

Solvent-free dehydrogenation of γ -terpinene in a ball mill: investigation of reaction parameters†

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Received 12th February 2010, Accepted 14th April 2010

First published as an Advance Article on the web 4th June 2010

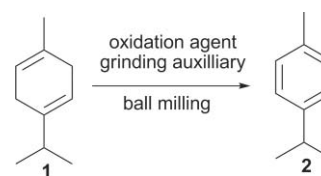
DOI: 10.1039/c002819c

The present article reports on the solvent-free dehydrogenation of γ -terpinene (**1**) in a planetary ball mill affording *p*-cymene (**2**) as the predominant reaction product. The influence of various reaction parameters and technical variables on the transformation of **1** has been assessed. Thus, it is shown that KMnO_4 can be substituted by other, less-toxic and environmentally-benign oxidation agents (Oxone®, NaIO_4 , I_2). In most cases the reaction yielded **2** with high selectivities, whereby conversion can be fine-tuned by variation of the oxidant-to-substrate ratio, the rotation frequency ν_{rot} , the number of milling balls n_{ball} or the type of grinding auxiliary employed. Contrary to particle refinement processes, the size of the milling balls d (constant mass) has no influence on the conversion and chemical yield.

Introduction

In organic chemistry oxidation is an important method for the synthesis of basic compounds in complex synthetic sequences. The growing interest in the implementation of sustainable chemistry in scientific work has led to the development of a myriad of new methods to perform chemical reactions. In this regard, the replacement of organic solvents is an important issue culminating in the accomplishment of solvent-free syntheses, whereby solvent is omitted during chemical synthesis. Solid inorganic oxidants are widely-used in organic transformations at the lab-scale,^{1–5} but catalytic procedures employing oxygen or hydrogen peroxide as oxidizing agent are preferred in large scale synthesis.^{6,7} Transformation of catalytic heterogeneous oxidation into solvent-free reaction procedures is difficult, whereas in the case of stoichiometric oxidants such experimental procedures are well-known.^{1–7} Solvent-free oxidation reactions can be arranged by simple grind-stone chemistry using mortar and pestle,^{1,2} by stirring either heated conductively^{3,6} or by microwave irradiation,^{4,5} and by the employment of specialized laboratory ball mills.^{4a} Within this work we take a closer look at the solvent-free oxidation of γ -terpinene (**1**) to *p*-cymene (**2**; Scheme 1) enhanced by grinding in a planetary ball mill.

The selective synthesis of **2** is a poorly investigated area of chemical research. Predominantly, **2** plays a major role as a by-product during the isomerization of terpenes like α - and β -pinene, or of *p*-menthadienes like limonene or α -phellandrene.⁸ Predominantly, **2** is used as a solvent or as a ligand in ruthenium(II) complexes: $[(\eta^6\text{-cymene})\text{RuCl}_2]_2$, which



Scheme 1 Oxidative dehydrogenation of γ -terpinene (**1**).

are often applied in selective hydrogenation or catalytic transfer hydrogenation reactions.⁹ In solution it has been shown that **2** can be generated by dehydrogenation of **1** or α -terpinene, whereby inorganics (permanganates, manganates, chromates)¹⁰ or oxygen¹¹ are the most common oxidants. The insolubility of inorganic oxidants in most organic solvents requires the application of biphasic reaction mixtures or the employment of phase transfer catalysts or similar auxiliaries (e.g. [18]crown-6). Accordingly, the employment of oxygen necessitates the presence of a catalyst to induce electron transfer. The oxidative dehydrogenation of **1** in acetone at 0 °C with KMnO_4 was investigated by Singaram and co-workers.¹² Nüchter *et al.* performed the oxidation of aromatic compounds with KMnO_4 , but without any solvents in a ball mill.^{4a} In the present work this procedure was applied to perform the oxidative dehydrogenation of **1**.

Therefore, a solvent-free method for the oxidative dehydrogenation of **1** to **2** in a ball mill was established. The use of solvents was unnecessary during the reaction process. After completion, an easy extraction procedure followed. The product **2** could be formed in quantitative yields after a reaction time of 5 min. In addition, the investigation of reaction parameters (oxidant, reaction time), the influence of variables like number of milling balls (n_{ball}) or rotation frequency (ν_{rot}) was assessed.

Results and discussion

The oxidative dehydrogenation of **1** (Scheme 1) was performed under solvent-free conditions, applying a planetary ball mill

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† Electronic supplementary information (ESI) available: Experimental results for different aluminas and silicas as grinding auxiliaries and the influence of doped solvents are reported. DOI: 10.1039/c002819c

Table 1 Time-dependency of the solvent-free oxidative dehydrogenation of γ -terpinene (**1**) in the presence of alumina or quartz sand as milling auxiliaries^a

<i>t</i> /min	alumina		quartz sand	
	<i>X</i> ₁ [%]	<i>Y</i> ₂ [%]	<i>X</i> ₁ [%]	<i>Y</i> ₂ [%]
5	96	95	74	73
10	97	96	85	84
20	99	99	93	92
30	99	99	96	94

^a Batch (per beaker): 3.8 g auxiliary, 2 mmol **1**, 6 mmol KMnO₄, 0.1 g H₂O; Ball milling: 2 milling beakers (ZrO₂, *V* = 45 ml), 6 milling balls (ZrO₂, *d* = 15 mm) per beaker; *v*_{rot} = 800 rpm (13.3 Hz).

(Pulverisette 7, Fritsch GmbH, Idar-Oberstein Germany) for efficient mixing of the reactants and for the application of energy. Before the investigation of various variables and their influence on the reaction course, the dependency of conversion *X*₁ and yield *Y*₂ from reaction time *t* of **1** and **2** was studied. The reaction time was concluded as the limiting factor for transformations in a ball mill within previous studies.¹³ Within these experiments we studied the difference between alumina[‡] and quartz sand[§], which have been applied as common grinding auxiliaries. As shown in Table 1, reactions in the presence of alumina afforded nearly quantitative conversion, accompanied by high selectivity *S* after 5 min. In contrast to experiments in solution, side-chain oxidation products (e.g. toluene, benzoic acids) were not identified during the reaction in a planetary ball mill under solvent-free conditions. In the case of quartz sand a conversion of 81% was reached within a similar time range. An extension of *t* to 30 min resulted in complete conversion of **1** in the presence of quartz sand. Neither in the case of experiments with alumina or quartz sand was a decrease in *S* observed, when increasing *t*. Therefore, it was decided to perform all following reactions at *t* = 5 min to guarantee a fast procedure.

It was shown recently, that addition of water or the presence of physisorbed water on the grinding auxiliary surface is beneficial for solvent-free transformation in ball mills.^{4a} However, reactions in the presence of different amounts of water (0–0.1 g) resulted in indifferent yields and selectivities (cf. Electronic Supporting Information; ESI[†]). Nonetheless, doping the reaction mixture with water, non-agglomerated free-flowing powders after treatment in the ball mill were obtained. Thus, it was easy to remove the reaction mixture from the beaker prior to following work-up by extraction.

Grinding auxiliaries

As mentioned in the section above the grinding auxiliary influences *X*₁ and therein *Y*₂. However, the product selectivity remains unaffected (Table 1). Generally the applied auxiliaries are also used as solid supports for the preparation of catalysts or as catalysts themselves.¹⁴ Different surface properties often

[‡] If not otherwise indicated “alumina” refers to acidic α -Al₂O₃ for chromatography purchased from Fluka® with a particle size between 0.063–0.2 mm (purity >95%).

[§] If not otherwise stated “quartz sand” refers to crude, calcinated SiO₂ (purity >95%) for cleaning of platinum crucibles purchased from Sigma-Aldrich®.

influence reactions. In this work the materials should mimic the function of a classical solvent. Thus, they are responsible for diluting the reactants, and therewith realizing a homogeneous reaction mixture. Furthermore, the support is responsible for heat transport through the whole beaker. Therewith, overheating and side-reactions can be minimized or completely avoided.

The reactions were performed as described above, once with KMnO₄ as oxidant and once without any oxidant to determine the oxidation potential of the pure auxiliary. As shown in Fig. 1, all filling materials render yields between 70 and 99% in the presence of KMnO₄. The aluminium oxides are all suitable to give yields between 90 and 99%. Five different aluminas were employed, which mainly differ in their surface characteristics, modification and particle size distribution (cf. ESI[†]). Due to insignificant differences in *Y*₁ and *S*₂, the mean value is provided within Fig. 1. Similar to aluminas, four different silicas have been employed as auxiliaries. Concerning *X*₁, *Y*₂, and *S*_F² they resemble each other. Thus, Fig. 1 reports the mean value (cf. ESI[†]). Contrary to silicas, quartz sand induces only moderate yields about 70%. This effect can be attributed to differences in particle sizes between silicas and quartz sand. The former (as well as alumina) offers a narrow particle size distribution (0.063–0.5 mm), which guarantees a good dispersion of the reaction mixture and therefore an efficient mass- and heat-transfer. In the case of quartz sand, the particle size is unknown but it is recognizable that it consists of small pebbles. Normally the energy generated by the movement of the milling balls is devolved to the reaction mixture and initiates the reaction. In the case of larger particle sizes, parts of the kinetic energy are consumed for particle refinement. Hence, quartz sand

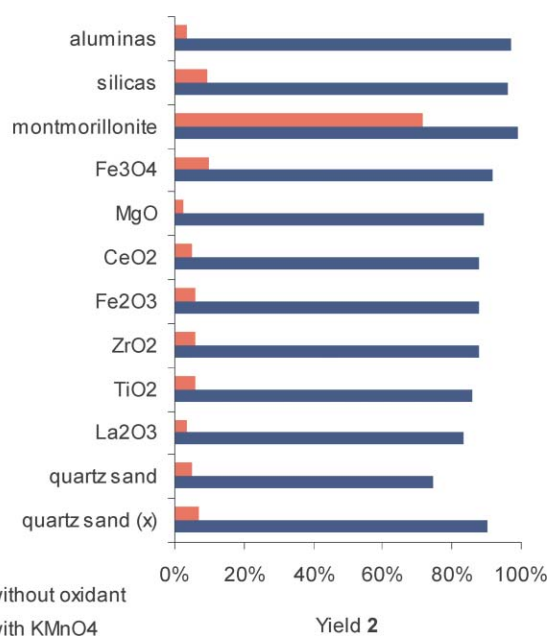


Fig. 1 Solvent-free oxidative dehydrogenation of γ -terpinene (**1**, 2 mmol) to *p*-cymene (**2**) in the presence of different milling auxiliaries (3.8 g) and in the presence or absence of KMnO₄ (6 mmol; 0.1 g H₂O; Ball milling: 2 milling beakers (ZrO₂, *V* = 45 ml), 6 milling balls (ZrO₂, *d* = 15 mm) per beaker; *v*_{rot} = 800 rpm (13.3 Hz), *t* = 5 min; x: pre-grinded quartz sand – cf. text).

afforded moderate yields, because a part of the overall kinetic energy is used to refine the quartz grains. This statement can be supported by an experiment where quartz sand was grinded before its use. Hence, 3.8 g quartz sand were ground without the reactants. After $t = 10$ min the reactants were added and the mixture was treated for another 5 min. As shown in Fig. 1 the yield of **1** rises up to 90% in the presence of KMnO_4 , and therewith to a level comparable with alumina or silica. Beside aluminas and silicas, basic and amphoteric metal oxides as well as montmorillonite (phyllosilicate) have been employed as grinding auxiliaries. Except for the latter, the conversions in the presence of the oxidant are between 85 (La_2O_3) and 90% (Fe_3O_4).

All grinding auxiliaries revealed negligible reactivity in the dehydrogenation of **1** without potassium permanganate, except montmorillonite. Pure montmorillonite is known to act as a catalytically active material, because of its acidity. Therefore it is used for ring-opening and isomerization reactions.¹⁵ Beside its inherent acidic properties, this phyllosilicate also offers a natural oxidation potential (bleaching soil).¹⁶ Assessment of the natural oxidation potential of montmorillonite in the dehydrogenation of **1** to **2** (Scheme 1) is pictured in Fig. 2. With increasing amounts of montmorillonite both Y_2 and S_2 reach up to 70%. Lower amounts of montmorillonite support isomerization affording various *p*-menthadiene-isomers ($\text{C}_{10}\text{H}_{16}$; e.g. terpinolene, α -terpinene). In the case of pure montmorillonite ($W_{\text{montmorillonite}} = 1$) the conversion of **1** is quantitative whereby the formation of **2** predominates ($S = 72\%$). Nevertheless, 28% of **1** undergoes a rearrangement reaction (*p*-menthadiene-isomers) instead of dehydrogenation to **2**.

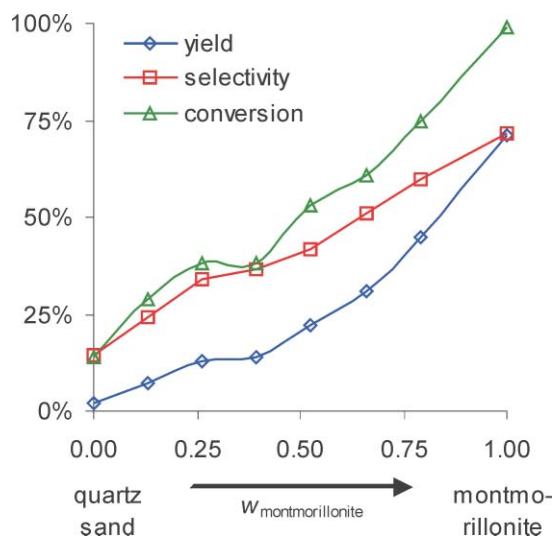


Fig. 2 Solvent-free oxidative dehydrogenation of γ -terpinene (**1**, 2 mmol) to *p*-cymene (**2**) with montmorillonite as oxidation agent in different mass fractions with quartz sand ($\Sigma = 3.8$ g; 0.1 g H_2O); Ball milling: 2 milling beakers (ZrO_2 , $V = 45$ ml), 6 milling balls (ZrO_2 , $d = 15$ mm) per beaker; $v_{\text{rot}} = 800$ rpm (13.3 Hz), $t = 5$ min).

Oxidation agents

Potassium permanganate is a commonly-used and well-established solid oxidant in organic synthesis.¹⁷ It was proved to be a suitable oxidizing agent for the oxidative dehydrogenation

Table 2 Solvent-free oxidative dehydrogenation of γ -terpinene (**1**) to *p*-cymene (**2**) in the presence of alumina or quartz sand as milling auxiliaries and different oxidation agents^a

Oxidation agent	Y_2 [%] ^a	
	alumina	quartz sand
KMnO_4	99	53
<i>p</i> -Benzoquinone	95	37
I_2	93	52
Oxone® ^b	84	8
NaMnO_4	82	73
$(\text{NH}_4)_4\text{Ce}(\text{SO}_4)_4 \cdot 2\text{H}_2\text{O}$	71	11
NaIO_4	67	41
K_2MnO_4	54	18
BaMnO_4	47	24
KIO_4	47	40
V_2O_5	39	19
DDQ ^c	29	29
KIO_3	22	8
PCC ^d	16	13
NaBrO_3	13	36
$\text{K}_2\text{Cr}_2\text{O}_7$	12	7
2,6-Dimethoxy- <i>p</i> -benzoquinone	11	5
$\text{Na}_2\text{S}_2\text{O}_8$	11	10
$\text{Mn}(\text{AcO})_3 \cdot 2\text{H}_2\text{O}$	10	4
$(\text{NH}_4)_2\text{S}_2\text{O}_8$	7	7
Anthraquinone	5	4
urea- H_2O_2 -adduct (28%)	5	6
MnO_2	4	2
$\text{NaBO}_3 \cdot 4\text{H}_2\text{O}$	2	4
9-Fluorenone	0	7

^a Batch (per beaker): 3.8 g auxiliary, 2 mmol **1**, 6 mmol oxidant, 0.1 g H_2O ; Ball milling: 2 milling beakers (ZrO_2 , $V = 45$ ml), 6 milling balls (ZrO_2 , $d = 15$ mm) per beaker; $v_{\text{rot}} = 800$ rpm (13.3 Hz), $t = 5$ min. ^b Triple salt: 2 $\text{KHSO}_5 \cdot \text{KHSO}_4 \cdot \text{K}_2\text{SO}_4$. ^c 2,3-Dichloro-5,6-dicyano-*p*-benzoquinone. ^d Pyridiniumchlorochromate: $[\text{PyH}][\text{CrO}_3\text{Cl}]$.

of **1** in the presence of aluminium oxide (Table 1, Fig. 1). In comparison to quartz sand, an increased yield of **2** was observed. However, KMnO_4 has a high toxicity and a complete removal of manganese residues is required for the application of reaction products in further synthesis. Due to this fact, a variety of other inorganic as well as organic oxidants were employed in the model reaction (Table 2). For application as the oxidant in the reaction according to Scheme 1, the reagents have to be unable to oxidize the substrate by oxygen transfer. Rather, they must have the ability to abstract the hydrogen atoms.

In the majority of all experiments, the dehydrogenation is more effective with alumina as the grinding auxiliary than with quartz sand. However, the results underline the good performance of KMnO_4 in combination with alumina as the grinding auxiliary. As shown in Fig. 3 a great excess of KMnO_4 is necessary to guarantee quantitative yields. Ball milling in the presence of alumina afforded a molar ratio of 3:1 for quantitative conversion after 5 min. A maximum yield of >95% at an oxidant-to-substrate ratio of 4:1 was assigned for reactions with quartz sand as a milling auxiliary. A further increase of the oxidant afforded a decrease in selectivity due to formation of *p*-cymenene (**3**; 1-methyl-4-(prop-1-en-2-yl)benzene; $S = 4\%$) as major side product (Scheme 2). The envisioned ideal molar ratio of KMnO_4 to **1** of 2:3, as indicated by the redox-equation (eqn (1)) is far away from reality. However, elongation of t might enhance the exploitation of the oxidant; thus, lower molar ratios can be chosen.

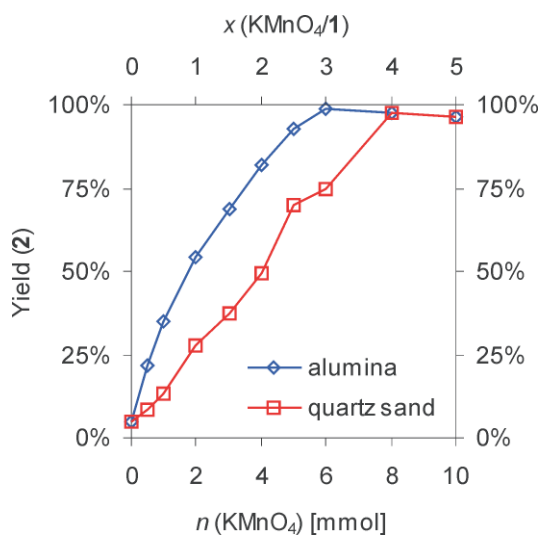
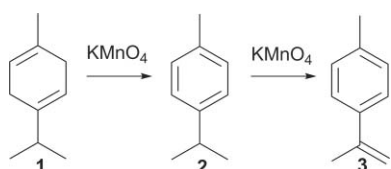
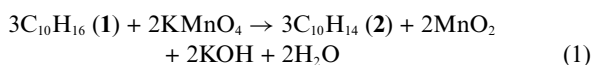


Fig. 3 Solvent-free oxidative dehydrogenation of γ -terpinene (**1**, 2 mmol) to *p*-cymene (**2**) with KMnO_4 as oxidant (3.8 g auxiliary, 0.1 g H_2O ; Ball milling: 2 milling beakers (ZrO_2 , $V = 45$ ml), 6 milling balls (ZrO_2 , $d = 15$ mm) per beaker; $v_{\text{rot}} = 800$ rpm (13.3 Hz), $t = 5$ min).



Scheme 2 Dehydrogenation of γ -terpinene (**1**) with excess of KMnO_4 .



Beside KMnO_4 , further potent oxidizing agents have been identified (Table 2). *p*-Benzoquinone (BQ) is also known as an effective dehydrogenation agent in organic synthesis.¹⁸ Nearly quantitative yields of **2** are formed by way of transfer hydrogenation affording *p*-hydroquinone as a side product. Further oxidation by-products were not observed. Compared to KMnO_4 , the remaining BQ and the formed *p*-hydroquinone have to be removed from the extraction mixture during purification. Thus BQ is disadvantageous due to complex work-up. DDQ (2,3-dichloro-5,6-dicyano-*p*-benzoquinone), 2,6-dimethoxy-*p*-benzoquinone, and anthraquinone have a similar structure to BQ. Thus, their oxidation potential should be in the same range. Table 2 reports yields of 29, 11, and 5%, respectively. Apparently, steric repulsion of the crowded benzoquinones prevent a higher reactivity under solvent-free reaction conditions.

Interestingly, elemental iodine is suitable for the dehydrogenation of **1** also.¹⁹ High yields combined with high selectivity (94%) were received. Neither, the formation of addition products to the double bond (iodination, hydroiodination) nor core-substitution products of **2** (from electrophilic substitution) were identified. However, the employment of iodine has a big disadvantage: excess oxidant has to be removed by washing with an aqueous solution of $\text{Na}_2\text{S}_2\text{O}_8$, prior to extraction to prevent solution of iodine in the organic eluent. A rather simple solution for overcoming the problem is the application of NaIO_4 as the oxidizing agent, which revealed a similar performance as shown

for KMnO_4 (Table 2). Due to its ionic nature, it is insoluble in organic solvents and therefore no further purification step was necessary. Similar to the employment of KMnO_4 (Fig. 3), the molar ratio of NaIO_4 -to-**1** has been assessed (Fig. 4). An increased ratio of NaIO_4 to **1** only resulted in linear increase of Y_2 with alumina as the grinding auxiliary. In contrast, the reaction in the presence of quartz sand afforded a maximum Y_2 of 50% at the ratio of 2:1. The product selectivity (>99%) is independent from both the amount of NaIO_4 and the grinding auxiliary. Thus, the reported yields in Fig. 4 represent the overall conversion of **1**.

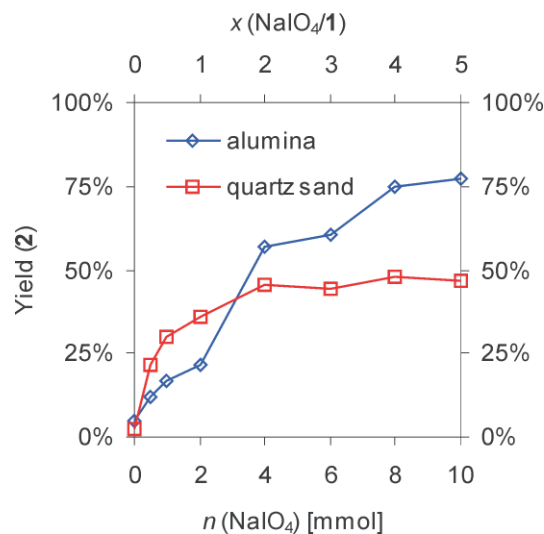


Fig. 4 Solvent-free oxidative dehydrogenation of γ -terpinene (**1**, 2 mmol) to *p*-cymene (**2**) with NaIO_4 as oxidant (3.8 g auxiliary, 0.1 g H_2O ; Ball milling: 2 milling beakers (ZrO_2 , $V = 45$ ml), 6 milling balls (ZrO_2 , $d = 15$ mm) per beaker; $v_{\text{rot}} = 800$ rpm (13.3 Hz), $t = 5$ min).

Oxone® (triple salt $2\text{KHSO}_5 \cdot \text{KHSO}_4 \cdot \text{K}_2\text{SO}_4$) is well known as a good oxidation agent;²⁰ it is also suitable for this reaction type (Scheme 1), but only in combination with aluminium oxide ($Y_2 = 85\%$; Table 2). With quartz sand as the auxiliary, a lower conversion of **1** was observed ($Y_2 = 8\%$). In comparison to KMnO_4 and NaIO_4 , Oxone® is non-toxic and also insoluble in organic solvents. However, due to its high molecular weight and combined with the high price it is an expensive oxidation agent.

Contrary to Oxone®, the oxidation potential of NaMnO_4 is independent from the milling auxiliary since yields of 80% were reached (Table 2). Instead of KMnO_4 , the yields in the presence of quartz sand are 20% higher ($Y_2 = 80\%$). Other Mn-containing compounds (K_2MnO_4 , BaMnO_4 , MnO_2 , $\text{Mn}(\text{AcO})_3$) afforded moderate yields only, which is assumed to be due to their lower oxidation potential. Additionally, Mn(IV) and Mn(V) species are the reaction products when KMnO_4 is employed as the oxidant (eqn 1). Despite their acceptable oxidation potential, the high molar weight of Na_2MnO_4 and $(\text{NH}_4)_4\text{Ce}(\text{SO}_4)_4 \cdot 2\text{H}_2\text{O}$ is the reason for the lower overall efficiency (economic and ecologic) of these oxidants. Other tested oxidation agents provided **2** in yields below 50% (e.g. $\text{PCC} = [\text{PyH}][\text{CrO}_3\text{Cl}]$, $\text{K}_2\text{Cr}_2\text{O}_7$, $\text{Na}_2\text{S}_2\text{O}_8$, urea- H_2O_2 -adduct). It has to be stated, that further improvement of reaction parameters (t , v_{rot}) might enhance the reaction.

Rotation frequency v_{rot}

Besides chemical variables, technical parameters like rotation frequency or the density of the milling material also significantly influence the outcome of reactions performed in ball mills. These effects are well understood in the case of particle refinement and inorganic processing.²¹ Recent publications indicate that for organic synthesis consideration of these parameters is also important.¹³ Therefore, the influence of the rotation frequency v_{rot} on the yield of the solvent-free dehydrogenation of **1** is assessed. Reactions at different frequencies from 100 to 800 rpm (1.7–13.3 Hz) were performed for two milling auxiliaries (Fig. 5). From 500 to 800 rpm (8.3–13.3 Hz) a relatively constant level for Y_2 occurs in the presence of Al_2O_3 . With regards to energy costs, this seems to be an interesting fact: lower v_{rot} means less energy consumption and therewith lower costs, thus improvement of the energy efficiency of the process.²² Within the decrease of v_{rot} below 500 rpm (8.3 Hz), significantly lower product yields were found (75%). In the case of quartz sand, the increase is more distinctive, since below 500 rpm Y_2 just reaches values about 50%.

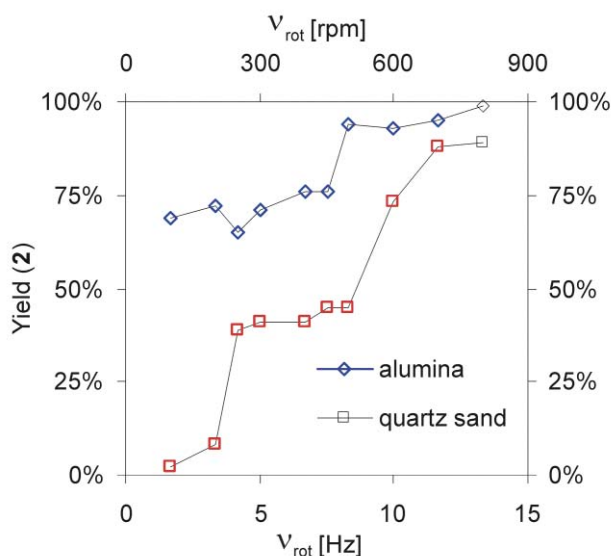


Fig. 5 Influence of rotation frequency v_{rot} on the solvent-free oxidative dehydrogenation of γ -terpinene (**1**, 2 mmol) to p -cymene (**2**) with KMnO_4 as oxidant (6 mmol; 3.8 g auxiliary, 0.1 g H_2O); Ball milling: 2 milling beakers (ZrO_2 , $V = 45$ ml), 6 milling balls (ZrO_2 , $d = 15$ mm) per beaker; $t = 5$ min).

Number of milling balls n_{ball}

Another critical parameter in ball-milling experiments is the number of milling balls, n_{ball} . So far, the experiments were performed with 6 milling balls made of ZrO_2 with a diameter d of 15 mm. Fig. 6 summarizes the results from experiments with n_{ball} varying from 1–7. It has to be stated expressly that the performance of experiments with one milling ball is not in line with the manufacturer's advice, due to strong abrasion.²³ In the presence of alumina as the milling auxiliary, a minimum of 4 milling balls are necessary to guarantee a quantitative yield of **2**. In the case of quartz sand, an increasing amount of milling balls

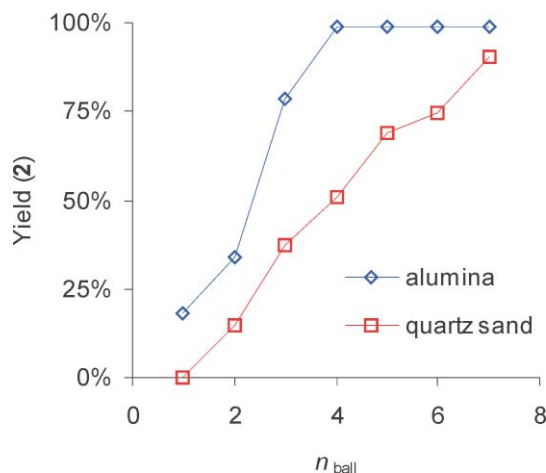


Fig. 6 Influence of number of milling balls n_{ball} on the solvent-free oxidative dehydrogenation of γ -terpinene (**1**, 2 mmol) to p -cymene (**2**) with KMnO_4 as oxidant (6 mmol; 3.8 g auxiliary, 0.1 g H_2O); Ball milling: 2 milling beakers (ZrO_2 , $V = 45$ ml), milling balls (ZrO_2 , $d = 15$ mm) per beaker; $v_{\text{rot}} = 800$ rpm (13.3 Hz), $t = 5$ min).²³

lead to a rise of Y_2 up to 90% when applying 7 milling balls. Loading of the milling beakers with $n_{\text{ball}} > 7$ ($d = 15$ mm) is not possible, since the required space prevents homogeneous mixing and therefore enhances abrasion of the milling balls. According to the manufacturer, a volume-ratio of substance to milling balls to free space of 1 : 1 : 1 is ideal.²²

Diameter of milling balls d

The following experiment should demonstrate the coherence between energy and mass. From physical mechanics it is known that kinetic energy is a function of mass and velocity. For our conception this means, independently Y_2 must be the same when using milling balls with different d but with the same total mass (Σm_{ball}). Our results verify this theory. As shown in Table 3 ball milling experiments with 120 milling balls with a diameter of 2 mm have nearly the same mass as 15 and 5 milling balls of 10 and 15 mm, respectively. Therefore, the same application of energy at the same rotation speed should be assured. With both, alumina and quartz sand, variation of d but constant Σm_{ball} leads to similar yields of **2**. This is due to the theory mentioned above. The energy, which depends on mass and velocity, is similar in all three cases. The surface area of the different milling ball diameters does not seem to have any effect on the yield, which

Table 3 Variation of the diameter of milling balls d in the solvent-free oxidative dehydrogenation of γ -terpinene (**1**) in the presence of alumina or quartz sand as milling auxiliaries^a

d/mm^b	n_{ball}	$\Sigma m_{\text{balls}}/\text{g}^c$	Y_2 [%]	
			alumina	quartz sand
15	5	46.33	99	75
10	15	45.37	99	79
2	120	45.84	99	72

^a Batch (per beaker): 3.8 g auxiliary, 2 mmol **1**, 6 mmol KMnO_4 , 0.1 g H_2O ; Ball milling: 2 milling beakers (ZrO_2 , $V = 45$ ml), ZrO_2 milling balls; $v_{\text{rot}} = 800$ rpm (13.3 Hz), $t = 5$ min. ^b Average milling ball diameter.

^c Overall mass of milling balls = $1/6\pi \cdot \rho_{\text{ZrO}_2} \cdot n_{\text{ball}} \cdot (d)^3$.

is in clear contrast to the application of ball mills in particle refinement processes.²¹

Conclusion

As shown, the solvent-free oxidative dehydrogenation of γ -terpinene (**1**) to *p*-cymene (**2**) initiated by grinding in a planetary ball mill is a very time-efficient method. After 5 min and in the presence of alumina as a grinding auxiliary, with KMnO_4 as the oxidant quantitative yields were obtained. Other auxiliary materials like silica or other metal oxides can also be applied. The employment of montmorillonite causes moderate yields without the addition of any further oxidizing agent. The assessment of other oxidants like *p*-benzoquinone, NaIO_4 or Oxone® revealed high conversions, accompanied by excellent selectivities. Widely-used oxidation agents like $\text{K}_2\text{Cr}_2\text{O}_7$ or H_2O_2 (as urea- H_2O_2 -adduct) are less effective. Finally, KMnO_4 and NaIO_4 are the best oxidants regarding cost, toxicity, and work-up of the reaction mixture. Nevertheless, an excess of these oxidants has to be applied to receive quantitative yields. The assessment of variables like rotation frequency or number of milling balls, revealed a significant influence on the outcome of the reaction. Thus, variation of these parameters and of the reaction time allows fine-tuning of the reaction conditions, achieving high yields and excellent selectivities. As optimum milling parameters $t = 5$ min at $v_{\text{rot}} = 800$ rpm (13.3 Hz) with 6 milling balls were identified.

Experimental

General

All chemicals were purchased from commercial suppliers and used without further purification. Montmorillonite K-10 was purchased from Sigma-Aldrich. The parameters of employed aluminas and silicas are provided within the ESI.†

Analyses were carried out with a 6890 Series GC-MSD and a 7890 Series II GC-FID from Agilent Technologies. Products were identified by comparison with either retention times and/or mass spectra of pure reference compounds. GC-FID: HP 5, 30 m \times 0.32 mm \times 0.25 μm , 5 psi H_2 ; program: 35 °C (hold 1 min), 4 K min^{-1} up to 80 °C, 4.5 K min^{-1} up to 90 °C, 35 K min^{-1} up to 280 °C (hold 3 min); injector temperature: 250 °C; detector temperature: 280 °C. GC-MS: HP 5, 30 m \times 0.32 mm \times 0.25 μm , 7 psi He; program: 55 °C (hold 1 min), 5 K min^{-1} up to 150 °C, 20 K min^{-1} up to 280 °C (hold 5 min); injector temperature: 280 °C, EI (70 eV).

All product yields reported herein are GC-determined yields and are comparable with the isolated ones. Nevertheless, the reported yields were corrected by means of different FID-sensitivity for substrate and product. The reported yields are mean values from at least two independent experimental runs.

The grinding beakers and the milling balls were purified with 10 wt% hydrochloric acid in ethanol for complete removal of residual Mn-species.

Reaction procedure

A milling beaker was equipped with 6 milling balls (ZrO_2 , d : 15 mm). Afterwards, the grinding auxiliary (3.8 g), γ -terpinene (**1**; 2 mmol, 272 mg), the oxidant (6 mmol), and H_2O (0.1 g)

were placed into the milling beaker (ZrO_2 , $V = 45$ ml). Finally, the beaker was sealed with a PTFE-gasket and the ZrO_2 -lid. Two similar loaded beakers are mounted into the planetary ball mill (*Pulverisette 7 classic line*, Fritsch GmbH, Idar-Oberstein, Germany). The parameters, rotations per minute and milling time, were set-up and the milling process was started. After the milling process, the beakers were opened and the milling balls were removed. The reaction mixture was transferred into a glass tube and subsequently demineralized water (3 ml) as well as ethyl acetate (5 ml) were added. The organic layer was separated and the composition was analyzed by GC-FID respective GC-MSD.

Acknowledgements

This work is funded by the German Federal Environmental Foundation (DFG; grant No. 27281-31).

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- 23 Reproduction of experiments with one milling ball is critical, due to extreme abrasion. Manufacturers of planetary ball mills advise to employ at least 2 milling balls.