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Synthesis and stabilization of nano-sized titanium dioxide

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Contents

I.	Introduction	873
II.	The effect of synthesis conditions on the degree of dispersion, phase composition and properties of titanium dioxide	874
III.	Synthesis of nano-sized TiO_2 based on titanium alkoxides; product dispersion and phase composition	875
IV.	Nano-sized TiO_2 synthesis based on $TiCl_4$; product dispersion and phase composition	881
V.	Synthesis of TiO_2 based on miscellaneous titanium-containing precursors	882
VI.	Stabilization of the disperse state and phase composition of nano-sized TiO_2 sols	883

Abstract. The published data on the preparation and the dispersion-structural properties of nano-sized TiO_2 are considered. Attention is focused on its sol – gel synthesis from different precursors. The possibilities for the purposeful control and stabilization of properties of TiO_2 nanopowders and sols are analyzed. Information on physicochemical methods used in studies of the particle size and the phase composition of nanodisperse TiO_2 is presented. The prospects of using nano-sized TiO_2 in medicine and nanobiotechnology are considered. The bibliography includes 95 references.

I. Introduction

Due to its unique properties, nano-sized titanium dioxide represents a promising research subject for various modern fields of science and technology, including microbiology, nanobiotechnology and fundamental medicine. Thus the most popular directions include the design of a new generation of drugs based on synthetic nanobioconstructions containing TiO_2 nanoparticles and aimed at curing cancer and viral or genetic diseases. The necessity of developing new approaches to fight against these diseases is associated with the limitations inherent in conventional methods of therapy and profilaxis. Thus for viral infections, the therapy efficacy tends to decrease due to permanent mutation of viruses.

Development of methods for the targeted influence on specific RNA and DNA molecules includes studies of the conjugates of oligonucleotides containing biologically active or photoreactive ligands targeted to a certain fragment of a nucleic acid.[1 – 3] Numerous oligonucleotides and their derivatives capable *in vitro* selective interact with nucleic acids were synthesized. The main problem of these compounds was associated with the absence of reliable and efficient methods of their delivery into cells, because viruses are localized inside a cell and oligonucleotides fail to effectively penetrate there due to their relatively high molecular weight and the hydrophobic nature of cell membranes. To solution of this problem, the methods of nanotechnology and nanobiotechnology oriented at employing nanoparticles as drug-loaded 'nanovectors' are engaged.[4] TiO_2 nanoparticles were used as a carrier for oligonucleotides.[5] Covalently linked TiO_2 – DNA nanocomposites were shown to possess the unique property of a light-inducible nucleic acid endonuclease.[6]

The first publication[7] on the use of titanium dioxide in microbiology for photoelectrochemical sterilization of microbial cells dates back to 1985; since that time, the number of studies devoted to the bactericidal effect of nanodisperse TiO_2 with respect to different pathogenic bacteria is being permanently increased.[8 – 17] Data on the efficient blood purification from residual viruses by filtering it through nanoceramic membranes or nanofibres containing nanostructured TiO_2 are documented.[18]

Recently, publications have appeared devoted to studies on the possibility of using TiO_2 in oncology.[19 – 22] This is associated with the quest for an alternative to two main methods of treating malignant tumours, *i.e.*, radio- and chemotherapy. For example, it was demonstrated[22] that the growth of the Ls-174-t culture of human colon carcinoma

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cells can be suppressed by treating these cells with a dilute TiO_2 colloid solution followed by irradiation. The tumour cells were effectively killed *in vitro* by photoexcited TiO_2 nanoparticles. The survival ratio after 30-min irradiation decreased rapidly with the increase in TiO_2 concentration.

In Russia, studies devoted to the development of synthetic nanoconstructs involving TiO_2 particles for the targeted viral genome cleavage are of the innovating nature and largely represented by proceeding of conferences.[23–27] It was demonstrated[27] that nanocomposites built of titanium dioxide nanoparticles with immobilized polyamine-containing oligonucleotides interact with 30-mer [^{32}P]RNA and [^{32}P]DNA targets. It was shown that UV irradiation of the complexes formed results in modification of the targets. Nanocomposites based on complexes of amorphous TiO_2–polylysine nanoparticles with oligonucleotides exhibited antiviral activity, which was especially pronounced under UV radiation carried out 2–3 h after infection. Obviously, the prerequisite for the use of TiO_2 in such constructs was its nanoscale size and colloidal state, which ensured the efficient penetration of nanostructures into cells.

The low cytotoxicity of TiO_2 nanoparticles was noted,[25,26] which, however, varied for different cell cultures and depended on the titanium dioxide phase composition. The low toxicity of TiO_2 nanoparticles was also demonstrated in another study.[28] A well-known *in vitro* procedure was used to assess the organism response to dust from the induction of proinflammatory cytokines IL-6 and IL-8 generated by respiratory tract epithelium cells treated with relevant particles. It was shown that nanoparticles of commercial metal oxides including TiO_2 are not too toxic with respect to lung cells as compared with the environmental dust particles. It also followed from the results of this study that contrary to expectations, the metal oxide nanoparticles were not more toxic than micron-sized particles.

Nano-sized titanium dioxide finds wide application in other modern scientific and technological fields including photocatalysis, electrochemistry, optics, microelectronics, in the production of dyes, ceramics, cosmetics, gas sensors, inorganic membranes, dielectrics, in the synthesis of mesoporous film coatings, catalysts for environmental cleaning processes, *etc*.[29–44]

Thus, the synthesis and stabilization of nanodisperse forms of TiO_2 is a challenge for science and practice.

The most popular method of synthesis of disperse deposits of metal oxides including TiO_2 is their precipitation from the solutions of the corresponding salts with ammonia, alkalis and alkali-metal carbonates. Numerous studies have shown that the minimum size of primary particles is independent of the nature of the precipitating agent being equal to 45 ± 10 Å.[45] Depending on the synthesis conditions, the primary particles coalesce to form different-sized aggregates. The degree of aggregation depended on many factors and was controlled by the synthesis conditions. Varying the temperature, the synthesis time and pH of the medium allowed fabrication of titanium dioxide with different phase compositions, namely, amorphous TiO_2, anatase, brookite or rutile.

The present review summarizes studies on the synthesis of nano-sized titanium dioxide and the control and stabilization of the dispersed state, morphology and phase composition of TiO_2 nanoparticles and also discusses the prospects of their use in nanobiotechnology.

II. The effect of synthesis conditions on the degree of dispersion, phase composition and properties of titanium dioxide

According to early studies,[45] hydrolysis of different titanium compounds (titanium alkoxides and inorganic salts, mainly, $TiCl_4$) in aqueous solutions with low pH (2–6) resulted in basic salts with variable compositions as the primary products. At higher pH, titanium dioxide hydrates, form presumably, with the composition $TiO(OH)_2$ or $TiO_2 \cdot n\,H_2O$, where n depends on the ageing and drying conditions.

Freshly precipitated titatium(IV) dioxide hydrate exhibited high adsorbability with respect to both cations and anions; the content and the nature of impurities in TiO_2 depended on the pH of the medium and the nature of both the precipitating agent and the starting titanium compound.[45] According to the data from transmission electron microscopy (TEM), the TiO_2 gel represents spherical nonporous particles with the sizes 30–60 Å aggregated into chains and bunches. The gel specific surface (S) varied from 250 to 500 $m^2\ g^{-1}$ (Refs 45 and 46) and depended on the precipitation conditions and the presence of impurities (Fig. 1, 2).[45]

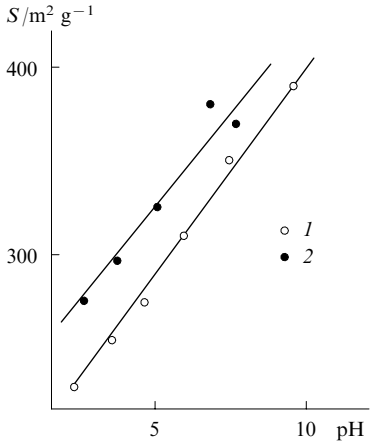


Figure 1. Dependence of the specific surface of titanium dioxide hydrate on the pH of the medium in the course of sedimentation at room temperature (*1*) and 70 °C (*2*).[45]

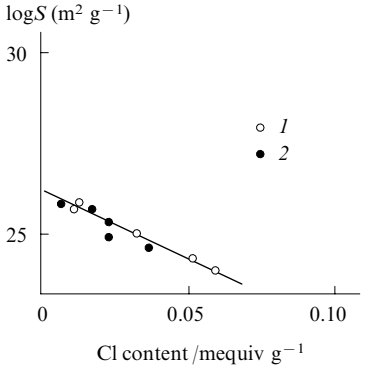


Figure 2. Dependence of the specific surface of titanium dioxide hydrate on the chloride ion content.[45]
(*1*) Sedimentation at room temperature, (*2*) at 70 °C.

The specific surface of titanium dioxide hydrate formed upon hydrolysis under hydrothermal conditions also depended substantially on the temperature and the duration of the process.[47] Strong effect of the initial concentration of $TiCl_4$, which determines the reaction medium acidity, on the degree of crystallinity of the hydrothermal hydrolysis product was obsewed.[48]

A simple and accessible method for the synthesis of pure and stable nano-sized TiO_2 (anatase) under mild hydrothermal conditions using $TiCl_4$ as the precursor was proposed.[49] Solvothermal hydrolysis of titanium ethoxide in anhydrous ethanol containing strictly definite amount of ultrapure water, carried out under mild conditions (< 200 °C, 2 h), also afforded pure ultradisperse nanocrystalline anatase with high specific surface (up to 250 $m^2\ g^{-1}$).[50]

Thermal treatment of gels of different titanium dioxide hydrates resulted in their crystallization to form anhydrous TiO_2. Depending on the calcination temperature, hydrated TiO_2 could be transformed into anatase, rutile or brookite, which was accompanied by changes in its specific surface and porous structure. Thus at temperatures below 600 °C, crystallization produced anatase with the virtually constant pore volume and specific surface.[51] For higher temperatures, the transition of anatase to rutile occurred with concomitant sharp decrease in both the pore volume and the specific surface (Fig. 3). Mineral impurities could also exert a strong effect on the polymorphous transition temperature.

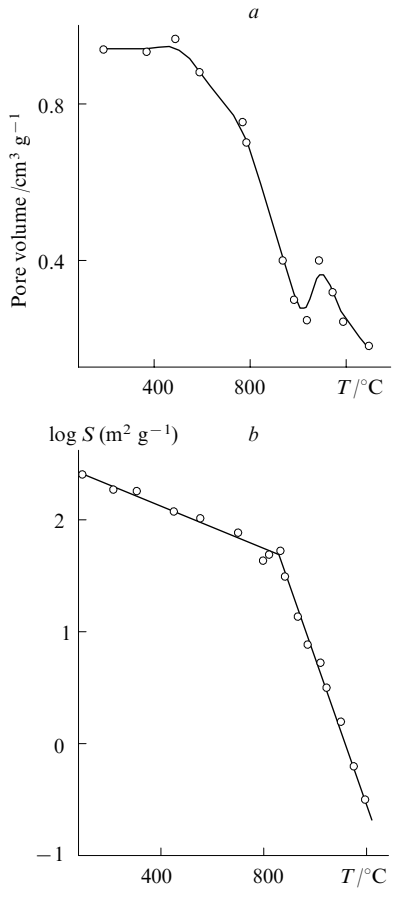


Figure 3. Changes in the porous structure (*a*) and the specific surface (*b*) of titanium dioxide in the calcination.[51]

Numerous data have shown that besides the phase composition, the conditions of thermal treatment of TiO_2 gels determined other important performance characteristics of titanium dioxide, namely, its morphology and the particle size.

The production of TiO_2 is carried out, most often, by the sulfate and chloride methods (from ilmenite and $TiCl_4$, respectively). Titanium tetrachloride can be processed according to three different schemes, namely, hydrothermal hydrolysis, vapour-phase hydrolysis and combustion in an oxygen flow. Recently, the sol–gel method that affords TiO_2 particles with desired structures and properties has gained in importance and, hence, has attracted attention from the viewpoint of development of nanotechnologies. Titanium alkoxides or titanium tetrachloride were used as the titanium-containing precursors in the sol–gel method.

In the following sections, the most significant results in the control over dispersion, morphology, phase composition and stability of nano-sized TiO_2 are considered.

III. Synthesis of nano-sized TiO_2 based on titanium alkoxides; product dispersion and phase composition

In the synthesis of TiO_2 from alkoxides, titanium tetraisopropoxide (from hereon, isopropoxide) and titanium tetrabutoxide (butoxide) are preferred.

Colloid solutions of TiO_2 with different particle sizes and stability were synthesized[52] from acetylacetone-modified $Ti(OPr^i)_4$ using organic solvents that differed in polarity and molar volume. According to data from X-ray phase analysis, irrespective of the nature of organic solvents used in the hydrolysis, all freshly prepared sols obtained both with or without acetylacetone contained amorphous TiO_2 that was transformed into the nanocrystalline anatase phase when heated to 450 °C. However, the use of solvents with small molar volumes and modification of the precursor with acetylacetone resulted in stabilization of the TiO_2 colloid solution, which actually was the principal result of the study cited above. An IR spectroscopic investigation suggested the formation of a chelate complex of titanium isopropoxide with acetylacetone (Fig. 4), which presumably slowed down the hydrolysis and condensation and, hence, decreased the degree of agglomeration of TiO_2 particles; the effect of solvent on the aggregate size (Fig. 5) was rationalized in terms of the Hansen solubility parameters. The Hansen solubility parameters found for TiO_2 samples prepared in different solvents in the presence of acetylacetone may be useful in the synthesis of stable colloidal TiO_2.

The data of the size of TiO_2 particles in colloid solutions and the degree of their aggregation in dry powders were obtained using light scattering, scanning electron microscopy (SEM) and TEM.[52]

Titanium isopropoxide, diethanolamine (DEA) and ethanol (3 : 1 : 20 by volume) were used[53] as the starting reagents in the fabrication of TiO_2 sols. The mixing order played an important role. Thus the introduction of EtOH before DEA led to very fast sedimentation of TiO_2 due to the high reactivity of the alkoxide in ethanol. Hence, first, half volume of ethanol was mixed with DEA and then titanium isopropoxide was added; the mixture was stirred for 30 min and the remaining amount of EtOH was added. The resulting mixture was vigorously stirred at room temperature. The obtained sol was stable for a week and then transformed into gel. A considerable increase in sol

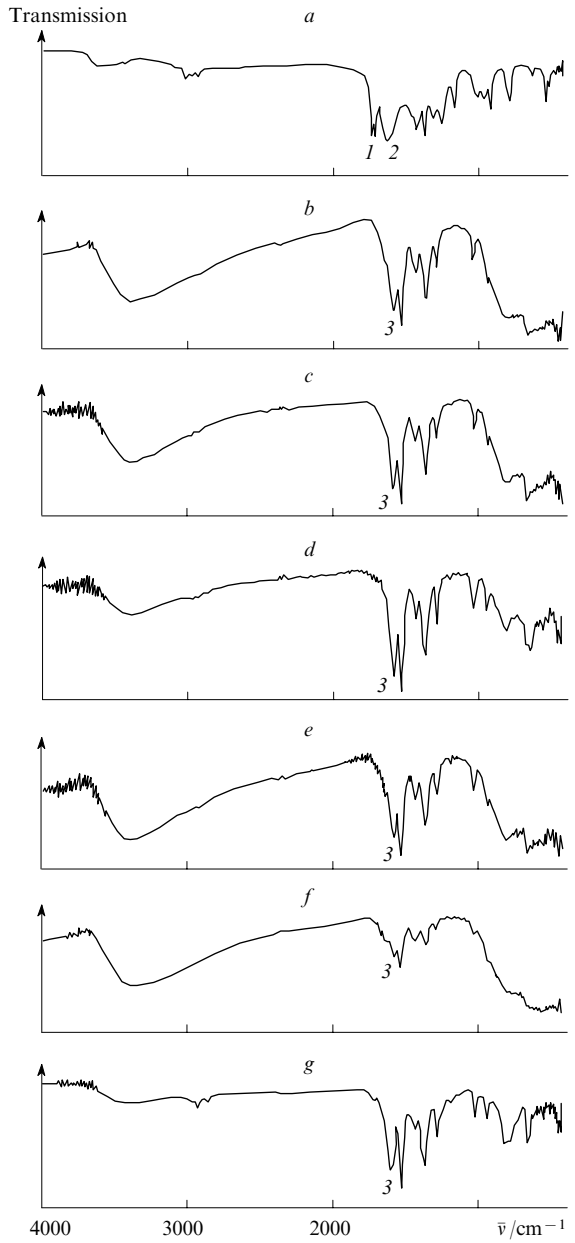


Figure 4. IR spectra of acetylacetone (*a*) and titanium dioxide sols prepared in the presence of acetylacetone in different organic solvents: THF (*b*), acetone (*c*), butanol (*d*), chloroform (*e*), toluene (*f*), hexane (*g*).[52]
(*1*) Peak of the C=O group of the keto form, (*2*) peak of the C=O group of the enol form, (*3*) peak of the C=O group of the chelate complex.

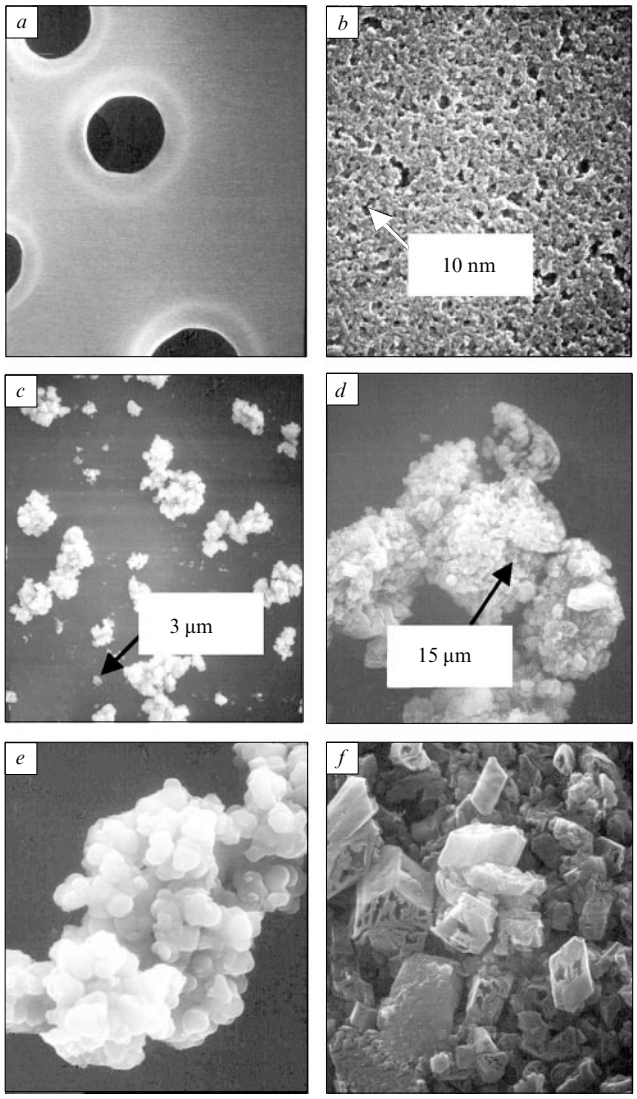


Figure 5. SEM microimages of titanium dioxide sols synthesized in the presence of acetylacetone in acetone (*a*), butanol (*b*), toluene (*c*, *e*) and hexane (*d*, *f*).[52]
Images (*e*) and (*f*) were obtained at larger magnification.

stability was observed with a decrease in its stirring time. The sol stability also substantially increased under low humidity conditions. In the course of drying, the formation of a xerogel considerably 'shrinked' as compared with the starting gel was observed, the volume decreased five- to tenfold.

A pure anatase phase with particle sizes of 10–20 nm was prepared[54] by a very simple low-temperature (100 °C) procedure using only water as the medium and titanium isopropoxide as the precursor (without additives). The size, shape and phase composition of particles were studied by X-ray phase analysis and TEM.

Nanoparticles of TiO_2 obtained by hydrolysis of $Ti(OPr^i)_4$ at various pH were studied.[55] For the subsequent preparation of nanopowders with narrow size distribution, the final suspension was peptized. The effect of pH on the size and morphology of particles in nanopowders was evaluated. According to XRD, SEM and TEM data, the as-prepared powders entirely consisted of the anatase crystalline phase. Only the powder prepared in a strongly acidic solution contained fine spherical particles. It was shown that the anatase to rutile transformation occurred at temperatures below 600 °C.

In a different study,[56] the preparation of colloidal titania with the concentration of 0.9 mol litre^{-1} involved hydrolysis of titanium isopropoxide in a mixture of isopropyl alcohol with 2 M hydrochloric acid.

In yet another study,[57] the synthesis of nanostructural films involved the preparation of a TiO_2 sol by hydrolysis of titanium isopropoxide in a mixture of ethanol with hydrochloric acid [molar ratio $Ti(OPr^i)_4 : HCl : EtOH : H_2O = 1 : 1.1 : 10 : 10$], which was followed by the addition of an

aqueous methylcellulose (MC) solution. It was shown that an increase in the water content and the sol dilution retards gelation.

Calcination of a titanium dioxide sol afforded TiO_2 nanopowder to be used in the preparation of homogeneous suspensions for the purpose of producing films. The stability of TiO_2 suspensions was investigated [57] by measuring the sedimentation rate. The anatase powder concentration in liquid was varied (5 mass % – 10 mass %) in the presence and in the absence of MC. It was shown that the sedimentation rate of the TiO_2 nanopowder sharply decreased in the presence of MC. For example, in 5% and 10% suspensions containing no MC, the sedimentation took 1 h and 30 min, respectively, whereas, in the presence of MC the 5% suspension remained stable for 3 days and the settlement in 10% suspension began after 10 h. Thus, MC served as the dispersant. The SEM data pointed to a considerable increase in homogeneity and uniformity of TiO_2 films and their higher specific surface in the presence of MC (Fig. 6).

The synthesis of nano-sized TiO_2 by the sol – gel method

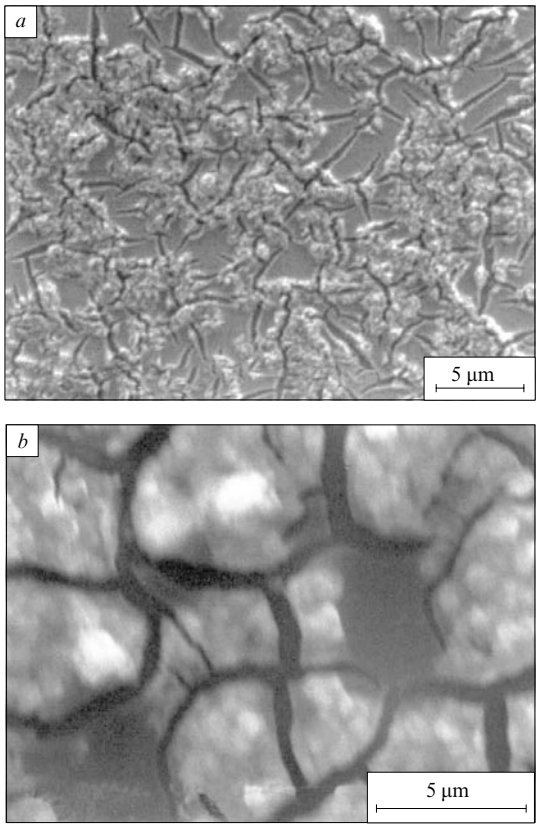


Figure 6. SEM microimages of TiO_2 films after thermal treatment at 500 °C of samples with (*a*) and without addition of methylcellulose (*b*).[57]

on the basis of titanium isopropoxide was carried out in the presence of a peptide, poly-L-lysine (PLL), as an additive.[58] In this case, peptide served not only as the dispersant but also as the structure-determining additive: it was only in the presence of PLL that tubular TiO_2 particles were formed (Fig. 7 *a*). The particles retained their shape after calcination at 700 °C (Fig. 7 *b*). For a sample obtained in the absence of PLL, calcination at the same temperature led to titanium dioxide with irregular structure (Fig. 8). Accord-

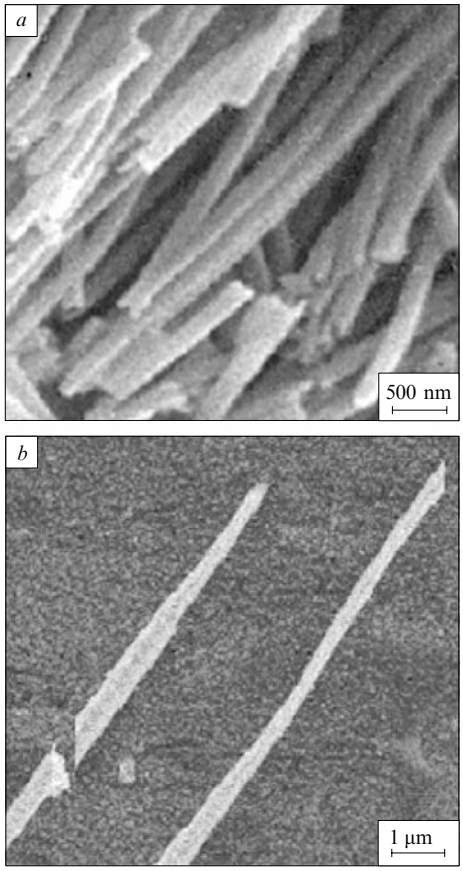


Figure 7. SEM microimages of TiO_2 syntheized in the presence of poly-L-lysine.[58]
(*a*) As-prepared sample, (*b*) sample after calcination at 700 °C.

ing to XRD data, titanium dioxide obtained in the presence of PLL and calcined at 700 °C represented anatase with a rutile admixture. In TEM microimages, nanoparticles with the anatase diffraction pattern looked as either coupled tubes with the diameter of 20 nm and the Y-shaped junction in the lower part or nanorods with the diameter from 10 to 25 nm. Materials based on nano-sized TiO_2 with the tubular structure can successfully be used in medicine, biotechnology, microelectronics, optics, *etc*.[58]

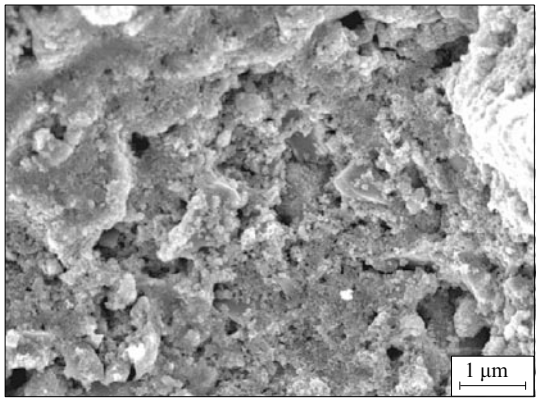


Figure 8. SEM microimage of a TiO_2 sample prepared without poly-L-lysine after calcination at 700 °C.[58]

Nano-sized mixed colloids with the composition PAA – TiO_2 [PAA is poly(acrylic acid)] were synthesized[59] by an *in situ* sol – gel method using titanium isopropoxide and a PAA solution in butanol. Depending on whether titanium isopropoxide was added before or after the complete dissolution of PAA, the solid phase separation and gelation scenarios differed; however, after heating, stable colloidal solutions were formed in both cases. To confirm the presence of interactions between PAA and Ti, the PAA : isopropoxide : water molar ratio was varied. The formation of chelate complexes was reliably confirmed by IR spectroscopy. Differential scanning calorimetry (DSC) also demonstrated strong interaction between PAA and Ti, which confined the motion of PAA chains. Moreover, according to the data from thermogravimetric analysis (TGA), the thermal stability of PAA chelate was higher as compared with the free acid. On the whole, as followed from TEM results, the order in which reagents were mixed and the PAA : isopropoxide : water molar ratio substantially affected the size and the shape of PAA – TiO_2 hybrid aggregates and the degree of aggregation.[59]

Nanocrystalline TiO_2 was deposited from an ethanolic solution of titanium isopropoxide and hydrogen peroxide by refluxing at 80 °C for 2 days.[60] The resulting particles were filtered and dried at 100 °C. Elucidation of the role of subsequent treatment on the physicochemical and electrochemical properties of nanocrystalline TiO_2 was carried out using XRD and TEM of as-prepared powder, a sample calcined at 400 °C and a sample following sonication. According to the data from X-ray diffraction analysis, all samples represented the anatase phase. The TEM studies have shown that the dried sample consisted of uniform spherical particles measuring 5 nm. In the sample calcined at 400 °C, the particles retained their spherical shape but their size increased to 10 nm. The sample subjected to sonication for 5 h contained a considerable fraction of particles with the average diameter of 5 nm and the length of 20 nm.

Mesoporous titanium dioxide with bimodal pore size distribution was prepared[61] by sonication-assisted hydrolysis of titanium isopropoxide in EtOH : water with the molar ratio equal to 1:1 (sample R1) and 10:1 (sample R10) and also in pure water (sample R0). According to data from XRD, nanostructured xerogels formed after drying of the hydrolysis products of R0, R1 and R10 at 100 °C represented an anatase and brookite mixture, pure anatase and the amorphous TiO_2 phase, respectively.

With the increase in calcination temperature, substantial changes in the qualitative and quantitative composition of the samples studied were observed (Fig. 9). Thus in R0 sample, the rutile phase appeared as soon as at 600 °C when the brookite phase was still present in a noticeable amount; at 700 °C, virtually all anatase was transformed to rutile. In R1 sample, small amount of brookite appeared at 400 °C but disappeared at 600 °C. This was accompanied by an increase in the anatase fraction, but the rutile admixture also appeared. At 700 °C, approximately half amount of anatase transformed to rutile. For amorphous xerogel R10, anatase nanocrystals appeared only at ~373 °C and underwent no phase transitions up to 600 °C. Only at 700 °C, the transformation of anatase to rutile started.

Figure 10 shows that phase transitions in samples R0, R1 and R10 were accompanied by the increase in the size of TiO_2 particles, which was more pronounced at temperatures above 500 °C being associated with the rutile formation. All TiO_2 powders calcined at 400 – 600 °C were characterized by bimodal pore size distributions with maximum pore diameters at 2 – 4 and 16 – 24 nm. At 700 °C, all samples demonstrated monomodal pore size distribution as the result of destruction of fine pores.

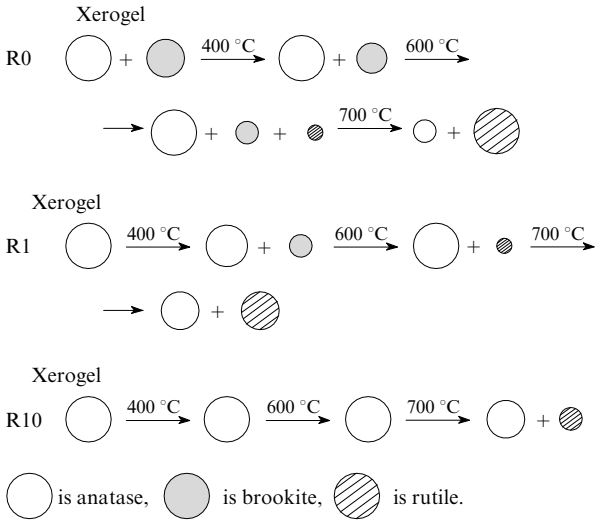


Figure 9. Scheme of phase transformations in samples R0, R1 and R10 (see text) for different calcination temperatures.[61]
The content of individual phases is roughly proportional to the surface of the corresponding circle.

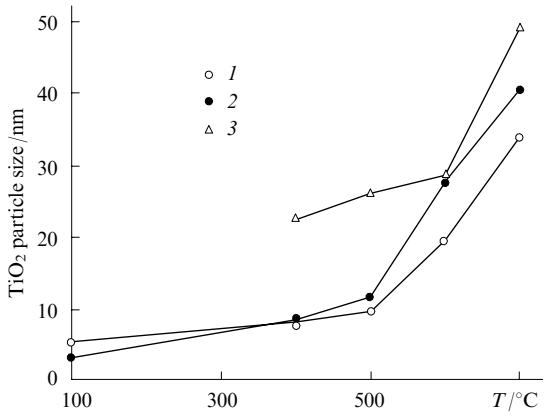


Figure 10. Average particle size of TiO_2 in R0 (*1*), R1 (*2*) and R10 (*3*) samples (see text) at different calcination temperatures.[61]

Pyrolysis of homogeneous TiO_2 gels prepared by hydrolysis of titanium isopropoxide pretreated with formic[62] or oxalic[63] acids with the aim of controlling the gelation process was studied. The amorphous titanium dioxide gel was characterized by FTIR spectroscopy, XRD and N_2 adsorption. Detection, qualitative analysis and identification of organic impurities in the TiO_2 gel and also the determination of the degree of their removal in the course of pyrolysis were carried out by TGA methods in combination with the gas chromatographic analysis and mass spectrometry.

Titanium isopropoxide was diluted with isopropyl alcohol in a flow of nitrogen; then, a carboxylic acid (formic or oxalic) was added with vigorous stirring, which was followed by dropwise addition of hydrochloric acid, which

served as the hydrolysis catalyst. This produced an emulsion that transformed into a uniform gel in 4 days. The molar ratio $Ti(OPr^i)_4$: carboxylic acid : isopropyl alcohol : water : HCl = 1 : 1 : 20 : 1 : 0.0184 was found to be optimum.[62,63] However, the physicochemical characteristics of TiO_2 samples synthesized in the presence of formic and oxalic acids[63,64] substantially differed.

Thus according to N_2 adsorption isotherms, a mesoporous material was formed in the presence of HCOOH that was characterized by specific surface of 480 $m^2\ g^{-1}$ and the average pore diameter of 2.7 nm.[62] IR Spectroscopic studies showed that the sample contained Ti—O—Ti fragments, formate groups coordinated with titanium and non-hydrolyzed titanium isopropoxide. Absorption bands belonging to organic impurities in the TiO_2 gel completely disappeared upon heating of the samples above 340 °C. According to data from XRD, the gel represented an amorphous product that crystallized at temperatures above 400 °C to form the anatase phase.

According to the data on N_2 adsorption, the sample formed in the presence of $(COOH)_2$ represented a macroporous material with specific surface of 18 $m^2\ g^{-1}$ and the average pore diameter of 24.4 nm.[63] IR Spectroscopic studies showed that titanium dioxide samples contained oxalate groups coordinated with titanium and also non-hydrolysed titanium isopropoxide. Absorption bands of organic impurities in the TiO_2 gel completely disappeared in samples heated above 550 °C. According to data from XRD, the original gel also represented an amorphous product (*cf.* Ref. 62), but the anatase crystallization occurred at temperatures above 550 °C.

As was shown by different physicochemical methods [XRD, IR spectroscopy, TGA, electron spectroscopy of diffuse reflectance (ESDR), ammonia thermoprogrammed desorption (TPD), adsorption methods],[64] the introduction of the sulfate ions into TiO_2 decreased the particle size, stabilized the anatase phase and increased both the specific surface and the pore volume (Table 1). The dependences of all parameters on the amount of sulfuric acid added in the impregnation had extrema. The sol–gel hydrolysis product of titanium isopropoxide in the presence of nitric acid was employed for the impregnation. After ageing, the sol formed was concentrated, dried, impregnated with sulfuric acid (0.5 mol $litre^{-1}$, 2–10 ml) and calcined.

Among modified methods for the preparation of nano-sized TiO_2, mention should be made of hydrolysis and condensation of titanium isopropoxide in anhydrous ethanol using a cellophane membrane that makes it possible to control the diffusion rate.[65] Hydrolysis combined with sonication is advantageous controlling the size of titanium dioxide nanoparticles.[66]

Table 1. Adsorption characteristics of sulfated TiO_2.[64]

Sample[a]	Specific surface /$m^2\ g^{-1}$	Pore volume /$cm^3\ g^{-1}$	Particle size /nm	Rutile content (%)	Pore diameter /Å
T	35	0.09	12.71	46.6	103.4
ST2	91	0.21	9.62	0	95.0
ST4	98	0.18	8.62	0	74.1
ST6	79	0.12	7.48	0	58.1
ST8	57	0.11	11.05	0	78.4
ST10	48	0.10	11.74	18.3	85.5

[a] The following designations were used: T is the original TiO_2; ST2–ST10 are samples prepared by impregnation with 2, 4, 6, 8 and 10 ml, respectively, of sulfuric acid (0.5 mol $litre^{-1}$).

TiO_2 Nanoparticles of different shapes (spherical, cubic and hexagonal rods) and sizes (50–500 nm) were prepared from titanium butoxide as the precursor.[67] Hydrolysis of $Ti(OBu^n)_4$ was carried out in the presence of different surfactant compositions and concentrations. The prepared TiO_2 nanoparticles were studied for photocatalytic decomposition of Methyl Orange in fixed film batch reactors. It was shown that the shape is more important than the size: TiO_2 nanorods had higher photocatalytic activities than spherical and cubic TiO_2 nanoparticles.

The dependence of the morphology, the size and the crystal structure of nano-sized crystalline titanium dioxide on the hydrolysis conditions of titanium butoxide was studied in detail.[68] Hydrolysis of $Ti(OBu^n)_4$ was carried out at room temperature in inverse micellar systems formed by an aqueous solution of a mineral acid, cyclohexane and a surfactant Igepal® CO-520 [4-(n-C_9H_{19})$C_6H_4O(CH_2$. .$CH_2O)_4CH_2CH_2OH$]. The effect of the hydrolysis conditions, such as concentration (c) and type of acid (hydrochloric, nitric, sulfuric or phosphoric), molar content of water [$w = H_2O$: surfactant and $h = H_2O : Ti(OBu^n)_4$], and hydrolysis time (t) on the formation, crystal phase, morphology, and size of the TiO_2 particles were investigated.

It was shown that the pH of the reaction medium had a significant effect on the crystal structure of the obtained TiO_2 nanoparticles. For example, according to TEM data, an amorphous product was formed when the hydrochloric acid concentration was below 2 mol $litre^{-1}$, all other conditions being equal. At the HCl concentration of 2 mol $litre^{-1}$, the resulting TiO_2 particles represented a mixture of anatase and rutile. The pure rutile phase was formed as the acid concentration reached 2.5 mol $litre^{-1}$. At still higher HCl concentration (to 4 mol $litre^{-1}$), the amorphous TiO_2 was formed again.

In the case of HCl at $c = 2.5$ mol $litre^{-1}$, $h = 28$, $t = 20$ days and $w = 3$, finely disperse shuttle-like TiO_2 nanoparticles with widths 35–40 nm and lengths 150–160 nm with the crystalline structure of rutile were formed. As the parameter w increased from 3 to 5, both the widths and the lengths of the particles increased slightly without changes in their morphology. For $w = 10$, the particles formed petal-shaped aggregates with retention of their crystalline structure. It is believed that the aqueous cores of inverse micelles served as microreactors for the hydrolysis of titanium butoxide. With the increase in parameter w, the number of these micelles increased, they had to coalesce; and thus, shuttle-like rutile nanoparticles from different micelles formed petal-like aggregates with the same crystal phase. However, the anatase phase appeared in aggregates for $w = 12$, probably because micelles were destroyed in the course of reaction with such a high water content.

For $c = 2.5$ mol $litre^{-1}$, $w = 8$, $t = 20$ days, the effect of parameter h was similar to the aforementioned effect of parameter w. For $h < 6$, *i.e.*, below the coordination number of Ti(IV) ions, the amount of water in micelle cores was insufficient for the complete hydrolysis of titanium butoxide. It this case, the crystallization slowed down and amorphous TiO_2 was formed. For $h > 10$, the amorphous product transformed into crystalline rutile. For $h = 10–20$, the nanoparticle size remained virtually unchanged; however, for $h = 36$, flower-shaped aggregates were formed.

High h values accelerated the butoxide hydrolysis and the crystalline TiO_2 particles formed were capable of aggregation both inside the aqueous cores of micelles and also in their environment.

As the hydrolysis time increased from 5 to 10 and 20 days all other conditions remaining standard (see above), the growth of particles with subsequent aggregation and morphological changes (Fig. 11) was observed.

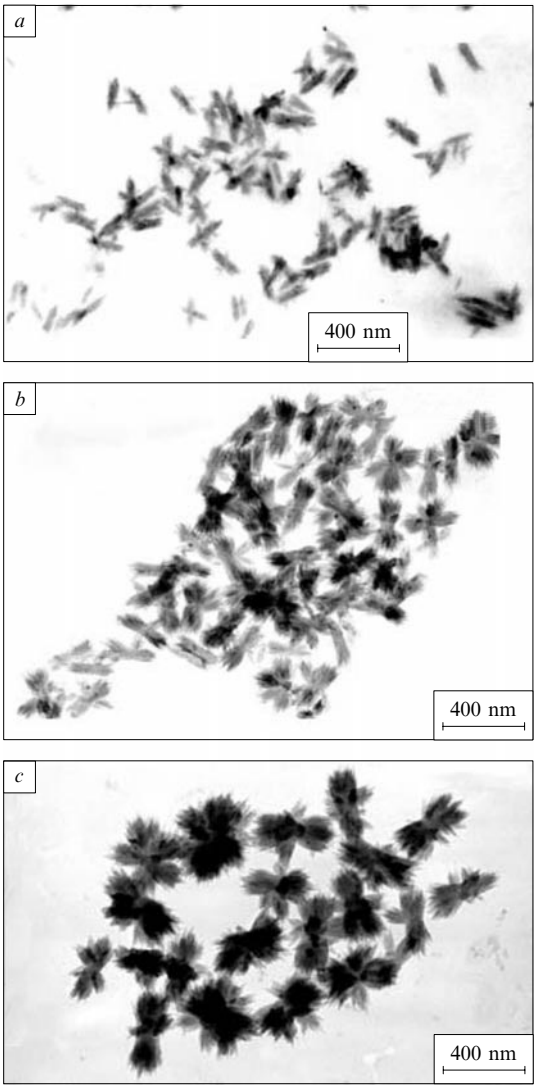


Figure 11. TEM microimages of TiO_2 particles formed upon hydrolysis of $Ti(OBu^n)_4$ under standard conditions for 5 (*a*), 10 (*b*) and 20 days (*c*).[68]

Hydrochloric, nitric, sulfuric and phosphoric acids used to adjust the pH of the medium were employed to examine the effect of the nature of acids.[68] The parameters w and h were taken to be 8 and 28, respectively, and the acid concentration was equivalent to 2.5 M HCl, all other parameters being the same. The nature of acid was found to substantially affect the crystalline phase composition, morphology and also the size of TiO_2 nanoparticles. Thus substitution of nitric acid for hydrochloric acid decreased the width of shuttle-like particles to 20–25 nm and their length to ~120 nm. The use of sulfuric or phosphoric acids irrespectively of their concentration resulted in the formation of amorphous rather than crystalline spherical TiO_2, namely, uniform small spheres with diameter of ~40 nm for sulfuric acid and coarse spheres with diameter of ~240 nm for phosphoric acid (Fig. 12). Presumably, this can be associated with different affinity of the anions with respect to Ti(IV) ions in aqueous solutions (Cl^- and NO_3^- exhibited weak affinity, while SO_4^{2-} demonstrated strong affinity). The strong affinity of SO_4^{2-} for titanium inhibits the titanium dioxide rearrangement and, hence, the overall crystallization process. It thus follows[68] that phosphoric acid, like sulfuric acid, is the crystallization inhibitor.

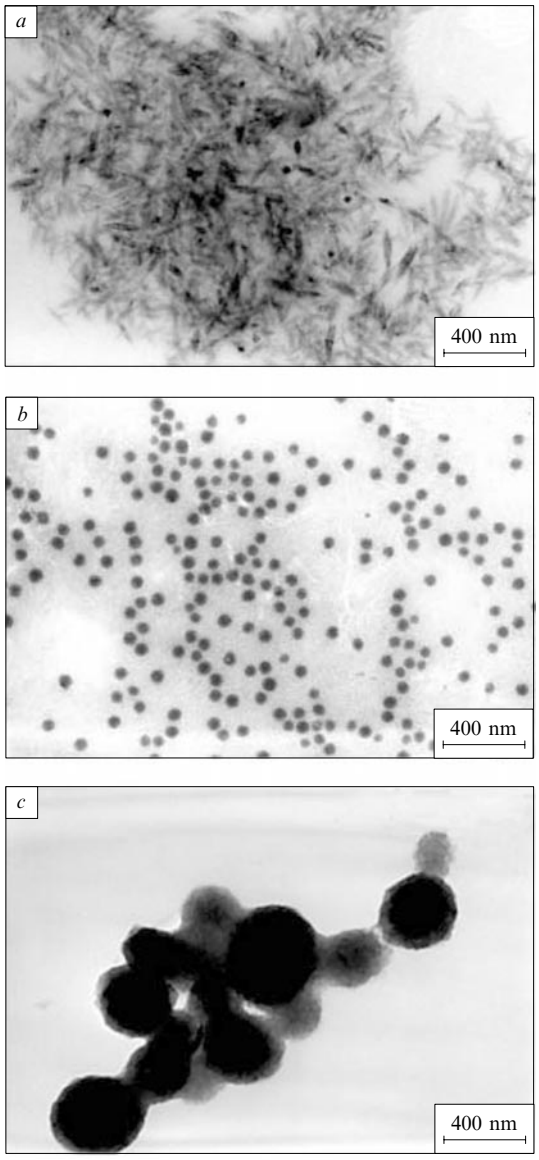


Figure 12. TEM microimages of TiO_2 particles formed upon hydrolysis of $Ti(OBu^n)_4$ in the presence of different mineral acids.[68] (*a*) Nitric acid, (*b*) sulfuric acid, (*c*) phosphoric acid.

Acetic acid often used in the hydrolysis of titanium-containing precursors can also serve as an efficient stabilizer of the anatase phase in the calcination. Thus the hydrolysis of an acetic-acid solution of $Ti(OPr^i)_4$ with aqueous ammonia at pH 3–4 and 70 °C afforded a gel that showed an anatase phase even at 1000 °C.[69] However, as the hydrolysis

medium pH increased to 5, pure rutile was formed at 1000 °C, whereas at pH 6, anatase to rutile transformation is complete at 800 °C (Table 2), as for samples prepared by hydrolysis in the absence of acetic acid.

Table 2. Phase composition [a] of calcined TiO_2 samples as a function of the pH of acetic acid-containing solution of titanium isopropoxide during the hydrolysis.[69]

Calcination temperature /°C	Hydrolysis medium pH			
	3	4	5	6
1000	A + R	A + R	R	R
800	A + R (traces)	A + R (traces)	A + R	R
600	A	A	A	A
400	A	A	A	A

[a] Used designations: A is anatase, R is rutile.

Monodisperse non-aggregated nanoparticles of titanium dioxide were prepared [70] by hydrolysis of titanium butoxide at 60 °C in the presence of acetylacetone and *p*-toluenesulfonic acid. It was shown that a thorough choice of synthesis conditions that rule out gelation makes it possible to produce particles with the anatase structure and the average size of 1 – 5 nm. It was found [70] that the optimum conditions for synthesizing nanodisperse TiO_2 sols are as follows: the initial molar ratio (a) acetylacetone : metal $1 \leqslant a \leqslant 6$; the molar ratio $h = H_2O : Ti$ $5 \leqslant h \leqslant 10$ and the acidity of the medium expressed through the molar ratio $h^+ = H^+ : Ti$, $0 \leqslant h^+ \leqslant 0.8$. In the mentioned variation ranges of parameters a, h and h^+, the titanium concentration in the sol could change from 0.5 to 1 mol litre^{-1}. Drying of a nanodisperse sol to form a xerosol could be accomplished by centrifugation, evaporation of solvent in vacuum at room temperature or by heating at 100 °C.

The prepared xerosol could be dispersed again without aggregation in a water – ethanol or ethanol solution. This afforded sufficiency concentrated sols (> 1 mol litre^{-1} with respect to titanium) containing TiO_2 particles with the size of 1 – 5 nm, the same as in the original sol.[70] This was proved by the data from TEM and quasi-elastic light scattering. The use of other physicochemical research methods (XRD, IR spectroscopy, ^{13}C, ^{17}O and ^{1}H NMR, mass spectrometry, *etc.*) in studying TiO_2 nanoparticles has shown that particles were protected from aggregation by complexes with acetylacetone formed on their surface, which agreed with other results,[52] and also by a mixed organic-inorganic adsorption layer formed from acetylacetone, *p*-toluenesulfonic acid and water.

Nanodisperse (particle size 3.8 nm) pure anatase with the specific surface of 359.1 m^2 g^{-1} was prepared based on the same precursor, *i.e.*, titanium butoxide.[71]

IV. Nano-sized TiO_2 synthesis based on $TiCl_4$; product dispersion and phase composition

Titanium tetrachloride belongs to the most widely used titanium dioxide precursors; it was employed in both the synthesis of substrates and catalysts by the precipitation method [72, 73] and preparation of nano-sized TiO_2 colloid solutions by the sol – gel method.

Thus a colloid solution of TiO_2 nanoparticles (40 – 60 Å), was prepared [74, 75] by dropwise addition of $TiCl_4$ to cold water (pH 3.5 – 4.0). The temperature and the reactant mixing rate were regulated by an apparatus designed for automatic preparation of colloid systems.[76] The TiO_2 concentration (0.1 – 0.6 mol litre^{-1}) was determined from the concentration of the peroxide complex after dissolving the colloid in concentrated sulfuric acid by a known procedure.[77] The possibility of preparation of surface complexes of titanium dioxide colloid nanoparticles with cysteine to be used in photocatalysis was demonstrated.[74, 75]

Titanium dioxide was also synthesized [78] by thermal hydrolysis of $TiCl_4$ in a propanol – water mixture. The dependence of the precipitate morphology on the propanol : water volume ratio, the $TiCl_4$ concentration, temperature and the presence of a dispersant, namely, hydroxypropylcellulose (HPC), was studied. It was shown that titanium dioxide prepared in a 3:1 (by volume) propanol : water mixture contained uniform-dispersed spherical particles. With the addition of HPC, the nanoparticle size distribution became narrower. The spherical shape of TiO_2 particles was independent of the $TiCl_4$ concentration, but their sizes increased with an increase in the suspension concentration. An increase in the synthesis temperature favoured the broader size distributions of particles. The effect of the liquid-phase temperature gradient on the morphology of TiO_2 particles was also noted. The morphology and size of titanium dioxide particles were studied by SEM and TEM methods; phase transitions were investigated by the XRD method.

In another study,[79] titanium dioxide was synthesized by the hydrolysis of $TiCl_4$ in a strongly acidic aqueous solution in the absence and in the presence of poly(ethylene glycol) PEG-1000 that served as the dispersant for controlling the shape and size of the TiO_2 particles. It was shown that in the absence of PEG-1000, uniform shuttle-shaped TiO_2 nanocrystals were formed and the degree of their aggregation increased with an increase in the acid content and a decrease in the $TiCl_4$ concentration. In the presence of PEG-1000, TiO_2 particles with sufficiently narrow size distributions were prepared, with the particle diameter decreasing with an increase in the PEG-1000 amount. The process was characterized by simplicity and a low cost and could be carried out in a continuous mode. The products were studied by the XRD and TEM methods.

In yet another study,[80] titanium dioxide sols were prepared by acid hydrolysis of $TiCl_4$ (pH of the medium was adjusted by addition of an ammonia solution), followed by peptization of precipitates with nitric acid. Stable titania sol (particle size 14 nm) was prepared at the molar ratio $H^+ : Ti = 0.5$ with vigorous stirring for 1 day at 70 °C (Table 3). It is remarkable that the activity of TiO_2 in photocatalytic reactions was largely determined by the degree of dispersion of TiO_2 rather than by the promoting effect of modifying additives (0.5% Pt or 10% of Si, Zr, W, Mo oxides) introduced into TiO_2 to increase its activity.

Nanosized TiO_2 powders prepared by controlled hydrolysis of $TiCl_4$ in aqueous solutions in the presence of small amounts of sulfate ions were studied [81] by TEM, high-resolution EM, XRD and electron diffraction; the specific surface was determined from adsorption isotherms using the Brunauer – Emmett – Teller (BET) equation. It was shown that the hydrolysis of $TiCl_4$ at 70 °C carried out in the presence of the sulfate ions produced a powder that consisted of the pure anatase phase with the predominant particle size of 3.5 nm, which is much smaller than in

Table 3. TiO_2 sol particle size at different concentrations of HNO_3 (TiO_2 concentration 0.3125 mol litre^{-1}).[80]

H^+ : Ti (mol.)	Particle size /nm	Sol stability
0.08		precipitate was not peptized
0.2	102	stable
0.4	45	"
0.5	14	"
0.7	56	"
1.0	96	"
1.2	–	unstable

powders prepared from titanium alkoxides. Moreover, the anatase–rutile phase transformation retarded. However, at the same hydrolysis temperature but in the absence of the sulfate ions, the product represented a mixture of anatase and rutile, the primary particle size in the rutile phase was 4.3 nm. Hydrolysis at 20 °C led to TiO_2 powders with the amorphous structure and high specific surfaces ($\sim$500 m^2 g^{-1}). According to the electron spectroscopic data, the presence of the sulfate ions accelerated the anatase phase formation.

According to the literature data, from the practical viewpoint, TiO_2 in the form of anatase is often preferred to rutile. Optical and electrochemical properties of anatase and the third modification of titanium dioxide, *i.e.*, brookite, were compared and the conditions of synthesis of each phase by the sol–gel method were described.[82] It was demonstrated that the formation of one or another phase was determined by not only the pH of the solution, but also the molar ratio Cl : Ti, which was controlled in the interval 17–35 by the addition of NaCl. In addition, the simultaneously formed brookite and rutile phases were characterized by different degrees of dispersion and could easily be separated.

Studies by XRD and Raman spectroscopy[83] revealed traces of brookite in anatase in nano-sized TiO_2 samples prepared by precipitation from $TiCl_4$ at different pH. The average size of TiO_2 crystals after 2-h treatment at 450 °C was 7–9 nm. The lattice parameter *c* of anatase increased as the pH of the medium increased during the synthesis, while the volume fraction of the brookite phase increased with a decrease in pH. It was shown that the temperature range of anatase transformation to rutile shifted to low temperatures as the brookite volume fraction increased, *i.e.*, the brookite phase was to a certain extent responsible for the anatase transformation to rutile.

A simple method of synthesis of high purity brookite nanoparticles was described.[84] Hydrolysis of $TiCl_4$ was carried out in acidified isopropyl alcohol at ambient temperature and the peptization and crystallization of the gel formed occurred on refluxing. The data from SEM and TEM revealed the formation of spherical TiO_2 with the average size of 30 nm. The data from XRD confirmed the presence of the brookite crystalline structure. The degree of particle agglomeration could be predicted based on the amount of heat released during the hydrolysis of $TiCl_4$.

Ultradisperse TiO_2 samples with the structures of anatase, rutile and their mixture were synthesized[85,86] by hydrolysis of $TiCl_4$ and assayed for the photocatalytic degradation of phenol. The resulting product was studied by high resolution EM, XRD, BET and electron spectroscopy. In the catalytic process mentioned, the highest selectivity (very low concentrations of side products, namely, *p*-benzoquinone and hydroquinone) was observed for catalyst particles in the anatase phase measuring 4 nm, whereas rutile particles of the same size exhibited selectivity that differed insignificantly from that of coarse-grain rutile. Presumably, calcination was effective in increasing the activity of the TiO_2 catalyst because this favoured perfection of its crystal structure.

The addition of $(NH_4)_2SO_4$ and adjustment of the pH to 7 (with NH_4OH) resulted in anatase in the final stage; in the absence of ammonium sulfate, a mixture of anatase and rutile was formed. To prepare rutile, the same process was carried out with no ammonium sulfate, nor ammonium hydroxide. In each case, the hydrolysis product represented titanium dioxide hydrate ($TiO_2 \cdot n\,H_2O$), which was centrifuged off, dried and, if necessary, calcined.

Nanodisperse titanium dioxide was fabricated[87] by CO_2-laser-assisted pyrolysis of $TiCl_4$ in a gas–vapour mixture. The effect of synthesis conditions, namely, the laser power and the oxidant (air) delivery rate, on the structural characteristics of synthesized TiO_2 was studied. It was shown that moderate acceleration of the air delivery increased the degree of crystallinity, the grain size, and the rutile content.

V. Synthesis of TiO_2 based on miscellaneous titanium-containing precursors

Besides alkoxides and $TiCl_4$, yet another TiO_2 precursor used in the preparation of anatase nanocrystals, namely, ammonium dihydroxodilactatotitanate(IV) (ALT), deserves mention.[88] According to the available published data, this compound attracted attention as the starting material in the preparation of catalysts,[89] fabrication of electrodes for medicinal purposes[90] and production of UV-radiation-proof films on different surfaces.[91] In contrast to titanium alkoxides that are rapidly hydrolyzed, ALT is stable in neutral solutions at ambient temperatures and decomposes to form TiO_2 (anatase), NH_3 and sodium lactate only above 100 °C or in aqueous NaOH solutions. However, even under these conditions, ALT undergoes hydrolysis more slowly; this makes it possible to synthesize nanocrystalline TiO_2 with predominantly oblate-shaped particles and a narrow size distribution; the latter is especially important for the synthesis of TiO_2 films.

Studies on ALT thermohydrolysis (up to 300 °C) in sealed glass tubes or in a titanium autoclave has shown[88] that the size of formed anatase nanoparticles increased with the increase in the hydrolysis temperature (Fig. 13) and ALT concentration. Thus, it can be controlled by varying these parameters. In all the cases, extremely narrow particle size distributions were obtained. With the addition of ammonium lactate to the reaction mixture, the effects of ALT concentration and the reaction time on the size of TiO_2 particles became negligibly small, and the growth of particles stopped. This simple trick can be used for the interruption of the process to afford high yields of virtually uniform size anatase nanocrystals. The final product contains no admixtures (ions Cl^-, Na^+).

Nanocrystalline TiO_2 was prepared[92] using an unconventional method, namely, plasma synthesis from a titanium hydride TiH_2 powder.

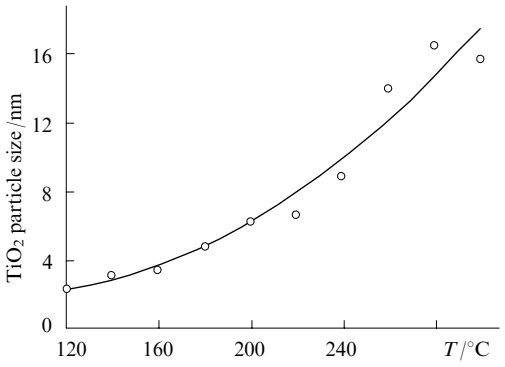


Figure 13. Dependence of the average TiO_2 particle size on the hydrolysis temperature.[88]
ALT Concentration in water is 0.415 mol litre^{-1}, duration of process is 24 h.

VI. Stabilization of the disperse state and phase composition of nano-sized TiO_2 sols

Despite the efficacy of using the sol–gel method for the synthesis of nanocrystalline TiO_2 sols, the pronounced trend of TiO_2 particles to aggregation during both the hydrolysis of a titanium-containing precursor and long-term storage of sols still remains the main drawback of this method; aggregation is often accompanied by variations in the phase composition. The analysis of published data allowed the ways for solving this problem to be outlined.

Thus an acidic medium (pH = 1.8) and a low storage temperature (4 °C) favoured higher stability of TiO_2 colloid solutions.[22] Moreover, the stability of non-aqueous sols tended to increase under low humidity conditions.[53] The nature of solvent also affected the size and the stability of TiO_2 colloid particles.[52] On the whole, the majority of studies stressed that strict observance of the synthesis conditions (pH, temperature, precursor concentration) and also of the stoichiometric ratio of the reactants and the addition order is very important for the targeted synthesis of TiO_2 with desired properties.[53, 59, 68–70]

Stable nanodisperse TiO_2 sols can be prepared if organic disaggregating and stabilizing additives, namely, acetylacetone,[52, 70] diethanolamine,[53] polyacrylic acid,[59] methylcellulose,[57] hydroxypropylcellulose,[78] poly(ethylene glycol),[79] *etc.*, are introduced into the reaction mixture. Disaggregating additives operate through different mechanisms, namely, the inhibition of hydrolysis and condensation,[52, 53] which favoured the lower degree of aggregation of particles; the formation of surface organic-inorganic complexes with TiO_2 nanoparticles, which prevented aggregation;[52, 70] the shift of balance of attractive and repulsive forces as a result of which the sedimentation rate decreased.[57]

One of the most popular methods of sol stabilization was the peptization of the hydrolysis product (after its centrifugation and rinsing with water) with nitric acid on vigorous stirring. The peptized precipitate was again centrifuged and dispersed in water.[80, 82]

In certain practical applications of nano-sized TiO_2, the stabilization of its phase composition was of no less importance than the definite size of nanoparticles. The amorphous TiO_2 phase was as a rule formed upon hydrolysis at 20 °C.[45, 81] The sol–gel method not only provided a possibility for regulation and reproduction of the ratio of TiO_2 crystal phases (anatase, rutile and brookite) in the final product, but also allowed preparation of each phase in its pure form. Like the control over the grain size of TiO_2, this was achieved[70] by accurate choice of the conditions of hydrolysis of titanium-containing precursors (pH, temperature, time, ratio of main components).[22, 68, 81, 82, 85, 93, 94]

Certain specific conditions for the formation of different TiO_2 phase compositions were mentioned. For example, the hydrolysis of $TiCl_4$ (Ref. 81) or titanium isopropoxide[64] in the presence of a small amount of the sulfate ions favoured the formation of the individual anatase phase, whereas in the absence of the sulfate ions, a mixture of anatase and rutile was formed under the same conditions.[64, 81] However, it was shown[68] that the strong affinity of SO_4^{2-} ions for titanium suppressed rearrangement of titanium dioxide and, hence, the overall crystallization process.

From the viewpoint of synthesizing pure anatase, it was of interest to use titanyl sulfate as the precursor. The substitution of an aqueous solution of $TiOSO_4$ (0.25 mol litre^{-1}) for the amorphous $TiO_2 \cdot n\,H_2O$ gel in the hydrothermal synthesis of nano-sized TiO_2 decreased the temperature of anatase formation from 250 to 150 °C, all other conditions being the same.[95] According to Table 4, this afforded highly disperse anatase with the particle size that increased with the increase in the temperature of hydrothermal treatment to 250 °C but nonetheless remained smaller than in anatase synthesized from amorphous TiO_2 gel. With the increase in the $TiOSO_4$ solution concentration to 0.44 mol litre^{-1}, the anatase particle size increased and the use of a $TiOSO_4$ solution in sulfuric acid (0.25 mol litre^{-1}) led to the appearance of the rutile phase at 250 °C. This is consistent with the data of Ref. 64 (see Table 1).

Table 4. Grain size of nanocrystalline anatase prepared by hydrothermal synthesis from an amorphous $TiO_2 \cdot n\,H_2O$ gel and an aqueous $TiOSO_4$ solution.[95]

Precursor	Concentration /mol litre^{-1}	Synthesis conditions		Particle size[a] /nm		Specific surface[a] /m^2 g^{-1}
		T/°C	time	XRD	TEM	
Gel		250	10 min	27	35	60
$TiO_2 \cdot n\,H_2O$		250	6 h	28	38	–
$TiOSO_4$	0.25	250	10 min	16	20	–
in water		250	6 h	18	24	–
		150	10 min	10	8	–
		150	6 h	14	16	–
	0.44	250	6 h	20	28	98
$TiOSO_4$	0.25	250	10 min	24	26	–
in 1 M H_2SO_4		250	6 h	see[b]	22	–

[a] These parameters were determined with the accuracy of ±10%.
[b] In this case, a mixture of anatase (85%) and rutile (15%) was formed; the particle size was 20 nm for anatase and 30 nm for rutile.

The synthesis of pure and stable nano-sized anatase was described[49, 50] (hydrothermal and solvothermal syntheses). Acetic acid added in the stage of hydrolysis strictly at pH 3–4 served as an efficient agent for stabilizing the anatase phase up to 1000 °C (see Table 2).[69]

As was mentioned above, unconventional titanium-containing precursors and synthesis conditions were sometimes used in the preparation of pure anatase and for controlling the quantitative ratio of anatase, rutile and brookite.[60, 65, 66, 88, 92]

* * *

The material of the present review clearly demonstrated that the problem of synthesizing stable forms of nano-sized titanium dioxide is being successfully solved. Materials with desired structural and morphological characteristics were fabricated using either conventional methods by scrupulous selecting synthesis conditions or by new approaches (new reactants, unusual methods of treatment of the reaction mixtures, improved instrumental implementation). It can be assumed that the directions of further studies in this field will be determined by the requirements imposed by practical application of nano-sized TiO_2, first of all, in medicine. The first positive results in this field will undoubtedly attract attention of scientists and engineers and the quest for new applications of nano-sized TiO_2 will pose new problems for synthetic chemists.

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