

New/Surface-Modified Biocompatible Polymer for ICD Lead Insulation

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Zusammenfassung

Die durchschnittliche Standzeit einer implantierten Herzschrittmacher- oder Defibrillator-elektrode (Lead) beträgt etwa 10 Jahre. Zu den häufigsten Ausfallursachen zählt Materialermüdung der Isolierung, verursacht durch chemische, biologische oder mechanische Einflüsse. Jeder Ausfall eines Leads erfordert eine zeitnahe Operation, in der das defekte Bauteil ausgetauscht werden muss, um die Gesundheit des Patienten zu gewährleisten. Sowohl der Ausfall des Leads als auch der erforderliche operative Eingriff stellen für den Patienten Gesundheitsrisiken dar und verursachen darüber hinaus hohe Kosten. Vor diesem Hintergrund beschäftigt sich die vorgelegte Arbeit mit der Frage, ob eines der zurzeit handelsüblichen Materialien, wie es von der Herzschrittmacherindustrie eingesetzt wird, durch chemische Modifikation verbessert und die Standzeit von Leads im besten Fall verlängert werden kann.

Üblicherweise werden Polyurethane und Silikone zur Leadisolierung verwendet. Polyurethane werden dabei unter anderem für ihre hohe Abriebfestigkeit geschätzt, die nicht zuletzt auf ihren guten Gleiteigenschaften bei Kontakt mit menschlichem Gewebe in wässriger Umgebung beruht. Allerdings sind Polyurethane sehr empfindlich gegenüber Metallionenoxidation (MIO). Silikone hingegen sind gegenüber MIO unempfindlich, haben aber aufgrund ihres stark wasserabweisenden Verhaltens schlechte Reibeigenschaften im Vergleich zu Polyurethanen. Einige Studien an Polyurethanen haben jedoch in den letzten Jahren erfolgreich gezeigt, dass es möglich ist, die Oberflächeneigenschaften in Bezug auf Biodegradation durch das Einbringen sogenannter surface-modifying end-groups (SMEs) deutlich zu verbessern. Es wurde nachgewiesen, dass SMEs, die sich im Inneren des Materials befinden, dank der hohen Molekülbeweglichkeit zur Oberfläche des Materials wandern und dort die Oberflächeneigenschaften verändern können.

In dieser Arbeit wird gezeigt, dass die Technologie der SMEs auch für Silikone nutzbar gemacht werden kann. Das Ziel ist Silikon, welches für seine Eigenschaft stark hydrophob zu sein bekannt ist, hydrophil zu machen. Dabei wird ein kommerziell erhältliches Silikon, wie es von der Herzschrittmacherindustrie häufig zur Isolation von Leads verwendet wird, chemisch modifiziert. Zwei verschiedene SMEs werden auf zwei unterschiedliche Arten

ins Material eingebracht: Im ersten Fall werden die SMEs kovalent an das Silikonnetzwerk gebunden; im zweiten Fall wird dem Silikon ein Trägermolekül beigemischt, welches seinerseits die SMEs trägt. Die Trägermoleküle selbst bestehen dabei aus Silikon in der Hauptkette.

Um die zwei SMEs zunächst zu identifizieren werden 16 Komponenten auf ihre Kompatibilität mit dem Silikonssystem, wie es von der Herzschrittmacherindustrie verwendet wird, überprüft. Dabei handelt es sich um Hydrogen- und Vinylterminierte Siloxanologomere, die unter Verwendung des Karstedt-Katalysators via Hydrosilylierung eine kovalente Bindung formen. Es sei angemerkt, dass in dieser Arbeit eine modifizierte Version des Karstedt-Katalysators verwendet wird.

Zugversuch, Weiterreißfestigkeit und Härtemessung werden an den modifizierten Materialien durchgeführt, um diese mit den handelsüblichen Materialien vergleichen sowie die Mischungsverhältnisse optimieren zu können. Des Weiteren werden Proteinanhaftung an der Materialoberfläche, Wasseraufnahme des Kernmaterials sowie Kontaktwinkelmessung an der Oberfläche durchgeführt.

Es wird gezeigt, dass die mechanischen Eigenschaften der modifizierten Silikone zwar nicht konkurrenzfähig, jedoch vergleichbar gegenüber den Eigenschaften der kommerziell erhältlichen Materialien sind. Des Weiteren sind die mechanischen Eigenschaften der modifizierten Silikone ausreichend, um die Silikone weiteren Versuchen zu unterziehen. Die Untersuchung der Proteinanhaftung an der Oberfläche zeigt eine niedrigere Anhaftung an den modifizierten Silikonen gegenüber dem unmodifizierten Material. Darüber hinaus reduziert die Modifikation des Silikons durch SMEs den Kontaktwinkel von $\sim 114^\circ$ bei unmodifiziertem Material auf $\sim 55^\circ$ bei modifiziertem Silikon. Mit SMEs modifiziertes Silikon ist somit deutlich hydrophiler als unmodifiziertes Material. Folglich sind sowohl die zwei vorgestellten SMEs in ihrer Funktionalität als auch die Technologie der SMEs in ihrer Anwendbarkeit auf Silikone bestätigt.

Keywords: Hydrophiles Silikon, hydrophil, Schrittmacher, Defibrillator, Lead, Isolierung

Abstract

The average lifetime of an implanted pacemaker or defibrillator cable (lead) is approximately 10 years. One of the main lead failure mechanisms is deterioration of the insulation, which can be caused by chemical, biological, and mechanical processes. Each time lead failure occurs, an operation for its prompt replacement is required, in order to guarantee the patients' well-being. Since lead failure poses a health risk for the patients, and replacement operations are costly, this study aims at the improvement of one of the materials which is used by the cardiac pacing industry.

Silicone polymers are commonly used for pacemaker and defibrillator lead insulation. Previous studies showed that some modified polyurethane polymers exhibit very different as well as favorable mechanical surface properties, as compared to their unmodified counterparts. This was due to the fact that polymeric blocs within the network can migrate to the materials' surface, and thereby act as surface-modifying end-groups (SMEs).

In this study, a commercially available silicone system was modified by introducing two different SMEs and using two different approaches. In one approach the SMEs were covalently bonded to the silicone backbone, and in the second approach carrier molecules with the SMEs attached to them were admixed to the silicone. The carriers themselves had a siloxane backbone. The tensile properties, tear strength, and hardness were measured in order to describe the material as compared to commercially available mixtures, and to improve the mixing ratio of the components. Protein adhesion, water uptake, and surface wettability were evaluated to investigate the effect of the SMEs on the surface properties of the novel silicone formulations. While the mechanical properties of the silicone mixtures are comparable to but not competitive with the commercially available materials, contact angle measurement showed a significant reduction of the surface hydrophobicity: The initial contact angle of $\sim 114^\circ$ could be reduced to $\sim 55^\circ$. It was concluded that the two novel SMEs can be used in order to make initially hydrophobic silicone hydrophilic.

Keywords: Hydrophilic silicone, pacemaker lead insulation, surface-modifying end-groups, SMEs.

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Abbreviations, terms, and units

^1H NMR	proton nuclear magnetic resonance
2-PCA	2-propene carboxylic acid
3-BCA	3-butene carboxylic acid
3-BCEE	3-butene carboxylic ethylester
3-BPDEE	3-butene phosphonic diethylester
4-AM	4-acryloylmorpholine
AAc	allylacetone
AAm	acrylamide
AB	allylbenzene
ABr	allyl bromide
AEE	allyl ethyl ether
APDEE	allyl phosphonic diethylester
APS	allyl phenyl sulfone
aq.	aqueous
ASA	allylsuccinic anhydride
ATC	acid treated clay
BA	boric acid
BB	bromobutane
BCA	bicinchoninic acid
BO	biological oxidation
BSA	bovine serum albumin
CAS #	Chemical Abstracts Service Registry Number
CDCl_3	deuterated chloroform
cm	centimeter
$^\circ$	degree (contact angle)
$^\circ\text{C}$	degree Celsius
d	doublet in ^1H NMR
D_2O	deuterated water, i.e. heavy water
DBS	dibutyl sulfide
DBSO	dibutyl sulfoxide

DBSO ₂	dibutyl sulfone
DCHI-TFB	dicyclohexylimidazolium tetrafluoroborate
DCM	dichloromethane
DMAM	dimethyl allylmalonate
DVS	divinylsulfone
DVTMS	divinyltetramethyldisiloxane
e.g.	exempli gratia; for example
ELISA	enzyme-linked immunosorbent assay
ESC	environmental stress cracking
FBS	fetal bovine serum
FS	fumed silica
FTIR	Fourier transform infrared spectroscopy
g	gram
GPC	gel permeation chromatography
H	hydrogen
H ₂ O	water
H ₂ O ₂	hydrogen peroxide
HEPES	4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid
HMDSz	hexamethyldisilazane
HRP	horseradish peroxidase
i.e.	id est; that is
kN	kilonewton
lead	pacemaker or defibrillator cable
Lead	Herzschrötmacher- oder Defibrillatorelektrode
m	multiplet in ¹ H NMR; meter in tear testing
M	molar concentration in mole per liter
m ²	square meter
µg	microgram
µm	micrometer
mg	milligram
MIO	metal ion oxidation; Metallionenoxidation
mL	milliliter

mm	millimeter
mmol	millimole
mod. Pt-cat	modified version of the Karstedt's-catalyst; CAS # 400758-55-6
mol	mole
MP35N	cobalt nickel chrome molybdenum alloy
MPa	megapascal; $1 \text{ MPa} = 1 \text{ N/mm}^2$
mPa*s	dynamic viscosity in millipascal-second
MSB	molecular sieve beads
nm	nanometer
Na ₂ CO ₃	sodium carbonate
NaOH	sodium hydroxide
OM-CTS	octamethyl-cyclotetrasiloxane
OVA	ovalbumin
P 1300	Silopren [®] U base compound P 1300
Pa*s	dynamic viscosity in pascal-second
PDMS	polydimethylsiloxane
PDMS _{vinyl}	vinyl-terminated polydimethylsiloxane
P(DMS-co-MHS)	poly(dimethylsiloxane-co-methylhydrosiloxane)
PEO	polyethylene oxide
PMHS	polymethylhydrosiloxane
% _{NMR}	percent by ¹ H NMR signal
% _{wt}	percent by weight
PMDS	pentamethyldisiloxane
ppm	chemical shift of ¹ H NMR in parts per million
PPS	polypropylene sulfide
PPS _{allyl}	allyl-terminated polypropylene sulfide
PPS _{butyl}	butyl-terminated polypropylene sulfide
PPSO	polypropylene sulfoxide
PPSO ₂	polypropylene sulfone
pro-hydrophile	hydrophobic component capable of becoming hydrophilic
PS	propylene sulfide
PT	propyl thioacetate

PTB	potassium tert butoxide
Pt-cat	Karstedt's-catalyst
Pt-cat _s	Karstedt's-catalyst in vinyl-terminated PDMS matrix
Pt-cat _x	Karstedt's-catalyst in xylene
PTFE	polytetrafluoroethylene
q	quartet in ¹ H NMR ; quintet in ¹ H NMR
s	singlet in ¹ H NMR
SAS	sodium allyl sulfonate
Si	the chemical element silicon, not to be confused with silicone polymer
SM	sodium methylate
SME	surface-modifying end-group
t	triplet in ¹ H NMR
T _R	room temperature
TBCEE-TM-CTS	tetraBCEE-tetramethyl-cyclotetrasiloxane
TEA	triethylamine
THF	tetrahydrofuran
TFMSA	trifluoromethanesulfonic acid
TK(DMS)S	tetrakis(dimethylsiloxy)silane
TM-CTS	tetramethyl-cyclotetrasiloxane
TMB substrate	tetramethylbenzidine substrate
U 1	Silopren [®] U 1 linear vinyl terminated polydimethylsiloxane
U 430	Silopren [®] U cross-linking agent 430
VCEE	vinyl carboxylic ethylester
VPDEE	vinyl phosphonic diethylester
VSEE	vinyl sulfonic ethylester

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1 Motivation

Biodegradation of polyurethane elastomers still remains a limiting factor to their application in the field of implantable biomedical devices. In spite of extensive research, none of the changes made to the chemical composition of these segmented thermoplastic polymers could fully inhibit the biodegradation mechanisms. [1-3]. Widespread representatives of this material group for biomedical applications are ElasthaneTM by the Polymer Technology Group, Berkeley, CA, and PellethaneTM by the Dow Chemical Company, Midland, MI. These materials are block copolymers, made from aliphatic glycols representing the soft segment, and aromatic cyanates representing the hard segment [4, 5]. The polymerization scheme of PellethaneTM is depicted in **Fig. 1**.

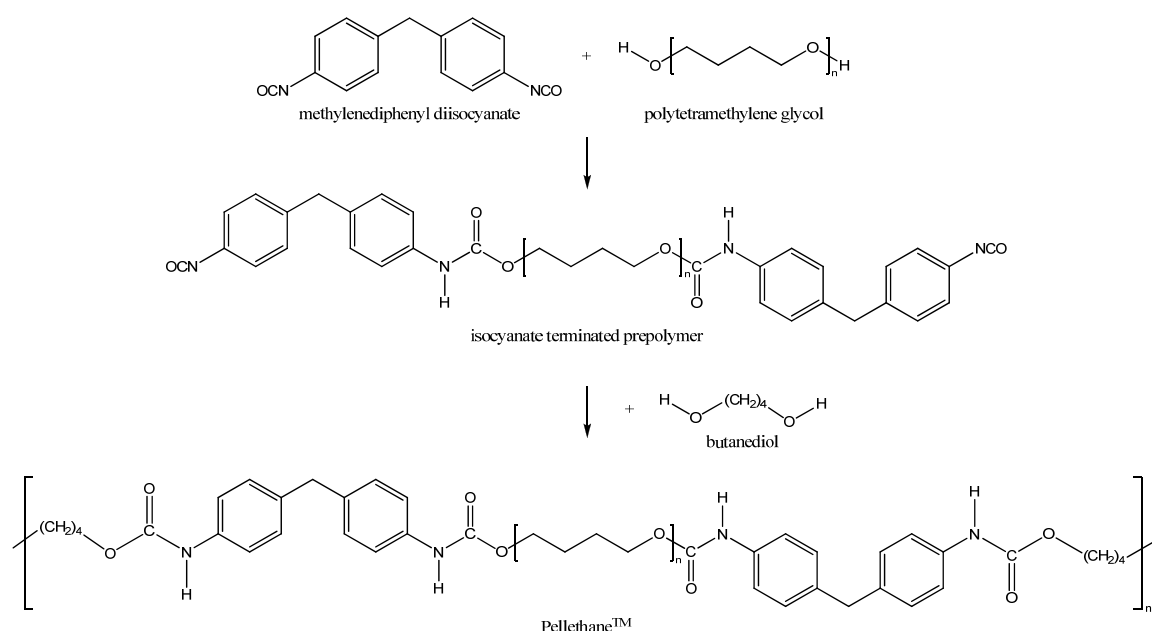


Fig. 1: Polymerization scheme of PellethaneTM with aliphatic glycols representing the soft segment, aromatic cyanates representing the hard segment, and butanediol used as chain extender.

Variation of the components' ratios of segmented polyether polyurethanes allows for the production of materials with a large spectrum of mechanical, physical and chemical properties. High resistance to wear and fatigue, as well as good tensile properties made them become the first choice for many applications like arteriovenous shunts, artificial heart diaphragms, heart valves, ventricular assist bladders, drug delivery systems, joint prosthesis, vascular grafts, and neurologic as well as cardiac pacing leads [6-8]. However, they are

susceptible to biologic oxidation (BO), environmental stress cracking (ESC), and in the case of use as pacemaker lead insulation also metal ion oxidation (MIO) [7-10]. At the present time it can be assumed that these degradation mechanisms will remain an imminent problem in the use of polyether polyurethanes as cardiac pacing lead insulation.

In recent years, many attempts have been made to improve the biostability of well-known polyurethanes by introducing surface modifying end-groups (SMEs). Even though only some of the published results were positive, the general approach still seems promising [11-16]. Detailed information about the findings will be given below in **chapter 3.1 Materials for cardiac pacing lead insulation**.

Using SMEs in combination with materials which are not as susceptible to BO, ESC, and MIO as polyether polyurethanes may lead to a new or modified biomaterial with a combination of positive properties: On the one hand, the good bulk properties of the initial material may be preserved, providing the bulk with high resistance to the various degradation mechanisms. On the other hand, surface properties may be enhanced by the SMEs, leading to surface properties comparable to those of polyether polyurethanes, e.g. high resistance to wear and fatigue. This would make the new or modified material competitive to polyether polyurethanes, allowing for a replacement of polyether polyurethanes in applications requiring high resistance to BO, ESC, and MIO.

2 Overall goal and two possible pathways

The main goal of this work is to modify an existing polymer, which is known to have high resistance to BO, ESC, and MIO, by adding SMEs to the material. Only polymeric materials which are well-established in the biomedical field and commercially available at low cost will be considered. The desired effect of the SMEs is improving the surface properties of the material with regard to surface hydrophilicity. Furthermore, over the lifetime of an implant the positive surface effect of the SMEs should not be obliterated. Since removal of some of the implants surface is likely to occur by wear and tear, the modification of the material will not be limited to the materials surface, but involve the bulk material, leading to a self-renewing surface.

Silicone as used by the cardiovascular pacing industry was chosen as the bulk material of interest. This is due to the fact that these silicone types are commercially available at reasonable cost, the processing techniques are well-established, and the silicones are known for their high resistance to BO, ESC, and MIO. The drawback of these silicones, however, is that they are characterized by low resistance to wear and tear as compared to polyether polyurethanes. Furthermore, they are known for their high hydrophobicity, again in stark contrast to polyether polyurethanes. With regard to SMEs these two downsides of silicones go hand in hand: If it were possible to make the silicone surface hydrophilic, its resistance to wear and tear may be drastically increased. Hence, the SMEs have to be capable of making the materials surface hydrophilic. Due to the hydrophobic nature of silicone, however, incompatibility of the silicone precursors with hydrophilic SMEs is likely to occur. Thus, SMEs should be hydrophobic as long as they are within the bulk, but should be able to become hydrophilic on the materials surface. Prof. J.A. Hubbell coined the term “pro-hydrophile” to describe SMEs that show this behavior. Last but not least, the SMEs must be chemically compatible to the silicone precursors, i.e. not cause adverse effects like side reactions or degradation, in order to allow for material polymerization.

Two general pathways will be proposed in the course of this work in order to provide silicones with a hydrophilic surface: One pathway is the introduction of oxidation sensitive SMEs, and the other pathway is the introduction of hydrolytically sensitive SMEs. In both

cases the pro-hydrophile components capable of undergoing change from hydrophobic to hydrophilic should be stable in their hydrophobic state throughout the entire production process of the silicone. Once the silicone material is polymerized, a subsequent step should occur only on the materials surface, changing it from hydrophobic to hydrophilic. If this step requires processing prior to implantation, or if this change occurs after implantation, is both an option.

If one of these pathways leads to a new/modified silicone, physical properties of the modified silicone will be evaluated in order to describe the material properties as compared to unmodified silicone. Finally, results from in vitro testing regarding protein adhesion and surface hydrophilicity will show, if this novel material may be a candidate for future biomedical applications.

3 State of the art

3.1 Materials for cardiac pacing lead insulation

The three major degradation mechanisms of polyurethane elastomers are BO, ESC, and MIO. The latter occurs when polyurethane is used as pacemaker lead insulation where the CoNiCrMo-alloy MP35N is present [7-9]. It has been shown that the amount of polyether in polyether polyurethanes has a major influence on the severity of the degradation by ESC. In consequence, ether-free polyurethanes were suggested as more biostable polyurethanes [17]. Replacing parts of the polyether with polydimethylsiloxane (PDMS) is another solution to this problem which has lead to polysiloxane polyether polyurethanes with reduced BO, ESC and MIO [11, 12, 18, 19]. Furthermore, PDMS-based polyurethane materials were shown to be unaffected by commercially available sterilization techniques [20].

Over the years, different building blocks were used as SMEs in the attempt to improve the biostability of previously tested polyurethanes. It was shown for polyethylene oxide (PEO) and polytetrafluoroethylene (PTFE) SMEs that chain mobility within the polymer network allows for migration of the SMEs to the material surface. There, the end-groups can form a layer, changing the polymers' surface characteristics [13-16]. PEO was chosen as it is known for its ability to increase the hydrophilicity of a polymer surface and to reduce cellular adhesion as well as protein adsorption [21-25]. On the other hand, hydrophilic PEO SMEs as well as hydrophobic PTFE SMEs were shown to have no influence on macrophage adhesion, fusion and apoptosis, whereas macrophage fusion and apoptosis can be affected by the presence of PDMS SMEs [26]. While in vitro tests indicated that MIO is accelerated for both PEO SMEs and PTFE SMEs, in vivo tests showed that PEO SMEs have no effect on MIO resistance, whereas PTFE SMEs slow down but do not prevent MIO in vivo. Particularly interesting is the misleading result from the in vitro tests, where materials showed the opposite behavior than in vivo [13]. Similar results were obtained regarding BO and ESC: There was no difference between samples with and without PEO SMEs [14], and samples with PTFE SMEs performed better than the control [15]. In the latter case, again the onset of degradation was delayed, but degradation not fully prevented.

The experiments with PEO SMEs and PTFE SMEs used polyurethanes of Shore hardness 80A, which is commonly referred to as a soft type [13-15]. It is difficult to test the biostability of harder polyurethane types, e.g. Shore 55D, as degradation mechanisms proceed much slower than in softer types. However, the positive effect of PTFE SMEs on the in vivo biostability could be demonstrated even for higher hardness polyurethane: MIO resistance is increased in samples containing PTFE SMEs, and resistance to ESC is the same in samples with and without PTFE SMEs [16].

For the clinical application of cardiac pacing leads, physicians regard the improvement of lead implantability and explantability as the main concerns, while manufacturers are on a continuous search for materials which will provide a longer implant lifetime, i.e. about 10 years at present. For the implantation, high surface hydrophilicity will yield a surface which is slippery when in contact with biological liquids and/or tissue. This will ease implantation, since inserting the pacing lead into and moving through the blood vessels become easier. As for implant lifetime and explantation, surface hydrophobicity plays, among other factors, a major role in the response of the host organism to an implant [27]. This is due to the fact that the degree of surface hydrophobicity strongly influences the degree of protein adhesion to the implant surface. Protein adhesion to the implant surface is the first step in the inflammatory response cascade of the host organism [28, 29]. Antibody response has been shown not only for polymeric materials, but also for implant-bound proteins [30]. Numerous attempts are made to reduce or avoid protein adhesion to implant surfaces in order to reduce the inflammatory response [31-39].

Protein adhesion also prepares the ground for tissue growth on the implant surface. Encapsulation of transvenous cardiac pacing leads through the formation of a collagenous capsule has been shown [40]. Furthermore, BO, ESC, and MIO are known to lead to a micro-cracked surface or even cracked bulk material. This allows for collagenous tissue ingrowth which represents a strong bond between the implant and the surrounding tissue. It is the main cause for difficult lead extraction, and was the motivation for the development of a wide range of explantation techniques and tools [41-44].

3.2 Selected materials used today by the cardiac pacing industry

In this chapter some of the commercially available materials which are typically used by the cardiac pacing industry will be presented, i.e. three types of silicones and one polyurethane. The latter is PellethaneTM 2363, which is used in spite of the fact that it is susceptible to BO, ESC and MIO. In order to reduce the materials degradation by MIO, PellethaneTM is never brought in direct contact with the conductors made from MP35N, which is a cobalt nickel chrome molybdenum alloy and the origin of cobalt ions causing MIO. PellethaneTM is used as a tubing with a wall-thickness of 0.08 mm as the outer insulation of the leads, harboring the conductors, which themselves are placed within a silicon tubing. With this multilayer design, the polyurethane serves as a barrier between the human body and the silicone rubber. This is done because of the good surface properties of the polyurethane, e.g. offering a hydrophilic as well as smooth and even surface, high resistance to tribological wear, and a slippery surface when in contact with biological tissue which simplifies the implantation of the lead.

The three silicone types are MED by NuSil Technology LLC, Carpinteria, Ca, Silastic[®] by Dow Corning, Midland, MI, and Silopren[®], by Momentive Performance Materials, Leverkusen, Germany, formerly GE Bayer Silicones, Leverkusen, Germany. These three materials are similar inasmuch as they are all silicone elastomers, delivered as 2 separate components with one containing the hydrogen-terminated species and the other containing the vinyl terminated species, mixing ratio is always 1:1, and polymerizing via platinum-catalyzed addition reaction.

The producers of the silicones for lead insulation offer information about their materials to very different extents, as can be seen in **Tab. 1**, where the polyurethane and the three silicones for cardiac pacing leads are listed with information regarding their composition. NuSil Technology LLC as well as Momentive Performance Materials actually offers a catalogue of silicone precursors. Different monomers, cyclic and non-cyclic, cross-linkers, and catalysts are available to allow for preparing tailor-made polymer compositions.

Polyurethane	Composition
Pellethane™ <ul style="list-style-type: none"> • P55DE [45, 46] • P75D [47, 48] 	polytetramethylene glycol, methylenediphenyl diisocyanate, 1,4-butanediol
Silicones	Composition
MED <ul style="list-style-type: none"> • MED-4750 [49-51] • MED-4755 [52-54] • MED-4765 [49, 55, 56] 	amorphous silica, dimethyl and methylhydrogen siloxane copolymer
Silastic® LSR <ul style="list-style-type: none"> • 7-4870 [57, 58] • 7-6830 [57, 59] • 7-6860 [57, 60] 	7-4870: dimethyl siloxane, dimethylvinyl-terminated; dimethylvinylated and trimethylated silica, dimethyl, methylvinylsiloxane, dimethylvinyl-terminated; dimethyl, methylhydrogen siloxane with methyl silsesquioxane; 2-methylbutanol 7-6830: dimethyl siloxane, dimethylvinyl-terminated; trimethylated silica, dimethyl, methylvinyl siloxane, dimethylvinyl-terminated; dimethyl, methylhydrogen siloxane; dimethylcyclsiloxanes 7-6860: dimethyl siloxane, dimethylvinyl-terminated; trimethylated silica, dimethyl, methylvinyl siloxane, dimethylvinyl-terminated; dimethyl, methylhydrogen siloxane
Silopren® LSR <ul style="list-style-type: none"> • LSR 4030 [61-63] • LSR 4050 [61, 64, 65] • LSR 4070 [61, 66, 67] 	vinylpolydimethylsiloxane; treated filler, siloxanes and silicones, di-Me, Me vinyl, vinyl group-terminated; dimethylhydrogenpolysiloxane

Tab. 1: Selected materials used today by the cardiac pacing industry. All material names and chemicals are listed with the notations used in publications, manufacturers' product profiles, and material safety data sheets.

Tab. 2 shows information about the catalysts that are offered by the producers and used in the three silicones. While the term “platinum catalyzed” is the only information available for Silastic® LSR, for Silopren® LSR the catalyst Additive Pt is available, described as “polydimethylsiloxane containing vinyl groups, with platinum catalyst and fillers”. Three catalysts are available for MED-type silicones: CAT-07 is an ammonium siloxanolate, intended for the use with siloxane cyclics, and CAT-53 is a phenyl containing platinum catalyst. Neither cyclics nor phenyl containing substances are listed in the contents of the materials precursors, see **Tab. 1** above. The third catalyst, CAT-50, is described as “platinum-divinyltetramethylsiloxane complex in a low molecular weight, functional vinyl polymer”, its Chemical Abstracts Service Registry Number (CAS #) is 68478-92-2.

Product name	Catalyst name	Catalyst composition	CAS #
MED <ul style="list-style-type: none"> • MED-4750 [49-51] • MED-4755 [52-54] • MED-4765 [49, 55, 56] 	CAT-07 [68, 69] silicone catalyst	tetramethyl-ammonium siloxanolate polymerization catalyst, 90 % tetramethylammonium silanolate, 10 % cyclohexane	68440-88-0 00110-82-7
	CAT-50 [70, 71] vinyl platinum catalyst	platinum-divinyltetramethylsiloxane complex in a low molecular weight, functional vinyl polymer	68478-92-2
	CAT-53 [72, 73] phenyl platinum catalyst	platinum-divinyltetraphenylsiloxane complex in a functional diphenyl copolymer	68478-92-2
Silastic [®] LSR <ul style="list-style-type: none"> • 7-4870 [57, 58] • 7-6830 [57, 59] • 7-6860 [57, 60] 	n. a. [57]	“platinum-catalyzed”	n. a.
Silopren [®] LSR <ul style="list-style-type: none"> • LSR 4030 [61-63] • LSR 4050 [61, 64, 65] • LSR 4070 [61, 66, 67] 	Additive Pt [74]	polydimethylsiloxane containing vinyl groups, with platinum catalyst and fillers	n. a.

Tab. 2: Catalysts for addition reaction of materials used today by the cardiac pacing industry. All material names and chemicals are listed with the notations used in publications, manufacturers’ product profiles, and material safety data sheets.

3.3 The Karstedt’s-catalyst and a modified version thereof

The Karstedt’s-catalyst (Pt-cat) shown in **Fig. 2** is a platinum(0)-1,3-divinyl-1,1,3,3-tetramethyl-disiloxane complex. It is commercially available and commonly supplied as a liquid solution. Its intended use is hydrosilylation [75, 76]. In the case of the siloxanes used today by the cardiac pacing industry this obviously works well in the absence of solvents, but the catalyst has also been applied successfully in the presence of different solvents, e.g. dichloromethane (DCM), toluene, and tetrahydrofuran (THF) [77-79]. The Karstedt’s-catalyst, as commercially available, is commonly supplied either in a vinyl terminated PDMS matrix, or in xylene. As it is a platinum catalyst, these two types will be referred to in the further course of this work as Pt-cat_s and Pt-cat_x, respectively.

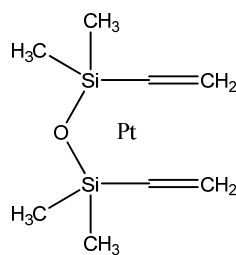


Fig. 2: Karstedt's-catalyst: Platinum(0)-1,3-divinyl-1,1,3,3-tetramethyldisiloxane complex, CAS # 68478-92-2, for hydrosilylation.

As we will see later in **chapters 6 Exploring the oxidative pathway** and **7 Exploring the hydrolytical pathway** there is also the necessity for a modified version of the Pt-cat. The reason is a possible deactivation of the Pt-cat, which may be the result of the formation of a colloidal platinum species. A yellow coloration of the reaction mixture was described in the literature as a typical sign for this deactivation [80]. This kind of coloration was also observed in reactions conducted later in this work. In a recent publication this phenomenon was addressed, and also the problem of by-product formation during hydrosilylation of olefins, when the Pt-cat is used. In consequence, a modification of the Pt-cat was proposed. **Fig. 3** shows the scheme of a simple method for the production of this modified Pt-cat [81].

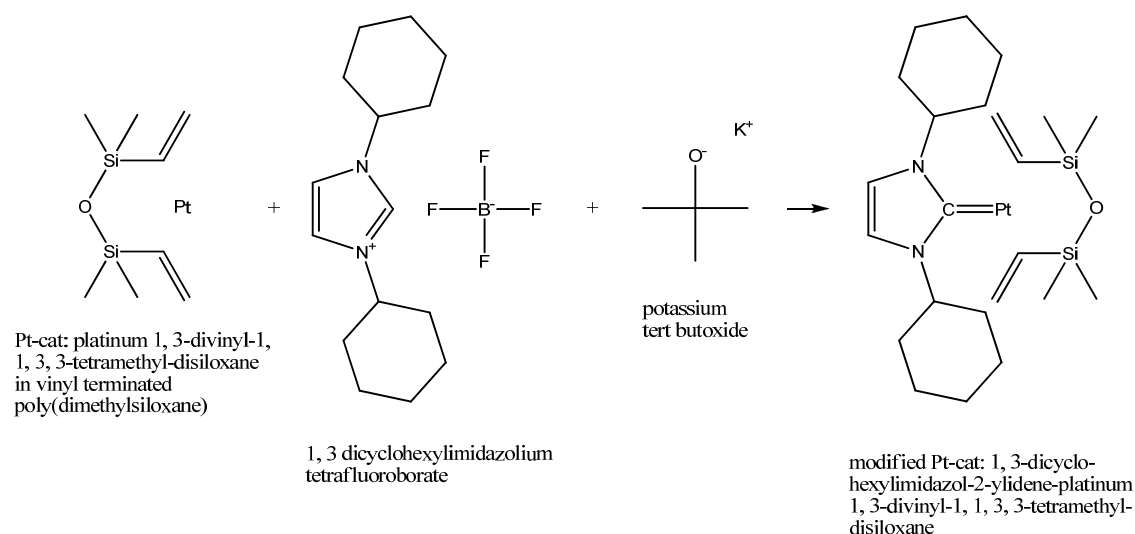


Fig. 3: Method for production of the mod. Pt-cat in a one-pot process, using the Pt-cat_s and two commercially available components.

For simplicity, and since the modified Karstedt's-catalyst was not given a name yet in the literature, it will be referred to as mod. Pt-cat in the further course of this work. Since the mod. Pt-cat is not commercially available, it was produced as described in the literature [81]. The production process will not be described here, since it is not part of this research work. After verification of the product via ^1H NMR the mod. Pt-cat was dissolved in xylene to form a 0.1 M solution. As suggested in the literature, the mod. Pt-cat was stored under protection from light.

In order to establish the state of the art for the use of the mod. Pt-cat, a literature research was conducted with SciFinder ScholarTM. The search yielded numerous hits, 8 sources describing the production of the catalyst [81-88], two using the mod. Pt-cat for hydrosilylation of linear or cyclic alkyl structures containing different functional groups [81, 89, 90], one reporting the use of the mod. Pt-cat for the preparation of high temperature stable silicones [91], and 5 sources reporting the modification of the mod. Pt-cat for the production of an amine platinum II complex and its application in cancer treatment [92-94]. But no literature reports the use of the mod. Pt-cat for the modification of silicones as used by the cardiac pacing industry, nor the attempt to introduce SMEs to silicone.

3.4 The oxidative pathway

For the oxidative pathway one polymer is proposed as SME-candidate: Polypropylene sulfide (PPS). This hydrophobic polymer can be rendered hydrophilic by oxidation to polypropylene sulfoxide (PPSO) and further to polypropylene sulfone (PPSO₂).

One of the prerequisites of introducing PPS into silicone is that PPS and the silicone precursors be miscible. Since PPS is a hydrophobic oil at T_R , producing a homogeneous mixture without phase separation can be possible. It is hypothesized that after polymerization of the silicone the PPS on the surface or within surface near regions of the silicone can be oxidized to form PPSO, and by a second oxidization step to PPSO₂. In case the linear initial PPS chains are covalently bonded to the silicone network at only one end, and chain mobility within the silicone network may allow for migration of the PPS chains to the material surface. There, the end-groups can form a layer, changing the polymers' surface

characteristics. As mentioned above in **chapter 3.1 Materials for cardiac pacing lead insulation**, this approach was shown to work in the case of PEO and PTFE SMEs [13-16]. Considering the energetic aspect, the motivation for the initial PPS chains to migrate to the materials' surface is the nucleophilic character of the sulfur in the PPS.

It is known that PPS can be oxidized by hydrogen peroxide (H_2O_2) to form PPSO and PPSO₂, using pathways with and without catalysts and in different solvents [95-97]. The general pathway of the oxidation of PPS by H_2O_2 , as shown in **Fig. 4**, has also been shown to work [98-100]. H_2O_2 is known to be present in inflammation sites, and first benefits from the use of PPS as a surface coating in vivo have been reported [101]. When the PPS-containing silicone is applied as an implant, the polymer surface is exposed to a much more oxidative environment than the bulk material. Additionally, if oxidation of PPS to PPSO or PPSO₂ should already occur within the bulk, the hydrophilic oxidation product would strive even more to leave the hydrophobic silicone bulk and migrate to its surface. However, this process may be lessened if PPSO and PPSO₂ were to exhibit reduced chain mobility within the bulk as compared to PPS, which could be caused by steric rotation hindrance.

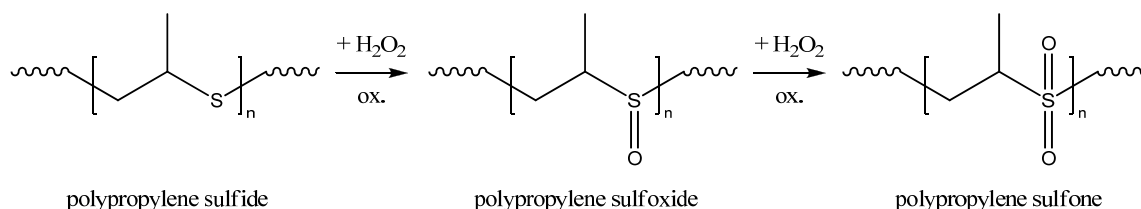


Fig. 4: Oxidation of PPS with H_2O_2 to form PPSO and subsequently PPSO₂.

PPS can be produced in a one pot process under inert gas atmosphere, by anionic ring opening polymerization. As initiator a thioacetate that can be deprotected with sodium methylate (SM) in dry THF is needed. The reactive species sodium thiolate will be formed in situ. When adding the desired equivalents of propylene sulfide (PS), the anionic ring opening polymerization will take place. The mechanism was shown to have controlled and living polymerization character. Further advantages are both the mild character of the reactive species as well as the process' tolerance to impurities - all reagents can be used as deliv-

ered and without any further purification [102]. **Fig. 5** shows the entire reaction scheme, with propyl thioacetate (PT) as the initiator.

In order to form a polymer with a functional group allowing for hydrosilylation, allyl bromide (AB) can be used as an end-capping reagent [103]. Side products are methyl acetate and sodium bromide. This polymerization must be conducted under inert gas atmosphere, since the presence of oxygen causes the formation of a sulfur-sulfur bond between two reactive species [98, 102-105]. Dimerization would obviously represent a chain termination mechanism, inhibiting the chain growth to its foreseen length, producing a low molecular weight polymer, and inhibit the end-capping with the molecule containing the functional group required for further use of the PPS.

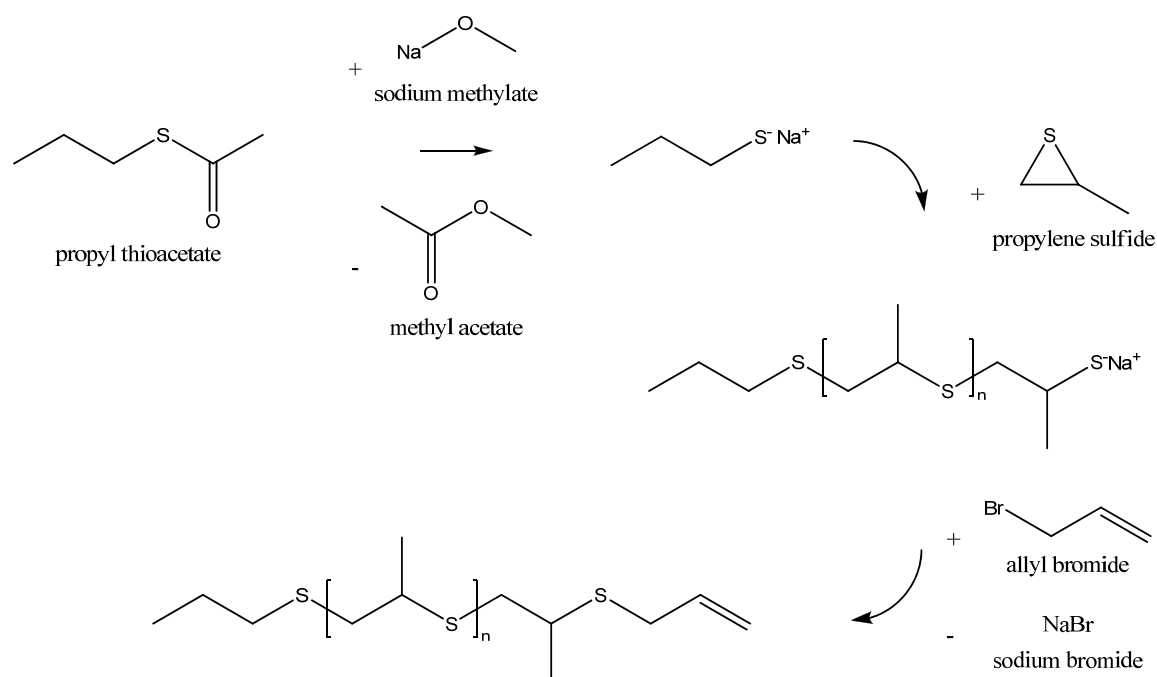


Fig. 5: Polymerization scheme of PPS with ring opening polymerization of propylene sulfide, using propyl thioacetate as initiator and allyl bromide as end-capping reagent.

3.5 The hydrolytical pathway

For the hydrolytical pathway numerous substances will be proposed as SME-candidates. All of the candidates must meet two requirements: First, they must contain either an ether group or an ester group, which can undergo hydrolysis in order to form a hydrophilic spe-

cies. The second requirement is that in case a side product is formed during hydrolysis, this side product must be of no harm to the host organism. The concept of the hydrolytical pathway is described using vinyl sulfonic ethylester (VSEE) as an example.

VSEE is proposed as SME-candidate, because the ester group can be hydrolyzed, the product being a hydrophilic sulfonic acid. The expectation that VSEE SMEs will migrate from the hydrophobic bulk to the surface is based upon the same reasoning as for PPS SMEs in **chapter 3.4 The oxidative pathway**. At the surface of the material the ester group is expected to undergo hydrolysis due to direct contact with water and/or hydrolizing media [106]. Hydrolysis will form ethanol as a low molecular weight side product which is split off, and in low concentrations ethanol should be of no harm to the host organism. **Fig. 6** shows the hydrolytical pathway of VSEE after polymerization.

After hydrolysis, the part remaining covalently bonded to the silicone is a sulfonic acid. This is not only hydrophilic but also presents a negative charge. This may reduce cell adhesion due to two mechanisms: Decreased interaction of bacterial cells with a hydrophilic surface on the one hand [107-113], and the repulsive force between the anionic cortex of the bacteria and the negative surface charge of the polymer on the other hand [107-109].

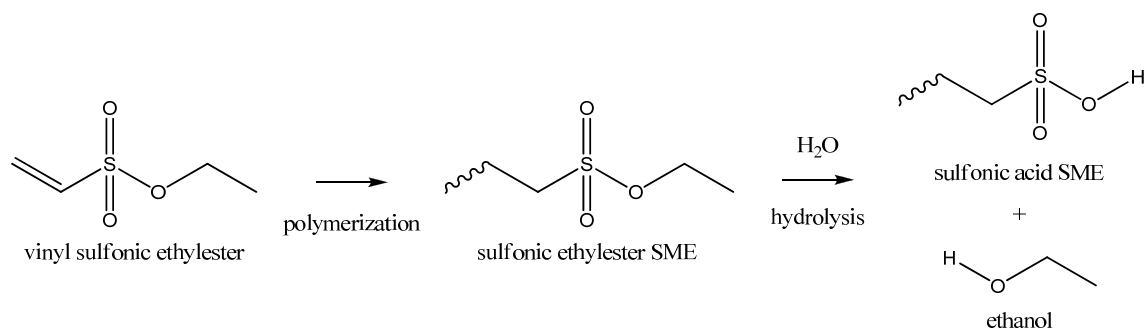


Fig. 6: Hydrolytical pathway of VSEE after polymerization: Hydrolysis leads to the formation of sulfonic acid and ethanol.

VSEE can be synthesized as shown in **Fig. 7** in a reaction of chloroethanesulfonyl chloride and ethanol in the presence of triethylamine. As a base the latter serves as both a dehydrohalogenating agent as well as a halogen acid acceptor [114, 115].

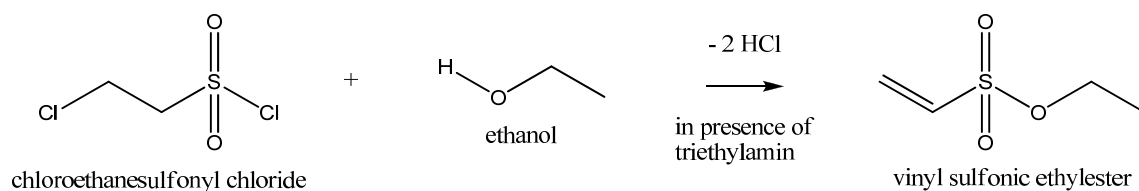


Fig. 7: Scheme for the formation of VSEE from chloroethanesulfonyl chloride and ethanol.

In this chapter, the hydrolytical pathway was exemplarily described for VSEE as the pro-hydrophile SME. Since this approach is imaginable for many other substances containing either an ether group or an ester group, which are capable of undergoing hydrolysis, a wide variety of SME-candidates will be tested. This will include linear carboxylic-, phosphonic, and sulfonic substances, yielding the respective acids, as well as cyclic substances like allylsuccinic anhydride, all of which capable of undergoing hydrolysis.

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4 Materials and methods

4.1 Materials

All materials were used as received. THF for PPS synthesis was dried with molecular sieve beads (MSB). Toluene for the production of the mod. Pt-cat was dried using a Dean-Stark trap, and stored using MSB. For materials without acronym please refer to **chapter 4.2 Methods**.

2-PCA	2-propene carboxylic acid, Aldrich, 134716, CAS # 625-38-7
3-BCA	3-butene carboxylic acid, Aldrich, 245925, CAS # 591-80-0
3-BCEE	3-butene carboxylic ethylester, Alfa Aesar, A12422, CAS # 1968-40-7 [116], and the analogue material from ABCR, AB116601, CAS # 1968-40-7 [117, 118]
3-BPDEE	3-butene phosphonic diethylester, Aldrich, 640522, CAS # 15916-48-0
4-AM	4-acryloylmorpholine, Aldrich, 448273, CSA # 5117-12-4
96 well plate	NUNC, F96 Maxisorp immuno plate, 442404
AAc	allylacetone, Aldrich, H13001, CAS # 109-49-9
AAm	acrylamide, Fluka, 01700, CAS # 79-06-1
AB	allylbenzene, Aldrich, A29402, CAS # 300-57-2
ABr	allyl bromide, Fluka, 05860, CAS # 106-95-6
AEE	allyl ethyl ether, Fluka, 02900, CAS # 557-31-3
antibodies	primary: polyclonal rabbit anti-OVA IgG A6D secondary: HRP conjugated goat anti-rabbit IgG, Bio-Rad, 170-6515
APDEE	allyl phosphonic diethylester, Aldrich, 565415, CAS # 1067-87-4
APS	allyl phenyl sulfone, Fluka, 06061, CAS # 16212-05-8
ASA	allylsuccinic anhydride, ABCR, AB135099, CAS # 7539-12-0
ATC	acid treated clay, Tonsil Optimum 210FF, Süd-Chemie, CAS # 70131-50-9
BA	boric acid, AppliChem, A2940,0500, CAS # 10043-35-3
BB	bromobutane, Sigma-Aldrich, B59497, CAS # 109-65-9

BCA kit	Pierce BCA Protein Assay Kit, Perbio, 23225
BSA	bovine serum albumin, PAA Laboratories GmbH, K41-001, CAS # 9048-46-8
casein	casein from bovine milk, Sigma, C3400, CAS # 9000-71-9
CDCl ₃	deuterated chloroform, Aramar Chemicals, 013300.2040, CAS # 865-49-6
D ₂ O	deuterated water, Aldrich, 151882, CAS # 7789-20-0
DBS	dibutyl sulfide, Merck, 8.20252.0100, CAS # 544-40-1
DBSO	dibutyl sulfoxide, Aldrich, B102407, CAS # 2168-93-6
DBSO ₂	dibutyl sulfone, Aldrich, B102202, CAS # 598-04-9
DCHI-TFB	dicyclohexylimidazolium tetrafluoroborate, Aldrich, 666181, CAS # 286014-38-8
DCM	dichloromethane, Fisher Chemical, D/1856/17, CAS # 75-09-2
DMAM	dimethyl allylmalonate, Aldrich, 476420, CAS # 40637-56-7
DVS	divinylsulfone, Aldrich, V3700, CAS # 77-77-0
DVTMS	divinyltetramethyldisiloxane, Aldrich, 371904, CAS # 2627-95-4 [119]
ethanol	Biosolve, 05250502, CAS # 64-17-5
FACS tube	Micronic, MP32022, 1.4 mL U-bottom, certified RNase/DNase free
FBS	fetal bovine serum, Gibco, 10270-106
FS	fumed silica, Sigma, S5505, CAS # 112945-52-5 [120, 121]
H ₂ O	water, tap, distilled, bi-distilled, or milli-q
H ₂ O ₂	hydrogen peroxide, Reactolab SA, 3000265, CAS # 7722-84-1
HEPES	4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid, Sigma, H3375, CAS # 7365-45-9
HMDSz	hexamethyldisilazane, Fluka, 52619, CAS # 999-97-3 [122]
mod. Pt-cat	modified version of the Karstedt's-catalyst, produced as described in the literature [81], CAS # 400758-55-6
MSB	molecular sieve UOP Type 3A beads, Fluka, 02573, CAS # 308080-99-1
Na ₂ CO ₃	sodium carbonate, Fluka, 71352, CAS # 497-19-8
NaOH	sodium hydroxide, Merck, 1.06498.1000, CAS # 1310-73-2
OM-CTS	octamethyl-cyclotetrasiloxane, Aldrich, 235695, CAS # 556-67-2 [123]

OVA	ovalbumin, Albumin from chicken egg white, Grade VI, Sigma, A2512, CAS # 9006-59-1
P 1300	Silopren [®] U base compound P 1300, Momentive Performance Materials [124, 125]
PBS 1x	phosphate buffered saline solution of pH 7.4 was produced by dilution of PBS with a concentration of 10x, pH 6.8, as delivered by the EPFL, SV-IN, using milli-q water.
PDMS _{vinyl}	vinyl-terminated polydimethylsiloxane, Aldrich, 433012, 25,000 g/mol, CAS # 68083-19-2 [126], used for the production of the high molecular weight 3-BCEE carrier in chapter 8.2.3 Non-functionalized SME carrier ; ABCR, AB109355, 770 g/mol, CAS # 68083-19-2 [127, 128], used in chapters 9.1 Unmodified silicone - proof of concept and 9.2 Modified silicone - proof of concept .
P(DMS-co-MHS)	poly(dimethylsiloxane-co-methylhydrosiloxane), Aldrich, 482196, 950 g/mol, CAS # 68037-59-2 [129], and the analogue product by ABCR, AB109381, CAS # 68037-59-2 [130, 131]
PMHS	polymethylhydrosiloxane, Fluka, 81330, CAS # 63148-57-2 [132], and the analogue from Aldrich, 176206, CAS # 63148-57-2 [133], please note: ¹ H NMR showed that these two components are identical
PMDS	pentamethyldisiloxane, Aldrich, 76840, CAS # 1438-82-0
PPS	polypropylene sulfide, synthesized as described in the literature [98, 102, 104, 105]
PPS _{allyl}	allyl-terminated polypropylene sulfide, synthesized as described in the literature [98, 102-105]
PPS _{butyl}	butyl-terminated polypropylene sulfide, synthesized as described in the literature [98, 102, 104, 105]
PS	propylene sulfide, Fluka, 82330, CAS # 1072-43-1
PT	propyl thioacetate, Alfa Aesar, B21875, CAS # 2307-10-0
PTB	potassium tert butoxide, Merck, 8.04918.0100, CAS # 865-47-4
Pt-cat	Karstedt's-catalyst, either Pt-cat _S or Pt-cat _X
Pt-cat _S	Karstedt's-catalyst in vinyl-terminated PDMS matrix, Aldrich, 479527, CAS # 68478-92-2

Pt-cat _x	Karstedt's-catalyst in xylene, Aldrich, 479519, CAS # 68478-92-2
SAS	sodium allyl sulfonate, ABCR, AB111813, CAS # 2495-39-8
SM	sodium methylate, Sigma-Aldrich, 403067, CAS # 124-41-4
TBCEE-TM-CTS	tetraBCEE-tetramethyl-cyclotetrasiloxane, produced as described in chapter 8.2.1 Functionalized SME carrier using TFMSA
TEA	triethylamine, Sigma-Aldrich, 90340, CAS # 121-44-8
THF	tetrahydrofuran, Fisher Chemical, T/0706/PB17, CAS # 109-99-9
TFMSA	trifluoromethanesulfonic acid, Aldrich, 347817, CAS # 1493-13-6 [134]
TK(DMS)S	tetrakis(dimethylsiloxy)silane, Aldrich, 497509, CAS # 17082-47-2 [135]
TM-CTS	tetramethyl-cyclotetrasiloxane, Aldrich, 512990, CAS # 2370-88-9 [136]
TMB substrate	Tetramethylbenzidine substrate solution for ELISA, eBioscience, 00-4201-56
toluene	VWR, 28676.322, CAS # 108-88-3
Tween [®] 20	Polyethylene glycol sorbitan monolaurate, Sigma-Aldrich, P7949, CAS # 9005-64-5
U 1	Silopren [®] U 1 linear vinyl terminated polydimethylsiloxane, Momentive Performance Materials [137, 138]
U 430	Silopren [®] U cross-linking agent 430, Momentive Performance Materials [139, 140]
VCEE	vinyl carboxylic ethylester, Fluka, 01750, CAS # 140-88-5 [141]
VPDEE	vinyl phosphonic diethylester, Aldrich, 116130, CAS # 682-30-4
xylene	Sigma-Aldrich, 33817, CAS # 1330-20-7

4.2 Methods

Hydrosilylation reactions were carried out in standard laboratory glass ware, i.e. round bottom flasks unless stated otherwise, in normal air atmosphere, and under constant stirring with a magnetic Teflon covered stir bar. Reactions at elevated temperature were heated using a silicone oil bath, and temperature control was ensured with an automatic control

loop measuring the temperature of the oil bath. In case solvents were used in reactions at elevated temperature, either a coil condenser or a Dimroth condenser was mounted on top of the reaction vessel. Tap water was used as cooling medium.

The amount of liquid reactants was measured volumetrically, using pipettes for liquids of low viscosity and below 1 mL of volume. For liquids of high viscosity or above 1 mL syringes of 1 mL, 2.5 mL, 5 mL, and 10 mL were used. Furthermore, syringes with needle were used for liquid reactants which were delivered in a glass bottle with septum, e.g. PMDS. The amount of highly viscous and of solid reactants, e.g. P 1300 and fumed silica, was determined gravimetrically.

Reactions requiring protective gas atmosphere were conducted under argon. For reactions requiring the absence of oxygen, i.e. the polymerization of PPS, Schlenk tubes with a septum were used, and the reagents degassed therein three times after freezing with liquid nitrogen, and subsequently melted under argon.

Proton nuclear magnetic resonance (^1H NMR) was conducted in an UltraShieldTM 400, Bruker, Fällanden, Switzerland, in combination with Bruker TopSpin software version 2.1, using 5 mm tubes, Aramar, Type 5UP, 203 mm, 032315.5030, and deuterated chloroform as solvent unless stated otherwise. All substances for chemical reactions were examined by ^1H NMR prior to use. Spectra of reaction products were analyzed in comparison to the initial spectra, following the results from ^1H NMR prediction using ChemDraw Ultra 11.0, Cambridgesoft, Cambridge, UK, and literature values [142-144].

Fourier transform infrared spectroscopy (FTIR) was measured as attenuated total reflection using the Spectrum One Universal ATR Sampling Accessory, Perkin Elmer, Schwerzenbach, Switzerland, in combination with Perkin Elmer Spectrum software, Version 5.3.

Gel permeation chromatography (GPC) was conducted using the Waters 515 HPLC pump, 996 Photodiode Array Detector, and 410 Differential Refractometer. Columns used were Styragel[®] THF guard column, WAT 054405, Styragel[®] HR3 THF, WAT 044222, and Styragel[®] HR2 THF, WAT 044237. The GPC was run with THF, using polystyrene stan-

dards for calibration, and Empower Pro software build 2154 for recording. Evaluation was done using MS Excel.

Mixing of the precursors of the 12 series of silicone was done in a SpeedMixerTM, DAC 15 SP, Hauschild Engineering, Hamm, Germany. Polypropylene beakers of appropriate size received from the same supplier were used. Injection molding was performed by manually transferring the silicone mixtures to EFD OptimumTM syringe barrels, with dispensing using standard EFD adapters and pistons, and an EFD dispenser allowing for air pressure regulation, and individual as well as timed shots. Polymerization of the samples in the molds was induced by heating the injection molds in a metal heating press controlled with a Z124/2/10 temperature control unit, Hasco, Lüdenscheid, Germany. Tempering of the samples was performed in an oven with normal air atmosphere. Samples produced by injection molding were handled following DIN ISO 23529, and ISO 23529 [145, 146].

Tensile testing was performed using a Z 2.5 single column testing machine, Zwick/Roell, Ulm, Germany, equipped with a 1 kN KAF-TC load cell, AST, Wolnzach, Germany. Evaluation was performed with TestXpert software V12.0. Tensile testing was conducted as described in DIN EN ISO 527-1, DIN EN ISO 527-2, and DIN 53504, using the test specimen size S3 as shown in the latter norm [147-150].

Hardness measurement for determination of hardness Shore A was performed using the DTE digitest 6016 in combination with the IRHD M test device, 1250 g, Bareiss, Ulm, Germany, following DIN ISO 48, DIN EN ISO 868, and DIN 53505 [151-153].

Tear strength was also conducted on the Z 2.5 and tested as described in ASTM D 624-00, and DIN ISO 34-1 using the crescent test piece, which is referred to as Die B in the ASTM norm [154-156]. For small test specimen ISO 34-2 was considered but dismissed in order to provide for comparability with the values given in the literature for Silopren® materials [157, 158]. Further norms for testing of tear strength were available, but as they are designed for coated fabrics, films, and sheets they are not applicable here [159-162].

Results were calculated following DIN 53598-1. The arithmetic mean value and its standard deviation are displayed in the diagrams [163, 164].

Light microscopy pictures were taken on Leica equipment, a M205 FA microscope with a DFC 350 FX Low Light Monochrome Digital Camera, using LAS AF software version 2.4.1 build 6384.

The Pierce BCA Protein Assay Kit, Perbio, 23225, was used as received. Silicone samples of 5 mm diameter and 1 mm thickness were produced from the flat silicone specimens shown in **chapter 11 Light microscopy** using a hollow punch, and rinsed gently with ethanol and bi-distilled water. For the compatibility test 0.050 mL of bovine serum albumin solution (BSA) or ovalbumin solution (OVA), both of 2 mg/mL concentration, were mixed with 0.200 mL working reagent in a 1.4 mL U-bottom tube (FACS tube). Dilution series were made by adding 0.250 mL of phosphate buffered saline solution (PBS 1x) of pH 7.4, mixing, and transferring 0.250 mL to the next FACS tube containing only 0.250 mL PBS 1x. The mixtures were allowed to react for 30 minutes, and 0.050 mL were pipetted to a 96 well plate for measurement of the optical density at 562 nm. For the test with fetal bovine serum (FBS) 0.250 mL of pure FBS were given to a FACS tube, dilution series were made as above. Silicone samples were immersed in the FBS solutions for 2 days at 37°C. The silicone samples were removed from the solutions and placed in a new FACS tube. 0.250 mL of working reagent was added to both the silicone samples in the fresh FACS tubes, as well as the FACS tubes containing the FBS solutions which were used. The mixtures were allowed to react for 30 minutes. For measurement 0.070 mL were transferred to a 96 well plate and measured at 562 nm. Fresh FBS solutions were measured in an analogous manner.

The enzyme-linked immunosorbent assay (ELISA) was conducted as follows: 1. Silicone samples and OVA dilution series were produced as for the use with the BCA assay. 2. The samples were placed in FACS tubes and immersed in 0.300 mL of the OVA solutions of different concentrations over night at 4°C. 3. The OVA solutions were removed using an aspirator, and 0.300 mL casein solution with a concentration of 2.5% was added for blocking at T_R for 2 hours. 4. The samples were washed 3 times with a 0.05% solution of

Tween[®] 20 in PBS 1x. 5. Antibody tagging was performed using 0.300 mL solution of polyclonal rabbit anti-OVA IgG A6D in PBS 1x with an antibody concentration of 1:4000 for 2 hours at T_R. 6. The antibody solution was removed and the samples were washed 3 times with a 0.05% solution of Tween[®] 20 in PBS 1x. 7. Secondary antibody tagging was performed using 0.300 mL solution of horseradish peroxidase (HRP) conjugated goat anti-rabbit IgG in PBS 1x with an antibody concentration of 1:2000 for 1 hour at T_R. 8. The samples were washed 5 times with a 0.05% solution of Tween[®] 20 in PBS 1x. 9. The samples were transferred to fresh FACS tubes. 10. 0.200 mL tetramethylbenzidine (TMB) substrate for HRP was added and allowed to react for 30 minutes at T_R. 11. The enzymatic reaction was stopped by adding 0.200 mL of H₂SO₄ of concentration 9.8%. 12. Three measurements were conducted for each sample by transferring 0.100 mL into a 96 well plate. Absorbance was measured at 450nm.

Optical densities were measured at 450 nm and 562 nm in a safire² microplate reader, Tecan, Männedorf, Switzerland, using XFluor4SafireII software, V 4.62b.

Buffer solutions were prepared using 4-(2-hydroxyethyl)-1-piperazineethane-sulfonic acid (HEPES) for pH 8, boric acid (BA) for pH 9, sodium carbonate (Na₂CO₃) for pH 10, and triethylamine (TEA) for pH 11. Solutions of 0.1 M were prepared by mixing 0.01 mol of substance with 100 mL of bi-distilled water, and subsequently adjusting the solutions to the desired pH using hydrochloric acid. The saturated solution of sodium carbonate was produced by adding 0.205 mol of substance to 100 mL of bi-distilled water and subsequently adjusting the solution to the desired pH using hydrochloric acid.

Contact angle measurement was performed using the DataPhysics OCA 35 in combination with the SCA 202 software, version 3.4.8 build 81, DataPhysics, Filderstadt, Germany.

5 Hydrosilylation in silicones for cardiac pacing lead insulation

As can be seen in **Tab. 1** and **Tab. 2**, a wide variety of silicone compositions and different catalyst systems exist for silicones used by the cardiac pacing industry for cardiac pacing lead insulation. However, the most frequently used silicone system consists of basically two types of species: One species is a hydride-terminated siloxane, and the second species is a vinyl-terminated silicone siloxane. The polymerization reaction is an addition reaction where hydride- and vinyl-terminated species react to form two neighbouring CH₂-groups, and thereby covalently bond the reactants. For this reaction, the hydrosilylation, most commonly the Karstedt's-catalyst is used. This catalyst, depicted in **Fig. 2**, is popular due to its availability, high turnover number, and high reaction rate even at low temperatures. Furthermore it is known to work well in bulk and in solvents [75-79].

For this work, a choice had to be made with regard to the silicones under investigation. The decision was made to understand the hydrosilylation reaction only as described above as the reaction between a hydride- and a vinyl-terminated species, forming a covalent bond between the two species, and yielding two neighbouring CH₂-groups. The catalyst system used for this hydrosilylation reaction will be the Karstedt's-catalyst.

5.1 Representing silicones for lead insulation in a universal model reaction

In order to determine, whether or not a SME candidate can be incorporated into silicone, the chemical compatibility of the SME candidate with the silicone precursors and with the Pt-cat for hydrosilylation has to be explored. To do so, a universal set up of a model reaction, in which the hydrosilylation reaction can be performed and analyzed, is needed. Performing the model reaction must be possible under a variety of conditions, such as in bulk or in different solvents, under protective gas atmosphere or in contact of air, and at different temperatures. All reagents and reactants should be commercially available at reasonable price. The set up of the model reaction would optimally allow for qualitative and quantitative analysis of the reaction products, e.g. by analysis via proton nuclear magnetic resonance, Fourier transform infrared spectroscopy, gel permeation chromatography, and

also gravimetrically. Last but not least, the model reaction must well represent the hydrosilylation reaction of the silicone precursors as used for cardiac pacing lead insulation.

From the compositions of the materials listed in **Tab. 1** on page 8 the conclusion can be drawn that, in order to represent a hydrosilylation reaction which is representative for the materials used for cardiac pacing lead insulation, the model compounds must be comparable to vinyl-terminated siloxanes on the one hand, and to hydride-terminated siloxanes on the other hand. For our purposes, however, if both species for the hydrosilylation reaction were siloxane species, the product of the hydrosilylation model reaction would only be an even bigger siloxane molecule. This means that in the case of side product formation, e.g. by reaction of one species with itself, ^1H NMR results may become difficult to interpret. Therefore, only one of the two components in the model reaction should be a siloxane species, whereas the second component should be clearly distinguishable from it in the chemical analysis by ^1H NMR. Hence, a component is needed, which does not show any signals in the ^1H NMR near the signals of the other components.

Siloxane signals in ^1H NMR are to be found at around 0 ppm. The product of a hydrosilylation reaction between a vinyl-terminated species and a hydride-terminated species will always be two neighbouring CH_2 -groups, with ^1H NMR signals depending on their respective neighbours, but frequently in the range between 1 ppm and 4 ppm. The functional groups of the precursors for a hydrosilylation reaction, namely the hydride-terminated siloxane and the vinyl-terminated siloxane, will have signals of the functional groups between 4 ppm and 5 ppm for the hydride-terminated species and approximately between 5 ppm and 6 ppm for the vinyl-terminated species. Therefore a species is needed which will have a clear ^1H NMR signal beyond 6 ppm in order to avoid the overlapping of signals, which would make analysis difficult.

Allylbenzene (AB) was chosen as a replacement for the vinyl-terminated siloxane species, because the benzene ring has clear ^1H NMR signals between 7 ppm and 8 ppm. Furthermore, in AB the vinyl group which is needed for the hydrosilylation step is shielded from the benzene ring by an additional CH_2 group, therefore the hydrosilylation reaction should remain undisturbed. Last but not least, AB is commercially available at reasonable price.

allylbenzene + pentamethyldisiloxane $\xrightarrow[\text{mod. Pt-cat}]{\text{Pt-cat}}$

allylbenzene + $\text{H}_3\text{C}-\text{Si}(\text{CH}_3)_2-\text{O}-\left[\text{Si}(\text{CH}_3)_2-\text{O}-\text{Si}(\text{CH}_3)_2-\text{O}\right]_m-\left[\text{Si}(\text{CH}_3)_2-\text{O}-\text{Si}(\text{CH}_3)_2-\text{O}\right]_n-\text{Si}(\text{CH}_3)_2-\text{CH}_3 \xrightarrow[\text{mod. Pt-cat}]{\text{Pt-cat}}$

Poly(dimethylsiloxane-co-methylhydrosiloxane), trimethylsilyl terminated

The reaction scheme shows allylbenzene reacting with a polydimethylsiloxane-co-methylhydrosiloxane terminated with trimethylsilyl groups. The reaction is catalyzed by Pt-cat or modified Pt-cat. The product is a functionalized polysiloxane where the allyl group has been converted to a benzyl group.

The model reactions as shown in **Fig. 8** and **Fig. 9** were performed in round bottom flasks under constant stirring with a magnetic Teflon coated stir bar, and in normal air atmosphere. The reactants were added in stoichiometric amounts, i.e. 0.339 mL AB, 0.500 mL PMDS, and 0.470 mL P(DMS-co-MHS). The reactions using the Pt-cat were conducted at T_R in THF, the hydrosilylation was started by adding 0.020 mL of the Pt-cat to the mixture, and allowed to react for three hours. Both the Pt-cat_S and the Pt-cat_X were tested. The reac-

tion using the mod. Pt-cat was conducted at 80°C in xylene, the hydrosilylation was started by adding 0.020 mL of the mod. Pt-cat to the mixture, and allowed to react over night. Solvent was removed from the reaction mixtures using a rotary evaporator. Analysis was performed by ^1H NMR in deuterated chloroform (CDCl_3).

In all cases the model reactions worked as expected. ^1H -NMR showed that the hydrosilylation took place as predicted under the formation of three neighboring CH_2 -groups: Benzene- CH_2 - CH_2 (t, 2.60-2.65 ppm, 2H), CH_2 - CH_2 - CH_2 (m, 1.60-1.70 ppm, 2H), CH_2 - CH_2 -Si (m, 0.54-0.60 ppm, 2H). In the case of the model reactions using P(DMS-co-MHS) peak broadening of the CH_2 -peaks could be observed, which is normal for polymers that contain several chemically identical functional groups. The reactions worked without the formation of a side product.

5.2 Conclusions for further experiments of this work

As an overall result it can be said that the setup of this model reaction is suitable for the testing of the feasibility of hydrosilylation. Furthermore, there is no difference in functionality between the Pt-cat_S and the Pt-cat_X. From the point of view of handling and analysis, the Pt-cat_S will increase the Si- CH_3 -signal in the ^1H NMR slightly, due to the fact that the matrix of this catalyst is siloxane based. The Pt-cat_X will, on the other hand, cause some residual solvent peaks, due to the fact that the matrix of this catalyst is xylene, which is hard to remove on a rotary evaporator. As known from the literature, the Pt-cat_S and Pt-cat_X are capable of performing hydrosilylation at T_R and at a high rate, whereas the mod. Pt-cat works only at elevated temperatures.

In further experiments of this work PMDS will be preferred as the hydride-terminated siloxane species for the hydrosilylation in order to avoid peak broadening in the ^1H NMR and thereby facilitate the analysis of the reaction products. No distinction will be made between the Pt-cat_S and the Pt-cat_X, but they will both be referred to as Pt-cat. Next to the Pt-cat the mod. Pt-cat will also be tested.

6 Exploring the oxidative pathway

The aim of this chapter is to evaluate whether the hydrophobic polymer PPS can be incorporated into silicone. PPS is considered to be a SME candidate because it is a pro-hydrophile polymer: It can be oxidized from its hydrophobic state to PPSO and further to hydrophilic PPSO₂. Furthermore PPS is suggested as SME candidate because of its high hydrophobicity, which may allow for good miscibility with the also hydrophobic silicone precursors. The optimal result of combining PPS and silicone would be a new silicone composition, containing hydrophobic PPS SMEs, which will be rendered hydrophilic on the material's surface once exposed to an oxidative environment. This can be expected to lead to a self-renewing hydrophilic surface. The crucial point for the application of PPS as SME is its chemical compatibility with the silicone precursors and the Pt-cat which is used for hydrosilylation. Any incompatibility would mean the immediate elimination of PPS from the list of possible SME-candidates.

6.1 Hydrosilylation in the presence of PPS

The goal is to investigate whether PPS is compatible with the hydrosilylation reaction, as described in **chapter 5 Hydrosilylation in silicones for cardiac pacing lead insulation**. This can be accomplished by conducting the model reaction shown in **Fig. 8** in the presence of PPS. Should PPS interfere with the hydrosilylation reaction, e.g. cause a side reaction or inhibit the hydrosilylation reaction, this would be a knock-out criterion for the application of PPS in silicones for cardiac pacing lead insulation.

PPS was produced as described in the literature [98, 102, 104, 105]. **Fig. 5** shows the reaction scheme, this polymerization yielded the vinyl-terminated species PPS_{allyl}. A second type of PPS was produced, with the only difference that it was end-capped with bromobutane (BB) [103]. The result was the butyl-terminated species PPS_{butyl}. The production of both types of PPS will not be elucidated here, because it is well described in the literature and not part of this research work. Analysis of the PPS by ¹H-NMR in CDCl₃ showed, that the polymerization of PPS was successful: S-CH (m, 2.56-2.67 ppm, 1H), S-CH₂ (m, 2.82-2.97 ppm, 2H), CH-CH₃ (m, 1.34-1.40 ppm, 3H), S-CH₂-CH₂-CH₃ (m, 1.55-1.65 ppm, 2H),

S-CH₂-CH₂-CH₃ (t, 0.96-1.01 ppm, 3H), S-CH₂-CH=CH₂ (m, 5.75-5.88 ppm, 1H), S-CH₂-CH=CH₂ (m, 5.06-5.17 ppm, 2H).

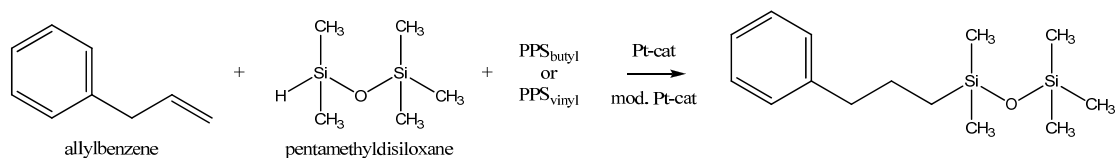


Fig. 10: Model reaction for hydrosilylation in the presence of PPS: Allylbenzene and pentamethyldisiloxane are the reactants, either PPS_{butyl} or PPS_{allyl} being present, testing both the Pt-cat and the mod. Pt-cat.

The model reaction to test the compatibility of both types of PPS with the hydrosilylation reaction was carried out as schematically shown above in **Fig. 10**. It was performed in round bottom flasks under constant stirring with a magnetic Teflon coated stir bar, and in normal air atmosphere. First, 0.5 mL of PPS was given to the flasks. The reaction using the Pt-cat was conducted at T_R in THF, and 0.020 mL of the Pt-cat were added to the mixture. The reaction using the mod. Pt-cat was conducted at 80°C in xylene, and 0.020 mL of the mod. Pt-cat were added to the mixture. PPS, solvent and catalysts were allowed to mix thoroughly. In a last step, the reactants were added in stoichiometric amounts, i.e. 0.339 mL AB, and 0.500 mL PMDS. The reaction using the Pt-cat was and allowed to react for three hours, and the reaction using the mod. Pt-cat was allowed to react over night. Solvent was removed from the reaction mixtures using a rotary evaporator. Analysis was performed by ¹H NMR.

In all cases the model reactions did not work as expected. The most obvious flaw was the formation of a reaction product which phase separated while on the rotary evaporator. Allowing it to settle produced two clearly separated phases, a colorless lighter one, the top phase, and a yellowish heavier one, the bottom phase. All phases were analyzed separately by ¹H-NMR in CDCl₃. The result was that the hydrosilylation did not take place, but the reactants AB and PMDS were found almost completely in their initial state, the only change being the nonexistence of the hydride peak of the PMDS. The top phase contained the PMDS and only some AB, whereas the PPS could be found together with AB in the bottom phase. Only traces of PMDS were found in the bottom phase. Centrifugation of the

reaction product yielded a solid sediment of yellowish-brownish color. Such a coloration of the reaction mixture has been described in the literature as a typical sign of the deactivation of the Pt-cat due to the formation of colloidal platinum species [80]. If this were the case, it would have to be concluded that PPS is not compatible with the hydrosilylation reaction as it is conducted here. In order to verify that this coloration and possible deactivation of the two catalysts is not a specific problem of the PPS that was produced for this model reaction, a general setup is needed. See the next three chapters for details.

6.2 Hydrosilylation in the presence of sulfides, sulfoxides, and sulfones

In order to determine, if silicone will generally be compatible with PPS, a test setup is needed to rule out possible specific problems of the PPS which was produced for this study. The deactivation of the catalyst by PPS is suspected. Platinum is known to interact with sulfur in its atomic state, due to the high nucleophilic character of the latter. This could lead to the observed deactivation of the catalyst. But it is not clear, if this also applies for components containing sulfur, like PPS. This may depend on the number of atomic valencies of the sulfur which are occupied. In PPS, two of the atomic valencies of the sulfur are occupied. PPS can be oxidized to PPSO, where four of the atomic valencies of the sulfur are occupied, and by further oxidation to PPSO₂ all of the atomic valencies of the sulfur are occupied.

To represent PPS, PPSO, and PPSO₂, model compounds are needed which represent sulfides, sulfoxides, and sulfones, but which do not contain any other functional group other than the sulfur. The compatibility with the Pt-cat and the mod. Pt-cat can then be tested, analogous to the model reaction described in **chapter 6.1 Hydrosilylation in the presence of PPS**. This is done by exposing the model reaction between AB and PMDS to the model compounds representing the sulfides, sulfoxides, and sulfones. In the case that both the Pt-cat and the mod. Pt-cat lost their catalytic function in the presence of the sulfide and the sulfoxide, PPS and PPSO can not be incorporated into silicones. Incorporating PPSO₂ into silicone is not an option, because it does not represent a pro-hydrophile component.

Dibutyl sulfide (DBS), dibutyl sulfoxide (DBSO), and dibutyl sulfone (DBSO₂) were chosen as model compounds to represent sulfides, sulfoxides, and sulfones. The reason is that no reaction of the alkyl chains of the model compounds with any of the reactants in the hydrosilylation was to be expected. **Fig. 11** shows the model reaction in the presence of dibutyl sulfide, dibutyl sulfoxide, and dibutyl sulfone, and testing both catalysts.

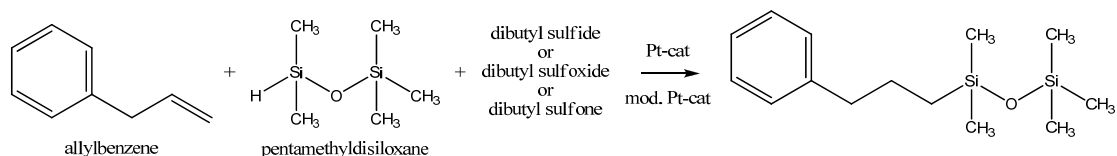


Fig. 11: Model reaction for hydrosilylation in the presence of dibutyl sulfide, dibutyl sulfoxide, and dibutyl sulfone: Allylbenzene and pentamethyldisiloxane are the reactants, using either the Pt-cat or the mod. Pt-cat.

The model reaction to test if the hydrosilylation can be performed in the presence of sulfide, sulfoxide, and sulfone was carried out in round bottom flasks under constant stirring with a magnetic Teflon coated stir bar, and in normal air atmosphere. First, 0.5 mL of sulfide, sulfoxide, or sulfone was given to the flasks. The reaction using the Pt-cat was conducted at T_R in THF, and 0.020 mL of the Pt-cat were added to the mixture. The reaction using the mod. Pt-cat was conducted at 80°C in xylene, and 0.020 mL of the mod. Pt-cat were added to the mixture. Sulfide, sulfoxide, or sulfone, solvent, and catalysts were allowed to mix thoroughly. Finally, the reactants were added in stoichiometric amounts, i.e. 0.339 mL AB, and 0.500 mL PMDS. The reaction using the Pt-cat was allowed to react for three hours, and the reaction using the mod. Pt-cat was allowed to react over night. Solvent was removed from the reaction mixtures using a rotary evaporator. Analysis was performed by ¹H NMR.

In the two cases, in which the model compounds representing the sulfides and the sulfoxides were present, the hydrosilylation reaction did not work. Furthermore, a yellowish colouring of the reaction mixture was observed. However, it worked as expected with the model compounds representing the sulfoxides being present. Analysis by ¹H-NMR in CDCl₃ showed that in the case of sulfides and sulfoxides being present, the hydrosilylation did not take place, and the reactants AB and PMDS were found almost completely in their

initial state. In the case of sulfone being present the hydrosilylation reaction did take place, as described above in **chapter 5 Hydrosilylation in silicones for cardiac pacing lead insulation**. Signals found here were identical with those previously established, and the results were identical for both catalysts.

6.3 Results

It was shown that the functionality of both the Pt-cat and the mod. Pt-cat is affected by sulfides and sulfoxides: Hydrosilylation does not occur when sulfides and sulfoxides are present in the reaction mixture. It can be assumed that sulfides and sulfoxides deactivate the catalyst by the formation of a colloidal platinum species. In conclusion, neither PPS nor PPSO can be incorporated into the silicone matrix when the hydrosilylation process relies on the two catalysts used in this work. However, the functionality of the catalysts seems to be unaffected in the case of sulfones being present. Hence, the incorporation of PPSO₂ into silicone may be possible. Since PPSO₂ is not a pro-hydrophile polymer, due to the fact that it is already in its oxidized and therefore most hydrophilic state, the introduction of PPSO₂ into silicone is not an option for this work - it will not lead to pro-hydrophile SMEs which could remain hydrophobic within the bulk and turn hydrophilic on the material surface. The oxidative pathway, as proposed here, is consequently not feasible with PPS.

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7 Exploring the hydrolytical pathway

Analogous to **chapter 6 Exploring the oxidative pathway** the goal is furnishing a commonly used hydrophobic silicones for cardiac pacing lead insulation with SMEs, leading to a self-renewing hydrophilic layer on the silicone surface. Here, the approach is to incorporate a hydrolytically sensitive pro-hydrophile SME. After having undergone hydrolysis the SME should be hydrophilic and exhibit a negative charge. This approach was described in **chapter 3.5 The hydrolytical pathway** using VSEE as an example. VSEE was proposed as SME, due to its ability to be hydrolyzed, splitting off only ethanol in the process. The remaining sulfonic group will be both hydrophilic as well as present a negative charge. Following the same principle as for VSEE, any component capable of undergoing hydrolysis and forming a negatively charged hydrophilic end-group can be a SME candidate. In the next chapter possible SME candidates will be presented and discussed. To evaluate if VSEE or any other possible SME candidate is compatible with the hydrosilylation reaction, a model reaction analogous to the reaction as established in **chapter 5.1 Representing silicones for lead insulation in a universal model reaction** will be conducted. The reaction scheme of VSEE undergoing hydrosilylation is shown below in **Fig. 12**.

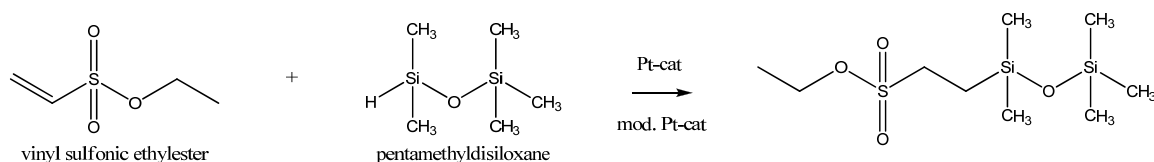


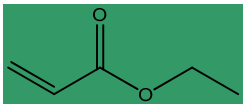
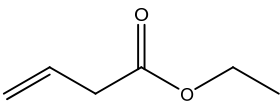
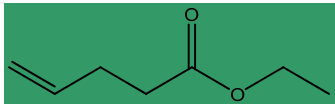
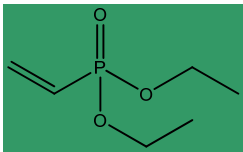
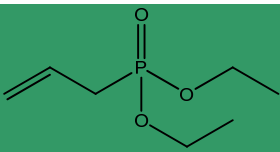
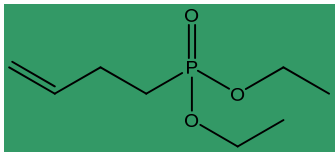
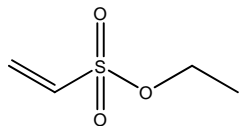
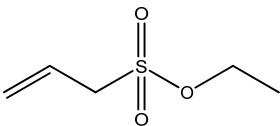
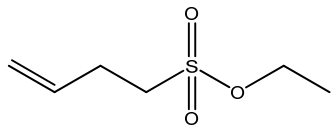
Fig. 12: Model reaction of VSEE and pentamethyldisiloxane, using both the Pt-cat and the mod. Pt-cat.

7.1 Possible SME candidates

Possible SME candidates must meet two general requirements: First, they must be able to undergo hydrosilylation, as defined in **chapter 5 Hydrosilylation in silicones for cardiac pacing lead insulation**. This hydrosilylation must be quantitative and without the formation of any side products. The second requirement is that they can undergo hydrolysis and form a hydrophilic species which represents a negative charge. Whether this hydrolytical step produces a side product or not, is not of any relevance, as long as the possible side

product can be expected to be of no harm to a host organism, e.g. an animal or a human. Furthermore, the SME candidates should preferably be commercially available, or at least producible at reasonable cost.

The second requirement, which is the ability to undergo hydrolysis to form a hydrophilic species with a negative charge, can theoretically be met by any carboxylic ester, phosphonic ester, and sulfonic ester. When the group that is split off during the process were a short alkyl chain like an ethyl group, the product which is split off during the hydrolysis, is ethanol. In low amounts, ethanol can be assumed of being of no harm to a host organism. This is especially true when the material were placed in the venous part of the blood system, where ethanol would be carried away quickly and thus the local concentration kept low. The carboxylic- phosphonic-, and sulfonic compounds are not restricted to being vinyl terminated, but may also be allyl or 3-butene terminated. In the latter two cases the additional CH₂ groups may shield the C-C double bond, which is needed for the hydrosilylation, from the functional group. This may provide for hydrosilylation as required. Theoretically, 9 components may serve as SME candidates. However, only 5 of these components are commercially available. They are highlighted in green in **Tab. 3**.

	vinyl-terminated	allyl-terminated	3-butene-terminated
carboxylic ethylester			
phosphonic diethylester			
sulfonic ethylester			

Tab. 3: The 9 possible SME candidates from carboxylic-, phosphonic-, and sulfonic ethylester, terminated by either a vinyl, allyl, or 3-butene group. The 5 commercially available components are highlighted in green.

As for possible SME candidates containing a carboxylic- or a phosphonic group, sufficient candidates were identified. But since none of the three suggested components containing a sulfonic group is commercially available, the search was broadened, omitting the prerequisite that the substance has to be able to undergo hydrolysis. This was done in order to be able to find components with which at least the feasibility of hydrosilylation of a sulfone containing component can be evaluated. Divinylsulfone (DVS) and allyl phenyl sulfone (APS) were identified as possible SME candidates. DVS bears two identical C-C double bonds, which can undergo hydrosilylation, and APS is very similar to AB, which has been used successfully to establish a universal setup of a model reaction for hydrosilylation, see **chapter 5.1 Representing silicones for lead insulation in a universal model reaction** for details. For want of a component containing a sulfonate group, sodium allyl sulfonate (SAS) was chosen as a possible SME candidate. This choice was made even though SAS does not represent a pro-hydrophile component. These three components are depicted below in **Fig. 13**.

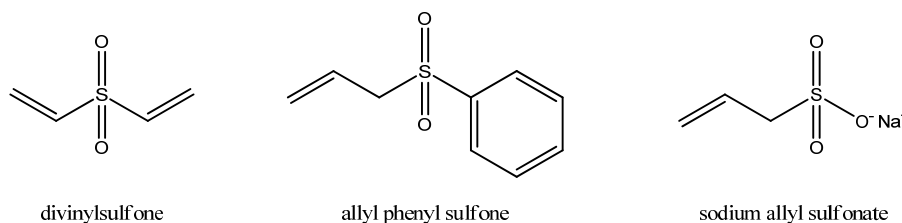


Fig. 13: Three possible SME candidates containing a sulfone: Divinyl sulfone, allyl phenyl sulfone, and sodium allyl sulfonate.

So far, only components forming carboxylic acid groups by splitting off an alkyl of low molecular weight were proposed. It is possible, however, to form carboxylic acid by hydrolysis from cyclic components. One representative of this group is allylsuccinic anhydride (ASA), and it was chosen as a possible SME candidate. ASA is known to hydrolyze readily in the presence of water and form two carboxylic acid groups in the process. The advantage of ASA is that two hydrophilic end-groups are formed by each molecule, which may double the effect of increasing the hydrophilicity. However, some moisture is frequently present in the silicone precursors, and if the ring opening hydrolysis of ASA were to occur during the polymerization of the silicone, the carboxylic acid groups may interfere

with the polymerization of the silicone. In order to evaluate the effect of carboxylic acid groups on the hydrosilylation reaction, the following two components were chosen as possible SME candidates: 2-propene carboxylic acid (2-PCA) and 3-butene carboxylic acid (3-BCA). All three components are shown below in **Fig. 14**.

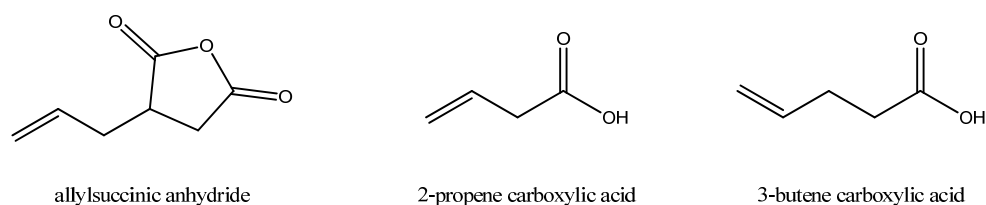


Fig. 14: Three possible SME candidates, two are carboxylic acids and one can form carboxylic acid by ring opening hydrolysis: Allylsuccinic anhydride, 2-propene carboxylic acid, and 3-butene carboxylic acid.

Searching for substances capable of forming carboxylic acid groups yielded another result: Dimethyl allylmalonate (DMAM). Just like ASA it can form two carboxylic acid groups, but here the alkyl rest which is split off in the process will be methanol. That would not be acceptable for a medical application, but is acceptable for the research purposes of this work. Therefore DMAM, see **Fig. 15**, is considered a possible SME candidate.

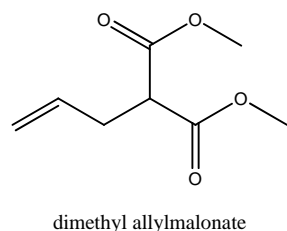


Fig. 15: Dimethyl allylmalonate: A possible SME candidate for this research work, but not for medical applications, due to the formation of methanol in the hydrolysis step.

Two amines were added to the list of possible SME candidates, even though amines are known in some cases to increase rather than decrease the adhesion of proteins [28]. They were included in this work to determine the general feasibility of hydrosilylation of amines. The two substances are acrylamide (AAM) and 4-acryloylmorpholine (4-AM), see **Fig. 16** below.

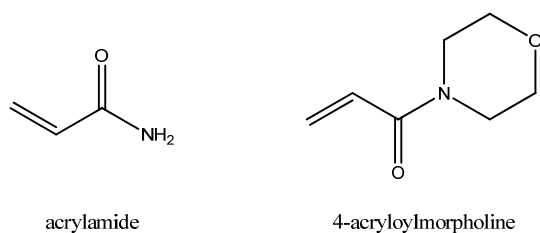


Fig. 16: Two possible SME candidates based on amines: Acrylamide and 4-acryloylmorpholine.

Finally, two substances were added to the list of compounds to test, see **Fig. 17** below, but in this case for comparison only. In the literature which described the production and functionality of the mod. Pt-cat, allylacetone (AAc) was used as model compound. The purpose was to demonstrate the ability of the mod. Pt-cat to process functionalized olefins via hydrosilylation. AAc was reacted successfully with a siloxane species, and a high yield was reported [81]. Here, AAc was chosen for comparison of results because AAc contains a carbonyl group. Allyl ethyl ether (AEE) was chosen because it contains an ether functional group, which was not tested yet.

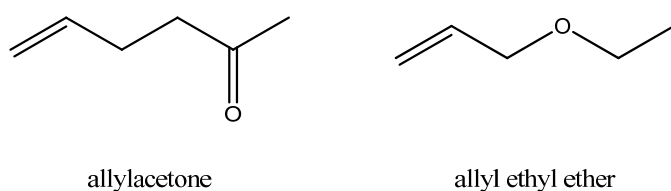


Fig. 17: Two components for comparison in the hydrosilylation reaction: Allylacetone and allyl ethyl ether, the first one was reported in the literature as olefin which can undergo hydrosilylation in the presence of the mod. Pt-cat.

7.2 Literature research for hydrosilylation of possible SME candidates

A literature research was conducted with the software SciFinder ScholarTM in order to gain knowledge about the state of the art of using the 16 components under investigation in hydrosilylation reactions. Searches were conducted for each of the 16 components in combination with a silane and a siloxane. The search mode was set to exact search, meaning the possible SME candidates had to match exactly. The structure for the silane and the siloxane was not restricted in any other way, but requiring a hydride-termination of the species

which is necessary for the hydrosilylation reaction. The number of hits for each of the 16 possible SME candidates is shown in **Tab. 4**. Literature was evaluated under the aspect whether it is useful for this research work; the most important results are summarized in the last column of **Tab. 4**.

possible SME candidate	Hits silane	Hits siloxane	Results regarding the catalyst system for the hydrosilylation reaction
vinyl carboxylic ethylester	1	0	copper oxide and ethanediamine [165]
3-butene carboxylic ethylester	0	1	mod. Pt-cat [81]
vinyl phosphonic diethylester	0	0	-
allyl phosphonic diethylester	0	0	-
3-butene phosphonic diethylester	0	0	-
divinylsulfone	0	0	-
allyl phenyl sulfone	0	0	-
sodium allyl sulfonate	0	0	-
allylsuccinic anhydride	0	0	-
2-propene carboxylic acid	0	0	-
3-butene carboxylic acid	0	0	-
dimethyl allylmalonate	0	0	-
acrylamide	0	0	-
4-acryloylmorpholine	0	0	-
allylacetone	1	1	chloroplatinic acid [166], mod. Pt-cat [81]
allyl ethyl ether	0	0	-

Tab. 4: Result of the literature research with the software SciFinder ScholarTM; search was conducted for each of the 16 components and in combination with both a siloxane and a silane. The number of hits for the hydrosilylation reaction is displayed.

The literature search yielded rather few results in general, and only 3 of the 16 components have been shown in the literature to undergo hydrosilylation with a siloxane or a silane species. In 2 of these 3 cases the mod. Pt-cat works. This suggests that the functional groups of the 16 components may inhibit or disturb the hydrosilylation reaction. On the other hand, it is also possible that not all of the 16 substances have been tested yet with all available catalysts. The mod. Pt-cat, for example, was first published in 2004, and even though there are some recent publications presenting possible applications for this catalyst, only little use has been made of it for hydrosilylation. This may be due to the fact that the mod. Pt-cat has been shown to have low activity at low temperatures and shows a high degree of activity only at elevated temperatures. This may actually bring the advantage of unproblematic storage of ready to use mixtures of silicones, with only a low content of or even without an inhibitor for the polymerization reaction [81, 85-87]. Up to date, silicones as used by the cardiac pacing industry are always delivered as two separate components, and are mixed only prior to their use.

7.3 Hydrosilylation of the 16 commercially available components

In order to determine whether or not a possible SME candidate can be incorporated into silicone, the model reaction as described in **chapter 5.1 Representing silicones for lead insulation in a universal model reaction** and shown in **Fig. 8** was conducted for each of the 16 components. Analysis was done by ^1H NMR in all cases, and in the case of ASA also GPC was used to verify the result. The mod. Pt-cat was used in all cases, due to its functionality even in the presence of olefins. The Pt-cat was tested in some cases.

All model reactions were performed applying the following procedure under constant stirring and in normal air atmosphere: First, a magnetic Teflon coated stir bar was placed in a round bottom flask. Solvent was added, using THF for reactions with the Pt-cat, and xylene for reactions with the mod. Pt-cat. Next, catalyst was added, using 0.020 mL in either case of the two catalysts. The reactants were added in stoichiometric amounts, i.e. 0.500 mL PMDS, and a respective amount of the substance under investigation. The reactions using the Pt-cat were conducted at T_R , and allowed to react for three hours. The reactions using the mod. Pt-cat were conducted at 80°C, and allowed to react over night. Sol-

vent was removed from the reaction mixtures using a rotary evaporator. Analysis was performed by ^1H NMR in CDCl_3 . GPC was conducted in THF.

7.3.1 Vinyl carboxylic ethylester

The proposed reaction scheme for vinyl carboxylic ethylester (VCEE) and PMDS is shown below in **Fig. 18**. Analysis by ^1H NMR showed similar results for the Pt-cat and the mod. Pt-cat. The vinyl group of the VCEE had been consumed, also the hydride group of the PMDS. However, the signals found in the spectrum could not indisputably be attributed to the formation of two neighboring CH_2 groups. There are numerous unidentified peaks, and the ratio between the PMDS and all possible modifications of the VCEE is not stoichiometric, but $\gg 1$. It can be concluded that some VCEE has reacted with PMDS in different ways, and some has evaporated on the rotary evaporator. Hence, the model reaction does not work as necessary for further use of VCEE in this study.

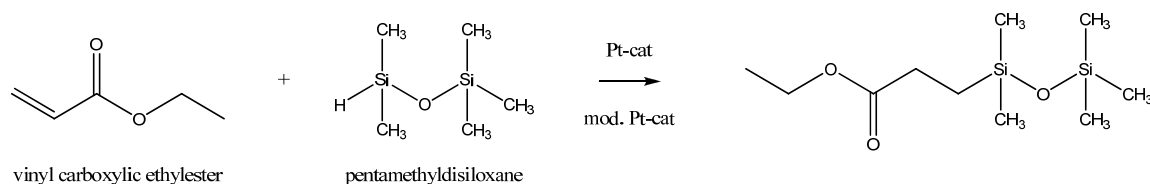


Fig. 18: Proposed reaction scheme for the hydrosilylation of VCEE with PMDS.

7.3.2 3-Butene carboxylic ethylester

Fig. 19 shows the reaction scheme for the hydrosilylation of 3-butene carboxylic ethylester (3-BCEE) with PMDS, as it was verified for the use of the mod. Pt-cat. ^1H NMR showed that the peaks of the ethylester remained unchanged, and the four neighboring CH_2 groups were detected as follows: $\text{OOC}-\underline{\text{CH}_2}$ (t, 2.26-2.32 ppm, 2H), $\text{OOC}-\text{CH}_2-\underline{\text{CH}_2}$ (q, 1.61-1.70 ppm, 2H), $\underline{\text{CH}_2}-\text{CH}_2-\text{Si}$ (m, 1.30-1.39 ppm, 2H), $\text{CH}_2-\underline{\text{CH}_2}-\text{Si}$ (m, 0.48-0.55 ppm, 2H). There were no signs of side product formation, and the ratio of 3-BCEE to PMDS found in the product was stoichiometric. Hence, the model reaction worked as expected, and as described in the literature [81].

Using the Pt-cat produced the same results regarding the ^1H NMR data. However, the initially colorless reaction mixture developed a yellowish coloration during the reaction. Furthermore, black particles were formed when the solvent was removed from the reaction mixture on the rotary evaporator. As mentioned above, both are signs for the deactivation of the catalyst due to the formation of colloidal platinum species [80, 81].

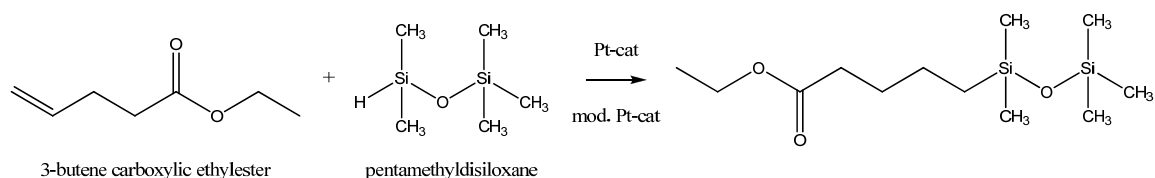


Fig. 19: Proposed reaction scheme for the hydrosilylation of 3-BCEE with PMDS.

7.3.3 Vinyl phosphonic diethylester

Similar results were found for the reaction between vinyl phosphonic diethylester (VPDEE) and PMDS using either the Pt-cat or the mod. Pt-cat. Almost only unreacted VPDEE was found in the reaction mixture, and its allyl group was not consumed. There was no sign of the formation of two neighboring CH_2 groups as proposed below in **Fig. 20**. The model reaction does not work, and VPDEE is not a SME candidate.

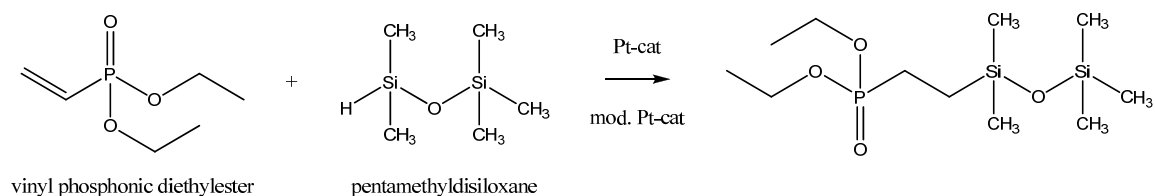


Fig. 20: Proposed reaction scheme for the hydrosilylation of VPDEE with PMDS.

7.3.4 Allyl phosphonic diethylester

The proposed reaction scheme between allyl phosphonic diethylester (APDEE) and PMDS is shown below in **Fig. 21**. Different results were found for the use of the Pt-cat and the mod. Pt-cat. In the first case, signals for the formation of three neighboring CH_2 groups could be identified by ^1H NMR: $\text{P}-\underline{\text{CH}_2}$ (m, 1.70-1.82 ppm, 2H), $\text{P}-\text{CH}_2-\underline{\text{CH}_2}$ (m, 1.58-

1.70 ppm, 2H), $\text{CH}_2\text{-Si}$ (m, 0.58-0.65 ppm, 2H). However, numerous peaks were found, suggesting the reaction between APDEE and PMDS yielded two neighboring CH_2 groups, and a terminal CH_3 group. Furthermore, the ratio between APDEE and PMDS was not stoichiometric, but PDMS was slightly overrepresented. In the case of the mod. Pt-cat almost only unconsumed APDEE was found in the reaction mixture. In consequence, APDEE was not considered a SME candidate.

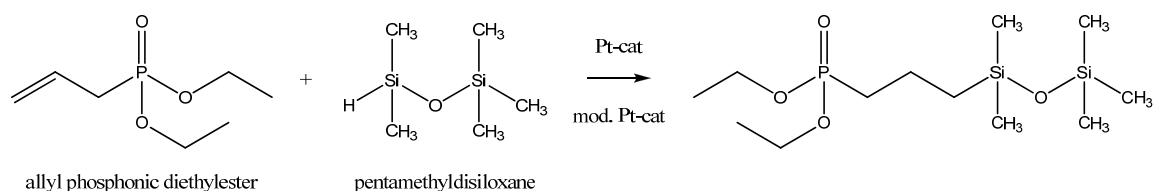


Fig. 21: Proposed reaction scheme for the hydrosilylation of APDEE with PMDS.

7.3.5 3-Butene phosphonic diethylester

In **Fig. 22** the proposed reaction scheme between 3-butene phosphonic diethylester (3-BPDEE) and PMDS is displayed. For the application of the Pt-cat, signals for the formation of four neighboring CH_2 groups could be identified by ^1H NMR: P-CH_2 (m, 1.67-1.80 ppm, 2H), $\text{P-CH}_2\text{-CH}_2$ (m, 1.55-1.67 ppm, 2H), $\text{CH}_2\text{-CH}_2\text{-Si}$ (m, 1.34-1.41 ppm, 2H), $\text{CH}_2\text{-Si}$ (m, 0.47-0.54 ppm, 2H). However, unidentified peaks were found, suggesting a side reaction. Furthermore, the ratio between 3-BPDEE and PMDS was not stoichiometric, but PDMS was slightly overrepresented. In the case of application of the mod. Pt-cat the 3-BPDEE remained unchanged in the reaction mixture. In consequence, 3-BPDEE was not considered a SME candidate.

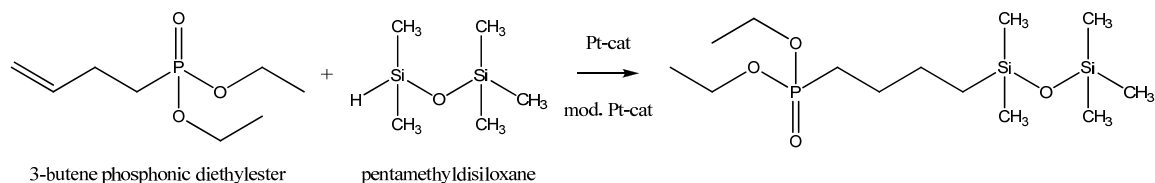


Fig. 22: Proposed reaction scheme for the hydrosilylation of 3-BPDEE with PMDS.

7.3.6 Divinylsulfone

Analysis of the reaction mixture by ^1H NMR showed almost only unreacted DVS for the model reaction using the mod. Pt-cat. Traces of two neighboring CH_2 groups formed by the reaction suggested in **Fig. 23** were found: $\text{Si}-\underline{\text{CH}_2}$ (t, 1.30-1.41 ppm, 2H), $\text{Si}-\text{CH}_2-\underline{\text{CH}_2}$ (t, 2.94-3.05 ppm, 2H). Due to the almost complete absence of reactivity, DVS was not considered a SME candidate.

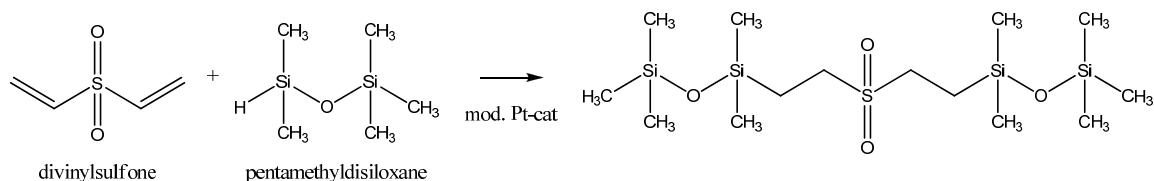


Fig. 23: Proposed reaction scheme for the hydrosilylation of DVS with PMDS.

7.3.7 Allyl phenyl sulfone

Reacting APS with PMDS as shown in **Fig. 24** produced only a low yield of the desired adduct. The result was similar for the Pt-cat and the mod. Pt-cat. The product phase separated into two phases while on the rotary evaporator. The first phase being colorless in both cases, and the second phase yellowish when the Pt-cat was used, and black when the mod. Pt-cat was used. ^1H NMR showed that the colorless phase contained almost only PMDS, while the yellowish and the black phase contained mainly APS. The hydride groups of the PMDS were consumed, while the allyl groups of the APS were still completely present. Traces of the three neighboring CH_2 groups of the adduct were found: $\text{S}-\underline{\text{CH}_2}$ (m, 3.04-3.09 ppm, 2H), $\text{S}-\text{CH}_2-\underline{\text{CH}_2}$ (m, 1.68-1.79 ppm, 2H), $\underline{\text{CH}_2}-\text{Si}$ (t, 0.95-1.02 ppm, 2H). In conclusion, APS is not used as a SME candidate in the further course of this work. The coloration in both cases is interpreted as a sign of the deactivation of the catalyst due to the formation of colloidal platinum species [80, 81].

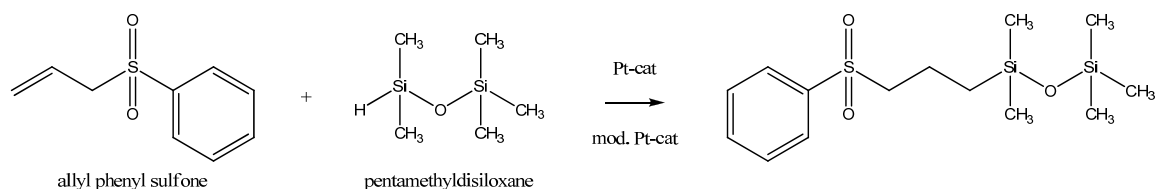


Fig. 24: Proposed reaction scheme for the hydrosilylation of APS with PMDS.

7.3.8 Sodium allyl sulfonate

Fig. 25 shows the proposed reaction mechanism of SAS with PMDS. Analysis of the reaction product by ^1H NMR was conducted in D_2O . No formation of a product could be seen in the reaction using the mod. Pt-cat, and SAS was found unchanged. PMDS was obviously completely removed on the rotary evaporator with the solvent. Hence, SAS is not considered a SME candidate.

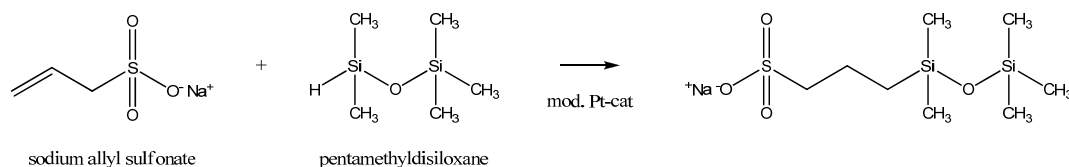


Fig. 25: Proposed reaction scheme for the hydrosilylation of SAS with PMDS.

7.3.9 Allylsuccinic anhydride

ASA was reacted with PMDS as proposed in **Fig. 26** using the mod. Pt-cat. Analysis of the reaction product by ^1H NMR showed the formation of three neighboring CH_2 groups: $\text{CH}_2\text{-CH}_2\text{-Si}$ (2m, 1.61-1.73 and 1.91-2.02 ppm, 2H), $\text{CH}_2\text{-CH}_2\text{-Si}$ (m, 1.38-1.49 ppm, 2H), $\text{CH}_2\text{-Si}$ (m, 0.47-0.61 ppm, 2H). Note: The splitting up of the signal of the CH_2 group next to the succinic anhydride ring can be explained by stereoisomerism [167, 168]. However, some unconsumed ASA was found in the reaction mixture. Furthermore, the ratio between ASA and PMDS was not stoichiometric, but the representation of the PMDS was too high.

ASA is capable of undergoing hydrolysis easily in the presence of water. Since some moisture may be contained in the solvents used for the model reaction, and since the model re-

actions are conducted in a normal air atmosphere where moisture is usually also present, hydrolysis of the ASA may have occurred during the model reaction. The result would be the formation of two carboxylic acid groups, which may not only interfere with the hydrosilylation reaction by reacting with the hydride of the PMDS, but which may allow for reaction of hydrolyzed ASA molecules with one another. As a result, multiple combinations with different products are imaginable.

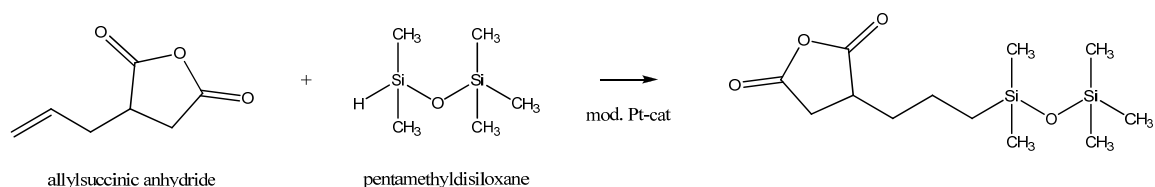


Fig. 26: Proposed reaction scheme for the hydrosilylation of ASA with PMDS.

In order to verify the assumption that ASA may hydrolyze and the thus formed carboxylic acids cause side reactions, the model reaction was repeated offering the ASA a 3-fold excess of PMDS. As in the model reaction using stoichiometric amounts, the analysis by ^1H NMR showed the formation of the three neighboring CH_2 groups: $\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-Si}$ (2m, 1.61-1.73 and 1.92-2.02 ppm, 2H), $\text{CH}_2\text{-CH}_2\text{-Si}$ (m, 1.39-1.49 ppm, 2H), $\text{CH}_2\text{-Si}$ (m, 0.48-0.61 ppm, 2H). However, in stark contrast to the reaction using stoichiometric amounts, no unreacted allyl groups of the ASA could be detected, and the representation of the PMDS had increased by $\sim 30\%_{\text{NMR}}$. The reaction mixture was analyzed by GPC in THF, see **Fig. 27** below. ASA and PMDS were measured by GPC for reference purposes, the peaks of their curves can be found at ~ 100 g/mol, and 190 g/mol, respectively. The adduct of the stoichiometric reaction between ASA and PMDS has its peak at ~ 310 g/mol, and traces of unconsumed ASA can be seen as well for the reaction with stoichiometric amounts. In the reaction with high excess of PMDS, the ratio of ASA to PMDS being 1:3, the peak of the desired adduct at ~ 310 g/mol is also present. However, no unconsumed ASA can be seen, which matches the findings by ^1H NMR. But most importantly, the presence of a second signal with its peak at ~ 700 g/mol proves the presence of a product of higher molecular weight than the desired adduct. This peak extends way beyond 5,000 g/mol, but only the range up to 1,100 g/mol is shown in order to increase the obviousness of **Fig. 27**. It can be concluded, that ASA causes a side reaction, as suggested above by ring opening of the suc-

cinic anhydride, and reacting either with PMDS or with its own species. In consequence, ASA is not considered a SME candidate. Furthermore, if carboxylic acids can cause side reactions under the applied conditions, the two components 2-PCA and 3-BCA just below will also not prove to be SME candidates.

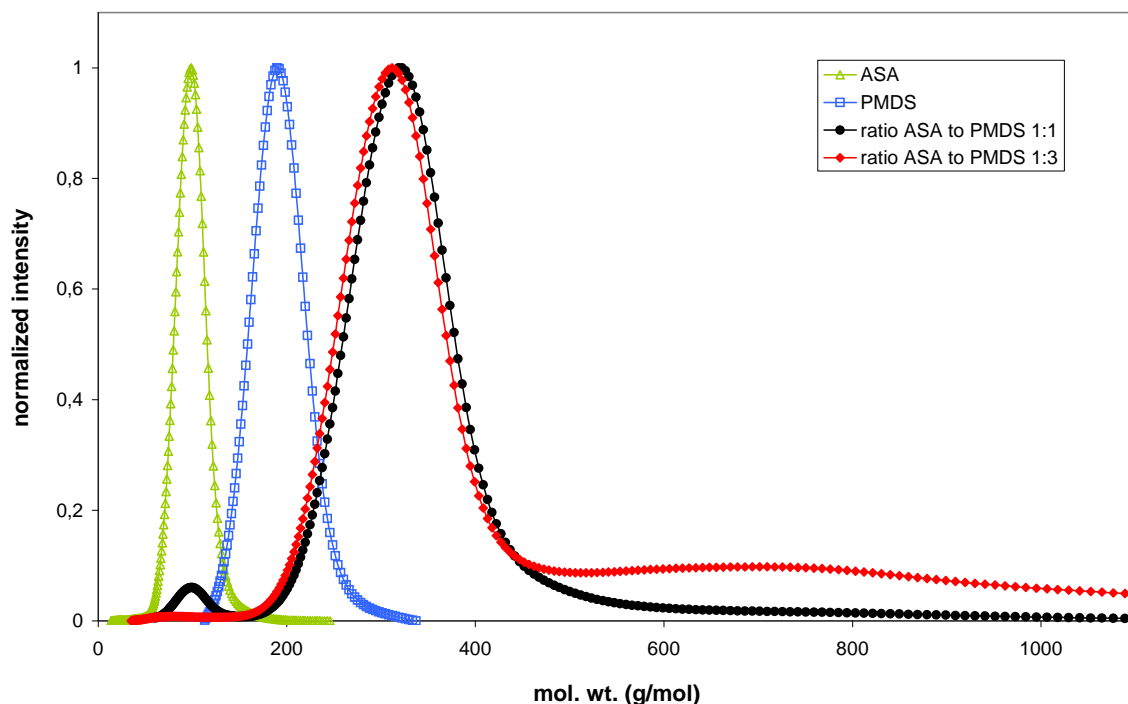


Fig. 27: GPC analysis of the reaction between ASA and PMDS, using different ratios of the reactants. Using excess PMDS leads to the formations of oligomers caused by the ring opening of the succinic anhydride ring and subsequent reaction with either PMDS or its own species.

7.3.10 2-Propene carboxylic acid

The proposed reaction between 2-PCA and PMDS is depicted in **Fig. 28**. The model reaction was conducted using the mod. Pt-cat. ^1H NMR showed that the three neighboring CH_2 groups are formed as suggested: $\text{OOC}-\underline{\text{CH}_2}$ (t, 2.26-2.32 ppm, 2H), $\text{OOC}-\text{CH}_2-\underline{\text{CH}_2}$ (m, 1.58-1.64 ppm, 2H), $\underline{\text{CH}_2}-\text{Si}$ (m, 0.52-0.59 ppm, 2H). However, the signals were partially overlapped by other peaks, and unidentified peaks were present, indicating a side reaction. Furthermore, some of the allyl of the 2-PCA was present after the reaction, and PMDS was overrepresented. The difficulty of hydrosilylation using the Karstedt's-catalyst in the pres-

ence of alcohol- or carboxylic acid-terminated species has been described in the literature to disturb the envisaged reaction mechanism [169]. It is safe to assume that this also applies for the hydrosilylation of 2-PCA and 3-BCA. In conclusion, 2-PCA can not be considered as SME candidate.

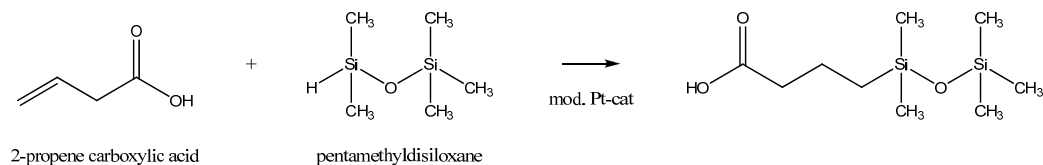


Fig. 28: Proposed reaction scheme for the hydrosilylation of 2-PCA with PMDS.

7.3.11 3-Butene carboxylic acid

Even though a negative outcome was expected analogous to the findings of the model reaction of 2-PCA, the reaction of 3-BCA and PMDS was carried out using the mod. Pt-cat. See **Fig. 29** for the reaction scheme. ^1H NMR showed the formation of four neighboring CH_2 groups: $\text{OOC}-\underline{\text{CH}_2}$ (t, 1.62-1.68 ppm, 2H), $\text{OOC}-\text{CH}_2-\underline{\text{CH}_2}$ (m, 1.31-1.42 ppm, 2H), $\underline{\text{CH}_2}-\text{CH}_2-\text{Si}$ (m, 0.89-0.96 ppm, 2H), $\underline{\text{CH}_2}-\text{Si}$ (m, 0.49-0.56 ppm, 2H). As for 2-PCA, the signals were partially overlapped by other peaks, and unidentified peaks were present. Again, some allyl of the 3-BCA was present in the reaction mixture, and PMDS was over-represented, all of which indicating a side reaction. Hence, 3-BCA is not a SME candidate.

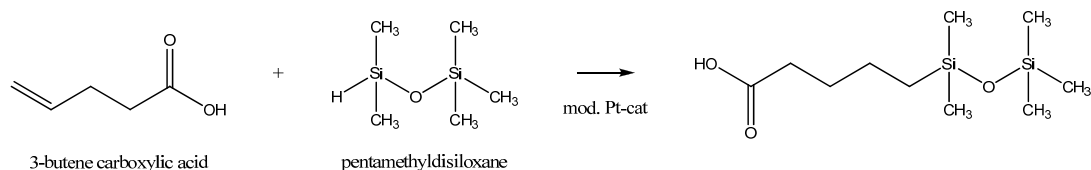


Fig. 29: Proposed reaction scheme for the hydrosilylation of 3-BCA with PMDS.

7.3.12 Dimethyl allylmalonate

Fig. 30 shows the reaction scheme for the reaction of DMAM and PMDS. The reaction was conducted using the mod. Pt-cat. The formation of three neighboring CH_2 groups was

clearly seen in the ^1H NMR analysis: $\text{CH}-\underline{\text{CH}_2}$ (q, 1.88-1.97 ppm, 2H), $\text{CH}-\text{CH}_2-\underline{\text{CH}_2}$ (m, 1.28-1.39 ppm, 2H), $\underline{\text{CH}_2}-\text{Si}$ (m, 0.48-0.56 ppm, 2H). The ratio between DMAM and PMDS was stoichiometric, no unconsumed material was found in the reaction mixture, and no sign of a side reaction was observed. Hence, DMAM is considered a SME candidate.

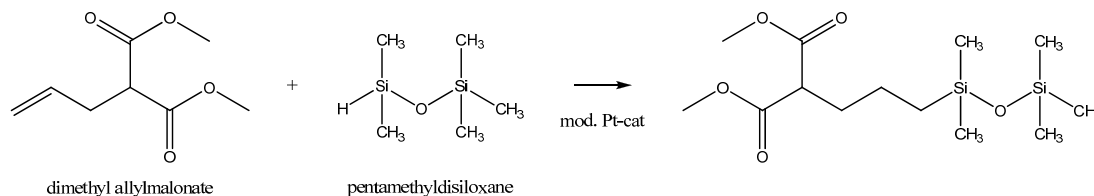


Fig. 30: Proposed reaction scheme for the hydrosilylation of DMAM with PMDS.

7.3.13 Acrylamide

AAM was reacted with PMDS using the mod. Pt-cat, as suggested in **Fig. 31**. Analysis by ^1H NMR showed no sign of a reaction, only unreacted AAM was found. This is most likely due to deactivation of the mod. Pt-cat by the NH_2 group in the AAM. Such an effect was described in the literature for allylamine and using the Pt-cat. The author did not investigate the mechanism of deactivation, and only stated that the Pt-cat was “poisoned” by the amine group [170]. Such a “poisoning” comes as no surprise since, as mentioned above in **chapter 3.3 The Karstedt’s-catalyst and a modified version thereof**, where the mod. Pt-cat was purposely combined with amines in order to form a platinum anticancer drug [92-94]. In consequence, AAM is not a SME candidate.

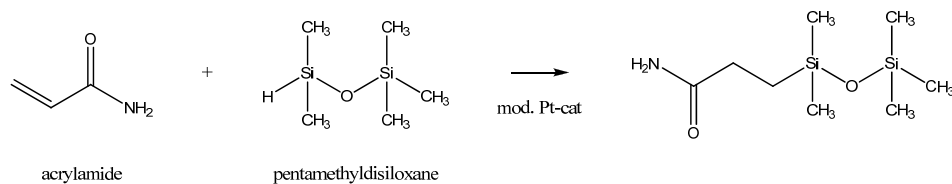


Fig. 31: Proposed reaction scheme for the hydrosilylation of AAM with PMDS.

7.3.14 4-Acryloylmorpholine

The result of reacting 4-AM with PMDS using the mod. Pt-cat was similar to that of AAm: Almost only unreacted material was found in the analysis of the reaction mixture by ^1H NMR. Some unidentified peaks were found, suggesting either a reaction as proposed in the reaction scheme in **Fig. 32**, or a side reaction. 4-Am will not be used as SME candidate.

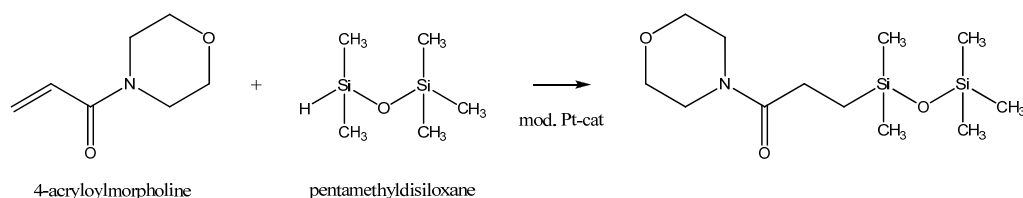


Fig. 32: Proposed reaction scheme for the hydrosilylation of 4-AM with PMDS.

7.3.15 Allylacetone

Fig. 33 shows the reaction scheme of AAc and PMDS; the model reaction was conducted using the mod. Pt-cat. ^1H NMR analysis showed the formation of four neighboring CH_2 groups as suggested, and as reported in the literature [81]. $\text{OC}-\underline{\text{CH}_2}$ (t, 2.39-2.44 ppm, 2H), $\text{OC}-\text{CH}_2-\underline{\text{CH}_2}$ (q, 1.54-1.63 ppm, 2H), $\underline{\text{CH}_2}-\text{CH}_2-\text{Si}$ (m, 1.26-1.36 ppm, 2H), $\underline{\text{CH}_2}-\text{Si}$ (m, 0.48-0.56 ppm, 2H). Unconsumed material was not found in the reaction mixture; the ratio between AAc and PMDS was almost stoichiometric with a slight overrepresentation of PMDS, and no sign of a side reaction was observed. AAC was tested only for comparison in order to establish comparability with the findings in the literature. It is not considered as SME candidate.

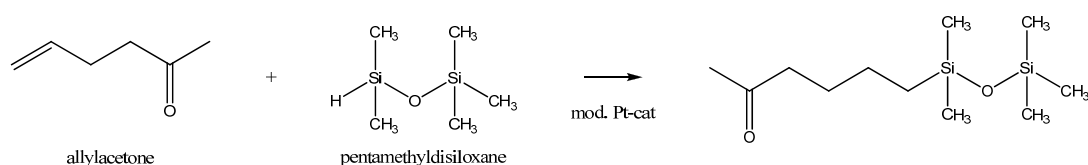


Fig. 33: Proposed reaction scheme for the hydrosilylation of AAc with PMDS.

7.3.16 Allyl ethyl ether

AAE was reacted with PMDS using the mod. Pt-cat as shown in **Fig. 34**. ^1H NMR analysis showed the formation of three neighboring CH_2 groups: $\text{O}-\text{CH}_2$ (t, 3.34-3.39 ppm, 2H), $\text{O}-\text{CH}_2-\text{CH}_2$ (m, 1.55-1.65 ppm, 2H), CH_2-Si (m, 0.47-0.53 ppm, 2H). No unconsumed material was found in the reaction mixture, the ratio between AEE and PMDS was stoichiometric, and no sign of a side reaction was observed. However, like AAc, AEE is not considered a SME candidate. It was used here only for comparison with the findings in the literature.

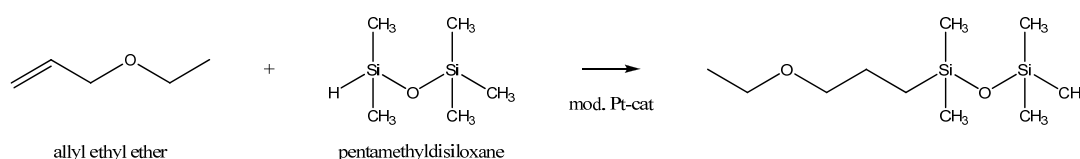


Fig. 34: Proposed reaction scheme for the hydrosilylation of AEE with PMDS.

7.4 Conclusions

Of the 16 possible SME candidates, only 4 underwent hydrosilylation in the model reaction with PMDS as required. All other components either caused side reactions, or deactivated the catalyst. The requirements for the hydrosilylation are firstly stoichiometric reaction under the given conditions, i.e. the presence of oxygen from the surrounding air atmosphere. The second requirement is the absence of side reactions, e.g. a side reaction with moisture which may be present in the solvent, the reactants, or the surrounding air. Finally, the catalyst may not be deactivated during the process.

Two of the 4 compounds which were shown to react properly in the hydrosilylation reaction will not be used as SME candidates, namely AAc and AEE. These two components were used only for comparison.

The remaining two components, 3-BCEE and DMAM, will be used as SME candidates to modify silicone, which will be described in the further course of this research work. They

were chosen, because they meet the two requirements for SME candidates: First, as stated above, they must be able to undergo hydrosilylation, as defined in **chapter 5 Hydrosilylation in silicones for cardiac pacing lead insulation**. The second requirement is that they can undergo hydrolysis and form a hydrophilic species which represents a negative charge. Both requirements are met only by 3-BCEE and DMAM.

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8 Incorporation of the SME candidates into silicone - two approaches

In order to combine the two SME candidates 3-BCEE and DMAM with the silicone, two general approaches are imaginable: One is the direct attachment of the SME candidates to the silicone backbone by hydrosilylation. The second approach is attaching the SME candidates to a carrier molecule and admixing this carrier to the silicone precursors prior to the polymerization of the silicone. Both approaches have their advantages and drawbacks.

The first approach, attaching the SME candidates directly to the silicone backbone, will form a covalent bond between the siloxane and the SME candidate. This would in any case prevent the SME candidate from being leached out of the silicone. However, forming this covalent bond would rely on the hydride-terminated siloxane species, which is originally meant to undergo hydrosilylation with a vinyl-terminated siloxane species, in order to form a silicone network. Hence, any use of the hydride-terminated siloxane species for bonding of SME candidates, will affect, i.e. decrease, the amount of interconnections within the silicone network. Reducing the cross-linking density of a polymer will in any case lead to a decrease of the mechanical properties like tensile strength of the silicone. Additional cross-linker can be added in order to rebalance the ratio between silicone hydride and vinyl, but can not fully make up for the change made to the cross-linking density. This is due to the fact that each cross-linker molecule will be partly saturated with SMEs and has fewer connections to the silicone backbone. Again, the overall cross-linking density of the polymer will decrease, causing a change of the mechanical properties.

The second approach, attaching the SME candidates to a carrier molecule, and admixing this carrier to the silicone precursors, will produce a blend of silicone and carrier. In this approach, the initial cross-linking-density of the silicone will be influenced less than in the first approach. In the best imaginable case, mixing the carrier and the silicone precursors would lead to a three-dimensional interpenetrating network, where the carrier molecule is entangled in the silicone matrix in such a manner, that any leaching of the carrier from the silicone is prevented. Leaching of the carrier from the silicone could be completely prevented, however, if the carrier were functionalized either by a silicone hydride group or a vinyl group. Either one could covalently bond to the silicone backbone. Since fewer bonds

would be needed to attach a carrier molecule to the silicone backbone, as compared to attaching every single SME candidate to the silicone backbone, the influence on the mechanical properties of the silicone would be lower as compared to the first approach. Furthermore, if the carrier were covalently bonded to the silicone backbone with more than one bonds, this may even contribute to the mechanical properties of the silicone.

8.1 Covalent bonding of SME candidates to the silicone backbone

Attaching one of the 2 SME candidates to the silicone backbone with a covalent bond can be done by hydrosilylation using the mod. Pt-cat. This was shown in **chapters 7.3.2 3-Butene carboxylic ethylester** and **7.3.12 Dimethyl allylmalonate**. However, this will consume hydride groups of the silicone precursors, which are intended for the formation of a silicone network. Hence, for the hydride groups which will be needed to bond the SME candidates, additional hydride groups have to be supplied. This can be done by adding supplemental cross-linker, like the P(DMS-co-MHS) shown in **chapter 5.1 Representing silicones for lead insulation in a universal model reaction**, and which was used to establish the universal hydrosilylation model reaction. Since the compatibility of P(DMS-co-MHS), 3-BCEE and DMAM with the hydrosilylation reaction has been shown in the universal model reactions, no further experiment is required. Silicone series produced by this approach will be discussed in **chapter 9 Production of 12 series of silicone**.

8.2 Admixing of a SME carrier to the silicone

For the second approach, which is covalently binding the SME candidates to a carrier, and then admixing the carrier to the silicone precursors, different options are theoretically available: The carrier molecule could either be non-functionalized, or functionalized with either hydride or vinyl groups, in order to allow for covalent bonding of the carrier to the silicone backbone. Secondly, the carrier could be either linear, or have a branched structure. There are numerous methods for producing silicone precursors, and they are well described in the literature. The idea is to use one of these methods and modify it as such, that a carrier for the 2 SME candidates can be synthesized.

Two methods of producing a functionalized 3-BCEE carrier will be examined below. Both involve the ring opening polymerization of a cyclotetrasiloxane species. In the first case trifluoromethanesulfonic acid (TFMSA) was used as a catalyst, and in the second case acid treated clay (ATC), namely the product Optimum 210 FF provided by Süd-Chemie AG, München, Germany. As the last section in this chapter, the production of a non-functionalized carrier for 3-BCEE and DMAM will be demonstrated.

8.2.1 Functionalized SME carrier using TFMSA

The ring opening polymerization of a cyclotetrasiloxane species by TFMSA is described well in the literature [171-177]. The procedure was shown to work well in a two step reaction for octamethyl-cyclotetrasiloxane (OM-CTS), with tetrakis(dimethylsiloxy)silane (TK(DMS)S) as the initiator for chain growth, TFMSA as the catalyst, and hexamethyldisilazane (HMDSz) to neutralize the reaction mixture. The synthesis yields a star shaped hydride-terminated siloxane molecule with 4 arms [178]. **Fig. 35** shows the reaction scheme of this two step process.

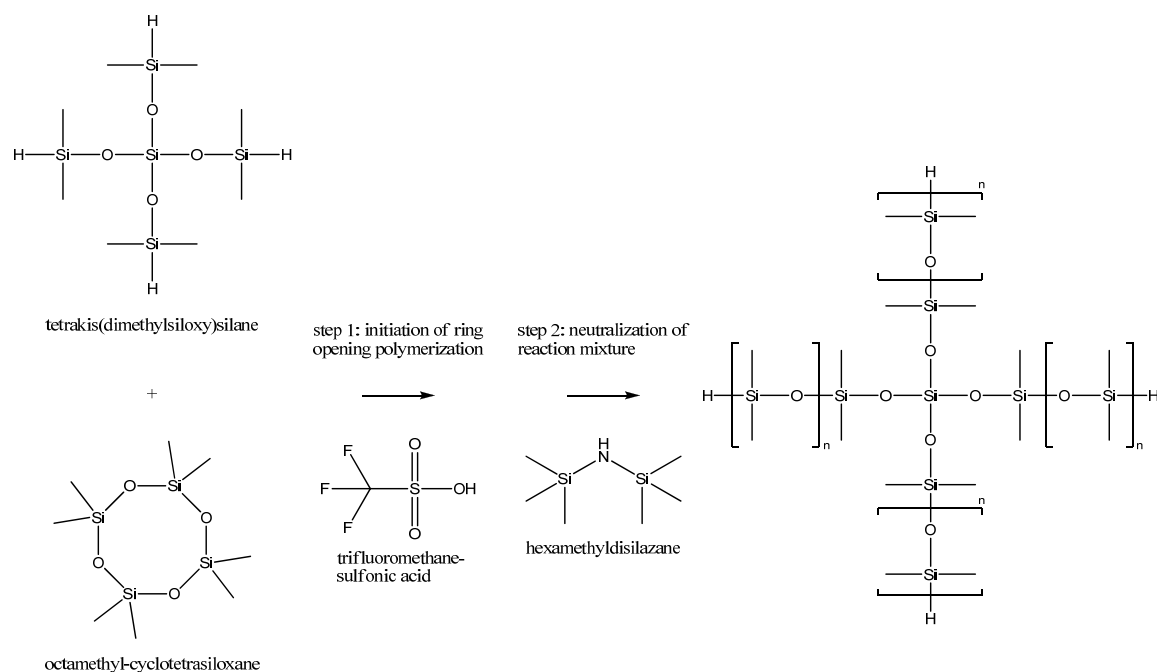


Fig. 35: Reaction scheme for the ring opening polymerization of OM-CTS: TK(DMS)S allows for the start of the chain growth, TFMSA acts as the catalyst, and HMDSz is used to neutralize the reaction mixture. The product is hydride-terminated.

In order to produce a 3-BCEE carrier in a polymerization reaction analogous to the reaction depicted in **Fig. 35** a cyclotetrasiloxane with 3-BCEE side groups is needed. Preparing such a species is possible by covalently bonding 3-BCEE to tetramethyl-cyclotetrasiloxane (TM-CTS) as shown below in **Fig. 36**. The product is tetraBCEE-tetramethyl-cyclotetrasiloxane (TBCEE-TM-CTS), and its short notation is shown in **Fig. 37**. Ring opening polymerization of TBCEE-TM-CTS can then be attempted as shown in **Fig. 38**.

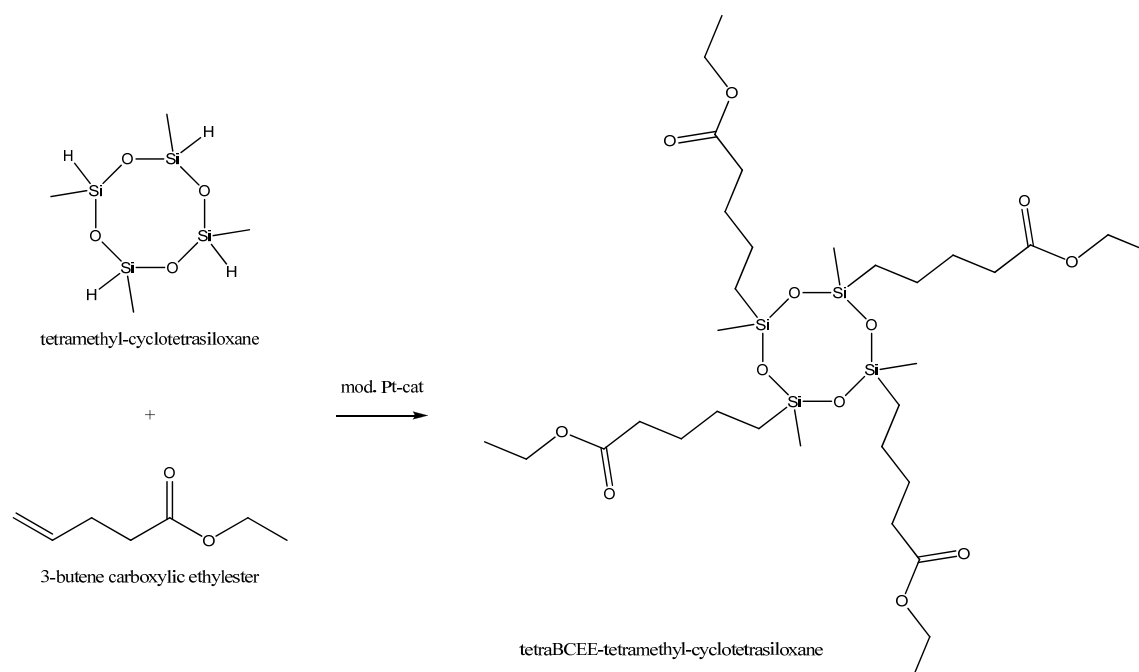


Fig. 36: Reaction scheme for the preparation of a 3-BCEE carrying cyclosiloxane: 3-BCEE is bonded to TM-CTS via hydrosilylation using the mod. Pt-cat. The product is TBCEE-TM-CTS.

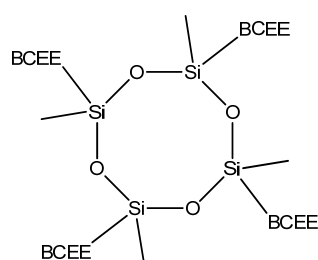


Fig. 37: Short notation of TBCEE-TM-CTS, the product of the reaction shown in Fig. 36.

TBCEE-TM-CTS was produced in a one pot process similar to the universal model reaction described in **chapter 5.1 Representing silicones for lead insulation in a universal**

model reaction: 2.0 mL of TM-CTS and 4.65 mL of 3-BCEE were reacted in a round bottom flask under constant stirring with a Teflon covered stir bar. The reaction was started by adding 0.020 mL of a 0.1 M solution of the mod. Pt-cat. The reaction vessel was heated to 80°C and the mixture allowed to react for 4 days. After the reaction the solvent was removed with a rotary evaporator, and analysis conducted by ^1H NMR and GPC. Yield was calculated gravimetrically and found to be ~92.6%_{wt}. ^1H NMR showed the formation of the desired product with four neighboring CH_2 groups as suggested in **Fig. 36**: $\text{OOC}-\underline{\text{CH}_2}$ (t, 2.25-2.31 ppm, 2H), $\text{OOC}-\text{CH}_2-\underline{\text{CH}_2}$ (q, 1.59-1.70 ppm, 2H), $\underline{\text{CH}_2}-\text{CH}_2-\text{Si}$ (m, 1.35-1.43 ppm, 2H), $\text{CH}_2-\underline{\text{CH}_2}-\text{Si}$ (m, 0.48-0.55 ppm, 2H). There were no signs of side product formation, and the ratio of 3-BCEE to each ring of TM-CTS was 4:1. Analysis by GPC showed an unimodal distribution curve with a sharp peak, and its maximum at ~950 g/mol. Hence, the production of TBCEE-TM-CTS worked as expected.

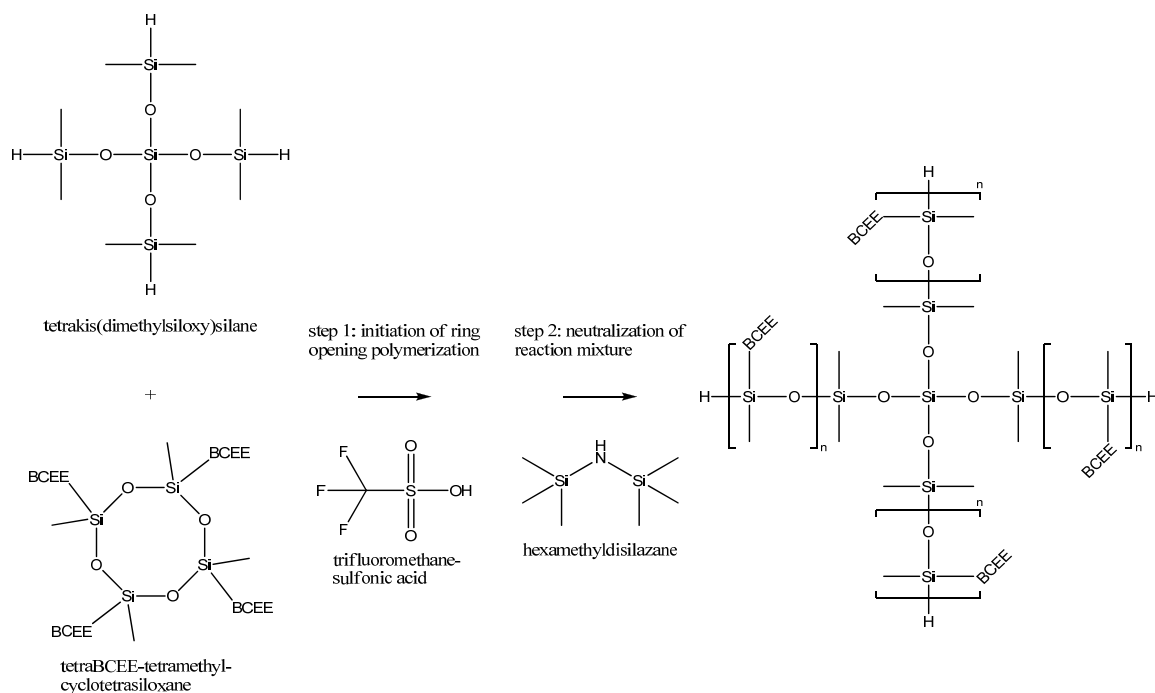


Fig. 38: Reaction scheme for the production of a 3-BCEE carrier with functional groups: TBCEE-TM-CTS is expected to undergo a ring opening polymerization, where TK(DMS)S allows for the start of the chain growth, TFMSA acts as the catalyst, and HMDSz is used to neutralize the reaction mixture.

The ring opening polymerization reactions of OM-CTS and TBCEE-TM-CTS, shown in **Fig. 35** and **Fig. 38**, were carried out using the procedure as described in the literature

[178]. This process will not be elucidated here, since it is state of the art and not part of this research work. The products of the reactions were checked by ^1H NMR and GPC. For the polymerization of OM-CTS, ^1H NMR showed that the hydride groups are slightly under-represented, but other than that there was no sign that the polymerization may not have worked. In contrast, there were no hydride functional groups in the product of the polymerization of TBCEE-TM-CTS. It is noteworthy that the BCEE was not affected by the polymerization procedure and remained unchanged. However, the GPC showed that the degree of polymerization is significantly lower for TBCEE-TM-CTS than for OM-CTS, as can be seen below in **Fig. 39**. The polymerization of OM-CTS produced a polymer, while the polymerization of TBCEE-TM-CTS only produced an oligomeric substance, and large parts of the monomer remained unchanged, i.e. the peak at $\sim 1,000$ g/mol is TBCEE-TM-CTS.

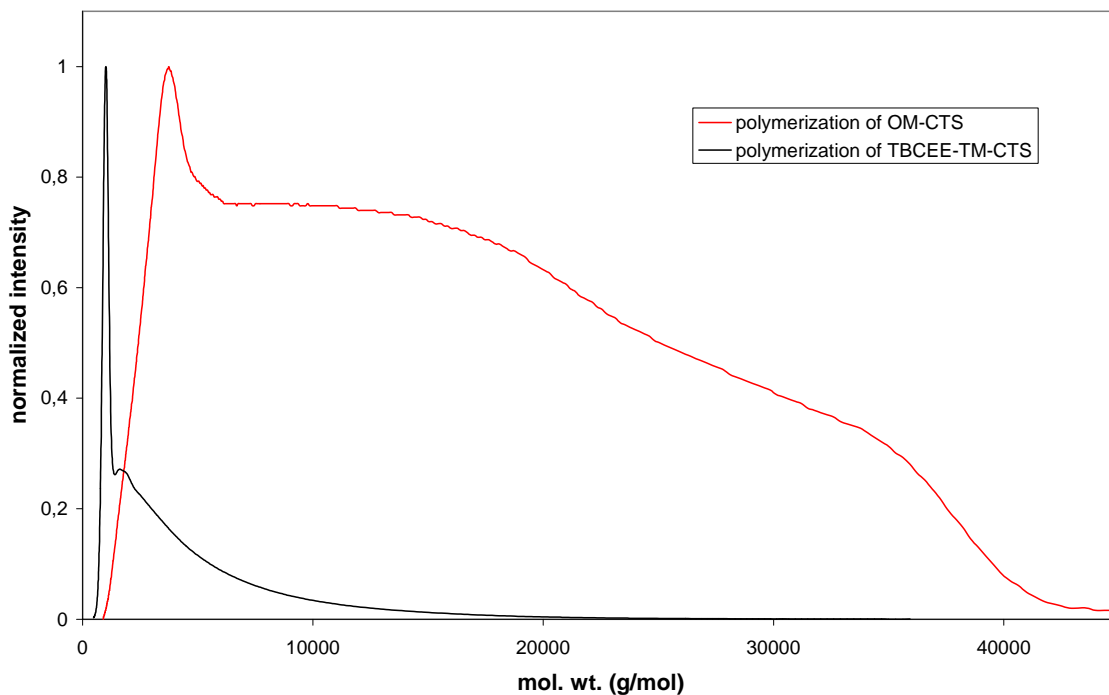


Fig. 39: GPC results of polymerization of OM-CTS and TBCEE-TM-CTS: The ring opening reaction works well for OM-CTS, but does not work for TBCEE-TM-CTS. In the latter case, the large part of the monomer remains unchanged and a small fraction is converted to an oligomer.

The polymerization reaction of TBCEE-TM-CTS was repeated using the same procedure, but at elevated temperature, i.e. 80°C, and for different time lengths, i.e. between 1 and 8 days. The analysis of the polymerization was again analyzed by GPC, see **Fig. 40**, where a higher molecular weight distribution of the product can be seen, as compared to the reaction conducted at room temperature, see **Fig. 39** for comparison. The increase in temperature lead to a higher molecular weight, but still a large part of the monomer remained unchanged in the reaction mixture. Reaction times above one day did not improve the results. In the literature, this polymerization reaction is described as an equilibrium reaction [178]. Hence, it can be assumed that the maximum degree of polymerization for the procedure described in the literature has been reached after one day. Since the result is not satisfying, in terms of producing a hydride-terminated SME carrier with good yield, this approach to produce a carrier molecule was discontinued.

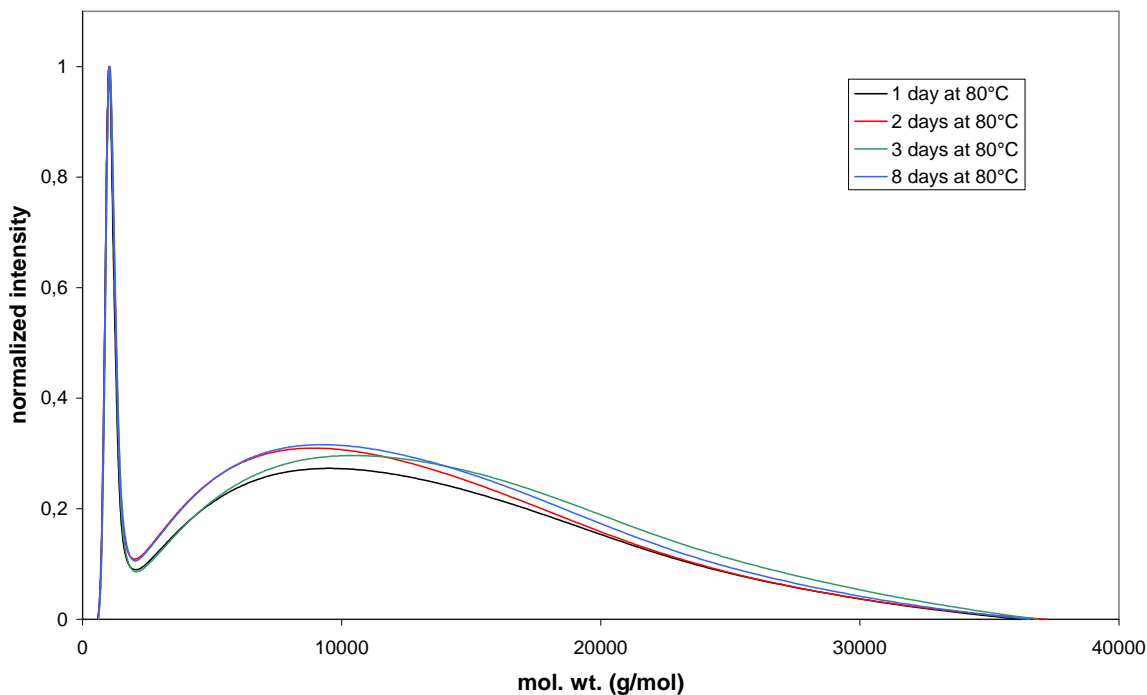


Fig. 40: GPC results of polymerization of TBCEE-TM-CTS conducted at 80°C: The ring opening reaction works better than at room temperature, but does not work as well as the ring opening reaction of OM-CTS, see Fig. 39 for comparison. A large part of the monomer still remains unchanged in spite of elevated reaction temperature and longer reaction times.

8.2.2 Functionalized SME carrier using ATC

A very simple way of producing a functionalized silicone polymer is to initiate the ring opening polymerization of OM-CTS with ATC [179]. This method is a one step bulk process, and purification of the product is possible by simple filtration [180]. Since this process is state of the art and not part of this thesis, it will not be described in detail here. ATC is commercially available at low cost and in large amounts, since it is commonly used at large scale for the purification of vegetable and animal oils and greases [181, 182]. **Fig. 41** shows the reaction scheme for the polymerization of OM-CTS, using divinyltetramethyldisiloxane (DVTMS) as the chain terminating agent. The result is a linear vinyl-terminated siloxane species with one functional group at either end.

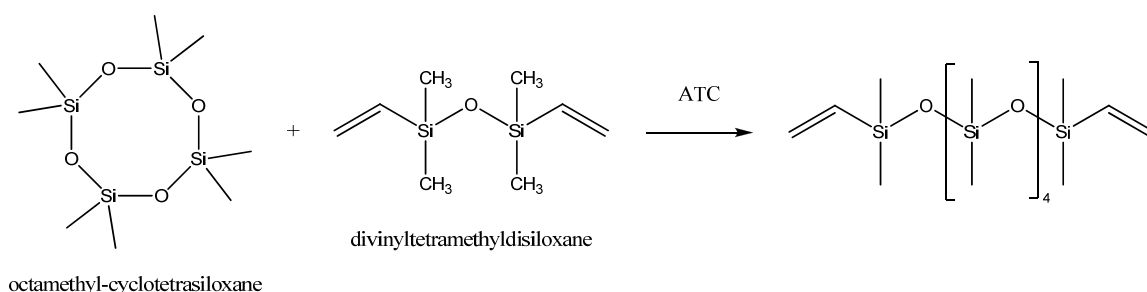


Fig. 41: Reaction scheme of the ring opening polymerization of OM-CTS using ATC: DVTMS acts as chain terminating agent and is split up during the process.

Analogous to the polymerization of OM-CTS the ring opening polymerization of TBCEE-TM-CTS with ATC can be attempted, see **Fig. 42** for the suggested reaction scheme.

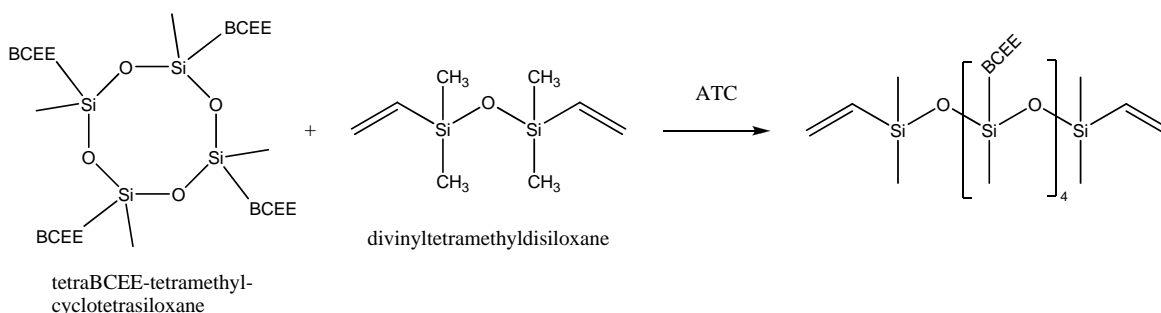


Fig. 42: Reaction scheme of the ring opening polymerization of TBCEE-TM-CTS using ATC: DVTMS acts as chain terminating agent, and is split up during the process.

Analysis by ^1H NMR showed, that the polymerization of OM-CTS led to a vinyl-terminated siloxane species: $\text{Si}-\text{CH}$ (q, 6.07-6.18 ppm, 1H), $\text{Si}-\text{CH}-\text{CH}_2$ (q, 5.90-5.97 and 5.69-5.78 ppm, 2H). However, in the case of TBCEE-TM-CTS no vinyl-functional group was detected. The BCEE was not changed by the polymerization process. GPC analysis showed that the polymerization process worked quantitatively only for the polymerization of OM-CTS, but not for the polymerization of TBCEE-TM-CTS, see **Fig. 43**. In the case of OM-CTS no unconsumed monomer was found. In stark contrast, the curve of the TBCEE-TM-CTS polymerization only shows a narrow distribution curve with its maximum at ~ 980 g/mol, which is the TBCEE-TM-CTS itself. In conclusion, the ring opening polymerization using ATC can not be applied for the production of a 3-BCEE carrier.

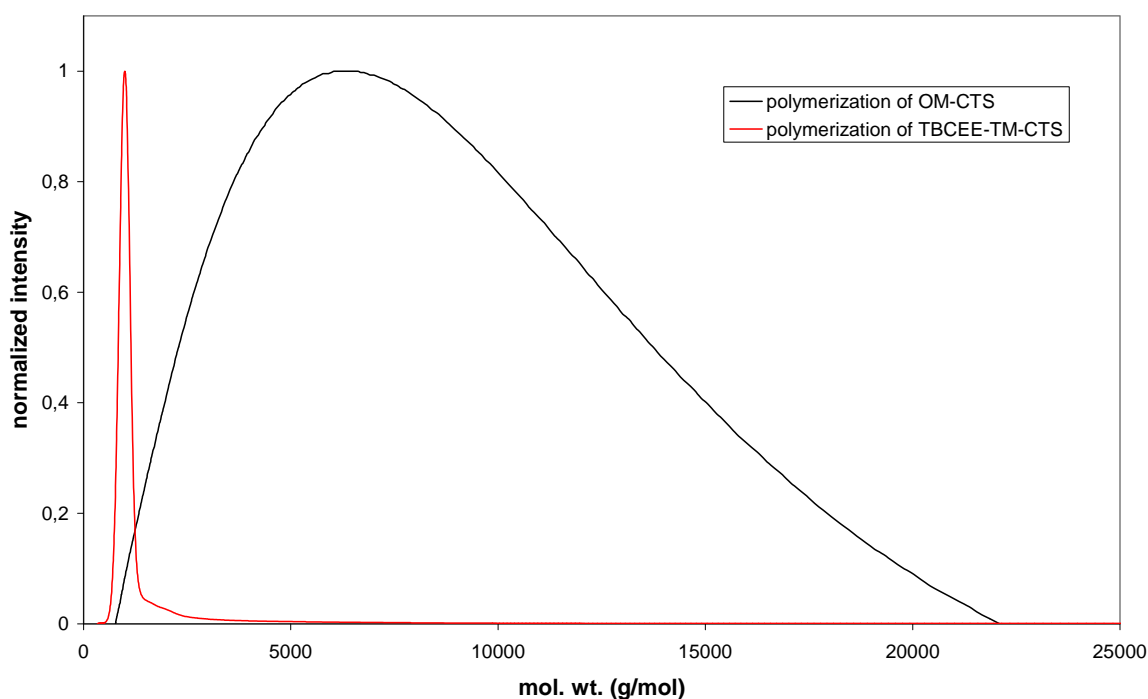


Fig. 43: GPC results of polymerization of OM-CTS and TBCEE-TM-CTS using ATC catalyst: The ring opening reaction works well for OM-CTS, but does not work for TBCEE-TM-CTS. In the latter case, the monomer remains unchanged.

8.2.3 Non-functionalized SME carrier

The basic idea for producing a non-functionalized 3-BCEE carrier is to attach many molecules of 3-BCEE to a silicone backbone. Silicone was chosen for the backbone in order to provide for as much similarity between the carrier molecule and the matrix as possible. Hence, a silicone backbone capable of covalently binding 3-BCEE or DMAM is needed. The most obvious approach is using the cross-linker molecule P(DMS-co-MHS) as the backbone, because it provides for several binding sites per molecule. Theoretically, saturating all hydride binding sites of P(MHS-co-MHS) would already yield a carrier molecule. However, P(DMS-co-MHS) is rather small, i.e. 950 g/mol, and even if it were saturated with SME candidates it may be small enough to easily migrate out of the silicone network. Thus, a larger molecule of P(DMS-co-MHS) must also be taken into consideration.

By combining P(DMS-co-MHS) with a chain extender, such as the short DVTMS, several cross-linker molecules can be attached to another, and the cross-linker would grow in size but keep its functionality. Some of the hydride groups of the P(DMS-co-MHS) will be used up in this process, but the majority will still be present. Those remaining hydride groups can then be saturated with 3-BCEE, and a much larger molecule would be obtained.

Since 3-BCEE and DMAM can be assumed to be more hydrophilic than the silicone precursors, the miscibility of the carrier molecules saturated with 3-BCEE or DMAM can not be taken for granted. Phase separation may occur. This problem may be overcome, if a part of the carrier were pure siloxane. This can be achieved by including a large molecule of vinyl-terminated polydimethylsiloxane (PDMS_{vinyl}) in the carrier. This way the produced carrier will consist of both a hydrophobic PDMS block and the less hydrophobic blocks on either end made from P(DMS-co-MHS) which are saturated with 3-BCEE or DMAM.

The reaction scheme for the production of large 3-BCEE or DMAM carriers is shown below in **Fig. 44**. It is a two step reaction, where P(DMS-co-MHS), DVTMS and PDMS_{vinyl} are reacted in the first step, and all remaining hydride binding sites are saturated with either 3-BCEE or DMAM in the second step. The mod. Pt-cat can be used for the hydrosilylation reaction of the siloxane species with one another, but also for saturating the molecule with

either one of the two SME candidates. By variation of the ratios of the siloxane components, i.e. by adding more or less of the chain extender DVTMS, the size of the backbone can be adjusted to the desired value.

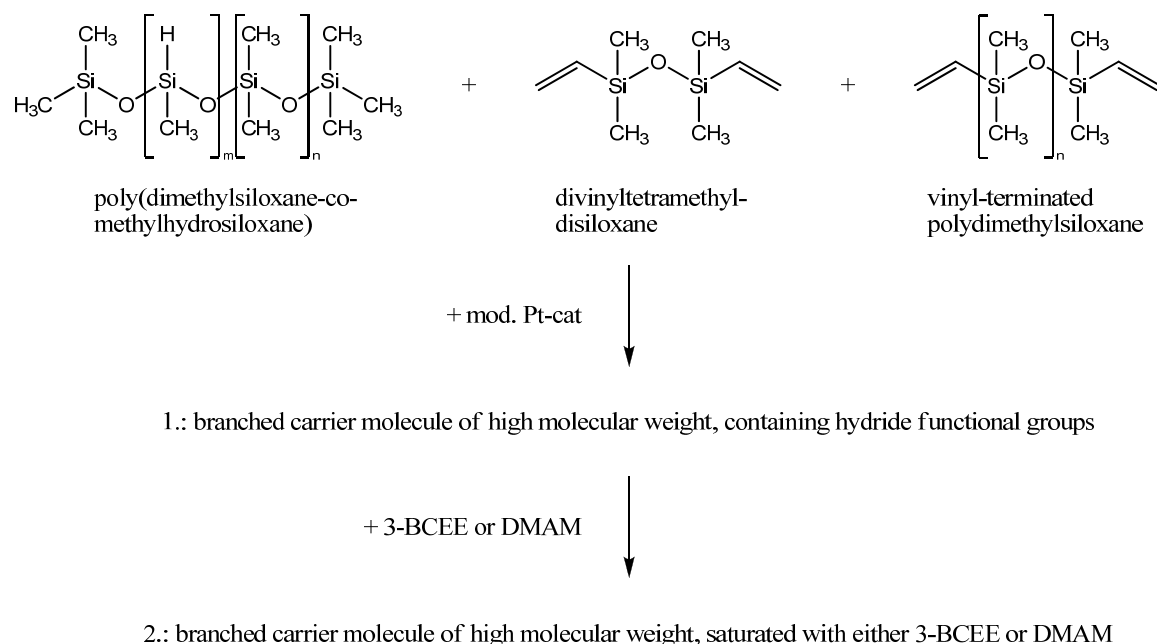


Fig. 44: Reaction scheme for the production of a 3-BCEE or DMAM carrier without functional groups: The first step of the reaction yields a carrier molecule of high molecular weight, where the blocks made from P(DMS-co-MHS) still bear the majority of the hydride binding sites. In the second step these binding sites are saturated with either 3-BCEE or DMAM.

Overall, five different carriers were produced following the scheme in **Fig. 44**, three carriers were saturated with 3-BCEE, and two were saturated with DMAM. The five carriers were produced with three different sizes, and only one, the largest one, contained a block of pure PDMS. **Tab. 5** shows the composition of the five carriers, giving both the molar ratios between the components and the actual amounts used for the siloxane backbone. The weight percentages of 3-BCEE and DMAM in the carriers were calculated from the initial amounts used.

The five carriers were produced in a one pot process similar to the universal model reaction described in **chapter 5.1 Representing silicones for lead insulation in a universal model reaction**: The reaction for the production of the carrier was performed in a round

bottom flask under constant stirring with a Teflon covered stir bar. Xylene was given to the reaction vessel first, followed by the 0.1 M solution of the mod. Pt-cat. The three siloxane components P(DMS-co-MHS), DVTMS, and PDMS_{vinyl} were given to the mixture, and the reaction vessel was heated to 80°C. The mixture was allowed to react over night, and checked by ¹H NMR. Once the vinyl groups were consumed, either 3-BCEE or DMAM was added in the amount required to saturate the siloxane backbone, and the mixture was allowed to react until all hydride groups were consumed. After the reaction the solvent was removed with a rotary evaporator, and analysis of the SME carrier was conducted by ¹H NMR and GPC. The resulting polymer was a yellowish liquid in all five cases, with the viscosities increasing with increasing molecular weight.

Carrier for silicone series #	P(DMS-co-MHS)	DVTMS	PDMS _{vinyl}	3-BCEE	DMAM	Mn (g/mol)
8	27 parts 28.5 mL	25 parts 6.335 mL	1 part 28.5 mL	18.96 mL 22.0% _{wt}	-	63,500
9	1 part 12.5 mL	-	-	11.87 mL 46.5% _{wt}	-	5,580
10	1 part 12.5 mL	-	-	-	13.48 mL 53.8% _{wt}	5,900
11	16 parts 12.5 mL	15 parts 2.81 mL	-	8.42 mL 34.2% _{wt}	-	17,000
12	16 parts 12.5 mL	15 parts 2.81 mL	-	-	9.56 mL 41.1% _{wt}	16,700

Tab. 5: Molar ratios and amounts of precursors for the preparation of the silicone backbone of the 3-BCEE and DMAM carriers. Mn as determined by GPC is shown in the last column.

In all five cases ¹H NMR showed the formation of the desired product with four neighboring CH₂ groups in the case of 3-BCEE, and three neighboring CH₂ groups in the case of DMAM, as first discussed in **chapters 7.3.2 3-Butene carboxylic ethylester** and **7.3.12 Dimethyl allylmalonate**. Furthermore, the reaction between a vinyl-terminated species

and a hydride-terminated siloxane species in the first step of the reaction led to the formation of two neighboring CH₂ groups. For 3-BCEE: Si-CH₂-CH₂-Si, (m, 0.35-0.52 ppm, 4H), OOC-CH₂ (m, 2.24-2.30 ppm, 2H), OOC-CH₂-CH₂ (m, 1.59-1.68 ppm, 2H), CH₂-CH₂-Si (m, 1.31-1.42 ppm, 2H), CH₂-Si (m, 0.47-0.56 ppm, 2H). For DMAM: Si-CH₂-CH₂-Si, (m, 0.35-0.52 ppm, 4H), CH-CH₂ (m, 1.86-1.96 ppm, 2H), CH-CH₂-CH₂ (m, 1.29-1.41 ppm, 2H), CH₂-Si (m, 0.48-0.58 ppm, 2H). There were no signs of side product formation. In the case of DMAM some unconsumed DMAM was found. Analyses by GPC showed unimodal distribution curves in all cases, see **Fig. 45**, and in the case of the 3-BCEE carrier for series # 8 a peak of some oligomeric material. This curve extends up to 450,000 g/mol, but only the region up to 100,000 g/mol is displayed in order to avoid crowdedness of the diagram in the regions of lower molecular weight. The molecular weight of the carriers as determined by GPC is given in the last column of **Tab. 5**. From the ¹H NMR and GPC results it can be concluded, that the production of the five carriers worked as predicted.

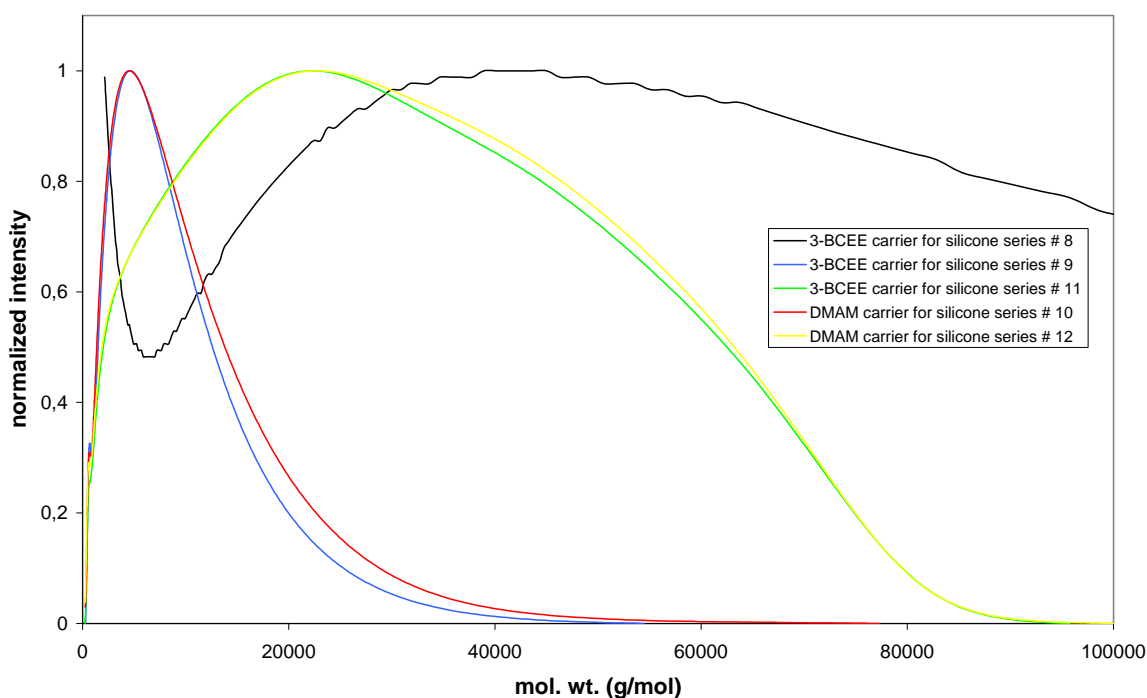


Fig. 45: Molecular weight distribution curves of the five carriers as determined by GPC. Some oligomeric material can be seen in the case of the 3-BCEE carrier for silicone series # 8. This curve extends up to 450,000 g/mol, but only the region up to 100,000 g/mol is displayed in order to avoid crowdedness of the diagram in the regions of lower molecular weight.

8.2.4 Thermal stability of the 3-BCEE and DMAM carriers

The silicones for cardiac pacing lead insulation are processed at high temperatures, and exposed to 200°C for up to 4 hours during the production process. Since SME carriers which are admixed to silicones will face the same conditions, the 3-BCEE carrier and the DMAM carrier were checked for temperature stability. The carriers for the silicone series # 11 and # 12 were chosen, and heated to 200°C for 4 hours in a round bottom flask with internal cold trap. The trap was cooled with tap water, and represented a cold surface where evaporated substance may condense. ¹H NMR was conducted of the material in the bottom of the flask, and GPC was performed on the material which condensed on the cold trap. ¹H NMR showed no difference between the initially produced carriers, and the results after exposure to 200°C for 4 hours. GPC showed the presence of low molecular weight substances, none larger than 2,000 g/mol. It is assumed that the condensed substances are residual solvent, oligomeric siloxanes, and in the case of the DMAM carrier unconsumed DMAM.

8.2.5 Hydrolysis of the SME carrier

One of the prerequisites of the SME candidates is their ability to undergo hydrolysis and form a carboxylic group. After it was shown above that both a 3-BCEE and a DMAM carrier can be produced, now the question has to be addressed, how 3-BCEE and DMAM can be hydrolyzed. Literature research with SciFinder ScholarTM yielded two procedures, one suggesting potassium hydroxide in aqueous (aq.) methanolic medium for the hydrolysis of 3-BCEE [183]. Another source reported that 3-aminopropan carboxylic ethylester was hydrolyzed with sodium hydroxide [184]. Here, sodium hydroxide (NaOH) was used both in aqueous solution and aqueous methanolic solution, and hydrolysis conducted as shown below in **Fig. 46**. To verify if the hydrolysis will also occur in blood, 3-BCEE was exposed to rat serum, see **Fig. 47** for the reaction scheme.

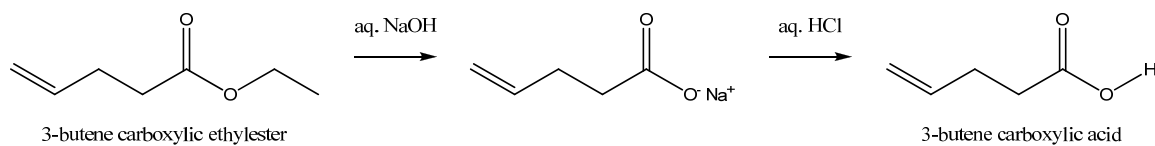


Fig. 46: Hydrolysis of 3-BCEE using sodium hydroxide in aqueous media leads to the formation of 3-butene carboxylic acid.

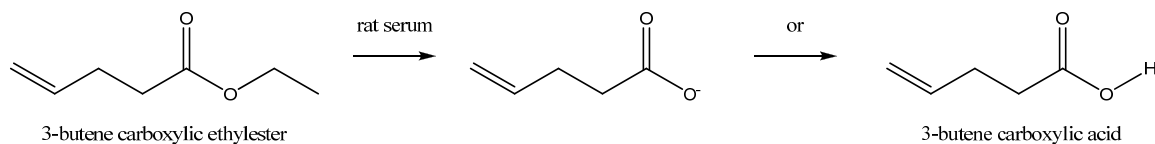


Fig. 47: Hydrolysis of 3-BCEE by the reaction with rat serum for 12 hours at 37°C leads to the formation of 3-butene carboxylic acid.

The hydrolysis of 3-BCEE with NaOH was conducted as follows: In a round bottom flask 0.3 mL of 3-BCEE, 9 mL H₂O and 0.256 g NaOH were mixed with a Teflon covered stir bar. In the case of using the methanolic solution 9 mL of methanol were added as well. The mixtures were allowed to react for 12 hours at reflux temperature. Dilute hydrochloric acid was then used to acidify the solution to pH ~4. The mixtures were worked up by addition of 25 mL of DCM, thorough mixing, and separation using a separating funnel. The last step was repeated three times. The collected DCM solution was concentrated using a rotary evaporator. The product was analyzed by ¹H NMR. The hydrolysis of 3-BCEE using rat serum was conducted the same way, only using pure rat serum at 37°C instead of the aqueous NaOH solution.

Analysis by ^1H NMR showed the formation of carboxylic acid as predicted in both cases: The ethyl group was split off, while all other signals of the 3-BCEE remained unchanged. The peak of the carboxylic acid was very broad, and could be found in the range of 9.5-12 ppm.

In a next step the hydrolysis of the 3-BCEE carrier was attempted using buffer solutions. Four 0.1 M buffer solutions of different pH were prepared: HEPES for pH 8, BA for pH 9, Na_2CO_3 for pH 10, and TEA for pH 11. For the hydrolysis reaction 25 mL of each buffer solution were given to a round bottom flask, and 0.5 mL of the 3-BCEE carrier for silicone

series # 9 was added. The mixtures were allowed to react for 3 days at T_R under constant stirring with a Teflon covered stir bar. The four reaction mixtures were worked up by addition of 25 mL of DCM, thorough mixing, and separation using a separating funnel. The last step was repeated three times. The collected DCM solutions were concentrated using a rotary evaporator, and the products were analyzed by ^1H NMR. In the case of HEPES and TEA no change of the 3-BCEE carrier could be observed. In the case of BA the signal of the ethyl group decreased by ~6%, and the best result was achieved for Na_2CO_3 with a decrease of the signal of the ethyl group of ~18%. In conclusion, Na_2CO_3 was chosen for further hydrolysis experiments in the course of this work.

8.3 Conclusions

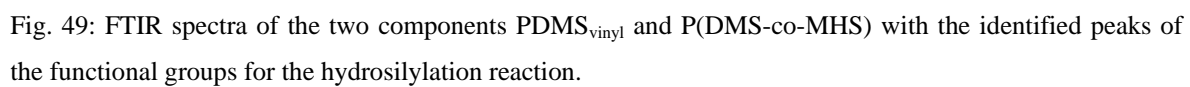
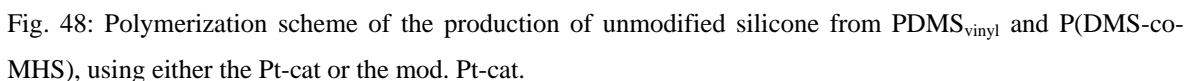
In this chapter it has been shown that the production of a SME carrier is possible for both 3-BCEE and DMAM. However, the state of the art processes of ring opening polymerization using TFMSA or ATC can not be applied for cyclic tetrasiloxanes carrying 3-BCEE. Instead, building a siloxane backbone with hydride functional groups which can be saturated with either 3-BCEE or DMAM has been shown to allow for the production of SME carriers of different molecular weights. The carrier is thermally stable within the temperature range commonly applied in the production of silicones for cardiac pacing leads. Finally, the SMEs which are attached to the carrier molecule can be hydrolyzed using Na_2CO_3 buffer solution.

9 Production of 12 series of silicone

In this chapter the production of 12 different silicone series will be described. The proof of concept for the production of unmodified and modified silicone using the mod. Pt-cat will be presented first, in order to establish the basis of both feasibility and evaluation. Once the basis is established, five different silicone precursors will be presented, which will be used in the 12 series of silicone. Series # 1-3 will deal with the composition of unmodified silicones, the aim will be to find a mixture which will produce a silicone with mechanical properties as close to the commercially available materials as possible. Series # 4-7 will contain 3-BCEE which will be covalently bonded to the siloxane backbone. Finally, series # 8-12 will contain each one of the SME carriers which were described in the previous chapter.

9.1 Unmodified silicone - proof of concept

A three-dimensionally cross-linked silicone network can be produced by combining any vinyl-terminated siloxane species with any hydride-terminated siloxane species via hydrosilylation. Provided that one component has at least two functional groups per molecule, and the other component has at least three functional groups per molecule, a network will be formed. The catalyst for the hydrosilylation reaction can be either the Pt-cat or the mod. Pt-cat. The mechanical properties of a thus formed silicone will depend on the cross-linking density, i.e. the number of interconnections between the molecules per volume unit, the length of the siloxane chains between the interconnections, and the amount of silica filler. Here, for proof of concept, PDMS_{vinyl} and P(DMS-co-MHS) were used to prepare a simple silicone using both the Pt-cat and the mod. Pt-cat for the hydrosilylation reaction. No attention will be paid to the mechanical properties in the proof of concept. The goal is to first identify the functional groups of the silicone components, and then to show that both catalysts lead to the same result. The polymerization scheme for this proof of concept is shown in **Fig. 48**. The FTIR spectra of the two precursors are displayed in **Fig. 49**, where the characteristic peaks of the functional groups which are needed for the hydrosilylation reaction are pointed out.



The polymerization was carried out in a simple one pot process: 1.00 mL of PDMS_{vinyl} and 0.444 mL of P(DMS-co-MHS) were mixed in 10 mL Falcon tube. To start the hydrosilylation reaction 0.020 mL of a 0.1 M solution of the catalysts were added and the silicone precursors again mixed. The mixture was allowed to react over night. In the case of the Pt-cat the reaction started immediately, and the mixture was solid within less than five minutes. In the case of the mod. Pt-cat, however, the mixture remained liquid for ~30 min. **Fig. 50** shows the FTIR spectra of the two silicones which were produced using the Pt-cat and the mod. Pt-cat. The arrows used to indicate the functional vinyl- and hydride groups are identical with those used in **Fig. 49**. It can be seen that the peaks of the vinyl groups and the hydride groups are not present any longer or in some cases at least much reduced in size. This was to be expected, as these functional groups were consumed during the polymerization process via hydrosilylation. No difference between the results obtained with the Pt-cat and the mod. Pt-cat could be found.

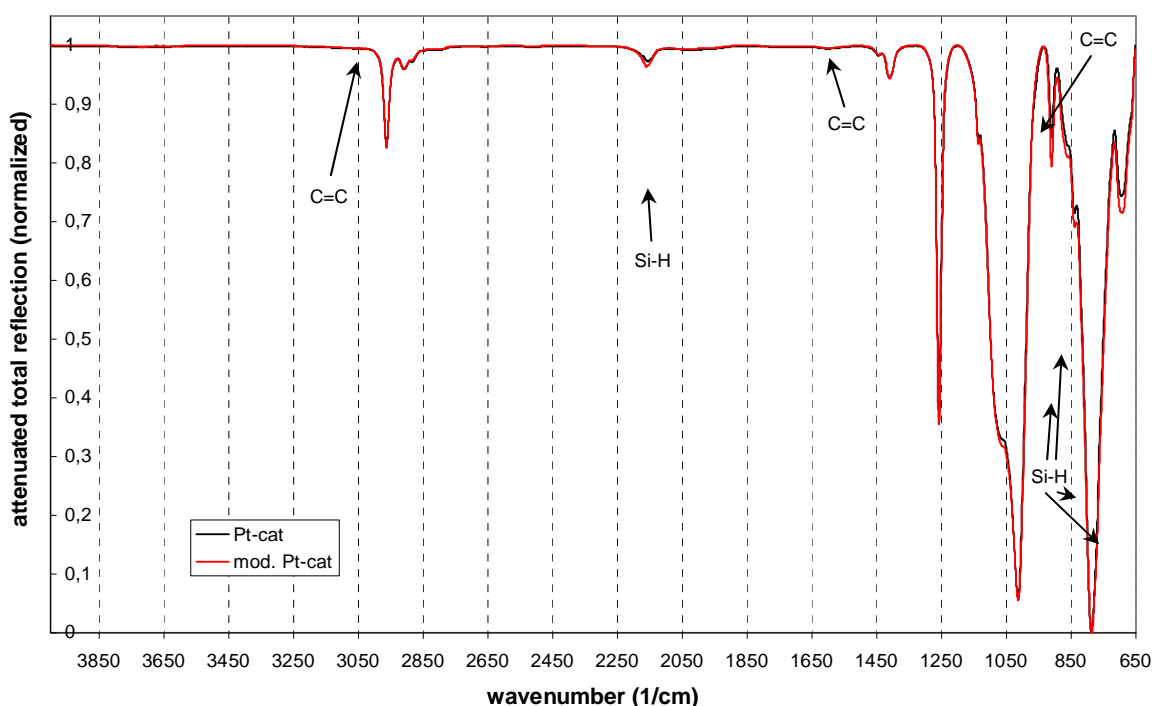


Fig. 50: FTIR spectra of silicone produced from the two components PDMS_{vinyl} and P(DMS-co-MHS), using the Pt-cat and the mod. Pt-cat. Characteristic peaks of the hydride- and vinyl-groups are pointed out. No difference can be seen between the silicones produced with the Pt-cat and with the mod. Pt-cat.

9.2 Modified silicone - proof of concept

For the proof of concept for the polymerization of modified silicone, silicone is polymerized in the presence of 3-BCEE. The reaction is analogous to the reaction in the previous chapter, but here 50mol% of the hydride functional groups are saturated with 3-BCEE. Again, no attention will be paid to the mechanical properties of the produced material. The reaction scheme is displayed in **Fig. 51**. The FTIR spectrum of 3-BCEE is shown in **Fig. 52**, characteristic peaks are pointed out. The polymerization was carried out exactly like the reaction in the previous chapter: 0.500 mL of PDMS_{vinyl}, 0.444 mL of P(DMS-co-MHS), and 0.171 mL of 3-BCEE were mixed in 10 mL Falcon tube. To start the hydrosilylation reaction 0.020 mL of a 0.1 M solution of the mod. Pt-cat was added and the silicone precursors again mixed. The mixture was allowed to react over night. FTIR was conducted on the material as produced, and again after extraction over night in DCM. Extraction was performed to verify, that the 3-BCEE is covalently bonded to the silicone.

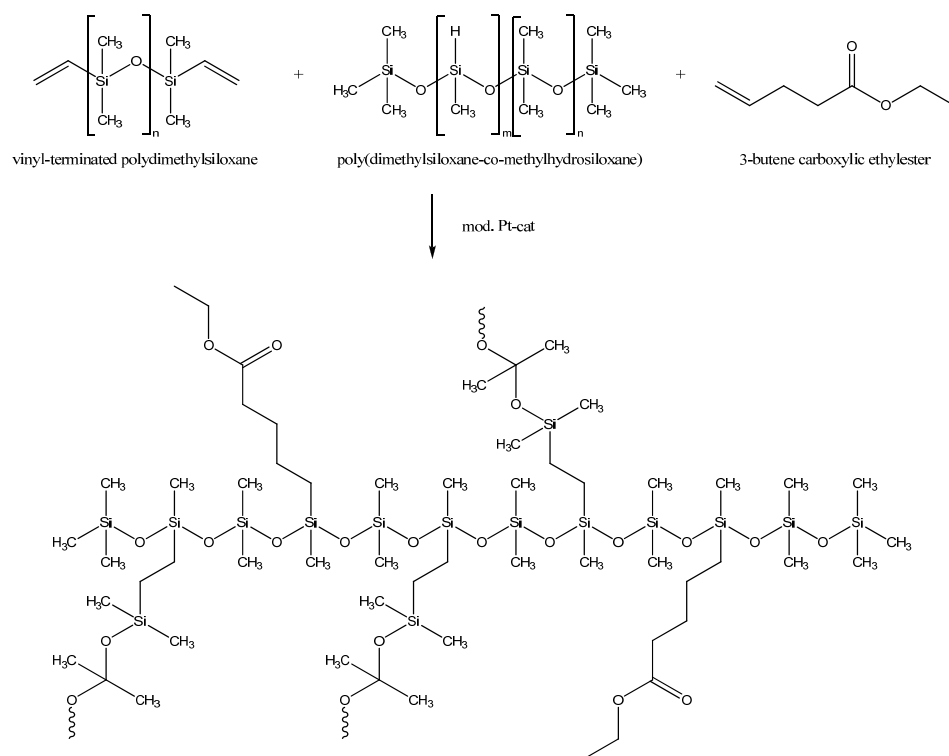


Fig. 51: Polymerization scheme of the production of unmodified silicone from PDMS_{vinyl} and P(DMS-co-MHS), using either the Pt-cat or the mod. Pt-cat.

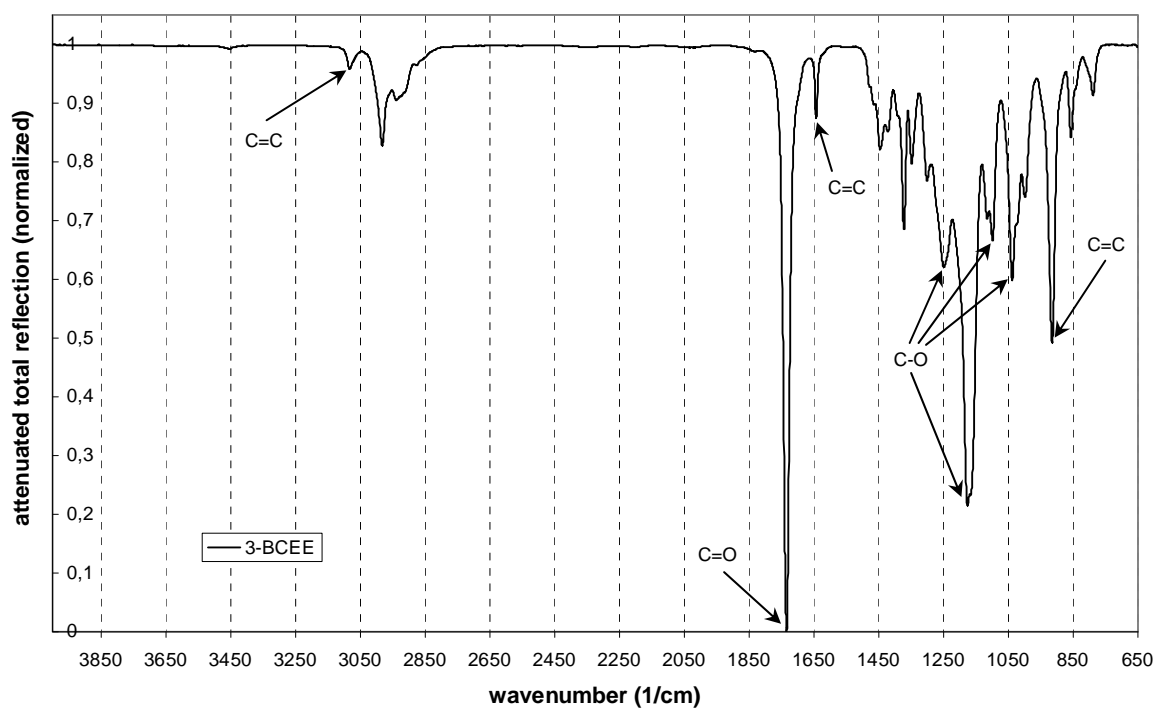


Fig. 52: FTIR spectrum of 3-BCEE, characteristic peaks of functional groups are pointed out.

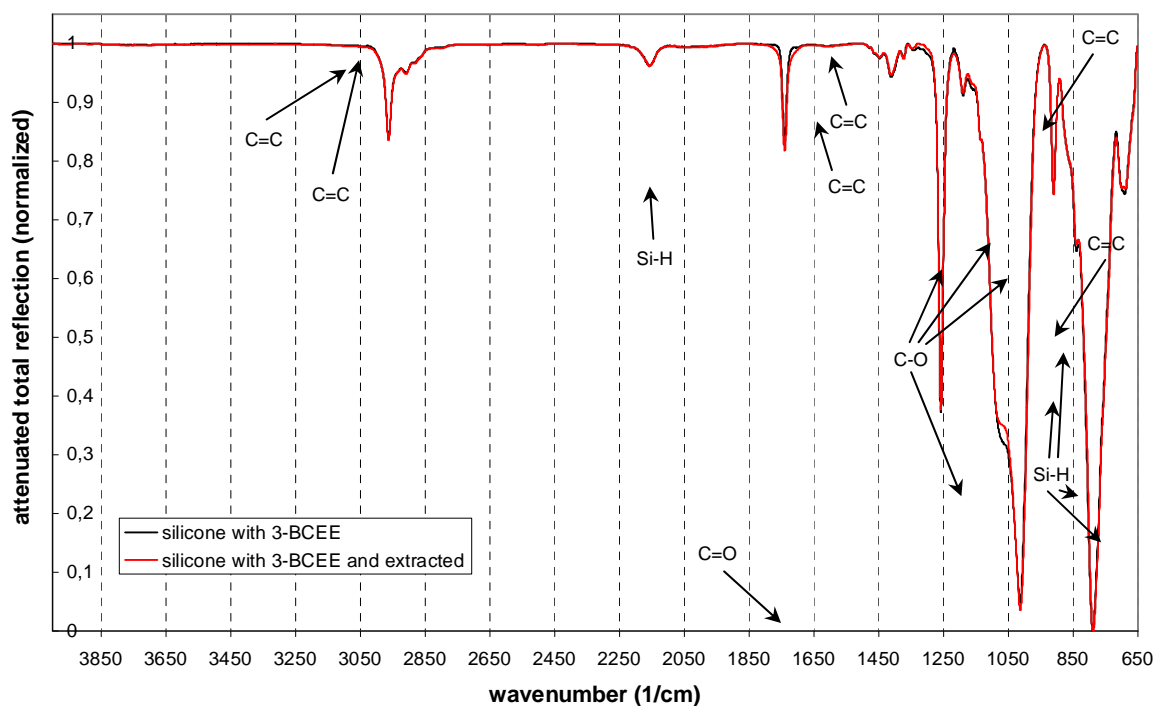


Fig. 53: FTIR spectra of silicone containing 3-BCEE before and after extraction in DCM. After extraction the same amount of 3-BCEE is present in the silicone, it is covalently bonded to the silicone network.

In **Fig. 53** the FTIR spectra of silicone containing 3-BCEE are shown before and after the extraction. The curves are identical, with the characteristic peaks of the 3-BCEE having the same size before and after the extraction. Hence, the material composition remained unchanged. It can be concluded that the 3-BCEE is covalently bonded to the silicone backbone of the polymer network and can not be washed out. The overall conclusions are that silicone can not only be produced in the presence of 3-BCEE, which will be required when adding non-functionalized 3-BCEE carrier, but the 3-BCEE can also be covalently bonded to the silicone backbone during the polymerization process.

9.3 Commercially available silicone precursors - 5 components

In the two previous chapters it was shown that the polymerization of a silicone is possible using both the Pt-cat, as well as the mod. Pt-cat. Furthermore, the resulting polymers are identical. It was also shown that the polymerization using the mod. Pt-cat is not only possible in the presence of 3-BCEE, but covalent bonding of the 3-BCEE to the silicone is feasible during the polymerization process. However, silicone of only very poor mechanical properties was obtained using the components PDMS_{vinyl} and P(DMS-co-MHS). It was so brittle that it could easily be brayed by hand. For the further studies, however, silicone of mechanical properties comparable to those of commercially available silicones is needed. Not only would that allow for mechanical testing of the produced material, e.g. tensile testing, tear testing, and hardness measurement, but it would also allow for the evaluation of the effect each modification has on the mechanical properties. In order to produce a silicone with mechanical properties comparable to those of commercially available silicones, other components than the PDMS_{vinyl} and P(DMS-co-MHS) which were used so far are needed. Below, 5 components are described, which will be used for the production of the 12 series of silicone next to 3-BCEE and the five SME carriers. Three of the five components are supplied courtesy of Momentive Performance Materials GmbH, Leverkusen, Germany. They are precursors of the silicone types named Silopren[®] which is one of the materials that is used for cardiac pacing lead insulation, see **Tab. 1**. The three silicone precursors are part of a set of ingredients, allowing for the production of custom mixtures of silicone. The other two components are standard chemicals.

9.3.1 Silopren[®] U 1 linear vinyl terminated polydimethylsiloxane

Silopren[®] U 1 (U 1) is a linear and vinyl terminated PDMS, see Fig. 54. Its typical viscosity is 1,000 mPa*s and its vinyl-contents 0.13 mmol/g [137, 138, 185]. U 1 is a chemical analog of the PDMS_{vinyl} which has been described numerous times in the previous chapters. It is one of the three compounds used for the silicone type named Silopren[®], which are used as insulation material by the cardiac pacing industry.

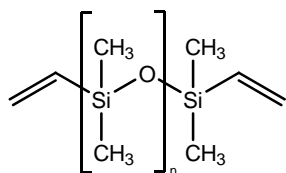


Fig. 54: Linear vinyl terminated polydimethylsiloxane Silopren[®] U 1, a chemical analog of PDMS_{vinyl}.

9.3.2 Silopren[®] U cross-linking agent 430

This component, the Silopren[®] U cross-linking agent 430 (U 430), contains dimethylsiloxane repeating units and methylhydrogensiloxane repeating units, see Fig. 55. Its typical viscosity is 40 mPa*s and its Si-H contents 4.3 mmol/g [139, 140, 186]. It is a chemical analog of the P(DMS-co-MHS) described frequently above. It is meant to be reacted with Silopren[®] U 1 via hydrosilylation using the Pt-cat.

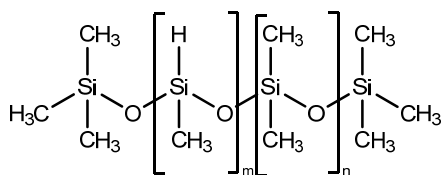


Fig. 55: Silopren[®] U cross-linking agent 430, a chemical analog of P(DMS-co-MHS).

9.3.3 Silopren[®] U base compound P 1300

The third component in the Silopren[®] series and which is supposed to be used in combination with the two previous silicone precursors, is the Silopren[®] U base compound P 1300

(P 1300), see Fig. 56. It is a paste-like mixture of silica which is used as a filler and vinyl-group containing silicones. Its typical viscosity is 1,300 Pa*s and its vinyl-contents 0.04 mmol/g [124, 125, 187]. Due to the filler in the base compound, the hardness of a silicone will increase with increasing proportion of this so-called base compound.

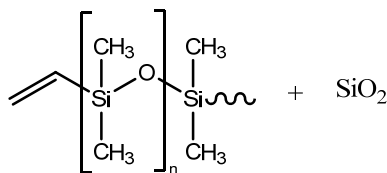


Fig. 56: Silopren[®] U base compound P 1300, a mixture of silica fillers and vinyl-terminated siloxanes.

9.3.4 Fumed silica

Fumed silica (FS) is amorphous silicon dioxide, with a typical particle size of 0.014 μm , and a surface area of $\sim 200 \text{ m}^2/\text{g}$ [120, 121]. In silicone mixtures it is used as filler, contributing to the viscosity of the mixture due to its thixotropic behaviour. Furthermore, it contributes to the hardness of the polymerized silicone.

9.3.5 Polymethylhydrosiloxane

Polymethylhydrosiloxane (PMHS) is a linear silicone oligomer, which contains only methylhydrogen repeating units, see **Fig. 57**. Its typical Si-H contents is 15 mmol/g and its viscosity ranges between 15 and 40 mPa*s. It was chosen to be used, as it contains a higher concentration of hydrosiloxane binding groups per volume unit than P(DMS-co-MHS). The reasoning for this choice was that cross-linker has to be added to the silicone mixture in order to provide enough binding sites for the 3-BCEE. The higher the hydrosiloxane content of the cross-linker is, the less of it needs to be added in terms of volume. Therefore, the overall silicone mixture undergoes less change in the ratio between the filler batch which has a high viscosity, and the other components, which have a rather low viscosity.

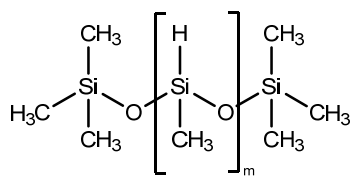


Fig. 57: Polymethylhydrosiloxane, a siloxane oligomer.

9.4 Mixing ratios

All 12 series of silicone were produced using the same procedure: The amount of the components Silopren[®] U 1, Silopren[®] U 430 and PMHS were measured volumetrically using syringes without needle. Silopren[®] P 1300 and fumed silica were measured gravimetrically. Only the mod. Pt-cat was used. The components were mixed using a speed mixer, transferred to a cartouche, and compressed air was used to inject the mixtures into injection moulds where they were polymerized. The molds were made from aluminum and steel, the shape of the specimen was that for tensile testing, tear testing, and hardness measurement. Their exact shapes will be described in the chapters for mechanical properties below. Curing of the silicones was allowed in the molds for 15 minutes at 120-160°C, where the temperature variation was due to heat uptake of the molds. The samples were removed from the molds and tempered for 4 hours at 200°C in normal air atmosphere. The tempering step is the standard procedure for silicone types like Silopren[®]. All samples were then allowed to rest for at least 16 hours at room temperature prior to any further testing.

As stated at the beginning of **chapter 9 Production of 12 series of silicone** the results from mechanical testing of series # 1-3 will be used to determine optimal composition of the remaining series of silicone. Series # 4-7 will contain 3-BCEE covalently bonded to the siloxane backbone, and series # 8-12 will contain the SME carriers.

9.4.1 Series # 1: Effect of ratio between hydrosiloxane and vinyl

The first series of silicone was a shot in the dark and the ratio between the filler batch P 1300 and the linear siloxane U 1 chosen randomly, and kept constant. Three mixtures were produced, and the amount of cross-linker U 430 varied so that the ratios between hy-

drogensiloxane and vinyl were 1:1, 2:1, and 3:1. Two mixtures, Si 008-1 and Si 008-3, were polymerized with the mod. Pt-cat dissolved in xylene, and one mixture, Si 008-2, was prepared adding the mod. Pt-cat directly to the mixture. **Tab. 6** shows the amounts used.

mixture	U 1 (mL)	U 430 (mL)	P 1300 (g)	ratio Si-H / vinyl
Si 008-1	4.50	0.35	10.5	1.04
Si 008-2	4.50	0.70	10.5	2.07
Si 008-3	4.50	1.05	10.5	3.11

Tab. 6: Series # 1 of silicone, the amounts of U 1 and P 1300 were chosen randomly and kept constant, while the ratio between Si-H and vinyl was varied between 1:1 and 3:1.

The first observation in this series was that all samples contained air bubbles. This is caused by the fact that the mixtures were of low viscosity, and air bubbles which get into the silicone precursors during the mixing process were not squeezed out during the process of injection molding. This is usually the case when mixtures of high viscosity are injected into molds.

The second important observation was that only the mixture Si 008-2 did not show any coloration, but remained colorless even after tempering at 200°C. This is the mixture where the mod. was Pt-cat directly added to the mixture. It is noteworthy, though, that in this mixture small brown spots were found. In contrast, mixtures containing the mod. Pt-cat in xylene turned evenly yellowish during tempering. Silopren[®] usually stays colorless, so the coloration can be attributed to the xylene which was used to dissolve the mod. Pt-cat, and the small brown spots are caused by catalyst which has not dissolved in the silicone precursors due to the absence of xylene or any other proper solvent.

In conclusion, for the next four series of silicone, namely series # 2-5, the mod Pt-cat was not dissolved in xylene, but admixed to the component U 1. A stock solution of U 1 with the mod. Pt-cat was prepared, and it could be seen that the catalyst did not fully dissolve in it.

9.4.2 Series # 2: Effect of ratio between hydrogensiloxane and vinyl - repeated

In order to increase the mixtures' viscosity and thereby produce a silicone mixture without bubbles, series # 1 was repeated with a higher amount of the component P 1300 and a lower amount of the component U 1 as compared to series # 1. Again the ratio between the two components was kept constant. The amount of the cross-linker U 430 used was again varied, this time using ratios of hydrogensiloxane to vinyl between 1 and 4. **Tab. 7** shows the quantities used.

mixture	U 1 (mL)	U 430 (mL)	P 1300 (g)	ratio Si-H / vinyl
Si 006-1	0.50	0.30	14.5	1.02
Si 006-2	0.50	0.60	14.5	2.05
Si 006-3	0.50	0.90	14.5	3.07
Si 006-4	0.50	1.20	14.5	4.09

Tab. 7: Series # 2 of silicone, the amount of U 1 was decreased and the amount of P 1300 was increased as compared to series # 1. The ratio between Si-H and vinyl was varied between 1:1 and 4:1.

As a result, all samples could be produced almost without bubbles, and no coloration occurred during tempering. Some samples contained brown spots. In the samples of mixture Si 006-2, where the component U 1 was drawn deliberately from the top of the stock solution containing the mod. Pt-cat, almost no brown spot appeared. This seems logical, as the non-dissolved fractions of the mod. Pt-cat were visible and found mainly at the bottom of the container of the stock solution.

Tensile testing, which will be presented in detail below in **chapter 10 Mechanical properties of the 12 series of silicone** showed that the ratio of hydrogensiloxane to vinyl of ~2.5 should be preferred. This is due to the fact that a good compromise between Young's Modulus and elongation at break can be achieved that way. This will come to play starting with series # 6.

For the next series of silicone it was decided to continue with a ratio between Si-H and vinyl of 1:1, even if a higher ratio between Si-H and vinyl may lead to higher results in tensile testing. Using small quantities of the cross-linker U 430 and thereby keeping the viscosity high was regarded more important than improving the mechanical properties at this stage of this work. Producing samples without bubbles was of greater importance than fine tuning the polymer mixture.

9.4.3 Series # 3: Effect of ratio between base compound and linear siloxane

In this third series of silicones the mixtures were prepared starting with the composition of mixture Si 006-1 from series # 2. The amount of P 1300 was reduced, and the amount of the linear siloxane U 1 increased stepwise. The amount of the cross-linker U 430 was only slightly adjusted in order to keep the ratio between Si-H and vinyl near 1:1, see **Tab. 8**.

mixture	U 1 (mL)	U 430 (mL)	P 1300 (g)	ratio Si-H / vinyl
Si 001	3.00	0.35	12.0	1.09
Si 002	2.50	0.34	12.5	1.08
Si 003	2.00	0.33	13.0	1.07
Si 004	1.50	0.32	13.5	1.05
Si 005	1.00	0.31	14.0	1.04
Si 006-1	0.50	0.30	14.5	1.02

Tab. 8: Series # 3 of silicone, starting from mixture Si 006-1 the amount of U 1 was increased and the amount of P 1300 was decreased step by step. The ratio between Si-H and vinyl was kept near 1:1 by adjusting the amount of cross-linker U 430 accordingly.

During the production of this series it could be observed that with increased amount of the linear siloxane U 1 the viscosity of the reaction mixture was decreased, and with that the amount of air bubbles in the samples increased. Again, some samples showed brown spots. As the ratio between P 1300 and U 1 came closer to 4:1, the reaction mixture became so

non-viscous that injection molding without producing air bubbles became impossible with the equipment at hand.

Results from tensile testing, which will be presented in detail below in **chapter 10 Mechanical properties of the 12 series of silicone** showed, that the ratio of P 1300 to U 1 of about 15:1 leads to maximal results. This is true for Young's Modulus, elongation at break, and tensile strength. Starting with series # 6 this will be made use of.

9.4.4 Series # 4: Effect of amount of 3-BCEE

Series # 4 is the first attempt to injection mold silicones with 3-BCEE being present in the mixture. The amount of 3-BCEE was varied between 2%_{wt} and 8%_{wt}. **Tab. 9** shows the ratios of the components. PMHS was added to the mixture in order to provide sufficient hydrosiloxane binding sites for the 3-BCEE. The amounts of the components U 1, U 430, and P 1300 are the same as in the composition of Si 006-1 of series # 2, but here they were kept constant. The ratio between Si-H and vinyl was set to ~1.2:1 and adjusted by adding more or less PMHS.

Three striking phenomena were observed with increasing contents of 3-BCEE: First of all, a yellowish coloration, secondly the mixtures became more non-viscous which allowed for the amount of bubbles in the injection molded samples to increase, and thirdly the samples started to stick to the polished steel tray which was used as a sample holder during tempering. The samples of mixtures Si 009 and Si 010 could not be removed from the sample holder without being damaged. Such a tackiness of silicones is usually caused by incomplete polymerization. The coloration can be attributed to the presence of the 3-BCEE, since the mod. Pt-cat was added by using the stock solution of U 1 which contained the catalyst.

mixture	3-BCCE (mL)	U 1 (mL)	U 430 (mL)	P 1300 (g)	PMHS (mL)	ratio Si-H / vinyl	3-BCCE (% _{wt})
Si 007	0.40	0.50	0.30	14.5	0.25	1.21	2.3
Si 008	0.80	0.50	0.30	14.5	0.50	1.24	4.4
Si 009	1.20	0.50	0.30	14.5	0.75	1.26	6.4
Si 010	1.60	0.50	0.30	14.5	1.00	1.26	8.2

Tab. 9: Series # 4 of silicone, the first series containing 3-BCCE. The amounts of the components U 1, U 430, and P 1300 are the same as in the mixture Si 006-1. The 3-BCCE contents ranges between 2.3%_{wt} and 8.2%_{wt}. PMHS was added to provide hydrogensiloxane binding sites for the 3-BCCE. The ratio between Si-H and vinyl was set to 1.2:1.

The testing of the tensile properties of the mixtures Si 009 and Si 010 was not possible, since the samples got damaged when they were removed from the sample holder which was used for tempering. It was decided to repeat this series with smaller steps when increasing the amount of the 3-BCCE contents.

9.4.5 Series # 5: Effect of amount of 3-BCCE - repeated

Series # 5 is a modified version of series # 4: The amount of 3-BCCE was increased in smaller steps, the ratio between Si-H and vinyl was reduced to ~1.1:1, and the mixtures were allowed to rest prior to injection molding. This was done because it is known that polymeric silicone precursors which are thoroughly mixed have a lower viscosity than those, which have been allowed to rest after the mixing process. In order to avoid sticking of the samples to the sample holder during tempering, the polished steel tray was greased with a thin layer of soap as a release agent. **Tab. 10** shows the compositions of the mixtures that were prepared.

mixture	3-BCEE (mL)	U 1 (mL)	U 430 (mL)	P 1300 (g)	PMHS (mL)	ratio Si-H / vinyl	3-BCEE (% _{wt})
Si 011	0.18	0.50	0.30	14.5	0.10	1.09	1.1
Si 012	0.36	0.50	0.30	14.5	0.20	1.11	2.1
Si 013	0.54	0.50	0.30	14.5	0.30	1.12	3.0
Si 014	0.72	0.50	0.30	14.5	0.40	1.12	4.0
Si 015	0.90	0.50	0.30	14.5	0.50	1.13	4.9
Si 016	1.08	0.50	0.30	14.5	0.60	1.13	5.8
Si 017	1.26	0.50	0.30	14.5	0.70	1.13	6.7
Si 018	1.44	0.50	0.30	14.5	0.80	1.13	7.5
Si 019	1.62	0.50	0.30	14.5	0.90	1.14	8.3

Tab. 10: Series # 5 of silicone, a modified version of series # 4. The amount of 3-BCEE was increased in smaller steps, and the ratio between Si-H and vinyl was reduced to 1.1:1.

Allowing the mixtures to rest after the mixing process and prior to injection molding helped to reduce but could not prevent the air bubbles in all cases. The coloration of the samples was as striking as in series # 4, and increased with increasing contents of 3-BCEE. As in series # 4 the coloration can be attributed to the presence of the 3-BCEE, since the mod. Pt-cat was added by using the stock solution of U 1 which contained the catalyst. Due to the soap that was used on the polished steel tray as a releasing agent, the samples stuck less to the tray, but still had to be removed very carefully, and sometimes needed to be cut off the tray with a razor blade.

FTIR was conducted to verify that the 3-BCEE which was admixed to the silicone precursors is present in the samples after tempering. The result of the FTIR measurement is shown in **Fig. 58**. It can be seen that there are only small peaks of the hydroxylic group of the 3-BCEE at 1740 cm^{-1} . This peak is shown enlarged in **Fig. 59**. Furthermore, the peaks do not correlate directly in all cases to the amount of admixed 3-BCEE. During the production of the silicone samples of this series a strong smell of 3-BCEE was noticed, especially

during tempering of the samples. It is safe to assume that a large part of the 3-BCEE has evaporated. This would suggest that some of the 3-BCEE was not covalently bonded to the silicone backbone during the production process as expected. One way this could happen is if the hydrosilylation reaction between two siloxane species were faster than between 3-BCEE and a hydride-terminated siloxane species. This would allow for the formation of a silicone network, in which the 3-BCEE is present but yet unbound. During tempering it could then evaporate. The difference in reactivity between two siloxane species and 3-BCEE and a siloxane species is, however, an assumption and was not verified. Furthermore, the formation of a siloxane bond is possible between two hydride-terminated siloxane species, using oxygen which is present in the material or later in the surrounding air during tempering. This would of course support the evaporation of the 3-BCEE, since the hydride functional groups would be consumed. In **Fig. 59** it can also be seen that the peaks of the five samples with the highest content of 3-BCEE can be found in the same range. This may be a sign of a saturation of the silicone with 3-BCEE.

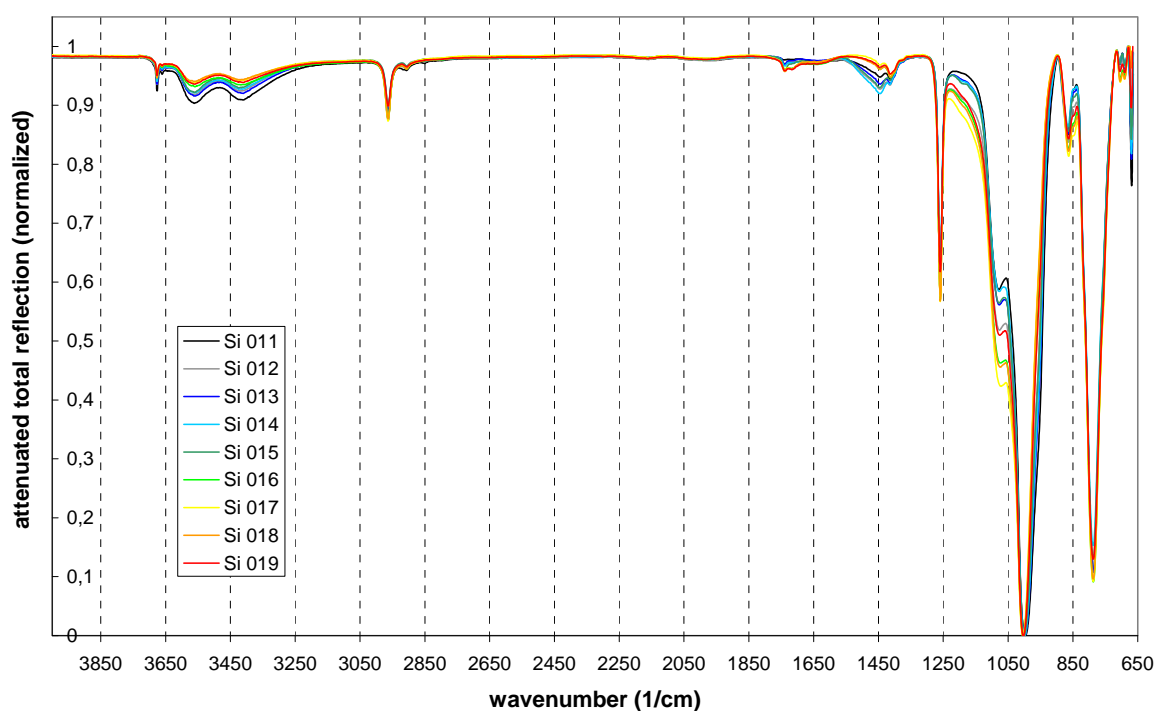


Fig. 58: FTIR of series #5, the peak of the carboxylic group at 1740 cm^{-1} is little pronounced and does not correlate directly to the amount of 3-BCEE admixed to the silicone precursors.

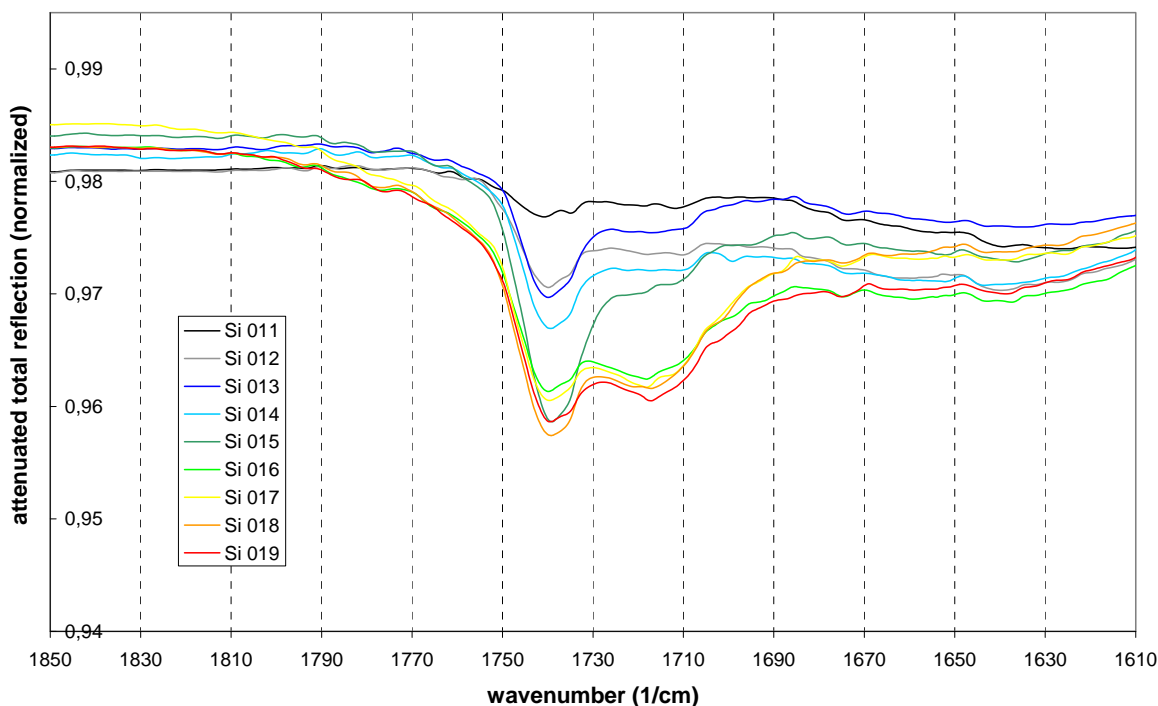


Fig. 59: FTIR of series # 5, the carboxylic peak at 1740 cm^{-1} enlarged, the signal does not correlate directly to the amount of 3-BCEE in the silicone mixtures, and the peaks of the five samples with the highest content of 3-BCEE can be found in the same range which may be a sign of a saturation of the silicone with 3-BCEE.

9.4.6 Series # 6 and series # 7: Using fumed silica and U 430 instead of PMHS

In the two silicone series # 6 and series # 7 a different approach was made in the attempt to avoid the presence of air bubbles in the samples. The idea was to increase the viscosity of the mixture by adding fumed silica as filler to the silicone precursors. Furthermore, when fumed silica is used and does increase the viscosity of the mixture, the need for PMHS becomes obsolete, and the original Silopren[®] cross-linker U 430 can be used. PMHS was used only because it contains more hydride-functional groups per volume unit than U 430, and the idea was to reduce the volume of silicone precursors as much as possible.

In **Tab. 11** and **Tab. 12** the compositions of series # 6 and # 7 are given. The ratio between P 1300 and U 1 is kept constant at 15:1 in both series. By adjusting the amount of U 430 in series # 6 the ratio between Si-H and vinyl is kept constant at 2.50. These two values were identified in series # 2 and # 3 as optimal for producing silicones with high tensile proper-

ties. The amount of 3-BCEE ranges from 0.00%_{wt} to 3.01%_{wt} in series # 6, which is lower than in the previous series. Series # 7 does not contain any 3-BCEE, and therefore less fumed silica was used. The absence of 3-BCEE changes the ratio between Si-H and vinyl as can be seen in the last column of **Tab. 12**. No 3-BCEE was added to series # 7 in order to evaluate if the admixing of the 3-BCEE to the silicone has a significant impact on the mechanical properties of the resulting material. Results of mechanical testing will be discussed in **chapter 10 Mechanical properties of the 12 series of silicone**. It is noteworthy that starting with these two series the mod. Pt-cat was used again as a 0.1 M solution in xylene. The reason is that the catalyst was thereby spread evenly throughout the mixture, as it dissolves well in xylene.

mixture	3-BCEE (mL)	U 1 (mL)	U 430 (mL)	P 1300 (g)	fumed silica (g)	3-BCEE (% _{wt})
Si 020	-	2.70	2.15	40.5	0.26	-
Si 021	0.51	2.54	4.18	38.1	0.56	1.01
Si 022	1.01	2.38	6.17	35.7	0.86	2.00
Si 023	1.53	2.22	8.25	33.3	1.17	3.01

Tab. 11: Series # 6 of silicone, in conclusion from previous series the ratio between P 1300 and U 1 is kept constant at 15:1, and the ratio between Si-H and vinyl is kept constant at 2.50.

mixture	3-BCEE (mL)	U 1 (mL)	U 430 (mL)	P 1300 (g)	fumed silica (g)	3-BCEE (% _{wt})	ratio Si-H / vinyl
Si 020	-	2.70	2.15	40.5	0.26	-	2.50
Si 024	-	2.54	4.18	38.1	0.50	-	5.18
Si 025	-	2.38	6.17	35.7	0.74	-	8.16
Si 026	-	2.22	8.25	33.3	0.99	-	11.68

Tab. 12: Series # 7 of silicone: This series is analogous to series # 6 but does not contain any 3-BCEE, which in consequence changes the ratio between Si-H and vinyl. The amount of fumed silica was reduced as compared to series # 6.

FTIR was conducted on series # 6 in order to verify the presence of 3-BCEE in the modified silicone series, see **Fig. 60** and **Fig. 61**. No 3-BCEE was added to the mixtures of series # 7. It was measured for comparison, and as expected no samples show a signal. In series # 6 the height of the peaks for the carboxylic group at 1740 cm^{-1} is very low, which was already the case in series # 5. Again it can be concluded that there is only little 3-BCEE covalently bonded to the silicone backbone, and that large parts of the 3-BCEE must have evaporated during the tempering of the samples. Furthermore, the coloration of the samples of series # 6 increases with increasing contents of 3-BCEE, while the samples of series # 7 remained colorless. This allows for the conclusion that not the presence of xylene alone in the silicone mixture causes any significant coloration, but the combined presence of xylene and 3-BCEE.

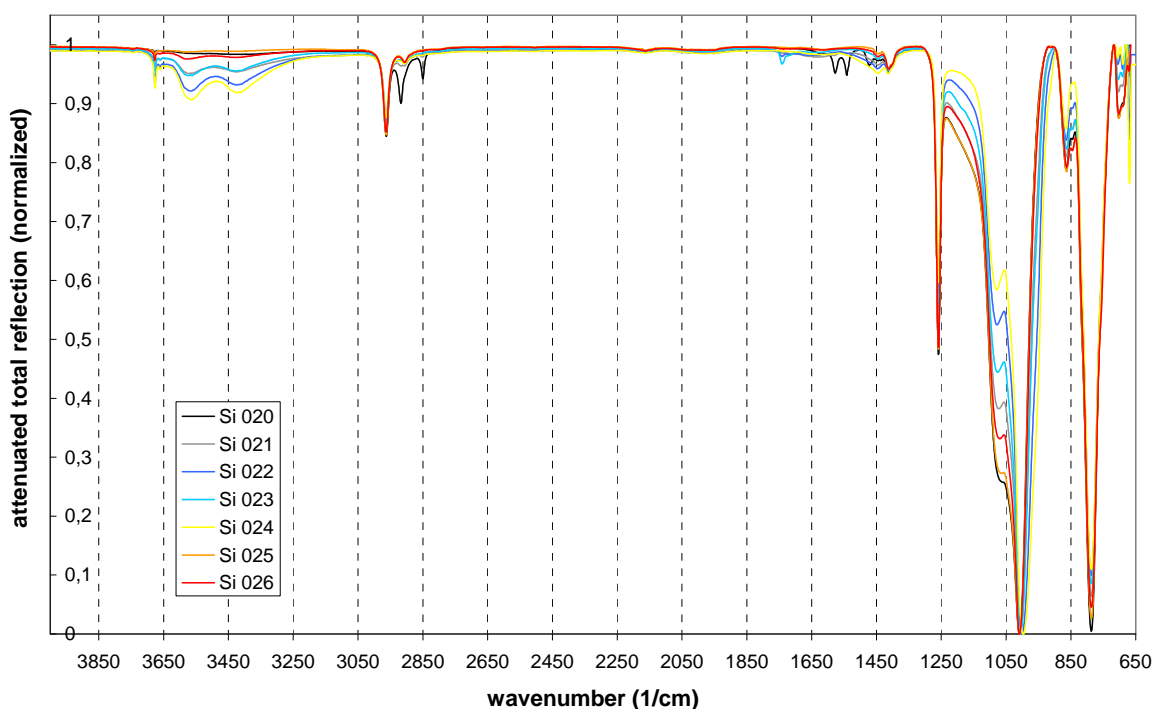


Fig. 60: FTIR of samples of series # 6 and series # 7 after production: For series # 6 the peaks of the carboxylic group at 1740 cm^{-1} are less pronounced than expected. It is again concluded that large parts of the 3-BCEE evaporated during tempering.

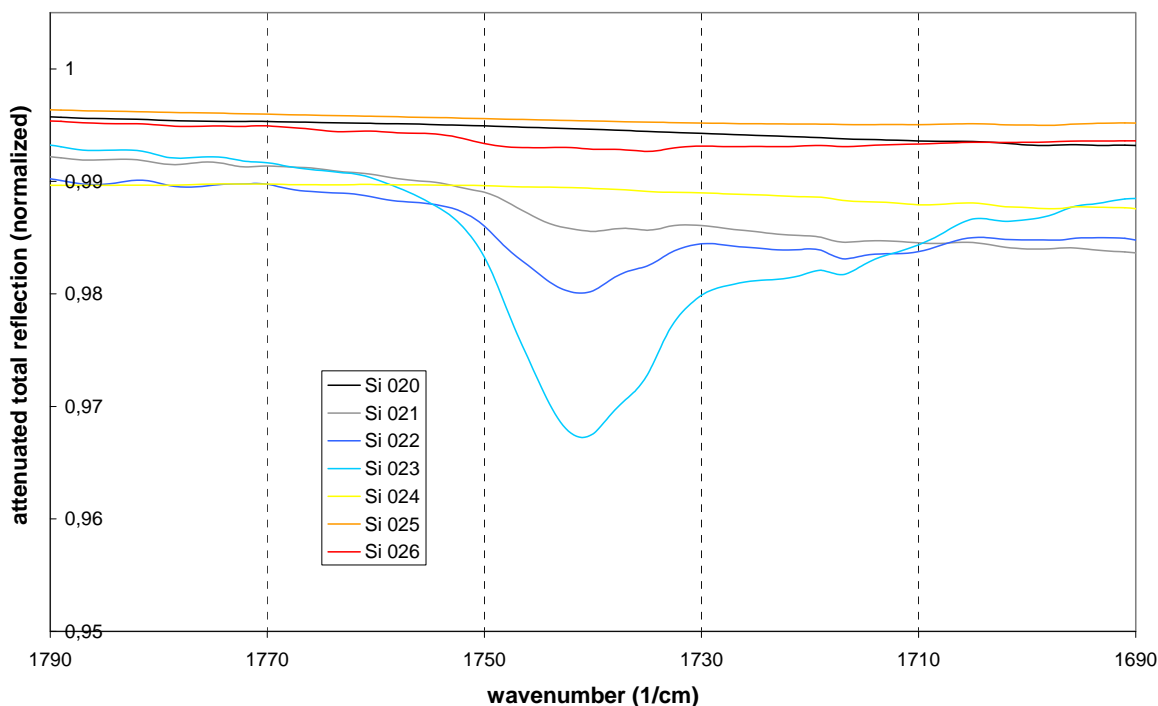


Fig. 61: FTIR of samples of series # 6 and series # 7 after production, the carboxylic peak at 1740 cm^{-1} enlarged: No 3-BCEE was added to series # 7, and accordingly no samples show a signal. For series # 6 the peaks are less pronounced than expected and it is concluded that large parts of the 3-BCEE evaporated during tempering.

9.4.7 Series # 8: Using the 3-BCEE carrier of highest molecular weight

The series # 8 of silicone is different from the previous series in as much, as 3-BCEE was not mixed with the silicone precursors in order to be bonded to the silicone backbone, but a non-functionalized 3-BCEE carrier was admixed to the silicone precursors. This carrier is described in **chapter 8.2.3 Non-functionalized SME carrier**. The composition of the silicone mixture is analogous to that of series # 6: The ratio between Si-H and vinyl was kept constant at 2.50, the ratio between P 1300 and U 1 was kept constant at 15:1, but no fumed silica was added. The amount of 3-BCEE which was present due to the admixing of the carrier ranged between $0.00\%_{\text{wt}}$ and $4.66\%_{\text{wt}}$ and is given in the last column of **Tab. 13**. The mod. Pt-cat was used as 0.1 M solution in xylene.

mixture	3-BCEE carrier (mL)	U 1 (mL)	U 430 (mL)	P 1300 (g)	3-BCEE (% _{wt})
Si 027	-	2.70	2.15	40.5	-
Si 028	0.50	2.30	1.83	34.5	0.28
Si 029	1.00	2.27	1.81	34.0	0.57
Si 030	1.50	2.23	1.78	33.5	0.85
Si 031	2.00	2.33	1.86	35.0	1.07
Si 032	2.50	2.30	1.83	34.5	1.34
Si 033	3.00	2.27	1.81	34.0	1.61
Si 034	3.50	2.23	1.78	33.5	1.89
Si 035	4.00	2.20	1.75	33.0	2.16
Si 036	4.50	2.17	1.73	32.5	2.43
Si 037	5.50	2.10	1.67	31.5	2.99
Si 038	7.00	2.00	1.59	30.0	3.82
Si 039	8.50	1.90	1.51	28.5	4.66

Tab. 13: Series # 8 of silicone: This series is an analogue of series # 6 but does not contain any fumed silica. The ratio between Si-H and vinyl was kept constant at 2.50, the ratio between P 1300 and U 1 was kept constant at 15:1, and the amount of 3-BCEE was varied between 0.00%_{wt} and 4.66%_{wt} by adding the according amount of 3-BCEE carrier.

During the production of the samples an unexpected observation was made: The viscosity of the mixture of the silicone precursors increased drastically with increasing contents of the 3-BCEE carrier. This caused the mixing process to become very difficult, as the heat production of the increasingly viscous paste in the speed mixer was large enough to start the polymerization process. Due to this, the duration of the mixing process had to be reduced with increasing contents of the 3-BCEE carrier. In consequence, the silicone mix-

tures of series # 8 have not undergone the same mixing duration, and some may be well mixed, whereas others may be not. This can cause inhomogeneity and may have an adverse effect on the material properties, but can also result in differences between samples of the same silicone series. The increasing viscosity also caused the injection process to become difficult: The commonly supplied pressure of 8 bar did not suffice any longer to inject the mixtures from the cartouches to the moulds. Special equipment and up to 40 bar were needed for the injection of the mixtures of this silicone series.

Further observations were made: The silicone samples did not stick to the injection mould as some of the previous series did. This was interpreted as a sign for complete polymerization of the mixtures. The final observation was that the initially colorless samples turned yellowish during the tempering process. The degree of coloration increased with increasing contents of 3-BC EE carrier, and it is attributed to both the 3-BC EE but also the xylene in the catalyst solution.

Samples of series # 8 were checked by FTIR to verify the presence of the 3-BC EE in the material. **Fig. 62** shows the complete spectrum as recorded, and **Fig. 63** shows an enlarged range of the carboxylic peak. It can be observed that the signal of the carboxylic peak is more pronounced than in the previously produced series containing 3-BC EE. Furthermore, the signal increases with increasing contents of admixed 3-BC EE carrier.

Testing if more 3-BC EE is present at the material's surface than within the bulk was conducted by cutting the mixture Si 039 which has the highest content of 3-BC EE carrier in half with a razor blade, and testing it again. The FTIR measurement was repeated on the bulk material, and is also displayed in **Fig. 63**. The height of the carboxylic peak is significantly lower within the bulk than at the material's surface. This allows for the conclusion that more 3-BC EE is present in the surface near regions than within the bulk. This is the first time within this research work that reason is given to believe that 3-BC EE may act as an SME and travel to the material's surface.

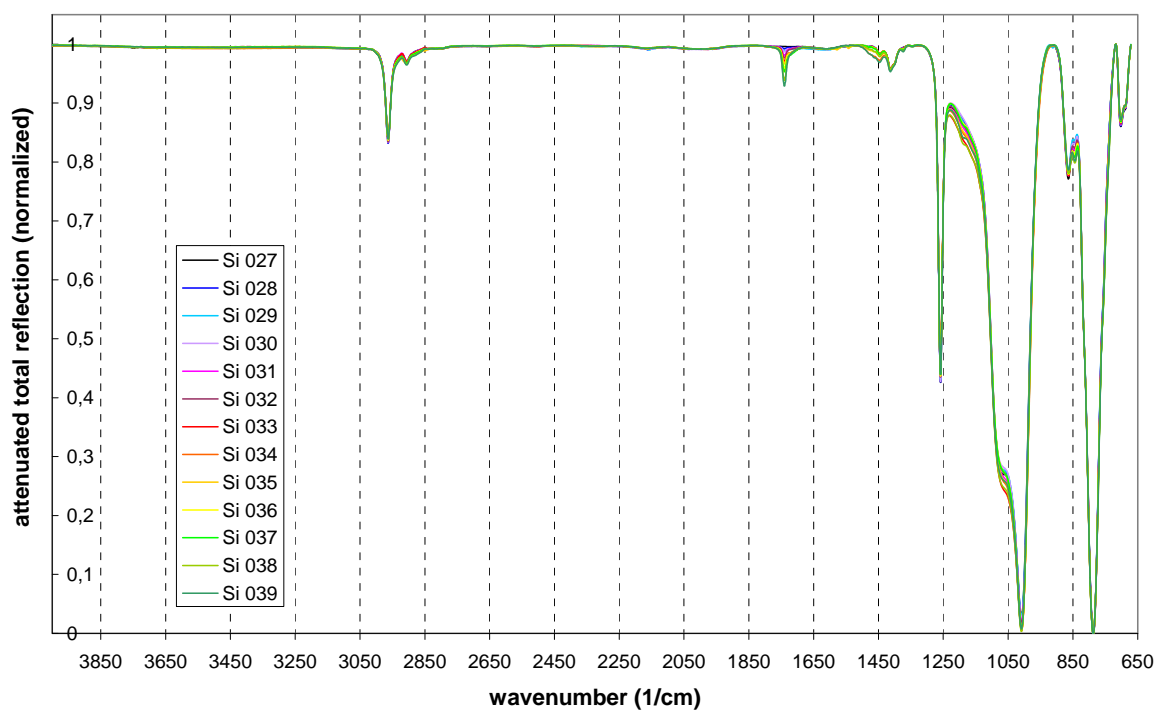


Fig. 62: FTIR of samples of series # 8 after production: The peaks of the carboxylic group at 1740 cm^{-1} are more pronounced than for the previously produced series.

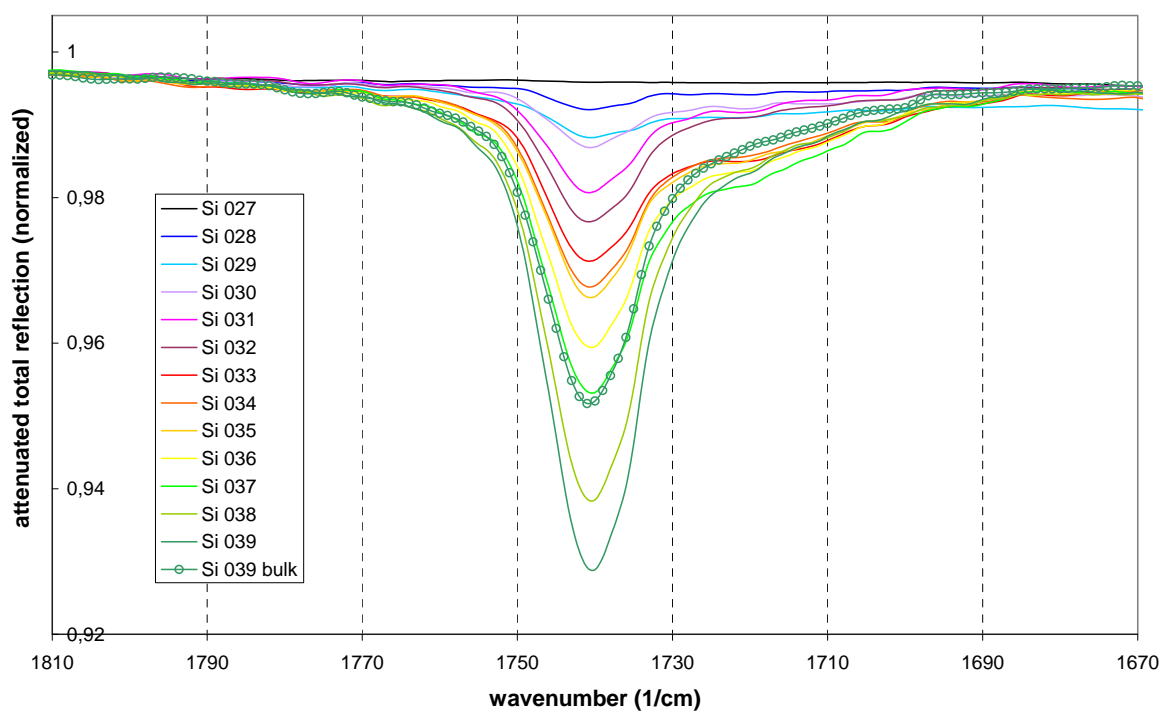


Fig. 63: FTIR spectrum of the carboxylic peak of series # 8 enlarged: The peaks increase with increased amount of 3-BCEE carrier, and the 3-BCEE contents within the bulk is lower than at the material's surface.

9.4.8 Series # 9: Using the 3-BCEE carrier of lowest molecular weight

Series # 9 of silicone, see **Tab. 14**, is an analogue of series # 8: The ratio between Si-H and vinyl was kept constant at 2.50, the ratio between P 1300 and U 1 was kept constant at 15:1, and the mod. Pt-cat was used as 0.1 M solution in xylene. In this series the 3-BCEE carrier with the lowest molecular weight was used and admixed to the silicone precursors. The amount of 3-BCEE was thereby varied between 0.00%_{wt} and 22.0%_{wt}.

mixture	3-BCEE carrier (mL)	U 1 (mL)	U 430 (mL)	P 1300 (g)	3-BCEE (% _{wt})
Si 040	-	2.70	2.15	40.5	-
Si 041	1.00	0.333	0.265	5.00	7.07
Si 042	2.00	0.333	0.265	5.00	12.3
Si 043	3.00	0.333	0.265	5.00	16.3
Si 044	4.00	0.333	0.265	5.00	19.4
Si 045	5.00	0.333	0.265	5.00	22.0

Tab. 14: Series # 9 of silicone: Analogous to series # 8 the ratio between Si-H and vinyl was kept constant at 2.50, and the ratio between P 1300 and U 1 was kept constant at 15:1. The amount of 3-BCEE was varied between 0.00%_{wt} and 22.0%_{wt} by adding the according amount of low molecular weight 3-BCEE carrier.

The mixing process of this series was not as problematic as that for series # 8. It can be assumed that the low molecular weight of the carrier which was used in this series is advantageous. However, in mixtures containing a high amount of the low molecular weight carrier air bubbles could not be prevented. During the production of this series it was observed that the samples were increasingly yellowish with increasing contents of the 3-BCEE carrier. This was attributed to both the presence of xylene and 3-BCEE.

FTIR was conducted on the samples and the carboxylic peak at 1740 cm⁻¹ was found to be well pronounced, see **Fig. 64**. However, the signal intensities of the peaks did not directly

correlate the amount of 3-BCEE carrier which was added to the mixtures, as can be seen in **Fig. 65**. Inhomogeneity caused by the insufficient mixing in the speed mixer may be the cause.

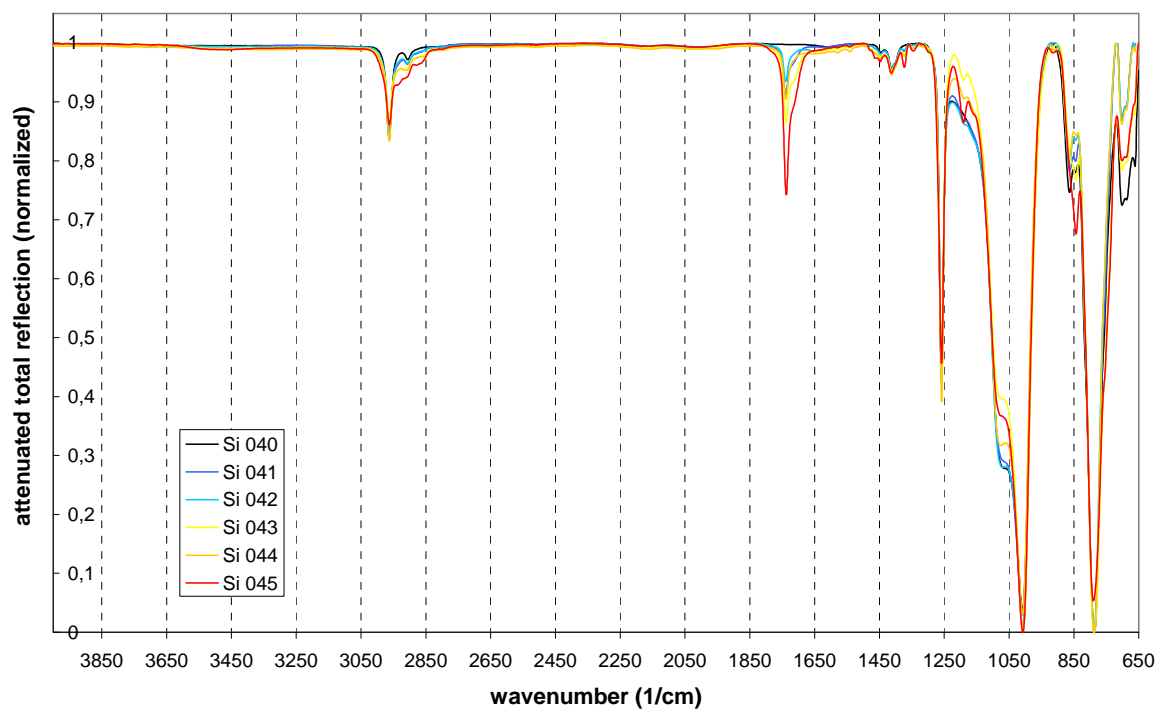


Fig. 64: FTIR of samples of series # 9 after production: The peaks of the carboxylic group at 1740 cm^{-1} are well pronounced.

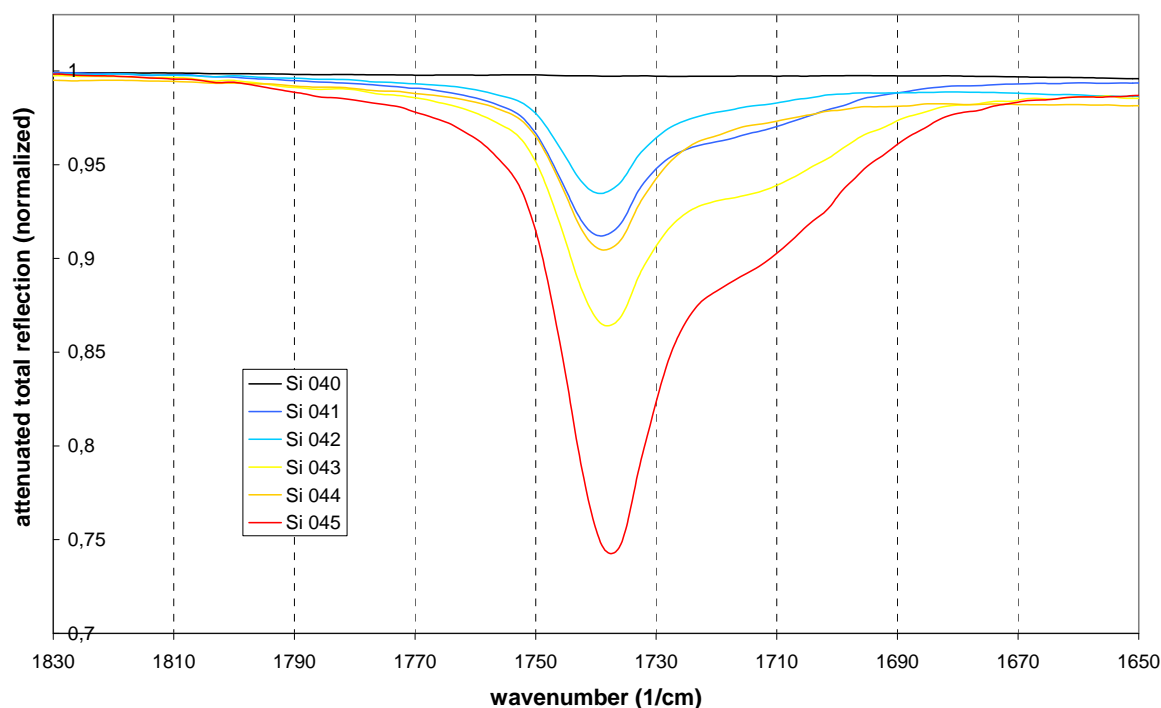


Fig. 65: FTIR spectrum of the carboxylic peak of series # 9 enlarged: The peak intensity does not directly correlate in all cases to the amount of 3-BCEE carrier which was admixed, inhomogeneity within the material from insufficient mixing are suspected to be the cause.

9.4.9 Series # 10: Using the DMAM carrier of lowest molecular weight

This series is again an analogue of series # 8, with the ratio between Si-H and vinyl kept constant at 2.50, the ratio between P 1300 and U 1 kept constant at 15:1, and the mod. Pt-cat used as 0.1 M solution in xylene. Here, the DMAM carrier with the lowest molecular weight was used and admixed to the silicone precursors, the amount of DMAM was thereby varied between 0.00%_{wt} and 22.5%_{wt}. **Tab. 15** below shows the compositions of the mixtures. Please note that the mixture Si 040 is the same as in series # 9.

As in series # 9 the coloration of the samples increased with increasing contents of DMAM carrier, which is assumed to be caused by DMAM and xylene. Furthermore, the samples with high contents of DMAM carrier exhibited a seemingly porous structure. Pictures of this will be shown later in the course of this research in the **chapter 11 Light microscopy**. FTIR analysis, which can be seen below in **Fig. 66** and enlarged in **Fig. 67**, showed that

the carboxylic peaks at 1710 cm^{-1} and at 1740 cm^{-1} are well pronounced. Furthermore, the peak intensity increases with increasing amount of admixed DMAM carrier.

mixture	DMAM carrier (mL)	U 1 (mL)	U 430 (mL)	P 1300 (g)	DMAM (% _{wt})
Si 040	-	2.70	2.15	40.5	-
Si 046	0.40	0.133	0.106	2.00	8.18
Si 047	0.80	0.133	0.106	2.00	14.2
Si 048	1.20	0.133	0.106	2.00	18.8
Si 049	1.60	0.133	0.106	2.00	22.5

Tab. 15: Series # 10 of silicone: Analogous to series # 8 the ratio between Si-H and vinyl was kept constant at 2.50, and the ratio between P 1300 and U 1 was kept constant at 15:1. The amount of DMAM was varied between 0.00%_{wt} and 22.5%_{wt} by adding the according amount of low molecular weight DMAM carrier.

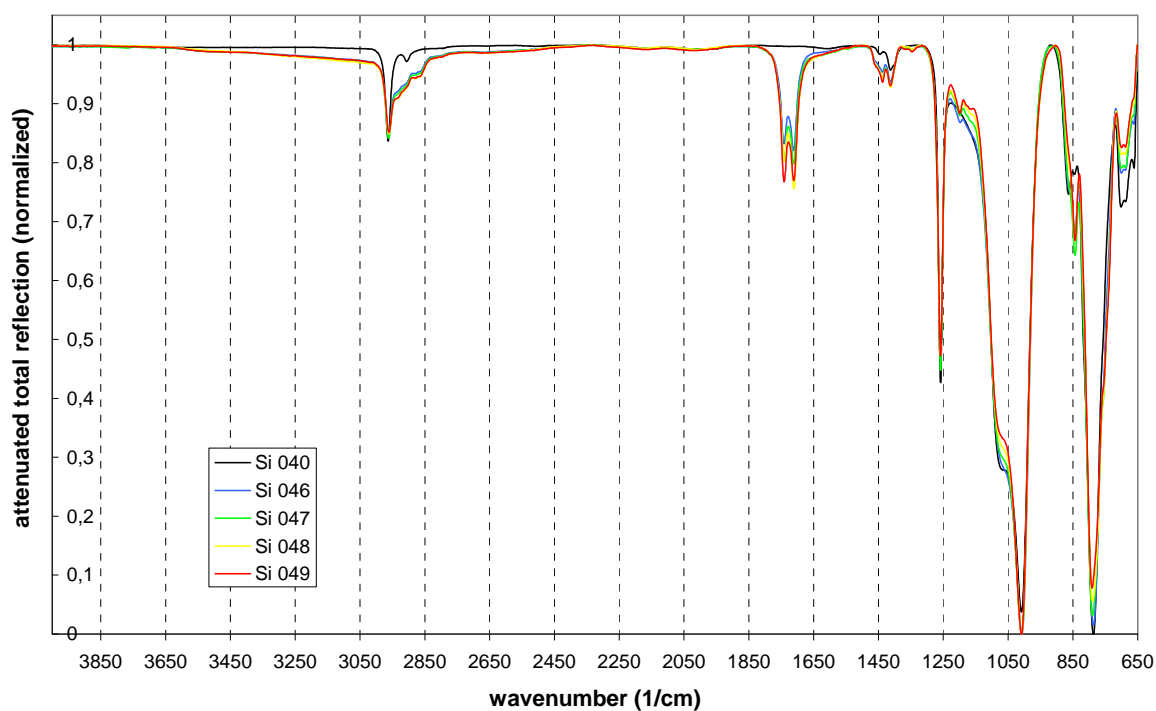


Fig. 66: FTIR of samples of series # 10 after production: The peaks of the carboxylic group at 1710 cm^{-1} and at 1740 cm^{-1} are well pronounced.

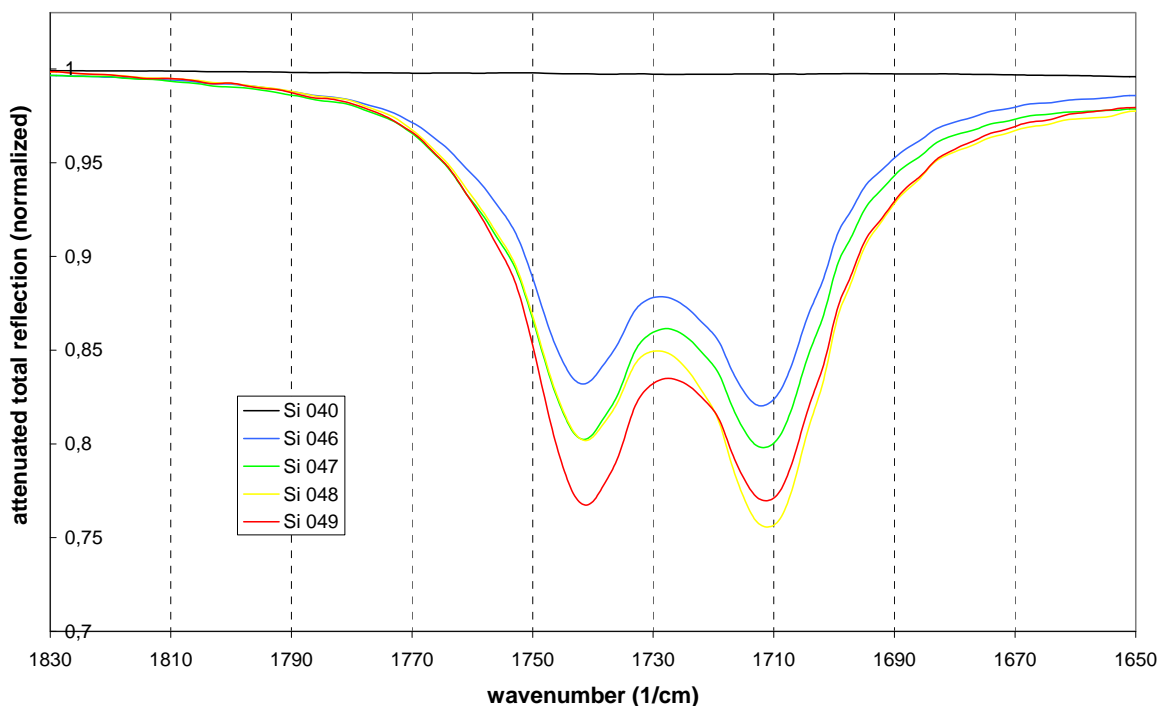


Fig. 67: FTIR spectrum of the carboxylic peak of series # 10 enlarged: The peaks increase with increased amount of DMAM carrier, and correlate well to the amount of DMAM carrier which was admixed.

9.4.10 Series # 11: Using the 3-BCEE carrier of medium molecular weight

Series # 11 is again an analogue of series # 8, but contains the 3-BCEE carrier with the medium molecular weight. The ratio between Si-H and vinyl is again kept constant at 2.50, the ratio between P 1300 and U 1 is kept constant at 15:1, and the mod. Pt-cat was used as 0.1 M solution in xylene. The amount of 3-BCEE in the mixture ranges between 0.00%_{wt} and 16.2%_{wt}. Note that the mixture Si 040 is the same as in series # 9 and # 10. The amounts of silicone precursors used are given below in **Tab. 16**.

Just like in the previous two series the coloration of the samples increased with increasing contents of 3-BCEE carrier. Again this is attributed to the 3-BCEE and the xylene. Some samples were inhomogeneous and pictures will be discussed below in the **chapter 11 Light microscopy**. FTIR analysis showed that the carboxylic peak at 1740 cm⁻¹ is well pronounced and that peak intensity increases with increasing amount of admixed 3-BCEE carrier, see **Fig. 68** and **Fig. 69**.

mixture	3-BCEE carrier (mL)	U 1 (mL)	U 430 (mL)	P 1300 (g)	3-BCEE (% _{wt})
Si 040	-	2.70	2.15	40.5	-
Si 050	0.50	0.133	0.106	2.00	6.26
Si 051	1.00	0.133	0.106	2.00	10.6
Si 052	1.50	0.133	0.106	2.00	13.7
Si 053	2.00	0.133	0.106	2.00	16.2

Tab. 16: Series # 11 is an analogue of series # 8: The ratio between Si-H and vinyl was kept constant at 2.50, and the ratio between P 1300 and U 1 was kept constant at 15:1. The amount of 3-BCEE was varied between 0.00%_{wt} and 16.2%_{wt} by adding the according amount of medium molecular weight 3-BCEE carrier.

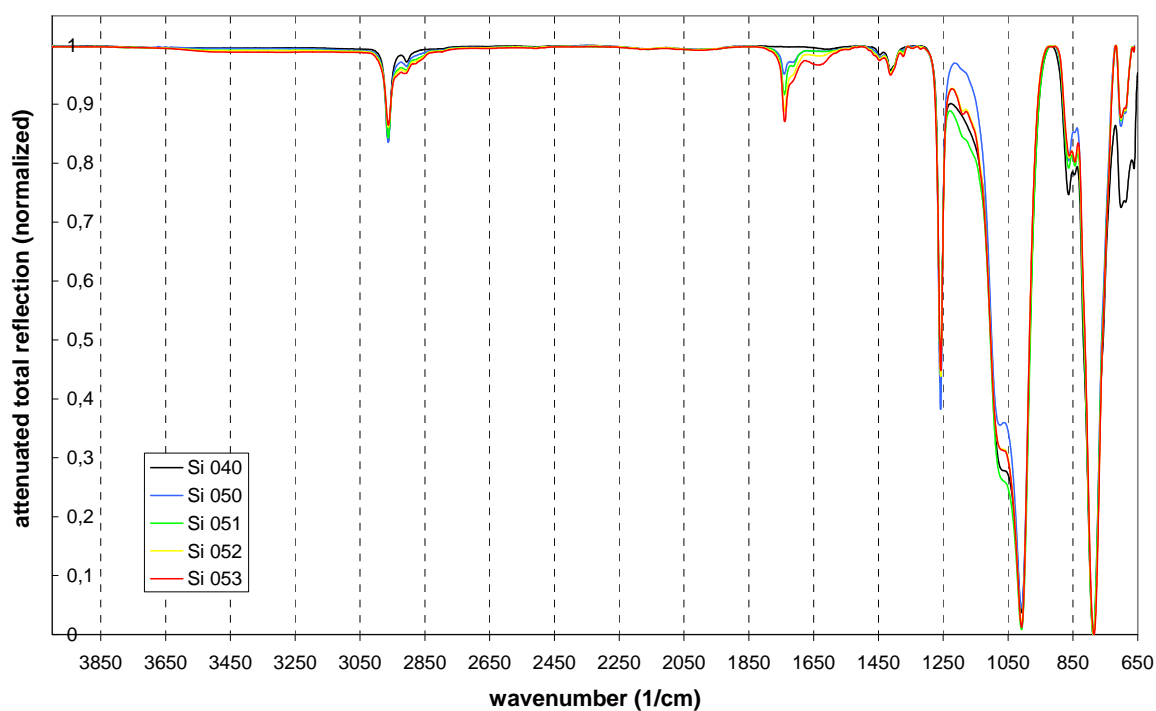


Fig. 68: FTIR of samples of series # 11 after production: The peak of the carboxylic group at 1740 cm⁻¹ is well pronounced.

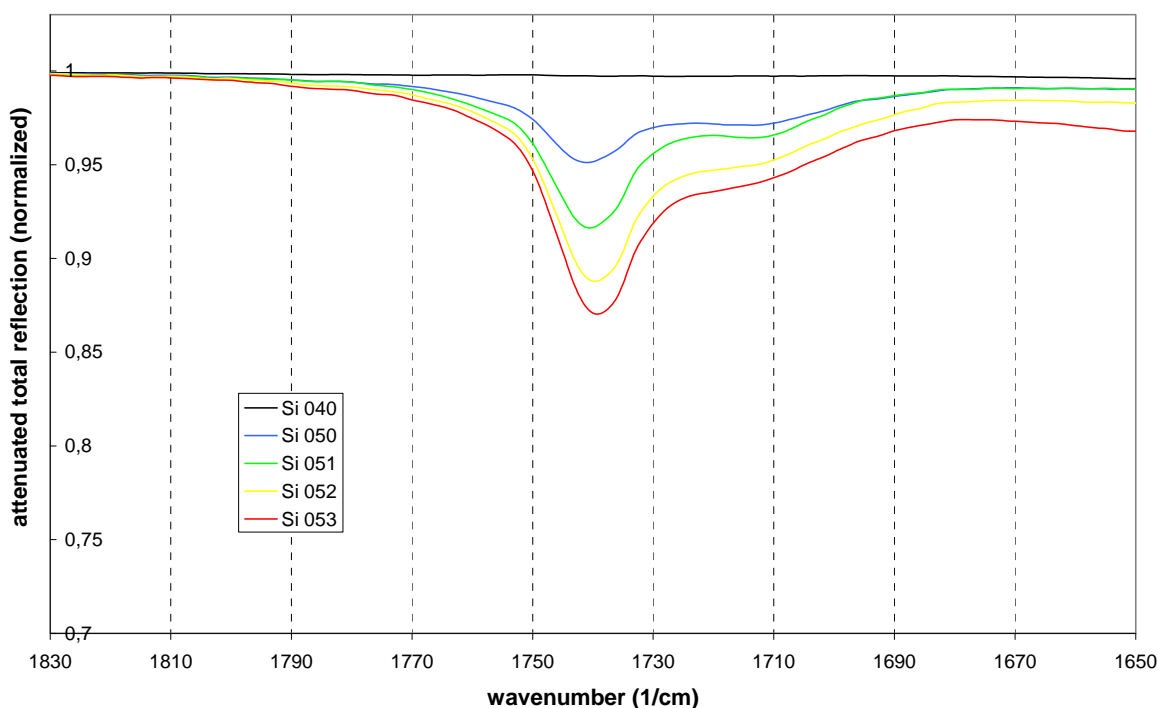


Fig. 69: FTIR spectrum of the carboxylic peak of series # 11 enlarged: The peaks increase with increased amount of 3-BCEE carrier, and correlate well to the amount of 3-BCEE carrier which was admixed.

9.4.11 Series # 12: Using the DMAM carrier of medium molecular weight

The last series in this chapter, series # 12, is an analogue of series # 8 like the three previous series. It contains the DMAM carrier of medium molecular weight. The ratio between Si-H and vinyl is kept constant at 2.50 as before, the ratio between P 1300 and U 1 is kept constant at 15:1 likewise, and as above in series # 6 to series # 11 the mod. Pt-cat was used as 0.1 M solution in xylene. The amount of DMAM in the mixture ranges between 0.00%_{wt} and 16.5%_{wt}. The amounts of silicone precursors used are given below in **Tab. 17**. Please note that the mixture Si 040 is the same as in series # 9, #10, and # 11.

Just like in the previous two series the coloration of the samples increased with increasing contents of DMAM carrier. As above this is attributed to the DMAM and the xylene. Some samples were porous and pictures will be shown below in the **chapter 11 Light microscopy**. FTIR analysis showed that the carboxylic peak at 1740 cm⁻¹ is well pronounced, but that the peak intensity does not directly correlate in all cases to the amount of DMAM car-

rier which was admixed, see **Fig. 70** and **Fig. 71**. Inhomogeneity within the material caused by insufficient mixing are suspected to be the cause.

mixture	3-BCEE carrier (mL)	U 1 (mL)	U 430 (mL)	P 1300 (g)	DMAM (% _{wt})
Si 040	-	2.70	2.15	40.5	-
Si 054	0.50	0.133	0.106	2.00	7.52
Si 055	1.00	0.133	0.106	2.00	12.7
Si 056	1.50	0.133	0.106	2.00	16.5

Tab. 17: Series # 12, an analogue of series # 8: The ratio between Si-H and vinyl was kept constant at 2.50, and the ratio between P 1300 and U 1 was kept constant at 15:1. The amount of DMAM was varied between 0.00%_{wt} and 16.5%_{wt} by adding the according amount of medium molecular weight DMAM carrier.

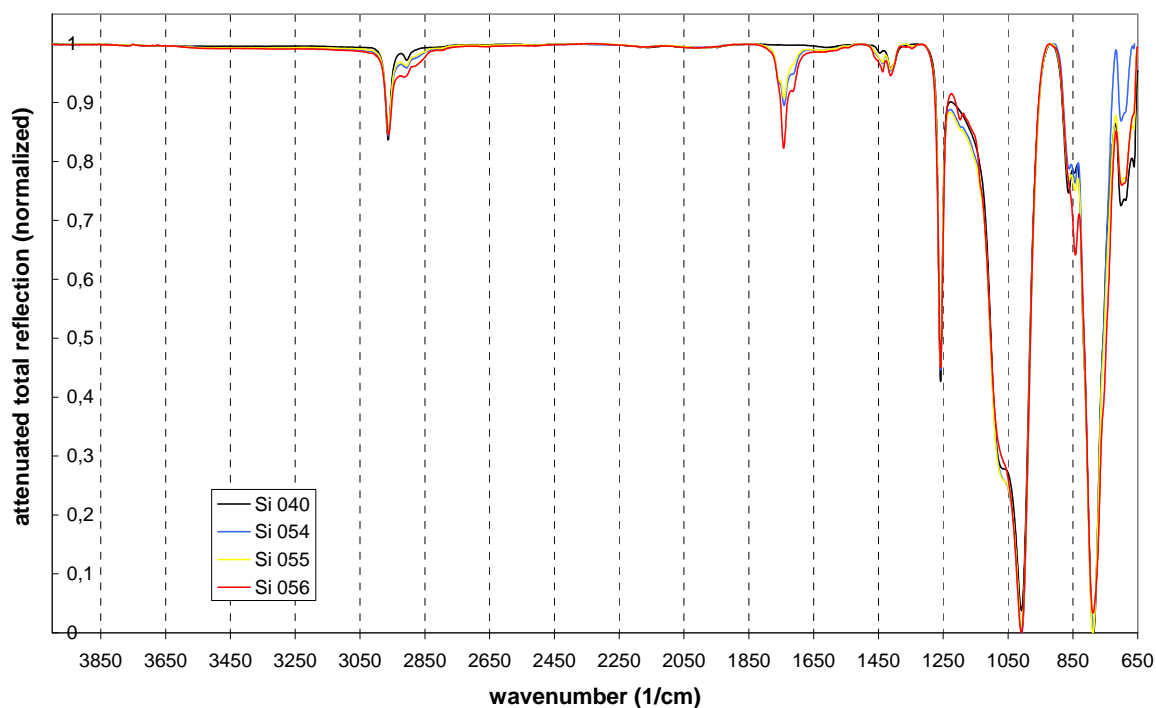


Fig. 70: FTIR of samples of series # 12 after production: The peak of the carboxylic group at 1740 cm⁻¹ is well pronounced.

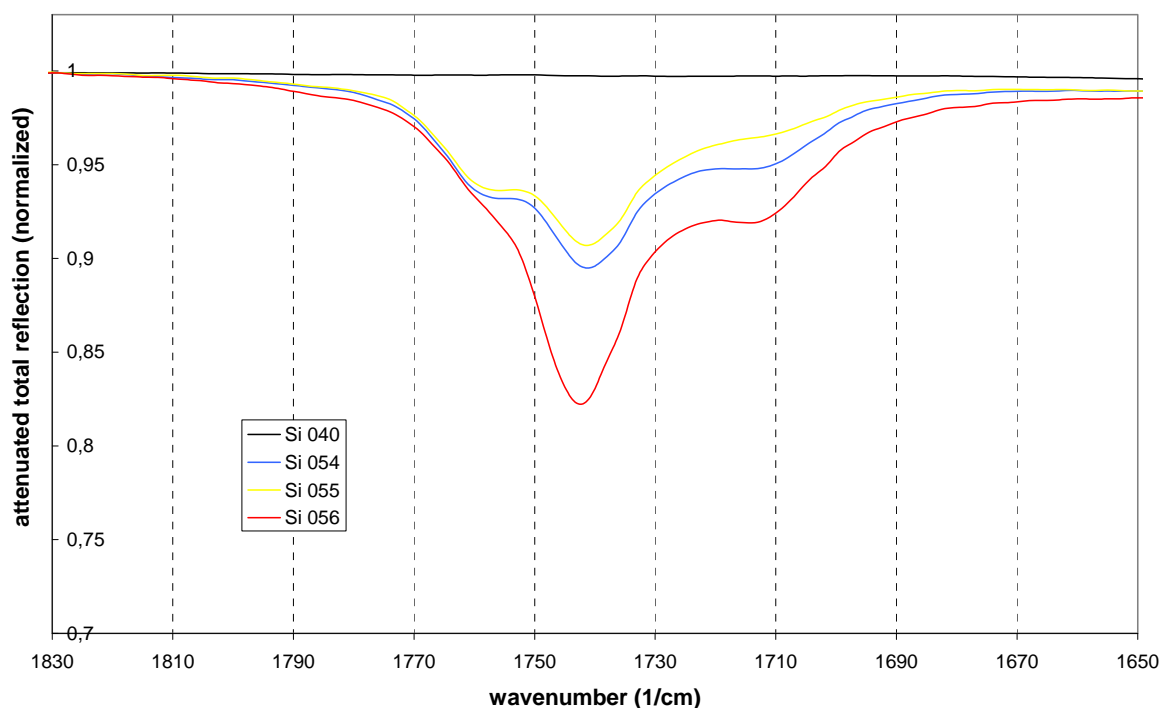


Fig. 71: FTIR spectrum of the carboxylic peak of series # 12 enlarged: The peak intensity does not directly correlate in all cases to the amount of DMAM carrier which was admixed; inhomogeneity within the material from insufficient mixing is suspected to be the cause.

9.5 Conclusions

In the beginning of this chapter it was shown that the polymerization of a silicone is possible using either the Pt-cat or the mod. Pt-cat. Furthermore, the polymerization of silicone is possible in the presence of 3-BCEE, and covalent bonding of 3-BCEE to the silicone backbone is feasible during this polymerization process. A silicone polymer can be produced using simple standard silicone precursors like PDMS_{vinyl} and P(DMS-co-MHS). However, the resulting polymers are of low mechanical properties as compared to commercially available materials.

In order to produce silicone mixtures with mechanical properties comparable to those of commercially available silicones, three silicone precursors of the silicone type named Silopren[®] have been used. It is one of the materials that are used for cardiac pacing lead insulation.

Two possibilities of introducing the two SME candidates 3-BCEE and DMAM to the silicone were evaluated: Firstly, it was shown that 3-BCEE could be directly attached to the silicone backbone. Secondly, 3-BCEE and DMAM carriers could be admixed to the silicone precursors, and a silicone produced successfully. However, attaching 3-BCEE to the silicone backbone did not yield satisfying results with regard to the efficiency of this approach, because a large part of the 3-BCEE seems to have evaporated during the production process. In contrast, admixing a carrier to the silicone precursors produced higher readouts in the FTIR for the functional group of interest, i.e. the carboxylic group. However, the molecular weight of the carrier plays a vital role in the processability of the silicone mixture: The silicone series # 8, in which the 3-BCEE carrier of highest molecular weight was used, became very difficult to process due to a drastic increase of viscosity.

The silicone series # 9 to # 12 contain amounts of 3-BCEE and DMAM of up to 22.5%_{wt}, which are the highest amounts achieved. Furthermore, they exhibit mechanical stability which allows for further testing, i.e. exposure to hydrolyzing media, contact angle measurement and ELISA. Hence, these four silicone series were chosen for further experiments.

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10 Mechanical properties of the 12 series of silicone

The goal of this chapter is to establish an overview over the mechanical properties of the 12 series of silicone which were described in the previous chapter. This will allow comparing of the 12 silicone series to the commercially available materials. Furthermore, the impact of introducing different amounts of the SME candidates to the silicones can be evaluated. In general, this will show if the changes made within the polymer have an unacceptable adverse effect on the material properties, or if the produced polymer may be a candidate for application as pacing lead insulation. Drawing such conclusions from standard test methods as described in DIN, ISO, EN, or ASTM test norms always has to be done very carefully, as the test conditions demanded in these norms do not have much in common with the conditions under which biomaterials are usually applied. However, mechanical testing is one of the bases for characterizing material properties.

Since the 12 silicone series were produced using mainly Silopren[®] silicone precursors, the 12 series will always be compared either among each other or to the commercially available Silopren[®] materials. The following data is available for Silopren[®] types LSR 4030...4070: Elongation (DIN 53504, S2) 400...800%, tensile strength (DIN 53504, S2) 8.0...10.0 MPa, hardness (DIN 53505, Shore A) 31...70, density (DIN 53479 A) 1.10...1.14 g/cm³, and tear strength (ASTM D 624, die B) 18...35 kN/m[158].

10.1 Tensile testing

Tensile testing was conducted for 10 of the 12 series of silicone. Series # 1 and # 4 were not tested, because the samples of series # 1 contained air bubbles, and most of the samples of series # 4 could not be removed from the sample holder without being damaged. Both would have certainly falsified the results.

10.1.1 Series # 2

Fig. 72 shows the Young's Modulus, **Fig. 73** the elongation at break, and **Fig. 74** the tensile strength of series # 2. In this series the ratio between hydrogensiloxane and vinyl was

varied between 1:1 and 4:1. The Young's Modulus increases with increasing ratio of Si-H to vinyl, showing almost a plateau between 2 and 3, whereas the elongation at break decreases with increasing ratio of Si-H to vinyl. The tensile strength does not change significantly. In conclusion, the ratio between Si-H and vinyl of 2.5 was found optimal for a compromise between the gain of Young's Modulus and the loss of elongation at break.

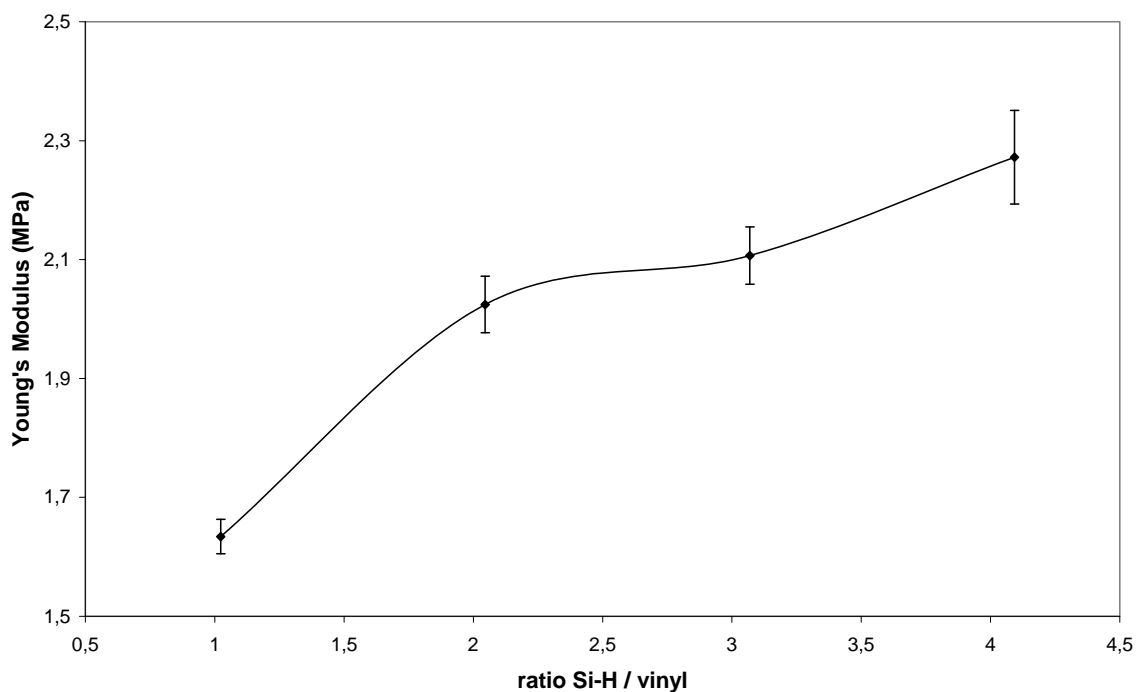


Fig. 72: Young's Modulus of Series # 2 as a function of the ratio between hydrosiloxane and vinyl, indicating a plateau for a ratio of Si-H to vinyl between 2 and 3.

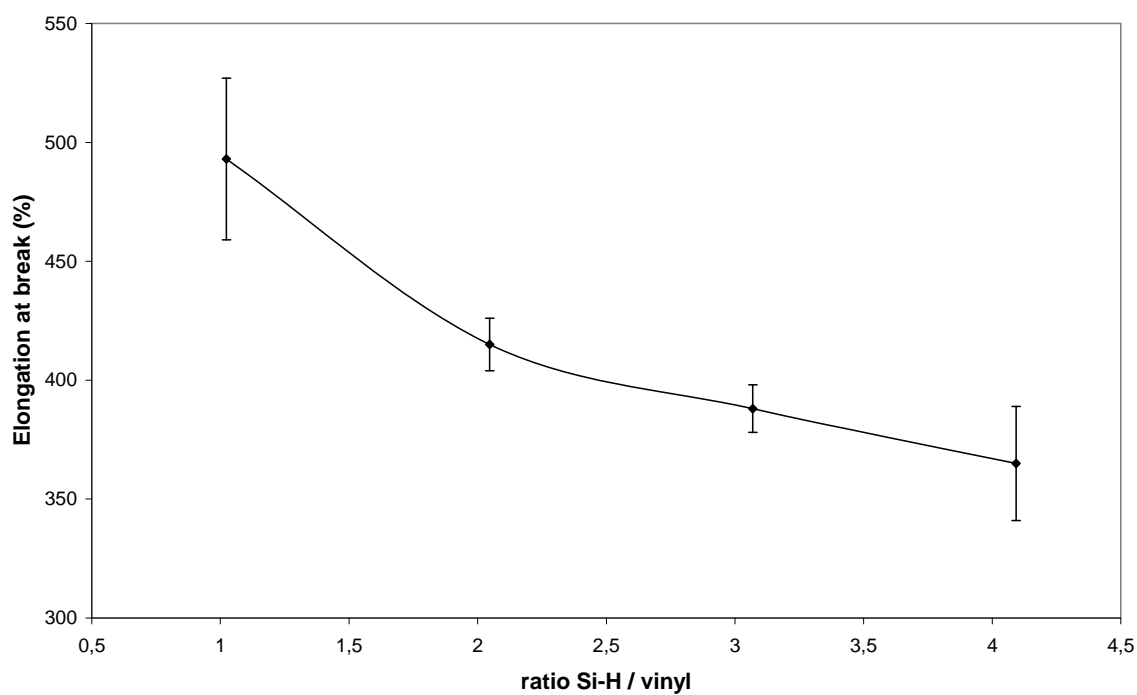


Fig. 73: Elongation at break of Series # 2 as a function of the ratio between hydrosiloxane and vinyl.

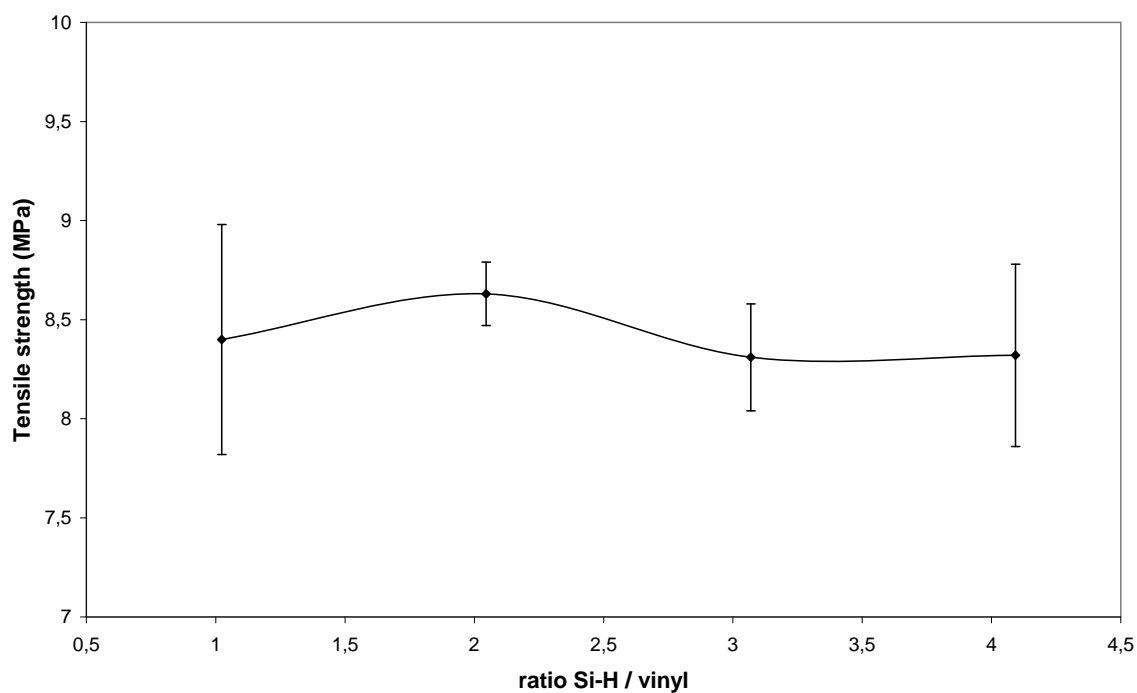


Fig. 74: Tensile strength of Series # 2 as a function of the ratio between hydrosiloxane and vinyl, no significant change can be seen in the within the tested range.

10.1.2 Series # 3

Fig. 75 shows the Young's Modulus, **Fig. 76** the elongation at break, and **Fig. 77** the tensile strength of series # 3. In this series, the ratio between the filler batch P 1300 and the linear vinyl terminated polydimethylsiloxane U 1 was varied. The overall trends of all three tensile properties suggest maxima at a ratio of P 1300 to U 1 of about 15:1. For future series it was thus decided to set the ratio between the filler batch P 1300 and the linear vinyl terminated polydimethylsiloxane U 1 to 15:1 in order to achieve maximal mechanical properties.

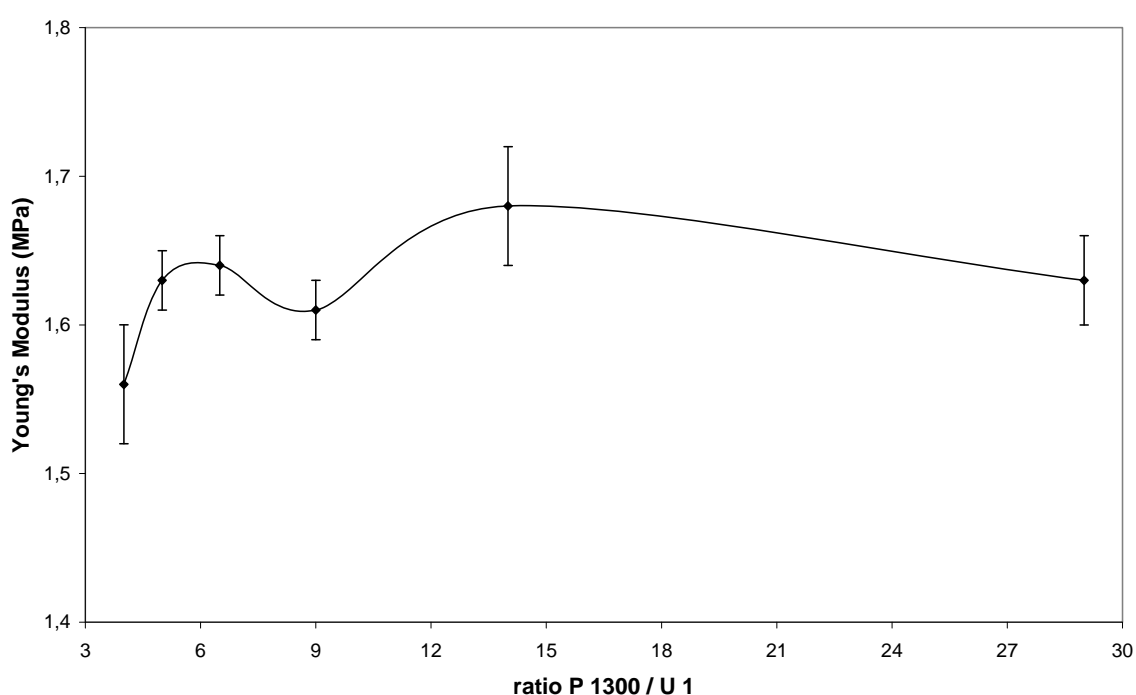


Fig. 75: Young's Modulus of series # 3 as a function of the ratio between the filler batch P 1300 and the linear vinyl terminated polydimethylsiloxane U 1, a maximum can be seen at a ratio of about 15:1.

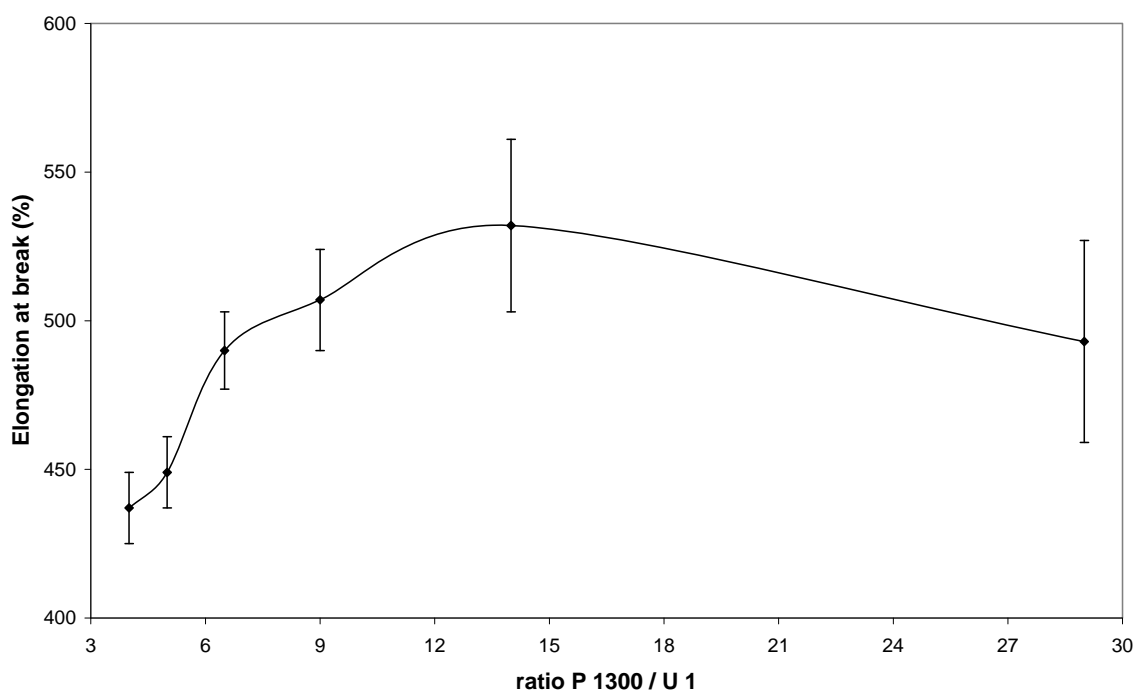


Fig. 76: Elongation at break of series # 3 as a function of the ratio between the filler batch P 1300 and the linear vinyl terminated polydimethylsiloxane U 1, with a maximum at a ratio of ~15:1.

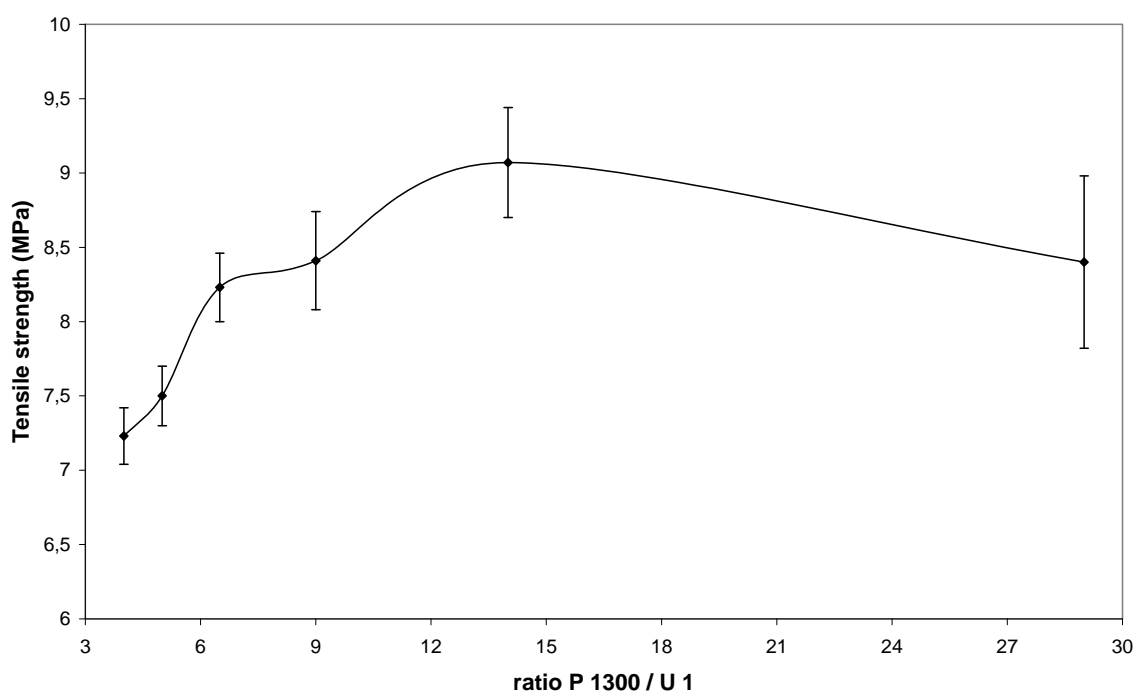


Fig. 77: Tensile strength of series # 3 as a function of the ratio between the filler batch P 1300 and the linear vinyl terminated polydimethylsiloxane U 1, again a maximum can be seen at a ratio of ~15:1.

10.1.3 Series # 5

Fig. 78 shows the Young's Modulus, **Fig. 79** the elongation at break, and **Fig. 80** the tensile strength of series # 5. The amount of 3-BCEE in the silicone mixtures was varied between 0.00 and 8.31%_{wt}, and PMHS was added in order to provide enough hydrogensiloxane binding sites for the 3-BCEE. In the figures it can be seen that the Young's Modulus increases slightly with increasing content of 3-BCEE, whereas the elongation at break and the tensile strength decrease significantly with increasing content of 3-BCEE. This behavior is explainable: The two latter properties depend largely on the cross-linking density of the silicone polymer. As the 3-BCEE does not contribute to the formation of the three-dimensional network of the silicone, the cross-linking density and thus both the elongation at break and the tensile strength are decreased with increasing contents of 3-BCEE.

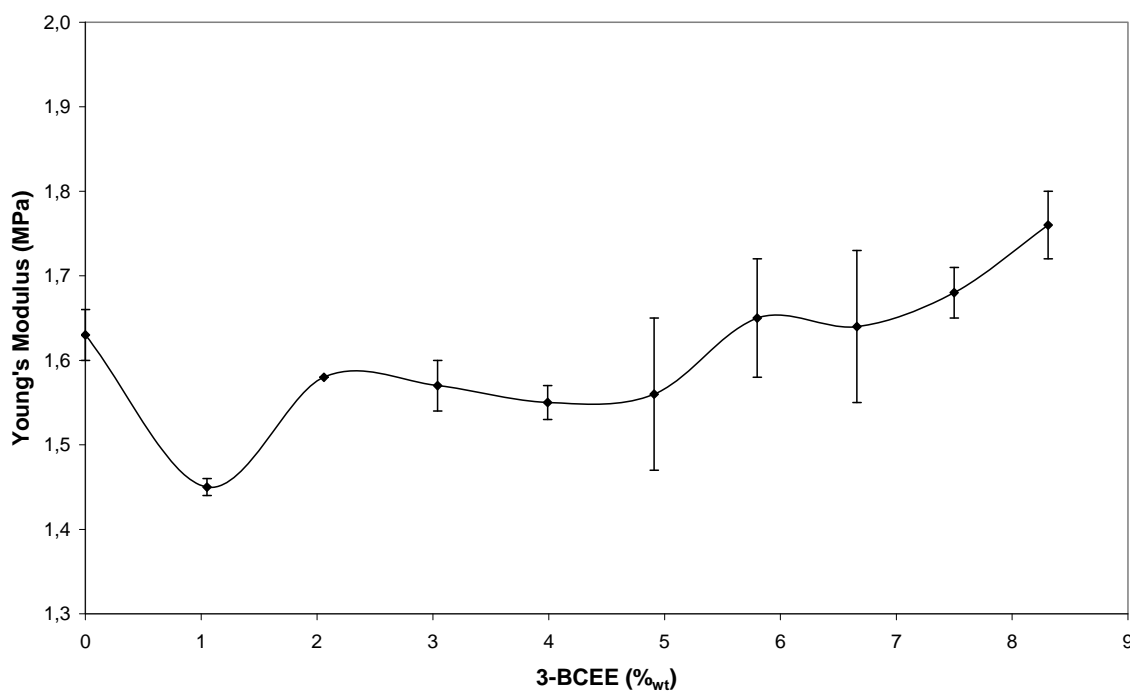


Fig. 78: Young's Modulus of series # 5 as a function of the contents of 3-BCEE, showing a slight increase with increasing contents of 3-BCEE.

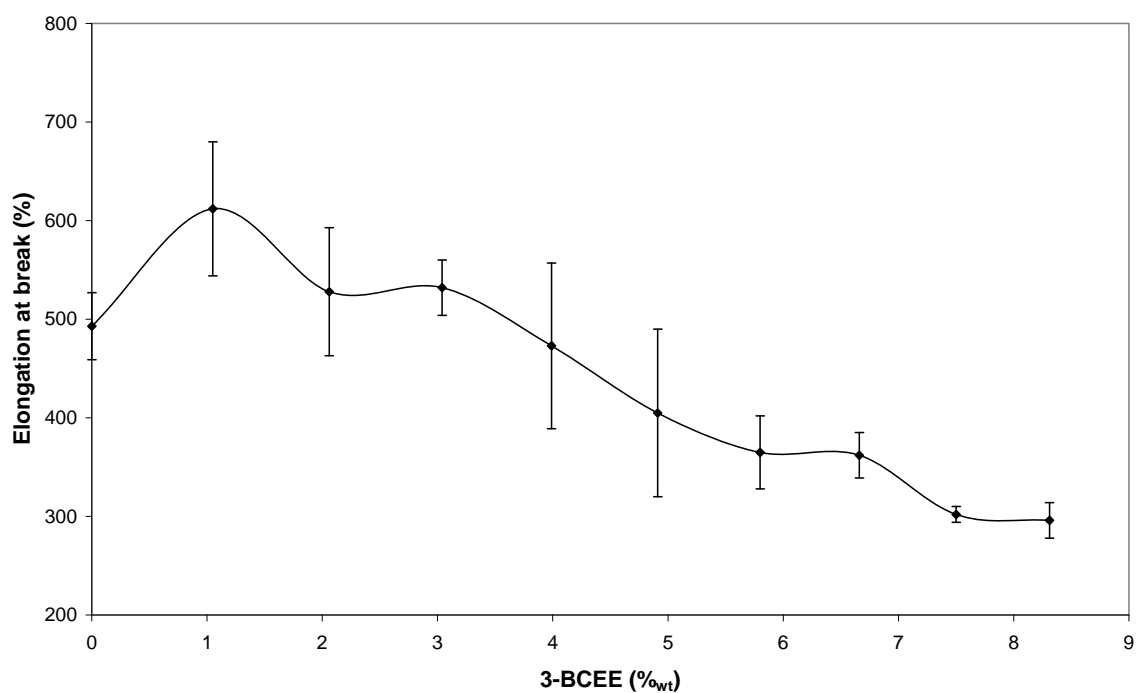


Fig. 79: Elongation at break of series # 5 as a function of the amount of 3-BCEE, the elongation at break decreases significantly with increasing contents of 3-BCEE.

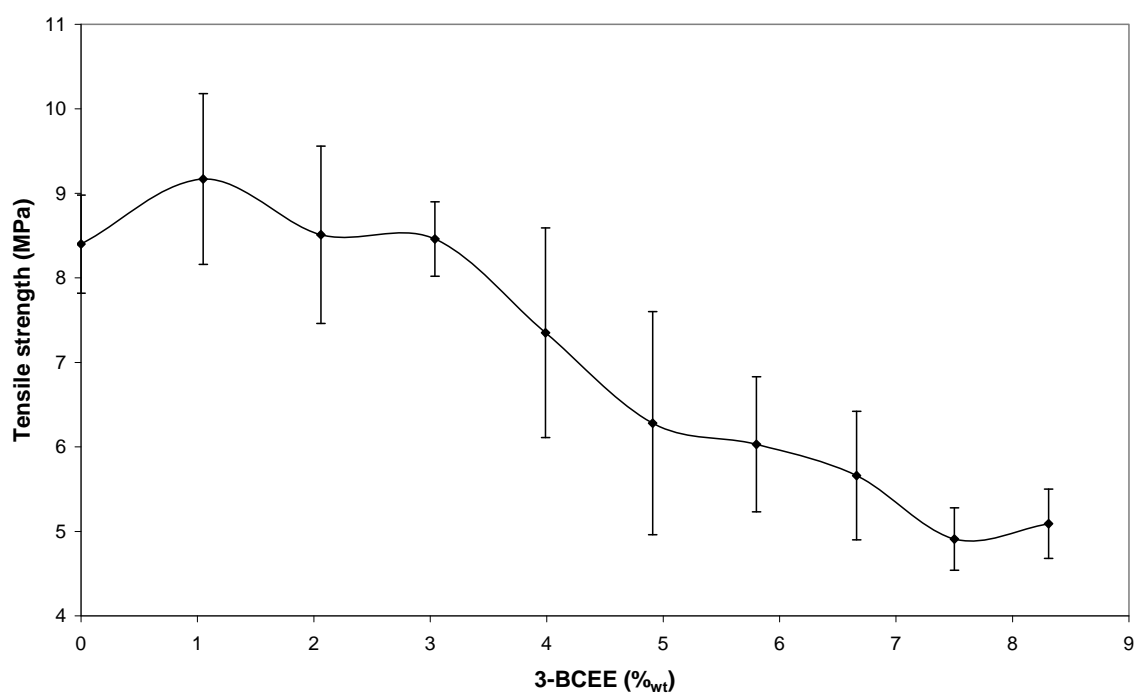


Fig. 80: Tensile strength of series # 5 as a function of the amount of 3-BCEE, the tensile strength decreases significantly with increasing contents of 3-BCEE.

10.1.4 Series # 6 and series # 7

The amount of 3-BCEE in series # 6 was varied between 0.00 and 3.01%_{wt}. The analogous series # 7 was produced without 3-BCEE. **Fig. 81** shows the Young's Modulus, **Fig. 82** the elongation at break, and **Fig. 83** the tensile strength of series # 6 and series # 7. In short, no significant differences could be seen between the two series. The conclusion is that the admixing of 3-BCEE to the silicone precursors does not have an adverse effect on the overall formation of the silicone network. However, in series # 7 the 3-BCEE is not added, leading to a variation of the ratio between Si-H and vinyl groups, which can be assumed to influence the mechanical properties of the material. However, this influence was not significant within the error of production and measurement techniques as conducted here.

FTIR, as presented above in **chapter 9.4.6 Series # 6 and series # 7: Using fumed silica and U 430 instead of PMHS**, in **Fig. 60** and **Fig. 61** showed that there is almost no 3-BCEE present in the samples of series # 6. Evaporation of the 3-BCEE was assumed. Therefore the series # 6 and series # 7 have the same overall composition. Hence, the two series must be expected to show the same properties. This reasoning allows for explication of the curves: In **Fig. 81** the Young's Modulus increases with increasing 3-BCEE contents. But since the 3-BCEE was not present in both of the series, the diagram must be read as increasing Young's Modulus with increasing ratio of Si-H to vinyl. This reasoning applies for the other diagrams as well: In **Fig. 82** the elongation at break decreases with increasing ratio of SI-H to vinyl. In **Fig. 83**, even though the error bars are large, with increasing ratio of SI-H to vinyl the trend of a slight initial increase of the tensile strength to a maximum can be seen, and then a subsequent decrease below the initial values.

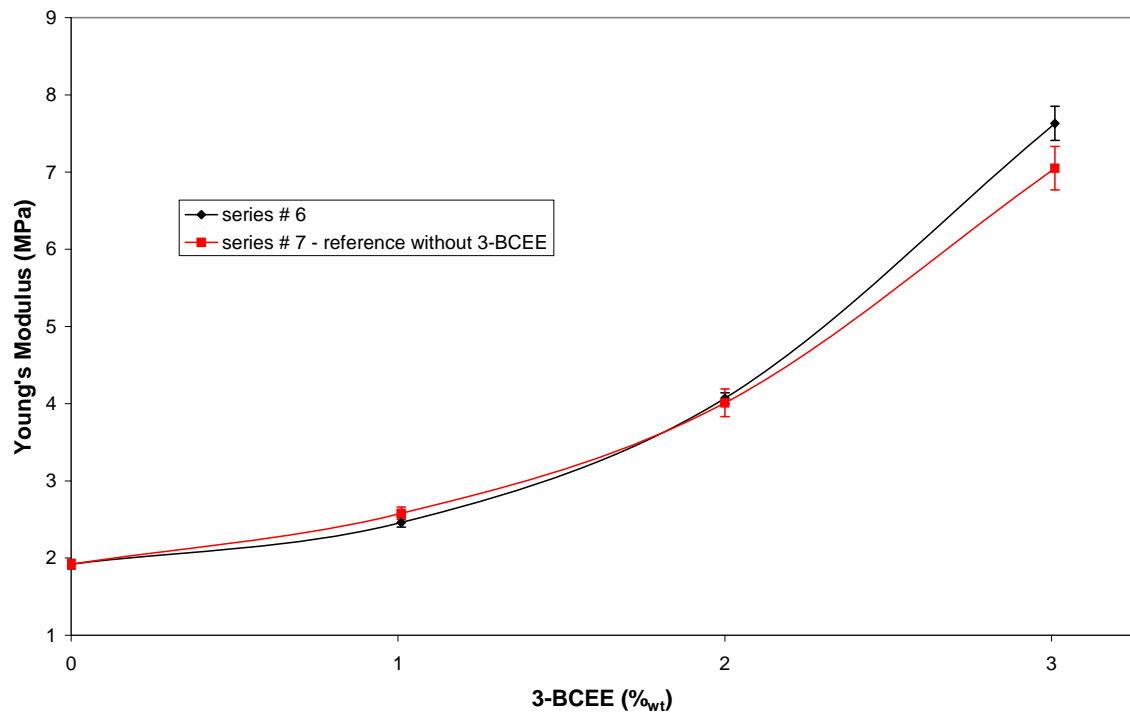


Fig. 81: Young's Modulus of series # 6 and # 7: No significant difference can be seen between the two series.

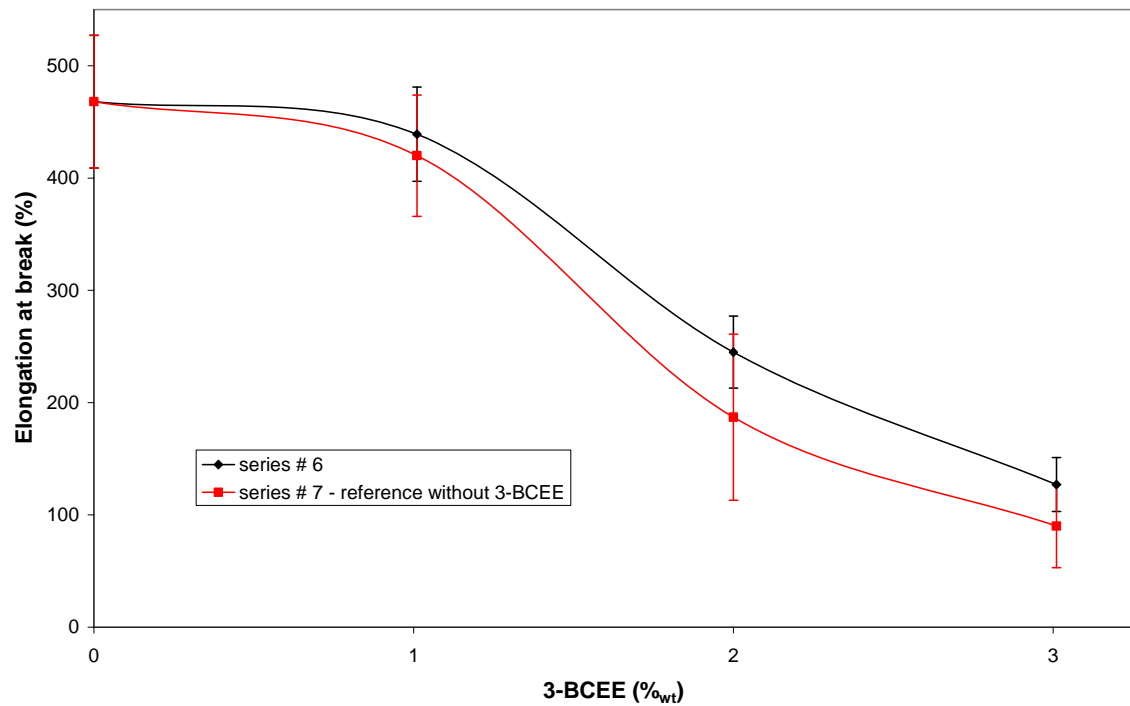


Fig. 82: Elongation at break of series # 6 and # 7: No significant difference can be seen between the two series.

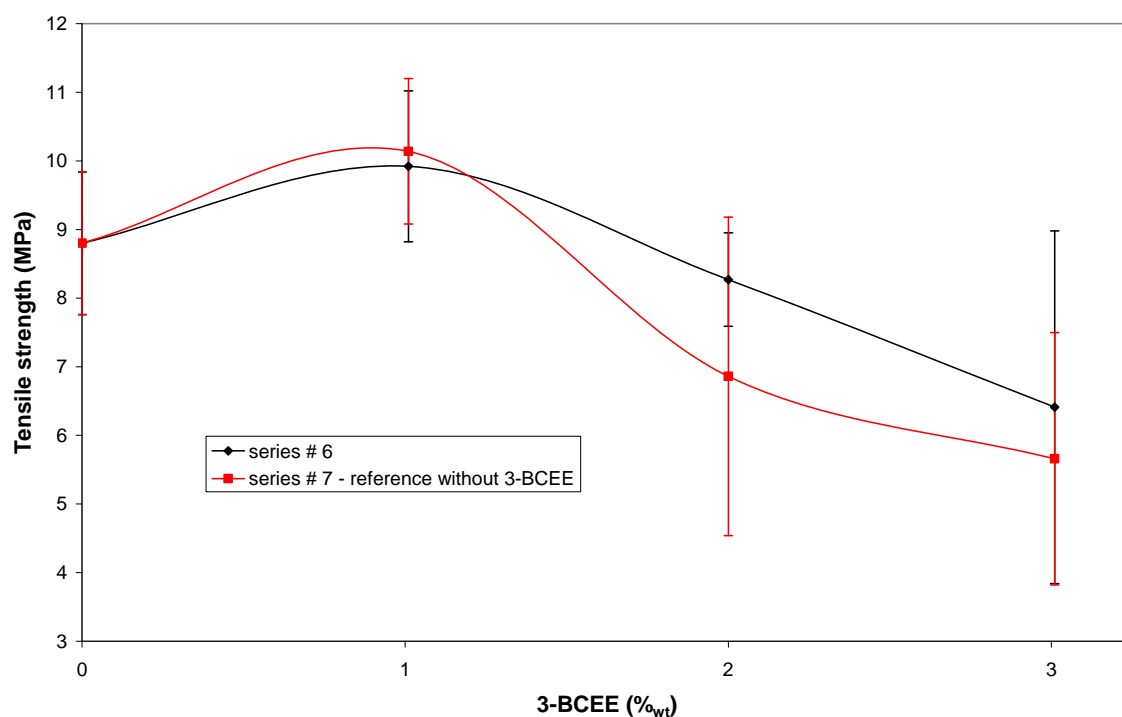


Fig. 83: Tensile strength of series # 6 and # 7: No significant difference can be seen between the two series.

10.1.5 Series # 8

Series # 8 is the first series containing a SME carrier, in this case the 3-BCEE carrier of highest molecular weight. The amount of 3-BCEE ranges between 0.00 and 4.66%_{wt}. For increasing amount of 3-BCEE in the samples the tensile testing shows a significant decrease of Young's Modulus, elongation at break, and tensile strength, see **Fig. 84**, **Fig. 85**, and **Fig. 86**, respectively. However, this trend is less pronounced for the elongation at break, and even shows a significant variability over the course of the diagram. The decrease of the tensile properties can be explained as follows: The 3-BCEE carrier does not have any functional groups to bond to the silicone network. In consequence, the 3-BCEE carrier does not contribute to but instead reduces the overall cross-linking density. This reduces the mechanical properties of the material. The large error bars are likely to be caused by the inhomogeneity of the silicone mixture, as discussed above in **chapter 9.4.7**

Series # 8: Using the 3-BCEE carrier of highest molecular weight.

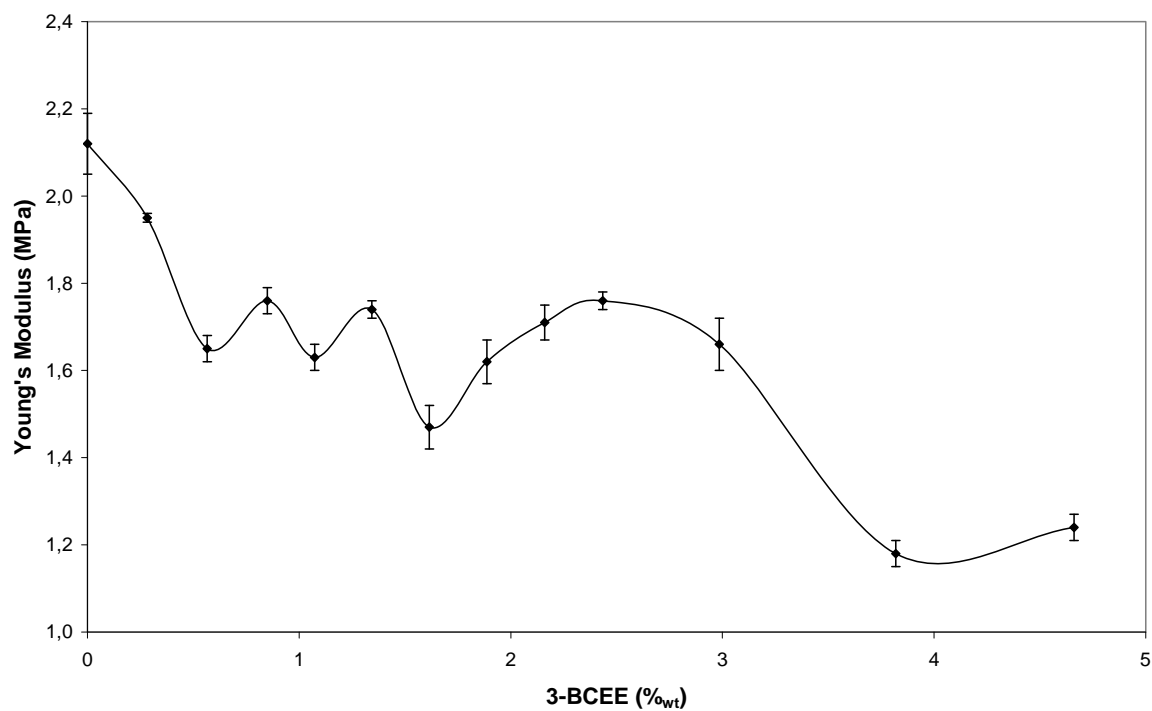


Fig. 84: Young's Modulus of series # 8, decreasing with increasing amount of 3-BCEE, large error bars may be caused by inhomogeneous silicone mixtures.

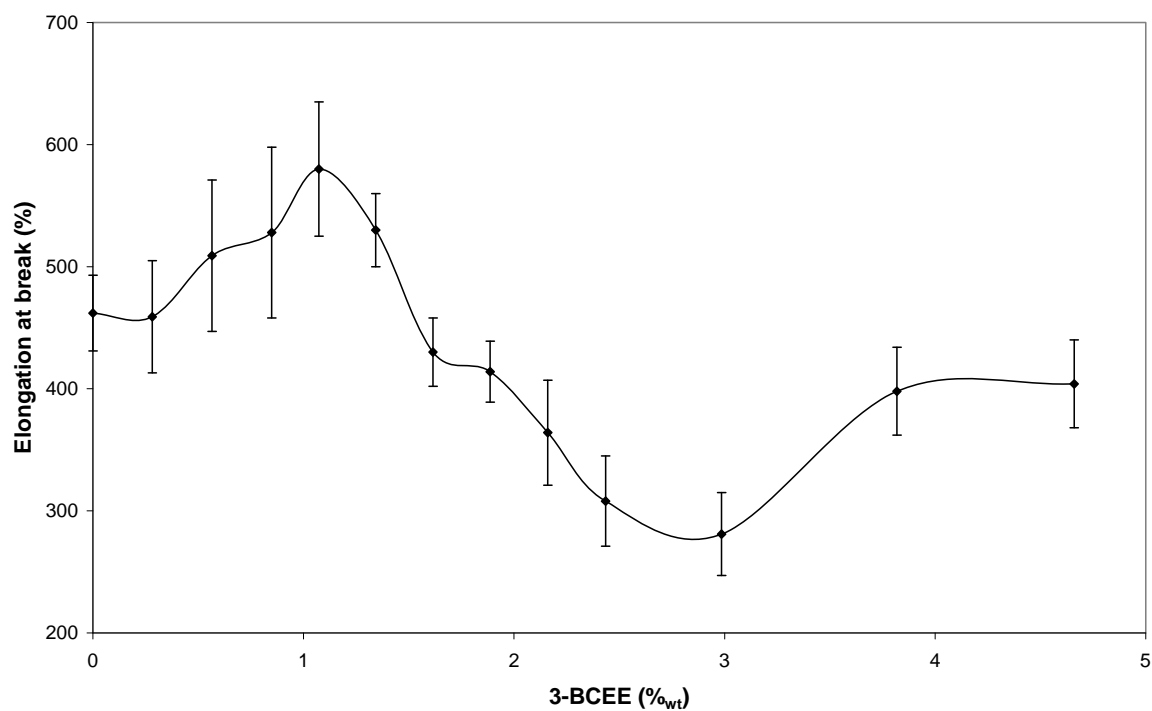


Fig. 85: Elongation at break of series # 8, decreasing with increasing amount of 3-BCEE, large error bars may be caused by inhomogeneous silicone mixtures.

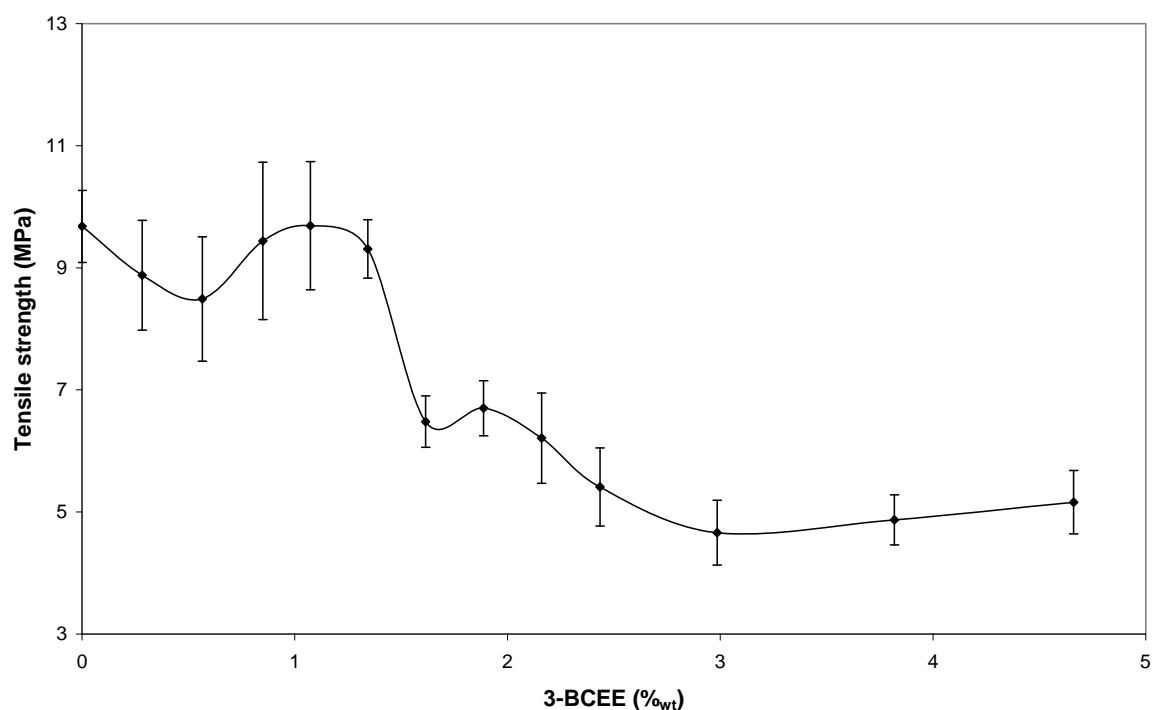


Fig. 86: Tensile strength of series # 8, decreasing with increasing amount of 3-BCEE, large error bars may be caused by inhomogeneous silicone mixtures.

10.1.6 Series # 9 to # 12

The tensile properties of series # 9 to # 12 are displayed and discussed together. This is due to the fact that the general composition of P 1300, U1 and U 430 was established in the previous series. Furthermore, the mechanical properties of these four series of silicone are very similar. Here, only the effect of the admixing of the carriers is evaluated. It is noteworthy that the series # 9 to # 12 contained 3-BCEE and DMAM of up to 22.0%_{wt}, and 22.5%_{wt} respectively. However, the mixtures with a content of either of these two SME candidates above ~14%_{wt} had mechanical properties which were too low as if to allow for tensile testing. **Fig. 87** shows the Young's Modulus, **Fig. 88** the elongation at break, and **Fig. 89** the tensile strength of series # 9 to # 12.

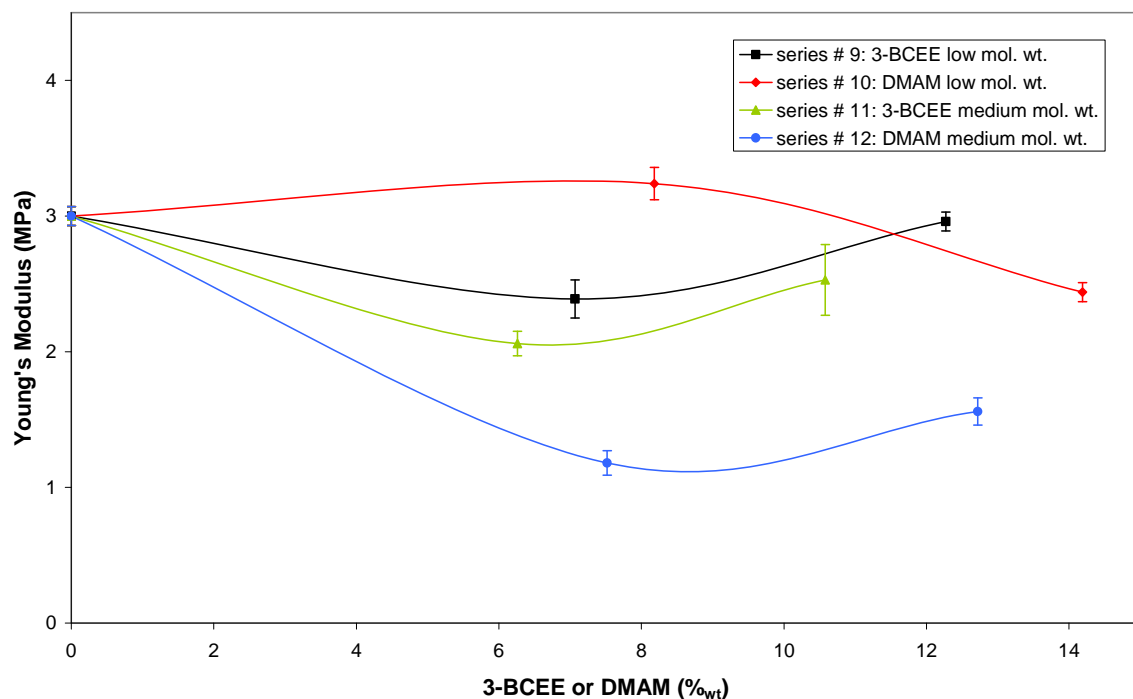


Fig. 87: Young's Modulus of series # 8 to # 12, not showing a clear trend. The measurement for series # 10 at ~8%_{wt} DMAM may be wrong due to insufficient mixing of the silicone precursors.

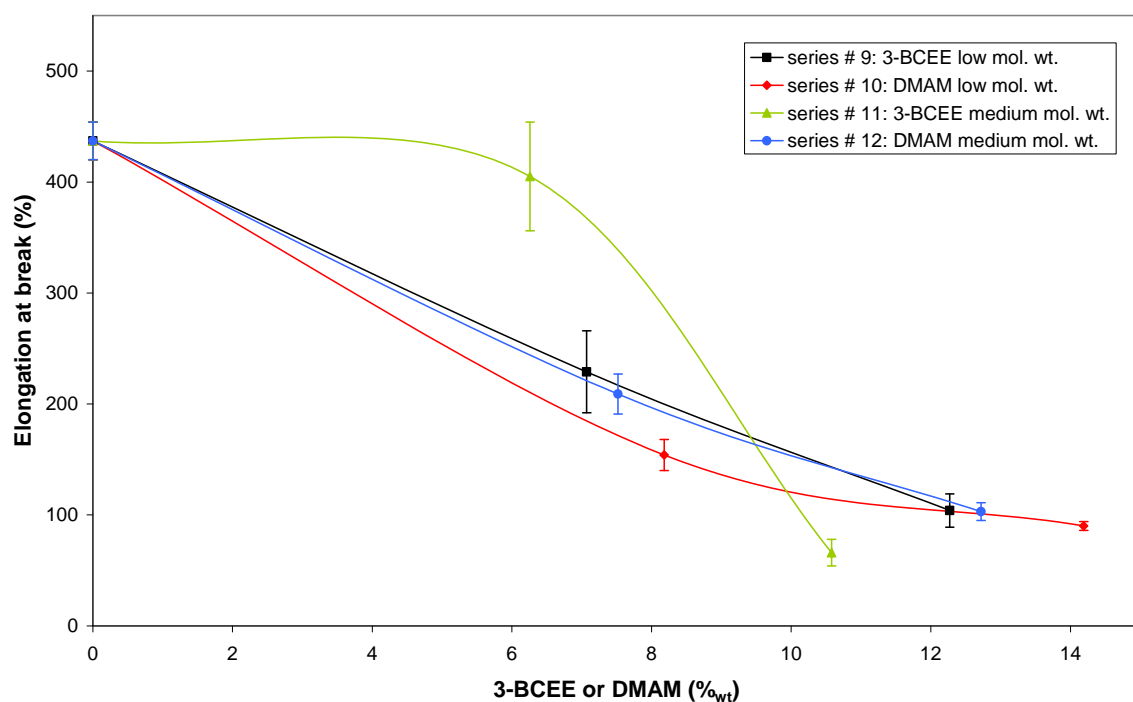


Fig. 88: Elongation at break of series # 9 to # 12, decreasing with increasing contents of 3-BCEE and DMAM. The measurement for series # 11 at ~6%_{wt} 3-BCEE may be wrong due to insufficient mixing.

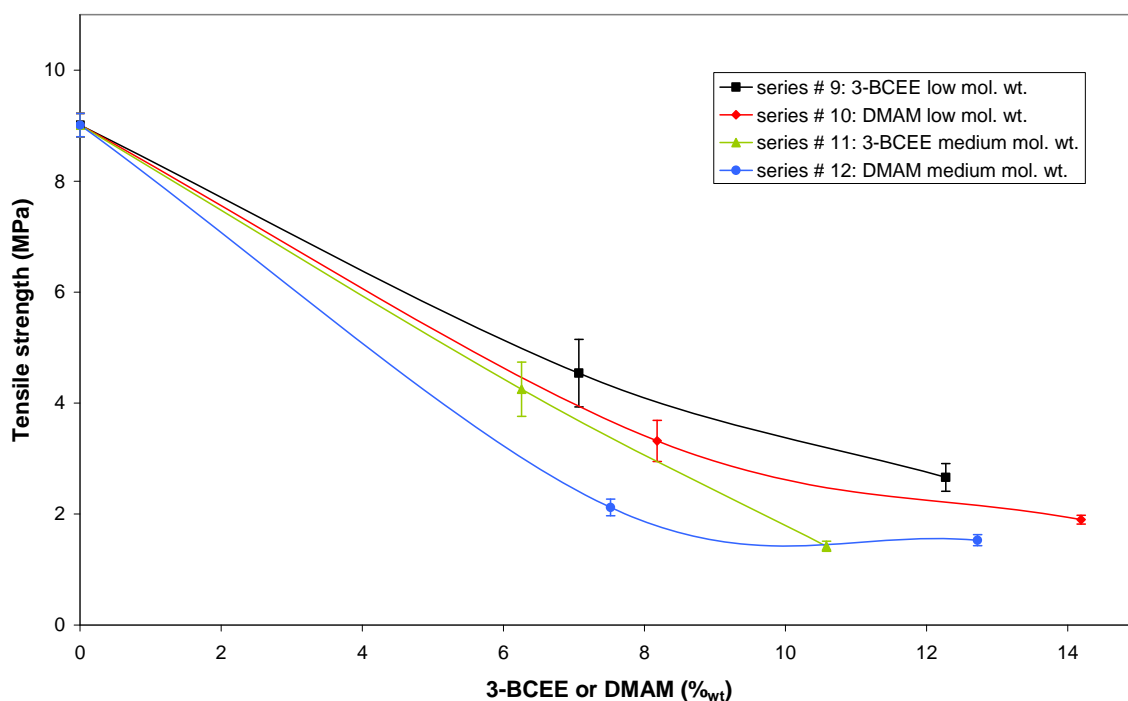


Fig. 89: Tensile strength of series # 9 to # 12, decreasing with increasing amount of both 3-BCEE and DMAM.

While the Young's Modulus does not show a clear trend, the elongation at break and the tensile strength decrease significantly with increasing amount of added carrier. This can be explained, analogous to series # 8, since the carriers do not contribute to the three-dimensional silicone network. Thus, any admixing of a non-functional SME carrier can be expected to reduce the overall cross-linking density, which in turn reduces the tensile properties of the material. The measurement for series # 10 at ~8%_{wt} DMAM in **Fig. 87** may be wrong, just like the measurement for series # 11 at ~6%_{wt} 3-BCEE in **Fig. 88**. The reason may be inhomogeneity in the mixtures in both cases. As will be shown later in **chapter 11 Light microscopy** the inhomogeneity, which can be observed in some of the samples, is severe and gives reason to believe that there is still room for improvement regarding the mixing process.

10.2 Hardness measurement

Hardness measurement was conducted here mostly as a descriptive measure. No conclusions resulting in the adjustment of a mixing ratio of the 12 series of silicone was drawn. This is due to the fact that the desired hardness of commercially available materials is mainly adjusted by adding the necessary amount of silica and other fillers to the silicone precursors, by changing the cross-linking density, and by changing the average chain-length between interconnections in the three-dimensional silicone network. In this work, however, the main goal is the incorporation of SMEs to silicone. The hardness is only regarded as a by-product of the modifications made to unmodified material.

10.2.1 Series # 1

Fig. 90 shows the hardness of series # 1. The hardness increases with increasing ratio of hydrogensiloxane to vinyl. The reason is that hydrogensiloxane functional groups can form a siloxane bond with one another in the presence of oxygen. As the polymerization was conducted in normal air atmosphere, and the silicone precursors were also not degassed, oxygen was present. Hence, the excess of hydrogensiloxane resulted in the formation of many additional bonds between the molecules, thus increasing the cross-linking density per volume unit, which increased the hardness.

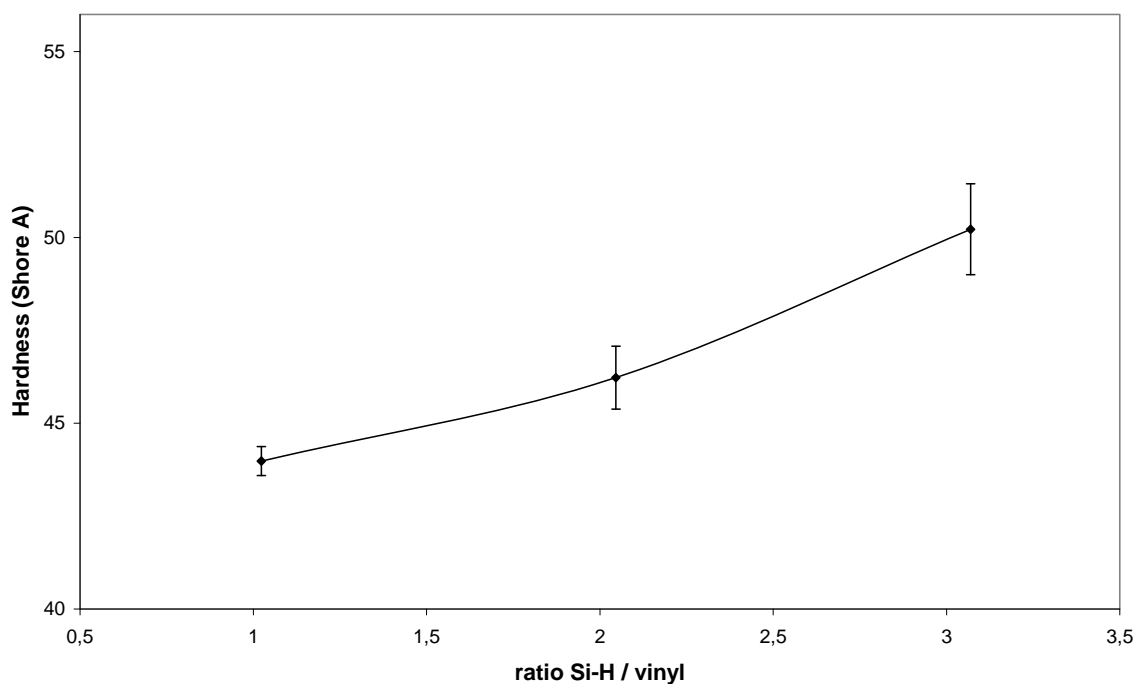


Fig. 90: Hardness of series # 1, increasing with increasing ratio of hydrogensiloxane to vinyl due to the reaction of hydrogensiloxane groups with one another under the formation of additional siloxane bonds, and thus increasing the cross-linking density, which in turn increases the hardness of the material.

10.2.2 Series # 2

Fig. 91 shows the hardness of series #2. As for series # 1 the hardness increases with increasing ratio of hydrogensiloxane to vinyl. The seeming decrease for the measurement of the samples with a ratio of Si-H to vinyl of ~ 3 can not immediately be explained, and is therefore doubted. It may be caused by insufficient mixing of the silicone precursors.

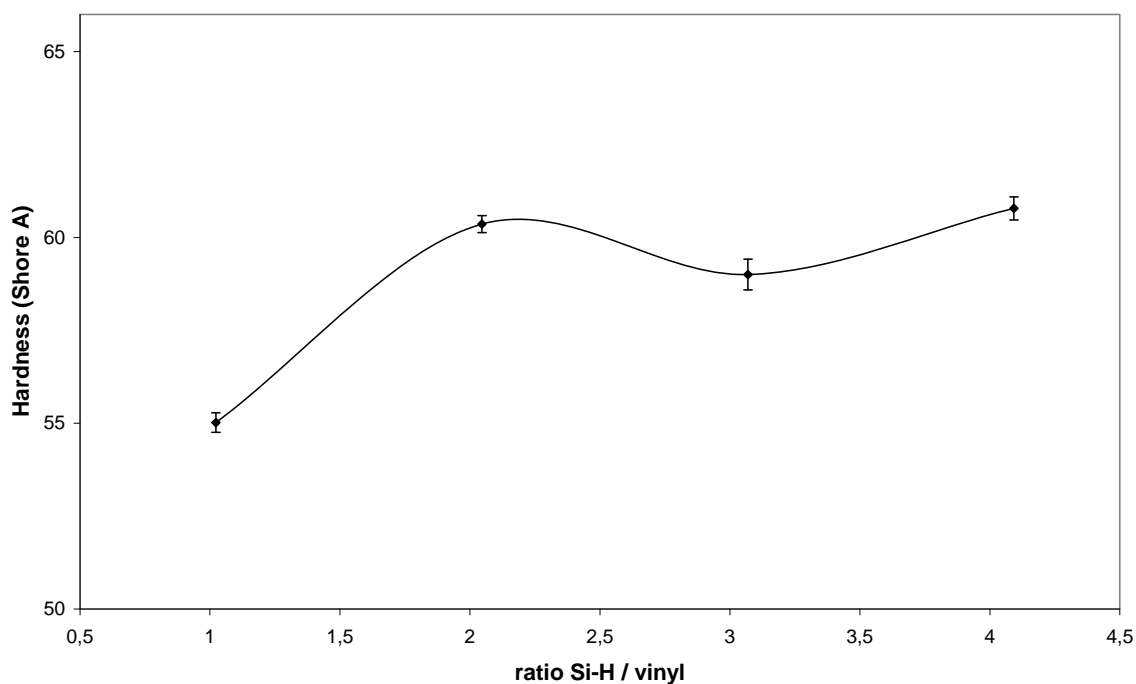


Fig. 91: Hardness of series # 2, overall increasing with increasing ratio of Si-H to vinyl. Insufficient mixing of the silicone precursors is suspected to be the cause of the fluctuation in the curve.

10.2.3 Series # 3

Fig. 92 shows the hardness of series # 3, which increases with increasing ratio between the filler batch P 1300 and die linear vinyl terminated polydimethylsiloxane U 1. This makes sense, as the filler batch is the only Silopren[®] component used here which contains amorphous silica, the substance which is commonly used as filler to increase the hardness of silicone materials. Therefore, the hardness can be expected to increase with increasing contents of P 1300 in the mixture.

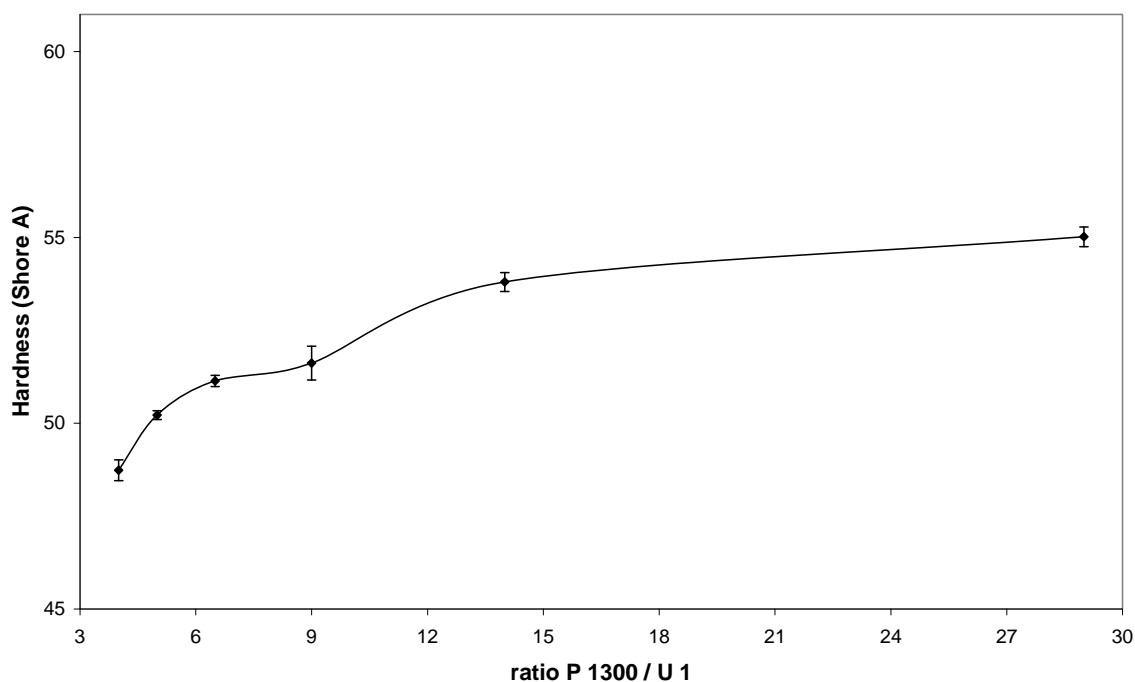


Fig. 92: Hardness of series # 3, increasing with increasing ratio of the filler batch P 1300 to the linear vinyl terminated polydimethylsiloxane U 1 as expected, as P 1300 contains silica as filler which is mainly responsible for the hardness of silicone mixtures.

10.2.4 Series # 4

Fig. 93 shows the hardness of series # 4 which increases with increasing content of 3-BCCE. The presence of 3-BCCE alone is not able to explain the increase of the hardness. However, with increasing contents of 3-BCCE, the content of PMHS was also increased in order to provide the hydrogensiloxane binding sites which are needed to covalently bond the 3-BCCE via hydrosilylation. In **chapter 9.4.5 Series # 5: Effect of amount of 3-BCCE - repeated** the conclusion was made that large parts of the 3-BCCE evaporated, and were not covalently bonded to the silicone backbone. Hence, this series had a large excess of Si-H functional groups. The increasing hardness can be explained since these groups are able to react with one another to form siloxane bonds in the presence of oxygen, and thereby increase the cross-linking density. This was already shown above in this **chapter**, see **10.2 Hardness measurement** for series # 1 and # 2.

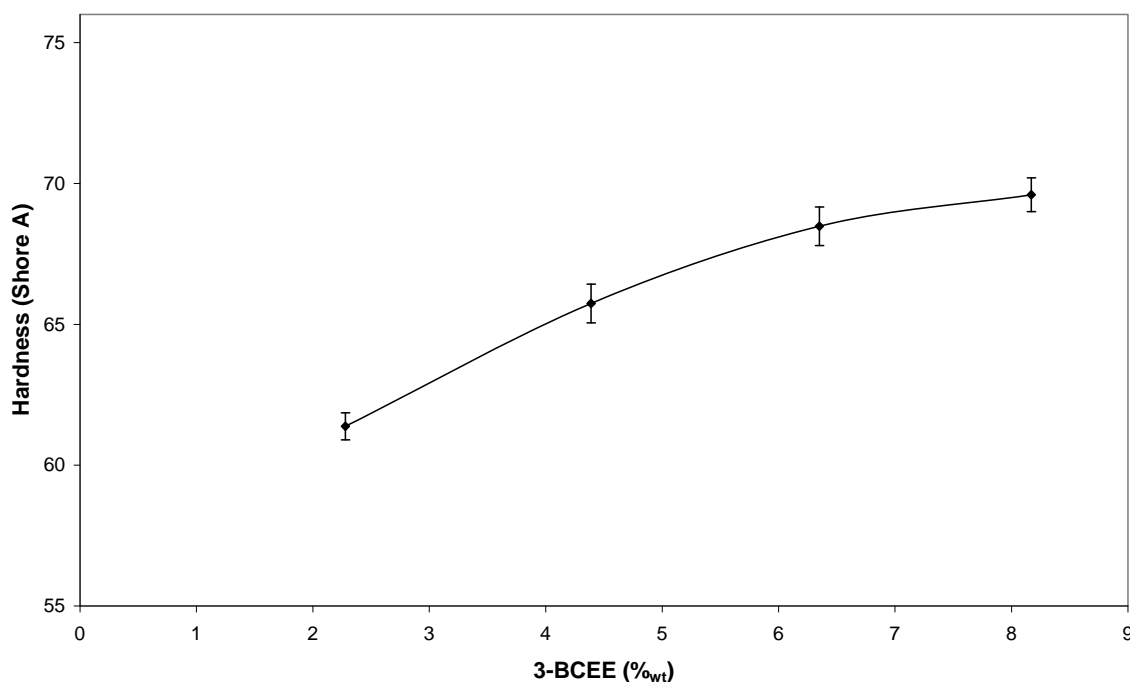


Fig. 93: Hardness of series # 4 as a function of the amount of 3-BCEE that was added to the mixture. Since large parts of the 3-BCEE evaporated this material has an increasing excess of Si-H to vinyl with increasing addition of 3-BCEE, leading to the increasing hardness analogous to series # 1 and # 2.

10.2.5 Series # 5

Series # 5 is a repetition of series # 4, with the difference that the overall ratio of Si-H to vinyl was decreased slightly. Fig. 94 shows the hardness of series # 5 which increases with increasing content of 3-BCEE. As in series # 4, this can be explained by the evaporation of large parts of the 3-BCEE, which causes an excess of Si-H functional groups resulting in the increase in hardness by increasing the cross-linking density through the formation of siloxane bonds in the presence of oxygen.

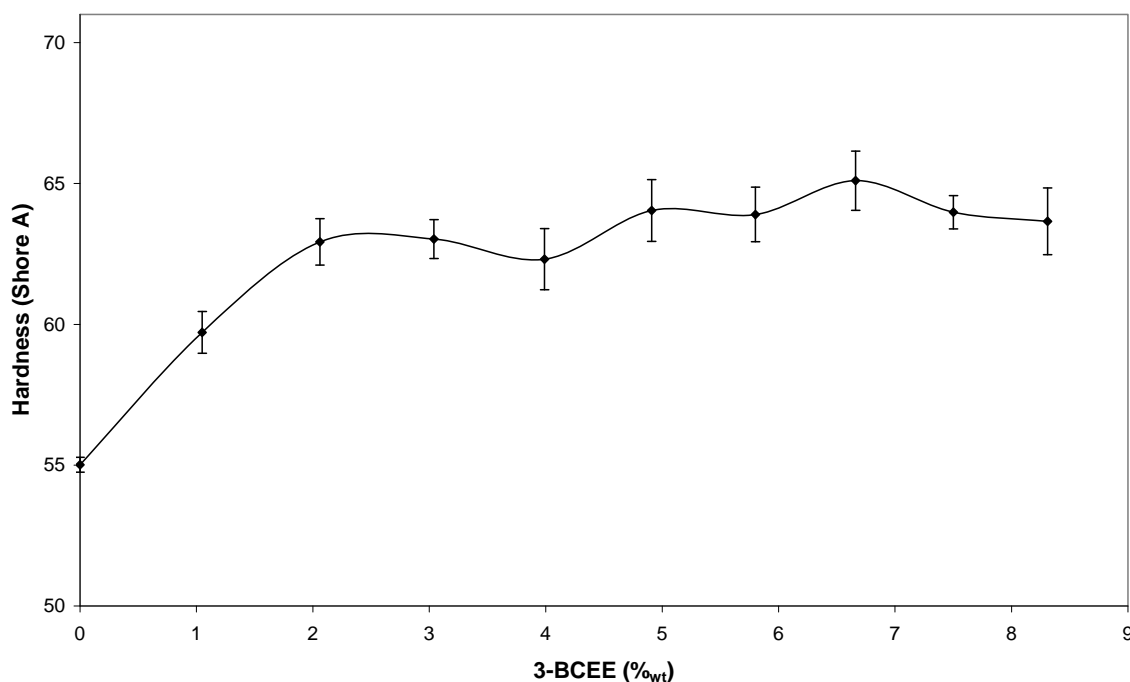


Fig. 94: Hardness of series # 5 as a function of the amount of 3-BCEE that was added to the mixture. Since large parts of the 3-BCEE evaporated this material has an increasing excess of Si-H to vinyl with increasing addition of 3-BCEE, leading to the increasing hardness analogous to series # 1 and # 2.

10.2.6 Series # 6 and series # 7

Fig. 95 shows the hardness of series # 6 and series # 7. The two series have the same composition regarding P 1300, U 430, and U 1, but series # 7 does not contain any 3-BCEE, and in consequence also less fumed silica was added. Hence, the steady increase of hardness of series # 6 with increasing contents of 3-BCEE may be due to the fumed silica which was added. In series # 7 less fumed silica was added as compared to series # 6, and the hardness of samples of series # 7 could therefore be expected to increase less. However, the decrease of the hardness of series # 7 at a content of 3-BCEE of $\sim 3\%_{\text{wt}}$ can not immediately be explained. It may be possible, that in series # 6 the hydrogensiloxane which was added to allow binding of the 3-BCEE interacted with the fumed silica. This is, however, only a speculation.

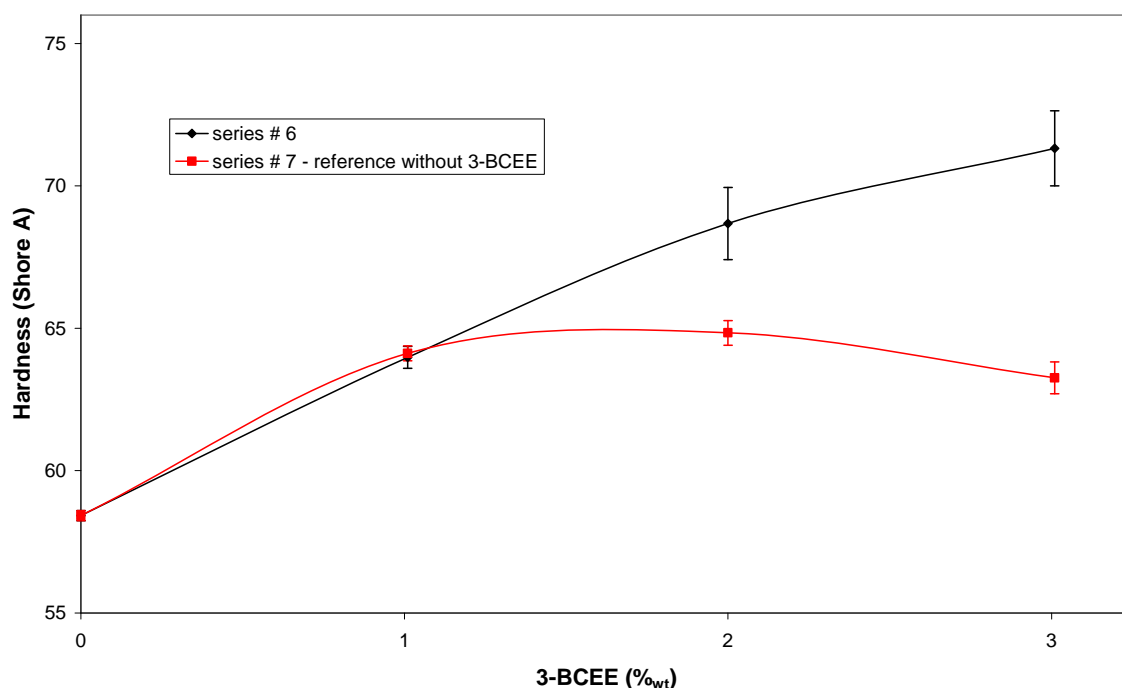


Fig. 95: Hardness of series # 6 and series # 7: The hardness of series # 6 steadily increases as the amount of fumed silica was increased with the amount of 3-BCEE which was added to the silicone precursors. In series # 7 less fumed silica was added as compared to series # 6, since no 3-BCEE was added.

10.2.7 Series # 8

In general, the hardness of the samples of series # 8 decreases with increasing amount of the 3-BCEE. Only for amounts of 3-BCEE below $\sim 1.5\%_{wt}$ the hardness initially increases as compared to the sample without 3-BCEE, see **Fig. 96**. It is noteworthy, that the error bars for samples with high contents of 3-BCEE are larger than those for samples with low contents of 3-BCEE. The reason for the difference in the size of the error bars is that as the amount of admixed 3-BCEE carrier was increased the viscosity of the mixtures also increased, which made thorough mixing of the silicone precursors in the speed mixer difficult. Samples with high contents of 3-BCEE may therefore be less well mixed, which can explain the larger error bars of these samples.

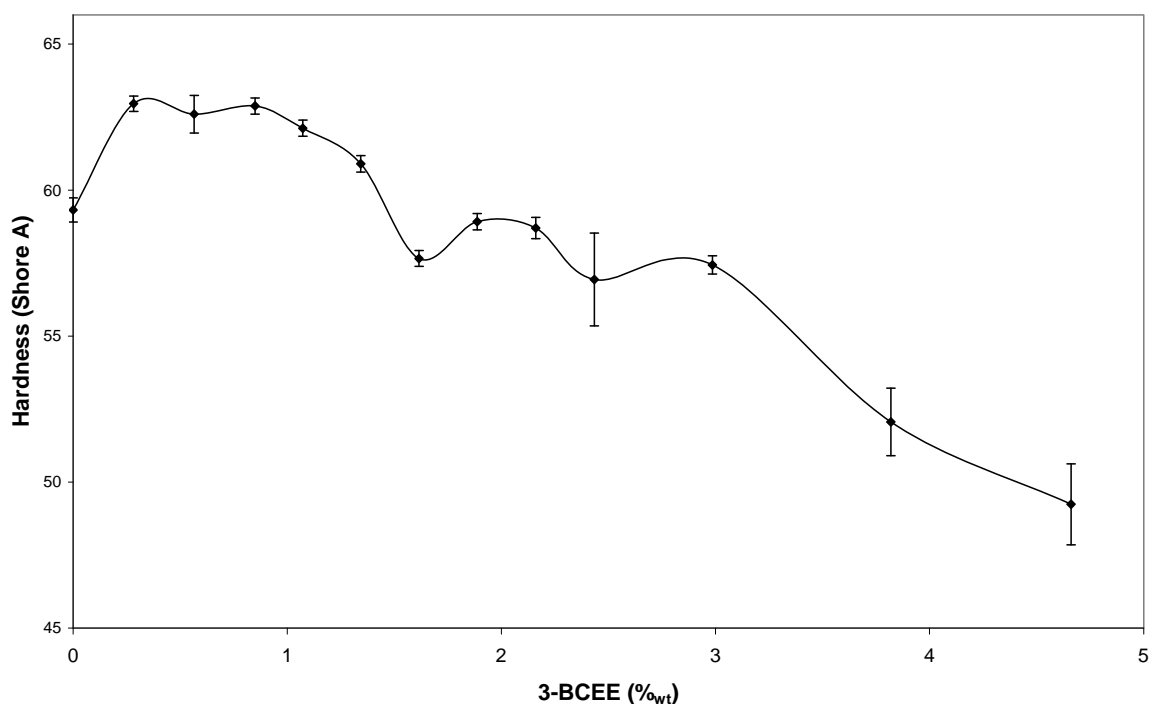


Fig. 96: Hardness of series # 8: For low amounts of 3-BCEE present in the silicone the hardness increases, whereas it decreases for larger amounts of 3-BCEE. Larger error bars with increasing contents of the 3-BCEE carrier may be caused by the mixing problems encountered during production of the mixtures, caused by a raise of viscosity with increasing contents of the 3-BCEE carrier.

10.3 Tear strength

Like the hardness measurement, the tear test was conducted only as a descriptive measure. The goal was to be able to compare the series of silicone with 3-BCEE attached to the silicone backbone, and the silicone series containing a 3-BCEE carrier to the commercially available Silopren[®] materials. However, the sample size used by Momentive Performance Materials for tear testing requires rather large amounts of material, which is why tear testing will only be conducted for two series with the approach of covalently bonding 3-BCEE to the silicone backbone, and one series containing a 3-BCEE carrier. Series # 6 to # 8 were chosen.

10.3.1 Series # 6 and series # 7

Fig. 97 shows the tear strength for silicone series # 6 and # 7. As above for the tensile properties of these two series, there is no difference between them. The tear strength decreases with increasing amount of 3-BCEE that was added to series # 6. But as no 3-BCEE was added to series # 7 and the values are the same between the two series, it can be concluded that it is not the 3-BCEE which is responsible for the decrease of the tear strength. Fumed silica and an increasing amount of U 430 were added to both series, the latter to provide the hydrogensiloxane binding sites needed to covalently bond the 3-BCEE, and the fumed silica to increase the viscosity of the two mixtures. Since less fumed silica was added to series # 7 than to series # 6, but no difference can be seen between the two series, it is not the fumed silica either, which is responsible for the decrease of the tear strength. This leaves only the additionally added cross-linker U 430 as a possible cause for the decrease of the tear strength.

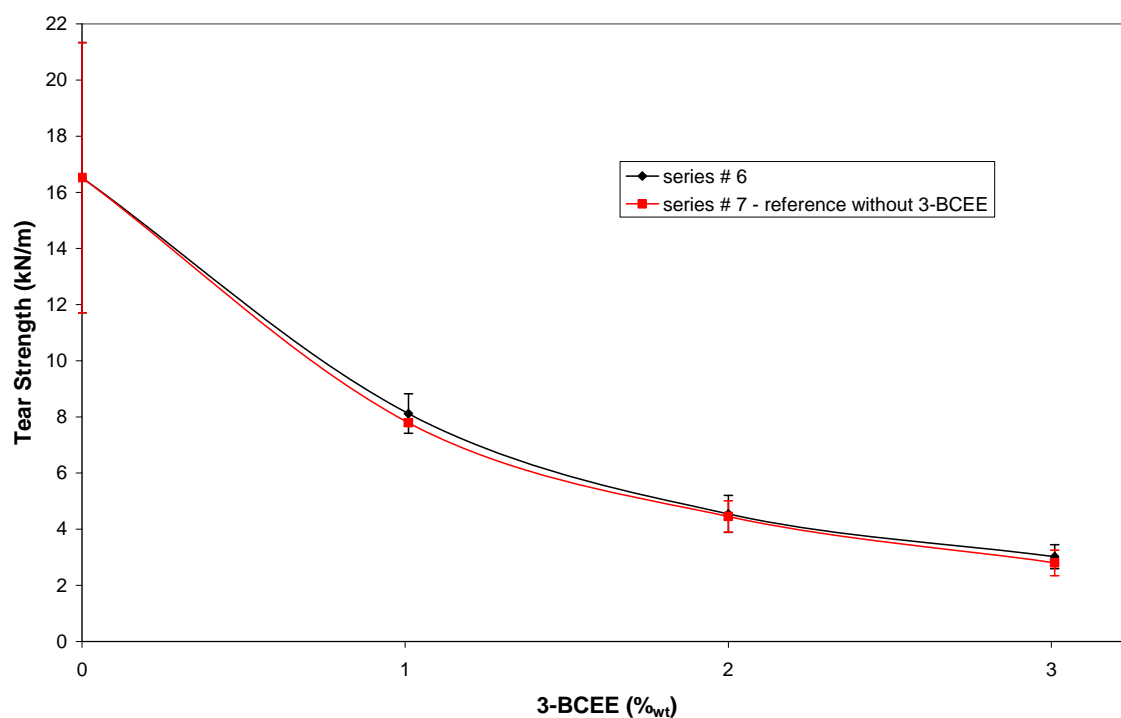


Fig. 97: Tear strength of series # 6 and series # 7: No significant difference can be seen between the two series. The decrease is caused by the additionally added cross-linker U 430.

10.3.2 Series # 8

The tear strength of series # 8 decreases with increasing amount of 3-BCEE, as can be seen in **Fig. 98**. This is not surprising, as the 3-BCEE carrier which was admixed to the silicone precursors is a non-functionalized carrier, which does not form any covalent bonds to the silicone backbone. Hence, no bonds which could enhance the mechanical properties of the three-dimensional network are formed. The large error bars of the samples and the variations in the shape of the curve are attributed to the inhomogeneity of the silicone mixtures caused by insufficient mixing of the silicone precursors.

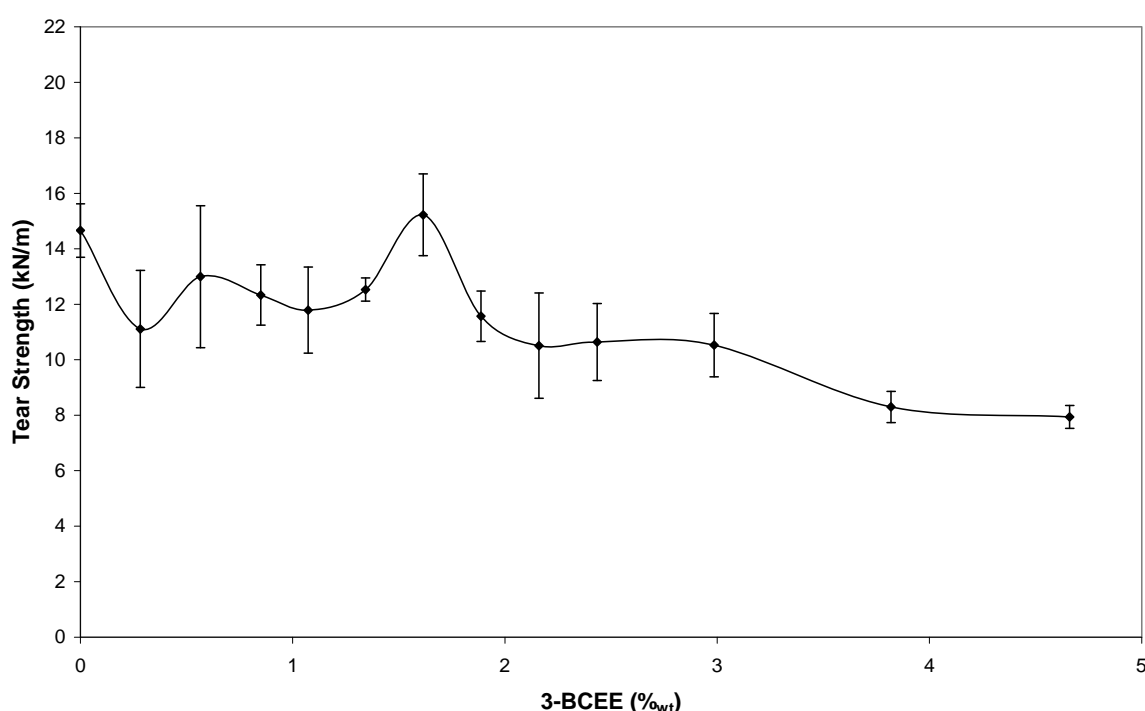


Fig. 98: Tear strength of series # 8: With increasing amount of 3-BCEE the tear strength decreases. Large error bars and variations in the curve shape are attributed to inhomogeneous silicone mixtures.

10.4 Conclusions

In the catalogue of Momentive Performance Materials the following values are given for the mechanical properties of the commercially available Silopren[®] types LSR 4030...4070: Elongation (DIN 53504, S2) 400...800%, tensile strength (DIN 53504, S2) 8.0...10.0 MPa,

hardness (DIN 53505, Shore A) 31...70, density (DIN 53479 A) 1.10...1.14 g/cm³, and tear strength (ASTM D 624, die B) 18...35 kN/m[158].

The maximum values for the elongation at break and the tensile strength that were obtained in the 12 series of silicone by using P 1300, U 430, and U 1 were ~440% and ~9 MPa, respectively. Thus, in comparison to the commercially available Silopren[®] types 4030...4070, the materials produced here without any SME-candidates or carriers were well in the range of the commercially available materials. Using 3-BCEE by attaching it directly to the silicone backbone or using a 3-BCEE or DMAM carrier produced significantly lower results. But while the materials containing SME-candidates or carriers show tensile properties too low as if to be able to compete with the commercially available materials on the market, the mechanical properties do suffice as if to allow for the use of the thus modified materials for research purposes.

Measurement of the hardness and the tear strength were conducted only as a descriptive means. The values for Shore hardness A which were found in the 12 silicone series as produced here ranged from ~44 to ~71, which is well in the range of the commercially available materials used for comparison.

The maximum values of the tear strength were ~15.2 kN/m, which is at the lower end of the range of the commercially available materials. Silicones which were modified by attaching 3-BCEE directly to the silicone backbone performed drastically worse, while the silicone in series # 8 showed a decrease of the initial values of ~48%.

The overall conclusion from tensile and tear testing is that any change which is made to the three-dimensional network of the silicone will alter, i.e. most likely reduce, the tensile properties and tear strength. This is especially true when the chemical change is so extensive, as the changes that were made here. The effect was less pronounced but still significant when non-functionalized carrier was admixed. In order to maintain the high mechanical properties of the silicone, however, a functionalized carrier would have to be used. That way the carrier could contribute to the mechanical properties in such a manner, as if to replace the silicone which is displaced by the admixing of a carrier.

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11 Light microscopy

Light microscopy was used to document the series # 9 to # 12. The purpose was to show how the admixing of the carriers changed the silicone from colorless to opaque. Furthermore, in some cases mixtures with an inhomogeneous composition or uneven structures could be observed. The samples that were photographed are band shaped with a width of 7 mm and of 1 mm thickness. They were produced by injection molding using the same equipment and technique like for the samples for mechanical testing.

Fig. 99 shows the mixture Si 040, which was produced using only the Silopren[®] precursors P 1300, U 430, and U 1. It is the mixture with a ratio of P 1300 to U 1 of 15: 1, and Si-H to vinyl of 2.5:1. This mixture represents the basic mixture to which the four carriers were admixed. The particles within the material and on its surface are dirt and dust. Since the mixture is colorless particles within the sample and on both the top and the bottom surface can be seen. The scratches in the surface are a reproduction of the scratches in the injection mold which was used for the production of all the samples. Please note for all light microscopy pictures that only the top light of the microscope was used. The background and the sample holder, which is a glass table, therefore appear black.

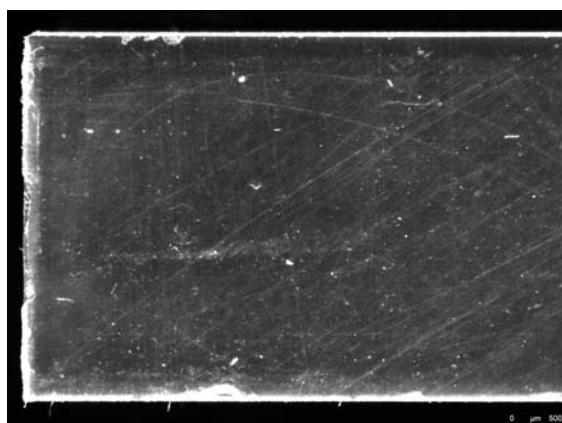


Fig. 99: Light microscopy picture of silicone mixture Si 040: This is the mixture produced only from Silopren[®] precursors P 1300, U 430, and U 1. The particles within the material and on its surface are dirt and dust, while the scratches in the surface are a reproduction of the scratches in the injection mold.

11.1 Series # 9

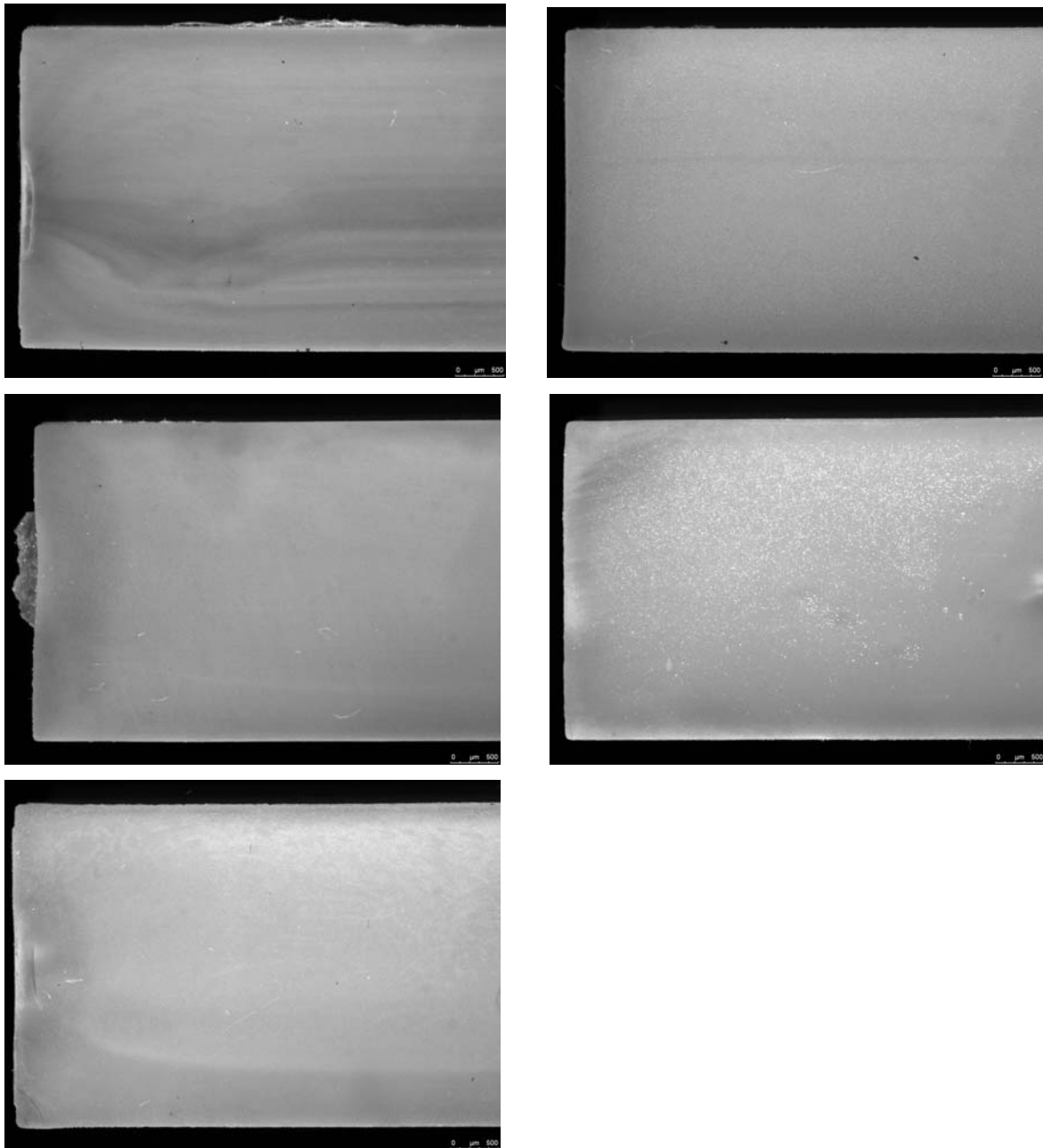


Fig. 100: Light microscopy picture of silicone mixture Si 041 (top left), Si 042 (top right), Si 043 (middle left), Si 044 (middle right), and Si 045 (bottom). All mixtures are opaque, showing different degrees of inhomogeneity. In the picture of sample Si 041 the flow of the mixture in the mold can be seen.

Fig. 100 shows the photographs of series # 9. All samples are opaque, and the flow of the mixture in the injection mold can be seen well for the mixture Si 041 (top left). The mix-

ture was injected into the mold on the middle of the left hand side, the air outlet was on the right. It is assumed that the inhomogeneity is not a result of a demixing process which takes place during the injection of the mixture into the mold, but that insufficient mixing in the speed-mixer is the cause.

11.2 Series # 10

The mixtures of series # 10 are shown in **Fig. 101**. As in series # 9 all samples are opaque, showing a different degree of inhomogeneity. The mixtures Si 048 and Si 049 exhibit an uneven porous structure, which may be the result of insufficient mixing or phase separation at molecular level. It is clear that such a structure must have a weak performance in tensile testing, and may be inapplicable as isolation material for cardiac pacing leads.

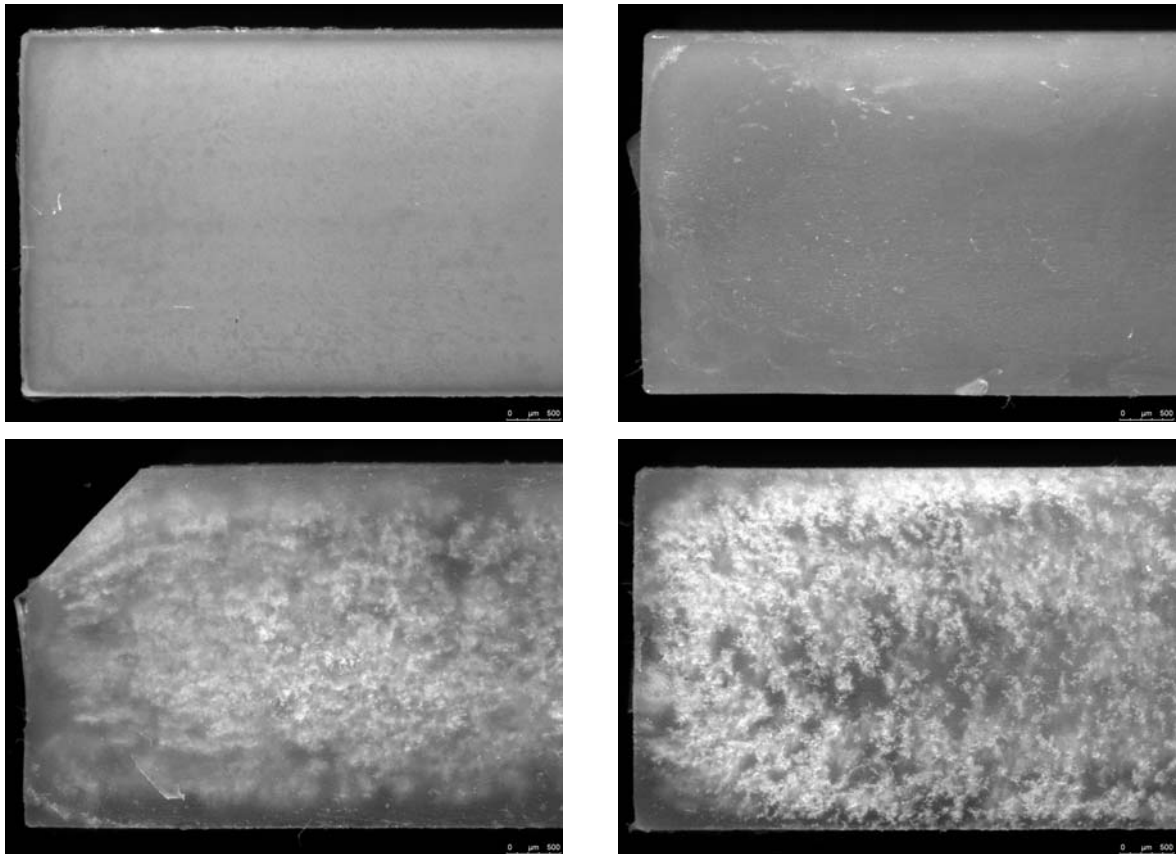


Fig. 101: Light microscopy picture of silicone mixture Si 046 (top left), Si 047 (top right), Si 048 (bottom left), and Si 049 (bottom right). As in series # 9 all mixtures are opaque, showing different degrees of inhomogeneity. In the pictures of samples Si 048 and Si 049 an uneven porous structure is visible.

11.3 Series # 11

Fig. 102 shows the mixtures of series # 11. As above in both the series # 9 and # 10 all samples are opaque. Different degrees of inhomogeneity are visible, which is a sign for incomplete mixing of the silicone precursors.

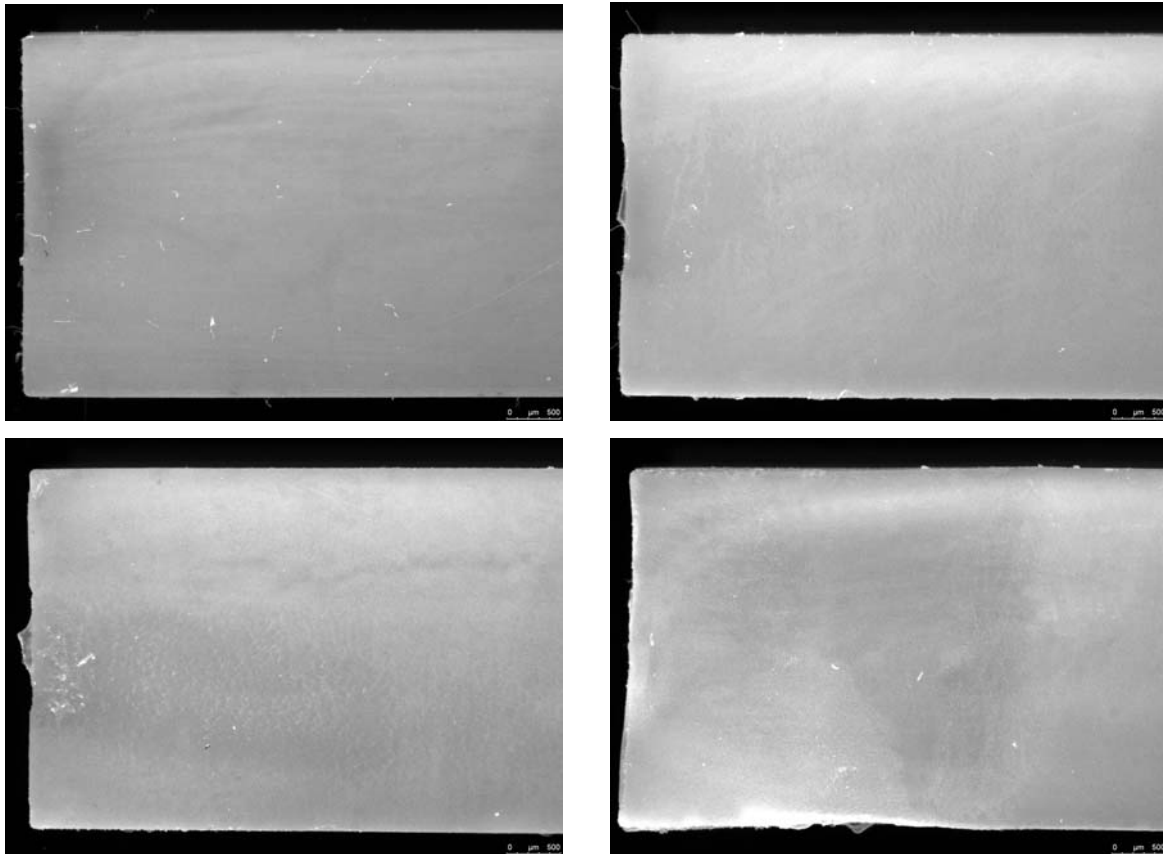


Fig. 102: Light microscopy picture of silicone mixture Si 050 (top left), Si 051 (top right), Si 052 (bottom left), and Si 053 (bottom right). As in the two previous series all mixtures are opaque, again showing different degrees of inhomogeneity.

11.4 Series # 12

In **Fig. 103** the photographs of series # 12 can be seen. Once again all samples are opaque and exhibit different degrees of inhomogeneity. The mixture Si 056 contains pores at macroscopical level. The cause of the inhomogeneity may be either insufficient mixing before the injection molding or phase separation in the mold while the mold is heated during the

polymerization step. The shape of the pores does not allow for an indisputable statement to whether the pores are formed by air in the mixture or by material “falling out” of the sample. Such a “falling out” can be imagined in the case that the DMAM carrier was not mixed well enough and therefore not entangled enough with the silicone precursors. Also, it can be imagined that phase separation may allow for material “falling out”. As for series # 10 it is clear that such a material will have poor performance in tensile testing, and will certainly be inapplicable as isolation material for cardiac pacing leads.

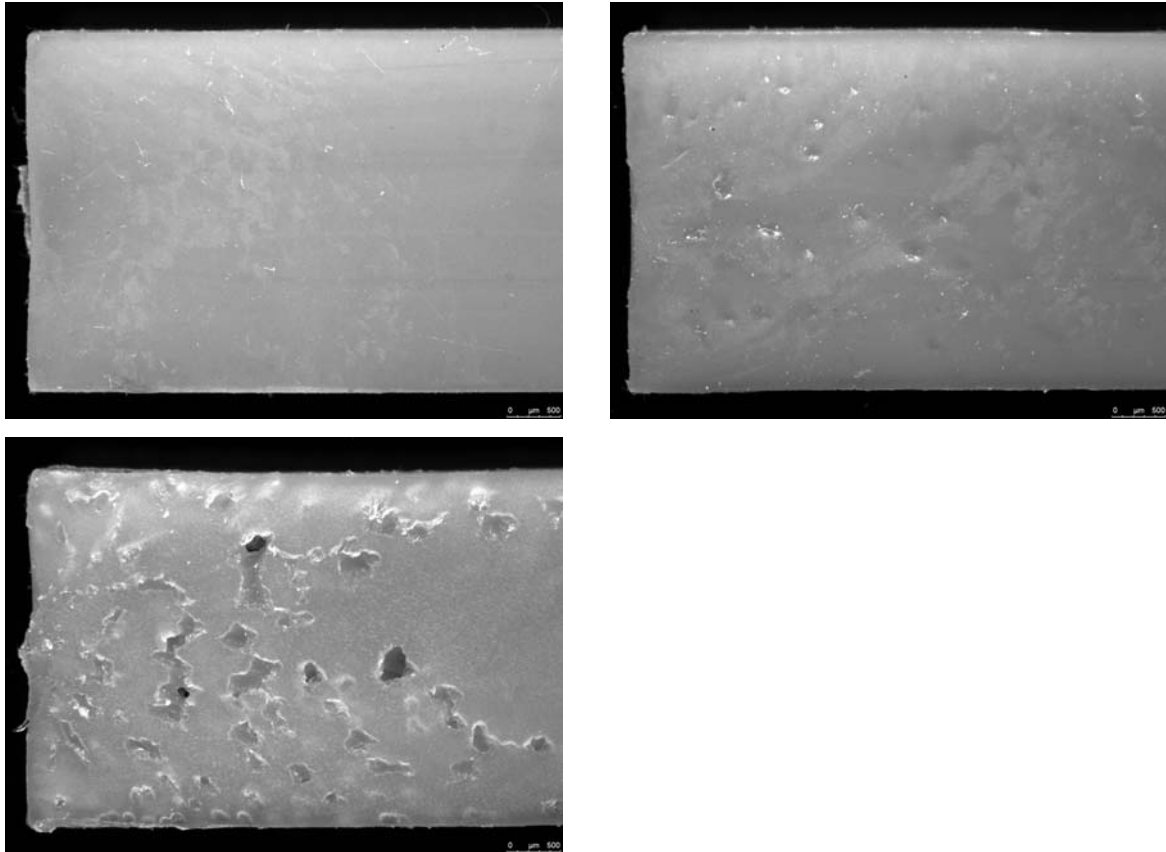


Fig. 103: Light microscopy picture of silicone mixture Si 054 (top left), Si 055 (top right), and Si 056 (bottom). Not surprisingly, all mixtures are again opaque and show different degrees of inhomogeneity. The sample of mixture Si 056 has pores at macroscopical level. It is not clear, whether the pores are caused by air in the silicone mixture, or if material “fell out” due to insufficient mixing of the silicone precursors or phase separation.

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12 Protein adhesion to silicone series # 9 to # 12

Two different methods for measuring the protein adhesion to silicone were examined with regard to their applicability in this study. The first was using the commercially available Pierce BCA Protein Assay Kit from Thermo Fischer Scientific Inc., Rockford, USA, and the second method was an ELISA protocol using OVA, two antibodies with one of them being HRP conjugated, and TMB substrate. Please refer to **chapter 4 Materials and methods** for more details. The four series # 9 to # 12 were examined.

12.1 BCA assay

For using the BCA assay, first the compatibility of the BCA assay with BSA and OVA was examined. Standard curves for different concentrations of both BSA and OVA were made, using dilution series with concentrations ranging from $7.81 \cdot 10^{-4}$ mg/mL to 0.2 mg/mL. As result, no difference in the optical signal can be seen between the two, see **Fig. 104**.

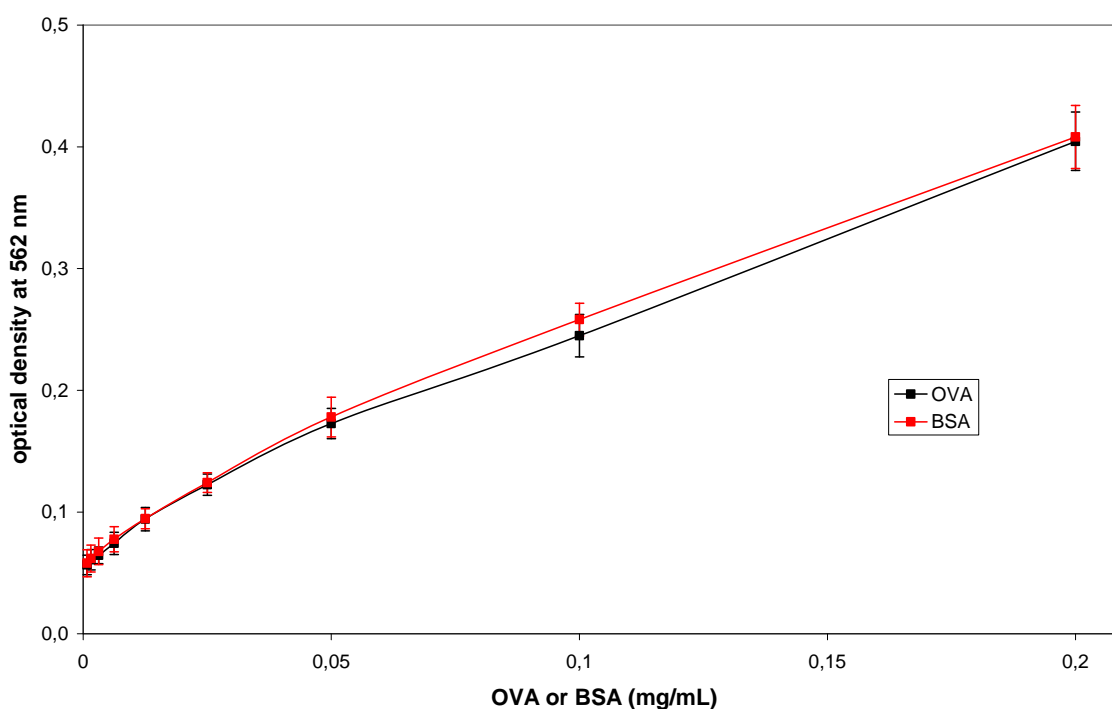


Fig. 104: Standard curves of the BCA assay for BSA and OVA, no difference in the optical signal can be seen between BSA and OVA.

In a second step FBS was used. Samples of the silicone mixture Si 040 were immersed in it for 2 days at 37°C to allow for adhesion of protein to the silicone surface. The BCA assay was tested on the FBS alone, on the FBS in which the silicone samples had been immersed, and on the silicone samples which were exposed to the FBS. **Fig. 105** shows the read out of the optical density. For the FBS alone and the FBS in which the silicone samples had been immersed, no difference in the signal intensity can be seen. For the silicone samples, however, the signal intensity was the same for all concentrations. It must be concluded that the BCA assay either does not work with protein which adheres to the silicone surface, or that the amount of protein on the silicone surface was below the detection limit of the assay. The latter assumption is the more probable one. In consequence, the BCA assay was not used for further studies.

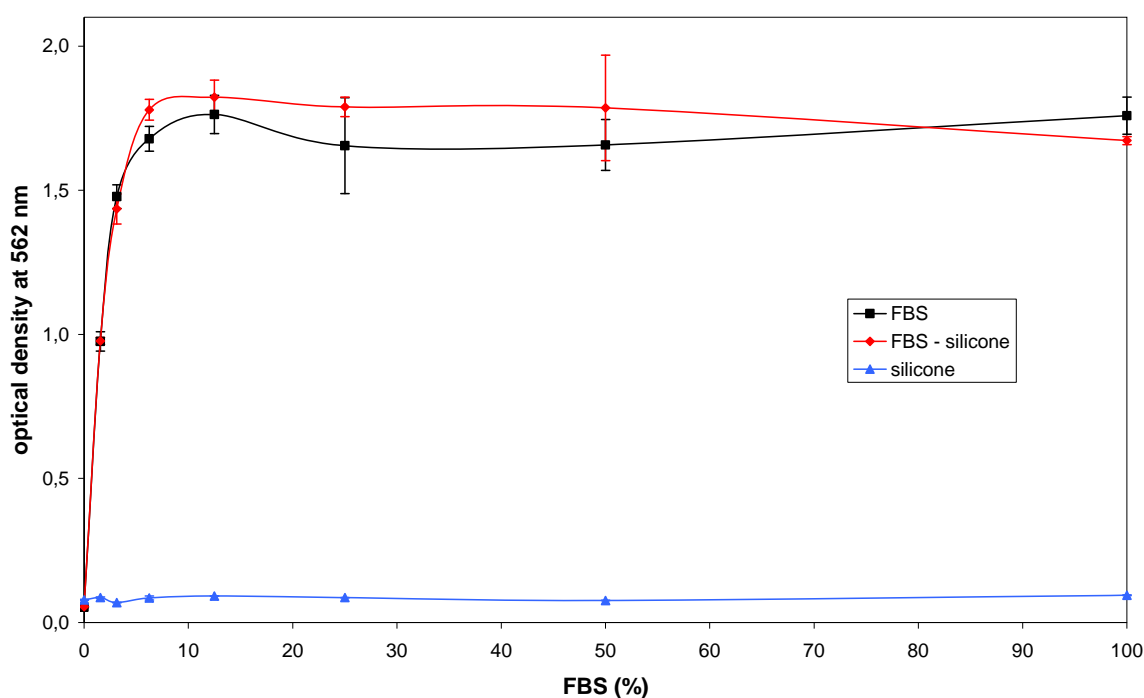


Fig. 105: Optical density of the BCA assay for FBS, FBS in which silicone samples had been immersed, and the silicone samples which were immersed. No difference in the optical signal can be seen between the FBS and the FBS in which the silicone samples had been placed. The silicone samples themselves do not have different signal intensities.

12.2 ELISA

In this approach the silicone samples were exposed to solutions of OVA with different concentrations. The OVA was then tagged with a primary antibody, which in turn was tagged with a secondary HRP conjugated antibody. TMB substrate was used as an indicator. Below, **Fig. 106**, **Fig. 107**, **Fig. 108**, and **Fig. 109** show the signal for series # 9 to # 12. In all four series the optical density of the mixtures containing one of the carriers is lower than the signal of the mixture without any carrier, i.e. Si 040. However, there is no difference between the mixtures containing one of the four carriers, even though the amount of carrier in the mixtures was varied. Since all four series produce very similar results, an influence of the molecular weight of the carrier on the protein adhesion can not be noticed - the carriers for series # 9 and # 10 were of low molecular weight, and the carriers for series # 11 and # 12 of medium molecular weight.

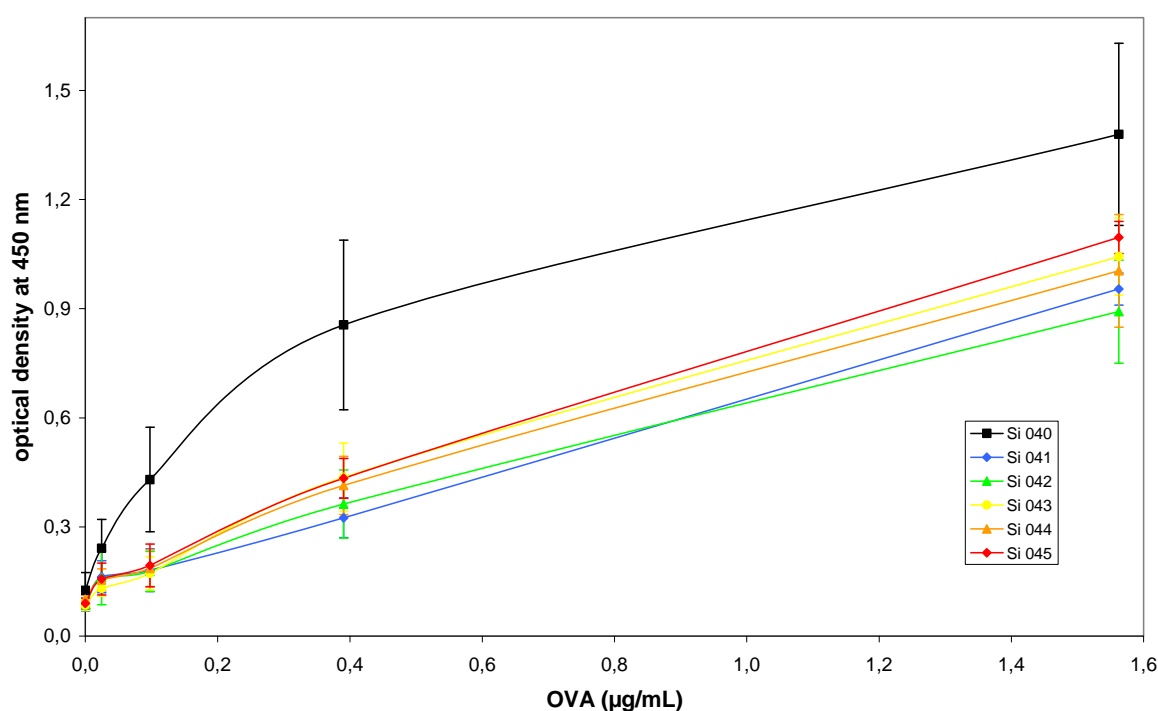


Fig. 106: ELISA of series # 9, the optical density of the mixtures containing the 3-BCEE carrier of low molecular weight is lower than the signal of the mixture without any carrier, i.e. Si 040.

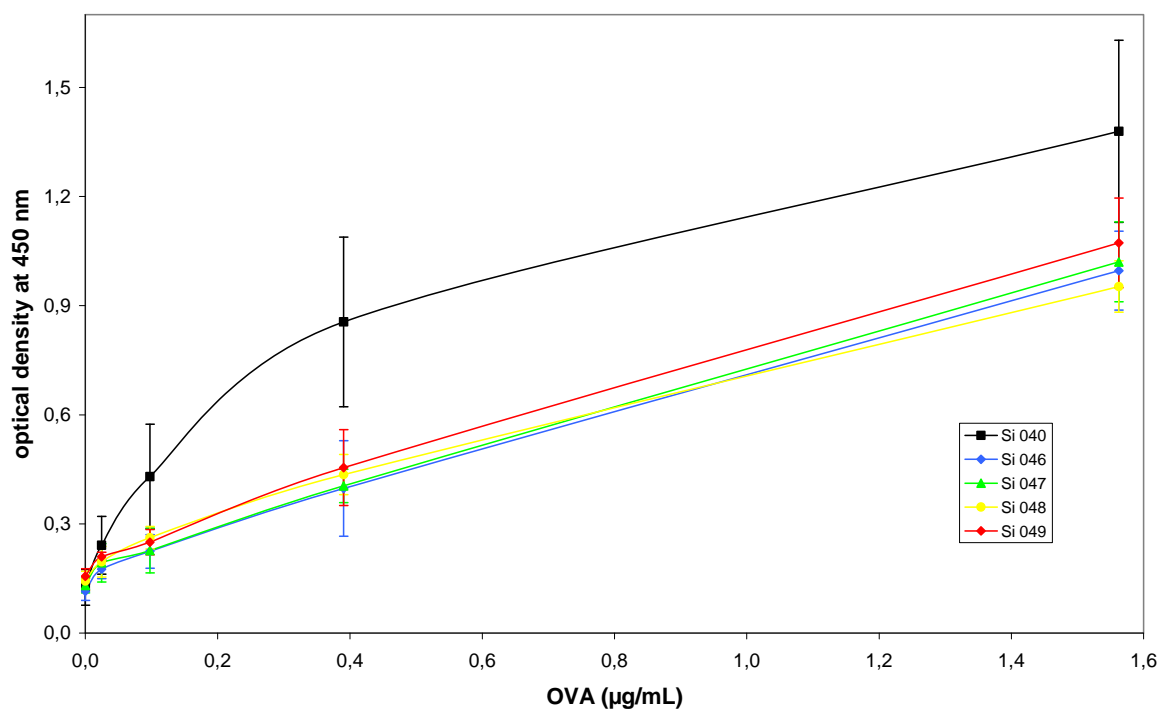


Fig. 107: ELISA of series # 10, the optical density of the mixtures containing the DMAM carrier of low molecular weight is lower than the signal of the mixture without any carrier, i.e. Si 040.

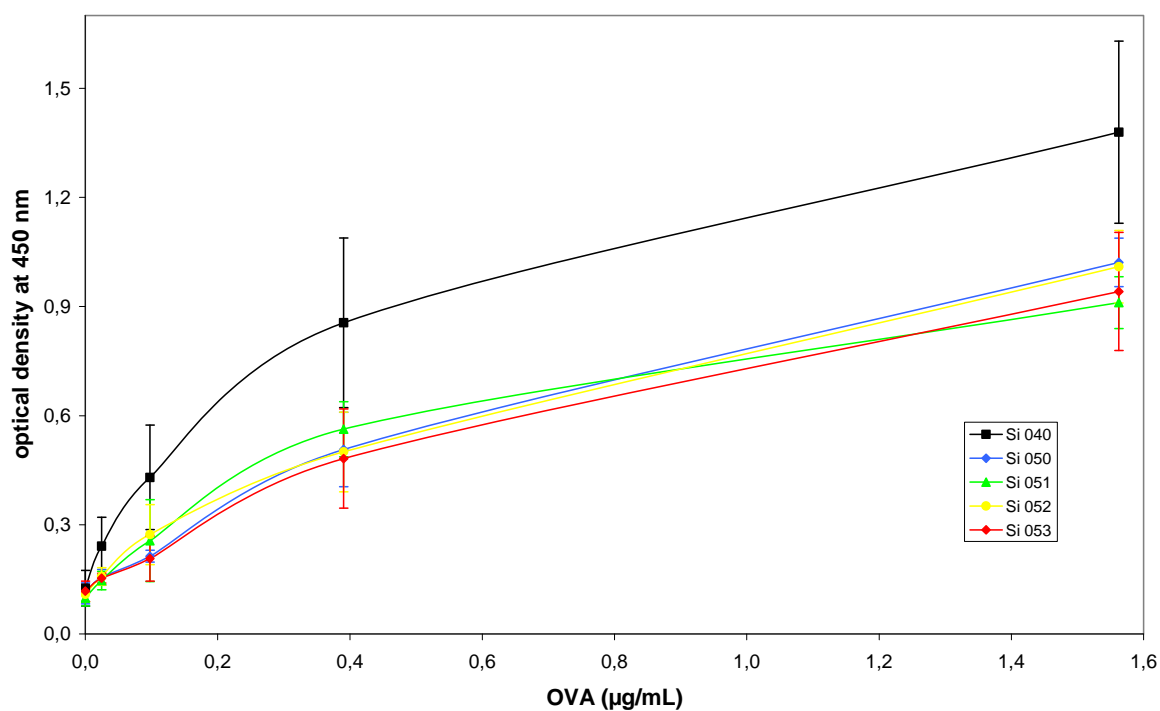


Fig. 108: ELISA of series # 11, the optical density of the mixtures containing the 3-BCEE carrier of medium molecular weight is lower than the signal of the mixture without any carrier, i.e. Si 040.

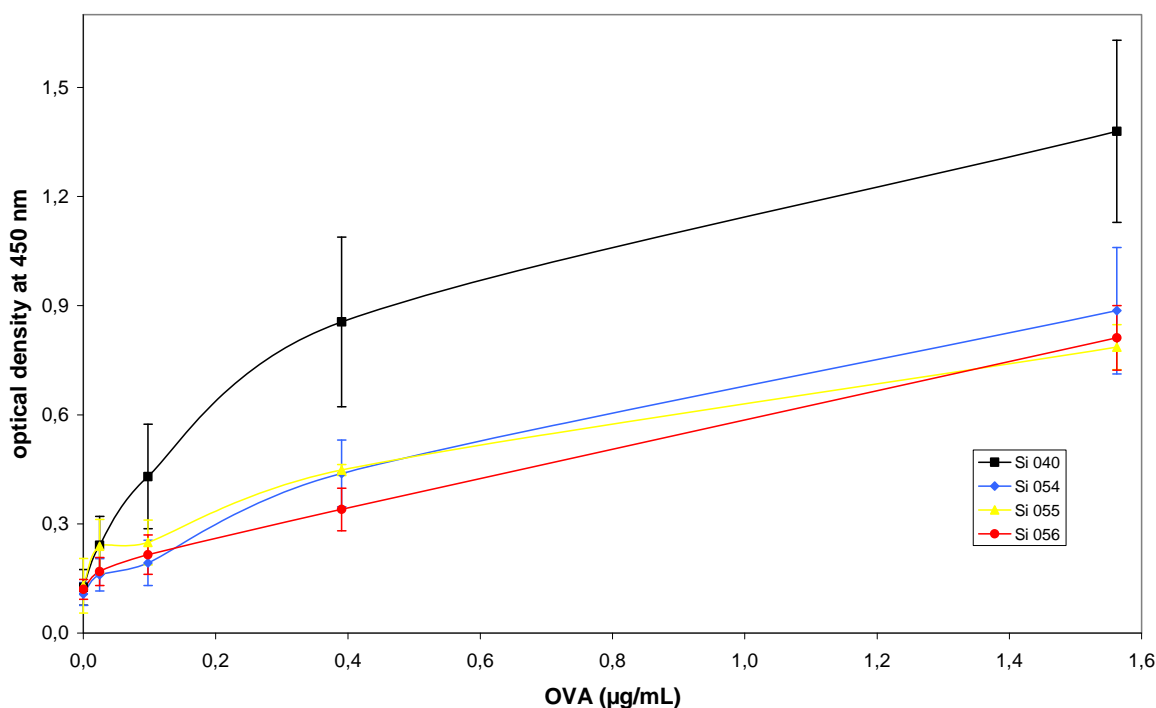


Fig. 109: ELISA of series # 12, the optical density of the mixtures containing the DMAM carrier of medium molecular weight is lower than the signal of the mixture without any carrier, i.e. Si 040.

It must be noted that the conclusiveness of this approach is rendered in question by the fact that the ELISA worked only for rather low concentrations of OVA, i.e. up to 1.6 µg/mL. In comparison, the concentrations of proteins in the human blood are up to $5 \cdot 10^4$ times higher. Furthermore, OVA is not present in the human blood and was used here only because the ELISA using OVA is well established and was available. Another important point is that the materials were tested as produced. It can not be assumed that any hydrolysis of the 3-BCEE and DMAM has occurred. Materials containing carriers which have undergone hydrolysis at the material's surface may perform differently.

12.3 Conclusions

Only the ELISA but not the BCA assay yielded results allowing for interpretation about the protein adhesion to the silicones. The BCA assay, which is made for the use with solutions, is either not sensitive enough, or does not work with proteins which are attached to a surface. According to the ELISA the materials containing one of the carriers perform better,

i.e. show less protein adhesion. However, the ELISA is not representative for the conditions which will be found in human blood. Furthermore, the samples were used as produced, i.e. prior to any hydrolysis of the 3-BCEE and DMAM which they contained. Hence, the hydrophilic carboxylic acid groups presenting a negative charge were not yet produced. After hydrolysis of these two components on the surface or within surface near regions the materials may perform differently. It is assumed that the materials will show even less protein adhesion once the SME-candidates have undergone hydrolysis.

13 Exposure of silicone series # 9 to # 12 to hydrolyzing medium

In order to hydrolyze the 3-BCEE and the DMAM in the silicone series # 9 to # 12 the samples were exposed to a saturated Na_2CO_3 buffer solution at 80°C for up to 16 days. FTIR spectra of the surface and the bulk material were recorded after this treatment in order to determine the impact of the buffer solution on the 3-BCEE and the DMAM. For measuring the bulk material the samples were simply cut in half with a razor blade. **Fig. 110, Fig. 111, Fig. 112, and Fig. 113** show the measurement at the samples' surfaces. Please note that the scale bar of the Y-axis was kept identical with the scale bar used in the original measurements after the production to allow for comparison, see **chapter 9 Production of 12 series of silicone**. There, the peaks after the production are shown in **Fig. 65, Fig. 67, Fig. 69, and Fig. 71**. Comparison with the initial peaks of the samples shows that the peaks are decreased in all mixtures in all four series, and some are reduced to zero. A possible explanation is that the exposure to saturated Na_2CO_3 buffer solution leached the carriers out of the surface near regions, thus reducing the signal intensity.

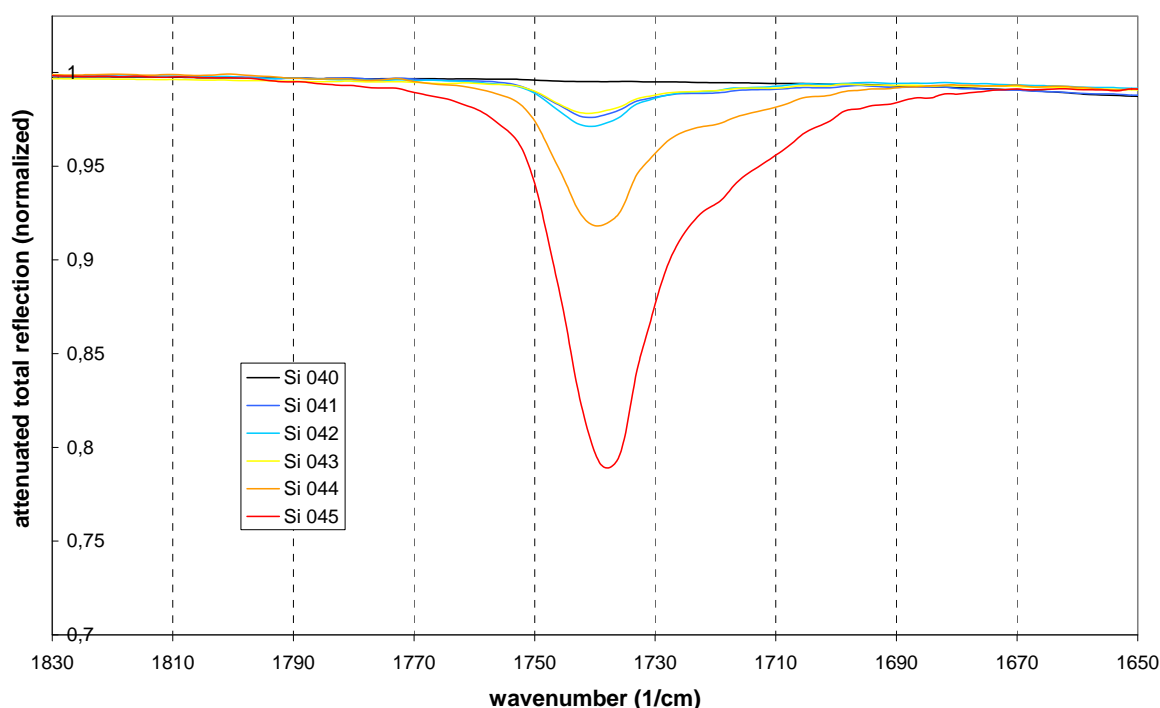


Fig. 110: FTIR at the surface of series # 9 after 16 days in Na_2CO_3 buffer: The peaks of the carboxylic group at 1740 cm^{-1} are reduced in size as compared to the peaks measured after the production of the samples.

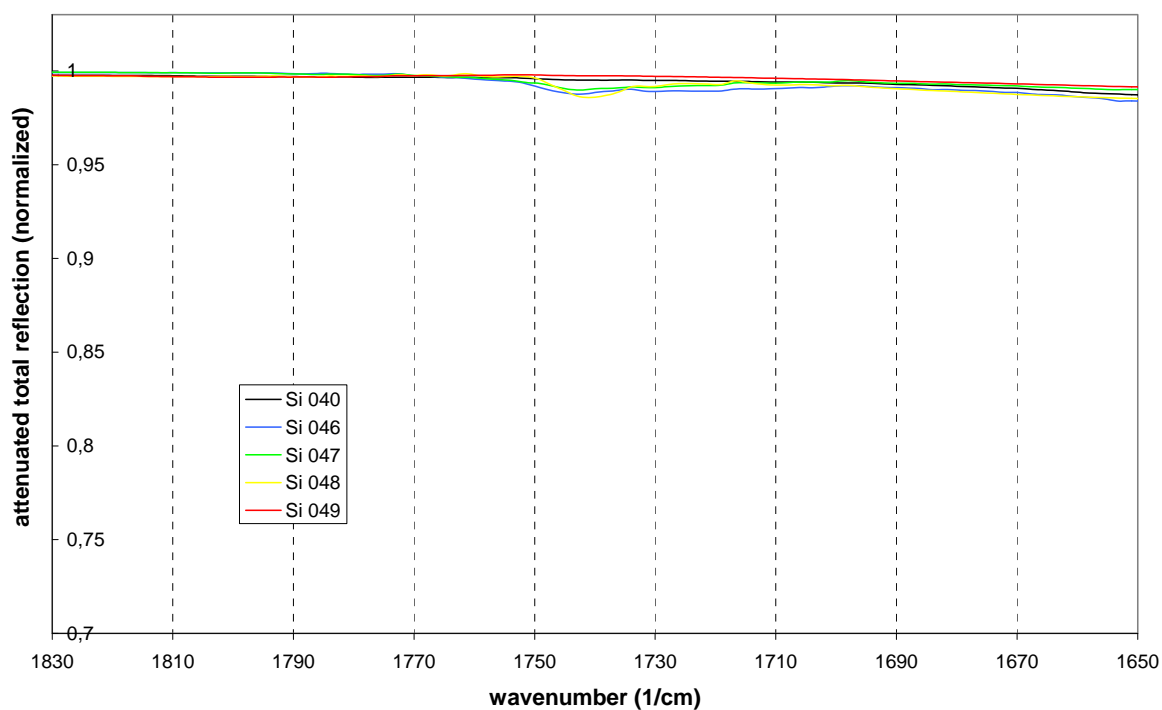


Fig. 111: FTIR at the surface of series # 10 after 16 days in Na_2CO_3 buffer solution: The peaks of the carboxylic group at 1740 cm^{-1} are reduced to zero.

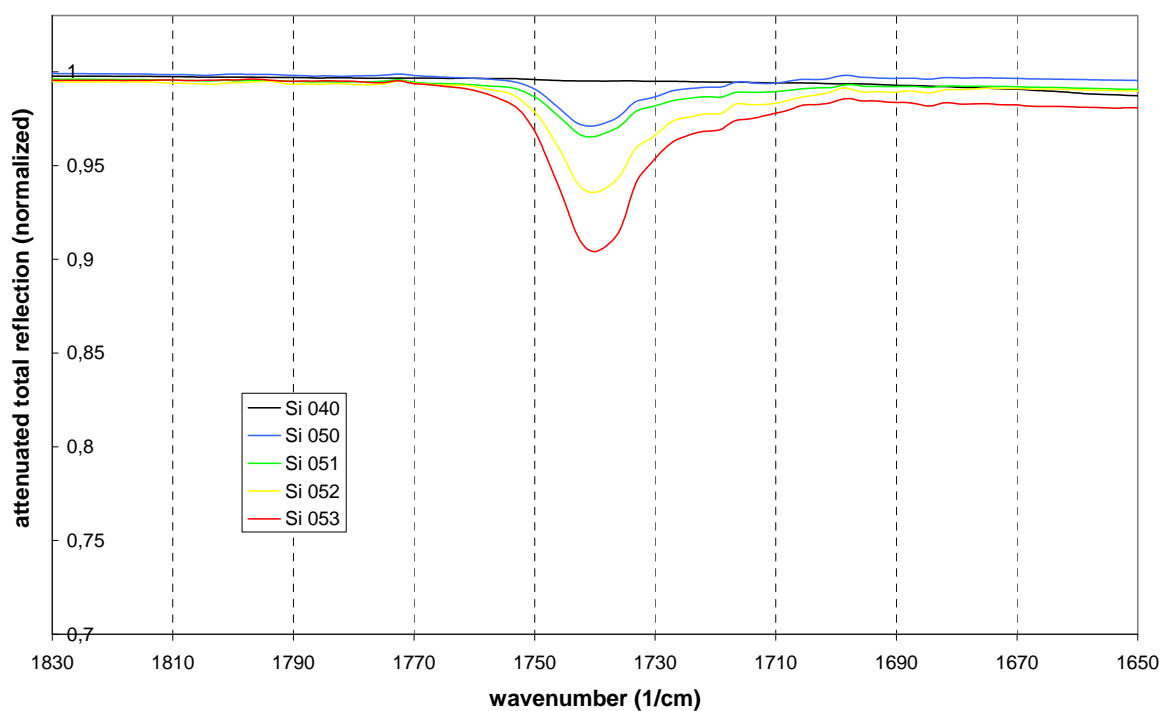


Fig. 112: FTIR at the surface of series # 11 after 16 days in Na_2CO_3 buffer: The peaks of the carboxylic group at 1740 cm^{-1} are reduced in size as compared to the peaks measured after the production of the samples.

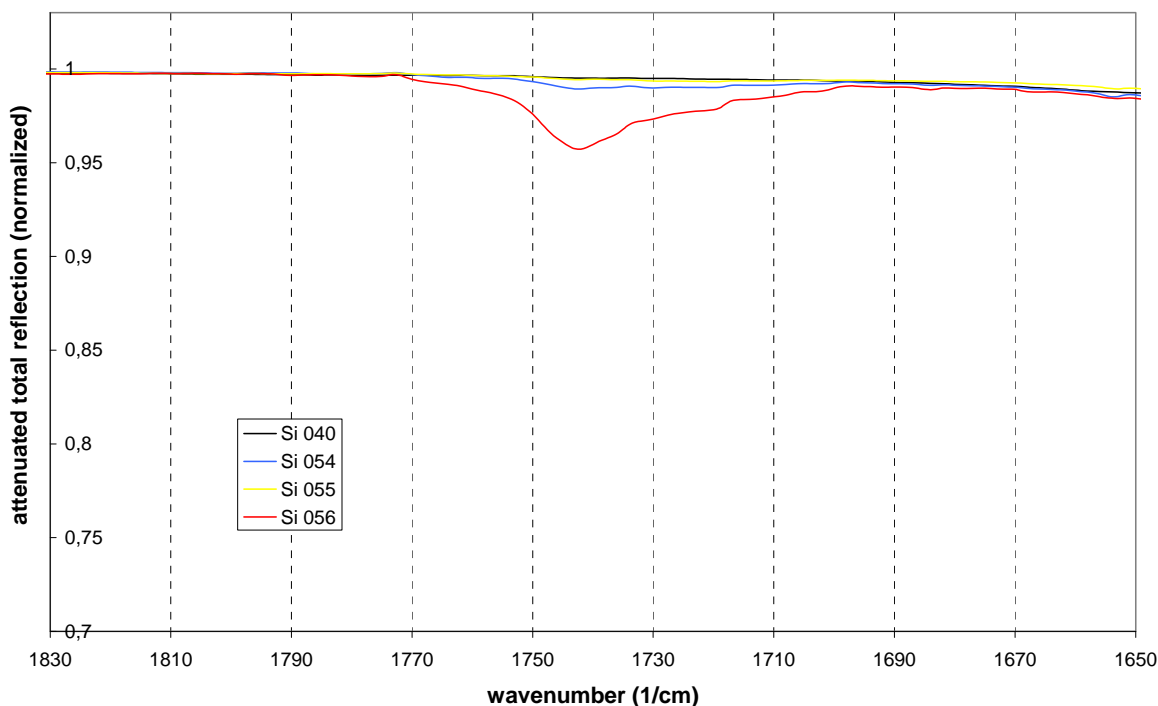


Fig. 113: FTIR at the surface of series # 12 after 16 days in Na_2CO_3 buffer: The peaks of the carboxylic group at 1740 cm^{-1} are reduced in size as compared to the peaks measured after the production of the samples.

Below, **Fig. 114**, **Fig. 115**, **Fig. 116**, and **Fig. 117** show the enlarged view of the carboxylic peak at 1740 cm^{-1} in the bulk material after 16 days in Na_2CO_3 buffer solution. The signal intensity is higher in all mixtures as compared to the signal at the surface after 16 days in Na_2CO_3 buffer solution. This supports the theory that the carrier molecules may have been leached from the surface near regions during the exposure to Na_2CO_3 buffer solution.

It is noteworthy that the signals of the 3-BCEE containing series # 9 and # 11 in **Fig. 114** and **Fig. 116** are similar to the original measurements after production, see **Fig. 65** and **Fig. 69** for comparison. In contrast, the signals of the DMAM containing series shown in **Fig. 115** and **Fig. 117** have changed notably from their initial intensities displayed in **Fig. 67** and **Fig. 71**. Furthermore, **Fig. 115** even suggests a higher loss of intensity for samples containing a higher concentration of the DMAM carrier of low molecular weight. Hence, the treatment of the silicone series # 9 to # 12 does not only affect the materials' surface, but also the bulk. Since the carriers are not covalently bonded to the silicone backbone, diffusion of the carriers within the bulk and also leaving the bulk may be possible.

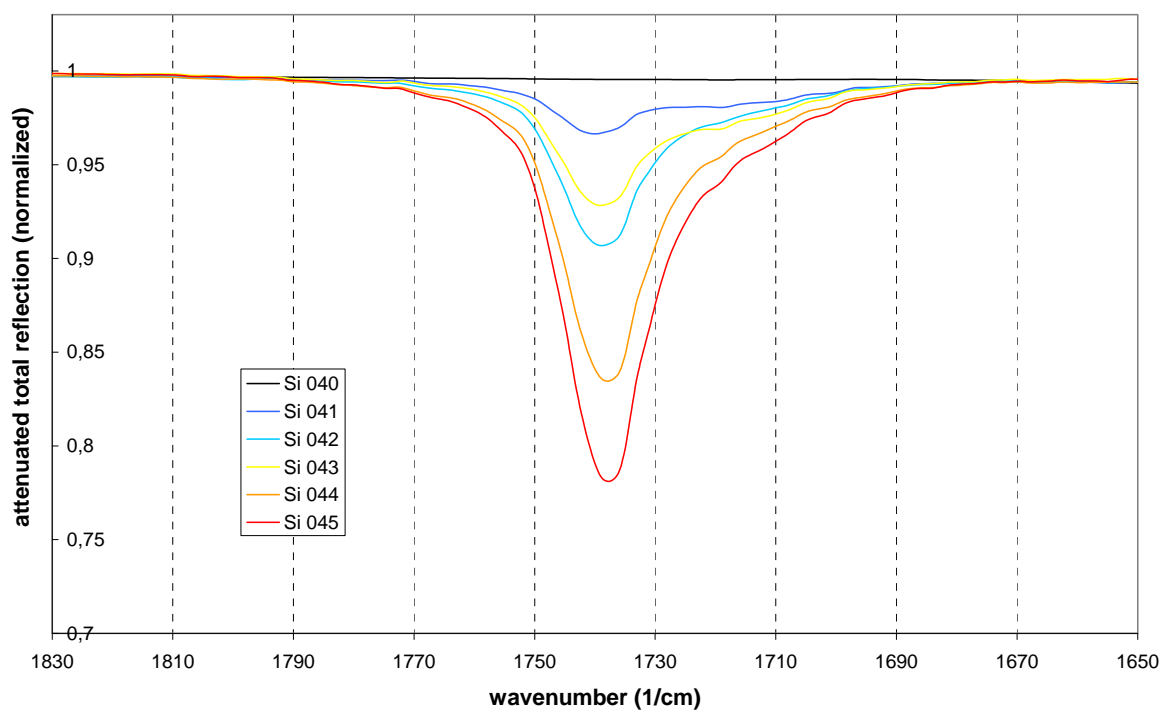


Fig. 114: FTIR in the bulk of series # 9 after 16 days in Na_2CO_3 buffer solution: The peaks of the carboxylic group at 1740 cm^{-1} are similar to those measured after the production of the samples.

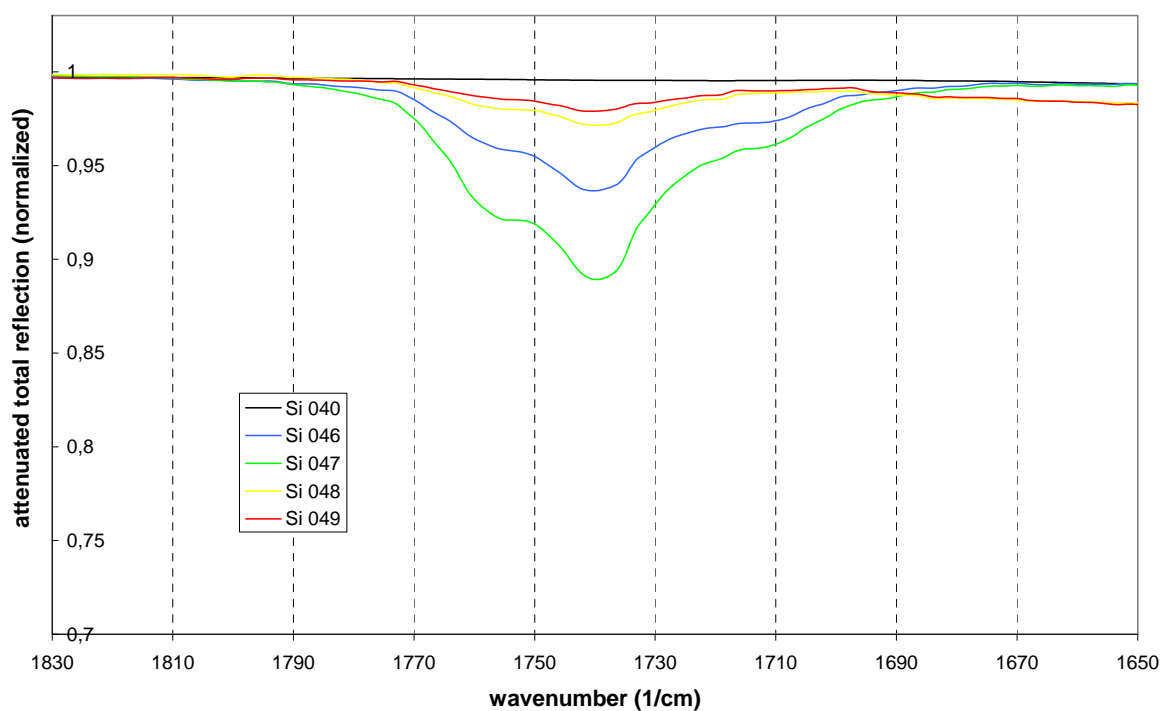


Fig. 115: FTIR in the bulk of series # 10 after 16 days in Na_2CO_3 buffer solution: The peaks of the carboxylic group at 1740 cm^{-1} are reduced in size as compared to the peaks measured after the production of the samples.

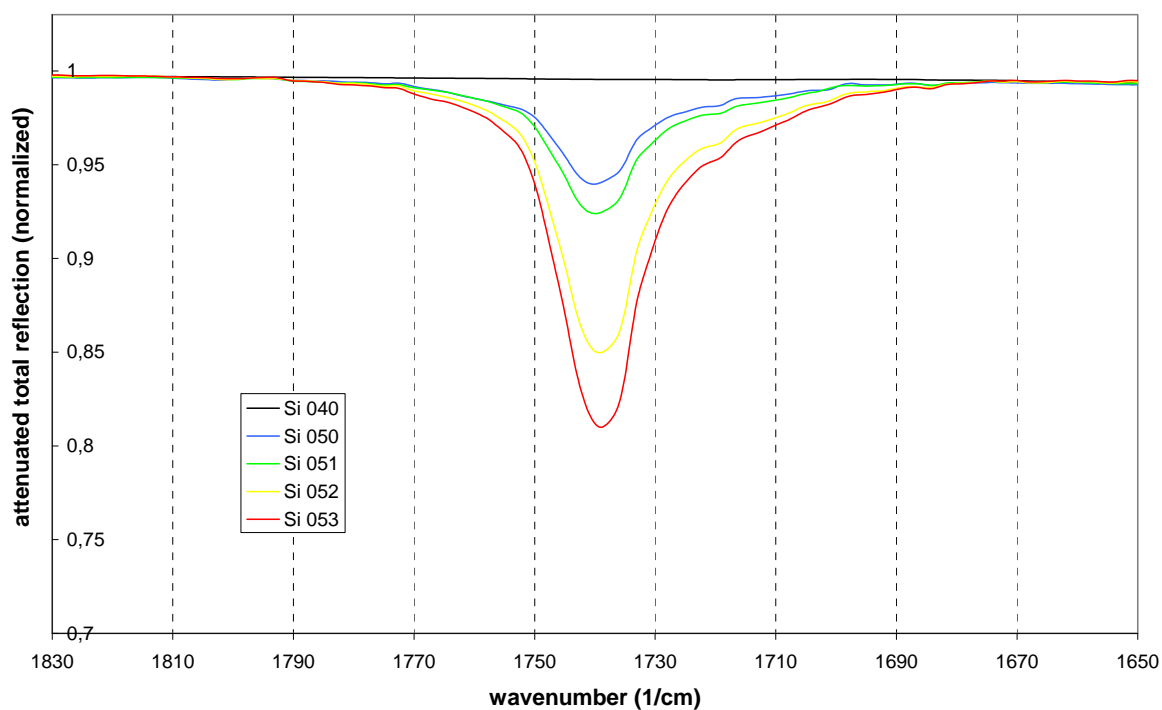


Fig. 116: FTIR in the bulk of series # 11 after 16 days in Na_2CO_3 buffer solution: The peaks of the carboxylic group at 1740 cm^{-1} are similar to those measured after the production of the samples.

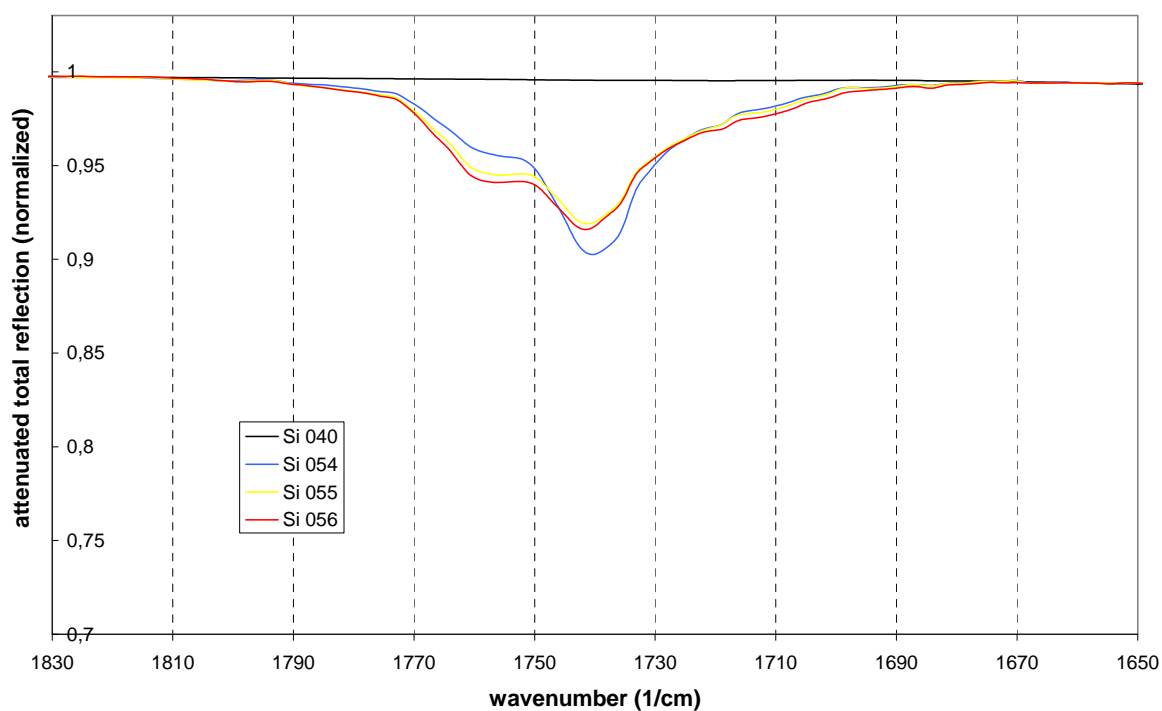


Fig. 117: FTIR in the bulk of series # 12 after 16 days in Na_2CO_3 buffer solution: The peaks of the carboxylic group at 1740 cm^{-1} are reduced in size as compared to the peaks measured after the production of the samples.

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14 Water uptake of silicone series # 9 to # 12

The water uptake of the silicone series # 9 to # 12 was investigated after 16 days of treatment with saturated Na_2CO_3 buffer solution. The calculation only involved the measurement of the sample weight directly after the treatment with the buffer solution, and a second measurement after drying the samples over night. This way, the need for determination of the mixtures' densities was avoided. It is clear that the densities will vary with the amount of carrier which is added to the silicone precursors. However, the densities of the mixtures are of no importance in this study, whereas the water uptakes of the mixtures are of major importance. This is due to the fact that the silicone should only become hydrophilic on its surface. The goal is to develop a system in which the SMEs only undergo hydrolysis in the surface near regions. If SMEs within the bulk underwent quantitative hydrolysis, the bulk material may become hydrophilic. This may in turn result in extensive swelling, causing the loss of the original shape, and the loss of the electrical insulation. Both would be unacceptable and render the material inapplicable as pacing lead insulator.

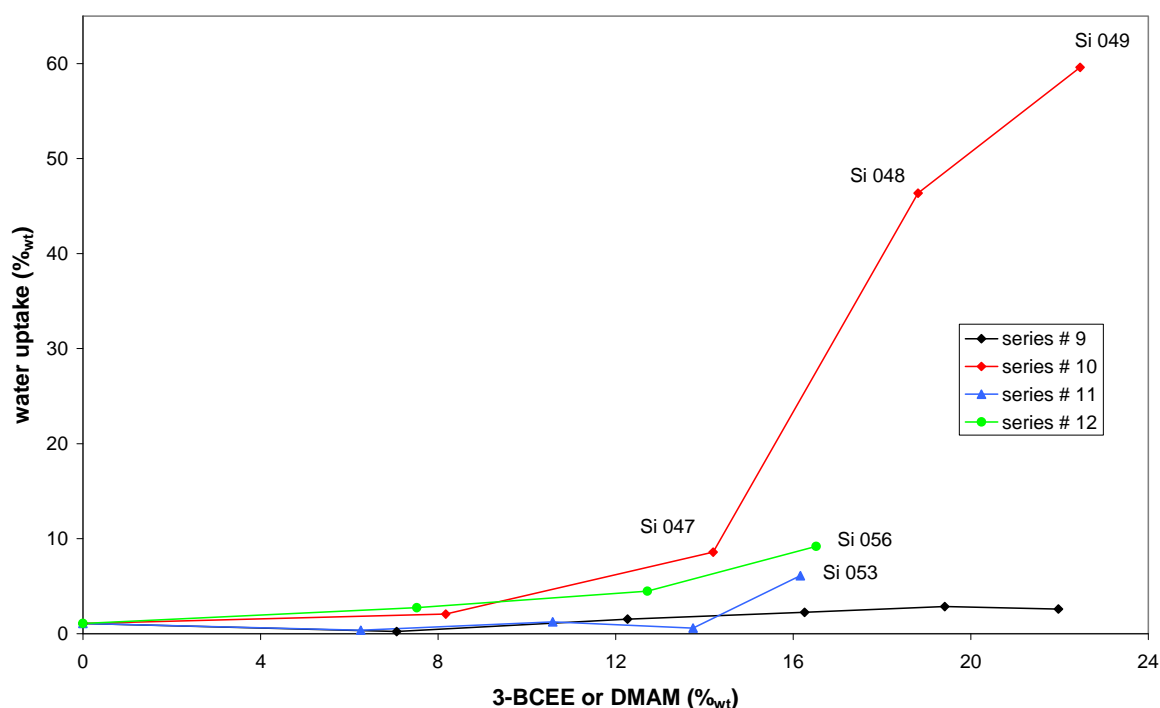


Fig. 118: Water uptake of series # 9 to # 12 after 16 days in Na_2CO_3 buffer solution, the mixtures with the highest water uptake are pointed out, i.e. Si 047...049 of series # 10, Si 053 of series # 11, and Si 056 of series # 12.

Fig. 118 shows the water uptake of the silicone series # 9 to # 12 after 16 days of immersion in Na_2CO_3 buffer solution. The mixture with the highest water uptake are pointed out, i.e. Si 047 to Si 049 of series # 10, Si 053 of series # 11, and Si 056 of series # 12. As water uptake is a bulk property, these five mixtures have to be discussed with regard to the results from **chapter 11 Light microscopy**, and **chapter 13 Exposure of silicone series # 9 to # 12 to hydrolyzing medium**.

The samples of Si 047 to Si 049 of series # 10 were shown above in **Fig. 101**. Only Si 048 and Si 049 showed pores, which are of course predestined to allow for extensive water uptake. **Fig. 115** shows the FTIR measurement after hydrolysis of the material, and the mixtures Si 048 and Si 049 have the lowest read out for the carboxylic peak at 1740 cm^{-1} . This suggests that the water uptake in these two mixtures is more a function of the porosity of the material than it is influenced by the composition with regard to the presence of DMAM carrier.

In **Fig. 102** the sample Si 053 of series # 11 can be seen. Just like the mixture Si 047 it does not contain any pores. But in contrast, it has the highest read out for the carboxylic peak at 1740 cm^{-1} , as can be seen in **Fig. 116**. This now suggests that the water uptake may well be a function of the amount of 3-BCEE carrier which is present in the mixture.

Finally, **Fig. 103** shows a photograph of the silicone mixture Si 056 of series # 12. Pores are clearly visible, but in contrast to the two porous mixtures of series # 10 the pores are at a rather macroscopic level. In **Fig. 117** the carboxylic peak of mixture Si 056 at 1740 cm^{-1} has the same size as the other mixtures of this series. In conclusion, the water uptake may equally be caused by both the pores as well as the DMAM carrier which is present in the mixture.

As an overall conclusion it can be said, that the presence of pores enhanced the water uptake of the silicone mixtures in any case, even when only little carrier was present. Furthermore, pores may enhance the ability of liquid to penetrate the silicone bulk, causing hydrolysis within the bulk, which may further increase the water uptake.

15 Contact angle measurement

The goal of this research work is to make silicone hydrophilic on its surface. Contact angle measurement is a standard technique for the evaluation of the surface hydrophilicity. Here, contact angle measurement was conducted using water, and the proceeding contact angle was measured. Calculation of the contact angle was done by tangent leaning as implemented in the software, see **chapter 4 Materials and methods** for more details. Tangent leaning was chosen because in the case that the water drops on the surface of the samples are asymmetric, it leads to more accurate results than other calculations. Asymmetric water drops were observed numerous times and may be caused by inhomogeneity within the samples. Please note that the range of the Y-axis is the same for all figures in this chapter to allow for comparison.

15.1 Series # 9

Fig. 119 shows the contact angle measurement of series # 9. At the beginning of the measurement all samples containing the 3-BCEE carrier of low molecular weight are more hydrophilic than the unmodified mixture Si 040. However, the difference is only small in some cases, but it increases with increasing contents of the 3-BCEE carrier. The mixture Si 045 which contains the largest amount of carrier performs best. Over the course of the 16 days of exposure to Na_2CO_3 buffer solution the difference between the mixtures with and without the carrier levels out. For some mixtures this process occurs fast, while it is slow for other mixtures. No clear trend is visible. Comparison with the FTIR measurement of the surface after 16 days, see **Fig. 110**, allows for another conclusion: There, the carboxylic peak at 1740 cm^{-1} increases with increasing contents of 3-BCEE carrier only for the two series of highest carrier contents. This difference is not reflected in the contact angle measurement after 16 days. It must be concluded that the contents of 3-BCEE carrier which was present after the 16 days of immersion in the Na_2CO_3 buffer solution does not suffice as if to make a difference in the contact angle any more. However, it did suffice right after the production of the mixtures. Hence, the loss of carrier during the 16 days annihilated the positive effect of the 3-BCEE carrier on the surface hydrophilicity. In the previous chapter

leaching of the carrier from the silicone was proposed as mechanism. The findings here support that theory.

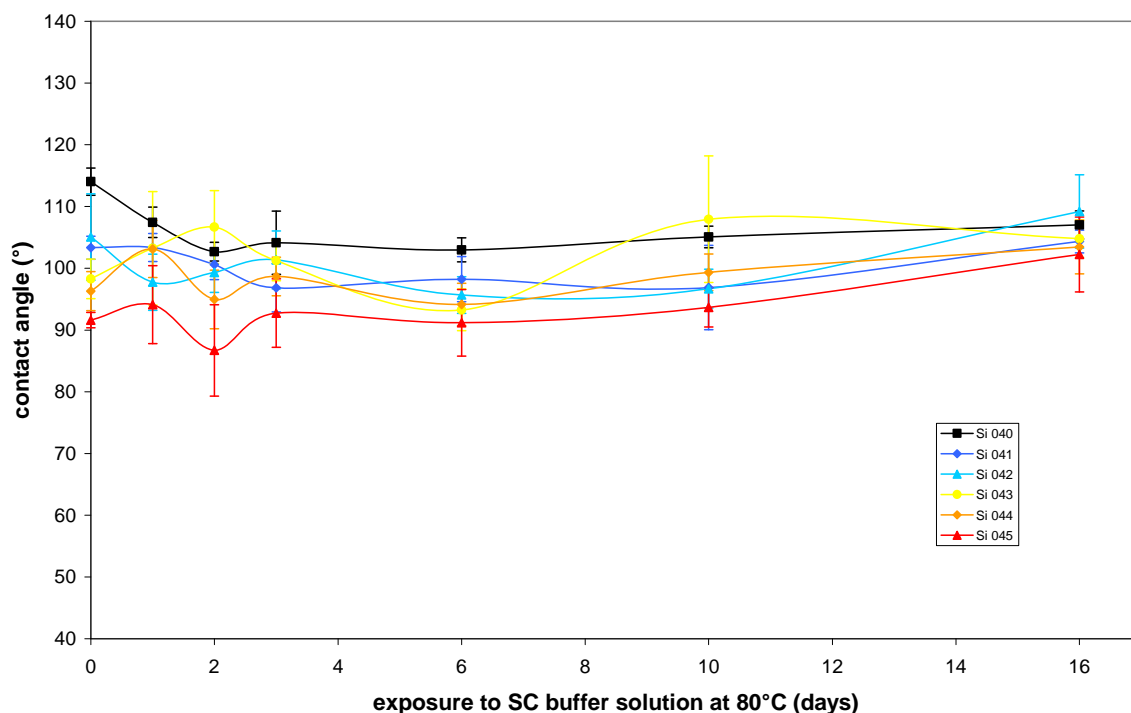


Fig. 119: Contact angle of series # 9: The contact angle of all mixtures containing the 3-BCEE carrier of low molecular weight is lower than that of unmodified silicone after production of the mixtures. Treatment with Na_2CO_3 buffer solution levels out the difference after different periods of time.

15.2 Series # 10

The contact angle measurement of series # 10 can be seen below in **Fig. 120**. After only 1 to 3 days in Na_2CO_3 buffer solution the three samples with the highest contents of low molecular weight DMAM carrier perform significantly better than the silicone without carrier. This allows for the conclusion, that the silicones are rendered hydrophilic by the contact with the hydrolyzing medium. However, this effect is gone after 5 days in Na_2CO_3 buffer solution. Moreover, after one week in Na_2CO_3 buffer solution the two samples with the highest content of carrier perform significantly worse than the other materials. It is noteworthy that these two mixtures were the ones showing pores after their production, photographs were shown in **Fig. 101**. The FTIR measurement of the surface after 16 days was

shown above in **Fig. 111**. The carboxylic peak at 1740 cm^{-1} at the surface was reduced to zero for all mixtures after 16 days. In comparison, the contact angle of all but the two porous mixtures has leveled out, while the two latter ones performed significantly worse. This allows for the conclusion that the increase of hydrophobicity of the two porous mixtures is influenced by the porosity, and therefore the surface structure of the samples. As in the series # 9, it can be concluded that leaching of the carrier from the material annihilated the positive effect of the carrier.

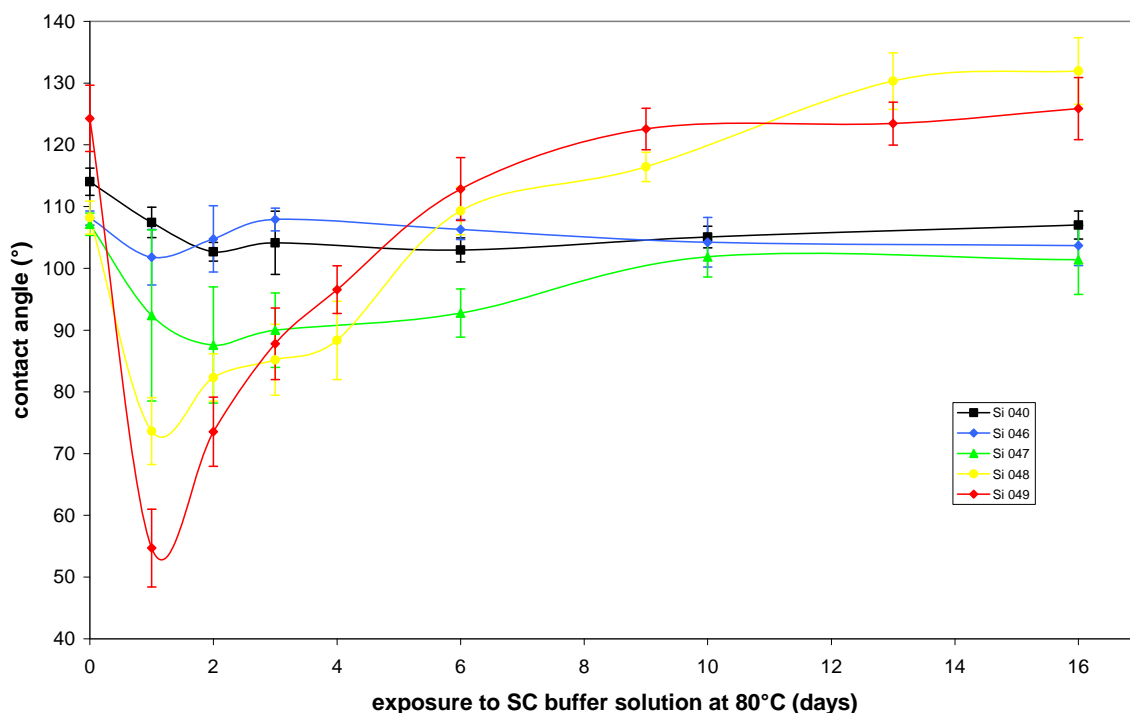


Fig. 120: Contact angle of series # 10: After exposure to Na_2CO_3 buffer solution for 1 to 3 days mixtures with high content of low molecular weight DMAM carrier perform significantly better than mixtures without carrier. The effect is annihilated by longer exposure times.

15.3 Series # 11

Fig. 121 shows the contact angle of series # 11 after production and after exposure to Na_2CO_3 buffer solution. The mixtures containing the 3-BCEE carrier of medium molecular weight are more hydrophilic after production. Furthermore, the hydrophilicity of the mixture with the highest contents of carrier, i.e. Si 053, performs best after 1 day exposure to

Na_2CO_3 buffer solution. As in series # 10 this allows for the conclusion, that the mixture is rendered hydrophilic by the contact with the Na_2CO_3 buffer solution. However, the positive effect of the carrier is gone after 5 days for this mixture. Furthermore, and in contrast to the previous two series, the hydrophilicity of all mixtures containing the carrier does not level out with the mixture without carrier. Instead, all mixtures containing the carrier are more hydrophobic than the mixture without carrier at the end of the test period.

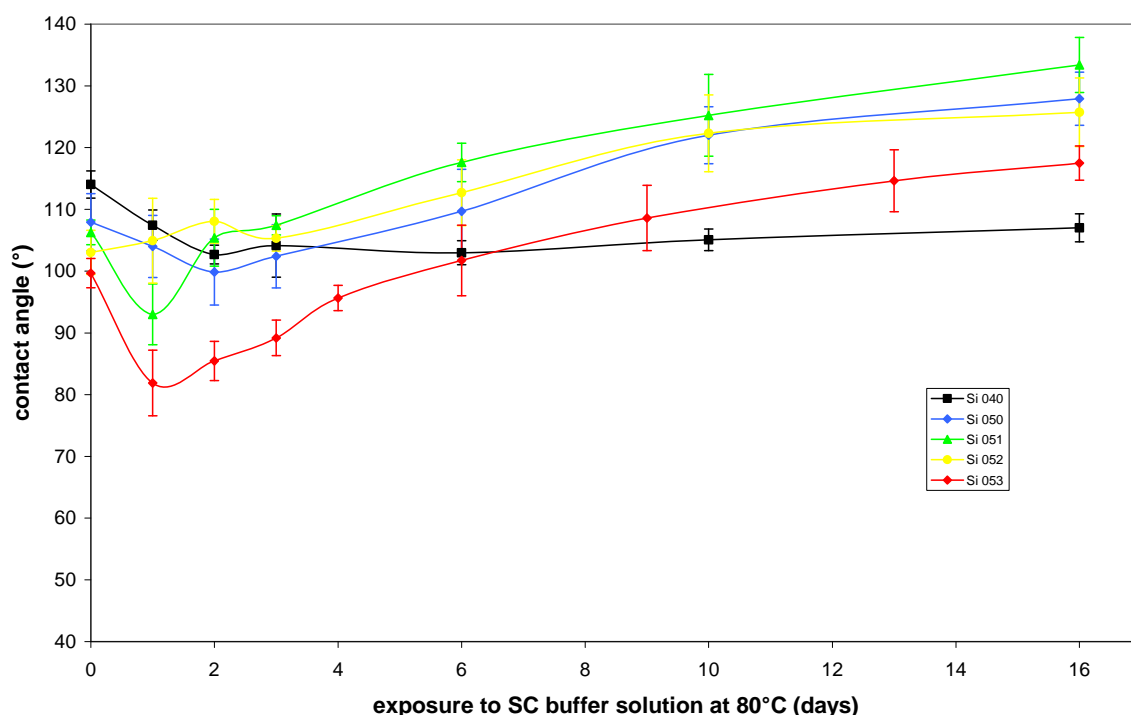


Fig. 121: Contact angle of series # 11: After 1 day of exposure to Na_2CO_3 buffer solution the mixture with the highest content of medium molecular weight 3-BCEE carrier performs significantly better than the other mixtures. The effect is annihilated by longer exposure times.

Comparison with the FTIR measurement of the surface after 16 days, see **Fig. 112**, suggests an interesting correlation: The lower the peak of the carboxylic group at the surface after 16 days, the higher is the surface hydrophobicity. Hence, the content of hydrolyzed carrier in the mixtures can be assumed to be one factor for the surface hydrophilicity. However, the increase of the hydrophobicity of the mixtures containing the carrier to values above the values of the mixture without carrier still requires clarification. A possible explanation can be that leaching of the carrier from the samples leaves behind a micro-

porous structure. This is possible, since the molecular weight of the carrier was large as compared to the molecular weight of the two carriers used in series # 9 and # 10, see **Tab. 5** for details. In conclusion, the increase of hydrophobicity of the mixtures is influenced by the presence of the hydrolyzed carrier on the one hand, and the surface porosity on the other hand. Leaching of the carrier from the material would explain both the decrease of hydrophilicity due to a loss of hydrophilic carboxylic groups which are attached to the carrier, and the increase of hydrophobicity due to the formation of micro-pores.

15.4 Series # 12

The observations for series # 12, see **Fig. 122**, are similar to those of series # 11: The hydrophilicity of the mixture with the highest content of medium molecular weight DMAM carrier, i.e. Si 056, performs best after 1 day exposure to Na_2CO_3 buffer solution. Longer exposure times to Na_2CO_3 buffer solution annihilate the positive effect. Like in the series # 10 and # 11 this allows for the conclusion, that the mixture is first rendered hydrophilic by the contact with the hydrolyzing medium. Then, as in series # 11, the hydrophilicity of all mixtures containing the carrier decreases until they are more hydrophobic than the mixture without carrier.

FTIR at the surface of series # 12 after 16 days in Na_2CO_3 buffer solution showed that the peaks of the carboxylic group at 1740 cm^{-1} are reduced to zero in two cases, and the mixture Si 056 shows only a small peak. See **Fig. 113** for results. This again supports the theory of carrier being leached from the silicone samples. In light microscopy pictures in **Fig. 103** pores could be seen only for mixture Si 056. However, these were large pores as compared to the pores seen in mixtures Si 048 and Si 049 shown in **Fig. 101**. This does not contradict the theory developed with series # 11 that leaching of the carrier from the samples leaves behind a micro-porous structure. The leaching of carrier molecules from the samples was assumed to decrease the hydrophilicity due to a loss of hydrophilic carboxylic groups, and to further increase the hydrophobicity due to the formation of micro-pores.

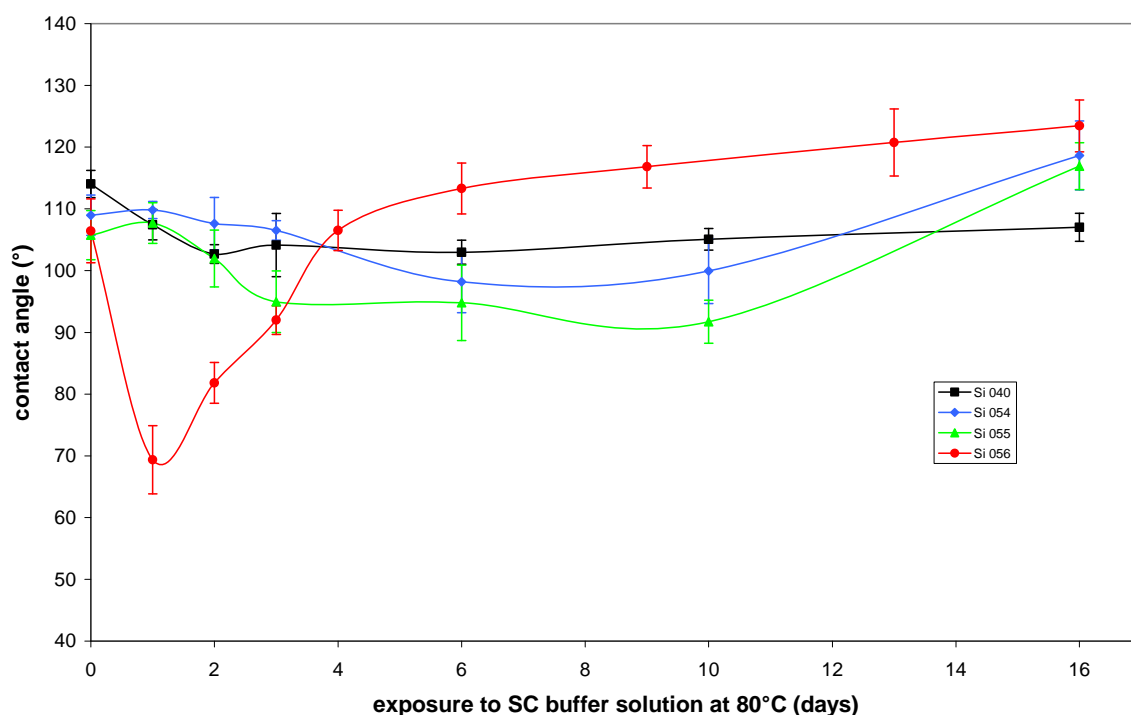


Fig. 122: Contact angle of series # 12: One day of exposure to Na_2CO_3 buffer solution renders the silicone mixture with the highest content of medium molecular weight DMAM carrier significantly more hydrophilic than all other mixtures of this series. The effect is annihilated by longer exposure times.

15.5 Conclusions

In this chapter it was shown that initially hydrophobic silicones can be rendered hydrophilic by the admixing of either a 3-BCEE carrier or a DMAM carrier. After the production of the silicones the effect is little pronounced, but treatment of the silicones with hydrolyzing medium largely increases the effect. The initial contact angle of material without any carrier was $\sim 114^\circ$, while the lowest contact angle for silicone containing a carrier was $\sim 55^\circ$ after exposure to hydrolyzing medium.

Extended exposure of the silicones containing carrier to hydrolyzing medium annihilates the effect, and leaching of the carriers from the samples can be assumed to be responsible. Furthermore, carrier molecules leached from the material may leave behind a micro-porous structure, which makes the material even more hydrophobic and susceptible to the penetration by liquid at the same time. In conclusion, preventing the carrier from leaching out of

the silicones may solve the problem. A solution would be the production of a functionalized carrier, which can form covalent bonds with the silicone backbone, and in consequence can not be leached from the material any more.

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16. Results and discussion

The overall goal of this work was to make the surface of a silicone hydrophilic - and it was achieved. At the beginning of this work numerous restrictions were made regarding the materials of interest, the technology for inducing surface hydrophilicity, and the desired effect: Only silicone materials which are commercially available at low cost and also well established in the biomedical field of cardiovascular applications were considered. The application field was narrowed to materials which are used as pacemaker and defibrillator lead insulators. These materials are known for their inherent hydrophilicity and appreciated for their high resistance to BO, ESC, and MIO. The hydrophilicity was to be induced only at the surface, but the bulk material was to be changed in order to allow for a self-renewing of the surface in the case that wear and tear removed parts of the material. In consequence, SMEs were chosen as the technology for achieving the goal. The SMEs had to be pro-hydrophile, meaning they have to be capable of undergoing hydrolysis and thereby change from their initial hydrophobic state to a hydrophilic state. Furthermore, they must present a negative charge in their hydrophilic state. Finally, the chemistry had to be compatible with that of the materials of interest. This meant the silicone chemistry was reduced to a system in which hydride- and a vinyl-terminated siloxane species react with one another to form a three-dimensionally cross-linked elastomer via hydrosilylation using the Karstedt's catalyst, or a modified version thereof. The latter point proved to be the bottleneck of this work: Of the 16 possible SME candidates that were tested only two proved to be compatible with the hydrosilylation reaction as defined for this work, and were thus accepted as SME candidates for the further research in this study.

The two SME candidates that were identified in the hydrosilylation model reactions are 3-BCEE and DMAM. The latter component has the advantage, that it carries two pro-hydrophile groups per molecule, and therefore doubles the surface effect. In order to incorporate these two components into a silicone polymer two pathways were proposed: The covalent bonding of the SME candidates to the silicone backbone, and the admixing of a carrier molecule with the SME candidates attached to it. While the first approach yielded silicone of very poor mechanical properties and large parts of the 3-BCEE evaporated during the process, the second approach yielded silicone samples with mechanical properties

high enough as if to allow for further use of the samples in this study. Mechanical testing showed that it is possible to use the 3-BCEE and DMAM carriers of different molecular weights to produce silicones with mechanical properties comparable to, but not competitive with the mechanical properties of commercially available silicones. Furthermore, high amounts of the SME candidates could be incorporated into the silicone using the second approach: 22.0%_{wt} of 3-BCEE, and 22.5%_{wt} of DMAM.

The carrier molecules that were produced in this work were non-functionalized, i.e. they contained neither hydrogen- nor vinylsiloxane functional groups. The synthesis of functionalized carrier molecules by ring-opening polymerization of cyclic tetrasiloxanes carrying 3-BCEE was of no avail. In consequence, the absence of functional groups for covalently binding of the carrier molecules to the silicone backbone meant, that the carrier molecules were free to move within the silicone network. The only restrictions for such movement are entanglement of the carrier molecules with the silicone network, and possibly physical interactions between the carrier molecules and the silicone. However, since the SME carriers will be less hydrophobic even in their unhydrolyzed state, the carriers will strive to diffuse to the surface of the silicone, where they may leave the material. This is obviously the drawback of the non-functionalized SME carriers, as it would mean a loss of SMEs, and therefore a loss of functionality.

The assumption that the 3-BCEE and the DMAM carrier may diffuse out of the silicone was verified by FTIR. With the measurements at the material's surface after the production of the samples as reference, a significant decrease of carrier both at the surface as well as within the bulk was observed after treatment of the samples with Na₂CO₃ buffer solution for 16 days. Two other issues with the carriers were firstly the miscibility with the silicone precursors, and secondly the formation of pores in cases of high contents of the carrier in the mixture. Regarding the first point all samples containing a SME carrier were opaque, while mixtures without carrier were transparent. This is a clear sign of the fact that the miscibility of the carrier with the silicone precursors is less than that of the silicone precursors among each other. Furthermore, it was possible to see that the mixtures were not homogeneous, as some parts of the samples were more opaque than others. While the latter point is due to the equipment which was available for mixing and can thus be resolved by

adjusting the mixing process, the reduced miscibility will remain an issue inherent to the system due to differences in hydrophobicity between the silicone precursors with the carriers.

Silicones containing either the 3-BCEE or the DMAM carrier perform differently regarding protein adhesion to the material's surface, water uptake, and contact angle. The material's behavior is clearly dependant on type and amount of carrier present in the mixture, as well as the exposure time to Na_2CO_3 buffer solution.

ELISA showed that all mixtures containing either one of the carriers allow for reduced protein adhesion as compared to the mixture without any carrier. However, the ELISA only covered a limited range of protein concentration per volume unit, and this range is much lower than the protein concentration which is present in human blood. Furthermore, the ELISA was conducted using the silicones as produced, without allowing for hydrolysis by exposure to Na_2CO_3 buffer solution prior to testing. Hence, the results of the ELISA may not represent the situation which will be encountered in vivo.

Water uptake was greatest for the silicone mixtures with the highest contents of the low molecular weight DMAM carrier, followed by the mixtures with the highest contents of high molecular weight 3-BCEE and DMAM carrier. However, the largest part of the water uptake can be attributed to the presence of pores in the material, which were present in the samples already after the production process. The smaller part of the water uptake may be due to the formation of micro-pores, which are formed by diffusion of the carrier molecules from the carrier, leaving voids in the silicone network.

Last but not least, contact angle measurement revealed a significant improvement in surface wettability of the silicone mixtures containing the carriers as compared to the silicone mixture without any carrier. For the latter material a contact angle of $\sim 114^\circ$ was found after production and $\sim 103^\circ$ after exposure to the Na_2CO_3 buffer solution. In stark contrast, the treatment of the samples containing carrier with Na_2CO_3 buffer solution lead to the following results: The contact angle of the sample containing the highest amount of low molecular weight DMAM carrier decreased to $\sim 55^\circ$; the samples containing the highest

amount of medium molecular weight 3-BCEE and DMAM carrier showed reduced contact angles of $\sim 82^\circ$ and $\sim 69^\circ$, respectively; the mixture containing the low molecular weight 3-BCEE carrier showed only little change, with a value of $\sim 86^\circ$. These improvements of the surface wettability were observed after only 1 and 2 days of exposure to Na_2CO_3 buffer solution. Longer exposure times annihilated the effect.

As an overall conclusion it can be stated that the two components 3-BCEE and DMAM both act as SMEs. They are capable of rendering an initially hydrophobic silicone hydrophilic at its surface. Furthermore, they are compatible with the hydrosilylation system that is used in the commercially available silicone materials which are applied in the field of cardiac rhythm management for pacemaker and defibrillator lead insulation.

17 Outlook and future suggestions

It was shown in this work that by using either 3-BCEE or DMAM as SMEs, initially hydrophobic silicone can be made hydrophilic. However, the effect was not yet proven to be long-lasting. Since the 3-BCEE and DMAM carriers were non-functionalized, and therefore not covalently bonded to the silicone network, diffusion of the carriers from the silicones was observed. In order to avoid this loss and ensure the long term presence of the SMEs in the material, the carriers should be functionalized. The presence of either hydrogen- or vinylsiloxane groups would allow for the permanent fixation of the carriers within the silicone network via covalent bonds to the silicone backbone. Furthermore, using hydrogen- or vinylsiloxane functional groups would bear the advantage that the formation of the covalent bond to the silicone backbone uses the same platinum catalyst, which is already present for the polymerization of the silicone.

As a second suggestion, using carrier molecules which have more than one functional group is imaginable. By doing that the carrier would not only be connected to the silicone network, but become an integrated part of it and thereby positively contribute to the mechanical properties of the material, e.g. increase the tensile strength.

Thirdly, if it were possible to build a functionalized SME carrier, it will be possible to replace all silicone precursors which were used here by analogue silicones carrying the SMEs. The three following precursors were used: P 1300, U 430, and U 1, and all three have a dimethylsiloxane backbone, but contain only either hydrogen- or vinylsiloxane functional groups. If each of these three precursors also carried some SMEs, the miscibility problems between the silicone precursors and the carriers would be prevented.

The bottleneck of this work was the restriction to a silicone system which relies on hydrosilylation between a hydrogensiloxane- and a vinyl-terminated species, using the Karstedt's-catalyst or the modified version thereof. Many more catalysts are available on the market, allowing for a vast field of chemical possibilities. By using a different catalyst system even some of the 16 components which could not be used here may be possible SME candidates.

Finally, in order to determine whether or not a material may be used in the biomedical field, experiments regarding the biomechanical properties, the in vitro behavior of the material, and in vivo experiments will be needed. For the application as pacemaker or defibrillator lead insulation the issue of tribological behavior is of major importance, as leads are constantly being subjected to many different types of friction. There is the contact with the walls of the venous part of the blood system, the rubbing against the constantly moving heart valves, the friction between two neighboring leads, but also the wear which occurs in contact with the housing of the pacemaker or defibrillator. As strange as it seems, numerous testing norms are available for polymers, but none for the kind of wear situation that a pacemaker cable will encounter [188-198]. Hence, test setups for the reproducible simulation of the wear situations of cardiac pacing leads are still needed. Further tests which will have to be conducted are cytotoxicology and haemocompatibility. Last but not least, in vivo tests will be needed. For both in vitro and in vivo testing, the Guidance for the Submission of Research and Marketing Applications for Permanent Pacemaker Leads and for Pacemaker Lead Adaptor, as published by the FDA, as well as the ISO 10993 will supply essential directions [199, 200].

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