New Monomers for Dental Application

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Summary: The currently used commercial restoratives composites and self-etching enamel-dentin adhesives usually contain various functionalised and cross-linking methacrylates. New developments of polymeric composites for restorative filling materials are mainly focused on the reduction of the polymerization shrinkage and improvement of biocompatibility and wear resistance. This can be partially achieved by using new monomers, for example, cyclic monomers for the radical polymerisation such as bicyclic cyclopropyl-acrylates or polycondensates generated by the hydrolytic condensation of triethoxypropylsilane dimethacrylates. In the presence of water and strongly acidic monomers, methacrylates undergo hydrolysis, which results in decrease of the performance of the adhesive. This problem can be overcome with new polymerizable acrylic phosphonic acids and cross-linking bis(acrylamide)s, which show improved hydrolytic stability.

Keywords: adhesives; composites; dental materials; polymerisation shrinkage; ring-opening polymerisation; sol-gel process

Introduction

In restorative dentistry, tooth-coloured resin-based composites have been used as direct restorative material to restore both the form and function to a tooth. These restorative composites are applied in the adhesive technology in combination with suitable enamel-dentin bonding agents to generate a strong bond between the dental hard tissues (enamel and dentin) and the composite to prevent the formation of a marginal gap.

Many of the currently used commercial direct restorative composites are composed of a mixture of about 70-80 wt.-% of different surface-modified inorganic fillers and 20-30 wt.-% of a organic matrix (Figure 1).[1] The micro-filled composites are based on nanofillers such as silica with a primary particle size of 10-50 nm, whereas the hybrid-filled composites additionally contain radiaopaque glass fillers. The organic matrix consists of a mixture of cross-linking dimethacrylates, a photoinitiator system and further additives. Frequently used dimethacrylates are

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Bis-GMA (2,2-bis[4-(2-hydroxy-3-methacryloyloxypropyl)phenyl]propane), UDMA (1,6-bis-[2-methacryloyloxyethoxycarbonylamino]-2,4,4-trimethylhexane) and D_3MA (decanediol dimethacrylate), which show a polymerisation shrinkage of 6.1, 6.7, and 10.3 vol.-% (Figure 2).

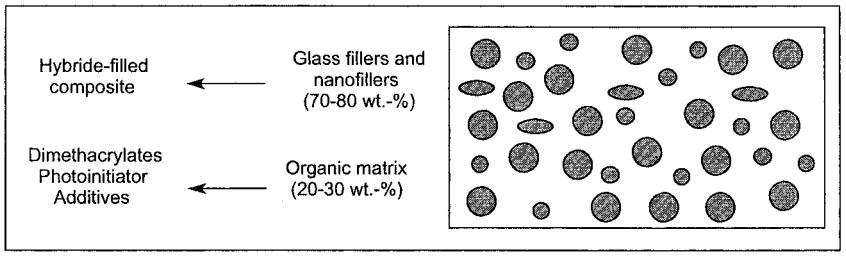

Figure 1. Composition of currently used restorative composites

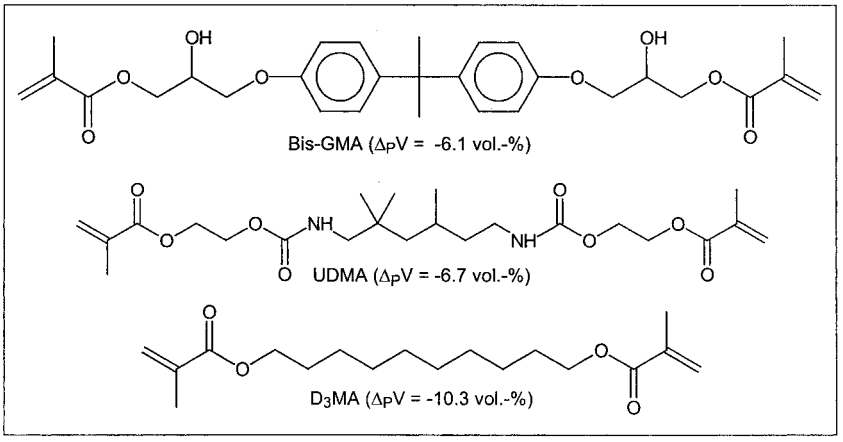

Figure 2. Structure of frequently used cross-linking monomers in restorative composites

Although the polymerisation shrinkage of the composites is reduced to a value of 2.0-4.0 vol.-% by the addition of filler, it may cause the formation of a marginal gap during the curing of the composite in the oral cavity. Composites for dental fillings have to meet a number of physico-chemical requirements (Figure 3). The main efforts for improving the presently used restorative composites involve the reduction of the polymerisation shrinkage and the increase of the abrasion resistance and biocompatibility.[2] This can be achieved by using new components such as cyclic

monomers or sol-gel monomers as shown in the following part of this paper.

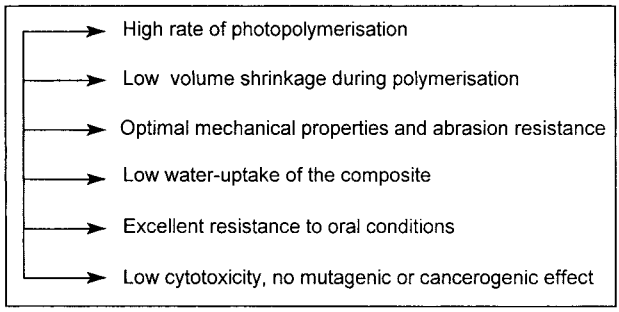

Figure 3. Physico-chemical requirements for direct resin based restorative composites

The currently used self-etching enamel-dentin adhesives contain different monomer components besides the initiator system and the solvent, such as water, ethanol and acetone or mixtures thereof. The main components include adhesive monomers (Figure 4), such as polymerisable carboxylic acids, for example, 4-MET (4-methacryloyloxyethyl trimellitic acid) or methacrylate phosphates, for example, MDP (10-methacryloyloxydecamethylene phosphoric acid), which are able to modify the enamel and dentin surface, promote the diffusion of the monomers into the dental hard tissue structure and mediate a strong bond between the dentin and the restorative composite.[3] Furthermore, hydrophilic cross-linking dimethacrylates, such as Bis-GMA, TEGDMA (triethyleneglycol dimethacrylate) and GDMA (glycerol dimethacrylate) are used in order to improve both the polymerisation reactivity of the adhesive and the mechanical properties of the adhesive layer formed. Finally, hydrophilic monomers such as HEMA (2-hydroxyethyl methacrylate) improve the miscibility of the adhesive components, the wetting behaviour of the adhesive and the monomer diffusion into the dentin structure. In self-etching adhesive water is primarily used as solvent or cosolvent. Thus, especially in the case of the easy-to-handle one-bottle-adhesives, the methacrylates may undergo hydrolysis of the methacrylate ester bonds in the presence of the strongly acidic adhesive monomers, which changes the chemical composition of the adhesive and also impairs its performance. Therefore, new monomers with improved hydrolytical stability under acidic conditions, which are described in the third part of this paper are necessary.

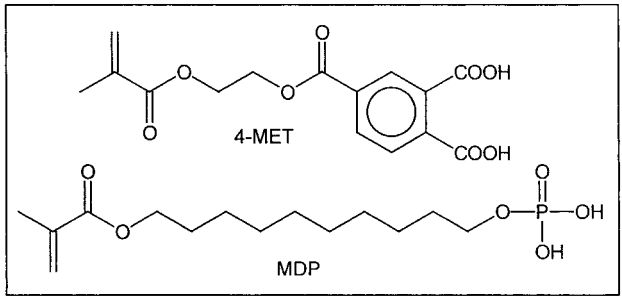

Figure 4. Structure of strongly acidic monomers presently used in self-etching adhesives

New monomers for restorative composites

We synthesised and evaluated a number of new cyclic monomers, which show a low volume shrinkage during their ring-opening polymerisation, for example, spiro orthocarbonates[4], cyclic ketene acetales[5,6] and 1,1,-disubstituted 2-vinylcyclopropanes[7,8] (Figure 5). Among theses monomers the vinylcyclopropanes showed the most promising properties. Therefore, a number of different new vinylcyclopropanes derivatives were synthesised, such as hybrid monomers, silanes and cross-linking vinylcyclopropanes (Figure 6).[9-13] In this context, the lowest polymerisation

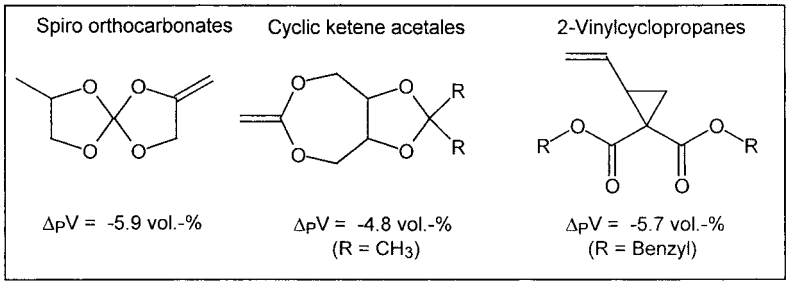

Figure 5. Structure of low shrinking monomers for the radical ring-opening polymerisation

shrinkage was shown by the cross-linking resorcinol derivative 1,3-bis[(1-ethoxycarbonyl-2-vinylcyclopropane-1-yl)carboxy]benzene ($\Delta_P V$ = -3.9 vol.-%).[13] However, 1,1-disubstituted 2-vinylcyclopropanes are less reactive than corresponding methacrylates. Nowadays, the market demands fast-curinge composites. Unfortunately, fast-curing composites cannot prepared based

on these vinylcyclopropanes. Therefore, more reactive vinylcyclopropanes have to be synthesised. In order to increase the reactivity of vinylcyclopropanes different approaches were made (Figure 6). However, neither the introduction of strong electron-withdrawing substituents nor the variation of the substitution pattern led to more reactive vinylcyclopropane derivatives. The increase of the functionality did also not result in a corresponding increase in the polymerisation reactivity. More promising results were obtained with bicyclic derivatives and the combination with an acrylic unit. When the last two concepts were brought together, the best results were obtained, that means with bicyclic cyclopropyl-acrylates.[14] It was found, that the polymer yield of the radical homopo-

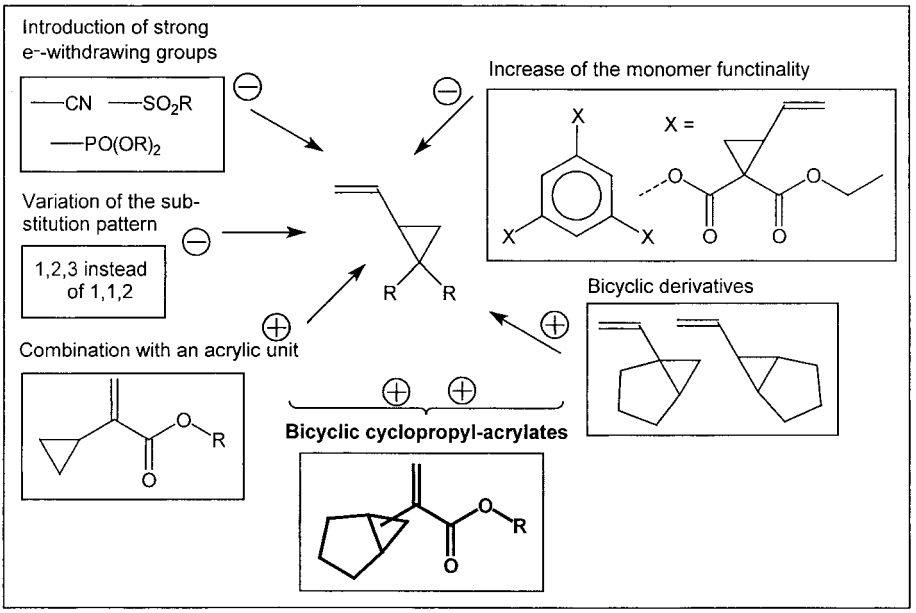

Figure 6. Approaches for the variation of the vinylcyclopropane structure

lymerisation of the different bicyclic cyclopropyl-acrylates in solution of chlorobenzene and in the presence of 2,2'-azobisisobutyronitrile (AIBN) as initiator depends on the size of the second ring. The highest polymer yields were obtained with the monomer containing a 5-membered ring, in other words, with a bicyclo[3.1.0]-acrylate (Figure 7).

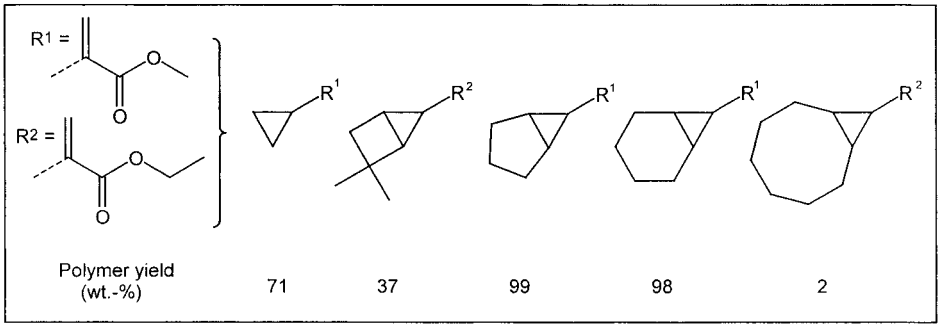

Figure 7. Polymerisation of bicyclic cyclopropyl-acrylates (2.0 mol/L) of different ring size with AIBN (2.0 mol-%) in chlorobenzene at 65 °C (15 h)

Good evidence of the change of the monomer reactivity is provided by the copolymerisation with MMA. The 1,1-disubstituted 2-vinylcyclopropanes were significant less reactive than MMA (Figure 8). Clearly, the content of vinylcyclopropyl-derived units in the copolymers increases in the case of the cyclopropyl-acrylates and is slightly lower or higherr in the case of the bicyclo[3.1.0]-acrylate. Furthermore, the results confirm that the bicyclic monomer, in which the bicylic ring was substituted at the bridgeheads showed the highest reactivity. The most promising results were obtained with methyl 2-(bicyclo[3.1.0]hex-1-yl)acrylate (AVCP), which showed a polymerisation shrinkage of about 10.6 vol.-%. [15] The ^{1}H NMR and ^{13}C NMR spectra of

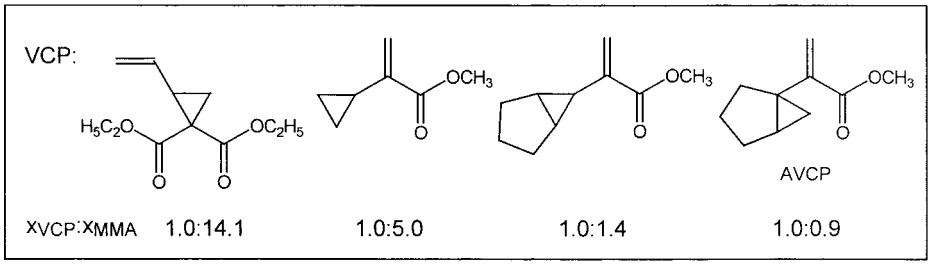

Figure 8. Composition of copolymers prepared by copolymerisation of vinylcyclopropyl monomers (VCP, 1.0 mol/L) and MMA (1.0 mol/L) with AIBN (2.0 mol-%) in chlorobenzene at 65 °C (2 h)

poly(AVCP) obtained in the solution polymerisation confirmed the opening of the cyclopropane

ring with the formation of a 1,5-substituted ring-opened unit and a unstrained cyclohexane ring (Figure 9). A further decrease of the polymerisation shrinkage can be achieved by increasing the molecular weight of the bicyclic acrylates. This can be done, for example, by substitution of the methyl ester group by larger substituents.

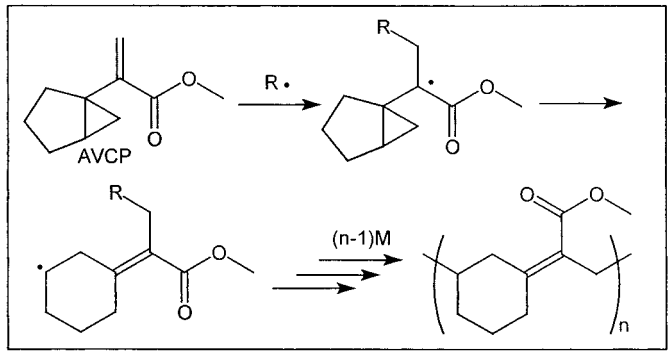

Figure 9. Proposed mechanism of the radical ring-opening polymerisation of vinylcyclopropyl monomer AVCP

A further possibility to improve dental filling composites is the use of new polymerisable sol-gel polycondensates.[16] Sol-gel polycondensates can be obtained by hydrolysis and condensation, for example, of methacrylic group-containing trialkoxysilanes (Figure 10). These polycondensates, which are also called Ormocers®, can be cross-linked in a second step under formation of organic-inorganic hybrids. In these hybrids the organic and inorganic components are combined at a nanoscopic or molecular scale and, therefore, enable the fabrication of composites with tailor-made properties. This makes these sol-gel-components very attractive for use in dental materials, for example, as an organic matrix for dental fillings. For this purpose two classes of new silanes, i.e. amino- or amidopropyltriethoxysilane dimethacrylates were synthesised in which the hydrolytically condensable silyl and the polymerisable methacrylic groups are linked by amine or amide-linking groups (Figure 11).[17] The hydrolytic condensation of the dimethacrylate silanes 1 and 2 was carried out with ethanol as the solvent in the presence of ammonium fluoride as the catalyst. ^{29}Silicon-NMR-spectroscopy was used to follow the course of hydrolytic condensation. After 20 h the starting silanes were completely consumed under formation of linear and branched polysiloxane chains with pendant dimethacrylate groups. After evaporation of the solvent pure

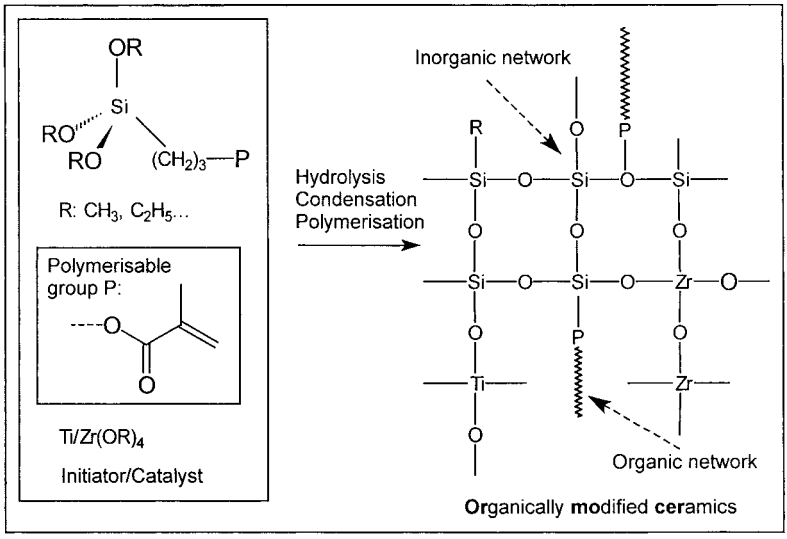

Figure 10. Synthesis strategy for sol-gel components starting from organically modified silanes

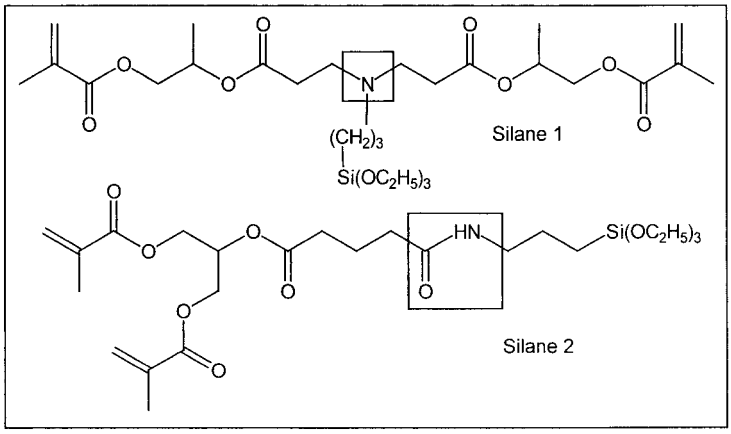

Figure 11. New triethoxypropylsilane dimethacrylates for the synthesis of sol-gel polycondensates

liquid polycondensates (PC) remained. The polycondensates of silane 1 and 2 (PC-1 and PC-2), respectively, and of corresponding PC-based composites, which contained about 81% of a barium

silicate glass filler, were cured using a visible-light source. The mechanical properties of these materials (Table 1) meet the minimal demands for dental composites according to the ISO-standard. One main advantage of such sol-gel-monomer-based composites is their improved biocompatibility. These composites are free of dimethacrylate diluents, which generally cause a certain amount of uncured and therefore extractable monomer content. This was confirmed by the fact, that the ethanol-soluble part of a visible-light-cured mixture of UDMA with the polycondensate PC-1 (53/47) was only 0.9% compared to 6.6% of a visible-light cured mixture of Bis-GMA and UDMA (53/47).[18] Finally, it should be mentioned that the properties of sol-gel composites can be further improved, for example, by the addition of methacrylate substituted oxozirconium clusters (Table 1).[19]

Table1. Mechanical properties of sol-gel polycondensates and composites based thereon (filler content: 80.7 wt.-%)

Sample	Flexural strength (MPa)	Flexural modulus (GPa)
PC-1	40	1.13
PC-2	65	1.79
PC-2 + Zr-cluster [a)]	70	2.40
Composite of PC-1	85	7.58
Composite of PC-2	89	8.85

a) Addition of 20 wt.-% of a methacrylate-substituted oxozirconium cluster.

New monomers for self-etching adhesives

Our synthetic concept for producing hydrolytically stable, strongly acidic monomers firstly involves the substitution of the instable methacrylic ester bond by a hydrolytically stable ether bond and secondly, the use of a phosphonic group instead of a phosphoric acid ester group (Figure 12). Starting from this concept a number of new phosphonic acid monomer with improved hydrolytically stability were synthesized (Figure 13).[20,21] Among these monomers the acrylic phosphonic acid 1a showed the most promising adhesive properties and, therefore, is used

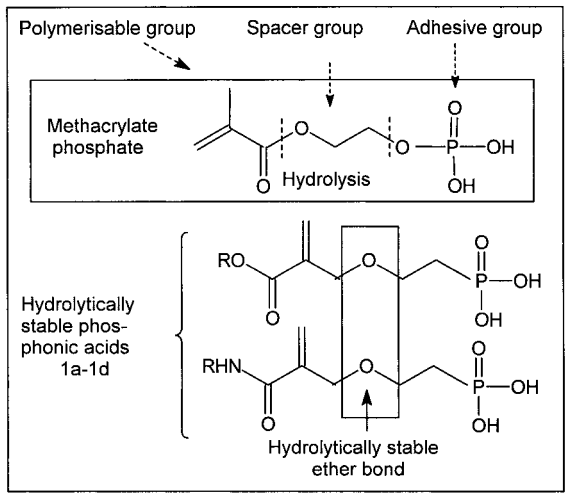

Figure 12. Synthetic concept for producing strongly acidic monomers with improved hydrolytic stability

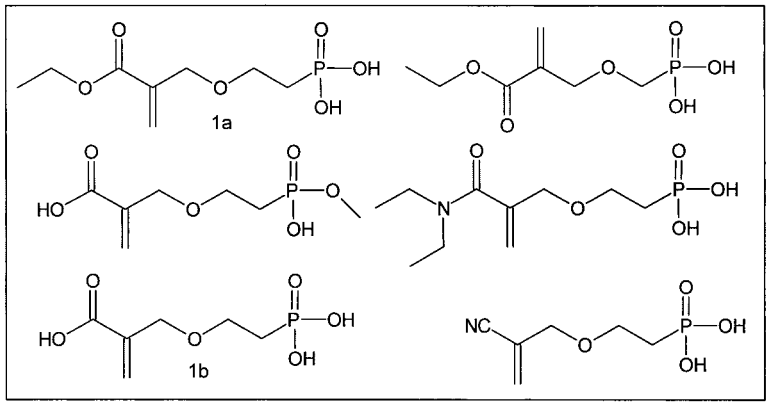

Figure 13. Examples of polymerisable phosphonic acids with improved hydrolytic stability

in our current dentin adhesives. In addition, two new phosphonic acids were synthesised by the reaction of the carboxylic group of the dimethyl phosphonate with mesitol in the presence of p-toluenesulfonyl chloride (PTSCl) in the case of monomer 1c, followed by silylation with

trimethylsilyl bromide (TMSBr) and methanolysis under formation of the phosphonic acid 1c (Figure 14). Monomer 1d was obtained by amidation with propylamine in the presence of 1,3-dicyclohexylcarbodiimide (DCC) as condensation agent. Monomer 1c, in particular, shows a very high hydrolytical stability under acidic conditions.

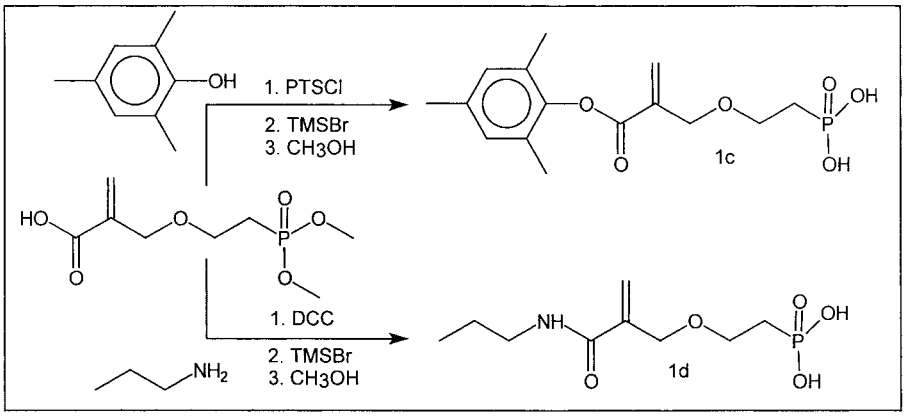

Figure 14. Synthesis of phosphonic acids 1c and 1d

New hydrolytically stable polymerisable bisacrylamides 2a-e, which can be used to substitute the dimethacrylates, for example, glycerol dimethacrylate (GDMA) in self-etching dentin adhesives were successfully synthesized.[22] Thereby, it was possible to influence the properties of the cross-linking monomers such as polymerisability, solubility and toxicity, by varying the spacer group X and the substituent R of amide nitrogen (Figure 15). Bis(meth)acrylamides 2a-e were synthesized by the reaction of acryloyl- or methacryloyl chloride with the corresponding diamine in the presence of triethylamine. The synthesised bifunctional monomers demonstrate excellent solubility both in water and organic solvents. Gel formation experiments were used to compare the reactivity of the synthesised bisacrylamides with that of GDMA, which is used as a cross-linker in current adhesives. The longer the gel time the lower is the reactivity of the cross-linkers. The results showed that the bisacrylamides are equally or slightly more or less reactive than GDMA.

From the recent acrylamide discussions with regard to the presence of this substance in various foodstuffs,it is known that the toxicity of such compounds may be a serious problem. Therefore,

the toxicity of the synthesised bisacrylamides was investigated very intensively. Consequently, several of the synthesised bisacrylamides were found to show a mutagenic potential. However, the bisacrylamides 2c and 2d did not show any mutagenic effect in the Ames test or the Comet assay.

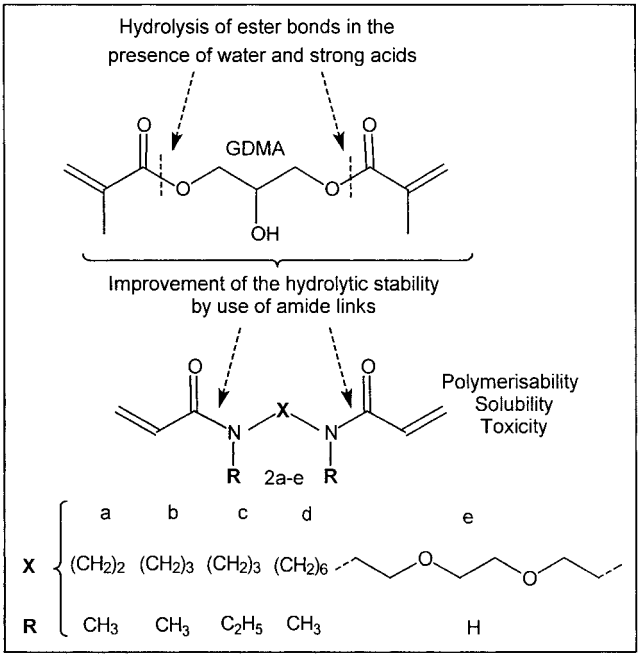

Figure 15. Examples of cross-linking bis(acrylamide)s with improved hydrolytical stability

The Comet assay is a very sensitive test for the potential of compounds to induce primary DNA-breakage. Finally, it should be mentioned, that many bisacrylamides showed a significantly lower cytotoxicity than commonly used dimethacrylates, such as TEGDMA.

Conclusion

On the basis of bicyclic cyclopropyl acrylates, which undergo a radical ring-opening polymerization, new monomers with a higher reactivity and lower polymerization shrinkage than

corresponding methacrylates can be developed for dental filling composites. Furthermore, polycondensates of new silane dimethacrylates in combination with oxozirconium clusters can be used for the preparation of diluent-free VL-cured composites, which meet the requirements for dental filling materials and show improved biocampatibility. New hydrolytically stable acrylate ether phosphonic acids and cross-linking bisacrylamides enables the preparation of self-etching enamel-dentin adhesives with improved hydrolytical and storage stability.

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