Palladium(II)-Catalyzed Conjugate Phosphination of Electron-Deficient Acceptors

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Verena T. Trepohl,[†] Susumu Mori,[‡] Kenichiro Itami,^{*,‡} and Martin Oestreich^{*,†}

Organisch-Chemisches Institut, Westfälische Wilhelms-Universität, Corrensstrasse 40, D-48149 Münster, Germany, and Department of Chemistry, Graduate School of Science, Nagoya University, Furo-cho, Chikusa-ku, Nagoya 464-8602, Japan

martin.oestreich@uni-muenster.de; itami@chem.nagoya-u.ac.jp

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ABSTRACT



 $P = PPh_2$ or PCy_2 or Pt-Bu₂ and Si = t-BuMe₂Si or Me₂PhSi

A general protocol for the conjugate transfer of diphenyl-, dicyclohexyl-, and di-*tert*-butylphosphinyl groups from silylphosphines to cyclic and acyclic electron-deficient acceptors employing a bench-stable palladium(II) catalyst is reported. Several *E* and *Z* configured $\alpha_{,\beta}$ -unsaturated carbonyl and carboxyl acceptors (including imides) as well as nitroalkenes participate in this palladium(II)-catalyzed process in high chemical yields.

The area of transition-metal-catalyzed conjugate element transfer onto α,β -unsaturated carbonyl and carboxyl acceptors is currently witnessing tremendous growth.¹ Prior to the C-element bond forming event, an interelement linkage is usually activated by a ligand-stabilized transition metal either through oxidative addition of the element–element bond to the low-valent metal center^{2,3} or through element-to-metal transmetalation.³ Indicators for the recent substantial progress are several novel (asymmetric) C-B (B-B bond activation⁴), C-Si (B-Si⁵ or Si-Si bond activation⁶), as well as C-P bond forming

[†] Universität Münster.

^{*} Nagoya University.

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reactions (Si–P bond activation⁷). Our contribution is the disclosure of a rhodium(I)-catalyzed activation of interelement compounds in basic aqueous media,^{5,7} a process believed to hinge upon a hydroxyrhodium(I) complex as the active catalyst. Its Lewis basic oxygen will interact chemoselectively with the more electronegative element of the interelement reagent, thereby weakening the element–element bond eventually resulting in transmetalation of the less electronegative element transfer was inspired and guided by the related 1,4-addition of arylboronic acids⁸ and its mechanism of action.⁹

As the logical next step, we reasoned that palladium(II)catalyzed protocols for conjugate arylation,¹⁰ which are tantamount to the aforementioned rhodium(I) catalysis,^{8,9} might also qualify for our purposes.^{5,7} Accordingly, a transmetalation mechanism involving a hydroxypalladium(II) complex was verified.¹¹ As we had elaborated an efficient rhodium(I)-catalyzed 1,4-addition of phosphinyl groups yet limited in substrate scope,⁷ we decided to investigate its unprecedented palladium(II)-catalyzed counterpart. In this Letter, we report a robust method for the conjugate phosphination of electron-deficient acceptors¹² using silylphosphines^{7,13} as a source of nucleophilic trivalent phosphorus.¹⁴

Catalyst identification commenced with bench-stable palladium(II) catalyst **1** developed by Itami et al. for the hydroarylation of fullerene with arylboronic acids.¹⁵ This work also included examples of conjugate arylation of cyclic and acyclic α,β -unsaturated carbonyls. We were then delighted to see that **1** also facilitated the phosphinyl transfer from *t*-BuMe₂Si–PPh₂

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 $(2a)^{7,16}$ to cyclic acceptor 4 (Scheme 1). Variation of reaction conditions (only a selection is shown) led to a straightforward procedure, affording the adduct in high chemical yield.

Table 1. Ligand [Pd(OAc)₂·L] and Additive Screening^a



entry	ligand ${f L}$	mol %	$C_6F_5CO_2H\ (mol\ \%)$	yield (%)
1	Ph_3P	20	_	45
2	L1	20	-	76
3	L2	20	-	64
4	L3	20	-	55
5	$Ph_{3}P$	5.0	-	36
6	L1	5.0	-	74
7	L2	5.0	-	66
8	L3	5.0	-	58
9	$Ph_{3}P$	5.0	10	41
10	L1	5.0	10	80
11	L2	5.0	10	71
12	L3	5.0	10	63

^{*a*} Conjugate phosphinations of **4** were conducted using $Pd(OAc)_2$ and an equimolar amount of the indicated ligand **L1–L3** (twice the amount in the case of Ph₃P) as well as **2a** (2.5 equiv) in 1,4-dioxane:H₂O = 10:1 (0.20 M) at 60 °C. Yields after oxidation and flash chromatography.

To ascertain whether $\mathbf{1} (= Pd(O_2CC_6F_5)_2\cdot\mathbf{L1})$ is the ideal counteranion—ligand combination, we surveyed four different ligands—Ph₃P and $\mathbf{L1}-\mathbf{L3}$ —with Pd(OAc)₂ as the palladium(II) source with or without C₆F₅CO₂H as additive^{15a} (Table 1). Independent of the catalyst loading and the presence of added acid, a clear trend was observed: Ph₃P^{10a} performed poorly, while all nitrogen-based ligands^{10b} were superior in the order $\mathbf{L1} > \mathbf{L2} > \mathbf{L3}$. Any further decrease in the amount of Pd(OAc)₂ gave lower yields.

⁽⁶⁾ Palladium(0) catalysis: (a) Hayashi, T.; Matsumoto, Y.; Ito, Y. J. Am. Chem. Soc. **1988**, 110, 5579–5581. Copper(I) catalysis: (b) Ito, H.; Ishizuka, T.; Tateiwa, J.-i.; Sonoda, M.; Hosomi, A. J. Am. Chem. Soc. **1998**, 120, 11196–11197. Rhodium(I) catalysis: (c) Nakao, Y.; Chen, J.; Imanaka, H.; Hiyama, T.; Ichikawa, Y.; Duan, W.-L.; Shintani, R.; Hayashi, T. J. Am. Chem. Soc. **2007**, 129, 9137–9143.

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Table 2. Conjugate Phosphination of Cyclic α , β -Unsaturated Carbonyl Compounds



entry	silyiphosphine SI-P	acceptor	n	adduct	yield (%)
1	t-BuMe ₂ Si-PPh ₂ (2a)	3	1	6a	94
2	t-BuMe ₂ Si-PPh ₂ (2a)	4	2	7a	84
3	t-BuMe ₂ Si-PPh ₂ (2a)	5	3	8a	90
4	$Me_2PhSi-PCy_2$ (2b)	3	1	6b	72
5	$Me_2PhSi-PCy_2$ (2b)	4	2	7b	80
6	$Me_2PhSi-PCy_2$ (2b)	5	3	8b	88

We then continued to apply this procedure to conventional cyclic α , β -unsaturated carbonyl compounds **3**–**5** using both *t*-BuMe₂Si–PPh₂ (**2a**) and Me₂PhSi–PCy₂ (**2b**) representative for diaryl- and dialkylphosphinyl groups (Table 2). As in all preceding and subsequent examples, phosphinyl—phosphinoyl oxidation with H₂O₂ or sulfurization with S₈ allowed facile purification by flash chromatography on silica gel. The yields obtained with substrates **3**–**5** compare well with those of the rhodium(I)-catalyzed variant.^{7a}

Table 3. Conjugate Phosphination of Acyclic α , β -Unsaturated Carbonyl Compounds



Acyclic α,β -unsaturated carbonyl compounds, e.g., acceptors **9–11**, had emerged as unreactive with the rhodium(I) catalytic system but reacted cleanly under the palladium(II) catalysis (Table 3). We note that isolated yields were invariably higher for *Z* than for *E* configured precursors (vide infra).

Gratifyingly, α , β -unsaturated imides **15** and **16** with *E* and *Z* double bond geometry extended the scope (Table 4), opening

Table 4. Conjugate Phosphination of α , β -Unsaturated Imides

Si_{P} 2a or 2b (2.5 equiv) 1 (5.0 mol %) 1,4-dioxane-H ₂ O 10:1 R ⁻¹ O R P O R P P O R P P P P P P P P					
<i>E</i> -15/16 and <i>Z</i> -15/16 H_2O_2 (30% in H_2O) 17a,b-18a,b rt, 2 h					
entry	silylphosphine Si-P	acceptor	R	adduct	yield (%)
1	t-BuMe ₂ Si-PPh ₂ (2a)	E-15	Ph	17a	62
2	t-BuMe ₂ Si-PPh ₂ (2a)	Z-15	Ph	17a	73
3	t-BuMe ₂ Si-PPh ₂ (2a)	E-16	<i>n</i> -Bu	18a	58
4	t-BuMe ₂ Si-PPh ₂ (2a)	<i>Z</i> -16	<i>n-</i> Bu	18a	64
5	$Me_2PhSi-PCy_2$ (2b)	E-15	Ph	17b	51
4	$Me_2PhSi-PCy_2$ (2b)	Z-15	Ph	17b	55
5	$Me_2PhSi-PCy_2$ (2b)	<i>E</i> -16	<i>n-</i> Bu	18b	63
6	$Me_2PhSi-PCy_2$ (2b)	<i>Z</i> -16	<i>n-</i> Bu	18b	82

the door for auxiliary-based, diastereoselective 1,4-additions.¹⁷ Again, Z alkenes performed better than E alkenes. Maleimide **19** afforded even higher yields (Scheme 2).

Scheme 2. Conjugate Phosphination of a Maleimide



Being aware of the fact that α,β -unsaturated carboxyls are intrinsically less reactive than carbonyl compounds, we were nevertheless surprised to learn these were reluctant to participate in this reaction.¹⁸ Conversely, both fumaric (*E*-**21**) and maleic ester (*Z*-**21**) gave the desired products in chemical yields expected for the respective double bond isomer (Scheme 3).



The range of conceivable substrates for this reaction was completed with nitroalkene E-23, furnishing the 1,4-adduct in good isolated yield (Scheme 4).





After identification of all these acceptors, we tested Me₂PhSi-Pt-Bu₂ (**2c**) to realize the transfer of the electronrich di-*tert*-butylphosphinyl group (Figure 1). Although chemical yields were somewhat lower, conjugate phosphination worked except for α , β -unsaturated imides, thereby rounding off the scope of this palladium(II) catalysis.

In summary, we elaborated a general method for the conjugate phosphinyl transfer employing easy-to-handle silylated diaryl- and dialkylphosphines $2\mathbf{a}-\mathbf{c}^7$ (Figure 2). This novel palladium(II) catalysis for interelement bond activation is superior to the rhodium(I)-catalyzed process previously reported by us.⁷ Future work will be devoted to mechanistic investigations and the development of enantio-selective¹⁹ and substrate-controlled^{17,20} variants.

(20) A remarkable reagent-contolled 1,4-addition of a metalated *P*-stereogenic phosphine oxide is known: Haynes, R. K.; Lam, W. W.-L.; Yeung, L.-L. *Tetrahedron Lett.* **1996**, *37*, 4729–4732.



Figure 1. Selected examples of conjugate $Pt-Bu_2$ transfer using $Me_2PhSi-Pt-Bu_2$ (2c).

<i>t</i> -BuMe₂Si〜 PPh₂	Me ₂ PhSi~PCy ₂	Me₂PhSi∼ Pt-Bu₂		
2a	2b	2c		
igure 2. Silylphosphines surveyed in this work. ^{7,16}				

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Supporting Information Available: General procedure, characterization data, as well as ¹H, ¹³C, and ³¹P NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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