

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

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Received 13 February 1997; accepted 9 June 1997

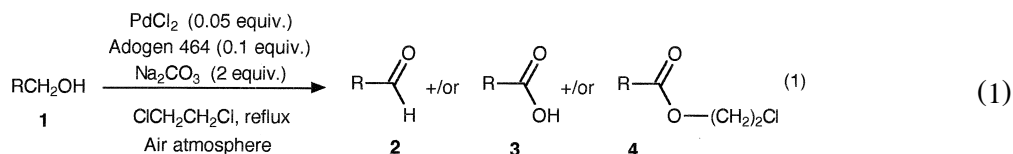
Abstract

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.

Keywords: Palladium-catalysis; Lactonisation; 1,2-dichloroethane; Oxidation; 1,*n*-diols

1. Introduction

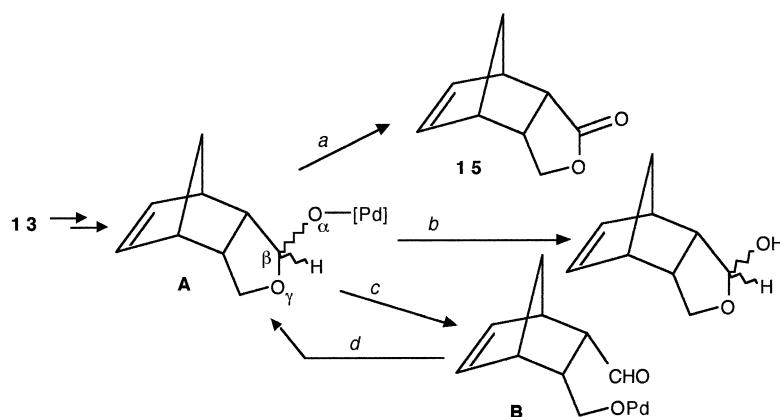
Recently, we have described the oxidation of alcohols using 1,2-dichloroethane (DCE), sodium carbonate and catalytic amounts of both palladium chloride and Adogen 464 [1]¹. This procedure led cleanly to ketones from saturated secondary alcohols. In contrast, the primary alcohols afforded mixtures which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



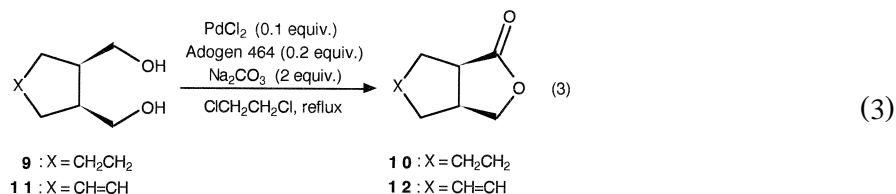
We have shown that the catalytic cycle involves the insertion of reduced palladium species into a C–Cl bond of DCE followed by an elimination reaction leading to ethylene and to the regeneration of

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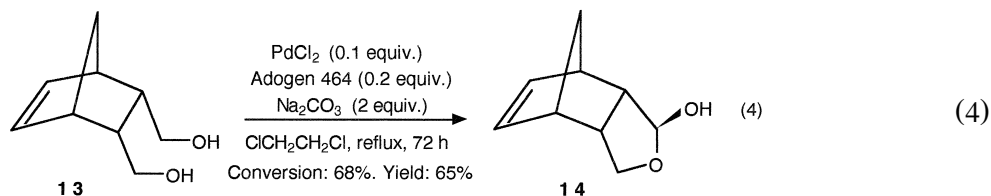
¹ Adogen 464 is a registered trademark of Ashland Chemical for methyltrialkyl(C₈–C₁₀)ammonium chloride.

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** ($\approx 4\%$ 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).



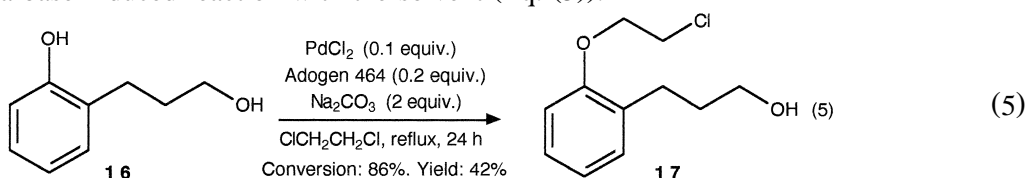
The isolation of **14** instead of **15** could be explained in considering **A** as intermediate (Scheme 1). The transformation of **A** into **15** would involve an intramolecular abstraction of hydrogen by Pd (path a) which requires a *syn*-orientation of O_α -Pd and C_β -H bonds. Since the formation of **15** is not observed, we postulate that such an arrangement is not obtained. Consequently, **A** would evolve through either alcoholysis of the alkoypalladium 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**.

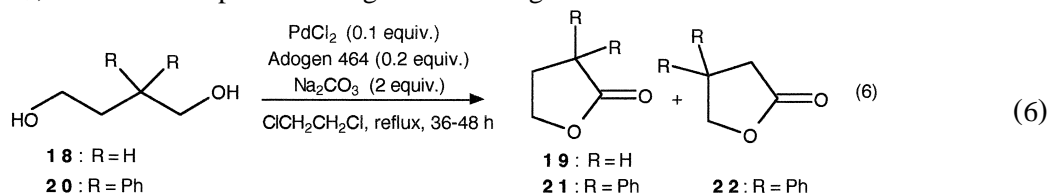
$C_{\beta}-O_{\gamma}$ bonds would be stabilized by intramolecular coordination of O_{γ} to Pd. This reaction pathway is reminiscent to the mechanism of dealkoxypalladation recently suggested by Sinou in the course of Heck-type cyclizations on carbohydrate templates [21,22]. From **B**, the intramolecular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

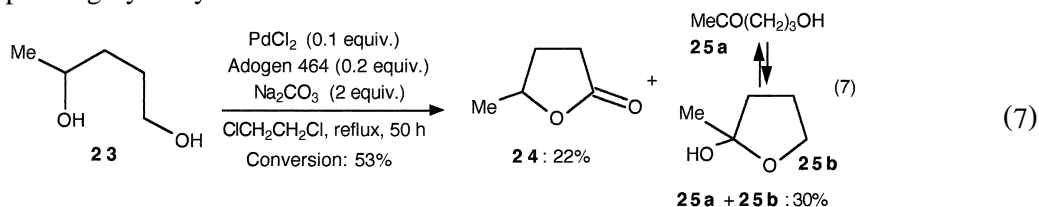
The oxidation of hydroxyphenol **16** gave many products, the main one being the chloroether **17** produced from a base-induced reaction with the solvent (Eq. (5)).



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 PdCl₂ (0.1 mmol) and Adogen 464 (0.2 mmol) was added ClCH₂CH₂Cl (10 ml), the diol (1 mmol) and Na₂CO₃ (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) δ = 1.60 (wide d, 1 H, *J* = 11.4, OH), 1.90 (quint, 2 H, *J* = 6.7, PhCH₂CH₂), 2.75 (t, 2 H, *J* = 7.2, PhCH₂), 3.60 (t, 2 H, *J* = 6.2, HOCH₂), 3.80 (t, 2 H, *J* = 5.7, ClCH₂), 4.30 (t, 2 H, *J* = 5.7, ArOCH₂), 6.75–7.25 (C₆H₄). ¹³C NMR 62.89 MHz (CDCl₃) δ = 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.

Acknowledgements

We are grateful to “Région Champagne–Ardenne” and CNRS for a Ph.D. studentship to S.A.-M., to the Engelhard Company for a generous gift of palladium chloride and to Dr. G. Bird (Zeneca Pharma, Reims) for help with the english. The work was partly carried out within the INTAS program (Research project INTAS-94-1515).

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