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Preparation of Aryldiazonium-, Aryldiazo-, and Arylazido-Derivatized Copolymers and Their Surface Photografting

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ABSTRACT: The photochemical surface grafting method based on the photochemistry of aryldiazonium, aryldiazo, and arylazido groups was explored. Five hydrophilic photoreactive copolymers containing these three photosensitive groups in their side chains were prepared by a *one-pot* procedure from two precursors, which were obtained by radical copolymerization of *N*,*N*-dimethylacrylamide and styrene derivatized with appropriate functional groups. The photoreactivity of the copolymers was verified by Fourier transform infrared (FT-IR) and ultraviolet (UV) spectroscopies. Upon coating of a photoreactive copolymer on poly(ethylene terephthalate) (PET) film as a model substrate and subsequent UV light irradiation, the surface became wettable by water irrespective of the type of copolymers. The photochemical fixation of the copolymers on PET surface was demonstrated by X-ray photoelectron spectroscopy analyses and water contact angle measurements. The potential application in the biomedical devices is discussed.

Introduction

In the past few decades, intensive efforts have been directed toward the development of nonfouling surfaces in various industrial fields such as coating, shipbuilding, automobiles, and artificial organs. For example, the biocompatible surface design is the most urgent topic in artificial device development. The surface chemical composition, structure, and properties of a given material influence greatly the biological responses when it comes in contact with body fluids and tissues. These include the adsorption, adhesion, activation, or growth of biocolloids such as proteins, polysaccharides, lipids, cells, and bacteria.

Various surface modification methods for minimizing the adsorption and adhesion of biocolloids have been attempted.[1−3] However, a simple physical coating of a polymeric substance often leads to delamination under severe working conditions. Therefore, it is necessary to ensure the durability of the coating layer. The use of photochemistry leading to the chemical fixation of a coated polymer onto a substrate is one of the most elegant approaches applied in the surface processing technology.

The surface modification of various polymer substrates has been investigated in this laboratory by using the photochemistry of aryl azides. When irradiated with ultraviolet light, an azido group is photolyzed into a very reactive nitrene which can make covalent bonds with neighboring groups.[4,5] We have reported in our previous studies the surface modification of polymeric substrates by phenylazido-derivatized copolymers to provide ionic, nonionic, hydrophilic, or hydrophobic character.[6−10] Bioactive substances such as proteins, peptides, and polysaccharides have also been photochemically grafted to provide the functionalization of the surface.[11,12]

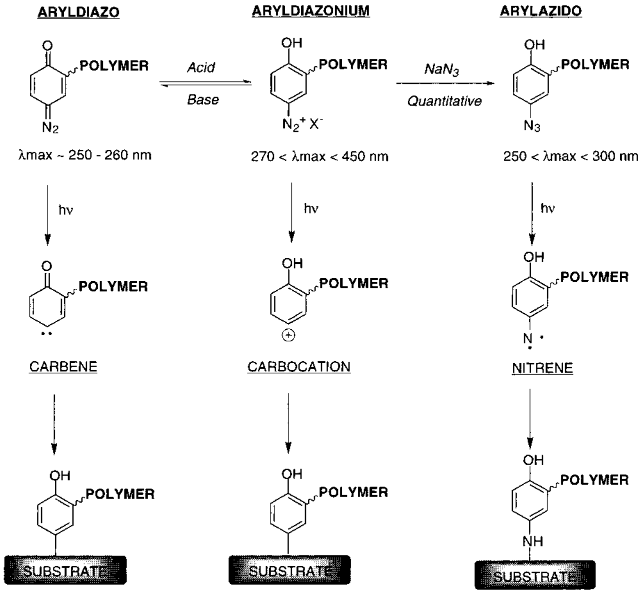

Figure 1. Schematic representation of the photochemical processes involved in the surface modification of polymer substrate.

To extend the scope of our photochemical surface modification technology, we herein describe a new approach based on the photochemistry of aryldiazonium and aryldiazo groups. These two photoreactive groups generate under UV light irradiation a highly reactive species, an arylcation and arylcarbene, respectively, that are able to make covalent bonds with a wide range of neighboring atoms (Figure 1).[13] The photochemistry of diazonium and diazo groups has found broad application in photoresist coatings technology and photoaffinity labeling of membrane receptors.[14−17]

The key feature of the newly developed technology lies on the generation of the three photoreactive groups (diazonium, diazo, and azido) from a common precursor. That is, a primary arylamine can be easily transformed to an arylazido group via a diazonium intermediate. If, in addition, a hydroxy substituent is introduced in the

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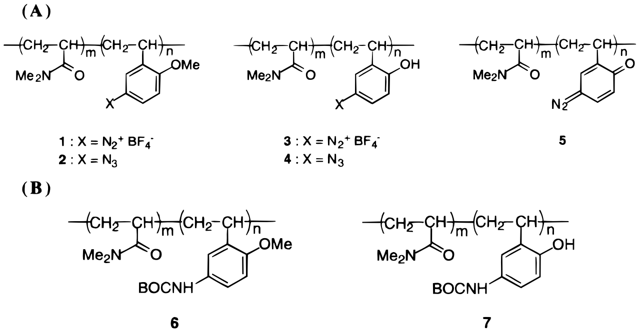


Figure 2. Chemical structures of (A) photoreactive copolymers **1**−**5** and (B) precursor copolymers **6** and **7**.

para position to the diazonium, a *p*-diazocyclohexadienone can be reversibly formed by an acid−basic exchange. The physicochemical characteristics and spectroscopic properties of these three groups make them attractive for photochemical surface processing. We have prepared hydrophilic photoreactive polymers containing diazonium, diazo, and azido groups by radical copolymerization of *N*,*N*-dimethylacrylamide (DMAA) with two styrene monomer derivatives. These monomers, designed with the required functionalities to generate the photoreactive groups and to ensure enough stability and hydrophilicity to the copolymer, were obtained by multistep synthesis. Both of them contain a para-electron-donating substituent (methoxy, hydroxy) to stabilize the diazonium group. On the other hand, the *p*-hydroxydiazonium served as a precursor for the diazo group. The photoreactive copolymers (listed in Figure 2) were coated on a substrate and subsequently irradiated with UV light. The synthesis, photochemical fixation, and surface modification using these polymers are discussed.

Experimental Section

Reagents and Materials. 2-Methoxy-5-nitrobenzyl bromide, 2-hydroxy-5-nitrobenzaldehyde, di-*tert*-butyl dicarbonate, *n*-tetrabutylammonium fluoride, 2-(trimethylsilyl)-ethoxymethyl chloride, and pyridinium dichromate were purchased from Aldrich Chemical Co. Inc. (Milwaukee, WI). Sodium acetate, sodium iodide, potassium carbonate, palladium on carbon catalyst (10% Pd contents), triethylamine, *n*-butyllithium (1.6 M solution in hexanes), sodium hydride (65% dispersion in oil), sodium nitrite, sodium azide, manganese dioxide, methyltriphenylphosphonium bromide and *N*,*N*-dimethylacrylamide were purchased from Wako Pure Chemicals Inc. (Osaka, Japan). Hexamethylphosphortriamide (HMPT) and 2,2′-azobis(isobutyronitrile) (AIBN) were purchased from Tokyo Casei Co. (Tokyo, Japan). All reagents and solvents used were of special reagent grade. Solvents were used without further purification except for tetrahydrofuran, which was freshly distilled prior to the Wittig reaction. Poly(ethylene terephthalate) (PET) film was obtained from Bellco Glass Inc. (Vineland, NJ).

2-Methoxy-5-nitrobenzyl Acetate (9). To a solution of 2-methoxy-5-nitrobenzyl bromide **8** (15.0 g, 61 mmol) in acetonitrile (300 mL) were added anhydrous sodium acetate (25 g, 305 mmol), HMPT (3 mL), and sodium iodide (1.5 g, 10 wt %). The mixture was stirred under reflux for 12 h and then concentrated under reduced pressure. Water was added and the product extracted with ethyl acetate. The organic phase was successively washed with hydrochloric acid (10% aqueous solution), sodium hydrogen carbonate (saturated aqueous solution), water, and sodium chloride (saturated aqueous solution) and then dried over sodium sulfate. After filtration and evaporation of the solvent under reduced pressure, the product was purified by silica gel column chromatography (elution with methylene chloride) to afford (13.7 g, 100%) a pale yellowish solid. $R_f = 0.37$ (silica gel, CH_2Cl_2). ^1H NMR ($CDCl_3$) (δ ppm): 2.17 (s, 3H, OAc); 3.97 (s, 3H, OMe); 5.18 (s, 2H, Hbenz); 6.96 (d, 1H, $J = 9.8$ Hz, Har); 8.2−8.25 (m, 2H, Har).

2-Methoxy-5-nitrobenzyl Alcohol (10). To a solution of acetate **9** (13.7 g, 61 mmol) in methanol (500 mL) was added potassium carbonate (42.15 g, 305 mmol), and the suspension was stirred overnight at 25 °C. After completion, the reaction mixture was concentrated under reduced pressure and ice was added, followed by hydrochloric acid (50% aqueous solution) to acidic pH. The product was extracted with ethyl acetate (300 mL), and the organic phase was successively washed with sodium hydrogen carbonate (saturated aqueous solution) and sodium chloride (saturated aqueous solution) and then dried over sodium sulfate. After filtration and evaporation of the solvent under reduced pressure, the product was purified by silica gel column chromatography (elution with methylene chloride) to afford (11.17 g, 100%) a pale yellowish solid. $R_f = 0.11$ (silica gel, CH_2Cl_2). ^1H NMR (acetone-d_6) (δ ppm): 3.99 (s, 3H, OMe); 4.52 (t, 1H, $J = 5.3$ Hz, OH); 4.69 (d, 2H, $J = 5.3$ Hz, Hbenz); 7.17 (d, 1H, $J = 9$ Hz, Har); 8.18 (dd, 1H, $J = 9$ Hz, $J = 2.9$ Hz, Har); 8.37 (d, 1H, $J = 2.9$ Hz, Har).

2-Methoxy-5-aminobenzyl Alcohol (11). To a solution of nitro compound **10** (11.16 g, 61 mmol) in methanol (300 mL) was added Pd/C catalyst (10%) (1.2 g) under argon. The reaction mixture was carefully evacuated from argon and filled with hydrogen and then stirred at 25 °C for 6 h. Amine formation was characterized on TLC by deep purple staining with a ninhydrin spray solution. After completion and removal of hydrogen, the catalyst was filtered on a pad of Celite, and methanol was evaporated under reduced pressure. The product was purified by silica gel column chromatography (elution with chloroform/methanol: 90/10, with 1% triethylamine) to afford a pale brownish solid (9.34 g, 100%). $R_f = 0.15$ (silica gel, $CHCl_3$/MeOH: 90/10).

2-Methoxy-5-*tert*-butoxycarbonylaminobenzyl Alcohol (12). To a solution of amino compound **11** (9.34 g, 61 mmol) in methylene chloride (200 mL) was added triethylamine (11 mL, 79.3 mmol) followed by dropwise addition of a di-*tert*-butyl dicarbonate (14.6 g, 67 mmol) solution in methylene chloride (10 mL). The reaction mixture was stirred overnight at 25 °C. Upon completion, the solvent was evaporated under reduced pressure, and the product was purified by silica gel column chromatography (gradient elution with chloroform/methanol: 100/0 to 95/5) to afford (15.4 g, 100%) of colorless solid. $R_f = 0.61$ (silica gel, $CHCl_3$/MeOH: 90/10). ^1H NMR ($CDCl_3$) (δ ppm): 1.51 (s, 9H, $(CH_3)_3C$); 3.83 (s, 3H, OMe); 4.65 (m, 2H, Hbenz); 5.29 (1H, OH); 6.40 (s, 1H, NH); 6.80 (d, 1H, Har); 7.25 (m, 2H, Har).

2-Methoxy-5-*tert*-butoxycarbonylaminobenzaldehyde (13). To a suspension of pyridinium dichromate (PDC) (48.9 g, 130 mmol) in methylene chloride (500 mL), was added dropwise a solution of benzylic alcohol **12** (13.2 g, 52.1 mmol), and the reaction mixture was stirred vigorously for 10 h under argon atmosphere at 25 °C. Upon completion, silica gel was added to the reaction mixture, and then the solvent was evaporated under reduced pressure. The crude mixture was filtered on silica gel (elution with methylene chloride). After evaporation of the solvent, ethyl acetate was added, and the product was successively washed with hydrochloric acid (10% aqueous solution), sodium hydrogen carbonate (saturated aqueous solution), and sodium chloride (saturated aqueous solution) and then dried over sodium sulfate. After filtration and evaporation of the solvent under reduced pressure, the product was purified by recrystallization in chloroform/hexane to afford (11.6 g, 89%) pure aldehyde. $R_f = 0.64$ (silica gel, CH_2Cl_2). ^1H NMR ($CDCl_3$) (δ ppm): 1.51 (s, 9H, $(CH_3)_3C$); 3.90 (s, 3H, OMe); 6.42 (s, 1H, NH); 6.95 (d, 1H, Har); 7.57 (m, 1H, Har); 7.75 (m, 1H, Har); 10.41 (s, 1H, CHO).

2-Methoxy-5-*tert*-butoxycarbonylaminostyrene (14). To a cooled suspension (−78 °C) of methyltriphenylphosphonium bromide (18.75 g, 52.48 mmol) in freshly distilled tetrahydrofuran (200 mL) was added dropwise a solution of *n*-butyllithium (1.5 M in hexane) (32.8 mL, 49.2 mmol) under argon. The bright orange mixture was stirred for 0.5 h at −78 °C before a solution of aldehyde **13** (8.25 g, 32.8 mmol) in tetrahydrofuran (165 mL) was added dropwise. The reaction mixture was stirred at −78 °C for 1 h and then slowly warmed to 25 °C. Upon completion, the mixture was hydrolyzed with ammonium chloride (saturated aqueous solution), and the product was extracted with ethyl acetate. The organic phase was washed with sodium chloride (saturated aqueous solution) and dried over sodium sulfate. After evaporation of the solvent under reduced pressure, the product was purified by silica gel chromatography (elution chloroform/hexane: 70/30). The styrene was recrystallized in hexane to afford (7.4 g, 91%) a colorless solid. $R_f = 0.62$ (silica gel, $CHCl_3$). ^1H NMR ($CDCl_3$) (δ ppm): 1.51 (s, 9H, $(CH_3)_3C$); 3.80 (s, 3H, OMe); 5.22−5.27 (dd, 1H, CH_2); 5.67−5.75 (dd, 1H, CH_2); 6.44 (s, 1H, NH); 6.76−6.79 (d, 1H, Har); 6.93−7.04 (dd, 1H, CH); 7.22−7.25 (m, 1H, Har); 7.41 (m, 1H, Har).

2-Hydroxy-5-nitrobenzyl Alcohol (16). To a cooled solution (−20 °C) of 2-hydroxy-5-nitrobenzaldehyde (20 g, 0.12 mol) in methanol (500 mL) was added sodium borohydride (9.05 g, 0.24 mol) in small portions. The reaction mixture was stirred for 2 h at −20 °C and then acidified with acetic acid at 0 °C. After evaporation under reduced pressure, tetrahydrofuran (300 mL) was added, and the solution was filtered on a pad of Celite. Evaporation of the solvent afforded (20.2 g, 100%) alcohol **16**. The product was enough pure to be used in the next step without further purification. $R_f = 0.12$ (silica gel, CH_2Cl_2/MeOH: 95/5).

2-Hydroxy-5-*tert*-butoxycarbonylaminobenzyl Alcohol (18). To a solution of nitrophenol **16** (10.0 g, 59.1 mmol) in ethyl acetate (500 mL) was added Pd/C catalyst (1.0 g, 10 wt %) under argon. The reaction mixture was carefully evacuated from argon and filled with hydrogen and then stirred at 25 °C for 8 h. After completion and removal of hydrogen, the catalyst was filtered on a pad of Celite, and the solvent was evaporated under reduced pressure to afford a brownish solid (8.22 g, 100%). $R_f = 0.37$ (silica gel, CH_2Cl_2/MeOH: 90/10). The crude mixture was dissolved in tetrahydrofuran (270 mL) and methanol (70 mL). Triethylamine (12.3 mL, 88.5 mmol) was added, followed by a dropwise addition of a di-*tert*-butyl dicarbonate (15.5 g, 70.9 mmol) solution in tetrahydrofuran (20 mL). The reaction mixture was stirred overnight at 25 °C under argon atmosphere. After evaporation of the solvent under reduced pressure, the product was purified by silica gel chromatography (elution with methylene chloride/methanol: 95:5) to afford (10.45 g, 74% overall) of pale yellow solid. $R_f = 0.44$ (silica gel, CH_2Cl_2/MeOH: 95/5). ^1H NMR ($CDCl_3$) (δ ppm): 1.51 (s, 9H, $(CH_3)_3C$); 4.81 (m, 2H, Hbenz); 6.30 (s, 1H, NH); 6.79−6.82 (d, 1H, Har); 6.99 (m, 1H, Har); 7.20 (m, 1H, Har).

2-[2-(Trimethylsilyl)ethoxymethoxy]-5-*tert*-butoxycarbonylaminobenzyl Alcohol (19). To a cooled solution (0 °C) of phenol **18** (10.0 g, 41.8 mmol) in DMF (250 mL) was added sodium hydride (65% dispersion in oil, 1.23 g, 33.4 mmol). The mixture was stirred under argon for 1 h at 0 °C. 2-(Trimethylsilyl)ethoxymethyl chloride (5.9 mL, 33.4 mmol) in solution in DMF (10 mL) was added dropwise, and the reaction mixture was stirred at 0 °C for 4 h. Upon completion of the reaction (followed by TLC), DMF was evaporated under reduced pressure, and ammonium chloride (saturated aqueous solution) was added. The product was extracted with ethyl acetate and the organic phase washed with sodium chloride (saturated aqueous solution) and then dried over sodium sulfate. The product was purified by silica gel column chromatography (elution hexane/ether: 70/30) to afford (14.0 g, 91%) a colorless oil. $R_f = 0.2$ (silica gel, hexane/ether: 50/50). ^1H NMR ($CDCl_3$) (δ ppm): 0.00 (s, 9H, $(Me)_3Si$); 0.95 (m, 2H, $CH_2{-}Si$); 1.50 (s, 9H, $(CH_3)_3C$); 2.67 (s, 1H, OH); 3.74 (m, 2H, $CH_2{-}O$); 4.64 (s, 2H, Hbenzylic); 5.20 (s, 2H, OCH_2O); 6.64 (s, 1H, NH); 7.03−7.29 (m, 3H, Har).

2-[2-(Trimethylsilyl)ethoxymethoxy]-5-*tert*-butoxycarbonylaminobenzaldehyde (20). To a solution of alcohol **19** (7.6 g, 20.6 mmol) in methylene chloride (150 mL) was added in portions MnO_2 (26.8 g, 308.7 mmol), and the suspension was stirred for 6 h at 25 °C under argon atmosphere. After completion, the mixture was filtered on a pad of Celite and the solvent evaporated under reduced pressure. The aldehyde was purified by silica gel column chromatography (elution with hexane/ether: 80/20) to afford (7.18 g, 95%) a bright yellow oil. $R_f = 0.51$ (silica gel, hexane/ether: 50/50). ^1H NMR ($CDCl_3$) (δ ppm): 0.00 (s, 9H, $(Me)_3Si$); 0.93 (t, 2H, $CH_2{-}Si$); 1.51 (s, 9H, $(CH_3)_3C$); 3.75 (t, 2H, $CH_2{-}O$); 5.29 (s, 2H, OCH_2O); 6.44 (s, 1H, NH); 7.33 (m, 1H, Har); 7.61 (m, 2H, Har); 10.42 (s, 1H, CHO).

2-[2-(Trimethylsilyl)ethoxymethoxy]-5-*tert*-butoxycarbonylaminostyrene (21). To a cooled suspension (−78 °C) of methyltriphenylphosphonium bromide (8.3 g, 23.3 mmol) in freshly distilled tetrahydrofuran (150 mL) was added dropwise a solution of *n*-butyllithium (1.5 M in hexane) (14.6 mL, 21.96 mmol) under argon. The yellow reaction mixture was stirred for 0.5 h at −78 °C. A solution of aldehyde **20** (4.5 g, 12.2 mmol) in tetrahydrofuran (50 mL) was added dropwise, and the reaction mixture was stirred at −78 °C for 1 h and then slowly warmed to 25 °C for 12 h. Upon completion, the mixture was hydrolyzed with aqueous ammonium chloride solution, and the product was extracted with ethyl acetate and then washed with sodium chloride (saturated aqueous solution) and dried over sodium sulfate. After evaporation of the solvent, the product was purified by silica gel chromatography (elution with hexane/ether: 90/10) to afford (3.9 g, 88%) a colorless oil. $R_f = 0.71$ (silica gel, hexane/ether: 50/50).^1H NMR ($CDCl_3$) (δ ppm): 0.00 (s, 9H, $(Me)_3Si$); 0.95 (t, 2H, $CH_2{-}Si$); 1.51 (s, 9H, $(CH_3)_3C$); 3.75 (t, 2H, $CH_2{-}O$); 5.19 (s, 2H, OCH_2O); 5.27 (d, 1H, CH_2); 5.73 (d, 1H, CH_2); 6.36 (s, 1H, NH); 6.95−7.20 (m, 3H, 2Har+CH); 7.48 (s, 1H, Har).

2-Hydroxy-5-*tert*-butoxycarbonylaminostyrene (22). To a solution of styrene **21** (3.5 g, 9.58 mmol) in tetrahydrofuran (45 mL) was added hexamethylphosphortriamide (400 μL) and tetra-*n*-butylammonium fluoride (48 mL, 48 mmol, solution 1 M in THF). The mixture was stirred at 70 °C for 12 h under argon atmosphere. Upon completion, the reaction was hydrolyzed with aqueous ammonium chloride, and the product was extracted with ethyl acetate, washed with brine, and dried over sodium sulfate. The styrene **22** was purified by silica gel column chromatography (elution with hexane/ether: 50/50) to afford (1.21 g, 54%) a colorless oil. $R_f = 0.34$ (silica gel, hexane/ether: 50/50).^1H NMR ($CDCl_3$) (δ ppm): 1.51 (s, 9H, $(CH_3)_3C$); 5.29 (d, 1H, CH_2); 5.70 (d, 1H, CH_2); 6.38 (s, 1H, NH); 6.64 (d, 1H, Har); 6.84−6.94 (dd, 1H, CH); 7.04 (d, 1H, Har); 7.31 (s, 1H, Har).

General Procedure for Polymerization. The solution radical copolymerization was carried out at 60 °C in Pyrex glass tubes that were sealed under reduced pressure after three freeze−thaw cycles.

Poly(*N*,*N*-dimethylacrylamide-*co*-2-methoxy-5-*tert*-butoxycarbonylaminostyrene) (6). Copolymer **6** was obtained from the radical copolymerization of freshly distilled *N*,*N*-dimethylacrylamide (8.9 g, 90.0 mmol) with 2-methoxy-5-*tert*-butoxycarbonylaminostyrene **14** (2.5 g, 10.0 mmol) in the presence of AIBN (164 mg, 1.0 mmol) as an initiator in DMF (450 mL). After 20 h polymerization, the solvent was evaporated under reduced pressure. The residue was dissolved in MeOH (5 mL) and precipitated in ether (1000 mL) to yield a white powder (8.5 g, 74.5%).^1H NMR (DMSO-d_6) (δ ppm): 1.45 (broad, CH_2); 2.77 (broad, CH); 3.32 (NMe_2); 3.60 (broad, OMe); 6.77 (broad, Har); 7.18 (broad, Har); 8.99 (broad, Har). IR ($CHCl_3$) (υ_{max}): 3485.7, 3292.3, 2974.0, 2933.5, 1716.5, 1624.0, 1541.0, 1506.3, 1458.1, 1419.5, 1404.1, 1363.6, 1242.1, 1159.1, 1095.5, 1056.9, 1026.1, 752.2. The molar ratio of monomer units was determined from ^1H NMR chemical shifts of methoxy protons to *N*,*N*-dimethylamide protons as (styrene/DMAA = 1/8). The molecular weight was estimated by GPC analysis: $M_n = 11\,750$.

Poly(*N*,*N*-dimethylacrylamide-*co*-2-hydroxy-5-*tert*-butoxycarbonylaminostyrene) (7). Copolymer **7** was obtained from the radical copolymerization of freshly distilled *N*,*N*-dimethylacrylamide (569 mg, 5.74 mmol) with 2-hydroxy-5-*tert*-butoxycarbonylaminostyrene **22** (150 mg, 0.64 mmol) in the presence of AIBN (10.5 mg, 0.064 mmol) as an initiator in DMF (28.7 mL). After 20 h polymerization, the solvent was evaporated under reduced pressure. The residue was dissolved in MeOH (1 mL) and precipitated in ether (300 mL) to yield a white powder (286.7 mg, 39%).^{1}H NMR (DMSO-d_6) (δ ppm): 1.44 (broad, CH_2); 2.2−2.8 (broad, CH); 3.32 (NMe_2); 6.64 (broad, Har); 7.05 (broad, Har); 8.91 (broad, Har). IR ($CHCl_3$) (υ_{max}): 3446.6, 3296.1, 2976.0, 2938.5, 1716.5, 1622.0, 1541.0, 1506.3, 1456.2, 1434.9, 1404.1, 1365.5, 1249.8, 1163.0, 1095.5, 1056.9, 754.1. The molar ratio of monomer units was determined from ^{1}H NMR chemical shifts of aromatic protons to *N*,*N*-dimethylamide protons as (styrene/DMAA = 1/5). The molecular weight was estimated by GPC analysis: $M_n = 7080$.

General Procedure for Diazotization Reaction. To an ice-cooled (0 °C) solution of the protected copolymer **7** (20 mg) in methylene chloride (1 mL) was added dropwise trifluoroacetic acid (1 mL), and the solution was stirred for 0.5 h. After evaporation of the solvent and trifluoroacetic acid under reduced pressure, water (1 mL) was added to the residue. The stirred mixture was protected from light, and tetrafluoroboric acid (42%, 10 μL) was added, followed by a solution of $NaNO_2$ (5 mg, 7×10^{-5} mol) in water (300 μL) in (20 μL) portions over 0.5 h at 0 °C. The reaction was followed by UV spectroscopy. We observed the appearance of a band at 355 nm characteristic of the diazonium species. The addition of $NaNO_2$ was stopped when no more formation of the diazonium was observed in UV. Water was evaporated under reduced pressure at −78 °C, and the residue was redissolved in methanol. The methanol solution was filtered on a microfilter (Millipore 5.0 μm) and stored at −30 °C, in the dark.

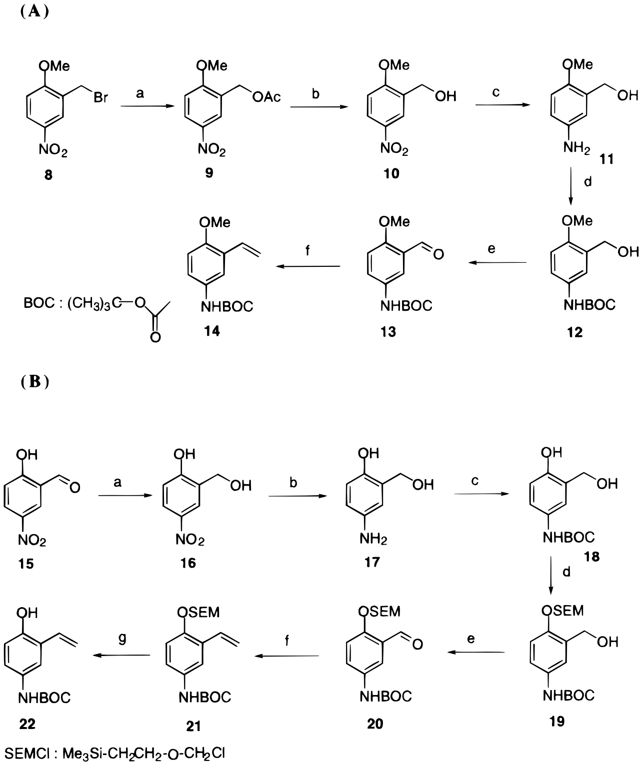
General Procedure for Diazo Species Formation. To 500 μL of the diazonium solution in water, protected from light, was added dropwise NaOH (100 μL, 0.1 M solution in water) at 0 °C, and the reaction was followed by UV spectroscopy. We observe the formation of the diazo species progressively at 260 nm and the simultaneous disappearance of the diazonium absorption band at 350 nm.

General Procedure for Azidation Reaction. A 5 mL aliquot of copolymer **1** (300 mg) solution in water (prepared as decribed above) was neutralized with $NaHCO_3$ until pH 7−8. A solution of NaN_3 (20 mg, 3×10^{-4} mol) in water (100 μL) was added dropwise at 25 °C. The reaction was followed by UV which showed an instantaneous disappearance of the diazonium absorption at 316 nm. Water was evaporated under reduced pressure, and the residue was redissolved in methanol (2 mL) and filtered. After evaporation of the solvent, deionized water was added, and the solution was dialyzed for 3 days. The product was then freeze-dried. A white solid was obtained (291 mg, 97%) which showed an absorption at 2111.9 cm^{-1} in FT-IR characteristic of the azido group.

Casting and Fixation of Photoreactive Copolymers. A cold solution (0 °C) of the photoreactive copolymer **1** (20 mg) in methanol (9.2 mL) was spread on PET film (diameter, 15 mm; thickness, 1 μm) in the dark. The film was air-dried for 3 h and vacuum-dried for 8 h and then irradiated with UV light using a Toshiba lamp (H-400P; 400 W) at a distance of 30 cm (intensity, 2.2 mW/cm^2) at different times (30, 60, 90, 120, 150, 180, and 240 s). The samples were then thoroughly washed with water and dried overnight under vacuum. Samples for ESCA measurements were further washed with deionized water. The photochemical fixation of copolymers **2**−**5** onto PET film was carried out similarly to **1**. ESCA spectra were recorded to verify the photochemical fixation.

Physical Measurements. ^{1}H NMR spectra were recorded on a JEOL GX-270 (Tokyo, Japan) in $CDCl_3$ with $(CH_3)_4Si$ as internal standard. FT-IR spectra were recorded on a Shimadzu FT-IR-8200A (Kyoto, Japan). UV absorption spectra were measured on a Ubest-30 UV/vis spectrophotometer (JASCO, Tokyo, Japan). GPC analyses were carried out with a HPLC-8020 instrument (Tosoh, Tokyo, Japan). The columns (Tosoh TSKgel 3000 and 5000) were calibrated with narrow weight distribution poly(ethylene glycol) standards. Electron spectroscopy for chemical analysis (ESCA) spectra were recorded on Shimadzu ESCA 750 (Kyoto, Japan). The C 1s, O 1s, and N 1s spectra deconvolution in subpeaks was computer-aided processed. Static advancing contact angles toward deionized water were measured by a Kyowa contact angle meter (Kyowa Kagaku Co, Ltd., Tokyo, Japan) at 25 °C by the sessile drop method.

Scheme 1. Syntheses of (A) 2-Methoxy-5-*tert*-butoxycarbonylaminostyrene (14)[a] and (B) 2-Hydroxy-5-*tert*-butoxycarbonylaminostyrene (22)[b]



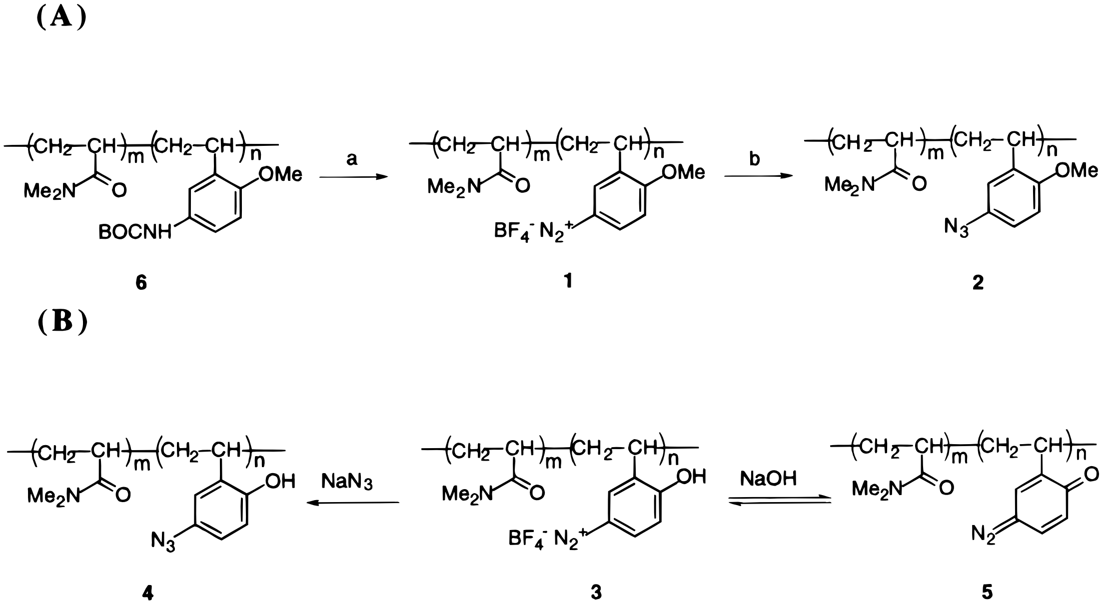
[a] Reagents and conditions: (a) 5.0 equiv of AcONa, NaI (cat), CH_3CN, HMPT (10%), reflux, quant; (b) 10.0 equiv of K_2CO_3, MeOH, 25 °C, quant; (c) H_2, Pd−C (10%), MeOH, 25 °C, quant; (d) 1.1 equiv of BOC_2O, 2.0 equiv of NEt_3, 25 °C, quant; (e) 1.6 equiv of PDC, CH_2Cl_2, 25 °C, 89%; (f) 1.6 equiv of methyltriphenylphosphonium bromide, 1.5 equiv of *n*-BuLi, THF, −78 to −10 °C, 91%. [b] Reagents and conditions: (a) 2.0 equiv of $NaBH_4$, MeOH, −20 °C, quant; (b) H_2, Pd−C (10%), EtOAc, 25 °C; (c) 1.2 equiv of BOC_2O, NEt_3, THF, 25 °C, 74% overall; (d) 0.79 equiv of NaH, 0.79 equiv of SEMCl, DMF, 0 °C, 91%; (e) 15.0 equiv of MnO_2 95%; (f) 1.9 equiv of methyltriphenylphosphonium bromide, 1.8 equiv of *n*-BuLi, THF, −78 to 25 °C, 88%; (g) 5.0 equiv of *n*-Bu_4NF, THF, 80 °C, 54%.

Results

The concept described in this paper, by which the surface modification of a polymer substrate is achieved, is based on the photoreactivity of aryldiazonium salts, paradiazoquinone, and arylazido species (Figure 1). Under appropriate UV light irradiation, these three photoreactive groups generate a highly reactive species, namely arylcation, arylcarbene, and arylnitrene, respectively, that are able to covalently bind a wide range of neighboring groups.[5,13,17] Photoreactive hydrophilic copolymers of DMAA and suitably polysubstituted styrene bearing these photosensitive groups on the styrene moiety were prepared and photografted on PET films. The chemical structures of these photoreactive copolymers are presented in Figure 2A.

Monomers Synthesis and Preparation of Precursor Copolymers 6 and 7. Figure 2B shows the structures of copolymers **6** and **7** which were designed and prepared as precursors of the photoreactive copolymers described above. The copolymers **6** and **7** were

Scheme 2. (A) Synthesis of Copolymers 1 and 2[a] and (B) Preparation of Copolymers 4 and 5



[a] Reagents and conditions: (a) CF_3COOH, CH_2Cl_2, 0 °C, then $NaNO_2$ aqueous, HBF_4, 0 °C; (b) $NaHCO_3$ (pH 7−8), NaN_3 excess, 25 °C, in the dark.

prepared by radical copolymerization of DMAA with respective monomers 2-methoxy-5-*tert*-butoxycarbonylaminostyrene **14** and 2-hydroxy-5-*tert*-butoxycarbonylaminostyrene **22**, respectively. The *tert*-butyl carbamate (BOC) protection of the arylamino group was introduced during the monomer synthesis and removed with trifluoroacetic acid after copolymerization.[18] Subsequently, the generated amine was transformed into the photoreactive species as will be discussed later.

A detailed description of monomers syntheses will be described below. Scheme 1A outlines the preparation of the methoxystyrene intermediate **14** from the commercially available bromide **8**. Thus, displacement of the bromide in **8** with sodium acetate led to the acetoxy derivative **9** (100%). Subsequent methanolysis with potassium carbonate furnished the expected alcohol **10** (100%). The hydrogenation of the nitro group using Pd−C catalyst (10% Pd contents), which proceeded smoothly producing the amino alcohol **11**, was followed by selective protection of the amino group with di-*tert*-butyl dicarbonate (BOC_2O), leading efficiently to the requisite benzylic alcohol **12** (quantitative yield overall). Oxidation of benzylic alcohol **12** was achieved by using pyridinium dichromate (PDC)[19] in methylene chloride and proceeded smoothly to give the desired aldehyde **13** with 89% yield. The generation of the styrene double bond has been performed by a Wittig reaction on the aldehyde **13**, which afforded the desired BOC-protected aminostyrene derivative **14** with 91% yield. Scheme 1B summarizes the synthesis of the hydroxystyrene derivative **22**. Selective reduction of the commercially available nitro aldehyde **15** with sodium borohydride produced the nitrophenol **16** (100%). Subsequent catalytic hydrogenation of the nitro group led to the expected aminophenol **17,** which was not isolated, but selectively protected as a crude material to afford the hydroxyphenol **18** with 74% overall yield, after purification on silica gel chromatography. The selective protection of the phenol **18** as a 2-(trimethylsilyl)-ethoxymethoxy ether (SEM ether) under the standard conditions[18] proceeded smoothly to give the compound **19** with 91% yield. Oxidation of the benzylic alcohol with MnO_2 furnished the required aldehyde **20** (82% yield). The generation of the styrene double bond by a Wittig reaction proceeded smoothly, leading to the styrene **21** with 88% yield. Finally, the deprotection of SEM ether was performed with $^nBu_4NF$, resulting in the desired styrene **22** with 54% yield.

Preparation of Photoreactive Copolymers. The photoreactive copolymer **1** bearing a diazonium species was prepared by deprotection of carbamate groups of copolymer **6** with excess trifluoroacetic acid, followed by diazotization with aqueous sodium nitrite at 0 °C, in the dark (Scheme 2A).

Figure 3 represents the UV spectra corresponding to the preparation of photoreactive copolymer **1**. Figure 3a shows the UV spectrum of the BOC-deprotected copolymer. The diazotization of amino groups generated progressively the corresponding diazonium species which show a characteristic absorption band at 316 nm (Figure 3b). For assessment of the presence and the photoreactivity of the diazonium species, the photoreactive copolymer was irradiated with UV light (254−313 nm); a complete photodecomposition of the diazonium species occurred upon irradiation, as demonstrated by the disappearance of the corresponding absorption at 316 nm (Figure 3c).

The photoreactive center in the copolymer **1** appeared to decompose slowly in water or methanol solution. After standing for 20 h at 25 °C, 30% decomposition was observed by UV spectroscopy.

The azido-derivatized copolymer **2** was prepared by reaction of the photoreactive copolymer **1** with excess sodium azide, at 25 °C in the dark (Scheme 2A). The diazonium absorption at 316 nm disappeared completely after addition of sodium azide. The copolymer **2** was characterized by FT-IR spectroscopy which displayed an azido absorption band at 2111.9 cm^{-1} that disappeared after photolysis (Figure 4).

The diazonium-derivatized copolymer **3** (Figure 2) was prepared similarly to the copolymer **1**. The removal of BOC protection in copolymer **7**, followed by diazotization, afforded the photoreactive copolymer **3**. Figure 5 summarizes the UV spectral characteristics of the

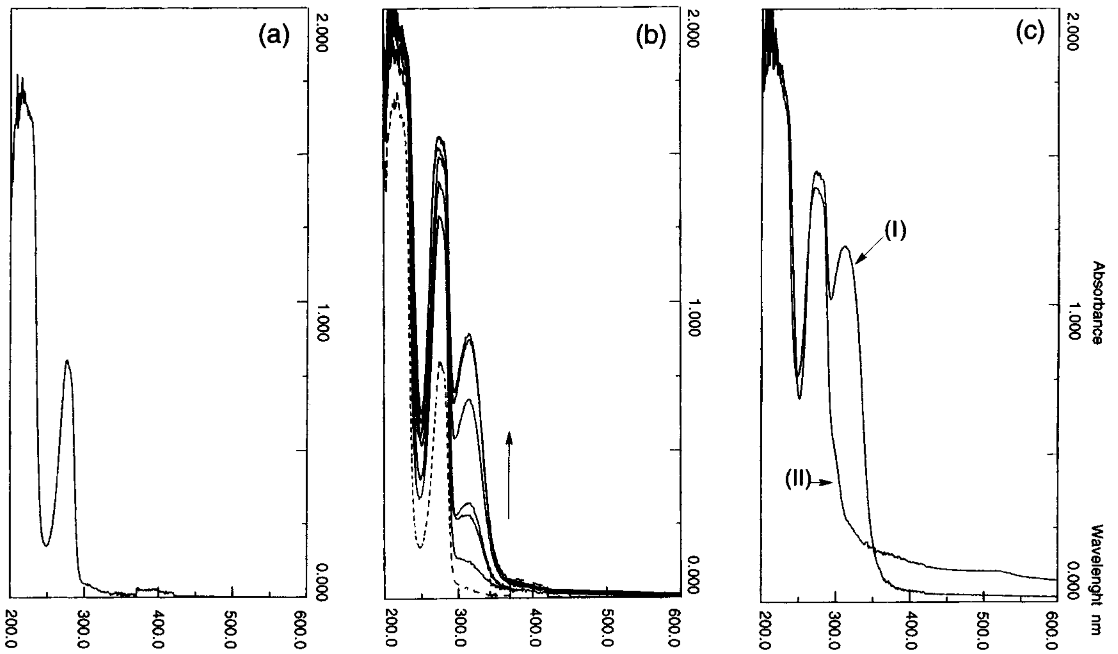


Figure 3. UV absorption spectral change of poly(dimethylacrylamide-*co*-2-methoxy-5-diazoniumstyrene) **(1)**: (a) BOC-deprotected copolymer **6**; (b) progressive diazonium formation; (c) curve I, copolymer **1**, curve II, UV-irradiated copolymer **1**.

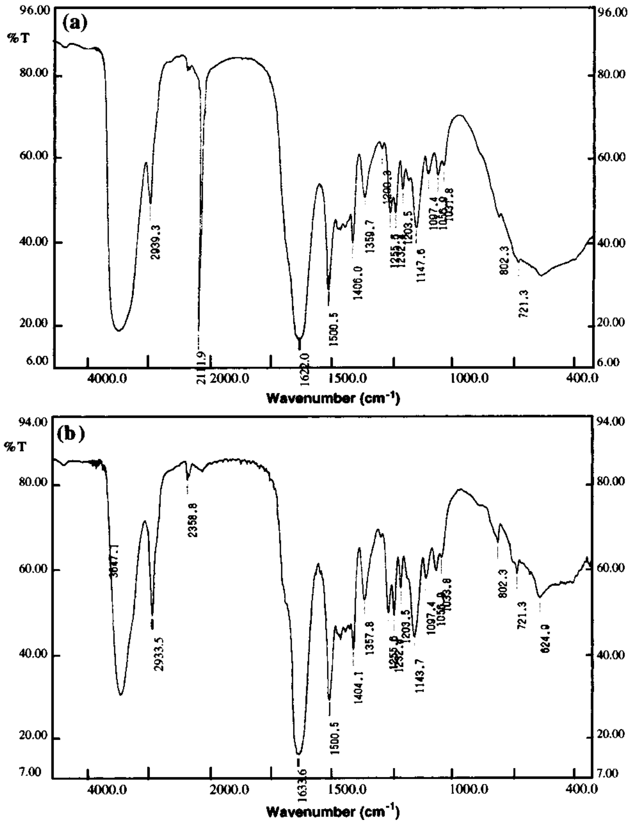


Figure 4. FT-IR spectra of (a) poly(dimethylacrylamide-*co*-2-methoxy-5-azidostyrene) (**2**) and (b) after UV light irradiation at 254–313 nm for 60 s.

photoreactive copolymers **3** and **5**. Curve I in Figure 5a corresponds to the copolymer **3** with an absorption band at 355 nm ascribed to the diazonium species. The assessment of the diazonium group and its photoreactivity was performed by UV irradiation of the copolymer. As shown in curve II of Figure 5a, a complete photodecomposition of the diazonium group occurred upon irradiation. The copolymer **3** was also decomposed similarly to **1** in methanol or water.

The conversion of a *p*-hydroxybenzenediazonium salt into the corresponding *p*-diazocyclohexadienone is a well-known equilibrium process, which is shifted toward the diazo species at pH > 11. As shown in Scheme 2B, copolymer **5** with the diazo photoreactive group was obtained by reaction of the diazonium-containing copolymer **3** with sodium hydroxide. Figure 5b shows the UV spectrum related to the formation of the diazo-containing copolymer **5**. The diazonium absorption band at 355 nm decreased gradually in favor of the formation of the diazo species with a characteristic absorption at 260 nm. The UV irradiation of copolymer **5** has shown a complete disappearance of the diazo at 260 nm. The azido-derivatized copolymer **4** was prepared similarly to the copolymer **2**, with an azido absorption at 2050.2 cm^{-1} in FT-IR spectroscopy. The photoreactive copolymers (**1**–**5**) contained a tertiary amide group in their molecules that were confirmed by FT-IR spectroscopy, which displayed the two amide bands at 1685.7 and 1635.5 cm^{-1}, indicating that the various treatments of copolymers **6** and **7** did not induce the hydrolysis of amide linkage of DMAA unit.

Photochemical Fixation. The photoreactive copolymers **1**–**5** were cast on PET films from methanol solution and vacuum-dried prior to UV irradiation and then thoroughly washed with water. Figure 6 shows the ESCA spectra of nontreated PET surface (a) and those of photochemically treated surfaces (b–f). For the nontreated surface, a negligible N 1s signal and three peaks in the C 1s spectrum, ascribed to hydrocarbon-like C at 285 eV, C–O at 287 eV, and C=O at 289 eV, whose intensities were close to the expected ones, were observed.

Irrespective of the photoreactive copolymers, substantial changes in the ESCA spectra were observed as a result of photoirradiation. Parts b and d of Figure 6 show the ESCA spectra of the irradiated diazonium-containing copolymers **1** and **3**. For both spectra, a neat increase in nitrogen signals were observed (N/C = 0.005

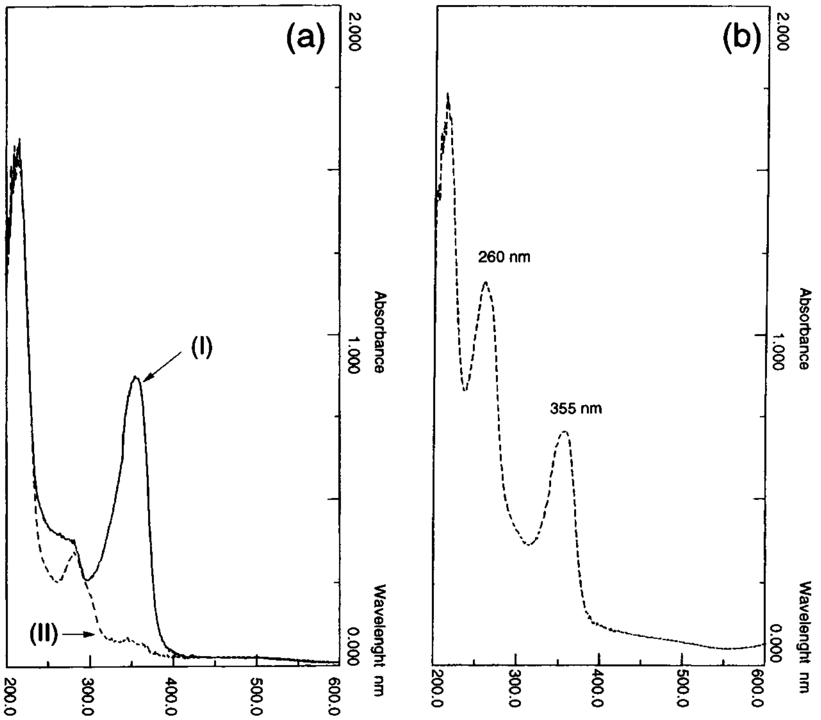


Figure 5. UV absorption spectral change of poly(dimethylacrylamide-*co*-2-hydroxy-5-diazoniumstyrene) (**3**): (a) curve I, copolymer **3**, curve II, UV-irradiated copolymer **3**; (b) formation of the diazo-derivatized copolymer **5**.

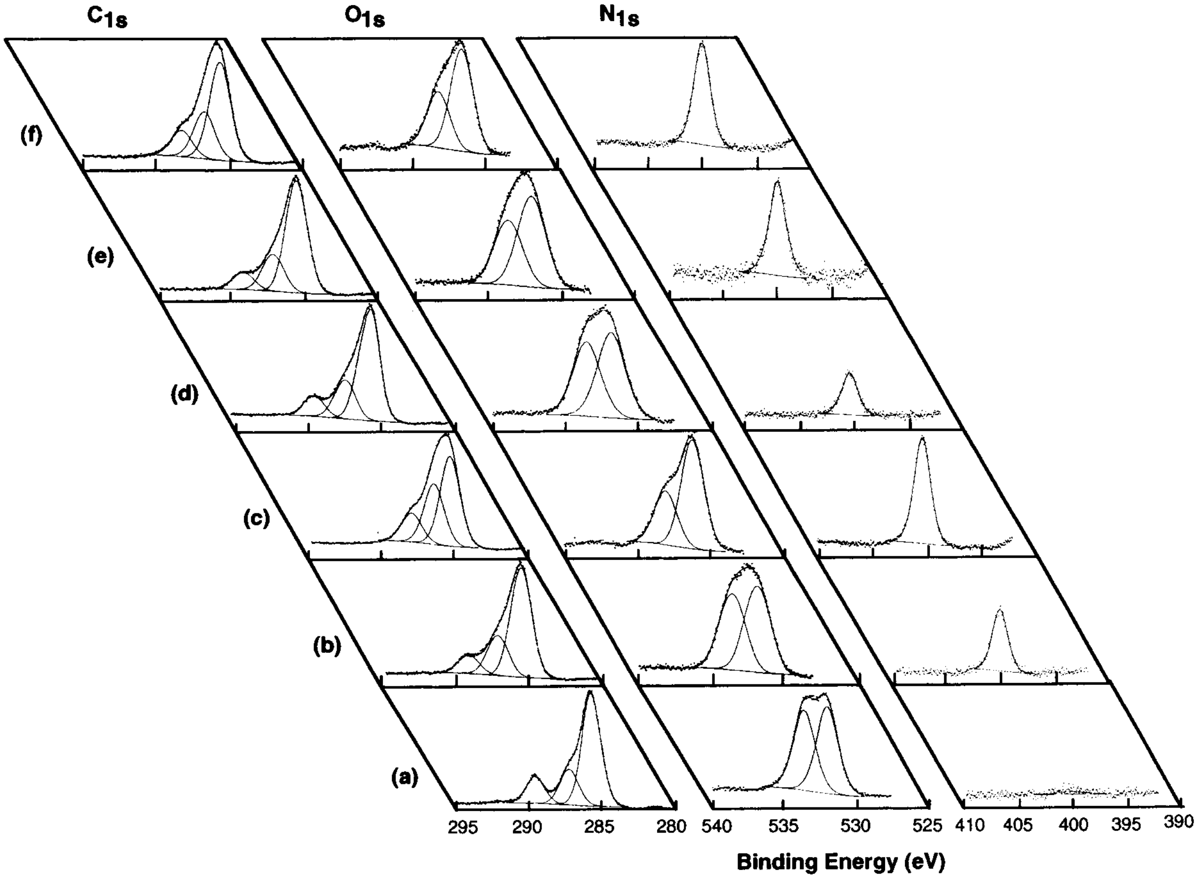


Figure 6. ESCA spectra of (a) nontreated PET surface, (b) **1**-treated surface, (c) **2**-treated surface, (d) **3**-treated surface, (e) **5**-treated surface, and (f) **4**-treated surface.

for nontreated surface, N/C = 0.082 for **1**-treated surface, and N/C = 0.062 for **3**-treated surface). The relative intensities of the signals ascribed to carbonyl C=O and C−O + C−N to total C 1s were as follows: 11.0% at 289 eV and 23.8% at 287 eV for **1**-treated surface and 11.9% at 289 eV and 22.7% at 287 eV for **3**-treated surface, respectively. C=O/C−O + C−N peak area ratios were close to the theoretical values. This indicates that the copolymers **1** and **3** were photochemically fixed on the PET surface (Table 1). The water

Table 1. Relative Intensities of Deconvoluted C 1s, N 1s, and O 1s ESCA Spectra[a]

sample	C 1s (%)			C=O/C−O + C−N	N 1s/C 1s	O 1s/C 1s
	C−O + C−N	C=O	C−C			
PET[b]	20.3 (20.0)	15.2 (20.0)	64.4 (60.0)	0.75 (1.00)	0.005 (0.0)	0.34 (0.40)
1	23.8 (36.7)	11.0 (16.3)	65.2 (46.9)	0.46 (0.44)	0.08 (0.16)	0.26 (0.18)
2	33.9 (38.8)	16.2 (16.3)	49.9 (44.9)	0.48 (0.42)	0.17 (0.18)	0.19 (0.18)
3	22.7 (33.3)	11.9 (15.2)	65.4 (51.5)	0.52 (0.45)	0.06 (0.15)	0.27 (0.18)
4	27.5 (36.4)	15.5 (15.1)	56.9 (48.5)	0.56 (0.41)	0.16 (0.18)	0.19 (0.18)
5	22.1 (33.3)	10.2 (15.2)	67.7 (51.5)	0.46 (0.45)	0.08 (0.15)	0.25 (0.18)

[a] Theoretical values are in parentheses. [b] Nontreated PET.

Table 2. Water Contact Angles of Nontreated and Photochemically Treated Surfaces

sample	water contact angle (deg)	
	advancing	receding
PET[a]	68 ± 2.9	59 ± 3.0
1	52 ± 2.3	32 ± 1.6
2	37 ± 1.6	26 ± 1.3
3	52 ± 2.2	28 ± 1.4
4	45 ± 1.9	27 ± 2.1
5	49 ± 2.1	30 ± 1.5

[a] Nontreated PET.

contact angle measurements showed that PET surface became quite hydrophilic. The receding contact angles were 59 ± 3.0° for nontreated PET and 32 ± 1.6° and 28 ± 1.4° for the copolymer **1**-treated and copolymer **3**-treated surface, respectively (Table 2).

Similarly to the copolymer **3**, UV irradiation of copolymer **5**-coated PET surface resulted in the ESCA spectral changes shown in Figure 6e. The N 1s signal appeared, and the C 1s subpeaks corresponding to C=O and the sum of two components, C−O + C−N, with the relative intensities (10.2% at 289 eV and 22.1% at 287 eV), respectively, were observed. Taken together with the C=O/C−O + C−N peak area ratio of 0.46 (theoretical 0.45), this shows that the copolymer **5** was fixed onto PET surface. The receding water contact angle was 30 ± 1.5°, showing that PET surface became more hydrophilic after treatment.

Parts c and f of Figure 6 present the ESCA spectra of the PET surface coated with the copolymers **2** and **4**. Upon irradiation, a markedly high elemental ratios of N/C were observed (0.167 for **2**-treated surface and 0.155 for **4**-treated surface), which were very close to the calculated values (0.184 and 0.182, respectively). The intensities of the subpeaks ascribed to carbonyl C=O and the sum of two components, C−O + C−N, in the C 1s spectrum, which were (16.2% at 288 eV and 33.9% at 286 eV for **2**-treated PET) and (15.5% at 288 eV and 27.5% at 286 eV for **4**-treated PET), reflected well those of the casting materials and were close to the calculated values (Table 1). The water wettability measurement showed that PET surface became more wettable after the photografting. The receding water contact angles were 26 ± 1.3° for **2**-treated PET and 27 ± 2.1° for **4**-treated PET. These results indicate that the copolymers **2** and **4** were effectively fixed on the PET surface. The time dependency of the photografting of copolymers **1**−**5** upon irradiation was assessed. Figure 7 depicts the contact angle dependency on photoirradiation time for the five differents photoreactive copolymer systems.

For each copolymer **1**−**5** we observed that the contact angle exhibited a constant value after 60 s irradiation. This result indicates that the photochemical reactions proceeded within 60 s; surface photografting and intra- and intermolecular cross-linking occurred on the surface during this lapse of time with no further change upon prolonged irradiation period.

Discussion

The growing need for providing surface functional properties such as adhesivity, hydrophilicity, nonfouling nature, and biocompatibility has led to the development of various methods for polymer surface modification with minimum alteration of bulk properties. The interfacial interaction between proteins or cells and polymeric surfaces under aqueous environment may be controllable by modulation of the surface chemical composition and structure of polymers.[1−3] For example, a nonionic, hydrophilic polymer-grafted surface reduces protein adsorption as well as cell adhesion. The essential feature of photochemically driven surface modification using photoreactive polymers, the photolysis of which forms covalent bonding between the surface and the polymer, is that reaction proceeds at room temperature and in air only at the photoirradiated region during photoirradiation, producing a relatively durable graft layer with micron-order dimensional precision.[6−11] This gives us considerable advantages over conventional coating or electron-beam surface modification methods.

To extend the scope of surface-processing technology based on arylazido photochemistry, we investigated a new photoinduced surface modification method utilizing the photochemistry of aryldiazonium and aryldiazo groups. Upon UV light irradiation these groups generate a highly reactive arylcarbocation and arylcarbene, respectively, that are capable of forming a covalent bond with neighboring atoms.[13] Similarly, the azido group is photolyzed into a nitrene species that binds covalently a wide range of neighboring groups. The photochemistry of diazonium, diazo, and azido groups has been extensively used to produce heavily cross-linked polymers and found a broad application in photoresist coatings and photoaffinity labeling of membrane receptors and enzymes.[14−17] When a polymer material derivatized with these groups is coated and irradiated on a substrate, intramolecular cross-linking within absorbant copolymer and fixation of the absorbant copolymer on the surface occur. On the basis of this concept, we attempted the surface modification of PET substrate with these photoreactive polymers.

We prepared the photoreactive hydrophilic copolymers **1**−**5** by radical copolymerization of DMAA and polysubstituted styrene monomers, which were obtained in high yields by a multistep synthesis. The selection of the substituents in the monomers was done on the rational basis of the type of photochemistry to be applied. Aryldiazonium molecules are thermally unstable and light sensitive. Their stability may be enhanced by the introduction of a para-electron-donating substituent such as hydroxy or methoxy groups. Styrene

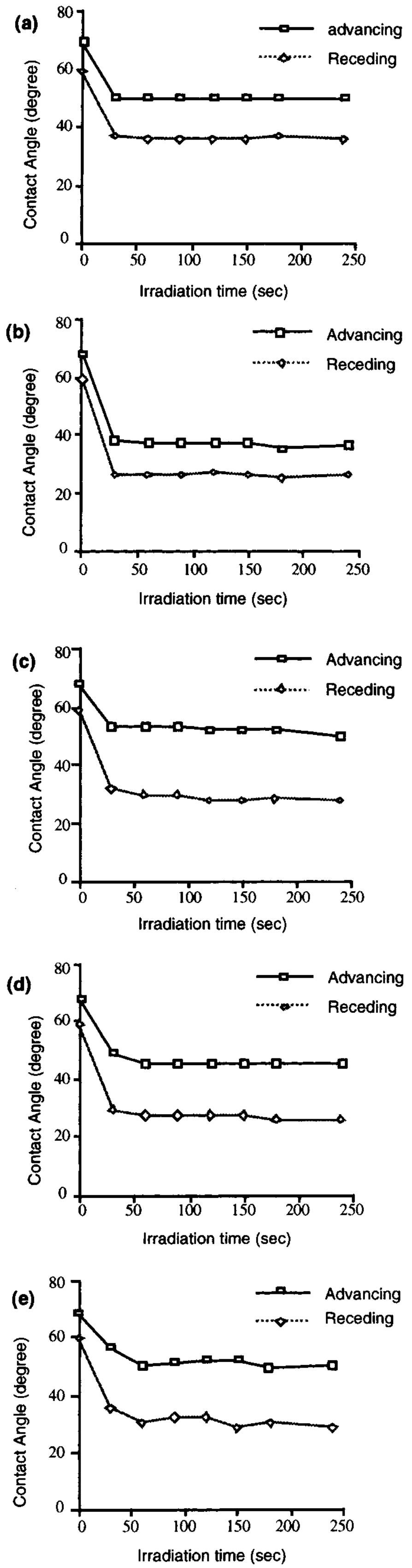


Figure 7. Contact angle−photoirradiation time relationships for the copolymers **1**−**5**: (a) copolymer **1**, (b) copolymer **2**, (c) copolymer **3**, (d) copolymer **4**, (e) copolymer **5**. Irradiation conditions: PET film, thickness = 1 μm, UV (H-400P; 400 W), intensity (2.2 mW/cm^2), distance = 30 cm.

derivative **14** contained a methoxy substituent in the para position to the diazonium for providing the required stability. On the other hand, the other styrene derivative **22** was substituted with a hydroxy group in the para position to the diazonium. The hydroxy substituent not only was designed for increasing the stability of the diazonium but also served as a precursor of the diazo group. An increase in the hydrophilicity of the styrene monomer was also aimed through its hydrophilic property. The photoreactivity of the copolymers in solution was demonstrated by UV and FT-IR spectroscopies. Within 60 s of irradiation with UV light, the photoreactive copolymers were completely photolyzed. This was further confirmed after photografting by the water contact angle measurements which showed that the contact angle remained constant for surfaces irradiated at longer times. The PET surface became hydrophilic after photoirradiation. However, relatively high advancing contact angles were observed for copolymers **1**, **3,** and **5**. The coating of very thin layers of diazonium- and diazo-containing copolymers on PET film was less uniform than azido-containing copolymers. This difference in the coating ability is very probably due to the physicochemical properties of the diazonium and azido groups. The highly polar nature of diazonium confers a different interaction with PET surface than the neutral azido-containing polymers. There exists also a hysteresis effect between the advancing and receding contact angles, suggesting that a surface reorganization occurs upon immersion into water. The hydrophobic main chain of the polymer, which is a hydrocarbon chain, dominates at the outermost surface in the dry state, whereas after immersion into water, the hydrophilic amide groups become oriented at the water−polymer interface. The general trend shows that, within 30−60 s photoirradiation, surface grafting occurred regardless of the photoreactive group. The photochemical fixation of the copolymers on PET surface was clearly demonstrated by XPS analyses as shown in Figure 6. Even upon vigorous washing, little spectral difference was observed, indicating that surface covalent bonding of the copolymer occurred, irrespective of the type of copolymer. Interestingly, the azido-derivatized photochemistry appears to be more suitable for the surface modification of PET than diazonium or diazo groups in terms of comparable irradiation time required for photografting, better coating ability, lower contact angle, and lesser degree of hysteresis. Thus, in addition to the azido group as a photoreactive species, aryldiazonium- and aryldiazo-derivatized copolymers are utilized in surface modification technology. As schematically shown in Figure 1, such photografting proceeds via carbocation and carbene as a reactive intermediate.

Conclusion

We have demonstrated the photochemical surface modification of PET film using aryldiazonium-, aryldiazo-, and arylazido-derivatized copolymers. A common feature shared by these three photoreactive groups is that, although these groups generate different species of reactive intermediates, surface grafting of copolymers derivatized with these groups occurred at almost the same extent. Since photochemical reaction occurs only at the irradiated portion of a surface, regional dimensional photoinduced fixation may be achieved. Finally, it is hoped that the described technology will be useful for surface functionalization without deleterious effects on the polymers and find versatile application in various industrial fields including biomedical devices. We are currently working in upgrading the blood compatibility of artificial hearts by the surface process technology developed here.

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