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Palladium(II)-Catalyzed Conjugate Addition of Arylsiloxanes in Water

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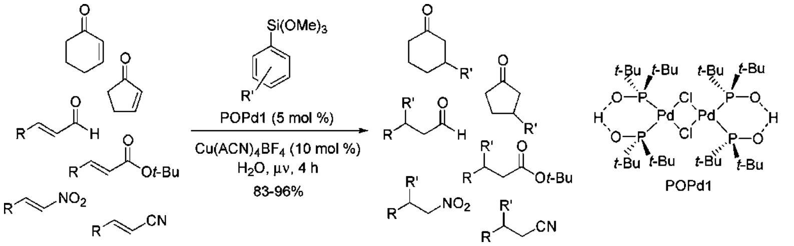
ABSTRACT



Palladium–phosphinous acids catalyze the conjugate addition of arylsiloxanes to a wide range of α,*β*-unsaturated substrates in water. A microwave-assisted procedure is described that uses 5 mol % of POPd1 to afford *β*-substituted ketones, aldehydes, esters, nitriles, and nitroalkanes in 83% to 96% yield within 4 h. This method eliminates the need for stoichiometric additives and an excess of arylsiloxane, and does not require an inert atmosphere.

In recent years, increasing efforts have been devoted to transition metal-catalyzed conjugate additions of organometallic reagents to α,*β*-unsaturated ketones and other Michael acceptors.[1] This important carbon−carbon bond-forming reaction is usually accomplished with organoboronic acids in the presence of rhodium catalysts.[2] The use of palladium catalysts is less common because they can form carbon-bound enolates that undergo *β*-hydride elimination toward Heck reaction products.[3] Miyaura and others demonstrated that this can be controlled with dicationic palladium(II) complexes which effectively catalyze 1,4-additions with minimal formation of Heck-type byproducts.[4] Copper catalysts have proved very useful in combination with Grignard[5] or organozinc[6] reagents, and rhodium-catalyzed conjugate additions of arylstannanes[7] and aryltitanium[8] compounds have also been described.

The use of silicon compounds provides an attractive alternative to these methods due to the general availability, low toxicity, and insensitivity of arylsiloxanes to various functional groups.[9] Several protocols suitable for rhodium-catalyzed 1,4-addition of arylsiloxanes or arylchlorosilanes to α,*β*-unsaturated ketones, esters, and amides have been developed.[10] By contrast, few palladium(II)-catalyzed con-

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jugate additions with arylsiloxanes are known.[11] Among Michael acceptors, α,β-conjugated aldehydes and ketones have been identified as the most reactive substrates and have been studied more extensively than unsaturated esters and nitroalkenes.[12] To date, a broadly applicable method that allows 1,4-additions of arylsiloxanes to a wide range of Michael acceptors providing the corresponding β-substituted products in high yields has not been reported.

We have recently introduced palladium−phosphinous acid catalysts to Hiyama cross-coupling and oxidative esterification of aldehydes with tetramethyl orthosilicate.[13] This class of catalysts shows remarkable stability to air and water, which facilitates operation and catalyst recycling, and has been successfully applied in Suzuki, Stille, Sonogashira, and other cross-coupling reactions (Figure 1).[14] Since palladium(II) complexes have been found to undergo relatively fast transmetalation with organosilicon species, we decided to investigate the usefulness of palladium−phosphinous acids for conjugate addition of arylsiloxanes to α,β-unsaturated compounds.

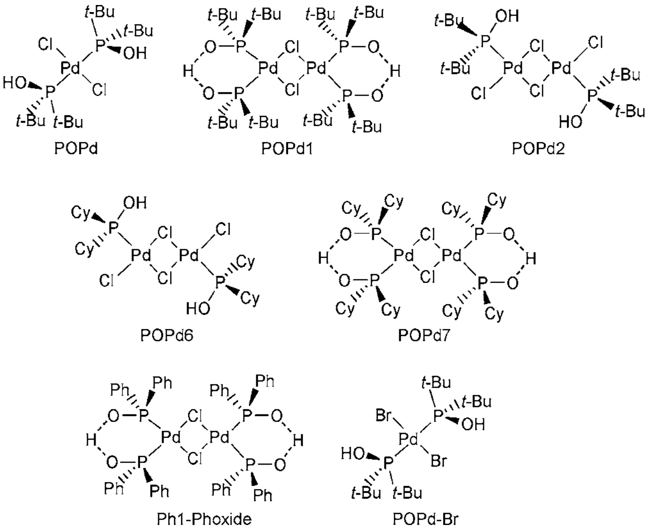
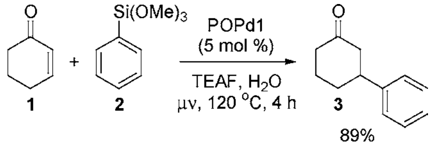


Figure 1. Structures of palladium−phosphinous acids.

Initial screening of the palladium−phosphinous acids shown above in acetonitrile or aqueous solvents revealed that the reaction between 2-cyclohexen-1-one, **1**, and phenyltrimethoxysilane, **2**, proceeds in the presence of 5 mol % of POPd1 and tetrabutylammonium fluoride in refluxing water, generating 3-phenylcyclohexanone, **3**, in 52% yield after 24 h. Further screening of KF, CsF, and several tetraalkylammonium fluoride sources showed that **3** can be obtained in 85% yield when tetraethylammonium fluoride, TEAF, is employed. We were pleased to find that the POPd1-catalyzed conjugate addition of **2** to **1** can be conveniently conducted in a microwave, providing **3** in 89% yield within 4 h.

We then decided to study the scope of the palladium−phosphinous acid-catalyzed conjugate addition using the conditions summarized in Scheme 1. To our disappointment, yields decreased significantly when we applied our procedure to other arylsiloxanes or Michael acceptors such as unsaturated nitriles.

Scheme 1. POPd1-catalyzed Conjugate Addition



Following Miyaura's reports on copper-promoted 1,4-additions of arylsiloxanes to enones we realized that the addition of catalytic amounts of $Cu(BF_4)_2$ or $Cu(ACN)_4PF_6$ to the reaction mixture overcomes these problems.[11a] In particular, the use of 5 mol % of POPd1 and 10 mol % of $Cu(ACN)_4PF_6$ as cocatalyst resulted in a broadly applicable conjugate addition procedure that tolerates a range of arylsiloxanes and α,β-unsaturated substrates (Table 1). Under these conditions, conjugate addition of arylsiloxanes, including 4-aminophenyltrimethoxysilane, **8**, 3-furyltrimethoxysilane, **10**, and 2-thienyltrimethoxysilane, **12**, to 2-cyclohexen-1-one, **1**, or 2-cyclopenten-1-one, **14**, furnishes the corresponding β-substituted cycloalkanones **3**, **5**, **7**, **9**, **11**, **13**, and **15** in 83−96% yield (entries 1−7). Excellent results were also obtained with α,β-unsaturated aldehyde **16** and ester **18** (entries 8 and 9). Importantly, our procedure is applicable to unsaturated nitriles and nitroalkenes. Addition of **2** to cinnamonitrile, **20**, and methacrylonitrile, **22**, gave 3,3-diphenylpropionitrile, **21**, and 2-methyl-3-phenylpropionitrile, **23**, in 83% and 93% yield, respectively (entries 10 and 11). (*E*)-β-Nitrostyrene, **24**, and 1-nitrocyclohexene, **26**, undergo POPd1-catalyzed 1,4-addition to form 2,2-diphenylnitroethane, **25**, and 2-phenylnitrocyclohexane, **27**, in 88% and 87% yield (entries 12 and 13).

Important features of microwave-assisted palladium−phosphinous acid-catalyzed conjugate additions with arylsiloxanes include high yields and short reaction times while

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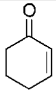
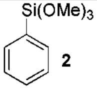
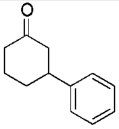
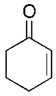
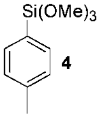
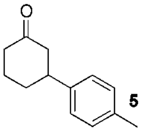
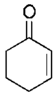
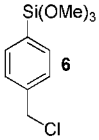
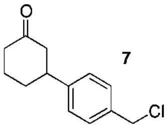
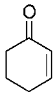
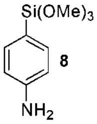
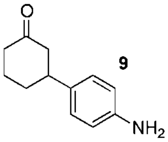
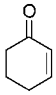
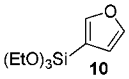
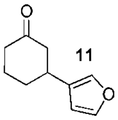
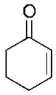
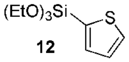
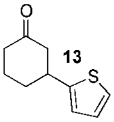
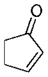
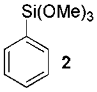
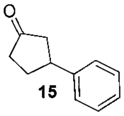
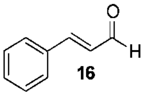
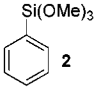
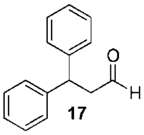
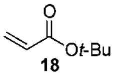
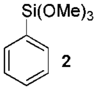
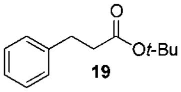
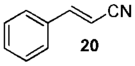
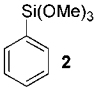
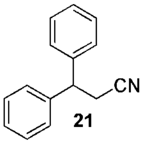
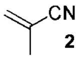
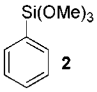
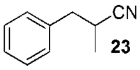
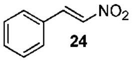
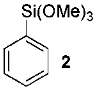
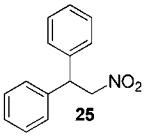
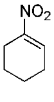
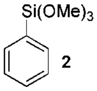
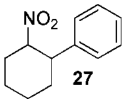
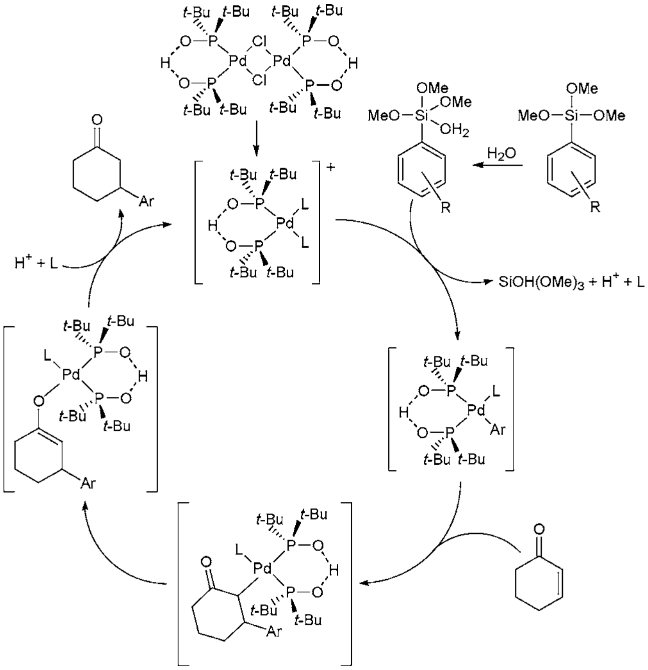
Table 1. POPd1-Catalyzed Conjugate Addition of Arylsiloxanes to α,*β*-Unsaturated Substrates[a]

entry	substrate	siloxane	addition product	yield
1	 **1**	 **2**	 **3**	96%
2	 **1**	 **4**	 **5**	91%
3	 **1**	 **6**	 **7**	83%
4	 **1**	 **8**	 **9**	87%
5	 **1**	 **10**	 **11**	84%
6	 **1**	 **12**	 **13**	93%
7	 **14**	 **2**	 **15**	87%
8	 **16**	 **2**	 **17**	86%
9	 **18**	 **2**	 **19**	92%
10	 **20**	 **2**	 **21**	83%
11	 **22**	 **2**	 **23**	93%
12	 **24**	 **2**	 **25**	88%
13	 **26**	 **2**	 **27**	87%

[a] General procedure: The Michael acceptor (1.00 mmol), arylsiloxane (1.30 mmol), $Cu(ACN)_4PF_6$ (0.1 mmol), and POPd1 (0.05 mmol) in 0.25 mL of water, 120 °C, 4 h.

an inert atmosphere and the use of organic cosolvents are unnecessary. The results summarized in Table 1 compare favorably with yields obtained by previously developed methods.[11,12] For example, palladium-catalyzed formation of cycloalkanones **3** and **15** in 73−78% and 60% yield, respectively, has been reported. However, these procedures generally require the use of 2.5 equiv of phenylsiloxane **2**, significantly longer reaction times (at least 23 h), and organic solvents or water/dioxane mixtures under inert atmosphere. 2,2-Diphenylnitroethane **25** has been prepared in 70% yield from **2** and **24** with palladium acetate as catalyst in the presence of 4 equiv of TBAF and $SbCl_3$, but no product was obtained when 1-nitrocyclohexene **26** was employed in the same reaction. To the best of our knowledge, the palladium-catalyzed addition of arylsiloxanes to unsaturated esters and nitriles is unprecedented.

Scheme 2. Proposed Mechanism of the POPd1-Catalyzed Conjugate Addition



A proposed catalytic cycle is shown in Scheme 2. Dissociation of POPd1 generates a cationic palladium(II) catalyst that undergoes transmetalation with a hypervalent arylsiloxane. Coordination of an α,*β*-unsaturated substrate such as 2-cyclohexen-1-one to the arylpalladium(II) species then affords a *C*-bound enolate that dissociates, presumably via formation of the corresponding palladium *O*-enolate, to form the Michael addition product while the catalytically active palladium complex is regenerated. Since palladium(II) enolates are known to undergo fast hydrolytic cleavage,[15] the last step is likely to be faster than *β*-hydride elimination when the reaction is carried out in aqueous solvents.[16] The usefulness of POPd1 in conjugate additions of arylsiloxanes

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(15) Albeniz, A. C.; Catalina, N. M.; Espinet, P.; Redon, R. *Organometallics* **1999**, *18*, 5571−5576.

to a wide range of Michael acceptors with pure water as solvent can therefore be attributed to the general stability of palladium−phosphinous acids under aqueous conditions which prevents precipitation of palladium black, and fast dissociation of intermediate palladium(II) enolates toward β-substituted conjugate addition products.

In summary, we have successfully employed a palladium−phosphinous acid catalyst in microwave-assisted conjugate additions of arylsiloxanes to a wide range of α,β-unsaturated substrates in water. This reaction provides access to β-substituted ketones, aldehydes, esters, nitriles, and nitroalkanes which are obtained in high yields. Attractive features of the POPd1-catalyzed procedure are the broad application spectrum, tolerance of functional groups, short reaction times, and operational simplicity due to the stability of palladium−phosphinous acids to water and air.

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Supporting Information Available: Synthetic procedures and NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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(16) Formation of Heck reaction products was not observed.