## **ARTICLE IN PRESS**

#### Tetrahedron Letters xxx (2013) xxx-xxx

Contents lists available at ScienceDirect



**Tetrahedron Letters** 

journal homepage: www.elsevier.com/locate/tetlet



# Selective hydroformylation-acetalization of various olefins using simple and efficient Rh-phosphinite complex catalyst

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#### ARTICLE INFO

Article history: Received 29 June 2013 Revised 16 August 2013 Accepted 18 August 2013 Available online xxxx

Keywords: Hydroformylation Acetalization Aldehydes Acetals Rh-phosphinite complex

#### ABSTRACT

A simple and efficient Rh-phosphinite complex catalyst was studied for the selective hydroformylation of various olefins. The influence of various reaction parameters including the effect of temperature, pressure, catalyst loading, time, and solvents was studied. The protocol was also applied for the synthesis of various acetals via tandem hydroformylation–acetalization of olefins in alcohols as solvents. High activity and selectivity for acetal formation was achieved in the absence of co-catalysts with admirable substrate to catalyst mole ratio (TON 2500). The developed protocol works for a wide range of olefins to synthesize corresponding aldehydes and acetals under optimized reaction conditions.

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Hydroformylation is one of the well studied homogeneously catalyzed reaction and also one of the large scale industrial applications of homogeneous catalysis. The annual production of several million tons of oxo chemicals attests its importance. The catalytic hydroformylation is an elegant, clean, and atom-efficient method to prepare wide range of aldehydes by the reaction of olefins with syngas.<sup>1</sup> In many cases, aldehydes are not the final products and are further converted into alcohols, esters, amines, acetals, and many more.<sup>2</sup> The tandem reaction is always advantageous over multistep synthesis since it minimizes the waste, multiple reaction steps and the number of purification processes which fulfills the criteria of sustainability and green chemistry. Several transition metal-based catalysts involving Rh, Pt, Co, and Ru are used for this reaction. Rhodium complexes of modified phosphorous containing ligand show high activity and selectivity at mild reaction conditions and hence are generally preferred for hydroformylation reactions.<sup>3</sup>

The direct synthesis of acetals from olefins is one of the interesting applications of tandem reaction. Acetal formation under hydroformylation conditions may be needed either to protect the sensitive aldehyde group from side reactions or for synthetic purposes.<sup>4</sup> Considering the importance of acetals as organic solvents, additives for fuel and intermediates in the pharmaceutical, perfumery, and agricultural industries,<sup>5</sup> several methods have been developed for their synthesis. Fernandez and Castillon reported the acetalization of olefins using  $[Rh_2(\mu-OMe)_2-(cod)_2]$  with pyridinium *p*-toluenesulfonate (PPTS) as co-catalyst.<sup>6</sup> The acetal formation under hydroformylation condition can be increased in the presence of acid catalyst or by acidified resins.<sup>7</sup> and special ligands with rhodium which can provide an acidic pH.<sup>8</sup> Besides this, there are a few reports wherein acetal formation was achieved under acid-free conditions. El Ali et al. reported acid-free acetalization of alkenes using RhCl<sub>3</sub>·3H<sub>2</sub>O/P(OPh)<sub>3</sub> as an effective catalytic system for this transformation.<sup>9</sup> Recently, Gusevskaya and co-workers reported the synthesis of fragrance acetals using Rh/P(O-o-tBuPh)<sub>3</sub> catalytic system in the absence of acid co-catalyst.<sup>10</sup> In spite of their potential utility, most of the reported protocols suffer from one or more drawbacks such as use of acid co-catalysts, harsh reaction conditions, or low substrate to catalyst mole ratio. Literature reports reveal that the hydroformylation as well as hydroformylation-acetalization reactions using rhodium metal with phosphite/ phosphinite ligands are more effective than the conventional Rhtriphenyl phosphine based catalysts.<sup>11</sup> Even with high activity, performance, and stability there are very few reports on Rh-phosphite/phosphinite complexes.<sup>12</sup> Some of the best results with these ligands are obtained using the family of calixarenes, which are known as sophisticated molecular cages and claw-like ligands,<sup>1</sup> pyranoside,<sup>14</sup> and furanoside<sup>15</sup> ligands. However, multistep synthetic procedures and high cost of these ligands limit their industrial applications.

Hence, the development of simple and atom efficient catalytic system is always a key issue in the case of hydroformylation and related reactions. In continuation of our interest in the development of homogeneous catalytic system,<sup>16</sup> we herein report a facile

Please cite this article in press as: Khan, S. R.; Bhanage, B. M. Tetrahedron Lett. (2013), http://dx.doi.org/10.1016/j.tetlet.2013.08.061

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and highly efficient protocol for hydroformylation reaction and for one-pot hydroformylation-acetalization process under acid-free condition using a known Rh-phosphinite complex catalyst.

To optimize the reaction conditions, series of experiments were performed on the hydroformylation of hexene as a model system using Rh-phosphinite complex as a catalyst (Scheme 1). The Rh-phosphinite complex used was synthesized according to the reported procedure in the literature.<sup>18</sup> The influences of various reaction parameters such as effect of temperature, solvent, catalyst loading, syngas pressure, and time were studied and the results obtained are summarized in Table 1.

Initially, the reaction was studied at different temperatures in the range of 50–110 °C (Table 1, entries 1–4). A high temperature significantly promotes the side reaction like hydrogenation with suppression of  $\alpha$ -formylation and thus provided higher branched selectivity (Table 1, entry 1).<sup>19</sup> It was found that regioselectivity for linear aldehvde formation increases with a decrease in temperature to 60 °C without affecting the conversion. Further decrease in the reaction temperature to 50 °C led to the poor conversion of hexene. Thus, further studies were carried out at 60 °C, which was found to provide optimum conversion and selectivity toward desired aldehyde (Table 1, entry 3). It was observed that the nature of solvent affects the selectivity of the reaction product. The small amount of substrate isomerization was observed when toluene was used as a reaction solvent provided moderate conversion and poor selectivity for linear aldehyde, whereas low conversion and considerable amount of acetal formation were obtained in methanol (Table 1, entries 5 and 6). It was observed that tetrahydrofuran (THF) provides good yield and selectivity of the desired product and hence was used for further studies (Table 1, entry 3). Next, we studied the substrate to catalyst molar ratio. It was found that increasing the molar ratio from 1000:1 to 2500:1 does not have a significant impact in the conversion and selectivity of the desired aldehyde products (Table 1, entries 7, 3, and 8), whereas, with further increase in the substrate to rhodium mole ratio up to 3333:1, decreases the conversion of hexene (Table 1, entry 9). This decrease in conversion was due to a decrease in the amount of catalyst from 0.04 mol % (Sub/Rh mole ratio 2500:1) to 0.03 mol % (Sub/Rh mole ratio 3333:1). The influence of syngas (CO/H<sub>2</sub>) pressure on the hydroformylation reaction was then investigated. It was observed that lowering the syngas pressure from 40 to 30 bar did not have any prominent effect on the reaction outcome, but with further decrease in pressure to 25 bar decreases the conversion of the desired product (Table 1, entry 11). We further studied the effect of reaction time ranging from 8 to 4 h and it was found that within a period of 6 h, reaction provided maximum vield and selectivity for linear aldehyde formation (Table 1. entries 3, 12, and 13). To check the activity and selectivity of the developed Rh-phosphinite complex with a ligand-free system, the reaction of 1-hexene was carried out using [Rh(cod)Cl]<sub>2</sub> as a catalyst and was compared. However, low conversion addresses the importance of the ligand in hydroformylation reaction (Table 1, entry 14). Hence, the optimized reaction conditions for the hydroformylation of hexene were; hexene (5 mmol), Rh-phosphinite complex (0.002 mmol), and  $CO/H_2$  (30 bar) at a temperature of 60 °C for 6 h in THF (15 mL) as solvent.

With these optimized reaction conditions, the scope of the developed protocol was extended for the hydroformylation of a variety of aliphatic, aromatic, and cyclic olefins and the results obtained are summarized in Table 2.<sup>20</sup> The model reaction of hexene provided good conversion and selectivity toward linear aldehyde (Table 2, entry 1).



Scheme 1. Hydroformylation of hexene using Rh-phosphinite complex catalyst.

Table 1				
Effect of reaction	parameters	on hydroformyl	ation of	hexene <sup>a</sup>

Entry	Temp (°C)	Solvent	Sub/Rh (mole ratio)	CO/H <sub>2</sub> pressure (bar)	Time (h)	Conversion <sup>c</sup> (%)	Aldehyde (%)	Linear:iso <sup>c</sup> (%)	Reduction (%)
1	110	THF	2000	30	8	100	92	43:57	8
2	90	THF	2000	30	8	100	95	49:51	5
3	60	THF	2000	30	8	100	99	71:29	_
4	50	THF	2000	30	8	44	99	69:31	1
5	60	Toluene	2000	30	8	94	97	52:48	3
6	60	MeOH	2000	30	8	68	13:87 <sup>d</sup>	67:33	_
7	60	THF	1000	30	8	100	99	71:29	_
8	60	THF	2500	30	8	100	99	72:28	1
9	60	THF	3333	30	8	73	97	69:31	3
10	60	THF	2500	40	8	100	96	65:35	4
11	60	THF	2500	25	8	88	99	70:30	1
12	60	THF	2500	30	6	100	99	72:28	-
13	60	THF	2500	30	4	89	99	73:27	1
14 <sup>b</sup>	60	THF	2500	30	6	34	73	67:33	27

<sup>a</sup> Reaction conditions: hexene (5 mmol), Rh-phosphinite complex (as indicated), solvent (15 mL), 600 rpm.

<sup>b</sup> [Rh(cod)Cl]<sub>2</sub> used as a catalyst.

<sup>c</sup> Conversion and selectivity (lin/iso) were determined by GC analysis.

<sup>d</sup> Acetal formation.

**Table 2**Hydroformylation of various olefins<sup>a</sup>

Entry	Olefins	Conversion (%)	Aldehyde <sup>e</sup> (%)	Lin:iso <sup>d</sup> (%)	Reduction (%)
1	$\sim \sim \sim$	100	99	72:28	1
2	$\sim$	98	99	69:31	1
3	$\sim$	95	98	73:27	2
4	$\sim$	96	96	67:33	4
5		79	97	36:74	3
6 <sup>b</sup>		100	99	12:88	_
7 <sup>b</sup>		99	99	17:83	-
8 <sup>b</sup>		100	99	19:81	_
9 <sup>b</sup>	CI	100	99	10:90	_
10 <sup>b,c</sup>	$\bigcirc$	100	97	_	3
11 <sup>b,c</sup>	$\bigcirc$	97	98	_	2

 $^a$  Reaction conditions: olefin (5 mmol), Rh-phosphinite complex (0.002 mmol), THF (15 mL), CO/H<sub>2</sub> (1:1) 30 bar, temperature (60 °C), time (6 h), 600 rpm.

<sup>b</sup> Toluene as solvent.

<sup>c</sup> Reaction time 8 h.

 $^{\rm d}\,$  Conversion and selectivity (lin/iso) were determined by GC analysis.

<sup>e</sup> Chemoselectivity for aldehyde product to total reaction product.

The screened aliphatic olefins such as 1-octene, 1-decene, and 1-dodecene also offered good selectivity for aldehyde formation with almost 98% conversion (Table 2, entries 2–4). The aromatic olefin such as styrene reacts efficiently in both THF and toluene as solvents providing 2-phenylpropanal as a major product. Toluene was a promising solvent for aromatic olefins since good regioselectivity for branched aldehydes was achieved (Table 2, entry 6). The poor selectivity in THF may be due to the interaction of the polar solvent with a benzylrhodium intermediate promoting the linear aldehyde formation. Substituted styrene like 3-methylstyrene and *p-tert*-butylstyrene were found to react efficiently, furnishing good yield and selectivity for the corresponding products (Table 2, entries 7 and 8). Furthermore, *p*-chlorostyrene also provided almost complete conversion and good selectivity for branched aldehyde formation (Table 2, entry 9).

It was observed that the regioselectivity for branched product faintly increases with electron-withdrawing substituent on a phenyl ring in the order p-(CH<sub>3</sub>)<sub>3</sub>CPh < m-CH<sub>3</sub>Ph < HPh < p-ClPh. This

might be due to an increase in  $\pi$ -electron density on the  $\alpha$ -carbon of styrene, which favors the attack of electropositive Rh metal, providing higher selectivity for branched aldehyde.<sup>17</sup> The cyclic olefins are known to react slowly for their hydroformylation, but under present catalytic conditions cyclic olefins also endow with very good conversion and selectivity for the formation of cyclopentane-carbaldehyde and cyclohexanecarbaldehyde (Table 2, entries 10 and 11).

The scope of developed catalytic protocol was further extended for the hydroformylation–acetalization tandem reaction. This domino reaction involves the hydroformylation of olefin to an aldehyde followed by the reaction of resulting aldehyde with alcohol to produce hemiacetal which finally reacts with another equivalent of an alcohol to give the acetal (Scheme 2). The acetal formation generally takes place in acidic condition, because a base simply deprotonates the –OH group of the hemiacetal. The developed Rh-phosphinite complex contains RhCl residue which could derive the acidic condition in the system and hence was not activated by hydrogen to eliminate the HCl under vacuum before performing the reaction.

In order to get the maximum conversion and selectivity for the desired acetal, the reaction was optimized with respect to various parameters and the optimum reaction conditions for the hydroformylation–acetalization reaction of olefins were; Rh-phosphinite complex (0.002 mmol), olefins (5 mmol) in alcohol (15 mL), and 30 bar of  $CO/H_2$  pressure at 80 °C for 8 h.

These optimized reaction conditions were then applied for the hydroformylation–acetalization reaction of various olefins with different alcohols, which provided good to excellent yields of the corresponding acetals (Table 3, entries 1–9).<sup>21</sup> The reaction of hexene in methanol confers very good conversion and selectivity for acetal formation (Table 3, entry 1).

The acetalization of hexene was also studied by varying the type of alcohols. Hexene reacts smoothly with ethanol providing an excellent yield of corresponding acetal (Table 3, entry 2). Hexene with *n*-butanol undergoes the acetalization with high conversion (95%) and selectivity (81%) for the formation of the desired acetal (Table 3, entry 3). It was observed that the regioselectivity toward the linear acetal formation increases from methanol to nbutanol at the expense of acetal selectivity. This change in the selectivity might be due to the increase in steric hindrance from methanol to *n*-butanol.<sup>11d</sup> The scope of developed protocol was then further investigated for different olefins in methanol to produce their corresponding acetals (Table 3, entries 4-9). Styrene reacts efficiently in the presence of methanol to provide (1,1dimethoxypropan-2-yl)benzene as a major product. The presence of an electron donating or electron withdrawing substituent on the styrene did not affect the reactivity and offered good conversion and selectivity for acetal formation (Table 3, entries 5-7). Likewise hydroformylation, in case of aryl olefins the branched product was formed predominantly because of the formation of stable benzyl rhodium intermediate. With cyclic olefins (cyclopentene and cyclohexene here), the reaction was quite slow (Table 3, entries 8



Scheme 2. One-pot hydroformylation-acetalization sequence.

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Table	3

Hydroformylation-acetalization of various olefins

Entry	Olefins	Alcohol	Conversion <sup>c</sup> (%)	Acetal <sup>d</sup> (%)	Lin:iso <sup>c</sup> (%)	Other (%)
1	$\sim \sim \sim$	CH₃OH	100	99	46:54	1
2	$\sim \sim$	EtOH	97	98	55:45	2
3		n- butanol	95	81	62:38	19
4		CH₃OH	100	99	38:62	1
5		CH₃OH	99	98	37:63	2
6	+	CH₃OH	96	97	39:61	3
7	CI	CH₃OH	100	99	36:64	1
8 <sup>b</sup>	$\bigcirc$	CH₃OH	97	98	-	2
9 <sup>b</sup>	$\bigcirc$	CH₃OH	95	99	-	1

<sup>a</sup> Reaction conditions: olefin (5 mmol), Rh-phosphinite complex (0.002 mmol), alcohol (15 mL), CO/H<sub>2</sub> (1:1) 30 bar, temperature (80 °C), time (8 h), 600 rpm.

<sup>b</sup> Reaction temperature 100 °C.

<sup>c</sup> Conversion and selectivity (lin/iso) were determined by GC analysis.

<sup>d</sup> Chemoselectivity for acetal product to total reaction product.

and 9). However, very good conversion (up to 97%) and remarkable acetal selectivity were obtained at 100 °C.

In conclusion, the present study reports a simple and efficient protocol for hydroformylation reactions by using a well-defined Rh-phosphinite complex as a versatile catalyst. The reaction system was optimized with respect to various parameters and applied for the hydroformylation of a range of substrate furnishing good to excellent yields of the desired products. Furthermore, the catalytic system was also useful for the synthesis of various acetals via hydroformylation-acetalization sequence in alcohol as a solvent. Different olefins in various alcohols are well tolerated under the optimized reaction conditions and lead to the highly selective formation of the corresponding acetals in the absence of any acid cocatalysts. The developed protocol works at milder reaction conditions with the additional advantage of high TON in comparison with previously reported protocols. Thus, we believe that the present catalytic system constitutes a versatile and economically attractive method for the synthesis of valuable chemicals.

#### Acknowledgments

The author (S.R.K.) is greatly thankful to the Council of Scientific and Industrial Research (CSIR) India for providing senior research fellowship (SRF).

### Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2013.08.061.

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- 19. The thermogravimetric analysis (TGA) of the Rh-phosphinite complex was carried out to provide information on the degradation pattern when decomposed under nitrogen. The complex was found to be stable up to 220 °C with a weight loss of only 3.55% which might be due to solvent loss. After that it gradually decomposes with temperature to 64.85% at 350 °C. Hence, the decomposition temperature of the complex was determined to be 220 °C. A total weight loss was observed at 430 °C. Thus TGA of the Rh-phosphinite catalyst shows that the catalyst is thermally stable at the reaction temperature.
- 20. General procedure for catalytic hydroformylation reaction: in a typical experiment, to a high pressure reactor (autoclave) of 100 mL capacity, Rh-phosphinite complex (0.002 mmol, 2 mg), olefin (5 mmol), and THF (15 mL) were added. The reactor was then flushed with nitrogen, followed by syngas (1:1 mixture of CO and H<sub>2</sub> gas) at room temperature; next, the reaction was pressurized to 30 bar syngas and heated to 60 °C at a stirring speed of 600 rpm for 6 h. After completion of reaction, the reactor was cooled to room temperature, and the remaining  $CO/H_2$  gas was carefully vented, and the reactor was opened. The reaction mixture was analyzed by gas chromatography (GC).
- 21. General procedure for catalytic hydroformylation-acetalization reaction: reactions were performed in high pressure reactor (autoclave) of 100 mL capacity. The autoclave was charged with olefin (5 mmol), Rh-phosphinite complex (0.002 mmol, 2 mg), and alcohol (as a solvent and reactant) (15 mL). The reactor was then flushed with nitrogen, followed by syngas (1:1 mixture of CO and H<sub>2</sub> gas) at room temperature. Subsequently, the autoclave was pressurized to 30 bar syngas and heated to 80 °C at a stirring speed of 600 rpm for 8 h. Further procedures were same as discussed earlier. All products obtained are well known in the literature and were confirmed by GC-MS analysis.