

Homogeneous Radiopaque Polymers with Organobismuth Compounds

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Synopsis

The effectiveness of triphenylbismuth and a few other bismuth compounds for use as a radiopacifying (X-ray contrast) additive in polymeric materials was tested. Ph_3Bi was found to be compatible (sometimes up to 70 wt %) with a wide range of monomers and polymers. It yields homogeneous mixtures with polystyrene, poly(vinyl chloride), polyacrylates, polyethylene, and other polymers. They can be formed by solvent casting, by melt processing, or by polymerizing a Ph_3Bi /monomer mixture. Polymerization is not affected by the presence of Ph_3Bi even when amine accelerators are used. Radiopacities of the polymer mixtures are proportional to the molar content of Ph_3Bi , and can easily exceed that of aluminum. The bismuth compound lowers the T_g of PVC, PMMA, and polystyrene by $1.3^\circ\text{C}/\text{wt } \%$ Ph_3Bi . The additive is moisture-insensitive, water-insoluble, and heat-stable. It does not leach into water and has a low toxicity index. Leaching even in organic solvents can be prevented entirely by covalently binding bismuth to the polymer matrix through the use of monomers such as styryldiphenyl bismuth.

INTRODUCTION

The availability of radiopaque (X-ray contrast) polymeric materials is of increasing importance in applications of plastics in dentistry, or in medical devices such as implants, sutures, and catheters.¹⁻³ Such materials permit the use of radiography as a rapid and nondestructive method for their detection and analysis. The difficulty in detecting plastic fireweapons by current screening devices can be cited as another reason for the need of radiopaque resins.

Most developments in this field have been concerned with polymers in which heavy metal salts such as BaSO_4 , or radiopaque glasses, are embedded in the polymer matrix.⁴⁻⁸ However, their incompatibility frequently has an adverse effect on the mechanical or esthetic properties of the resins. Halogenated polymers have also been used,⁹ for example, iodated hydrogel particles in endovascular embolization.¹⁰

Our work has focused on radiopacifying agents that are compatible with a polymeric material. This can in a number of cases be achieved when the heavy metal salt is chelated with the polymer. For example, transparent, radiopaque resins can be obtained with barium bromide dihydrate for polymers which contain barium chelating oligo-oxyethylene side chains.^{11,12} More versatile are the bismuth halides or a salt such as uranyl nitrate hexahydrate which solubilize into carbonyl or phosphonate containing monomers.^{13,14} On polymerization homogeneous transparent polymers, e.g., poly(methyl methacrylate), can be obtained with radiopacities exceeding that of aluminum by at least a factor 2.

A disadvantage of the bismuth halides in forming homogeneous mixtures with polymers is their limited applicability. Also, the transparent BiBr_3 or BiCl_3 containing resins slowly turn opaque on prolonged exposure to moisture. Water penetration causes the formation of insoluble bismuthoxyhalides. Bismuth halides also inhibit the room temperature polymerization of monomers carried out with a mixture of a peroxide and an amine accelerator (e.g., N,N' -dimethyl-*p*-toluidine). The bismuth salts are known to complex with amines.

This paper describes the application of organobismuth compounds and more specifically triphenylbismuth as compatible X-ray contrast additives for a variety of polymers.¹⁵ Triphenylbismuth does not exhibit the difficulties encountered with the bismuth halides, and its insolubility in water prevents any leaching out of the resin into water. It can also be covalently incorporated into a polymer matrix by using a monomer such as styryldiphenylbismuth.

EXPERIMENTAL

Materials. Methyl methacrylate (MMA) and styrene were distilled prior to use. Benzoyl peroxide (BPO) and azobisisobutyronitrile (AIBN) were recrystallized from methanol and N,N' -dimethyl-*p*-toluidine was distilled. Polymers used in the experiments were available in our laboratory, or acquired from Aldrich or Polysciences. Triphenylbismuth, triphenylbismuth dichloride, and triphenylantimony (Alfa) were used without purification. Diphenylbismuth chloride and bromide were synthesized according to reported procedures¹⁶ and recrystallized from hot benzene. Tri(*p*-bromophenyl)bismuth (mp 119–121°C) was synthesized in 30% yield as described.¹⁷ Bismuth tris(*p*-bromophenyl) was an Alfa product, while the monomer styryldiphenylbismuth was synthesized in 50% yield from diphenylbismuth chloride and *p*-bromostyrene via its Grignard compound.¹⁸

Polymer-Organobismuth Mixtures. Up to 70 wt % of the radiopacifying agent was dissolved in styrene, MMA, or other monomers, and the homogeneous mixtures polymerized for 48 h at 60–70°C with 0.5 wt % AIBN or BPO. Room temperature polymerizations of Ph_3Bi -MMA mixtures were carried out with 2.5 wt % BPO and 1.5 wt % N,N' -dimethyl-*p*-toluidine. A hard, transparent material formed after a few minutes. Styryldiphenylbismuth mixtures with styrene or MMA were polymerized with 0.5 wt % BPO. Radiopaque resins were also made by dissolving the radiopacifying agent (usually Ph_3Bi) and the polymer in an appropriate solvent (CHCl_3 , THF, ethyl acetate, hexane). The solvent was then slowly evaporated under a stream of nitrogen, and the last traces of solvent removed in a vacuum oven.

Measurements. IR spectra of the polymers were recorded on a Nicolet 20 DX FTIR spectrometer. A Varian XL100 was employed to record the ^1H - and ^{13}C -NMR spectra of the synthesized products and of mixtures of Ph_3Bi and MMA. The effect of Ph_3Bi on the T_g of some of the polymers was measured on a Perkin-Elmer DSC-4 differential scanning calorimeter under a nitrogen atmosphere at a heating rate of 20°C/min. The instrument was calibrated with indium. Each sample was scanned until a constant T_g was recorded (usually on the second scan). T_g values were taken at the inflection point.

Radiopacities were measured with a Picker X-ray unit operating at 90 kV and 6 mA. The transparent materials were cut into 1 or 2 mm thick cylindrical

pellets and placed next to an aluminum stepwedge (1 mm steps) on a Kodak ultraspeed double sided X-ray film no. DF 49. The film was placed 22 in. below the tungsten anode. The developed film was scanned with a Joyce microdensitometer and the radiopacities of the specimens measured relative to that of the aluminum stepwedge. Radiopacities are expressed in mm of aluminum.

RESULTS AND DISCUSSION

For many years organobismuth compounds, specifically triphenylbismuth, have been added in small quantities to monomers as well as polymers for use as catalysts or cocatalysts, stabilizers, inhibitors, antioxidants, bactericides, fungicides, flame retardants, coatings for magnetic recording tape, and the like.¹⁹ However, no report has appeared on its application in polymeric materials as a radiopacifying agent.

Strong interaction between carbonyl oxygen and bismuth is the reason for the high solubility of bismuth chloride and bromide in monomers such as acrylates and vinyl acetate.^{8,13,14} This can be demonstrated from infrared, ¹H- and ¹³C-NMR spectra of carbonyl-containing compounds in which bismuth salts or other Lewis acids are dissolved.²⁰⁻²² For example, the 1727 cm⁻¹ carbonyl absorption of MMA shows an additional peak at 1705 cm⁻¹ in the presence of sufficient BiBr₃, while in a mixture of PMMA/BiBr₃ two distinct carbonyl absorptions are seen, namely, at 1732 cm⁻¹ (as in salt free PMMA) and one at 1685 cm⁻¹ belonging to the C=O ··· BiBr₃ adduct.¹³ A 2 : 1 mixture of MMA/BiBr₃ is still homogeneous and exhibits a ¹³C-NMR shift of 3.6 ppm for the carbonyl carbon and a 4.8 ppm shift for the β-vinyl carbon. The combined results are consistent with the formation of an adduct between the bismuth halide and the carbonyl group. BiBr₃ also was found to form a sharp melting 1 : 1 adduct with dimethyl malonate in which only one of the carbonyl groups appears to be complexed with the bismuth.¹³

In contrast, triphenylbismuth when dissolved in acrylates or their polymers does not cause significant ¹³C-NMR or IR shifts in the carbonyl group. For example, addition of 40 wt % Ph₃Bi to MMA (6 : 1 molar ratio) shifts the ¹³C-NMR peak of C=O by only 0.1 ppm. Triphenylbismuth, a white solid melting at 78°C and thermally stable to at least its boiling point (242°C at 14 mm), has no dipole moment. Its apolar character makes it soluble in a wide range of solvents, including hexane, benzene, chloroform, tetrahydrofuran, and acetone. It also solubilizes in a variety of monomers, for example, acrylates, styrene, isoprene, acrylonitrile, and vinyl acetate.

When Ph₃Bi is added to monomers such as MMA or styrene (up to at least 70 wt %), colorless, transparent polymeric materials are formed when the mixtures are heated with BPO or AIBN at 65°C for a day or two. A distinct advantage of this organobismuth compound over the bismuth halides is the observation that polymerization of acrylates proceeds equally smoothly when carried out at room temperature with BPO and an amine accelerator. A transparent, hard PMMA was formed in a few minutes with BPO and *N,N'*-dimethyl-*p*-toluidine as accelerator under conditions outlined in the experimental section. This, of course, makes Ph₃Bi an attractive radiopacifying agent for restorative dental materials and similar applications. Apparently, Ph₃Bi does not easily form adducts with amines, unlike the bismuth halides which deactivate the accelerator by complexing with the amine.

An alternative method to form homogeneous, transparent polymers with Ph_3Bi as radiopacifying additive is by casting films from solutions of polymer and Ph_3Bi in appropriate solvents. For example, clear films of Ph_3Bi with PMMA or PSt can be cast from THF or CHCl_3 , those with polyacrylonitrile from dimethylformamide, with polyethylene from hot hexane and poly(vinyl chloride) from hot THF. In the latter system PVC is dissolved in warm THF and up to 40 wt % Ph_3Bi is added. After dissolving the bismuth compound, the THF is slowly evaporated under a stream of nitrogen. The clear, colorless film is then dried under vacuum. Transparent films containing Ph_3Bi were also made from polycarbonate (Lexan) in CHCl_3 , from an ethylene-propylene copolymer in hexane and from an ethylene-acrylate copolymer in THF. The results demonstrate that a variety of polymers is able to form homogeneous mixtures with Ph_3Bi as radiopacifying additive.

Homogeneous radiopaque materials can also be acquired by processing a polymer that is compounded with Ph_3Bi . This is commercially an attractive method. For example, isotactic polypropylene (iPP) mixed with up to 40 wt % Ph_3Bi gives a clear, transparent melt when heated under vacuum to about 200°C. On cooling, the material, like crystalline iPP itself, turns opaque but no free Ph_3Bi can be detected in the DSC scans of the product. The good thermal stability of Ph_3Bi (at least up to 240°C for brief periods) permits melt processing with other polymers as well.

Effect of Ph_3Bi on the T_g of Polymers. DSC scans of transparent specimens of PMMA/ Ph_3Bi mixtures are depicted in Figure 1. Since the T_g of PMMA is lowered considerably in the presence of water,²³ moisture was avoided by working under dry conditions. The T_g gradually decreases from 117°C for atactic PMMA to 86°C for PMMA containing 26 wt % Ph_3Bi . Similar measurements were carried out for PSt and PVC. Plots of T_g vs. wt % of Ph_3Bi are depicted in Figure 2. The decrease in T_g is essentially linear with the Ph_3Bi content up to at least 20 wt %. For the three polymers it amounts to $1.3 \pm 0.1^\circ\text{C}/\text{wt \%}$ bismuth compound. The results suggest that Ph_3Bi largely functions as

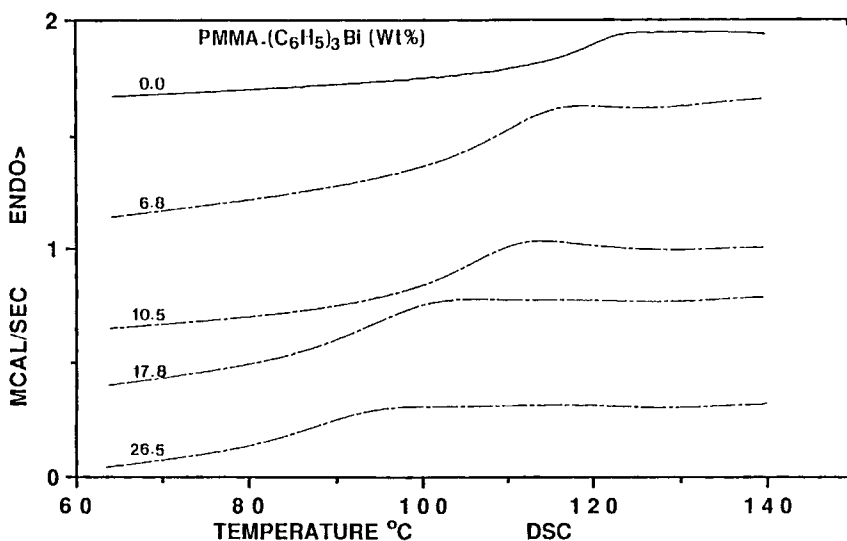


Fig. 1. DSC scans of transparent mixtures of Ph_3Bi and PMMA for different wt % of Ph_3Bi .

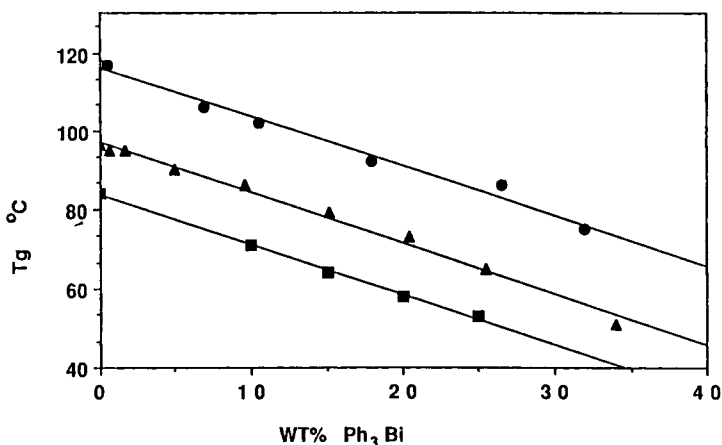


Fig. 2. Plots of T_g vs. wt % of Ph_3Bi for mixtures of Ph_3Bi with: (●) PMMA; (▲) polystyrene; (■) PVC.

a plasticizer. The addition of a bismuth halide to PMMA causes a much smaller decrease in T_g ,¹³ probably because its plasticizing effect is in part compensated for by its adduct formation with the carbonyl group and the resulting hindrance in segmental chain motion.

To avoid lowering the T_g on adding Ph_3Bi as radiopacifying agent, the bismuth compound can be covalently incorporated into the polymer matrix by using styryldiphenylbismuth. This monomer, reported as early as 1963¹⁸ readily copolymerizes with styrene, MMA, and other vinyl monomers. For example, a transparent, hard material was obtained by polymerizing MMA and the bismuth monomer at 65°C with BPO as initiator. The polymerization is also rapid at room temperature when an amine accelerator is added. The T_g of this product was found to be 110°C as compared to 80°C for a PMMA specimen with 30 wt % Ph_3Bi . The result is not surprising as the homopolymer of styryldiphenylbismuth was found to have a T_g of 110°C, close to that of PMMA. Another distinct advantage of covalently polymer-bound bismuth is that it will not leach out when the radiopaque material is exposed to organic solvents in which Ph_3Bi itself is soluble.

The addition of Ph_3Bi to the partially crystalline iPP lowers both the T_g and the T_m (Fig. 3) of this polymer. For example, 30 wt % Ph_3Bi decreases the T_g of iPP from 0 to -31°C and the T_m from 158 to 152°C. At the same time the heat of fusion, ΔH_f , decreases from 23.1 to 16.1 cal/g. This amounts to a decrease in the crystallinity, $W_c = 100 \Delta H_f / \Delta H_u$, from 66 to 46%, the heat of fusion, ΔH_u , of 100% crystalline iPP being 35 cal/g.²⁴ These data imply that the Ph_3Bi causes considerably more plasticization in the amorphous domains than in the crystalline domains, although the lowering of both T_m and W_c indicates that crystallization is definitely hindered by the presence of the bismuth additive. The results are consistent with data on the effect of flame-retardant triphenylantimony compounds on the structural and mechanical behavior of iPP.²⁵

Radiopacity Characteristics. Figure 4 shows positive radiographs of 2 mm thick transparent pellets of Ph_3Bi mixtures with PSt and of 1 and 2 mm pellets of a copolymer of MMA with different weight percentages of styryldi-

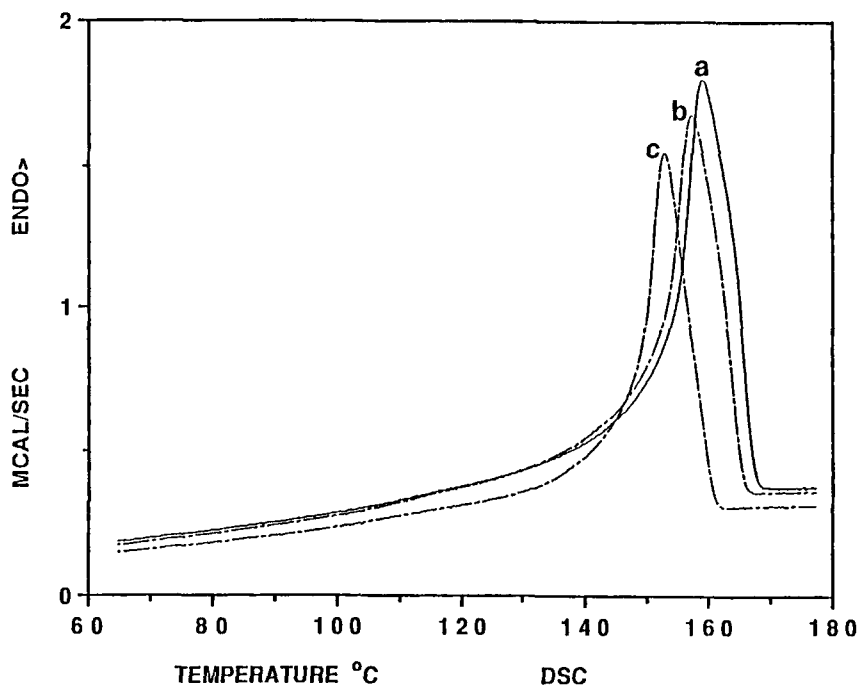


Fig. 3. DSC scans of Ph_3Bi mixtures with isotactic polypropylene: (a) unfilled iPP; (b) 10 wt % Ph_3Bi ; (c) 30 wt % Ph_3Bi .

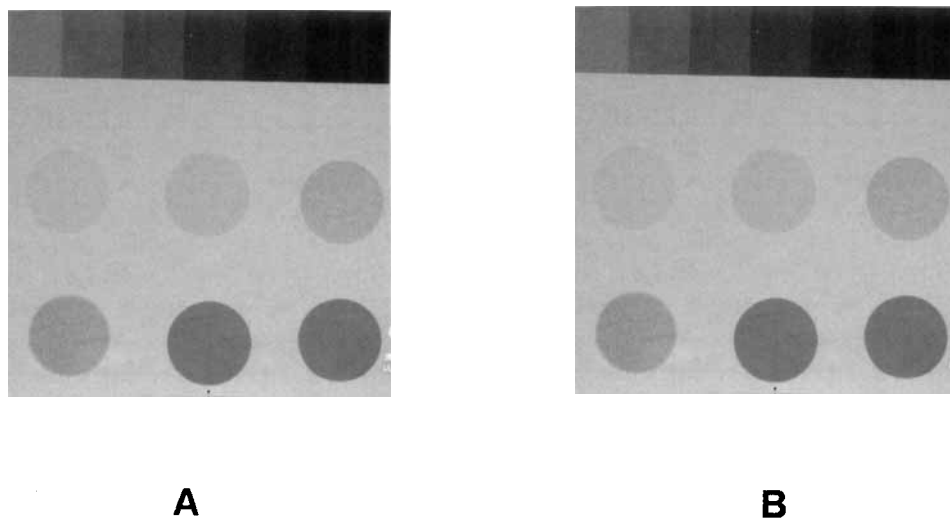


Fig. 4. Positive radiographs of transparent 1 and 2 mm thick pellets of (A) PSt/ Ph_3Bi and (B) random copolymer of MMA and styryldiphenylbismuth (STDPB). From left to right, top, then bottom: (A) 0, 10, 15, 20, 25, and 30 wt % Ph_3Bi , all 2 mm pellets; (B) 10.2, 21, and 32.3 wt % STDPB, top = 1 mm, bottom = 2 mm pellets.

phenylbismuth. Comparison with an aluminum stepwedge permits the radiopacity to be expressed in mm of aluminum. The radiopacities of 2 mm thick PMMA pellets are plotted in Figure 5 vs. the molar concentration of Ph_3Bi . The latter was calculated from the wt % of the additive and the weight and volume of the pellet. Included in the figure are data for triphenylantimony, BiCl_3 , and those reported earlier for BiBr_3 .^{13,26} The plots are all linear unlike those in which the radiopacity was plotted vs. the wt % of radiopacifying agent.¹³ In that case the lines slightly curve upwards due to the increase in the density of the specimens. From the data of Figure 5 it can be calculated that 24 wt % Ph_3Bi or a concentration of $0.67M$ is required in a 2 mm thick specimen of PMMA to impart to this material a radiopacity equivalent to that of 2 mm aluminum. The latter is a radiopacity standard proposed for medical applications.²⁷ For BiBr_3 and BiCl_3 the respective numbers are 13.5 wt % or $0.36M$ and 15.3 wt % or $0.62M$. The amounts required for the halides are less because the three chlorine atoms in BiCl_3 and even more so the bromine atoms in BiBr_3 contribute to the radiopacity. Although Ph_3Sb also gives transparent mixtures with PMMA, PSt, PVC, and other polymers, the smaller atomic weight of antimony reduces its efficiency as a radiopacifying agent. An amount of 52 wt % or $1.77M$ Ph_3Sb is needed in PMMA to render its radiopacity equal to that of aluminum.

Radiopacity plots similar to those for PMMA were obtained for iPP, PVC, and PSt (Fig. 6). For these three polymers radiopacity equivalence with aluminum is obtained with 34 wt % or $0.75M$ Ph_3Bi , 18 wt % or $0.47M$ Ph_3Bi , and 24.4 wt % or $0.61M$ Ph_3Bi , respectively. The much lower value for PVC results from the inherent radiopacity of the polymer itself.

A few other organobismuth compounds were tested but found to be more expensive or less effective. Low solubilities (less than 5 wt % in MMA, somewhat higher in styrene) were recorded for diphenylbismuth chloride and bromide. Triphenylbismuth dichloride is soluble in MMA up to 11 wt %, but its mixtures

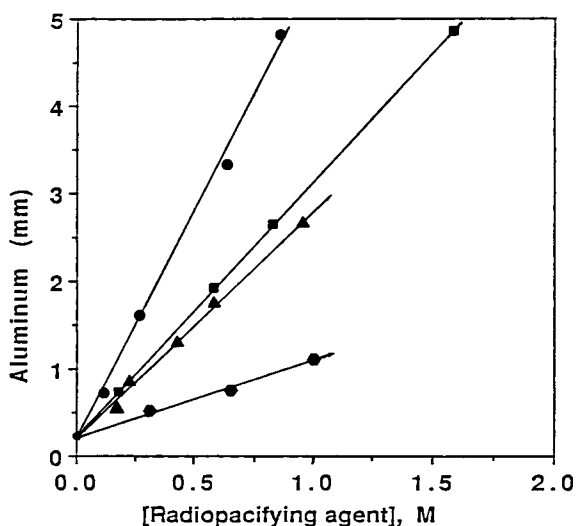


Fig. 5. Radiopacities (in mm of aluminum) of transparent, 2 mm thick pellets of PMMA and its mixtures with BiBr_3 (●), BiCl_3 (■), Ph_3Bi (▲), and Ph_3Sb (●) as a function of their molar concentration.

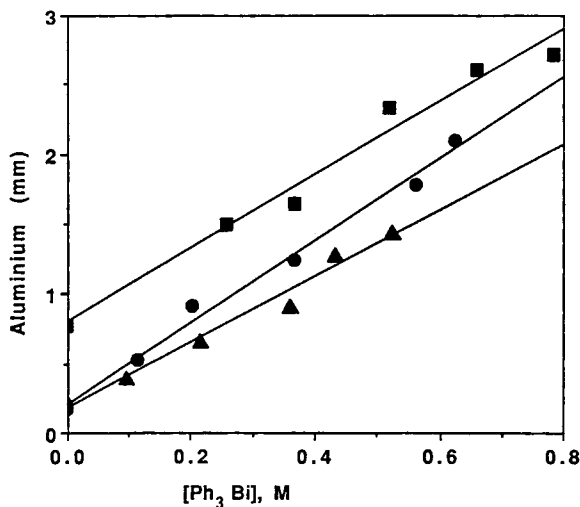


Fig. 6. Radiopacities (in mm of aluminum) of transparent, 2 mm thick pellets of mixtures of Ph_3Bi with PVC (■), isotactic polypropylene (▲), and polystyrene (●) as a function of the molar concentration of Ph_3Bi .

with PMMA are somewhat opaque. We also synthesized tri(*p*-bromophenyl)bismuth, but, although this compound has good solubility properties in MMA and styrene and is more effective on a molar basis than Ph_3Bi , its radiopacity on a weight basis is no improvement. A relatively inexpensive bismuth compound is bismuth tris (*p*-bromophenate) but its solubility is poor.

A distinct advantage of Ph_3Bi over the bismuth halides is its water insensitivity. Bismuth halide-containing PMMA turns hazy in a matter of weeks when exposed to moist air, especially when the halide content is more than 10 wt %.^{8,13} Exposure to warm water rapidly turns a transparent PMMA/ BiBr_3 mixture opaque. The problem is formation of insoluble bismuthoxyhalide. Ph_3Bi is not attacked by water, and a 30 wt % mixture with PMMA remains transparent in water for prolonged periods of time, even at elevated temperatures. Its insolubility in water also prevents the leaching of Ph_3Bi into the surrounding water. Leaching, even in organic solvents, can be entirely eliminated by using monomers such as styryldiphenylbismuth (vide supra). Ph_3Bi also has good thermal stability (at least up to 250°C). A transparent mixture of PMMA with 30 wt % Ph_3Bi remains optically clear up to at least 150°C.

CONCLUSIONS

Triphenylbismuth is an effective radiopacifying additive because of its compatibility (up to 70 wt %) with many monomers and polymers. Interference with polymerization procedures is minimal even when amine accelerators are used. Homogeneous X-ray contrast resins can be obtained by polymerizing monomer/ Ph_3Bi mixtures, by solvent casting polymer/ Ph_3Bi mixtures from appropriate solvents, or by melt processing. Radiopacities can often exceed that of aluminum by at least a factor 2. Ph_3Bi is water-insoluble, moisture-insensitive, and heat-stable. It does not leach into an aqueous medium, and the use

of bismuth-containing monomers can prevent leaching in any solvent as it becomes covalently bound to the polymer matrix. As mentioned at the start of the discussion, the presence of Ph_3Bi in a polymer has other beneficial effects since it can function as a bactericide, stabilizer, plasticizer, and so on. Testing of mechanical properties of the radiopaque materials is underway, as are experiments to check its carcinogenicity. Its toxicity index appears to be low.²⁸

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