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Highly Linear-Selective Hydroformylation of 1-Alkenes using Formaldehyde as a Syngas Substitute

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Abstract: A highly linear-selective hydroformylation of 1-alkenes using formaldehyde without the direct use of syngas is described. One rhodium(I) complex catalyzes two processes in the overall hydroformylation of 1-alkenes using formaldehyde as the syngas substitute to give hydroformylated aldehydes with excellent regioselectivities. A high regioselectivity (linear/branched = up to 98/2) and chemical yield (up to 95%) can be achieved by the simultaneous use of two types of phosphanes as ligands.

Keywords: alkenes; formaldehyde; homogeneous catalysis; hydroformylation; rhodium

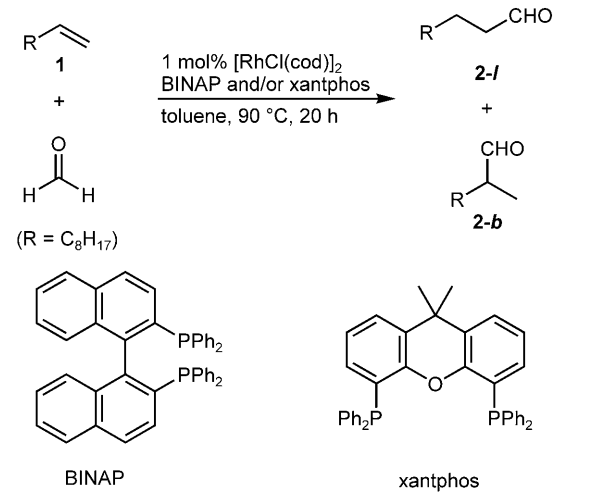
Hydroformylation involves the addition of carbon monoxide and hydrogen (CO/H_2, syngas) to alkenes in the presence of a transition metal catalyst to give homologous linear (***l***) and/or branched (***b***) aldehydes.[1] Because of its versatility, it represents synthetic routes to various aldehydes that are useful in a wide range of areas from fine and specialty chemicals production to pharmaceuticals synthesis.[2] Since the discovery of the reaction by Roelen in 1938,[3] considerable efforts have been devoted to the development of new catalysts including new ligands and the utilization of novel reaction media, such as the use of an aqueous biphase, supercritical carbon dioxide, fluorous biphase, or ionic liquids, in attempts to improve the efficiency and selectivity (regio- and enantioselectivity) of the reaction. A recent innovation in this chemistry involves the development of a protocol using formaldehyde (HCHO) as a syngas substitute. This promises to be an experimentally convenient alternative to the transformation. Some reports have appeared regarding the use of paraformaldehyde in hydroformylation reactions without the direct use of syngas,[4,5,6] although they have not yet afforded synthetically useful levels of productivity and regioselectivity.[7] The method using formaldehyde consists of two cooperative catalytic processes: the catalytic decarbonylation of formaldehyde to give a carbonyl moiety and hydrogen, and their use in the subsequent hydroformylation of alkenes. Regardless of the complexity involved in the overall catalysis, the aforementioned reports have used only a single catalyst for the two different processes. It is, however, possible that two discrete catalysts could be used in the decarbonylation and hydroformylation processes. Herein we wish to report on a highly selective, highly efficient hydroformylation without the direct use of syngas by using two different types of catalysts, which are suitable for each process.

In order to simultaneously generate two types of rhodium catalysts in one reaction system, we adopted a strategy in which two different rhodium species are generated *in situ* by adding two phosphanes to a single rhodium complex. For the success of the strategy, it is essential that the decarbonylation process is controlled by one phosphane more strongly than the other and that the hydroformylation process is reversed. BINAP was a promising candidate as an effective ligand for a rhodium catalyst in the decarbonylation process, because it is known that the rhodium complex having BINAP is a more efficient catalyst for the decarbonylation of aldehydes than xantphos.[8] In addition, we also have recently reported that the use of BINAP ligand facilitates a rhodium(I)-catalyzed CO gas-free carbonylation reaction using paraformaldehyde as the CO substitute.[5e] Towards a regioselective hydroformylation process, we selected xantphos, which is a representative ligand for the ex-

tremely highly linear-selective hydroformylation catalyzed by a rhodium complex.[9]

We initially carried out the rhodium-catalyzed hydroformylation reaction of 1-decene (**1**) with formalin under the catalytic conditions consisting of $[RhCl(cod)]_2$, BINAP, and xantphos: **1** (1 mmol), formalin (0.37 mL of 37 wt% aqueous solution, 5 mmol equivalents to formaldehyde), $[RhCl(cod)]_2$ (0.01 mmol), BINAP (0.02 mmol), xantphos (0.02 mmol) in toluene (6 mL) at 90 °C for 20 h. The reaction proceeded with an extremely high regioselectivity to give the linear aldehyde **2-*l*** and the branched aldehyde **2-*b*** in 80% yield in a ratio of **2-*l*/2-*b*** = 97/3, along with 18% of isomers of 1-decene (Table 1, entry 1).[10] In contrast, the use of BINAP or xantphos resulted in a low selectivity or a low efficiency (entries 2 and 3). These results indicate that, when a combination of BINAP and xantphos was used, each phosphane functions uniquely and specifically (BINAP in the decarbonylation and xantphos in the hydroformylation), to achieve the highly linear-selective hydroformylation, as we expected.

Table 1. Effective use of a combination phosphanes in Rh(I)-catalyzed hydroformylation of 1-decene **1** using formalin.[a]



Entry	BINAP	xantphos	Conv.[b]	Yield (**2-*l*/2-*b***)[b]
1	2 mol%	2 mol%	98%	80% (97/3)
2	4 mol%	–	85%	85% (64/36)
3	–	4 mol%	77%	8% (88/12)

[a] *Conditions:* **1** (1 mmol), formalin (37%; 0.37 mL, 5 mmol), $[RhCl(cod)]_2$ (0.01 mmol), ligand (0.04 mmol), toluene (6 mL), 90 °, 20 h.

[b] Yields are the sum of **2-*l*** and **2-*b***. Values in parentheses are the ratios of **2-*l*/2-*b***. Conversions, yields, and ratios were determined by GC. cod = 1,5-cyclooctadiene; BINAP = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl; xantphos = 9,9-dimethyl-4,5-bis(diphenylphosphino)xanthene.

Next, we investigated the effect of BINAP or xantphos on the efficiency and selectivity of hydroformylation using syngas. Using BINAP and/or xantphos as ligand(s), the turnover frequency (TOF) in the early stage (1 h) of the hydroformylation of 1-decene (**1**) with atmospheric syngas was examined: 1-decene (1 mmol), $[RhCl(cod)]_2$ (0.005 mmol), and phosphane(s) (0.02 mmol) in toluene (6 mL) under atmospheric syngas ($CO/H_2 = 1/1$) at 90 °C for 1 h. When only BINAP was used as a ligand, linear (**2-*l***) and branched (**2-*b***) aldehydes were formed in a ratio of **2-*l*/2-*b*** = 65/35 (TOF = 3.05 h^{-1}). When only xantphos was used, the reaction proceeded much more smoothly (TOF = 19.9 h^{-1}) to give these aldehydes with a high linear-selectivity of **2-*l*/2-*b*** = 93/7. Furthermore, the use of a combination of BINAP (0.01 mmol) and xantphos (0.01 mmol) resulted in a slight decrease in the reaction rate (TOF = 10.9 h^{-1}), although the linear-selectivity (**2-*l*/2-*b*** = 94/6) remained the same. These findings suggest that, for the simultaneous use of BINAP and xantphos, the rhodium species associated with the xantphos ligand controls the regioselectivity and the efficiency of the overall reaction.

Furthermore, ^{31}P NMR experiments (Figure 1) implied that two rhodium species participate in the reaction of entry 1 in Table 1. A mixture of $[RhCl(cod)]_2$, (*R*)-BINAP, and xantphos (1:2:2) in toluene-d_8 at room temperature showed two signals at $\delta = 49.5$ ppm (d, $J_{P,Rh} = 195$ Hz) and 2.3 ppm (d, $J_{P,Rh} = 91$ Hz), which correspond to $[RhCl((R)\text{-BINAP})]_2$[11] and RhCl(cod)(xantphos),[12] respectively. When 100 equivalents of formalin were added to the mixture, these signals vanished, and two new signals appeared at $\delta = 45.6$ ppm (dd, $J_{P,P} = 45$ Hz, $J_{P,Rh} = 160$ Hz) and 20.9 ppm (d, $J_{P,Rh} = 127$ Hz), which are assigned to RhCl(CO)((*R*)-BINAP)[11b] and $RhH(CO)_2$(xantphos),[9] respectively. These two rhodium species, RhCl(CO)((*R*)-BINAP) and $RhH(CO)_2$(xantphos), would be directly involved in the linear-selective hydroformylation catalysis using formaldehyde in the presence of both BINAP and xantphos.

From the above results, an acceptable reaction pathway is as follows. Thus, the present reaction includes two catalytic processes: the decarbonylation of formaldehyde leading to the formation of a carbonyl moiety and H_2 and subsequent hydroformylation using the resulting carbonyl moiety and H_2 (Scheme 1). Each process proceeds in a general manner. Oxidative addition of the aldehydic C–H bond in formaldehyde to Rh, followed by decarbonylative hydride migration and subsequent reductive elimination, yields an Rh-CO species and H_2. On the other hand, addition of *in situ* generated Rh-H species to 1-alkene and subsequent insertion of the carbonyl formed earlier, followed by hydrogenolysis by H_2, afford the aldehyde with the regeneration of the Rh-H species. These are taken up by two different rhodi-

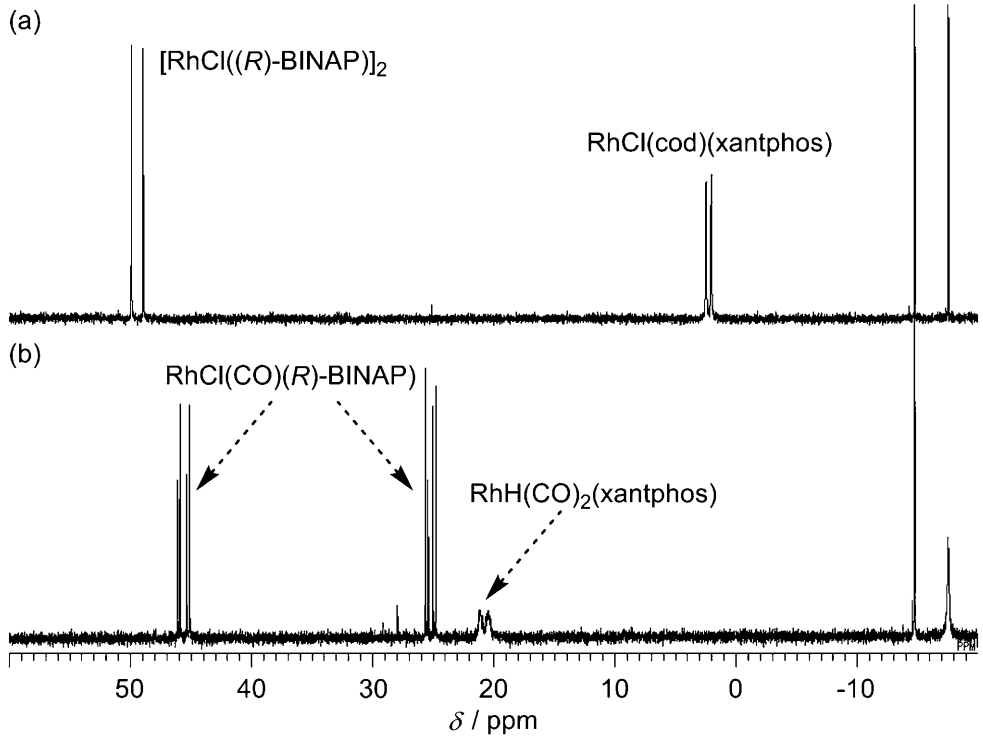
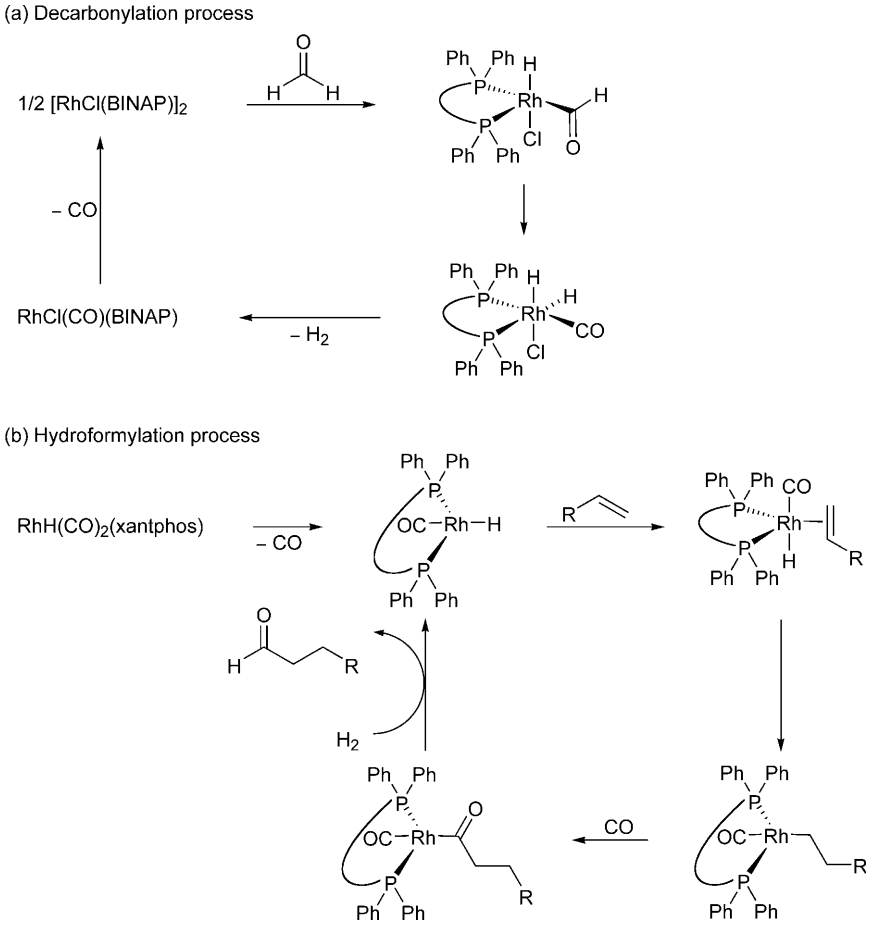


Figure 1. ^{31}P NMR spectra of (a) a mixture of $[RhCl(cod)]_2$, (*R*)-BINAP, and xantphos (1:2:2) in toluene-d_8 solution and (b) the reaction of the mixture with formalin.

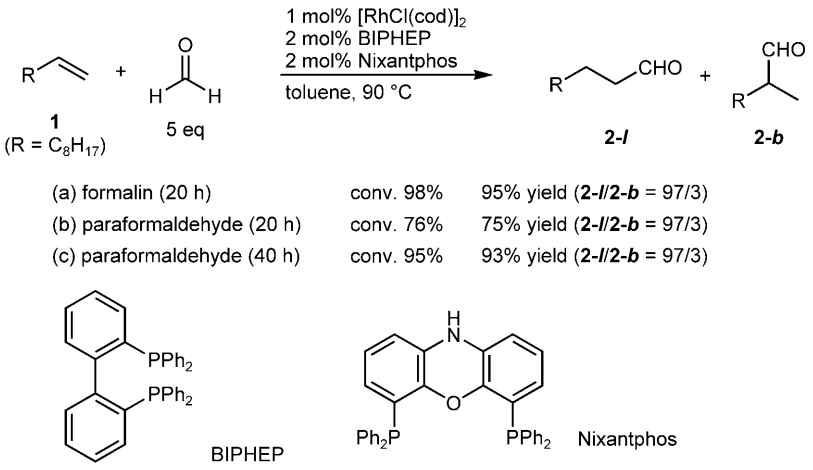
um species, $[RhCl(BINAP)]_2$ and RhCl(cod)(xantphos), which are formed from a mixture of the catalyst precursors $[RhCl(cod)]_2$, BINAP, and xantphos. From the known property that a rhodium catalyst associated with the BINAP ligand has a higher ability to decarbonylate aldehydes,[5e,7] $[RhCl(BINAP)]_2$ is responsible for the decarbonylation of formaldehyde to yield RhCl(CO)(BINAP) and H_2 [process (a)]. RhCl(cod)(xantphos) receives the resulting carbonyl and H_2 "formally" from the process (a), to afford $RhH(CO)_2$(xantphos),[13] and then catalyzes the hydroformylation of 1-decene [process (b)]. The finding obtained from the kinetic study suggests the consideration that, for the combined use of BINAP and xantphos, the rhodium species associated with xantphos controls the efficiency and regioselectivity of the hydroformylation process. The origin of the high linear-selectivity follows the mechanism reported by van Leeuwen.[9] Consequently, the sequence of events leads to a highly regioselective hydroformylation without the direct use of syngas.

The best result was obtained when BIPHEP and Nixantphos were used instead of BINAP and xantphos: the yield of products increased dramatically to 95% GC yield without any detectable loss in linear-selectivity (**2-*l*/2-*b*** = 97/3) [Scheme 2(a)]. The observed high linear selectivity is almost the same as the selectivity (***l*/*b*** = 98/2) in the $Rh(acac)(CO)_2$/nixantphos-catalyzed hydroformylation of 1-octene using pressurized synthesis gas.[14] Thus, using this system, it was possible to perform a similar transformation more simply and conveniently. Furthermore, under the catalytic conditions employed, even when paraformaldehyde was used instead of formalin, **2-*l*** regioselectivity was observed, although with somewhat lower efficiency (76% conversion) [Scheme 2(b)]. Prolonging the reaction time to 40 h led to the regioselective formation of **2-*l*** [Scheme 2(c)] in high yield.

Reactions of other 1-alkenes also proceeded efficiently with a high regioselectivity to yield the corresponding linear aldehydes. In all cases, no side reaction products, except for linear/branched aldehydes and isomers of 1-alkenes, were detected. Under the above standard conditions, the reaction of 1-octene proceeded well to give nonanal (***l***) and 2-methyloctanal (***b***) in 90% yield in a ratio of ***l*/*b*** = 97/3 (Table 2, entry 1). The present method using formalin tolerates not only simple alkenes, but also functionalized alkenes. Thus, for reactions of 1-alkenes having functional groups, such as an ether (entry 3), an ester (entry 5), a siloxy (entry 7), and a phthaloyl (entry 9) group, linear aldehydes were formed predominantly in ratios of ***l*/*b*** = 94/6 up to 97/3, however substantial isomerization of the substrates to internal alkenes was observed. Importantly, during the course of the reaction, these functional groups in the remaining substrates and their isomers as well as in products (aldehydes) remained intact. Regarding Scheme 1, when



Scheme 1. Possible reaction pathway of hydroformylation using formaldehyde catalyzed by two different Rh species.

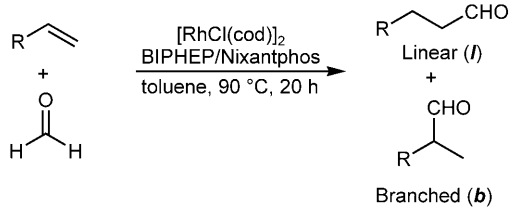


Scheme 2. Rh(I)-catalyzed highly linear-selective hydroformylation of 1-decene (**1**) with formaldehyde.

paraformaldehyde was used, instead of formalin, in all of the reactions, the regioselectivity remained extremely high with a slightly slower consumption of substrates (entries 2, 4, 6, 8, and 10).

In conclusion, we have reported on the highly linear-selective hydroformylation of 1-alkenes using formaldehyde as a syngas substitute. The high regioselectivity (linear/branched = up to 98/2) and efficiency (up to 95%) can be attributed to the simultaneous use of two types of phosphanes as ligands. Two rhodium species associated with each phosphane separately catalyze the decarbonylative decomposition of form-

Table 2. Highly linear-selective hydroformylation of 1-alkenes using formaldehyde.[a]



Entry	R	HCHO[b]	Conv.[c]	Yield (*l*/*b*)[c]
1	$-C_6H_{13}$	A	94%	90% (97/3)
2		B	76%	72% (97/3)
3	$-(CH_2)_7CH_2OBn$	A	94%	68% (97/3)
4		B	71%	47% (96/4)
5	$-(CH_2)_7CH_2OPiv$	A	96%	79% (97/3)
6		B	90%	73% (98/2)
7	$-(CH_2)_7CH_2OTBS$	A	94%	85% (97/3)
8		B	77%	68% (97/3)
9	$-(CH_2)_7CH_2NPhth$	A	93%	37% (94/6)
10		B	80%	26% (92/8)

[a] *Conditions:* 1-alkene (1 mmol), formaldehyde (5 mmol), $[RhCl(cod)]_2$ (0.01 mmol), BIPHEP (0.02 mmol), Nixantphos (0.02 mmol), toluene (6 mL), 90 °C, 20 h.

[b] A: formalin (0.37 mL of 37 wt% aqueous solution); B: paraformaldehyde (150 mg).

[c] Yields are the sum of formed linear and branched aldehydes. Values in parentheses are the ratios of linear/branched aldehydes. Conversions, yields, and ratios were determined by GC. BIPHEP = 2,2′-bis(diphenylphosphino)-1,1′-biphenyl; Nixantphos = 4,6-bis(diphenylphosphino)phenoxazine; Bn = benzyl; Piv = pivaloyl (trimethylacetyl); TBS = *tert*-butyl(dimethyl)silyl; Phth = phthaloyl.

aldehyde to a CO moiety and hydrogen and the hydroformylation of 1-alkenes. Further investigations of the details of the reaction mechanism are currently in progress.

Experimental Section

Typical Procedure for the Hydroformylation of 1-Decene (1) Using Formalin

A 10-mL Schlenk tube containing a stirring bar was charged with $[RhCl(cod)]_2$ (4.93 mg, 0.01 mmol), BIPHEP (10.5 mg, 0.02 mmol), and Nixantphos (11.0 mg, 0.02 mmol) under nitrogen. After adding toluene (6 mL), 1-decene (140.3 mg, 1 mmol), and formalin (37%, 0.37 mL, 5 mmol), the mixture was degassed and purged with nitrogen (three freeze-pump-thaw cycles). The mixture was stirred in a preheated oil bath at 90 °C for 20 h. The reaction mixture was diluted with ether (2 mL), and dodecane (70 mg) was then added as the internal standard for GC analysis. Conversion, yield, and selectivity were determined by GC. The mixture was concentrated under vacuum, and the residue was purified by column chromatography on silica gel (eluent; hexane/Et_2O = 5/1) to afford the linear (R_f 0.71) and branched (R_f 0.70) aldehydes as colorless oils.

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