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PII:	S0920-5861(20)30524-1
DOI:	https://doi.org/10.1016/j.cattod.2020.07.051
Reference:	CATTOD 13056
To appear in:	Catalysis Today
Received Date:	15 December 2019
Revised Date:	27 April 2020
Accepted Date:	13 July 2020

Please cite this article as: { doi: https://doi.org/

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Catalytic oxidative transformation of betulin to its valuable oxo-derivatives over gold supported catalysts: Effect of support nature

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Graphical abstract

- Betulin can be transformed into its oxo-derivatives by liquid-phase oxidation over gold-based catalysts under mild conditions
- Gold catalyzed betulin oxidation is a structure sensitive reaction
- An optimum gold particle size of 3.3 nm gave the highest TOF in betulin oxidation
- Alumina materials are suitable supports for gold nanoparticles
- A certain oxo-derivative of betulin be preferentially formed by adjusting the experimental conditions

ABSTRACT

Liquid-phase oxidation of betulin extracted from birch bark was studied over gold catalysts supported on a range of supports (hydrotalcite, ZrO₂, ZnO, MgO, CeO₂, La₂O₃, HMS and various alumina) with different morphology and properties. Gold catalysts as well as the corresponding supports were characterized by XRD, BET, ICP-OES, XPS and TEM. It was found that the nature of the support plays a decisive role in betulin oxidation over gold-based catalysts, expressed in the influence on the average size and distribution of gold nanoparticles and, thereby, on their catalytic performance (activity and selectivity) in betulin oxidation. Moreover, it was revealed that betulin oxidation catalyzed by gold is a structure sensitive reaction, requiring an optimal size of gold nanoparticles of ca. 3.3 nm. The most suitable support for gold was found to be alumina. Kinetic studies allowed determination of reaction orders and conditions favorable for selective formation of a particular oxoderivative of betulin (betulone, betulinic and betulonic aldehydes, betulinic acid).

Keywords: Gold catalyst, betulin oxidation, support nature, structure sensitivity

1. Introduction

Medical drugs obtained by chemical transformations of natural compounds have several advantages over synthetic analogues. They show low toxicity, provide a multilateral effect on the

organism, rarely cause side effects. It is especially valuable that many promising objects of chemical transformations can be obtained in almost unlimited quantities from the waste of the forest and wood processing industry. One such example is birch bark, a large-tonnage waste product from birch processing with a share is 15-17% from the total harvested wood volume. The outer part of the birch bark is a source of a number of valuable organic substances. The birch extracts are dominated by cyclic triterpenoids of the lupane series, the main of which is betulin - (lup-20 (29)-ene-3, 28-diol, $C_{30}H_{50}O_2$, CAS: 473-98-3) [1]. Betulin is produced from birch bark of various species [2]. The content of betulin in the outer part of the bark varies (10-35 %) depending on the species of birch, the place and conditions of its growth, the age of the tree and other factors [3]. Betulin is easily and almost completely extracted from birch bark by such extracting agents as aliphatic hydrocarbons, alcohols C1 – C4 or acetone [1, 2, 4-8], and, therefore, is considered as an available feedstock.

Betulin, and especially its oxo-derivatives (betulone, betulinic and betulonic aldehydes, betulinic and betulonic acids, as well as their derivatives) exhibit a broad-spectrum biological activity per se (immunostimulatory, antioxidant, hepatoprotective, anti-inflammatory, antiviral, etc.) and, moreover, can serve as building blocks for the creation of new generation of drugs, thereby representing an exceptional interest for the pharmaceutical, cosmetic and food industries [2, 9-24]. The main method for the synthesis of betulin oxo-derivatives is its oxidation. Complexity of betulin oxidation is due to several reasons: presence of three reaction centers in the molecule, namely a primary hydroxyl group at C-28, a secondary alcohol group at C-3 and a multiple bond at the C-20 - C-29 position; difficulty of regulating selectivity to a specific product, lability of the betulin structure and its solubility [2]. The most commonly used oxidizing agents are Cr(VI) compounds, for example, the Jones reagent, pyridinium dichromate, pyridinium chlorochromate, pyridinedichromate complex with acetic anhydride, etc. [2, 25-30]. However, despite numerous studies aimed at modifying the method of betulin oxidation by chromium compounds, the synthesis of oxo-derivatives is a quite complex process characterized by low yields of the target products, low temperature and long reaction times, low selectivity leading to a mixture of products, as well as complexity of toxic Cr(III) disposal and

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handling of very toxic residual Cr(VI). Subsequently, product isolation requires complex purification, the use of a large number of different types of organic solvents and different techniques for removing Cr(III). There are also several approaches in which betulin oxo-derivatives are synthesized using mixtures: TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl) - NaClO₂-NaOCl; butyl acetate, phosphate buffer, 4-acetamido-TEMPO and Bu₄NBr×H₂O in an aqueous solution of NaClO₂ and NaOCl [31]. In addition, methods of biological transformation by microorganisms are used to obtain betulin oxoderivatives, in particular, this is the main way to obtain betulone, due to the fact that during chemical transformation it is very difficult to keep other groups intact. However, despite a possibility to obtain the target products with a high degree of regio- and stereoselectivity using biocatalysts, this approach is characterized by an even larger set of disadvantages than chemical transformation methods (complex nutrient media, long duration, low substrate concentrations, etc.) [12, 32-35].

Earlier in a series of articles [36-39], some of the authors of this work demonstrated that a more environmentally and economically viable alternative to existing stoichiometric methods for producing betulin oxo-derivatives can be heterogeneous catalytic oxidation of betulin with synthetic air over catalysts based on Pd, Ru, Ag and Au nanoparticles deposited on various carbon and oxide supports. The best results were achieved over gold catalysts supported on modified titania [39]. Gold catalysts have been shown to be more stable and less sensitive to changes in reaction conditions and the inhibitory effect of water. A more detailed comparative analysis of the catalysts (Pd, Ag, and Au) previously studied in betulin oxidation is given in [39].

It should be noted that, gold-based nanosized catalysts due to their unique properties are one of the most studied systems for aerobic oxidation of all types of alcohols [40-42], as well as others substrates and reactions [43-49].

The aim of this work is to further explore the liquid phase betulin oxidation with synthetic air over supported nanogold catalysts, with a focus on assessing the effect of oxide support nature on the catalytic behavior of supported gold catalysts.

2. Materials and methods

2.1. Catalysts preparation

Hydrotalcite (HT, Merck), ZrO₂ (Alfa Aesar), ZnO (Merck), MgO (Merck), CeO₂ (Merck), La₂O₃ (Merck), Al₂O₃V (Versal gamma alumina (VGL-25), UOP), AlOOH_L (pseudoboehmite (LaRoche V-280), LaRoche Chemicals), AlOOH_C (boehmite (Catapal B), Sasol), AlOOH_S (silica-alumina hydrate (Siral 5), Sasol), AlOOH and HMS (hexagonal mesoporous silica) were used as supports. AlOOH was obtained by water oxidation of Al nanopowder obtained by electric explosion of Al wire in an atmosphere of nitrogen (or argon), according to the procedure previously described [50]. 1.0 g of the powder was placed in a thermally insulated vessel containing 100 ml of distilled water and heated to 60[°] C under stirring. The oxidation reaction was performed for 1 hour. Thereafter, the resulting suspension was filtered, followed by washing the precipitate was washed with distilled water and drying at 120 °C for 2 hours. HMS was synthesized by a neutral S⁰I⁰ templating route (S⁰: neutral primary amine surfactant; I⁰: neutral inorganic precursor), according to the procedure previously described [51]. Dodecylamine was employed as a surfactant, tetraethyl orthosilicate as an inorganic precursor and mesitylene as a swelling organic agent. The reaction mixture was aged at ambient temperature for 18 hours. This was followed by filtration of the reaction products, washing with distilled water, and drying at room temperature for 24 h and at 100 ° C for 2 h. The template was then removed by calcination at 550 ° C for 3.5 h in air.

Gold catalysts (denoted as Au/HT, Au/ZrO₂, Au/ZnO, Au/MgO, Au/CeO₂, Au/La₂O₃, Au/HMS, Au/Al₂O₃_V, Au/AlOOH_L, Au/AlOOH_S, AlOOH_C and Au/AlOOH) were prepared by deposition–precipitation with urea, according to the procedure previously described [52-55]. The nominal gold content in all catalysts was 4 wt%. The gold precursor (HAuCl₄×3H₂O, Merck) and urea (Merck) were dissolved in distilled water, and thereafter the support was added to the solution. The resulting mixture was heated to 80 0 C and kept at constant temperature for 16 h, with stirring. Thereafter, the catalysts were pretreated at 300 0 C for 1 hour under H₂ atmosphere.

2.2. Catalysts characterization

The phase composition of ZnO, ZrO₂, MgO, HT and Al₂O₃_V supports was studied by the stepscanning procedure (step size: 0.02^{0} ; 0.5 s) with a Philips XPert PRO diffractometer, using CuK α radiation ($\lambda = 0.15406$ nm) and a Ni-filter. The measured diffractograms were analyzed with the ICDD-2013 powder diffraction database. For other studied materials, structural characterization was carried out by X-ray powder diffraction (XRD) in a PAN'alytical X'Pert MPD equipped with a X'Celerator detector and secondary monochromator (Cu K α $\lambda = 0.154$ nm, 50 kV, 40 mA; data recorded at a 0.017⁰ step size, 100 s/step). The collected spectra were analyzed by the Rietveld refinements using the Highscore Plus 4.8 program (from PANalytical), allowing determination of the crystallite size by means of the Williamson-Hall plot. To determine the amount of each phase, refinements were performed using the Highscore Plus 4.8 program (from PANalytical), except Au/HMS, when amorphous phases were present. In the latter case, a more appropriate PowderCell software was used.

The samples texture was analyzed using an ASAP 2060 (Micromeritics) apparatus. Materials were previously degassed in vacuum, at 300 ^o C for 5 hours. The surface area was determined using the Brunauer-Emmett-Teller (BET) equation applied for the adsorption isotherm at the relative pressures between 0.005 to 0.25. The pore size distribution was determined by the Barrett-Joyner-Halenda (BJH) method (desorption branch).

The metal loading of the catalysts was determined by inductively coupled plasma optical emission spectrometry (ICP-OES) using a Horiba JobinYvon (France) Ultima apparatus. The solids were treated by aqua regia, digested in microwave oven, diluted to 100 mL and analyzed in the spectrometer.

The surface composition and the chemical state of each element were determined by X-ray photoelectron spectroscopy (XPS), performed on a VG Scientific ESCALAB 200A spectrometer using Al Kα radiation (1486.6 eV) in CEMUP. The charge effect was corrected using the C1s peak as a reference (binding energy of 285 eV). The CASA XPS software (http://www.casaxps.com/) was used for data analysis.

The size of gold nanoparticles was investigated by high resolution transmission electron microscopy (HRTEM) using JEM-2100F instrument. The samples were ground to a fine powder and sonicated in hexane at room temperature. Then a part of the suspension was placed on a lacey carbon-coated Cu grid. For each sample, at least 150 particles were counted.

2.3. Catalytic testing

Betulin (90–94%) was extracted from birch bark with a non-polar solvent and recrystallized from 2-propanol according to the procedure, previously reported [5]. Typically oxidation of betulin was carried out using 200 mg of betulin in 100 ml of mesitylene (the initial betulin concentration was 4.5 mmol/l) and 200 mg of Au catalyst (betulin to gold molar ratio was 11:1) under atmospheric pressure with synthetic air (AGA, 20% oxygen, 80% nitrogen) as an oxidant at 140 ° C. The gas phase was bubbled through the liquid with an inlet for the gas (flow rate: 50 ml/min) located at the bottom of the reactor to enhance the gas–liquid mass transfer. Moreover, a metallic sinter was applied to diminish the size of air bubbles. The reaction started when the desired temperature was reached via turning on stirring (500 rpm). Small catalyst particles (<63 μ m) and a high stirring rate of 500 rpm were used to suppress the internal and external mass transfer limitations. To confirm reliability of the results of catalytic studies, the tests were performed twice for each studied catalyst. Kinetic experiments were performed in the temperature range of 80 - 140 ° C using 0.05 – 0.4 g catalyst and the initial betulin concentration varied from 1.13 mmol/l – 9.04 mmol/l. In addition, the oxygen content in the gas atmosphere was changed from 0% to 100% by adjusting the oxygen level with nitrogen (Table 1).

The samples for analysis were withdrawn from the reactor at regular intervals. Prior to GCanalysis, the samples (150 μ L) were silvlated by adding 150 μ L of the mixture of pyridine (VWR International, Fontenay-sous-Bois, France), N,O-bis(trimethylsilyl) trifluoroacetamide (BSTFA, Supelco Analytical, Bellefonte, PA, USA), and trimethylsilyl chloride (TMCS, Merck KGaA, Darmstadt, Germany) with the 1:4:1 volume ratio followed by heating of a mixture was heated in an oven at 70 ^o C for 45 min. GC analysis was performed on a Crystallux-4000M Meta-chrome gas

chromatograph using an Agilent HP-1 capillary column, 25 m (L) \times 0.2 mm (ID), film thickness: 0.11 mm. Hydrogen was used as a carrier gas, with a flow rate of 30 ml/min. Betulinic aldehyde, betulonic acid and betulinic acid (90% purity), used as standards, were purchased from MedChem Express and Merck, respectively. The products were confirmed by GC-MS. The conditions of betulin oxidation and the analytical procedure were previously published [36-39].

The TOF values were calculated as the number of converted moles of betulin per mole of exposed catalytic site per unit time, during the first 5 min, taking into account the metal dispersion:

$$TOF = \frac{n_{Betulin}}{n_{Metal}Dt} \tag{1}$$

where n_{Betulin} is the number of converted moles of betulin, n_{Metal} is the number of moles of the metal in the catalyst, *D* is dispersion and *t* is time [39]. The metal dispersion was calculated knowing the average gold particle size measured by transmission electron microscopy (TEM), according to the following equation:

$$D = \frac{6M}{\rho d_{Au} N_A cs} \tag{2}$$

where d_{Au} - average gold particle size, ρ and *cs* its bulk density and cross-section, N_A is the Avogadro number.

For determination of the activation energy of betulone formation from the Arrhenius equation the initial rate of this reaction was calculated as moles of formed betulone in 30 min divided by that time.

3. Results and discussion

3.1. Betulin oxidation over gold supported on various oxide supports

3.1.1. Catalyst characterization results

Table 2 summarizes the textural and structural data of supports and catalysts, Au content and the average gold particle size. Analysis of X-ray powder diffraction data of the studied supports and the

corresponding catalysts showed that the deposition of gold leads to a change in the support structure and composition in only three cases, namely transformations of MgO to Mg(OH)₂, La₂O₃ to (La(OH)₃ and La₂(CO₃)₂(OH)₂) and Al₂O₃ to (Al₂O₃ and AlO(OH)) (Supporting Information, Fig. S1, S4). Such changes can be explained by the chemical properties of these supports, manifested by interactions with water and urea hydrolysis products (Eq. 3) during the catalyst preparation [52,56,57].

$$CO(NH_2)_2 + 3H_2O = 2NH_4^+ + CO_2(g) + 2OH^-$$
(3)

At the same time, the average crystal sizes d_c of the supports decreased after gold deposition for almost all samples. It can be hypothesized that interactions of a support with the gold precursor and urea hydrolysis products during the catalyst preparation lead to deagglomeration depending on the surface charge density of particles and repulsion forces between them [58,59].

Au was detected by XRD in all catalysts except Au/La₂O₃ and Au/CeO₂ (Table 2). The reasons for a lack of diffraction peaks of gold in XRD patterns of Au/La₂O₃ and Au/CeO₂ were previously discussed in [60], namely, that the size of gold nanoparticles is lower than 3–4 nm (i.e. sensitivity of XRD) or that they are X-ray amorphous. The gold loading in the studied catalysts determined by XRD was in good agreement with elemental analysis by ICP (Table 2), as well as very close to the nominal value of 4 wt.%. The average gold particle size determined by HRTEM for almost all studied catalysts is more than 3 nm and varies from 3.6 (for Au/La₂O₃) to 18.2 nm (for Au/HMS). For Au/CeO₂ and Au/Al₂O₃_V, the size is 2.6 and 3.1 nm, respectively (Table 2, Supporting Information Fig.S2). It should be noted that the average particle size of gold is not directly related to the specific surface area (S_{BET}) of the support. For example, for HMS with S_{BET} is 478 m²/g, the average Au particle size is 18.2 nm; while for ZnO these values are 5 m²/g and 7.4 nm, respectively. It was demonstrated in [52] that the average size of gold nanoparticles depends on the point of zero charge (PZC) of the support surface, determining the efficiency of interactions of gold precursor with the support surface during the catalyst preparation. According to the mechanism of interactions of the gold precursor, urea and the support during catalyst preparation by DP with urea proposed in [52]: during the initial time (up to 1

hour) the pH of media ~ 3. Under these conditions the surface of such supports as TiO_2 (PZC ~ 6), Al₂O₃ (PZC ~ 7.5) and CeO₂ (PZC ~ 6) is positively charged, and gold species in the solution are [AuCl₄]⁻ or [Au(OH)Cl₃]⁻. Subsequently, there are initially electrostatic interactions between the support and these gold species, followed by growth of the gold precipitate on the support surface. Formation of this gold precipitate occurs fast within the first hour of the preparation. Thereafter, with increasing pH due to urea hydrolysis, there is a change in the surface charge density of the gold precipitate particles, which leads to fragmentation, and then to a decrease in the size of the gold particles with increasing deposition time. As a result it was possible to obtain gold particles in the range of 2.3 - 5 nm for these supports. The largest gold particles were obtained on the silica surface [52], which has the lowest zero charge point (PZC \sim 2), thereby complicating adsorption of gold species [AuCl₄]⁻ or [Au(OH)Cl₃]⁻ on the negatively charged silica surface. It should be noted that in the case of magnesia, the introduction of MgO into the aqueous media leads to its rapid hydration to Mg(OH)₂ and a rapid increase of pH to 9-10, due to its high solubility [57]. As shown in [61,62], the adsorption rate of the gold precursor is linearly proportional to the difference between the pH of media and the point of zero charge of the support (PZC), which is about 12 in the case of magnesia. With such a small difference, the adsorption of the gold precursor is very slow, leading to the formation of gold(I) polynuclearhydroxo complexes in the solution along with gold(III) polynuclearhydroxo complexes, resulting in a broad particle size distribution with a predominance of particles larger than 5 nm on the magnesia surface (Supporting Information, Fig.S2).

It should be noted that because the size of gold nanoparticles depends on the point of zero charge of a particular support and pH of deposition [63], in general regulation of the deposition pH can optimize dispersion of gold on the supports, which are otherwise less active when the same preparation method is applied. Understanding of the influence of preparation and pretreatment methods, as well as gold loading on the catalytic behavior, clearly requires a stand-alone comprehensive study, going beyond the scope of the current work aiming at elucidation of selectivity in catalytic transformations of betulin. Moreover, differences between the pzc and the pH during metal deposition are certainly not

the only criterium for formation of gold clusters with an optimum dispersion. A suitable method for obtaining gold catalysts for a particular support should take, into account not only its chemical nature and pH during introduction of the metal onto a support, but also textural and structural features of the latter, including potential phase transformations.

It is worth mentioning that Au addition led to a significant change in the specific surface area only for Au/HT, Au/MgO and Au/HMS, while for other supports it remained practically unaffected. Herewith, for Au/HT and Au/HMS, the surface area decreases by 4.3 and 2.9 fold, even increasing for Au/MgO 2.2 fold after gold deposition. For the latter case, an increase in the specific surface area after gold addition is probably due to changes in the structure and composition of the support, namely, transformations of an oxide to a hydroxide and/or decrease in the crystallite size, resulting from reasons described above. For Au/HT and Au/HMS, the reason for a decrease in the specific surface area is most likely pore plugging by gold nanoparticles [51].

To study the electronic state of gold on the surface of different oxide supports, the catalysts were analyzed by XPS (Supporting Information, Fig. S3 and Table S1). Analysis of XPS results shows that most of gold (50 - 100%) on the surface of the studied catalysts is in a metallic state with BE (Au $4f_{7/2}$) in the range of 84.0 - 84.2 eV [39, 60,64,65]. Gold is only in the metallic (Au⁰) state on the surface of ZrO₂, MgO and HMS. For Au/HT and Au/ZnO, Au $4f_{7/2}$ BE is lower than the standard of metallic Au (84.0 - 84.2 eV), namely, 83.7 eV. In these cases, sometimes it is assumed that there is a donation of electrons from the support to gold with generation of Au^{δ-} [66-68], although most authors attribute this value of BE to metallic gold [69-76]. It should be noted that in the XPS spectra of Au/HT, Au/ZnO and Au/MgO catalysts, there was an overlapping of the Au4f peak with the Mg2s, Zn3p and Mg2s peaks, respectively, leading to challenges in interpretation of these peaks. At the same time, because the Au4f_{7/2} line is clearly visible, it can be assumed that the states are defined correctly. In the XPS spectra of Au/CeO₂ (21 %), Au/La₂O₃ (12 %) and Au/Al₂O₃_V (13 %) another state of Au appears with BE (Au 4f_{7/2}) in the range 85.0 - 85.3 eV related to single charged ions (Au⁺) [39, 60, 69, 76-79].

As previously reported [60], Au/CeO₂ (22 %) and Au/La₂O₃ (38 %) are characterized by the presence of Au^{δ -} state with BE (Au 4f_{7/2}) within the range of 83.3 - 83.5 eV.

3.1.2. Catalytic results

It was found that the support nature plays a crucial role in the betulin oxidation over gold supported catalysts. From the results presented in Table 3 it can be seen that for most of the studied materials, betulin conversion does not exceed 8% (i.e., for 6 out of 8 samples), including Au/HT, Au/ZrO₂, Au/ZnO and Au/HMS, for which betulin conversion is less than 2%, despite different textural and structural properties (Table 2), as well as the average size of gold nanoparticles and their distribution. At the same time, for all these catalysts, the gold particle size exceeds 3 nm displaying a wide distribution, with a significant fraction of gold particles being larger than 10 nm (Supporting Information, Fig. S2). This is probably the reason for low activity of such catalysts in betulin oxidation.

For Au/CeO₂ with gold particles of 2.6 nm, betulin conversion after 6 h was 27% with selectivity to betulone (B), betulonic (D) and betulinic aldehydes (C) of 43, 18 and 39 %, respectively (Fig. 1, Table 3). For Au/Al₂O₃_V with gold particles of 3.1 nm, betulin conversion reaches already 71% in 30 minutes, being 97% after 6 h with selectivity to betulone (B), betulonic aldehyde (D) and betulinic acid (E) of 29, 64 and 7 %, respectively. Even if the particle size of gold in Au/Al₂O₃_V is 1.2 fold larger than in Au/CeO₂, betulin conversion is 3.6 fold higher, meaning that, the size of gold particles is not only factor determining catalytic behaviour. The textural and structural properties of supports should be also taken into account. Ceria has large pores exhibiting the specific surface area of 38 m²/g. Alumina is characterized by a better developed porous structure and a higher specific surface area of $277 \text{ m}^2/\text{g}$.

For deeper understanding of the reasons for the observed catalytic behavior of Au/Al₂O₃, a series of materials based on gold nanoparticles supported on alumina with different morphology and modification was prepared, characterized and tested in betulin oxidation (Section 3.2.).

3.2. Betulin oxidation over gold on various types of alumina supports

3.2.1. Catalyst characterization results

Structural characteristics of bare alumina supports and catalysts containing gold were determined by X-ray diffraction (Supporting Information, Fig. S4). Table 4 shows the phases detected for each alumina support, their crystallite sizes, and some other characterization data. Four out of five aluminas are in the boehmite phase with an orthorhombic framework. For Al₂O₃V, γ or η -alumina with a cubic framework was found. The average crystal size for the bare supports varies slightly from 4 nm (for Al₂O₃_V) to 6.4 nm (for AlOOH_C). Gold deposition leads to a change in the structure and composition of the support only in the case of Al_2O_3 V, for which, along with the main phase of γ or η-alumina (89%), also the boehmite phase was present (7%), resulting from a change in the support during the catalyst preparation [56]. Au phase was detected by XRD for all Au/alumina materials. The gold loading determined by the Rietveld refinements is in good agreement with elemental analysis data (Table 4). For three out of five studied samples, the average crystal size of gold obtained from XRD data is close to the average particle size of gold determined by HRTEM (Table 4). For Au/Al₂O₃_V and Au/AlOOH_L, the values obtained from XRD are slightly higher than those determined by HRTEM (Table 4). It is well known that lower particles are not detected by XRD, therefore it is possible that XRD gives an overestimation of the average size. Fig. 2 shows Au particle size distribution and HRTEM images of Au/alumina materials. Gold on AlOOH S shows the broadest nanoparticle size distribution (2 - 19 nm) with the largest average nanoparticle size of 4.2 nm. A broad distribution of Au particles (1 - 14 nm) was also observed for Au/AlOOH_L, while the average Au size was 3.2 nm. Gold on AlOOH shows the large average nanoparticle size (3.7 nm), not exhibiting

such a wide distribution (1-11 nm). Smaller Au nanoparticles are found on the surface of AlOOH_C and Al₂O₃_V with average sizes of 2.9 and 3.1 nm, and with the narrowest distributions, i.e., 2 - 5 and 2 - 11 nm, respectively.

Table 4 also shows the BET surface area, pore size and pore volume of the bare supports and Au/alumina materials. After deposition of Au, specific surface area for almost all studied catalysts noticeably decreased, except Au/Al₂O₃_V, for which it remained practically unchanged. A decrease in the specific surface area probably originated from an increase in the average crystal size of aluminas after gold deposition, as well as a decrease in the accessible pores. All studied materials exhibited a mesoporous structure. For supports, pores size vary from 5.7 (for AlOOH_S) to 11.7 nm (for Al₂O₃_V). For the corresponding catalysts, these values are slightly lower, which can be caused by partial blocking of the pores by gold [80].

Au/alumina materials were further investigated by XPS (Fig. 3). The chemical state of Au found on the alumina supports and their relative atomic concentrations are listed in Table 5. On the surface of Au/AlOOH_S and Au/AlOOH_L, gold is only in the metallic (Au⁰) state with BE (Au 4f_{7/2}) in the range of 84.0 - 84.2 eV [39, 60,64,65], while for Au/Al₂O₃_V (13%), Au/AlOOH (10%) and Au/AlOOH_C (19%) an additional state of gold with BE (Au 4f_{7/2}) in the range 85.0 - 85.3 eV [39, 60, 69, 77-79] related to Au⁺ ions was found.

A special focus is given to surface oxygen species (Fig. 3), since, as repeatedly noted in the literature, they play a special role in different type of reactions [81-89], namely, chemisorbed oxygen species are affirmed as the most reactive oxygen species for phenol photocatalytic degradation, oxidative coupling of alcohol and amine, phenol wet oxidation, NO oxidation, low-temperature CO oxidation, etc. For all studied catalysts, the O 1s peak can be deconvoluted into three bands associated

with the lattice oxygen at 530 - 531 eV (marked as O_I), the low coordination oxygen species, surface defects/vacancies, and hydroxyl groups at 531 - 532 eV (marked as O_{II}), carbonate species and/or adsorbed water at 532 - 534 eV (marked as O_{II}) [85-94]. The relative contribution of each oxygen species is presented in Table 5. According to this Table, the main contribution is from O_{II} species, with their surface concentration varying from 46% (for Au/AlOOH) to 72% (for Au/AlOOH_C) in good agreement with the structural data. In Table 2, four out of five materials are present in the boehmite phase. Moreover, for Al₂O₃_V after gold deposition this phase is also observed, which means the presence of a large amount of OH specie on the surface. The contribution of lattice oxygen (O₁) is higher for Au/AlOOH, almost the same value is observed for Au/Al₂O₃_V and Au/AlOOH_L, while for Au/AlOOH_S and Au/AlOOH_C this value is almost 1.5 and 2 folds lower than for the previous ones. The amount of O_{III} species does not exceed 7%.

3.2.2. Catalytic results

Catalytic data for a series of catalysts bearing gold nanoparticles on several alumina supports with different texture and morphology in betulin oxidation are presented in Table 6 and Fig. 4.

The highest betulin conversion of 97% in 6 h was achieved on Au/Al₂O₃_V and Au/AlOOH_L, giving mainly betulonic aldehyde (D), followed by betulone (B) and betulinic acid (E) (Table 6, entries 1 and 5). Despite high conversion, the mass balance closure (GCLPA - the sum of the reactant and product masses in GC analysis (%)) was far from complete (ca. 60%). For Au/AlOOH betulin conversion was lower, while the product yield was almost the same (62%) due to better GCPLA – 72% (Table 6, entry 2). For the catalysts mentioned above, the distribution of products was rather similar. For Au/AlOOH_S and Au/AlOOH_C, betulin conversion was significantly lower than for other catalysts (Table 6, entries 3 and 4). At the same time, for Au/AlOOH_C, the total product yield was the highest (69%) among the studied catalysts with the highest GCLPA (91%) (Table 6, entry 4). In both latter cases, the main product was betulone (B), followed by betulonic aldehyde (D) and betulinic acid (E).

It should be noted that in the reaction products, betulinic aldehyde (C) was observed only in the initial period of reaction contrary to a previous study [39], when for the most active Au/La₂O₃/TiO₂, the selectivity to betulin aldehyde (C) was 27%. It can be assumed that in current case it was very quickly transformed into betulonic aldehyde (D) or betulinic acid (E) (Fig. 1). It should be taken into account that for Au/Al₂O₃_V, Au/AlOOH_L and Au/AlOOH, the concentration of betulinic acid (E) in the reaction media increased only up to betulin conversion level of 80%, followed by a decrease (Fig. 4). This may be explained by further transformations of betulinic acid (E), giving higher molecular weight products, not detectable by GC, thereby giving lower values of GCPLA for these catalysts. Similar trends for the discrepancy between the total yield of products and conversion were previously observed in our recent work [39] (Table 6, entry 6). This was ascribed to an incomplete mass balance caused by side reactions of oligomerization/polymerization occurring with the participation of strong acid sites on the catalyst surface. Most likely, in the case of Au/alumina materials, similar centers are responsible for side reactions. It is difficult, however, to have an unequivocal conclusion because of difficulties in an adequate determination of the acidic properties of used aluminas. The following reasons can be mentioned. When using the Hammett indicator method, water cannot be considered inert as upon its adsorption on the Lewis centers, additional Brønsted acid centers are created, being absent in the initial catalyst [95]. Surface layers of alumina in an aqueous media can be transformed by surface dissociation, deprotonation and dimerization via a hydroxyl bridge into various types of ions and multinuclear cations [96,97]. According to temperature-programmed desorption of ammonia (TPD of NH₃), boehmite structure contains ca. 20% of weakly and strongly bound water giving an overestimation of acidity, while at elevated temperature boehmite starts to be transformed into γ -alumina [98,99], not present in the catalysts studied here.

Analyzing the kinetic plots and the yields of the main products at the same conversion level of 70% (Table 6 and Fig. 4), it is interesting to note that for three of the five studied catalysts

(Au/Al₂O₃_V, Au/AlOOH_L and Au/AlOOH) the product yields are very close. For Au/AlOOH_S and Au/AlOOH_C, the yields of the main products differ significantly from other materials. Namely, for Au/AlOOH_S, the yield of betulone (B) was 39%, otherwise not exceeding 27%. For Au/AlOOH_C, the yield of betulonic aldehyde (D) was 20%, while for other catalysts it was below 9%. A possible explanation may be the involvement of active oxygen species (O_{II}) on the catalyst surface. Such species can promote betulin oxidation, in line with their maximum concentration on the surface of Au/AlOOH_S and Au/AlOOH_C (Table 5). For the latter materials, the largest yields of betulone (B) and betulonic aldehyde (D) were observed (Table 6, entries 3 and 4) at 70% conversion of betulin. Confirmation that these species are involved in betulin oxidation comes from an experiment carried out under neat nitrogen, with all other conditions being the same. In such experiment, betulin conversion was 69% in 6 h (Table 7, entry 8) compared to 77% obtained using synthetic air (Table 6, entry 4). It is also worth noting that the betulin conversion on bare supports did not exceed 5% in 6 h.

Table 6 also shows the TOF values calculated after 5 min. The highest TOF values among the studied catalysts were obtained for Au/Al₂O₃_V and Au/AlOOH_L, followed by Au/AlOOH and Au/AlOOH_C, and finally Au/AlOOH_S. For comparison, Table 6 also contains the TOF value for the most active Au/La₂O₃/TiO₂ from the previous study [39], which is significantly lower than the TOF values calculated for Au/alumina materials. Visualization of TOF dependence on the average particle size of gold is given in Fig. 5 (including data for Au/La₂O₃/TiO₂) showing a volcano type behaviour. Previously [100], structure sensitivity of the same type was observed for the gold catalyzed aerobic selective oxidation of lignan hydroxymatairesinol (HMR) into oxomatairesinol (oxoMAT).

In [100] noncompetitive adsorption of the reactant and molecular oxygen on different sites was assumed and the rate expression was simplified considering the zero order in oxygen and a fractional reaction order in HMR. Similar kinetic regularities have been observed in the current work as will be discussed in section 3.2.3, thus leading to the following expression for TOF:

$$TOF = \frac{ke^{\alpha\chi/d_{cluster}K_BC_B}}{1+K_Be^{\chi_B/d_{cluster}C_B}}$$
(4)

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where α is the Polanyi parameter, χ - reflects differences in the Gibbs energy of betulin adsorption on edges and terraces, k and K correspond to the rate constant of betulin transformations and its adsorption constant on terraces, respectively.

While in [100] a modified version of eq. (4) was used to describe a maximum in the rates per mass of catalyst, eq. (4) *per se* can also be applied to describe an optimum in TOF dependence as a function of the cluster size as demonstrated for decarboxylation of stearic acid [101].

In the present study, the same mathematical model as in [100] was applied, and a similar trend of the dependence of TOF on Au cluster size was obtained. As can be seen from Fig. 5, the applied model adequately describes the experimental data for TOF dependence on the average particle size of gold. Thus, it can be concluded that the oxidation of betulin is also a structure sensitive reaction, requiring an optimum of ca. 3.3 nm.

It should be noted, that while TOF dependence on the average gold particle size has a very clear trend, not only the cluster size, but the nature of the support should be also taken into account. In the case of Au/La₂O₃, deposition of gold on the surface of lanthana led to a change in the phase composition as mentioned in section 3.1.1. Presence of La₂(CO₃)₂(OH)₂ also affects catalytic activity of Au/La₂O₃ in betulin oxidation in a unique way, therefore not only the average size of gold particles determines catalytic behavior.

3.2.3. Kinetic regularities in betulin oxidation over Au/AlOOH_C

The effect of the catalyst mass on betulin concentration as a function of normalized time (i.e., time multiplied by catalyst mass) is shown in Fig. 6. The curves should overlap with each other if there is no deactivation or influence of gas/liquid mass transfer [102]. In the current case, betulin concentration after 6 h was higher with a lower amount of catalyst, indicating presence of catalyst deactivation due to strong adsorption of the reactant. The corresponding conversion levels for different masses of catalysts are shown in Table 7 (entries 1-4).

3.2.3.1. Reaction rates, conversion levels and liquid phase mass balance closure in betulin oxidation over Au/AlOOH_C

The initial rates calculated from formation of the products between 0 to 5 min are shown in Fig.7, as a function of the oxygen content, initial betulin concentration and temperature.

The effect of temperature on the initial reaction rate, calculated from formed products increased from 80 to 140 °C (Table 7, entries 3, 5-7, Fig. 7c). The mass balance closure in the liquid phase was under these conditions ($C_{0,bet}$.=4.5 mmol/l, 0.2 g catalyst, 20% oxygen), above 90% in the whole studied temperature range (Table 7, entries 3, 6, 7) except entry 5 (GCLPA = 82%).

Effect of oxygen amount in the reaction atmosphere in betulin oxidation showed that the initial reaction rate was rather independent on the reaction atmosphere (Fig. 7a). Moreover, the initial reaction rate, in the case of pure nitrogen was the same as when using 20% oxygen in nitrogen (Table 7, entries 3 and 8). The highest liquid phase mass balance closure was observed in nitrogen atmosphere, being 94%, while in the presence of 12%, 48% and 100% oxygen, the GCLPA varied in the range of 70-78 %. Interestingly, high GCLPA was obtained when using 20% oxygen, being 91%. Betulin conversion was slightly lower in a neat nitrogen atmosphere, being 69% after 6 h, while with oxygen, the conversion levels were in the range of 77 - 82%.

The initial rates calculated from formed products between 0 - 5 min increased with increasing initial betulin concentration (Fig. 7b), indicating that the reaction order was higher than zero. Nearly complete conversion of betulin was observed for the two lowest initial betulin concentrations, (Table 7, entries 12, 13). The liquid phase mass balance closure, GCLPA, was very small for these experiments because of large available specific surface area, compared to the amount of betulin or products.

3.2.3.2. Product distribution in betulin oxidation over Au/AlOOH_C

The concentration profiles of betulin and the main products, betulone and betulonic aldehyde as a function of time, are shown in Fig. 8, varying the initial concentration of betulin, at different reaction

temperatures, in Fig. 9, and with different oxygen contents, in Fig. 10, while the concentration profiles of the minor products. betulinic aldehyde and betulinic acid are shown in Fig. S5-S7 (Supporting information). In all experiments the yield of the final product, betulonic acid was very low (Table 7). The two primary products in betulin oxidation are betulone and betulinic aldehyde (Fig. 1). The highest concentrations of betulone were obtained under 20% oxygen with 4.52 mmol/l initial betulin concentration at 140 °C (Fig. 8b, Table 7, entry 3), while betulinic aldehyde formation is favored with the highest initial betulin concentration (Fig. S5a, Table 7, entry 14). The selectivity to betulone was also plotted as a function of conversion, showing that slightly lower betulone selectivity was obtained with the highest initial betuline concentration, while with the initial betulin concentration varying in the range of 1.13 mmol/l – 4.52 mmol/l, the difference in betulone selectivity was minor (Fig. 11).

The effect of temperature can be clearly seen for betulone formation, which increased with increasing temperature (Fig. 9b, Table 7, entries 3, 5-7). This can also be clearly seen when plotting betulinic aldehyde concentration vs betulone concentration at different temperatures (Fig. 12c). Oxidation of C3 hydroxyl group and formation of betulone was favored at high temperature (Fig. 9c, 12c), indicating that betulone formation has a higher activation energy than competing routes. The activation energy for betulone formation was calculated to be 38 kJ/mol. This value is in agreement with the upper limit for activation energy for transformation of adsorbed benzyl carboxylate to benzoic acid, over a Pd/C catalyst, in benzyl alcohol oxidation, with oxygen, being below 40 kJ/mol [103].

In nitrogen atmosphere a low conversion of betulin was obtained due to its rapid reaction to betulonic aldehyde (Fig. 10, Table 7, entry 8). A low yield of betulone was obtained also in nitrogen atmosphere (Table 7, entry 8) due to a fast formation of betulonic aldehyde under nitrogen (Fig. 10a, c). In addition to an optimum oxygen amount, also an optimum initial concentration of betulin and the highest studied reaction temperature were favorable for the formation of betulone (Fig. 10b, Table 7, entry 3), while the lowest betulone concentrations being observed both with low and high initial betulin concentrations.

The highest concentrations of betulinic aldehyde, when oxidation of betulin is occurring at C27 hydroxyl group, were observed at a high initial betulin concentration and at intermediate temperature 100 - 120 °C (Fig. S6a), when the adsorption through this hydroxyl group seems to be is favored. According to the reaction scheme (Fig. 1), the consecutive reaction from betulinic aldehyde and betulone is the formation of betulonic aldehyde, which was most prominent under nitrogen atmosphere at 140 °C with 0.2 g catalyst and 4.52 mmol/l initial betulin concentration. At low initial betulin concentrations, betulinic aldehyde reacted further, giving a maximum of betulonic aldehyde concentration at 30 min. Nearly the same concentrations and yields of betulonic aldehyde were observed in the temperature range of 100 - 140 °C, while, at 80 °C, betulonic aldehyde formation was very small (Fig. S6b, Table 7, entries 3, 5 - 7). This result can be explained by the slow rates of both reactions. A sharp decrease in the concentration of betulinic aldehyde after 30 minutes when using 20% oxygen (Table 7, entry 3, Fig. S7a) can be noted and explained by rapid transformations of betulinic aldehyde preferentially into betulinic acid. Such transformations are becoming more apparent when analyzing the effect of oxygen content on the changes in the concentration of betulinic aldehyde (Fig. S7a) and betulinic acid (Fig. S7b) with time. A sharp increase in the concentration of betulinic acid occurs simultaneously with a sharp decrease in the concentration of betulinic aldehyde.

Betulinic acid is only formed by oxidation of betulinic aldehyde, which has an aliphatic aldehyde group attached to a cyclic group. It is known from literature that benzyl alcohol oxidation via benzaldehyde to benzylic acid is favored at high temperatures, i.e., at 100 °C, in air, over a Pt/C catalyst, in 7 h [104]. In the current case, the highest yield of betulinic acid by betulinic aldehyde oxidation was obtained at 4.52 mmol/l initial betulin concentration, at 140 °C, with 12 and 20% oxygen (Figs 8e, S6c), while with higher oxygen concentration and in the absence of oxygen, nearly no betulinic acid was formed (Table 7, entry 8, Fig. S7b).

Formation of the final product, betulonic acid, under the studied reaction conditions was minor (Table 7), due to catalyst deactivation, which is caused by strong reactant/product adsorption on the

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catalyst surface as well as by poisoning water, which is formed in stoichiometric amounts, blocking the active sites.

4. Conclusions

The current work is a continuation of the study of the liquid phase oxidation of betulin over supported gold catalysts. Gold was deposited on oxide supports characterized by different textural, structural and chemical properties (hydrotalcite, ZrO₂, ZnO, MgO, CeO₂, La₂O3, HMS, various types of alumina). It was found, that the support nature determines the uniformity of gold particle distribution and their mean size, and as a result, the catalytic behavior of supported gold catalysts in betulin oxidation. Such supports as hydrotalcite, ZrO₂, ZnO, MgO, La₂O₃, HMS were characterized by a wide distribution of gold nanoparticles with a significant fraction of particles being larger than 10 nm, and as a consequence, resulting in a very poor activity in betulin oxidation. Alumina materials proved to be more suitable supports for gold nanoparticles. Gold catalysts based on them were characterized by a narrower distribution of gold nanoparticles (1 - 11 nm), and the highest catalytic activity in betulin oxidation among studied materials. The highest betulin conversion of ca. 100% in 6 h was achieved on Au/Al₂O₃_V and Au/AlOOH_L having almost the same mean size of gold nanoparticles, exhibiting, however, different phases, namely, boehmite and γ -alumina. Similar to the recently studied gold supported on a modified titania, Au/alumina materials also gave side reactions, leading to a discrepancy between the observed conversion and the products yield, as well as an activity decrease due to strong adsorption of reactant and products. As a result, the highest products yield of 69% was achieved on Au/AlOOH_C, having a lower level of betulin conversion of 77%, but the highest mass balance closure among studied Au/alumina catalysts. In the latter case, the main product was betulone (47 %), followed by betulonic aldehyde (34%) and betulinic acid (17%). It should be noted that among all catalysts studied by the authors in betulin oxidation, appearance of betulinic acid in the reaction products was observed only for Au/alumina catalysts. In addition, in the present study, it was revealed that betulin oxidation is a structure sensitive reaction. The highest turnover frequency for betulin oxidation was found for an optimum gold particle size of 3.3 nm.

Kinetics of betulin oxidation over Au/AlOOH_C catalyst was investigated with different initial betulin concentrations, oxygen amounts and temperatures in mesitylene as a solvent. The reaction order in the substrate was higher than zero, being zero toward oxygen. The conditions favorable for obtaining a specific oxo-derivative of betulin with higher selectivity were determined. In the case of betulone, these conditions are a low initial concentration of betulin, a high temperature and a high catalyst loading, while the oxygen content had practically no effect. For betulinic aldehyde, a low initial concentration of betulin and catalyst loading, an intermediate temperature ($100 - 120^{\circ}$ C) and neat oxygen were favorable. The amount of betulonic aldehyde in the reaction products increased with an increase in the initial concentration of betulin and temperature and lower catalyst loading. The oxygen content did not affect the amount of betulonic aldehyde; at the same time, its highest concentration was obtained in neat nitrogen. Betulinic acid was formed only in the case of initial betulin concentration of 4.52 mmol/l, 140 ° C and a low oxygen content of 12 – 20%. Regardless of the reaction conditions, the amount of betulonic acid did not exceed 2%.

E. Kolobova: Investigation; Writing -Original draft, P. Mäki-Arvel: Writing- review and editing, Conceptualization; Supervision; A. Grigoreva: Investigation, E. Pakrieva: Investigation; S.A.C. Carabineiro; : Investigation; Supervision; J. Peltonen: Investigation; S. Kazantsev: Investigation, N. Bogdanchikova: : Investigation; A. Pestryakov: Conceptualization; Funding acquisition; D. Yu. Murzin : Writing- review and editing, Conceptualization; Supervision

Declaration of interests

☑ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The research is funded from the Russian Science Foundation project No. 18-73-00019 and Tomsk Polytechnic University Competitiveness Enhancement Program, project VIU-ISHBMT-65/2019 (Russia). This work was partially supported by Fundação para a Ciência e a Tecnologia, Portugal (2020-2023 multiannual funding to Centro de Química Estrutural). Authors thank Dr. Carlos Sá

(CEMUP) for the assistance with XPS analyses and Prof. Pedro Tavares (UTAD) for assistance with XRD analyses.

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Fig. 1. Reaction scheme for betulin oxidation (adapted from [39]).









0,

Au/AlOOH_C

Au/AlOOH_C





Fig. 3. Au 4f and O 1s XPS spectra of studied catalysts.



a)



Fig. 4. Kinetics of betulin oxidation on a) Au/Al₂O₃_V, b) Au/AlOOH, c) Au/AlOOH_S, d) Au/AlOOH_C, e) Au/AlOOH_L, data are presented taking into account the mass balance; Conditions: 140 0 C, synthetic air (50 ml/min) as oxidant, solvent - mesitylene, initial betulin concentration – 4.5 mmol/l, 0.2 g catalyst.



Fig. 5. Dependence of TOF on the average Au particle size.*data from [39] for Au/La₂O₃/TiO₂.



Fig. 6. Concentration of betulin as a function of normalized time (time multiplied by catalyst mass) in betulin oxidation at 140 °C with 20% oxygen. Symbols: 0.05 g (\blacksquare), 0.1 g (\square), 0.2 g (\bullet) and 0.4 g (\blacktriangle) of Au/AlOOH_C.





Fig. 7. Initial rate for formation of products between 0 - 5 min in betulin oxidation as a function of a) oxygen amount, b) initial betulin concentration and c) temperature.



c)

Fig. 8. Effect of the initial betulin concentration on a) betulin, b) betulone and c) betulonic aldehyde concentration as a function of time in betulin oxidation at 140 ^o C under 20% oxygen with 0.2 g catalyst. Symbols: (O) 1.13 mmol/l, (\Box) 2.26 mmol/l, (\blacksquare) 4.52 mmol/l and (\blacktriangle) 9.04 mmol/l.



Fig. 9. Effect of temperature on a) betulin, b) betulone and c) betulonic aldehyde concentration as a function of time in betulin oxidation with 4.52 mmol/l initial betulin concentration under 20% oxygen with 0.2 g catalyst. Symbols: (\Box) 80 °C, (o) 100 °C, (•) 120 °C and (**=**) 140 °C.



Fig. 10. Effect of oxygen content on a) betulin, b) betulone and c) betulonic aldehyde concentration as a function of time in betulin oxidation at 140 °C with with 4.52 mmol/l initial betulin concentration with 0.2 g catalyst. Symbols: (x) 0%, (\Box) 12 %, (**\blacksquare**) 20%, (\bullet) 48% and (O) 100%.



Fig. 11. Selectivity to betulone as a function of conversion in betulin oxidation at 140 $^{\circ}$ C under 20% oxygen with 0.2 g catalyst. Symbols: (O) 1.13 mmol/l, (\Box) 2.26 mmol/l, (\blacksquare) 4.52 mmol/l and (\blacktriangle) 9.04 mmol/l.



Fig. 12. Concentration of betulinic aldehyde as a function of betulone concentration with different a) initial betulin concentrations, symbols: (O) 1.13 mmol/l, (\Box) 2.26 mmol/l, (\blacksquare) 4.52 mmol/l and (\blacktriangle) 9.04 mmol/l, b) oxygen amounts, symbols: (x) 0%, (\Box), 12 %, (\blacksquare) 20%, (\bullet) 48% and (O) 100% and c) temperatures, symbols: (\Box) 80 °C, (o), 100 °C, (\bullet) 120 °C and (\blacksquare) 140 °C.

Table 1

The values of experimental variables (temperature, catalyst mass, initial betulin concentration and

Entry	T (°C)	m _{catalyst} (g)	C _{0,Betulin} (mmol/l)	Oxygen content (%)
1	140	0.05	4.52	20
2	140	0.1	4.52	20
3	140	0.2	4.52	20
4	140	0.4	4.52	20
5	80	0.2	4.52	20
6	100	0.2	4.52	20
7	120	0.2	4.52	20
8	140	0.2	4.52	0*
9	140	0.2	4.52	12
10	140	0.2	4.52	48
11	140	0.2	4.52	100
12	140	0.2	1.13	20
13	140	0.2	2.6	20
14	140	0.2	9.04	20

oxygen content).

Table 2

X-ray powder diffraction data for the studied supports and the corresponding gold catalysts, specific surface area, contents of Au and average Au particle size. The obtained phase weight proportions $w_i/\Sigma w$ and estimated average crystal sizes d_c for the measured samples, are based on the Rietveld refinements.

Sample	Observed phase (framework)	w _i /Σw (%)	d _c (nm)	$R_{wp} (\%)^a$	S _{BET} (m²/g)	Au content (wt.%) by ICP	Au average particle size (nm) by HRTEM
UТ	MgO (cubic)	98	7.0 ± 1	5 ^d	13		
111	CaCO ₃ (rhombohedral)	2	45.0 ± 10	5 ^d	+5		-
ZrO_2	ZrO ₂ (monoclinic)	100	107.0 ± 3	4 ^d	5	-	-
ZnO	ZnO (hexagonal)	100	270.0 ± 40	5 ^d	5	-	-
MgO^b	MgO (cubic)	100	18.0 ± 1	-	141	-	-
$\mathrm{CeO}_2^{\mathrm{c}}$	CeO ₂ (cubic)	100	-	-	37	-	-
LanOn ^c	La ₂ O ₂ (CO ₃) (hexagonal)	-	-		3		
$La_2O_3^{\circ}$	La ₂ O ₂ (CO ₃) (monoclinic)	-	-		7	-	-
HMS	SiO ₂ amorphous	100	-	-	478	-	-
$Al_2O_3_V$	Al ₂ O ₃ (γ or η , cubic)	100	4.0 ± 1	5 ^d	274	-	-
A.,./IIT	Hydrotalcite	97	3.8 ± 0.5	24	10	3.85	5 4
Au/111	Au	3	1.6 ± 1	24	10	5.65	5.4
$\Delta u/7r\Omega_{c}$	ZrO ₂ (monoclinic)	96	24.6 ± 3	12	5	3.86	13.0
$Au/2iO_2$	Au	4	6.3 ± 0.5	12	J	5.00	15.0
$\Delta u/7nO$	ZnO (hexagonal)	96	25.6 ± 0.5	10	3	3.99	7 4
Au/ZIIO	Au	4	4.5 ± 0.5	10	7	5.00	/.4
Au/MaO	Mg(OH) ₂ (hexagonal)	9 9	7.7 ± 0.5	13	210	2.95	61
Au/MgO	Au	< 1	3.2 ± 0.5	13	512	5.65	0.1
Au/CeO2 ^b	CeO ₂ (cubic)		-	-	38	4.30	2.6
	La(OH) ₃ (hexagonal)						
Au/La ₂ O ₃ ^b	$La_2(CO_3)_2(OH)_2$	-	-	-	10	4.50	3.6
	(orthorhombic)	-	-	-			
	SiO ₂ amorphous	98	-	-	162	2 70	10.2
Au/HMS	Au	2	13.8 ± 1.6	8	105	5.19	18.2
	Al ₂ O ₃ (cubic)	89	-	13			
Au/Al_2O_3V	AlO(OH) (orthorhombic)	7	10.0 ± 0.5	13	277	3.95	3.1
	Au	4	4.5 ± 0.3	13			

 ${}^{a}R_{wp}$ (%) - the weighted profile R-factor

^bTwo peaks remained unidentified and are ascribed to unidentified phases

^cdata from [60]

 $^d\mbox{The}$ quality of the Rietveld refinement fit is described by the parameter $R_{exp},$ where a smaller value of

 R_{exp} indicates a better fit to the measured data.

Table 3

Catalytic behaviour of Au supported on different metal oxides in betulin oxidation.

Entry	Catalyst	X (%)	Selectivity (%)						
	5	`` <i>`</i>	SB	\mathbf{S}_{D}	\mathbf{S}_{F}	Sc	$S_{\rm E}$		
1	Au/HT	1	0	0	0	0	100		
2	Au/ZrO ₂	1	0	0	0	0	100		
3	Au/ZnO	1	0	0	0	0	100		
4	Au/MgO	8	41	20	0	0	39		
5	Au/CeO ₂	27	43	18	tr.	39	0		
6	Au/La ₂ O ₃	8	39	3	2	56	0		
7	Au/HMS	2	31	0	0	0	69		
8	$Au/Al_2O_3_V$	97	29	64	0	0	7		

X – conversion of betulin after 6 h (%); S_B – selectivity to betulone (%); S_D – selectivity to betulonic aldehyde (%); S_F – selectivity to betulonic acid (%); S_C – selectivity to betulinic aldehyde (%); S_E – selectivity to betulinic acid; Conditions: 140°C, synthetic air (50 ml/min) as oxidant, solvent – mesitylene, initial betulin concentration – 4.5 mmol/l, catalyst mass - 0.2 g.

Table 4

Physico-chemical characterization data for alumina supports and the corresponding gold catalysts.

Sample	Observed phase (framework)	w _i /∑w ^a (%)	d _c (nm) ^a	$R_{wp} (\%)^b$	S _{BET} (m ² /g)	Pore size (nm)	Pore volume (cm ³ /g)	Au content (wt.%) by ICP	Au average particle size (nm) by HRTEM
Al ₂ O ₃ _V	Al ₂ O ₃ (γ or η , cubic)	100	4.0 ± 1	5°	274	11.7	1.14	-	-
Alooh	AlO(OH) (orthorhombic)	100	4.8 ± 0.1	15	398	7.5	1.07	-	-
AlooH_S	AlO(OH) (orthorhombic)	100	5.6 ± 0.1	17	385	5.7	0.67	-	-
AlOOH_C	AlO(OH) (orthorhombic)	100	6.4 ± 0.1	18	321	5.8	0.41	-	-
AlOOH_L	AlO(OH) (orthorhombic)	100	5.2 ± 0.1	15	334	8.8	0.98	-	-
	Al ₂ O ₃ (cubic)	89	-	13					
Au/Al ₂ O ₃ _V	AlO(OH) (orthorhombic)	H) (orthorhombic) 7 10.0 ± 0.5 13 277		11.4	4 1.06	3.95	3.1		
	Au	4	4.5 ± 0.3	13					
Au/Alooh	AlO(OH) (orthorhombic)	96	12.0 ± 0.5	12	350	69	0.78	3.80	37
110/110011	Au	4	3.5 ± 0.3	12	550	0.9	0.70	5.00	5.7
	AlO(OH) (orthorhombic)	96	9.1 ± 0.5	13	293	6.0	0.55	3.94	4.2
nu/noon_b	Au	4	4.0 ± 0.3	13	275	0.0	0.55	5.74	7.2
Au/Alooh C	AlO(OH) (orthorhombic)	97	8.4 ± 0.5	13	254	56	0.52	3.95	29
nu/noon_c	Au	3	3.0 ± 0.3	13	2.54	5.0	0.52	5.75	2.7
	AlO(OH) (orthorhombic)	96	5.8 ± 0.5	13	285	82	0.82	3.92	3.2
/ M// MOOII_L	Au	4	3.7 ± 0.3	13	205	0.2		5.72	5.2

^aThe weight fractions $w_i/\Sigma w$ and the estimated average crystal sizes d_c were based on the Rietveld refinements.

 ${}^{b}R_{wp}\left(\%\right)$ - the weighted profile R-factor

^cThe quality of the Rietveld refinement fit is described by the parameter Rexp, where a smaller value of Rexp indicates a better fit to the measured data.

Table 5

Contribution of electronic states of gold and oxygen calculated according to XPS for studied catalysts.

Sample	Au 4f _{7/2}		O 1s					
	Au ⁰ (%) (84.0 – 84.2 eV)	Au ⁺ (%) (85.0 – 85.3 eV)	O _I (%) (530 – 531 eV)	O _{II} (%) (531 - 532)	O _{III} (%) (532 – 534)			
Au/Al ₂ O ₃ _V	87	13	43	51	6			
Au/AlOOH	90	10	47	46	7			
Au/AlOOH_S	100	0	32	61	7			
Au/AlOOH_C	81	19	24	72	4			

Au/AlOOH_L	100	0	45	50	5	
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Table 6

Catalytic behaviour of Au/alumina catalysts in betulin oxidation.

Entry Catalyst	Catalyst	X (%)	TOF (s ⁻¹) ^a	GCLPA	Select	Selectivity (%)				$\mathbf{V}_{\mathrm{P}}(\%)$	$\mathbf{V}_{\mathrm{P}}(\%)$	$\mathbf{V}_{\mathrm{E}}(\%)$	$\Sigma Y_{\text{product}}(\%)$
	Cataryst	Α(/0)		(%)	SB	SD	$S_{\rm F}$	Sc	SE	IB(/0)	10(/0)	1 E (70)	
1	Au/Al ₂ O ₃ _V	97	0.549	59	29	64	0	0	7	23	9	7	57
2	Au/AlOOH	90	0.469	72	40	48	0	0	12	23	9	6	62
3	Au/AlOOH_S	74	0.185	81	56	21	0	0	23	39	7	9	56
4	Au/AlOOH_C	77	0.263	91	47	34	0	2	17	27	20	9	69
5	Au/AlOOH_L	97	0.533	65	35	56	0	0	9	23	6	6	62
6	Au/La ₂ O ₃ /TiO ₂ ^b	69	0.007 ^c	80	42	31	0	27	0	20	15	0 (13 ^d)	48

X – conversion of betulin after 6 h (%); GCLPA - the sum of reactant and product masses in GC analysis (%); S_B – selectivity to betulone after 6 h (%); S_D – selectivity to betulonic aldehyde after 6 h (%); S_F – selectivity to betulonic acid after 6 h (%); S_C – selectivity to betulinic aldehyde after 6 h (%); S_E – selectivity to betulinic acid after 6 h (%); Y_B , Y_D , Y_E - yield of betulone, betulonic aldehyde and betulinic acid at 70% conversion of betulin (%), respectively; $\sum Y_{product}$ - total product yield after 6 h (%); ^aTOF was calculated after 5 min; ^bData from [39]; ^cTOF was calculated after 15 min; ^dYield of betulinic aldehyde; Conditions: 140 ^o C, synthetic air (50 ml/min) as oxidant, solvent - mesitylene, initial betulin concentration – 4.5 mmol/l, 0.2 g catalyst.

Table 7

The initial rate calculated from formation of all products visible in GC analysis between 0 - 5 min, liquid phase mass balance determined by GC analysis, conversion after 6 h and yields of different products at 60 % conversion and in parenthesis after 6 h^{a,b} in betulin oxidation in mesitylene as a solvent.

Entry T	T (°C)	m _{catalyst}	$C_{0,Betulin}$	Oxygen	r ₀	GCLPA	X (%)	$\mathbf{Y}_{\mathbf{p}}(\%)$	$\mathbf{Y}_{c}(\%)$	$\mathbf{Y}_{\mathbf{p}}(\%)$	$\mathbf{Y}_{\mathrm{r}}(\%)$	$\mathbf{Y}_{r}(\%)$
Lifting	1(0)	(g)	(mmol/l)	content (%)	$(mmol/min/g_{cat})$	(%)	A (70)	I B(/0)	10(70)	1 D(/0)	1 E(/0)	1 F(70)
1	140	0.05	4.52	20	0.009	97	12	^a (5)	(5)	(5)	(1)	(<1)
2	140	0.1	4.52	20	0.015	88	38	^a (8)	(6)	(11)	(<1)	(<1)
3	140	0.2	4.52	20	0.077	91	77	(32)	(1)	(23)	(11)	(0)
4	140	0.4	4.52	20	0.041	21	~ 100	^a (19)	^a (<1)	^a (1)	^a 0 (0)	^a (<1)
5	80	0.2	4.52	20	0.007	82	41	^a (4)	^a (6)	^a (13)	^a (<1)	^a (<1)
6	100	0.2	4.52	20	0.031	95	53	^a (14)	^a (11)	^a (23)	^a (<1)	^a (<1)
7	120	0.2	4.52	20	0.045	90	71	17	10	21	<1	<1
/ 1	120	0.2	4.52	20	0.045	50	/1	(24)	(12)	(25)	(<1)	(<1)
8	140	10 0.2	4.52	0	0.078	9/	60	n.a.	n.a.	n.a.	n.a.	n.a.
0	140	0.2	4.52	0	0.078	94	09	(20)	(11)	(36)	(<1)	(<1)
9	140	0.2	4.52	12	0.070	78	81	^b (29)	^b (9)	^b (18)	^b (<1)	^b (<1)
10	140	0.2	4.52	18	0.070	73	87	15	17	14	<1	<1
10	140	0.2	4.32	40	0.070	13	02	(26)	(10)	(19)	(<1)	(<1)
11	140	0.2	4.50	100	0.070	70	01	13	7	14	<1	<1
11	140	0.2	4.52	100	0.070	/0	81	(22)	(11)	(17)	(<1)	(<1)
12	140	0.2	1.13	20	0.031	58	~ 100	^b (56)	^b (<1)	^b (1)	^b (<1)	^b (0)
13	140	0.2	2.26	20	0.034	58	~ 100	^b (53)	^b (<1)	^b (2)	^b (<1)	^b (0)
14	140	0.2	9.04	20	0.090	97	35	^a (9)	^a (7)	^a (15)	^a (<1)	^a (<1)

^ayields are given after 6 h due to either very slow or ^bvery rapid disappearance of betulin, n.a. not available