Gold-catalyzed stereoselective cycloisomerization of allenoic acids for two types of common natural \( \gamma \)-butyrolactones

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\( \gamma \)-(E)-Vinylic and \( \gamma \)-alkylc \( \gamma \)-butyrolactones are two different types of lactones existing extensively in animals and plants and many of them show interesting biological activities. Nature makes alkylc \( \gamma \)-butyrolactones by many different enzymatic lactonization processes. Scientists have been mimicking the natural strategy by developing new catalysts. However, direct and efficient access to \( \gamma \)-(E)-vinylic \( \gamma \)-butyrolactones is still extremely limited. Here, we wish to present our modular allene approach, which provides an efficient asymmetric approach to (E)-vinylic \( \gamma \)-butyrolactones from allenoic acids by identifying a new gold complex as the catalyst. Based on this cycloisomerization strategy, the first syntheses of racemic xestospongiene and xestospongienes E, F, G, and H have been realized and the absolute configurations of the chiral centers in xestospongienes E and F have been revised. In addition, by applying a C–O bond cleavage-free hydrogenation, the syntheses of naturally occurring \( \gamma \)-alkylc \( \gamma \)-lactones, (R)-4-tetradecalactone, (S)-4-tetradecalactone, (R)-\( \gamma \)-palmitolactone, and (R)-4-decalactone, have also been achieved.
Natural products are a big treasure for human beings, which exhibit rich academic and industrial potentials due to their structural diversity and biological activities. As we know, \(\gamma\)-butyrolactones with common structures of \(\gamma-(E)\)-vinyl and \(\gamma\)-alkylic \(\gamma\)-butyrolactones, \(\text{E-I}\) and \(\text{II}\), exist extensively in nature and many of them have been identified with interesting biological potentials, such as anti-HIV, anti-fungal, cytotoxic, anti-bacterial, anti-proliferative activities, etc., featuring applications in pharmacy (Fig. 1). Some of these lactones, especially for aliphatic \(\gamma\)-butyrolactones, are also common flavor source in plants and food, which involved in several metabolic pathways.

So far, very few highly selective asymmetric synthesis of \(\text{E-I}\) type \(\gamma\)-butyrolactones with a \(\text{trans} 1,3\)-disubstituted \(\text{C} = \text{C}\) bond has been reported\(^{22,23}\). The approaches for the synthesis of unique \(\gamma-(2,2\text{-disubstituted or 1-iodo})\) vinyl \(\gamma\)-butyrolactones\(^{14-18}\) are not applicable for the synthesis of the natural \(\gamma\)-butyrolactones due to the substrate limitation. It is well reasoned that in the Au-catalyzed enantioselective approach the control of \(\text{E/Z selectivity}\) and enantioselectivity are most likely the challenge when 6-monosubstituted allenoic acids were used (Fig. 2d).\(^{14-16}\) We envisioned a Au-catalyzed cycloisomerization\(^{19-25}\) of optically active 4,5-alkadienoic acids, readily available from terminal alkynes and aldehydes, for the direct access to various natural and non-natural enantioenriched \(\text{E-I}\)-type common \(\gamma\)-butyrolactones, which could further be easily hydrogenated to provide naturally occurring \(\gamma\)-alkyl \(\gamma\)-butyrolactones \(\text{II}\) (Fig. 2e). The latter was usually prepared via the lactonization (Fig. 2a)\(^{26-29}\), Baeuer–Villiger oxidation (Fig. 2b)\(^{30}\), and dihydroxylation-lactonization-elimination (Fig. 2c), etc.\(^{31-34}\) The challenge for strategy in Fig. 2e is the efficiency of axial-to-central chirality transfer\(^{35-43}\) and the control of \(\text{Z/E selectivity} (\text{E-I vs. Z-I})\), which after hydrogenation would afford the enantiomers of lactones \(\text{II}\), respectively, thus, leading to a much lower ee during the cyclic anti-nucleometalation and the efficiency of the proto demetalation process to deliver the required 1,3-disubstituted \(\text{E-C} = \text{C}\) bond finishing the catalytic cycle. Overall it is highly desirable to identify a suitable ligand \(\text{L}\) for a much more stable complex \(\text{I}\) over complex \(\text{II}\).

Herein, we present the highly stereoselective cycloisomerization of optically active 5-monosubstituted 4,5-alkadienoic acids affording various non-natural and natural enantioenriched \(\gamma-(E)\)-alkenyl-\(\gamma\)-butyrolactones by using \(\text{AuCl(LB-Phos)}\) as the catalyst.

**Results**

**Synthesis of \(\text{AuCl(LB-Phos)}\).** At the beginning, we treated \((R)\)-4,5-tridecadienoic acid \((R)\)-5a (for its synthesis from aldehyde and terminal alkyne, see: Supplementary Tables 1 and 2) as the model substrate. After screening of some commonly used gold catalysts such as \(\text{AuCl, Au(Cl(IPr)), Au_2Cl_2(dppm), Au_2Cl_2(dpmm)}\) combined with \(\text{AgOTs}\) was identified as the first generation catalyst to afford the desired \(\gamma-1(E)-alkenyl\)-(S)-\(\gamma\)-butyrolactone \((S, E)\)-6a in a quantitative yield with a \(\text{E/Z selectivity} 93:7\) and 96% ee in \(\text{CHCl}_3\) at room temperature for 3 h (Table 1, entry 1). For the purpose of improving the \(\text{E/Z selectivity}\), we tried to identify a more stereoselective catalyst. Based on our recent development of monophosphine ligands\(^{44}\), some of the gold complexes of these ligands have been prepared. \(\text{AuCl(LB-Phos)}\), the structure of which was determined by X-ray single crystal diffraction study (Fig. 3)\(^{45}\), is one of them.

**Optimization of reaction conditions.** With this rather sterically bulky \(\text{AuCl(LB-Phos)}\), gladly, an \(\text{E/Z selectivity} 97:3\) with 100% yield and 97% ee was observed, indicating that the new catalyst was able to control both the \(\text{C} = \text{C}\) stereoselectivity and ensure the efficiency of chirality transfer (Table 1, entry 2). Inspired by this result, we explored the effect of solvents: \(\text{CH}_2\text{Cl}_2\) gave a similar

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**Fig. 1** Representative examples of \(\gamma-(E)\)-vinyl and \(\gamma\)-alkylic-\(\gamma\)-butyrolactones. **a** Common structure unit and representative examples of \(\gamma-(E)\)-vinyl-\(\gamma\)-butyrolactones \((\text{E-I})\); **b** Common structure unit and representative examples of \(\gamma\)-alkylic-\(\gamma\)-butyrolactones \((\text{II})\).
E/Z and ee (Table 1, entry 3), while 1,2-DCE led to a rather poor E/Z selectivity of 91:9 (Table 1, entry 4); CH₃NO₂ showed a better E-selectivity of 98:2, but a much lower ee of 90% (Table 1, entry 6); other solvents such as toluene, dioxane, and CH₃CN failed to yield any better results even with a prolonged time of 12 h (Table 1, entries 5, 7–8). In the absence of AgOTs, the expected product 6a was obtained in only 8% yield with 92% recovery of (R)-5a after 24 h (Table 1, entry 9), and the lactonization couldn’t take place by just using AgOTs (Table 1, entry 10), indicating the significance of the gold-catalysis. Examining the effect of different salts showed the importance of the counter anion: AgPF₆ resulted in the same E/Z-selectivity but with a lower ee of 92% (Table 1, entry 11), while other common silver salts such as AgOTf, AgSbF₆, and AgOAc, etc. all caused a dropped E/Z selectivity ranging from 82:18 to 93:7 (Table 1, entries 12–16).

Thus, we defined the standard reaction conditions as follows: 5 mol% Au(LB-Phos)/AgOTs in CHCl₃ at 25 °C for 3 h (Table 1, entry 2).

**Substrate scope.** With the optimized reaction conditions in hand, differently substituted 4,5-allenoic acids (Rₐ)-5 were treated with AuCl(LB-Phos) to afford γ-1(E)-alkenyl (S)-γ-butyrolactones in high yields (93–98%) with an excellent axial-to-center chirality transfer and E/Z-selectivity (up to >99:1 E/Z) (Table 2): R could be primary alkyl: n-heptyl (6a), n-butyl (6b), n-undecyl (6c), and phenylethyl (6g), or branched alkyl: i-Pr (6d), and Cy (6e). The reaction of benzyl-substituted (Rₐ)-5f should be conducted at −40 °C for 6 h to keep the enantioselectivity due to the observed racemization at 25 °C (6f) (compare entry 6 with entry 7 in
Table 2). Functional groups including benzyl group, C= C, and C≡C bonds were also tolerated (6f, 6g, 6h, and 6i).

As expected, the enantiomer (R,E)-butyrolactone (6j) could also be prepared from the enantiomer of the starting allene, (S,a)-4,5-dienoic acid (S,a)-5j, in a high yield and an excellent E/Z-selectivity (Fig. 4a). After some further optimization (see Supplementary Table 3), a 10 mmol scale reaction with just 1.5 mol% each of AuCl(LB-Phos) and AgOTs in CHCl₃ at −20 °C for 15 h was realized, delivering an excellent yield of chiral lactone (S,E)-6b with 97% ee and 98:2 E/Z selectivity (Fig. 4b).

**The effect of different gold catalysts.** The results of different gold catalysts combined with AgOTs in CHCl₃ are listed in Table 3, which showed that AuCl(LB-Phos) was indeed the best catalyst (Table 3, entry 6).

**Synthesis of racemic xestospongiene.** Such a strategy should deliver a direct entry to the optically active natural γ-butyrolactone with common structure E-I as shown in Fig. 1a. Xestospongienes are a series of brominated polyunsaturated lipids isolated from the Chinese marine sponge Xestospongia testudinaria (shown in Fig. 1a). No total synthesis has been reported yet. Thus, 7-((tert-butyldimethylsilyl)oxy)heptanal 7 underwent 1,2-addition reaction with ethyl magnesium bromide to yield propargylic alcohol 8. Methylation of 8 via deprotonation with NaH, followed by quenching with MeI, and subsequent removal

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**Table 1 Optimization of the reaction conditions for AuCl(LB-Phos)-catalyzed stereoselective cyclization of 4,5-allenoic acid (R,a)-5a**

| Entry | [Ag]  | solvent   | t (h) | Yield (%) (S,E)/(R,Z) | ee (%) of (S,E)-6a (%) |
|-------|-------|-----------|-------|-----------------------|------------------------|
| 1,c,d | AgOTs | CHCl₃     | 4     | 100                   | 93.7                   | 96                     |
| 2,d   | AgOTs | CHCl₃     | 3     | 100                   | 97.3                   | 97                     |
| 3     | AgOTs | CH₂Cl₂    | 3     | 100                   | 96.4                   | 95                     |
| 4     | AgOTs | 1,2-DCE  | 3     | 98                    | 92.2                   | 96                     |
| 5     | AgOTs | toluene   | 12    | 100                   | 94.6                   | 95                     |
| 6     | AgOTs | CH₃NO₂    | 3     | 99                    | 98.2                   | 90                     |
| 7     | AgOTs | dioxane   | 12    | 100                   | 94.6                   | 96                     |
| 8     | AgOTs | CH₃CN     | 12    | 100                   | 97.3                   | 95                     |
| 9     | AgOTs | CHCl₃     | 24    | 0                     | –                      | –                      |
| 10     | AgOTs | CHCl₃     | 24    | 0                     | –                      | –                      |
| 11     | AgPF₆ | CHCl₃     | 3     | 100                   | 97.3                   | 92                     |
| 12     | AgOMs | CHCl₃     | 12    | 99                    | 93.7                   | 97                     |
| 13     | AgOTf | CHCl₃     | 2     | 100                   | 92.8                   | –                      |
| 14     | AgSbF₆| CHCl₃     | 2     | 96                    | 91.9                   | –                      |
| 15     | AgOAc | CHCl₃     | 8.5   | 100                   | 82.8                   | –                      |
| 16     | AgBF₄ | CHCl₃     | 2     | 99                    | 92.8                   | –                      |

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AgOTs (0.01 mmol), AuCl(LB-Phos) (0.01 mmol), and solvent (2 mL) were stirred at room temperature for 15 min under nitrogen atmosphere; then 0.2 mmol (R,a)-5a and solvent (1 mL) were added

*a* Determined by 1H NMR of the crude product using 1,3,5-trimethylbenzene as internal standard

*b* Determined by chiral high-performance liquid chromatography (HPLC) analysis

*c* 2.5 mol% Au₂Cl₂(dppm) was used instead of AuCl(LB-Phos)

*d* The reaction was conducted at 25 °C

*e* 1,2-DCE: 1,2-dichloroethane

*f* The reaction was conducted in the absence of AuCl(LB-Phos); 100% recovery of (R,a)-5a
of the TBS group via acidic hydrolysis yielded the primary alcohol \( \text{9} \) with a terminal C-C triple bond in 88% yield. Fe(III)-catalyzed aerobic oxidation of \( \text{9} \) afforded aldehyde \( \text{10} \) in 62% yield\(^6\). Wittig olefination of the aldehyde functionality in \( \text{10} \) afforded the terminal alkyne \( \text{1c} \)\(^7\), which underwent the ATA (allenylation of terminal alkynes) reaction with methyl 4-oxobutanoate \( \text{2k} \) (readily available from \( \gamma \)-butyrolactone) reaction with methyl 4-oxobutanoate \( \text{2k} \) to afford (5\( \text{S,E} \))\(-\text{butyrolactone} \ 6\text{b} \).

Asymmetric synthesis of xestospongiens E–H. It is well known that different stereoisomers of drug molecules may show very distinct biological activities. After methylation, deprotection, aerobic oxidation, and Wittig olefination reaction, (R)-\( \text{8} \) and (S)-\( \text{8} \) (for their syntheses, see Supplementary Tables 5, 6 and Supplementary Methods\(^50\)) were easily converted to terminal propargylic methyl ethers (R)-\( \text{1c} \) and (S)-\( \text{1c} \), respectively (Fig. 6a, b).

The reaction of (R)-\( \text{1c} \), \( \text{2k} \), and (S)-diphenylprolinol (S)-\( \text{3a} \) in a ratio of 1:1.5:1.5 afforded (R)\( \text{R,R} \)-\( \text{4ck} \) as a single stereoisomer in 47% yield with >99% ee and >99:1 d.r. Hydrolysis of (R)\( \text{R,R} \)-\( \text{4ck} \) was conducted subsequently by its treatment with LiOH\( \cdot \)H\( \text{2O} \) at 90 °C for 1.5 h affording (R)\( \text{R,R} \)-\( \text{5k} \), which was cycloisomerized with 10 mol% of AuCl\( (\text{LB-Phos}) \) at −30 °C to afford (5\( \text{S,I',E',E'} \))-\( \text{R} \)-\( \text{6k} \), i.e., xestospongienne F (reported as xestospongienne F\(^5\)) in 94% yield with >99% ee and >99:1 d.r. (Fig. 6c).

Xestospongienes G, H, and (5\( \text{R,I',E',S'} \))-\( \text{R} \)-\( \text{6k} \), i.e., xestospongienne E (reported as Xestospongienne E\(^\ddagger\)) could also be obtained easily with high stereo- and enantioselectivity in a similar way by just replacing amino alcohol (S)-\( \text{3a} \) with (R)-\( \text{3a} \) or propargylic alcohol (R)-\( \text{1c} \) with (S)-\( \text{1c} \) (Fig. 6d–f). Subsequently, gram scale synthesis of xestospongienne F was easily realized with a high enantiopurity (99% ee and 98:2 d.r.) (for details, see Supplementary Methods).

### Table 2 Highly stereoselective synthesis of \((S,E)\)-6

| Entry | \((R)_5\)-S | \((S,E)\)-6 Yield | (S,E)/(R,Z) | ee (%) |
|-------|-----------|-------------------|-------------|--------|
| 1     | \(n\)-C\(_5\)H\(_{10}\) \((R)_5\)-5\(a\) | 96 | 96 \(6\text{a}\) | 96 |
| 2     | \(n\)-C\(_5\)H\(_{10}\) \((R)_5\)-5\(b\) | 97 | 93 \(6\text{b}\) | 96 |
| 3     | \(n\)-C\(_5\)H\(_{10}\) \((R)_5\)-5\(c\) | 97 | 98 \(6\text{c}\) | 96 |
| 4     | \(\mu\)-Pr \((R)_5\)-5\(d\) | 98 | 94 \(6\text{d}\) | 98 |
| 5     | Cy \((R)_5\)-5\(e\) | 97 | 96 \(6\text{e}\) | 99.1\(^\ddagger\) |
| 6     | Bn \((R)_5\)-5\(f\) | 96 | 90 \(6\text{f}\) | 95.5 (95:5) |
| 7     | Bn \((R)_5\)-5\(g\) | 95 | 95 \(6\text{g}\) | 98.2 (97:3) |
| 8     | \(\text{BnCH}=	ext{CH(CH}_2\text{)}\text{H}_9 \((R)_5\)-5\(h\) | 97 | 97 \(6\text{h}\) | 97.3 (95.5) |
| 9     | \(\text{H}_2\text{C}=	ext{C} \text{CH(CH}_2\text{)}\text{H}_9 \((R)_5\)-5\(i\) | 96 | 94 \(6\text{h}\) | >99:1 (97.3) |
| 10    | \(\text{TBSCH}=	ext{C} \text{CH(CH}_2\text{)}\text{H}_9 \((R)_5\)-5\(l\) | 96 | 96 \(6\text{i}\) | 97.3 (97.3) |

AgOTs (0.05 mmol), AuCl\((\text{LB-Phos})\) (0.05 mmol), and CHCl\(_3\) (5 mL) were stirred at room temperature for 15 min under nitrogen atmosphere; then 1.0 mmol \((R)_5\)-6 and CHCl\(_3\) (5 mL) were added at 25 °C.

\(\ddagger\) Isolated yield

\(\ddagger\) Determined by \(\text{H}\) NMR of the isolated product; the data in parentheses were determined by \(\text{H}\) NMR of crude product using 1,3,5-trimethylbenzene as internal standard

\(\ddagger\) Reaction time was 2.5 h

\(\ddagger\) Not able to be determined in the crude product; determined by quantitative \(13\text{C}\) NMR of the isolated product

\(\ddagger\) The reaction was conducted at −40 °C for 6 h.

\(\ddagger\) The reaction time was 2 h.
Asymmetric syntheses of naturally occurring \( \gamma \)-alkyllic \( \gamma \)-lactones. As stated above, aliphatic \( \gamma \)-butyrolactones are the major aroma components of many industrial fragrances and ingredients in flavors and as food additives\(^\text{11}\), some of which also work as quorum-sensing molecules in vivo\(^\text{51}\). Hydrogenation of the C=C bond in (E)-alkenyl \( \gamma \)-butyrolactones E-I would provide an efficient entry to these naturally occurring \( \gamma \)-alkyllic \( \gamma \)-lactones II listed in Fig. 1b, provided that the cleavage of the allylic C–O bond causing racemization to the chiral center under the transition metal catalysis may be avoided.

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Fig. 6 First total synthesis of xestospongiene E–H. a Synthesis of (R)-1c; b Synthesis of (S)-1c; c Total synthesis of xestospongiene F; d Total synthesis of xestospongiene G; e Total synthesis of xestospongiene H; f Total synthesis of xestospongiene E. Reagents and conditions: i. NaH (1.0 equiv.), THF, 0 °C, then rt; then Mel (1.2 equiv.), 0 °C–rt; then HCl (aq., 3.0 M), MeOH, rt; ii. Fe(NO₃)₃·9H₂O (10 mol%), TEMPO (10 mol%), NaCl (10 mol%), O₂ balloon, DCM, rt; iii. CBr₄ (1.5 equiv.), PPh₃ (3.0 equiv.), DCM, 0 °C; iv. methyl 4-oxobutanoate 2k (1.5–1.7 equiv.), CuBr₂ (20 mol%), dioxane, 120 °C; v. LiOH·H₂O (1.5 equiv.), EtOH/H₂O = 1:1, 90 °C; vi. AuCl(LB-Phos) (10 mol%), AgOTs (10 mol%), CHCl₃, −30 °C.
It has been established that the two enantiomers of γ-alkyl-γ-butyrolactones make some differences in odor quality and odor intensity.11,32,33 Thus, we tried to synthesize both (R) and (S)-γ-lactones by utilizing the current strategy. Starting from asymmetric allenylation of readily available ethyl pent-4-ynoate 1b with nonanal 2j in the presence of 5 mol% H2 (25 atm), EtOH/H2O (1.5 equiv.) and H2 (25 atm), EtOAc, rt (Fig. 7a).30,31,34,35

The enantiomer (S)-4-tetradecalactone was executed by following the same synthetic route just by replacing (S)-3a with (R)-3a in the step of EATA (enantioselective allenylation of terminal alkynes) reaction, giving the desired product with a similar yield and enantioselectivity. Similarly, naturally occurring aromatic (R)-γ-palmolactone was synthesized in 96% ee by just using undecanal 2l as the starting aldehyde in EATA reaction (Fig. 7c).34 (R)-4-Deocalactone is a sex pheromone of Osmoderma eremita released mainly or exclusively by male beetles35, which has also been proven to be cytotoxic38,39, and synthesized with biocatalysts26,28,59 or by other strategies29,33,60. Gram scale synthesis of (R)-4-decalactone was also realized easily in 43% total yield for 4 steps with 94% ee (Fig. 7d).

Discussion

A facile strategy for general asymmetric synthesis of two types of common γ-butyrolactones from readily available common chemicals-terminal alkynes and aldehydes has been developed by applying the newly identified catalyst, AuCl(LB-Phos), with the stereoselectivity of up to >99:1 E/Z and >99% ee. The first total syntheses of xestospigniones E, F, G, and H have been realized with high stereoselectivity. In addition, the C–O bond cleavage-free hydrogenation led to a general access to naturally occurring γ-alkyl-γ-butyrolactones, such as (R)-4-tetradecalactone, (S)-4-tetradecalactone, (R)-γ-palmolactone, and (R)-4-decalactone, efficiently with ee of 93–96%. Such a modular solution to two different types of optically active γ-butyrolactones will surely stimulate further interest in the synthetic and bio-potential of these compounds and identifying even better aromas for human life. Further studies on this area are being carried out in our laboratory.

Methods

General method for cycloisomerization of alkanedioic acids. To a dry Schlenk tube were added AgOAc (0.014 g, 0.05 mmol, weighed in glove box), AuCl (LB-Phos) (0.0299 g, 0.05 mmol), and CHCl3 (5 mL) under nitrogen atmosphere sequentially. After stirring for 15 min, (R)-4-decalactone (0.2108 g, 1 mmol) and CHCl3 (5 mL) were added. After being continuously stirred at 25 °C for 3 h, the reaction was complete as monitored by thin layer chromatography (TLC). Filtration through a short column of silica gel [eluent: EtOAc (20 mL × 3)] and evaporation afforded a crude mixture of (S,E)-6a and (R,Z)-6a (S,E)/R,Z = 98:2 as determined by 1H NMR analysis] [silica gel (60–200 mesh, 10 g)] [eluent: petroleum ether (60–90 °C)/ethyl acetate = 15/1 (400 mL) to 10/1 (550 mL)] as an oil with pleasant flavor: 96% ee (HPLC conditions: Chiralcel OJ-H column, n-hexane/i-PrOH = 200:1, 1.0 mL/min, λ = 214 nm, tR (major) = 22.73 min, tR (minor) = 20.86 min; [α]D = +29.6 (c = 1.01, CHCl3).] 1H NMR (300 MHz, CDCl3) δ 5.81 (dt, J1 = 15.3 Hz, J2 = 7.2 Hz, 1H, =CH2), 5.49 (dd, J1 = 15.3, J2 = 7.2 Hz, 1H, =CH =CH), 4.90 (q, J = 7.2 Hz, 1H, CH2), 2.61–2.50 (m, 2H, CH2), 2.46–2.31 (m, 1H, one proton from CH2), 2.13–1.90 (m, 3H, CH3, one proton from CH3), 1.45–1.18 (m, 10H, CH2), 0.88 (t, J = 6.6 Hz, 3H, CH3); the following signals are discernible for (R,Z)-6a: δ 5.72–5.62 (m, 1H, =CH), 5.31–5.21 (m, 1H, =CH); 13C NMR (75 MHz, CDCl3) δ 177.0, 135.6, 127.2, 81.1, 32.0, 31.6, 5.99, 28.7, 28.8, 28.6, 28.61, 22.15, 14.0; IR (neat) ν (cm−1): 2955, 2925, 2855, 2778, 1673, 1459, 1415, 1378, 1327, 1296, 1216, 1177, 1123, 1010; GC-MS (GC condition: injector: 280 °C; column: DB5 column 30 m × 0.25 mm, temperature programming: 60 °C (2 min), 20 °C/min to 280 °C, 280 °C (30 min); detector: 280 °C) (70 ev, El) m/z (%): for (S,E)-6a: tR (major) = 5.83 min: 210 (M+, 23.1), 111 (100); for (R,Z)-6a: tR (minor) = 5.76 min: 210 (M+, 0.75), 111 (100). HRMS calcld for C13H19O2 [M+]: 210.1620, found: 210.1624.

Data availability. All data that support the findings of this study are available in the online version of this paper in the accompanying Supplementary Methods (including experimental procedures, compound characterization data).

The X-ray crystallographic coordinates for structure of AuCl(LB-Phos) reported in this study has been deposited at the Cambridge Crystallographic Data Centre (CCDC), under deposition number CCDC 1558142. This data can be obtained free
of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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Author contributions

S.M. directed the research and developed the concept of the reaction with J.Z., who also performed the experiments and prepared the Supplementary Materials. J.Z., C.F., and S.M. checked the experimental data. J.Z. and S.M. wrote the manuscript with contributions from the other authors.

Additional information

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