# 30. On the Regioselectivity Control in the Palladium-Catalyzed Hydro-alkoxycarbonylation of α,β-Unsaturated Esters

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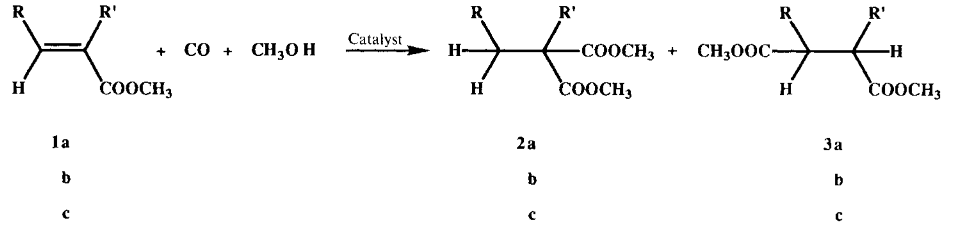
The regioselectivity of the hydro-alkoxycarbonylation of methyl acrylate, methacrylate, and crotonate catalyzed by $[PdCl_2L_2]$ complexes (L = phosphine ligands) can be largely controlled by variation of the ligands. $PPh_3$ promotes preferential carbonylation at the α-position, whereas with [(2,2-dimethyl-1,3-dioxolane-4,5-diyl)bis(methylene)]bis[diphenylphosphine] as ligand, the β-position is overwhelmingly carbonylated.

**Introduction.** – A complete control of the regioselectivity in carbonylation reactions of olefinic substrates is still an open problem which limits the applicability of this reaction to the preparative organic chemistry [1] [2]. We [3] [4] and others [5] [6] found that in the hydro-alkoxycarbonylation (*i.e.*, in the synthesis of esters from olefins, CO, and alcohols) using palladium catalysts of the type $[PdCl_2L_2]$ [7] (where L are phosphorus ligands), the regioselectivity can be controlled to a large extent at least in the case of aromatic olefins (such as styrene and 2-phenylpropene). In fact, monophosphine ligands cause almost exclusive formation of the branched (or more branched) isomer, whereas with the chelating diphosphine ligands, the alternative regioisomer largely prevails. Similarly, a good control of the regioselectivity was reached on hydro-carboxylation and hydro-alkoxycarbonylation of 3,3,3-trifluoropropene and pentafluorostyrene with the same or similar catalytic palladium systems [8]. Very recently it was reported that hydro-alkoxycarbonylation of acrylates by iron pentacarbonyl gives methyl malonates with fair to high regioselectivities [9]. This is claimed to be the only report on the catalytic carbonylation of acrylates exhibiting such regioselectivity. Therefore, we refer herein on the results obtained on such substrates obtained in connection with our interest in enantioselective carbonylation [10] [11]. In fact, even though the hydroformylation of these substrate has been extensively investigated [12], much less is known about their hydro-alkoxycarbonylation [10].

**Results and Discussion.** – The results obtained on hydro-methoxycarbonylation of acrylate **1a**, crotonate **1b**, and methacrylate **1c** (*Scheme*) are reported in the *Table*. The use of $[PdCl_2(PPh_3)_2]$ [7] as catalyst precursor brings about overwhelming (> 80%) carbonylation at the α-position leading to the formation of the branched (or more branched) diester **2**; in the case of **1a**, the reaction is practically regiospecific. By contrast, when $[PdCl_2\{(R,R)\text{-diop}\}]$ [13] (diop = [(2,2-dimethyl-1,3-dioxolane-4,5-diyl)bis(methylene)]bis[diphenylphosphine]) is used as catalyst precursor, carbonylation takes place prevailingly at the β-position with formation of diester isomer **3**. For **1c**, the reaction gives essentially exclusively dimethyl 2-methylbutanedioate (**3c**). As for the

*Scheme*



a R = R' = H  b R = $CH_3$, R' = H  c R = H, R' = $CH_3$

Table. *Hydro-methoxycarbonylation of the Methyl Esters of Some α,β-Unsaturated Acids*[a])

| Substrate | Catalyst precursor | Reaction time [h] | Conversion [%] | Selectivity **2**/**3**[b]) |
|---|---|---|---|---|
| $CH_2$=CH–$COOCH_3$ (**1a**) | [$PdCl_2(PPh_3)_2$] | 18 | 95 | > 97:3 |
| | [$PdCl_2${(*R*,*R*)-diop}] | 19 | 87 | 40:60 |
| $CH_3$–CH=CH$COOCH_3$ (**1b**) | [$PdCl_2(PPh_3)_2$] | 18 | 44 | 83:17[c]) |
| | [$PdCl_2${(*R*,*R*)-diop}] | 19 | 39 | 30:60[d]) |
| $CH_2$=C($CH_3$)–$COOCH_3$ (**1c**) | [$PdCl_2(PPh_3)_2$] | 18 | 50 | 80:20 |
| | [$PdCl_2${(*R*,*R*)-diop}] | 19 | 49 | < 2:98 |

[a]) Reaction conditions: 30 mmol of substrate and 60 mmol of $CH_3OH$ in 15 ml of benzene solution, catalyst, *ca.* 0.3 mmol, 120°/200 atm.

[b]) Molar ratio of α-carbonylated *vs.* β-carbonylated product.

[c]) Traces of dimethyl adipate were formed.

[d]) *Ca.* 10% of dimethyl adipate was contemporaneously formed.

previously reported case of aromatic olefins [3], the monodentate $PPh_3$ ligand promotes prevailing formation of the branched (or more branched) product, whereas the bidentate ligand favours the linear (or less branched isomer). It appears possible that the regioselectivity shown in the *Table* could be still better controlled by a judicious variation of the other reaction parameters, as it was shown in the case of 2-phenylpropene [3] [4] [7].

It has been more recently reported that phosphinepalladium complexes with non-hydrogen halide acids (such as trifluoromethanesulfonic or heptadecafluorooctanesulfonic acid) give catalytic systems with increased activity for the hydro-methoxycarbonylation of some aliphatic olefins [14]. Similar systems containing anions of other strong (mostly organic) acids ($pK_a > 2$) have been used for aliphatic olefins and for ethyl crotonate [15]. We have performed preliminary hydro-methoxycarbonylation experiments with methyl acrylate using [$Pd(CH_3COO)_2$]/$CF_3SO_3H$ (molar ratio 1:10) modified with either $PPh_3$ or diop as catalyst precursor in tetrahydrofuran as solvent. In this case, however, the effect of ligand change on the regioselectivity is small (if any); furthermore, the yield of addition products is rather low, due to the parallel formation of oligomeric materials, the structure of which is under investigation.

## Experimental Part

*Materials*. [$PdCl_2(PPh_3)_2$] [7] and [$PdCl_2${(*R*,*R*)-diop}] [13] were prepared as previously reported. Methyl acrylate, methacrylate, crotonate, and the alcohols used as H-donor (*Fluka*) were used without further purification.

*Procedure.* A soln. containing the substrate, the solvent (when used), and the H-donor (for rel. quantities, see *Table*) was placed under $N_2$ in a stainless-steel autoclave together with the catalyst precursor. The reactor was pressurized with CO and heated to the desired temp. After the reported reaction time, the autoclave was cooled to r.t., and the residual gas was released. The mixture was analyzed by GLC. The products were identified after distillation by NMR and mass spectroscopy.

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