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Surface functionalization of PEEK films using photochemical routes

Catherine Henneuse-Boxus, Eric Dulière, Jacqueline Marchand-Brynaert *

Laboratoire de Chimie organique de Synthèse, Université catholique de Louvain, Bâtiment Lavoisier, place Louis Pasteur 1, B-1348 Louvain-la-Neuve, Belgium

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Abstract

Two photochemical routes have been considered for the surface topologically defined functionalization of poly(ether ether ketone) (PEEK) films, based, respectively, on the covalent coupling of molecules protected with a photoclivable group (indirect way A), and on the photografting of various azide derivatives (direct way B). (4,5-Dimethoxy-2-nitrophenyl)methyl succinamate **3** could be coupled to the PEEK–OH film surface, under wet-chemistry conditions, but in rather low yield. 4-Azido-benzoic acid **9**, 4-azido-tetrafluorobenzoic acid **6** and *N*-butyl-*N*′-(4-azidophenyl)thiourea **8** were grafted on the PEEK and PEEK–OH films surface, under mild photochemical conditions, in moderate to good yields. Attempts to obtain patterned surfaces with 4-azido-benzoic acid **9** and sodium 5-azido-naphthalene-1-sulphonate **10**, under microlithographic conditions, failed.

Keywords: PEEK film; PEEK–OH film; Photografting; Aryl azide; XPS analysis

1. Introduction

The controlled surface modification of synthetic polymers has been in great demand over the last years for the development of new biomaterials [1]. It appeared recently that the surface heterogeneity is an important feature, strongly influencing the cellular adhesion on biomaterials [2]. Heterogeneity concerns the alternance of physicochemical [3] and biochemical [4] properties located on defined domains of the surface, as well as the alternance of microstructures resulting from different topographies [5] and chain mobilities [6].

The micropatterning of surfaces actually develops according to three main strategies, namely the processing of block copolymers or polymer blends [7], the formation of self-assembled monolayers on gold [8], and the photochemical surface modification of homopolymers, most usually via microlithographic methods [9].

In the course of our studies devoted to the chemical modification of the poly(ether ether ketone) (PEEK) film [10–13], we envisaged the photochemical approach as a possible way to attach functionalized molecules on topologically defined regions of the polymer surface. For this purpose, we considered two routes depicted in Fig. 1. The first route A (two-step process) was based on the uniform covalent derivatization of the film surface with molecules bearing a photocleavable protecting group, followed by the photolysis of the protected functions by UV exposure through a photolithographic mask [14]. The second route B (one-step process) consisted the irradiation, through a photolithographic mask, of the film surface previously coated with molecules equipped with a photoactivable group [15]; after rinsing, only the exposed regions should be covalently grafted with the reagents. As photocleavable and photoactivable groups, we selected respectively the *ortho*-nitrobenzyloxycarbonyl motif [16], and the aromatic azide function [17].

* Corresponding author. Tel.: +32-10-47-27-40; fax: +32-10-47-41-68.

E-mail address: marchand@chor.ucl.ac.be (J. Marchand-Brynaert).

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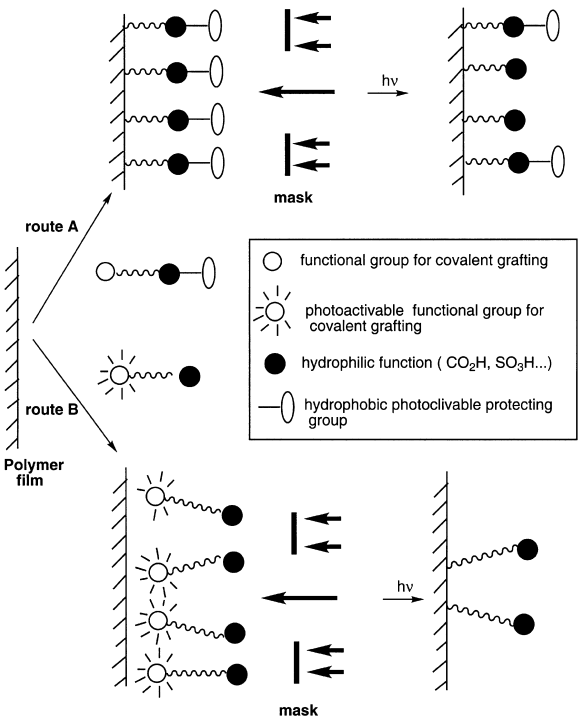

Fig. 1. Selected strategies for the photochemical functionalization of the PEEK film surface.

This paper reports the results we obtained by exploring the photochemical functionalization of PEEK (native and/or reduced films), and our attempts to reach controlled heterogeneities. To our knowledge, only a few papers deal with the surface photochemistry of PEEK [18–22]; they mainly describe unspecific oxidations.

2. Experimental

2.1. Chemistry in solution

2.1.1. Materials and methods

The reagents were of analytical grade and purchased from Aldrich (Bornem, Belgium) and Acros Chimica (Beerse, Belgium). The solvents were dried and distilled as usual. Merck silica gel 60 (70–230 mesh ASTM) was used for the column-chromatographies. The R_F values were determined on Merck TLC 60 F_{254} plates with a thickness of 0.2 mm (visualization with UV).

Melting points are uncorrected (digital melting point apparatus, Electrothermal, UK). The IR spectra were taken on a Perkin–Elmer 1710 instrument and calibrated with polystyrene. The NMR spectra were recorded on Varian Gemini-200 and Varian Gemini-300 spectrometers with tetramethylsilane as internal standard. The mass spectra were obtained with a Finnigan MAT TSQ-70 instrument. The microanalyses were performed at the University College (London, UK).

2.1.2. 1-(Bromomethyl)-4,5-dimethoxy-2-nitrobenzene (**2**)

To a solution of 6-nitroveratraldehyde **1** (2.51 g, 9.53 mmol) in methanol (35 ml) was added $NaBH_4$ (0.474 g, 12.3 mmol, 1.3 eq.) in methanol (15 ml). After 1 h of stirring at 20°C, water was added (20 ml), and the solution was extracted with CH_2Cl_2 (5 × 20 ml). The organic layers were dried over $MgSO_4$, concentrated and chromatographed on silica gel (eluent: CH_2Cl_2) to furnish (4,5-dimethoxy-2-nitrophenyl)methanol as a yellow solid (2 g, 99% yield). R_F (SiO_2; CH_2Cl_2) = 0.17; IR (KBr) ν 3499, 2850, 1618, 1581, 1517, 1355, 1270, 1072 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.71 (t, 1H), 3.97 (s, 3H), 4.02 (s, 3H), 4.97 (d, 2H), 7.18 (s, 1H), 7.72 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) ppm 56.4, 62.7, 108.3, 111.1, 132.3, 139.9, 148.1, 153.9. The alcohol (0.371 g, 1.8 mmol) dissolved in benzene (48 ml) was treated, under argon atmosphere, with pyridine (three drops) and PBr_3 (90 μl, 0.26 g, 0.9 mmol) in benzene (2 ml), added dropwise with a syringe through a rubber-stopper. The mixture was stirred at 20°C for 24 h; then, water was added (10 ml). The organic layer was washed twice with water, dried over $MgSO_4$ and concentrated to furnish the bromide **2** (0.474 g) which was recrystallized from toluene (0.423 g of orange crystals, 88% yield). R_F (Al_2O_3; CH_2Cl_2–cyclohexane, 70:30) = 0.77; IR (KBr) ν 3071, 1612, 1585, 1527, 1368, 1277, 1064 cm^{-1}; ^1H-NMR (300 MHz, $CDCl_3$) δ 3.97 (s, 3H), 4.0 (s, 3H), 4.88 (s, 2H), 6.95 (s, 1H), 7.68 (s, 1H); ^{13}C-NMR (50 MHz, $CDCl_3$) ppm 29.9, 56.5, 108.7, 113.9, 127.4, 140.4, 149.1, 153.3.

2.1.3. (4,5-Dimethoxy-2-nitrophenyl)methyl succinamate (**3**)

A solution of **2** (0.382 g, 1.4 mmol), succinamic acid (0.173 g, 1.4 mmol), and potassium fluoride (0.171 g, 3 mmol) in acetone (5 ml) and methanol (2 ml) was heated with stirring at 60°C, under argon atmosphere and in the dark, for 72 h. After adding water (20 ml), the mixture was extracted with ethyl acetate. The organic phase was dried over $MgSO_4$, concentrated, and purified by column chromatography on silica gel (elution with CH_2Cl_2–ether, 80:20) to give **3** (0.391 g, 90% yield) as an orange powder. R_F (SiO_2; CH_2Cl_2) = 0.31; m.p. = 156.7–157.9°C; MS (EI) m/e 312 (M^+), 196, 167, 151, 136, 100; IR (KBr) ν 3430, 2943, 1721, (ester), 1686 (amide), 1580, 1525, 1364, 1171 cm^{-1}; ^1H-NMR (300 MHz, $CDCl_3$) δ 2.60 (t, 2H, J = 6.6 Hz), 2.81 (t, 2H, J = 6.6 Hz), 3.96 (s, 3H), 4.03 (s, 3H), 5.35 (s, 1H, NH), 5.55 (s, 2H), 5.56 (s, 1H, NH), 7.05 (s, 1H), 7.72 (s, 1H); ^{13}C-NMR (50 MHz, DMSO-d6) ppm 28.91, 29.53, 56.22, 56.42, 62.40, 108.37, 110.95, 126.82, 139.53, 147.95, 153.52, 172.21 (C=O ester), 172.72 (C=O amide).

*2.1.4. (4,5-Dimethoxy-2-nitrophenyl)methyl N-(4,4′-dimethoxybenzhydryl) succinamate (**4**)*

A solution of **3** (0.15 g, 0.48 mmol) and 4,4′-dimethoxybenzhydrol (59 mg, 0.24 mmol) in acetic acid (2 ml), containing one drop of H_2SO_4 as the catalyst, was stirred overnight at 20°C, under argon atmosphere and in the dark. The crude mixture was poured into ice-cold water (15 ml). The precipitate was filtered off, dissolved in CH_2Cl_2 (20 ml) and washed with 5% $NaHCO_3$. The aqueous phase was extracted with CH_2Cl_2. The organic layers were gathered, dried over $MgSO_4$ and concentrated to furnish crude **4** which was purified by column chromatography on neutral alumina (elution with CH_2Cl_2–ether, 80:20). Pure **4** (0.069 g, 53% yield) was recovered as a yellow solid. R_F (Al_2O_3; CH_2Cl_2) = 0.35; m.p. = 152.2–153.1°C; MS (FAB$^+$) m/e = 539.3 ($M+1$), 227; IR (KBr) ν 3454, 2935, 2852, 1726 (C=O ester), 1647 (C=O amide), 1582, 1517, 1460, 1422, 1163 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 2.61 (t, 2H, J = 6.3 Hz), 2.83 (t, 2H, J = 6.3 Hz), 3.76 (s, 6H), 3.89 (s, 3H), 3.95 (s, 3H), 5.55 (s, 2H), 6.06 (d, 1H, J = 7.5 Hz), 6.20 (d, 1H, J = 7.5 Hz), 6.78 (d, 4H, J = 8.6 Hz), 6.95 (s, 1H), 7.09 (d, 4H, J = 8.6 Hz), 7.71 (s, 1H); ^{13}C-NMR (50 MHz, $CDCl_3$) ppm 29.56, 31.02, 55.23, 56.75, 56.34, 56.58, 63.37, 108.22, 110.05, 114.02, 127.55, 128.36, 133.83, 139.54, 148.16, 153.97, 158.93, 170.09 (C=O amide), 172.32 (C=O ester); anal. calcd. (%) for $C_{28}H_{30}N_2O_9 \cdot H_2O$ (556.5): C, 60.37; H, 5.75; N, 5.03 – found (%): C, 60.62; H, 5.73; N, 4.69.

*2.1.5. 4-Azido-tetrafluorobenzoic acid (**6**)*

A solution of methyl pentafluorobenzoate **5** (1.305 ml, 2 g, 8.757 mmol) and NaN_3 (0.609 g, 9.37 mmol) in acetone–water (18/7 ml) was refluxed in the dark during 8 h. After the addition of water (25 ml), the mixture was extracted three times with ether. The organic layer was dried over $MgSO_4$ and concentrated to give methyl 4-azido-tetrafluorobenzoate (2.168 g, 99% yield) as a white powder. R_F (SiO_2; CH_2Cl_2–cyclohexane, 50:50) = 0.45; IR (film) ν 2969, 2926, 2133 (N_3), 1735 (C=O ester), 1648, 1481, 1331, 1292, 1269 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.98 (s); ^{13}C-NMR ($CDCl_3$, 75 MHz) ppm 52.94, 107.52, 123.3, 140.3, 140.5, 145.1, 145.3, 159.54; ^{19}F-NMR ($CDCl_3$, 300 MHz) δ −150.27 (m), −139.07 (m); MS (EI) m/e = 249 (M$^+$), 221, 206, 190, 178, 162, 93, 59. A solution of the previous ester (1.698 g, 6.819 mmol) and NaOH (1.556 g, 38.53 mmol) in H_2O (8 ml) and methanol (30 ml) was stirred for 24 h at 20°C in the dark. The mixture was acidified to reach pH 1 with 2 N HCl, then extracted three times with $CHCl_3$ (3 × 30 ml). Drying over $MgSO_4$ and concentration gave the acid **6** (1.564 g, 98% yield) as a white solid. R_F (SiO_2; *i*-PrOH) = 0.37; IR (KBr) ν 2855, 2134 (N_3), 1702 (CO_2H), 1641, 1484, 1263 cm^{-1}; ^{13}C-NMR (75 MHz, $CDCl_3$) ppm 106.23, 124.5, 140.4, 140.6, 145.97, 146.1, 163.84 (CO_2H); ^{19}F-NMR (300 MHz, $CDCl_3$) δ −149.8 (m), −136.2 (m); MS (EI) m/e = 235.1 (M$^+$), 207.1, 204, 162.1, 151.1, 131.1, 113.1, 93.1, 45.

*2.1.6. N-Butyl-N′-(4-azidophenyl) thiourea (**8**)*

A solution of 4-azidophenyl isothiocyanate **7** (50 mg, 0.28 mmol) and *n*-butylamine freshly distilled (27.8 μl, 20.5 mg, 0.28 mmol) in benzene (2.5 ml) was stirred for 2 h 30 min at 20°C in the dark. After concentration, the residue was dissolved in CH_2Cl_2 and washed with 1.2 N HCl, then with water. Drying and concentration furnished the thiourea **8** (70 mg, 100% yield) as a yellow solid. R_F (SiO_2; CH_2Cl_2) = 0.40; IR (film) ν 3275, 3213, 3051, 2951, 2867, 2411, 2254, 2115 (N_3), 1542, 1500, 1289, 1259 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.92 (t, 3H, J = 7.3 Hz), 1.30 (m, 2H), 1.58 (m, 2H), 3.62 (td, 2H), 5.85 (br s, 1H, NH), 7.07 (d, 2H, J = 8.7 Hz), 7.20 (d, 2H, J = 8.7 Hz), 7.64 (br s, 1H, NH); ^{13}C-NMR (75 MHz, $CDCl_3$) ppm 13.67, 20.04, 31.02, 45.28, 120.55, 127.02, 132.95, 139.19, 180.86 (C=S); MS (EI) m/e = 250.2 ($M+1$), 249.2 (M$^+$), 221.2, 107.1, 106.1, 79.1, 57.1, 43.1.

2.2. Chemistry on polymer films

2.2.1. Materials and methods

Amorphous PEEK film (Stabar K200; thickness of 25 μm) received from ICI (UK) was surface reduced according to Refs. [23, 24]. The amount of hydroxylated monomer units was determined by XPS considering the C=O/C–O and the O=C/O–C atomic ratios in the fine structures of the C_{1s} and O_{1s} peaks. The percentage of surface reduction was about 80% for the samples used in this study. The PEEK–OH disks (1.12 cm^2) and squares (4 cm^2) used for the surface derivatizations were cut off a large PEEK–OH sample (rectangle of 30 cm × 15 cm).

Water used for the rinsing of the modified polymer samples was of HPLC grade and obtained with a Milli-Q system (Millipore, Bedford, MA). The other solvents were of analytical grade and purchased from Acros Chimica (Beerse, Belgium).

The X-ray photoelectron spectroscopy (XPS) was performed with an SSI X-probe (SSX-100/206) spectrometer from Fisons (Surface Science Laboratories, Mountain View, CA), equipped with an aluminium anode (10 kV, 20 mA) and a quartz monochromator. The direction of photoelectron collection made angles of 55° and 75° with the normal to the sample and the incident X-ray beam, respectively. The electron flood gun was set at 6 eV. The vacuum in the analysis chamber was 2.5×10^{-7} Pa. The binding energies of the peaks were determined by setting the C_{1s} component due to carbon bound only to carbon and hydrogen at a value of 284.8 eV. The peak areas were determined using linear background subtraction. Intensity ratios were converted into atomic concentration ratios by using the SSI ESCA

8.3D software package. The XPS experimental technique was fully described in Refs. [11,24].

For the photoactivation experiments, we used RPR lamps (Rayonet Preparative Reactor equipped with three lamps) of 254 nm or 300 nm (21 and 24 W, respectively). The distance between the lamps and the polymer films was 15 cm. For the microelectronic experiments, we used a mercury vapour lamp (KASPER), HBO type (short arc) of 350 W, covering a wave length domain of 250–750 nm. The mask displayed parallel slits of 50 μm, spaced at a distance of 130–150 μm.

The SEM images were obtained with a HITACHI-570 microscope (electron gun set at 15 KV). The samples were coated with a Au/Pd layer of 10 nm of thickness, and placed at an angle of 45°.

The fluorescence microscopy analyses used a POLYVAR apparatus with two different filters (BP 330–380 nm and BP 390–450 nm).

2.2.2. Preparation of PEEK–ester

PEEK–OH film (disk of 1.2 cm of diameter) was immersed at room temperature in a solution of succinamate **3** (0.35 g) in acetic acid (11.7 ml, concentration of **3** = 3% w/v) containing sulphuric acid (0.058 g, concentration of H_2SO_4 = 0.5% w/v). After 72 h of stirring in the dark, the sample was taken off the solution and rinsed as follows: 2 × 10 min in HOAc, 4 × 10 min in H_2O, 2 × 10 min in acetone. The sample was dried at 60°C under vacuum. The blank sample was prepared as before, but by omitting the catalyst (H_2SO_4) in the reactive solution. XPS analysis: PEEK–ester: C_{1s}, 86.11% (284.8 eV); O_{1s}, 13.69% (533.23 eV); N_{1s}, 0.20% (399.9 eV) – blank: C_{1s}, 83.71%, O_{1s}, 16.28%.

From the experimental N/C atomic ratio of 0.0023, we calculated the level of surface functionalization considering the following monomer unit: $(\text{PEEK} + \text{PEEK–OH})_x + (\text{PEEK–ester})_y$, or $(C_{19}O_3)_x + (C_{32}N_2O_9)_y$ where $x + y = 1$. For $x = 0.98$ and $y = 0.02$, the N/C value is $2 \times 0.02/(19 \times 0.98) + (32 \times 0.02) = 0.0021$ (expt. = 0.0023), corresponding to about 2% of grafting.

2.2.3. Preparation of PEEK–Ph–CO_2H

The PEEK–OH film was embedded between two glass rings (home-made equipment) to furnish an insert with an internal diameter of 1 cm. A solution of 4-azidobenzoic acid **9** in benzene (2%, w/v) was prepared in the dark; 40 μl of this solution was deposited into the polymer insert, and the solvent was evaporated. This coated insert was irradiated with three RPR lamps at 254 or 300 nm for 6 h, then rinsed as follows: 3 × 10 min with benzene, 3 × 10 min with MeOH, 3 × 10 min with acetone. The polymer sample was air dried before XPS analysis. The native PEEK film was similarly treated. The blank samples (PEEK–OH and PEEK) were obtained as previously, but by omitting the UV irradiation; they were stored for 6 h in the dark before rinsing. XPS analysis of PEEK–Ph–CO_2H obtained from PEEK–OH (+**9**) irradiated at 300 nm (Table 1, entry 2): C_{1s}: 284.8 eV (82.78%); O_{1s}: 533.23 eV (16.51%); N_{1s}: 399.90 eV (0.70%).

From the experimental N/C atomic ratio of 0.0084, we calculated the level of surface functionalization considering the following monomer unit: (PEEK + PEEK–OH)$_x$ + (PEEK–Ph–CO_2H)$_y$, or $(C_{19}O_3)_x + (C_{26}NO_5)_y$, where $x + y = 1$. For $x = 0.83$ and $y = 0.17$, the N/C value is $0.17/(19 \times 0.83) + (26 \times 0.17) = 0.0084$.

The surface morphology of the samples (photografting on PEEK–OH and PEEK films) was examined by SEM (images not shown).

2.2.4. Preparation of PEEK–Ph(F_4)–CO_2H

The PEEK–OH and PEEK films were treated as above using 4-azido-tetrafluorobenzoic acid **6** as reagent; the irradiation time was 5 min at 254 nm, or 30 min at 300 nm. XPS analysis of PEEK–Ph(F_4)–CO_2H from PEEK–OH (+**6**) irradiated at 254 nm (Table 1, entry 7): C_{1s}: 284.81 eV (49.21%), 286.34 eV (16.73%), 287.41 eV (4.74%), 288.84 eV (2.57%), 291.58 eV (5.67%); O_{1s}: 533.39 eV (10.50%), 532.24 eV (4.77%), 531.35 eV (2.15%), 540.08 eV (0.73%); N_{1s}: 400.36 eV (0.79%); F_{1s}: 687.85 eV (2.12%).

From the experimental N/C and F/C atomic ratios of, respectively, 0.0100 and 0.0268, we calculated the level of surface functionalization considering the following monomer unit: $(\text{PEEK} + \text{PEEK–OH})_x + (\text{PEEK–Ph}(F_4)CO_2H)_y$, or $(C_{19}O_3)_x + (C_{26}NO_5F_4)_y$, where $x + y = 1$. For $x = 0.80$ and $y = 0.20$, the N/C value is $0.20/(19 \times 0.8) + (26 \times 0.2) = 0.0098$. For $x = 0.87$ and $y = 0.13$, the F/C value is $4 \times 0.13/(19 \times 0.87) + (26 \times 0.13) = 0.0261$.

2.2.5. Preparation of PEEK–Ph–NHC(S)NH–But

The PEEK–OH and PEEK films were treated as above using the azide **8** as reagent (concentration in benzene: 0.2% or 2%, w/v); the irradiation times were 5 and 17 h at 300 nm. XPS analysis of PEEK–Ph–NHC(S)NH–But obtained from PEEK–OH(+**8**, 0.2%) irradiated at 300 nm for 5 h (Table 1, entry 15): C_{1s}: 284.72 eV (79.87%); O_{1s}: 533.23 eV (18.02%); N_{1s}: 400.13 eV (1.60%); S_{2p}: 164.29 eV (0.51%).

From the experimental N/C and S/C atomic ratios of respectively 0.0200 and 0.00638, we calculated the level of surface functionalization considering the following monomer unit: $(\text{PEEK} + \text{PEEK–OH})_x + (\text{PEEK–Ph–NHC(S)NH–But})_y$, or $(C_{19}O_3)_x + (C_{30}N_3O_3S)_y$, where $x + y = 1$. For $x = 0.86$ and $y = 0.14$, the N/C value is $3 \times 0.14/(19 \times 0.86) + (30 \times 0.14) = 0.0204$. For $x = 0.87$ and $y = 0.13$, the S/C value is $0.13/(19 \times 0.87) + (30 \times 0.13) = 0.00636$.

Table 1
Surface analyses by XPS

Entry	Surface chemistry		XPS data (atomic composition)					Atomic ratios×100 (% derivatization)		
	Polymer film	Conditions (conc. in benzene, *hv*, time)	C (%)	O (%)	N (%)	F (%)	S (%)	N/C	F/C	S/C
1	PEEK–OH	**9** (2%), 254 nm, 6 h	83.31	16.69	0.0	–	–	0.0 (0%)	–	–
2	PEEK–OH	**9** (2%), 300 nm, 6 h	82.78	16.51	0.70	–	–	0.84 (17%)	–	–
3	PEEK–OH	**9** (2%), dark, 6 h	84.21	15.79	0.0	–	–	0.0 (0%)	–	–
4	PEEK	**9** (2%), 254 nm, 6 h	84.81	15.19	0.0	–	–	0.0 (0%)	–	–
5	PEEK	**9** (2%), 300 nm, 6 h	82.28	17.14	0.58	–	–	0.70 (14%)	–	–
6	PEEK	**9** (2%), dark, 6 h	84.98	15.02	0.0	–	–	0.0 (0%)	–	–
7	PEEK–OH	**6** (2%), 254 nm, 5 min	78.92	18.15	0.79	2.12	–	1.0 (20%)	2.69 (13%)	–
8	PEEK–OH	**6** (2%), 300 nm, 30 min	80.99	17.76	0.51	0.74	–	0.63 (12.5%)	0.91 (4.5%)	–
9	PEEK–OH	**6** (2%), dark, 5 min	77.56	21.49	0.51	0.44	–	0.66 (4%)	0.57 (3%)	–
10	PEEK–OH	**6** (2%), dark, 30 min	79.70	18.86	0.36	1.08	–	0.45 (3%)	1.35 (6.5%)	–
11	PEEK	**6** (2%), 254 nm, 5 min	82.41	14.98	0.76	1.86	–	0.92 (19%)	2.26 (11%)	–
12	PEEK	**6** (2%), 300 nm, 30 min	80.77	18.70	0.0	0.55	–	0.0 (0%)	0.68 (3%)	–
13	PEEK	**6** (2%), dark, 5 min	84.76	14.96	0.0	0.28	–	0.0 (0%)	0.33 (1.5%)	–
14	PEEK	**6** (2%), dark, 30 min	82.79	16.92	0.0	0.28	–	0.0 (0%)	0.34 (1.6%)	–
15	PEEK–OH	**8** (0.2%), 300 nm, 5 h	79.87	18.02	1.60	–	0.51	2.0 (14%)	–	0.64 (13%)
16	PEEK–OH	**8** (0.2%), 300 nm, 17 h	81.82	15.40	2.34	–	0.45	2.86 (20%)	–	0.55 (11%)
17	PEEK–OH	**8** (0.2%), 300 nm, 5 h	83.01	14.80	1.72	–	0.48	2.07 (14%)	–	0.58 (12%)
18	PEEK–OH	**8** (0.2%), dark, 17 h	79.35	20.65	0.0	–	0.0	0.0 (0%)	–	0.0 (0%)
19	PEEK	**8** (0.2%), 300 nm, 5 h	80.80	16.99	1.82	–	0.38	2.25 (15.5%)	–	0.47 (9.5%)
20	PEEK	**8** (0.2%), 300 nm, 17 h	79.16	20.84	0.0	–	0.0	0.0 (0%)	–	0.0 (0%)

2.2.6. Microlithographic experiments

The PEEK–OH film was embedded between two glass rings as before. A solution of sodium 5-azido-naphthalene-1-sulphonate **10** in benzene (0.5%, w/v) was prepared; 40 μl of this solution was deposited into the polymer insert, and the solvent was evaporated. The sample was taken off the glass rings and placed in contact with the microlithographic mask. Irradiation with the microlithographic lamp was performed for 1, 2, 5, 10, 50, or 180 min, then the polymer film was rinsed as follows: 3×10 min with methanol, 2×10 min with water, 2×10 min with acetone. After air drying, the samples were examined by fluorescence microscopy, and analyzed by XPS. The same experiments were realized with 4-azido-benzoic acid **9**. The surface morphologies were analyzed by SEM, in both cases (photographting of **9** and **10**; images not shown).

3. Results and discussion

3.1. Route A

We have previously demonstrated the synthetic versatility of the PEEK–OH film [23] for the covalent surface derivatization of the polymer [10–12]. This key-intermediate, readily prepared by the surface reduction of PEEK film with $NaBH_4$ in hot DMSO, displayed about 80% of hydroxylated monomer units from the XPS analysis [24]. The hydroxyl groups of the polymer benzhydryl motifs could be substituted with primary amides dissolved in acetic acid containing 0.5% of sulphuric acid as the catalyst [11,12]. We decided thus to apply this wet-chemistry method for the covalent fixation of (4,5-dimethoxy-2-nitrophenyl) methyl succinamate **3** (Fig. 2).

Compound **3** is a succinamic acid derivative which carboxyl function has been masked by a photoremovable ester [25,26] derived from 1-(bromomethyl)-4,5-dimethoxy-2-nitrobenzene **2** (Fig. 2). The 4,5-dimethoxy-2-nitrobenzyl moiety has been selected because its λ_{max} is above 350 nm [27]; moreover, the efficiency of this photosensitive group has been well established, in medicinal chemistry, for the fast controlled release of physiologically active compounds [28], and in parallel chemical synthesis on solid support [29]. The required precursor was prepared in two steps from 6-nitroveratraldehyde **1**, by reduction into alcohol and substitution with PBr_3 [27]. The alkylation of succinamic acid with **2** was performed in acetone–methanol, in the presence of potassium fluoride; the ester **3** was purified by column chromatography and well characterized by the usual spectroscopies (see experimental).

The reactivity of **3** has been tested by a model coupling reaction with 4,4′-dimethoxybenzhydrol, under the experimental conditions recommended for the PEEK–OH surface derivatization. The secondary amide **4** (model of the functionalized PEEK–OH monomer unit), was obtained in reasonable yields, and fully characterized as usual (see experimental) (Fig. 2). Thus, the reaction of **3** with the PEEK–OH film could be envisaged. However, the results were somewhat disappointing; only a low level of surface derivatization was reached. The best conditions we found correspond to the immersion of the PEEK–OH film into acetic acid containing 3% (w/v) of the amide **3** and 0.5% (w/v) of H_2SO_4, for three days at room temperature (Fig. 3). The resulting film sample, called PEEK–ester was analyzed by XPS: from the experimental N/C atomic ratio of 0.0023, we concluded that about 2% of the monomer units have fixed the molecule **3**. Such a low level of functionalization could result from the progressive dissolution of the chemically modified interface. This gravely handicaps the feasibility of route A (Fig. 1) which has been therefore abandoned.

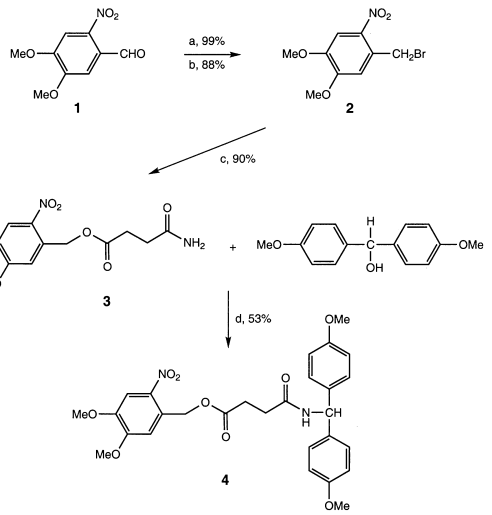

Fig. 2. Chemistry in solution (route A).

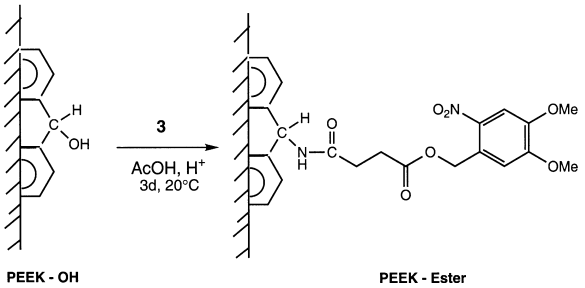

Fig. 3. Chemistry on polymer film (route A).

3.2. Route B

Aromatic azides constitute the more popular class of photoactivable reagents [30]. They were originally developed for the photoaffinity labelling of biological receptors [31,32]: a modified ligand, incorporating the arylazide moiety, is used to form the receptor–ligand complex; upon irradiation, a reactive nitrene intermediate is produced that will bond covalently to aminoacid residues of the active site. More recently, aromatic azides were used for the surface modification of polymers by photografting with spacial control [33]. Interesting applications were developed in the grafting of biologically active molecules which improved the hemocompatibility of polyurethanes [34].

The photochemistry of arylazides is somewhat complicated and not totally understood [35,36]. The singlet nitrenes generated upon irradiation, by loss of nitrogen, could rearrange and/or perform insertion reactions into all kinds of C–H and X–H bonds (X = heteroatom); such reactions are thus totally unselective. Therefore, we considered the PEEK–OH film, as well as the native PEEK material, for the photografting of 4-azido-benzoic acid **9**, 4-azido-tetrafluorobenzoic acid **6**, and *N*-butyl-*N*′-(4-azidophenyl)thiourea **8** (Fig. 4).

4-Azido-tetrafluorobenzoic acid **6** was prepared in two steps from methyl pentafluorobenzoate **5**: aromatic nucleophilic substitution with sodium azide was followed by ester saponification to furnish **6** in almost quantitative yield [37]. *N*-butyl-*N*′-(4-azidophenyl)thiourea **8** was quantitatively obtained by addition of *n*-butylamine on 4-azidophenyl isothiocyanate **7** [38,39].

The feasibility of photografting on PEEK supports was first controlled without patterning mask. After deposition of a benzene solution of 4-azido-benzoic acid **9** on the PEEK and PEEK–OH films, and evaporation of the solvent, the coated polymers were exposed to three UV lamps of 24 W at 254 nm, or 300 nm, for 6 h (the

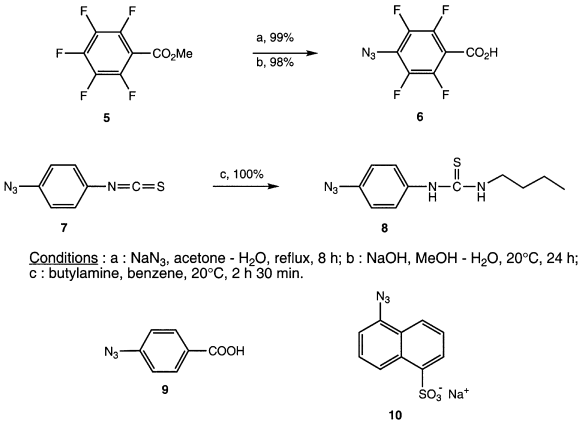

Fig. 4. Chemistry in solution (route B).

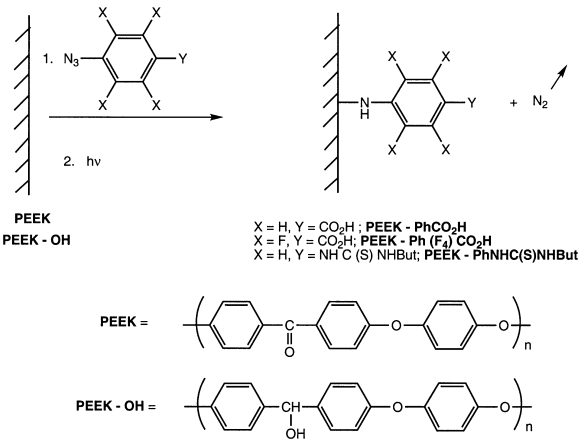

Fig. 5. Chemistry on polymer film (route B).

λ_{max} of compound **9** is 269 nm, with a shoulder at 290 nm). After appropriate washing, the polymer films were analysed by XPS (Table 1). The samples treated at 254 nm (entries 1 and 4), and the blank samples maintained in the dark (entries 3 and 6) did not contain nitrogen atoms. On the other hand, the samples irradiated at 300 nm showed nitrogen atoms in their surface atomic composition (entries 2 and 5); this result is consistent with the absorption spectrum of **9**. The label grafting could be quantified considering the N/C atomic ratio: the PEEK–Ph–CO_2H films (Fig. 5) obtained from PEEK–OH and from PEEK displayed respectively 17% and 14% of derivatized manomer units.

In order to increase the level of surface grafting, we next considered the more reactive perfluoroazide **6** as the photoactivable reagent. As a matter of fact, fluorine substituents have been proved to slow down the rate of intramolecular rearrangements versus the rate of intermolecular insertion reactions of aryl nitrenes [30]. The PEEK–OH and PEEK films were coated with **6** and irradiated at 254 nm or 300 nm, for 5 min and 30 min respectively (the λ_{max} of compound **6** is 259 nm, with a shoulder at 300 nm). The various PEEK–Ph(F_4)–CO_2H samples obtained were analyzed by XPS (Fig. 5). The results listed in Table 1 showed the presence of nitrogen and fluorine atoms in significant amount on the PEEK–OH and PEEK samples treated at 254 nm (entries 7 and 11); this is in agreement with the absorption spectrum of **6**. The percentage of surface derivatization was about 20%, as calculated from the N/C atomic ratio. The PEEK–OH film treated at 300 nm was less grafted (entry 8), while the functionalization of PEEK film at 300 nm (entry 12) could not be detected considering the nitrogen incorporation (XPS limit of detection for this atom). Some physisorption of **6** was detected on PEEK–OH (entries 9 and 10), but not on the less polar PEEK (entries 13 and 14). The percentages of surface derivatization calculated from the F/C atomic ratios appeared

systematically lower than the ones obtained from the N/C atomic ratios. This could result from some degradation of the samples under X-ray bombardment; such phenomenon has been already mentioned in the case of perfluorinated polymers [40,41]. Fig. 6 gives a picture of the C_{1s} region of the XPS spectrum of PEEK–Ph(F_4)–CO_2H (entry 7); the presence of carboxyl– and C–F motifs [42] could be visible around 288–290 eV, corresponding to about 3.3% of the C_{1s} signal. This value is in agreement with an average of 15% of derivatized monomer units.

Also, we examined the grafting of azide **8** on which *n*-butylamine has been fixed (Fig. 4); this molecule represents a model for the grafting of biologically active compounds equipped with a spacer arm terminated by NH_2. The PEEK–OH and PEEK films were coated with **8** and irradiated with UV lamps at 300 nm for 5 h or 17 h (the two λ_{max} of **8** are 256 nm and 283 nm with a shoulder at 320 nm). The best results were obtained after 5 h of treatment: PEEK–OH (Table 1, entry 15) and PEEK (entry 19) displayed respectively 14% and 15% of grafting as determined from the N/C atomic ratios obtained by XPS. Similar values were calculated from the S/C atomic ratios. The same results were obtained when using 0.08 M (2%, w/v) or 0.008 M (0.2%, w/v) solutions of **8** for the coating (entry 17). We confirmed that the label fixation does not occur in the absence of light (entry 18). When the irradiation time was 17 h, the PEEK–OH film still displayed grafted molecules **8**, in 20% yield from the XPS N/C atomic ratio (entry 16), while the PEEK film appeared devoid of any substitution (entry 20); this could result from surface degradation upon prolonged irradiation.

The successful photografting of azides **6**, **8** and **9** led us to further consider the possibility of surface patterning by using a microlithographic technique. After coating of PEEK–OH film with 4-azido-benzoic acid **9** and irradiation with a microlithographic mercury vapour lamp of 350 W, through a mask with parallel slits of 50 μm, or without the mask, we did not obtain surface functionalization as evidenced by the absence of nitrogen atoms in the XPS spectra recorded for different exposition times (from 1 min to 3 h). In order to visualize a possible patterning, we then used sodium 5-azido-naphthalen-1-sulphonate **10** [43] (Fig. 4) as label in our microlithographic experiments. Indeed, after insertion, this strongly fluorescent compound should be easily detected by fluorescence microscopy [43]. Disappointingly, the label **10** could not be fixed on the PEEK–OH film, whatever the irradiation time applied; examination of the samples by fluorescence microscopy gave no visible signal, and the XPS analyses did not reveal the presence of nitrogen and sulphur atoms in the surface atomic composition. We speculated that surface degra-

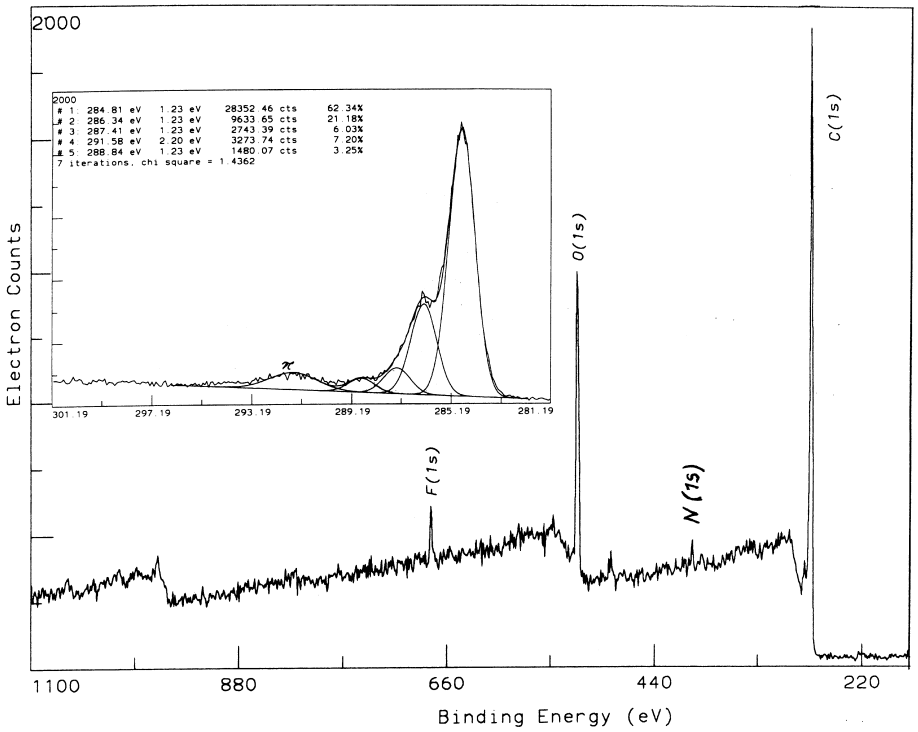

Fig. 6. XPS spectrum of PEEK–Ph(F_4)–CO_2H.

dation occurs under irradiation with a microlithographic lamp of high power and covering a large range of wavelengths (250–750 nm); after the usual washings, the modified polymer interface is most probably removed. Examination of the samples submitted to photolithography by scanning electron microscopy (SEM) clearly showed the presence of numerous surface defects and cracks, already visible after only 1 min of exposition. On the other hand, PEEK and PEEK–OH films remained almost smooth after UV irradiation at 300 nm under the mild conditions of the organic synthesis.

4. Conclusion

Under the usual wet-chemistry conditions, succinamate **3** equipped with a photoremovable protecting group was fixed on the PEEK–OH film surface in very low yield. Therefore, the preparation of patterned surfaces by photochemical deprotection of the so-called PEEK–ester film was not considered (Fig. 1, route A).

On the other hand, functionalized arylazides could be readily grafted on the PEEK and PEEK–OH films surface by UV irradiation (3×24 W) at 254–300 nm. The level of derivatization was in the range of 10% to 20%, from the XPS analysis. We previously calculated [1] that an interface domain of 10 atomic layers (XPS sampling depth) "covered" by 1 cm^2 of surface contains about 2000 pmol of monomer units; thus the surface photografting we reached corresponds to 200–400 pmol/cm^2 of fixed probes, i.e. a value significantly higher than those usually reported in the same type of experiments [44–46].

Generally, the yields of grafting were found to be slightly superior on the PEEK–OH film than on the native PEEK material. This could be explained by the fact that nitrene insertion reactions are more efficient when aliphatic C–H and O–H bonds are involved in the process. However, the difference between the two substrates is not very high and does not justify significant mechanistical discussions about the competition of nitrene insertion reactions towards non-productive rearrangement reactions. Also, the PEEK film is more susceptible to give photoactivated side reactions than the PEEK–OH film, due to the presence of benzophenone moieties in a large quantity. Indeed, benzophenone is a well-known photosensitizer, used in photolithography [47].

Under microlithographic irradiation, the surface of PEEK and PEEK–OH films were degraded, making impossible the patterning with functionalized molecules (Fig. 1, route B); most probably polymer chain cleavages occurred under such drastic irradiation conditions [18,48]. Thus, the use of light to perform selective reactions at the PEEK or PEEK–OH surface is limited to the mild conditions usually applied in synthetic organic chemistry.

Acknowledgements

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