OL | Organic Letters

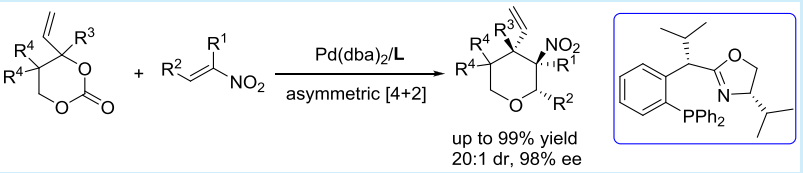
pubs.acs.org/OrgLett Letter

Palladium-Catalyzed Asymmetric Decarboxylative [4+2] Dipolar Cycloaddition of 4-Vinyl-1,3-dioxan-2-ones with α,β-Disubstituted Nitroalkenes Enabled by a Benzylic Substituted P,N-Ligand

Juan Du,[‖] Yuan-Da Hua,[‖] Yang-Jie Jiang, Shuai Huang, Di Chen, Chang-Hua Ding,* and Xue-Long Hou*

Cite This: https://dx.doi.org/10.1021/acs.orglett.0c01638 Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information



ABSTRACT: The Pd-catalyzed asymmetric [4+2] cycloaddition reaction of an aliphatic 1,4-dipole with singly activated electron-deficient alkenes is realized for the first time, enabled by using a newly developed benzylic substituted P,N-ligand, affording tetrahydropyrans having three continuous chiral centers in high yields with high diastereo- and enantioselectivities. The rational transition states of the reaction as well as the role of the benzylic chiral center are proposed.

The transition metal-catalyzed asymmetric [3+2] dipolar cycloaddition of vinyl three-membered rings and their analogues with unsaturated compounds through a zwitterionic Pd-π-allyl intermediate (1,3-dipole) has become an important strategy for the construction of five-membered rings, which as basic and important subunits have widely been found in natural products as well as medicines (Scheme 1a).[1] It seems that a similar zwitterionic Pd-π-allyl complex can also be formed from 2-vinyl azitidines and 2-vinyl oxetanes or their analogues, which as a 1,4-dipole could react with unsaturated compounds under transition metal catalysis via [4+2] dipolar cycloaddition to afford the corresponding tetrahydropyrans and piperidines. Larksarp and Alper were the first to report the Pd-catalyzed [4+2] dipolar cycloaddition of vinyl oxetanes with isocyanates and carbodiimides to provide racemic 1,3-oxazines in 1999.[2] Since then, some reports of Pd-catalyzed [4+2] dipolar cycloadditions have appeared by using different starting materials as a precursor of the 1,4-dipole, activated alkenes, and some other C═X compounds as the dipolarophile (Scheme 1b).[3] In addition, benzoxazinanones have been used as benzo analogues of the 1,4-dipole to react with different kinds of alkenes to afford dihydroquinolines (Scheme 1c).[4] An asymmetric version has also been reported; however, it was mainly limited to those using benzoxazinanones as the 1,4-dipole with excellent results.[4] The reaction of an aliphatic 1,4-dipole from vinyl oxetanes and its analogue with C═X, such as azadienes,[5a] formaldehyde,[5b] and isocyanates,[5c] afforded the products in good ee, the only exception appearing in a report by Yamamoto in 2001, in which a few examples using doubly activated alkenes[3a] could be found in moderate yields with unsatisfying diastereo- and enantioselectivities.

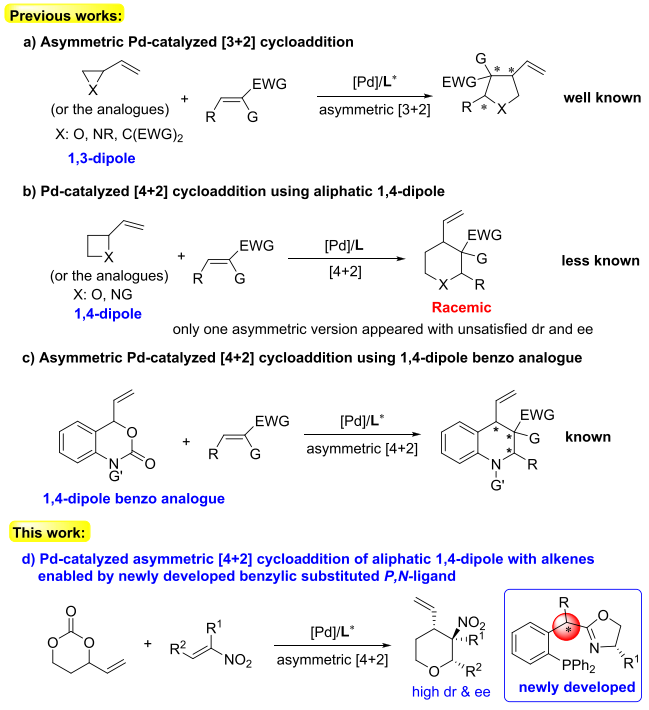
How to realize Pd-catalyzed asymmetric [4+2] cycloaddition of aliphatic 1,4-dipoles with alkenes remains the great challenge. It could be deduced that the lack of a successful example of the reaction using aliphatic 1,4-dipoles might be caused by the fact that they are more flexible than their benzo analogues so that it should be more difficult to control the stereochemistry of the reaction when aliphatic dipoles were the reagent. To address this challenge, the development of new and efficient chiral ligands as well as the catalyst system should be pursued. We have designed and synthesized a new type of benzylic substituted chiral P,N-ligand, with which high catalytic activity and asymmetric induction as well as the switch of enantioselectivity have been observed in many enantioselective reactions.[6] Recently, we found that when we modified this type of ligand by introducing a new chiral center at the benzylic position and used it in Pd-catalyzed asymmetric [4+2] cycloaddition of 4-vinyl-1,3-dioxan-2-one with α,β-disubstituted nitroalkenes, high diastereo- and enantioselectivities were realized. Herein, we report our preliminary study of this reaction.

Initially, several 1,4-dipole precursors were adopted to react with substituted nitroalkenes under Pd catalysis. It was found that tetrahydropyrans **3a** and **4a** were afforded in 92% yield in

Received: May 17, 2020

https://dx.doi.org/10.1021/acs.orglett.0c01638
Org. Lett. XXXX, XXX, XXX−XXX

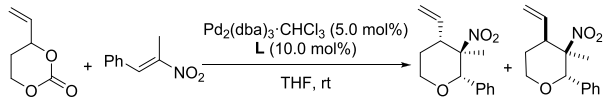
Scheme 1. Pd-Catalyzed Dipolar Cycloaddition through a Zwitterionic Pd-π-Allyl Intermediate



a 3/1 ratio when 4-vinyl-1,3-dioxan-2-one (**1a**) reacted with (*E*)-1-methyl-2-phenyl nitroethene (**2a**) in the presence of $Pd_2(dba)_3{\cdot}CHCl_3$ and achiral PHOX **L5** as the catalyst (entry 5, Table 1) by trial and error (*vide infra*), while the reaction with 2-phenyl nitroethene provided more diastereomers of the corresponding [4+2] cycloadduct in 65% yields with poor selectivity. These results are in accord with our previous findings that the yields and the diastereo- and enantioselectivities are better for the reaction of α,β-disubstituted nitroalkenes than that of β-substituted nitroalkenes.[7] The low yield of the cycloadduct with low selectivity was also realized for the reaction of (*E*)-5-hydroxypent-2-en-1-yl methyl carbonate with 2-phenyl nitroethene by using $[Pd(C_3H_5)Cl]_2/PPh_3$ as the catalyst. On the basis of the results described above, the investigation of the reaction with α,β-disubstituted nitroalkenes continued.

From the preliminary screen of different types of ligands (Figure 1), it was found that only by using a P,N-ligand were the desired cycloadducts **3a** and **4a** afforded while no reaction occurred by using ligands **L1**−**L4** (entries 1−4, respectively, Table 1). The reaction using P,N-ligands **L6**−**L10** produced **3a** in high yield with varied enantioselectivity, but with very low diastereoselectivity (entries 6−10, respectively, Table 1). However, both the yield and diastereo- and enantioselectivities were improved if benzylic substituted P,N-ligands **L11** with two methyls as substituents at the benzylic position were used (entry 11). Previously, we observed a dramatic switch in enantioselectivity in Pd-catalyzed asymmetric Heck reaction using ligands **L10** and **L11** with and without substituents at the benzylic position and provided a rational explanation for such observations.[6d] Therefore, we envisioned that the diastereo- and enantioselectivities would be improved further if a new chiral center were introduced at the benzylic position of the ligand. Indeed, the diastereo- and enantioselectivities increased greatly by using these newly designed and synthesized benzylic

Table 1. Influence of Ligands on Pd-Catalyzed [4+2] Cycloaddition of 4-Vinyl-1,3-dioxan-2-one 1a and Nitroalkene 2a[a]



entry	L	yield (%)[b]	dr[c]	ee (%)[d]
1	**L1**	nr[e]	–	–
2	**L2**	nr[e]	–	–
3	**L3**	nr[e]	–	–
4	**L4**	nr[e]	–	–
5	**L5**	92	3/1	–
6	**L6**	96	2/1	40
7	**L7**	92	2/1	84
8	**L8**	96	6/1	0
9	**L9**	92	1/1	20
10	**L10**	33	2/1	59
11	**L11**	62	4/1	86
12	(*S,S*)-**L12**	92	6/1	65
13	(*S,S*)-**L13**	83	11/1	94
14	(*S,S*)-**L14**	92	3/1	93
15	(*S,S*)-**L15**	70	4/1	90
16	(*R,S*)-**L16**	64	6/1	71
17	(*R,S*)-**L17**	21	2/1	98
18	(*R,S*)-**L18**	8	4/1	94
19	(*R,S*)-**L19**	12	3/1	90
20[f]	(*S,S*)-**L13**	92	17/1	96

[a]At a 5.0/10.0/200/100 $Pd_2dba_3{\cdot}CHCl_3$/**L**/**1a**/**2a** molar ratio and 25 °C. [b]Isolated yield of diastereomers **3a** and **4a**. [c]dr (**3a**/**4a** ratio) determined by ^{1}H NMR. [d]ee of **3a** determined by chiral HPLC. [e]nr = no reaction. [f]At a 5.0/5.0/150/100 $Pd(dba)_2$/**L13**/**1a**/**2a** molar ratio and 0 °C.

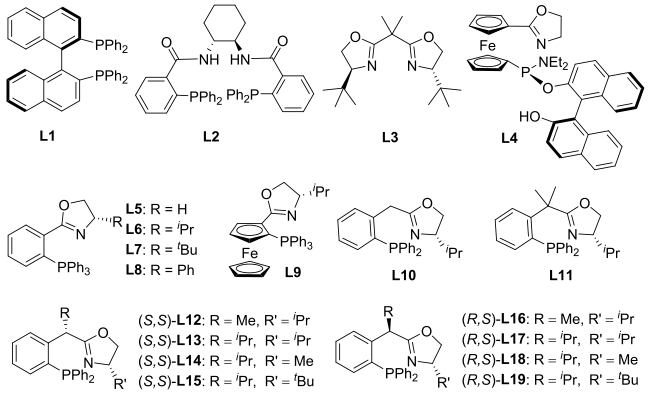


Figure 1. Various chiral ligands screened for the asymmetric cycloaddition.

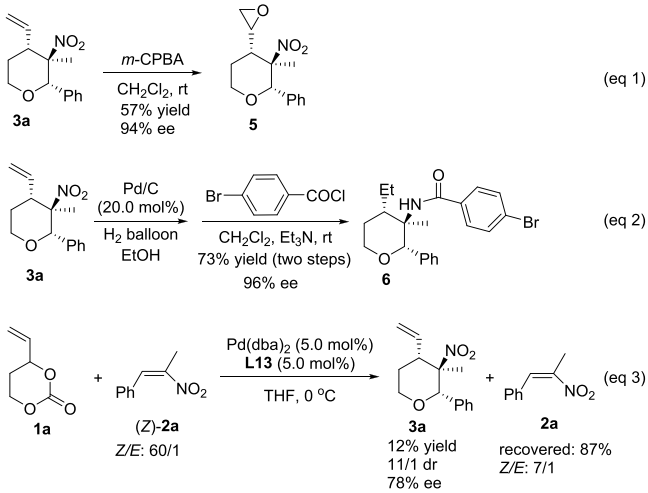
substituted P,N-ligands (Figure 1; entries 12−19) (for detailed synthesis of ligands **L12**−**L19**, see the Supporting Information). The best results were afforded when (*S,S*)-**L13** was the ligand, the yield being 83% with the dr being 11/1 and the ee being 94% for **3a** (entry 13). With **L13** as the ligand, the influence of other reaction conditions, including the palladium source, solvent, and temperature, on the cycloaddition was investigated (for details, see the Supporting Information). Using $Pd(dba)_2$ and ligand **L13** as the catalyst and performing the reaction in THF at 0 °C, the [4+2] cycloaddition afforded tetrahydropyran **3a** in 92% yield with a 17/1 dr and a 95% ee

https://dx.doi.org/10.1021/acs.orglett.0c01638
Org. Lett. XXXX, XXX, XXX−XXX

(entry 20). It was found that better yields and diastereoselectivity were obtained by using (*S*,*S*)-ligands **L12**−**L15** than by using (*R*,*S*)-**L16**−**L19**, though the ee values were slightly higher when using (*R*,*S*)-ligands (entries 12−15 vs entries 16−19), suggesting the chiralities in the former are matched. More interestingly, the reaction with both ligands (*S*,*S*)-**L12**−**L15** and (*R*,*S*)-**L16**−**L19** delivered the same enantiomer for product **3a** as the major stereoisomer, which was identified by their HPLC spectra (for details, see the Supporting Information). These results suggest the absolute configuration of product **3a** is controlled by the chiral center on the oxazoline ring of the ligand, while the chiral center on the benzylic position mainly affects the yield and the diastereoselectivity of the reaction.

Under the optimized conditions, the substrate scope was examined. A range of disubstituted nitroalkenes **2a**−**e** containing both electron-donating and -withdrawing substituents at the *para* or *meta* position of the phenyl ring (R^2) were well-tolerated to produce the corresponding tetrahydropyrans **3a**−**e**, respectively, in high yields with high diastereoselectivity and excellent enantioselectivity (entries 1−5), while **2f** and **2g** with *ortho* substituents on the phenyl ring as well as a β-naphthyl or β-furanyl substituent with α-methyl nitroethene **2h** or **2i**, respectively, delivered products **3f**−**i** in moderate yields with reduced ee (entries 6−9, respectively). β-Pyridyl-substituted nitroalkene **2j** was also a suitable substrate for the cycloaddition to give a high dr and excellent ee (entry 10). The cycloaddition with nitroalkenes **2k**−**2m** bearing an α-phenyl, isopropyl, or ethyl substituent worked well to afford the corresponding products in high yields with excellent enantioselectivity, but the dr ratio decreased when the steric hindrance of the α-substituent became bulkier (entries 11−13). Notably, the cycloaddition with a cyclic nitroalkene **2n** proceeded well to form 1,8-dioxadecalin **3n**, which is the core structure of the bioactive natural product,[8] with a 12/1 dr and a 96% ee (entry 14). Furthermore, substituted vinyldioxanones **1b** and **1c** also reacted smoothly with nitroalkene **2a** to provide adducts **3o** bearing two vicinal chiral quaternary carbon centers with excellent dr and ee (entry 15) and **3p** (entry 16). In addition, nitroalkene **2o** bearing a BnO-ether functional group was tested, leading to the corresponding product **3q** with 83% ee but in a low yield and dr (entry 17). Unfortunately, no reaction was observed in the case of using (*E*)-4-(prop-1-en-1-yl)-1,3-dioxan-2-one (**1d**) and 4-(prop-1-en-2-yl)-1,3-dioxan-2-one (**1e**) as the reactant (entries 18 and 19, respectively).

The absolute configurations of reaction product **3c** were determined to be (2*S*,3*R*,4*R*) by X-ray diffraction analysis of its single crystal (Figure 2).[9] The transformation of the reaction product was also carried out to demonstrate the utility of the protocol (eqs 1 and 2). Product **3a** was easily converted into the corresponding epoxide **5** through oxidation using *m*-CPBA in CH_2Cl_2 in 57% yield (eq 1). Moreover, a sequential Pd/C-catalyzed reduction and amide formation of **3a** delivered compound **6** in 73% yield in two steps (eq 2).



To improve our understanding of this cycloaddition, (*Z*)-**2a** with a *Z*/*E* ratio of 60/1 reacted with 4-vinyl-1,3-dioxan-2-one (**1a**) under the optimized reaction conditions (eq 3). Cycloadduct **3a** was obtained in 12% yield with a 11/1 dr and a 78% ee, while **2a** was recovered in a 87% yield with a *Z*/*E* ratio of 7/1. Comparison of the *Z*/*E* ratio of recovered **2a** with that of starting material **2a** indicated that (*Z*)-**2a** was isomerized to (*E*)-**2a** during the reaction, probably through a reversible oxo-Michael addition of Pd alkoxide generated via the decarboxylative oxidative addition of the Pd(0) catalyst to cyclic carbonate **1a** with (*Z*)-**2a**.[10] Upon comparison of the reaction with (*Z*)-**2a** (eq 3) and (*E*)-**2a** (entry 1, Table 2), these results suggested that the geometry of nitroalkene has a significant effect on the cycloaddition.

To explain the stereochemistry of the reaction, the plausible transition states were proposed (Figure 3). The reaction should proceed through a stepwise mechanism involving Michael addition followed by intramolecular allylic alkylation.[3a] For the reaction with (*S*,*S*)-**L13** as the ligand, the isopropyl substituent at the benzyl site is oriented away from the Pd center as shown from the crystal structure of the $PdCl_2$-(*S*,*S*)-**L13** complex (Figure 4).[11] Intermediate **A** is dominant for the Michael addition step, because intermediate **B** has both nitro and phenyl groups in axial positions and should be less stable. In the second intramolecular allylic alkylation step, intermediate **E** should be favorable due to the bulky nitro group occupying an axial position in intermediate **F** and thus leading to product **3** with a (2*S*,3*R*,4*R*) configuration. Similarly, in the case of the reaction using (*R*,*S*)-**L17**, intermediates **C** and **G** should be favored, also affording (2*S*,3*R*,4*R*)-**3**. However, the isopropyl substituent at the benzyl site is oriented toward the Pd center as indicated by X-ray crystal structure of the $PdCl_2$-(*R*,*S*)-**L17** complex[12] (Figure 4). The orientation of the isopropyl substituent at the benzyl position may decrease the energy gap between transition states **G** and **H**, thus decreasing the diastereoselectivity of the reaction. These plausible transition states provided some explanations for why the major enantiomer was same for the reactions by using ligands (*S*,*S*)-**L13** and (*R*,*S*)-**L17** and

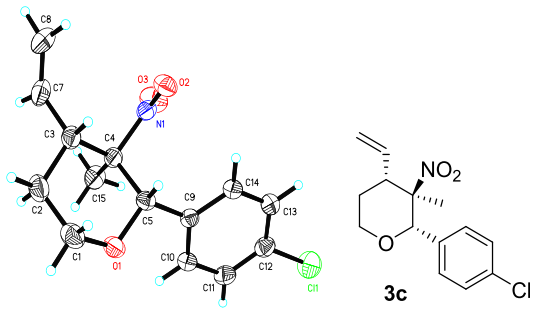
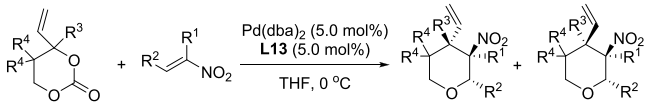


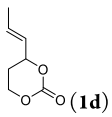
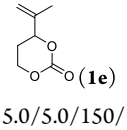
Figure 2. ORTEP drawing of product **3c**.

https://dx.doi.org/10.1021/acs.orglett.0c01638
Org. Lett. XXXX, XXX, XXX−XXX

Table 2. Substrate Scope of the Pd-Catalyzed Asymmetric [4+2] Cycloaddition of 4-Vinyl-1,3-dioxan-2-ones 1 with Nitroalkenes 2[a]



1 2 3 4

entry	R^3, R^4 (**1**)	R^1, R^2 (**2**)	yield/%[b]	dr[c]	ee/%[d]
1	H, H (**1a**)	Me, Ph (**2a**)	92 (**3a**)	17/1	96
2[f]	H, H (**1a**)	Me, *p*-MeOC$_6$H$_4$ (**2b**)	68 (**3b**)	7/1	97
3	H, H (**1a**)	Me, *p*-ClC$_6$H$_4$ (**2c**)	99 (**3c**)	16/1	97
4	H, H (**1a**)	Me, *m*-MeC$_6$H$_4$ (**2d**)	92(**3d**)	13/1	94
5	H, H (**1a**)	Me, *m*-ClC$_6$H$_4$ (**2e**)	75 (**3e**)	7/1	91
6[e,f]	H, H (**1a**)	Me, *o*-MeC$_6$H$_4$ (**2f**)	69 (**3f**)	6/1	85
7	H, H (**1a**)	Me, *o*-ClC$_6$H$_4$ (**2g**)	64 (**3g**)	11/1	83
8	H, H (**1a**)	Me, 1-naphthyl (**2h**)	47 (**3h**)	7/1	73
9	H, H (**1a**)	Me, 2-furanyl (**2i**)	38 (**3i**)	13/1	85
10	H, H (**1a**)	Me, 3-pyridyl (**2j**)	60 (**3j**)	12/1	98
11	H, H (**1a**)	Et, Ph (**2k**)	77 (**3k**)	17/1	97
12	H, H (**1a**)	Ph, Ph (**2l**)	96 (**3l**)	8/1	96
13	H, H (**1a**)	*i*-Pr, Ph (**2m**)	87 (**3m**)	5/1	93
14	H, H (**1a**)	 (**2n**)z	60 (**3n**)	12/1	96
15[e,f]	Me, H (**1b**)	Me, Ph (**2a**)	42 (**3o**)	20/1	91
16[f]	H,-(CH$_2$)$_5$- (**1c**)	Me, Ph (**2a**)	44 (**3p**)	6/1	92
17	H, H (**1a**)	Me, CH2OBn (**2o**)	24 (**3q**)	3/1	83
18	 (**1d**)	Me, Ph (**2a**)	nr[g]	--	--
19	 (**1e**)	Me, Ph (**2a**)	nr[g]	--	--

[a]At a 5.0/5.0/150/100 Pd(dba)$_2$/**L13**/**1**/**2** molar ratio with a reaction time of 4.0 days. [b]Isolated yield of diastereomers **3** and **4**. [c]dr (ratio of 3/4) determined by ^{1}H NMR. [d]ee of **3a** determined by chiral HPLC. [e]With 0.1 mmol of **1** added in 1 day via a syringe pump. [f]Reaction temperature of 10 °C. [g]nr = no reaction.

implied that the chiral center on the benzylic position did influence the stereoselectivities (dr and ee). The experimental

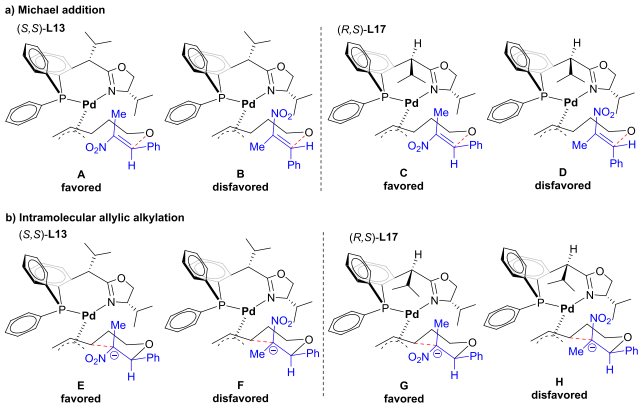


Figure 3. Plausible transition states of the cycloaddition.

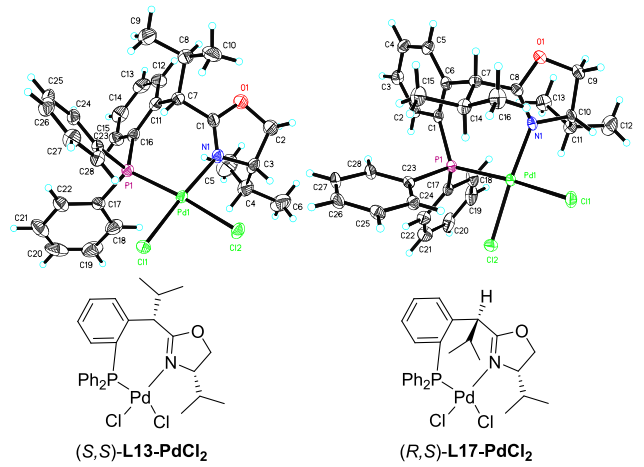


Figure 4. ORTEP drawings of X-ray crystal structures of PdCl$_2$-(*S*,*S*)-**L13** and PdCl$_2$-(*R*,*S*)-**L17** complexes.

results provided some support for these plausible transition states (*vide supra*). Further investigations are needed to improve our understanding of the reaction mechanism.

In conclusion, a new type of benzylic substituted P,N-ligand has been designed and synthesized. It enables a Pd-catalyzed asymmetric [4+2] cycloaddition of an aliphatic 1,4-dipole with singly activated electron-deficient alkenes with high enantioselectivity for the first time. Further exploration of this type of [4+2] cycloaddition as well as more applications in asymmetric catalysis by using these benzylic substituted P,N-ligands is ongoing.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.0c01638.

Screening data, experimental procedures, preparation of ligands **L12**−**L19**, crystallographic data of **3c**, the PdCl$_2$-(*S*,*S*)-**L13** complex, and the PdCl$_2$-(*R*,*S*)-**L17** complex, and NMR and HPLC spectra (PDF)

Accession Codes

CCDC 1999956, 1999962, and 1999970 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

https://dx.doi.org/10.1021/acs.orglett.0c01638
Org. Lett. XXXX, XXX, XXX−XXX

Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

AUTHOR INFORMATION

Corresponding Authors

Chang-Hua Ding − *Department of Chemistry, Innovative Drug Research Center, Shanghai University, Shanghai 200444, China;* orcid.org/0000-0002-4628-4016; Email: dingchanghua@shu.edu.cn

Xue-Long Hou − *State Key Laboratory of Organometallic Chemistry, Center for Excellence in Molecular Synthesis and Shanghai-Hong Kong Joint Laboratory in Chemical Synthesis, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, China;* orcid.org/0000-0003-4396-3184; Email: xlhou@sioc.ac.cn

Authors

Juan Du − *State Key Laboratory of Organometallic Chemistry, Center for Excellence in Molecular Synthesis, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, China*

Yuan-Da Hua − *State Key Laboratory of Organometallic Chemistry, Center for Excellence in Molecular Synthesis, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, China*

Yang-Jie Jiang − *State Key Laboratory of Organometallic Chemistry, Center for Excellence in Molecular Synthesis, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, China*

Shuai Huang − *State Key Laboratory of Organometallic Chemistry, Center for Excellence in Molecular Synthesis, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, China*

Di Chen − *State Key Laboratory of Organometallic Chemistry, Center for Excellence in Molecular Synthesis, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, China*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.orglett.0c01638

Author Contributions

‖J.D. and Y.-D.H. contributed equally.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

The authors thank the National Natural Science Foundation of China (21772215 and 21532010), the Strategic Priority Research Program of the Chinese Academy of Sciences (XDB20030100), the Chinese Academy of Sciences, the Technology Commission of Shanghai Municipality, and the Croucher Foundation of Hong Kong for financial support. This work is dedicated to Professor Henry N. C. Wong on the occasion of his 70th birthday.

REFERENCES

(1) (a) He, J.; Ling, J.; Chiu, P. *Chem. Rev.* **2014**, *114*, 8037−8128. (b) Khan, A.; Zhang, Y. J. *Synlett* **2015**, *26*, 853−860. (c) Ganesh, V.; Chandrasekaran, S. *Synthesis* **2016**, *48*, 4347−4380. (d) Allen, B. D. W.; Lakeland, C. P.; Harrity, J. P. A. *Chem. - Eur. J.* **2017**, *23*, 13830−13857. (e) De, N.; Yoo, E. J. *ACS Catal.* **2018**, *8*, 48−58. (f) Huang, G.; Yin, B. *Adv. Synth. Catal.* **2019**, *361*, 405−425. (g) Liu, Y.; Oble, J.; Pradal, A.; Poli, G. *Eur. J. Inorg. Chem.* **2020**, *2020*, 942−961. (h) Patil, N. T.; Yamamoto, Y. *Synlett* **2007**, *2007*, 1994−2005.

(2) Larksarp, C.; Alper, H. *J. Org. Chem.* **1999**, *64*, 4152−4158.

(3) (a) Sekido, M.; Aoyagi, K.; Nakamura, H.; Kabuto, C.; Yamamoto, Y. *J. Org. Chem.* **2001**, *66*, 7142−7147. (b) Wang, C.; Tunge, J. A. *Org. Lett.* **2006**, *8*, 3211−3214. (c) Wang, L.; Li, P.; Menche, D. *Angew. Chem., Int. Ed.* **2010**, *49*, 9270−9273. (d) Wang, L.; Menche, D. *J. Org. Chem.* **2012**, *77*, 10811−10823. (e) Wang, L.; Menche, D. *Angew. Chem., Int. Ed.* **2012**, *51*, 9425−9427. (f) Wu, A.; Feng, Q.; Sung, H. H. Y.; Williams, I. D.; Sun, J. *Angew. Chem., Int. Ed.* **2019**, *58*, 6776−6780. (g) Uno, H.; Imai, T.; Harada, K.; Shibata, N. *ACS Catal.* **2020**, *10*, 1454−1459. (h) Mao, B.; Liu, H.; Yan, Z.; Xu, Y.; Xu, J.; Wang, W.; Wu, Y.; Guo, H. *Angew. Chem., Int. Ed.* **2020**, DOI: 10.1002/anie.202002765. (i) Shintani, R.; Ito, T.; Nagamoto, M.; Otomo, H.; Hayashi, T. *Chem. Commun.* **2012**, *48*, 9936−9938.

(4) (a) Wang, C.; Tunge, J. A. *J. Am. Chem. Soc.* **2008**, *130*, 8118−8119. (b) Sun, M.; Ma, Y.-N.; Li, Y.-M.; Tian, Q.-P.; Yang, S.-D. *Tetrahedron Lett.* **2013**, *54*, 5091−5095. (c) Li, T.-R.; Tan, F.; Lu, L.-Q.; Wei, Y.; Wang, Y.-N.; Liu, Y.-Y.; Yang, Q.-Q.; Chen, J.-R.; Shi, D.-Q.; Xiao, W.-J. *Nat. Commun.* **2014**, *5*, 5500−5510. (d) Wei, Y.; Lu, L. Q.; Li, T. R.; Feng, B.; Wang, Q.; Xiao, W. J.; Alper, H. *Angew. Chem., Int. Ed.* **2016**, *55*, 2200−2204. (e) Guo, C.; Fleige, M.; Janssen-Müller, D.; Daniliuc, C. G.; Glorius, F. *J. Am. Chem. Soc.* **2016**, *138*, 7840−7843. (f) Leth, L. A.; Glaus, F.; Meazza, M.; Fu, L.; Thogersen, M. K.; Bitsch, E. A.; Jorgensen, K. A. *Angew. Chem., Int. Ed.* **2016**, *55*, 15272−15276. (g) Mei, G.-J.; Li, D.; Zhou, G.-X.; Shi, Q.; Cao, Z.; Shi, F. *Chem. Commun.* **2017**, *53*, 10030−10033. (h) Li, M.-M.; Wei, Y.; Liu, J.; Chen, H.-W.; Lu, L.-Q.; Xiao, W.-J. *J. Am. Chem. Soc.* **2017**, *139*, 14707−14713. (i) Mei, G.-J.; Bian, C.-Y.; Li, G.-H.; Xu, S.-L.; Zheng, W.-Q.; Shi, F. *Org. Lett.* **2017**, *19*, 3219−3222. (j) Wang, C.; Li, Y.; Wu, Y.; Wang, Q.; Shi, W.; Yuan, C.; Zhou, L.; Xiao, Y.; Guo, H. *Org. Lett.* **2018**, *20*, 2880−2883. (k) Li, T. R.; Wang, Y. N.; Xiao, W. J.; Lu, L. Q. *Tetrahedron Lett.* **2018**, *59*, 1521−1530. (l) Wang, Y.-N.; Xiong, Q.; Lu, L.-Q.; Zhang, Q.-L.; Wang, Y.; Lan, Y.; Xiao, W. J. *Angew. Chem., Int. Ed.* **2019**, *58*, 11013−11017. (m) Suo, J.-J.; Du, J.; Jiang, Y.-J.; Chen, D.; Ding, C.-H.; Hou, X.-L. *Chin. Chem. Lett.* **2019**, *30*, 1512−1514. (n) Zhao, H.-W.; Feng, N.-N.; Guo, J.-M.; Du, J.; Ding, W.-Q.; Wang, L.-R.; Song, X.-Q. *J. Org. Chem.* **2018**, *83*, 9291−9299.

(5) (a) Wang, Y.-N.; Yang, L.-C.; Rong, Z.-Q.; Liu, T.-L.; Liu, R.; Zhao, Y. *Angew. Chem., Int. Ed.* **2018**, *57*, 1596−1600. (b) Xu, H.; Khan, S.; Li, H.; Wu, X.; Zhang, Y. J. *Org. Lett.* **2019**, *21*, 214−217. (c) Khan, I.; Shah, B. H.; Zhao, C.; Xu, F.; Zhang, Y. J. *Org. Lett.* **2019**, *21*, 9452−9456.

(6) (a) Hou, X. L.; Wu, X. W.; Dai, L. X.; Cao, B. X.; Sun, J. *Chem. Commun.* **2000**, 1195−1196. (b) Wu, H.; Wu, X. W.; Hou, X. L.; Dai, L. X.; Wang, Q. R. *Chin. J. Chem.* **2002**, *20*, 816−818. (c) Hou, X. L.; Dong, D. X.; Yuan, K. *Tetrahedron: Asymmetry* **2004**, *15*, 2189−2191. (d) Wu, W.-Q.; Peng, Q.; Dong, D.-X.; Hou, X.-L.; Wu, Y.-D. *J. Am. Chem. Soc.* **2008**, *130*, 9717−9725. (e) Ding, C.-H.; Hou, X.-L. *Bull. Chem. Soc. Jpn.* **2010**, *83*, 992−1003.

(7) Du, J.; Jiang, Y.-J.; Suo, J.-J.; Wu, W.-Q.; Liu, X.-Y.; Chen, D.; Ding, C.-H.; Wei, Y.; Hou, X.-L. *Chem. Commun.* **2018**, *54*, 13143−13146.

(8) Wang, X.-J.; Zhang, J.; Wang, J.-D.; Qian, P.-T.; Liu, C.-X.; Xiang, W.-S. *Nat. Prod. Res.* **2013**, *27*, 1863−1869.

(9) CCDC 1999956 contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(10) Nising, C. F.; Bräse, S. *Chem. Soc. Rev.* **2008**, *37*, 1218−1228.

(11) CCDC 1999962 contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(12) CCDC 1999970 contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.