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Highly Regioselective and Rapid Hydroformylation of Alkyl Acrylates Catalyzed by a Rhodium Complex with a Tetraphosphorus Ligand

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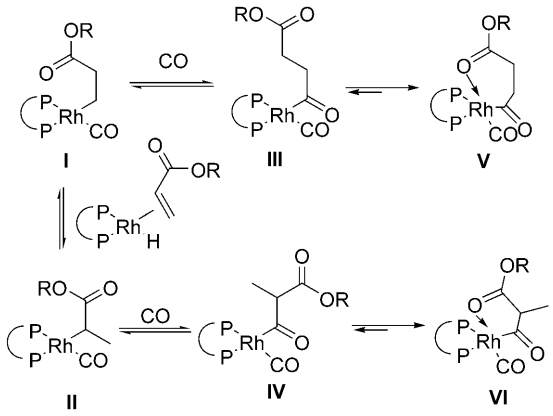
Abstract: Alkyl acrylates have been hydroformylated to the linear aldehydes with high regioselectivity (linear/branch > 99/1) and extraordinarily high average turnover frequencies (up to 5400 h^{-1}) by using a rhodium complex with a tetraphosphorus ligand. This protocol is in sharp contrast to the most of other processes that favor production of the branched aldehyde (typically > 95% branched for most Rh-catalyzed reaction systems). The high turnover number achieved by this new catalytic system is also remarkable considering the less reactive character of alkyl acrylates to the hydroformylation reaction conditions.

Keywords: aldehydes; alkyl acrylates; hydroformylation; P ligands; regioselectivity

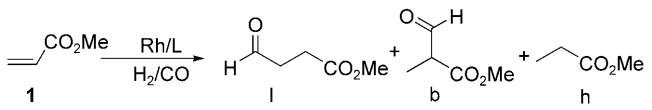
Hydroformylation of alkenes represents a highly attractive method to prepare aldehydes and alcohols, and is one of the most important reactions in industry catalyzed by homogeneous catalysts. Production of aldehyde is estimated at over 9 million tons per year.[1] Many efforts have been devoted to the development of systems with improved regioselectivity toward the formation of the industrially important linear aldehydes. Both phosphine- and phosphite-based systems giving high regioselectivities to linear aldehydes for the hydroformylation of terminal and internal alkenes have been reported.[2] Recently, there has been increased interest in the regioselective hydroformylation of ready available functionalized alkenes.[3] One such cheap, useful feedstock is alkyl acrylate.[4] Hydroformylation of alkyl acrylate produces 1,3- and 1,4-bifunctional compounds, which can be further converted into synthetically useful intermediates such as malonic acid, 1,4-dicarboxylic acid derivatives and butyrolactones.[5]

The hydroformylation of alkyl acrylate has three distinct characters. Firstly, alkyl acrylate is less reactive to H_2/CO compared to terminal alkenes.[6] The lower rate was ascribed to be a result of the formation of thermodynamically stable five- or six-membered rings through the coordination of carbonyl group to the metal center (See Scheme 1 for the formation of



Scheme 1. Coodination of a carbonyl group to the rhodium.

complexes **V** and **VI**). Thus, the rate-determining step has been suggested to be the dissociation of the chelated carbonyl group to afford a coordinatively unsaturated species that is active towards the oxidative addition of H_2.[7] In this context, high temperature (150 °C) and/or high pressure (100 bar) are often required to achieve high turnover.[8] Recently, significant progresses have been made to carry out the process under mild conditions, such as using an organo-aquo biphasic system[6b] or supported aqueous phase catalyst[7b] or in supercritical CO_2.[9] Secondly, hydroformylation of alkyl acrylate with the rhodium complex generally gives the branched aldehyde with few exceptions[10] (For typical results catalyzed by an Rh complex with P ligands, see Scheme 2).[11] It is highly desirable to develop a process that gives linear alde-



Rh complex/ligand	Production and yield	Ref.
$Rh(COD)BPh_4$	b:l = 30:70	[4e]
$Rh(acac)(CO)_2/PPh_3$	l + b = 94%, b:l > 200	[11b]
$[Rh(COD)Cl_2]_2$/DPPB	l + b = 94%, b:l = 99:1	[4d]
$Rh(COD)(\eta^6\text{-}PhBPh_3)/P(OPh)_3$	b:l = 98:2	[4d]
$Rh(acac)(CO)_2$/TPPMS	l + b = 83%, b:l = 63:1, h = 17%	[6c]
$Rh(acac)(CO)_2$/Phosoxophite AA	l = 91%, b = 1%, h = 8%	[10b]
$Rh(acac)(CO)_2/P(OPh)_3$	l = 28%, h = 38%	[12]

DPPB: 1, 4-bis(diphenylphosphino)butane; TPPMS: [3-(sodium sulfonato)phenyl]diphenylphosphine.

Scheme 2. Typical results for rhodium-catalyzed hydroformylation of methyl alkylates.

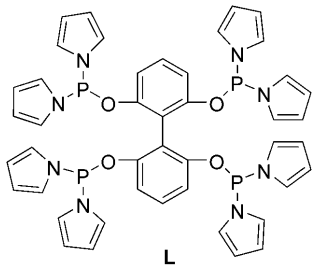


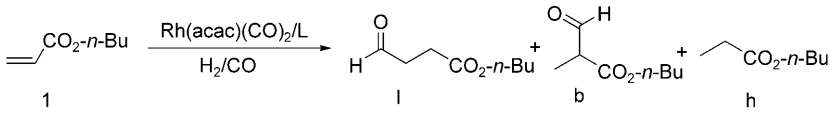
Figure 1. Ligand used in this study.

hydes as the major product with high efficiency due to the wide application of 1,4-bifunctional compounds in organic synthesis.[5] Thirdly, the hydroformylation process is usually accompanied with significant amounts of hydrogenation product.[6c,12] Thorough tuning of the reaction condition can suppress the formation of the hydrogenation product in some degree.

We have recently developed a protocol for the highly regioselective isomerization-hydroformylation of internal alkenes to linear aldehydes catalyzed by an Rh complex with a tetraphosphorus ligand (Figure 1).[13] This very selective catalytic system was not tested for alkyl acrylate in our initial study, but it occurred to us that this catalytic system might allow a regioselective hydroformylation of alkyl acrylates to linear aldehydes. In this paper, we report the first highly regioselective and rapid hydroformylation of alkyl acrylates to the linear aldehydes in the presence of $Rh(acac)(CO)_2$ and the tetraphosphorus ligand **L**.

The hydroformylation of *n*-butyl acrylate with the tetraphosphine ligand **L** was first investigated (Table 1). The reaction was conducted in toluene and decane was used as an internal standard. The rhodium catalyst was prepared *in situ* by mixing the tetraphosphine ligand **L** with $Rh(acac)(CO)_2$. The substrate to catalyst ratio was 10,000 and the catalyst concentration was 0.17 mM. The reaction was terminated after 1 h. To our surprise, the $Rh(acac)(CO)_2$-tetraphosphrus systems smoothly catalyzed the hydroformylation of *n*-butyl acrylate, and the linear aldehyde was obtained as the main product with a very high turnover

Table 1. Optimization of reaction conditions for the hydroformylation of butyl acrylate.[a]



Entry	Rh/L	T [°C]	CO/H_2 [atm]	Conv. [%][b]	h [%][c]	Aldehyde l:b[d]	Aldehyde TOF[e]
1	1:1	100	5/5	64	12.6	>99	4.8×10^3
2	1:2	100	5/5	57	5.3	>99	4.9×10^3
3	1:3	100	5/5	62	6.6	>99	5.1×10^3
4	1:4	100	5/5	63	5.4	>99	5.4×10^3
5	1:5	100	5/5	64	5.7	>99	5.4×10^3
6	1:4	100	10/10	62	4.6	>99	4.6×10^3
7	1:4	100	20/20	68	5.2	>99	3.4×10^3
8	1:4	100	30/30	85	5.9	>99	1.3×10^3
9	1:4	60	5/5	13	2.1	>99	9.8×10^2
10	1:4	80	5/5	25	1.4	>99	2.2×10^3
11[f]	1:4	100	5/5	30	2.4	>99	2.7×10^3

[a] S/C = 10,000, [Rh] = 0.17 mM, time = 1 h, toluene as solvent, decane as internal standard.
[b] Conversion of the *n*-butyl acrlate, determined on the basis of GC, polymetric products account for the product balance.
[c] Percentage of hydrogenated product in all products.
[d] Linear/branched ratio, analyzed by proton NMR.
[e] Average turnover frequency, determined based on GC, reaction time = 1 h.
[f] THF used as solvent.

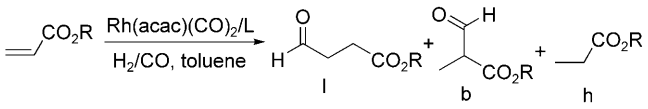
frequency. No branched aldehydes were formed under these reaction conditions. A slight increase of turnover frequency was observed when the ratio of ligand to Rh complex was increased from 1:1 to 5:1 (entries 1–5). The effects of CO/H_2 pressure were tested, too. At high CO/H_2 pressure, the consumption of starting material greatly increased, however the formation of the linear aldehyde decreased due to the formation of polymetric products (entries 4, 6–8). Finally, the effects of reaction temperature on the hydroformylation reaction were also investigated (entries 4, 9 and 10). The reaction rate was greatly improved when the reaction temperature increased from 60 °C to 100 °C. The reaction can also be carried out in THF, albeit with lower activity (entry 11).

We then applied the optimized reaction conditions (100 °C, $CO/H_2 = 5/5$ atm, ligand/metal = 4) to the hydroformylation of other alkyl acrylates in toluene. The reactions were also carried out for 1 h and the results are summarized in Table 2. In all cases, only the linear aldehydes were observed, which is in sharp contrast with the literature reports that the hydroformylation of acrylates usually affords branched aldehydes as the dominant product. Much more significantly, the turnover frequency still remains at a high level. For comparison, the bisphosphorus ligand was prepared[14] and employed in the hydroformylation of *n*-butyl acrylate under identical reaction conditions (Table 2, entry 4). The bisphosphorus ligand was found also to show high regioselectivity for linear aldehyde and a high turnover frequency was observed.

Currently, the mechanism of the linear regioselectivity for the hydroformylation of the alkyl acrylates is still unclear. From our results, it seemed that a ligand with larger natural bite angle and electron-withdrawing moieties was preferred for the formation of the linear aldehyde. Further studies are required to reconcile these results. As for the high turnover frequency, one possibility is that the 9-membered P-Rh-P ring might inhibit the formation of another 5- or 6-membered carbonyl coordinated ring due to the steric repulsion.

In summary, we have shown that the hydroformylation of alkyl acrylates can be achieved with essentially high regioselectivity (linear selectivity is up to 99:1) and extraordinarily high average turnover frequencies (up to 5400 h^{-1}) by using a tetraphosphorus-based Rh catalyst. This protocol is complementary to other processes catalyzed by rhodium complexes that produce mainly branched aldehydes. Further ligands, applications and mechanism studies are now under investigation and will be reported in due course.

Table 2. Hydroformylation of alkyl acrylates with ligand L.[a]



Entry	R	Conv. [%][b]	h [%][c]	Aldehyde l:b[d]	Aldehyde TOF[e]
1	*i*-Bu	59	5.2	>99	5.1×103
2	*t*-Bu	48	5.8	>99	3.9×103
3	Me	56	5.2	>99	4.8×103
4[f]	*n*-Bu	44	6.1	>99	3.5×103

[a] S/C = 10,000, [Rh] = 0.17 mM, ligand/Rh ratio = 4:1, temperature = 100 °C, $CO/H_2 = 5/5$ atm, time = 1 h, toluene as solvent, decane as internal standard.
[b] For footnotes [b] to [e], see Table 1.
[f] The bisphosphorus ligand 1,1′-biphenyl-2,2′-diyl-bis(dipyrrolylphosphoramidite) was used.

Experimental Section

General Procedure for the Regioselective Hydroformylation of *n*-Butyl Acrylate with Ligand L

A 10-mL vial with a magnetic stirring bar was charged with ligand **L** (4 μmol, 3.6 mg) and $Rh(acac)(CO)_2$ (1 μmol, 0.1 mL of 10 mM solution in toluene). The mixture was stirred for 5 min, *n*-butyl acrylate (10 mmol, 1.43 mL) was then added, followed by decane (0.1 mL) as internal standard and toluene (4.36 mL). The reaction mixture was transferred to an autoclave. The autoclave was purged with nitrogen three times and subsequently charged with CO (5 atm) and H_2 (5 atm). The autoclave was then heated to 100 °C and the pressure was set to 10 atm. After 1 h, the autoclave was cooled in ice/water, and the pressure was carefully released in a well-ventilated hood. The reaction mixture was immediately analyzed by GC and ^1H NMR to determine the conversion and regioselectivity.

Acknowledgements

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