

Pd-catalysed arylation of propan-1-ol and derivatives: oxidative role of the arylating agent

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With excess PhI under Pd catalysis, 1-PrOH was converted to a mixture of 3,3-diphenylpropenal and *trans*-2,3-diphenylpropenal by a concerted, oxidative sequence that involved two arylation couplings and an olefinic aldehyde that was generated *in situ*.

Recently in our laboratory, Pd on porous glass was developed as a heterogeneous catalyst¹ for promoting Glaser-type and Heck arylation couplings² without the need for solubilising or activating ligands. Significantly, with excess allyl alcohol and with PhI in air, Pd on porous glass gave *trans*-cinnamaldehyde (**1**) along with 3-phenylpropanal (**2**; see entry 2, Table 1).¹ Consistent with literature reports,^{3,4} in the absence of air, and without the addition of Ag⁺ salts, **2** predominated and **1** was not obtained (entry 1, Table 1).

With PhI in excess, the diarylated compounds **3** and **4** appeared as major products from allyl alcohol, along with **1** and **2** (entry 3, Table 1). This diarylation appeared to contrast with a wealth of literature data on the Pd catalysed arylation of that alcohol.³ Without Ag⁺ salts,⁴ one might expect that the first arylation of allyl alcohol would be accompanied by rapid migration of the olefinic bond to afford mainly 3-phenylpropanal (**2**), thereby removing the opportunity for a second Heck arylation to occur.

Although air facilitated the dehydrogenation for the reaction in entry 2 of Table 1,⁵ the results in entry 3 and co-formation of biphenyl suggested that the arylating agent may have had an additional role. To support this contention, we now report that 1-PrOH with excess PhI can afford a mixture of 3,3-diphenylpropenal (**4**) and *trans*-2,3-diphenylpropenal (**5**), even under an inert gas atmosphere (see entry 9). This remarkable transformation has been performed with either Pd(OAc)₂ or Pd on porous glass as catalyst^{6,7} (which was used for all entries in Table 1) includes microwave heating⁸ in a reactor of our design.⁹

A comparable stepwise process would require oxidation of the hydroxy function of 1-PrOH, dehydrogenation of the hydrocarbon chain and two Heck-like arylation couplings of the resultant olefin. However, for the one reaction, successive intermolecular Heck arylation couplings onto the same olefin are rare.¹⁰ Intramolecular examples usually have involved mono-arylations of more than one carbon-carbon double bond.¹¹

Mono-arylated products were not observed in the reaction of 1-PrOH, rendering as unlikely, a multi-step sequence involving successive intermolecular Heck arylation couplings with an olefin formed by dehydrogenation *in situ*.¹² The absence of detectable intermediates implies that the process was concerted and may constitute a new reaction.

Formation of biphenyl and benzene as by-products indicates that PhI served as both an oxidant and a reactant. Buchwald and Palucki observed similar behaviour of their arylating agent in the 'Pd' catalysed reaction of cyclohexanol with 4-*tert*-butylbromobenzene to produce the corresponding α -arylated cyclohexanone and *tert*-butylbenzene.¹³ They surmised that some of the haloarene was simultaneously reduced during oxidation of the alcohol to cyclohexanone.

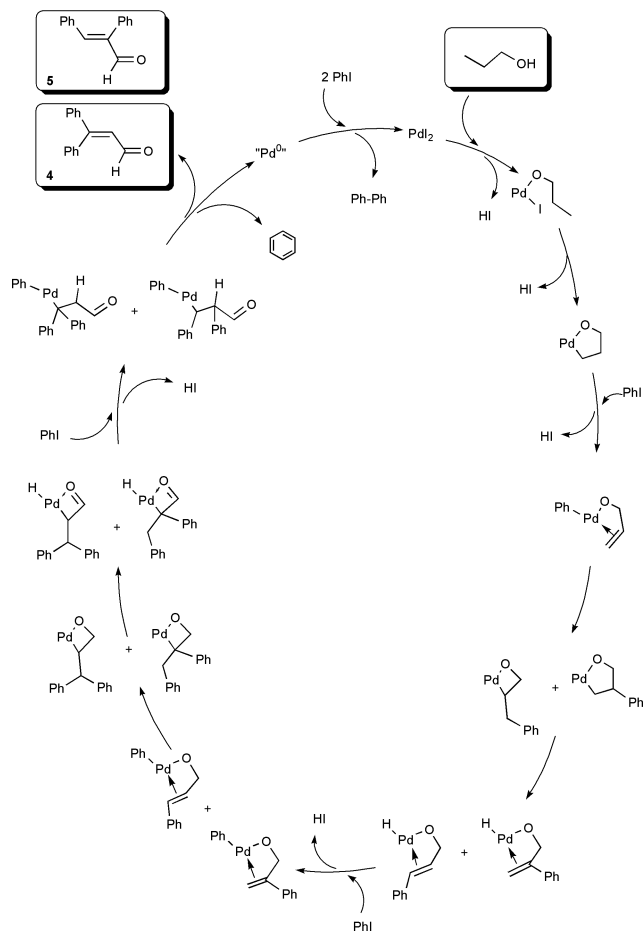
Although variations in the order of transformations and alternative routes are possible for the present reaction, the pathway in Scheme 1 appears to account for the products, by-products and their relative proportions.

Preliminary investigations (see Table 1) into the process utilised cinnamaldehyde (**1**),¹⁴ cinnamyl alcohol (**6**), 3-phenylpropanol (**7**) and 3-phenylpropanal (**2**). Cinnamyl alcohol (**6**) afforded diarylenal **4** as a major product (along with **3** and the 2,3-diphenylpropenal isomer **8**), irrespective of whether or not the atmosphere contained air (entries 5 and 6). Under argon, 3-phenylpropanal (**2**) gave 2,3-diphenylpropanal (**9**) and products of higher oxidation state, including **1**, **4** and **5** (entry 7). 3-Phenylpropanol (**7**) afforded **4** and **5** as major products, along with traces of **1** and **2** (entry 8). The product distributions obtained from Pd catalysed reactions of excess PhI with **6**, **7** and **2** suggest that several competing processes were operating, including α -arylation,¹³ Heck-like arylation coupling of olefinic bonds² as well as the new process described herein and illustrated by Scheme 1.

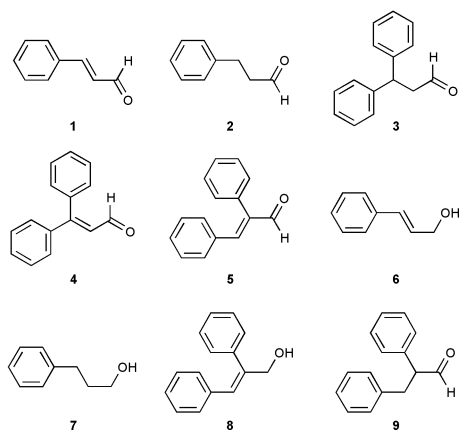
These outcomes may have depended on whether or not coordination of the olefin to Pd occurred in conjunction with the establishment of a strong Pd-O bond, leading to a chelation controlled reaction. Such bonds have been suggested for palladium catalysed oxidation of alcohols.¹⁵ Scheme 1, proposed for the reaction of 1-PrOH commences with Pd-O chelation and proceeds preferably through metallaoxetane intermediates,¹⁶ which account for the observed products and their relative distribution. In the case of allyl alcohol (entry 3), it appears that the double bond and the hydroxy group of the

Table 1 Example reactions and conditions

Entry	Starting material (mmol)	PhI/mmol	Ar or Air	Major products (percentage of total detected)	Turnover Number
1	CH ₂ =CH-CH ₂ OH (13)	6	Ar	2 (59), CH ₃ CH(Ph)CHO (23)	170
2	CH ₂ =CH-CH ₂ OH (13)	6	Air	1 (60), 2 (40)	120
3	CH ₂ =CH-CH ₂ OH (14)	34	Air	1 (16), 2 (7), 3 (24), 4 (26)	450
4	PhCH=CH-CHO, 1 (13)	34	Ar or Air	4 (99)	245 (Ar), 170 (Air)
5	PhCH=CHCH ₂ OH, 6 (13)	34	Ar	3 (36), 4 (18), 8 (15), 9 (10)	700
6	PhCH=CHCH ₂ OH, 6 (13)	34	Air	3 (6), 4 (62), 8 (13)	560
7	PhCH ₂ CH ₂ CHO, 2 (6)	34	Ar	1 (5), 3 (16), 4 (39), 5 (6), 9 (18)	270
8	PhCH ₂ CH ₂ CH ₂ OH, 7 (10)	34	Ar	4 (60), 5 (18)	50
9	CH ₃ CH ₂ CH ₂ OH (20)	34	Ar	4 (80), 5 (18)	30



Scheme 1



alcohol compete for the Pd and products from both Heck-type arylation (2 and 3) as well as the sequence in Scheme 1 (diarylenal 4) result.

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- A** Into a dry, two-necked flask fitted with a reflux condenser and an inert gas (Ar) bleed line was placed a solution of 1-PrOH (0.784 g; 13.06 mmol) and PhI (12.674 g; 62.12 mmol) in dry, deoxygenated *N,N*-dimethyl acetamide (DMA; 50 mL). Anhydrous NaOAc (5.80 g; 70.70 mmol) and Pd(OAc)₂ (0.564 g; 2.51 mmol) were added and the mixture was heated at 125 °C for 16 h, then cooled, quenched with 80 mL H₂O and extracted with Et₂O (1 × 80 mL, 2 × 50 mL). The ether extract was washed thrice with water, dried with MgSO₄ and the ether removed *in vacuo*. Unconverted PhI was recovered by vacuum distillation at 40 °C and 1 × 10⁻² mbar and biphenyl was removed by sublimation (80 °C and 1 × 10⁻² mbar) and biphenyl was removed by sublimation (80 °C and 1 × 10⁻² mbar). Flash chromatography (silica gel 60, dichloromethane: pentane 1:1) afforded pure product **4** (395 mg). **B** Into a dry, two-necked flask fitted with a reflux condenser and an inert gas (Ar) bleed line was placed a solution of 1-PrOH (749 mg; 12.48 mmol) and PhI (6.971 g; 34 mmol) in dry, deoxygenated *N,N*-dimethyl acetamide (DMA; 50 mL). Anhydrous NaOAc (4.127 g; 50 mmol) and Pd on porous glass (containing 19 μmol Pd)¹ were added and the mixture was heated at 125 °C for 16 h, then cooled. Work up as above yielded pure product **4** (73 mg).
- Although Pd(OAc)₂ undergoes thermal decomposition to give finely divided Pd metal and gases including CO₂, methane and ethane (see M. T. Reetz and M. Maase, *Adv. Mat.*, 1999, **11**, 773; M. T. Reetz and G. Lohmer, *Chem. Commun.*, 1996, 1921), no evidence was obtained to associate that redox process with the present reaction.
- Into a dry PTFE vessel under nitrogen was placed a solution of 1-PrOH (0.803 g; 13.4 mmol) and PhI (6.853 g; 33.6 mmol) in dry, deoxygenated *N,N*-dimethyl acetamide (DMA; 50 mL). Anhydrous NaOAc (4.19 g; 51.0 mmol) and Pd(OAc)₂ (50.4 mg; 0.22 mmol) were added and the mixture was heated for 10 min at 220 °C in a microwave batch reactor⁹, then cooled. Work up as in footnote 6 yielded pure product **4** (280 mg). For other examples of Pd catalysed reactions under microwave heating, see M. Larhed and A. Hallberg, *J. Org. Chem.*, 1996, **61**, 9582; U. Bremberg, M. Larhed, C. Moberg and A. Hallberg, *J. Org. Chem.*, 1999, **64**, 1082; M. Larhed, M. Hoshino, S. Hadida, D. P. Curran and A. Hallberg, *J. Org. Chem.*, 1997, **62**, 5583.
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