Palladium(II)-catalysed Oxidation of Carbon–Carbon Double Bonds of Allylic Compounds with Molecular Oxygen; Regioselective Formation of Aldehydes

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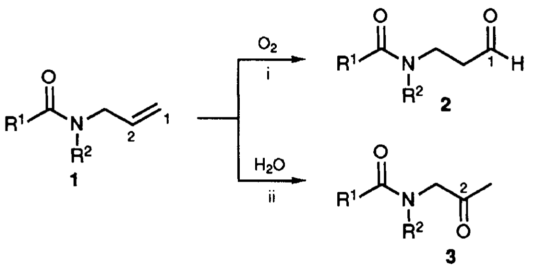
Treatment of *N*-allylamides **1a–c** and lactams **1d–f** with molecular oxygen in the presence of $[PdCl_2(MeCN)_2]$–CuCl catalyst in anhydrous 1,2-dichloroethane containing hexamethylphosphoric triamide gives the corresponding aldehydes **2** regioselectively, while methyl ketones **3** become the major products in the presence of water.

In the Wacker oxidation of alk-1-enes, O-atom transfer to C=C double bonds occurs from water.[1] In contrast to this well known process, we have now found that alk-1-enes are directly oxidised with molecular oxygen in anhydrous, aprotic solvents, when a catalyst system consisting of $PdCl_2(MeCN)_2$ and CuCl is used together with hexamethylphosphoric triamide (HMPA). The oxidation is unique in that regioselective production of aldehydes **2** from *N*-allylamides **1** occurs (Scheme 1), which is in sharp contrast with the usual Wacker oxidation to give methyl ketones **3**. Although regioselective formation of aldehydes from terminal alkenes has been observed even in the usual Wacker oxidation[2] or by the use of $[Pd(MeCN)_2Cl(NO_2)]$ as catalyst in Bu^tOH,[3] there is no precedent for such a complete reversal of the regioselectivity in the $PdCl_2$-catalysed oxidation of alkenes.

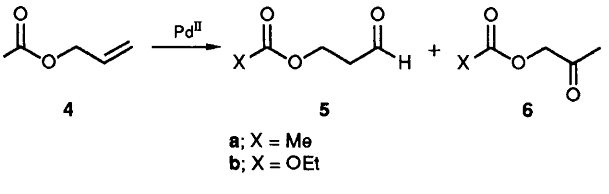
The oxygenation of *N*-allylamides **1** with molecular oxygen proceeds in a variety of anhydrous, aprotic solvents such as benzene, 1,2-dimethoxyethane (DME), dichloromethane and 1,2-dichloroethane. Halogenated solvents such as 1,2-dichloroethane led to a higher regioselective production of aldehyde **2**. When aqueous DME (DME : H_2O = 3 : 1) was used as the solvent, the product composition was completely reversed, resulting in the predominant formation of ketone **3** as shown in Table 1 (entry 1).



Scheme 1 *Reagents and conditions*: i, $PdCl_2(MeCN)_2$, CuCl, HMPA; ii, $PdCl_2$, $CuCl_2$, O_2

To promote the oxidation under anhydrous conditions, it is essential to use HMPA as an additive. In the absence of HMPA, virtually no reaction takes place. The use of a smaller amount of HMPA (HMPA : Pd = 1 : 1) does induce the oxygenation, but it leads to deallylation of **1**. For instance, the oxygenation of **1a** (R^1 = Ph, R^2 = Me) in DME gives a 11% isolated yield of *N*-methylbenzamide along with the aldehyde **2a** and the ketone **3a** (69%, **2a** : **3a** = 66 : 34). The deallylation can be suppressed by using an excess of HMPA (HMPA : Pd = 20 : 1). Under these conditions, *N,N*-disubstituted amides **1a–c** are predominantly converted into aldehydes **2** as shown in Table 1 (entries 1–3). Similarly the oxygenation of *N*-allyllactams **1d–f** under anhydrous conditions (Table 1, entries 4–7) gives aldehydes **2** regioselectively, while the corresponding ketones **3** become the major products under aqueous conditions. The use of $CuCl_2$ in place of CuCl in aqueous tetrahydrofuran (THF) containing HMPA at 50 °C has been found to give the ketones **3** with higher regioselectivity. Representative results are also given in Table 1.

From allyl acetate **4a** and allyl carbonate **4b** (Scheme 2) a reasonable excess of aldehydes **5** is formed under anhydrous conditions (CH_2Cl_2, room temp.) (**5a** : **6a** = 65 : 35, 76% yield; **5b** : **6b** = 48 : 52, 56% yield), while the corresponding ketones **6** again become the major products under aqueous conditions (**5a** : **6a** = 5 : 95, 76% yield; **5b** : **6b** = 0 : 100, 59% yield).

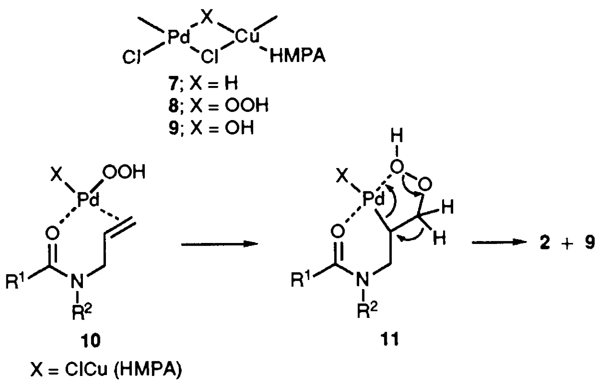


Scheme 2

Table 1 Pd^{II}-catalysed oxidation of *N*-allylamides and related compounds under anhydrous and aqueous conditions

				O_2[a]		H_2O[b]	
Entry	Substrate	R^1	R^2	Yield (%)[c]	Aldehyde : Ketone[d] **2** **3**	Yield (%)[c]	Aldehyde : Ketone[d] **2** **3**
1	**1a**	Ph	Me	52 (71)	90 : 10 (75 : 25)[e]	62 (58)	6 : 94 (28 : 72)[e,f]
2	**1b**	Me	Ph	68	90 : 10	57	8 : 92
3	**1c**	Me	Me	58	85 : 15	50	7 : 93
4	**1d**	$-[CH_2]_5-$		62	90 : 10	86	17 : 83
5	**1e**	$-[CH_2]_4-$		50	90 : 10	74	15 : 85
6	**1f**	$-[CH_2]_3-$		55	89 : 11[g]	72[h]	4 : 96[g]

[a] The reaction was performed by using *N*-allylamides **1** (2 mmol), $PdCl_2(MeCN)_2$ (0.2 mmol), CuCl (0.2 mmol) and HMPA (4 mmol) in anhydrous 1,2-dichloroethane (2 ml) at room temperature under oxygen (balloon) for 2–12 h. [b] Using $CuCl_2$ (0.2 mmol) and THF (4 ml) containing water (40 mmol), the reaction was carried out at 50 °C for 9–20 h under otherwise the same conditions as above. [c] Isolated yield. [d] Determined by GLC analysis. [e] The data shown in parentheses were obtained from reactions using 1,2-dimethoxyethane as a solvent. [f] CuCl was used as co-catalyst. [g] Determined by ^1H NMR analysis. [h] *N*-(2-Formylethenyl)pentane-5-lactam (18%) was formed as by-product.



Scheme 3

Under anhydrous conditions, normal alkenes are also oxidised, but the corresponding ketones are the exclusive products. For example, the reaction of dec-1-ene with O_2 (anhydrous $ClCH_2CH_2Cl$, 50 °C, 4 h) affords a 50% isolated yield of decan-2-one as the sole product. Similarly, cyclopentene gives cyclopentanone (44%, 19 h). These results reflect the direction of the regioselectivity by the carbonyl group for the formation of aldehydes. Among carbonyl compounds examined, *e.g.* simple ketones, esters and amides, palladium(II) interacts strongly with amido-carbonyl groups to form a chelate complex which effects a directed O-atom transfer to the alkenes.

The oxidation is effected by a Pd–OOH species derived from Pd–H and molecular oxygen.[4] The Pd–H species **7** is probably formed by chloropalladation by $PdCl_2$ of the alkene followed by β-hydride elimination. When HMPA is present, the bimetallic Pd–H species **7** is oxidised smoothly by O_2 to give **8**. In the chelating hydroperoxo complex **10** (Scheme 3), the regioselective transfer of O-atom to the alkene is attained *via* a pseudocyclic hydroperoxopalladation (**10** → **11**).[5] Monitoring the O_2 uptake and the amounts of products (**1** + **2**) indicated that 0.5 mole of O_2 is consumed for the production of 1 mole of the products, and thus both O atoms of molecular oxygen are incorporated into the substrate. Accordingly, the Pd–OH species **9** arising from **11** undergoes further O atom transfer *via* hydroxypalladation.[6] When water is present in the reaction system, coordination of H_2O to Pd^{II} competitively takes place to interfere with the chelation of the amido-carbonyl group. Water then attacks the alkenes in the usual manner to give methyl ketones.

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