A Journal of the Gesellschaft Deutscher Chemiker

Angewandte International Edition GDCh Chemie

www.angewandte.org

Accepted Article

Title: Palladium-Catalyzed Asymmetric Decarboxylative Addition of β-Keto Acids to Heteroatom-substituted Allenes

Authors: Dong-Jin Jang, Sukhyun Lee, Juyeol Lee, Dohyun Moon, and Young Ho Rhee

To be cited as: *Angew. Chem. Int. Ed.* 10.1002/anie.202107990

Link to VoR: https://doi.org/10.1002/anie.202107990

WILEY-VCH

10.1002/anie.202107990

WILEY-VCH

Palladium-Catalyzed Asymmetric Decarboxylative Addition of β-Keto Acids to Heteroatom-substituted Allenes

Dong-Jin Jang, [a]† Sukhyun Lee, [a]† Juyeol Lee, [a] Dohyun Moon[b] and Young Ho Rhee*[a]

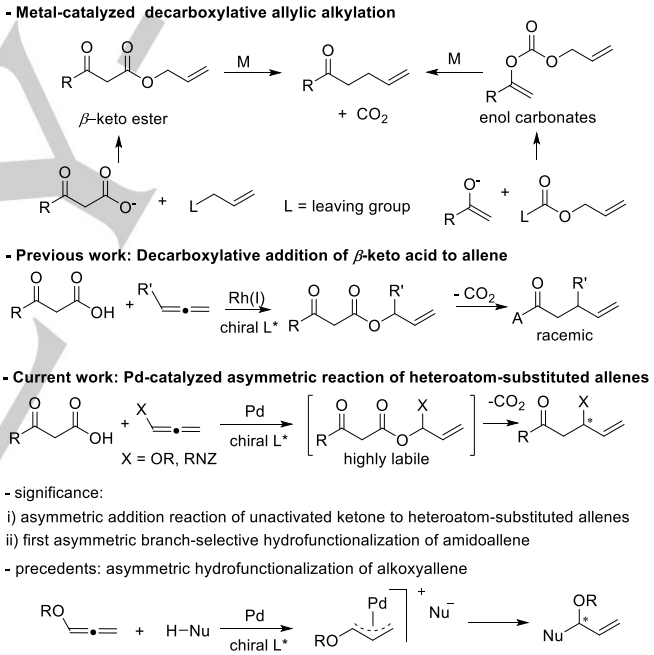
[a] D.-J. Jang, S. Lee, J. Lee, Prof. Y. H. Rhee
Department of Chemistry
Pohang University of Science and Technology
Cheongam-ro 77, Nam-gu, Pohang, Gyeongbuk 37673, Republic of Korea
E-mail: yhrhee@postech.ac.kr
†These authors contributed equally to the manuscript
[b] Dr. D. Moon
Beamline Department
Pohang Accelerator Laboratory
80 Jigokro-127-beongil, Nam-gu, Pohang, Gyeongbuk 37673, Republic of Korea

Supporting information for this article is given via a link at the end of the document.

Abstract: Pd-catalyzed asymmetric addition reaction of β-keto acids to heteroatom-substituted allene is reported. This reaction generates β-substituted ketones in an asymmetric manner by way of a branch-selective decarboxylative allylation pathway. The reaction accommodates various alkoxyallenes as well as amidoallenes.

Over the last decades, metal-catalyzed asymmetric allylic alkylation (AAA) has become one of the most powerful carbon-carbon bond forming reactions.[1] Traditionally, the reaction accomodates structurally diverse soft carbon nucleophiles. In recent years, however, some examples of unactivated carbonyl compounds have been reported. Decarboxylative allylation reaction has emerged as a new and highly useful variant of the AAA reaction utilizing carbonyl groups as nucleophiles.[2,3] In general, this method employs allylic β-keto esters[4] or enol allyl carbonates[5] as the substrates, which needs to be prepared in separate steps prior to the desired reaction (Scheme 1). In this regard, a more direct protocol would be to initiate the reaction with the addition of β-keto acid to allene precursors. Moreover, the use of substituted allene offers potential to introduce a stereogenic center via branch-selecive C-C bond formation. Despite intriguing features of this method discussed above, development of an asymmetric reaction is limited, particularly with carbon-substituted allenes.[6,7] This is presumably due to the complicated kinetic behavior of π-allyl complexes associated with the generation and utilization of the allylic β-keto ester intermediates.

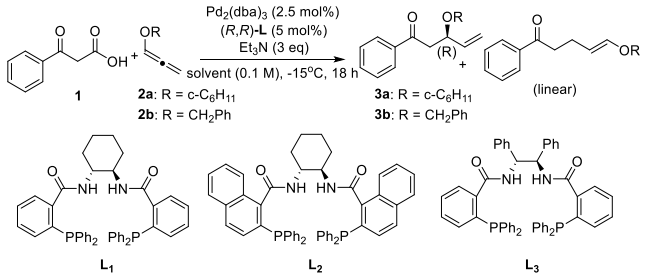
Since the seminal work of Trost, numerous asymmetric Pd-catalyzed hydrofunctionalization reactions of alkoxyallene have been developed.[8,9] Within this context, we reported asymmetric addition reaction of heteroatom nucleophiles to alkoxyallene, which emerged as a unique *de novo* glycosylation method.[10] Here, we disclose an unprecedented Pd-catalyzed asymmetric decarboxylative addition reaction of β-keto acid to hetereoatom-substituted allenes such as alkoxy- and amido-allenes.[11-13] The latter is noteworthy because asymmetric hydrofunctionalization of amidoallene is rare. Extensive mechanistic studies established the initial hydrocarboxylation as the key event (Scheme 1), which facilitates the subsequent asymmetric decarboxylative allylation. From a synthetic viewpoint, the proposed reaction produces highly functionalized γ,δ-unsaturated ketones possessing stereogenic heteroatom substituents at the β-position.



Scheme 1. Basic concept of the research

In a preliminary reaction using β-keto acid **1** and allene **2a** at -15°C in CH_2Cl_2 along with $Pd_2(dba)_3$ (2.5 mol%), standard Trost-type ligand **L_1** (5 mol%) and triethylamine (3 eq), the desired product **3a** was obtained in low 34% yield but with significant 53% ee (entry 1, Table 1). Switching the ligand to **L_2** improved the yield of **3a** to 61% with 91% ee (entry 2). Further increase of the yield (91%) and ee (97%) arose when **L_3** was employed (entry 3). Employing more polar solvents such as THF and acetonitrile as well as using benzyloxyallene **2b** dropped the conversion with slight decrease of ee (entries 4-6). [14] Notably, no linear isomer was observed, as with the other hydrofunctionalization of alkoxyallenes.

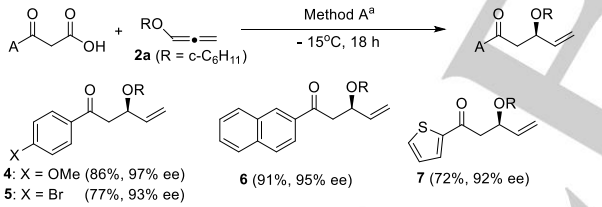
Table 1. Optimization of the reaction of alkoxyallene



entry	ligand	allene	solvent	Yield[a] (%)	ee[b](%)
1	L_1	**2a**	CH_2Cl_2	34	53
2	L_2	**2a**	CH_2Cl_2	61	91
3	L_3	**2a**	CH_2Cl_2	91	97
4	L_3	**2a**	THF	55	89
5	L_3	**2a**	CH_3CN	37	74
6	L_3	**2b**	CH_2Cl_2	42	87

[a] Isolated yield. [b] Determined by HPLC analysis

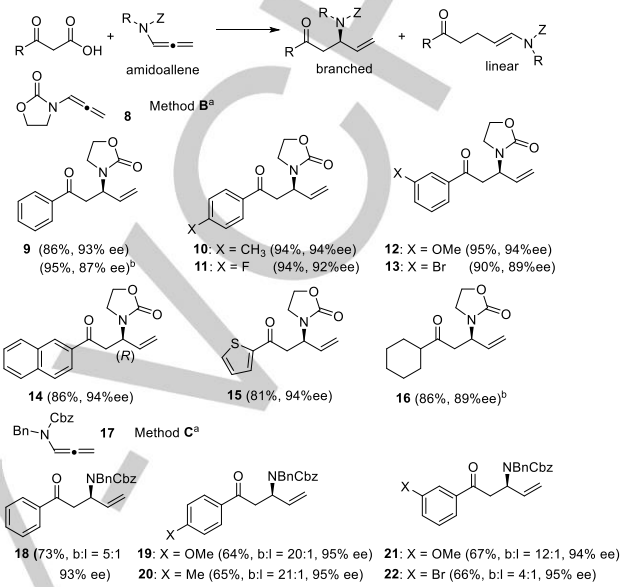
With the optimized condition described (entry 3, Table 1) in hand, we explored the scope of this reaction. Varying the *para*-substituents of the phenyl ring provided the products **4** and **5** in comparable yield and ee to that of **3a**. In addition, *β*-keto acids containing bulkier naphthyl and heterocyclic thiophenyl group were well accommodated into the reaction, as demonstrated by the high yield and ee of **6** and **7** (Scheme 2).



[a] Method A: acid (1 eq), allene (1 eq), $Pd_2(dba)_3$ (2.5 mol%), ligand L_3 (5 mol%) and Et_3N (3 eq) was reacted in CH_2Cl_2(0.1M)

Scheme 2. Scope of nucleophiles with alkoxyallene **2a**

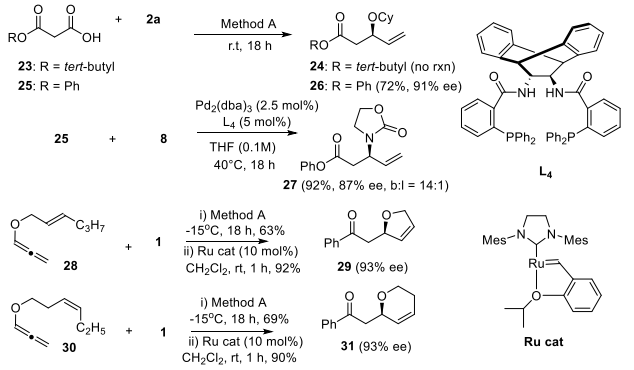
Encouraged by this promising result with the alkoxyallene, we then decided to explore oxazolidinone-allene **8**. After further modification, the reaction of **8** (1 eq), acid **1** (1 eq), $Pd_2(dba)_3$ (2.5 mol%) and ligand L_2 (5 mol%) in THF generated the desired product **9** in 95% yield and 87% ee with no formation of the linear isomer (Scheme 3). Interestingly, addition of 5 mol% trifluoroacetic acid slightly improved the ee to 93%. Under this new condition, a number of *β*-keto acids bearing aryl groups worked well to provide the corresponding *β*-amido-arylketones **10**~**15** in high yield and ee. In addition, *β*-amido-alkylketone **16** was also obtained in significant 86% yield and 89% ee. [14] The absolute configuration of **14** verified by the X-ray crystallographic analysis (CCDC deposition No. 2084084) proved consistent with β-alkoxyketone **3a** (For the detailed analysis, see the SI). Meanwhile, the reaction of acylic amidoallene **17** was slower than **8**. Full conversion required higher loading of $Pd_2(dba)_3$ (5 mol%) and the use of excess *β*-keto acids (2 eq). Nevertheless, the corresponding *β*-amido-ketones **18**~**22** were obtained in high yield and enantioselectivity.[15] Interestingly, small amount linear isomer was obtained, presumably due to the increased steric effect of the amide substituents on **17**.



[a] Method B: acid (1 eq), allene (1 eq), $Pd_2(dba)_3$ (2.5 mol%), ligand L_2 (5 mol%) and CF_3CO_2H (5 mol%) was reacted in THF(0.1M) at -15°C for 3-24h/ Method C: acid (2 eq), allene (1 eq), $Pd_2(dba)_3$ (5 mol%), ligand L_2 (10 mol%) and Et_3N (0.1 eq) was reacted in toluene(0.2M) at -15°C for 18 h
[b] CF_3CO_2H was not used

Scheme 3. Reaction of the amidoallenes **8** and **17**

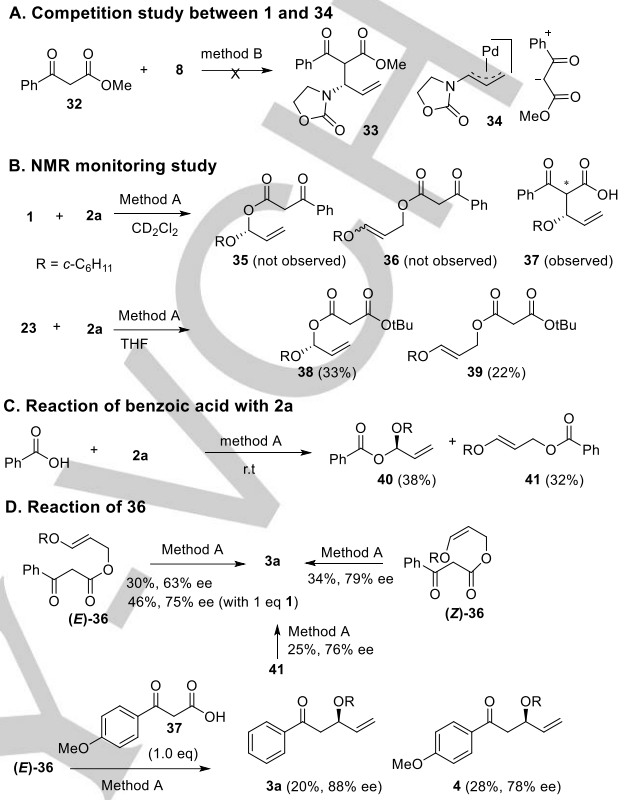
Next, we tested malonic acid monoester to further broaden the scope of the reaction (Scheme 4). Initial attempts to use *tert*-butyl ester **23** with alkoxyallene **2a** failed to provide the desired *β*-alkoxy ester **24**. Notably, switching to phenyl ester **25** produced **26** in significant 72% yield and 91% ee. Also, an analogous reaction of **25** and **8** performed with ligand L_4 at 40°C in THF furnished *β*-amido ester **27** in 92% yield and 87% ee with ~14:1 branch selectivity. Thus, the proposed reaction could be used in preparation of new functionalized *β*-amino acid derivatives. [16] We also tested ene-alkoxyallenes **28** and **30** to explore the synthesis of cyclic ethers. The reaction of allene **28** with **1** under the method A followed by the ring-closing-metathesis reaction using 2nd-generation Hoveyda-Grubbs catalyst (10 mol%) provided enantioenriched dihydrofuran **29** in 58% yield (over two steps) and 93% ee. Analogously, dihydropyran **31** was prepared in 62% yield and 93% ee from **30**. Based upon these results, the current method may find further use in the total synthesis of various bioactive *C*-glycoside natural products. [17]



Scheme 4. Synthetic applications

From a mechanistic viewpoint, the initial hydrocarboxylation seems crucial for the desired transformation.[18] This is highlighted by the competition reaction of methyl ester **32** with amidoallene **8**. Under the method B, **32** showed no reactivity towards formation of **33** (Scheme 5), which strongly suggests that the ion pair **34** could not be formed. We also conducted ^{1}H NMR monitoring studies for the reaction of **1** and **2a**. In this case, only **37** was observed with no detection of adduct **35** nor **36**. Interestingly, the reaction of *tert*-butyl ester **23** and **2a** described scheme 4 showed formation of analogous adducts **38** and **39**. We further tested the addition of benzoic acid to allene **2a** to determine the regioselectivity of the initial hydrocarboxylation step. Under the method A, this reaction quickly generated unstable branch adduct **40** as the major regioisomer, which migrated to the more stable **41**.[19] Based upon these results, it is reasonable to assume that branch adduct such as **35** is formed as the kinetic product in the proposed reaction. To gain further insight into the C-C bond formation, we tested (*E*)-**36**, which could be readily prepared by alternative route (For the details, see the supporting information). This experiment generated **3a** in 30% yield and 63% ee. Interestingly, (*Z*)-**36** provided the same enantiomer **3a** in comparable yield and ee. This enantioconvergent result reasonably excludes a potentially competing concerted migration pathway from **36**.[20] Furthermore, it confirms that the rapid equilibration of kinetically formed π-allyl intermediates generated from **36** precedes the C-C bond formation.[19] This hypothesis is further supported by the reaction of **41** with **1**, which again exhibited comparable yield and ee. Interestingly, ee of **3a** from (*E*)-**36** could be improved by the use of additional amount of **1**. Moreover, crossover experiment using **37** as the exogeneous nucleophile generated a mixture of the product **3a** and **4** possessing the identical absolute stereochemistry as that from the reaction of alkoxyallene depicted in Scheme 2.

Based upon the experimental results and a related working model,[21] a plausible mechanism is proposed (Scheme 6). Pd-H species (generated by the oxidative addition of Pd(0) into carboxylic acids) adds to the allene to form thermodynamically favorable syn-π allyl complex A, which is in rapid equilibrium with the adduct B. The subsequent intramolecular C-C bond formation via enol Pd-carboxylate complex C is likely to be the enantio-determining (and rate-determining) event, which generates D by way of inner-sphere mechanism. This picture is consistent with a related study[22] and our own report.[10d,23] Decarboxylation afterwards generates the desired ketone product. Finally, maintaining a tight ion pair between the Pd complex and carboxylate counteranion (A^- in Scheme 6) is crucial in achieving high enantioselection.

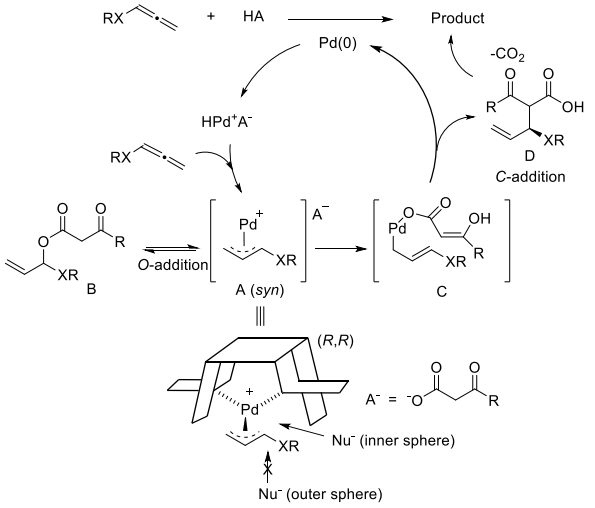


Scheme 5. Mechanistic studies

In summary, we developed a Pd-catalyzed asymmetric decarboxylative addition of *β*-keto acids to alkoxy- and amidoallenes, which enabled hydrocarboxylation-induced decarboxylative allylation. This reaction significantly broadens the scope of asymmetric hydrofunctionalization of heteroatom-substituted allenes. Currently, we are working on expanding the scope of the reaction as well as applying this method into the total synthesis of complex bioactive natural products.

Acknowledgements

This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT) (No. NRF-2020R1A3B2079988 and NRF-2018R1A4A1024713).



Scheme 6. Proposed catalytic cycle

Keywords: Allene • Addition • Palladium • Catalysis • Decarboxylation

[1] For selected reviews on the Pd-catalyzed AAA reactions, see: a) O. Pàmies, J. Margalef, S. Cañellas, J. James, E. Judge, P. J. Guiry, C. Moberg, J.-E. Bäckvall, A. Pfaltz, M. A. Pericàs, M. Diéguez, *Chem. Rev.* **2021**, *121*, 4373-4505; b) N. A. Butt, W. Zhang, *Chem. Soc. Rev.* **2015**, *44*, 7929-7967; c) B. M. Trost, *Org. Process Res. Dev.* **2012**, *16*, 185-194; d) Z. Lu, S. Ma, *Angew. Chem. Int. Ed.* **2007**, *47*, 258-297; *Angew. Chem.* **2007**, *120*, 264-303; e) B. M. Trost, M. L. Crawley, *Chem. Rev.* **2003**, *103*, 2921-2944

[2] For selected reviews on the decarboxylative allylation, see: a) J. James, M. Jackson, P. J. Guiry, *Adv. Synth. Catal.* **2019**, *361*, 3016-3049; b) A. Y. Hong, B. M. Stoltz, *Eur. J. Org. Chem.* **2013**, 2745-2759; c) J. D. Weaver, A. Recio III, A. J. Grenning, J. A. Tunge, *Chem. Rev.* **2011**, *111*, 1846-1913; d) S.-L. You, L.-X. Dai, *Angew. Chem. Int. Ed.* **2006**, *45*, 5246-5248; *Angew. Chem.* **2006**, *118*, 5372-5374.

[3] For selected examples using non-stabilized carbonyl compounds in AAA reactions, see: a) B. M. Trost, G. M. Schroeder, *J. Am. Chem. Soc.* **1999**, *121*, 6759-6760. b) M. Braun, F. Laicher, T. Meier, *Angew. Chem. Int. Ed.* **2000**, *39*, 3494–3497. 3) S.-L. You, X.-L. Hou, L.-X. Dai, X.-Z. Zhu, *Org. Lett.* **2001**, *3*, 149–151.4) B. M. Trost, G. M. Schroeder, *Chem. Eur. J.* **2005**, *11*, 174–184. 5) M. Braun, T. Meier, *Angew. Chem. Int. Ed.* **2006**, *45*, 6952–6955. f) M. Braun, P. Meletis, M. Fidan, *Org. Synth.* **2009**, *86*, 47-58. G) X.-X. Yan, C.-G. Liang, Y. Zhang, W. Hong, B.-X. Cao, L.-X. Dai, X.-L. Hou, *Angew. Chem. Int. Ed.* **2005**, *44*, 6544–6546. H) W.-H. Zheng, B.-H. Zheng, Y. Zhang, X.-L. Hou, *J. Am. Chem. Soc.* **2007**, *129*, 7718–7719. I) X.-H. Li, B.-H. Zheng, C.-H. Ding, X.-L. Hou, *Org. Lett.* **2013**, *15*, 6086–6089. J) J.-P. Chen, C.-H. Ding, W. Liu, X.-L. Hou, L.-X. Dai, *J. Am. Chem. Soc.* **2010**, *132*, 15493–15495. K) F.-L. Yu, D.-C. Bai, X.-Y. Liu, Y.-J. Jiang, C.-H. Ding, X.-L. Hou, *ACS Catal.* **2018**, *8*, 3317–3321. L) B. M. Trost, M. U. Frederiksen, *Angew. Chem. Int. Ed.* **2005**, *44*, 308–310. M) Y.-J. Jiang, G.-P. Zhang, J.-Q. Huang, D. Chen, C.-H. Ding, X.-L. Hou, *Org. Lett.* **2017**, *19*, 5932–5935. N) P. Meletis, M. Patil, W. Thiel, W. Frank, M. Braun, *Chem. Eur. J.* **2011**, *17*, 11243–11249. O) M. Braun, *Org. Synth.* **2020**, *97*, 79-95.

[4] a) A. Ngamnithiporn, T. Iwayama, M. D. Bartberger, B. M. Stoltz, *Chem. Sci.* **2020**, *11*, 11068-11071; b) D. C. Duquette, A. Q. Cusumano, L. Lefoulon, J. T. Moore, B. M. Stoltz, *Org. Lett.* **2020**, *22*, 4966-4969; c) B. M. Trost, A. Nagaraju, F. Wang, Z. Zuo, J. Xu, K. L. Hull, *Org. Lett.* **2019**, *21*, 1784-1788; d) S. Qin, T. Liu, Y. Luo, S. Jiang, G. Yang, *Org. Chem. Front,* **2019**, *6*, 732-735; e) J.-S. Yu, H. Noda, M. Shibasaki, *Angew. Chem. Int. Ed.* **2018**, *57*, 818-822; *Angew. Chem.* **2018**, *130*, 826-830; f) J. James, P. G. Guiry, *ACS Catal*. **2017**, *7*, 1397-1402.

[5] a) M.-Y. Cao, B.-J. Ma, Z.-Q. Lao, H. Wang, J. Wang, J. Liu, K. Xing, Y.-H. Huang, K.-J. Gan, W. Gao, H. Wang, X. Hong, H.-H. Lu, *J. Am. Chem. Soc.* **2020**, *142*, 12039-12045; b) R. Lavernhe, E. J. Alexy, H. Zhang, B. M. Stoltz, *Org. Lett.* **2020**, *22*, 4272-4275; c) E. J. Alexy, H. Zhang, B. M. Stoltz, *J. Am. Chem. Soc.* **2018**, *140*, 10109-10112; d) H. Kondo, M. Maeno, K. Hirano, N. Shibata, *Chem. Commun.* **2018**, *54*, 5522-5525; e) P. Starkov, J. T. Moore, D. C. Duquette, B. M. Stoltz, I. Marek. *J. Am. Chem. Soc.* **2017**, *139*, 9615-9620.

[6] For recent reviews on hydrofunctionalization of allenes, see: a) R. Blieck, M. Taillefer, F. Monnier, *Chem. Rev*. **2020**, *120*, 13545-13598; b) G. Li, X. Huo, X. Ziang, W. Zhang, *Chem. Soc. Rev.* **2020**, *49*, 2060-2118. c) M. Holmes, L. A. Schwartz, M. J. Krische, *Chem. Rev*. **2018**, *118*, 6026−6052.

[7] a) C. Li, B. Breit, *J. Am. Chem. Soc.* **2014**, *136*, 862-865. b) F. A. Cruz, Z. Chen, S. I. Kurtoic, V. M. Dong, *Chem. Commun*. **2016**, *52*, 5836-5839; c) C. Li, C. P. Grugel, B. Breit, *Chem. Commun.* **2016**, *52*, 5840-5843.

[8] a) M. Zhu, Q. Zhang, W. Zi, *Angew. Chem. Int. Ed.* **2021**, *60*, 6545-6552; *Angew. Chem.* **2021**, *133*, 6619-6626; b) H. Zhou, Z. Wei, J. Zhang, H. Yang, C. Xia, G. Jiang, *Angew. Chem. Int. Ed.* **2017**, *56*, 1077-1081; *Angew. Chem.* **2017**, *129*, 1097-1101; c) B. M. Trost, J. Xie, J. D. Sieber, *J. Am. Chem. Soc.* **2011**, *133*, 20611-20622; d) B. M. Trost, A. B. C. Simas, B. Plietker, C. Jäkel, J. Xie, *Chem. Eur. J.* **2005**, *11*, 7075-7082; e) B. M. Trost, C. Jäkel, B. Plietker, *J. Am. Chem. Soc.* **2003**, *125*, 4438-4439.

[9] For an early report on Pd-catalyzed racemic hydroalkoxylation and hydroamidation of alkoxyallene, see: S. S. Kinderman, R. Doodeman, J. W. van Beijma, J. C. Russcher, K. C. M. F. Tjen, T. M. Kooistra, H. Mohaselzadeh, J. H. van Maarseveen, H. Hiemastra, H. E. Schoemaker, F. P. J. T. Rutjes, *Adv. Synth. Catal.* **2002**, *344*, 736-748.

[10] a) K. Lee, M. Kim, Y. H. Rhee, *Bull. Korean Chem. Soc.* **2021**, *42*, 679-682; b) J. Lee, J. Kang, S. Lee, Y. H. Rhee, *Angew. Chem. Int. Ed.* **2020**, *59*, 2349-2353; *Angew. Chem.* **2020**, *132*, 2369-2373; c) J. Lee, S. Kang, J. Kim, D. Moon, Y. H. Rhee, *Angew. Chem. Int. Ed.* **2019**, *58*, 628-631; *Angew. Chem.* **2019**, *131*, 638-641; d) S. H. Jang, H. W. Kim, W. Jeong, D. Moon, Y. H. Rhee, *Org. Lett.* **2018**, *20*, 1248-1251; e) S. Kang, S. H. Jang, J. Lee, D. Kim, M. Kim, W. Jeong, Y. H. Rhee, *Org. Lett.* **2017**, *19*, 4684-4687. f) W. Lim, J. Kim, Y. H. Rhee, *J. Am. Chem. Soc.* **2014**, *136*, 13618-13621

[11] For selected examples on metal-catalyzed intermolecular linear-selective and racemic branch-selective hydrofunctionalization of amidoallenes, see: a) Y. Liu, N. Ding, X. Tan, X. Li, Z. Zhao, *Chem. Commun.* **2020**, *56*, 7507-7510; b) R. Blieck, R. A. A. Abdine, M. Taillefer, F. Monnier, *Org. Lett.* **2018**, *20*, 2232-2235; c) T. R. Pradhan, H. W. Kim, J. K. Park, *Angew. Chem. Int. Ed.* **2018**, *57*, 9930-9935; *Angew. Chem.* **2018**, *130*, 10078-10083; d) L. A. Perego, R. Blieck, A. Groué, F. Monnier, M. Taillefer, I. Ciofini, L. Grimaud, *ACS Catal.* **2017**, *7*, 4253-4264; e) J. Fernández-Casado, R. Nelson, J. L. Mascareñas, F. López, *Chem. Commun.* **2016**, *52*, 2909-2912; f) J. M. Alonso, M. P. Muñoz, *Org. Lett.* **2019**, *21*, 7639-7644.

[12] For recent examples involving asymmetric umpolung reaction derived from hydrofuctionalization of alkoxy- and amidoallene, see: a) K. Spielmann, M. Xiang, L. A. Schwartz, M. J. Krische, *J. Am.Chem. Soc.* **2019**, *141*, 14136–14141. b) S. B. Han, H. Han, M. J. Krische, *J. Am. Chem. Soc.* **2010**, *132*, 1760–1761. c) M. Xiang, D. E. Pfaffinger, E. Ortiz, G. A. Brito, M. J. Krische, *J. Am. Chem. Soc.* **2021**, *143*, 8849−8854.

[13] For a recent example on decarboxylative asymmetric C-C bond formation of alkoxyallene under photocatalytic conditions, see: J. Zheng, A. Nikbakht, B. Breit, *ACS Catal.* **2021**, *11*, 3343-3350.

[14] For the determination of the absolute configuration of **3b**, see the supporting information.

[15] In this case, the use of acidic additive did not improve the enantioselectivity.

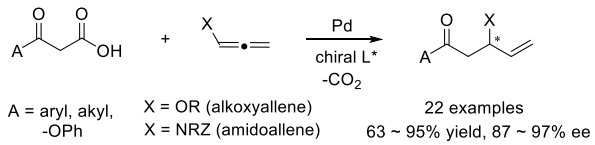
[16] S. M. Kim, J. W. Yang, *Org. Biomol. Chem.* **2013**, *11*, 4737-4749.

[17] a) H. Liao, J. Ma, H. Yao, X.-W. Liu, *Org. Biomol. Chem.* **2018**, *16*, 1791-1806; b) Y. Yang, B. Yu, *Chem. Rev.* **2017**, *117*, 12281-12356.

[18] For early examples on hydrocarboxylation of allenes, see: a) M. Al-Masum, Y. Yamamoto, *J. Am. Chem. Soc.* **1998**, *120*, 3809–3810. b) I. S. Kim, M. J. Krische, *Org. Lett.* **2008**, *10*, 513–515.
[19] Amidoallene **8** showed a similar pattern in the reaction with benzoic acid.
[20] M. F. Carroll, *J. Chem. Soc.* **1940**, 704**–**706.
[21] B. M. Trost, M. R. Machacek, A. Aponick, *Acc. Chem. Res.* **2006**, *39*, 747**–**760.
[22] D. C. Behenna, J. T. Mohr, N. H. Sherden, S. C. Marinescu, A. M. Harned, K. Tani, M. Seto, S. Ma, Z. Novak, M. R. Krout, R. M. McFadden, J. L. Roizen, J. A. Enquist, D. E. White, S. R. Levine, K. V. Petrova, A. Iwashita, S. C. Virgil, B. M. Stoltz, *Chem. Eur. J.* **2011**, *17*, 14199–14223.
[23] This behaviour is in sharp contrast to alkyl-substituted π-allyl complexes invoking outer-sphere reaction. For a reference, see: B. M. Trost, F. D. Toste, *J. Am. Chem. Soc.* **1999**, *121*, 4545–4554.

10.1002/anie.202107990

Entry for the Table of Contents



A = aryl, akyl, -OPh

X = OR (alkoxyallene)
X = NRZ (amidoallene)

22 examples
63 ~ 95% yield, 87 ~ 97% ee

We report here an asymmetric decarboxylative allylation reaction initiated by the hydrocarboxylation reaction of heteroatom-substituted allene. The reaction works particularly well with heteroatom-substituted allenes such as alkoxyallenes and amidoallenes. A number of aryl and alkyl *β*-keto acids as well as malonic acid mono-phenyl ester participates in the reaction to generate *γ*,*δ*-unsaturated carbonyl compounds possessing stereogenic heteroatom substituents at the *β*-position.

Institute and/or researcher Twitter usernames: @CPostech