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The oxo-synthesis catalyzed by cationic palladium complexes, selectivity control by neutral ligand and anion

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Abstract

Catalyst systems consisting of a palladium(II) diphosphine complex with weakly or non-coordinating counterions are efficient catalysts for the hydrocarbonylation of both aliphatic and functionalized olefins. Moreover, variations of ligand, anion and/or solvent can be used to steer the reaction towards alcohols, aldehydes, ketones or oligoketones. Non-coordinating anions and arylphosphine ligands produce primarily (oligo)ketones; increasing ligand basicity or anion coordination strength shifts selectivity towards aldehydes and alcohols. For the mechanisms of the aldehyde-producing step, we propose heterolytic dihydrogen cleavage, assisted by the anion. At high electrophilicity of the palladium center, selective ketone formation is observed. The reactions described here constitute the first examples of *selective* formation of ketones by hydrocarbonylation of higher olefins.

Keywords: Oxo synthesis; Ketones; Aldehydes; Copolymerization; Cationic palladium complexes

1. Introduction

The discovery of the oxo-synthesis in 1938 [1] by Otto Roelen at Ruhrchemie has marked the birth of the large scale industrial application of homogeneous catalysis by organometallic complexes. The term oxo-synthesis denotes the synthesis of oxygenates by hydro-carbonylation of olefins, i.e. the reaction of olefins with mixtures of carbon monoxide and hydrogen. It was based upon the original finding that with a cobalt catalyst and ethene as olefinic substrate both propionaldehyde and diethylketone were produced. Roelen expected [2] that 'one day it would be possible to convert olefins in general to aldehydes or ketones at choice'. Despite later observations that only ethene gives rise to significant formation of ketone product, the term oxo-synthesis remained in use in the chemical community. However, the term hydroformylation, which originated from a paper by Atkins and Krsek [3], is a more correct expression for the widely applicable aldehyde and alcohol synthesis reactions (Eq. (1)).

$$R\text{–}CH{=}CH_2 + CO + H_2 \rightarrow R\text{–}CH_2\text{–}CH_2\text{–}CHO$$

$$R\text{–}CH{=}CH_2 + CO + 2H_2 \rightarrow R\text{–}CH_2\text{–}CH_2\text{–}CH_2OH \quad (1)$$

Driven by the need to produce oxygenates from petrochemical hydrocarbons, hydroformylation has become the largest-scale industrial chemical application of homogeneous catalysis by transition-metal complexes, with a present worldwide volume of about 6.5 million ton per annum of aldehydes and alcohol products.

Several advances in homogeneous catalysis have made this development possible. In the 1960s, it was discovered that ligand substitution in the original cobalt carbonyl catalyst $HCo(CO)_4$ could influence the performance significantly. The resulting catalyst $HCoL(CO)_3$ (in which L represents a tertiary alkylphosphine) is much more stable and can be used at higher temperatures [4]. A unique feature of these catalysts is that they possess a high olefin isomerization activity combined with a high regio-selectivity for terminal olefin hydroformylation. This allows the production of predominantly linear alcohols from internal straight-chain olefins. This process was first commercialized by Shell.

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Another major breakthrough in catalyst activity and regio-selectivity was made possible by advances in organometallic chemistry [5]. Based on this, workers at Union Carbide, Johnson and Matthey, and Davy Powergas jointly developed a rhodium–phosphine based hydroformylation process to produce *n*-butanal from propene. This process was first commercialized in 1976. In the last 2 decades, numerous hydroformylation catalysts, predominantly based on the metals Co and Rh combined with a wide variety of ligands, have become available. However, none of these catalysts has allowed the full and general exploitation of the oxo-synthesis: the *selective* production of ketones has thus far remained an elusive goal [6].

Our interest in the *palladium-catalysed hydrocarbonylation* of olefins was awakened by the discovery of a class of highly efficient cationic palladium catalysts for the alternating copolymerization of olefins with carbon monoxide (Eq. (2)) [7].

$$n\ R\text{–}CH{=}CH_2 + n\ CO \longrightarrow \left(CHR\text{–}CH_2\text{–}CO\right)_n \qquad (2)$$

The active catalysts for this Reppe-type reaction can be represented by the general formula L_2PdX_2, in which L_2 stands for a *bidentate* ligand (e.g. phosphine, pyridyl or thioether) and X represents a weakly or non-coordinating anion. When these copolymerization catalyst were exposed to olefins and carbon monoxide in the presence of small amounts of hydrogen in aprotic solvents, ketonic end-groups were generally observed. However, with some catalysts containing moderately strongly coordinating anions, both ketone and aldehyde end-groups could be observed, indicating that chain transfer by H_2 is possible both at the Pd–alkyl and the Pd–acyl stage of the growing chain. It was hoped that under sufficiently high hydrogen pressure relative to that of carbon monoxide, chain growth of the copolymerization could be efficiently interrupted, resulting in low-molecular weight products and ultimately in aldehydes and monoketones. In this paper, we will show that with L_2PdX_2 complexes as catalysts, aldehydes and ketones can indeed be produced from olefinic substrates in general. Moreover, we will show that by a proper choice of the ligand (L_2) and the anion (X^-), hydrocarbonylation of olefins can be tuned to proceed selectively towards *either* aldehydes (alcohols) *or* ketones. The reported class of catalysts, thus provides for the first time a means of control for the selective production of both possible oxo-type products.

Table 1
Abbreviations used for ligands and acids

Name	R	*n*
Ligands	$R_2P(CH_2)_nPR_2$	
DPPP	Ph	3
DsBPE	*sec*-Bu	2
DEPP	Et	3
DnBPP	*n*-Bu	3
DsBPP	*sec*-Bu	3
DtBPP	*tert*-Bu	3
Acids		
HOAc	CH_3COOH	Acetic acid
TFA	CF_3COOH	Trifluoroacetic acid
HOTf	CF_3SO_3H	Trifluoromethanesulfonic acid
HOMs	CH_3SO_3H	Methanesulfonic acid
HOtBs	$(CH_3)_3CSO_3H$	*t*-Butylsulfonic acid
HOTs	p-$CH_3C_6H_4SO_3H$	*p*-Toluenesulfonic acid

2. Results

The catalysts tested were formed by the combination of a suitable bidentate ligand (L_2) with a palladium (II) species, e.g. $Pd(OAc)_2$, and an acid containing the weakly or non-coordinating anions (X^-), via ligand complexation–anion displacement reaction (Eq. (3)) [8,9].

$$L_2 + Pd(OAc)_2 + 2HX \rightarrow L_2PdX_2 + 2HOAc \qquad (3)$$

The catalysts are conveniently generated in situ by applying some excess of ligand and acid over the stoichiometric quantities required by Eq. (3) (see Section 5).

We will describe the effects of variations of the ligand and acid components of the catalysts on the chemo-selectivity in oxo-synthesis. In addition, we will illustrate their effects on the regio-isomeric product distribution, both in aldehyde–alcohol and ketone formation. Steric and electronic (basicity) properties of the diphosphine ligands $R_2P(CH_2)_nPR_2$ were varied by variation of R and *n* (no active catalysts could be obtained with monodentate ligands). In the text, we will use abbreviations for both ligands and acids; these abbreviations are explained in Table 1.

2.1. Chemo-selectivity in palladium catalyzed oxo-synthesis

It appears appropriate to distinguish between aliphatic olefinic and functionalized vinylic substrates.

2.1.1. Aliphatic olefins as substrate

A series of catalyst systems examined for the chemo-selectivity of hydrocarbonylation of propene and 1-octene is given in Table 2. Inspection of the table shows that variation of the ligand and the acid component of the catalyst system resulted in very significant changes in chemo-selectivity. For one substrate (propene) and one acid (HOTs), ligand variation can shift the chemo-selectivity from simultaneous production of aldehydes, monoketones and co-oligomers (with the DPPP ligand),

Table 2
Chemoselectivity in olefin hydrocarbonylation [a]

Ligand	Acid	Olefin	T (°C)	Rate [b]	Solvent	Products (%) [c]	
						Aldehydes/Alcohols	Ketones
DPPP	TFA	Propene	125	200	Diglyme	95/–	4
	HOTs	Propene	125	500	Diglyme	30/–	50 [d]
	HOTf	Propene	125	100	Diglyme	–/–	70 [d]
	TFA	1-Octene	125	100	Diglyme	98/–	Trace
DnBPP	TFA	Propene	125	300	Diglyme	95/–	Trace
	HOTs	Propene	125	1000	Diglyme	15/25	50
	HOTf	Propene	125	500	Diglyme	–/–	90
	TFA	1-Octene	90	60	Diglyme	96/–	Trace
	HOTs	1-Octene	90	100	Diglyme	80/5	10
	HOTs [e]	1-Octene	125	120	Diglyme	3/93	Trace
	HOTs	1-Octene	125	100	Methanol	–/–	95
	HOTf	1-Octene	125	80	Diglyme	–/–	98
DsBPP	HCl	Propene	115	0	Diglyme	–	–
	HOAc	Propene	115	0	Diglyme	–	–
	TFA	Propene	125	500	Diglyme	98/–	Trace
	HOTs	Propene	100	800	Diglyme	84/2	7
	HOTf	Propene	125	800	Diglyme	–/–	95
	TFA	1-Octene	115	100	Diglyme	96/2	Trace
	HOTs[e]	1-Octene	125	150	Diglyme	3/95	Trace
	HOTf	1-Octene	125	40	Diglyme	–/–	98
DsBPE	TFA	Propene	90	100	Diglyme	98/–	Trace
	HOTf	Propene	90	300	Diglyme	–/–	93
DtBPP	TFA	Propene	80	<10	Diglyme	–	–
	HOTs	Propene	80	30	Diglyme	85/10	4
	HOTf	Propene	80	10	Diglyme	14/11	75

[a] Batch experiments, 250 ml Hastelloy C autoclave, 45 ml solvent, $P_{CO} = P_{H_2} = 30$ bar (at room temperature). Propene reactions: 20 ml propene, 0.1 mmol $Pd(OAc)_2$, 0.2 mmol ligand, 0.5 mmol acid. 1-Octene reactions: 20 ml octene, 0.25 mmol $Pd(OAc)_2$, 0.6 mmol ligand, 1 mmol acid. Rates averaged over $<30\%$ olefin conversion.
[b] Turnover/h (mol/mol/h).
[c] Remaining products are diketones and/or keto-aldehydes.
[d] Higher oligoketones formed.
[e] $P_{CO} = 20$ bar, $P_{H_2} = 40$ bar.

through simultaneous production of aldehydes and monoketones (with the DnBPP ligand) to the selective production of aldehydes (with the ligands DsBPP and DtBPP).

Likewise, for one selected ligand, e.g. DnBPP, acid variation can bring about a remarkable shift in chemo-selectivity from selective aldehydes formation (with TFA) towards selective monoketones formation (with HOTf).

Generally, the monoketones formed are both saturated- and α-β unsaturated ketones (vide infra, Table 4).

With hydrogen chloride and weak carboxylic acids (e.g. HOAc) as acid catalyst components, no active catalysts could be generated.

The variation in chemo-selectivity for propene hydrocarbonylation under conditions specified in Table 2, has been summarized schematically in a graphical representation given in Fig. 1. Along the horizontal axis the acid catalyst components have been ordered for increasing pK_a: HOTf $(-5.1 <$ HOTs $(-2.7) <$ TFA (-0.7) [10]. Along the vertical axis the ligand catalyst components have been ordered for increasing basicity: DPPP < DnBPP < DsBPP < DtBPP. Three different regions of chemo-selectivity can be distinguished: co-oligomerization, monoketone formation and

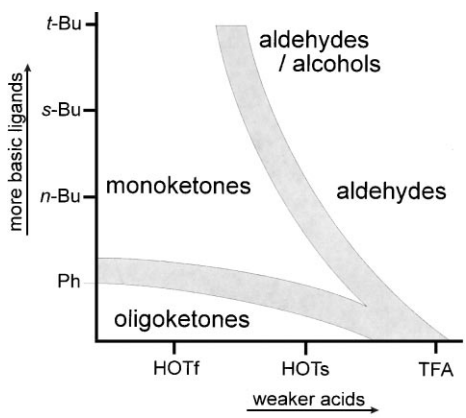


Fig. 1. Schematic representation of chemoselectivity as a function of ligand and acid properties.

Table 3
Chemoselectivity in hydrocarbonylation of functionalized olefins [a]

Ligand	Acid	Olefin (ml)	T (°C)	Rate [b]	Solvent	Products (%)	
						Aldehydes	Ketones [c]
DPPP	TFA	Styrene (20)	115	100	Anisole	98	<1
DPPP	HOTf	Styrene (20)	115	120	Anisole	50	50
DEPP	TFA	Styrene (20)	115	250	Anisole	98	<1
DEPP	HOTf	Styrene (20)	115	100	Anisole	–	99
DnBPP	TFA	Methyl acrylate (20)	90	100	Diglyme	12	34 (54)
DnBPP	HOTf	Methyl acrylate (20)	90	200	Diglyme/methanol	–	88 (12)
DnBPP	HOTf	Acrylic acid (20)	75	600	Water/THF	–	60 [d]
DnBPP	HOTf	Acryl-amide (5 g)	100	50	Diglyme	–	30 [e]
DEPP	HOTf	Methyl acrylate (15)/1-octene (40)	70	100	THF	–	95 (5) [f]
DEPP	HOTf	Acrylic acid (10)/1-octene (40)	60	250	THF	–	80 [g]

[a] Batch experiments, 250 ml Hastelloy C autoclave, 0.25 mmol $Pd(OAc)_2$, 0.3 mmol ligand, 1 mmol acid, 50 ml solvent.
[b] Turnover/h (mol/mol/h).
[c] Percentage byproduct methylpropionate in parentheses.
[d] Detected as dispirolactone (see text); byproduct propionic acid (40%).
[e] Detected as dispirolactam (see text); byproduct propionamide (70%).
[f] Mixed ketone selectivity 90% based on acrylate, 95% based on 1-octene.
[g] Mixed ketone selectivity 75% based on acrylic acid, 92% based on 1-octene; byproducts propionic acid (10%), dispirolactone (10%).

aldehyde–alcohol. The regions are separated by fairly discrete boundary regions. For example, the DnBPP–HOTs combination is located in the boundary region between ketone and aldehyde–alcohol formation (50/40%), while the combination of DsBPP with the same acid shifts chemo-selectivity to within the region of selective aldehyde–alcohol formation (86%). Likewise, the DPPP–HOTf combination is located in the boundary region between co-oligomerization and monoketone formation, while the combinations of DnBPP and DsBPP with the same acid are located well within the region of selective monoketone formation (90–95%). The combination of all ligands investigated with TFA is located in the region of selective aldehyde formation; reduction of the aldehydes to alcohols does not take place to a significant extent, with this acid as catalyst component.

The location of the chemo-selectivity boundary regions, e.g. between monoketone and aldehyde–alcohol formation, depends on the olefinic substrate as well as on the reaction conditions. Thus, the above-mentioned DnBPP–HOTs combination becomes more selective for aldehyde formation with 1-octene as the substrate. The DPPP–TFA combination is clearly located well within the region of selective aldehyde formation with 1-octene. At a higher H_2:CO ratio (of 2), and with the combination DnBPP–HOTs, ketones formation is completely suppressed and alcohols are formed selectively (93%).

The reaction solvent could also bring about a dramatic effect on the chemo-selectivity. This is demonstrated with the DnBPP–HOTs combination and 1-octene as substrate. Whereas this ligand–acid combination in diglyme as solvent resulted in selective aldehydes–alcohols formation (85%), exclusively ketones were formed in the more polar methanol solvent. The same shift towards ketone formation is observed by changing (in the diglyme solvent) the acid from HOTs to HOTf. Thus, HOTs in methanol behaves similar as HOTf in diglyme.

With all catalysts, the rate of hydrocarbonylation with propene was considerably higher than with 1-octene. This is at least partly due to the fact that 1-octene was isomerized to internal octenes in the course of the hydrocarbonylation experiments. In separate experiments with internal olefins as substrate, it was found that these are converted to the same products as the terminal olefins. However, the rate of conversion of internal olefins was about a factor of eight lower than the initial rate (at $<15\%$ conversion) observed with 1-octene.

2.1.2. Functionalized olefins as substrate

Some results obtained with functionalized olefins are collected in Table 3. The catalyst systems studied in this case contained a near stoichiometric amount of ligand combined with a small excess of acid. For styrene, the dependence of chemo-selectivity on acid variation is very similar to that for propene and 1-octene. With DPPP as ligand and TFA as acid component, aldehydes were formed with high selectivity (98%), whereas a 1:1 mixture of aldehydes and ketones could be produced with HOTs in apolar solvents such as anisole. With DEPP as ligand, selectivity could be directed towards aldehydes (98%) using TFA, or towards ketones (99%) using HOTf. Higher oligo-ketones were not observed.

With acrylic olefins, such as methyl acrylate, ketone formation dominated over aldehyde formation. Even with TFA, which in other cases gave very selective hydroformylation, the proportion of aldehydes did not rise over

≈ 15% under conditions specified in Table 3. With HOTf, ketones were formed exclusively. However, we observed that *hydrogenation* sometimes strongly competed with hydrocarbonylation. This is noteworthy, since we never observed more than 2% hydrogenation in the hydrocarbonylation of aliphatic olefins. Hydrogenation could, however, be suppressed by using HOTf as acid component, in particular in a polar reaction medium containing methanol as (co)-solvent. Thus, methyl acrylate could be converted with good selectivity (≈ 90%) to the di-ester ketone, di-methyl-4-oxopimilate.

With acrylic olefins containing active hydrogen atoms, such as acrylic acid and acrylamide, formation of di-spirolactone or di-spirolactam was observed. The initially formed diacid and diamide ketones apparently undergo an intramolecular double *cyclo*-condensation (see Sections 2.2.2 and 3.3).

The high propensity of acrylic olefins for ketone formation suggested that insertion of these olefins in palladium–acyl intermediates is facile compared to that of aliphatic olefins. This prompted us to test hydrocarbonylation using mixtures of functionalized olefins and 1-alkenes. Indeed, these reactions turned out to produce mixed ketones with good selectivity. Thus, with DEPP as ligand and HOTf as acid, 1-octene could be converted under mild conditions with acrylic acid or methyl acrylate to 4-oxo-dodecanoic acid or its methyl ester, respectively.

These results clearly illustrate that in cationic palladium catalysts, variation of the ligand and acid components can be used to control chemo-selectivity in hydrocarbonylation of olefins.

2.2. Regio-selectivity in the palladium catalyzed oxo-synthesis

Catalyst composition not only affects chemo-selectivity, but also influences the regio-selectivity of the palladium-catalyzed hydrocarbonylation. In this section, we will focus on regio-selectivity; the effects of ligand variation are illustrated in Table 4, and the effect of acid variation on regio- selectivity of hydroformylation is summarized in Table 5.

2.2.1. Regio-selectivity in aldehyde–alcohol formation

With propene only two aldehydes can be formed: *n*- and *iso*-butanal. From Table 4 it can be observed that, with TFA or HOTs as acid component, hydroformylation linearity increases with the steric bulk of the ligand from 60 to 65% with DnBPP to 84% with DsBPP. The C_2-bridged ligand DsBPE afforded a significantly lower product linearity (76%) than the corresponding C_3-bridged DsBPP ligand (84%).

The acid component also affects regio-selectivity, with stronger acids affording lower product linearity. For example, using the DsBPP ligand, linearity falls from 90% with TFA to 77% with HOTs. The effect of acid strength on product linearity was more pronounced at lower reaction temperatures (Table 5).

Similar effects could be noted with 1-octene as sub-

Table 4
Regioisomer distribution in hydrocarbonylation [a]

Ligand	Acid	Olefin	Aldehydes/alcohols [b]	Ketones [c]		
			Percent linear	h to t	h to h	t to t
DPPP	TFA	Propene	72	–	–	–
DPPP	HOTs	Propene	62	50(63)	20(90)	30(85)
DPPP	HOTf	Propene	–	52(79)	17(91)	31(85)
DnBPP	TFA	Propene	68	–	–	–
DnBPP	HOTs	Propene	60	83(16)	11(25)	6(20)
DnBPP	HOTf	Propene	–	82(5)	11(24)	7(5)
DsBPP	TFA	Propene	84	–	–	–
DsBPP	HOTf	Propene	–	92(10)	6(15)	2(10)
DsBPE	TFA	Propene	76	–	–	–
DsBPE	HOTf	Propene	–	81(12)	10(15)	9(4)
DnBPP	TFA	1-Octene	70 [e]	–	–	–
DnBPP	HOTf	1-Octene	–	98(10)	2	<1
DPPP	TFA	Styrene	85	–	–	–
DEPP	HOTs	Styrene	83	2(80)	–	98(67)
DEPP	TFA	Styrene	72	–	–	–
DEPP	HOTf	Styrene	–	16(5)	–	84(4)
DnBPP	HOTf	Methyl acrylate	–	<2	–	98(0)
DEPP	HOTf	Methyl acrylate/1-octene	–	8(0)	–	92(0) [d]

[a] Reaction conditions as specified in Tables 2 and 3.
[b] Linear aldehydes + alcohols as percentage of total aldehydes + alcohols.
[c] Saturated + unsaturated ketones as percentage of total ketones; fraction of unsaturated ketones given in parentheses.
[d] Mixed ketone.
[e] 20% α-methyl branched, 10% α-ethyl and α-propyl branched aldehydes.

Table 5
Effect of acid on regioisomer distribution of hydroformylation [a]

Acid	pK_a	Olefin	Rate [b]	Aldehyde selectivity (%) [c]	Linearity (%) [d]
HOTs	−2.7	Propene	150	86 (11, 3)	77
HOMs	−1.9	Propene	80	94 (4.5, 1.5)	84
HOtBs	−1.2	Propene	80	95 (3.5, 1)	88
TFA	−0.7	Propene	20	99	90
HOTs	−2.7	1-Octene	80	98	78
HOtBs	−1.2	1-Octene	30	98	85

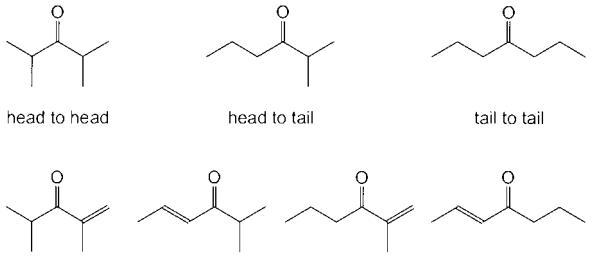
[a] Batch experiments, 250 ml Hastelloy C autoclave, $P_{CO} = P_{H_2} = 30$ bar (at room temperature), solvent diglyme, 0.25 mmol $Pd(OAc)_2$, 0.6 mmol ligand (DsBPP), 0.5 mmol acid, $T = 75$°C.
[b] Turnover/h (mol/mol/h).
[c] Byproducts $CH_3CH_2CH_2COCH(CH_3)CH_2CHO$ and $CH_3CH_2CH_2COC(CH_3)=CH_2$ given in parentheses.
[d] Linear aldehyde as percentage of total aldehyde.

strate. Mainly linear nonanals were formed under aldehyde formation conditions using TFA. With DnBPP as the ligand, *n*-nonanal comprised 70% of the total amount of aldehydes formed. In addition to the branched isomer α-methyloctanal (20%), the product also contained branched isomers derived from internal octenes (α-ethylheptanal and α-propylhexanal, together 10%). These latter products are a consequence of concomitant isomerization of 1-octene under hydrocarbonylation conditions as noted earlier. As with propene, the acid component also affected aldehyde product linearity (Table 5). With DsBPP as ligand, it changed from 78% with HOTs to 85% with HOtBs.

Under aldehyde forming conditions with TFA as catalyst component, similar phenomena could also be noticed with *styrene*. The main product was the linear aldehyde 3-phenylpropionaldehyde. Product linearity increased with ligand bulk, e.g. from 72% for DEPP to 85% for DPPP. Acid variation (TFA vs. HOTs) had little effect on the regio-selectivity of aldehyde formation, possibly because these reactions were carried out at a relatively high temperature.

2.2.2. Regio-selectivity in ketone formation

With a higher olefin such as *propene*, a variety of regio-isomeric ketones can, in principle, be obtained. Three *saturated* monoketones with, respectively, h (head) to h (head), h (head) to t (tail) and t (tail) to t (tail) enchainment of the propyl groups via carbonyl can be formed. Likewise, four *unsaturated* ketones can be produced with h to h, h to t (twice) and t to t enchainment of the propyl and the propenyl moiety via carbonyl, respectively.



The observed distribution of regio-isomeric ketones, under conditions specified in Table 2, is illustrated in Table 4. Of the two different unsaturated h to t isomers, *iso*-propenyl-*n*-propyl ketone was consistently formed in much higher amounts than the alternative isomer *n*-propenyl-*iso*-propyl ketone. Only traces of the latter isomer could be observed with all catalysts containing alkylphosphine ligands. With DPPP as ligand, however, a small but non-negligible quantity could be detected (about 5% of total ketones). The h to t ketone contents given in Table 4, denote the combined amount of both unsaturated h to t isomers.

It can be seen that the ligand structure has a very significant influence on the regio-isomer distribution of the ketone products. With all ligands mentioned in Table 4, the h to t isomer was predominantly formed, but this preference was considerably stronger with alkyl phosphines (up to 92%) than with the arylphosphine DPPP ($\approx 50\%$). The preference for the h to t regio-isomer increased with the steric bulk of the alkylphosphine, from 82% with DnBPP to 92% with DsBPP. The C_3-bridged diphosphine DsBPP gave a significantly higher preference (92%) for h to t enchainment than the C_2-bridged analogue DsBPE (81%).

No significant influence of the anion on the isomeric distribution of the ketones could be established. This was illustrated in two instances, with DPPP and DnBPP as ligand (Table 4). Whereas the hydrocarbonylation could be shifted from simultaneous production of aldehydes and ketones towards exclusive production of ketones by changing the acid from HOTs to HOTf, the regio-isomer distribution of the ketone products remained virtually unchanged.

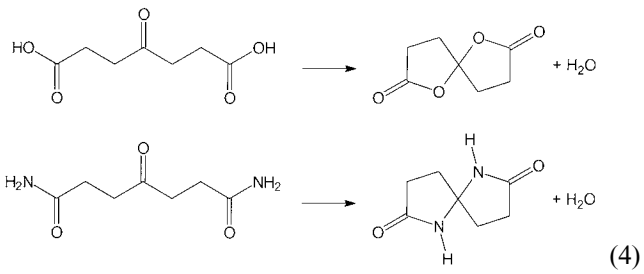
The proportion of unsaturated ketones depends on the ligand and changes from predominantly unsaturated ($\approx 85\%$) with DPPP towards mainly saturated with alkylphosphines (≈ 80–85%). Generally, unsaturation was found to decrease with increasing temperature and increasing hydrogen pressure. It can be noted

that the highest degree of unsaturation was consistently found in the h to h coupled ketone isomer.

With 1-octene, the h to t regio-isomeric ketone was almost exclusively formed under ketone formation conditions with BnDPP and HOTf as catalyst components. Thus, regio-specificity with the bulkier olefin, 1-octene, for h to t ketone formation is considerably higher than observed with propene.

Ketone formation with *styrene* proceeded with a remarkably high regio-selectivity to the t to t isomer (98%) with DPPP and HOTs. Under these conditions predominantly unsaturated ketones were formed. With DEPP and HOTf, preference for t to t coupling was less pronounced. As observed with propene and 1-octene, mainly saturated ketones were formed with the alkyl phosphine. It is noteworthy that the unsaturated fraction of the h to t regio-isomer was exclusively 1,4 diphenylpent-1-ene-3-one with both types of ligand.

Acrylic olefins also showed a *high preference for t to t coupling* of the olefinic moieties both with aryl- and alkylphosphine ligands. This is exemplified in Table 4 for methyl acrylate with DnBPP and HOTf. In this case, saturated ketones are formed exclusively. The formation of di-spirolactone and di-spirolactam from acrylic acid and acrylamide can be explained by initial t to t coupling followed by cyclocondensation (Eq. (4)).



(4)

In cross-hydrocarbonylation experiments with mixtures of *acrylic and aliphatic olefins*, it was observed that the mixed ketone products consisted predominantly of t to t regio-isomers. Thus, the mixed ketone from methyl acrylate and 1-octene (using DEPP–HOTf) contained 92% of methyl 4-oxo-dodecanoate. The h to t regio-isomer by-product was exclusively methyl 4-oxo-5-methylundecanoate. No unsaturated mixed ketones were observed.

3. Discussion

The above reported results indicate that cationic palladium(II) catalyst systems of the type L_2PdX_2, easily prepared from e.g. $Pd(OAc)_2$, a chelating ligand L_2 and an acid HX, have a wide applicability in olefin carbonylation chemistry, in addition to being efficient olefin–carbon monoxide copolymerization catalysts [7]. The electrophilic palladium center can not only activate nucleophiles, such as olefins, carbon monoxide and alcohols to facilitate insertion reactions, but also allows reactions of dihydrogen with intermediate Pd–alkyl and/or Pd–acyl species. By a suitable choice of the ligand and acid, the reaction with dihydrogen can efficiently prevent copolymerization chain growth. Depending on the ligand and acid, the chain growth can be interrupted selectively at the Pd–acyl stage to produce aldehydes (and alcohols by further reduction) or at the second Pd–alkyl stage to produce monoketones. This class of catalysts thus provides a link between the Reppe-type olefin carbonylation chemistry and the Roelen-type oxo-chemistry.

We consider it worthwhile to comment on the interplay between the catalysts' ligand and anion and their effect on the course of the hydrocarbonylation reactions (chemo-selectivity). Subsequently, we will consider their role in the mode of olefin insertion at the palladium center, both in aldehyde–alcohol and ketone forming reactions (regio-selectivity).

3.1. Chemo-selectivity

3.1.1. Elementary steps in hydrocarbonylation

The catalyst systems we describe contain a square-planar d^8 16-electron palladium(II) center surrounded by a neutral *cis*-chelating diphosphine (L_2) and two anionic ligands (X^-). The anions are provided by the acid component of the catalyst via the reaction given in Eq. (3) [7].

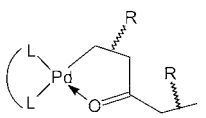
The proposed aldehyde- and ketone-forming reactions and their link to olefin–CO copolymerization have been summarized in Scheme 1. In analogy with the term hydroformylation for aldehyde–alcohol forming reactions, the ketone forming reactions can best be termed as hydro-acylation of olefins [11].

The actual active species in both hydroformylation and hydro-acylation is thought to be a cationic Pd–hydride complex L_2PdH^+, formed by heterolytic splitting of dihydrogen at the electrophilic palladium center of the precursor L_2PdX_2 (Eq. (5)).

$$L_2Pd^{2+}X_2^- \rightarrow L_2PdH^+X^- + HX \quad (5)$$

The next step would involve coordination of the olefin to the Pd hydride, followed by migratory insertion of the olefin to generate a Pd–alkyl complex L_2PdR^+. Coordination and subsequent migratory insertion of carbon monoxide then yields the Pd–acyl complex $L_2PdC(O)R^+$. It is at this stage that hydroformylation and hydro-acylation reactions are thought to diverge.

In hydroformylation, hydrogenolysis of the Pd–acyl bond takes place to give the aldehyde product and regenerate the hydride L_2PdH^+. In hydro-acylation, a second olefin molecule coordinates to the Pd–acyl, and migratory insertion gives an internally coordinated Pd–alkyl complex (see structure **1** below).



(1)

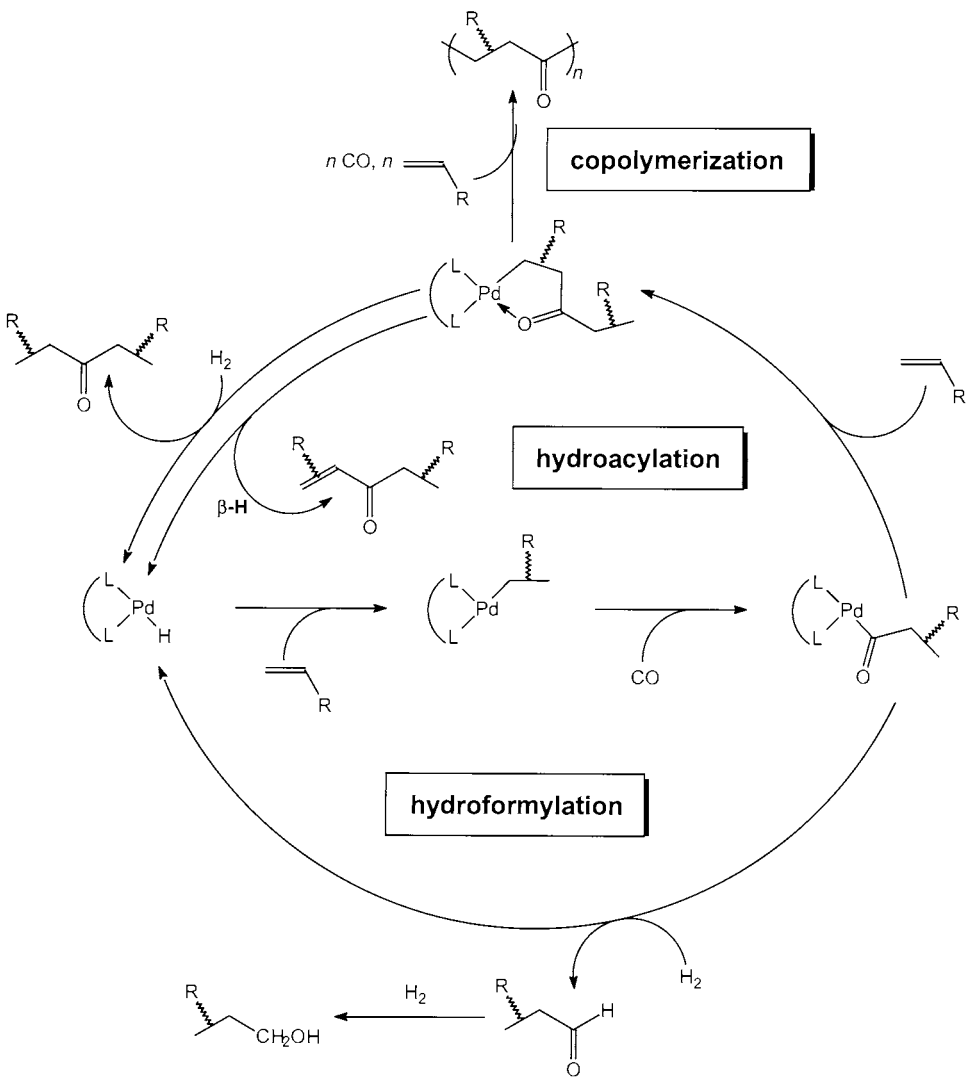
Stable species of this type have recently been observed spectroscopically in the studies of olefin insertion in L_2Pd–acyl complexes [12]. They are also thought to play a key role as intermediates in the alternating olefin–CO copolymerization. Termination of hydroacylation can proceed by hydrogenolysis of complex **1** to form a saturated ketone and regenerate the hydride L_2PdH^+. Alternatively, complex **1** can undergo β-elimination to give the hydride and an unsaturated ketone. These terminating reactions compete with further insertion steps to give oligo- or poly-ketones.

We will now discuss the factors which determine the fate of the crucial Pd–acyl intermediate.

3.1.2. The interplay of ligands and anions in electrophilicity

Inspection of Table 2 and Fig. 1 suggests that the steric properties of the ligand and anions are probably not a very crucial factor for the observed variation in chemo-selectivity. No correlation between chemo-selectivity and ligand size, as manifested by the estimated cone-angle [13] at the phosphorus atoms of the ligand, could be established. However, the steric properties of the ligand can indeed have a significant effect on regiochemistry in hydrocarbonylation, as will be discussed in Section 3.2.

Instead, Fig. 1 suggests that the electronic properties of both the neutral ligand L_2 and the anion X^- determine the course of hydrocarbonylation. An increasing ligand basicity should lead to a decreasing electrophilicity of the palladium(II) center. Likewise, weaker acids are generally associated with increasing coordination strength of the anion to the palladium center and also



Scheme 1. Proposed mechanisms of Pd-catalyzed hydroformylation, hydroacylation and olefin–CO copolymerization.

decrease the electrophilicity of the metal center. Apparently, highly electrophilic complexes are efficient copolymerization or hydroacylation catalysts, whereas less electrophilic complexes give rise to hydroformylation.

One essential requirement of the anions should be their easy displacement by reactants from the coordination sites around palladium. Too strong coordination, e.g. with halogen or weak carboxylic acids, leads to inactive catalysts (Table 2). Even when the anions can be displaced by the reactants, as evidenced by the observed catalytic activity, their basicity still affects chemoselectivity. It is thought that more basic anions stay in closer proximity to the palladium(II) center than less basic anions during the elementary steps of the catalytic cycle. For example, they could remain at or near a fifth coordination site below or above the coordination plane.

Cation–anion coordination, just like acidity, will depend on the reaction solvent. Thus, it can be understood that the OTs^- anion, as far as chemo-selectivity is concerned, behaves as a non-coordinating anion in a polar solvent, i.e. very similar to the non-coordinating OTf^- anion in a less polar solvent under the same conditions (see Table 2, experiments with DnBPP–1-octene). Cation–anion dissociation in methanol is facilitated by solvation, whereas in diglyme such ion-pairs stay in closer proximity.

3.1.3. Hydroformylation versus hydro-acylation

Apparently, selective hydroformylation requires a not too strongly electrophilic palladium center. This can be achieved by using a very basic ligand (DsBPP, DtBPP) and/or a not too poorly coordinating anion (e.g. TFA^-). It is interesting to note that, for one particular ligand (DsBPP, Table 5), the *selectivity* for hydroformylation increases with increasing coordination of the anion, whereas the *rate* of hydroformylation decreases, presumably because anion displacement at the palladium center becomes more difficult.

Selective hydro-acylation requires a more strongly electrophilic palladium center, such as achievable with basic ligands (DnBPP through DtBPP) in combination with a non-coordinating anion (OTf^-). The even more electrophilic palladium center obtained with OTf^- and the less basic DPPP ligand leads to oligo- or polyketones.

Since the catalytic cycles for hydroformylation and hydroacylation diverge at the Pd–acyl stage, the electrophilicity of the Pd center apparently determines the ratio of hydrogenolysis (to give aldehydes) and olefin insertion (to give ketones). A more electrophilic metal center appears to favor olefin insertion over hydrogenolysis. The substrate molecules (CO, olefin) can easily displace the weakly coordinating anion in $L_2Pd(acyl)(X)$. Carbon monoxide insertion in the Pd–acyl bond will not occur for thermodynamic reasons. However, once the olefin enters the coordination sphere, both a low barrier of insertion into the Pd–acyl bond and a strong thermodynamic driving force for olefin insertion are expected. The insertion product is stabilized by internal coordination of the β-carbonyl group to the metal center (structure **1**) [12]. Since part of this stabilization will already be felt in the transition state, the insertion barrier should be lower than for a normal olefin insertion. A more electrophilic metal center should therefore favor olefin insertion over hydrogenolysis.

However, this is probably not the whole story. Generally, hydro-acylation (with non-coordinating anions) proceeds with a somewhat *lower* rate than hydroformylation (with weakly coordinating anions). It is reasonable to expect that olefin insertion in the Pd–acyl bond represents the overall rate-determining step in hydroacylation. Therefore, it is thought that additional factors must come into play which make hydrogenolysis of the Pd–acyl less probable with catalysts containing non-coordinating anions. Hydrogenolysis of the Pd–acyl bond is thought to require the electrophilic activation of dihydrogen. One factor may be that strong coordination of CO and/or olefin under these conditions prevents the approach of dihydrogen. In addition, it could be that the coordinating anions giving rise to hydroformylation play an *active* role in the hydrogenolysis reaction. The *mechanism* of the Pd–acyl hydrogenolysis is not known, but we currently favor a pathway involving heterolytic H_2 dissociation at a single Pd center. This would produce a Pd(hydride)(acyl) complex, which could eliminate aldehyde and then react with H^+ to regenerate a palladium hydride [14] (a similar hydrogenolysis mechanism has been proposed for hydrogenolysis of ruthenium–acyl complexes [15]). The anion may assist the heterolytic dissociation by (temporarily) binding H^+. Non-coordinating anions like OTf^- are not basic enough to fulfill this role, and also do not stay close to the Pd center.

Thus, the ligand–anion combination affects the catalysis in a number of ways:

- By changing the electrophilicity of the metal center. More electrophilic catalysts tend to give higher hydroformylation rates, but at high electrophilicity hydroacylation is preferred.
- Coordinating anions block a coordination site and thus result in lower insertion rates.
- More basic anions assist hydrogenolysis and favor aldehyde formation.

The low activity of catalysts containing the strongly basic DtBPP as a ligand is noteworthy. With the more coordinating TFA^- anion, in particular, hydroformylation activity is negligible (Table 2). In this case, the palladium center seems to be too weakly electrophilic for the required heterolytic dihydrogen dissociation.

The alternative possibility of steric hindrance by the bulky phosphine during olefin insertion can be almost certainly excluded. When the hydroformylation of propene or 1-octene was attempted in the presence of methanol, methyl esters were produced exclusively and with high rate [16]. This proves that intermediate Pd–acyl species are not only formed rapidly but also undergo rapid alcoholysis by the already pre-polarized CH_3O^- H^+ molecule. Thus, the problem in this case seems to be hydrogenolysis of the Pd–acyl by the non-polar dihydrogen molecule. Apparently, electrophilicity of the palladium center and anion basicity have to work together for efficient heterolytic dissociation of dihydrogen.

Finally, we comment on the terminating hydrogenolysis of the Pd–alkyl bond to yield the monoketone hydro-acylation products. The chelate formation in structure **1** could affect the subsequent fate of the Pd–alkyl intermediate in a number of ways. On one hand, chelate formation could prevent or slow down termination by β-hydride elimination (to yield unsaturated ketones) or hydrogenolysis (to yield saturated ketones). Inhibition of β-H elimination in metallacycles is known [17]. For β-hydride elimination to occur the β-H atom has to approach the palladium ion, but this requires loss of Pd–O coordination. For hydrogenolysis, the dihydrogen molecule has to approach the palladium center. This process might therefore also be inhibited by strong carbonyl coordination to palladium. In the extreme case of high electrophilicity, with DPPP as ligand and OTf^- as anion (Table 2 and Fig. 1), termination indeed seems to be difficult, since significant amounts of *higher* ketones were obtained. The monoketone products in this case were mainly unsaturated, indicating termination by β-elimination.

On the other hand, it is also possible that chelate formation *assists* hydrogenolysis of the Pd–alkyl bond. This seems to be the case at intermediate electrophilicity, and thus moderately strong coordination of the chelating carbonyl group, with basic alkylphosphine ligands and weakly to non-coordinating anions. Here efficient and fast hydrogenolysis produces mainly *saturated* monoketones. The notion that chelating Pd–alkyl moieties can undergo rapid hydrogenolysis is supported by observations made with acrylic substrates. The insertion of these olefins in Pd–hydride immediately affords a five-membered chelate ring similar to structure **1**, but now involving the ester, acid or amide carbonyl group. With these substrates, unlike with aliphatic olefins, hydrogenation of the substrate *itself* strongly competes with hydrocarbonylation.

We suggest that the coordinated carbonyl group of the chelate ring can assist heterolytic H_2 dissociation by temporarily binding H^+. This would be similar to the proposed intermolecular assistance of the (weakly) basic anions as proton acceptors in Pd–acyl hydrogenolysis. The resulting Pd(hydride)(alkyl) species can eliminate the saturated ketone and then bind a proton to regenerate the cationic hydride. This assisted hydrogenolysis can occur after the *second* olefin insertion with *aliphatic* olefins, or already after the *first* insertion with *acrylic* olefins. The first insertion of aliphatic olefins, however, cannot follow this pathway, and therefore we find only a negligible amount of hydrogenation products with such olefins.

3.2. Regio-selectivity

In this section, we will consider the effects of the ligand and anion on the mode of olefin insertion at the palladium center, both in hydroformylation and hydroacylation reactions.

3.2.1. Hydroformylation

For hydroformylation, the regio-selectivity of olefin insertion at palladium can directly be related to the linearity of the product as given in Table 3. Obviously, linear hydroformylation products can only be obtained via 1,2-(*n*) insertion of olefins in Pd–hydride intermediates, whereas branched products are only accessible via 2,1-(*iso*) insertion. It can be seen from Table 4 that the *n*/*iso* insertion ratios of olefins in Pd–hydride clearly increase with increasing bulk of the ligand. For example, the C_2-bridged bidentate DsBPE affords a significantly lower preference for 1,2-insertion than the C_3-bridged ligand DsBPP.

These observations indicate that the mode of olefin insertion is determined primarily by the space available at the palladium center. It is thought that both olefin insertion in Pd–hydride and CO insertion in the Pd–alkyl bond are reversible [18] and that in subsequent aldehyde formation, the respective acyl intermediate is trapped irreversibly by hydrogenolysis (see also Section 3.2.2 for additional support of this proposal). Thus, formation and/or trapping of *n*-acyl intermediates is favored over that of the sterically more demanding *iso*-acyl intermediates.

The results given in Tables 4 and 5, indicate that the anion also has a distinct effect on the mode of olefin insertion at palladium. The stronger the basicity of anion, as judged from the pK_a of the associated acid, the greater is the observed product linearity both in propene and 1-octene hydroformylation.

As described earlier, it is suggested that the measure of coordination of the anion towards the palladium center determines the proximity of the anion and cation in apolar media. Therefore, the observed higher preference for *n*-acyl- over *iso*-acyl intermediates with the more coordinating anions could be a consequence of the greater congestion at the palladium center. It could also be that the anion-assisted hydrogenolysis reaction discriminates between a Pd–*n*-acyl and Pd–*iso*-acyl species, with more strongly coordinating anions favoring *n*-acyl hydrogenolysis.

Table 6
Regioselectivity in hydrocarbonylation [a]

Ligand	Acid	Olefin	Aldehydes [b]	Ketones [c]	
			1,2-Insertion (%)	1,2-Selectivity (%)	*n*-Acyl selectivity (%)
DPPP	TFA	Propene	72	–	–
DPPP	HOTs	Propene	62	65	74
DPPP	HOTf	Propene	–	64	78
DnBPP	HOTs	Propene	60	93	88
DnBPP	HOTf	Propene	–	92	88
DsBPP	TFA	Propene	84	–	–
DsBPP	HOTf	Propene	–	98	94
DsBPE	TFA	Propene	76	–	–
DsBPE	HOTf	Propene	–	90	89
DnBPP	TFA	1-Octene	70	–	–
DnBPP	HOTf	1-Octene	–	99	98
DPPP	TFA	Styrene	85	–	–
DPPP	HOTs	Styrene	84	0	98
DEPP	TFA	Styrene	72	–	–
DEPP	HOTf	Styrene	–	0	84
DnBPP	HOTf	Methyl acrylate	–	0	98
DEPP	HOTf	Methyl acrylate/1-octene	–	0 [d]	92 [e]

[a] Based on the data in Table 4.
[b] Percentage 1,2-insertion in Pd–H, percentage linear aldehydes + alcohols of total aldehydes + alcohols.
[c] Percentage 1,2-selectivity, percentage of 1,2-insertion in *any* Pd–acyl; percentage *n*-acyl selectivity, percentage of *any* insertion in a Pd *n*-acyl (see text).
[d] Percentage 1,2 acrylate insertion in Pd–nonoyl.
[e] Percentage acrylate insertion in Pd–*n*-nonoyl.

3.2.2. Hydro-acylation

Obtaining the regio-selectivity data from the isomer distribution of *ketone* products is somewhat more complicated. We will use propene hydroacylation as an example. Both saturated and unsaturated ketones are formed. The h to h ketones (both saturated and unsaturated) can only be formed by 2,1-insertion in Pd–hydride, followed by 1,2-insertion in Pd–acyl. Similarly, t to t isomers must be formed by 1,2-insertion followed by 2,1-insertion. The saturated h to t isomer, however, can be formed *either* by two 1,2-insertions *or* by two 2,1-insertions. Two different unsaturated isomers, h to t and t to h, can be formed, respectively by two 1,2-insertions *and* two 2,1-insertions. The percentage of all ketones formed via 1,2-insertion in *any* acyl is thus given by the amounts of (h to h) + (h to t) — the amount of saturated h to t isomer formed by double 2,1-insertions. From the structure of the unsaturated isomers, which is predominantly of the *iso*-propenyl-type for all catalysts, it can be concluded that there is a clear preference for 1,2-insertions in Pd–acyl. The correction for double 2,1-insertion is small but not negligible. In particular, with catalysts based on DPPP we have detected a small quantity of *n*-propenyl-*iso*-propylketone, which must have been formed by two consecutive 2,1-insertions. We approximate the percentage of double 2,1-insertion leading to *saturated* ketone by $0.01 \times (\text{h to h}) \times (\text{t to t})$ (%), so that the overall selectivity for 1,2-insertion in any acyl becomes:

$$(\text{h to t}) + (\text{h to h}) \times [1 - 0.01 \times (\text{t to t})] \ (\%).$$

Similarly, the selectivity for any insertion in an *n*-acyl is given by:

$$(\text{h to t}) + (\text{t to t}) \times [1 - 0.01 \times (\text{h to h})] \ (\%).$$

The latter selectivity, of course, corresponds with the apparent selectivity for 1,2 insertion in Pd–hydride of the first olefinic fragment in ketone formation. The selectivities calculated in this way from the data in Table 4 have been collected in Table 6. For comparison, the selectivity for 1,2-insertion in Pd–hydride in aldehyde formation is included in the table.

It can be seen from the results tabulated in Tables 4 and 6, that in hydro-acylation of aliphatic olefins there is a strong preference for h to t coupling of the olefinic fragments and this preference becomes larger with the steric bulk of the ligand. Thus, olefin insertion in both the Pd–hydride and the Pd–acyl bond is preferentially 1,2. Bulkier ligands and higher olefins (cf 1-octene vs. propene) strongly increase this preference, due to increased steric congestion at the palladium center. The aryl phosphine ligand DPPP has a surprisingly low regio-selectivity for 1,2-insertion in Pd–acyl, even though it is larger than the smallest alkylphosphine used in the examples. This suggests that not only steric, but also electronic factors (e.g. electrophilicity) are important. A two-methylene bridged ligand affords a lower preference for 1,2-insertion in Pd–acyl than a

three-methylene bridged ligand, consistent with the larger space available around the palladium center.

It can be seen from a comparison of the results on regio-selectivity in hydro-acylation with those in hydroformylation that the proportion of ketones derived from *n*-acyl intermediates is *consistently and substantially higher* than the proportion of *n*-aldehydes derived from the same intermediates. Whereas anion variation can shift the balance from the simultaneous production of aldehydes and ketones to pure ketone formation, the regio-selectivities for *olefin insertion in Pd–acyl* remain practically constant (Tables 4 and 6, see DPPP and DnBPP examples). This is an indication that both the olefin insertions in the Pd–hydride bond and CO insertions in the Pd–alkyl bonds are indeed reversible as suggested above. The acyl intermediate can, thus, be trapped either by hydrogenolysis to yield hydroformylation products or by olefin insertion to give an intermediate like **1** and eventually a ketone. Apparently, the olefin insertion reaction is more sensitive than hydrogenolysis to the steric difference between *n*- and *iso*-acyl intermediates, and therefore has a higher preference for trapping the *n*-acyl selectively. This preference becomes even higher with bulkier ligands or larger olefins.

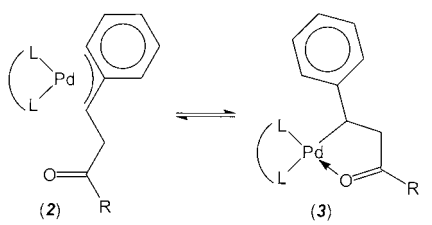
The degree of unsaturation of the product ketones reflects the relative rates of β-H elimination and hydrogenolysis (Scheme 1). The highest degree of unsaturation is consistently found in the h to h coupled ketone isomer. This may be related to the strength of the internal coordination of the carbonyl group in structure **1**. Above, we have argued that internal coordination stabilizes this structure and suppresses β-elimination. Substituents in both olefinic units of the intermediate (**1**) could destabilize the chelate structure and so promote β-elimination. This effect should be the largest for the h to h coupled ketone, where both substituents are closest to the carbonyl group. Apparently, hydrogenolysis is not hindered as much by chelate formation; as suggested above, this reaction could even be promoted by chelate coordination.

3.3. Hydrocarbonylation of functionalized olefins

The hydrocarbonylation of *styrene* shows no significant deviations from those of aliphatic olefins, discussed above, as far as chemo-selectivity is concerned (Table 3).

With respect to regio-selectivity, the proportion of ketones produced via styrene insertion in Pd–*n*-acyl is considerably higher than the proportion of linear aldehydes produced via the same Pd–*n*-acyl intermediate. This indicates that styrene, like aliphatic olefins, preferentially traps the *n*-acyl intermediate, presumably for steric reasons. However, a peculiar deviation from the aliphatic alkenes discussed above is seen in the regio-selectivity of insertion of styrene in the Pd–acyl bond (Tables 4 and 6). We find a high preference for t to t enchainment of the styrene moieties via carbonyl. This t to t ketone isomer can only be formed by 1,2-insertion in Pd–hydride and a consecutive 2,1-insertion in Pd–acyl intermediates. As the unsaturated h to t isomer observed is exclusively 1,4 diphenylpent-1-ene-3-one, it can be concluded that styrene insertion in Pd–acyl takes place exclusively in the 2,1-fashion. Ketones produced with similar catalysts containing bipyridyl type chelating ligands show the same selectivity [20], and 2,1-insertion of styrene in Pd–acyl bonds is also observed in styrene–CO copolymerization [19].

Thus, the most surprising aspect is that styrene, unlike aliphatic olefins, inserts into the Pd–acyl bond *exclusively* in a 2,1-fashion. One factor may be that the steric hindrance between the acyl group and the phenyl group in the 1,2-insertion transition state inhibits the 1,2 regio-chemistry. It could also be that the interaction between the palladium center and the phenyl ring during the insertion provides a lower-energy reaction pathway. Brookhart et al. [21] have shown that in styrene–CO copolymerization with bipyridyl containing catalysts, the intermediate after each styrene insertion exists as a rapidly exchanging mixture of allylic and chelate structures **2** and **3** ($K \approx 0.3$ at -80°C).



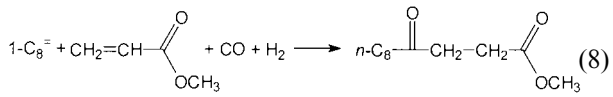
This indicates that allylic coordination is, indeed, quite strong and should favor 2,1-insertion in the Pd–acyl bond. Such an allylic coordination would, of course, also favor the initial 2,1-insertion of styrene in the Pd–H bond. However, if — as we believe — both this first insertion and the subsequent CO insertion are reversible, this does not affect the apparent regio-chemistry of the first insertion as observed in the final product.

It can be seen from Table 2, that *acrylic olefins* deviate from aliphatic olefins in chemo-selectivity: hydro-acylation dominates over hydroformylation even with the more coordinating TFA^- anions. Apparently, these olefins insert into the Pd–acyl bond very easily. Again, a strong preference is observed for t to t coupling. Thus, hydro-acylation of methyl acrylate produces 4-oxo-dimethylpimelate exclusively. The same regioselectivity is observed with acrylic acid and acrylamide. In these cases the primary hydro-acylation products can undergo a double cyclization, as indicated in Eq. (5), to form a di-spirolactone and a di-spirolac-

tam, respectively. These cyclizations may have occurred after hydroacylation itself. Alternatively, it is possible that the spiro-products are directly formed by the catalyst, similar to poly-spiro-ketal formation in the copolymerization of carbon monoxide with higher olefins using similar catalysts [22].

In any case, these products can only be formed via 1,2-insertion in Pd–hydride and 2,1-insertion in Pd–acyl intermediates (Table 6). As with styrene, it is suggested that both steric effects and the interaction of the electron-rich functionality with the electrophilic palladium center contribute to the observed high selectivity to α, ω-functionalized products.

The cross-hydro-acylation between acrylic olefins and aliphatic olefins also leads to the predominantly t to t coupled linear mixed ketone, i.e. methyl 4-oxo-dodecanoate with methyl acrylate and 1-octene (Tables 3 and 6, Eq. (8)).



(8)

In view of the results obtained with aliphatic and acrylic olefins separately, it is thought that the mixed t to t coupled ketone must be formed by 1,2 insertion of the aliphatic olefin (present in excess) in Pd–hydride followed by the very facile 2,1 insertion of the acrylic olefin in the Pd–C(O)-*n*-C_n acyl intermediate. The observed small quantity of h to t mixed ketone, methyl 4-oxo-5-methylundecanoate, must be formed by 2,1 insertion of 1-octene, also followed by 2,1 insertion of methyl acrylate. The 2,1 insertion of methyl acrylate, thus, selectively traps the *n*-C_8 acyl intermediate from an equilibrium mixture of *n*- and *iso*-C_8 acyl intermediates. This may, again, be attributed to the greater steric hindrance experienced by methyl acrylate for insertion in a Pd–iso-C_8-acyl intermediate.

4. Conclusions

The cationic palladium complexes, L_2PdX_2, previously shown to be excellent catalysts for the alternating copolymerization of olefins with carbon monoxide [7], owe their catalytic properties to the electrophilic nature of the palladium(II) center. The metal has a square-planar environment made up of the *cis*-chelating neutral ligand (L_2) and anionic ligands (X^-). *Cis*-chelation by the neutral ligand is considered essential for placing the intermediate palladium–hydride- and palladium–carbon bonds *cis* to the fourth coordination site available to a substrate molecule. This is an ideal situation for the migratory insertion of the substrate molecules to generate intermediate Pd–alkyl- and Pd–acyl species. In addition, this arrangement favors reductive elimination and oxidative addition steps, which may be involved in product generating termination steps like hydrogenolysis. The electrophilic palladium center not only can bind and activate nucleophilic molecules, such as olefins, carbon monoxide and alcohols, but also dihydrogen.

The possibility of interrupting the chain-growth of CO–olefin co-polymerization by an efficient chain-transfer with dihydrogen either at the Pd–alkyl or the Pd–acyl stage, forms the basis of the results on olefin hydrocarbonylation (oxo-synthesis) described in this paper. With these palladium catalysts, the oxo-synthesis can, thus, be fully exploited to produce, at choice, aldehydes–alcohols by hydroformylation or ketones by hydro-acylation.

We believe that the electrophilicity of the palladium center is a key parameter for chemo-selectivity control of the catalysis towards either reaction. Both the neutral ligand and the anions can be used to adjust the electrophilicity and the steric environment of the palladium center with high precision. Apart from this, it seems likely that the anions associated with the cationic palladium center play an important role of their own. Apparently anion basicity determines the efficiency of hydrogenolysis at the Pd–acyl stage.

The interplay between the neutral chelating ligand and the anion allows an almost perfect control over selectivity. Both chemo- and regio-control can be achieved; particularly in hydro-acylation, a nearly perfect selectivity to a single regio-isomeric ketone can be obtained. We have demonstrated the principles with only a limited number of ligands, anions and substrates, but it is clear that they can be extended to many other possible combinations. The application of chiral neutral and/or anionic ligands would be another logical extension. It can be expected that stereo-selective hydroacylation, in particular, is achievable, since stereoselective CO–olefin copolymerization has already been demonstrated [23].

Although we have rationalized most of the observed phenomena in a qualitative way it is clear that further detailed studies of the elementary steps involved in the catalysis are required to gain full insight into the factors that control rate and selectivity in the palladium catalyzed oxo-synthesis.

5. Experimental

5.1. Analytical equipment

Product analysis of reaction mixtures was routinely performed by gas–liquid chromatographic (GLC) analysis on a Perkin–Elmer 8500 equipped with two capillary columns, Chrompack 50 m CP-sil-5 and 50 m FFAP. Structural analysis was performed with GLC-

mass spectroscopic (GC/MS) analysis on a Finnagin-9610 gas chromatograph fitted with the CP-sil-5 column and coupled to a Finnigan-4000 triple-stage mass-spectrometer using electron impact ionization. This technique was applied to identify reaction products by comparison with authentic samples.

^{13}C-NMR spectra were recorded on a Bruker WM 250 spectrometer. ^{1}H- and ^{13}P-NMR spectra were recorded on a Bruker WM 250 spectrometer.

5.2. Materials

Palladium acetate, diglyme, THF, the Brønstedt acids, *p*-toluenesulfonic acid, methanesulfonic acid, trifluoroacetic acid and trifluoromethanesulfonic acid, 1-octene (p.a.), styrene (p.a.), methyl acrylate, acrylic acid and acryl amide were all obtained from Merck and were used as supplied. *t*-Butylsulfonic acid was prepared in house by oxidation of *t*-butylthiol with hydrogen peroxide. Of the phosphine ligands, DPPP was obtained from Strem, whereas DnBPP, DsBPP, DsBPE, DEPP and DtBPP were all synthesized by standard preparation techniques [24], involving the reaction between the respective di-alkylphosphine and 1,3 dibromopropane or 1,2 dibromoethane to give the double HBr salt of the respective di-phosphine. Neutralisation with sodium hydroxide, and subsequent destillation afforded the di-phosphine. Purity of the applied phosphines was always higher than 95% as observed with ^{1}H- and ^{31}P-NMR. Phosphine–monoxide was observed as the main impurity. The enantiomeric composition of DsBPP and DsBPE was statistical. The air-sensitive phosphines were all stored and handled in a Glove box under nitrogen. Propene of polymer grade quality was used and was obtained from in house sources. Commercial quality carbon monoxide (98%) and hydrogen ($>99\%$) were obtained from Air Products.

5.3. Batch autoclave procedure

All hydrocarbonylation experiments were carried out in 250 or 300 ml magnetically stirred Hastelloy™ C autoclaves, heated electrically. A typical experimental procedure was as follows.

In a nitrogen glove box, the catalyst components, 0.25 mmol (56.1 mg) palladium acetate, 0.6 mmol (199.6 mg) DsBPP were dissolved in 10 ml diglyme contained in a small sealable bottle. The components were allowed to react until no solid palladium acetate was visible. The solution was transferred in the closed bottle from the glove box and introduced in the autoclave prefilled with 40 ml degassed diglyme and 0.5 mmol (95.1 mg) *p*-toluenesulfonic acid (mono-hydrate), which was blanketed under a continuous stream of nitrogen. The autoclave was subsequently closed and evacuated. Liquid propene (30 ml) was pumped in the autoclave from a high pressure ISCO pump. Subsequently, the autoclave was first pressurized with 30 bar of CO and then with 30 bar of hydrogen.

In about 10 min, the autoclave was heated to 70°C and kept at this temperature by a Thermo-Electric 100 temperature control unit. The pressure was continuously recorded by using a Transamerica Instruments pressure transducer, series 2000. Activity data during the experiment were calculated from the pressure decrease in time and from GLC analysis of the reaction product at the end of a reaction period of 5 h. After that time, the autoclave was allowed to cool, depressurized and opened. Selectivity data were obtained from a standard analysis of the final reaction product by GLC. From these analyses it appeared that *n*-butanal and isobutanal were produced with a combined rate of about 150 mol mol^{-1} Pd h^{-1} and selectivity of 86%. The linearity of the aldehydes formed was determined from the $n/(n+iso)$ product ratio, being 77% in this case. The byproducts, 4-oxo-3-methylheptanal and *iso*-propenyl-*n*-propyl ketone (2-methylhex-1-ene-3-one) were identified by GC/MS analysis and were produced with a respective selectivity of 11 and 3%. Reaction rates can vary over time with the level of substrate conversion; the rate data in the tables are initial rates, averaged over a period corresponding to $<30\%$ conversion.

In the example above, the catalyst system was generated in situ by applying an excess of ligand over the stoichiometric quantity required by Eq. (3). Under the rigorous exclusion of oxygen, the same results could be obtained with stoichiometric complexes prepared in situ or in advance. We have observed that the application of some excess of ligand (and acid) leads to more robust catalysts, enabling easy handling under nitrogen blanketing to achieve reproducible, stable catalyst performance.

Whereas reaction product analysis in general was performed with GLC-MS, some of the less common products, such as dimethyl 4-oxopimelate, di-spirolactone and di-spirolactam were isolated from reaction media and characterized by ^{1}H- and ^{13}C-NMR to provide additional structural evidence.

5.3.1. Di-methyl 4-oxo-pimelate

Following the procedure described above, a solution of 30 ml of methylacrylate in 30 ml diglyme–20 ml methanol was introduced in the autoclave. Subsequently, catalyst components, 0.25 mmol (56.1 mg) palladium acetate, 0.3 mmol DnBPP and 0.5 mmol (75.1 mg) HOTf were introduced under nitrogen. After closure of the autoclave it was pressurized with 30 bar CO and 30 bar H_2 and heated to 75°C for 5 h. After cooling to room temperature and slow depressurizing, the autoclave was opened and its content was cooled to -5°C overnight. Di-methyl 4-oxopimelate (12 g) was

recovered by filtration as colorless needles. ^{13}C-NMR ($CDCl_3$, 300Mhz: δ(*C*H3–O) 51.8 ppm, δ(CH_3O–*C*=O) 173.5 ppm, δ(CH_3O–C(O)–*C*H_2–) 27.7 ppm, δ(–*C*H_2–C(O)–) 37.1 ppm; ^{1}H-NMR ($CDCl_3$, 200MHz): δ(C*H*$_3$O–) 3.6 ppm (s), δ(–C(O)–C*H*$_2$–) 2.5 ppm (t), δ(–C*H*$_2$–C(O)–) 2.7 ppm (t).

5.3.2. Di-spirolactone

The same procedure with 10 ml of acrylic acid as the substrate and 30 ml of diglyme as solvent, was followed with the synthesis of di-spirolactone. After cooling and addition of an equal volume of cyclohexane, 4.5 g of di-spirolactone was recovered as a white solid: ^{13}C-NMR($CDCl_3$, 300 MHz) δ(–O–*C*=O) 174.5 ppm, δ(–O–C(O)–*C*H_2–) 27.8 ppm, δ(–O–C(O)–CH_2–*C*H_2–) 32.3 ppm, δ((–CH_2–)$_2$*Cspiro*(–O–)$_2$) 112.7 ppm.

5.3.3. Di-spirolactam

Following the same procedure with 15 g of acryl amide, instead of acrylic acid, yielded 7.4 g of di-spirolactam as a white crystalline solid: ^{13}C-NMR (D2O, 300 MHz), δ(–N(H)–*C*=O) 180.6 ppm, δ(–N(H)–C(O)–*C*H_2–) 25.7 ppm, δ(–N(H)–C(O)–CH_2–*C*H_2–) 42.8 ppm, δ((–CH_2)$_2$–*Cspiro*–(N(H)–)$_2$) 62.4 ppm; ^{1}H-NMR (D_2O, 200 MHz) δ(–N(*H*)–C(O)–) 7.7 (weak due to D/H exchange with D_2O), δ(–C(O)–C*H*$_2$–) 2.2 (br), δ(–C(O)–CH_2–C*H*$_2$–) 1.6 (br).

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