Accepted Manuscript

Title: Heteropoly acid catalysis for the isomerization of biomass-derived limonene oxide and kinetic separation of the *trans*-isomer in green solvents

Authors: Rafaela F. Cotta, Rafael A. Martins, Matheus M. Pereira, Kelly A. da Silva Rocha, Elena F. Kozhevnikova, Ivan V. Kozhevnikov, Elena V. Gusevskaya



PII: DOI:	S0926-860X(19)30328-X https://doi.org/10.1016/j.apcata.2019.117173
Article Number:	117173
Reference:	APCATA 117173
To appear in:	Applied Catalysis A: General
Received date:	15 May 2019
Revised date:	19 July 2019
Accepted date:	22 July 2019

Please cite this article as: Cotta RF, Martins RA, Pereira MM, da Silva Rocha KA, Kozhevnikova EF, Kozhevnikov IV, Gusevskaya EV, Heteropoly acid catalysis for the isomerization of biomass-derived limonene oxide and kinetic separation of the *trans*-isomer in green solvents, *Applied Catalysis A, General* (2019), https://doi.org/10.1016/j.apcata.2019.117173

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Heteropoly acid catalysis for the isomerization of biomass-derived limonene oxide and kinetic separation of the *trans*-isomer in green solvents

Rafaela F. Cotta ^a, Rafael A. Martins ^a, Matheus M. Pereira ^b, Kelly A. da Silva Rocha ^b, Elena F. Kozhevnikova ^c, Ivan V. Kozhevnikov ^c, Elena V. Gusevskaya^{a,*}

^aDepartamento de Química, Universidade Federal de Minas Gerais, 31270-901, Belo Horizonte, MG, Brazil

^bDepartamento de Química, Universidade Federal de Ouro Preto, 35400-000, Ouro Preto, MG, Brazil ^cDepartment of Chemistry, University of Liverpool, Liverpool L69 7ZD, UK

* Corresponding author. Tel.: +55 31 34095741; fax: +55 31 34095700.

E-mail address: <u>elena@ufmg.br</u> (E. V. Gusevskaya).

Graphical Abstract



Research Highlights

• HPW/SiO₂ promotes selective isomerization of bimass-based limonene oxide into valuable fragrance ingredients.

- The reaction pathway can be switched between dihydrocarvone and carvenone (obtained in ca. 90% unprecedented yield each) simply by changing the reaction temperature.
- *trans*-Limonene oxide can be kinetically separated from the commercial isomeric mixture, with the *cis*-isomer being stereoselectively converted into *trans*-dihydrocarvone.
- Eco-friendly dimethylcarbonate and diethylcarbonate can replace toxic hazardous solvents commonly used in this reaction.

Abstract

Terpenes are an abundant class of natural products, which is important for flavor and fragrance industry. Many acid catalyzed reactions used for upgrading terpenes still involve mineral acids as homogeneous catalysts and/or toxic solvents. Heteropoly acids represent a well-established eco-friendly alternative to conventional acid catalysts. As these reactions are usually performed in the liquid phase, solvents play a critical role for the process sustainability. In the present work, we developed a catalytic route to valuable fragrance ingredients, dihydrocarvone and carvenone, from limonene oxide by its isomerization using silica-supported tungstophosphoric acid as a heterogeneous catalyst and dialkylcarbonates as green solvents. The reaction pathway can be switched between dihydrocarvone and carvenone (obtained in 90% yield each) simply by changing the reaction temperature. In addition, we developed an efficient method for kinetic separation of *trans*-limonene oxide from commercial *cis/trans*-limonene oxide mixture and stereoselective synthesis of *trans*-dihydrocarvone.

Keywords: Bio-renewables; isomerization; heteropoly acid catalysis; kinetic resolution; limonene oxide.

1. Introduction

The sustainability of chemical processes and their environmental footprint are nowadays among the main concerns of chemical industry. In this context, the use of biomass based raw materials in the production of chemicals is particularly important [1]. The most abundant class of natural products consists of terpenic compounds, which are available at a relatively low cost from essential oils. Besides direct applications in flavor and fragrance industry [2], terpenes can be

chemically converted in a variety of value-added products [3-7]. Acid catalyzed reactions are widely used for upgrading terpenes; however, many of these processes still involve mineral acids as homogeneous catalysts and/or toxic solvents as reaction media.

Heteropoly acids of the Keggin series (HPAs) are a well-established eco-friendly alternative to conventional acid catalysts for the clean synthesis of fine and specialty chemicals [8,9]. HPA catalysts have been successfully applied in various reactions of terpenes [7]. For example, we have reported the isomerization [10-12] and etherification/esterification [13-15] of terpenic compounds over the HPA catalysts as well as their coupling with aldehydes [16,17]. Due to the high reactivity of terpenes in the presence of acids and their tendency to oligomerization, most of these transformations require the use of solvents. Moreover, some of these reactions, for instance, the isomerization of limonene oxide [10], have been found to be strongly dependent on the solvent nature.

Limonene oxide is a natural compound available from citric essential oils and also from the epoxidation of limonene, one of the most widespread terpenic compounds. In the presence of acid catalysts, limonene oxide can be converted into various valuable products for flavor and fragrance industry, such as carveol, exocarveol, dihydrocarvone and carvenone [18]. In most cases, good selectivities were achieved only for para-menthenic allylic alcohols such as carveol and exocarveol [19-25]. Reports on the selective synthesis of carbonyl compounds from limonene oxide are scarce and usually describe the procedures which require the use of hazardous solvents or drastic conditions. For example, dihydrocarvone was obtained in 50-70% yield in benzene solutions using a homogeneous ZnBr₂ catalyst [18] or in toluene solutions using nearly stoichiometric amounts of solid LiClO₄ [26], BF₃-etherate [26] or alumina [21]. Carvenone was produced from limonene oxide in modest 50-60% yields in toluene solutions over H₂SO₄/SiO₂ [26] or Cu/SiO₂-Al₂O₃ [27] and in 80-90% yields over zeolite [28] or montmorillonite [29] at high temperature (140–190 °C) or microwave radiation.[29] The first application of HPA catalysts for the isomerization of limonene oxide was reported in our previous work [10]. The reaction resulted in dihydrocarvone as the main product; however, satisfactory yields (ca. 80%) were achieved only in toxic and rigorously regulated solvents such as 1,4-dioxane, dichloromethane and 1,2-dichloroethane. For this reason, our further efforts were directed to the reduction of the environmental impact of the process by finding "greener" alternatives for these solvents.

Here, we report the isomerization of limonene oxide over silica-supported tungstophosphoric acid H₃PW₁₂O₄₀ (HPW) in eco-friendly solvents, dimethylcarbonate (DMC) and diethylcarbonate (DEC). Low-toxic and biodegradable DMC and DEC are highly recommended green solvents with an eco-friendly ranking, comparable to that of ethanol and water [30-33]. We found that the reaction in these solvents can be directed to either dihydrocarvone or carvenone simply by changing the reaction temperature. Moreover, a thorough control of the reaction variables allowed for kinetic separation of trans-limonene oxide and stereoselective synthesis of *trans*-dihydrocarvone to be developed. More reactive *cis*-limonene oxide was selectively transformed to the highly valuable trans-dihydrocarvone, with translimonene oxide remaining largely unconverted. Enantiomerically pure epoxides are versatile building blocks in asymmetric synthesis. In particular, the *trans*-limonene oxide is used for the production of special biodegradable polymers such as polycarbonates and polyesters [34-36]. Commercial limonene oxide is a mixture of *cis* and *trans* isomers (hardly separable by physical means) and their kinetic separation has attracted much attention. Most separation methods developed so far involve the cleavage of the epoxy ring by water or methanol to give limonene diol or its methoxy derivatives [37-43]. Only a few reports on the kinetic separation of limonene oxide isomers has been published, which are based on their difference in reactivity toward isomerization reactions [25,27,44].

2. Experimental

The reagents and solvents employed for the catalyst synthesis and catalytic tests were from Sigma-Aldrich, except Aerosil 300 silica, which was acquired from Degussa. (+)-Limonene oxide (a mixture of *cis* and *trans* isomers in a ratio of 43/57) was also from Aldrich. Anhydrous dimethylcarbonate (DMC) was used without additional treatment. Diethylcarbonate (DEC) was distilled under argon and stored over 4Å molecular sieves.

The silica-supported $H_3PW_{12}O_{40}$ (HPW) catalyst (HPW/SiO₂) was synthesized by wet impregnation of Aerosil 300 silica (BET surface area of 300 m²g⁻¹) with an aqueous solution of HPW and dried at 130°C/0.2-0.3 Torr for 1.5 h, as described elsewhere [45]. From nitrogen physisorption (Micromeritics ASAP 2010 instrument), the HPW/SiO₂ catalyst had a BET surface area of 200 m²g⁻¹, pore volume of 0.53 cm³g⁻¹ and average pore diameter of 144 Å. ³¹P MAS

NMR of HPW/SiO₂ (Bruker Avance DSX 400 NMR, room temperature, spinning rate of 4 kHz, 85% H₃PO₄ as the reference) revealed only one signal at ca. -15 ppm characteristic of the Keggin structure of HPW (Figure S1) [46]. X-ray diffraction analyses (Rigaku Geigerflex-3034 diffractometer with CuK_a radiation) showed that most of HPW was finely dispersed on the surface, with only small amounts of crystalline phase being detected (Figure S2). The content of tungsten and phosphorus was determined by inductively coupled plasma atomic emission spectroscopy (ICP, SpectroCiros CCD instrument) and corresponded to 20 wt% of HPW loading in the catalyst. The characterization data for the HPW/SiO₂ catalyst are presented in Supporting Information (Figures S1 – S3) and also documented in ref [8]. The acid properties of the HPW/SiO₂ catalyst have been discussed in detail elsewhere [47], including the number and the nature of acid sites and their strength.

Catalytic experiments were performed under air in a 10 mL glass reactor. In a typical run, a mixture of limonene oxide (0.45-3.00 mmol), dodecane (GC internal standard, 0.30 mmol) and HPW/SiO₂ catalyst (1–25 mg, 0.07–1.75 µmol of HPW) in a specified solvent (total volume of 3.0 mL) was stirred with a magnetic stirrer at 25–90 °C for a required time. The stirring was stopped periodically and, after a quick catalyst settling, the samples of the supernatant liquid were taken for the gas chromatography (GC) analysis (Shimadzu 17 instrument, Carbowax20 M capillary column, flame ionization detector). Due to the small volume of the samples taken for the GC analysis (5 µL) the changes in catalyst bulk density were insignificant. The reaction rate was not dependent on the intensity of stirring within the range used, suggesting the absence of mass transfer limitations. Conversions and selectivities were calculated from GC analysis using dodecane as the internal standard. Reaction products were identified by GC-MS (Shimadzu QP2010-PLUS spectrometer, 70 eV) by comparison with authentic samples and by ¹H and ¹³C-NMR (Bruker 400 MHz spectrometer, CDCl₃, TMS) after the separation by a column chromatography (silica gel 60, hexane/CH₂Cl₂ mixtures). The product characterization data are presented in Supplementary material (Figures S4-S10). To control the leaching of HPW from silica, the reaction mixture after reaction was submitted to centrifugation (1.5 h, 18000 rpm) or vacuum filtration (10-20 microns filter) to separate the catalyst then the supernatant was allowed to react further under the same conditions. The absence of any additional conversion of limonene oxide indicated the absence of dissolved HPW, i.e., the absence of any significant HPW leaching.

3. Results and discussion

3.1. Synthesis of dihydrocarvone

The data on the isomerization of limonene oxide (1) over the HPW/SiO₂ catalyst are presented in Tables 1 and 2. In the absence of catalyst or in the presence of pure silica, the substrate was not converted at all in blank reactions in all solvents used. The structures of identified reaction products such as dihydrocarvone (2), carvenone (3), 1-methyl-3-isopropenylcyclopentyl-1-carboxaldehyde (4), and limonene-1,2-diol (5) are presented in Schemes 1 and 2. Previously, we have reported that the isomerization of limonene oxide over HPA catalysts resulted mainly in dihydrocarvone [10]. Among various solvents tested, 1,4-dioxane gave the best result, however 1,4-dioxane is a hazardous solvent. Organic carbonates, in particularly dimethylcarbonate (DMC) and diethylcarbonate (DEC), have recently attracted our attention as alternative eco-friendly solvents for the catalytic transformations of terpenic substrates.

In the present work, it was found that DMC and DEC could be successfully used to perform the isomerization of limonene oxide over the silica-supported HPW. It is especially important that HPW is not soluble in DMC and DEC in contrast to 1,4-dioxane, hence the reaction can be conducted under truly heterogeneous conditions.

The reaction in anhydrous DMC occurred rapidly in the presence of small amounts of HPW/SiO₂ (0.2 wt% based on the whole reaction mixture) at room temperature, reaching complete conversion in 15 min (Table 1, run 1). *Cis* and *trans* isomers of dihydrocarvone were formed in total 84% yield derived from the *trans* and *cis* isomers of the original limonene oxide, respectively (Scheme 1). This result is better than that obtained in homogeneous 1,4-dioxane solutions of HPW previously [10]. After reaction (runs 1 and 9, Table 1), the solid catalyst was removed and the supernatant was allowed to react with a new portion of limonene oxide under the same conditions. No further reaction was observed to confirm the heterogeneous nature of the process without any significant HPW leaching.

In an attempt to improve the catalyst efficiency in terms of turnover number (TON), the concentration of the substrate was increased (Table 1, run 2). Although the reaction was fast, the selectivity for dihydrocarvone dropped to 64% probably due to concomitant oligomerization of the substrate. The GC analysis of the supernatant after the reaction showed the presence of high-

boiling products with the mass spectra similar to that of limonene oxide (probably, limonene oxide dimers or trimers). Optimization of the catalyst loading and substrate concentration allowed to achieve high TONs (6000–13000) while maintaining excellent selectivity for dihydrocarvone (Table 1, runs 3–6). Minor products in all these runs were ring-contracted aldehyde **4** and diol **5**, with the latter being probably formed due to the residual water in the system. After reaction, the catalyst was separated by centrifugation from the reaction mixture, washed with chloroform and reused two times without a significant decrease in activity and selectivity (Table 1, runs 2, 2a and 2b).

The reactions in DMC at 40 °C gave dihydrocarvone in nearly 90% yield, the best result ever reported for this product as far as we know (Table 1, runs 7 and 8). DEC, a solvent ranked in sustainability guides even better that DMC and close to water [30], can also be used as the solvent for the isomerization of limonene oxide. In the DEC, dihydrocarvone was obtained in 80–85% yields (Table 1, runs 9 and 10). The limonene oxide conversion occurred slower in DEC than in DMC (Table 1: run 9 vs. run 6; run 10 vs. run 7).

Thus, both organic carbonates, DMC and DEC, can perfectly substitute hazardous 1,4dioxane, dichloromethane and 1,2-dichloroethane as the reaction media for the synthesis of dihydrocarvone from limonene oxide over the HPW catalyst.

Furthermore, an unexpected observation allowed us to change the reaction selectivity in these solvents and obtain another valuable limonene oxide isomer in excellent yields. When the reaction mixture was left in contact with the catalyst for 5 hours at 40 °C, a new reaction product appeared in appreciable concentrations at the expense of dihydrocarvone (Table 1, run 8). The product was identified as carvenone (compound **3** in Scheme 1), which is a high-value natural compound used as a constituent for perfume, flavor and fragrance formulations. Therefore, we further attempted to develop an efficient and eco-friendly synthesis of carvenone from limonene oxide (Table 2).

3.2. Synthesis of carvenone

The selectivity for the formation of carvenone was found to be strongly dependent on the reaction temperature. The yield of carvenone in a 5-hour reaction was 9% at 40 °C (Table 1, run 8), 18% at 50 °C, 35% at 60 °C and 68% at 70 °C (Table 2, runs 1, 2 and 3). Keeping the reaction

mixture in contact with the catalyst for 10 h at 70 °C resulted in 84% yield of carvenone along with 5% of remaining dihydrocarvone (Table 2, run 3). All the reactions presented in Table 2 reached a nearly 100% conversion of limonene oxide at first sampling in 15 min, with dihydrocarvone being the major product at that moment. The formation of carvenone was accompanied by the gradual decrease in the concentration of dihydrocarvone. It is important that the combined selectivity for dihydrocarvone and carvenone was nearly the same (85–90%) along the whole reaction course. Thus, the catalytic process consists of two consecutive steps including fast formation of dihydrocarvone from limonene oxide and slow isomerization of dihydrocarvone into carvenone, with both steps catalyzed by HPW (Scheme 1).

The results obtained clearly showed that higher temperatures were required to accelerate the second reaction step. In order to be able to increase the reaction temperature, we substituted DMC (b.p. 90 °C) by a less volatile DEC (b.p. 126 °C). The catalytic performance of HPW/SiO₂ was nearly the same in DMC and DEC at 70 °C (Table 2, runs 3 and 4). At 90 °C in DEC solutions, carvenone was obtained in 93% yield in only 2 hours, which is the best result ever reported for this product as far as we know (Table 2, run 5). The catalyst was reused two times (Table 2, runs 5, 5a and 5b). A complete conversion of limonene oxide was observed in these runs in 15 min, without a significant decrease in the yield of carvenone after 2 hours (ca. 90%).

The initial rate of carvenone formation, the second slower step in Scheme 1, was estimated and the TOF values are presented in Table 2. It was found that the reaction had the same activation energy of 82 kJ mol⁻¹ in both DMC and DEC solutions (in the range of 40–70 °C in DMC and 70–90 °C in DEC). It should be emphasized that turnover frequencies given in Table 2 are refered to the formation of carvenone from dihydrocarvone.

In run 10 (Table 2), catalyst was removed from the reaction mixture after 60 min and the supernatant was allowed to react further under the same conditions with no additional conversion of dihydrocarvone being observed thereupon to confirm the absence of significant HPW leaching. HPW is insoluble in low polar DEC and DMC and thermally stable under the conditions used, thus ensuring the stability of the catalyst.

The effectiveness of organic carbonates as the reaction medium for the synthesis of carvenone from limonene oxide appears particularly remarkable when compared to that of other solvents (Table 2, runs 6–9). In 1,4-dioxane, not a trace of carvenone was detected under the same conditions used for the reactions in DMC and DEC (Table 2, runs 6 and 7 vs. runs 3 and 4).

Both solid HPW/SiO₂ and dissolved HPW have been tested in the corresponding amounts in 1,4dioxane (HPW is soluble in 1,4-dioxane). In 1,2-dichloroethane and toluene, the formation of carvenone occurred 3 times slower than in DMC and DEC (Table 2, runs 8 and 9 vs. runs 3 and 4). In all cases, the main product rapidly formed from limonene oxide was dihydrocarvone, which was then slowly converted into carvenone (except for 1,4-dioxane). The rate of the second reaction step was strongly dependent on the solvent nature.

The data obtained demonstrate that the solvent effect in dihydrocarvone isomerization is complex and does not correlate with the solvent polarity and basicity. The reaction in the most polar solvent studied, 1,2-dichloroethane ($\varepsilon = 10.4$), had a similar rate as in nonpolar toluene ($\varepsilon = 2.4$) (Table 2, run 8 vs. run 9). Both 1,2-dichloroethane and toluene are nonbasic solvents. On the other hand, weakly basic and weakly polar DMC and DEC ($\varepsilon = 3.1$ and 2.8, respectively) showed much better efficiency than 1,2-dichloroethane and toluene. Finally, the reaction did not occur at all at 70 °C in nonpolar 1,4-dioxane, the solvent with the highest basicity among the solvents tested in the present work. This may be due to a decrease of HPA acid strength in 1,4-dioxane solutions. Further studies are required for better understanding the solvent effects in this reaction.

3.3. Kinetic separation of trans-limonene oxide

Epoxidation of limonene usually results in an almost equimolar mixture of *cis* and *trans* diastereomers of limonene oxide. Working with a commercial sample of limonene oxide (*cis/trans* ratio of 43:57) we noticed a great difference in reactivity of the two isomers toward the isomerization into dihydrocarvone. A larger steric hindrance of the oxygen atom in the *trans* isomer and consequently more difficult access to the active acid sites of the catalyst probably accounts for its lower reactivity in comparison to the *cis*-limonene oxide [27]. This difference provides the possibility for the kinetic separation of *trans*-limonene oxide from the commercial mixture over the HPW catalyst and for the selective synthesis of *trans*-dihydrocarvone (**2a**) (Scheme 1).

The reactions aiming at the kinetic separation of *trans*-limonene oxide were performed under ambient conditions in the presence of small amounts of HPW/SiO₂ (0.015 mol% of HPW, corresponding to a TON of ca. 6500). The data presented in Table 3 clearly show much higher reactivity of *cis* isomer **1a** as compared to *trans* isomer **1b**. In DMC solutions, complete

conversion of **1a** was observed in 10 min, whereas only 15% of **1b** was converted.

Dihydrocarvone**2** (85% *trans*) was formed in 91% chemoselectivity, with the remaining limonene oxide having exclusively *trans* geometry. However, under such conditions the reactivity of the *trans*-isomer was too high to allow sufficient time for the catalyst separation in order to quench the reaction at this step. In 15 min, the conversion of the *trans*-isomer was already 27% decreasing the diastereomeric purity of the dihydrocarvone product (Table 3, run 1). The reaction rate could be diminished at lower temperatures, but this would bring about a technical problem related to the low-temperature catalyst separation (centrifugation or filtration). In a 5-fold diluted solution of DMC, the reaction occurred slower and showed complete conversion of the *cis* isomer in 5 h (Table 3, run 2). Nearly 80% of the *trans* isomer remained unconverted ensuring the diastereoisomeric purity of 82% of the resulting dihydrocarvone. Another way to decelerate the reaction could be the use of DEC as the solvent, as in DEC the reaction occurred slower than in DMC (Table 1, runs 6 vs. run 9)

It is important that the kinetic diastereo-discrimination between the *cis* and *trans* isomers of limonene oxide in DEC solutions was found not only as efficient as in DMC but also more convenient technically due to the lower reactivity of both isomers (Table 3, run 3 vs. run 1). Best purity of the remaining limonene oxide (100% *trans*) and dihydrocarvone (84% *trans*) was obtained in 30 min. To achieve this, the reaction must be terminated at a very low conversion of *trans*-limonene oxide. Conversely, a long contact with the catalyst resulted in nearly complete conversion of both isomers, with the final isomeric composition of dihydrocarvone corresponding to the isomeric ratio in the original limonene oxide (Table 3, runs 1 and 3). It should be taken into account that the *cis* isomer of limonene oxide gives *trans*-dihydrocarvone, whereas *trans*-limonene oxide gives *cis*-dihydrocarvone (Scheme 1).

In a special experiment (Table 3, run 4), the reaction in DEC was stopped in 30 min and the catalyst was quickly separated by vacuum filtration. No further reaction was observed in the supernatant for the next two hours confirming the technical viability of isomer separation under these conditions and also the absence of catalyst leaching problems. The remaining *trans*-limonene oxide after fractional distillation from the reaction mixture can be further processed over the HPW/SiO₂ catalyst to produce pure *cis*-dihydrocarvone. The individual isomers of dihydrocarvone have different organoleptic characteristics and would be much more valuable

than their mixture. The *trans* isomer has the odor of spearmint, whereas the *cis* isomer has a musty and woody scent [44].

3.4. Comments on reaction mechanism

The suggested mechanism of the transformations of limonene oxide 1 in the presence of HPW catalyst is schematically represented in Scheme 2. Protonation of the oxygen atom opens the epoxy ring in limonene oxide resulting in carbenium ion **A**, which can further undergo several competing rearrangements. The C2-C1 hydride shift in **A** gives carbenium ion **B**, which then loses a proton to give dihydrocarvone **2**. As mentioned above, the formation of carvenone **3** was accompanied by the gradual decrease in the concentration of dihydrocarvone **2**. The isomerization of dihydrocarvone into carvenone can be induced by its protonation resulting in the formation of intermediate carbenium ions **C** and **D**. Alternatively, carbenium ion **A** can rearrange into carbenium ion **E** via the transfer of the electron pair of the C2– C3 σ -bond to C3 carbon atom. Proton abstraction from **E** would result in ring-contracted aldehyde **4**. Finally, the residual water can react with carbeniumion **A** to give limonene diol **5**.

4. Conclusions

In has been demonstrated that dimethylcarbonate (DMC) and diethylcarbonate (DEC) are effective and eco-friendly alternatives for conventional hazardous solvents for the isomerization of limonene oxide to valuable fragrance ingredients. The HPA catalyst was applied for the first time for the efficient synthesis of carvenone from limonene oxide. The reaction can be selectively directed to either dihydrocarvone or carvenone simply by changing the reaction temperature. These compounds are obtained in ca. 90 yield each using silica-supported tungstophosphoric acid $H_3PW_{12}O_{40}$ as a heterogeneous catalyst. This is the highest yield reported for these compounds so far, to the best of our knowledge. The catalyst and the solvents can be easily recovered and reused. Different reactivity of *cis*- and *trans*-limonene oxide can be effectively utilized for kinetic separation of *trans*-limonene oxide and stereoselective synthesis of *trans*-dihydrocarvone.

Acknowledgments

The authors acknowledge financial support and scholarships from CNPq, CAPES, FAPEMIG, INCT-Catálise (Brazil) and PROPP-UFOP.

References

- [1] A. Behr, L. Johnen, Alternative Feedstocks for Synthesis, in Ch-J. Li (Ed.), Handbook of Green Chemistry, Volume 7: Green Synthesis, first ed., Wiley-VCH, Weinheim, 2012, pp. 69–92.
- [2] E. Breitmaier, Terpenes. Flavors, Fragrances, Pharmaca, Pheromones, Wiley-VCH, Weinheim, 2006.
- [3] A. Behr, A.J. Vorholt, K.A. Ostrowski, T. Seidensticker, Green Chem. 16 (2014) 982– 1006.
- [4] E.V. Gusevskaya, J. Jimènez-Pinto, A. Börner, ChemCatChem 6 (2014) 382–411.
- [5] K.A.D. Swift, Top. Catal. 27 (2004) 143–155.
- [6] J.L.F. Monteiro, C.O. Veloso, Top. Catal. 27 (2004) 169–180.
- [7] E.V. Gusevskaya, ChemCatChem 6 (2014) 1506–1515.
- [8] I.V. Kozhevnikov, Catalysts for Fine Chemicals, Catalysis by Polyoxometalates, Vol. 2, Wiley, Chichester, 2002.
- [9] Y. Kamiya, T. Okuhara, M. Misono, A. Miyaji, K. Tsuji, T. Nakajo, Catal. Surv. Asia 12 (2008)101–113.
- [10] V.V. Costa, K.A. da Silva Rocha, I.V. Kozhevnikov, E.F. Kozhevnikova, E.V. Gusevskaya, Catal. Sci. Technol, 3 (2013) 244–250.
- [11] A.L.P. de Meireles, M. dos Santos Costa, K.A. da Silva Rocha, E.V. Gusevskaya, Appl. Catal. A 502 (2015) 271–275.
- [12] K.A. da Silva Rocha, P.A. Robles-Dutenhefner, I.V. Kozhevnikov, E.V. Gusevskaya, Appl. Catal. A 352 (2009) 188–192.
- [13] A.L.P. de Meireles, M. dos Santos Costa, K.A. da Silva Rocha, E.F. Kozhevnikova, I.V. Kozhevnikov, E.V. Gusevskaya, ChemCatChem 6 (2014) 2706–2711.
- [14] K.A. da Silva Rocha, N.V.S. Rodrigues, I.V. Kozhevnikov, E.V. Gusevskaya, Appl. Catal. A 374 (2010) 87–94.
- [15] A.L.P. de Meireles, M. dos Santos Costa, K.A. da Silva Rocha, E.F. Kozhevnikova, I.V. Kozhevnikov, E.V. Gusevskaya, ChemCatChem 6 (2014) 2706–2711.
- [16] V.V. Costa, K.A. da Silva Rocha, R.A. Mesquita, E.F. Kozhevnikova, I.V. Kozhevnikov,E.V. Gusevskaya, ChemCatChem 5 (2013) 3022–3026.

- [17] R.F. Cotta, K.A. da Silva Rocha, E.F. Kozhevnikova, I.V. Kozhevnikov, E.V. Gusevskaya, Appl. Catal. B 217 (2017) 92–99.
- [18] R. L. Settine, G. L. Parks, G. L. K. Hunter, J. Org. Chem. 29 (1964) 616–618.
- [19] I. C. Nigam, L. Levi, Can. J. Chem. 46 (1968) 1944–1947.
- [20] E. H. Eschinasi, Israel J. Chem. 6 (1968) 713–721.
- [21] K. Arata, K. Tanabe, Chem. Lett. (1976) 321–322.
- [22] J. Jayasree, C. S. Narayanan, Res. Chem. Intermed. 23 (1997) 169–178.
- [23] G. G. Kolomeyer, J. S. Oyloe (Millennium Specialty Chemicals), EP Patent 1404635 (2003).
- [24] C. Raptis, H. Garcia, M. Stratakis, Angew. Chem. Int. Ed. 48 (2009) 3133–3136.
- [25] G. G. Kolomeyer, D. A. Ferone (LyondellBasell Flavors & Fragrances Company), US Patent 7884252 (2011).
- [26] K. Arata, S. Akutagatva, K. Tanabe, J. Catal. 41 (1976) 173–179.
- [27] N. Ravasio, F. Zaccheria, M. Guidotti, R. Psaro, Top. Catal. 27 (2004) 157–168.
- [28] Y. Fujiwara, M. Nomura, K. Igawa (Toyo Soda Mfg. Company), JP Patent 62114926 (1987).
- [29] T.-T.T. Nguyen, D.-K.N. Chau, F. Duus, T.N. Le, Int. J. Org. Chem. 3 (2013) 206–209.
- [30] C.M. Alder, J.D. Hayler, R. K. Henderson, A. M. Redman, L. Shukla, L. E. Shuster, H. F. Sneddon, Green Chem. 18 (2016) 3879–3890.
- [31] D. Prat, A.Wells, J. Hayler, H. Sneddon, C.R. McElroy, S. Abou-Shehada, P.J. Dunn, Green Chem. 18 (2016) 288–296.
- [32] F. Aricò, P. Tundo, Rus. Chem. Rev. 79 (2010) 479–489.
- [33] B. Schäffner, F. Schäffner, S. P. Verevkin, A. Börner, Chem. Rev. 110 (2010) 4554–4581.
- [34] C.M. Byrne, S.D. Allen, E.B. Lobkovsky, G.W. Coates, J. Am. Chem. Soc. 126 (2004) 11404–11405.
- [35] O. Hauenstein, M. Reiter, S. Agarwal, B. Riegerb, A. Greiner, Green Chem. 81 (2016) 760–770.
- [36] R.C. Jeske, A.M. DiCiccio, G.W. Coates, J. Am. Chem. Soc. 129 (2007) 11330–11331.
- [37] L. Salles, A.F. Nixon, N.C. Russell, R. Clarke, P. Pogorzelec, D.J. Cole-Hamilton, Tetrahedron: Asymmetry 10 (1999) 1471–1476.

- [38] M.J. van der Werf, H. Jongejan, M.C.R. Franssen, Tetrahedron Lett. 42 (2001) 5521– 5524.
- [39] D. Steiner, L. Ivison, C. T. Goralski, R.B. Appel, J.R. Gojkovic, B. Singaram, Tetrahedron: Asymmetry 13 (2002) 2359–2363.
- [40] B.K. Bettadaiah, P.J. Srinivas, Photochem. Photobiol. A 167 (2004) 137–140.
- [41] P.C. Andrews, M. Blair, B.H. Fraser, P.C. Junk, M. Massi, K.L. Tuck, Tetrahedron: Asymmetry 17 (2006) 2833–2838.
- [42] M. Blair, P.C. Andrews, B.H. Fraser, C.M. Forsyth, P.C. Junk, M. Massi, K.L. Tuck, Synthesis (2007) 1523–1527.
- [43] C.S. Kumar, J.R. Manjunatha, P. Srinivas, B.K. Bettadaiah, J. Chem. Sci. 126 (2014) 875–880.
- [44] C. G. Cardenas, Z.U. Din (SCM Corporation), US Patent 4 296 257 (1981).
- [45] I.V. Kozhevnikov, A. Sinnema, A.J.A. van der Weerdt, H. van Bekkum, J. Mol. Catal. A 120 (1997) 63–70.
- [46] I.V. Kozhevnikov, Chem. Rev. 98 (1998) 171–198.
- [47] E.F. Kozhevnikova, I.V. Kozhevnikov, J. Catal. 224 (2004) 164–169.

Scheme and Table captions

Scheme 1. Main products of limonene oxide isomerization of over HPW/SiO₂.

Scheme 2. Schematic presentation of acid catalyzed transformations of limonene oxide (1),

Table 1. Isomerization of limonene oxide (1) over HPW/SiO₂: synthesis of dihydrocarvone (2).

 Table 2. Isomerization of limonene oxide (1) over HPW/SiO2: synthesis of carvenone (3).

Table 3. Kinetic separation of *trans*-limonene oxide induced by HPW/SiO₂^a

Run	1	Catalyst/HPW	Т	Time	Conversion	Selectivity (%)		TON ^b			
	(mmol)	(mg/µmol)	(°C)	(min)	(%)	2	3	4	5	-	
Solvent: dimethylcarbonate											
1 ^c	0.45	5/0.35	25	15	100	84	0	8	7	1290	
2^d	3.00	5/0.35	25	15	81	64	0	11	14		
				60	100	64	0	11	14	8570	
2a ^d	3.00	5/0.35	25	15	76	65	0	12	11		
				60	100	65	0	10	13	8570	
$2b^d$	3.00	5/0.35	25	15	75	62	0	13	10		
				60	100	64	0	12	11	8570	
3	3.00	1/0.07	25	15	63	62	0	12	10		
				60	99	64	0	10	12	42400	
4	1.50	1/0.07	25	15	65	65	0	9	8		
				60	94	63	0	8	6	20100	
5	0.90	1/0.07	25	15	62	82	0	9	9		
				60	100	81	0	9	9	12900	
6	0.45	1/0.07	25	15	60	88	0	3	4		
				60	98	83	0	7	7	6040	
7	0.45	1/0.07	40	15	100	87	0	6	6	6430	
8	0.45	25/1.75	40	15	100	88	0	2	6		
				300	100	77	9	2	0	257	
Solvent: diethylcarbonate											
9°	0.45	1/0.07	25	15	34	89	0	0	10		
				120	94	82	0	6	11	6040	
10	0.45	1/0.07	40	15	76	87	0	5	8		
				60	100	85	0	7	9	6430	

Table 1. Isomerization of limonene oxide (1) over HPW/SiO₂: synthesis of dihydrocarvone (2)^a

^a Total volume 3.0 mL. Conversion and selectivity (based on converted limonene oxide) were determined by GC. ^b Turnover number in moles of substrate converted per mole of a total amount of HPW in the catalyst. ^c After the run, the catalyst was removed, the solution was recharged with fresh substrate (0.45 mmol) and the reaction was allowed to proceed further under the same conditions for 1 h, with no further conversion observed thereupon. ^d After run 2, the catalyst was reused two times (runs 2a and 2b).

Run	Solvent	Т	Time	Conversion	Selectivity (%)		TON ^b	TOF ^c
		(°C)	(min)	(%)	2	3	-	(\min^{-1})
1	dimethylcarbonate	50	15	100	85	3		0.15
			300	100	72	18	257	
2	dimethylcarbonate	60	15	100	84	4		0.30
			300	100	61	35	257	
3	dimethylcarbonate	70	15	100	66	23		1.62
			300	100	20	68		
			600	100	6	84	257	
4	diethylcarbonate	70	15	100	66	27		1.63
			300	100	20	75		
			600	100	11	77	257	
5 ^d	diethylcarbonate	90	15	100	47	41		7.08
			120	100	2	93	257	
5a ^d	diethylcarbonate	90	15	100	52	38		6.50
			120	100	4	91	257	
5b ^d	diethylcarbonate	90	15	100	54	35		6.00
			120	100	4	90	257	
6	1,4-dioxane	70	15	100	85	0		0
			300	100	86	0	257	
7 ^e	1,4-dioxane	70	15	100	88	0		0
			300	100	88	0	257	
8	1,2-dichloroethane	70	15	100	83	3		0.56
			300	100	51	37	257	
9	toluene	70	15	100	81	1		0.50
			300	100	46	34	257	
10 ^f	diethylcarbonate	70	60	100	45	52		1.70
			600	100	45	52	257	

Table 2. Isomerization of limonene oxide (1) over HPW/SiO₂: synthesis of carvenone (3)^a

^a Limonene oxide, 0.45 mmol; catalyst 20% HPW/SiO₂, 25 mg (1.75 μmol of HPW); total volume 3.0 mL.

Conversion and selectivity (based on converted limonene oxide) were determined by GC. ^b Turnover number in

moles of substrate converted per mole of a total amount of HPW in the catalyst. ^c Initial turnover frequency for the formation of carvenone **3** (up to 25–40% conversion of dihydrocarvone). ^d After run 5, the catalyst was reused two times (runs 5a and 5b). [e] Homogeneous HPW catalyst, 5 mg (1.75 μ mol). ^f After 60 min, the catalyst was removed from the reaction mixture and the supernatant was allowed to react further under the same conditions with no additional conversion of dihydrocarvone being observed thereupon.

Run	Solvent	Time	Conversion (%)		Composition of remaining 1	Selectivity for 2 (%)		
		(min)	1a (<i>cis</i>)	1b (trans)	(1b trans/ 1c cis)	(2a trans/2b cis)		
1	DMC	10	100	15	100/0	91 (85/15)		
		15	100	27	100/0	88 (80/20)		
		30	100	51	100/0	85 (65/35)		
		60	100	95	100/0	83 (52/48)		
		300	100	100	-	76 (47/53)		
2 ^b	DMC	30	24	5	61/39	95 (72/28)		
		180	78	9	84/16	90 (83/17)		
		300	100	20	100/0	85 (82/18)		
3	DEC	15	64	3	77/23	89 (89/11)		
		25	90	9	92/8	87 (87/13)		
		30	100	19	100/0	87 (84/16)		
		60	100	52	100/0	84 (67/33)		
		120	100	90	100/0	82 (52/48)		
4 ^c	DEC	30	100	19	100/0	87 (84/16)		
		150	100	20	100/0	87 (84/16)		

Table 3. Kinetic separation of *trans*-limonene oxide induced by HPW/SiO₂^a

^a Limonene oxide (1) (commercial mixture of *cis* and *trans* isomers in a ratio of 43/57), 0.45 mmol; catalyst 20% HPW/SiO₂, 1 mg (0.07 μmol of HPW); 25 °C; total volume 3.0 mL. Conversion and selectivity (based on converted limonene oxide) were determined by GC. ^b Total volume 15.0 mL ^c After 30 min, the catalyst was centrifuged from the reaction mixture and the supernatant was allowed to react further under the same conditions with no additional conversion of limonene oxide being observed thereupon.



Scheme 1. Main products of limonene oxide isomerization over HPW/SiO₂.



Scheme 2. Schematic presentation of acid catalyzed transformations of limonene oxide (1).