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Manufacture of Citronellal by the Rhodium-Catalyzed Homogeneous Hydrogenation of Neral

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Abstract. The highly chemoselective hydrogenation of neral affording citronellal is described. The reaction has been conducted with homogeneous rhodium complexes. Among the set of ancillary diphosphane ligands tested, Xantphos was found to be superior. The relevant precatalyst has been generated from neutral metal sources such as $Rh(acac)(CO)_2$ or the carbon monoxide free rhodium source Rh(acac)(cod) in the absence of any base. A high activity and chemoselectivity in favor of the desired citronellal is achieved at 0.1 MPa and room temperature. Under the same conditions, geranial is also reduced to citronellal. The addition of carbon monoxide to the hydrogen stream as used in an industrial process is not necessary.

Keywords: Catalyst precursors; Chemoselective hydrogenation; Enones; Rhodium; Xantphos

Introduction

Catalytic hydrogenation with molecular hydrogen is one of the most important transformations in chemistry. Heterogeneous[1] as well as homogeneous hydrogenations[2] represent key technologies not only in academic labs but also for the chemical and pharmaceutical industries. For example, in 2013, 25% of marketed drugs required at least one hydrogenation step in their production.[3] In this context, the development of highly chemoselective hydrogenation reactions of functionalized olefins is a challenging task.[4] Among such multifunctional substrates, the transformation of α,β-unsaturated carbonyl compounds, e.g., enones, plays a pivotal role. Frequently, this transformation is assisted by the application of heterogeneous catalysts offering several advantages over the homogeneous version with respect to separation of the product and recycling of the catalyst.[5] On the other hand, problems with the toleration of other functionalities in the substrate may be faced. Especially, poor chemoselectivities and over-reduction represent serious issues.

A typical substrate in this regard is the monoterpene citral (**1**, Scheme 1), representing a mixture of the two configurational isomers neral (**1a**) and geranial (**1b**). Citral is a natural product and widely used as a starting material for the manufacturing of fragrances, flavors, pharmaceuticals, nutrients and vitamins.[6] Citronellal (**2**), as one of the hydrogenation products, is an important ingredient for perfumes and other flavor compounds. (±)-Citronellal is found in nature in herbs and spices. It possesses anti-inflammatory and redox protective activities, and it is used against fungal infections.[7] Enantioenriched citronellal (**2**) serves as an educt for the total synthesis of menthol, which is another important flavor material. Besides the preparation of (*R*)-citronellal for special applications, e.g., for the synthesis of L-menthol,[8] the synthesis of racemic citronellal is also of similarly high industrial interest.[9] The most preferential route to **2** is based on the chemoselective hydrogenation of neral or geranial. In this regard, only the activated conjugated C=C double bond should be hydrogenated, while keeping the aldehyde group unaffected in order to avoid the formation of citronellol (**3**). The latter may cause heavy allergies when used in perfumes or other odorants. Another challenge is the *E/Z*-isomerization equilibrium between neral (**1a**) and geranial (**1b**). This reaction is catalyzed by several hydrogenation catalysts and may therefore alter the composition and thus consequently the chemical properties of the substrate. Additionally, full saturation of the substrates or of relevant intermediates such as nerol (**4a**) or geraniol (**4b**) to give 3,7-dimethyloctanol (**5**) should be strictly avoided.

A common way to approach the regio- and chemoselective hydrogenation of the conjugated C=C-double bond in citral is the application of heterogeneous metal catalysts. Thus, considerable selectivities were reached with the use of a range of palladium-based systems.[10] Other noble metals such as platinum, nickel, and ruthenium often performed less selectively or simultaneously affected the carbonyl group.[11] In addition, chiral heterogeneous

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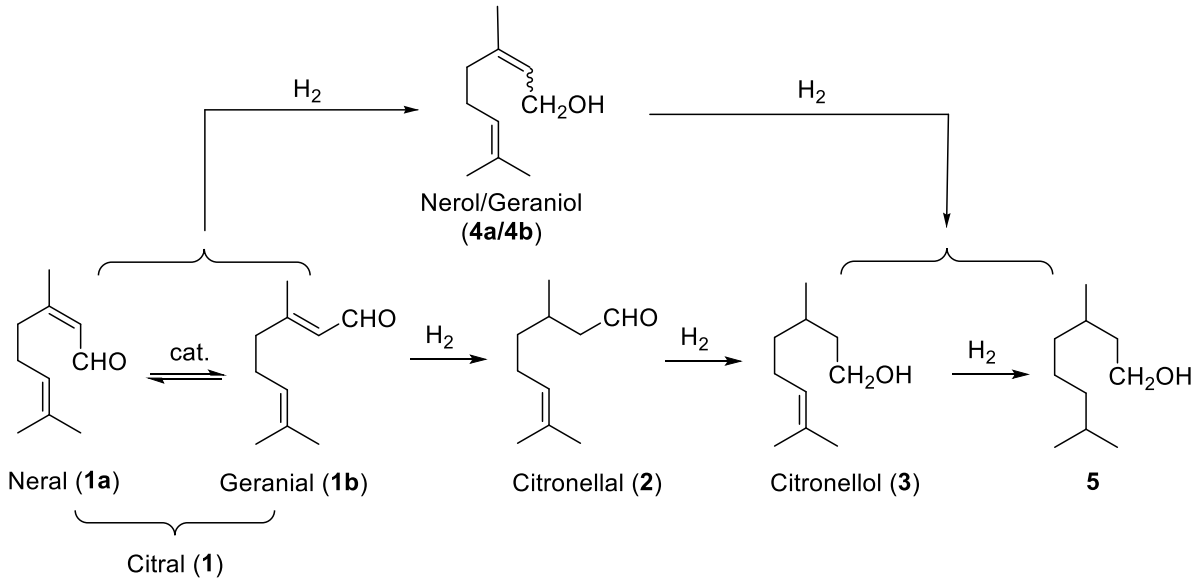

Scheme 1. Synthesis of Citronellal (**2**) by the Chemoselective Hydrogenation of Citral Isomers **1**.

as well as homogeneous hydrogenation catalysts have been screened for the synthesis of enantiomerically enriched citronellal.[12] The technical BASF-process running on a scale of 3 to 5 metric tons for the synthesis of L-menthol commences with the asymmetric homogeneous hydrogenation of citral with a ratio of neral (**1a**)/geranial (**1b**) ≥ 95:5.[8b] It is based on a rhodium complex modified with the chiral diphosphane ligands (*R*,*R*)- or (*S*,*S*)-Chiraphos ((2*S*,3*S*)-butane-2,3-diyl)bis(diphenylphosphane)).[13] Remarkably, the transformation is started under typical "hydroformylation" conditions, where the precatalyst is generated by treatment of $Rh(acac)(CO)_2$ and the phosphorus ligand in a syngas atmosphere (CO/H_2 = 1:1, 8 MPa). The hydrogenation itself proceeds only in the presence of 1000 ppm carbon monoxide in a hydrogen stream with a pressure of 8 MPa. Another approach claimed by the Nikki Chemical Co. employs a $Rh(PPh_3)$-catalyst and operates likewise under syngas (CO/H_2 = 1:1).[14] A group at Rhône-Poulenc suggested rhodium carbonyl complexes, such as $HRh(CO)(PPh_3)_3$, $Rh_6(CO)_{16}$ or $Rh_4(CO)_{12}$, for the formation of the relevant precatalyst.[15] Up until now, the role of CO has not been fully clarified. NMR spectroscopic investigations by Scheuermann and Jaekel with a catalyst prepared from $Rh(acac)(CO)_2$ and Chiraphos using cyclic enones as the substrate indicated that only by the addition of a carefully adjusted amount of CO is the formation of a catalytically inactive bis(diphosphane)Rh-complex prevented.[16] Moreover, it was claimed that CO-free metal sources such as Rh(acac)(cod) (cod = 1,5-cyclooctadiene) or $[Rh(cod)_2]BF_4$ did not catalyze the hydrogenation even at high H_2-pressure.

In order to find less severe hydrogenation conditions and to facilitate the tricky technical set-up for the hydrogenation of citral isomers by avoiding the handling of toxic CO gas at different concentrations with respect to hydrogen, we investigated the subtle relationship between the rhodium source, phosphane ligand and CO in the hydrogenation. As commercially available ligands diphosphanes were tested.

Results and Discussion

Our preliminary attempts under enhanced hydrogen pressure showed that some of the chosen rhodium source/ligand systems are not able to catalyze the hydrogenation of pure neral (**1a**). Frequently, before the hydrogenation, the isomerization of neral (**1a**) into geranial (**1b**) took place, which is a typical behavior of some rhodium-based hydrogenation catalysts.[17] Especially, in the asymmetric hydrogenation, this isomerization may significantly affect the results.[8b] Moreover, under these circumstances the completion of the hydrogenation was difficult to evaluate. Often the hydrogenation to citronellal (**2**) was accompanied by the subsequent transformation of the latter to citronellol (**3**). In some cases, the formation of nerol (**4a**) by the hydrogenation of the aldehyde group was the predominant reaction. Nerol (**4a**) or a mixture of nerol and geraniol (**4a**/**4b**) can also react further to form citronellol (**3**). Occasionally, full saturation to give 3,7-dimethyloctanol (**5**) was also noted.

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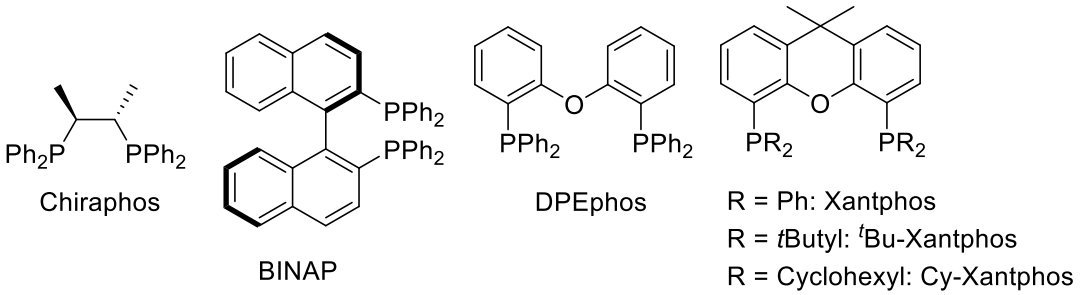
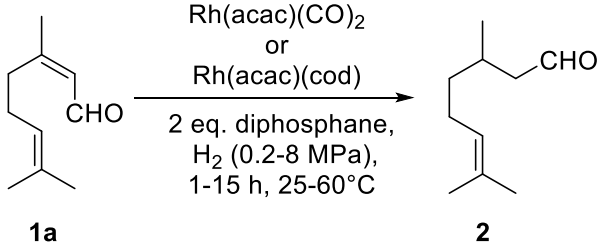
Table 1. Results of the Hydrogenation of Neral (**1a**)[a].



Entry	[Rh]	Ligand	S:Rh	*T* [°C]	*p* [MPa]	*t* [h]	Composition of Final Mixture[b] [Mol-%]				
							1a	**1b**	**2**	**3**	**4**
1	**A**	Chiraphos	200:1	60	8	4	88	7	5		
2	**A**	Chiraphos	200:1[c]	60	8	4	37	23	40		
3	**B**	Chiraphos	500:1[c]	60	8	10	46	41	13		
4	**B**	BINAP	500:1[c]	60	8	10	21	1	10	32	36
5	**A**	BINAP	500:1[c]	60	8	15	46		35	11	8
6	**A**	DPEphos	500:1[c]	60	8	15			95	5	
7	**B**	DPEphos	500:1[c]	60	8	15			90	10	
8	**A**	DPEphos	500:1[c]	30	1	10	93		7		
9	**A**	Xantphos	500:1[c]	60	4	10			12	88	
10	**A**	Xantphos	200:1	40	2	4			23	77	
11	**A**	Xantphos	200:1[c]	40	2	4			4	96	
12	**B**	Xantphos	200:1	30	1	4			84	16	
13	**B**	Xantphos	200:1	25	0.5	2			94	6	
14	**B**	Xantphos	800:1	25	2	4			87	13[d]	
15	**B**	Xantphos	800:1	25	2	1			95	5[d]	
16	**B**	Xantphos	800:1	25	0.2	5			97	3[d]	
17	**B**	Xantphos	600:1	25	2	0.3			96	4[d]	
18[e]	**B**	Xantphos	600:1	25	2	0.3			96	4[d]	
19	**A**	[t]Bu-Xantphos	500:1[c]	60	6	10				18	82[f]
20	**B**	Cy-Xantphos	200:1	25	2	4	91	9			

[a] *Conditions:* 10 µmol Rh-Precursor **A** (Rh(acac)(CO)$_2$) or **B** (Rh(acac)(cod)), 20 µmol Ligand, 7.5 ml Toluene; If Not Otherwise Indicated, Neral (**1a**) Was Used as the Substrate. [b] Estimation of the Composition Was Carried out by NMR. [c] Neat. [d] 3.33 µmol Rh-Precursor, 6.66 µmol Ligand. [e] Geranial (**1b**) Was Used as the Substrate. [f] *Z/E* = 54:28.

A range of prominent phosphane ligands was screened at various temperatures, pressures and substrate/rhodium ratios (Scheme 2). The catalysts were generated by the reaction of either Rh(acac)(CO)$_2$ or Rh(acac)(cod) with two equivalents of the diphosphane.



Scheme 2. Hydrogenation of Neral (**1a**).

Table 1 summarizes some typical results. It should be noted that trials with PPh_3, dppb [1,4-bis(diphenylphosphanyl)butane] or dppf [1,1'-bis(diphenylphosphanyl)ferrocene] as ligands gave only poor yields, and therefore, the results are not listed. Additionally, rhodium complexes bearing Chiraphos and BINAP (2,2'-bis(diphenylphosphanyl)-1,1'-binaphthalene) were not able to catalyze the hydrogenation of neral (**1a**) to citronellal (**2**) in a satisfactory manner under these conditions. The reactions did not go to completion and were accompanied by the isomerization of neral (**1a**) to geranial (**1b**) (Entries 1-5).

Only the application of the ether diphosphane DPEphos ((oxybis(2,1-phenylene))bis(diphenylphosphane)) gave some early results that were promising. At elevated temperature and a H_2-pressure of 6 MPa, complete hydrogenation took place; 90% or even higher chemoselectivities in favor of **2** could be obtained (Entries 6 and 7).

Table 2. Results of the Hydrogenation of Neral (**1a**) with Various Solvents[a].

Solvent	$t_{100\%}$ [min][b]	t_{total} [min][c]	Conversion [%]	Portion of **2** [Mol-%][d]
toluene	25	-	100	98
methanol	-	60	0	-
tetrahydrofuran	70	-	100	99
dichloromethane	-	90	34	99
hexane	55	-	100	99
PC[e]	-	180	72	99
PC[e]/hexane	300	-	100	99
neat	60	-	100	99

[a] Conditions: 1 mmol of 1a, 1a/Rh(acac)(cod)/Xantphos = 100:1:2, 25°C, 0.1 MPa, 7.5 mL of Solvent. [b] The Reaction Was Stopped at the Inflexion Point of the Hydrogen Consumption Curve. [c] Reaction Time Before the Complete Consumption of Hydrogen.[d] Estimated by NMR. [e] PC = Propylene Carbonate.

It is noteworthy that the hydrogenation proceeds well regardless of the metal source used, $Rh(acac)(CO)_2$ (Condition A) or the CO-free version Rh(acac)(cod) (Condition B). However, under less severe conditions, the hydrogenation with DPEphos became sluggish (Entry 8).

Unexpectedly, this problem could be overcome by use of the structurally similar ligand Xantphos ((9,9-dimethyl-9H-xanthene-4,5-diyl)bis(diphenylphosphane)) bearing a rigid ether backbone. It should be noted, that Xantphos and the closely related diphosphane Nixantphos (4,6-bis(diphenylphosphanyl)-10-methyl-10H-phenoxazine) have been recommended as ligands in a patent of Firmenich for the selective hydrogenation of various conjugated dienals.[18] The relevant catalyst was generated from an ionic complex of the type [Rh(diolefin)(diphosphane)]X (diolefin = cod, nbd (nbd = norbornadiene); X = Cl, BF_4, TfO) due to the effect of bases (KOAc, KOC(O)Ph), and it was operated at elevated hydrogen pressures of 1-5 MPa.

Remarkably, our rhodium (Xantphos) complexes display their high chemoselectivity only under mild conditions (Entries 12-17); at higher hydrogen pressures and temperatures, citronellol (**3**) was the major product (Entries 9-11). At 25 °C and a H_2 pressure of 0.2-0.5 MPa, citronellal (**2**) was formed in excellent chemoselectivities even at higher substrate/rhodium ratios of up to 800:1 (Entries 12-17). In order to avoid over-reduction to citronellol (**3**), it was necessary to shorten the reaction time (Entry 14 versus Entry 17). Under more drastic conditions, the formation of **3** was favored. This also holds for larger amounts of the catalyst and prolonged reaction times (Entries 9-11). Investigations using geranial (**1b**) as the substrate instead off neral (**1a**) showed a similar tendency in the hydrogenation. After complete conversion of both substrates, 96% of **2** was obtained in each case (compare Entries 17 and 18).

The careful monitoring of the hydrogen consumption during the reaction helps to interrupt the hydrogenation at the inflexion point.[19] Structural variations of the parent Xantphos ligand did not improve the results. Additionally, the replacement of phenyl with aliphatic groups (cyclohexyl, *t*-butyl) influenced the hydrogenation negatively (Entries 19, 20). Reduction of the carbonyl group was noted with ^{t}Bu-Xantphos ((9,9-dimethyl-9H-xanthene-4,5-diyl)bis(di-tert-butylphosphane)) (Entry 19). Mainly isomerization of the substrate was observed with the relevant Cy-Xantphos ((9,9-dimethyl-9H-xanthene-4,5-diyl)bis(dicyclohexylphosphane)) complex (Entry 20). Apparently, electron-rich *P*-atoms in the diphosphane ligand lead to a different coordination behavior and alter the catalytic properties of the rhodium complexes. Thus, after mixing Rh(acac)(cod) and ^{t}Bu-Xantphos in a ratio of 1:1 in toluene-d_8, no complexation of the ligand to the rhodium center by substitution of cyclooctadiene was observed. Only the uncoordinated ^{t}Bu-Xantphos was detected in the ^{31}P NMR spectrum (δ_p +10.4 ppm). This is in strong contrast to the behavior of Xantphos (*vide infra*) and demonstrates the importance of the P-phenyl groups.[20]

The high hydrogenation activity of the Xantphos catalyst under rather mild conditions prompted us to try the reaction even at a H_2 pressure of 0.1 MPa and 25°C, which allowed the switch from a stainless steel pressure reactor to a glass vessel. Indeed, we were pleased to see that under these conditions, the hydrogenation of **1a** also took place in the desired manner. Our solvent screening clearly showed that the best catalytic performance can be reached in toluene (Table 2). Methanol as a solvent failed entirely. The reactions in tetrahydrofuran and hexane, respectively, also proceeded well, but they required a longer time compared to the transformation in toluene. Reactions in other solvents such as dichloromethane or propylene carbonate (PC) were slower or did not lead to complete conversions due to our NMR analysis. Interestingly, the reaction under neat conditions also gave full conversion and almost complete chemoselectivity. Nevertheless, the reaction in toluene was superior in terms of the reaction half-life, conversion and chemoselectivity of **2**.

In Figure 1a, a typical curve of hydrogen consumption is depicted. After ca. 30 minutes, the conversion of substrate **1a** is complete. The isolated

product contained 98% of the desired aldehyde **2** and only 2% of alcohol **3**. Figure 1b illustrates the situation when the hydrogenation of **1a** was prolonged to approximately 21 hours.

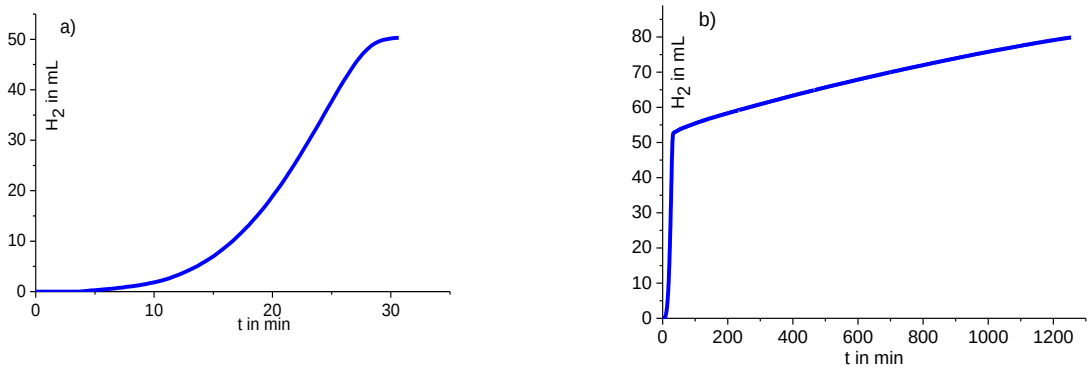


Figure 1. H_2-Consumption During the Hydrogenation of **1a** at Ambient Conditions (25 °C, 0.1 MPa) in Toluene with Rh(cod)(acac)/Xantphos (**1a**/[Rh]/ligand = 200:1:2). **Figure 1a)** Hydrogenation of the C=C-Bond. **Figure 1b)** Fast Reduction of the Olefin and Subsequent Slow Hydrogenation of the C=O-Group.

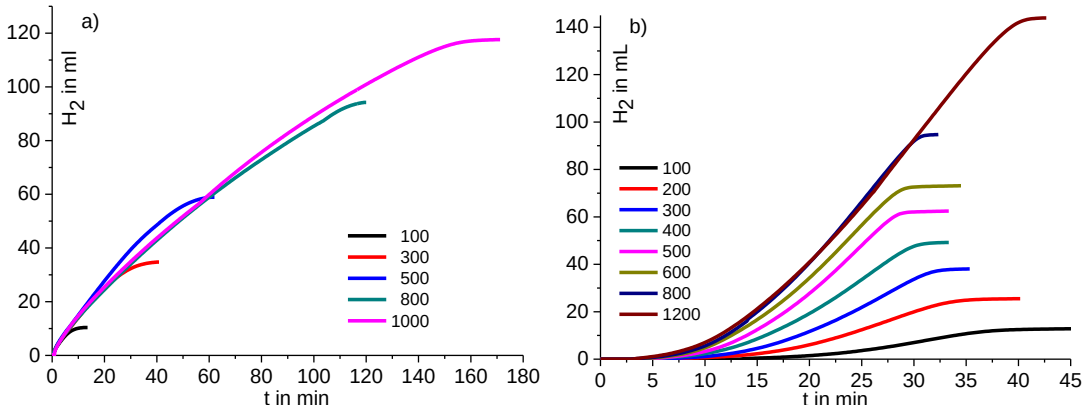


Figure 2. Hydrogenation of Neral (**1a**) with Two Different Metal Sources and Varying **1a**/[Rh]/Ligand Ratios = x:1:2 by Using Rh(acac)$(CO)_2$ (**Figure 2a**) or Rh(acac)(cod) (**Figure 2b**) [(x = 100…1000/1200), 5 µmol Rhodium Source, 0.1 MPa H_2 Pressure, at 25°C in Toluene (7.5 mL)].

The inflexion point at ca. 35 minutes indicates the end of the hydrogenation to citronellal (**2**). The second part of the curve corresponds to the slow hydrogenation of **2** to citronellol (**3**). At the end, the isolated product consisted of a mixture of **2** and **3** in a ratio of approximately 66:34.

By application of the alternative rhodium source Rh(acac)$(CO)_2$ instead off Rh(acac)(cod), the reaction also proceeded well. However, inspection of the hydrogen consumption curves shows that the shapes are different (Figure 2).

Whereas the hydrogenation started immediately using Rh(acac)$(CO)_2$ (Figure 2a), the reaction with Rh(acac)(cod) is characterized by an induction period of a few minutes. With Rh(acac)$(CO)_2$, an increase of the substrate/rhodium ratio did not influence the turnover frequency of the hydrogenation, and the curves essentially overlap (Figure 2a). Obviously, the reaction follows zero-order kinetics regarding the substrate. In contrast, with Rh(acac)(cod), the reaction rate increased with increasing substrate/rhodium ratios (Figure 2b, Table 3) and a positive reaction order can be assumed. The reaction rate became constant at a ratio of approximately 800:1 (Table 3, Entries 1-7). This ratio could be further increased to 2000:1 without affecting the rate of the transformation (Table 3, Entries 8 and 9). Only at a ratio of 3000:1 did the turnover frequency of the hydrogenation drop dramatically (Entry 10).

Remarkably, high substrate/catalyst ratios could only be obtained by using freshly distilled substrate. In previous trials, it was observed that the hydrogenations were incomplete and slowed down even with ratios of 600/1-800/1. Our first speculation that the reaction was inhibited by the product citronellal could be excluded by the addition of the product to the hydrogenation. Under these conditions, no effect was observed. However, it was found that the activity of hydrogenation dropped with increasing storage time of the substrate neral (**1a**). For example, Entry 4 in Table 3 shows the result when a sample of neral that was stored in the presence of air for two

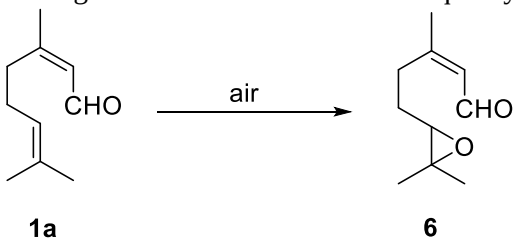
days was employed. Under these conditions, no consumption of hydrogen occurred. However, by the application of freshly distilled neral or the use of substrate which has been strictly stored under inert gas, the substrate/catalyst ratio could be further increased.

Table 3. Results of the Hydrogenation of Neral (**1a**) with Rh(acac)(cod) at Ambient Conditions (25°C, 0.1 MPa)[a].

Entry	[S]:[Rh]	t_{100} [min]	t_{total} [min]	Composition of Final Mixture [Mol-%][b]		
				1a	**2**	**3**
1	100:1	43	45		93	7
2	200:1	37	40		96	4
3	300:1	34	35		97	3
4[c]	300:1		180	100	-	-
5	400:1	32	33		97	3
6	600:1	32	34		98	2
7	800:1	31	32		98	2
8	1200:1	41	43		99	1
9[d]	2000:1	52	55		98	2
10[d]	3000:1		1400	4	>96	<1

[a] Conditions: 5 µmol (1.55 mg) (Rh(acac)(cod), 10 µmol (5.8 mg) Xantphos, 7.5 ml Toluene. [b] Estimation of the Composition Was Carried out by NMR. [c] Neral Was Stored under Aerobic Conditions for Two Days. [d] 3.33 µmol (1.03 mg) Rh(acac)(cod), 6.66 µmol Xantphos, 7.5 ml Toluene.

By keeping a sample of neral in the presence of air after three days, approximately 10 mol% of the corresponding 6,7-epoxide **6** was formed (Scheme 3).[21] This epoxide is apparently a poison to the catalyst and/or ligand and causes the deactivation. Therefore, the larger the substrate/catalyst ratio, the larger the proportion of this inhibitor compared to the catalyst, and thus, the larger the effect on the turnover frequency.



Scheme 3. Formation of the 6,7-Epoxide of Neral.

Varying results with different rhodium sources led us to the assumption that the resulting catalytic systems are different, and hence, the kinetics of the reactions are also different. Mixing Rh(acac)(cod) with Xantphos (1.5 eq.) in toluene-d_8 showed that after four hours, only ca. 20 mol% of Rh(acac)(cod) was converted into a Rh(acac)(Xantphos) complex. Besides the released cyclooctadiene, no uncoordinated acetylacetone was found in the ^{1}H NMR spectrum. The resulting Rh(acac)(Xantphos) complex was characterized by a doublet in the ^{31}P NMR spectrum (δ_P +34.4 ppm, $J_{Rh,P}$ = 202 Hz) (Figure 3a).

Approximately 24 hours later, only 65 mol% of the desired Rh complex could be detected. Additionally, an attempt to shift the equilibrium of the ligand exchange between cyclooctadiene and Xantphos failed. Thus, after one hour of stirring a mixture of Rh(acac)(cod) and 1.5 eq. Xantphos in toluene, all of the volatile materials were evaporated under vacuum (30 min), and the residue was dissolved again in toluene-d_8. By comparison of the relevant NMR spectrum with that of the untreated sample, no differences were visible. After ca. four hours, in both cases only ~20 mol% of the targeted precatalyst was formed, which is in contrast to a reaction suggested for the complete substitution of diolefins in rhodium precatalysts in the literature.[22] In contrast, by submission of Rh(acac)$(CO)_2$ to the same procedure, one equivalent of Xantphos was almost fully consumed after three hours, and a broad doublet at approximately (δ_P +13.5 ppm, $^1J_{Rh,P}$ = 88 Hz) became visible (Figure 3b). The spectroscopic data of the formed complex are close to those of Rh(acac)(CO)(Xantphos) described by Dingwall and co-workers (δ_P +11.0 ppm, $J_{Rh,P}$ = 88 Hz).[23]

Next, we investigated the effect of the ligand/Rh ratio on the reaction. In Figure 4a, it is demonstrated that in both trials (**1a**/[Rh]/Xantphos = 600:1:x and 300:1:x; x = 1, 2, or 3 eq.) with a diminishing amount of Xantphos, the time for the induction period is shortened, but the turnover frequency in the range of 30 and 70 % conversion remains constant. It seems that the excess diphosphane blocks vacant positions at the rhodium center and therefore retards the start of the hydrogenation. It was also quite surprising to note that pre-treatment of the Rh(acac)(cod)/Xantphos system with hydrogen in the absence of the substrate for up to 60 minutes did not show any effect on the subsequent hydrogenation of neral (Figure 4b), as all three curves of the hydrogen consumption are almost identical. Apparently, the hydrogenation of coordinated 1,5-cyclooctadiene to cyclooctene and cyclooctane is rather slow.

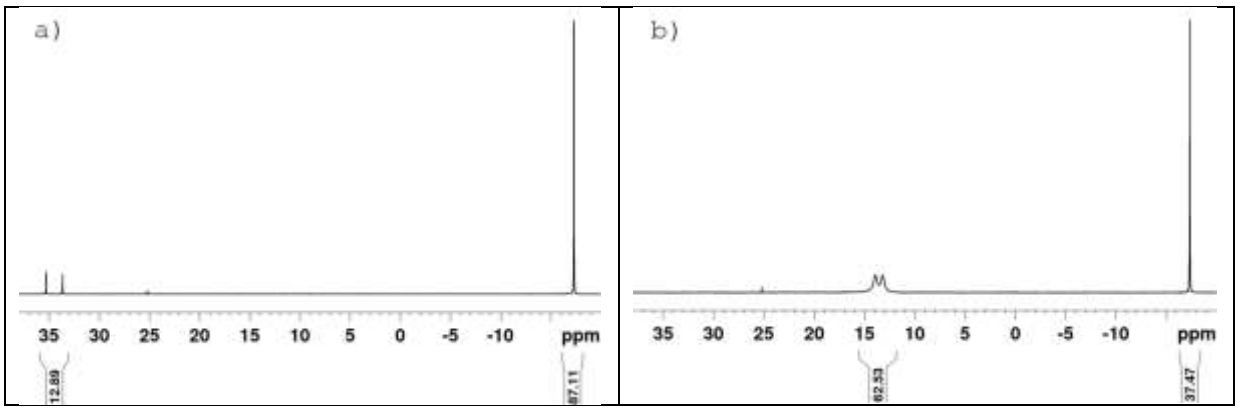


Figure 3. ^{31}P NMR Spectra Registered After 3-4 Hours of Complex Formation using 1.5 eq. of Xantphos and Rh(acac)(cod) (**Figure 3a**) or 1.5 eq. of Xantphos and Rh(acac)$(CO)_2$ (**Figure 3b)**.

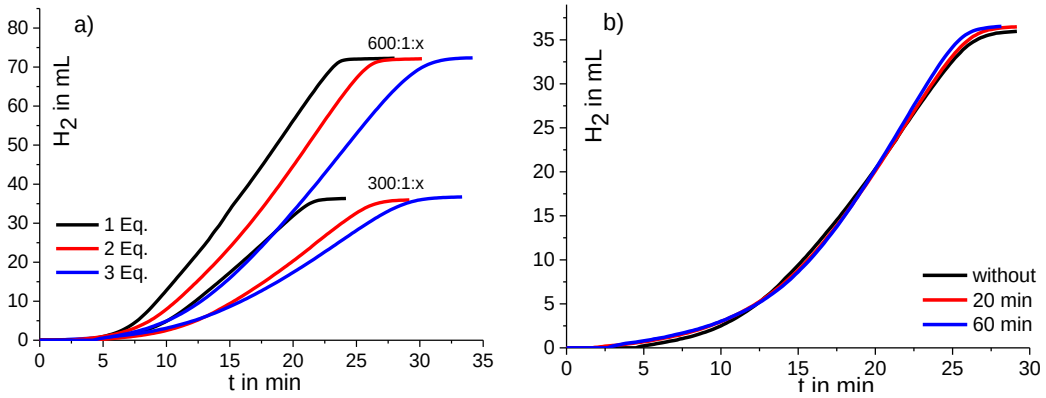


Figure 4a) Influence of the Ratio **1a**/[Rh]/Xantphos on the Reaction Time (600:1:x and 300:1:x; x =1, 2, or 3 eq.). **Figure 4b)** Influence of the Time of Pre-Hydrogenation on the Hydrogenation of Neral in Ambient Conditions (Rh(acac)(cod), **1a**/[Rh]/Xantphos = 300:1:2). Reaction Conditions: 5 µmol Rhodium Precursor, 0.1 MPa H_2-Pressure, at 25°C in Toluene (7.5 mL).

Conclusion

For the industrially relevant chemo- and regioselective hydrogenation of neral to citronellal, a homogeneous rhodium catalyst based on the ether diphosphane Xantphos endowed with a large bite angle was developed. In strong contrast to other catalytic approaches suggested in the past, the new catalytic system can be conveniently generated from Rh(acac)$(CO)_2$ or the CO-free metal source Rh(acac)(cod). The catalytic system operates best at 0.1 MPa hydrogen pressure, at 25°C in toluene or even under neat conditions. The reaction operates with excellent conversion and gives the desired product citronellal in greater than 95 % chemoselectivity. Under the optimized conditions, *E/Z*-isomerization of the substrate does not play a role, which might be a precondition for the success of a described stereoselective version.[8b] It is noteworthy that the homogeneous hydrogenation proceeds without the presence of CO in the precatalyst. Moreover, the addition of CO to the hydrogen gas during the hydrogenation is not required. We speculate that after coordination to rhodium, the large bite angle of diphosphane Xantphos more strongly inhibits the formation of bis-ligand rhodium complexes as found for the corresponding Chiraphos complexes. The latter displays a smaller bite angle, and therefore, CO has the function of loosely coordinating to the metal and preventing the formation of catalytically inactive bis-ligated complexes.[8b, 16] The mild reaction conditions found may offer a possibility for a more facile enantioselective version of the reaction, provided that suitable chiral Xantphos-type ligands with the correct electronic and steric structure become available.

Experimental Section

General Procedure for the Hydrogenation Studies of Neral (1a) at Elevated Pressure

All reactions were carried out using an automatic device [HPChemScan, Fa. HEL Ltd.], which allows the parallel hydrogenation in up to eight mini-

autoclaves (16 mL). Each autoclave was equipped with a proper glass vial along with a cross-stirrer and loaded with 10 µmmol of Rh-precursor, 20 µmol of ligand, and the indicated amount of neral (**1a**). After assembly of the autoclaves into the device, the system was purged with argon five times (0.6 MPa), and in the cases indicated in Table 2, the solvent was added. After purging three times with hydrogen (1 MPa) and heating at ambient pressure, in the next step, the indicated hydrogen pressure was adjusted. After the scheduled time interval, the reaction was finished automatically. The system was cooled down, and after release of pressure, the autoclaves were purged again with argon (5 cycles). The conversion and contents of products were estimated by NMR.

Procedure for the Hydrogenation of 4 mmol Neral (1a) with Rh(acac)(cod) and Xantphos at Ambient Conditions (0.1 MPa, 25 °C, 1a:[Rh]:Xantphos = 800:1:2)

In a double-walled glass-reactor, freshly distilled neral (**1a**) (608 mg, 4 mmol) and Xantphos (5.79 mg, 10 µmol) were placed, and toluene (7.5 mL) was added. Rh(acac)(cod) (1.55 mg, 5 µmol) was placed in a small Teflon-sagger. The solution was stirred slowly, and the device was exhausted and purged five times with hydrogen. The temperature was adjusted to 25°C. With increasing the speed of stirring, the catalyst was dissolved in the solution, and the hydrogenation process was started. After ca. 30 min of reaction, the initially fast H_2 consumption slowed down, indicating that the hydrogenation of the olefin unit neighboring the aldehyde group was finished. This corresponds to an inflexion point during the automatically measured hydrogen consumption of 95 mL (4 mmol). In order to avoid over-reduction, the reaction must be stopped at this time. The product consists of 598 mg (97 %) citronellal (**2**) and 18 mg (3 %) citronellol (**3**).[24]

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Manufacture of Citronellal by the Rhodium-Catalyzed Homogeneous Hydrogenation of Neral

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