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Intermolecular Chirality Transfer from Silicon to Carbon: Interrogation of the Two-Silicon Cycle for Pd-Catalyzed Hydrosilylation by Stereoisotopochemical Crossover

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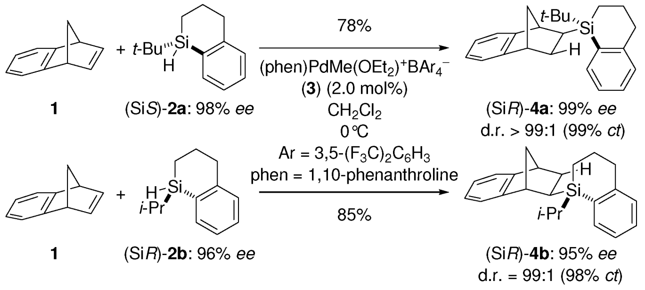
Despite long-standing interest in silicon-stereogenic reagents,[1] it was only recently that highly efficient intra-[2] and intermolecular[3] silicon-to-carbon chirality transfers were achieved. The intermolecular process involves the hydrosilylation of norbornene and norbornene-derivative **1** by chiral silanes **2**, employing cationic Pd precatalyst **3** (Scheme 1).[3] Cyclic silanes such as **2a** and **2b** emerged as excellent reagents for this process.[3] Although these silanes are readily prepared in very high ee,[4] it is the *diastereoisomeric* ratio in the quaternary silane products, for example, **4a** or **4b**, that reveals the exceptionally high *net* chirality transfer (98−99% ct).[3] We have also shown that scalemic samples of **2a** (1.2 equiv, 16−65% ee) give rise to a marked asymmetric amplification: the hydrosilylation product of norbornene (but not **1**) being generated in greater ee than that of the reagent **2**.[3]

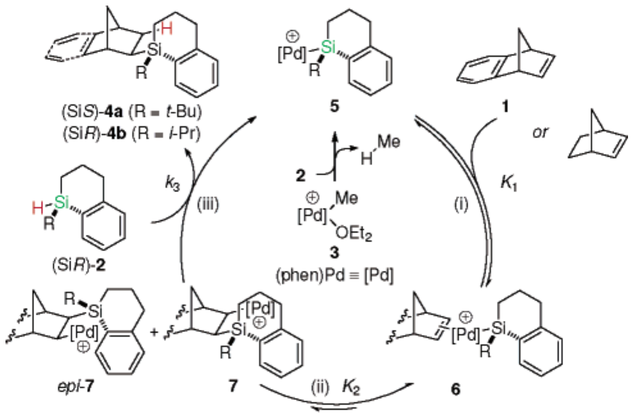
The Pd-catalyzed hydrosilylation of alkenes[5] and dienes[6] by achiral silanes such as Et_3SiH has been studied in great detail by Brookhart et al.[5] and Widenhoefer et al.[6] However, many facets of the stereochemistry in such processes remain to be explored. Herein, we report on the mechanism of the reaction of **1** with **2a** or **2b**, on the elucidation of which step(s) in the catalytic cycle induce the chirality transfer, and on the origin and attenuation (masking) of asymmetric amplification.

Applying the Brookhart model[5] to the reaction of *chiral* silanes **2** with **1** yields the catalytic cycle outlined in Scheme 2. Key features are a silane-mediated precatalyst activation (**3** → **5**), followed by a three-step propagation (i, ii, and iii). In such a "two-silicon cycle", the chirality transfer from silicon to carbon can occur at one or both of two stages: the C−Si bond forming migratory insertion step ii (**6** → **7**) or the C−H bond forming σ-bond metathesis step iii (**7** → **4**). Starting from these considerations, we have designed experiments that both validate the proposed two-silicon cycle and reveal whether the highly efficient chirality transfer arises from step ii or step iii, or both.

Scheme 1. Chirality Transfer (ct) in a Pd-Catalyzed Hydrosilylation



Scheme 2. A Two-Silicon Cycle for Hydrosilylation by **2**



As shown in step iii of Scheme 2, the R_3Si and H moieties of product **4** are delivered from *two separate molecules of* **2** via two sequential turnovers of the catalytic cycle. To test for this, we reacted **1** with a mixture of [^{13}C]-**2a** and [^{2}H]-**2a**. A two-silicon cycle will give rise to a mixture of all four isotopomers (**4a**, [^{13}C]-**4a**, [^{2}H]-**4a**, and [^{2}H,^{13}C]-**4a**) with proportions dependent on the primary kinetic isotope effect (PKIE) attending step iii. For a one-silicon cycle *only* two isotopomers ([^{13}C]-**4a** and [^{2}H]-**4a**) should be obtained, thereby allowing distinction on the basis of isotopic distributions. However, Brookhart has demonstrated that [Pd]-SiR_3 species (cf. **5**) undergo rapid exchange of the silyl moiety with R'_3Si-H.[5] Such a process will have the net effect of scrambling H and ^{2}H between [^{13}C]-**2a** and [^{2}H]-**2a**, thus precluding distinction of a one-silicon from a two-silicon cycle. A series of five experiments, in which conversion (11−38%) and [**1**]/[Pd] (330−3300) were varied, were analyzed by $^{29}Si\{^{1}H\}$ NMR, exploiting a combination of $^{1}J_{SiC}$ and γ-^{2}H isotope shifts.[7] Under conditions of high [**1**] (biasing k_1[**1**][**5a**] towards **6a**) the scrambling of reagents [^{13}C]-**2a**/[^{2}H]-**2a** could be sufficiently suppressed to allow conclusive analysis. A single model, based on the two-silicon cycle (Scheme 2), in which a PKIE of $k_H/k_D = 2.5$ attends cleavage of Si−^{2}H in step iii and in which scrambling is inversely proportional to [**1**], gave an excellent fit for the ^{2}H/^{13}C distributions in **2a** and **4a** in all five runs.[7] The outcome from one run after 38% conversion (127 turnovers) is given in Scheme 3. The magnitude of the PKIE (independently determined as $k_H/k_D = 3.0 \pm 0.5$)[7] suggests small transfer angles[8] in the transition state for step iii, fully consistent with a σ-bond metathesis process.[5,6]

With good evidence for propagation via the two-silicon cycle, we then tested for chirality transfer in step iii by co-reacting enantioenriched (Si*R*)-**2b**[9] (97% ee) with an *achiral* ^{2}H-labeled silane, [^{2}H]-**8** (Scheme 4). These partners were chosen for their comparable reactivity, and we again employed high [**1**] to suppress ^{1}H/^{2}H scrambling (vide supra).[5] Chiral HPLC analysis followed

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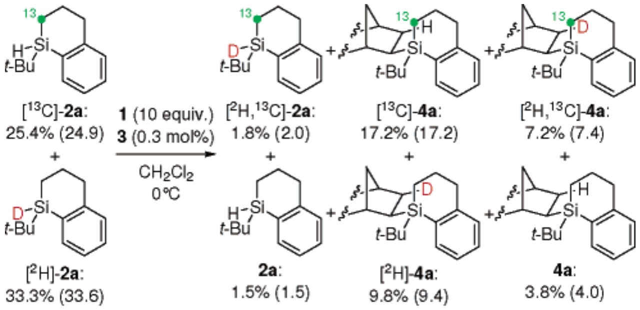
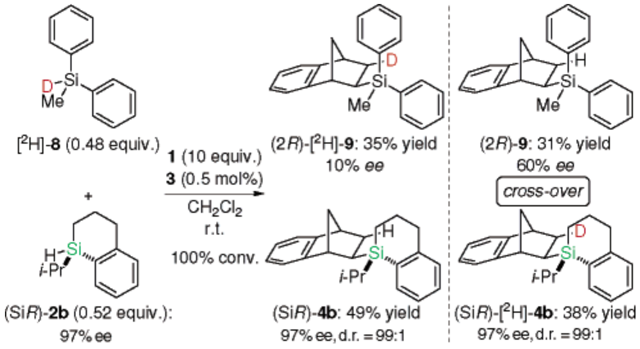
Scheme 3. Analysis of the Two-Silicon Cycle by ^{2}H/^{13}C Crossover[a]



[a] obsd % (calcd) at 38% conversion by ^{29}Si{^{1}H} NMR; 127 turnovers.

Scheme 4. "Traceless Chirality Transfer" from **2b** to Generate **9**

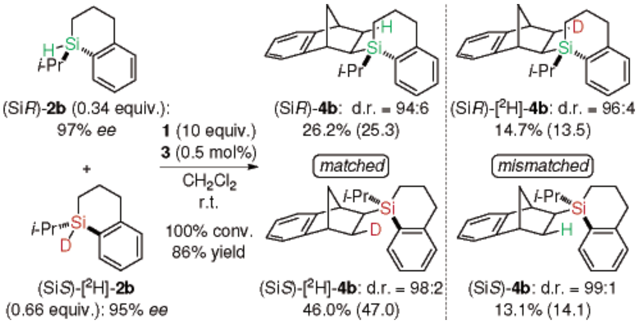


by MS facilitated the quantification of isotopomeric ratios for all four stereoisomers of **4b** and both enantiomers of **9**.[7]

Two distinct conclusions can be drawn from analysis of the chirality transfer in the crossover products, (2*R*)-**9** and (Si*R*)-[^{2}H]-**4b**. First, there is significant asymmetric induction (60% ee) in the generation of **9**, which is liberated by reaction of a racemic Pd-alkyl intermediate (cf. **7**) with (Si*R*)-**2b**, while the solely [^{2}H]-**8** derived product [^{2}H]-**9** is essentially racemic.[7,10] The "traceless chirality transfer" exerted in generation of 60% ee for (2*R*)-**9** demonstrates the profound stereochemical impact of a single chiral silicon moiety in the transition state of step iii of the reaction and confirms reversible silapalladation of alkene **1** by (±)-[Pd]-SiPh$_2$-Me: in effect there is a dynamic kinetic resolution of the Pd-alkyl intermediate. Second, (Si*R*)-[^{2}H]-**4b**, which is liberated by σ-bond metathesis of **7b** with achiral [^{2}H]-**8**, is generated with the same chirality transfer as (Si*R*)-**4b** (dr = 99:1), and thus the chirality transfer arises from step ii alone.

When an excess (1.2 equiv) of scalemic silane **2a** is employed, norbornene gives rise to asymmetric amplification[3] (vide supra). Scheme 2 provides a ready explanation for such a phenomenon: step iii involves *two* silicon-stereogenic units (**7** and **2**), and thus subtle match (m)−mismatch (mm) effects ($k_3^{\mathrm{m}}/k_3^{\mathrm{mm}}$) can kinetically select for the major enantiomer of the reagent **2a**. Modeling of the two-silicon cycle suggests that $k_3^{\mathrm{m}}/k_3^{\mathrm{mm}} = 3$ is sufficiently large to give rise to the observed asymmetric amplification. Given the equally high chirality transfer obtained with **1**, the lack of asymmetric amplification with this alkene is beguiling. However, the model also reveals that the exchange of (Si*S*)-SiR$_3$ with (Si*R*)-SiR$_3$ at the stage of the [Pd]-SiR$_3$ species **5** (vide supra)[5] can completely "mask" the amplification despite substantial match−mismatch effects (see Supporting Information for a full discussion). Efficient capture of **5** by alkene, so as to minimize silane exchange, is thus a prerequisite for efficient asymmetric amplification. As such, the lower reactivity of **1** as compared to norbornene, would explain the lack of amplification with **1**. Conclusive evidence for substantial match−mismatch with **1** was obtained by reaction of quasiscalemic silane **2b** with excess **1**. Analysis by chiral HPLC followed by MS confirmed that the "same-silane" (matched) products are prevalent over the crossover (mismatched) products (Scheme 5). Modeling of the product distributions according to the two-silicon cycle suggests $k_3^{\mathrm{m}}/k_3^{\mathrm{mm}} = 2.5$.[7]

Scheme 5. Match−Mismatch Effects Detected by Crossover[a]



[a] obsd % (calcd); by chiral HPLC and MS, $k_3^{\mathrm{m}}/k_3^{\mathrm{mm}} = 2.5$, PKIE = 2.5.

In summary, the mechanism of intermolecular chirality transfer via a two-silicon cycle has been investigated by means of stereoisotopochemical probes in catalytic crossover experiments. Three important observations emerge: (1) A thermodynamically controlled diastereo-discrimination in the migratory insertion (K_2 vs K_2^{diast}) is the major source of chirality transfer by hydrosilylation (**2** → **4**), albeit manifested by the irreversible σ-bond metathesis reaction (step iii). (2) Under appropriate conditions (scalemic reagent **2**, high K_1; low [**5**]), chirality match−mismatch effects in step iii ($k_3^{\mathrm{m}}/k_3^{\mathrm{mm}}$) can induce asymmetric amplification. (3) Reaction of a silicon-stereogenic silane with a racemic but racemizing σ-alkyl palladium(II) species is able to induce remarkable enantioselectivity (cf. **9**, Scheme 4). These observations bode well for the design of other processes using silicon-based stereoinducers[12] in asymmetric catalysis.

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Supporting Information Available: Full experimental data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(9) **2b** was used instead of **2a** because of the slightly diminished diastereo-selectivity allowing for the detection and separation of all four possible stereoisomers.
(10) The nonzero ee in [^{2}H]-**9** can be ascribed to the generation of traces of [^{2}H]-**2b** through silane exchange.
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