Asymmetric Catalysis

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Catalytic Asymmetric C–Si Bond Formation to Acyclic α,β-Unsaturated Acceptors by Rh^I-Catalyzed Conjugate Silyl Transfer Using a Si–B Linkage**

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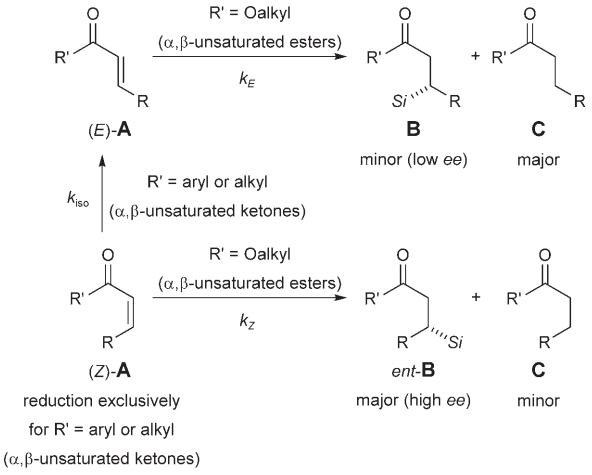
Dedicated to Professor Larry E. Overman on the occasion of his 65th birthday

Transition-metal-catalyzed activation of interelement linkages[1] for the subsequent functionalization of unsaturated carbon skeletons is now part of the standard repertoire of synthetic organic chemistry;[2] currently its elusive enantioselective variants are garnering considerable attention.[3] In this context, the catalytic asymmetric addition of both a Si–Si (Cl_2PhSi-$SiMe_3$)[4,5] and a Si–B (Me_2PhSi-Bpin)[6] (pin = pinacolato) bond across α,β-unsaturated acceptors[7] is particularly attractive as it provides direct access[8,9] to synthetically versatile, chiral β-silyl carbonyl compounds.[10] Indeed, an exciting report disclosed a Pd^0-catalyzed disilylation of an acyclic enone with promising enantiomeric excess (92% *ee*) almost two decades ago.[4] It remained, however, the sole example until we recently devised a Rh^I-catalyzed silaboration of cyclic enones and a lactone with useful enantioselectivity (92–98% *ee*).[6]

We soon learned that application of this procedure to acyclic α,β-unsaturated acceptors is certainly not a simple task (Scheme 1). Strikingly, conjugate reduction was found to occur with α,β-unsaturated ketones (R′ = aryl or alkyl) exclusively (**A**→**C**), a reaction pathway that is not seen in related cyclic systems.[6] Moreover, a *Z* double bond rapidly isomerized [(*Z*)-**A**→(*E*)-**A**] prior to any product formation ($k_{iso} > k_E$ and k_Z). To our delight, α,β-unsaturated esters (R′ = Oalkyl) underwent the desired C–Si bond formation (**A**→**B**) but 1,4-reduction was again competing (**A**→**C**). As for the conjugate silyl transfer, *Z* acceptors were markedly more reactive than the corresponding *E* precursors ($k_Z > k_E$) and were, in this case, not prone to isomerization ($k_{iso} = 0$).



Scheme 1. Unexpected reaction pathways of acyclic acceptors. Reaction conditions: $[Rh(cod)_2]OTf$ (5.0 mol%), (*R*)-binap (10 mol%[11]), Me_2PhSi-Bpin (**1**)[12] (2.5 equiv), Et_3N (1.0 equiv), 1,4-dioxane/H_2O (10:1, 0.20 M), 50 °C. *Si* = $SiMe_2Ph$, R = aryl or alkyl, OTf = trifluoromethanesulfonate, (*R*)-binap = (*R*)-2,2′-bis(diphenylphosphanyl)-1,1′-binaphthyl, cod = cycloocta-1,5-diene.

The unexpected isomerization and 1,4-reduction are still not understood at all. A few control experiments were inconclusive; we were able to rule out Rh^I-catalyzed hydrosilylation after hydrolysis of **1**. We currently believe that the boron reagent Me_2PhSi-Bpin (**1**)[12] in aqueous media might provide an entry into radical chemistry.[13,14] With the focus on methodology development, we then continued to assess α,β-unsaturated esters with *Z* geometry in this Rh^I catalysis. In this communication, we present an unprecedented conjugate silyl transfer onto *Z*-configured carboxyl compounds with exceptional levels of enantioselection.

With ethyl (*Z*)-cinnamate (R = Ph and R′ = OEt) as a model, we tested selected chiral ligand motifs using [Rh(cod)$_2$]OTf as a precatalyst [(*Z*)-**2a**→(*S*)-**3a**, Table 1]. In the presence of (*R*)-binap the catalysis afforded (*S*)-**3a** along with some reduced material with impressive enantioselecitivity of > 99% *ee* (Table 1, entry 1). In contrast, the surrogate ligands (*S*)-Cl-MeO-biphep and (*R*)-solphos failed to produce appreciable quantities of the product (Table 1, entries 2 and 3). Other privileged ligands such as (R,S_p)-josiphos and Carreira's diene[15] were totally inefficient in this reaction (Table 1, entries 4 and 5).

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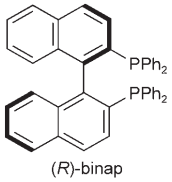
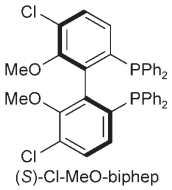
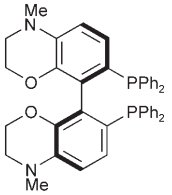
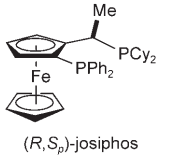
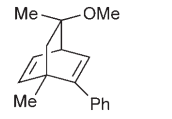
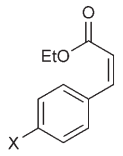
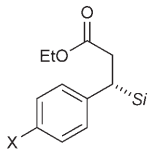
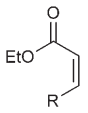
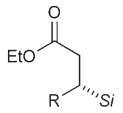
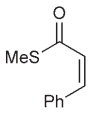
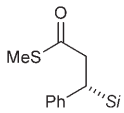
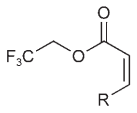
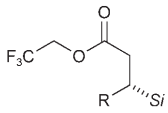
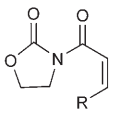
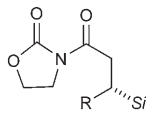
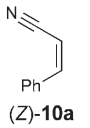
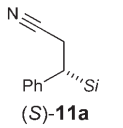
Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

Table 1: Ligand screening in the enantioselective conjugate silyl transfer onto ethyl (*Z*)-cinnamate [(*Z*)-**2a** → (*S*)-**3a**].[a,b]

Entry	Ligand	*t* [h]	Substrate yield [%]	Reduced acceptor yield [%]	Conjugate silyl transfer yield [%]	Conjugate silyl transfer *ee* [%][c]
1	 (*R*)-binap	2	0	10	56	> 99
2	 (*S*)-Cl-MeO-biphep	3	40	30	5	–
3	 (*R*)-solphos	2	15	75	10	–
4	 (R,S_p)-josiphos	2	15	50	10	–
5	 Carreira´s diene	0.5	0	75	0	–

[a] All reactions were conducted using [Rh(cod)$_2$]OTf (5.0 mol%), the indicated ligand (10 mol%[11]), **1**[12] (2.5 equiv), and Et_3N (1.0 equiv) in 1,4-dioxane/H_2O (10:1; 0.20 M) at 50 °C. [b] Absolute configuration assigned by comparison with reported optical rotation values.[8a] [c] Determined by HPLC analysis using a Daicel Chiralcel IA column (baseline separation of enantiomers).

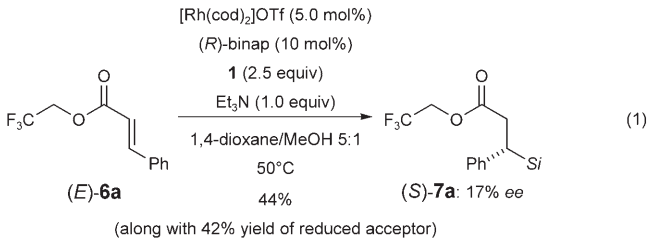
Table 2: Enantioselective conjugate silyl transfer onto *Z*-configured acceptors.[a]

Entry	Acceptor	Product		Yield [%][b]	*ee* [%][c]
1	 (*Z*)-**2a–d**	 (*S*)-**3a–d**	**a**: X = H	66[d]	> 99
2			**b**: X = Me	58[d]	> 99
3			**c**: X = OMe	50	> 99
4			**d**: X = Cl	58[d]	> 99
5	 (*Z*)-**2e,f**	 (*R*)-**3e,f**	**e**: R = *n*Bu	55	> 99
6			**f**: R = *i*Bu	44	> 99
7	 (*Z*)-**4a**	 (*S*)-**5a**		–[e]	–
8	 (*Z*)-**6a** and (*Z*)-**6b**	 (*S*)-**7a** and (*R*)-**7b**	**a**: R = Ph	65	> 99
9			**b**: R = *n*Bu	72[d]	98
10	 (*Z*)-**8a** and (*Z*)-**8b**	 (*S*)-**9a** and (*R*)-**9b**	**a**: R = Ph	60	> 99
11			**b**: R = *n*Bu	58[d]	> 99
12	 (*Z*)-**10a**	 (*S*)-**11a**		–[e]	–

[a] Unless otherwise noted, all reactions were conducted using [Rh(cod)$_2$]OTf (5.0 mol%), (*R*)-binap (10 mol%[11]), **1**[12] (2.5 equiv), and Et_3N (1.0 equiv) in 1,4-dioxane/H_2O (10:1; 0.20 M) at 50 °C. [b] Yield of analytically pure product after flash chromatography; in some cases, trace amounts of the reduced acceptor were removed under high vacuum. [c] Determined by HPLC analysis using Daicel Chiralcel columns (baseline separation of enantiomers). [d] Yield obtained when the reaction temperature was carefully maintained at 45 °C. [e] No reaction.

Subsequent variation of the substitution pattern of the *Z*-configured α,β-unsaturated ethyl ester (*Z*)-**2** underscored the generality of the enantioselective conjugate silyl transfer (Table 2, entries 1–6). Both aryl and alkyl groups, including a branched alkyl chain, are tolerated. (*S*)-**3a–d** and (*R*)-**3e,f** were invariably formed with > 99 % *ee* in reasonable yields. In order to improve the yields, we employed the activated acceptors (*Z*)-**4a** and (*Z*)-**6a,b** (Table 2, entries 7–9). The methyl thioester (*Z*)-**4a** was inert, but the trifluoroethyl esters (*Z*)-**6** were more reactive than the parent compounds, furnishing (*S*)-**7a** and (*R*)-**7b** in slightly improved yields at the cost of enantioselectivity in the case of (*R*)-**7b** (98 % *ee*). Diastereoselective conjugate silylation using cuprates[9] had also been developed using Evans' auxiliary.[9e] Application of our catalyst-controlled enantioselective 1,4-silylation of achiral imides is also possible (Table 2, entries 10 and 11); (*Z*)-**8a** and (*Z*)-**8b** cleanly reacted to yield (*S*)-**9a** and (*R*)-**9b** in > 99 % *ee*. α,β-Unsaturated nitrile (*Z*)-**10a** showed, however, no reaction (Table 2, entry 12).

In this substrate screening (Table 2), we had identified reactive trifluoroethyl esters to be ideal in terms of reactivity and susceptibility to reduction. We therefore returned to the problematic acceptors having *E* configuration [Eq. (1)]. When we treated (*E*)-**6a** with **1** under standard reaction conditions (MeOH instead of H_2O), we were indeed able to isolate moderate amounts of (*S*)-**7a** with poor enantiomeric



(1)

excess. Unexpectedly, the absolute configuration is the same as that of the product obtained from the *Z* precursor. As depicted in Scheme 1, we had anticipated the opposite enantiomer. This outcome indicates to us that *Z* und *E* isomers pass through totally different enantioselectivity-determining transition states.

In summary, this catalytic asymmetric silaboration[16] of acyclic α,β-unsaturated carboxyl compounds complements existing methods for the formation of stereodefined α-chiral organosilanes. The present work also revealed a surprising 1,4-reduction, which will require serious efforts towards its mechanistic elucidation.

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