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Journal of Organometallic Chemistry 624 (2001) 372–375

Journal of Organo metallic Chemistry

www.elsevier.nl/locate/jorganchem

Communication

Cross-coupling of vinylpolysiloxanes with aryl iodides

Scott E. Denmark *, Zhigang Wang

Roger Adams Laboratory, Department of Chemistry, University of Illinois, Urbana, IL 61801, USA

Received 16 October 2000; accepted 14 November 2000

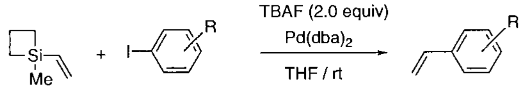
Abstract

Commercially available vinylpolysiloxane (**1**) rapidly undergoes cross-coupling reactions with aryl and alkenyl iodides in the presence of tetrabutylammonium fluoride (two to three equivalents) and Pd(dba)$_2$ (1–5 mol%) at room temperature to afford coupling products in high yield. This process employs an inexpensive and non-toxic siloxane reagent and shows good functional group compatibility and high stereospecificity. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Cross-coupling; Vinylpolysiloxanes; Palladium catalysis; Styrenes; Alkenes

1. Introduction

The palladium-catalyzed cross-coupling of aryl or alkenyl halides with organometallic reagents (Li, Mg. Al, Zn, B, Sn) has emerged as one of the most general carbon–carbon forming reactions in the past 30 years [1]. Despite early efforts by Kumada and Ito [2], only recently have organosilicon compounds been incorporated into the set of agents that are able to participate in transferring an organic unit in this process. In all of these cases, primarily studied by Hiyama and Deshong, the silafunctional unit contained one or more heteroatoms to assist in the activation of the transmetalation [3–5]. The focus of efforts in these laboratories in recent years has been to develop new classes of silicon coupling reagents that allow for mild and selective cross-coupling reagents. Initial studies led to the development of a trialkylsilyl moiety (silacyclobutane) which was successfully employed in cross-coupling reactions with aryl or alkenyl halides [6]. Importantly, this unique process affords the desired products in high yields under mild conditions and with good functional group compatibility. Moreover, the coupling reactions with alkenyl halides are also stereospecific.



Scheme 1. Cross-coupling of vinylsilacyclobutane.

As part of a rapidly expanding program to explore the scope of structural types capable of participating in these coupling reactions, we investigated the simplest alkenyl derivative, 1-methyl-1-vinylsilacyclobutane. This stable, low boiling liquid was easily synthesized and its coupling to aryl and alkenyl halides was explored (Scheme 1) [6c]. For electron poor aryl iodides, the coupling reactions proceeded rapidly to afford the products in good yields. For electron-rich iodides, the coupling reactions proceed more slowly, though without deleterious consequences on the yield. In the latter cases, the addition of triphenylarsine was necessary for the reaction to reach completion [7]. The compatibility with a variety of functional groups and substituent patterns revealed that the vinylsilacyclobutane is a very useful vinylation reagent for aryl and alkenyl halides.

In the course of efforts to deduce the mechanism of this reaction, both silanols and disiloxanes were found to be the effective coupling components under conditions nearly identical to those used with alkenyl silacyclobutanes [8,9]. These observations encouraged us to test the cross-coupling reaction of commercially available vinylpolysiloxanes with aryl and alkenyl iodides. Herein, we report our preliminary studies on the palla-

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* Corresponding author.

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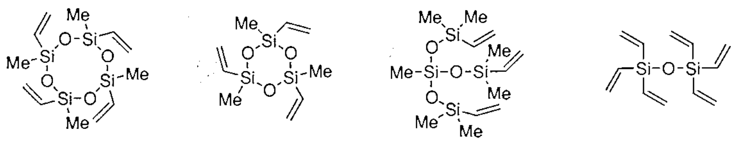
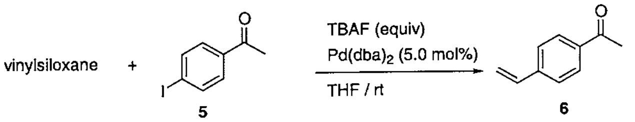
PII: S0022-328X(00)00894-9



1 2 3 4

Fig. 1. Structures of 1,3,5,7-tetramethyl-1,3,5,7-tetravinylcyclotetrasiloxane (D_4^V, **1**) 1,3,5-trimethyl-1,3,5-trivinylcyclotrisiloxane (D_3^V, **2**), tri(vinyldimethylsiloxy)-methylsilane (**3**) and hexavinyldisiloxane (**4**).

Table 1
Optimization of the coupling of vinylpolysiloxanes with **5**



Entry	Vinylsiloxane (equivalents)	TBAF (equivalents)	Time (min)	Conversion (%)[a]
1	**1** (1.2/4)	2.0	10	100 (88)
2	**2** (1.2/3)	2.0	10	100 (85)
3	**3** (1.2/3)	2.0	10	100 (89)
4	**4** (1.2/6)	2.0	10[b]	78
5	**4** (1.5/6)	2.0	10	94 (51)
6	**4** (1.5/6)	3.0	10	93 (53)

[a] The numbers in parentheses are isolated yields from 2.0 mmol scale experiments.
[b] r.t., 5 h, 92% conversion by GC, the reaction then stalled.

dium-catalyzed cross-coupling of vinylpolysiloxanes with aryl iodides.

2. Results and discussion

To initiate these studies we selected four, commercially available vinylsiloxanes which represented three different classes of silicon functional groups, cyclooligodisiloxanes (**1** and **2**), orthosiliconate (**3**) and hexavinyldisiloxane (**4**) (Fig. 1). These reagents were chosen to explore their potential to deliver each of the vinyl groups as well as for their ease of handling and cost [10].

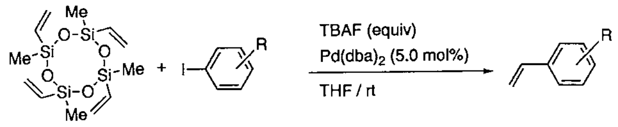
For orienting experiments, 4-iodoacetophenone (**5**) was chosen to test the coupling of vinylpolysiloxanes using reaction conditions employed previously with minimum modification (5 mol% Pd(dba)$_2$, two equivalents tetrabutylammonium fluoride (1.0 M in THF, room temperature)) [6a,c,8a]. The established stoichiometry of transferable vinyl group to iodide was maintained at 1.2/1, thus the molar equivalents of each precursor was divided by the number of available vinyl groups. The results are compiled in Table 1.

Silanes **1**, **2** and **3** underwent rapid coupling to 4-iodoacetophenone (**5**). In all of these cases, the starting iodide was completely consumed at room temperature within 10 min to afford the product **6** in 88, 85 and 89% yields, respectively. The coupling reaction of **4** was discouraging since it did not proceed to completion. The initial rate of coupling, however, was not slow (78% conversion at 10 min). Disappointingly, extending the reaction time at 5 h still did not reach completion. Further increasing the loading of reagent **4** to 1.5/6 equivalents and also increasing the amount of TBAF to three equivalents gave 93% conversion at 10 min (entry 6), but the progress of the reaction once again stalled. A 2.0 mmol scale descriptive run under these conditions afforded the coupling product in low yield (53%).

From these results it is clear that vinylation precursors **1**, **2** or **3** could each be employed for this transformation. On the basis of cost and efficiency of vinyl transfer [10], we chose the vinylpolysiloxane (**1**) for further examination of scope of the coupling reaction with a number of different aryl and alkenyl iodides. The results are collected in Table 2.

As had been previously observed, the coupling reaction between **1** and electron poor iodides (4-iodoacetophenone (**5**), ethyl 4-iodobenzoate (**7**) and 3-iodonitrobenzene (**11**)) proceeded smoothly to afford the corresponding products in high yields. When the loading of Pd(dba)$_2$ was decreased to 1 mol%, the reaction of **1** with **7** was also complete in 1 h to afford the product in comparable yield (83%). In all these experiments, the catalyst was added last which caused a significant exotherm (up to 55°C on a 2 mmol scale) for the fast acting substrates (**5**, **7**, **11**). A modified procedure in which a solution of **5** was added last such that

Table 2
Cross-coupling of **1** (D_4^V)with aryl iodides [a]



Entry	Aryl, R	**1** (equivalents)	TBAF (equivalents)	Time (min)	Product	Yield (%)
1	4-COMe (**5**)	1.2/4	2.0	10	**6**	88
2 [b]	4-COMe (**5**)	1.2/4	2.0	10	**6**	80
3	4-COOEt (**7**)	1.2/4	2.0	10	**8**	85
4 [c]	4-COOEt (**7**)	1.2/4	2.0	60	**8**	83
5	4-OMe (**9**)	1.5/4	3.0	240	**10**	46
6 [d]	4-OMe (**9**)	1.5/4	3.0	360	**10**	63
7	3-NO_2 (**11**)	1.2/4	2.0	10	**12**	87
8 [c]	3-CH_2OH (**13**)	1.2/4	2.0	480	**14**	59
9 [d]	2-OMe (**15**)	1.5/4	3.0	24 h	**16**	72
10 [d]	2-COOMe (**17**)	1.2/4	2.0	480	**18**	83
11	1-naphthyl-I (**19**)	1.2/4	2.0	180	**20**	64

[a] All the reactions were conducted under argon on 2.0 mmol scale.

[b] 4-Iodoacetophenone added last over 45 min at <30°C.

[c] 1 mol% $Pd(dba)_2$ loading.

[d] 10 mol% $AsPh_3$ added.

the temperature was maintained at < 30°C, gave comparable results in the same time period (entry 2).

From foregoing studies on the coupling with electron rich iodides [6c], it is not surprising that the reaction of 4-iodoanisole with **1** was very sluggish under the same conditions. Although **9** was consumed after 4 h under the standard conditions (with three equivalents of TBAF), the isolated yield was quite low 46% (entry 4) and 15% of the corresponding Heck reaction product ((*E*)-4,4′ dimethoxystilbene) was also isolated.

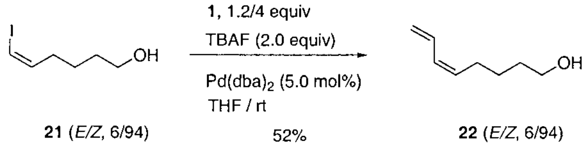
In the cross coupling with 1-methyl-1-vinylsilacyclobutane, the Heck reaction byproducts were primarily observed with **9** and **19**. In those cases, the intervention of the stilbene byproducts was suppressed simply by increasing the amount of one to 1.2 and 1.5 equivalents, respectively [6c]. In this system, however, it seems that the Heck reaction is more competitive since a trace of stilbene was observed in the coupling reaction of **1** with **7** as well as with **9** and **19** (entries 2, 3). Moreover, in the coupling reaction of **9** and **19**, increasing the amount of **1** was not effective in suppressing the side reaction. The yields of the desired products improved upon addition of 10 mol% Ph_3As (entry 5) although Heck product was still observed. Nevertheless, this material can be easily separated from the product by chromatography. The use of Ph_3As was beneficial for most of the slower coupling substrates. This allowed for the solubilization of the palladium(0) through many catalytic cycles.

The effect of sterically demanding substituents observed in the coupling of 1-methyl-1-vinylsilacyclobutane was also seen in reactions with **1**. Thus, reaction of **1** with 2-iodoanisole (**15**) was extremely sluggish compared with that of 4-iodoanisole (**9**) (6 vs. 24 h for completion). The importance of steric effects was apparent in the reaction of methyl 2-iodobenzoate (**17**), an electron poor iodide, which required 8 h to go to completion (entry 9, in the presence of 10 mol% Ph_3As) compared with just 10 min for the *para*-isomer **7** (entry 2). The compatibility of a free hydroxyl functional group was demonstrated in the successful coupling of 3-iodobenzyl alcohol (entry 7) at a reasonable rate and in good yield.

Finally, we also examined the coupling of vinylpolysiloxane (**1**) with (*Z*)-6-iodo-5-hexen-1-ol (**21**) [11] (Scheme 2). Although the reaction was sluggish, it proceeded to completion in 24 h to give the diene **22** in 52% yield. Gratifyingly, the process was stereospecific as established by GC–MS analysis. The compatibility with the free hydroxyl group is also noted.

3. Conclusions

The commercially available, inexpensive siloxanes **1** (D_4^V), **2** (D_3^V), and **3** are the effective vinylation reagents



Scheme 2. Cross-coupling of **1** with an alkenyl iodide.

of aryl and alkenyl iodides under mild condition in the presence of TBAF (two equivalents) and Pd(dba)$_2$. In view of the mildness and generality of the transformation along with the cost and non-toxic nature of the silicon reagents and byproducts, this procedure should become the reaction of choice for large scale and laboratory preparations. Studies on the use of in-situ generated siloxanes for cross-coupling reactions are in progress.

4. Experimental

A representative procedure for the cross-coupling of **1** with **5** follows. To a solution of **1** (207 mg, 0.6 mmol, 1.2 equivalents) in THF (0.2 ml) was added a solution of TBAF (Fluka, 1 M in THF, 4.0 ml). After 10 min, 4-iodoacetophenone (**5**) (492 mg, 2.0 mmol) and Pd(dba)$_2$ (58 mg, 0.10 mmol, 5 mol%) were added sequentially. A strong exotherm was observed (the temperature of reaction solution increased from 24 to 55°C within 6 min). After 10 min, GC analysis showed that the iodide was consumed (HP-5, 200°C, 15 psi: t_R **6**, 5.40 min). Diethyl ether (10 ml) was added and the mixture was stirred for an additional 5 min. The mixture was filtered though a short column of silica gel, which was further eluted with ether (50 ml). The combined eluate was concentrated by rotary evaporation and vacuum drying to give the crude product which was purified by silica gel chromatography (24 × 162 mm, pentane–ethyl acetate, 40:1) to afford **6** as a white solid 258 mg (88%). Spectroscopic and analytical data matched those reported in the literature [3c].

Procedure II for the cross-coupling of **1** with **5**: to a solution of **1** (207 mg, 0.6 mmol) in THF (0.2 ml) was added a solution of TBAF (Fluka, 1 M in THF, 4.0 ml). After 10 min, Pd(dba)$_2$ (58 mg, 0.10 mmol, 5 mol%) was added. Then a solution of **5** in THF (2.0 ml, 1.0 M) was slowly added by syringe such that the reaction temperature did not exceed 30°C (45 min). After complete addition of **5**, the reaction mixture was stirred at room temperature for 10 min, whereupon GC analysis showed that the iodide was consumed. Ether (10 ml) was added and the mixture was stirred for an additional 5 min. The mixture was filtered though a short column of silica gel, then was eluted with ether (50 ml). The combined eluate was concentrated by rotary evaporation and vacuum drying to give the crude product which was purified by silica gel chromatography (24 × 155 mm, hexane–ethyl acetate, 40:1) to afford **6** as a white solid 233 mg (80%).

Acknowledgements

We gratefully acknowledge the National Science Foundation for financial support (NSF CHE-9800398).

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[10] 1,3,5,7-Tetramethyl-1,3,5,7-tetravinylcyclotetrasiloxane (D_4^{V}, **1**, US$0.76 per g), 1,3,5-trimethyl-1,3,5-trivinylcyclotrisiloxane (D_3^{V}, **2**, US$4.60 per g), tris(vinyldimethylsiloxy)methylsilane (**3**, US$3.30 per g) and hexavinyldisiloxane (**4**, US$5.30 per g) purchased from Gelest were used directly without any further purification.

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