

Mechanistic Studies on the Pd-Catalyzed Vinylation of Aryl Halides with Vinylalkoxysilanes in Water: The Effect of the Solvent and NaOH Promoter

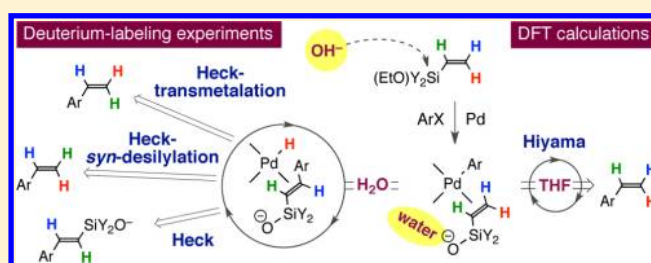
Alvaro Gordillo,[†] Manuel A. Ortuño,[‡] Carmen López-Mardomingo,[†] Agustí Lledós,[‡] Gregori Ujaque,^{*,‡} and Ernesto de Jesús^{*,†}

[†]Departamento de Química Orgánica y Química Inorgánica, Universidad de Alcalá, Edificio de Farmacia, Campus Universitario, E28871 Alcalá de Henares, Madrid, Spain

[‡]Departament de Química Física, Universitat Autònoma de Barcelona, Edifici C.n, 08193 Cerdanyola del Vallès, Catalonia, Spain

S Supporting Information

ABSTRACT: The mechanism of the Pd-catalyzed vinylation of aryl halides with vinylalkoxysilanes in water has been studied using different catalytic precursors. The NaOH promoter converts the initial vinylalkoxysilane into a highly reactive water-soluble vinylsilanolate species. Similarly, deuterium-labeling experiments have shown that, irrespective of the catalytic precursor used, vinylation occurs exclusively at the CH vinylic functionality via a Heck reaction and not at the C–Si bond via a Hiyama cross-coupling. The involvement of a Heck mechanism is interpreted in terms of the reduced nucleophilicity of the base in water, which disfavors the transmetalation step. The Heck product (β -silylvinyllarene) undergoes partial desilylation, with formation of a vinylarene, by three different routes: (a) hydrolytic desilylation by the aqueous solvent (only at high temperature); (b) transmetalation of the silyl olefin on the PdH Heck intermediate followed by reductive elimination of vinylarene; (c) reinsertion of the silyl olefin into the PdH bond of the Heck intermediate followed by β -Si *syn*-elimination. Both the Hiyama and Heck catalytic cycles and desilylation mechanisms b and c have been computationally evaluated for the [Pd(en)Cl₂] precursor in water as solvent. The calculated Gibbs energy barriers support the reinsertion route proposed on the basis of the experimental results.



INTRODUCTION

Recent work in the field of Pd-catalyzed C–C coupling reactions between aryl or vinyl halides and organometallic species (organoboron, -tin, -silicon, -magnesium, etc.) has tended to concentrate on the search for processes that occur under mild conditions, employ readily available cost- and atom-efficient starting materials, and avoid the formation of byproducts or the use of toxic reagents.¹ In this context, organosilicon compounds are remarkable for their low toxicity, environmental friendliness, and high chemical stability.² The development of organosilanes as cross-coupling partners has lagged behind that of other organometallic compounds because of the lower reactivity of the low-polarized silicon–carbon bond. Although the first examples of the vinylation of aryl halides with vinyltrimethylsilanes were reported in the early 1980s,³ these actually involved one of the C–H bonds of the vinyl group in a Mizoroki–Heck⁴ process (Figure 1a).⁵ As a result, the major product of the reaction was often a styrene due to loss of the silicon group via a hydrodesilylation process subsequent to the Heck coupling. The increasing synthetic interest in β -silylstyrene intermediates stimulated the search by groups such as those of Hallberg,⁶ Kikukawa,⁷ or Jeffery⁸ for reaction conditions that could inhibit this desilylation step. A major breakthrough in this respect was reported in 1989, when

Hiyama and Hatanaka published the fluoride-promoted cross-coupling of organosilanes and haloarenes (Figure 1b).⁹ It was assumed that the formation of pentacoordinate silicates accelerated the rate-determining transmetalation step (Figure 1c). Accordingly, the alkenylsilanes became more reactive when their fluorophilicity was increased upon replacing methyl substituents with fluorides.¹⁰ However, the preformation of a stable, pentacoordinate silicate intermediate prior to the transmetalation step may not be key to the cross-coupling reaction because theoretical calculations have suggested that formation of the Si–F bond may occur in a concerted manner with transfer of the vinyl group from Si to Pd, thus stabilizing the transition state of the transmetalation step.¹¹

The subsequent introduction of silanols as coupling partners was aimed at improving the reactivity and selectivity of these reactions as a result of their ability to coordinate to palladium via the oxygen atom. In the course of these studies, Mori, Hiyama, and co-workers discovered that silver oxide promoted the cross-coupling of aryl- or alkenylsilanols under fluoride-free conditions.¹² A major breakthrough in this respect was the finding by Denmark and Sweis that the deprotonation of

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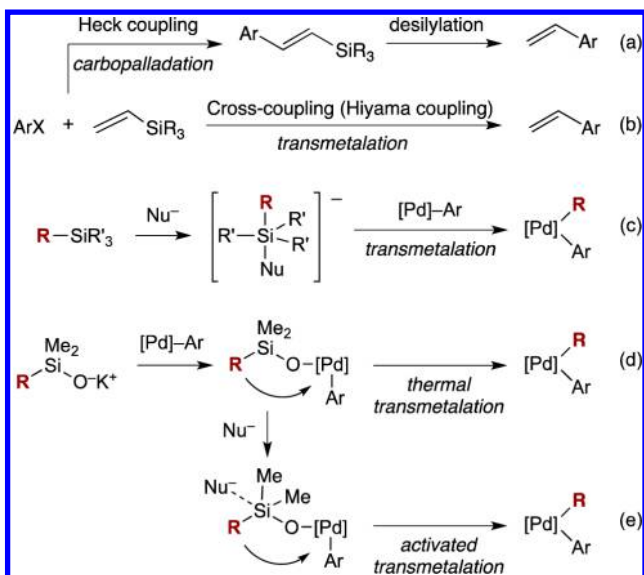


Figure 1. Heck–desilylation (a) and Hiyama–Denmark (b) couplings. The transmetalation step in the Hiyama–Denmark couplings occurs via preformation of pentacoordinate silicates (c) or coordination of tetracoordinate silanolate followed by thermal (d) or activated (e) transfer of the organyl group.

silanols with a Brønsted base meant that the use of fluorides or other external activators could be avoided.¹³ After coordination to the Pd(II) center, the tetracoordinate silanolate formed under these conditions can undergo transmetalation without requiring the formation of a pentacoordinate species (Figure 1d).^{14,15} Nevertheless, the transmetalation is accelerated by silanolate excesses (or by addition of fluorides)¹⁶ probably due to nucleophilic attack at the silicon and subsequent formation of hypervalent intermediates (or transition states, Figure 1e).¹⁵ Although the diversity of modes in which alkenylsilanes can potentially be arylated is synthetically challenging, the methods developed in the past few years, together with the current level of mechanistic understanding, allow a high degree of control over the synthesis of multisubstituted olefins and other complex molecules.^{17–19}

Research on palladium-catalyzed organic transformations in water has progressed rapidly since the discovery of carbon–carbon bond-formation processes.²⁰ Indeed, most of the progress achieved in this field has been based on the development of efficient protocols together with the synthesis of new water-soluble catalysts.²¹ In contrast, considerably less effort has been spent on understanding the specific mechanisms of catalytic reactions in aqueous media, despite the advantages this would bring as regards the rational optimization of such processes.²² Because water is a reactive medium, the possible active participation of water solvent molecules in the chemical process makes the study of reaction mechanisms in this medium more difficult. The mechanism of cross-coupling reactions in conventional organic solvents has been extensively studied using theoretical methods.²³ The Heck reaction has also been widely computed.²⁴ As mentioned above for the Hiyama reaction, the promoting role of fluoride and hydroxide anions in the transmetalation has been computationally proven.¹¹ In this regard, theoretical calculations, which give a microscopic description of the solvent, have contributed notably to revealing the specific mechanistic features of a number of reactions performed in water.^{25,26} However, to the

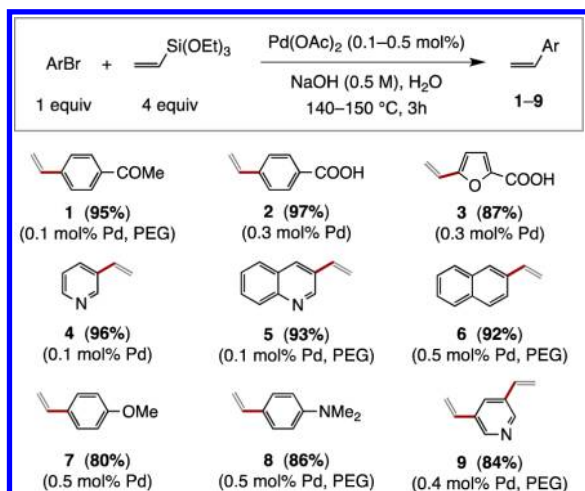
best of our knowledge, very few computational studies of cross-coupling reactions in the presence of water have been published to date.²⁷

The first example of a cross-coupling reaction involving arylsilanes in water was reported by Huang and Li,²⁸ and subsequent work by the groups of Wolf, Nájera, and some of us revealed the synthetic potential of organosilanes for the formation of C–C bonds in the aqueous phase and established appropriate conditions for the high-yield coupling of aryl^{29–32} and vinyl^{33–35} derivatives. The methodologies developed were based on the use of aryl- or vinyltri(alkoxy)silanes as coupling partners³⁶ and sodium hydroxide as promoter,³⁷ often under aerobic conditions. It is important to note that almost all the above-mentioned reports highlighted the lower efficiency of fluorides as promoters for this reaction in water.

In the course of our studies, we observed that the vinylation of bromoarenes with triethoxyvinylsilane in water requires only low loadings of a simple salt such as palladium acetate and afforded styrene and stilbene derivatives with excellent efficiencies in terms of both selectivities and yields.³⁴ The synthetic effectiveness and simplicity of these aqueous and “ligand-free” reactions prompted us to undertake the study of their inner workings in more detail. These mechanistic studies were aimed at clarifying the nature of the coupling reaction (Heck–desilylation versus Hiyama) and the role played by the sodium hydroxide promoter in activation of the organotri(alkoxy)silane precursor. In a preliminary communication,³⁸ we reported the use of deuterium-labeling experiments to establish the essential mechanistic pathways of the reaction under these ligand-free and aqueous-phase conditions. Herein, we describe a detailed study of the mechanism involved in the palladium-catalyzed vinylation of aryl halides with alkoxy-silanes in water. Kinetic and isotopic labeling studies involving partially deuterated triethoxyvinylsilanes suggest that the predominant reaction mechanism critically depends on the solvent and, to a lesser extent, the palladium precursor. The involvement of tetracoordinate silanolate species in the reaction is also described. These observations are supported by DFT calculations; the full catalytic cycles for the diamine [Pd(en)-Cl₂] precursor, explicitly considering water molecules within a continuum method, attempt to shed light on the competitive pathways that lead to the products detected experimentally.

RESULTS AND DISCUSSION

Synthesis of Vinylarene and (*E*)-1,2-Diarylethene Derivatives. The initial screening of conditions was based on the reaction of 4-bromoacetophenone with triethoxyvinylsilane (Table S1, Supporting Information). Low loadings (0.1 mol %) of simple salts such as palladium acetate were found to efficiently catalyze the formation of **1** (Scheme 1) at 140 °C. The formation of diarylethene byproducts was minimized using a 3-fold excess of the vinylsilane.³⁹ Nevertheless, the most relevant point for the subsequent discussion was the use of sodium hydroxide in view of the poor efficiency of fluorides and other bases as promoters of this aqueous-phase reaction (Table 1). Under similar conditions, other activated and inactivated bromoarenes reacted quantitatively with the vinylsilane to afford compounds **2–9** (Scheme 1) in high yields after separation of the small amounts of (*E*)-1,2-diarylethene byproducts observed (usually less than 3%). The palladium loadings (from 0.1 to 0.5 mol %) were adjusted on the basis of bromoarene reactivity and solubility. Addition of PEG as a cosolvent improved the selectivities and yields for less activated

Scheme 1. Vinylarene Derivatives^a

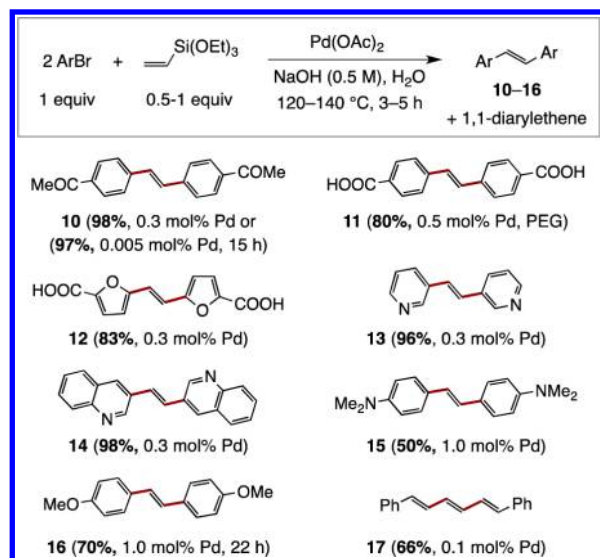
^aPercentages in bold represent isolated yields after chromatographic purification. See Supporting Information for details.

Table 1. Screening of Bases in the Synthesis of 1

base (0.5 M)	reaction time (h)	conversion (%) ^a	yield (%) ^a
NaOH	1.5	97	76
CsF	3	35	<5
Cs ₂ CO ₃	3	0	0

^aConversions are given with respect to reacted ArBr and yields to the amount of 1 after workup. Percentages were determined by ¹H NMR spectroscopy, using (Me₃Si)₂O as standard.

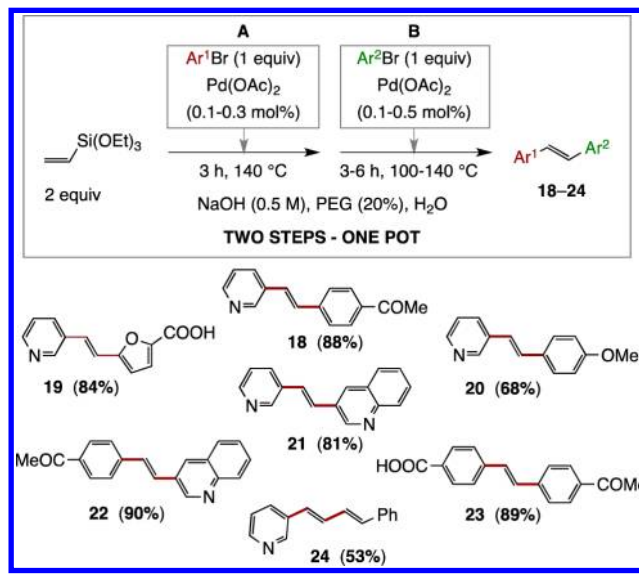
or soluble substrates. (*E*)-1,2-Diarylethenes 10–16 were obtained under similar reaction conditions except for the use of a lower vinylsilane/bromoarene ratio (Scheme 2). Although

Scheme 2. Symmetric (*E*)-1,2-Diarylethene Derivatives

electronically activated 4-bromoacetophenone quantitatively afforded stilbene 10 in 15 h at 120 °C with a Pd loading of only 0.005 mol % (turnover number 19 400), Pd loadings ranging from 0.3 to 1 mol % were usually needed to attain full conversions in 3–5 h. Selectivities were generally higher than 95% (except in the case of 11 and 16). This synthetic

methodology was extended to the preparation of triene 17 using vinyl bromide as starting material.

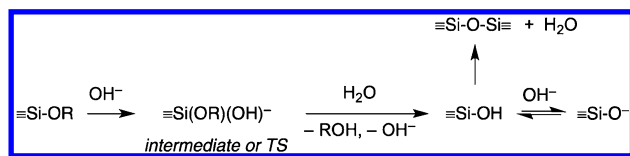
Most of the approaches used to prepare unsymmetrically substituted (*E*)-1,2-diarylethenes, such as those based on Wittig-type reactions, Ti-catalyzed McMurry couplings or Ru-catalyzed olefin metathesis, have either the length of the synthetic routes, low functional group tolerance, or limited diastereoselectivity as drawbacks.⁴⁰ A versatile and atom-economical alternative to these approaches is the one-pot sequential double Heck arylation of ethylene, the success of which depends on the degree of selectivity achieved in the intermediate vinylarene.⁴¹ In this context, vinylsilanes have been explored as ethylene surrogates because the selectivity of the reaction can take advantage of the dual C–H versus C–Si alkene reactivity.^{19,42} We performed the synthesis of unsymmetrical (*E*)-1,2-diarylethenes by the sequential one-pot, two-step process shown in Scheme 3. The bromoarenes suitable for

Scheme 3. Unsymmetric (*E*)-1,2-Diarylethene Derivatives

step A were those almost quantitatively converted into their corresponding vinylarenes under the aqueous conditions described above. In addition, an additional portion of palladium acetate had to be added at the beginning of the second step (B). Under these conditions, the unsymmetric (*E*)-1,2-diarylethenes 18–23 and diene 24 were obtained with good selectivities and isolated in high yields (68–90%) after separation of the small amounts of symmetric 1,2-diarylated derivatives formed as byproducts (<5%, except for 4-bromoanisole).

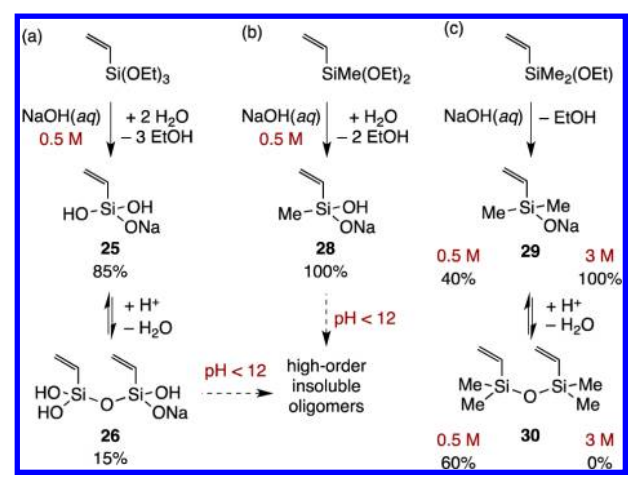
The Role of the NaOH Promoter. In the absence of mechanistic studies, it has been proposed that the NaOH-promoted coupling of organotrialkoxysilanes with aryl halides in water occurs via the formation of pentacoordinate silicates RSi(OR)₃(OH)[−] (Figure 1c, where Nu[−] = OH[−]).^{29,31,35} However, this proposal can be questioned because such silicates are the probable intermediates (or transition states) in the hydroxide-promoted hydrolysis of Si–OR bonds in alkoxy silanes under basic conditions (Scheme 4).^{43,44} As such, it seemed reasonable to assume that the triethoxyvinylsilane reagent is quickly hydrolyzed under the conditions of the coupling reactions, with the corresponding formation of silanol, silanolate, or siloxane species.

Scheme 4. Hydroxide-Promoted Hydrolysis of Alkoxyxilanes



Stirring the water-insoluble triethoxyvinylsilane reagent under the basic conditions of the catalytic reaction (0.5 M NaOH(aq)) gave a clear solution in less than 10 min at room temperature. The ESI-TOF mass spectrum of this solution, recorded in negative mode, showed two large peaks corresponding to the silanolates [25-Na]⁻ and [26-Na]⁻ (Scheme 5a).⁴⁵ Complete hydrolysis of the silicon-ethoxide

Scheme 5. Hydrolysis of Alkoxyvinylsilanes in Aqueous NaOH Solutions

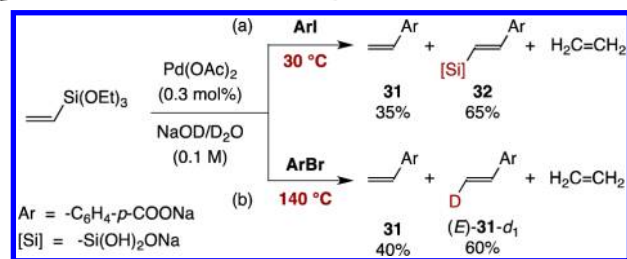


bonds and the formation of a mixture of **25** (85%) and **26** (15%) in 0.5 M NaOH was supported by NMR spectroscopy. The monomeric and dimeric structures proposed for these silanolate species were supported by diffusion (DOSY) NMR measurements. The protonation and condensation of these silanolate species in less basic media led to higher order insoluble oligomers that began to precipitate at a pH of around 11.5–12. The hydrolysis of diethoxy(methyl)vinylsilane and ethoxydimethylvinylsilane was also fast under the same conditions (Schemes 5b,c). Solutions of (vinyl)SiMe(OEt)₂ in 0.5 M NaOH contained only the silanolate monomer **28**, which was transformed into insoluble polysiloxanes at a pH of less than 12. In contrast, the dissolution of (vinyl)SiMe₂(OEt) in 0.5 M NaOH yielded a mixture containing 40% of the anionic and water-soluble silanolate **29** and 60% of the neutral and water-insoluble 1,3-divinyltetramethyldisiloxane **30** (dvtms). In accordance with the expected effect of the electron-donating methyl groups on the protic acidity of the conjugated silanol, this equilibrium shifted completely to the formation of the silanolate in 3 M NaOH.

Once the structure of the silane reagent obtained under these reaction conditions had been elucidated, we tried to understand the role of the NaOH promoter. According to Hiyama's proposal (Figure 1c), the activation of organosilicon compounds by fluorides (or hydroxides) is easily interpretable in terms of the very strong bonds formed by such hard Lewis bases with silicon.⁴⁶ In contrast, in light of the ubiquitous role of fluorides in Hiyama cross-couplings, the experimental

evidence showing that organoalkoxyxilanes are more readily activated by hydroxides than fluorides in water^{29,30,33,35} cannot be understood exclusively in terms of Lewis basicity. In this regard, the transformation of organoalkoxyxilanes into organosilanolates under the effect of the base provides a bridge between these aqueous-phase processes and the cross-coupling chemistry developed by Denmark based on the activation of organosilicon compounds by formation of silanolate anions (Figures 1d,e). On the other hand, the hydrolysis of a base in water increases the concentration of hydroxide anions to an extent determined by the Brønsted strength of that base, according to the equilibrium $B^- + H_2O \leftrightarrow HB + OH^-$. This fundamental difference between the aprotic organic solvents usual in Hiyama reactions and water or other protic solvents led us to investigate to what extent the reactivity under aqueous conditions was determined by the Brønsted strength of the base instead of the nature of the electron-pair donor. To this end, we undertook a study of the aqueous-phase coupling reactions in the presence of bases of different Brønsted basicity.

Unless otherwise stated, the mechanistic studies included in this work have been performed on the model reaction between *p*-iodobenzoic acid and triethoxyvinylsilane under the conditions shown in Scheme 6a. Both reagents are solubilized by

Scheme 6. Products of the Vinylation of Sodium *p*-Iodo and *p*-Bromobenzoate in NaOD/D₂O

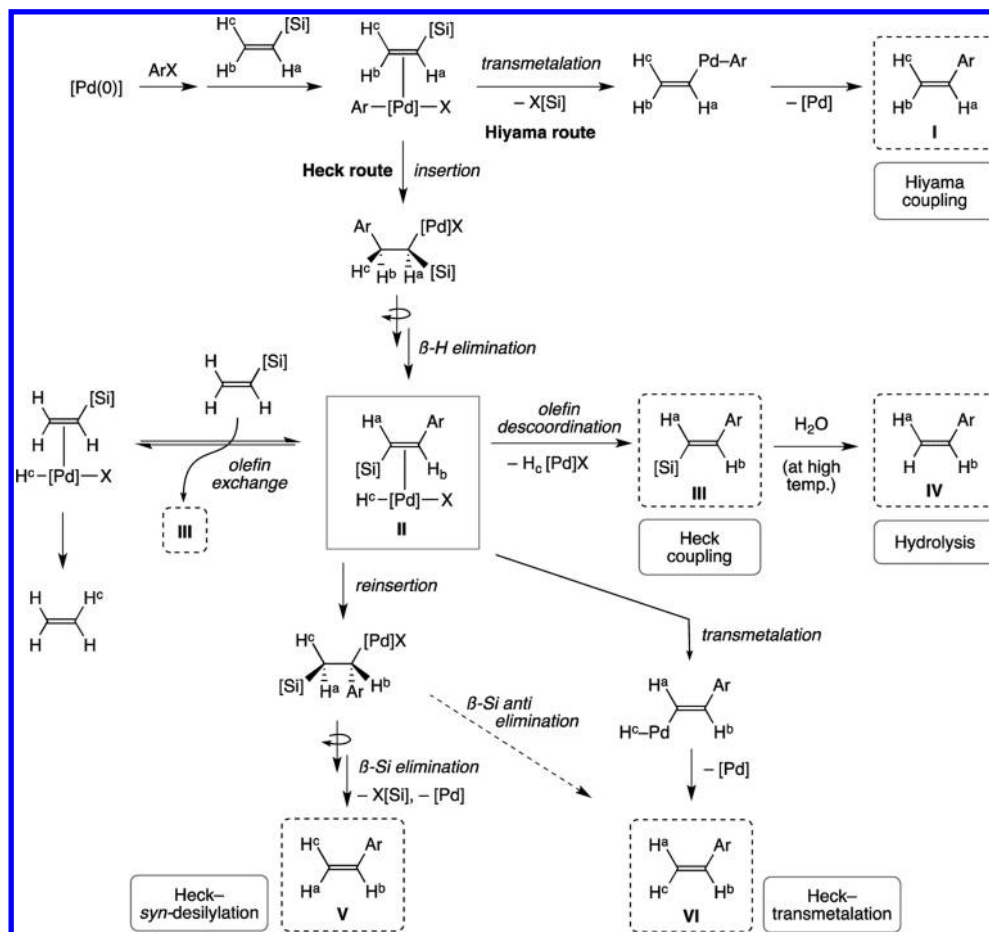
the effect of the base, thus allowing the aqueous reaction to be monitored by ¹H NMR spectroscopy. Moreover, the aryl iodide substrate is activated at lower temperatures than aryl bromides, thus allowing the experiments to be performed close to room temperature (30 °C). In the particular case of the experiments described in Table 2, the triethoxyvinylsilane reagent was replaced by a preisolated sample of the corresponding sodium silanolate **25** (and *p*-iodobenzoic acid by its sodium salt) to avoid possible artifacts produced by a slower hydrolysis of the

Table 2. Vinylation of Sodium 4-Iodobenzoate with **25** in Different Basic Media

base	pH ^a	observed media	conversion ^b (%)
<i>c</i>	11.8–11.6	heterogeneous	24
Na ₂ CO ₃ (1 M)	11.4–11.4	heterogeneous	15
Na ₃ PO ₄ (0.1 M)	11.9–11.6	heterogeneous	25
Na ₃ PO ₄ (1 M)	12.0–11.8	homogeneous	100
NaOH (0.1 M)	12.7–12.0	homogeneous	100
NaOH (1 M)	13.7–13.5	homogeneous	100

^aInitial and final pH. ^bConversion of ArI determined by ¹H NMR spectroscopy. ^cThis reaction was performed in the absence of any base other than 4-iodobenzoate and silanolate **25**.

Scheme 7. Competing Mechanisms in the Coupling of Vinylsilanes with Aryl Halides



Si-OEt bonds with certain bases. The conversions shown in Table 2 were determined with respect to the aryl iodide reagent after 22 h of reaction at 30 °C. In an initial experiment, the reaction was performed in the absence of any base other than the reagents themselves. Subsequent experiments were performed in 0.1 or 1 M solutions of bases of increasing Brønsted strength, namely, CO_3^{2-} ($\text{p}K_b = 3.7$), PO_4^{3-} ($\text{p}K_b = 1.7$), and OH^- ($\text{p}K_b = -1.7$). These experiments revealed a correspondence between reactivity and pH that appeared to be independent of the nature of the base. Efficient activations were achieved with the stronger bases (hydroxide and phosphate) at concentrations that maintained the pH of the reaction above 12. The progress of the reaction therefore clearly depends on the addition of a base of sufficient Brønsted strength to attain the pH values required to stabilize silanolate species. In light of these results, the limited effectiveness of fluoride promotion should be interpreted in terms of the low Brønsted basicity of this anion ($\text{p}K_b = 10.8$).⁴⁷

In the reactions performed at a pH below 12, the condensation of **25** into high-order siloxane oligomers was apparent by the formation of copious precipitates. Therefore, the effect of the alkalinity may be ascribed to either an intrinsically higher reactivity of the silanolate anions formed at high pH or to precipitation of the vinyl donors in the form of siloxanes at lower pH values. This point was clarified by way of another set of experiments based on the use of commercial 1,3-divinyltetramethyldisiloxane (dvtms, **30**) as silicon coupling partner and poly(ethylene glycol) as cosolvent. Dvtms is a liquid that is insoluble in water but soluble in water/PEG

mixtures. In pure water, the reaction had to be performed in 3 M NaOH in order to obtain reasonable yields, in agreement with the strongly alkaline medium required to displace the equilibrium in Scheme 5c toward **29**. Despite the solubility of reagents under less alkaline conditions, the use of 3 M NaOH was still required in the presence of PEG. This result suggests that silanolates are key species in the reaction mechanism of these aqueous-phase couplings.

General Mechanistic Scheme. In a preliminary communication,³⁸ we reported some initial mechanistic findings based on experimental studies of the reaction between *p*-iodobenzoic acid and triethoxyvinylsilane under aqueous basic conditions. This homogeneous reaction was monitored by ¹H NMR spectroscopy in NaOD/D₂O at close to room temperature (30 °C, Scheme 6a). Under these low-temperature conditions, the reaction afforded a mixture of vinylarene **31** and the *trans*- β -silyl derivative **32**. The analogous reaction with the less reactive *p*-bromobenzoic acid required temperatures of 120–140 °C (Scheme 6b). Under such high-temperature conditions, a mixture of **31** and its isotopologue (*E*)-**31**-*d*₁ was obtained irrespective of the starting aryl halide used (*p*-bromo- or *p*-iodobenzoic acid). Evolution of nondeuterated ethylene was observed in both cases. In light of the product distributions, it appeared obvious that similar amounts of the silyl derivative **32** were formed in both reactions, although only vinylarene end-products were observed at high temperature due to rapid hydrolysis of the alkenylsilane C–Si bonds.⁴⁸ Because none of the products observed at 30 °C included deuterium, we assumed that both reactions shared a common underlying

mechanism in which the direct involvement of water hydrogens had to be excluded.

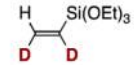
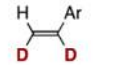
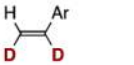
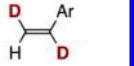
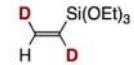
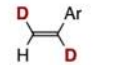
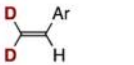
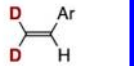
As noted in the Introduction, arylation of vinylsilanes can occur at the carbon–silicon functionality via a Hiyama reaction, which includes a transmetalation step and gives a vinylarene (I, Scheme 7), or at the alkene functionality via a Heck reaction, which gives a *trans* β -silylated vinylarene (III) after the insertion and β -H elimination steps.⁴⁹ Formation of the vinylarene by hydrolysis of the *trans* β -silylated vinylarene (III \rightarrow IV) is slow at temperatures below 100 °C. Nevertheless, vinylarene formation can also occur by hydrogenative desilylation of the silyl olefin coordinated to palladium in the hydride intermediate II. In Heck–desilylation reactions with stereochemically marked vinylsilanes or alkenylsilanes, the usual stereochemistry of the reaction has been explained by a process involving reinsertion of the olefin into the palladium–hydride bond of intermediate II, followed by a *syn* Pd–Si β -elimination (Heck–*syn*-desilylation route, V).^{6,17,49} The preliminary deuterium-labeling experiments that we performed under the above NaOH-aqueous conditions showed that the formation of 31 occurred essentially via a Heck–desilylating instead of a Hiyama route, as may have been anticipated considering that the Heck coupling product 32 was the major reaction product.³⁸ However, the stereochemistry of the major deuterated vinylarene product corresponded to an apparent β -Si *anti* elimination^{7,50} instead of the usual *syn* elimination. As an alternative to the *anti* mechanism,⁵¹ a Heck–transmetalation mechanism (VI) is proposed in this work to explain the main stereochemistry observed (see computational study on the [PdCl₂(en)] precursor below).

The evolution of ethylene, which was particularly obvious at the beginning of the reaction, was postulated to occur by displacement of the Heck product from the coordination sphere of the palladium hydride II by a molecule of vinylsilane, which is subsequently desilylated. This mechanism was supported by deuterium-labeling and other key experiments that demonstrated the intermolecular transfer of hydrogen atoms between olefins.³⁸ It should be noted that this exchange is very favorable and accounts for the formation of almost all the Heck product III when an almost one-fold excess of vinylsilane was used under low-temperature conditions. This result is quite intriguing because it implies an unexpected reluctance of the [Pd(olefin)HX] intermediate to reductively eliminate HX in a rather basic aqueous solution.^{52,53}

Stereochemically Marked Vinylsilanes. Isotopic labeling techniques permit the competing routes involved in the formation of vinylarenes (I and IV–VI) under a specific set of reaction conditions to be identified and quantified. Using the deuterium-marked triethoxyvinylsilane (*E*)-33-*d*₂ (Table 3), we performed preliminary experiments that confirmed the essential Heck nature of the coupling but did not allow us to discard the partial existence of Hiyama cross-coupling.³⁸ The identification of the three hydrogen positions of a vinyl group (H^a, H^b, and H^c in Scheme 7) requires the use of two vinylsilanes that differ in their deuterium distribution. To this end, we recently prepared the (*Z*) isotopic stereoisomer of 33-*d*₂.⁵⁴ Arylation of these deuterated vinylsilanes is expected to afford the styrene isotopomers (*E*)-31-*d*₂, (*Z*)-31-*d*₂, or 1,1-31-*d*₂, depending on the starting vinylsilane and the reaction path, as indicated in Table 3. The use of these deuterated silanes in the elucidation of reaction mechanisms is shown below.

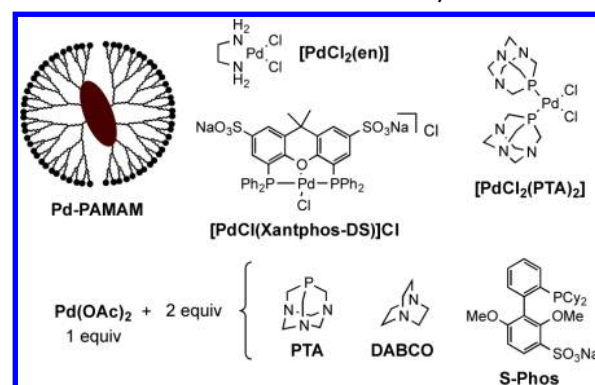
The Effect of the Palladium Precursor. The reaction in Scheme 6a was also studied, under similar conditions (30 °C,

Table 3. Vinylarene Isotopomers Expected from Reaction Routes Depicted in Scheme 7

starting vinylsilane	Hiyama product (I)	Heck-desilylation products	
		<i>syn</i> -desilylation (V)	transmetalation (VI)
 (<i>E</i>)-33- <i>d</i> ₂	 (<i>E</i>)-31- <i>d</i> ₂	 (<i>E</i>)-31- <i>d</i> ₂	 (<i>Z</i>)-31- <i>d</i> ₂
 (<i>Z</i>)-33- <i>d</i> ₂	 (<i>Z</i>)-31- <i>d</i> ₂	 1,1-31- <i>d</i> ₂	 1,1-31- <i>d</i> ₂

0.3 mol % Pd), with the water-soluble Pd catalysts shown in Scheme 8 (preformed complexes or 1:2 mixtures of palladium-

Scheme 8. Water-Soluble Palladium Catalytic Precursors



(II) acetate with P- or N-donor ligands, and 1.6 \pm 0.3 nm Pd nanoparticles stabilized by fourth-generation hydroxy-terminated PAMAM dendrimers). All the reactions were completed in a maximum of 24 h. Nevertheless, the Pd precursors exhibited appreciable differences in their catalytic activities (Figure S3, Supporting Information). The more active catalysts were the complex [PdCl₂(PTA)₂] and the mixture Pd(OAc)₂/DABCO (initial TOFs = 290 and 650 h⁻¹, respectively, compared with 135 h⁻¹ obtained with Pd(OAc)₂).⁵⁵

Excluding the special case of the ethylenediamine complex [PdCl₂(en)], the chemoselectivities (vinylarene 31 versus silyl derivative 32, Table S3) and stereoselectivities (Table 4) found for the different catalysts were comparable to those obtained with Pd(OAc)₂ under ligand-free conditions. Thus, the Heck-coupling product 32 was the main product of the reaction with molar ratios of 31 versus 32 in the relatively narrow range of 0.56 to 0.77. Furthermore, (*E*)-33-*d*₂ always gave (*Z*)-31-*d*₂ as the major desilylated product (62–75% of the total amount of 31, Table 4, entries 1–4), which corresponds to the Heck–transmetalation route VI (see Table 3).⁵⁶ The minor isotopomer (*E*)-31-*d*₂ was essentially formed via the Heck–*syn*-desilylation route V. The alternative Hiyama route I was ruled out by a second experiment with palladium(II) acetate in which only 3% of (*Z*)-33-*d*₂ was converted into the expected Hiyama product (*Z*)-31-*d*₂ (Table 4, entry 6). In the case of the ethylenediamine complex [PdCl₂(en)], the reaction also proceeded via a Heck mechanism but with significant differences in terms of product distribution. First of all, this catalyst largely favored formation of the vinylarene 31 with

Table 4. Stereochemistry of the Arylation of (*E*)- and (*Z*)-Triethoxy(vinyl-*d*₂)silane

		$\begin{array}{c} \text{H} \quad \text{Si(OEt)}_3 \\ \diagdown \quad / \\ \text{C} = \text{C} \\ / \quad \backslash \\ \text{D} \quad \text{D} \end{array} \xrightarrow[\text{NaOD/D}_2\text{O 0.1 M}]{\text{Arl, [Pd] 0.3 mol\%}} \begin{array}{c} \text{H} \quad \text{Ar} \\ \diagdown \quad / \\ \text{C} = \text{C} \\ / \quad \backslash \\ \text{D} \quad \text{D} \end{array} + \begin{array}{c} \text{D} \quad \text{Ar} \\ \diagdown \quad / \\ \text{C} = \text{C} \\ / \quad \backslash \\ \text{H} \quad \text{D} \end{array} + \begin{array}{c} \text{D} \quad \text{Ar} \\ \diagdown \quad / \\ \text{C} = \text{C} \\ / \quad \backslash \\ \text{D} \quad \text{D} \end{array} + \text{[Si]} \begin{array}{c} \text{Ar} \\ \diagdown \quad / \\ \text{C} = \text{C} \\ / \quad \backslash \\ \text{D} \quad \text{D} \end{array}$		
		(<i>E</i>)-31- <i>d</i> ₂	(<i>Z</i>)-31- <i>d</i> ₂	32- <i>d</i> ₂
entry	[Pd]	yields (%) ^a		
		(<i>E</i>)-31- <i>d</i> ₂ (I or V)	(<i>Z</i>)-31- <i>d</i> ₂ (VI)	32- <i>d</i> ₂ (III)
1	Pd(OAc) ₂	12	23	60
2	Pd(OAc) ₂ + 2 DABCO	9	27	55
3	[PdCl ₂ (PTA) ₂]	10	16	70
4	[PdCl(Xantphos-DS)]Cl	11	22	58
5	[PdCl ₂ (en)]	63	4	30

		$\begin{array}{c} \text{D} \quad \text{Si(OEt)}_3 \\ \diagdown \quad / \\ \text{C} = \text{C} \\ / \quad \backslash \\ \text{H} \quad \text{D} \end{array} \xrightarrow[\text{NaOD/D}_2\text{O 0.1 M}]{\text{Arl, [Pd] 0.3 mol\%}} \begin{array}{c} \text{D} \quad \text{Ar} \\ \diagdown \quad / \\ \text{C} = \text{C} \\ / \quad \backslash \\ \text{H} \quad \text{D} \end{array} + \begin{array}{c} \text{D} \quad \text{Ar} \\ \diagdown \quad / \\ \text{C} = \text{C} \\ / \quad \backslash \\ \text{D} \quad \text{H} \end{array} + \begin{array}{c} \text{D} \quad \text{Ar} \\ \diagdown \quad / \\ \text{C} = \text{C} \\ / \quad \backslash \\ \text{D} \quad \text{D} \end{array} + \text{[Si]} \begin{array}{c} \text{Ar} \\ \diagdown \quad / \\ \text{C} = \text{C} \\ / \quad \backslash \\ \text{H} \quad \text{H} \end{array}$		
		(<i>Z</i>)-31- <i>d</i> ₂	1,1-31- <i>d</i> ₂	32- <i>d</i> ₁
entry	[Pd]	yields (%) ^a		
		(<i>Z</i>)-31- <i>d</i> ₂ (I)	1,1-31- <i>d</i> ₂ (V or VI)	32- <i>d</i> ₂ (III)
6	Pd(OAc) ₂	3	36	56
7	[PdCl ₂ (en)]	1	79	20

^aDetermined by ¹H NMR analysis of the crude reaction mixture.

respect to that of the pure Heck product 32 (molar ratio 31/32 = 3.4, Table S3). Second, formation of the vinylarene occurred almost exclusively via a Heck–*syn*-desilylation route (V), as was clearly demonstrated by the almost exclusive formation of (*E*)- and 1,1-31-*d*₂ vinylarenes from (*E*)- and (*Z*)-33-*d*₂, respectively (Table 4, entries 5 and 7).

It can be concluded from these experiments that the arylation of triethoxyvinylsilane with the Pd precursors examined here occurs exclusively via a Heck mechanism in aqueous NaOH. According to this, when performed at low temperature, the major reaction product is almost invariably the Heck-coupling product 32, whereas styrene 31 is formed by Pd-catalyzed desilylation of 32. In the presence of the ethylenediamine Pd complex, the reaction also occurs via Heck mechanism, although this catalyst notably favors the desilylation of the Heck-coupling product 32 via reinsertion of the olefin into the Pd–H bond of hydride II, followed by a classical Si β-elimination in the *syn* position (in contrast to the remaining catalysts). An explanation for this dual behavior can be found in the transmission electronic microscopy (TEM) images obtained from samples of a selected number of reactions containing different catalytic precursors. Two samples were studied for each reaction: the first was taken at low conversion levels (<33%) and the second after reaching full conversion. All these images, even those taken at low conversions and reaction temperatures, showed the presence of Pd nanoparticles (see Supporting Information). The ethylenediamine complex was again the only exception to this general behavior. The formation of Pd nanoparticles is interesting, irrespective of their direct involvement or not in the catalytic cycle, because it is indicative of a labile coordination of the ligands to the Pd(0) centers in the molecular species. The particular behavior of the ethylenediamine complex might therefore be ascribed to a more

long-lasting coordination of this ligand during the full catalytic cycle under these low-temperature conditions.

Other experimental evidence indirectly supports the above model. Thus, in the reactions catalyzed by Pd(OAc)₂, the Heck coupling product 32 and ethylene are rapidly formed at the beginning of the reaction, whereas the formation of vinylarene 31 tends to occur after the first hour of reaction and coincides with the slowing of ethylene evolution (Figure 2a; see also

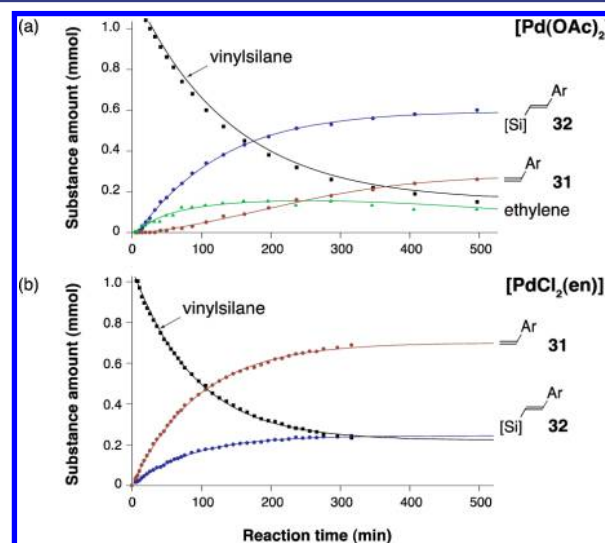
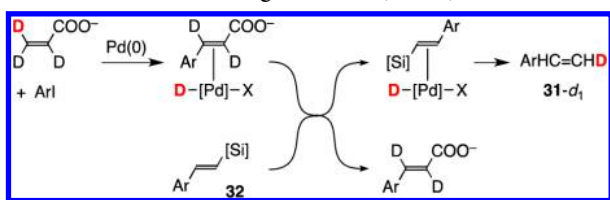


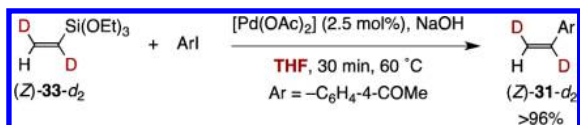
Figure 2. Kinetic profiles for the reaction of *p*-iodobenzoic acid and triethoxyvinylsilane in NaOD/D₂O at 30 °C catalyzed by 0.3 mol % of [Pd(OAc)₂] (a) or [PdCl₂(en)] (b).

Figure S4 in Supporting Information).⁵⁷ This behavior can be straightforwardly explained on the basis of the olefin exchange process shown in Scheme 7. Thus, at short reaction times, the large excess of the vinyl silanolate reagent favors the displacement of 32 from the coordination sphere of the Pd hydride complex II, thereby explaining the formation of similar amounts of this olefin and ethylene. This exchange becomes less favorable as the concentration of the starting vinyl silanolate decreases, and from this point, the desilylation of 32 prevails and the production of 31 increases. In the case of the ethylenediamine complex, the vinylarene 31 is the major product, even at the beginning of the reaction, and the evolution of ethylene is much less intense (Figure 2b). We can hypothesize that coordination of the en ligand slows the rate of exchange of olefin at the Pd hydride II. In a previous report,³⁸ we devised a simple experiment to demonstrate this exchange in the case of the Pd(OAc)₂ catalyst. This experiment consisted in the addition of a deuterated and nonsilylated olefin (sodium acrylate-*d*₃) to an initial reaction mixture comprising the vinylsilanolate and an excess of the iodoarene under the usual reaction conditions (Scheme 9). The Heck coupling of the deuterated olefin with the iodoarene presumably afforded a deuterido PdD(arylacrylate) complex. Exchange of the aryl acrylate with the silyl olefin 32 on this deuterido intermediate was evidenced by complete conversion of the latter into the deuterated styrene 31-*d*₁. In contrast, the formation of this deuterated compound was essentially not observed when a similar experiment was performed with the [PdCl₂(en)] catalyst, according to the proposed blockage of the olefin exchange by the en ligand.

Scheme 9. Olefin Exchange on PdH(olefin) Intermediates^a

^aThe transferred deuterium is marked in bold red.

The Effect of the Solvent. The NaOH-promoted cross-coupling of organosilicon compounds with organic halides was first reported by Hatanaka and co-workers,³⁷ who studied the reaction between bromoarenes and alkenylchlorosilanes in THF using Pd(OAc)₂ as catalyst. Although not explicitly mentioned in the original report, it can be assumed that alkenylchlorosilanes were converted into their corresponding alkenylsilanolates by action of the base. The observed retention of the original *cis* or *trans* stereochemistry around the double bond was coherent with a cross-coupling (Hiyama) reaction. It should be observed that, except for the solvent (THF instead of water), these reactions were performed under conditions comparable to those used in this work. Intrigued by the apparent fundamental role played by the solvent, we tested the reactivity of (*Z*)-**33-d₂** under the Hatanaka conditions because this isomer can discriminate between the Hiyama and Heck routes. The retention of the configuration in the reaction (Scheme 10) confirmed the dramatic effect of the solvent on

Scheme 10. Reaction of (*Z*)-Triethoxy(vinyl-*d*₂)silane and *p*-Iodoacetophenone in THF

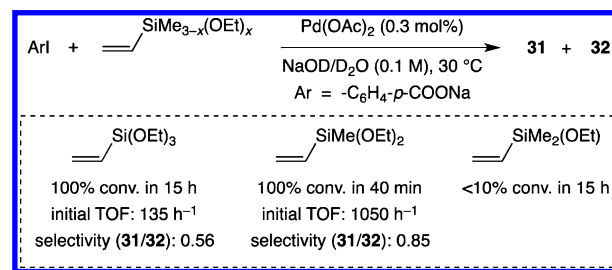
the operating mechanism, which switched from Heck in water to Hiyama in THF. Nucleophilic attack of the hydroxide anion at the silicon center is possibly the key step in the transmetalation process. However, the nucleophilicity of the hydroxide (or fluoride) anion is notably reduced in protic solvents such as water, where the anion is strongly solvated by means of hydrogen bonds, thus probably making the transmetalation step less favorable (the free energies of hydration for fluoride and hydroxide are around 440 and 410 kJ/mol, respectively).⁵⁸ In the absence of powerful solvation effects, nucleophilicity follows approximately the same order as basicity. Basicity is thermodynamically controlled and, thus, the affinity of the hard fluoride or hydroxide bases for the hard silicon acid center can be easily rationalized in terms of the exceptionally high energy of the resulting Si–X bonds (565 kJ/mol for Si–F and 452 kJ/mol for Si–O bonds). However, the order of kinetically controlled nucleophilicity is typically altered for small negatively charged ions in protic polar solvents in which the shell of hydrogen-bonded solvent molecules constitutes a barrier between them and the substrate.⁵⁹ For instance, even small amounts of water in an aprotic solvent can produce dramatic effects as regards the reactivity of fluoride salts as fluorinating agents.⁶⁰

These results point to a general prevalence of Heck- over Hiyama-type reactivity under alkaline aqueous conditions and could shed new light on results previously published in the

literature. For instance, it has been reported that the arylation of (*E*)-styryltriethoxysilane with several aryl halides in NaOH aqueous solutions under MW heating afforded mixtures of 1,1- and 1,2-(*E*) disubstituted olefins.³⁵ Formation of the latter was interpreted as being result of a Hiyama cross-coupling, whereas the 1,1 regioisomer was justified on the basis of a Heck–desilylation mechanism. The report concluded that the “ α -arylation was observed in higher proportions with aryl iodides than bromides or chlorides”. We can now reinterpret the formation of the 1,2-(*E*) regioisomer as being due to a Heck coupling between the aryl halide and the styrene formed in situ by thermal hydrolysis of the (*E*)-styryltriethoxysilane Si–C bond at the high reaction temperature (120 °C). Fast-reacting substrates such as aryl iodides will encounter lower proportions of styrene versus (*E*)-styryltriethoxysilane in the reaction medium and will therefore afford higher proportions of the 1,1 regioisomer, which is formed by Heck coupling of the latter. Following similar reasoning, the formation of significant amounts of 1,1-diarylethene with some of the substrates in Scheme 2 might be related to the slower hydrolysis kinetics of the Si–C bond in the (*E*)-silyl intermediate **III**.

The Effect of the Silane. The partial replacement of ethoxy by methyl groups had a marked effect on the alkoxyvinylsilane reactivity (Scheme 11). Thus, the diethoxy-

Scheme 11. The Effect of Silane Substituents



ymethylvinylsilane substrate markedly accelerated the reaction under the standard conditions used (0.1 M NaOD), attaining a TOF of 1050 h⁻¹ at 30 °C (compared with 135 h⁻¹ for triethoxyvinylsilane).⁵⁵ In contrast, the chemoselectivity was only slightly affected, thus pointing to a marginal influence of the silane on the prevalent Heck routes. Hatanaka and co-workers observed a similar effect of methyl substituents on the kinetics of the above-mentioned NaOH-promoted reactions of alkenylchlorosilanes in THF.^{37,61} This coincident trend in two reactions that progress via different routes may indicate a common origin in a step prior to the bifurcation of the Heck and Hiyama paths. One possible explanation is that silanetriol species are more likely to lead to condensed structures that reduce the accessibility of the vinyl group. Furthermore, the introduction of a methyl substituent must increase the nucleophilic strength of the silanolate oxygen-donor atom, thus making the foreseeable coordination of this oxygen to the palladium(II) center prior to the transmetalation (Hiyama) or insertion (Heck) steps more favorable.

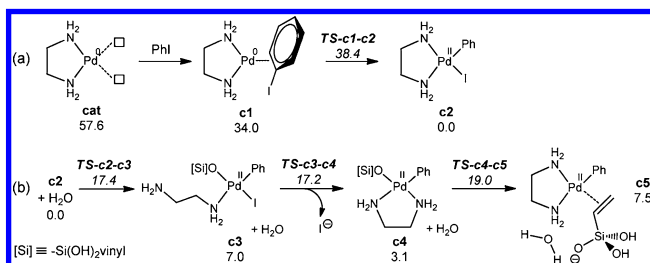
In contrast with the above trend, the dimethylated silane was almost unreactive. We initially ascribed this lack of reactivity to the low concentration of silanolate **29** under our reaction conditions (0.1 M NaOD). However, the concentration of **29** in solution represents around 15% of the added vinylsilane (as determined by ¹H NMR) and should remain invariant during the reaction by equilibration with the insoluble dtvms **30**.⁶² We

arrived at a more satisfactory explanation from our observation that the addition of *dvmts* completely inhibited the catalytic cycle in the reaction of ArI with (vinyl)Si(OEt)₃ (see Supporting Information for details). *Dvmts* forms fairly stable complexes by chelate coordination of the vinyl groups to Pd(0) or Pt(0). Coordination alone, however, cannot explain the drastic inhibition effect of *dvmts*. Thus, (vinyl)Si(OEt)₃ is an efficient coupling partner despite the significant amounts of divinyl disiloxane **26** present in solution (see Scheme 5). It is foreseeable that Pd complexes formed by the *dvmts* ligand are extracted into the immiscible phase formed by this disiloxane, thereby restricting the accessibility of the vinylsilanolates to the catalytic centers. This type of mechanism is compatible with the absence of inhibiting effects in similar reactions performed in organic solvents in the presence of *dvmts*.⁶²

Computational Study of the Reaction Mechanism Involving the [PdCl₂(en)] Precursor. Although the experimental study provided several mechanistic clues, the [PdCl₂(en)] precursor behaves in a different manner from the other catalysts surveyed in terms of both the nature of the major product (formation of vinylarene **31** favored over the formation of the silyl derivative **32**) and the stereochemistry of the desilylation product (*syn* product favored). These differences have been ascribed above to stable coordination of the ethylenediamine ligand to the palladium center during the catalytic cycle. This coordination hampers olefin exchange on the palladium intermediate **II** and simplifies the global mechanism shown in Scheme 7. Moreover, no Pd nanoparticles were observed during the reaction. As a result, we chose this catalyst to perform a theoretical investigation of the full catalytic cycles, which involved analyzing the competitive pathways that lead to the possible experimental products (**I**, **III**, **V**, and **VI**, see Scheme 7). Unsaturated [Pd(en)]²⁺ cat was employed as catalyst and vinyl-Si(OH)₂O⁻ [2S-Na]⁻ and iodobenzene as reagents. The solvent was represented by continuum methods that also explicitly included a solvent water molecule. The Hiyama and Heck reaction mechanisms were computed first because they should explain the formation of products **I** and **III**, respectively. Two desilylation pathways to yield products **V** and **VI** via intermediate **II** (from Heck mechanism) were then proposed.

The Hiyama and Heck reaction mechanisms share the first two reaction steps, namely, oxidative addition and iodide substitution (Scheme 12). The oxidative addition is characterized by a three-center interaction, TS-c1-c2, and proceeds quickly because it involves a relative barrier of only 4.4 kcal mol⁻¹ (Scheme 12a).⁶³ The resulting complex, [Pd(en)(Ph)I]

Scheme 12. Common Steps for the Hiyama and Heck Reaction Mechanisms: (a) Oxidative Addition and (b) Iodide Substitution^a



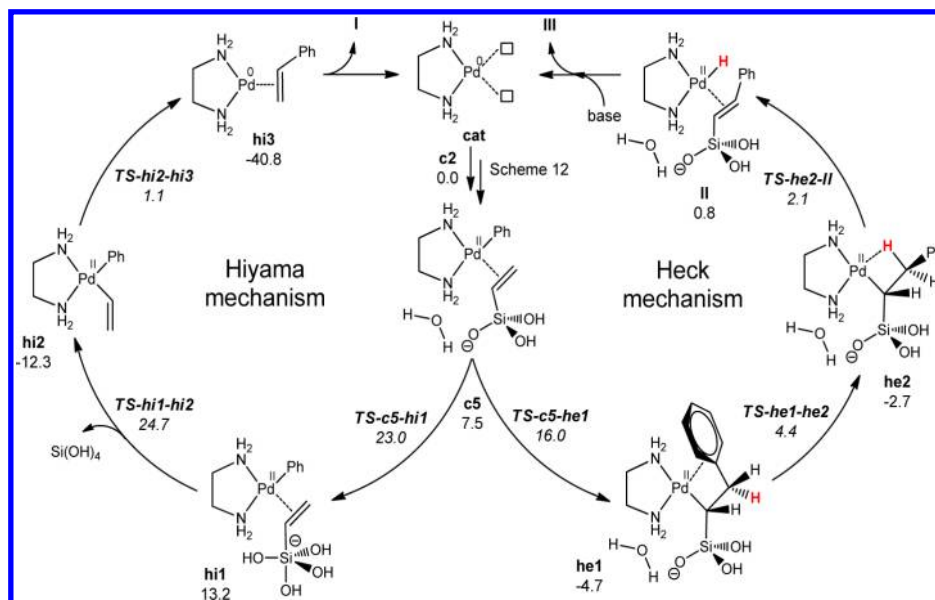
^aGibbs energies (water) in kcal mol⁻¹.

c2, was taken as our zero of energies. No transition state was located for direct iodide substitution by the vinylsilanolate compound. Instead, a stepwise substitution route involving an intermediate **c3**, in which a nitrogen arm of the didentate amine ligand is displaced, was found (Scheme 12b). The oxygen of the vinylsilanolate species initially replaces the amine group located *trans* to the halide (the process *cis* to the halide is less favored, see Supporting Information), then the amine arm coordinates again, substituting the iodide ligand. Both processes involve five-coordinate transition states (TS-c2-c3 and TS-c3-c4 located at 17.4 and 17.2 kcal mol⁻¹, respectively). An explicit water molecule was included at this point to better represent the environment of the vinylsilanolate ligand, which bears a negative charge. As a result, this ligand changes its coordination mode from η¹-O **c4** to η²-C=C **c5** via TS-c4-c5 (19.0 kcal mol⁻¹). Once intermediate **c5** has formed, the reaction mechanism splits into two different routes for the Hiyama and Heck catalytic cycles *per se*.

Starting from intermediate **c5**, the Hiyama mechanism (Scheme 13, left) continues via a transmetalation step, which is promoted by the addition of a water molecule to the silanolate ligand in order to weaken the C–Si bond. One hydrogen from the water is abstracted by the charged oxygen of the silanolate and the freshly formed hydroxide anion binds to the silicon atom.⁶⁴ The activation process needs 23.0 kcal mol⁻¹ to reach TS-c5-hi1 and the resulting five-coordinate silicon species **hi1** can now undergo the transmetalation step via TS-hi1-hi2 (24.7 kcal mol⁻¹).⁶⁵ Finally, reductive elimination takes place via the three-centered transition state TS-hi2-hi3, with an activation barrier of 13.4 kcal mol⁻¹. The Hiyama product **I** is obtained, and the catalyst **cat** is regenerated. The rate-determining step of the entire catalytic cycle concerns the transmetalation process and requires 24.7 kcal mol⁻¹ above intermediate **c2**. According to labeling studies, since hydrogen does not participate in the reaction, the deuterium distribution in the product should not be affected.

In the Heck mechanism (Scheme 13, right), the vinylsilanolate ligand of intermediate **c5** can insert into the Pd–Ph bond by means of TS-c5-he1. Subsequent rotation of the C–C bond changes the coordination mode via TS-he1-he2, located at 9.1 kcal mol⁻¹ above **he1**, and generates an agostic intermediate **he2**. This agostic interaction lengthens the C–H bond distance, thus allowing it to be more easily cleaved via a β-elimination process. The corresponding transition state TS-he2-II, which lies 4.8 kcal mol⁻¹ above **he1**, gives the palladium hydride **II** from which the Heck product **III** can be released. The rate-determining step for this catalytic cycle corresponds to the coordination change (Scheme 12b), which demands 19.0 kcal mol⁻¹ above **c2**. In this case, although one hydrogen atom takes part in the reaction, it is not included in the final product so the deuterium pattern will remain unchanged.

To enable a better comparison between pathways, Figure 3 shows the Gibbs energy profiles for the Hiyama (dotted line) and Heck (solid line) reaction mechanisms. After the rapid oxidative addition of iodobenzene, the resulting complex **c2** evolves until intermediate **c5**, that is, the iodide substitution followed by the coordination change required for coordination of the vinyl group to the palladium center. At this point, the catalytic cycle can follow two different pathways. For the Hiyama route, **c5** should reach TS-c5-hi1, which is located at 23.0 kcal mol⁻¹ above **c2**, in order to achieve C–Si bond activation. Moreover, the subsequent transmetalation step requires even more energy (24.7 kcal mol⁻¹). On the other

Scheme 13. Hiyama and Heck Reaction Mechanisms^a

^aParticipating hydrogen is marked in bold red. Gibbs energies (water) in kcal mol⁻¹.

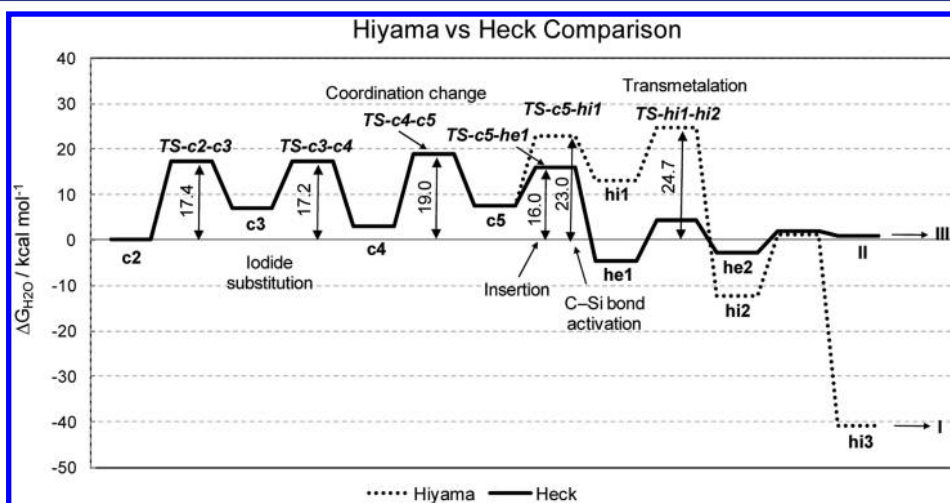
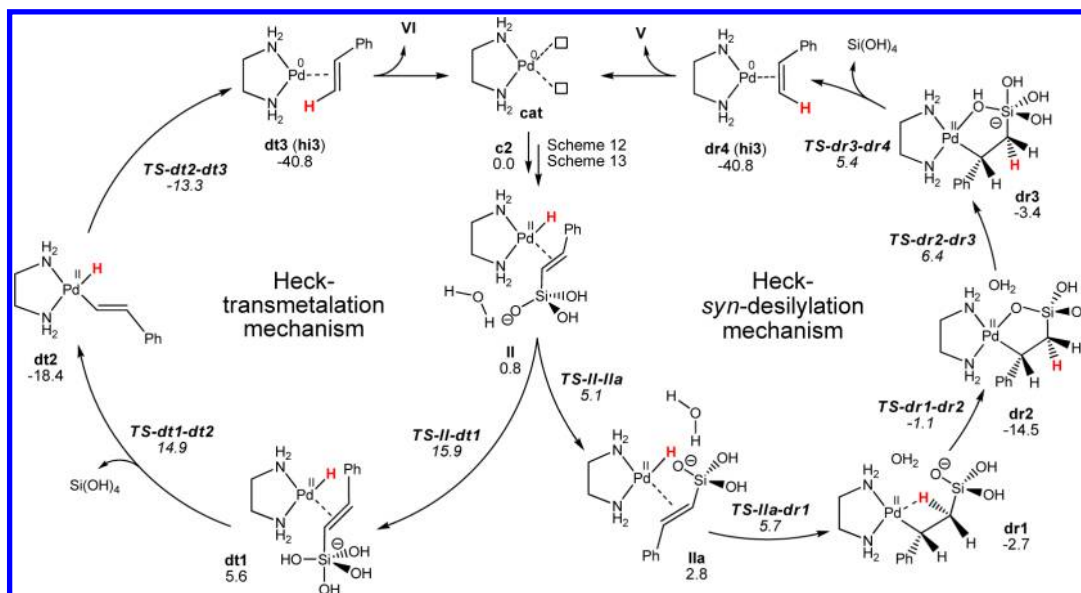


Figure 3. Gibbs energy (water) profiles for Hiyama (dotted line) and Heck (solid line) reaction mechanisms.

hand, as shown in the Heck route, the evolution of **c5** may also proceed via insertion of the vinyl group into the Pd–Ph bond, which requires 16.0 kcal mol⁻¹. Focusing on the rate-determining step for each route, the coordination change in the Heck cycle demands 5.7 kcal mol⁻¹ less than the transmetalation step in the Hiyama one. This result, together with the more facile evolution of intermediate **c5** via the insertion step (16.0 vs 24.7 kcal mol⁻¹), clearly favors the Heck reaction mechanism.

Once the Hiyama reaction mechanism can be ruled out, two desilylation mechanisms can be proposed to account for the experimentally observed product distribution. Both pathways are initiated using palladium hydride intermediate **II**, which is obtained through the Heck reaction mechanism, as starting point. The so-called Heck–transmetalation route (Scheme 14, left) suggests a transmetalation step, whereas the Heck–*syn*-desilylation alternative (Scheme 14, right) entails reinsertion of the olefin and subsequent *syn* Pd–Si β -elimination, as shown previously in Scheme 7.

The Heck–transmetalation mechanism (Scheme 14, left) occurs in an analogous manner to the Hiyama one. Thus, the C–Si bond of intermediate **II** is initially activated by nucleophilic attack of a water molecule via **TS-II-dt1** (located at 15.9 kcal mol⁻¹).⁶⁴ Transmetalation of the activated complex **dt1** takes place via **TS-dt1-dt2**, which requires 14.9 kcal mol⁻¹ and releases the silanol Si(OH)₄.⁶⁵ Notably, the transmetalation step in this mechanism requires much less energy than the Hiyama one (**TS-hi1-hi2** at 24.7 kcal mol⁻¹). The resulting styryl complex **dt2** undergoes reductive elimination via **TS-dt2-dt3**, which finally yields the product **VI** and regenerates the catalyst **cat**. The C–Si bond activation step is the rate-determining step in the process, although the transmetalation process has a very similar barrier. Due to the nature of this mechanism, product **VI** includes the hydrogen atom in the *trans* position with respect to the phenyl group coming from an *anti* desilylation process. A competitive proposal to generate **VI** (without a transmetalation step) is described in the Supporting Information (Scheme S5).

Scheme 14. Heck–Transmetalation and Heck–*syn*-Desilylation Reaction Mechanisms^a

^aThe participating hydrogen is marked in bold red. Gibbs energies (water) in kcal mol⁻¹.

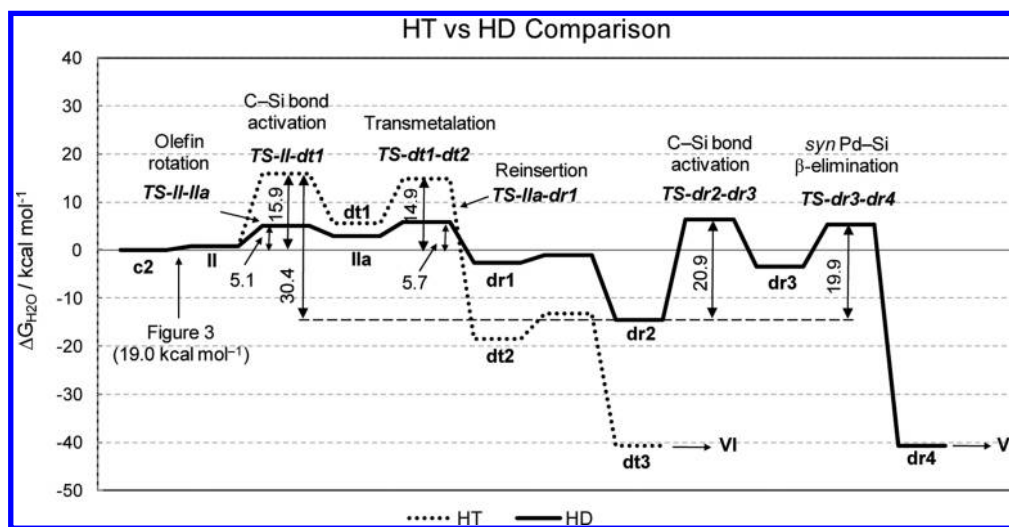


Figure 4. Gibbs energy (water) profiles for Heck–transmetalation (HT, dotted line) and Heck–*syn*-desilylation (HD, solid line) reaction mechanisms.

The second proposal, the so-called Heck–*syn*-desilylation mechanism (Scheme 14, right), starts with the conformational change of the *trans*-silylated styrene ligand. Olefin rotation occurs via **TS-II-Ia**, which lies 9.8 kcal mol⁻¹ above **he1**.⁶⁶ The *trans*-silylated styrene ligand of **IIa** can then insert into the Pd–H bond via **TS-IIa-dr1**, which lies 10.4 kcal mol⁻¹ above **he1**. This reaction produces the corresponding agostic intermediate **dr1**, which quickly evolves to the more stable compound **dr2** by forming a new Pd–O bond. From **dr1**, the addition of a water molecule to promote a β -Si *anti* elimination process could not be found. The coordination change via **TS-dr1-dr2** requires only 1.6 kcal mol⁻¹ with respect to **dr1** and the resulting intermediate **dr2** lies 14.5 kcal mol⁻¹ below **c2**. The ability of the silanolate group to coordinate the metal via its oxygen atom allows a *syn* configuration to be established between the silicon and palladium atoms. A C–Si bond activation is eventually required in order to carry out the desilylation step. Once again, a water molecule attacks the

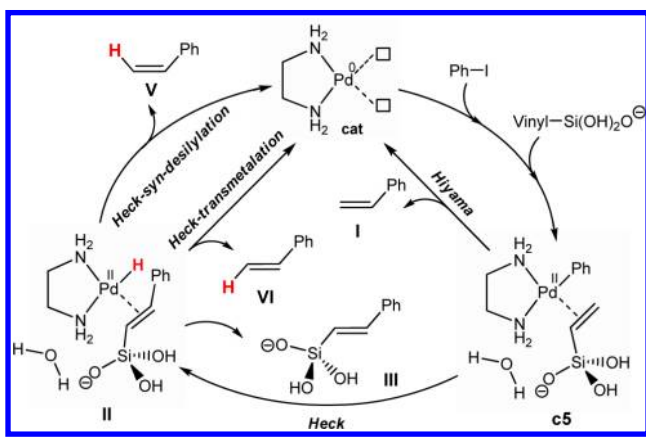
silicon atom via **TS-dr2-dr3** with a barrier of 20.9 kcal mol⁻¹ from **dr2**. Intermediate **dr3** then undergoes a *syn* Pd–Si β -elimination via **TS-dr3-dr4**, which yields complex **dr4** through a barrier of 19.9 kcal mol⁻¹. As shown in the previous Heck–transmetalation mechanism, the rate-determining step also involves the C–Si bond activation, although the coordination change (Scheme 12) and β -elimination processes are also close in energy. As far as labeling aspects are concerned, olefin rotation together with the formation of intermediate **dr2** locates the hydrogen atom *cis* to the phenyl group, thus forming the *syn* desilylation product **V**. As suggested experimentally, this result relates the reinsertion process with the observed *syn* stereochemistry.

The Gibbs energy profiles for both desilylation pathways are displayed in Figure 4, where the dotted line represents the Heck–transmetalation (HT) and the solid line the Heck–*syn*-desilylation (HD). Starting from the common intermediate **II**, the reinsertion process (**TS-IIa-dr1**) is favored over C–Si bond

activation (TS-II-dt1) by $10.2 \text{ kcal mol}^{-1}$, thus meaning that the former mechanism evolves faster. Once the reaction has reached intermediate **dr2**, the Gibbs energy barrier for the HD route becomes $20.9 \text{ kcal mol}^{-1}$, which is indeed higher than that for the HT route ($15.9 \text{ kcal mol}^{-1}$). However, the retro-HD route from **dr2** to obtain **II** and subsequent C–Si bond activation via TS-II-dt1 is not possible because the new energy barrier is $30.4 \text{ kcal mol}^{-1}$. In other words, intermediate **dr2** drives the reaction toward the formation of *syn* product **V**. Finally, formation of the *anti* product **VI** should follow a pathway that does not include an olefin reinsertion process.

In summary, four catalytic cycles have been investigated to explain the formation of four types of products (**I**, **III**, **V**, and **VI**; see Scheme 15). Labeling experiments with the

Scheme 15. General Scenario Summarizing All the Pathways Studied



[PdCl₂(en)] precursor have shown that the major product **V** corresponds to reinsertion and subsequent *syn* desilylation processes, whereas the yields for both the *anti* desilylation and Hiyama routes are quite low (see Table 4, entries 5 and 7, respectively). According to theoretical calculations, the Hiyama route (product **I**) can be ruled out since water-promoted transmetalation in this mechanism ($24.7 \text{ kcal mol}^{-1}$) is less favored than both coordination change ($19.0 \text{ kcal mol}^{-1}$) and insertion ($16.0 \text{ kcal mol}^{-1}$) in the Heck route (product **III**). As such, the Gibbs energy barriers support the Heck mechanism as the most feasible pathway. However, the catalytic engine has not stopped and can continue to evolve via the Heck intermediate **II** by removal of the silanolate fragment. Two water-assisted desilylation mechanisms are possible: the first involves a transmetalation step (HT) and generates the desilylation *anti* product **VI**, whereas the other (HD) suggests reinsertion and *syn*-elimination processes to yield the *syn* desilylation product **V**. Starting from intermediate **II**, the Gibbs energy barriers show the reinsertion step in the HD route (TS-IIa-dr1 at $5.7 \text{ kcal mol}^{-1}$) to be favored over C–Si bond activation in the HT route (TS-II-dt1 at $15.9 \text{ kcal mol}^{-1}$) by $10.2 \text{ kcal mol}^{-1}$. Finally, the structure of intermediate **dr2** imposes and explains the *syn* stereochemistry observed experimentally.

CONCLUSION

The experimental and computational studies presented herein have furnished mechanistic insights into the Pd-catalyzed vinylation of aryl halides with alkoxyvinylsilanes in water. Specifically, the reaction between *p*-iodobenzoic acid and

triethoxyvinylsilane has been investigated in the presence of different catalytic Pd precursors. Irrespective of the catalytic precursor, vinylation occurs exclusively at the CH vinylic functionality to afford a mixture of Heck and Heck–desilylation products (*β*-silylvinylarene and vinylarene, respectively). Only vinylarenes are obtained in reactions performed at high temperature due to rapid hydrolysis of the Si–vinylarene bonds under these conditions. It is usually assumed that Heck–desilylation occurs via a reinsertion–*β*-Si-*syn*-elimination mechanism. However, deuterium-labeling experiments have revealed the concurrence of a second (usually major) route for which we propose a transmetalation mechanism. The participation of the competing routes in the reaction as a whole does not appear to be markedly affected by the nature of the catalyst. However, it should be taken into account that most of the Pd precursors studied are degraded to Pd(0) nanoparticles under our reaction conditions. In this respect, the [PdCl₂(en)] complex was the only Pd precursor that showed a significantly different behavior by favoring the Heck–*syn*-desilylation route and the only complex for which Pd NP formation was never observed. Computational studies on this diamine precursor clearly rule out the Hiyama mechanism, thereby enhancing the Heck pathway as the most favored. As far as elimination of the silicon moiety is concerned, the calculated Gibbs energy barriers show that the Heck–*syn*-desilylation mechanism is lower in energy than the Heck–transmetalation one. In an aqueous medium, a solvent molecule is suggested to activate the corresponding C–Si bonds. However, the Heck–transmetalation pathway can be accessible for other precursors if the reinsertion route is blocked.

Vinylation is efficiently promoted by sodium hydroxide or other strong Brønsted bases. These bases afford an aqueous solution of sufficient alkalinity to stabilize the silicon vinyl donor in the form of highly reactive water-soluble silanolate species. Under these aqueous NaOH conditions, we have never observed the involvement of the C–Si bond in cross-coupling (Hiyama) reactions. The influence of the aqueous solvent in this result is apparent from the comparison with reactions performed in THF under similar conditions, which follow a Hiyama mechanism. The reduced nucleophilicity of the hydroxide or fluoride Hiyama activators probably represents an important hindrance to the transmetalation step in water. We have shown that the alternative Denmark-type activation via silanolate formation also accelerates the Heck coupling. It is important to note that an efficient control of the Hiyama/Heck/Heck–desilylation routes has provided a notable synthetic flexibility to the synthesis of complex olefins using alkenylsilanes in nonaqueous solvents. Thus, while the viability of performing Hiyama vinylation in water remains to be demonstrated, it appears that Heck/desilylation processes can be appropriately controlled by way of the Pd catalyst. In this respect, it is important to develop water-soluble catalysts for the coupling of inactivated aryl halides at moderate temperatures to avoid C–Si bond hydrolysis, in addition to finding conditions that favor olefin displacement/HX elimination versus competing desilylation steps. Finally, the critical influence of the silicon substituents on the vinylsilane reactivity should be taken into account when designing new synthetic protocols.

EXPERIMENTAL SECTION

General Procedure for the Vinylation Experiments under Different Basic Conditions. Sodium dihydroxyvinylsilanolate (**25**; 0.2324 g, 1.81 mmol), sodium 4-iodobenzoate (0.2700 g, 1.00 mmol),

and an aqueous solution of the base at the appropriate concentration (8 mL) were introduced into a 35 mL Ace pressure tube and stirred vigorously for 5 min at room temperature. The initial pH of the solution was then measured. After addition of the palladium acetate catalyst (0.7 mg, 3 μmol), the tube was placed into a silicone bath warmed to 30 $^{\circ}\text{C}$ and vigorously stirred for 22 h. The final pH of the solution was then measured. The solvent was removed under vacuum, and the conversions were determined by ^1H NMR spectroscopy.

General Procedure for ^1H NMR Monitoring Experiments. 4-Iodobenzoic acid (50.6 mg, 0.20 mmol) was introduced into a 5 mL vial and dissolved in a 0.35 M NaOD solution in D_2O (2.0 mL). After addition of triethoxyvinylsilane (0.052 mL, 0.24 mmol), the mixture was stirred vigorously for several minutes until complete dissolution, then a 1.0×10^{-2} M solution of the appropriate palladium catalyst in D_2O (60.0 μL , 0.60 μmol) added. An aliquot of this solution (0.20 mL) was immediately transferred to a 5 mm NMR tube fitted with a J. Young valve containing D_2O (0.50 mL) at 0 $^{\circ}\text{C}$. The tube was quickly introduced into the NMR probe previously thermostatted at 30 $^{\circ}\text{C}$, and the automatic data collection program was then started. Concentrations were determined from the relative integrals of the well-resolved vinylic resonances with respect to the overall integration of aryl protons.

Computational Details. All calculations were performed at the DFT level using the M06 functional⁶⁷ with an ultrafine grid,⁶⁸ as implemented in Gaussian09.⁶⁹ Pd and I atoms were described using an effective core potential SDD⁷⁰ for the inner electron and its associated double- ζ basis set for the outer ones, complemented with a set of f-polarization functions.⁷¹ The 6-31G** basis set was used for the H,⁷² C, N, O, and Si atoms.⁷³ Diffuse function was added for the O atom in all calculations.⁷⁴ Solvent effects (water, $\epsilon = 78.35$) were introduced via SMD⁷⁵ single-point calculations on gas-phase-optimized geometries using the 6-311++G** basis set for H, C, N, O, and Si atoms.^{74,76} The structures of all reagents, intermediates, transition states, and products were fully optimized without any symmetry restriction. Transition states were identified by having one imaginary frequency in the Hessian matrix. It was confirmed that transition states connect with the corresponding intermediates by applying the eigenvector corresponding to the imaginary frequency and subsequent optimization of the resulting structures. Gibbs energies in solution (water), ΔG_{solv} , were calculated using the following formula, where a "gp" subscript indicates gas phase and TZ and DZ labels represent the 6-311++G** and 6-31G** basis sets respectively.

$$\Delta G_{\text{solv}} = \Delta E_{\text{solv}}(\text{TZ}) + \Delta G_{\text{gp}}(\text{DZ}) - \Delta E_{\text{gp}}(\text{DZ})$$

■ ASSOCIATED CONTENT

■ Supporting Information

Full experimental procedures, characterization data, kinetic profiles for all the catalysts, NMR spectra, ball-and-stick representations of selected structures, alternative iodide substitution, additional transition states, and Cartesian coordinates, absolute energies, and Gibbs energies in gas-phase and water (hartrees) of all the optimized structures. This material is available free of charge via the Internet at <http://pubs.acs.org>.

■ AUTHOR INFORMATION

Corresponding Authors

*ernesto.dejesus@uah.es

*gregori@klingon.uab.es

Notes

The authors declare no competing financial interest.

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