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Functional Nanobeads

Covalently Functionalized Cobalt Nanoparticles as a Platform for Magnetic Separations in Organic Synthesis**

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The product separation and postprocessing of organic compounds, proteins, nucleic acids, and natural products from complex reaction mixtures remain labor-intensive and costly. A possible solution to this problem is the magnetic separation of products from mixtures,[1] as routinely applied in biochemistry.[2–5] Unfortunately, the exorbitant price of magnetic microbeads[6] and their low binding capacity (approximately 700 pmol g^{-1}) limit their use for organic synthesis.

Recently there has been an increased interest in air-stable core–shell magnetic nanoparticles.[7] These materials combine the beneficial magnetic properties of the core with the possible functionalization of the surface. Optimal magnetic properties can be achieved by the use of metals. However, if the size of the magnets is reduced to the nanometer size range they become air-sensitive (typically pyrophoric), impeding the application in standard separation processes. Up to now this has promoted a widespread use of oxides (mainly magnetite) for nanomagnets.[8–10] To access the much higher magnetic moments of metallic nanomagnets, the core could be protected by an additional surface coating that should be chemically inert towards air and acids, and stable at elevated temperatures. Further, the surface must be suitable for the formation of covalent bonds and the binding of functional groups, as is the case for the solid supports for Merrifield synthesis.[11] Several coating materials such as silica,[12,13] transition-metal oxides,[14,15] gold,[16] and carbon[17] have been suggested. While the use of gold does not seem to be cost-efficient, covalent bonds on silica and other metal oxides are prone to hydrolysis, leaving carbon coatings as the most promising option. The synthesis of carbon-coated metals such as cobalt,[18,19] cobalt–iron alloys,[20] and nickel[21] has recently been reported at very limited production rates (<1 g h^{-1}). The functionalization of such nanomaterials has been attempted previously, but Seo et al.[20] obtained only noncovalent ligand bonding, and Ma et al.[21] achieved carboxylate functionalizations by oxidation in concentrated acids at yields below 20%.

Herein we present the one-step, large-scale (>30 g h^{-1}) production of carbon-coated nanomagnets with high air and thermal stabilities. We demonstrate covalent functionalization of the carbon surface with chloro, nitro, and amino groups, the most frequently used linkers presently applied in solid supports. The particles were prepared by reducing flame synthesis, a process which we recently derived from the industrially most prominent nanomaterials-manufacturing method, flame-aerosol synthesis; currently this method accounts for the preparation of several million tons of carbon, silica, and titania.[22] We have most recently demonstrated the synthesis of pure cobalt nanoparticles.[23] These uncoated particles (see Table 1, material prepared under N_2) were only protected by oxide layers and could not be used as magnetic beads with a covalent functionalization. The core–shell arrangement presented here was achieved by adding acetylene to the cobalt-nanoparticle-forming process, resulting in the controlled deposition of carbon on the particles.

Figure 1 shows the freshly produced metallic nanopowder in air. (See the Supporting Information for details on reducing flame synthesis.) The unexpected stability can be explained by looking at the structure of the individual particles with a transmission electron microscope (Figure 1, right). Several carbon layers coat the particles in an onion-type arrangement and protect the metallic core from oxidation.

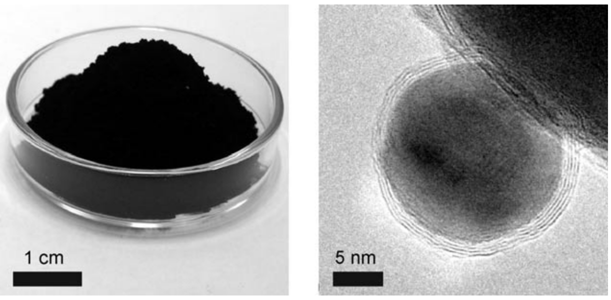

Figure 1. Left: Photograph of about 5 g of the air-stable, carbon-coated nanomaterial. Right: Transmission electron microscopic image of the powder shows two to four homogeneous graphene layers coating the metallic cobalt core.

The mean thickness of the carbon layer could be calculated from the carbon content (2.1 wt%, Table 1) and the particle specific surface area (15 $m^2 g^{-1}$, Table 1) as approximately 1 nm, which is equivalent to a coating with roughly three carbon layers. The average particle diameter could be derived from the specific surface area, assuming the presence of spheres, as 50 nm, and the particle size distribu-

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Table 1: Synthesis conditions and properties of the magnetic beads.

Conditions[a]	C content [wt%][c]	SSA[d] [$m^{-2}g^{-1}$]	*d* [nm][e]	SM [$A m^2 kg^{-1}$][f]
under N_2[b]	<0.5	19	<0.1	124
with 5 $L min^{-1}$ C_2H_2	2.1	15	0.7	158
bulk cobalt[g]	–	<0.01	–	163[26]

[a] See the Supporting Information for experimental setup and detailed conditions. [b] Reference material.[23] [c] Carbon content as measured by microanalysis. [d] Particle surface area as measured by nitrogen adsorption; errors ±10%. [e] Average thickness of carbon layer coating the particles calculated from carbon content and particle surface area (i.e. carbon content/carbon density/surface area, assuming a carbon density of 2200 $kg m^{-3}$). [f] Saturation magnetization (SM) at room temperature at $B = 2$ T; error: ±2%. [g] Reference values.

tion of flame-spray-derived materials has been shown to be lognormal, with a geometric standard deviation of ≈ 1.4.[23–25]

The carbon-coated core–shell particles exhibited a high thermal stability and did not show any indications of oxidation (weight change) at temperatures of up to 190 °C (Figure 2). This is in sharp contrast to the spontaneous ignition of uncoated, pyrophoric metal nanopowders. At higher temperatures the oxidation occurred as a two-step process: the first oxidization step corresponded to a weight gain of $\approx 25\%$ at 195–240 °C and a second oxidation step starting at ≈ 280 °C led to a total weight gain of 31.5%.

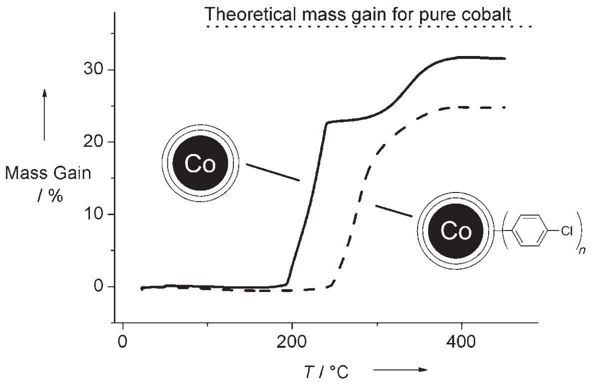


Figure 2. Powder mass gain upon oxidation measured by thermogravimetry in air of untreated carbon-coated cobalt nanoparticles (solid line) and chlorobenzene-functionalized nanobeads (broken line).

The as-prepared carbon-coated cobalt nanobeads exhibited excellent magnetic properties with a saturation magnetization of 158 $A m^2 kg^{-1}$. This is, when calculated as saturation magnetization per unit metal, equivalent to the bulk saturation magnetization[26] of metallic cobalt and gives further evidence of the high purity of the metallic core. These superior magnetic properties (see the Supporting Information for full hysteresis) enabled the fast and complete recovery of the magnetic nanobeads from a suspension (Figure 3).

The results presented here on untreated carbon-coated magnetic nanobeads motivated us to investigate possible surface modifications. As it can be assumed that the carbon coating of the magnetic beads is chemically related to the structure of graphite layers or multiwalled carbon nanotubes, similar functionalization chemistry could be applied. Such methods have been thoroughly investigated for applications in printing inks and the solvatization and exfoliation of carbon nanotubes.[27] From the large range of possible reactions reported,[28,29] the conversions of aryl diazonium salts appeared most promising.

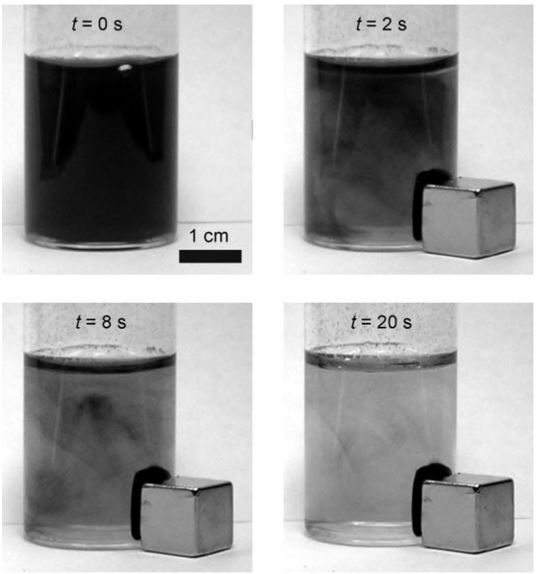
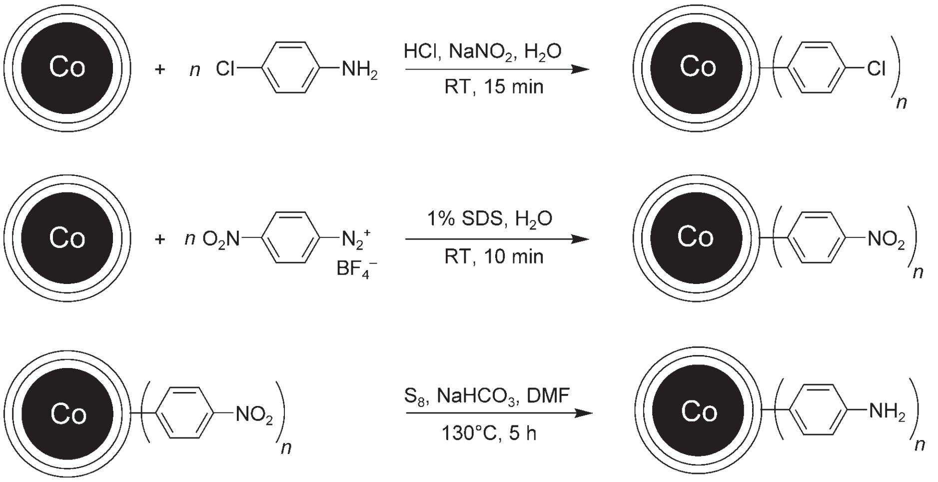


Figure 3. Separation of cobalt nanoparticles from a suspension (1 $g L^{-1}$) in water by a commercial neodymium magnet ($B = 1.4$ T). Photographs were taken at indicated times after placement of the magnet.

Scheme 1 shows two different diazotation reactions. Chloro groups were introduced to the surface of the cobalt nanobeads by reaction with the diazonium salt formed in situ from 4-chloroaniline.[30] The reaction quickly proceeded at room temperature in an ultrasound bath and the evolution of nitrogen could be observed. The derivatized material could be removed easily from the reaction mixture with a magnet and was washed consecutively with water, hexane, and ethyl acetate and dried in vacuo.

Since the presence of the magnetic cobalt core made product analysis by NMR spectroscopy impossible, the material produced was analyzed by IR spectroscopy. The IR spectrum of the chloro-functionalized magnetic nanobeads (Figure 4, second trace from the bottom) strongly differs from that of the untreated carbon-coated magnetic beads (Figure 4, bottom trace) and shows peaks characteristic of a 4-substituted chlorobenzene group. This is supported by the good match with the IR spectrum of chloro-4-ethyl-benzene (Figure 4, second trace from the top) and the deviation from that of chlorobenzene (Figure 4, top trace). This observation rules out the possible physisorption of chlorobenzene on the graphite surface. The absence of the azo group ($\nu = 1400$—$1500\ cm^{-1}$)[31] is in line with earlier investigations on the diazotation of carbon nanotubes and supports the radical-mediated reaction path suggested by Dyke et al.[32] The temperature stability of the carbon nanobeads was



Scheme 1. Functionalization of carbon-coated magnetic nanobeads with chlorobenzene[30] and nitrobenzene[34] and reduction of the nitro groups to amino groups with elemental sulfur. SDS = sodium dodecylsulfate.[35]

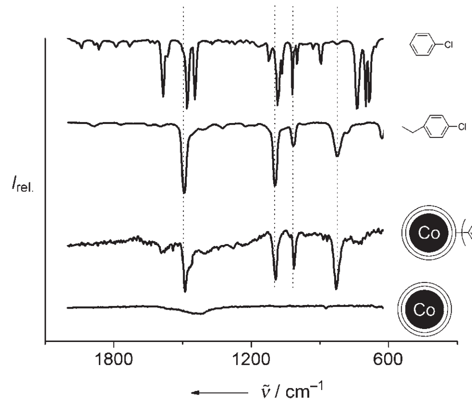


Figure 4. IR spectra of the unreacted C/Co powder (bottom trace) and after reaction with chlorobenzenediazonium salt (second trace from the bottom); reference spectra of 1-chloro-4-ethylbenzene (second trace from the top) and chlorobenzene (top trace).[33]

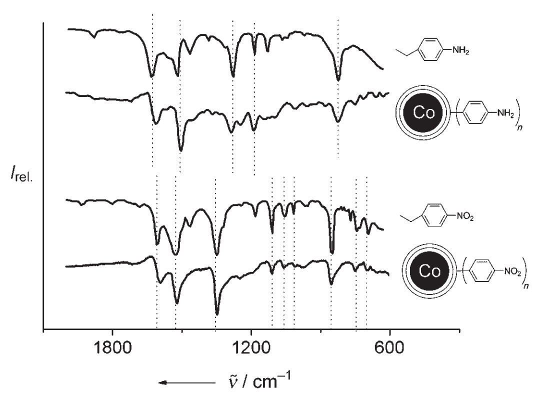


Figure 5. IR spectra of the C/Co powder after reaction with 4-nitrobenzenediazonium salt (bottom trace) and after subsequent reduction with S_8/$NaHCO_3$ (second trace from the top); reference spectra of 4-ethylaniline (top trace) and 4-ethylnitrobenzene (second trace from the bottom).[33]

increased even further by the functionalization with chlorobenzene, as indicated in Figure 2.

The degree of functionalization can be calculated from quantitative microanalysis. The measured Cl content of 1.1 % corresponds to a loading of approximately 0.3 mmol g^{-1}. This is on the order of magnitude of solid supports currently used. No morphological changes of the magnetic nanobeads could be observed by transmission electron microscopy (see the Supporting Information), and the specific surface area of the material increased by roughly 15 %.

Alternatively, the carbon-coated magnetic beads were derivatized using 4-nitrobenzenediazonium tetrafluoroborate salt, which was previously used for the exfoliation of carbon nanotubes.[34] Again the IR spectrum of the derivatized sample shows peaks characteristic of 4-substituted nitrobenzene moieties and no indications of azo groups. The degree of functionalization was determined from quantitative C,H,N analysis and yielded 0.1 mmol g^{-1}.

Following the most recent approach by McLaughlin[35] the nitro groups were reduced to amino groups (Figure 5, Scheme 1). These amino-functionalized magnetic nanobeads can now be used for standard peptide coupling.

In summary, carbon-coated magnetic nanobeads were synthesized at a rate of more than 30 g h^{-1} by reducing flame synthesis by the addition of acetylene to a nanoparticle-forming flame. Beads consisting exclusively of carbon and cobalt exhibited excellent magnetic properties and high stability in air at temperatures up to 190 °C. The core–shell particles could be functionalized by the use of diazonium chemistry yielding chloro-, nitro-, and amino-functionalized magnetic nanobeads. The high capacity for ligand binding and rapid removal of the nanobeads from reaction mixtures suggests possible application of these functionalized nanomagnets in organic synthesis and biotechnological applications.

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