Terpenoid transformations over gold catalysts

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+H$_2$

Au

+PhNH$_2$

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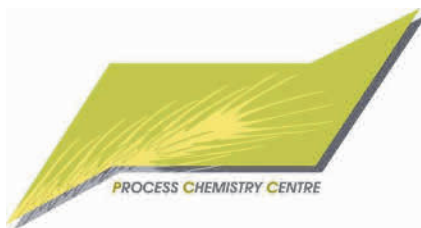

Ph.D. Kinetics and Catalysis, 2013

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Preface

Abstract

Yuliya S. Demidova

Terpenoid transformations on gold catalysts

Nowadays biomass transformation has a great potential for the synthesis of value-added compounds with a wide range of applications. Terpenoids, extracted from biomass, are inexpensive and renewable raw materials which often have a biological activity and are widely used as important organic platform molecules in the development of new medicines as well as in the synthesis of fine chemicals and intermediates. At the same time, special attention is devoted to the application of gold catalysts to fine chemical synthesis due to their outstanding activity and/or selectivity for transformations of complex organic compounds. Conversion of renewable terpenoids in the presence of gold nanoparticles is one of the new and promising directions in the transformation of biomass to valuable chemicals. In the doctoral thesis, different kinds of natural terpenoids, such as α-pinene, myrtenol and carvone were selected as starting materials. Gold catalysts were utilized for the promising routes of these compounds transformation.

Investigation of selective α-pinene isomerization to camphene, which is an important step in an industrial process towards the synthesis of camphor as well as other valuable substrates for the pharmaceutical industry, was performed. A high activity of heterogeneous gold catalysts in the Wagner-Meerwein rearrangement was demonstrated for the first time. Gold on alumina carrier was found to reach the α-pinene isomerization conversion up to 99.9% and the selectivity of 60-80%, thus making this catalyst very promising from an industrial viewpoint. A detailed investigation of kinetic regularities including catalyst deactivation during the reaction was performed.

The one-pot terpene alcohol amination, which is a promising approach to the synthesis of valuable complex amines having specific physiological properties, was investigated. The general regularities of the one-pot natural myrtenol amination in the presence of gold catalysts as well as a correlation between catalytic activity, catalyst redox treatment and the support nature were obtained. Catalytic activity and product distribution were shown to be strongly dependent on the support properties, namely acidity and basicity. The gold-zirconia (Au/ZrO_2) catalyst pretreated under oxidizing atmosphere was observed to be rather active, resulting in the total conversion of myrtenol and the selectivity to the corresponding amine of about 53%. The reaction kinetics was modelled based on the mechanistic considerations with the catalyst deactivation step incorporated in the mechanism.

Carvone hydrogenation over a gold catalyst was studied with the general idea of investigating both the activity of gold catalysts in competitive hydrogenation of different functional groups and developing an approach to the synthesis of valuable carvone derivatives. Gold was found to promote stereo- and chemoselective carvone hydrogenation to dihydrocarvone with a predominant formation of the *trans*-isomer, which generally is a novel synthetic method for an industrially valuable dihydrocarvone. The solvent effect on the catalytic activity as well as on the ratio between *trans*- and *cis*-dihydrocarvone was evaluated.

Referat

Yuliya S. Demidova
Omvandling av terpenoider med guldkatalysatorer

Nuförtiden har omvandling av biomassa en stor potential för syntes av värdefulla komponenter med många tillämpningar. Terpenoider, som har extraherats ur biomassan, är billiga förnyelsebara råmaterial, vilka ofta är biologiskt aktiva och de används som viktiga organiska intermediärer vid utveckling av nya läkemedel samt vid syntes av finkemikalier och specialkemikalier. Samtidigt har det ägnats mycket uppmärksamhet för tillämpning av guld som katalysatormetall för syntes av finkemikalier, därför guldnanopartiklar har visat sig vara mycket aktiva och selektiva i kemisk omvandling av komplexa organiska föreningar. Omvandling av förnybara terpenoider i närvaro av guldnanopartiklar är en av de nya och lovande inriktningarna vid omvandling av biomassa till värdefulla kemikalier. I doktorsavhandlingen valdes olika typers naturligt förekommande terpenoider, s.s. α-pinen, myrtenol och karvon som råmaterial. Guldkatalysatorer utnyttjades vid omvandling av dessa komponenter i lovande reaktionsrutter.

Selektiv isomerisering av α-pinen till kamfen, vilket är ett viktigt steg i en industriell process mot syntes av kamfor och andra värdefulla komponenter inom läkemedelsindustrin, undersöktes i avhandlingen. En hög aktivitet av heterogena guldkatalysatorer i Wagner-Meervein-omvandlingen demonstrerades för första gången. Guld på aluminiumoxidbärare möjliggjorde en omsättning av α-pinen up till 99.9% med selektiviteten 60-80% och visade sig vara en lovande katalysator även ur industriell synvinkel. En detaljerad undersökning av kinetiska regelbundenheter och katalysatordeaktivering under reaktionens förlopp utfördes.

Aminering av terpenalkohol i ett steg, vilket är ett lovande system för syntes av värdefulla komplexa aminer med specifika fysiologiska egenskaper, undersöktes. De allmänna regelbundenheterna i ettstegsaminering av naturligt förekommande myrtenol i närvaro av guldkatalysatorer samt korrelationer mellan katalytisk aktivitet, katalysatorns redoxtillstånd och bärarmaterialets egenskaper utvecklades. Den katalytiska aktiviteten och produktfördelningen visade sig vara starkt beroende av bärarmaterialets egenskaper, nämligen surhet och bashet. Guld på zirkoniumoxid (Au/ZrO_2) som behandlades under en oxiderande atmosfär observerades vara ganska aktiv samt resultera i fullständig omsättning av myrtenol och ca 53%:s selektivitet för respektive amin. Reaktionskinetiken modellerades med hjälp av mekanistiska idéer samt genom att beakta katalysatorns deaktivering.

Karvonhydrering på guldkatalysatorer undersöktes som ett exempel på konkurrerande hydrering av olika funktionella grupper och en metod för syntes av värdefulla karvonbaserade produkter utvecklades. Guld upptäcktes gynna stereo- och kemoselektiv karvonhydrering till dihydrokarvon med bildning av trans-isomeren som huvudprodukt. Detta förfarande är en ny syntesmetod för industriellt viktig dihydrokarvon. Inverkan av lösningsmedlet på katalysatorns aktivitet samt förhållandet mellan trans- och cis-dihydrokarvon undersöktes också i arbetet.

Реферат

Юлия Сергеевна Демидова

Превращения терпеноидов в присутствии золотых катализаторов

В настоящее время переработка компонентов возобновляемого растительного сырья с использованием гетерогенных катализаторов для получения ценных соединений с широким спектром применения имеет большой потенциал. Терпеноиды, содержащиеся в составе эфирных масел и живиц хвойных деревьев, зачастую обладают биологической активностью и широко используются для получения их производных с новыми физиологическими свойствами, а также ценных продуктов тонкого органического синтеза. Вместе с тем применение наночастиц золота в реакциях тонкого органического синтеза представляет особый научный интерес в связи с их необычайно высокой активностью и/или селективностью, обнаруженной для некоторых реакций. В данной работе в качестве исходных субстратов были выбраны разные типы соединений природного происхождения – α-пинен, миртенол, карвон – и исследованы перспективные маршруты их превращения.

Изучена изомеризация α-пинена в камфен, которая является важной стадией промышленного процесса синтеза камфары, а также некоторых биологически активных веществ. Впервые показана высокая активность гетерогенных нанесенных золотосодержащих катализаторов в перегруппировке Вагнера-Меервейна. Предложена оптимальная Au/γ-Al$_2$O$_3$ каталитическая система для изомеризации α-пинена в камфен, позволяющая достичь 99.9%-ной конверсии при 60-80%-ной селективности, что делает данный катализатор привлекательным с промышленной точки зрения. Изучены основные кинетические закономерности реакции в присутствии Au/γ-Al$_2$O$_3$, включая исследование процессов дезактивации катализатора.

Изучены основные закономерности жидкофазного аминирования миртенола в присутствии гетерогенных Au катализаторов. Исследовано влияние природы носителя, окислительно-восстановительных условий формирования активного Au компонента на активность и селективность образования основных продуктов в этой реакции. Показано, что наиболее активным и селективным является Au/ZrO$_2$ катализатор, прошедший окислительную термообработку, в котором соотношение основных и кислотных центров на поверхности носителя наиболее благоприятно среди исследованных катализаторов. Исследованы кинетические закономерности аминирования миртенола с учетом вклада процессов дезактивации. Предложены схема механизма и кинетическая модель реакции.

Исследована реакция гидрирования карвона в присутствии Au катализатора с целью изучения активности золотых катализаторов в конкурентном гидрировании различных функциональных групп, а также разработки подхода для синтеза ценных производных карвона. Показана высокая активность гетерогенных нанесенных золотосодержащих катализаторов в стерео- и хемоселективном гидрировании карвона в дигидрокарвон с преимущественным образованием *транс*-изомера, что является новым методом синтеза промышленно ценного дигидрокарвона. Изучено влияние растворителя на каталитическую активность и соотношение между *транс*- и *цис*-дигидрокарвоном.

List of publications

I. I.L. Simakova, **Yu. S. Solkina (Demidova)**, B. L. Moroz, O.A. Simakova, S.I. Reshetnikov, I.P. Prosvirin, V.I. Bukhtiarov, V.N. Parmon, D.Yu. Murzin, *Selective vapour-phase α-pinene isomerization to camphene over Au catalysts.* Appl. Catal. A, 2010, 385, 136–143.

II. **Yu.S. Solkina (Demidova)**, S. Reshetnikov, M. Estrada, A.V. Simakov, D.Y. Murzin, I.L. Simakova, *Evaluation of gold on alumina catalyst deactivation dynamics during α-pinene isomerization.* Chem. Eng. J., 2011, 176-177, 42-48.

III. **Yu.S. Demidova**, I.L. Simakova, M. Estrada, S. Beloshapkin, E.V. Suslov, D.V. Korchagina, K.P. Volcho, N.F. Salakhutdinov, A.V. Simakov, D.Yu. Murzin, *One-pot myrtenol amination over Au nanoparticles supported on different metal oxides.* Appl. Catal. A, 2013, 464-465, 348-356.

IV. **Yu.S. Demidova**, I.L. Simakova, J. Wärnå, A.V. Simakov, D.Yu. Murzin, *Kinetic modelling of one-pot myrtenol amination over Au/ZrO$_2$ catalyst.* Chem. Eng. J., 2014, 238, 164–171.

V. **Yu.S. Demidova**, E.V. Suslov, O.A. Simakova, I.L. Simakova, K.P. Volcho, N.F. Salakhutdinov, D.Yu. Murzin, *Selective carvone hydrogenation to dihydrocarvone over titania supported gold catalyst.* Catal. Today, 2013 (submitted).

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4. D.Yu. Murzin, **Y. Demidova**, B. Hasse, B. Etzold, I.L. Simakova, *Synthesis of fine chemicals using catalytic nanomaterials: structure sensitivity, in Producing Fuels and Fine Chemicals from Biomass Using Nanomaterials*, Chapter 10, CRC Press, 2013, 267-283.

5. **Yu.S. Demidova**, O.V. Ardashov, O.A. Simakova, I.L. Simakova, K.P. Volcho, N.F. Salakhutdinov, D.Yu. Murzin, *Isomerization of bicyclic terpene epoxides into allylic alcohols without changing of the initial structure.* J. Mol. Catal., 2013 (accepted).

6. **Yu.S. Solkina (Demidova)**, I.L. Simakova, B.L. Moroz, O.A. Simakova, S.I. Reshetnikov, A.V. Simakov, D.Yu. Murzin, V.N. Parmon. *Devepolopment of selective camphene synthesis by vapor-phase α-pinene isomerization over nanosized Au catalyst.* //9th Congress on catalysis applied to fine chemicals, Zaragoza, Spain, September 13-16, 2010, p. 95.

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8. **Yu. Demidova**, I. Simakova, S. Reshetnikov, I. Prosvirin, O. Simakova, M. Estrada, A. Simakov, D. Murzin. *Dynamics of Au/Al$_2$O$_3$ deactivation during a-pinene to camphene isomerization in hydrogen atmosphere. Kinetic and deactivation aspects in the transformation of α-pinene to camphene over gold catalysts.* //Catalysis in Multiphase Reactors Multifunctional Reactors CAMURE 8 & ISMR 7, Naantali, Finland, May 22-25, 2011, p. 59.

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14. **Yu.S. Demidova**, I.L. Simakova, M. Estrada, S. Beloshapkin, J. Wärna, E.V. Suslov, K.P. Volcho, N.F. Salakhutdinov, A.V. Simakov, D.Yu. Murzin. *Nanosized gold catalysts for one-pot natural monoterpene alcohol amination.* //XIth European congress on catalysis, Lyon, France, September 1-6, 2013, S7-T6-DS22-02.

Contents

1. Introduction

The attention of the world scientific community is increasingly focused on environmental protection and efficient use of natural resources. A huge number of scientific publications on biomass transformation into valuable commercial chemicals have appeared recently [1-3]. Currently, the design of the new catalytic routes starting from renewables and different from traditional chemical synthesis routes is one of the key issues of sustainable development and holds a great potential for further investigation as well as synthesis of a range of valuable compounds [4].

Natural terpenoids, based on multiples of the five -carbon isoprene subunit, represent a large and diverse class of organic compounds which often have biological activity and are widely used as important organic platform molecules in the development of new medicines as well as in the synthesis of fine chemicals and intermediates [5-7]. More than 22 000 individual terpenoids are currently known, making them the largest group of natural compounds.

Nowadays, special attention is devoted to the utilization of gold catalysts for fine chemical synthesis due to its unique activity for transformations of complex organic compounds. Many reviews concerning the application of nano-gold catalysis in organic reactions have been published, including those of Hashmi and Hutchings in 2006 [8], Corma and Garcia in 2008 [9], Stratakis and Garcia [10] and Zhang et al. in 2012 [11]. Moreover, some examples of outstanding activity and/or selectivity of nanosized gold catalyst in the conversion of biomass-derived compounds have been also described recently [12]. Nevertheless, the conversion of renewable terpenoids in the presence of gold nanoparticles is one of the new and promising directions in transformation of biomass to valuable chemicals.

In this work different kinds of natural terpenoids, such as α-pinene, its oxygenated derivative myrtenol and carvone, which are hydrocarbon, alcohol and ketone, respectively, were selected as starting materials. Gold catalysts were utilized for the perspective routes of these compounds transformation.

Isomerization of α-pinene, which is the major component of turpentine oil derived from coniferous trees, in the presence of acid catalysts results in the formation of different mono-, bi- and tricyclic terpenes (Scheme 1) [2].

α–Pinene

Camphene

Tricyclene

p-Cymene   **Limonene**   **α–Terpinene**
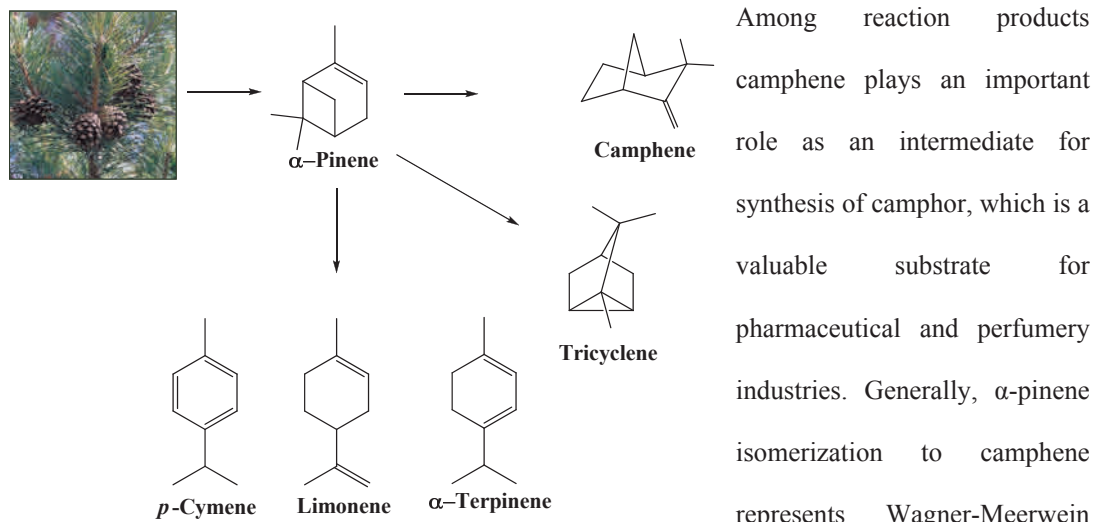
Scheme 1. Reaction pathways of α-pinene isomerization catalyzed by acid catalysts.

Among reaction products camphene plays an important role as an intermediate for synthesis of camphor, which is a valuable substrate for pharmaceutical and perfumery industries. Generally, α-pinene isomerization to camphene represents Wagner-Meerwein rearrangement, namely alkyl group migration from one carbon to a neighboring carbon.

In industry, the transformation of α-pinene into camphene is performed in liquid phase at 423-443 K over TiO_2 catalyst activated *in situ* by H_2SO_4 with rather low reaction rates, giving yields from 35 to 50% [13]. Other acidic catalysts such as natural [14-17] and synthetic zeolites [18-20], activated carbon [21], clays [13, 22], ion exchange resins [23] and silica supported - rare earth oxides [24] have been also examined. However, in the presence of these catalysts a complex mixture of isomers was obtained in most cases, particularly without selective formation of camphene. At the same time, taking into account the fact that cationic gold(I) complexes have recently evolved as excellent Lewis acid catalysts for various Wagner-Meerwein shifts, such as the ring expansion of cyclopropanols to the corresponding cyclobutanones [25, 26], utilization of heterogeneous gold catalysts have a great potential for this reaction [**I, II**]. To the best of our

knowledge, supported gold metal catalysts have never been tested before for α-pinene isomerization.

Another challenge in the organic catalysis for fine chemicals is to develop selective amination of alcohols to yield amines of a certain structure having specific physiological properties. Complicated amines based on natural monoterpene alcohols are of high practical interest for the development of new pharmaceuticals. In particular complicated terpene amines, synthesized from renewable raw materials, were recently shown to exhibit specific physiological properties, such as antiparkinsonian, anxiolytic, antiepileptic activities, and can be used as intermediates of potential drugs for neurological diseases [27-30].

The one-pot alcohol amination is a perspective approach to the synthesis of complicated amines with different structures. The synthesis generally consists of three consecutive steps: dehydrogenation of an alcohol to a reactive aldehyde, which reacts with an amine to produce a corresponding imine and the hydrogen transfer from the alcohol to the imine *via* metal-hydride intermediates with the amine formation (Scheme 2).
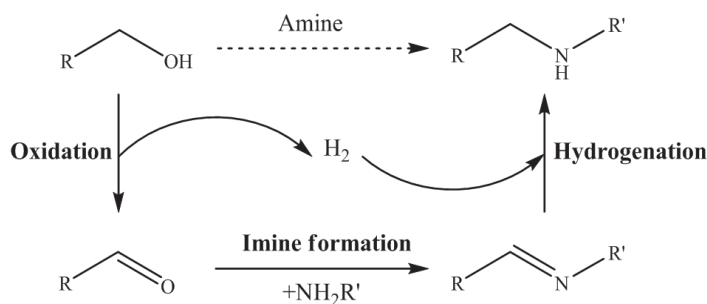
Scheme 2. Schematic view of the one-pot alcohols amination.

The one-pot multistep reaction holds a high potential for increasing the efficiency for chemical synthesis of medicinally and biologically important compounds. At the same time, the complexity of this process is reflected by a large number of parameters which can influence each step. Thus the integrated study of the one-pot alcohol amination is a difficult, but necessary task in the development of an effective process for the synthesis of valuable amines. For a long time, special attention was focused on this process, initially in the presence of homogeneous catalysts [31-34] and more recently, different heterogeneous metal

catalysts [35-38]. Gold catalysts are shown to be highly effective for the direct alcohol amination by using benzyl alcohol and aniline as typical model substrates [39-41]. In order to study general regularities of one-pot natural terpene alcohol amination in the presence of gold catalysts, myrtenol, which represents a natural terpene alcohol with a primary hydroxyl group, was selected as a model substrate [**III, IV**].

Ultimately, the last part of the work is devoted to the investigation of carvone hydrogenation [**V**], which is one of the most widespread natural monoterpenoids [42] and is widely used in food and perfumery industry [43] as well as in the synthesis of fine chemicals [44-47]. This process is of great practical interest to obtain a range of valuable products, including dihydrocarvone (Scheme 3), which is formed as a mixture of two stereoisomers and has spearmint-like odor and is used as a flavoring additive in various food products [43, 48].
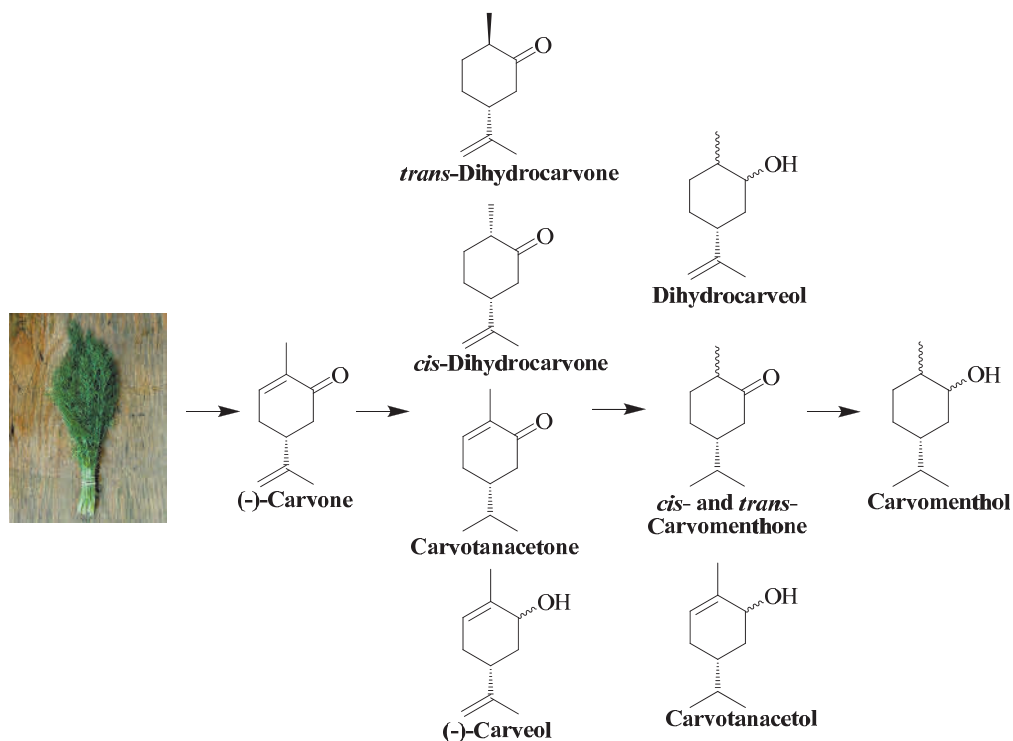
Scheme 3. Reaction pathways of carvone hydrogenation.

At the same time, carvone is an interesting substrate to explore the catalyst activity in stereo- and chemoselective hydrogenation, because it contains an asymmetric center with a specific configuration as well as three types of functional groups, which can be hydrogenated: $C=O$, conjugated $C=C$ and isolated $C=C$ groups. In general, the selective hydrogenation of multifunctional organic molecules is one of the topics, which is actively studied in catalytic fine chemistry.

Carvone can be hydrogenated to dihydrocarvone by using $Bu_3SnH/Pd(PPh_3)_4$ in the presence of protonic or Lewis acids [49], metal hydrides [50, 51], zinc powder in the presence of $NiCl_2$ [52] and alkali alcohol solution [47], $Me(EtO)_2SiH$ in the presence of various complexes of copper and palladium [53], sodium dithionite [54] and using enzymatic methods [55]. At the same time, carvone hydrogenation by molecular hydrogen in the presence of heterogeneous catalysts is a more effective approach in terms of green chemistry. There are a lot of examples of carvone hydrogenation over different heterogeneous catalysts as well [56-64]. However, in the presence of these catalysts dihydrocarvone was not found or was formed only in small yields up to 30% as a part of complex mixtures. To the best of our knowledge, there is no heterogeneous catalyst that allows the formation of dihydrocarvone via carvone hydrogenation at high selectivity.

Gold has been used in hydrogenation reactions acting as a very promising catalyst, especially in selective hydrogenations. For a long time, enormous attention was given to chemoselective hydrogenation of unsaturated carbonyl compounds to the corresponding unsaturated alcohols over gold catalysts [8-10, 65-71]. The advantage of using gold was the ability to selectively hydrogenate the $C=O$ group in presence of to $C=C$ group, as the latter hydrogenation is kinetically and thermodynamically favored. At the same time, in the case of carbonyl compounds containing different conjugated and isolated $C=C$ double bonds, predominant conjugated $C=C$ double bond hydrogenation was observed over the gold catalysts, for example, in the case of citral [68]. Additionally, the $C=C$ double bond in ketones, having more sterically unhindered $C=O$ group

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compared to aldehydes, was observed to be predominantly hydrogenated [68]. Therefore, utilization of gold catalysts for carvone hydrogenation to valuable dihydrocarvone is a promising approach.

Thus, summarizing it can be stated that, terpenoids are a rich source for the chemical synthesis of value-added compounds with a wide range of applications. The general idea of this work was to study some commercially interesting pathways of natural terpenoid transformations in the presence of gold catalysts.

2. Experimental

2.1. Substrates

α-Pinene was isolated from turpentine oil by vacuum distillation and contained the following impurities: tricyclene – 0.19 wt. %, camphene – 1.61 wt. %, β-pinene – 3.54 wt. %, 3-carene – 1.30 wt. %. (1 R)-(-)-Myrtenol of 95.0% purity, (1 R)-(-)-myrtenal (≥97.0%) and aniline (99.5%) for alcohol amination as well as (-)-carvone (98.0%), D-(+)–dihydrocarvone of 98.0% purity (mixture *cis*- and *trans*-isomers, *cis*-/*trans*- = 20:80), L-(-)-carveol of 97.0% purity (mixture *cis*- and *trans*-isomers, *cis*-/*trans*- = 54:46) and (-)-limonene (97.0%) were supplied by Sigma-Aldrich (Germany) and used as received.

n-Octane and toluene applied as solvents for α-pinene isomerization and one-pot myrtenol amination, respectively, were purchased from Reakhim (Russia) and purified by vacuum distillation. The monoterpenoids hydrogenation was studied utilizing methanol (Sigma-Aldrich, Germany), ethanol (Reakhim, Russia) and 2-propanol (Reakhim, Russia), which were additionally dried before experiments.

2.2. Catalysts

2.2.1. Gold catalysts for α-pinene isomerization

The gold catalysts for investigation of α-pinene isomerization were synthesized at Surface Science Laboratory at Boreskov Institute of Catalysis (Novosibirsk) by Boris L. Moroz and Pavel A. Pyrjaev.

2.2.1.1. Supports

A series of the following supports were selected for α-pinene isomerization:

1. ceria was synthesized from $Ce(NO_3)_3 \cdot 6H_2O$ by Pechini method and granulated (particle size 200-500 μm, $S_{BET} = 110$ m^2/g, lattice parameter 5.403 Å).

2. γ-alumina modified by lanthanide (Ln) oxides was synthesized by impregnation of alumina support by water solution of nitrate La (III) or a mixture of Ln nitrate followed by calcination in air at 1073 K. Microspheroidal γ-Al_2O_3 was produced at Boreskov Institute of Catalysis from pseudoboehmite (particle size 500-700 μm, S_{BET} = 185 m^2/g, total pore volume 0.93 cm^3/g).

3. carbon composite material Sibunit was supplied by Institute of Hydrocarbon Processing (Omsk) (particle size 200-500 μm, S_{BET} = 281 m^2/g, total pore volume 0.39 cm^3/g).

4. γ-alumina (R,S) was synthesized from boehmite and granulated at Boreskov Institute of Catalysis (particle size 200-500 μm, S_{BET} = 149 m^2/g, total pore volume 0.45 cm^3/g).

5. γ-alumina was supplied by Ryazan Oil Refinery Company (Russia) (particle size 200-500 μm, S_{BET} = 268 m^2/g, total pore volume 0.69 cm^3/g)

2.2.1.2. Catalyst preparation

Hydrogen tetrachloroaurate HAuCl₄·aq (49.47 wt. % Au) used as a gold precursor was purchased from Aurat (Russia) and used without further purification. Several methods of catalyst preparation were applied:

1. deposition-precipitation technique with NaOH for Au supported on CeO_2, γ-Al_2O_3 (R,S) and γ-Al_2O_3 modified by lanthanide oxides. The samples obtained were washed with water, filtered, dried at room temperature and then calcined at 673 K for 4 h.

2. modified deposition-precipitation technique with ethylenediamine instead of NaOH for carbon-supported gold catalyst;

3. wetness impregnation for Au/γ-Al_2O_3 was similar to the methods previously described in ref. [72]. After treatment in flowing H_2 at 673 K for 4 h, the sample was additionally treated with an aqueous 1M NaOH solution for removal of Cl⁻ and neutralization of acidic sites on the support surface. Thereafter, it was thoroughly washed with warm distilled water to remove Na⁺ and excess hydroxide ions. Finally, the sample was dried at 373 K for 8 h using

a vacuum system and calcined in air at 473 K for 4 h. Some catalysts were additionally calcined in air at 473 K for 4 h and at 873 K for 4 h and 21 h.

2.2.2. Gold catalysts for one-pot myrtenol amination

The gold catalysts for one-pot myrtenol amination were synthesized at Centro de Nanociencias y Nanotecnología de la Universidad Nacional Autónoma de México by the group of Prof. Andrey V. Simakov.

2.2.2.1. Supports

Commercial CeO_2, Al_2O_3, La_2O_3, ZrO_2 (Alfa Aesar) and MgO (Mallinckrodt) oxides were used as supports. The specific surface area and pores of oxides are presented in [**III**].

2.2.2.2. Catalyst preparation

Catalysts with 3% wt. Au over such oxides as CeO_2, Al_2O_3, La_2O_3, ZrO_2 (Alfa Aesar) and MgO (Mallinckrodt), respectively, were synthesized by deposition-precipitation technique using $HAuCl_4$ (Alfa-Aesar) as a gold precursor and urea as a precipitating agent similar to the procedure described elsewhere [73]. In order to remove the excess of chloride after gold deposition, the samples were washed with a 25 M solution of NH_4OH (pH ca. 10), in accordance with [74, 75]. Thereafter, the samples were washed with deionized water, filtered and dried at room temperature for 24 h. Then the samples were calcined in oxygen while heating from room temperature up to 623 K with a ramp rate of 20°/min.

2.2.3. Gold catalysts for carvone hydrogenation

The 2 wt. % Au/TiO_2 catalyst was prepared at Åbo Akademi University by Dr. Olga A. Simakova from $HAuCl_4$ aqueous solution (5×10^{-4} M) by deposition-precipitation with urea (DPU) at 354 K during 24 h onto TiO_2 (Degussa AG, Aerolyst 7708, anatase >70%,

$S_{BET} = 45$ m^2/g). The obtained slurry was washed with NH$_4$OH aqueous solution (4 M) and deionized water. Thereafter, the catalyst was dried at 333 K for 12 h and calcined at 573 K for 4 h. The catalyst was characterized by a variety of state of the art physical methods described in detail in [76].

2.3. Catalyst characterization

2.3.1. Inductively coupled plasma atomic emission spectroscopy

The metal loading of the gold catalysts supported on alumina modified by lanthanide oxides, titania as well as in catalysts for myrtenol amination was determined by inductively coupled plasma atomic emission spectroscopy (ICP-AES) using a Varian Liberty 110 ICP Emission Spectrometer.

2.3.2. X-ray fluorescence

The Au and Cl contents of the catalysts for α-pinene isomerization except gold supported on alumina modified by lanthanide oxides were measured using X-ray fluorescence (XRF) technique on a VRA-30 instrument equipped with a Cr-anode. Diffuse reflectance UV–vis spectra were recorded on a Shimadzu UV-2501 PC spectrometer equipped with an ISR-240 integrating sphere attachment for diffuse reflectance measurements, using BaSO$_4$ as a reference, in the range of 200–1000 nm and presented in Kubelka–Munk function F(R)-wavelength coordinates.

2.3.3. Nitrogen adsorption

Specific surface areas and pore size distribution determined by physisorption of nitrogen in a Tristar II 3020 Micromeritics equipment. Prior to surface area measurements, the samples were treated in vacuum (0.05 mbar) at 623 K for 12 hours.

2.3.4. Transmission electron microscopy

Transmission electron microscopy (TEM) studies were carried out on a JEOL JEM-2010 electron microscope operated at 200 kV and giving an information limit of 0.14 nm. Before the TEM measurements, the samples were dispersed in isopropanol and dropped on a copper grid coated with a carbon film. To estimate the value of the mean diameter of the Au nanoparticles more than 250 particles were chosen. The mean diameter (d_m) of particles was calculated using the following equation: $d_m = \dfrac{\sum_i (x_i d_i)}{\sum_i x_i}$, where x_i is the number of particles with diameter d_i.

2.3.5. X-ray photoelectron spectroscopy (XPS)

Photoelectron spectra were recorded using SPECS spectrometer with PHOIBOS-150 hemispherical energy analyzer and MgK_α irradiation (hν = 1253.6 eV, 100 W). Binding energy scale was preliminarily calibrated by the position of the peaks of $Au4f_{7/2}$ (84.0 eV) and $Cu2p_{3/2}$ (932.67 eV) core levels. For recording the spectra, the samples were supported to a conductive scotch tape. The binding energy of peaks was corrected to take into account the sample charging by referencing to the Al2p (74.5 eV) (internal standard). This reference was applied since the spectrometer was equipped with turbomolecular pumps, and calibration on the basis of the position of C1s core level, typically used in the case of vacuum systems with diffusion pumps, was difficult. The ratio of surface atomic concentrations of the elements was calculated from the integral intensities of photoelectron peaks corrected by corresponding atomic sensitivity factors. In addition to the conventional survey of photoelectron spectra, more narrow spectral regions Al2p, Au4f, Al2s, C1s, and O1s have been recorded. For the survey spectra the pass energy of the analyzer was 50 eV, while for the narrow spectral regions the pass energy was 10 eV.

The electronic state of gold species was also studied with Kratos AXIS 165 photoelectron spectrometer using monochromatic AlK_α radiation (hv=1486.58 eV) and fixed analyzer pass energy of 20 eV. All measured binding energies (BE) were referred to the C1s line of adventitious carbon

at 284.8 eV. The spectra fitting was done using Shirley background estimation over the energy range of the fit.

2.3.6. Temperature programmed oxidation

Analysis of organic deposits formed on the catalyst surface due to the side reactions was carried out in a lab made set-up including a flow reactor, quadrupole HP-20 mass-spectrometer (Hiden) with gas sampling at atmospheric pressure and AvaSpec-2048-USB2 UV-Vis spectrometer (Avantes) equipped with a reflectance fiber probe for high temperature measurements. The temperature programmed oxidation (TPO) with recording of UV-Vis spectra *in situ* (every 15 seconds) and in-line mass-spectrometric analysis of oxygen consumption and products formation was studied over a sample of Au/Al_2O_3 catalyst (0.2 g) in a flow of a gas mixture containing 5 vol. % O_2 and 5 vol. % Ar (rest He) under heating up to 800 K with a ramp 20K/min. A reactor filled with MgO was used as a reference sample for UV-Vis spectra recording. UV-Vis spectra were obtained by subtraction of the initial spectrum recorded at room temperature from others measured at elevated temperatures.

2.3.7. X-ray diffraction

X-ray diffraction (XRD) analysis of studied samples was carried out with a Philips X'pert diffractometer equipped with a curved graphite monochromator applying Cu K_{α} ($\lambda = 0.154$ nm) radiation. In order to identify the crystal phases, the diffractograms obtained were compared with the features presented in JCPDS-ICCD (Joint Committee on Powder Diffraction Standards International-Centre for Diffraction Data (2000)).

2.4. Experimental setup

2.4.1. Continuous mode

Vapour-phase isomerization of α-pinene was carried out under continuous flow conditions at atmospheric pressure using a solution of α-pinene in *n*-octane of the determined concentration as the initial reaction mixture and H_2 or N_2 as a carrier gas. A catalyst sample (0.2 g) was placed in a U-shaped glass tubular reactor of 4 mm i.d. equipped with a thermocouple which was fixed in the middle of the catalyst bed outside the reactor tube. The carrier gas was passed through the catalyst bed at the desired space velocity and the temperature was raised up to 463–483 K. Then α-pinene solution in *n*-octane was supplied via a heated pre-chamber of U-reactor to be vapourized and mixed with the carrier gas before passing to the catalyst bed. The catalyst was pre-activated *in-situ* by heating under hydrogen flow at 473 K for 1h.

2.4.2. Batch mode

The reactions of liquid-phase myrtenol amination and carvone hydrogenation were carried out in a stainless steel reactor (150 ml), equipped with an electromagnetic stirrer (1100 rpm) and the sampling system.

The one-pot myrtenol amination was performed by using a mixture of myrtenol (1 mmol), aniline (1 mmol) and the Au catalysts (92 mg, Au 1.4 mol. % to substrate) in toluene (10 ml) at 453 K under N_2 atmosphere (9 atm).

In the case of competitive hydrogenation of different functional groups, the solution of the substrate (10 mmol) in the corresponding solvent (36 ml) and Au/TiO_2 catalyst (336 mg, Au 0.3 mol. % to substrate) was used as the initial mixture. The experiments were conducted at 373 K under H_2 atmosphere (9 bar).

In both cases, at appropriate time intervals, aliquots were withdrawn form the reactor and analyzed by gas chromatography.

2.5. Product analysis

Generally, the reaction products were analyzed by gas chromatography using different columns and appropriate conditions of analysis. The products were confirmed by analysis with gas chromatograph-mass spectrometer (Agilent Technologies 7000 GC/MS Triple Quad, HP-5MS column) and NMR in some cases as well.

2.5.1. α-Pinene isomerization

The concentrations of reaction components in the reaction mixture were analyzed by a gas chromatograph («Tzvet-500») equipped with a flame-ionization detector and a capillary Carbowax-20M column (50 m/0.2 mm/0.5 μm) at 393 K. The temperature of the detector and evaporator was 473 K.

2.5.2. One-pot myrtenol amination

The reaction mixture was analyzed by using a SLB-5ms column (length 30 m, inner diameter 0.25 mm and film thickness 0.25 μm) and flame ionization detector operating at 573 K. The initial temperature of column was 323 K for 15 min and the temperature was increased at a rate 9 K/min to 553 K. The temperature of the evaporator was 573 K.

^{1}H- and ^{13}C-NMR spectra: *Bruker DRX-500* spectrometer (500.13 MHz (^{1}H) and 125.76 MHz (^{13}C)) in the CDCl$_3$ solutions of the substances; chemical shifts δ in ppm rel. to residual chloroform [δ(H) 7.24, δ(C) 76.90 ppm], *J* in Hz. The structure of the compounds was elucidated by analyzing the NMR spectra of ^{1}H and ^{13}C with the attraction of the spectra of the dual resonance of ^{1}H – ^{1}H, two-dimensional spectra of the heteronuclear of ^{13}C – ^{1}H of correlation on the straight constants of spin-spin interaction (C – H COSY, $^{1}J_{C,H}$ 160 Hz). The signal multiplicity in the ^{13}C NMR spectra was determined from the *J* modulation (JMOD).

Elemental composition was determined by mass spectra data recorded on a *DFS Thermo Scientific* spectrometer in full scanning mode in the range 0-500 *m/z*, ionization by electron impact 70 eV with direct insertion of the sample.

2.5.3. Carvone hydrogenation

The reaction mixture was analyzed by gas chromatograph («Tzvet-500») equipped with a Carbowax-20M column (length 50 m, inner diameter 0.2 mm and film thickness 0.5 μm) at 433 K and a flame ionization detector operating at 523 K. The temperature of the evaporator was 493 K. ^{1}H-NMR spectra were recorded by *Bruker AV-400* spectrometer (400.13 MHz (^{1}H)) in the CDCl$_3$ solutions of the reaction mixture. The chemical shifts of the *cis-* and *trans*-dihydrocarvones were determined in accordance with ref. [77].

3. Results and Discussion

3.1. Selective α-pinene isomerization to camphene [I, II]

3.1.1. Effect of catalyst support and thermal treatment

First in order to study the general regularities of α-pinene isomerization over gold catalysts, the gold catalysts with *ca.* 2% wt. Au over different supports including ceria, carbon composite material Sibunit, alumina as well as alumina modified by lanthanide oxides were examined.

As mentioned above, α-pinene isomerization has been actively studied mainly in the presence of heterogeneous catalysts such as zeolites [14-20], activated carbon [21], clays [13, 22], ion exchange resins [23] and silica supported rare earth oxides [24]. Thus, in the case of metal supported catalysts it is important to estimate the catalytic activity of the support *per se* as well as determine its role in the reaction. In our work, special attention was given to investigation of the activity of both the active metal, namely gold, and the support.

Basic supports CeO_2 and $\gamma-Al_2O_3$ modified by basic type lanthanide were not active *per se* in the reaction. Gold supported on these oxides showed a high α-pinene conversion and a high selectivity to camphene (Figure 1), but rapid deactivation was observed in the presence of these catalysts.

Figure 1. Catalytic activity of CeO_2 (1); Al_2O_3/La_2O_3 (2); Au/CeO_2 (3); $Au/Al_2O_3/LnO_x$ (4); $Au/Al_2O_3/La_2O_3$ (5) in α-pinene isomerization. Reaction conditions: T = 473 K, α-pinene concentration in *n*-octane 0.4 vol. %, τ = 0.33 s.

At the same time, carbon composite material Sibunit and γ-alumina *per se*, which contains the acid surface sites, catalyzed α-pinene isomerization (Figure 2). However, camphene formation was not selective and a significant amount of limonene was also observed. After neutralization of acid sites by alkaline treatment Sibunit (C/NaOH in Figure 2a) as well as γ-Al₂O₃ (γ-Al₂O₃/NaOH in Figure 2b) become inactive. The Au/γ-Al₂O₃ and Au/C catalysts

on modified supports exhibited high activity, with camphene and *p*-cymene being the main products. Among the catalysts investigated, the highest conversion and selectivity were achieved over Au/γ-Al$_2$O$_3$ catalyst. Compared to conventional α-pinene –to- camphene transformations over acid-hydrated TiO$_2$, resulting in camphene yields from 35% to 50%, gold on alumina was found to afford α-pinene isomerization conversion up to 99.9% and selectivity 60-80%. Generally speaking, the high activity of heterogeneous gold catalysts in Wagner-Meerwein rearrangement reactions, such as α-pinene isomerization to camphene was demonstrated for the first time in the open literature.

In order to confirm the role of gold nanoparticles in α-pinene transformation as well as to avoid possibility of support modification during the catalyst preparation, a blank experiment was performed in the presence of γ-Al$_2$O$_3$ lacking gold but subjected to the same kind of chemical and thermal treatment that was used at different stages of the gold catalyst preparation (except that a solution of 0.01M HCl was taken instead of HAuCl$_4$ solution for γ-alumina impregnation). As a result, only very low conversion (2.7%) was observed with a wide product distribution in which camphene and limonene were the main products. The data obtained suggested that gold as such plays the key role in the α-pinene transformation to camphene.

Figure 2. Catalytic activity of carbon composite material Sibunit (a) and γ-alumina supported (b) gold catalysts and supports *per se* in α-pinene isomerization. Reaction conditions: T = 473 K, α-pinene concentration in *n*-octane 0.4 vol. %, τ = 0.33 s.

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For Au/γ-Al$_2$O$_3$ the effect of thermal treatment on the catalytic activity was also studied. The conditions of the catalyst treatment are presented in the Table 1. Despite the high treatment temperature gold particle siz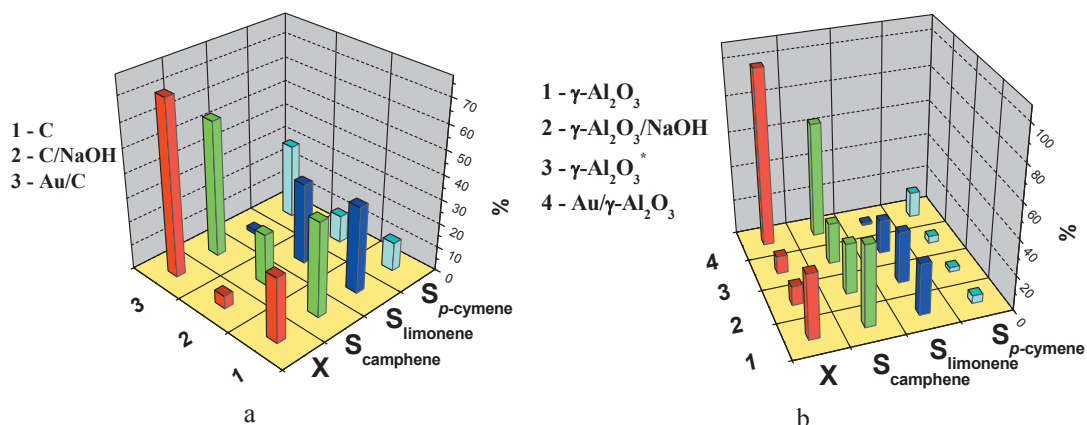es did not change significantly, while a treatment of Au/γ-Al$_2$O$_3$ under oxidizing conditions besides reducing atmosphere led to an increase in the ratio between the main reaction products, camphene and *p*-cymene. At the same time, the most stable catalyst was the sample exposed to thermal treatment first under reducing atmosphere for 4 hours at 673 K and then under oxidizing atmosphere for 4 hours at 673 K.

Table 1. Effect of Au/γ-Al$_2$O$_3$ catalyst thermal treatment on the ratio of camphene and *p*-cymene.

Sample	Temperature, K	Duration, h	Atmosphere	$S_{camphene}/S_{p\text{-}cymene}$	d_{Au}, nm
1	673	4	H$_2$	3.8	2.7±0.6
2	673	4	H$_2$	7.9	3.1±0.7
		4	O$_2$		
3	673	4	H$_2$	7.3	3.9±0.9
	873	4	O$_2$		
4	673	4	H$_2$	7.4	3.9±0.9
	873	21	O$_2$		

The study of the reaction mechanism was not the main focus of this work. However, to explain the outstanding activity of the Au/γ-Al$_2$O$_3$ catalyst in α-pinene isomerization to camphene, the following reaction mechanism based on kinetic observations as well as the literature data [15, 78] can be proposed. In the isomerization of α-pinene, the activity was shown to be strongly associated with the catalyst acidity, in particular it is supposed that the type of the active sites (Brønsted or Lewis) and their strength affect the selectivity to bicyclic and monocyclic products [78]. Taking into account that cationic gold(I) complexes have recently evolved as excellent Lewis acid catalysts for various Wagner-Meerwein shifts such as the ring expansion of cyclopropanols to the corresponding cyclobutanones [25, 26], participation of Au$^+$ species in the catalytic cycle of α-pinene isomerization over the Au/Al$_2$O$_3$ catalyst can be hypothesized. Thus, α-pinene was proposed to coordinate on Lewis acid sites (Au$^+$) through the electron-rich double bond.
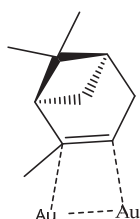
Figure 3. Proposed scheme for α-pinene adsorption on gold catalysts.

The molecule is oriented in a way, that the gem dimethyl groups are positioned away from the surface (Figure 3) and the double bond is then protonated since the support possesses Brønsted acidity. Such interactions with the surface favor the formation of camphene. In the absence of Lewis sites, α-pinene orients differently and can reach the surface with gem dimethyl groups and protonation of four member ring gives preferably limonene or *p*-cymene.

3.1.2. Reaction kinetics

A study of the effect of the support as well as of the thermal treatment allowed us to choose an optimum Au/γ-Al$_2$O$_3$ system for further investigations of kinetic regularities. The effects of temperature, residence time and initial α-pinene concentration on the α-pinene conversion and selectivity to camphene were studied over the Au/γ-Al$_2$O$_3$ catalyst.

The impact of internal diffusion was determined through evaluation of the catalyst effectiveness factor for spherical particles:

$$\eta_{ef} = \frac{3}{\varphi}\left(\frac{1}{\tanh\varphi} - \frac{1}{\varphi}\right) \tag{1}$$

If $\eta_{ef} \rightarrow 1$, the diffusion restriction is negligible. Parameter φ is Thiele modulus given:

$$\varphi = R\sqrt{\frac{k}{D_{ef}}} \tag{2}$$

where $R = 1.75 \times 10^{-4}$ m is the mean radius of the catalyst particles (200-500 μm) and the rate constant of the first order reaction k = 4.75 s^{-1} was found from the experimental data. Effective diffusion coefficient of α-pinene D_{ef} in hydrogen is defined as $D_{ef} = D\dfrac{\xi}{\chi}$, where D is the combined the molecular diffusivity and the Knudsen diffusivity calculated according to Bosanquet equation:

$$D = \left(\frac{1}{D_{mol}} + \frac{1}{D_k}\right)^{-1} \tag{3}$$

The ratio between catalyst porosity (ξ) and tortuosity (χ) was taken as 0.1. The molecular diffusion coefficient for hydrogen and α-pinene in the vapour phase was calculated according to Chapman-Enskog equation for binary gas diffusivities:

$$D_{mol} = 1.8583 \cdot 10^{-3} \frac{\sqrt{T^3 \left(\dfrac{1}{M_A} + \dfrac{1}{M_B} \right)}}{p(\sigma_{AB})^2 \Omega_{AB}} \tag{4}$$

In equation (4), T is temperature (K), M_A and M_B are molar masses of hydrogen and α-pinene molecules (g/mol) respectively, p is total pressure (atm), σ_{AB} (Å) is the collision diameter for pair hydrogen and α-pinene; Ω_{AB} is a collision integral (dimensionless) that is a function of $k_B T / \varepsilon_{AB}$, where ε_{AB} (J) is Lennard-Jones parameter and k_B ($1.38 \cdot 10^{-23}$ J/K) is the Bolzmann constant.

The collision diameter σ_{AB} for pair hydrogen and α-pinene, was calculated by the following equation,

$$\sigma_{AB} = \frac{1}{2}(\sigma_A + \sigma_B) \tag{5}$$

while the collision integral depends on the constant ε_{AB}, which was calculated for a binary system from

$$\varepsilon_{AB} = \sqrt{\varepsilon_A \varepsilon_B} \tag{6}$$

The Knudsen diffusivity was calculated by

$$D_k = \frac{2}{3} r \sqrt{\frac{8RT}{\pi M}} \tag{7}$$

where r, R, T, and M are respectively pore radius, ideal gas law constant, temperature, and molar mass of gas molecules.

The pore radius in the case of cylindrical pores can be calculated from the total pore volume $V_p = 0.69 \cdot 10^{-6}$ m^3/g and the total surface area S= 268 m^2/g.

$$\frac{V_p}{S} = \frac{\pi r^2 L}{2\pi r L} = 0.5r \tag{8}$$

Hence eq.8 takes the form

$$D_k = \frac{2}{3} \frac{2V_p}{S} \sqrt{\frac{8RT}{\pi M}} \qquad (9)$$

Finally estimation of the effectiveness factor under reaction conditions gave a value 0.91, which is close to unity, indicating that α-pinene diffusion inside the catalyst pores does not affect the reaction rate notably.

An isomerization reaction for α-pinene conversion catalyzed by Au/γ-Al$_2$O$_3$ is similar to that catalyzed by conventional acid catalysts (Scheme 4). The main product of vapour-phase α-pinene isomerization is camphene, but also minor components tricyclene, *p*-cymene and limonene were obtained during the reaction. The selectivity to these products as a function of α-pinene conversion seems to be rather constant in the reaction temperature range studied 463-483 K [**I, II**]. Consequently, the reaction products are formed in parallel pathways. Activation energies for their formation are approximately the same, and the difference in the rate constants is probably due to the difference in the activation entropy of the products formation. The key intermediate in the α-pinene isomerization seems to be the pinylcarbonium ion, which is formed from α-pinene and is the precursor for all of the reaction products, produced in turn in subsequent steps. Camphene and tricyclene are formed from the bornylcarbonium ion in parallel steps, while limonene and *p*-cymene originate from the terpenylcarbonium ion also in parallel steps (Scheme 4).

The effect of residence time on the α-pinene isomerization over Au/γ-Al$_2$O$_3$ was studied at different temperatures 463, 473 and 483 K during the initial period of the reaction to avoid the influence of Au/γ-Al$_2$O$_3$ catalyst deactivation on α-pinene conversion with time-on-stream. To facilitate a comparison between experiments with different initial α-pinene concentrations the analyzed samples of reaction products were withdrawn when approximately the same amount of α-pinene passed through the catalyst bed (e.g. for higher α-pinene concentration the initial period was lower) in order to assure that the sampling times corresponded to approximately the same extent of deactivation. Figure 4a displays α-pinene conversion measured during the initial period of testing versus residence time τ for three different reaction temperatures.
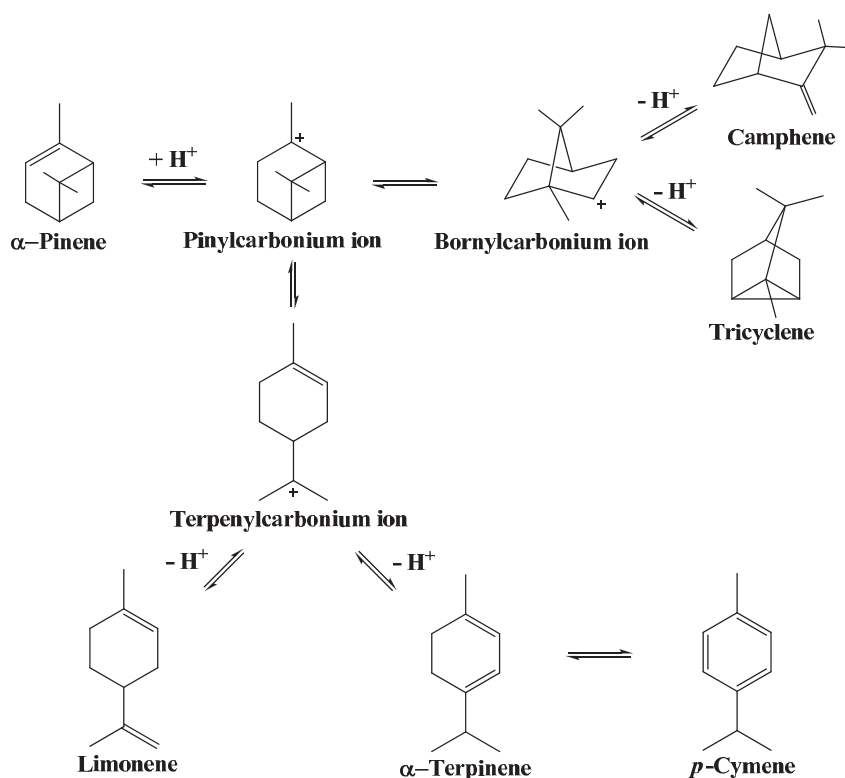
Scheme 4. Scheme of α-pinene isomerization catalyzed by acid catalysts.

The experimental dependence of the α-pinene conversion on the residence time is well described by the following equation:

$$X = 1 - e^{-k\tau} \tag{10}$$

This indicates that the reaction is of the first-order with respect to α-pinene (Figure 4a). The apparent activation energy calculated from these data is 51 kJ/mol (with 95% confidence limits), which is in a good agreement with that for TiO_2 catalyst (Figure 4b) [79]. It should be noted that during all tests, the carbon balance between the feed and outlet stream was within $100 \pm 5\%$.

However, the increase of the α-pinene concentration in the initial mixture from 0.4 to 20.0 vol. % was observed to result in the strong catalyst deactivation [**II**]. Thereby, taking into account the high potential of this catalyst from an industrial viewpoint, a special attention in our work was given to investigation of the deactivation process.
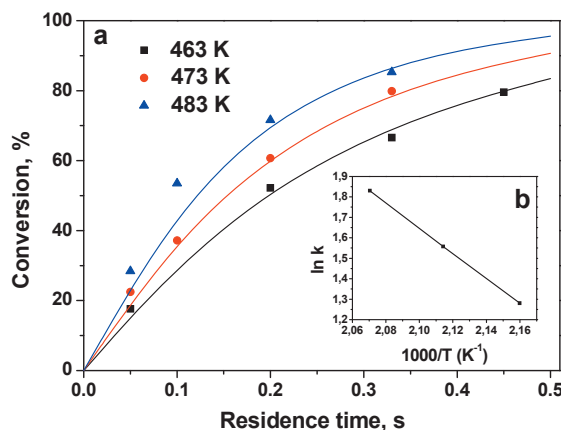
Figure 4. (a) Dependence of α-pinene conversion on residence time over 2.2 wt. % Au/γ-Al$_2$O$_3$ at different temperatures (symbols - experiments; line - calculated). (b) Arrhenius plot of rate constant (k, s^{-1}) of α-pinene isomerization. Reaction conditions: T = 463-483 K, α-pinene concentration in *n*-octane 20.0 vol. %.

3.1.3. Catalyst deactivation and regeneration

According to nitrogen physisorption, both the catalyst specific surface area and the total pore volume decreased during the reaction. A detailed study of the spent Au/γ-Al$_2$O$_3$ catalyst by TPO with simultaneous recording of UV-Vis spectra *in situ* showed that deactivation is caused by hydrocarbons adsorption on gold species [**II**]. The obtained data are presented in Figure 5 (a, b). The first peak of water desorbed at 300-500 K is similar to that obtained on the fresh Au/Al$_2$O$_3$ catalyst (data not shown) and is caused by water removal from the sample being pre-exposed to air. Contrary to the fresh catalyst, desorption of water started at 308 K on the spent Au/Al$_2$O$_3$ catalyst resulting in the appearance of a band at 255 nm, which could be assigned to the metal- to-ligand charge transfer [80] in an organic compound adsorbed on gold species during the reaction. A maximum intensity was achieved at 519 K, while a further temperature increase leads to an intensity decrease due to this compound oxidation accompanied with oxygen consumption and desorption of water, CO and CO$_2$. The relative content of desorbed products was in a good correspondence with the stoichiometry of C$_{10}$H$_{16}$ (α-pinene or other reaction compounds) oxidation.

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As oxidation proceeds, the new band at 860 nm rises. This band is similar to the one found for metallic gold nanoparticles being in contact with oxygen-rich media [75]. Therefore, it could be concluded that partial oxidation of the organic deposit at 519-703 K results in the formation of oxygen containing deposit adsorbed on gold nanoparticles. The sample heating at higher temperatures provokes further oxidation of this intermediate which was indicated by the appearance of a new peak in the oxygen consumption profile and a new narrow peak of CO_2 desorption as well as by decrease of the band intensity at 860 nm. The oxidation of organic deposit was almost completed at 800 K.

a

b
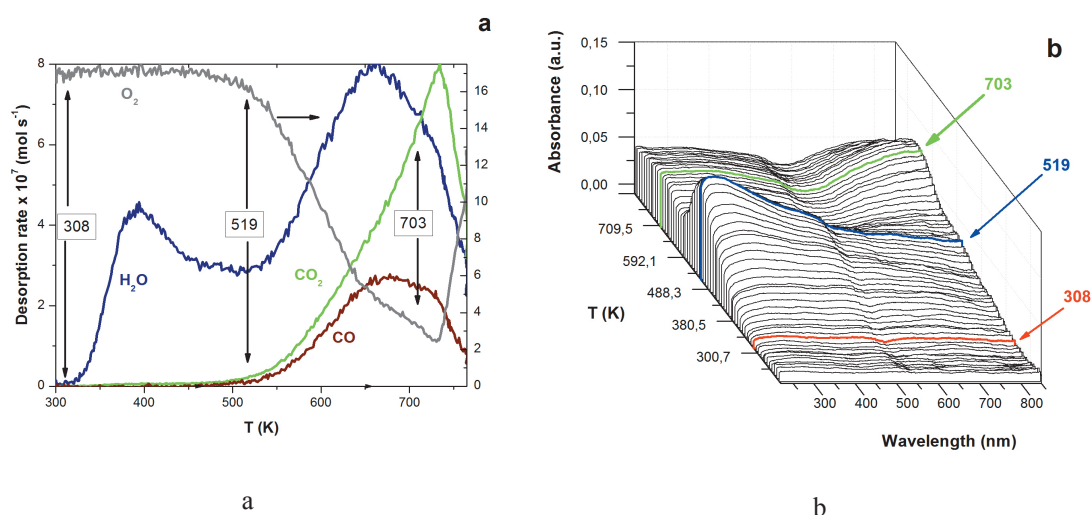
Figure 5. Profiles of oxygen consumption and product formation (a) and UV-Vis spectra *in-situ* (b) under temperature programmed oxidation of the spent Au/Al$_2$O$_3$ catalyst.

According to TEM, the size of gold nanoparticles was not changed noticeably during the α-pinene isomerization and TPO as well. The high sintering stability of the Au/Al$_2$O$_3$ catalyst used in this work provides a possibility of restoring its activity in α-pinene isomerization by burning the hydrocarbon deposits on the catalyst surface at temperature ≥800 K.

Au/γ-Al$_2$O$_3$ regeneration by coke burning was performed in oxygen for 1 h at 323 K and thereafter for 1 h at the temperature range of 323-873 K (ramping 10°/min). After this procedure, the catalyst was tested successively in two cycles. Regenerated Au/γ-Al$_2$O$_3$ at first exhibited

conversion of α-pinene in the range of 98-100% and selectivity to camphene 83% demonstrating complete catalyst regeneration at 473 K and α-pinene concentration 0.4 vol. % (τ = 0.33 s). In addition, the catalysts have shown the same activity during the reaction at 473 K and α-pinene concentration 4.0 vol. % (τ = 0.33 s). In this connection, the important issue is to predict the catalyst life time under current reaction conditions and the time required for catalyst regeneration.

The dynamics of catalyst deactivation during α-pinene isomerization was described based on the so-called "separable" deactivation model assumption [**II**]. According to this approach, the reaction rate under catalyst deactivation can be divided into two functions, one depends only on the main reaction kinetics, while another one ($a(C_o,t)$) is determined by deactivation steps. Finally, for predicting of the α-pinene conversion (X) at the different temperature and concentration the following expression is obtained:

$$X = 1 - e^{-k \cdot a \cdot \tau} \tag{11}$$

where k is the rate constant, τ is the residence time, $a(C_o, t)$ is the empirical expression, also called relative activity or function of deactivation, which in our case depends on initial α-pinene concentration and time-on-stream.

On the basis of experimental observations the deactivation function a was shown to be well described by a hyperbolic function and the following expression [**II**]:

$$a = \frac{1}{1 + K_t(C_o) \cdot t} \tag{12}$$

where $K_t (C_o)$ is deactivation parameter (min^{-1}), which depends on the initial concentration of α-pinene.

The developed kinetic model described well the experimental data for the α-pinene transformations on the Au/Al_2O_3 catalyst during the initial period of reaction as well as the dynamics of the catalyst deactivation. The parameter of the deactivation dependence on α-pinene concentration is well described by a parabolic function $K_t = BC_o^{2}$.

Moreover, in order to explain equation (12) from a mechanistic viewpoint the catalyst deactivation model taking into account deposits formation due to the interactions of two adsorbed α-pinene molecules was proposed [**II**]:

α−Pinene   α−Pinene*   Products + *
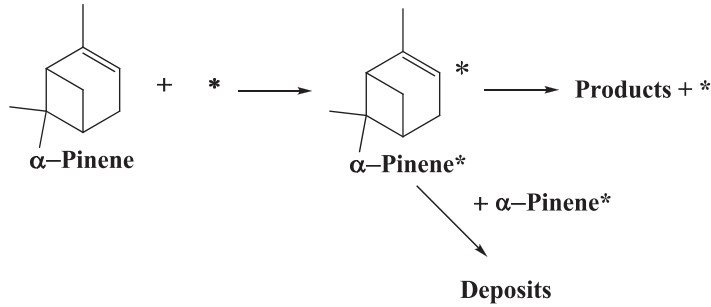
+ α−Pinene*

Deposits

where * is the surface site. From this scheme, an expression for the coverage of the deposit is valid by assuming Langmuir adsorption for α-pinene:

$$\frac{d\theta_{deposit}}{dt} = k_d \theta_{pinene}^2 = k_d \frac{K_p^2 C^2}{(1 + K_p C \ )^2} \theta_*^2 \tag{13}$$

where k_d is the deactivation constant, θ_* is vacant sites.

Since the reaction is first order in α-pinene, it in essence means that the coverage of α-pinene is very low compared to the fraction of available (vacant) sites, e.g. $\theta_Z \approx 1 - \theta_{deposit}$ and $1 >> K_p C$ giving a possibility to transform eq. (13) into

$$\frac{d\theta_{deposit}}{dt} = k_d \theta_{pinene}^2 = k_d K_p^2 C^2 (1 - \theta_{deposit})^2 \tag{14}$$

Defining the relative activity as the fraction of sites not occupied by deposit $a = (1 - \theta_{deposit})$ one gets

$$-\frac{da}{dt} = k_d K_p^2 C^2 a^2 \tag{15}$$

which after integration with the boundary conditions (t=0, a=1) results in

$$a = \frac{1}{1 + k_d K_p^2 C_o^2 t} \tag{16}$$

Eq. (16) provides a mechanistic explanation for utilization of deactivation function in eq. (12) and parabolic expression for the lumped constant K_t, which is defined as

$$K_t = BC_o^{\,2} = k_d K_p^2 C_o^{\,2}.$$

3.2. One-pot myrtenol amination [III, IV]

3.2.1. Effect of catalyst support and redox activation

The regularities of one-pot natural myrtenol amination in the presence of gold containing catalysts were studied with the general idea to systematically obtain the knowledge about the key parameters determining the catalyst performance including the investigation of the support nature and the catalyst redox activation effect.

First in order to study the role of the support in this reaction, a series of pre-oxidized gold catalysts supported on different metal oxides were examined for myrtenol amination with aniline using equimolar amounts of substrates under nitrogen pressure.

During myrtenol animation with aniline besides expected products, myrtenal and its imine (1) and amine (2), additionally the formation of myrtanol as well as myrtanal with saturated C-C bond and the corresponding imine (3) and amine (4) took place (Scheme 5).
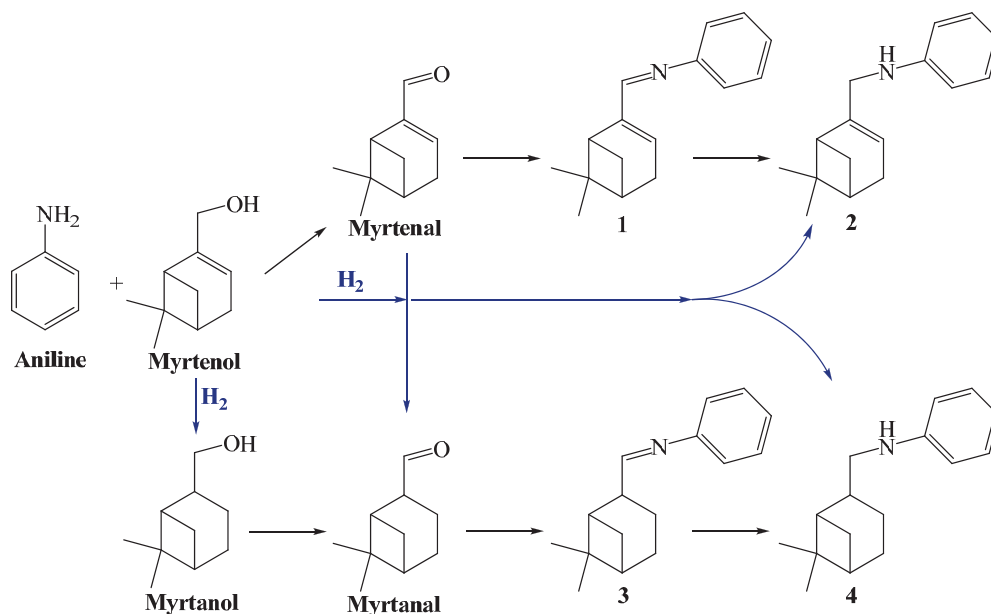
Scheme 5. Myrtenol amination with aniline on Au catalysts.

The product distribution during the reaction was found to strongly depend on the type of supports [**III**]. A nearly complete conversion of myrtenol was attained only in the presence of

Au/ZrO$_2$ and Au/Al$_2$O$_3$ catalysts (Figure 6). Gold supported on ceria, magnesia and lanthana showed a relatively high alcohol conversion only after 16 h, implying that the reaction rates were low. In general, gold catalysts on these basic metal oxides exhibited a very slow formation of the corresponding imine (1) without significant hydrogen transfer accompanied by the accumulation of significant amounts of myrtenal during the reaction.

In comparison with other catalysts, Au/ZrO$_2$ was observed to exhibit better selectivity to the corresponding amine (2) at the same myrtenol conversion (74%) with the selectivity to the target product (2) increasing up to 52% after 16 h. However, the reuse of the Au/ZrO$_2$ catalyst after the first reaction run led to a profound decline in activity. A detailed investigation of the catalyst deactivation was performed while studying the reaction kinetics.

a   b
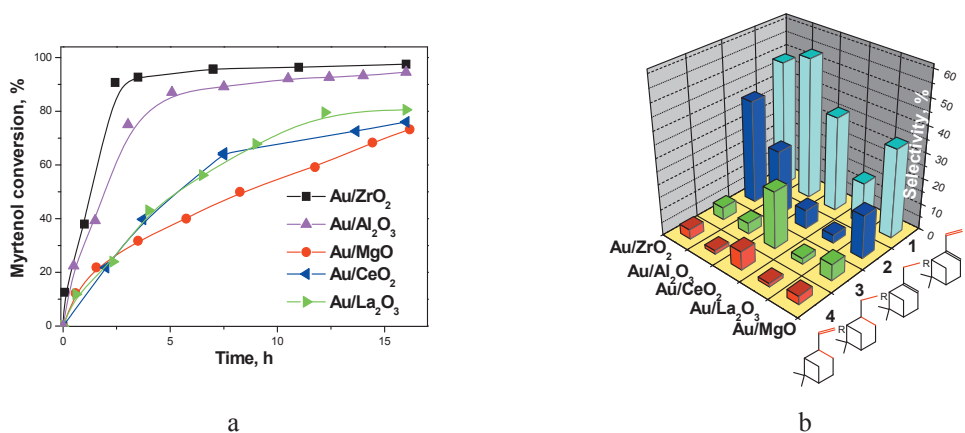
Figure 6. Myrtenol amination in the presence of pre-oxidized gold supported on the ZrO$_2$, Al$_2$O$_3$, CeO$_2$, La$_2$O$_3$ and MgO. (a) The myrtenol conversion, (b) the products selectivity at the same value of myrtenol conversion (74 %). The reaction conditions: T = 453 K, myrtenol 1 mmol, aniline 1 mmol, toluene 10 ml, catalyst 1.4 mol. % Au. R = aniline.

At the same time, the myrtenol amination over the supports *per se* of more active catalysts, ZrO$_2$ and Al$_2$O$_3$, resulted in the formation of the corresponding imine (1) only and the myrtenol conversion about 30-40% after 7 h.

The data obtained for the myrtenol conversion are in a good agreement with the results previously reported by Ishida et al. for the amination of benzyl alcohol over Au supported on the same metal oxides [40]. A direct correlation between the electronegativity of metal ions in metal oxide supports, which determines their acid-base properties, and the alcohol conversion as well as selectivity to the target amine was obtained (Figure 7).
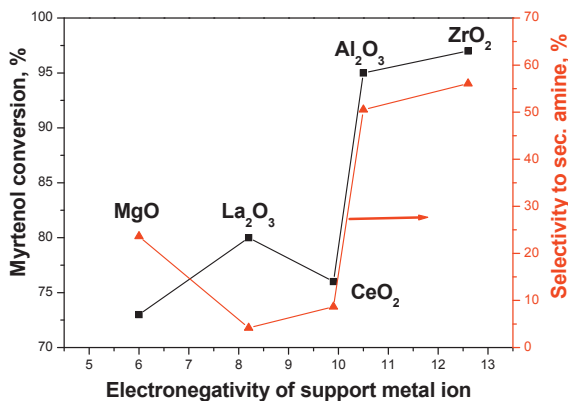
Figure 7. Correlation between myrtenol conversion (■) and selectivity to secondary amine (▲) and electronegativity of metal ions in metal oxide supports. The reaction conditions: T = 453 K, myrtenal 1 mmol, aniline 1 mmol, toluene 10 ml, pre-oxidized catalyst 1.4 mol. % Au.

Thus, the catalyst activity and product distribution are strongly dependent on the support nature, which seems to be related to the acid-base properties of the metal oxides. The highest activity in one-pot myrtenol amination among the catalysts investigated was obtained over Au/ZrO$_2$ with both acidic and basic surface sites. The initial alcohol activation was confirmed to require the presence of basic sites on metal oxide surfaces. At the same time, the availability of protonic groups on the support surface was suggested to be necessary in hydrogen transfer.

The regularities obtained for myrtenol amination are consistent with a plausible reaction mechanism for alcohol amination presented in ref. [40, 81] (Figure 8). The first step of the alcohol deprotonation is promoted at the basic sites of the support to give an alkoxide intermediate on the support surface with the consecutive β-hydride elimination catalyzed by gold to form the carbonyl

compound. The adsorbed aldehyde and amine interact to form hemiaminal, which then undergoes an attack by the hydride ion from Au nanoparticles and proton from the support surface resulting in the production of the final product. Meanwhile, the aldehyde can be desorbed into the solution giving the imine. The imine formation can be also a result of the direct hemiaminal conversion. Non-catalytic interactions between myrtenal and aniline were experimentally confirmed, although in the presence of the Au/ZrO_2 catalyst, the reaction rate significantly increases probably due to the substrates localization or water released sorption on the catalyst surface [**III**].
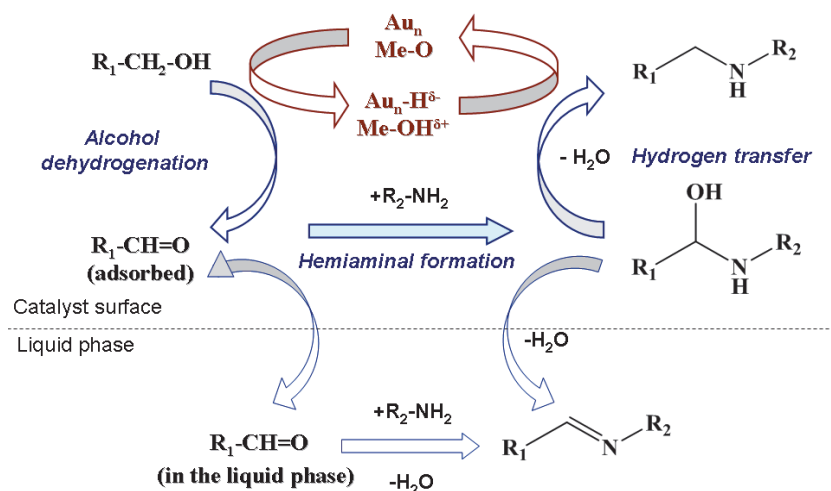
Figure 8. Proposed reaction mechanism for alcohol amination.

Thus, the support nature profoundly affects the catalytic activity and the product composition in the one-pot myrtenol amination. According to the data obtained, a certain balance between different sites, such as in the Au/ZrO_2 catalyst, is required for an efficient alcohol amination.

Catalyst treatment can also have an influence on the support and on the Au species taking part in the reaction, and consequently, affecting the activity and selectivity.

Therefore, a series of pre-reduced catalysts on the same metal oxides were tested. Generally, in the case of pre-reduced catalysts, despite the increase in the reaction rate for some catalysts, the decrease in the selectivity to the target amine was observed. According to XPS data, this is likely to

be connected to the decrease in the fraction of cationic gold species required for efficient hydrogen transfer.

3.2.2. Reaction kinetics

Since the one-pot amination is a complicated process including three consequence steps, a special attention in this part of the work was given to the investigation of its kinetics with the further development of the kinetic model to predict the catalyst performance in terms of stability as well as activity. Despite higher activity and selectivity to the target amine of the pre-oxidized zirconium-supported gold catalyst in comparison to the pre-reduced one, a less active catalytic system was used to provide correct data fitting and to model the process kinetics. In the presence of the pre-oxidized catalyst, only traces of myrtenal were observed during the reaction, which hinders a more complete kinetic analysis. The developed model is a very generic one and can be used for a number of hydrogen borrowing reactions.

In order to verify the absence of internal diffusion limitations the Weisz-Prater criterion was used [82]. For the maximal initial alcohol dehydrogenation rate ($5 \cdot 10^{-5}$ mol·l^{-1}·s^{-1}) obtained for the Au/ZrO$_2$ catalyst the estimated Weisz-Prater modulus was amounted to $\Phi=0.0003$, which indicates that the substrate diffusion inside the catalyst pores does not affect the reaction rate. The impact of external diffusion resistance was suppressed by conducting experiments at the stirring speed of 1100 rpm, which is proved to be efficient enough to avoid external mass transfer limitations.

The one-pot myrtenol amination over Au/ZrO$_2$ catalyst were studied in detail during the development of the kinetic model [**IV**].

As it was mentioned above, catalyst deactivation was shown to occur. In order to explore the catalyst deactivation in more detail and to verify the cause of deactivation, additional experiments were performed. First to exclude the leaching of the active metal as well as the influence of homogeneous catalysis, leaching analysis by hot filtration was performed in two consecutive experiments. As a result, no signs of leaching of the active component were found. According to ICP-AES, the gold content in the spent catalyst was the same as in the fresh one within the

experimental uncertainty. Moreover, no gold was observed in the solution. In the next step, a series of consecutive experiments, described in detail in [**IV**], allowed us to unequivocally conclude that the second step of the one-pot myrtenol amination with aniline and most likely imine oligomerization or polymerization results in deactivation of the active sites.

Thus, based on the data obtained for myrtenol amination over the Au/ZrO_2 catalyst and the literature data the reaction mechanism based on elementary steps was proposed (Scheme 6). It should be noted that the concept of competitive adsorption was used, assuming quasi-equilibria in the component adsorption. The catalyst deactivation and the non-catalytic reaction were taken into account in this kinetic model, along with the main reaction routes.

Scheme 6

	Elementary step	Constant	Basic routes			
			1	2	3	4
1	$Z + A \equiv ZA$	K_1	1	0	1	0
2	$ZA + Z \rightarrow ZB + ZH_2$	k_2	1	0	1	0
3	$Z + B \equiv ZB$	K_3	-1	1	-1	0
4	$Z + H_2 \equiv ZH_2$	K_4	-1	0	0	0
5	$ZB + ZE \leftrightarrow ZC' + Z$	$k_{+5} \rightarrow$ $k_{-5} \leftarrow$	0	1	0	0
6	$C + Z + H_2O \equiv ZC'$	K_6	0	-1	1	0
7	$Z + E \equiv ZE$	K_7	0	1	0	0
8	$ZC' + ZH_2 \leftrightarrow ZD + Z + H_2O$	$k_{+8} \rightarrow$ $k_{-8} \leftarrow$	0	0	1	0
9	$Z + D \equiv ZD$	K_9	0	0	-1	0
10	$Z + C \equiv ZC$	K_{10}	0	0	0	2
11	$2ZC \rightarrow$ deposits	k_{11}	0	0	0	1
12	$B + E \leftrightarrow C + H_2O$	$k_{+12} \rightarrow$ $k_{-12} \leftarrow$	Non-catalytic			

N^1: $A = B + H_2$; N^2: $B + E = C + H_2O$;

N^3: $A + C = B + D$; N^4: $2C =$ deposits

Scheme 6 on the right hand side contains the stoichiometric numbers along the basic routes. Steps 5, 8 and 12 (non-catalytic one) are reversible, steps 2, 11 are irreversible and steps 1, 3, 4, 6, 7, 9, 10 are quasi-equilibria. ZA, ZB, ZC', ZC, ZD and ZE represent adsorbed myrtenol, myrtenal, hemiaminal intermediate, imine (**C**), amine (**D**) and aniline, respectively. In the catalytic steps, Z denotes surface sites, and k and K are rate constants and equilibrium constants respectively. The number of basic routes was determined by using Horiuti-Temkin equation [82].

The basic routes N^1 - N^3 describe the transformations of the main reaction compounds, while N^4 depicts the formation of deposits resulting in catalyst deactivation.

The dependence of the coverage of the intermediates on the fraction of vacant sites can be obtained from the quasi-equilibrium approximation. Hence the coverage of the vacant sites (θ_Z) is determined by the following equation:

$$\theta_Z = \frac{1}{(1 + K_1 \cdot C_A + K_3 \cdot C_B + K_4 \cdot C_{H_2} + K_6 \cdot C_C \cdot C_{H_2O} + K_7 \cdot C_E + K_9 \cdot C_D + K_{10} \cdot C_C)} \tag{17}$$

The catalyst deactivation during the reaction was proposed to be caused by a decrease of the total available sites fraction due to the formation of deposits. The impact can be taken into account by using the function $f = 1 - \theta_{deposits}$, where $\theta_{deposits}$ is fraction of the catalyst sites occupied by deposits.

Therefore, the consumption/generation rates (r_i) are defined by

$$r_A = \frac{dC_A}{dt} = -r_2 = -k_2 \cdot K_1 \cdot C_A \cdot \theta_Z^2 \cdot (1 - \theta_{deposits}) \tag{18}$$

$$r_B = \frac{dC_B}{dt} = r_2 - r_5 - r_{12}$$
$$= (k_2 \cdot K_1 \cdot C_A - k_{+5} \cdot K_3 \cdot C_B \cdot K_7 \cdot C_E + k_{-5} \cdot K_6 \cdot C_C \cdot C_{H_2O}) \cdot \theta_Z^2 \cdot (1 - \theta_{deposits}) - r_{12} \tag{19}$$

$$r_C = \frac{dC_C}{dt} = r_5 - r_8 - 2 \cdot r_{11} + r_{12}$$
$$= (k_{+5} \cdot K_3 \cdot C_B \cdot K_7 \cdot C_E - k_{-5} \cdot K_6 \cdot C_C \cdot C_{H_2O} - k_{-8} \cdot K_6 \cdot C_C \cdot C_{H_2O} \cdot K_4 \cdot C_{H_2} +$$
$$+ k_{-8} \cdot K_9 \cdot C_D \cdot C_{H_2O}) \cdot \theta_Z^2 \cdot (1 - \theta_{deposits}) - 2 \cdot r_{11} + r_{12} \tag{20}$$

$$r_D = \frac{dC_D}{dt} = r_8$$
$$= (k_{+8} \cdot K_6 {\cdot} C_C \cdot C_{H_2O} \cdot K_4 \cdot C_{H_2} - k_{-8} \cdot K_9 \cdot C_D \cdot C_{H_2O}) \cdot \theta_Z^2 \cdot (1 - \theta_{deposits})$$

$$(21)$$

$$r_{H_2} = \frac{dC_{H_2}}{dt} = r_2 - r_8$$
$$= (k_2 \cdot K_1 \cdot C_A - k_{+8} \cdot K_6 {\cdot} C_C \cdot C_{H_2O} \cdot K_4 \cdot C_{H_2} + k_{-8} \cdot K_9 \cdot C_D \cdot C_{H_2O}) \cdot \theta_Z^2 \cdot (1 - \theta_{deposits})$$

$$(22)$$

$$r_E = \frac{dC_E}{dt} = -r_5 - r_{12}$$
$$= (-k_{+5} \cdot K_3 \cdot C_B \cdot K_7 \cdot C_E + k_{+5} \cdot K_6 {\cdot} C_C \cdot C_{H_2O}) \cdot \theta_Z^2 \cdot (1 - \theta_{deposits}) - r_{12}$$

$$(23)$$

$$r_{H_2O} = \frac{dC_{H_2O}}{dt} = r_5 + r_{12}$$
$$= (k_{+5} \cdot K_3 \cdot C_B \cdot K_7 \cdot C_E - k_{-5} \cdot K_6 {\cdot} C_C \cdot C_{H_2O}) \cdot \theta_Z^2 \cdot (1 - \theta_{deposits}) + r_{12}$$

$$(24)$$

$$r_{deposites} = \frac{d\theta_{deposites}}{dt} = r_{11} = k_{11} \cdot (K_{10} \cdot C_C)^2 \theta_Z^2 \cdot (1 - \theta_{deposits})$$

$$(25)$$

In order to verify whether the proposed mechanism can be applied for explaining the experimental data in a quantitative manner, parameter estimation through numerical data fitting was performed.

The kinetic constants *k* in the rate equations were assumed to follow the modified Arrhenius dependence [82]

$$k = A \exp\left(\frac{-E_a}{R_{gas}} \left(\frac{1}{T} - \frac{1}{T_{mean}} \right) \right)$$

$$(26)$$

In the expression above, A, E_a, R_{gas}, T, and T_{mean} denote frequency factor, activation energy, the gas constant, reaction temperature, and mean temperature of the experiments, correspondingly.

The validity of the model was determined by the closeness of the experimental data and the values predicted by the model. The nonlinear regression analysis is based on the minimization of an objective function (Q). The sum of residual squares is the most commonly used objective function

$$Q = \left\| c_{exp} - c_{est} \right\|^2 = \sum_t \sum_i (c_{exp,it} - c_{est,it})^2 ,$$

$$(27)$$

where c_{exp} and c_{est} denote the experimental and estimated data of the components, respectively.

The goodness of the fit is determined with the R^2-coefficient. It compares the residuals given by the model to the residual of the model using the average of all data points. The idea is to compare the residuals c-c_p given by the model to the residuals of the simplest model one may think of, the average value $\bar{c}$ of all data points. The R^2-value or degree of explanation is given by the expression

$$R^2 = \left(1 - \frac{\|c - c_p\|^2}{\|c - \bar{c}\|^2} \right) \tag{28}$$

Hence R^2 is typically <1. The closer the value is to unity, the more perfect is the fit.

The system of differential equations (18)-(25) was solved numerically with the backward difference method by minimization of the sum of residual squares (*SRS*) with non-linear regression analysis using the Simplex and Levenberg-Marquardt optimization algorithms implemented in the software Modest [83].

The values of the calculated frequency factors, equilibrium constants and activation energies (k_0 and E_a), the estimated standard errors, as well as the estimated relative standard errors (in %) of the tested reaction mechanisms were determined [**IV**].

Comparison between experimental and calculated data for different reaction temperature is presented in Figure 9, while the contour plots and sensitivity analysis of main parameters are presented in [**IV**]. As several parameters are calculated simultaneously, the solution was well identified with respect to some parameters, but rather badly identified with respect to some others. The calculated value of the activation energy for the first step of alcohol dehydrogenation is comparable with the activation energy (93.7 kJ/mol) of benzyl alcohol dehydrogenation on Au/TiO$_2$ [84].

The comparison in Figure 9 along with the value of R^2 equal to 94.7% confirms the applicability of the proposed mechanism and equations (18)-(25) as well as the deactivation function to describe experimental data of the one-pot myrtenol amination over Au/ZrO$_2$.
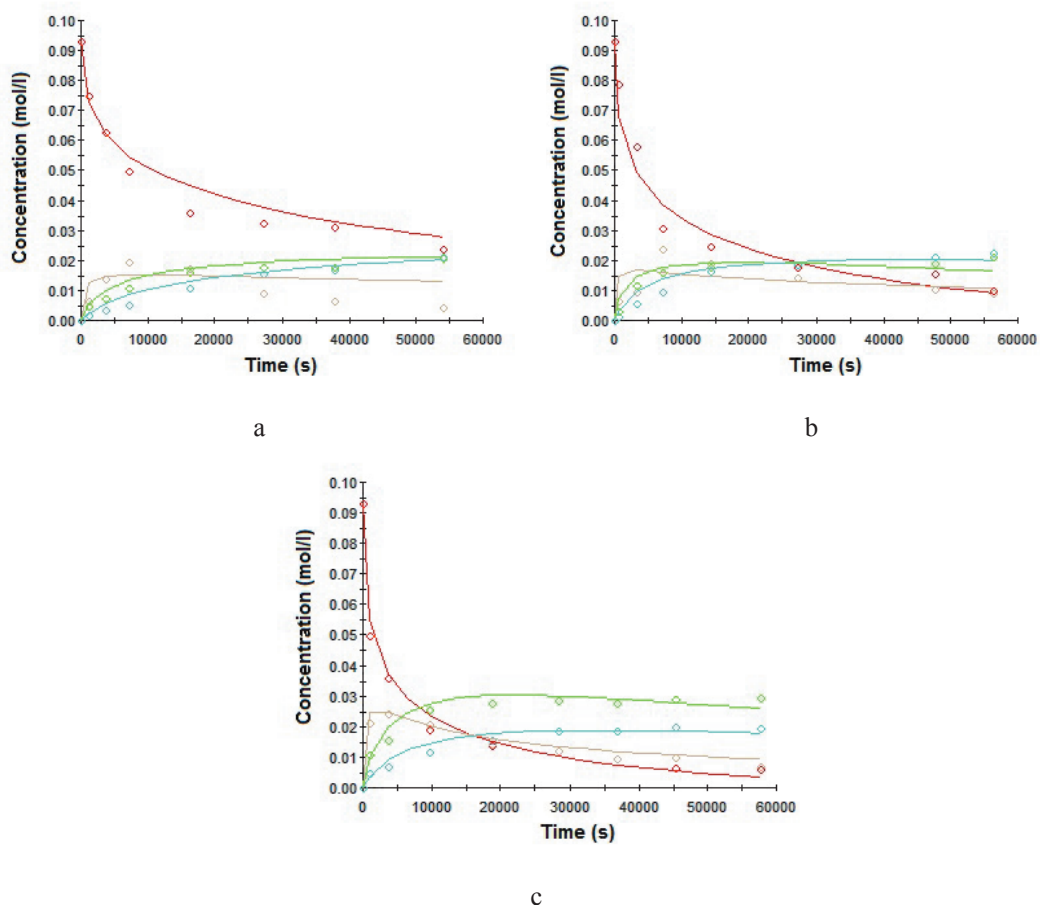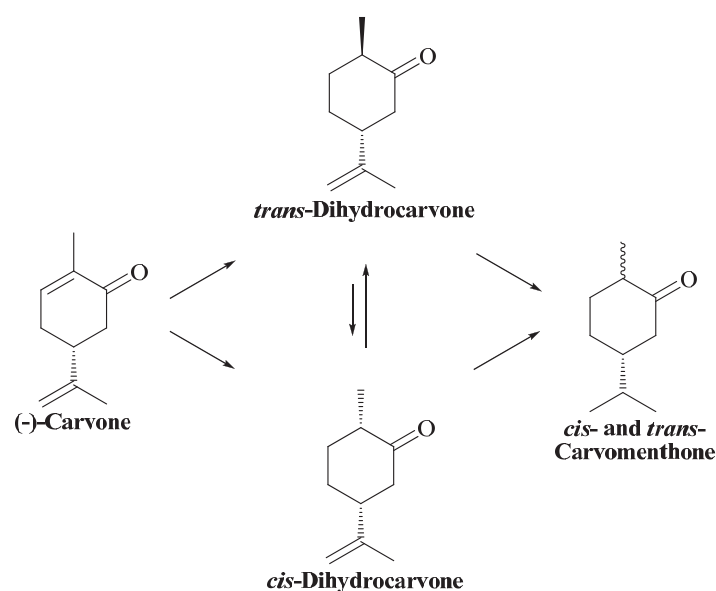
c

Figure 9. Comparison between experimental data (markers) of concentrations vs time (s) and calculations (solid lines): (—) myrtenol, (—) myrtenal, (—) imine (**C**) and (—) amine (**D**). Reaction conditions: (a) T = 413 K, (b) T = 433 K and (c) T = 453 K, myrtenol 1 mmol, aniline 1 mmol, toluene 10 ml, catalyst 1.4 mol. % Au, nitrogen atmosphere.

3.3. Selective carvone hydrogenation to dyhydrocarvone [V]

3.3.1. Solvent effect

Previous studies of gold-catalyzed α,β-unsaturated carbonyl compound hydrogenation have shown that the adsorption of the C=O group is favored by face atoms, while sites with low coordination strongly favor the activation of the C=C bond with its further hydrogenation [85, 86]. In the case of Au/TiO$_2$, which was selected as a catalyst in this work, the rounded particle structure accompanied by high relative amount of low-coordinate surface sites was found [87]. Carvone hydrogenation was performed in this work in different solvents by using the Au/TiO$_2$ catalyst with the Au particle size of *ca.* 2 nm.

A series of C$_1$-C$_3$ protic solvents including methanol (MeOH), ethanol (EtOH) and 2-propanol (2-PrOH) were used. The catalytic activity was shown to strongly depend on the solvent applied [V]. The carvone hydrogenation resulted mainly in *cis*-, *trans*-dihydrocarvone formation,

Scheme 7. Reaction pathways of carvone hydrogenation over Au/TiO$_2$ catalyst.

with *trans*-isomer being the main product in most cases (Scheme 7).

Moreover, the solvent nature profoundly affected the *cis*-to-*trans* isomer ratio (Figure 10). According to the data obtained both catalytic activity and *trans*-/*cis*-dihydrocarvone ratio increased in the following order: 2-propanol<ethanol<methanol. Thus, the highest activity as well as *trans*-to-*cis*- isomer ratio among the solvents applied for carvone hydrogenation were observed in the case of

methanol. The highest total selectivity to dihydrocarvone 62% was achieved at a nearly complete carvone conversion (90%) after 13 h. Further carvone hydrogenation was accompanied by increasing *trans*-to-*cis*-dihydrocarvone ratio along with an increasing impact of side reactions, such as the C=C double bond in dihydrocarvone hydrogenation to carvomenthone (Scheme 7).
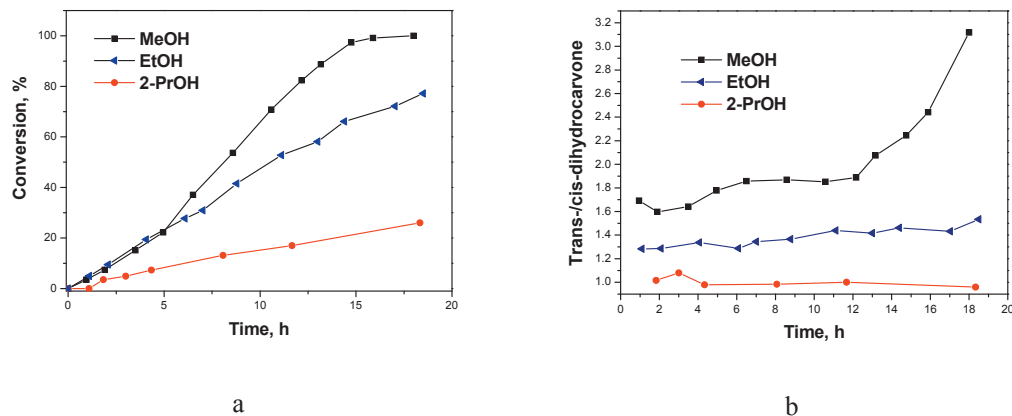

a   b

Figure 10. Solvent effect on carvone conversion and *trans*-to-*cis*-dihydrocarvone ratio over Au/TiO$_2$ catalyst. Reaction conditions: T = 373 K, p (H$_2$) = 9 bar, (-)-carvone (10 mmol), solvent (36 ml), Au catalyst (336 mg, Au 0.3 mol. % to substrate).

Two probable reasons for the increase of *trans*-to-*cis* -isomer ratio can be suggested. The first reason is predominant hydrogenation of the *cis*-isomer to carvomenthone while the second one is the isomerization of *cis*-dihydrocarvone to *trans*-dihydrocarvone. The activity of gold catalysts in *cis-trans* isomerization has recently been demonstrated for azobenzene [88]. In general, epimerization of cyclohexane derivatives is well-known and was reported in ref. [89-92]. In order to explain this observation as well as to clarify the reaction scheme, dihydrocarvone hydrogenation was performed over Au/TiO$_2$ under similar reaction conditions. As a result, the same changes in the ratio between *trans*- and *cis*-dihydrocarvone for the same reaction time were obtained with the formation of small amounts of the carvomenthone. Thus, it can be supposed that the thermodynamically controlled isomerization of *cis*- to *trans*-dihydrocarvone is likely to occur with

the further transformation of both isomers to carvomenthone. It is important to note that TiO_2 *per se* was not active in both carvone hydrogenation and dihydrocarvone isomerization.

In general the solvent effect can be related mainly to the specificity of the solvent interactions with reactants and the catalysts. Considering interactions between H_2 and solvents, namely variations in the hydrogen solubility in the liquid phase, no correlation for carvone hydrogenation was found, as it was observed in ref. [93]. At the same time, based on the transition state theory and the Kirkwood treatment [94], which considers the reaction between ions and dipolar molecules, or between two dipolar molecules, it is possible to account the solvent effects on the reaction. The reaction rate (k), proportional to $e^{-\Delta^{\neq}G^0/kT}$, for the case when the reactant and the transition state are not charged is defined by

$$\ln k = \ln k_0 - k' \frac{(\mu^{\neq})^2 - (\mu_A)^2}{\varepsilon}$$

(29)

where ε is the dielectric constant, μ denotes the dipole moment of the activated complex ($\mu^{\neq}$) and the reactant (μ_A) respectively, k' is constant, which depends on temperature.

Equation (29) is useful in predicting the influence of the solvent polarity on the reaction kinetics. For example, if the reaction occurs with the formation of an activated complex, which is less polar than the reactant, the rate constant decreases with an increasing dielectric constant. This approach was successfully applied recently for the investigation of the solvent effect in the enantioselective hydrogenation of 1-phenyl-1,2-propanedione [95] and ethyl benzoylformate [96]. Hence, the rate constant can be expressed in the following way:

$$k = k_0 e^{\alpha/\varepsilon}$$

(30)

where α is a constant.

Therefore, the ratio between the selectivity (S) to *trans*- and *cis*-dihydrocarvone can be written in the case of the same reaction orders for formation of *trans*- and *cis*-dihydrocarvone as

$$\ln \frac{S_{trans}}{S_{cis}} = \ln \frac{k_{trans}}{k_{cis}} = \frac{k_0^{trans}}{k_0^{cis}} + \Delta\alpha \frac{1}{\varepsilon}$$

(31)

where $\Delta\alpha$ is the difference between α constants for *trans*- and *cis*-isomers, k_0^{trans} and k_0^{cis} are the hypothetical rate constants.
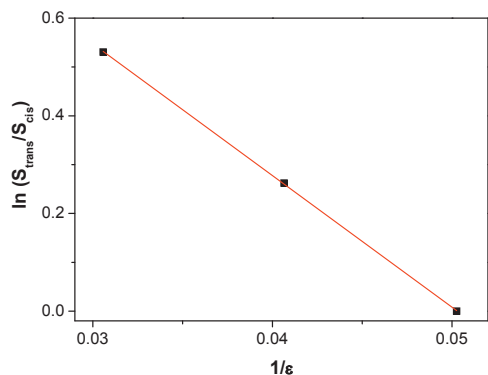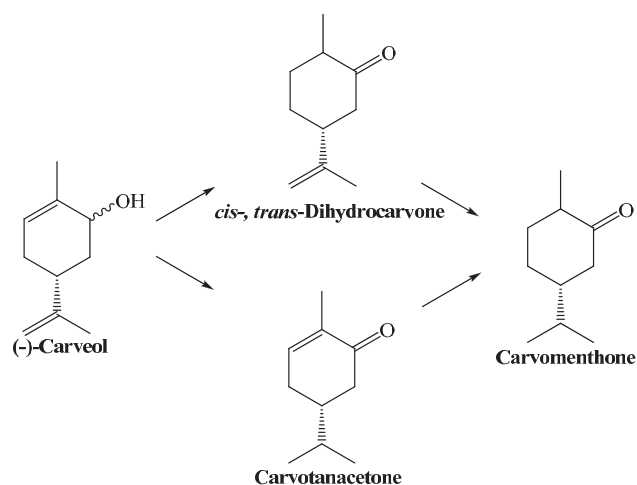

Figure 11. Dependence of the ratio between selectivity (S) to *trans*- and *cis*-dihydrocarvone on dielectric constants. Experimental data: points; calculations: solid line.

Equation (31) was used to describe the dependence of the ratio between the dihydrocarvone isomers on the dielectric constants. The values of dielectric constants are 32.7, 24.6, 19.9 for MeOH, EtOH, 2-PrOH, respectively. A good description was obtained as shown in Figure 11. The value of parameters were found to be equal $\Delta\alpha = -26.9$ and $\dfrac{k_0^{trans}}{k_0^{cis}} = 1.3$. Thus, the reaction rate of trans-

isomer formation as well as the total rate increase with an increasing solvent dielectric constant and H-donor ability. The developed correlation was able to describe the behavior of the system as a function of the solvent dielectric constant.

Scheme 8. Reaction pathways of carveol hydrogenation over Au/TiO₂ catalyst.

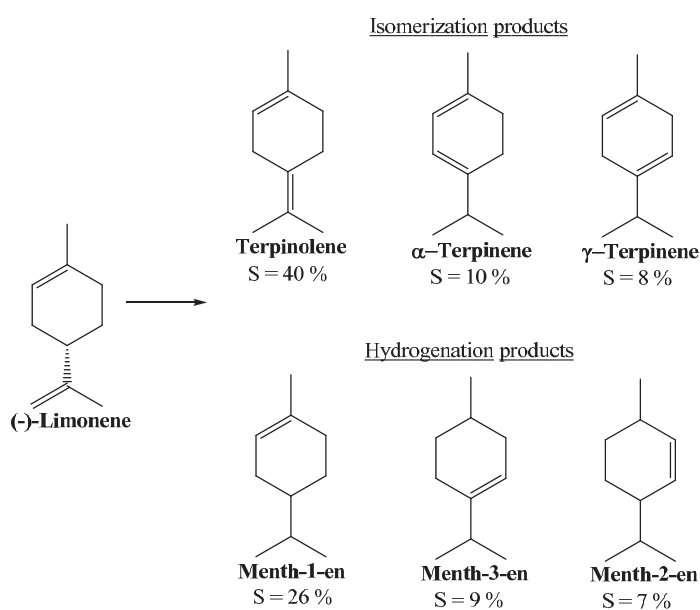### 3.3.2. Effect of substrate structure

In order to study the reaction regularities of the conjugated C=C bond hydrogenation in carvone and explore the possible ways of interactions between carvone and the catalyst surface, the hydrogenation of substrates with the structure to similar carvone but with different functional groups, such as limonene and carveol, was performed on Au/TiO₂ catalyst at

the same reaction conditions as for carvone.

In the case of carveol, the replacement of the C=O group by C-OH led to a significant decrease in the catalytic activity of Au/TiO$_2$ in exocyclic C=C bond hydrogenation, with its isomers being the main products (Scheme 8).

The isomerization products, such as dihydrocarvone, carvotanacetone, as well as carvomenthone, were mainly obtained. At the same time, among the products formed, the ratio between dihydrocarvone isomers was similar to one for carvone hydrogenation. It is worth noting that two carveol isomers had different reactivities and only *trans*-carveol conversion was observed, while the *cis*-isomers concentration was approximately constant during the reaction.

The lowest catalytic activity in the corresponding C=C group hydrogenation was obtained in the case of limonene, which is a hydrocarbon and does not possess any oxygen containing groups. The limonene conversion after 21 h was about 14%, with its isomers being the main products (Scheme 9). The limonene isomers, such as terpinolene, α-terpinene, γ-terpinene, were formed with the combined selectivity of

Scheme 9. Limonene hydrogenation over Au/TiO$_2$. Reaction conditions: T = 373 K, p (H$_2$) = 9 bar, (-)-limonene (10 mmol), methanol (36 ml), Au catalyst (336 mg, Au 0.3 mol % to substrate), 21 h. Product selectivity (S) is presented for 14 % limonene conversion.

about 58%. Among the hydrogenation products, menth-1-ene with an exocyclic C=C double bond was mainly observed with a selectivity of 26%.

Based on the results above it can be stated that the conjugation with C=O is important for selective C=C hydrogenation, which promotes C=C activation as well as influences the adsorption on the catalyst surface. According to the results reported previously, the adsorption mode of the substrate is a key parameter, determining the selectivity towards the product formation [97, 98].
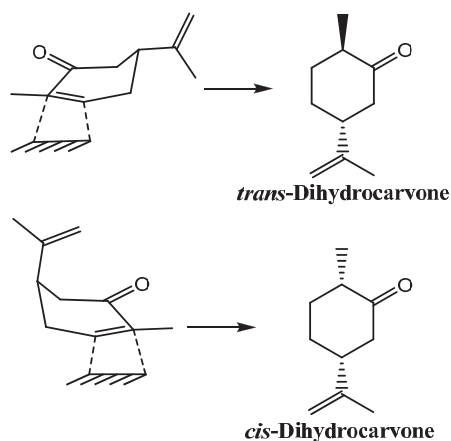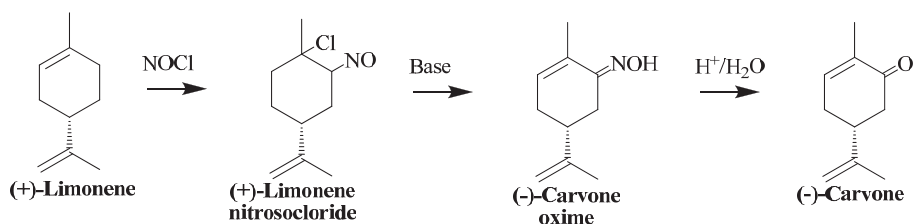

trans-**Dihydrocarvone**

cis-**Dihydrocarvone**

Figure 12. Proposed mechanism for conjugated C=C double bond hydrogenation in carvone over Au/TiO$_2$.

Thus the reaction mechanism for conjugated C=C double bond hydrogenation presented in Figure 12 can be envisaged. The predominant formation of *trans*-isomer can be explained by the specificity of carvone adsorption on the catalyst surface. Carvone conformation resulting in *trans*-dihydrocarvone contains an equatorially oriented isopropylene group, whereas to form *cis*-dihydrocarvone less favorable axial position of isopropylene group is required.

Thus, gold was found to promote the stereo- and chemoselective carvone hydrogenation to dihydrocarvone with a predominant formation of the *trans*-isomer, which is a novel synthetic method for industrially valuable dihydrocarvone.

In the past, (+)- and (-)-carvones were isolated by fractional distillation of caraway oil and spearmint oil, respectively. These carvones are now prepared synthetically, the preferred starting material being (+)- and (-)-limonenes, which are converted into the corresponding optically active carvones (Scheme 10). Carvone oxime is an intermediate, which is formed during carvone synthesis [43, 99]. From the point of view of increasing the chemical synthesis efficiency, a decrease of the number of synthesis steps is one of the general approaches. Therefore, a titania supported gold catalyst was also tested in the hydrogenation of carvone oxime with a general idea to combine synthesis steps.

Scheme 10. Industrial method of carvone synthesis.

Carvone and *trans*-, *cis*-dihydrocarvone were found to be mainly formed during carvone oxime hydrogenation (Scheme 11).
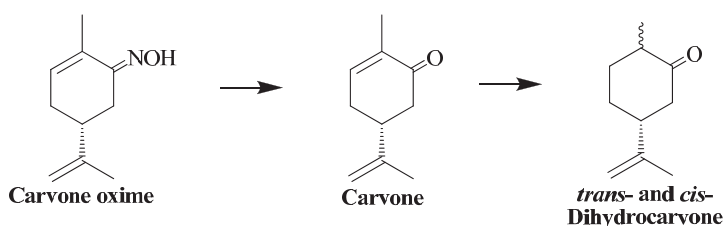
Scheme 11. Reaction pathways of carvone oxime hydrogenation over Au/TiO_2.

The reaction was shown to occur through carvone formation with the subsequent hydrogenation of its conjugated C=C double bond. Despite the decrease in the reaction rate, the increase in the stereoselectivity towards *trans*-dihydrocarvone was observed (Figure 13). In the case of oxime carvone conversion, the ratio between *trans*- and *cis*- dihydrocarvone was doubled compared to carvone hydrogenation (Figure 14).
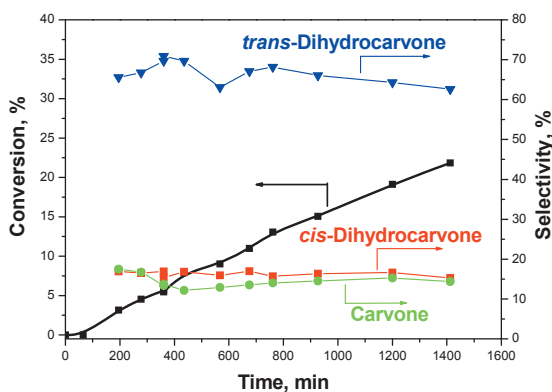
Figure 13. Carvone oxime hydrogenation over Au/TiO$_2$. Reaction conditions: T = 373 K, p (H$_2$) = 9 bar, carvone oxime (10 mmol), methanol (36 ml), Au catalyst (336 mg, Au 0.3 mol. % to substrate).
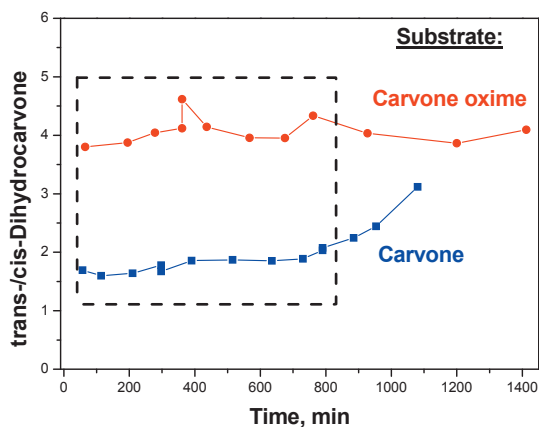

Figure 14. Effect of substrate structure on *trans*-/*cis*-dihydrocarvone ratio. Reaction conditions: T = 373 K, p (H$_2$) = 9 bar, initial substrate (10 mmol), methanol (36 ml), Au catalyst (336 mg, Au 0.3 mol. % to substrate).

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4. Conclusions

Gold catalysts were utilized for different industrially feasible pathways of natural terpenoids transformation, such as α-pinene isomerization, one-pot myrtenol amination and carvone hydrogenation.

For the first time, the outstanding activity of gold catalysts in Wagner-Meerwein rearrangement, such as α-pinene isomerization to camphene, were demonstrated. Compared to a conventional α-pinene to camphene transformation over acid-hydrated TiO_2 resulting in camphene yields from 35% to 50%, gold on alumina catalyst was found to afford α-pinene isomerization conversion up to 99.9% and selectivity 60-80%, making this catalyst very promising from an industrial viewpoint. A detailed investigation of kinetic regularities including the $Au/\gamma-Al_2O_3$ catalyst deactivation during α-pinene isomerization was performed. It was shown that deactivation is caused by adsorption of hydrocarbons on gold clusters. The possibility of complete catalyst regeneration by thermal treatment with oxygen was demonstrated.

The one-pot terpene alcohol amination, which is of high practical importance for the synthesis of complicated amines with specific physiological properties, was systematically studied in the presence of gold catalysts to obtain the knowledge about the key parameters determining the catalytic performance. The catalytic activity and product distribution were shown to be strongly dependent on the support properties, namely acidity and basicity, and conditions of the catalysts pretreatment. The Au/ZrO_2 catalyst pretreated under oxidizing atmosphere was observed to be rather active resulting in total conversion of myrtenol and selectivity to corresponding amine of about 53%. The reaction kinetics was modeled based on mechanistic considerations with the catalyst deactivation step included in the mechanism.

Moreover, gold was found to promote stereo- and chemoselective carvone hydrogenation to dihydrocarvone with predominant formation of the *trans*-isomer, which generally is a novel synthetic method for an industrially valuable dihydrocarvone. The obtained results demonstrate a possibility of catalysis by gold for preferential hydrogenation of a C=C bond conjugated with a

carbonyl group even when another C=C group is present in the substrate. The solvent effect on the catalytic activity as well as on the ratio between *trans*- and *cis*-dihydrocarvone was observed. A range of C_1-C_3 alcohol solvents was applied for carvone hydrogenation and the highest yield of dihydrocarvone was achieved in the case of methanol. Based on the transition state theory, the quantitative explanation of the *trans*-to-*cis*-dihydrocarvone ratio in different solvents was provided.

In summary, bio-derived natural extractives such as terpenoids represent very attractive starting materials for producing fine and specialty chemicals when an advantage can be taken from the molecular structures. Application of the gold catalysts for transformation of these compounds gives new possibilities in terms of both current processes improvements and development of new ones.

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