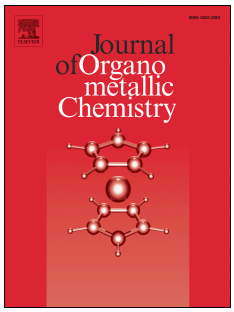
# Accepted Manuscript

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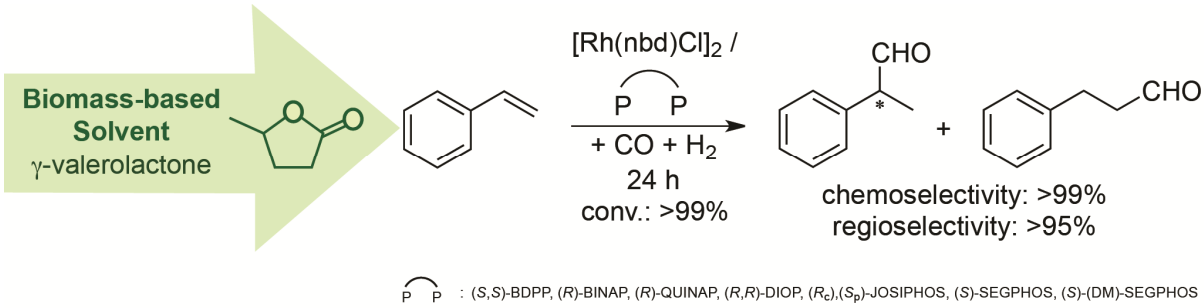


P P : (*S*,*S*)-BDPP, (*R*)-BINAP, (*R*)-QUINAP, (*R*,*R*)-DIOP, ($R_c$),($S_p$)-JOSIPHOS, (*S*)-SEGPHOS, (*S*)-(DM)-SEGPHOS

# Rhodium-catalyzed hydroformylation in γ-valerolactone as a biomass-derived solvent

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This paper is dedicated to Professor John A. Gladysz on the occasion of his 65th birthday

**Keywords**

Alternative solvent, gamma-valerolactone, hydroformylation, homogeneous catalysis, rhodium

**Abstract**

Rhodium-catalyzed hydroformylation of styrene, α-methylstyrene, dimethyl itaconate, and (*R*)-limonene was performed in gamma-valerolactone (GVL) as a proposed biomass-based environmentally benign solvent for hydroformylation referring to toluene as a generally used conventional solvent. Both achiral (triphenylphosphine, 1,3-bis(diphenylphoshino)propane) and enantiopure bidentate phosphine ligands ((*S*,*S*)-BDPP, (*R*)-BINAP, (*R*)-QUINAP, (*R*,*R*)-DIOP, ($R_c$),($S_p$)-JOSIPHOS, (*S*)-SEGPHOS, (*S*)-(DM)-SEGPHOS) were investigated in *in situ* generated Rh-diphosphine catalyst systems. In general, the catalysts' activity in GVL was lower than in toluene; however, remarkable chemo- (>99%) and regioselectivities (>95%) were achieved in GVL under identical conditions. The BDPP-modified Rh-catalyst was recycled for three consecutive cycles; however a decrease in its activity was detected.

## 1. Introduction

Since the accidental discovery of hydroformylation (or oxo-synthesis) concerning the cobalt-catalyzed Fischer-Tropsch reactions by Otto Roelen [1], the highly chemo-, regio- and enantioselective hydroformylation of alkenes to aldehydes has become one of the most important homogeneous transformations [2] even at industrial scale [3]. Regarding the variation of the substrates, two major topics can be distinguished *i)* hydroformylation of (terminal) alkenes with the aim of obtaining high linear selectivity and *ii)* the highly regio- and enantioselective hydroformylation of functionalized olefins to synthesize fine chemicals. The first group can be exemplified by the large scale production of $C_9$-$C_{11}$, so-called "oxo" aldehydes or highly regioselective hydroformylation of propene to n-butyraldehyde, which is the basic compound of 2-ethylhexanol built into diisooctyl phthalate plasticizers. The small scale enantioselective hydroformylation of vinylaromatics to 2-arylpropanals, the intermediate of non-steroidal anti-inflammatory drugs (NSAIDs) can be distinguished as an example for the second one [4]. Although, several industrial oxo-plants utilized both non-modified Co- and Rh-catalysts [4], to improve activity and selectivity hundreds of modified Co-, Rh- and Pt-containing catalysts were developed and some of them have been introduced on industrial scale. While, the large scale industrial oxo-synthesis is continuously performed in refinery olefin mixtures, the small scale hydroformylations very often take place in the presence of various conventional organic solvents such as benzene, toluene, or $C_6$-$C_{10}$ alkane [2], from which several have high toxicity, vapour pressure even at high temperature, and significant negative impact on the environment.

As for the technological, economic and environmental aspects of hydroformylation, several improvements have been completed including development of facile methods for catalyst separation and recycling [5] and even more introducing alternative solvents as a replacement of conventional, usually toxic and volatile organic media. The latter is crucial to achieve environmentally benign alternatives for hydroformylation reactions. The aqueous [6] and fluorous [7] biphasic systems as well as the application of supercritical carbon-dioxide [8] and room temperature ionic liquids [9] have been successfully applied for this purposes. Very recently, as a result of the intensive research activity on biomass conversion, a sustainable liquid, γ-valerolactone (GVL) was identified as a renewable platform molecule [10]. It can be used for the production of alkanes and alkenes [11], transportation fuels [12], polymer compounds [13], lighter fluid [14], as well as a surrogate of conventional organic solvents for synthesis and catalysis. Beyond its first application as a solvent for dehydration of carbohydrates [15,16], several important transition metal catalyzed reactions such as Heck [17] Sonogashira [18] and Hiyama cross-coupling reactions [ 19 ], Catellani-reaction [ 20 ], platinum-catalyzed hydroformylation [ 21 ] and palladium-catalyzed aminocarbonylation [22] were successfully performed in GVL without significant changes in the catalytic systems' efficiency. On the other hand, GVL can be produced from carbohydrate rich biomass or biomass-based wastes *via* levulinic acid [23, 24] making it fossil independent alternative reaction media. GVL

occurs naturally in fruits and fermented products such as wines and beers [25], accordingly it can be considered as a non-toxic substance. It should be noted that moisture content of GVL could be crucial as follows i) water content could have a serious influence on the operation of transition metal-based catalyst ii) the ring opening of GVL results in the formation of 4-hydroxyvaleric acid [26], which could lead to unwanted side reactions. The investigation of phase behaviour of GVL and water revealed that water can be completely separated by vacuum distillation without formation of azeotropic mixture in whole concentration range [30] overcoming this issue.

Herein we report, the investigation of hydroformylation of styrene as well as functionalized olefins such as α-methylstyrene, dimethyl itaconate, and limonene in the presence of *in situ* generated rhodium-chiral diphosphine catalyst in GVL. The activity, as well as chemo-, regio- and enantioselectivities of the aforementioned systems, obtained in toluene as conventional and GVL as non-toxic, biomass-based solvent, are compared.

## 2. Experimental

*General procedures*

Toluene, gamma-valerolactone, styrene, α-methylstyrene, dimethyl itaconate, and (*R*)-limonene and bidentate phosphine ligands were obtained from Sigma-Aldrich Kft. Budapest, Hungary. The $[Rh(nbd)Cl]_2$ precursor was synthesized using standard procedure [27]. Toluene was distilled and purified by standard methods and stored under argon. Substrates and ligands were used as obtained without any further purification. All reactions were carried out under argon atmosphere using standard Schlenk technique. Gamma-valerolactone was purified by vacuum distillation (2 Torr, 80–82 °C) and stored under nitrogen. The GC and chiral GC measurements were run on a Chrom-Card Trace GC-Focus GC gas-chromatograph. The enantiomeric excesses were determined on a capillary Cyclodex-column.

*Hydroformylation experiments*

In a typical hydroformylation experiment, a solution of $[Rh(nbd)Cl]_2$ (2.3 mg, 0.005 mmol), corresponding diphosphine (0.01 mmol) in 5 mL of toluene containing 0.115 mL (1.0 mmol) of styrene was transferred under argon into a 100 mL stainless steel autoclave. The reaction mixture was pressurized to 80 bar total pressure ($CO:H_2$ = 1:1) and placed in an oil bath of appropriate temperature and the mixture was stirred with an internal magnetic stirrer. Sample was taken from the mixture and the pressure was monitored throughout the reaction. After cooling and venting of the autoclave, the pale yellow solution was removed and immediately analysed by GC and chiral GC. For appropriate determination of enantiomeric excess, 10 mL of hexane was added to a sample of the reaction mixture (2 mL) and washed with water (twice 10 mL). The hexane phase was dried over $Na_2SO_4$, filtered and concentrated to a colorless oil. The $CH_2Cl_2$ solution of this GVL-free sample was applied for chiral GC.

## 3. Results and Discussion

The replacement of conventional organic solvents by environmentally benign alternative could result in a safer alternative of hydroformylation. In comparison to GVL, the temperature dependence of the vapor pressure of solvents that are generally utilized for hydroformylation, it can be stated that the replacement of these media with GVL could result in an environmentally benign catalytic system. The vapor pressures of GVL in the temperature range of hydroformylation reactions are two orders of magnitude less than hexane, benzene or toluene, just to name a few (Figure 1).

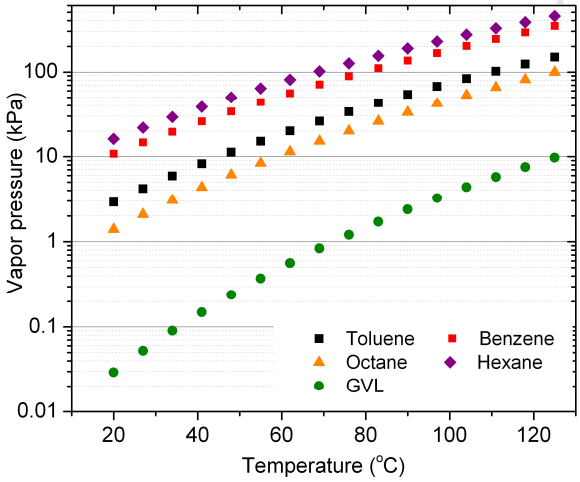
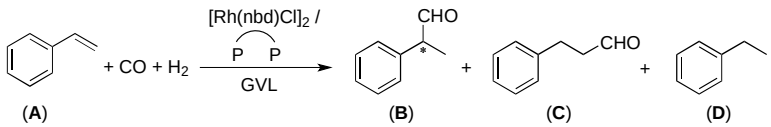



**Figure 1** Vapor pressures of commonly used solvents for hydroformylation and GVL. Data were obtained as follows: toluene, hexane, octane ref. 28, benzene ref 29; GVL ref. 30.

Although the platinum-chiral diphosphine-tin(II) chloride systems were successfully utilized in enantioselective hydroformylation, the rhodium-containing systems have shown the best performance due to their high activity and, since the discovery of Takaya's rhodium-BINAPHOS catalysts [31], due to excellent enantioselectivity as well. In order to demonstrate the applicability of GVL as a reaction medium for Rh-catalyzed hydroformylation of functionalized olefins, we initially investigated the conversion of styrene (**A**) as a model substrate (Scheme 1) in the presence of catalyst *in situ* formed from $[Rh(nbd)Cl]_2$ and chiral bidentate phosphine ligands (Figure 2).




**Scheme 1** Hydroformylation of styrene (**A**) in GVL

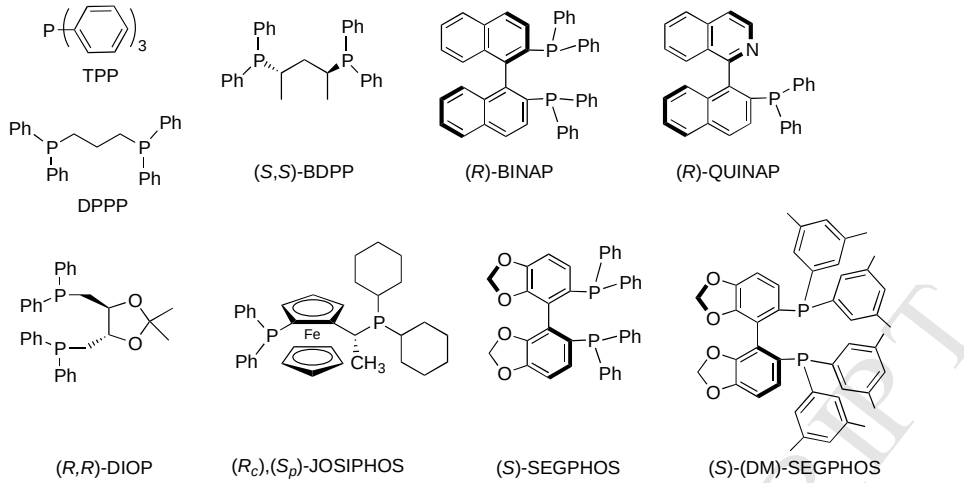



**Figure 2** Ligands used in this work

Initially, hydroformylation of styrene (Scheme 1) was performed in the presence of catalyst *in situ* formed from $[Rh(nbd)Cl]_2$ and achiral phosphines in GVL. When 6 eqv. of $PPh_3$ (*i.e.* $Rh:PPh_3$ = 1:3) was used, no significant difference in both conversion and chemoselectivity was observed. Chemoselectivity towards aldehydes were > 98.5% for both solvents. By the use of 2 eqv. of DPPP ligand *i.e.* Rh:Ligand = 1:1, slower reaction was detected in GVL than in toluene. However, the nearly chemospecific reaction is accompanied by the slight decrease of the regioselectivity *i.e.* more linear aldehyde was formed in GVL than in toluene (Table 1, entries 1-3). This is in accordance with our recent observation for Pt-catalyzed hydroformylation of styrene [21].

Subsequently, several diphosphines (mainly chiral enantiomerically pure diphosphines) were also tested in asymmetric hydroformylation of styrene in rhodium-catalyzed reaction. Carrying out the reaction in the presence of Rh-BDPP system (Table 1, entries 6-17) the following statements can be made:

i) The activity of the rhodium-BDPP system (and that of the rhodium-DPPP system) in GVL is lower than in toluene (compare for instance entries 9 and 18, and entries 4 and 5, respectively). However, as expected, lower conversions were obtained at low pressure (15/15 bar) (entry 13) and low temperature (25 $^{o}$C) (entry 10). It should be noted that GVL as a non-protic dipolar species could act as a coordinating solvent reducing the reaction rate. Similar observations were reported for tetrahydrofurane [ 32 , 33 ]. When Rh(CO)2(acac) was used as a precursor no significant changes in the activity and selectivity were observed (entries 7 and 8).

ii) The high chemoselectivities towards aldehydes obtained in toluene (*ca.* 99%, entries 16-18) was further increased in GVL. In general, aldehyde selectivity higher than 99.8% can be achieved. The only lower chemoselectivity was obtained at high hydrogen partial pressure obtained by the variation of the reaction conditions (Table 1, entry 14).

iii) The experiments carried out at variable temperatures have shown no significant dependence of chemoselectivity on the reaction temperature (entries 6-10).

It should be noted that in toluene the lowering of the temperature resulted in a slight increase of the chemoselectivity. As one of the important advantages of using GVL, as it has been revealed by detailed GC-MS investigations, the practically chemoselective reaction towards aldehydes in GVL has to be mentioned.

iv) As for the regioselectivity, nearly the same regioselectivities were obtained in toluene and GVL (Table 1, entries 16-18 and 6-9, respectively). Some decrease (less than 2%) in regioselectivity towards branched aldehyde can only be observed when the reaction was carried out at low temperatures.

v) The reactions carried out at various pressures have shown no strong dependence of regioselectivity data on the partial pressure of carbon monoxide or hydrogen (Table 1, entries 13-15).

vi) The enantioselectivities obtained in the presence of BDPP in GVL, similar to those obtained in toluene, are very low in general. The *ee* of the hydroformylation towards branched aldehyde (2-phenylpropanal) could be increased to 9% when higher BDPP/Rh (3/1) ratios were used (entries 12, 13).

Regarding the other diphosphines, such as BINAP, DIOP, JOSIPHOS and QUINAP (Table 1, entries 19-38) very similar results obtained in GVL can be mentioned. That is, the reaction is practically chemospecific regarding aldehydes, provides high regioselectivity towards branched aldehyde (2-phenylpropanal) at low temperature and can provide low enantioselectivities under various conditions. It is worth mentioning that a surprisingly high dependence of regioselectivity on the temperature was observed with BINAP in GVL (Table 1, entries 19-24). When SEGPHOS and DM-SEGPHOS ligands with a smaller dihedral angle were used, significantly lower activity and negligible enantioselectivities were detected in GVL (Table 1, entries 36-38).

Additionally, efforts were made to separate and re-use the catalyst. By applying Rh/BDPP system under condition given in Table 1 entry 11, the products as a GVL solution can be separated by vacuum (10 mmHg) distillation at 80–85 °C. The glue-like residue that remained at the bottom of distillation flask, was re-dissolved in in GVL and re-used in consecutive cycle under identical conditions. We demonstrated that the Rh-BDPP system could be recycled for 3 times at 60 $^{o}$C and 80 bar pressure ($CO:H_2$ = 1:1). While a perfect chemoselectivity towards aldehydes (>99.9%) was maintained throughout this procedure, some decrease in both conversion and regioselectivity was observed reflecting the partial degradation of the catalyst (Table 2.). Similar observation was reported for Pt-BINAP-tin(II)chloride system [21].

Table 1. Hydroformylation of styrene in GVL (and, for comparison in toluene) in the presence of Rh-phosphine *in situ* systems [a)]

| Entry | Ligand | Solvent | T (°C) | p(CO)/p($H_2$) (bar) | Time (h) | Conv. (%) | $R_c$ [b] (%) | $R_{br}$ [c] (%) | ee.[d] (%) |
|---|---|---|---|---|---|---|---|---|---|
| 1[e] | $PPh_3$ | GVL | 100 | 40/40 | 24 | 100 | 99.5 | 67 | - |
| 2[e] | $PPh_3$ | toluene | 100 | 40/40 | 1 | 10 | 90.6 | 93 | - |
| 3[e] | $PPh_3$ | toluene | 100 | 40/40 | 24 | 100 | 98.8 | 87 | - |
| 4 | DPPP | GVL | 80 | 40/40 | 24 | 100 | 99.5 | 83 | - |
| 5 | DPPP | Toluene | 80 | 40/40 | 1 | 87 | 98.7 | 89 | - |
| 6 | BDPP | GVL | 80 | 40/40 | 24 | 100 | 99.9 | 90 | 7 (*S*) |
| 7 | BDPP | GVL | 60 | 40/40 | 24 | 63 | 99.8 | 92 | 3 (*S*) |
| 8f | BDPP | GVL | 60 | 40/40 | 24 | 57 | 99.6 | 92 | 2 (S) |
| 9 | BDPP | GVL | 40 | 40/40 | 20 | 5 | 99.2 | 93.9 | 10 (S) |
| 10 | BDPP | GVL | 25 | 40/40 | 68 | 51 | 99.8 | 98 | 0 |
| 11 | BDPP | GVL | 60 | 15/15 | 24 | 76 | 99.8 | >99 | 0 |
| 12[e] | BDPP | GVL | 60 | 40/40 | 24 | >99 | >99 | 95.3 | 9 (*S*) |
| 13[e] | BDPP | GVL | 60 | 15/15 | 24 | 79 | 99.9 | 92.3 | 9 (*S*) |
| 14 | BDPP | GVL | 60 | 20/80 | 24 | 100 | 95.8 | 94 | 2 (*R*) |
| 15 | BDPP | GVL | 60 | 40/60 | 24 | 100 | >99.9 | 93 | 2 (*R*) |
| 16 | BDPP | toluene | 80 | 40/40 | 1 | 100 | 98.8 | 89 | 4 (*R*) |
| 17 | BDPP | toluene | 60 | 40/40 | 5 | 86 | 98.9 | 94 | 2 (*R*) |
| 18 | BDPP | toluene | 40 | 40/40 | 24 | 100 | 99.2 | 95 | 7 (*S*) |
| 19 | BINAP | GVL | 100 | 40/40 | 3 | 55 | 99.6 | 66 | 0 |
| 20 | BINAP | GVL | 80 | 40/40 | 3 | 86 | 99.5 | 77 | 1 (*S*) |
| 21[f] | BINAP | GVL | 80 | 40/40 | 3 | 51 | 99.7 | 88 | 1 (*S*) |
| 22 | BINAP | GVL | 40 | 40/40 | 45 | 68 | >99.9 | 95 | 5 (*R*) |
| 23[f] | BINAP | GVL | 60 | 40/40 | 24 | 87 | 99.7 | 91 | 2 (*S*) |
| 24 | BINAP | toluene | 80 | 40/40 | 1 | 99 | 98.4 | 91 | 4 (*R*) |
| 25 | JOSIPHOS | GVL | 80 | 40/40 | 4 | 92 | 99.9 | 87 | 4 (*S*) |
| 26 | JOSIPHOS | toluene | 80 | 40/40 | 3 | 100 | 99 | 92 | 2 (*S*) |
| 27 | DIOP | GVL | 60 | 20/20 | 24 | 99.8 | >99.9 | 99.4 | 2 (*S*) |
| 28 | DIOP | GVL | 40 | 20/20 | 4.5 | 18 | >99.9 | 98.3 | n.d. |
| 29 | DIOP | GVL | 40 | 20/20 | 24 | 28.6 | >99.9 | 98.3 | 2 (*S*) |
| 30 | DIOP | toluene | 60 | 20/20 | 24 | >99 | 99.9 | 90.1 | 1 (*S*) |
| 31 | QUINAP | GVL | 60 | 20/20 | 30 | 6.9 | 99.1 | 81.4 | 10 (*S*) |
| 32 | QUINAP | toluene | 60 | 20/20 | 30 | 99.9 | 99.4 | 79.3 | 2 (*R*) |
| 33 | SEGPHOS | GVL | 60 | 40/40 | 5 | 21 | 61 | 98 | n.d. |
| 34 | SEGPHOS | GVL | 60 | 40/40 | 24 | 81 | 90 | 91 | 1 (*S*) |
| 35 | SEGPHOS | toluene | 60 | 40/40 | 24 | >99 | 99 | 93 | 5 (*S*) |
| 36 | DM-SEGPHOS | GVL | 60 | 40/40 | 5 | 14 | 11 | 97 | n.d. |
| 37 | DM-SEGPHOS | GVL | 60 | 40/40 | 24 | 27 | 63 | 93 | 3 (*S*) |
| 38 | DM-SEGPHOS | toluene | 60 | 40/40 | 24 | >99 | 97 | 94 | 4 (*S*) |

**B**: 2-phenylpropanal, **C**: 3-phenylpropanal, **D**: ethylbenzene.

[a] Reaction conditions (unless otherwise stated): Catalyst precursor: $[Rh(nbd)Cl]_2$, Rh/Ligand/styrene = 1/1/100, 1 mmol of styrene, solvent: 5 mL of toluene (or GVL).

[b] Chemoselectivity towards aldehydes (B, C). [(moles of B + moles of C)/(moles of B + moles of C + moles of D) × 100].

[c] Regioselectivity towards branched aldehyde (B). [moles of B/(moles of B + moles of C) × 100].

[d] Enantioselectivities were determined by chiral GC. (*S*)-2-phenylpropanal was eluted before the (*R*) enantiomer.

[e] Rh:Ligand = 1:3

[f] $Rh(CO)_2(acac)$ was used as a precursor.

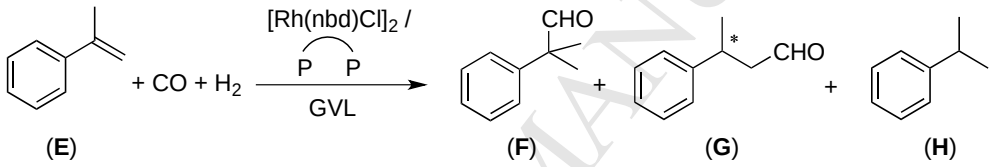
Table 2. Re-use of Rh-BDPP catalyst in the hydroformylation of styrene at 60 °C [a)]

| Cycle | Conversion (%) | $R_c$ | $R_{br}$ |
|---|---|---|---|
| 1 | >99 | >99 | 95.3 |
| 2 | >99 | >99 | 94.0 |
| 3 | 95 | >99 | 92.0 |
| 4 | 66 | >99 | 90.0 |

a) Reaction conditions: Catalyst precursor: $[Rh(nbd)Cl]_2$, Rh/Ligand/styrene = 1/1/100, 1 mmol of styrene, in 5 mL of GVL.

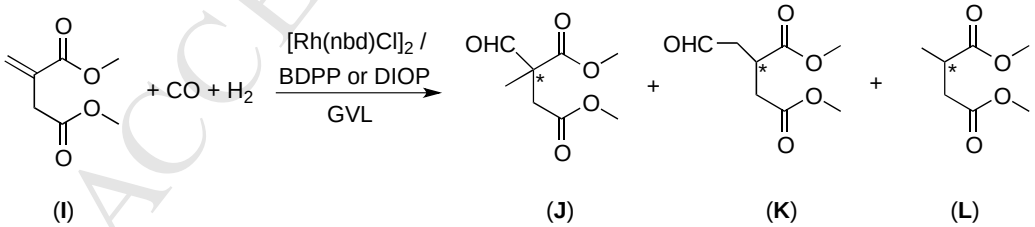
Two further substrates, α-methylstyrene (**E**) and dimethyl itaconate (**I**) were also subjected to hydroformylation.

The application of GVL in the hydroformylation of α-methylstyrene (Scheme 2) resulted in lower activity related to those obtained in toluene; however, resulted in higher chemoselectivity towards aldehydes while the extremely high regioselectivity towards the chiral aldehyde (**G**) was maintained. This is true for both BDPP- and BINAP-containing systems (Table 3, entries 1,3 and 2,4, respectively).




**Scheme 2** Hydroformylation of α-methylstyrene (**E**)

In contrary to styrene-type substrates, the hydroformylation of dimethyl itaconate (**I**) (Scheme 3) resulted in higher conversion in GVL. The difference in activity was surprisingly high at low temperature (Table 3, entries 5 and 6). However, low chemoselectivity towards aldehydes (**J**, **K**) were observed in general. That is, practically only hydrogenation takes place at high temperature in GVL both in the presence of BDPP and DIOP ligands (Table 3, entries 8 and 10).



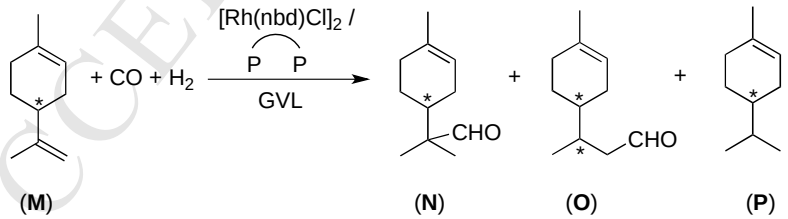

**Scheme 3** Hydroformylation of dimethyl itaconate (**I**)

Table 3. Hydroformylation of various substrates in GVL (and, for comparison in toluene) in the presence of Rh-phosphine '*in situ*' systems [a)]

| Entry | Substrate | Ligand | Solvent | T (°C) | Time (h) | Conv. (%) | $R_c$ [b] (%) | $R_{lin}$ [c] (%) | ee. (**J**)[d] (%) | ee. (**G/K**)[d] (%) | ee. (**L**)[d] (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | α-methylstyrene | BDPP | GVL | 60 | 24 | 9.2 | 95 | >99 | - | 0 | - |
| 2 | α-methylstyrene | BINAP | GVL | 60 | 24 | 3.6 | >99 | >99 | - | 0 | - |
| 3 | α-methylstyrene | BDPP | toluene | 60 | 24 | 44.6 | 77 | >99 | - | 0 | - |
| 4 | α-methylstyrene | BINAP | toluene | 60 | 24 | 23.1 | >99 | >99 | - | 0 | - |
| 5 | dimethyl itaconate | BDPP | toluene | 60 | 24 | 8 | 40 | 27 | 3.6 (-) | 0 | 0.2 (*R*) |
| 6 | dimethyl itaconate | BDPP | GVL | 60 | 24 | 47 | 9 | 1 | 0 | n.d. | 0.2 (*R*) |
| 7 | dimethyl itaconate | BDPP | toluene | 100 | 24 | >99 | 15 | 64 | 2.2 (-) | 0.5 (*S*) | 0.3 (*S*) |
| 8 | dimethyl itaconate | BDPP | GVL | 100 | 24 | >99 | <1 | n.d. | n.d. | n.d. | 0.3 (*R*) |
| 9 | dimethyl itaconate | DIOP | toluene | 100 | 20 | 73 | 25 | 22 | 0.8 (-) | 1.2 (*S*) | 0 |
| 10 | dimethyl itaconate | DIOP | GVL | 100 | 20 | >99 | <1 | n.d. | n.d. | n.d. | 1.8 (*R*) |

**F**: 2-methyl-2-phenylpropanal (or **J**: dimethyl 2-formyl-2-methylsuccinate) (branched aldehyde)
**G**: 3-phenylbutanal (or **K**: dimethyl 2-(formylmethyl)succinate) (linear/less branched aldehyde)
**H**: isopropylbenzene (or **L**: dimethyl 2-methylsuccinate) (hydrogenated product)
[a] Reaction conditions: Rh/Ligand/substrate = 1/1/100, 1 mmol of substrate, $p(CO)=p(H_2)$= 40 bar; solvent: 5 mL GVL (or toluene).
[b] Chemoselectivity towards aldehydes (**F/G**, **J/K**). [(moles of **F/J** + moles of **G/K**)/(moles of **F/J** + moles of **G/K** + moles of **H/L**) × 100].
[c] Regioselectivity towards linear aldehyde (**G/K**). [moles of **G/K**/(moles of **G/K** + moles of **F/J**) × 100].
[d] Enantioselectivities were determined by chiral GC.

A terpene derivative, (*R*)-limonene of practical importance was hydroformylated under similar conditions (Scheme 4). As observed before in platinum-catalyzed hydroformylation [34] and palladium-catalyzed hydroalkoxycarbonylation [35], high regioselectivity towards linear regioisomer (**O**) was obtained also in rhodium-catalyzed hydroformylation in GVL. The chemoselectivity towards aldehydes (**N**, **O**) is about 75%, *i.e.*, some hydrogenated product (**P**) was always present in the reaction mixture. The two diastereoisomers were formed in close to 1/1 ratio. A slight diastereoselection of 16% and 4% was observed with BDPP- and BINAP-containing catalysts, respectively.




**Scheme 4** Hydroformylation of (*R*)-limonene (**M**)

Table 4. Hydroformylation of (*R*)-limonene in GVL in the presence of Rh-phosphine '*in situ*' systems[a)]

| Entry | Substrate | Ligand | Solvent | T (°C) | Time (h) | Conv. (%) | $R_c$ [b] (%) | $R_{lin}$ [c] (%) | de. (**O**)[d] (%) |
|---|---|---|---|---|---|---|---|---|---|
| 1 | (*R*)-Limonene | BDPP | GVL | 100 | 20 | >99 | 75 | 95 | 16 |
| 2 | (*R*)-Limonene | BINAP | GVL | 100 | 20 | >99 | 77 | 96 | 4 |

[a]Reaction conditions: Rh/Ligand/substrate = 1/1/100, 1 mmol of substrate, $p(CO) = p(H_2)$ = 40 bar; solvent: 5 mL

[b]Chemoselectivity towards aldehydes (**N**, **O**). [(moles of **N** +moles of **O**)/(moles of **N** + moles of **O** + moles of **P**) × 100].
[c]Regioselectivity towards selected aldehyde (**O**). [moles of **O**/(moles of **O** + moles of **N**) × 100].
[d]Diastereomeric excess. [(moles of diastereomer 1-moles of diastereomer 2)/(moles of diastereomer 1 + moles of diastereomer 2) × 100

## 3. Conclusion

In summary, the application of gamma-valerolactone as a renewable and environmental friendly solvent was successfully utilized for bidentate phosphine ligand-modified rhodium-catalyzed hydroformylation of styrene, α-methylstyrene, dimethyl itaconate, and (*R*)-limonene. Although, the catalytic activities were lower in GVL compared to toluene as a conventional organic solvent for hydroformylation, remarkable chemo- and regioselectivities were observed in GVL. Results proved that GVL is a good biomass-based alternative solvent and could be very promising for its application in both industrial and academic processes.

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# Rhodium-catalyzed hydroformylation in γ-valerolactone as a biomass-derived solvent

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## Highlights

- γ-valerolactone was applied as a solvent for Rh-catalyzed hydroformylation.
- Results were compared to toluene as a FDA Class 2 solvent.
- Remarkable chemo- and regioselectivities were achived in GVL.