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Platinum Oxide Catalyzed Hydrosilylation of Unsymmetrical Internal Aryl Alkynes under Ortho-Substituent Regiocontrol

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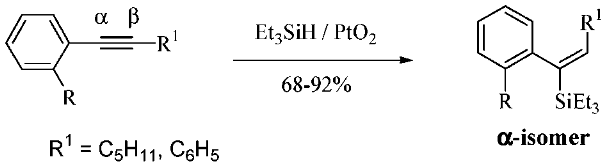
ABSTRACT



$R^1 = C_5H_{11}, C_6H_5$
$R = -NO_2, -CN, -CHO, -COOEt, -CH_2OAc, -OAc, -i\text{Pr}$

PtO_2- and H_2PtCl_6-catalyzed hydrosilylation of internal aryl alkynes having a para or an ortho substituent with triethylsilane are discussed and compared. The regioselectivity of the H–Si bond addition was found to be controlled by the ortho substituent rather than the nature of the platinum catalyst. Arylalkynes with an ortho substituent, regardless of its electronic nature, directed the silyl substituent mainly to the α-position. PtO_2 proved to be a versatile and powerful catalyst compared to H_2PtCl_6 since it prevents the alkyne reduction.

Vinylsilanes are very useful intermediates in organic synthesis, especially for palladium-catalyzed cross-coupling reactions.[1] Because of this, and their low toxicity, they are now being used increasingly in the construction of natural products and polymers.[2] Hydrosilylation of alkynes is still the simplest and most straightforward method for their preparation.[3] The main difficulty with this transformation is control of the stereo- and regiochemistry of the alkenylsilane products. Although radical[4] and Lewis acid[5] induced procedures have been reported, the transition-metal-catalyzed reaction continues to play a dominant role since it proceeds in a stereoselective manner.[6] Of the various transition metals used (Pd, Pt, Rh, Ru...), Speier's catalyst (H_2PtCl_6), which has the advantage of high turnover numbers (often >10 000), holds certain supremacy and is now routinely used for the

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(1) (a) *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, 1998. (b) Heck, R. F. *Palladium Reagents in Organic Synthesis*; Academic Press: New York, 1985. (c) Tsuji, J. *Palladium Reagents and catalysts, Innovations in Organic Synthesis*; Wiley: Chichester, UK, 1995. (d) *Silicon in Organic Synthesis*; Colvin, E. W., Ed.; Butterworth: London, 1981. (e) Hiyama, T.; Kusumoto, T. In *Comprehensive Organic Synthesis*; Fleming, I., Ed.; Pergamon: Oxford, 1991; Vol. 8.

(2) (a) Flann, C. J.; Overman, L. E. *J. Am. Chem. Soc.* **1987**, *109*, 6115−6118. (b) Blumenkopf, T. A.; Overman, L. E. *Chem. Rev.* **1986**, *86*, 857−873. (c) Oku, J.; Takeuchi, M.; Saito, A.; Asami, R. *Polym. J.* **1992**, *24*, 1409−1417.

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(4) (a) Benkeser, R. A.; Burrous, M. L.; Nelson, L. E.; Swisher, J. V. *J. Am. Chem. Soc.* **1961**, *83*, 4385−4389. (b) Benkeser, R. A. *Pure Appl. Chem.* **1966**, *13*, 133−140. (c) Amrein, S.; Timmermann, A.; Studer, A. *Org. Lett.* **2001**, *3*, 2357−2360.

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cis-hydrosilylation of terminal alkynes. However, the Pt-catalyzed reaction of unsymmetrical internal alkynes, particularly those with one or two aromatic rings, has received very little attention probably because of the difficulty in controlling the regioselectivity of the H−Si bond addition. To the best of our knowledge, only one example regarding the Pt/C-catalyzed hydrosilylation of 1-phenyl-1-propyne has been described, and in this case, a mixture of regioisomers was obtained.[7] Therefore, the search for new selective procedures and more selective catalysts presents an interesting challenge.

Previously, we reported the effect of ortho substituents on the regioselectivity in the palladium-catalyzed hydrostannylation of aryl-substituted alkynes.[8] We demonstrated that this ortho-substituent regiocontrol concept was especially well suited to the synthesis of stannylated stilbene derivatives via selective addition of tributyltin hydride to unsymmetrical diaryl- and heteroarylarylalkynes.[9] The results have been rationalized in terms of electronic polarization across the alkyne bond, induced by the ortho substituent whatever its electronic nature. It occurred to us that this unprecedented ortho-directing effect (ODE) could be extended to control the regiochemistry of the platinum-catalyzed hydrosilylation of internal arylalkylalkynes as well as diarylalkynes to provide trisubstituted vinylsilanes of defined stereochemistry. Herein, we report our first efforts realizing this goal and we also compare the hydrosilylation reaction selectivity of various para-substituted substrates with their corresponding ortho-substituted derivatives.

Since hexachloroplatinic acid (Speier's catalyst) is currently considered to be the catalyst of choice for *cis*-hydrosilylation of terminal alkynes with high regioselectivity,[10] we decided to examine its catalytic activity with Et_3SiH in the case of internal para- and ortho-substituted aryl alkynes **1a**,**b** as model systems (Scheme 1). At first, we studied the hydrosilylation of arylalkylalkyne **1a** bearing a para π-electron-withdrawing substituent and an ethoxycarbonyl group, and the results are summarized in Table 1.

Scheme 1

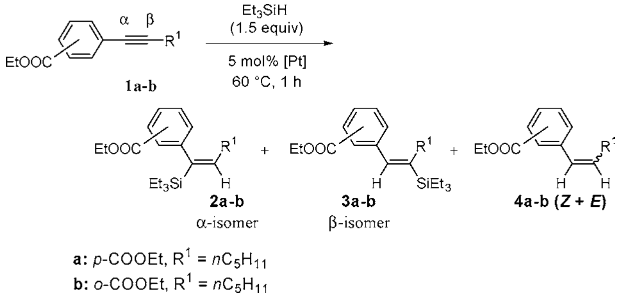

Table 1. Platinum-Catalyzed Hydrosilylation of Para- and Ortho-Substituted Alkynes **1a**,**b** with Triethylsilane[a]

entry	alkyne[i]	catalyst	solvent	ratio[b] **2/3/4**	yield[c] (%)
1	**1a**	H_2PtCl_6	THF[d]	82/18/0	65[e]
2	**1a**	H_2PtCl_6	neat	84/16/0	87[e]
3	**1b**	H_2PtCl_6	neat	82/0/18[g]	70[f]
4	**1b**	$Pt(PPh_3)_4$	neat		0
5	**1b**	Pt/C	neat	53/0/47	nd
6	**1b**	$PtCl_2$	neat	100/0/0	72[h]
7	**1b**	PtO_2	neat	100/0/0	90[h]
8	**1a**	$PtCl_2$	neat	83/17/0	88[e]
9	**1a**	PtO_2	neat	83/17/0	92[e]
10	**1a**	Pt/C	neat	80/20/0	91[e]

[a] All reactions were conducted with triethylsilane (1.5 equiv) in the presence of 5 mol % of platinum catalyst at 60 °C for 1 h. [b] Ratio was determined by ^1H NMR in the crude reaction mixture. [c] Isolated yields of the vinylsilane mixture after column chromatography. All of the reported compounds exhibited spectral data in agreement with the assigned structures. [d] A 4 M solution was used; other solvents such as toluene, MeCN, or CH_2Cl_2 could also be employed without affecting selectivity. [e] Isolated yields of an inseparable mixture of α and β isomers. [f] Isolated yield of pure α-isomer **2b** after flash column chromatography. [g] Mixture of *E/Z* isomers in a 64/36 ratio. [h] Exclusively *cis*-addition of H−Si bond occurred. [i] Alkynes were prepared according to ref 11.

Reaction of **1a** with triethylsilane (1.5 equiv) in THF (4 M) in the presence of H_2PtCl_6 (5 mol %) at 60 °C for 1 h afforded stereoselectively an inseparable 82:18 mixture of the vinylsilanes **2a** and **3a** in 65% yield (entry 1, Table 1). Performing the reaction without solvent increased the yield of the hydrosilylation reaction but had no significant change on the regioselectivity (entry 2). To evaluate the influence of the ortho substituent on the reaction selectivity (ODE), we next examined the platinum-catalyzed hydrosilylation of alkyne **1b** with an ortho π-electron-withdrawing group. In this case, when using Speier's catalyst, no β-isomer **3b** could be detected, but the reaction gave an 82/18 mixture of α-isomer **2b** and olefin **4b** (*E/Z* 64/36) which were easily separated by flash chromatography on silica gel (entry 3). Notwithstanding the hydrosilylation being regioselective, a notable amount of the side product **4b** was formed from a competing H_2PtCl_6-catalyzed direct reduction of alkyne **1b**.[12] This side reaction encouraged us to examine other platinum catalysts to avoid the reduction. In the presence of $Pt(PPh_3)_4$ (entry 4), no reaction took place, probably due to the fact that platinum does not catalyze the hydrosilylation in the presence of phosphine ligands.[13] Pt/C catalyzed this hydrosilylation reaction, but now the side reduction became dominant and a 53:47 mixture of α-isomer **2b** and **4b** was obtained (entry 5). The use of PtO_2 or $PtCl_2$ as catalysts

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[7] (a) Chauhan, M.; Hauck, B. J.; Keller, L. P.; Boudjouk, P. *J. Organomet. Chem.* **2002**, *645*, 1−13. (b) For other metal-catalyzed hydrosilylations of 1-phenyl-1-propyne, see: (b) Field, L. D.; Ward, A. J. *J. Organomet. Chem.* **2003**, *681*, 91−97.

[8] Liron, F.; Le Garrec, P.; Alami, M. *Synlett* **1999**, 246−248.

[9] (a) Alami, M.; Liron, F.; Gervais, M.; Peyrat, J. F.; Brion, J. D. *Angew. Chem., Int. Ed.* **2002**, *41*, 1578−1580. (b) Liron, F.; Gervais, M.; Peyrat, J. F.; Alami, M.; Brion, J. D. *Tetrahedron Lett.* **2003**, *44*, 2789−2794.

[10] Speier's catalyst is well-known to provide *cis*-addition processes for internal alkynes; see: Tsipis, C. A. *J. Organomet. Chem.* **1980**, *187*, 427−446.

[11] Alami, M.; Ferri, F.; Linstrumelle, G. *Tetrahedron Lett.* **1993**, *34*, 6403−6406.

[12] When exposing pure **2b** to Et_3SiH (1.5 equiv) in the presence of H_2PtCl_6 (5 mol %) at 70 °C for a prolonged time (3 h), no trace of **4b** was detected. This experiment exclude the formation of **4b** from a protodesilylation process. A similar result was obtained from a mixture of α- and β-regioisomers.

[13] Shimada, T.; Mukaide, K.; Shinohara, A.; Han, J. W.; Hayashi, T. *J. Am. Chem. Soc.* **2002**, *124*, 1584−1585.

(entries 6 and 7), however, allowed exclusive formation of α-isomer **2b** in excellent yields. Neither reduced product **4b** nor *β*-isomer **3b** was detected. NMR experiments (NOEs) between the Et group of the triethylsilyl substituent and the vinylic hydrogen substituent clearly indicated that syn addition of the silane had occurred on the alkyne.

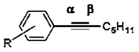
The hydrosilylation reaction of alkyne **1a** with a para *π*-electron-withdrawing group was less regioselective with these catalysts affording a mixture of α- and *β*-regioisomers with a selectivity similar to that obtained when the reaction is carried out in the presence of the H_2PtCl_6 catalyst (entries 8 and 9). These results clearly demonstrate the ortho-substituent regiocontrol concept in the hydrosilylation reactions (compare entries 6 and 7 with 8 and 9). One can note that Pt/C catalyzes the hydrosilylation reaction of **1a** to give a mixture of α- and *β*-isomers (entry 10) with levels of regiocontrol similar to that obtained with PtO_2 or $PtCl_2$ catalysts (entries 10 vs 8 and 9).

It should be noted that although platinum oxide has been utilized for hydrosilylation of alkenes,[14] to the best of our knowledge, this is the first example of the alkyne hydrosilylation being catalyzed by PtO_2 and $PtCl_2$. Significantly, the use of the heterogeneous catalyst PtO_2 (3 times less expensive than $PtCl_2$) offered other advantages compared to the Speier's catalyst (H_2PtCl_6) in that formation of reduced products in the case of ortho-substituted derivatives was avoided. The catalyst was easily removed from the reaction medium by simple filtration.

The PtO_2-catalyzed hydrosilylation reaction was next examined with several other para- and ortho-substituted aryl alkynes **1**, and the performance of this heterogeneous catalyst was compared with those of Speier's catalyst. Table 2 summarizes the results of the hydrosilylation reaction on internal arylalkylalkynes **1c**−**l**. The distribution of α- and *β*-isomers was mostly influenced by the position of the substituent R at the aromatic ring, and the nature of the platinum catalyst (H_2PtCl_6 or PtO_2) had no significant effect on the α/*β*-product composition. Substrate **1c** with a *p*-nitro group which induces strong polarization of the carbon−carbon triple bond afforded almost exclusively the α-regioisomer whichever catalyst was used (entries 1 and 2). With alkyne **1d** having a *p*-formyl group (which is a less powerful *π*-electron-withdrawing group), the PtO_2-catalyzed hydrosilylation reaction was less regioselective and gave a regioisomeric mixture with a preference for the α-isomer (α/*β* = 85:15, entry 4). It should be noted that the use of H_2PtCl_6 instead of PtO_2 (entry 3) resulted in the formation of a complex mixture probably due to incompatibility of the triethylsilane reactant with the formyl functionality in the presence of Speier's catalyst.

With arylalkylalkynes **1e**−**g** which all contain a para *σ*-electron-donating group, the selectivity of the hydrosilylation reaction decreased, and a mixture of silylated α- and *β*-isomers (α/*β* ∼75:25, entries 5−9) was obtained. However, on switching the substituent group from the para to the ortho position, regardless of its electronic nature (electron-withdrawing or electron-donating group), the reaction afforded mainly to exclusively the α-isomers in good yields (entries 10−18), though only a slight increase of the α-regioselectivity was observed in the case of alkyne **1l** bearing an isopropyl substituent (entry 18). In most cases, the use of PtO_2 proved to be a more efficient catalyst than H_2PtCl_6 since it prevented the alkyne reduction (compare entries 10, 11 and 14, 15). It should be noted that PtO_2-catalyzed hydrosilylation of nonsubstituted aryl alkyne (1-phenylheptyne as baseline control) led to a 65/35 mixture of α- and *β*-regioisomers in a 71% yield (not shown in Table 2).

Table 2. Hydrosilylation of Para and Ortho Arylalkylalkynes **1**[a] with Triethylsilane in the Presence of PtO_2 and H_2PtCl_6

Entry	 	catalyst	Ratio[b] **2/3/4**	Yields[c] (%)
1	**1c** R = *p*-NO_2	H_2PtCl_6	97/3/0	78
2		PtO_2	97/3/0	83
3	**1d** R = *p*-CHO	H_2PtCl_6	nd[d]	nd
4		PtO_2	85/15/0	62
5	**1e** R = *p*-CH_2OAc	H_2PtCl_6	78/22/0	87
6		PtO_2	77/23/0	90
7	**1f** R = *p*-OAc	H_2PtCl_6	80/20/0	75
8		PtO_2	78/22/0	82
9	**1g** R = *p*-*i*Pr	PtO_2	73/27/0	68
10	**1h** R = *o*-NO_2	H_2PtCl_6	73/0/27	nd
11		PtO_2	100/0/0	90
12	**1i** R = *o*-CHO	H_2PtCl_6	100/0/0	55
13		PtO_2	100/0/0	71
14	**1j** R = *o*-CH_2OAc	H_2PtCl_6	nd[d]	nd
15		PtO_2	100/0/0	74
16	**1k** R = *o*-OAc	H_2PtCl_6	95/5/0	76
17		PtO_2	95/5/0	76
18	**1l** R = *o*-*i*Pr	PtO_2	81/19/0	83

[a] Alkynes were prepared according to ref 11. [b] Ratio was determined by ^1H NMR in the crude reaction mixture. [c] Isolated yields of the vinylsilane mixture after column chromatography. All of the reported compounds exhibited spectral data in agreement with assigned structures. [d] The crude product was very complex.

The success of this ortho-substituent regiocontrol prompted additional investigations into the possible ortho-directing effect (ODE) of other substituents in the hydrosilylation of diarylalkynes. To our knowledge, the hydrosilylation of unsymmetrical diarylalkynes is not known.[15] Results summarized in Table 3 show that the selectivity of the hydrosilylation reaction is markedly in favor of the α-isomer in the case of diarylalkynes **1m**−**o** with a para *π*-electron-withdrawing group (entries 1−6) probably for electronic reasons. Both catalysts, PtO_2 as well as H_2PtCl_6, afford a similar distribution of α- and *β*-isomers. However, when the reaction is carried out with alkynes **1q**−**s** with an ortho

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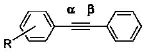
(14) Sabourault, N.; Mignani, G.; Wagner, A.; Mioskowski, C. *Org. Lett.* **2002**, *4*, 2117−2119.

(15) For transition-metal-catalyzed hydrosilylation of symmetrical diphenylacetylene, see: Sato, A.; Kinoshita, H.; Shinokubo, H.; Oshima, K. *Org. Lett.* **2004**, *6*, 2217−2220.

Table 3. Hydrosilylation of Para and Ortho Diarylalkynes **1**[a] with Triethylsilane in the Presence of PtO_2 and H_2PtCl_6

Entry		catalyst	Ratio[b] **2/3/4**	Yields[c] (%)
1	**1m** R = *p*-NO_2	H_2PtCl_6	83/17/0	60
2		PtO_2	80/20/0	80
3	**1n** R = *p*-COOEt	H_2PtCl_6	72/28/0	60
4		PtO_2	74/26/0	82
5	**1o** R = *p*-CN	H_2PtCl_6	72/28/0	60
6		PtO_2	72/28/0	65
7	**1p** R = *p*-CH_2OAc	H_2PtCl_6	59/41/0	57
8		PtO_2	54/46/0	67
9	**1q** R = *o*-NO_2	H_2PtCl_6	100/0/0	90
10		PtO_2	100/0/0	92
11	**1r** R = *o*-COOEt	H_2PtCl_6	72/0/28	nd
12		PtO_2	100/0/0	72
13	**1s** R = *o*-CN	H_2PtCl_6	72/0/28	nd
14		PtO_2	100/0/0	80
15	**1t** R = *o*-CH_2OAc	H_2PtCl_6	92/8/0	57
16		PtO_2	92/8/0	68

[a] Alkynes were prepared according to ref 11. [b] Ratio was determined by ^1H NMR in the crude reaction mixture. [c] Isolated yields of the vinylsilane mixture after column chromatography. All of the reported compounds exhibited spectral data in agreement with assigned structures.

π-electron-withdrawing substituent, total selectivity is obtained in favor of the α-hydrosilylation product (Et_3Si group being relative to the ortho-substituted aryl moiety, entries 9−14). As previously, the reduction process did not occur when PtO_2 was used (compare entries 11, 12 and 13, 14). More interestingly, the α-selectivity of this hydrosilylation was even more remarkable with diarylalkyne **1t** which contained an ortho σ-electron-donating substituent (R = *o*-CH_2OAc, $\alpha/\beta = 92{:}8$, entries 15, 16). By way of contrast, a 1:1 mixture of α- and β-isomers (entries 7 and 8) was obtained from diarylalkyne compound **1p** with the same σ-electron donating substituent in the para position.

In conclusion, we have studied the platinum-catalyzed hydrosilylation of internal arylalkynes and examined how the nature and the position of substituents on the aromatic ring influence the regioselectivity. We have shown that the ortho substituent in arylalkylalkynes, as well as in diarylalkynes, promotes the regioselective addition of triethylsilane to the triple bond and affords, efficiently, vinylsilanes of structure **2** regardless of the electronic nature of the substituent (π-electron-withdrawing group or σ-electron-donating group). Additionally, we have shown, for the first time, that PtO_2 can be used as a catalyst to mediate the addition of the H−Si bond across an alkyne bond. Interestingly, the use of this heterogeneous catalyst suppresses the undesired reduction process that was observed with H_2PtCl_6 in the case of hydrosilylation of ortho-substituted arylalkynes. Although the origins of this ortho-directing effect (ODE) are not clear presently, the electronic polarization of the alkyne bond induced by the ortho substituent[9a] could account for the observed α-selectivity. However, coordinative directing effects should not be discounted. At present, such explanations must be regarded as highly speculative. Nonetheless, our findings extend the list of synthetically useful hydrosilylation reactions that are now available and provide a selective route to arylated vinylsilanes **2**. The latter compounds, with their well-defined stereostructures, may serve as versatile precursors after further coupling reactions to allow the synthesis of combretastatins or resveratrol analogues. Additional developments in this area will be reported in due course.

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Supporting Information Available: Experimental procedures and spectroscopic data of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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