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Rhodium(I)-catalyzed enantioselective 1,4-addition of nucleophilic silicon

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ABSTRACT

A rhodium(I)-catalyzed activation of a silicon–boron linkage, that is, the transmetalation of silicon from boron to rhodium(I) by means of an Rh^{I}–OH complex, enables the conjugate transfer of nucleophilic silicon onto α,β-unsaturated acceptors. Pre- or in situ formed cationic rhodium(I)–binap complexes catalyze this novel carbon–silicon bond formation with exceptional enantiocontrol, 92 to >99% ee for cyclic carbonyl and carboxyl compounds as well as >99% ee for acyclic carboxyl compounds.

1. Introduction

The formation of a carbon–silicon bond is often achieved by 1,4-addition of a silicon nucleophile to an electron-poor α,β-unsaturated acceptor. The textbook reagents for this transformation are a variety of soft silicon-based cuprates, usually stoichiometric in copper.[1] While a stereogenic silicon-bearing carbon atom is formed in this reaction, merely a handful of substrate-controlled protocols were developed to access these synthetically useful[2] building blocks.[3] Reagent- or even catalyst-controlled procedures are still elusive. A few years ago, we had addressed the latter challenge with the development of a copper(I)-catalyzed conjugate silyl transfer employing bis(triorganosilyl) zincs.[4] This methodology had been designed to allow for straightforward screening of chiral ligands but the levels of enantiomeric excess were only minor; the disappointing outcome was rationalized by an uncatalyzed background reaction and the presence of substantial quantities of Lewis acidic lithium cations.[5] We then decided to abandon this strategy and seeked an alternative to realize a catalytic asymmetric silyl transfer onto electron-poor acceptors.

Whereas the copper–silicon reagents described above are directly derived from triorganosilyl lithiums or cognate zincs (along with (over)stoichiometric amounts of lithium chloride) through transmetalation, we envisioned isolable and genuine interelement compounds as sources of nucleophilic silicon. Activation of the interelement linkage[6] was planned to occur again through transmetalation and not oxidative addition. Our thinking was guided by the mechanistic picture established by Hayashi et al. for the rhodium(I)-catalyzed 1,4-addition of carbon nucleophiles to α,β-unsaturated carbonyl compounds.[7] This catalysis begins with a transmetalation step, in which an Rh^{I}–OH complex reacts with a C(sp^2)–B bond to produce the nucleophilic Rh^{I}–C(sp^2) complex. Consequently, we asked ourselves whether the same Rh^{I}–OH complex would show similar reactivity toward an Si–B linkage. We therefore proposed that, in our situation (Scheme 1),[8] the catalysis commences with chemoselective coordination of **1**[9] to the Rh^{I}–OH complex **A**, assuming that in **1** boron is more Lewis acidic than silicon (**A**→**B**). The silicon–boron bond in intermediate **B** is thereby weakened and might be cleaved as indicated by gray arrows, thus liberating a boric acid **C** and Rh^{I}–Si complex **D** (**B**→**D**). The acceptor **E** is then captured by **D**, and conjugate silyl transfer yields rhodium(I) enolate **F** (**D**→**F**), which ejects the active catalyst **A** upon hydrolysis (**F**→**G**).

We note that the Si–B linkage had already been used in several (asymmetric) palladium(0)-[10] and platinum(II)-catalyzed[11] reactions with considerable success but these are likely to be initiated by oxidative addition rather than transmetalation.[6,12] In this full account, we describe the implementation of this novel carbon–silicon bond formation in the racemic[13] and asymmetric[14] series. The enantioselective silyl transfer onto both cyclic carbonyl and carboxyl compounds[15] and acyclic carboxyl compounds[16] will be reported in detail.

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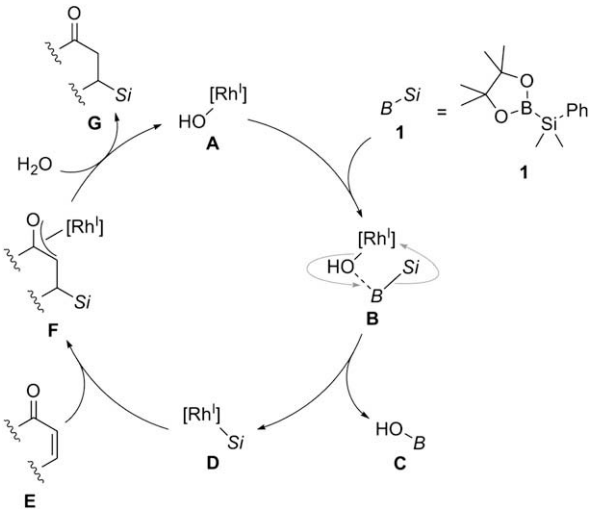


Scheme 1. Tentative catalytic cycle of conjugate silyl transfer.

2. Results and discussion

2.1. Rhodium(I)-catalyzed silyl transfer

On the basis of the aforementioned putative mechanism, we chose the reaction conditions established for the rhodium(I)-catalyzed 1,4-addition of aryl boronic acids as a reasonable starting point.[17] All reactions were performed in degassed aqueous 1,4-dioxane at elevated temperatures employing **1** as the silicon source; out of a number of cyclic α,β-unsaturated carbonyl and carboxyl acceptors (**2**–**4** and **5**–**7**, Fig. 1), 2-cyclohexenone (**3**) was selected as the model substrate.

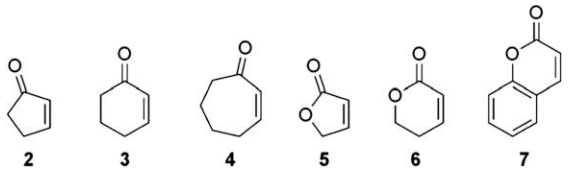
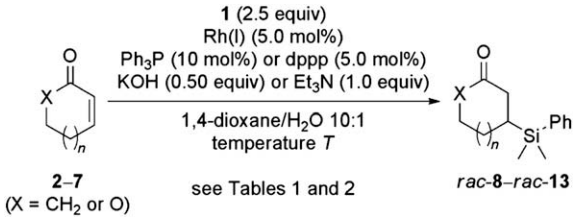


Figure 1. Cyclic α,β-unsaturated acceptors investigated in this study.

The search for catalysts that would facilitate silyl transfer from **1** to **3** commenced with a short screening of preformed rhodium(I)–phosphine complexes and bases (Scheme 2, Table 1); later, several precatalyst–ligand combinations were also tested (vide infra). While chloride-containing, dimeric $[(Ph_3P)_2RhCl]_2$ showed no conversion independent of the presence of KOH (entries 1 and 2, Table 1), minor quantities of *rac*-**9** were seen with cationic $[(dppp)Rh(cod)]ClO_4$ as catalyst even in the absence of KOH (entry 3, Table 1). The chemical yield increased substantially with added KOH but the addition of an equimolar amount of the free bidentate



Scheme 2. Conjugate silyl transfer onto cyclic acceptors (racemic series).

Table 1
Identification of the rhodium(I)–phosphine–base system[a]

Entry	Catalyst precursor[b]	Phosphine	Base	*T*	Yield (%)
1	$[(Ph_3P)_2RhCl]_2$	Ph_3P	—	100	0
2	$[(Ph_3P)_2RhCl]_2$	Ph_3P	KOH	50	0
3	$[(dppp)Rh(cod)]ClO_4$	dppp	—	100	8
4	$[(dppp)Rh(cod)]ClO_4$	dppp	KOH	50	65
5	$[(dppp)Rh(cod)]ClO_4$	—	KOH	50	18
6	$[(dppp)Rh(cod)]ClO_4$	dppp	Et_3N	50	76

[a] Screening (**3**→*rac*-**9**) was conducted using catalyst precursor (2.5 or 5.0 mol %), the indicated phosphine (5.0 or 10 mol %), **1** (2.5 equiv), and the indicated base (0.50 or 1.0 equiv) in 1,4-dioxane–H_2O=10:1 at 50 or 100 °C.
[b] dppp=1,3-bis(diphenylphosphanyl)propane, cod=1,5-cyclooctadiene.

ligand was still crucial (entries 4 and 5, Table 1); Et_3N instead of KOH as base gave an improved yield (entry 6, Table 1).

This protocol, $[(dppp)Rh(cod)]ClO_4$ (5.0 mol %) and dppp (5.0 mol %) in the presence of Et_3N (1.0 equiv), promoted the desired 1,4-addition to cyclic α,β-unsaturated carbonyls **2**–**4** (entries 1–3, Table 2) and carboxyls **5** and **6** (entries 4 and 5, Table 2) in good chemical yields (Scheme 2).

Extension of this general procedure to an acyclic acceptor was successful but required double the amount Rh(I)–dppp. Moderately reactive chalcone underwent the silyl transfer in acceptable yield (*E*-**14**→*rac*-**15**, Scheme 3).

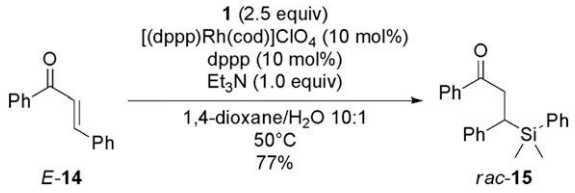
2.2. Cyclic electron-poor acceptors

We then addressed the elusive enantioselective 1,4-addition of nucleophilic silicon to the cyclic substrates depicted in Figure 1. In order to identify a suitable chiral ligand for this transformation

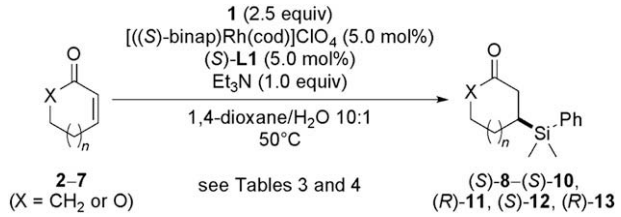
Table 2
Conjugate silyl transfer onto cyclic acceptor (racemic series)[a]

Entry	Acceptor	Product	Yield (%)
1	**2**	*rac*-**8**	82
2	**3**	*rac*-**9**	76
3	**4**	*rac*-**10**	81
4	**5**	*rac*-**11**	44
5	**6**	*rac*-**12**	76

[a] Reactions were conducted using $[(dppp)Rh(cod)]ClO_4$ (5.0 mol %), dppp (5.0 mol %), **1** (2.5 equiv), and Et_3N (1.0 equiv) in 1,4-dioxane–H_2O=10:1 at 50 °C.



Scheme 3. Conjugate silyl transfer onto *E*-chalcone (racemic series).



Scheme 4. Enantioselective conjugate silyl transfer onto cyclic acceptors.

(Table 3), we tested privileged motifs **L1**–**L4** (Fig. 2); **L1**[17] and **L4**[18] seemed particularly promising since these are exceptionally effective in the related asymmetric conjugate addition of Ar–B(OH)$_2$ to α,β-unsaturated carbonyl compounds.

Table 3
Testing of different chiral ligand motifs[a]

Entry	Ligand	Product	Time (h)	Yield (%)	ee[b] (%)
1	(*S*)-**L1**	(*S*)-**8**	12	70	98
2	**L2**	(*R*)-**8**	12	46	97
3	**L3**	*rac*-**8**	12	20	0
4[c]	**L4**	(*S*)-**8**	0.5	75	66

[a] Unless otherwise noted, testing (**2**→(*S*)-**8** or (*R*)-**8**) was conducted using pre-catalyst [Rh(cod)$_2$]OTf (5.0 mol %), the indicated ligand (10 mol %), **1** (2.5 equiv), and Et$_3$N (1.0 equiv) in 1,4-dioxane–H$_2$O=10:1 at 50 °C.
[b] Determined by HPLC analysis using a Daicel Chiralcel OJ-RH column (baseline separation of enantiomers).
[c] Using 5.0 or 10 mol % of **L4** had no influence on the level of enantioinduction while removal of liberated cod under reduced pressure prior to addition of reactants gave a markedly improved enantiomeric excess (85% ee instead of 66% ee).

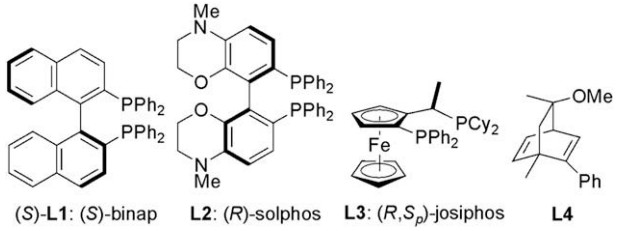


Figure 2. Chiral ligands tested in this survey.

The use of [Rh(cod)$_2$]OTf as a precatalyst rather than preformed rhodium(I)–ligand complexes greatly facilitated this screening; this time, 2-cyclopentenone (**2**), which had performed best in the racemic series, was the test substrate (**2**→**8**, Table 3). To our delight, a mixture of [Rh(cod)$_2$]OTf (5.0 mol %) and either axially chiral ligand **L1** or **L2** (10 mol %) brought about high enantiomeric excess (entries 1 and 2, Table 3). Conversely, planar chiral **L3** afforded essentially racemic material in poor chemical yield. Whereas these reactions were all relatively slow (hour time scale), the conjugate transfer occurred on a minute time scale in the presence of chiral diene ligand **L4** (entry 4, Table 3). It is important to note that the enantiomeric excess of 66% was further increased to 85% by pre-treatment of [Rh(cod)$_2$]OTf with **L4** and subsequent evaporation of liberated cod under reduced pressure.

With the optimal Rh(I)–**L1** combination in hand, we prepared preformed [((*S*)-binap)Rh(cod)]ClO$_4$ and applied the asymmetric conjugate silyl transfer to acceptors **2**–**7** (Scheme 4, Table 4). Carbonyl compounds **2**–**4** gave high enantiomeric excesses but yields varied significantly (entries 1–3, Table 4); 2-cycloheptenone (**4**) is known to be a peculiar substrate in the corresponding arylation[19] (51%, 92% ee vs 22%, 92% ee for (*S*)-**10**). As exemplified for **2**→(*S*)-**8**, [Rh(cod)$_2$]OTf–(*S*)-binap (1:2) and preformed [((*S*)-binap)Rh(cod)]ClO$_4$–(*S*)-binap (1:1) operated equally well (entry 1, Tables 3 and 4). Carboxyl compounds, that is, lactones **5**–**7**, performed extremely well in terms of the level of enantioinduction (entries 4–6, Table 4). Interestingly,

Table 4
Enantioselective conjugate silyl transfer onto cyclic acceptors[a]

Entry	Acceptor	Product	Yield (%)	ee[b] (%)
1	**2**	(*S*)-**8**	70	98
2	**3**	(*S*)-**9**	45	96
3	**4**	(*S*)-**10**	22	92
4	**5**	(*R*)-**11**	39	>99
5	**6**	(*S*)-**12**	58	98
6	**7**	(*R*)-**13**	9[c]	98

[a] All reactions were conducted using [((*S*)-binap)Rh(cod)]ClO$_4$ (5.0 mol %), (*S*)-**L1** (5.0 mol %), **1** (2.5 equiv), and Et$_3$N (1.0 equiv) in 1,4-dioxane–H$_2$O=10:1 at 50 °C.
[b] Determined by HPLC analysis using Daicel Chiralcel and Chiralpak columns (baseline separation of enantiomers).
[c] The reduced acceptor (formal 1,4-reduction) was isolated in 32% yield.

the formation of (*R*)-**13** from **7** was poor-yielding, and we observed the reduced acceptor (formal 1,4-reduction) for the first time, a fatal side reaction in the conjugate silyl transfer onto acyclic acceptors (vide infra).

The catalysis was sensitive toward the amount of **1** used, the rhodium(I)–ligand ratio and the base: (i) chemical yields collapsed when using less than 2.5 equiv of **1**; (ii) the uncommon ratio of 1:2 instead of 1:1 is not unprecedented[20a] and resulted in better overall performance (chemical yields and enantiomeric excesses)[20b] of the system; (iii) as summarized in Table 5, the choice of the base was also important;[17] remarkably the commonly used base KOH deteriorated the enantiomeric excess!

Table 5
Influence of the base on enantioselectivity[a]

Entry	Acceptor	Product	Base	Yield (%)	ee (%)
1	**2**	(*S*)-**8**	Et_3N	70	98
2	**2**	(*S*)-**8**	TMP[b]	75	96
3	**2**	(*S*)-**8**	Morpholine	0	—
4	**2**	(*S*)-**8**	K_3PO_4	71	98
5	**2**	(*S*)-**8**	KOH	68	59

[a] All reactions (**2**→(*S*)-**8**) were conducted using precatalyst [((*S*)-binap)Rh(cod)]ClO_4 (5.0 mol %), (*S*)-**L1** (5.0 mol %), **1** (2.5 equiv), and the indicated base (1.0 equiv) in 1,4-dioxane–H_2O=10:1 at 50 °C.
[b] TMP=2,2,6,6-tetramethylpiperidine.

Carbonyl compounds (*S*)-**8**–(*S*)-**10** failed to crystallize, which is why their configurational assignment is based on reported data.[21,22] Gratifyingly, the absolute configuration of carboxyl compounds (*S*)-**12** (Fig. 3) as well as (*R*)-**13** (Fig. 4) was unambiguously secured by X-ray diffraction, (*R*)-**11** was assigned accordingly. The latter configurations are in agreement with those of the carbonyl compounds.

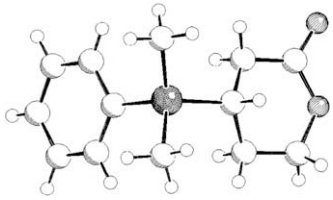


Figure 3. Molecular structure of (*S*)-**12**.

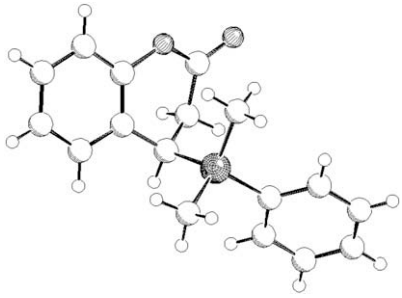
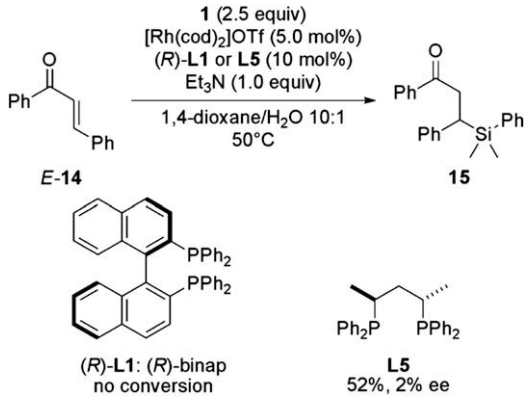


Figure 4. Molecular structure of (*R*)-**13**.

2.3. Acyclic electron-poor acceptors

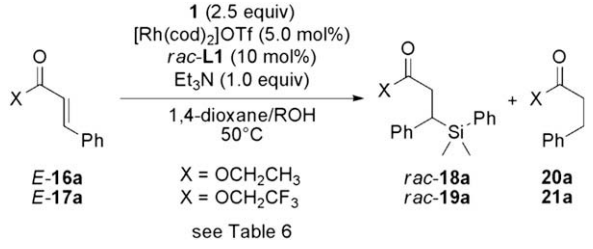
The next obvious step was to extend this methodology to acyclic α,β-unsaturated acceptors. Since we had already accomplished the conjugate silyl transfer onto *E*-**14** in the racemic series (Scheme 3), we logically supposed that replacing achiral dppp by chiral binap (**L1**) would render this transformation enantioselective. However, treatment of *E*-**14** with **1** in the presence of our established catalyst system showed no conversion at all; the starting material was reisolated in quantitative yield (Scheme 5). Realizing that **L1** is not a good ligand for this reaction, we used a ligand structurally and electronically very similar to dppp, ligand **L5**. Indeed, *E*-**14** was now successfully silylated to give **15** in 52% isolated yield yet in almost racemic form (Scheme 5). At this stage, it had already become clear that cyclic and acyclic acceptors display different reactivity patterns in this reaction.

As acyclic α,β-unsaturated enones failed to react, we turned to the corresponding esters. When subjecting *E*-**16a** and electron-



Scheme 5. Attempted enantioselective silyl transfer onto *E*-chalcone.

poorer *E*-**17a** to the standard reaction conditions (Scheme 6), we encountered an even more serious hurdle. Unexpectedly, *E*-**16a** furnished none of the desired adduct *rac*-**18a** but the reduced acceptor **20a** in high chemical yield (entry 1, Table 6). This reaction channel was first observed with benzannulated lactone **7** (entry 6, Table 4), also a β-aryl-α,β-unsaturated carboxyl compound. We had recently discussed competing conjugate addition and reduction pathways in connection with a transition metal-free stannyl transfer in basic aqueous media.[23] The tentative ionic mechanism outlined in that work might also apply to the present problem: an allylic and benzylic carbon–silicon bond in the intermediate β-silyl rhodium(I) enolate is relatively labile and might be prone to cleavage by nucleophilic attack at the silicon atom. While this might rationalize the experimental observations for β-arylated acceptors, we still cannot provide a general explanation for the formal conjugate reduction. We were at least able to rule out a rhodium(I)-catalyzed hydrosilylation (**1** is not hydrolyzed) and we are also considering radical pathways as the boron reagent **1** might provide an entry into radical chemistry in aqueous media.[24]



Scheme 6. Competing conjugate silyl transfer and reduction.

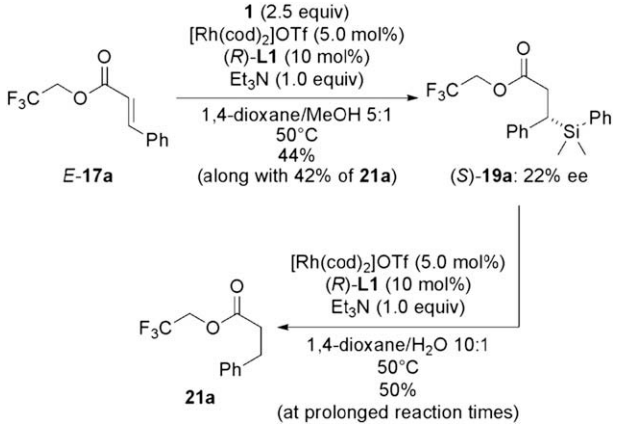
Table 6
Competing conjugate silyl transfer and reduction[a]

Entry	Ester	Solvent system		Conv[b] %	Silyl transfer versus reduction	
		ROH	Ratio[c]		Yield of *rac*-**18a** or *rac*-**19a** (%)	Yield of **20a** or **21a** (%)
1	*E*-**16a**	H_2O	10:1	100	0	75
2	*E*-**17a**	H_2O	10:1	100	5	65
3	*E*-**17a**	MeOH	5:1	100	45	30
4	*E*-**17a**	EtOH	5:1	90	20	35
5	*E*-**17a**	*i*-PrOH	5:1	90	40	35
6	*E*-**17a**	*t*-BuOH	5:1	70	25	30

[a] All reactions were conducted using [$Rh(cod)_2$]OTf (5.0 mol %), *rac*-**L1** (10 mol %), **1** (2.5 equiv), and Et_3N (1.0 equiv) in 1,4-dioxane–ROH=10:1 at 50 °C.
[b] Determined by GLC analysis using an SE-54 column with *n*-decane as an internal standard.
[c] 1,4-Dioxane–ROH ratio.

We then probed more reactive substrate *E*-**17a** under the same reaction conditions (Scheme 6). Again, saturated **21a** was formed in high yield but this time minor quantities of *rac*-**19a** were also detected (entry 2, Table 6). Based on the latter result, we started to systematically survey different 1,4-dioxane–alcohol mixtures, which is one of the few modifiable parameters in this reaction (no conversion is seen in toluene as solvent). In all cases, both *rac*-**19a** and **21a** were generated in varying ratios (entries 3–6, Table 6) with MeOH clearly favoring conjugate addition over reduction (entry 3, Table 6).

With this slightly modified solvent mixture, we returned to the asymmetric silyl transfer and repeated the reaction using (*R*)-**L1** as the chiral ligand (Scheme 7). As expected, we were able to isolate (*S*)-**19a** along with **21a** in yields similar to that of the racemic series. Unfortunately, the enantiomeric excess of 22% for (*S*)-**19a** was low. The above optimization to finally accomplish the silyl transfer onto an acyclic acceptor involved countless experiments, in the course of which we learned that the β-arylated β-silyl carboxyl compounds undergo protodesilylation upon being exposed to our reagent–solvent cocktail. In a control run, a pure sample of (*S*)-**19a** was maintained under the standard conditions for 12 h, at which approximately half of the material had suffered desilylation to give **21a** (Scheme 7). The intermediacy of an enolate formed in equilibrium with a weakened allylic and benzylic carbon–silicon bond might account for this (vide supra).[23]



Scheme 7. Enantioselective silyl transfer onto an *E*-configured electron-poor acceptor followed by decomposition.

After ongoing failure with *E*-configured α,β-unsaturated carbonyl and carboxyl compounds, we concluded that we would need acyclic substrates resembling the geometry of the successful cyclic systems. In other words, acyclic acceptors with a *Z* alkene unit would have been the more obvious choice right from the start! Hence, we prepared a couple of *Z*-configured α,β-unsaturated ketones but these, to our surprise, isomerized rapidly under the standard conditions. Conversely, *Z*-configured α,β-unsaturated esters proved to be configurationally stable, and we prepared several β-aryl- and β-alkyl-substituted esters *Z*-**16a**–**g**, 'active' esters *Z*-**17a**,**e**, and imides *Z*-**22a**,**e** (Fig. 5). These precursors were accessed by diastereoselective Lindlar reduction using 1-hexene as solvent in order to suppress any over-reduction.[16]

In the silyl transfer onto *Z*-α,β-unsaturated esters, reduction still occurred but was not prevailing, ranging from 10–20% if not less. Almost all acceptors depicted in Figure 5 reacted in the asymmetric 1,4-addition with good chemical yields (Scheme 8, Table 7). Importantly, exceptional levels of enantioselection were invariably detected for arylated (entries 1–4, 8, and 10, Table 7) and alkylated (entries 6, 9, and 11) acceptors, in some cases even if the alkyl chain

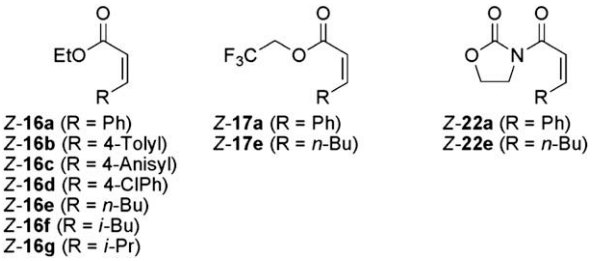
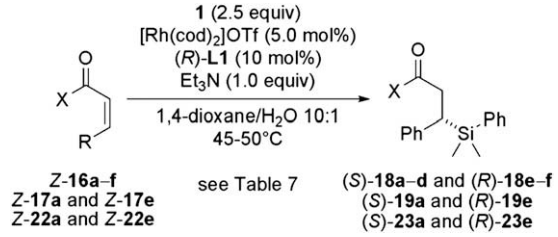
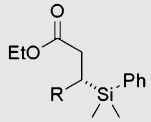
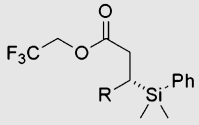
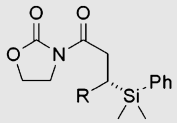


Figure 5. Acyclic *Z*-configured α,β-unsaturated acceptors investigated in this study.



Scheme 8. Enantioselective silyl transfer onto *Z*-configured acceptors.

Table 7
Enantioselective conjugate silyl transfer onto acyclic acceptors[a]

Entry	Acceptor[b]	Product	R	Yield (%)	ee[c] (%)
1	*Z*-**16a**	 (*S*)-**18a**–**d** and (*R*)-**18e**–**f**	Ph	66[d]	>99
2	*Z*-**16b**		4-Tolyl	58[d]	>99
3	*Z*-**16c**		4-Anisyl	50	>99
4	*Z*-**16d**		4-ClPh	58[d]	>99
5	*Z*-**16e**		*n*-Bu	55	>99
6	*Z*-**16f**		*i*-Bu	44	>99
7	*Z*-**16g**		*i*-Pr	0	—
8	*Z*-**17a**	 (*S*)-**19a** and (*R*)-**19e**	Ph	65	>99
9	*Z*-**17e**		*n*-Bu	72[d]	98[e]
10	*Z*-**22a**	 (*S*)-**23a** and (*R*)-**23e**	Ph	60	>99
11	*Z*-**22e**		*n*-Bu	58[d]	>99

[a] Unless otherwise noted, all reactions were conducted using $[Rh(cod)_2]OTf$ (5.0 mol %), (*R*)-**L1** (10 mol %), **1** (2.5 equiv), and Et_3N (1.0 equiv) in 1,4-dioxane–H_2O=10:1 at 50 °C.

[b] *Z*/*E* ratio determined by ^1H NMR spectroscopy and thus estimated to be *Z*/*E* >95:5.

[c] Determined by HPLC analysis using Daicel Chiralcel and Chiralpak columns (baseline separation of enantiomers).

[d] Yield obtained when the reaction temperature was carefully maintained at 45 °C.

[e] Slightly diminished because acceptor is not isomerically pure (*Z*/*E*=95:5).

was branched (entries 6 and 7, Table 7). Likely due to lower reactivity, a number of synthetically useful acceptors *Z*-**24**–*Z*-**27** failed to participate in this rhodium(I) catalysis; the starting materials were always recovered quantitatively (Fig. 6).

In the previous section on cyclic electron-poor acceptors, we had identified binap (**L1**) as an ideal ligand for this rhodium(I)-catalyzed process. We also tested ligands **L2**–**L4** (Fig. 2) in the

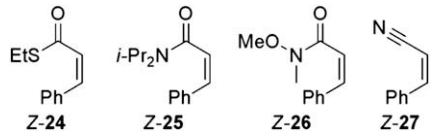


Figure 6. Unreactive acyclic *Z*-configured α,β-unsaturated acceptors.

reaction of *Z*-cinnamate *Z*-**16a** (Table 8). In contrast to (*R*)-**L1** (entry 1, Table 8), its surrogate (*R*)-solphos (**L2**) failed to promote the conjugate silyl transfer, reduction was seen instead (entry 2, Table 8). The same result was obtained with (R,S_p)-josiphos (**L3**) and chiral diene (**L4**) (entries 3 and 4, Table 8). The reaction rate in the presence of **L4** was once again high (vide supra).

Table 8
Testing of different chiral ligand motifs[a]

Entry	Ligand	Time (h)	Silyl transfer versus reduction		ee[b] (%)
			Yield of (*S*)-**18a** (%)	Yield of **20a** (%)	
1	(*R*)-**L1**	2	56	10	>99
2	**L2**	15	10	75	—
3	**L3**	15	10	50	—
4	**L4**	0.5	0	75	—

[a] Unless otherwise noted, testing (*Z*-**16a**→(*S*)-**18a**) was conducted using pre-catalyst [Rh(cod)$_2$]OTf (5.0 mol %), the indicated ligand (10 mol %), **1** (2.5 equiv), and Et_3N (1.0 equiv) in 1,4-dioxane–H_2O=10:1 at 50 °C.
[b] Determined by HPLC analysis using a Daicel Chiralpak IB column (baseline separation of enantiomers).

3. Summary

The asymmetric conjugate silyl transfer onto electron-poor α,β-unsaturated acceptors had been one of the open challenges of organosilicon chemistry. We developed a general highly enantioselective procedure based on a novel activation mode of the silicon–boron interelement linkage. Aside from this catalytic asymmetric carbon–silicon bond formation,[15,16] a number of alternative (general) approaches relying on established catalytic asymmetric carbon–carbon[25] and carbon–hydrogen[26] bond formation were developed yet starting from stereodefined silicon-containing substrates. We are currently extending our methodology to more complex substrates.

4. Experimental

4.1. General information

All reactions were performed in flame-dried glassware under a static pressure of argon. Liquids and solutions were transferred with syringes; 1,4-dioxane was purified following a standard procedure, both 1,4-dioxane and H_2O were thoroughly degassed prior to use. Et_3N was distilled from CaH_2 and stored at −20 °C under exclusion of air. Technical grade solvents for flash chromatography (cyclohexane and EtOAc) were distilled before use. Flash chromatography was performed on silica gel 60 (40–63 μm, 230–400 mesh, ASTM) by Merck. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on Bruker AM/AV 300 and, AM/AV 400 instruments as well as on a Varian MERCURY 300 HFCP instrument. Chemical shifts are reported in parts per million with the solvent reference as the internal standard (δ=7.26 ppm for ^{1}H NMR and δ=77.1 ppm for ^{13}C NMR). Gas liquid chromatography (GLC) was performed on a Shimadzu GC-17A with an SE-54 (30 m×0.32 mm×0.25 μm film thickness) column by CS-Chromatographie Service. Infrared spectra were recorded on a Digilab Excalibur Series FTS 4000 spectrophotometer. Enantiomeric ratios were determined by analytical HPLC analysis on an Agilent 1200 Series with a chiral stationary phase using Daicel Chiralpak AD-H and IB as well as Daicel Chiralcel OJ-H and OJ-RH columns (*n*-heptane–*i*-PrOH or MeCN–H_2O as solvent mixtures). Optical rotations were measured on a Perkin Elmer 341 polarimeter. High resolution mass spectrometry (HRMS) and electron spray ionization mass spectrometry (ESI-MS) were performed by the Analytic Department at the Organisch-Chemisches Institut, Universität Münster.

Full experimental data for *Z*-configured α,β-unsaturated acceptors and enantioenriched β-silylated carboxyl compounds (Table 6) are reported in the Supplementary data of Ref. 16.

4.2. General procedure for catalytic asymmetric silyl transfer

In a flame-dried Schlenk tube equipped with a magnetic stir bar, [(binap)Rh(cod)]ClO_4 (5.0 mol %) and binap (**L1**) (5.0 mol %) or [Rh(cod)$_2$]OTf (5.0 mol %) and binap (**L1**) (10 mol %) were dissolved in 1,4-dioxane–H_2O 10:1 (1.0 mL) and stirred for 10 min. The acceptor (0.2 mmol), Et_3N (0.2 mmol, 1.0 equiv), and **1**[9] (0.5 mmol, 2.5 equiv) were added in this order. The mixture was stirred at 50 °C (or the indicated temperature) until GLC showed almost complete conversion of the substrate. After quenching with ethyl acetate, the solvents were evaporated under reduced pressure. The residue was purified using flash chromatography (SiO_2, cyclohexane–ethyl acetate 98:2) yielding the product; if contaminated with the reduced acceptor, further purification was achieved by evaporation of the lower-boiling by-product under high vacuum at slightly elevated temperatures.

*4.2.1. (S)-3-Dimethylphenylsilylcyclopentanone, (S)-**8***

Colorless oil; yield: 70%; $[\alpha]_D^{20}$ −131 (*c* 4.3, $CHCl_3$); 98% ee. The enantiomeric excess was determined by HPLC using a chiral column [Chiralcel OJ-RH, column temperature 20 °C, MeCN–H_2O (50:50), 0.5 mL/min, 230 nm, retention times: 17.1 min (*S*) and 18.5 min (*R*)]. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.32–0.36 (m, 6H), 1.48–1.78 (m, 2H), 1.84–1.92 (m, 1H), 2.03–2.34 (m, 4H), 7.36–7.41 (m, 3H), 7.49–7.54 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ −5.0, −4.9, 23.9, 25.0, 39.3, 40.1, 127.9, 129.3, 133.8, 136.9, 220.9. IR (ATR) 1737 cm^{-1}. HRMS (ESI) calcd for $C_{13}H_{18}OSiNa$ ([M+Na]$^+$): 241.1019, found: 241.1015.

*4.2.2. (S)-3-Dimethylphenylsilylcyclohexanone, (S)-**9***

Colorless oil; yield: 45%; $[\alpha]_D^{20}$ −85.8 (*c* 2.9, $CHCl_3$); 96% ee. The enantiomeric excess was determined by HPLC using a chiral column [Chiralpak AD-H, column temperature 24 °C, *n*-heptane–*i*-PrOH (100:1), 0.8 mL/min, 230 nm, retention times: 9.45 min (*S*) and 10.7 min (*R*)]. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.31 (m, 6H), 1.29 (m, 1H), 1.42 (m, 1H), 1.70 (m, 1H), 1.78–1.85 (m, 1H), 2.05–2.18 (m, 2H), 2.21–2.40 (m, 3H), 7.35–7.40 (m, 3H), 7.46–7.50 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ −4.9, −4.7, 26.6, 28.2, 30.3, 42.5, 43.3, 128.4, 129.8, 134.4, 137.1, 213.3. IR (ATR) 1708 cm^{-1}. HRMS (ESI) calcd for $C_{14}H_{20}OSiNa$ ([M+Na]$^+$): 255.1176, found: 255.1164.

*4.2.3. (S)-3-Dimethylphenylsilylcycloheptanone, (S)-**10***

Colorless oil; yield: 22%; $[\alpha]_D^{20}$ −73.7 (*c* 0.70, $CHCl_3$); 92% ee. The enantiomeric excess was determined by HPLC using a chiral column [Chiralpak AD-H, column temperature 24 °C, *n*-heptane–*i*-PrOH (100:1), 0.8 mL/min, 230 nm, retention times: 13.5 min (*S*) and 14.9 min (*R*)]. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.30 (m, 6H), 1.02–1.37 (m, 3H), 1.49 (m, 1H), 1.83–2.06 (m, 3H), 2.28–2.63 (m, 4H), 7.33–7.40 (m, 3H), 7.46–7.52 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ −4.6, −4.4, 23.9, 25.0, 31.7, 32.5, 44.0, 45.1, 128.4, 129.8, 134.5, 137.6, 216.0. IR (ATR) 1696 cm^{-1}. HRMS (ESI) calcd for $C_{15}H_{22}OSiNa$ ([M+Na]$^+$): 269.1332, found: 269.1328.

*4.2.4. (R)-4-Dimethylphenylsilyl-3H-furan-2-one, (R)-**11***

Colorless oil; yield: 39%; $[\alpha]_D^{20}$ −5.64 (*c* 0.99, $CHCl_3$); >99% ee. The enantiomeric excess was determined by HPLC using a chiral column [Chiralpak IB, column temperature 20 °C, *n*-heptane–*i*-PrOH (90:10), 0.8 mL/min, 230 nm, retention times: 15.7 min (*R*) and 18.0 min (*S*)]. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.37 (m, 6H), 2.06 (m, 1H), 2.29 (dd, *J*=17.3, 12.6 Hz, 1H), 2.51 (dd, *J*=17.2, 8.7 Hz, 1H), 4.11 (dd, *J*=11.3, 9.0 Hz, 1H), 4.43 (dd, *J*=8.7, 8.7 Hz, 1H), 7.36–7.49 (m, 5H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ −5.0, −4.8, 23.9, 30.4, 70.9, 128.1, 130.0, 133.7, 135.2, 178.1. IR (ATR) 1769 cm^{-1}. HRMS (ESI) calcd for $C_{12}H_{16}O_2SiNa$ ($[M+Na]^+$): 243.0812, found: 243.0818.

*4.2.5. (S)-4-Dimethylphenylsilyltetrahydropyran-2-one, (S)-**12***

Colorless oil; yield: 58%; $[\alpha]_D^{20}$ −36.3 (*c* 1.0, $CHCl_3$); 98% ee. The enantiomeric excess was determined by HPLC using a chiral column [Chiralpak AD-H, column temperature 24 °C, *n*-heptane–*i*-PrOH (97:3), 0.8 mL/min, 230 nm, retention times: 19.3 min (*S*) and 20.3 min (*R*)]. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.33 (m, 6H), 1.40 (m, 1H), 1.65 (m, 1H), 1.85 (m, 1H), 2.27 (dd, *J*=17.4, 12.6 Hz, 1H), 2.57 (ddd, *J*=17.4, 5.7, 1.5 Hz, 1H), 4.20–4.33 (m, 2H), 7.33–7.42 (m, 3H), 7.45–7.50 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ −5.7, −5.6, 18.4, 23.7, 30.9, 70.3, 128.1, 129.7, 133.9, 135.5, 171.6. IR (ATR) 1732 cm^{-1}. HRMS (ESI) calcd for $C_{13}H_{18}O_2SiNa$ ($[M+Na]^+$): 257.0968, found: 257.0953.

*4.2.6. (R)-4-Dimethylphenylsilylchroman-2-one, (R)-**13***

Colorless oil; yield: 9%; $[\alpha]_D^{20}$ −4.30 (*c* 0.78, $CHCl_3$); 98% ee. The enantiomeric excess was determined by HPLC using a chiral column [Chiralcel OJ-H, column temperature 20 °C, *n*-heptane–*i*-PrOH (90:10), 0.7 mL/min, 230 nm, retention times: 17.3 min (*R*) and 19.6 min (*S*)]. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.25 (m, 6H), 2.56 (dd, *J*=7.6, 2.4 Hz, 1H), 2.72 (dd, *J*=16.2, 2.4 Hz, 1H), 2.78 (dd, *J*=16.2, 7.6, 1H), 6.82 (m, 1H), 6.94 (m, 2H), 7.10 (m, 1H), 7.26–7.37 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ −5.4, −4.8, 26.2, 30.3, 117.1, 124.1, 125.1, 126.8, 127.7, 128.0, 129.9, 134.0, 135.0, 151.2, 168.8. IR (ATR) 1773 cm^{-1}. HRMS (ESI) calcd for $C_{17}H_{18}O_2SiNa$ ($[M+Na]^+$): 282.1076, found: 282.1034.

4.3. X-ray data

4.3.1. General information

Datasets were collected with a Nonius KappaCCD diffractometer. Programs used: data collection COLLECT (Nonius B. V., 1998), data reduction Denzo-SMN,[27a] absorption correction Denzo,[27b] structure solution SHELXS-97,[27c] structure refinement SHELXL-97,[27d] graphics SCHAKL (Universität Freiburg, **1997**).

Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication. CCDC-700992 [(*S*)-**12**] and CCDC-700993 [(*R*)-**13**] contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336–033; E-mail: deposit@ccdc.cam.ac.uk].

*4.3.2. X-ray crystal structure analysis for (S)-**12***

Formula $C_{13}H_{18}O_2Si$, *M*=234.36, colorless crystal, 0.30×0.25×0.15 mm, *a*=6.6682(4), *b*=8.3843(5), *c*=12.7971(8) Å, α=77.805(5)°, β=75.402(1)°, γ=71.187(4)°, *V*=648.75(7) Å^3, ρ_{calcd}=1.200 g cm^{-3}, μ=1.467 mm^{-1}, empirical absorption correction (0.667≤*T*≤0.810), *Z*=2, triclinic, space group *P*1 (no. 1), λ=1.54178 Å, *T*=223(2) K, ω and φ scans, 5958 reflections collected ($\pm h$, $\pm k$, $\pm l$), $[(\sin\theta)/\lambda]$=0.60 Å^{-1}, 2719 independent (R_{int}=0.036) and 2607 observed reflections [$I\geq 2\sigma(I)$], 293 refined parameters, *R*=0.062, wR^2=0.173, Flack parameter 0.05(5), max (min) residual electron density 0.26 (−0.45) e/Å^3, two almost identical molecules in the asymmetric unit, hydrogen atoms calculated and refined as riding atoms.

*4.3.3. X-ray crystal structure analysis for (R)-**13***

Formula $C_{17}H_{18}O_2Si$, *M*=282.40, colorless crystal 0.40×0.30×0.10 mm, *a*=6.3217(1), *b*=13.4366(1), *c*=9.0172(1) Å, β=104.780(1)°, *V*=740.60(2) Å^3, ρ_{calcd}=1.266 g cm^{-3}, μ=1.382 mm^{-1}, empirical absorption correction (0.608≤*T*≤0.874), *Z*=2, monoclinic, space group $P2_1$ (no. 4), λ=1.54178 Å, *T*=223(2) K, ω and φ scans, 4777 reflections collected ($\pm h$, $\pm k$, $\pm l$), $[(\sin\theta)/\lambda]$=0.60 Å^{-1}, 2280 independent (R_{int}=0.031) and 2261 observed reflections [$I\geq 2\sigma(I)$], 183 refined parameters, *R*=0.036, wR^2=0.097, Flack parameter 0.05(3), max (min) residual electron density 0.38 (−0.15) e/Å^3, hydrogen atoms calculated and refined as riding atoms.

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