polymer communications

Polymer supports based on maleic anhydride copolymers: Preparation of beaded copolymers of maleic anhydride on dimethylacrylamide pre-polymers

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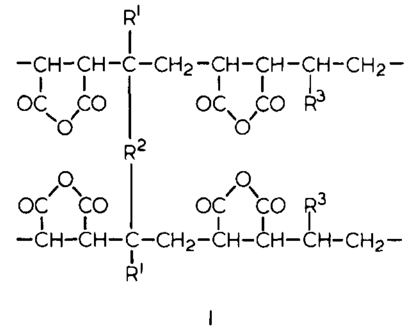
A new technique is described whereby maleic anhydride copolymers are formed within the swellable beads of dimethylacrylamide pre-polymers. Incorporation of a divinyl compound during the copolymerization, or diamine condensation of a pre-formed soluble copolymer, provides a wide range of anhydride containing resins whose conversion to the corresponding acidic or succinimido derivatives, is briefly described.

Keywords Polymer supports; maleic anhydride; dimethylacrylamide pre-polymers; polymer-supported polymerization

Copolymers of maleic anhydride (MAN) have been extensively studied due to their alternating structure[1], chemical and physico-chemical properties of their hydrolysed derivatives[2], or as their action as polymeric reagents[3-5]. Regarding the latter, soluble or insoluble copolymers of MAN have, in particular, been converted to polymeric *N*-hydroxysuccinimide for subsequent applications in peptide synthesis. Insoluble copolymers of MAN have been obtained by γ-radiation crosslinking of the soluble copolymer[3], or direct incorporation of divinylbenzene into the monomer mixture during the copolymerization[4]. The so-called macronet resins have been prepared by diamine-condensation crosslinking of some of the anhydride groups in the linear polymer[5]. Preparation of beaded copolymers of MAN by direct suspension copolymerization is relatively simple in the case of styrene[6], but is less (or not) practical in the case of other comonomers such as vinyl ethers (or ethylene). This communication reports on a simple technique, i.e., polymer-supported polymerization[7], whereby crosslinked copolymers of MAN are formed within the beads of dimethylacrylamide pre-polymers.

Two basically different strategies of crosslinking have been employed and two types of crosslinked copolymers of MAN (1 and 2) will be discussed here. General procedures for the preparation of both resin types are outlined, and further details of four typical preparations are summarized in *Table 1*. In the type 1 resin, crosslinking is achieved by the more usual inclusion of a divinyl compound into the monomer mixture during the copolymerization, whereas in a type 2 resin the crosslinked copolymer is obtained by diamine-condensation of the pre-formed soluble polymer. In either case the newly formed MAN copolymer is entrapped within the beads of a loosely crosslinked



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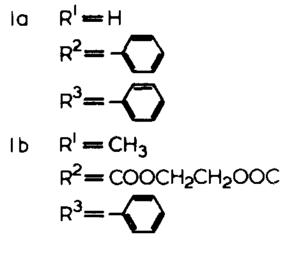

Ia $R^1=H$
$R^2=$
$R^3=$

Ib $R^1=CH_3$
$R^2=COOCH_2CH_2OOC$
$R^3=$

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Table 1 Details of crosslinked copolymers of maleic anhydride prepared on beaded dimethylacrylamide prepolymers

Resin type[a]	Pre-polymer	Monomer mixture[b,c] (mole ratio)[d]	Polymerization solvent[e]	Resin swellability[f]
1a (3.7)	3a	STY : MAN : DVB (10 : 12 : 1.0)	2.0 (1 : 1)	10
1b (3.7)	3b	STY : MAN : EDM (10 : 12 : 1.0)	2.0 (1 : 1)	12
2a (2.2)	3b	PEM : PDA (10 : 1.4)	12.5 (1 : 4)	9
2b (1.2)	3a	PMV : HDA (10 : 3.0)	17.0 (1 : 6)	13

[a] Theoretical anhydride content of the resins in mmol/g is given in parentheses

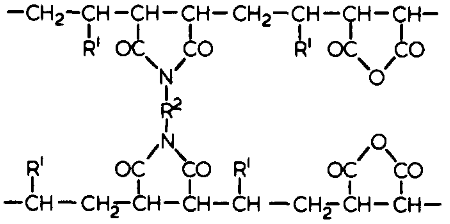
[b] STY, styrene; MAN, maleic anhydride; DVB, commercially available divinylbenzene (ethylvinylbenzene is counted as styrene); EDM, 1,2-ethanedimethacrylate; PEM, copoly(ethylene-maleic anhydride); PDA, 1,4-phenylenediamine; PMV, copoly(maleic anhydride-vinyl ethyl ether); HDA, 1,6-hexanediamine

[c] 2.2 gram monomer has been employed per gram pre-polymer (PEM and PMV are counted as monomer)

[d] Molar ratios in the case of PEM and PMV refer to the repeating units of the copolymer assuming alternative structure in either case

[e] Total volume of dimethylformamide and chlorobenzene employed per gram pre-polymer, the overall volume ratio of the solvents, respectively, is given in parentheses

[f] Bulk expanded volume of the resin in ml/g in dimethylformamide



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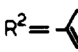
2a $R^1 = H$



2b $R^1 = OCH_2CH_3$

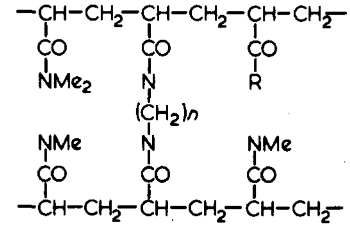
$R^2 = (CH_2)_6$

dimethylacrylamide resin whose structure (3a[8a] or 3b[8b]) is shown separately for the sake of clarity. Entrappment is assumed to be mainly physical in either case, although in a type 1 structure some covalent crosslinking is also likely due to the possibility of copolymerization with residual vinyl bonds in, or chain transfer to, the pre-polymer. In principle, a type 1 resin is preferred because of the higher anhydride content, higher chemical stability, and more control over matrix structure of the crosslinked resin. Practically, however, a type 2 resin is sufficiently stable for many applications, and may be more readily accessible through the use of the commercially available soluble polymers.

Experimental

General procedure for preparation of type 1 resin (see *Table 1*): The solution of the monomers in the indicated solvent containing 2% AIBN (based on the total weight of the solution) is placed in a wide neck flask and is vigorously shaken with the prepolymer until the former is completely absorbed by the latter. The swollen resin beads are then allowed to stand for about 30 min, flushed thoroughly with nitrogen, the flask is tightly stoppered, and kept at 60°C for 15 h. The coagulated beads are then stirred (or wet-sieved) in dichloromethane before being washed with several portions of dry dimethylformamide, dry acetone (or dioxane), ether, and dried in a vacuum desiccator.

General procedure for preparation of type 2 resin (see *Table 1*): The solution of the diamine in the indicated amount of dimethylformamide is shaken with the pre-polymer as described above, and allowed to stand for 30 min. This is then shaken with the solution of the MAN copolymer in chlorobenzene in the same manner, allowed to stand for 30 min, and kept at 60°C for 3 h. The final resin is recovered as described above.



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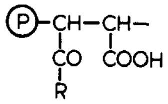

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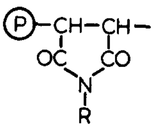

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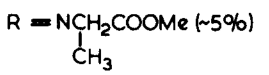
3a $n = 2 (6.1\%)$



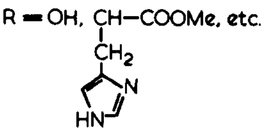
$R = N(CH_3)CH_2COOMe$ (~5%)

3b $n = 6 (8.0\%)$

$R = NMe_2$

4 $R = OH, OMe, NMe_2$, etc.

5 R = OH,



$CH(CH_2\text{-imidazolyl})COOMe$, etc.

Full characterization of the resins will be reported subsequently, but some of the basic characteristics are discussed below. The compositions and polymerization conditions were empirically adjusted to produce resins having various degrees of functionality and swellability as may be suitable for various applications. In all cases the expected structure of the resins has been confirmed by infra-red (i.r.) spectroscopy. For example an i.r. spectrum of structure 1b, showing the anhydride absorptions at ~1815 cm^{-1} and ~1780 cm^{-1} and the ester carbonyl absorption at 1720 cm^{-1}, is superimposed on the spectrum of the dimethylacrylamide pre-polymer with its main absorption at 1650–1600 cm^{-1}. Although considerable quantitative differences exist between the different resins, they all undergo typical reactions of the anhydride function to produce either acidic (4) or succinimido (5) derivatives. The acidic resins (4) have been generally obtained by reaction of the resins with water, methanol, phenol, and secondary amines at room temperature and, if necessary, in the presence of a base catalyst. The succinimido resins are prepared by treatment with primary amines (e.g., hydroxylamine, amino acids, etc.) at 60°–130°C depending on the nature of the amine.

The presently described technique provides by far the most convenient route to copolymers of maleic anhydride suitable for preparation of polymeric reagents and polymer supports. The method is simple and, as can be seen from *Table 1*, resins with a wide range of characteristics such as chemical structure, crosslinking, swellability, and degree of functionality are obtained equally easily. The technique should be equally applicable for the preparation of other copolymers of maleic anhydride and/or alternative types of prepolymers. However, the use of dimethylacrylamide-based prepolymers is thought to generally widen the range of solvent compatibility of the resulting resins. In particular preliminary results indicate that the use of these resins for peptide synthesis may be made more efficient as a result of catalytic effects of dimethylamide residues in aminolysis reactions[9].

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(b) This resin is prepared in an essentially similar manner, but in the presence of 3 ml/g monomer diluent (water–dimethylformamide, 1:1)

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