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## Carbonylation of alcohols in the Pd(OAc)<sub>2</sub>/TsOH/molten salt system

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A non-phosphine catalytic system, Pd(OAc)<sub>2</sub>/TsOH/NBu<sub>4</sub>Br, is suggested for the synthesis of acids by the carbonylation of alcohols.

The carbonylation of olefins and alcohols affords acids whose carbon skeletons are one carbon atom longer than that of the substrates. Phosphine–palladium complexes with acidic promoters are the most popular catalysts of this reaction.<sup>1</sup> Progress in carbonylation in the past decade is attributed to the use of two-phase systems where water<sup>2,3</sup> or ionic liquids, including pyridinium, imidazolinium and tetraalkylammonium salts,<sup>4,5</sup> serve as the polar phase. The latter salts are preferable because they do not require special water-soluble ligands for retaining palladium in solution and allow one to use ordinary phosphine complexes. What is more,  $NR_4^+X^-$  salts can stabilise nanoparticles of a transition metal in the colloidal state.<sup>6</sup> Phosphine-free catalytic systems of this kind were recently suggested for Heck and Suzuki coupling<sup>7–10</sup> and olefin carbonylation.<sup>11,12</sup>

We have shown for the first time that carboxylic acids can be obtained by carbonylation of alcohols in the presence of the phosphine-free catalytic system  $Pd(OAc)_2/TsOH$  in molten NBu<sub>4</sub>Br. The reaction was performed in a steel autoclave equipped with a magnetic stirrer and an automatic valve to maintain a constant CO pressure; the autoclave was heated with an electric furnace. The reactor was loaded with alcohol (4 mmol),  $Pd(OAc)_2$  (0.02 mmol), an acidic promoter (0.8 mmol) and  $NBu_4Br$  (2 g). The reactor was then purged with CO and heated to 110 °C; after that, CO was introduced to the required pressure and the stirrer was turned on. The substrate conversion and the product yields were determined chromatographically (Avtokhrom UE5 FID, a quartz capillary column 30 m×0.25 mm, the SE-30 stationary phase, and helium as a carrier gas), using authentic specimens to identify the peaks.

Primary and secondary alcohols, aliphatic and 1-phenyl-substituted alcohols undergo this reaction. The reactions with methanol, 1-phenylethanol and benzyl alcohol occur smoothly to give carboxylic acids in moderate to high yields. The carbonylation of *n*-butanol gives butyl valerate in 66% yield. The conversion of cyclohexanol was as small as 13% over 2 h; in this case, almost equal amounts of cyclohexanecarboxylic acid and its ester were formed. Water added to the starting mixture did not increase the yields of the carboxylic acids (Table 1).



Figure 1 Effect of pressure on the indicators of 1-phenylethanol carbonylation in the  $Pd(OAc)_2/TsOH/NBu_4Br$ . T = 110 °C, 2 h.

The carbonylation of 1-phenylethanol was studied in detail, since one of the products (hydratropic acid 1) is a structural fragment of ibuprofen and its analogues.<sup>13–15</sup> The reaction gives hydrocinnamic acid 2 as a by-product. Furthermore, styrene and traces of ethylbenzene were found in the reaction mass.

To ascertain Koch chemistry is not involved we carried out a blank run without a Pd catalyst. No carbonylation occurred. Styrene was the sole product formed in 45% yield, based on GLC data.

The reaction requires an acidic promoter. Experiments showed that HCl, HBr and TsOH were equally efficient. In the presence of these compounds, complete conversion of phenylethanol was reached for 2 h with 85–90% selectivity for the acids. The yield of compounds 1 + 2 in the presence of trichloroacetic acid was 8%, and the reaction did almost not occur in the presence of formic acid. Thus, a high acidity of the medium is a prerequisite for the reaction to be successful, whereas the nature of the anion is not important. This is reasonable because the system contains an excess of bromide ions.

We tested some other molten salts as reaction media. Only trace amounts of carboxylic acids were obtained in NBu<sub>4</sub>Cl, [BMIM][Cl], [BMIM][BF<sub>4</sub>] and [BMIM][PF<sub>6</sub>] with Pd(OAc)<sub>2</sub> as a catalyst precursor. Remarkably, 1-phenylethanol conversion of 14% or less was reached in Cl<sup>-</sup>-containing molten salts, while the substrate was completely converted in molten salts with complex anions. Styrene was the major product in all of the runs.

The high yields of the acids can be obtained at a CO pressure of 2 MPa or above. A decrease in the pressure affects the conversion of the alcohol only slightly, but the selectivity of carbonylation decreases abruptly. On the contrary, the yield of styrene increases, and styrene becomes the main reaction product at CO pressures lower than 0.7 MPa (Figure 1). Likewise, the regioselectivity depends considerably on the CO pressure. A pressure decrease increases the selectivity with respect to branched acid **1**. The **1:2** ratio is 0.25 at a pressure of 0.5 MPa and increases almost linearly with an increase in pressure to reach 1.05 at 5 MPa. Similar dependences were obtained in a study on the 1-(4-isobutylphenyl)ethanol carbonylation in the presence of a traditional Pd-phosphine catalyst.<sup>15</sup>

The time dependence of the reaction mixture composition has a shape typical of consecutive reactions. The styrene content

**Table 1** Carbonylation of alcohols in the 0.5%  $Pd(OAc)_2/20\%$  TsOH/ NBu<sub>4</sub>Br catalytic system. T = 110 °C, P = 5 MPa, 2 h.

Alcohol	Conversion (%)	Product	Yield (%) (GLC)
MeOH	73	MeCOOH	65
EtOH	32	EtCOOH	19
		EtCOOEt	9
Bu <sup>n</sup> OH	73	Bu <sup>n</sup> COOBu <sup>n</sup>	66
PhCH <sub>2</sub> OH	98	PhCH <sub>2</sub> COOH	87
PhCH(OH)Me	100	PhCH(Me)COOH 1	43.5
		PhCH <sub>2</sub> CH <sub>2</sub> COOH 2	44
cyclo-C <sub>6</sub> H <sub>11</sub> OH	13	cyclo-C <sub>6</sub> H <sub>11</sub> COOH	6
~ **		$c - C_6 H_{11} C(O) OC_6 H_{11} - c$	5



Figure 2 Carbonylation of 1-phenylethanol in the system 0.5% Pd(OAc)<sub>2</sub>/ 20% TsOH/NBu<sub>4</sub>Br/heptane. T = 110 °C, P = 5 MPa.

passes through a maximum. In this series of experiments, hexane was added to the reaction mixture to prevent the possible polymerisation of styrene and to determine its amount more accurately. As a result, the reaction rate was somewhat lower (Figure 2).

Based on the relationships obtained, it can be assumed that styrene, which results from the dehydration of 1-phenylethanol, is the true substrate of the carbonylation. Insertion of the olefin into the Pd–H bond gives a branched (3) or linear (4) alkylpalladium complex. Subsequent insertion of CO gives the corresponding acyl complexes. Hydrolysis of the latter gives acids 1 and 2. The selectivity of the olefin insertion stage is presumably determined by the CO pressure. As the carbon monoxide pressure is increased and hence its concentration in the solution increases, CO molecules compete more successfully for sites in the ligand sphere of Pd. As a result, the catalytic complex becomes more compact, which favours the formation of compound 3, and hence 1, in agreement with experimental and published data.<sup>15</sup>

If, for some reasons, carbonylation is hindered (for example, the CO pressure is insufficient), styrene becomes the main product. Furthermore, the reaction mixture contained traces of ethylbenzene, which was obviously formed by the hydrogenation of styrene (Figure 3).

Further evidence for the proposed consecutive scheme is the fact that styrene can be converted into corresponding acids under the reaction conditions giving the same regioselectivity.<sup>11,12</sup>

In the absence of phosphine ligands, palladium is retained in the system as suspended nanoparticles stabilised by  $NBu_4Br^{8,10}$ Presumably, nanoparticles do not show catalytic activity but





Figure 4 Repeated use of the 0.5% Pd(OAc)<sub>2</sub>/20% HCl/NBu<sub>4</sub>Br catalytic system. T = 110 °C, P = 5 MPa.

play the role of a reservoir of atomic Pd. This conclusion is based on the distinct dependence of the carbonylation regioselectivity on the CO pressure, which is the same as that for a certainly homogeneous catalyst.<sup>15</sup>

The catalytic system proposed can be used repeatedly. After the reaction, the reaction mass was extracted with diethyl ether. A mixture of acids 1 and 2 was isolated from the resulting extract, while the catalyst remained in the ionic liquid, and it was reused with a fresh portion of phenylethanol and HCl. Note that reloading was carried out in air. The catalyst maintained the original activity for seven cycles, after which the phenylethanol conversion and the yield of the acids started to decrease (Figure 4). Simultaneously, the colour of the reaction mass changed from light yellow to green and then to black, which is evidence for palladium-black precipitation. We hope that further studies will make it possible to prolong the life of the catalytic system, as well as reveal possible degradation of the molten salt under the reaction conditions.

## References

- 1 A. L. Lapidus and S. D. Pirozhkov, Usp. Khim., 1989, 58, 197 (Russ. Chem. Rev., 1989, 58, 117).
- 2 F. Bertiux, E. Monflier, Y. Castanet and A. Morteux, *J. Mol. Catal. A: Chem.*, 1999, **143**, 11.
- 3 B. Cornils and E. Wiebus, *CHEMTECH*, 1995, **25**, 33.
- 4 H. Olivier-Bourbigou and L. Magna, J. Mol. Catal. A: Chem., 2002, 182–183, 419.
- 5 C. M. Gordon, Appl. Catal. A: General, 2001, 222, 101.
- 6 M. T. Reetz, W. Helbig, S. A. Quaiser, U. Stimming, N. Breuer and R. Vogel, *Science*, 1995, **267**, 367.
- 7 T. Jeffery, Tetrahedron, 1996, 52, 10113.
- 8 M. T. Reetz, R. Breinbauer and K. Wanninger, *Tetrahedron Lett.*, 1996, 37, 4499.
- 9 T. Jeffery and M. David, Tetrahedron Lett., 1998, 39, 5751.
- 10 M. T. Reetz and E. Westermann, Angew. Chem., Int. Ed. Engl., 2000,
- 39, 165.
  11 A. L. Lapidus, O. L. Eliseev, N. N. Stepin and T. N. Bondarenko, *Izv. Akad. Nauk, Ser. Khim.*, 2004, 2458 (*Russ. Chem. Bull., Int. Ed.*, 2004, 53, 2564).
- 12 O. L. Eliseev, N. N. Stepin, T. N. Bondarenko and A. L. Lapidus, Dokl. Akad. Nauk, 2005, 401, 486 [Dokl. Chem. (Engl. Transl.), 2005, 401, 59].
- 13 J.-P. Rieu, A. Boucherle, H. Cousse and G. Mouzin, *Tetrahedron*, 1986, 42, 4095.
- 14 T. C. Wu and B. Rouge, US Patent 5254720, 1993.
- 15 E. J. Jang, K. H. Lee, J. S. Lee and Y. G. Kim, J. Mol. Catal. A: Chem., 1999, 138, 25.

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