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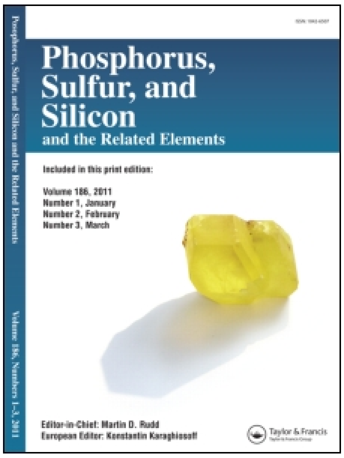

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Synthesis and Dental Aspects of Acrylic Phosphoric and Phosphonic Acids

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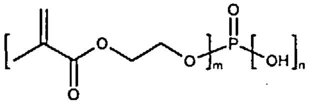
Introduction

Achieving a strong and durable bond to dentine is of great importance in restorative techniques. In recent years there has been a lot of debate as to how such a bond may be obtained. Bonding is believed to occur through either mechanical or chemical interaction or possibly a combination of both[1]. In this study we have focused on phosphorus compounds[2-4] which can form complexes with the Ca^{2+} ions of hydroxyapatite. Most of the hitherto known compounds can not afford a single step procedure in dental adhesion. To overcome this problem several new phosphonic and phosphoric methacrylates have been synthesized. Furthermore, polymerization capabilities and characteristics of physical and adhesive properties are described.

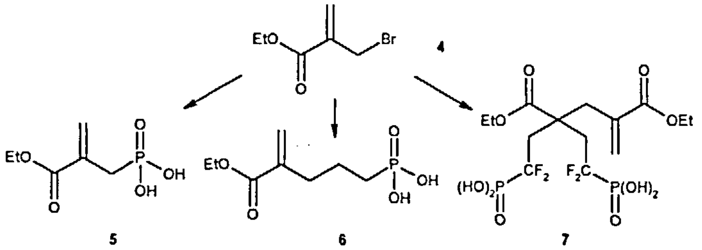
Materials and Methods

The reaction of 2-hydroxyethyl methacrylate with phosphorus oxychloride in a mole ratio of 2 : 1 produces a mixture with a statistical distribution of mono- **1**, di- **2** and triester **3**. From this mixture the bis-HEMA-ester **2** was easily enriched to 85 % by an extraction procedure. In the course of purification, the monophosphate **1** and the triphosphate **3** were also isolated for comparative tests.



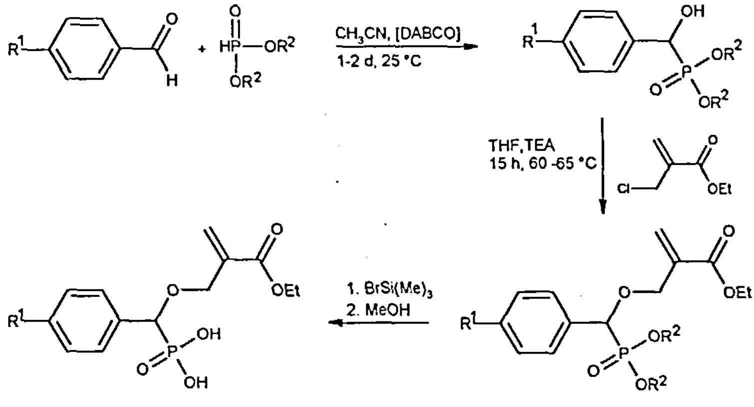
1 (m=1, n=2)
2 (m=2, n=1)
3 (m=3, n=0)

Introduction of the methacrylic substituent into phosphonates was achieved with ethyl 2-(hydroxymethyl)acrylate as the initial product[5]. Conversions to ethyl 2-(halogenomethyl)acrylates were conducted by $SOCl_2$ or HBr.



The 2-(bromomethyl)acrylate **4** was converted by the MICHAELIS-ARBUZOV reaction or by a reaction with organometallic phosphonates[6] respectively into several alkylene-linked acrylic phosphonates, which were selectively hydrolyzed into the phosphonic acids **5** - **7** by bromotrimethylsilane[7]. Cleavage of the phosphonic acid esters proceeded with yields of about 80 %.

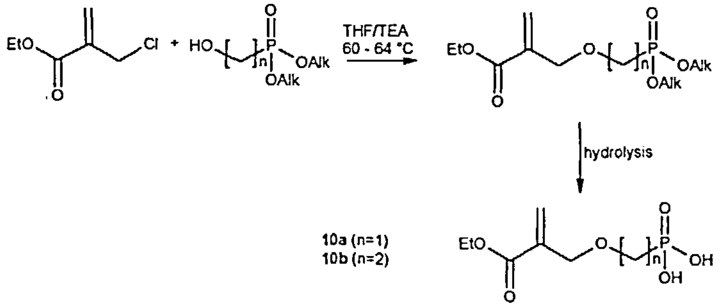
Synthesis of aromatic acrylic phosphonates[8] was carried out by the PUDOVIK-reaction[9], starting with benzaldehyde or terephthaldialdehyde. Reaction with dialkyl phosphite in the presence of a base (i.e. potassium fluoride, DABCO) produced dialkyl hydroxymethylphosphonates with a yield of 80 - 90 %. Further reaction with ethyl 2-(chloromethyl)acrylate in THF and triethylamine resulted in a 69 % yield of **8a** (R^1=H, R^2=Me) or 73 % of **8b** of (R^1=bis-compound, R^2=Et) respectively. In the last step, hydrolysis was carried out with bromotrimethylsilane to give 66 % of the phosphonic acids **9a** (R^1=H) or 76 % of **9b** (R^1=bis-compound) respectively. Purification proved to be somewhat difficult because of the good solubility of the product in water. Hydrolysis of the ethyl carboxylate **9a** with sodium hydroxide led to the corresponding acid **9c**.



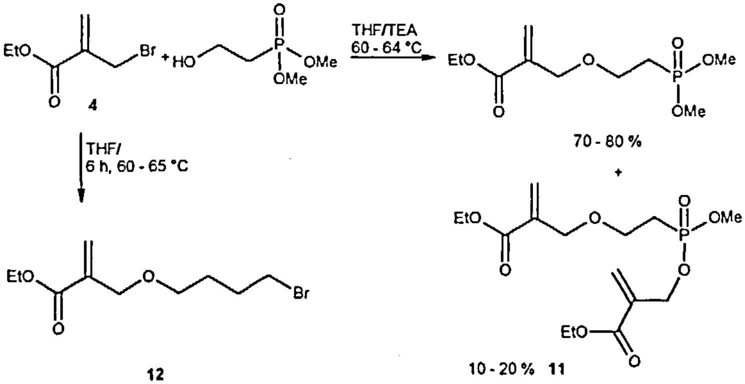
9a,b **8a,b**

The preparation of aliphatic ether-linked acrylic phosphonates[8] was started with commercially available hydroxyalkylphosphonates. In contrast to the aromatic derivatives bifunctional compounds are difficult to obtain in the aliphatic series. Etherification proceeded in the same manner as described above. In the transition from hydroxymethyl- to (2-hydroxyethyl)phosphonate, the reaction time could be decreased to one third. Obviously, this is due to the higher nucleophilic activity of the hydroxyethyl group. Finally, the needed phosphonic acids were obtained with a yield of 91 % (**10a**) and 86 % (**10b**) by the proven method with bromotrimethylsilane.

Examination of the etherification method using **4** instead of ethyl 2-(chloromethyl)-acrylate showed that in addition to 70 - 80 % of the desired product about 10 - 20 % of bismethacrylate **11** is obtained.



An explanation for the formation of this product could be transesterification of dimethyl phosphonate with cleavage of methylbromide. If the reaction is carried out in the absence of triethylamine and dimethyl (2-hydroxyethyl)phosphonate, **12** is formed.



In contrast to older generations, today's dentine adhesive systems are tested as 1-step system only without conditioning by primers and without additional bonding. The adhesion (shearbond strength) was measured using a universal testing machine (Zwick) at a crosshead speed of 0.8 mm/min. In general, a 40 % solution in $EtOH/H_2O$ is used.

Results and Discussion

HEMA-phosphates **1** and **2** were shown to undergo hydrolysis in an aqueous-ethanolic solution. Hydrolysis was even detected at 4 °C after 1 week. At higher temperatures hydrolysis increased rapidly. Thus, at 37 °C it was completed after 3 months. Nevertheless, the compounds can be successfully used for adhesive purposes, if they are mixed immediately before use. Acrylic phosphonic acids **9a,b** are resistant to hydrolysis, whereas the aliphatic ones **10a,b** slowly cleave at the carboxylic acid ester function. Because a strong connection exists between the methacrylic and the phosphonic part of the molecule, **10a,b** can be applied in a one-bottle system.

Phosphoric acid ester **1** - **3** and phosphonic acrylates clearly show that a minimum acidity (~ 1.0 - 1.4) is needed to afford good adhesion. The triester **3** without acidity but good polymerization reactivity shows very low bond strengths. Comparable results are achieved with the mono-ester **1**, which exhibits a strong acidity and low reactivity. The best bond strengths are achieved with the highly acidic di-ester **2**, which demonstrates excellent reactivity. The alkylene-linked phosphonates **5** - **7** show little adhesion or none at all. This is due to poor polymerization demonstrated by **7** which is converted by 4 % after 1 h at 65 °C (2.5 % AIBN, 20 % **7**). Similarly weak bond strengths are achieved by the aromatic ether-linked phosphonic acids **9a-c**. The investigation of the aliphatic ether-linked phoshonic acids **10a,b** indicates that the average molecular weight of polymerization is closely related to adhesion. Furthermore, the adhesive potential can be increased rapidly by the addition of bismethacrylates as comonomers.

Compound	Bond strength (MPa)	pH (40% in $EtOH/H_2O$ (1:1))	Polymerization
1	6.6 ± 3.5	0.7	
2	20.8 ± 3.4	0.85	conv.: 95 %
3	5.3 ± 2.5	7	
5	no adhesion detected	0.7	conv.: 0 (ester)
6	no adhesion detected	1.9	conv.: 0 (ester)
7	6.7 ± 2.8	0.4	conv.: 4 %
9a	no adhesion detected		conv.: 34 %
9b	3.8 ± 1.9 11.6 ± 2.0 (metal)	2.05	conv.: 48 %
9c	no adhesion detected		conv.: 0
10a	no adhesion detected 7.6 ± 4.3 (+ 10 % GDMA)	0.75	conv.: 100 % M_n = 2500 (ester)
10b	7.7 ± 2.8 16.1 ± 4.9 (+ 10 % GDMA)	1.4	conv.: 100 % M_n = 31400 (ester)

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