Palladium Catalysed Phenylation of Allylic Alcohols; Dramatic Effect of Tertiary Amines on the Reaction Rate

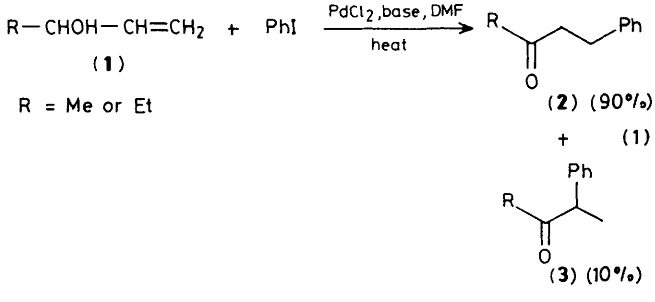
Rachida Benhaddou, Stanislas Czernecki,* and Guy Ville

Laboratoire de Chimie des Glucides, Université P. et M. Curie, Tour 54—55, E1, 4 Place Jussieu, 75005 Paris, France

The rate of palladium catalysed phenylation of allylic alcohols is markedly enhanced by addition of tertiary amines, presumably by co-ordination to the palladium atom to form very reactive species.

As part of a continuing programme[1] dealing with the study of the Heck reaction,[2] the kinetics of the title reaction (equation 1) have been investigated. For this reaction, a multi-step mechanism involving *cis*-addition of 'ArPdX' followed by *syn*-elimination of 'HPdX' is now well established.[1] A base is generally added to the reaction system to regenerate Pd^0 from 'HPdX' by neutralisation of HX.[3,4]

Since the determination of the rate law of such a complex reaction is usually difficult, the initial pseudo-first order rate of formation of the ketones (**2**) and (**3**) was evaluated† with different combinations of palladium salts, bases, and complexing agents (Table 1).



$$Pd^0L_n + PhI \longrightarrow PhPdIL_{n-2} + 2L \qquad (2)$$

---

† The rate was measured by monitoring the appearance of the ketones (**2**) and (**3**) by g.l.c. in the presence of triethyleneglycol dimethyl ether as internal standard.

Table 1. Initial pseudo-first-order rate constants for formation of the ketones (**2**) and (**3**).[a]

Entry	t/°C	Catalyst (10^{-2} mol. equiv.)	$10^5 k_i$/ s^{-1}	Other ligand (mol. equiv.)
1	74	$PdCl_2$ (1)	2.20	—
2[b]	74	$PdCl_2$ (1)	38.7	Et_3N (1)
3[b]	74	$PdCl_2$ (1)	70.0	$Bu^n{}_3N$ (1)
4	50	$PdCl_2$ (1)	0.06	Et_2NH (0.2)
5	54	$PdCl_2$ (1)	0.06	Pyridine (0.2)
6	74	$PdCl_2$ (1)	0.05	$[Me_2NCH_2]_2$ (0.1)
7	74	$Pd(dba)_2$ (5)[c]	3.9	—
8	74	$PdCl_2$ (4)	0.13	$(Ph)_3P$ (0.1)
9	74	$Pd[(Ph)_3P]_4$ (1)	0.26	—

[a] [But-3-en-2-ol] = [PhI] = [AcONa] = 1 M in dimethylformamide. [b] Without AcONa. [c] dba = dibenzylideneacetone.

Table 2. Initial rate constants in the presence of sodium acetate and/or tertiary amines.[a]

Entry	R	Base (mol. equiv.)	$10^5 k_i$/ s^{-1}
1	Me	AcONa (1)	2.2
2	Et	AcONa (1)	2.4
3	Me	Et_3N (1)	38.7
4	Me	Bu_3N (1)	70.0
5	Et	Et_3N (1)	30.6
6	Me	AcONa (1) + Et_3N (0.2)	70.3
7	Et	AcONa (1) + Et_3N (0.2)	66.7
8	Me	AcONa (1) + Bu_3N (0.2)	94.4

[a] $[RCH(OH)CH{=}CH_2]$ = [PhI] = 10^2 $[PdCl_2]$ = 1 M in dimethylformamide at 74 °C.

Reasonable reaction rates were obtained only with sodium acetate or tertiary amines as bases and palladium chloride in dimethylformamide; these systems were investigated further, and the results are summarised in Table 2.

For the two allylic alcohols employed in this study, the initial rate constants (k_i) were considerably higher with R'_3N (R' = Et or Bu) than with AcONa (compare entries 1 and 2 with 3, 4, and 5, Table 2). This observation strongly suggests that R'_3N not only neutralises the HX formed in the reaction but also acts as a ligand of the palladium atom to form a very reactive species in the oxidative addition step (equation 2) that could be rate-determining.

In order to clarify this aspect of the reaction, we carried out a kinetic study of the phenylation of but-3-en-2-ol with increasing amounts of Et_3N in the presence of an excess of AcONa (Figure 1). Our results clearly demonstrate the role of the amine as a ligand of the palladium catalyst. A ratio $(Et_3N)/(PdCl_2) = 20$ is necessary to ensure the complete formation of the active catalytic species, resulting in maximum rate constants. The same phenomenon was observed with pent-3-en-2-ol (entries 6 and 7 of Table 2).

Although it has been claimed that tertiary amines are not good ligands for palladium[5] our observations are in agreement with the *ortho*-palladation effect provided by benzylic tertiary amines allowing a remarkable regiochemical control of the Heck reaction[6] and isolation of stable *ortho*-palladated aromatic compounds.[6,7]

Variation of the temperature allowed us to determine the thermodynamic activation values for the phenylation of but-3-en-2-ol in the range 40—74 °C under these conditions:

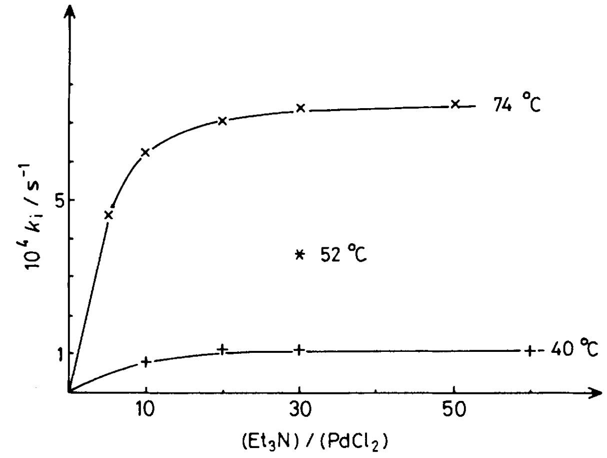


Figure 1. Plot of k_i against (Et_3N) for the phenylation of but-3-en-2-ol in the presence of sodium acetate.

$\Delta G^{\ddagger} = 46$ kJ mol^{-1}, $\Delta H^{\ddagger} = 43$ kJ mol^{-1}, and $\Delta S^{\ddagger} = -75$ J mol^{-1}K^{-1}. These activation values are in the range of the usually measured values for oxidative addition reactions with various transition metals[8] and the largely negative $\Delta S^{\ddagger}$ value is generally interpreted in terms of an increased solvation due to the increased dipole in going from the ground state to the transition state.[9]

Although not fully understood as yet, a strong synergistic effect has been observed. The initial rate constant of the reaction is greater when a small amount of R'_3N (0.2 mol equiv.) is used in the presence of AcONa than when a tertiary amine is employed alone (compare entry 6 with 3, 7 with 5, and 8 with 4 in Table 2).

We believe that this new aspect of the role of R'_3N should be studied in other palladium catalysed reactions.

In conclusion, we emphasise that the effect of added Et_3N on the initial rate allows this synthetically important reaction to be run at a lower temperature than those previously employed,[3,4] and under these conditions but-3-en-2-ol (**1**) was transformed to the arylated ketones (**2**) and (**3**) in 97% yield.‡

We acknowledge the financial support of the Centre National de la Recherche Scientifique.

Received, 21st May 1987;§ Com. 696

References

1 W. Smadja, S. Czernecki, G. Ville, and C. Georgoulis, *Organometallics*, 1987, **6**, 166.
2 R. F. Heck, *Pure Appl. Chem.*, 1978, **50**, 691; *Acc. Chem. Res.*, 1979, **12**, 146.
3 J. B. Melpolder and R. F. Heck, *J. Org. Chem.*, 1976, **41**, 265.
4 A. J. Chalk and S. A. Magennis, *J. Org. Chem.*, 1976, **41**, 273.
5 A. Spencer, *J. Organomet. Chem.*, 1983, **258**, 101.
6 B. M. Trost and T. R. Verhoeven in 'Comprehensive Organometallic Chemistry,' eds. G. Wilkinson, F. G. A. Stone, and E. W. Abel, Pergamon Press, Oxford, 1982, vol. 8, p. 799.
7 B. J. Brisdon, P. Nair, and S. F. Dyke, *Tetrahedron*, 1981, **37**, 173.
8 R. G. Pearson and P. E. Figdore, *J. Am. Chem. Soc.*, 1980, **102**, 1541 and references cited therein.
9 J. F. Harrod and C. A. Smith, *J. Am. Chem. Soc.*, 1970, **92**, 2699.

---

‡ The reaction was complete in 4 h at 74 °C with 2 mol. equiv. of PhI.

§ Received in revised form, 6th October 1987.