DIPLOMARBEIT

URETHANE BASED VINYLCYCLOPROPANES FOR LOW SHRINKAGE DENTAL COMPOSITES

ausgeführt am Institut für Angewandte Synthesechemie an der Technischen Universität Wien und in der Firma Ivoclar Vivadent in Schaan

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für meine Eltern!

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Abstract

Composite materials, which are used for dental restorations for more than 50 years are gradually replacing amalgams. Such dental composites have led to a breakthrough in modern dentistry since they are easy to manipulate, inexpensive and have excellent esthetic properties. Their organic matrix is mainly based on monomers such as dimethacrylates and additives (e.g. initiators, stabilizers, pigments). Before curing the monomer molecules are located at Van-der-Waals distance to each other, which changes during curing with the formation of covalent bonds. This causes a volumetric shrinkage during photocuring and has been a major challenge for research and industry.[1] The resulting shrinkage stress is supposed to generate microleakage, marginal staining, secondary caries and post-operative sensitivity.

Cyclic monomers like vinylcyclopropanes (VCPs) exhibit dramatically reduced shrinkage upon curing and can be a conceivable alternative to methacrylates for the development of low-shrinkage composites. In this study the synthesis of new difuncitonal VCPs **3-11** is described. The reactivity is studied with photo-differential scanning calorimetry using bis(4-methoxybenzoyl)diethylgermane (Ivocerin®) as photoinitiator. Real-time near-infrared photorheology measurements are performed to evaluate rheological behavior (i.e., time of gelation, polymerization-induced shrinkage force) and chemical conversion (i.e., double bond conversion at the gel point, final double bond conversion) of the vinylcyclopropanes in situ. Composites based on VCPs **3–11** show good mechanical properties and exhibit significantly lower volumetric shrinkage and shrinkage stress than corresponding dimethacrylate-based materials.

Kurzfassung

Komposite werden für zahnmedizinische Restaurationen seit über 50 Jahren verwendet und stellen mittlerweile eine gute Alternative zu Amalgam dar. Vor allem durch ihren geringen Preis, die gute Formbarkeit und die herausragende Ästhetik konnten sich solche Zahn-Komposite erfolgreich in der Zahnmedizin etablieren. Die organische Matrix besteht hauptsächlich aus Monomeren wie Dimethacrylaten und Additiven (z.B. Initiatoren, Stabilisatoren, Pigmenten,...). Bevor das Komposite ausgehärtet wird liegen die Monomere mit einer Van-der-Waals Distanz untereinander vor, welche sich während des Aushärtens zu einer kovalenten Bindung umformt. Diese Umformung führt zu einem Volumenschrumpf während der Photopolymerisation. Dieses Schrumpfverhalten ist eine der größten Herausforderungen für Forschung und Industrie.[1] Durch die zusätzlich auftretende Schrumpfspannung bilden sich Mikrorisse wodurch die Langlebigkeit der Füllung beeinträchtigt ist und der erneute Befall von Karies schneller eintreten kann.

Zyklische Monomere wie Vinylcyclopropane (VCPs) weisen einen signifikant reduzierten Volumenschrumpf bei der Photopolymerisation auf und sind eine gute Alternative für Methacrylate in der Entwicklung von schrumpfarmen Kompositen. In dieser Arbeit wird die Synthese von neuen difunktionellen VCPs **3-11** beschrieben und die Reaktivität mittels Photo-dynamischer Differenzkalorimetrie untersucht. Als Photoinitiator wurde für diese Untersuchungen Bis(4-methoxybenzoyl)diethylgermane (Ivocerin®) verwendet. Mit der Echtzeit NIR Photoreheologie Messung wurde das rheologische Verhalten (Zeit bis zum Gelieren, polimerisationsinduzierte Schrumpfkraft) und das chemische Verhalten (Doppelbindungsumastz am Gelpunkt, finaler Doppelbindungsumsatz) der synthetisierten VCPs in situ untersucht. Komposite basierend auf **VCP 3-11** zeigten gute mechanische Eigenschaften und der Volumenschrumpf und die Schrumpfkraft konnten im Verglich zu den methacrylat-basierenden Materialien signifikant reduziert werden.

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Tooth structure

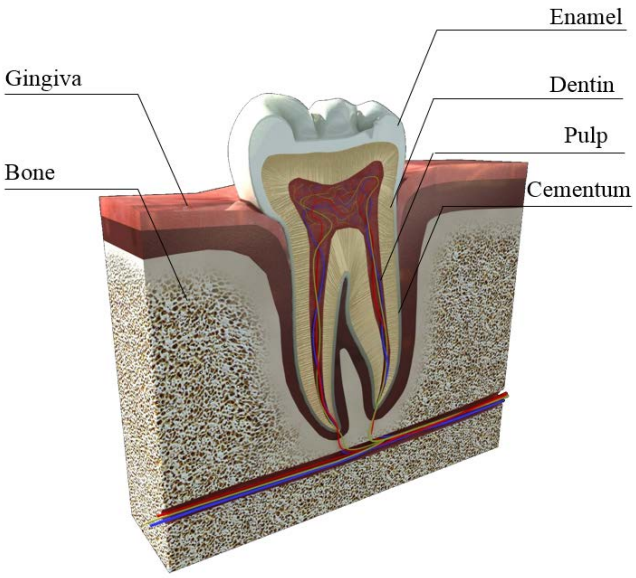


Figure 1: General structure of a tooth[2]

For the better understanding of the restauration process the structure of a tooth is shown in Figure 1 with the most important parts. The tooth represents one of the hardest structures in the human body and mainly consist out of the following materials:

- Enamel: it is the outer most layer and the hardest most mineralized tissue in the body. It consists of about 92 % hydroxyapatite (HAP), 2 % organic material and 6 % water. HPA is a tightly packed mixture of calcium and phosphate. This composition leads to a very high mechanical strength but a relatively low stability towards acids.

- Dentine: it is the layer underneath the enamel and builds up the largest part of the tooth. Dentine consists of about 70 % HPA, 20 % organic material (mainly collagen) and about 10 % water. Besides minerals it consists out of sensitive layer of living tissue and microscopic channels.

- Pulp: is the vascular region of soft connective tissue located under the dentine in the middle of the tooth. It manly consists out of blood vessels and nerves which supply the tooth with nutrition.

- Cementum: a mixture of calcium and collagen fibers (bone like structure) that connects the tooth firmly to the gingiva and jawbone.[3]

Dental Restoration

Restoration methods

There is a variety of materials which meet most of the criteria for the use as dental restoratives. The most commonly used are listed in Table 1. Amalgam was one of the first materials used for dental fillings but there are concerns regarding the health issues due to the mercury amount. Besides the health issues there is also the esthetic issue which is not satisfying with amalgam. Composites and ceramics have the benefit of an individual coloration with pigments and no health concerns.

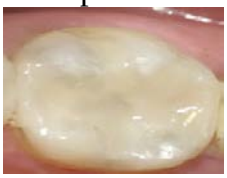
For a good dental restoration the composite material should be able to replace dentine and enamel nearly perfectly. Therefore it should be able to fulfill most of the following requirements:[4]

- Low acid solubility
- Sufficient long term strength to resist occlusal forces
- Abrasion resistance to maintain shape of the dental restorative
- Seamless filling of cavities to avoid the penetration of bacteria and secondary caries
- Excellent esthetic properties
- Easy handling properties
- Sufficient biocompatibility
- Ductile and prone to curing at room temperature
- Low price

Since many of the commonly used materials show substantial drawbacks the motivation was to develop and to create new improved dental materials. Polymer based dental composites are a good and improving class in dental restorations.[5-7]

Table 1: Commonly used materials for dental restorations

Material	Advantages	Disadvantages	Application

Amalgam[8] 	• cheap • easy processing • good chemical and mechanical resistance	• esthetic • controversial toxicity (Hg^0) • environmentally unfriendly • expands during curing	• dental fillings
Gold[9] 	• good chemical and mechanical resistance • decorative	• difficult to process • expensive	• dental fillings • inlays • onlays
Ceramics[10] 	• natural tooth color • good chemical and mechanical resistance	• expensive • difficult to process	• crowns • inlays • onlays
Composites[11] 	• natural tooth color • easy to process • relatively cheap	• shrinkage and shrinkage stress	• dental fillings

Resin-based composites

Dental caries is one of the major global health problems nowadays. It has been considered as the most important component of the oral disease burden. Dental caries affect about 60-90 % of school-aged children and also a vast majority of adults. For over 150 years amalgam was used for dental restoration, despite the concerns regarding the presence of mercury in the filling. In the past two decades, alternative ways for restorations have increased due to the environmental impact of mercury.[12] Not only because of health issue alternative filling materials are interesting. The esthetic properties are also getting more important in the field of dental restoration. Resin-based composites (RBCs) materials are the most common alternative. RBCs are made up of an organic matrix, fillers and a coupling agent. The organic matrix mainly contains dimethacrylates as well as various additives (photoinitiator system, stabilizers, pigments, etc).[13] To ensure a strong bond between the tooth and the RBC a dental adhesive is needed. [14]

Until today composites contain an organic matrix with about 10-65 wt% and inorganic fillers with about 35-90 wt% (Figure 2). Composited can be classified according to their viscosity if they are flowable or packed and according to their filler size (macrofiller, midifiller, minifiller etc.).[15]

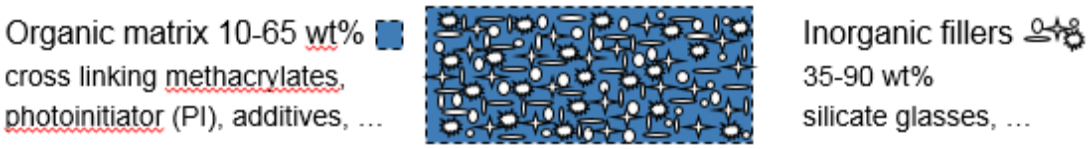


Figure 2: Schematic illustration of a dental composite

The organic matrix contains a mixture of different dimethacrylates. In a composite the organic matrix influences significantly the curing rate, the polymerization shrinkage, the color and the storage stability. The most commonly used dimethacrylates for composites are [2-hydroxy-3-[4-[2-[4-[2-hydroxy-3-(2-methylprop-2-enoyloxy)propoxy]phenyl]propan-2-yl]phenoxy]- propyl] 2-methylprop-2-enoate (Bis-GMA) and 2-[[3,5,5-trimethyl-6-[2-(2-methylprop-2-enoyloxy)ethoxycarbonylamino] hexyl]carbamoyloxy]ethyl 2-methylprop-2-enoate (UDMA). Both structures are shown in Figure 3. Bis-GMA has low water solubility and high viscosity and therefore a diluent is needed. The function of the diluent is to improve workability and decrease the viscosity of the organic matrix. A commonly used diluent is 2-[2-[2-(2-methylprop-2-enoyloxy)ethoxy]ethoxy]ethyl 2-methylprop-2-enoate (TEGDMA) (Figure 3).[7, 15, 16]

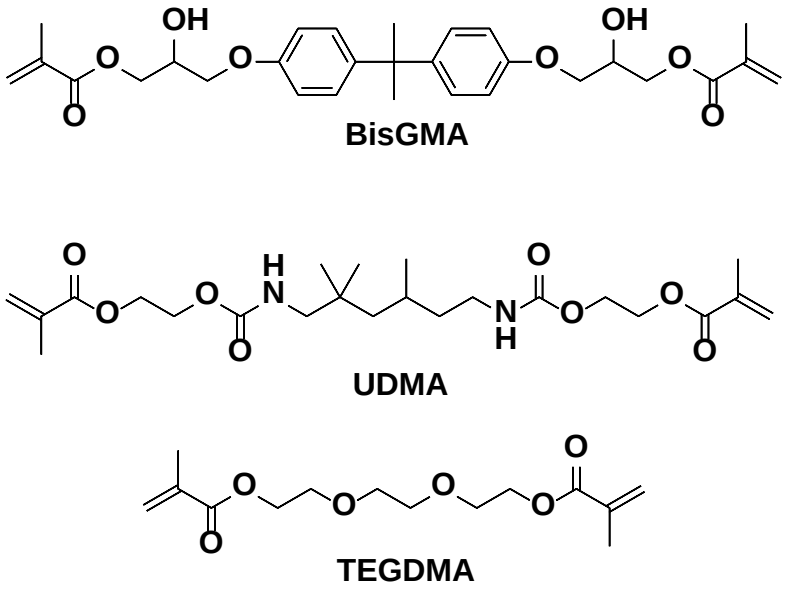


Figure 3: Structure of the most commonly used dimethacrylates for dental composites

Photopolymerization is the most common way to cure the RBCs. For the process a blue light emitting diode (LED) is used. The most commonly used photoinitiator systems contain camphoriquinone (CQ) as a photosensitizer and a tertiary amine such as ethyl 4-dimethylaminobenzoate (EDAB) as co-initiator (Figure 4).

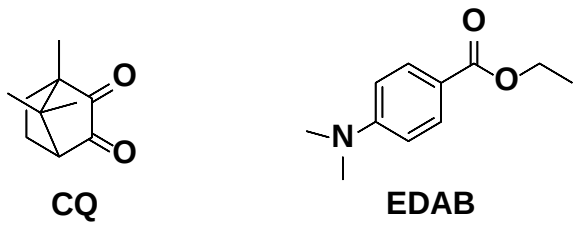


Figure 4: Structure of the Norrish type II photoinitiator system CQ-amine

Phosphine oxides such as bis(2,4,6-trimethylbenzoyl)-phenylphosphine oxide or diphenyl(2,4,6-trimethylbenzoyl)phosphine oxide) can also be used as Norrish type I photoinitiators. Both of them have been successfully used in dental composite formulations. Unfortunately the phosphine oxides exhibit a minimal absorption beyond 420 nm and they show no absorption for the wavelength of the blue LED.[17] Norrish type I photoinitiators based on benzoylgermanium have been reported and it was found that they exhibit a strong absorption in the blue domain. Ivocerin® is a highly efficient photoinitiator, which can be found in some commercially available dental composites (eg. Tetric Evo Ceram). The quantum yield of efficiency of the related structure to Ivocerin® (Φ_D = 0.85) was found to be significantly higher than the one from phenylbis(2,4,6-trimethylbenzoyl)phosphine oxide (Φ_D = 0.59) and the CQ based photoinitiator systems (Φ_D = 0.07).[18]

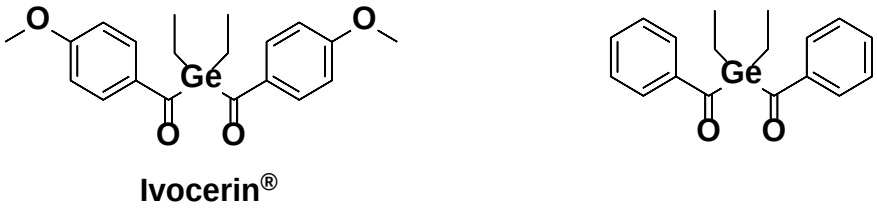


Figure 5: Structure of Ivocerin® the highly reactive related structure

The mechanism of Ivocerin® has been investigated and it turned out that the molecule cleavesunder irradiation to give both a benzoyl and a germyl radicals. In the further reaction these two radicals are responsible for the polymerization. [15, 17, 19, 20]

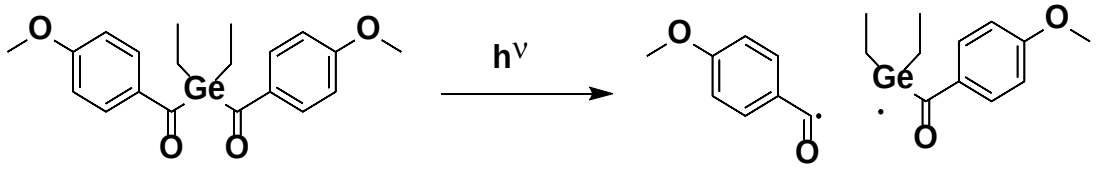


Figure 6: Cleavage of Ivocerin® under irradiation

Particulate fillers are incorporated in dental composites in order to directly influence properties such as radiopacity, abrasion resistance, flexural modulus and translucency. The fillers can be categorized according to their size: macrofillers (10-100 µm), midfillers (1-10 µm), minifillers (0.2-1 µm) and nanofillers (<0.2 µm). Various examples of different fillers used in RBCs are listed below: [15, 17, 19-21]

- Silicate glass fillers based on SiO_2 and contain other heavy elements oxides (BaO, SrO…) that give the material its radiopacity
- Ytterbium fluoride (YbF_3), which is usually incorporated to improve the radiopacity
- Pyrogenic silica
- Prepolymerized composite fillers: they were prepared from an initial microfilled composite (containing a mixture of dimethacrylates, a barium-aluminum-borosilicate glass, and YbF3), which was pre-polymerized (thermally) and then grounded to a fine powder

The filler amount correlates to the rheological properties of the RBC. The lower the amount of filler,the more flowable the composite. The filler size influences the polishability and the wear resistance of the material.

To get a good and strong bond between the organic matrix and the fillers of the RBC, in a previous step the fillers undergo a condensation reaction with a silane coupling agent. A commonly used coupling agent is the 3-(methacryloyloxy) propyltrimethoxysilane. During polymerization the methacrylate group forms a bond with the organic matrix and the silane group with the inorganic part of the composite.

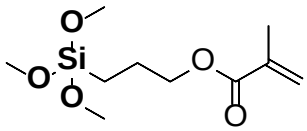


Figure 7: Structure of the silane coupling agent

The dental tissue, consisting out of dentine and enamel contains water, therefore it has hydrophilic character. Since the RBCs are hydrophilic a strong coupling agent is needed to form an optimal bond between dental tissue and RBC. Those coupling agents are called dental adhesives. [14]

Dental adhesives

RBCs have to fulfill a variety of requirements: they have to be stable, nontoxic, non-allergenic and without any mutagenic potential. On top of those requirements the used monomers should have a high reactivity towards homopolymerization and copolymerization with comonomers.[15]

If a tooth suffers from caries and needs a filling, the cavity first have to be prepared before applying the composite. The dentist will apply an adhesive on the tooth surface in order to generate a good bonding between composite and the dental tissue. Adhesives can be divided in in two major classes: the self-etch adhesives (SEAs) and the etch-and-rinse adhesives (E&RAs) and.[15]

SEAs are aqueous solutions which are strongly acidic and they are able to demineralize and infiltrate the dental tissue simultaneously. The ionization of a strongly acidic monomer in the aqueous solution is responsible for the etching of the tissue. SEAs do not require a rinsing step like the E&RAs, they can be seen as a major breakthrough because the need less steps, therefore they are less error-prone and as a result the all in all error risk during the application decreases.
SEAs are acidic, aqueous solutions with a pH between 0.8-2.5. They constist up to 40 wt% out of water, monofunctional, acidic and crosslinking monomers, solvent and additives (photoinitiator, co-initiator, stabilizers, etc.). The monomers can either be mehtacrylic monomers or acrylamides. The monofunctional monomers like 2-hydroxymethylmethacrylate (HEMA) acts as a surfactant between the hydrophobic and hydrophilic part.

In comparison the E&RAs the hard dental tissues are typically etched by a phosphoric acid gel at about 30-40 %. The demineralized tissues are subsequently rinsed with water and partially dried with air. In the first step a monomer mixture is applied to the prepared surface. The monomer infiltrates the demineralized tooth surface. In the next step there will be first a photopolymerization step followed by the application of the RBCs which provides the final adhesion. The procedure of the

E&RAs requires a significant higher amount of steps then the SEAs and the technique is sensitive to the drying procedure. Therefore E&RAs get more and more replaced by the less sensitive SEAs.[22]

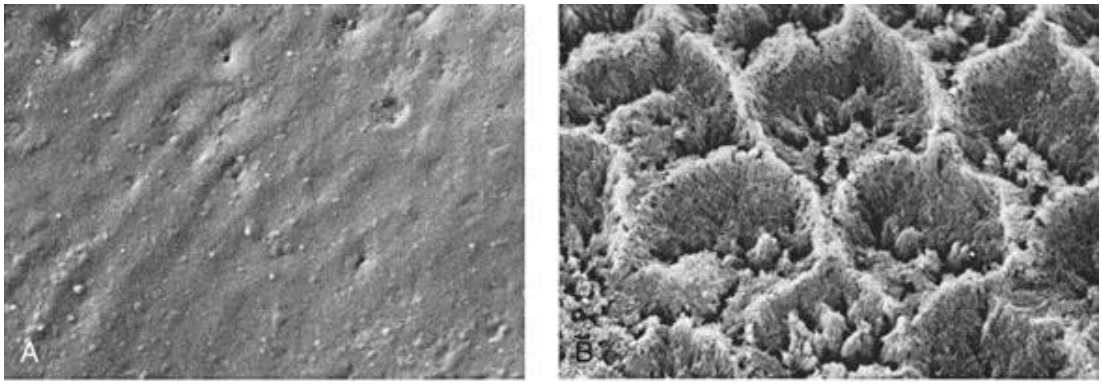


Figure 8: Picture of enamel surface berfore (left) and after (right) the acidic etching step

Reduction of shrinkage stress and volumetric shrinkage

RBCs have suffered some major drawbacks. One major problem is the volumetric shrinkage during the polymerization process. Before curing, the monomer molecules are located at Van-der-Waals distance and after the curing they are covalently bond in the polymer network. The conversion from Van-der-Waals distance (~ 3.40 Å) to the distance of a covalent bond, (~ 1.54 Å) causes a volumetric shrinkage.

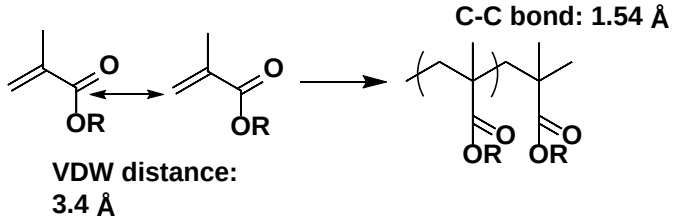
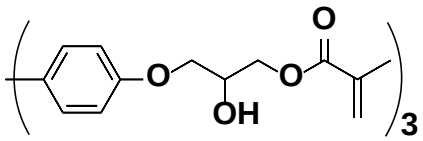


Figure 9: Change of the distance before and after curing a methacrylic monomer

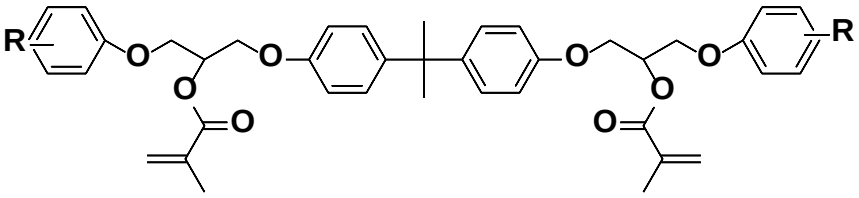
Due to the resulting shrinkage stress, microleakage, marginal staining, secondary caries and post-operative sensitivity could be the result. [23, 24] Therefore one of the major objectives in the last decades was to reduce the polymerization shrinkage of RBCs.

Because of the generated microleackage the durability of the filling cannot be granted. One of the first attempts to reduce the volumetric shrinkage was to use high molecular weight monomers in composite formulations. A typical composite consists of a dimethacrylate monomer, a dimethacrylate

diluent and a large quantity of inorganic fillers. Typical photocurable dental resins on the widely use are Bis-GMA/ TEGDEA mixtures (70:30 wt.%: wt.%). Alternative monomers to Bis-GMA, UDMA and TEGDMA are trifunctional methacrylates such as TTEMA or dimethacrylate monomers with bulky side groups such as MtBDMA and DtBDMA to increase the molecular weight. By using these monomers in dental composites the shrinkage could be reduced, but these monomers still need also a diluent to be formulated in composites. The amount of diluent correlates to the volumetric shrinkage and in addition to the mechanical properties which both diminish with the increase of used diluent. [25, 26]



TTEMA



MtBDMA R=4-tert-butyl
DtBDMA R=3,5-di-tert-butyl

Figure 10: High molecular weight monomers for shrinkage reduction

Thiol-ene chemistry and other methods for network regulation

A better network regulation can also be achieved by using thiol-ene chemistry where the reaction of thiols with a carbon double bond takes place. Thiol-ene chemistry is a powerful method to generate homogenous polymer networks. This homogenous network is generated by pushing the photopolymerization towards higher conversions. The major advantage for dental materials would be a high conversion, fast reaction rates, low oxygen inhibition and an easy tunabiltiy of the resulting polymer network. The generated polymer networks exhibit a more definded glass transition and less stiff networks with flexible thio-ether bridges which results in photopolymers with improved impact resistance. The major drawback of the thiols in dimethacrylate systems is the tendency to colorize the materials, the storage stability and the unpleasant smell.[27]

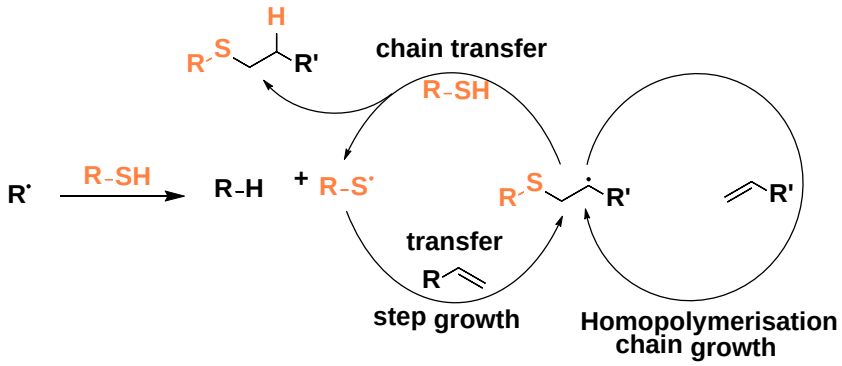


Figure 11: Mechanism of the thiol-ene reaction

Additional fragmentation chain Transfer (AFCT)

Pure dimethacrylate networks can be rapidly cured by photopolymerization and are therefore of interest in dental applications. The formed networks often exhibit a broad thermal phase transition and low impact resistance because of their high number of cross-links. These occurring cross-links lead to extremely dense networks. A drawback of curing methacrylates formulations is that the gel point, where the transition from liquid to solid takes place, is reached very fast and at low conversions which results in a high shrinkage stress. [28]

By using additional fragmentation chain transfer (AFCT) reagents the uncontrolled radical chain growth mechanism can be altered and the creation of more homogenous photopolymer networks with optimized properties is possible. Network modifiers push the gel point during the polymerization to higher conversions, which in turn reduces the occurring shrinkage stress. [29]

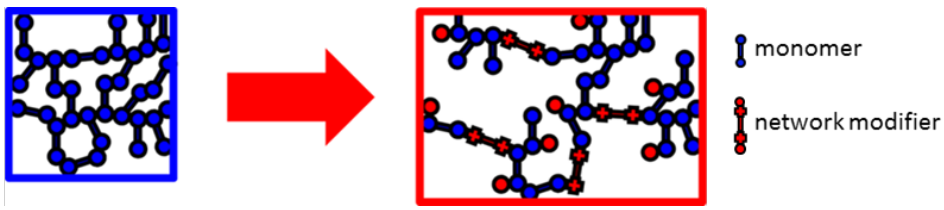


Figure 12: Illustration of a network without and with network modifier

An AFCT reagent has a reactive part towards radical attack (e.g., carbon double bond) and a leaving group that forms a reactive radical after fragmentation. After a radical attacks the double bond, an intermediate radical is formed which then can undergo the desired fragmentation to form the radical of the leaving group. This radical should be reactive enough to initiate a new radical chain.[30] Through AFCT reagents the shrinkage can be rescued but shifting the gel point to higher conversions leads also to an increase in irradiation time.

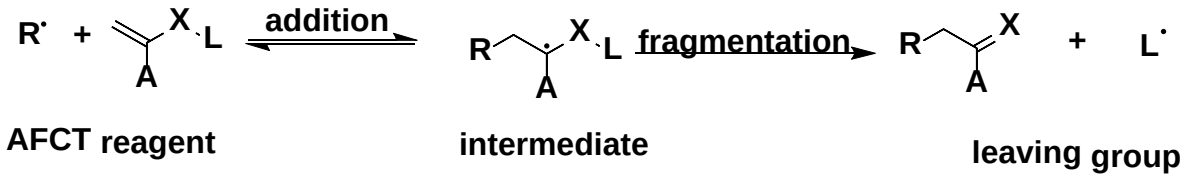


Figure 13: Reaction of a radical with an AFCT reagent

Nanogels for shrinkage reduction

Another way to reduce the volumetric shrinkage and the shrinkage stress is the use of high molecular weight polymeric nanoparticles (nanogels) as a swellable, potentially reactive additives in a secondary monomer. The goal is to reduce the overall reactive group concentration and in addition the volumetric shrinkage and the shrinkage stress without influencing other critical polymer properties. [31]

Nanogels are internally crosslinked and cyclized single or multi-chain polymeric particles typically well below 100 nm. The naonogels can be added to the monomer matrix to provide a stable, transparent solution of swollen particles. A physical enlargement and potential chemical crosslinking between nanogel structures and the resin network allow to reinforce the mechanical properties of the final network during polymerization. The reactive nanogels have shown the capability to reduce the shrinkage stress without significant influences on the mechanical properties of materials. By using nanogel to reduce the shrinkage and the shrinkage stress the consequence is an increasing viscosity of the monomer mixture which limits the applications. [32, 33]

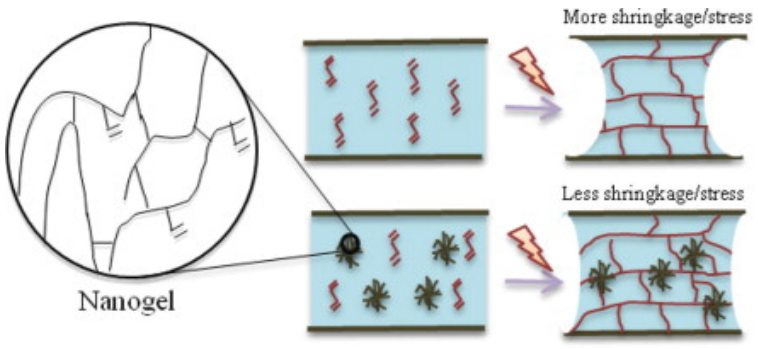
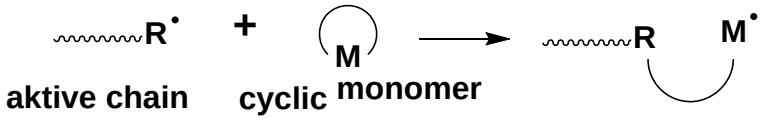


Figure 14: Nanogel network for shrinkage reduction

Radical ring opening polymerization (RROP)

RROP is also a powerful tool to reduce shrinkage and shrinkage stress during photopolymerization. It has been used since the beginning of the 1900s in order to synthesize polymers. With the RROP it is possible to produce polymers of the same or lower density than the monomers. This is important for application with the requirement of a similar volume after polymerization.



A high reactivity was observed by the copolymerization of bicyclic monomers such as 2-(bicyclo[3.1.0]hex-1-yl)acrylate, substituted at the bridgehead (Figure 15). The results showed a similar reactivity to methyl methacrylate (MMA) in contrast to the 1,1-disubstituated-VCPs where the reactivity was significantly lower. The shrinkage of these molecules was around 10.6 vol%. Through the increase of the molecular weight a decrease in shrinkage could be achieved. The major drawback in these structures was the very complex syntheses and that crosslinking monomers could not be easily prepared. In addition another problem was the low T_G of 52 °C. This is a disadvantage for dental applications regarding to the mechanical properties of the composite based on these monomers. [16]

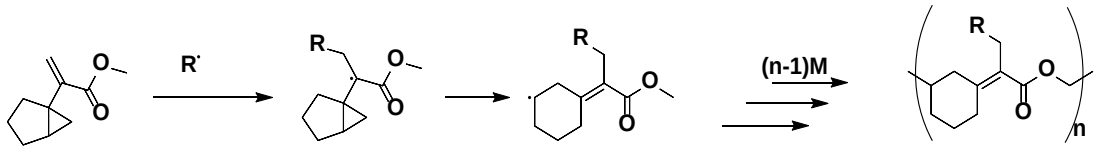


Figure 15: Proposed mechanism of the radical ring-opening polymerization of bicyclic cyclopropyl acrylate

Other cyclic structures like 3-methylene-1,5-dithiacyclooctane (MCO) are also able to perform ring-opening, but in this case the backbiting step leads to the closed ring structure which is limiting the polymerization. Therefore these structures are not favored for a RROP. [16]

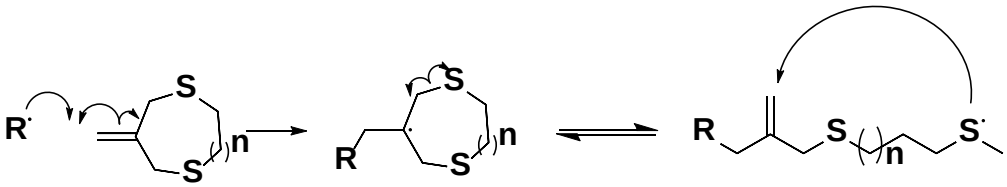
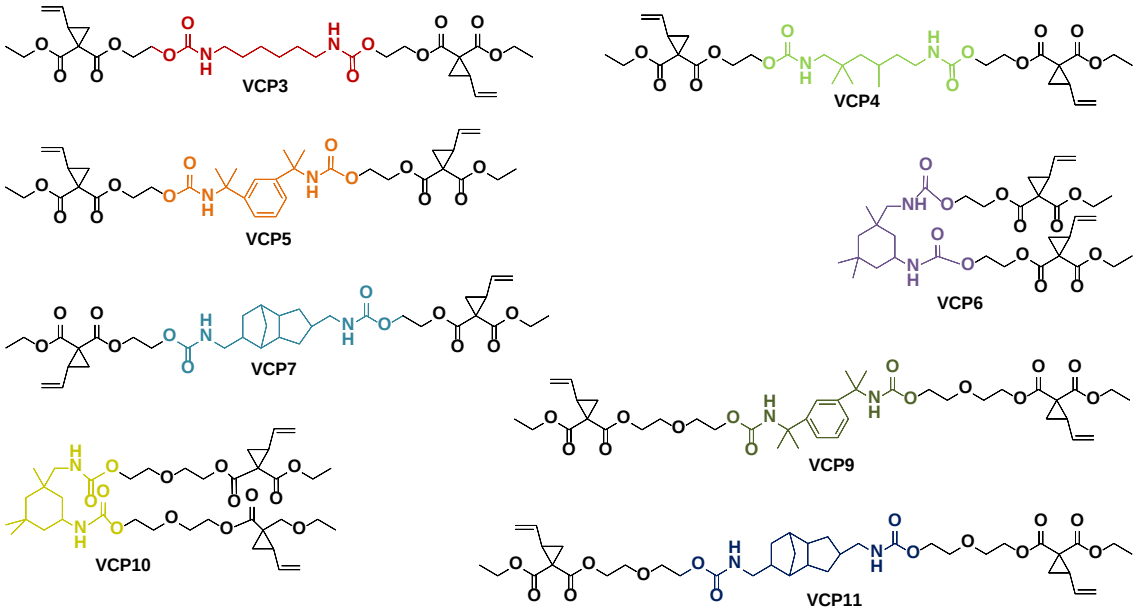


Figure 16: Polymerization mechanism of cyclic allylic sulfides

Objective

Dental caries is one of the major global health problems nowadays. It has been considered as the most important component of the oral disease burden. Dental caries affect about 60-90 % of school-aged children and also a vast majority of adults. For over 150 years amalgam was used for dental restoration, despite the concerns regarding the presence of mercury in the filling. In the past two decades, alternative ways for restorations have increased due to the environmental impact of mercury.[12] Not only because of health issue alternative filling materials are interesting. The esthetic properties are also getting more important in the field of dental restoration. Resin-based composites (RBCs) materials are the most common alternative. The major drawback of composite fillings is the resulting volumetric shrinkage and shrinkage stress after curing whereby mikroleakage and caries is generated again and a long lasting filling cannot be granted. There have been some approaches to reduce the volumetric shrinkage and the shrinkage stress by using large amounts of filler, high molecular weight monomers or soft-start polymerization. By using cyclic monomers which are able to undergo ring-opening polymerization (ROP), the polymerization shrinkage can also be reduced. Several cyclic monomers such as epoxides, oxetanes, spiro orthocarbonates or cyclic ketene acetals were tested in RBC but unfortunately they are not stable in presence of acidic or basic impurities, which is a major drawback for dental applications. On the other hand, it was found that 1,1-disubstituted vinylcyclopropanes (VCPs) are stable in usual dental composite formulations. However, VCPs have not found their place in restorative dentistry yet. Indeed, VCPs have been shown to exhibit a significantly lower reactivity in comparison to methacrylates when using camphorquinone (CQ) / tertiary amine as a photoinitiator system. It was found recently that the germanium based photoinitiator Ivocerin® was able to significantly increase the polymerization rate of VCPs. Therefore, composites containing VCPs instead of methacrylates and Ivocerin® as initiator were formulated. Those composites exhibit good mechanical properties as well as significantly lower polymerization shrinkage in comparison to corresponding methacrylate based composites. Although the syntheses of diluent VCP monomers has already been reported,[34] there is still a need for low-shrinkage monomers as 2-[[3,5,5-trimethyl-6-[2-(2-methylprop-2-enoyloxy) ethoxycarbonylamino]hexyl]carbamoyloxy] ethyl 2-methylprop-2-enoate (UDMA) or [2-hydroxy-3-[4-[2-[4-[2-hydroxy-3-(2-methylprop-2-enoyloxy)propoxy]phenyl]propan-2-yl]phenoxy]propyl] 2-methylprop-2-enoate (Bis-GMA) alternatives In this context, VCPs bearing urethane groups would be excellent candidates. Indeed, dimethacrylates bearing urethane groups have found applications in dental materials and are known to provide lower polymerization shrinkage as well as excellent mechanical properties. Monomers such as UDMA and TMX-UDMA, which has been used as an alternative to Bis-GMA, are excellent examples of such monomers.

The objective of this project was to synthesize the new difunctional VCPs **3-11** bearing urethane groups. The reactivity of these monomers as well as the mechanical properties, volumetric shrinkage and shrinkage stress of corresponding composites was investigated.



General Part

1 State of the art for VCPs

1,1-disubstituted VCPs are known to undergo ROP. Electron-withdrawing groups such as ester-, cyano- and chloro-groups have been shown to increase the reactivity of VCPs. Ester and amide groups are amongst the most efficient activating groups. As an example, polymerization of 1,1-dicyano-, 1,1-dichloro- and 1,1-diethoxycarbonyl-2-vinylcyclopropanes was investigated. [35-38]

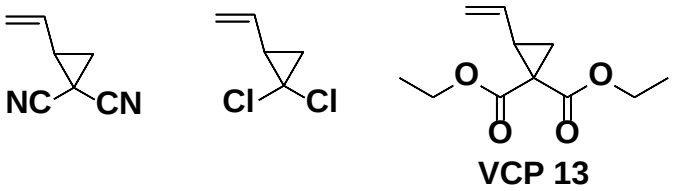


Figure 17: Examples of different 1,1-disubstituted-2-VCPs

The first attempt to copolymerize VCPs was to mix 1,1-dichloro-2-VCP with other comonomers, such as maleic anhydride (MAS), styrene (St), methyl acrylate (MA) and methyl methacrylate (MMA). Based on the polymerization conditions, the formation of a 1,5-type polymers was expected, but the amount of unsaturated units in the co-polymer was only small and changed with the monomer feed. The results were explain on the basis of the fast rearrangement of the radicals and the very fast cyclization of the growing chains (Figure 18).

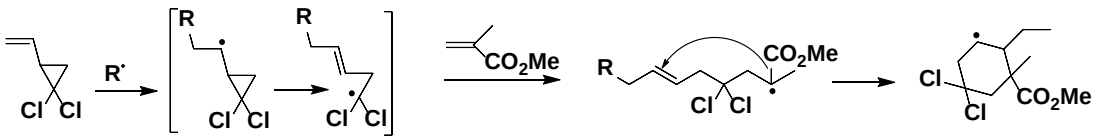


Figure 18: Ring opening and cyclization of the 1,1-dichloro-2-VCP

Analogous to VCPs with radical-stabilizing chloro groups, VCPs with electron withdrawing groups such as ester or cyano groups were tested. They also undergo radical polymerization to afford exclusively 1,5-ring-opened polymers. 1,1-Dicyano-2-VCP showed the highest monomer conversion. The polymerization of the 1,1-diethoxycarbonly-2-VCP resulted in a polymer that only consisted of ring-opened units, but through a temperature raise more cyclobutane units were formed. Therefore it was found that the radical polymerization depends strongly on the type and the position of the substituents.

In a side reaction cyclobutane units are built. The cyclobutane unit is formed over a backbiting step of the propagating radical to a double bond of the main chain. The backbiting step is the major drawback in the ROP of VCPs. Through the backbiting additional shrinkage is occurring. Nevertheless, the ROP of VCPs does allow a significantly reduction of the polymerization shrinkage compared to methacrylates. [39, 40] The propagating step and the backbiting is shown in Figure 19.

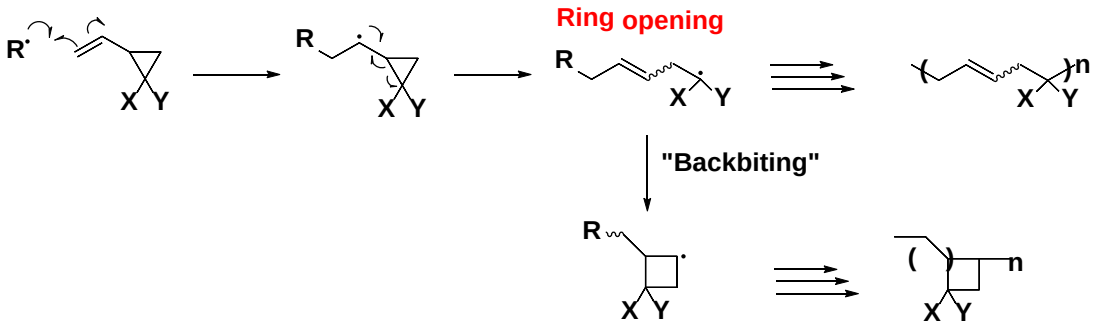


Figure 19: 1,5 Ring opening and backbiting step of the VCP reaction, X and Y represent the electron withdrawing groups

Because of their promising low shrinkage properties, different crosslinking 1,1-disubstitued VCPs were synthesized for an application in dental materials. They were obtained through an esterification of 1-alkoxycarbonyl-2-vinylcyclopropane-1-carboxylic acid with a diol. For the two examples in Figure 20 ethylene glycol and hydroquinone was used for the synthesis. [38, 41]

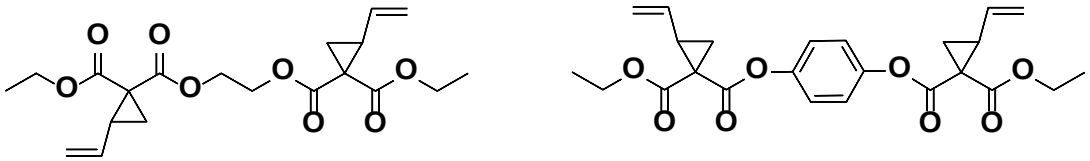


Figure 20: Previously synthesized VCPs by Moszner et al in 1999

Unfortunately by using of the common photoinitiator system CQ/amine the rate of polymerization of these monomers was significantly lower compared to the dimethacrylates. As a consequence, composites solely based on VCPs could not find an application in dental materials.

In 2015 it was stated by Contreras et al. that the reactivity of VCPs can be increased by using a different photoinitiator system. Therefore it was demonstrated that the addition of the onium salt diphenyliodonium hexafluorophosphate (DPIHFP) to the photoinitiator system CQ/ EDMAB brings a significant increase of the polymerization rate of the 1,1-bis(ethoxycarbonyl)vinylcyclopropane

(BECVCP). Subsequently they optimized this ternary photoinitiator system by increasing the amount of DPIHFP and showed that the formation of the cyclobutane units (backbiting) compared to the polymer obtained was even more reduced. The reduced amount of cyclobutane units was proportional to the volume shrinkage. To reach a conversion between 70-80 % Contreras et al. used a high amount of photoinitiator (1.0 mol% CQ + 2.0 mol% EDMAB + 2.0 mol% DPIHFP). These high amounts of initiator are not suitable for dental applications and therefore another way to increase the reactive has to be found. [40]

A year later Contreras et al. stated that through the introduction of amide groups in VCPs, incorporating intermolecular amide hydrogen bonds will lead to an even higher reactivity and a shrinkage reduction compared methacrylates. On the other hand was the amide group responsible for an increase in viscosity. The difference in reactivity between a VCP-hexaamid and a VCP-ester could be due to the molecular structure of the VCP-hexaamid allowing intermolecular hydrogen bonding via amid units, leading to a partial preorganization of monomer molecules.

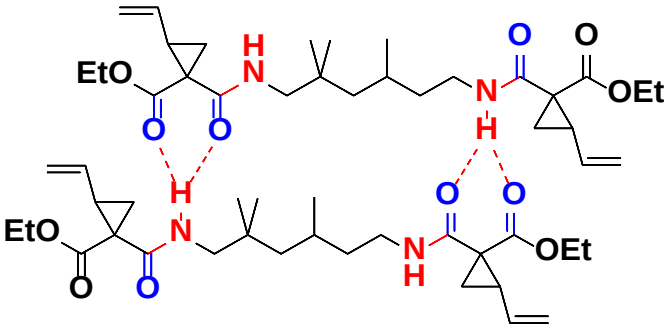


Figure 21: Intermolecular hydrogen bond of the amide units leading to a partial preoranziation

Catel et al. repeated the investigation of the reactivity, of of BECVCP using a ternary photoinitiator system (1.0 mol% CQ + 2.0 mol% EDMAB + 2.0 mol% DPIHFP) as described by Contreras et al. They used a Bluephase LED (20 mW cm^{-2}) as a irradiation source, and in his research it only lead to conversion of 20 % after 2 minutes of irradiation.[40] In 2016 Catel et al. found that the use of Ivocerin®, a highly efficient Norrish type I photoinitiator, leads to a strong increase of the VCP polymerization rate. It was found that using Ivoerin® (0.5 mol%) as a photoinitiatior, a conversion of 92 % using the monomer BECVCO could be reached after 2 min of irradiation. [38, 42]

So far composites are mainly based on methacrylates such as Bis-GMA, TEGDMA and UDMA as crosslinking monomers. These monomers are highly reactive in free radical polymerization, exhibit relatively low polymerization shrinkage and enable formation of polymer networks with excellent mechanical properties. To improve the mechanical properties high filler loading is required. Unfortunately high filler contents cannot be incorporated with high viscosity monomers such as Bis-

GMA. In order to circumvent this problem, diluents are added to the monomer mixture. The result is polymerization shrinkage. Therefore there is a need of low shrinkage diluent cross-linkers to replace the methacrylate components in the composite. By the syntheses of new VCPs (Figure 22) with similar structures to diluent methacrylates new composites could be formulated with Ivocerin® as a photoinitiator. The so far synthesized diluent VCPs had a higher reactivity, exhibited a significantly lower shrinkage stress and a higher DBC in comparison to TEGDMA.[34] The composites using the VCPs exhibit good mechanical properties as well as low polymerization shrinkage and volumetric shrinkage.

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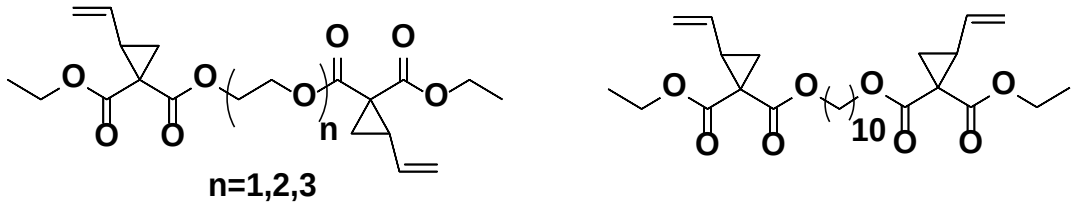


Figure 22: Structure of successfully synthesized and tested diluent VCPs

Those results showed the high potential of VCPs to replace methacrylates for the formulation of low-shrinkage composites. In order to further reduce the polymerization shrinkage and improve the mechanical properties of such VCP based materials, alternative structures to Bis-GMA would be needed. For dentistry a breakthrough would be to design a composite with a low volumetric shrinkage and a low shrinkage stress to avoid mircoleakage.

2 Syntheses of the monomers

Methacrylates tend to have a high volumetric shrinkage and shrinkage stress during curing. Since it was found that VCPs undergo ring opening during photopolymerization the objective was to synthesize VCP containing monomers as a replacement of methacrylates in dental composites. In addition the molecules should bear a urethane group because it is know from literature that methacrylates containing urethane groups are highly reactive and have good mechanical properties.[43]

Syntheses of VCPs 2 and 8

VCPs **2** and **8** were synthesized in two steps (Figure 23) starting from 1,1-diethoxycarbonyl-2-vinylcyclopropane. One ester group of 1,1-diethoxycarbonyl-2-vinylcyclopropane was cleaved with KOH. The reaction was carried out at room temperature for 2 h. The resulting carboxylic acid (VCP **1)** was recovered in a 71 % yield.

The second step was a Steglich esterification of the carboxylic acid (VCP **1**) with ethylene glycol (5 eq.) using the carbodiimide DCC as a coupling agent and DMAP as a catalyst. The resulting alcohol VCP **2** was isolated in a 65.0 % yield

VCP **8**, was synthesized form VCP **1** under the same conditions as VCP **2** just by the use of diethylene glycol (5 eq.) DCC and DMAP. VCP **8** was isolated in a 70 % yield

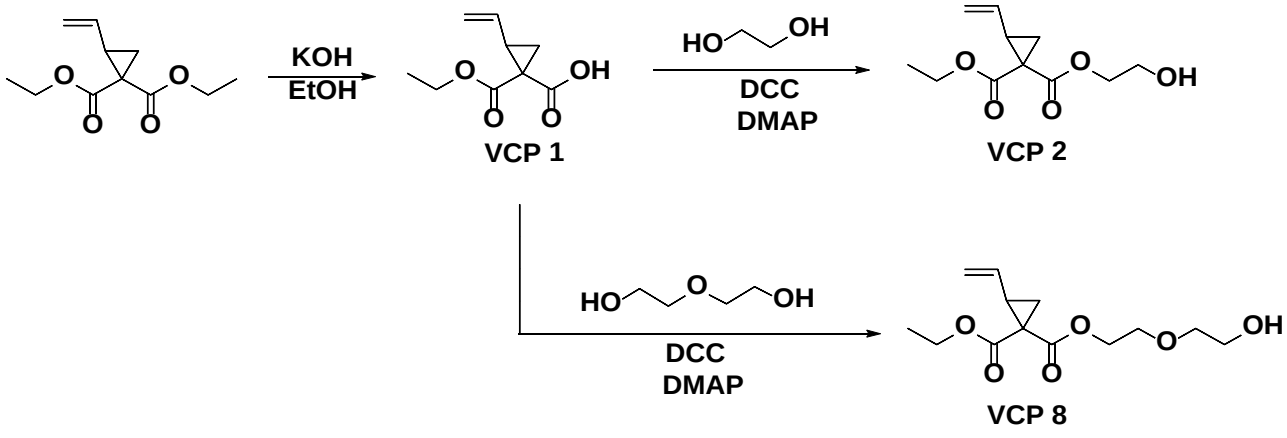


Figure 23: Syntheses of VCP 1, VCP 2 and VCP 8

Synthesis of VCPs 3-7 and 9-11

VCPs **3-7** were synthesized by reacting VCP **2** with the corresponding diisocyanate using DBTDL as a catalyst (Figure 24). For VCPs **9-11** the corresponding diisocyanate was reacted with VCP **8** (Figure 25). The reaction was carried out under reflux for 8 h. The resulting VCPs were isolated in good yields (69-92 %). All new VCP monomers were characterized by ^{1}H NMR and ^{13}C NMR spectroscopy. The NMR spectra of the pure compounds are attached in the appendix. VCPs **3** and **4** were found to have viscosity of 50-150 Pa*s. VCPs **5-7** were highly viscous (9.0-26.0 kPa*s) compared to UDMA (η=12-14 Pa*s) and bisGMA (η=0.7-1.4 kPa*s). The variation of the spacer length led to a decrease in viscosity. The refractive index is an important parameter for the development of dental composites. VCPs **3**, **4**, **6** and **10** had a significantly lower refractive index than Bis-GMA. VCP **5** has an almost equal and VCP **7**, VCP **9** and VCP **11** have slightly lower refractive indices as Bis-GMA. A Match between the refractive indices of both monomer matrix and the fillers is useful for an optimal depth of cure.

Table 2: Physical properties of VCPs 3-4 and TEGDMA

Monomer	**η [mPa*s]**	**n_D**
VCP **3**	0.34	1.4914
VCP **4**	1.50	1.4917
VCP **5**	140.0	1.5574
VCP **6**	260.0	1.4972
VCP **7**	97.10	1.5055
VCP **9**	4.54	1.5057
VCP **10**	3.02	1.4955
VCP **11**	1.30	1.5045
Bis-GMA	**7-14**	**1.5520**

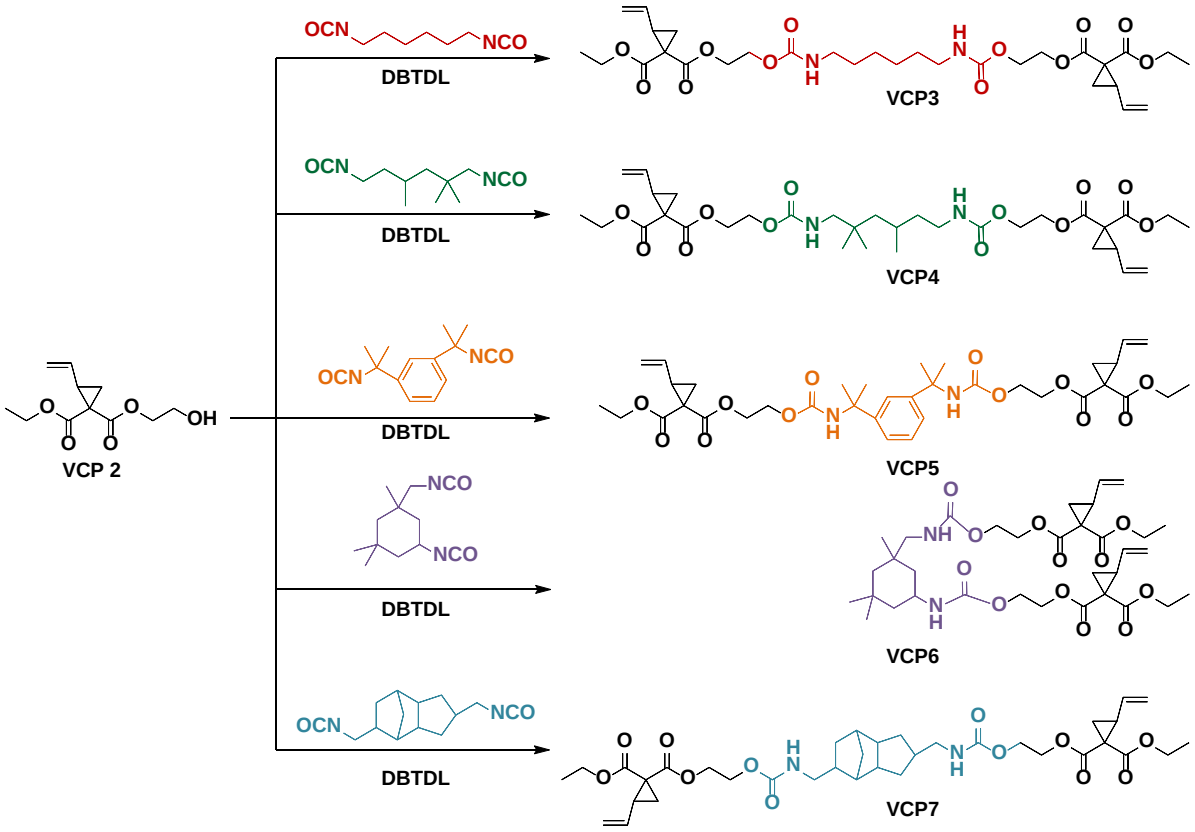


Figure 24: Synthesis of VCPs 3-7

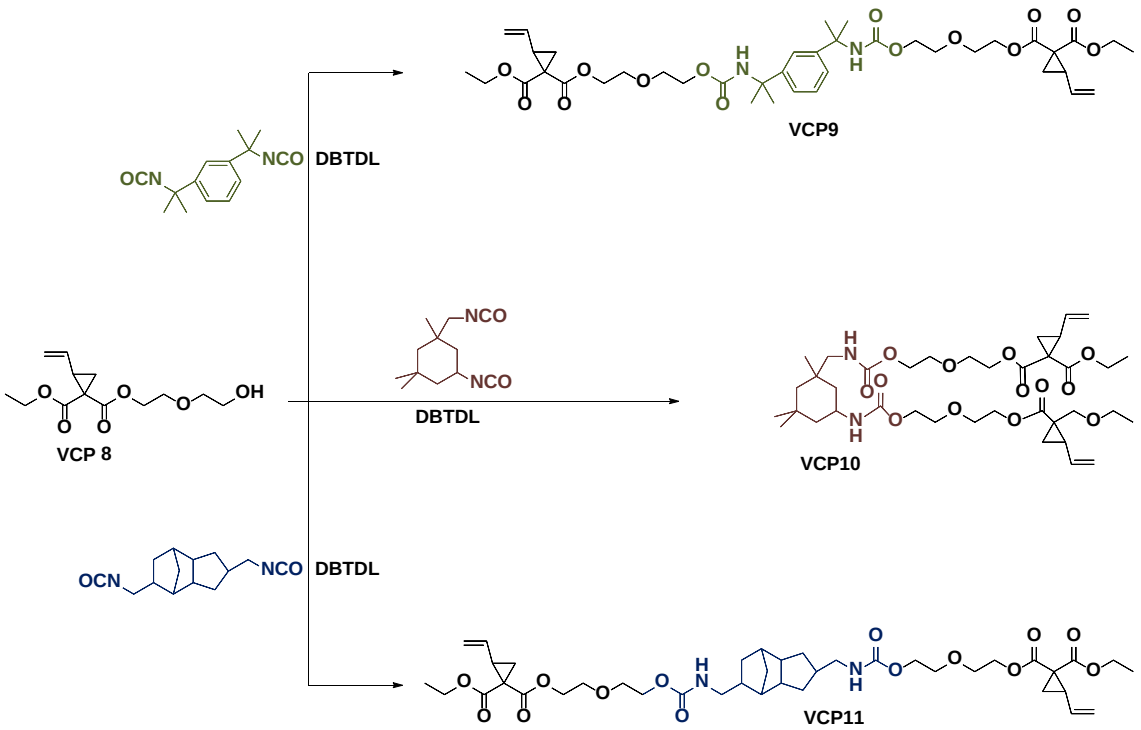


Figure 25: Synthesis of VCPs 9-11

Syntheses of VCP 12

VCP **12** was synthesized in two steps (Figure 26). The first step is described in section 3.1.1. The second step was a Steglich esterification of the carboxylic acid (VCP **1**) with hexadecanediol (0.5 eq.) using the carbodiimide DCC as a coupling agent and DMAP as a catalyst. The resulting VCP 1**2** was isolated in a 70.0 % yield.

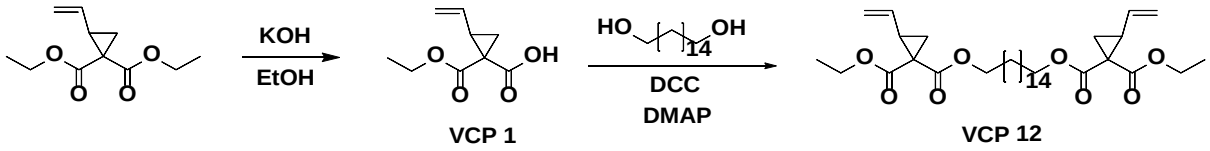


Figure 26: Syntheses of VCP 12

Investigation of the reactivity

Photopolymerization

The reactivity of the synthesized monomers VCPs **3-7** and VCPs **9-11**was studied using photo-DSC. Each polymerization was performed using a Bluephase LED curing light (20 mW*cm^{-2}) for 2 min at 37 °C. Ivocerin® (0,5 mol%) was used as photoinitiator. Due to the high viscosity of VCPs **5-7** and VCPs **9-11** homopolymerization could not performed. For VCPs **5-7** and VCPs **9-11**, VCP **13** was used as a diluent (Figure 27). For these monomers copolymerization was carried out in a 1:1 (mol:mol) mixture. VCP **14** was used as a reference since it was known and stated by Contreras et al. to be highly reactive.[40]

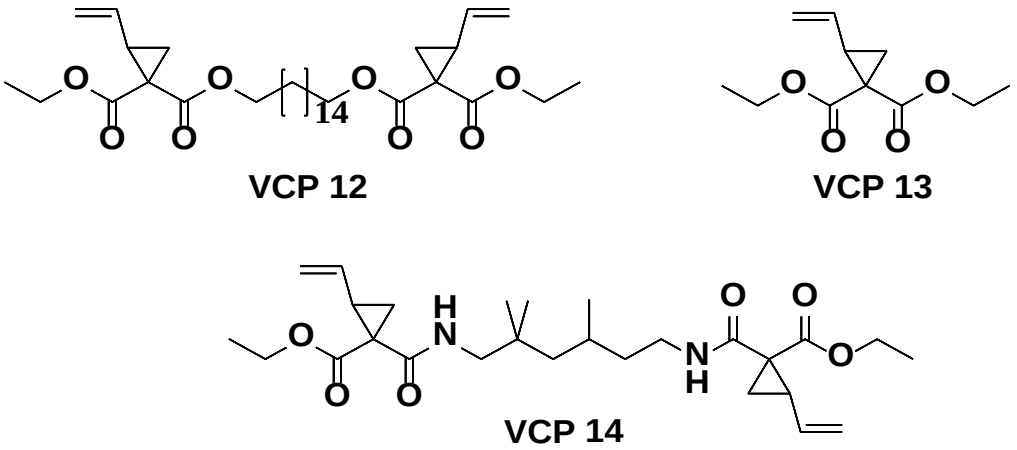


Figure 27: Structure of VCPs 12, 13 and 14

The first attempt to investigate the reactivity was to homopolymerize the monomers with a moderate viscosity. Therefore only VCPs **3** and **4** were found to have a viscosity low enough to perform homopolymerization. Figure 28 and Figure 29 represent the rate of polymerization (R_p) and the double bond conversion (DBC) of VCP **3** and VCP **4** as a function of time. VCP **12** and VCP **14** were used as a reference, to compare the influence of a long C16 spacer and an amide group in comparison to molecules baring a urethane group. According to the results, monomers could be classified from the most to the least reactive, in the following order: VCP **12** > VCP **14** >> VCP **3** ≈ VCP **4.** The result was unexpected, since the VCP **12** has a C14 spacer and the long spacer should result in a decrease of reactivity. VCP **14** was bearing an amide group whereby the reactivity was increased, this was expected since the amide group is the better activating group than the ester group. VCPs **3** and **4** were compared to VCP **12** and **14** highly viscous due to the urethane groups. VCPs **3** and **4** had also a lower DBC as the reference monomer. This was also expected considering the high viscosity difference and the different functional groups.

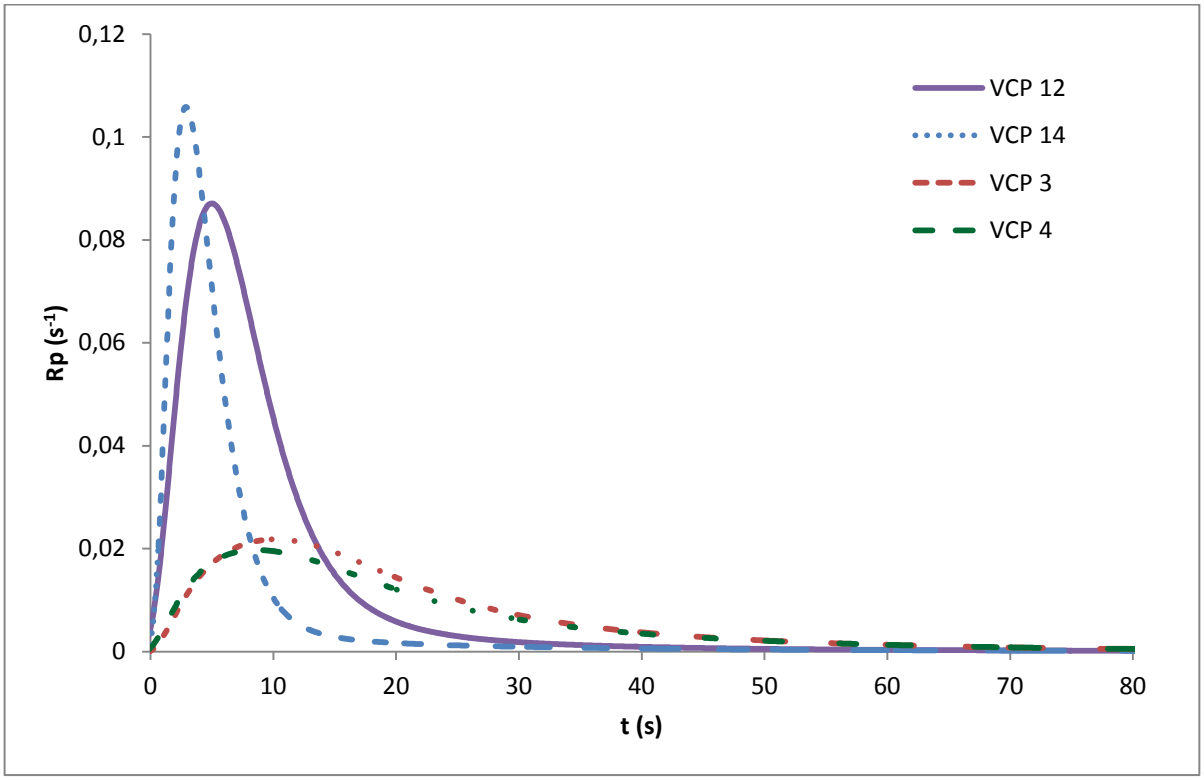


Figure 28: Rate of polymerization (R_p) versus irradiation time for the photopolymerization of VCPs 3, 4, 12 and 14. All monomers were mixed with 0.5 mol % Ivocerin®

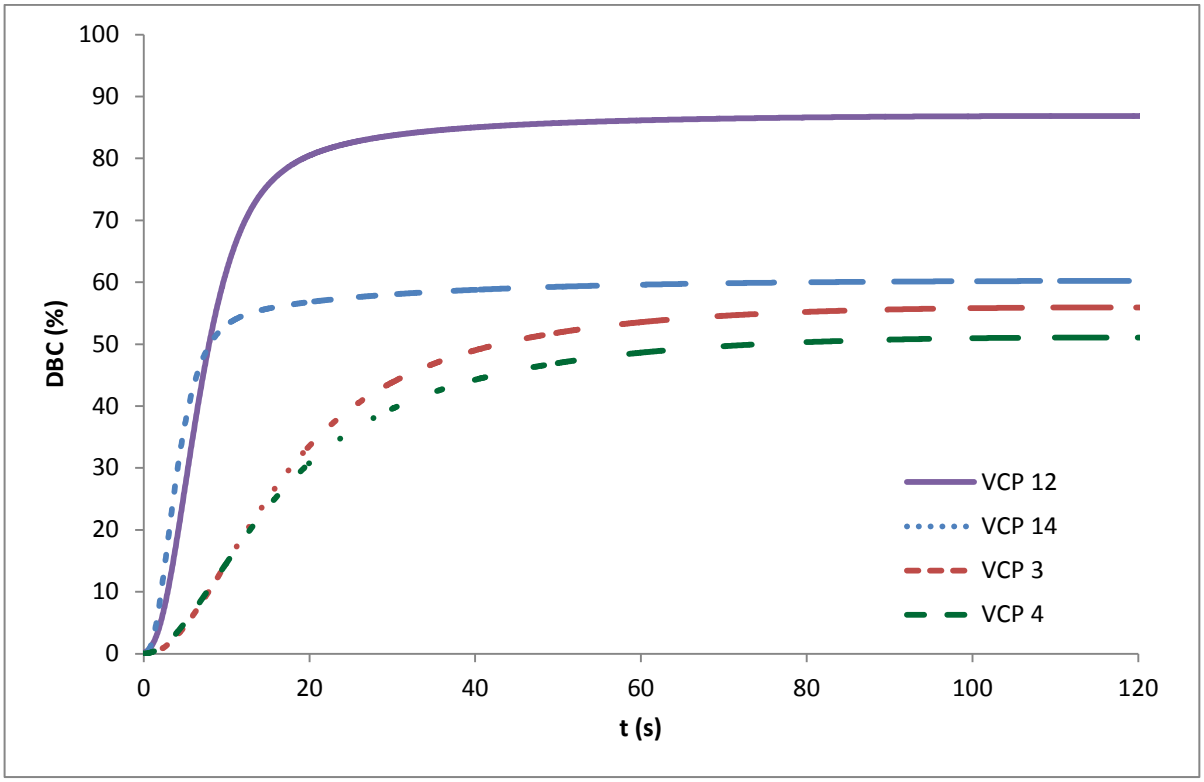


Figure 29: Double bond conversion (DBC) versus irradiation time for the photopolymerization of VCPs 3, 4, 12 and 14. All monomers were mixed with 0.5 mol % Ivocerin®

Table 3: Photo DSC results of the homo polymerization

Monomer	*t R_{pmax} [s]*	*ΔH [J/g]*	*Rp_{max}*10^3 [s^{-1}]*	*DBC [%]*
VCP ***3***	10.1 ± 0.08	179 ± 3.5	20 ± 0.1	60.8 ± 0.37
VCP **4**	8.6 ± 0.07	154 ± 1.5	20 ± 0. 2	53.9 ± 0.51
VCP **12**	**5.1 ± 0.08**	**185 ± 2.7**	**40 ± 0. 7**	**47.3 ± 0.60**
VCP **14**	**2.5 ± 0.03**	**235 ± 17.0**	**100 ± 0. 3**	**61.8 ± 0.11**

Because of the high viscosity of the monomers, especially VCPs **5-7** and **9-11**, no homopolymerization was possible, copolymerization was performed. Copolymerization was performed with VCP **13** (Figure 27) as a diluent in a 1:1 (mol:mol) ratio. As reference the highly reactive VCP **14** was also mixed in a 1:1 (mol:mol) ratio with VCP **13**. A significant increase of the reactivity in comparison with the homopolymerization was achieved. The double bond conversion of the monomer mixture with VCP **3** and **4** (73-76 %) was almost as high as the DBC from the reference monomer mixture VCP **14**/ VCP **12** (77%). The rate of polymerization for the monomer mixtures containing VCPs **6** and **7** were significantly lower than the reference mixture. The mixture

with VCP 5 was the least reactive of all. The DBC for the mixtures with VCPs **5-7** (55-62 %) was also significantly lower than the reference mixture (72 %).

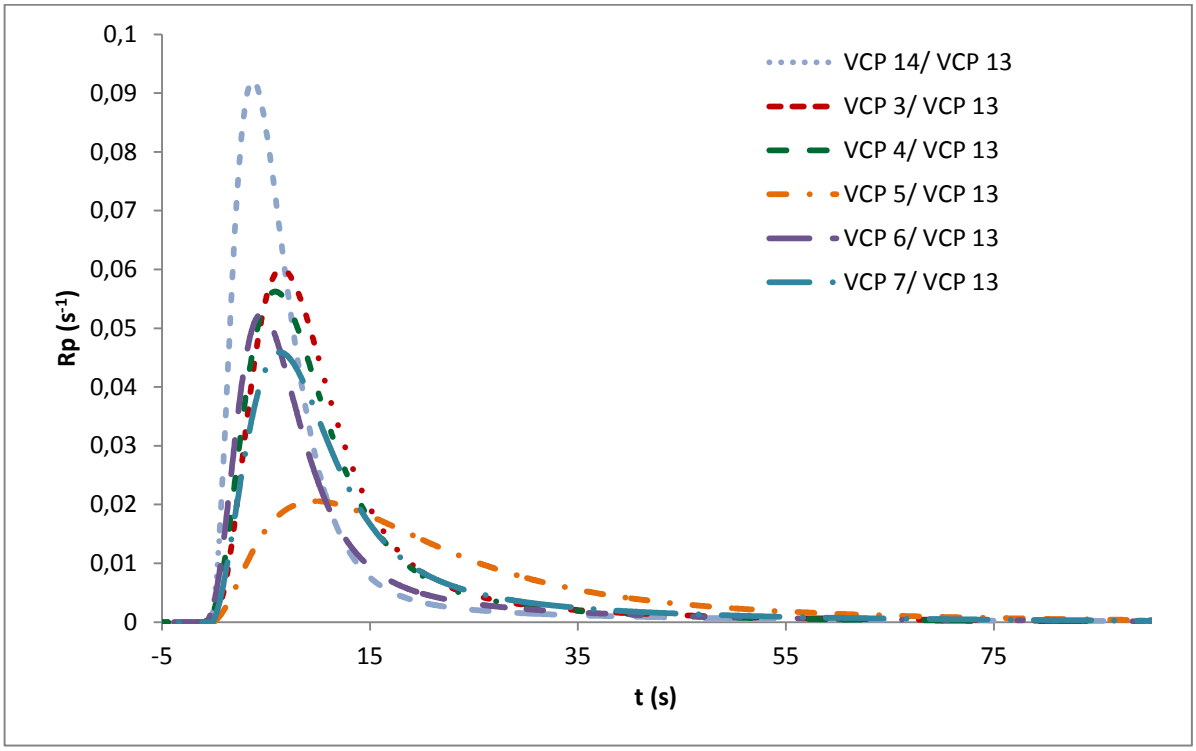


Figure 30: Rate of polymerization (R_p) versus irradiation time for the photopolymerization of VCPs 3-7 and 14 in a 1:1 (mol:mol) ratio with 13 and 0.5 mol% Ivocerin®

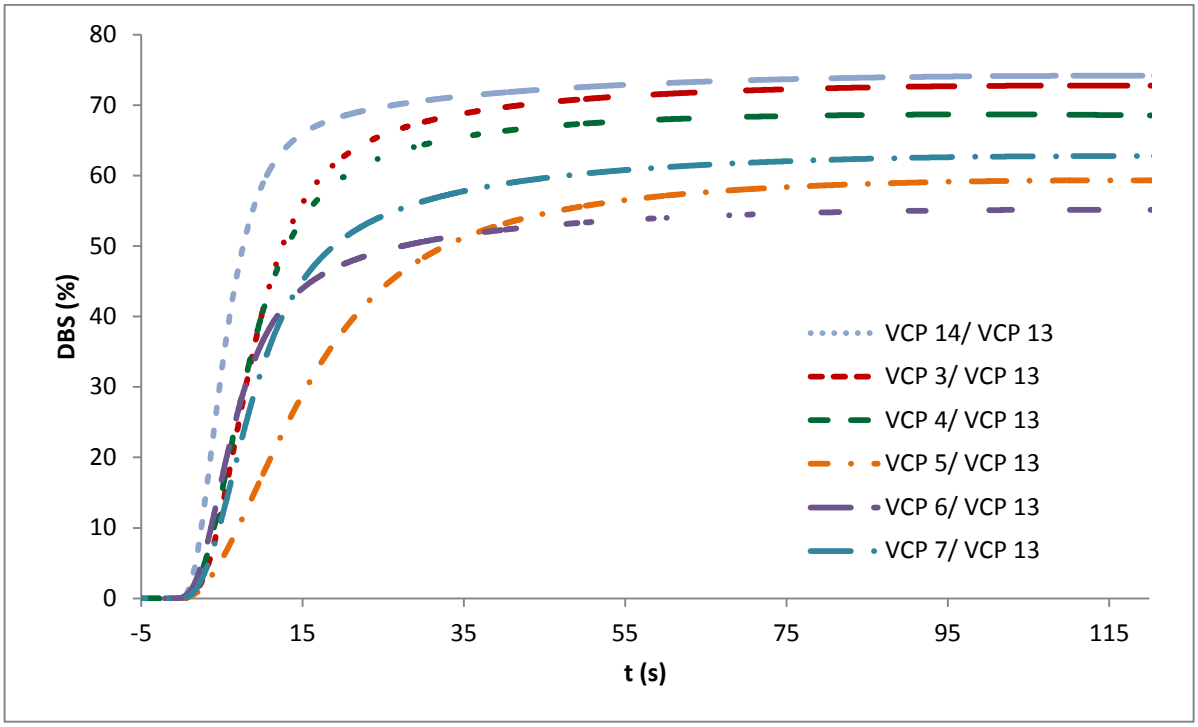


Figure 31: Double bond conversion (DBC) versus irradiation time for the photopolymerization of VCPs 3-7 and 14 in a 1:1 (mol:mol) ratio with 13 and 0.5 mol% Ivocerin®

The reference monomer mixture VCP **14**, bearing an amide group, exhibits a higher DBC (72 %) than the three most promising monomers (VCPs **9-11**). They had a slightly lower amount (63-70 %) for the DBC. By the extension of the spacer for VCPs **9-11** a significant increase of the reactivity in comparison to VCPs **5-7** was achieved and an increase of the DBC could also be obtained (Figure 32 and Figure 33). Normally a decrease in reactivity would have been expected by the extension of the spacer, because of the higher molecular weight, which leads to less molecules in the same volume. In our case a higher reactivity was observed which might be due to the decreased viscosity of the monomers. No monomer was able to reach higher rate of polymerization or DBC than the reference monomer (VCP **14**). It has been shown, recently, that the presence of an amide group (VCP **14**) results in a strong increase of the polymerization rate, a similar reactivity was expected for monomers bearing a urethane group because methacrylates bearing urethane groups are known for their high reactivity. [40]

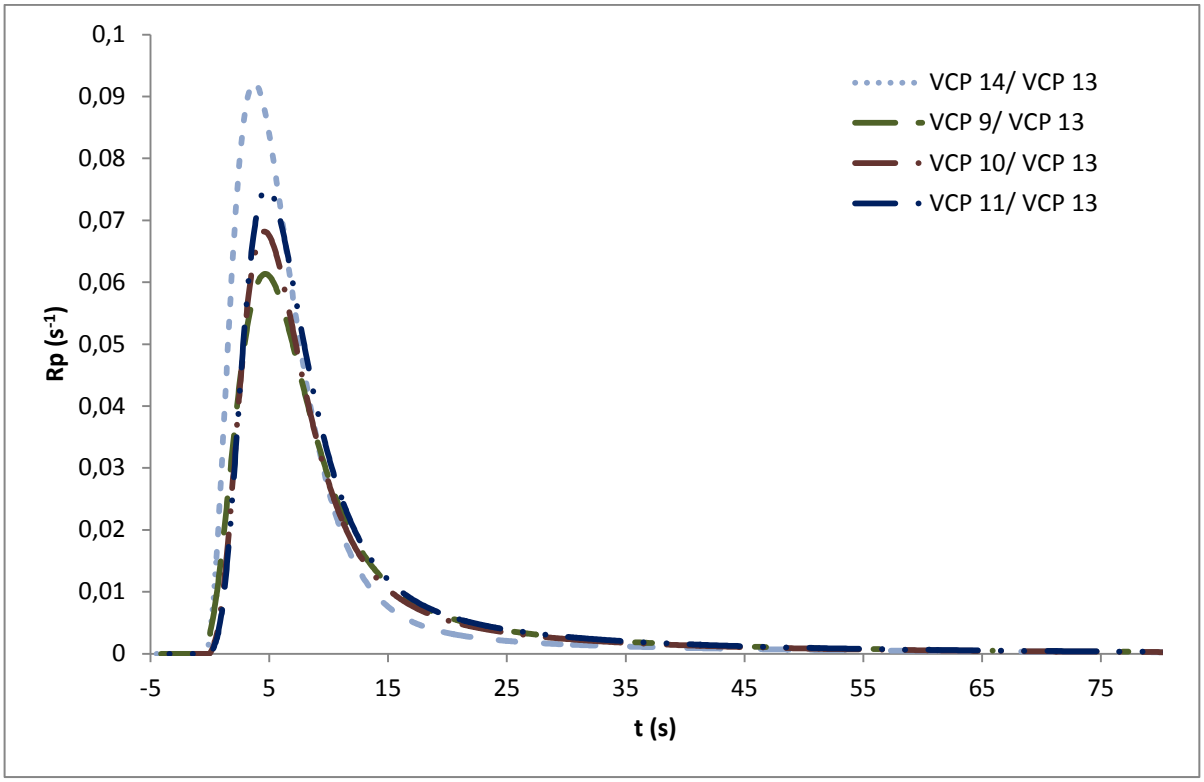


Figure 32: Rate of polymerization (R_p) versus irradiation time for the photopolymerization of VCPs 9-11 and 14 in a 1:1 (mol:mol) ratio with 13 and 0.5 mol% Ivocerin®

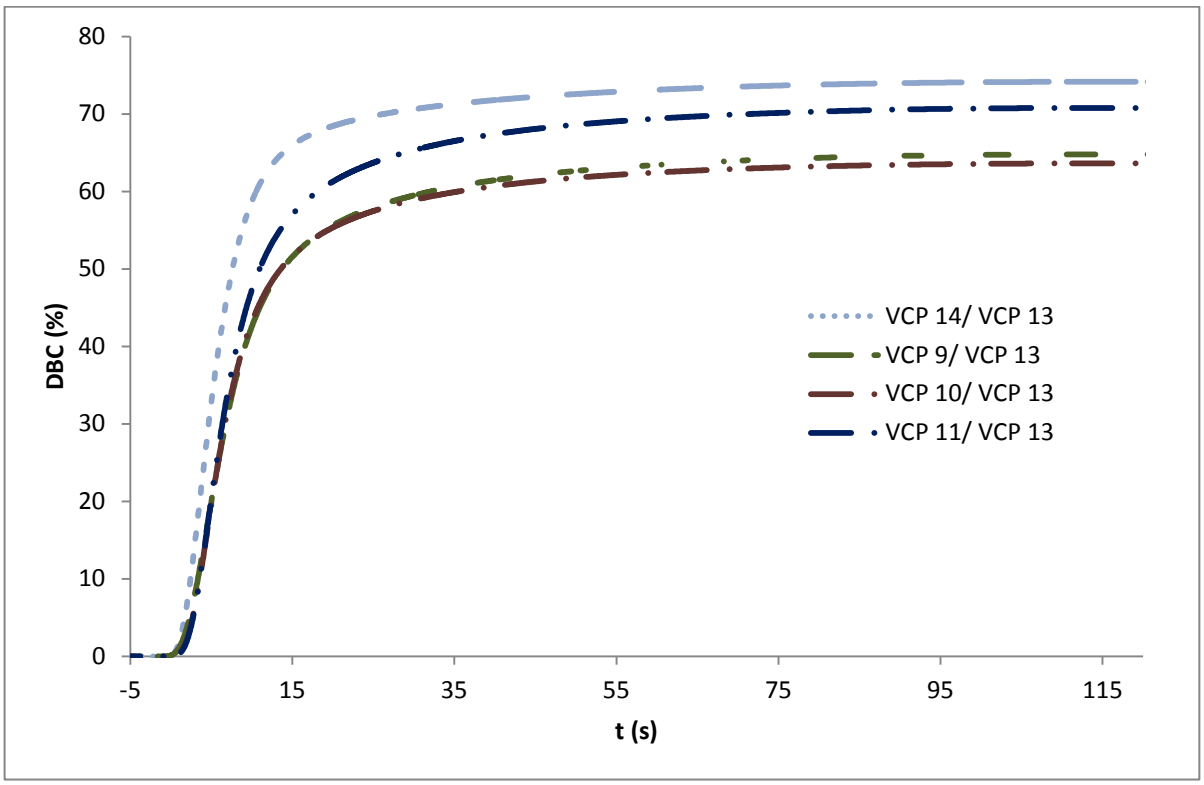


Figure 33: Double bond conversion (DBC) versus irradiation time for the photopolymerization of VCPs 9-11 and 14 in a 1:1 (mol:mol) ratio with 13 and 0.5 mol% Ivocerin®

Table 4: Photo DSC results of the co-polymerization

Monomer	*t R_{pmax} [s]*	*ΔH [J/g]*	*Rp_{max}*10^3 [s^{-1}]*	*DBC [%]*
VCP **3**/ VCP **13**	5.5 ± 0.09	259 ± 6.3	61 ± 1.3	76.2 ± 0.2
VCP **4**/ VCP **13**	5.2 ± 0.20	235 ± 8.4	62 ± 3.6	72.4 ± 0.3
VCP **5**/ VCP **13**	9.3 ± 0.18	191 ± 4.8	25 ± 0.6	61.1 ± 0.2
VCP **6**/ VCP **13**	4.7 ± 0.13	180 ± 3.1	51 ± 1.7	56.2 ± 0.1
VCP **7**/ VCP **13**	6.3 ± 0.36	203 ± 7.1	43 ± 2.3	65.2 ± 0.2
VCP **9**/ VCP **13**	4.7 ± 0.07	192 ± 2.6	60 ± 1.2	67.3 ± 0.9
VCP **10**/ VCP **13**	3.8 ± 0.10	190 ± 4.9	67 ± 1.7	65.1 ± 1.7
VCP **11**/ VCP **13**	3.8 ± 0.03	201 ± 3.7	75 ± 0.9	70.6 ± 1.3
VCP 14/ VCP 13	**5.5 ± 0.09**	**259 ± 6.3**	**61 ± 1.3**	**2.2 ± 1.8**

RT-NIR-Photorheology

For the further investigation of the reactivity of VCPs mixutres, the photoreactivity was analyzed by the coupled measurement of RT-NIR and photorheology. With the help of this hyphenated analytical device, characteristic parameters such as evolution of time to gel point (t_g) (defined by G′/G″ = 1), double bond conversion at the gel point DBCg, storage modulus G′ during curing, final DBC and polymerization-induced shrinkage force F [N] can be investigated for the tested resins. To the gelation point the ratio of initiation and termination remains unchanged. At the gelation point the resin changes from the liquid state to a solid gel. Through that change the mobility of the polymer chains in the forming network is decreasing. While initiation is still in progress, the termination of the propagation is hindered which leads to a high polymerization rate. The in situ characterization of rheological behavior and chemical conversion using a RT-NIR-photorheology setup was performed on mixtures of VCPs **3-7** and **9-11** with VCP **13** in a 1:1 mol: mol ratio. As a reference a mixture of UDMA/ AAEMA 1:1 (mol:mol) with 0.5 mol % Ivocerin® was also prepared. The formulations were prepared analogously to the photo-DSC samples and the measurement parameters are stated in Section 2.2. The results of the measurement showed that the gel time of mixtures for VCPs **3, 4, 9, 10** and **11** (t_g = 1.3-2.5 s) is about the same as the values from methacrylic mixture (UDMA/ AAEMA) (tg = 2.0 s). The mixtures of VCPs **3** reaches gelation earlier than all the other mixtures, which can be explained by their architecture. The monomer mixtures with VCPs **5-7** were highly viscous whereby they have not the same mobility as the linear monomers and this lead to a gelation at higher t_g (5.0-

13.3 s). Through the extension of the spacers the mixtures with VCPs **9-11** t_g is reached earlier (2.0-2.5 s). This confirms the photo-DSC results, which correlate with the RT-NIR-photorheology measurements. Gelation occurs at conversions between 15-18 % for the mixtures with VCPs **5-7** (Figure 38). For the mixtures containing VCPs **9-11** gelation started already at a DBC of 10-13 %. Through the enlargement of the spacer the gel point of the mixtures with VCPs **9-11** was shifted to lower conversions. At the gel point the volumetric shrinkage and shrinkage stress, due to formation of covalent bonds, starts to matter because the material cannot flow anymore. In the case of the mixtures for VCPs **3-7** (Figure 37) and **9-11** the DBCg values lie within the range of 10-18 % and therefore under the value of the reference UDMA/ AAEMA (DBCg = 29 %) (Table 5). The values for the storage modulus (G') were lower for all measured mixtures except for the one containing VCP **7**, there an almost equal value was reached. The mixtures with VCP **3** had one lowes G', which is due to the linear architecture and therefore correlates with the flexibility. Mixtures containing VCPs **5-7** (Figure 35: G' values of VCPs 3-7 mixtures with VCP 13 1:1 (mol:mol)) hat high G' (852-1184 MPa), but through the extension of the G' for the mixtures with VCP **9-11** (Figure 36) decreased (643-980 MPa). Therefore it can be stated the mixtures with the highly viscous VCPs were more rigid and through the extension of the spacer the flexibility increased. The reduction of shrinkage stress, has also been confirmed by the measurement of the shrinkage force. VCPs **3-4** mixtures had the highest values with 16-18 N but still significantly lower than the reference mixture. With the mixtures containing VCPs **5-7** and **9-11** the shrinkage fore was reduced even more with results of 12-14 N. Therefore, a significant reduction of shrinkage stress had even has been proven. This reduction can be attributed due to the RROP reaction during polymerization. In Figure 37 the DBC and in Figure 39 the shrinkage stress of VCP **3-7** are pictured. In Figure 39 and Figure 40 the correlation between VCP **5-7** and VCP **9-11** with enlarged spacers is shown. Since the volumetric shrinkage and the shrinkage stress start to matter at the gel point, it can be stated that the lower DBC of all mixtures is negligible since gelation starts already at conversions between 10-18 %. Therefore, a higher DBC would not result in a higher shrinkage stress. The DBC of VCPs **9-11** mixtures was significantly increased and the shrinkage force was slightly reduced compared to the correlating mixtures and the methacrylic reference.

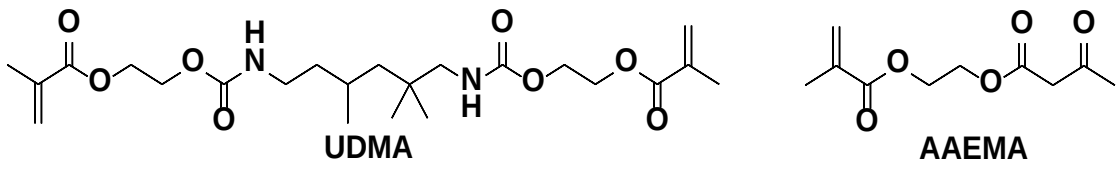


Figure 34: Methacrylic reference monomers for the RT-NIR-photorheology

Table 5: Restults of the RT-NIR-photorheology

Monomer	t_g [s]	DBC_g [%]	Final G' [MPa]	Final DBC [%]	F_N [N]
VCP **3**/ VCP **13**	1.3 ± 0.3	11.3 ± 1	684.2	76.7 ± 0.1	18.0 ± 0.9
VCP **4**/ VCP **13**	2.0 ± 0.2	16.0 ± 2	1022.0	73.0 ± 0.2	16.1 ± 0.2
VCP **5**/ VCP **13**	7.5 ± 0.5	17.7 ± 1	852.9	51.7 ± 0.1	12.1 ± 0.6
VCP **6**/ VCP **13**	13.3 ± 0.1	17.0 ± 1	1061.0	67.0 ± 0.1	14.3 ± 0.1
VCP **7**/ VCP **13**	5.0 ± 0.3	15.3 ± 1	1184.0	63.0 ± 0.2	14.0 ± 0.1
VCP **9**/ VCP **13**	2.5 ± 0.6	10.0 ± 2	643.8	71.0 ± 0.3	13.2 ± 0.3
VCP **10**/ VCP **13**	2.0 ± 0.2	13.0 ± 2	854.3	68.7 ± 0.2	13.1 ± 0.2
VCP **11**/ VCP **13**	2.0 ± 0.1	12.7 ± 1	980.4	72.0 ± 0.2	14.1 ± 0.4
UDMA/ AAEMA	**2.0 ± 0.1**	**28.7 ± 1**	**1178.5**	**84.0 ± 0.4**	**28.0 ± 0.3**

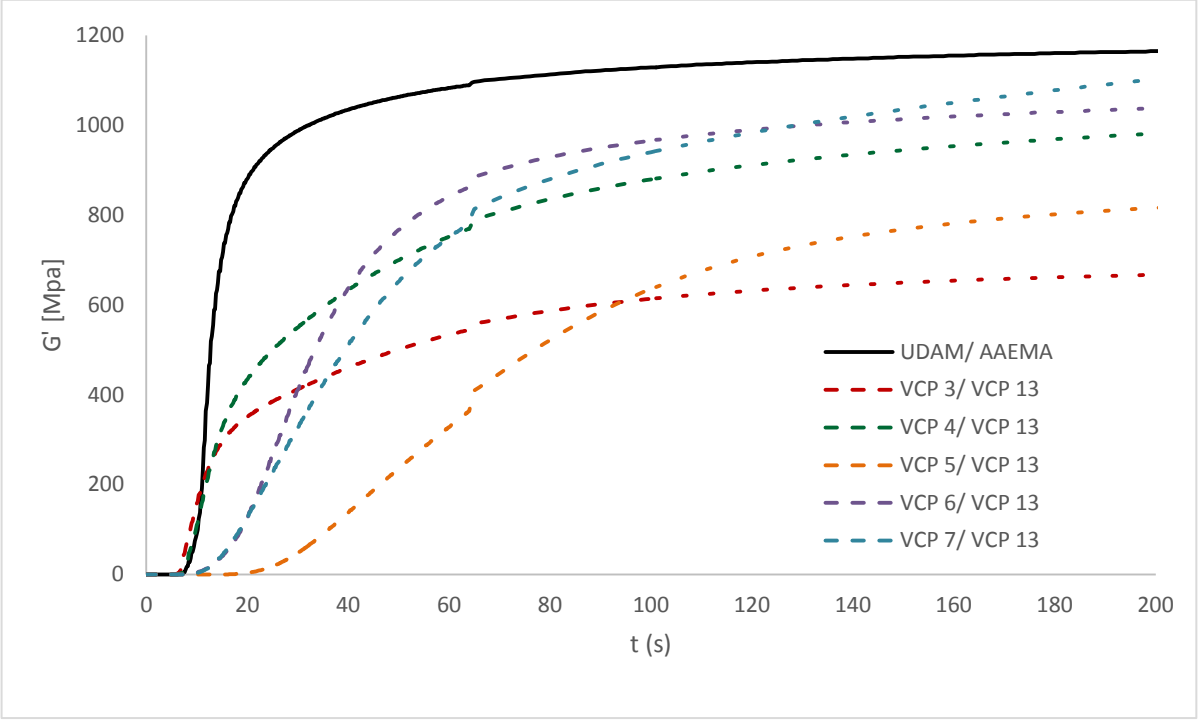


Figure 35: G' values of VCPs 3-7 mixtures with VCP 13 1:1 (mol:mol)

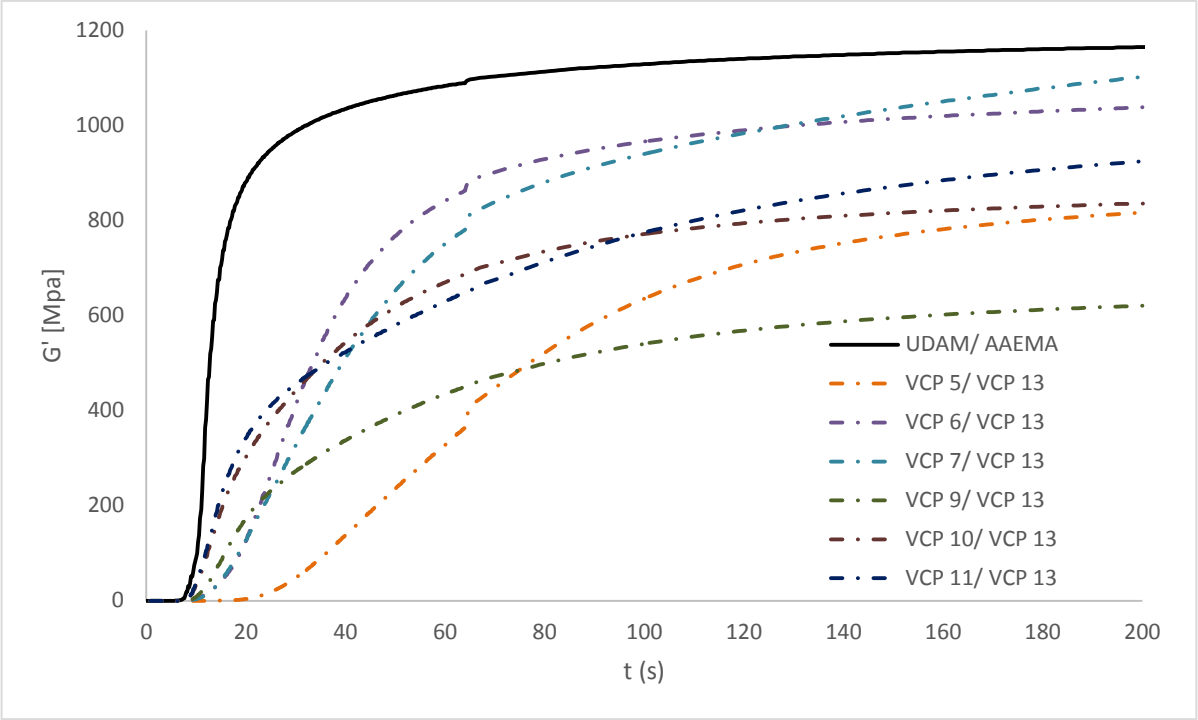


Figure 36: G' of VCPs 5-7 in comparison with VCPs 9-11, mixtures with VCP 13 1:1 (mol:mol)

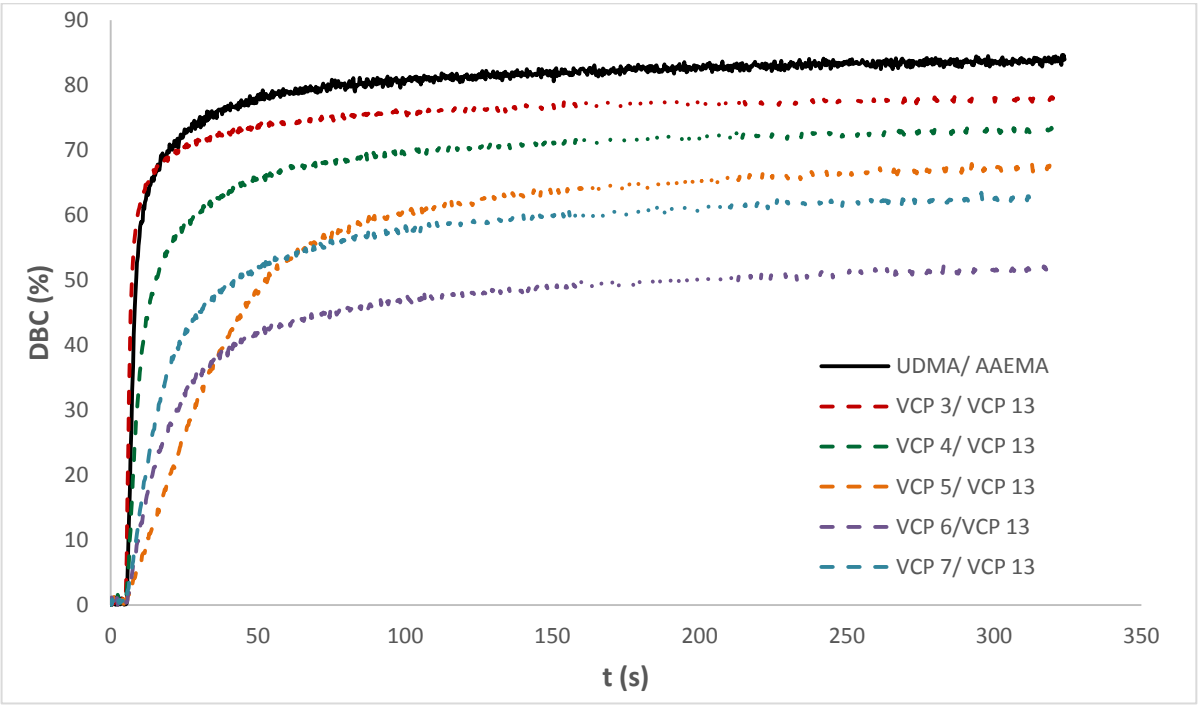


Figure 37: DBC of the VCP 3-7 mixture with VCP 13 1:1 (mol:mol) measured with the RT-NIR-photorheometer

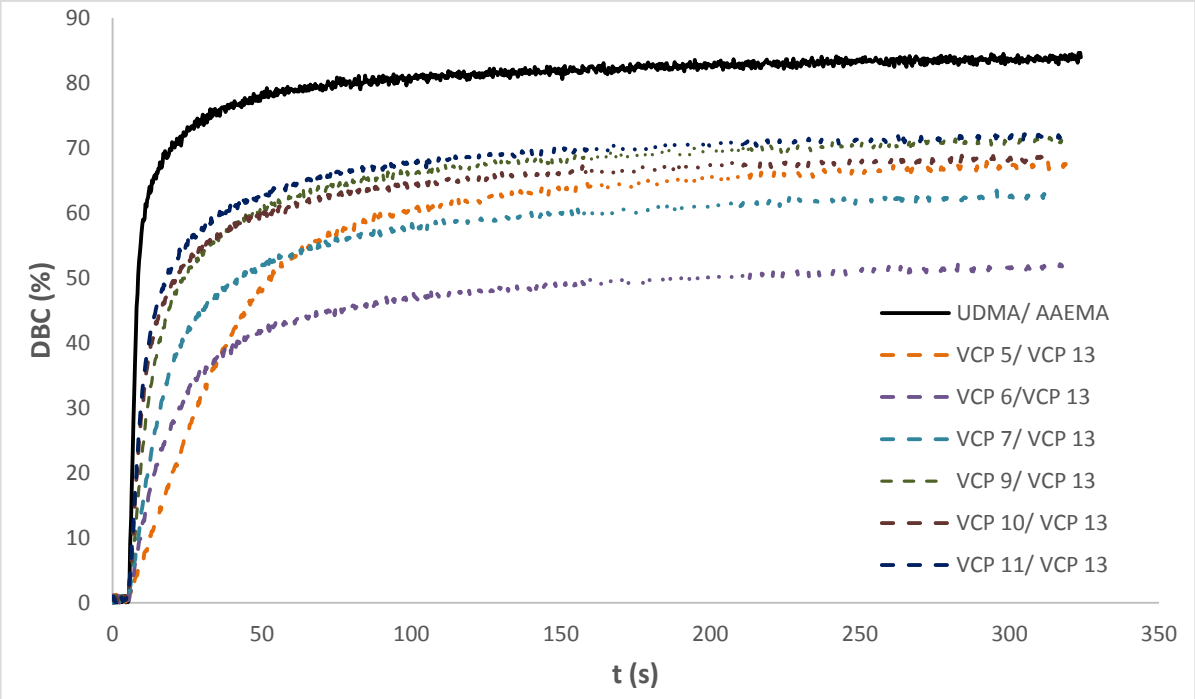


Figure 38: DBC of VCPs 5-7 in comparison with VCPs 9-11, mixtures with VCP 13 1:1 (mol:mol)

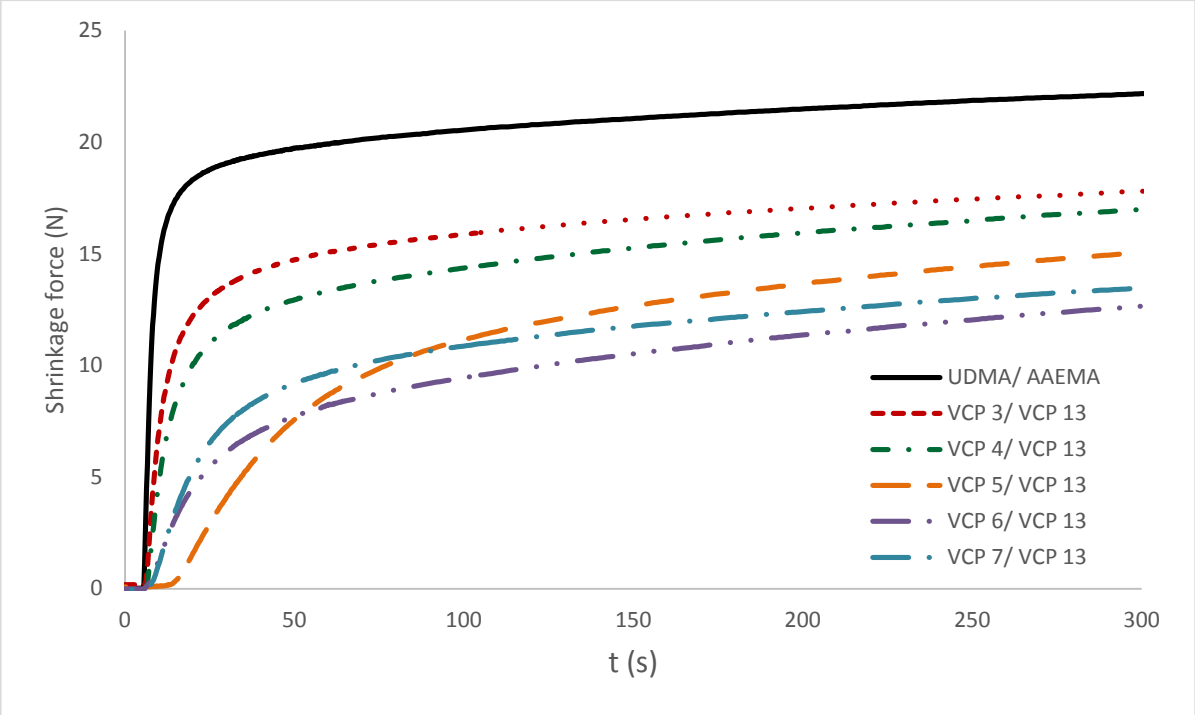


Figure 39: Shrinkage force of VCP 3-7 mixture with VCP 13 1:1 (mol:mol) measured with the RT-NIR-photorheometer

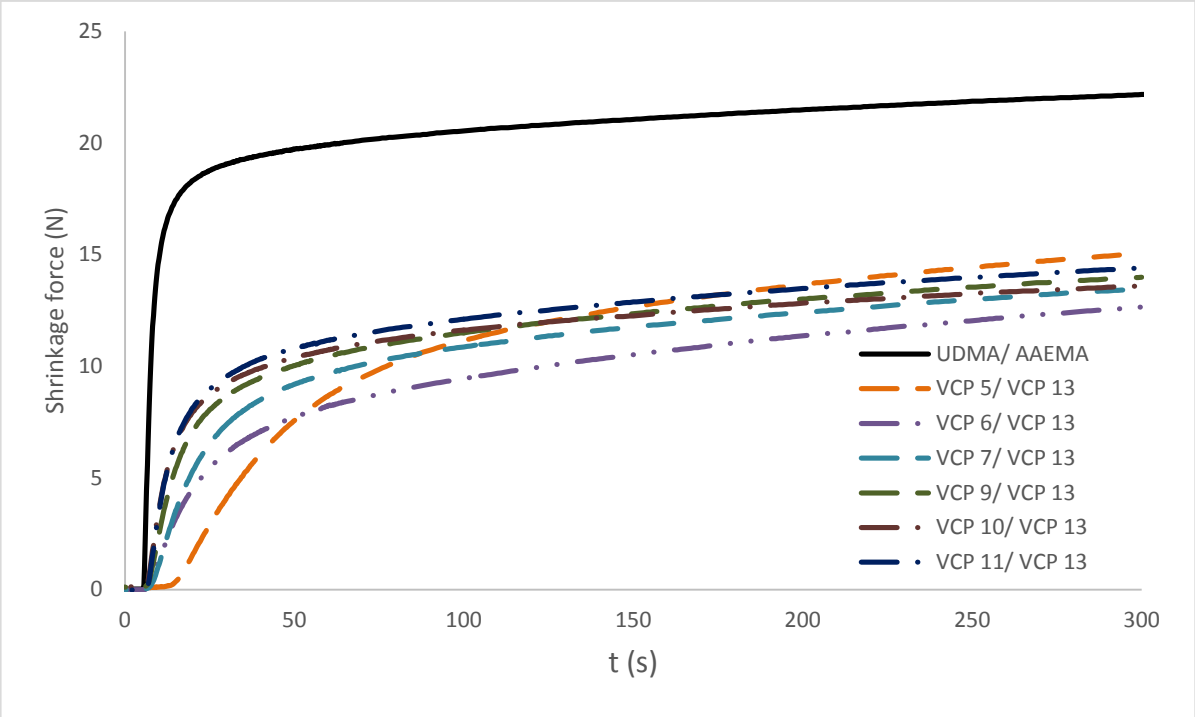


Figure 40: Shrinkage force of VCPs 5-7 in comparison with VCPs 9-11, mixtures with VCP 13 1:1 (mol:mol)

VCP-based dental composites

The flexural strength and the flexural modulus of the cured composite samples was measured by a three-point bending test with an universal testing machine (Zwick, Germany).[44] Because of the high viscosity of the monomers, diluent monomers have been used for the monomer mixture (Figure 41). The syntheses of VCP **14** was recently reported by Contreras et al.[45] This monomer was chosen as a UDMA alternative for the composites. VCP **15** and **16** had a very low viscosity and were used for the monomer mixtures with VCPs **3**-**7** to generate a homogenous mixture and dissolve Ivocerin®.

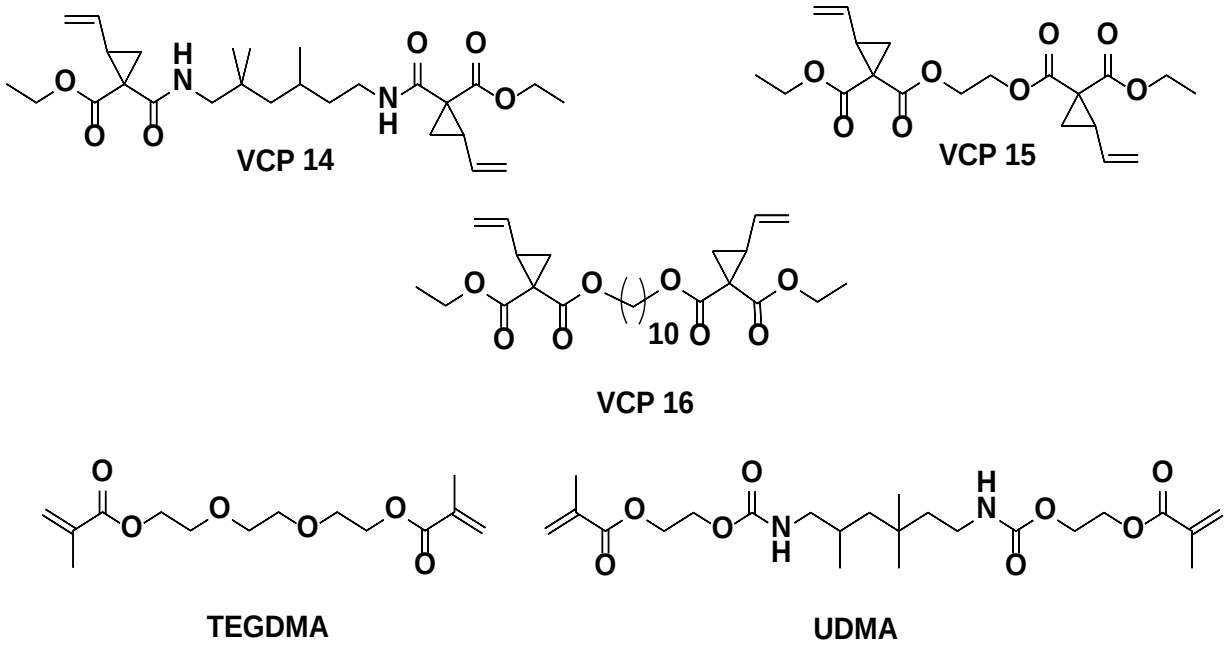


Figure 41: Structure of VCP 14-16 used diluent monomers and the reference methacrylates

1.0 wt% of Ivocerin® was added to the organic matrix as a photoinitiator. All composites were prepared with a filler loading of 82.5 wt%. In order to compare VCP-based with methacrylate based composites, a reference composite C9 containing UDMA and TEGDMA was also formulated and tested (Table 9). Flexural strength, flexural modulus and volumetric shrinkage were measured for each composite (Table 9).

Dental-based composites C1 and C2 based on VCPs **3-4** were formulated (Table 6) and the crosslinking VCP **15** (Figure 41) was used as a diluent in the organic matrix. Crosslinking VCPs **3** and **4** were added as main component (VCP **3** or **4**/ reactive diluent VCP **15**: 7/ 3 (wt/ wt)). The flexural strenght of C1 and C2 containing VCP **3** and **4** were higher than methacrylate based reference. The flexural modulus of both C1 and C2 was significantly lower than the corresponding reference but still exceeded the performance expectations. The volumetric shrinkage of C1 and C2 was with ~ 0.8 % lower than the reference.

For composites C3-C5 based on VCPs **5-7** (Table 7) two crosslinking diluents (VCP **14** and **16**) were needed because of the high viscosity of the monomers. The crosslinking VCPs **5-7** were added as the main component (VCP **5, 6** or **7**/ VCP **14/** VCP **16**: 5/ 3/ 2 (wt/ wt/ wt)). The flexural strength of C4 and C5 was equal to the methacrylic reference, C3 was with 126 MPa the weakest. The flexural modulus for C3-5 were almost the same but ~ 2000 GPa lower than the reference composite. The volumetric shrinkage was with ~1.5 % significantly lower for all three composites compared to the reference (2.5 %).

Table 6: Composite formulation of C1 and C2

Components	C1 [wt%]	C2 [wt%]
VCP **3**	12.17	-
VCP **4**	-	12.17
VCP **15**	5.15	5.15
Ivocerin®	0.18	0.18
Inorganic fillers	77.50	77.50
YbF3	5.00	5.00

Table 7: Composite formulation of C5–C7

Components	C3 [wt%]	C4 [wt%]	C5 [wt%]
VCP **5**	8.70	-	-
VCP **6**	-	8.70	-
VCP **7**	-	-	8.70
VCP **14**	5.21	5.21	5.21
VCP **16**	3.41	3.41	3.41
Ivocerin®	0.18	0.18	0.18
Inorganic fillers	77.50	77.50	77.50
YbF3	5.00	5.00	5.00

Table 8: Composite formulation of C6–C9

Components	C6 [wt%]	C7 [wt%]	C8 [wt%]	C9 [wt%]
VCP **9**	12.17	-	-	-

VCP **10**	-	12.17	-	-
VCP **11**	-	-	12.17	-
VCP **14**	5.15	5.15	5.15	-
UDMA	-	-	-	12.17
TEGDMA	-	-	-	5.15
Ivocerin®	0.18	0.18	0.18	0.18
Inorganic fillers	77.5	77.5	77.5	77.5
YbF3	5	5	5	5

Table 9: Flexural strength, flexural modulus and volumetric shrinkage for composites C1-C9

Composite	**Flexural strength [MPa]**	**Flexural modulus [GPa]**	**Volumetric shrinkage [Vol%]**	**Shrinkage force [N]**
C1	149.9 ± 11.5	8.5 ± 0.8	1.75 ± 0.04	27.9 ± 0.8
C2	143.5 ± 11.2	8.1 ± 1.1	1.70 ± 0.02	26.0 ± 1.5
C3	126.3 ± 4.6	8.3 ± 0.3	1.48 ± 0.02	22.2 ± 0.6
C4	137.5 ± 8.5	8.6 ± 0.7	1.50 ± 0.01	20.8 ± 0.9
C5	133.8 ± 7.0	8.3 ± 0.5	1.47 ± 0.03	21.5 ± 1.8
C6	103.7 ± 9.4	5.5 ± 0.6	1.46 ± 0.01	21.2 ± 0.9
C7	128.2 ± 8.9	7.7 ± 0.4	1.35 ± 0.02	17.4 ± 0.9
C8	136.6 ± 4.4	7.8 ± 0.5	1.39 ± 0.02	21.5 ± 0.9
C9	**134.7 ± 9.8**	**10.0 ± 0.4**	**2.50 ± 0.05**	44.4 ± 1.8

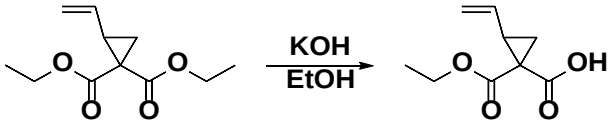
Composites C6-C8 containing the VCPs **9-11** with the longer spacers were mixed with the highly reactive VCP **14**. The main components in the organic matrix were represented by VCPs **9-11** and VCP **14** was used as a highly reactive diluent (VCP **9**, **10** or **11**/ reactive diluent VCP **14**: 7/ 3 (wt/ wt)). C6 had the lowest flexural strength and flexural modulus of all formulated composites. C7 and C8 had almost equal values for the flexural strength but significantly lower values for the flexural modulus compared to the reference. The volumetric shrinkage was for C6-8 more than 1 % lower than the reference shrinkage. Through the extension of the spacer a decrease in flexural strength could be observed. The results show that the methacrylate based composite (C9) shows higher flexural modulus than the VCP based composites (C1-C8). Nevertheless, the values measured with

composites C1-C5, C7 and C8 significantly exceeded performance expectations for dental materials (flexural strength > 80 MPa).[46] The replacement of methacrylates by VCPs results in a significantly lower volumetric shrinkage of the composite. The shrinkage force, which builds up during the photo-polymerization of composites C1-C9 was also determined (Table 9). Similar to the results of the volumetric shrinkage, VCP-based materials were found to have also a significantly lower shrinkage force than the reference composite. Therefore it can be stated that VCP based dental composites present a major advantage over methacrylate based composites.

Experimental Part

2.1 Synthesis

2.1.1 1-Ethoxycarbonyl-2-vinylcyclopropanecarboxylic acid (VCP 1)



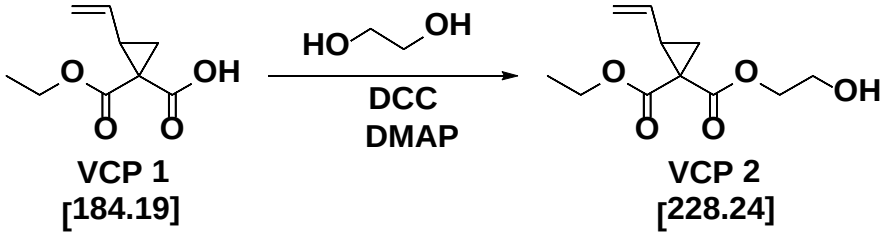
[212.25] VCP 1 [184.19]

Reagent	n [mmol]	m [g]	V [mL]
1,1-Diethoxycarbonyl-2-vinylcyclopropane	741.6	157.4	
KOH	821.6	46.1	
Ethanol			325

1,1-Diethoxycarbonyl-2-vinylcyclopropane (157.4 g, 714.6 mmol) was dissolved in ethanol (325 mL). The mixture was cooled down to 0 °C and KOH (46.1 g, 821.6 mmol) was added in small portions. The solution was stirred for 2 h at RT. The solution was filtered and concentrated under reduced pressure. Distilled water (150 mL) was added to the solution and the aqueous layer was extracted with Et_2O (diethyl ether) (2x60 mL). The organic phase was discarded. HCl 1N (120 mL) was added to the aqueous solution, which was subsequently extracted with Et_2O (3x90 mL). The organic layers were combined, dried over Na_2SO_4 and filtered. After concentration under reduced pressure, 96.25 g (522.56 mmol) of the desired product were isolated.

Yield: 71%. Aspect: slightly yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.32 (t, $^3J_{HH}$ = 7.1 Hz, 3H, $\underline{CH_3}CH_2O$); 2.01 (dd, $^2J_{HH}$ = 4.6 Hz, $^3J_{HH}$ = 8.4 Hz, 1H, $\underline{CH_2}CHCH=CH_2$); 2.17 (dd, $^2J_{HH}$ = 4.6 Hz, $^3J_{HH}$ = 9.3 Hz, 1H, $\underline{CH_2}CHCH=CH_2$); 2.76 (q, $^3J_{HH}$ = 8.8 Hz, 1H, $CH_2\underline{CH}CH=CH_2$); 4.22-4.37 (m, 2H, $CH_3\underline{CH_2}O$); 5.26 (dd, $^2J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 9.8 Hz, 1H, $CH=\underline{CH_2}$); 5.41 (dd, $^2J_{HH}$ = 1.0 Hz, $^3J_{HH}$ = 15.7 Hz, 1H, $CH=\underline{CH_2}$); 5.64-5.76 (m, 1H, $CH_2=\underline{CH}$). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.2 ($OCH_2\underline{C}H_3$); 23.5 ($CH_2=CHCH\underline{C}H_2$); 33.2 ($CO\underline{C}CO$); 39.1 ($C\underline{C}HCH$); 62.9 ($\underline{C}H_2OCO$); 120.9 ($CH=\underline{C}H_2$); 132.2 ($\underline{C}H=CH_2$); 171.2 (C=O); 172.9 (C=O).

2.1.2 1-(2-Hydroxyethoxycarbonyl)-1-ethoxycarbonyl-2-vinylcyclopropane (VCP 2)



VCP 1 **[184.19]** **VCP 2** **[228.24]**

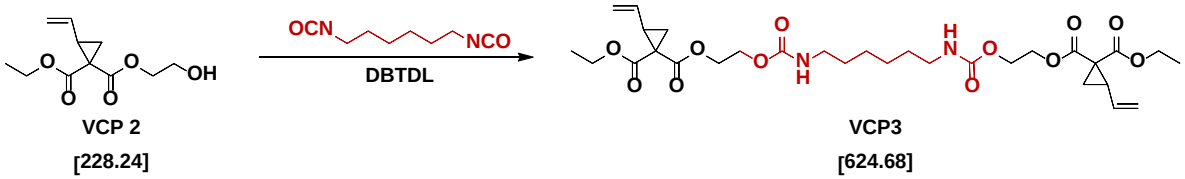
Reagent	n [mmol]	m [g]	V [mL]
VCP 1	343.3	80.0	
Ethylene glycole	2168.0	143.7	
DAMP	86.9	10.6	
DCC	434.3	89.6	
DCM			480

General Procedure A

Under Argon atmosphere, 1-ethoxycarbonyl-2-vinylcyclopropanecarboxylic acid (VCP **1**) (80g, 434.3 mmol), 4-dimethylaminiopyridine (DMAP, 10.6 g, 86.9 mmol) and ethylene glycol (134.8 g, 2.17 mol) were dissolved in dry DCM (240 mL). The solution was cooled to -5 °C. A solution of DCC (89.6 g, 434.3 mmol) in dry DCM (240 mL) was added to the reaction dropwise. The solution was stirred for 30 min. at 0°C and for 1.5 h at RT. The solution was filtered and washed with deionised water (100 mL). The aqueous layer was extracted with DCM (2x100 mL). The organic layers were combined, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified with flash column chromatography (eluent EA/ Hexane 1/ 3). 64.86 g (284.17 mmol) of the desired product were isolated.

Yield: 65 %. Aspect: slightly yellow liquid. ^{1}H NMR (400.1 MHz; $CDCl_3$): δ = 1.26 (t, $^3J_{HH}$ = 7.1 Hz, 3H, $OCH_2\underline{CH_3}$); 1.59 (dd, $^2J_{HH}$ = 4.9 Hz, $^3J_{HH}$ = 9.0 Hz, 1H, $\underline{CH_2}CHCH=CH_2$); 1.76 (dd, $^2J_{HH}$ = 4.9 Hz, $^3J_{HH}$ = 7.5 Hz, 1H, $\underline{CH_2}CHCH=CH_2$); 2.20 (bs, 1H, O$\underline{H}$); 2.61 (q, $^3J_{HH}$ = 8.1 Hz, 1H, $CH_2\underline{CH}CH=CH_2$); 3.82 (t, $^3J_{HH}$ = 4.6 Hz, 2H, $\underline{CH_2}OH$); 4.14-4.28 (m, 3H, $CH_3\underline{CH_2}OCO$ und $O\underline{CH_2}CH_2OH$); 4.33-4.41 (m, 1H, $O\underline{CH_2}CH_2OH$); 5.12-5.19 (m, 1H, $\underline{CH_2}$=CH); 5.27-5.35 (m, 1H, $\underline{CH_2}$=CH); 5.40-5.52 (m, 1H, $\underline{CH}=CH_2$). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.3 ($\underline{C}H_3CH_2O$); 21.0 ($\underline{C}H_2CHCH=CH_2$); 31.9 ($CH_2\underline{C}HCH=CH_2$); 35.9 (CO$\underline{C}$CO); 61.1 ($CH_2O$); 61.8 ($CH_2O$); 67.3 ($CH_2O$); 119.1 ($\underline{C}H_2$=CH); 132.8 ($CH_2=\underline{C}H$); 167.5 (C=O); 170.0 (C=O).

2.1.3 VCP 3



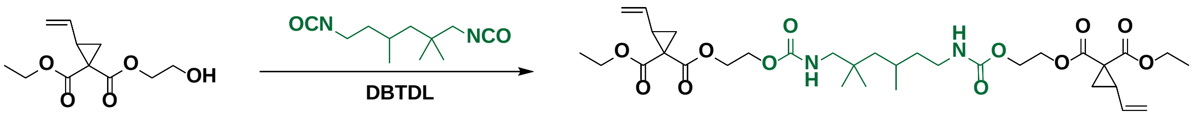
Reagent	n [mmol]	m [g]	V [mL]
VCP 2	87.6	20.0	
Hexamethylene diisocyanate	43.8	7.37	
DBTDL	0.44	0.27	
DCM			200

General Procedure B

Under Argon atmosphere, 1-(2-hydroxyethoxycarbonyl)-1-ethoxycarbonyl-2-vinylcyclopropane (VCP **2**) (20.0 g, 87.6 mmol), hexamethylene diisocyanate (7.37 g, 43.8 mmol) and DBTDL (0.272 g, 0.44 mmol) were dissolved in dry DCM (200 mL). The reaction was stirred under reflux for 8 h. The solution was subsequently concentrated under reduced pressure. The crude product was purified by flash column chromatography (eluent: EA/ Hexane 2/ 1). 25.55g (40.90 mmol) of the desired product was obtained. phenothiazine (50 ppm) and BHT (250 ppm) were added as stabilizers.

Yield: 93%. Aspect: slightly yellow high viscous liquid. ^{1}H NMR (400.1 MHz; $CDCl_3$): δ = 1.26 (t, $^{3}J_{HH}$ = 7.1 Hz, 6H, $OCH_2\underline{CH_3}$); 1.30-1.37 (m, 4H, CH_2); 1.43-1.55 (m, 4H, CH_2); 1.58 (dd, $^{2}J_{HH}$ = 4.9 Hz, $^{3}J_{HH}$ = 9.0 Hz, 2H, $\underline{CH_2}CHCH=CH_2$); 1.72 (dd, $^{2}J_{HH}$ = 4.9 Hz, $^{3}J_{HH}$ = 7.6 Hz, 2H, $\underline{CH_2}CHCH=CH_2$); 2.59 (q, $^{3}J_{HH}$ = 8.4 Hz, 2H, $CH_2\underline{CH}CH=CH_2$); 3.06-3.22 (m, 4H, $\underline{CH_2}NH$); 4.12-4.40 (m, 12H, CH_2OCO); 4.74 (bs, 2H, NH); 5.10-5.17 (m, 1H, $\underline{CH_2}$=CH); 5.25-5.34 (m, 1H, $\underline{CH_2}$=CH); 5.37-5.50 (m, 1H, CH_2=$\underline{CH}$). ^{13}C NMR ($CDCl_3$, 400 MHz, δ): 14.2 ($OCH_2\underline{CH_3}$); 20.6 ($\underline{C}H_2CHCH=CH_2$); 26.2 ($CH_2$); 29.8 ($CH_2$); 31.4 ($CH_2\underline{C}HCH=CH_2$); 35.8 (CO$\underline{C}$CO); 40.9 ($CH_2NH$); 61.5 ($\underline{C}H_2OCO$); 62.3 ($\underline{C}H_2OCO$); 63.7 ($\underline{C}H_2OCO$); 118.7 ($\underline{C}H_2$=CH); 132.9 ($CH_2$=$\underline{C}H$); 156.0 (C=O); 167.1 (C=O); 169.4 (C=O).

2.1.4 VCP 4



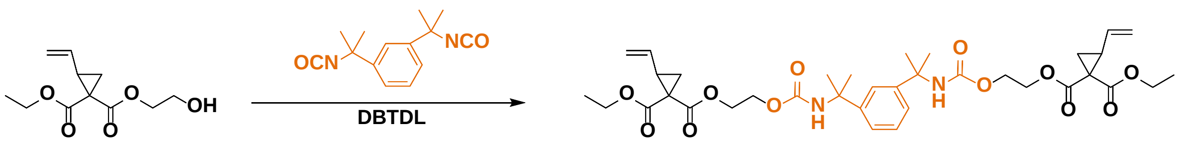
VCP 2 [228.24] VCP4 [666.77]

Reagent	n [mmol]	m [g]	V [mL]
VCP 2	87.6	20.0	
Trimethyl-1,6-diisocyanatohexane	43.8	9.21	
DBTDL	0.44	0.27	
DCM			200

VCP **4** was synthesized, from 1-(2-hydroxyethoxycarbonyl)-1-ethoxycarbonyl-2-vinylcyclopropane (VCP **2**) (20.0 g, 87.6 mmol) and trimethyl-1,6-diisocyanatohexane (9.21 g, 43.8 mmol) according to the general procedure B. 22.88 g of VCP **4** were isolated.

Yield: 78 %. Aspect: slightly yellow high viscous liquid. ^{1}H NMR (400.1 MHz; $CDCl_3$): δ = 0.85-0.96 (m, 9H, CH_3); 1.00-1.14 (m, CH_2), 1.18-1.30 (m, $OCH_2\underline{CH_3}$ and CH_2); 1.32-1.50 (m, CH and CH_2); 1.52-1.78 (m, $\underline{CH_2}CHCH{=}CH_2$, CH and CH_2); 2.60 (q, $^3J_{HH}$ = 8.4 Hz, 2H, $CH_2\underline{CH}CH{=}CH_2$); 2.80-3.24 (m, 4H, $\underline{CH_2}NH$); 4.10-4.42 (m, 12H, CH_2OCO); 4.62-5.00 (m, 2H, NH); 5.10-5.17 (m, 1H, $\underline{CH_2}{=}CH$); 5.25-5.34 (m, 1H, $\underline{CH_2}{=}CH$); 5.37-5.50 (m, 1H, $CH_2{=}\underline{CH}$). ^{13}C NMR ($CDCl_3$, 400 MHz, δ): 14.3 ($OCH_2\underline{C}H_3$); 20.6; 20.7 ($\underline{C}H_2CHCH{=}CH_2$); 22.5; 25.2; 25.4; 26.3; 27.5; 27.6; 29.5; 31.5 ($CH_2\underline{C}HCH{=}CH_2$); 33.0; 35.2; 35.9 ($CO\underline{C}CO$); 37.4 ($CH_2$); 39.2 ($CH_2$); 39.4 ($CH_2$); 42.1 ($CH_2$); 46.1 ($CH_2$); 46.7 ($CH_2$); 48.7 ($CH_2$); 51.6 ($CH_2$); 61.7 ($\underline{C}H_2OCO$); 62.4 ($\underline{C}H_2OCO$); 63.8 ($\underline{C}H_2OCO$); 118.8 ($\underline{C}H_2{=}CH$); 133.0 ($CH_2{=}\underline{C}H$); 156.1 (C=O); 156.4 (C=O); 156.5 (C=O); 167.2 (C=O); 169.6 (C=O).

2.1.5 VCP 5



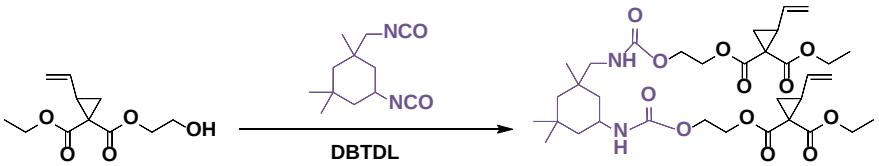
VCP 2 [228.24] VCP5 [700.78]

Reagent	n [mmol]	m [g]	V [mL]
VCP 2	65.72	15.0	
1, 3-bis(1-isocyanato-1-methylethyl)benzene	32.86	8.03	
DBTDL	0.33	0.21	
DCM			150

VCP 5 was synthesized, from 1-(2-hydroxyethoxycarbonyl)-1-ethoxycarbonyl-2-vinylcyclopropane (VCP **2**) (15.0 g, 65.72 mmol) and 1, 3-bis (1-isocyanato-1-methylethyl) benzene (8.03 g, 32.86 mmol), according to general procedure B. 19.76 g of VCP **5** were isolated.

Yield: 94 %. Aspect: slightly yellow high viscous liquid. ^{1}H NMR (400.1 MHz; $CDCl_3$): δ = 1.26 (t, $^{3}J_{HH}$ = 7.1 Hz, 6H, $OCH_2\underline{CH_3}$); 1.52-1.78 (m, 16H, CH_3 and $\underline{CH_2}CHCH=CH_2$); 1.32-1.52 (m, 2H, CH_2); 2.60 (q, $^{3}J_{HH}$ = 8.4 Hz, 2H, $CH_2\underline{CH}CH=CH_2$); 4.12-4.40 (m, 12H, CH_2OCO); 5.09-5.35 (m, 6H, $\underline{CH_2}$=CH and NH); 5.38-5.51 (m, 2H, $CH_2=\underline{CH}$); 7.22-7.33 (m, 3H, CH_{Ar}); 7.39-7.44 (m, 1H, CH_{Ar}). ^{13}C NMR ($CDCl_3$, 400 MHz, δ): 14.3 ($OCH_2\underline{C}H_3$); 20.6 ($\underline{C}H_2CHCH=CH_2$); 29.4 ($CH_3$); 31.5 ($CH_2\underline{C}HCH=CH_2$); 35.9 ($CO\underline{C}CO$); 55.6 ($CH_3\underline{C}NH$); 61.7 ($\underline{C}H_2OCO$); 62.0 $\underline{C}H_2OCO$); 63.9 ($\underline{C}H_2OCO$); 118.8 (s, $\underline{C}H_2$=CH); 121.3 (CH_{Ar}); 123.4 (CH_{Ar}); 128.6 (CH_{Ar}); 133.1 ($CH_2=\underline{C}H$); 147.0 (C_{Ar}); 154.2 (C=O); 167.3 (C=O); 169.6 (C=O).

2.1.6 VCP 6



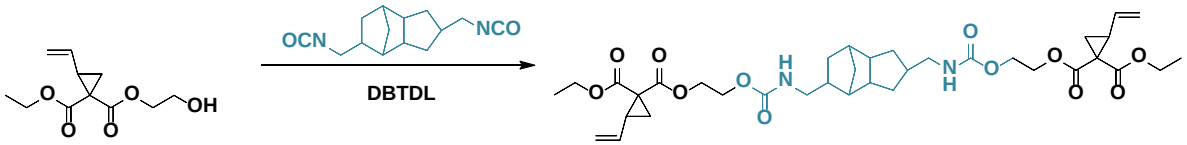
VCP 2 [228.24] **VCP6** [678.78]

Reagent	n [mmol]	m [g]	V [mL]
VCP 2	61.40	14.0	
Isophorone diisocyanate	30.67	6.82	
DBTDL	0.29	0.19	
DCM			140

VCP 6 was synthesized from 1-(2-hydroxyethoxycarbonyl)-1-ethoxycarbonyl-2-vinylcyclopropane (VPC **2**) (14.0 g, 61.4 mmol) and isophorone diisocyanate (6.82 g, 30.67 mmol) according to the general procedure B. 19.22 g of VCP **6** were isolated.

Yield: 92 %. Aspect: slightly yellow high viscous liquid. ^{1}H NMR (400.1 MHz; $CDCl_3$): δ = 0.82-1.12 (m, CH_3 and CH_2); 1.15-1.31 (m, CH_2 and $OCH_2\underline{CH_3}$); 1.52-1.80 (m, CH_2 and $\underline{CH_2}CHCH=CH_2$); 2.59 (q, $^{3}J_{HH}$ = 8.4 Hz, 2H, $CH_2\underline{CH}CH=CH_2$); 2.84-3.00 (m, $\underline{CH_2}NH$); 3.16-3.40 (m, $\underline{CH_2}NH$); 3.64-3.88 (m, 1H, $\underline{CH}NH$); 4.10-4.42 (m, 12H, CH_2OCO); 4.46-4.68 (m, 1H, NH); 4.75-4.92 (m, 1H, NH); 5.11-5.18 (m, 1H, $\underline{CH_2}=CH$); 5.26-5.35 (m, 1H, $\underline{CH_2}=CH$); 5.37-5.51 (m, 1H, $CH_2=\underline{CH}$). ^{13}C NMR ($CDCl_3$, 400 MHz, δ): 14.3 ($OCH_2\underline{C}H_3$); 20.7 ($\underline{C}H_2CHCH=CH_2$); 23.4 ($CH_3$); 27.7 ($CH_3$); 29.8; 31.5 ($CH_2\underline{C}HCH=CH_2$); 32.0 ($CH_2\underline{C}CH_2$); 35.2 ($CH_3$); 35.9 ($CO\underline{C}CO$); 36.5 ($CH_2\underline{C}CH_2$); 41.8 ($CH_2$); 44.8 (CH); 46.4 ($CH_2$); 47.1 ($CH_2$); 55.0 ($CH_2$); 61.6 ($\underline{C}H_2OCO$); 62.3 ($\underline{C}H_2OCO$); 62.6 ($\underline{C}H_2OCO$); 63.8 ($\underline{C}H_2OCO$); 118.8 ($\underline{C}H_2=CH$); 133.1 ($CH_2=\underline{C}H$); 155.4 (C=O); 156.6 (C=O); 167.3 (C=O); 169.6 (C=O).

2.1.7 VCP 7



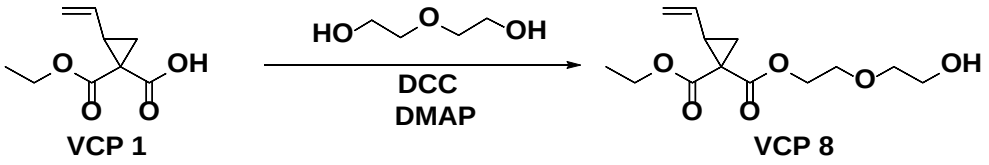
VCP 2 **[228.24]** **VCP7** **[702.80]**

Reagent	n [mmol]	m [g]	V [mL]
VCP 2	43.80	10.0	
4,8-bis(isocyanatomethyl)tricyclo[5.2.1.0^{2,6}]decane	24.10	5.40	
DBTDL	0.27	0.17	
DCM			100

VCP 7 was synthesized, from 1-(2-hydroxyethoxycarbonyl)-1-ethoxycarbonyl-2-vinylcyclopropane (VCP **2**) (10.0 g, 43.8 mmol) and 4,8-bis(isocyanatomethyl)tricyclo[5.2.1.0^{2,6}]decane (5.4 g, 24.10 mmol), according general procedure B. 13.11 g of **VCP 7** were isolated.

Yield: 85 %. Aspect: slightly yellow viscous liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.80-2.55 (m, 24H, $CH_{/aliphatic}$, $CH_{2/aliphatic}$, $\underline{CH_2}CHCH=CH_2$, $OCH_2\underline{CH_3}$); 2.60 (q, $^{3}J_{HH}$ = 8.3 Hz, 2H, $CH_2\underline{CH}CH=CH_2$); 2.88-3.14 (m, 4H, $\underline{CH_2}NH$); 4.13-4.45 (m, 12H, CH_2OCO); 4.67-4.90 (m, 2H, NH); 5.11-5.19 (m , 2H, $\underline{CH_2}=CH$); 5.26-5.35 (m , 2H, $CH=\underline{CH_2}$); 5.38-5.51 (m, 2H, $CH_2=\underline{CH}$).

2.1.8 1-(5-Hydroxy-3-oxa-pentoxycarbonyl)-1-ethoxycarbonyl-2-vinylcyclopropane (VCP 8)



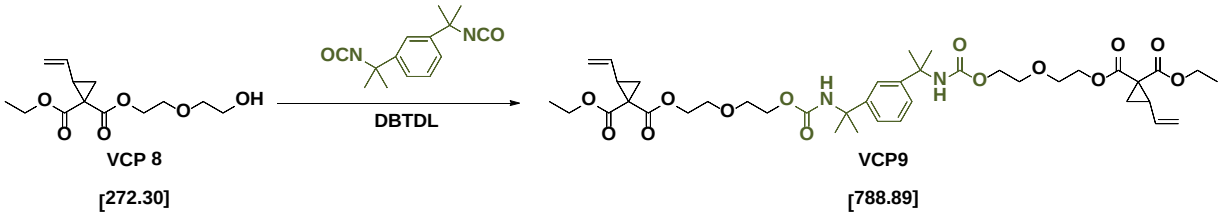
VCP 1 **[184.07]** **VCP 8** **[272.30]**

Reagent	n [mmol]	m [g]	V [mL]
VCP 1	135.7	25.0	
Diethylene glycole	678.65	72.0	
DAMP	27.2	3.30	
DCC	135.7	28.0	
DCM			480

VCP **8** was prepared from 1-ethoxycarbonyl-2-vinylcyclopropanecarboxylic acid (VCP **1**) (25 g, 135.7 mmol), DMAP (3.3 g, 27.2 mmol) and diethylene glycol (72.0 g, 678.65 mol) according to the general procedure A. The crude product was purified with flash column chromatography (eluent EA/ Hexane 1/ 2). 25.7 g (94.4 mmol) of the desired product were isolated.

Yield: 70 %. Aspect: slightly yellow liquid. ^{1}H NMR (400.1 MHz; $CDCl_3$): δ = 1.26 (t, $^{3}J_{HH}$ = 7.1 Hz, 3H, $OCH_2\underline{CH_3}$); 1.59 (dd, $^{2}J_{HH}$ = 4.9 Hz, $^{3}J_{HH}$ = 9.0 Hz, 1H, $\underline{CH_2}CHCH=CH_2$); 1.73 (dd, $^{2}J_{HH}$ = 4.9 Hz, $^{3}J_{HH}$ = 7.6 Hz, 1H, $\underline{CH_2}CHCH=CH_2$); 2.20 (bs, 1H, $CH_2O\underline{H}$); 2.60 (q, $^{3}J_{HH}$ = 8.4 Hz, 1H, $CH_2\underline{CH}CH=CH_2$); 3.54-3.64 (m, 2H, $OCH_2\underline{C}H_2OH$); 3.65-3.78 (m, 4H, CH_2O); 4.10-4.40 (m, 4H, CH_2OCO); 5.12-5.19 (m, 1H, $\underline{CH_2}$=CH); 5.26-5.34 (m, 1H, $\underline{CH_2}$=CH); 5.39-5.51 (m, 1H, CH_2=$\underline{CH}$). ^{13}C NMR ($CDCl_3$, 400 MHz, δ): 14.3 ($\underline{C}H_3CH_2O$); 21.0 ($\underline{C}H_2CHCH=CH_2$); 31.7 ($CH_2\underline{C}HCH=CH_2$); 35.9 (CO$\underline{C}$CO); 61.7 ($CH_2O$); 64.6 ($CH_2O$); 68.9 ($CH_2O$); 72.4 ($CH_2O$); 118.8 ($\underline{C}H_2$=CH); 133.0 ($CH_2$=$\underline{C}$H); 167.3 (C=O); 179.8 (C=O).

2.1.9 VCP 9

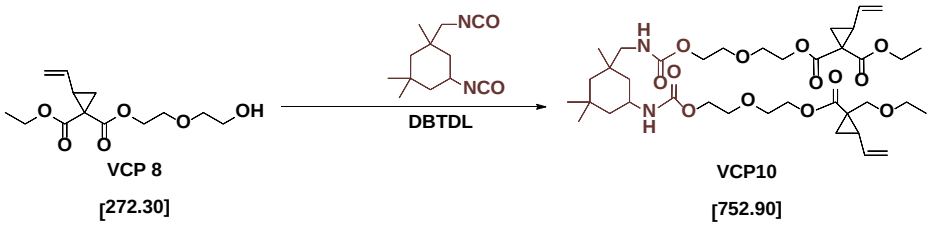


Reagent	n [mmol]	m [g]	V [mL]
VCP 8	73.5	20.0	
1, 3-bis(1-isocyanato-1-methylethyl)benzene	36.7	8.20	
DBTDL	0.44	0.27	
DCM			200

VCP **9** was prepared from 1-(5-Hydroxy-3-oxa-pentoxycarbonyl)-1-ethoxycarbonyl-2-vinylcyclopropane (VCP **8**) (20.0 g, 73.5 mmol) and 1,3-bis(isocyanatomethyl)benzene (8.2 g, 36.7 mmol) according to the general procedure B. 19.2 g (24.3 mmol) of the desired monomer were isolated.

Yield: 69 %. Aspect: slightly yellow high viscous liquid. ^{1}H NMR (400.1 MHz; $CDCl_3$): δ = 1.21-1.39 (m, 30H, CH_2 and $OCH_2\underline{CH_3}$); 1.54 (dd, $^{2}J_{HH}$ = 4.7 Hz, $^{3}J_{HH}$ = 9.0 Hz, 2H, $\underline{CH_2}CHCH=CH_2$); 1.58-1.71 (m, 6H, CH_2 and $\underline{CH_2}CHCH=CH_2$); 2.56 (q, $^{3}J_{HH}$ = 8.2 Hz, 2H, $CH_2\underline{CH}CH=CH_2$); 4.03-4.25 (m, 8H, CH_2OCO); 5.10-5.16 (m, 2H, $\underline{CH_2}=CH$); 5.25-5.33 (m, 2H, $\underline{CH_2}=CH$); 5.37-5.49 (m, 2H, $CH_2=\underline{CH}$). ^{13}C NMR ($CDCl_3$, 400 MHz, δ): 14.3 (CH_3); 20.5 ($\underline{C}H_2CHCH=CH_2$); 25.9 ($CH_2$); 28.6 ($CH_2$); 29.3 ($CH_2$); 29.6 ($CH_2$); 29.7 ($CH_2$); 29.8 (2s, CH_2); 31.2 ($CH_2\underline{C}HCH=CH_2$); 36.0 ($CO\underline{C}CO$); 61.6 ($CH_2OCO$); 65.9 ($CH_2OCO$); 118.5 ($\underline{C}H_2=CH$); 133.3 ($CH_2=\underline{C}H$); 167.5 (OCO); 169.9 (OCO).

2.1.10 VCP 10

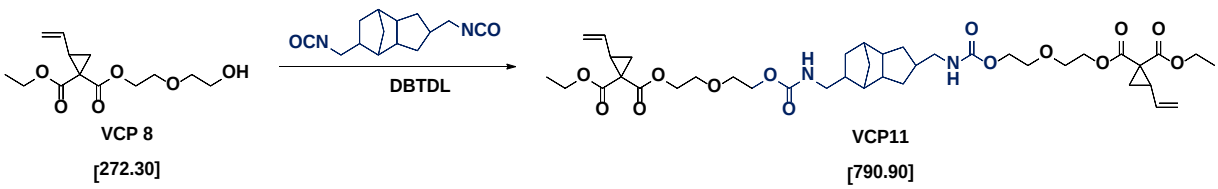


Reagent	n [mmol]	m [g]	V [mL]
VCP 8	73.5	20.0	
Isophorone diisocyanate	36.7	8.20	
DBTDL	0.44	0.27	
DCM			200

VCP **10** was synthesized, from 1-(5-Hydroxy-3-oxa-pentoxycarbonyl)-1-ethoxycarbonyl-2-vinylcyclopropane (VCP **8**) (20.0 g, 73.5 mmol) and isophorone diisocyanate (8.2 g, 36.7 mmol), according to the general procedure B. 23.4 g (30.1 mmol) of VCP **10** were isolated.

Yield: 83 %. Aspect: slightly yellow high viscous liquid. ^{1}H NMR (400.1 MHz; $CDCl_3$): δ = 0.82-1.12 (m, CH_3 and CH_2); 1.15-1.31 (m, CH_2 and $OCH_2\underline{CH_3}$); 1.52-1.80 (m, CH_2 and $\underline{CH_2}CHCH=CH_2$); 2.58 (q, $^{3}J_{HH}$ = 8.4 Hz, 2H, $CH_2\underline{CH}CH=CH_2$); 2.84-3.00 (m, $\underline{CH_2}NH$); 3.15-3.39 (m, $\underline{CH_2}NH$); 3.55-3.90 (m, 9H, $\underline{CH}NH$ and CH_2O); 4.05-4.47 (m, 12H, CH_2OCO); 4.50-5.02 (m, 2H, NH); 5.10-5.18 (m, 1H, $\underline{CH_2}=CH$); 5.25-5.34 (m, 1H, $\underline{CH_2}=CH$); 5.36-5.50 (m, 1H, $CH_2=\underline{CH}$). ^{13}C NMR ($CDCl_3$, 400 MHz, δ): 14.3 ($OCH_2\underline{C}H_3$); 20.5 ($\underline{C}H_2CHCH=CH_2$); 23.3 ($CH_3$); 27.6 ($CH_3$); 29.7; 31.4 ($CH_2\underline{C}HCH=CH_2$); 31.8 ($CH_2\underline{C}CH_2$); 35.0 ($CH_3$); 35.8 ($CO\underline{C}CO$); 36.4 ($CH_2\underline{C}CH_2$); 41.8 ($CH_2$); 44.7 (CH); 46.2 ($CH_2$); 46.9 ($CH_2$); 54.9 ($CH_2$); 61.5 ($\underline{C}H_2OCO$); 63.7 ($CH_2O$); 63.9 ($CH_2O$); 64.5 ($CH_2O$); 68.7 ($CH_2O$); 69.6 ($CH_2O$); 118.7 ($\underline{C}H_2=CH$); 133.0 ($CH_2=\underline{C}H$); 155.5 (C=O); 156.8 (C=O); 167.2 (C=O).

2.1.11 VCP 11

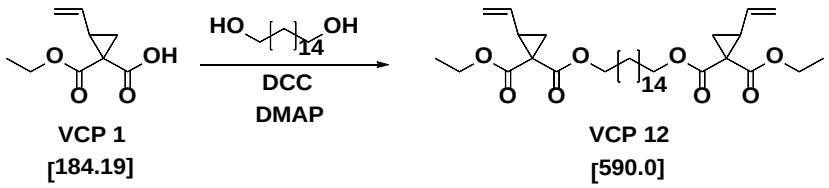


Reagent	n [mmol]	m [g]	V [mL]
VCP 8	73.5	20.0	
4,8-bis(isocyanatomethyl)tricyclo[5.2.1.0^{2,6}]decane	36.7	9.10	
DBTDL	0.44	0.27	
DCM			200

VCP 11 was synthesized, from 1-(5-Hydroxy-3-oxa-pentoxycarbonyl)-1-ethoxycarbonyl-2-vinylcyclopropane (VCP **8**) (20.0 g, 73.5 mmol) and 4,8-bis(isocyanatomethyl)tricyclo[5.2.1.$0^{2,6}$]decane (9.1 g, 36.7 mmol), according to the general procedure B. 23.8 g (30.1 mmol) of VCP **11** were isolated.

Yield: 82 %. Aspect: slightly yellow high viscous liquid. ^{1}H NMR (400.1 MHz; $CDCl_3$): δ = 0.76-2.52 (m, 24H, CH, CH_2, $\underline{CH_2}CHCH=CH_2$, $OCH_2\underline{CH_3}$); 2.59 (q, $^{3}J_{HH}$ = 8.3 Hz, 2H, $CH_2\underline{CH}CH=CH_2$); 2.84-3.32 (m, 4H, $\underline{CH_2}NH$); 3.61-3.76 (m, 8H, CH_2O); 4.08-4.41 (m, 12H, CH_2OCO); 4.42-5.03 (m, 2H, NH); 5.10-5.18 (m, 2H, $\underline{CH_2}=CH$); 5.27-5.34 (m, 2H, $\underline{CH_2}=CH$); 5.37-5.50 (m, 2H, $CH_2=\underline{CH}$).

2.1.12 VCP 12



Reagent	n [mmol]	m [g]	V [mL]
VCP 1	27.2	5.0	
Hexadecanediol	13.6	3.51	
DAMP	0.27	0.033	
DCC	27.2	5.61	
DCM			60

Under an argon atmosphere, 4-dimethylaminopyridine (DMAP, 33 mg, 0.27 mmol) was added to a solution of 1-ethoxycarbonyl-2-vinylcyclopropanecarboxylic acid (5.00 g, 27.2 mmol) and 1,16-hexadecanediol (3.51 g. 13.6 mmol) in dry DCM (60 mL). The solution was cooled down to 0 °C. DCC (5.61 g, 27.2 mmol) was added in small portions to the reaction mixture. The solution was stirred for 30 min at 0 °C and for 6 h at RT. The reaction mixture was filtered and washed with distilled water (2*50 mL). The organic layer was dried over sodium sulfate and concentrated under reduced pressure. The crude product was purified by flash column chromatography (eluent = EA/hexane: 1/9). 5.66 g (9.6 mmol) of the desired compound were isolated.

Yield: 70%. Aspect: colorless liquid. ^{1}H NMR ($CDCl_3$, 400 MHz, δ): 1.21-1.39 (m, 30H, CH_2 and $OCH_2\underline{CH_3}$); 1.54 (dd, $^{2}J_{HH}$ = 4.7 Hz, $^{3}J_{HH}$ = 9.0 Hz, 2H, $\underline{CH_2}CHCH=CH_2$); 1.58-1.71 (m, 6H, CH_2 and $\underline{CH_2}CHCH=CH_2$); 2.56 (q, $^{3}J_{HH}$ = 8.2 Hz, 2H, $CH_2\underline{CH}CH=CH_2$); 4.03-4.25 (m, 8H, CH_2OCO); 5.10-5.16 (m, 2H, $\underline{CH_2}$=CH); 5.25-5.33 (m, 2H, $\underline{CH_2}$=CH); 5.37-5.49 (m, 2H, CH_2=$\underline{CH}$). ^{13}C NMR ($CDCl_3$, 400 MHz, δ): 14.3 (CH_3); 20.5 ($\underline{C}H_2CHCH=CH_2$); 25.9 ($CH_2$); 28.6 ($CH_2$); 29.3 ($CH_2$); 29.6 ($CH_2$); 29.7 ($CH_2$); 29.8 (2s, CH_2); 31.2 ($CH_2\underline{C}HCH=CH_2$); 36.0 (CO$\underline{C}$CO); 61.6 ($CH_2OCO$); 65.9 ($CH_2OCO$); 118.5 ($\underline{C}H_2$=CH); 133.3 ($CH_2$=$\underline{C}$H); 167.5 (OCO); 169.9 (OCO).

2.2 **Photo-Differential Scanning Calorimetry (DSC) Investigation**

Photopolymerizations were carried out on a Perkin Elmer differential scanning calorimeter (DSC), Pyris Diamond. Ivocerin® (0.5 mol%) was added as photoinitiator for the polymerization of each mixture. A sample (ca 1.0 mg) of each mixture was placed in an uncovered aluminum DSC pan. The DSC chamber was purged with nitrogen for 4 min. The acquisition was then started. After 1 min of acquisition, the samples were irradiated for 2 min at 37 °C with an LED curing light (Bluephase, Ivoclar-Vivadent AG). The incident light intensity was 20 mW cm^{-2}. Each experiment was repeated three times. The heat flux was monitored as a function of time using the DSC under isothermal conditions. Double-bond conversion (DBC, %) was calculated as the quotient of the overall heat evolved [ΔH_p (J g^{-1})] and the theoretical heat of polymerization obtained for 100% conversion [ΔH_{0p} (J g^{-1})] (equation 1).

$$DBC = 100 * \frac{\Delta H_p}{\Delta H_{0p}} \quad (1)$$

ΔH_{0p} was calculated according to the following formula (equation 2):

$$\Delta H_{0p} = \frac{\sum x_i \cdot \Delta H_{0i}}{\sum x_i \cdot M_i} \quad (2)$$

where ΔH_{0i} is the theoretical enthalpy of monomer i (ΔH_{0i} = 95 kJ·mol^{-1} for monofunctional vinylcyclopropanes, ΔH_{0i} = 190 kJ·mol^{-1} for bifunctional vinylcyclopropanes), M_i its molecular weight and x_i the molar percentage of monomer i in the mixture.

The rate of polymerization (R_p) was calculated according to the following formula (Equation 3):

$R_p = Q / (m \Delta H_{0p})$ (3)

where *Q* (mW) is the heat flow per s during the reaction and m (mg) the mass of the mixture in the sample.

2.3 **Real-Time (RT)-Near-Infrared (NIR)-Photorheology**

RT-NIR-photorheology measurements were performed on an Anton Paar MCR 302 WESP rheometer coupled with a Bruker Vertex 80 FTIR spectrometer. Ivocerin® (0.5 mol%) was added as photoinitiator for the polymerization of each monomer. The IR beam (NIR light source and CaF_2 beam splitter) was guided through the optical channel and penetrates the sample, which is being analyzed by rheology. The rheometer is equipped with a P-PTD 200/GL Peltier glass plate and a PP25 measuring system (plate-plate setup with an upper plate diameter of 25 mm), which reflects the IR beam into an external Mercury Cadmium Telluride (MCT) detector. A PE tape was placed in between sample and glass plate for protection of the measurement setup due to the good adhesion of the cured materials to the glass surface. For all measurements, ≈130 µL of resin formulation were used and the measurements were performed at 20 °C with a gap of 200 µm. All sample formulations were measured in triplicate. Rheological measurements were conducted in oscillation mode with a strain of 1% and a frequency of 1 Hz. The materials were cured from the underside of the glass plate using an Exfo Omnicure S 2000 with a broadband Hg lamp and a double waveguide to ensure homogeneous irradiation (300 s, 400–500 nm, 10 mW cm^{-2} on the surface of the sample). The storage G′ and loss moduli G″ and the polymerization-induced shrinkage force (F [N]) on the measurement system were recorded during photopolymerization. The data were acquired with a frequency of 5 Hz during the first minute and then 1 Hz for the last 4 min of irradiation. IR measurements were recorded every ≈0.26 s and the measurements were started 5 s prior to irradiation. The conversion of the reactive double bonds was evaluated by following the decrease of the respective NIR signals (≈6139 cm^{-1} for vinylcyclopropane, ≈6165 cm^{-1} for methacrylate). The area ratio of the double bond signal at the start and the end of the measurement were used to calculate the final DBC. Conversion at the point of gelation DBC_g is defined by the conversion at the time when the storage and loss moduli intersect (G′/G″ = 1).[47]

2.4 **Formulation of Dental Composites**

Composites C1 – C8 contained 17.33 wt% of monomer mixture, 0.17% of Ivocerin, 33.50 wt% of barium-aluminium-borosilicate glass, 10.00 wt% of SiO2/ZrO2 mixed oxide Spherosil, 5.00 wt% of YbF3 and 34.00 wt% of prepolymer filler. Composite C9 contained 5.20 wt% of **TEGDMA**, 12.70 wt% of **UDMA**, 0.18% of Ivocerin® 33.50 wt% of barium- aluminum-borosilicate glass, 10.00 wt%

of SiO_2/ZrO_2 mixed oxide Spherosil, 5.00 wt% of YbF_3, and 34.00 wt% of prepolymer filler. The experimental composites were mixed using an LPM 0.1 SP kneading machine (Linden, Marienheide). Flexural strength specimens (2 × 2 × 25 mm3) were obtained by irradiating the resins with a visible light source (Spectramat SP2 polymerization unit) for 2 × 3 min. Mechanical properties were measured after storage in distilled water at 37 °C for 24 h. The measurements were carried out in three-point bending tests (span: 20 mm) with a speed of 0.8 mm min^{-1} using a BZ2.5/TS1S universal testing machine (Zwick, Germany).[46]

2.5 **Volumetric Shrinkage and Shrinkage Stress of dental Composites**

Volumetric polymerization shrinkage of the dental composites was measured using a mercury dilatometer (ADAHF, NIST). ≈0.12 g of composite were applied on a glass slide. A glass column was clamped to the glass slide. The column was filled with mercury and a LVDT (Linear Variable Differential Transducer) probe was placed on top of the mercury. The composite was light cured through the glass slide for 60 s using a Heliolux DLX (Ivoclar Vivadent AG) lamp. The volumetric shrinkage was measured 1 h after irradiation. The value was calculated using the recorded data and the density of the sample.

Shrinkage force was measured based on a method described by Watts et al. using a BZ2.5/TS1S universal testing machine (Zwick, Germany).[44] A steel rod (height: 50 mm, diameter: 10 mm) with a flat end was fixed to the load cell of the universal testing machine. A glass slide (2.85 × 30 × 75 mm^3) was placed on the stationary part of the machine framework. Both the flat surface of the steel rod and the middle of the glass slide were rubbed for 20 s with a primer (Monobond S, Ivoclar Vivadent AG). 3 min after the application of the primer, compressed air was blown on both surfaces. This step will provide a strong bond between the composite and both surfaces (steel rod and glass slide). The composite was applied on the flat surface of the steel rod. The crosshead was lowered (0.5 mm min^{-1}) until a composite layer with 0.8 mm thickness (between the steel rod and the glass slide) was reached. The excess of material around the steel rod was removed. The composite was subsequently light-cured underneath the glass slide for 10 s using an LED curing light Bluephase 20i (Ivoclar Vivadent AG). The shrinkage stress was measured as a function of time. Each experiment was repeated six times.

Materials and devices

Materials

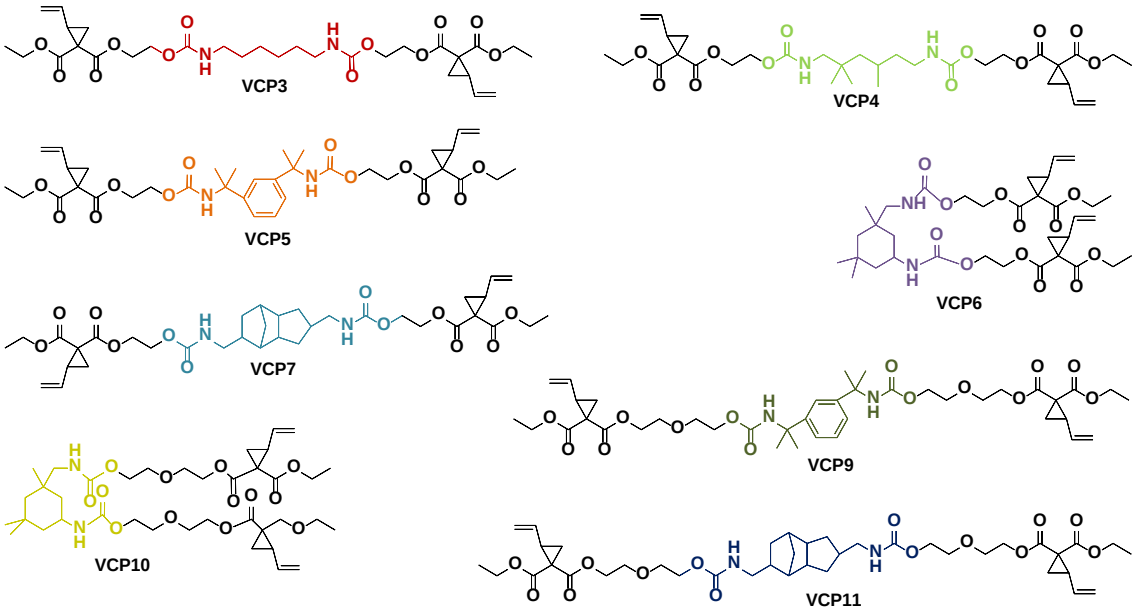
Dichloromethane (DCM) was dried over molecular sieves. 1-Ethoxycarbonyl-2-vinylcyclopropanecarboxylic acid [41], VCP **13,** VCP **14** and VCP **15** was prepared according to procedures described in the literature. All reagents used for the syntheses of VCPs were purchased from Sigma-Aldrich (Switzerland). Column chromatographies were performed on Macherey-Nagel silica gel 60 (40–63 μm). Thin layer chromatography (TLC) was performed on silica gel 60 F-254 plates. BMDG (Ivocerin®) was purchased from Synthon Chemicals GmbH (Germany). TEGDMA was produced by Ivoclar Vivadent AG (Liechtenstein)UDMA was produced by Ivoclar Vivadent AG (Liechtenstein). A prepolymer filler (Ivoclar Vivadent AG), ytterbium fluoride (YbF_3, Sukgyung AT Co. Ltd., Korea), and SiO_2/ZrO_2 mixed oxide Spherosil (Tokuyama Soda, Japan), and a bariumaluminum-borosilicate glass Ba-Al-B-SiO_2 (GM27884, Schott, (Germany) were used as fillers. The prepolymer filler was prepared from an initial microfilled composite (containing a mixture of dimethacrylates, a barium-aluminumborosilicate glass, and YbF_3), which was pre-polymerized (thermally) and then grounded to a fine powder. Before use, the SiO_2/ZrO_2 mixed oxide Spherosil and the barium-aluminum-borosilicate glass Ba-Al-B-SiO_2 were modified with the silane coupling agent 3-methacryloyloxy-propyltrimethoxysilane (MPTS, Union Carbide). The fillers were silanized by mixing them with 1.0 wt% of water and 5.0 wt% of MPTS at room temperature over a period of 2 h. The modified fillers were subsequently dried at 50 °C for 4 d

Measurement

^1H NMR and ^{13}C NMR spectra were recorded on a DPX-400 spectrometer using tetramethylsilane as internal reference. Data are given in the following order: chemical shift in ppm, multiplicity (s, singlet; d, doublet; q, quadruplet; m, multiplet), coupling constant in Hertz (Hz), assignment. High-resolution mass spectra (HRMS) were obtained with an ACQUITY UPLC H-Class system (Waters) coupled with a Xevo G2-Xs QTof mass spectrometer (Waters). The density of the composite materials was measured using an AccuPyc 1330 gas pycnometer (Micromeritics, Germany). Refractive indices were measured using an Abbe 5 refractometer (Bellingham & Stanley Ltd., UK). The monomer viscosities were assessed

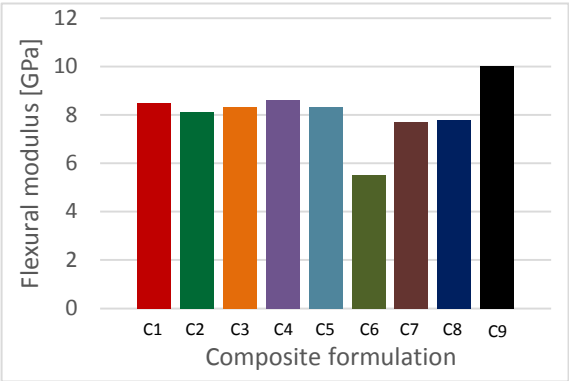
Conclusion

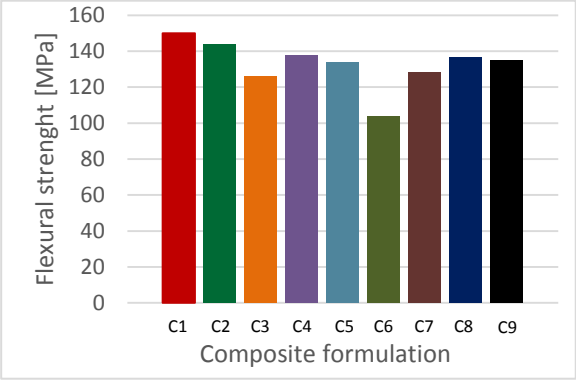
To reduce the shrinkage stress and the volumetric shrinkage of composite fillings, new monomers were synthesized. The synthesized difunctional monomers had vinylcyclopropanes instead of methacrylates and they were bearing urethane groups. The goal was to find Bis-GMA and UDMA replacing structures for composite formulations to avoid mirkoleakage and generate more lasting dental fillings.

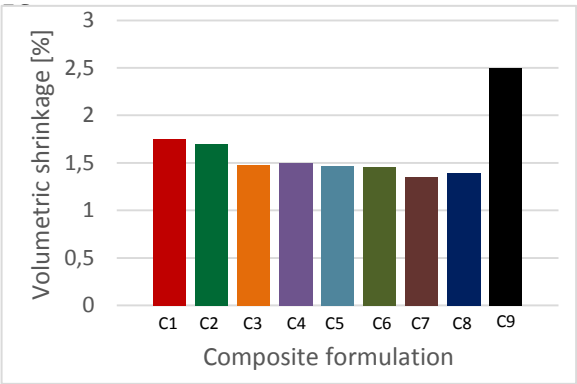


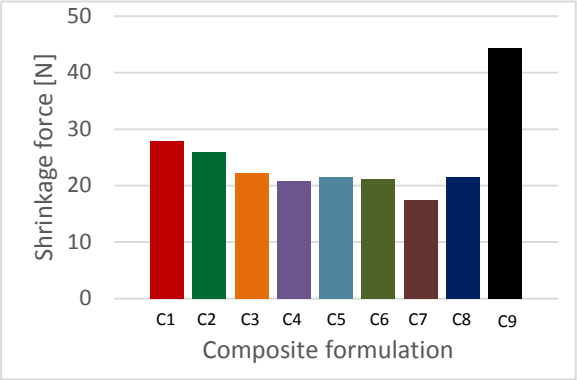
VCPs 3-7 and **9-11** bearing a urethane group could be successfully synthesized in three steps with good yields. The photopolymerization kinetics of those monomers was studied with a photo-DSC and using Ivocerin® as a photoinitiator. The viscosity of VCPs **5-7** and **9-11** was too high to perform a homopolymerization. Therefore the reactivity was investigated via copolymerization with VCP **13** in a 1:1 (mol:mol) ratio. The reactivity of the VCP **5**-7 was lower than expected and therefore it can be stated that VCPs bearing a urethane group are less reactive than VCPs baring an amide group. Through the extension of the spacer with diethylene glycole instead of ethylene glycole the viscosity could be significantly reduced and an increase in reactivity could be observed. VCP **11** was the most reactive monomer and the rate of polymerization was almost doubled in for the copolymerization compared to the mixture containing VCP **7**. An even higher effect of reaction increase by the enlargement of the spacer was observed for the mixture containing VCP **9**. In this case the reactivity tripled in comparison to the reference mixture with VCP **5**. For the mixtures containing VCP **6** and VCP **10** the rate of polymerization increased the least and stayed almost the same. RT-NIR-

photorheology experiments confirmed the results from the photo-DSC, where **VCP 11** was the most reactive followed by VCP **10** and **9**. The same effect of the increasing reactivity by the enlargement of the spacer was also observed with the correlating VCP mixtures (VCP **5**/ VCP **9**, VCP **6**/ VCP **10**, VCP **7**/ VCP **11**). In addition RT-NIR-photorheology enabled the correlation between gelation, polymerization-induced shrinkage stress and final double bond conversion. The DBC of the reference methacrylate based mixture could not be reached with the VCP mixtures. The DBC of 63-70 % is significantly lower than the methacrylic reference (83 %) but still exceeded the performance expectations. All synthesized VCPs revealed a significantly lower shrinkage stress in comparison to the reference methacrylates. The most promising composite formulation C8 (containing VCP **11**) with a volumetric shrinkage of 1.4 % and a shrinkage force of 21.5 N was significantly lower than the methacrylate based composite (C9) with a volumetric shrinkage value of 2.5 % and a shrinkage stress of 44.4 N. For all formulated composites the results of the flexural strength were higher or equal except C6 (containing VCP **9**). C6 had a significantly lower flexural strength which is possibly due to the enlargement of the spacer and the aromatic structure of the major monomer in the composite. The values for flexural modulus of all VCP-based composites were lower than the methacrylate-based, but nevertheless, the values measured with composites C1-C5 (containing VCP **3**-**7**), C7 (containing VCP **10**) and C8 (containing VCP **11**) significantly exceeded performance expectations for dental materials. Therefore the replacement of dimethacrylates with VCPs is a promising approach in the development of low shrinkage composites.

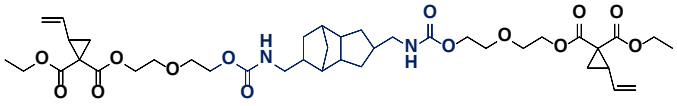








The most promising structure was VCP 11:



VCP11

[790.90]

η [MPs*s]	1.30
n_D	1.5045
G' [MPa]	980
DBC [%]	72.0
F [N]	14
Flexural strength in composite [MPa]	137
Flexural modulus in composite [GPa]	7.8
Volumetric shrinkage in composite [Vol %]	1.40
Shrinkage force in composite [N]	21.5

The next step in the research of VCPs for dental composties would be to make formulations with transfer agents to shift the T_g to higher conversions and therefore reduce the shrinkage and the shrinkage stress even more.

References

1. Poitevin, A., et al., *Bonding effectiveness of self-adhesive composites to dentin and enamel.* Dent Mater, 2013. **29**(2): p. 221-30.
2. *Tooth structure*. Available from: http://www.webmd.com/oral-health/picture-of-the-teeth#1.
3. Nanci, A., *Ten Cate's Oral Histology*. 8th Edition. 2012.
4. Albert, P.D., K.; Rentsch, H. , *Amalgam und die Alternativen.* Chemie Unserer Zeit, 2000. **34**: p. 300-305.
5. Francisconi, L.F., et al., *Glass Ionomer Cements And Their Role In The Restoration Of Non-Carious Cervical Lesions.* Journal of Applied Oral Science, 2009. **17**(5): p. 364-369.
6. Christmann, L.D. and M.T. Plaumann, *Polymer-modified glass ionomer cement*. 2010, Google Patents.
7. Moszner, N., et al., *Sol-gel materials 2. Light-curing dental composites based on ormocers of cross-linking alkoxysilane methacrylates and further nano-components.* Dent Mater, 2008. **24**(6): p. 851-6.
8. *Amalgam filling*. Available from: https://www.google.at/url?sa=i&rct=j&q=&esrc=s&source=images&cd=&ved=0ahUKEwjr6rD0tMzUAhUEtRQKHUv8CkwQjxwIAw&url=https%3A%2F%2Fwww.implantate-tuebingen.de%2Fbehandlungsspektrum%2Ffuellungstherapie%2Fdas-problem-amalgam.html&psig=AFQjCNGKSja7pA8JpndCQ1TiVrKSC2JTEw&ust=1498047604239094&cad=rjt.
9. *Gold filling*. Available from: http://www.zahnarzt-am-maarweg.de/de/behandlungen/zaehne-erhalten/fuellungen-und-inlays/.
10. *Ceramic crown*. Available from: http://www.zahnarzt-am-maarweg.de/de/behandlungen/zaehne-erhalten/fuellungen-und-inlays/.
11. *Composite filling*. Available from: http://www.zahnmedizin-waldshut.de/fuellungstherapie.html.
12. HQ, W., *Future Use of Materials for Dental Restoration.* 2009.
13. Ferracane, J.L., *Resin composite--state of the art.* Dent Mater, 2011. **27**(1): p. 29-38.
14. Van Meerbeek, B., et al., *State of the art of self-etch adhesives.* Dental Materials, 2011. **27**(1): p. 17-28.
15. Moszner, N. and T. Hirt, *New polymer-chemical developments in clinical dental polymer materials: Enamel-dentin adhesives and restorative composites.* Journal of Polymer Science Part A: Polymer Chemistry, 2012. **50**(21): p. 4369-4402.
16. Moszner, N. and U. Salz, *Recent Developments of New Components for Dental Adhesives and Composites.* Macromolecular Materials and Engineering, 2007. **292**(3): p. 245-271.
17. Cramer, N.B., J.W. Stansbury, and C.N. Bowman, *Recent advances and developments in composite dental restorative materials.* J Dent Res, 2011. **90**(4): p. 402-16.
18. Catel, Y., et al., *Synthesis of Acidic Vinylcyclopropanes for Dental Applications.* Polymer International, 2017.
19. Moszner, N., et al., *Benzoylgermanium Derivatives as Novel Visible-Light Photoinitiators for Dental Composites.* Macromolecular Materials and Engineering, 2009. **294**(12): p. 877-886.
20. *Ivoclar Vivadent Report, No. 19, Ivocerin – A milestone in the composite technology.* 2013.
21. Zeuner, F., J. Angermann, and N. Moszner, *Synthesis of Novel 2-Vinylcyclopropane Phosphonic Acids.* Synthetic Communications, 2006. **36**(24): p. 3679-3691.
22. Sahin, G., et al., *Synthesis and evaluation of new dental monomers with both phosphonic and carboxylic acid functional groups.* Journal of Polymer Science Part A: Polymer Chemistry, 2009. **47**(7): p. 1953-1965.
23. Janaina Bechtold, P.J.d.S., Andrea Anido-Anido, Vinícius Di Hipólito, Roberta Caroline Bruschi Alonso, Paulo Henrique Perlatti D'Alpino,, *Hardness, polymerization depth, and*

internal adaptation of Class II silorane composite restorations as a function of polymerization protocol. Dental Materials, 2005. **21**: p. 962-970.
24. Braga, R.R., R.Y. Ballester, and J.L. Ferracane, *Factors involved in the development of polymerization shrinkage stress in resin-composites: a systematic review.* Dent Mater, 2005. **21**(10): p. 962-70.
25. C.-M. Chung, J.-G.K., M.-S. Kim, K.-M. Kim, K.-N. Kim, *Development of a new photocurable composite resin with reduced curing shrinkage.* Dental Materials, 2002. **18**: p. 174-178.
26. Ge, J., M. Trujillo, and J. Stansbury, *Synthesis and photopolymerization of low shrinkage methacrylate monomers containing bulky substituent groups.* Dent Mater, 2005. **21**(12): p. 1163-9.
27. Cramer, N.B., et al., *Investigation of thiol-ene and thiol-ene-methacrylate based resins as dental restorative materials.* Dent Mater, 2010. **26**(1): p. 21-8.
28. Gorsche, C., et al., *Exploring the benefits of β-allyl sulfones for more homogeneous dimethacrylate photopolymer networks.* Polym. Chem., 2015. **6**(11): p. 2038-2047.
29. Park, H.Y., et al., *Stress Relaxation by Addition-Fragmentation Chain Transfer in Highly Crosslinked Thiol-Yne Networks.* Macromolecules, 2010. **43**(24): p. 10188-10190.
30. Colombani*, D., *Driving forces in free radical addition–fragmentation processes.* Progress in Polymer Science, 1999. **24**: p. 425–480.
31. Moraes, R.R., et al., *Control of polymerization shrinkage and stress in nanogel-modified monomer and composite materials.* Dent Mater, 2011. **27**(6): p. 509-19.
32. Liu, J., et al., *A Study of Shrinkage Stress Reduction and Mechanical Properties of Nanogel-Modified Resin Systems.* Eur Polym J, 2012. **48**(11): p. 1819-1828.
33. Han, J., et al., *Intramolecular-initiating photopolymerization behavior of nanogels with the capability of reducing shrinkage*. J. Mater. Chem. C, 2016. **4**(45): p. 10675-10683.
34. Catel, Y., et al., *Evaluation of Difunctional Vinylcyclopropanes as Reactive Diluents for the Development of Low-Shrinkage Composites.* Macromolecular Materials and Engineering, 2017: p. 1700021.
35. Fumio Sanda, T.T., and Takeshi Endo, *Radical Polymerizaion Behavior of 1,l-Disubstituted 2-Vin ylcyclopropanes.* Macromolecules 1993. **26**: p. 1818-1824.
36. Fumio Sanda, T.T., and Takeshi Endo, *Radical Ring-Opening Polymerization of Novel Vinylcyclopropanes Designed as Low Shrinkage Monomers. Structure of the Polymer, Mechanism of the Polymerization, and Volume Change on the Polymerization.* Macromolecules 1995. **28**: p. 1346-1355.
37. Sanda, F., T. Takata, and T. Endo, *Synthesis and radical ring-opening polymerization of a vinylcyclopropane bearing a cyclic carbonate moiety, 1-vinyl-5,7-dioxaspiro[2.5]octan-6-one*. Macromolecules, 1994. **27**(14): p. 3986-3991.
38. Moszner, N., et al., *Synthesis and polymerization of vinylcyclopropanes.* Macromol. Chem. Phys. , 1999. **200**: p. 2173–2187.
39. Ata, S., D. Mal, and N.K. Singha, *Copper catalyzed ring opening copolymerization of a vinyl cyclopropane and methyl methacrylate.* RSC Advances, 2013. **3**(34): p. 14486.
40. Contreras, P.P., P. Tyagi, and S. Agarwal, *Low volume shrinkage of polymers by photopolymerization of 1,1-bis(ethoxycarbonyl)-2-vinylcyclopropanes.* Polym. Chem., 2015. **6**(12): p. 2297-2304.
41. N. Moszner, F.Z., T. Völkel, U. K. Fischer, V. Rheinberger, *Polymerization of cyclic monomers. VII. Synthesis and radical polymerization of 1,3-bis[(1-alkoxycarbonyl-2-vinylcyclopropane-1-yl)carboxy]benzenes.* J. Appl. Polym. Sci. 1999, 72, 1775, 1999.
42. Catel, Y., et al., *Bis(4-methoxybenzoyl)diethylgermane: A Highly Efficient Photoinitiator for the Polymerization of Vinylcyclopropanes.* Macromolecular Chemistry and Physics, 2016. **217**(24): p. 2686-2691.
43. Moszner, N., et al., *A partially aromatic urethane dimethacrylate as a new substituent for BIS-GMA in restorative composites.* Dental Materials, 2008. **24**: p. 694-699.

44. Watts, D.C., A.S. Marouf, and A.M. Al-Hindi, *Photo-polymerization shrinkage-stress kinetics in resin-composites: methods development.* Dental Materials, 2003. **19**(1): p. 1-11.
45. Pineda Contreras, P., et al., *Renaissance for low shrinking resins: all-in-one solution by bi-functional vinylcyclopropane-amides.* Chem Commun (Camb), 2015. **51**(59): p. 11899-902.
46. *ISO 4049:2009(E), International Standard, Dentistry Resin-Based Filling Materials, p. 21*.
47. Gorsche, C., et al., *Real Time-NIR/MIR-Photorheology: A Versatile Tool for the in Situ Characterization of Photopolymerization Reactions.* Anal Chem, 2017. **89**(9): p. 4958-4968.

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A

AFCT	Additional fragmentation chain transfer

B

BECVCP	1,1-bis(ethoxycarbonyl)vinylcyclopropane
BHT	Butylated hydroxytoluene
BisGMA	[2-hydroxy-3-[4-[2-[4-[2-hydroxy-3-(2-methylprop-2-enoyloxy)propoxy]phenyl]propan-2-yl]phenoxy]propyl] 2-methylprop-2-enoate

D

DBC	Double bond conversion
DBCg	Double bond conversion at the gel point
DBTDL	Dibutyltin dilaurate
DCC	Dicyclohexylcarbodiimide, Dicyclohexylcarbodiimide
DCM	Dichlor methane
DPIHFP	Diphenyliodonium hexafluorophosphate

E

EA	Ethyl acetate
Et_2O	Diethyl ether

H

HCl	Hydrochloric acid

I

Ivocerin®	Bis-(4- methoxybenzoyl)diethylgermanium

M

MA	Methyl acrylate
MAS	maleic anhydride
MMA	Methyl methacrylate

N

Na_2SO_4	Sodium sulfateSiehe

R

RBC	Resin-based composite
RT	Room temperature

S

St	Styrene

T

TEGDMA	Triethylene glycol dimethacrylate
T_g	Glass-transition temperature

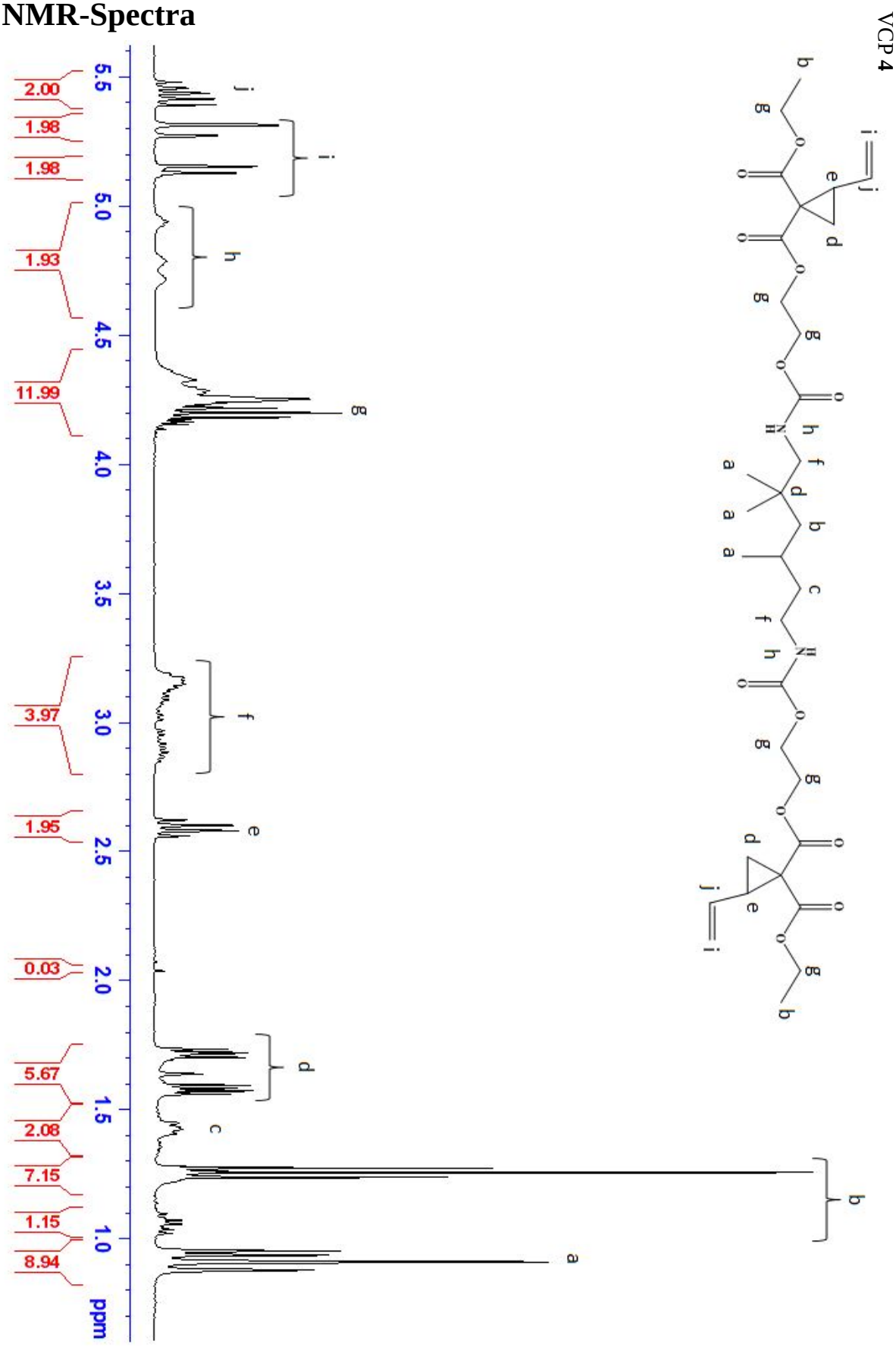
U

UDMA	1,6-bis-[2-methacryloyloxyethoxycarbonylamino]-2,4,4-trimethylhexane, 2-[[3,5,5-trimethyl-6-[2-(2-methylprop-2-enoyloxy)ethoxycarbonylamino]hexyl]carbamoyloxy]ethyl 2-methylprop-2-enoate

V

VCPs	Vinylcyclopropanes

NMR-Spectra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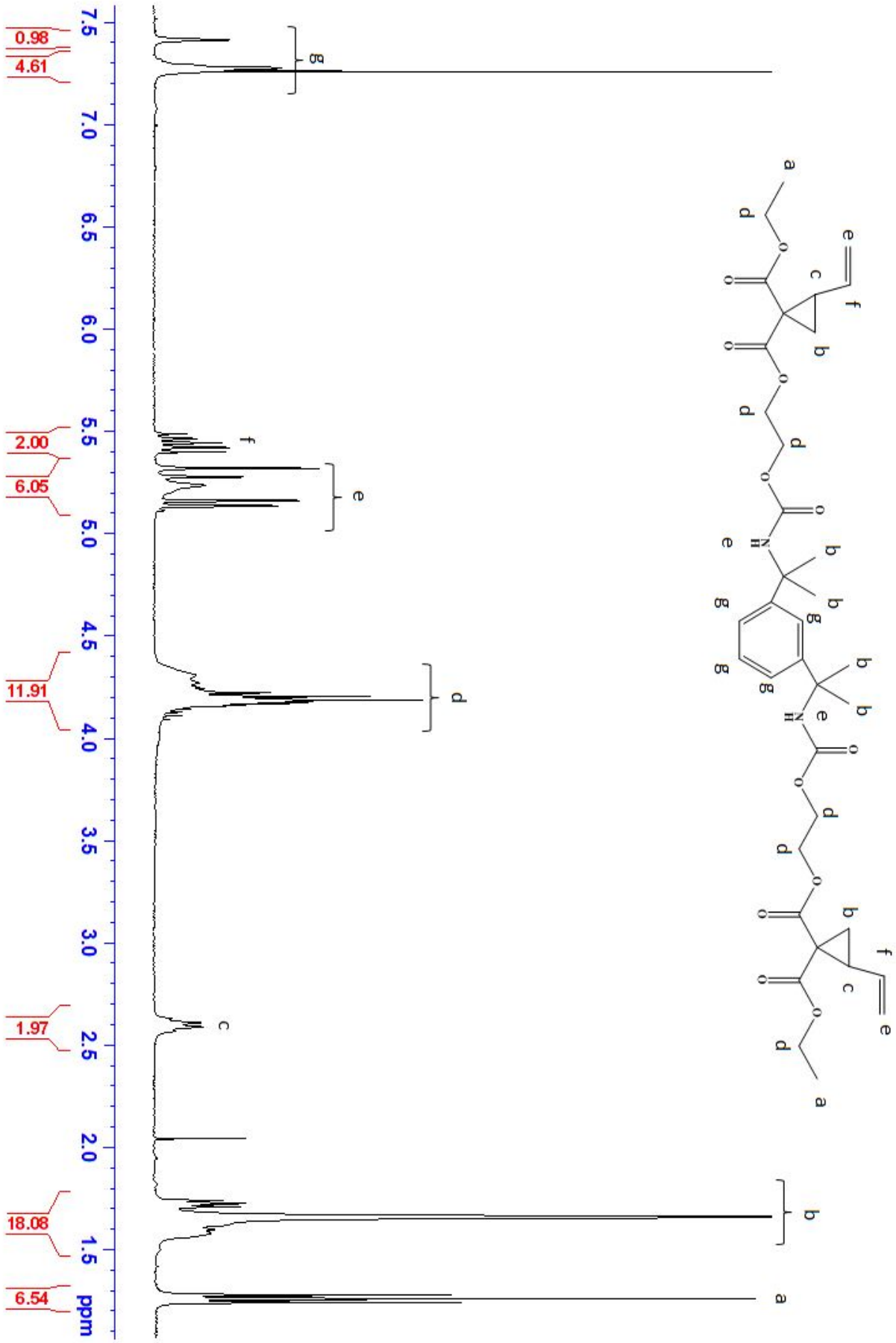
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
2.00
1.98
1.98
1.93
11.99
3.97
1.95
0.03
5.67
2.08
7.15
1.15
8.94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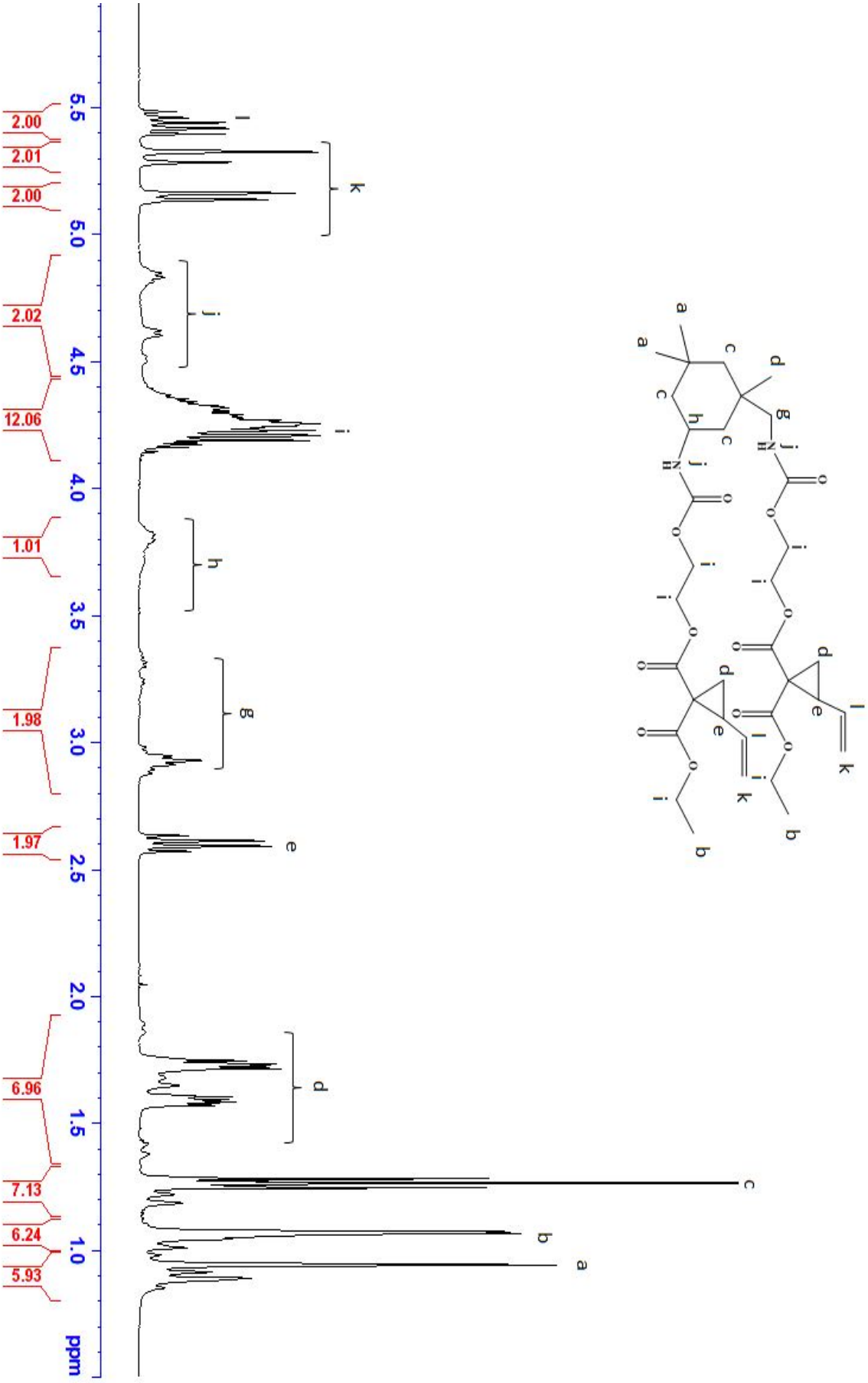
1.97
18.08
6.54
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm
a
b
c
d
e
f
g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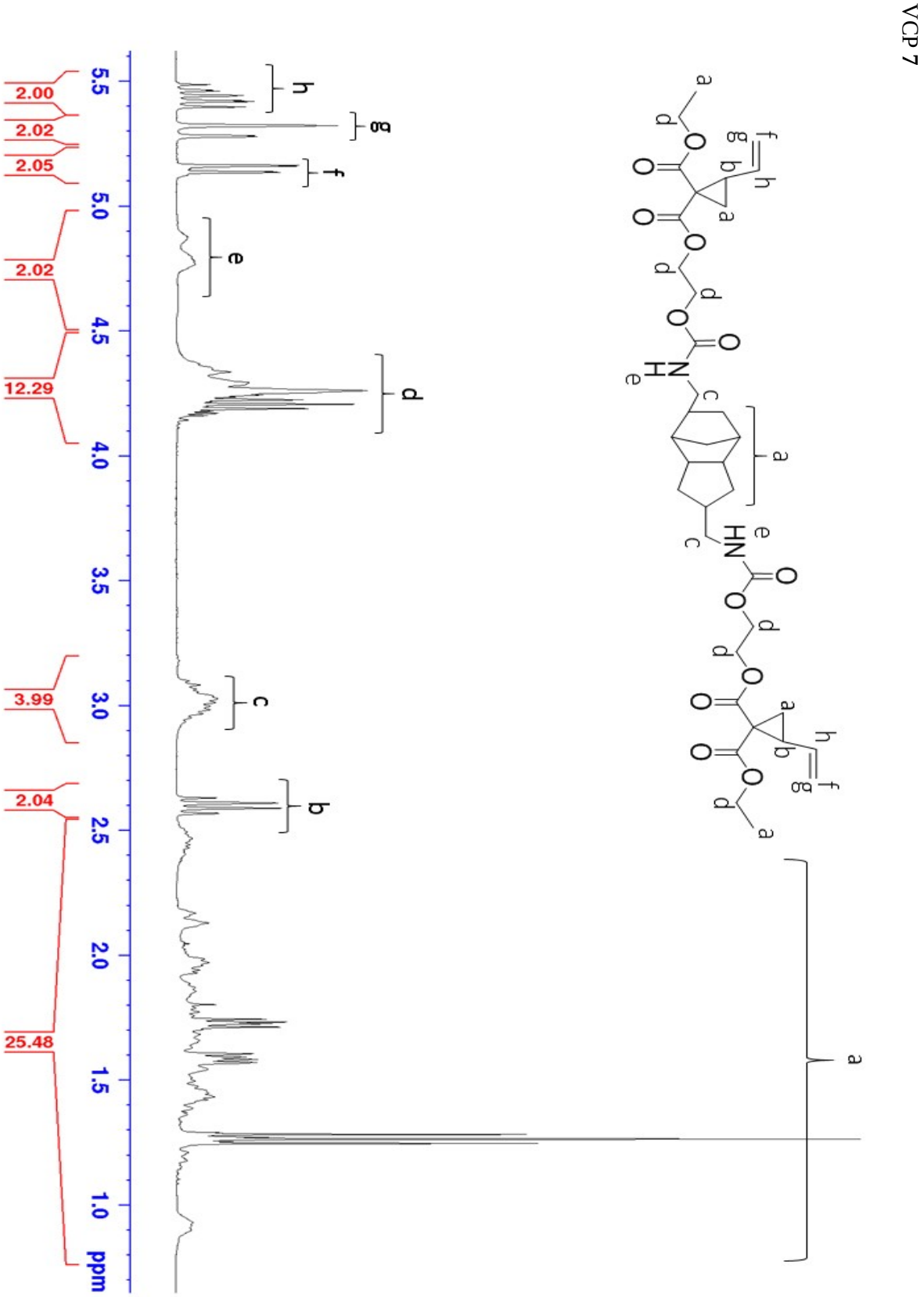
1.0
ppm
2.00
2.01
2.00
2.02
12.06
1.01
1.98
1.97
6.96
7.13
6.24
5.93
a
b
c
d
e
g
h
i
j
k
l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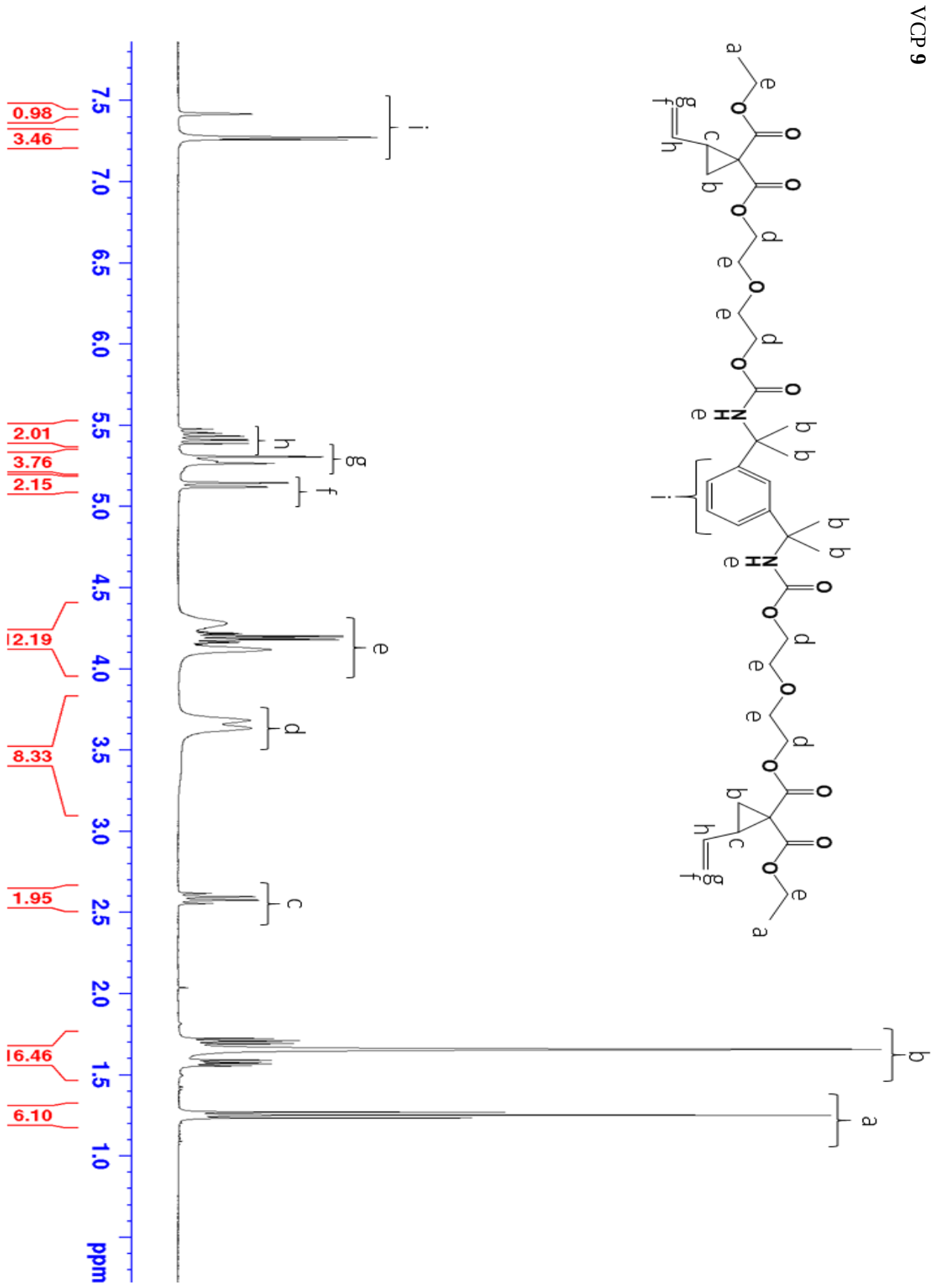
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
2.00
2.02
2.05
2.02
12.29
3.99
2.04
25.48
h
g
f
e
d
c
b
a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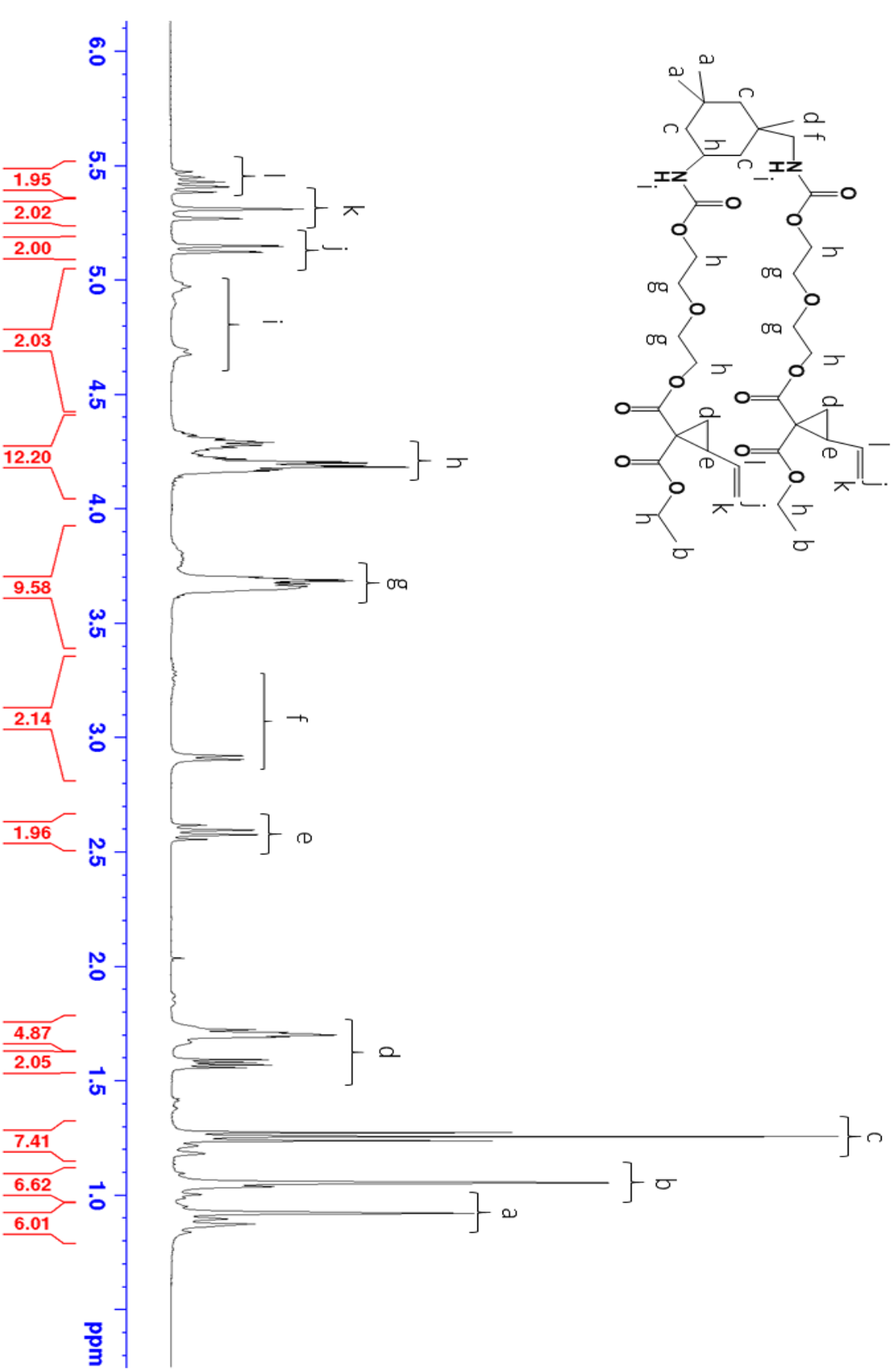
3.76
2.15
2.19
8.33
1.95
16.46
6.10
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
a
b
c
d
e
f
g
h
i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3.0
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1.5
1.0
ppm
1.95
2.02
2.00
2.03
12.20
9.58
2.14
1.96
4.87
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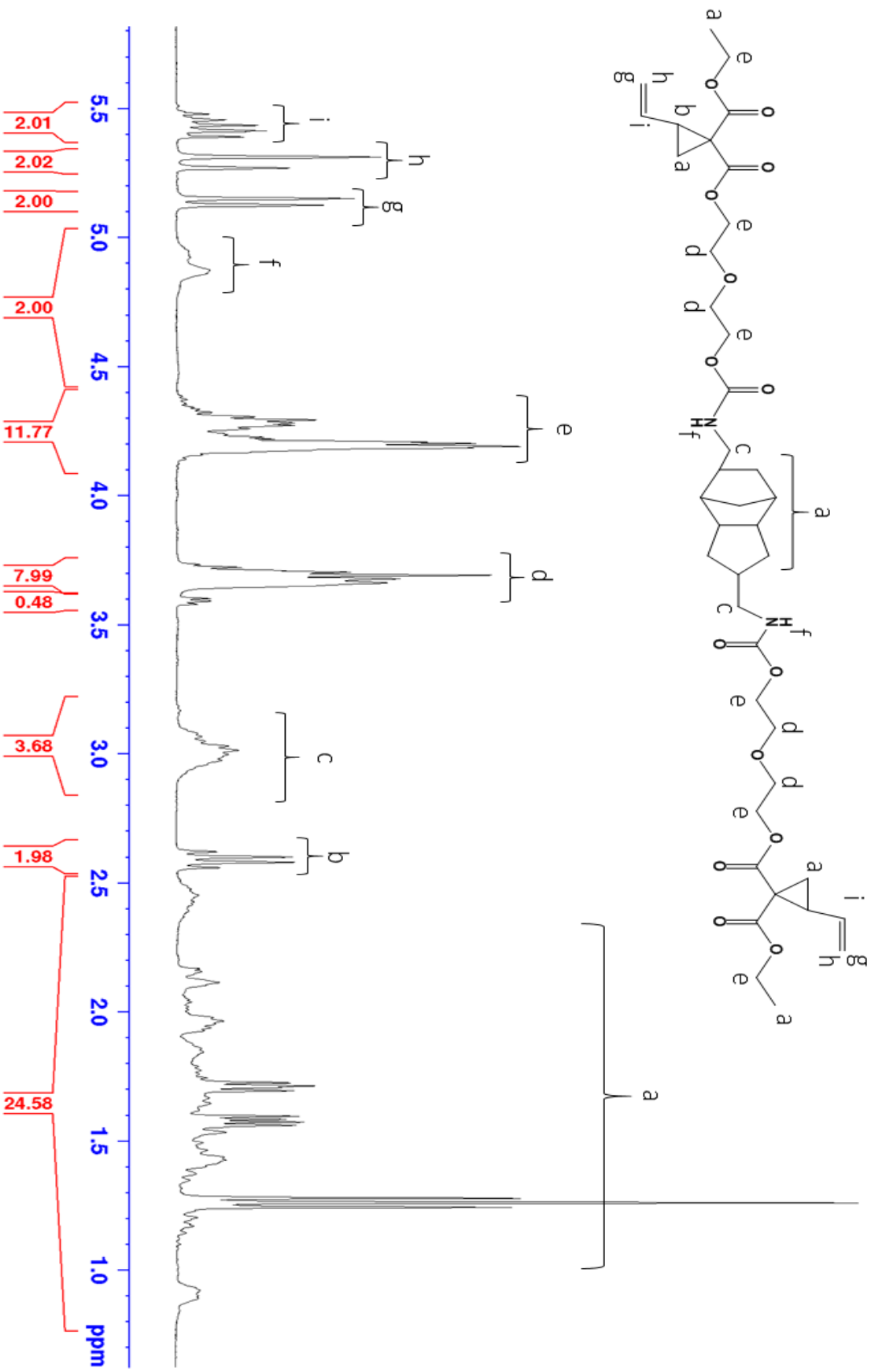
7.41
6.62
6.01
a
b
c
d
e
f
g
h
i
j
k
l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3.5
3.0
2.5
2.0
1.5
1.0
ppm
2.01
2.02
2.00
2.00
11.77
7.99
0.48
3.68
1.98
24.58