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Hydrocarboxylation of styrene in aqueous media with Pd-guanidinumphosphine systems

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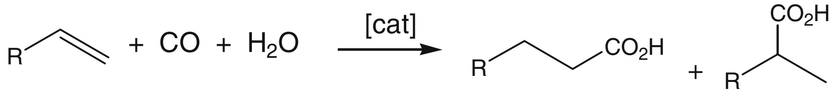
Hydrosoluble palladium complexes with guanidinumphosphine ligands are active catalyst precursors for the hydrocarboxylation of styrene forming the corresponding carboxylic acids using water as a solvent. The aryl guanidinum derivative is much more stable than the alkyl derivative studied and provided high selectivity in the acids with conversions up to 96%.

KEY WORDS: hydrocarboxylation; hydroxycarbonylation; aqueous biphasic systems.

1. Introduction

Catalytic hydrocarboxylation or hydroxycarbonylation is an attractive procedure for obtaining carboxylic acid from alkenes [1–3] (Eq. 1). The hydrocarboxylation of vinyl aromatics is important in the synthesis of 2-aryl propionic acid derivatives, a class of non-steroidal anti-inflammatory drugs [4]. (Scheme 1)

(1) 

Palladium catalysts with phosphorus ligands in the presence of variable amounts of Brønsted acids of different strength, as well as other co-catalysts, are the systems most often used for this process [5–12]. Usually, dimethoxyethane, toluene, tetrahydrofurane or dioxane are used as solvents. A more environmentally desirable solvent such as water [13,14] has been employed for this process introducing sulfonated aryl groups in the phosphine ligands [15]. In this reaction, as well as for environmental reasons, it is especially beneficial to use water as a solvent because it is also one of the reactants. The hydrosoluble catalyst precursor systems reported so far use recoverable palladium complexes with the sodium salt of trisulfonated triphenylphosphine (TPPTS) [16,17,18–20], the corresponding acid form TPPTSH [21], Pd-modified precursors with *β*-cyclodextrin in two-phase systems [22] or sulfonated diphosphines [23,24].

Within this catalogue, sulfonated phosphines are by far the most widely studied systems and, so far, the only ones with an industrial application in biphasic processes. However, the results obtained in hydrocarboxylations fall well short of any practical interest and leave plenty of possibilities for improvement. For this reason, new ligands are highly welcome candidates for exploration. Some of us reported a convenient synthesis of guanidinio phosphines **1** and **2**, which are readily soluble in water [25–28] and present higher stability than TPPTS, especially with regard to oxidation. In fact, these ligands were successfully used in the palladium-catalyzed Castro-Stephens coupling between iodobenzoate and *N*-(trifluoroacetyl)propargylamine in aqueous solution [25] and in the decoration of peptides and proteins with non-proteinogenic moieties under native aqueous conditions [26]. In this paper we report the application of these ligands in the palladium-catalyzed hydrocarboxylation of styrene in water.(figure 1)

2. Experimental

Standard catalysis experiment. A mixture of 0.04 mmol of $Pd(OAc)_2$ with the corresponding amount of ligand **1** or **2** in 10 ml of water was stirred for 1 h until total dissolution. The pH was then adjusted using H_2SO_4 (0.25 M) or NaOH (0.25 M). The substrate (4 mmol) was added and the mixture was placed in an evacuated autoclave and pressurised with CO up to the desired pressure. Final solutions were extracted with 3×5 ml of diethylether and analysed by GC with a Hewlet-Packard 5890A Chromatograf in an Ultra-2 (5% diphenylsilicone/95% dimethylsilicone) column (25 m × 0.2 mm Ø).

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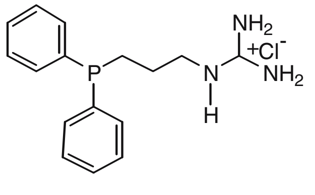

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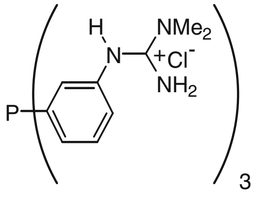

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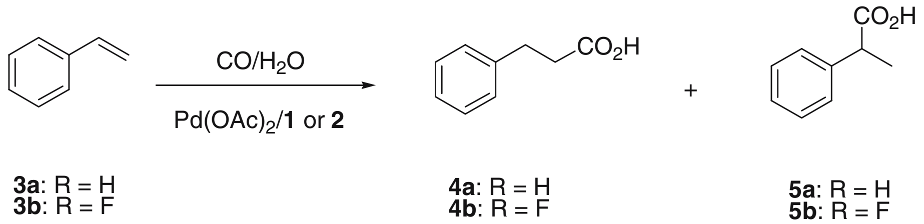
3. Results and discussion

The hydrocarboxylation of styrene **3a** yielded the corresponding linear **4a** and branched **5a** carboxylic acids (Scheme 2). Catalyst precursors were prepared *in situ* by adding the corresponding ligand (**1** or **2**) to a suspension of $Pd(OAc)_2$ in water and stirring at room temperature until total dissolution. Since it was reported that adding a Brønsted acid increases the activity of the catalytic systems [16], the pH of the solution was adjusted to 3.5 by adding diluted sulfuric acid (0.25 M). The results are shown in table 1. (Scheme 2).



The catalytic system $Pd(OAc)_2$/**1** (P/Pd = 4) at 20 atm of CO and 110 °C (entry 2, Table 1) provided an almost quantitative conversion after 6 h, but the selectivity in the desired product acids was only 54%. The major carboxylation product was the linear 3-phenylpropanoic acid. This is opposite to what is reported for Pd/TPPTS systems, for which the branched isomer is the main product formed [16,17, 21]. In the end, palladium black was formed in the final solution, which indicates that the catalytic system was decomposing. Black palladium also appeared when the reaction was run only for 2 h (entry 1, Table 1). To overcome this problem and improve the results, we studied several conditions. When the temperature was decreased to 80 °C (entry 3, Table 1) or the pressure was increased to 75 atm (entry 4, Table 1), the conversion and selectivity in the acids decreased but the regioselectivity in the linear acid increased. The final solution also showed some decomposition. Similar behaviour was observed when the P/Pd ratio increased to 6 (entry 5, Table 1).

In TPPTS Pd-systems [16], the presence of Cl^- anion in the media increased the stability of the catalytic system. In contrast, when we replaced the sulphuric acid with HCl to adjust the initial pH, the results did not improve (entries 6, Table 1). Likewise, adding NaCl up to a Cl/Pd ratio of 16 did not enhance the stability of the catalyst (entry 9, Table 1). Moreover, changing the pH to 2 or 7 showed no positive effects with this Pd/**1** system (entries 7–9, Table 1).

Much better selectivities were obtained with the tris-(guanidinioaryl) ligand **2**. In fact, the selectivity for carboxylic acid products was practically total in all cases studied (entries 10–12, table 1). Although the conversion obtained after 6 h (entry 10, Table 1) at the same conditions was lower than with system Pd/**1**, the final solution did not show any signs of decomposition. The major product was also the linear acid **4a** (up to 67%). However, when we decreased the temperature to 80 °C, we observed an inversion of the regioselectivity in favour of the branched product (entry 11, Table 1). A similar dependence of selectivity on temperature was reported for Pd/TPPTS [21] but with the TPPTS system the branched product was always the major one in the 90–130 °C range. The regioselectivity obtained with the guanidinum system was more sensitive to temperature changes. Our results for the hydrocarboxylation of 4-fluorostyrene **3b** (entry 12, Table 1) were similar.

4. Conclusion

In summary, palladium systems with guanidinum phosphine ligands form water-soluble active catalyst precursors for the hydrocarboxylation of styrene. Guanidinio-aryl derivatives are much more stable and provided high chemo-selectivities in carboxylic acids. The main product was the linear carboxylic acid, but regioselectivity could be reversed by decreasing the temperature.

Acknowledgements

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Table 1
Hydrocarboxylation of styrene catalysed by Pd(II)/**1** or **2**[a]

Run	L	pH[b]	P/Pd	*t*(h)	P (atm)	*T* (°C)	C_{tot}(%)	Selec[c](%)	**4/5** [d]
1[e]	**1**	4	4	2	20	110	33	47	62/38
2[e]	**1**	4	4	6	20	110	97	54	63/37
3[e]	**1**	4	4	2	20	80	5	41	79/21
4[e]	**1**	4	4	6	75	110	60	27	72/28
5[e]	**1**	4	6	6	20	110	60	22	65/35
6[e,f]	**1**	4	4	6	20	110	84	25	72/28
7[e]	**1**	7	4	6	20	110	12	49	61/39
8[e, f]	**1**	2	4	6	20	110	47	56	70/30
9[e, f, g]	**1**	2	4	6	20	110	28	21	78/22
10	**2**	4	4	6	20	110	58	100	67/33
11	**2**	4	4	6	20	80	16	100	39/61
12[h]	**2**	4	4	6	20	110	85	100	60/40

[a] Reaction Conditions: $Pd(OAc)_2 = 0.04$ mmol, Substrate/Pd = 100; H_2O = 10 ml;
[b] initial pH (adjusted with $H_2SO_4$0.25 M);
[c] Selectivity in acids;
[d] n = 3-phenyl propanoic acid, i = 2-phenylpropanoic acid;
[e] formation of black Pd at the end of the reaction;
[f] initial pH (adjusted with concentrated HCl);
[g] addition 16 eq of Cl^-(NaCl)/ mol of Pd.
[h] substrate: 4-fluorostyrene

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