Nickel(0)-catalyzed divergent reactions of silacyclobutanes with internal alkynes

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Transition metal-catalyzed reactions of silacyclobutanes with a variety of π units have attracted much attention and become one of the most straightforward and efficient approaches to rapidly access structurally diverse organosilicon compounds. However, the reaction of silacyclobutanes with alkynes still suffers from some limitations: (1) internal alkynes remain challenging substrates; (2) expensive Pd- or Rh-based catalysts have been employed in all existing systems; (3) controlling chemodivergence has not yet been realized. Herein we realize Ni-catalyzed chemodivergent reactions of silacyclobutanes with alkynes. In comparison with the previous Pd or Rh catalytic systems, our Ni-catalytic system features: 1) complementary substrate scope; 2) ligand-controlled chemodivergence; 3) low cost. The ligand precisely dictates the pathway selectivity, leading to the divergent formation of (benzo)silacyclohexenes and allyl vinylsilanes. Moreover, we demonstrate that employment of a chiral phosphine ligand is capable of forming silicon-stereogenic allyl vinylsilanes in high yields and enantioselectivities. In addition, DFT calculation is performed to elucidate the origin of the switchable selectivities, which is mainly attributed to different ligand steric effects.

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The discovery of general and efficient methodologies to approach silicon-containing organic compounds, including chiral silicons, has attracted great interest. Because these molecules are fundamentally important with a multitude of applications ranging from organic synthesis, materials science to medicinal chemistry. Sila-substitution often leads to the improvement of the potency and ADMET properties of drug-like candidates.

Silacyclobutanes (SCBs), which was first synthesized by Kipping, has proven to possess unique reactivity and served as synthetic linchpin to rapidly access a variety of organosilicon compounds. For example, low valent transition metals can facilely insert into the SCBs to form 5-membered silametallacycles, which is capable of undergoing the migratory insertion of a variety of π units into the M–Si bonds, cultivated in various fascinating transition metal-catalyzed reactions. Within this context, in 1975, Sakurai and Imai realized the first cycloaddition of the SCBs with alkynyl carboxylates or phenylacetylene by use of Pd-catalytic system, but giving the mixture of silacyclohexenes and allyl vinylsilanes, which severely hampers their practical applications. In 2012, Shintani et al. made an important breakthrough in the cycloaddition of the SCBs with alkynyl carboxylates. They disclosed that a palladium catalyst coordinated with a sterically demanding chiral phosphoramidite ligand could facilitate the reductive elimination step to highly chemoselective and enantioselective formation of the enantioenriched silicon-stereogenic silacyclohexenes. Unfortunately, less electron-deficient alkynes such as phenylacetylenes and diphenylacetylenes are clearly incompatible.

Until recently, Song and Xu independently have achieved the first highly efficient and chemoselective cycloaddition of the SCBs with alkynes to produce the silacyclohexenes by employment of Rh-catalyzed condition. Moreover, Song et al. further proved that the use of chiral phosphoramidite ligand during the reaction is capable of inducing moderate to good enantioselectivity at the stereogenic silicon center. Despite significant advances, the reaction still suffers from some limitations to date: (1) SCBs have not been shown to react with unactivated internal alkynes such as diarylacetylenes in an intermolecular manner; (2) expensive Pd- or Rh-based catalysts have been employed in all existing systems; (3) the steering of the reaction pathway exclusively toward chemoselective and enantioselective formation of allyl vinylsilanes has not yet been realized. Because Ni is smaller and more nucleophilic than Pd and Rh, nickel-based catalysts are generally more active than the corresponding complexes of palladium and rhodium at activating internal alkynes and cleaving the C–Si bond on SCBs. At the same time, nickel-based catalysts have not been shown to react with unactivated internal alkynes such as diarylacetylenes in an intermolecular manner.

Fig. 1 Research background and our work on the reaction of SCBs and benzosilacyclobutenes with alkynes. a Pd or Rh-catalyzed reaction of SCBs with alkynes in literature. b This work for Ni-catalyzed divergent reactions of SCBs with alkynes. c Medicinally relevant molecules possessing vicinal-diaryl structures. The potential "C/Si switch" site in those vicinal-diaryl structures has been highlighted by pink ball.
same time, β-H elimination is often more facile at Ni-center in comparison to Pd or Rh-centers. We questioned whether Ni(0) catalyst is capable of facilitating the reaction of SCBs with unactivated internal alkynes and simultaneously controlling the pathway selectivity in combination of proper ligands to selective formation of either the reductive elimination or β-H elimination product (Fig. 1b), thus further broadening the utility of this process in modular assembly of diverse silicon-containing scaffolds such as an array of vicinal-diaryl substituted silacyclohexenes and allyl-tethered vinylsilanes, which are difficult to be synthesized by the other methods. It is worthy to note that vicinal-diaryl structures with/without chiral centers are a common scaffold in numerous marketed drugs as shown in Fig. 1c. Considering the importance of "C/Si switch" for the development of new materials, drugs and pesticides, introduction of silyl moieties into 1,2-diaryl structures is of great significance and highly desired.

We herein disclose Ni-catalyzed ligand-controlled chemodivergent reactions of SCBs with alkynes. In comparison with the previous Pd or Rh catalytic systems, our Ni-catalytic system features: (1) complementary substrate scope; (2) ligand-controlled chemodivergence; (3) low cost. In our system, by use of a sterically hindered NHC ligand to highly-efficient suppress β-H elimination, SCBs undergo ring expansion to exclusively provide silacycles. In contrast, phosphine ligands permit the β-H elimination step to afford allyl vinylsilanes. Moreover, we further demonstrate that employment of a chiral phosphine ligand is capable of the asymmetric induction of the ring-opening reaction of SCBs and internal alkynes, forming silicon-stereogenic allyl vinylsilanes in high yields and enantioselectivities. Additionally, we find that [4 + 2] annulation of benzosilacyclobutanes with internal alkynes also proceeds regioselectively through Si−C(sp²) bond cleavage to produce an array of dihydrobenzo[c]silines by choice of proper ligands.

**Results and discussion**

**Condition screening.** We started our investigations by using SCB 1a and diphenyl acetylene 2a as the model substrates under the Pd- or Rh-catalyzed methods developed for the cycloaddition of SCBs with terminal alkynes; however, these conditions were found to be unreactive (Table 1, entries 1–2). To our delight, the reaction of 1a and 2a occurred smoothly in the presence of Ni(cod)₂ (10 mol%) and PCy₃ (20 mol%), yielding a mixture of silacycloclohexene 3aa and allyl vinylsilane 4aa in a 6:61 ratio (Entry 3). A large panel of ligands were then screened (see Supplementary Table 1). Finally, we found that the β-H elimination product 4aa was exclusively obtained in 83% yield by use of small phosphate PMe₃ as the ligand (Entry 5). In contrast, the reaction performed with commercially available NHC ligand IMes·HCl (1,3-dimesityl-4,5-dimethyl-1H-imidazol-3-ium chloride) resulted in exclusive formation of silacycle 3aa under identical reaction conditions (Entry 8). The best results for producing 3aa (84% isolated yield) were found in the presence of 20 mol% 1Pr-HCl (1,3-bis(2,6-didiisopropylphenyl)imidazolium chloride) with incorporation of 20 mol% LiO'Bu at 120 °C (Entry 10).

**Substrate scope for cycloaddition of SCBs with alkynes.** With this optimized protocol, we first investigated the substrate scope and functional group tolerance of the Ni-catalyzed ring expansion of SCBs with internal alkynes (Table 2). It is pleased that the reaction of SCB 1a and a wide variety of symmetric mono-substituted or multisubstituted diaryl alkynes afforded the desired products in good yields with nearly neglectable electronic and steric effects of substituents (3ab–an). Heteroaryl-substituted alkyne was also well tolerated (3ao). Importantly, this catalyst system is remarkably tolerant of various functional groups on the alkynyl ring of diaryl alkynes, such as F, CF₃, COOEt, and OMe groups. Additionally, various aliphatic internal alkynes are also well compatible with the established condition, enabling approach to the six-membered silacyclic products (3bp–br). In addition, various allylic internal alkynes were found in the presence of 20 mol% IPr·HCl (1,3-bis(2,6-diisopropylphenyl)imidazolium chloride) with incorporation of 20 mol% LiO'Bu at 120 °C (Entry 10).

### Table 1 Condition optimizationa.

| Entry | [M] cat. | Ligand | 3aa[%]b | 4aa[%]b | Entry | [M] cat. | Ligand | 3aa[%]b | 4aa[%]b |
|-------|---------|--------|---------|---------|-------|---------|--------|---------|---------|
| 1     | Pd(OAc)₂ | PMe₃   | 0       | 0       | 1     | Ni(cod)₂ | Xantphos | 6       | 74      |
| 2     | Rh(PPh₃)Cl | -      | 0       | 0       | 2     | Ni(cod)₂ | DPPB    | 0       | 0       |
| 3     | Ni(cod)₂ | PCy₃   | 6       | 61      | 3     | Ni(cod)₂ | IMes·HCl | 72      | 0       |
| 4     | Ni(cod)₂ | PPh₃   | 6       | 94      | 4     | Ni(cod)₂ | IrPr-HCl | 80      | 0       |
| 5     | Ni(cod)₂ | PMe₃   | trace   | 86 (83) | 5     | Ni(cod)₂ | IrPr-HCl | 85 (84) | 0       |

a[M] Catalyst (0.01 mmol), ligand (0.02 mmol), 1a (0.3 mmol), and 2a (0.1 mmol) in toluene for 24 h at 100 °C.
b20 mol% LiO'Bu as additive.
c120 °C for 24 h.
dYields were determined by ³H NMR analysis using CH₂Br₂ as the internal standard, and values in parentheses indicate the isolated yield.
led exclusively to the corresponding silacycles 3bw and 3bx in moderate yields (63% yield for 3bw and 55% yield for 3bx) and complete regioselectivity (rr > 20:1 for both 3bw and 3bx). However, terminal alkynes, such as phenylacetylene or 1-hexyne, which worked well with SCBs in previous Rh-catalyzed conditions, failed to participate in the reaction due to rapid self-oligomerization of the alkynes under the Ni-catalyzed condition. Then, the scope of SCBs with diverse substituents on silicon was expanded by the high efficiency and selectivity for the ring-opening reaction of SCBs with internal alkynes achieved that uses Ni catalysis in combination with phosphine ligand for the formation of allyl vinylsilanes 4, we attempt to develop an asymmetric version for enantioselective construction of highly enantioenriched silicon-stereogenic allylsilanes. We performed the evaluation of a variety of different chiral P-ligands by use of SCB 1b and diphenyl acetylene 2a as the model substrates in the presence of Ni(cod)$_2$ (10 mol%) in toluene at 100 °C for 24 h. Values represent isolated yields.

Table 2 Substrate scope for cycloaddition of SCBs with alkynes.

| Entry | Substrate | Yield (%) | ee (%) |
|-------|-----------|-----------|--------|
| 3a    | Ph        | 74%       |        |
| 3b    | Ph        | 60%       |        |
| 3c    | Ph        | 55%       |        |
| 3d    | Ph        | 70%       |        |
| 3e    | Ph        | 50%       |        |
| 3f    | Ph        | 75%       |        |
| 3g    | Ph        | 77%       |        |
| 3h    | Ph        | 85%       |        |
| 3i    | Ph        | 90%       |        |
| 3j    | Ph        | 82%       |        |
| 3k    | Ph        | 62%       |        |
| 3l    | Ph        | 70%       |        |
| 3m    | Ph        | 85%       |        |
| 3n    | Ph        | 73%       |        |
| 3o    | Ph        | 75%       |        |
| 3p    | Ph        | 70%       |        |
| 3q    | Ph        | 73%       |        |
| 3r    | Ph        | 55%       |        |
| 3s    | Ph        | 11%       |        |
| 3t    | Ph        | 10%       |        |
| 3u    | Ph        | 90%       |        |
| 3v    | Ph        | 85%       |        |
| 3w    | Ph        | 70%       |        |
| 3x    | Ph        | 70%       |        |
| 3y    | Ph        | 75%       |        |
| 3z    | Ph        | 85%       |        |

**Ring-opening reaction of SCBs with internal alkynes.** Encouraged by the high efficiency and selectivity for the ring-opening reaction of SCBs with internal alkynes achieved that uses Ni catalysis in combination with phosphine ligand for the formation of allyl vinylsilanes 4, we attempt to develop an asymmetric version for enantioselective construction of highly enantioenriched silicon-stereogenic allylsilanes. We performed the evaluation of a variety of different chiral P-ligands by use of SCB 1b and diphenyl acetylene 2a as the model substrates in the presence of Ni(cod)$_2$ (10 mol%) in toluene at 100 °C for 24 h. Values represent isolated yields.

| Entry | Substrate | Yield (%) | ee (%) |
|-------|-----------|-----------|--------|
| 4a    | Ph        | 74%       |        |
| 4b    | Ph        | 60%       |        |
| 4c    | Ph        | 55%       |        |
| 4d    | Ph        | 70%       |        |
| 4e    | Ph        | 50%       |        |
| 4f    | Ph        | 75%       |        |
| 4g    | Ph        | 77%       |        |
| 4h    | Ph        | 85%       |        |
| 4i    | Ph        | 90%       |        |
| 4j    | Ph        | 82%       |        |
| 4k    | Ph        | 62%       |        |
| 4l    | Ph        | 70%       |        |
| 4m    | Ph        | 85%       |        |
| 4n    | Ph        | 73%       |        |
| 4o    | Ph        | 75%       |        |
| 4p    | Ph        | 70%       |        |
| 4q    | Ph        | 73%       |        |
| 4r    | Ph        | 55%       |        |
| 4s    | Ph        | 11%       |        |
| 4t    | Ph        | 10%       |        |
| 4u    | Ph        | 90%       |        |
| 4v    | Ph        | 85%       |        |
| 4w    | Ph        | 70%       |        |
| 4x    | Ph        | 70%       |        |
| 4y    | Ph        | 75%       |        |
| 4z    | Ph        | 85%       |        |

**Table 2 Substrate scope for cycloaddition of SCBs with alkynes.**

| Entry | Substrate | Yield (%) | ee (%) |
|-------|-----------|-----------|--------|
| 3a    | Ph        | 74%       |        |
| 3b    | Ph        | 60%       |        |
| 3c    | Ph        | 55%       |        |
| 3d    | Ph        | 70%       |        |
| 3e    | Ph        | 50%       |        |
| 3f    | Ph        | 75%       |        |
| 3g    | Ph        | 77%       |        |
| 3h    | Ph        | 85%       |        |
| 3i    | Ph        | 90%       |        |
| 3j    | Ph        | 82%       |        |
| 3k    | Ph        | 62%       |        |
| 3l    | Ph        | 70%       |        |
| 3m    | Ph        | 85%       |        |
| 3n    | Ph        | 73%       |        |
| 3o    | Ph        | 75%       |        |
| 3p    | Ph        | 70%       |        |
| 3q    | Ph        | 73%       |        |
| 3r    | Ph        | 55%       |        |
| 3s    | Ph        | 11%       |        |
| 3t    | Ph        | 10%       |        |
| 3u    | Ph        | 90%       |        |
| 3v    | Ph        | 85%       |        |
| 3w    | Ph        | 70%       |        |
| 3x    | Ph        | 70%       |        |
| 3y    | Ph        | 75%       |        |
| 3z    | Ph        | 85%       |        |
electron-neutral, electron-deficient, and electron-rich substituents on different positions of the phenyl ring were compatible with the current reaction, enabling access to silicon stereogenic allyl vinylsilanes in 40 to 92% yield and 91:9 er to 96:4 er (4ca–co). Symmetrical aliphatic alkyne reacted with SCB 1q to furnish the desired product 4cp in 85% yield with moderate enantiomeric ratio (74:26 er for 4cp). In addition, unsymmetrical internal alkynes such as 1-phenylpropyne were inert. Then, a number of SCBs bearing diverse substituents on silicon were tested using 2-phenylpropyne was inert. Then, a number of SCBs bearing diverse substituents on silicon were tested using 2-phenylpropyne as the alkyne (0.1 mmol) in toluene (0.1 M) at 100 °C for 24 h.

Table 3 Condition optimization for asymmetric ring-opening reaction of SCBs with alkyne 2a.

| Entry | L*       | Yield (%)<sup>b</sup> | er<sup>c</sup> | Entry | L*       | Yield (%)<sup>b</sup> | er<sup>c</sup> | Entry | L*       | Yield (%)<sup>b</sup> | er<sup>c</sup> |
|-------|----------|------------------------|---------------|-------|----------|------------------------|---------------|-------|----------|------------------------|---------------|
| 1     | L1-9     | n.r.                   | -             | 9     | L18      | 22                      | 78:22         | 17    | L26      | 39                      | 80:20         |
| 2     | L10      | 70                     | 60:40         | 10    | L19      | 18                      | 60:40         | 18    | L27      | <5                      | 86:14         |
| 3     | L11      | 55                     | 50:50         | 11    | L20      | 90                      | 85:15         | 19    | L28      | 18                      | 87.5:13.5     |
| 4     | L12      | 37                     | 72:28         | 12    | L21      | 75                      | 82:18         | 20    | L29      | 80                      | 88:12         |
| 5     | L13      | 40                     | 80:20         | 13    | L22      | 80                      | 71:19         | 21<sup>d</sup> | L20      | 88                      | 89.5:11.5     |
| 6     | L14      | n.r.                   | -             | 14    | L23      | 65                      | 81:19         | 22<sup>e</sup> | L20      | 40                      | 90:10         |
| 7     | L15      | 10                     | 78:22         | 15    | L24      | <5                      | 93.5:6.5      | 23<sup>d</sup> | L20      | 90                      | 95:5:4.5      |
| 8     | L16-17   | 37                     | 50:50         | 16    | L25      | n.r.                   | -             | 24<sup>d</sup>,<sup>f</sup> | L20      | 92                      | 96:4          |

<sup>a</sup>Reactions were performed by use of Ni(cod)<sub>2</sub> (10 mol%), chiral ligand (L*: 10 mol%), 1b (0.2 mmol) and 2a (0.1 mmol) in toluene (0.1 M) at 100 °C for 24 h.

<sup>b</sup>Isolated yield is given.

<sup>c</sup>The enantiomeric ratio (er) was determined by chiral HPLC on commercial columns.

<sup>d</sup>40 °C for 24 h.

<sup>e</sup>*n.r.*

<sup>f</sup>-MeTHF was used as the solvent.

*SCBs by other alkyl groups such as ethyl, i-propyl, and cyclopropyl did not significantly affect the reaction efficiency and enantioselectivity, offering an array of chiral silicon-stereogenic allyl vinylsilanes (4ja–oa) in a 35–85% yield and 90:10 er to 92.5:7.5 er. Notably, as the products 4 are liquid, a chiroptical method was employed to determine the absolute configuration of the product 4cb.

The computational electronic circular dichroism (ECD) spectra for 4cb
calculated by time-dependent density functional theory (DFT) is well-matched with the experimental ECD spectra (see Supplementary Figs. 1–3). Thus 4cb was assigned to be S-configured.

**Cycloaddition of benzosilacyclobutenes with internal alkynes.** Following the success in Ni-catalyzed ligand-controlled divergent reaction of SCBs with internal alkynes, we proceeded to perform the reaction of benzosilacyclobutene 5a with diphenylacetylene 2a to try to further extend the practical application of this Ni-
Table 4 Substrate scope for enantioselective synthesis of silicon-stereogenic allyl vinylsilanes 4a.

| Internal alkynes | Silacyclobutanes |
|------------------|------------------|
| 4ca, R = Me, 91%, 96:4 er | 4a, R = Et, 85%, 90:10 er |
| 4cb, R = Me, 91%, 96:4 er | 4a, R = Et, 85%, 90:10 er |
| 4cc, R = Pr, 80%, 95:5 er | 4a, R = Et, 85%, 90:10 er |
| 4cd, R = Bu, 75%, 95:5:4.5 er | 4a, R = Et, 85%, 90:10 er |
| 4ce, R = OMe, 82%, 95:5 er | 4a, R = Et, 85%, 90:10 er |
| 4cf, R = NMe2, 40%, 95:5 er | 4a, R = Et, 85%, 90:10 er |
| 4cg, R = SMe, 70%, 95:5 er | 4a, R = Et, 85%, 90:10 er |
| 4ch, R = F, 86%, 95:5 er | 4a, R = Et, 85%, 90:10 er |

*Internal alkynes 2 (0.04 mmol), SCB 1 (0.4 mmol), Ni(cod)2 (0.02 mmol), L20 (0.04 mmol) in 2-MeTHF at 60 °C for 24 h. Values represent isolated yields. The er value was determined by chiral HPLC.

catalytic system in silacycle synthesis even the reaction of benzosilacyclobutenes with unactivated internal alkynes has also never been presented (Fig. 2a). Unfortunately, the reaction afforded a mixture of two components, 6aa and 6aa”, in a 55:45 ratio with full version under the optimized ring expansion reaction conditions due to the competitive Si−C(sp3) bond and Si−C(sp2) bond cleavage of 5a. The formation of 6aa” is likely attributed to the competitive migratory insertion of alkyne into the Ni−C bond, followed by an alkene isomerization and sequential regressive elimination42,43. To improve the regioselectivity in Si−C bond cleavage of benzosilacyclobutene 5a, we further screened a large set of reaction parameters, such as ligands, solvents and temperatures (Supplementary Table 2). Finally, we found that employing PMe3 as the ligand and 1,4-dioxane as the solvent resulted in a strong preference for Si−C(sp2) bond cleavage to afford 6aa in 86% yield. We next examined the substrate scope for the cycloaddition of benzosilacyclobutenes 5 with internal alkynes 2 to approach diverse dihydrobenzo[c]silines 6 under the modified conditions (Fig. 2, lower panel). Various diaryl alkynes bearing substituents at the meta- or para-position of the phenyl ring proceeded smoothly to afford the desired silacycles in satisfactory yields (6ab–ai). Again, our method could also be applied in dialkyl alkynes without any drop in yields (6bj–bk). Moderate regioselectivities of 1.9:1 to 6:1 were observed for the unsymmetrical internal alkynes (6bl–bn). Furthermore, we studied the benzosilacyclobutenes 5 for this reaction. To our delight, benzosilacyclobutenes containing different groups on silicon could be utilized to react with 1a by employing PAd3 as the ligand, providing cyclic products 6bj–bm and 6ba–ca in good yields and selectivities. Finally, we proved that the high yield and selectivity was unaffected by installation of diverse substituents at different positions of the phenyl ring on benzosilacyclobutenes (6da–ha).

**Synthetic utility.** To demonstrate the practicality of our method, we first scaled up the Ni-catalyzed cycloaddition reaction of SCB 1a with 2a as well as the enantioselective ring opening reaction of
SCB 1c with 2a to obtain 0.6 g of 3aa in 73% yield and ~1 g of 4ca in 85% yield with 92% ee, respectively (Fig. 3a, b). Furthermore, we demonstrated the synthetic usefulness of the 6-membered silacycle 3aa and the enantioenriched silicon-stereogenic allyloxy-silane 4ca by carrying out several additional downstream transformations. The C=−C bond of 3aa can be easily reduced by hydrogen in the presence of Pd/C catalyst to deliver compound 7 in 85% yield. Moreover, 3aa could also undergo the epoxidation reaction at room temperature in the presence of m-CPBA oxidant to afford epoxide 8 in 77% yield. Additionally, the product 4ca was treated with Schwartz’s reagent, followed by molecular iodine to deliver the corresponding primary iodide 9 in 90% yield with retention of the enantioselectivity. We further demonstrated that product 4ca can be converted to vicinal diol 10 with a 1:1 dr through a diboration/oxidation sequence. Hydroboration of the terminal C=−C bond on 4ca also proceeded smoothly to yield borylated vinylsilane 11 in 85% yield in the presence of AlEt3. The 4ca could also smoothly undergo hydrogenation as well as hydroboration-oxidation to yield and product 12 in 90% yield with 92% ee and 1:2:1 dr and enantioenriched silicon-stereogenic hydroxyl-functionalized vinylsilane 13 with 73% yield and 92% ee.

Mechanistic studies. To probe the reaction mechanism, several mechanistically insightful experiments were carried out (Fig. 4a). When we mixed 1,2-bis(3-fluorophenyl)ethyne with 1.0 equiv. of Ni(cod)₂ in the presence of 2.0 equiv. of Ni(cod)₂ in the presence of 2.0 equiv. IMes·HCl and LiO-Bu in toluene-d₈ for 1 h at 60 °C, signal splitting of the F atom occurred (see Supplementary Fig. 4). The addition of diphenyl acetylene to Ni(PPh₃)₄ resulted in the appearance of a new 3¹P NMR peak at δ = 39.84 ppm (see Supplementary Fig. 5). These results supported the existence of a nickel(0)-alkyne complex. In addition, there was no deuterium incorporation of 4aa in the Ni-catalyzed ring opening reaction of 1a and 2a in the presence of 5.0 equiv. of CD₃OD. It strongly implies that the ring opening reaction under the optimized condition most likely involved an intramolecular hydrogen shift process. Following our experimental observation

### Table

| Entry | Ligand | Solvent | Yield of 6aa | Yield of 6aa | Yield of 6aa |
|-------|--------|---------|--------------|--------------|--------------|
| 1     | IPr    | toluene | 55%          | 0            | 45%          |
| 2     | PMe₃   | toluene | 90%          | 10%          | 0            |
| 3     | PMe₃   | dioxane | 95% (86%)    | 0            | 5%           |

* The isolated yield was given in parentheses.
and the previous studies, we proposed a plausible mechanism to rationalize the ligand-controlled structure divergence in the Ni-catalyzed reaction of SCBs with unactivated internal alkynes (Fig. 4b). It begins with coordination of Ni0 to internal alkynes, thereby forming nickel(0)-alkyne complex A, which is followed by coordination-assisted oxidative cleavage of Si−C(sp3) on SCBs, thus producing Ni-silacycloheptene B. Ni-silacycloheptene B could smoothly undergo either reductive elimination to afford cyclic products 3 or β-hydride elimination to deliver allyl vinylsilanes 4. To unveil the origins of the ligand-controlled structure divergence in the Ni-catalyzed reaction of SCBs with unactivated internal alkynes, computational studies for the reaction of 1a and 2a were carried out by DFT44,45. As shown in Fig. 4c and Supplementary Fig. 6, the computed profiles disclosed that the reductive elimination of the intermediate B leads to the ring expansion product 3aa via a three-membered ring transition state TSRE and the β-H elimination from the intermediate B to form the ring opening product 4aa undergoes a ligand-to-ligand H transfer (LLHT) process via transition state TSLLHT. In a good agreement with experiments, the computed transition states clearly predict that IPr and PMe3 as the ligands favor the generation of 3aa and 4aa respectively with significant kinetic differentiation (7.1 kcal/mol for IPr-TSRE vs. IPr-TSLLHT and 2.7 kcal/mol for P2-TSRE vs. P-TSLLHT)46. Importantly, it is implicated by computations that a major difference between the competing TSs lies in the steric environment around the Ni center. The extra ligations of a hydride group and a partially formed C=C unit in TSLLHT render the first coordination sphere more crowded than that in TSRE. The latter only involves a relatively small three-membered-ring Ni–C–C array which is largely compatible with even the larger IPr ligand. These observations led us to question whether a steric control of reactivity is operative.

To clarify our hypothesis on the steric control of reactivity, a visual analysis of non-covalent interactions for transition state IPr-TSRE and IPr-TSLLHT was performed. It reveals that IPr-TSLLHT contains appreciable ligand-substrate steric repulsions while the competing IPr-TSRE mainly shows attractive dispersions (Fig. 5a). Evaluation of ligand distortion energies also suggests higher ligand deformations in the more congested LLHT pathway if using IPr as the ligand (Fig. 5b; $E_{\text{dist},L}$ for IPr-TSLLHT = 5.2 kcal/mol, $E_{\text{dist},L}$ for IPr-TSRE = 3.5 kcal/mol). By contrast, the repulsions can be circumvented by use of a small PMe3 ligand, as reflected by the almost ignorable ligand distortion energies ($\leq 0.5$ kcal/mol in both P2-TSRE and P-TSLLHT) and the occurrence of no repulsive atomic distances. We postulate that the LLHT pathway is plausibly intrinsically preferred against reductive elimination to form the ring opening product in this Ni-catalyzed reaction of SCBs with alkynes, which becomes a reality when small PMe3 ligand was used. However, the use of...
**Fig. 4** Mechanistic studies for this Ni-catalyzed divergent reactions of SCBs with alkynes. **a** Control experiments. **b** Plausible mechanism. **c** DFT investigation about mechanistic origin of the ligand-controlled structure divergence in the Ni-catalyzed reaction of SCB 1a with 2a. Free energies are shown in kcal/mol, distances in Å. Ni-silacycloheptene species was used as energy zero.

**Fig. 5** Ligand steric effects on divergent cycloaddition. **a** Visual analysis of non-covalent interactions. **b** Ligand distortion energies. **c** The reaction of SCB 1a with 2a by use of a much less sterically hindered NHC ligand. Free energies are shown in kcal/mol, distances in Å.
large sterically hindered IPr ligand in the reaction would lead to significantly destabilizing distortions of TS\textsubscript{LLHT}. It will steer the reaction pathway toward reductive elimination via a less crowded TS\textsubscript{RE} to afford the cycloaddition product. To provide experimental support for our standpoint, the reaction of SCB 1a with 2a was carried out in the presence of a much less sterically hindered NHC precursor 1,3-dimethyl-3-imidazolidine iodide (IMe-HI; Fig. 5c). The reaction unsurprisingly in turn favors LLHT pathway to obtain a high ratio between the ring opening product 4aa and ring expansion product 3aa (86:14). Notably, we have also carried out the computational studies to investigate the reaction pathway of the Ni-catalyzed cycloaddition of benzosila-
cyclobutenes 5 with internal alkynes 2 (see Supplementary Figs. 7 and 8). Those results are consistent with the experimental observations.

In summary, we have disclosed nickel-catalyzed reaction of (benzo)silacyclobutanes with alkynes. The choice of different ligands dictates whether the pathway involves cycloaddition or ring-opening. Moreover, by using a TADDOL-derived chiral phosphonite ligand, we achieved the high enantioselective ring-
opening reaction of SCBs with alkynes thereby constituting an efficient and general route for asymmetric synthesis of silicon-
stereogenic allyl vinylsilanes. The origins of the switchable selectivities were elucidated by DFT calculation. The results indicate that the two pathways share a Ni-silacycloheptene intermediate. IPr ligand promotes direct reductive elimination via a three-membered ring transition state from this intermediate to
afford an array of (benzo)silacyclohexenes. Alternatively, small PMe\textsubscript{3} ligand enables ring-opening via a LLHT process from Ni-
silacycloheptene to generate diverse allyl vinylsilanes. 

Methods

General procedure for Ni-catalyzed cycloaddition of silacyclobutanes with internal alkynes. In a glovebox, an oven-dried screw-capped 8 ml glass vial equipped with a magnetic stir bar was charged with Ni(cod)\textsubscript{2} (5.8 mg, 0.02 mmol), 1.0 ml 2-MeTHF, and the mixture was stirred at room temperature for 1 h. Then, rotary evaporation, and the residue was subjected to silica gel column chromatography. The volatile fraction, R, was subjected to preparative RP-HPLC with an Bonna-Agela CHEETAH HP series.

Data availability

The authors declare that the data supporting the findings of this study are available within the article and its Supplementary Information Files, and also are available from the corresponding author on request.

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References

1. Hiyama, T. & Oestreicher, M. Organosilicon Chemistry: Novel Approaches and Reactions (Wiley-VCH, 2019).

2. Oestreicher, M. Silicon-stereogenic silanes in asymmetric catalysis. Synlett 11, 1629–1643 (2007).

3. Xu, L.-W., Li, L., Lai, G.-Q. & Jiang, J.-X. The recent synthesis and application of silicon-stereogenic silanes: a renewed and significant challenge in asymmetric synthesis. Chem. Soc. Rev. 40, 1777–1790 (2011).

4. Xu, L.-W. Desymmetrization catalyzed by transition-metal complexes: enantioselective desymmetrization of silicon-stereogenic silanes. Angew. Chem. Int. Ed. 51, 12932–12934 (2012).

5. Cui, Y.-M., Lin, Y. & Xu, L.-W. Catalytic synthesis of chiral organoheteroatom compounds of silicon, phosphorus, and sulfur via asymmetric transition metal-catalyzed C–H functionalization. Coord. Chem. Rev. 330, 37–52 (2017).

6. Shintani, R. Catalytic asymmetric synthesis of silicon-stereogenic compounds by enantioselective desymmetrization of prochiral tetraorganosilanes. J. Synth. Org. Chem. Jpn. 76, 1163–1169 (2018).

7. Shintani, R. Recent progress in catalytic enantioselective desymmetrization of prochiral organosilanes for the synthesis of silicon-stereogenic compounds. Synlett 29, 388–396 (2018).

8. Diesel, F. & Cramer, N. Generation of heteroatom stereocenters by enantioselective C–H functionalization. ACS Catal. 9, 1916–1917 (2019).

9. Zhang, M. et al. Asymmetric synthesis of chiral organosilicon compounds via transition metal-catalyzed stereoselective C–H activation and silylation. Chem. Commun. 57, 8250–8263 (2021).

10. Ye, F., Xu, Z. & Xu, L.-W. The discovery of multifunctional chiral P ligands for the catalytic construction of quaternary carbon/silicon and multiple stereocenters. Acc. Chem. Res. 54, 452–470 (2021).

11. Jones, R. G., Ando, W. & Chojnowski, J. Silicon-Containing Polymers (Kluwer Academic Publishers, 2000).

12. Bairns, W. & Tacke, R. Silicon chemistry as a novel source of chemi-cal diversity in drug design. Curr. Opin. Drug. Discov. Dev. 6, 526–543 (2003).

13. Fukazawa, A. & Yamaguchi, S. Ladder n-conjugated materials containing main-group elements. Chem. Asian J. 4, 1386–1400 (2009).

14. Franz, A. K. & Wilson, S. O. Organosilicon Chemistry with Medicinal Applications. J. Med. Chem. 56, 388–405 (2013).

15. Zelisko, P. M. Bio-Inspired Silicon-Based Materials (Springer, 2014).

16. Ramesh, R. & Reddy, D. S. Quest for novel chemical entities through incorporation of silicon in drug scaffolds. J. Med. Chem. 61, 3779–3798 (2018).

17. Showell, G. A. & Mills, J. S. Chemistry challenges in lead optimization: silicon isosteres in drug discovery. Drug Discov. Today 8, 551–556 (2003).

18. Englebienne, P., Hoonacker, A. V. & Herst, C. V. The place of the bioisosteric sila-substitution in drug design. Drug Des. Rev. 2, 467–483 (2005).

19. Kipping, F. P. & Sands, J. E. XCIV. Organic derivatives of silicon. Part XXVI. Piperidines as an analytical reagent. J. Chem. Soc. 119, 848–850 (1921).

20. Kipping, F. P. CCC. Organic derivatives of silicon. Part XXVIII. Octaphenyldihexylsilocetane. J. Chem. Soc. 123, 2598–2603 (1923).

21. Kipping, F. P. CCCVIII. Organic derivatives of silicon. Part XXX. Complex silicyldrocarbons [SiPh\textsubscript{4}]. J. Chem. Soc. 125, 2291–2297 (1924).

22. Mu, Q. C., Chen, J., Xia, C. G. & Xu, L.-W. Synthesis of silacyclobutanes and their catalytic transformations enabled by transition-metal complexes. Coord. Chem. Rev. 374, 93–113 (2018).

23. Li, L., Zhang, Y., Gao, L. & Song, Z. L. Recent advances in Si–C bond activation via a direct transition metal insertion. Tetrahedron Lett. 56, 1466–1473 (2015).

24. Zhang, Q.-W. et al. Construction of chiral tetraorganosilicones by tandem desymmetrization of silacyclobutanes/intermolecular dehydrogenative silylation. Angew. Chem. Int. Ed. 56, 1125–1129 (2017).

25. Chen, H. et al. Rhodium-catalyzed reaction of silacyclobutanes with unactivated alkynes to afford silacyclohexenes. Angew. Chem. Int. Ed. 58, 4695–4699 (2019).

26. Wang, X.-R. et al. Controllable Si–C bond activation enables stereocenter in the palladium-catalyzed [4+2] annihilation of cyclopropanes with benzosilacyclobutenes. Angew. Chem. Int. Ed. 59, 790–797 (2020).

27. Sakurai, H. & Imai, T. Novel [r+n] cycladdition of silacyclobutanes with acetylenes catalyzed by palladium complexes. Chem. Lett. 4, 891–894 (1975).

28. Takeyama, Y., Nozaki, K., Matsumoto, K., Oshima, K. & Utimoto, K. Palladium catalyzed reaction of silacyclobutanes with acetylenes. Bull. Chem. Soc. Jpn. 64, 1461–1466 (1991).

29. Shintani, R., Moriya, K. & Hayashi, T. Palladium-Catalyzed desymmetrization of silacyclobutanes with alkynes: enantioselective synthesis of silicon-stereogenic 1-Sila-2-cyclohexenes and mechanistic considerations. Org. Lett. 14, 2902–2905 (2012).

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30. Wang, X. et al. Multifunctional P-ligand-controlled "silicon-centered" selectivity in Rh/Cu-catalyzed Si–C bond cleavage of silacyclobutanes. Org. Chem. Front. 8, 6577–6584 (2021).

31. Liu, W. & Kong, W. Ni-Catalyzed stereoselective difunctionalization of alkenes. Org. Chem. Front. 7, 3941–3955 (2020).

32. Nakao, Y. Hydroarylation of alkenes catalyzed by nickel. Chem. Rec. 11, 242–251 (2011).

33. Moslin, R. M., Miller-Moslin, K. & Jamison, T. F. Regioselectivity and enantioselectivity in nickel-catalysed reductive coupling reactions of alkenes. Chem. Commun. 2007, 4441–4449 (2007).

34. Jackson, E. P. et al. Mechanistic basis for regioselection and regiodivergence in nickel catalyzed reductive couplings. Acc. Chem. Res. 48, 1736–1745 (2015).

35. Tasker, S. Z., Standley, E. A. & Jamison, T. F. Recent advances in homogeneous nickel catalysis. Nature 509, 299–309 (2014).

36. Hirano, K., Yorimitsu, H. & Oshima, K. Nickel-catalysed reactions with trialkylboranes and silacyclobutanes. Chem. Commun. 44, 3234–3241 (2015).

37. Hirano, K., Yorimitsu, H. & Oshima, K. Nickel-catalyzed regio- and stereoselective silylation of terminal alkenes with silacyclobutanes: facile access to vinylsilanes from alkenes. J. Am. Chem. Soc. 129, 6094–6095 (2007).

38. Hirano, K., Yorimitsu, H. & Oshima, K. Nickel-catalyzed reactions of silacyclobutanes with aldehydes: ring opening and ring expansion reaction. Org. Lett. 8, 483–485 (2006).

39. Zhang, J., Yan, N., Ju, C.-W. & Zhao, D. Nickel(0)-catalyzed asymmetric ring expansion toward enantioenriched silicon-stereogenic benzosilolones. Angew. Chem. Int. Ed. 60, 25723–25728 (2021).

40. Tartaglia, S., Padula, D., Scafato, P., Chiumento, L. & Rosini, C. A chemical/computational approach to the determination of absolute configuration of flexible and transparent molecules: aliphatic diols as a case study. J. Org. Chem. 73, 4865–4873 (2008).

41. Polavarapu, P. L., Nafe, L. A. & Berova, N. Special issue "Advances in Chiroptical Methods". Chirality 21, E2–E3 (2009).

42. Liu, S. et al. Layered chirality relay model in Rh(I)-mediated enantioselective C–Si bond activation: a theoretical study. Org. Lett. 22, 2124–2128 (2020).

43. Zhang, J. et al. Palladium-catalyzed desymmetrization of silacyclobutanes with alkenes to silicon-stereogenic silanes: a DFT study. Chem. Asian J. 11, 2867–2875 (2016).

44. Gaussian 16, Revision A.03 (Gaussian, Inc.) (see Supplementary Information for full reference).

45. All DFT mechanistic studies were carried out at the level of (SMD-1)PBE0-D3(BJ)/def2-TZVP/M06-L/def2-SV(P) with quasi-harmonic corrections. References and full computational procedure are provided in the SI.

46. DFT calculations indicate that the P2-TSRe possesses higher energy of 21.3 kcal/mol than that of the P2e-monocoordinated reductive elimination transition state (P2-TSRe) (see Supplementary Fig. 6).

47. Visual analysis of non-covalent interactions was performed using the independent gradient model implemented in the Multiwfn program (see Supplementary Information for references).

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X.-C.W. and C.-W.J. carried out the experiments. B.L. performed the DFT calculation. D.Z. conceived the concept, directed the project and wrote the paper.

Competing interests
The authors declare no competing interests.

Additional information
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