Title: Enantioselective Hydroxylation of Dihydrosilanes to Si-Chiral Silanols Catalyzed by In Situ Generated Copper(II) Species

Authors: Wu Yang, Lin Liu, Jiandong Guo, Shou-Guo Wang, Jia-Yong Zhang, Li-Wen Fan, Yu Tian, Li-Lei Wang, Cheng Luan, Zhong-Liang Li, Chuan He, Xiaotai Wang, Qiang-Shuai Gu, and Xin-Yuan Liu

This manuscript has been accepted after peer review and appears as an Accepted Article online prior to editing, proofing, and formal publication of the final Version of Record (VoR). The VoR will be published online in Early View as soon as possible and may be different to this Accepted Article as a result of editing. Readers should obtain the VoR from the journal website shown below when it is published to ensure accuracy of information. The authors are responsible for the content of this Accepted Article.

To be cited as: Angew. Chem. Int. Ed. 2022, e202205743

Link to VoR: https://doi.org/10.1002/anie.202205743
Enantioselective Hydroxylation of Dihydrosilanes to Si-Chiral Silanols Catalyzed by In Situ Generated Copper(II) Species

Wu Yang*, Lin Liu*, Jiandong Guo*, Shou-Guo Wang, Jia-Yong Zhang, Li-Wen Fan, Yu Tian, Li-Lei Wang, Cheng Luan, Zhong-Liang Li, Chuan He, Xiaotai Wang,* Qiang-Shuai Gu,* and Xin-Yuan Liu*

Abstract: Catalytic enantioselective hydroxylation of prochiral dihydrosilanes with water is expected to be a highly efficient way to access Si-chiral silanols, yet has remained unknown up to date. Herein, we describe a strategy for realizing this reaction: using an alkyl bromide as a single-electron transfer (SET) oxidant for invoking CuII species and chiral multidentate anionic N,N,P-ligands for its subsequent σ-metathesis with dihydrosilanes. In addition, we manifest the synthetic potential by establishing two synthetic schemes for transforming the functional group compatibility. In addition, we report the synthesis of Si-chiral silanols with high enantioselectivity and excellent effective enantiocontrol. The reaction readily provides a broad range of Si-chiral silanols with highenantioselectivity and excellent functional group compatibility. In addition, we manifest the synthetic potential by establishing two synthetic schemes for transforming the obtained products into Si-chiral compounds with high structural diversity. Our preliminary mechanistic studies support a mechanism involving SET for recruiting chiral CuII species as the active catalyst and its subsequent σ-metathesis with dihydrosilanes.

Chiral organosilicon compounds featuring Si-stereogenic centers are important for developing synthetic reagents,[1] bioactive molecules,[2] and materials.[3] Among others, Si-chiral compounds with stereogenic Si–O bonds are of particular importance given their great potential for further synthetic transformations.[4] In addition, they are also emerging as promising drug candidates,[5] optically active materials,[6] and chiral ligands[7] (Figure 1A). Thus, efficient catalytic asymmetric methodologies for practical access to these molecules are in high demand, yet have so far remained underdeveloped.[8] In this aspect, the catalytic enantioselective alcoholsysis (silanolsysis) of prochiral dihydrosilanes[9] with achiral alcohols[10] (silanols[10b,10c]) or water is an ideal approach that is among the earliest investigated catalytic methods for access to Si-chiral compounds due to the ready availability of both starting materials (Figure 1B). However, reported successful examples have been focused on the use of precious metal rhodium catalysts for accessing siloxanes[10b,10c,11] and silyl ethers.[10b,10c,12] As such, the corresponding catalytic enantioselective hydroxylation of dihydrosilanes to Si-chiral silanols,[13] to the best of our knowledge, has hitherto remained unknown.

Notably, 3d transition metal copper is earth-abundant and inexpensive.[14] And CuII-mediated hydrosilation alkylation has been widely invoked for establishing a myriad of useful transformations involving CuIIH species.[15] Among others, Leighton[16] and Oestreich[17] have independently achieved the synthesis of Si-chiral silyl ethers with chiral alcohols by CuII catalysis. In addition, Oestreich[18] has also pioneered in establishing a series of (dynamic) kinetic resolution reactions of racemic alcohols. However, for the expedient construction of Si-stereogenic centers, the development of CuII-catalyzed enantioselective alkylation (siloxylation) or hydroxylation of hydrosilanes with achiral alcohols (silanols) or water, respectively, though highly demanded, has so far remained unknown (Figure 1C, left). The major reasons for the underdevelopment seem to be twofold. First, the diagonal positioning of the ligand-coordinated CuII and the evolving Si stereocenter in the commonly presumed σ-metathesis[19] transition state keeps the chiral ligand far away from the Si-stereocenters. Second, up to two-site ligand binding to CuII is commonly allowed for the σ-metathesis to proceed,[18–20] which renders the catalyst pocket insufficiently compact. These factors together likely render the enantiocontrol very challenging, particularly when the remarkably steric small water is
COMMUNICATION

A. Representative Si-chiral silanol and derivatives

(Left) Sila-procyclidine muscarinic antagonist
Optically active polysiloxane material
Phosphonamidite ligand

B. Prevalent catalytic asymmetric dihydrosilane alcoholysis or silanization with achiral alcohols or silanols

C. Challenges in developing Cu-catalyzed asymmetric hydrosililation or hydroxylation for Si-chirality

D. This work: CuII-mediated enantioselective hydroxylation of dihydrosilanes to Si-chiral silanols

Facile access to diverse Si-chiral skeletons

Figure 1. Importance, challenges, and development of copper-catalyzed enantioselective hydroxylation of dihydrosilanes to Si-chiral silanols.

employed. In this regard, we noticed that multisite ligand binding to the one-electron oxidized CuII is possible,[21] which would likely make the catalyst pocket more congested[22] and the stereodifferentiation more effective (Figure 1C, right).

With our longstanding interest in developing catalytic asymmetric reactions involving radical species,[24,25] we recently disclosed a series of single-electron transfer (SET) catalysts of copper together with chiral multidentate anionic ligands.[26] In these studies, CuI was continuously oxidized to CuII through SET[27] with mild oxidants, mostly alkyl halides, as the reactions proceeded. Intrigued by the aforementioned importance of Si-chiral silanols and their synthetic challenges, we envisioned that the use of an SET oxidant together with our copper/multidentate anionic ligand catalysts would be promising for realizing the speculated CuII-mediated enantioselective hydroxylation of dihydrosilanes. Herein, we report our efforts in achieving this goal using our copper/chiral N,N,P-ligand catalysts under mild conditions (Figure 1D). The introduction of an alkyl bromide to the reaction as the SET oxidant successfully ensures the continuous generation of catalytically active CuII species. The reaction exhibits high enantioselectivity and good functional group tolerance over a number of structurally distinct dihydrosilane substrates. We further demonstrate the synthetic utility of this methodology by converting the thus obtained Si-chiral silanols into diverse Si-chiral skeletons. Preliminary experimental and computational mechanistic investigations support the SET oxidant role of the alkyl bromide and CuII species as the active hydroxylation catalyst.

Our investigation began with screening various SET oxidants using dihydrosilane S1 and water as substrates in the presence of CuI, the Dixon’s ligand L1,[28] and Cs2CO3 in tetrahydrofuran (THF) at 0 °C (Table 1). We previously showed that mildly oxidizing alkyl bromides such as SX2–SX4 were excellent SET oxidants for our Cu(I)/N,N,P-ligand catalysts.[29,30] In fact, they all delivered high reaction efficiency and almost constant

<table>
<thead>
<tr>
<th>Entry</th>
<th>L*</th>
<th>SX</th>
<th>Yield/%</th>
<th>Ee/%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>L1</td>
<td>none</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>L1</td>
<td>SX1</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>L1</td>
<td>SX2</td>
<td>66</td>
<td>29</td>
</tr>
<tr>
<td>4</td>
<td>L1</td>
<td>SX3</td>
<td>72</td>
<td>29</td>
</tr>
<tr>
<td>5</td>
<td>L1</td>
<td>SX4</td>
<td>75</td>
<td>29</td>
</tr>
<tr>
<td>6</td>
<td>L2</td>
<td>SX4</td>
<td>16</td>
<td>69</td>
</tr>
<tr>
<td>7</td>
<td>L3</td>
<td>SX3</td>
<td>11</td>
<td>75</td>
</tr>
<tr>
<td>8</td>
<td>L4</td>
<td>SX4</td>
<td>18</td>
<td>76</td>
</tr>
<tr>
<td>9</td>
<td>L5</td>
<td>SX4</td>
<td>19</td>
<td>75</td>
</tr>
<tr>
<td>10</td>
<td>L6</td>
<td>SX4</td>
<td>68</td>
<td>95</td>
</tr>
</tbody>
</table>

[a] Reaction conditions: S1 (0.10 mmol), H2O (5.0 equiv.), CuI (10 mol%), L* (10 mol%), Cs2CO3 (2.0 equiv.), and SX (2.0 equiv.) in THF (1.0 mL) under argon (Ar) at 0 °C for 1 d. Yield was based on 1H NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard. The ee values were based on chiral HPLC analysis. [b] CuI (5.0 mol%) and L6 (5.0 mol%).

Table 1: Screening of reaction conditions.
enantioselectivity (entries 3–5; for results with BnBr, see Scheme S1). By contrast, the stronger peroxide oxidant SX1 afforded marginal conversion and substantially lower enantioselectivity (entry 2), possibly due to the oxidative decomposition of the copper catalyst. The control experiment without an oxidant indicated the marginal occurrence of essentially non-enantioselective base- and/or Cu(I)-catalyzed background reactions (entry 1). We next investigated our recently developed N,N,N-ligands L2–L6 of which all gave remarkably enhanced enantioselectivity (entries 6–10). Particularly, L6 featuring a benzyl substituent on the oxazoline moiety performed best in terms of both yield and ee (entry 10). We chose SX4 for these and the following studies due to the relatively low cost, easier product purification, and better performance. The catalyst loading could be decreased to 5 mol% without significantly affecting the overall reaction outcome (entry 11). Further screening of copper salts, base additives, solvents, and temperatures (Table S1) identified the optimal conditions as follows: 0.10 mmol S1, 5.0 equiv. H2O, 10 mol% CuI, 10 mol% L6, 2.0 equiv. Cs2CO3, and 2.0 equiv. SX4 in THF (0.1 M) at 0 °C for 1 d, providing 1 in 68% yield with 95% ee (entry 10 and Scheme S2A; 70% yield, 93% ee on 0.20 mmol scale, Scheme 1). Several Cu(I) salts gave comparable results with CuI (Table S1). Additional control experiments confirmed that all components were indispensable for the reaction (Table S2) and the amount of added water was flexible (Scheme S3). 

Regarding the scope of dihydrosilanes (Scheme 1), various additional aryl dihydrosilanes bearing ortho-, meta- or para-substituents of different electronic and steric properties on the phenyl rings were well tolerated (2–18). Noteworthy is the good tolerance of reactive functional groups such as aryl chloride (10), aryl tosylate (16), free phenol (11), ester (17), and carbonate (18). This prompted us to further explore other challenging functionalities, such as aryl iodide (19), heteroarene (20 and 21), amide NH (22 and 23), ketone (24), alkyne (25), and nitrile (26), of which all proved to be compatible with our reaction conditions. In addition, substrates bearing complex residues derived from bioactive molecules and natural products, such as isoxepac (27), phenylalanine (28), biotin (29), and dehydrocholic acid (30), were applicable to our reaction without any functional group or stereochemical interference. Furthermore, aryl dihydrosilanes possessing bicyclic or polycyclic (hetero)aryl rings were also suitable for the reaction (31–36). The reactions on substrates with the Si-aryl ring replaced by unsubstituted alkylenyl (37) or homobenzyl (38) groups or with the Si-Bu substituent switched to α,α-dimethylbenzyl (39) or cyclohexyl (40) groups still provided promising enantioselectivity albeit with low reaction yield, which are currently under further optimization in our lab. Unfortunately, the phenyl dihydrosilane with a small Si-aryl substituent (41) and unsymmetric diaryl-substituted dihydrosilanes (42 and 43) are currently unsuitable for this reaction due to low yield and poor ee (see Scheme S2B–D for details). The absolute configuration of 36 was established to be R on the basis of X-ray structural analysis31 (Scheme 1 and Figure S1) and those of others were assigned by analogy.

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>X</th>
<th>Y</th>
<th>Ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H</td>
<td></td>
<td>H</td>
<td>70%, 95% ee</td>
</tr>
<tr>
<td>2</td>
<td>Me</td>
<td></td>
<td>H</td>
<td>67%, 94% ee</td>
</tr>
<tr>
<td>3</td>
<td>R = F</td>
<td>54%, 87% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>R = OMe</td>
<td>63%, 93% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>R = Ph</td>
<td>65%, 89% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>R = 4-Bu</td>
<td>72%, 94% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>R = TMS</td>
<td>60%, 93% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>R = Ph</td>
<td>68%, 92% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>R = F</td>
<td>60%, 90% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>R = Cl</td>
<td>40%, 85% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>R = H</td>
<td>60%, 86% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>R = Me</td>
<td>61%, 91% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>R = Bn</td>
<td>70%, 91% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>R = Ph</td>
<td>64%, 90% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>R = TBS</td>
<td>51%, 90% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>R = Ts</td>
<td>54%, 91% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>R = 3-OMeBz</td>
<td>60%, 94% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>PhO(O)</td>
<td>42%, 85% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>R = Me</td>
<td>61%, 91% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>R = Ph</td>
<td>64%, 92% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>R = Ph</td>
<td>64%, 92% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>R = Ph</td>
<td>64%, 92% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>R = Ph</td>
<td>64%, 92% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>R = Ph</td>
<td>64%, 92% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>R = Ph</td>
<td>64%, 92% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>26</td>
<td>R = Ph</td>
<td>64%, 92% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>27</td>
<td>R = Ph</td>
<td>64%, 92% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>28</td>
<td>R = Ph</td>
<td>64%, 92% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>29</td>
<td>R = Ph</td>
<td>64%, 92% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>R = Ph</td>
<td>64%, 92% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>31</td>
<td>Ar = 1-Np</td>
<td>53%, 93% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>32</td>
<td>Ar = 2-Np</td>
<td>63%, 87% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>33</td>
<td>Ar = 1-Py</td>
<td>74%, 84% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>34</td>
<td>X = S</td>
<td>50%, 89% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>35</td>
<td>X = NPh</td>
<td>58%, 94% ee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>36</td>
<td>X = O</td>
<td>58%, 84% ee</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Scheme 1. Scope of dihydrosilanes. [a] Standard conditions: dihydrosilane (0.20 mmol), H2O (5.0 equiv.), CuI (10 mol%), L6 (10 mol%), Cs2CO3 (2.0 equiv.), and SX4 (2.0 equiv.) in THF (0.1 M) at 0 °C under argon for 10–72 h. Yield was isolated. The ee values were based on chiral HPLC analysis. [b] Cu (20 mol%) and L6 (20 mol%) [c] Dihydrosilane (0.10 mmol) was employed. [d] Ee was not determined. [e] Significant formation of disiloxanes and oligosiloxanes was observed. TMS, trimethylsilyl; TBS, tert-butyldimethylsilyl; Ts, 4-methylbenzenesulfonyl; Fmoc, 9-fluorenylmethyloxycarbonyl; NP, naphthalenyl; Py, pyrenyl; Cy, cyclohexyl; PMP, p-methoxyphenyl.
To demonstrate the practicality and synthetic potential of this methodology, we first carried out a gram-scale reaction on S1 to obtain Si-chiral silanol 1 with comparable efficiency and enantioselectivity (Scheme 2A). We readily obtained the antepode of 1 (ent-1) with almost the same yield and enantioselectivity using the enantiomer of L6 (ent-L6) under the otherwise standard conditions (Scheme 2B). Chiral silanol 1 remained stable, underwent slow condensation reactions, and otherwise standard conditions (Scheme 2B). Chiral silanol hydrosiloxane and chemoselective nucleophilic attack, delivering Si-chiral first silanol protection, then Si–H alkoxylation, and finally, ent-1, 69%, 94% ee.

Scheme 2. Scbility and synthetic utility. [a] Cu(OTrI)2 (10 mol%), Phen (12 mol%), and TMSCHN2 (2.0 equiv.) in CH2Cl2 at rt. [b] Cu(OTrI)2 (10 mol%), Phen (12 mol%), and N-ChOC(=O)2 (2.0 equiv.) in CH2Cl2 at rt. [c] MeLi (10 equiv.) and NaH (10 equiv.) in THF at rt. [d] LIAH4 (3.0 equiv.) in EtO at 40 °C. [e] DMAP (10 mol%), CISiPhMe2 (1.5 equiv.), and imidazole (1.5 equiv.) in CH2Cl2 at rt. [f] [Rh(COD)Cl]2 (1.0 mol%), rac-BINAP (2.0 mol%), and EVA (10 equiv.) in PhMe at 60 °C. [g] PMP (3.0 equiv.) in EtO at rt. [h] BuLi (3.0 equiv.) in EtO at rt. [i] BuLi (3.0 equiv.) in THF at rt. Phen, 1.07 g, 50%, 94% ee.

Concerning the mechanism of this reaction, we initially observed the formation of 53 in the control experiment with radical trap TEMPO ((2,2,6,6-tetramethylpiperidin-1-yl)oxyl) (Scheme 3A), likely indicating the formation of the corresponding alkyl radical from SX4 via SET[27] with CuI. Besides, the efficiency and enantioselectivity of the control reaction were almost unaffected by this radical trapping process, disproving the possible hydrogen atom abstraction of S1[32] by the alkyl radical for product formation. Therefore, we observed the formation of a roughly stoichiometric amount of the corresponding radical disproportionation product in the other control reaction using an analog of SX4 (Scheme 4; see Scheme S5 for details of the radical coupling product from benzylic bromide SX2). These results together suggest a dispensable role of this radical in the ensuing CuII-participated steps. The next control experiment with stoichiometric amounts of CuI salt and chiral ligand L6 provided 1 with essentially the same enantioselectivity (Scheme 3B), supporting CuII species as the active catalyst for the enantioselective hydroxylation. The subsequent control experiments with scalemic ligand L6 showed a linear relationship between the ee values of ligands and corresponding products (Figure S2), revealing a 1:1 molar ratio of CuI to the ligand in the enantiodetermining step. In addition, we also observed a relatively small but significant primary kinetic isotope effect (KIE) using the deuterated S1 (parallel KIE = 1.8; intermolecular competition KIE = 1.5). Thus, the Si–H bond cleavage is likely involved in the rate-determining steps. Our preliminary density functional theory (DFT) calculations lend further support to the conjectured CuII-mediated α-metathesis,[19] which proved to be facile to proceed with an activation barrier of 19.7 kcal/mol (Scheme 3C and Figure S3; see the Supporting Information for more details and discussions). Interestingly, the efficiency of the stoichiometric control reaction was greatly diminished (Scheme 3B) likely due to competing CuII reduction by hydrosilanes,[23] which highlights the additional advantage of our reaction design.

On the basis of these results and previous reports, we tentatively proposed a plausible mechanism, as shown in Scheme 3D. First, CuI salt reacts with ligand L* in the presence of base to generate the L*CuI complex I, entering the catalytic cycle. This complex subsequently undergoes SET[26,27] with alkyl bromide to afford alkyl radical II and L*CuI–Br III. The alkyl radical II then undergoes off-cycle radical coupling or radical disproportionation and polymerization for termination. Within the catalytic cycle, base-promoted hydrolysis converts III to L*CuI–OH IV. Its subsequent α-metathesis with dihydrosilane S1 delivers the final enantiopure silanol product 1 and L*CuI–OH V[23] through a four-membered cyclic transition state VI[19] Finally, tandem deprotonation of VI by base[34] and comproportionation of the resulting CuII species with III[35] regenerate the complex I from VI, closing the catalytic cycle. Assuming that the α-metathesis step was enantiodefining, we conjectured two transition states R-TS and S-TS (Scheme 3E) that led to 1 and ent-1, respectively. The latter (Scheme 3E, right) was rendered disfavored possibly due to the steric clash between the Si–phenyl ring and the hydroxide, leading to the favorable formation of 1. Further studies are underway in our lab to disclose more details of the reaction mechanism.
In summary, we have developed a practical and robust copper-catalyzed enantioselective synthesis of a wide range of secondary Si-chiral silanols through the hydroxylation of prochiral dihydrosilanes with water. The successful implementation of the reaction hinges on the use of alkyl bromide as an SET oxidant for in situ continuously generating catalytically active CuII species. In addition, the use of multidentate anionic ligands is also important for ensuring compact $\alpha$-metathesis transition states that result in highly efficient enantiocontrol. Further strategic derivatizations of these secondary Si-chiral silanols deliver a variety of Si-chiral skeletons. This work not only provides a practical synthetic tool to facilitate the development of Si-chiral organosilicon chemistry but also opens the door for exploring CuII-mediated enantioselective hydrosilane transformations.

Acknowledgements

Financial support from the National Natural Science Foundation of China (Nos. 22025103, 22001109, and 21831002), Guangdong Innovative Program (No. 2019B020335), Guangdong Provincial Key Laboratory of Catalysis (No. 2020B121201002), Shenzhen Special Funds (No. JCYJ202001091400101789), and Shenzhen Key Laboratory of Small Molecule Drug Discovery and Synthesis (No. ZDSYS2019JQ020932158777) is acknowledged. The authors appreciate the assistance of SUSTech Core Research Facilities.

Keywords: asymmetric catalysis • copper • metathesis • silanols • single-electron transfer (SET) oxidation


Copper(II)-mediated $\sigma$-metathesis with prochiral dihydrosilanes has been successfully leveraged to efficiently synthesize Si-chiral silanols as well as many other related Si-chiral skeletons. The reaction hinges on the continuous generation of catalytically active copper(II) species via single-electron transfer oxidation of copper(I) by alkyl halides and the efficient stereocontrol with multidentate anionic N,N,P-ligands.