



Heterogeneously Catalysed Oxidative Dehydrogenation of Menthol in a Fixed-Bed Reactor in the Gas Phase

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For the first time, the oxidative dehydrogenation of (–)-menthol to (–)-menthone and (+)-isomenthone in a marketable quality was carried out in a continuous gas phase reactor as a sustainable process using molecular oxygen as green oxidant and solid catalysts which do not contaminate the product mixture and which are easily to remove. The diastereomeric purity remained largely unchanged. Three types of catalysts were found to be very active and selective in the

formation of menthone and isomenthone: AgSr/SiO₂, CuO distributed on a basic support and RuMnCe/CeO₂, where Ru, Mn and Ce exist in an oxidized state. The best overall yield of menthon/isomenthone obtained with an Ag-based catalyst was 58 % at 64 % selectivity, with a Cu-based catalyst 41 % at 51 % selectivity and with a Ru-based catalyst 68 % at 73 % selectivity. Reaction conditions were widely optimized.

1. Introduction

(–)-Menthone and (+)-isomenthone are used in the fragrance industry in synthetic peppermint oils and bases.^[1] They can be easily epimerized via an enol tautomer using acidic catalysts. Both terpenes are minor ingredients of various *Mentha* species, together with menthol as main terpene-type component. Therefore a manufacture from menthol by oxidation with toxic chromic acid or catalytic dehydrogenation applying copper chromite was carried out on a larger scale.^[1] Furthermore, a couple of catalytic aerobic oxidations for the synthesis of menthone/isomenthone in the liquid phase using both homogeneous and heterogeneous catalysts were described in the scientific literature reported in the following part.

The application of TEMPO and TEMPO-analogue bicyclic N-oxides as catalysts in the aerobic oxidation of menthol were described several times,^[2–8] menthone yields of more than 90 % were obtained. Disadvantages are larger amounts of additive needed and salt loads formed. Different Cu-, Co- und Mo-complexes catalysed the oxidation of menthol also according to a radical mechanism.^[9–13] In this case, the necessary amounts of bases and/or additives are disadvantageous. Furthermore, a series of palladium- and ruthenium complexes, often together with co-catalysts and further additives, were successfully

investigated.^[14–20] In general, the costs for recycling of catalysts and solvent might prevent the application of such homogeneous catalysts in a larger scale.

The heterogenization of homogeneous catalysts onto the surface of organic or inorganic supports was also described for the aerobic oxidation of menthol. For example, TEMPO,^[21] Fe- or Co complexes,^[22–25] Pd(II) catalysts,^[26] MoO₂(acac)₂^[27] or polyoxometalates^[28] were immobilized. But a leaching of the active species of such catalysts into the liquid phase cannot be avoided, even if it cannot be proved due to the small scales described and the detection limits of ICP methods.

Heterogeneous catalysts were also applied in the liquid phase. Using Ru/CeO₂^[29] (15 % yield) or Ru(OH)_x/SiO₂@Fe₃O₄^[30] (17 % yield), only poor yields of menthone were produced. The latter catalyst could be removed from the reaction mixture by means of a magnet. Under the same reaction conditions, carveol was converted in the presence of this catalyst to 92 % of carvone. Au/MgO could be used as catalyst without an additional base, but the yield of carvone was also low. Albadi et al. investigated Au/CuO-ZnO^[31] or Co nanoparticles/Al₂O₃^[32] catalysts in H₂O, but a semi-stoichiometric amount of Cs₂CO₃ as base was necessary. Platinum nanoparticles on mesoporous, specially treated activated carbon were found to be very active and selective in the conversion of menthol (90 % conversion, 97 % selectivity) in an autoclave in the presence of dioxane at 10 bar air.^[33] The formation of ether hydroperoxides might be detrimental for an upscaling of the procedure. The polyoxometalate Na_{6.3}Fe_{0.9}[AlMo₁₁O₃₉]·2H₂O induced 92 % yield of menthone.^[34] V₂O₅ without any base produced 77 % of menthone.^[35] Unfortunately, the good yields of the latter two procedures could not be reproduced in own experiments. In general, a disadvantage of application of heterogeneous catalysts in the liquid phase is a frequently observed leaching of the active metal.

Without any catalyst in subcritical H₂O (50 bar total pressure, 5–20 bar O₂), 85 % menthone could be isolated.^[36] It seems a

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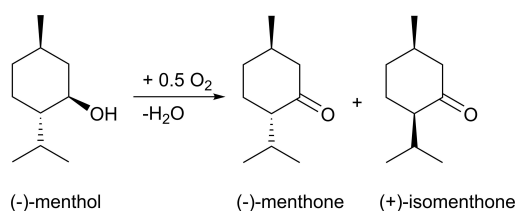
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sufficient processing from the chemical point of view but requires special design of the equipment.

It should be mentioned that the non-oxidative dehydrogenation of menthol was also successful in the presence of heterogeneous catalysts. Here, a reaction in the gas phase at Ni–Cu/Al₂O₃ doped with 0.1% CeO₂ resulted in 48% menthone and 24% thymol beside low amounts of by-products.^[37] The transfer dehydrogenation with styrene as H₂ acceptor at Cu/Al₂O₃ led to a mixture of menthone and isomenthone.^[38,39] But the stoichiometric amounts of styrene are detrimental. Patents^[40,41] were claimed, too, but we do not know if the procedure is really being used. Also the homogeneous Shvo catalyst or RuH₂CO(PPh₃)₃ were found to be suitable for the direct dehydrogenation of menthol in mesitylene at 165 °C.^[42]

Continuous processes for the synthesis of fine chemicals in the gas phase are rare but quite possible. From a sustainable point of view, a solvent-free process using heterogeneous catalysts and oxygen as the sole oxidant would be highly desirable. Such a process should be also very advantageous for a scale-up to technical scale. Neither solvent, catalysts, additives nor salts have to be removed and recycled, the products can be processed directly, and a leaching of the active metal species into the product mixture causing often deactivation is also precluded. For the first time, the oxidative dehydrogenation of (–)-menthol to (–)-menthone and (+)-isomenthone (Scheme 1)



Scheme 1. Aerobic oxidative dehydrogenation of (–)-menthol (identified by-products: 1-menthene, 2-menthene, 3-menthene, cymene, menth-2-enone, thymol).

was investigated in a flow reactor in the gas phase. Various heterogeneous catalysts were tested, and the reaction conditions were optimized.

2. Results and Discussion

Menthol is difficult to oxidize since all substituents are preferably arranged in the less reactive equatorial conformation, the OH group is not activated (Figure 1). Therefore many catalytic systems which work well in the oxidation of more

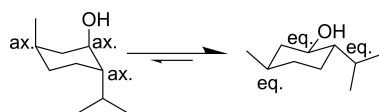


Figure 1. Position of the equilibrium between axial and equatorial conformation of substituents in (–)-menthol.

simple aliphatic or cycloaliphatic alcohols do not succeed with menthol as substrate.

Thus, a process management at higher temperatures as presented here might be favorable. Ag, Cu and Ru-based catalysts were identified to be active in the menthol oxidation as a result of a broader screening of various oxidation catalysts, whereby the non-active catalysts should not be discussed here in detail. For the first time, heterogeneous Ag catalysts were used for menthol oxidative dehydrogenation. The menthone/isomenthone yields obtained with heterogeneous Ru catalysts in this study are much better than described for solid Ru catalysts in the liquid phase in a batch reactor.^[29,30] In the following, both the composition of the active catalysts (see Tables 1 and 2) and reaction conditions were optimized in order to obtain the highest possible yields of menthone/isomenthone at the best possible selectivities.

The heterogeneous catalysts were prepared by incipient wetness impregnation (Ag and Cu catalysts) and precipitation with sodium hydroxide/carbonate (Ru catalysts).

With the exception of SiO₂-supported catalysts, compression of the powdery material (2.2 t/cm²), crushing and sieving were carried out (after deposition of active species and post-treatment such as reduction or calcination) because only the catalyst

Table 1. Composition, BET area and pore volume of Ag and Cu catalysts investigated in this study.

Catalyst	ICP [calc./found] Ag	[wt%] 2 nd metal	BET [m ² g ^{−1}]	Pore volume [cm ³ g ^{−1}]
Ag/SiO ₂	1.5/1.34		331.4	0.9050
1.5/4%AgSr/SiO ₂	1.5/1.30	4.0/3.56	284.5	0.7677
AgNa/SiO ₂	1.5/1.48	1.1/1.05	181.9	0.8339
AgLi/SiO ₂	1.5/1.38	0.3/0.3	221.4	0.8462
AgBa/SiO ₂	1.5/1.33	6.3/5.36	267.0	0.7920
AgMg/SiO ₂	1.5/1.50	2.6/1.02	288.7	0.8491
AgCa/SiO ₂	1.5/1.37	2.7/1.88	276.2	0.8445
AgK/SiO ₂	1.5/1.48	1.8/1.57	178.7	0.8140
Ag/MgO	1.5/1.59		115.8	0.2716
Ag/hydrotalcite	1.5/1.42		183.3	0.1239
AgSr/hydrotalcite	1.5/1.11	4.0/3.02	202.7	0.1509
AgSr/La ₂ O ₃	1.5/1.44	4.0/3.22	29.7	0.0868
AgSr/MgO	1.5/1.28	4.0/3.09	174.3	0.3573
AgSr/Nb ₂ O ₅	1.5/1.51	4.0/3.45	20.5	0.0299
0.5/4%AgSr/SiO ₂	0.5/0.53	4.0/3.47	276.1	0.7652
1/4%AgSr/SiO ₂	1.0/0.97	4.0/3.55	277.3	0.7698
3/4%AgSr/SiO ₂	3.0/3.10	4.0/3.54	283.7	0.7675
1.5/1%AgSr/SiO ₂	1.5/1.70	1.0/1.46	312.4	0.8175
1.5/3%AgSr/SiO ₂	1.5/1.56	3.0/2.82	289.2	0.7776
1.5/10%AgSr/SiO ₂	1.5/1.23	10.0/8.41	240.0	0.7024
CuO-0.2			0.2	
CuO-1.0			1.0	
CuO-1.6			1.6	
Cu/SiO ₂	1.3/1.14		346.5	0.8312
CuO/SiO ₂	1.5/1.14		361.9	0.8436
CuO/MgO	1.5/1.21		132.1	0.2231
CuO/hydrotalcite	1.5/1.20		148.0	0.1675
CuO/Nb ₂ O ₅	1.5/1.17		20.0	0.0288
CuO/La ₂ O ₃	1.5/1.06		24.4	0.0563
CuOSr/SiO ₂	1.5/1.16	4.0/3.61	275.8	0.8190
CuOMg/SiO ₂	1.5/1.21	2.6/1.15	299.2	0.8622
CuOBa/SiO ₂	1.5/1.13	6.3/5.82	299.6	0.8192
CuOCa/SiO ₂	1.5/1.19	2.7/1.80	293.2	0.8571

[a] 0.5 mmol 2nd metal g^{−1} support

Table 2. ICP analyses, BET areas and pore volumes of prepared Ru catalysts.

Catalyst	ICP [calc./found]			BET [m ² g ⁻¹]	Pore volume [cm ³ g ⁻¹]
	Ru	Mn	Ce		
0.2%Ru/CeO ₂	0.2/ 0.16			52.9	0.1381
0.5%RuMnCe/ CeO ₂	0.5/ 0.35	1.2/1.0	1.6/ n.d.	46.5	0.1198
1.0%RuMnCe/ CeO ₂	1.0/ 0.77	1.2/ 1.06	1.6/ n.d.	52.7	0.1233

fraction with a particle diameter between 400–800 μm was installed in the reactor.

The Ag- and Cu-based catalysts were prepared in adaption of a literature procedure.^[43] In case of Ag catalysts, an alkali or earth alkali dopant was investigated together with the variation of catalyst support. Since AgSr/SiO₂ was very active in the catalytic reaction, both the Ag and the Sr content were also optimized. In the series of Cu catalysts, earth alkali species were added as dopant, and the support was also varied.

Few Ru catalysts on ceria, investigated earlier by some of us in the oxidation of different alcohols,^[44] were also prepared and tested (Table 2).

As seen at Tables 1 and 2, the BET surface and pore volume of the catalysts strongly depends on the morphology and texture of the support, or in case of unsupported CuO, on the calcination temperature.

For determination of oxidation states, XPS spectra of 1.5/4% AgSr/SiO₂, CuO/hydrotalcite and 1.0%RuMnCe/CeO₂ were recorded exemplarily (see Figures S3–S5, respectively). Since for silver oxides only small shifts of the binding energy are observed, the position and shape of the Auger Ag MNN peaks were also used for interpretation. A binding energy of 368.0 eV was measured for the Ag3d_{5/2} peak of 1.5/4%AgSr/SiO₂. The shape and position of Ag M5N45N45 and Ag M4N45N45 peaks at kinetic energies of 348.3 eV and 353.9 eV, respectively, together with the Ag3d_{5/2} peak point to the existence of Ag₂O or mixed silver oxides at the surface.^[45] No significant shift of the Ag3d_{5/2} peak (367.8 eV) was observed for this catalyst after 120 h time on stream. The position of the Sr3d_{5/2} peak at 133.3 eV and the Sr3d_{3/2} peak at 135.1 eV indicates the existence of SrO.^[46] For CuO/hydrotalcite, the state of the Cu2p_{3/2} peak at 933.5 eV together with significant satellite features around 942 eV denote Cu²⁺ but also mixed oxides cannot be excluded completely.^[47] In 1.0%RuMnCe/CeO₂ the peak position of Ru3d_{5/2} at 281 eV proves the presence of Ru⁴⁺.^[48] In the Ce4d region, the binding energy of the Ce4d_{5/2} peak at 882.3 eV and the strong peak at 916.2 eV, belonging to Ce4d_{3/2}, reveal Ce⁴⁺ as the main oxidation state [5].^[49]

The investigations concerning catalytic oxidative dehydrogenation started with a blank experiment. The reactor was only filled with inert glass beads instead of the catalyst. An appreciable menthol conversion (X=3%) was not observed within a reaction time of 3 h, menthone and isomenthone yields were only 1% and 0.3%, respectively. This result

confirmed that the oxidative dehydrogenation can only occur in the presence of a suitable catalyst.

Starting with 1.5/4%AgSr/SiO₂ as catalyst, optimal conditions for reaction temperature, menthol/O₂ ratio and residence time were determined first. An increase in reaction temperature from 250 °C to 350 °C led to a nearly linear rise of both menthone and isomenthone yield and to an increased menthol conversion (see Figure S6). However, the proportion of by-products such as 1-, 2- and 3-menthene, cymene and thymol (see Table S4 for yields of by-products) also grew significantly, especially in the range between 300–350 °C. Considering higher conversion and yields vs. selectivity, both 300 and 350 °C were chosen as reaction temperature for subsequent experiments. Lowering the flow rate from 30 mL min⁻¹ to 20 mL min⁻¹ (see Figure S7), that means increasing the residence time by factor 1.5, caused an increase of menthol conversion from 49% to 81% and a rise in yield of menthone and isomenthone from 16% to 27% and 11% to 18%, respectively. Even though a further reduction of flow rate to 10 mL min⁻¹ led to a menthol conversion of 96%, the desired product selectivity decreased due to more undesired by-products. A flow rate of 30 mL min⁻¹ was chosen for further experiments due to the lowest proportion of by-products (6%), such as menthene, 1-, 2- and 3-menthene, cymene and thymol, under these conditions. The influence of menthol/O₂ ratio on conversion and yield of menthone/isomenthone was also investigated (see Figure S8). The volume flow rate of 5% O₂/Ar was adjusted constantly to 30 mL min⁻¹. According to the vapor pressure curves of menthol, a menthol/O₂ ratio of 1:2 should be achieved at 110 °C and a ratio of 1:4 at 91 °C. Therefore the thermostat temperature for the saturator was lowered from 120 °C (standard reaction condition) to 110 °C and 91 °C to diminish the proportion of the vaporized menthol. The evaporated amount was also controlled by weighing of the saturator vessel after the reaction. A reduction of the menthol/O₂ ratio from 1:1 to 1:2 led to an increase of menthol conversion from 49% to 71%, but only a very small increase of menthone/isomenthone yields by 2% and a growing formation of by-products were observed. The further lowering of the menthol content (menthol/O₂ ratio 1:6) effected poorer menthone/isomenthone yields of 14% and 10% at 71% menthol conversion. In addition, a lower menthol/O₂ ratio led to reduced recovery rates.

Regrettably, the suspected formation of compounds with higher molecular weight could not be proved. However, a high proportion of oxygen favors the formation of by-products. Therefore, a saturator temperature of 120 °C and thus a menthol/O₂ ratio of about 1:1 were applied in further experiments.

The control of diastereomeric purity confirmed that the oxidative dehydrogenation of menthol with 1.5/4%AgSr/SiO₂ leads almost exclusively to (–)-menthone (de ≥ 99.61%).

Since 1.5/4%AgSr/SiO₂ showed a good catalytic activity, the replacement of Sr by alkali metals Li, Na, K and other alkaline earth metals such as Mg, Ca and Ba was evaluated (see Figure 2). The idea behind was the assumption that a basic component in the catalyst might facilitate the hydrogen abstraction from the CH–OH group of menthol and thus, might

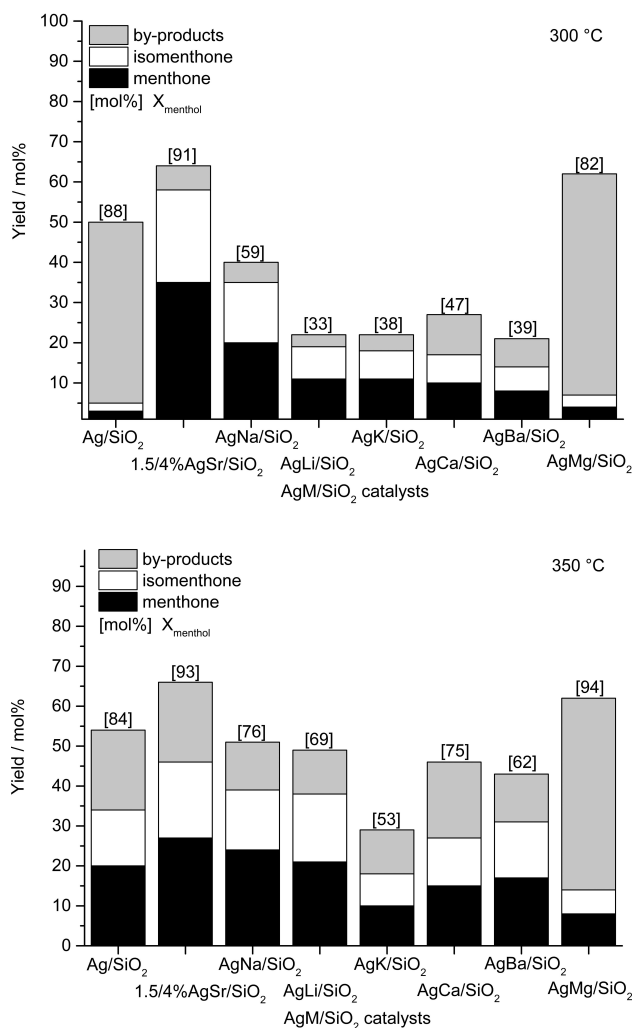


Figure 2. Variation of basic dopant in Ag/SiO₂ catalysts (reaction conditions: 3 mL catalyst (1.5 wt% Ag, 0.5 mmol 2nd metal/g support), 30 mL min⁻¹ 5 vol% O₂/Ar, menthol/O₂ ratio ~ 1:1; see Table S4 for spectrum and yields of by-products; X = conversion).

be the reason for the good catalytic performance. For direct comparison of the catalyst activity and selectivity, all catalysts were tested at 300 and 350 °C applying standard reaction conditions. Additionally, monometallic Ag/SiO₂ was included into the test series to check if doping with a second metal species is necessary.

At a reaction temperature of 300 °C, only low overall yields of menthone and isomenthone in the range of 19% at most, and a medium conversion of up to 47% could be observed with the catalysts containing Li, K, Ca and Ba. Higher conversions were obtained with AgMg/SiO₂, but this catalyst formed almost exclusively the by-products 3-, 2- and 1-menthene. The best results with 58% overall yield at 91% menthol conversion (64% selectivity for menthone and isomenthone), which could not be improved by increasing the temperature to 350 °C, provided the metal combination Ag/Sr. The direct comparison of the monometallic Ag/SiO₂ with the bimetallic AgSr/SiO₂ showed that especially at 300 °C, the pure Ag catalyst preferably formed by-products. TEM images of Ag/

SiO₂, AgK/SiO₂ and 1.5/4%AgSr/SiO₂ (see Figure S2) explained probably the reason for the excellent activity and selectivity of the Sr-doped catalyst.

Strontium obviously enables a very fine and uniform dispersion of silver particles, the average particle size distribution was measured to be 2 nm.

Both in the pure Ag/SiO₂ catalyst and in AgK/SiO₂, numerous Ag particles larger than 5 nm were found, and an uneven size distribution was observed. Almost identical, and in comparison to SiO₂ significantly higher, menthone and isomenthone yields were obtained at a reaction temperature of 300 °C if MgO and hydrotalcite were used as basic supports (Figure 3).

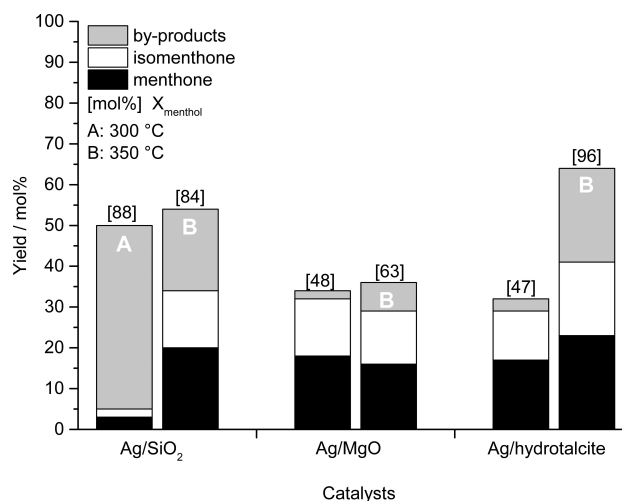


Figure 3. Monometallic Ag catalysts on different supports (reaction conditions: 3 mL 1.5% Ag catalyst, 30 mL min⁻¹ 5 vol% O₂/Ar, menthol/O₂ ratio ~ 1:1, 300 °C and 350 °C); numerical values and spectrum of by-products see Table S4 in ESI; X = conversion.

On the other hand, all catalysts showed similar yields for menthone/isomenthone of 41% at most if the temperature was increased to 350 °C. It is quite remarkably that Ag/MgO led to significantly lower yields of undesired by-products (7%) although it effected only a menthol conversion of 64%. Furthermore, the stereochemical analysis of the menthone produced with Ag/hydrotalcite at 350 °C resulted in 4% (+)- and 96% (–)-menthone.

Since a monometallic Ag catalyst from this test series was not able to exceed the best results of the bimetallic 1.5/4% AgSr/SiO₂, a variation of the support was investigated for 1.5/4%AgSr (Figure 4).

The comparison of Ag/MgO and Ag/hydrotalcite with AgSr/MgO and AgSr/hydrotalcite demonstrated that doping with Sr species did not reveal any positive effect regarding menthone/isomenthone yields. At a reaction temperature of 300 °C, SiO₂ was identified as the best support material for the combination of Ag (1.5%) and Sr (4%). Remarkably, the undesired formation of by-products, which frequently occurred when the reaction was executed at 350 °C, could be significantly minimized by La₂O₃ as support.

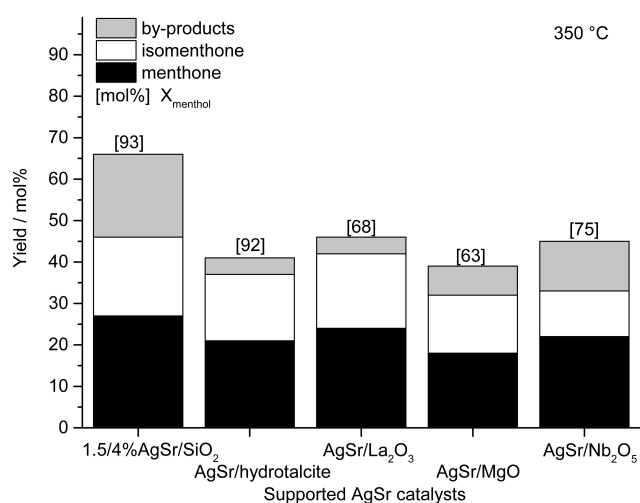
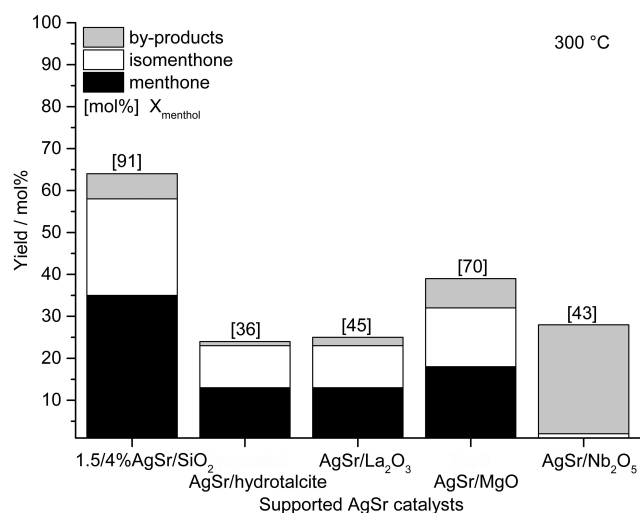


Figure 4. Variation of support for 1.5/4%AgSr as active species (reaction conditions: 3 mL catalyst (1.5 wt% Ag, 4 wt% Sr), 30 mL min⁻¹ 5 vol% O₂/Ar, menthol/O₂ ratio ~ 1:1, 300 °C and 350 °C); X = conversion, numerical values and spectrum of by-products see Table S4 in ESI.

Since 1.5/4%AgSr/SiO₂ showed a sufficient activity (91% menthol conversion) even at 300 °C, and only a slight tendency to by-product formation (6% overall yield), further investigations were directed on the optimization of the Ag and Sr loading.

Therefore four catalysts were first examined with an Ag content between 0.5–3.0 wt% at 300 and 350 °C, and a reaction period of 3 h (Figure 5). With an Ag loading of 0.5 and 1.0%, only very low menthol conversions (43% max.) and total selectivities for menthone and isomenthone (21% max.) were achieved at 300 °C. A temperature increase to 350 °C led to higher menthone/isomenthone yields (25% max.) and also to slightly higher selectivities of up to 33%. However, the best results were obtained using catalysts with Ag contents of 1.5 and 3.0%. As only few by-products had been formed, 1.5/4% AgSr/SiO₂ showed clearly an outstanding performance at a temperature of 300 °C. It seems that enough active sites for the oxidative dehydrogenation are available already at an Ag

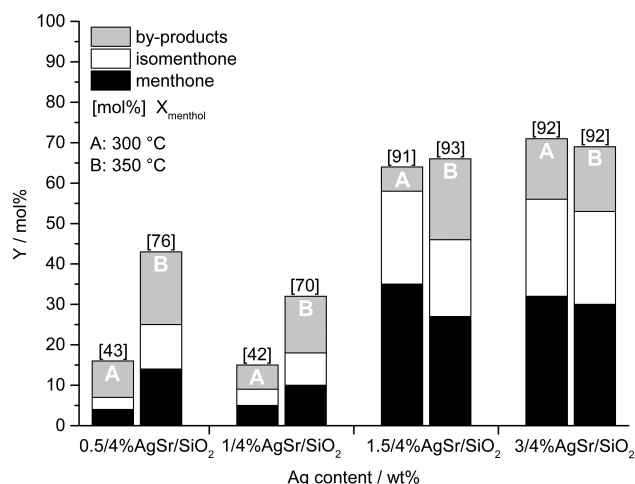


Figure 5. Variation of Ag content in AgSr/SiO₂ catalysts (reaction conditions: 3 mL catalyst (4 wt% Sr), 30 mL min⁻¹ 5 vol% O₂/Ar, menthol/O₂ ratio ~ 1:1, 300 °C and 350 °C); X = conversion, numerical values and spectrum of by-products see Table S4 in ESI.

loading of 1.5%, so that a continuous increase of the menthol conversion could be observed from 0.5 to 1.5 Ag. The lower selectivities at lower Ag loading could possibly be explained by a parallel dehydration occurring at other active sites, which are abundant even at low Ag loading. TEM analyses of the four catalysts could not explain why 1.5/4%AgSr/SiO₂ achieved the best results. A uniform Ag dispersion as well as small particles sizes and narrow particle size distributions were found for all Ag contents between 0.5–3.0%.

In a second series, further experiments were carried out to find the optimum loading of strontium. For this purpose, four catalysts were investigated with Sr contents between 1–10 wt% (Figure 6).

An increased Sr loading from 1.0 to 3.0% effected growing menthol conversion from 58% to 93% and menthone/isomenthone yields from 35% to 52% at a reaction temperature

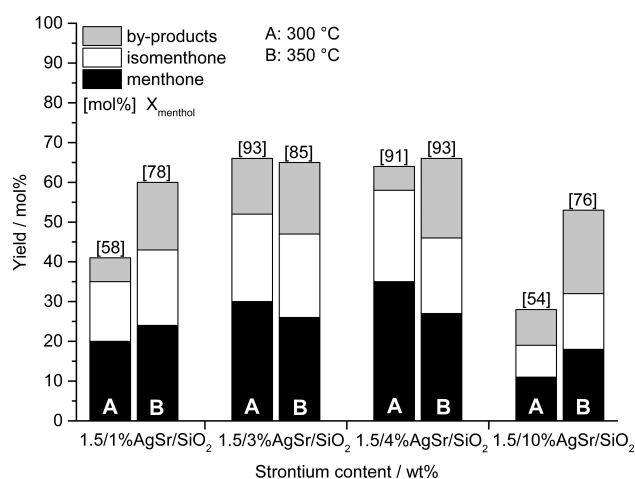


Figure 6. Influence of Sr content (reaction conditions: 3 mL catalyst (1.5 wt% Ag), 30 mL min⁻¹ 5 vol% O₂/Ar, menthol/O₂ ratio ~ 1:1, 300 °C and 350 °C); X = conversion, numerical values and spectrum of by-products see Table S4 in ESI.

of 300 °C. But effect of Sr content on activity and selectivity did not play this significant role when the temperature was raised to 350 °C. In a range between 3.0–4.0% of Sr loading, its optimum was found (58% maximum yield of menthone/isomenthone at 64% selectivity). However, a further increase of the Sr content to 10% caused the opposite effect and led only to 18% menthone and 14% isomenthone selectivity at most (at 32% total selectivity), and significantly lower yields at both 300 and 350 °C. The TEM analysis of the catalysts could not contribute to the clarification of the differences in activity and selectivity. All catalysts show the existence of many small Ag particles, and only very few larger particles could be detected. The distribution of Sr could not be visualized by TEM. In addition, Sr could not be detected by EDX because the SrL α line was superimposed by the SiK α line. A strong substrate-Sr

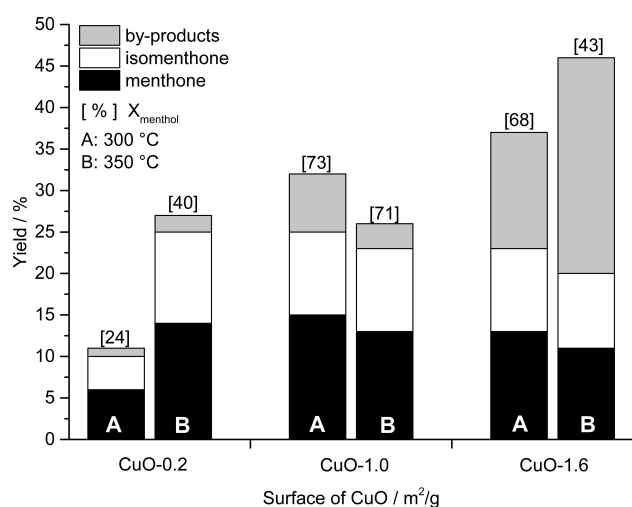


Figure 7. Variation of BET surface of pure CuO catalysts (reaction conditions: 3 mL catalyst, 30 mL min⁻¹ 5 vol% O₂/Ar, menthol/O₂ ratio ~ 1:1, 300 °C and 350 °C); X = conversion, numerical values and spectrum of by-products see Table S4 in ESI.

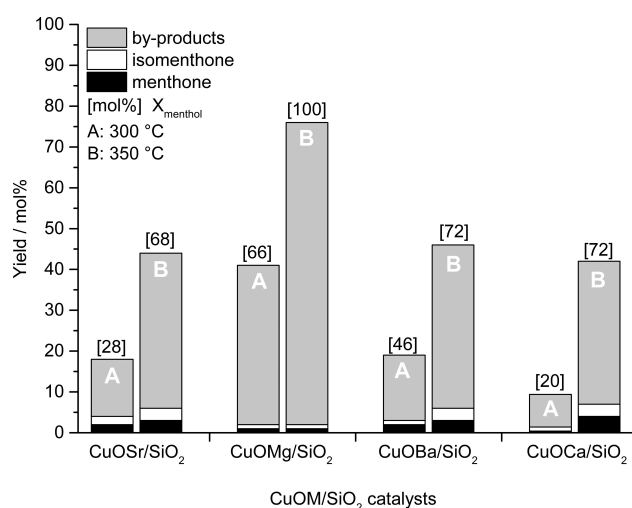


Figure 8. Variation of basic dopant in CuOM/SiO₂ catalysts (reaction conditions: 3 mL CuOM/SiO₂, 30 mL min⁻¹ 5 vol% O₂/Ar, menthol/O₂ ratio ~ 1:1, 300 °C and 350 °C); X = conversion, numerical values and spectrum of by-products see Table S4 in ESI.

interaction may interfere with the process of oxidative dehydrogenation. In addition, it is conceivable that a high Sr loading might lead to the partial coverage of the active Ag centers, resulting in the decreased activity.

Oxidic copper catalysts showed also catalytic activity in the reaction of menthol to menthone. Therefore pure CuO, CuO dispersed on several supports (SiO₂, MgO, hydrotalcite, Nb₂O₅, La₂O₃) and CuO doped with a second alkaline earth metal oxide (CuO–M, M = Sr, Mg, Ba, Ca) were investigated in this series of tests.

First, three copper oxides with different small BET surfaces between 0.2–1.6 m² g⁻¹ were applied at both 300 and 350 °C (Figure 7). The surface of the CuO had a significant influence on the catalyst activity and selectivity. A larger surface area also leads to an increased catalyst activity and consequently to a growing menthol conversion from 24% up to 73% at 300 °C.

In particular, the comparison of the product spectrum shows that the tendency to form by-products increased drastically (up to 26% yield for CuO-1.6 at 350 °C) with rising activity, resulting in diminished selectivities of menthone (16–18%) and isomenthone (13–14%). CuO with the smallest BET surface area of 0.2 m² g⁻¹ achieved the best overall selectivity of 64% menthone and isomenthone (at 25% overall yield) at 350 °C.

Analogously to the successful AgSr/SiO₂ catalysts, SiO₂-supported CuO catalysts with a further active component such as Sr, Mg, Ba, Ca (0.5 mmol second metal g⁻¹ support) were prepared and investigated at 300 and 350 °C (Figure 8).

Unfortunately, all doped CuOM/SiO₂ catalysts induced only a very low selectivity for menthone and isomenthone via oxidative dehydrogenation. All catalysts led almost exclusively to the formation of already above mentioned by-products (see Table S4) with an overall yield of up to 74% (CuOMg/SiO₂ at 350 °C).

Obviously, dehydration to menthenes and dehydrogenation to thermodynamically more stable aromatics were preferred with these more basic catalysts.

But since a positive effect of a basic dopant could not be observed, further investigations were directed on the influence of different supports for CuO.

Therefore five CuO catalysts with nominal 1.5% CuO content were synthesized on SiO₂, MgO, hydrotalcite, Nb₂O₅ and La₂O₃ as support materials. To find out if the catalytically active species CuO can also be formed during the reaction, a freshly reduced 1.2% Cu/SiO₂ catalyst was additionally tested (Figure 9). The application of both Cu/SiO₂ and CuO/SiO₂ led to comparable, but very low yields of desired products (max 7%). Similar to Ag/SiO₂, the yields of menthone and isomenthone could also be increased if basic MgO and hydrotalcite were used as support materials, whereby 41% menthone and isomenthone yield and a total selectivity of 51% were achieved. CuO/MgO also showed the lowest yield of unwanted by-products (4–9%) in the entire temperature range between 300–350 °C.

In contrast to all the catalysts described here, the menthone synthesis with CuO/hydrotalcite led to 6% (+)- and 94% (–)-

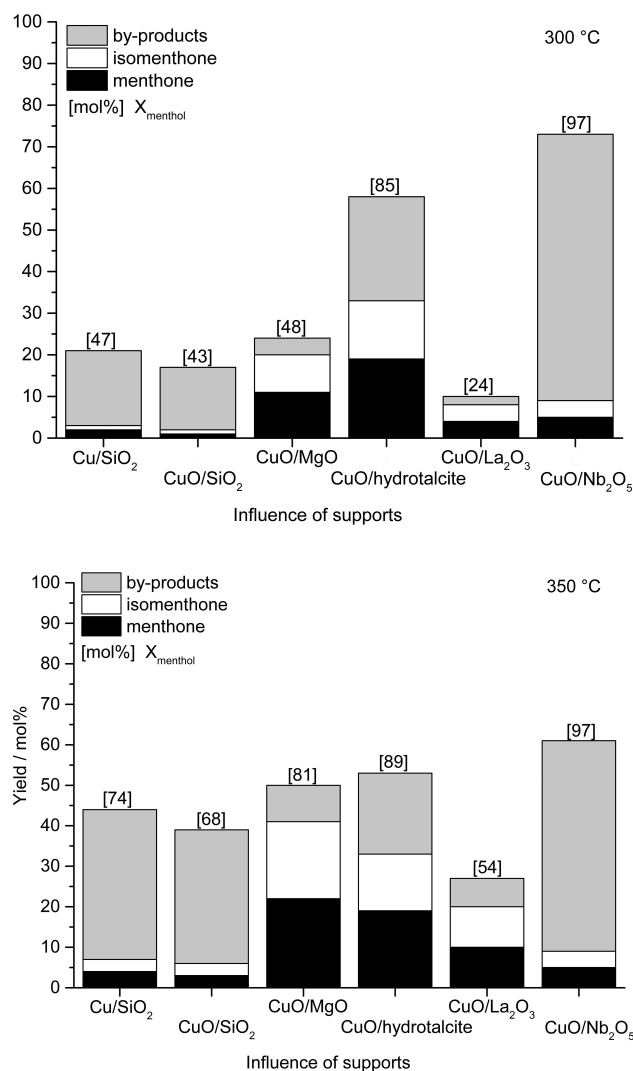


Figure 9. Variation of support in Cu-based catalysts (reaction conditions: 3 mL catalyst (1.2 wt% Cu or 1.5 wt% CuO), 30 mL min⁻¹ 5 vol% O₂/Ar, menthol/O₂ ratio ~ 1 : 1, 300 °C and 350 °C); X = conversion, numerical values and spectrum of by-products see Table S4 in ESI.

menthone, that was the lowest diastereomeric purity of (–)-menthone.

Finally, also some ruthenium-based catalysts were investigated that some of us earlier had developed for the oxidative dehydrogenation of other primary and secondary alcohols in liquid phase.^[44] Two catalysts with a Ru content of 0.5 and 1.0% together with MnO₂ and nanoparticulate ceria doping were prepared on ceria. In addition, a pure 0.2%Ru/CeO₂ was included into the tests (Figure 10). A ruthenium content in the range between 0.5–1.0% has proven to be optimal. Remarkably, 0.2%Ru/CeO₂ with the lowest Ru content already showed a significant activity, and all catalysts provoked a good selectivity for menthone/isomenthone and a low formation of by-products. In direct comparison with all previously used Ag- and Cu-based catalysts, the best results with respect to menthone/isomenthone yields (68% at most at 93% conversion) and

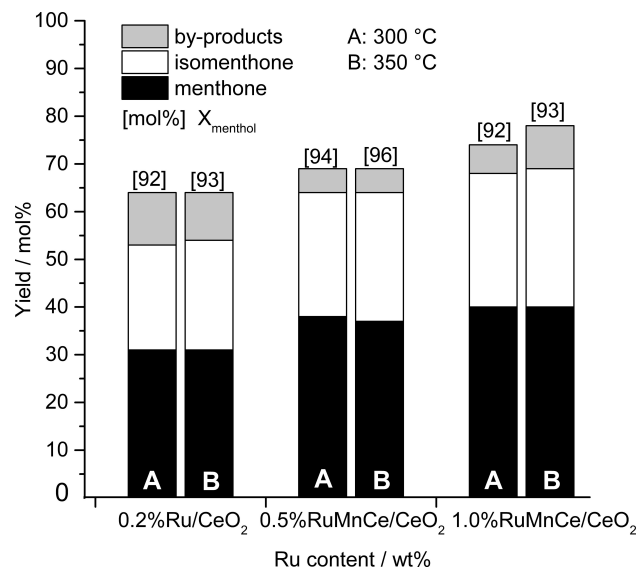


Figure 10. Influence of Ru content (reaction conditions: 3 mL catalyst (0.2 wt% Ru/CeO₂, 0.5 and 1.0 wt% RuMnCe/CeO₂), 30 mL min⁻¹ 5 vol% O₂/Ar, menthol/O₂ ratio ~ 1 : 1); X = conversion, numerical values and spectrum of by-products see Table S4 in ESI.

selectivities of menthone (43%) and isomenthone (30%) were obtained with 1.0%RuMnCe/CeO₂.

An observation in all experiments was the gap between conversion and identified yields of products that means the recovery rate was often lower than 90%. An assumption was that the total oxidation of menthol to CO₂ might play also a role at reaction temperatures of 300–350 °C. To verify this assumption, the experiment with 1.0%RuMnCe/CeO₂ was repeated and the gas stream at the reactor outlet (after the cold trap and sample collection) was fed into a concentrated Ba(OH)₂ solution to perform a gravimetric determination of CO₂ as precipitated BaCO₃. In a second experiment, the gas stream was collected in a He-filled gas mouse and analyzed by GC. The recovery rates (calculated as sum of moles of all products plus moles of unreacted menthol (collected per hour)/moles of menthol (fed into the reactor per hour)) of the gravimetric assay were 79% (300 °C) and 74% (350 °C), and for the experiment with subsequent GC analysis of the gas 84% (300 °C) and 72% (350 °C). With both analytical methods, a total oxidation could be detected as a side reaction of the oxidative menthol dehydrogenation. Using the Ru catalyst, 6% (GC determination) and 9% (gravimetric determination) of the substrate were totally oxidized to CO₂. Of course, the CO₂ content in the reaction gas depends on the catalyst used and on the temperatures prevailing in the reactor which has to be taken into account. Typical of continuous processing, an additional adjustment of residence time will open up further opportunities for improvement of selectivity.

3. Conclusions

For the first time, a sustainable oxidative dehydrogenation of menthol to menthone was performed in the gas phase in a continuous process. This study clearly demonstrates the great potential of Ag-, Cu- and Ru-based catalysts. The first series of experiments with Ag (1.5%) as the active component using SiO₂, hydrotalcite and MgO as support materials revealed that the monometallic SiO₂-supported catalyst essentially led to the formation of by-products, whereas a total selectivity of menthone and isomenthone of up to 67% (32% overall yield at 48% conversion) could be achieved with support materials such as MgO and hydrotalcite. The doping with Sr(II), which apparently prevents the sintering of the Ag particles during the preparation and consequently leads to the formation of small Ag particles, increases considerably both the catalyst activity (91% conversion) and the selectivity to menthone and isomenthone (64%). This effect was neither observed when using basic supports such as hydrotalcite, MgO, La₂O₃ as well as the acidic Nb₂O₅ nor using other alkali and alkaline earth metals as dopants. 1.5/4%AgSr/SiO₂ was found to be the best Ag-based catalyst so far.

The suitability of pure CuO as a catalyst in the oxidative dehydrogenation depends on the size of the BET surface area. The CuO with the lowest BET surface area gave the best results with 63% selectivity for menthone/isomenthone yield at 40% conversion at a reaction temperature of 350 °C. In contrast to the results of silver catalysts, doping with alkali and alkaline earth metal oxides did not improve the yields of menthone and isomenthone. Only by dispersion of CuO on basic supports such as MgO and hydrotalcite, the overall menthone/isomenthone yield (41% at most) and selectivity (51% at most) could be significantly increased.

In direct comparison to the Ag and CuO catalysts, Ru catalysts of the type RuMnCe/CeO₂ gave the best results of this study. Experiments to vary the Ru content showed that a Ru loading of 0.5–1.0% was optimal. Menthone/isomenthone yields of up to 68% at 73% overall selectivity could be observed. That means that the oxidation with Ru on ceria in a continuous reactor resulted in significantly better yields than it was already reported for discontinuous processing^[29] in a batch reactor. One of the advantages of continuous processing is the opportunity of adjusting and influencing the product selectivity by kinetic control of the reaction. In addition, a Ru-based catalyst was used to prove total oxidation as a side reaction of the oxidative dehydrogenation in the investigated temperature range. And not unimportant, the quality of the menthone/isomenthone product is marketable.

Experimental Section

Ag-Based Catalysts

The Ag-based catalysts were prepared in analogy to a literature procedure;^[43] 1.5/4%AgSr/SiO₂: For catalyst preparation, homemade SiO₂ (synthesis see ESI) was fractionally sieved (315–710 μm). Subsequently, 9.45 g of the support material (pore volume:

0.92 mL g⁻¹) was impregnated with a solution of 0.236 g AgNO₃ and 0.966 g Sr(NO₃)₂ in 10 mL water. The moist catalyst precursor was first dried at RT overnight and then at 120 °C for 3 h, calcined at 500 °C for 4 h (heating rate: 2 K min⁻¹) and reduced at 400 °C for 16 h in a H₂ stream. The catalyst powder was pressed in a tablet press, carefully crushed in a mortar and sieved (fraction 400–800 μm).

Compositions of precursors for further Ag-based catalysts can be found in ESI. Their preparation was carried out by analogy with the given procedure.

Cu-Based Catalysts

To prepare the CuO strands, 100 g of Cu(OH)₂ were first calcined at 400 °C for 3 h. Thereafter, 80 g of the calcined material was mixed with 37 mL of a 2% methylcellulose solution in deionized water to form a paste. With the help of a syringe, 2 mm strands were formed. These were heated slowly under synthetic air to 400 °C (heating rate: 5 K min⁻¹) and then faster to 900 °C (heating rate of 10 K min⁻¹). The calcination took place at 900 °C over a period of 6 h. The CuO particles were crashed carefully in a mortar and sieved into fractions before being used in the reaction.

The Cu-based catalysts on supports were prepared according to the same procedure as applied for the Ag-based materials;^[43] 1.5%Cu/SiO₂: For catalyst preparation, again homemade SiO₂ granules were used. Subsequently, 9.85 g of these SiO₂ granules (pore volume: 0.92 mL g⁻¹) were impregnated with a solution of 0.456 g of Cu(NO₃)₂ in 10 mL of water. The precursor was first dried at RT overnight and then at 120 °C for 3 h. Thereafter, the reduction was carried out in a H₂ stream at 300 °C for 3 h (heating rate: 2 K min⁻¹).

1.5%CuO/SiO₂: The preparation was performed as described for 1.5%Cu/SiO₂ with an additional calcination of the catalyst in synthetic air after reduction step at 400 °C for 4 h (heating rate: 2 K min⁻¹).

CuO catalysts on several supports were prepared similarly (see ESI).

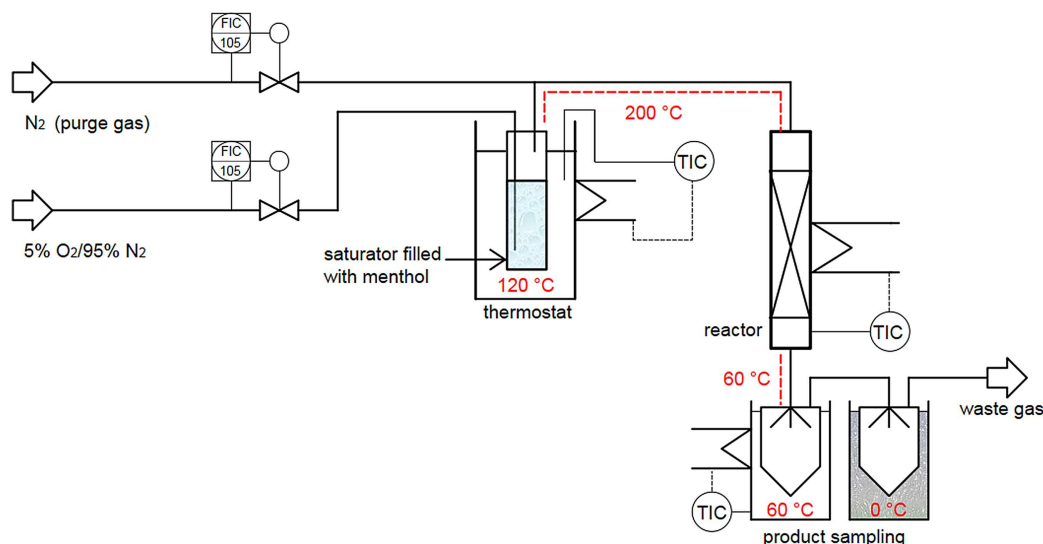
Ru-Based Catalysts

The Ru-based catalysts were prepared following a literature procedure;^[44] 1.0%RuMnCe/CeO₂: To a suspension of 10.0 g CeO₂ in 210 mL deionized water, a solution of 0.223 g RuCl₃ · H₂O, 0.548 g Mn(NO₃)₂ · 4H₂O and 0.496 g Ce(NO₃)₃ · 6H₂O in 40 mL water was added. Then, using a syringe pump, a solution of 0.930 g of NaOH and 0.704 g of Na₂CO₃ in 20 mL of water was continuously added dropwise while stirring the suspension over a period of 5 h. After completion of the addition, the reaction suspension was heated to 65 °C and stirred for 18 h. The solid was separated by centrifugation, washed three times with 20 mL of water and dried overnight at 90 °C in a drying oven. The active components Ru, Mn and Ce are present on the support as oxides and/or hydroxides.

Other compositions of Ru-based catalysts were prepared accordingly, amounts of used reagents can be found in ESI.

Catalyst Characterization

All catalysts were characterized by ICP-OES analysis, BET surface and pore volume. Additionally selected catalysts were characterized by TEM and XPS (see ESI).



Scheme 2. Flow sheet of the reactor set-up.

Catalytic Reaction

All reactions were conducted in a home-made set-up for the oxidative dehydrogenation in the gas phase (see Scheme 2). It consisted of a stainless steel fixed-bed tubular reactor (inside diameter 1.0 cm) enclosed by a heating oven, a saturator (filled with menthol) placed in a thermostat, digital MFCs for gas dosing and control, a vessel for collection of product samples (filled with 6 mL of *o*-xylene) placed in an oil bath, and gas lines heated by heating tapes. The set-up was monitored by control elements and thermocouples. To carry out the experiments, first the reactor was filled with 3 mL of the previously granulated catalyst. The saturator filled with menthol was then immersed in the thermostat solution, which was heated to the desired temperature (usually 120 °C). With the exception of the gas line to the saturator, the temperature of all other lines was set to 200 °C by heaters (heating bands) equipped with thermocouples and control units, and kept constant. During the heating phase, the complete test apparatus was flushed with N₂ via a gas line connected to the feed line after the saturator.

Subsequently, a gas mixture of 5/95 vol% O₂/Ar (e.g. 30 mL min⁻¹) was passed into the saturator, which was heated to 120 °C, when the N₂ purge gas feed had been closed. The evaporated volume fraction of menthol was determined on the basis of its vapour pressure curves and was about 4% by volume. Thus, by using 5% by volume O₂/Ar as reaction and carrier gas, a small excess of oxygen (theoretical menthol/oxygen ratio 0.8:1.0) was adjusted for oxidative dehydrogenation. The reaction was started by opening the gas valve from the saturator to the reactor. Each catalyst was investigated at 300 and 350 °C. In order to prevent crystallization of the unreacted menthol (mp: 41–45 °C) at the reactor outlet, the gas line from the reactor outlet to the collecting vessel was heated to 100 °C. In addition, 6 mL of *o*-xylene was placed into the collecting vessel serving as capture solution, and heated with an oil bath to 60 °C during the entire reaction time. Furthermore, a cold trap filled with ice for collection and identification of any volatile products, was located directly behind the collecting vessel. The hourly collected sample and the contents from the cold trap were transferred to a volumetric flask and analyzed by GC-MS. The total duration of an experiment was always 3 h per each temperature. When the experiment was finished, the oxygen supply was closed and the reactor was purged with N₂. The consumption of menthol

was calculated by removing and weighing the saturator after each test.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords: oxidative dehydrogenation · gas-phase reactions · supported silver catalyst · supported copper catalyst · supported ruthenium catalyst

- [1] H. Surburg, J. Panten, *Common Fragrance and Flavor Materials*, Wiley-VCH, Weinheim **2006**, p. 63.
- [2] M. B. Lauber, S. S. Stahl, *ACS Catal.* **2013**, *3*, 2612–2616.
- [3] WO2012008228 (19.1.2012).
- [4] WO2009145323 (3.12.2009).
- [5] M. Shibuya, Y. Osada, Y. Sasano, M. Tomizawa, Y. Iwabuchi, *J. Am. Chem. Soc.* **2011**, *133*, 6497–6500.
- [6] M. Shibuya, S. Nagasawa, Y. Osada, Y. Iwabuchi, *J. Org. Chem.* **2014**, *79*, 10256–10268.
- [7] CN101565344 (28.10.2009).
- [8] CN1796349 (5.7.2006).
- [9] T. Iwahama, Y. Yoshino, T. Keitoku, S. Sakaguchi, Y. Ishii, *J. Org. Chem.* **2000**, *65*, 6502–6507.
- [10] V. B. Sharma, S. L. Jain, B. Sain, *Tetrahedron Lett.* **2003**, *44*, 383–386.
- [11] T. Punniyamurthy, J. Iqbal, *Tetrahedron Lett.* **1994**, *35*, 4007–4010.
- [12] I. E. Marko, A. Gautier, I. Chelle-Regnaut, P. R. Giles, M. Tsukazaki, C. J. Urch, S. M. Brown, *J. Org. Chem.* **1998**, *63*, 7576–7577.
- [13] K. Jeyakumar, D. K. Chand, *Open Catal. J.* **2008**, *1*, 6–10.

- [14] T. Nishimura, T. Onoue, K. Ohe, S. Uemura, *J. Org. Chem.* **1999**, *64*, 6750–6755.
- [15] C. Melero, O. N. Shishilov, E. Álvarez, P. Palma, J. Cámpora, *Dalton Trans.* **2012**, *41*, 14087–14100.
- [16] G.-J. ten Brink, I. W. C. E. Arends, M. Hoogenraad, G. Verspui, R. A. Sheldon, *Adv. Synth. Catal.* **2003**, *345*, 1341–1352.
- [17] E. V. Johnston, E. A. Karlsson, L.-H. Tran, B. Åkermark, J.-E. Bäckvall, *J. Org. Chem.* **2010**, 1971–1976.
- [18] G. Csajnyik, A. H. Éll, L. Fadini, B. Pugin, J.-E. Bäckvall, *J. Org. Chem.* **2002**, *67*, 1657–1662.
- [19] G. B. W. L. Ligthart, R. H. Meijer, M. P. J. Donners, J. Meuldijk, J. A. J. M. Vekemans, L. A. Hulshof, *Tetrahedron Lett.* **2003**, *44*, 1507–1509.
- [20] S. Murahashi, T. Naota, N. Hirai, *J. Org. Chem.* **1993**, *58*, 7318–7319.
- [21] B. Karimi, E. Farhangi, *Chem. Eur. J.* **2011**, *17*, 6056–6060.
- [22] US20060167313 (27.7.2006).
- [23] A. K. Mandal, J. Iqbal, *Tetrahedron* **1997**, *53*, 7641–7648.
- [24] R. Naik, P. Joshi, R. K. Deshpande, *J. Mol. Catal. A* **2005**, *238*, 46–50.
- [25] S. R. Cicco, M. Latronico, P. Mastroilli, G. P. Suranna, C. F. Nobile, *J. Mol. Catal. A* **2001**, *165*, 135–140.
- [26] N. Kakiuchi, T. Nishimura, M. Inoue, S. Uemura, *Bull. Chem. Soc. Jpn.* **2001**, *74*, 165–172.
- [27] S. Velusamy, M. Ahamed, T. Punniyamurthy, *Org. Lett.* **2004**, *6*, 4821–4824.
- [28] A. Bordoloi, S. Sahoo, F. Lefebvre, S. B. Halligudi, *J. Catal.* **2008**, *259*, 232–239.
- [29] F. Vocanson, Y. P. Guo, J. L. Namy, H. B. Kagan, *Synth. Commun.* **1998**, *28*, 2577–2582.
- [30] V. V. Costa, M. J. Jacinto, L. M. Rossi, R. Landers, E. V. Gusevskaya, *J. Catal.* **2011**, *282*, 209–214.
- [31] J. Albadi, A. Alihoseinzadeh, A. Razeghi, *Catal. Commun.* **2014**, *49*, 1–5.
- [32] J. Albadi, A. Alihoseinzadeh, M. Jalali, M. Sharezaei, A. Mansourneshad, *Mol. Catal.* **2017**, *440*, 133–139.
- [33] P. Korovchenko, C. Donze, P. Gallezot, M. Besson, *Chem. Sustainable Dev.* **2006**, *14*, 577–582.
- [34] J. Wang, L. Yan, G. Qian, X. Wang, *Tetrahedron Lett.* **2006**, *47*, 7171–7174.
- [35] S. Velusamy, T. Punniyamurthy, *Org. Lett.* **2004**, *6*, 217–219.
- [36] R. Ozen, N. S. Kus, *Monatsh. Chem.* **2006**, *137*, 1597–1600.
- [37] S. Singh, S. Dev, *J. Indian Chem. Soc.* **1994**, *71*, 463–467.
- [38] F. Zaccaria, N. Ravasio, R. Psaro, A. Fusi, *Chem. Commun.* **2005**, 253–255.
- [39] F. Zaccaria, N. Ravasio, R. Psaro, A. Fusi, *Chem. Eur. J.* **2006**, *12*, 6426–6431.
- [40] DE4236111 (26.10.1992).
- [41] WO2005085160 (04.03.2005).
- [42] S. Muthaiah, S. H. Hong, *Adv. Synth. Catal.* **2012**, *354*, 3045–3053.
- [43] Y.-S. Sawayama, H. Shibahara, Y. Ichihashi, S. Nishiyama, S. Tsuruya, *Ind. Eng. Chem. Res.* **2006**, *45*, 8837–8845.
- [44] M. P. Chęciński, A. Brückner, J. Radnik, A. Köckritz, *J. Appl. Catal. A: Gen.* **2009**, *366*, 212–219.
- [45] A. M. Ferraria, A. P. Carapeto, A. M. Botelho do Rego, *Vacuum* **2012**, *86*, 1988–1991.
- [46] C. D. Wagner, A. V. Naumkin, A. Kraut-Vass, J. W. Allison, C. J. Powell, J. R. Rumble, NIST Standard Reference Database 20, Version 3.4 (web version) (<http://srdata.nist.gov/xps/>) 2003.
- [47] M. C. Biesinger, *Surf. Interface Anal.* **2017**, *49*, 1325–1334.
- [48] D. J. Morgan, *Surf. Interface Anal.* **2015**, *47*, 1072–1079.
- [49] E. Bêche, P. Charvin, D. Perarnau, S. Abanades, G. Flamant, *Surf. Interface Anal.* **2008**, *40*, 264–267.

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