

Catalytic oxidation of alcohols with allyl diethyl phosphate and palladium acetate

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Abstract

Allyl diethyl phosphate (ADP) was found to function as a stoichiometric hydrogen acceptor in a catalytic oxidation reaction of alcohols with Pd(OAc)₂. A variety of acyclic primary and secondary alcohols were oxidized in good yields and under mild conditions to the corresponding aldehydes and ketones, in the presence of Na₂CO₃ or K₂CO₃. Simple aliphatic primary alcohols yielded esters, exclusively. Polar ligand solvents (DMF, DMSO) were found to accelerate the reaction. Slow, but high yield reactions were encountered in THF and acetonitrile as solvents. The reactivity of several other allyl systems serving as H-acceptors, and several Pd compounds serving as catalysts, in the above oxidation reaction, was evaluated. It has been experimentally demonstrated (H-NMR) that ADP is capable of generating a π-allyl-Pd complex using a Pd(0) complex. Consequently, a catalytic cycle was proposed for the above oxidation reaction. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Oxidation; Alcohols; Palladium acetate; Allyl diethyl phosphate

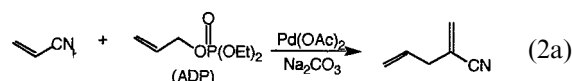
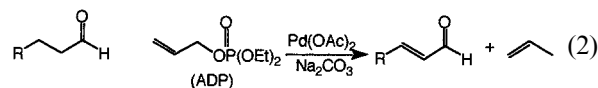
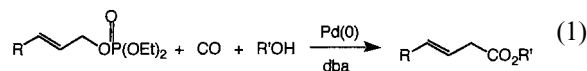
1. Introduction

Oxidation of alcohols to ketones and aldehydes is a fundamental reaction in organic chemistry. Economic and environmental aspects dictate a *catalytic* oxidation reaction. Indeed, alcohols can be catalytically oxidized with transition metal complexes of Ru [1], Ni [2], Pt [3], and Pd [4]. Several oxidation reactions of alcohols are known where a hydrogen acceptor was used, in conjunction with various Pd catalysts. Thus for example, bromobenzene [5] was reduced to benzene, with concomitant oxidation of an alcohol function. With 1,2-dichloroethane as hydrogen acceptor, the oxidation reaction generated ethylene and HCl [6]. Carbon tetrachloride was reduced to chloroform upon the oxidation of an alcohol function [7]. Allyl carbonate undergoes an *intramolecular* H transfer, generating the corresponding ketone, CO₂ and propene [8a,8b].

Noteworthy is the recent discovery by Sheldon co-workers [8c] of green aerobic oxidation of alcohols with a Pd(II) phenanthroline complex in a water–alcohol biphasic system. The reaction proceeded at reasonable

rates and good yields. Most of the above mentioned reactions proceeded in satisfactory yields.

Murahashi et al. [9] have recently demonstrated that various allyl diethyl phosphates (ADPs), in the presence of CO, alcohol, and Pd(0) as catalyst, undergo a *facile* alkyloxy carbonylation, giving rise to unsaturated carboxylic acid esters (Eq. (1)). The higher yields and rates (compared to other allyl esters and ethers) were attributed to the use of ADPs.



Recently we have discovered [10a] that aldehydes, in the presence of ADP, Pd(OAc)₂, and sodium carbonate, gave rise to a clean αβ-dehydrogenation reaction of aldehydes (Eq. (2)). Under the above conditions also, cyclic-ketones gave the corresponding αβ-unsaturated ketones. The yields were moderate to good. The dehy-

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drogenation of *aldehydes* under such non-oxidative conditions is significant, and useful.

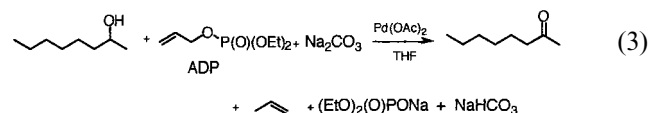
Very recently [10b], we have discovered a reaction between ADPs and acrylonitrile, catalyzed by $\text{Pd}(\text{OAc})_2$, to give a 1,4-diene (Eq. (2a)). Various substituted ADP compounds could also be used. This interesting intermolecular metallo-ene reaction involves C–C bond formation, and is currently being further investigated.

It is evident that *ADP is a unique substrate* in those catalytic reactions.

2. Results and discussion

In the present paper we shall report on still another new reaction of ADP that is also catalyzed by $\text{Pd}(\text{OAc})_2$. Thus, during the above dehydrogenation study [10a] we have noted that alcohols, in the presence of ADP, were readily oxidized to carbonyl compounds. Thus, cyclohexanol was oxidized to cyclohexanone, which was further transformed to phenol [10a] with excess ADP; cholesterol was similarly oxidized to cholestanone, that was further dehydrogenated to cholesta-1,4,6-triene-3-one in 75% yield [10a]. This observation, and the mild reaction condition, prompted us to study in detail the scope and mechanism of this oxidation reaction of alcohols with ADP, and $\text{Pd}(\text{OAc})_2$ as catalyst, which is the subject of the present report.

We have found that $\text{Pd}(\text{OAc})_2$, catalytically oxidized primary and secondary alcohols to the corresponding aldehydes and ketones, in the presence of stoichiometric amount of ADP. The allyl moiety of ADP was converted to propylene, as determined by brominating the evolving gas in CCl_4 . The stoichiometry of the reaction, exemplified with 2-octanol as a substrate and ADP, is described below in Eq. (3). Formally ADP is functioning as a hydrogen acceptor. The scope of the oxidation reaction was studied using a variety of alcohol substrates, and the results are presented in Table 1.



The following conclusions can be drawn from the data of Table 1:

1. The oxidation reaction of alcohols proceeds in polar ligand solvents. Best results were obtained in DMF (Experiments 1–3). The next best solvent is DMSO (Experiments 4 and 5). THF and acetonitrile are the best solvents from the reaction-work-up stand point. The yields with these solvents are good, but the reaction is slow (Experiments 1 and 2). Apparently the rate of the reaction was affected by the polarity, and ligand power of the reaction solvent.
2. In the present reaction, K_2CO_3 is a better base than Na_2CO_3 . It is, most probably, due to the better solubility of the former in DMF. A reaction time

Table 1
Experimental data for oxidation reactions with $\text{Pd}(\text{OAc})_2$ and ADP^a

Experiment	Substrate	Base	Time (h)	Solvent	Conversion ^b (%)	Products (yield %) ^b
1	2-Octanol	Na_2CO_3	37	THF	84	2-Octanone (80)
2	2-Octanol	Na_2CO_3	26	CH_3CN	84	2-Octanone
3	2-Octanol	Na_2CO_3	8	DMF	94	2-Octanone (85)
4	2-Octanol	K_2CO_3	2	DMF	97	2-Octanone (85)
5	2-Octanol	K_2CO_3	2	DMSO	76	2-Octanone (64)
6	1-Phenylethanol	Na_2CO_3	12	THF	78	Acetophenone
7	Benzyl alcohol	Na_2CO_3	2.5	DMF	86	Benzaldehyde (60)
8	4-OMe-benzyl alcohol	Na_2CO_3	46	CH_3CN	65	4-Methoxybenzaldehyde
9	4-OMe-benzyl alcohol	K_2CO_3	2	DMF	97	4-Methoxybenzaldehyde (88)
10	4-Cl-benzyl alcohol	K_2CO_3	4	DMF	71, 13	4-Chlorobenzaldehyde (32), 4-Chlorobenzyl-4-chlorobenzoate
11	1-Octene-3-ol	K_2CO_3	3.25	DMF	64	1-Octene-3-one (30)
12	Cinnamyl alcohol	K_2CO_3	2	DMF	97	Cinnamaldehyde (90)
13	(±) Menthol	K_2CO_3	4	DMF	92	(±) Menthone
14	Diisopropyl carbinol	K_2CO_3	1.5	DMF	98	Diisopropyl ketone
15	Diphenylcarbinol	K_2CO_3	5	DMF	100	Benzophenone (96)
16	Benzoin	K_2CO_3	6.5	DMF	60	Benzil (54)
17	1-Octanol	K_2CO_3	3.5	DMF	50	Octyl octanoate
18 ^c	Cyclohexanol	K_2CO_3	5	DMF	57, 32	Cyclohexanone, 2-cyclohexene-1-one

^a Reaction conditions: substrate 5 mmol, ADP 6.25 mmol, carbonate base 10 mmol, $\text{Pd}(\text{OAc})_2$ 0.2 mmol, solvent 4 ml. All reactions were carried out at 86 °C (bath temperature) under nitrogen blanket.

^b Conversions and yields were determined quantitatively by an internal standard (anisole) method, using gas chromatography, and are accurate to ± 5%.

^c Oil bath temperature was kept at 70 °C.

Table 2

Experimental data for oxidation reactions of 2-octanol with Pd(OAc)₂ and various allyl systems^a

Experiment	Allyl compound	Time (h)	Conversion (%)
1	ADP	2.0	97
2	Allyl acetate	7	18
3	Allyl bromide	7	0
4	Allyl methyl carbonate	6	93

^a The reactions were carried out under the same conditions described in the footnote to Table 1, in DMF–K₂CO₃.

Table 3

Experimental data for oxidation reactions of 2-octanol with ADP and various Pd compounds^a

Experiment	Pd catalyst	Time (h)	Conversion (%)
1	Pd(OAc) ₂	2.0	97
2	Pd(OAc) ₂ –PPh ₃	6	25
3	Pd–C (10%)	24	75
4	Pd ₂ (dba) ₃ ·CHCl ₃	6	93

^a The reactions were carried out under the same conditions described in the footnote to Table 1, in DMF–K₂CO₃.

factor of 4 was recorded in experiments 3 and 4, indicating the superiority of K₂CO₃.

- Primary aliphatic alcohols, viz 1-octanol, gave octyl octanoate as a sole product (Experiment 17). It must have originated via the formation of octanal, the subsequent formation of dioctyl hemiacetal, followed by its fast oxidation to the ester (the transient octanal was not dehydrogenated due to the fast formation of dioctyl hemiacetal). However, no benzyl benzoate ester could be detected with the primary benzyl alcohol (Experiment 7). This is attributed to the substantial smaller *K*(Eq) for hemiacetal formation of aromatic aldehydes compared to aliphatic aldehydes [11]. But 4-chlorobenzyl alcohol (Experiment 10) gave a mixture of both ester and aldehyde. The intermediate 4-chlorobenzaldehyde has a more electrophilic carbonyl C atom compared to benzaldehyde, thus inducing some hemiacetal formation, and subsequently an ester. 4-Methoxybenzyl alcohol (Experiment 9) was selectively oxidized to 4-methoxybenzaldehyde, faster than 4-chlorobenzyl alcohol (Experiment 10), as expected for an oxidation reaction.
- The oxidation of cyclohexanol was not selective. Cyclohexenone, the dehydrogenation product of cyclohexanone, was generated as a by-product (Experiment 18). This is in line with our previous finding that saturated *cyclic* ketones were dehydrogenated substantially faster than *acyclic* ketones [10a], which were practically inert. In fact this behavior makes feasible our oxidation reaction of secondary alcohols to ketones (acyclic).

- Attempts to oxidize ethyl lactate and 2,2,2-trifluoroethanol failed. Electron withdrawing groups next to the carbinol C atoms must impede the oxidation reaction.

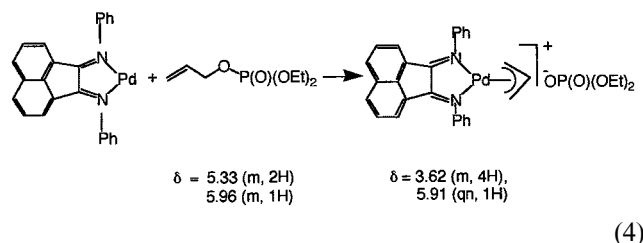
Finally, *N*-phenyl hydroxylamine could also be catalytically oxidized with Pd(OAc)₂ as catalyst in the presence of ADP–K₂CO₃ under the above reaction conditions. A transient GC peak of nitrosobenzene could be detected, which under the basic reaction condition was slowly transformed to azoxybenzene. After 24 h at 75°, azoxybenzene was obtained in 32% yield.

It is of interest to study and compare the efficiency of other allyl systems in the oxidation reaction of alcohols with Pd(OAc)₂ as catalyst. Several such systems were examined under identical reaction conditions, and the results are presented in Table 2. It can be seen from Table 2 that ADP (Experiment 1) gave the best results. Allyl methyl carbonate (Experiment 4) also exhibits a good reactivity, while allyl acetate and bromide (Experiments 2 and 3) are by far inferior.

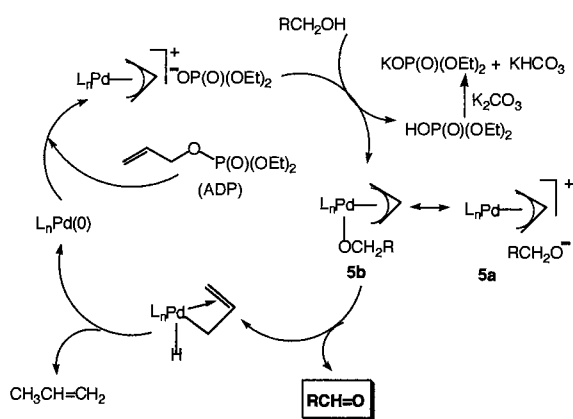
Examination of the catalytic activity of various Pd compounds in the oxidation of 2-octanol with ADP gave the following results (Table 3).

From the data of Table 3, it is evident that the oxidation reaction proceeds with Pd(II) (Experiments 1 and 2) as well as with Pd(0) (Experiments 3 and 4) as precatalysts. Thus, Pd(II) precatalyst is presumably reduced to Pd(0) in the presence of alcohols. Pd(0) is most probably the initial active catalytic species (vide infra). PPh₃ (Experiment 2) slows down the oxidation reaction, most probably through much stronger coordination to the Pd atom, as compared to a weaker solvent coordination. It is however gratifying that Pd–C, although slow, is reactive. A heterogeneous catalytic reaction is usually preferred for practical reasons. When Pd–C was used in the *absence of ADP*, no reaction could be detected, thus reflecting on the similarity between the heterogeneous and homogeneous reactions.

It will be of interest to briefly touch upon the mechanism of the present reaction. First we have addressed the question whether ADP is capable of forming a π -allyl Pd complex. For technical reasons it was difficult to determine its formation under the reaction conditions. The ¹H-NMR spectra of equimolar quantities of Pd(PPh₃)₄ and ADP in CDCl₃ or in benzene-*d*₆ at room temperature indicated a gradual disappearance of the allyl system H signals of the ADP. Broad ill-defined signals appeared at higher magnetic field. We have therefore resorted to the more stable and rigid known complex, (bis(phenylimino)acenaphthene)Pd(0). It was prepared from Pd₂(dba)₃·CHCl₃ and the (bis(phenylimino)acenaphthene) ligand [12]. The resulting Pd(0) complex was then reacted with ADP in acetone (Eq. (4)), and after work-up, the H-NMR spectrum was measured (we were unable to crystallize the product). The chemical shifts (ppm) of the allyl system H atoms are given below (Eq. (4)).



The resonance signals of the four terminal π -allyl protons in the product (3.62 ppm) were shifted to a higher magnetic field relative to the three vinyl protons of ADP (5.33 ppm), in line with a π -allyl Pd complex structure. Further support for the above π -allyl structure was gained by comparing the above chemical shifts of the product with those of the corresponding known [13] chloride and bromide complexes, $\delta = 3.34$ (br, 4H), 5.51 (qn, 1H). The allyl protons of the phosphate complex resonate at somewhat lower field than those of the above halogen complexes, implying that the phosphate complex is more positively charged, i.e. more



Scheme 1. Catalytic cycle for the oxidation of alcohols.

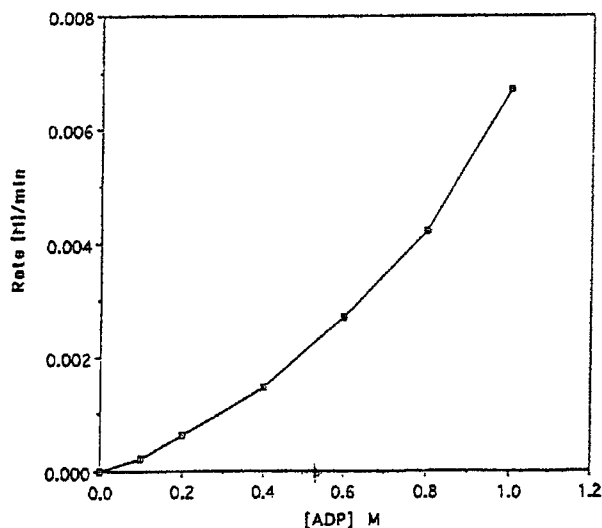


Fig. 1. Oxidation rate of 2-octanal as a function of ADP concentration.

ionic than the halogen complexes. However, more important, the above results indicate that ADP does form a π -allyl complex with Pd(0).

Granted that a π -allyl-Pd complex is also formed in the above described oxidation reaction of alcohols in the presence of a Pd(0) species, a catalytic cycle may now be constructed, using well known organometallic chemistry principles (Scheme 1). The step, following ADP complexation with L_n Pd(0), must consist of a phosphate anion exchange with the alcohol substrate, RCH_2OH (Scheme 1). The equilibrium of this exchange reaction must be shifted to the right due to the fast neutralization of the relatively strong diethyl phosphoric acid produced (Scheme 1). Significantly, no reaction was found to take place in the *absence* of base.

The product of such an exchange reaction is described by structures **5a** and **5b**, two extreme formulations of the alcoholate π -allyl-Pd complex. In the present experiment, the covalent structure **5b** is probably more important than the ionic structure **5a**, on the basis of the following grounds:

- The presence of the strong alkyloxy anion in the ionic formulation **5a** is expected to promote a nucleophilic attack on the positively charged π -allyl carbon system that would have eventually yielded an allyl ether. The latter is *not* a product of the present reaction.
- Mechanistically, β -elimination should take place in order for the oxidation reaction to occur. This in turn requires a structure RCH_2O-Pd- , such as in the covalent formulation **5b**, therefore better describing the catalytic reactive species.

Thus, β -elimination from **5b** generated the carbonyl product, and an allyl Pd hydride species (Scheme 1). The latter undergoes now reductive elimination of propylene (identified) and regeneration of Pd(0), which resumes the catalytic cycle by recomplexation with ADP. In the scheme it is assumed that the solvent ligand L stabilizes the Pd atom in the various complexes.

Brief kinetic studies indicated that the oxidation rate of 2-octanol depends on the concentrations of ADP, Pd(OAc)₂ and the alcohol (Figs. 1–3). This implies that the formation of the π -allyl-Pd complex (**5a–5b**) must be the slow step of the catalytic cycle. The subsequent β - and reductive eliminations are most probably fast reaction steps [14].

In conclusion, alcohols may be readily oxidized under mild conditions and satisfactory yields to ketones or aldehydes with ADP, and Pd(OAc)₂ as a precatalyst, in the presence of a carbonate base. ADP may be readily prepared from the commercially available diethyl chlorophosphate and allyl alcohol [9]. ADP is a *unique* stoichiometric H-acceptor ligand for the above oxidation reaction. A variety of polar solvents may be used, and the rate of the reaction is solvent dependent.

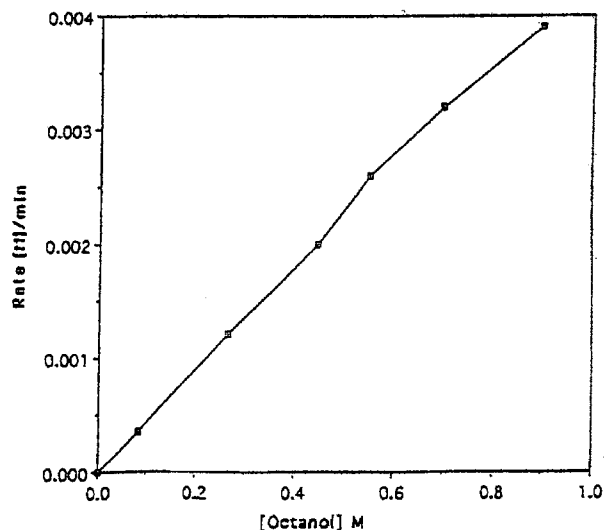


Fig. 2. Oxidation rate of 2-octonal as a function of octonal concentration.

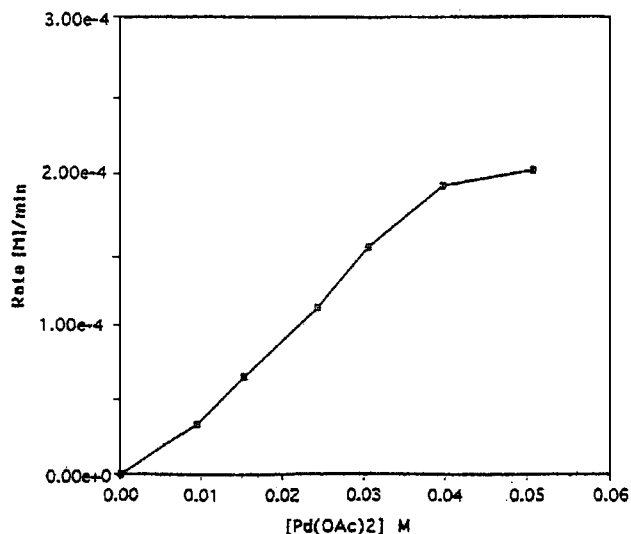


Fig. 3. Oxidation rate of 2-octonal as a function of Pd(OAc)₂ concentration.

In most cases the yields are good. The reaction was found to proceed via π -allyl-Pd diethyl phosphate intermediate complex. The above oxidation reaction may be particularly useful in cases where classical oxidative reaction conditions are prohibitive.

3. Experimental

3.1. General

Data related to the quantities of reactants and solvents, reaction temperature and time, as well as percent conversions and yields are given in Tables 1–3 and their accompanying footnotes.

ADP was prepared from the commercially available diethyl chlorophosphate and allyl alcohol [9].

All oxidation reactions were carried out under a nitrogen blanket, and GC monitored their progress. At the end of the reaction, the catalyst was filtered, the solvent was removed by evaporation under reduced pressure, and the residue was analyzed by GC, as well as by NMR and IR measurements. The oxidation products are known commercially available compounds, and were identified by GC co-injection with authentic commercial samples.

3.1.1. Azoxybenzene

N-Phenyl hydroxylamine was prepared according to the procedure of Vogel [15]. A solution of *N*-phenyl hydroxylamine (0.545 g, 5 mol), ADP (1.212 g, 6.25 mol), K₂CO₃ (1.38 g, 10 mol) and Pd(OAc)₂ (0.045 g, 0.2 mol) in DMF (4 ml), was heated overnight at 75 °C. GC injection of the reaction solution after 4 h indicated a nitrosobenzene signal (co-injection of an authentic sample) that disappeared at the end of the reaction to give an azoxybenzene signal, identified by co-injection of an authentic sample. The solvent was evaporated in vacuum, and the product was purified by column chromatography (silica) from pet ether (0.158 g, 32%). MS *m/z*: [M⁺] (198), and GC co-injection with an authentic sample of azoxybenzene.

3.1.2. Octyl octanoate (Experiment 17)

¹H-NMR (CDCl₃): 0.85–1.61 (28H), 2.29 (t, 7.4 Hz, 2H), 4.06 (t, 6.6 Hz, 2H) ppm. MS *m/z*: [M⁺ + H] (257), [M⁺ – O(CH₂)₇CH₃] (127).

3.1.3. Bis(phenylimino)acenaphthene) π -allyl palladium diethylphosphate

Bis(phenylimino)acenaphthene) ligand was prepared according to a literature procedure [12,13]. Bis(phenylimino)acenaphthene) (0.8 mmol), Pd₂(dba)₃·CHCl₃ (0.4 mmol) and ADP (1.12 mmol) were stirred in acetone (18 ml) for 1 h at room temperature. The solvent was evaporated in vacuum, the residue washed with ether (3 × 7 ml), CH₂Cl₂ (7 ml) was added to the residue, and the solution was filtered through celite. Evaporation of the filtrate gave a semi-solid red residue, ¹H-NMR (CDCl₃): 1.16 (t, 7.1 Hz, 6H), 3.62 (m, 4H), 3.9 (qn, 7.0 Hz, 4H), 5.91 (q, 9.7 Hz, 1H), 7.10 (d, 7.6 Hz, 2H), 7.55 (m, 10H), 8.17 (d, 8.3 Hz, 2H) ppm (proper integration of the signals was obtained upon addition of D₂O).

3.1.4. Kinetic measurements

All kinetic measurements were carried out in 10 ml volumetric flasks, in DMF, under nitrogen, with magnetic stirring, in an oil bath kept at 70 ± 2 °C. In all cases, the molar ratio for K₂CO₃–ADP was 10:6.25. Initial reaction rates were measured (GC) for variable

concentrations of 2-octanol, ADP and Pd(OAc)₂. Plots of the constant initial reaction rates versus variable concentrations were made for each of the above variables, and are presented in Figs. 1–3.

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