

## RESEARCH ARTICLE

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Pd((*R*)-DTBM-SEGphos)Cl<sub>2</sub>-catalyzed kinetic resolution of tertiary propargylic alcohols†Jie Wang,<sup>‡a</sup> Wei-Feng Zheng,<sup>‡a</sup> Yuling Li,<sup>b</sup> Yin-Long Guo,<sup>‡b</sup> Hui Qian<sup>‡\*a</sup> and Shengming Ma<sup>‡a,b</sup>

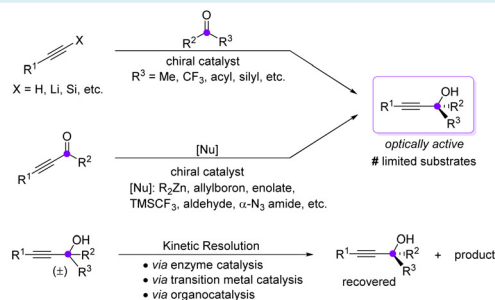
We report here an asymmetric carboxylation reaction based on kinetic resolution of tertiary propargylic alcohols by identifying Pd((*R*)-DTBM-SEGphos)Cl<sub>2</sub> as the pre-catalyst. A variety of optically active tertiary propargylic alcohols and tetrasubstituted 2,3-allenoic acids were obtained in good yields with excellent enantioselectivities. The salient features of this report include the use of readily available substrates, a readily available precatalyst, mild reaction conditions, remarkable functional group tolerance, gram-scale synthesis, and versatile synthetic transformations. Mass spectrometry experiments trapped some key intermediates, which revealed the mechanism.

## Introduction

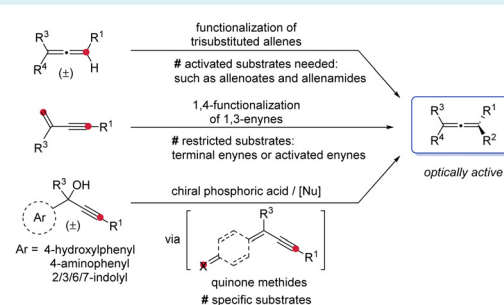
Optically active tertiary propargylic alcohols are useful building blocks in organic synthesis.<sup>1</sup> Typically, three catalytic strategies have been developed for asymmetric synthesis of tertiary propargylic alcohols (Scheme 1a):<sup>2–6</sup> (a) enantioselective alkylation of methyl ketones,<sup>2b,c,e,g,h</sup> trifluoromethyl ketones,<sup>3b–f</sup> α-carbonyl ketones,<sup>4</sup> and acyl silanes<sup>5</sup> with terminal alkynes or 1-alkynyl trimethylsilanes<sup>4b</sup> in >90% ee; (b) enantioselective addition of nucleophiles (including Me<sub>2</sub>Zn, Et<sub>2</sub>Zn, TMSCF<sub>3</sub>, aldehydes, α-N<sub>3</sub> amides, etc.) with 4-phenylbut-3-yn-2-one,<sup>6a</sup> pyridin-2-yl 1-alkynyl ketones,<sup>6d</sup> *tert*-butyl-substituted ethynyl ketones,<sup>6e</sup> propargylic ketoesters,<sup>6f</sup> or trifluoromethyl 1-alkynyl ketones<sup>6g,h</sup> in >90% ee; (c) catalytic kinetic resolution of racemic tertiary propargylic alcohols.<sup>7</sup> In 2019, Oestreich and coworkers reported the kinetic resolution by the enantioselective Si–O coupling catalyzed by MesCu/(*R,R*)-Ph-BPE affording tertiary 1-phenyl-1-(*n*-butyl)- or 1-cyclohexyl (or *N*-Boc-piperidinyl-4-yl)-1-methyl-2-alkynols in 92–96% ee;<sup>7c</sup> in 2021, Li and coworkers realized the kinetic resolution *via* chiral Rh(III)-catalyzed allenylation of benzamides affording tertiary 1-aryl-1-bulky alkyl (*tert*-butyl, adamantyl, cyclohexyl, isopropyl)-2-alkynols in >90% ee;<sup>7d</sup> in the same year, Zhou and coworkers demonstrated the kinetic resolution *via* Cu(I)-cata-

lyzed azide–alkyne cycloaddition affording tertiary 1-aryl-1-bis (cyclohexyloxy)methyl (or fluoroalkyl)-2-alkynols in >90% ee.<sup>7e</sup> On the other hand, due to the axial allenes serving as versatile

a) Three typical catalytic strategies for asymmetric syntheses of optically active tertiary propargylic alcohols



b) Representative methods for axially chiral tetrasubstituted allenes via asymmetric catalysis

c) this work: Kinetic resolution of tertiary propargylic alcohols by Pd((*R*)-DTBM-SEGphos)Cl<sub>2</sub> as the pre-catalyst

Scheme 1 Approaches to optically active tertiary propargylic alcohols and tetrasubstituted allenes.

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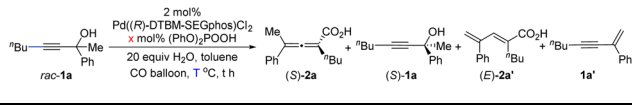
precursors in organic transformations and material science,<sup>8</sup> development of expeditious paths for constructing optically active tetrasubstituted allenes has been receiving increasing attention in the synthetic community. Representative catalytic methods for axially chiral tetrasubstituted allenes<sup>9,10</sup> are as follows (Scheme 1b): (a) direct asymmetric functionalization of trisubstituted allenes.<sup>9f-i</sup> These reported strategies are generally based on the formation of allenic carbanion analogues through the deprotonation of trisubstituted allenes to react with electrophiles, which demand the potential acidity of trisubstituted allenes such as trisubstituted allenolates and allenamides. (b) Asymmetric 1,4-functionalization of 1,3-enynes.<sup>9f-o</sup> It is restricted to terminal enynes or activated enynes. (c) Chiral phosphoric acid (CPA) catalyzed conjugate addition to quinone methides<sup>9p-r</sup> formed from specific substrates including 4-hydroxyphenyl, 4-aminophenyl, or 2/3/6/7-indolyl substituted propargylic alcohols. Therefore, catalytic asymmetric formation of tetrasubstituted allenes, especially from readily available chemicals, remains challenging. Recently, with the help of the supporting ligand PPh<sub>3</sub>, we reported a Pd-catalyzed kinetic resolution carboxylation reaction of tertiary propargylic alcohols for a series of chiral 2,3-allenoic acids<sup>11</sup> and chiral tertiary propargylic alcohols<sup>12</sup> under different reaction conditions. Here we wish to report the identification of pre-prepared Pd((R)-DTBM-SEGphos)Cl<sub>2</sub> as the pre-catalyst, and both optically active tertiary propargylic alcohols and tetrasubstituted 2,3-allenoic acids could be easily accessed under mild reaction conditions with high efficiency and enantioselectivities *via* a kinetic resolution process. Furthermore, the synthetic potential of the current method has been showcased by scale-up reactions and derivatization reactions of optically active products.

## Results and discussion

### Optimization of reaction conditions

With Pd((R)-DTBM-SEGphos)Cl<sub>2</sub> as the pre-catalyst, the reactions of 2-phenyloct-3-yn-2-ol *rac*-**1a** were conducted and some of the typical results are shown in Table 1. First of all, two sets of control experiments were conducted by using Pd((R)-DTBM-SEGphos)Cl<sub>2</sub> as the catalyst instead of PdCl<sub>2</sub> and a chiral phosphine ligand under our previous optimal conditions (entries 1 and 2):<sup>11,12</sup> no products were observed at −5 °C (entry 1), and the reaction only delivered (*S*)-**2a** in 23% NMR yield at 25 °C (entry 2). Interestingly, the reaction exhibited a moderate efficiency at 15 °C and provided (*S*)-**2a** in 17% NMR yield with 93% ee in the absence of the supporting ligand, which suggested that the catalytic species involved in the current Pd-complex-catalyzed reaction may be different from that of the former protocols (entry 3). By prolonging the reaction time to 36 hours, the yield of (*S*)-**2a** was slightly improved with a higher yield of the enyne product (entry 4). To our delight, 44% yield of (*S*)-**1a** with 90% ee was observed when the reaction was carried out at 20 °C (entry 5). By applying 10 mol% of (PhO)<sub>2</sub>POOH, the desired product (*S*)-**1a** was

**Table 1** Optimization of reaction conditions<sup>a</sup>



Entry	x	T (°C)	t (h)	( <i>S</i> )- <b>2a</b> Yield, <sup>b</sup> ee <sup>c</sup> (%)	( <i>S</i> )- <b>1a</b> Recovery, <sup>b</sup> ee <sup>c</sup> (%)	( <i>E</i> )- <b>2a'</b> Yield <sup>b</sup> (%)	<b>1a'</b> Yield <sup>b</sup> (%)
1 <sup>d</sup>	20	−5	18	0, —	100, —	—	—
2 <sup>d</sup>	2	25	18	23, 90	78, 30	—	—
3	20	15	18	17, 93	78, 16	—	5
4	20	15	36	20, 94	65, 19	—	13
5	20	20	18	51, 85	44, 90	2	4
6	15	20	18	51, 84	41, 93	2	4
7	10	20	18	51, 82	46, 98	2	2
8	10	20	12	45, 91	54, 70	—	—
9	5	20	18	55, 82	45, 96	—	—
10	2.5	20	18	51, 85	51, 91	—	—

<sup>a</sup> Reaction conditions: *rac*-**1a** (0.2 mmol), Pd((R)-DTBM-SEGphos)Cl<sub>2</sub> (2 mol%), (PhO)<sub>2</sub>POOH (x mol%), and H<sub>2</sub>O (20 equiv.) in toluene (1 mL) at T °C with a CO balloon unless otherwise noted. <sup>b</sup> Determined by <sup>1</sup>H NMR analysis using dibromomethane as the internal standard. <sup>c</sup> Determined by HPLC analysis. <sup>d</sup> 20 mol% PPh<sub>3</sub> was added.

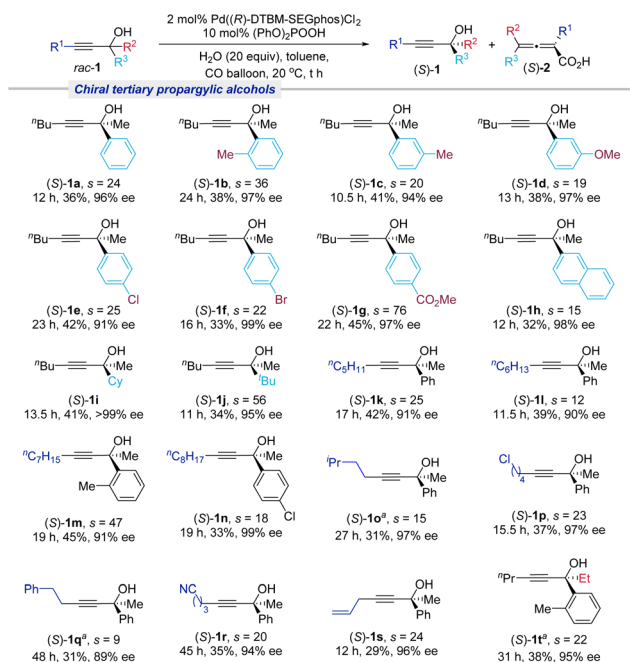
formed in 46% yield with 98% ee (entries 6–10). Thus, the optimal reaction conditions of this Pd((R)-DTBM-SEGphos)Cl<sub>2</sub>-catalyzed kinetic resolution carboxylation reaction for the optically active tertiary propargylic alcohols have been identified as shown in entry 7 of Table 1. Under the same conditions, optically active tetrasubstituted 2,3-allenoic acid (*S*)-**2a** could also be smoothly obtained in 45% yield with 91% ee by just shortening the reaction time to 12 hours (entry 8).

### Substrate scope

With the optimized reaction conditions in hand, the generality of this Pd((R)-DTBM-SEGphos)Cl<sub>2</sub>-catalyzed carboxylation reaction was investigated. As shown in Scheme 2, a range of tertiary propargylic alcohols containing electron-donating groups (**1b–1d**) or electron-withdrawing (**1e–1g**) on the phenyl ring furnished the corresponding products in good yields (33%–45%) with excellent ee (91%–99%). Naphthyl-substituted tertiary propargylic alcohol (**1h**) was compatible with the current system. Moreover, the substrates employing aliphatic substituents (Cy and <sup>t</sup>Bu) were also successfully resolved to afford the desired products (*S*)-**1i** and (*S*)-**1j** in good yields with excellent enantioselectivities. Besides <sup>n</sup>Bu substitution at the R<sup>1</sup> position, a series of tertiary propargylic alcohols containing different carbon chains ranging from C<sub>3</sub> to C<sub>8</sub> and versatile functional groups, such as the halogen atom (Cl), cyano, and allyl, were all suitable, affording the corresponding optically active tertiary propargylic alcohol products (*S*)-**1k–(S)-1s** in 29–45% yields with up to 99% ee. For the R<sup>2</sup> group, the methyl substituent may also be replaced with ethyl to recover (*S*)-**1t** in 38% yield with 95% ee.

Next, we turned our attention to the substrate scope for the formation of chiral 2,3-allenoic acids (Scheme 3). No obvious steric effect was observed since the substrates containing the



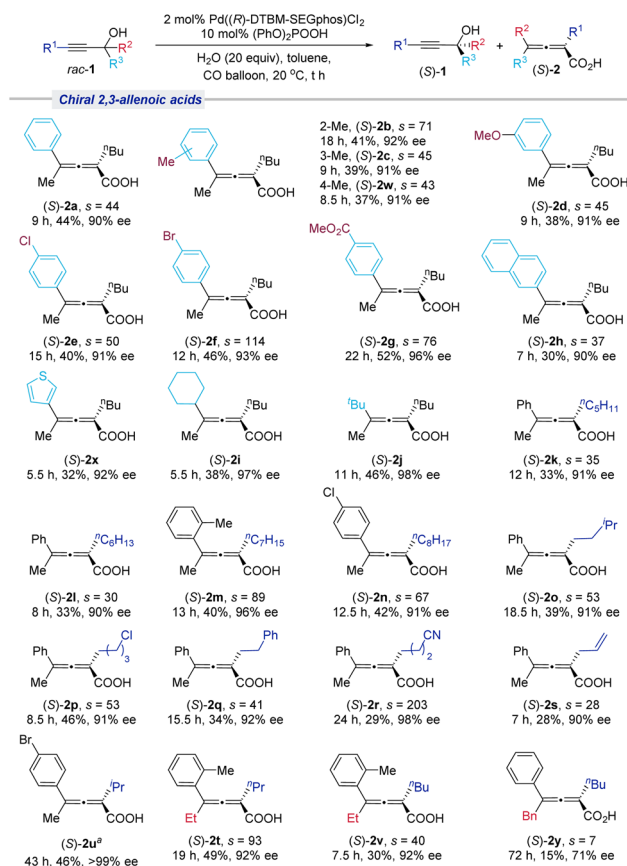


**Scheme 2** The substrate scope of chiral tertiary propargylic alcohols. Reaction conditions: *rac*-1 (0.5 mmol), Pd((*R*)-DTBM-SEGphos)Cl<sub>2</sub> (2 mol%), (PhO)<sub>2</sub>POOH (10 mol%), and H<sub>2</sub>O (20 equiv.) in toluene (2.5 ml) at 20 °C with a CO balloon unless otherwise noted. *s* is the selectivity factor. *s* =  $k_{\text{fast}}/k_{\text{slow}} = \ln[1 - (1 - \text{recovery})(1 + \text{ee})]/\ln[1 - (1 - \text{recovery})(1 - \text{ee})]$ . Recovery is determined by <sup>1</sup>H NMR analysis, and ee is the enantiomeric excess value determined by HPLC analysis. <sup>a</sup> The reaction was carried out with 12 mol% (PhO)<sub>2</sub>POOH.

methyl group at the 2-, 3- or 4-position of the phenyl group provided the targeted products (*S*)-2b, (*S*)-2c and (*S*)-2w in good yields (37%–41%) with high ee (91%–92%). The substrates bearing the functional groups OMe, Cl, Br, and CO<sub>2</sub>Me on the phenyl ring also underwent the carboxylation reaction efficiently, affording the corresponding products (*S*)-2d–(*S*)-2g in good yields with more than 90% ee. 2-Naphthyl substituted and 3-thienyl substituted propargylic alcohols were also well tolerated (**1h** and **1x**). Notably, the alkyl substituted substrates at R<sup>3</sup> could also be converted to the desired products (*S*)-2i and (*S*)-2j smoothly. R<sup>1</sup> with different carbon chains bearing a variety of different functional groups (halide, cyano, allyl) afforded the desired products (*S*)-2k–(*S*)-2s and (*S*)-2u in good yields with no less than 90% ee. Furthermore, when R<sup>2</sup> was an ethyl group, the reaction also formed the chiral 2,3-allenoic acids (*S*)-2t and (*S*)-2v with high enantioselectivities. However, when R<sup>2</sup> was Bn, the reaction was slow, affording 15% of (*S*)-2y with 71% ee after 72 hours.

### Gram scale reactions and synthetic applications

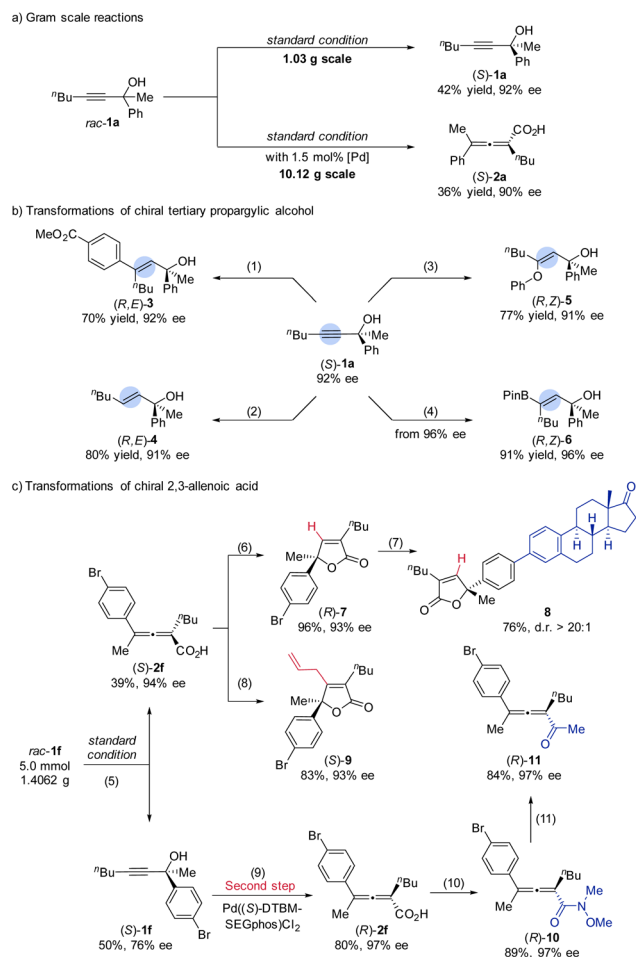
A gram-scale carboxylation reaction worked smoothly, delivering the corresponding chiral product (*S*)-1a in 42% yield with 92% ee (Scheme 4a); the 50 mmol scale reaction of *rac*-1a afforded 4.24 g of (*S*)-2a in 36% isolated yield and 90% ee. To exhibit the synthetic utility, several transformations of (*S*)-1a have been carried out as shown in Scheme 4b: rhodium cata-



**Scheme 3** The substrate scope of chiral 2,3-allenoic acids. Reaction conditions: *rac*-1 (0.5 mmol), Pd((*R*)-DTBM-SEGphos)Cl<sub>2</sub> (2 mol%), (PhO)<sub>2</sub>POOH (10 mol%), and H<sub>2</sub>O (20 equiv.) in toluene (2.5 ml) at 20 °C with a CO balloon unless otherwise noted. *s* is the selectivity factor. *s* =  $k_{\text{fast}}/k_{\text{slow}} = \ln[1 - (1 - \text{recovery})(1 + \text{ee})]/\ln[1 - (1 - \text{recovery})(1 - \text{ee})]$ . Yield is determined by <sup>1</sup>H NMR analysis, and ee is the enantiomeric excess value determined by HPLC analysis. <sup>a</sup> The reaction was carried out with 4 mol% Pd((*R*)-DTBM-SEGphos)Cl<sub>2</sub>.

lyzed highly regioselective hydroarylation of (*S*)-1a with boronic acid afforded the desired product (*R,E*)-3 in good yields without erosion of ee;<sup>13</sup> the reaction of (*S*)-1a with red-Al afforded the allylic alcohol (*R,E*)-4 in 80% yield with 91% ee;<sup>14</sup> (*S*)-1a could be selectively transformed to phenyl enol ether (*R,Z*)-5 in 77% yield with 91% ee under gold catalysis.<sup>15</sup> Moreover, the copper-catalyzed hydroboration of (*S*)-1a delivered the useful intermediate (*R,Z*)-6 in 91% yield.<sup>16</sup> On the other hand, 1.4 g of *rac*-1f was smoothly converted to (*S*)-2f in 39% yield with 94% ee and 50% of (*S*)-1f was recovered in 76% ee under the standard conditions (Scheme 4c). Subsequently, a successful successive kinetic resolution of the recovered (*S*)-1f to afford (*R*)-2f in higher yield (80%) and ee (97%) was realized with Pd((*S*)-DTBM-SEGphos)Cl<sub>2</sub>. Employing this pair of enantiomeric allenoic acids (*S*)-2f and (*R*)-2f, a series of transformations were investigated. A CuCl-catalyzed cycloisomerization reaction was realized affording (*R*)-7 in excellent yield without the loss of ee.<sup>17</sup> Furthermore, a Suzuki coupling reaction with the estrone-derived boronic acid afforded **8** in good yield and dr (>20 : 1).<sup>18</sup> A cyclization reaction of (*S*)-2f catalyzed by PdCl<sub>2</sub>





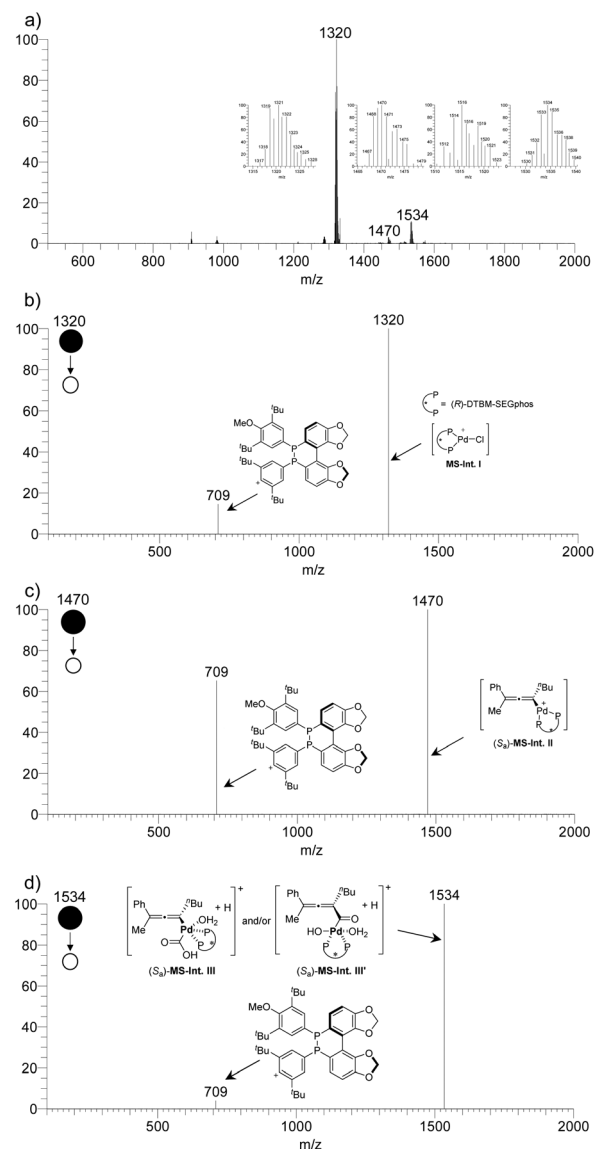
**Scheme 4** The gram scale reactions and synthetic applications. Reaction conditions: (1)  $(\text{Cp}^*\text{RhCl}_2)_2$  (2.5 mol%),  $(4\text{-MeO}_2\text{C})\text{C}_6\text{H}_4\text{B}(\text{OH})_2$  (2.0 equiv.),  $\text{AgBF}_4$  (15 mol%),  $\text{NaOAc}$  (20 mol%),  $\text{MeOH}$ , rt, air, 12 h; (2) red-Al (3.5 equiv.),  $\text{Et}_2\text{O}$ ,  $-78^\circ\text{C}$ , 1 min, rt, 6 h; (3)  $\text{PPh}_3\text{AuNTf}_2$  (2 mol%),  $\text{PhOH}$  (1.2 equiv.),  $\text{K}_2\text{CO}_3$  (1.0 equiv.),  $\text{CHCl}_3$ ,  $50^\circ\text{C}$ , 16 h; (4)  $\text{B}_2\text{Pin}_2$  (1.3 equiv.),  $\text{CuCl}$  (15 mol%),  $\text{PCy}_3$  (18 mol%),  $\text{NaO}^t\text{Bu}$  (15 mol%),  $\text{MeOH}$  (2.0 equiv.), toluene, rt, 12 h; (5) *rac*-1f (5.0 mmol),  $\text{Pd}((R)\text{-DTBM-SEGphos})\text{Cl}_2$  (2 mol%),  $(\text{PhO})_2\text{POOH}$  (10 mol%),  $\text{H}_2\text{O}$  (20 equiv.), toluene, CO balloon,  $20^\circ\text{C}$ , 11 h; (6)  $\text{CuCl}$  (4 mol%),  $\text{MeOH}$ ,  $60^\circ\text{C}$ , 1 h; (7)  $\text{Pd}(\text{dppf})\text{Cl}_2$  (10 mol%), boronic acid (1.1 equiv.),  $\text{K}_2\text{CO}_3$  (2.0 equiv.),  $\text{DMSO}$ ,  $80^\circ\text{C}$ , 1.5 h; (8)  $\text{PdCl}_2$  (5 mol%), allyl bromide (6 equiv.),  $\text{DMA}$ ,  $50^\circ\text{C}$ , 18 h; (9)  $\text{Pd}((S)\text{-DTBM-SEGphos})\text{Cl}_2$  (2 mol%),  $(\text{PhO})_2\text{POOH}$  (10 mol%),  $\text{H}_2\text{O}$  (20 equiv.), toluene, CO balloon,  $20^\circ\text{C}$ , 16 h; (10) methyl methoxylamine hydrochloride (1.3 equiv.),  $\text{EDC}\cdot\text{HCl}$  (1.3 equiv.),  $\text{NEt}_3$  (1.3 equiv.),  $\text{DMAP}$  (0.1 equiv.),  $\text{DCM}$ ,  $0^\circ\text{C}$  to rt, 3 h; (11)  $\text{MeMgBr}$  (4.0 equiv.),  $\text{THF}$ ,  $-78^\circ\text{C}$  to  $0^\circ\text{C}$ , 1 h.

in the presence of allyl bromide afforded allyl furanone (*S*)-9 in 83% yield with 93% ee.<sup>19</sup> The reaction of (*R*)-2f with methyl methoxylamine hydrochloride led to the formation of Weinreb amide (*R*)-10 in 89% yield with 97% ee.<sup>20</sup> In addition, the treatment of (*R*)-10 with  $\text{MeMgBr}$  could afford chiral allenone (*R*)-11 in 84% yield and with 97% ee.

### SAESI-MS studies

To further reveal the process of this  $\text{Pd}((R)\text{-DTBM-SEGphos})\text{Cl}_2$ -catalyzed reaction, solvent-assisted electrospray ionization

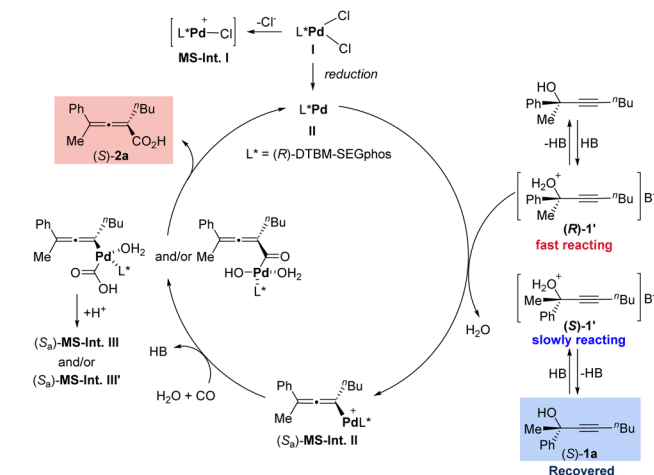
mass spectrometry (SAESI-MS) studies were carried out (Scheme 5).<sup>21</sup> Under standard conditions, the resulting mixture was analyzed after stirring for 10 min. A signal at  $m/z$  1320 was observed, which matched the  $m/z$  of the intermediate  $[\text{Pd}((R)\text{-DTBM-SEGphos})\text{Cl}]^+$  (calcd for  $\text{C}_{74}\text{H}_{100}^{35}\text{ClO}_8\text{P}_2^{106}\text{Pd}^+$ : 1319.5611) **MS-Int. I** (Scheme 5b). The reaction of the catalyst with the  $\text{H}^+$ -activated tertiary propargylic alcohols,  $\text{H}_2\text{O}$ , and CO could afford the allenylpalladium intermediate (*S<sub>a</sub>*)-**MS-Int. II** (Scheme 5c,  $m/z$  1470). Moreover, the carboxylation inter-



**Scheme 5** The SAESI-MS studies. (a) SAESI-MS spectrum of the reaction solution after stirring for 10 min; the inset SAESI-MS spectrum shows the major signal from  $m/z$  1315 to 1330, 1465 to 1480, 1510 to 1525 and 1525 to 1540; (b) SAESI-MS/MS spectrum of the complex ion  $[\text{Pd}((R)\text{-DTBM-SEGphos})\text{Cl}]^+$  (**MS-Int. I**) at  $m/z$  1320; (c) SAESI-MS/MS spectrum of the complex ion (*S<sub>a</sub>*)-**MS-Int. II** at  $m/z$  1470; (d) SAESI-MS/MS spectrum of the complex ion (*S<sub>a</sub>*)-**MS-Int. III** and/or (*S<sub>a</sub>*)-**MS-Int. III'** at  $m/z$  1534.







**Scheme 6** The proposed mechanism.

mediate ( $S_A$ )-MS-Int. III and/or ( $S_A$ )-MS-Int. III' (Scheme 5d,  $m/z$  1534) was also detected.

Combining the  $^1\text{H}$  NMR monitoring experiment (for details see ESI Table 1†) and mass spectrometric studies, a catalytic cycle was proposed as shown in Scheme 6. First,  $\text{Pd}((R)\text{-DTBM-SEGphos})\text{Cl}_2$  I would be reduced *in situ* to form the catalytically active species  $\text{Pd}(0)((R)\text{-DTBM-SEGphos})$  II. Then II would react with the configuration-matched  $\text{H}^+$ -activated propargylic alcohol ( $R$ )-1' to afford the allenylpalladium intermediate ( $S_A$ )-MS-Int. II *via* stereo-defined *anti*- $\text{S}_{\text{N}}2'$ -type oxidative addition. The subsequent reaction of ( $S_A$ )-MS-Int. II with CO and  $\text{H}_2\text{O}$  delivered the carboxylation intermediate ( $S_A$ )-MS-Int. III and/or ( $S_A$ )-MS-Int. III', which generated the product 2,3-allenoic acid ( $S$ )-2a *via* reductive elimination. Moreover, the slowly reacting propargylic alcohol ( $S$ )-1a could be recovered in excellent ee.

## Conclusions

In summary, a  $\text{Pd}((R)\text{-DTBM-SEGphos})\text{Cl}_2$ -catalyzed carboxylative kinetic resolution reaction of racemic tertiary propargylic alcohols has been developed. Under this set of mild reaction conditions, a variety of enantioenriched tertiary propargylic alcohols and optically active tetrasubstituted 2,3-allenoic acids were obtained in good yields with excellent ee (up to >99%). Gram-scale reactions were easily realized and the optically active tertiary propargylic alcohols and 2,3-allenoic acids could be converted to a series of optically active functionalized products indicating the generality and practicality of this strategy. Mass spectrometry experiments revealed the catalytic process. Further studies in this topic are currently underway in our laboratory.

## Conflicts of interest

There are no conflicts to declare.

## Acknowledgements

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## References

- For selected reviews, see: (a) O. Riant and J. Hannedouche, Asymmetric catalysis for the construction of quaternary carbon centres: nucleophilic addition on ketones and ketimines, *Org. Biomol. Chem.*, 2007, **5**, 873–888; (b) P. G. Cozzi, R. Hilgraf and N. Zimmermann, Enantioselective catalytic formation of quaternary stereogenic centers, *Eur. J. Org. Chem.*, 2007, 5969–5994; (c) M. Shibasaki and M. Kanai, Asymmetric synthesis of tertiary alcohols and  $\alpha$ -tertiary amines *via* Cu-catalyzed C–C bond formation to ketones and ketimines, *Chem. Rev.*, 2008, **108**, 2853–2873; (d) B. M. Trost and A. H. Weiss, The enantioselective addition of alkyne nucleophiles to carbonyl groups, *Adv. Synth. Catal.*, 2009, **351**, 963–983; (e) T. Ohshima, H. Morimoto and K. Morisaki, Catalytic Asymmetric 1,2-Alkynylation, in *Reference Module in Chemistry, Molecular Sciences and Chemical Engineering*, Elsevier, 2015 (an update of Comprehensive Chirality, 2012, Vol. 4, pp. 355–377); (f) V. Bisai and V. K. Singh, Recent developments in asymmetric alkynylations, *Tetrahedron Lett.*, 2016, **57**, 4771–4784; (g) Y.-L. Liu and X.-T. Lin, Recent advances in catalytic asymmetric synthesis of tertiary alcohols *via* nucleophilic addition to ketones, *Adv. Synth. Catal.*, 2019, **361**, 876–918.
- For examples of enantioselective alkynylations of methyl ketones, see: (a) P. G. Cozzi, Enantioselective alkynylation of ketones catalyzed by  $\text{Zn}(\text{Salen})$  complexes, *Angew. Chem., Int. Ed.*, 2003, **42**, 2895–2898; (b) G. Lu, X. Li, X. Jia, W. L. Chan and A. S. C. Chan, Enantioselective alkynylation of aromatic ketones catalyzed by chiral camphorsulfonamide ligands, *Angew. Chem., Int. Ed.*, 2003, **42**, 5057–5058; (c) Y. Zhou, R. Wang, Z. Xu, W. Yan, L. Liu, Y. Kang and Z. Han, Highly enantioselective phenylacetylene additions to ketones catalyzed by ( $S$ )-BINOL-Ti complex, *Org. Lett.*, 2004, **6**, 4147–4149; (d) L. Liu, R. Wang, Y.-F. Kang, C. Chen, Z.-Q. Xu, Y.-F. Zhou, M. Ni, H.-Q. Cai and M.-Z. Gong, Highly enantioselective phenylacetylene addition to aromatic ketones catalyzed by cinchona alkaloid-aluminum complexes, *J. Org. Chem.*, 2005, **70**, 1084–1086; (e) C. Chen, L. Hong, Z.-Q. Xu, L. Liu and R. Wang, Low ligand loading, highly enantioselective addition of phenylacetylene to aromatic ketones catalyzed by Schiff-base amino alcohols, *Org. Lett.*, 2006, **8**, 2277–2280; (f) T. Ueda, K. Tanaka, T. Ichibakase, Y. Orito and



- M. Nakajima, Enantioselective alkynylation of carbonyl compounds with trimethoxysilylalkynes catalyzed by lithium binaphtholate, *Tetrahedron*, 2010, **66**, 7726–7731; (g) S. Kotani, K. Kukita, K. Tanaka, T. Ichibakase and M. Nakajima, Lithium binaphtholate-catalyzed asymmetric addition of lithium acetylides to carbonyl compounds, *J. Org. Chem.*, 2014, **79**, 4817–4825; (h) K. Yamashita, Y. Tabata, K. Yamakawa, T. Mochizuki, K. Matsui, M. Hatano and K. Ishihara, Chiral macrocyclic catalysts for the enantioselective addition of lithium acetylides to ketones, *J. Am. Chem. Soc.*, 2023, **145**, 26238–26248.
- For examples of enantioselective alkynylations of trifluoromethyl ketones, see: (a) R. Motoki, M. Kanai and M. Shibasaki, Copper(I) alkoxide-catalyzed alkynylation of trifluoromethyl ketones, *Org. Lett.*, 2007, **9**, 2997–3000; (b) G.-W. Zhang, W. Meng, H. Ma, J. Nie, W.-Q. Zhang and J.-A. Ma, Catalytic enantioselective alkynylation of trifluoromethyl ketones: pronounced metal fluoride effects and implications of zinc-to-titanium transmetallation, *Angew. Chem., Int. Ed.*, 2011, **50**, 3538–3542; (c) A. M. Cook and C. Wolf, Efficient access to multifunctional trifluoromethyl alcohols through base-free catalytic asymmetric C–C bond formation with terminal ynarnides, *Angew. Chem., Int. Ed.*, 2016, **55**, 2929–2933; (d) J.-i. Ito, S. Ubukata, S. Muraoka and H. Nishiyama, Enantioselective direct alkynylation of ketones catalyzed by chiral CCN pincer Rh<sup>III</sup> complexes, *Chem. – Eur. J.*, 2016, **22**, 16801–16804; (e) Y. Zheng, Y. Tan, K. Harms, M. Marsch, R. Riedel, L. Zhang and E. Meggers, Octahedral ruthenium complex with exclusive metal-centered chirality for highly effective asymmetric catalysis, *J. Am. Chem. Soc.*, 2017, **139**, 4322–4325; (f) D. Park, C. I. Jette, J. Kim, W.-O. Jung, Y. Lee, J. Park, S. Kang, M. S. Han, B. M. Stoltz and S. Hong, Enantioselective alkynylation of trifluoromethyl ketones catalyzed by cation-binding salen nickel complexes, *Angew. Chem., Int. Ed.*, 2020, **59**, 775–779.
  - For examples of enantioselective alkynylations of  $\alpha$ -carbonyl ketones, see: (a) B. Jiang, Z. Chen and X. Tang, Highly enantioselective alkynylation of  $\alpha$ -keto ester: an efficient method for constructing a chiral tertiary carbon center, *Org. Lett.*, 2002, **4**, 3451–3453; (b) K. Aikawa, Y. Hioki and K. Mikami, Highly enantioselective alkynylation of trifluoropyruvate with alkynylsilanes catalyzed by the BINAP-Pd complex: access to  $\alpha$ -trifluoromethyl-substituted tertiary alcohols, *Org. Lett.*, 2010, **12**, 5716–5719; (c) T. Ohshima, T. Kawabata, Y. Takeuchi, T. Kakinuma, T. Iwasaki, T. Yonezawa, H. Murakami, H. Nishiyama and K. Mashima, C<sub>1</sub>-symmetric Rh/Phebox-catalyzed asymmetric alkynylation of  $\alpha$ -ketoesters, *Angew. Chem., Int. Ed.*, 2011, **50**, 6296–6300; (d) R. Infante, J. M. Martin-Alvarez, C. Andrés and J. Nieto, Dimethylzinc-mediated addition of phenylacetylene to  $\alpha$ -diketones catalyzed by chiral perhydro-1,3-benzoxazines, *Org. Lett.*, 2017, **19**, 1516–1519; (e) B. P. Zavesky and J. S. Johnson, Direct zinc(II)-catalyzed enantioconvergent additions of terminal alkynes to  $\alpha$ -keto esters, *Angew. Chem., Int. Ed.*, 2017, **56**, 8805–8808; (f) M. C. Schwarzer, A. Fujioka, T. Ishii, H. Ohmiya, S. Mori and M. Sawamura, Enantiocontrol by assembled attractive interactions in copper-catalyzed asymmetric direct alkynylation of  $\alpha$ -ketoesters with terminal alkynes: OH...O/ $sp^3$ -CH...O two-point hydrogen bonding combined with dispersive attractions, *Chem. Sci.*, 2018, **9**, 3484–3493.
  - For examples of terminal alkyne asymmetric addition to acyl silanes, see: (a) P. Smirnov, J. Mathew, A. Nijs, E. Katan, M. Karni, C. Bolm, Y. Apeloig and I. Marek, One-pot zinc-promoted asymmetric alkynylation/Brook-type rearrangement/ene-allene cyclization: highly selective formation of three new bonds and two stereocenters in acyclic systems, *Angew. Chem., Int. Ed.*, 2013, **52**, 13717–13721; (b) P. Smirnov, E. Katan, J. Mathew, A. Kostenko, M. Karni, A. Nijs, C. Bolm, Y. Apeloig and I. Marek, Formation of three new bonds and two stereocenters in acyclic systems by zinc-mediated enantioselective alkynylation of acylsilanes, Brook rearrangement, and ene-allene carbocyclization reactions, *J. Org. Chem.*, 2014, **79**, 12122–12135.
  - For examples of enantioselective addition to ynones, see: (a) M. Yus, D. J. Ramón and O. Prieto, Highly enantioselective addition of dialkylzinc reagents to ketones promoted by titanium tetraisopropoxide, *Tetrahedron: Asymmetry*, 2002, **13**, 2291–2293; (b) S. E. Denmark and Y. Fan, Catalytic, enantioselective Aldol additions to ketones, *J. Am. Chem. Soc.*, 2002, **124**, 4233–4235; (c) S. Lou, P. N. Moquist and S. E. Schaus, Asymmetric allylboration of ketones catalyzed by chiral diols, *J. Am. Chem. Soc.*, 2006, **128**, 12660–12661; (d) D. K. Friel, M. L. Snapper and A. H. Hoveyda, Aluminum-catalyzed asymmetric alkylations of pyridyl-substituted alkynyl ketones with dialkylzinc reagents, *J. Am. Chem. Soc.*, 2008, **130**, 9942–9951; (e) H. Kawai, K. Tachi, E. Tokunaga, M. Shiro and N. Shibata, Cinchona alkaloid-catalyzed asymmetric trifluoromethylation of alkynyl ketones with trimethylsilyl trifluoromethane, *Org. Lett.*, 2010, **12**, 5104–5107; (f) J. M. García, J. M. Odriozola, J. Razkin, I. Lapuerta, A. Odriozola, I. Urruzuno, S. Vera, M. Oiarbide and C. Palomo, Catalytic enantioselective quick route to Aldol-tethered 1,6- and 1,7-enynes from  $\omega$ -unsaturated aldehydes, *Chem. – Eur. J.*, 2014, **20**, 15543–15554; (g) E. Sánchez-Díez, M. Fernández, U. Uria, E. Reyes, L. Carrillo and J. L. Vicario, Enantioselective synthesis of tertiary propargylic alcohols under *N*-heterocyclic carbene catalysis, *Chem. – Eur. J.*, 2015, **21**, 8384–8388; (h) H. Noda, F. Amemiya, K. Weidner, N. Kumagai and M. Shibasaki, Catalytic asymmetric synthesis of CF<sub>3</sub>-substituted tertiary propargylic alcohols via direct Aldol reaction of  $\alpha$ -N<sub>3</sub> amide, *Chem. Sci.*, 2017, **8**, 3260–3269; (i) F. W. van der Mei, C. Qin, R. J. Morrison and A. H. Hoveyda, Practical, broadly applicable,  $\alpha$ -selective, *Z*-selective, diastereoselective, and enantioselective addition of allylboron compounds to mono-, di-, tri-, and polyfluoroalkyl ketones, *J. Am. Chem. Soc.*, 2017, **139**, 9053–9065.
  - For examples of kinetic resolution of racemic tertiary propargylic alcohols, for enzyme catalysis, see: (a) S. Bartsch,



- R. Kourist and U. T. Bornscheuer, Complete inversion of enantioselectivity towards acetylated tertiary alcohols by a double mutant of a *bacillus subtilis* esterase, *Angew. Chem., Int. Ed.*, 2008, **47**, 1508–1511; For transition metal catalysis, see: (b) Z. Li, V. Boyarskikh, J. H. Hansen, J. Autschbach, D. G. Musaev and H. M. L. Davies, Scope and mechanistic analysis of the enantioselective synthesis of allenes by rhodium-catalyzed tandem ylide formation/[2,3]-sigmatropic rearrangement between donor/acceptor carbenoids and propargylic alcohols, *J. Am. Chem. Soc.*, 2012, **134**, 15497–15504; (c) J. Seliger, X. Dong and M. Oestreich, Kinetic resolution of tertiary propargylic alcohols by enantioselective Cu–H-catalyzed Si–O coupling, *Angew. Chem., Int. Ed.*, 2019, **58**, 1970–1974; (d) R. Mao, Y. Zhao, X. Zhu, F. Wang, W.-Q. Deng and X. Li, Rhodium-catalyzed and chiral zinc carboxylate-assisted allenylation of benzamides via kinetic resolution, *Org. Lett.*, 2021, **23**, 7038–7043; (e) K. Liao, Y. Gong, R.-Y. Zhu, C. Wang, F. Zhou and J. Zhou, Highly enantioselective CuAAC of functional tertiary alcohols featuring an ethynyl group and their kinetic resolution, *Angew. Chem., Int. Ed.*, 2021, **60**, 8488–8493; For organocatalysis, see: (f) S. Niu, H. Zhang, W. Xu, P. R. Bagdi, G. Zhang, J. Liu, S. Yang and X. Fang, Access to enantioenriched compounds bearing challenging tetrasubstituted stereocenters via kinetic resolution of auxiliary adjacent alcohols, *Nat. Commun.*, 2021, **12**, 3735; (g) T. Desrues, X. Liu, J.-M. Pons, V. Monnier, J.-A. Amalian, L. Charles, A. Quintard and C. Bressy, Indirect tertiary alcohol enantiocontrol by acylative organocatalytic kinetic resolution, *Org. Lett.*, 2021, **23**, 4332–4336; (h) G. Wang, L. Li, Y. Jiang, X. Zhao, X. Ban, T. Shao, Y. Yin and Z. Jiang, Kinetic resolution of azaarylethynyl tertiary alcohols by chiral Brønsted acid catalysed phosphine-mediated deoxygenation, *Angew. Chem., Int. Ed.*, 2023, **62**, e202214838; (i) S. Xie, X. Gao, F. Zhou, H. Wu and J. Zhou, Enantioselective carboxylative cyclization of propargylic alcohol with carbon dioxide under mild conditions, *Chin. Chem. Lett.*, 2020, **31**, 324–328.
- 8 (a) R. Zimmer, C. U. Dinesh, E. Nandanan and F. A. Khan, Palladium-catalyzed reactions of allenes, *Chem. Rev.*, 2000, **100**, 3067–3125; (b) S. Ma, Transition metal-catalyzed/mediated reaction of allenes with a nucleophilic functionality connected to the  $\alpha$ -carbon atom, *Acc. Chem. Res.*, 2003, **36**, 701–712; (c) S. Ma, Some typical advances in the synthetic applications of allenes, *Chem. Rev.*, 2005, **105**, 2829–2871; (d) S. Ma, Electrophilic addition and cyclization reactions of allenes, *Acc. Chem. Res.*, 2009, **42**, 1679–1688; (e) S. Yu and S. Ma, Allenes in catalytic asymmetric synthesis and natural product syntheses, *Angew. Chem., Int. Ed.*, 2012, **51**, 3074–3112; (f) P. Rivera-Fuentes and F. Diederich, Allenes in molecular materials, *Angew. Chem., Int. Ed.*, 2012, **51**, 2818–2828; (g) J. Ye and S. Ma, Palladium-catalyzed cyclization reactions of allenes in the presence of unsaturated carbon-carbon bonds, *Acc. Chem. Res.*, 2014, **47**, 989–1000; (h) M. P. Muñoz, Silver and platinum-catalysed addition of O–H and N–H bonds to allenes, *Chem. Soc. Rev.*, 2014, **43**, 3164–3183; (i) J.-Y. Wang, W.-J. Hao, S.-J. Tu and B. Jiang, Engaging yne-allenes in cycloaddition reactions: recent developments, *Chin. J. Chem.*, 2022, **40**, 1224–1242.
- 9 Selected reviews for the synthesis of axially chiral allenes: (a) S. Yu and S. Ma, How easy are the syntheses of allenes?, *Chem. Commun.*, 2011, **47**, 5384–5418; (b) W.-D. Chu, Y. Zhang and J. Wang, Recent advances in catalytic asymmetric synthesis of allenes, *Catal. Sci. Technol.*, 2017, **7**, 4570–4579; (c) W. Xiao and J. Wu, Recent advances in the metal-catalyzed asymmetric synthesis of chiral allenes, *Org. Chem. Front.*, 2022, **9**, 5053–5073; (d) X. Wang, X. Chen, W. Lin, P. Li and W. Li, Recent advances in organocatalytic enantioselective synthesis of axially chiral allenes, *Adv. Synth. Catal.*, 2022, **364**, 1212–1222; (e) T. T. Nguyen, Organocatalytic synthesis of axially chiral tetrasubstituted allenes, *Org. Biomol. Chem.*, 2023, **21**, 252–272; For asymmetric functionalization of trisubstituted allenes, see: (f) T. Hashimoto, K. Sakata, F. Tamakuni, M. J. Dutton and K. Maruoka, Phase-transfer-catalysed asymmetric synthesis of tetrasubstituted allenes, *Nat. Chem.*, 2013, **5**, 240–244; (g) C. T. Mbofana and S. J. Miller, Diastereo- and enantioselective addition of anilide-functionalized allenates to *N*-acylimines catalyzed by a pyridylalanine-based peptide, *J. Am. Chem. Soc.*, 2014, **136**, 3285–3292; (h) G. Wang, X. Liu, Y. Chen, J. Yang, J. Li, L. Lin and X. Feng, Diastereoselective and enantioselective alleno-Aldol reaction of allenates with isatins to synthesis of carbinol allenates catalyzed by gold, *ACS Catal.*, 2016, **6**, 2482–2486; (i) Y. Hu, W. Shi, B. Zheng, J. Liao, W. Wang, Y. Wu and H. Guo, Organocatalytic asymmetric C(sp<sup>2</sup>)-H allylic alkylation: enantioselective synthesis of tetrasubstituted allenates, *Angew. Chem., Int. Ed.*, 2020, **59**, 19820–19824; For asymmetric 1,4-functionalization of 1,3-enynes, see: (j) A. Tap, A. Blond, V. N. Wakchaure and B. List, Chiral allenes via alkynylogous Mukaiyama Aldol reaction, *Angew. Chem., Int. Ed.*, 2016, **55**, 8962–8965; (k) Y. Liao, X. Yin, X. Wang, W. Yu, D. Fang, L. Hu, M. Wang and J. Liao, Enantioselective synthesis of multisubstituted allenes by cooperative Cu/Pd-catalyzed 1,4-arylboration of 1,3-enynes, *Angew. Chem., Int. Ed.*, 2020, **59**, 1176–1180; (l) Y. Zeng, M.-F. Chiou, X. Zhu, J. Cao, D. Lv, W. Jian, Y. Li, X. Zhang and H. Bao, Copper-catalyzed enantioselective radical 1,4-difunctionalization of 1,3-enynes, *J. Am. Chem. Soc.*, 2020, **142**, 18014–18021; (m) X.-Y. Dong, T.-Y. Zhan, S.-P. Jiang, X.-D. Liu, L. Ye, Z.-L. Li, Q.-S. Gu and X.-Y. Liu, Copper-catalyzed asymmetric coupling of allenyl radicals with terminal alkynes to access tetrasubstituted allenes, *Angew. Chem., Int. Ed.*, 2021, **60**, 2160–2164; (n) H. Huang, H. Zhang, Q. Wang, Y. Sun, L. Su, W. Xu, Y. Ma, S. Kong, G. Zhang and R. Guo, Copper-catalyzed asymmetric 1,4-aryl/alkynylation of 1,3-enynes to access axially chiral tetrasubstituted allenes, *ChemCatChem*, 2023, **15**, e202300697; (o) Y. Zhang, J. Wu, L. Ning, Q. Chen, X. Feng and X. Liu, Enantioselective synthesis of tetrasubstituted allenes via addition/arylation tandem reaction of 2-activated 1,3-



- enynes, *Sci. China: Chem.*, 2023, **66**, 526–533; For chiral phosphoric acid (CPA) catalyzed conjugate addition to quinone methides formed from propargylic alcohols, see: (p) D. Qian, L. Wu, Z. Lin and J. Sun, Organocatalytic synthesis of chiral tetrasubstituted allenes from racemic propargylic alcohols, *Nat. Commun.*, 2017, **8**, 567; (q) P. Zhang, Q. Huang, Y. Cheng, R. Li, P. Li and W. Li, Remote stereocontrolled construction of vicinal axially chiral tetrasubstituted allenes and heteroatom-functionalized quaternary carbon stereocenters, *Org. Lett.*, 2019, **21**, 503–507; (r) W.-R. Zhu, Q. Su, H.-J. Diao, E.-X. Wang, F. Wu, Y.-L. Zhao, J. Weng and G. Lu, Enantioselective dehydrative  $\gamma$ -arylation of  $\alpha$ -indolyl propargylic alcohols with phenols: access to chiral tetrasubstituted allenes and naphthopyrans, *Org. Lett.*, 2020, **22**, 6873–6878; Selected other examples: (s) T. Hayashi, N. Tokunaga and K. Inoue, Rhodium-catalyzed asymmetric 1,6-addition of aryl titanates to enynones giving axially chiral allenes, *Org. Lett.*, 2004, **6**, 305–307; (t) M. Hammel and J. Deska, Enantioselective synthesis of axially chiral tetrasubstituted allenes *via* lipase-catalyzed desymmetrization, *Synthesis*, 2012, **44**, 3789–3796; (u) Y. Tang, J. Xu, J. Yang, L. Lin, X. Feng and X. Liu, Asymmetric three-component reaction for the synthesis of tetrasubstituted allenates *via* allenolate-copper intermediates, *Chem*, 2018, **4**, 1658–1672; (v) B. Shi, J.-B. Liu, Z.-T. Wang, L. Wang, Y. Lan, L.-Q. Lu and W.-J. Xiao, Synthesis of chiral endocyclic allenes by palladium-catalyzed asymmetric annulation followed by Cope rearrangement, *Angew. Chem., Int. Ed.*, 2022, **61**, e202117215; (w) J. Wang, W.-F. Zheng, X. Zhang, H. Qian and S. Ma, Stereoselectivity control in Rh-catalyzed  $\beta$ -OH elimination for chiral allene formation, *Nat. Commun.*, 2023, **14**, 7399.
- 10 Selected examples for heteroatom-substituted chiral tetrasubstituted allenes: (a) M. Wang, Z.-L. Liu, X. Zhang, P.-P. Tian, Y.-H. Xu and T.-P. Loh, Synthesis of highly substituted racemic and enantioenriched allenylsilanes *via* copper-catalyzed hydrosilylation of (Z)-2-alken-4-ynoates with silylboronate, *J. Am. Chem. Soc.*, 2015, **137**, 14830–14833; (b) J. Yang, Z. Wang, Z. He, G. Li, L. Hong, W. Sun and R. Wang, Organocatalytic enantioselective synthesis of tetrasubstituted  $\alpha$ -amino allenates by dearomative  $\gamma$ -addition of 2,3-disubstituted indoles to  $\beta,\gamma$ -alkynyl- $\alpha$ -imino esters, *Angew. Chem., Int. Ed.*, 2020, **59**, 642–647; (c) A. G. Woldegiorgis, Z. Han and X. Lin, Organocatalytic asymmetric dearomatization reaction for the synthesis of axial chiral allene-derived naphthalenones bearing quaternary stereocenters, *Org. Lett.*, 2021, **23**, 6606–6611; (d) F. Li, S. Liang, Y. Luan, X. Chen, H. Zhao, A. Huang, P. Li and W. Li, Organocatalytic regio-, diastereo- and enantioselective  $\gamma$ -additions of isoxazol-5(4H)-ones to  $\beta,\gamma$ -alkynyl- $\alpha$ -imino esters for the synthesis of axially chiral tetrasubstituted  $\alpha$ -amino allenates, *Org. Chem. Front.*, 2021, **8**, 1243–1248; (e) C. Sheng, Z. Ling, J. Xiao, K. Yang, F. Xie, S. Ma and W. Zhang, Enantio- and diastereoselective synthesis of chiral tetrasubstituted  $\alpha$ -amino allenates bearing a vicinal all-carbon quaternary stereocenter with dual-copper-catalysis, *Angew. Chem., Int. Ed.*, 2023, **62**, e202305680; (f) T. J. O'Connor, B. K. Mai, J. Nafie, P. Liu and F. D. Toste, Generation of axially chiral fluoroallenes through a copper-catalyzed enantioselective  $\beta$ -fluoride elimination, *J. Am. Chem. Soc.*, 2021, **143**, 13759–13768; (g) J. S. Ng and T. Hayashi, Asymmetric synthesis of fluorinated allenes by rhodium-catalyzed enantioselective alkylation/defluorination of propargyl difluorides with alkylzincs, *Angew. Chem., Int. Ed.*, 2021, **60**, 20771–20775.
  - 11 W.-F. Zheng, W. Zhang, C. Huang, P. Wu, H. Qian, L. Wang, Y.-L. Guo and S. Ma, Tetrasubstituted allenes *via* the palladium-catalysed kinetic resolution of propargylic alcohols using a supporting ligand, *Nat. Catal.*, 2019, **2**, 997–1005.
  - 12 J. Wang, W. Zhang, P. Wu, C. Huang, Y. Zheng, W.-F. Zheng, H. Qian and S. Ma, Chiral tertiary propargylic alcohols *via* Pd-catalyzed carboxylative kinetic resolution, *Org. Chem. Front.*, 2020, **7**, 3907–3911.
  - 13 W. Wang, H. Qian and S. Ma, Rh-catalyzed reaction of propargylic alcohols with aryl boronic acids-switch from  $\beta$ -OH elimination to protodemetalation, *Chin. J. Chem.*, 2020, **38**, 331–345.
  - 14 W. Zhang and S. Ma, Palladium/ $H^+$ -cocatalyzed kinetic resolution of tertiary propargylic alcohols, *Chem. Commun.*, 2018, **54**, 6064–6067.
  - 15 V. Laserna, C. J. Rojas and T. D. Sheppard, Gold-catalyzed hydrophenoxylation of propargylic alcohols and amines: synthesis of phenyl enol ethers, *Org. Lett.*, 2019, **21**, 4443–4447.
  - 16 A. L. Moure, R. G. Arrayás, D. J. Cárdenas, I. Alonso and J. C. Carretero, Regiocontrolled  $Cu^I$ -catalyzed borylation of propargylic-functionalized internal alkynes, *J. Am. Chem. Soc.*, 2012, **134**, 7219–7222.
  - 17 S. Ma, Z. Yu and S. Wu,  $CuCl$ -catalyzed cycloisomerization reaction of 1,2-allenyl carboxylic acids. A cost-effective synthesis of  $\beta$ -unsubstituted butenolides, *Tetrahedron*, 2001, **57**, 1585–1588.
  - 18 N. Miyaura, T. Yanagi and A. Suzuki, The palladium-catalyzed cross-coupling reaction of phenylboronic acid with haloarenes in the presence of bases, *Synth. Commun.*, 1981, **11**, 513–519.
  - 19 S. Ma and Z. Yu,  $Pd(II)$ -catalyzed coupling cyclization of 2,3-allenoic acids with allylic halides. An efficient methodology for the synthesis of  $\beta$ -allylic butenolides, *J. Org. Chem.*, 2003, **68**, 6149–6152.
  - 20 K. P. Melnykov, D. S. Granat, D. M. Volochnyuk, S. V. Ryabukhin and O. O. Grygorenko, Multigram synthesis of  $C_4/C_5$  3,3-difluorocyclobutyl-substituted building blocks, *Synthesis*, 2018, **50**, 4949–4957.
  - 21 J.-T. Zhang, H.-Y. Wang, W. Zhu, T.-T. Cai and Y.-L. Guo, Solvent-assisted electrospray ionization for direct analysis of various compounds (complex) from low/nonpolar solvents and eluents, *Anal. Chem.*, 2014, **86**, 8937–8942.

