OL | Organic Letters

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

Letter

pubs.acs.org/OrgLett

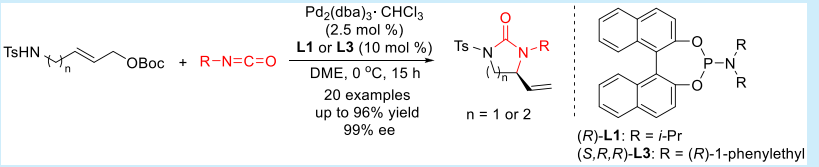
Pd-Catalyzed Asymmetric Allylic Cycloaddition of N-Containing Allylic Carbonates with Isocyanates

Ijaz Khan,[†] Babar Hussain Shah,[†] Can Zhao,[†] Feng Xu,[*,‡] and Yong Jian Zhang[*,†]

[†]School of Chemistry and Chemical Engineering, and Shanghai Key Laboratory of Electrical Insulation and Thermal Aging, Shanghai Jiao Tong University, 800 Dongchuan Road, Shanghai 200240, P.R. China

[‡]Shanghai Jiao Tong University Affiliated Sixth People's Hospital South Campus, 6600 Nanfeng Highway, Shanghai 201400, P.R. China

Supporting Information



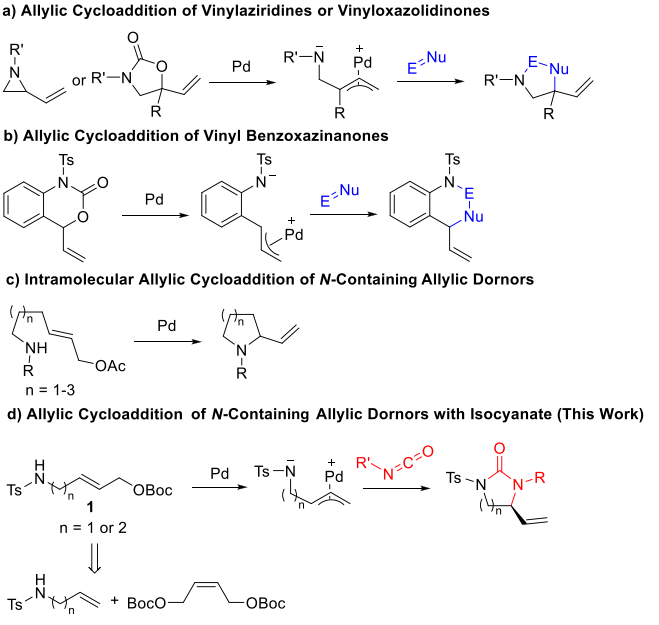
ABSTRACT: An efficient method for the enantioselective synthesis of cyclic ureas has been developed through Pd-catalyzed asymmetric allylic cycloaddition of readily accessible nitrogen-containing allylic carbonates with isocyanates. By using a palladium complex in situ generated from $Pd_2(dba)_3{\cdot}CHCl_3$ and phosphoramidite **L1** or **L3** as a ligand under mild reaction conditions, the process afforded imidazolidinones and tetrahydropyrimidinones with high yields and high levels of enantioselectivities.

The Pd-catalyzed allylic cycloaddition via zwitterionic allylpalladium intermediates has been extensively studied for the preparation of a variety of cyclic frameworks.[1] Various allylic donors have been productively applied in the transformations with diverse unsaturated electrophiles. Since the pioneering work of Ohfune on the Pd-catalyzed allylic cycloaddition of vinylaziridines with carbon monoxide in 1991,[2] vinylaziridines have served as efficient 1,3-*C*,*N*-dipoles in the Pd-catalyzed allylic cycloaddition with various unsaturated electrophiles to afford functionalized aza-heterocycles,[3] and the asymmetric variants have also been documented recently (Scheme 1a).[4] 5-Vinyloxazolidin-2-ones as the vinylaziridine equivalent have recently been applied to Pd-catalyzed decarboxylative allylic cycloadditions with unsaturated electrophiles with high efficiency (Scheme 1a).[5] Most recently, Tunge and Wang reported Pd-catalyzed asymmetric allylic cycloaddition of vinyl benzoxazinanones with Michael acceptors to provide hydroquinolines with high enantio- and diastereoselectivities.[6] Subsequently, vinyl benzoxazinanones have served as useful 1.4-*C*,*N*-dipoles in Pd-catalyzed decarboxylative allylic cycloadditions with a variety of reaction partners to form aza-heterocycles with diverse functionalities (Scheme 1b).[7]

Even though these three types of nitrogen-containing allylic donors have successfully been applied in the Pd-catalyzed allylic cycloaddition, some limitations have emerged, such as limited structural diversity and/or multistep preparation for the allylic substrates.

Most recently, our group developed vinylethylene carbonates (VECs) as stable and readily accessible *C*,*O*-dipoles and achieved the Pd-catalyzed asymmetric decarboxylative allylic cycloaddition of VECs with various unsaturated electrophiles to afford diverse oxo-heterocycles in high efficiencies.[8] Based on these research results, we are interested in the development of readily accessible nitrogen-containing allylic donors and their

Scheme 1. Pd-Catalyzed Allylic Cycloaddition of *C*,*N*-Dipoles



Received: October 16, 2019

DOI: 10.1021/acs.orglett.9b03662
Org. Lett. XXXX, XXX, XXX−XXX

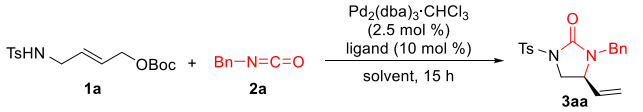
applications in the Pd-catalyzed allylic cycloaddition to afford aza-heterocycles. In 1996, Trost reported intramolecular allylic cycloaddition of nitrogen-containing linear allylic donors to form five- to seven-membered N-heterocycles (Scheme 1c).[9] In contrast with this report, we envisioned that the N-containing allylic carbonates **1** (n = 1 or 2) could afford stable zwitterionic allylpalladium intermediates (Scheme 1d). The intermediates could be intercepted by unsaturated electrophiles to form five- or six-membered aza-heterocycles. Allylic carbonates **1** can be readily synthesized by cross-metathesis of allylic or homoallylic amines with Boc-protected 2-butene-1,4-diol. However, to the best of our knowledge, there have been no reports for the allylic cycloaddition using this type of readily accessible allylic donors. Herein, we report Pd-catalyzed asymmetric allylic cycloaddition of nitrogen-containing allylic carbonates with isocyanates, a practical and efficient approach which allows rapid access to imidazolidinones and tetrahydropyrimidinones as useful chiral building blocks[10] in high yields with high levels of enantioselectivities.

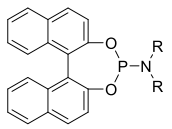
Initial studies were focused on the investigation of the allylic cycloaddition of nitrogen-containing allylic carbonate **1a**[11] with commercially available benzyl isocyanate **2a** as typical reaction partners using palladium(0) catalyst bearing different chiral phosphoramidite[12] ligands (Table 1). To our delight, the reaction proceeded smoothly with phosphoramidite-derived Binol ligand (*R*)-**L1** at 20 °C in THF for 15 h, affording imidazolidinone **3aa** with 80% yield and 87% ee (entry 1). It is observed that the enantioselectivity could be enhanced using the ligand (*S*,*R*,*R*)-**L3** (93% ee, entry 3). However, Zhou's spiro-type phosphoramidite,[13] Phox-type **L7**, and Segphos ligands showed no reactivity under the reaction conditions (entries 4−8). Lower yields and enantioselectivities were observed using Binap or the Trost ligand for the reaction (entries 9 and 10). By further screening of solvent (entries 11−18), we found that the reaction was very sensitive to the reaction solvent. When the reaction proceeded in 1,2-dimethoxyethane (DME), the yield was improved to 94% without the deterioration of enantioselectivity (entry 18). The enantioselectivity could be further improved when the reaction was performed at 0 °C (93% yield, 96% ee, entry 19). The enantioselectivities were remarkably decreased when the reaction proceeded at higher temperature (entries 20 and 21).

With optimal conditions in hand, we evaluated the generality of this process by the reaction of nitrogen-containing allylic carbonate **1a** with various substituted isocyanates (Scheme 2). The reaction proceeded smoothly with 2-phenylethylisocyanate **2b** to afford imidazolidinone **3ab** in 85% yield with 93% ee. The functional group of chloride **3ac** and allylic group **3ad** could also be introduced with high yields with good to high enantioselectivities. A wide range of phenyl-substituted isocyanates bearing different electronic and steric properties was tolerated under the reaction conditions, affording the corresponding imidazolidinones **3ae**−**3al** in high yields with good to excellent enantioselectivities.

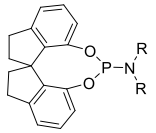
Next, we investigated the allylic cycloaddition of N-containing allylic carbonate **1b**[11] with isocyanates. Under the optimal conditions (Table 1, entries 19), the cycloaddition of **1b** with benzyl isocyanate **2a** proceeded smoothly to afford tetrahydropyrimidinone **3ba** in 83% yield, albeit with moderate enantioselectivities (65% ee). After further condition optimizations (see Supporting Information), we found that the reaction with phosphoramidite (*R*)-**L1** as the ligand under otherwise identical conditions with Scheme 2 gave the cycloadduct **3ba** in

Table 1. Condition Optimization[a]

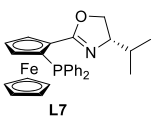




(*R*)-**L1**: R = *i*-Pr
(*S*,*S*,*S*)-**L2**: R = (*S*)-1-phenylethyl
(*S*,*R*,*R*)-**L3**: R = (*R*)-1-phenylethyl



(*R*)-**L4**: R = *i*-Pr
(*R*,*R*,*R*)-**L5**: R = (*R*)-1-phenylethyl
(*S*,*R*,*R*)-**L6**: R = (*R*)-1-phenylethyl



L7

entry	ligands	solvents	T (°C)	yield (%)[b]	ee (%)[c]
1	(*R*)-**L1**	THF	20	80	−87
2	(*S*,*S*,*S*)-**L2**	THF	20	trace	
3	(*S*,*R*,*R*)-**L3**	THF	20	77	93
4	(*R*)-**L4**	THF	20	trace	
5	(*R*,*R*,*R*)-**L5**	THF	20		
6	(*S*,*R*,*R*)-**L6**	THF	20		
7	**L7**	THF	20		
8	(*R*)-Segphos	THF	20	trace	
9	(*R*)-Binap	THF	20	35	−20
10	Ph-Trost	THF	20	52	−26
11	(*S*,*R*,*R*)-**L3**	toluene	20	34	60
12	(*S*,*R*,*R*)-**L3**	DCM	20	60	78
13	(*S*,*R*,*R*)-**L3**	Et_2O	20	12	49
14	(*S*,*R*,*R*)-**L3**	CyH	20		
15	(*S*,*R*,*R*)-**L3**	dioxane	20	trace	
16	(*S*,*R*,*R*)-**L3**	CH_3CN	20	83	90
17	(*S*,*R*,*R*)-**L3**	MTBE	20	60	23
18	(*S*,*R*,*R*)-**L3**	DME	20	94	93
19	(*S*,*R*,*R*)-**L3**	DME	0	93	96
20	(*S*,*R*,*R*)-**L3**	DME	40	95	53
21	(*S*,*R*,*R*)-**L3**	DME	60	95	43

[a]Reaction conditions: $Pd_2(dba)_3{\cdot}CHCl_3$ (2.5 mol %), ligand (10 mol %), **1a** (0.2 mmol), **2a** (0.2 mmol), solvent (1.0 mL), 15 h. [b]Isolated yields. [c]Determined by HPLC using a chiral stationary phase. The minus sign means the obtained product with opposite configuration.

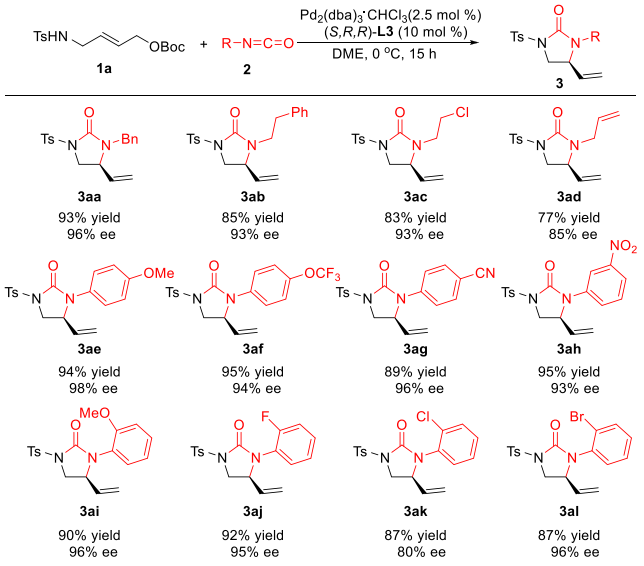
84% yield with excellent enantioselectivity (99% ee, Scheme 3). The allylic cycloaddition of **1b** with various isocyanates was examined with (*R*)-**L1** as ligand (Scheme 3). The reaction of **1b** with alkyl-substituted isocyanates gave cycloadducts **3bb** and **3bd** with high yields with good to excellent enantioselectivities. The allylic cycloaddition of **1b** with phenyl-substituted isocyanates bearing different electronic and steric properties performed smoothly to afford the corresponding tetrahydropyrimidinones **3be**−**3bj** in high yields with good enantioselectivities. Interestingly, the opposite stereochemistry was observed for the allylic cycloaddition of **1b** in comparison to that of **1a**.

We next investigated the allylic cycloaddition of N-containing allylic carbonate **1c**[11] with benzyl isocyanate **2a** under optimal conditions, as described in Table 1 (entry 19). However, the reaction provided pyrrolidine **4** in 72% yield with 43% ee. The desired cycloadduct **3ca** was not observed (Scheme 4). This result implied that the allylic carbonate **1c** (n = 3) underwent zwitterionic allylpalladium intermediate, which occurs intramolecular cycloaddition to afford favored pyrrolidine rather than intercepted by isocyanate **2a**.

The synthetic utility of the protocol has been demonstrated by the gram-scale transformation and product elaboration (Scheme 5). Under the standard conditions, the allylic

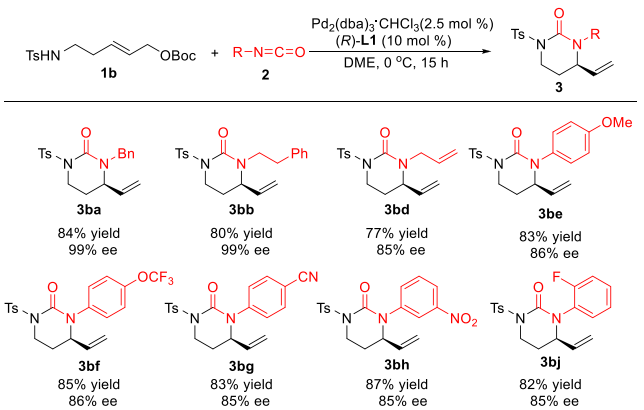
DOI: 10.1021/acs.orglett.9b03662
Org. Lett. XXXX, XXX, XXX−XXX

Scheme 2. Pd-Catalyzed Asymmetric Allylic Cycloaddition of 1a with Isocyanates 2[a]



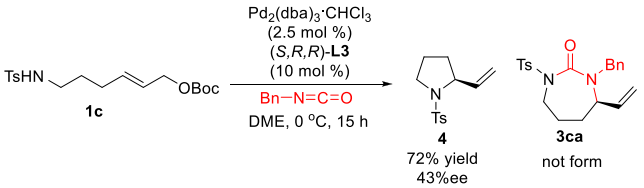
[a]Reaction conditions: $Pd_2(dba)_3{\cdot}CHCl_3$ (2.5 mol %), (*S*,*R*,*R*)-**L3** (10 mol %), **1a** (0.2 mmol), **2** (0.2 mmol), DME (1.0 mL), 0 °C, 15 h. The enantiomeric excesses were determined by HPLC using a chiral stationary phase. The absolute configuration of **3ae** was confirmed by X-ray crystallography (see Supporting Information). Those of the other products were assigned by analogy.

Scheme 3. Pd-Catalyzed Asymmetric Allylic Cycloaddition of 1b with Isocyanates 2[a]



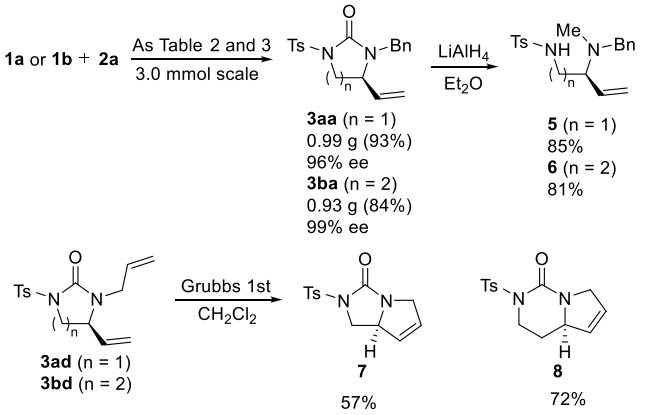
[a]Reaction conditions: $Pd_2(dba)_3{\cdot}CHCl_3$ (2.5 mol %), (*R*)-**L1** (10 mol %), **1a** (0.2 mmol), **2** (0.2 mmol), DME (1.0 mL), 0 °C, 15 h. The enantiomeric excesses were determined by HPLC using a chiral stationary phase. The absolute configuration of **3bj** was confirmed by X-ray crystallography (see Supporting Information). Those of the other products were assigned by analogy.

Scheme 4. Pd-Catalyzed Allylic Cycloaddition of 1c with 2a



cycloaddition of **1a** or **1b** with benzyl isocyanate **2a** at the 3.0 mmol scale performed smoothly to furnish corresponding

Scheme 5. Gram-Scale Transformation and Product Elaboration



cycloadducts **3aa** and **3ba** in high yields with excellent enantioselectivities. Reduction of **3aa** and **3ba** in the presence of $LiAlH_4$ gave diamines **5** and **6**, respectively, in high yields.[14] *N*-Allylic-substituted cycloadducts **3ad** and **3bd** could convert into the bicyclic heterocycles **7** and **8**, respectively, through ring-closing metathesis using Grubbs first generation catalyst.

In conclusion, we have developed an efficient method for the enantioselective synthesis of imidazolidinones and tetrahydropyrimidinones via Pd-catalyzed allylic cycloaddition of readily accessible N-containing allylic carbonates with isocyanates. By using a palladium complex generated in situ from $Pd_2(dba)_3{\cdot}CHCl_3$ and phosphoramidite **L3** or **L1** as a catalyst under mild conditions, the process afforded formal [3 + 2] and [4 + 2] cycloadducts in high yields with good to excellent enantioselectivities. The synthetic utility of the protocol has been demonstrated by the gram-scale transformation and the product derivatizations. Further studies on extending the scope of the cycloaddition of nitrogen-containing allylic carbonates with other unsaturated electrophiles are currently underway and will be reported in due course.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.9b03662.

Detailed experimental procedures; characterization data of all the new compounds; copies of HPLC chromatography, ^1H and ^{13}C NMR spectra of the products (PDF)

Accession Codes

CCDC 1879205−1879206 contain 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 Authors

*E-mail: xuf@smu.edu.cn.

*E-mail: yjian@sjtu.edu.cn.

ORCID

Yong Jian Zhang: 0000-0001-5808-1745

DOI: 10.1021/acs.orglett.9b03662
Org. Lett. XXXX, XXX, XXX−XXX

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the National Natural Science Foundation of China (21572130, 21871179), the Innovation Fund from Joint Research Center for Precision Medicine set up by Shanghai Jiao Tong University & Affiliated Sixth People's Hospital South Campus (IFPM2017B008). We thank the Instrumental Analysis Center of Shanghai Jiao Tong University for HRMS analysis.

■ REFERENCES

(1) For selected reviews, see: (a) Souillart, L.; Cramer, N. Catalytic C−C Bond Activations via Oxidative Addition to Transition Metals. *Chem. Rev.* **2015**, *115*, 9410−9464. (b) Weaver, J. D.; Recio, A.; Grenning, A. J.; Tunge, J. A. Transition Metal-Catalyzed Decarboxylative Allylation and Benzylation Reactions. *Chem. Rev.* **2011**, *111*, 1846−1913. (c) Chan, D. M. T. In *Cycloaddition Reactions in Organic Synthesis*; Kobayashi, S., Jørgensen, K. A., Eds.; Wiley-VCH: Weinheim, Germany, 2002; p 57.

(2) Spears, G. W.; Nakanishi, K.; Ohfune, Y. Novel Entry to a 3, 4-Disubstituted 2-Azetidinone Derivative via Palladium-Assisted Carbonylation of a 2-Substituted 3-Vinylaziridine. *Synlett* **1991**, *1991*, 91−92.

(3) (a) Spielmann, K.; van der Lee, A.; de Figueiredo, R. M.; Campagne, J.-M. Diastereoselective Palladium-Catalyzed (3 + 2)-Cycloadditions from Cyclic Imines and Vinyl Aziridines. *Org. Lett.* **2018**, *20*, 1444−1447. (b) Lin, T.-Y.; Wu, H.-H.; Feng, J.-J.; Zhang, J. Divergent Access to Functionalized Pyrrolidines and Pyrrolines via Iridium-Catalyzed Domino-Ring-Opening Cyclization of Vinyl Aziridines with β-Ketocarbonyls. *Org. Lett.* **2017**, *19*, 6526−6529. (c) Rivinoja, D. J.; Gee, Y. S.; Gardiner, M. G.; Ryan, J. H.; Hyland, C. J. The Diastereoselective Synthesis of Pyrroloindolines by Pd-Catalyzed Dearomative Cycloaddition of 1-Tosyl-2-Vinylaziridine to 3-Nitroindoles. *ACS Catal.* **2017**, *7*, 1053−1056. (d) Yuan, Z.; Wei, W.; Lin, A.; Yao, H. Bifunctional Organo/Metal Cooperatively Catalyzed [3 + 2] Annulation of para-Quinone Methides with Vinylcyclopropanes: Approach to Spiro [4.5] deca-6, 9-diene-8-ones. *Org. Lett.* **2016**, *18*, 3370−3373. (e) Fontana, F.; Chen, C. C.; Aggarwal, V. K. Palladium-Catalyzed Insertion of CO_2 into Vinylaziridines: New Route to 5-Vinyloxazolidinones. *Org. Lett.* **2011**, *13*, 3454−3457. (f) Lowe, M. A.; Ostovar, M.; Ferrini, S.; Chen, C. C.; Lawrence, P. G.; Fontana, F.; Calabrese, A. A.; Aggarwal, V. K. Palladium-Mediated Annulation of Vinyl Aziridines with Michael Acceptors: Stereocontrolled Synthesis of Substituted Pyrrolidines and Its Application in a Formal Synthesis of (−)-α-Kainic Acid. *Angew. Chem., Int. Ed.* **2011**, *50*, 6370−6374. (g) Aoyagi, K.; Nakamura, H.; Yamamoto, Y. Palladium-Catalyzed Aminoallylation of Activated Olefins with Allylic Halides and Phthalimide. *J. Org. Chem.* **2002**, *67*, 5977−5980. (h) Butler, D. C. D.; Inman, G. A.; Alper, H. Room Temperature Ring-Opening Cyclization Reactions of 2-Vinylaziridines with Isocyanates, Carbodiimides, and Isothiocyanates Catalyzed by $[Pd(OAc)_2]/PPh_3$. *J. Org. Chem.* **2000**, *65*, 5887−5890.

(4) (a) Suo, J.-J.; Liu, W.; Du, J.; Ding, C.-H.; Hou, X. L. Diastereo- and Enantioselective Palladium-Catalyzed Dearomative [3 + 2] Cycloaddition of 3-Nitroindoles. *Chem. - Asian J.* **2018**, *13*, 959−963. (b) Zhang, J.-Q.; Tong, F.; Sun, B.-B.; Fan, W.-T.; Chen, J.-B.; Hu, D.; Wang, X.-W. Pd-Catalyzed Asymmetric Dearomative Cycloaddition for Construction of Optically Active Pyrroloindoline and Cyclopentaindoline Derivatives: Access to 3a-Aminopyrroloindolines. *J. Org. Chem.* **2018**, *83*, 2882−2891. (c) Jiang, F.; Yuan, F.-R.; Jin, L.-W.; Mei, G.-J.; Shi, F. Metal-Catalyzed (4 + 3) Cyclization of Vinyl Aziridines with para-Quinone Methide Derivatives. *ACS Catal.* **2018**, *8*, 10234−10240. (d) Næsborg, L.; Tur, F.; Meazza, M.; Blom, J.; Halskov, K. S.; Jørgensen, K. A. Synergistic Catalysis for the Asymmetric [3 + 2] Cycloaddition of Vinyl Aziridines with α, β-Unsaturated Aldehydes. *Chem. - Eur. J.* **2017**, *23*, 268−272. (e) Li, T. R.; Cheng, B.-Y.; Fan, S.-Q.; Wang, Y.-N.; Lu, L. Q.; Xiao, W. J. Highly Stereoselective [3 + 2] Cycloadditions of Chiral Palladium-Containing N1−1, 3-Dipoles: A Divergent Approach to Enantioenriched Spirooxindoles. *Chem. - Eur. J.* **2016**, *22*, 6243−6247. (f) Xu, C.-F.; Zheng, B.-H.; Suo, J.-J.; Ding, C.-H.; Hou, X.-L. Highly Diastereo-and Enantioselective Palladium-Catalyzed [3 + 2] Cycloaddition of Vinyl Aziridines and α, β-Unsaturated Ketones. *Angew. Chem., Int. Ed.* **2015**, *54*, 1604−1607. (g) Trost, B. M.; Fandrick, D. R. Dynamic kinetic asymmetric cycloadditions of isocyanates to vinylaziridines. *J. Am. Chem. Soc.* **2003**, *125*, 11836−11837.

(5) (a) Imagawa, N.; Nagato, Y.; Ohmatsu, K.; Ooi, T. Multiple Absolute Stereocontrol in Pd-Catalyzed [3 + 2] Cycloaddition of Oxazolidinones and Trisubstituted Alkenes Using Chiral Ammonium−Phosphine Hybrid Ligands. *Bull. Chem. Soc. Jpn.* **2016**, *89*, 649−656. (b) Ohmatsu, K.; Kawai, S.; Imagawa, N.; Ooi, T. Palladium-Catalyzed Asymmetric [3 + 2] Cycloaddition of 5-Vinyloxazolidinones with Imines Using Chiral Ammonium-Phosphine Hybrid Ligand. *ACS Catal.* **2014**, *4*, 4304−4306. (c) Ohmatsu, K.; Imagawa, N.; Ooi, T. Ligand-Enabled Multiple Absolute Stereocontrol in Metal-Catalysed Cycloaddition for Construction of Contiguous all-Carbon Quaternary Stereocentres. *Nat. Chem.* **2014**, *6*, 47. (d) Knight, J. G.; Stoker, P. A.; Tchabanenko, K.; Harwood, S. J.; Lawrie, K. W.M. Synthesis of Highly Substituted Pyrrolidines via Palladium-Catalyzed Cyclization of 5-Vinyloxazolidinones and Activated Alkenes. *Tetrahedron* **2008**, *64*, 3744−3750. (e) Knight, J. G.; Tchabanenko, K.; Stoker, P. A.; Harwood, S. J. Synthesis of Highly Substituted Pyrrolidines via Palladium Catalysed Formal [2 + 3] Cycloaddition of 5-Vinyl-oxazolidin-2-ones to Activated Alkenes. *Tetrahedron Lett.* **2005**, *46*, 6261−6264.

(6) (a) Wang, C.; Pahadi, N.; Tunge, J. A. Decarboxylative Cyclizations and Cycloadditions of Palladium-Polarized aza-ortho-Xylylenes. *Tetrahedron* **2009**, *65*, 5102−5109. (b) Wang, C.; Tunge, J. A. Asymmetric Cycloadditions of Palladium-Polarized aza-o-Xylylenes. *J. Am. Chem. Soc.* **2008**, *130*, 8118−8119. (c) Wang, C.; Tunge, J. A. Decarboxylative Ring Contractions and Olefin Insertions of Vinyl Oxazinanones. *Org. Lett.* **2006**, *8*, 3211−3214.

(7) (a) Jin, J.-H.; Wang, H.; Yang, Z.-T.; Yang, W.-L.; Tang, W.; Deng, W.-P. Asymmetric Synthesis of 3, 4-Dihydroquinolin-2-ones via a Stereoselective Palladium-Catalyzed Decarboxylative [4+ 2]-Cycloaddition. *Org. Lett.* **2018**, *20*, 104−107. (b) Duan, S.; Cheng, B.; Duan, X.; Bao, B.; Li, Y.; Zhai, H. Synthesis of cis-5, 5a, 6, 10b-Tetrahydroindeno [2, 1-b] indoles through Palladium-Catalyzed Decarboxylative Coupling of Vinyl Benzoxazinanones with Arynes *Org. Org. Lett.* **2018**, *20*, 1417−1420. (c) Zhao, H.-W.; Feng, N.-N.; Guo, J.-M.; Du, J.; Ding, W.-Q.; Wang, L.-R.; Song, X.-Q. Diastereoselective and Enantioselective Synthesis of Barbiturate-Fused Spirotetrahydroquinolines via Chiral Palladium (0)/Ligand Complex Catalyzed [4+ 2] Cycloaddition of Vinyl Benzoxazinanones with Barbiturate-Based Olefins. *J. Org. Chem.* **2018**, *83*, 9291−9299. (d) Wang, C.; Li, Y.; Wu, Y.; Wang, Q.; Shi, W.; Yuan, C.; Zhou, L.; Xiao, Y.; Guo, H. Enantioselective Construction of Tetrahydroquinazoline Motifs via Palladium-Catalyzed [4 + 2] Cycloaddition of Vinyl Benzoxazinones with Sulfamate-Derived Cyclic Imines. *Org. Lett.* **2018**, *20*, 2880−2883. (e) Li, M.-M.; Wei, Y.; Liu, J.; Chen, H.-W.; Lu, L.-Q.; Xiao, W.-J. Sequential Visible-Light Photoactivation and Palladium Catalysis Enabling Enantioselective [4 + 2] Cycloadditions. *J. Am. Chem. Soc.* **2017**, *139*, 14707−14713. (f) Guo, C.; Janssen-Müller, D.; Fleige, M.; Lerchen, A.; Daniliuc, C. G.; Glorius, F. Mechanistic Studies on a Cooperative NHC Organocatalysis/Palladium Catalysis System: Uncovering Significant Lessons for Mixed Chiral Pd (NHC)(PR_3) Catalyst Design. *J. Am. Chem. Soc.* **2017**, *139*, 4443−4451. (g) Mei, G.-J.; Li, D.; Zhou, G.-X.; Shi, Q.; Cao, Z.; Shi, F. A Catalytic Asymmetric Construction of a Tetrahydroquinoline-Based Spirooxindole Framework via a Diastereo-and Enantioselective Decarboxylative [4 + 2] Cycloaddition. *Chem. Commun.* **2017**, *53*, 10030−10033. (h) Wei, Y.; Lu, L.-Q.; Li, T.-R.; Feng, B.; Wang, Q.; Xiao, W.-J.; Alper, H. P, S Ligands for the Asymmetric Construction of Quaternary Stereocenters in Palladium-Catalyzed Decarboxylative [4+ 2] Cycloadditions. *Angew. Chem., Int. Ed.* **2016**, *55*, 2200−2204. (i) Wang, Q.; Qi, X.; Lu, L.-Q.; Li,

DOI: 10.1021/acs.orglett.9b03662
Org. Lett. XXXX, XXX, XXX−XXX

T.-R.; Yuan, Z.-G.; Zhang, K.; Li, B.-J.; Lan, Y.; Xiao, W.-J. Iron-Catalyzed Decarboxylative [4 + 1] Cycloadditions: Exploiting the Reactivity of Ambident Iron-Stabilized Intermediates. *Angew. Chem., Int. Ed.* **2016**, *55*, 2840. (j) Leth, L. A.; Glaus, F.; Meazza, M.; Fu, L.; Thøgersen, M. K.; Bitsch, E. A.; Jørgensen, K. A. Decarboxylative [4+ 2] Cycloaddition by Synergistic Palladium and Organocatalysis. *Angew. Chem., Int. Ed.* **2016**, *55*, 15272−15276. (k) Guo, C.; Fleige, M.; Janssen-Müller, D.; Daniliuc, C. G.; Glorius, F. Cooperative N-heterocyclic Carbene/Palladium Catalyzed Enantioselective Umpolung Annulations. *J. Am. Chem. Soc.* **2016**, *138*, 7840−7843.

(8) (a) Xu, H.; Khan, S.; Li, H.; Wu, X.; Zhang, Y. J. Pd-Catalyzed Asymmetric Allylic Cycloaddition of Vinyloxetanes with Formaldehyde. *Org. Lett.* **2019**, *21*, 214−217. (b) Liu, K.; Khan, I.; Cheng, J.; Hsueh, Y. J.; Zhang, Y. J. Asymmetric Decarboxylative Cycloaddition of Vinylethylene Carbonates with *β*-Nitroolefins by Cooperative Catalysis of Palladium Complex and Squaramide. *ACS Catal.* **2018**, *8*, 11600−11604. (c) Khan, I.; Li, H.; Wu, X.; Zhang, Y. J. Asymmetric Decarboxylative Cycloaddition of Vinylethylene Carbonates with Aldehydes by Cooperative Catalysis of Palladium Complex and Chiral Squaramide. *Huaxue Xuebao* **2018**, *76*, 874−877. (d) Khan, I.; Zhao, C.; Zhang, Y. J. Enantioselective Decarboxylative Cycloaddition by Palladium Catalysis. *Chem. Commun.* **2018**, *54*, 4708−4711. (e) Khan, A.; Khan, S.; Khan, I.; Zhao, C.; Mao, Y.; Chen, Y.; Zhang, Y. J. Enantioselective Construction of Tertiary C−O Bond via Allylic Substitution of Vinylethylene Carbonates with Water and Alcohols. *J. Am. Chem. Soc.* **2017**, *139*, 10733−10741. (f) Yang, L.; Khan, A.; Zheng, R.; Jin, L. Y.; Zhang, Y. J. Pd-Catalyzed Asymmetric Decarboxylative Cycloaddition of Vinylethylene Carbonates with Imines. *Org. Lett.* **2015**, *17*, 6230−6233. (g) Khan, A.; Zhang, Y. J. Palladium-Catalyzed Asymmetric Decarboxylative Cycloaddition of Vinylethylene Carbonates with Electrophiles: Construction of Quaternary Stereocenters. *Synlett* **2015**, *26*, 853−860. (h) Khan, A.; Xing, J.; Zhao, J.; Kan, Y.; Zhang, W.; Zhang, Y. J. Palladium-Catalyzed Enantioselective Decarboxylative Cycloaddition of Vinylethylene Carbonates with Isocyanates. *Chem. - Eur. J.* **2015**, *21*, 120−124. (i) Khan, A.; Zheng, R.; Kan, Y.; Ye, J.; Xing, J.; Zhang, Y. J. Palladium-Catalyzed Decarboxylative Cycloaddition of Vinylethylene Carbonates with Formaldehyde: Enantioselective Construction of Tertiary Vinylglycols. *Angew. Chem., Int. Ed.* **2014**, *53*, 6439−6442. (j) Khan, A.; Yang, L.; Xu, J.; Jin, L. Y.; Zhang, Y. J. Palladium-Catalyzed Asymmetric Decarboxylative Cycloaddition of Vinylethylene Carbonates with Michael Acceptors: Construction of Vicinal Quaternary Stereocenters. *Angew. Chem., Int. Ed.* **2014**, *53*, 11257−11260.

(9) Trost, B. M.; Krische, M. J.; Radinov, R.; Zanoni, G. On Asymmetric Induction in Allylic Alkylation via Enantiotopic Facial Discrimination. *J. Am. Chem. Soc.* **1996**, *118*, 6297−6298.

(10) (a) Wright, W. B., Jr; Brabander, H. J.; Hardy, R. A., Jr; Osterberg, A. C. Central Nervous System Depressants. I. 1-Aminoalkyl-3-aryl Derivatives of 2-Imidazolidinone, 1a-c 2-Imidazolidinethione, and Tetrahydro-2 (1*H*)-pyrimidinone1d. *J. Med. Chem.* **1966**, *9*, 852−857. (b) Li, C.-D.; Mella, S. L.; Sartorelli, A. C. Cyclic Urea and Thiourea Derivatives as Inducers of Murine Erythroleukemia Differentiation. *J. Med. Chem.* **1981**, *24*, 1089−1092. (c) Salituro, F. G.; Baker, C. T.; Court, J. J.; Deininger, D. D.; Kim, E. E.; Li, B.; Novak, P. M.; Rao, B. G.; Pazhanisamy, S.; Porter, M. D.; et al. Design and Synthesis of Novel Conformationally Restricted HIV Protease Inhibitors. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 3637−3642. (d) Sun, S.; Zhang, Z.; Kodumuru, V.; Pokrovskaia, N.; Fonarev, J.; Jia, Q.; Leung, P.-Y.; Tran, J.; Ratkay, L. G.; McLaren, D. G.; et al. Systematic Evaluation of Amide Bioisosteres Leading to the Discovery of Novel and Potent Thiazolylimidazolidinone Inhibitors of SCD1 for the Treatment of Metabolic Diseases. *Bioorg. Med. Chem. Lett.* **2014**, *24*, 520−525. (e) Moreau, F.; Florentin, D.; Marquet, A. Synthesis of New Biotin Derivatives. *Tetrahedron* **2000**, *56*, 285−293. (f) Lien, E. J.; Hussain, M.; Golden, M. P. Structure-Activity Correlations for the Central Nervous System Depressant 2-Imidazolidinones. *J. Med. Chem.* **1970**, *13*, 623−626. (g) Kazmierski, W. M.; Furfine, E.; Gray-Nunez, Y.; Spaltenstein, A.; Wright, L. Potent Inhibitors of the HIV-1 Protease Incorporating Cyclic Urea P1−P2 Scaffold. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 5685−5687. (h) Li, J. J.; Sutton, J. C.; Nirschl, A.; Zou, Y.; Wang, H.; Sun, C.; Pi, Z.; Johnson, R.; Krystek, S. R.; Seethala, R. Discovery of Potent and Muscle Selective Androgen Receptor Modulators Through Scaffold Modifications. *J. Med. Chem.* **2007**, *50*, 3015.

(11) Only *E*-isomers were obtained for the synthesis of **1a**, **1b**, and **1c** by the cross-metathesis.

(12) Feringa, B. L.; Pineschi, M.; Arnold, L. A.; Imbos, R.; de Vries, A. H. Highly Enantioselective Catalytic Conjugate Addition and Tandem Conjugate Addition−Aldol Reactions of Organozinc Reagents. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2620−2623.

(13) Zhou, H.; Wang, W.-H.; Fu, Y.; Xie, J.-H.; Shi, W.-J.; Wang, L.-X.; Zhou, Q.-L. Highly Enantioselective Copper-Catalyzed Conjugate Addition of Diethylzinc to Enones Using Chiral Spiro Phosphoramidites as Ligands. *J. Org. Chem.* **2003**, *68*, 1582−1584.

(14) Struble, T. J.; Lankswert, H. M.; Pink, M.; Johnston, J. N. Enantioselective Organocatalytic Amine-Isocyanate Capture-Cyclization: Regioselective Alkene Iodoamination for the Synthesis of Chiral Cyclic Ureas. *ACS Catal.* **2018**, *8*, 11926−11931.

DOI: 10.1021/acs.orglett.9b03662
Org. Lett. XXXX, XXX, XXX−XXX