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# Palladium-Catalyzed Efficient Enantioselective Synthesis of Chiral Allenes: Steric and Electronic Effects of Ligands

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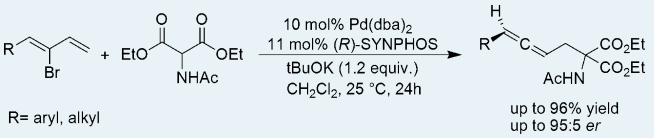
Supporting Information

**ABSTRACT:** Asymmetric synthesis of chiral allenes starting from prochiral substrates under mild reaction conditions promoted by Pd-SYNPHOS catalyst is reported. This protocol provides an efficient access to various enantioenriched aryl- and alkyl- substituted allenes, which are versatile building blocks of high utility to both organic and medicinal chemists, in excellent isolated yields (up to 96%) and high enatiomeric ratio values (up to 95:5). In addition, a comparative study using several $C_2$-symmetric atropisomeric diphosphine ligands revealed the overwhelming impact of the steric and electronic properties of the ligands for the catalytic efficiency of this process.




**KEYWORDS:** *allene, synthetic method, asymmetric catalysis, enantioselective, palladium*

Optically active allenes are useful building blocks for synthesizing organic compounds of importance to medicinal chemistry.[1] For example, they are widely considered as excellent substrates for a multitude of synthetic transformations[2] and have been recently introduced as chiral ligands in asymmetric catalysis.[3] Furthermore, because they are key structural motifs of a wide range of biologically active natural products,[4] such as compound **I**, which is a potent antifungal agent,[5] they are frequently incorporated in pharmaceuticals to finely tune their biological and pharmacological properties.[4] For example, Enprostil **II** is a potent $PGE_2$ analogue currently used for preventing and treating gastric and duodenal ulcers;[6] and (*R*)-(−)-adenallene **III** is a nucleoside analogue with impressive biological activities as a cytotoxic and antiviral agent[7] (Figure 1). Accordingly, during the last two decades, considerable research efforts have been devoted to the development of efficient methods toward the synthesis of chiral allenes.[8]

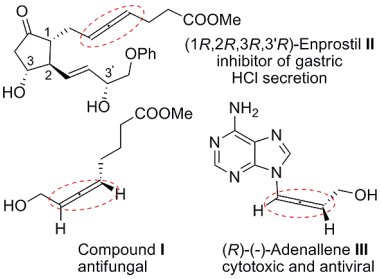



**Figure 1.** Structure of natural and pharmaceutically active products containing an allenic moiety.

Classical pathways for constructing such a framework rely on the resolution of racemic allenic precursors[8b,g,9] and the chirality transfer between, for example, nonracemic propargylic derivatives and incoming nucleophiles.[8f,h,10]

Although these protocols proved to be highly effective, there are some drawbacks associated with these methods, such as the use of stoichiometric amounts of chiral sources as either substrates or reagents. In 2001, a major breakthrough was made by Hayashi et al.,[11] who reported the first efficient Pd-catalyzed asymmetric synthesis of axially chiral allenylsilanes and allenes with enantioselectivities up to 90% and 89%, respectively, starting from prochiral substrates.[12] Although highly efficient, this process is rather limited in substrate scope and requires the use of noncommercially available, highly air- and moisture-sensitive CsO$^t$Bu base for optimal catalytic efficiency. Since these seminal reports, several other catalytic systems based on Pd,[13] Rh,[14] Cu,[15] and Fe[16] have been developed. However, although moderate to excellent results have been obtained using these catalyst systems, the substrate scope for these processes is generally rather limited. To date, despite the progress made in this area, the enantioselective synthesis of allenic derivatives from prochiral substrates is still an underdeveloped topic in synthetic organic chemistry.

Therefore, development of asymmetric methods that allow a rapid and efficient access to enantiomerically enriched axially chiral allenes with high levels of enantioselectivities for a broad

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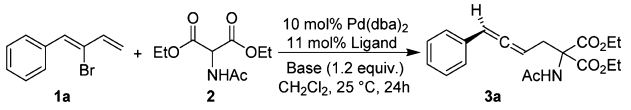
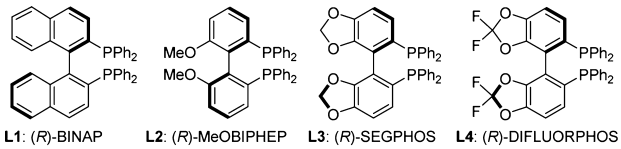
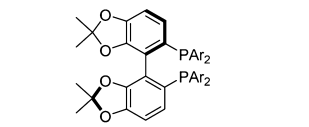
**Table 1. Optimization of Pd-Catalyzed Enantioselective Synthesis of Axially Chiral Allene 3a[a]**

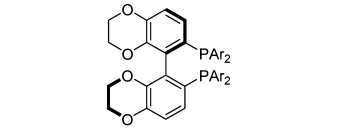



| entry | ligand | base | yield (%)[b] | er (%)[c] |
|---|---|---|---|---|
| 1 | **L1** | $^t$BuOK | 92 | 85.5:14.5 |
| 2 | **L2** | $^t$BuOK | 80 | 84:16 |
| 3 | **L3** | $^t$BuOK | 95 | 81:19 |
| 4 | **L4** | $^t$BuOK | 92 | 55.5:44.5 |
| 5 | **L5** | $^t$BuOK | 93 | 71.5:28.5 |
| 6 | **L6** | $^t$BuOK | 92 | 80:20 |
| 7 | **L7** | $^t$BuOK | 86 | 86.5:13.5 |
| 8 | **L8** | $^t$BuOK | 90 | 87:13 |
| 9 | **L9** | $^t$BuOK | 92 | 94:6 |
| 10 | **L10** | $^t$BuOK | 85 | 92:8 |
| 11 | **L11** | $^t$BuOK | 88 | 91:9 |
| 12 | **L12** | $^t$BuOK | 87 | 91:9 |
| 13 | **L13** | $^t$BuOK | 88 | 63:37 |
| 14 | **L9** | $K_2CO_3$ | 60 | 76:24 |
| 15 | **L9** | $Cs_2CO_3$ | 79 | 54.5:45.5 |
| 16 | **L9** | NaH | 81 | 53.5:46.5 |
| 17 | **L9** | $Et_3N$ | 0 | 0 |
| 18 | **L9** | DBU | 81 | 94:6 |

[a]Reactions were conducted at 25 °C using 0.5 mmol of bromodiene **1a** and 1.1 mmol of **2** in $CH_2Cl_2$ with 10 mol % of Pd-(R)-SYNPHOS catalyst for 24h. [b]Isolated yields. [c]Determined by HPLC or chiral stationary phase supercritical-fluid chromatography (CSP-SFC) using a Chiralcel IA column.



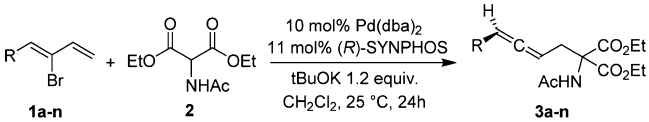



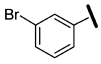
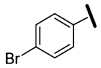
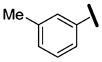
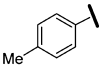
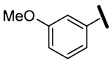
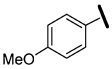
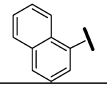




substrate scope is still a major challenge. As part of our ongoing research program dedicated to the design and synthesis of atropisomeric diphosphine ligands and their applications in transition-metal-catalyzed asymmetric reactions,[17] we report our progress toward this goal, which resulted in designing an optimized Pd/ligand catalyst for the enantioselective synthesis of a full set of aryl- and alkyl-substituted axially chiral allenes **3**.

Initially, we first explored the catalytic performance of a number of chiral $C_2$-symmetric atropisomeric diphosphine ligands **L1**−**L13** that were commercially available or developed in our laboratories[18,19] for the reaction of (*Z*)-2-bromo-1-phenyl-1,3-butadiene **1a** with malonate **2** as a nucleophile using 10 mol % of Pd-catalyst, prepared in situ from $Pd(dba)_2$ and the corresponding diphosphines **L1**−**L13**, in the presence of $^t$BuOK as a base at 25 °C in $CH_2Cl_2$ for 24 h. The results of these experiments are shown in Table 1. In all cases, the allene product **3a** was isolated in good to excellent yields in a range of

**Table 2. Substrate Scope of Pd-Catalyzed Enantioselective Synthesis of Axially Chiral Allenes 3[a]**




| entry | bromodiene | | yield (%)[b] | *er* (%)[c] |
|---|---|---|---|---|
| | **1** | R | | |
| 1 | **1a** |  | 92 | 94:6 (−) |
| 2 | **1b** |  | 96 | 91.5:8.5 (−) |
| 3 | **1c** |  | 95 | 92:8 (−) |
| 4 | **1d** |  | 92 | 90.5:9.5 (−) |
| 5 | **1e** |  | 92 | 91.5:8.5 (−) |
| 6 | **1f** |  | 89 | 94:6 (−) |
| 7 | **1g** |  | 92 | 94:6 (−) |
| 8 | **1h** |  | 96 | 95:5 (−) |
| 9 | **1i** |  | 92 | 93.5:6.5 (−) |
| 10 | **1j** |  | 94 | 92.5:7.5 (−) |
| 11 | **1k** |  | 89 | 91:9 (−) |
| 12 | **1l** |  | 88 | 85:15 (−) |
| 13 | **1m** |  | 90 | 83:17 (−) |
| 14 | **1n** |  | 88 | 84:16 (−) |

[a]Reactions were conducted at 25 °C using 0.5 mmol of bromodienes **1** in $CH_2Cl_2$ with 10 mol % of Pd-(*R*)-SYNPHOS catalyst for 24h. [b]Isolated yields. [c]Determined by HPLC or chiral stationary phase supercritical-fluid chromatography (CSP-SFC) using a Chiralcel IA column.

80−95% (Table 1, entries 1−13), but the stereochemical course of the reaction proved to be highly dependent on both the steric and electronic properties of the ligand employed. Reactions carried out with catalyst derived from electron-rich diphosphines (*R*)-BINAP[20] **L1** and (*R*)-MeO-BIPHEP[21] **L2** provided **3a** in good yields and moderate enantiomeric ratios (Table 1, entries 1−2, 92−80% yields, 85.5:14.5−84:16 enantiomeric ratio (er), respectively). Similar results in terms of both reactivity and selectivity were obtained with the electron-rich (*R*)-SEGPHOS[22] **L3**, whereas the use of the electron-deficient (*R*)-DIFLUORPHOS[23] ligand **L4**, having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similar narrower dihedral angle, gave adduct **3a** in comparable high yield but with significantly lower selectivity (Table 1, entries 3−4, 95−92% yields, 81:19−55.5:44.5 er, respectively). These results clearly indicate that the electronic properties of the ligand have a strong influence on the stereochemical course of the reaction.

This trend was confirmed by comparing the results obtained when the reaction was conducted with catalysts bearing (*R*)-3,5-diMe−$C_6H_3$−SYNPHOS **L11**[18a,b] and (*R*)-3,5-di$CF_3$−$C_6H_3$−SYNPHOS ligands **L13**,[18a,b] which are differentiated electronically by only the substituent on the phosphorus phenyl rings (Table 1; compare entries 11 and 13, 88% yield, 91:9−63:37 er, respectively). The data of Table 1 also illustrate that the steric properties of the bidentate diphosphine ligands have an impact on the stereochemical outcome of the reaction. This steric effect was demonstrated by comparing the enantioselectivities observed using catalysts bearing the SUNPHOS[19] family of ligands (Table 1, entries 5−8). In all cases, full conversions were obtained, compound **3a** being isolated in high yields ranging from 86 to 93%. SUNPHOS ligand **L5** and the corresponding 4-Me-$C_6H_4$-substituted diphosphine **L6** afforded lower selectivities compared with ligands **L1**−**L3**, with 71.5:28.5 and 80:20 er, respectively (Table 1, entries 5−6), whereas ligands 4-MeO-3,5-diMe-$C_6H_2$−(*R*)-SUNPHOS **L7** and 4-MeO-3,5-($^t$Bu)$_2$-$C_6H_2$−(*R*)-SUNPHOS **L8** having bulky 3,5-dialkyl substituents on the P-phenyl rings led to a significant increase in enantioselectivity (Table 1, entries 7−8, 86.5:13.5 and 87:13 er, respectively).

To our delight, a marked improvement in catalytic activity was achieved by using the electron-rich (*R*)-SYNPHOS[18] family of ligands **L9**−**L12**, compound **3a** being isolated in good to excellent yields (85−92%) with enantiomeric ratio values ranging from 91:9 to 94:6 (Table 1, entries 9−12). Finally, other nucleophiles have been tested in this transformation using the optimized reaction conditions; however, poor to modest catalytic activity was observed in all cases (see the Supporting Information for details).

Finally, from those experiments, (*R*)-SYNPHOS **L9** turned out to be the ligand of choice for this reaction, providing the desired allenic compound **3a** in 92% yield and with an excellent enantiomeric ratio of 94:6. Taking into account that Ogasawara, Hayashi et al.[11] showed that both the yield and the enantioselectivity of such transformation could be dramatically influenced by the nature of the base, we thus decided to test other organic or inorganic bases. As shown in Table 1, inferior results in terms of both reactivity and selectivity were obtained with $K_2CO_3$ and $Cs_2CO_3$, and no reaction occurred with $Et_3N$, probably because of catalyst poisoning (Table 1, entries 14−17). Interestingly, the use of DBU furnished **3a** with a similar excellent enantiomeric ratio of 94:6, but with a lower chemical isolated yield due to incomplete conversion (85%) (Table 1, compare entries 9 vs 18). Through these screenings, the best reaction conditions for the asymmetric synthesis of **3a** were therefore set as the following: 10 mol % of Pd(dba)$_2$/(*R*)-SYNPHOS as catalyst, in the presence of 1.2 equiv of $^t$BuOK as base, in $CH_2Cl_2$ at 25 °C for 24h.

Considering these results, we decided to explore the scope of the reaction. Using the optimal reaction conditions, a variety of aryl- and alkyl-substituted bromodienes **1a**−**n** were easily prepared in two steps according to a known procedure[11] and subsequently reacted with compound **2a** as the nucleophile partner. As the synthesis of compounds **3a**−**k** demonstrates (Table 2), all aryl-bromodiene derivatives **1a**−**k** were smoothly converted to their corresponding allenic derivatives **3a**−**k** in excellent yields and good to excellent selectivities (Table 2, entries 1−11, 89−96% yields and 90.5:9.5−95:5 er). Regarding the substitution pattern of the aryl moiety, whereas the yields were essentially the same, the stereoinduction proved to be influenced by both the nature and the relative position of the substituents in the substrates. Compounds **1b**−**d** bearing an electron-withdrawing group, such as chloro and bromo substituents, afforded the desired allenic products **3b**−**d** in slightly lower enantiomeric ratios than those obtained with substrates **1e**−**j** possessing an electron-donating group, such as methyl and methoxy substituents, with 90.5:9.5 to 92:8 and 91.5:8.5 to 95:5 er, respectively (Table 2, compare entries 2−4 vs entries 5−10). It should be noted that except for substrate **1h**, compounds **1b**, **1e**, and **1k**, bearing an ortho substituent on the 1-phenyl group, gave uniformly lower enantioselectivities, probably as a result of unfavorable steric hindrance between the ortho-substituted group of the substrate and the catalyst during the reaction (Table 2, entries 2, 5, and 11, 91:9 to 91.5:8.5 er). In addition, the reaction can also be extended to aliphatic bromodienes **1l**−**n**. Although the reaction proceeds well with all substrates to give the corresponding allenes **3l**−**n** in good yields ranging from 88 to 90%, a significant drop in enantioselectivity was observed, regardless of the length and the size of the alkyl chain (Table 2, entries 12−14, 83:17−85:15 er).

In conclusion, a straightforward route to chiral allenes, which are versatile building blocks of high utility to both organic and medicinal chemists, through Pd-catalyzed asymmetric $S_N2'$ substitution of easily available prochiral bromodienes is described. We demonstrated that the reaction can be accomplished in the presence of a variety of functional groups, providing efficient access to both enantioenriched aryl- and alkyl-substituted allenes in excellent isolated yields (up to 96%) and with high er values (up to 95:5). Most importantly, the process involves a comparative study using various $C_2$-symmetric atropisomeric diphosphine ligands and revealed the overwhelming impact of the steric and electronic properties of the ligands. On the basis of these experiments, (*R*)-SYNPHOS, with a narrow dihedral angle and a strong basic character, emerged as the best ligand in term of stereoelectronic features to fit the requirements for achieving high levels of enantioselectivities. Further investigations to fully understand the intimate role of the stereoelectronic profile of the diphosphine ligands in this Pd-catalyzed asymmetric reaction are the focus of our current studies.

## ■ ASSOCIATED CONTENT

### Ⓢ Supporting Information

Experimental procedures, spectroscopic data for all new compounds, and HPLC or SFC charts for the determination of the er values of compounds **3**. This material is available free of charge via the Internet at http://pubs.acs.org.

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### Notes

The authors declare no competing financial interest.

## ■ ACKNOWLEDGMENTS

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## ■ REFERENCES

(1) (a) *Modern Allene Chemistry*; Krause, N., Hashmi, A. S. K., Eds.; Wiley-VCH: Weinheim, 2004. (b) Bruneau, C.; Renaud, J.-L. *Allenes and Cumulenes in Comprehensive Organic Functional Group Transformations II*, Katritzky, A. R., Taylor, R. J. K., Cossy, J., Eds.; Elsevier Ltd: Oxford, 2005; Vol. *1*; pp 1019−1081.

(2) For recent reviews on allenes, see: (a) Ma, S. *Chem. Rev.* **2005**, *105*, 2829−2871. (b) Ma, S. *Aldrichim. Acta* **2007**, *40*, 91−102. (c) Brasholz, M.; Reissig, H.-U.; Zimmer, R. *Acc. Chem. Res.* **2009**, *42*, 45−56. (d) Ma, S. *Acc. Chem. Res.* **2009**, *42*, 1679−1688. (e) Alcaide, B.; Almendros, P.; Campo, T. M. *Chem.—Eur. J.* **2010**, *16*, 5836−5842. (f) Aubert, C.; Fensterbank, L.; Garcia, P.; Malacria, M.; Simonneau, A. *Chem. Rev.* **2011**, *111*, 1954−1993. (g) Inagaki, F.; Kitagaki, S.; Mukai, C. *Synlett* **2011**, 594−614. (h) Lopez, F.; Mascarenas, J. L. *Chem.—Eur. J.* **2011**, *17*, 418−428. (i) Yu, S.; Ma, S. *Angew. Chem., Int. Ed.* **2012**, *51*, 3074−3112. (j) Shichao, S.; Ma, S. *Angew. Chem., Int. Ed.* **2012**, *51*, 2−41. (k) Rivera-Fuentes, P.; Diederich, F. *Angew. Chem., Int. Ed.* **2012**, *51*, 2−13.

(3) (a) Pu, X.; Qi, X.; Ready, J. M. *J. Am. Chem. Soc.* **2009**, *131*, 10364−10365. (b) Cai, F.; Pu, X.; Lynch, V.; Radha, A.; Ready, J. M. *J. Am. Chem. Soc.* **2011**, *133*, 18066−18069.

(4) Hoffmann-Röder, A.; Krause, N. *Angew. Chem., Int. Ed.* **2004**, *43*, 1196−1216.

(5) Ohigashi, H.; Kawazu, K.; Egawa, H.; Mitsui, T. *Agric. Biol. Chem.* **1972**, *36*, 1399−1403.

(6) (a) Collins, P. W.; Djuric, S. W. *Chem. Rev.* **1993**, *93*, 1533−1564. (b) Carpio, H.; Cooper, G. F.; Edwards, J. A.; Fried, J. H.; Garay, G. L.; Guzman, A.; Mendez, J. A.; Muchowski, J. M.; Roszkowski, A. P.; Van Horn, A. R. *Prostaglandins* **1987**, *33*, 169−180.

(7) (a) Phadtare, S.; Kessel, D.; Corbett, T. H.; Renis, H. E.; Court, B. A.; Zemlicka, J. *J. Med. Chem.* **1991**, *34*, 421−429. (b) Megati, S.; Goren, Z.; Silverton, J. V.; Orlina, J.; Nishimura, H.; Shirasaki, T.; Mitsuya, H.; Zemlicka, J. *J. Med. Chem.* **1992**, *35*, 4098−4104.

(8) (a) Sydnes, L. K. *Chem. Rev.* **2003**, *103*, 1133−1150. (b) Rossi, R.; Diversi, P. *Synthesis* **2003**, 25−36. (c) Ma, S. *Eur. J. Org. Chem.* **2004**, 1175−1183. (d) Krause, N.; Hoffmann-Röder, A. *Tetrahedron* **2004**, *60*, 11671−11694. (e) Miesch, M. *Synthesis* **2004**, 746−752. (f) Brummond, K. M.; DeForrest, J. E. *Synthesis* **2007**, 795−818. (g) Ogasawara, M. *Tetrahedron: Asymmetry* **2009**, *20*, 259−271. (h) Yu, S.; Ma, S. *Chem. Commun.* **2011**, *47*, 5384−5418. (i) Kolakowski, R. V.; Manpadi, M.; Zhang, Y.; Emge, T. J.; Williams, L. J. *J. Am. Chem. Soc.* **2009**, *131*, 12910−12911.

(9) (a) Nogushi, Y.; Takiyama, H.; Katsuki, T. *Synlett* **1998**, 543−545. (b) Sweeney, Z. K.; Salsman, J. L.; Andersen, R. A.; Bergman, R. G. *Angew. Chem., Int. Ed.* **2000**, *39*, 2339−2343. (c) Nyhlén, J.; Eriksson, L.; Bäckvall, J. E. *Chirality* **2008**, *20*, 47−51. (d) Manzuna Sapu, C.; Bäckvall, J. E.; Deska, J. *Angew. Chem., Int. Ed.* **2011**, *50*, 9731−9734.

(10) Ohno, H.; Nagaoka, Y.; Tomioka, K. in *Modern Allene Chemistry*; Krause, N.; Hashmi, A. S. K., Eds.; Wiley-VCH: Weinheim, 2004; Vol. *1*; pp 141−181.

(11) (a) Ogasawara, M.; Ikeda, H.; Nagano, T.; Hayashi, T. *J. Am. Chem. Soc.* **2001**, *123*, 2089−2090. (b) Han, J. W.; Tokunaga, N.; Hayashi, T. *J. Am. Chem. Soc.* **2001**, *123*, 12915−12916.

(12) For seminal examples of transition metal catalyzed asymmetric synthesis of chiral allenes with low selectivity, see: (a) De Graff, W.; Boersma, J.; Van Koten, G.; Elsevier, C. J. *J. Organomet. Chem.* **1989**, *378*, 115−124. (b) Matsumoto, Y.; Naito, M.; Uozumi, Y.; Hayashi, T. *J. Chem. Soc. Chem. Commun.* **1993**, 1468−1469. (c) Tillack, A.; Michalik, D.; Koy, C.; Michalik, M. *Tetrahedron Lett.* **1999**, *40*, 6567−6568.

(13) For Pd-catalyzed enantioselective synthesis of allenes, see: (a) Ogasawara, M.; Ueyama, K.; Nagano, T.; Mizuhata, Y.; Hayashi, T. *Org. Lett.* **2003**, *5*, 217−219. (b) Ogasawara, M.; Nagano, T.; Hayashi, T. *J. Org. Chem.* **2005**, *70*, 5764−5767. (c) Imada, Y.; Nishida, M.; Kutsuwa, K.; Murahashi, S. I.; Naota, T. *Org. Lett.* **2005**, *7*, 5837−5839. (d) Ogasawara, M.; Ngo, H. L.; Sakamoto, T.; Takahashi, T.; Lin, W. *Org. Lett.* **2005**, *7*, 2881−2884. (e) Ogasawara, M.; Ge, Y.; Uetake, K.; Takahashi, T. *Org. Lett.* **2005**, *7*, 5697−5700. (f) Trost, B. M.; Fandrick, D. R.; Dinh, D. C. *J. Am. Chem. Soc.* **2005**, *127*, 14186−14187. (g) Ogasawara, M.; Fan, L.; Ge, Y.; Takahashi, T. *Org. Lett.* **2006**, *8*, 5409−5412. (h) Ogasawara, M.; Okada, A.; Nakajima, K.; Takahashi, T. *Org. Lett.* **2009**, *11*, 177−180. (i) Nemoto, T.; Kanematsu, M.; Tamura, S.; Hamada, Y. *Adv. Synth. Catal.* **2009**, *351*, 1773−1778. (j) Liu, H.; Leow, D.; Huang, K. W.; Tan, C. H. *J. Am. Chem. Soc.* **2009**, *131*, 7212−7213. (k) Ogasawara, M.; Okada, A.; Subbarayan, V.; Sörgel, S.; Takahashi, T. *Org. Lett.* **2010**, *12*, 5736−5739. (l) Ogasawara, M.; Suzuki, M.; Takahashi, T. *J. Org. Chem.* **2012**, *77*, 5406−5410. (m) Ogasawara, M.; Ge, Y.; Okada, A.; Takahashi, T. *Eur. J. Org. Chem.* **2012**, 1656−1663. (n) Wan, B.; Ma, S. *Angew. Chem., Int. Ed.* **2013**, *51*, 441−445. (o) Crouch, I. T.; Neff, R. K.; Frantz, D. E. *J . Am. Chem. Soc.* **2013**, *135*, 4970−4973.

(14) For Rh-catalyzed enantioselective synthesis of allenes, see: (a) Hayashi, T.; Tokunaga, N.; Inoue, K. *Org. Lett.* **2004**, *6*, 305−307. (b) Li, Z.; Boyarskikh, V.; Hansen, J. H.; Autschbach, J.; Musaev, D. G.; Davies, H. M. L. *J . Am. Chem. Soc.* **2012**, *134*, 15497−15504.

(15) For Cu-catalyzed enantioselective synthesis of allenes, see: (a) Ye, J.; Li, S.; Chen, B.; Fan, W.; Kuang, J.; Liu, J.; Liu, Y.; Miao, B.; Wan, B.; Wang, Y.; Xie, X.; Yu, Q.; Yuan, W.; Ma, S. *Org. Lett.* **2012**, *14*, 1346−1349. (b) Li, H.; Müller, D.; Guénée, L.; Alexakis, A. *Org. Lett.* **2012**, *14*, 5880−5883.

(16) For Fe-catalyzed enantioselective synthesis of allenes, see: Li, C. Y.; Wang, X. B.; Sun, X. L.; Tang, Y.; Zheng, J. C.; Xu, Z. H.; Zhou, Y. G.; Dai, L. X. *J. Am. Chem. Soc.* **2007**, *129*, 1494−1495.

(17) (a) Pautigny, C.; Jeulin, S.; Ayad, T.; Zhang, Z. G.; Genet, J.-P.; Ratovelomanana-Vidal, V. *Adv. Synth. Catal.* **2008**, *350*, 2525−2532. (b) Tone, H.; Buchotte, M.; Mordant, C.; Guittet, E.; Ayad, T.; Ratovelomanana-Vidal, V. *Org. Lett.* **2009**, *11*, 1995−1997. (c) Tadaoka, H.; Cartigny, D.; Nagano, T.; Gosavi, T.; Ayad, T.; Genet, J.-P.; Ohshima, T.; Ratovelomanana-Vidal, V.; Mashima, K. *Chem.—Eur. J.* **2009**, *15*, 9990−9994. (d) Pautigny, C.; Debouit, C.; Vayron, P.; Ayad, T.; Ratovelomanana-Vidal, V. *Tetrahedron: Asymmetry* **2010**, *21*, 1382−1338. (e) Cartigny, D.; Puntener, K.; Ayad, T.; Scalone, M.; Ratovelomanana-Vidal, V. *Org. Lett.* **2010**, *12*, 3788−3791. (f) Cartigny, D.; Nagano, T.; Ayad, T.; Genet, J.-P.; Ohshima, T.; Mashima, K.; Ratovelomanana-Vidal, V. *Adv. Synth. Catal.* **2010**, *352*, 1886−1891. (g) Prevost, S.; Ayad, T.; Phansavath, P.; Ratovelomanana-Vidal, V. *Adv. Synth. Catal.* **2011**, *353*, 3213−3226. (h) Cartigny, D.; Berhal, F.; Nagano, T.; Phansavath, P.; Ayad, T.; Genet, J.-P.; Ohshima, T.; Mashima, K.; Ratovelomanana-Vidal, V. *J. Org. Chem.* **2012**, *77*, 4544−4556. (i) Wu, Z.; Perez, M.; Ayad, T.; Scalone, M.; Ratovelomanana-Vidal, V. *Angew. Chem., Int. Ed.* **2013**, *52*, 4925−4928.

(18) (a) Duprat de Paule, S.; Champion, N.; Ratovelomanana-Vidal, V.; Genet, J.-P.; Dellis, P. French Patent 2830254, 2001. (b) Duprat de Paule, S.; Champion, N.; Ratovelomanana-Vidal, V.; Genet, J.-P.; Dellis, P.; WO Patent 03029259, 2003. (c) Duprat de Paule, S.; Jeulin, S.; Ratovelomanana-Vidal, V.; Genet, J.-P.; Champion, N.; Dellis, P. *Eur. J. Org. Chem.* **2003**, 1931−1941. (d) Duprat de Paule, S.; Jeulin, S.; Ratovelomanana-Vidal, V.; Genet, J.-P.; Champion, N.; Deschaux, G.; Dellis, P. *Org. Process Res. Dev.* **2003**, *7*, 399−406. (e) Pautigny, C.; Jeulin, S.; Ayad, T.; Zhang, Z.; Genet, J.-P.; Ratovelomanana-Vidal, V. *Adv. Synth. Catal.* **2008**, *350*, 2525−2532. (f) Berhal, F.; Esseiva, O.; Martin, C. H.; Tone, T.; Genet, J.-P.; Ayad, T.; Ratovelomanana-Vidal, V. *Org. Lett.* **2011**, *13*, 2806−2809. (g) Wu, Z.; Ayad, T.; Ratovelomanana-Vidal, V. *Org. Lett.* **2011**, *13*, 3782−3785. (h) Berhal, F.; Wu, Z.; Genet, J.-P.; Ayad, T.; Ratovelomanana-Vidal, V. *J. Org. Chem.* **2011**, *76*, 6320−6326. (i) Berhal, F.; Wu, Z.; Zhang, Z.; Ayad, T.; Ratovelomanana-Vidal, V. *Org. Lett.* **2012**, *14*, 3308−3311. (j) Jackowski, O.; Wang, J.; Xie, X.; Ayad, T.; Zhang, Z.; Ratovelomanana-Vidal, V. *Org. Lett.* **2012**, *14*, 4006−4009.

(19) (a) Sun, Y.; Wan, X.; Guo, M.; Wang, D.; Dong, X.; Pan, Y.; Zhang, Z. *Tetrahedron: Asymmetry* **2004**, *15*, 2185−2188. (b) Meng, Q.; Sun, Y.; Ratovelomanana-Vidal, V.; Genet, J.-P.; Zhang, Z. *J. Org. Chem.* **2008**, *73*, 3842−3847. (c) Tao, X.; Li, W.; Ma, X.; Li, X.; Fan, W.; Xie, X.; Ayad, T.; Ratovelomanana-Vidal, V.; Zhang, Z. *J. Org. Chem.* **2012**, *77*, 612−616. (d) Ma, X.; Li, W.; Li, X.; Tao, X.; Fan, W.; Xie, X.; Ayad, T.; Ratovelomanana-Vidal, V.; Zhang, Z. *Chem. Commun.* **2012**, *48*, 5352−5354.

(20) Miyashita, A.; Yasuda, A.; Takaya, H.; Toriumi, K.; Ito, T.; Souchi, T.; Noyori, R. *J. Am. Chem. Soc.* **1980**, *102*, 7932−7934.

(21) Schmidt, R.; Broger, E. A.; Cereghetti, M.; Crameri, Y.; Foricher, J.; Lalonde, M.; Müller, R. K.; Scalone, M.; Schoettel, G.; Zutter, U. *Pure Appl. Chem.* **1996**, *68*, 131−138.

(22) Saito, T.; Yokozawa, T.; Ishizaki, T.; Moroi, T.; Sayo, N.; Miura, T.; Kumobayashi, H. *Adv. Synth. Catal.* **2001**, *343*, 264−267.

(23) (a) Jeulin, S.; Duprat de Paule, S.; Ratovelomanana-Vidal, V.; Genet, J.-P.; Champion, N.; Dellis, P. *Angew. Chem., Int. Ed.* **2004**, *43*, 320−325. (b) Jeulin, S.; Duprat de Paule, S.; Ratovelomanana-Vidal, V.; Genet, J.-P.; Champion, N.; Dellis, P. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5799−5804.



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