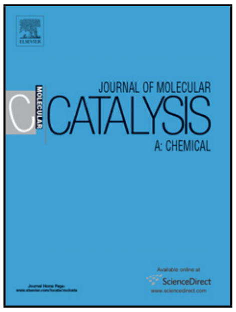

Title: Prins cyclization: Synthesis of compounds with tetrahydropyran moiety over heterogeneous catalysts

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Prins cyclization: Synthesis of compounds with tetrahydropyran moiety over heterogeneous catalysts

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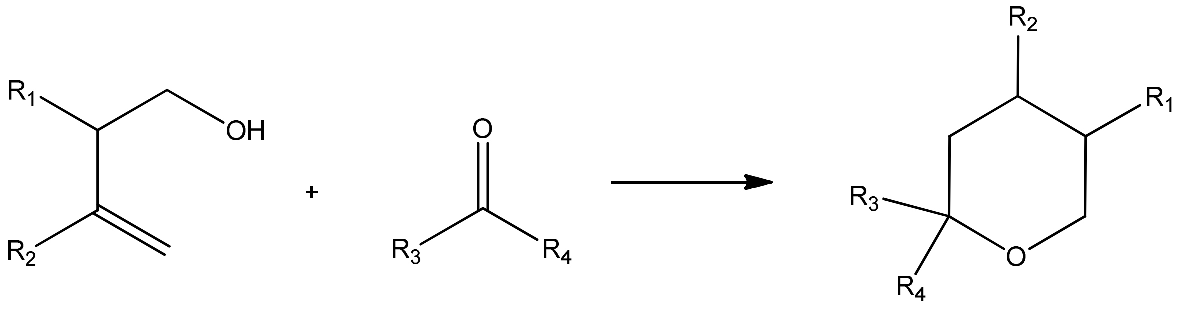
Graphical Abstract



Highlights

- acidic catalyzed Prins cyclization of homoallylic alcohol with simple aldehydes
- isopulegol and 3-methyl-6-(prop-1-en-2-yl)cyclohex-3-ene-1,2-diol as alcohols
- comparative investigation of zeolites, metal modified forms and mesoporous materials
- correlation of performance with physico-chemical properties
- high selectivity to tetrohydropyran structure with Ce-MCM-41 in reaction of isopulegol and benzaldehyde

Abstract

Tetrahydropyrans, compounds with 6-membered oxygen-containing heterocycles, are widely used for the synthesis of biologically active compounds with analgesic, anti-inflammatory or cytotoxic activity. Synthesis of compounds with the desired structure can be realized by several methods, including the acidic catalyzed Prins cyclization of homoallylic alcohol with simple aldehydes. In the current study, synthesis of compounds with the desired tetrahydropyran framework by Prins cyclization of benzaldehyde and alcohols with different structure, namely isopulegol and 3-methyl-6-(prop-1-en-2-yl)cyclohex-3-ene-1,2-diol, was investigated. Different parent zeolites as well as their metal modified forms and mesoporous materials were employed in the comparative investigation. Activity and selectivity of the tested catalysts were correlated with their physico-chemical properties. The highest conversion and selectivity toward the product with the tetrohydropyran structure was achieved using Ce-MCM-41 in the interactions of isopulegol and benzaldehyde.

Keywords: Prins cyclization; Isopulegol, 3-Methyl-6-(prop-1-en-2-yl)cyclohex-3-ene-1,2-diol (diol) ; Benzaldehyde; Zeolites; Metal supported catalysts

1. Introduction

New biologically active substances are often synthesized from a variety of compounds isolated from natural sources. It has been discovered that compounds with 6-membered oxygen-containing heterocycles with tetrahydropyran moiety are widely used for the synthesis of biologically active compounds with a potential for use in medicine [1]. These compounds can exhibit analgesic, anti-inflammatory or cytotoxic activity [1-4]. Synthesis of compounds with the desired tetrohydropyran structure can be realized by several important methods, including Prins cyclization onto oxocarbenium ions, oxy-Michael reactions, transition metal catalyzed cyclizations, reduction of cyclic hemi ketals and hetero-Diels-Alder cycloaddition [1]. Recently an in-depth review on the synthesis of tetrahydropyrans and related heterocycles via Prins cyclization has been reported by Olier et al. [5].

Preparation of compounds with the desired tetrohydropyran structure can be performed by the acidic catalyzed ene-Prins cyclization of homoallylic alcohol with simple aldehydes [1,2,6]. It is known that Brønsted as well as Lewis acids can catalyze Prins cyclization reactions**.** Reaction mechanism of Prins cyclization over various heterogeneous solid acid catalysts such as sulfated zirconia and cellulose-SO_3H has been proposed [7, 8]. The influence of types and strength of acid sites on the formation of tetrahydropyrans was described by Breugst et al. [9]. Synergic effects between weak Brønsted and Lewis acids were analyzed by Density Functional Theory in Prins cyclization of but-3-en-1-ol and 2-methoxybenzaldehyde [8]. Yadav et al. reported synthesis of octahydro-2H-chromen-4-ol from (*R*)-citronellal and aldehydes using scandium triflate at ambient temperature in dichloromethane [6]. Synthesis of the same product, octahydro-2*H*-chromen-4-ol, from isopulegol and vanillin over acid modified montmorillonite clays at 35 °C was described by Timofeeva et al. [2]. Synthesis of 4-OH-tetrahydropyrans over Ni(II)-N,N´-dioxide complex and $FeCl_3$ as catalysts was described by Zheng et. al. [10]. A broad range of substrates was tested in the reaction under mild reaction conditions [10]. Synthesis of 8-oxabicyclo [3.2.1] oct-2-enes and 9-oxabicyclo [3.3.1] nona-2, 6-dienes from enynol via oxonium /Prins-type cyclization using Au(1) catalyst has been reported by Vandavasi et al. [11].

In the current study, synthesis of compounds with the desired tetrahydropyran framework was investigated (Fig. 1a, b). Two alcohols with a different structure, namely isopulegol (Fig. 1a) and 3-methyl-6-(prop-1-en-2-yl)cyclohex-3-ene-1,2-diol (Fig. 1b), were tested in the Prins cyclization reaction with benzaldehyde.

Isopulegol (Fig. 1a), a monoterpene alcohol, belongs to natural compounds and can be isolated from a variety of essential oils (e.g. from Eucalyptus citriodora) [12]. It can be synthetically prepared by the catalytic cyclization of citronellal [13]. Isopulegol is widely used in flavor and perfume industry for the production of fragrances and is an important intermediate for the synthesis of menthol, a fine chemical widely used in pharmaceuticals, agrochemicals and various cosmetics.

Diol (3-methyl-6-(prop-1-en-2-yl)cyclohex-3-ene-1,2-diol) (Fig. 1b) is product of verbenol oxide isomerization. It has been discovered that this diol possesses potent activity against Parkinson disease [14] which is one of the most common neurological diseases. Decisive influence of absolute configuration of *diol* on its biological activity was shown in ref. [14]. (1*R*,2*R*,6*S*)-*Diol* can be synthesized from carvone [15], but the most effective way leading to this compound with high stereoselectivity starts from (-)-verbenone and includes three stages: epoxidation of verbenone to verbenone oxide with hydrogen peroxide in alkali/methanol solution, reduction of verbenone oxide using $LiAlH_4$ and subsequent isomerisation of obtained verbenol oxide [16,17]. Verbenone is a natural organic compound which can be found in a variety of plants or synthesized by allylic oxidation of α-pinene [18].

The aim was to prepare compounds with the desired tetrahydropyran moiety (product **4** in Fig. 1a and product **8** in Fig. 1b) using solid acid and metal (Fe, Ce, Au) modified heterogeneous catalysts. The criteria for the selection of catalysts were based on the assumptions of an important role of the type of acid sites (Brønsted and Lewis), their amount and strength and the structure of catalytic materials in Prins cyclization reaction. A further aim was to study the function of metals such as Au, Ce and Fe in the synthesis of compounds with tetrahydropyran moiety via Prins cyclization, as their catalytic behavior was described in the literature for similar substrates. Detail catalyst characterization was carried out using various techniques in order to study the physico-chemical properties of catalysts and explain the catalytic results. It should also be pointed out that despite of the fact that (-)-isopulegol was used as one of the reagents, the emphasis was not put into stereoselectivity and only racemic products were analyzed.

2. Experimental methods

Metal-modified zeolites (Beta-25 and Beta-150) and mesoporous MCM-41 were prepared, characterized and tested in the present study. As a comparison proton forms of zeolites were tested in Prins cyclization reactions. Furthermore, one commercial gold catalyst was tested in the same reaction. Zeolites and other support materials were modified by iron, gold and cerium and tested in Prins cyclization reaction of two different monoterpenoid alcohols with benzaldehyde.

2.1. Materials

NH_4-Beta-25 (25 = SiO_2/Al_2O_3 molar ratio), NH_4-Beta-150 and NH_4-Beta-300 zeolites were purchased from Zeolyst International. Aluminum oxide used as another support was obtained from UOP Inc.

Ferric nitrate and cerium nitrate used as the metal precursors were purchased from Fluka. The gold precursor, in the form of hydrogen tetrachloroaurate(III) hydrate, 99.9% (metals basis), was supplied by Alfa Aesar.

(-)-Isopulegol (SAFC, 98.9%), benzaldehyde (Fluka, 99.0 %) and toluene (99.8 %) were supplied by Sigma-Aldrich (Germany) and used as received. Diol (3-methyl-6-(prop-1-en-2-yl)cyclohex-3-ene-1,2-diol) was synthesized at the Vorozhtsov Novosibirsk Institute of Organic Chemistry, with a purity of 98.5 %.

2.2. Catalysts preparation

NH_4^+ form of zeolites were transformed to proton forms at 500 °C in a muffle oven using a step calcination procedure.

MCM-41 was synthesized in the sodium form (Na-MCM-41) using a Parr autoclave (300 mL) as mentioned in ref. [19] with few modifications [20]. After synthesis of MCM-41, it was filtered, washed with distilled water, dried overnight at 100 °C and calcined at 450 °C.

Iron and cerium modified catalysts were prepared using conventional evaporation impregnation (IMP) method. Ferric nitrate ($Fe(NO_3)_3.9H_2O$) and cerium nitrate ($Ce(NO_3)_3.6H_2O$) were used as iron and cerium precursors, respectively, in all cases. In the evaporation impregnation method aqueous solutions of metal nitrates were applied. The mixtures were stirred for 24 hours at 60 °C. The other steps of the synthesis were evaporation, drying at 100 ˚C overnight and calcination at 450 ˚C for 4 hours.

Au-Beta-25 was prepared by the deposition-precipitation method. The proton form of zeolite Beta-25 was dispersed in an aqueous solution of the gold precursor. In the next step, aqueous ammonium hydroxide was added into the suspension in order to increase pH to 10.5. The suspension was stirred for 3 h at 50 °C. The final catalyst was filtered, washed by deionized water, dried overnight at 100 °C and calcined at 300 °C for 3 h.

2.3. Catalysts characterization

The characterization of catalysts was carried out using nitrogen adsorption and FTIR spectroscopy with pyridine as a probe molecule. For selected catalysts also transmission electron microscopy was applied.

The specific surface area of supports and metal modified catalysts was determined by nitrogen adsorption using Sorptometer 1900 (Carlo Erba instruments). The samples were outgassed at 150 °C for 3 h before each measurement. The BET equation was used for calculation of the specific surface area of mesoporous materials, silica and alumina and the Dubinin equation was used for calculation of the specific surface area of microporous zeolites.

The acidity of the proton and metal modified catalyst was measured by infrared spectroscopy (ATI Mattson FTIR) using pyridine ($\geq$ 99.5%) as a probe molecule for qualitative and quantitative determination of both Brønsted and Lewis acid sites. The samples were pressed into thin pellets (10–25 mg), which were pretreated at 450 °C before the measurements. Pyridine was first adsorbed for 30 min at 100 °C and then desorbed by evacuation at different temperatures. Three different temperatures were used for desorption of pyridine, namely at 250 °C – 350 °C, which corresponds to all (weak, medium and strong) sites, 350 °C – 450 °C, reflecting medium and strong sites and 450 °C, which is related only to strong sites [21]. The amount of Brønsted and Lewis acid sites was calculated from the intensities of the corresponding spectral bands, 1545 cm^{-1} and 1450 cm^{-1} respectively, using the molar extinction parameters reported by Emeis [22].

The textural properties and metal particle size of the catalysts were also characterized using transmission electron microscope, JEM 1400 plus with acceleration voltage of 120 kV and resolution of 0.98 nm using Quemsa I MPx bottom mounted digital camera.

XPS analysis was performed with Perkin-Elmer PHI 5400 spectrometer using monochromatized Al Ka X-ray source at 14 kV and 300 W. The analyzer pass energy was 18 eV with energy step of 0.1 eV. The measurement was performed in a vacuum chamber under pressure of 10 $^{-9}$ mbar.

2.4. Catalytic tests

Prins cyclization reactions of isopulegol and benzaldehyde over H-Beta with varying SiO_2 to Al_2O_3 ratio, Fe-Beta-150, Au-Beta-25, Ce-Beta-150 and Ce-MCM-41 catalysts were carried out in the liquid phase using a batch-wise glass reactor. In a typical experiment the initial concentration of isopulegol and the catalyst mass were 0.04 mol/l and 0.3 g, respectively. The catalyst was treated in the reactor at 250 °C in an inert atmosphere for 30 min before the reaction. This pretreatment was selected, since it was decided to keep the same procedure as reported in the previous publication [23], in which addition of verbenol oxide with benzaldehyde was studied. For the latter reaction the presence of water can be detrimental in terms of selectivity to the desired product. The adopted protocol thus allows a fair comparison between these two reactions. Benzaldehyde was used in excess (V_L=50 ml) without any other solvents. The reaction temperature was 70 °C. The catalyst particle size below 90 μm and the stirring rate of 390 rpm were used in order to suppress the internal and external mass transfer limitations. The samples were taken at different time intervals and analyzed by GC with a capillary column HP-5 (30 m x 320 μm x 0.5 μm) using the following temperature program: initial temperature 100 °C (held for 5 min), increased at 20 °C /min to 280 °C and held at the final temperature for 3 min. The products were confirmed by GC-MS by comparing retention times of components and their complete mass spectra with the corresponding data for pure compounds. Agilent 7890A gas chromatograph equipped with a quadrupole mass spectrometer Agilent 5975C as a detector with quartz column HP-5MS (copolymer 5%–diphenyl–95%–dimethylsiloxane) of length 30 m, internal diameter 0.25 mm and stationary phase film thickness 0.25 µm was used for the analysis.

Prins cyclization reactions of 3-methyl-6-(prop-1-en-2-yl)cyclohex-3-ene-1,2-diol with benzaldehyde were performed under similar conditions. The initial concentration of diol and the catalyst mass were 0.04 mol/l and 0.3 g, respectively. Benzaldehyde was used in excess (V=40 ml) and toluene (V=10 ml) was used as a co-solvent. Because of different solubility of isopulegol and diol in benzaldehyde for the latter substrate addition of toluene was needed, while isopulegol was readily dissolved in benzaldehyde.

3. Results and discussion

Synthesis of tetrahydropyran type compounds has been previously investigated using different homoallylic alcohols and various aldehydes over a range of acid catalysts [1,2,6,10]. In the current work different parent zeolites as well as their metal modified forms and mesoporous materials were employed in the comparative investigation focused on Prins cyclization of isopulegol and 3-methyl-6-(prop-1-en-2-yl)cyclohex-3-ene-1,2-diol (diol) with benzaldehyde.

3.1. Catalysts characterization results

Two methods of catalyst synthesis were used, namely conventional impregnation and deposition-precipitation. The in-depth characterization of some of the tested catalysts (H-Beta-25, H-Beta-150, H-Beta-300, Fe-Beta-150, Ce-MCM-41) was carried out using various methods (scanning electron microscopy, X-ray absorption spectroscopy, nitrogen adsorption, FTIR with pyridine as a probe molecule) and was published previously [24, 25]. Also the parent material Na-MCM-41 used for Ce-MCM-41 was fully characterized in ref. [26], including XRD pattern of Na-MCM-41.

Specific surface areas and pore specific volumes of supports and metal modified catalysts are given in Table 1. The parent zeolites are characterized by very high surface areas being up to 800 m^2/g. Their specific surface areas decreased in all cases after the metal introduction due to some pore blocking. Significantly lower specific surface area was measured for iron modified alumina and cerium modified MCM-41. A large decrease in specific surface area in the case of ceria modification of MCM-41 is probably caused by high loading of ceria (32 wt. %) and probably by partial distortion of the mesoporous hexagonal phase [20].

Loaded amounts of metals on the supports are given in Table 1 as well. In most cases, zeolites and other supports were modified by small amounts of metals in the range 1 – 3 wt. %. An exception was Ce-MCM-41 prepared in order to achieve 32 wt. % loading of ceria.

The highest concentration of Brønsted acid sites was determined (Table 2) for Beta zeolites with a higher content of alumina in their structure (SiO_2/Al_2O_3 = 25 and 150) as well as for their iron, gold and cerium modified forms (Fe-Beta-150, Au-Beta-25 and Ce-Beta-150). Modification of zeolite H-Beta-25 with gold caused a slight decrease of total concentration of Brønsted acid sites with a simultaneous increase of strong Brønsted acid sites. Analogous results on the effect of metal on the support acidity have been previously published in [27]. The opposite trend was observed in the case of iron modification of H-Beta-150 where the total concentration of Brønsted acid sites increased along with a decrease of strong acid sites. An increase of strong Brønsted acidity as well the total concentration of Brønsted acid centers was observed after cerium modification of H-Beta-150.

The highest concentration of Lewis acid sites was as well determined for Beta zeolites with a higher content of alumina in their structure (SiO_2/Al_2O_3 = 25 and 150) and for their iron, gold and cerium modified forms (Fe-Beta-150, Au-Beta-25 and Ce-Beta-150) and for iron modified alumina. Modification of H-Beta-25 zeolite with gold caused a decrease in the total concentration of Lewis acid sites, mainly strong ones. On the other hand, as expected the concentration of Lewis acid sites significantly increased after iron and ceria modification of H-Beta-150.

The characterization of the porosity, periodicity and structural uniformity of the pores of pure H-Beta-25 zeolite prior to the modification with Au nanoparticles was done using transmission electron microscope. It was observed that the H-Beta-25 zeolite catalytic material exhibited presence of regular uniform pores without any interruption or distortion of pores periodicity (Fig. 2a). The Au nanoparticles modified H-Beta-25 zeolite catalyst also showed structural integrity of the pores and intact crystal morphology of Beta zeolite in Au-Beta-25 zeolite catalyst. It was inferred from the transmission electron micrographs of Au-H-Beta-25 zeolite catalyst that the majority of Au nanoparticles were homogeneously distributed and were circular in shape. However, few agglomerates of Au nanoparticles, large in size were also observed (Fig. 2b). The Au nanoparticle size distribution was also determined from the transmission electron micrographs of Au-H-beta-25 zeolite catalyst and the average Au particle size was 7 nm. The gold was most probably in the metallic state according to XPS measurements showing that Si2p peak, being partially charged, was at 2.345 eV. Taking this value into account the $Au4f_{7/2}$ peak was at 83.6 eV corresponding to metallic gold. These results are in accordance with Casaletto et al. [28].

3.2. Catalytic results

3.2.1. Initial rates, rate constants and conversion levels

The initial reaction rate was calculated according to $r_0 = \left((c_0 - c_t)t^{-1}(m_{cat})^{-1}\right)$, where c_0,c_t are initial and actual concentration of isopulegol (mmol/L), t is reaction time (1 min) and m_{cat} is the mass of catalyst (g). In addition, first order rate constant was calculated from the kinetic data. The preliminary experiments were performed by varying catalyst mass, stirring speed and catalyst particle size in order to check whether the experiments are under the kinetic regime. The initial rate obtained using 0.3 g of H-Beta-300 was 23.8 mmol/(l min) (Table 3), whereas with 0.15 g it is nearly the same, 20 mmol/(l min) showing that productivity correlated with the catalyst amount. The effect of stirring speed was studied with 360 rpm and 390 rpm, respectively, using H-Beta-300 with particle size below 90 μm. Both of these experiments gave the same rates and conversion. In the third test the effect of the catalyst particle size was elucidated for the one of the most active catalyst, namely H-Beta-300, by using the catalyst fractions below 63 μm or 90 μm. In the latter case the initial rate was 60% of the former one indicating that some internal diffusional limitations might be present using particle size below 90 μm for very active catalysts and the kinetic constants in those cases have an apparent nature.

The highest initial rate in Prins cyclization of isopulegol was achieved using Ce-MCM-41 containing 32 wt. % of ceria (Table 3), which exhibited a mild acidity and large pore size. High initial rates were also obtained with the parent H-Beta zeolites and acidity had only a minor effect on initial reaction rate. On the other hand, slightly lower initial rates were obtained for metal modified zeolites, except Ce-Beta-150, which also exhibited very high acidity. Especially low initial rates were found for Fe-Beta-150. The first order rate constant was the highest for the most acidic catalyst, H-Beta-25 and slightly lower k values were achieved for H-Beta-150 and H-Beta-300. Noteworthy is also that the mildly acidic Ce-MCM-41 exhibited a very high rate. Generally the fits were very good, except for Ce-MCM-41, for which the relative error was the largest one.

Total conversion of isopulegol was achieved over all three parent beta zeolites and Ce-MCM-41 within 60 min from the beginning of the reaction, over Ce-Beta-150 within 120 min and over Au-Beta-25 within 240 min. High conversion was obtained over Fe-Beta-150 being 93 % after 240 min. Ceria modified materials exhibited the highest activity among the metal modified materials expressed per catalyst weight. Plausible explanations for such activity is besides loading of ceria (in Ce-MCM-41) its variable state (Ce $^{3+}$, Ce $^{4+}$) attributed to mobile nature of oxygen species present in Ce-MCM-41 and Ce-Beta-25. Furthermore, in addition to mild acidity and large pore size (4.5 nm), Ce-MCM-41 also exhibited presence of 2.53 mmol/g of basic sites. A detail description regarding the state of Ce in Ce-MCM-41 determined by XPS and basic sites measured by CO_2 TPD can be found in [20]. It was recently reported in the literature [29], that neither only weak Lewis nor weak Brønsted acidic homogeneous catalysts were able to catalyze Prins cyclization of homoallylic alcohol with 2-methoxybenzaldehyde. However, a combination of these catalysts showed a synergetic effect [28]. When comparing these results [29] with the current case, it can be stated that mildly acidic, bifunctional H-Beta-300 and Ce-MCM-41 catalysts exhibit an analogous type of synergetic effect of Brønsted and Lewis acid sites.

Conversion of isopulegol as a function of reaction time over zeolites and metal modified materials is depicted in Fig. 3 a,b. It is obvious that the proton forms of the parent beta zeolites were very active giving total conversion within 60 min (Fig. 3a). On the other hand, metal modification of zeolites caused decrease of activity in most cases (Fig. 3b). This was visible for Fe-Beta material. As mentioned above, the most active catalysts among metal modified materials were ceria based materials (Fig. 3b).

In the second model reaction, Prins cyclization reaction of 3-methyl-6-(prop-1-en-2-yl)cyclohex-3-ene-1,2-diol (diol) with benzaldehyde the following catalysts were investigated: proton forms of beta zeolites, Fe-Beta-150 and Ce-MCM-41 under similar reaction conditions as with isopulegol (Figure 4).

The highest initial reaction rate for diol reaction with benzaldehyde was obtained with a mesoporous, mildly acidic, mesoporous Ce-MCM-41 (Table 4) analogously to the case of isopulegol. The initial rates with different zeolites were more than two fold less than that for Ce-MCM-41. The rate constant was also the highest for Ce-MCM-41 being 1.8 fold larger than that for H-Beta-25. Analogously to the case of isopulegol reaction, the error in the *k* value was the highest for Ce-MCM-41. When comparing the rate constants for isopulegol and diol reactions, it can be noted that the rate constants were higher for isopulegol reaction compared to diol in all other cases except for Fe-Beta-150.

Total conversion of diol was achieved over H-Beta-25 and H-Beta-150 catalysts within 240 min of the reaction and very high conversions of diol were obtained using all other tested catalysts, being over 90 % (Fig. 4). On the other hand, low conversion of diol was observed after 60 min of the reaction over ceria catalyst, therefore just 93 % conversion was achieved within 240 min. It can be in general concluded, that transformation of diol proceeds slower than transformation of isopulegol under the same reaction conditions. This fact might be related to the presence of an additional hydroxyl group in the structure of *diol* decreasing the electron density of the neighboring hydroxyl group which acts as a reaction center in Prins cyclization. Moreover the *diol* has another stereochemical arrangement of isopropenyl and hydroxyl groups in comparison with isopulegol (*cis*- for diol and *trans*- for isopulegol) which also may influence the reaction rate.

3.2.2. Product distribution and selectivity

In the Prins cyclization of isopulegol the selectivity as a function of conversion are shown in Fig. 5 a, b. The highest selectivity toward the product with the tetrahydropyran structure (93

%) at 90 % conversion was achieved using a mildly acidic, mesoporous hybrid material Ce-MCM-41, which contains 32 wt. % CeO_2 at total conversion of isopulegol (Fig. 5b, Table 3). Subsequently a very low formation of side products was observed in comparison with other catalysts. Ce-MCM-41 catalyst showed the highest weight based activity and selectivity also in our previous study focused on acidic catalyzed isomerizations of α-pinene and verbenol oxide [25, 30].

Selectivity to minor often encountered products (compounds **1-3** and **unidentified products**) in isopulegol reaction is also given in Table 3. A relatively high selectivity to tetrahydropyran type of product **4** (around 74 %) was achieved over H-Beta-25 and H-Beta-300. On the other hand, the lowest selectivity to the product with the tetrahydropyran moiety was seen for Fe-Beta-150 which was caused by significant formation of byproducts, namely a dehydrated product **1** and a dioxinol type product **3**.

It was observed that the selectivity to the desired product with the tetrahydropyran structure slightly increased with conversion and significantly decreased over some catalysts after reaching the total conversion. Such significant decrease of selectivity towards the desired compound with tetrahydropyran structure was observed mainly with H-Beta-25 and H-Beta-150 (Fig. 5a) as well as using cerium modified catalysts (Fig. 5b). The two former catalysts exhibited strong Brønsted acid sites promoting dehydration reaction, whereas the latter catalyst was a mildly acidic mesoporous structure being able to form dioxinol, product **3** (Table 3). It was observed that pyran product **4** transformed to the dehydration product **1** and the ring rearrangement of **4** to **3** occurred also during the reaction.

Very similar selectivities to the desired product **8** were achieved over all tested catalysts in Prins cyclization of diol (Table 4, Fig. 6). Slightly higher selectivity to **8** was achieved again using H-Beta-25 and Ce-MCM-41, being 67 %. These selectivities are, however, lower than selectivity in the case of Prins cyclization of isopulegol with benzaldehyde.

Selectivities to minor often encountered products (compounds **5-7** and **unidentified products**) are also given in Table 4. In comparison with isopulegol as a substrate, high amounts of **unidentified products** as well product **9** were detected. Product **9**, formed by reaction of diol with two molecules of benzaldehyde, was generated mainly over H-Beta-300 and Fe-Beta-150 but not with Ce-MCM-41.

The obtained conversions of both alcohols as well as selectivities towards the desired products are slightly higher in comparison with already published data for similar systems. The maximum achieved yield of the product with the tetrahydropyran moiety was around 76 % in isopulegol reaction with vanillin over acid-modified clays [2].

3.2.3. Side reactions

Two types of side reactions can occur in Prins cyclization of isopulegol and diol, namely dehydration of tetrahydropyran type compounds **4** and **8** to **1** and **5**, respectively (Fig. 7) and ring arrangement of tetrahydropyran compound **4** and **8** to dioxinol type compounds **3** and **7**, respectively (Fig. 8).

In Prins cyclization of isopulegol concentration of the product with the tetrahydropyran structure (**4**) as a function of the dehydration product (**1**) concentration over catalysts with highly Brønsted acidic catalysts showed that the formation of tetrahydropyran type product **4** is preferred mainly at the beginning of the reaction (Fig. 9a) while the formation of dehydration product **1** is taking over at higher conversion levels. High formation of the dehydrated byproduct **1** (over 20 %) was observed over Fe-Beta-150 and Au-Beta-25 (Table 3). Especially the latter catalyst exhibited relatively high amount of strong acidic sites being responsible for dehydration. In addition, gold was in metallic state in Au-Beta-150, which could partially decrease its selectivity towards tetrahydropyran, since Au(I) has been active in Prins cyclisation [11]. The most significant decrease in the selectivity to **4** can be seen over H-Beta-25, H-Beta-150 and Ce-Beta-150 (Fig. 9a). The selectivity to products **4** and **1** at the moment of achieving total conversion of isopulegol was 73 and 13 %, respectively, over H-Beta-25 changing to 61 and 22 % after another 180 min. The selectivity to products **4** and **1** at complete conversion of isopulegol over H-Beta-150 and Ce-Beta-150 was similar, 65 and 18 %, respectively. Dehydration was faster over cerium containing Ce-Beta-150 catalyst giving selectivity 47 and 28 % towards **4** and **1** respectively after 240 min, while 53 and 27 % were obtained for H-Beta-150.

Concentration of the product with the tetrahydropyran structure (**8**) as a function of concentration of dehydration product (**5**) is depicted in Fig. 9b for the second studied reaction. In the case of *diol* reaction, the most active catalyst for tetrahydropyran formation was initially H-Beta-300, which exhibited mild acidity (Fig. 9b). Formation of the dehydration product was the lowest with this catalyst, whereas with highly acidic H-Beta-25 and H-Beta-150 the amount of tetrahydropyran type product **8** decreased significantly with increasing the amount of dehydration product **5**. The highest amount of the dehydration product **5** was formed over a mildly acidic Ce-MCM-41 (Fig. 9b, Table 4), but its amount was only 25% of the amount of the yield of dehydration product **1** in the case of isopulegol. However, in the case of *diol* reaction also formation of other side products was observed because a significant decrease of selectivity to **8** is not equal to an increase of selectivity to **5**. On the other hand, the decrease in selectivity to the dehydrated product **5** was observed in the reaction catalyzed by Ce-MCM-41 (Fig. 9) being 5 % at 50 % conversion and just 2 % after 240 min. Unfortunately, tetrahydropyran type product **8** was transformed to unidentified products.

The effect of Brønsted acid sites concentration on the (**4**)/(**1**) molar ratio is illustrated in Fig. 10a showing that the molar ratio of products (**4**)/(**1**) was decreasing with increasing Brønsted acidity of different studied catalysts. Analogously it has been published previously, that an increasing amount of Brønsted acid sites led to the decrease in the ratio tetrahydropyran to dehydrated product molar ratio in Prins cyclization of isopulegol with vanillin [2]. A similar trend, a decrease in (**8**)/(**5**) molar ratio with Brønsted acid sites concentration increase can be seen also in the cyclization of diol over all tested catalysts (Fig. 10b). Thus it can be concluded that dehydration of tetrahydropyran types of compounds was catalyzed by highly Brønsted acidic catalysts, whereas the transformation of tetrahydropyran compounds to dioxinol was quite independent on the catalyst acidity.

The ring rearrangement of tetrahydropyran compounds, **4** and **8** to dioxinol type compounds **3** and **7**, respectively, is depicted in Fig. 11 and 12. The ring rearrangement can be seen mainly in the reaction catalyzed by Ce-MCM-41 in isopulegol reaction (Fig. 11a). Selectivity to products **4** and **3** after 60 min over Ce-MCM-41 was 93 and 3 %, respectively, changing to 83 and 13 % after 240 min. The formation to tetrahydropyran type of product **4** also significantly decreased over H-Beta-25, H-Beta-150 and Ce-Beta-150 (Fig. 11a) and high formation of the byproduct **3** (over 10 %) was noticed. Parallel formation of products **4** and **3** is observed for H-Beta-300 and all metal modified Beta zeolites (Fig. 11b).

In the case of diol, zeolites gave analogous trends for formation of **8** and **7** (Fig. 12). Opposite to isopulegol reaction, dioxinol type of product **7** was only formed to a minor extent in the case of diol reaction over Ce-MCM-41. Prins cyclization of diol was thus much less selective than isopulegol reaction to the main identified products (Table 3 and 4). On the other hand, much more dioxinol was formed over different parent zeolites and Fe-modified zeolites (Fig. 12). The ratio between the yields of tetrahydropyran and dioxinol was nearly unaffected by the acidity of different zeolites as can also been seen in Fig. 13.

One way of investigating dehydration and ring rearrangement of tetrahydropyran type of compound to dioxinol is to plot the yields of **4** to **1** and **8** to **5** and **4** to **3** as well as **8** to **7**, respectively, as a function of conversion (Fig. 13a,b). These plots revealed clearly that the formation tetrahydropyran type compounds was more favored over the formation of the dehydration product, when using mildly acidic catalysts, such as H-Beta-300 and Ce-MCM-41 (Fig. 13). Dehydration was strongly enhanced with highly Brønsted acidic catalysts, as expected, such as H-Beta-150 (Fig. 12), H-Beta-25, Au-Beta-25 and Fe-H-Beta-150 (Table 3). From the viewpoint of the catalyst structure it can also be stated, that mildly acidic, mesoporous catalyst exhibited very high selectivity to pyran and less formation of dehydration product than mildly acidic, microporous H-Beta-300 catalyst in case of isopulegol transformation (Fig. 13a). Analogous trends were observed for Prins cyclization of diol (Fig. 13b). It was also interesting to observe that in the ring rearrangement of tetrahydropyran to dioxinol type compound both the acidity and structure of catalysts exhibited only a minor role especially in case of diol (Fig. 13b).

Finally it should be mentioned, that conventional explanation of Prins cyclization is related to formation of oxocarbenium ions which can be generated by the dehydrative condensation of alcohols with aldehydes in the presence of Brønsted or Lewis acids. Subsequent Prins-type cyclization by reacting this nucleophile with an alkene forms a carbocation reacting further with an additional nucleophile derived from the acid catalyst [31]. Such complex mechanism makes it difficult to access precisely the role of different acid sites and the role of metals in the studied main and side reactions.

Introduction of metals leads to the activity decline (conversion and rate constant) for H-Beta-25, H-Beta-150, H-Beta-300 catalysts which can be attributed not only to suppression of strong Brønsted sites, but also to the variations in the amount and strength of Brønsted and Lewis acid sites (Table 2).

Recently, in the work of Čejka and co-workers different types of MOFs materials were used in Prins condensation of β-pinene and paraformaldehyde [32, 33]. The results are somewhat in line with the current work, since strong Brønsted acid sites of zeolites BEA and FAU showed significantly lower selectivity to the target Nopol than MOFs with Lewis sites resulting in the former case in an unwanted reaction of pinene isomerization [33]. Activity was also seen to be influenced by the Lewis acidity.

Apparently further work is needed to quantitatively access the role of different types of sites in the Prins cyclization reaction as well as in the side reactions.

4. Conclusions

In the current study, a wide range of heterogeneous catalysts was tested in selective synthesis of compounds with tetrahydropyran moiety by Prins cyclization reaction of isopulegol or 3-methyl-6-(prop-1-en-2-yl)cyclohex-3-ene-1,2-diol (diol) with benzaldehyde. Activity and selectivity of the tested catalysts were correlated with their physico-chemical properties.

Very high conversions of both substrates (up to 100 % within 60 min) were achieved using various tested catalysts. Higher activity was observed mainly in the case of proton forms of beta zeolites and ceria modified catalysts. It was concluded, that transformations of diol proceed slower than transformations of isopulegol under the same reaction conditions. This fact might be related to the presence of an additional hydroxyl group in the structure of diol decreasing the electron density of the neighboring hydroxyl group which acts as a reaction center in Prins cyclization or to different stereochemical arrangement of isopropenyl and hydroxyl groups in the compounds.

Lower selectivities toward the products with the tetrohydropyran moiety were achieved as well in the case of using diol because of higher formation of unidentified products as well as generation of heavier condensation products.

The highest weight-based activity and selectivity toward the product with the tetrohydropyran structure along with a very low formation of side products was achieved using Ce-MCM-41.

The selectivity to the desired products was decreased by subsequent transformations of tetrahydropyrans, dehydrations and ring rearrangements. In particular, it was found that the products with tetrahydropyran structure are transformed via dehydration over catalysts characterized by high concentration of Brønsted acid sites.

Acknowledgements

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References

[1] N.M. Nasir, K. Ermanis, P.A. Clarke, Org. Biomol. Chem. 12 (2014) 3323-3335.

[2] M.N. Timofeeva, K.P. Volcho, O.S. Mikhalschenko, V.N. Panchenko, V.V. Krupskaya, S.V. Tsybulya, A. Gil, M.A. Vincente, N.F. Salakhutdinov, J. Mol. Cat. A: Chem. 398 (2015) 26-34.

[3] I. Il’ina, O. Mikhalchenko, A. Pavlova, D. Korchagina, T. Tolstikova, K. Volcho, N. Salakhutdinov, E. Pokushalov, Med. Chem. Res. 23 (2014) 5063-5073.

[4] O.S. Mikhalschenko, D.V. Korchagina, K.P. Volcho, N.F. Salakhutdinov, Helv. Chim. Acta 97 (2014) 1406-1421.

[5] C. Olier, M. Kaafarani, S. Gastaldi, M. P. Bertrand, Tetrahedron 66 (2010) 413-445.

[6] J.S. Yadav, B.V. Subba Reddy, A.V. Ganesh, G.G.K.S. N. Kumar, Tetrahedron Lett. 51 (2010) 2963-2966.

[7]. B. V. Subba Reddy, A. Venkateswarlu, G. G. K. S. N. Kumar, A. Vinu, Tetrahedron Lett. 51 (2010) 6511-6515.

[8] V. S. Marakatti, G. V. Shanbhag, A. B. Halgeri, Appl. Catal. A: Gen. 451 (2013) 71-78.

[9] M. Breugst, R. Grée, N.K. Houk, J. Org. Chem. 78 (2013) 9892-9897.

[10] K. Zheng, X. Liu, S. Qin, M. Xie, L. Lin, C. Hu, X. Feng, J. Am. Chem. Soc. 134 (2012) 17564-17573.

[11] J. K. Vandavasi, W. P. Hu, S. S. K., Boominathan, Chem. Comm. 51 (2015) 12435-12438.

[12] B.R. Rajeswara Rao, P.N. Kaul, K. Syamasundar, S. Ramesh, Flavour and Frag. J. 18 (2003) 133-135.

[13] M. Fuentes, J. Magraner, C. De Las Pozas, R. Roque-Malherbe, Appl. Cat. 47 (1989) 367-374.

[14] O.V. Ardashov, A.V. Pavlova, I. Il´ina, E.A. Morozova, D.V. Korchagina, E.V. Karpova, K.P. Volcho, T.G. Tolstikova, N.F. Salkhutdinov, J. Med. Chem. 54 (2011) 3866-3874.

[15] H. Kim, L. Su, H. Jung, S. Koo, Org. Lett. 13 (2011) 2682-2685.

[16] I.V. Il´ina, K.P. Volcho, D.V. Korchagina, V.A. Barkhash, N.F. Salakhutdinov, Helv. Chim. Acta 90 (2007) 353-368.

[17] O.V. Ardashov, I.V. Il´ina, D.V. Korchagina, K.P. Volcho, N.F. Salakhutdinov, Mendeleev Commun. 17 (2007) 303-305.

[18] M.K. Lajunen, T. Maunula, A.M.P. Koskinen, Tetrahedron 56 (2000) 8167-8171.

[19] K.M. Reddy, C. Song, Catal. Lett. 36 (1996) 103-109.

[20] N. Kumar, E. Leino, P. Mäki-Arvela, A. Aho, M. Käldström, M. Tuominen, P. Laukkanen, K. Eränen, J.-P. Mikkola, T. Salmi, D.Yu. Murzin, Microp. Mesop. Mater. 152 (2012) 71-77.

[21] D. Kubicka, N. Kumar, P. Mäki-Arvela, M. Tiitta, V. Niemi, T. Salmi, D.Yu. Murzin, J. Catal. 222 (2004) 65-79.

[22] C.A. Emeis, J. Catal. 141 (1993) 347-354.

[23] A. Torozova, P. Mäki-Arvela, A. Aho, N. Kumar, A. Smeds, M. Peurla, R. Sjöholm, I. Heinmaa, D. V. Korchagina, K. P. Volcho, N. F. Salakhutdinov, D. Yu. Murzin, J. Mol. Catal. A: Chem. 397 (2015) 48-55.

[24] M. Stekrova, N. Kumar. S. F. Diáz, P. Mäki-Arvela, D. Yu. Murzin, Catal. Today 241 (2015) 237-245.

[25] M. Stekrova, N. Kumar, P. Mäki-Arvela, O.V. Ardashov, K.P. Volcho, N. F. Salakhutdinov, D. Yu. Murzin, Materials 6 (2013) 2103-2118.

[26] N. Kumar, P. Mäki-Arvela, T. Yläsalmi, J. Villegas, T. Heikkilä, A.-R. Leino, K. Kordás, T. Salmi, D. Yu. Murzin, Microp. Mesop. Mater. 147 (2012) 127-134.

[27] D. Kubicka, N. Kumar, T. Venäläinen, H. Karhu, I. Kubicka, H. Österholm, D. Yu. Murzin, J. Phys. Chem. B 110 (2006) 4937-4946.

[28] M. P. Casaletto, A. Longo, A. Martorana, A. Prestianni, A. M. Venezia, Surf. Interface Anal. 38 (2006) 215–218.

[29] P. Borkar, P. van de Weghe, B. V. S. Reddy, J. S. Yadav, R. Grée, Chem. Comm. 48 (2012) 9316-9318.

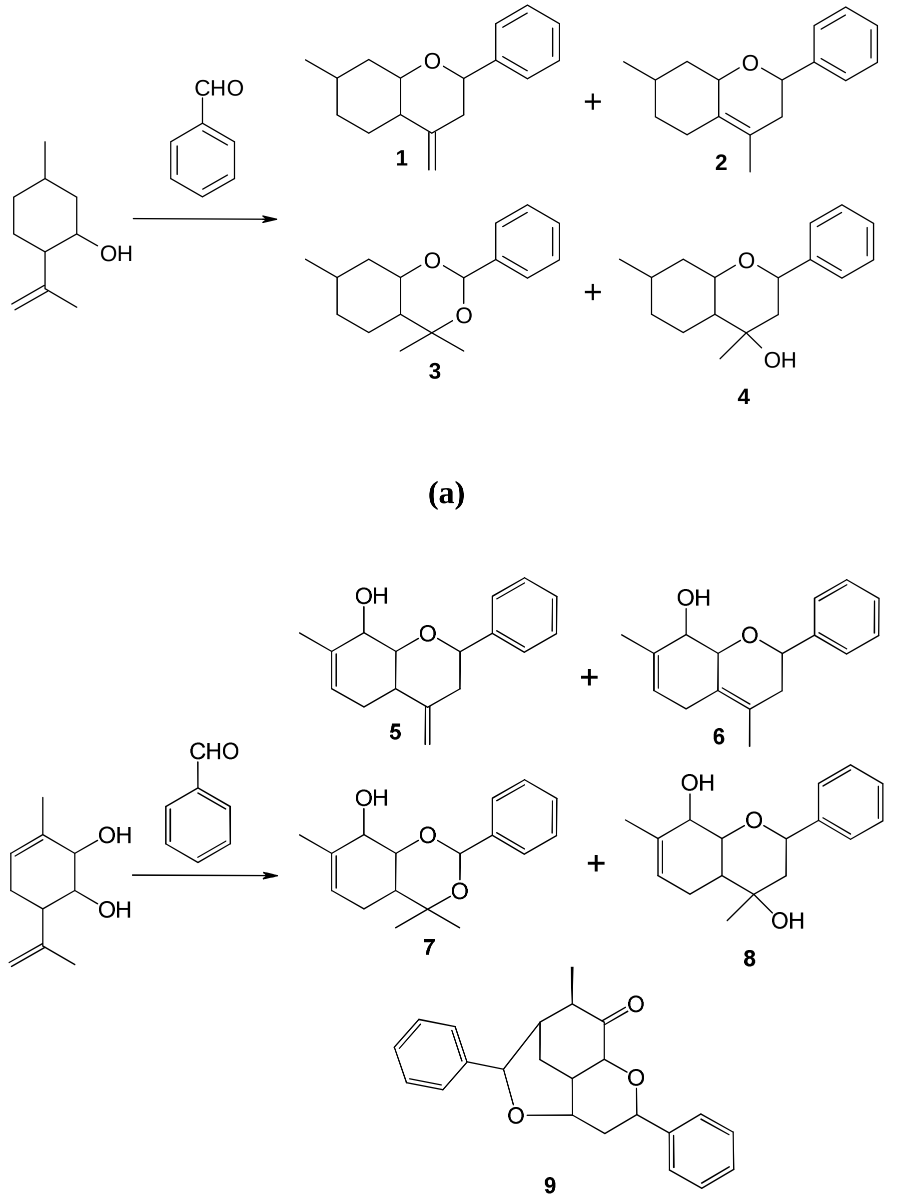
[30] M. Stekrova, N. Kumar, P. Mäki-Arvela, A. Aho, J. Linden, K. P. Volcho, N. F. Salakhutdinov, D. Yu. Murzin, React. Kin. Mech. Catal. 110 (2013) 449-458.

[31] X. Han, G. Peh, P. E. Floreancig, Eur. J. Org. Chem. 2013 (2013), 1193–1208.

[32] M. Shamzhy, M. Opanasenko, O. Shvets, J. Cejka, Front. Chem. 1 (2013), A 11: 1-11.

[33] M. Opanasenko, A. Dhakshinamoorthy, Y. K. Hwang, J.-S. Chang, H.Garcia, J. Čejka, 6 (2013) 865–871.

Figure Captions



(a)

(b)

Fig. 1. Reaction scheme for Prins cyclization of a) isopulegol with benzaldehyde and b) diol (3-methyl-6-(prop-1-en-2-yl)cyclohex-3-ene-1,2-diol) with benzaldehyde.

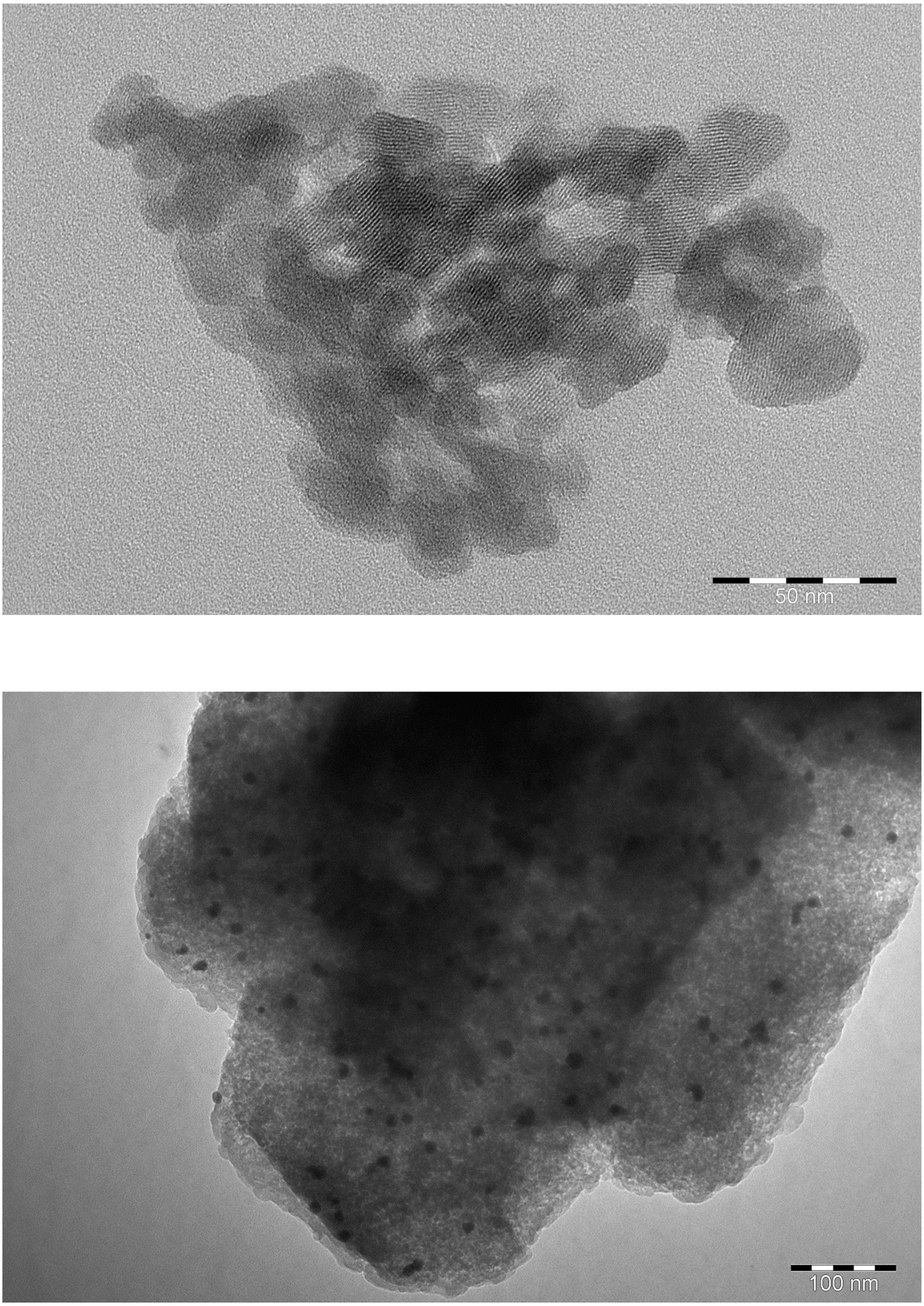
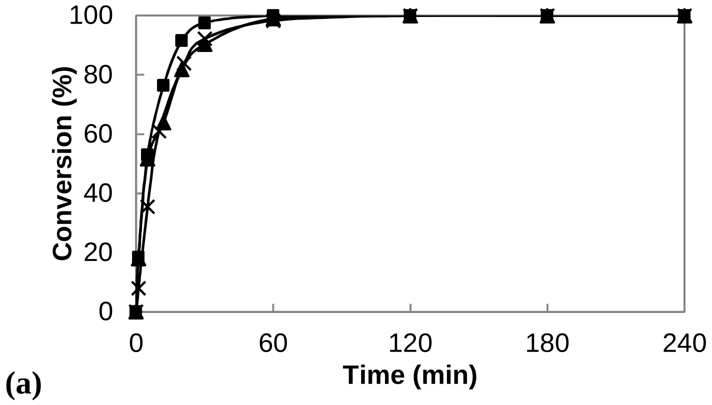


Fig. 2. Transmission electron micrograph of a) H-Beta-25 and b) Au-Beta-25 zeolite catalysts.



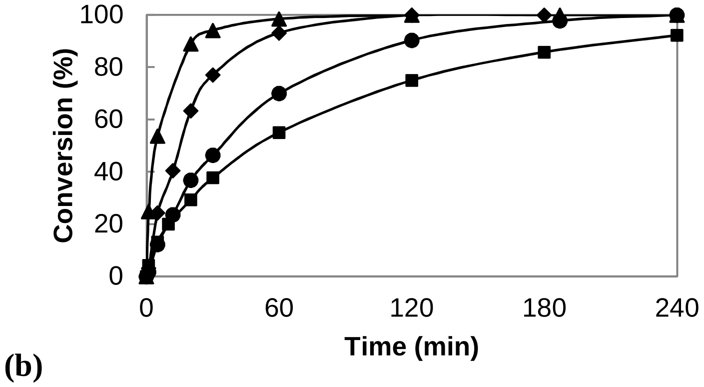


Fig. 3. Conversion of isopulegol as a function of the reaction time over **(a)** zeolites H-Beta-25 (■), H-Beta-150 (x) and H-Beta-300 (▲) and over **(b)** metal modified catalyst: Fe-Beta-150 (■), Au-Beta-25 (●), Ce-Beta-150 (♦) and Ce-MCM-41 (▲).

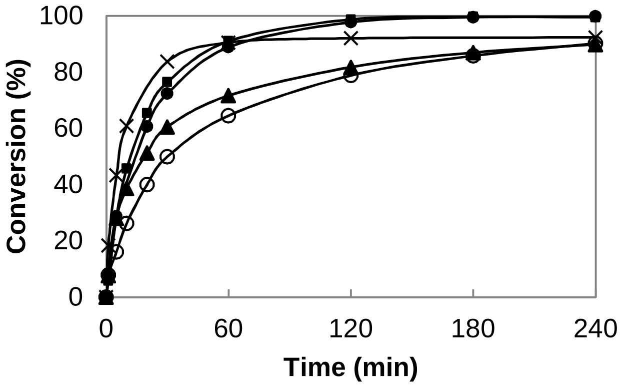
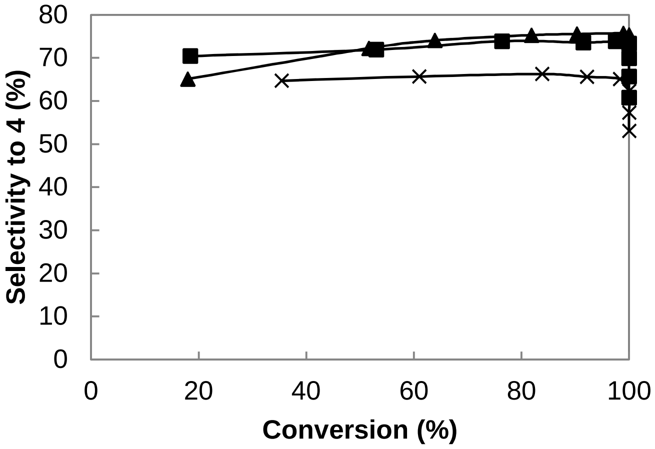
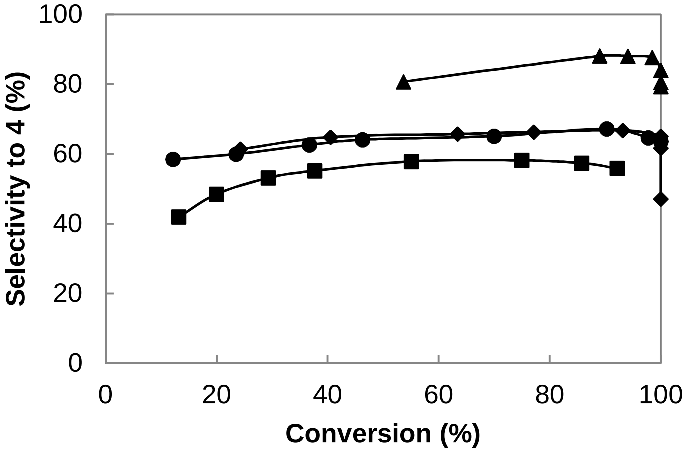


Fig. 4. Conversion of diol as a function of the reaction time over zeolites H-Beta-25 (■), H-Beta-150 (●), H-Beta-300 (▲), Fe-Beta-150 (○) and Ce-MCM-41 (x).



(a)



(b)

Fig. 5. Selectivity to the product 4 as a function of isopulegol conversion over **(a)** zeolites H-Beta-25 (■), H-Beta-150 (x) and H-Beta-300 (▲) and over **(b)** metal modified catalyst: Fe-Beta-150 (■), Au-Beta-25 (●), Ce-Beta-150 (♦) and Ce-MCM-41 (▲).

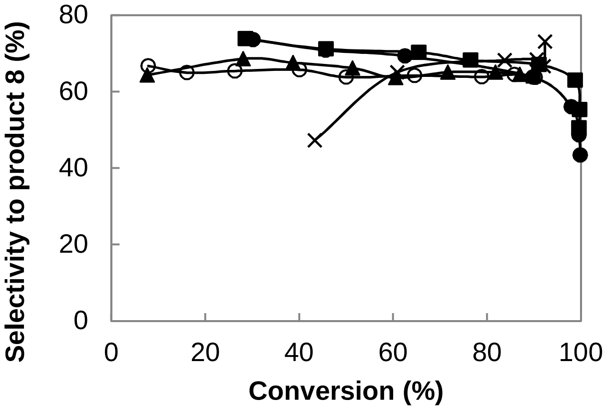
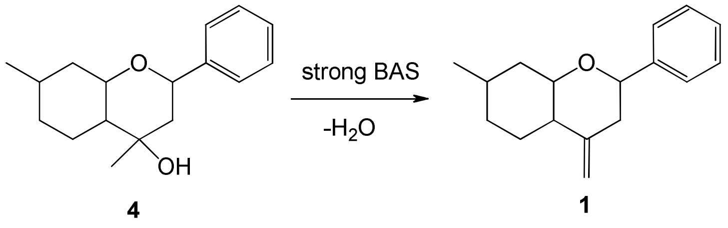
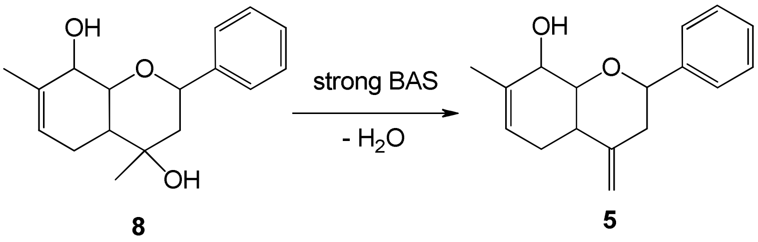


Fig. 6. Selectivity to product **8** as a function of diol conversion over H-Beta-25 (■), H-Beta-150 (●), H-Beta-300 (▲), Fe-Beta-150 (○) and Ce-MCM-41 (x).



(a)



(b)

Fig. 7. Dehydration of tetrahydropyran type product: **(a) 4** to **1** and **(b) 8** to **5.**

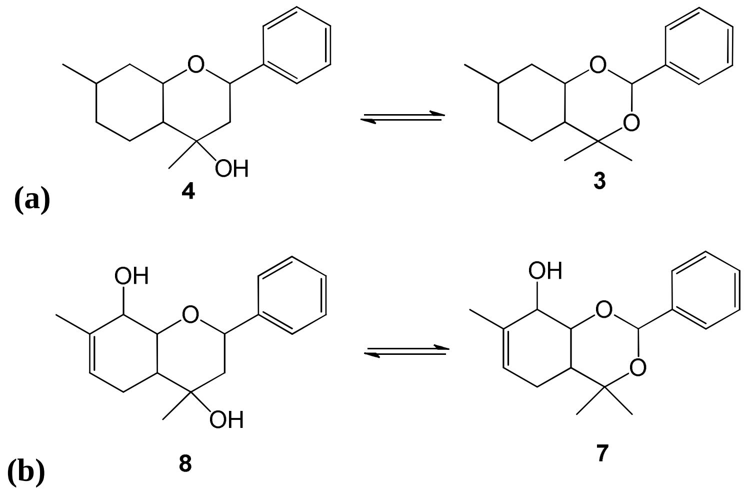
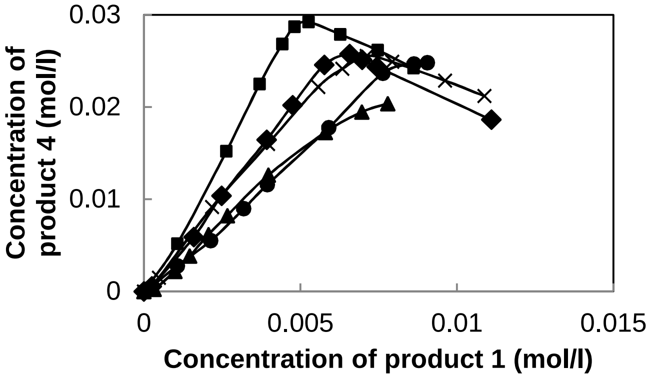
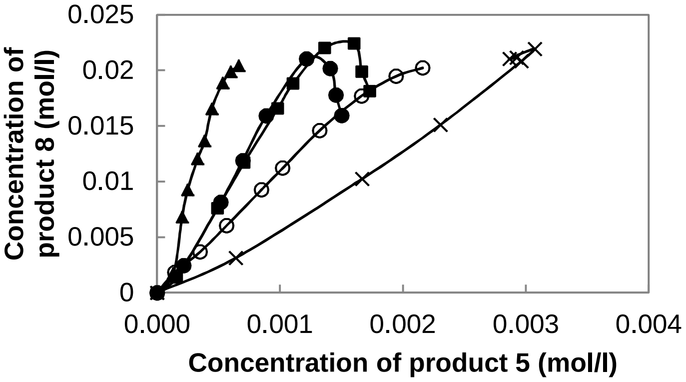


Fig. 8. Ring rearrangement of (a) tetrahydropyran type product **4** to dioxinol type product **3** in isopuleogol reaction and of (b) terahydropyran type product **8** to dioxinol type product **7** in diol reaction.

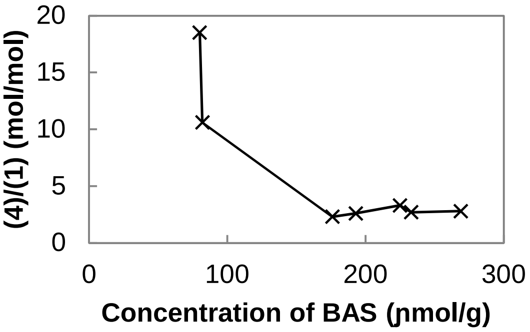


(a)



(b)

Fig. 9. Concentration of a) tetrahydropyran type product **4** as a function of dehydration product **1** concentration over H-Beta-25 (■), H-Beta-150 (x), Fe-Beta-150 (▲), Au-Beta-25 (●) and Ce-Beta-150 (♦) in isopulegol reaction and b) tetrahydropyran type product **8** as a function of dehydration product **5** concentration over H-Beta-25 (■), H-Beta-150 (●), H-Beta-300 (▲), Fe-Beta-150 (○) and Ce-MCM-41 (x) in diol reaction.



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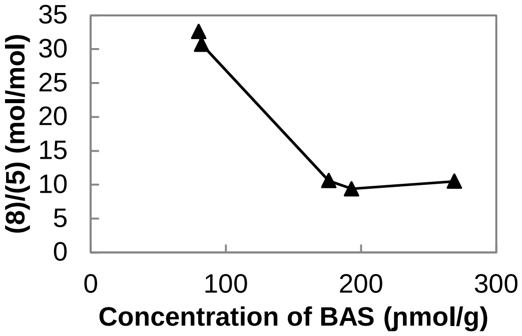
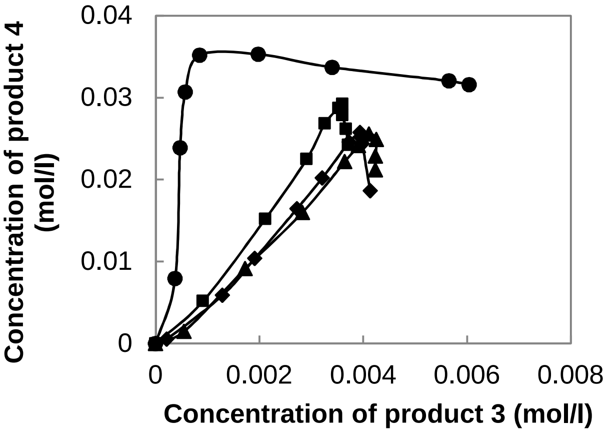


(b)

Fig. 10. Effect of Brønsted acid sites concentration on the molar ratio between tetrahydropyran product to dehydration product: a) (**4**)/(**1**) molar ratio (x) in isopulegol reaction and b) the (**8**)/(**5**) molar ratio (▲) in diol reaction over different catalysts tested.



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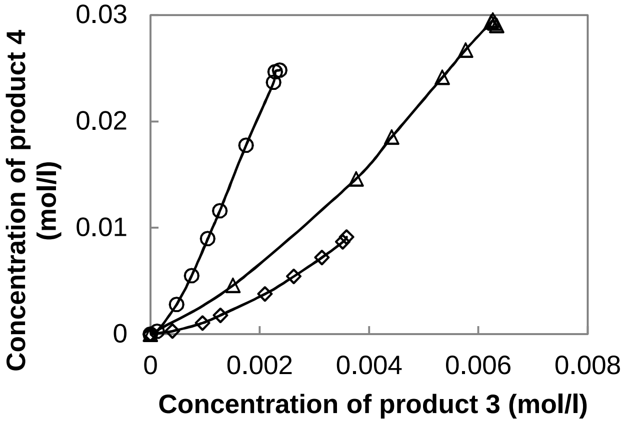


(b)

Fig. 11. Concentration of tetrahydropyran type product **4** as a function of concentration of dioxinol type product **3** over **(a)** H-Beta-25 (■), H-Beta-150 (▲), Ce-Beta-150 (♦) and Ce-MCM-41 (●) and over **(b)** H-Beta-300 (Δ), Fe-Beta-150 (◊) and Au-Beta-25 (○) in isopulegol reaction.

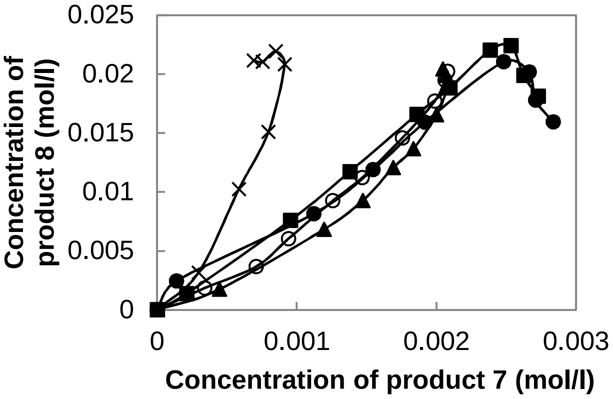
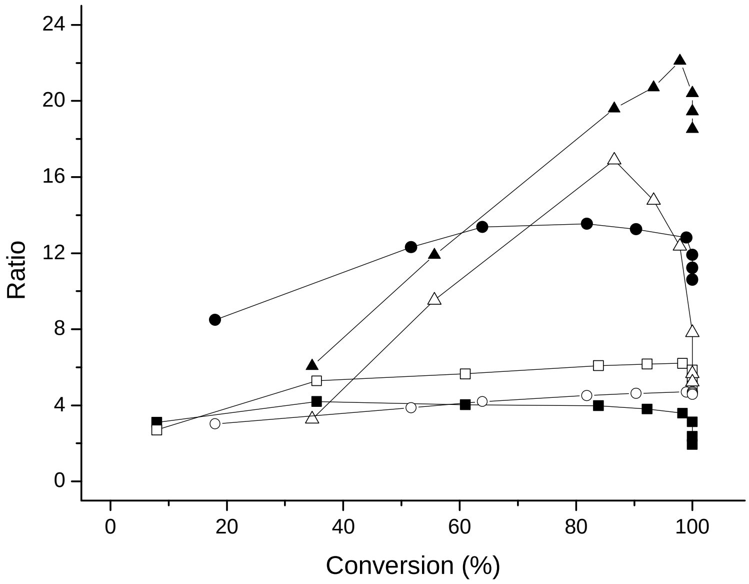


Fig. 12. Concentration of terahydropyran type product **8** as a function of concentration of dioxinol type product **7** over H-Beta-25 (■), H-Beta-150 (●), H-Beta-300 (▲), Fe-Beta-150 (○) and Ce-MCM-41 (x) in diol reaction.



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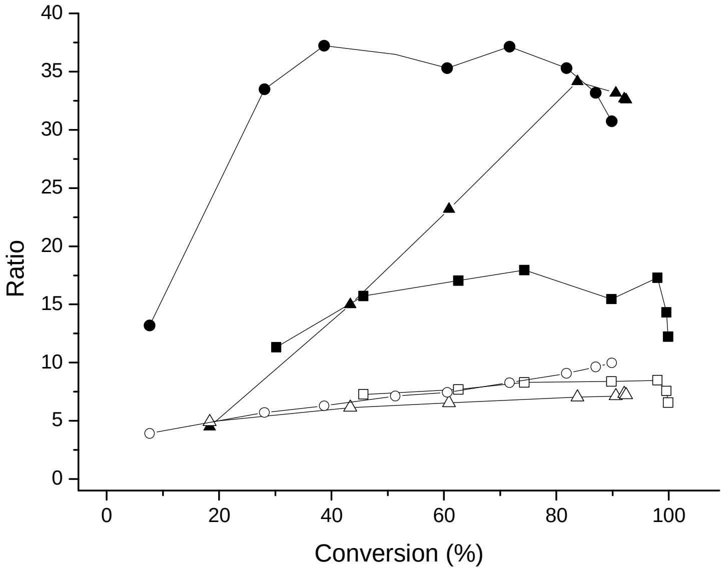

(b)

Fig. 13. The ratio between tetrahydropyran to dehydration product (solid symbol) and terahydropyran to dioxinol product (open symbol) for H-Beta-300 (●), H-Beta-150 (■) and Ce-MCM-41 (▲), in the reaction between **(a)** isopulegol and benzaldehyde and **(b)** diol and benzaldehyde.

Tables

Table 1 Main textural characteristics of the studied catalysts.

Catalyst/support	Metal content (wt. %)	Specific Surface Area (m^2/g)	Pore Specific Volume (cm^3/g)
H-Beta-25 [23]	-	807	-
H-Beta-150 [23]	-	664	-
H-Beta-300 [23]	-	805	-
Fe-Beta-150 [23]	3	467	0.59
Au-Beta-25	2.1[a]	652	0.23
Ce-Beta-150	2[b]	n.d.	
Ce-MCM-41 [24]	32[a]	384	-

[a] determined by EDXA, [b]nominal loading.

Table 2 Brønsted and Lewis acidities of the tested catalyst determined by FTIR.

Catalysts	Brønsted acidity (µmol/g)			Lewis acidity (µmol/g)		
	250 °C	350 °C	450 °C	250 °C	350 °C	450 °C
H-Beta-25	269	207	120	162	128	113
H-Beta-150	176	161	72	43	23	10
H-Beta-300	82	67	10	30	4	4
Fe-Beta-150	193	137	45	119	41	6
Au-Beta-25	233	202	141	143	82	33
Ce-Beta-150	225	198	125	99	57	43
Ce-MCM-41	80	49	10	67	12	9

Table 3 Conversion of isopulegol, initial reaction rate, first order rate constant and selectivities to products at 90 and 100 % conversion of isopulegol.

Catalyst	Initial reaction rate (mmol/(l·min·g_{cat}))	k (min^{-1})	Conversion (%) 120 min (240 min)	Selectivity at 90 % conversion (100 % conversion)				
				1	**2**	**3**	**Unident. products**	**4**
H-Beta-25	24.3	0.143±0.006	100	12 (13)	2 (2)	9 (9)	3 (2)	74 (73)
H-Beta-150	11.3	0.091±0.002	100	17 (19)	3 (3)	11 (11)	4 (6)	66 (62)
H-Beta-300	23.8	0.100±0.010	100	6 (6)	1 (1)	16 (16)	2 (1)	75 (75)
Fe-Beta-150	5.4	0.012±0.001	76 (93)	21	4	13	6	56
Au-Beta-25	5.2	0.021±0.001	90 (100)	22 (23)	3 (3)	6 (6)	2 84)	67 (64)
Ce-Beta-150	15.1	0.050±0.001	100	16 (17)	2 (3)	10 (10)	5 (6)	67 (65)
Ce-MCM-41	33.5	0.137±0.018	100	5 (3)	0 (0)	1 (13)	2 (1)	93 (83)

Table 4 Initial reaction rate, first order rate constant, conversion and selectivities to products at 90 % conversion of diol.

Catalyst	Initial reaction rate (mmol/(l·min·g_{cat}))	k (min^{-1})	Conversion (%) 120 min (240 min)	Selectivity at 90 % conversion (%)				
				5	**7**	**8**	**Unidentified products**	**9**
H-Beta-25	6.9	0.052±0.003	99 (100)	4	7	67	17	4
H-Beta-150	10.0	0.048±0.003	98 (100)	4	8	64	20	5
H-Beta-300	8.5	0.024±0.005	81 (90)	2	6	64	19	9
Fe-Beta-150	8.7	0.016±0.002	78 (90)	7	7	64	15	8
Ce-MCM-41	22.3	0.093±0.014	92 (93)	9	3	67	21	0