

Catalysts for enantioselective Biginelli reaction based on the composite silica-zirconia xerogels prepared using different zirconium sources

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Abstract The composite silica-zirconia xerogels have been prepared via sol–gel method using zirconium oxychloride, oxynitrate, acetate and sodium silicate as the precursors. The prepared materials have been characterized using FTIR, TG/DTA, EDX and surface area analyses. It has been established that surface area of silica-zirconia xerogels significantly depends on the zirconium source, but phase transitions and structural features of the xerogels seem to be unaffected by the choice of the zirconia precursor. Prepared xerogels increase the activity of chiral inductor in the asymmetric Biginelli reaction. The anion of the zirconium salt adsorbed on the surface of the synthesized material and the presence of Si–O–Zr heterolinkages determines the reaction yield. The highest chemo- and enantioselectivity towards formation of *ee* isomer have been provided by the catalyst prepared from zirconium oxychloride.

Keywords Silica-zirconia · Biginelli reaction · Enantioselective catalyst · Sol–gel method

1 Introduction

Composite silica-zirconia materials are well known for their unique properties. They are successfully applied as the supports and heterogeneous catalysts in a number of organic reactions [1–4]. The preparation of silica-zirconia composites with a high level of molecular homogeneity is not an easy task, since the isomorphous substitution of silicon by zirconium atoms in the silica matrix is hindered because of the difference of their atomic radii, and also the sources of silica and zirconia have significantly different reactivity [5]. Using alkoxide precursors, such as zirconium *n*-propoxide or butoxide, TEOS or TMOS, and equalizing their reactivity by addition of organic complexing agents have solved above mentioned problems [6]. However, these types of precursors are toxic, expensive and unstable under water–vapor rich atmosphere. That is why the search for less expensive and easily handled precursors has arisen. In substantial number of papers the results of formation of silica-zirconia xerogels using zirconium oxychloride [7], oxynitrate [8] and acetate [4] are reported, but in the analyzed literature we have not found any data containing the comparison of thermal, morphological, structural and textural properties of the silica-zirconia sol–gel composites prepared from this kind of precursors, as well as their catalytic activity in Biginelli reactions. Our previous studies on silica-zirconia xerogels prepared from zirconium oxychloride and sodium silicate using different precipitation routes have shown that it is possible to obtain highly homogeneous materials in absence of any structure-directing agents and organic ligands [9]. On the basis of the data obtained earlier [10] it has been assumed, for the present research, that the most homogeneous, in terms of presence of Si–O–Zr linkages, silica-zirconia xerogels are prepared when SiO₂/ZrO₂ molar ratio equals two, that is

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why the composites synthesized at this molar ratio have been characterized. There are several examples of the efficient application of acid catalysts in Biginelli reaction. In case of heterogeneous inorganic catalysis the attention is attracted mostly to other acidic oxides and clay materials [11–13], but the authors of study [14] also reported the high selectivity and reaction yields in homogeneously catalyzed Biginelli reaction in the presence of ZrOCl_2 and ZrCl_4 . However, the separation of the catalyst after the reaction can prove not an easy task, so in the present communication we report the application of silica-zirconia xerogels, prepared from different zirconium sources, as heterogeneous catalysts for the enantioselective Biginelli reaction.

2 Materials and methods

All reagents used in the current study were of analytical grade. Zirconium oxychloride, oxynitrate and acetate solutions were obtained from MEL Chemicals, sodium silicate solution was purchased from Aldrich. Sodium hydroxide and hydrochloric, nitric or acetic acids were used to adjust pH values of the reaction mixtures.

Sol-gel method was applied to synthesize composite silica-zirconia gels. During gel preparation the solution of sodium silicate was added dropwise to the solution of zirconium salt until the desired molar $\text{SiO}_2/\text{ZrO}_2$ composition was reached. Then the pH of the reaction mixture was adjusted to the value of 3.0 (4.5 while using zirconium acetate as the precursor) with sodium hydroxide or a solution of the corresponding acid, and the opalescent sols were formed. The sols were mixed for an hour and left for 24 h at room temperature in order to obtain monolithic gel. Gels were synthesized at $\text{SiO}_2/\text{ZrO}_2$ molar ratio equaling two. Final concentrations of the zirconia precursors and sodium silicate in the reaction mixtures were 0.05 and 0.1 M correspondingly. Prepared hydrogels were dried at 50 °C, and then washed with deionized water until the negative reaction to the byproduct ions. Finally, the gels were dried again at 50 °C under vacuum (930 Pa) for 72 h. The xerogels prepared using zirconium oxychloride, oxynitrate or acetate were designated as ZSCL, ZSN and ZSAC correspondingly. For the comparison of the activity in the reaction the pure zirconia xerogel (ZCL) was prepared by the similar method to ZSCL sample, but in the absence of silica source.

2.1 Characterization

Thermoanalytical curves have been registered using Netzsch 449 F1 simultaneous TG/DTA thermal analyzer. Measurements have been carried out at the heating rate of 10 °C min^{-1} in platinum crucibles in 40 mL min^{-1} flow of

dry air, in the temperature range from 25 to 1,100 °C. Infrared spectra have been collected in the range 2,000–400 cm^{-1} using Bruker Tensor 27 spectrometer. Samples have been pressed in potassium bromide (KBr) pellets under dynamic vacuum, in order to reduce the amount of air and physically adsorbed water, with sample/KBr mass ratio equaling 1/100. For each spectrum no less than 120 scans with the resolution of 2 cm^{-1} have been recorded and averaged. Specific surface area has been determined by low temperature nitrogen adsorption method with the help of Sorbi-MS analyzer. Prior to measurement the samples were heat treated at 150 °C for 2 h, then degassed in the helium flow at 140 °C. No less than three measurements have been carried out for each sample and the systematic error for this type of measurement was found to be not higher than 5 %. Elemental composition of the samples has been obtained with the help of EDS attachment by Oxford Instruments to scanning electron microscope Jeol JSM7001F.

Determination of the Stereoselectivity of the Biginelli Reaction Performed in the Presence of Silica-Zirconia composite xerogels and Chiral Inductor. Benzaldehyde (1.06 g, 10 mmol), urea (0.6 g, 10 mmol), the chiral organic catalyst (10 mol %) and a xerogel (10 mol %) were dispersed in tetrahydrofuran (10 mL). The reaction mixture was stirred for 30 min at room temperature, after that acetoacetate (1.30 g, 10 mmol) was added. The reaction mixture was stirred for 40 h at room temperature. Then the xerogel was centrifuged, and the solvent was evaporated. The yield of the product 1 was determined using ^1H NMR spectroscopy and HPLC. An enantiomeric excess in the product 1 was determined by HPLC using a YMC-Pack, Chiral-NEA-R chiral column (hexan/ H_2O 35:65, 1.0 mL min^{-1}) and a UV-visible detector (254 nm). The retention times of the (R)-1 and (S)-1 were 10.90 and 12.11 min, respectively.

3 Results and discussion

As we showed in our previous study on silica-zirconia materials, thermal analysis and FTIR spectroscopy were informative analyzing techniques for investigating structural features of amorphous xerogels [10]. Based on the results obtained using these methods one can determine the degree of molecular homogeneity and track the processes of thermally induced phase segregation. Moreover, since the materials have been prepared from inorganic salts under acidic conditions, the corresponding anions and hydroxyls might stay adsorbed on the xerogel surfaces, they can be also detected applying FTIR and TG/DTA analyses. There are two stages of the mass loss observed for ZSN and ZSAC samples with the maxima on DTG at

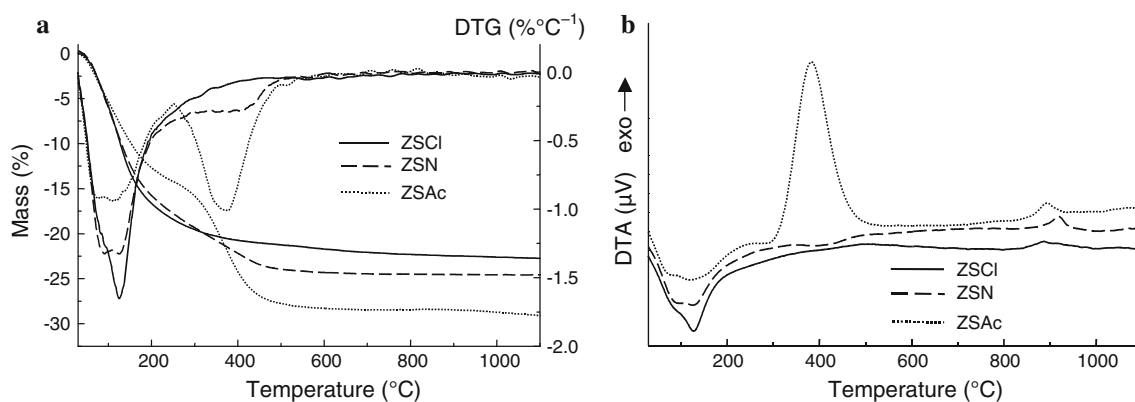


Fig. 1 TG and DTG curves of the composite xerogels (**a**), and their DTA profiles (**b**)

80–130 °C and 360–410 °C, and only one stage is found for ZSCI sample (Fig. 1a). It is worth mentioning that the mass loss in the temperature range 80–130 °C, when the adsorbed and chemically bonded water is removed, is decreasing in the order ZSCI>ZSN>ZSAc, this sequence is reversed for the total mass loss. Sample ZSAc loses 29.3 %, for ZSN and ZSCI this value equals 24.5 and 22.6 % correspondingly. The second decomposition stage in the range of 360–410 °C allows obtaining some information about anions attached to the surface of the xerogels. Mass loss in this region was estimated as 3.9 wt% for NZS and 14.1 wt% for ZSAc samples. These values are supposed to be close to the amount of the NO_3^- and CH_3COO^- groups on the xerogel surfaces. As chlorine is not removed under thermal treatment, it is impossible to determine its content using TG even approximately, but EDS analysis has shown that it equals 1 wt%.

The most important feature on the DTA curves is the presence of the exothermic effect in the region near 900 °C (Fig. 1b). Earlier we reported that this effect reflected the transition of amorphous zirconia in the crystalline tetragonal form, but it was shifted to the higher temperatures in the mixed $\text{SiO}_2/\text{ZrO}_2$ system compared to pure zirconia [9]. The results of the thermogravimetric studies (not presented) confirm this presupposition; all free samples stay amorphous up to 800 °C and then tetragonal zirconia is formed. Thus, the intense exothermic effect on the DTA curve of ZSAc sample is assigned to combustion of organic part of the xerogel and not to zirconia phase transition.

The data obtained from FTIR studies confirm the similarity of the structural features of all three samples. On the spectra of the samples there is a distinctive broad band at approximately $1,050\text{ cm}^{-1}$ corresponding to the TO_3 mode of Si–O–Si vibrations with partially substituted silicon atoms by zirconium ones (Fig. 2). With the rise of the temperature of the heat treatment, this band is gradually shifting towards the higher wavenumbers, indicating the

separation of Zr oxoclusters from the silica matrix. After 700 °C the segregation of the composite phase is obvious and ZrO_2 starts transitioning into crystalline form. The other characteristic band at 800 cm^{-1} attributed to the TO_2 mode of Si–O–Si vibrations also helps us track the segregation process. It can be seen that it appears only after heat treatment at 700 °C. The anions attached to the surface of the xerogels reveal themselves on IR spectra at $1,385\text{ cm}^{-1}$ indicating the presence of NO_3^- (Fig. 2b) groups in the ZSN sample, and bands at $1,571$, $1,452$, $1,350\text{ cm}^{-1}$ are characteristic for CH_3COO^- anion on the surface of ZSAc (Fig. 2c). Thus, FTIR study, as well as thermal analysis and XRD, show that the use of different zirconium salts in synthesis of the silica-zirconia composite does not have great effect on the phase formation and homogeneity of the xerogels. The homogeneity of silica-zirconia materials can be achieved by the equalizing the hydrolysis rates of the silica and zirconia sources, which differ a lot. We reached this goal by the optimizing the synthetic conditions. Highly acidic conditions used to prepare the ZSCI and ZSN samples, where the rates of silica hydrolysis and condensation are low, promoted formation of Si–O–Zr linkages in the solution before the process of fast condensation of zirconia aqua-complexes started. When the hydrolysis of zirconium, while preparing the ZSAc sample is inhibited, because of formation of the complex with acetic acid, which stability is higher than it is for zirconium inorganic salts.

The surface area of the catalysts was determined by low-temperature nitrogen adsorption, the values were found to be: $<10\text{ m}^2/\text{g}$ for ZSCI, 168 m^2 for ZSN and $46\text{ m}^2/\text{g}$ for ZSAc. This difference can be explained by considering the measurement conditions of the xerogels. As the prepared materials had not been subjected to the treatment at high temperatures prior to using in the reaction, it was important to measure their textural properties in the similar state to the same xerogels tested in the reaction. The anions of the salts used for synthesis and some amount of water could be

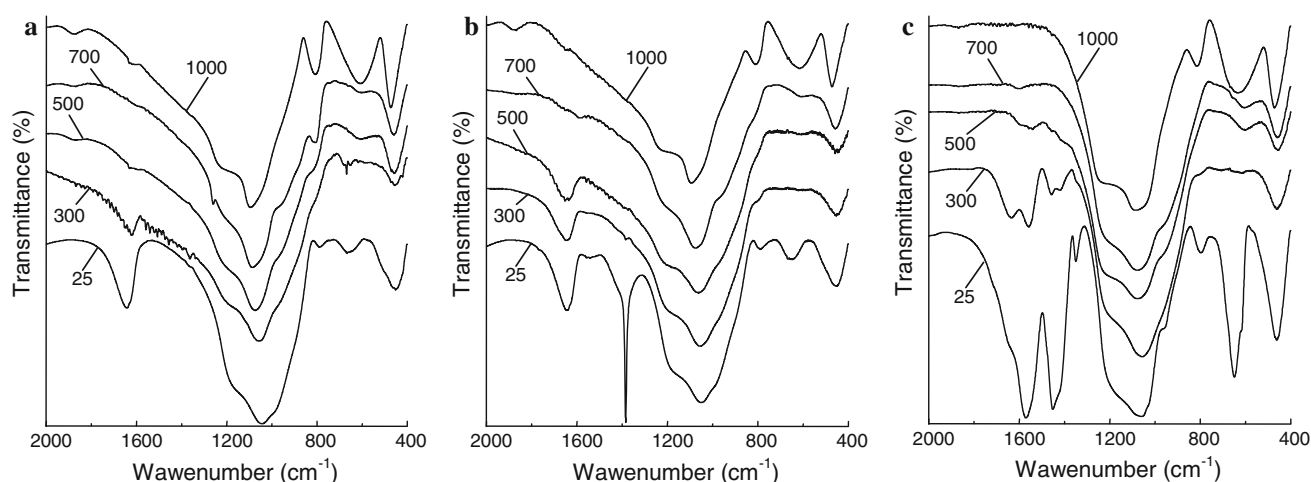


Fig. 2 FTIR spectra of the samples ZsCl (**a**), ZsN (**b**) and ZsAc (**c**) registered at different heat treatment temperatures

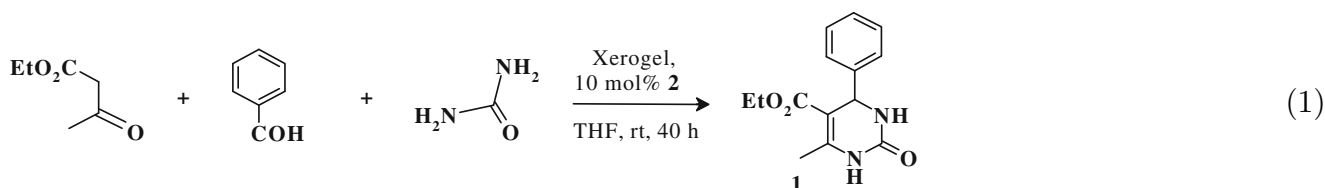
present in the materials, blocking the access of nitrogen molecules inside the pores. The difference in the hydrated state of the surface, as well as the type of the anion, could result in the variations of the surface area values obtained for the xerogels. However, the explanation of that feature by the difference in the solution chemistry of the zirconium salts and as a consequence the difference in polymerization and condensation behavior of zirconia species should not be excluded.

In the previous studies we showed that the addition of the nanosized Ni-C composite increases the enantioselective effect of *L*-proline in the Biginelli reaction (**1**). The enantiomeric excess (*ee*) of the reaction was raised from 0 to 18 % [15, 16]. Silica-zirconia materials have been found to be more active in the same reaction in the presence of (2*S*,4*R*)-4-hydroxyprolyl-(*S*)-1-phenylethylamine **2** described in the study [17].

Table 1 The results of the enantioselective synthesis of the compound **1**

No	Xerogel (10 mol %)	Yield (%)	<i>Ee</i> (%)
1	Without a catalyst [17]	29	39
2	ZsCl	82	52
3	ZsN	51	46
4	ZsAc	46	51
5	ZCl	36	54

correspondingly, but the enantioselectivity does not differ significantly. It is clearly seen that enantioselectivity of the reaction with pure zirconia xerogel (ZCl) is comparable with the results obtained for the composite xerogels. However, the yield of the reaction is only slightly improved in comparison



The yields and enantioselectivity of the reaction in the presence of the silica-zirconia xerogels are summarized in the Table 1. The highest yield and enantioselectivity are observed for the xerogel prepared from zirconium oxychloride. In case of using ZsCl the yield of the reaction is 1.6 and 1.8 times higher than it is for ZsN and ZsAc samples,

with blank experiment. We attribute the enhanced activity of the composite xerogels to the formation of Si–O–Zr heterolinkages, which can generate new acid sites of different strength, and increase the hydroxylation of the material, thus improve adsorption properties, resulting in more effective anchoring of the chiral inductor on the xerogels.

4 Conclusion

It has been found that the use of different inorganic sources of zirconium for preparation of the composite silica-zirconia materials does not have significant effect on the structural features of the prepared materials such as thermally induced phase transition or molecular mixing of SiO_2 and ZrO_2 in the amorphous phase, which has been confirmed by TG/DTA, FTIR and XRD analyses. The nature of the anions attached to the surface and the formation of Si–O–Zr heterolinkages are supposed to be of the greatest significance, as the reaction yield is lower for pure zirconia xerogel. In our opinion, it is probable that the adsorption properties and strength of the acid sites both determine the yield of the reaction, since the strength of the corresponding acids is decreasing in the same order as the activity of the samples $\text{HCl} > \text{HNO}_3 > \text{CH}_3\text{COOH}$, then the selectivity is probably the function of the total concentration of the acid sites or structural features. Silica-zirconia xerogels hold promise for their efficient utilization as heterogeneous catalysts in the enantioselective Biginelli reaction, since the high yields of the products can be achieved and the catalyst is easily separated from the solution. The detailed investigation of the enantioselective properties of this kind of materials is the topic for the further study.

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References

1. Ward AJ, Pujari AA, Costanzo L, Masters AF, Maschmeyer T (2011) The one-pot synthesis, characterisation and catalytic behaviour of mesoporous silica-sulfated zirconia solids. *Catal Today* 178:187–196
2. Chen X-R, Ju Y-H, Mou C-Y (2007) Direct synthesis of mesoporous sulfated silica-zirconia catalysts with high catalytic activity for biodiesel via esterification. *J Phys Chem C* 111:18731–18737
3. Zhuang Q, Miller JM (2001) $\text{ZrO}_2/\text{SiO}_2$ mixed oxides as catalysts for alcohol dehydration. *Appl Catal A* 209:1–6
4. Gomez R, Lopez T, Tzompantzi F, Garciafigueroa E, Acosta DW, Novaro O (1997) Zirconia/silica sol – gel catalysts: effect of the surface heterogeneity on the selectivity of 2-propanol decomposition. *Langmuir* 13:970–973
5. Landau MV, De Jong K (2009) Synthesis of solid catalysts. Wiley, Weinheim, pp 83–110
6. Zhan Z, Zeng HC (1999) A catalyst-free approach for sol–gel synthesis of highly mixed ZrO_2 – SiO_2 oxides. *J Non-Cryst Solids* 243:26–38
7. Navio JA, Colon G, Macias M, Sanchez-Soto PJ, Augugliaro V, Palmisano L (1996) ZrO_2 – SiO_2 mixed oxides: surface aspects, photophysical properties and photoreactivity for 4-nitrophenol oxidation in aqueous phase. *J Mol Catal A* 109:239–248
8. Nagarajan VS, Rao KJ (1989) Crystallization studies of ZrO_2 – SiO_2 composite gels. *J Mater Sci* 24:2140–2146
9. Avdin VV, Krivtsov IV, Dyachuk VV, Zhrebtsov DA (2012) Thermal behavior of the composite xerogels of zirconium oxyhydroxide and silicic acid. *J Therm Anal Calorim* 109:1261–1265
10. Krivtsov IV, Ilkaeva MV, Avdin VV, Zhrebtsov DA (2013) Properties and segregation stability of the composite silica-zirconia xerogels prepared via “acidic” and “basic” precipitation routes. *J Non-Cryst Solids* 362:95–100
11. Mondal J, Sen T, Bhaumik A (2012) Fe_3O_4 @mesoporous SBA-15: a robust and magnetically recoverable catalyst for one-pot synthesis of 3,4-dihydropyrimidin-2(1H)-ones via the Biginelli reaction. *Dalton Trans* 41:6173–6181
12. Martínez S, Meseguer M, Casas L, Rodríguez E, Molins E, Moreno-Mañas M, Roig A, Sebastián RM, Vallriber A (2003) Silica aerogel-iron oxide nanocomposites: recoverable catalysts in conjugate additions and in the Biginelli reaction. *Tetrahedron* 59:1553–1556
13. Bigi F, Carloni S, Frullanti B, Maggi R, Sartori G (1999) A revision of the Biginelli reaction under solid acid catalysis. Solvent-free synthesis of dihydropyrimidines over montmorillonite KSF. *Tetrahedron* 40:3465–3468
14. Rodríguez-Domínguez JC, Bernardi D, Kirsch G (2007) ZrCl_4 or ZrOCl_2 under neat conditions: optimized green alternatives for the Biginelli reaction. *Tetrahedron Lett* 48:5777–5780
15. Uhm YR, Lee HM, Fedorova O, Ovchinnikova I, Valova M, Rusinov G, Charushin V, Rhee CK (2010) Synthesis of carbon encapsulated metal (Ni and Cu) nano particles and applications for chiral catalysts. *Res Chem Intermed* 36:867–873
16. Fedorova OV, Valova MS, Titova YuA, Ovchinnikova IG, Grishakov AN, Uimin MA, Mysik AA, Ermakov AE, Rusinov GL, Charushin VN (2011) Catalytic effect of nanosized metal oxides in the Biginelli reaction. *Kinet Catal* 52:226–233
17. Xin J, Chang L, Hou Z, Shang D, Liu X, Feng X (2008) An enantioselective Biginelli reaction catalyzed by a simple chiral secondary amine and achiral brønsted acid by a dual-activation route. *Chem Eur J* 14:3177–3181