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 [PdCl₂(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 PdCl₂(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 oxidation² or by the use of [Pd(MeCN)₂Cl(NO₂)] as catalyst in BuⁱOH,³ there is no precedent for such a complete reversal of the regioselectivity in the PdCl₂-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).

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 CuCl₂ 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 (CH₂Cl₂, 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).



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

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	Entry	Substrate	R ¹	R ²	O_2^a			H_2O^b			
					Yield (%) ^c	Aldehyde : 2	Ketone ^d 3	Yield (%) ^c	Aldehyde : 2	Ketone ^d 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 O₂ (anhydrous ClCH₂CH₂Cl, 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

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probably formed by chloropalladation by PdCl₂ 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 $(10 \rightarrow 11)$.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 H₂O to Pd¹¹ competitively takes place to interfere with the chelation of the amidocarbonyl group. Water then attacks the alkenes in the usual manner to give methyl ketones.

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