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Advances in the Sol-Gel Synthesis of Nanoparticles for Optical and X-ray Bio-Imaging

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Introduction :

The interest to mixed metal oxides and sulfides in biological and environmental applications is due to their high potential as sensor materials and as contrasting agents in the medical diagnostics (de Chermont 2007). The objectives of medical imaging is to introduce chemically inert nanoparticles into the metabolic fluids and follow the major fluxes in them, indicating the enhanced biochemical activity associated commonly with the development of cancer tumors. The characteristics, exploited in imaging can be the luminescent or magnetic properties and also high electron density for contrasting in electron microscopy or X-ray studies (Bridot 2007, Choi 2007).

Materials and methods :

In a typical procedure for preparation of oxide particles a mixture of single-source precursors or a mixed-metal precursor, such as $(\text{Ba}_{1-x}\text{Eu}_x)_2\text{Ti}_2(\text{thd})_4(\text{O}^n\text{Pr})_{8+x}(\text{PrOH})_{2-x}$, $x = 0.01$, obtained according to (Pazik 2008), with a total weight of about 1 g was dissolved in 10 ml toluene and hydrolyzed by stoichiometric amount of water (1 eq. H_2O per each OR-group) on continuous stirring on reflux. The drop wise addition of hydrolyzing solution resulted first in a clear colloid that became slightly turbid after $\frac{1}{2}$ h of reflux. The colloid remained rather stable and its solid content had to be separated by centrifugation and dried in air at room temperature, producing extremely fine white powder, containing about 40% of organic volatiles (by TG). It was then treated thermally in 4 h in air at 700°C , 800°C , 900°C , and 1000°C respectively and characterized by powder X-ray diffraction (SMART CCD 1k). The standard procedure in approach to sulfide particles included dissolution of ≈ 0.25 g of metal oxoalkoxide, oxide or acetylacetonate in a solution prepared by mixing 5 ml toluene with 0.5 ml DMTF at room temperature.

The size of initial particles in aqueous sols was measured by dynamic light scattering (ZetaSizer 3000 HSA, Malvern). FTIR spectra of sols and gels were recorded with Perkin-Elmer Spectrum 100 instrument without dilution in a cell supplied with CaF_2 glasses. The morphology of the xerogels was studied with a Hitachi TM-1000- μDeX 15 kV scanning electron microscope (SEM) and the agglomerate size and crystallinity were studied with a Topcon EM-002 B Ultrahigh resolution analytical electron microscope (TEM). UV-Vis spectra were recorded using Hitachi U-2001 spectrophotometer.

Results and Discussion :

Perovskite materials based on barium titanate or yttrium aluminate are good candidates for the role of nanoparticulate contrasting agents: they are highly chemically inert in the bulk, which can be explained through their stable crystal structure ABO_3 . The latter permits doping these materials with different cations. Doping can be made in two directions: in A-position they can be doped with Rare Earths to produce luminescent nanopowders and in B position they can be enriched with high-valent heavy metal cations, such as, for example, tantalum or tungsten, to achieve high electron concentration.

In the present work the synthesis of nanoparticles of complex composition was achieved by hydrolytic treatment of molecular single-source precursor complexes in refluxing solutions in hydrocarbon solvents. The primary particles formed in this approach conserved the composition of the molecular precursor when the amounts of added water (5% in parent alcohol solution) was equal or exceeding the stoichiometric ones, i.e. 1 eq. of water per each alkoxide group. Application of polar solvents is less favorable as it opens ways for equilibria involving liberation of hydroxo- β -diketonates of main group elements soluble in these media. In contrast, less polar solvents will favor the preservation of all metal cations within the self-assembling particle. It is necessary to mention that formation of self-assembling nanoparticles covered by heteroligands (designated as Micelles Templated by Self-Assembly of Ligands, MTSALs) lays in the background of the generally observed sol-gel mechanism for the formation of metal oxides (Kessler 2006).

The hydrolysis on reflux in toluene resulted in originally amorphous (in X-rays) powders, not sensitive to ambient atmosphere, and gaining pronounced crystallinity already after the thermal treatment at 700°C (see Fig. 1). They contain then exclusively a phase-pure tetragonal $BaTiO_3$ -type phase.

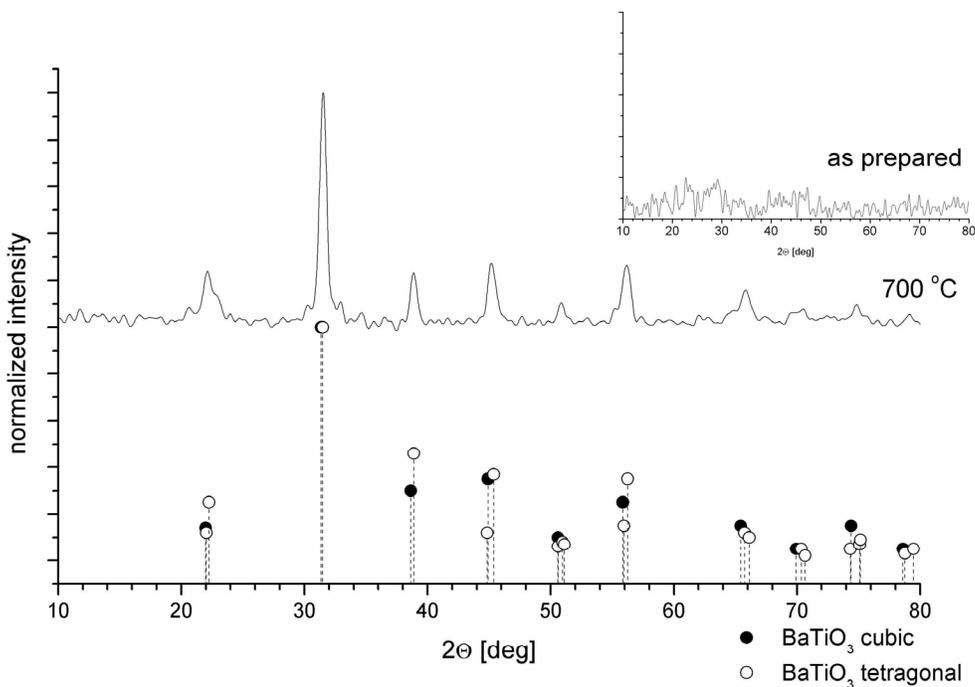


Figure (1) : X-ray powder diffraction pattern of the $BaTiO_3$ nanopowders.

The uniform distribution of europium cations was confirmed by spot-analyses in SEM-EDS. The TEM image of the powder heat-treated at 800°C displays mainly loosely aggregated partially crystalline particles with the average size of 6 nm. Minor part of the sample is represented by bigger particles formed through coalescence of several small ones, where the different crystalline domains, corresponding to the original small particles are clearly distinguishable. These aggregates are more numerous in the samples heat-treated at 900°C and they start dominating the picture after thermal treatment at 1000°C.

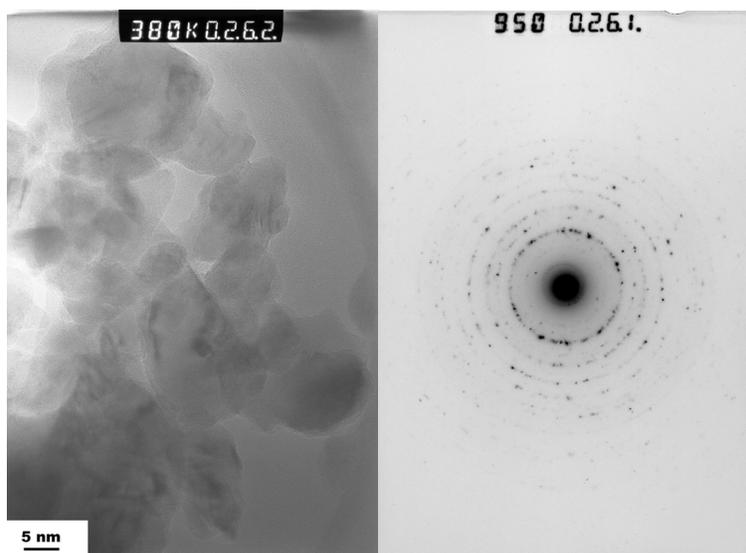


Figure 2 Eu-BaTiO₃ nanoparticles heat treated at 800°C and their electron diffraction pattern.

The controlled increase in the size of the produced particles is provided by subsequent hydrothermal treatment, permitting to obtain uniform polycrystalline aggregate with the size between 20 and 30 nm dependent on the treatment time. The hydrolysis in less polar media is providing thus a facile approach to nanoparticles of Perovskite phases without violation of their original stoichiometry in agreement with the supposition made on the basis of studies of molecular transformations of precursor molecules on hydrolysis (Seisenbaeva 2008). The prepared particles are of interest for further application as contrasting agents in bio-imaging as they display a sharp luminescence band at 610-630 nm.

A new and attractive approach to extremely small, about 5 nm, crystalline nanoparticles can be offered through non-hydrolytic synthesis. The most attractive reaction for this purpose is the ether elimination from metal alkoxides, the Bradley reaction (Turova 1991). It is most efficient when the aprotic polar solvents, such as aldehydes and ketones are applied (Kessler 1998).

The most often used and broadly recognized contrasting agents for X-ray absorption and even X-ray fluorescence studies of tissues suspected to incorporate cancer tumors are solutions of rhenium sulfide, Re₂S₇, nanoparticles often incorporating the ⁹⁹Tc isotope. The most convenient way in the introduction of the latter is the neutron irradiation of a stable ⁹⁸Mo isotope. The efficient development of such nanoparticles requires thus preparation of sulfide samples with a truly uniform distribution of molybdenum on molecular level.

In our approach the formation of sulfides was achieved through solution sulfidation reaction, a general pathway typical of all transition metal complexes with O-donor ligands (see Fig. 3). The

most facile transfer of a sulfur atom is achieved using dimethylthioformamide, a sterically unhindered thiocarbonyl compound (Seisenbaeva 2003).

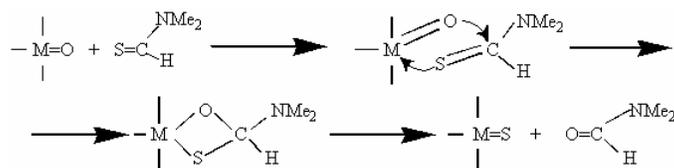


Figure (3) : Mechanism of the solution sulfidation reaction.

The most reasonable precursor of Re_2S_7 in this synthesis is the oxide, Re_2O_7 , easily soluble in majority of polar organic solvents due to its molecular nature. Molybdenum oxide, MoO_3 , cannot be used in combination with rhenium oxide because it has polymeric structure and is insoluble in aprotic solvents. We have applied instead the molybdenum alkoxide, $\text{MoO}(\text{OMe})_4$, amphiphilic species easily soluble in both polar and non-polar solvents. An additional advantage in its application lies in its facile reaction with Re_2O_7 in the presence of methanol, resulting in formation of a heterometallic cluster compound $\text{ReMoO}_2(\text{OMe})_7$ (Seisenbaeva 2001).

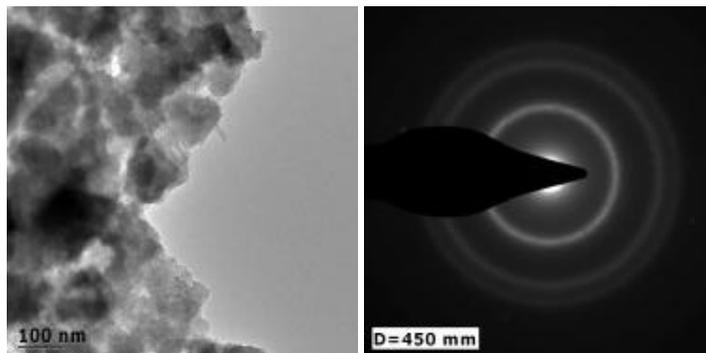


Figure (4) : TEM view and electron diffraction pattern of obtained sulfide nanoparticles.

The prepared particles are crystalline with an anion-deficient Re_2S_7 structure. They are rather uniform in size with an average of 5 nm. In spite of their hydrophobic nature they are readily redispersible in aqueous media and are currently under investigation for X-ray imaging applications.

Conclusions :

Application of solution reactions involving single source precursor complexes provide under controlled conditions a facile and efficient approach to mixed-metal oxide and sulfide nanoparticles – attractive materials for bio-imaging applications.

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