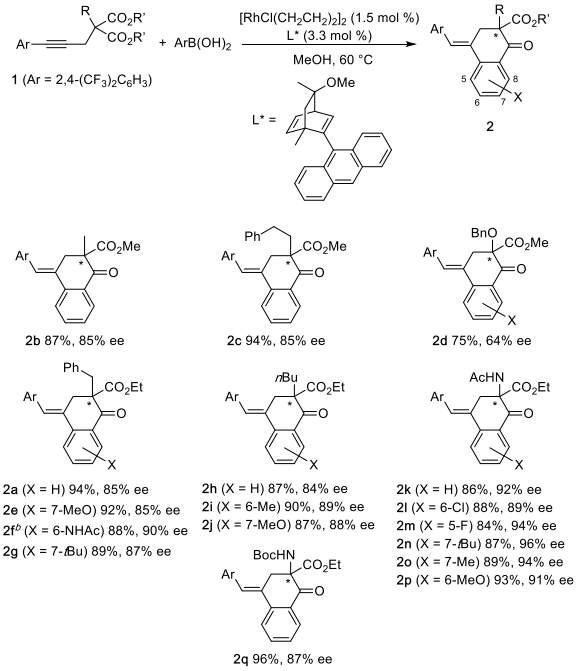
The structure of 1-tetralone **2j** was confirmed unambiguously by single-crystal X-ray analysis (Figure 1). The absolute configuration of the stereogenic center of **2j** was determined to be (*R*) when anthracen-9-yl-MSBod was used as ligand.

We next examined the reactivity of the 1-tetralones, which can further be functionalized thanks to its versatile functional groups such as an ester, a ketone, and an exocyclic olefin. As an illustration, the reactivity of the exocyclic double bond has been studied: the ruthenium-catalyzed oxidative cleavage[17] of tetralone **2p** gave the corresponding chiral dihydronaphthoquinone **3p** in 74% yield, with no erosion of the enantioselectivity, a motif prevalent in a wide range of natural and synthetic compounds (Scheme 3).[18]

In summary, we have described, for the first time, an efficient atom-economic asymmetric arylative cyclization to access chiral enantioenriched 1-tetralones bearing a quaternary carbon stereocenter. The success of the overall process relies on a highly regioselective alkyne insertion, a 1,4-Rh shift, and

DOI: 10.1021/acs.orglett.9b03153
Org. Lett. XXXX, XXX, XXX–XXX

Scheme 2. Chiral 1-Tetralones from Rh/Chiral Diene-Catalyzed Arylative Desymmetrization of 1[a]



[a]The reactions were conducted with **1** (0.3 mmol) and arylboronic acid (0.6 mmol), in the presence of in situ generated chiral L*–rhodium complex (3 mol % Rh) in degassed methanol at 60 °C. Isolated yields indicated and ee were determined by HPLC analysis using a chiral stationary phase (see Supporting Information). [b]90% yield and 90% ee on reaction conducted with 1.2 mmol of starting material.

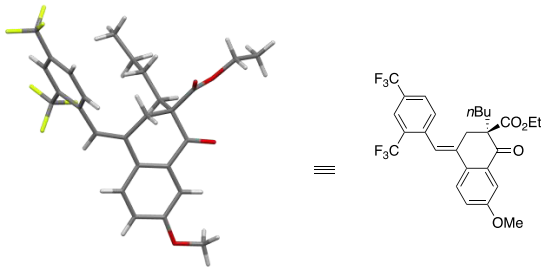
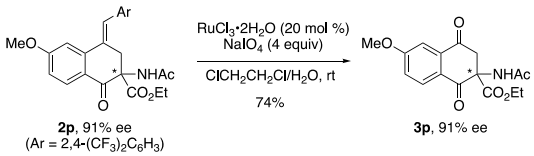


Figure 1. X-ray crystal structure of (*R*)-**2j**.

Scheme 3. Formation of Chiral Dihydronaphthoquinones



an acylation step via the desymmetrization of the malonate moiety thanks to an appropriate chiral diene ligand.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.9b03153.

Experimental procedures, description of the compounds, and X-ray diffraction of **2j** (PDF)

Accession Codes

CCDC 1926608 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

*E-mail: sylvain.darses@chimie-paristech.fr.

ORCID

Sylvain Darses: 0000-0003-3350-1736

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

A.S. thanks the Ministère de l'Éducation Nationale et de l'Enseignement Supérieur et de la Recherche for a grant. We gratefully acknowledge Geoffrey Gontard and Lise-Marie Chamoreau for the X-ray analyses (Sorbonne Université, Paris).

■ REFERENCES

(1) For some recent examples, see: (a) Taber, G. P.; Pfisterer, D. M.; Colberg, J. C. A New and Simplified Process for Preparing *N*-[4-(3,4-Dichlorophenyl)-3,4-dihydro-1(2H)-naphthalenylidene]methanamine and a Telescoped Process for the Synthesis of (1*S*-cis)-4-(3,4-Dichlorophenol)-1,2,3,4-tetrahydro-*N*-methyl-1-naphthalenamine Mandelate: Key Intermediates in the Synthesis of Sertraline Hydrochloride. *Org. Process Res. Dev.* **2004**, *8*, 385–388. (b) Yang, R.-Y.; Kizer, D.; Wu, H.; Volckova, E.; Miao, X.-S.; Ali, S. M.; Tandon, M.; Savage, R. E.; Chan, T. C. K.; Ashwell, M. A. Synthetic methods for the preparation of ARQ 501 (*β*-Lapachone) human blood metabolites. *Bioorg. Med. Chem.* **2008**, *16*, 5635–5643. (c) Pinto-Bazurco Mendieta, M. A. E.; Negri, M.; Jagusch, C.; Müller-Vieira, U.; Lauterbach, T.; Hartmann, R. W. Synthesis, Biological Evaluation, and Molecular Modeling of Abiraterone Analogues: Novel CYP17 Inhibitors for the Treatment of Prostate Cancer. *J. Med. Chem.* **2008**, *51*, 5009–5018. (d) Ortega, R.; Hübner, H.; Gmeiner, P.; Masaguer, C. F. Aromatic ring functionalization of benzolactam derivatives: New potent dopamine D3 receptor ligands. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 2670–2674. (e) Cueva, J. P.; Gallardo-Godoy, A.; Juncosa, J. I., Jr.; Vidi, P. A.; Lill, M. A.; Watts, V. J.; Nichols, D. E. Probing the Steric Space at the Floor of the D_1 Dopamine Receptor Orthosteric Binding Domain: 7*α*-,7*β*-,8*α*-, and 8*β*-Methyl Substituted Dihydrexidine Analogues. *J. Med. Chem.* **2011**, *54*, 5508–5521. (f) Odagi, M.; Furukori, K.; Takayama, K.; Noguchi, K.; Nagasawa, K. Total Synthesis of Rishirilide B by Organocatalytic Oxidative Kinetic Resolution: Revision of Absolute Configuration of (+)-Rishirilide B. *Angew. Chem., Int. Ed.* **2017**, *56*, 6609–6612. (g) Umihara, H.; Yokoshima, S.; Inoue, M.; Fukuyama, T. Total Synthesis of (−)-Morphine. *Chem. - Eur. J.* **2017**, *23*, 6993–6995.

(2) (a) Allen, J. G.; Danishefsky, S. J. The Total Synthesis of (±)-Rishirilide B. *J. Am. Chem. Soc.* **2001**, *123*, 351–352. (b) Charest, M. G.; Siegel, D. R.; Myers, A. G. Synthesis of (−)-Tetracycline. *J. Am. Chem. Soc.* **2005**, *127*, 8292–8293. (c) Yao, S.; Tang, C.-P.; Ke, C.-Q.; Ye, Y. Abietane Diterpenoids from the Bark of Cryptomeria fortunei. *J. Nat. Prod.* **2008**, *71*, 1242–1246. (d) Stoessl, A.; Stothers, J. B. Tetrahydroaltersolanol B, a hexahydroanthronol from Alternariasolani. *Can. J. Chem.* **1983**, *61*, 378–382. (e) Devkota, K. P.; Covell, D.; Ransom, T.; McMahon, J. B.; Beutler, J. A. Growth

DOI: 10.1021/acs.orglett.9b03153
Org. Lett. XXXX, XXX, XXX–XXX

Inhibition of Human Colon Carcinoma Cells by Sesquiterpenoids and Tetralones of Zygogynum calothyrsum. *J. Nat. Prod.* **2013**, *76*, 710−714. (f) Leng, J.; Qin, H.-L.; Zhu, K.; Jantan, I.; Hussain, M. A.; Sher, M.; Amjad, M. W.; Naeem-ul-Hassan, M.; Ahmad, W.; Bukhari, S. N. A. Evaluation of multifunctional synthetic tetralone derivatives for treatment of Alzheimer's disease. *Chem. Biol. Drug Des.* **2016**, *88*, 889−898. (g) Rajagopalan, N.; Nelson, K. M.; Douglas, A. F.; Jheengut, V.; Alarcon, I. Q.; McKenna, S. A.; Surpin, M.; Loewen, M. C.; Abrams, S. R. Abscisic Acid Analogues That Act as Universal or Selective Antagonists of Phytohormone Receptors. *Biochemistry* **2016**, *55*, 5155−5164. (h) Legoabe, L. J.; Van der Walt, M. M.; Terre'Blanche, G. Evaluation of 2-benzylidene-1-tetralone derivatives as antagonists of A_1 and A_2 adenosine receptors. *Chem. Biol. Drug Des.* **2018**, *91*, 234−244.

(3) For some examples, see: (a) Liard, A.; Quiclet-Sire, B.; Saicic, R. N.; Zard, S. Z. A new synthesis of α-tetralones. *Tetrahedron Lett.* **1997**, *38*, 1759−1762. (b) Nishimura, T.; Ohe, K.; Uemura, S. Oxidative Transformation of tert-Cyclobutanols by Palladium Catalysis under Oxygen Atmosphere. *J. Org. Chem.* **2001**, *66*, 1455−1465. (c) Yu, J.; Zhao, H.; Liang, S.; Bao, X.; Zhu, C. A facile and regioselective synthesis of 1-tetralones via silver-catalyzed ring expansion. *Org. Biomol. Chem.* **2015**, *13*, 7924−7927. (d) Xia, Y.; Lu, G.; Liu, P.; Dong, G. Catalytic activation of carbon−carbon bonds in cyclopentanones. *Nature* **2016**, *539*, 546−550. (e) Chang, S.; Holmes, M.; Mowat, J.; Meanwell, M.; Britton, R. α-Arylation and Ring Expansion of Annulated Cyclobutanones: Stereoselective Synthesis of Functionalized Tetralones. *Angew. Chem., Int. Ed.* **2017**, *56*, 748−752. (f) Arunprasath, D.; Devi Bala, B.; Sekar, G. Stereoselective Construction of α-Tetralone-Fused Spirooxindoles via Pd-Catalyzed Domino Carbene Migratory Insertion/Conjugate Addition Sequence. *Org. Lett.* **2017**, *19*, 5280−5283. (g) Plaza, M.; Paraja, M.; Florentino, L.; Valdés, C. Domino Synthesis of Benzo-Fused β,γ-Unsaturated Ketones from Alkenylboronic Acids and *N*-Tosylhydrazone-Tethered Benzonitriles. *Org. Lett.* **2019**, *21*, 632−635.

(4) For some examples, see: (a) Lan, Q.; Wang, X.; Shirakawa, S.; Maruoka, K. Phase-Transfer Catalyzed Asymmetric Conjugate Additions of β-Ketoesters to Acetylenic Ketones. *Org. Process Res. Dev.* **2010**, *14*, 684−686. (b) Odagi, M.; Furukori, K.; Watanabe, T.; Nagasawa, K. Asymmetric α-Hydroxylation of Tetralone-Derived β-Ketoesters by Using a Guanidine−Urea Bifunctional Organocatalyst in the Presence of Cumene Hydroperoxide. *Chem. - Eur. J.* **2013**, *19*, 16740−16745. (c) Roiban, G.-D.; Agudo, R.; Ilie, A.; Lonsdale, R.; Reetz, M. T. CH-activating oxidative hydroxylation of 1-tetralones and related compounds with high regio- and stereoselectivity. *Chem. Commun.* **2014**, *50*, 14310−14313. (d) Chen, W.; Chen, M.; Hartwig, J. F. Diastereo- and Enantioselective Iridium-Catalyzed Allylation of Cyclic Ketone Enolates: Synergetic Effect of Ligands and Barium Enolates. *J. Am. Chem. Soc.* **2014**, *136*, 15825−15828. (e) Odagi, M.; Furukori, K.; Yamamoto, Y.; Sato, M.; Iida, K.; Yamanaka, M.; Nagasawa, K. Origin of Stereocontrol in Guanidine-Bisurea Bifunctional Organocatalyst That Promotes α-Hydroxylation of Tetralone-Derived β-Ketoesters: Asymmetric Synthesis of β- and γ-Substituted Tetralone Derivatives via Organocatalytic Oxidative Kinetic Resolution. *J. Am. Chem. Soc.* **2015**, *137*, 1909−1915. (f) Sim, S.-B. D.; Wang, M.; Zhao, Y. Phase-Transfer-Catalyzed Enantioselective α-Hydroxylation of Acyclic and Cyclic Ketones with Oxygen. *ACS Catal.* **2015**, *5*, 3609−3612. (g) Yu, L.; Wu, X.; Kim, M. J.; Vaithiyanathan, V.; Liu, Y.; Tan, Y.; Qin, W.; Song, C. E.; Yan, H. Asymmetric Synthesis of 2-Thiocyanato-2-(1-aminoalkyl)-substituted 1-Tetralones and 1-Indanones with Tetrasubstituted Carbon Stereogenic Centers via Cooperative Cation-Binding Catalysis. *Adv. Synth. Catal.* **2017**, *359*, 1879−1891. (h) Shang, M.; Cao, M.; Wang, Q.; Wasa, M. Enantioselective Direct Mannich-Type Reactions Catalyzed by Frustrated Lewis Acid/Brønsted Base Complexes. *Angew. Chem., Int. Ed.* **2017**, *56*, 13338−13341. (i) Rao, X.; Li, N.; Bai, H.; Dai, C.; Wang, Z.; Tang, W. Efficient Synthesis of (−)-Corynoline by Enantioselective Palladium-Catalyzed α-Arylation with Sterically Hindered Substrates. *Angew. Chem., Int. Ed.* **2018**, *57*, 12328−12332.

(5) (a) Ishida, N.; Sawano, S.; Murakami, M. Synthesis of 3,3-disubstituted α-tetralones by rhodium-catalysed reaction of 1-(2-haloaryl)cyclobutanols. *Chem. Commun.* **2012**, *48*, 1973−1975. (b) Hu, Z.-P.; Zhuang, Z.; Liao, W.-W. Asymmetric Synthesis of Dihydronaphthoquinones Containing Adjacent Stereocenters via a Sulfa-Michael Addition Triggered Ring-Expansion Approach. *J. Org. Chem.* **2015**, *80*, 4627−4637. (c) Zhang, G.; Yang, S.; Zhang, X.; Lin, Q.; Das, D. K.; Liu, J.; Fang, X. Dynamic Kinetic Resolution Enabled by Intramolecular Benzoin Reaction: Synthetic Applications and Mechanistic Insights. *J. Am. Chem. Soc.* **2016**, *138*, 7932−7938.

(6) Nath, U.; Pan, S. C. Organocatalytic Asymmetric Tamura Cycloaddition with α-Branched Nitroolefins: Synthesis of Functionalized 1-Tetralones. *J. Org. Chem.* **2017**, *82*, 3262−3269.

(7) Collar, A. G.; Trujillo, C.; Connon, S. J. Highly Enantio- and Diastereoselective Catalytic Asymmetric Tamura Cycloaddition Reactions. *Chem. - Eur. J.* **2019**, *25*, 7270−7274.

(8) (a) Serpier, F.; Flamme, B.; Brayer, J.-L.; Folléas, B.; Darses, S. Chiral Pyrrolidines and Piperidines from Enantioselective Rhodium-Catalyzed Cascade Arylative Cyclization. *Org. Lett.* **2015**, *17*, 1720−1723. (b) Serpier, F.; Brayer, J.-L.; Folléas, B.; Darses, S. Access to Polyfunctionalized Chiral Piperidines through Enantioselective Addition−Carbocyclization Cascade Reaction Catalyzed by a Rhodium(I)−Diene Complex. *Org. Lett.* **2015**, *17*, 5496−5499. (c) Claraz, A.; Serpier, F.; Darses, S. Organoboron Initiated Rh-Catalyzed Asymmetric Cascade Reactions: A Subtle Switch in Regioselectivity Leading to Chiral 3-Benzazepine Derivatives. *ACS Catal.* **2017**, *7*, 3410−3413. (d) Selmani, A.; Serpier, F.; Darses, S. From Tetrahydrofurans to Tetrahydrobenzo[d]oxepines via a Regioselective Control of Alkyne Insertion in Rhodium-Catalyzed Arylative Cyclization. *J. Org. Chem.* **2019**, *84*, 4566−4574.

(9) For some examples of reactions involving a 1,4-shift, see: (a) Hayashi, T.; Inoue, K.; Taniguchi, N.; Ogasawara, M. Rhodium-Catalyzed Hydroarylation of Alkynes with Arylboronic Acids: 1,4-Shift of Rhodium from 2-Aryl-1-alkenylrhodium to 2-Alkenylarylrhodium Intermediate. *J. Am. Chem. Soc.* **2001**, *123*, 9918−9919. (b) Shintani, R.; Okamoto, K.; Hayashi, T. Rhodium-Catalyzed Isomerization of α-Arylpropargyl Alcohols to Indanones: Involvement of an Unexpected Reaction Cascade. *J. Am. Chem. Soc.* **2005**, *127*, 2872−2873. (c) Shintani, R.; Tsurusaki, A.; Okamoto, K.; Hayashi, T. Highly Chemo- and Enantioselective Arylative Cyclization of Alkyne-Tethered Electron-Deficient Olefins Catalyzed by Rhodium Complexes with Chiral Dienes. *Angew. Chem., Int. Ed.* **2005**, *44*, 3909−3912. (d) Matsuda, T.; Shigeno, M.; Murakami, M. Asymmetric Synthesis of 3,4-Dihydrocoumarins by Rhodium-Catalyzed Reaction of 3-(2-Hydroxyphenyl)cyclobutanones. *J. Am. Chem. Soc.* **2007**, *129*, 12086−12087. (e) Panteleev, J.; Menard, F.; Lautens, M. Ligand Control in Enantioselective Desymmetrization of Bicyclic Hydrazines: Rhodium(I)-Catalyzed Ring-Opening versus Hydroarylation. *Adv. Synth. Catal.* **2008**, *350*, 2893−2902. (f) Sasaki, K.; Nishimura, T.; Shintani, R.; Kantchev, E. A. B.; Hayashi, T. Rhodium/diene-catalyzed tandem 1,4-shift/1,4-addition of (E)-1,2-diphenylethenylboronic acid to enones: density functional theory modeling and asymmetric catalysis. *Chem. Sci.* **2012**, *3*, 1278−1283 and references cited .

(10) Miura, T.; Sasaki, T.; Nakazawa, H.; Murakami, M. Ketone Synthesis by Intramolecular Acylation of Organorhodium(I) with Ester. *J. Am. Chem. Soc.* **2005**, *127*, 1390−1391.

(11) For some examples, see: (a) Cauble, D. F.; Gipson, J. D.; Krische, M. J. Diastereo- and Enantioselective Catalytic Carbometallative Aldol Cycloreduction: Tandem Conjugate Addition−Aldol Cyclization. *J. Am. Chem. Soc.* **2003**, *125*, 1110−1111. (b) Shintani, R.; Okamoto, K.; Otomaru, Y.; Ueyama, K.; Hayashi, T. Catalytic Asymmetric Arylative Cyclization of Alkynals: Phosphine-Free Rhodium/Diene Complexes as Efficient Catalysts. *J. Am. Chem. Soc.* **2005**, *127*, 54−55. (c) Shintani, R.; Tsurusaki, A.; Okamoto, K.; Hayashi, T. Highly Chemo- and Enantioselective Arylative Cyclization of Alkyne-Tethered Electron-Deficient Olefins Catalyzed by Rhodium Complexes with Chiral Dienes. *Angew. Chem., Int. Ed.* **2005**, *44*, 3909−3912. (d) Tsukamoto, H.; Matsumoto, T.; Kondo, Y.

DOI: 10.1021/acs.orglett.9b03153
Org. Lett. XXXX, XXX, XXX−XXX

Enantioselective Arylative Cyclization of Allenyl Aldehydes with Arylboronic Acids under Pd(II)-diphosphine Catalysis. *Org. Lett.* **2008**, *10*, 1047−1050. (e) Shintani, R.; Isobe, S.; Takeda, M.; Hayashi, T. Rhodium-Catalyzed Asymmetric Synthesis of Spirocarbocycles: Arylboron Reagents as Surrogates of 1,2-Dimetalloarenes. *Angew. Chem., Int. Ed.* **2010**, *49*, 3795−3798. (f) Williams, F. J.; Jarvo, E. R. Palladium-Catalyzed Cascade Reaction for the Synthesis of Substituted Isoindolines. *Angew. Chem., Int. Ed.* **2011**, *50*, 4459−4462. (g) Shen, K.; Han, X.; Lu, X. Cationic Pd(II)-Catalyzed Highly Enantioselective Arylative Cyclization of Alkyne-Tethered Enals or Enones Initiated by Carbopalladation of Alkynes with Arylboronic Acids. *Org. Lett.* **2012**, *14*, 1756−1759. (h) Johnson, T.; Choo, K.-L.; Lautens, M. Rhodium-Catalyzed Arylative Cyclization for the Enantioselective Synthesis of (Trifluoromethyl)cyclobutanols. *Chem. - Eur. J.* **2014**, *20*, 14194−14197. (i) Li, Y.; Xu, M.-H. Rhodium-Catalyzed Asymmetric Tandem Cyclization for Efficient and Rapid Access to Underexplored Heterocyclic Tertiary Allylic Alcohols Containing a Tetrasubstituted Olefin. *Org. Lett.* **2014**, *16*, 2712−2715. (j) Zhang, X.; Han, X.; Lu, X. Cationic Pd(II)-Catalyzed Cyclization of *N*-Tosyl-aniline Tethered Allenyl Aldehydes with Arylboronic Acids: Diastereo- and Enantioselective Synthesis of Tetrahydroquinoline Derivatives. *Org. Lett.* **2015**, *17*, 3910−3913.

(12) (a) Bocknack, B. M.; Wang, L.-C.; Krische, M. J. Desymmetrization of enone-diones via rhodium-catalyzed diastereo- and enantioselective tandem conjugate addition-aldol cyclization. *Proc. Natl. Acad. Sci. U. S. A.* **2004**, *101*, 5421−5424. (b) He, Z.-T.; Tian, B.; Fukui, Y.; Tong, X.; Tian, P.; Lin, G.-Q. Rhodium-Catalyzed Asymmetric Arylative Cyclization of meso-1,6-Dienynes Leading to Enantioenriched cis-Hydrobenzofurans. *Angew. Chem., Int. Ed.* **2013**, *52*, 5314−5318. (c) Keilitz, J.; Newman, S. G.; Lautens, M. Enantioselective Rh-Catalyzed Domino Transformations of Alkynylcyclohexadienones with Organoboron Reagents. *Org. Lett.* **2013**, *15*, 1148−1151. (d) Partridge, B. M.; Solana González, J.; Lam, H. W. Iridium-Catalyzed Arylative Cyclization of Alkynones by 1,4-Iridium Migration. *Angew. Chem., Int. Ed.* **2014**, *53*, 6523−6527. (e) Clarke, C.; Incerti-Pradillos, C. A.; Lam, H. W. Enantioselective Nickel-Catalyzed anti-Carbometallative Cyclizations of Alkynyl Electrophiles Enabled by Reversible Alkenylnickel E/Z Isomerization. *J. Am. Chem. Soc.* **2016**, *138*, 8068−8071. (f) Karad, S. N.; Panchal, H.; Clarke, C.; Lewis, W.; Lam, H. W. Enantioselective Synthesis of Chiral Cyclopent-2-enones by Nickel-Catalyzed Desymmetrization of Malonate Esters. *Angew. Chem., Int. Ed.* **2018**, *57*, 9122−9125.

(13) For the regioselective insertion of aryl-substituted alkynes, see: (a) Hayashi, T.; Inoue, K.; Taniguchi, N.; Ogasawara, M. Rhodium-Catalyzed Hydroarylation of Alkynes with Arylboronic Acids: 1,4-Shift of Rhodium from 2-Aryl-1-alkenylrhodium to 2-Alkenylarylrhodium Intermediate. *J. Am. Chem. Soc.* **2001**, *123*, 9918−9919. (b) Lautens, M.; Yoshida, M. Regioselective Rhodium-Catalyzed Addition of Arylboronic Acids to Alkynes with a Pyridine-Substituted Water-Soluble Ligand. *Org. Lett.* **2002**, *4*, 123−125. (c) Lautens, M.; Yoshida, M. Rhodium-Catalyzed Addition of Arylboronic Acids to Alkynyl Aza-Heteroaromatic Compounds in Water. *J. Org. Chem.* **2003**, *68*, 762−769. (d) Genin, E.; Michelet, V.; Genet, J.-P. Efficient synthesis of trisubstituted alkenes in an aqueous-organic system using a versatile and recyclable Rh/m-TPPTC catalyst. *Tetrahedron Lett.* **2004**, *45*, 4157−4161. For the specific case of propargylic amines, see: (e) Arcadi, A.; Aschi, M.; Chiarini, M.; Ferrara, G.; Marinelli, F. Rhodium- and Palladium-Catalyzed Hydroarylation of Propargylic Amines with Arylboronic Acids. *Adv. Synth. Catal.* **2010**, *352*, 493−498. (f) Panteleev, J.; Zhang, L.; Lautens, M. Domino Rhodium-Catalyzed Alkyne Arylation/Palladium-Catalyzed N Arylation: A Mechanistic Investigation. *Angew. Chem., Int. Ed.* **2011**, *50*, 9089−9092.

(14) Enantioselectivities obtained with diphosphine ligands: (*R*)-binap 28%, (*R*)-dtbm-segphos 7%, (*S*)-difluorphos 27%, (*R,R*)-Me-duphos 8%.

(15) (a) Tokunaga, N.; Otomaru, Y.; Okamoto, K.; Ueyama, K.; Shintani, R.; Hayashi, T. C2-Symmetric Bicyclo[2.2.2]octadienes as Chiral Ligands: Their High Performance in Rhodium-Catalyzed Asymmetric Arylation of N-Tosylarylimines. *J. Am. Chem. Soc.* **2004**, *126*, 13584−13585. (b) Okamoto, K.; Hayashi, T.; Rawal, V. H. Simple Chiral Diene Ligands Provide High Enantioselectivities in Transition-Metal-Catalyzed Conjugate Addition Reactions. *Org. Lett.* **2008**, *10*, 4387−4389. (c) Okamoto, K.; Hayashi, T.; Rawal, V. H. Electronic and steric tuning of chiral diene ligands for rhodium-catalyzed asymmetric arylation of imines. *Chem. Commun.* **2009**, 4815−4817. (d) Roy, I. D.; Burns, A. R.; Pattison, G.; Michel, B.; Parker, A. J.; Lam, H. W. A second-generation ligand for the enantioselective rhodium-catalyzed addition of arylboronic acids to alkenylazaarenes. *Chem. Commun.* **2014**, *50*, 2865−2868.

(16) (a) Fischer, C.; Defieber, C.; Suzuki, T.; Carreira, E. M. Readily Available [2.2.2]-Bicyclooctadienes as New Chiral Ligands for Ir(I): Catalytic, Kinetic Resolution of Allyl Carbonates. *J. Am. Chem. Soc.* **2004**, *126*, 1628−1629. (b) Gendrineau, T.; Chuzel, O.; Eijsberg, H.; Genet, J.-P.; Darses, S. C_1-symmetric monosubstituted chiral diene ligands in asymmetric rhodium-catalyzed 1,4-addition reactions. *Angew. Chem., Int. Ed.* **2008**, *47*, 7669−7672. (c) Selmani, A.; Serpier, F.; Darses, S. Chiral Bicyclo[2.2.2]octa-2,5-dienyltrifluoroborate Derivative as a Useful and Stable Precursor of C_1-Symmetric Chiral Dienes. *Org. Lett.* **2019**, *21*, 4378−4382.

(17) Yang, D.; Zhang, C. Ruthenium-Catalyzed Oxidative Cleavage of Olefins to Aldehydes. *J. Org. Chem.* **2001**, *66*, 4814−4818.

(18) (a) Fronza, M.; Murillo, R.; Ślusarczyk, S.; Adams, M.; Hamburger, M.; Heinzmann, B.; Laufer, S.; Merfort, I. In vitro cytotoxic activity of abietane diterpenes from Peltodon longipes as well as Salvia miltiorrhiza and Salvia sahendica. *Bioorg. Med. Chem.* **2011**, *19*, 4876−4881. (b) Nematollahi, A.; Aminimoghadamfarouj, N.; Wiart, C. Reviews on 1,4-naphthoquinones from Diospyros L. *J. Asian Nat. Prod. Res.* **2012**, *14*, 80−88. (c) Widhalm, J. R.; Rhodes, D. Biosynthesis and molecular actions of specialized 1,4-naphthoquinone natural products produced by horticultural plants. *Hortic. Res.* **2016**, *3*, 16046.

DOI: 10.1021/acs.orglett.9b03153
Org. Lett. XXXX, XXX, XXX−XXX