Phenoxaphosphino-Modified Xantphos-Type Ligands in the Rhodium-Catalysed Hydroformylation of Internal and Terminal Alkenes

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Dedicated to Dr. Joe P. Richmond on the occasion of his 60th birthday.

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Abstract: The solubility of the modifying ligand is an important parameter for the efficiency of a rhodium-catalysed hydroformylation system. A facile synthetic procedure for the preparation of well-defined xanthene-type ligands was developed in order to study the influence of alkyl substituents at the 2-, and 7-positions of the 9,9-dimethylxanthene backbone and at the 2-, and 8-positions of the phenoxaphosphino moiety of ligands **1**–**16** on solubility in toluene and the influence of these substituents on the performance of the ligands in the rhodium-catalysed hydroformylation. An increase in solubility from 2.3 $mmol \cdot L^{-1}$ to >495 $mmol \cdot L^{-1}$ was observed from the least soluble to the most soluble ligand. A solubility of at least 58 $mmol \cdot L^{-1}$ was estimated to be sufficient for a large-scale application of these ligands in hydroformylation. Highly active and selective catalysts for the rhodium-catalysed hydroformylation of 1-octene and *trans*-2-octene to nonanal, and for the hydroformylation of 2-pentene to hexanal were obtained by employing these ligands. Average rates of >1600 (mol aldehyde) $\times$ (mol Rh)$^{-1} \times h^{-1}$ {conditions: $p(CO/H_2) = 20$ bar, $T = 353$ K, [Rh] = 1 mM, [alkene] = 637 mM} and excellent regio-selectivities of up to 99% toward the linear product were obtained when 1-octene was used as substrate. For internal olefins average rates of >145 (mol aldehyde) $\times$ (mol Rh)$^{-1} \times h^{-1}$ {$p(CO/H_2) = 3.6-10$ bar, $T = 393$ K, [Rh] = 1 mM, [alkene] = 640–928 mM} and high regio-selectivities up to 91% toward the linear product were obtained.

Keywords: homogeneous catalysis; hydroformylation; kinetics; phosphane ligands; rhodium; substituent effects; xanthene-type ligands

Introduction

To date the rhodium-catalysed hydroformylation using phosphorus-based ligands is one of the most important industrial applications of organometallic complexes as homogeneous catalysts.[1–5] Most research focuses on tuning electronic and steric properties of the ligands in order to gain insight into the relation between ligand structure and catalyst performance, and to optimise the regio- and chemoselectivity and overall catalytic activity.[6–12] In academia, issues concerning deactivation and decomposition of the catalytic system are rarely addressed.[13] For commercial applications, however, these factors are crucial. Next to catalyst selectivity and activity, stability has been a key issue for the many industrial processes that have come on stream during the last decades.[14,15] In that respect the ligand concentration and thereby the solubility of the ligand is an important parameter for a number of reasons. Firstly, decomposition of (phosphine) ligands is followed readily by precipitation of metal clusters, as CO will be the only remaining stabilising ligand. Ligand-free catalysis will lead to loss in catalytic activity or selectivity, but might also catalyse further ligand decomposition. Secondly, a sufficiently high concentration of catalyst is required to obtain a high space-time yield (weight of aldehyde produced per volume of catalyst per time unit, e.g., hour). Thirdly, ligand deposition during continuous hydroformylation

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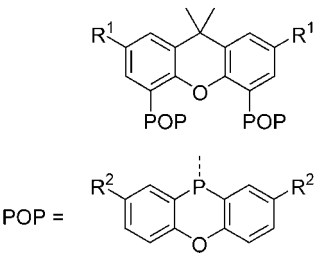
processes might lead to obstruction of tubes or filters,[16] and additionally volatile phosphorus compounds in the off-gas can lead to corrosion.

Recently, the first diphosphine ligand that shows a good compromise between selectivity toward the linear aldehyde and activity in the rhodium-catalysed hydroformylation of aliphatic *internal* alkenes was developed (Figure 1, **7**).[12,17] Especially from an economical and environmental point of view the selective hydroformylation of internal alkenes to linear aldehydes is an important reaction as Raffinate II (a mixture of different butenes obtained during the Naphtha steam-cracking[18]) can be used as feedstock. An inherent problem of these xanthene-based ligands is their low solubility in most solvents that are used for hydroformylation, like pure substrate, product aldehyde, toluene, xylene and anisole. Also the ligand is hardly soluble in other solvents such as ethers, ketones, and the high-boiling condensation products from aldehydes, the side-products that may be formed during the hydroformylation reaction. A possible way to improve the ligand solubility is modification of the ligand by introduction of aliphatic substituents. Here we report efficient and short routes for the synthesis of new Xantphenoxaphos-type ligands **1**–**16** (Figure 1) with highly improved solubility, thus circumventing loss of activity and selectivity by ligand precipitation.[16,19] A systematic variation of the ligand backbone and the phenoxaphosphino moiety was initiated in order to study the effect of different alkyl groups on the solubility in toluene. Furthermore, the effect of the substituents on catalytic performance in the hydroformylation of 1-octene and *trans*-2-octene has been investigated. To understand the crucial reaction parameters, we studied the kinetics for the hydroformylation of 1-octene and 2-pentene using **13** as modifying ligand.



No.	R^1	R^2	No.	R^1	R^2
1	H	Me	**9**	neohexyl	H
2	Me	Me	**10**	neohexyl	Me
3	Me	neohexyl	**11**	neohexyl	neohexyl
4	Me	*n*-hexyl	**12**	neohexyl	*n*-hexyl
5	*i*-Pr	Me	**13**	*n*-hexyl	Me
6	*s*-Bu	Me	**14**	*n*-hexyl	*n*-hexyl
7	*t*-Bu	H	**15**	*t*-octyl	Me
8	*t*-Bu	Me	**16**	*n*-decyl	Me

Figure 1. Xantphenoxaphos-type ligands.

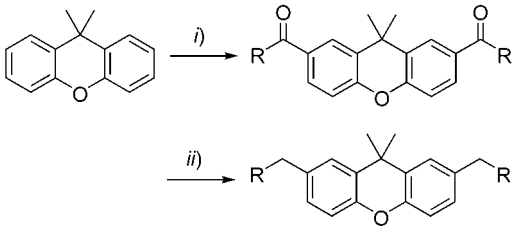
For the kinetic investigation of internal alkenes 2-pentene was preferred over *trans*-2-octene to simplify product analysis.

In order to quantify the effects of alkyl substituents, and in order to facilitate identification of the ligands we prepared a range of well-defined ligands. For industrial applications, however, a mixture of ligands with different alkyl groups are preferred, because they can be prepared from less expensive and readily available starting materials and a mixture of alkyl-substituted ligands is advantageous for solubility (*vide infra*).

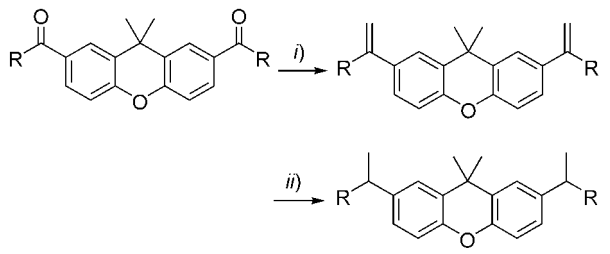
Results and Discussion

Synthesis

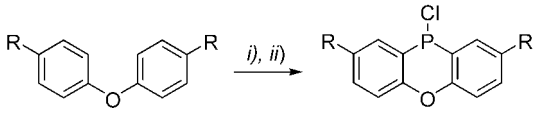
The different xanthene backbones of ligands **1**–**16** were synthesised using a variety of methods. 2,7-Di-*n*-hexyl-9,9-dimethylxanthene, 2,7-dineohexyl-9,9-dimethylxanthene and 2,7-di-*n*-decyl-9,9-dimethylxanthene were synthesised by Friedel–Crafts acylation of 9,9-dimethylxanthene[20] with the corresponding acid chloride followed by the Huang–Minlon modification of the Wolff–Kischner reduction (Scheme 1).[21,22] 2,7-Di-*s*-butyl-9,9-dimethylxanthene (as racemic mixture of different diastereomers), and 2,7-di-*i*-propyl-9,9-dimethylxanthene were obtained *via* a Wittig reaction of the appropriate diketone with *in situ* generated methylenetriphenylphosphorane followed by a palladium-catalysed hydrogenation (Scheme 2). It was found that Friedel–Crafts acylation followed by ketone reduction was the most efficient method for preparing the substituted xanthene derivatives. Due to the deactivating nature of acyl groups for electrophilic aromatic substitution only one acid chloride will react with an aromatic ring. Using two equivalents of acid chloride leads to selective formation of 2,7-disubstituted xanthenes. Other methods also yielded the desired xanthenes albeit with many side-reactions, resulting in tedious work-up procedures and/or in low yield. Obvious procedures that were explored comprise Friedel–Crafts alkylation, variations on the acid-catalysed condensation reaction of *p*-cresol with



Scheme 1. Synthesis of 2,7-dialkyl-9,9-dimethylxanthenes (yields in parenthesis) – conditions: *i*) 2.2 equivs. $AlCl_3$/2.2 equivs. acid chloride (90–97%); *ii*) 1) $H_2NNH_2 \cdot H_2O$/NaOH/120–220 °C (19–65%).



Scheme 2. Synthesis of 2,7-dialkyl-9,9-dimethylxanthenes (yields in parenthesis) – conditions: *i*) CH_3PPh_3I/*n*-BuLi (51–74%), *ii*) Pd(0), H_2 (3 bar) (38–99%).



Scheme 3. Synthesis of 2,8-dialkyl-10-chlorophenoxaphosphines (yields in parenthesis) – conditions: *i*) 1.5 equivs. $AlCl_3/PCl_3$/8 h, *ii*) pyridine/1 h (65–87%).

acetone to yield 2,7,9,9-tetramethylxanthene as proposed by Caruso et al.,[23] or palladium-catalysed cross-coupling reactions using 2,7-dibromoxanthene and alkylmagnesium chlorides. Especially the former two synthetic procedures give a mixture of substituted xanthene backbones that require elaborate identification and/or purification procedures, but from an industrial point of view these methods are attractive for their straightforward synthesis from low-cost starting compounds, additionally the mixture of alkyl substituted xanthene backbones is advantageous for solubility reasons.

In order to study the effect of different alkyl groups on the phenoxaphosphino moiety on the solubility and catalytic performance, four different 10-chlorophenoxaphosphines were prepared. Again, Friedel–Crafts acylation of diphenyl ether followed by a reduction proved to be the most efficient way of synthesizing the required 4,4′-dialkyldiphenyl ether, the starting material for the 10-chloro-2,8-dialkylphenoxaphosphine synthesis. The 10-chloro-2,8-dialkylphenoxaphosphines were prepared by an 8 h reflux of 4,4′-dialkyldiphenyl ether in PCl_3 in the presence of $AlCl_3$.

Selective dilithiation of the modified xanthenes followed by the reaction of 10-chlorophenoxaphosphines at low temperature yielded the corresponding ligands in moderate to high yields (30–80%, based on the amount of xanthene backbone).

Solubility Data

The solubility of the ligands in toluene at room temperature was determined by slow addition of toluene to the ligand under continuous stirring until all ligand had dissolved. Additionally, saturated solutions of ligand in toluene were prepared followed by separation of the dissolved ligand from the non-dissolved ligand by decantation and evaporation of the toluene under vacuum. The residue was weighed to calculate the amount of dissolved ligand in the saturated solution. Both experimental methods gave results that agreed within 5%. Toluene was used to study the solubility instead of Texanol®, which is a widely applied mimic for the heavy ends that are produced during hydroformylation, because toluene is easier to remove by evaporation and consequently results in a higher accuracy. Additionally, we used toluene in all our hydroformylation experiments. Only the solubility of the ligands itself was measured and not of their metal complexes as in industry often a large excess of ligand (L/Rh ratio > 10) is used during catalysis. In addition, during catalysis many different complexes are formed, which probably all have a different solubility. Measurement under catalytic conditions would also be cumbersome.

Table 1. Ligand solubility; effect of changing ligand backbone.

No.	Ligand[a]	R^1	R^2	Solubility[b] [mmol/L]
1	**1**	H	Me	2.6
2	**2**	Me	Me	4.3
3	**5**	*i*-Pr	Me	4.7
4	**6**	*s*-Bu	Me	17
5	**8**	*t*-Bu	Me	13
6	**10**	neohexyl	Me	58
7	**13**	*n*-hexyl	Me	118
8	**15**	*t*-octyl	Me	2.3
9	**16**	*n*-decyl	Me	127

[a] See Figure 1.
[b] Solubility in toluene determined at room temperature.

Table 1 shows the effects of changing the substituent R^1 at the backbone while keeping the substituent at the phenoxaphosphino moiety constant (R^2 = Me). The first significant increase in solubility is observed for *tert*-butyl- and *sec*-butyl-substituted xanthene backbones, while the sharpest increase in solubility is observed for substituents with six carbons in the chain. In that respect, the *n*-hexyl group (118 $mmol \cdot L^{-1}$) causes a larger increase in solubility than the bulky neohexyl group (58 $mmol \cdot L^{-1}$) (Table 1, entries 6 and 7). Relative to *n*-hexyl-substituted backbones a further increase in carbon chain length to *n*-decyl only causes a small improvement in solubility from 118 $mmol \cdot L^{-1}$ to 127 $mmol \cdot L^{-1}$. Interestingly, the highly branched *tert*-octyl- (1,1,3,3-tetramethylbutyl-)substituted ligand **15** shows a solubility that is even lower (2.3 $mmol \cdot L^{-1}$) than the solubility of the parent compound **1** (2.6 $mmol \cdot L^{-1}$) (Table 1, entries 1 and 8).

To investigate the effect of alkyl substituents at the phenoxaphosphino moiety, four different structural variants have been synthesised. Table 2 shows that modifi-

Table 2. Ligand solubility; effect of changing the phenoxaphosphino moiety.

No.	Ligand[a]	R^1	R^2	Solubility[b] [mmol/L]
1	**2**	Me	Me	4.3
2	**3**	Me	neohexyl	20
3	**4**	Me	*n*-hexyl	330
4	**7**	*t*-Bu	H	4.6
5	**8**	*t*-Bu	Me	13
6	**9**	neohexyl	H	77
7	**10**	neohexyl	Me	58
8	**11**	neohexyl	neohexyl	283
9	**12**	neohexyl	*n*-hexyl	324
10	**13**	*n*-hexyl	Me	118
11	**14**	*n*-hexyl	*n*-hexyl	>495[c]
12	**16**	*n*-decyl	Me	127

[a] See Figure 1.
[b] Solubility in toluene determined at room temperature.
[c] The solubility of this ligand is too high for an accurate measurement concerning the amount of tested ligand.

cation of the phenoxaphosphino moiety, by changing R^2, has a more pronounced effect on the solubility of the ligands than placing substituents on the backbone. This effect is partially caused by the number of extra alkyl groups that are attached to the ligand since modification of the phenoxaphosphino moiety results in four additional alkyl groups compared to the two additional alkyl groups obtained by modification of the ligand backbone. For ligands based on the 2,7,9,9-tetramethylxanthene backbones a 76-fold increase in solubility was found for *n*-hexyl-substituted phenoxaphosphines compared to methyl-substituted phenoxaphosphines (Table 2, entries 1 and 3). Also for the other ligand backbones, the *n*-hexyl-substituted phenoxaphosphines showed improved solubilities, although the effects were less pronounced (Table 2, compare entries 7, 9 and 10, 11). The neohexyl substituent enhances the ligand's solubility to a considerably lesser extent (Table 2, compare entries 1, 2 and 7, 8). This is probably the result of the close proximity of the bulky neohexyl groups on the phenoxaphosphino moieties of ligands **3** and **11**, which might cause hindered rotation (*vide infra*). Loss of degeneracy of the different protons is observed when the constrained AA′BB′ splitting patterns of PP-Ar$C\underline{H}_2$-$C\underline{H}_2$ $C(CH_3)_3$ on the phenoxaphosphino moiety are compared to the splitting patterns of the neohexyl groups attached to the ligand backbone. In the latter case the A and A′ protons have (nearly) the same chemical shift, while in the former case a significant difference in chemical shift between A and A′ is observed (Figure 2).

The results indicate that the longer carbon chain and the decreased overall aromatic character of the ligands lead to more soluble systems. This can be rationalised as follows: the modification causes more steric repulsion hampering π-π stacking interactions.[24] Secondly, by increasing the carbon chain length the number of possible conformers increases and consequently the configurational entropy of the system becomes larger. The latter effect is clearly observed for the neohexyl and *t*-octyl modified systems. In the series *n*-hexyl, neohexyl to *t*-octyl the rigidity of the alkyl chain increases dramatically; this reduces the number of possible conformations and gives rise to a decrease in solubility. The results obtained for the *t*-butyl and *t*-octyl modified ligands suggest that the increase of configurational entropy has a larger effect on solubility than on hampering π-π stacking interactions.

Comparison of the reactor content after hydroformylation reactions using 10 equivalents of ligand revealed that reaction solutions containing ligands that have a solubility $< 13\ \mathrm{mmol \cdot L^{-1}}$ show precipitation of the ligand upon cooling the reaction mixture to room temperature. It must be noted that we already started with sus-

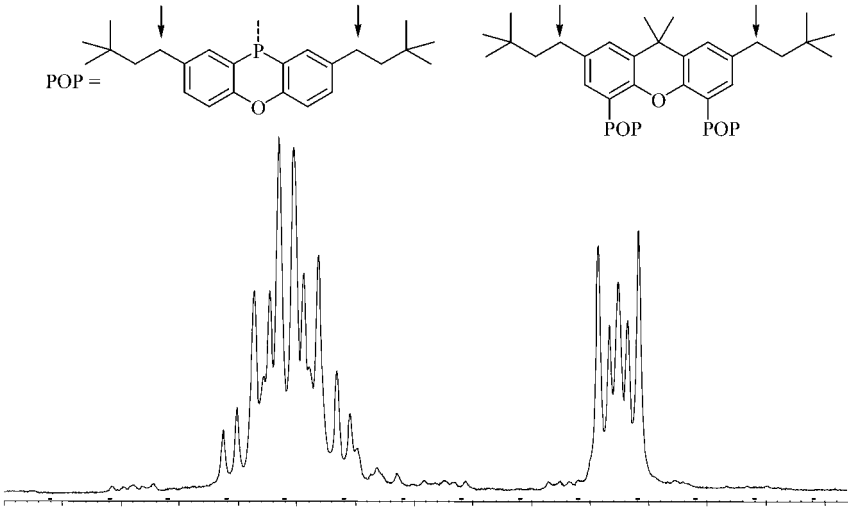


Figure 2. Ligand **11**, AA′BB′ splitting pattern for neohexyl groups on the phenoxaphosphino moiety (left) and on the ligand backbone (right).

Table 3. Hydroformylation of 1-octene at 80 °C.[a]

Ligand	R^1	R^2	TOF[b, c]	l/b[b]	Isom.[b] [%]	Sel[b] [%]
1	H	Me	1800	97 : 3	9.8	87
2	Me	Me	1660	97 : 3	10	87
3		neohexyl	1200	92 : 8	8.6	84
4		*n*-hexyl	1800	95 : 5	11.3	84
5	*i*-propyl	Me	1640	97 : 3	10.4	87
6	*s*-butyl	Me	1700	97 : 3	10.4	87
7	*t*-Bu	H	1900	99 : 1	12	87
8		Me	1500	97 : 3	9.8	87
9	neohexyl	H	2100	99 : 1	12.3	87
10		Me	1900	98 : 2	10.7	87
11		neohexyl	1900	96 : 4	8.3	88
12		*n*-hexyl	1350	96 : 4	9.3	87
13	*n*-hexyl	Me	1700	97 : 3	9	87
14		*n*-hexyl	1200	96 : 4	8.3	88
15	*t*-octyl	Me	1800	96 : 4	10.5	86
16	*n*-decyl	Me	1400	95 : 5	10.4	85

[a] Conditions: $p(CO/H_2)(1:1) = 20$ bar, ligand/Rh = 5, substrate/Rh = 637, [Rh] = 1.00 mM in toluene, number of experiments is 3 (data represent average numbers). In none of the experiments was hydrogenation observed.
[b] Linear to branched ratio, percent linear aldehyde, percent isomerisation to 2-octene and turnover frequency were determined at ~20% alkene conversion.
[c] Turnover frequency = (mol aldehyde) × (mol Rh)$^{-1}$ × h^{-1}.

pensions of these ligands in toluene before the catalytic reactions were run (with the exception of **8** that gave a clear solution in toluene). From the reaction mixture with ligand **6**, which has a solubility of 17 mmol·L^{-1}, crystals were formed within two days after stopping the reaction. The ligands that have a higher solubility did not show any precipitation or crystallisation.

It has been reported that the application of **10** in a continuous hydroformylation process did not show any loss in activity or selectivity during at least the first 168 h of application {substrate was either a mixture of *cis*- and *trans*-2-butene or Raffinate II, $T = 125$ °C, $p(CO/H_2)$-$(1:1) = 25$ bar, [rhodium] = 1.85 mM, [ligand] = 28 mM, catalysis was performed at 73% conversion of the substrate}.[16]

Hydroformylation of 1-Octene

The effect of the different alkyl substituents on the performance of the ligands during the hydroformylation of 1-octene was investigated. The reactions were performed in toluene at 80 °C under 20 bar of 1 : 1 CO/H_2 using a 1.0 mM solution of rhodium diphosphine catalyst prepared from $Rh(CO)_2(acac)$ and 5 equivalents of ligand. The formation of octene isomers, nonanal, and 2-methyloctanal was monitored by gas chromatography. Turn-over frequencies were determined and averaged over the initial ~20% conversion. The results of the hydroformylation experiments are shown in Table 3.

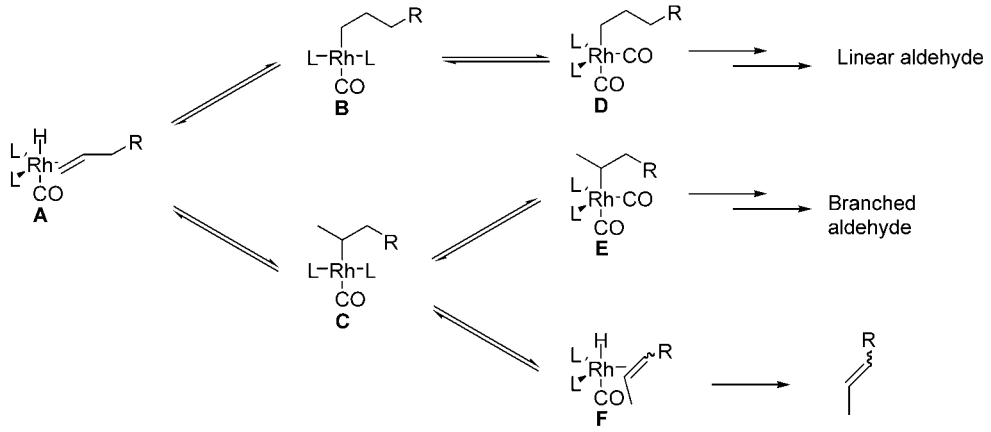
Comparisons of the ligands with small substituents on the phenoxaphosphino moiety (R^2 = H or Me) show that there is hardly any effect of changes of the ligand backbone on the catalytic performance. This is different for the ligands bearing the more bulky neohexyl- and *n*-hexyl-substituted phenoxaphosphino moieties (Table 3, entries 3, 4, 11, 12 and 14). In the latter cases both activity and linear/branched (l/b) ratio are clearly affected.

Comparison of the effect of different substituents on the phenoxaphosphino moieties shows that both the rate of isomerisation and the l/b ratio increase when less bulky substituents are applied. As the overall selectivity for the linear product is hardly influenced, the results imply that the amount of branched alkyl-rhodium species formed during the reaction is about equal in all cases (Scheme 4). Small changes in ligand structure determine the ratio between the rate of β-hydrogen elimination (Scheme 4, **C** → **F**) versus the rate of CO-insertion (Scheme 4, **C** → **E**).

Apparently it is more favourable to perform CO insertion (steric requirement diminishes) than β-hydrogen elimination (steric requirement increases) in the case of large steric hindrance, e.g., when large substituents are used on the phenoxaphosphino moieties. The negative effect of bulky substituents (of either the ligand or substrate) on selectivity for the linear aldehyde is commonly encountered.[25,26]

Hydroformylation of *trans*-2-Octene

Previous studies with related phenoxaphosphino-modified xanthene backbones showed that these types of ligands are suitable for efficient hydroformylation of in-



Scheme 4. Partitioning of the branched alkyl species **C** to **E** and **F**. **B** reverts almost directly to the linear aldehyde.

ternal alkenes to linear aldehydes.[12],[17] Therefore, the current series of ligands was used to investigate the effects of the different alkyl groups on the catalytic activity and selectivity using 2-alkenes as substrate. Hydroformylation of *trans*-2-octene was carried out at 120 °C under 3.6 bar of 1:1 CO/H_2 using a 1.0 mM solution of rhodium diphosphine catalyst prepared from $Rh(PPh_3)_3H(CO)$ and 10 equivalents of ligand. We chose to use $Rh(PPh_3)_3H(CO)$ as catalyst precursor instead of $Rh(CO)_2(acac)$ for several reasons: 1) no incubation time is needed and under the applied hydroformylation conditions the catalyst formation is less efficient when starting from $Rh(CO)_2(acac)$ and ligand, 2) the presence of PPh_3 might additionally stabilise the active species, and 3) ligand exchange of PPh_3 for these diphosphines occurs rapidly, already at room temperature. The production of octene isomers, nonanal, and branched C_9-aldehydes was monitored by gas chromatography. Turnover frequencies were determined and averaged over the initial 2 h of reaction time. The results of the hydroformylation experiments are shown in Table 4.

By applying catalytic conditions that promote β-hydrogen elimination[27] (a high reaction temperature and low syngas pressure), the rate of isomerisation in these systems is substantially enhanced, thereby continuously replenishing the reacting terminal alkenes. With all ligands preferential formation of the linear aldehyde was observed. Better selectivities can be obtained by employing even lower syn-gas pressures [$p(CO/H_2)$ (1:1) = 2 bar instead of $p(CO/H_2)$ (1:1) = 3.6 bar] although at a slight expense of activity (Table 4, entry 7). These results are in line with the influence of CO and H_2 on activity and selectivity as observed for the hydroformylation of 2-pentene (*vide infra*). Again, the use of different ligands bearing the same phenoxaphosphino moiety gives similar activity and selectivity. Ligands bearing sterically less hindered phenoxaphosphino moieties show a higher selectivity for the linear aldehyde albeit with lower activity. This effect can also be explained by the preference of β-hydrogen elimination over CO insertion from the rhodium branched alkyl species with the less hindered phenoxaphosphino-moieties. CO insertion leads to (branched) product formation, and therefore to an increased activity and a decreased selectivity, while β-hydrogen elimination is non-productive.

Table 4. Hydroformylation of *trans*-2-octene at 120 °C.[a]

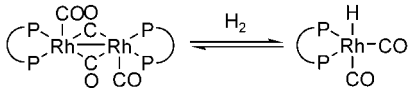
Ligand	R^1	R^2	TOF[b, c]	l/b[b]	Sel[b, d] [%]
1	H	Me	143	4.3	81
2	Me	Me	144	4.3	81
3		neohexyl	155	2.9	74
5	*i*-propyl	Me	149	4.3	81
6	*s*-butyl	Me	141	4.9	83
7	*t*-Bu	H	140	6.6	87
7[e]		H	112	9.5	90
8		Me	134	4.8	83
9	neohexyl	H	142	6.6	87
10		Me	134	4.9	83
11		neohexyl	152	3.4	77
12		*n*-hexyl	144	4.6	82
13	*n*-hexyl	Me	144	4.3	81
14		*n*-hexyl	179	3.2	76
15	*t*-octyl	Me	150	4.2	81
16	*n*-decyl	Me	162	3.6	78

[a] Conditions: $p(CO/H_2)(1:1) = 3.6$ bar, ligand/Rh = 10, substrate/Rh = 637, [Rh] = 1.00 mM in toluene, number of experiments is 2 (data represent average numbers). In none of the experiments was hydrogenation observed.
[b] Linear to branched ratio, percent linear aldehyde and turnover frequency were determined at ~50% alkene conversion.
[c] Turnover frequency = (mol aldehyde) × (mol Rh)$^{-1}$ × h^{-1}.
[d] Percentage of linear aldehyde of all products other than octenes.
[e] $p(CO/H_2) = 2.0$ bar.

Kinetic Studies

The rate equations of the hydroformylation of 1-octene at $T=80\,^{\circ}C$ and 2-pentene at $T=120\,^{\circ}C$ using **13** were determined by a kinetic study. The concentration dependency of all the reactants was investigated (see Table 5). The initial rate of aldehyde production was determined by HP-IR spectroscopy or by taking samples during the first ~10% conversion. The results for 1-octene hydroformylation are summarised in Tables 6 and 7.

The dimerisation reaction of (diphosphine)RhH-$(CO)_2$ to $[(\text{diphosphine})Rh(CO)_2)]_2$ is an important side-reaction observed under hydroformylation conditions (Scheme 5). Low hydrogen pressures, low temperatures and high rhodium concentrations promote the formation of these dimeric rhodium species.[28] The first order dependency of reaction rate on rhodium concentration indicates that within these concentration limits the dimerisation reaction is directed toward the rhodium monomer. A small influence of ligand concentration on initial activity was observed. From 1 mM to 5 mM no change in activity was observed, indicating a very strong binding of the ligand to the rhodium. The very small effect on activity at higher ligand concentrations indicates that association of a second ligand is very difficult, but feasible. The association of a second ligand effectively reduces the concentration of the active hydroformylation species, which results in a lower activity. At very low hydrogen pressures ($pH_2=2.5$ bar) only half the activity was measured compared to catalysis run at hydrogen pressures > 5 bar. This might indicate the presence of rhodium dimers at very low hydrogen pressures since at higher pressures a zero order dependency in pH_2 was measured. Alternatively, at very low pressures hydrogenolysis may become rate limiting. For the CO pressure a -0.9 order rate dependence and for the alkene concentration a reaction order of 0.9 were measured. The reaction orders of all parameters indicate that similar reaction kinetics as reported for the triphenylphosphine-based catalyst are applicable for (**13**)$Rh(CO)_2H$ and agree with the Type I kinetics [Eq. (7)] as proposed by van Leeuwen et al.[29] Both ligand concentration and CO pressure influence the formation of the coordinatively unsaturated rhodium intermediate ((diphosphine)RhH(CO)), but since there exists a 0.9 order in al-



Scheme 5. Equilibrium between Rh-dimer and Rh-hydride species.

Table 5. Concentration ranges of all reactants used for kinetic study.

1-Octene hydroformylation	2-Pentene hydroformylation
0.5 mM ≤ [Rh] ≤ 4.0 mM	0.25 mM ≤ [Rh] ≤ 2.0 mM
212 mM ≤ [1-octene] ≤ 1062 mM	213 mM ≤ [1-octene] ≤ 1067 mM
1 mM ≤ [**13**] ≤ 30 mM	5 mM ≤ [**13**] ≤ 48 mM
2.5 bar ≤ pH_2 ≤ 32 bar	2 bar ≤ pH_2 ≤ 16 bar
5.5 bar ≤ pCO ≤ 30 bar	2 bar ≤ pCO ≤ 8 bar

Table 6. Hydroformylation of 1-octene at 80 °C using **13**.[a]

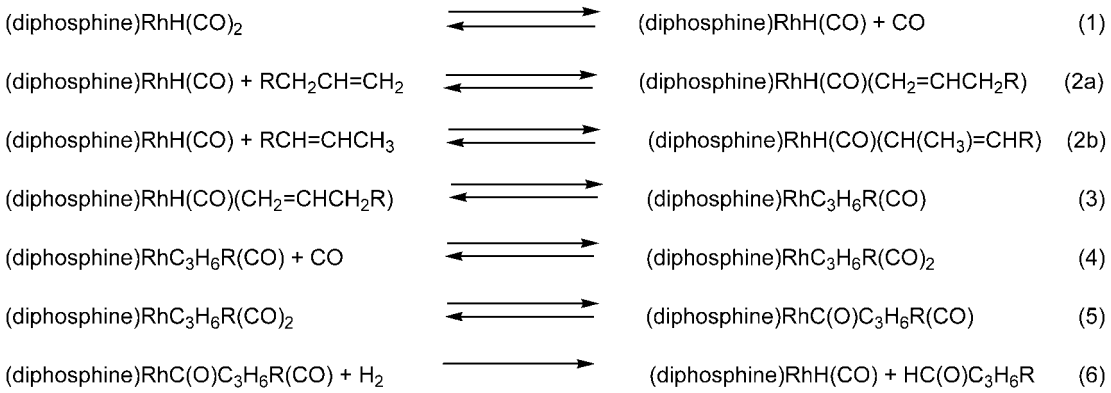
No.	pH_2 [bar]	pCO [bar]	% isom. [%]	TOF[b, c]	l/b[b]	Sel[b, d] [%]
1	9.5	5.5	16.5	3150	59	82
2	10.0	10.0	9.4	1550	39	88
3	10.5	14.5	5.4	1200	17	89
4	10.4	29.9	3.0	700	14	90
5	2.4	9.4	15.3	850	32	82
6	5.5	9.4	10.6	1450	31	87
7	10.0	10.0	11.9	1550	36	86
8	14.6	10.5	14.6	1550	33	83
9	20.6	9.3	12.0	1700	31	85
10	31.6	8.7	12.9	1550	34	85
Reaction order: $pH_2=0$; $pCO=-0.9$ ($R^2=0.981$)						

[a] Conditions: ligand/Rh = 5, substrate/Rh = 637, [Rh] = 1.00 mM in toluene, number of experiments is 2. In none of the experiments was hydrogenation observed.
[b] Linear to branched ratio, percent linear aldehyde and turnover frequency were determined during ~10% alkene conversion.
[c] Turnover frequency = (mol aldehyde) × (mol Rh)$^{-1}$ × h^{-1}.
[d] Percentage of linear aldehyde of all products other than octenes.

Table 7. Hydroformylation of 1-octene at 80 °C using **13**.[a]

[Rh][b]	AU/min[c]	[Substrate][b]	AU/min[c]	[Ligand][b]	AU/min[c]
0.5	0.124	212	0.087	1	0.244
1.0	0.246	425	0.174	5	0.246
2.0	0.441	637	0.246	10	0.226
3.0	0.637	849	0.309	22	0.217
4.0	0.886	1062	0.361	30	0.207
Reaction order = 1 (R^2 = 0.998)		Reaction order = 0.9 (R^2 = 0.996)		Reaction order = −0.05 (R^2 = 0.97)	

[a] General conditions: ligand/Rh = 5, substrate/Rh = 637, [Rh] = 1.00 mM in toluene, number of experiments is 2.
[b] [Rh], [Substrate], and [Ligand] in mM.
[c] Arbitrary units per minute



Scheme 6. Separate reaction steps of hydroformylation for the production of linear aldehydes. For internal alkenes the internal alkene has to isomerise toward the terminal alkene [Eq. (2b) → Eq. (2a) *via* β-hydrogen elimination).

kene concentration also a step later in the reaction cycle is rate limiting. The two rate influencing reactions that both fit the observed kinetics are alkene coordination followed by rapid alkene insertion into the Rh–H bond or rate determining hydride migration to the coordinated alkene preceded by fast reversible coordination of this alkene [Scheme 6, Eqs. (2a) and (3)].[29] The rate of CO dissociation does not play a role as this reaction is 10–100 times faster than the rate of hydroformylation as was found by van der Veen et al.[12,30]

$$\text{Rate(Type I)} = \frac{A[\text{Rh}][\text{alkene}]}{B + C[\text{CO}]} \quad (7)$$

The CO pressure has a very large influence on the regioselectivity. An increase in CO pressure of 5.5 bar to 30 bar results in a drop of l/b ratio from 59 to 14, but the selectivity for the linear product increases since the amount of isomerisation decreases to a large extent.

The 2-pentene hydroformylation experiments were conducted under slightly different reaction conditions than the 1-octene hydroformylation experiments. The reactions were run at a lower CO pressure and higher temperature to increase the rate of isomerisation and to suppress carbonylation from the branched alkyl-rhodium species. Usually hydroformylation reactions are conducted under a 1:1 atmosphere of CO/H_2 and thus the hydrogen pressure was also reduced, this might favour the formation of rhodium dimers. The rhodium concentration was investigated up to concentrations of 2 mM, since at high rhodium concentrations ([Rh] ≥ 2.5 mM) the catalyst is not stable under the chosen reaction conditions. The results for the hydroformylation of 2-pentene are summarised in Tables 8 and 9. Within the chosen limits a broken order of 0.5 in the rhodium concentration was observed and thus the dimerisation reaction does play a role under these conditions. The reaction order of −0.07 in ligand concentration is comparable to the one found for 1-octene hydroformylation. The 0.6 reaction order in the concentration of 2-pentene indicates that either fast, reversible alkene coordination followed by rate determining hydride-migration or rate determining alkene coordination are rate influencing [Scheme 6, Eqs (2b) and (3)]. The latter is most likely due to the steric requirements of internal alkenes. Clearly other steps later in the catalytic cycle are also included in the rate equation. For the CO pressure a reaction dependence of −0.5 was found, which is the result of slow CO insertion at low CO pressures, especially CO insertion from the branched alkyl rhodium species. The low CO pressure also leads to an increase of the coordina-

tively unsaturated rhodium intermediate [(diphosphine)RhH(CO)], which might give rise to an increase in activity. The rate of isomerisation is strongly influenced by the CO pressure [Scheme 6, Eq. (2b) → Eq. (2a)]. Isomerisation is an important reaction for internal olefin kinetics; the rate of isomerisation and the concentration of terminal alkenes in the reaction mixture are influenced by the CO pressure, but also by the concentration of the internal alkenes. At hydrogen pressures < 3 bar a large influence of hydrogen pressure was observed, but at hydrogen pressures > 5 bar the reaction is zero order in hydrogen pressure. The most likely explanation for the influence of hydrogen pressure at pressures < 3 bar is the formation of inactive rhodium dimers. At higher hydrogen pressures the rhodium dimer/monomer equilibrium shifts to the rhodium monomer. For 1-octene the rate limiting steps are predominantly Eq. (1), Eqs. (2a)–(3) in Scheme 6, but for 2-pentene hydroformylation these steps are only partially rate limiting, thus step Eq. (2b) → Eq. (2a) and the equilibrium Eqs. (4) – (5)/(6) should be included in the rate equation. It seems that for 2-pentene hydroformylation the reaction is changing toward Type II kinetics.

Both hydrogen and CO pressure have a large impact on the regioselectivity. An increase in the hydrogen pressure results in a slight increase in regioselectivity, while raising the *p*CO leads to a lower regioselectivity. The latter observation is attributed to differences in rate of β-hydrogen elimination versus CO insertion as was shown in previous studies.[31] The effect of hydrogen pressure is not fully understood, because a zero reaction order in hydrogen pressure was found at sufficiently high pressures and according to the 1-octene hydroformylation experiments the hydrogen pressure has no influence on the rate of isomerisation. At low hydrogen pressures rate determining hydrogenolysis could have an effect on the regio-selectivity since differences in rate of hydrogenolysis or CO deinsertion between the branched and linear rhodium acyl species could exist.

Table 8. Hydroformylation of 2-pentene at 120 °C using **13**.[a]

No.	pH_2 (bar)	*p*CO (bar)	TOF[b, c]	l/b[b]
1	2	2	180	7.0
2	2	3	149	5.4
3	2	5	116	4.1
4	2	8	99	3.8
5	4	2	361	7.7
6	5	2	313	8.7
7	8	2	358	9.7
8	16	2	358	9.1
Reaction order: $pH_2 = 0$; *p*CO = -0.5 ($R^2 = 0.994$)				

[a] Conditions: ligand/Rh = 5, substrate/Rh = 928, [Rh] = 1.00 mM in toluene, number of experiments is 2. In none of the experiments was hydrogenation observed.
[b] Linear to branched ratio, percent linear aldehyde and turnover frequency were determined and averaged over the first 0.5 h.
[c] Turnover frequency = (mol aldehyde) × (mol Rh)$^{-1}$ × h^{-1}.

Conclusions

In conclusion, we have presented an easy synthetic route for the preparation of a series of novel diphosphine ligands that show large differences in solubility. The developed synthetic procedure can easily be converted to modify other ligands in order to improve the solubility or to study the effects of different aliphatic groups on catalytic performance. The configurational entropy of the alkyl chains plays a more important role on solubility than hampering π-π stacking interactions. In that respect, the effect of linear alkyl groups on solubility is larger than the effect of branched alkyl groups, e.g., the effect of *n*-hexyl groups is larger than the effect of neohexyl groups. Modifications close to the active centre (i.e., modification of the phenoxaphophino-moiety) have a larger effect on catalysis than modification further away from the active centre (i.e., modification of the xanthene backbone).

Table 9. Hydroformylation of 2-pentene at 120 °C using **13**.[a]

[Rh][b]	AU/min[c]	[Substrate][b]	AU/min[c]	[Ligand][b]	TOF[d, e]
0.25	0.017	213	0.0177	5	180
0.5	0.024	427	0.0266	10	163
0.75	0.031	640	0.035	14	160
1.0	0.035	853	0.04	20	156
1.25	0.039	1067	0.0466	48	153
1.5	0.044				
2.0	0.051				
Reaction order = 0.5 ($R^2 = 0.999$)		Reaction order = 0.6 ($R^2 = 0.999$)		Reaction order = −0.07 ($R^2 = 0.85$)	

[a] General conditions: ligand/Rh = 5, substrate/Rh = 928, [Rh] = 1.00 mM in toluene, number of experiments is 2.
[b] [Rh], [substrate], and [Ligand] in mM.
[c] Arbitrary units per minute.
[d] Turnover frequencies were determined and averaged over 0.5 h.
[e] Turnover frequency = (mol aldehyde) × (mol Rh)$^{-1}$ × h^{-1}.

For the hydroformylation of 1-octene the simplest kinetics (Type I) can be used as starting point. For 2-pentene several broken reaction orders are found and thus a simple model cannot be used explain the kinetic results.

Experimental Section

General Procedures

All air- or water-sensitive reactions were performed using standard Schlenk techniques under an atmosphere of purified argon. Toluene was distilled from sodium, THF from sodium/benzophenone, and hexanes from sodium/benzophenone/triglyme. Isopropyl alcohol and dichloromethane were distilled from CaH_2. Chemicals were purchased from Acros Chimica, and Aldrich Chemical Co. 9,9-Dimethylxanthene,[32] 2,7,9,9-tetramethylxanthene,[23] 2,7-di-*t*-butyl-9,9-dimethylxanthene,[33] 10-chlorophenoxaphosphine,[12] 2,7-di-*t*-butyl-9,9-dimethyl-4,5-bis(10-phenoxaphosphino)xanthene (**7**)[12] and 2,8-dimethyl-10-chlorophenoxaphosphine[33] were prepared according to literature procedures. 2,7-Di-*t*-octyl-9,9-dimethyl-4,5-bis(2,8-dimethyl-10-phenoxaphosphino)xanthene (**15**) was kindly provided by Celanese Chemicals Europe, GmbH, Germany.[16] Syntheses of compounds **1–14**, **16–36** are provided in the Supporting Information. Silica gel 60 (230–400 mesh) purchased from Merck was used for column chromatography. Melting points were determined on a Gallenkamp MFB-595 melting point apparatus in open capillaries and are reported uncorrected. NMR spectra were recorded on Varian Mercury 300 and Inova 500 spectrometers. ^{31}P and ^{13}C NMR spectra were measured in the ^{1}H decoupled mode. TMS was used as an external standard for ^{1}H and ^{13}C NMR and H_3PO_4 as an external standard for ^{31}P NMR. Hydroformylation reactions were carried out in a 200-mL home-made stainless steel autoclave. The hydroformylation reactions were stirred at 800 rpm. The alkene was filtered over neutral activated alumina to remove peroxide impurities. The reactions were stopped by quenching the reactions with tri-*n*-butyl phosphite, cooling on ice and venting the gases. Synthesis gas (CO/H_2, 1:1, 99.9%) was purchased from Air Liquide. Gas chromatographic analysis were run on an Interscience HR GC Mega 2 apparatus (split/splitless injector, J&W Scientific, DB-1 30-m column, film thickness 3.0 mm, carrier gas 70 kPa He, FID detector) equipped with a Hewlett Packard Data system (Chrom-Card) using decane as an internal standard.

1-Octene Hydroformylation

In a typical experiment the autoclave was charged with a solution of $Rh(CO)_2(acac)$ (2.6 mg, 10 μmol) and 5 equivalents of ligand in toluene (8.5 mL). After purging the autoclave three times with CO/H_2 (1:1), the reactor was brought to 16 bar of CO/H_2 (1:1). Next the autoclave was heated to 80 °C. After 1 hour at 80 °C the substrate and internal standard (decane) were charged to the reaction mixture by overpressure of CO/H_2 (1:1).

trans-2-Octene Hydroformylation

In a typical experiment the autoclave was charged with a solution of $Rh(PPh_3)_3H(CO)$ (9.2 mg, 10 μmol) and 10 equivalents of ligand in toluene (8.5 mL). After purging the autoclave three times with CO/H_2 (1:1), the reactor was brought to 2 bar of CO/H_2 (1:1). Next the autoclave was heated to 120 °C. After 30 minutes at 120 °C the substrate and internal standard (decane) were charged to the reaction mixture by overpressure of CO/H_2 (1:1).

High-Pressure FT-IR Experiments

The high pressure FT-IR experiments were conducted in a similar way as the standard hydroformylation experiments only using a 50-mL home-made stainless steel autoclave equipped with mechanical stirrer and ZnS windows. Infrared spectra were recorded on a Nicolet 510 FT-IR spectrophotometer and on a Bio-Rad FTS-60A spectrophotometer. The production of aldehydes was determined by the following the increase in intensity of the aldehyde peak at 1734 cm^{-1}.

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