ChemComm

Cite this: Chem. Commun., 2012, 48, 5419-5421

www.rsc.org/chemcomm

COMMUNICATION

Aryl-aryl interactions as directing motifs in the stereodivergent iron-catalyzed hydrosilylation of internal alkynes[†]

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Received 24th February 2012, Accepted 16th April 2012 DOI: 10.1039/c2cc31395b

The defined Fe hydride complex FeH(CO)(NO)(Ph₃P)₂ is highly active as a catalyst for selective hydrosilylation of internal alkynes to vinylsilanes. Depending on the silane employed either *E*- or *Z*-selective hydrosilylation products were formed in excellent yields and good to excellent stereoselectivities.

Alkynes are versatile building blocks in organic syntheses and allow for a plethora of transformations.¹ Amongst them the direct transformation of an alkyne into a vinylsilane-the hydrosilylation-offers the chance to generate vinylanion equivalents for various applications in organic synthesis or materials science.² Due to the stability of the Si-H bond this type of reaction is usually achieved by means of metal catalysts. However, although the metal catalyzed hydrosilylation of terminal alkynes is well documented³⁻¹³ the corresponding transformation of internal alkynes lacks behind.14-19 Whereas the field of alkyne hydrosilylations has largely been dominated by the use of noble transition metal catalysts defined Fe-,²⁰ Co-²¹ or Ni-complexes²² have proven to be interesting alternatives to the established protocols. The low price and the high reactivity of these complexes have kindled serious interest in extending their application.

Herein we report a stereodivergent iron-catalyzed hydrosilylation of internal alkynes using a defined Fe-hydride complex 1. Depending on the silane source various diarylalkynes were transformed into the corresponding *E*- or *Z*-configured vinylsilanes (Fig. 1).

Complex 1 is prepared in good yields from readily available $Fe(CO)_5$ (4) in a one-pot procedure following a slightly modified literature procedure.²³

This complex turned out to be highly active in the hydrosilylation of 1,2-diphenylacetylene (5) which served as a model reaction throughout the optimization study (Table 1).²⁴

These studies indicated the hydrosilylation to be efficiently performed using only 1 mol% of the Fe-hydride catalyst 1 in the presence of 0.5 equiv. of NEt₃ and 1.1 equiv. of PhSiH₃ (2) in THF at 40 °C. Although the exact role of the amine additive is

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Fig. 1 Fe-catalyzed E- or Z-selective hydrosilylation of alkynes.

Table 1Fe-catalyzed hydrosilylation of 1,2-diphenylacetylene**5**—thesilane effect^a

Ph—≡	<u></u> ₽h +	R¹ R²-Si−H R³	1 [1 mc NEt ₃ [0 THF, 40	I%] .5 equiv.] ⊃ °C, 12 h Ph	$ \begin{array}{c} $	$R^{1} R^{2}$ $R^{3} R^{3}$ Ph Z
Entry	\mathbb{R}^1	\mathbf{R}^1	\mathbb{R}^1	Product	$E:Z^b$	Yield ^c [%]
1	Ph	Н	Н	6	1/>20	98
2	n-Hex	Н	Н	7	1/5	94
3	Ph	Ph	Н	8	1/2	92^d
4	Ph	Ph	Ph	9		_
5	Ph	Me	Me	10	> 20/1	97^d
6	Vinyl	Me	Ph	11	> 20/1	97^d
7	Et	Et	Et	12	4/1	90^e

^{*a*} The reactions were performed on a 1 mmol-scale using 1 mol% **1**, 0.5 equiv. NEt₃ and 1.1 equiv. R¹R²R³SiH at 40 °C in dry THF (1 mL) for 12 h under a N₂-atmosphere. ^{*b*} Determined by ¹H NMR-integration. ^{*c*} Isolated yields. ^{*d*} The reactions were performed using 2.5 mol% catalyst **1** at 60 °C. ^{*e*} The reaction was performed using 5 mol% catalyst **1** at 60 °C.

not clear at the current state of research the fact that in most cases addition of 10 mol% of DMAP leads to comparable results suggests that the additive might be involved in proton transfer or ligand dissociation events. Surprisingly, under these conditions the Z-configured vinyl silane Z-6, which is obtained by a formal *trans*-addition of the Si–H-bond across the $C \equiv C$ -triple bond, was obtained with excellent selectivity in almost quantitative yield (entry 1, Table 1). The stereochemical course of this transformation proved to be dependent on the substitution of the silane source and was mainly directed by its steric demand (entries 5 and 6, Table 1). Using densely substituted silane **3** a total inversion of the stereochemistry was observed.

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[a] An reactions were performed as indicated in ratio 1, [b] Determined by H NMR-integration. [c] Isolated yields. [d] The reaction was performed using 5 mol% catalyst 1 at 60 $^{\circ}$ C for 36 hours.

Scheme 1 Fe-catalyzed hydrosilylation of 1,2-disubstituted alkynes—the aryl effect.

Changing the silane source from $PhSiH_3$ to *n*-HexSiH₃ led to a decrease in the *E*–*Z*-selectivity (entry 2, Table 1).

In order to showcase the interplay of the silane source and an alkyne substitution pattern a diaryl-, an aryl/alkyl- and a dialkylacetylene were subjected to the standard reaction conditions using either PhSiH₃ (2) or PhMe(CH₂=CH)SiH (3) (Scheme 1). These experiments indicate that the substitution pattern of the alkyne is the decisive regioselectivity directing structural motif. The C-Si-bond is formed with almost exclusive preference proximal to the aryl-group (eqn (2), Scheme 1). However, the data also suggest that the stereoselective course of the hydrosilylation is mainly directed by an interaction between the silvl group and the second alkyne substituent. Employing a diarylalkyne in the hydrosilylation using silane 2 led to almost exclusive formation of Z-configured vinylsilane Z-6 (eqn (1), Scheme 1). The use of an arylalkylalkyne under otherwise identical reaction conditions resulted in predominant formation of the E-configured vinylsilane E-13 (eqn (2), Scheme 1). Subjecting dialkylalkynes to the hydrosilylation led to the formation of the E-configured products independent of the silane source (eqn (3), Scheme 1).

The *trans*-addition of a silane across a C \equiv C-triple bond is usually believed to follow an Ojima–Crabtree-mechanism *via* a carbanionic intermediate which is formed by electron-donation from the metal center into the C \equiv C-double bond of the metallavinylsilane (Fig. 2).²⁵ With regard to the results summarized in Scheme 1 we propose the following mechanistic rationale for the unexpected stereoselectivity. If the Fe-catalyzed hydrosilylation using monosubstituted silane RSiH₃ is regioselective with the Si–C bond ending up proximal to the aryl group the formation of a stable benzylic carbanion and the isomerization of the metallavinylsilane appear to be favorable.

The stereoselectivity however is mainly directed by the distal alkyne substituent. Using sterically less hindered silane PhSiH₃ (2)



Fig. 2 π -Bond isomerization in metal catalyzed hydrosilylations.

the primarily formed metallavinylsilane can undergo a π -bond isomerization that is mainly driven by a favorable π - π -interaction in the Z-configured vinylsilane between the β -aryl group of the olefin and the phenyl group bound to the Si-atom (eqn (1), Fig. 3). Employing the sterically hindered silane **3** such a positive interaction in the resulting vinylsilane is prohibited due to unfavorable steric repulsions (eqn (2), Fig. 3).

We finally set out to analyze the generality of the aryl–aryldirected stereoselective iron-catalyzed hydrosilylation of diarylsubstituted alkynes (Table 2).

Various bis-aryl alkynes were hydrosilylated in good to excellent yields and stereoselectivities. However, since a mixture of regioisomers was obtained in the majority of cases the crude reaction mixture was directly employed in a desilylation to give the corresponding olefins. The reaction proved to possess a good level of functional group tolerance. Esters, amides, ethers, alcohols, amines and nitriles were tolerated. However, electron-withdrawing groups within the aromatic moiety led to an erosion in π -bond selectivity employing method A.

The synthetic value of Fe-catalyzed hydrosilylation reported in this manuscript was finally demonstrated by the stereodivergent synthesis of *E*- and *Z*-combrestatin A-4 **27**, a class of microtubuli-stabilizing agents, that has attracted significant attention within the past years (Scheme 2).²⁶ Starting from readily accessible alkyne **26** both natural products were obtained



Fig. 3 π -Bond isomerization in metal catalyzed hydrosilylations.

 Table 2
 Scope and limitations^a

	R	1. 1 [1 - 2.5 mol ⁶ silane [1.1 equ NEt ₃ [0.5 equi THF, 40 / 60 ⁶ 2. Desilylation	$ \begin{array}{c} \overset{\text{\%}}{}_{\text{uiv.]}} \\ \overset{\text{iv.]}}{}_{\text{C}} \\ \overset{\text{C}}{}_{\text{R}^2} \\ R^2 \\ R^2 \\ R^2 \\ R^2 \\ R^1 \end{array} $			
Entry	\mathbf{R}^1	R ²	Product	$E: Z^{b,c}$ (Method)	Yield ^d [%] (Alkane)	
1	Ph	p-MeOC ₆ H ₄	17	17:1(A)	96	
2				1:20 (B)	93	
3	Ph	p-ClC ₆ H ₄	18	7:1(A)	93	
4 58	DI	MOCCU	10	1 : 10 (B)	95	
5° 6	Pn	p-MeO ₂ CC ₆ H ₄	19	1 : 1 (A) 1 : 10 (B)	50 (11) 76	
0 7 ^e ,g	Ph	n-CH-C(O)C-H	20	$3 \cdot 1 (\Delta)^{f}$	25 (4)	
8 ^e	1 11	<i>p</i> -CI13C(0)C6I14	20	$1 \cdot 10$ (B)	23 (1) 92	
9^e	Ph	p-HOCH ₂ C ₆ H ₄	22	9:1(A)	76	
10^e		1 2 0 4		1:9(B)	95	
11^g	Ph	p-NCC ₆ H ₄	23	3:1(A)	71 (10)	
12				1:12 (B)	73	
13^e	Ph	$p-H_2NC_6H_4$	24	20:1(A)	92	
14^e				1 : 20 (B)	89	
15 ^e	Ph	p-CH ₃ C(O)NHC ₆ H ₄	25	14 : 1 (A)	90	
16 ^e				1:20 (B)	82	

^a The reactions were performed on a 1 mmol-scale using 1 mol% 1, 0.5 equiv. NEt₃ in dry THF (1 mL) for 12 h under a N₂-atmosphere. ^b Determined by ¹H NMR-integration. ^c Method A: hydrosilylations were performed under the standard conditions using 1 mol% 1, 2 (1.1 equiv.) at a temperature of 40 °C. Desilvlation: 1.5 equiv. of 1 M TBAF-solution in 7.5 mL THF at 0 °C for 2 h. Method B: hydrosilylations were performed under the standard conditions using 2.5 mol% 1, 3 (1.1 equiv.) at a temperature of 60 °C. Desilylation: addition of 1.5 mL THF, 1 mL MeOH and 1 mL of 2 N NaOH-solution to the reaction mixture and MW for 10 min at 130 °C. ^d Isolated yields. ^e 2.1 equiv. of the silane were used. ^f The product was isolated as the alcohol.^g Partial overreaction to the corresponding alkane was observed.



Scheme 2 Stereodivergent synthesis of E- and Z-combrestatin A-4 27 (Reagents and conditions: 2.5 mol% 1, 2.1 equiv. 2, 0.5 equiv. NEt₃, 60 °C were used for method A; 5 mol% 1, 2.1 equiv. 3, 0.5 equiv. NEt₃, 80 °C were used for method B).

using our hydrosilylation-desilylation strategy in good yields and promising E-Z-selectivities. Interestingly protection of the free phenolic OH-group was not necessary.

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