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Umpolung α -Silylation of Cyclopropyl Acetates via Low-Temperature Catalytic C–C Activation

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Abstract

We report a redox-neutral, catalytic C–C activation of cyclopropyl acetates to produce silicon-containing five-membered heterocycles in a highly region- and chemoselective fashion. The umpolung α -selective silylation leading to dioxasilolanes is opposed to contemporary β -selective C–C functionalization protocols of cyclopropanols. Lewis base activation of dioxasilolanes as α -silyl carbinol equivalents undergoes the unconventional [1,2]-Brook rearrangement to form tertiary alcohols. Notably, mechanistic studies indicate that an electrophilic metal- π interaction harnessing highly fluorinated $\text{Tp}^{(\text{CF}_3)_2}\text{Rh}(\text{nbd})$ catalyst permitted a low-temperature C–C activation.

Graphical Abstract

Keywords

cyclopropanols; C–C activation; silylation; rhodium; tris(pyrazolyl)borate

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ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acscatal.8b04252. Experimental details and spectroscopic characterization data for all compounds (PDF) (CIF)

Notes

The authors declare no competing financial interest.

INTRODUCTION

Carbon–carbon (C–C) functionalization approaches offer new synthetic strategies involving traditionally unimaginable bond disconnection to build important molecular architectures rapidly for chemistry, biology, and medicine.^{1–14} Current strategies of C–C σ -bond metal insertion and succeeding functionalization have centered on new C–C formation. For example, carbonylation,^{9,14,15} an insertion of alkene,¹⁶ alkynes,^{15,17} and C=N,¹⁸ and others^{7,19} to C–C single bond has been well demonstrated. Emerging interests in synthetic chemistry are to develop new synthetic strategies to construct carbon–heteroatom (e.g., B, F, Si) bonds. Among them, carbon–silicon (C–Si) bond formation is attractive because of the environmental sustainability and ready diversification nature of organosilanes, aiming at rapid preparation of a range of bioactive molecules and new materials.^{20,21} Despite their established synthetic benefits, catalytic C–C silylation has been underdeveloped, primarily because of a lack of efficient catalytic protocol to effect the crucial bond scission and formation. Recently, Murakami and co-workers have demonstrated the first C–C silylation reactions through unique Pd-catalyzed cross metathesis of C–C and C–Si bonds within cyclobutanones and silacyclobutanes, respectively, which builds structurally unique silacycles.^{22–24}

Another important issue in C–C activation^{14–17} has arisen in regioselective bond functionalization. For example, conventional C–C activation approaches of cyclopropanol derivatives^{25–29} are limited to the β -C–C functionalization to provide ketones **2** via metallohomoenolate **3** (Figure 1a).³⁰ However, to the best of our knowledge, catalytic α -functionalization of cyclopropanols has not been reported. Herein, we report umpolung α -C–C silylation of cyclopropyl acetates with highly fluorinated $\text{Tp}^{(\text{CF}_3)_2}_2\text{Rh}(\text{nbd})$ catalyst. The redox-neutral, catalytic C–C activation provides dioxasilolanes **6** in a highly region- and chemoselective fashion at low temperature (e.g., room temperature) (Figure 1b).

DISCUSSION

To address the synthetic challenge associated with regioselective C–C silylation of cyclopropanols, we envisioned Rh-catalyzed redox-neutral, umpolung α -selective C–C silylation of cyclopropyl acetates (Figure 1b). Specifically, loading of metal catalyst onto cyclopropyl hydrosilyl acetals **5**, accessed via Ir-catalyzed ester hydrosilylation,³¹ followed by cross σ -bond metathesis between C–C and Si–M bonds in **7** provides regioselective C(α)–Si bond formation and leads to dioxasilolanes **6** via **8** (Figure 2a). The resulting dioxasilolanes **6** can serve as stable, α -silylcarbinol equivalents. Although they can be accessed by a silyl anion addition approach to ketones, the potential setbacks with this stoichiometric approach include a 1,2-silyl migration from carbon to oxygen (Brook rearrangement) of the resulting oxyanion after the nucleophilic addition,³² enolization, and preferential 1,4-silyl nucleophile addition to α,β -unsaturated ketones to afford β -silyl ketones.^{33–35}

Furthermore, chemoselective metal insertion into C–C bonds in the presence of largely abundant C–H bonds in close proximity is challenging.¹⁷ To address this issue, our strategy for chemoselective C–C silylation is predicated on the transition-state-guided reaction

design, harnessing analysis of each putative cyclometalated structure generated through either C–H or C–C activation. We recognized the importance of metalated transition state (TS) to activate and functionalize specific chemical bonds successfully and selectively. Our hypothesis is that the highly chemoselective Rh-catalyzed C–C activation of **5** is achievable with adopting the five-membered TS geometry, depicted in **7** (Figure 2a). In contrast, two proximal arene and cyclopropyl C–H activation^{36,37} requires unfavorable eight-membered TS for **9** and seven-membered TS for **10**, respectively (Figure 2b).

As a proof-of-concept of performing region- and chemoselective catalytic C–C silylation, we prepared phenyl-cyclopropyl acetate **4a** (Table 1). This substrate includes proximal arene and cyclopropyl C–H bonds and cyclopropyl C–C bond. To assess the feasibility of the α -selective C–C silylation, **4a** was subjected to a sequence of Ir-catalyzed ester hydrosilylation and Rh-catalyzed C–C silylation conditions in a single pot. A series of supporting ligands including pentamethylcyclopentadienyl (Cp*) (entry 1) and tris-(pyrazolyl)borate (Tp) (entries 2–7) screened showed that the C–C silylation was viable to afford a pair of constitutional isomers (**6a** and **11a**) (Table 1). Among them, the electron-poor Tp ligand, [Tp^{(CF₃)₂][–] led to the highest yield of **6a** (entry 4).^{38,39} Among a number of cyclic olefin promoters having different ring strains (entries 4–7),⁴⁰ the norbornene was found to be the most effective and generally applicable for the C–C silylation (see the Supporting Information). In any case the competing proximal arene and cyclopropyl C–H silylations were not observed, as rationalized by the TS analysis shown in Figure 2.}

[Tp^{(CF₃)₂][–] coordinates to Rh(I) in bidentate fashion as evident from the X-ray structure of Tp^{(CF₃)₂ Rh(nbd) is shown in Figure 3.⁴¹ The use of isolated Tp^{(CF₃)₂ Rh(nbd) for the C–C silylation under essentially identical conditions led to **6a** in 76% yield and 12:1 diastereoselectivity. A substoichiometric amount of nbe was indeed required for efficient reaction (cf., 39% yield without nbe), inferring that nbe is not innocent for an overall catalytic cycle.}}}

Unexpectedly, we found that the Tp^{(CF₃)₂ Rh(nbd) catalyst permitted the room temperature C–C silylation of aryl-, alkenyl-, and alkynyl-substituted cyclopropyl hydrosilyl acetals (Figure 4).⁴² The lower yield observed in the C–C silylation of **5a** at room temperature is attributed to partial instability of **5a** during the extended reaction time (24 h). In contrast to the sluggish kinetics in the formation of **6a**, the reactions of the alkene and alkyne-substituted cyclopropyl hydrosilyl acetals, **5b** and **5c**, respectively, were remarkably fast to afford **6b** and **6c** within 40 and 30 min at room temperature, with good yields (87% and 83%, respectively) and excellent diastereoselectivity (both >20:1). We rationalize that increasing electrophilicity of the rhodium center by highly fluorinated tris(pyrazolyl)borate ligand facilitates the donor–acceptor interaction between the neighboring π -donor and the electrophilic rhodium and thus develops the Rh–(C–C) agostic interaction^{8,43} for the ready C–C activation, leading to facile C(α)–Si bond formation. When alkyl-substituted cyclopropyl hydrosilyl acetals in the absence of a neighboring π donor were subjected to the catalytic conditions, the C–C silylation reactions ultimately failed and the starting materials}

were recovered. This result indicates the importance of the Rh- π interaction for the successful catalytic C–C activation of cyclopropyl hydrosilyl acetals.

Under the optimized reaction conditions for a single-pot, redox-neutral C–C silylation, a range of a new class of silicon-containing heterocycles **6** were prepared from **4** with moderate to excellent yield and diastereoselectivity (Table 2). Dioxasilolanes **6** presented in Table 2 were chromatographically stable and a range of common functional groups including alkenes (**6b**, **6d**), alkyne (**6c**), amine (**6h**), ethers (**6i–6p**), halides (**6m**, **6n**), trifluoromethyl (**6o**), 3,5-dimethyl (**6p**), acetal (**6q**), naphthalene (**6r**), furan (**6s**), thiophene (**6t**), and indole (**6u**) were tolerated either at rt or 100 °C. However, a reaction with allene (**6e**) gave a complex mixture. The reactions with substrates holding substituted cyclopropyl ring also proceeded to furnish **6v–6x** with good yield and excellent diastereoselectivity. In these cases, we observed the preferential activation of a more kinetically accessible C–C bond. An NOE experiment with **6v** revealed that the diastereoselection was consistent with the proposed TS model **7** (Figure 2a and see the Supporting Information), which permitted high diastereoselectivity.

The cyclic silyl acetals **6** are chromatographically stable, yet willing acceptors of organometallic nucleophiles.^{31,44,45} Upon a nucleophilic attack to **6** leading to a putative, pentacoordinated silicon species **14**, the high thermodynamic driving force drives them rapidly and irreversibly to **15** in equilibrium with a strained, pentacoordinated species **16** (Figure 5a). This spring-loaded nature makes **6** suitable for rapid diversification to tertiary alcohol derivatives. To demonstrate this aspect, we first performed the [1,2]-Brook rearrangement of **6a** as α -silylcarbinol equivalents.³² Specifically, a ring opening of **6a** with MeLi releases acetaldehyde, which can engage in additional MeLi, and a spontaneous ring closure of **15** produces **16**. Upon addition of electrophiles and raising of the temperature, the reactions furnished tertiary alcohols capped with a diethylmethylsilyl group, **12** and **13**, respectively. When the reaction was quenched at –78 °C, α -silylcarbinol **17** was produced (88% yield). This protocol was applied to a complex molecular setting, where estrone-derived cyclopropyl acetate **18** was converted into silyl ether **19** (85% yield, a three-step single pot from **18**) (Figure 5b).

To gain insight into the mechanism of this reaction, we conducted a series of mechanistic experiments. First, we performed the Hammett study to understand a linear free-energy relationship of a redox-neutral C–C silylation mechanism (Figure 6a). The rate acceleration by electron-withdrawing groups was observed in the process. Specifically, the ρ value of 0.80 indicates no appreciable accumulation of the electron density in the transition state of the C–C cleavage step. The results infer that the M- π coordination is not likely the turnover-determining step, but increasing the electron-withdrawing nature of the aryl moiety would rather facilitate the cleavage of the neighboring cyclopropyl C–C bond. Labeling experiments with tetradeuterated cyclopropyl hydrosilyl acetal and a fully deuterated phenyl group-substituted hydrosilyl acetal conclude that no obvious cyclopropyl and arene C–H cleavage occurs in the course of the C–C silylation (Figure 6b,c, respectively). We then conducted the kinetic isotope effect (KIE) study with **5a-CP-H₄** and **5a-CP-D₄** in a single vessel (Figure 6d). The reaction afforded inverse secondary KIE. These results along with

the Hammett studies described above suggest that the turnover-determining step is likely the C–C cleavage.

On the basis of our preliminary mechanistic studies along with literature precedents,^{46–49} the proposed mechanisms accounting for formation of **6** and **11** proceeds through a common bis-silyl rhodium intermediate **C** (Figure 7). Oxidative addition of cyclopropyl hydrosilyl acetal **5** to $\text{Tp}^{(\text{CF}_3)_2}\text{Rh}(\text{nbd})$ generates Rh-silyl hydride **A**, which was identified as a major species observed through ^1H NMR spectroscopy (see the Supporting Information).^{48,49} Norbornene is indispensable in producing **C** efficiently; olefin migratory insertion to form **B**, followed by oxidative addition of **5** and reductive elimination, could generate norbornane (observed by ^1H NMR) and **C**, which is in equilibrium with **D**. Considering the bonding similarities between the Cp^* and Tp ligands, structurally similar $\text{Cp}^*\text{Rh}(\text{SiEt}_3)_2$ species were proposed by Berry and co-workers in the context of C–H silylation.⁴⁸ Once the rhodium- π interaction that facilitates a tightly organized geometry and thus would develop putative C–C agostic interaction with the metal center are established within **D**, direct cross metathesis of Si–Rh and C–C within **D**, which is a turnover-determining step, can give rise to the intermediates **E** (major) and **F** (minor). We rationalize that **F** requires a significantly distorted geometry for the putative intramolecular bond exchange process. Because the steric bulk from the proximal, fully substituted carbon center is present next to the metal, σ -bond metathesis between hydrosilyl acetal **5** and **E** furnishes **6**, where the β -hydride elimination adduct **G** was not observed. The crossover experiment between protiosilyl acetal and deuteriosilyl acetal established that the final hydrogen transfer occurs intramolecularly (see the Supporting Information). On the other hand, the reaction between the alkylrhodium species **F** holding the bidentate RhTp and **5** leads to a minor constitutional isomer **11** (**H** was not observed). We made an observation on the alkene transposition adduct **20** (9% yield) along with **6d** (79% yield) from **4d**, suggesting that formation of the fully substituted alkylrhodium species **21** underwent [1,3]-rhodium shift²⁵ to produce less hindered **22** and thus **F** is responsible for formation of dioxasilepanes **11**.

CONCLUSION

In summary, we have developed umpolung α -silylation of cyclopropyl acetates via redox-neutral catalytic C–C activation to produce silicon-containing five-membered heterocycles with high region- and chemoselectivities. Synthetic applicability of the methods was demonstrated through the rapid preparation of tertiary alcohols vis Lewis base-mediated unconventional [1,2]-Brook rearrangement of the resulting chromatographically stable dioxasilolanes. Finally, preliminary mechanistic studies suggest that the electrophilic metal center present in highly fluorinated $\text{Tp}^{(\text{CF}_3)_2}\text{Rh}(\text{nbd})$ catalyst is a key to the facile, low-temperature C–C silylation. Studies toward an enantioselective variant of this reaction are underway and will be reported in due course.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGMENTS

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REFERENCES

- (1). Crabtree RH The Organometallic Chemistry of Alkanes. *Chem. Rev.* 1985, 85, 245–269.
- (2). Jones WD The Fall of the C–C Bond. *Nature* 1993, 364, 676–677.
- (3). Murakami M; Amii H; Ito Y Selective Activation of Carbon–Carbon Bonds Next to a Carbonyl Group. *Nature* 1994, 370, 540–541.
- (4). Rybtchinski B; Milstein D Metal Insertion into C–C bonds in Solution. *Angew. Chem. Int. Ed.* 1999, 38, 870–883.
- (5). Murakami M; Ito Y Cleavage of Carbon–Carbon Single Bonds by Transition Metals. *Top. Organomet. Chem.* 1999, 3, 97–129.
- (6). Jun C-H; Lee H Catalytic Carbon–Carbon Bond Activation of Unstrained Ketone by Soluble Transition-Metal Complex. *J. Am. Chem. Soc.* 1999, 121, 880–881.
- (7). Xia Y; Lu G; Liu P; Dong G Catalytic Activation of Carbon–Carbon Bonds in Cyclopentanones. *Nature* 2016, 539, 546–550. [PubMed: 27806379]
- (8). Jun C Transition Metal-Catalyzed Carbon-Carbon Bond Activation. *Chem. Soc. Rev.* 2004, 33, 610–618. [PubMed: 15592626]
- (9). Murakami M; Matsuda T Metal-Catalysed Cleavage of Carbon-Carbon Bonds. *Chem. Commun.* 2011, 47, 1100–1105.
- (10). Seiser T; Saget T; Tran DN; Cramer N Cyclobutanes in Catalysis. *Angew. Chem. Int. Ed.* 2011, 50, 7740–7752.
- (11). Soullart L; Cramer N Catalytic C–C Bond Activations via Oxidative Addition to Transition Metals. *Chem. Rev.* 2015, 115, 9410–9464. [PubMed: 26044343]
- (12). Fumagalli G; Stanton S; Bower JF Recent Methodologies That Exploit C–C Single-Bond Cleavage of Strained Ring Systems by Transition Metal Complexes. *Chem. Rev.* 2017, 117, 9404–9432. [PubMed: 28075115]
- (13). Gao X-F; Fu Z-X In C–C Bond Activation; Dong D, Ed.; Springer: Berlin, 2014; Vol. 346, pp 195–232.
- (14). Wang G-W; Bower JF Modular Access to Azepines by Directed Carbonylative C–C Bond Activation of Aminocyclopropanes. *J. Am. Chem. Soc.* 2018, 140, 2743–2747. [PubMed: 29461050]
- (15). Shaw MH; Melikhova EY; Kloor DP; Whittingham WG; Bower JF Directing Group Enhanced Carbonylative Ring Expansions of Amino-Substituted Cyclopropanes: Rhodium-Catalyzed Multicomponent Synthesis of N-Heterobicyclic Enones. *J. Am. Chem. Soc.* 2013, 135, 4992–4995. [PubMed: 23488745]
- (16). Li H; Li Y; Zhang X; Chen K; Wang X; Shi Z Pyridinyl Directed Alkenylation with Olefins via Rh(III)-Catalyzed C–C Bond Cleavage of Secondary Arylmethanols. *J. Am. Chem. Soc.* 2011, 133, 15244–15247. [PubMed: 21875139]
- (17). Zeng R; Dong G Rh-Catalyzed Decarbonylative Coupling with Alkynes via C–C Activation of Isatins. *J. Am. Chem. Soc.* 2015, 137, 1408–1411. [PubMed: 25569352]
- (18). Li B; Wang Y; Jin Z; Zheng P; Ganguly R; Chi Y Carbon-carbon Bond Activation of Cyclobutenones Enabled by the Addition of Chiral Organocatalyst to Ketone. *Nat. Commun.* 2015, 6, 6207. [PubMed: 25652912]
- (19). Xia Y; Wang J; Dong G Distal-Bond-Selective C–C Activation of Ring-Fused Cyclopentanones: An Efficient Access to Spiroindanones. *Angew. Chem. Int. Ed.* 2017, 56, 2376–2380.
- (20). Nakao Y; Hiyama T Silicon-Based Cross-Coupling Reaction: An Environmentally Benign Version. *Chem. Soc. Rev.* 2011, 40, 4893–4901. [PubMed: 21755089]
- (21). Ramesh R; Reddy DS Quest for Novel Chemical Entities through Incorporation of Silicon in Drug Scaffolds. *J. Med. Chem.* 2018, 61, 3779–3798. [PubMed: 29039662]

- (22). Ishida N; Ikemoto W; Murakami M Intramolecular σ -Bond Metathesis Between Carbon–Carbon and Silicon–Silicon Bonds. *Org. Lett.* 2012, 14, 3230–3232. [PubMed: 22651103]
- (23). Ishida N; Ikemoto W; Murakami M Cleavage of C–C and C–Si σ -Bonds and Their Intramolecular Exchange. *J. Am. Chem. Soc.* 2014, 136, 5912–5915. [PubMed: 24720573]
- (24). Okumura S; Sun F; Ishida N; Murakami M Palladium-Catalyzed Intermolecular Exchange Between C–C and C–Si σ -Bonds. *J. Am. Chem. Soc.* 2017, 139, 12414–12417. [PubMed: 28837766]
- (25). Chen DY-K; Pouwer RH; Richard J-A Recent Advances in the Total Synthesis of Cyclopropane-Containing Natural Products. *Chem. Soc. Rev.* 2012, 41, 4631–4642. [PubMed: 22592592]
- (26). Kulinkovich OG The Chemistry of Cyclopropanols. *Chem. Rev.* 2003, 103, 2597–2632. [PubMed: 12848581]
- (27). Lee J; Kim H; Cha JK A New Variant of the Kulinkovich Hydroxycyclopropanation. Reductive Coupling of Carboxylic Esters with Terminal Olefins. *J. Am. Chem. Soc.* 1996, 118, 4198–4199.
- (28). Rubin M; Rubina M; Gevorgyan V Transition Metal Chemistry of Cyclopropenes and Cyclopropanes. *Chem. Rev.* 2007, 107, 3117–3179. [PubMed: 17622181]
- (29). Carson CA; Kerr MA Heterocycles from Cyclopropanes: Applications in Natural Product Synthesis. *Chem. Soc. Rev.* 2009, 38, 3051–3060. [PubMed: 19847340]
- (30). Epstein OL; Lee S; Cha JK Formation of Seven-Membered Carbocycles by the Use of Cyclopropyl Silyl Ethers as Homoenols. *Angew. Chem.* 2006, 118, 5110–5113.
- (31). Hua Y; Asgari P; Avullala T; Jeon J Catalytic Reductive ortho-C–H Silylation of Phenols with Traceless, Versatile Acetal Directing Groups and Synthetic Applications of Dioxasilines. *J. Am. Chem. Soc.* 2016, 138, 7982–7991. [PubMed: 27265033]
- (32). Brook AG Molecular Rearrangements of Organosilicon Compounds. *Acc. Chem. Res.* 1974, 7, 77–84.
- (33). Gilman H; Lichtenwalter GD The Syntheses and Some Reactions of α -Silylcarbinols. *J. Am. Chem. Soc.* 1958, 80, 2680–2682.
- (34). Chénéde A; Rahman NA; Fleming I Dehydration of α -Silyl alcohols in the Reductive Conversion of Esters and Ketones into Alkenes. *Tetrahedron Lett.* 1997, 38, 2381–2382.
- (35). Still WC Conjugate Addition of Trimethylsilyllithium. A Preparation of 3-Silyl Ketones. *J. Org. Chem.* 1976, 41, 3063–3064.
- (36). Lee T; Hartwig JF Rhodium-Catalyzed Enantioselective Silylation of Cyclopropyl C–H Bonds. *Angew. Chem., Int. Ed.* 2016, 55, 8723–8727.
- (37). Rousseaux S; Liégault B; Fagnou K Palladium (0)-Catalyzed Cyclopropane C–H Bond Functionalization: Synthesis of Quinoline and Tetrahydroquinoline Derivatives. *Chem. Sci.* 2012, 3, 244–248.
- (38). Silver, [tris(3,5-bis(trifluoromethyl)-1H-pyrazolato- κ N1)]hydroborato(1-)- κ N2, κ N2', κ N2'']-. In *e-EROS Encyclopedia of Reagents for Organic Synthesis*; Wiley, 2006; DOI: 10.1002/047084289X.rm00663.
- (39). Dias HR; Kim H-J; Lu H-L; Rajeshwar K; de Tacconi NR; Derecskei-Kovacs A; Marynick DS Investigation of the Electronic and Geometric Effects of Trifluoromethyl Substituents on Tris(pyrazolyl)borate Ligands Using Manganese(I) and Copper(I) Complexes. *Organometallics* 1996, 15, 2994–3003.
- (40). Allinger NL; Sprague JT Conformational analysis. LXXXIV. Study of the Structures and Energies of Some Alkenes and Cycloalkenes by the Force Field Method. *J. Am. Chem. Soc.* 1972, 94, 5734–5747.
- (41). Del Ministro E; Renn O; Ruegger H; Venanzi LM; Burckhardt U; Gramlich V Rhodium (I) Complexes of the Type [Tp3R,5RRh(LL)] (LL= 2CO, NBD, COD) with Trifluoromethyl Substituted Tris(pyrazolyl)borate Ligands and Their Dynamic Behaviour in Solution. The X-Ray Crystal Structure of TpCF3,MeRh-(CO)2. *Inorg. Chim. Acta* 1995, 240, 631–639.
- (42). Tamaki T; Ohashi M; Ogoshi S [3+ 2] Cycloaddition Reaction of Cyclopropyl Ketones with Alkynes Catalyzed by Nickel/Dimethylaluminum Chloride. *Angew. Chem., Int. Ed.* 2011, 50, 12067–12070.
- (43). Halpern J Determination and Significance of Transition Metal-Alkyl Bond Dissociation Energies. *Acc. Chem. Res.* 1982, 15, 238–244.

- (44). Frauenrath H Vinyl Acetals and Related Compounds in Organic Synthesis. *Synthesis* 1989, 1989, 721–734.
- (45). Nasveschuk CG; Jui NT; Rovis T A Modular Approach to the Synthesis of 2,3,4-Trisubstituted Tetrahydrofurans. *Chem. Commun.* 2006, 3119–3121.
- (46). Karmel C; Li B-J; Hartwig JF Rhodium-Catalyzed Regioselective Silylation of Alkyl CH Bonds for the Synthesis of 1, 4-Diols. *J. Am. Chem. Soc.* 2018, 140, 1460–1470. [PubMed: 29293327]
- (47). Cheng C; Hartwig JF Mechanism of the Rhodium-Catalyzed Silylation of Arene C–H Bonds. *J. Am. Chem. Soc.* 2014, 136, 12064–12072. [PubMed: 25082802]
- (48). Ezbiansky K; Djurovich PI; LaForest M; Sinning DJ; Zayes R; Berry DH Catalytic C–H Bond Functionalization: Synthesis of Arylsilanes by Dehydrogenative Transfer Coupling of Arenes and Triethylsilane. *Organometallics* 1998, 17, 1455–1457.
- (49). Bromberg SE; Yang H; Asplund MC; Lian T; McNamara B; Kotz K; Yeston J; Wilkens M; Frei H; Bergman RG The Mechanism of a CH Bond Activation Reaction in Room-Temperature Alkane Solution. *Science* 1997, 278, 260–263.

a. Previous reports: Catalytic ring-opening C–C activation of cyclopropanols–
 β -functionalization for C–C, C–N, C–S bond formations

b. This work: A redox-neutral, catalytic C–C activation of cyclopropyl hydrosilyl acetals–
Umpolung α -silylation of cyclopropanols

Figure 1. Catalytic C–C activation of cyclopropanol derivatives: Complementary α - and β -regioselective functionalization.

a. Regioselectivity: cross α -bond metathesis in **7** for Si-C(α) bond formation

b. Chemoselectivity: conceptual transition state (TS)-guided reaction design for chemoselective C-C silylation vs. **arene C-H** and **cyclopropyl C-H** silylations

Figure 2.
Proposed mechanism for region- and chemoselective C-C silylation.

Figure 3.

Isolation and X-ray structure of $\text{Tp}^{(\text{CF}_3)_2}\text{Rh}(\text{nbd})$ a catalyst for redox-neutral, catalytic α -C–C silylation of cyclopropyl hydrosilyl acetal **5a**.

Figure 4.

Room temperature, C-C silylation with electron-poor $\text{Tp}^{(\text{CF}_3)_2}\text{Rh}$ catalyst.

a. [1,2]-Brook rearrangement of dioxasilolanes **6**

proposed mechanism

b. C-C silylation of estrone-derived cyclopropyl acetate and [1,2]-Brook rearrangement

Figure 5.
Synthetic applications of dioxasilolanes **6**.

Figure 6. Mechanism studies. (a) Hammett plot. (b) Deuterium-labeling studies with tetradeuterated cyclopropane. (c) Deuterium-labeling studies with a pentadeuterated phenyl group. (d) Kinetic isotope effect (KIE) study.

Figure 7.
Proposed mechanism.

Table 1.

Reaction Optimization of Rhodium-Catalyzed C–C Silylation^a

entry	supporting ligand	promotor ^b	6a (%) ^b	11a (%) ^b
1	[Cp*] ^{-c}	nbe	73	6
2	Tp(CH ₃) ₂ K	nbe	70	9
3	Tp(CH ₃)Ph Na(THF)	nbe	76	11
4	Tp(CH ₃) ₂ Na(THF)	nbe	78	8
5	Tp(CH ₃) ₂ Na(THF)	nbd	37	
6	Tp(CH ₃) ₂ Na(THF)	cod	20	
7	Tp(CH ₃) ₂ Na(THF)	coe	18	

^a Conditions: (i) cyclopropanoacetate **4a** (0.2 mmol), [Ir(coe)₂Cl]₂ (0.1 mol %), H₂SiEt₂ (3 equiv), THF (0.33 M). (ii) [Rh(nbd)Cl]₂ (0.8 mol %), supporting ligand (1.6 mol %), promotor (2 equiv), THF (0.33 M).

^b Isolation yield. The major diastereomer of **6a** is shown; in all cases, the minor diastereomer of **6a** was observed as determined by ¹H NMR and GC-MS spectrometry analyses of the crude reaction mixture. A diastereomeric ratio of **11a** was not determined.

^c [RhCp*Cl₂]₂ was used. nbe, norbornene; nbd, norbornadiene; cod, 1,5-cyclooctadiene; coe, *cis*-cyclooctene.

Table 2.

Scope of Redox-Neutral Catalytic C–C Silylation of Cyclopropyl Acetates^a

$\text{4} \xrightarrow[\text{THF, temp.}]{\text{i) } [\text{Ir}(\text{coe})_2\text{Cl}_2]_2 \text{ (0.1 mol \%)} \text{ H}_2\text{SiEt}_2 \text{ (3 equiv)}} \text{5} \xrightarrow[\text{THF, temp.}]{\text{ii) } [\text{Rh}(\text{ndd})\text{Cl}_2]_2 \text{ (0.8 mol \%)} \text{ Tp}^t\text{C}^t\text{Si}^t\text{Na}(\text{THF}) \text{ (1.6 mol \%)} \text{ nbe (10 mol \%)} \text{ 6}$
6a rt: ^b 48% >20:1 dr 100 °C: 78% (71% ^c) 13:1 dr
6b rt: 87% >20:1 dr 100 °C: 75% 12:1 dr
6c rt: 83% >20:1 dr 100 °C: 81% >20:1 dr
6d rt: 79% 3:1 dr 100 °C: 70% 2.5:1 dr
6e rt: 0% 100 °C: 0% 15:1 dr
6f rt: ^b 49% >20:1 dr 100 °C: 69% 15:1 dr
6g rt: ^b 60% 20:1 dr 100 °C: 77% 9:1 dr
6h rt: ^b 57% >20:1 dr 100 °C: 73% 10:1 dr
6i rt: ^b 59% >20:1 dr 100 °C: 67% 11:1 dr
6j rt: ^b 55% 20:1 dr 100 °C: 69% 10:1 dr
6k rt: ^b 50% >20:1 dr 100 °C: 72% 10:1 dr
6l rt: ^b 44% >20:1 dr 100 °C: 72% 10:1 dr
6m rt: ^b 46% >20:1 dr 100 °C: 71% >20:1 dr
6n rt: ^b 52% >20:1 dr 100 °C: 70% >20:1 dr
6o rt: ^b 44% >20:1 dr 100 °C: 77% 11:1 dr
6p rt: ^b 43% >20:1 dr 100 °C: 73% 13:1 dr
6q rt: ^b 49% >20:1 dr 100 °C: 74% 14:1 dr
6r rt: ^b 57% >20:1 dr 100 °C: 72% 13:1 dr
6s rt: ^b 59% >20:1 dr 100 °C: 79% 10:1 dr
6t rt: ^b 63% >20:1 dr 100 °C: 79% 10:1 dr
6u rt: ^b 64% >20:1 dr 100 °C: 82% 10:1 dr
6v rt: ^b 44% >20:1 dr 100 °C: 73% >20:1 dr
6w rt: ^b 51% >20:1 dr 100 °C: 73% >20:1 dr
6x rt: ^b 47% >20:1 dr 100 °C: 78% >20:1 dr

^aYields are for isolated material over a single-pot, two-step sequence from **4** (0.2 mmol). Diastereomeric ratio (dr) was determined by ¹H NMR spectroscopy and GC-MS spectrometry analyses of the crude reaction mixture.

^b[Rh(nbd)Cl]₂, Tp (5 mol %), (CF₃)₂Na(THF) (10 mol %), norbornene (10 mol %), THF (0.33 M), rt.

^c1 mmol of **4a** was used.