Motivation & Goal
Preparative chromatography is still mainly performed with silica-based retention phases. [1,2] Unfortunately, the small stability range of silica, approximately pH 2–8, limits the possible parameter space of chromatographic protocols. In order to fully protonate or deprotonate common product types (i.e. amino acids), or to routinely clean and reuse the columns (typically with concentrated sodium hydroxide solutions), stationary phases with stability ranges outside pH 2–12 would be desired. [1,3] Previous work shows promising results with other oxide materials, such as alumina (Al(OH)3), titanio (TiO2), or zirconia (ZrO2). [4]

Materials & Methods
Porous spheres of zirconia, alumina and titania were produced either by a precursor route or by controlled aggregation (PICA method, [5]) of nanoparticle dispersions. In the former approach, aqueous solutions of nitrate or chloride salts with organic monomers (urea and formaldehyde) were either dispersed by agitator or dispersed dropwise (by one of two different dispenser types) into a curing bath based on silicone or mineral oil. Variation of the viscosity of the oil phase, dispersants and heating rate led to a set of different particles. Alternatively, the dispersed phase contained alginate instead of monomers while the continuous phase contained calcium hydroxide, both to coagulate the alginate and to precipitate the precursor salts.

After calculation of the particles, surface modifications with different polymers were performed. Particle sizes and pore sizes were compared in the prepared state and after surface modifications. The stability against dissolution of various materials was tested in buffer solutions at pH 1 and pH 12. According to these trials, zirconia, alumina, titania, and ceria were selected. Non-oxidic materials such as silicon carbide or silicon nitride were further dispersants.

After sintering, these particles exhibited specific surface areas (ca. 100-3000 Hz). Producing small amounts (ca. 50 -100 mg) of monodispersed spheres would be accessible using a smaller die.

Conclusions
Several methods for producing spheres by batchwise emulsification were tested. The one using the precursor route produced spheres of relatively narrow size distribution around the targeted sphere size range of 10-30 µm. Nevertheless, gel-casting formulations using dispersions with alginate based binders or PICA type reactions may be more promising for producing and controlling the targeted pore size distribution. As long as perfect monodispersity is not the highest priority, batch emulsification is clearly the method of choice for practical production of spheres in the targeted size range and screening of materials with different pore size distributions.

Through the PICA process high yields of various, practically monodispersed, oxide spheres could be achieved. Underneath the initial simplicity of the process, surprising difficulties arose: The increase of sphere size to the 10–30 µm range requires more development and the control of pore size distribution requires new concepts as well. So-far, the PICA process seems to be rather a “black box” system, where its unclear which handles exist to influence particle size or porosity.

Since dispersing methods offer inherent control over the droplet size (and thus finally the particle size), they are an attractive option to close the “size gap” opened by the above discussed methods. On the other hand, it has to be considered that when dispersing the rate of sphere production is highly dependent on the sphere diameter. For example, producing the same mass of spheres with diameters of 10 µm would take a factor of 10² longer than for 30 µm spheres. Irrespective of the type of dispenser system, one of the main obstacles at present for production of spheres by dispersing is the curing and collection of the spheres. Fusing or aggregation of not fully cured droplets (in flight, on the interface to the curing liquid, in the curing liquid) has to be avoided. Although some parameters to influence this seem obvious (i.e. dispersing frequency, surface tension of the curing liquid, curing speed), finding practical solutions to this issue is not trivial.

Results
A first set of experiments using agitation synthesis (“water in oil”) aimed at the preparation of particles of ZrO2 or yttrium doped ZrO2 (zirconia, YSZ). After sintering, these particles exhibited specific surface areas around 50 m²/g. Considering the density of zirconia, which is approximately 2.5 times larger than the density of silica, this compares to a silica of approx. 125 m²/g (Fig. 1).

Due to difficulties with reproductibility, this approach was abandoned in favor of other methods.

The first disperser used a piezo driven nozzle, allowing the production of particles in the desired size range of 10-30 µm. Producing small amounts (ca. 50-100 mg) of monodispersed spheres could be achieved with this system at moderate rates (ca. 100-3000 Hz).

Again, the pore volumes calculated by the BJH method are significantly higher than those derived from DFT (Tab. 1, Fig. 5). The main reason for this is the absence of pore size information in the DFT data above about 150 Å (i.e. the pore volume of pores larger than 150 Å is not taken into account). The DFT also predicts unrealistic average pore sizes around 19 Å for TiO2 and CeO2 which are not consistent with the particle sizes. All in all, the values of the BJH appear more consistent and reliable here to be considered as guidelines.

Conclusions
Several methods for producing spheres by batchwise emulsification were tested. The one using the precursor route produced spheres of relatively narrow size distribution around the targeted sphere size range of 10-30 µm. Nevertheless, gel-casting formulations using dispersions with alginate based binders or PICA type reactions may be more promising for producing and controlling the targeted pore size distribution. As long as perfect monodispersity is not the highest priority, batch emulsification is clearly the method of choice for practical production of spheres in the targeted size range and screening of materials with different pore size distributions.

Through the PICA process high yields of various, practically monodispersed, oxide spheres could be achieved. Underneath the initial simplicity of the process, surprising difficulties arose: The increase of sphere size to the 10–30 µm range requires more development and the control of pore size distribution requires new concepts as well. So-far, the PICA process seems to be rather a “black box” system, where its unclear which handles exist to influence particle size or porosity.

Since dispersing methods offer inherent control over the droplet size (and thus finally the particle size), they are an attractive option to close the “size gap” opened by the above discussed methods. On the other hand, it has to be considered that when dispersing the rate of sphere production is highly dependent on the sphere diameter. For example, producing the same mass of spheres with diameters of 10 µm would take a factor of 10² longer than for 30 µm spheres. Irrespective of the type of dispenser system, one of the main obstacles at present for production of spheres by dispersing is the curing and collection of the spheres. Fusing or aggregation of not fully cured droplets (in flight, on the interface to the curing liquid, in the curing liquid) has to be avoided. Although some parameters to influence this seem obvious (i.e. dispersing frequency, surface tension of the curing liquid, curing speed), finding practical solutions to this issue is not trivial.

Literature