Synthesis and Cyclopolymerization of Bis(2-Alkoxycarbonyl-2-Propenyl) Ether

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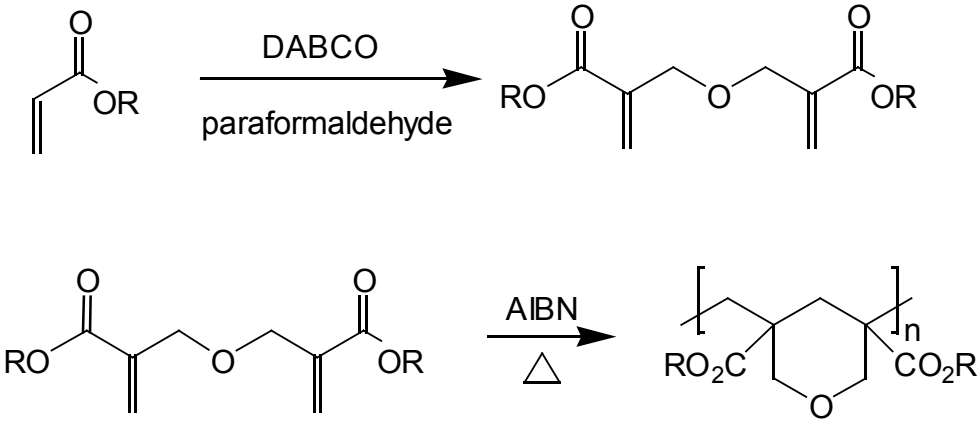

1. Synthesis (Ethers)

Bis(2-alkoxycarbonyl-2-propenyl) ethers may be obtained as major by-products in the DABCO catalyzed synthesis of the alkyl "-(hydroxymethyl)acrylates[3] (see previous method, this volume). Alternatively, they may readily be prepared in good yield directly from the acrylate by allowing the hydroxymethylation reaction and subsequent ether-forming dimerization to proceed to completion. The following method is typical.

Ethyl acrylate (20.0 ml, 0.188 mol), paraformaldehyde (2.82 g, 0.0957 mol), 1,4-diazabicyclo[2.2.2.]octane (DABCO, 1.05 g, 0.0094 mol) and a teflon-coated stirring magnet are charged to a 20 oz. Quorpak wide-mouth jar with polyethylene lined phenolic cap. Excess ethyl acrylate is used as solvent. All reagents were used as received from Aldrich Chemicals.

It has been found that submerging the closed reaction vessel in the heating medium[4] is necessary to avoid vaporization and subsequent recondensation of the formaldehyde out of the reaction medium. This also avoids DABCO catalyst deposition at the edge of the reaction solution as the ether product concentration increases due to decreased solubility.

The jar is sealed and submerged in an oil-bath which is then heated to approximately 70°C. After three days the vessel is removed and its contents added to 30 ml diethyl ether. The organic solution is then washed with a solution of 1% aqueous HCl (3 times, 10 ml each). The aqueous layer is back-extracted with 10 ml diethyl ether. Organics are combined, and solvents and unreacted ethyl acrylate removed using a rotary evaporator. A large pinch of copper(II) chloride is added as a free-radical inhibitor and the solution fractionally distilled to produce 5.8 g of 91% pure bis(2-ethoxycarbonyl-2-propenyl) ether (yield 50%, Note 1).

The ethyl derivative is a liquid (bp 101-102°C at 0.2 mm Hg) while the methyl derivative is a solid (mp 48°C) that is readily recrystallized from methanol or pentane.[5] The n-butyl and t-butyl compounds boil so high, even under vacuum, that they are difficult to distill without spontaneous polymerization. However, extraction and distillation to remove catalyst and all by-products generally leaves the ether as the only product left in the distillation flask. Copper(II) chloride (or other inhibitor) should be added for vacuum distillation and storage of the crude reaction mixtures and purified ethers.

2. Characterization (Ethers)

Bis(2-alkoxycarbonyl-2-propenyl) ethers are readily soluble in DMSO, chloroform, and methylene chloride; slightly soluble in pentane and methanol; and insoluble in water. The infrared spectrum for the methoxycarbonyl derivative exhibits the following absorption bands [cm-1]: 2980-2870 (CH stretch), 1716 (carbonyl stretch), 1636 (C=C stretch), 1463 (asymmetric CH_2 bend), 859 ($C=CH_2$ out-of-plane bend), and 1111 (R-O-R stretch). Other derivatives display essentially identical spectra except for increased intensity for the alkane peaks.

The proton spectrum of the ethoxycarbonyl derivative in $CDCl_3$ shows alkene proton singlets at * 6.29 and 5.90; a 2-proton singlet at 4.26 attributed to the ether "-methylene; a 2-proton quartet at 4.13 attributed to the ester methylene; and a 3-proton triplet at 1.30 attributed to the ester methyl. The carbon spectrum of this monomer shows a carbonyl at * 165.7; alkene peaks at 137.6 and 125.3; and peaks for the ether methylene (69.0), ester methylene (60.7), and ester methyl (14.2). The C-H coupled spectrum confirms these assignments.

3. Cyclopolymerization

Bis(2-methoxycarbonyl-2-propenyl) ether (10.16 g, 47.5 mmol), 2,2'-azobis(isobutyronitrile) (AIBN, 640 mg, Note 2) and chloroform (240 ml, Note 3) are placed in a capped round-bottom flask and degassed by bubbling nitrogen through the solution. The mixture is then heated at 65°C for 6 h to give a clear solution having only a small quantity of insoluble material.

The solution is cooled in an ice bath, insolubles removed by filtration (0.09 g, 0.9%), and the filtrate slowly added to diethyl ether to give the cyclopolymer as a white precipitate. The polymer is purified by repeated dissolution, precipitation, washing and drying under vacuum. The yield of soluble polymer is 8.8-9.6 g, 87-95%.[6] The cyclopolymers of bis(2-ethoxycarbonyl-2-propenyl) ether and bis(2-n-butoxycarbonyl-2-propenyl) ether are prepared in a similar manner. The monomeric t-butyl ester dimer spontaneously gave soluble, high molecular weight cyclopolymer on attempted distillation. This polymer can be readily converted to the free acid material by treatment with neat trifluoracetic acid.[7]

4. Characterization (Cyclopolymers)

The cyclopolymers are soluble in chloroform and 1,1,1,3,3,3-hexafluoroisopropyl alcohol (HFIP, Note 4) and insoluble in diethyl ether except for the t-butyl ester polymer which is soluble in diethyl ether and petroleum ether. The intrinsic viscosities in chloroform (Note 5) are 0.15 to 0.45 dL/g. (The checkers obtained a value of 0.21 dL/g).

The infrared spectrum (Note 6) for the methoxycarbonyl polymer exhibits the following absorption bands [cm-1]: 3009-2861 (CH stretch), 1745 (carbonyl stretch), 1261 and 1171 (ester C-O-C stretches). The 50 MHz carbon NMR spectrum (Note 7) in $CDCl_3$ at room temperature of the methoxycarbonyl polymer shows absorptions at [*]: 173.5, 172.9 (carbonyls), 71.2 (CH_2O), 51.4 (OCH_3) and 43.5 (backbone). Nutation NMR analysis of a dimer labeled with ^{13}C confirms formation of the 6-membered ring pyran structure rather than the tetrahydrofuran possibility.[8]

TGA thermograms (Note 8) display two weight loss transitions, one at 200°C apparently due to residual solvent desorption, and a second at about 300°C involving catastrophic weight loss through depolymerization and degradation. The DSC thermogram for the methoxycarbonyl polymer shows a strong glass transition at about 160°C while that of the t-butyl polymer is 136°C. Decomposition onset occurs at 270°C for the former and ca 180°C for the latter.

5. Notes

1. Purity is determined by gas chromatography using a Hewlett Packard 5890A gas chromatograph with HP3396A integrator and J & W 5% phenyl methyl polysiloxane column. Yield is based on initial paraformaldehyde concentration.
2. AIBN is purified by recrystallization from methanol.
3. Benzene and acetone may give insoluble polymers.
4. HFIP is a corrosive material and should be used with care.
5. A Cannon-Ubbelohde #50 semimicro viscometer is used.
6. A Nicolet 5DX FTIR is used to obtain the infrared spectra.

7. A Bruker MSL-200 is used to obtain ^{1}H and ^{13}C NMR spectra.
8. A DuPont 9900 thermal analyzer equipped with a DuPont 910 DSC and a DuPont 951 TGA is used to obtain thermograms.

6. Method of Preparation

Free-radical cyclopolymerizations are well known.[9,10] A study of cyclopolymerization in a number of solvents of different dielectric constants has been published.[11] Intramolecular cyclization reactions were first discovered by Butler and co-workers who found that the radical polymerization of quaternary diallylammonium salts gives soluble, uncrosslinked polymers.[12]

The products synthesized in this report are related to DIVEMA, a cyclopolymer of divinyl ether and maleic anhydride. DIVEMA shows a broad range of biological activity:[13,14] it acts as an antitumor agent, an antiviral agent, an antibacterial and antifungal agent; it stimulates immune system response; and it acts as an anticoagulant. DIVEMA does suffer from some disadvantages: its molecular weight distribution is hard to control, and it may posses a microstructure which includes furan as well as pyran ring structures. Although a 1:2 repeat unit is reported for DIVEMA, other ratios of comonomers scattered along the backbone may be present, leading to configurational and compositional inhomogeneities.

7. References

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