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Palladium-catalyzed oxidative cyclization of 1,4- and 1,5-diols in 1,2-dichloroethane

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Abstract

 β - and δ -lactones have been obtained from diols in 1,2-dichloroethane containing sodium carbonate and catalytic amounts of both palladium chloride and Adogen 464. In one case, the reaction stopped at the level of the lactol; a dealkoxypalladation is thus suggested. © 1998 Elsevier Science B.V.

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1. Introduction

Recently, we have described the oxidation of alcohols using 1,2-dichloroethane (DCE), sodium carbonate and catalytic amounts of both palladium chloride and Adogen 464 [1]¹. This procedure led cleanly to ketones from saturated secondary alcohols. In contrast, the primary alcohols afforded mixtures which can contain the corresponding aldehydes, acids and/or chloroethyl esters (Eq. (1)).



We have shown that the catalytic cycle involves the insertion of reduced palladium species into a C–Cl bond of DCE followed by an elimination reaction leading to ethylene and to the regeneration of

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¹ Adogen 464 is a registered trademark of Ashland Chemical for methyltrialkyl($C_8 - C_{10}$) ammonium chloride.

Pd(II) [1]. Since the achievement of this mechanistic study, the elimination of ethylene from a transient complex — $ClCH_2CH_2PdCl(dppe)$ — has been proposed [2] while formation of Pd–Cl bonds from Pd species and DCE have been reported [3,4]. The emergence of **4** as product of the oxidation of **1** (Eq. (1)) has been explained by the esterification of **3** by DCE in the presence of sodium carbonate and Adogen 464 as depicted in an independent study [5]. Therefore, the lactonisation of diols under our Pd(II)/DCE oxidative conditions could be expected.

The originality of the reoxidation of Pd(0) species by DCE made the subject challenging. Furthermore, we were aware of only a few reports describing the palladium-catalyzed oxidation of diols to lactones [6–9]. This letter discloses our results concerning lactonisation under our recently described Pd-conditions.

2. Results and discussion

The oxidation of 1,4-diol **5** bearing two primary benzylic hydroxy groups, was firstly carried out under the conditions we used previously for alcohols [1] (Eqs. (1) and (2)). Thus a 87% conversion of **5** was obtained in 22 h and phthalide [10,11] was isolated with 66% yield. Doubling the quantities of PdCl₂ and Adogen 464 led to complete reaction and a 70% yield of **6**. When the reaction was performed under argon instead of an air atmosphere, the chemical yield was lower but the process remained catalytic in palladium (conversion: 100% in 24 h, **6** yield: 51%). Therefore, it appeared clearly that the solvent was here also involved in the catalytic cycle.

$$\begin{array}{c} \begin{array}{c} & PdCl_{2} (cat.) \\ Adogen 464 (cat.) \\ \hline Base \\ \hline C(CH_{2})_{n}OH \end{array} \xrightarrow{PdCl_{2} (cat.)} \\ \hline Base \\ \hline CICH_{2}CH_{2}CI, reflux \\ \hline CICH_{2}C$$

From these initial results, we decided to examine the oxidation of various diols under an air atmosphere using 0.1 equivalent of $PdCl_2$, 0.2 equivalent of Adogen 464 and 2 equivalents of Na_2CO_3 .

The 1,5-diol **7** where only one hydroxy group is benzylic, was fully converted in 7 h leading to 79% yield of the corresponding δ -lactone **8** [10]. Therefore, it appears that a benzylic primary alcohol is more prone to oxidation than an aliphatic one under these conditions.

A benzylic hydroxy group is nevertheless not required to observe the lactonisation since the 1,4-diol **9** yielded **10** [12] cleanly (Eq. (3); reaction time: 20 h, conversion: 100%, yield: 79%). The presence of an isolated double bond as in **11** lowered the efficiency of the process: the conversion was thus reduced to 76% in 24 h and the γ -lactone **12** [12] was isolated in 46% yield after chromatography. The high reactivity of the double bonds with Pd(II) is well known [13–15]; a portion of the catalyst is likely trapped by the unsaturation and is not available to react with the hydroxy groups. The ¹H NMR spectrum of the crude mixture of organic compounds obtained from the oxidation of **11** revealed the presence of aromatic hydrogens. This observation indicated a reaction of the double bond



Scheme 1. Suggested pathways for the oxidation of diol 13.

with palladium leading to dehydrogenation of the cyclohexenyl fragment ². Indeed, we have been able to prove (TLC, ¹H NMR, IR) the formation of small amounts of lactone $6 \ (\approx 4\% \text{ yield})$.



Since the double bond of the norbornene derivative **13** is not susceptible to lead to an η^3 -allylpalladium complex in the presence of Pd(II) [13–15,18], a cleaner reaction was expected. Indeed, the oxidation was highly selective (more than 95% selectivity) but provided the unanticipated lactol **14** [19,20] (Eq. (4)). The treatment of **14** under palladium-oxidative conditions did not produced lactone **15** (89% of **14** was recovered after 42 h).



The isolation of 14 instead of 15 could be explained in considering A as intermediate (Scheme 1). The transformation of A into 15 would involve an intramolecular abstraction of hydrogen by Pd (path a) which requires a *syn*-orientation of O_{α} -Pd and C_{β} -H bonds. Since the formation of 15 is not observed, we postulate that such an arrangement is not obtained. Consequently, A would evolve through either alcoholysis of the alkoxypalladium bond by 13 to afford a lactol (path b) or palladium-assisted cleavage of the C_{β} -O_{γ} bond (path c) giving B. A *syn*-orientation of O_{α} -Pd and

² Aromatisations carried out by Pd(II) have been already described [16–18]. An η^3 -allylpalladium complex [13–15,18] is postulated as an intermediate for the formation of **6**.

 $C_{\beta}-O_{\gamma}$ bonds would be stabilized by intramolecular coordination of O_{γ} to Pd. This reaction pathway is reminiscent to the mechanism of dealkoxypalladation recently suggested by Sinou in the course of Heck-type cyclizations on carbohydrate templates [21,22]. From **B**, the intramolecular nucleophilic addition of OPd on the aldehyde would regenerate **A** (path d).

In the course of the process, the formation of the lactol with an *endo*-hydroxy group is imaginable. This hemiacetal will be in equilibrium with the corresponding hydroxyaldehyde to afford the lactol with an *exo*-hydroxy group as the thermodynamic compound [19,20].

The oxidation of hydroxyphenol 16 gave many products, the main one being the chloroether 17 produced from a base-induced reaction with the solvent (Eq. (5)).



The reactivity of acyclic primary diols was also examined (Eq. (6)). The reaction of **18** was slow but clean: after two days, 51% of the diol was converted leading to **19** [10,11] with high selectivity (50% yield). In contrast, **20** afforded low amounts of lactones (reaction time: 36 h, conversion: 36%, **21**: 1%, **22**: 5%), the main compounds being esters arising from side-reactions with DCE.



Finally, the 1,4-diol **23** which bears one primary and one secondary hydroxy group has been subjected to the process (Eq. (7)). The concurrent reactions between the two hydroxy groups caused the formation of the two heterocycles: lactone **24** [11] and lactol **25b**, the latter being in equilibrium with the corresponding hydroxyketone.



3. Conclusion

We have shown that β - and δ -lactones can be obtained when 1,4- and 1,5-diols respectively are subjected to catalytic amounts of palladium chloride and Adogen 464 at reflux of 1,2-dichloroethane in the presence of sodium carbonate, the efficiency of the process being greatly dependent on the structure of the starting diol.

4. Experimental

4.1. General procedure

In a round-bottomed flask containing $PdCl_2$ (0.1 mmol) and Adogen 464 (0.2 mmol) was added $ClCH_2CH_2Cl$ (10 ml), the diol (1 mmol) and Na_2CO_3 (2 mmol). The stirred mixture was refluxed under an air atmosphere for the time indicated in the equations. After cooling to room temperature, the mixture was filtered on a short pad of silica gel and eluted with dichloromethane. After evaporation of solvents, the compounds were separated by flash-chromatography or preparative TLC eluting with AcOEt/petroleum ether. Products were identified by IR, NMR and comparison with literature data [10–12,19,20].

3-[2-(2'-*Chloroethoxy*)-*phenyl*]-*propanol* **17**. ¹H NMR 250 MHz (CDCl₃) $\delta = 1.60$ (wide d, 1 H, J = 11.4, OH), 1.90 (quint, 2 H, J = 6.7, PhCH₂C H_2), 2.75 (t, 2 H, J = 7.2, PhC H_2), 3.60 (t, 2 H, J = 6.2, HOC H_2), 3.80 (t, 2 H, J = 5.7, ClC H_2), 4.30 (t, 2 H, J = 5.7, ArOC H_2), 6.75–7.25 (C₆H₄). ¹³C NMR 62.89 MHz (CDCl₃) $\delta = 26.1$ (ArCH₂CH₂), 32.9 (ArCH₂), 42.2 (ClCH₂), 62.1 (HOCH₂), 68.1 (ArOCH₂), 111.5, 121.4, 127.1, 130.3, 130.7, 156.0 (aromatic C). IR (neat): 3391, 2932, 2866, 1493, 1240, 752, 484. MS, m/e: 214, 196, 169, 133.

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