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POLYMERS WITH FUNCTIONAL GROUPS

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Abstract - Examples for the synthesis of functional polymers are discussed. Functional oligomers are prepared by endcapping of oligomers with terminal reactive groups with a functional reagent. Functionalization of a high polymer was done similarly. The synthesis of a functional monomer and its homo- and copolymerization is exemplified by discussing 3-vinylsalicylic acid derivatives. Bithionol and other bisphenols were used as monomers for the synthesis of condensation polymers, i.e. polycarbonates, polyesters and polyurethanes.

INTRODUCTION

Polymers with functional groups are desired because of their specific chemical and spectroscopic properties, rather than their mechanical properties (1). Polymers have been synthesized which have active groups effective as catalysts (2,3) for chemical reactions or hydrogenations, UV absorbers (4-6), antioxidants (7), photo (8), thermo (9) and electro-active (10) as well as biologically active groups (11-15). Such polymers range over a diverse group of polymers and include homopolymers and copolymers, polymers of various kinds of solubility, swellability and even completely insoluble materials; they include oligomers and polymers of low, medium and high molecular weights.

Polymers have been prepared in order to modify such basic chemical and physical properties as the glass transition temperature, melting point, solubility, crystallinity and other fundamental properties which depend directly upon steric requirements, polarity and interaction of functional groups.

It has been estimated that polymers in the health and food industry and for the production and preservation of energy, will be the main thrust of the research development in polymer science over the next decade; as polymer engineering, polymer physics and polymer chemistry respectively were important in the development of polymer science in each of the preceeding decades. If one compares the number of meetings, symposia and seminars concerned with the aspects, preparation, characterization and utilization of polymers with functional groups, it is clear that this area is probably the field of greatest growth in polymer research development.

In this discussion examples of polymers with various and specific functional groups will be given but we will not stress the more traditional polymers of low or moderate molecular weights with functional groups which are used for postreactions (16,17). These polymers have the functional and reactive group either at the end of the polymer chain such as in glycidyl ether terminated-Bisphenol A epoxy polymers, or isocyanate terminated polyurethanes of low and medium molecular weight copolymers consisting of reactions of 2,4-toluene diisocyanates, or methylene-bis(4,4'-diphenyl diisocyanate) with polymeric glycols of polyethers or polyesters. Telechelic polymers which are acrylate terminated low molecular weight polyesters or polyamides and the common unsaturated polyesters where polymerizable double bonds are in the middle of the oligomeric polymer chain or phenol-, urea-, or melamine-formaldehyde prepolymers could also be classified in this category.

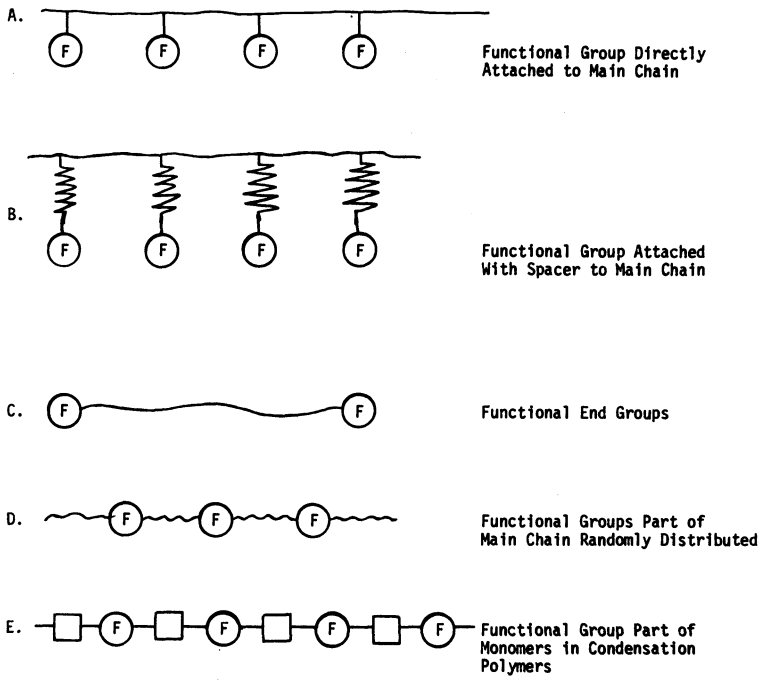
Polymeric materials with functional groups have potential advantages or disadvantages over small molecules with functional groups as their usefulness may be related to the functional groups and/or to the polymeric nature of the substances (6,18). The importance of this behavior has been particularly well recognized in the area of polymeric pharmaceuticals or polymeric drugs but the concept can very well be applied to other areas of functional polymers.

Reactions on oligomers and polymers are qualitatively similar; however, solubility of the starting material and the final reaction product may require different reaction conditions. When reactions are carried out on oligomers or polymers, the active group of the polymers may have to be further activated by introducing a more reactive group in order to guarantee

that the desired reaction can be carried out under mild conditions. The preparation of more reactive derivatives, however, suffers from the normal problems of polymer reactions as it is plagued by side reactions (18).

In principle, the active groups may be (a) part of the polymer main chain, (b) the functional group may be linked to the chain as a pendant group either directly or with the spacer group of specific chain length or (c) the active agent may be at the end of a low or moderate molecular weight polymer chain.

FIGURE 1

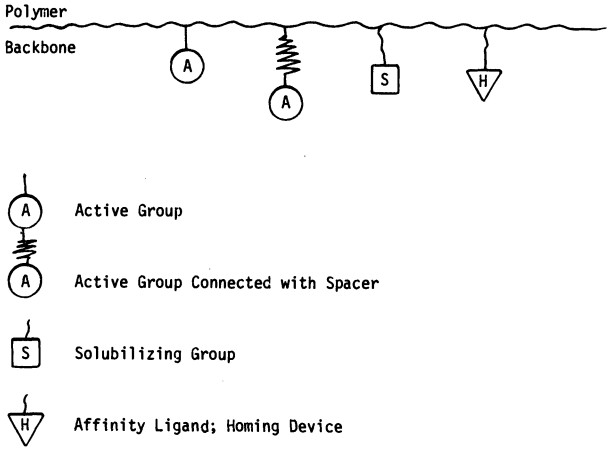


For the preparation of relatively low molecular weight materials or oligomers, endcapping reactions on polymers can be achieved by reacting the properly substituted active compound onto the reactive group of the chain ends as, for example, in hydroxyl terminated polymers of relatively low molecular weight (1,18). The value of oligomeric types of functional polymers has been demonstrated in the area of polymer stabilizers as a short paraffinic chain to active stabilizers is an effective means of increasing compatibility, lowering mobility and decreasing solubility and volatility (19). It has indeed been argued that future antioxidant and UV stabilizer systems may consist not only of low molecular weight functional compounds but also of materials of medium and high molecular weight compounds with compatibilizing groups appropriately attached.

The simplest way to prepare high molecular weight polymers with functional groups is by starting with an already formed polymer with reactive groups and replacing them by the desirable functional groups. Advantages of such polymer reactions are that the molecular weight and the molecular weight distribution of the polymer have already been established. It must, however, be established that polymer degradation does not occur during this substitution reaction. This is particularly important for reactions on polymers whose polymer chain is sensitive for chemical reactions. An example is a nucleophilic substitution reaction on polyepichlorohydrin where even relatively weak nucleophiles at high temperature and long reaction times can cause a cleavage of the polymer chains.

If copolymers are used for the substitution reaction, comonomer distribution and the run number of the comonomers having the reactive group are important. Additional advantages of reactions on polymers include the possibility of introducing several different functional groups in sequence which not only includes the desired functional group but may include solubilizing and compatibilizing groups, anchoring groups, and hydrophilic or hydrophobic groups (20) as it is outlined in Figure 2. In the case of polymeric drugs, specific

FIGURE 2



groups may have specific characteristics including an affinity or have a homing device to direct the polymer to the desired reaction site (21). For the introduction of functionality into a polymer it is important that the same chemical reaction, for example, a nucleophilic displacement reaction, be used for the introduction of all groups.

Reactions on polymers have some inherent and major problems; they must be carried out under mild conditions and the yield of all reactions must be quantitative because every undesirable group that is formed by a side reaction of the substitution will become an integral part of the polymer chain. Experience has shown that many reactions on polymers form discoloration; this problem has been frequently observed in dehydrohalogenation reactions and other nucleophilic displacement reactions; another undesirable side reaction may be crosslinking of the polymer. As a result of these polymer reactions not only the chemical but also the physical nature of the polymers changes and often the solubility of the starting material is not the same as that of the final product. The solubility change has been observed in the formation of poly(vinyl alcohol) from poly(vinyl acetate) and in the case of poly(vinyl butyral) from poly(vinyl alchol) (16). During any of these reactions the starting polymer might either dissolve or precipitate depending on the reaction conditions and the solvents used for the reaction.

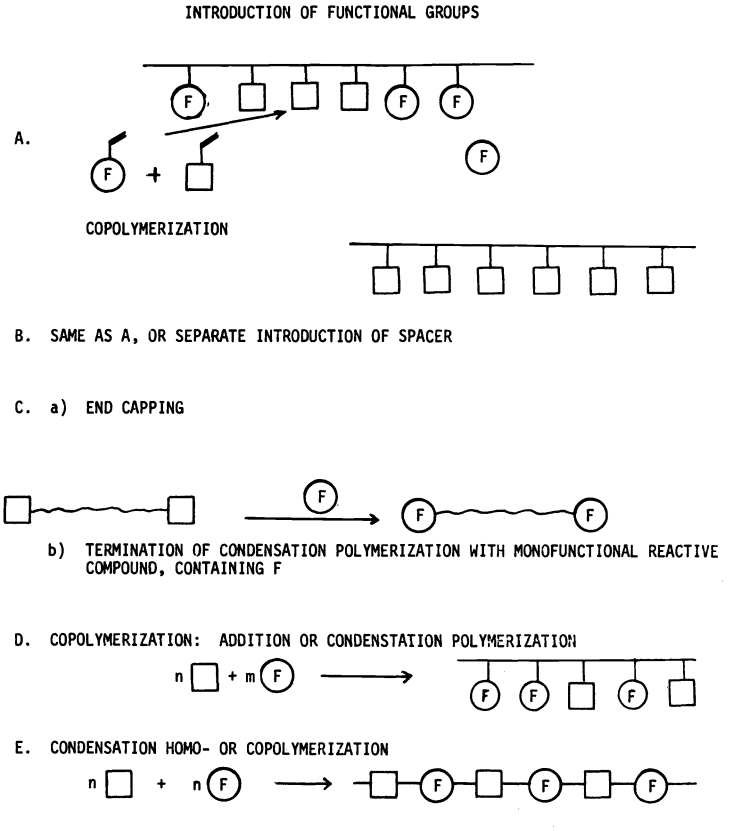
One of the limitations of the reactions on polymers is the fact that the reactivity of a functional group may be low when it is directly attached to the main chain which may be caused by steric hindrance by neighboring side groups. Rate constants of reactions often decrease as the degree of substitution increases which normally means that the overall substitution reaction cannot go to completion (22,23). The problem of incomplete reaction on polymers has been overcome by spacing the reactive side group several atoms from the main chain via spacer groups. The work on polymers with spacer groups between the main chain and the reactive group is still in its infancy and only a few well documented polymers have been prepared; these polymers are primarily in the field of biologically active polymers. Spacing the reactive side group more than the usual two carbon atoms along the polymer chain, as for example, in poly(ethylene oxide), or the use of copolymers has overcome the problem of decreasing reactivity as substitution reaction proceeds.

Functional polymers can also be prepared by the synthesis and polymerization of functional monomers. Monomers of high purity must be prepared to obtain reasonable molecular weight of polymer. Monomer synthesis of monomers with functional groups is often difficult and generally low yields of the desired monomers is obtained as a result of multi-step syntheses. The polymerization of functional monomers to polymers of optimum molecular weight and molecular weight distribution and of desirable sequence distribution and compositional homogeneity of the copolymers may also be achieved only with difficulty. In many cases, the functional monomer could be synthesized and was obtained in sufficient purity, but great difficulties were encountered in the polymerization or copolymerization. When functional monomers with spacer groups were used as comonomer for polymerization it was difficult to carry out addition polymerization of the ethylene double bond or the epoxide group because of adverse reactivity. As a consequence the literature involving these kinds of monomers

is very scarce (24,25). Functional monomers with polymerizable vinyl groups as in acrylates, methacrylates or styrenes, usually polymerize and copolymerize readily.

Advantages and disadvantages of the two approaches, the preparation of functional monomers and their homo- and copolymerization as well as the efficient reactions on polymers are in many ways complementary. One of the two methods may be preferred for the preparation of a particular functional polymer or copolymer while being totally impractical in another system. The requirements of the individual system must be thoroughly examined in order to take full advantage of each of the preparative techniques.

FIGURE 3



The functional group may also be part of the polymer main chain. For example, an active diamine, glycol, bisphenol could be allowed to react with dicarboxylic acid derivatives, i.e. bisisocyanates, acid chlorides or other bifunctional monomers capable of forming condensation polymers. Prime candidates for the polymer structure in this category are polyamides, polyesters or polycarbonates and carbonate polyurethanes.

In this paper we will discuss our work and give examples from each of these categories without specific regard to the usefulness of the ultimately prepared functional polymer.

Endcapping of Oligomers

The endcapping of high molecular weight polymers has been used as a means of stabilization of polymers (26) and endcapping of poly(alkylene oxide) glycols with bisisocyanates have been used for the preparation of elastomeric fibers (27). Pharmaceuticals, particularly steroids have been attached to the terminal OH groups of hydroxyl terminated butadiene polymers (28).

We have attached groups with UV absorbing characteristics onto low molecular weight poly(oxyethylene) glycols. Oligo(oxyethylene) glycols of molecular weight 100 - 400 were endcapped with N,N-dimethyl-p-aminobenzoate by a sodium methoxide catalyzed ester interchange reaction of oligo(oxyethylene) glycol with methyl N,N-dimethyl-p-aminobenzoate (1,29)

and good yields of purified products were obtained. Other reactions, the esterification of the N,N-dimethyl-p-aminobenzoyl chloride or the reaction of the di-p-toluenesulfonate with the potassium salt in DMAc offered no advantage.

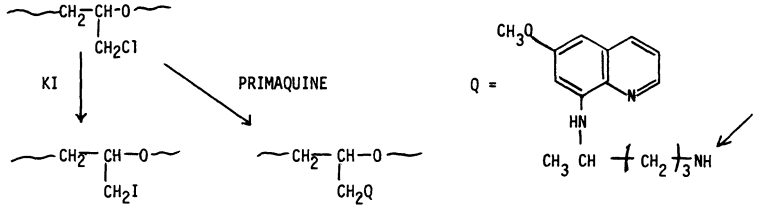
Disalicylate of low molecular weight oligo(oxyethylene) glycols were prepared by a sodium salicylate displacement reaction on the corresponding oligo(oxyethylene) glycol di-p-toluenesulfonates in DMAc at about 70°C. Direct esterification of the glycols with salicylic acid and p-toluenesulfonic acid as the catalyst was also successful although the reaction was substantially slower than in previous reactions.

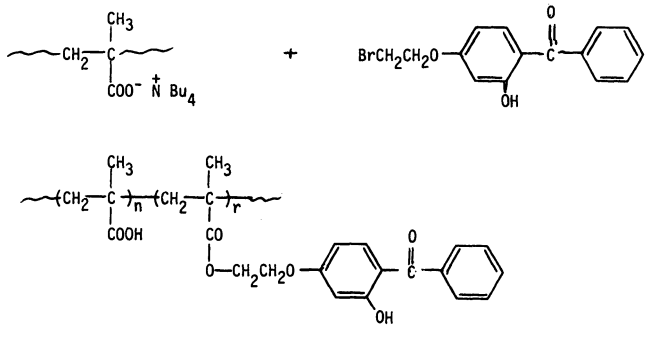
Reactions on Polymers

Reactions on polymers are most conveniently carried out in highly polar nonprotic solvents such as DMSO and DMAc (30). This reaction condition allows nucleophilic displacement reactions to be carried out under very mild conditions. Important examples for polymers to undergo such reactions are poly(acrylic acid) or poly(methacrylic acid) and polyepichlorohydrin. Well characterized polymers whose molecular weight and molecular weight distribution is known can be used for these reactions. Polyepichlorohydrin is perhaps the best studied example. It has been reacted with potassium cinnamate (31) or quartenized with various nitrogen containing tertiary bases (32); most of these reactions were carried out at 100°C. and caused serious problems of degradation. Other nucleophiles were found to be effective under milder reaction conditions (33). Polyepichlorohydrin was also allowed to react with sodium thiosulfate (34), N,N-dimethyl dithiocarbamate (35), 2-mercaptoethanol (36) thiourea (37), sodium sulfide (38) and sodium thiocyanate (39). Severe degradation and molecular weight decrease has, however, been reported especially when reactions were carried out at 100°C. and amines were used for these reactions (40). We have carried out displacement reactions on polyepichlorohydrin with tetraethylammonium N,N-dimethyl-p-aminobenzoate in DMF and obtained copolymers which contained 90% glycidyl N,N-dimethyl-p-aminobenzoate repeat units. Compositions with a lower percentage of glycidyl N,N-dimethyl-p-aminobenzoate units could also be easily obtained.

FIGURE 4

REACTION ON POLYMERS





Displacement reaction of polyepichlorohydrin was also carried out with a known antimalarial drug, primaquine (41,42), which has two amino groups in the molecule but only the aliphatic primary amino group is reactive. Nucleophilic displacement reactions could be carried out in DMAc under mild conditions to obtain degrees of substitutions of primaquine from 25% to 100% (43).

In order to increase the reactivity of the reactive polymers we have also prepared polyepiiodohydrin with a degree of substitution of 93% by carrying out a modified Finkelstein reaction which consists of allowing to react polyepichlorohydrin in methylethylketone with KI (44).

A specific esterification reaction has been worked out in our laboratory by reacting tetraalkylammonium salts of carboxylic acids particularly the tetraethyl- and tetrabutylammonium salts in DMAc with aliphatic bromides or chlorides (4,45). This reaction is actually a modification of a reaction first discovered for low molecular weight compounds but has been adapted with some modification for reactions on polymers.

One amplification of this reaction of a aliphatic carboxylate described earlier was the reaction of the tetraethylammonium N,N-dimethylaminobenzoate with the aliphatic halide which is part of a polymer chain (polyepichlorohydrin) (4). It has also been shown that tetraalkylammonium acetate reacted readily with butyl bromide or butyl chloride (30). Poly(tetrabutylammonium methacrylate) was also allowed to react with 4-(2-bromoethoxy)-2-hydroxybenzophenone at room temperature; approximately 30% of this compound was used for this reaction and a 70:30 copolymer of methacrylic acid and 2-hydroxy-4-(2-methacryloxyethoxy) benzophenone was prepared (29). It had earlier been shown that poly(tetrabutylammonium methacrylate) gave a quantitative reaction with butyl bromide to yield the well known poly(butyl methacrylate).

Synthesis and Polymerization of Functional Monomers

We have been interested in the preparation of functional monomers as UV absorbers, complexing agents, polymeric catalysts and polymeric drugs.

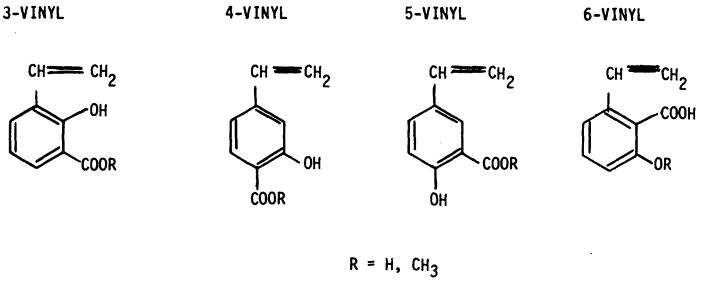
2,4-Dihydroxybenzophenone derivatives are an example of so-called broad spectrum UV absorbers since they do not exhibit a sharp decrease in extinction coefficient above 320 nm; it was therefore found desirable to synthesize 2,4-dihydroxy-4'-vinylbenzophenone. The synthesis of this compound was achieved in five steps with an overall yield of about 15%; the starting material for this synthesis was p-ethylbenzoic acid (46), and the final step was the dehydrobromination of 2,4-dihydroxy-4'-(1-bromoethyl)-benzophenone. The compound was homopolymerized with AIBN as the initiator, or polymerized with methacrylic acid and styrene. The last step of the synthesis of 2,4-dihydroxy-4'-vinylbenzophenone consisted of a bromination reaction with NBS with subsequent dehydrobromination.

The bromination/dehydrobromination technique is one of the classic methods for the preparation of styrene derivatives. The second method is the dehydration of either the 1-hydroxy- or the 2-hydroxyethyl group substituted on the benzene ring. This latter reaction requires that the product formed has a sufficient solubility because the dehydration is done under reduced pressure and the desired product is immediately removed from the reaction; the dehydration route to styrenes normally gives purer products.

For our study on functional monomers for polymerization, we selected the family of salicylic acid derivatives. Methyl esters are known UV absorbers, the free acids are excellent complexing agents and broad spectrum antimicrobial agent in addition to their activities as an analgesic (acetylsalicylic acid).

We have decided to synthesize the whole family of salicylic acid derivatives: There are four possible vinylsalicylic acids known - the 3-vinyl, 4-vinyl, 5-vinyl- and 6-vinylsalicylic acid (Figure 5). We have accomplished the synthesis of the 3-vinyl- and 4-vinylsalicylic acid derivatives in addition to our earlier synthesis of the 5-vinylsalicylic acid derivatives.

FIGURE 5



VINYL SALICYLIC ACID DERIVATIVES

We are describing here in more detail the synthesis of the 3-vinylsalicylic acid derivatives which was accomplished in an overall yield of about 35% from o-ethylphenol (47). 2-Ethylphenol was carbonated by a modification of the Kolbe-Schmitt reaction and gave 3-ethylsalicylic acid in 80% yield. This reaction was carried out in a glass lined stainless steel autoclave at 1000 psi and 175°C. 3-Ethylsalicylic acid was esterified with methanol and sulfuric acid and gave in 90% yield methyl 3-ethylsalicylate which was then acetylated with acetic anhydride and sulfuric acid to give methyl 3-ethylacetylsalicylate in nearly quantitative yield. The phenol group was acetylated in order to avoid complications (ring bromination) in the bromination with NBS. Benzylic bromination of methyl 3-ethylacetylsalicylate was carried out smoothly and gave the desired monobromide in quantitative yield. If a radical initiator, AIBN, was used for the bromination, the disubstitution product, methyl 3-(1,1-dibromoethyl)-acetylsalicylate, was obtained as the primary reaction product. Methyl 3-(1-bromoethyl)-acetylsalicylate was dehydrobrominated in good yield with triethyl amine in acetonitrile or with tributyl amine in DMAc (Figure 6).

Methyl 3-vinylacetylsalicylate was converted to methyl 3-vinylsalicylate in over 80% yield by treating it with methanolic sodium methoxide; 3-vinylsalicylic acid was obtained from methyl 3-vinylacetylsalicylate by saponification in aqueous sodium hydroxide. 3-Vinylacetylsalicylic acid was prepared from 3-vinylsalicylic acid by acetylation with acetic anhydride and sulfuric acid. Methyl 3-vinylsalicylate was polymerized at 60°C. with AIBN in bulk and gave the homopolymer with high inherent viscosity.

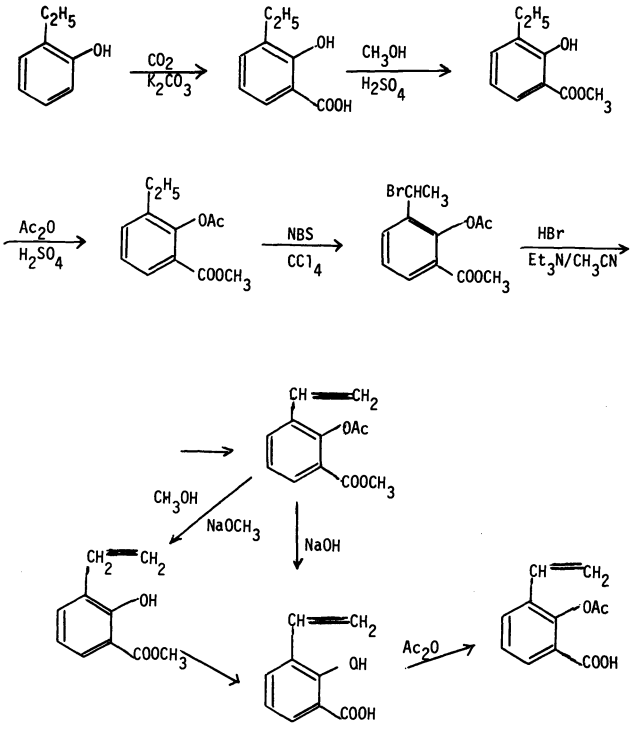
Derivatives of 4-vinylsalicylic acid were prepared by a similar route except that the starting material was 3-ethylphenol. It is very interesting to note that the carbonation occurs exclusively in the 2 position of the benzene ring to give 4-ethylsalicylic acid, which is the para position to the ethyl group; no 6-ethylsalicylic acid was isolated. The synthesis steps from 4-ethylsalicylic acid to methyl 4-vinylacetylsalicylate were essentially the same as for the synthesis of methyl 3-vinylacetylsalicylate (esterification, acetylation, NBS bromination and dehydrobromination). The individual derivatives of 4-vinylsalicylic acid were prepared from the key intermediate methyl 4-vinylacetylsalicylate as indicated for the 3-vinyl isomer (48).

Methyl 5-vinylsalicylate was prepared in an overall yield of about 60% in a sequence of six reactions. Methyl salicylate was acetylated in para position to the phenol group by a modified Friedel-Craft acetylation to methyl 5-acetylsalicylate which was acetylated and the acetyl product reduced with sodium borohydride to the 5-(1-hydroxymethyl) salicylate which was dehydrated with $KHSO_4$ at 225°C. and 0.1 mm. During this dehydration step, some of the acetyl groups of methyl 5-vinylacetylsalicylate were hydrolyzed and a reaction mixture was obtained which consisted of methyl 5-vinylacetylsalicylate and methyl 5-vinylsalicylate. The reaction mixture could be hydrolyzed with sodium methoxide and methanol to the methyl 5-vinylsalicylate or acetylated to methyl 5-vinylacetylsalicylate. The mixture could also be hydrolyzed directly under more vigorous conditions to 5-vinylsalicylic acid which in turn could be acetylated to 5-vinylacetylsalicylic acid.

All three vinyl salicylic acid monomers, the 3-vinyl-, 4-vinyl- and 5-vinyl isomers, have been polymerized and copolymerized. The copolymerization studies with various comonomers is now underway.

FIGURE 6

SYNTHESIS OF 3-VINYLSALICYLATE DERIVATIVES



Functional Group as Part of the Polymer Main Chain

Hindered bisphenols which were active as antioxidants or antibacterial agents (50) were selected to be incorporated into the polymer backbone chain by using their phenolic hydroxyl groups as bifunctional monomers for condensation polymerization. This work was primarily done for the possible use of these polymers as polymeric release agents.

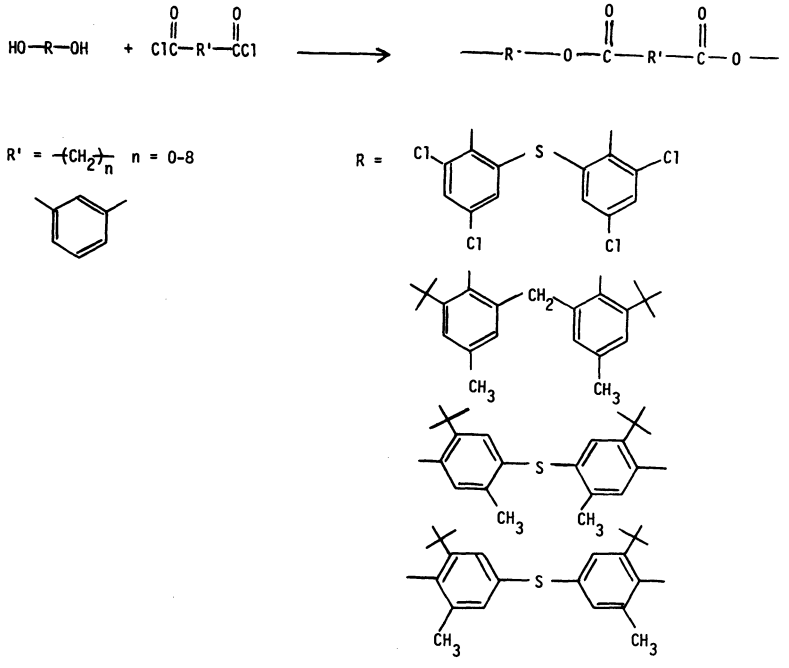
Bithionol [2,2'-thiobis(4,6-dichlorophenol)], an effective bacteriostat (51,52), was condensed with a number of aliphatic or aromatic dicarboxylic acids. The diacids ranged in chain length from oxalic acid to sebacic acid; in all cases aromatic polyesters of relatively low molecular weight (inherent viscosity of 0.3 - 0.4) were obtained (Figure 6). Most of these polymers were insoluble in the medium in which the reaction was carried out (aprotic solvent particularly DMSO and DMAc).

Two candidates of bisphenol type antioxidants, 4,4'-methylenebis(2-tertiarybutyl-6-methylphenol) and 4,4'-methylene(2-tertiarybutyl-5-methylphenol were also subjected to the condensation reaction with diacid chloride in polar inert solvents (53). The corresponding 4,4'-thiobis{2-tertiarybutyl-6-methylphenol) and 4,4'-thiobis{2-tertiarybutyl-5-methylphenol) were also used since they have a thioether link similar to bithionol. The polyesterification reaction occurred readily although the molecular weights of the final products were not very high. It can, however, be concluded from this study that the steric hindrance in ortho position of the bisphenol monomers, even with tertiarybutyl groups, was not sufficient to prevent the condensation reaction; the steric hindrance of the polymer chain which developed during the polymerization together with the insolubility of the polymers prevented, however, the formation of polymers of high molecular weights. It was found that polymers with an inherent viscosity as high as 0.6 can readily be obtained when sebacyl chloride which has a flexible chain was used as the acid chloride.

It is also important to note that the condensation reaction depended to a greater extent on the type of substituents rather than on the size and consequently the steric hindrance of

FIGURE 7

POLYESTERS FROM BISPHENOLS



individual groups in ortho-positions. No substantial difference was noticed when 2,2'-bisphenols were used (ortho linkage) as compared to 4,4'-bisphenols (para linkage) for polyesterification reactions; it was found that the more flexible thio- linkage allowed the formation of polyesters of molecular weights substantially higher (η = 0.6) than that obtained from a bisphenol with a methylene linkage (η = 0.3). Polyphosphates, polyphosphinates and polyphosphonates of bithionol were also prepared with the corresponding acid chlorides.

We have also shown that bithionol could also react with phosgene by solution but even better by melt polymerization or by melt polymerization of bithionol with diphenol carbonate to form the polycarbonate.

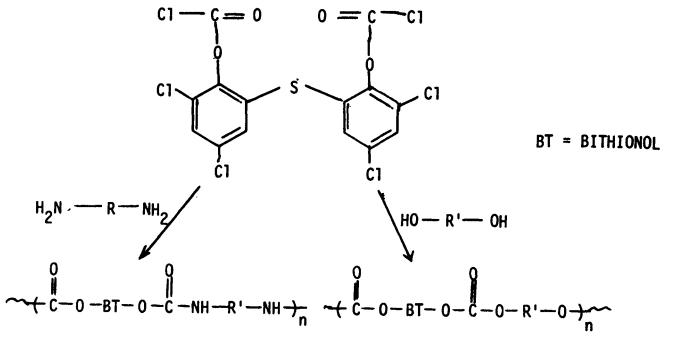
The formation of alternating polycarbonates of bithionol or the synthesis of polyurethanes containing bithionol was achieved by the use of the bischloroformate of bithionol (which had been obtained in 45% yield from bithionol and phosgene).

Polyurethanes of medium molecular weight were obtained in good yield by reacting aliphatic diamines with 2 to 8 carbon atoms or aromatic diamines with the bischloroformate of bithionol.

Alternating polycarbonates were prepared by reacting the bischloroformate of bithionol with glycols, bisphenols and particularly with the polymeric glycol of ethylene oxide of the medium molecular weight range (600 - 4000). The alternating copolycarbonate with carbowax 4000 gave an attractive tough and flexible polymer which was soluble in water, could be cast into tough films and degraded to bithionol at a rate of about 1%/day at room temperature at PH of 4 and 10.

FIGURE 8

COPOLYCARBONATES AND POLYURETHANES OF BITHIONOL



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