

STUDIES ON THE SYNTHESIS OF MESOPOROUS ALUMINOSILICATES AS CARRIES FOR DRUG DELIVERY SYSTEMS

Laura BĂJENARU¹, Silviu NĂSTASE², Cristian MATEI³, Daniela BERGER⁴

Sistemele pentru eliberare de medicamente formate prin depunerea unei substanțe biologic active pe un suport mezoporos, netoxic, oferă posibilitatea de a controla eliberarea moleculelor de medicament în organism. Aceasta lucrare prezintă sinteza de aluminosilicăți mezoporoși de tip AlMCM-41 prin combinarea metodei sol-gel cu tratamentul hidrotermal și folosirea de precursori de aluminiu diferenți ($NaAlO_2$, $Al(NO_3)_3$, $Al(OsecBu)_3$) ca posibili suporți pentru molecule biologic active. Cele mai mari valori ale suprafeței specifice și volumului total de pori s-au obținut în cazul utilizării $Al(OsecBu)_3$ drept sursă de aluminiu.

Drug delivery systems formed by loading a biological active substance on mesoporous, nontoxic support, offer the possibility to control the release of the drug molecules in the organism. The paper deals with the synthesis of mesoporous aluminosilicates AlMCM41 by sol-gel method combined with hydrothermal treatment, using different aluminum precursors ($NaAlO_2$, $Al(NO_3)_3$, $Al(OsecBu)_3$) as possible carriers for biological active molecules. The highest values for specific surface area and pore volume were obtained when $Al(OsecBu)_3$ was used as aluminum precursor.

Keywords: AlMCM-41, mesoporous material, sol-gel method, hydrothermal treatment

1. Introduction

There is an increasing interest in efficient administration of drugs and in the last years, several groups have reported the use of mesoporous materials as drug carriers [1-3]. Among the drug supports, the mesostructured silica-based materials present some advantages: biocompatibility, tunable pores size and morphology, large specific surface area, high pore volume that allow a good adsorption of biologic active molecules [3,4], the possibility to modify their surface properties by grafting different functional groups *via* postsynthesis silylation reactions [5] etc.

¹ PhD Student, Dept. of Inorganic Chemistry, University POLITEHNICA of Bucharest, Romania

² PhD Eng., Dept. of Inorganic Chemistry, University POLITEHNICA of Bucharest, Romania

³ Reader, Dept. of Inorganic Chemistry, University POLITEHNICA of Bucharest, Romania

⁴ Reader, Dept. of Inorganic Chemistry, University POLITEHNICA of Bucharest, Romania, corresponding author, e-mail: danaberger01@yahoo.com

In 2001, MCM-41 mesoporous silica, which has cubic structure and one-dimensional hexagonal mesopores array, was proposed for the first time as drug delivery system [1] and up to now it is one of the most used silica-type carriers in drug controlled release systems.

The delivery rate of biologic active molecules can be controlled by increasing the interaction between drug molecule and mesophase by tuning the pore size, hydrophobic/hydrophilic nature of carrier surface, introduction of different heteroatoms (aluminum, titanium, phosphorous etc.) in the silica arrays altering the surface acidic properties etc.

Al-containing mesoporous materials present stability and enhanced acidity towards silica [6] and could be applied as drug carriers. AlMCM41-type molecular sieves have well defined system of pores and are synthesized in the presence of cationic surfactant, alkyltrimethylammonium cations in basic reaction medium [7]. The pore size, the specific surface area, the pore volume and the other properties can be modified by varying different synthesis parameters [8].

In this paper, we report a combined sol-gel with hydrothermal approach for the synthesis of mesoporous aluminosilicates AlMCM41 by using tetraethylorthosilicate as silicon source, and different aluminum precursors (sodium aluminate, aluminum nitrate and aluminum *sec*-butoxide).

2. Experimental

2.1 Reagents

Tetraethylorthosilicate (TEOS, Fluka 99,0%), sodium aluminate (NaAlO_2 , Sigma Aldrich), aluminum nitrate ($\text{Al}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$, Sigma Aldrich) and aluminum *sec*-butoxide ($\text{Al}(\text{OsecBu})_3$, Sigma) were used as silicon and aluminum sources and 1-hexadecyltrimethyl ammonium bromide (CTAB, Merck) as template agent.

2.2. AlMCM41 synthesis using NaAlO_2 (**P1**), $\text{Al}(\text{NO}_3)_3$ (**P2**) and $\text{Al}(\text{OBu})_3$ (**P3**) as aluminum precursors

10 mL of 25% (wt) aqueous ammonia solution as catalyst were added to the solution previously prepared by dissolving 2.4 g CTAB in 120 mL deionized water. The mixture of TEOS (10 mL) and aluminum precursor (0.093 g NaAlO_2 or 0.4257 g $\text{Al}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ or 0.4519 g $\text{Al}(\text{OsecBu})_3$ dissolved in 3 mL of absolute ethanol) was dropwise added for 0.5 h under magnetic stirring. The reaction mixture was kept for 2 h, at room temperature, to take place the hydrolysis and condensation reactions and then the formed white gel was ageing for 20 h. To improve the ordering of aluminosilicate samples structure, the obtained gels were hydrothermal treated at 150 °C/ 6 h, at autogene pressure. Then the hydrothermal treated gel was filtered off and washed with ethanol and water to remove the surfactant. To stabilize the mesoporous structure and to

remove completely the template agent, the aluminosilicate samples were calcined at 600 °C for 5 h.

2.3 Characterization

The aluminosilicates samples were characterised by X-ray diffraction (XRD; Rigaku Miniflex II), FTIR spectroscopy (Bruker Tensor 27) in the 400-4000 cm⁻¹ range, scanning electron microscopy coupled with energy dispersive X-ray analysis (SEM-EDX, Tescan Vega III scanning electron microscope), as well as by N₂ adsorption-desorption isotherms performed at liquid nitrogen temperature (Micromeritics Gemini IV porosimeter).

3. Results and discussions

The FTIR spectra of AlMCM-41 samples are similar. In the figure 1 it can be observed the asymmetric stretching vibration of Si-O-Si units from 1066 cm⁻¹, which overlapped the Al-OH deformation band, the vibration from 463 cm⁻¹ characteristic to bending vibrations of Si-O-Si groups, the stretching band from 950-960 cm⁻¹ characteristic to silanol groups, as well as the vibrations from 1630 cm⁻¹ of adsorbed water molecules. In the FTIR spectrum of **P3** sample before calcination (Fig. 1, curve red) are present the vibrations of methyl and methylene groups in the range of 2800-2900 cm⁻¹, which prove that the surfactant was not completely removed by washing the samples. No organic traces are present in the calcined aluminosilicate samples (Fig. 1, curve black).

Scanning electron microscopy investigation of **P3** sample showed primary nanometric spherical particles that have the tendency of spherical agglomerates formation with uniform size and less than 100 nm (Fig. 2A). EDX analysis of this sample has demonstrated a relatively uniform composition and the presence of sodium ions as charge balancing cations, indicating the formation of AlMCM-41 sample with the Si/Al average ratio of ~15.

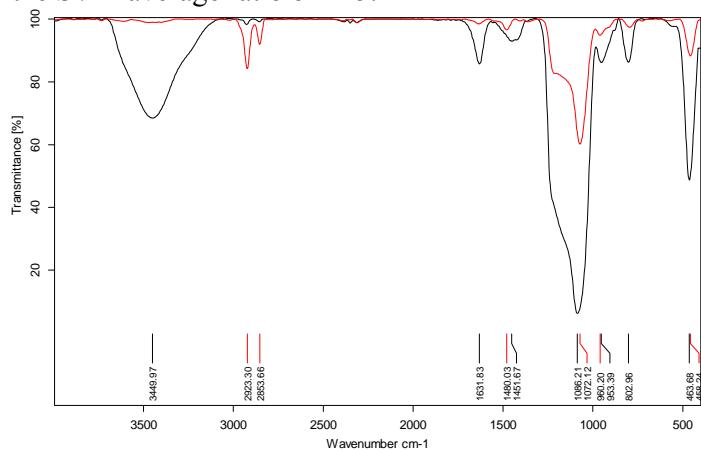


Fig.1. FTIR spectra of **P3** sample before (red curve) and after (black curve) calcination

EDX analysis of P1 and P2 samples have revealed a Si/Al molar ratio of around 30. Both samples were obtained in hydrogen form. The SEM investigation of P1 sample proves a small tendency of spherical agglomerates formation with 50-100 nm diameter and a narrow size distribution (Fig. 2B).

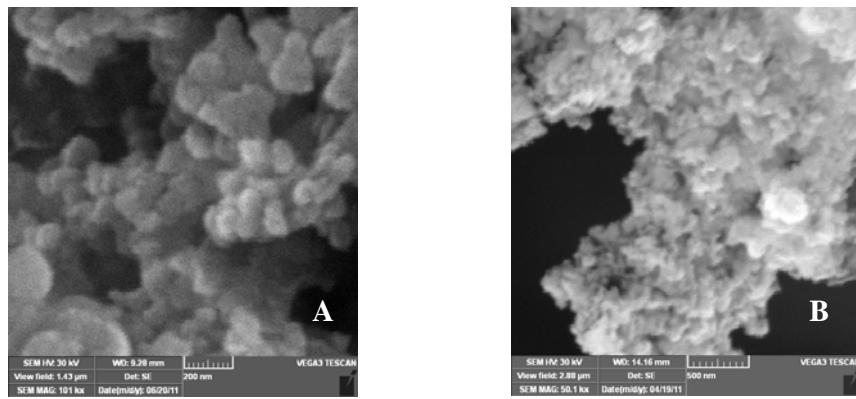


Fig. 2. SEM micrographs of P3 sample (A) and P1 sample, respectively (B)

Table 1

Textural properties of AlMCM41 samples

Sample	S_{BET} (m^2/g)	d_{pore} (nm)	V_{pore} (ads/desorption) (cm^3/g)	$V_{\text{micropore}}$ (cm^3/g)
P1	595	3.45	0.59 / 0.64	0.0037
P2	518	3.35	0.47 / 0.51	0.0064
P3	993	3.34	0.71 / 0.84	0.00

S_{BET} – total specific surface area obtained by BET method, V_{p} – pore volume in terms of equivalent liquid volume, d_{pore} – the average pore size

AlMCM-41 samples were characterized by adsorption-desorption isotherms performed at liquid nitrogen temperature. All three samples present type-IV isotherms typical for good quality MCM41 materials [9]. The nitrogen isotherms are completely reversible, indicating size uniformity and tubular unidirectional mesopores (Figs. 3, 4 and 5). It is evident from the isotherms that all samples have high pore volume and narrow pore size distribution (Figs. 3, 4 and 5, insets). The pore size distributions were calculated using the Barrett-Joyner-Halenda method (BJH) from the corresponding isotherm desorption branch. Although it is well known that the BJH method is inaccurate in absolute terms, the pore size distribution curves presented on the inset of the corresponding isotherms (Fig. 3, 4 and 5, insets) provide useful information for comparative purposes. Table 1 lists some textural properties of prepared AlMCM-41 samples.

Aluminosilicate samples were investigated by XRD at small angles. Usually, the introduction of a heteroatom like aluminum in the silica array induces a disorder degree and only three diffraction peaks can be usually displayed on

SAXS patterns [10]. Unlike MCM41 (Sigma-Aldrich), whose X-ray diffraction pattern reveals a strong sharp peak corresponding at 41.0 Å Bragg distance, and weaker reflections at 23.3, 20.3 and 15.1 Å, AIMCM-41 samples (Fig. 6) have only 2 or 3 less intense and broader peaks. AlMCM41 sample obtained from aluminum *sec*-butoxide precursor shows reflections that correspond to 42.6 Å Bragg distance and two weaker reflections at 24.0 Å and 20.4 Å, which proved an ordered structure. The **P1** and **P2** samples have also hexagonal array, but a less ordered mesophase.

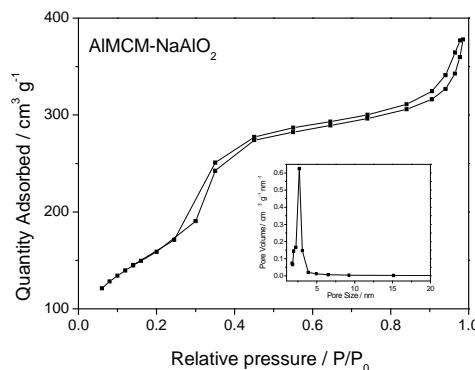


Fig.3. N_2 adsorption-desorption isotherm and the pore size distribution (inset) of **P1** sample

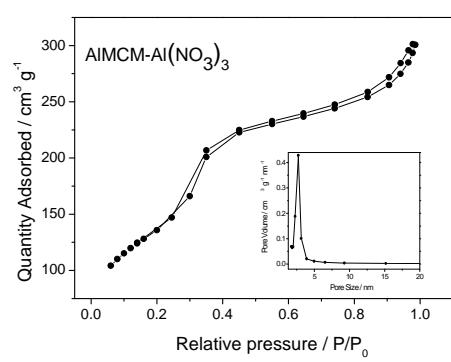


Fig.4. N_2 adsorption-desorption isotherm and the pore size distribution (inset) of **P2** sample

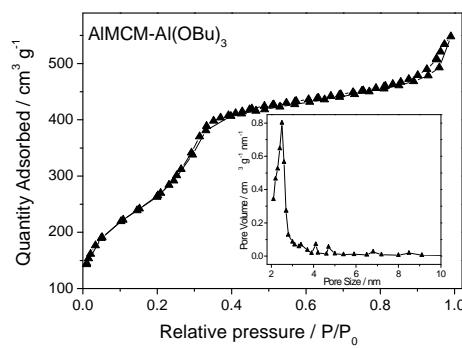


Fig.5. N_2 adsorption-desorption isotherm and the pore size distribution (inset) of **P3** sample

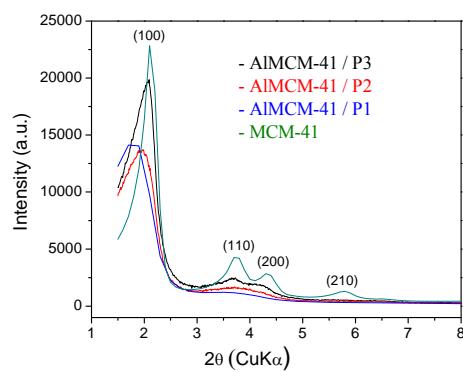


Fig.6. XRD analysis of AlMCM-41 samples

6. Conclusions

All aluminosilicate samples obtained by combining sol-gel method with solvothermal treatment, are good quality MCM41-type mesoporous materials as N_2 adsorption-desorption isotherms performed at 77 K have proved. AlMCM41

sample obtain from aluminum tri *sec*-butoxide as metallic source has more ordered mesopore array and higher values for specific surface area and pore volume than the aluminosilicate samples prepared from aluminum inorganic salts. The good textural features of this AlMCM41 sample, comparable with those of commercially available silica MCM41 [11], recommend this as biological active molecule carrier in drug controlled release systems.

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