Master Thesis

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Coating of glass substrates to prevent diffusion of alkali ions into pharmaceutical solutions

Beschichtung von Glassubstraten zur Verhinderung von Alkali-Diffusion in pharmazeutische Lösungen

vorgelegt von
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in Zusammenarbeit mit
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1 Acknowledgement

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2 Abstract

Within the framework of this thesis a novel approach for a diffusion-impeding coating for soda-lime glass containers was developed. The reason why a barrier layer is desirable is that leaching of alkaline metals and alkaline earth metals out of the glass material into the solution may occur. The treated glass containers are used for pharmaceutical purposes, mainly for storage of solutions for parenteral use. The leaching of these ions leads to an increased pH-value, which can cause undesired interactions with the API. Other requirements which had to be taken into account are a stability of the film for at least 12 months, suitability for pharmaceutical application (no toxicity, only very little leaching of the components of the film etc.), a certain mechanical stability and it should withstand heat sterilization at 121°C. In preliminary studies the basic key points of the process were determined, like washing procedures, activation (acid/base treatment), APTES loading, TiO_2 loading and temperature. The underlying principle was inspired by a paper by *Wang et al.* (1). Various production methods were assessed; with the outcome that spraying seems to be the most promising method. At the beginning the inner surface of the glass container is activated with HCl and NaOH. This is not done by spraying; the acid/base is poured into the bottles and shaken. In the next step a layer of (3-aminopropyl)triethoxysilane (APTES) is applied to provide binding sites for the next layer. The final step is the application of a titanium-alcoholate via spraying. The used $Ti(iOPr)_4$ hydrolyzes at the surfaces yielding TiO_2. The TiO_2 particles should be chemically bound to the amino-group of an APTES molecule. The coated bottle is put in the oven at app. 100°C after each process step. The finished bottles were sent to our industrial partner for analysis of the hydrolytic class according to ISO specification 4802-1:1988 (E) (2). Many different laboratory experiments were carried out to determine the best process parameters. The conclusions that could be drawn out of the experiments are that the most important process parameters are the APTES spraying step and the annealing. To evaluate the other properties like leaching behavior appropriate analysis methods had to be established. The results showed that ICP-OES is a suitable method for determination of the TiO_2 leaching and total organic carbon (TOC) measurements can be used for determination of the APTES leaching. With all these efforts it was possible to develop a coating which is capable of increasing the hydrolytic resistance to the desired level.

3 Kurzfassung

Im Rahmen dieser Arbeit wurde eine neuartige Beschichtung entwickelt, um die Diffusion von Alkali- und Erdalkaliionen aus Kalk-Natron Glasflaschen zu verlangsamen bzw. zu stoppen. Die beschichteten Glassubstrate sollen anschließend als Behälter für parenteral verwendete Lösungen zum Einsatz kommen. Wenn Alkali- und Erdalkaliionen aus dem Glas leachen, wird der pH-Wert der Lösung in der Flasche erhöht, was zu unerwünschten Wechselwirkungen mit dem pharmazeutischen Wirkstoff führen kann. Kritische Parameter des entwickelten Beschichtungsprozesses sind etwaige Waschschritte, eine Aktivierungsprozedur (Behandlung mit Säure bzw. Base), die verwendete Temperatur des Glassubstrates und die Beladung mit den beiden Hauptkomponenten 3-Aminopropyltriethoxysilan (APTES) und Titanisopropylat. Weitere Anforderung an die beschichteten Flaschen sind neben der gesteigerten hydrolytischen Resistenz noch mechanische Stabilität, sehr wenig bis kein Leaching der Beschichtungskomponenten in die Lösung, eine Stabilität von mindestens 12 Monaten sowie die Fähigkeit unbeschadet eine Hitzesterilisation bei 121°C (Autoklav) zu überstehen. In vorausgehenden Untersuchungen wurden die Eckpunkte des Beschichtungsprozesses festgelegt. Als Produktionsmethode sollte Sprühen zum Einsatz kommen; vor den ersten Beschichtungsschritten wird die Oberfläche mit HCl und NaOH aktiviert (jedoch nicht im Sprühverfahren, die Flaschen werden mit Säure/Base befüllt und geschüttelt). Die Beschichtung selbst besteht aus 2 Komponenten, nämlich dem Silan, welches an die Glasoberfläche gebunden wird um eine Bindungsstelle für das im nächsten Schritt aufgebrachte $Ti(iOPr)_4$ bereitzustellen, welches schnell zu TiO_2 hydrolysiert. Das zugrunde liegende Konzept wurde von *Wang et al.* (1) inspiriert. In einer Reihe von Experimenten wurden dann die einzelnen Parameter untersucht und optimiert, wobei sich vor allem die Glastemperatur während des Sprühvorganges sowie die APTES-Beladung als sehr bedeutend erwiesen haben. Zur Bestimmung der hydrolytischen Klasse wurden die beschichteten Flaschen an unseren Unternehmenspartner gesandt, welcher die Untersuchung gem. ISO Norm 4802-1:1988 (E) (2) durchführte. Um die anderen Eigenschaften wie das Leaching-Verhalten von APTES und TiO_2 zu untersuchen, mussten als Erstes geeignete Analysemethoden etabliert werden. Für TiO_2 stellten sich ICP-OES Messungen als Mittel der Wahl heraus, für APTES wurden „Total organic carbon“ (TOC) Messungen herangezogen. Somit konnte erfolgreich eine Beschichtungsmethode

entwickelt werden, welche die hydrolytische Klasse der verwendeten Glassubstrate auf das gewünschte Niveau anhebt.

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7 List of Abbreviations, Symbols and Nomenclature

ann.	Annealing
API	Active pharmaceutical ingredient
app.	Approximately
APTES	3-Aminopropyltriethoxysilane
ATR	Attenuated total reflection
b.	Bottle
cm^{-1}	wavenumber
CO_2	Carbon dioxide
CVD	Chemical vapor deposition
ESI	Electron spray ionization
EtOH	Ethanol
ger.	German
HC	Hydrolytic class
HCl	Hydrochloric acid
HPLC	High Performance Liquid Chromatography
H_2O	Water
ICP	Inductively coupled plasma
IR	Infrared
ISO	International Organization for Standardization
J	Joule
K	Kelvin
KCN	Potassium Cyanide
l	Liter
m	Meter
m.	Microscope
M	Molar (=mol/l)
MEK	Methylethylketone
MS	Mass spectrometry
MVDA	Multivariate data analysis
m/q	Mass to charge ratio
N	Newton
NaOH	Sodium hydroxide

NDIR	Non-dispersive IR detector
NH_3	Ammonia
$(NH_4)_2SO_4$	Ammonium sulfate
nm	Nanometer
OES	Optical emission spectroscopy
PDA	Photo diode array
pH	Negative logarithm (base 10) of the conc. of dissolved H_3O^+
ppm	Parts per million (for example mg/L)
RT	Room temperature (app. 25°C)
s	Second
sil.l.	Silane layer
SiO_2	Silicon dioxide
sl.	Slide
SO_2	Sulfur dioxide
SO_3	Sulfur trioxide
t	Time
T_g	Glass transition temperature
TiO_2	Titanium Dioxide
T_m	Melting point
TOC	Total organic carbon
UHPLC	Ultra High Performance Liquid Chromatography
unw.	Unwashed
UV	ultraviolet
VIS	Visible
v/v	Concentration in percent volume per volume
W	Watt
wa.	Washed
w/w	Concentration in percent weight per weight
#	Number
°C	Degree Celsius

8 Goals and Motivation

Glass containers are widely used in pharmaceutical industry. A major concern regarding these glass containers is their hydrolytic stability (this means their “corrosion resistance” in aqueous environments), particularly when soda-lime-glass (also called type 3 glass (2)) are used. When these containers are filled with pharmaceutical solutions, alkali metals and alkaline earth metals can be leached out of the glass and alter the pH-value of the solution in the glass container. This may cause undesired interactions with the API. Possible examples for such undesired interactions are degradation of the API, which leads to inefficacy of the drug or precipitation of biopharmaceuticals (3).

To improve the hydrolytic resistance the glass manufacturer can use high quality glass like borosilicate glass, but this raises the costs significantly. The hydrolytic resistance is measured according to ISO specification 4802-1:1988 (E) (2). This specification divides glass containers into 3 different types: class 1 (best hydrolytic resistance), class 2 (intermediate hydrolytic resistance) and class 3 (worst hydrolytic resistance), including class B and D. The analysis itself is done by titrating an aqueous sample, which has received a certain exposure to the glass surface (1 hour at 121°C), with HCl.

Another approach to solve this problem is the application of an appropriate coating onto the interior surface of the containers. Several types of coatings and other methods to improve the hydrolytic class are currently known, including SiO_2 based coatings (4) or a depletion of surface alkali metals and alkaline earth metals with (for example) $(NH_4)_2SO_4$ (5).

With respect to the current situation, the goal of this work is the development of a novel approach for coating soda-lime-glass containers to improve their hydrolytic resistance. Soda-lime glass products are among the cheapest types of glass and it would be a great economic benefit if it would be possible to upgrade their hydrolytic class with a suitable treatment. (Comparison of prices: 1 bottle made of borosilicate glass is app. 3 times more expensive than a bottle of the same size made of soda lime glass (6) (7).)

The major objective of this thesis is to improve the hydrolytic class of the treated containers as far as possible, but at least from class 3 to class 2. This work has a great focus towards a simple application of the coating because the whole coating process should be incorporated in a glass container production line without major changes of the current process. Further requirements are:

- The coating has to be stable for at least 12 months.
- It must be suitable for application in the pharmaceutical industry (this means non-toxic, virtually no leaching of the components of the coating etc.).
- A certain mechanical stability is desired.
- It must withstand heat sterilization at 121°C.

To achieve these goals a completely new approach should be developed in order to prevent overlaps with existing processes, because the principal wants to avoid problems with existing patents.

The development of the coating and the process can be divided into three different stages:

Stage 1: Systematic optimization of the coating

Stage 2: Systematic optimization of the coating process

Stage 3: Development of a concept for process implementation

9 Introduction

9.1 The history of glass making

Glass making (8) (9) has a long and rich history of almost 5000 years, although natural glass (so called obsidian) was used before that. The first traces can be found in Mesopotamia, from where the knowledge of glass making came to ancient Egypt. There the prevailing glass type was soda-lime glass. A great improvement in the art of glassmaking was the invention of glassblower's pipe in the area of Judea in the centuries around Jesus Christ's birth. This invention made glass much cheaper compared to pottery and therefore the popularity of glass was increasing throughout the Roman Empire.

The Romans brought the art of glass making to Europe, where Trier/Cologne became a major spot of glass manufacturing, but instead of sodium carbonate they added potassium carbonate to produce so called "forest glass", a type of greenish glass material.

Glass became interesting for construction purposes when MnO_2 was introduced, which allowed the production of transparent glasses. Throughout the centuries many different types of glasses have been developed, each one with a different composition, for example lead crystal glass was invented in England in the late 17th century. The next major step in glass development was the production of optical glasses. This was a big improvement, because they have virtually no imperfections.

At the beginning of the 20th century another big change in glass making was the introduction of automatic processing in glass production. Famous processes for automatized glass making are the Focault process (Belgium, 1914), the Libbey-Owens process (USA, 1917) and the Pittsburgh-process (USA, 1928).

Another major improvement in glass making was the introduction of the float glass process. Step by step the whole process of glass making was mechanized and automated.

Due to the outstanding significance of the surface properties of glass, the methods of surface treatment like grinding, polishing, cleaning and coating became very important. The first glass coatings invented were various kinds of single layer antireflection coatings.

9.2 Glass as a material

There are several definitions for glass, for example the definition of the American Society for Testing and Materials (similar in DIN specification 1259: Glas – Begriffe für Glasarten und Glasgruppen from September 1986):

"Glass is an inorganic product of fusion which has been cooled to a rigid condition without crystallizing."

This definition is not entirely true, because it excludes organic glasses (like poly (methyl methacrylate) (10). A better definition includes the physicochemical properties of glass. Figure 9-1 shows the glass manufacturing process looking at the property of specific volume with respect to the temperature.

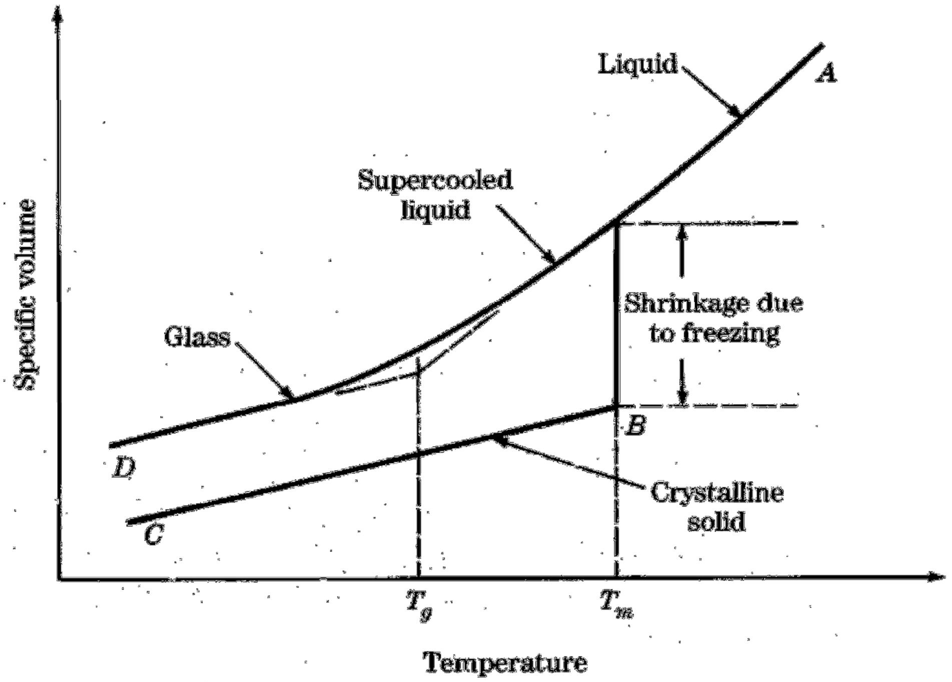


Figure 9-1: Schematic diagram of the temperature - volume relationship of glass (11)

Usually the volume of a melting is decreasing while cooling. The curves shown in the figure above represent thermodynamic equilibriums. When we look at curve A, the liquid/melting starts to crystallize after the melting has reached the temperature of the melting point (T_m) and the volume of the melting is decreasing sharply to point B. After that, further cooling is slower due to a smaller temperature coefficient (curve B-C).

When following the upper curve, an area called super cooled liquid can be seen, which is still in a (metastable) thermodynamic equilibrium. But when this curve starts to run parallel to curve C (the crystal curve) we do not have equilibrium. This is due to the increasing viscosity, which slows down the arrangement of the proper structures inside the material. At the point where it is impossible for the material to obtain the correct equilibrium structure the liquid/melting has become a solid. The temperature referring to this viscosity is called glass transition (area). This approach leads to a second definition of glass (12): “From a physicochemical point of view glass is a supercooled liquid”.

Considering this definition we get a clue of the glass structure. Liquids have a random structure; therefore we can expect that glasses show similar features.

9.2.1 The glassy state

Several theories have been developed to describe this glassy non-crystalline state. Very fruitful was the random network theory, developed by *Zachariasen* (13). It states that the basic silicate structure in glass forms a random network of SiO_2-units (this random network is the backbone of glass) if the following 4 conditions are fulfilled:

- The coordination number of the cation must be small.
- An oxygen ion must not be bonded to more than 2 cations.
- The oxygen polyhedrons are only allowed to share common corners, they are not allowed to share common edges or areas.
- At least 3 corners of every oxygen-polyhedron must be connected to other polyhedrons.

These requirements are met by the typical glass forming oxides, like B_2O_3, SiO_2, As_2O_3, P_2O_5, GeO_2, As_2O_5 and Sb_2O_3. Most of the important technical glasses are made by silica. To alter the properties of the glass, such as chemical durability, electrical conductivity etc. glass property modifying oxides can be added during the manufacturing process. Some of these are listed in Table 9-1.

Table 9-1: Glass property modifying oxides (8) (14)

Modified property	Compound
Network modifiers	Na_2O
	K_2O
	CaO
Optical properties	TiO_2
	PbO
	Li_2O
Chemical durability	PbO
	ZnO
	Al_2O_3
Thermal properties	PbO
	ZnO
	MgO
Electrical properties	B_2O_3
	Na_2O
	CaO
Mechanical properties	Na_2O

LiO_2
K_2O

In binary systems R_2O – SiO_2 (R = Alkali) the introduction of species like Na_2O leads to a big change in the glass structure. The introduced compound can cleave O^{2-} ion bridges and therefore alter the structure of the glass network. Bridging oxygens are transformed into non-bridging oxygens. An example of the change is shown in Figure 9-2:

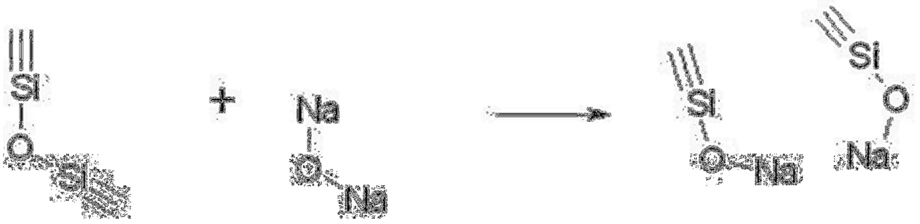


Figure 9-2: Chemical equation of the introduction of alkali oxides in glass (8)

Every glass must form a three-dimensional network for structural integrity, therefore the glass formation stops theoretically when each $[SiO_4]$-tetrahedron is connected at 3 edges, that means when the composition reaches R_2O - 2 SiO_2. Nevertheless, the glass formation occurs up to composition of R_2O-SiO_2, due to inhomogeneities in the linkage of the tetrahedrons. The compounds that form the network, which is the backbone of the material (in most cases this backbone of the glass network is formed by $[SiO_4]$-tetrahedrons) are called network formers. On the other hand cations that degrade and alter the structure of the glass network are called network modifiers. Different unmodified and modified networks are shown in Figure 9-3.

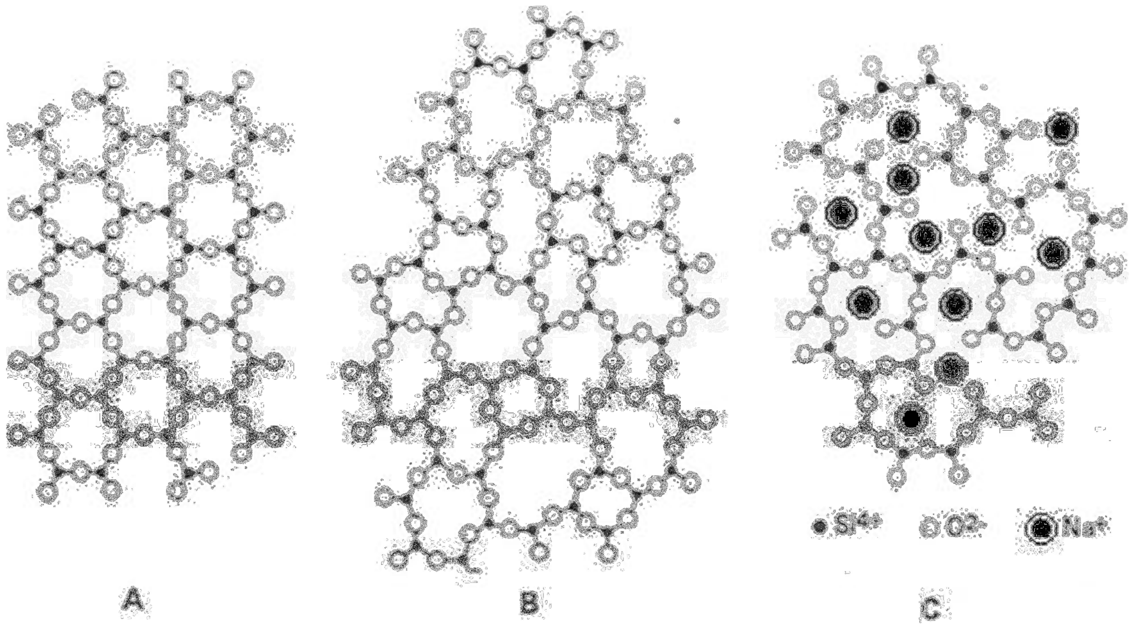


Figure 9-3: Structure of crystallized silica (A), fused silica (B) and soda silicate glass (C) (9)

9.3 Leaching and diffusion

Different types of diffusion can be encountered in nature (15; 16), for example thermal diffusion (Fourier's law (17)) or diffusion of mass (Fick's law). In this section the focus will be on the latter. Diffusion is of great relevance for this work, because leaching of ions into the pharmaceutical solution contained by the glass bottle is depending on diffusion. Therefore, the diffusion theory gives a better understanding of the underlying principles. The temperature dependence of diffusion is of great importance, because it is very likely that the glass containers have to undergo heat sterilization before usage.

Diffusion is a transport phenomenon, where particles spread in a medium through their own thermal movement. In an area where a certain substance A has a higher concentration, more particles are available to move randomly and statistically more particles A move into areas of a low A concentration. This leads to a reduction of the concentration gradient on a microscopic level. When considering diffusion in glass, the driving force for leaching (this means the movement of alkaline metals and alkaline earth metals out of the glass into the pharmaceutical solution) is the endeavor of the sodium and calcium ions to eliminate the concentration gradient. The movement of the particles is completely randomized, but during a longer period of time the transport can occur in only one direction, because the particles have a higher probability of movement out of the areas of higher concentration. This increased probability leads to a net flux in the direction of lower concentration. After some time the system reaches steady state, this means thermodynamic equilibrium. When the system is in that equilibrium, the concentration of particles is the same at every (coordinate) point within the borders of the system.

Such diffusion depends, as stated above, on the difference of the concentrations (C2 – C1), on the interface area (A) and the length l of the way of the diffusing species. In 1855 Adolf Eugen Fick, a German physiologist described diffusion in two laws, called Fick's first and Fick's second law of diffusion. (18)

Fick's first law (Equation 1) describes steady state diffusion, this means the system is in a thermodynamic equilibrium and a change of time does not influence the system and the particle flux of a certain species.

$$J_X = -D\frac{dC}{dx} \qquad \text{Equation 1}$$

J_x … Diffusion flux [kg/(m^2*s)]

D … Diffusion coefficient [m²/s]

C … Concentration [kg/m^3]

X … Coordinate point / Position [m]

The negative sign in Equation 1 indicates a flux from high concentration to low concentration. Typical values for diffusion coefficients (D) are 5*10^{-6} to 10^{-5} m²/s for gases (19), 10^{-10} to 10^{-9} m²/s for liquids (20) and 10^{-14} to 10^{-10} m²/s for solids (20).

If a linear concentration profile (this means concentration plotted vs. the distance) is assumed, the concentration gradient can be written according to Equation 2.

$$\frac{dC}{dX} = \frac{C_A - C_B}{X_A - X_B} \qquad \text{Equation 2}$$

C_A … concentration at point A [kg/m^3]

X_A … coordinate point A [m]

C_B … concentration at point B [kg/m^3]

X_B … coordinate point B [m]

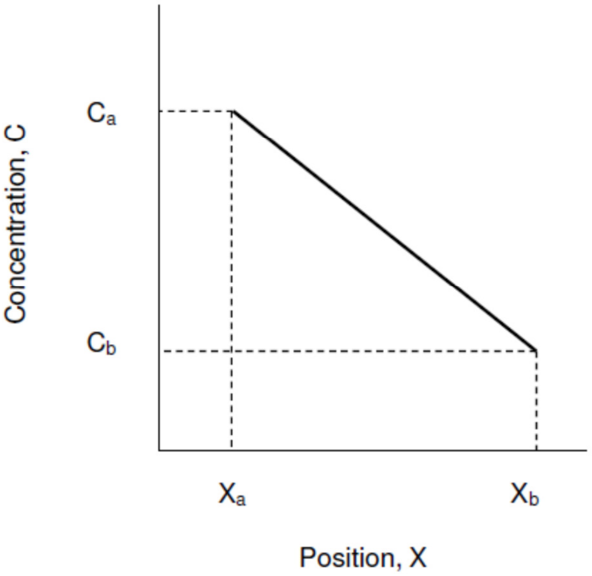


Figure 9-4: Steady state diffusion (slope = concentration gradient)

On the other hand Fick's second law deals with time dependent processes. If temperature distribution is taken as an example, the following setup can be used to clarify Fick's second law. When one end of a metal rod is heated up and then left for a certain period of time, the differences in temperature will be compensated until the whole rod has the same temperature. Another example (which is much closer to the presented thesis) is the concentration distribution in a solution. (16)

The central equation to describe time dependent diffusion processes is "Fick's second law", also called diffusion equation:

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2} \qquad \text{Equation 3}$$

c … concentration [kg/m^3]
x … coordinate point [m]
t … time [s]

If a small cuboid (Figure 9-5) with a cross section A from coordinate point x to point x + l is imagined, the concentration of a dissolved species at a certain point x at time t is c. The quantity of particles diffusing into the cuboid (volume = l*A) equals to J*A. The rise of the concentration in the cuboid due to the flow of particles from the left side is

$$\frac{dc}{dt} = \frac{J * A}{A * l} = \frac{J}{l} \qquad \text{Equation 4}$$

c … concentration [kg/m^3]

J … diffusion flux into the cuboid [kg/(m^2*s)]

A … cross sectional area of the cuboid [m^2]

l … length of the cuboid [m]

t … time [s]

Through the interface on the right side of the cuboid particles are diffusing out of the cuboid. This flux is called J’. The change of concentration due to this flux is

$$\frac{dc}{dt} = \frac{J' * A}{A * l} = \frac{J'}{l} \qquad \text{Equation 5}$$

c … concentration [kg/m^3]

J’ … diffusion flux out of the cuboid [kg/(m^2*s)]

A … cross sectional area of the cuboid [m^2]

l … length of the cuboid [m]

t … time [s]

Joining of Equation 4 and Equation 5 yields Equation 6.

$$\frac{dc}{dt} = \frac{J - J'}{l} \qquad \text{Equation 6}$$

J’ … diffusion flux out of the cuboid [kg/(m^2*s)]

J … diffusion flux into the cuboid [kg/(m^2*s)]

l … length of the cuboid [m]

c … concentration [kg/m^3]

t … time [s]

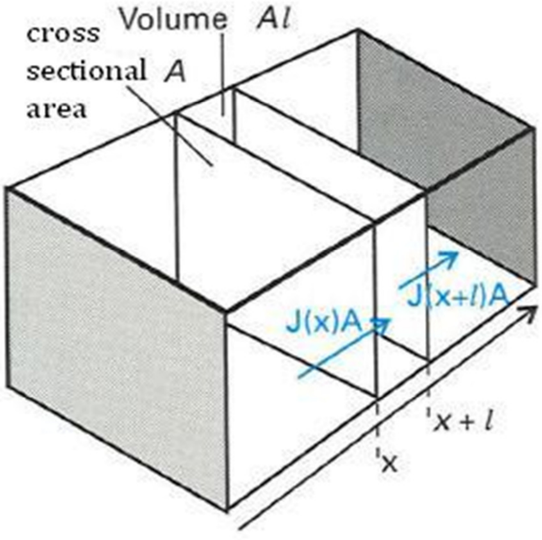


Figure 9-5: Net-flow of particles from an area of high concentration to an area of low concentration (16)

Each flux is proportional to the concentration gradient at the cross sectional areas at the borders of the cuboid. If we apply Fick's first law to these considerations, we can establish the following correlation:

$$J - J' = -D\frac{dc}{dx} + D\frac{dc'}{cx} =$$ Equation 7

$$= -D\frac{dc}{dx} + D\frac{d}{dx}\left(c + \left(\frac{dc}{dx}\right)l\right) =$$

$$= Dl\frac{d^2c}{dc^2}$$

J' … diffusion flux out of the cuboid [kg/(m^2*s)]

J … diffusion flux into the cuboid [kg/(m^2*s)]

l … length of the cuboid [m]

c … concentration at x [kg/m^3]

c' … concentration at x+l [kg/m3]

t … time [s]

If the final result of the equation above is substituted into Equation 6 Fick's second law (Equation 3) is obtained. However, the solutions of Fick's second law can involve many different approaches, depending on initial and boundary conditions. One approach uses Gaussian error functions, derived from statistics (error functions). The solution is as follows:

$$\frac{C_S - C_{(x,t)}}{C_S - C_0} = \operatorname{erf}\left(\frac{x}{2\sqrt{Dt}}\right)$$ Equation 8

$c_{(x,t)}$ … concentration at depth x after time t [kg/m³]
c_S … concentration at the surface [kg/m^3]
c_0 … concentration at time t=0 [kg/m^3]
x … coordinate point [m]
D … diffusion coefficient [m²/s]
erf(z) … Gaussian error function

It is known that diffusion processes change with temperature. The diffusion coefficient depends on an Arrhenius-style equation:

$$D = D_0 \exp\left(\frac{-E_A}{RT}\right)$$ Equation 9

D_0… temperature independent pre exponential [m²/s]
E_A … activation energy [J/mol]
R … ideal gas constant [8.314 J/(mol*K)]
T … temperature [K]

As mentioned before, diffusion is very important to understand leaching. The assumption that the bulk structure of the glass is not altered by depletion of sodium and calcium ions can be made. Furthermore, the following consideration regarding the mechanisms of leaching can be made: If an as film as continuous as possible is applied onto the surface of the glass substrate, the length of diffusion is increased. The diffusion coefficient of the applied coating is not known; nevertheless an extension of the way of the diffusing species will lead to fewer Na- and Ca-ions in the pharmaceutical solution.

9.4 Surface morphology

Another theory regarding the hindrance of diffusion of alkali metals and alkaline earth metals out of the glass bulk is the following: A layer of small particles may lead to an increased surface roughness resulting in worse wetting properties of the pharmaceutical solution contained by the glass bottle; this means the hydrophobicity of the inner surface is increased.

The "gold standard" for evaluating the hydrophobicity/hydrophilicity and the surface energy of a material is contact angle measurement. Particles at the surface produce a structured pattern which leads to an increasing roughness of the surface. Thus, the contact angle is rising, which means that the water has worse wetting properties with respect to the glass surface, as shown in Figure 9-6.

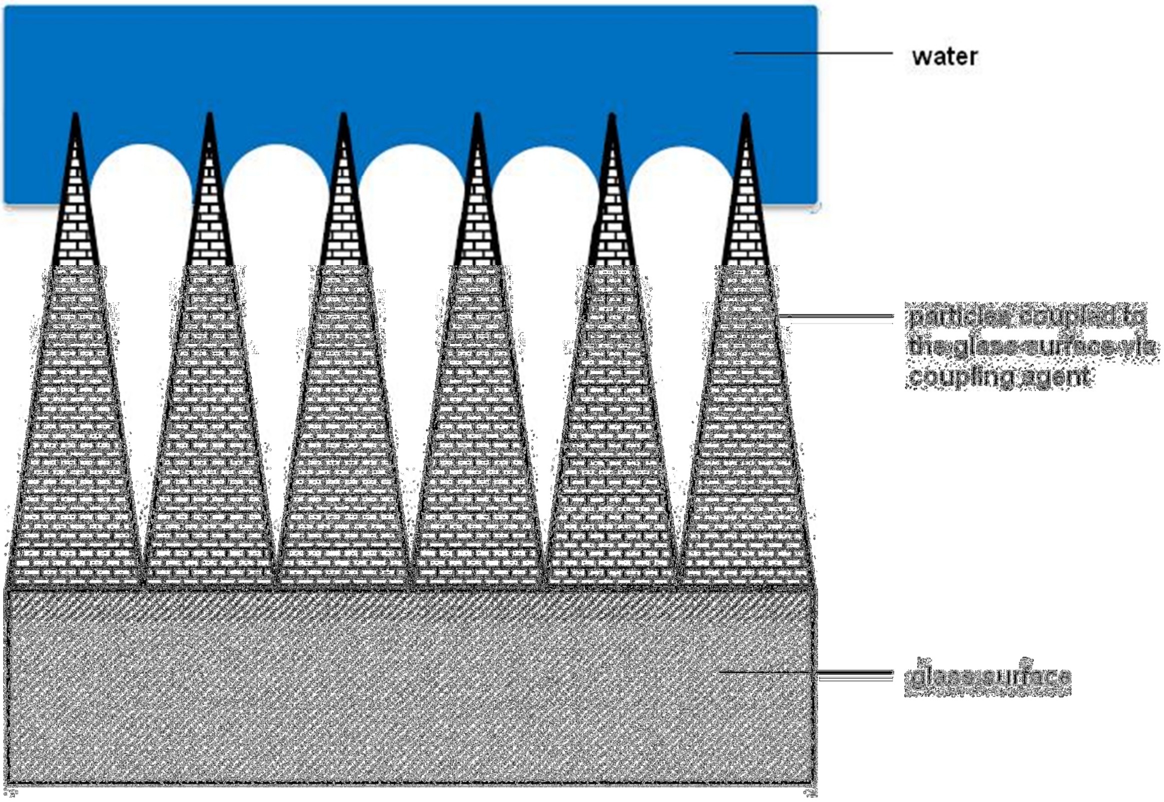


Figure 9-6: Water in contact with a structured surface (21)

9.4.1 Different models to describe surface tension

If we consider a homogenous liquid on a surface and we cleave it in two parts, the work done can be defined as

$$W_{ii} = 2\sigma \qquad \text{Equation 10}$$

W_{ii} …work of cohesion [J/m²]
σ …surface tension [N/m]

The work of cohesion was defined by *Dupre* as work, which has to be done to divide a liquid (and create the new surfaces) related to the newly formed area. If we have two liquids that are immiscible and we separate them, two new surfaces are created but the interface disappears. Equation 10 can rewritten as

$W_{ij} = \sigma_i + \sigma_j - \gamma_{ij}$ Equation 11

W_{ii} …work of cohesion [J/m^2]
σ …surface tension [N/m]
γ_{ij} … interfacial tension between the two phases [N/m]

The calculation of the interfacial tension as the difference between the two surface tensions was done by *Antonow* (22). But it was proven that this approach was more like an approximation.

$\gamma_{ij=}|\sigma_i - \sigma_j|$ Equation 12

σ …surface tension [N/m]
γ_{ij} … interfacial tension between the two phases [N/m]

A different approach was proposed by *Good and Girifalco* (23), shown in Equation 13.

$W_{ij} = 2\varphi\sqrt{\sigma_i * \sigma_j}$ Equation 13

σ …surface tension [N/m]
W_{ij} …work of cohesion [J/m^2]
φ … interaction parameter

The so-called interaction parameter Φ is a complex function of molecular properties and was initially only available through experiments.

If we combine Equation 13 and Equation 11 and transpose for γ_{ij}, we get

$\gamma_{ij} = \sigma_i + \sigma_j - 2\varphi\sqrt{\sigma_i * \sigma_j}$ Equation 14

σ …surface tension [N/m]
γ … interfacial tension [N/m]
φ … interaction parameter

Fowkes (24) developed a new approach, in which he proposed that only similar interaction can occur between two different phases, for example that nonpolar matter (this means only dispersive interactions) can only interact with dispersive parts of the second phase.

$$\gamma_{ij} = \sigma_i + \sigma_j - 2\sqrt{\sigma_i^D * \sigma_j^D} \qquad \text{Equation 15}$$

σ …surface tension (“D” represents the dispersive nature of the interactions) [N/m]
γ … interfacial tension [N/m]

This theory was expanded by OWENS, WENDT, RABEL und KAELBLE (25). Their method proposes that the total surface tension consists of two part, the disperse part and a polar part (derived from the polarity of the liquid).

$$\sigma = \sigma^D + \sigma^P \qquad \text{Equation 16}$$

σ …total surface tension [N/m]
σ^D … disperse share of the total surface tension [N/m]
σ^P … polar share of the total surface tension [N/m]

If we use Equation 16 to extend Equation 15, we get Equation 17.

$$\gamma_{ij} = \sigma_i + \sigma_j - 2(\sqrt{\sigma_i^D * \sigma_j^D} + \sqrt{\sigma_i^P * \sigma_j^P}) \qquad \text{Equation 17}$$

σ …surface tension [N/m]
γ … interfacial tension [N/m]
σ^D … disperse share of the total surface tension [N/m]
σ^P … polar share of the total surface tension [N/m]

Another theory, known as “extended Fowkes” (26) introduces a third kind of interaction, namely interactions caused by hydrogen bonds.

$$\sigma = \sigma^D + \sigma^P + \sigma^H \qquad \text{Equation 18}$$

σ …total surface tension [N/m]
σ^D … disperse share of the total surface tension [N/m]
σ^P … polar share of the total surface tension [N/m]
σ^P … hydrogen bond caused share of the total surface tension [N/m]

This extends the total equation to

$$\gamma_{ij} = \sigma_i + \sigma_j - 2(\sqrt{\sigma_i^D * \sigma_j^D +} \sqrt{\sigma_i^P * \sigma_j^P} + \sqrt{\sigma_i^H * \sigma_j^H} \qquad \text{Equation 19}$$

σ …surface tension [N/m]
γ … interfacial tension [N/m]
σ^D … disperse share of the total surface tension [N/m]
σ^P … polar share of the total surface tension [N/m]

All the equations (this means Equation 15, Equation 17 and Equation 19) use the geometric mean of the single surface tension components. They produce sufficiently good results for a broad range of surface energies. (27) Other models are the *"Oss and Good"* model (28), which uses the acid-base model of Lewis to describe the polar interactions and the model according to *Wu* (29) , which uses the harmonic mean instead of the geometric mean, but limits the interactions to disperse and polar interactions. The Wu approach is particularly useful for systems with low surface energy.

The models described above can be used to describe the interfacial tension between liquids, if the surface tensions and the polar, disperse and (if used) hydrogen bond fraction are known.

9.4.2 Contact angle measurement

As stated above, the assumption that the wettability of the surface may influence the leaching out of the glass substrate can be made. To evaluate this approach, it is necessary to have an adequate method for measuring the underlying irregularities of the surface, which may cause this effect (also known as "Lotus-effect").
In 1805, *Young* (30) developed a theory to give a description of the contact line between three phases. The situation at the contact line is shown in Figure 9-7. The relationship

between the factors shown in this figure (this means the surface and the interfacial tensions) was described by Young in the following equation (31):

$$\sigma_s = \gamma_{sl} + \sigma_l \cos\theta \qquad \text{Equation 20}$$

σ_s …surface tension (solid phase) [N/m]
σ_l …surface tension (liquid phase) [N/m]
γ_{sl} … interfacial tension (solid-liquid phase) [N/m]
θ … contact angle [°]

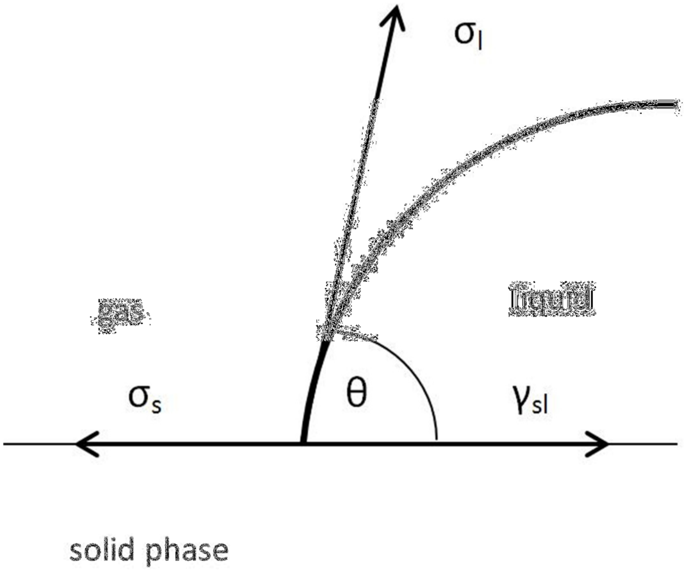


Figure 9-7: Contact angle formation on a solid surface according to Young (σ_s … surface tension (solid phase); σ_l … surface tension (liquid phase); γ_{sl} … interfacial tension between the liquid and the solid phase; θ … contact angle) (27)

If we apply the OWRK (Owens, WENDT, RABEL und KAELBLE) model to our contact angle measurements, we split the interactions between different phases in a disperse and a polar fraction. Equation 17 is used in combination with Equation 20. To solve this system of equations, the contact angles of different liquids were measured by *Rabel* (32). Values for the disperse and polar fraction are obtained by a linear regression. This means the equation resulting from the combination of Equation 17 and Equation 20 is rewritten in the general form of the linear equation (y = m*x+b). This operation yields Equation 21.

$$\frac{(1+\cos\theta)*\sigma_l}{2\sqrt{\sigma_l^D}}\{y\} = \sqrt{\sigma_S^P}\{m\}\sqrt{\frac{\sigma_l^P}{\sigma_l^D}}\{x\} + \sqrt{\sigma_S^D}\{b\} \qquad \text{Equation 21}$$

σ_s …surface tension (solid phase) [N/m]
σ_l …surface tension (liquid phase) [N/m]
θ … contact angle [°]

The superscripts P and D represent the polar and disperse fraction, respectively. The letters in den curved brackets represent the linear equation.

The graphical representation of Rabel’s approach is shown in Figure 9-8.

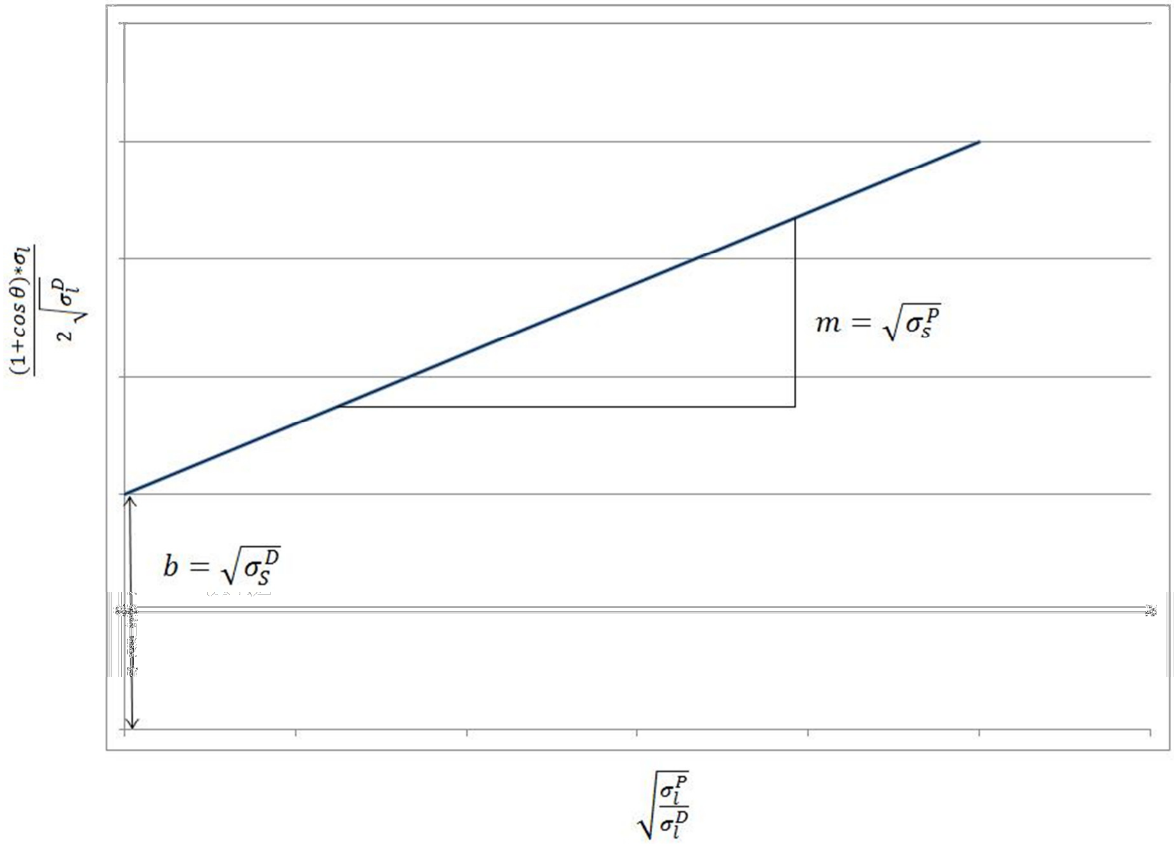


Figure 9-8: Determination of polar and disperse fraction according to Rabel

In summary we can say that a bad wettability of the inner glass surface may decreases the interactions between the aqueous solution and the glass surface. This can impede the leaching of alkali metal ions and alkaline earth metal ions.

9.5 “State of the art” technology

9.5.1 Impeding alkali leaching – State of the art

There are several possibilities to impede the leaching of alkali metals and alkaline earth metals into an aqueous solution that is filled into a glass container (4).

1. Use of a glass type which does not contain any diffusing alkali metal ions, like
    a. High-silica glass (Vycor-glass)
    b. Non-alkali containing aluminum silicate glass
    c. Lower-alkali borosilicate (Pyrex-glass)

    However, soda-lime glasses are relatively inexpensive compared to other glass types and therefore much more suitable for mass production of glass containers.

2. Removal of the alkali-ions prior to filling.
    a. The surface is brought in contact with sulfur at high temperature (300°C) in vacuum. An electric field (direct current) is applied subsequently to drive the Na^+-ions to the opposite side of the fielding surface.
    b. The glass material is boiled in acid, such as HCl, H_2SO_4 etc. Metal ions, particularly the reactive alkali-ions are replaced by protons under formation of silanol-groups. (5) Disadvantages of this method are a lack of reproducibility and that it is time-consuming (4).

3. Application of thin coatings on the glass surface. (5) Commonly used are SiO_x thin films, but other types of metal oxides are known as well. Possible options for applications are: (33)
    a. Evaporation
    b. Ion beam sputtering
    c. Thermal chemical vapor deposition (CVD)
    d. Metal-organic CVD
    e. Plasma-enhanced CVD

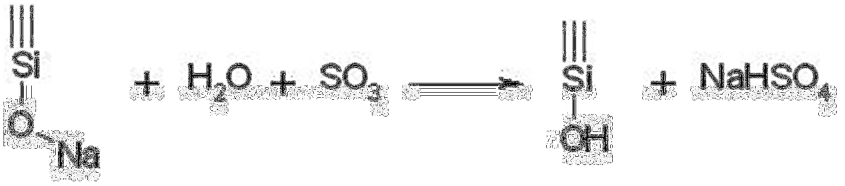
4. Improvement of the glass by ion exchange with gases (5).

The containers are exposed to acidic gases in the range of T_g. Very often sulfur oxides are being used, which can be introduced in the form of SO_2 or SO_3 gases or as ammonia sulfate tablets, which dissociate at higher temperatures according to Figure 9-9.

$$(NH_4)_2SO_4 \longleftrightarrow 2\ NH_3 + H_2O + SO_3$$

Figure 9-9: Dissociation of ammonia sulfate at elevated temperatures (5)

In both cases SO_3 is the reactant and the reaction with the alkali occurs corresponding to Figure 9-10. This leads to the generation of alkali sulfates at the surface of the glass container. Before using them for pharmaceutical purposes the containers have to be washed thoroughly. Instead of sulfur oxides HCl, HF or organic compounds can also be used.



$$\equiv Si{-}O{-}Na + H_2O + SO_3 \longrightarrow \equiv Si{-}OH + NaHSO_4$$

Figure 9-10: Reaction of alkali ions with acids or acid anhydrides in the presence of trace amounts of water

The surface enhancement with sulfur (ger.: “Vergütung mit Hüttenrauch”) is commonly used to enhance the surface of glass. When using solid tablets, there are several advantages that make this method popular, but on the other hand several disadvantages make new developments desirable.

Table 9-2: Advantages and disadvantages of surface treatment with sulfur compounds (5)

Advantages	Disadvantages
Easy to remove	Devitrification at the surface
Rather cheap	Parts of the glass can break away, if too many protons are brought into the glass
Easy to handle	-
Good improvement of the hydrolytic resistance	-

9.5.2 Our approach - TiO_2 films

With respect to the requirements (stable for at least 12 months; suitable for application in the pharmaceutical industry; withstand heat sterilization at 121°C) we have chosen TiO_2 for coating of the soda-lime glass because of the following reasons:

1. Preliminary work has shown that a process based on SiO_2 dip-coating does not show the desired results; therefore, we excluded this option from our considerations. Furthermore, many different kinds of SiO_x films are known, which lead to the consideration that this fact may be hindering a successful patent application.
2. TiO_2 is non-toxic and thermo-stable. (The coated glass container has to withstand autoclaving at a temperature of 121°C for 1 hour.)
3. TiO_2 is commonly used as an excipient in the pharmaceutical industry. (34)
4. The coated glass remains transparent and the film is mechanical stable. (35)
5. TiO_2 is well known for its properties as a photo catalyst (36), but photo catalytic degradation of the API will be prevented due to the UV light absorbing properties of the soda-lime glass (see Figure 10-7). Doping of the glass can be used as well to reduce its transparency in the UV region.

9.5.3 Surface silanization

According to (37) (38) we have to provide adequate binding sites for the TiO_2 particles to get a good TiO_2 barrier layer at the inner glass surface of the bottle. A straightforward approach is treatment of the inner surface with silanes, because glass surfaces are rich in hydroxyl groups which allow bonding of the silane coupling agents. The amino group at the other end of the silane molecule can be utilized to establish a coordinative bond to the inorganic particles (in our case TiO_2). Silane layers at the surface show good stability due to the covalent nature of the bonding and the fact that the silanes can form cross-linked networks. After the activation procedure (see *Chen et al.* (39) (The activation has to be done to remove adsorbed hydrocarbons (this contamination may impede the availability of the silanol-groups (9)) and to generate as many OH-groups at the surface as possible), the surface is exposed to the silane (in our case (3-aminopropyl)triethoxysilane (APTES)). The silane can be dissolved in either organic or aqueous solvents. Application of silane dissolved in anhydrous organic solvent leads to continuous, monomolecular layers, because the occurrence of hydrolysis reactions is rather unlikely. In protic solvents silanes tend to form three-dimensional polymerized networks because of hydrolysis reactions. The silanization reaction itself is very sensitive to water content, because depletion in surface water leaves some ethoxy groups unreacted (40).

The condensation reaction between the OH-groups at the surface and the silane can be catalyzed with amines (41). In our case the amino - group of APTES can self-catalyze this reaction. After this step the glass substrate is heated up and held at elevated temperate to allow cross-linkage of silanes, which are solely adsorbed with adjacent silane molecules. It is common to rinse the glass substrates after coating to remove unbound silane, but we could not find any beneficial influence on the final results.

9.6 Analytical technologies used

It is desired that the loss of TiO_2 and APTES into the pharmaceutical solution is as small as possible. Therefore, it was necessary to establish appropriate methods for qualitative and quantitative analysis of these analytes.

9.6.1 TiO_2 analysis

9.6.1.1 ICP-OES

The method we have chosen for TiO_2 analysis is ICP-OES. Referring to (42), OES (optical emission spectroscopy) is a well-established method based on atom spectroscopy. Atom spectroscopy is, generally spoken, a method where an atom is excited and subsequently emits electromagnetic radiation or absorbs electromagnetic radiation of a particular wavelength or energy, respectively. The wavelength is used for qualitative analysis; the intensity of the signal is used for quantification.

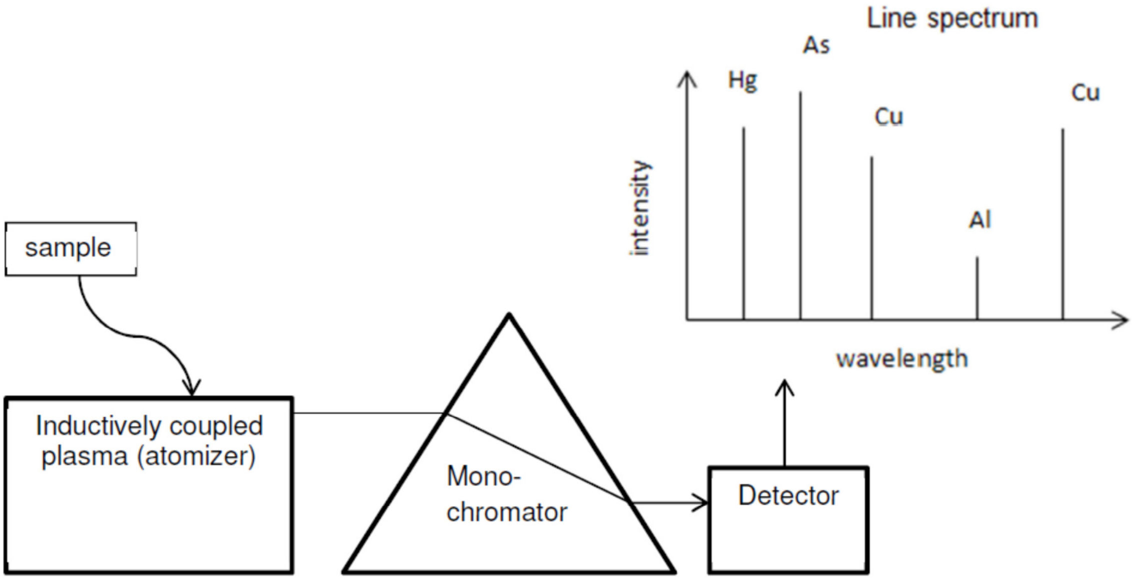


Figure 9-11: Block diagram of an ICP-OES

The basic setup of an ICP-OES is shown above in Figure 9-11. In ICP-OES analysis an inductively coupled plasma coil is used as atomizer. The plasma flame (with a temperature of app. 10000K) leads to a very high degree of atomization. Because of this high degree of atomization the precision and reproducibility is very high and low detection limits (and limit of quantification) are achieved. If a suitable spectrometer unit is used, the simultaneous measurement of up to 70 elements can be done. These advantages make the ICP-OES perfectly suitable to fulfill our demands.

9.6.2 APTES analysis

9.6.2.1 Fourier-Transform-IR-spectroscopy (FT-IR)

According to (43), the basic principle of IR spectroscopy is the following: a light source which emits infrared light sends electromagnetic radiation of certain energy into the sample where it is absorbed, because it induces rotations in small molecules or vibrations in molecular bonds. The wavelength of the absorbed light is related to the nature of the rotation or vibration. Usually infrared light is divided in three different regions:

- Near-infrared: 14000 – 4000 cm^{-1}
- Mid-infrared: 4000 – 400 cm^{-1}
- Far-infrared: 400 – 10 cm^{-1}

As seen above the wavelength of the light is expressed as wavenumber, which is related to the wavelength according to Equation 22.

$$\nu\sim = \frac{10^4}{\lambda} \qquad \text{Equation 22}$$

$\nu\sim$…wavenumber [cm^{-1}]
λ … wavelength [µm]

IR spectroscopy can be used for structure elucidation and for quantitative analysis as well. Many functional groups (for example amines, acid-groups etc.) have characteristic vibrational modes which show absorption bands in defined areas of the spectrum. This allows convenient identification of functional groups with rather small efforts (this means comparison with reference spectra). Today the usage of Fourier-Transform-IR equipment is standard because it allows almost simultaneous detection of every wavelength. This is achieved through the following procedure: the whole spectrum of IR radiation (with continuous intensity) is sent through a so-called Michelson interferometer, which conducts the transformation in an interferogram. The interferometer can be placed behind or before the sample. The interferometer allows the recording of the light intensity as a function of the mirror position. The resulting interferogram is subject to a mathematical operation called Fourier transformation, which transforms the interferogram into a spectrum (Figure 9-12).

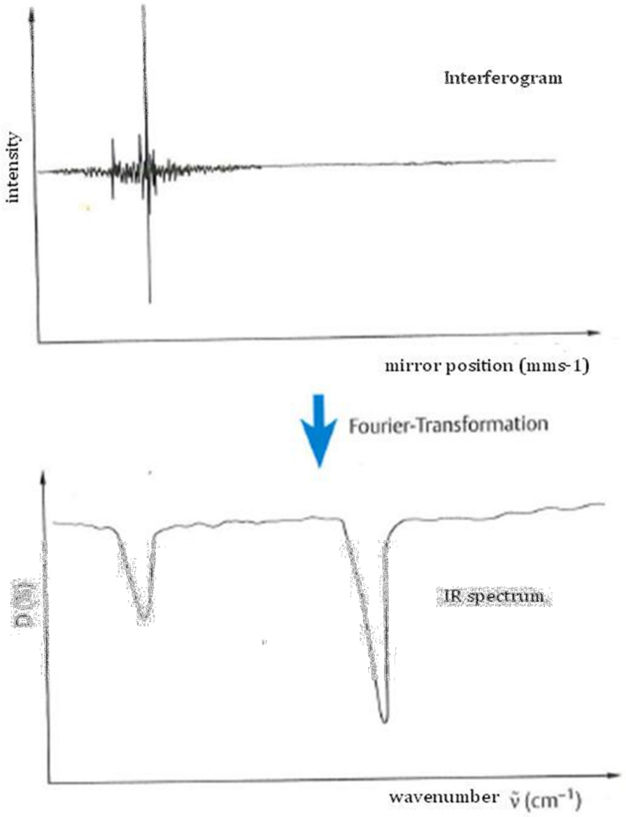


Figure 9-12: Fourier transformation (43)

9.6.2.1.1 Attenuated Total Reflectance (ATR)

In our measurements we used an ATR system. The underlying principle of ATR (44) is shown in Figure 9-13. The IR radiation is guided onto an optically dense crystal, which creates an evanescent wave. This wave reaches out of the surface of the crystal for some micrometer (0.5 – 5 µm (app. one wavelength, also depending on the angle of incidence and the type of ATR crystal)) and enters the sample, which has to be in good contact with the analyzer crystal. If the sample shows absorption the evanescent wave will be altered / attenuated. This leads to an attenuation of the IR beam in the optical waveguide, which can be retransformed into an IR spectrum.

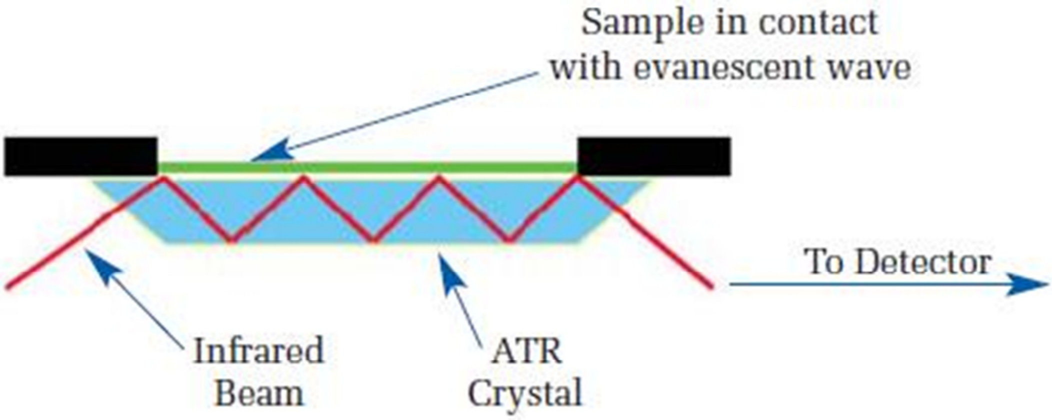


Figure 9-13: ATR system (multiple reflection) (44)

9.6.2.2 Ultra high performance liquid chromatography (UHPLC)

As described in (45), chromatography is a commonly used separation technique. Together with a solvent (mobile phase) the examined substance (analyte) is pumped through the separation column (stationary phase). In analytical chromatography a detector is installed at the end of column. At the end of the column the separated compounds show different retention times due to their individual interactions with the stationary phase, the composition of the mobile phase and the flow rate of the mobile phase. Two different combinations of mobile and stationary phase exist:

- Normal phase: polar stationary phase (for example silica gel) and non-polar mobile phase (for example various hydrocarbons)
- Reversed phase: non-polar stationary phase (for example modified silica gel) and polar mobile phase (for example water)

To get very fast separations without a lost in N (column plate number - a higher N results in a better separation performance) the classical High Performance Liquid Chromatography (HPLC) technique has been evolved to the more sophisticated Ultra high performance liquid chromatography. Smaller particles (usually < 2 µm diameter), relatively small columns and higher flow rates are key features of UHPLC. With these parameters the separation performance can be improved if the run time remains the same and vive versa. In our UHPLC setup we used two different types of detectors:

Photo Diode Array Detector (PDA)

The PDA (46) allows simultaneous detection of all wavelengths at every time of the chromatogram. The basic principle of a PDA detector is shown in Figure 9-14. The full light spectrum is sent through the sample and then divided at the polychromator. After this step the light falls onto the diode array, where a large quantity of light-sensing diodes register the incident light. The advantages are, as stated above, the possibility to record a full spectrum at every point of the elution and the possibility to set the detection wavelength to a particular value and record a chromatogram for the selected wavelength.

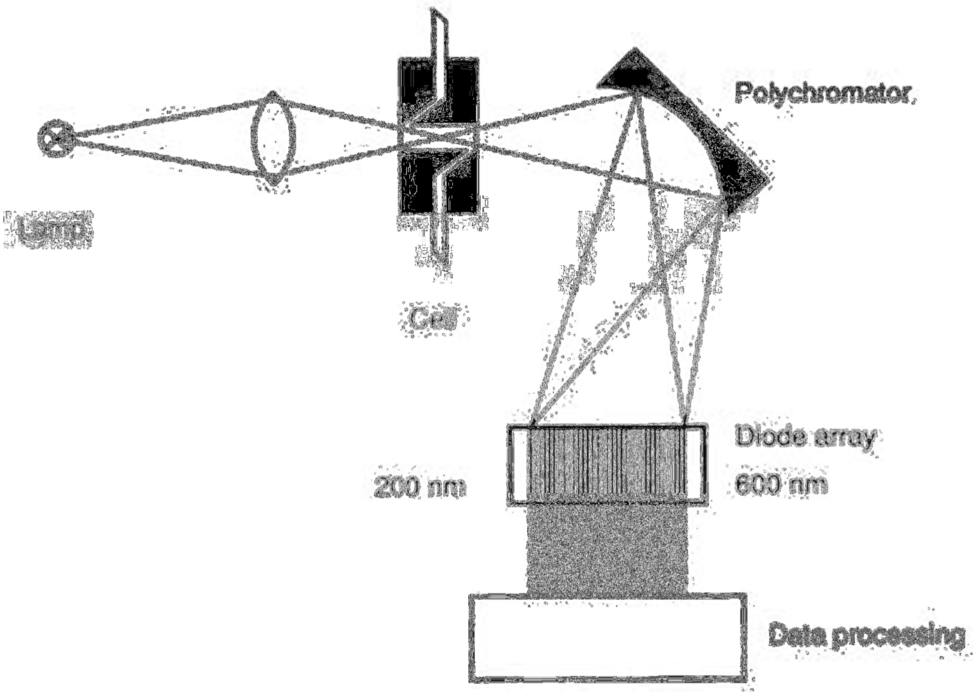


Figure 9-14: Basic principle of a diode array detector (46)

Mass spectrometry (MS)

According to (46), the basic concept of a mass spectrometry detector is that the analyte is vaporized and subsequently ionized (the technique we have used for ionization will be described below). The ions produced are accelerated in an electric field and directed towards the analyzer, which separates the incoming ions depending on their mass to charge ratio (m/q) (47). The resulting particle beams are sent towards the detector to give a mass spectrum. Depending on the ionization method the analyte molecule can be fragmented (so-called “hard” ionization). The MS we have used utilizes electron spray ionization (This is a “soft-ionization” technique which causes virtually no fragmentation.) (Figure 9-15). A MS unit consists of the following major parts:

- Interface (entrance and ionization)
- Mass analyzer (for example Quadrupole mass filter)
- Detector (for example an electron multiplier)

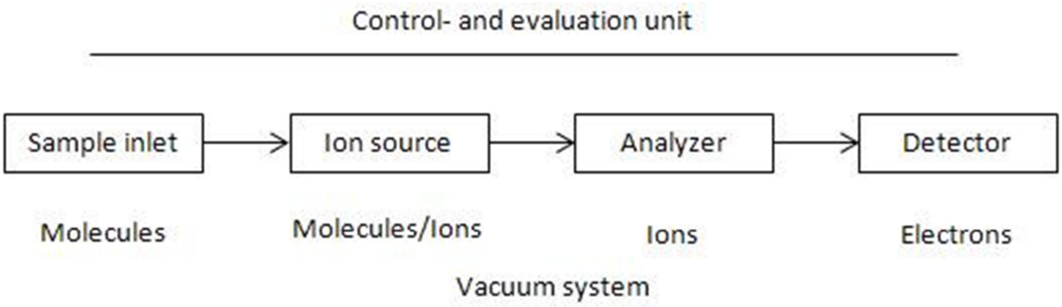


Figure 9-15: Block diagram of a mass spectrometry unit (42)

9.6.2.3 Total organic carbon (TOC)

The TOC method is using the following principle (48) (Figure 9-16). The aqueous sample is fully oxidized using a catalyst (for example Platinum) in an oxygen rich atmosphere. The whole carbon is transformed into CO_2, which is measured with a non-dispersive IR detector (NDIR). In our case the limited capabilities of the catalyst set the limit of quantification to 5 ppm (5 mg per liter).

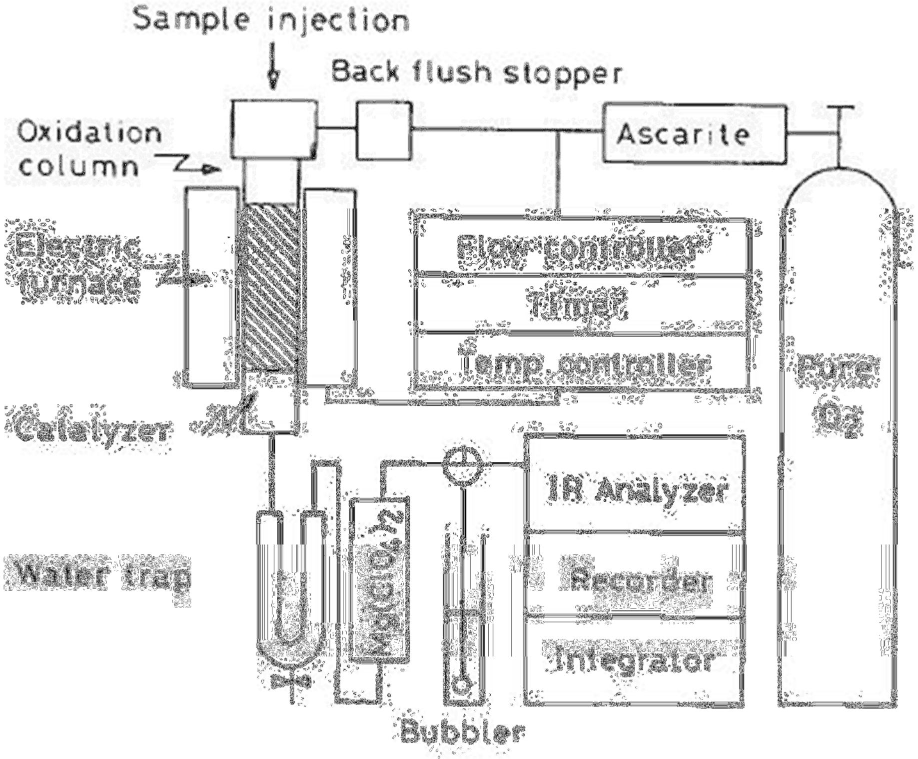


Figure 9-16: Dissolved TOC measuring apparatus (48)

9.6.2.4 Ultraviolet–visible spectroscopy (UV-VIS)

UV-VIS spectroscopy (43) is a type of absorption spectroscopy. Samples are illuminated with ultraviolet and/or visible light, which can excite valence electrons of molecules. The main application for this technique is the analysis of organic molecules or metal complexes. The Beer-Lambert's law (Equation 23) is used for quantification.

$$A = \log(\frac{I_0}{I}) = \varepsilon * c * L \qquad \text{Equation 23}$$

A …absorption
I … intensity of light beam (before sample)
I_0 … intensity of light beam (after sample (this means transmitted light))
ε … molar absorptivity [$l*mol^{-1}*cm^{-1}$]
c … concentration [mol/l]
L … path length through the sample [cm]

The basic setup of a dual-beam UV/VIS spectrometer is shown below.

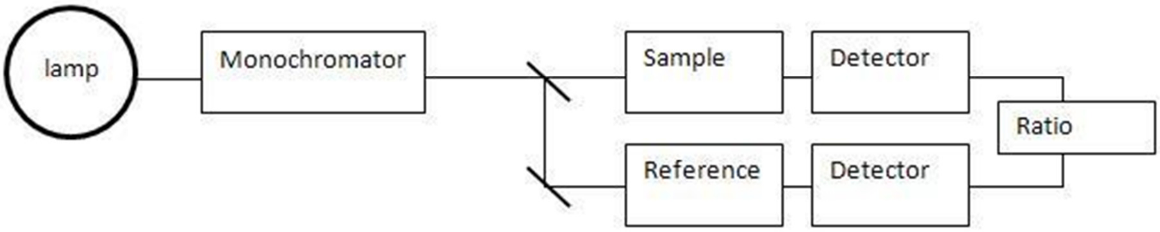


Figure 9-17: Block diagram of an UV-VIS spectrophotometer

Amine detection reaction with ninhydrin

APTES itself shows very little UV absorption and has no significant absorbance in the visible region of the electromagnetic spectrum. A frequently used method for derivatization of amines (particularly amino acids) is the reaction of the amine group with ninhydrin (49). This reaction yields a compound called "Ruhemann's purple", which shows a strong absorption band at 570 nm. The reaction mechanism is shown in Figure 9-18.

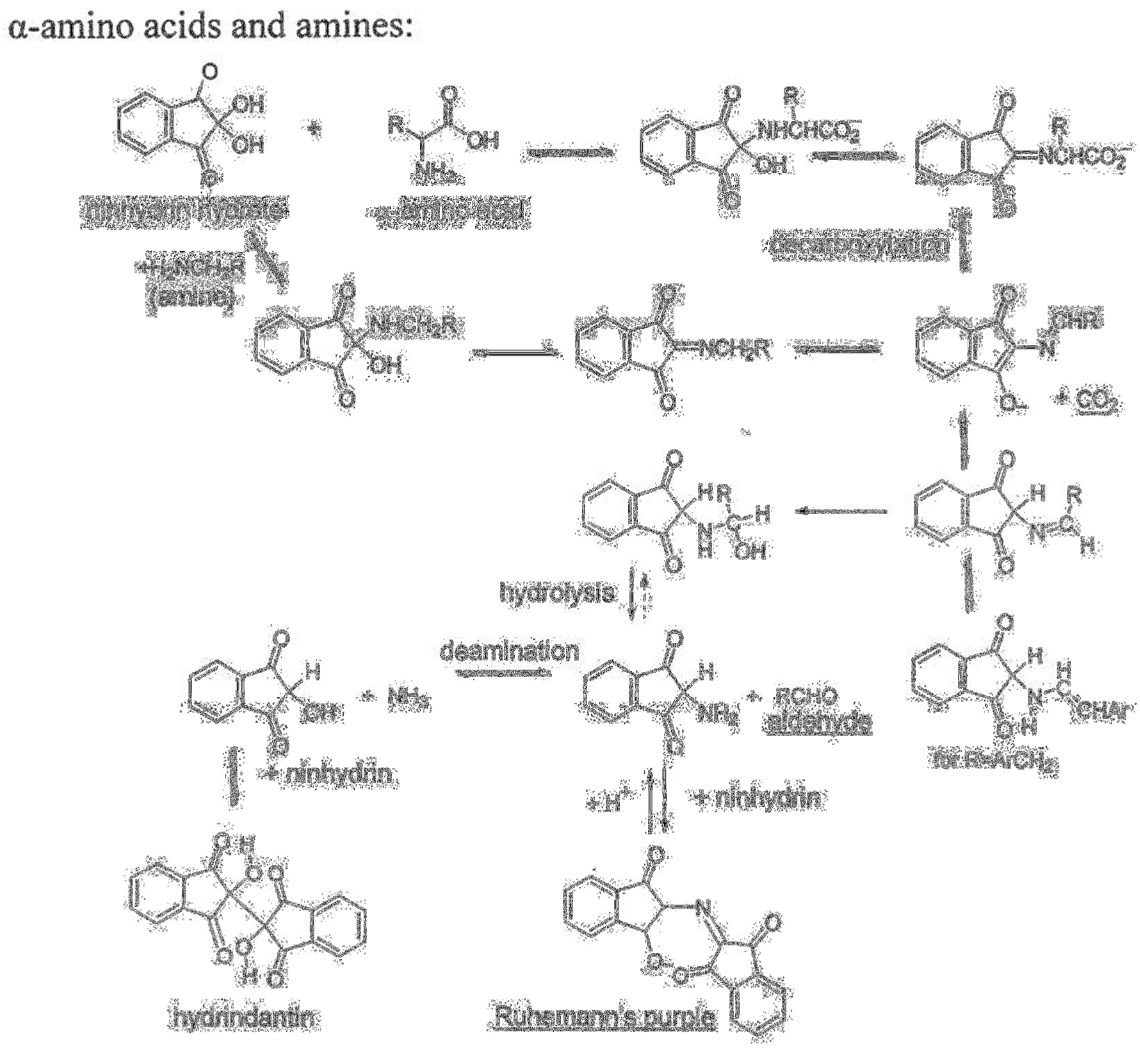


Figure 9-18: Detection reaction of amines with ninhydrin (50)

In literature (51) an experimental procedure for reaction of ninhydrin with APTES is described as follows: "*Three stock solutions including 80 % phenol in ethanol, KCN in H_2O/pyridine, and 5% ninhydrin in ethanol were prepared, and a known weight equivalent to 3 drops of each were added to test tubes with a solution of APTES (…) The mixture was heated to 393 K for 2 min in an air-tight vessel at constant pressure. After cooling down to room temperature, the solution was characterized by UV-visible spectroscopy.*" For security reasons (KCN!) it was not possible to follow the proposed procedure. In (49) a general experimental procedure is described (but not particularly for APTES analysis): *"1 to 2 mg of substance (analyte) is dissolved in water. Add 4 to 5 drops of a 1% ninhydrin solution and boil it for a short period of time."*

Therefore we tried to adapt the experiment for our needs. The approaches we developed and the outcome are shown in Chapter 10.5.4.

10 Experimental, Results and Discussion

10.1 Preliminary study

Preliminary studies were conducted by *Heidrun Gruber-Wölfler* to figure out the most promising approach for the coating and to find a production method that fulfills all the requirements. The developed method should be capable of handling 200,000 glass containers per day. To resolve this issue different manufacturing processes were examined in the preliminary study. As described below dipping, spin coating and spraying was taken into consideration. Each method was assessed in order to determine the eligibility in the manufacturing. Furthermore, the resulting increase in the hydrolytic resistance was evaluated for all methods. The model substrates we used in this part of the work were microscope slides.

10.1.1 Manufacturing methods

In the first step of the examination the slides were degreased using two different methods. In the method developed by *Jokinen et al.* (52) the slides are being submerged in acetone for 5 minutes and in the second step submerged in ethanol for another 5 minutes. Finally, the slides were air-dried at room temperature.

The other method was reported by *Pucher* (53): the microscope slides are dipped in NaOH (1M), then rinsed with distilled water and acetone and dried with paper.

After degreasing the slides they were submerged in a solution of titanium(IV)isopropylate in ethanol (app. 10% w/w) for app. 1 second. After a short period of drying at room temperature the slides were further dried in an oven at 150°C for 1 hour. One fraction of these slides was rinsed with ethanol and cleaned with paper; the other fraction was left untreated.

10.1.1.1 Assessment of the procedures

To assess the eligibility of the tested methods a process similar to the ISO 4802-1:1988 was established. Representative samples (3 parts with an area of app. 0.25 cm²) were cracked off the slides and put into a test tube (made of Borosilicate glass). 10 ml of deionized water were added; the test tube was sealed and heated to 80°C for 1h. After cooling down to room temperature 5 ml of the extracts were dosed with 2 droplets of pH indicator (25 mg methyl red in 100 ml testing water, referring to ISO 4802-1:1988) and titrated with HCl (0.1 mM). The results of the titration are shown in Table 10-1.

Table 10-1: Results of the first titration of the coated slide extracts (Ac. = acetone)

Sample	Consumption 1 (0.1 mM HCl) [ml]	Consumption 2 (0.1 mM HCl) [ml]	Average [ml]	Mass of the sample [g]	Consumption related to sample mass [ml/g]
Deion. Water	1.4	1.4	1.4	-	-
Testing water	1.2	1.1	1.2	-	-
Blank	1.6	1.6	1.6	-	-
Slides without treatment	4.3	4.0	4.2	0.664	6.25
Slides Ac/EtOH	4.0	4.0	4.0	0.811	4.93
Slides Ac/EtOH/TiO_2/rinsed	3.6	3.6	3.6	0.863	4.17
Slides NaOH	3.0	3.0	3.0	0.744	4.03
Slides NaOH/TiO2/rinsed	2.9	2.8	2.9	0.767	3.72

A second titration was performed another day. The results are shown in Table 10-2.

Table 10-2: Results of the second titration of the coated slide extracts (Ac. = acetone)

Sample	Consumption 1 (0.1 mM HCl) [ml]	Consumption 2 (0.1 mM HCl) [ml]	Average [ml]	Mass of sample [g]	Consumption related to sample mass [ml/g]
Deion. Water	1.0	0.8	0.9	-	-
Testing water	0.8	0.7	0.8	-	-
Slides without treatment	2.1	2.2	2.2	0.546	3.94
Slides Ac/EtOH/TiO_2/ not rinsed	2.0	1.9	2.0	0.553	3.53
Slides Ac/EtOH/TiO_2/rinsed	1.4	1.5	1.5	0.567	2.56
Slides NaOH/TiO2/rinsed	1.4	1.5	1.5	0.624	2.32

Furthermore, the appearance of the slides was evaluated (Figure 10-1):

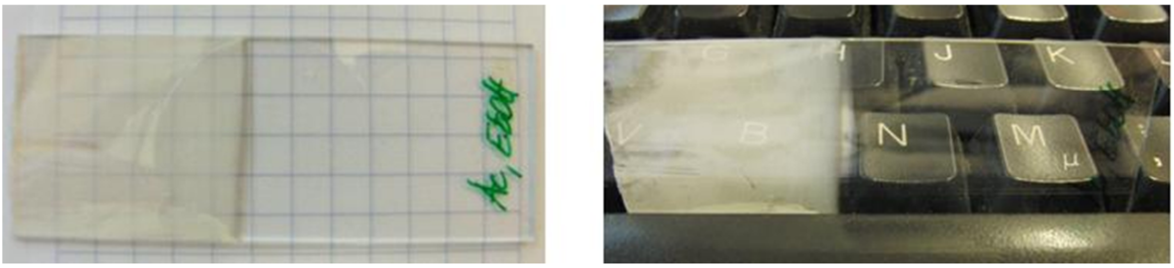


Figure 10-1: Treated, but unwashed slide. The slide was degreased with acetone and ethanol, the left part was coated with titanium dioxide.

Additionally, contact angle measurements of 2 different types of slides were conducted. The results are shown in Table 10-3:

Table 10-3: Contact angle measurements of different slides

Type of slide	Contact angle [°]
untreated	16.3
Slides degreased with NaOH | coated with TiO_2 | after drying washed with EtOH	58.9
Slides degreased with NaOH | after drying washed with EtOH (no TiO_2 coating)	30.9

These first experiments showed that the process meets the requirements in the following points:

- Slides coated with TiO_2 and washed after drying remain transparent (optical requirements).
- Coating of the slides reduced alkali leaching.

Additionally, the following processes were taken into consideration:

- Coating with TiO_2 based on a sol-gel process
- Coating with Ti(i-OPr_4) in ethanol after degreasing with subsequent annealing (52) (53)
- Application of a coating in a gaseous state is possible according to *Mills et al.* (35)

Considering these facts and the possibilities given by the laboratory equipment the following three methods of manufacturing were chosen for further evaluation:

- Dipping sol gel process (see above)
- Spin coating (on a magnetic stirrer with a rotating plate)
- Spraying

Regarding the optical appearance, the tested methods yielded the results shown in Figure 10-2, Figure 10-3, Figure 10-4 and Figure 10-5. The corresponding process parameters are shown in the caption.

Spin coating process:

Figure 10-2: unwashed, concentration of coating solution is 1% w/w

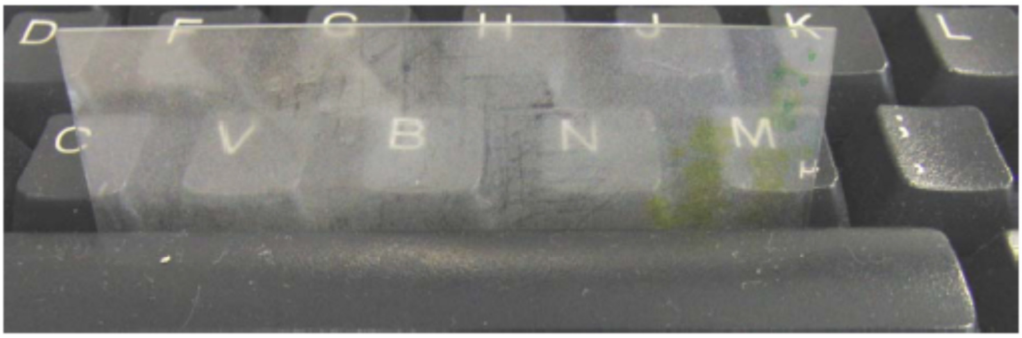


Figure 10-3: unwashed, concentration of coating solution is 10% w/w

Spraying process

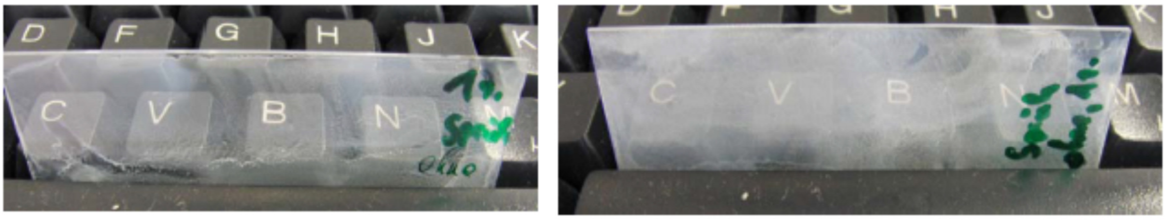


Figure 10-4: unwashed, concentration of coating solution is 1% w/w

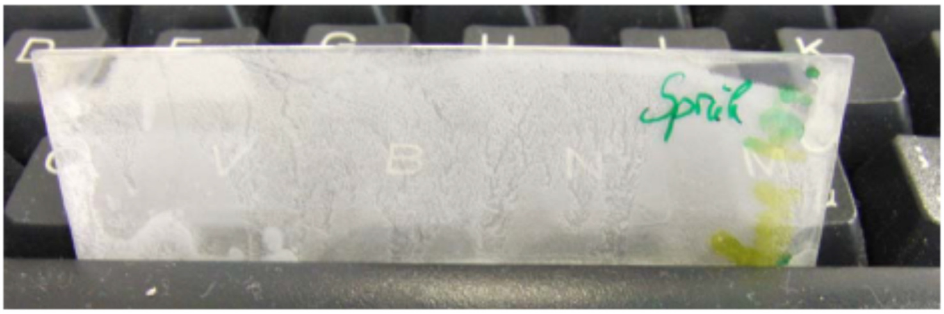


Figure 10-5: unwashed, concentration of coating solution is 10% w/w

The results of the evaluation of the barrier layer suitability of dip-coated slides are shown in Figure 10-6. The results of spin-coated and spray-coated slides are shown in Table 10-4.

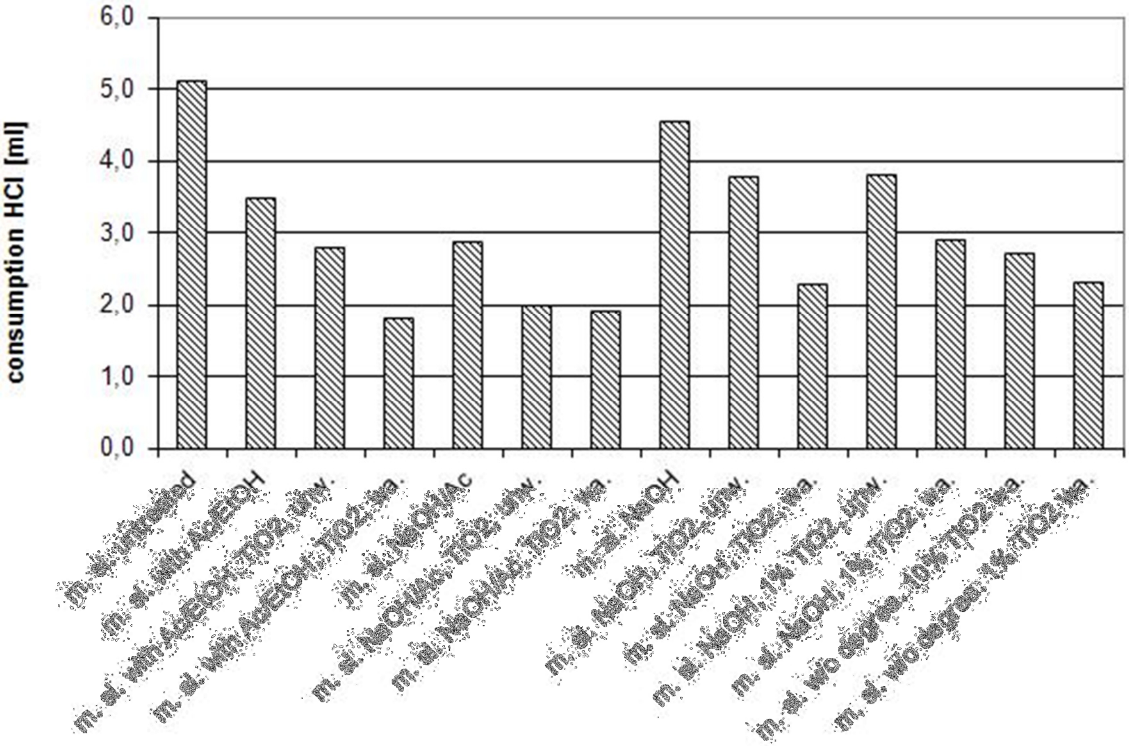


Figure 10-6: Titrations of slides coated by dipping (unless otherwise stated, the Ti(iOPr)$_4$ solution had a concentration of 10% w/w

Table 10-4: Titration of microscope slides after Spin-Coating and Spraying

Name	Degreasing	Ti(iOPr)$_4$ [% w/w]	Washing?	Consumption [0.1 mM HCl]
Untreated	-	-	-	5.1
Spin coat.	-	1	Yes	4.2
Spin coat.	NaOH	10	Yes	3.0
Spraying	-	1	Yes	2.9
Spraying	-	10	Yes	2.8

Another issue which was taken into consideration was that TiO_2 particles show photo catalytic activity when exposed to UV light (54). This fact may be very uncomfortable, because the containers should protect organic molecules (the drugs containing the API) from external influences. To study and evaluate this problem a UV/VIS spectrum of several specimens was recorded. The results are shown below in Figure 10-7.

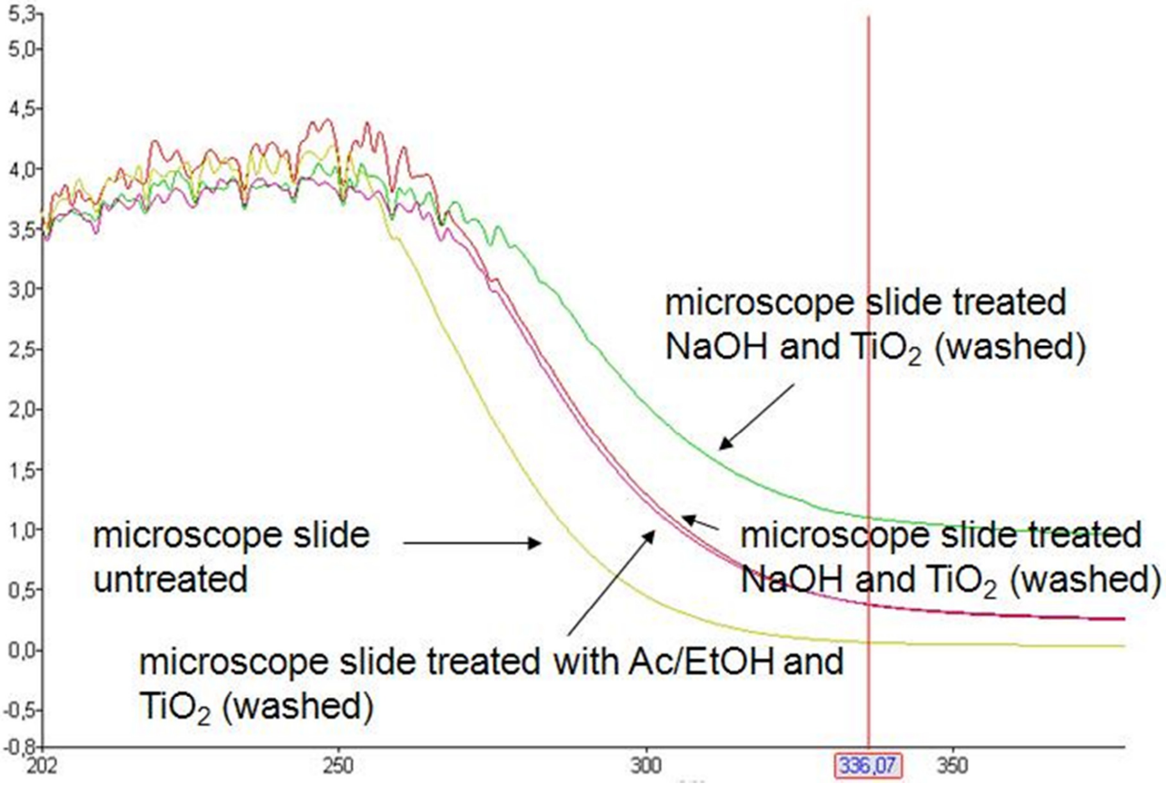


Figure 10-7: UV/VIS spectra of several treated or untreated microscope slides; x-axis = wavelength in nm; y-axis = absorption

The soda lime glass is not entirely impermeable for UV radiation with an adequate wavelength to trigger photo catalytic activity of the titanium oxide particles. This shows that this problem cannot be completely ignored. Possible ways to solve this problem may be the application of eligible glass ingredients to alter the UV transmission of the glass.

Conclusions of these studies:

- Slides coated with TiO_2 and washed with EtOH fulfill the optical requirements. (Remain transparent after treatment.)
- Coating increases the hydrophobicity (this means the contact angle).
- Coated slides show a higher UV absorption.

- The coating decreases the HCl consumption; this means the leaching of alkaline and alkaline earth metals is apparently decreased. (Improvement of the hydrolytic class)

With this knowledge the experiments were continued using glass bottles provided by Stölzle Oberglas GmbH, which are also the substrate in the final stage (manufacturing in the industrial production site).

10.1.2 Coating of glass bottles – Approach 1 (Use of stage one spraying apparatus and $Ti(i\text{-}OPr)_4$)

The bottles were degreased using NaOH and subsequently rinsed with deion. H_2O. After this, they were dried in the oven at 150°C. The coating itself was done using a solution of titanium isopropoxide ($Ti(i\text{-}OPr)_4$) in ethanol (99.8%). The applied spraying device was the stage 1 spraying apparatus (see chapter 10.2.1). The following $Ti(i\text{-}OPr)_4$ concentrations were tested:

- 3 bottles using 10% w/w $Ti(i\text{-}OPr)_4$
- 3 bottles using 2% w/w $Ti(i\text{-}OPr)_4$
- 3 bottles using 1% w/w $Ti(i\text{-}OPr)_4$
- 3 bottles using 0.5% w/w $Ti(i\text{-}OPr)_4$
- 4 bottles using 0.1% w/w $Ti(i\text{-}OPr)_4$

After a short period of drying at room temperature the bottles were further dried in an oven at 150°C for 1 hour. After the treatment the bottles were sent to our industrial partner for the determination of the hydrolytic class according to Method ISO 4802-1. The results are shown in Table 10-5.

Table 10-5: Determination of the hydrolytic class of the glass containers (ISO 4802-1); Approach 1

Sample description	Specification Type II	Results [ml 0.01 N HCl/100 ml]	Average [ml]
Untreated	Max. 0.40 mL 0.01 N HCl / 100 mL	2.86	2.86
Only NaOH		2.76	2.76
Unwashed 0.1 % old		2.28	2.28
Unwashed 0.1%		2.54 / 2.66	2.6
Unwashed 0.5%		2.30 / 2.32	2.31
Unwashed 1%		2.52 / 2.58	2.55
Unwashed 2%		2.40 / 2.42	2.41
Unwashed 10%		1.28 / 2.12	1.7

These values do not match the requirements for hydrolytic class 2 (this means below 0.4 ml consumption of 0.01 N HCl), therefore another approach was tested.

10.1.3 Coating of glass bottles – Approach 2 (Treatment of the surface with APTES)

Wang et al. (1) presented a method for binding 3-aminopropyltriethoxysilane (APTES) to the glass surface with subsequent binding of silver nano particles to the amino group of APTES, shown in Figure 10-8.

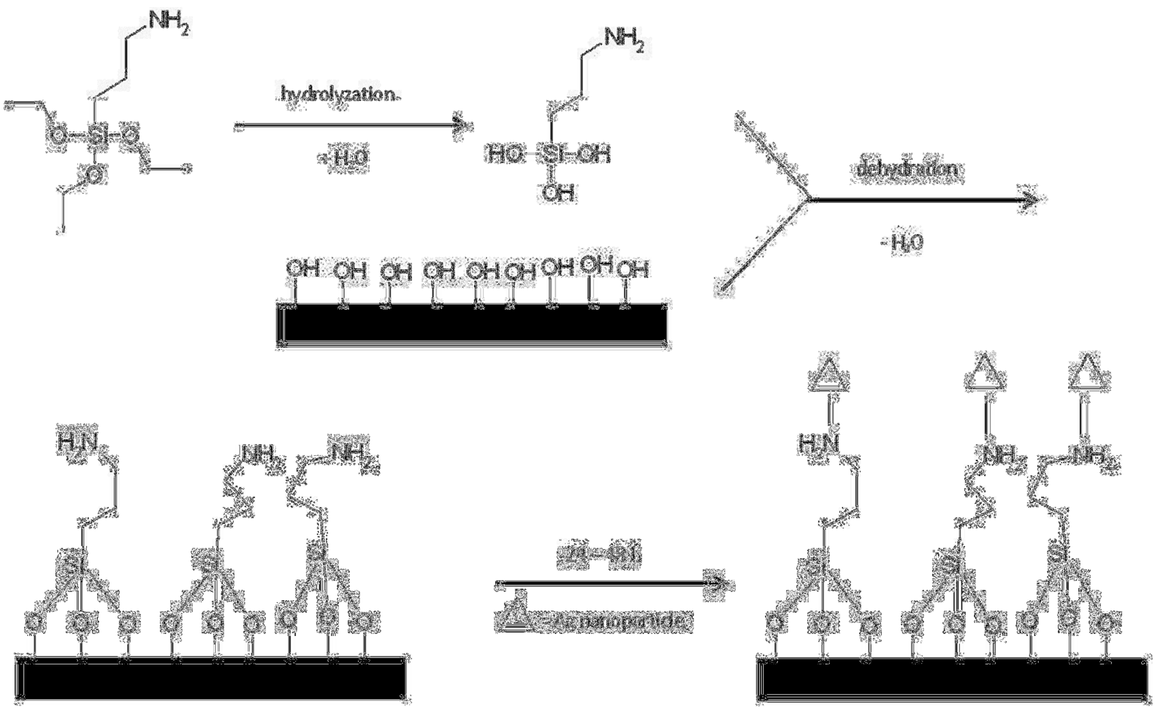


Figure 10-8: Reaction scheme of the immobilization of Ag nanoparticles at a glass surface via APTES (1)

Various experiments were conducted to assess this approach.

- Activation of the glass surface (39):
    - Treatment with 1 M HCl (30 Minutes at 25°C)
    - Rinsing with deion. water
    - Treatment with 1 M NaOH (30 Minutes at 25°C)
    - Rinsing with deion. water

- APTES Treatment
    - Filling the bottles with a 1% solution of APTES in purified EtOH (the pH of the solution was set to app. 4 with 100% acetic acid)
    - Treatment for app. 30 minutes
    - Washing with EtOH
    - Drying for 2 hours at 70°C in the oven

- TiO_2 / $Ti(i\text{-}OPr)_4$ Coating
    - One fraction of the samples was filled with a 10% solution of TiO_2-particles in EtOH from Degussa for app. 30 minutes at 25°C.
    - Another fraction of the samples was filled with a 10% solution of $Ti(i\text{-}OPr)_4$ in EtOH for app. 30 Minutes at 25°C.
    - The third fraction of the samples was treated with a 10% solution and a 1% solution of $Ti(i\text{-}OPr)_4$ in EtOH by spraying into the bottles. The spraying was done with the stage 1 spraying apparatus (see chapter 10.2.1).

- Drying
    - Drying at 80°C for 3 hours and subsequent washing with EtOH

The results of the titration of the bottles treated according to approach 2 are shown in Table 10-6 and Figure 10-9.

Table 10-6: Determination of the hydrolytic class of the glass containers (ISO 4802-1), the results are shown from approach 2

Specification Type II	Sample description	Results [mL 0.01 N HCl/100 mL test water]
Max. 0.40 mL 0.01 N HCl / 100 mL	Untreated	2.80
	Activated, APTES	2.84
	Activated, APTES, 10% $Ti(i\text{-}OPr)_4$ in EtOH, filled in bottle	0.84
	Activated, APTES,	0.88

10% Ti(i-OPr)$_4$ in EtOH, sprayed	
Activated, APTES, 1% Ti(i-OPr)$_4$ in EtOH, sprayed	1.00
Not activated, APTES, TiO$_2$ Degussa	2.56

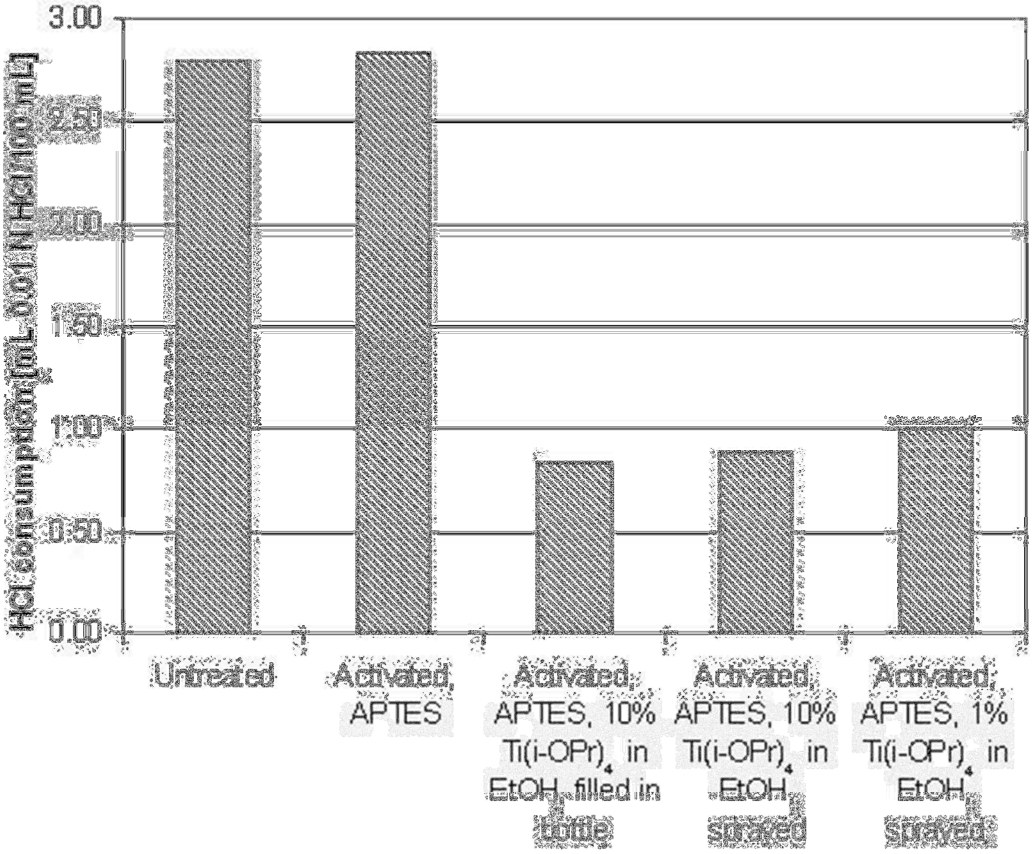


Figure 10-9: Determination of the hydrolytic class of the glass containers (ISO 4802-1), preliminary study - approach 2

10.2 Design and construction of the spraying apparatus

The only appropriate manufacturing method to fulfill the process requirements is the use of spraying methods. During the course of this work a spraying apparatus was designed and constructed to provide reproducible results.

In this thesis the different development stages of the spraying apparatus are denoted as follows:

10.2.1 Stage 1

Use of a single-action “Conrad Airbrush starter set”, consisting of a

- Spray gun; nozzle diameter 0.5 mm
- Container for the spraying material
- Tube to connect the gun to a pressurized air system

The system is shown in Figure 10-10. The feed stream of the spraying material is carried to the top by under-pressure. In the air stream it is nebulized and the spray is carried to the targeted spot. When stage 1 was used, the spray gun was operated manually. Therefore this method yielded low reproducibility. To solve these problems stage 2 of the spraying apparatus was introduced.

Figure 10-10: Stage 1 spraying apparatus / airbrush gun (55)

10.2.2 Stage 2

While operating the spraying apparatus manually the spraying times were fluctuating severely. This issue was resolved with the introduction of a relay controlled magnetic valve, which allows exact control of the spraying time. The whole apparatus was mounted on a stand as shown in Figure 10-11. A major drawback of stage 2 was the fact, that it was virtually impossible to align the spraying nozzle completely parallel to the bottle. Therefore, it was decided that a completely rigid stand would be necessary.

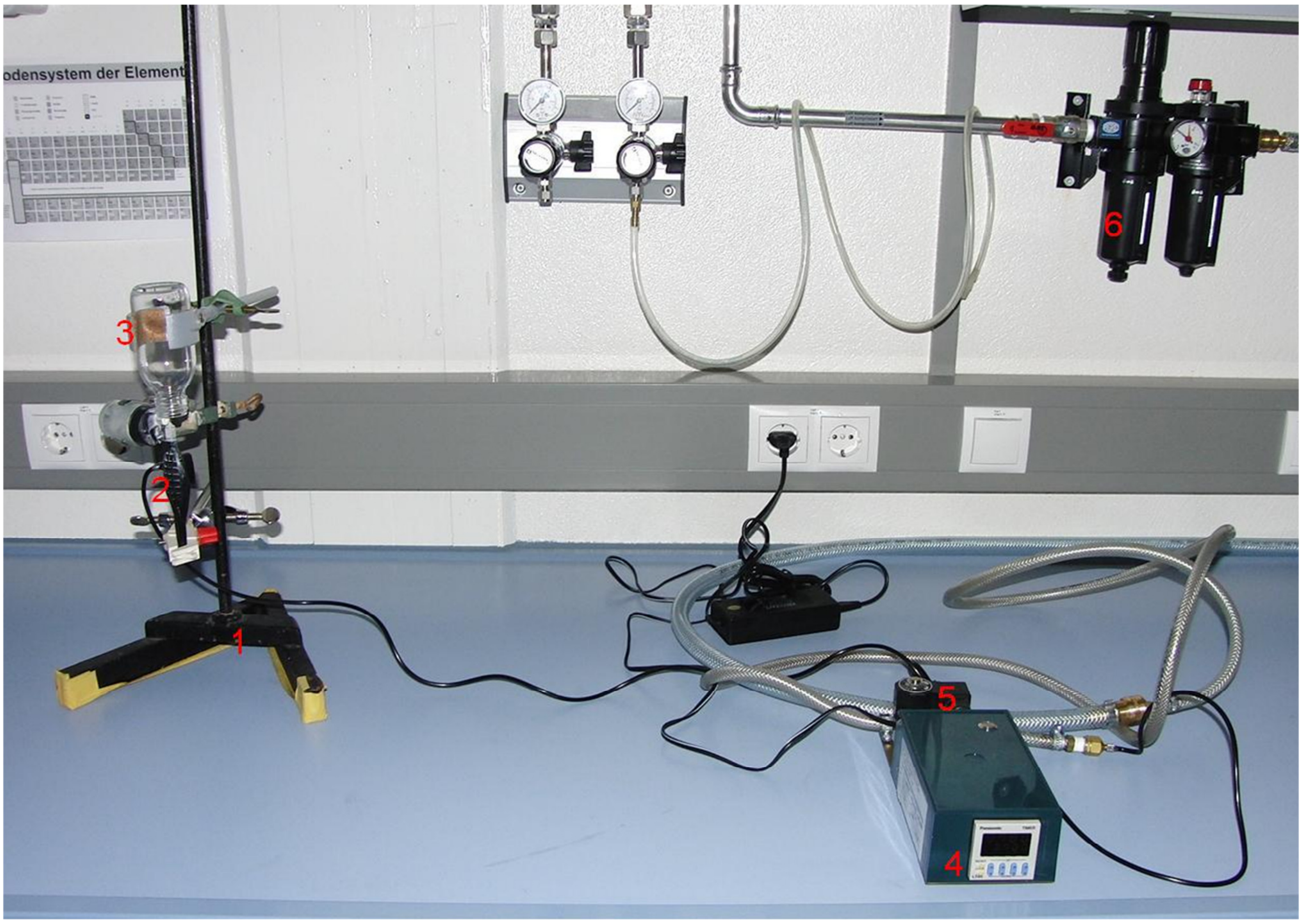


Figure 10-11: Stage 2 spraying apparatus (1…sample mounting 2…airbrush gun 3…sample 4…time relay to open the magnetic valve (5) for a well-defined time 5…magnetic valve 6…pressure regulator)

10.2.3 Stage 3

Due to not completely reproducible array of the components in the sample mounting it became necessary to develop a third stage. A framework was designed to fix the sample and the spray gun permanently without any scope. To heat the sample during the spraying process a heating sleeve was built, using a heating foil (Power: 20 W) with a jacket made of cellular rubber.

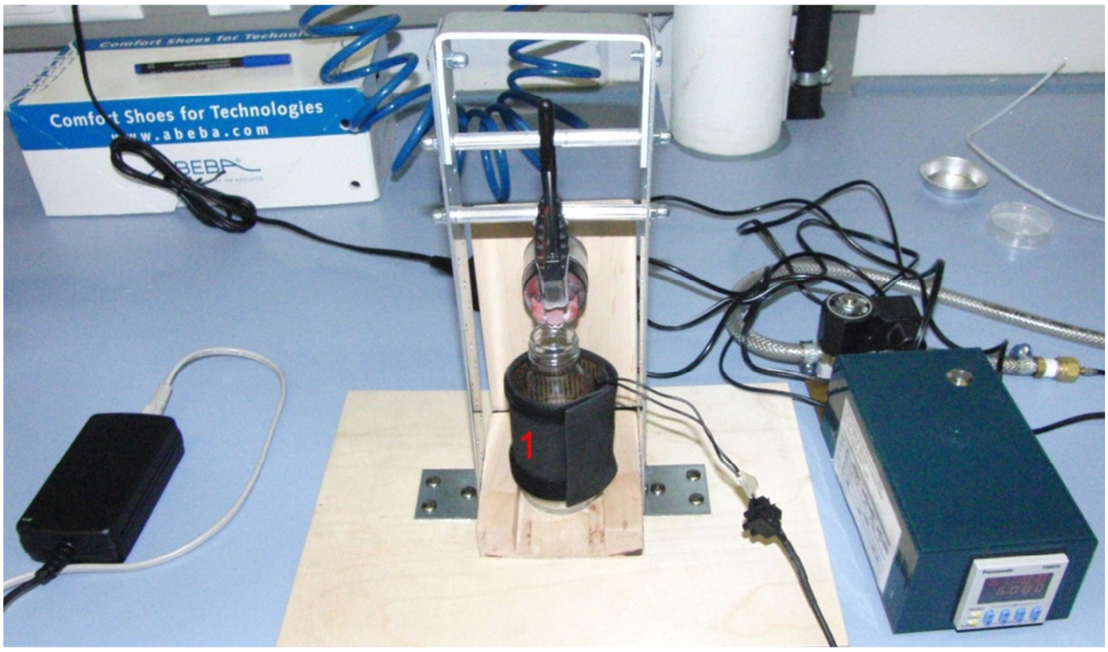


Figure 10-12: Stage 3 spraying apparatus (1… heating sleeve)

10.2.4 Characterization of the spraying apparatus

To assess the properties of the apparatus, several tests were conducted.

10.2.4.1 Application of material

These tests were done using glass bottles and a pressure of 4 bars.

The results are shown in Table 10-7 and Figure 10-13. There exists a linear relationship between spraying time and material input.

Table 10-7: Material application vs. time

Spraying time [s]	Material input [mg]
0.5	4.9
1.0	7.4
1.5	9.4
2.0	14.4
2.5	17.6

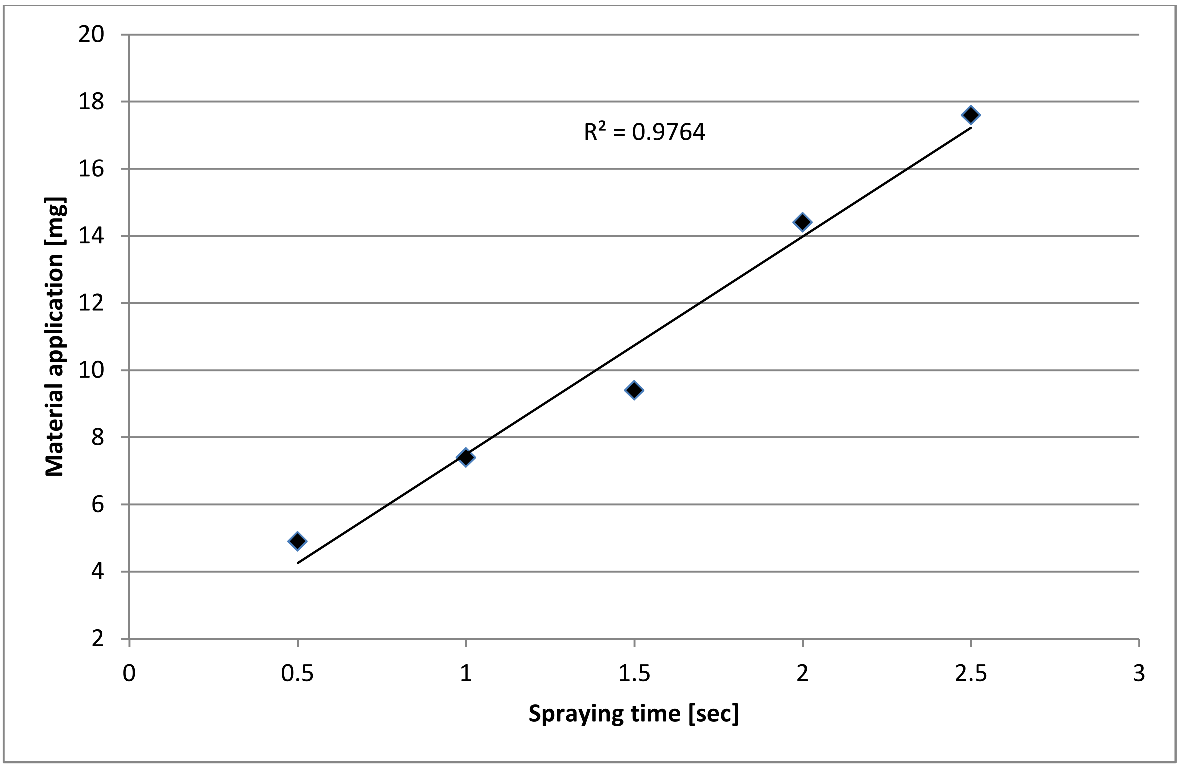


Figure 10-13: Plot of material input vs. time

10.2.4.2 Spraying properties

To assess the spraying properties of the apparatus the following procedure was developed. A solution of red acrylic varnish was dissolved in ethanol to enhance the visibility of the spatial distribution of the coating material. The test runs which were conducted are shown in Table 10-8, the results are shown in Table 10-9.

Table 10-8: Determination of the spatial spraying behavior. Each sample was coated at room temperature, apart from sample Q which was coated at 60°C.

Sample label	Working pressure (at the pressure reduction valve) [bar]	Distance to bottleneck [mm]	Number of spray burst x time [s]
A	4.55	20	5 x 0.7
B	4.55	0	5 x 0.7
C	4.90	20	5 x 0.7
D	4.90	0	5 x 0.7
E	4.00	0	7 x 0.5
F	4.00	0	5 x 0.7
G	4.65	0	4 x 0.7
H	5.00	0	3 x 0.7
I	4.00	0	8 x 0.7
J	4.15	0	7 x 0.5
K	4.15	0	7 x 0.5

L	4.15	0	5 x 0.5
M	4.15	0	3 x 0.5
N	4.15	0	3 x 0.4
O	4.00	0	6 x 0.5
P	4.00	0	7 x 0.5
Q	4.00	0	5 x 0.5

Table 10-9: Results of the determination of the spatial spraying behavior

Sample label	Results (optical appearance)
A	Bad, virtually all dye is at the bottleneck
B	Rather good, but the dye is accumulating at some points
C	Rather good, the dye is accumulating at some points, but this effect is weaker than at sample B
D	Rather bad, strong accumulation effects
E	Good
F	Thinly coated, continuous, little accumulation at the bottom of the bottle, better than sample G
G	Thinly coated, continuous, little accumulation at the bottom of the bottle
H	Thinly coated, continuous, little accumulation at the bottom of the bottle
I	Good, but accumulation, formation of a ring at the bottom of the bottle
J	Good, but accumulation, formation of a ring at the bottom of the bottle
K	Rather thinly coated, formation of a ring at the bottom of the bottle
L	Rather thinly coated, formation of a ring at the bottom of the bottle
M	Rather thinly coated, formation of a ring at the bottom of the bottle, better than sample K
N	Thinly coated, continuous, formation of a ring at the bottom of the bottle
O	Virtually no coating, only formation of a ring at the bottom of the bottle
P	Thinly coated, even gaps in the coating
Q	Thickly coated on one side of the bottle, formation of a big ring at the bottom of the bottle

Due to these results we know that the following settings give a continuous barrier film.

- Working pressure (at the pressure reduction valve) = 4.0 bar
- Distance to bottleneck = 0 mm

Two examples for a badly and a well coated bottle are shown below in Figure 10-14 and Figure 10-15.

Figure 10-14: Sample E - good coating

Figure 10-15: Sample N - bad coating

Summarizing, we can say that the stage 3 spraying apparatus gives satisfying results regarding spraying properties and reproducibility. Nevertheless, it was observed that the spraying nozzle is not directly above the bottleneck and this gives slight irregularities. To compensate these irregularities the bottles were turned after each spray burst.

10.3 Production of samples

With respect to the preliminary studies, several parameters were identified as crucial. These critical factors are presented in Table 10-10:

Table 10-10: Critical process parameters and influenced factor

Critical factor	Potential impact
Washing procedure	Removal of unbound reaction products / side products / reagents
Activation	Creation of as many silanol groups at the surface (act as binding sites) as possible
APTES loading	Coupling agent between glass surface (OH-groups) and TiO_2 particles
TiO_2 loading	Transparency of the samples; Resistance

	against leaching
Annealing (temperature and time)	Homogeneity of the coating; Quality of the layers

Referring to the critical parameters which have been defined (Table 10-10) the samples were used to examine how those parameters influence the hydrolytic resistance.

10.3.1 Activation

It was assessed if the activation procedure is necessary and which procedure is most eligible for the desired purpose.

The first experiments were done with respect to the best results from the preliminary study. Samples 1 to 24 were manufactured to check if the activation is imperative. The procedure is shown in Figure 10-16 and Table 10-11.

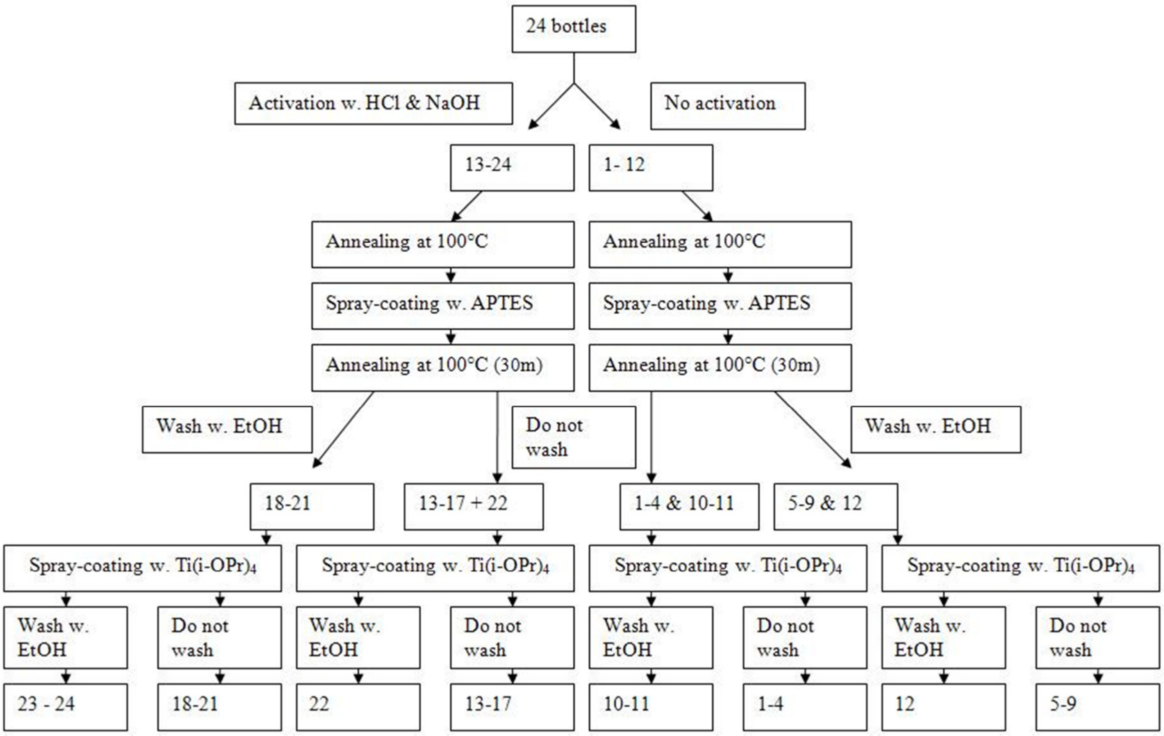


Figure 10-16: Manufacturing of samples 1-24; each sample was activated for 1 minute, except samples 17 and 24 which were activated for 30 minutes

Table 10-11 Production of 1-24 (activation; washing steps)

Process step
Put 12 bottles in the oven (100°C)
Preparation of the solutions; 40 ml 1% w/w APTES in EtOH; 40 ml 10% w/w $Ti(i\text{-}OPr)_4$ in EtOH

Activation of 12 bottles with HCl (2M); 10 bottles for 1 minute, 2 bottles for 30 minutes; subsequently rinsing with H_2O
Activation of 12 bottles with NaOH (2M); 10 bottles for 1 minute, 2 bottles for 30 minutes; subsequently rinsing with H_2O
Drying every activated bottle in the oven (100°C)
Spray-coating of all the non-activated bottles with APTES solution (3-5 seconds each) (p = ~ 5 bars)
Drying all the non-activated bottles in the oven (100°C)
Spray-coating of all the activated bottles with APTES solution (3-5 seconds each) (Observation: Some of the bottles are still wet from the rinsing with H_2O) (p = ~ 5 bars)
The pH of the APTES solution was set to 4 with acetic acid (100%).
Once again spray-coating of all the non-activated bottles with APTES solution (3-5 seconds each) (p = ~ 5 bars)
Once again spray-coating of all the activated bottles with APTES solution (3-5 seconds each) (Observation: Some of the bottles are still wet from the rinsing with H_2O) (p = ~ 5 bars)
Washing of 6 non-activated bottles with EtOH; back in the oven 5 minutes later
Washing of 6 activated bottles with EtOH; back in the oven 5 minutes later
Spray-coating of all the non-activated bottles with $Ti(i\text{-}OPr)_4$ solution (3-5 seconds each); back in the oven 5 minutes later (p = ~ 5 bars)
Spray-coating of all the activated bottles with $Ti(i\text{-}OPr)_4$ solution (3-5 seconds each); back in the oven 5 minutes later (p = ~ 5 bars)
Washing of 3 non-activated bottles with EtOH; back in the oven 5 minutes later
Washing of 3 activated bottles with EtOH; back in the oven 5 minutes later
All the samples were dried in the oven (100°C) over night.

The results of the titration of these samples are shown in Table 10-12.

Table 10-12: Results of the determination of the hydrolytic class; samples 1-79 (solvent for the APTES-solution 53-58; washing steps 1-24; activation 49-79; $Ti(iOPr_4)$-conc. 53-79; APTES-conc. 53-79)

Specification Type II	#	Results [ml 0.01 N HCl/100 ml]	#	Results [ml 0.01 N HCl/100 ml]
Max. 0.40 ml 0.01 N HCl / 100 ml	1	0.44	52	0.70
	2	0.46	53	1.28

	4	0.44	54	0.88
	5	0.50	55	1.12
	6	0.46	56	0.88
	7	0.50	57	0.88
	9	0.40	58	0.92
	10	0.42	59	0.80
	11	1.00	61	0.86
	12	1.08	62	0.80
	13	0.48	63	1.00
	14	0.40	64	0.88
	15	0.38	65	0.94
	16	0.36	66	0.90
	17	0.38	67	0.84
	18	0.40	69	0.92
	19	0.50	70	1.00
	20	0.40	72	0.66
	21	0.42	73	0.80
	22	0.40	74	0.70
	23	0.52	75	0.84
	24	0.88	76	0.70
	49	0.70	77	0.78
	50	0.96	78	0.80
	51	0.68	79	0.78

Remark: Sample 80 was made using the same parameter as for samples 49 – 52 with the following exceptions: The bottle was preheated to 160°C before activation. A ten minutes annealing step at 160 °C was introduced after the last activation step. Sample 80 was used for determination of the leaching behavior; this means the hydrolytic class was not determined.

The samples 3, 8, 60, 68, 71 and 80 were used to investigate the APTES and TiO_2 leaching.

According to the results presented in Table 10-12 the activation has great influence on the hydrolytic class, it improves the results tremendously (bottles 13-24). One of the non-activated samples (number 9) has hydrolytic class 2, this proofs that the activation is not absolutely necessary. But due to the much better results of the activated samples it was decided to keep the activation procedure.

In the next production cycle various changes in the activation procedure were made, each one with little success. The following attempts were tested:

- Usage of 1 M reagents (acid and base), left in the bottle for 30 minutes each
    - samples 49-52 - Table 10-15
    - samples 56-58 - Table 10-20
    - samples 65-67 - Table 10-37
    - samples 71-73 - Table 10-22
    - samples 74 – 76 - Table 10-23
- Usage of 1 M reagents, left in the bottle for 15 minutes at 70°C after each step
    - samples 59-61 - Table 10-16
    - samples 62-64 - Table 10-21
    - samples 68-70 - Table 10-38
    - samples 77-79 - Table 10-39
- Spraying acid/base (2M) into the bottle, left there for 15 minutes
    - samples 53-55 - Table 10-19

A summary of all the related results from production cycle 1 (samples 1- 80) can be seen in Table 10-12. As stated above, the methods did not show the desired results, therefore the better method from samples 1 – 24 will be used for future samples, this means using 2 M acid/base for app. 1 min with shaking. Later more experiments were conducted to verify the conclusions from samples 1 to 24. The samples 147 – 164 (the manufacturing is shown in Figure 10-17 and Table 10-13) compared activated to the results of non-activated samples. Generally, the activated samples had less HCl consumption in the tests, therefore the activation procedure will be kept for future glass bottles. The results of the titration are shown in Table 10-14.

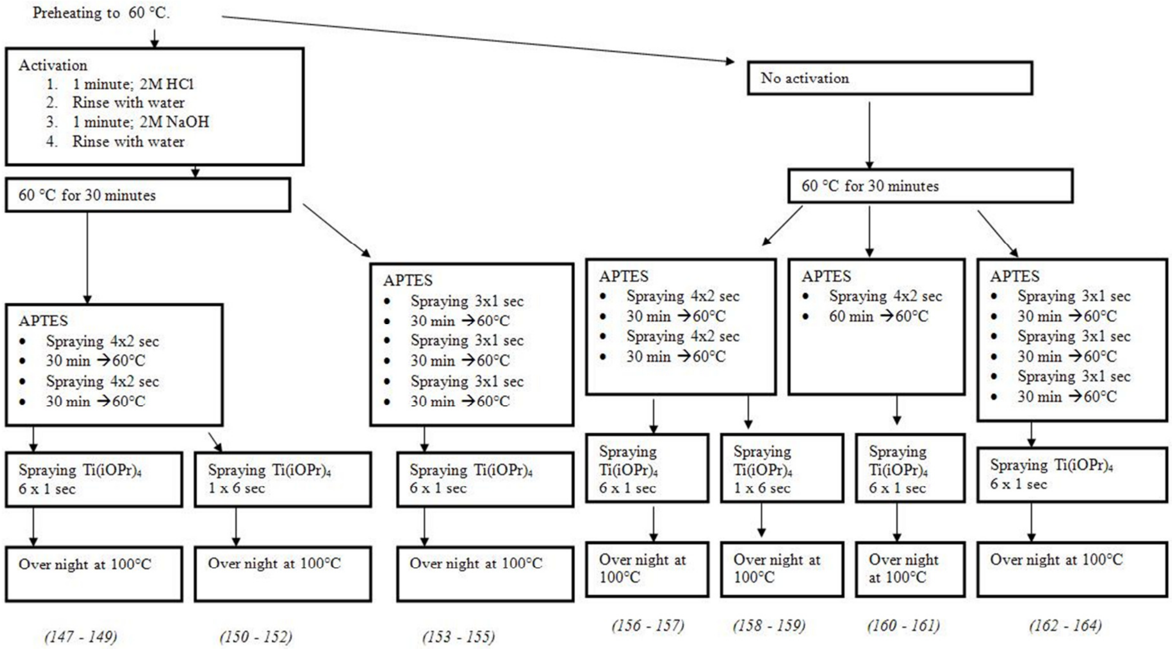


Figure 10-17: Production of samples 149-164

Table 10-13 Production of samples 147-164 (activation; APTES spraying time; number of Ti(iOPr)$_4$ spraying bursts)

Process step
The bottles were preheated to a temperature of 60°C.
Preparation of the solutions; 1% w/w APTES in EtOH; 10% w/w Ti(i-OPr)$_4$ in EtOH; the pH of the APTES solution was not adjusted
Activation of samples 147 - 155: • Filling the bottles with HCl (2M) for 1 min • The bottles were thoroughly rinsed with water • Filling the bottles with NaOH (2M) for 1 min • The bottles were thoroughly rinsed with water
The samples 156 - 164 were not activated.
Annealing of samples 147 – 155 in the oven for 60 min at 60°C
Spray-coating of samples 158 and 159 with APTES for 4 x 2 s (The bottle was rotated 90° after each spray burst), subsequently dried in the oven for 30 min at 60°C (p = ~ 5 bars)
Samples 156 – 157 and 160 - 161: • Spray-coating with APTES for 4 x 2 s (The bottle was rotated 90° after each spray burst) (p = ~ 5 bars) • Drying in the oven for 30 min at 60°C • Spray-coating with APTES for 4 x 2 s (The bottle was rotated 90° after each spray burst) (p = ~ 5 bars) • Drying in the oven for 30 min at 60°C
Samples 162 - 164: • Spray-coating with APTES for 3 x 1 s (The bottle was rotated 120° after each spray

burst) (p = ~ 5 bars)

- Drying in the oven for 30 min at 60°C
- These two steps were repeated twice.

Samples 147 – 152:

- Spray-coating with APTES for 4 x 2 s (The bottle was rotated 90° after each spray burst) (p = ~ 5 bars)
- Drying in the oven for 30 min at 60°C
- Spray-coating with APTES for 4 x 2 s (The bottle was rotated 90° after each spray burst) (p = ~ 5 bars)
- Drying in the oven for 30 min at 60°C

Samples 153 - 155:

- Spray-coating with APTES for 3 x 1 s (The bottle was rotated 120° after each spray burst) (p = ~ 5 bars)
- Drying in the oven for 30 min at 60°C
- These two steps were repeated twice.

Spray-coating of samples 158 and 159 with $Ti(i\text{-}OPr)_4$ for 6 x 1 s; (The bottle was rotated 120° after each spray burst) (p = ~ 5 bars)

Spray-coating of samples 156 and 157 with $Ti(i\text{-}OPr)_4$ for 6 x 1 s; (The bottle was rotated 120° after each spray burst) (p = ~ 5 bars)

Spray-coating of samples 160 and 161 with $Ti(i\text{-}OPr)_4$ for 6 s (p = ~ 5 bars)

Spray-coating of samples 147 - 149 with $Ti(i\text{-}OPr)_4$ for 6 x 1 s; (The bottle was rotated 120° after each spray burst) (p = ~ 5 bars)

Spray-coating of samples 150 - 152 with $Ti(i\text{-}OPr)_4$ for 6 s (p = ~ 5 bars)

Spray-coating of samples 162 - 164 with $Ti(i\text{-}OPr)_4$ for 6 x 1 s; (The bottle was rotated 120° after each spray burst) (p = ~ 5 bars)

Spray-coating of samples 153 - 155 with $Ti(i\text{-}OPr)_4$ for 6 x 1 s; (The bottle was rotated 120° after each spray burst) (p = ~ 5 bars)

After the final spray-coating step and/or washing step every sample was dried in the oven (100°C) over night.

Table 10-14: Results of the determination of the hydrolytic class; samples 147-164 (activation; APTES spraying time; number of Ti(iOPr)$_4$ spraying bursts)

Specification Type II	#	Results [ml 0.01 N HCl/100 ml]	#	Results [ml 0.01 N HCl/100 ml]
Max. 0.40 ml 0.01 N HCl / 100 ml	147	2.46	156	1.02
	148	2.42	157	1.12
	149	2.86	158	0.98
	150	2.38	159	0.94
	151	0.84	160	1.52
	152	0.88	161	2.08
	153	0.76	162	0.86
	154	0.76	163	0.90
	155	0.90	164	1.04

Table 10-15: Production of samples 49-52 (activation)

Process step
Preparation of the solutions; 40 ml 1% w/w APTES in EtOH; 40 mL 10% w/w Ti(i-OPr)$_4$ in EtOH; the pH of the APTES solution was set to app. 4 with acetic acid (100%).
Activation of the bottles with HCl (1M) for 30 minutes; subsequently rinsed with H_2O
Activation of the bottles with NaOH (1M) for 30 minutes; subsequently rinsed with H_2O
Spray-coating with APTES solution (3-5 seconds each) (p = ~ 5 bars)
Drying of the non-activated bottles in the oven (75°C) for 1.75 h
Washing of the samples with EtOH
Spray-coating of the bottles with Ti(i-OPr)$_4$ solution (3-5 seconds each); back in the oven 5 minutes later (p = ~ 5 bars)
Drying of the bottles in the oven (80°C) for 3 h

Table 10-16: Production of samples 59-61 (activation; Ti(iOPr$_4$)-conc.; APTES-conc.)

Process step
The bottles were preheated to a temperature of 160°C.
Preparation of the solutions; 2% v/v APTES in EtOH; 10% v/v Ti(i-OPr)$_4$ in EtOH; the pH

of the APTES solution was set to app. 4 with acetic acid (100%).
Activation of samples: the bottles were filled with HCl (1M) for 15 min; these bottles were left at 70°C for 15 min
The samples were thoroughly rinsed with water
Activation of samples: the bottles were filled with NaOH (1M) for 15 min; these bottles were incubated for 15 min at 70°C
The samples were thoroughly rinsed with water
Annealing of the samples for 15 min at 120 °C
Spray-coating of the samples with APTES solution for app. 5 s (p = ~ 5 bars)
Silanization (this means annealing in the oven) for 35 min at 120°C
The samples were rinsed with EtOH
Annealing in the oven for 15 min at 120°C
Spray-coating of the samples with $Ti(i\text{-}OPr)_4$ 10% v/v solution for app. 5 s (p = ~ 5 bars)
Drying of the bottles in the oven (80°C) for 6h20m

10.3.2 Washing

In the first production cycle the benefit of the washing steps was also examined. The basic idea of the washing steps is to remove unbound reaction products from the glass surface. The manufacturing process is shown in Table 10-11 and Figure 10-16, the according results in Table 10-12 (bottles 1 - 24).

The results showed no measurable influence on the hydrolytic resistance. The results have a certain statistical dispersion, but there was no improvement of the hydrolytic class. But it might be necessary to introduce washing steps with respect to the leaching of film components into the pharmaceutical solution (this means washing to avoid contamination of the pharmaceutical solution by the coating). For now the decision was made to discard the washing steps to get a manufacturing process as simple as possible.

A second experiment was done to check the results of the first experiment. In the first part of the third production cycle (samples 97 – 112) washed and unwashed samples were compared. The washing was done after the last APTES spraying step. The manufacturing is presented in Figure 10-18 and Table 10-17, the results in Table 10-18. These results confirm that washing has no beneficial influence on the hydrolytic resistance (bottles 97-

104 compared to bottles 105-112). The abandonment of washing steps will be kept. Blowing out the bottles with pressurized air (bottle 97 and 109) instead of washing them with EtOH (bottle 99 and 111) after the final annealing step does not improve the results and will not be taken into consideration.

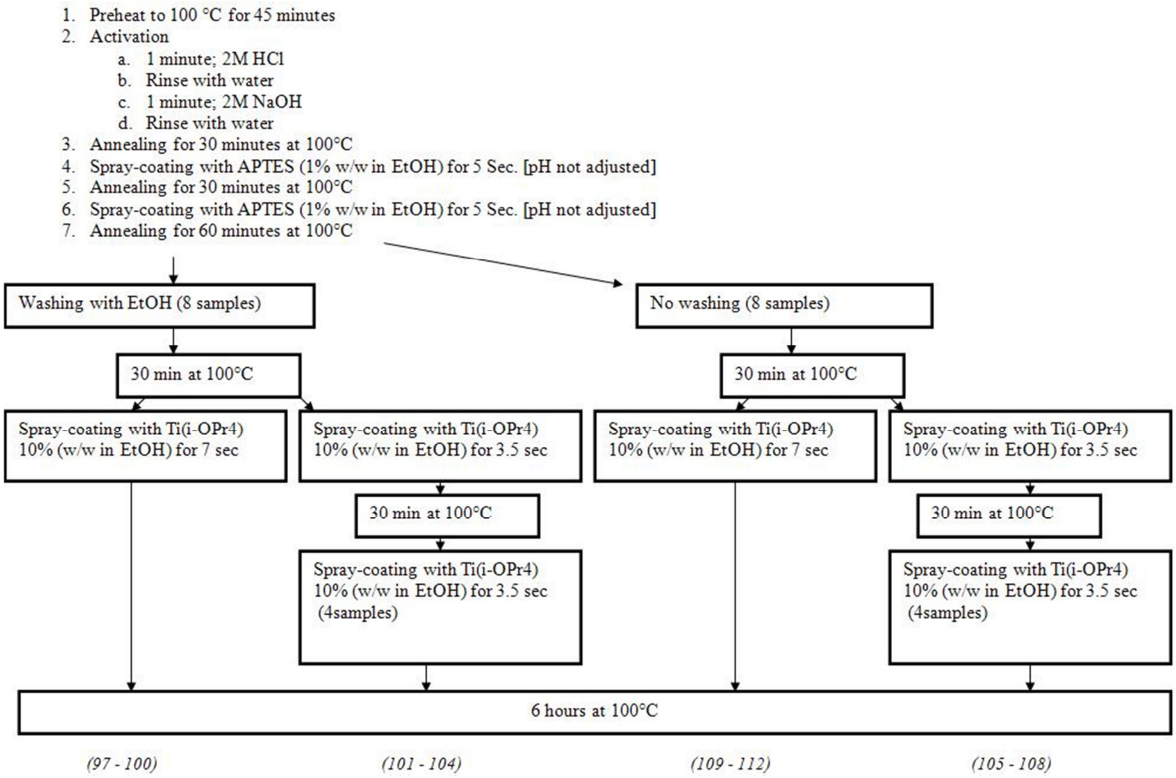


Figure 10-18: Production of samples 97-112

Table 10-17: Production of samples 97-112 (number of APTES spraying cycles 101-108; washing 97-104)

Process step
The bottles were preheated to a temperature of 100°C.
Preparation of the solutions; 1% w/w APTES in EtOH; 10% w/w Ti(i-OPr)$_4$ in EtOH; the pH of the APTES solution was not adjusted
Activation of samples: • Filling the bottles with HCl (2M) for 1 min • The bottles were thoroughly rinsed with water • Filling the bottles with NaOH (2M) for 1 min • The bottles were thoroughly rinsed with water
Annealing in the oven for 30 min at 100°C
Spray-coating of samples 97 – 112 with APTES for 5 s (p = ~ 4 bars)
Annealing in the oven for 30 min at 100°C
Spray-coating of samples 97 – 112 with APTES for 5 s (p = ~ 4 bars)

Annealing in the oven for 60 min at 100°C
Samples 97 – 104: Rinsed with Ethanol
Samples 97 – 104: Drying in the oven for 30 min at 100°C
Spray-coating of samples 105 - 112 with $Ti(i\text{-}OPr)_4$ for - 7 s (samples 109-112) - 3.5 s (samples 105-108)
Drying of the samples 105-108 in the oven (100°C) for 30 min
Spray-coating of samples 97 - 104 with $Ti(i\text{-}OPr)_4$ for - 7 s (samples 97-100) (p = ~ 4 bars) - 3.5 s (samples 101-104) (p = ~ 4 bars)
Drying of the samples 101-104 in the oven (100°C) for 30 min
Spray-coating of samples 105 - 108 with $Ti(i\text{-}OPr)_4$ for 3.5 s (p = ~ 4 bars)
Spray-coating of samples 101 - 104 with $Ti(i\text{-}OPr)_4$ for 3.5 s (p = ~ 4 bars)
Preparation of new solutions; 1% w/w APTES in EtOH; 10% w/w $Ti(i\text{-}OPr)_4$ in EtOH; the pH of the APTES solution was not adjusted
Spray-coating of samples 109 - 112 with $Ti(i\text{-}OPr)_4$ for 7 s (p = ~ 4 bars)
Spray-coating of samples 97 - 100 with $Ti(i\text{-}OPr)_4$ for 7 s (p = ~ 4 bars)
Sample 109 was blown out with pressurized air, sample 111 was washed with Ethanol
Samples 105 – 108 were taken out of the oven
Samples 101 – 104 were taken out of the oven
Sample 97 was blown out with pressurized air, sample 99 was washed with Ethanol
The samples 97-100 and 109-112 remain in the oven over night.

Table 10-18: Results of the determination of the hydrolytic class samples; samples 97 - 112(number of APTES spraying cycles 101-108; washing 97-104)

Specification Type II	#	Results [ml 0.01 N HCl/100 ml]	#	Results [ml 0.01 N HCl/100 ml]
Max. 0.40 ml 0.01 N HCl / 100 ml	97	0.54	105	0.64
	98	0.56	106	0.54
	99	0.62	107	0.64
	100	0.54	109	1.20
	101	0.66	110	2.58

	103	0.66	111	0.64
	104	0.68	112	0.58

Remark: The samples 102 and 108 were used to investigate the APTES and TiO_2 leaching.

10.3.3 Influence of APTES

In order to get a good and a preferably continuous coating it was tried to optimize the parameters that influence the APTES coating, this means

- solvent for the APTES solution
- concentration of the APTES solution
- pH adjustment of the APTES solution
- APTES solution spraying time
- APTES solution spraying pressure

10.3.3.1 Influence of the solvent

First the solvent was examined. The preliminary study showed good results with EtOH, but in literature organic solvents are widely used. Therefore, it was tried to use cyclohexane as solvent. The manufacturing of the corresponding samples (53 - 58) is shown in Table 10-19 and Table 10-20, the results are presented in Table 10-12 (samples 53-58). It can be noticed that the use of an organic solvent does not increase the hydrolytic resistance of the glass bottles. Apart from that the use of an organic solvent has many disadvantages, cyclohexane for example is dangerous for the environment (N) and harmful (Xn).

Table 10-19: Production of samples 53-55 (activation; $Ti(iOPr_4)$-conc.; solvent for APTES solution; APTES-conc.)

Process step
Preparation of the solutions; 2% v/v APTES in cyclohexane; 40 ml 10% v/v $Ti(i\text{-}OPr)_4$ in EtOH
Activation of the bottles with spraying of HCl (2M) for app. 5 sec; then left at RT for 15 min (p = ~ 5 bars)
The samples were thoroughly rinsed with water
Activation of the bottles with spraying of NaOH (2M) for app. 5 sec; then left at RT for 15 min (p = ~ 5 bars)

The samples were thoroughly rinsed with water
Annealing of samples 53 - 55 for 15 min at 120 °C
Spray-coating of samples 53 - 55 with APTES solution for app. 15 sec (p = ~ 5 bars)
Silanization (this means annealing in the oven) for 30 min at 120°C
The samples were rinsed with cyclohexane and water
Annealing in the oven for 10 min at 120°C
Spray-coating of the samples with $Ti(i\text{-}OPr)_4$ solution for app. 5 sec (p = ~ 5 bars)
Drying of the bottles in the oven (80°C) for 3 h

Table 10-20: Production of samples 56-58 (activation; $Ti(iOPr_4)$-conc.; solvent for APTES solution; APTES-conc.)

Process step
Preparation of the solutions; 2% v/v APTES in cyclohexane; 40 ml 10% v/v $Ti(i\text{-}OPr)_4$ in EtOH
Activation of the samples; the bottles were filled with HCl (1M) for 30 min
The samples were thoroughly rinsed with water
Activation of the samples; the bottles were filled with NaOH (1M) for 30 min
The samples were thoroughly rinsed with water
Annealing of the samples for 15 min at 120 °C
Spray-coating of the samples with APTES solution for app. 5 sec (p = ~ 5 bars)
Silanization (this means annealing in the oven) for 30 min at 120°C
The samples were rinsed with cyclohexane and water
Annealing in the oven for 10 min at 120°C
Spray-coating of the samples with $Ti(i\text{-}OPr)_4$ solution for app. 5 sec (p = ~ 5 bars)
Drying of the bottles in the oven (80°C) for 3 h

The hydrolytic resistance of the bottles treated with APTES in cyclohexane (bottle 53-58) is worse than the resistance of bottles treated with APTES in ethanol. In future experiments EtOH will be used as solvent.

10.3.3.2 Influence of APTES-concentration

Different APTES concentrations were tested (samples 62 – 64 and 71 – 76) to find the ideal concentration of the APTES spraying solution. To enhance our knowledge in this field, different solutions were prepared, namely 1% v/v, 2% v/v and 1% w/w (from the preliminary study). In the preliminary study the influence of the APTES concentration was not tested. The manufacturing of these samples is shown in Table 10-21, Table 10-22 and Table 10-23; the corresponding results are shown in Table 10-12 (samples 62-64 and 72-76. It does not seem that a higher APTES concentration improves the results. Due to these facts the APTES concentration was left at the concentration 1% w/w (as for the samples 1 to 24, which had a satisfying hydrolytic resistance.

Table 10-21: Production of samples 62-64 (activation; Ti(iOPr$_4$)-conc.; APTES concentration)

Process step
The bottles were preheated to a temperature of 160°C.
Preparation of the solutions; 2% v/v APTES in EtOH; 5% v/v Ti(i-OPr)$_4$ in EtOH; the pH of the APTES solution was set to app. 4 with acetic acid (100%).
Activation of samples: the bottles were filled with HCl (1M) for 15 min; these bottles were incubated for 15 min at 70°C
The samples were thoroughly rinsed with water
Activation of samples: the bottles were filled with NaOH (1M) for 15 min; these bottles were incubated for 15 min at 70°C
The samples were thoroughly rinsed with water
Annealing of the samples for app. 15 min at 120 °C
Spray-coating of the samples with APTES solution for app. 5 s (p = ~ 5 bars)
Silanization (this means annealing in the oven) for 35 min at 120°C
The samples were rinsed with EtOH
Annealing in the oven for 15 min at 120°C
Spray-coating of the samples with Ti(i-OPr)$_4$ 5% v/v solution for app. 5 s (p = ~ 5 bars)
Drying of the bottles in the oven (80°C) for 6h20m

Table 10-22: Production of samples 71-73 (activation; Ti(iOPr$_4$)-conc.; APTES-conc.)

Process step
The bottles were preheated to a temperature of 160°C.
Preparation of the solutions; 2% v/v APTES in EtOH; 5% v/v Ti(i-OPr)$_4$ in EtOH; the pH

of the APTES solution was set to app. 4.2 with acetic acid (100%).
Activation of samples: the bottles were filled with HCl (1M) for 30 min
The samples were thoroughly rinsed with water
Activation of samples: the bottles were filled with NaOH (1M) for 30 min
The samples were thoroughly rinsed with water
Annealing of the samples for 15 min at 120 °C
Spray-coating of the samples with APTES solution for 3.5 s (p = ~ 5 bars)
Silanization (this means annealing in the oven) for 30 min at 120°C
The samples were rinsed with EtOH
Annealing in the oven for 15 min at 120°C
Spray-coating of the samples with Ti(i-OPr)$_4$ 5% v/v solution for 3.5 s, but sample 71 got spray-coated for 4.9 s (p = ~ 5 bars)
Drying of the bottles in the oven (80°C) for 3h

Table 10-23: Production of samples 74-76 (activation; Ti(iOPr$_4$)-conc.; APTES-conc.)

Process step
The bottles were preheated to a temperature of 160°C.
Preparation of the solutions; 2% v/v APTES in EtOH; 10% v/v Ti(i-OPr)$_4$ in EtOH; the pH of the APTES solution was set to app. 4 with acetic acid (100%).
Activation of samples: the bottles were filled with HCl (1M) for 30 min
The samples were thoroughly rinsed with water
Activation of samples: the bottles were filled with NaOH (1M) for 30 min
The samples were thoroughly rinsed with water
Annealing of the samples for 15 min at 120 °C
Spray-coating of the samples with APTES solution for 3.5 s (p = ~ 5 bars)
Silanization (this means annealing in the oven) for 30 min at 120°C
The samples were rinsed with EtOH
Annealing in the oven for 10 min at 120°C
Spray-coating of the samples with Ti(i-OPr)$_4$ 10% v/v solution for 3 5 s; sample 75 was coated for 4 s (p = ~ 5 bars)

Drying of the bottles in the oven (80°C) for 3h

10.3.3.3 Influence of the pH-value

pH-Adjustment of the APTES solution with 100% acetic acid is described in literature. During the manufacturing process of the samples 1 – 24 it was forgotten to adjust the pH value of the APTES solution, therefore a second APTES spraying step with adjusted pH-value was applied. To evaluate the necessity of the pH-value alteration a series of bottles (81-96) was prepared and tested. The manufacturing is shown in Figure 10-19 and Table 10-24. As we can see in the results (Table 10-25) discarding the pH value has no negative influence on the hydrolytic resistance, this means in future production cycles the pH-adjustment will be skipped. Comparing the samples 174-176 with sample 177 we can see once again that pH adjustment shows no advantages.

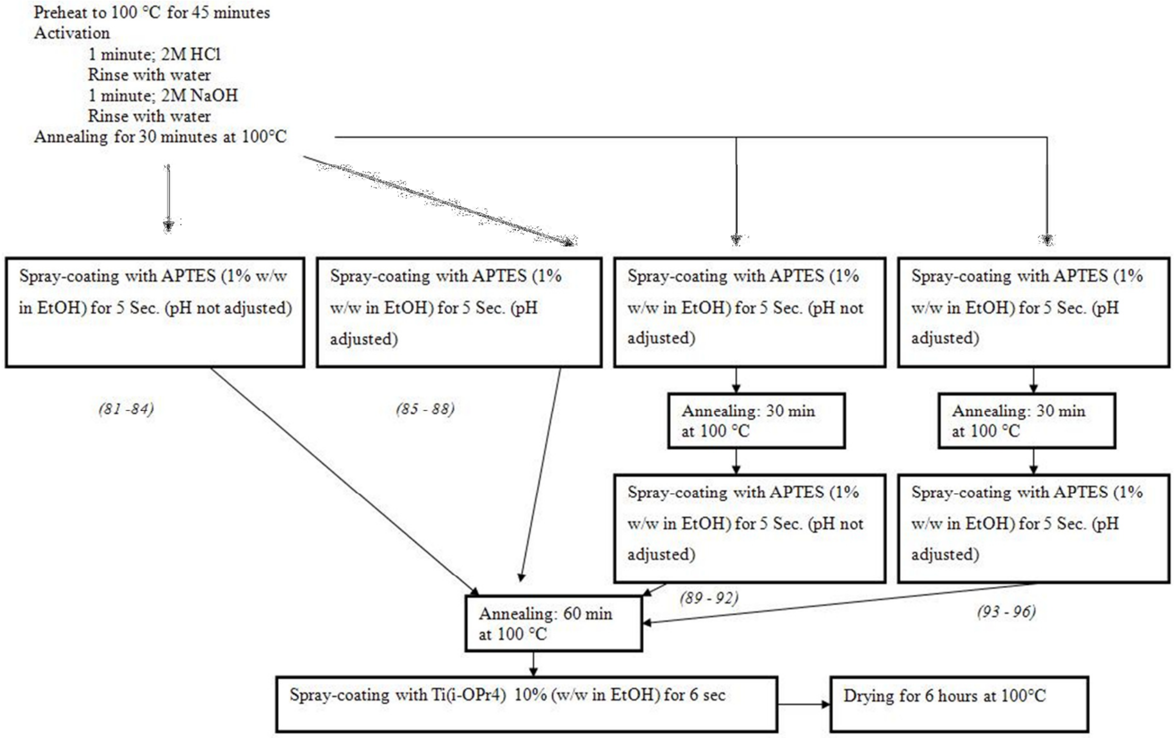


Figure 10-19: Production of samples 81-96

Table 10-24: Production of samples 81-96 (APTES spraying time/cycles 89-96; pH-adjustment 85-88, 93-96)

Process step
The bottles were preheated to a temperature of 100°C.
Preparation of the solutions; 1% w/w APTES in EtOH; 10% w/w Ti(i-OPr)$_4$ in EtOH; the pH of one half of the APTES solution was set to app. 4 with acetic acid (100%); the pH value other half was not adjusted

Activation of samples:

- Filling the bottles with HCl (2M) for 1 min
- The bottles were thoroughly rinsed with water
- Filling the bottles with NaOH (2M) for 1 min
- The bottles were thoroughly rinsed with water

Annealing in the oven for 30 min at 100°C

Spray-coating of samples 81 – 84 with APTES for 5 s (pH not adjusted) (p = ~ 4 bars)

Spray-coating of samples 85 – 88 with APTES for 5 s (pH adjusted) (p = ~ 4 bars)

Spray-coating of samples 89 – 92 with APTES for 5 s (pH not adjusted) (p = ~ 4 bars)

Spray-coating of samples 93 – 96 with APTES for 5 s (pH adjusted) (p = ~ 4 bars)

Samples 89 – 96: Annealing in the oven for 30 min at 100°C

Spray-coating of samples 89 – 92 with APTES for 5 s (pH not adjusted) (p = ~ 4 bars)

Spray-coating of samples 93 – 96 with APTES for 5 s (pH adjusted) (p = ~ 4 bars)

Every sample was silanized in the oven at 100°C for 60 minutes after the final APTES spraying step

Spray-coating of samples 81 - 84 with $Ti(i\text{-}OPr)_4$ for 5 s (p = ~ 4 bars)

Spray-coating of samples 85 - 88 with $Ti(i\text{-}OPr)_4$ for 5 s (p = ~ 4 bars)

Spray-coating of samples 89 - 92 with $Ti(i\text{-}OPr)_4$ for 5 s (p = ~ 4 bars)

Spray-coating of samples 93 - 96 with $Ti(i\text{-}OPr)_4$ for 5 s (p = ~ 4 bars)

Drying of the bottles in the oven (100°C) for app. 6h

Table 10-25: Results of the determination of the hydrolytic class; samples 81-96 (APTES spraying time/cycles 89-96; pH-adjustment 86-88, 93-96)

Specification Type II	#	Results [ml 0.01 N HCl/100 ml]	#	Results [ml 0.01 N HCl/100 ml]
Max. 0.40 mL 0.01 N HCl / 100 mL	81	0.62	90	0.46
	83	0.56	91	0.52
	84	0.58	93	0.54
	86	0.86	95	0.62
	88	0.66	96	0.60
	89	0.52	-	-

Remark: The samples 82, 87, 92 and 94 were used to investigate the APTES and TiO_2 leaching. Sample 85 was not manufactured properly and therefore removed.

10.3.3.4 Influence of the number of spraying cycles, spraying pressure and spraying time

During the manufacturing of the samples 1 – 24 APTES was sprayed twice. Therefore, it was tested if spraying for x seconds or spraying two times x*0.5 sec yields better results. The samples 147-164 were made to evaluate different spraying pattern. The manufacturing is shown in Table 10-13 and Figure 10-17, the results are shown in Table 10-14. The results suggest that one long spraying burst is worse than several short spraying bursts. This conclusion is concurrent with the results form 1 -24; where more, but shorter spraying bursts were used.

Another parameter which should be taken into consideration is the spraying pressure. The samples 1 – 80 were made with a pressure of 5 bars, the samples 81 – 112 were manufactured with 4 bars, all the other samples (unless stated otherwise) were made with 5 bars. In order to characterize the spraying properties of the apparatus (see chapter 10.2.4), it was found out that a pressure of 4 bars gives a better appearance of the bottles. But it seems that a pressure of 5 bars (this means more application of the components of the coating) gives a higher hydrolytic resistance. In future samples a spraying pressure of 4 bars will not be used.

Different spraying times (this means duration of all the spray bursts together) were tested as well. With respect to the results obtained so far, it is supposed that this will be one of the most influential factors regarding the hydrolytic resistance. As it is already known two spraying steps with a certain period of annealing between the two APTES applications improves the results, the experiments shown in Table 10-26 were conducted to find the best APTES spraying pattern.

Table 10-26: Experiments conducted to find the ideal parameters for APTES application

Sample Number	Manufacturing shown in	Results shown in	1st APTES application	2nd APTES application
183 - 185	Figure 10-20 and Table 10-27	Table 10-36	6x1 s	5x1 s
186 - 188	Figure 10-20 and Table 10-28	Table 10-36	5x1 s	5x1 s
189 – 191	Figure 10-20	Table 10-36	6x1 s	-

	and Table 10-29			
192-194	Figure 10-21 and Table 10-31	Table 10-36	6x1 s	6x1 s
206 - 208	Figure 10-21 and Table 10-30	Table 10-36	4x1 s	4x1 s
218 – 220	Figure 10-21 and Table 10-32	Table 10-36	5x1 s	5x1 s + 4x1 s
233 – 235	Figure 10-22 and Table 10-33	Table 10-36	8x1 s	8x1 s
236 - 238	Figure 10-22 and Table 10-34	Table 10-36	8x1 s	8x1 s
242 – 244	Figure 10-22 and Table 10-35	Table 10-36	7x1 s	7x1 s

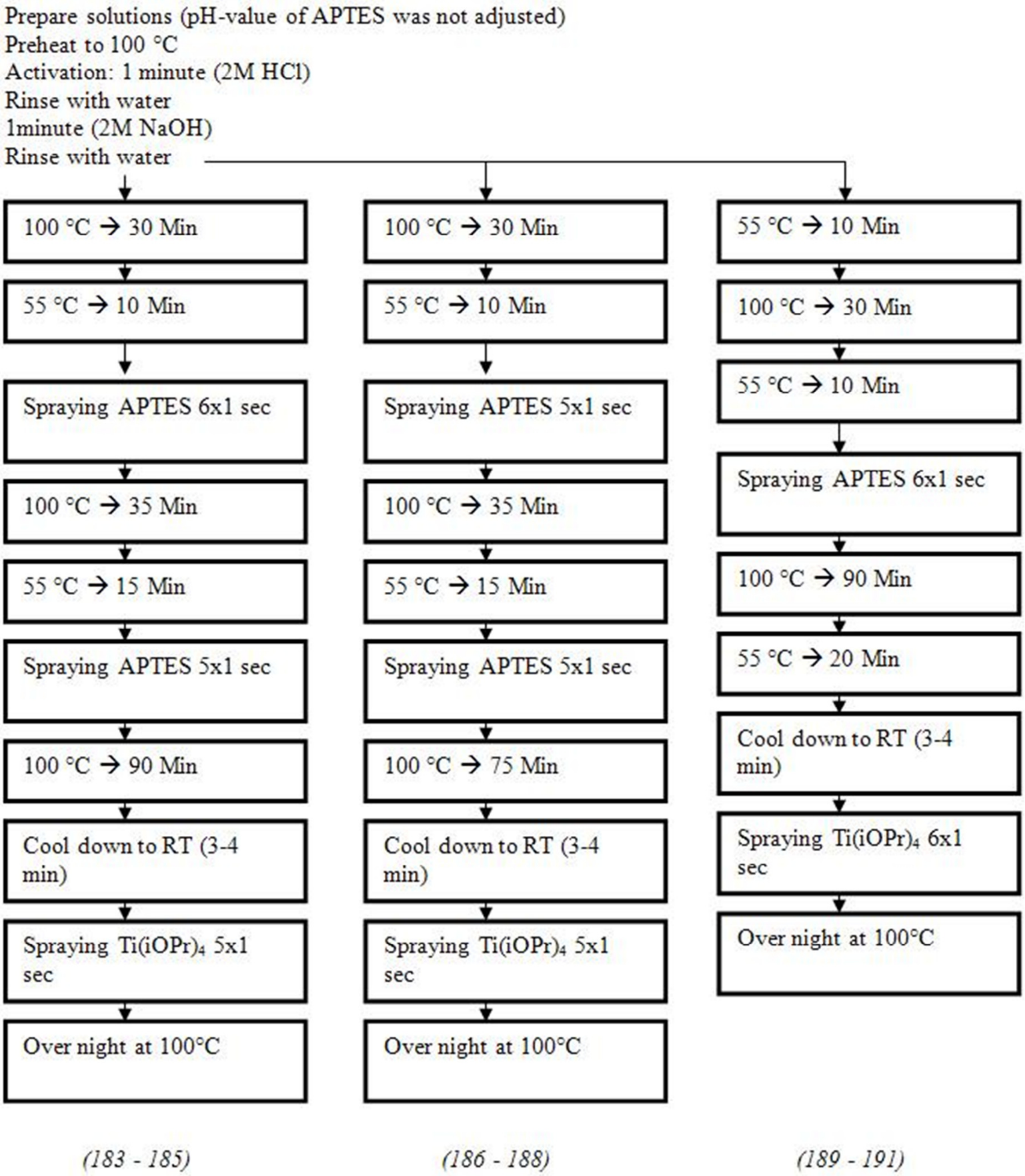


Figure 10-20: Production of samples 183-191

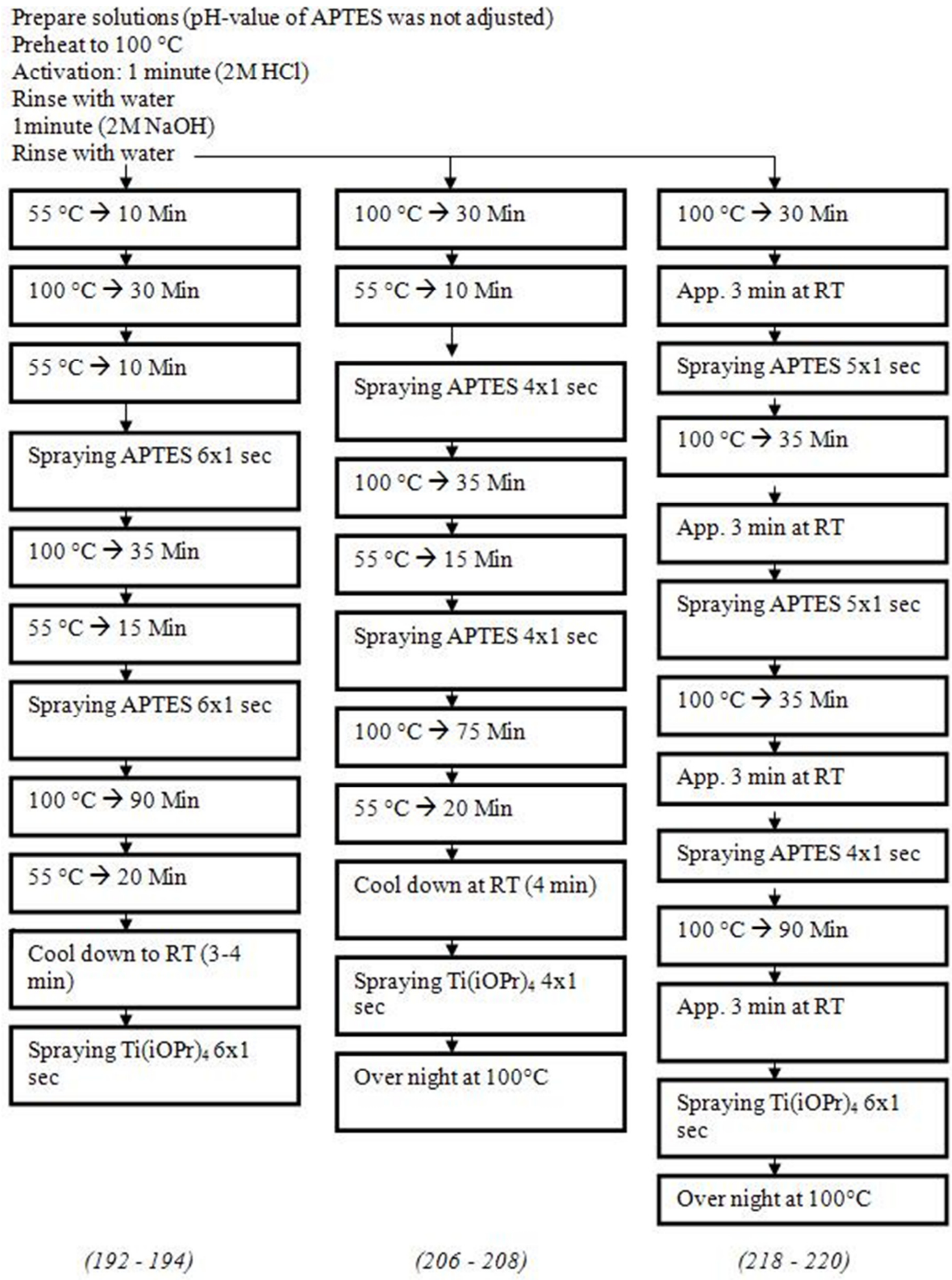


Figure 10-21: Production of samples 192-194, 206-208 and 218-220

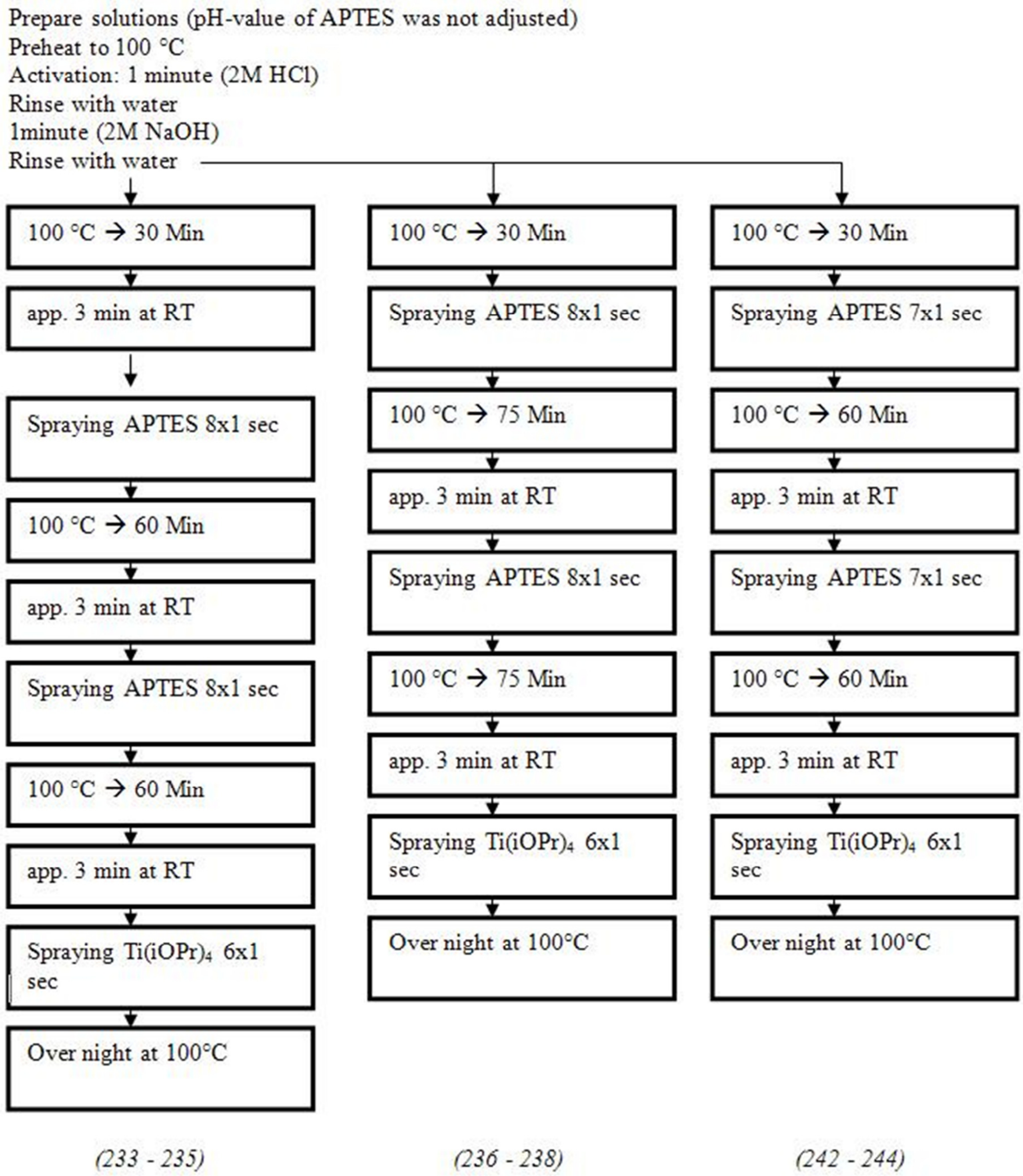


Figure 10-22: Production of samples 233-238 and 242-244

Table 10-27: Production of samples 183-185 (APTES spraying time)

Process step
The bottles were preheated to a temperature of 100°C.
Preparation of the solutions: 1% w/w APTES in EtOH (pH not adjusted); 10% w/w Ti(i-OPr)$_4$ in EtOH
Activation : • Filling the bottles with HCl (2M) for 1 min • The bottles were thoroughly rinsed with water • Filling the bottles with NaOH (2M) for 1 min

• The bottles were thoroughly rinsed with water
Drying in the oven: • 10 minutes at 55°C • 30 minutes at 100°C
Spray-coating of the samples with APTES for 6 x 1 s (The bottle was turned randomly after each spray burst), subsequently dried in the oven for 35 min at 100°C and 15 min at 55°C (p = ~ 5 bars)
Spray-coating of the samples with APTES for 5 x 1 s (The bottle was turned 120° after each spray burst), subsequently dried in the oven for 90 min at 100°C and 15 min at 55°C (p = ~ 5 bars)
The bottle was left at RT for 3 to 4 minutes to cool down
Spray-coating of samples 183 – 185 with $\mathrm{Ti(i\text{-}OPr)_4}$ for 6 x 1 s (the bottle was turned randomly after each spray burst) (p = ~ 5 bars)
After the final spray-coating step every sample was dried in the oven (100°C) over night.

Table 10-28: Production of samples 186-188 (APTES spraying time)

Process step
The bottles were preheated to a temperature of 100°C.
Preparation of the solutions: 1% w/w APTES in EtOH (pH not adjusted); 10% w/w $\mathrm{Ti(i\text{-}OPr)_4}$ in EtOH
Activation : • Filling the bottles with HCl (2M) for 1 min • The bottles were thoroughly rinsed with water • Filling the bottles with NaOH (2M) for 1 min • The bottles were thoroughly rinsed with water
Drying in the oven: • 10 minutes at 55°C • 30 minutes at 100°C
Spray-coating of the samples with APTES for 5 x 1 s (The bottle was turned randomly after each spray burst), subsequently dried in the oven for 35 min at 100°C and 15 min at 55°C (p = ~ 5 bars)
Spray-coating of the samples with APTES for 5 x 1 s (The bottle was turned 120° after each spray burst), subsequently dried in the oven for 75 min at 100°C (p = ~ 5 bars)
The bottle was left at RT for 3 to 4 minutes to cool down
Spray-coating of the samples with $\mathrm{Ti(i\text{-}OPr)_4}$ for 6 x 1 s (the bottle was turned randomly after each spray burst) (p = ~ 5 bars)
After the final spray-coating step every sample was dried in the oven (100°C) over night.

Table 10-29: Production of samples 189-191 (APTES spraying time)

Process step
The bottles were preheated to a temperature of 100°C.
Preparation of the solutions: 1% w/w APTES in EtOH (pH not adjusted); 10% w/w Ti(i-OPr)$_4$ in EtOH
Activation : • Filling the bottles with HCl (2M) for 1 min • The bottles were thoroughly rinsed with water • Filling the bottles with NaOH (2M) for 1 min • The bottles were thoroughly rinsed with water
Drying in the oven: • 10 minutes at 55°C • 30 minutes at 100°C • 10 minutes at 55°C
Spray-coating of the samples with APTES for 6 x 1 s (The bottle was rotated 120° after each spray burst), subsequently dried in the oven for 90 min at 100°C and 20 min at 55°C (p = ~ 5 bars)
The bottle was left at RT for 3 to 4 minutes to cool down
Spray-coating of the samples with Ti(i-OPr)$_4$ for 6 x 1 s (the bottle was turned randomly after each spray burst) (p = ~ 5 bars)
After the final spray-coating step every sample was dried in the oven (100°C) over night.

Table 10-30: Production of samples 206-208 (APTES spraying time)

Process step
The bottles were preheated to a temperature of 100°C.
Preparation of the solutions: 1% w/w APTES in EtOH (pH not adjusted); 10% w/w Ti(i-OPr)$_4$ in EtOH
Activation : • Filling the bottles with HCl (2M) for 1 min • The bottles were thoroughly rinsed with water • Filling the bottles with NaOH (2M) for 1 min • The bottles were thoroughly rinsed with water
Drying in the oven: • 45 minutes (206 and 207) or 40 minutes (208) at 100°C • 4 minutes at RT
Spray-coating of the samples with APTES for 4 x 1 s (The bottle was turned randomly after each spray burst), subsequently dried in the oven for 35 min at 100°C, then left at RT for 4 minutes (p = ~ 5 bars)
Spray-coating of the samples with APTES for 4 x 1 s (The bottle was turned randomly after each spray burst), subsequently dried in the oven for 75 min at 100° (p = ~ 5 bars)

The bottle was left at RT for 4 minutes to cool down
Spray-coating of samples 203 – 205 with Ti(i-OPr)$_4$ for 6 x 1 s (the bottle was turned randomly after each spray burst) (p = ~ 5 bars)
After the final spray-coating step every sample was dried in the oven (100°C) over night.

Table 10-31: Production of samples 192-194 (APTES spraying time)

Process step
The bottles were preheated to a temperature of 100°C.
Preparation of the solutions: 1% w/w APTES in EtOH (pH not adjusted); 10% w/w Ti(i-OPr)$_4$ in EtOH
Activation : • Filling the bottles with HCl (2M) for 1 min • The bottles were thoroughly rinsed with water • Filling the bottles with NaOH (2M) for 1 min • The bottles were thoroughly rinsed with water
Drying in the oven: • 10 minutes at 55°C • 30 minutes at 100°C • 10 minutes at 55°C
Spray-coating of the samples with APTES for 6 x 1 s (The bottle was turned randomly after each spray burst), subsequently dried in the oven for 35 min at 100°C and 15 min at 55°C (p = ~ 5 bars)
Spray-coating of the samples with APTES for 6 x 1 s (The bottle was turned randomly after each spray burst), subsequently dried in the oven for 90 min at 100°C and 20 minutes at 55°C (p = ~ 5 bars)
The bottle was left at RT for 3 to 4 minutes to cool down
Spray-coating of the samples with Ti(i-OPr)$_4$ for 6 x 1 s (the bottle was turned randomly after each spray burst) (p = ~ 5 bars)

Table 10-32: Production of samples 218-220 (APTES spraying time)

Process step
The bottles were preheated to a temperature of 100°C.
Preparation of the solutions: 1% w/w APTES in EtOH (pH not adjusted); 10% w/w Ti(i-OPr)$_4$ in EtOH
Activation : • Filling the bottles with HCl (2M) with shaking for 1 min • The bottles were thoroughly rinsed with water

• Filling the bottles with NaOH (2M) with shaking for 1 min • The bottles were thoroughly rinsed with water
Drying in the oven: • 30 minutes at 100°C • 3 minutes at RT
Spray-coating of the samples with APTES for 5 x 1 s (The bottle was turned randomly after each spray burst, then put in the oven for 35 minutes at 100°C, then left at RT for another 3 minutes (p = ~ 5 bars)
Spray-coating of the samples with APTES for 5 x 1 s (The bottle was turned randomly after each spray burst, then put in the oven for 35 minutes at 100°C, then left at RT for another 3 minutes (p = ~ 5 bars)
Spray-coating of the samples with APTES for 4 x 1 s (The bottle was turned randomly after each spray burst, then put in the oven for 90 minutes at 100°C, then left at RT for another 3 minutes (p = ~ 5 bars)
Spray-coating of samples 218 – 220 with Ti(i-OPr)$_4$ for 6 x 1 s (the bottle was turned randomly after each spray burst) (p = ~ 5 bars)
After the final spray-coating step every sample was dried in the oven (100°C) over night.

Table 10-33: Production of samples 233-235 (APTES spraying time)

Process step
The bottles were preheated to a temperature of 100°C.
Preparation of the solutions: 1% w/w APTES in EtOH (pH not adjusted); 10% w/w Ti(i-OPr)$_4$ in EtOH
Activation : • Filling the bottles with HCl (2M) and shaking for 1 min • The bottles were thoroughly rinsed with water • Filling the bottles with NaOH (2M) and shaking for 1 min • The bottles were thoroughly rinsed with water
Drying in the oven for 30 minutes at 100°C, then left at RT for 3 minutes
Spray-coating of the samples with APTES for 8 x 1 s (The bottle was turned randomly after each spray burst) , then put in the oven for 60 minutes at 100°C, then left at RT for another 3 minutes (p = ~ 5 bars)
Spray-coating of the samples with APTES for 8 x 1 s (The bottle was turned randomly after each spray burst) , then put in the oven for 60 minutes at 100°C, then left at RT for another 3 minutes (p = ~ 5 bars)
Spray-coating of samples 233 – 235 with Ti(i-OPr)$_4$ for 6 x 1 s (the bottle was turned randomly after each spray burst) (p = ~ 5 bars)
After the final spray-coating step every sample was dried in the oven (100°C) over night.

Table 10-34: Production of samples 236-238 (APTES spraying time)

Process step
The bottles were preheated to a temperature of 100°C.
Preparation of the solutions: 1% w/w APTES in EtOH (pH not adjusted); 10% w/w Ti(i-OPr)$_4$ in EtOH
Activation : • Filling the bottles with HCl (2M) and shaking for 1 min • The bottles were thoroughly rinsed with water • Filling the bottles with NaOH (2M) and shaking for 1 min • The bottles were thoroughly rinsed with water
Drying in the oven for 30 minutes at 100°C, then left at RT for 3 minutes
Spray-coating of the samples with APTES for 8 x 1 s (The bottle was turned randomly after each spray burst) , then put in the oven for 75 minutes at 100°C, then left at RT for another 3 minutes (p = ~ 5 bars)
Spray-coating of the samples with APTES for 8 x 1 s (The bottle was turned randomly after each spray burst) , then put in the oven for 75 minutes at 100°C, then left at RT for another 3 minutes (p = ~ 5 bars)
Spray-coating of samples 236 – 238 with Ti(i-OPr)$_4$ for 6 x 1 s (the bottle was turned randomly after each spray burst) (p = ~ 5 bars)
After the final spray-coating step every sample was dried in the oven (100°C) over night.

Table 10-35: Production of samples 242-244 (APTES spraying time)

Process step
The bottles were preheated to a temperature of 100°C.
Preparation of the solutions: 1% w/w APTES in EtOH (pH not adjusted); 10% w/w Ti(i-OPr)$_4$ in EtOH
Activation : • Filling the bottles with HCl (2M) and shaking for 1 min • The bottles were thoroughly rinsed with water • Filling the bottles with NaOH (2M) and shaking for 1 min • The bottles were thoroughly rinsed with water
Drying in the oven for 30 minutes at 100°C, then left at RT for 3 minutes
Spray-coating of the samples with APTES for 7 x 1 s (The bottle was turned randomly after each spray burst) , then put in the oven for 60 minutes at 100°C, then left at RT for another 3 minutes (p = ~ 5 bars)
Spray-coating of the samples with APTES for 7 x 1 s (The bottle was turned randomly after each spray burst) , then put in the oven for 60 minutes at 100°C, then left at RT for another 3 minutes (p = ~ 5 bars)
Spray-coating of samples 242 – 244 with Ti(i-OPr)$_4$ for 6 x 1 s (the bottle was turned

randomly after each spray burst) (p = ~ 5 bars)
After the final spray-coating step every sample was dried in the oven (100°C) over night.

Table 10-36: Results of the determination of the hydrolytic class; samples 183-194, 206-208, 218-220, 233-238 and 242-244 (APTES spraying time)

Specification Type II	#	Results [ml 0.01 N HCl/100 ml]	#	Results [ml 0.01 N HCl/100 ml]
Max. 0.40 ml 0.01 N HCl / 100 ml	183	0.56	208	0.70
	184	0.54	218	0.54
	185	0.56	219	0.56
	186	0.48	220	0.50
	187	0.54	233	0.62
	188	0.52	234	0.70
	189	0.50	235	0.52
	190	0.60	236	0.42
	191	0.60	237	0.46
	192	0.64	238	0.40
	193	0.88	242	0.62
	194	0.82	243	0.72
	206	0.58	244	0.64
	207	0.74	-	-

As one can see in the next chapter (TiO_2 loading), the amount of TiO_2 used has virtually no influence on the final result, this means in this case the different TiO_2 spraying times do not influence the comparability of the results. The obtained data shows no clear results, but it seems that spraying more APTES gives better results. Furthermore, it seems that the amount of APTES used and the annealing conditions have a very delicate interplay. But applying too much APTES worsens the protective layer. The optimal conditions for a well-established APTES layer are in a very narrow range and hard to achieve. The results of samples 236 – 238 show that the combination of rather much APTES spraying and long heat treatment is a very promising approach.

10.3.4 TiO_2-Loading

Similar to the assessment of the APTES loading the influence of the TiO_2 layer was evaluated. The preliminary study has shown that higher $Ti(i\text{-}OPr)_4$ concentrations yield better results. Different concentrations of the $Ti(i\text{-}OPr)_4$ were tested, namely

- 5% v/v
  - samples 62-64 - Table 10-21
  - samples 65-67 - Table 10-37
  - samples 68-70 - Table 10-38
  - samples 71-73 - Table 10-22
- 10% v/v
  - samples 53-55 - Table 10-19
  - samples 56-58 - Table 10-20
  - samples 59-61 - Table 10-16
  - samples 74-76 - Table 10-23
  - samples 77-79 - Table 10-39
- 10% w/w
  - samples 49-52 - Table 10-15

Table 10-37: Production of samples 65-67 (activation; $Ti(iOPr_4)$-conc.; APTES-conc.)

Process step
The bottles were preheated to a temperature of 160°C.
Preparation of the solutions; 1% v/v APTES in EtOH; 5% v/v $Ti(i\text{-}OPr)_4$ in EtOH; the pH of the APTES solution was set to app. 3.7 with acetic acid (100%).
Activation of samples: the bottles were filled with HCl (1M) for 30 min
The samples were thoroughly rinsed with water
Activation of samples: the bottles were filled with NaOH (1M) for 30 min
The samples were thoroughly rinsed with water
Annealing of the samples for 15 min at 120 °C
Spray-coating of the samples with APTES solution for app. 5 s (p = ~ 5 bars)
Silanization (this means annealing in the oven) for 30 min at 120°C

The samples were rinsed with EtOH
Annealing in the oven for 10 min at 120°C
Spray-coating of the samples with $Ti(i\text{-}OPr)_4$ 5% v/v solution for app. 5 s (p = ~ 5 bars)
Drying of the bottles in the oven (80°C) for 3h

Table 10-38: Production of samples 68-70 (activation; $Ti(iOPr_4)$-conc.; APTES-conc.)

Process step
The bottles were preheated to a temperature of 160°C.
Preparation of the solutions; 1% v/v APTES in EtOH; 5% v/v $Ti(i\text{-}OPr)_4$ in EtOH; the pH of the APTES solution was set to app. 3.7 with acetic acid (100%).
Activation of samples: the bottles were filled with HCl (1M) for 15 min; these bottles were incubated for 15 min at 70°C
The samples were thoroughly rinsed with water
Activation of samples: the bottles were filled with NaOH (1M) for 15 min; these bottles were incubated for 15 min at 70°C
The samples were thoroughly rinsed with water
Annealing of the samples for 15 min at 120 °C
Spray-coating of the samples with APTES solution for app. 5 s (p = ~ 5 bars)
Silanization (this means annealing in the oven) for 30 min at 120°C
The samples were rinsed with EtOH
Annealing in the oven for 10 min at 120°C
Spray-coating of the samples with $Ti(i\text{-}OPr)_4$ 5% v/v solution for app. 5 s (p = ~ 5 bars)
Drying of the bottles in the oven (80°C) for 3h

Table 10-39: Production of samples 77-79 (activation; $Ti(iOPr_4)$-conc.; APTES-conc.)

Process step
The bottles were preheated to a temperature of 160°C.
Preparation of the solutions; 1% v/v APTES in EtOH; 10% v/v $Ti(i\text{-}OPr)_4$ in EtOH; the pH of the APTES solution was set to app. 4 with acetic acid (100%).
Activation of samples: the bottles were filled with HCl (1M) for 15 min; these bottles were incubated for 15 min at 70°C
The samples were thoroughly rinsed with water
Activation of samples: the bottles were filled with NaOH (1M) for 15 min; these bottles

were incubated for 15 min at 70°C
The samples were thoroughly rinsed with water
Annealing of the samples for 15 min at 120 °C
Spray-coating of the samples with APTES solution for app. 5 s (p = ~ 5 bars)
Silanization (this means annealing in the oven) for 30 min at 120°C
The samples were rinsed with EtOH
Annealing in the oven for 15 min at 120°C
Spray-coating of the samples with $Ti(i\text{-}OPr)_4$ 10% v/v solution for app. 5 s (p = ~ 5 bars)
Drying of the bottles in the oven (80°C) for 3h

It can be seen that a lower $Ti(iOPr)_4$ concentration did not yield better results (see Table 10-12). A concentration of 10% w/w was kept, because the best results (samples 1 – 24) were made with 10% w/w. Another solvent was not taken into consideration, because the outcome using EtOH was good enough.

Similar to APTES it was tested if spraying for x seconds or spraying two times x*0.5 sec gives a higher hydrolytic resistance. The production of the corresponding samples (97-112) is presented in Table 10-18. The results suggest that more, but shorter spraying steps do not improve the results. Therefore, the decision was made that one $Ti(i\text{-}OPr)_4$ spraying step is enough.

It is obvious that higher pressures and longer spraying times lead to application of more TiO_2. In the next experiment different spraying times and spraying pressures were tested. The used parameters are shown in Figure 10-23 and Table 10-40. The corresponding results are shown in Table 10-42. Another attempt with a $Ti(i\text{-}OPr)_4$ spraying times of 4 seconds is shown in Figure 10-24 and Table 10-41.

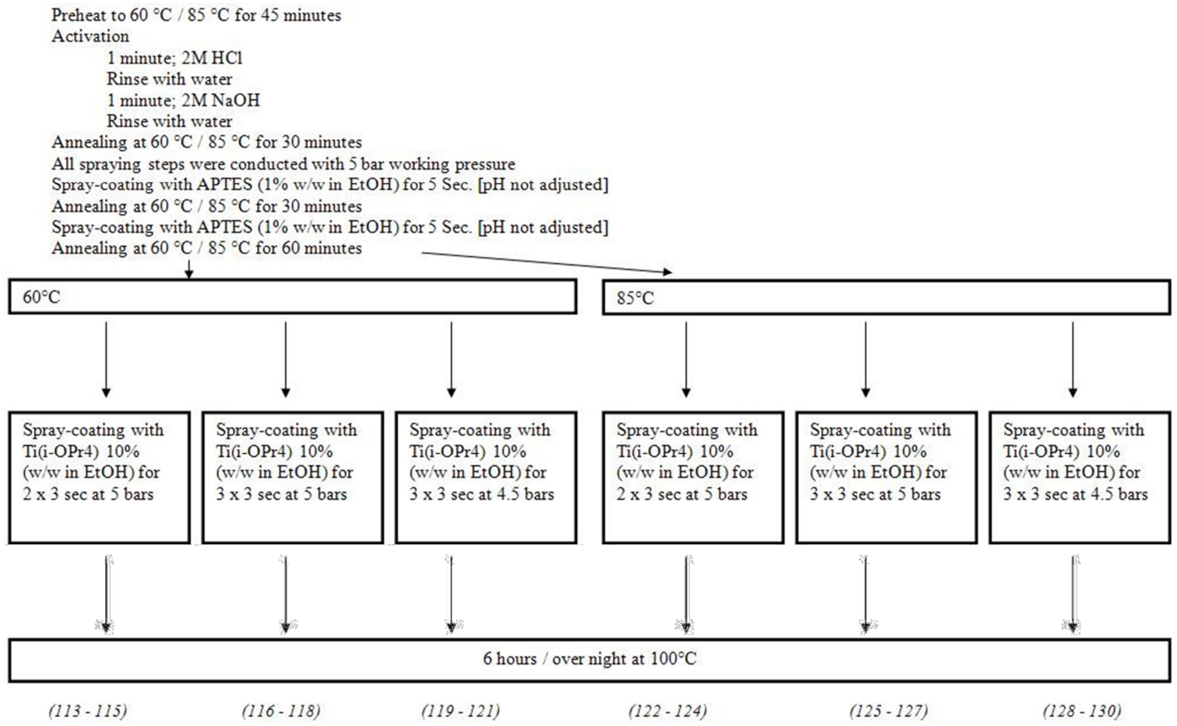


Figure 10-23: Production of samples 113-130

Table 10-40: Production of samples 113-130 (annealing temperature; Ti(iOPr$_4$) spraying time)

Process step
The bottles were preheated to a temperature of 85°C.
Preparation of the solutions; 1% w/w APTES in EtOH; 10% w/w Ti(i-OPr)$_4$ in EtOH; the pH of the APTES solution was not adjusted
Activation of samples: • Filling the bottles with HCl (2M) for 1 min • The bottles were thoroughly rinsed with water • Filling the bottles with NaOH (2M) for 1 min • The bottles were thoroughly rinsed with water
Annealing of samples 113 – 121 in the oven for 30 min at 60°C
Annealing of samples 122 – 130 in the oven for 30 min at 85°C
Spray-coating of samples 113 – 121 with APTES for 5 s (p = ~ 5 bars)
Spray-coating of samples 122 – 130 with APTES for 5 s (p = ~ 5 bars)
Annealing of samples 113 – 121 in the oven for 30 min at 60°C
Annealing of samples 122 – 130 in the oven for 30 min at 85°C
Spray-coating of samples 113 – 121 with APTES for 5 s (p = ~ 5 bars)
Spray-coating of samples 122 – 130 with APTES for 5 s (p = ~ 5 bars)
Annealing of samples 113 – 121 in the oven for 60 min at 60°C

Annealing of samples 122 – 130 in the oven for 60 min at 85°C
Spray-coating of samples 113 - 115 with Ti(i-OPr)$_4$ for 2 x 3 s (p = ~ 5 bars)
Spray-coating of samples 116 - 118 with Ti(i-OPr)$_4$ for 3 x 3 s (p = ~ 5 bars)
Spray-coating of samples 119 - 121 with Ti(i-OPr)$_4$ for 3 x 3 s (p = ~ 4.5 bars)
Spray-coating of samples 122 - 124 with Ti(i-OPr)$_4$ for 2 x 3 s (p = ~ 5 bars)
Spray-coating of samples 125 - 127 with Ti(i-OPr)$_4$ for 3 x 3 s (p = ~ 5 bars)
Spray-coating of samples 128 - 130 with Ti(i-OPr)$_4$ for 3 x 3 s (p = ~ 4.5 bars)
After spray-coating with Ti(i-OPr)$_4$ all samples were dried in the oven (100°C) over night.

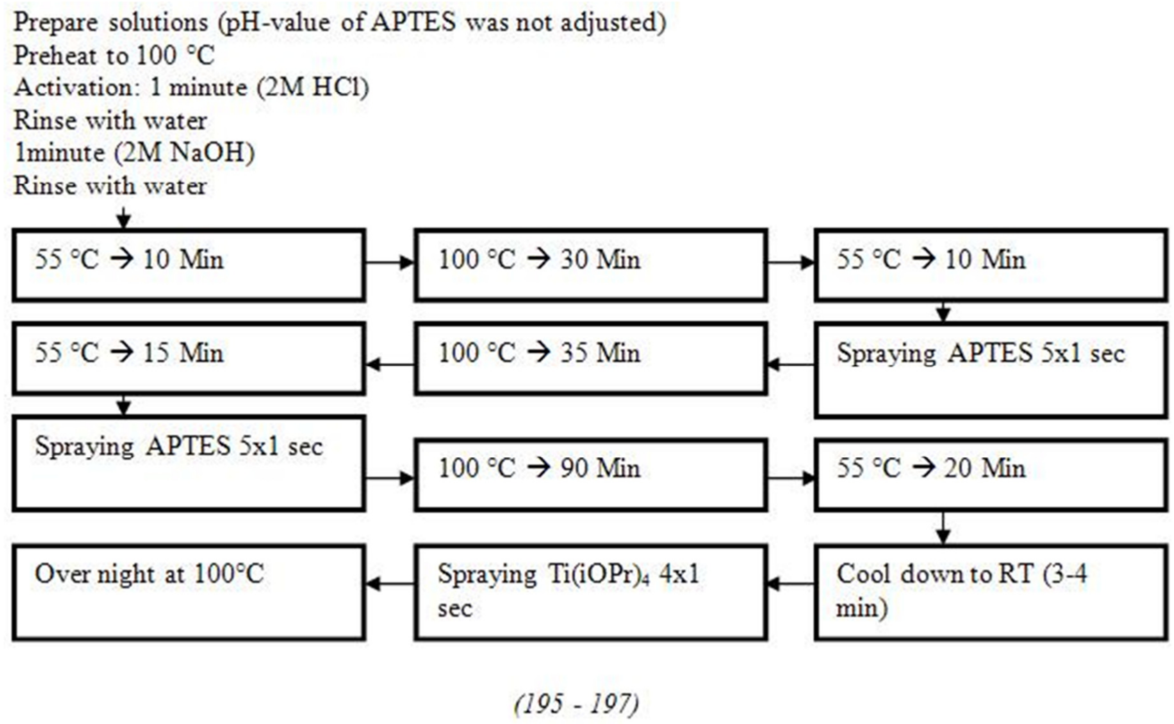


Figure 10-24: Production of samples 195-197

Table 10-41: Production of samples 195-197 (APTES spraying time; Ti(iOPr$_4$) spraying time)

Process step
The bottles were preheated to a temperature of 100°C.
Preparation of the solutions: 1% w/w APTES in EtOH (pH not adjusted); 10% w/w Ti(i-OPr)$_4$ in EtOH
Activation : • Filling the bottles with HCl (2M) for 1 min • The bottles were thoroughly rinsed with water • Filling the bottles with NaOH (2M) for 1 min • The bottles were thoroughly rinsed with water

Drying in the oven: • 10 minutes at 55°C • 30 minutes at 100°C • 10 minutes at 55°C
Spray-coating of the samples with APTES for 5 x 1 s (The bottle was turned randomly after each spray burst), subsequently dried in the oven for 35 min at 100°C and 15 min at 55°C (p = ~ 5 bars)
Spray-coating of the samples with APTES for 5 x 1 s (The bottle was turned randomly after each spray burst), subsequently dried in the oven for 90 min at 100°C and 20 min at 55°C (p = ~ 5 bars)
The bottle was left at RT for 3 to 4 minutes to cool down
Spray-coating of samples 165 – 170 with Ti(i-OPr)$_4$ for 4 x 1 s (the bottle was turned randomly after each spray burst) (p = ~ 5 bars)
After the final spray-coating step every sample was dried in the oven (100°C) over night.

Table 10-42: Results of the determination of the hydrolytic class samples (annealing temperature 113-130; Ti(iOPr$_4$) spraying time 113-130, 195-197; APTES spraying time 195-197)

Specification Type II	#	Results [ml 0.01 N HCl/100 ml]	#	Results [ml 0.01 N HCl/100 ml]
Max. 0.40 ml 0.01 N HCl / 100 ml	113	0.52	124	0.70
	114	0.60	125	0.62
	115	0.64	126	0.64
	116	0.52	127	0.58
	117	0.54	128	0.72
	118	0.62	129	0.74
	119	0.52	130	0.74
	120	0.58	195	0.46
	121	0.58	195	0.54
	122	0.70	197	0.56
	123	0.58	-	-

Apparently, the influence of different spraying pressures and spraying times is negligible. The TiO$_2$ layer seems to have a comparably small influence on the resulting hydrolytic class. But we can see that different temperatures while spraying have a great influence on the results. This will be examined and discussed later (see chapter 10.3.5 (annealing)).

In another experiment it was tested, if a different spraying pattern influences the hydrolytic resistance. In the experiments (samples 147-152 (shown in Table 10-13 and Figure 10-17; results shown in Table 10-14)) spraying 1x6 seconds and 6x1 second were compared. Similar to the experiments with APTES several bursts are better than one long burst. This may be due to the fact, that more of the inner surface is covered and voids in the coating are avoided. To enlarge the covered area of the inner surface the bottles will be turned after each spraying burst.

To check if the application of the TiO_2 is necessary a series of bottles was prepared without application of $Ti(i\text{-}O\text{-}Pr)_4$ (this means only an APTES layer was applied). The manufacturing is shown in Figure 10-25 and Table 10-43, the results are presented in Table 10-44. As one can see, the results are terrible and it is proven that usage of $Ti(i\text{-}OPr)_4$ is mandatory.

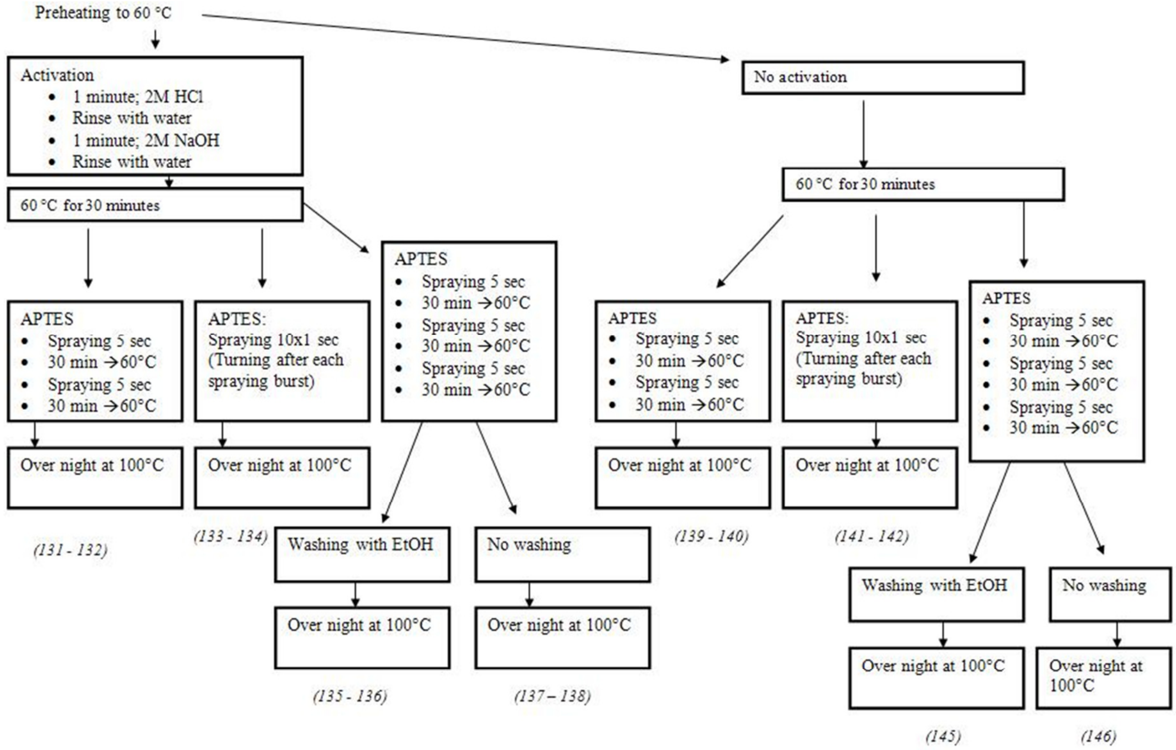


Figure 10-25: Production of samples 131-146

Table 10-43: Production of samples 131-146 (activation 139-146; Ti(iOPr₄) application)

Process step
The bottles were preheated to a temperature of 60°C.
Preparation of the solutions; 1% w/w APTES in EtOH; 10% w/w $Ti(i\text{-}OPr)_4$ in EtOH; the

pH of the APTES solution was not adjusted

Activation of samples 131 - 138:
- Filling the bottles with HCl (2M) for 1 min
- The bottles were thoroughly rinsed with water
- Filling the bottles with NaOH (2M) for 1 min
- The bottles were thoroughly rinsed with water

The samples 139 - 142 and 145 - 146 were not activated.

Annealing of samples 131 – 138 in the oven for 30 min at 60°C

Samples 131 – 132:
- Spray-coating with APTES for 5 s (p = ~ 5 bars)
- Drying in the oven for 30 min at 60°C
- Spray-coating with APTES for 5 s (p = ~ 5 bars)

Spray-coating of samples 133 and 134 with APTES for 10 x 1 s (p = ~ 5 bars)

Samples 135 – 138:
- Spray-coating with APTES for 5 s (p = ~ 5 bars)
- Drying in the oven for 30 min at 60°C
- Spray-coating with APTES for 5 s (p = ~ 5 bars)
- Drying in the oven for 30 min at 60°C
- Spray-coating with APTES for 5 s (p = ~ 5 bars)
- Drying in the oven for 30 min at 60°C

Washing of samples 135 and 136 with EtOH for 1 min.

Samples 139 – 140:
- Spray-coating with APTES for 5 s (p = ~ 5 bars)
- Drying in the oven for 30 min at 60°C
- Spray-coating with APTES for 5 s (p = ~ 5 bars)

Spray-coating of samples 141 and 142 with APTES for 10 x 1 s (p = ~ 5 bars)

Samples 145 and 146:
- Spray-coating with APTES for 5 s (p = ~ 5 bars)
- Drying in the oven for 30 min at 60°C
- Spray-coating with APTES for 5 s (p = ~ 5 bars)
- Drying in the oven for 30 min at 60°C
- Spray-coating with APTES for 5 s (p = ~ 5 bars)
- Drying in the oven for 30 min at 60°C

Washing of sample 145 with EtOH for 1 min.

After the final process step every sample was dried in the oven (100°C) over night.

Table 10-44: Results of the determination of the hydrolytic class; samples 131-146 (activation 139-146; Ti(iOPr$_4$) application)

Specification Type II	#	Results [ml 0.01 N HCl/100 ml]	#	Results [ml 0.01 N HCl/100 ml]

Max. 0.40 ml 0.01 N HCl / 100 ml	131	13.60	139	2.02
	132	8.58	140	18.76
	133	7.42	141	2.72
	134	5.12	142	3.38
	135	2.04	143	2.42
	136	1.86	144	2.28
	137	14.92	145	2.08
	138	16.86	146	18.98

10.3.5 Annealing (temperature and time)

In several experiments it was noticed that the temperature of the heat treatment and the duration of the treatment change the results severely. The samples 1 to 24 were put out of the oven and were cooled down for a short period of time. Maybe this circumstance led to the good results of the first bottles. In literature heat treatment is always used after surface silanization, but different temperatures are described. This led to the decision that different temperatures for the annealing step should be tested as well.

In the experiments (samples 165-179) different annealing times and temperatures before spraying were tested, shown in Figure 10-26, Table 10-45, Table 10-46, Table 10-47 and Table 10-49. The results are shown in Table 10-50.

Sample 177 (Figure 10-26 and Table 10-48) was an attempt to reproduce sample 16, to check if the overall-procedure is still working.

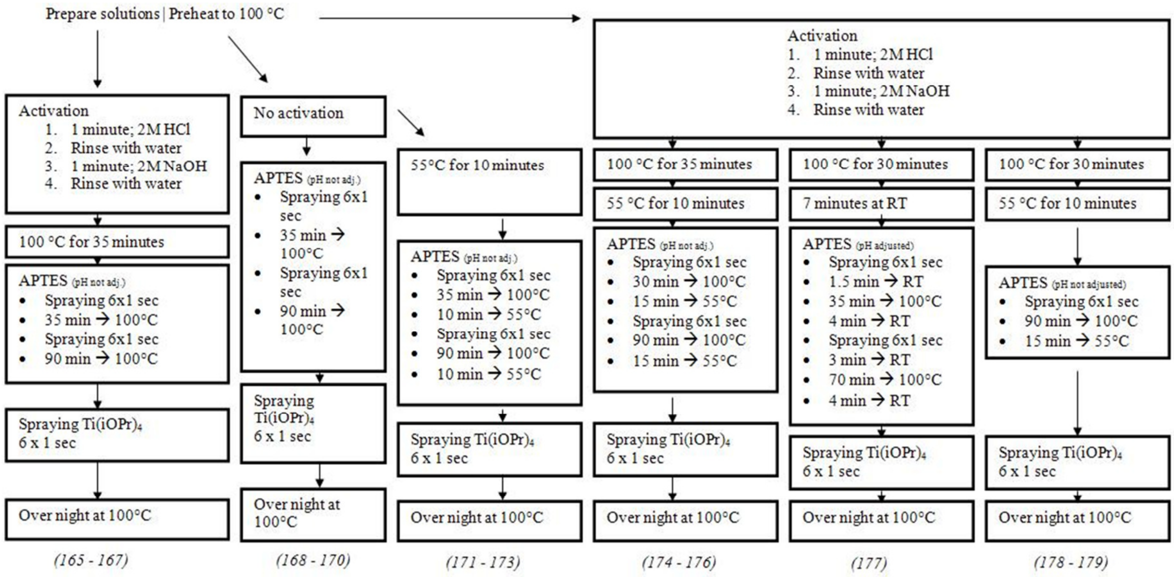


Figure 10-26: Production of samples 165-179

Table 10-45: Production of samples 165-170 (annealing time)

Process step
The bottles were preheated to a temperature of 100°C.
Preparation of the solutions: 2 x 1% w/w APTES in EtOH (pH adjusted and not adjusted); 10% w/w $Ti(i\text{-}OPr)_4$ in EtOH
Activation of samples 165 - 167: • Filling the bottles with HCl (2M) for 1 min • The bottles were thoroughly rinsed with water • Filling the bottles with NaOH (2M) for 1 min • The bottles were thoroughly rinsed with water Samples 168 – 170 were not activated.
Annealing of samples 165 – 167 in the oven for 35 min at 100°C
• Spray-coating of samples 165 - 170 with APTES for 6 x 1 s (The bottle was turned 120° after each spray burst) (p = ~ 5 bars) • Drying in the oven for 35 min at 100°C • Spray-coating of samples 165 - 170 with APTES for 6 x 1 s (The bottle was turned 120° after each spray burst) (p = ~ 5 bars) • Drying in the oven for 35 min at 100°C
After coating with APTES each sample was annealed for 90 minutes at 100°C.
Spray-coating of samples 165 – 170 with $Ti(i\text{-}OPr)_4$ for 6 x 1 s (the bottle was rotated 120° after each spray burst) (p = ~ 5 bars)
After the final spray-coating step every sample was dried in the oven (100°C) over night.

Table 10-46: Production of samples 171-173 (annealing time)

Process step
The bottles were preheated to a temperature of 100°C.
Preparation of the solutions: 1% w/w APTES in EtOH (pH not adjusted); 10% w/w Ti(i-OPr)$_4$ in EtOH
These samples were not activated (no HCL / NaOH treatment)
Put in the oven for 10 min at 55°C
Spray-coating of the samples with APTES for 6 x 1 s (The bottle was turned 120° after each spray burst), subsequently dried in the oven for 35 min at 100°C and 10 min at 55°C (p = ~ 5 bars)
Spray-coating of the samples with APTES for 6 x 1 s (The bottle was turned 120° after each spray burst), subsequently dried in the oven for 90 min at 100°C and 15 min at 55°C (p = ~ 5 bars)
Spray-coating of samples 165 – 170 with Ti(i-OPr)$_4$ for 6 x 1 s (the bottle was turned 120° after each spray burst) (p = ~ 5 bars)
After the final spray-coating step every sample was put in the oven (100°C) over night.

Table 10-47: Production of samples 174-176 (annealing time)

Process step
The bottles were preheated to a temperature of 100°C.
Preparation of the solutions: 1% w/w APTES in EtOH (pH not adjusted); 10% w/w Ti(i-OPr)$_4$ in EtOH
Activation : • Filling the bottles with HCl (2M) for 1 min • The bottles were thoroughly rinsed with water • Filling the bottles with NaOH (2M) for 1 min • The bottles were thoroughly rinsed with water
Drying in the oven: • 10 minutes at 55°C • 30 minutes at 100°C • 10 minutes at 55°C
Spray-coating of the samples with APTES for 6 x 1 s (The bottle was turned 120° after each spray burst), subsequently dried in the oven for 30 min at 100°C and 15 min at 55°C (p = ~ 5 bars)
Spray-coating of the samples with APTES for 6 x 1 s (The bottle was turned 120° after each spray burst), subsequently dried in the oven for 90 min at 100°C and 15 min at 55°C (p = ~ 5 bars)
Spray-coating of samples 165 – 170 with Ti(i-OPr)$_4$ for 6 x 1 s (the bottle was turned

randomly after each spray burst) (p = ~ 5 bars)
After the final spray-coating step every sample was dried in the oven (100°C) over night.

Table 10-48: Production of sample 177 (annealing time; reproduction of sample 16)

Process step
The bottles were preheated to a temperature of 100°C.
Preparation of the solutions: 1% w/w APTES in EtOH (pH adjusted); 10% w/w Ti(i-OPr)$_4$ in EtOH
Activation : • Filling the bottles with HCl (2M) for 1 min; remove the HCl, wait for 10 min • The bottles were thoroughly rinsed with water, wait for 10 min • Filling the bottles with NaOH (2M) for 1 min; remove the NaOH, wait for 10 min • The bottles were thoroughly rinsed with water, wait for 10 min
Drying in the oven for 30 min at 100°C, then left at RT for 7 min
Spray-coating of the samples with APTES for 6 x 1 s (The bottle was turned 120° after each spray burst), left at RT for 1.5 min, then dried in the oven for 30 min at 100°C, finally left at RT for 4 min (p = ~ 5 bars)
Spray-coating of the samples with APTES for 6 x 1 s (The bottle was turned 120° after each spray burst), left at RT for 3 min, then dried in the oven for 70 min at 100°C, finally left at RT for 4 min (p = ~ 5 bars)
Spray-coating with Ti(i-OPr)$_4$ for 6 x 1 s (the bottle was turned randomly after each spray burst) (p = ~ 5 bars)
After the final spray-coating step the sample was dried in the oven (100°C) over night.

Table 10-49: Production of samples 178-179 (annealing time; APTES spraying time)

Process step
The bottles were preheated to a temperature of 100°C.
Preparation of the solutions: 1% w/w APTES in EtOH (pH not adjusted); 10% w/w Ti(i-OPr)$_4$ in EtOH
Activation : • Filling the bottles with HCl (2M) for 1 min • The bottles were thoroughly rinsed with water • Filling the bottles with NaOH (2M) for 1 min • The bottles were thoroughly rinsed with water
Drying in the oven for 30 min at 100°C and 10 min at 55°C
Spray-coating of the samples with APTES for 6 x 1 s (The bottle was turned 120° after each spray burst), subsequently dried in the oven for 90 min at 100°C and 15 min at 55°C (p = ~ 5 bars)
Spray-coating with Ti(i-OPr)$_4$ for 6 x 1 s (the bottle was turned 120° after each spray burst) (p = ~ 5 bars)
After the final spray-coating step every sample was dried in the oven (100°C) over night.

Table 10-50: Results of the determination of the hydrolytic class; samples 165-179 (annealing time; APTES spraying time 178-179)

Specification Type II	#	Results [ml 0.01 N HCl/100 ml]	#	Results [ml 0.01 N HCl/100 ml]
Max. 0.40 ml 0.01 N HCl / 100 ml	165	0.48	173	0.50
	166	0.48	174	0.36
	167	0.52	175	0.36
	168	0.54	176	0.40
	169	0.56	177	0.38
	170	0.58	178	0.54
	171	0.56	179	0.62
	172	0.48	-	-

It seems that a comparably low temperature of the bottle before the spraying steps is the only way to get samples which fulfill the requirements of hydrolytic class 2. Furthermore, an increased annealing time after application of the silane coupling agent seems to improve the results.

Several experiments (Table 10-51) were conducted to assess the helpfulness of a cool down period before spraying the APTES solution and the effect of an alteration of the annealing parameters (time and temperature).

Table 10-51: List of experiments to find the ideal annealing conditions

Sample Number	Manufacturing shown in	Results shown in	Ann. I (after 1st APTES application)	Ann. II (after 2nd APTES application)	Ann. III (after $Ti(i\text{-}OPr)_4$ application)
180 – 182	Figure 10-27 and Table 10-52	Table 10-58	35 minutes at 100°C	90 minutes at 100°C	Overnight at 100°C
200 - 202	Figure 10-27 and Table 10-53	Table 10-58	35 minutes at 100°C	75 minutes at 100°C	Overnight at 100°C
212 - 214	Figure 10-26 and Table 10-54	Table 10-58	30 minutes at RT	90 minutes at RT	-
215 – 217	Figure 10-28 and Table 10-55	Table 10-58	30 minutes at 100°C	90 minutes at 100°C	Overnight at 100°C

224 – 226	Figure 10-28 and Table 10-56	Table 10-58	60 minutes at 100°C	60 minutes at 100°C	Overnight at 100°C
227 - 229	Figure 10-28 and Table 10-57	Table 10-58	75 minutes at 100°C	75 minutes at 100°C	Overnight at 100°C

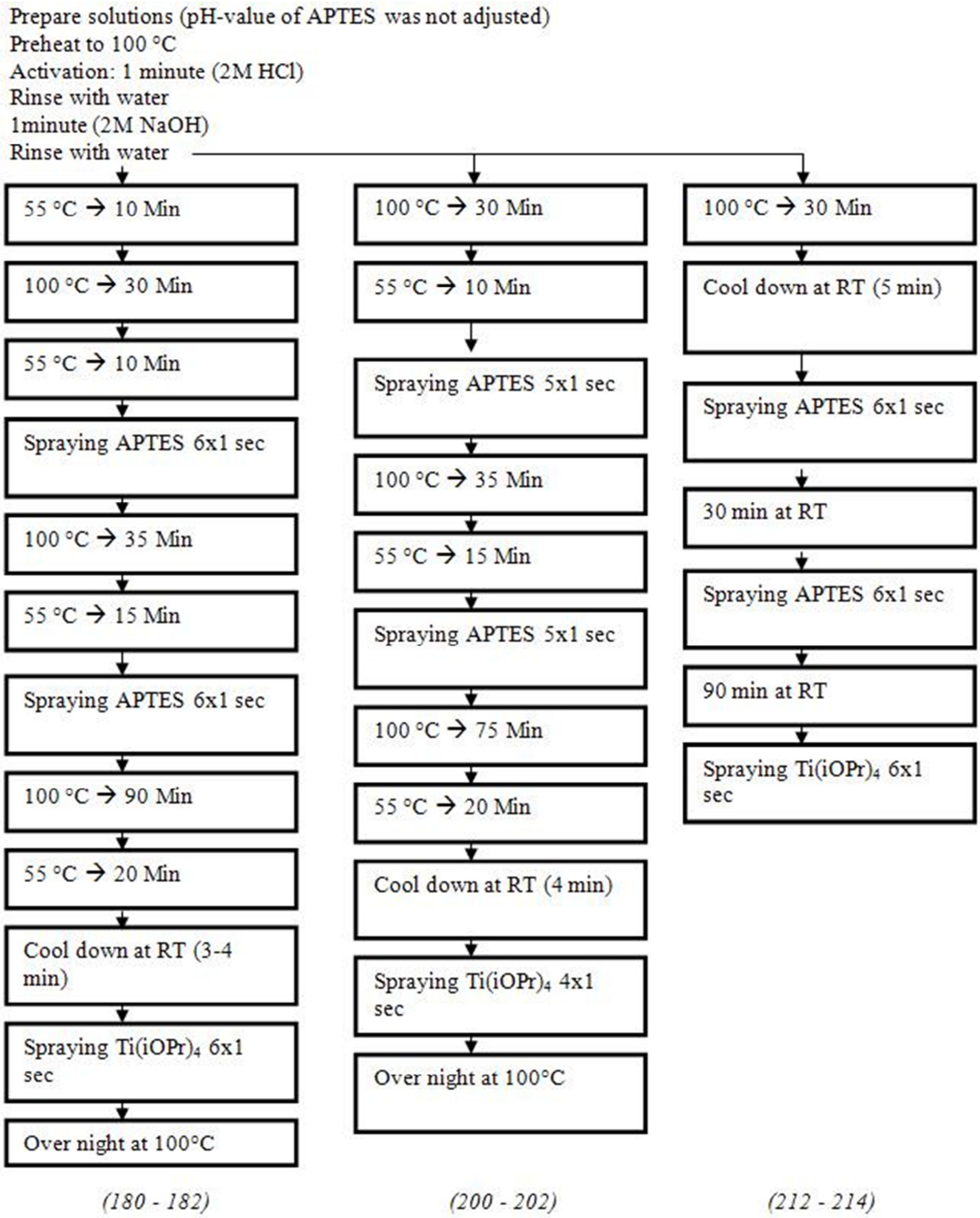


Figure 10-27: Production of samples 180-182, 200-202 and 212-214

Table 10-52: Production of samples 180-182 (annealing time)

Process step
The bottles were preheated to a temperature of 100°C.
Preparation of the solutions: 1% w/w APTES in EtOH (pH not adjusted); 10% w/w Ti(i-OPr)$_4$ in EtOH
Activation : • Filling the bottles with HCl (2M) for 1 min • The bottles were thoroughly rinsed with water • Filling the bottles with NaOH (2M) for 1 min • The bottles were thoroughly rinsed with water
Drying in the oven: • 10 minutes at 55°C • 30 minutes at 100°C • 10 minutes at 55°C
Spray-coating of the samples with APTES for 6 x 1 s (The bottle was turned randomly after each spray burst), subsequently dried in the oven for 35 min at 100°C and 15 min at 55°C (p = ~ 5 bars)
Spray-coating of the samples with APTES for 6 x 1 s (The bottle was rotated 120° after each spray burst), subsequently dried in the oven for 90 min at 100°C and 15 min at 55°C (p = ~ 5 bars)
The bottle was left at RT for 3 to 4 minutes to cool down
Spray-coating of samples 180 – 182 with Ti(i-OPr)$_4$ for 6 x 1 s (the bottle was turned randomly after each spray burst) (p = ~ 5 bars)
After the final spray-coating step every sample was dried in the oven (100°C) over night.

Table 10-53: Production of samples 200-202 (annealing time; APTES spraying time; Ti(iOPr)$_4$ spraying time)

Process step
The bottles were preheated to a temperature of 100°C.
Preparation of the solutions: 1% w/w APTES in EtOH (pH not adjusted); 10% w/w Ti(i-OPr)$_4$ in EtOH
Activation : • Filling the bottles with HCl (2M) for 1 min • The bottles were thoroughly rinsed with water • Filling the bottles with NaOH (2M) for 1 min • The bottles were thoroughly rinsed with water
Drying in the oven: • 60 minutes (200 and 201) or 50 minutes (202) at 100°C • 4 minutes at RT

Spray-coating of the samples with APTES for 5 x 1 s (The bottle was turned randomly after each spray burst), subsequently dried in the oven for 35 min at 100°C, then left at RT for 4 minutes (p = ~ 5 bars)
Spray-coating of the samples with APTES for 5 x 1 s (The bottle was turned randomly after each spray burst), subsequently dried in the oven for 75 min at 100° (p = ~ 5 bars)
The bottle was left at RT for 4 minutes to cool down
Spray-coating of samples 200 – 202 with $Ti(i\text{-}OPr)_4$ for 4 x 1 s (the bottle was turned randomly after each spray burst) (p = ~ 5 bars)
After the final spray-coating step every sample was dried in the oven (100°C) over night.

Table 10-54: Production of samples 212-214 (annealing time)

Process step
The bottles were preheated to a temperature of 100°C.
Preparation of the solutions: 1% w/w APTES in EtOH (pH not adjusted); 10% w/w $Ti(i\text{-}OPr)_4$ in EtOH
Activation : • Filling the bottles with HCl (2M) with shaking for 1 min • The bottles were thoroughly rinsed with water • Filling the bottles with NaOH (2M) with shaking for 1 min • The bottles were thoroughly rinsed with water
Drying in the oven: • 30 minutes at 100°C • 5 minutes at RT
Spray-coating of the samples with APTES for 6 x 1 s (The bottle was turned randomly after each spray burst, then left at RT for 30 minutes.) (p = ~ 5 bars)
Spray-coating of the samples with APTES for 6 x 1 s (The bottle was turned randomly after each spray burst, then left at RT for 90 minutes) (p = ~ 5 bars)
Spray-coating of samples 212 – 214 with $Ti(i\text{-}OPr)_4$ for 6 x 1 s (The bottle was turned randomly after each spray burst) (p = ~ 5 bars)

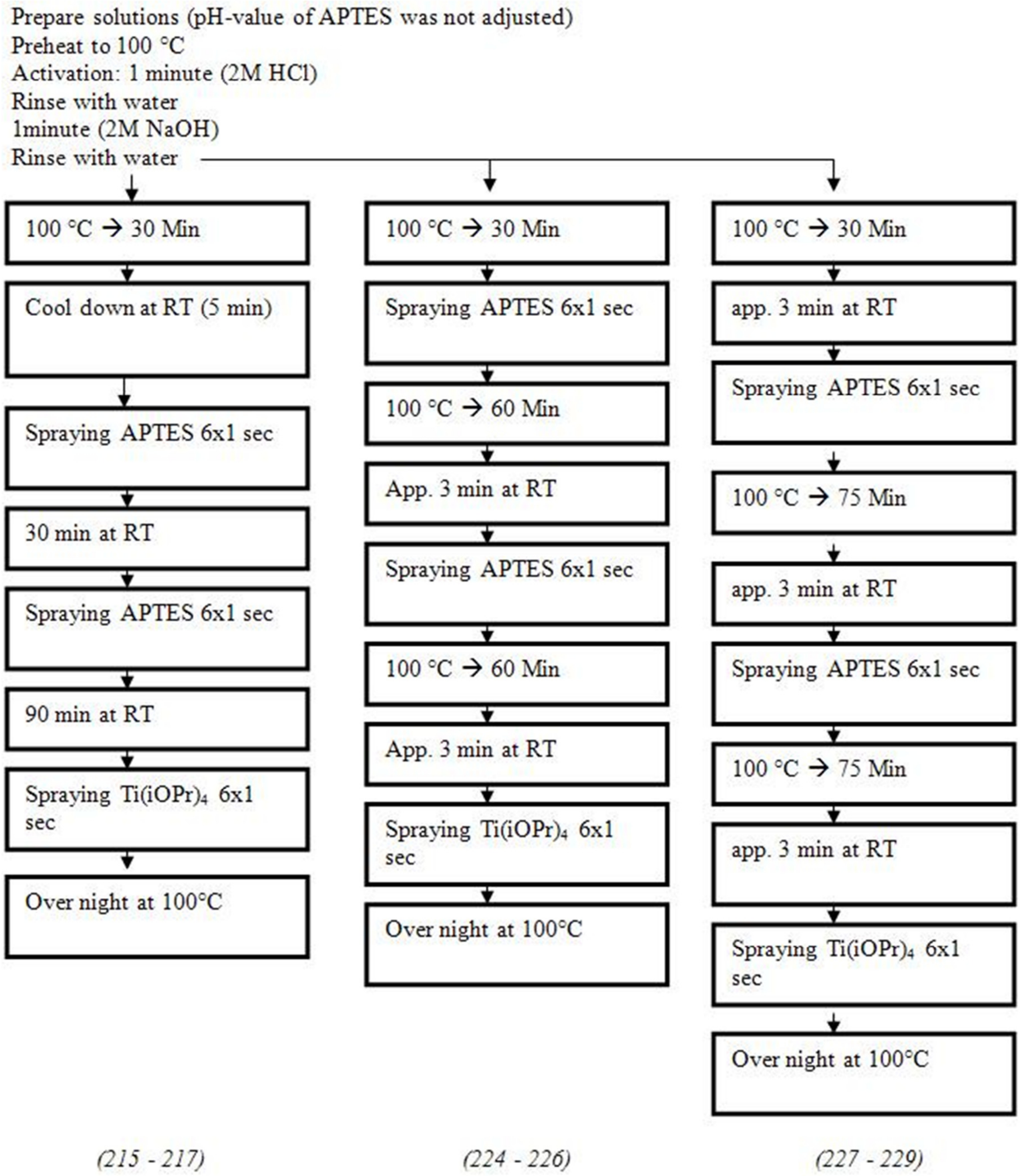


Figure 10-28: Production of samples 215-217 and 224-229

Table 10-55: Production of samples 215-217 (annealing time)

Process step
The bottles were preheated to a temperature of 100°C.
Preparation of the solutions: 1% w/w APTES in EtOH (pH not adjusted); 10% w/w Ti(i-OPr)$_4$ in EtOH
Activation : • Filling the bottles with HCl (2M) with shaking for 1 min • The bottles were thoroughly rinsed with water • Filling the bottles with NaOH (2M) with shaking for 1 min

• The bottles were thoroughly rinsed with water
Drying in the oven: • 30 minutes at 100°C • 5 minutes at RT
Spray-coating of the samples with APTES for 6 x 1 s (The bottle was turned randomly after each spray burst, then left at RT for 30 minutes) (p = ~ 5 bars)
Spray-coating of the samples with APTES for 6 x 1 s (The bottle was turned randomly after each spray burst, then left at RT for 90 minutes) (p = ~ 5 bars)
Spray-coating of samples 212 – 214 with Ti(i-OPr)$_4$ for 6 x 1 s (the bottle was turned randomly after each spray burst) (p = ~ 5 bars)
After the final spray-coating step every sample was dried in the oven (100°C) over night.

Table 10-56: Production of samples 224-226 (annealing time)

Process step
The bottles were preheated to a temperature of 100°C.
Preparation of the solutions: 1% w/w APTES in EtOH (pH not adjusted); 10% w/w Ti(i-OPr)$_4$ in EtOH
Activation : • Filling the bottles with HCl (2M) with shaking for 1 min • The bottles were thoroughly rinsed with water • Filling the bottles with NaOH (2M) with shaking for 1 min • The bottles were thoroughly rinsed with water
Drying in the oven: • 30 minutes at 100°C • 3 minutes at RT
Spray-coating of the samples with APTES for 6 x 1 s (The bottle was turned randomly after each spray burst, then put in the oven for 60 minutes at 100°C, then left at RT for another 3 minutes) (p = ~ 5 bars)
Spray-coating of the samples with APTES for 6 x 1 s (The bottle was turned randomly after each spray burst, then put in the oven for 60 minutes at 100°C, then left at RT for another 3 minutes) (p = ~ 5 bars)
Spray-coating of samples 224 – 226 with Ti(i-OPr)$_4$ for 6 x 1 s (the bottle was turned randomly after each spray burst) (p = ~ 5 bars)
After the final spray-coating step every sample was dried in the oven (100°C) over night.

Table 10-57: Production of samples 227-229 (annealing time)

Process step
The bottles were preheated to a temperature of 100°C.
Preparation of the solutions: 1% w/w APTES in EtOH (pH not adjusted); 10% w/w Ti(i-

OPr)$_4$ in EtOH
Activation : - Filling the bottles with HCl (2M) and shaking for 1 min - The bottles were thoroughly rinsed with water - Filling the bottles with NaOH (2M) and shaking for 1 min - The bottles were thoroughly rinsed with water
Drying in the oven for 30 minutes at 100°C, then left at RT for 3 minutes
Spray-coating of the samples with APTES for 6 x 1 s (The bottle was turned randomly after each spray burst) , then put in the oven for 75 minutes at 100°C, then left at RT for another 3 minutes (p = ~ 5 bars)
Spray-coating of the samples with APTES for 6 x 1 s (The bottle was turned randomly after each spray burst), then put in the oven for 75 minutes at 100°C, then left at RT for another 3 minutes (p = ~ 5 bars)
Spray-coating of samples 227 – 229 with Ti(i-OPr)$_4$ for 6 x 1 s (the bottle was turned randomly after each spray burst) (p = ~ 5 bars)
After the final spray-coating step every sample was dried in the oven (100°C) over night.

Table 10-58: Results of the determination of the hydrolytic class; samples 180-182, 200-202, 212-217 and 224-229 (annealing time; Ti(iOPr)$_4$ spraying time 200-202; APTES spraying time 200-202)

Specification Type II	#	Results [ml 0.01 N HCl/100 ml]	#	Results [ml 0.01 N HCl/100 ml]
Max. 0.40 ml 0.01 N HCl / 100 ml	180	0.56	215	2.56
	181	0.54	216	3.48
	182	0.88	217	2.94
	200	0.74	224	0.44
	201	0.86	225	0.48
	202	0.54	226	0.48
	212	3.22	227	0.56
	213	2.42	228	0.52
	214	2.64	229	0.56

As one can see, the annealing has an enormous influence on the hydrolytic resistance. No annealing decreases the hydrolytic resistance in any event (bottles 212-214). Using two annealing steps with a longer duration yields better results than one short and one very long annealing step (For example 60 minutes and 60 minutes is better than 30 minutes and

90 minutes) (bottles 224-229 compared to 180-182/200-202/215-217). An annealing time of 60 to 75 minutes after each APTES spraying step gives the best results.
Letting the glass substrates cool down to a temperature of app. 60°C improves the results a lot. If the temperature of the bottle is too high, the carrier material (ethanol) is evaporated before it reaches the lower regions of the bottle. This leads to a bad coating in this area and therefore to a higher HCl consumption.

10.3.6 General remarks

Different types of bottles were used in the course of this thesis, shown in Table 10-59.

Table 10-59: Types of glass substrates (sample 177 was made with a bottle from shipment 1)

Shipment number	Color	Used for samples	HCl consumption (blank)
1	white (full transparency)	1 - 80	2.28
2	white (full transparency)	81 - 179	2.42
3	brown	180 - 244	2.91

As one can see, the blank values for the second and the third shipment are worse than the blank value of the first ship (app. 25% difference). It is assumed, that this is one of the major reasons why the results of the last bottles (180-244) are worse than the results in the beginning.

It was noticed as well that shaking the bottle during activation gives better results than just filling them and leave them untouched for a certain period of time.

The following samples are completely the same (for reasons of comparability) and therefore they are not described in detail.

- 180-182 (Hydrolytic resistance: does not fulfill the requirements of HC 2)
- 203-205 (Hydrolytic resistance: does not fulfill the requirements of HC 2)
- 209-211 (Hydrolytic resistance: does not fulfill the requirements of HC 2)
- 221-223 (Hydrolytic resistance: does not fulfill the requirements of HC 2)
- 230-232 (Hydrolytic resistance: does not fulfill the requirements of HC 2)

10.4 Mechanical stability

For assessment of the mechanical stability of the coating, the following experimental setup was created.

10.4.1 Microscope slides

Referring to the results of the preliminary study microscope slides were coated (following the plan shown in Table 10-60). The activation followed a procedure similar to the activation which was used for sample 80, which means submerging the microscope slides in HCl (1M) and NaOH (1M) for 30 minutes, respectively. To account for the autoclaving the slides were submerged in hot water (80°C) hot for 1 hour.
Two different testing methods were used:

- Step 1: Scotch tape test - a stripe of pressure sensitive tape was put on the slide and removed at once
- Step 2: Friction based testing - a paper towel was used to rub at the surface of the slide

Not every microscope slide was tested. The results, presented in Table 10-61, were evaluated optically.

Table 10-60: Production of the samples for assessment of the mechanical stability

Sample #	Activation	APTES	Washing 1	Ti-(i-OPr)$_4$	Washing 2
25	Yes	1% w/w sprayed	Rinsed with EtOH	10% w/w sprayed	Rinsed with EtOH
26	Yes	1% w/w sprayed	Rinsed with EtOH	10% w/w sprayed	Rinsed with EtOH
27	Yes	1% w/w sprayed	Rinsed with EtOH	10% w/w sprayed	Rinsed with EtOH
28	Yes	1% w/w sprayed	Rinsed with EtOH	10% w/w sprayed	No Washing
29	Yes	1% w/w sprayed	Rinsed with EtOH	10% w/w sprayed	No Washing
30	Yes	1% w/w sprayed	Rinsed with EtOH	10% w/w sprayed	No Washing
31	Yes	1% w/w sprayed	No Washing	10% w/w sprayed	Rinsed with EtOH
32	Yes	1% w/w sprayed	No Washing	10% w/w sprayed	Rinsed with EtOH
33	Yes	1% w/w	No Washing	10% w/w	Rinsed with

		sprayed		sprayed	EtOH
34	Yes	1% w/w sprayed	No Washing	10% w/w sprayed	No Washing
35	Yes	1% w/w sprayed	No Washing	10% w/w sprayed	No Washing
36	Yes	1% w/w sprayed	No Washing	10% w/w sprayed	No Washing
37	No	1% w/w sprayed	Rinsed with EtOH	10% w/w sprayed	Rinsed with EtOH
38	No	1% w/w sprayed	Rinsed with EtOH	10% w/w sprayed	Rinsed with EtOH
39	No	1% w/w sprayed	Rinsed with EtOH	10% w/w sprayed	Rinsed with EtOH
40	No	1% w/w sprayed	Rinsed with EtOH	10% w/w sprayed	No Washing
41	No	1% w/w sprayed	Rinsed with EtOH	10% w/w sprayed	No Washing
42	No	1% w/w sprayed	Rinsed with EtOH	10% w/w sprayed	No Washing
43	No	1% w/w sprayed	No Washing	10% w/w sprayed	Rinsed with EtOH
44	No	1% w/w sprayed	No Washing	10% w/w sprayed	Rinsed with EtOH
45	No	1% w/w sprayed	No Washing	10% w/w sprayed	Rinsed with EtOH
46	No	1% w/w sprayed	No Washing	10% w/w sprayed	No Washing
47	No	1% w/w sprayed	No Washing	10% w/w sprayed	No Washing
48	No	1% w/w sprayed	No Washing	10% w/w sprayed	No Washing

Table 10-61: Results for testing of the mechanical stability

Sample #	Results
25	Moderate detachment of the coating, but a continuous layer remains
27	Moderate detachment with both testing methods, but a continuous layer remains
28	Moderate detachment of the coating, but a continuous layer remains
29	Removal of the coating with both methods
31	Removal of the coating with both methods
33	Moderate detachment at scotch tape test, good resistance with paper towel
36	Detachment with scotch tape test, good resistance with paper towel
37	No detachment with scotch tape test, slight detachment at paper towel test
38	Slight detachment at scotch tape test, virtually no detachment at paper towel test
40	Moderate detachment, but a continuous layer remains
41	Bad resistance at scotch tape test, good resistance at paper towel test
43	This slide was heavily coated, therefore the detachment was very strong
44	Virtually no detachment

47	Slight detachment at scotch tape test, no detachment at paper towel test
48	Slight detachment at scotch tape test, some detachment at paper towel test

It seems that the activation procedure has a negative influence on the mechanical stability and that washing steps have a slightly positive influence on the mechanical stability. It is assumed that an increased TiO_2 application leads to a worse mechanical stability.

10.4.2 Testing of the bottles MS 1 and MS 2

Table 10-62: Production of MS1 and MS2

Process step	MS1	MS2
Preheating	85°C	85°C
Activation	1 min HCl (2M) Rinse with water 1 min NaOH (2M) Rinse with water	1 min HCl (2M) Rinse with water 1 min NaOH (2M) Rinse with water
Annealing	30 minutes at 60°C	30 minutes at 85°C
APTES	1% w/w for 5 s	1% w/w for 5 s
Annealing	30 minutes at 60°C	30 minutes at 85°C
APTES	1% w/w for 5 s	1% w/w for 5 s
Annealing	60 minutes at 60°C	60 minutes at 85°C
$Ti(i\text{-}OPr)_4$	10% w/w for 2 x 3 sec	10% w/w for 2 x 3 sec

First the stage 3 airbrush system (see chapter 10.2.3) was filled with water. It was tried to spray water into the bottle to assess the stability of the coating with regard to spray cleaning procedures commonly used in pharmaceutical industry. Unfortunately the water was not nebulized properly and these experiments were skipped.

In the next test compressed air was used to apply stress on the coating. MS 1 showed no change, MS 2 was emitting TiO_2 particles through the bottleneck. In the next step the coating was rubbed with a finger to check if any coating is removed. MS 1 showed good stability, MS 2 showed strong detachment of coating. Then a scrubbing brush was shoved into the bottle and turned. MS 1 showed good stability, MS 2 had a moderate stability.

This is concurrent with the outcome of the other experiments that showed better results with a temperature before spraying of app. 60°C.

10.5 Leaching behavior of APTES and TiO_2

To determine the leaching behavior of the components of the coating (APTES and TiO_2), the following procedure was developed:

A coated bottle is filled with 100 ml purified water (Grade II) (56) and incubated for 1 week at room temperature. After this period of time the water is transferred to a storage container made of borosilicate glass. To establish suitable methods for analyzing the compounds the approaches shown in Table 10-63 were used:

Table 10-63: Methods for evaluation of leaching

Analyte	Method
TiO_2	ICP-OES
APTES	ATR-FTIR spectroscopy
APTES	UPLC-PDA
APTES	UPLC-MS
APTES	TOC measurement
APTES	Ninhydrin derivatization coupled with UV-VIS spectroscopy

The leaching behavior of the samples shown in Table 10-64 was tested.

Table 10-64: Methods used to analyze the leaching behavior of APTES and TiO_2, respectively

Sample #	Method for analysis of APTES	Method for analysis of TiO_2
3	ATR-FTIR	ICP-OES
8	ATR-FTIR	ICP-OES
60	ATR-FTIR	ICP-OES
68	ATR-FTIR	ICP-OES
71	ATR-FTIR	ICP-OES
80	ATR-FTIR	ICP-OES
82	ATR-FTIR / TOC	Not analyzed
87	ATR-FTIR / TOC	Not analyzed
92	ATR-FTIR	Not analyzed
94	ATR-FTIR	Not analyzed

For all methods the amount of the aqueous solution (100 ml - the solution containing the analyte) was reduced to a volume of app. 5 to 10 ml using a rotary evaporator.

10.5.1 IR-measurements

A reference spectrum was recorded to choose a proper peak for calibration. The spectra were recorded with an ATR device. Accurate ATR reference spectra were not available, therefore it was rather tricky to assign the wavenumber to the related vibrational modes. Additionally; the peaks in the area of higher wavenumbers vanished (for example NH_2 peaks in the neighborhood of 3300 – 3500 cm^{-1}). A band with good visibility was the C-O-Si vibration in the area of 1045 cm^{-1}. For quantification only the peak height and not the peak area was used and applied to the law of Beer-Lambert (Equation 23). For the calculations spectra at different concentrations (for example Figure 10-30) were recorded. The results are shown in Table 10-65.

Table 10-65: FTIR calibration curve for the APTES measurement

Concentration [mol/l]	Dilution	Absorption at ~1045cm^{-1}
4.27E+00	-	0.72524
8.55E-01	1 to 5 (=1+4)	0.10266
4.27E-01	1 to 10	0.04784
1.71E-01	1 to 25	0.0206
8.55E-02	1 to 50	0.0108
6.10E-02	1 to 70	0.00672
4.75E-02	1 to 90	0.00536
4.27E-02	1 to 100	0.00641
3.88E-02	1 to 110	0.00512
3.29E-02	1 to 130	0.00335
2.85E-02	1 to 150	0.00307
2.37E-02	1 to 180	0.00296
1.94E-02	1 to 220	-

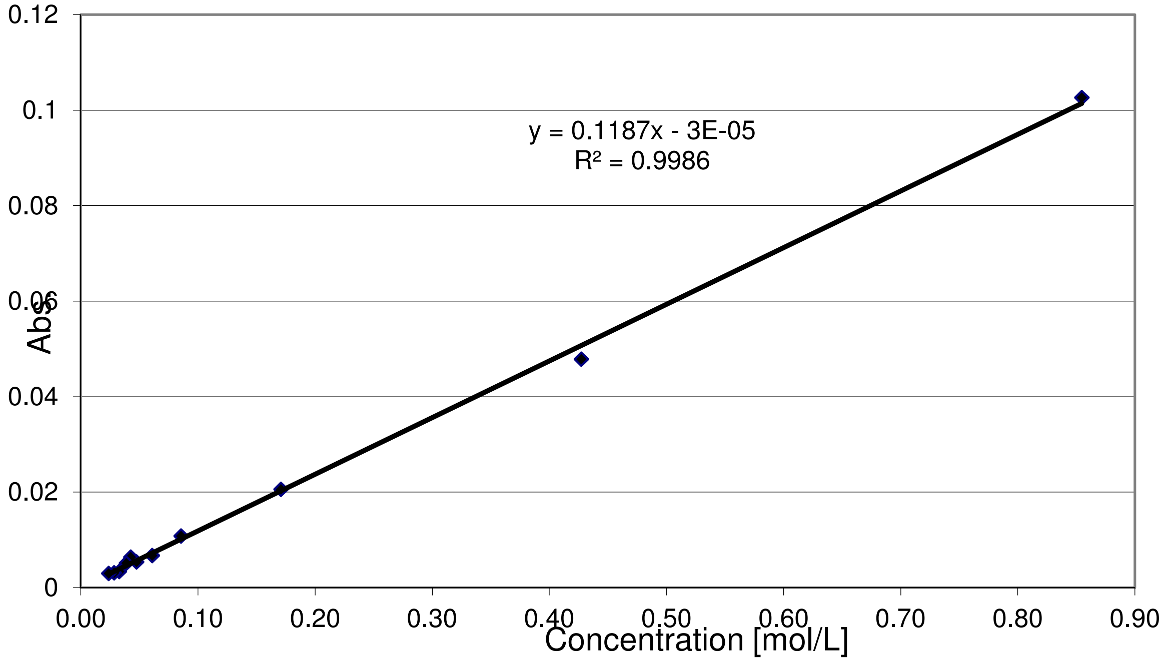


Figure 10-29: FTIR calibration curve for APTES analysis

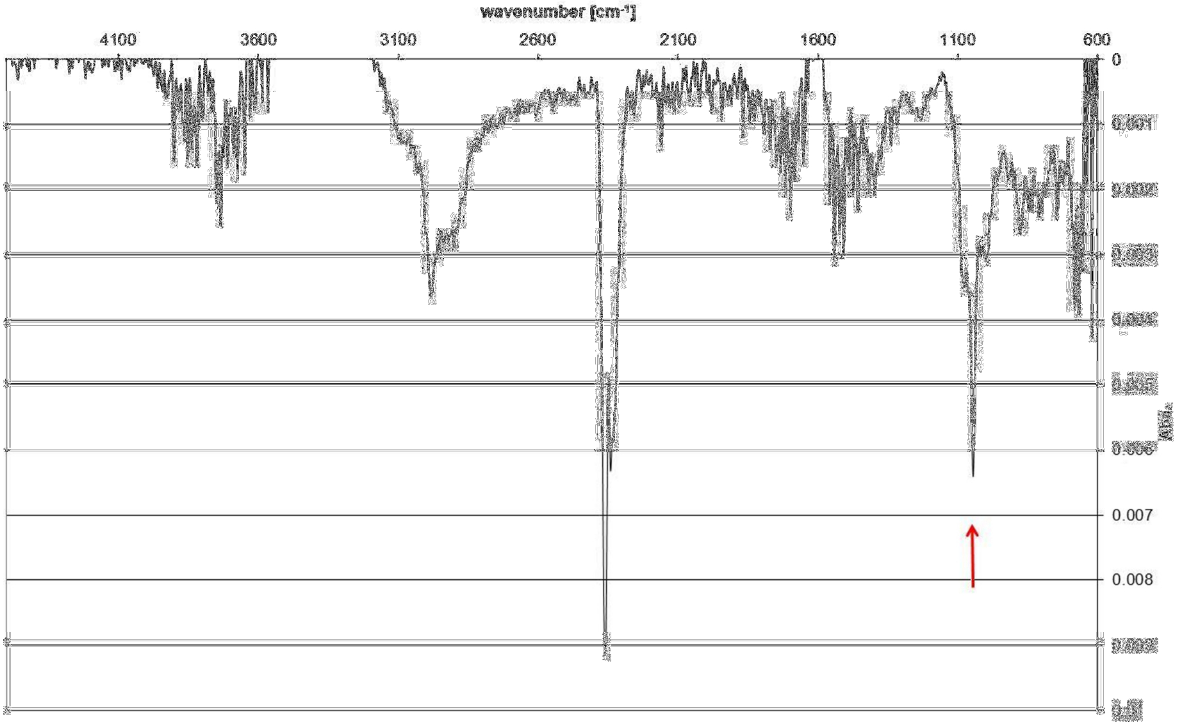


Figure 10-30: Example of an IR spectrum (1 to 100 dilution). The red arrow indicates the selected vibrational mode.

The last dilution (1 to 220) showed no significant extinction. Using these results we were able to compute the calibration curve shown in Figure 10-29. Using the calibration curve we got the concentrations shown in Table 10-66 and Figure 10-31.We have to consider that hydrolysis reactions can lead to a cleavage of the ethoxy side chains, which leave as ethanol. This means that we have to expect a decline of the peak strength with increasing time. Due to these limitations other analysis techniques were taken into consideration, as shown in the other chapters of section 10.5.

Table 10-66: APTES concentrations of leaching samples

Sample #	Concentration [mol/l]
3	2.84E-02
8	1.51E-02
60	1.27E-02
68	9.01E-03
71	7.83E-03
80	no visible peak

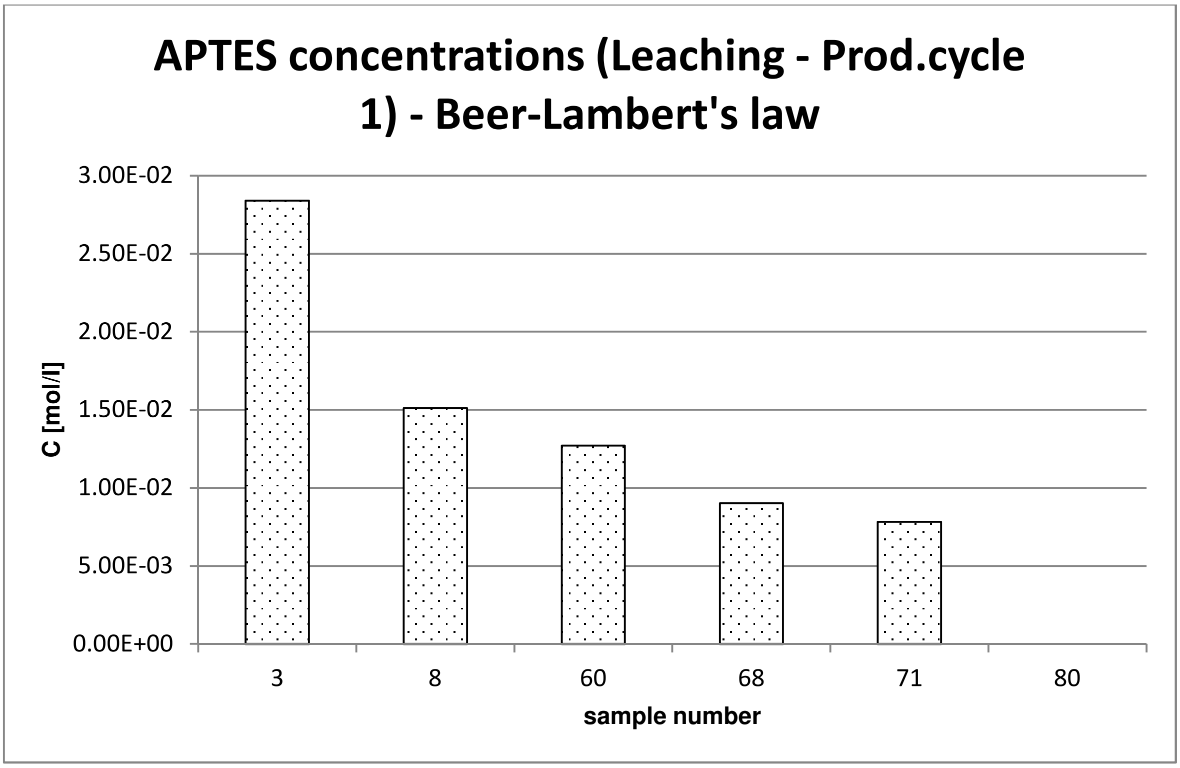


Figure 10-31: IR spectrometer APTES measurements – results using Beer-Lambert's law

The results show that the bottle with short annealing, but rather long spraying shows bad results steps. Decreasing the spraying times improves the leaching behavior. Increasing the silanization time improves the results a lot; no APTES in the solution was observable.

In a second attempt the data obtained was processed using a multivariate data analysis approach, carried out by RCPE. The calculated results of the ATR-IR measurement are shown in Table 10-67 and Figure 10-32. "Cut" means the range of data points which were taken into consideration was limited from 1494.7 cm^{-1} to 839.0 cm^{-1}. The results denoted with uncut include the whole range of data point (4500 cm^{-1} to 600 cm^{-1}).

Table 10-67: APTES concentrations of leaching samples (MVDA)

	Conc. [mol/l]	
Sample number	„cut“	„uncut“
80	0.0009	0.0150
71	0.0084	0.0238
68	0.0094	0.0214
60	0.0106	0.0282
8	0.0147	0.0236
3	0.0528	0.0348

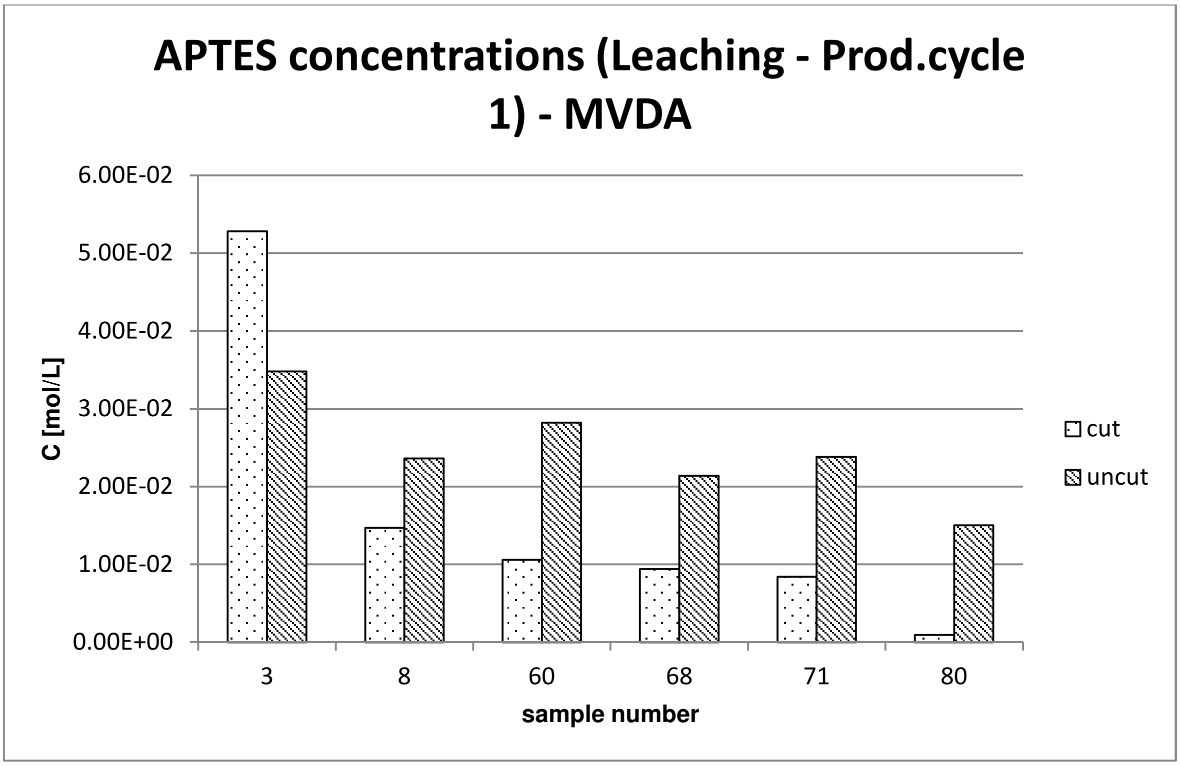


Figure 10-32: IR spectrometer APTES measurements – results using the MVDA

The European Pharmacopoeia (57) knows no threshold values for APTES, but it is defined that the maximal value for the total organic carbon content in water for parenteral use is 0.5 ppm. Therefore, it is important to be below this value.

These results are in good accordance with the results of the hydrolytic resistance determination. This means activation as well as prolonged annealing times improves the quality of the coating which leads to a decreased loss of film components and a better hydrolytic resistance. Due to the mentioned drawbacks FTIR is not the ideal method for determination of the APTES leaching.

10.5.2 UHPLC-measurement

In the following attempt the eligibility of UHPLC separation followed by UV/VIS-photo diode array detection or MS with ESI was tested.

However, pre-experiments showed that this method is of little use. The analyte (APTES) showed far too little UV activity to measure at low concentrations. (Another approach where the APTES is derivatized to increase its UV activity will be part of future experiments, shown in chapter 10.5.4.) APTES tends to form oligomers and because the ethoxy side chain is very prone to hydrolysis. Therefore, the MS spectrum showed lots of artifacts. Many different m/q peaks were visible (monomers, dimers, trimers, monomers which lost one side chain …). Furthermore, the separation was not good enough and would need thorough optimization. Therefore, UHPLC separation was discarded for the moment. One of the recorded mass spectra is shown in Figure 10-33.

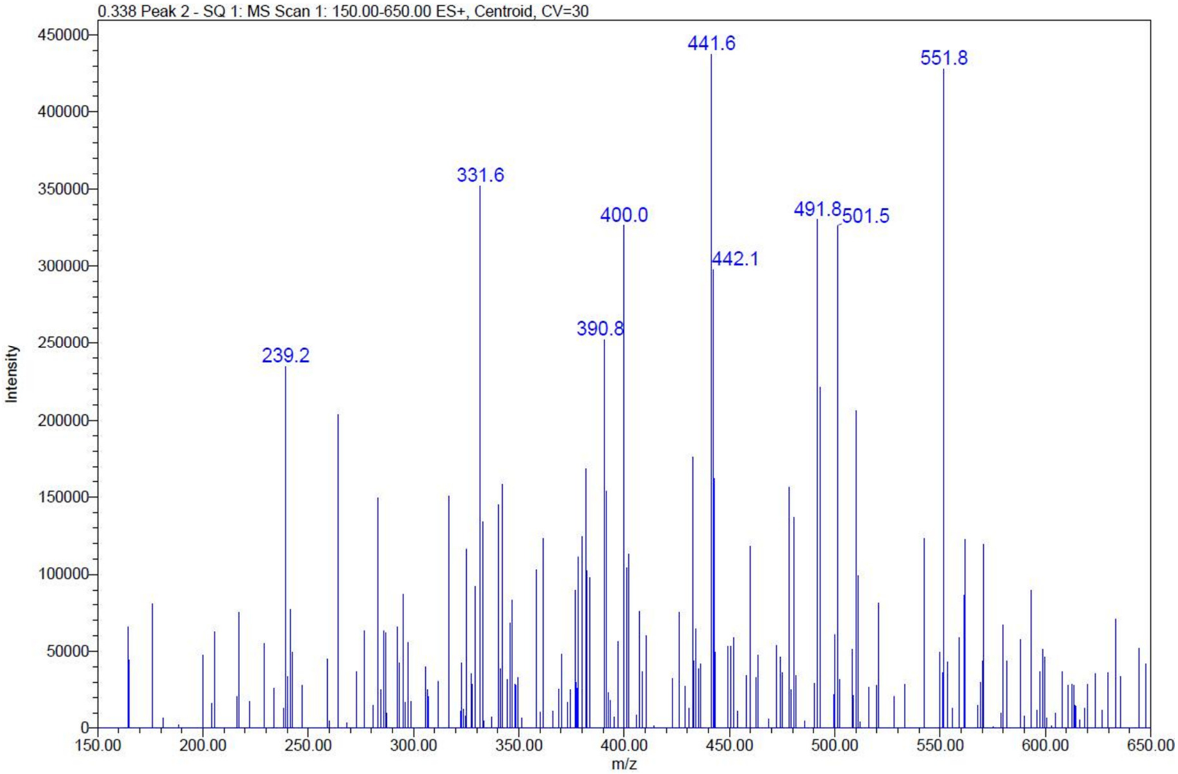


Figure 10-33: Mass spectrum of APTES at t=0.338 min

10.5.3 TOC-measurement

If we assume that the only organic compound in the aqueous solution is APTES, we can take TOC measurements into consideration. The TOC measurements were conducted at the “Institute of Chemical Engineering and Environmental Technology“ at Graz University of Technology. For a first estimation of the usability of this method two samples were measured. A suitable method should be capable of detecting TOC concentrations of less than 0.5 ppm. 0.5 ppm is the threshold for the total organic carbon content in bulk water used to make parenterals (57). Unfortunately the limit of quantification of the TOC analysis method is 5 ppm. Nevertheless, some samples were measured with TOC assess if the method might be useful in the future. (An improvement of the catalyst will be taken into consideration if the results show that the method is applicable). Before handing the samples over to the analyzing institute, their volume was reduced using a rotavapor (as stated above). The concentration was increased app. twentyfold. (Starting volume: 100 ml; final volume app. 5 ml)

The results of the TOC measurements are shown below:

- Sample number 82: Total organic carbon content: 36.44 mg/l
- Sample number 87: Total organic carbon content: 30.84 mg/l

These values are above the limit of 0.5 ppm, but maybe the usage of the rotavapor led to a contamination with other organic compounds.

10.5.4 UV/VIS-measurement with ninhydrin derivatization

As mentioned above, another analysis method for APTES determination which was taken into consideration was the derivatization of APTES with ninhydrin (Chapter 9.6.2.4). The method was working, but it is limited to an amine concentration of app. 1 mmol/l. This is the same as 105 ppm TOC, so the ninhydrin derivatization was discarded because the method is less sensitive than the TOC measurement.

10.6 Assessment of the appearance of coated bottles

Another requirement was that the coated bottles should have enough transparency to be inspected optically and no visible particles should be transferred into the solution. It is not a requirement that the coating is uniform.

Examples of treated and untreated bottles are shown in Figure 10-34 to Figure 10-41. The results indicate that

- the appearance of the bottles is influenced exclusively by the TiO_2 layer.
- the relation of TiO_2 application and appearance of the coating depends on the spraying pressure and the spraying time.
- a lower spraying pressure gives a better transparency.
- a higher spraying time leads to a decreased transparency.
- less coating particularly in the bottom region leads to a decreased hydrolytic resistance.
- washing steps do not change the optical appearance of the samples.

A complete description of every sample can be found in the appendix, chapter 12.1.

Figure 10-34: An uncoated (untreated) bottle

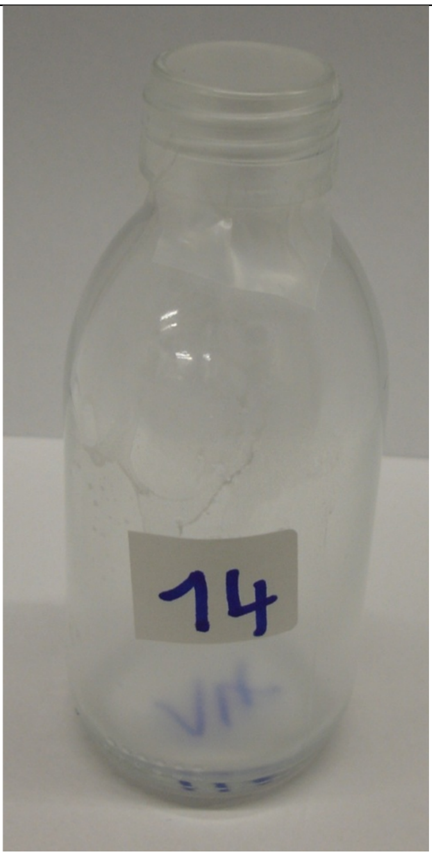


Figure 10-35:Sample 14 (3-5 sec 10% w/w $Ti(iOPr)_4$ at 100°C; p=5bars)

Figure 10-36: Sample 55 (15 sec 10% v/v $Ti(iOPr)_4$ at 100°C; p=5bars)

Figure 10-37: Sample 84 (6 sec 10% w/w $Ti(iOPr)_4$ at 100°C; p=4bars)

Figure 10-38: Sample 102 (3.5 sec 10% w/w $Ti(iOPr)_4$ at 100°C; p=4bars)

Figure 10-39: Sample 100 (7 sec 10% w/w $Ti(iOPr)_4$ at 100°C; p=4bars)

Figure 10-40: Sample 163 (6 sec 10% w/w $Ti(iOPr)_4$ at 60°C; p=5bars)

Figure 10-41: sample 117 (9 sec 10% w/w $Ti(iOPr)_4$ at 65°C; p=5bars)

Figure 10-42: Sample 202 (6 sec 10% w/w Ti(iOPr)4 at 60°C; p=5bars)

10.7 Contact angle measurements

To elaborate our knowledge about the basic principles of the barrier layer some contact angle measurements were conducted. The samples were prepared using the well-established process described in Table 10-52, but instead of bottles the whole process was done with soda-lime glass microscope slides. Due to the fact that the stage 3 spraying apparatus is not suitable for coating microscope slide, the slides were put into a beaker and treated in the same way as the bottles. This yielded coatings with less homogeneity. The slides were not uniformly coated and had areas with different thicknesses, denoted “high thickness” and “low thickness”.

Several slides were made and contact angles were measured for each point (this means high and low thickness). The obtained data is shown in Table 10-68. The method used was the sessile drop technique with deionized grade II water and a droplet size of app. 2 µl. Water at 22°C has the following properties (58):

- Interfacial tension	72.3 mN/m
- Disperse fraction	18.7 mN/m
- Polar fraction	53.6 mN/m
- Density	0.997 g/cm³
- Viscosity	0.995 mPa*s

Table 10-68: Results of the contact angle measurements

Slide label	Description	Contact angle [°]
Blank	Slide No. 1	22.3
	Slide No. 2	24.9
	Slide No. 3	18.8
	Slide No. 4	20.5
CA_1	High thickness	132.9
	Low thickness	66.4
CA_2	High thickness	129.1
	Low thickness	87.5
CA_3	High thickness	134.8
	Low thickness	57.7
CA_4	High thickness	132.0
	Low thickness	57.9

It is uncertain, if we can transfer the obtained results to the bottles because of the large inhomogeneities. As we can see in the table above, thickly coated areas show significant higher contact angles than rather thinly coated areas. We can say that thickly coated areas show super-hydrophobic behavior. This is good, because we want to prevent transfer of alkali metals and alkaline earth metals from the glass surface to the liquid.

11 Summary and conclusions

Different samples were produced to evaluate the influence of variations of the key process parameters (as defined in Table 10-10) on the final result (mainly the hydrolytic class, but also leaching behavior, transparency, mechanical stability etc.).

After the first production cycles the following process parameters were defined as crucial:

a. Washing steps
b. Activation with HCl/NaOH
c. Application of APTES
d. Application of $Ti(i\text{-}O\text{-}Pr)_4$
e. Annealing (temperature and time)

The results concerning the influence of these parameters can be summarized as follows:

11.1 Washing steps

Washing steps before and after silanization and after $Ti(iOPr)_4$ coating showed no significant improvement of the hydrolytic resistance. For reasons of process simplification washing was discarded. Nevertheless washing may be beneficial to reduce APTES and TiO_2 leaching.

11.2 Activation with HCl/NaOH

The activation step has a great influence on the resulting hydrolytic class. Although one sample which was not treated with HCl/NaOH showed HC 2 (sample 9), it was observed that samples which were activated showed far better results. Different activation procedures were tested, like

- Spraying of acid and base, respectively
- Different reaction temperatures
- Different reaction times

Surprisingly, it makes a difference if the bottles are shaken after filling with acid or base. Apparently the energy input while shaking improves the results. Unfortunately, we had no method to directly analyze the surface properties; therefore we could only conclude from the final results of the hydrolytic class determination. It was observed that activation using solutions with a concentration of 2 M for 1 minute without heating gives the best results. On the other hand the mechanical stability is better if the bottles are not activated.

11.3 Application of APTES

For the APTES spraying various pressure settings were examined. (See 10.2.4 - Characterization of the spraying apparatus). In the course of this thesis it was noticed that the APTES application is one of the most influential parameters. Many different approaches were tested and the following conclusions were drawn:

- Better results were achieved when a series of one second spray bursts is used instead of one long burst. It improves the hydrolytic resistance if the APTES application is divided in two parts with an annealing step in between.
- In general, we can say that more APTES gives better results. The formation of a densely packed APTES layer at the glass surface is the most critical step for a good barrier layer.
- In literature the most popular solvents for surface silanization with APTES are organic solvents like cyclohexane and toluene, but there are also other approaches that use solvents like ethanol (59) or water (60). The advantages of ethanol are quite obvious: it is comparably cheap, its non-toxic (unlike methanol) and has a high volatility. Tests using cyclohexane did not show good result. Therefore, we may say that ethanol as solvent gives satisfying results for our purposes. Potential drawbacks are that ethanol is inflammable and the explosion risk.
- A higher APTES concentration (1% vs. 2%) did not decrease the HCl consumption. For economic reasons the concentration used was 1% w/w.
- It is unnecessary to adjust the pH-value of the APTES solution, although in literature it is stated that it is necessary (1).

The temperature of the glass substrate while spraying has a great influence on the formation of the APTES layer. If the temperature is too high the carrier material (boiling point of ethanol ~ 78°C) evaporates too fast. This leads to a bad spatial distribution and worsens the quality of the coating. If the temperature is too low, the results are also bad. Reasons for this can be that the liquid is gathering at the bottom of the bottle and the deposition of APTES is concentrated in some areas of the bottle which leaves voids in other areas. Temperatures of app. 60°C (= app. 3 minutes cool down at room temperature after preheating the bottles to 100°C) give good results. It is virtually impossible to obtain good results without a reduced temperature during the spraying process.

11.4 Application of Ti(i-O-Pr)$_4$

The Ti(i-O-Pr)$_4$ spraying step has surprisingly little influence on the final result. Different concentrations were examined (5% vs. 10%) and also different spraying times (from 3.5 to 9 seconds), but the influence on the obtained results was negligible. With regard to the transparency criterion shorter Ti(i-O-Pr)$_4$ spraying times should be preferred over longer spraying times.

The coating itself has no influence on the HCl consumption. This was tested by application of the coating on SCHOTT-DURAN borosilicate glass substrate. No change in the HCl titration was observable.

11.5 Annealing

The second high-impact key parameter is the annealing time. In order to form a good APTES layer, which is also crucial for the formation of a good TiO_2 layer the reaction time must be long enough. A temperature of 100°C is preferable. The resulting hydrolytic resistance is better if two rather long (60-75 minutes) annealing steps are used instead of one short and one very long annealing step.

11.6 Mechanical stability

All the bottles will be thoroughly washed before use, this leads to the following considerations:

- All TiO_2 particles which are loosely bound to the glass surface will be removed. This reduces the issue of film component leaching into the pharmaceutical solution.
- All the particles that stay at the surface should have a satisfying mechanical stability.

- The hydrolytic class of the bottles should be determined after the final washing to check if the washing and a possible removal of film areas reduces the hydrolytic resistance.

11.7 Leaching behavior

The use of ICP-OES for quantification of the TiO_2 leaching is proposed, because the method is perfectly suitable to satisfy our demands. Furthermore it would make sense if the TOC measurements are used for the APTES determination (if it is possible to use a TOC analyzer with a catalyst good enough to get a limit of quantification of 0.5 ppm), because the method allows convenient comparison of the values prescribed in the European Pharmacopoeia (57). It seems that a longer annealing time decreases the leaching of film components. The TiO_2 leaching could be adjusted by spraying less $Ti(iOPr)_4$. If the leaching of the film components is too high washing should be considered. But the bottles will be washed before use, so this problem might be comparably small.

11.8 Optical transparency

At the beginning of this thesis we were trying to find the best spraying conditions in order to get a continuous and "nice" layer at the inner surface of the bottle. But as we found out later a spraying pressure of 5 bars gives better a hydrolytic resistance than 4 bars. Regarding this fact we abandoned the goal to get a uniform coating. When spraying $Ti(iOPr)_4$ for 6 seconds with 5 bars, the opacity of the bottles is too high. Spraying less $Ti(iOPr)_4$ will improve the transparency.

11.9 The "ideal" coating process

The following process gives the most promising results:

- Activation with 2M HCl and NaOH for 1 minute each
    - Shaking the bottles during the activation
    - Rinsing the bottles with deionized water after acid and base treatment
- Drying in the oven for 30 minutes at 100°C
- Cool down to 60°C (app. 3 minutes at room temperature)
- Spray APTES (1% w/w in EtOH) for 6 to 8 seconds with 5 bars
- Annealing for 60 to 75 minutes at 100°C

- Cool down to 60°C (app. 3 minutes at room temperature)
- Spray APTES (1% w/w in EtOH) for 6 to 8 seconds with 5 bars
- Annealing for 60 to 75 minutes at 100°C
- Cool down to 60°C (app. 3 minutes at room temperature)
- Spray Ti(iOPr)4 (10% w/w in EtOH) for 4 to 6 seconds with 5 bars
- Annealing for several hours at 100°C

The results are strongly influenced by the quality of the used glass substrate. It is virtually impossible to reach hydrolytic class 2 with the last shipment of bottles. A certain quality of the raw material is highly desirable.

11.10 Outlook

The last results (Table 12-34 - Table 12-37) show clearly that the most influential step on the hydrolytic resistance is the APTES application. An increase of the spraying time leads to an improvement of the hydrolytic resistance as well as an extension of the silanization time. An appropriate temperature while spraying is also absolutely necessary to get satisfying results. Future work will go into this direction.

It may be useful to improve the spraying apparatus. A different nozzle would allow alteration of the spraying process (for example other droplet sizes). This may lead to an increased hydrolytic resistance.

Besides that, the activation process could be optimized if proper methods for surface characterization are established. It might be useful to examine the influence of washing on the leaching behavior of APTES and TiO_2 particles. If we take into account that containers used in pharmaceutical industry are washed thoroughly before use sufficient emphasis should be put on these issue. The washing steps are mandatory. Commonly used cleaning procedures will apply stress on the coating; therefore this issue is closely related to mechanical stability.

12 Appendix

12.1 Optical transparency

General remarks (if not denoted differently):

- front face = side with labeling
- low opacity = fulfills the transparency requirements

- medium opacity = does not fulfill the transparency requirements
- high opacity = does not fulfill the transparency requirements
- Sample 180 and all further samples were made using brown glass bottles. It was very difficult to assess the transparency correctly. If possible, we tried to describe the opacity, but these descriptions have a reduced reliability.

Table 12-1: Optical appearance of samples 81-96

Sample number	Sample description Opacity	Consistency	Anomalies
81	Low	Formation of a ring in the center of the bottle	-
82	Low	Less coating in the lower region	-
83	Low	Less coating in the lower region	-
84	Low	Formation of a ring in the center of the bottle	-
86	Low	Less coating in the lower region	-
87	Low	Less coating in the lower region	-
88	Low	Formation of a ring in the center of the bottle	-
89	Medium	Less coating in the lower region	-
90	Medium	Good	-
91	Medium	Good	-
92	Medium	Good	-
93	Medium	Formation of a ring in the center of the bottle	-
94	Medium	Formation of a ring in the center of the bottle	-
95	High	Formation of a ring in the center of the bottle	-
96	High	Good	-

Table 12-2: Optical appearance of samples 97-112

Sample number	Sample description Opacity	Consistency	Anomalies
97	High	Good	Beginning formation of a ring at the bottom of the bottle
98	High	Less coating in the lower region	-
99	High	Less coating in the lower region	-
100	High	Less coating in the lower region	TiO_2 trickles down from the bottleneck on the front face
101	-	Less coating in the lower region	-
102	High opacity in the upper part, low opacity in the lower part		-
103	High opacity in the upper part, low opacity in the lower part		-
104	High opacity in the upper part, low opacity in the lower part		-
105	Medium	Less coating in the lower region	-
106	Medium	Good	-
107	High opacity in the upper part, low opacity in the lower part		-

108	Medium	Less coating in the lower region	-
109	Medium	„Web structure“ in the lower region	stains
110	High	Bad	stains
111	High	Good	some splashes
112	High	Good	-

Table 12-3: Optical appearance of samples 113 - 130

Sample number	Sample description		
	Opacity	Consistency	Anomalies
113	High	Continuous	TiO_2 trickles down from the bottleneck on the front face
114	High	Less coating in the lower region	TiO_2 trickles down from the bottleneck on the front face
115	High	A little less coating in the lower region	TiO_2 trickles down from the bottleneck on the front face
116	High	Continuous	TiO_2 trickles down from the bottleneck on the front face
117	High	Continuous	TiO_2 trickles down from the bottleneck on the right side of the bottle
118	High	Continuous	TiO_2 trickles down from the bottleneck on the right side of the bottle
119	High	Continuous	„Web structure“ on the rear side
120	High	Continuous	TiO_2 trickles down a little bit from the bottleneck on the front face
121	High	Continuous	TiO_2 trickles down from the bottleneck on the front face
122	Medium	A little less coating in the lower region	-
123	Medium	Continuous	More coating on the rear side
124	Medium	Less coating in the lower region	Anomaly on the right side of the bottle
125	High	Less coating in the lower region	TiO_2 trickles down from the bottleneck on the front face
126	High	Less coating in the lower region	TiO_2 trickles down from the bottleneck on the right side of the bottle
127	High in the upper region, medium in the lower part		TiO_2 trickles down from the bottleneck on the front face
128	Medium	Virtually no coating in the lower region	Rather little coating on the rear side of the bottle
129	Low	Strongly coated in the middle region	„Web structure“; little coating on the rear side of the bottle
130	High	Strongly coated in the middle region	-

Table 12-4: Optical appearance of samples 131 - 146

Sample number	Sample description		
	Opacity	Consistency	Anomalies

131	Transparent	-	Whitish in the lower half of the bottle, dirty appearance
132	Transparent	-	dirty appearance in the lower part of the bottle, “droplet”-structure
133	Transparent	-	Good appearance; a little bit limy
134	Transparent	-	Good appearance; a little bit limy
135	Transparent	-	“droplet”-structure; limy
136	Transparent	-	Good appearance; limy
137	Transparent	-	The lower half of the bottle is very “dirty”
138	Transparent	-	“droplet”-structure; “dirty” in the middle of the bottle
139	Transparent	-	Good appearance
140	Transparent	-	Good appearance
141	Transparent	-	Good appearance
142	Transparent	-	Good appearance
143	-	-	Blank
144	-	-	Blank
145	Transparent	-	Good appearance; limy in the upper part of the bottle
146	Transparent	-	Good appearance; a little bit opaque in the upper part of the bottle

Table 12-5: Optical appearance of samples 147 - 164

Sample	Sample description		
number	Opacity	Consistency	Anomalies
147	High	Good	Stains on the rear side of the bottle
148	High	Good	A little bit “dirty” on the rear side
149	High	Good	A big stain on the rear side; Unsteady in the lower part of the bottle
150	Medium	poor	TiO2 trickles down on the front side
151	High	Good	-
152	High	Good	Some voids on the rear side
153	High	Good	White stains on the right side
154	High	Good	Some stains on the rear side
155	High	Good	Droplets on the right side; a big stain on the left side
156	High	Good	Unsteady in the lower part of the bottle
157	High	Poor	Trickles down on each side of the bottle
158	High	Good	A little less coating in the upper half of the bottle
159	High	Good	-
160	Medium	Big voids in the coating	-
161	Medium	Big voids in the coating	-
162	High	Good	Voids on the front side
163	High	Good	Some voids on the front and rear side

164	High	Good	Voids on each side

Table 12-6: Optical appearance of samples 165 - 179

Sample number	Opacity	Sample description Consistency	Anomalies
165	Medium	A little less coating in the lower region	-
166	Medium	Continuous	-
167	Medium	Less coating in the lower region	-
168	Medium	Continuous	-
169	Medium	Less coating in the lower part of the bottle	Some white splashes on the rear side
170	Medium	Less coating in the lower part of the bottle	-
171	Medium	Continuous	Some white splashes on the rear side
172	Medium	Continuous	-
173	Medium	Continuous	Accumulation at the bottleneck
174	High	Formation of a ring in the center of the bottle	Really bad appearance, strong segmentation
175	High	Less coating in the lower region	Really bad appearance
176	Medium	Too much coating in the upper region	Really bad appearance, more coating on the rear side, TiO_2 trickles down
177	High	Formation of a ring in the center of the bottle	Bad appearance
178	Medium	Continuous	some white splashes on the rear side
179	Medium	Formation of a ring in the center of the bottle	TiO_2 trickles down on the rear side of the bottle

Table 12-7: Optical appearance of samples 180 – 188

Sample number	Opacity	Sample description Consistency	Anomalies
180	?	Formation of a ring in the middle of the bottle	TiO_2 trickles down on front of the bottle, more coating on the bottom of the bottle
181	?	Formation of a ring in the middle of the bottle	More coating on the bottom of the bottle
182	?	Formation of a ring in the middle of the bottle	TiO_2 trickles down on front of the bottle, more coating on the bottom of the bottle

183	?	Formation of a ring in the middle of the bottle	-
184	?	Formation of a ring in the middle of the bottle	TiO_2 trickles down on front of the bottle
185	?	-	-
186	?	Formation of a ring in the middle of the bottle	More coating on the bottom of the bottle
187	?	Formation of a ring in the middle of the bottle	TiO_2 trickles down on front of the bottle, more coating on the bottom of the bottle
188	?	Formation of a ring in the middle of the bottle	TiO_2 trickles down on front of the bottle, more coating on the bottom of the bottle

Table 12-8: Optical appearance of samples 189 - 197

Sample number	Sample description		
	Opacity	Consistency	Anomalies
189	?	Formation of a ring in the middle of the bottle	-
190	?	More coating in the upper part of the b., more coating on the rear side of the b.	-
191	?	Formation of a ring in the left front section of the b.	-
192	?	Bad	TiO_2 trickles down on each side of the bottle
193	?	Bad; more coating in the upper part of the b.	TiO_2 trickles down on the front side of the bottle
194	?	Bad; more coating in the upper part of the b.	TiO_2 trickles down on each side of the bottle
195	?	Formation of a ring in the middle of the bottle	-
196	?	Formation of a ring in the middle of the bottle	-
197	?	Formation of a ring in the middle of the bottle	-

Table 12-9: Optical appearance of samples 200 – 208

Sample	Sample description		

number	Opacity	Consistency	Anomalies
200	Low	Good	One big stain on the right front side
201	Low	More coating in the front section	-
202	Low	Good	One big stain on the left front side
203	Low	“Patterns”	Cracks in the coating at the bottom of the bottle
204	Low	More coating in the upper and the front section of the b.; “patterns”	Cracks in the coating at the bottom of the bottle
205	Low	More coating in the upper section of the bottle	Cracks in the coating at the bottom of the bottle
206	Low	More coating in the front section of the bottle	-
207	High in the upper section, rather good transparency in the lower section of the bottle	More coating in the upper third of the bottle	-
208	Low	-	One big stain at the rear side of the bottle

Table 12-10: Optical appearance of samples 209 - 217

Sample	Sample description		
number	Opacity	Consistency	Anomalies
209	Low	Good	One big stain on the left front side; TiO_2 trickles down on the rear side
210	Low	Good	TiO_2 trickles down on front of the bottle; on big stain on the rear side of the bottle
211	Low	Good	-
212	High in the upper 2/3 of the bottle	Bad	Individual particles at the bottom of the bottle; formation of a hole in the bottom; TiO_2 trickles down on each side of the bottle
213	High	Bad	Cracks in the coating at the bottom of the bottle; TiO_2 trickles down on each side of the bottle
214	High in the upper 2/3 of the bottle	Bad	Individual particles at the bottom of the bottle; TiO_2 trickles down on each side of the bottle
215	Low in the upper 2/3 of the bottle, good	Bad	Individual particles at the bottom of the bottle; when turning the bottle upside down TiO_2 is fluttering out of the

	transparency in the lower 1/3 of the bottle		bottle; TiO_2 trickles down on each side of the bottle
216	High opacity in upper section of the bottle, virtually no coating in the lower 1/3 of the bottle	Bad	Individual particles at the bottom of the bottle; when turning the bottle upside down TiO_2 is fluttering out of the bottle; TiO_2 trickles down on each side of the bottle
217	High opacity in upper section of the bottle, virtually no coating in the lower 1/3 of the bottle	Bad	When turning the bottle upside down TiO_2 is fluttering out of the bottle; TiO_2 trickles down on each side of the bottle; some parts of the bottom are uncoated

Table 12-11: Optical appearance of samples 218 – 226

Sample number	Sample description		
	Opacity	Consistency	Anomalies
218	Low	Strong fragmentation	Dots at the rear side of the bottle; some voids in the coating
219	Medium	Good	TiO_2 trickles down a little bit
220	Medium	Rather good	TiO_2 trickles down a little bit on the left side of the bottle; when turning the bottle upside down TiO_2 is fluttering out
221	Low	Formation of a ring in the middle of the bottle	-
222	Medium	Good	“Patterned” structure
223	Low medium	More coating in the front and upper section of the bottle	TiO_2 trickles down on the rear side of the bottle
224	Low	Strong fragmentation	TiO_2 trickles down a little bit
225	Low	Fragmentation; less coating in the lower part of the bottle	TiO_2 trickles down
226	Low	Less coating in the lower part of the bottle	When turning the bottle upside down TiO_2 is fluttering out; TiO_2 trickles down on the rear side of the sample

Table 12-12: Optical appearance of samples 227 - 235

Sample number	Sample description		
	opacity	consistency	Anomalies
227	Low	Rather good	One stain on the rear side of the

			bottle; TiO_2 trickles down on the right side of the bottle
228	Low	Rather good	One stain at the rear side of the bottle; TiO_2 trickles down on the front side of the bottle
229	Low	Rather good	One stain on the front side of the bottle; TiO_2 trickles down on the rear side of the bottle
230	Low	Rather good	One stain on the rear side of the bottle
231	Medium	Formation of a ring in the middle of the bottle	-
232	Low	Good	-
233	Low	Rather good	One stain on the rear side of the bottle; TiO_2 trickles down a little bit
234	Low	Rather good	One stain on the rear side of the bottle
235	Low	Rather good	One stain on the right side of the bottle; TiO_2 trickles down a little bit

Table 12-13: Optical appearance of samples 236 – 244

Sample number	Sample description		Anomalies
	opacity	consistency	
236	Medium	Rather bad	“Patterned” structure
237	Medium	Rather good	“Patterned” structure
238	Medium	Rather good	“Patterned” structure
239	Medium	Rather good	Additional coating in the bottom region of the bottle
240	Medium	rather good	Stains on the rear side of the bottle
241	Medium	Good	Stains; additional coating in the bottom region of the bottle
242	Medium	Formation of a ring in the middle of the bottle	-
243	Low	Rather good	One stain on the right side of the bottle
244	Low	Good	-

12.2 List of the samples produced, including the process used for manufacturing and the results of the corresponding hydrolytic class analysis

Table 12-14: List of the samples produced including analysis of the hydrolytic class – part 1

#_Date	Activation	Ann. 1	APTES 1	Ann. 2 (sil.l.)	APTES 2	Ann. 3 (sil.l.)	Washing 1	Ti-i-pr-oxid 1	Washing 2	Ann. 4	Ti-i-pr-oxid 2	Ann. 5	Remarks	Tit. [mL 0,1 mM HCl]
01_17/02	No activation	90 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed, pH not adjusted	40 min. at 100°C	APTES in EtOH pur 1% w/w sprayed pH ~ 4	30 min. at 100°C	Add. 40 min. in the oven at 100°C	Ti sprayed 10% w/w	Add. 30 min. in the oven at 100°C	-	-	In the oven over night at 100°C	Ann.1 is before the treatment, pH was not adjusted; therefore the samples were put out of the oven after 40 min at 100°C and once again coated with APTES	0,44
02_17/02	No activation	90 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed, pH not adjusted	40 min. at 100°C	APTES in EtOH pur 1% w/w sprayed pH ~ 4	30 min. at 100°C	Add. 40 min. in the oven at 100°C	Ti sprayed 10% w/w	Add. 30 min. in the oven at 100°C	-	-	In the oven over night at 100°C	Ann.1 is before the treatment, pH was not adjusted; therefore the samples were put out of the oven after 40 min at 100°C and once again coated with APTES	0,46
03_17/02	No activation	90 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed, pH not adjusted	40 min. at 100°C	APTES in EtOH pur 1% w/w sprayed pH ~ 4	30 min. at 100°C	Add. 40 min. in the oven at 100°C	Ti sprayed 10% w/w	Add. 30 min. in the oven at 100°C	-	-	In the oven over night at 100°C	Ann.1 is before the treatment, pH was not adjusted; therefore the samples were put out of the oven after 40 min at 100°C and once again coated with APTES	x
04_17/02	No activation	90 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed, pH not adjusted	40 min. at 100°C	APTES in EtOH pur 1% w/w sprayed pH ~ 4	30 min. at 100°C	Add. 40 min. in the oven at 100°C	Ti sprayed 10% w/w	Add. 30 min. in the oven at 100°C	-	-	In the oven over night at 100°C	Ann.1 is before the treatment, pH was not adjusted; therefore the samples were put out of the oven after 40 min at 100°C and once again coated with APTES	0,44
05_17/02	No activation	90 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed, pH not adjusted	40 min. at 100°C	APTES in EtOH pur 1% w/w sprayed pH ~ 4	30 min. at 100°C	With EtOH	Ti sprayed 10% w/w	Add. 30 min. in the oven at 100°C	-	-	In the oven over night at 100°C	Ann.1 is before the treatment, pH was not adjusted; therefore the samples were put out of the oven after 40 min at 100°C and once again coated with APTES	0,50
06_17/02	No activation	90 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed, pH not adjusted	40 min. at 100°C	APTES in EtOH pur 1% w/w sprayed pH ~ 4	30 min. at 100°C	With EtOH	Ti sprayed 10% w/w	Add. 30 min. in the oven at 100°C	-	-	In the oven over night at 100°C	Ann.1 is before the treatment, pH was not adjusted; therefore the samples were put out of the oven after 40 min at 100°C and once again coated with APTES	0,46
07_17/02	No activation	90 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed, pH not adjusted	40 min. at 100°C	APTES in EtOH pur 1% w/w sprayed pH ~ 4	30 min. at 100°C	With EtOH	Ti sprayed 10% w/w	Add. 30 min. in the oven at 100°C	-	-	In the oven over night at 100°C	Ann.1 is before the treatment, pH was not adjusted; therefore the samples were put out of the oven after 40 min at 100°C and once again coated with APTES	0,50
08_17/02	No activation	90 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed, pH not adjusted	40 min. at 100°C	APTES in EtOH pur 1% w/w sprayed pH ~ 4	30 min. at 100°C	With EtOH	Ti sprayed 10% w/w	Add. 30 min. in the oven at 100°C	-	-	In the oven over night at 100°C	Ann.1 is before the treatment, pH was not adjusted; therefore the samples were put out of the oven after 40 min at 100°C and once again coated with APTES	x
09_17/02	No activation	90 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed, pH not adjusted	40 min. at 100°C	APTES in EtOH pur 1% w/w sprayed pH ~ 4	30 min. at 100°C	With EtOH	Ti sprayed 10% w/w	Add. 30 min. in the oven at 100°C	-	-	In the oven over night at 100°C	Ann.1 is before the treatment, pH was not adjusted; therefore the samples were put out of the oven after 40 min at 100°C and once again coated with APTES	0,40
10_17/02	No activation	90 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed, pH not adjusted	40 min. at 100°C	APTES in EtOH pur 1% w/w sprayed pH ~ 4	30 min. at 100°C	Add. 40 min. in the oven at 100°C	Ti sprayed 10% w/w	With EtOH	-	-	In the oven over night at 100°C	Ann.1 is before the treatment, pH was not adjusted; therefore the samples were put out of the oven after 40 min at 100°C and once again coated with APTES	0,42

Table 12-15: List of the samples produced including analysis of the hydrolytic class – part 2

#_Date	Activation	Ann. 1	APTES 1	Ann. 2 (sil.l.)	APTES 2	Ann. 3 (sil.l.)	Washing 1	Ti-i-pr-oxid 1	Washing 2	ann. 4	Ti-i-pr-oxid 2	Ann. 5	Remarks	Tit. [mL 0,1 mM HCl]
11_17/02	No activation	90 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed, pH not adjusted	40 min. at 100°C	APTES in EtOH pur 1% w/w sprayed pH ~ 4	30 min. at 100°C	Add. 40 min. in the oven at 100°C	Ti sprayed 10% w/w	With EtOH	-	-	In the oven over night at 100°C	Ann.1 is before the treatment, pH was not adjusted; therefore the samples were put out of the oven after 40 min at 100°C and once again coated with APTES	1,00
12_17/02	No activation	90 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed, pH not adjusted	40 min. at 100°C	APTES in EtOH pur 1% w/w sprayed pH ~ 4	30 min. at 100°C	With EtOH	Ti sprayed 10% w/w	With EtOH	-	-	In the oven over night at 100°C	Ann.1 is before the treatment, pH was not adjusted; therefore the samples were put out of the oven after 40 min at 100°C and once again coated with APTES	1,08
13_17/02	1 min. w. 2 M HCl, rinsed w. H2O; 1 min. w. 2M NaOH; rinsed w. H2O	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed, pH not adjusted	30 min. at 100°C	APTES in EtOH pur 1% w/w sprayed pH ~ 4	35 min. at 100°C	Add. 30 min. in the oven at 100°C	Ti sprayed 10% w/w	Add. 30 min. in the oven at 100°C	-	-	In the oven over night at 100°C	Ann.1 is before the treatment, pH was not adjusted; therefore the samples were put out of the oven after 40 min at 100°C and once again coated with APTES	0,48
14_17/02	1 min. w. 2 M HCl, rinsed w. H2O; 1 min. w. 2M NaOH; rinsed w. H2O	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed, pH not adjusted	30 min. at 100°C	APTES in EtOH pur 1% w/w sprayed pH ~ 4	35 min. at 100°C	Add. 30 min. in the oven at 100°C	Ti sprayed 10% w/w	Add. 30 min. in the oven at 100°C	-	-	In the oven over night at 100°C	Ann.1 is before the treatment, pH was not adjusted; therefore the samples were put out of the oven after 40 min at 100°C and once again coated with APTES	0,40
15_17/02	1 min. w. 2 M HCl, rinsed w. H2O; 1 min. w. 2M NaOH; rinsed w. H2O	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed, pH not adjusted	30 min. at 100°C	APTES in EtOH pur 1% w/w sprayed pH ~ 4	35 min. at 100°C	Add. 30 min. in the oven at 100°C	Ti sprayed 10% w/w	Add. 30 min. in the oven at 100°C	-	-	In the oven over night at 100°C	Ann.1 is before the treatment, pH was not adjusted; therefore the samples were put out of the oven after 40 min at 100°C and once again coated with APTES	0,38
16_17/02	1 min. w. 2 M HCl, rinsed w. H2O; 1 min. w. 2M NaOH; rinsed w. H2O	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed, pH not adjusted	30 min. at 100°C	APTES in EtOH pur 1% w/w sprayed pH ~ 4	35 min. at 100°C	Add. 30 min. in the oven at 100°C	Ti sprayed 10% w/w	Add. 30 min. in the oven at 100°C	-	-	In the oven over night at 100°C	Ann.1 is before the treatment, pH was not adjusted; therefore the samples were put out of the oven after 40 min at 100°C and once again coated with APTES	0,36
17_17/02	30 min. w. 2 M HCl, rinsed w. H2O; 30 min. w. 2M NaOH; rinsed w. H2O	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed, pH not adjusted	30 min. at 100°C	APTES in EtOH pur 1% w/w sprayed pH ~ 4	35 min. at 100°C	Add. 30 min. in the oven at 100°C	Ti sprayed 10% w/w	Add. 30 min. in the oven at 100°C	-	-	In the oven over night at 100°C	Ann.1 is before the treatment, pH was not adjusted; therefore the samples were put out of the oven after 40 min at 100°C and once again coated with APTES	0,38
18_17/02	1 min. w. 2 M HCl, rinsed w. H2O; 1 min. w. 2M NaOH; rinsed w. H2O	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed, pH not adjusted	30 min. at 100°C	APTES in EtOH pur 1% w/w sprayed pH ~ 4	35 min. at 100°C	With EtOH	Ti sprayed 10% w/w	Add. 30 min. in the oven at 100°C	-	-	In the oven over night at 100°C	Ann.1 is before the treatment, pH was not adjusted; therefore the samples were put out of the oven after 40 min at 100°C and once again coated with APTES	0,40
19_17/02	1 min. w. 2 M HCl, rinsed w. H2O; 1 min. w. 2M NaOH; rinsed w. H2O	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed, pH not adjusted	30 min. at 100°C	APTES in EtOH pur 1% w/w sprayed pH ~ 4	35 min. at 100°C	With EtOH	Ti sprayed 10% w/w	Add. 30 min. in the oven at 100°C	-	-	In the oven over night at 100°C	Ann.1 is before the treatment, pH was not adjusted; therefore the samples were put out of the oven after 40 min at 100°C and once again coated with APTES	0,50
20_17/02	1 min. w. 2 M HCl, rinsed w. H2O; 1 min. w. 2M NaOH; rinsed w. H2O	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed, pH not adjusted	30 min. at 100°C	APTES in EtOH pur 1% w/w sprayed pH ~ 4	35 min. at 100°C	With EtOH	Ti sprayed 10% w/w	Add. 30 min. in the oven at 100°C	-	-	In the oven over night at 100°C	Ann.1 is before the treatment, pH was not adjusted; therefore the samples were put out of the oven after 40 min at 100°C and once again coated with APTES	0,40
21_17/02	1 min. w. 2 M HCl, rinsed w. H2O; 1 min. w. 2M NaOH; rinsed w. H2O	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed, pH not adjusted	30 min. at 100°C	APTES in EtOH pur 1% w/w sprayed pH ~ 4	35 min. at 100°C	With EtOH	Ti sprayed 10% w/w	Add. 30 min. in the oven at 100°C	-	-	In the oven over night at 100°C	Ann.1 is before the treatment, pH was not adjusted; therefore the samples were put out of the oven after 40 min at 100°C and once again coated with APTES	0,42

Table 12-16: List of the samples produced including analysis of the hydrolytic class – part 3

#_Date	Activation	Ann. 1	APTES 1	Ann. 2 (sil.l.)	APTES 2	Ann. 3 (sil.l.)	Washing 1	Ti-i-pr-oxid 1	Washing 2	Ann. 4	Ti-i-pr-oxid 2	Ann. 5	Remarks	Tit. [mL 0,1 mM HCl]
22_17/02	1 min. w. 2 M HCl, rinsed w. H2O; 1 min. w. 2M NaOH; rinsed w. H2O	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed, pH not adjusted	30 min. at 100°C	APTES in EtOH pur 1% w/w sprayed pH ~ 4	35 min. at 100°C	Add. 30 min. in the oven at 100°C	Ti sprayed 10% w/w	with EtOH	-	-	In the oven over night at 100°C	Ann.1 is before the treatment, pH was not adjusted; therefore the samples were put out of the oven after 40 min at 100°C and once again coated with APTES	0,40
23_17/02	1 min. w. 2 M HCl, rinsed w. H2O; 1 min. w. 2M NaOH; rinsed w. H2O	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed, pH not adjusted	30 min. at 100°C	APTES in EtOH pur 1% w/w sprayed pH ~ 4	35 min. at 100°C	With EtOH	Ti sprayed 10% w/w	with EtOH	-	-	In the oven over night at 100°C	Ann.1 is before the treatment, pH was not adjusted; therefore the samples were put out of the oven after 40 min at 100°C and once again coated with APTES	0,52
24_17/02	30 min. w. 2 M HCl, rinsed w. H2O; 30 min. w. 2M NaOH; rinsed w. H2O	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed, pH not adjusted	30 min. at 100°C	APTES in EtOH pur 1% w/w sprayed pH ~ 4	35 min. at 100°C	With EtOH	Ti sprayed 10% w/w	with EtOH	-	-	In the oven over night at 100°C	Ann.1 is before the treatment, pH was not adjusted; therefore the samples were put out of the oven after 40 min at 100°C and once again coated with APTES	0,88
49_29/03	Act. W. 1 M HCl/NaOH at RT for 0.5 hours, poured in bottle, rinsed with H2O after each step	10 min. at 160°C	APTES in EtOH pur. 1% w/w sprayed, pH ~ 4.05	1 3/4 h at 75°C	-	-	-	Ti sprayed 10% w/w	-	-	-	3h at 80°C	Process from the preliminary study, Probe 80 is using the same process	0,70
50_29/03	Act. W. 1 M HCl/NaOH at RT for 0.5 hours, poured in bottle, rinsed with H2O after each step	10 min. at 160°C	APTES in EtOH pur. 1% w/w sprayed, pH ~ 4.05	1 3/4 h at 75°C	-	-	-	Ti sprayed 10% w/w	-	-	-	3h at 80°C	Process from the preliminary study, Probe 80 is using the same process	0,96
51_29/03	Act. W. 1 M HCl/NaOH at RT for 0.5 hours, poured in bottle, rinsed with H2O after each step	10 min. at 160°C	APTES in EtOH pur. 1% w/w sprayed, pH ~ 4.05	1 3/4 h at 75°C	-	-	-	Ti sprayed 10% w/w	-	-	-	3h at 80°C	Process from the preliminary study	0,68
52_29/03	Act. W. 1 M HCl/NaOH at RT for 0.5 hours, poured in bottle, rinsed with H2O after each step	10 min. at 160°C	APTES in EtOH pur. 1% w/w sprayed, pH ~ 4.05	1 3/4 h at 75°C	-	-	-	Ti sprayed 10% w/w	-	-	-	3h at 80°C	Process from the preliminary study	0,70
53_31/03	Act. w. 2 M HCl/NaOH at RT; sprayed; left for 15 min	15 min. at 120°C	APTES in Cyclohexane 2% v/v; sprayed; pH not adjusted	30 min. at 120°C	-	-	Cyclohexane and Ethanol	Ti sprayed 10% v/v	-	-	-	3h at 80°C	The APTES spraying time was increased because it seemed that less Vol. was nebulized (app. 15 s spraying time)	1,28
54_31/03	Act. w. 2 M HCl/NaOH at RT; sprayed; left for 15 min	15 min. at 120°C	APTES in Cyclohexane 2% v/v; sprayed; pH not adjusted	30 min. at 120°C	-	-	Cyclohexane and Ethanol	Ti sprayed 10% v/v	-	-	-	3h at 80°C	The APTES spraying time was increased because it seemed that less Vol. was nebulized (app. 15 s spraying time)	0,88
55_31/03	Act. w. 2 M HCl/NaOH at RT; sprayed; left for 15 min	15 min. at 120°C	APTES in Cyclohexane 2% v/v; sprayed; pH not adjusted	30 min. at 120°C	-	-	Cyclohexane and Ethanol	Ti sprayed 10% v/v	-	-	-	3h at 80°C	The APTES spraying time was increased because it seemed that less Vol. was nebulized (app. 15 s spraying time)	1,12

Table 12-17: List of the samples produced including analysis of the hydrolytic class – part 4

#_Date	Activation	Ann. 1	APTES 1	Ann. 2 (sil.l.)	APTES 2	Ann. 3 (sil.l.)	Washing 1	Ti-i-pr-oxid 1	Washing 2	Ann. 4	Ti-i-pr-oxid 2	Ann. 5	Remarks	Tit. [mL 0,1 mM HCl]
56_31/03	Act. w. 1 M HCl/NaOH at RT for 0.5 hours, poured in bottle, rinsed with H2O after each step	15 min. at 120°C	APTES in Cyclohexane 2% v/v; sprayed; pH not adjusted	30 min. at 120°C	-	-	Cyclohexane and Ethanol	Ti sprayed 10% v/v	-	-	-	3h at 80°C	The APTES spraying time was increased because it seemed that less Vol. was nebulized (app. 15 s spraying time)	0,88
57_31/03	Act. w. 1 M HCl/NaOH at RT for 0.5 hours, poured in bottle, rinsed with H2O after each step	15 min. at 120°C	APTES in Cyclohexane 2% v/v; sprayed; pH not adjusted	30 min. at 120°C	-	-	Cyclohexane and Ethanol	Ti sprayed 10% v/v	-	-	-	3h at 80°C	The APTES spraying time was increased because it seemed that less Vol. was nebulized (app. 15 s spraying time)	0,88
58_31/03	Act. w. 1 M HCl/NaOH at RT for 0.5 hours, poured in bottle, rinsed with H2O after each step	15 min. at 120°C	APTES in Cyclohexane 2% v/v; sprayed; pH not adjusted	30 min. at 120°C	-	-	Cyclohexane and Ethanol	Ti sprayed 10% v/v	-	-	-	3h at 80°C	The APTES spraying time was increased because it seemed that less Vol. was nebulized (app. 15 s spraying time)	0,92
59_01/04	Act. w. 1 M HCl/NaOH at 70°C for 15 min; poured in bottle, rinsed with H2O after each step	18 min. at 110°C	APTES in EtOH pur.; 2% v/v sprayed, pH ~ 4.05	35 min. at 120°C	-	-	Ethanol	Ti sprayed 10% v/v	-	-	-	6h20m at 80°C	Duration of annealing 3 increased	0,80
60_01/04	Act. w. 1 M HCl/NaOH at 70°C for 15 min; poured in bottle, rinsed with H2O after each step	18 min. at 110°C	APTES in EtOH pur.; 2% v/v sprayed, pH ~ 4.05	35 min. at 120°C	-	-	Ethanol	Ti sprayed 10% v/v	-	-	-	6h20m at 80°C	Duration of annealing 3 increased	x
61_01/04	Act. w. 1 M HCl/NaOH at 70°C for 15 min; poured in bottle, rinsed with H2O after each step	18 min. at 110°C	APTES in EtOH pur.; 2% v/v sprayed, pH ~ 4.05	35 min. at 120°C	-	-	Ethanol	Ti sprayed 10% v/v	-	-	-	6h20m at 80°C	Duration of annealing 3 increased	0,86
62_01/04	Act. w. 1 M HCl/NaOH at 70°C for 15 min; poured in bottle, rinsed with H2O after each step	18 min. at 110°C	APTES in EtOH pur.; 2% v/v sprayed, pH ~ 4.05	35 min. at 120°C	-	-	Ethanol	Ti sprayed 5% v/v	-	-	-	6h20m at 80°C	Duration of annealing 3 increased	0,80
63_01/04	Act. w. 1 M HCl/NaOH at 70°C for 15 min; poured in bottle, rinsed with H2O after each step	18 min. at 110°C	APTES in EtOH pur.; 2% v/v sprayed, pH ~ 4.05	35 min. at 120°C	-	-	Ethanol	Ti sprayed 5% v/v	-	-	-	6h20m at 80°C	Duration of annealing 3 increased	1,00
64_01/04	Act. w. 1 M HCl/NaOH at 70°C for 15 min; poured in bottle, rinsed with H2O after each step	18 min. at 110°C	APTES in EtOH pur.; 2% v/v sprayed, pH ~ 4.05	35 min. at 120°C	-	-	Ethanol	Ti sprayed 5% v/v	-	-	-	6h20m at 80°C	Duration of annealing 3 increased	0,88
65_04/04	Act. w. 1 M HCl/NaOH at RT for 30 min; poured in bottle, rinsed with H2O after each step	15 min. at 120°C	APTES in EtOH pur.; 1% v/v sprayed, pH ~ 3.7	30 min. at 120°C	-	-	Ethanol	Ti sprayed 5% v/v	-	-	-	3h at 80°C	pH-value APTES	0,94

Table 12-18: List of the samples produced including analysis of the hydrolytic class – part 5

#_Date	Activation	Ann. 1	APTES 1	Ann. 2 (sil.l.)	APTES 2	Ann. 3 (sil.l.)	Washing 1	Ti-i-pr-oxid 1	Washing 2	Ann. 4	Ti-i-pr-oxid 2	Ann. 5	Remarks	Tit. [mL 0,1 mM HCl]
66_04/04	Act. w. 1 M HCl/NaOH at RT for 30 min; poured in bottle, rinsed with H2O after each step	15 min. at 120°C	APTES in EtOH pur.; 1% v/v sprayed, pH ~ 3.7	30 min. at 120°C	-	-	Ethanol	Ti sprayed 5% v/v	-	-	-	3h at 80°C	pH-value APTES	0,90
67_04/04	Act. w. 1 M HCl/NaOH at RT for 30 min; poured in bottle, rinsed with H2O after each step	15 min. at 120°C	APTES in EtOH pur.; 1% v/v sprayed, pH ~ 3.7	30 min. at 120°C	-	-	Ethanol	Ti sprayed 5% v/v	-	-	-	3h at 80°C	pH-value APTES	0,84
68_04/04	Act. w. 1 M HCl/NaOH at 70°C for 15 min; poured in bottle, rinsed with H2O after each step	15 min. at 120°C	APTES in EtOH pur.; 1% v/v sprayed, pH ~ 3.7	30 min. at 120°C	-	-	Ethanol	Ti sprayed 5% v/v	-	-	-	3h at 80°C	pH-value APTES	x
69_04/04	Act. w. 1 M HCl/NaOH at 70°C for 15 min; poured in bottle, rinsed with H2O after each step	15 min. at 120°C	APTES in EtOH pur.; 1% v/v sprayed, pH ~ 3.7	30 min. at 120°C	-	-	Ethanol	Ti sprayed 5% v/v	-	-	-	3h at 80°C	pH-value APTES	0,92
70_04/04	Act. w. 1 M HCl/NaOH at 70°C for 15 min; poured in bottle, rinsed with H2O after each step	15 min. at 120°C	APTES in EtOH pur.; 1% v/v sprayed, pH ~ 3.7	30 min. at 120°C	-	-	Ethanol	Ti sprayed 5% v/v	-	-	-	3h at 80°C	pH-value APTES	1,00
71_11/04	Act. w. 1 M HCl/NaOH at RT for 30 min; poured in bottle, rinsed with H2O after each step	15 min. at 120°C	APTES in EtOH pur.; 2% v/v sprayed, pH ~ 4.2	30 min. at 120°C	-	-	Ethanol	Ti sprayed 5% v/v	-	-	-	3h at 80°C	"Awkward" spraying because a combination of manual spraying and the stage II spraying apparatus was used	x
72_11/04	Act. w. 1 M HCl/NaOH at RT for 30 min; poured in bottle, rinsed with H2O after each step	15 min. at 120°C	APTES in EtOH pur.; 2% v/v sprayed, pH ~ 4.2	30 min. at 120°C	-	-	Ethanol	Ti sprayed 5% v/v	-	-	-	3h at 80°C	"Awkward" spraying because a combination of manual spraying and the stage II spraying apparatus was used	0,66
73_11/04	Act. w. 1 M HCl/NaOH at RT for 30 min; poured in bottle, rinsed with H2O after each step	15 min. at 120°C	APTES in EtOH pur.; 2% v/v sprayed, pH ~ 4.2	30 min. at 120°C	-	-	Ethanol	Ti sprayed 5% v/v	-	-	-	3h at 80°C	"Awkward" spraying because a combination of manual spraying and the stage II spraying apparatus was used	0,80
74_11/04	Act. w. 1 M HCl/NaOH at RT for 30 min; poured in bottle, rinsed with H2O after each step	15 min. at 120°C	APTES in EtOH pur.; 2% v/v sprayed, pH ~ 4.2	30 min. at 120°C	-	-	Ethanol	Ti sprayed 10% v/v	-	-	-	3h at 80°C	"Awkward" spraying because a combination of manual spraying and the stage II spraying apparatus was used	0,70
75_11/04	Act. w. 1 M HCl/NaOH at RT for 30 min; poured in bottle, rinsed with H2O after each step	15 min. at 120°C	APTES in EtOH pur.; 2% v/v sprayed, pH ~ 4.2	30 min. at 120°C	-	-	Ethanol	Ti sprayed 10% v/v	-	-	-	3h at 80°C	"Awkward" spraying because a combination of manual spraying and the stage II spraying apparatus was used. Ti sprayed for 6 x 0,7 s	0,84

Table 12-19: List of the samples produced including analysis of the hydrolytic class – part 6

#_Date	Activation	Ann. 1	APTES 1	Ann. 2 (sil.l.)	APTES 2	Ann. 3 (sil.l.)	Washing 1	Ti-i-pr-oxid 1	Washing 2	Ann. 4	Ti-i-pr-oxid 2	Ann. 5	Remarks	Tit. [mL 0,1 mM HCl]
76_11/04	Act. w. 1 M HCl/NaOH at RT for 30 min; poured in bottle, rinsed with H2O after each step	15 min. at 120°C	APTES in EtOH pur.; 2% v/v sprayed, pH ~ 4.2	30 min. at 120°C	-	-	Ethanol	Ti sprayed 10% v/v	-	-	-	3h at 80°C	"Awkward" spraying because a combination of manual spraying and the stage II spraying apparatus was used	0,70
77_05/04	Act. w. 1 M HCl/NaOH at 70°C for 15 min; poured in bottle, rinsed with H2O after each step	15 min. at 115°C	APTES in EtOH pur.; 1% v/v sprayed, pH ~ 4	30 min. at 120°C	-	-	Ethanol	Ti sprayed 10% v/v	-	-	-	3h at 80°C	-	0,78
78_05/04	Act. w. 1 M HCl/NaOH at 70°C for 15 min; poured in bottle, rinsed with H2O after each step	15 min. at 115°C	APTES in EtOH pur.; 1% v/v sprayed, pH ~ 4	30 min. at 120°C	-	-	Ethanol	Ti sprayed 10% v/v	-	-	-	3h at 80°C	-	0,80
79_05/04	Act. w. 1 M HCl/NaOH at 70°C for 15 min; poured in bottle, rinsed with H2O after each step	15 min. at 115°C	APTES in EtOH pur.; 1% v/v sprayed, pH ~ 4	30 min. at 120°C	-	-	Ethanol	Ti sprayed 10% v/v	-	-	-	3h at 80°C	-	0,78
80_12/04	Act. w. 1 M HCl/NaOH at RT for 30 min; poured in bottle, rinsed with H2O after each step	10 min. at 160°C	APTES in EtOH pur.; 1% v/v sprayed, pH ~ 4	1 3/4 h at 75°C	-	-	-	Ti sprayed 10% w/w	-	-	-	3h at 80°C	Process from the preliminary study	x
81_22/06	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. , pH not adj.	60 min. at 100°C	-	-	-	6 s. Ti sprayed 10% w/w	-	-	-	6h at 100°C	Working pressure ~4.1 bar	0,62
82_22/06	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. , pH not adj.	60 min. at 100°C	-	-	-	6 s. Ti sprayed 10% w/w	-	-	-	6h at 100°C	Working pressure ~4.1 bar	x
83_22/06	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. , pH not adj.	60 min. at 100°C	-	-	-	6 s. Ti sprayed 10% w/w	-	-	-	6h at 100°C	Working pressure ~4.1 bar	0,56
84_22/06	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. , pH not adj.	60 min. at 100°C	-	-	-	6 s. Ti sprayed 10% w/w	-	-	-	6h at 100°C	Working pressure ~4.1 bar	0,58
85_22/06	x	x	x	x	x	x	x	x	x	x	x	x	The bottle was not mounted properly in the spraying apparatus and coating did not work; this sample was discarded	x

Table 12-20: List of the samples produced including analysis of the hydrolytic class – part 7

#_Date	Activation	Ann. 1	APTES 1	Ann. 2 (sil.l.)	APTES 2	Ann. 3 (sil.l.)	Washing 1	Ti-i-pr-oxid 1	Washing 2	Ann. 4	Ti-i-pr-oxid 2	Ann. 5	Remarks	Tit. [mL 0,1 mM HCl]
86_22/06	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 10 s. ; pH not adj.	60 min. at 100°C	-	-	-	6 s. Ti sprayed 10% w/w	-	-	-	6h at 100°C	Working pressure ~4.1 bar	0,86
87_22/06	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 10 s. ; pH not adj.	60 min. at 100°C	-	-	-	6 s. Ti sprayed 10% w/w	-	-	-	6h at 100°C	Working pressure ~4.1 bar	x
88_22/06	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 10 s. ; pH not adj.	60 min. at 100°C	-	-	-	6 s. Ti sprayed 10% w/w	-	-	-	6h at 100°C	Working pressure ~4.1 bar	0,66
89_22/06	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 100°C	-	6 s. Ti sprayed 10% w/w	-	-	-	6h at 100°C	Working pressure ~4.1 bar	0,52
90_22/06	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 100°C	-	6 s. Ti sprayed 10% w/w	-	-	-	6h at 100°C	Working pressure ~4.1 bar	0,46
91_22/06	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 100°C	-	6 s. Ti sprayed 10% w/w	-	-	-	6h at 100°C	Working pressure ~4.1 bar	0,52
92_22/06	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 100°C	-	6 s. Ti sprayed 10% w/w	-	-	-	6h at 100°C	Working pressure ~4.1 bar	x
93_22/06	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH ~ 4	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH ~ 4	60 min. at 100°C	-	6 s. Ti sprayed 10% w/w	-	-	-	6h at 100°C	Working pressure ~4.1 bar	0,54
94_22/06	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH ~ 4	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH ~ 4	60 min. at 100°C	-	6 s. Ti sprayed 10% w/w	-	-	-	6h at 100°C	Working pressure ~4.1 bar	x
95_22/06	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH ~ 4	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH ~ 4	60 min. at 100°C	-	6 s. Ti sprayed 10% w/w	-	-	-	6h at 100°C	Working pressure ~4.1 bar	0,62

Table 12-21: List of the samples produced including analysis of the hydrolytic class – part 8

#_Date	Activation	Ann. 1	APTES 1	Ann. 2 (sil.l.)	APTES 2	Ann. 3 (sil.l.)	Washing 1	Ti-i-pr-oxid 1	Washing 2	Ann. 4	Ti-i-pr-oxid 2	Ann. 5	Remarks	Tit. [mL 0,1 mM HCl]
96_22/06	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH ~ 4	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH ~ 4	60 min. at 100°C	-	6 s. Ti sprayed 10% w/w	-	-	-	6h at 100°C	Working pressure ~4.1 bar	0,60
97_05/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	80 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 100°C	Ethanol	7 s. Ti sprayed 10% w/w	-	6h at 100°C	7 s. Ti sprayed 10% w/w	In the oven over night at 100°C	Working pressure ~4.1 bar; the pressure in the first APTES spraying step was 3.5 bar. 1 h after the 2nd Ti spraying step the bottle was blown out with compressed air.	0,54
98_05/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	80 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 100°C	Ethanol	7 s. Ti sprayed 10% w/w	-	6h at 100°C	7 s. Ti sprayed 10% w/w	In the oven over night at 100°C	Working pressure ~4.1 bar; the pressure in the first APTES spraying step was 3.5 bar.	0,56
99_05/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	80 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 100°C	Ethanol	7 s. Ti sprayed 10% w/w	-	6h at 100°C	7 s. Ti sprayed 10% w/w	In the oven over night at 100°C	Working pressure ~4.1 bar; the pressure in the first APTES spraying step was 3.5 bar. 1 h after the 2nd Ti spraying step the bottle was rinsed with ethanol.	0,62
100_05/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	80 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 100°C	Ethanol	7 s. Ti sprayed 10% w/w	-	6h at 100°C	7 s. Ti sprayed 10% w/w	In the oven over night at 100°C	Working pressure ~4.1 bar; the pressure in the first APTES spraying step was 3.5 bar.	0,54
101_05/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	60 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 100°C	Ethanol	3,5 s. Ti sprayed 10% w/w	-	-	-	6,5h at 100°C	Working pressure ~4.1 bar; the pressure in the first APTES spraying step was 3.5 bar.	0,66
102_05/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	60 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 100°C	Ethanol	3,5 s. Ti sprayed 10% w/w	-	-	-	6,5h at 100°C	Working pressure ~4.1 bar; the pressure in the first APTES spraying step was 3.5 bar.	x
103_05/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	60 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 100°C	Ethanol	3,5 s. Ti sprayed 10% w/w	-	-	-	6,5h at 100°C	Working pressure ~4.1 bar; the pressure in the first APTES spraying step was 3.5 bar.	0,66
104_05/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	60 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 100°C	Ethanol	3,5 s. Ti sprayed 10% w/w	-	-	-	6,5h at 100°C	Working pressure ~4.1 bar; the pressure in the first APTES spraying step was 3.5 bar.	0,68
105_05/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	45 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 100°C	-	3,5 s. Ti sprayed 10% w/w	-	-	-	6,25h at 100°C	Working pressure ~4.1 bar; the pressure in the first APTES spraying step was 3.5 bar.	0,64

Table 12-22: List of the samples produced including analysis of the hydrolytic class – part 9

#_Date	Activation	Ann. 1	APTES 1	Ann. 2 (sil.l.)	APTES 2	Ann. 3 (sil.l.)	Washing 1	Ti-i-pr-oxid 1	Washing 2	Ann. 4	Ti-i-pr-oxid 2	Ann. 5	Remarks	Tit. [mL 0,1 mM HCl]
106_05/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	45 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 100°C	-	3,5 s. Ti sprayed 10% w/w	-	-	-	6,25h at 100°C	Working pressure ~4.1 bar; the pressure in the first APTES spraying step was 3.5 bar.	0,54
107_05/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	45 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 100°C	-	3,5 s. Ti sprayed 10% w/w	-	-	-	6,25h at 100°C	Working pressure ~4.1 bar; the pressure in the first APTES spraying step was 3.5 bar.	0,64
108_05/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	45 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 100°C	-	3,5 s. Ti sprayed 10% w/w	-	-	-	6,25h at 100°C	Working pressure ~4.1 bar; the pressure in the first APTES spraying step was 3.5 bar.	x
109_05/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 100°C	-	7 s. Ti sprayed 10% w/w	-	6h at 100°C	7 s. Ti sprayed 10% w/w	In the oven over night at 100°C	The samples show white stains after ann. 1. working pressure ~4.1 bar; the pressure in the first APTES spraying step was 3.5 bar. 1 h after the 2nd Ti spraying step the bottle was blown out with compressed air.	1,20
110_05/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 100°C	-	7 s. Ti sprayed 10% w/w	-	6h at 100°C	7 s. Ti sprayed 10% w/w	In the oven over night at 100°C	The samples show white stains after ann. 1. working pressure ~4.1 bar; the pressure in the first APTES spraying step was 3.5 bar.	2,58
111_05/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 100°C	-	7 s. Ti sprayed 10% w/w	-	6h at 100°C	7 s. Ti sprayed 10% w/w	In the oven over night at 100°C	The samples show white stains after ann. 1. working pressure ~4.1 bar; the pressure in the first APTES spraying step was 3.5 bar. 1 h after the 2nd Ti spraying step the bottle was rinsed with EtOH.	0,64
112_05/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 100°C	-	7 s. Ti sprayed 10% w/w	-	6h at 100°C	7 s. Ti sprayed 10% w/w	In the oven over night at 100°C	Working pressure ~4.1 bar; the pressure in the first APTES spraying step was 3.5 bar.	0,58
113_12/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	120 min. at 65°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 65°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 65°C	-	2x3 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	Working pressure ~5.1 bar	0,52
114_12/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	120 min. at 65°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 65°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 65°C	-	2x3 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	Working pressure ~5.1 bar	0,60
115_12/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	120 min. at 65°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 65°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 65°C	-	2x3 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	Working pressure ~5.1 bar	0,64

Table 12-23: List of the samples produced including analysis of the hydrolytic class – part 9

#_Date	Activation	Ann. 1	APTES 1	Ann. 2 (sil.l.)	APTES 2	Ann. 3 (sil.l.)	Washing 1	Ti-i-pr-oxid 1	Washing 2	Ann. 4	Ti-i-pr-oxid 2	Ann. 5	Remarks	Tit. [mL 0,1 mM HCl]
116_12/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	120 min. at 65°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 65°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 65°C	-	3x3 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	Working pressure ~5.1 bar	0,52
117_12/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 65°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 65°C	-	3x3 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	Working pressure ~5.1 bar	0,54
118_12/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	90 min. at 65°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 65°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 65°C	-	3x3 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	Working pressure ~5.1 bar	0,62
119_12/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	90 min. at 65°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 65°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 65°C	-	3x3 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	Working pressure ~4.5 bar	0,52
120_12/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	80 min. at 65°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 65°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 65°C	-	3x3 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	Working pressure ~4.5 bar	0,58
121_12/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	80 min. at 65°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 65°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 65°C	-	3x3 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	Working pressure ~4.5 bar	0,58
122_12/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	75 min. at 80°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 85°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 85°C	-	2x3 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	Working pressure ~5.1 bar	0,70
123_12/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	60 min. at 80°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 85°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 85°C	-	2x3 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	Working pressure ~5.1 bar	0,58
124_12/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	60 min. at 80°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 85°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 85°C	-	2x3 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	Working pressure ~5.1 bar	0,70
125_12/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	55 min. at 80°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 85°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 85°C	-	3x3 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	Working pressure ~5.1 bar	0,62

Table 12-24: List of the samples produced including analysis of the hydrolytic class – part 10

#_Date	Activation	Ann. 1	APTES 1	Ann. 2 (sil.l.)	APTES 2	Ann. 3 (sil.l.)	Washing 1	Ti-i-pr-oxid 1	Washing 2	Ann. 4	Ti-i-pr-oxid 2	Ann. 5	Remarks	Tit. [mL 0,1 mM HCl]
126_12/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	55 min. at 80°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 85°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 85°C	-	3x3 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	Working pressure ~5.1 bar	0,64
127_12/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	45 min. at 80°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 85°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 85°C	-	3x3 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	Working pressure ~5.1 bar	0,58
128_12/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	45 min. at 80°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 85°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 85°C	-	3x3 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	Working pressure ~4.5 bar	0,72
129_12/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	35 min. at 80°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 85°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 85°C	-	3x3 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	Working pressure ~4.5 bar	0,74
130_12/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	35 min. at 80°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 85°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 85°C	-	3x3 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	Working pressure ~4.5 bar	0,74
131_26/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	-	-	-	-	-	-	In the oven over night at 100°C	Working pressure ~5.2 bar	13,60
132_26/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	-	-	-	-	-	-	In the oven over night at 100°C	Working pressure ~5.2 bar	8,58
133_26/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 10x1 s. ; pH not adj.	-	-	-	-	-	-	-	-	In the oven over night at 100°C	Working pressure ~5.2 bar	7,42
134_26/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 10x1 s. ; pH not adj.	-	-	-	-	-	-	-	-	In the oven over night at 100°C	Working pressure ~5.2 bar	5,12
135_26/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 60°C	1 min w. EtOH	-	-	-	-	In the oven over night at 100°C	Working pressure ~5.2 bar; The APTES spraying process was repeated a third time after drying at 60°C for 30 min	2,04

Table 12-25: List of the samples produced including analysis of the hydrolytic class – part 11

#_Date	Activation	Ann. 1	APTES 1	Ann. 2 (sil.l.)	APTES 2	Ann. 3 (sil.l.)	Washing 1	Ti-i-pr-oxid 1	Washing 2	Ann. 4	Ti-i-pr-oxid 2	Ann. 5	Remarks	Tit. [mL 0,1 mM HCl]
136_26/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 60°C	1 min w. EtOH	-	-	-	-	In the oven over night at 100°C	Working pressure ~5.2 bar; The APTES spraying process was repeated a third time after drying at 60°C for 30 min	1,86
137_26/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 65°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 65°C	-	-	-	-	-	In the oven over night at 100°C	Working pressure ~5.2 bar; The APTES spraying process was repeated a third time after drying at 60°C for 30 min	14,92
138_26/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 85°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 85°C	-	-	-	-	-	In the oven over night at 100°C	Working pressure ~5.2 bar; The APTES spraying process was repeated a third time after drying at 60°C for 30 min	16,86
139_26/07	No activation	60°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	-	-	-	-	-	-	In the oven over night at 100°C	Working pressure ~5.2 bar; ann. 1 is before the start of the treatment	2,02
140_26/07	No activation	60°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	-	-	-	-	-	-	In the oven over night at 100°C	Working pressure ~5.2 bar; ann. 1 is before the start of the treatment	18,76
141_26/07	No activation	60°C	APTES in EtOH pur. 1% w/w sprayed f. 10x1 s. ; pH not adj.	-	-	-	-	-	-	-	-	In the oven over night at 100°C	Working pressure ~5.2 bar; ann. 1 is before the start of the treatment	2,72
142_26/07	No activation	60°C	APTES in EtOH pur. 1% w/w sprayed f. 10x1 s. ; pH not adj.	-	-	-	-	-	-	-	-	In the oven over night at 100°C	Working pressure ~5.2 bar; ann. 1 is before the start of the treatment	3,38
143_26/07	-	-	-	-	-	-	-	-	-	-	-	-	Blank from the 2nd shipment of bottles	2,42
144_26/07	-	-	-	-	-	-	-	-	-	-	-	-	Blank from the first shipment of bottles	2,28
145_26/07	No activation	60°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 60°C	1 min w. EtOH	-	-	-	-	In the oven over night at 100°C	Working pressure ~5.2 bar; The APTES spraying process was repeated a third time after drying at 60°C for 30 min ; ann. 1 is before the start of the treatment	2,08

Table 12-26: List of the samples produced including analysis of the hydrolytic class – part 12

#_Date	Activation	Ann. 1	APTES 1	Ann. 2 (sil.l.)	APTES 2	Ann. 3 (sil.l.)	Washing 1	Ti-i-pr-oxid 1	Washing 2	Ann. 4	Ti-i-pr-oxid 2	Ann. 5	Remarks	Tit. [mL 0,1 mM HCl]
146_26/07	no activation	60°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	30 min. at 65°C	APTES in EtOH pur. 1% w/w sprayed f. 5 s. ; pH not adj.	60 min. at 65°C	-	-	-	-	-	In the oven over night at 100°C	Working pressure ~5.2 bar; The APTES spraying process was repeated a third time after drying at 60°C for 30 min ; ann. 1 is before the start of the treatment	18,98
147_28/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	60 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 4x2 s. ; pH not adj.	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 4x2 s. ; pH not adj.	30 min. at 60°C	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was rotated 90° after each APTES spray burst. The bottle was rotated 120° after each Ti spray burst.	2,46
148_28/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	60 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 4x2 s. ; pH not adj.	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 4x2 s. ; pH not adj.	30 min. at 60°C	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was rotated 90° after each APTES spray burst. The bottle was rotated 120° after each Ti spray burst.	2,42
149_28/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	60 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 4x2 s. ; pH not adj.	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 4x2 s. ; pH not adj.	30 min. at 60°C	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was rotated 90° after each APTES spray burst. The bottle was rotated 120° after each Ti spray burst.	2,86
150_28/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	60 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 4x2 s. ; pH not adj.	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 4x2 s. ; pH not adj.	30 min. at 60°C	-	1x6 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was rotated 90° after each APTES spray burst.	2,38
151_28/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	60 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 4x2 s. ; pH not adj.	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 4x2 s. ; pH not adj.	30 min. at 60°C	-	1x6 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was rotated 90° after each APTES spray burst.	0,84
152_28/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	60 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 4x2 s. ; pH not adj.	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 4x2 s. ; pH not adj.	30 min. at 60°C	-	1x6 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was rotated 90° after each APTES spray burst.	0,88
153_28/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	60 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 3x1 s. ; pH not adj.	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 3x1 s. ; pH not adj.	30 min. at 60°C	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was rotated 120° after each APTES spray burst. The bottle was rotated 120 after each Ti spray burst. The APTES spraying process was repeated a third time after drying at 60°C for 30 min	0,76
154_28/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	60 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 3x1 s. ; pH not adj.	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 3x1 s. ; pH not adj.	30 min. at 60°C	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was rotated 120° after each APTES spray burst. The bottle was rotated 120 after each Ti spray burst. The APTES spraying process was repeated a third time after drying at 60°C for 30 min	0,76
155_28/07	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	60 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 3x1 s. ; pH not adj.	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 3x1 s. ; pH not adj.	30 min. at 60°C	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was rotated 120° after each APTES spray burst. The bottle was rotated 120 after each Ti spray burst. The APTES spraying process was repeated a third time after drying at 60°C for 30 min	0,90

Table 12-27: List of the samples produced including analysis of the hydrolytic class – part 13

#_Date	Activation	Ann. 1	APTES 1	Ann. 2 (sil.l.)	APTES 2	Ann. 3 (sil.l.)	Washing 1	Ti-i-pr-oxid 1	Washing 2	Ann. 4	Ti-i-pr-oxid 2	Ann. 5	Remarks	Tit. [mL 0,1 mM HCl]
156_28/07	No activation	-	APTES in EtOH pur. 1% w/w sprayed f. 4x2 s. ; pH not adj.	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 4x2 s. ; pH not adj.	30 min. at 60°C	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was rotated 90° after each APTES spray burst. The bottle was rotated 120° after each Ti spray burst.	1,02
157_28/07	No activation	-	APTES in EtOH pur. 1% w/w sprayed f. 4x2 s. ; pH not adj.	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 4x2 s. ; pH not adj.	30 min. at 60°C	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was rotated 90° after each APTES spray burst. The bottle was rotated 120° after each Ti spray burst.	1,12
158_28/07	No activation	-	APTES in EtOH pur. 1% w/w sprayed f. 4x2 s. ; pH not adj.	30 min. at 60°C	-	-	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was rotated 90° after each APTES spray burst. The bottle was rotated 120° after each Ti spray burst.	0,98
159_28/07	No activation	-	APTES in EtOH pur. 1% w/w sprayed f. 4x2 s. ; pH not adj.	30 min. at 60°C	-	-	-	1x6 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was rotated 90° after each APTES spray burst. The bottle was rotated 120° after each Ti spray burst.	0,94
160_28/07	No activation	-	APTES in EtOH pur. 1% w/w sprayed f. 4x2 s. ; pH not adj.	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 4x2 s. ; pH not adj.	30 min. at 60°C	-	1x6 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was rotated 90° after each APTES spray burst.	1,52
161_28/07	No activation	-	APTES in EtOH pur. 1% w/w sprayed f. 4x2 s. ; pH not adj.	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 4x2 s. ; pH not adj.	30 min. at 60°C	-	1x6 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was rotated 90° after each APTES spray burst.	2,08
162_28/07	No activation	-	APTES in EtOH pur. 1% w/w sprayed f. 3x1 s. ; pH not adj.	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 3x1 s. ; pH not adj.	30 min. at 60°C	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was rotated 120° after each APTES spray burst. The bottle was rotated 120 after each Ti spray burst. The APTES spraying process was repeated a third time after drying at 60°C for 30 min	0,86
163_28/07	No activation	-	APTES in EtOH pur. 1% w/w sprayed f. 3x1 s. ; pH not adj.	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 3x1 s. ; pH not adj.	30 min. at 60°C	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was rotated 120° after each APTES spray burst. The bottle was rotated 120 after each Ti spray burst. The APTES spraying process was repeated a third time after drying at 60°C for 30 min	0,90
164_28/07	No activation	-	APTES in EtOH pur. 1% w/w sprayed f. 3x1 s. ; pH not adj.	30 min. at 60°C	APTES in EtOH pur. 1% w/w sprayed f. 3x1 s. ; pH not adj.	30 min. at 60°C	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was rotated 120° after each APTES spray burst. The bottle was rotated 120 after each Ti spray burst. The APTES spraying process was repeated a third time after drying at 60°C for 30 min	1,04

Table 12-28: List of the samples produced including analysis of the hydrolytic class – part 14

#_Date	Activation	Ann. 1	APTES 1	Ann. 2 (sil.l.)	APTES 2	Ann. 3 (sil.l.)	Washing 1	Ti-i-pr-oxid 1	Washing 2	Ann. 4	Ann. 5	Remarks	Tit. [mL 0,1 mM HCl]
165_05/08	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	45 min at 100 °C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 min. at 100°C	-	6x1 s. Ti sprayed 10% w/w	-	-	In the oven over night at 100°C	The bottle was rotated 120° after each APTES spray burst. The bottle was rotated 120 after each Ti spray burst. The bottles were preheated to a temperature of 100°C. Working pressure = 5 bar	0,48
166_05/08	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	45 min at 100 °C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 min. at 100°C	-	6x1 s. Ti sprayed 10% w/w	-	-	In the oven over night at 100°C	The bottle was rotated 120° after each APTES spray burst. The bottle was rotated 120 after each Ti spray burst. The bottles were preheated to a temperature of 100°C. Working pressure = 5 bar	0,48
167_05/08	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	35 min at 100 °C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 min. at 100°C	-	6x1 s. Ti sprayed 10% w/w	-	-	In the oven over night at 100°C	The bottle was rotated 120° after each APTES spray burst. The bottle was rotated 120 after each Ti spray burst. The bottles were preheated to a temperature of 100°C. Working pressure = 5 bar	0,52
168_05/08	No activation	-	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 min. at 100°C	-	6x1 s. Ti sprayed 10% w/w	-	-	In the oven over night at 100°C	The bottle was rotated 120° after each APTES spray burst. The bottle was rotated 120 after each Ti spray burst. The bottles were preheated to a temperature of 100°C. Working pressure = 5 bar	0,54
169_05/08	No activation	-	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 min. at 100°C	-	6x1 s. Ti sprayed 10% w/w	-	-	In the oven over night at 100°C	The bottle was rotated 120° after each APTES spray burst. The bottle was rotated 120 after each Ti spray burst. The bottles were preheated to a temperature of 100°C. Working pressure = 5 bar	0,56
170_05/08	No activation	-	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min. at 100°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 min. at 100°C	-	6x1 s. Ti sprayed 10% w/w	-	-	In the oven over night at 100°C	The bottle was rotated 120° after each APTES spray burst. The bottle was rotated 120 after each Ti spray burst. The bottles were preheated to a temperature of 100°C. Working pressure = 5 bar	0,58
171_05/08	No activation	10 min 55°C before APTES 1	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min. at 100°C & 10 min at 55°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 min. at 100°C & 15 min at 55°C	-	6x1 s. Ti sprayed 10% w/w	-	-	In the oven over night at 100°C	The bottle was rotated 120° after each APTES spray burst. The bottle was rotated 120 after each Ti spray burst. The bottles were preheated to a temperature of 100°C. Working pressure = 5 bar	0,56
172_05/08	No activation	10 min 55°C before APTES 1	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min. at 100°C & 10 min at 55°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 min. at 100°C & 15 min at 55°C	-	6x1 s. Ti sprayed 10% w/w	-	-	In the oven over night at 100°C	The bottle was rotated 120° after each APTES spray burst. The bottle was rotated 120 after each Ti spray burst. The bottles were preheated to a temperature of 100°C. Working pressure = 5 bar	0,48
173_05/08	No activation	10 min 55°C before APTES 1	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min. at 100°C & 10 min at 55°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 min. at 100°C & 15 min at 55°C	-	6x1 s. Ti sprayed 10% w/w	-	-	In the oven over night at 100°C	The bottle was rotated 120° after each APTES spray burst. The bottle was rotated 120 after each Ti spray burst. The bottles were preheated to a temperature of 100°C. Working pressure = 5 bar	0,50
174_05/08	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min at 100 °C & 10 min at 55°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	30 min at 100 °C & 15 min at 55°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 min. at 100°C & 15 min at 55°C	-	6x1 s. Ti sprayed 10% w/w	-	-	In the oven over night at 100°C	The bottle was rotated 120° after each APTES spray burst. The bottle was turned randomly after each Ti spray burst. The bottles were preheated to a T of 100°C. Working pressure = 5 bar. The bottles were at RT when the Ti spraying started.	0,36

Table 12-29: List of the samples produced including analysis of the hydrolytic class – part 15

#_Date	Activation	Ann. 1	APTES 1	Ann. 2 (sil.l.)	APTES 2	Ann. 3 (sil.l.)	Wash. 1	Ti-i-pr-oxid 1	Ann. 5	Remarks	Tit. [mL 0,1 mM HCl]
175_05/08	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min at 100 °C & 10 min at 55°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	30 min at 100 °C & 15 min at 55°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 min. at 100°C & 15 min at 55°C	-	6x1 s. Ti sprayed 10% w/w	Oven over night at 100°C	The bottle was rotated 120° after each APTES spray burst. The bottle was turned randomly after each Ti spray burst. The bottles were preheated to a T of 100°C. Working pressure = 5 bar. The bottles were at RT when the Ti spraying started.	0.36
176_05/08	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min at 100 °C & 10 min at 55°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	30 min at 100 °C & 15 min at 55°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 min. at 100°C & 15 min at 55°C	-	6x1 s. Ti sprayed 10% w/w	Oven over night at 100°C	The bottle was rotated 120° after each APTES spray burst. The bottle was turned randomly after each Ti spray burst. The bottles were preheated to a T of 100°C. Working pressure = 5 bar. The bottles were at RT when the Ti spraying started.	0.40
177_05/08	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min at 100 °C & 7 min at RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH adj.	1,5 min (RT), 35 min (100°C), 4 min (RT)	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH adj.	3 min. at RT & 70 min at 100°C & 4 min at RT	-	6x1 s. Ti sprayed 10% w/w	Oven over night at 100°C	pH = adjusted; The b. was rotated 120° after each APTES spray burst. The b. was turned rand. after each Ti spray burst. The b. was preheated to a T. of 100°C. Before Act. it was taken out of the oven and left at RT for 4 min. After each step of the activation procedure the bottle was left for 10 m.	0.38
178_05/08	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min at 100 °C & 10 min at 55°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 min. at 100°C & 15 min at 55°C	-	-	-	6x1 s. Ti sprayed 10% w/w	Oven over night at 100°C	The bottle was rotated 120° after each APTES spray burst. The bottle was rotated 120 after each Ti spray burst. The bottles were preheated to a temperature of 100°C. Working pressure = 5 bar	0.54
179_05/08	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min at 100 °C & 10 min at 55°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 min. at 100°C & 15 min at 55°C	-	-	-	6x1 s. Ti sprayed 10% w/w	Oven over night at 100°C	The bottle was rotated 120° after each APTES spray burst. The bottle was rotated 120 after each Ti spray burst. The bottles were preheated to a temperature of 100°C. Working pressure = 5 bar	0.62
180_22/08	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	10 m. 55°C + 30 m. 100 °C + 10 m. 55°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min (100°C), 15 min (55°C)	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 m at 100°C & 20 m at 55°C + 3 m at RT	-	6x1 s. Ti sprayed 10% w/w	Oven over night at 100°C	The bottle was rotated 120° after each APTES spray burst. The b. was rotated randomized after each Ti spray burst.	0.56
181_22/08	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	10 m. 55°C + 30 m. 100 °C + 10 m. 55°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min (100°C), 15 min (55°C)	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 min. at 100°C & 20 min at 55°C + 3 min at RT	-	6x1 s. Ti sprayed 10% w/w	Oven over night at 100°C	The bottle was rotated 120° after each APTES spray burst. The b. was rotated randomized after each Ti spray burst.	0.54
182_22/08	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	10 m. 55°C + 30 m. 100 °C + 10 m. 55°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min (100°C), 15 min (55°C)	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 min. at 100°C & 20 min at 55°C + 3 min at RT	-	6x1 s. Ti sprayed 10% w/w	Oven over night at 100°C	The bottle was rotated 120° after each APTES spray burst. The b. was rotated randomized after each Ti spray burst.	0.88
183_22/08	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min at 100 °C & 10 min at 55°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min (100°C), 15 min (55°C)	APTES in EtOH pur. 1% w/w sprayed f. 5x1 s. ; pH not adj.	90 min. at 100°C + 4 min at RT	-	5x1 s. Ti sprayed 10% w/w	Oven over night at 100°C	The bottle was rotated 120° after each APTES spray burst. The b. was rotated randomized after each Ti spray burst.	0.56
184_22/08	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min at 100 °C & 10 min at 55°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min (100°C), 15 min (55°C)	APTES in EtOH pur. 1% w/w sprayed f. 5x1 s. ; pH not adj.	90 min. at 100°C + 4 min at RT	-	5x1 s. Ti sprayed 10% w/w	Oven over night at 100°C	The bottle was rotated 120° after each APTES spray burst. The b. was rotated randomized after each Ti spray burst.	0.54

Table 12-30: List of the samples produced including analysis of the hydrolytic class – part 16

#_Date	Activation	Ann. 1	APTES 1	Ann. 2 (sil.l.)	APTES 2	Ann. 3 (sil.l.)	Wash. 1	Ti-i-pr-oxid 1	Wash.2	Ann. 4	Ti-i-pr-o. 2	Ann. 5	Remarks	Tit. [mL 0,1 mM HCl]
185_22/08	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min at 100 °C & 10 min at 55°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min (100°C), 15 min (55°C)	APTES in EtOH pur. 1% w/w sprayed f. 5x1 s. ; pH not adj.	90 min. at 100°C + 4 min at RT	-	5x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was rotated 120° after each APTES spray burst. The b. was rotated randomized after each Ti spray burst. The activ. Solutions were just poured into the b., no shaking was done.	0,56
186_22/08	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min at 100 °C & 10 min at 55°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min (100°C), 15 min (55°C)	APTES in EtOH pur. 1% w/w sprayed f. 5x1 s. ; pH not adj.	75 min. at 100°C + 4 min at RT	-	5x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was rotated 120° after each APTES spray burst. The b. was rotated randomized after each Ti spray burst. The activ. Solutions were just poured into the b., no shaking was done.	0,48
187_22/08	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min at 100 °C & 10 min at 55°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min (100°C), 15 min (55°C)	APTES in EtOH pur. 1% w/w sprayed f. 5x1 s. ; pH not adj.	75 min. at 100°C + 4 min at RT	-	5x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was rotated 120° after each APTES spray burst. The b. was rotated randomized after each Ti spray burst. The activ. Solutions were just poured into the b., no shaking was done.	0,54
188_22/08	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min at 100 °C & 10 min at 55°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min (100°C), 15 min (55°C)	APTES in EtOH pur. 1% w/w sprayed f. 5x1 s. ; pH not adj.	75 min. at 100°C + 4 min at RT	-	5x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was rotated 120° after each APTES spray burst. The b. was rotated randomized after each Ti spray burst. The activ. Solutions were just poured into the b., no shaking was done.	0,52
189_23/08	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min at 100 °C & 10 min at 55°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	-	-	90 min. at 100°C + 4 min at RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst. During Ti coating there was a leak in the air tube.	0,50
190_23/08	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min at 100 °C & 10 min at 55°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	-	-	90 min. at 100°C + 4 min at RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst. During Ti coating there was a leak in the air tube.	0,60
191_23/08	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min at 100 °C & 10 min at 55°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	-	-	90 min. at 100°C + 4 min at RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst. During Ti coating there was a leak in the air tube.	0,60
192_23/08	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	10 m. 55°C + 30 m. 100 °C + 10 m. 55°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min (100°C), 15 min (55°C)	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 min. at 100°C & 20 min at 55°C + 3 min at RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	-	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst. During Ti coating there was a leak in the air tube.	0,64
193_23/08	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	10 m. 55°C + 30 m. 100 °C + 10 m. 55°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min (100°C), 15 min (55°C)	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 min. at 100°C & 20 min at 55°C + 3 min at RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	-	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst. During Ti coating there was a leak in the air tube.	0,88

Table 12-31: List of the samples produced including analysis of the hydrolytic class – part 17

#_Date	Activation	Ann. 1	APTES 1	Ann. 2 (sil.l.)	APTES 2	Ann. 3 (sil.l.)	Wash. 1	Ti-i-pr-oxid 1	Wash.2	Ann. 4	Ti-i-pr-o. 2	Ann. 5	Remarks	Tit. [mL 0,1 mM HCl]
194_23/08	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	10 m. 55°C + 30 m. 100 °C + 10 m. 55°C	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min (100°C), 15 min (55°C)	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 min. at 100°C & 20 min at 55°C + 3 min at RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	-	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst. During Ti coating there was a leak in the air tube.	0,82
195_23/08	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	10 m. 55°C + 30 m. 100 °C + 10 m. 55°C	APTES in EtOH pur. 1% w/w sprayed f. 5x1 s. ; pH not adj.	35 min (100°C), 15 min (55°C)	APTES in EtOH pur. 1% w/w sprayed f. 5x1 s. ; pH not adj.	90 min. at 100°C & 20 min at 55°C + 3 min at RT	-	4x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst. During Ti coating there was a leak in the air tube.	0,46
196_23/08	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	10 m. 55°C + 30 m. 100 °C + 10 m. 55°C	APTES in EtOH pur. 1% w/w sprayed f. 5x1 s. ; pH not adj.	35 min (100°C), 15 min (55°C)	APTES in EtOH pur. 1% w/w sprayed f. 5x1 s. ; pH not adj.	90 min. at 100°C & 20 min at 55°C + 3 min at RT	-	4x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst. During Ti coating there was a leak in the air tube.	0,54
197_23/08	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	10 m. 55°C + 30 m. 100 °C + 10 m. 55°C	APTES in EtOH pur. 1% w/w sprayed f. 5x1 s. ; pH not adj.	35 min (100°C), 15 min (55°C)	APTES in EtOH pur. 1% w/w sprayed f. 5x1 s. ; pH not adj.	90 min. at 100°C & 20 min at 55°C + 3 min at RT	-	4x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst. During Ti coating there was a leak in the air tube.	0,56
198_23/08	-	-	-	-	-	-	-	-	-	-	-	-	Blank from the third shipment of bottles	2,92
199_23/08	-	-	-	-	-	-	-	-	-	-	-	-	Blank from the third shipment of bottles	2,90
200_05/09	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	60 m. 100 °C + 4 min RT	APTES in EtOH pur. 1% w/w sprayed f. 5x1 s. ; pH not adj.	35 min (100°C) + 4 min RT	APTES in EtOH pur. 1% w/w sprayed f. 5x1 s. ; pH not adj.	75 min. at 100°C + 4 min at RT	-	4x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst. During Ti coating there was a leak in the air tube.	0,74
201_05/09	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	60 m. 100 °C + 4 min RT	APTES in EtOH pur. 1% w/w sprayed f. 5x1 s. ; pH not adj.	35 min (100°C) + 4 min RT	APTES in EtOH pur. 1% w/w sprayed f. 5x1 s. ; pH not adj.	75 min. at 100°C + 4 min at RT	-	4x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst. During Ti coating there was a leak in the air tube.	0,86
202_05/09	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	52 m. 100 °C + 4 min RT	APTES in EtOH pur. 1% w/w sprayed f. 5x1 s. ; pH not adj.	35 min (100°C) + 4 min RT	APTES in EtOH pur. 1% w/w sprayed f. 5x1 s. ; pH not adj.	75 min. at 100°C + 4 min at RT	-	4x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst. During Ti coating there was a leak in the air tube.	0,54

Table 12-32: List of the samples produced including analysis of the hydrolytic class – part 18

#_Date	Activation	Ann. 1	APTES 1	Ann. 2 (sil.l.)	APTES 2	Ann. 3 (sil.l.)	Wash. 1	Ti-i-pr-oxid 1	Wash.2	Ann. 4	Ti-i-pr-o. 2	Ann. 5	Remarks	Tit. [mL 0,1 mM HCl]
203_05/09	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	60 m. 100 °C + 4 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min (100°C) + 4 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 min. at 100°C + 4 min at RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	0,56
204_05/09	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	48 m. 100 °C + 4 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min (100°C) + 4 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 min. at 100°C + 4 min at RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	0,60
205_05/09	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	48 m. 100 °C + 4 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min (100°C) + 4 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 min. at 100°C + 4 min at RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	0,54
206_05/09	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	44 m. 100 °C + 4 min RT	APTES in EtOH pur. 1% w/w sprayed f. 4x1 s. ; pH not adj.	35 min (100°C) + 4 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	75 min. at 100°C + 4 min at RT	-	4x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	0,58
207_05/09	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	44 m. 100 °C + 4 min RT	APTES in EtOH pur. 1% w/w sprayed f. 4x1 s. ; pH not adj.	35 min (100°C) + 4 min RT	APTES in EtOH pur. 1% w/w sprayed f. 4x1 s. ; pH not adj.	75 min. at 100°C + 4 min at RT	-	4x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	0,74
208_05/09	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	37 m. 100 °C + 4 min RT	APTES in EtOH pur. 1% w/w sprayed f. 4x1 s. ; pH not adj.	35 min (100°C) + 4 min RT	APTES in EtOH pur. 1% w/w sprayed f. 4x1 s. ; pH not adj.	75 min. at 100°C + 4 min at RT	-	4x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	0,70
209_07/09	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 m. 100 °C + 10 min 55°C + 2m RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min (100°C) + 15 m 55°C + 2 m RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 m. at 100°C + 20 m. at 55°C + 2 m. RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	0,62
210_07/09	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 m. 100 °C + 10 min 55°C + 2m RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min (100°C) + 15 m 55°C + 2 m RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 m. at 100°C + 20 m. at 55°C + 2 m. RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	0,54
211_07/09	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 m. 100 °C + 2 min 55°C + 2 m RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min (100°C) + 15 m 55°C + 2 m RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 m. at 100°C + 20 m. at 55°C + 2 m. RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	0,58

Table 12-33: List of the samples produced including analysis of the hydrolytic class – part 19

#_Date	Activation	Ann. 1	APTES 1	Ann. 2 (sil.l.)	APTES 2	Ann. 3 (sil.l.)	Wash. 1	Ti-i-pr-oxid 1	Wash.2	Ann. 5	Remarks	Tit. [mL 0,1 mM HCl]
212_07/09	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min 100°C + 5 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	30 min at RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 min at RT	-	6x1 s. Ti sprayed 10% w/w	-	-	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	3,22
213_07/09	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min 100°C + 5 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	30 min at RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 min at RT	-	6x1 s. Ti sprayed 10% w/w	-	-	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	2,42
214_07/09	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min 100°C + 5 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	30 min at RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 min at RT	-	6x1 s. Ti sprayed 10% w/w	-	-	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	2,64
215_07/09	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min 100°C + 5 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	30 min at RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 min at RT	-	6x1 s. Ti sprayed 10% w/w	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	2,56
216_07/09	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min 100°C + 5 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	30 min at RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 min at RT	-	6x1 s. Ti sprayed 10% w/w	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	3,48
217_07/09	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min 100°C + 5 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	30 min at RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 min at RT	-	6x1 s. Ti sprayed 10% w/w	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	2,94
218_19/09	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 5x1 s. ; pH not adj.	35 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 5x1 s. ; pH not adj.	90 min at 100°C + 3 min RT	-	6x1 s. Ti sprayed 10% w/w	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst. After APTES 2 another APTES spraying step was introduced, with the same subsequent annealing procedure. (this means like Ann.2)	0,54
219_19/09	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 5x1 s. ; pH not adj.	35 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 5x1 s. ; pH not adj.	90 min at 100°C + 3 min RT	-	6x1 s. Ti sprayed 10% w/w	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst. After APTES 2 another APTES spraying step was introduced, with the same subsequent annealing procedure. (this means like Ann.2)	0,56
220_19/09	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 5x1 s. ; pH not adj.	35 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 5x1 s. ; pH not adj.	90 min at 100°C + 3 min RT	-	6x1 s. Ti sprayed 10% w/w	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst. After APTES 2 another APTES spraying step was introduced, with the same subsequent annealing procedure. (this means like Ann.2)	0,50

Table 12-34: List of the samples produced including analysis of the hydrolytic class – part 20

#_Date	Activation	Ann. 1	APTES 1	Ann. 2 (sil.l.)	APTES 2	Ann. 3 (sil.l.)	Wash. 1	Ti-i-pr-oxid 1	Wash.2	Ann. 4	Ti-i-pr-o. 2	Ann. 5	Remarks	Tit. [mL 0,1 mM HCl]
221_19/09	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 m. 100 °C + 10 min 55°C + 2m RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min (100°C) + 15 m 55°C + 2 m RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 m. at 100°C + 20 m. at 55°C + 2 m. RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	0,56
222_19/09	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 m. 100 °C + 10 min 55°C + 2m RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min (100°C) + 15 m 55°C + 2 m RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 m. at 100°C + 20 m. at 55°C + 2 m. RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	0,66
223_19/09	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 m. 100 °C + 10 min 55°C + 2m RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min (100°C) + 15 m 55°C + 2 m RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 m. at 100°C + 20 m. at 55°C + 2 m. RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	0,56
224_19/09	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 m. 100 °C + 10 min 55°C + 2m RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	60 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	60 min 100°C + 3 min RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	0,44
225_19/09	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 m. 100 °C + 10 min 55°C + 2m RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	60 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	60 min 100°C + 3 min RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	0,48
226_19/09	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 m. 100 °C + 10 min 55°C + 2m RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	60 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	60 min 100°C + 3 min RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	0,48
227_03/10	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	75 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	75 min 100°C + 3 min RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	0,56
228_03/10	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	75 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	75 min 100°C + 3 min RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	0,52
229_03/10	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	75 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	75 min 100°C + 3 min RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	0,56

Table 12-35: List of the samples produced including analysis of the hydrolytic class – part 21

#_Date	Activation	Ann. 1	APTES 1	Ann. 2 (sil.l.)	APTES 2	Ann. 3 (sil.l.)	Wash. 1	Ti-i-pr-oxid 1	Wash.2	Ann. 4	Ti-i-pr-o. 2	Ann. 5	Remarks	Tit. [mL 0,1 mM HCl]
230_03/10	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 m. 100 °C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min (100°C) + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 m. at 100°C + 3 min RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	0,54
231_03/10	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 m. 100 °C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min (100°C) + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 m. at 100°C + 3 min RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	0,48
232_03/10	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 m. 100 °C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min (100°C) + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 m. at 100°C + 3 min RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	0,58
233_03/10	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 8x1 s. ; pH not adj.	60 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 8x1 s. ; pH not adj.	60 min 100°C + 3 min RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	0,42
234_03/10	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 8x1 s. ; pH not adj.	60 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 8x1 s. ; pH not adj.	60 min 100°C + 3 min RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	0,46
235_03/10	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 8x1 s. ; pH not adj.	60 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 8x1 s. ; pH not adj.	60 min 100°C + 3 min RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	0,40
236_03/10	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 m. 100 °C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 8x1 s. ; pH not adj.	75 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 8x1 s. ; pH not adj.	75 min 100°C + 3 min RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	0,42
237_03/10	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 8x1 s. ; pH not adj.	75 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 8x1 s. ; pH not adj.	75 min 100°C + 3 min RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	0,46
238_03/10	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 8x1 s. ; pH not adj.	75 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 8x1 s. ; pH not adj.	75 min 100°C + 3 min RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	0,40

Table 12-36: List of the samples produced including analysis of the hydrolytic class – part 22

#_Date	Activation	Ann. 1	APTES 1	Ann. 2 (sil.l.)	APTES 2	Ann. 3 (sil.l.)	Wash. 1	Ti-i-pr-oxid 1	Wash.2	Ann. 4	Ti-i-pr-o. 2	Ann. 5	Remarks	Tit. [mL 0,1 mM HCl]
239_03/10	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 m. 100 °C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min (100°C) + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 m. at 100°C + 3 min RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst. Glass substrate = SCHOTT DURAN bottle	0,12
240_03/10	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 m. 100 °C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min (100°C) + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 m. at 100°C + 3 min RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst. Glass substrate = SCHOTT DURAN bottle	0,12
241_03/10	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 m. 100 °C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	35 min (100°C) + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 6x1 s. ; pH not adj.	90 m. at 100°C + 3 min RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst. Glass substrate = SCHOTT DURAN bottle	0,12
242_03/10	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 m. 100 °C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 7x1 s. ; pH not adj.	60 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 7x1 s. ; pH not adj.	60 min 100°C + 3 min RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	0,62
243_03/10	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 7x1 s. ; pH not adj.	60 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 7x1 s. ; pH not adj.	60 min 100°C + 3 min RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	0,72
244_03/10	Act. w. 2 M HCl/NaOH at RT for 1 min. each; poured in bottle; rinsed w. H2O after each step	30 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 7x1 s. ; pH not adj.	60 min 100°C + 3 min RT	APTES in EtOH pur. 1% w/w sprayed f. 7x1 s. ; pH not adj.	60 min 100°C + 3 min RT	-	6x1 s. Ti sprayed 10% w/w	-	-	-	In the oven over night at 100°C	The bottle was turned randomly after each APTES spray burst. The b. was turned randomly randomized after each Ti spray burst.	0,64
245_03/10	-	-	-	-	-	-	-	-	-	-	-	-	Blank (DURAN SCHOTT bottles)	0.14
246_03/10	-	-	-	-	-	-	-	-	-	-	-	-	Blank (DURAN SCHOTT bottles)	0.12

Remarks for chapter 12.2 (if not denoted differently):

- The pH value of the APTES solution was adjusted with 100% acetic acid and the usage of a pH-electrode.
- The concentration of the APTES solution does not consider the addition of acetic acid.
- The pressure was set to 5 bars at the pressure reduction valve.
- Duration of spraying: app. 3-5 s. From sample 80 on the spraying times are well defined.
- The samples 1-24 were preheated to 100°C over night before the first APTES coating step.
- The samples 49-80 were preheated to 160°C over night before the first APTES coating step.
- The samples 81-112 were preheated to 100°C for 45 min before the first APTES coating step.
- The samples 113-121 were preheated to 65°C for 45 min before the first APTES coating step.
- The samples 122-130 were preheated to 80°C for 45 min before the first APTES coating step.
- The samples 131-164 were preheated to 60°C for 45 min before the first APTES coating step.
- If the sample number is printed **BOLD**: sample was used up for in-house testing of TiO_2 and APTES leaching or testing of the mechanical stability.

12.3 Equipment and materials

Equipment

Water purification system: TKA MicroPure UV Ultra-Pure Water System

(The deionized water used in this work was made with this water purification system.)

ICP-OES: Varian Vista-MPX CCD Simultaneous ICP-OES

FTIR: Bruker Vertex 70; DLaTGS detector with an ATR unit: MVP Pro Star; Diamond crystal; resolution 4cm-1; 16 scans; 4500-600 cm-1

UHPLC: Waters Acquity UPLC H-Class system with 2D-technology with a Waters Acquity SQ Detector mass spectrometer and a Waters Acquity UPLC PDA photo diode array detector

TOC analyzer: Shimadzu SSM-5000A

UV-VIS spectrometer: Perkin Elmer Lambda 950

Goniometer: Krüss Easydrop

Materials

Pasteur pipettes: Roth soda-lime glass 150 mm pipettes

Microscope slides: Menzel GmbH & Co KG app. 76x26 mm cut edges (soda-lime glass)

Table 12-37: Chemicals used

Compound	Abbr.	Note	Product number	Company
Ethanol	EtOH	99.8%; 1% MEK	9065.6	Roth
(3-Aminopropyl)triethoxysilane	APTES	98%	919-302	Fluka
Titanium-isopropylate	$Ti(i\text{-}O\text{-}Pr)_4$	97%	546-689	Aldrich
TiO2 nano particles	-	VP90	-	Degussa
Sodium hydroxide	NaOH	2 mol/L	1310-73-2	Roth
Hydrochloric acid	HCl (fuming)	37%	32862-91-2	Roth
Acetic acid	HAc	100%	64-19-7	Roth

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