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Palladium-catalyzed electrochemical carbonylation of 2-amino-1-alkanols to oxazolidin-2-ones under very mild conditions

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Abstract—A new procedure for an efficient synthesis of oxazolidin-2-ones was developed. 2-Amino-1-alkanols undergo oxidative carbonylation under atmospheric pressure of carbon monoxide at room temperature using Pd(II) catalyst in combination with its anodic recycling at a graphite electrode. © 2001 Elsevier Science Ltd. All rights reserved.

Oxazolidin-2-ones, a well-known class of organic compounds, have many chemical and biological uses; they are, in fact, employed as chiral auxiliaries (Evans' chiral auxiliaries)[1] in asymmetric synthesis and some oxazolidin-2-ones have been found to have activity as immunosuppressants[2] and as antimicrobials.[3]

Oxazolidin-2-ones are usually obtained by reaction of 1,2-amino alcohols with phosgene or derivatives.[1] Also palladium-catalyzed carbonylation of 2-amino alcohols has been described in literature: Tam[4] used 3 atm of CO and a quite high temperature (80°C) to afford oxazolidin-2-ones in 34–94% yields. This method has the disadvantage of not being suitable for primary amines, and $CuCl_2$ is used to reoxidize palladium(0) to palladium(II), which is the reactive species. Imada and co-workers[5] carried out this reaction under atmospheric pressure with a mixture of CO and O_2, at 50°C and catalytic CuI, with fair to good yields in oxazolidin-2-ones; however, in this case the reaction does not work with primary amines. 80 atm of CO are necessary to carbonylate primary amines. More recently, Gabriele and co-workers[6] synthesized oxazolidin-2-ones by direct palladium-catalyzed oxidative carbonylation of 2-amino-1-alkanols in good yields (with primary amines), but this method suffers from several drawbacks. A high pressure of gases (CO, O_2 and air, 60 atm) and a temperature of 100°C are required.

In this study, we wish to report a new procedure for the electrochemical synthesis of oxazolidinones from 2-amino-1-alkanols, under very mild conditions, using a palladium(II) complex as catalyst and carbon monoxide (pCO = 1 atm). The process is outlined in Eq. (1).

The following general procedure was used: in a cell with three separated compartments, kept at 50±0.1°C, the electrolysis was carried out on a solution of 2-amino-2-phenylethanol (0.5 mmol) in 0.03 dm^3 of CH_3CN containing n-Bu_4NBF_4 (0.2 mol dm^{-3}) as supporting electrolyte, in the presence of $Pd(OAc)_2$ (0.05 mmol) and NaOAc (2 mmol), under 1 atm of CO, at +0.4 V versus SCE. A graphite electrode, of apparent area of 3 cm^2, was used as the working electrode. The counter electrode was a Pt wire and the reference was a

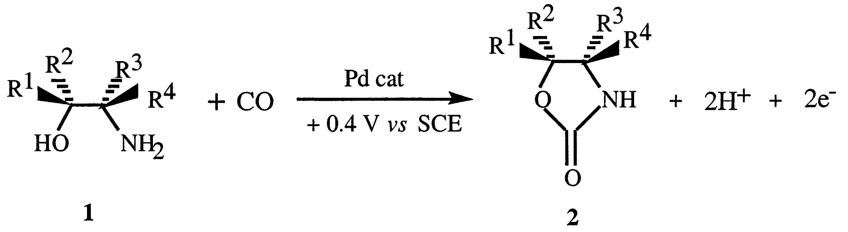

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Table 1. Electrochemical carbonylation of (*R*)-(−)-2-amino-2-phenylethanol to (*R*)-(−)-4-phenyloxazolidin-2-one using different Pd(II) complexes as catalyst

Catalyst	Base	F/mol[a]	Yield (%)[b] **2**	Current efficiency (%)
$PdCl_2$	AcONa	1.04	62	100
$Pd(PPh_3)_2(OAc)_2$	AcONa	1.63	79	85
$Pd(OAc)_2$	AcONa	1.27	75	100
$PdCl_2$	NEt_3	1.27	75	99

[a] With respect to starting **1**.

[b] Isolated yields relative to starting **1**.

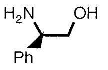
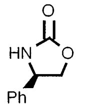
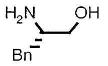
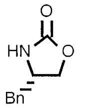
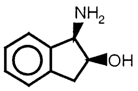
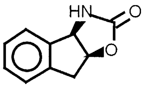
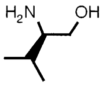
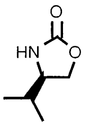
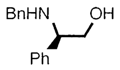
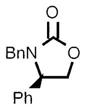
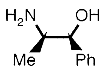
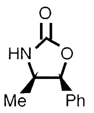
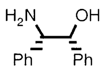
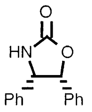
saturated calomel electrode (SCE). The results for the electrolyses using various palladium complexes are summarized in Table 1.

It was found that the reaction proceeded efficiently under atmospheric pressure of carbon monoxide with all the catalyst systems taken into account. The choice of the $Pd(OAc)_2$/NaOAc system derives from the necessity to use a chloride-free system and to avoid the presence of triphenylphosphine during the work-up.[7] On the basis of these considerations we used this catalyst system for the reaction with various 2-amino-1-alkanols (Table 2).

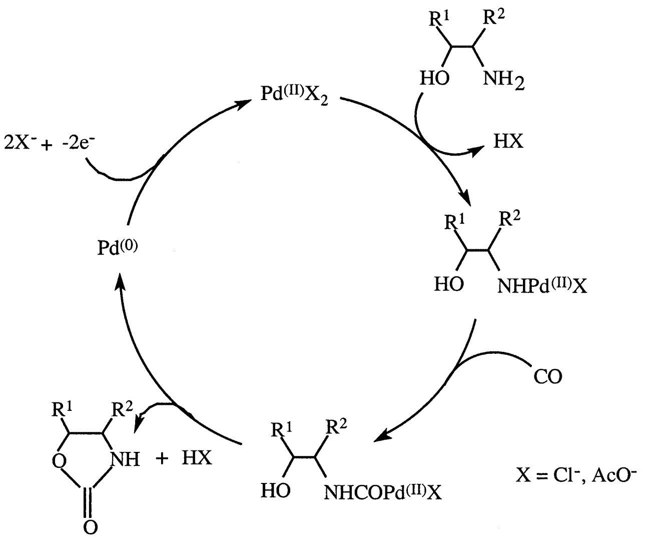
Oxazolidin-2-ones were obtained in very good current yields, with all the 2-amino-1-alkanols bearing a primary amino group. In the case of *N*-benzyl-2-phenyl-2-amino-1-ethanol (Table 2, entry 5) the reaction was very slow; it was probably due to the lower reactivity of this secondary amino group versus the palladium catalyst in our reaction conditions.

The possible reaction mechanism is outlined in Scheme 1. The use of a base is necessary to avoid the formation of $HPd(II)(PPh_3)_2{}^+$ or of $HPd(II)^+$, that do not react in this reaction.[8]

Table 2. Electrochemical carbonylation of 2-amino-1-alkanols **1**, by $Pd(OAc)_2$ catalyst, to oxazolidin-2-ones **2**

Entry	**1**	**2**	Yield (%)[a]	Current efficiency (%)	F/mol[b]
1			75	100	1.27
2			96	96	1.80
3			58	57	1.70
4			79	95	1.45
5			29	57	0.64
6			86	84	1.80
7			69	97	1.22

[a] Isolated yields relative to starting **1**. [b] With respect to starting **1**



Scheme 1.

In conclusion, we have reported the use of electrochemistry in the reoxidation of Pd(0) to Pd(II), in very mild conditions, during the synthesis of chiral oxazolidin-2-ones from chiral 2-amino-1-alkanols.

Acknowledgements

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7. After the end of the electrolysis, the anodic solution was concentrated, analyzed by TLC, and the reaction products purified by flash-chromatography (*n*-hexane/ethyl acetate 6:4). The isolated oxazolidin-2-ones were identified by comparison of their physical and spectral data (^{1}H, ^{13}C NMR, MS, $[\alpha]_D$) with those of authentic samples.
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