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Synthesis and Radical Polymerization of Hydrolytically Stable Dentin Bonding Agents

Norbert Moszner, Frank Zeuner, Volker Rheinberger*

Ivoclar AG, Research & Development, FL-9494 Schaan, Liechtenstein

SUMMARY: Acrylic groups containing phosphonic acids were synthesized by ether formation of ethyl α-chloromethylacrylate with hydroxyalkyl phosphonates and subsequent hydrolysis to the corresponding phosphonic acid α-methylsubstituted acrylates. Furthermore, phosphonic acids derived from acrylonitrile and acrylamide were synthesized. The monomers are hydrolytically stable in aqueous ethanol. The radical polymerization of the monofunctional phosphonic acids results in water soluble polymers, whereas in case of a phosphonic acid diacrylate a cross-linked polymer was formed. The most radical polymerizable phosphonic acids can be used to promote the adhesion to dentin.

Introduction

To achieve a strong bond between the filling material and the tooth substance (dentin and enamel), coupling agents are used in restorative dentistry[1,2]. In general, these coupling agents are bifunctional molecules, containing a polymerizable group, for example, a methacrylic group, which can react with the restorative material by copolymerization. Furthermore, an adhesive group AD, such as an ionic (e.g. a phosphonic group) or chelating group (e.g. acetoacetate group) is capable to react with the tooth substance. And finally, a spacer R, is responsible to influence the hydrophilicity, flexibility and the wetting properties of the adhesive monomer (*Scheme 1*).

In this respect, phosphoric acid esters of hydroxyalkyl methacrylates are favourable as primers for dentine adhesion, because they are well soluble in water or ethanol and remove the smear layer on the dentine surface. However, one disadvantage of these polymerizable phosphoric acids is their low hydrolytic stability. For example, in an aqueous solution of di(2-methacryloyloxyethyl)-hydrogenphosphate (**MEP**), a hydrolysis of both the methacrylic ester (**A**) and phosphoric ester bond (**B**) takes place under the formation 2-hydroxyethyl methacrylate (**HEMA**), resulting in a significant decrease of the adhesive properties of the **MEP** solution[3] (*Scheme 2*).

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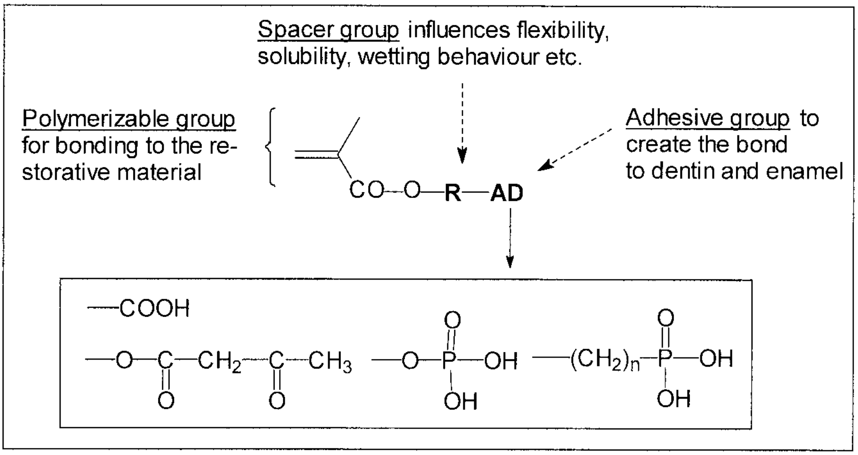
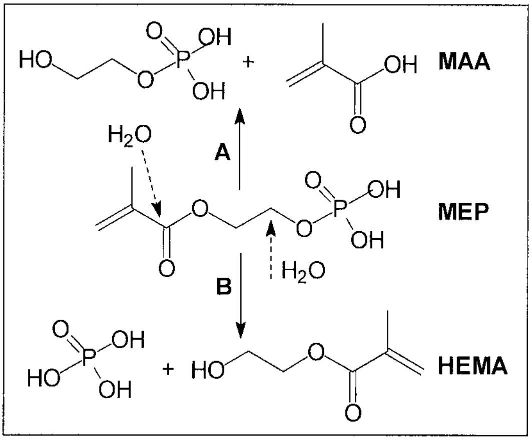
Scheme 1:



Scheme 2:



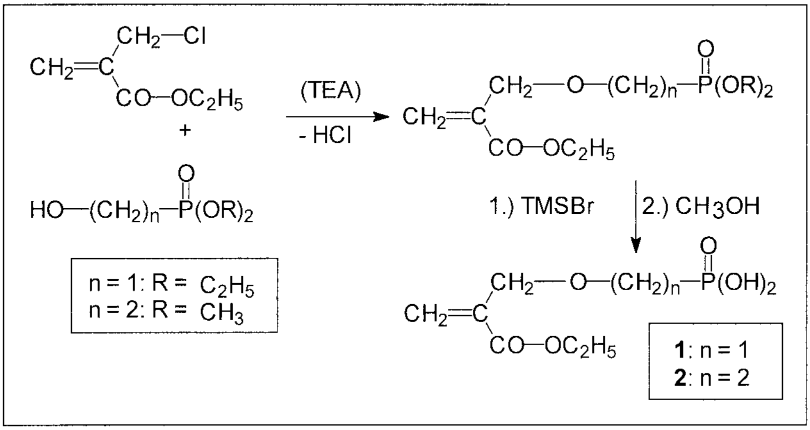
This problem can be overcome with monomers containing more hydrolytically stable bonds between the polymerizable methacrylic group and the strongly acidic phosphorus group. This requirement fulfil a number of polymerizable phosphonic acids, for example, vinylphosphonic acid or 4-vinylbenzylphosphonic acid. However, vinylphosphonic acid show a poor radical polymerizability and 4-vinylbenzylphosphonic acid is less reactive than methacrylates[4]. In conjunction with the preparation of polymeric scale inhibitors, a number of polymerizable phosphonic acids are described[5,6], which are well radical polymerizable and demonstrate higher hydrolytical stability, for example, 2-acrylamido or 2-methacrylamido-2-methyl-1-propanephosphonic acid.

This paper summarizes our results of the synthesis and radical polymerization of hydrolytically stable polymerizable groups containing phosphonic acids.

Synthesis of polymerizable phosphonic acids

The polymerizable phosphonic acids **1** and **2** were synthesised by ether formation of ethyl α-chloromethylacrylate with the diethyl hydroxymethylphosphonate or dimethyl 2-hydroxyethylphosphonate in the presence of triethylamine (TEA), and subsequent silylation of the reaction products with trimethylsilyl bromide (TMSBr) and metha-nolysis of the silyl ester to the phosphonic acid α-methylsubstituted acrylates **1** or **2** (*Scheme 3*)[7].

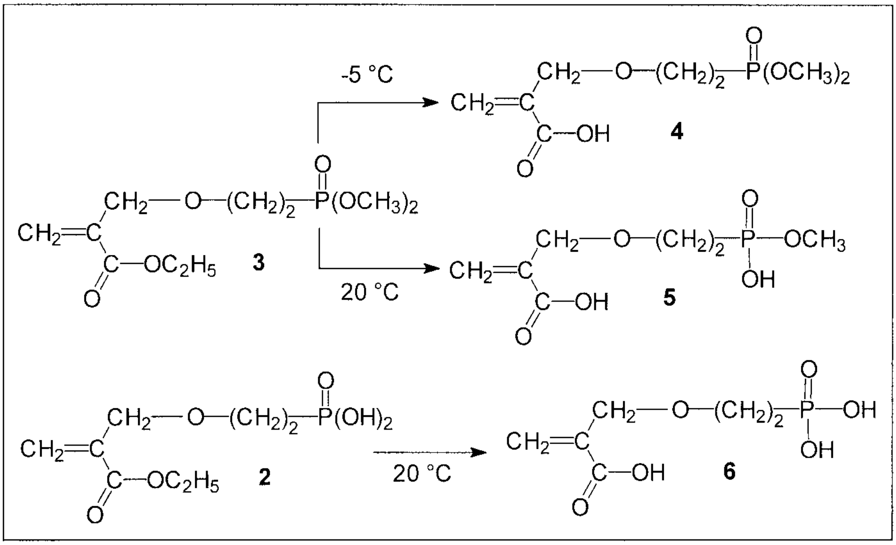
Scheme 3:



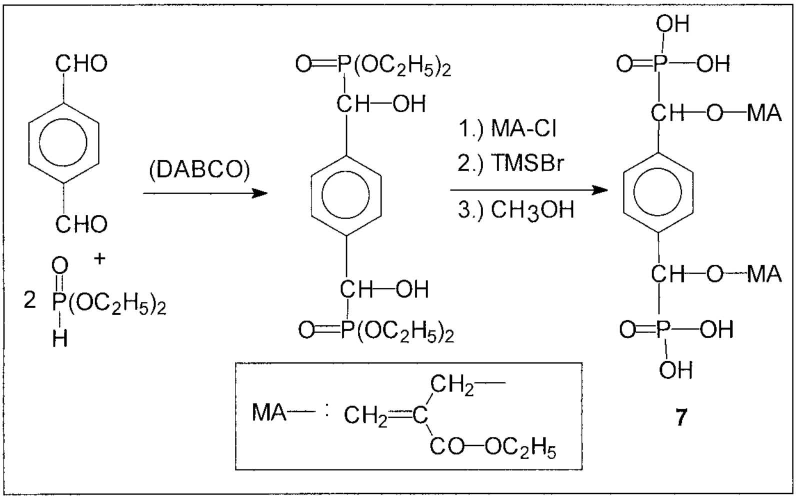
Further derivatives of monomer **2** can be obtained by partial hydrolysis of monomer **2** or **3** (*Scheme 4*)[8]. Thus, the partial hydrolysis of monomer **3** with KOH results in monomer **4** at –5°C or monomer **5** at 20 °C, wheareas monomer **6** is formed by alkaline hydrolysis of monomer **2** at 20 °C. The monomers **2-6** are well soluble in both water or ethanol and corresponding mixtures, which is very important for dental

application. However, in comparison to monomer **2**, the phosphonic acids **5** and **6** are less soluble in **HEMA** or glycerol dimethacrylate (**GDMA**), which are often used as comonomers in dental adhesives. Beside the solubility, the carboxylic group in these monomers influences also the storage stability of corresponding mixtures with other methacrylates or alcohols, because of the tendency of the carboxylic group for esterification or transesterification.

Scheme 4:

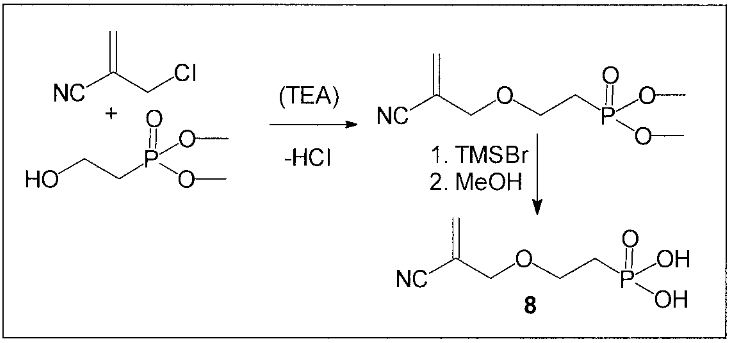


Scheme 5:

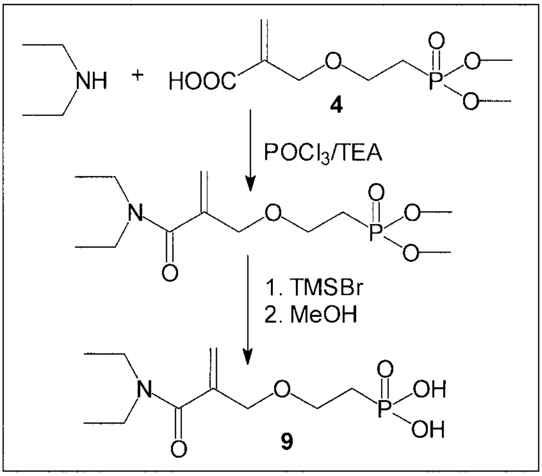


Monomer **7** is accessible by the reaction of diethyl phosphite with terephthalaldehyde in the presence of 1,4-diazabicyclo[2.2.2]octane (DABCO), followed by the reaction with ethyl α-chloromethylacrylate, the silylation with TMSBr, and methanolysis of the silyl ester to the difunctional phosphonic acid α-methylsubstituted diacrylate **7** (*Scheme 5*). In comparison to monomer **2**, compound **7** is less soluble in organic solvents. Monomer **8** can be synthesized by ether formation of ethyl α-chloromethacrylonitrile with the dimethyl 2-hydroxyethylphosphonate, and subsequent silylation and methanolysis (*Scheme 6*). Finally, the reaction of diethyl amine with monomer **4** followed by the silylation and methanolysis results in acrylamidophosphonic acid **9** (*Scheme 7*). The monomers **8** and **9** show excellent solubility in water, polar and non-polar solvents.

Scheme 6:



Scheme 7:



The above described phosphonic acids can be synthesized in a high purity. Therefore, their ^{31}P-NMR spectra show only single peak. This is in contrast to methacrylate phosphoric acid esters, for example, HEMA-phosphate, that ^{31}P-NMR spectrum usually shows three signals, which are caused by the presence of both mono- or di ester and diphosphate. According to our expectations, the monomers **1-9** were stable in aqueous ethanol at 25 °C during the 3 months of the investigation, that means no hydrolysis of the ether bond between the polymerizable group and the phosponic acid moiety was observed. The pH-values of aqueous solutions of the synthesized

phosphonic acids (20 wt.-%) shows an increase in the following order: **5** (0.61)< **9** (0.81) < **2** (1,12) < **6** (1.25) < **9** (1.76). Therefore, aqueous solutions of phosphonic acids are able to etch enamel.

Polymerization and adhesion properties

The radical solution polymerisation of the synthesized phosphonic acids was carried out in tetrahydrofuran (THF), ethanol, water or N,N-dimethylformamide.(DMF) in the presence of 2,2`-azoisobutyronitrile (THF, DMF, ethanol) or 2,2`-azobis(2-methylpropionamidine) dihydrochloride (water) at 65 °C. Water soluble polymers were obtained in case of monomers **1-6** and **8-9**. In contrast to this, the radical polymerization of the diacrylate **7** resulted in a insoluble cross-linked polymer. In case of the aqueous solution polymerization of monomer **2** and **4-6** high molecular weight polymers are formed with an almost complete monomer conversion within one hour. In contrast to this, the monomers **8** and **9** are significantly less reactive.

Based on the results of the polymerization, the adhesive properties of the most promising hydrolytically stable phosphonic acid monomers were investigated. Therefore, the shear bond strength of a corresponding ethanol based dentin adhesives containing the synthesized monomers was measured (Tab. 1). The adhesive based on monomer **2** shows the highest shear bond strength. The most acidic monomer **5** is significant less active, which is probably caused by the presence of the phosphonic acid monoester group.

Tab. 1: Shear bond strength of model dentin adhesives based on various polymerizable phosphonic acids.

Monomer	Shear bond strength (MPa)
1	14.1
2	24.2
5	10.3
8	9.3
9	23.2

Moreover, the lower shear bond strength of the adhesive with monomer **1** in comparison to that of monomer **2** can be explained on the basis of the lower reactivity of monomer **1** in the radical polymerization. Altogether, the investigation of the phosphonic acid monomers demonstrated that the shear bond strength both increases with the monomer reactivity in the radical polymerization and the monomer solubility in the adhesives mixture. Furthermore, the adhesion properties of primers can be strongly improved by the addition of cross-linking monomers, such as dimethacrylates.

References

1. L-A.-Lindén, in: Radiation Curing in Polymer Science and Technology, Ed.: J. P. Fouassier, J.F. Rabek, Vol. IV, Elsevier Apllied Science, London- New York 1993, 387.
2. A. Peutzfeldt, Eur. J. Oral Sci. **105** (1997) 97.
3. N. Moszner, F. Zeuner, A. Rumphorst, U. Salz, V. Rheinberger, Phillip J, in press.
4. W.-D. Schröder, in: *Methoden der organischen Chemie*, Makromolekulare Stoffe, Eds.: H. Bartl, J. Falbe, Vol. E20/2, Thieme-Verlag, Stuttart-New York 1987, 1300.
5. DOS 3210775 (1982), Hoechst AG, invs.: M. Finke, W. Rupp; *Chem. Abstr.* **100**, 68909 (1983).
6. DOS 3313819 (1983), Hoechst AG, invs.: E, Weiss, W. Rupp; *Chem. Abstr.* **102**, 62666 (1984).
7. N. Moszner, F. Zeuner, U. K. Fischer, V. Rheinberger, Macromol. Chem. Phys. **200** (1999) 1062.
8. N. Moszner, F. Zeuner, S. Pfeiffer, J. Angermann, I, Schurte, V. Rheinberger, M. Drache, Macromol. Chem. Phys., in preparation