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Synthesis of fragrance compounds from renewable resources: the aqueous biphasic hydroformylation of acyclic terpenes

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The rhodium-catalyzed hydroformylation of acyclic terpenic compounds, *i.e.*, β-citronellene, linalool and nerolidol, was performed in a water/toluene biphasic system. The addition of the cationic surfactant cetyltrimethylammonium chloride remarkably increased the reaction rates, with the surfactant effect being substrate dependent. A water-soluble phosphine ligand was used to immobilize the rhodium catalyst in water, an environmentally benign solvent, whereas non-polar products were collected in the organic phase. A complete phase separation was easily achieved by switching the magnetic stirrer off and cooling the mixture to room temperature. Linalool and nerolidol gave cyclic hemiacetals with excellent stereoselectivity, whereas the hydroformylation of β-citronellene resulted in two isomeric aldehydes with a linear-to-branched product ratio of approximately 85/15. Several fragrance compounds with pleasant sweet floral and woody scents were obtained in high yields through a simple and green one-pot procedure starting from the substrates easily available from natural bio-renewable resources.

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Introduction

Terpenes are an important class of natural substrates widely used in the flavor and fragrance industry.[1–4] Since many natural aroma compounds contain an aldehyde group, the hydroformylation of terpenes has been extensively studied in attempts to obtain aldehydes and compounds derived from aldehydes with interesting organoleptic properties.[5–16] However, the practical application of these processes faces a general problem of homogeneous hydroformylation, which is especially crucial for long-chain alkenes: the separation of high-cost rhodium catalysts. The distillation of high-boiling terpenic aldehydes in the presence of the catalyst could promote undesirable side reactions, the catalyst decomposition and loss of the metal. Aqueous biphasic hydroformylation represents one of the most promising strategies to overcome the problem with the catalyst separation; however, it is seriously restricted to short-chain alkenes due to the insufficient water solubility of higher alkenes.[17]

The alternatives to avoid transfer limitations in aqueous biphasic hydroformylation and extend the substrate scope to more hydrophobic alkenes have been recently revised.[18] The strategies include the use of co-solvents, amphiphilic ligands, modified cyclodextrins, supported aqueous phase catalysts and surfactants, with the latter being one of the most practical and effective alternatives.[19–29] Although anionic and non-ionic surfactants have been tested in the systems with industrially used Rh-sulfonated phosphines showing some success, cationic surfactants provide the most remarkable effects. The positively charged moiety of the cationic surfactant is directed to the aqueous phase, favoring the approach of the anionic Rh-sulfonated phosphine complex to the water/organic phase interface where the substrate can coordinate to the catalyst.[20,22]

The hydroformylation of more abundant terpenes, such as limonene, β-pinene and camphene, was quite extensively studied;[5–15] however, the data on the hydroformylation of β-citronellene, linalool and nerolidol are really scarce.[5,30–36] Acyclic monoterpenes β-citronellene (dihydromyrcene) and linalool are produced commercially from one of the most widespread monoterpene hydrocarbons, α-pinene, a cheap major constituent of turpentine oils. Both compounds are used for the industrial synthesis of various vitamins and/or fragrance ingredients.[3] In addition, linalool, a monoterpenic allylic alcohol with a pleasant lily odor, is also found in the essential oils of various plants, *e.g.*, Brazilian rosewood and Chinese Ho leaf oils. Nerolidol (also known as peruviol or melaleucol), a sesquiterpenic allylic alcohol with a delicate sweet floral woody odor and strong therapeutic potential, is also available from various essential oils, which may contain up to 50–90% of nerolidol.

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The hydroformylation of allylic alcohols is a simple and direct method for the synthesis of substituted tetrahydrofurans since primarily formed hydroxyl aldehydes undergo a spontaneous intramolecular cyclization to give five-membered hemiacetals. The products resulting from the hydroformylation of β-citronellene and linalool have been reported as promising fragrance compounds with fresh floral and/or green citrus odors,[5] and those derived from nerolidol are known to provide perfume with the sweet smell of a natural flower.[35]

In continuation of our ongoing project on valorization of natural ingredients of essential oils, we report herein for the first time the rhodium-catalyzed hydroformylation of β-citronellene (**1a**), linalool (**2a**) and nerolidol (**3a**) in a water/toluene biphasic system giving special attention to the effect of the cationic surfactant cetyltrimethylammonium chloride (CTAC) on these reactions.

Results and discussion

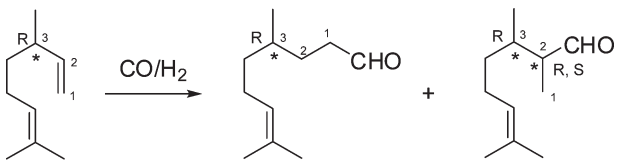
We have studied the behavior of β-citronellene (**1a**), linalool (**2a**) and nerolidol (**3a**) under hydroformylation conditions in a water/toluene biphasic system using $[Rh(COD)(OMe)]_2$ as the catalyst precursor and a water-soluble *tris*(3-sulfonatophenyl)phosphine trisodium salt (TPPTS) ligand to keep the catalyst dissolved in the aqueous phase. Under hydroformylation conditions in the biphasic system, all three substrates gave one or two major products derived from the direct carbonylation of their terminal double bonds. The substrates and corresponding products are numbered in the present communication by the same number with the addition of the letter "a" to indicate the substrate and other letters to indicate the products derived from this substrate. The total selectivity for the hydroformylation products in most of the runs was 90–100% for all substrates.

Hydroformylation of β-citronellene

The homogeneous hydroformylation of β-citronellene (**1a**) occurred smoothly in toluene solutions in the presence of PPh_3 or $P(O\text{-}o\text{-}^tBuPh)_3$ under mild conditions as reported in our previous publications.[32] The linear aldehyde **1b** was formed as the major product (70–85% of the mass balance) along with the branched isomer **1c** detected as a mixture of two diastereoisomers, (2*R*,3*R*) and (2*S*,3*R*), as the molecule of the starting β-citronellene has *R* configuration at asymmetric carbon C-3 (Scheme 1). The diastereoisomers could not be separated at GC analysis under the conditions used; however, their NMR spectra were different.

In the present work, the hydroformylation of β-citronellene was performed in a water/toluene biphasic system employing the water-soluble combination of $[Rh(COD)(OMe)]_2$ and TPPTS under conditions similar to those used in the homogeneous system. The results are presented in Table 1. In the absence of the surfactant at 20 atm (CO/H_2 = 1) and 80 °C, no conversion of β-citronellene was observed after 2 h (Table 1, run 1). The addition of small amounts of CTAC (2.5 mM, considering only the volume of the aqueous phase) promoted the hydroformylation of β-citronellene at a slow rate resulting in 10% conversion for 2 h (Table 1, run 2). The increase in the surfactant amount resulted in a gradual increase in the rate of the reaction which occurred with an excellent selectivity for aldehydes and a high linearity of *ca.* 85% (Table 1, runs 2–5). In the presence of 50 mM of CTAC, a 2 hour reaction resulted in 87% substrate conversion to give aldehydes **1b** and **1c** with nearly 100% selectivity. The variation of the total pressure of the equimolar gas mixture had no significant effect on the β-citronellene hydroformylation (Table 1, runs 3, 6 and 7). It is noteworthy that switching the magnetic stirrer off and cooling the reaction mixture to room temperature result in a rapid and complete phase separation. The organic phase contains the products, whereas the rhodium catalyst is well retained in the aqueous phase.

Thus, in the absence of the surfactant, no hydroformylation of β-citronellene was observed in the biphasic system due to the low solubility of the substrate in water where the rhodium



Scheme 1 Hydroformylation of β-citronellene (**1a**).

Table 1 Rhodium-catalyzed hydroformylation of β-citronellene (**1a**) catalyzed by Rh/TPPTS in an aqueous/toluene biphasic system[a]

Run	CTAC (mmol)	[CTAC][b] (mM)	*P* (atm)	Conversion (%)	Selectivity for aldehydes (%) (**1b**/**1c**)
1	0	0	20	0	—
2	0.01	2.5	20	10	100 (85/15)
3	0.05	12.5	20	40	100 (87/13)
4	0.10	25.0	20	46	100 (87/13)
5	0.20	50.0	20	87	100 (90/10)
6	0.05	12.5	60	36	98 (84/16)
7	0.05	12.5	80	35	100 (88/12)
8[c]	0	0	60	8	100 (85/15)

[a] Conditions: β-citronellene, 2.0 mmol; $[Rh(COD)(OMe)]_2$, 2.5×10^{-3} mmol; TPPTS, 0.1 mmol; toluene, 10.0 mL; water, 4.0 mL; 80 °C; CO/H_2 = 1/1; reaction time, 2 h. Conversion and selectivity are based on the substrate reacted. [b] Considering the volume of the aqueous phase. [c] Reaction time, 6 h.

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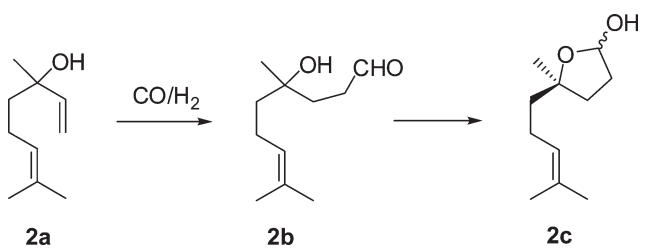
catalyst was immobilized. However, the use of the cationic surfactant allowed one to remarkably increase the reaction rate. The presence of the surfactant above the critical micelle concentration results in the formation of a micellar system with a consequent increase in the interfacial area. The hydrophobic molecules of β-citronellene could be solubilized within the hydrophobic cores of the micelles, thus leading to the improvement in the mass transfer process.[18a,23] Besides, the cationic nature of the surfactant results in the increase in the concentration of the Rh catalyst in the interfacial layer due to the electrostatic attraction between the anionic sulfonate group of the TPPTS ligand and the positively charged micelle surface covered by the cationic moiety of the surfactant.[18a,20,22] Considering the relative amounts of the liquid phases used in the present work (water/oil ≈ 3/7), the formation of reverse micelles, *i.e.*, the small droplets of water containing surfactant molecules on their surface suspended in the non-polar medium, can also be possible.

Hydroformylation of linalool

The hydroformylation of linalool (**2a**) in toluene solutions gave hemiacetal **2c** as the main product (Scheme 2).[31,32] This product formally results from the intramolecular cyclization of the primarily formed hydroxy aldehyde **2b**, which we have never detected in the reaction solutions. The hemiacetal was formed in the homogeneous system as a mixture of *cis* and *trans* isomers with respect to the position of the methylpentenyl and hydroxyl groups around the tetrahydrofuran ring (Scheme 2), with the ratio between the isomers being strongly dependent on the reaction variables.

In the biphasic system without the surfactant, at 60 atm and 80 °C, the hydroformylation of linalool occurred slowly, with 10% of the substrate being converted in 2 h (a standard reaction time used for comparison in most of the runs) and 24% in 6 h (Table 2, runs 1 and 2). Although in homogeneous systems in toluene solutions, the rates of the hydroformylation of β-citronellene and linalool were similar,[32] in the biphasic system, linalool was much more reactive than β-citronellene. Under the same conditions without the surfactant, 24% of linalool was converted in a 6 hour reaction (Table 2, run 2), whereas the conversion of β-citronellene was only 8% (Table 1, run 8). This can be explained by the higher hydrophilicity of linalool, which allows the reaction to occur not only in the interface water/organic medium but also in the aqueous phase. Although the solubility of linalool in water is rather modest (6.7×10^{-3} M at 25 °C), this value is *ca.* 1000 times higher than that of β-citronellene (7.5×10^{-6} M at 25 °C).



Scheme 2 Hydroformylation of linalool (**2a**).

The addition of small amounts of CTAC drastically increased the rate of the hydroformylation of linalool (Table 2, run 3 *vs.* run 1). The reactions in the presence of 5.0–25.0 mM of the surfactant were nearly completed in 2 h with no loss in the product selectivity (Table 2, runs 4–6). Hemiacetal **2c** was formed in 93–97% chemoselectivity in all runs with an excellent stereoselectivity of 97–99% for the *cis* isomer. In a further study, we have decreased the temperature to slow down the reaction and be able to more precisely follow the surfactant effect. At low concentrations, the surfactant significantly increased the reaction rate (Table 2, runs 1, 7 and 8); however, further addition CTAC from 12.5 mM up to 50.0 mM had only a slight effect on the substrate conversion (Table 2, runs 8–11).

A 3-fold decrease in the total pressure of the CO/H_2 equimolar gas mixture had no significant effect on the hydroformylation of linalool, similarly to that observed with β-citronellene (Table 2, run 12 *vs.* run 8). After the reaction in run 13 (Table 2), the aqueous phase containing the catalyst was separated under argon and reused 5 times without the loss of activity and selectivity.

The inductively coupled plasma analysis showed <0.005 ppm of rhodium in the organic phase after the first reaction in run 13 (<0.008% loss of rhodium) and no rhodium after the first recycling. To further verify the possible catalyst loss, fresh linalool was added to the recovered organic phase and the solution was placed in the autoclave under hydroformylation conditions (60 °C, 80 atm of CO/H_2 = 1/1). No further conversion of linalool was observed, which indicated the lack of significant rhodium leaching to the organic phase during the biphasic process.

Hydroformylation of nerolidol

There are two natural isomers of nerolidol (**3a**) which differ in the geometry of the central double bond: *cis* (*Z*-nerolidol) and *trans* (*E*-nerolidol). The starting substrate was a mixture of *Z* and *E* isomers with a ratio of *ca.* 40/60. The hydroformylation of nerolidol in both homogeneous[36] and biphasic systems gave hemiacetal **3c** as the main product (Scheme 3). This product formally results from the intramolecular cyclization of the primarily formed hydroxy aldehyde **3b**, which has never been detected in the reaction solutions in our studies. The stereoselectivity of the reaction was only slightly dependent on the reaction variables, and hemiacetal **3c** was formed predominantly (almost exclusively in the biphasic system) as *Z-cis* and *E-cis* isomers in the same *Z*/*E* proportion as the starting substrate.

The total selectivity for the hydroformylation products in most of the runs was 90–95%, with only one minor product being responsible for almost all the rest of the mass balance. The minor product was identified in our previous work[36] as a non-functionalized sesquiterpenic acyclic triene, which formally

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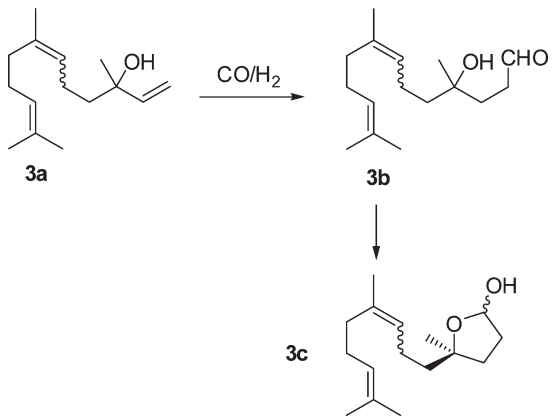
Table 2 Rhodium-catalyzed hydroformylation of linalool (**2a**) catalyzed by Rh/TPPTS in an aqueous/toluene biphasic system[a]

Run	CTAC (mmol)	[CTAC][b] (mM)	T (°C)	Conversion (%)	Selectivity for **2c** (%) (*cis*/*trans*)
1	0	0	80	10	95 (95/5)
2[c]	0	0	80	24	95 (95/5)
3	0.01	2.5	80	72	94 (99/1)
4	0.02	5.0	80	97	95 (99/1)
5	0.05	12.5	80	98	93 (99/1)
6	0.10	25.0	80	98	93 (97/3)
7	0.01	2.5	60	43	93 (98/2)
8	0.05	12.5	60	58	94 (98/2)
9	0.10	25.0	60	59	93 (98/2)
10	0.15	37.5	60	68	93 (98/2)
11	0.20	50.0	60	71	90 (92/8)
12[d]	0.05	12.5	60	55	91 (99/1)
13[d,e]	0.25	62.5	80	35	97 (97/3)
		1st recycle		33	97 (97/3)
		2nd recycle		44	96 (97/3)
		3rd recycle		40	97 (97/3)
		4th recycle		41	97 (97/3)
		5th recycle		41	96 (97/3)

[a] Conditions: linalool, 2.0 mmol; $[Rh(COD)(OMe)]_2$, 2.5×10^{-3} mmol; TPPTS, 0.1 mmol; toluene, 10.0 mL; water, 4.0 mL; CO/H_2 = 1/1; 60 atm; reaction time, 2 h. Conversion and selectivity are based on the substrate reacted. [b] Considering the volume of the aqueous phase. [c] Reaction time, 6 h. [d] 20 atm. [e] TPPTS (0.5 mmol). The aqueous phase containing the catalyst was separated under argon and used in recycling experiments.



Scheme 3 Hydroformylation of nerolidol (**3a**).

resulted from the dehydration and monohydrogenation of the nerolidol molecule.

In the absence of the surfactant at 20 atm and 80 °C, no conversion of nerolidol was observed after 2 h (Table 3, run 1). The addition of the surfactant gradually increased the reaction rate (Table 3, runs 2–6). The reactions with 12.5–50.0 mM of CTAC were nearly completed in 2 h (Table 3, runs 4–6). Hemiacetal **3c** was formed in *ca.* 90% chemoselectivity with an excellent stereoselectivity of 96–98% for the *cis* isomers. In a further study, we have decreased the temperature to slow down the reaction and be able to more precisely follow the surfactant effect. The correlation was very similar to that found for linalool: at low concentrations, the surfactant significantly increased the reaction rate, whereas from 12.5 mM up to 50.0 mM, there was only a slight effect (Table 3, runs 7–9).

The saturation of the surfactant effect observed for linalool and nerolidol could be explained by the fact that at high surfactant concentrations, the micelles begin to expand and oil/water or water/oil microemulsions might be formed. Thus, starting from a certain point, the increase in the surfactant concentration does not result in a significant increase in the interfacial area and the hydroformylation rate increases only slowly. However, the fact that the hydroformylation of β-citronellene has greatly benefited from the surfactant even above the 12.5 mM concentration (a saturation value for linalool and nerolidol) suggests that the effect of the surfactant is substrate dependent.

Indeed, we have previously found that the optimal concentration of the surfactant (CTAC) at the hydroformylation of terpenes in the biphasic water/toluene system strongly depends on the conformational characteristics of the substrate and its capacity to accommodate among the surfactant molecules in order to permeate through their layer and reach the catalyst in the aqueous phase.[37] In particular for acyclic monoterpene myrcene, a significant promotion effect was observed up to the CTAC concentration of *ca.* 25 mM; after that, even a slight decrease in the reaction rate occurred. The promotion by CTAC was less pronounced for monocyclic monoterpene limonene and turned into an inhibition effect for the bulky bicyclic monoterpene camphene.[37] The surfactant accumulates in the interface water/oil region and the substrate has to permeate the oriented membrane-like array of the surfactant molecules to approach the catalyst sites. For this reason, the excess of the surfactant can inhibit the contact between the catalyst and the substrate and decrease the hydroformylation rate.

A similar effect seems to operate for the molecules of linalool and nerolidol compared to β-citronellene. Due to their hydrophilic parts, the first two substrates are expected to have more difficulty than the hydrophobic molecule of

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Table 3 Rhodium-catalyzed hydroformylation of nerolidol (**3a**) catalyzed by Rh/TPPTS in an aqueous/toluene biphasic system[a]

Run	CTAC (mmol)	[CTAC][b] (mM)	T (°C)	Conversion (%)	Selectivity for **3c** (%) (*cis*/*trans*)
1	0	0	80	0	—
2	0.01	2.5	80	45	90 (98/2)
3	0.03	7.5	80	85	91 (96/4)
4	0.05	12.5	80	90	91 (98/2)
5	0.10	25.0	80	95	90 (98/2)
6	0.20	50.0	80	96	91 (98/2)
7	0.05	12.5	60	48	92 (98/2)
8	0.10	25.0	60	49	92 (96/4)
9	0.20	50.0	60	57	94 (95/5)
10[c]	0.05	12.5	60	75	90 (95/5)
11[d]	0	0	80	30	96 (98/2)

[a] Conditions: nerolidol, 2.0 mmol; $[Rh(COD)(OMe)]_2$, 2.5×10^{-3} mmol; TPPTS, 0.1 mmol; toluene, 10.0 mL; water, 4.0 mL; CO/H_2 = 1/1; 20 atm; reaction time, 2 h. Conversion and selectivity are based on the substrate reacted. [b] Considering the volume of the aqueous phase. [c] $[Rh(COD)(OMe)]_2$, 5.0×10^{-3} mmol. [d] Reaction time, 6 h; 60 atm.

β-citronellene to permeate through the hydrophobic part of the surfactant layer that accumulated on the oil side of the interface water/oil region. For this reason, the strong promoting effect of CTAC for linalool and nerolidol is limited to the 12.5 mM concentration. At higher concentrations, the surfactant molecules become more densely packed at the interface making the approximation of the substrate to the catalytic centre more difficult. Thus, the increase in the CTAC concentration and in the interfacial area is not fully accompanied by the increase in the hydroformylation rate.

The total pressure of the equimolar gas mixture had no significant effect on the hydroformylation of nerolidol (Table 4, runs 1–3), which is similar to that observed for β-citronellene and linalool. This could reflect a net result of the opposite kinetic effects of the gas reagents as it was observed in homogeneous systems.[31,32,36] In homogeneous systems, a positive order in hydrogen and a negative order in carbon monoxide were found for all three substrates. The accelerating effect of hydrogen suggested that the oxidative addition of hydrogen to the rhodium acyl intermediate could be a rate-determining step at the hydroformylation of these substrates in toluene solutions. However, in the biphasic system, neither carbon monoxide (Table 4, *cf.* runs 3–5) nor hydrogen (Table 4, *cf.* runs 1 and 5; runs 3 and 6) partial pressure had a kinetic effect on the hydroformylation of nerolidol. On the other hand, we observed a strong positive kinetic effect of the concentration of the rhodium catalyst (Table 3, *cf.* runs 7 and 10). This suggests that a rate-determining step at the nerolidol hydroformylation in the biphasic system should involve rhodium species (*e.g.*, substrate coordination to rhodium); however, the existence of mass transference limitations in the system cannot be ruled out.

In order to compare the reactivity of all three terpenes in the conventional biphasic system without the surfactant, the reactions were run under the same conditions for 6 h. The highest conversion was obtained for nerolidol (30%, Table 3, run 11), followed by linalool (24%, Table 2, run 2) and β-citronellene (8%, Table 1, run 8).

Thus, among the acyclic terpenes studied, *i.e.* nerolidol, linalool and β-citronellene, the first two substrates can be hydroformylated in a conventional surfactant-free aqueous biphasic system at a reasonable rate probably due to their higher water solubility. The addition of CTAC resulted in a significant increase in the rate of the hydroformylation of all three substrates, with the effect being more pronounced for the substrates with higher water solubility: linalool > nerolidol > β-citronellene (6.70, 0.02 and 0.0075 mM, respectively, at 25 °C). With small CTAC amounts (12.5 mM), the reactions with nerolidol and linalool still occurred much faster than that with β-citronellene (run 6 in Table 1 *vs.* run 5 in Table 2; run 3 in Table 1 *vs.* run 4 in Table 3). In the presence of CTAC, the reactions with linalool were faster than those with nerolidol (run 12 in Table 2 *vs.* run 7 in Table 3; run 8 in Table 2 *vs.* run 2 in Table 4), which is an inverse

Table 4 Rhodium-catalyzed hydroformylation of nerolidol (**3a**) catalyzed by Rh/TPPTS in an aqueous/toluene biphasic system: effect of pressure[a]

Run	P (CO) (atm)	P (H_2) (atm)	Conversion (%)	Selectivity for **3c** (%) (*cis*/*trans*)
1	10	10	48	92 (98/2)
2	30	30	45	94 (99/1)
3	40	40	46	94 (99/1)
4	20	40	48	95 (99/1)
5	10	40	42	92 (96/4)
6	40	20	43	90 (98/2)

[a] Conditions: nerolidol, 2.0 mmol; $[Rh(COD)(OMe)]_2$, 2.5×10^{-3} mmol; TPPTS, 0.1 mmol; toluene, 10.0 mL; water, 4.0 mL; CTAC, 0.05 mmol, 12.5 mM; 60 °C; reaction time, 2 h. Conversion and selectivity are based on the substrate reacted.

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tendency compared to the system without CTAC. The reaction rate for β-citronellene increases almost linearly with the addition of CTAC, whereas the surfactant effect on the hydroformylation of nerolidol and linalool becomes weaker at higher CTAC concentrations. As a result, in the presence of relatively high amounts of surfactant, the reactions with β-citronellene and nerolidol occurred at comparable rates (run 5 in Table 1 *vs.* run 6 in Table 3, [CTAC] = 0.05 M).

Conclusion

The study of the rhodium-catalyzed hydroformylation of β-citronellene, linalool and nerolidol in a water/toluene biphasic system revealed a remarkable effect of the cationic surfactant on the reaction rates. The reactions with all substrates give the same products as in the corresponding homogeneous systems in toluene solutions and can be performed under optimized biphasic conditions at reasonable rates. A complete phase separation can be achieved by simply switching the magnetic stirrer off after the reaction and cooling the mixture to room temperature. Several fragrance compounds can be obtained in high yields through a simple and green one-pot procedure starting from the substrates easily available from natural bio-renewable resources. It is important to point out that the rhodium catalyst is immobilized in water, an environmentally benign solvent, and can be easily separated after the reaction from the products dissolved in the organic phase.

Experimental section

All chemicals were purchased from commercial sources and used as received unless otherwise indicated. A mixture of *Z* and *E* isomers of nerolidol [3,7,11-trimethyl-1,6,10-dodecatrien-3-ol] (*Z*/*E* ≈ 40/60), racemic linalool [(±)-3,7-dimethyl-1,6-octadien-3-ol] and (−)-β-citronellene [dihydromyrcene, (*R*)-(−)-3,7-dimethyl-1,6-octadiene] were acquired from Aldrich. $[Rh(COD)(OMe)]_2$ (COD = 1,5-cyclooctadiene) was prepared by a published method.[38] Tris(3-sulfonatophenyl)phosphine trisodium salt (TPPTS) was prepared as described previously.[39] Toluene was purified under reflux with sodium wire–benzophenone for 8 h and then distilled under argon. Deionized water was deoxygenated by reflux for 6 h under argon.

Catalytic experiments were carried out in a homemade stainless steel reactor with magnetic stirring. In a typical run, two solutions were prepared separately in Schlenk tubes under argon: a toluene (10.0 mL) solution of $[Rh(COD)(OMe)]_2$ (2.5 μmol), substrate (2 mmol) and dodecane (1 mmol, internal standard) and a water (4.0 mL) solution of TPPTS (0.1 mmol) and CTAC (0–0.20 mmol). The solutions were mixed and stirred for 10 minutes at room temperature in a Schlenk tube under argon. Then, the biphasic mixture was transferred into the reactor, which was pressurized to 20–80 atm (typically CO/H_2 = 1/1), placed in an oil bath (60–80 °C) and stirred for the reported time. The reaction rate was not dependent on the intensity of stirring within the range used. After the reaction was carried out and cooled to room temperature, the excess CO and H_2 were slowly vented. In all experiments, the emulsion was broken after cooling the mixture to room temperature. In recycling runs, the aqueous phase containing the catalyst was separated under argon and repeatedly used in consequent runs.

The products were analyzed in the organic phase by gas chromatography (GC, Shimadzu QP2010, Rtx®-5MS capillary column, FID detector). Conversion and selectivity were determined by GC. The GC mass balance was based on the substrate charged using dodecane as an internal standard.

The products were identified by GC-MS (Shimadzu QP2010-PLUS instrument operating at 70 eV). The NMR and MS data of the products were reported in our previous publications.[31,32,36]

The rhodium content in the organic phase was measured using a SPECTRO ARCOS ICP-OES (inductively coupled plasma optical emission spectrometer). Reference solutions of Rh (1000 mg L^{-1}) with a high degree of analytical purity (ICP Standard, SpecSol) were used to obtain the calibration curves. Deionized water (MILLI-Q) was used to prepare all solutions. The organic medium was evaporated before the sample digestion, which was carried out at 115 °C for 3 h with 5 mL of HNO_3. The volume of the samples was then adjusted to 10 mL using DI water. The rhodium content was quantified in triplicate for each sample.

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