DOI: 10.1002/adsc.200700423

Selectivity of Rhodium-Catalyzed Hydroformylation of 1-Octene during Batch and Semi-Batch Reaction using Trifluoromethyl-Substituted Ligands

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Received: August 28, 2007; Published online: December 20, 2007

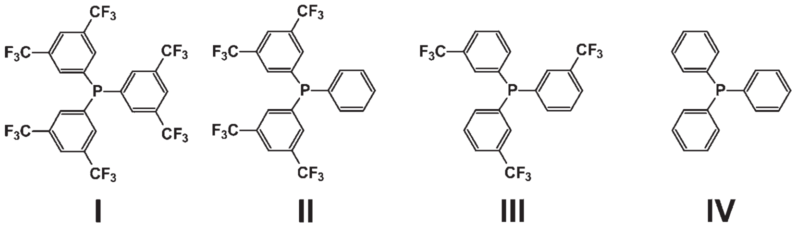
Abstract: The regioselectivity of catalysts generated *in situ* from dicarbonyl rhodium(I)(2,4-pentanedione) and trifluoromethyl-substituted triphenylphosphine ligands has been evaluated during the hydroformylation of 1-octene. The influence of batch or semi-batch operation, the solvent, and the number of trifluoromethyl substituents has been investigated. During batch operation in a supercritical carbon dioxide (CO_2)-rich system the differential *n*:*iso* ratio increases from approximately 4 to a value of 12–16 at about 90–95% conversion for the catalyst based on bis[3,5-bis(trifluoromethyl)phenyl]phenylphosphine. For semi-batch conditions using hexane a constant *n*:*iso* ratio is obtained over a broad conversion range. Batch hydroformylation in neat 1-octene is faster than in a supercritical CO_2-rich, one-phase system, with a similar overall selectivity as observed in the supercritical case. The results provide further directions for the development of ligands that are especially designed for the separation of homogeneous catalysts in continuously operated hydroformylation in $scCO_2$.

Keywords: fluorinated ligands; homogeneous catalysis; hydroformylation; organic solvents; supercritical carbon dioxide

Introduction

The hydroformylation of alkenes is an important example of homogeneous catalysis on an industrial scale.[1] Organometallic complexes of rhodium have proven to be the most active and selective catalysts in hydroformylation. In the hydroformylation of propene a water-soluble rhodium catalyst is used, facilitating an easy separation from the organic product phase.[1,2] However, water-soluble catalysts have limited application in the hydroformylation of long-chain alkenes as the low solubility of long-chain alkenes in water will result in relatively low reaction rates.[2] Research dealing with hydroformylation of long-chain alkenes, therefore, focuses on alternative solvents in conjunction with the development of ligands and additives to make rhodium catalysts more active and selective and easier to separate from the product.[3] Perfluorinated solvents,[4] ionic liquids,[5] water in combination with a phase-transfer agent,[6] PEGs,[7] and supercritical fluids[8] are regarded as promising alternative solvents, which can facilitate catalyst separation.[9–12] Another approach to catalyst recycling is the attachment of ligands to soluble or insoluble macromolecular supports, which can be separated by filtration or decantation.[13,14] The development of, for example, diphosphines,[15] diphospites,[16] diphosphines by self-assembly,[17] and tetraphosphines[18] has led to rhodium-catalyzed hydroformylation of long-chain alkenes with a very good regioselectivity for the linear aldehyde product.

The advantages of the application of carbon dioxide as a solvent for homogeneously catalyzed reactions include the possibility to create a one-phase supercritical reaction mixture in which phase boundaries are absent, high diffusivity of the different species, and high solubility of carbon monoxide and hydrogen.[8] The solubility of common homogeneous catalysts in supercritical carbon dioxide, $scCO_2$, is limited.[19] This can be seen as an advantage in of view of the possibilities to separate the catalyst, because CO_2 has been applied as an anti-solvent in order to precipitate and recycle the catalyst.[20] However, the changes in pressure required to apply CO_2 in this manner are possibly not very energy efficient. Therefore, to employ the promising solvent characteristics of CO_2, an alter-



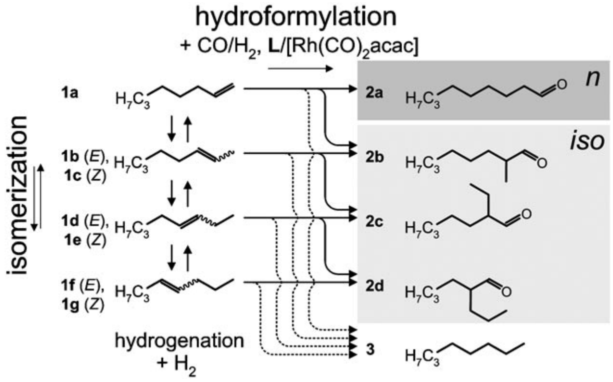
Scheme 1. Ligands used in the rhodium-catalyzed hydroformylation: tris[3,5-bis(trifluoromethyl)phenyl]phosphine (**I**), bis-[3,5-bis(trifluoromethyl)phenyl]phenylphosphine (**II**), tris(3-trifluoromethylphenyl)phosphine (**III**), triphenylphosphine (**IV**). In the text, the catalytic complexes L/[Rh(CO)$_2$acac] (acac: 2,4-pentanedione) are indicated by the ligand only.

native separation method and a catalyst, which is soluble in a CO$_2$-enriched supercritical mixture, have to be developed. Membrane separation is regarded as a promising method to separate catalysts from a supercritical reaction mixture.[21] In order to influence and improve the solubility of Wilkinson-type hydroformylation catalysts in CO$_2$-rich reaction environments, perfluorinated groups or "tails" can be attached to the triphenylphosphine ligands.[21–23] Besides the improvement of catalyst solubility in scCO$_2$ or flourous systems, phosphine ligands with perfluoroalkyl groups also significantly influence the hydroformylation catalysis.[24–28]

Here we present a detailed study about the application of trifluoromethyl-substituted triphenylphosphines in the rhodium-catalyzed hydroformylation of 1-octene. Results obtained under batch conditions in scCO$_2$ are compared with results obtained under batch and semi-batch conditions in organic solvents, which is relevant for further development of continuous hydroformylation in scCO$_2$.

Results and Discussion

Previously it was shown that, for the rhodium-catalyzed hydroformylation of 1-octene, the influence of the trifluoromethyl substituents on the phosphine on the activity and overall selectivity is about the same when scCO$_2$,[29] hexane or toluene are applied as solvent.[26] In this comparison it was observed that the (final) ratio of linear over branched aldehydes (*n*:*iso* ratio) was almost always comparable although the experimental conditions, like pressure and concentration of the syngas, were considerably different. Therefore, a closer look is taken at the cumulative (or overall or integral) selectivity and the differential (or intrinsic) selectivity in the application of *in situ* prepared catalysts generated from [Rh(CO)$_2$acac] and four different ligands. Three trifluoromethyl-substituted triphenylphosphine ligands and the triphenylphosphine ligand, shown in Scheme 1, have been used in the hydroformylation of 1-octene (**1a**) (Scheme 2). In particular, the use of **II** and **III** has been evaluated in four situations: batch and semi-batch with hexane as solvent, batch with scCO$_2$ as solvent, and solventless (neat). The experimental conditions and main results for the 12 cases studied are summarized in Table 1. A high ligand to rhodium ratio, L:Rh = 50:1, is applied, which approaches industrial conditions. An enhanced regioselectivity towards the linear product can be expected at higher ligand concentrations.[1,30] The differential selectivity indicates to what extent 1-octene is converted into the desired products at some moment in the batch reactor. For commercial hydroformylation processes predominantly CSTRs or loop reactors are being used,[31] and for these types of reactor configurations the overall selectivity is equal to the differential selectivity.



Scheme 2. Reaction scheme for the hydroformylation of 1-octene (**1a**), with the two main products nonanal (**2a**) and 2-methyloctanal (**2b**). The side products are (*E,Z*)-2-octene (**1b**, **1c**), (*E,Z*)-3-octene (**1d**, **1e**), (*E,Z*)-4-octene (**1f**, **1g**), 2-ethylheptanal (**2c**), 2-propylhexanal (**2d**), and *n*-octane (**3**). **L** is the phosphine ligand.

Concentration Profile

For **III** (Scheme 1) it has been observed that during the reaction the aldehyde selectivity decreased be-

Table 1. Summary of conditions and results.

Entry[a]	Solvent	L	$n_{\mathbf{1a}}$ [mmol]	$n_{CO}:n_{H_2}$[mmol]	P_{max}[b] [MPa]	$TOF_{\mathbf{1a}}$[c,d]	$TOF_{\mathbf{ald}}$[c,e]	X[f] [%]	$S_{\mathbf{ald}}$ [%]	$S_{\mathbf{2a}}$ [%]	$S_{\mathbf{1b-1g}}$ [%]	*n*:*iso* [-]
1	hexane[g]	**II**	49.8	49.9:49.2	4.5	3.04	2.89	97.7	95.4	78.4	4.1	4.60
2	hexane[g]	**III**	49.9	51.6:50.8	4.6	1.79	1.69	97.0	96.8	78.7	2.7	4.34
3	hexane[g]	**II**	49.7	[h]	5.0	3.10	3.01	99.0	98.4	76.6	1.0	3.52
4	hexane[g]	**III**	49.9	[h]	4.6	2.07	2.02	99.4	98.8	76.8	1.0	3.50
5	CO_2	**I**	105	108:108	50.1	9.82	8.87	99.2	90.5	69.6	6.1	3.33
6	CO_2	**II**	105	109:109	49.5	3.29	3.13	97.2	94.0	78.4	5.1	5.02
7	CO_2	**III**	105	109:109	49.6	1.33	1.28	91.7	96.6	79.3	2.9	4.59
8[k]	CO_2	**IV**	107	108:109	51.0	0.463	0.455	93.0	99.0	77.1	0.1	3.53
9	Neat	**I**	104	104:103	6.5	15.4 [l]	14.3 [l]	98.7	94.3	77.8	4.5	4.71
10	Neat	**II**	100	104:105	6.5	7.38	6.79	99.9	94.7	79.8	4.6	5.37
11	Neat	**III**	100	104:105	6.5	3.50	3.16	99.8	96.7	79.1	2.7	4.48
12	Neat	**IV**	100	104:105	6.5	1.03	1.00	95.9	98.3	75.8	1.1	3.38

[a] General applied conditions: $T=70\,°C$, $S/C=2.0\times10^3$ $mol_{\mathbf{1a}}$ mol_{Rh}^{-1}. For entries 1–4 and 9–12: $V_{reactor}=0.103$ L; for entries 5–8: $V_{reactor}=0.108$ L. Results in entries 5 and 7 have also been reported in a previous communication.[26]

[b] Maximum pressure reached upon injection of **1a**.

[c] Obtained from multiplying S/C with the slope of a linear fit through conversion ($TOF_{\mathbf{1a}}$) or yield ($TOF_{\mathbf{ald}}$) data up to a conversion of 60% (40% for **IV**).

[d] [10^3 $mol_{\mathbf{1a}}$ mol_{Rh}^{-1} h^{-1}].

[e] [10^3 $mol_{aldehydes}$ mol_{Rh}^{-1} h^{-1}].

[f] Conversion (X), selectivity for aldehydes ($S_{\mathbf{ald}}$), selectivity for nonanal ($S_{\mathbf{2a}}$), selectivity for isomers of **1a** ($S_{\mathbf{1b\text{–}ä1g}}$) and the *n*:*iso* after 3 h of reaction.

[g] Amount of hexane used for entry 1: 44.7 mL; entry 2: 42.8 mL; entry 3: 47.2 mL; entry 4: 43.9 mL.

[h] Semi-batch, $CO:H_2=1.0:1.0$.

[k] Results after 9 h reaction.

[l] The $TOF_{\mathbf{ald}}$ was determined from the pressure change in the first 5 min of reaction. $TOF_{\mathbf{1a}}$ and $TOF_{\mathbf{2a}}$ are estimated based on $TOF_{\mathbf{ald}}$ and the composition of the first sample taken after 12 min.

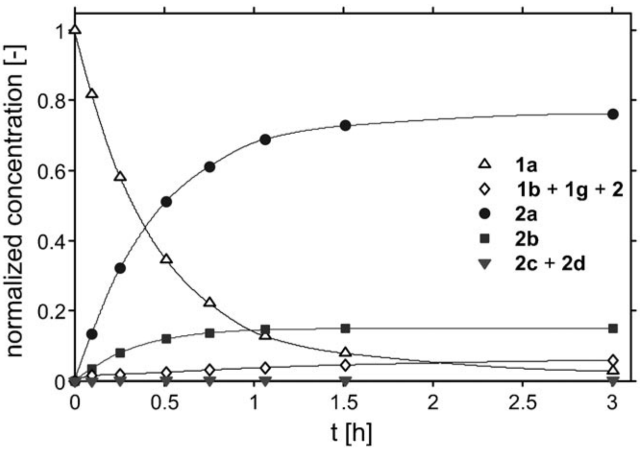


Figure 1. Normalized concentration profile of the hydroformylation of **1a** in CO_2 using **II**. The reaction conditions are given in Table 1, entry 6.

cause of a slow buildup of **1a** isomers.[26] For ligand **II** a similar behavior is observed. In Figure 1 it is seen that after approximately 1 hour of reaction the concentration of **2a** still increases slowly, while the concentrations of **2b** to **2d** remain constant, which implies that the selectivity of the catalyst changes during the reaction.

Cumulative *n*:*iso* Ratio

To investigate whether there is a change in regioselectivity, in particular a change in *n*:*iso* ratio as a result of the mode of operation, **II** and **III** have been applied in batch and semi-batch modes with respect to syngas and using hexane as the solvent. In Figure 2 it can be seen that during semi-batch operation a constant *n*:*iso* ratio over a broad conversion range is observed, while during batch operation the *n*:*iso* ratio increases clearly with an increase in conversion. The initial activity of **III** in hexane is similar for the batch case (entry 2), the semi-batch case (entry 4) and for the case where a lower syngas pressure has been applied (as reported in ref.[26]). The same holds for **II** even when taking into account the reaction in $scCO_2$ (entry 6). It appears that the finding that the reaction rate is only slightly dependent on the concentration of CO/H_2 (1:1) as reported by Cavalieri d'Oro et al. for the hydroformylation of propene with [HRhCO(**IV**)$_3$] as the pre-catalyst also holds for **II** and **III**.[32]

To study the influence of solvent on the selectivity in more detail, the *n*:*iso* ratio as a function of conversion has been obtained using **I** to **IV** in a one-phase supercritical system, shown in Figure 3a, or in neat **1a**, given in Figure 3b, both in batch. The results for the *n*:*iso* ratio obtained for the neat experiments

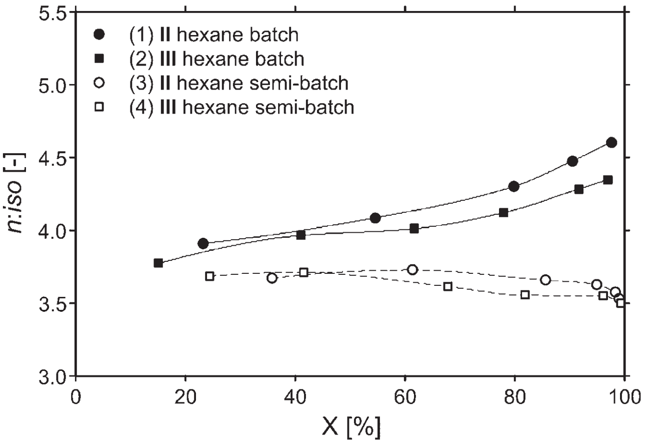


Figure 2. The *n:iso* ratio as a function of conversion (X) for the experiments with ligand **II** and **III** in hexane for the batch and semi-batch case (entries 1 to 4 in Table 1).

show more or less the same dependence on the conversion as the results obtained in $scCO_2$. For **II** and **III** a clear increase is observed in the *n:iso* ratio as the reaction progresses. The increase in *n:iso* ratio is more pronounced for the supercritical batch system than for the two-phase hexane batch system. For **IV** in CO_2, the *n:iso* ratio is more or less constant as a function of the conversion up to a conversion of 80% but then also starts to increase at higher conversion.

For **I**, which is the most active catalyst in this comparison, a small increase in the *n:iso* ratio is observed up to a conversion of approximately 90% when $scCO_2$ is used. At high conversion, a decrease in *n:iso* ratio is observed. Initially, **I** gives rise to a substantial amount of **1a** isomerization. Moreover, **I** has sufficient activity towards the hydroformylation of internal alkenes (**1b** to **1g**), and as a result the *n:iso* ratio drops at a high **1a** conversion because of the production of **2b** to **2d** through hydroformylation of **1a** isomers. It is noted that for neat conditions the highest values for the *n:iso* after three hours of reaction ratio have been obtained. Additionally, the rhodium catalysts modified with **I**, **II**, or **III** are very active in the solventless hydroformylation of **1a**.

The final outcome of the reaction in terms of *n:iso* ratio observed for neat **1a** is roughly the same when compared to the reaction in $scCO_2$ except for **I** (entries 5 and 9). However, the *n:iso* as a function of conversion for the neat experiments appears to increase linearly, while in CO_2 the *n:iso* ratio increases in a non-linear manner. The large difference between the observed overall *n:iso* ratio for **I** can possibly be explained by the fact that the reaction is very fast and solubility of H_2 and CO is low in neat **1a** and aldehydes. Possibly, as a result of mass transfer limitations the concentration of CO in the liquid phase is at a minimum and this favors the formation of linear aldehydes.[33]

Catalytic Activity versus Selectivity

Based on the TOF values (Table 1) the hydroformylation in neat **1a** is about 1.5 to 2 times faster, as compared to reaction rates obtained in the other solvents. This can probably be attributed to a higher local concentration of catalyst in the liquid **1a** phase in combination with the highest concentration of **1a** possible. The activity of the rhodium complex clearly increases when a triarylphosphine is applied with a greater number of trifluoromethyl substituents. Both in CO_2 and in neat **1a** the initial TOF values observed for ligand increase in the order: **I**>**II**>**III**>**IV**. As can be deduced from Table 1 by comparing $TOF_{\mathbf{1a}}$ and $TOF_{\mathbf{ald}}$, the initial rate of isomerization and hydroge-

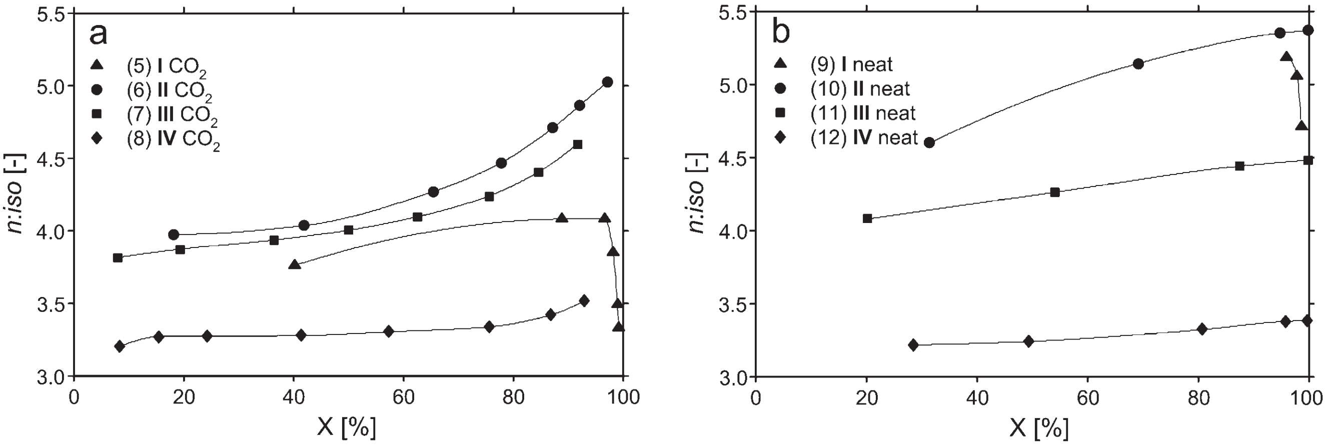


Figure 3. a) Ratio of linear to branched product, *n:iso*, ratio as a function of conversion for the experiments with ligand **I** to **IV** in the one-phase supercritical CO_2. **b)** *n:iso* ratio as a function of conversion for the experiments with ligand **I** to **IV** in neat **1a**. It should be noted that in particular for **I** to **III** in neat **1a** a minimum amount of samples were taken to minimize the effect of sampling on the reaction.

nation of **1a** towards the isomers **1b** to **1g** and **3**, respectively, also increases for the ligand in the order: **I**>**II**>**III**>**IV**. The regioselectivity in terms of *n*:*iso* ratio, however, increases in the order **II**>**III**>**I**≈**IV**. The difference in regioselectivity of **I**, **II**, and **III** observed in CO_2 becomes most pronounced at a conversion above 60% (Figure 3a).

It has been demonstrated by Moser et al.[34] that the (hydroformylation and isomerization) activity and the regioselectivity in terms of *n*:*iso* ratio of the catalyst generated from rhodium and a *para*-substituted triarylphosphine increases with decreasing basicity of the phosphine ligand. The basicity of the phosphine ligand decreases upon attaching trifuoromethyl substituents on the aryl ring of a triarylphosphine.[24] Moreover, for monodentate triarylphosphines it is expected that electron-withdrawing groups induce a higher fraction of the diequatorial coordinated $[HCO(alkene)Rh(PAr_3)_2]$ intermediate (with regard to the phosphines) responsible for a higher selectivity towards the linear aldehyde.[35,36] Additionally, the electron-withdrawing groups present in this diequatorial intermediate should lead to an even better selectivity towards the linear aldehyde, which was demonstrated by Casey et al. for the diphosphines BISBI and T-BDCP.[35] Indeed, a similar dependence as observed by Moser et al.[34] of the regioselectivity (*n*:*iso*) and activity on the basicity of the ligand is observed here when the ligands **II** to **IV** are considered, see Table 1. The results obtained with **I**, however, deviate from the behavior described by Moser et al.,[34] because for **I** a lower regioselectivity is observed than for **II** (in neat **1a**) and **III** (in CO_2 and neat **1a**). Furthermore, in the application of **II** to **IV** in $scCO_2$ the regioselectivity (*n*:*iso*) is not clearly coupled with the overall selectivity for **2a** (*n*-aldehyde selectivity, S_{2a}, in Table 1) as observed by Casey et al. for the bidentate phosphines.[35] The *n*-aldehyde selectivity increases in the order **I**<**IV**<**II**<**III** in $scCO_2$. Palo and Erkey also tested **I** and **III** in the rhodium-catalyzed hydroformylation of **1a** in $scCO_2$, but they did not observe a significant change in *n*:*iso* ratio with an increase in basicity of ligands (**I**: *n*:*iso*=3.02, **III**: *n*:*iso*=3.13).[24] Probably the reaction conditions they applied (T=50°C and L:Rh=3:1) can account for this. This clear deviation of **I** from the expected dependence of the catalytic behaviour on the number of electron-withdrawing substituents in the series **I** to **IV**, which appears to be independent of the solvent has not been established before.

Differential *n*:*iso* Ratio

An increase in (cumulative or overall) *n*:*iso* ratio with an increase in conversion implies that as the reaction proceeds the catalyst converts **1a** with an increasing differential *n*:*iso* ratio. In Figure 4a and Figure 4b a comparison is made between the differential *n*:*iso* ratio, calculated from the cumulative *n*:*iso* ratio, obtained with **II** and **III**, respectively. Additionally, the differential *n*:*iso* obtained with **IV** in CO_2 is shown in Figure 4b. From this comparison the influence of the operating conditions, a one-phase supercritical batch system, a two-phase batch system, and a two-phase semi-batch system, becomes clear. For all cases where an additional solvent is used, the differential *n*:*iso* ratio is initially about 3.7 and increases continuously with increasing conversion.

For the batch case with **II** and **III** in CO_2 and hexane the increase in differential *n*:*iso* becomes more pronounced at a conversion of above 50%. For **IV** in CO_2 the increase in differential ratio becomes more apparent above a conversion of 70%. The highest value for the differential *n*:*iso* ratio is obtained for **II** in $scCO_2$; the differential *n*:*iso* ratio increases to a

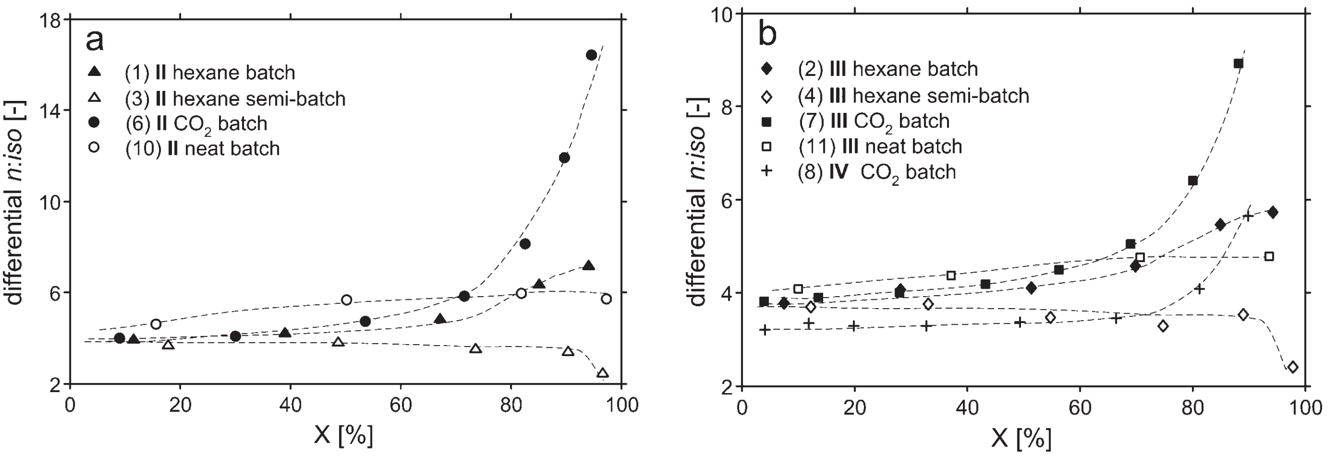


Figure 4. a) Differential *n*:*iso* ratio as a function of conversion for **II** (entries 1, 3, 6, and 10). **b)** Differential *n*:*iso* ratio as a function of conversion for **III** (entries 2, 4, 7, and 11). The dashed lines indicate the trend.

value of approximately 14–16. In hexane, the differential *n*:*iso* increases less sharply, the highest value obtained is 6–6.5. For the semi-batch experiment performed in hexane the differential *n*:*iso* ratio is constant up to a conversion of about 90% and then drops to a value of about 2.5, as a result of the hydroformylation of internal octenes. For neat **1a** and using **II** the maximum differential *n*:*iso* ratio observed is about 6.0 at a conversion around 82%. For **III** a similar behaviour is observed; the highest differential *n*:*iso* ratio obtained is about 8–9 and 5–6 for $scCO_2$ and hexane, respectively.

Screening of new hydroformylation catalysts is predominantly done at "low" pressures and semi-batch with respect to the gaseous reactants. Usually, during semi-batch hydroformylation, using rhodium catalysts in the presence of excess phosphine ligand, a constant or a decrease in *n*:*iso* ratio has been observed for a variety of solvents.[32,37,38] For hydroformylation with **IV** applying a lower CO partial pressure results in a higher regioselectivity, that is, a higher *n*:*iso* ratio, at the cost of a lower chemoselectivity, that is, a higher degree of hydrogenation and/or isomerization.[30,32,33]

For supercritical conditions it is more convenient to work batch-wise. To keep the concentration of syngas constant in a supercritical reaction mixture, during semi-batch operation, requires a dosing mechanism that delivers syngas at high pressures. Moreover, the pressure of the supercritical mixture not only changes as a result of the conversion of syngas but also as a result of a different interaction between **1a** and CO_2 as compared to the interaction between the aldehydes and CO_2. Remarkably, for the batch hydroformylation of **1a** no change in selectivity during the reaction in $scCO_2$ has been reported before in the literature.[24,39–42] This is most likely a result of either the application of a more than two-fold excess of syngas with respect to the alkene, or the use of a "low" ligand to rhodium ratio, which in most cases is not higher than 10:1. Only in the case when tris[3-(1*H*,1*H*,2*H*,2*H*-perfluorooctyl)phenyl] phosphite was used a clear increase in *n*:*iso* ratio as function of the conversion was observed.[39]

In the application of the triphenylphosphine analogues tris[4-(1*H*,1*H*,2*H*,2*H*-perfluorooctyl)phenyl]-phosphine or tris[3-(1*H*,1*H*,2*H*,2*H*-perfluorooctyl)-phenyl]phosphine in the rhodium-catalyzed hydroformylation of **1a** in $scCO_2$ Koch et al.[39] observed a constant *n*:*iso* ratio of about 5.5. In this case, the electron-withdrawing effect of the perfluoroalkyl group on the phosphorus is counteracted by the ethyl "spacers" between the perfluoroalkyl group and the aryl ring. The electron density on the phosphorus of these phosphines with perfluoroalkyl chains is similar to that of triphenylphosphine. So, the constant (differential) *n*:*iso* ratio obtained with **IV** in $scCO_2$ up to 70% conversion and the subsequent moderate increase in (differential) *n*:*iso* ratio (Figure 3a) is in good agreement with the observations by Koch et al.[39] The difference in regioselectivity can probably be attributed to the steric effects caused by the perfluoroalkyl substituents. Finally, the catalytic activity we observed (entry 8 in Table 1) is close to the activity of 430 $mol_{ald}\ mol_{Rh}^{-1}\ h^{-1}$ reported by Koch et al. for tris[4-(1*H*,1*H*,2*H*,2*H*-perfluorooctyl)phenyl]phosphine at 65°C.[39]

Based on the differential *n*:*iso* of entries 2 and 4 as a function of conversion the similar overall *n*:*iso* found previously[26] when applying **III** during batch operation in $scCO_2$ [*n*:*iso* (3 h) = 4.6] or during semi-batch operation in hexane [*n*:*iso* (3 h) = 4.8] can be explained. The syngas pressure applied in the semi-batch experiment using hexane as the solvent was 1 MPa. This syngas pressure corresponds to the pressure at about 80% conversion in the case of entry 10. The value of 5 for the differential *n*:*iso* ratio observed at 80% conversion is close to the value of 4.8 for the overall *n*:*iso* observed previously.

Differential Selectivity

By plotting the differential selectivity towards nonanal, Σ_{2a}, and towards the nonanal isomers, Σ_{2b-2d}, as a function of the conversion, the origin for the increase in the differential *n*:*iso* ratio is further clarified. In Figure 5a the differential selectivity obtained with **II** in CO_2 and hexane, batch and semi-batch, are compared. For the supercritical system (entry 6), the selectivity towards the linear aldehyde product is more or less constant up to a conversion of 90%, while Σ_{2b-2d} decreases from 18.5% at 9% conversion to 4% at approximately 95% conversion. For the batch hydroformylation in hexane (entry 1) a similar but more moderate behavior is observed. For the semi-batch case (entry 3), Σ_{2a} decreases and Σ_{2b-2d} increases slightly. Above 90% conversion Σ_{2a} decreases by about 10%, and Σ_{2b-2d} increases by about 20%, which is reflected in the lower differential *n*:*iso* ratio. For **IV** in CO_2, both Σ_{2a} and Σ_{2b-2d} remain constant, in the conversion range of 5% to about 70%, above 70% Σ_{2a} increase to a value of about 80% and Σ_{2b-2d} decreases to a value of about 15%.

For the catalyst **III** a similar but more moderate behavior of Σ_{2a} and Σ_{2b-2d} as a function of conversion is observed than for **II** as can be seen in Figure 5b. In the batch experiments in CO_2 and hexane Σ_{2a} only increases up to values of 85% at about 90% conversion. However, in the conversion range of 80 to 95% the differential *n*:*iso* ratio observed for **III** is somewhat lower than for **II**, because Σ_{2b-2d} for **III** does not decrease as much as observed for **II**. It seems that **III** maintains a higher chemoselectivity towards aldehydes than **II** at low CO partial pressure. For the

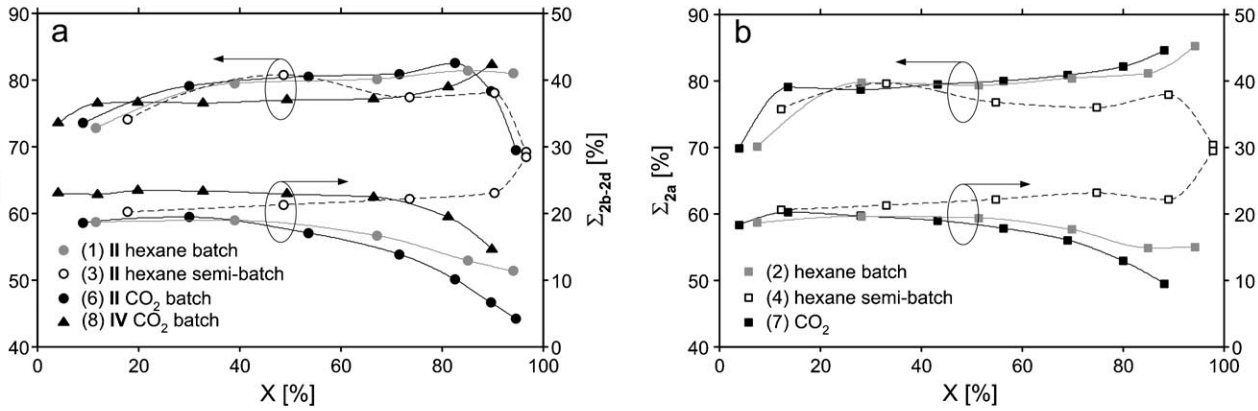


Figure 5. a) Differential selectivity for **2a** (nonanal), Σ_{2a}, and the differential selectivity towards the branched aldehydes, Σ_{2b-2d}, 2-methyloctanal (**2b**), 2-ethylheptanal (**2c**) and 2-propylhexanal (**2d**) using **II** as a function of conversion for entries 1, 3 and 6. **b)** Differential selectivity using **III** as a function of conversion for entries 2, 4 and 7.

semi-batch case (entry 4), Σ_{2a} and Σ_{2b-2d} remain more or less constant up to a conversion of about 90%. Above 90% conversion a similar behaviour as for **II** is observed, Σ_{2a} decreases to 70% while Σ_{2b-2d} increases to about 30%.

Conclusions

By following the reaction in time it was observed that a low CO partial pressure induces a higher differential *n*:*iso* ratio for **II** and **III** than expected based on the overall *n*:*iso* ratio, especially in $scCO_2$. This appears to be caused by a slower hydroformylation of 1-octene to the branched aldehyde. For **IV** in $scCO_2$ this phenomenon also takes place but in a more moderate manner at a lower CO concentration.

The hydroformylation and isomerization activity increases with the number of trifluoromethyl substituents and decreasing basicity of the ligand in the order: **I** < **II** < **III** < **IV**. When the catalysts **II** to **IV** are considered, also the regioselectivity selectivity (*n*:*iso*) increases with the number of electron-withdrawing trifluoromethyl groups. From the various results it can be derived that it could be attractive if the hydroformylation of **1a** could be operated continuously using **II** with a *n*:*iso* ratio of about 12–16. The preferred conditions are a one-phase CO_2 enriched mixture at a low CO partial pressure (for entry 6 approximately 0.3–0.6 MPa). As can be deduced from Figure 5 a, this will be at the expense of a lower overall aldehyde selectivity (*n* + *iso*) as the selectivity towards isomerization products **1b** and **1c** will be higher.

The results obtained in $scCO_2$ and the effect of different substitution patterns on the ligands provide directions for further development of ligands that are especially designed for the separation of homogeneous catalysts in continuously operated hydroformylation in $scCO_2$.

Experimental Section

Materials

Ligands **I**, **II** and **III** were supplied by Arkema (Vlissingen). Ligand **IV** was purchased from Aldrich. Dicarbonyl rhodium(I) 2,4-pentanedione ($[Rh(CO)_2acac]$) was obtained from Fluka. Ligands **I**, **II**, **III** and $[Rh(CO)_2acac]$ were stored under argon. **1a** was purchased from Aldrich, passed over a column of activated alumina (Brockmann I, Sigma-Aldrich), dried over molecular sieves and stored under argon. Hydrogen grade 5.0, carbon monoxide 4.7 and carbon dioxide grade 5.0 were purchased from Hoekloos. Prior to use carbon dioxide was passed over a Messer Oxisorb filter to remove oxygen and moisture. Analytical grade hexane was obtained from Merck and dried over molecular sieves and stored under argon. Toluene (analytical grade, Merck) and decane (99% purity, Aldrich) used to prepare the samples for GC analysis were used as received.

Hydroformylation in $ScCO_2$

The procedure for the hydroformylation in CO_2 was described in a previous communication.[26]

Hydroformylation in Neat 1a

The conditions during catalyst pre-formation for the experiments without solvent were the same as in the experiments with CO_2 as the solvent. After the pre-formation time of approximately one hour the reactor was cooled rapidly to room temperature and the gases were carefully vented. The catalyst and excess ligand remained in the reactor and were stored overnight under an argon atmosphere. After evacuating the reactor, carbon monoxide and hydrogen were fed to the reactor up to 4.9 MPa at room temperature after the stirrer speed was set to 1400 rpm. Then the reactor was heated up to 70 °C. When the reactor temperature was stabilized, **1a** was pressurized to a pressure just above reactor pressure and subsequently the desired volume was injected into the reactor within 30 s. This marked the start of the reaction. The samples taken from the liquid phase were immediately diluted with a solution of 0.01 molL^{-1} of decane in toluene and cooled to room temperature.

Hydroformylation in Hexane

The experimental procedure was started by conveying the desired amounts of catalyst (on average 26.0 μmol [Rh(CO)$_2$acac] and 1.31 mmol phosphine ligand) into the reactor. The reactor was closed and alternately evacuated and rinsed with argon three times. The reactor was evacuated and the desired amount of hexane was injected at room temperature. Then carbon monoxide and hydrogen were fed to the reactor up to 4.3 MPa. The stirrer was turned at a revolution rate of 1400 rpm and the pressure typically dropped to a pressure of 3.6 MPa. After stirring at 50 °C for half an hour the reactor was heated and kept for another half hour at 70 °C before injecting **1a** in a similar manner described for the scCO$_2$ and the neat experiments. In the semi-batch experiments the pressure was kept constant at 4.7 ± 0.2 MPa. Samples were taken from the liquid phase and treated in a similar way as in the neat experiments.

Analysis

The samples were analyzed offline on the same day as the reaction was conducted using a Fisons Instruments GC-FID equipped with a Restek Rtx-5 column (fused silica, length 30 m, internal diameter 0.53 mm) with helium as the carrier gas. Calibration was done for **1a**, **1b**, **1c**, **3** and **2a**, the sensitivity coefficients for the other octene and aldehyde isomers were taken to be equal to those of **1a** and **2a**, respectively.

Reaction Parameters

To obtain consistent concentration profiles for **1a** and its reaction products, each concentration obtained by GC analysis was normalized to the sum of all obtained concentrations [Eq. (1)]:

$$[\mathrm{i}]_\mathrm{n} = \frac{[\mathrm{i}]}{\sum [\mathrm{i}]} \tag{1}$$

where i = **1a–1g**, **2a–2d** and **3**, and the subscript n refers to the normalized values. The activity and selectivity of the different catalytic complexes was expressed in one of the following parameters. The conversion, X, was given by [Eq. (2)]:

$$\mathrm{X} = \frac{[\mathbf{1a}]_{\mathrm{n.0}} - [\mathbf{1a}]_\mathrm{n}}{[\mathbf{1a}]_{\mathrm{n.0}}} \tag{2}$$

with $[\mathbf{1a}]_{\mathrm{n.0}} = 1$.

The (overall or cumulative) *n:iso* ratio was calculated as follows:

$$n : iso = \frac{[\mathbf{2a}]}{[\mathbf{2b}] + [\mathbf{2c}] + [\mathbf{2d}]} \tag{3}$$

The overall selectivity, S$_\mathrm{j}$, towards a product *i* was defined as [Eq. (4)]:

$$\mathrm{S_j} = \frac{[\mathrm{j}]_\mathrm{n}}{\{[\mathbf{1a}]_{\mathrm{n.0}} - [\mathbf{1a}]_\mathrm{n}\}} \tag{4}$$

where j = **1b–1g**, **2a–2d** and **3**.

The overall yield for a product p was [Eq. (5)]:

$$\mathrm{Y_p} = \frac{[\mathrm{p}]_\mathrm{n}}{[\mathbf{1a}]_{\mathrm{n.0}}} \tag{5}$$

where p = **1b–1g**, **2a–2d** and **3**.

The differential selectivity $\Sigma_{\mathrm{q,k}}$ for product q was determined by [Eq. (6)]:

$$\Sigma_{\mathrm{q,k}} = \frac{\mathrm{Y_{q,sample_{k+1}}} - \mathrm{Y_{q,sample_k}}}{\mathrm{X_{sample_{k+1}}} - \mathrm{X_{sample_k}}} \tag{6}$$

with q = **1b**–**1g**, **2a–2d** and **3**. k runs from 1 to the total number of samples taken during an experiment minus 1. $\Sigma_{\mathrm{q,k}}$ was only evaluated for **2a** and the sum of the branched aldehydes **2b** to **2d**.

The differential *n:iso* ratio was calculated as follows [Eq. (7)]:

$$\text{differential } n:iso_\mathrm{k} = \frac{\Sigma_{\mathbf{2a},\mathrm{k}}}{\Sigma_{\mathbf{2b},\mathrm{k}} + \Sigma_{\mathbf{2c},\mathrm{k}} + \Sigma_{\mathbf{2d},\mathrm{k}}} \tag{7}$$

The differential parameters were evaluated as a function of conversion. The conversion values corresponding to differential parameter values were calculated as follows [Eq. (8)]:

$$\mathrm{X_k} = \frac{(\mathrm{X_{sample_{k+1}}} + \mathrm{X_{sample_k}})}{2} \tag{8}$$

The substrate to catalyst ratio S/C was calculated as follows [Eq. (9)]:

$$\frac{\mathrm{S}}{\mathrm{C}} = \frac{\mathrm{m}_{\mathbf{1a}} \times \mathrm{MW_{Rh}}}{\mathrm{m_{Rh}} \times \mathrm{MW}_{\mathbf{1a}}} \tag{9}$$

with $\mathrm{m}_{\mathbf{1a}}$ the mass of **1a** injected, $\mathrm{MW}_{\mathbf{1a}}$ the molar mass of **1a**, and $\mathrm{m_{Rh}}$ and $\mathrm{MW_{Rh}}$ the mass conveyed to the reactor and the molar mass of the rhodium precursor, respectively.

The turnover number based on the conversion of **1a**, $\mathrm{TON}_{\mathbf{1a}}$, was calculated as follows [Eq. (10)]:

$$\mathrm{TON}_{\mathbf{1}a} = \frac{\mathrm{S}}{\mathrm{C}} \times \mathrm{X} \tag{10}$$

The "initial" turnover frequency based on either **1a**, **2a**, or aldehydes (**2a**–**2d** also abbreviated as "**ald**") was calculated by multiplying $\mathrm{n}_{\mathbf{1a},0}$ (initial amount of **1a** in mol) with the slope of a line fitted through the conversion, $\mathrm{Y}_{\mathbf{2a}}$ or $\mathrm{Y}_{\mathbf{ald}}$ data points up to a conversion where there was a linear trend (typically up to a conversion of 0.6).

Acknowledgements

This work was supported by an EET grant from SenterNovem (agency of the Dutch Ministry of Economic Affairs). The contribution of Paul van Bavel to the experimental work is gratefully acknowledged.

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