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Synthesis of a Sequence-Ordered Copolymer. Hydrogenation of Alternating Butadiene–Methyl Methacrylate Copolymer

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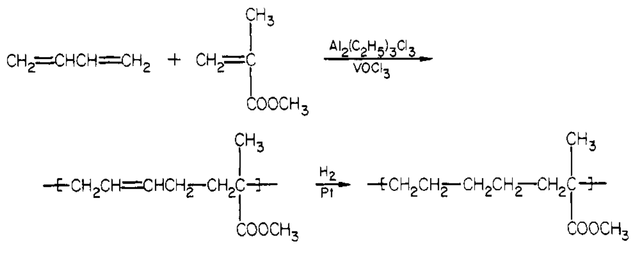
ABSTRACT: Alternating butadiene–methyl methacrylate copolymer was hydrogenated at atmospheric pressure with platinum black catalyst. The hydrogenated copolymer structure was identified by elemental analysis and infrared, ^{1}H NMR, and ^{13}C NMR spectra. It has repeating ethylene–ethylene–methyl methacrylate sequences and is a 2:1-type sequence-ordered copolymer. It dissolves in benzene, chloroform, and tetrahydrofuran, shows a partially crystalline X-ray diffraction pattern, melts at 90 °C, and decomposes slowly above 200 °C. A tensile test shows it is a soft and tough material.

Syntheses of sequence-ordered copolymers in radical copolymerization have been developed for the preparation of block, graft, and alternating copolymers. Copolymers in which the two monomer units appear alternatingly on the copolymer chain can be obtained[1-3] either from the specific combination of electron-donating and -accepting monomers, such as styrene–maleic anhydride, or from various combinations in the presence of Lewis acids, such as styrene–methyl acrylate with ethylaluminum sesquichloride. Alternating copolymers exhibit physical properties different from those of random copolymers and some have been shown to be useful materials.[4,5]

Sequence-ordered copolymers, however, in which three or more monomer units appear in a definite order have not yet been obtained by copolymerization of three or more vinyl monomers.

In this work we report the hydrogenation of alternating butadiene–methyl methacrylate (MMA) copolymer and physical properties of the product hydrogenated copolymer. This product is a 2:1 sequence-ordered copolymer in which the repeating sequences are ethylene–ethylene–MMA. A short communication on this work has been given elsewhere.[6]



$$\mathrm{CH_2{=}CHCH{=}CH_2 + CH_2{=}\overset{\displaystyle CH_3}{\underset{\displaystyle COOCH_3}{C}}} \xrightarrow[\mathrm{VOCl_3}]{\mathrm{Al_2(C_2H_5)_3Cl_3}}$$

$$\mathrm{{+}CH_2CH{=}CHCH_2{-}CH_2\overset{\displaystyle CH_3}{\underset{\displaystyle COOCH_3}{C}}{+}} \xrightarrow[\mathrm{Pt}]{\mathrm{H_2}} \mathrm{{+}CH_2CH_2{-}CH_2CH_2{-}CH_2\overset{\displaystyle CH_3}{\underset{\displaystyle COOCH_3}{C}}{+}}$$

Experimental Section

Materials. Commercial butadiene and MMA were used. Butadiene was passed through columns of potassium hydroxide pellets, Drierite, and molecular sieves 3A and condensed to feed. MMA was washed with 5% sodium hydrogen sulfite, 5% sodium hydroxide, and 20% sodium chloride solutions and distilled under reduced nitrogen pressure. It was stored over calcium hydride and redistilled before use. Ethylaluminum sesquichloride from Ethyl Corp. was distilled under vacuum and dissolved in hexane (4.4 mol/L). Vanadyl chloride was commercially available and dissolved in hexane as received (0.25 mol/L). Platinum black was prepared according to Willstätter's method.[7] Other reagents were commercially available and used as received.

Polymerization. Preparation of alternating butadiene–MMA copolymer was carried out according to Furukawa et al.'s description.[8] In a nitrogen-purged test tube (25 mm in diameter and 200 mm in length) were placed at −78 °C butadiene (4 mL) and MMA (5 mL). Ethylaluminum sesquichloride (2 mL) and vanadyl chloride (1 mL) solutions were added and mixed well. The test tube was immersed in an ice-water bath and shaken occasionally for 24 h. The solidified content was stirred with methanol (200 mL) containing 1% concentrated hydrochloric acid. The precipitated copolymer was reprecipitated twice from benzene into methanol and freeze-dried from benzene. The yield was 78%. Addition of a trace of *tert*-butylcatechol was effective in avoiding gel formation. The alternating structure of the copolymer has been well identified by Furukawa et al.[8] Infrared (IR) (Figure 1a) and ^{1}H nuclear magnetic resonance (NMR) (Figure 2a) spectra show that the copolymer contains equimolar amounts of butadiene and MMA units, that successive butadiene and MMA units are absent, and that the butadiene units are of 1,4-trans structure. The molecular weight was 1.5×10^5 as estimated by gel permeation chromatography.

Hydrogenation of Alternating Butadiene–MMA Copolymer. The copolymer sample (1.5 g) was dissolved in tetrahydrofuran (50 mL) and magnetically stirred with platinum black catalyst (65 mg) in a test tube. Tiny hydrogen bubbles were passed into the suspension from a capillary for 4 days. The catalyst was precipitated and to the supernatant solution was added methanol. The quantitatively recovered polymer was freeze-dried from benzene.

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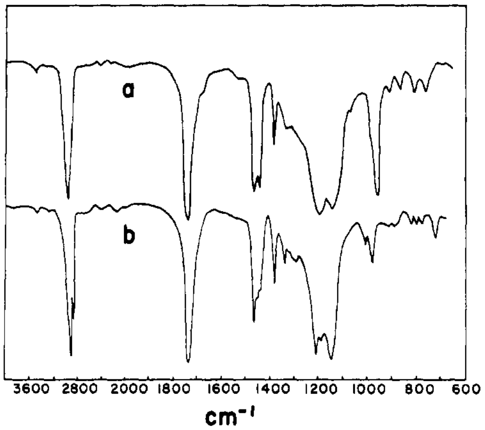


Figure 1. IR spectra of (a) alternating butadiene–MMA copolymer and (b) the hydrogenated copolymer; determined as films.

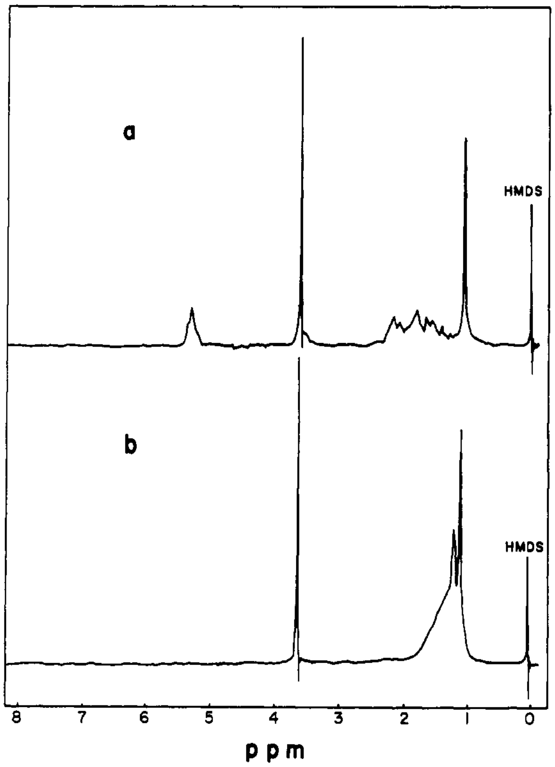


Figure 2. ^{1}H NMR spectra of (a) alternating butadiene–MMA copolymer and (b) the hydrogenated copolymer; in deuteriochloroform at 60 °C.

Measurements. IR spectra were recorded on a Jasco IR-E spectrometer. NMR spectra were recorded on a Hitachi R-20B spectrometer (^{1}H, 60 MHz) and a JEOL JNM-FX100 spectrometer (^{13}C, 25 MHz), using hexamethyldisiloxane (HMDS) as an internal standard. Thermal analyses were taken on a Rigaku-Denki Thermoflex with a thermogravimetry unit and a low-temperature differential scanning calorimetry unit. The X-ray diffraction pattern was recorded on a Shimadzu VD-1 diffractometer. The tensile test was carried out on a Toyo-Sokki Tensilon.

Results and Discussion

Identification of the Hydrogenated Copolymer Structure. Figures 1 and 2 show the IR and ^{1}H NMR spectral changes of the copolymer before and after hydrogenation. The IR absorptions due to the carbon–carbon double bond of alternating butadiene–MMA copolymer, i.e., the strong absorption at 970 cm^{-1} ($\delta_{trans\text{-}CH=CH\text{-}}$) and the weak shoulder at 1670 cm^{-1} ($\nu_{\text{-}C=C\text{-}}$) in Figure 1a, do not appear in the spectra of the hydrogenated product, which is shown in Figure 1b. Changes of methylene group absorptions are also observed. In the ^{1}H NMR spectra, the absorption at 5.32 ppm due to *trans*-CH=CH- (Figure 2a) is not present after the hydrogenation, and the methylene absorptions at 1.2–2.4 ppm markedly change in shape and increase in intensity to correspond to 10 H rather than 6 H.

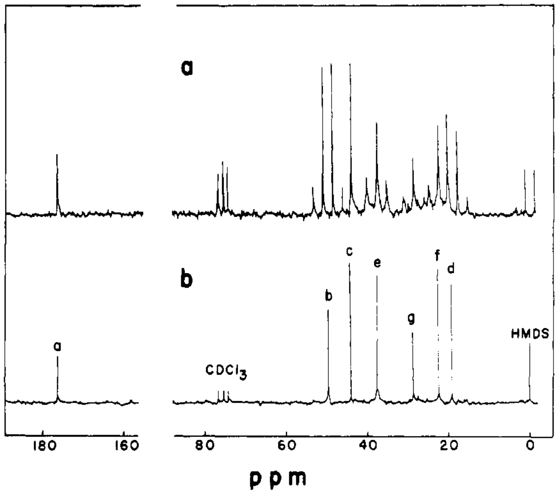
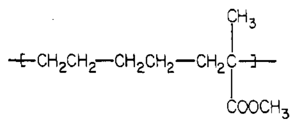


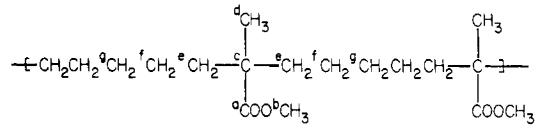
Figure 3. ^{13}C NMR spectra of the hydrogenated copolymer: (a) proton off-resonance and (b) proton noise-decoupled spectra in deuteriochloroform at ambient temperature.

Because the alternating structure of alternating butadiene–MMA copolymer has been sufficiently proven by Furukawa et al.,[8] the copolymer after hydrogenation should have the expected repeating ethylene–ethylene–MMA sequences.



$$-\!\!\left[CH_2CH_2-CH_2CH_2-CH_2\overset{\overset{\large CH_3}{|}}{\underset{\underset{\large COOCH_3}{|}}{C}}\right]\!\!-$$

The ^{13}C NMR spectrum of the hydrogenated copolymer (Figure 3) clearly demonstrates this structure. The proton noise-decoupled spectrum in Figure 3b shows only seven peaks in spite of the apparent presence of nine carbon atoms in one repeating sequence. This is because the structure is symmetrical around the quaternary carbon atom of the MMA unit.



$$-\!\!\left[CH_2CH_2{}^{g}CH_2{}^{f}CH_2{}^{e}CH_2-{}^{c}\overset{\overset{\large {}^{d}CH_3}{|}}{\underset{\underset{\large {}^{a}COO{}^{b}CH_3}{|}}{C}}-{}^{e}CH_2{}^{f}CH_2{}^{g}CH_2CH_2CH_2-\overset{\overset{\large CH_3}{|}}{\underset{\underset{\large COOCH_3}{|}}{C}}\right]\!\!-$$

Assignment of peaks was carried out by referring to the proton off-resonance spectrum in Figure 3a. The three methylene peaks are tentatively assigned as shown. The peak at 28.7 ppm shows about half the intensity of the peaks at 22.5 and 37.5 ppm and therefore it is assigned to $^{g}CH_2$. The peak at 37.5 ppm may be assigned to $^{e}CH_2$ because this is nearest the $COOCH_3$ group. Signals other than the seven peaks are hardly observed and therefore the copolymer has a very high sequential purity. The seven peaks are all sharp, indicating that the possible two configuration types at the quaternary carbon atoms of MMA units do not split the peaks. This is probably because of the long repeating sequence of six carbon atoms.

Elemental analysis of the hydrogenated copolymer is as follows. Calcd for $C_9H_{16}O_2$: C, 69.20; H, 10.32. Found: C, 68.85; H, 10.36.

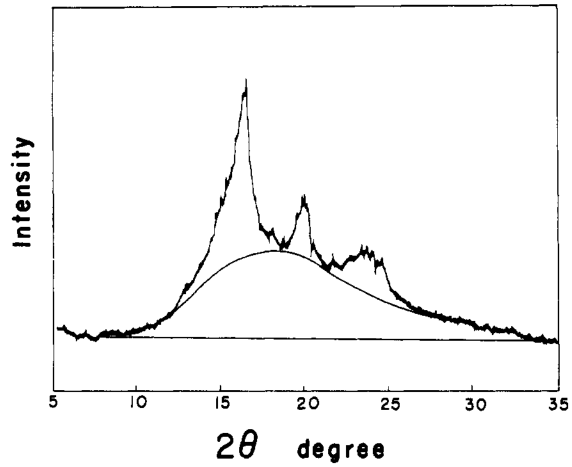


Figure 4. X-ray diffraction pattern of the hydrogenated copolymer with nickel-filtered Cu Kα radiation.

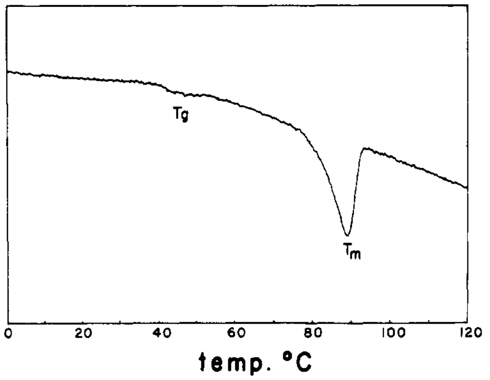


Figure 5. Differential scanning calorimetry diagram of the hydrogenated copolymer.

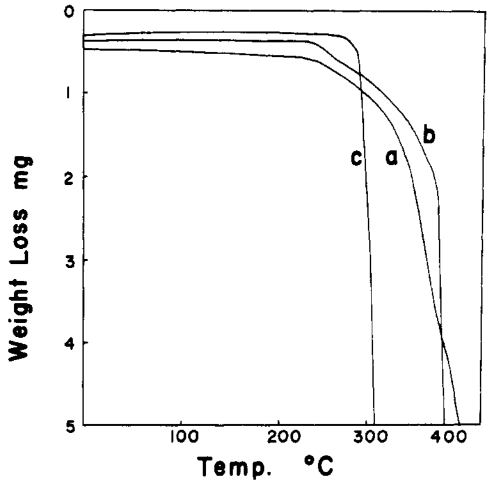


Figure 6. Thermogravimetry diagram of (a) the hydrogenated copolymer, (b) polyethylene, and (c) poly(methyl methacrylate).

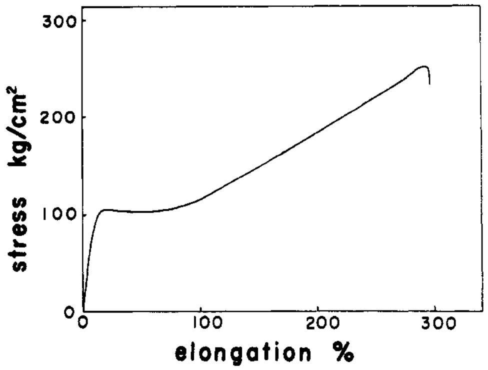


Figure 7. Stress–elongation curve of the hydrogenated copolymer.

Physical Properties of the Hydrogenated Copolymer. The hydrogenated copolymer freeze-dried from benzene is a white spongy material and can be cast from a tetrahydrofuran solution to give an almost transparent tough film. It is soluble in benzene, tetrahydrofuran, and chloroform and insoluble in methanol, ether, petroleum ether, acetone, and acetonitrile.

The X-ray diffraction pattern of an unoriented film on a slide glass shows crystalline peaks at 2θ = 16.1, 19.8, and 23.4° as shown in Figure 4. The crystalline peak area ratio to the total diffraction is about 30%.

Differential scanning calorimetry of a film sample showed (Figure 5) a small endothermic peak at 90 °C and a much smaller but reproducible peak at 45 °C. The former peak is ascribed to the polymer melting temperature and the latter to the glass transition temperature. According to Flory's relation,[9] the melting temperature of a copolymer in which only one monomer unit is able to crystallize is given by

$$\frac{1}{T_m} - \frac{1}{T_m{}^\circ} = -\frac{R}{\Delta H_m} \ln p$$

where T_m is the copolymer melting temperature, $T_m{}^\circ$ is the melting temperature of the crystallizable homopolymer (here for polyethylene $T_m{}^\circ$ = 141 °C[10]), R is the gas constant, ΔH_m is the melting enthalpy per crystallizable monomer unit (here for polyethylene ΔH_m = 1.92 kcal/CH_2CH_2[11]), and p is the propagation probability of the crystallizable sequence (here we assume $p = {}^2/_3$, i.e., random propagation). Using the above values, T_m = 80 °C, which is somewhat lower than observed. This discrepancy probably comes from the assumed random and the observed sequence-ordered propagation. For the glass transition temperature, we use Fox's relation,[12] given by

$$\frac{1}{T_g} = \frac{w_1}{T_{g1}} + \frac{w_2}{T_{g2}}$$

where w_1 and w_2 are the weight fractions of ethylene and MMA units and T_{g1} and T_{g2} are the glass transition temperatures of the homopolymers. When we use w_1 = 0.359, w_2 = 0.641, T_{g1} = −21 °C,[13] and T_{g2} = 105 °C[14] for the present copolymer, we obtain T_g = 47 °C, which is in good agreement with the observed T_g. However, since we again assumed random propagation and conflicting glass transition temperatures are reported in the literature,[13] further analysis cannot be made. The peak area at the polymer melting temperature gives the heat of melting of the copolymer as 8 cal/g, which is much smaller than that of polyethylene (68.6 cal/g[11]), and, together with the X-ray diffraction experiment, indicates the partial crystallinity of the hydrogenated copolymer.

The hydrogenated copolymer decomposes slowly above 200 °C in air or nitrogen at a rate resembling that of polyethylene. This behavior is in contrast to that of poly(methyl methacrylate), which decomposes catastrophically above 290 °C (Figure 6).

A preliminary tensile test on the film, shown in Figure 7, gave the following data: Young's modulus, 10^3 kg/cm^2; stress at yield, 10^2 kg/cm^2, stress at break, 2.6×10^2 kg/cm; elongation at break, 300%. These data indicate that the hydrogenated copolymer is a soft and tough material resembling low-density polyethylene and that it has excellent elasticity.

Conclusion

The hydrogenation of alternating butadiene-MMA copolymer gives a sequence-ordered copolymer which has repeating ethylene-ethylene-MMA sequences. It is a partially crystalline, soft, and tough material.

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Schiff Base Coupling of Cyclic and High-Polymeric Phosphazenes to Aldehydes and Amines: Chemotherapeutic Models

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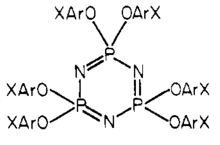
ABSTRACT: Prototype systems have been investigated for the synthesis of polymer-bound chemotherapeutic agents in which bioactive molecules are linked to poly(organophosphazenes) through Schiff base linkages. The sodium salts of the phenols 4-hydroxybenzaldehyde, 2-hydroxy-9-fluorenone, and 4-nitrophenol were allowed to react with hexachlorocyclotriphosphazene (III) to yield hydrolytically stable species of general formula $[NP(OArX)_2]_3$ (IV), where X = CHO, C=O, or NO_2. The 4-nitrophenolic group of IV was reduced to the corresponding 4-aminophenolic unit with PtO_2 and molecular hydrogen. Species IV formed Schiff base products with 2,4-dinitrophenylhydrazine, sulfadiazine, 3-hydroxytyramine, 2-amino-4-picoline, or citral. High-polymeric analogues of IV were synthesized with both phenoxy and OArX side groups (X = CHO, C=O, or NH_2) by techniques similar to those used for the cyclic trimers, and the macromolecules formed Schiff base species with 2,4-dinitrophenylhydrazine, sulfadiazine, phenylhydrazine, hydralazine, or citral. The physical and chemical properties of the Schiff base products are discussed.

Considerable interest exists in the use of synthetic macromolecules as carriers for the controlled release of chemotherapeutic agents.[1-3] Relatively few conventional polymers are suitable for this purpose because of the need for biocompatibility and facile side-group release mechanisms in aqueous media.

Poly(organophosphazenes) possess a number of advantages as potential carrier macromolecules. Synthetic routes are known for the introduction of a wide range of different substituent groups,[4-8] and the subtlety of structural variation is almost unique in macromolecular synthesis. Moreover, biodegradable polyphosphazenes have been prepared which can be designed to hydrolyze to innocuous small-molecule products.[9-11]

In this paper we explore the possibility that bioactive molecules might be attached to poly[(aryloxy)phosphazenes)] through a hydrolyzable Schiff base linkage. The reactions reported here are prototypes only since the use of aryloxy cosubstituent groups precludes the possibility of total biodegradation of these polymers. In later work we hope to extend these studies to systems that possess more biologically compatible spacer groups and cosubstituent units.

Inherent in our approach has been the need to perform exploratory reactions with small-molecule models, rather than with the high polymers themselves. Hence, cyclic trimeric phosphazenes such as I have been used as preliminary models for reactions with high polymers of type II. The group OArX represents a "spacer" aryloxy residues bearing a carbonyl or amino group X for reaction with amines or carbonyl compounds, respectively, to form Schiff bases. Because little was known about the reactivity or stability of the carbonyl or amino units in molecules such as I or II, it was necessary to carry out preliminary reactions with nonchemotherapeutic analogues before extension of these coupling processes to more complex reactants.



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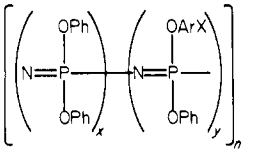

II

Results and Discussion

Synthesis of Cyclic Trimeric Model Systems. The specific reaction sequences used for the phosphazene cyclic trimers are outlined in Scheme I.

The cyclic model systems were synthesized by treatment of hexachlorocyclotriphosphazene (III) with the sodium salt of an aldehydic or ketonic phenol or of a nitrophenol. Specifically, one of three types of spacer units was introduced at this stage—those derived from the sodium salts of 4-hydroxybenzaldehyde, 2-hydroxy-9-fluorenone, or 4-nitrophenol. The 4-nitrophenoxy side groups were reduced with hydrogen over PtO_2 to the 4-aminophenoxy derivative. These derivatives are depicted in the general structures shown in IV, VI, and VII. The spacer units were chosen as the simplest aldehydic, planar ketonic, and amino derivatives that should form stable aryl Schiff bases. The 9-fluorenone unit had the added advantage that its reactions could be monitored readily by ultraviolet spectroscopy. The indirect formation of the 4-aminophenoxy

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