Olefin Carbonylation Catalysis with Cationic Palladium Complexes: Selectivity and Possible Intermediates

Martin Sperrle and Giambattista Consiglio*

Eidgenössische Technische Hochschule, Laboratorium für Technische Chemie,
ETH Zentrum, CH-8092 Zürich

Received Mai 14, 1997

Keywords: Carbonylations / Alkenes / Palladium / Asymmetric catalysis / P and N ligands

Palladium complexes L_2PdX_2 containing various group Va ligands and weakly coordinating anions are active catalysts for the carbonylation of olefin substrates. These catalytic systems, though gaining significance in industry for the synthesis of polyketones, are normally characterised by a low chemoselectivity. This derives from the numerous possibilities for initiation and termination reactions which lead to different catalytic cycles and from facile multiple alternating insertion reactions of olefins and carbon monoxide. Based on experiments carried out under conditions of low selectivity and on previously published data, the factors involved in the control of the regio-, chemo- and stereoselectivity for those reactions are discussed, taking current ideas and model studies involving the above palladium complexes into consideration.

Introduction

Carbonylation reactions of olefins are the basis of many synthetic transformations, which are highly significant for industrial and laboratory processes[1]. In this context, palladium catalysis is of particular significance, and is widely used in the laboratory, whereas important commercial applications seem to be rare[2][3]. Hydro-alkoxycarbonylation, catalysed by palladium complexes of the type L_2PdX_2 (X = halide) has been known for a long time[4], but the reaction conditions have usually been rather severe[5]. Therefore, with few exceptions, good control of the regiochemistry and stereochemistry of the reaction has not been achieved[6][7].

The catalytic precursor properties of complexes of the above type, where X is an anionic ligand that can be displaced easily in a second coordination sphere, have not been investigated to the same extent[8]. However, in the last decade there has been growing interest in these types of systems,

Giambattista Consiglio (right) was born in Foggia, Italy, in 1941. He had his university education in Pisa where he obtained the title of doctor in industrial chemistry in 1965 and where he remained for a postdoctoral appointment until 1967. After service in the army he joined the group of Prof. P. Pino at the ETH-Zürich at the end of 1968. He was appointed as a professor of inorganic chemistry at the university of Cagliari in 1980. Back at the ETH in 1982 he obtained the professor title in 1988. He was visiting scientist at the Central Research and Development Department, DuPont, Wilmington (De), U.S.A. in 1986. His research interests are in the field of the stereochemistry of organotransition metal compounds mostly in connection with aspects of homogeneous catalysis.

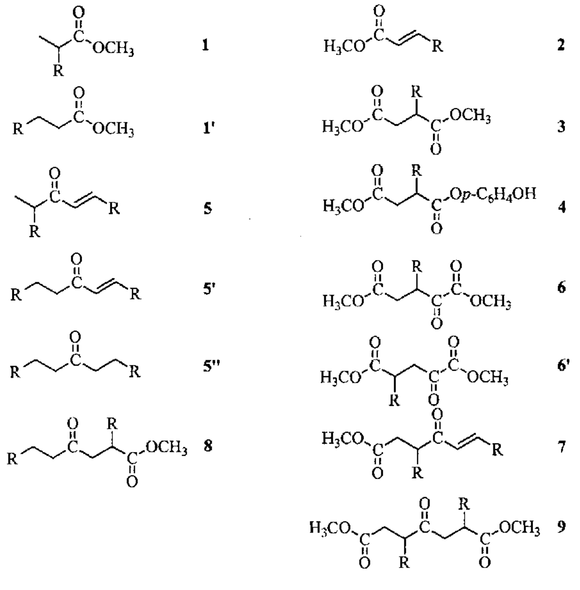
Martin Sperrle (left) obtained his "Vordiplom" in 1987 from the University of Tübingen. After one year of doing research in the group of Prof. Dr. F. Calderazzo at the University of Pisa, Italy (coordination chemistry of early transition metals), he returned to Tübingen for his "Hauptdiplom" exam. He then carried out his "Diplomarbeit" at the Laboratoire de Chimie de Coordination du CNRS in Toulouse, France under the supervision of Dr. D. Ballivet-Tkatchenko and Prof. Dr. J. Strähle (the use of tin alkoxides as catalyst precursors for the synthesis of dimethylcarbonate). In 1993 he started his doctorate studies at the ETH Zürich with Prof. Dr. G. Consiglio on enantioselective palladium-catalysed carbonylations of olefins. As a Feodor-Lynen-Fellow of the Alexander-von-Humboldt-Foundation he is currently a postdoctoral fellow at Stanford University, USA with Prof. Dr. B. M. Trost. The project deals with the application of ruthenium catalysts in organic synthesis.

MICROREVIEWS: This feature introduces Berichte's readers to the authors' research through a concise overview of the selected topic. Reference to important work from others in the field is included.

0009–2940/97/1111–1557 $ 17.50+.50/0

probably due to their recent industrial application for the synthesis of Carilon, an alternating olefin–carbon monoxide terpolymer based mostly on ethene[9]. Moreover, due to the fact that copolymers of 1-olefins are chiral[10], interest in enantioselective copolymerisation has grown[11][12][13][14][15][16]. It is peculiar that the most successful application in the field of palladium-catalysed olefin carbonylation is concerned with a reaction in which chemoselectivity is a secondary factor. In fact, for a copolymerisation process initiation and termination are less important, since they are related to minor events (see below)[17]. However, the benefit of these cationic palladium complexes for olefin carbonylation has been shown recently[18][19]. In fact, we have achieved a highly enantioselective synthesis of succinates[20] and of oxo-glutarates[21] through multiple carbonylation of olefins and a selective synthesis of ketones[22]. The fact that very similar reaction conditions are applied for those syntheses prompted us to look for non-chemoselective reaction conditions for olefin carbonylation reactions which could help clarify the crucial matter of the actual catalytic palladium intermediates involved. This could lead to a better understanding of aspects related to monomer insertion. Such experiments should allow the compilation of a list of compounds which, although formed under the same conditions, display different chemo-, regio-, and stereoselectivite effects. Figure 1 summarises carbonylation products other than the styrene copolymer which have been identified during carbonylation reactions of styrene (R = C_6H_5).

Figure 1. Various carbonylation products from 1-olefins[a]



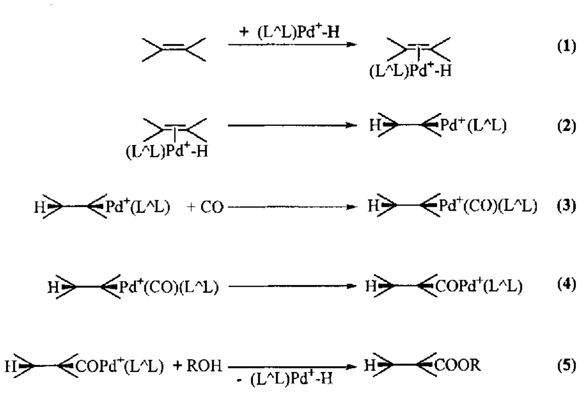
[a] **a**: R = C_6H_5; **b**: R = CH_3.

The factors responsible for chemo-, regio-, and enantioselectivity during carbonylation reactions catalysed by cationic palladium complexes are analysed in this paper along with their dependence on the reaction conditions used. Some of the problems that still need to be solved are also outlined. The discussion is mostly based on the use of styrene as a substrate although some comparison with aliphatic olefins, in particular propene, is also made. As the starting point for our discussion we will use an account by Milstein[23], which addressed the question of whether the species responsible for hydro-alkoxycarbonylation are metal hydrides (M–H) or metalcarbalkoxy species (M–COOR) or both[24].

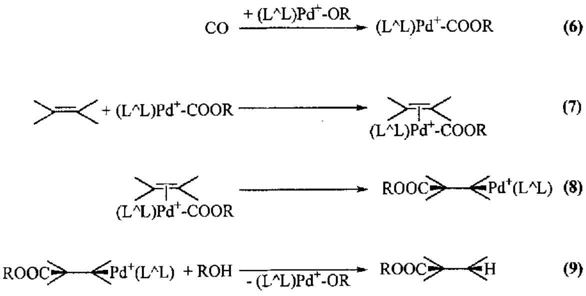
Hydridopalladium vs. (Alkoxycarbonyl)palladium Intermediates

Schemes 1 and 2 show the two alternative mechanistic descriptions of olefin hydro-alkoxycarbonylation in which cationic palladium complexes containing chelate ligands act as the initiating species.

Scheme 1. Hydride route for hydro-alkoxycarbonylation

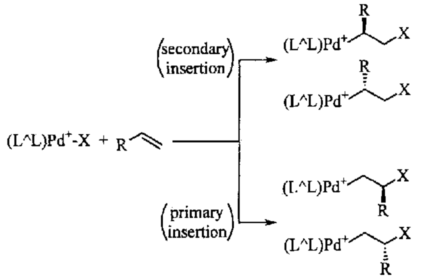


Scheme 2. Carbalkoxy route for hydro-alkoxycarbonylation



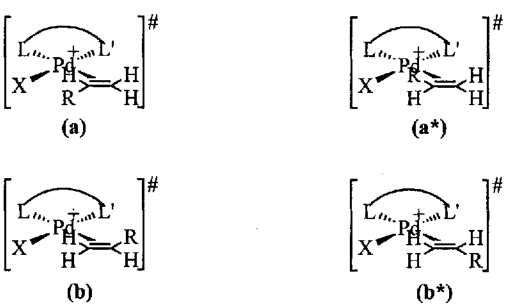
Both mechanistic routes appear possible, and at present there is no clear-cut experimental evidence which allows the true pathway to be identified[24]. That both initiating species, $(L^\wedge L)Pd^+-H$ and $(L^\wedge L)Pd^+-COOR$, are simultaneously possible is demonstrated by the analysis of the copolymerisation products of ethene with carbon monoxide. Indeed, chains containing two carbalkoxy, two alkyl or one alkyl and one alkoxy termination have been shown to be present[17][25][26][27]. The question is a very important one since it involves a consideration of the regiochemistry of the insertion of the olefin substrate into two different species (eqs. 2 and 8 and Scheme 3) and, therefore, with different steric and electronic requirements. Furthermore, olefin insertion in a Pd–H species is quite often reversible and, for the present systems in particular, the reaction has been claimed to be highly reversible[17]. Regio- and stereoselectivity of the carbonylation process is therefore not determined before the insertion of carbon monoxide. It has been argued recently that this may be a reason for rather low enantioselectivities during asymmetric hydro-alkoxycarbonylation[28]. On the other hand, proof of the reversibility of olefin insertion in palladium−acyl or in palladium−carbomethoxy species are very rare[29].

Scheme 3. Possible intermediates due to the insertion of a 1-olefin into an (L^L)Pd$^+$−X bond



Let us first consider enantioface discrimination of the insertion in either palladium species. On the basis of a simple model for insertion, based on a coordinated olefin leading to a four-centre intermediate[30], one might intuitively expect that discrimination caused by the presence of elements of chirality would be more effective when the groups at which the double bond is inserted are large (Scheme 4). This is supported by the identification of the factors determining stereoselectivity for olefin insertion in the related Ziegler−Natta catalysis[31]. In this case, an effective enantioface discrimination of the substrate is possible only with a minimum size of the growing chain. Therefore, a hydro-alkoxycarbonylation catalysis running exclusively via a (L^L)Pd$^+$−COOR intermediate might be envisaged as a possible solution to the problem of low enantioface discrimination during olefin insertion in the synthesis of substituted propanoates.

Scheme 4. Model for olefin insertion during carbonylation (X = H, COOR or CO−; L = or ≠L')



One way to switch the mechanism of the hydro-alkoxycarbonylation is to add an oxidant. The latter is believed to transform the palladium hydride species (L^L)Pd$^+$−H into the corresponding palladium−carbalkoxy species (L^L)Pd$^+$−COOR according to eq. 10 and eq. 6[26]. Indeed, it has been shown that in the copolymerisation reaction of ethene the amount of carbalkoxy termination increases when the concentration of an oxidant is increased without influencing the molecular weight[17]. In contrast, when styrene is the substrate, with a catalytic system containing 1,10-phenanthroline as the ligand, the presence of excess oxidants was found to cause not only a shift towards ester end-groups, but also a decrease in the molecular weight of the products formed[19][32][33][34]. In particular, when the catalyst precursors contained diphosphine ligands, only low molecular weight products were formed (Figure 1).

$$(L\hat{}L)Pd^+\text{-}H + ROH + \text{"Ox"} \longrightarrow (L\hat{}L)Pd^+\text{-}OR + \text{"Ox"}H2 \qquad (10)$$

The various carbonylation products summarised in Figure 1 are divided into two groups. The formation of the products on the left-hand side of the figure does not require the presence of an oxidant and therefore does not necessarily imply initial olefin insertion in a (L^L)Pd$^+$−COOR species. In particular, only hydride cycles should be involved in the formation of the ketones **5a**, **5'a** and **5"a** (eqs. 1−4 and Scheme 5).

Scheme 5. Pathways for the formation of ketones

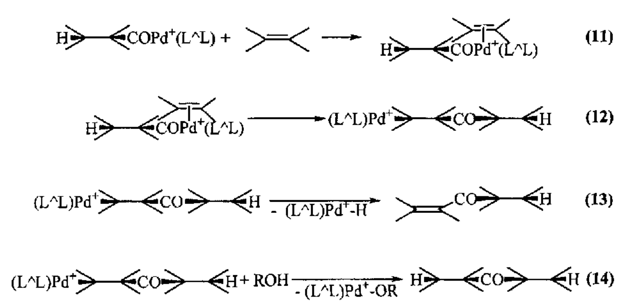


Table 1 reports the results of experiments aimed at the carbonylation of styrene using [{(*S*)-MeO-Biphep}Pd(H_2O)$_2$](OTf)$_2$ [MeO-Biphep is (6,6'-dimethoxy biphenyl-2,2'-diyl)bis(diphenylphosphine)][8] as the catalyst precursor and carried out using different amounts of oxidant (usually 1,4-benzoquinone) and of catalyst. The presence of increased amounts of 1,4-benzoquinone has two effects; we observed an increased conversion of styrene and an increased selectivity towards products, the formation of which implies a cycle starting with a (L^L)Pd$^+$−COOR species. The selectivity for products for which the catalytic cycle undoubtedly starts with (L^L)Pd$^+$−H, namely the ketones **5**, decreases. It is most interesting that the other two products for which a decreased selectivity is observed are the monoesters **1** and the ketoester **8**.

These observations suggest that, as expected, the oxidant is able to transform (L^L)Pd$^+$−H into a (L^L)Pd$^+$−COOR species (eqs. 10 and 6) and that the insertion of the olefin into the latter species is more productive in terms of carbonylation products. Moreover, it seems that the hydro-alkoxycarbonylation of olefins is a process which is probably not accessible when starting with a (L^L)Pd$^+$−COOR species but usually needs to start with a (L^L)Pd$^+$−H species. In fact, the formation of the saturated ketone **5"a** (eq. 14) shows that protonation is possible after olefin insertion but is a minor event with respect to β-hydrogen elimination (consider the **5'a**:**5"a** molar ratios and the formation of **2a**)[35].

Table 1. Influence of the concentration of the oxidant (1,4-benzoquinone) and of the catalyst on the enantioselective carbonylation of styrene (data in%) using $[\{(S)\text{-MeO-Biphep}\}Pd(H_2O)_2](OTf)_2$ as the catalyst precursor [a]

[catalyst] /mmol	[styrene] /[oxidant]	conv.	Σ 1 [1'a:1a]	1a ee	Σ 5 [5'a:5a:5"a]	5a ee	8a [8a ee]	2a	3a [3a ee]	4a	7a	9a	6a
0.140	1	71	2 [50:50]	28 (S)	4 [76:14:10]	38	1 [33]	12	56 [91 (S)]	1	12	12	--
0.140	10	20	16 [42:58]	39 (S)	21 [79:17:4]	30	10 [42]	6	36 [91 (S)]	--	5	6	--
0.035	8	12	—	—	—	—	—	6	48 [92 (S)]	1	3	3	37 [91]
0.035	2	40	—	—	—	—	—	2	68 [93 (S)]	8	1	2	19 [92]
0.070	2	64	1 [43:57]	29 (S)	2 [77:14:9]	48	1 [42]	4	48 [92 (S)]	3	3	8	30 [92]
0.140	2	60	4 [44:56]	33 (S)	7 [80:15:5]	54	3 [41]	11	51 [93 (S)]	1	11	12	—

[a] Reaction conditions: 35 mmol styrene; 20 ml CH_3OH; T = 50°C; reaction time = 20h; 350 bar CO.

Table 2. Influence of the nature of the anion on the enantioselective carbonylation of styrene (data in%) using $[\{(S)\text{-MeO-Biphep}\}Pd(H_2O)_2](X)_2$ as the catalyst precursor [a]

anion X {complex}	conv.	Σ 1 [1'a:1a]	1a ee	Σ 5 [5'a:5a:5"a]	5a ee	8a [8a ee]	2a	3a [3a ee]	4a	7a	9a	6a [6a ee]
$CF_3SO_3^-$	60	4 [44:56]	33 (*S*)	7 [80:15:5]	54	3 [41]	11	51 [93 (*S*)]	1	11	12	—
BF_4^-	63	3 [50:50]	30 (*S*)	3 [78:14:8]	61	1 [39]	12	53 [91 (*S*)]	—	14	14	—
p-$CH_3C_6H_4SO_3^-$	53	4 [41:59]	30 (*S*)	10 [85:9:6]	39	4 [41]	10	51 [92 (*S*)]	2	8	11	—
$CF_3CO_2^-$	48	—	—	—	—	—	12	66 [92 (*S*)]	6	4	7	5 [92]

[a] Reaction conditions: 35 mmol styrene; 20 ml CH_3OH; [styrene]/[catalyst] = 250; [styrene]/[1,4-benzoquinone] = 2; T = 50°C; reaction time = 20h; 350 bar CO.

Table 2 shows the influence of the nature of the anion on chemoselectivity. The results demonstrate the influence of the anion on the relative concentration (and/or activity) of the two initiating species. With the trifluoroacetate anion, which is the most strongly coordinating anion[35], suppression of the hydride cycles takes place.

Most important with the catalytic system used, and as far as we know with all systems containing phosphine ligands, the yield of products containing more than two olefin units is essentially zero[35].

Nature of the Catalytic Species: Mono- vs. Binuclear

Model investigations of palladium complexes similar to those involved in the present study seem to infer that the catalytic species are of the type $[(L^\frown L)Pd^+{-}R(Solv)]^+X^-$[36]. However, compounds of the type $[\{L^\frown L\}Pd(H_2O)_2](X)_2$ are usually used as the catalyst precursor[37][38]. At the very beginning it was observed that these compounds transform rather easily into binuclear species with possible concurrent reduction[39][40]. The possibility of the involvement of species of higher nuclearity during the catalytic cycles is usually revealed by the influence of the catalyst concentration on the normalised activity and on the selectivity of the reactions.

The last three entries in Table 1 show that, in this case, a decrease in the catalyst concentration is not accompanied by the expected loss in catalytic activity. In contrast, the turnover number with respect to converted styrene increases, while the concentration of the palladium precursor decreases. Furthermore, the chemoselectivity shifts towards the formation of products not involving initiating hydride species. It is remarkable that, even when the concentration of the catalyst precursor was low, decreasing the amount of oxidant, to the disadvantage of the $(L^\frown L)Pd^+{-}COOR$ cycle, did not lead to the formation of olefin carbonylation products as a result of initiating $(L^\frown L)Pd^+{-}H$ species (Table 1, entry 3).

Recent investigations of the catalyst precursor used for the experiments in Table 1 showed that these complexes transform in methanol and under carbon monoxide pressure into the binuclear species $[\{L^\frown L\}Pd(\mu{-}H)(\mu{-}CO)Pd\{L^\frown L\}](X)$ [41][42][8]. Such species are considered to be a palladium (II) hydride stabilised by palladium (0) species[41]. No transformation was observed for these compounds in the presence of styrene ($L^\frown L$ is dppp or bdpp)[42]. Despite this, when $L^\frown L$ was dippp they were found to exchange the bridging hydrogen with olefins[41], thus suggesting that olefin insertion into the metal–hydride bond is indeed possible but rapidly reversible, possibly due to the low stability of the insertion product. Furthermore, previous investigations using labelled styrene suggest reversible insertion of the olefin into a metal hydride species both for ester **1** and for ketone **5** formation[19]. The influence of the concentration of the catalyst precursor on the chemoselectivity of the olefin carbonylation reaction (Table 1) suggests that binuclear species may be involved in the catalysis through hydride cycles but not in the alternative carboalkoxy cycles. Whether these stable binuclear palladium species[41][42] represent actual catalytic intermediates or serve, as mentioned below, as a reservoir for the highly reactive and unstable mononuclear palladium hydride species requires further investigation. It is noteworthy, however, that an increase in productivity was observed in the copolymerisation of ethene with carbon monoxide by decreasing the catalyst concentration[37][43].

Olefin Insertion

Styrene as the Substrate

The results discussed above infer that, depending on the reaction involved, insertion of the olefin into a palladium−hydride, $(L^\frown L)Pd^+-H$, intermediate or into a palladium−alkoxycarbonyl, $(L^\frown L)Pd^+-COOR$, intermediate occurs and that the former type of insertion is probably involved as the first step in hydro-alkoxycarbonylation (Scheme 1). Consider the relationship of the regio- and stereochemistry of the two types of insertion to the nature of the possible products when styrene is used as the substrate (Scheme 3). The data in Table 1 show that productive styrene insertion into $(L^\frown L)Pd^+-H$ is much less regioselective than into $(L^\frown L)Pd^+-COOR$ (or more generally into a $(L^\frown L)Pd^+-CO-X$ species), at least on the basis of the composition of the isomeric products, the formation of which infers without doubt the nature of the initiating species. Only secondary insertion (Scheme 3) into $(L^\frown L)Pd^+-CO-X$ species, i.e., in the formation of **2a**, **5a**, **5'a**, and **5"a**, and **7a**, is observed. Due to the absence of regioisomers of **4a**, **6a**, **8a**, and **9a**, it is concluded that only one type of regioselectivity of the insertion is involved. Considering the similarity of both series of products, the most probable type of insertion for the latter series is also secondary . In the absence of isomers of **4a**, **6a** and **2a**, we assume that a secondary insertion is also involved in the formation of **3a** (see below).

Insertion into $(L^\frown L)Pd^+-H$ to give the esters **1** does not shown any particular regioselectivity, the isomer ratio being close to unity. In contrast, regioselectivity in the formation of ketones **5a**, **5'a**, and **5"a** is largely in favour of a primary insertion. The reasons for this difference in regioselectivity are not clear. However, if we assume that the same catalytic species are involved in the formation of the esters and the ketones, then we conclude that the selectivity must be driven by the step following carbon monoxide insertion. The formation of acyl species should therefore be reversible (Curtin−Hammett conditions)[44].

It is remarkable that, depending on the type of ligand used, the regioselectivity of the first olefin insertion in the formation of the ketones **5a**, **5'a**, and **5"a** (insertion into a $(L^\frown L)Pd^+-Pd-H$ species) can be controlled to a large extent[22][45]. In contrast, we observed practically no effect of the ligand on the regioselectivity of the insertion of the second olefin unit. The regioselective synthesis of syndiotactic poly[1-oxo-2-phenylpropane-1,3-diyl] was found to be a consequence of exclusive secondary insertions of the substrate[32]. No system is known in which regioirregular styrene−carbon monoxide copolymers are obtained, even if primary insertion seems possible when P N ligands are used, as demonstrated by the existence of terminations arising from β-hydrogen elimination[46].

Let us return to the problem of the enantioface discrimination of insertion into both species. The model described in Scheme 4 suggests that, in the most simple case (L=L'), there is competition among four different transition-states and the control of regio- and enantioselectivity is related[47]. With the atropisomeric ligand used, we observed (Table 1) a good enantioface discrimination in the formation of **3a** and **6a** (ca. 96:4) but a much less effective discrimination for the formation of **1a**, **5a**, and **8a**. Accordingly, for this ligand, there is a larger and more efficient enantioface discrimination when the insertion takes place between the groups which are largest in size (i.e., for $(L^\frown L)Pd^+-COOR$ vs. $(L^\frown L)Pd^+-H$). We have already identified ligands for which the opposite is true; however, in this case, only a fair asymmetric induction was achieved[48]. The factors determining the final enantioselectivity may be very different for the two pathways. Theoretical calculations made on the evolution of hydridic species for the ethene−carbon monoxide alternating copolymerisation suggest that hydrido-olefin-π-complexes $(L^\frown L)Pd^+-H(Olefin)$ do not represent true intermediates (Scheme 1, eq. 1), whereas acyl-olefin-π-complexes $(L^\frown L)Pd^+-(CO-)(Olefin)$ do[49][50]. On the other hand, the reversibility of the olefin insertion into the palladium−hydride species causes enantioselectivity to be determined by the next irreversible step, probably not the carbon monoxide insertion (see below).

Another important aspect is related to the influence of the reaction variables on the enantioface discrimination. In addition to the results in Tables 1 and 2, Table 3 describes the influence of carbon monoxide partial pressure on the enantioselective carbonylation. The enantioface discrimination remains high and substantially invariant in the formation of **3a** and **6a** (ca. 96:4) but does show some dependence on the reaction conditions for **1a**, **5a**, and **8a**. Unfortunately, only the absolute configurations of **1a** and **3a** are known; moreover, we did not succeed in identifying the enantiomeric excess of **4a**, **7a**, and **9a**. However, it was possible to evaluate the diastereoselectivity in the formation of the dimeric species **9a** which remained substantially constant at around 80 to 85%. We assume that the dominant diastereomer of the codimer **9a** is the *l*-diastereomer, since the opposite diastereomer is formed using the 1,10-phenantroline ligands under conditions in which the syndiotactic poly(1-oxo-2-phenyl-1,3-propanediyl) is simultaneously produced[33].

Aliphatic Olefins

The most important differences observed in the carbonylation of aliphatic olefins (such as propene) with the same $[\{(S)\text{-MeO-Biphep}\}Pd(H_2O)_2](OTf)_2$ catalyst precursor under reaction conditions similar to those used for styrene are the formation of oligomeric and polymeric materials corresponding to alternating insertions of the aliphatic olefin and carbon monoxide. The poor regioselectivity control of the insertion of the olefin into $(L^\frown L)Pd^+-CO-X$ bonds is also of importance[45]. As far as the regioselectivity of the olefin insertion into the $(L^\frown L)Pd^+-COOR$ species is concerned, the formation of both isomeric glutarates **6b** and **6'b** is always observed[21]. Consistent with the interplay between regio- and enantioselectivity discussed above, the asymmetric induction in the formation of the succinates **3b** is lower than that observed for at least one of the two possible glutarates. Furthermore, not only the codimer **9b**, but

Table 3. Influence of the carbon monoxide pressure on the enantioselective carbonylation of styrene (data in%) using [{(*S*)-MeO-Biphep}Pd(H_2O)$_2$](OTf)$_2$ as the catalyst precursor [a]

pressure / bar	conv.	Σ **1** [**1'a**:**1a**]	**1a** ee	Σ **5** [**5'a**:**5a**:**5"a**]	**5a** ee	**6a** [**6a** ee]	**2a**	**3a** [**3a** ee]	**4a**	**7a**	**9a**	**6a** [**6a** ee]
50	40	2 [36:64]	23 (*S*)	11 [82:7:11]	37	1 [2]	42	36 [91 (*S*)]	1	6	1	—
125	44	3 [40:60]	28 (*S*)	7 [81:10:10]	31	2 [17]	26	47 [91(*S*)]	1	10	4	—
250	50	4 [49:51]	32 (*S*)	8 [72:11:17]	52	3 [34]	15	48 [91 (*S*)]	1	12	10	—
350	60	4 [56:44]	33 (*S*)	7 [80:15:5]	54	3 [41]	11	51 [93 (*S*)]	1	11	12	—

[a] Reaction conditions: 35 mmol styrene; 20 ml CH_3OH; [Styrene]/[catalyst] = 250; [Styrene]/[1,4-benzoquinone] = 2; T = 50°C; reaction time = 20h.

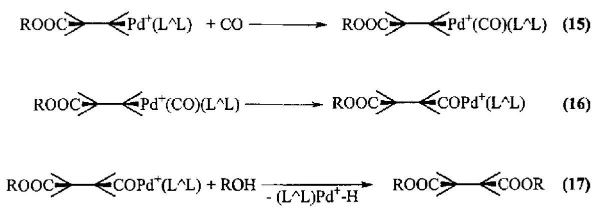
also the other two possible regioisomers have been identified[45]. The preferred regioselectivity of the insertion of propene into the (L^L)Pd^+-CO- species is primary; however, in the formation of the low molecular weight compounds a regiospecific insertion has never been observed, irrespective of the ligand used. The use of more basic diphosphine ligands (i.e., diphosphine ligands having alkyl substituents at the phosphorus centre) causes a further shift in the regioselectivity towards primary insertion; however, a completely regiospecific, most probably primary, insertion is observed only for the copolymerisation reaction[11]. A similar effect is observed for enantioface discrimination. In the formation of the codimers (**9b** and regioisomers) as well as the two 2-oxo-glutarates (**6b** and **6'b**) a lower level of enantioselectivity with respect to the formation of the copolymers is observed[51]. A regiospecific primary insertion of propene into a palladium−acetyl bond was observed at low temperature for a complex containing a phosphine−phosphite chelate ligand (L^L')Pd^+-COCH_3][14]. This system also catalyses the highly enantioselective and completely regioselective formation of poly[1-methyl-2-oxopropane-1,3-diyl]. However, preliminary investigations[52] show that the system is not regioselective under conditions leading to the 2-oxo-glutarates (**6b** and **6'b**)[21] and to the codimers (**9b** and regioisomers thereof)[45].

Carbon Monoxide Insertion

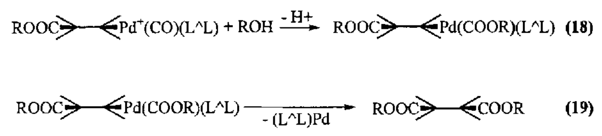
For the processes discussed in this paper, the step corresponding to the insertion of carbon monoxide (e.g., Scheme 1, eq. 4) should provide the initial control for the regio- and enantioselectivity of the olefin insertion. However, experiments[53] and theoretical calculations[49][50] suggest that the insertion of carbon monoxide into a Pd−C(sp^3) bond is rapidly reversible. Therefore, the possible influence of the concentration of carbon monoxide on those selectivities is of mechanistic significance. As already stated, the carbon monoxide partial pressure does not influence the enantioselectivity during the formation of **3a** and **6a** (ca. 96:4) but does for **1a**, **5a** and **8a**. Moreover, there is also no change in the diastereoselectivity during the formation of the dimeric species **9a**.

The lack of influence of the carbon monoxide concentration on the enantioselectivity of the formation of the succinate **3a** (and also of the glutarate **6a**) can be easily understood on the basis of Scheme 6. If we assume the existence of a single catalytic species and that step 8 (Scheme 2) is irreversible, then a change in the concentration of carbon monoxide should not influence the diastereomeric ratio of the species shown in Scheme 6 with respect to that formed in step 8. Model reactions suggest possible alternatives for the formation of the succinates (Scheme 7)[54]. A possible competition between the two pathways (eqs. 16 and 17 vs. eqs. 18 and 19) cannot be inferred easily from the present data.

Scheme 6. Route for bis-alkoxycarbonylation of olefins to succinates

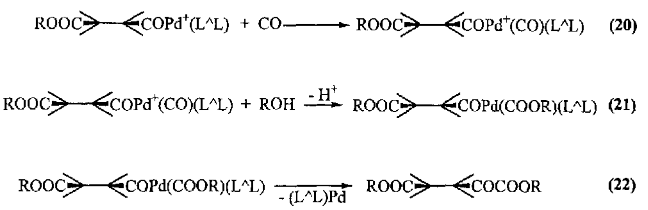


Scheme 7. Alternative route for bis-alkoxycarbonylation of olefins to succinates



Remarkably we observe the same enantioselectivity in the formation of both **3a** and **6a**; this strongly suggests that both compounds probably derive from the same reaction intermediate. Furthermore, when the carbon monoxide pressure was increased, we observed an increased yield of **6a** at the expense of **3a**. Formation of the 2-oxoglutarate **6a** could arise from steps corresponding to two successive insertions of carbon monoxide after olefin insertion. Based on model compound studies[55][56][57] and theoretical calculations[49][50][58] this is considered to be unfavourable. Therefore, the formation of the glutarates **6** is described according to Scheme 8[21], starting with the intermediate formed in eq. 16 that is also responsible for the formation of the succinate. It is noteworthy that species similar to that formed in eq. 20 (Scheme 8) correspond to the catalyst resting-state during the copolymerisation of olefins with carbon monoxide[14]. Interestingly, the diastereoselectivity during the formation of **9a** is lower than that expected if the enantioface discrimination were the same for both olefin units and as high as in the formation of succinates and glutarates. Even though we cannot exclude kinetic resolu-

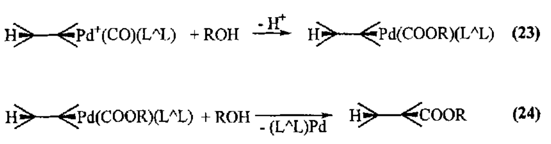
Scheme 8. Triple carbonylation of olefins to 2-oxoglutarates



tion effects leading to either **7a** or **9a**, this decreased stereoselectivity might result from some bias of the first inserted styrene unit toward *ul*-enchainment, as happens in the synthesis of syndiotactic poly[1-oxo-2-phenylpropane-1,3-diyl][59].

The influence of carbon monoxide pressure on the regio- and enantioselectivity of the formation of the esters **1′a** and **1a** has precedents in the field of carbonylation[5]. The results were interpreted assuming either the existence of different catalytic species having a different carbon monoxide to chiral-ligand molar ratio or to relatively slow reversibility of the olefin insertion (Scheme 1, eq. 2) with respect to the rate of carbon monoxide insertion (Scheme 1, eq. 4) (absence of Curtin–Hammett regime)[60]. Similar explanations might be proposed for the formation of the ketones **5a** and **5′a** (and **5″a**). With our catalytic systems, an excess of ligands was not observed to have an effect on the stereochemical outcome of the reaction. We cannot, however, determine whether or not our conditions correspond to the Curtin–Hammett regime. As far as hydro-alkoxycarbonylation is concerned, a possible alternative might be the competition of another mechanism not involving an acylation step (Scheme 9).

Scheme 9. Hydride route (eqs. 1–3) for hydro-alkoxycarbonylation not involving acyl formation



Much more puzzling is the influence of the reaction variables on the enantioselectivity of the formation of **8a**. Based on the regioselectivity of the internal olefin unit and on the fact that when this compound is not formed **1** and **5** are also not formed, we believe that this product derives from the intermediate formed in eq. 12, followed by the reactions shown in Scheme 6 or 7. The much lower enantioselectivity for the insertion of styrene into a (L^L)$Pd^+-CO-CH_2CH_2Ph$ than into a (L^L)Pd^+-COOR species was somewhat surprising; furthermore, no influence of the carbon monoxide pressure on the enantioselectivity was expected due to the very probable nonreversibility of the olefin insertion. Therefore, we assume that kinetic resolution effects, which imply competition between the formation of **8a** vs. **5′a** after the second styrene insertion, are operative.

Completion of the Catalytic Cycles

The following termination reactions must be considered for the palladium catalysis of the carbonylation of olefins. When methanol is present, termination reactions can take place which lead either to carbomethoxy (e.g. eq. 5) or to hydrocarbyl end-groups (e.g. eq. 4). Otherwise β-hydrogen elimination, leading to unsaturated end-groups, is the termination event if the unsaturated ligand thus formed is released (e.g. eq. 13)[46][51]. The role of possible reductive elimination reactions[54] (e.g. eq. 24) remains to be established. Considering the products shown in Figure 1 and taking into account that the catalytic systems involved are known to copolymerise olefins with carbon monoxide, the control of chemoselectivity is strongly related to the possibility of influencing the relative reaction rates of monomer insertions with respect to termination events. In this context, it is noteworthy that, in all cases, we observed the complete alternation of olefin and carbon monoxide insertion. The factors responsible for this alternation have been investigated both experimentally and theoretically[49][50][57][58]. In fact, the production of the 2-oxoglutarates **6** does not seem to imply consecutive carbon monoxide insertions[21].

The potentially unsaturated nature of the catalytic complexes makes β-hydrogen elimination facile. With styrene as the substrate, diphosphine ligands cause somewhat slower olefin insertion than termination with respect to dinitrogen ligands such as 2,2′-bipyridine or 1,10-phenanthroline[33]. This therefore allows a fairly chemoselective synthesis of the succinate[20] or the ketones[35]. Under appropriate reaction conditions (low temperature in aprotic solvents), the latter catalytic systems were even found to exhibit the characteristics of living polymerisation for the copolymerisation of 4-*tert*-butylstyrene[61]. Carbon monoxide insertion between palladium and a benzylic secondary carbon atom is apparently not difficult[32]. Competitive β-hydrogen elimination is relatively slow but always seems to cause breaking of chain growth[46]. In contrast, carbon monoxide insertion seems to be rather difficult when the secondary carbon atom is bound to an alkyl substituent. This causes low molecular weights for cyclic[62] and internal olefins[16] and gives rise to preferential 1,3-enchainment. This type of enchainment has also been observed for propene when the ligands of the catalytic system used do not cause regioselective primary insertion[63]. These results, however, show that β-hydrogen elimination does not always cause dissociation of the unsaturated ligands thus formed.

Final Remarks

An important aspect of the results discussed is that we now have the potential for synthesis of different products in an enantioselective way. It is evident that we have realized the first enantioselective synthesis of succinates, ketones and polyketones, 4-oxo-pimelates and 2-oxoglutarates through very simple carbonylation reactions with rather good enantioselectivities. A major task in the near future will be modelling of the catalysts and improvement of the reaction conditions in order to realise the goal of a good chemoselectivity for the multiple carbonylation reactions[64] discussed here.

The results reported suggest that a hydride route is responsible for the formation of mono-esters. Alkoxycarbonyl intermediates, even if their formation is possible and can be forced by the presence of the oxidant under the conditions used, do not guarantee the necessary regioselectivity of the insertion for styrene in order to produce a chiral ester. For aliphatic olefins regioselectivity would be appropriate for attaining this goal, but the necessary chemoselectivity appears difficult to achieve.

Finally, the problems aring from the observation that e.g. the propene–carbon monoxide alternating copolymer forms exclusively as a polyiro-2,5-(3-methyltetrahydrofuran)][65] and that this structure is less stable than the isomeric poly[1-methyl-2-oxopropane-1,3-diyl] deserves to be tackled[16][66][67][68].

---

[1] H. M. Colquhoun, D. J. Thompson, M. V. Twigg, *Carbonylation. Direct Synthesis of Carbonyl Compounds*, Plenum Press, New York 1991.

[2] J. Tsuji, *Palladium Reagents and Catalysts - Innovations in Organic Synthesis*, John Wiley & Sons, New York 1995.

[3] J. Tsuji, *Synthesis* **1990**, 739–749.

[4] K. Bittler, N. V. Kutepow, D. Neubauer, H. Reis, *Angew. Chem.* **1968**, *80*, 352–359; *Angew. Chem. Int. Ed. Engl.* **1968**, *7*, 329–335.

[5] G. Consiglio, in I. Ojima (Ed.): *"Catalytic Asymmetric Synthesis"*, VCH, New York 1993, p. 273–302.

[6] S. Oi, M. Nomura, T. Aiko, Y. Inoue, *J. Mol. Catal. A-Chem.* **1997**, *115*, 289–295.

[7] H. Zhou, S. Lu, J. Hou, J. Chen, H. Fu, H. Wang, *Chem. Lett.* **1996**, 339–340.

[8] M. Sperrle, V. Gramlich, G. Consiglio, *Organometallics* **1996**, *15*, 5196–5201.

[9] [9a] E. Drent, *Eur. Pat. Appl.* 121 965 (1984) (*Chem. Abstr.* **1985**, 102, 4623). – [9b] A. Sen, T. -W. Lai, *J. Am. Chem. Soc.* **1982**, *104*, 3520–3352. – [9c] A. Wakker, H. G. Kormelink, P. Verbeke, J. C. M. Jordaan, *Kunststoffe* **1995**, *85*, 1056–1064.

[10] A. Batistini, G. Consiglio, U. W. Suter, *Polym. Mater. Sci. Eng.* **1992**, *67*, 104–105.

[11] S. Bronco, G. Consiglio, R. Hutter, A. Batistini, U. W. Suter, *Macromolecules* **1994**, *27*, 4436–4440.

[12] M. Brookhart, M. I. Wagner, G. G. A. Balavoine, H. A. Haddou, *J. Am. Chem. Soc.* **1994**, *116*, 3641–3642.

[13] E. Amevor, S. Bronco, G. Consiglio, S. Di Benedetto, *Macromol. Symp.* **1995**, *89*, 443–454.

[14] K. Nozaki, N. Sato, H. Takaya, *J. Am. Chem. Soc.* **1995**, *117*, 9911–9912.

[15] S. Bartolini, C. Carfagna, A. Musco, *Macromol. Rapid Commun.* **1995**, *16*, 9–14.

[16] Z. Jiang, A. Sen, *J. Am. Chem. Soc.* **1995**, *117*, 4455–4467.

[17] E. Drent, J. A. M. van Brockhoven, M. J. Doyle, *J. Organomet. Chem.* **1991**, *417*, 235–251.

[18] E. Drent, *Pure Appl. Chem.* **1990**, *62*, 661–669.

[19] G. Consiglio, S. C. A. Nefkens, C. Pisano, *Inorg. Chim. Acta* **1994**, *220*, 273–281.

[20] S. C. A. Nefkens, M. Sperrle, G. Consiglio, *Angew. Chem.* **1993**, *105*, 1837–1838; *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 1719–1720.

[21] M. Sperrle, G. Consiglio, *J. Organomet. Chem.* **1996**, *506*, 177–180.

[22] C. Pisano, A. Mezzetti, G. Consiglio, *Organometallics* **1992**, *11*, 20–22.

[23] D. Milstein, *Acc. Chem. Res.* **1988**, *21*, 428–434.

[24] V. V. Grushin, *Chem. Rev.* **1996**, *96*, 2011–2033.

[25] E. Drent, J. A. M. van Broekhoven, M. J. Doyle, P. K. Wong, in G. Fink, R. Mühlhaupt, H. H. Brintzinger (Eds.): *Ziegler Catalysts*, Springer-Verlag, Berlin Heidelberg 1995, p. 481–494.

[26] E. Drent, P. H. M. Budzelaar, *Chem. Rev.* **1996**, *96*, 663–681.

[27] E. Drent, J. A. M. van Broekhoven, P. H. M. Budzelaar, *Recl. Trav. Chim. Pays-Bas* **1996**, *115*, 263–270.

[28] I. Tóth, C. J. Elsevier, J. G. de Vries, *10th International Symposium on Homogeneous Catalysis* (Princeton, New Jersey USA), **1996**, pp. PP–A5 .

[29] B. A. Markies, D. Kruis, M. H. P. Rietveld, K. A. N. Verkerk, J. Boersma, H. Kooijman, M. T. Lakin, A. L. Spek, G. van Koten, *J. Am. Chem. Soc.* **1995**, *117*, 5263–5274.

[30] D. L. Thorn, R. Hoffmann, *J. Am. Chem. Soc.* **1978**, *100*, 2079–2090.

[31] A. Zambelli, C. Pellecchia, L. Oliva, *Makromol. Chem., Macromol. Symp.* **1991**, *48/49*, 297–316.

[32] M. Barsacchi, G. Consiglio, L. Medici, G. Petrucci, U. W. Suter, *Angew. Chem.* **1991**, *103* 992–994; *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 989–991.

[33] C. Pisano, S. C. A. Nefkens, G. Consiglio, *Organometallics* **1992**, *11,* 1975–1978.

[34] V. Busico, P. Corradini, L. Landriani, M. Trifuoggi, *Makromol. Chem., Rapid Commun.* **1993**, *14*, 261–266.

[35] C. Pisano, G. Consiglio, *Gazz. Chim. Ital.* **1994**, *124,* 393–401.

[36] G. P. C. M. Dekker, C. J. Elsevier, K. Vrieze, P. W. N. M. van Leeuwen, C. F. Roobeek, *J. Organomet. Chem.* **1992**, *430,* 357–372.

[37] C. Pisano, G. Consiglio, A. Sironi, M. Moret, *J. Chem. Soc., Chem. Commun.* **1991**, 421–423.

[38] F. Benetollo, R. Bertani, G. Bombieri, L. Toniolo, *Inorg. Chim. Acta* **1995**, *233*, 5–9.

[39] J. A. Davies, F. R. Hartley, S. G. Murray, G. Marshall, *J. Mol. Cat.* **1981**, *10,* 171–176.

[40] P. H. M. Budzelaar, P. W. N. M. van Leeuwen, C. F. Roobeek, A. G. Orpen, *Organometallics* **1992**, *11* 23–25.

[41] [41a] M. Portnoy, F. Frolow, D. Milstein, *Organometallics* **1991**, *10*, 3960–3962. – [41b] M. Portnoy, D. Milstein, *Organometallics* **1994**, *13*, 600–609.

[42] I. Tóth, C. J. Elsevier, *Organometallics* **1994**, *13*, 2118–2122.

[43] A. Vavasori, L. Toniolo, *J. Mol. Catal. A-Chem.* **1996**, *110*, 13 -23.

[44] J. I. Seeman, *Chem. Rev.* **1983**, *83,* 83–134.

[45] M. Sperrle, G. Consiglio, *J. Am. Chem. Soc.* **1995**, *117,* 12130–12136.

[46] M. Sperrle, A. Aeby, G. Consiglio, A. Pfaltz, *Helv. Chim. Acta* **1996**, *79,* 1387–1392.

[47] P. Pino, A. Stefani, G. Consiglio, in B. Pullman (Ed.): *Catalysis in Chemistry and Biochemistry. Theory and Experiment*, Reidel, D., Dordrecht 1979, p. 347–354.

[48] S. C. A. Nefkens, Dissertation No. 9939, ETH, Zürich, Switzerland, 1992.

[49] P. Margl, T. Ziegler, *J. Am. Chem. Soc.* **1996**, *118,* 7337–7344.

[50] P. Margl, T. Ziegler, *Organometallics* **1996**, *15,* 5519–5523.

[51] S. Bronco, G. Consiglio, *Macromol. Chem. Phys.* **1995**, *197,* 355–365.

[52] M. Sperrle, unpublished results, 1996.

[53] E. Drent, J. A. M. van Broekhoven, P. H. M. Budzelaar, in B. Cornils, W. A. Herrmann (Eds.): *Applied Homogeneous Catalysis with Organometallic Compounds, Vol. 1*, VCH, Weinheim 1996, p. 333–335.

[54] [54a] I. Tóth, C. J. Elsevier, *J. Am. Chem. Soc.* **1993**, *115*, 10388–10389. – [54b] I. Tóth, C. J. Elsevier, *J. Chem. Soc., Chem. Commun.* **1993**, 529–531.

[55] [55a] J.-T. Chen, A. Sen, *J. Am. Chem. Soc.* **1984**, *106*, 1506–1507. – [55b] A. Sen, J.-T. Chen, W. M. Vetter, R. R. Whittle, *J. Am. Chem. Soc.* **1987**, *109*, 148–156.

[56] [56a] A. Yamamoto, F. Ozawa, K. Osakada. L. Huang, T. Son, N. Kawasaki, M. -K. Doh, *Pure Appl. Chem.* **1991**, *63*, 687–696. – [56b] A. Yamamoto, *Bull. Chem. Soc. Jpn.* **1995**, *68*, 433–446.

[57] F. C. Rix, M. Brookhart, P. S. White, *J. Am. Chem. Soc.* **1996**, *118*, 4746–4764.

[58] M. Svensson, T. Matsubara, K. Morokuma, *Organometallics* **1966**, *15*, 5568–5576.

[59] P. Corradini, C. De Rosa, A. Panunzi, G. Petrucci, P. Pino, *Chimia* **1990**, *44,* 52–54.

[60] A. Scrivanti, V. Beghetto, A. Bastianini, U. Matteoli, G. Menchi, *Organometallics* **1996**, *15*, 4687–4694.

[61] M. Brookhart, F. C. Rix, J. M. DeSimone, J. C. Barborak, *J. Am. Chem. Soc.* **1992**, *114*, 5894–5895.

[62] E. Amevor, R. Bürli, G. Consiglio, *J. Organomet. Chem.* **1995**, *497*, 81–89.

[63] A. Batistini, Thesis, Università di Pisa, Italy, 1991.

[64] A. Yamamoto, T. Yamamoto, F. Ozawa, *Pure Appl. Chem.* **1985**, *57*, 1799–1808.

[65] A. Batistini, G. Consiglio, *Organometallics* **1992**, *11*, 1766–1769.
[66] P. K. Wong, J. A. van Doorn, E. Drent, O. Sudmeijer, H. A. Stil, *Ind. Eng. Chem. Res.* **1993**, *32*, 986–988.
[67] S. Bronco, G. Consiglio, S. Di Benedetto, M. Fehr, F. Spindler, A. Togni, *Helv. Chim. Acta* **1995**, *78*, 883–886.
[68] M. W. Holtcamp, J. A. Labinger, J. E. Bercaw, *J. Am. Chem. Soc.* **1997**, *119*, 848–849

[97117]