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A Catalytic System for Allylic Acetoxylation Consisting of Palladium(II) and Nitrate and Using Oxygen as Final Oxidant.

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Abstract: Cyclohexene is oxidized to cyclohexenyl acetate in 92% yield by 5 mol% palladium acetate and 5 mol% iron(III) nitrate in acetic acid under an atmosphere of oxygen. Addition of chloride or acetate are negative for the yield while addition of acetic anhydride will give a more reproducible reaction. A mechanism for the reoxidation, including a palladium nitro-nitrosyl redox couple is suggested.

Palladium catalyzed oxidation reactions are extensively used in synthetic organic chemistry. In many of these reactions the necessary reoxidant for palladium is another metal compound such as copper(II) chloride or manganese dioxide. Since large amounts of metal salts are produced in these reactions it is desirable to couple the palladium promoted reactions to systems that utilize molecular oxygen as oxidant.[1] During the last decades, a number of different solutions to this problem have been presented and several processes have been developed which are based on molecular oxygen as final reoxidant. Examples are the Wacker reaction,[2] the diacetoxylation of 1,3-dienes,[3] and the acetoxylation of alkenes.[4] With the exception of the Wacker process, these systems are not yet suited for industrial applications due to complicated design and/or limited stability.

It has earlier been shown that palladium(II) salts together with a nitrate can oxidize alkenes to glycol monoesters[5] and, in some cases, allyl acetates.[6] It has also been shown that certain palladium(II) nitro complexes react with alkenes to give glycol monoacetates,[7] epoxides[8-10] and ketones.[11] We therefore decided to study if reaction conditions could be developed which use only a catalytic amount of nitrate, in combination with molecular oxygen, as reoxidant for palladium in allylic acetoxylations.

Allylic acetoxylation of cyclohexene was selected as the model reaction for the present investigation. The reactions were performed at 50°C in acetic acid with ca 2 mol% palladium acetate as catalyst and between 5 and 15 mol% of nitrate added in the form of iron(III), copper(II) or lithium salt.[12] Under argon atmosphere, all the nitrates gave a few catalytic turnovers, resulting in about 10% yield of cyclohexenyl acetate. Under an oxygen atmosphere, the yield of cyclohexenyl acetate decreased and became essentially stoichiometric in palladium (ca 3%) when lithium nitrate was added. Use of iron(III) nitrate instead led to a 55% yield of cyclohexenyl acetate, but the reaction started only after a considerable lag period (several hours). When acetic anhydride (10% by volume of acetic acid) was added to the acetic acid solution of palladium acetate, followed by iron(III) or lithium nitrate a considerably shorter lag period was observed (10-30 minutes). Rapid acetoxylation occurred, giving about 80% yield of cyclohexenyl acetate when iron nitrate was used and ca 70% yield with lithium nitrate. The lag period can be completely eliminated if the reaction mixture is heated at 50 °C for 30 minutes before any cyclohexene is added. Interestingly, this lag period can also be eliminated by the addition of water (5% by volume) instead of the acetic anhydride. The yield is in this case lower, 61%, and substantial amounts of cyclohexenol are formed, presumably via hydrolysis of cyclohexenyl acetate. The product from a Wacker type of oxidation, ie cyclohexanone, could not be detected in any of the reactions in this investigation. Addition of lithium chloride (20 mol%) or lithium acetate (100 mol%) gave a decrease in yield. If nitric acid was added in place of nitrates, ca 70% yield of cyclohexenyl acetate was obtained.

An optimization of the reaction was done at 40 °C, using the lithium salt as nitrate source and a reaction time of 15 h. The optimum stoichiometry of lithium nitrate was ca 30 mol% and the acetic anhydride concentration 5-20% by volume. Under those conditions 75-77% cyclohexenyl acetate was obtained (Figure 1). A similar optimization with iron(III) nitrate gave also an optimum in the same region but with a yield of ca 83%.

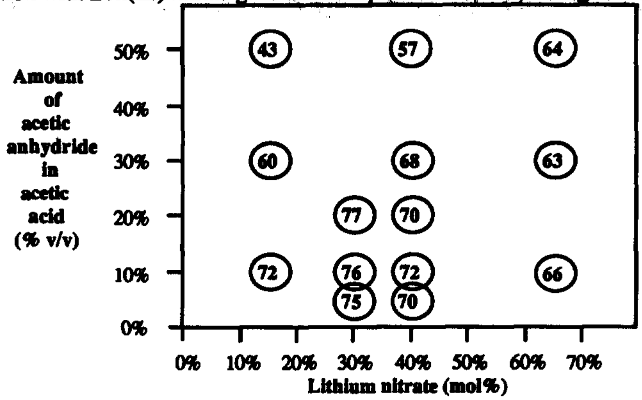


Figure 1. Encircled figures shows yield (GLC) of cyclohexenyl acetate for that specific reaction mixture. Reactions run for 15 hours at 40°C with 2 mol% palladium acetate.

When a larger amount of palladium acetate was used, 5 mol%, together with 5 mol% iron(III) nitrate, cyclohexenyl acetate was formed in 92% yield. Some other substrates were also tried under those conditions: Oxidation of 1-methylcyclohexene produced a mixture of 6-acetoxy-1-methylcyclohexene and 3-acetoxy-1-methylcyclohexene (57:43) in 40% isolated yield. When 3- and 4-methylcyclohexene were oxidized they produced a complex mixture of regio- and stereoisomeric acetoxymethylcyclohexenes in 55% resp. 61% yield.[13] Cholest-5-ene-3β-yl acetate gave a mixture of cholest-5-ene-3β,7α-diyl diacetate and cholest-5-ene-3β,7β-diyl diacetate (35:65) in a rather low yield (c:a 20%) and low conversion. A terminal olefin, 1-decene, was also tried but gave a very low conversion to a complex mixture of products.

Also the temperature had an effect on the yield of cyclohexenyl acetate. As the temperature was reduced from 50 °C to 25 °C, the yield increased from 73% to 88% when iron(III) nitrate was used. A similar trend was observed for lithium nitrate, except that at 25 °C the reaction became prohibitively slow (Table 1). Reactions run at 60 °C showed considerable decomposition of the product whereas at 40 °C no decomposition could be observed.

Table 1. Acetoxylation of cyclohexene with different nitrate sources and of different temperatures.

	Reaction temperature/time		
Nitrate source	50°C/5h	40°C/15h	25°C/60h
$Fe(NO_3)_3 \cdot 9\ H_2O$	73% (14%)[a]	83% (6%)	88% (2%)
$LiNO_3$	68% (18%)	72% (9%)	25% (50%)

a, Yield of cyclohexenyl acetate, amount of recovered cyclohexene in brackets.

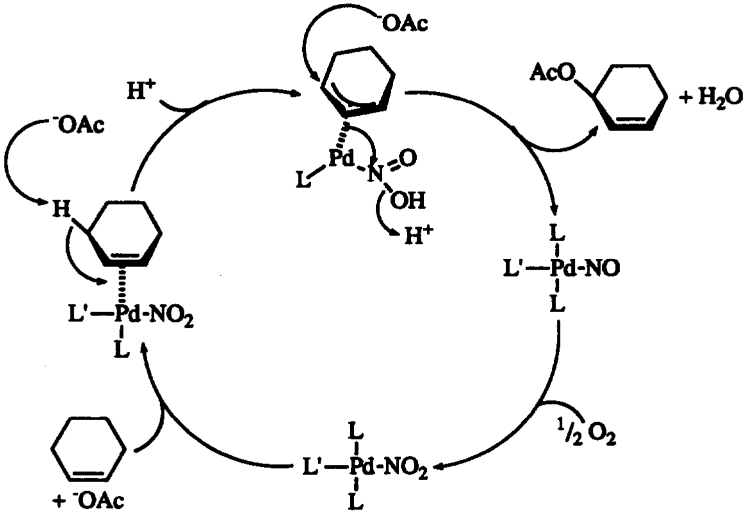
The nitrate was slowly consumed in the reaction and if only 2.5 mol% of iron(III) nitrate (7.5 mol% nitrate) was added the reaction was halted at about 50% yield of cyclohexenyl acetate. An extra addition of nitrate restarted the reaction and even dissolved precipitated palladium(0). It could also be shown that nitrate is involved in an unidentified side-reaction, which consumes cyclohexene, and that the yield of cyclohexenyl acetate is independent of whether all nitrate is added from start or if it is added in portions.

When palladium acetate was excluded a mixture of different products was formed, but no cyclohexenyl acetate. This mixture has not been fully characterized but shows a similar ^{1}H-NMR spectrum as the crude product mixture from the reaction of acetyl nitrate with cyclohexene.[14] This would indicate that acetyl nitrate is formed also under acetoxylation conditions. However, an investigation of the by-products formed in the acetoxylation reaction with lithium nitrate showed that the major part of these products are <u>not</u> identical to products formed from the reaction of acetyl nitrate with cyclohexene. Only traces of 3-nitrocyclohexene and no 4-nitrocyclohexene was formed while these are the major products in the reaction without palladium. A control experiment demonstrated that nitrocyclohexenes are stable under the conditions used. This might indicate that acetyl nitrate is formed but to a very large extent intercepted by palladium before it can react with cyclohexene.

Because it seemed possible that some type of nitropalladium complex could be the active catalyst, bis(acetonitrile)chloronitropalladium(II) (5 mol%) was reacted with cyclohexene under an oxygen atmosphere, to give a good yield (68%) of cyclohexenyl acetate. The reaction produces some cyclohexenyl chloride and cyclohexenol as by-products. The chloride is rapidly formed, faster than the acetate, but will decrease during the reaction while the alcohol is fairly stable under the reaction conditions. When the reaction is run under argon only 3% cyclohexenyl acetate is formed and almost no cyclohexenol. No cyclohexene epoxide or 1,2-cyclohexanediol monoacetate was detected.

If cyclohexene was added to a mixture of cyclohexyl nitrite (5 mol%) and palladium acetate (2 mol%) under oxygen, the nitrite disappeared rapidly while the reaction mixture turns dark red and cyclohexenyl acetate (38%) and cyclohexanol were formed. When no oxygen is present, the mixture also turned dark red and after a while a heavy red-brown precipitate is formed. This precipitate does not contain any organic residues besides acetate (three different peaks at 2.59; 1.87; 1.74 ppm in $CDCl_3$). Infra-red analysis showed the presence of an broad absorption at 1605 cm^{-1} which was interpreted as acetate and a bridged nitrosyl in accordance with literature.[15] Thus, the product is probably oligomeric $(Pd(NO)_yOAc)_x$ in analogy with reactions of manganese(0) which reacts with organic nitrites in the presence of acid to form manganese nitrosyls.[16]

Scheme 1



Is seems possible that a palladium nitrosyl complex is a common product formed in these oxidation systems, since in all reactions, regardless of the starting oxidant, the same red colour appears. In reactions with nitrates the colour is weaker than in reactions with either nitro-complexes or organic nitrites. Nitrosyl complexes are known to be oxidized to nitro complexes by oxygen[17] but the complex isolated from the reaction with cyclohexyl nitrite under anaerobic conditions reacts rather slowly with oxygen. Therefore, the successful reaction under aerobic conditions might simply mean that the nitrosyl complexes are oxidized to nitro complexes before a less reactive bridge nitrosyl complex is formed.

Based on these results a reoxidation sequence is presented in scheme 1. This sequence resembles the mechanism suggested for the formation of glycol monoacetates from terminal olefins and palladium nitro complexes in acetic acid.[18] Since the same active catalyst is postulated but different products are obtained it is likely that the reactions go via different intermediates. Thus, since the reaction with terminal olefins go via an acetoxy-palladate we suggest that the formation of allylic acetate go via a π-allylic palladium intermediate.

Acknowledgement

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