UNIVERSITY OF AMSTERDAM

UvA-DARE (Digital Academic Repository)

S,O-Ligand-Promoted Palladium-Catalyzed C-H Functionalization Reactions of Nondirected Arenes

Naksomboon, K.; Valderas, C.; Gomez-Martinez, M.; Alvarez-Casao, Y.; Fernández Ibáñez, M.A.

DOI
10.1021/acscatal.7b02356

Publication date
2017

Document Version
Final published version

Published in
ACS Catalysis

License
CC BY-NC-ND

Link to publication

Citation for published version (APA):
Naksomboon, K., Valderas, C., Gomez-Martinez, M., Alvarez-Casao, Y., & Fernández Ibáñez, M. A. (2017). S,O-Ligand-Promoted Palladium-Catalyzed C-H Functionalization Reactions of Nondirected Arenes. *ACS Catalysis*, *7*(9), 6342-6346. https://doi.org/10.1021/acscatal.7b02356

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: https://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, P.O. Box 19185, 1000 GD Amsterdam, The Netherlands. You will be contacted as soon as possible.
UvA-DARE is a service provided by the library of the University of Amsterdam (https://dare.uva.nl)

Download date:15 Sep 2026

This is an open access article published under a Creative Commons Non-Commercial No Derivative Works (CC-BY-NC-ND) Attribution License, which permits copying and redistribution of the article, and creation of adaptations, all for non-commercial purposes.

ACS Catalysis

Letter

pubs.acs.org/acscatalysis

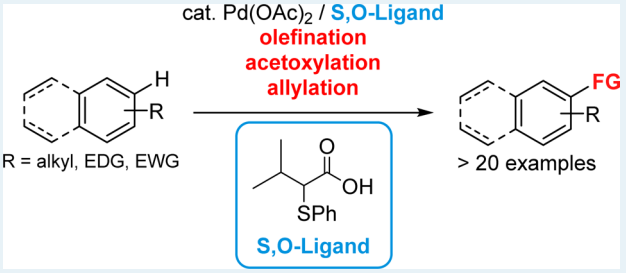
S,O-Ligand-Promoted Palladium-Catalyzed C−H Functionalization Reactions of Nondirected Arenes

Kananat Naksomboon, Carolina Valderas, Melania Gómez-Martínez, Yolanda Álvarez-Casao, and M. Ángeles Fernández-Ibáñez*

Van't Hoff Institute for Molecular Sciences, University of Amsterdam, Science Park 904, 1098 XH Amsterdam, The Netherlands

Supporting Information

ABSTRACT: Pd(II)-catalyzed C−H functionalization of nondirected arenes has been realized using an inexpensive and easily accessible type of bidentate S,O-ligand. The catalytic system shows high efficiency in the C−H olefination reaction of electron-rich and electron-poor arenes. This methodology is operationally simple, scalable, and can be used in late-stage functionalization of complex molecules. The broad applicability of this catalyst has been showcased in other transformations such as Pd(II)-catalyzed C−H acetoxylation and allylation reactions.



KEYWORDS: *C−H activation, S,O-ligand, olefination, palladium, arenes*

Over the past decade, metal-catalyzed C−H functionalization has emerged as a powerful methodology for the synthesis of valuable chemicals and materials.[1] This approach brings the opportunity to introduce complexity in organic molecules in a most efficient manner, since no prefunctionalization of the starting materials is required. Many elegant and efficient methodologies have been described for the direct functionalization of C−H bonds, but the vast majority of these examples require the presence of a directing group to enhance the reactivity and selectivity of the process.[2] Reports of direct C−H functionalization of simple arenes, without a directing group, are still scarce.[3] An attractive alternative to the use of directing groups is the development of suitable ligands that may lead to the discovery of new catalytic systems capable of promoting these transformations. However, to date, the arsenal of ligands that enable metal-catalyzed C−H functionalization reactions is very limited.[4] The research in our group aims at the development of novel ligands/catalytic systems capable of promoting selective C−H functionalization reactions to broaden the applicability of this strategy in organic synthesis. In this field, groundbreaking developments by the groups of Yu,[5] Sanford,[6] Stahl,[7] and Glorius[8] have identified pyridine-based ligands as very versatile and efficient ligands for nondirected Pd-catalyzed C−H functionalization reactions. In the particular case of the Pd-catalyzed C−H olefination (the Fujiwara−Moritani reaction) of simple arenes,[9] Yu's initial report shows good results with electron-poor arenes using a bulky pyridine ligand.[5] Subsequent investigations on the topic from Sanford's group describe the beneficial effect of 3,5-dichloropyridine ligand as a promotor of the Fujiwara−Moritani reaction for electron-rich and electron-poor arenes.[10]

Recently, our group reported an increase in reactivity and site selectivity in the C−H acetoxylation of simple arenes in the presence of picolinic acid ligands.[11] We postulate that the carboxylic acid functionality of the picolinic acid ligand promotes the C−H bond cleavage via a concerted metalation-deprotonation (CMD) mechanism.[12] In addition, the chelating ability of the ligand enhances the stability of the catalyst. However, the irreversible formation of an inactive palladium complex bearing two picolinic acid molecules is a major drawback for this system. We envisioned that a bidentate ligand with weaker coordination ability to $Pd(OAc)_2$ than the bidentate picolinic acid ligand would lead to a more efficient catalyst. Thus, we decided to investigate the performance of bidentate thioethercarboxylates, which are easily accessible and have hemilabile behavior in palladium chemistry.[13] To the best of our knowledge, this type of ligand has never been used in metal catalysis. Here, we report the discovery of a new class of S,O-ligands, that enable nondirected Pd-catalyzed C−H functionalization reactions of arenes. These S,O-ligands show higher activity and stronger influence on the site selectivity than the well-established pyridine-based ligands in the C−H olefination of simple arenes. The new methodology is also successful in preparative scale and in late-stage functionalization of complex molecules, a step that could not be taken with previously described catalytic systems. Moreover, the new Pd/S,O-ligand catalyst is also active in the C−H acetoxylation and allylation of benzene.

Thioethercarboxylic acid ligands can be easily made in gram scale in two steps, starting from commercially available carboxylic acids.[14,15] We started our investigations by studying the performance of these thioethercarboxylic acid ligands in the Pd(II)-catalyzed C−H olefination reaction employing benzene

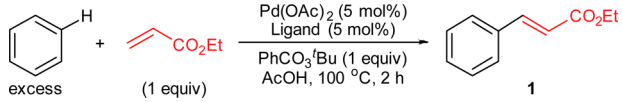
Received: July 17, 2017
Revised: August 17, 2017
Published: August 18, 2017

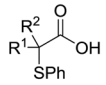
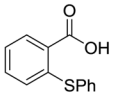
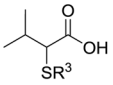
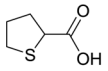
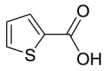
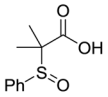
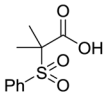
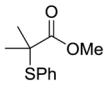
© 2017 American Chemical Society

DOI: 10.1021/acscatal.7b02356
ACS Catal. 2017, 7, 6342−6346

and ethyl acrylate as model substrates under standard reaction conditions (see Table 1). The reaction, in the absence of a ligand, provided, after 2 h, the alkenylated product **1** in only 16% yield. In contrast, the presence of 2-ethy-2-(phenylthio)-acetic acid (**L1**) resulted in an increase in yield, up to 64%. Other thioethercarboxylic acid ligands with different side chains of the thioetheracetic acid were studied. Similar yields were obtained with ligands bearing aliphatic chains in α-position (**L2** and **L3**), including the gem-dimethyl (**L4**) and cyclopropane (**L5**) ligands. The phenylthioetheracetic acid (**L6**), 2-phenyl-2-(phenylthio)acetic acid (**L7**), and the 2-(phenylthio)benzoic acid (**L8**) furnished the olefinated product **1** in lower yields (20%–40%) than **L1**–**L5**. We next explored the reactivity of the catalytic system regarding the substituents attached to the sulfur atom. In particular, electron-rich, electron-poor, bulky aromatic (**L9**–**L14**), and aliphatic substituents (**L15** and **L16**) were investigated. Unfortunately, all these ligands provided similar or slightly lower yields than those obtained with **L1**–**L5**, with the exception of the bulky ligand **L10**, with a triphenylmethyl group, which did not furnish any product. The reaction with the tetrahydro-2-thiophenecarboxylic acid (**L17**) and the 2-thiophenecarboxylic acid (**L18**) provided the desired product, in 61% and 26% yield, respectively. From these initial studies, we concluded that, in general, thioethercarboxylic acid ligands bearing aliphatic substituents in α-position and with a neutral aromatic ring attached to the sulfur atom constitute the most active catalyst for the Pd-catalyzed C–H olefination of benzene.

Table 1. Ligand Optimization of Dehydrogenative Heck Reaction

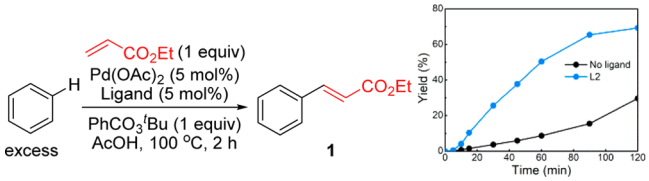


Entry	Ligand			Yield (%)[a]
1	No ligand			16
		R^1 R^2		
2		Et H	(**L1**)	64
3		^{i}Pr H	(**L2**)	63
4		^{t}Bu H	(**L3**)	64
5		Me Me	(**L4**)	71
6		-CH_2CH_2-	(**L5**)	61
7		H H	(**L6**)	40
8		Ph H	(**L7**)	20
9			(**L8**)	16
		R^3		
10		Mes	(**L9**)	62
11		Tr	(**L10**)	NR
12		*p*-OMe-C_6H_4	(**L11**)	53
13		2,4,6-$(OMe)_3$-C_6H_2	(**L12**)	40
14		C_6F_5	(**L13**)	39
15		*p*-CF_3-C_6H_4	(**L14**)	46
16		$CH_2C_6H_5$	(**L15**)	37
17		^{i}Pr	(**L16**)	44
18			(**L17**)	61
19			(**L18**)	26
20			(**L19**)	16
21			(**L20**)	20
22			(**L21**)	27
23			(**L22**)	37

[a]Yields were determined by ^{1}H NMR analysis of the crude mixture, using CH_2Br_2 as internal standard.

The kinetic profile in Scheme 1 clearly indicates that 2-*i*-propyl-2-(phenylthio)acetic acid (**L2**) increased the reaction rate dramatically. Having established the positive effect of the S,O-ligand in the dehydrogenative Heck reaction, different experiments were conducted to ascertain the role of each functionality in the ligand (Table 1). First, we performed the reaction with the corresponding sulfoxide (**L19**) and sulfone (**L20**) to confirm that these species are not responsible for the observed catalytic activity. Indeed, the reaction in the presence of either of these ligands proceeded with similar outcome as the reaction carried out without any ligand. The use of thioanisole (**L21**) or methyl 2,2-dimethyl-2-(phenylthio)acetate (**L22**) as ligands furnished the olefinated product **1** in 27% and 37% yield, respectively. These results confirmed that the presence of both functionalities, the thioether and the carboxylic acid, are crucial for the acceleration of the reaction. Different conditions for the oxidative Heck reaction were examined in the presence of **L2** (see Tables S2–S5 in the Supporting Information), but no improvement was observed, compared to the standard conditions.

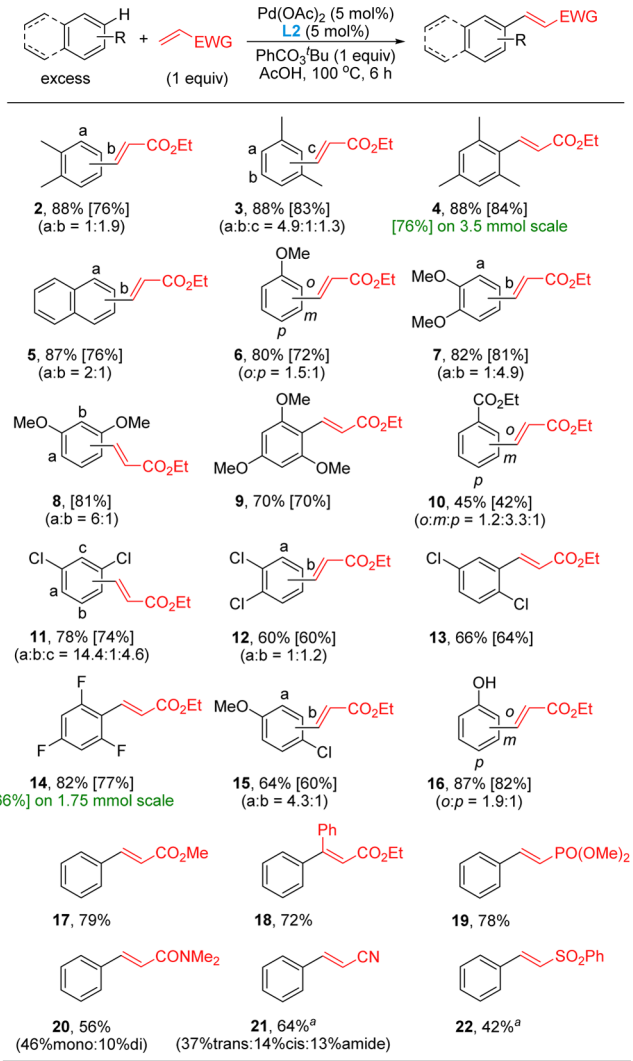
Scheme 1. Kinetic Profile of the Dehydrogenative Heck Coupling of Benzene and Ethyl Acrylate without Ligand and in the Presence of L2



With the optimized conditions in hand, we set out to explore the substrate scope of this transformation with different substituted arenes (see Table 2).[16] All the reactions were performed in a pressure tube using 5 mol % of catalyst and stirring at 100 °C for 6 h. At this time, the formation of Pd black was observed in most cases. The reaction of arenes with alkyl substituents such as *ortho*- and *meta*-xylene and mesitylene provided the alkenylated products **2**, **3**, and **4** with excellent yields (76%, 83%, and 84%, respectively). Regarding the selectivity, the *ortho*-xylene provided a 1:1.9 ratio of the α(a) and β(b) isomers, respectively, and the *meta*-xylene provided a mixture of isomers (a:b:c = 4.9:1:1.3 ratio) in favor of the less sterically *ortho* olefinated product. In a similar manner, 76% yield was obtained in the reaction using naphthalene as starting material with a ratio of 2:1 in favor of the α-olefinated product **5**. We also tested the reaction of arenes bearing strong electron-donating groups. Excellent yields were obtained employing anisole, 1,2- and 1,3-dimethoxybenzene, and 1,3,5-trimethoxybenzene as starting materials (70%–81%). Anisole provided a

DOI: 10.1021/acscatal.7b02356
ACS Catal. 2017, 7, 6342–6346

Table 2. Substrate Scope*

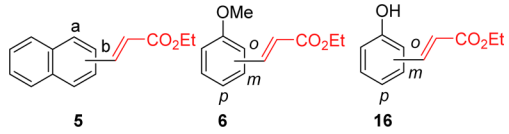


*Yields were determined by ^{1}H NMR analysis of the crude mixture using CH_2Br_2 as internal standard. Isolated yields are given in square brackets. [a]The reaction was stirred overnight.

1.5:1 ratio of the *ortho* and *para* isomers, respectively, and only traces of the *meta* isomer were detected. 1,2-Dimethoxybenzene yielded a 1:4.9 ratio of the corresponding α(a) and β(b) isomers. Similarly, the C−H olefination of 1,3-dimethoxybenzene occurred mainly at the least sterically hindered C−H bond at the *ortho* position of the methoxy group (6:1 ratio). The C−H olefination of electron-poor arenes was also explored. The reaction with ethyl benzoate provided the desired olefinated products **10** in 42% yield, as a mixture of isomers in favor of the *meta* olefinated product (*o*:*m*:*p* = 1.2:3.3:1). When 1,2- 1,3-, and 1,4-dichlorobenzene were employed as starting materials, the desired products were obtained as a mixture of regioisomers in good yields (60%−74%). The reaction with 1,3,5-trifluorobenzene furnished the desired product **14** in 77% yield. When 4-chloroanisole was subjected to standard reaction conditions, the olefinated product **15** was obtained in 60% yield in 4.3:1 ratio in favor of the *ortho* product, with respect to the methoxy substituent. Moreover, the direct C−H olefination of unprotected phenol provided the *ortho*- and *para*-olefinated product **16** in excellent yield (82%) and in a ratio of 1.9:1, respectively. Taking into consideration that only a few reports have addressed the direct functionalization of phenols, both the yield obtained and the preference for the *ortho* olefination are remarkable.[17] In all cases, we observed much higher yields using **L2**, in comparison with those in which the ligand was absent (see Table S6 in the Supporting Information). Finally, the C−H olefination in preparative scale, using mesitylene and 1,3,5-trifluorobenzene as starting materials, afforded the corresponding olefinated products **4** and **14** with good yields without any significant erosion from the original values.

Regarding the site selectivity of the reaction, our results indicate that it is mainly dictated by the substrate and controlled by electronic factors, with preferential functionalization at the most electronic-rich position in the arene. However, when we compare the site selectivity of the reaction with and without **L2**, it is evident the influence of **L2** on the site selectivity (see Table S6 in the Supporting Information). In Table 3, we show some substrates where a different trend in site

Table 3. Comparison of the Site Selectivity



5 **6** **16**

ligand	**5** (a:b)	**6** (*o*:*m*:*p*)	**16** (*o*:*p*)
no ligand[a]	1:1	1:0:1.7	1:1.3
L2[a]	2:1	1.5:0:1	1.9:1
3,5-dichloropyridine	1.1:1[b]	4.1:1:7.4[b]	1.4:1[c]

[a]Site selectivity was determined by ^{1}H NMR analysis of the isolated olefinated product. [b]Site selectivity reported previously in ref 10. [c]Site selectivity was determined by ^{1}H NMR analysis of the crude mixture.

selectivity in the presence of **L2** was observed in comparison with the reaction without ligand. The reaction of naphthalene in the absence of ligand provided a 1:1 ratio of isomers versus the 2:1 ratio obtained in the presence of **L2** in favor of the α-olefinated product. The reactions of anisole or phenol without ligand provided a mixture of *ortho* and *para* products, with a clear preference for the former. In contrast, in the presence of **L2**, the *ortho*-olefinated products were preferred. On the other hand, a similar trend in the site selectivity of the reaction of naphthalene and anisole was observed without ligand and with 3,5-dichloropyridine, which was the best ligand reported by Sanford for the C−H olefination of simple arenes.[10] The reaction of phenol using 3,5-dichloropyridine provided a mixture of *ortho* and *para* products in 50% NMR yield with a small preference for the *ortho* product (1.4*o*:1*p*). These results indicate that the S,O-ligand has stronger influence on the site selectivity of the C−H olefination reaction than the pyridine-based ligand.

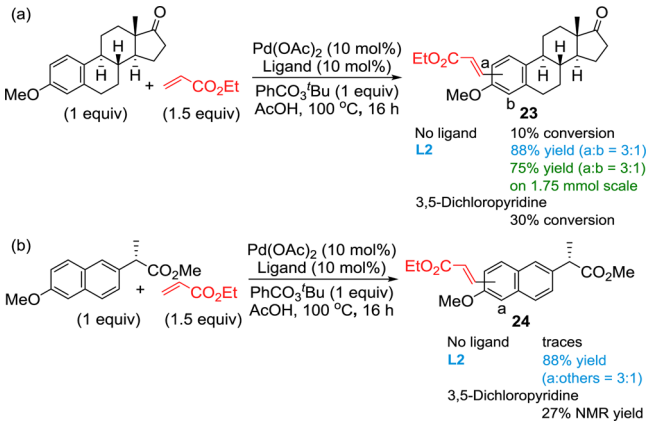
Next, we explored the olefin scope. The reaction with methyl acrylate and ethyl cinnamate furnished the olefinated products **17** and **18**, respectively, in high yields. Other electrophilic alkenes such as vinyl phosphonates, vinyl amides, vinyl nitriles, and vinyl sulfonates reacted efficiently with benzene, leading to the olefinated products **19**−**22** in good yields (42%−78%). Unfortunately, we did not observe any improvement in the yield using nonactivated alkenes such as styrene when using **L2**, in comparison with the reaction without ligand.

Having revealed the high reactivity of the new catalytic system in simple arenes, we assessed the suitability of this methodology for late-stage functionalization of complex

DOI: 10.1021/acscatal.7b02356
ACS Catal. 2017, 7, 6342−6346

molecules (see Scheme 2). To the best of our knowledge, the intermolecular Fujiwara–Moritani reaction of arenes without

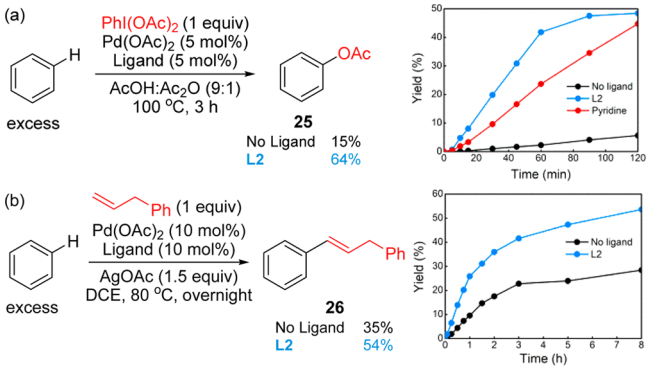
Scheme 2. Late-Stage C–H Olefination of (a) Estrone and (b) Naproxen Derivatives



directing groups has not been applied in late-stage functionalization. The reaction of *O*-methylestrone (1 equiv) with ethyl acrylate (1.5 equiv) and 10 mol % of $Pd(OAc)_2$ provided the desired product **23** in only 10% conversion. In contrast, when the reaction was performed in the presence of **L2**, the olefinated product **23** was obtained in 88% yield as a mixture of *ortho*-olefinated isomers, with respect to the methoxy substituents (a:b = 3:1). Moreover, we compared our catalytic system with the one previously reported by Sanford for the C–H olefination of simple arenes using 3,5-dichloropyridine as a ligand.[10] Under the same reaction conditions, only 30% conversion was obtained. Similarly, when the reaction of the naproxen derivative was carried out in the absence of a ligand, only traces of olefinated product **24** were detected by ^1H NMR. The same reaction in the presence of **L2** furnished a mixture of products with a combined isolated yield of 88%, being the main isomer the *ortho*-olefinated product, with respect to the methoxy substituent (a:other isomers = 3:1). Again, for comparison, we performed the reaction of the naproxen derivative using 3,5-dichloropyridine as ligand. Under the standard conditions, we obtained a mixture of olefinated products in 27% NMR yield. To further prove the applicability of the new catalytic system, the C–H olefination in preparative scale of *O*-methylestrone (1.75 mmol) was performed. To our delight, yield comparable to that of the original value was found.

In search for a general and efficient catalytic system capable of promoting a large number of C–H functionalization reactions, we decided to test **L2** in C–H acetoxylation and allylation reactions (see Scheme 3). The C–H acetoxylation reaction was performed using benzene as the substrate and $PhI(OAc)_2$ as the oxidant. Under the standard reaction conditions, the presence of **L2** significantly increased the reaction rate of the process. A 64% yield was reached, compared to the 15% obtained in the absence of the ligand (Scheme 3a). We monitored the reaction over time with **L2** and without ligand. Also, the reaction in the presence of pyridine was performed for comparison.[6a] The kinetic profile of these reactions indicates that the presence of **L2** dramatically accelerated the reaction. Moreover, the S,O-ligand showed higher activity than the pyridine ligand. In addition, the C–H allylation reaction using benzene and allylbenzene as substrates

Scheme 3. S,O-Ligand-Promoted Pd-Catalyzed (a) C–H Acetoxylation and (b) Allylation of Benzene



was also conducted with and without **L2**.[18] Again, we observed an acceleration of the reaction rate in the presence of the S,O-ligand **L2** and the corresponding allylated product was obtained in 54% yield (Scheme 3b). In this case, no acceleration using pyridine as ligand was observed.

The precise role of the S,O-ligand in the C–H olefination, acetoxylation, and allylation reactions remains under investigation.[19] However, considering that the C–H activation of the inert C–H bond of the arene is common in all these transformation, it seems reasonable to propose that the S,O-ligand is assisting the C–H bond cleavage.

In summary, we have found a new catalytic system based on $Pd(OAc)_2$ and easily accessible S,O-ligands that enables nondirected C–H functionalization reactions of arenes. The catalyst promotes the C–H olefination reaction of both electron-rich and electron-poor arenes in high yields. Remarkably, the Pd/S,O-ligand system shows higher activity and influence in the site selectivity than the well-established Pd/pyridine-based catalytic system. The catalytic power of the new methodology is convincingly demonstrated in late-stage functionalization of complex molecules. Furthermore, the new catalyst is also active in the C–H acetoxylation and allylation reaction of benzene. We expect this new class of ligands to find broad application in C–H functionalization reactions.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acscatal.7b02356.

Experimental procedures and compounds characterization (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: m.a.fernandezibanez@uva.nl.

ORCID

M. Ángeles Fernández-Ibáñez: 0000-0002-7694-5911

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We acknowledge financial support from NWO though a VIDI grant (No. 723.013.006). We acknowledge Daniël Verdoorn for the synthesis of **L5**. M. Gómez-Martínez acknowledges the Vicerrectorate of Research, Development, and Innovation at

DOI: 10.1021/acscatal.7b02356
ACS Catal. 2017, 7, 6342–6346

the University of Alicante (Spain) for the travel grant. We thank Prof. S. R. Harutyunyan, Prof. B. Macia, Dr. Sergio Maroto and Dr. Alejandro Orden for their helpful comments on the manuscript.

REFERENCES

(1) For general reviews on C−H functionalization, see: (a) Alberico, D.; Scott, M. E.; Lautens, M. *Chem. Rev.* **2007**, *107*, 174−238. (b) Yu, J.-Q.; Shi, Z. *C−H Activation*; Yu, J.-Q., Shi, Z., Eds.; Topics in Current Chemistry, Vol. *292*; Springer: Berlin, 2010. (c) Hartwig, J. F. *J. Am. Chem. Soc.* **2016**, *138*, 2−24. (d) Davies, H. M. L.; Morton, D. *J. Org. Chem.* **2016**, *81*, 343−350. For a special issue dedicated to this topic, see: (e) Doyle, M. P.; Goldberg, K. I. *Acc. Chem. Res.* **2012**, *45*, 777.10.1021/ar300096z

(2) (a) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147−1169. (b) Chen, Z.; Wang, B.; Zhang, J.; Yu, W.; Liu, Z.; Zhang, Y. *Org. Chem. Front.* **2015**, *2*, 1107−1295. (c) Maes, J.; Maes, B. U. W. *Adv. Heterocycl. Chem.* **2016**, *120*, 137−194. (d) Pototschnig, G.; Maulide, N.; Schnürch, M. *Chem.—Eur. J.* **2017**, *23*, 9206−9232. (e) Ma, W.; Gandeepan, P.; Li, J.; Ackermann, L. *Org. Chem. Front.* **2017**, *4*, 1435−1467.

(3) For a review on C−H functionalization of substrates that do not bear directing groups, see: (a) Kuhl, N.; Hopkinson, M. N.; Wencel-Delord, J.; Glorius, F. *Angew. Chem., Int. Ed.* **2012**, *51*, 10236−10254. For selected examples, see: (b) Robbins, D. W.; Hartwig, J. F. *Angew. Chem., Int. Ed.* **2013**, *52*, 933−937. (c) Shrestha, R.; Mukherjee, P.; Tan, Y.; Litman, Z. C.; Hartwig, J. F. *J. Am. Chem. Soc.* **2013**, *135*, 8480−8483. (d) Ricci, P.; Krämer, K.; Larrosa, I. *J. Am. Chem. Soc.* **2014**, *136*, 18082−18086. (e) Cheng, C.; Hartwig, J. F. *J. Am. Chem. Soc.* **2015**, *137*, 592−595. (f) Larsen, M. A.; Wilson, C. V.; Hartwig, J. F. *J. Am. Chem. Soc.* **2015**, *137*, 8633−8643. (g) Paudyal, M. P.; Adebesin, A. M.; Burt, S. R.; Ess, D. H.; Ma, Z.; Kürti, L.; Falck, J. R. *Science* **2016**, *353*, 1144−1147. (h) Luan, Y.-X.; Zhang, T.; Yao, W.-W.; Lu, K.; Kong, L.-Y.; Lin, Y.-T.; Ye, M. *J. Am. Chem. Soc.* **2017**, *139*, 1786−1789.

(4) For a general review, see: Engle, K. M.; Yu, J.-Q. *J. Org. Chem.* **2013**, *78*, 8927−8955.

(5) Zhang, Y.-H.; Shi, B.-F.; Yu, J.-Q. *J. Am. Chem. Soc.* **2009**, *131*, 5072−5074.

(6) (a) Emmert, M. H.; Cook, A. K.; Xie, Y. J.; Sanford, M. S. *Angew. Chem., Int. Ed.* **2011**, *50*, 9409−9412. (b) Cook, A. K.; Emmert, M. H.; Sanford, M. S. *Org. Lett.* **2013**, *15*, 5428−5431. (c) Gary, J. B.; Cook, A. K.; Sanford, M. S. *ACS Catal.* **2013**, *3*, 700−703. (d) Cook, A. K.; Sanford, M. S. *J. Am. Chem. Soc.* **2015**, *137*, 3109−3118.

(7) Izawa, Y.; Stahl, S. S. *Adv. Synth. Catal.* **2010**, *352*, 3223−3229.

(8) Wang, C.; Rakshit, S.; Glorius, F. *J. Am. Chem. Soc.* **2010**, *132*, 14006−14008.

(9) Moritanl, I.; Fujiwara, Y. *Tetrahedron Lett.* **1967**, *8*, 1119−1122.

(10) Kubota, A.; Emmert, M. H.; Sanford, M. S. *Org. Lett.* **2012**, *14*, 1760−1763.

(11) Valderas, C.; Naksomboon, K.; Fernández-Ibáñez, M. Á. *ChemCatChem* **2016**, *8*, 3213−3217.

(12) (a) Lafrance, M.; Fagnou, K. *J. Am. Chem. Soc.* **2006**, *128*, 16496−16497. (b) García-Cuadrado, D.; Braga, A. A. C.; Maseras, F.; Echavarren, A. M. *J. Am. Chem. Soc.* **2006**, *128*, 1066−1067. (c) Ackermann, L. *Chem. Rev.* **2011**, *111*, 1315−1345. (d) Granell, J.; Martínez, M. *Dalton Trans.* **2012**, *41*, 11243−11258.

(13) (a) Meyer, W. H.; Brüll, R.; Raubenheimer, H. G.; Thompson, C.; Kruger, G. J. *J. Organomet. Chem.* **1998**, *553*, 83−90. (b) Esterhuysen, M. W.; Brüll, R.; Raubenheimer, H. G.; Esterhuysen, C.; Kruger, G. J. *J. Organomet. Chem.* **2001**, *619*, 164−178.

(14) (a) Zhang, L. H.; Duan, J.; Xu, Y.; Dolbier, W. R., Jr. *Tetrahedron Lett.* **1998**, *39*, 9621−9622. (b) Yeh, P.-P.; Daniels, D. S. B.; Cordes, D. B.; Slawin, A. M. Z.; Smith, A. D. *Org. Lett.* **2014**, *16*, 964−967.

(15) The preferred ligand **L2** is prepared in one step from commercial available 2-bromo-3-methylbutanoic acid in 73% isolated yield. See the Supporting Information.

(16) We also tested the reaction of other arenes in the presence of **L4** (NMR yields): naphthalene, 89% (2.2a:1b); mesitylene, 93%; and 1,3,5-trifluorobenzene, 62%. The yields obtained are similar or lower than those provided using **L2** as ligand.

(17) For selected examples of direct C−H functionalization of unprotected phenols, see: (a) Bedford, R. B.; Coles, S. J.; Hursthouse, M. B.; Limmert, M. E. *Angew. Chem., Int. Ed.* **2003**, *42*, 112−114. (b) Bedford, R. B.; Limmert, M. E. *J. Org. Chem.* **2003**, *68*, 8669−8682. (c) Luo, J.; Preciado, S.; Larrosa, I. *J. Am. Chem. Soc.* **2014**, *136*, 4109−4112. (d) Yu, Z.; Ma, B.; Chen, M.; Wu, H.-H.; Liu, L.; Zhang, J. *J. Am. Chem. Soc.* **2014**, *136*, 6904−6907.

(18) Jin, W.; Wong, W.-T.; Law, G.-L. *ChemCatChem* **2014**, *6*, 1599−1603.

(19) In our preliminary investigations on the mechanism of this transformation, we have isolated and fully characterized by X-ray analysis the palladium complex bearing two molecules of **L4** attached (CCDC 1567101 contains the supplementary crystallographic data for $Pd[OCOC(SPh)Me_2]_2$). The model reaction using this complex as catalyst furnished the olefinated product **1** in a similar yield (22% NMR yield) to that obtained with $Pd(OAc)_2$ (Table 1, entry 1), suggesting that this complex is not involved in our catalytic system.

DOI: 10.1021/acscatal.7b02356
ACS Catal. 2017, 7, 6342−6346