OL | Organic Letters

Letter

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

pubs.acs.org/OrgLett

Asymmetric Hydroarylation of Enones via Nickel-Catalyzed 5-*Endo*-*Trig* Cyclization

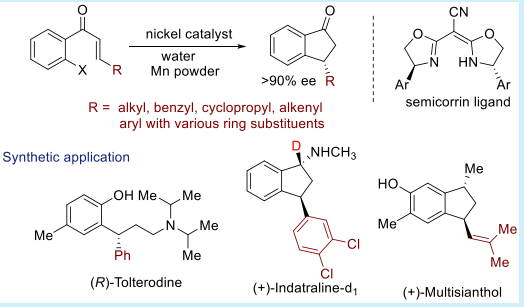
Xurong Qin,[‡] Marcus Wen Yao Lee,[‡] and Jianrong Steve Zhou*[,†]

[†]State Key Laboratory of Chemical Oncogenomics, Key Laboratory of Chemical Genomics, School of Chemical Biology and Biotechnology, Peking University Shenzhen Graduate School, Nanshan District, Shenzhen 518055, China

[‡]Division of Chemistry and Biological Chemistry, School of Physical and Mathematical Sciences, Nanyang Technological University, 21 Nanyang Link, Singapore 637371

Supporting Information

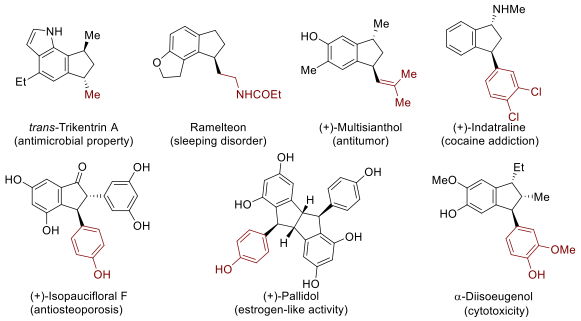
ABSTRACT: A nickel-catalyzed reductive cyclization of enones affords a wide array of indanones in high enantiomeric induction. The reaction is featured with an unprecedented broad scope of substrates. The versatility of the new method is demonstrated in several short stereoselective syntheses of medically valuable (*R*)-tolterodine, parent and deuterated (+)-indatraline, and an antitumor natural product, (+)-multisianthol. In comparison, these compounds cannot be prepared satisfactorily via analogous processes catalyzed by palladium.



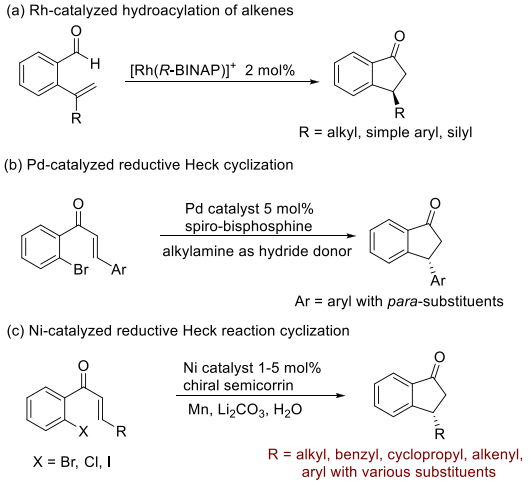
Substituted indanones are core motifs in many bioactive natural products and medicines. They are also used as key intermediates in stereoselective synthesis of some pharmaceuticals and bioactive compounds.[1] For example, *trans*-trikentrin A bearing an alkylated indane has good antimicrobial activity,[2] whereas ramelteon is used for the treatment of insomnia.[3] Moreover, (+)-multisianthol bearing an alkenyl group was reported to have antitumor activity.[4] Other examples of bioactive indanes containing aryl substituents include (+)-indatraline for the treatment of depression and cocaine addiction,[5] (+)-isopaucifloral F with antiosteoporosis activities,[6] (+)-pallidol possessing estrogen-like properties, and α-diisoeugenol, which is cytotoxic (Scheme 1).[7] Consequently, efficient stereoselective construction of substituted indanones is still an important task in organic synthesis.

Several stereoselective catalytic methods have been developed that allowed the formation of the indane ring and simultaneous establishment of new stereocenters on indanes (Scheme 2).[8] However, they often suffered from tedious preparation of precursors for cyclization, limited scope of ring substituents, or the use of expensive noble metals (as part of catalysts) in relatively high loading. One example is catalytic hydroacylation of *o*-vinyl benzaldehydes catalyzed by Rh or Co, which offered indanones carrying different types of C3

Scheme 1. Selected Indane-Based Pharmaceuticals and Bioactive Natural Products



Scheme 2. Selected Examples of Catalytic Asymmetric Synthesis of Substituted Indanones



Received: June 20, 2019

DOI: 10.1021/acs.orglett.9b02130
Org. Lett. XXXX, XXX, XXX–XXX

substituents with good ee values (Scheme 2a).[9] Another example is Rh-catalyzed cyclization of aryl boronates onto enones, but the substrates were not readily accessible.[10]

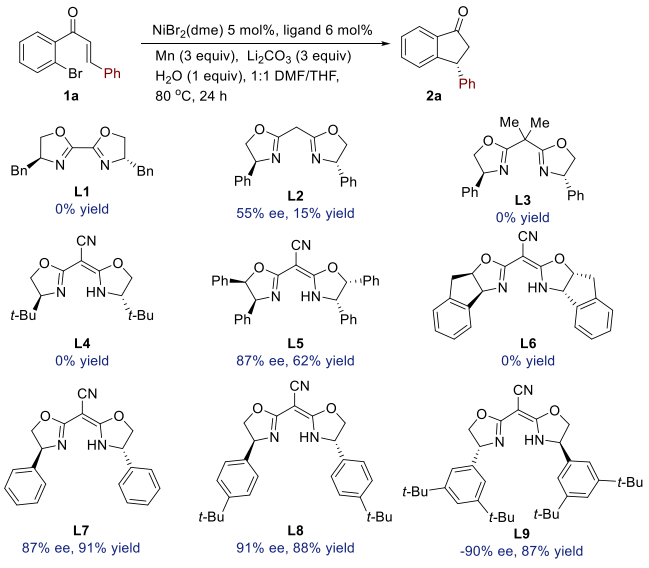
In recent years, there has been a resurgence of research interest in developing enantioselective variants of the reductive Heck reaction.[11] For example, in 2015, our group reported a reductive Heck cyclization of *o*-bromochalcone derivatives via 5-*endo*-*trig* cyclization of cationic arylpalladium species, which afforded 3-arylated indanones, but only those bearing C3-aryl rings with simple *para* substituents provided moderate-to-good yields and >90% ee (Scheme 2b).[12] Other substrates carrying alkenyl groups, alkyl chains, or C3-aryl rings with other substitution patterns resulted in poor yields and/or poor enantiomeric ratios (see the Supporting Information).

Herein, we describe nickel-catalyzed enantioselective reductive Heck reaction,[13] which produced a wide array of substituted indanones with substrate generality (Scheme 2c). The new reaction was successfully applied to concise syntheses of several bioactive indanes of medicinal value. Of note, recent DFT studies indicated that 5-*endo*-*trig* cyclization of 3-butenylmetals was kinetically less favored than 4-*exo*-*trig* in both cases of palladium and nickel.[14]

Nickel is an abundant base metal and is much cheaper than noble metals such as palladium and rhodium. In terms of reactivity, nickel-based catalysts may offer some advantages over palladium catalysts in Heck-type reactions;[15] for example, faster oxidative addition of challenging aryl−chlorine bonds, faster olefin insertion, and closer interaction between substrates and chiral ligands due to shorter nickel−ligand bonds.[16]

Initially, we chose a model reaction of (*E*)-*o*-bromochalcone to search for a suitable nickel catalyst (Scheme 3). We found

Scheme 3. Effect of Bisoxazoline Ligands on Reductive Cyclization on a Model Enone

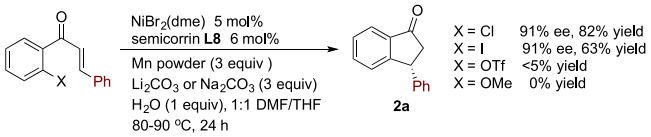


that many commercially available chiral diphosphines did not form catalytically active nickel catalysts, while bisoxazolines **L1**−**L3** led to incomplete conversion of **1a** and low ee values. To our satisfaction, diarylated semicorrin[17] **L7** gave the desired product **2a** in good yield and 87% ee. To improve further the stereoselectivity of the cyclization reaction, introduction of bulky *tert*-butyl substituents on bisarylated semicorrins (**L8** and **L9**)[18] improved the ee value to greater than 90% at 80 °C. Presumably, the active nickel catalyst was probably ligated with anionic forms of semicorrins **L7**−**L9** via in situ deprotonation of these ligands.

With regard to other reaction parameters, most of other nickel(II) salts gave similarly good performance in the catalytic process. Manganese powder was the only reductant that was effective for this purpose. Li_2CO_3 and Na_2CO_3 were similarly effective as bases. The best yield of **2a** was obtained in a 1:1 mixed solvent of DMF and THF, and the yield reduced to 53% in DMF alone.

Having optimized the reaction conditions, we next tested the applicability of different aryl electrophiles (Scheme 4). Aryl

Scheme 4. Asymmetric Cyclization of Different Aryl Electrophiles



chloride was a competent electrophile and afforded **2a** in good yield and 91% ee after the base was switched to Na_2CO_3. In comparison, (*E*)-*o*-iodochalcone gave **2a** in high ee, but only moderate yield was observed. The main side reaction was hydrodehalogenation of the aryl−I bond caused by manganese powder. In the reaction of an aryl triflate, **2a** was formed in very low yield because of basic hydrolysis of the aryl triflate. In the reaction of an arylmethoxide, **2a** was not produced, and the main side reaction was conjugate reduction of the enone moiety.

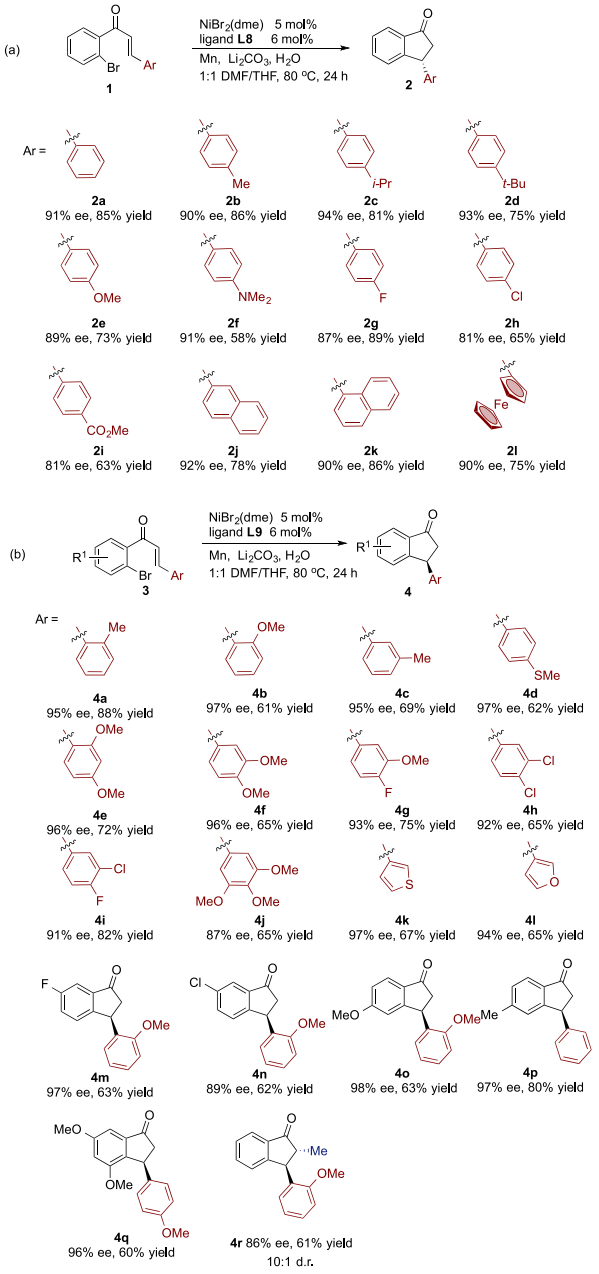
Next, in asymmetric cyclization of chalcones bearing a *para*-substituted *β*-aryl ring, we found that a nickel catalyst of **L8** afforded better ee values than those of **L7** or **L9** (Scheme 5a). Most substrates provided the desired indanones in good yields and over 90% ee, while a common side reaction was determined to be hydrogenation of enones. In the case of **2i**, partial ester hydrolysis accounted for the material balance.

When we examined the cyclization of other chalcones bearing *ortho* or *meta* substituents on aryl rings, however, the nickel catalyst of **L9** consistently afforded better ee values than that of **L8** (Scheme 5b). Both electron-donating and electron-withdrawing groups can be present on the aryl rings. In the example of **4d** carrying a *p*-SMe group, switching from **L8** to **L9** led to improvement of its ee value from 88% to 97%. Moreover, reactions of enones bearing two or more substituents on *β*-aryl rings also proceeded in good yields and excellent enantiomeric excess (**4e**−**j**). Heterocyclic rings of thiophene and furan were compatible with the nickel catalysis (**4k**−**l**), but a pyridine ring interfered with the desired process. Moreover, both an electron-donating methoxy group and electron-withdrawing fluorine and chlorine can be present on the benzo-fused rings (**4m**−**q**).

Finally, our catalyst also allowed cyclization of a chalcone bearing an *α*-methyl group, yielding the *trans*-isomer selectively (**4r**). In some cases above that gave moderate yields of indanones, the main side reaction was the reduction of aryl halides. Notably, indanone **4q** is a common precursor to many biologically active resveratrol-based oligomers, such as (+)-quadranglularin A, (+)-isopaucifloral F, (+)-pauciflorol F, and (+)-pallidol.[1d]

DOI: 10.1021/acs.orglett.9b02130
Org. Lett. XXXX, XXX, XXX−XXX

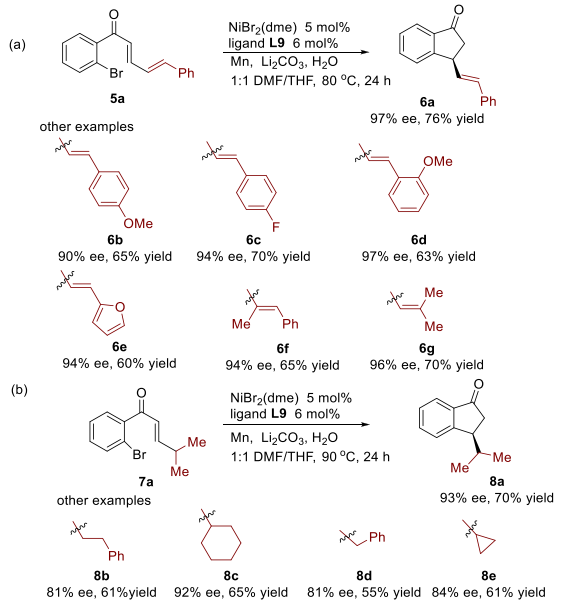
Scheme 5. Asymmetric Synthesis of Indanones from 3-Arylated Chalcones Using Nickel Catalysts of Semicorrins



The nickel catalyst of semicorrin **L9** was applicable to enantioselective synthesis of indanones carrying alkenyl or alkyl chains at the C3 positions (Scheme 6). The C3-alkenyl substituents can carry β-aryl groups (**6a**–**e**) and can have three substituents (**6f**,**g**). Furthermore, the nickel catalyst can be applied to the synthesis of indanones carrying C3-alkyl groups (including isopropyl, *n*-hexyl, benzyl, and homobenzyl and a cyclopropyl group (**8a**–**e**), but a large *tert*-butyl group impeded the cyclization step. In comparison, under Pd-catalyzed reductive Heck conditions (Scheme 2b), these products were formed in low yields and low ee values (see the Supporting Information).[12]

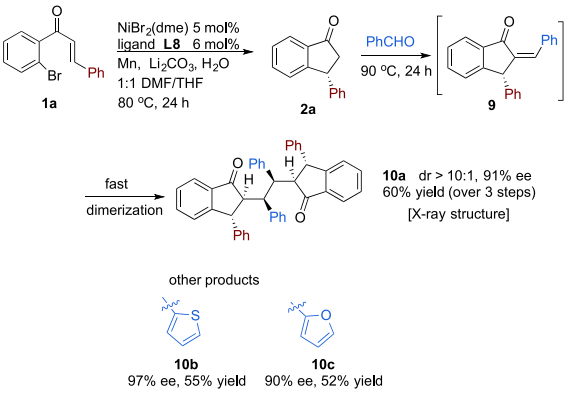
Furthermore, we wondered whether indanone **2a**, once produced, will undergo aldol condensation with an aldehyde such as benzaldehyde under catalytic conditions and whether aldol adduct **9** will be further reduced in situ by manganese

Scheme 6. Asymmetric Synthesis of Indanones from Enones Carrying 3-Alkenyl, Alkyl, and Cyclopropyl Groups



powder. Surprisingly, when the crude reaction mixture of **2a** was directly treated with benzaldehyde, the resulting enone **9** underwent facile reductive dimerization in one pot to form diketone **10a** with excellent dr (Scheme 7).[19] We determined that both the nickel catalyst and manganese powder were required for the reductive dimerization from control experiments.

Scheme 7. One-Pot Reductive Cyclization, Aldehyde Condensation, and Dimerization



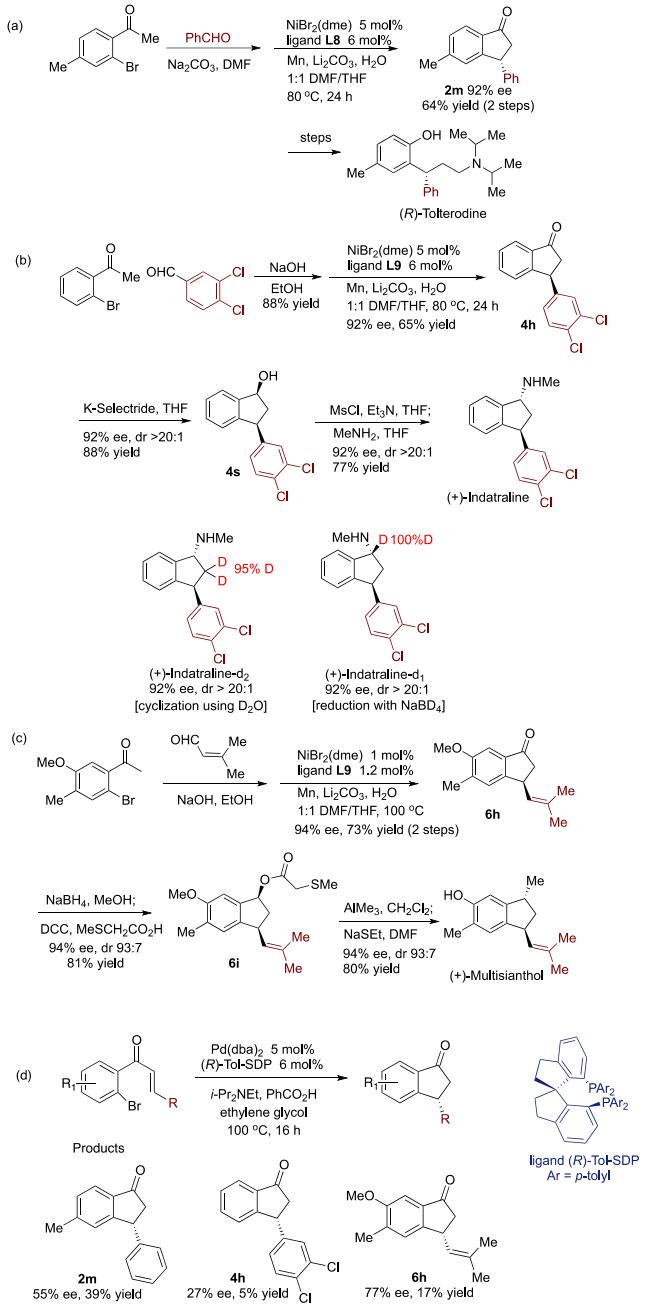
(*R*)-Tolterodine is currently used for the treatment of overactive bladder.[20] The new method was applied to a formal synthesis toward (*R*)-tolterodine,[21] starting from an aldol condensation and subsequent hydroarylation (Scheme 8a).

(+)-Indatraline is a nonselective monoamine transporter inhibitor that blocks the reuptake of neurotransmitters including dopamine, serotonin, and norepinephrine, and it has been subjected to a few stereoselective syntheses.[22] We successfully devised a short synthesis of (+)-indatraline (Scheme 8b), which was followed by *syn*-selective reduction with K-Selectride and amination of a mesylate derivative.

Deuteration of medicines at metabolic positions can slow metabolic rates of drugs in the body, allow a lower dosage to be used, and thus minimize side effects caused by drugs.[23] We

DOI: 10.1021/acs.orglett.9b02130
Org. Lett. XXXX, XXX, XXX−XXX

Scheme 8. Synthetic Applications: (a) Formal Synthesis of (*R*)-Tolterodine; (b) Asymmetric Synthesis of (+)-Indatraline and Its Deuterated Derivatives; (c) Synthesis of (+)-Multisianthol; (d) Comparison with Palladium-Catalyzed Reductive Heck Cyclization



thus prepared a doubly labeled (+)-indatraline at both α-positions of the ketone group by using an excess amount of D_2O during reductive Heck cyclization (see the Supporting Information). Furthermore, a new deuterologue of (+)-indatraline with the label at the benzylic position was synthesized by stereoselective ketone reaction using $NaBD_4$.

We then achieved a concise asymmetric synthesis of (+)-multisianthol, an antitumor natural product (Scheme 8c). The reductive cyclization of the enone at an 8 mmol scale produced 1.38 g of **6h** (75% yield, 95% ee) at 80 °C. Alternatively, the nickel catalyst was reduced from 5 to 1 mol % at 100 °C, which gave 73% yield and 94% ee. Subsequent selective reduction with $NaBH_4$ and esterification provided ester **6i** in 81% yield and 13:1 dr. Later, stereoinvertive methylation using $AlMe_3$ and deprotection with NaSEt yielded (+)-mutisianthol in an overall yield of 47% over six steps. It compares well with a reported synthesis via a key step of iridium-catalyzed asymmetric hydrogenation (90% ee, 33% yield over seven steps starting from a tetralone derivative).[4c]

Finally, we made a comparison with palladium-catalyzed reductive Heck cyclization under conditions that we reported previously (Scheme 8d), which failed to afford the substituted indanones in good yields or >80% ee.

In summary, we report a nickel-catalyzed versatile reductive cyclization of chalcones to quickly access indanones carrying various substituents at the C3 positions, including alkyl, benzyl, cyclopropyl, alkenyl, and aryl groups. The catalytic process was successfully used in short syntheses of (*R*)-tolterodine, two deuterated analogues of (+)-indatraline, and an anticancer natural product, (+)-multisianthol. In comparison, the palladium-catalyzed reductive Heck reaction could not afford these compounds in good yields or high ee values.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.9b02130.

Experimental procedures (PDF)
Spectra for all new compounds (PDF)

Accession Codes

CCDC 1844641 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: jrzhou@pku.edu.cn.

ORCID

Jianrong Steve Zhou: 0000-0002-1806-7436

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank Shenzhen Graduate School, Peking University, Nanyang Technological University, Singapore GSK-EDB Trust Fund (2017 GSK-EDB Green & Sustainable Manufacturing Award), Singapore A*STAR Science & Engineering Research Council (AME IRG A1783c0010), and the National Natural Science Foundation of China (21502157) for financial support. X.Q. conducted most experiments in this work. We thank Prof. Gregory C. Fu at Caltech for a free sample of chiral semicorrins.

■ REFERENCES

(1) (a) Keylor, M. H.; Matsuura, B. S.; Stephenson, C. R. *Chem. Rev.* **2015**, *115*, 8976−9027. (b) Gabriele, B.; Mancuso, R.; Veltri, L. *Chem.—Eur. J.* **2016**, *22*, 5056−5094. (c) Borie, C.; Ackermann, L.; Nechab, M. *Chem. Soc. Rev.* **2016**, *45*, 1368−1386. (d) Patil, S. A.;

DOI: 10.1021/acs.orglett.9b02130
Org. Lett. XXXX, XXX, XXX−XXX

Patil, R.; Patil, S. A. *Eur. J. Med. Chem.* **2017**, *138*, 182−198. (e) Turek, M.; Szczęsna, D.; Koprowski, M.; Bałczewski, P. *Beilstein J. Org. Chem.* **2017**, *13*, 451−494.
(2) Capon, R. J.; Macleod, J. K.; Scammells, P. J. *Tetrahedron* **1986**, *42*, 6545−6550.
(3) Uchikawa, O.; Fukatsu, K.; Tokunoh, R.; Kawada, M.; Matsumoto, K.; Imai, Y.; Hinuma, S.; Kato, K.; Nishikawa, H.; Hirai, K.; Miyamoto, M.; Ohkawa, S. *J. Med. Chem.* **2002**, *45*, 4222−4239.
(4) (a) Bianco, G. G.; Ferraz, H. M. C.; Costa, A. M.; Costa-Lotufo, L. V.; Pessoa, C.; de Moraes, M. O.; Schrems, M. G.; Pfaltz, A.; Silva, L. F. *J. Org. Chem.* **2009**, *74*, 2561−2566. (b) Dethe, D. H.; Boda, R.; Murhade, G. M. *Org. Chem. Front.* **2015**, *2*, 645−648. (c) Bhorkade, S. B.; Gavhane, K. B.; Shinde, V. S. *Tetrahedron* **2016**, *72*, 1954−1959.
(5) (a) Bogeso, K. P.; Christensen, A. V.; Hyttel, J.; Liljefors, T. *J. Med. Chem.* **1985**, *28*, 1817−1828. (b) Kuhar, M. J.; Ritz, M. C.; Boja, J. W. *Trends Neurosci.* **1991**, *14*, 299−302. (c) Froimowitz, M.; Wu, K.-M.; Moussa, A.; Haidar, R. M.; Jurayj, J.; George, C.; Gardner, E. L. *J. Med. Chem.* **2000**, *43*, 4981−4992.
(6) (a) Ito, T.; Tanaka, T.; Iinuma, M.; Nakaya, K.-i.; Takahashi, Y.; Sawa, R.; Murata, J.; Darnaedi, D. *J. Nat. Prod.* **2004**, *67*, 932−937. (b) Snyder, S. A.; Zografos, A. L.; Lin, Y. *Angew. Chem., Int. Ed.* **2007**, *46*, 8186−8191. (c) Kerr, D. J.; Miletic, M.; Manchala, N.; White, J. M.; Flynn, B. L. *Org. Lett.* **2013**, *15*, 4118−4121. (d) Tang, M. L.; Peng, P.; Liu, Z. Y.; Zhang, J.; Yu, J. M.; Sun, X. *Chem. - Eur. J.* **2016**, *22*, 14535−14539.
(7) Atsumi, T.; Murakami, Y.; Shibuya, K.; Tonosaki, K.; Fujisawa, S. *Anticancer Res.* **2005**, *25*, 4029−4036.
(8) (a) Shintani, R.; Yashio, K.; Nakamura, T.; Okamoto, K.; Shimada, T.; Hayashi, T. *J. Am. Chem. Soc.* **2006**, *128*, 2772−2773. (b) Nørager, N. G.; Lorentz-Petersen, L. L. R.; Lyngso, L. O.; Kehler, J.; Juhl, K. *Synlett* **2011**, *2011*, 1753−1755. (c) Li, X.-H.; Zheng, B.-H.; Ding, C.-H.; Hou, X.-L. *Org. Lett.* **2013**, *15*, 6086−6089. (d) Heravi, M. M.; Dehghani, M.; Zadsirjan, V. *Tetrahedron: Asymmetry* **2016**, *27*, 513−588. (e) Burns, A. R.; Lam, H. W.; Roy, L. D. *Org. React.* **2017**, *93*, 1−686.
(9) (a) Hydroacylation: Kundu, K.; McCullagh, J. V.; Morehead, A. T., Jr. *J. Am. Chem. Soc.* **2005**, *127*, 16042−16043. (b) Yang, J.; Yoshikai, N. *J. Am. Chem. Soc.* **2014**, *136*, 16748−16751. (c) Rastelli, E. J.; Truong, N. T.; Coltart, D. M. *Org. Lett.* **2016**, *18*, 5588−5591.
(10) Yu, Y.-N.; Xu, M.-H. *J. Org. Chem.* **2013**, *78*, 2736−2741.
(11) (a) Cacchi, S. *Pure Appl. Chem.* **1990**, *62*, 713. (b) Minatti, A.; Zheng, X.; Buchwald, S. L. *J. Org. Chem.* **2007**, *72*, 9253−9258. (c) Liu, S.; Zhou, J. *Chem. Commun.* **2013**, *49*, 11758−11760. (d) Shen, C.; Liu, R.-R.; Fan, R.-J.; Li, Y.-L.; Xu, T.-F.; Gao, J.-R.; Jia, Y.-X. *J. Am. Chem. Soc.* **2015**, *137*, 4936−4939. (e) Rh-catalyzed reductive arylation: Jang, Y. J.; Larin, E. M.; Lautens, M. *Angew. Chem., Int. Ed.* **2017**, *56*, 11927−11930. (f) Kong, W.; Wang, Q.; Zhu, J. *Angew. Chem., Int. Ed.* **2017**, *56*, 3987−3991. (g) Mannathan, S.; Raoufmoghaddam, S.; Reek, J. N. H.; de Vries, J. G.; Minnaard, A. J. *ChemCatChem* **2017**, *9*, 551−554. (h) Zhang, Z. M.; Xu, B.; Qian, Y.; Wu, L.; Wu, Y.; Zhou, L.; Liu, Y.; Zhang, J. *Angew. Chem., Int. Ed.* **2018**, *57*, 10373−10377.
(12) Yue, G.; Lei, K.; Hirao, H.; Zhou, J. *Angew. Chem., Int. Ed.* **2015**, *54*, 6531−6535.
(13) (a) Qin, X.; Lee, M. W. Y.; Zhou, J. S. *Angew. Chem., Int. Ed.* **2017**, *56*, 12723−12726. (b) Wang, K.; Ding, Z.; Zhou, Z.; Kong, W. *J. Am. Chem. Soc.* **2018**, *140*, 12364−12368. (c) Anthony, D.; Lin, Q.; Baudet, J.; Diao, T. *Angew. Chem., Int. Ed.* **2019**, *58*, 3198−3202. (d) Jin, Y.; Wang, C. *Angew. Chem., Int. Ed.* **2019**, *58*, 6722−6726. (e) Tian, Z.-X.; Qiao, J.-B.; Xu, G.-L.; Pang, X.; Qi, L.; Ma, W.-Y.; Zhao, Z.-Z.; Duan, J.; Du, Y.-F.; Su, P.; Liu, X.-Y.; Shu, X.-Z. *J. Am. Chem. Soc.* **2019**, *141*, 7637−7643.
(14) Fiser, B.; Cuerva, J. M.; Gómez-Bengoa, E. *Organometallics* **2018**, *37*, 390−395.
(15) (a) Lebedev, S. A.; Lopatina, V. S.; Petrov, E. S.; Beletskaya, I. P. *J. Organomet. Chem.* **1988**, *344*, 253−259. (b) Iyer, S.; Ramesh, C.; Ramani, A. *Tetrahedron Lett.* **1997**, *38*, 8533−8536. (c) Lin, P. S.; Jeganmohan, M.; Cheng, C. H. *Chem. - Asian J.* **2007**, *2*, 1409−1416. (d) Gøgsig, T. M.; Kleimark, J.; Nilsson Lill, S. O.; Korsager, S.; Lindhardt, A. T.; Norrby, P.-O.; Skrydstrup, T. *J. Am. Chem. Soc.* **2012**, *134*, 443−452. (e) Ehle, A. R.; Zhou, Q.; Watson, M. P. *Org. Lett.* **2012**, *14*, 1202−1205. (f) Tasker, S. Z.; Gutierrez, A. C.; Jamison, T. F. *Angew. Chem., Int. Ed.* **2014**, *53*, 1858−1861. (g) Desrosiers, J.-N.; Hie, L.; Biswas, S.; Zatolochnaya, O. V.; Rodriguez, S.; Lee, H.; Grinberg, N.; Haddad, N.; Yee, N. K.; Garg, N. K.; Senanayake, C. H. *Angew. Chem., Int. Ed.* **2016**, *55*, 11921−11924. (h) Asymmetric cyclization to form oxindoles: Desrosiers, J.-N.; Wen, J.; Tcyrulnikov, S.; Biswas, S.; Qu, B.; Hie, L.; Kurouski, D.; Wu, L.; Grinberg, N.; Haddad, N.; Busacca, C. A.; Yee, N. K.; Song, J. J.; Garg, N. K.; Zhang, X.; Kozlowski, M. C.; Senanayake, C. H. *Org. Lett.* **2017**, *19*, 3338−3341. (i) Medina, J. M.; Moreno, J.; Racine, S.; Du, S.; Garg, N. K. *Angew. Chem., Int. Ed.* **2017**, *56*, 6567−6571.
(16) (a) Lin, B.-L.; Liu, L.; Fu, Y.; Luo, S.-W.; Chen, Q.; Guo, Q.-X. *Organometallics* **2004**, *23*, 2114−2123. (b) Menezes da Silva, V. H.; Braga, A. A. C.; Cundari, T. R. *Organometallics* **2016**, *35*, 3170−3181.
(17) Fritschi, H.; Leutenegger, U.; Pfaltz, A. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1005−1006.
(18) Zuo, Z.; Cong, H.; Li, W.; Choi, J.; Fu, G. C.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2016**, *138*, 1832−1835.
(19) Wang, C.-C.; Lin, P.-S.; Cheng, C.-H. *Tetrahedron Lett.* **2004**, *45*, 6203−6206.
(20) Nilvebrant, L.; Andersson, K.-E.; Gillberg, P.-G.; Stahl, M.; Sparf, B. *Eur. J. Pharmacol.* **1997**, *327*, 195−207.
(21) (a) Chen, G.; Tokunaga, N.; Hayashi, T. *Org. Lett.* **2005**, *7*, 2285−2288. (b) Hedberg, C.; Andersson, P. G. *Adv. Synth. Catal.* **2005**, *347*, 662−666. (c) Ulgheri, F.; Marchetti, M.; Piccolo, O. *J. Org. Chem.* **2007**, *72*, 6056−6059. (d) Sun, C.; Potter, B.; Morken, J. P. *J. Am. Chem. Soc.* **2014**, *136*, 6534−6537.
(22) (a) Bennani, Y. L.; Hanessian, S. *Chem. Rev.* **1997**, *97*, 3161−3196. (b) Davies, H. M. L.; Gregg, T. M. *Tetrahedron Lett.* **2002**, *43*, 4951−4953. (c) Yoo, K.; Kim, H.; Yun, J. *Chem. - Eur. J.* **2009**, *15*, 11134−11138. (d) Roesner, S.; Casatejada, J. M.; Elford, T. G.; Sonawane, R. P.; Aggarwal, V. K. *Org. Lett.* **2011**, *13*, 5740−5743. (e) Taylor, J. G.; Correia, C. R. D. *J. Org. Chem.* **2011**, *76*, 857−869. (f) Wei, W. T.; Yeh, J. Y.; Kuo, T. S.; Wu, H. L. *Chem. - Eur. J.* **2011**, *17*, 11405−11409. (g) Li, Y.; Dong, K.; Wang, Z.; Ding, K. *Angew. Chem., Int. Ed.* **2013**, *52*, 6748−6752.
(23) (a) Gant, T. G. *J. Med. Chem.* **2014**, *57*, 3595−3611. (b) Timmins, G. S. *Expert Opin. Ther. Pat.* **2017**, *27*, 1353−1361.

DOI: 10.1021/acs.orglett.9b02130
Org. Lett. XXXX, XXX, XXX−XXX