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Surface amination of PEEK film by selective wet-chemistry

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Using 4,4′-dimethoxybenzhydrol as soluble mimic of the reduced poly(aryl ether ether ketone) (PEEK) monomer unit, we established the best experimental conditions to replace the hydroxyl group with an amine function, on the one hand, and to fix an amino acid residue, on the other hand. The selected strategies were then adapted to the surface functionalization of the PEEK-OH film obtained by reduction of the PEEK precursor. Thus, reaction with phenylcarbamate followed by LiOH hydrolysis gave the PEEK-NH_2 film characterized by θ_w, multiple internal reflection (MIR) and X-ray photoelectron spectroscopy (XPS). The PEEK-NH_2 was further derivatized with 1,3-propanesultone. Reaction of PEEK-OH with *N*′-(9-fluorenylmethoxycarbonyl) (*L*) glutamine followed by piperidine deprotection gave the PEEK-glutamine film characterized by θ_w, MIR and XPS. © 1998 Published by Elsevier Science Ltd. All rights reserved.

(Keywords: poly(ether ether ketone); PEEK film; surface wet-chemistry)

INTRODUCTION

Biocompatibilization[1] of synthetic polymers constitutes a major objective of our laboratory[2–5]. Pursuing our work devoted to the controlled surface modification of poly(aryl ether ether ketone) (PEEK) film[5–8], we report in this paper the preparation of aminated surfaces using the wet-chemistry approach[9,10].

Surface-modified PEEK films are used as new substrates for the *in vitro* cultivation of anchorage-dependent mammalian cells[11,12]. It was previously demonstrated that supports displaying free amine functions significantly improve the cellular adhesion[13–16]. This could result from a primarily non-specific electrostatic interaction between the negatively charged polysaccharides (proteoglycans) on the cell surface[17] and the positively charged aminated support at physiological pH. In addition, specific interactions could also take place, mediated by proteins adsorbed on the polar substrate. Interestingly, such interactions can be directed by the covalent grafting of peptide ligands containing the active sequence (Arg-Gly-Asp) of the extracellular matrix proteins[18–20]. In this respect, surface amine functions offer potential anchorage points for the covalent coupling of peptides, and other biologically active agents susceptible to interact with cell receptors.

We have already established the synthetic versatility of the PEEK-OH film obtained by surface reduction of the PEEK precursor[6]; the hydroxyl groups displayed on the surface could be easily substituted by weak nucleophilic reagents (anilines, amides) dissolved in acetic acid. These reactions led to the preparation of original modified PEEK films, the surface of which exposed fluorinated motifs[7] or carboxylic acids[8].

In the present work, we further make use of this substitution strategy for the introduction of (protected) amine functions, (i) directly on the benzhydryl motifs of the PEEK-OH film and (ii) *via* a short spacer arm derived from glycinamide or glutamine. Using 4,4′-dimethoxybenzhydrol **1** as a model compound[21], we first examined, in solution, the feasibility of the envisaged sequences of reactions. The best results were then adapted to the heterogeneous chemistry on polymer films.

The modified PEEK surfaces were characterized by water contact angle measurements, and by multiple internal reflection (MIR) and X-ray photoelectron spectroscopy (XPS) spectroscopies. Secondary ion mass spectrometry (SIMS) and fluorescence spectroscopies were punctually used.

EXPERIMENTAL

Chemistry on model compounds

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 and 40–63 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 u.v., potassium permanganate and ninhydrine).

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Melting points are uncorrected (digital melting point apparatus, Electrothermal, UK). The i.r. spectra were taken with a Perkin-Elmer 1710 instrument (infra red Fourier transformer spectrometer) and calibrated with polystyrene (1601 cm^{-1}). The n.m.r. spectra were recorded on Varian Gemini 200 and 300 spectrometers with tetramethylsilane as internal standard. The mass spectra were obtained with a Finnigan MAT TSQ-70 instrument (EI mode, electronic impact or FAB mode, fast atom bombardment, Xe, Ion Tech 8 kV). The microanalyses were performed at the University College of London (Dr Alan Stones).

*Preparation of compounds **3** (compounds **3a, 3b** and **3d** were prepared according to* [21]*)*

N*-(4,4′-Dimethoxybenzhydryl)phenylcarbamate **3e***). A solution of 4,4′-dimethoxybenzhydrol (0.6 g, 2.41 mmol, 1 equiv.) and phenylcarbamate (0.68 g, 4.81 mmol, 2 equiv.) in dry HOAc (15 ml) containing 1% of H_2SO_4 (catalyst) was stirred overnight at room temperature. The mixture was poured into ice-cold water (150 ml). The precipitate was filtered off, dissolved in CH_2Cl_2 (30 ml), washed with 5% $NaHCO_3$, dried over $MgSO_4$ and concentrated to furnish 0.73 g (82%) of **3e** as a white powder: m.p. 163–164.5°C (recrystallization from i-propanol); R_F (SiO_2, CH_2Cl_2) = 0.38; MS (EI) *m/e* = 363 (M^+), 269, 227; i.r. (KBr) ν 3321, 2836, 1733, 1702, 1611, 1539, 1512, 1252 cm^{-1}; ^1H n.m.r. ($CDCl_3$, 300 MHz) δ 7.2 (d, $J = 8.7$ Hz, 4 H), 7.42–7.1 (m, 5H), 6.8 (d, $J = 8.7$ Hz, 4 H), 5.96 (d, $J = 8.1$ Hz, 1 H), 5.68 (d, $J = 8.1$ Hz, 1 H), 3.8 (s, 3 H); ^{13}C n.m.r. ($CDCl_3$, 50 MHz) ppm 159.12, 153.75, 151.16, 133.92, 129.90, 128.42, 125.24, 121.5, 114.17, 58.12, 55.31; Anal. Calc. for $C_{22}H_{21}NO_4$ (363.41): C, 72.64; H, 5.78; N, 3.85—Found: C, 72.58; H, 5.81; N, 3.80%.

*Deprotection of compounds **3** (preparation of 4,4′-dimethoxybenzhydrylamine **4**)*

*Deprotection of **3b***. A solution of *N*-(4,4′-dimethoxybenzhydryl) chloroacetamide **3b** (0.102 g, 0.317 mmol) in dry pyridine (10 ml) was heated at 80°C for 1.5 h. Concentration under vacuum gave the corresponding pyridinium salt which was dissolved in aqueous NaOH (0.264 g NaOH, 20 equiv., in 50 ml H_2O). The mixture was stirred at 40°C for 17 h, then extracted with CH_2Cl_2 (3 × 10 ml). The organic phase was washed with water, dried over $MgSO_4$, concentrated and chromatographed on silica gel with hexane-ethyl acetate (1:1) to give 33 mg (42%) of pure amine **4** as a white powder.

Deprotection of **3e**. A solution of *N*-(4,4′-dimethoxybenzhydryl) phenylcarbamate **3e** (0.2 g, 0.55 mmol) and $LiOH.H_2O$ (0.118 g, 2.75 mmol, 5 equiv.) in CH_3CN-H_2O (1:1; 20 ml) was heated at 50°C for 3 h. After evaporation under vacuum, the residue was dissolved in CH_2Cl_2 (20 ml), washed with water, dried over $MgSO_4$ and concentrated to furnish 0.12 g (90%) of **4**: m.p. 59–60.5°C; R_F (SiO_2, CH_2Cl_2) = 0.12; MS (EI) *m/e* 243 (M^+), 227, 212, 135; ^1H n.m.r. ($CDCl_3$, 200 MHz) δ 7.27 (d, $J = 8.7$ Hz, 4 H), 6.85 (d, $J = 8.7$ Hz, 4 H), 5.12 (s, 1 H), 3.77 (s, 6 H), 1.85 (br s, 2 H); ^{13}C n.m.r. ($CDCl_3$, 50 MHz) ppm 158.4; 138.1, 127.8, 113.7, 58.4, 55.2; Anal. calc. for $C_{15}H_{17}NO_2$ (243.3): C, 74.04; H, 7.04; N, 5.75—Found: C, 74.09; H, 7.06; N, 5.57%.

*Preparation of protected amino acids **5***

N′*-Trifluoroacetyl glycinamide **5a***. To a suspension of glycinamide chlorohydrate (1 g, 8.86 mmol) in pyridine (15 ml), was added trifluoroacetic anhydride (1.26 ml, 8.86 mmol). The mixture was stirred overnight at room temperature, then poured into brine (100 ml) and extracted with ethyl acetate (3×20 ml). The organic phase was washed with 0.3 N HCl, dried over $MgSO_4$, concentrated and flash chromatographed on silica gel with CH_2Cl_2-ethyl acetate (98:2) to give 0.6 g (40%) of **5a** as a yellow powder: m.p. 45.5–46.5°C; $R_F = 0.26$; MS (EI) *m/e* 169 (M − 1), 152, 83, 69, 56; i.r. (film) ν 3305, 1724, 1556, 1421, 1219, 1166, 728 cm^{-1}; ^1H n.m.r. ($CDCl_3$, 300 MHz) δ 6.9–7.1 (br m, 3 H), 4.35 (d, $J = 6.2$ Hz, 1 H).

N′*-Trifluoroacetyl* (L)*-glutamine **5b***. This product is commercially available from Acros.

N′*-Dansylglycinamide **5c***. To a solution of glycinamide hydrochloride (0.721 g, 6.4 mmol) in dry pyridine (4 ml) was added dropwise, under argon atmosphere, dansyl chloride (2.62 g, 9.5 mmol, 1.5 equiv) in pyridine (6 ml). The mixture was stirred (in the dark) under heating at 50°C during 20 h. Addition of water (50 ml), extraction with EtOAc (5 × 20 ml), washing of the organic layers with brine (5 × 10 ml) and with 0.1 N HCl (5 × 10 ml), drying over $MgSO_4$ and concentration gave 2.13 g of crude **5c**. Column-chromatography on silica gel (100 g) with CH_2Cl_2-iPrOH (95:5) yielded 1.28 g (65%) of pure **5c**: m.p. 132.2–133.7°C; R_F (SiO_2, CH_2Cl_2-iPrOH, 95:5) = 0.26; MS (FAB) *m/e* 308; i.r. (KBr) ν 2873, 2787, 1666, 1574, 1459, 1319, 1144, 786, 625 cm^{-1}; ^1H n.m.r. ($CDCl_3$, 200 MHz) δ 8.52 (d, $J = 7.97$ Hz, 1 H), 8.20–8.27 (dd, $J = 8.58$ Hz and 6.87 Hz, 2 H), 7.48–7.61 (dd, 2 H), 7.24 (d, $J = 7.62$ Hz, 1 H), 6.38 (s, 1 H), 5.93 (t, $J = 6.19$ Hz, 1 H), 5.75 (s, 1 H), 3.52 (d, $J = 6.14$ Hz, 2 H), 2.89 (s, 6 H); ^{13}C n.m.r. ($CDCl_3$, 75 MHz) ppm 171.1, 153.3, 132.4, 132.2, 131.2, 129.96, 129.4, 126.5, 124.2, 119.2, 116.5, 46.6, 46.4; Anal. calc. for $C_{14}H_{17}N_3O_3S$ (307.36): C, 54.70; H, 5.57; N, 13.67—Found: C, 54.63; H, 5.48; N, 12.87%.

N′*-(9-Fluorenylmethoxycarbonyl)* (L)*-glutamine **5d***. To a mixture of (L)-glutamine (1 g, 6.77 mmol), dioxane (10 ml) and 10% aqueous Na_2CO_3 (20 ml), vigorously stirred at 0°C, was added dropwise 9-fluorenylmethyl chloroformate (1.98 g, 7.45 mmol, 1.1 equiv.) dissolved in dioxane (15 ml). After complete addition, the mixture was further stirred for 2 h at 20°C. The mixture was then poured into water (200 ml) and extracted twice with ether. The aqueous phase was acidified with conc. HCl to reach pH 2 (formation of a white precipitate) and extracted with ethyl acetate (2 × 50 ml). The organic layers were washed with water and concentrated under high vacuum to furnish 2.35 g (94%) of **5d** as a white solid: m.p. 195.8–196.7°C; R_F (SiO_2, i-PrOH) = 0; MS (EI) *m/e* 368 (M^+), 196, 179, 178, 165; i.r. (KBr) ν 3429, 3334, 1724, 1698, 1645, 1532, 1468, 1416 cm^{-1}; ^1H n.m.r. (DMSO-d6, 300 MHz) δ 12.8–12.4 (br m, 1 H), 7.9 (d, 2 H), 7.7 (d, 2 H), 7.5–7.2 (m, 6 H), 6.8 (br s, 1 H), 4.2 (d, 2 H), 3.95 (t, 1 H), 3.5–3.2 (br m, 1 H), 2.2 (t, 2 H), 2.1–1.9 (m, 1H), 1.9–1.7 (m, 1 H); ^{13}C n.m.r. (DMSO-d6, 50 MHz) ppm 173.6, 173.5, 156.1, 143.9, 140.7, 127.6, 127.1, 125.3, 120.1, 65.8, 53.6, 46.8, 31.5, 26.7; Anal. calc. for $C_{20}H_{20}N_2O_5$ (368.38): C, 65.2; H, 5.47; N, 7.6—Found: C, 64.79; H, 5.41; N, 7.28%.

*Coupling of **5** to 4,4′-dimethoxybenzhydrol **1** (preparation of the model compounds **6**)*

N*-(4,4′-Dimethoxybenzhydryl)-*N′*-(dansyl)glycinamide **6c***. A mixture of **5c** (95 mg, 0.31 mmol) and **1** (39 mg, 0.16 mmol) in HOAc (2 ml) (plus one drop of H_2SO_4) was stirred overnight, at room temperature (in the dark). The mixture was poured in ice-cold water (15 ml) and filtered. The precipitate was dissolved in CH_2Cl_2 (5 ml). The aqueous phase was extracted with CH_2Cl_2 (5 × 10 ml). The organic layers were washed with 5% $NaHCO_3$ (3 × 15 ml), dried over $MgSO_4$ and concentrated to give 76 mg (90%) of crude **6c**. Column-chromatography on silica gel (CH_2Cl_2-iPrOH, 98.5:1.5) yielded 54 mg (64%) of pure **6c**: $R_F = 0.09$; MS (FAB) *m/e* = 534; i.r. (KBr) ν 2927, 1727, 1657, 1177, 831, 627 cm^{-1}; ^1H n.m.r. ($CDCl_3$, 200 MHz) δ 8.55 (d, 1 H), 8.19–8.24 (d, 2 H), 7.43-7.54 (m, 2 H), 7.14 (d, 1 H), 6.98 (d, 1 H), 6.89 (d, J = 8.6 Hz, 4 H), 6.75 (d, J = 8.8 Hz, 4 H), 5.97 (d, J = 8.36 Hz, 1 H), 5.73 (t, J = 6.42 Hz, 1 H), 3.76 (s, 6 H), 3.52 (d, J = 6.46 Hz, 2 H), 2.86 (s, 6 H); ^{13}C n.m.r. ($CDCl_3$, 75 MHz) ppm 166.6, 158.98, 133.4, 131.3, 130.8, 130.3, 129, 128.8, 128.3, 125.5, 123.2, 118.2, 115.5, 114.1, 55.9, 55.3, 46.1, 45.4; Anal. calc. for $C_{29}H_{31}N_3O_5S$ (533.64): C, 65.27; H, 5.85; N, 7.87—Found: C, 65.16; H, 5.92; N, 7.35%.

N*-(4,4′-Dimethoxybenzhydryl)-*N′*-(9-fluorenylmethoxy-carbonyl)-(*L*)-glutamine **6d***. A mixture of **5d** (0.856 g, 2.32 mmol) and **1** (0.289 g, 1.16 mmol) in HOAc (15 ml) containing 1% of H_2SO_4 (catalyst) was stirred overnight at 20°C.

The mixture was poured in ice-cold water (100 ml); the white precipitate was filtered off, washed with ether and dried under vacuum to give 0.644 mg (93%) of **6d**: m.p. 165.6–166.6°C; R_F (SiO_2, i- PrOH) = 0.16; MS (FAB) *m/e* 595 (M + 1), 534, 453, 307, 242, 227, 154, 136; i.r. (KBr) ν 3295, 2835, 1692, 1640, 1611, 1543, 1510, 1450 cm^{-1}; ^1H n.m.r. (DMSO-d6, 300 MHz) δ 12.7–12.6 (br m, 1 H), 8.7 (d, 1 H), 7.9 (d, 2 H), 7.7 (d, 2 H), 7.5–7.2 (m, 6 H), 7.1 (d, 4 H), 6.8 (d + br d, 5 H), 6.0 (d, 1 H), 4.3–4.2 (br s, 2 H), 4.0–3.9 (br s, 1 H), 3.69 (s, 6 H), 3.37 (m, 1 H), 2.3 (m, 2 H), 2.1–1.9 (m, 1 H), 1.9–1.7 (m, 1 H); ^{13}C n.m.r. (DMSO-d6, 50 MHz) ppm 173.7, 170.3, 158.1, 156.2, 143.7, 140.6, 134.9, 128.2, 127.5, 126.9, 125.1, 119.9, 113.55, 65.5, 54.96, 54.5, 53.5, 46.6, 31.7, 26.8; Anal. calc. for $C_{35}H_{34}N_2O_7$ (594.66): C, 70.69; H, 5.76; N, 4.71—Found: C, 70.70; H, 5.70; N, 4.46%.

*Deprotection of compound **6d***

N*-(4,4′-Dimethoxybenzhydryl) (*L*) glutamine **7d***. Method A: a solution of **6d** (100 mg, 0.168 mmol) in piperidine (0.5 ml) was left for 45 min at room temperature, then poured into ice-cold water (15 ml). The precipitate of *N*-(9-fluorenylmethyl) piperidine[22] was filtered off. The filtrate was concentrated under high vacuum to furnish **7d** (~100%) containing piperidine. Method B: a solution of **6d** (50 mg, 0.084 mmol) in CH_3CN (2 ml) was treated with piperidine (0.017 ml, 0.168 mmol, 2 equiv.) and left for 3 h at 20°C. CH_3CN was removed under vacuum, water was added and the mixture was extracted with CH_2Cl_2. The organic layer contained *N*-(9-fluorenylmethyl) piperidine[22]. The aqueous phase was lyophilized to give **7d** (14 mg, 70%). Method C: FMOC deprotection was conducted in toluene, as described in Method B (yield 80%). Method D: FMOC deprotection was conducted in DMSO, as described in Method B (yield 100%): ^1H n.m.r. (DMSO-d6, 300 MHz) δ 9.0 (d, J = 4 Hz, 1 H), 7.16 (d, J = 8.5 Hz, 4 H), 6.84 (d, J = 8.5 Hz, 4 H), 5.98 (d, J = 4 Hz, 1 H), 3.70 (s, 6 H), 3.15 (m, 1 H), 2.32 (m, 2 H), 2.0–1.7 (m, 2 H).

CHEMISTRY ON POLYMER FILMS

Materials and methods

Amorphous PEEK film (Stabar K200; thickness of 25 μm) received from ICI (UK), was surface-reduced according to Refs 6–8. The amount of hydroxylated monomer units was determined by X-ray photoelectron spectroscopy (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 percentages of surface reduction were within 70–90%, depending on the experimental conditions (temperature: 100–120°C, and duration of the treatment with $NaBH_4$-DMSO: 2–4 h). From SEM analysis, the surface of PEEK-OH was smooth. The PEEK-OH disks (1.12 cm^2) used for the surface derivatizations were cut off a large PEEK-OH sample (rectangle of 30 cm in length and 15 cm in width).

Water used for the rinsing of the modified polymer disks was of HPLC grade and obtained with a Milli-Q system (Millipore, Bedford, MA, USA).

The contact angles of water were measured at room temperature using the sessile drop technique and an image analysis system (CCD camera of MXR 5010 type and contour processor PIO-12 with computer monitor 80 from Electronish Ontwerp Bureau De Boer, The Netherlands). The values given in *Table 6* are the average of 10 measurements. The standard deviation is indicated in parentheses.

The surface i.r. spectra (MIR mode) were recorded on PE 580 and PE 1760 spectrometers using an optical deviation system from Perkin-Elmer and a thallium bromide-iodide crystal KRS-5 (incidence angle: 45°); the instrument was coupled with a PE 3600 computer.

The scanning electron miscroscopy (SEM) was performed using a Hitachi (Tokyo, Japan) S-570 system with an accelerating voltage of 15 kV and a working distance of approximatively 10 mm. The samples were gold coated in a Balzers Union SCD 040 vapour disposition unit, at 15 mA, for a period of 120 sec.

The XPS spectra were obtained with a SSI X-probe (SSX-100/206) spectrometer from Fisons (Surface Science Laboratories, Mountain View, CA, USA), 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 only bound to carbon and hydrogen at a value of 284.8 eV. The peak areas were determined with a linear background subtraction. Intensity ratios were converted into atomic concentration ratios by using the SSI ESCA 8.3D software package. The peaks were curve-fitted using a non-linear least square routine and assuming a Gaussian/Lorentzian (85/15) function. The XPS experimental technique was fully described in Ref. 8.

The TOF-SIMS analyses were realized with a TRIFT-TFS 4000 MMI spectrometer (ion beam of 15 keV, with a diameter of 0.5 μm).

The fluorimetric analysis was performed with a SLM-Aminco 48000 S DW 2000 apparatus (incidence angle: 45°).

*Reaction of PEEK-OH with amide (carbamate) **2***

PEEK-NHCOCH$_2$Cl. PEEK-OH disks (15 disks of 1.12 cm^2) were immersed into a solution of chloroacetamide **2b** (3 g) in HOAc (100 ml) containing H_2SO_4 as catalyst (0.1 g). The disks were stirred at 20°C for 48 or 72 h, then removed from the solution and rinsed with HOAc (2 × 10 min), water (2 × 10 min) and acetone (2 × 10 min). The disks were dried under vacuum (60°C, 3 h). The blank samples were obtained by similarly treating PEEK-OH disks, but with omitting the acid catalyst; they did not contain chlorine atoms. XPS analysis of PEEK-NHCOCH$_2$Cl (48 h): C$_{1s}$, 84.42% (284.9 eV); O$_{1s}$, 13.49% (533.4 eV); N$_{1s}$, 1.13% (400 eV); Cl, 0.66% (200–202 eV)—PEEK-NHCOCH$_2$Cl (72 h): C$_{1s}$, 82.82%; O$_{1s}$, 14.93%; N$_{1s}$, 0.89%; Cl, 1.35%.

PEEK-NHCOOPh. PEEK-OH disks (15 disks of 1.12 cm^2) were immersed into a solution of phenyl carbamate **2e** (3 g) in HOAc (100 ml) containing H$_2$SO$_4$ as catalyst (0.5 g). The disks were stirred at 20°C for 72 h, then removed from the solution and rinsed with HOAc (3×10 min), water (3×10 min) and acetone (3×10 min). The disks were dried under air atmosphere (20°C). The blank samples were obtained by similarly treating PEEK-OH disks, but with omitting the acid catalyst; they did not contain nitrogen atoms.

XPS analysis of PEEK-NHCOOPh 1 (from PEEK-OH displaying 82% of hydroxyl functions): C$_{1s}$, 82.86% (284.8 eV); O$_{1s}$, 14.17% (533.31 eV); N$_{1s}$, 2.97% (400.13 eV)—PEEK-NHCOOPh 2 (from PEEK-OH displaying 75% of hydroxyl functions): C$_{1s}$, 83.55% (284.8 eV); O$_{1s}$, 13.86% (533.31 eV); N$_{1s}$, 2.59% (400.21 eV).

Deprotection of PEEK-NHCOR (preparation of PEEK-NH$_2$)

PEEK-NH$_2$ from PEEK-NHCOCH$_2$Cl. Disks of PEEK-NHCOCH$_2$Cl (treatment of 72 h; 5 disks of 1.12 cm^2) were immersed into pyridine (25 ml) at 80°C for 1 h 30 min, then into 0.5 M aqueous NaOH (25 ml) at 40°C for 24 h, under stirring. The disks were removed from the solution and rinsed with water (3 × 15 min), and acetone (2 × 15 min), and then dried under vacuum (60°C, 3 h). The blank samples were obtained by similarly treating PEEK-OH disks. XPS analysis of PEEK-NH$_2$: C$_{1s}$, 79.96% (284.8 eV); O$_{1s}$, 17.77% (533.4 eV); N$_{1s}$, 1.45% (399 eV); Cl, 0.44% (200–202 eV)-Blank: C$_{1s}$, 80.46%; O$_{1s}$, 18.88%; N$_{1s}$, 0.61%.

PEEK-NH$_2$ from PEEK-NHCOOPh. Disks of PEEK-NHCOOPh (2 disks of 1.12 cm^2) were immersed into a solution of LiOH-H$_2$O (0.203 g) in CH$_3$CN-H$_2$O (1:1; 20 ml), and stirred at 50°C during 3 h. The disks were removed from the solution and rinsed with water (3 × 10 min) and acetone (3 × 10 min), then dried under air atmosphere (20°C). The blank samples were obtained by similarly treating PEEK-OH disks; they did not contain nitrogen atoms. SEM analysis: smooth surfaces; no visible defects. XPS analysis of PEEK-NH$_2$ (from PEEK-NHCOOPh, 90%): C$_{1s}$, 85.27% (284.8 eV), O$_{1s}$, 11.27% (533.39 eV); N$_{1s}$, 3.46% (398.87 eV)—PEEK-NH$_2$ (from PEEK-NHCOOPh, 75%): C$_{1s}$, 83.75%; O$_{1s}$, 13.12%; N$_{1s}$, 3.12%.

Reaction of PEEK-OH with compounds **5**

PEEK-dansyl. PEEK-OH disks (2 disks of 1.12 cm^2) were immersed into a solution of **5c** (respectively 0.086 g (1%), 0.172 g (2%) and 0.351 g (4%)) in HOAc (9 ml) containing H$_2$SO$_4$ (0.025 ml, 0.5%). The disks were stirred for 72 h at 20°C, in the dark, then removed from the solution and rinsed with HOAc (2 × 10 min), water (4 × 10 min) and acetone (2 × 10 min). The samples were dried under vacuum (60°C, 3 h) and storred in the dark. XPS analysis of PEEK-dansyl (1%): C$_{1s}$, 76.44% (284.9 eV); O$_{1s}$, 16.82% (533.1 eV); N$_{1s}$, 4.23% (399.9 eV); S$_{2p}$, 2.52% (168.7 eV)—Blank (1%): C$_{1s}$, 78.03%; O$_{1s}$, 16.8%; N$_{1s,}$ 2.39%; S$_{2p}$, 1.86%. PEEK-dansyl (2%): C$_{1s}$, 83.06%; O$_{1s}$, 14.97%; N$_{1s}$, 1.75%; S$_{2p}$, 0.31%—Blank (2%): C$_{1s}$, 85.88%; O$_{1s}$, 13.63%; N$_{1s}$, 0.42%; S$_{2p}$, 0.06%. PEEK-dansyl (4%): C$_{1s}$, 85.46%; O$_{1s}$, 14.05%; N$_{1s}$, 0.39%; S$_{2p}$, 0.11%—Blank (4%): C$_{1s}$, 85.95%; O$_{1s}$, 13.82%; N$_{1s}$, 0.20%; S$_{2p}$: 0.03%.

PEEK-FMOC. PEEK-OH disks (5 disks of 1.12 cm^2) were immersed into a solution of **5d** (0.25 g) in HOAc (25 ml) containing H$_2$SO$_4$ as catalyst (0.068 ml; 0.125 g). The disks were stirred for 72 h at 20°C, then removed from the solution and rinsed with HOAc (3 × 10 min), water (3 × 10 min) and acetone (3 × 10 min). The samples were dried under air atmosphere (20°C). The blank samples prepared as usual, did not contain nitrogen atoms. XPS analysis of PEEK-FMOC (from PEEK-OH displaying 82% of hydroxyl functions): C$_{1s}$, 80.35%; (284.88 eV); O$_{1s}$, 18.37% (533.39 eV); N$_{1s}$, 1.26% (400.21 eV)—PEEK-FMOC (from PEEK-OH displaying 75% of hydroxyl functions): C$_{1s}$, 82.69%; O$_{1s}$, 15.62%; N$_{1s}$, 1.69%.

Preparation of PEEK-glutamine

Disks of PEEK-FMOC (4 disks of 1.12 cm^2, samples of entry 5, *Table 5*) were immersed into a solution of piperidine (0.581 ml, 1%) in toluene (50 ml) and stirred for 3 h at room temperature. The disks were removed from the solution and rinsed with toluene (3 × 10 min), acetone (1 × 10 min), water (2 × 10 min) and acetone (1 × 10 min). The samples were dried under air atmosphere (20°C). The blank sample was obtained by similarly treating a PEEK-OH disk; the blank did not contain nitrogen atoms. XPS analysis: C$_{1s}$, 81.59% (284.8 eV); O$_{1s}$, 16.23% (533.3 eV); N$_{1s}$, 2.18% (399.6 eV). SEM analysis: smooth surface, no visible defects.

Preparation of PEEK-SO$_3$H

Disks of PEEK-NH$_2$ (3 disks of 1.12 cm^2, samples of entry 4, *Table 2*) were immersed into a solution of 1,3-propanesultone (0.25 g, 1%) in toluene (25 ml) and stirred respectively at 20°C for 31 h, at 80°C for 10 h and at 80°C for 20 h. The samples were rinsed with toluene (3 × 10 min), methanol (3 × 10 min) and acetone (3 × 10 min), then dried under air atmosphere (20°C).

XPS analysis of PEEK-SO$_3$H (20°C, 31 h). C$_{1s}$, 83.12% (284.6 eV); O$_{1s}$, 13.24% (533.2 eV), N$_{1s}$, 2.62% (398.9 eV); S$_{2p}$, 0.81% (168.9 eV)—Blank: C$_{1s}$, 85.34%; O$_{1s}$, 14.23%; N$_{1s}$, 0.27%; S$_{2p}$, 0.16%. PEEK-SO$_3$H (80°C, 10 h): C$_{1s}$, 74.99% (284.8 eV); O$_{1s}$, 20.44% (533.0 eV); N$_{1s}$, 1.97% (401.4 eV); S$_{2p}$, 2.60% (168.6 eV). PEEK-SO$_3$H (80°C, 20 h): C$_{1s}$, 78.16%; O$_{1s}$, 17.92%; N$_{1s}$, 1.88%; S$_{2p}$, 2.04%—Blank: C$_{1s}$, 78.77%; O$_{1s}$, 18.87%; N$_{1s}$, 0.66%; S$_{2p}$, 1.71%.

RESULTS AND DISCUSSION

PEEK derivatization with amine functions is poorly documented in the literature. Some bulk modifications resulted from the use of functionalized units in the polymer synthesis, i.e. aromatic amine-terminated PEEK oligomers[23] and *p*-aminophenyl(4,4′-difluorobenzophenone)imine[24].

Surface modifications of PEEK films, under wet-conditions, were initially reported by McCarthy[25]; in particular, the reactions with hydroxylamine and 2,4-dinitrophenylhydrazine were performed[26], but the subsequent reductive depotections to furnish aminated surfaces were not achieved. At last, plasma treatments with N$_2$ and N$_2$/O$_2$ mixtures were examined; however, the incorporation of amine functions could not be detected[27].

Amorphous PEEK film was easily reduced by immersion

Table 1 Preparation of 4,4′-dimethoxybenzhydrylamine

Entry	R (**2**)	Yield **3**^{a}	Deprotection conditions	Yield **4**^{b}
1	H	**a**, 85%	KOH, THF-H_2O-MeOH (3:1:1), reflux, 25 h	~30%
2	CH_2Cl	**b**, 85%	(i) pyr., 80°C, 1 h 30 min; (ii) NaOH, H_2O, 40°C, 16 h	~50%
3	CF_3	**c**, 0%	—	—
4	OCH_3	**d**, 75%	KOH, THF-H_2O-MeOH (3:1:1), 60°C, 60 h	~20%
5	OPh	**e**, 82%	LiOH, CH_3CN-H_2O (1:1), 50°C, 3 h	~90%

^{a}Yield after recrystallization ^{b}Yield after purification by column chromatography on silica gel

Table 2 XPS analysis of PEEK-NHCOR and PEEK-NH_2

Entry	PEEK-OH (% of reduction)	PEEK-NHCOR				PEEK-NH_2	
		R	Treatment	X/C atomic ratio	%^{a}	X/C atomic ratio	% (corrected)^a
1	89	CH_2Cl	48 h	Cl/C × 100 = 0.782	15	—	—
2	89	CH_2Cl	72 h	Cl/C × 100 = 1.630	32	N/C × 100 = 1.052	21 (10)
						Cl/C × 100 = 0.550	11
3	82	OPh	72 h	N/C × 100 = 3.584	90	N/C × 100 = 4.058	78
4	75	OPh	72 h	N/C × 100 = 3.099	75	N/C × 100 = 3.725	72

^{a}Percentage of modified polymer units

Table 3 XPS analysis of PEEK-SO_3H

Entry	Conditions	N/C × 100	Corrected	S/C × 100	Corrected	% of grafted sultone
1	1% sultone, toluene, 20°C, 31 h	3.152	2.836	0.974	0.787	15
	PEEK-OH blank	0.316		0.187		
2	1% sultone, toluene, 80°C, 10 h	2.627	1.789	3.467	1.296	25
	PEEK-OH blank	0.838		2.171		
3	1% sultone, toluene, 80°C, 20 h	2.405	1.567	2.610	0.439	9
	PEEK-OH blank	0.838		2.171		

into a solution of sodium borohydride in dimethylsulfoxide at 120°C for a few hours. The resulting surface exposed hydroxyl functions in high amounts (70–90% of reduced monomer units from XPS analysis), the reactivity of which has been previously demonstrated[6–8]. This film, called PEEK-OH, constitutes our actual starting material for the development of amination procedures by wet-chemistry.

Direct amination of the PEEK-OH film

Our synthetic plan for the surface amination of PEEK-OH film was based on the substitution of the hydroxyl groups with protected amines, followed by selective deprotection. This strategy was first examined in homogeneous solution, with 4,4′-dimethoxybenzhydrol **1** considered as a good mimic of the reduced PEEK monomer unit. Using our standard conditions,[21] we reacted **1** with formamide **2a**, chloroacetamide **2b**, methyl carbamate **2d** and phenyl carbamate **2e**, to furnish the corresponding *N*-(4,4′-dimethoxybenzhydryl) amides **3a** and **3b**, and *N*-(4,4′-dimethoxybenzhydryl) carbamates **3d** and **3e** (*Scheme 1*, *Table 1*). The trifluoroacetamide **2c** was not nucleophilic enough to give the substitution[21]. Various deprotection conditions of compounds **3** were systematically studied[28]: treatment of **3a** with a solution of KOH in aqueous tetrahydrofurane-methanol for one day at 70°C gave 30% of 4,4′-dimethoxybenzydrylamine **4** (entry 1); similarly, the basic hydrolysis of **3d** yielded 20% of **4** (entry 4). The deprotection of chloroacetamide **3b** was performed in two steps[29]: reaction with pyridine at 80°C produced a pyridinium salt by chlorine substitution, the basic hydrolysis of which was more easily conducted in aqueous NaOH, overnight at 40°C, to give 50% of the free amine **4** (entry 2). Finally, the carbamate **3e** was found to be quantitatively cleaved by LiOH in aqueous acetonitrile, for 3 h at 50°C (entry 5). The procedures 2 and 5 were selected for the polymer modification.

PEEK-OH samples were immersed into a solution of chloroacetamide **2b** in acetic acid containing 0.1% of H_2SO_4 as catalyst; after 48 and 72 h of reaction, the samples were adequately rinsed and analysed by X-ray photoelectron spectroscopy (XPS). They contained nitrogen and chlorine atoms; from the Cl/C × 100 atomic ratios, we calculated*, respectively, 15% and 32% of surface derivatization (*Scheme 2*, *Table 2*). Blank samples were prepared by omitting the acid catalyst in the wet-chemistry procedure. These films did not contain chlorine atoms from XPS analysis, thus confirming that protonation of the polymer hydroxyl functions is necessary for the substitution to occur. The two step deprotection procedure was applied to the PEEK-$NHCOCH_2Cl$ sample of entry 2. The film was successively treated with pyridine for 1 h 30 min at 80°C and with aqueous NaOH for one day at 40°C, then rinsed as usual. The XPS analysis (entry 2) revealed the presence of nitrogen atoms and residual chlorine atoms corresponding

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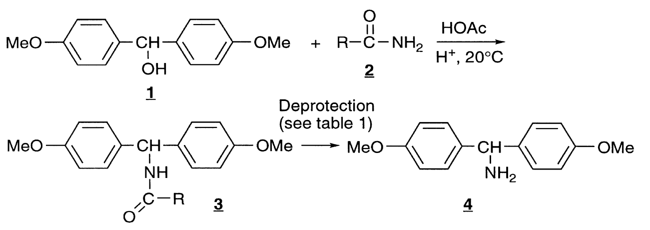
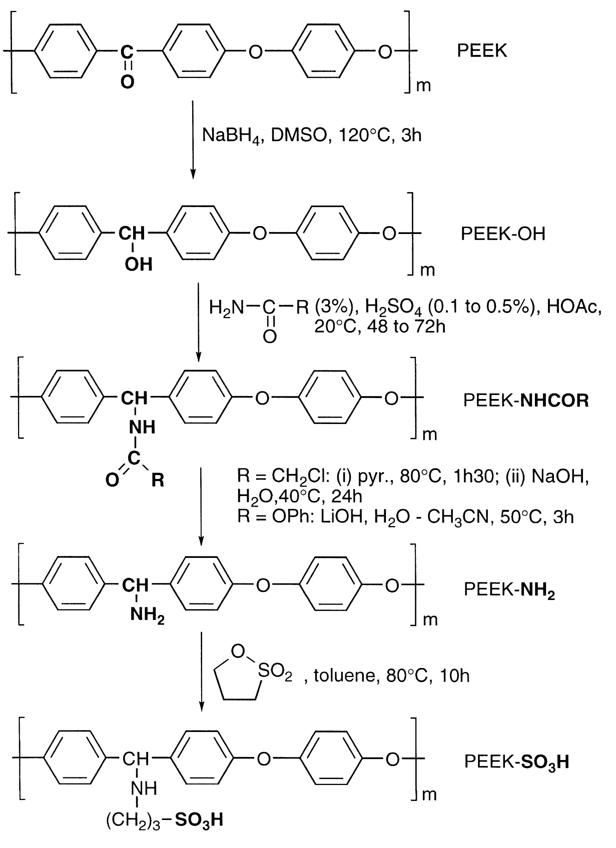
* We considered a theoretical monomer unit consisting of $[(\text{PEEK-OH})_x + (\text{PEEK-NHCOCH}_2\text{Cl})_y]$, i.e. $[(C_{19}O_3)_x + (C_{21}O_3NCl)_y]$, where $x + y = 1$. For $x = 0.68$ and $y = 0.32$, the calculated Cl/C × 100 atomic ratio was $0.32/19.64 \times 100 = 1.629$ (experimental value = 1.63).



Scheme 1 Preparation of 4,4′-dimethoxybenzhydrylamine from 4,4′-dimethoxybenzhydrol



Scheme 2 Preparation of PEEK-NH_2 and PEEK-SO_3H

to 21% and 11% of surface functionalization, respectively†. The chloroacetamide hydrolysis was thus uncomplete (corrected yield of PEEK-NH_2: 10%); but under more drastic conditions, surface erosion occurred (SEM analysis).

The reaction of PEEK-OH with phenyl carbamate **2e**, in acetic acid containing 0.5% of H_2SO_4, gave PEEK-$NHCO_2Ph$ film in high yield (*Scheme 2*, *Table 2*). The MIR spectrum clearly showed the carbamate function at 1739 cm^{-1} (*Figure 1A*). The water contact angle of 78.8° (*Table 6*) indicated a more hydrophobic surface in comparison to the starting PEEK-OH film (75.8°). The XPS analysis of two samples of different origins (entries 3 and 4) gave N/C × 100 atomic ratios of 3.584 and 3.099, corresponding to 90% and 75% of modified polymer units‡.

Figure 1 MIR spectrum of PEEK-$NHCO_2Ph$ and PEEK-NH_2 films. (A) PEEK-$NHCO_2Ph$ film; (B) PEEK-NH_2 film

The fine structure of the C_{1s} peak (*Figure 2*) revealed the presence of carbon atoms simply bound to a nitrogen atom (*C*-N at 285.5 eV) and carbon atoms doubly bound to the oxygen atom of the carbamate function (N-*C*(= O)O at 289.5 eV). The secondary ion mass spectrometry (SIMS, negative mode) confirmed the presence of phenyloxycarbonyl groups (*m/z* 121).

The deprotection of PEEK-$NHCO_2Ph$ was realized by immersing the film into a solution of LiOH in aqueous acetonitrile for 3 h at 50°C. The MIR spectrum confirmed the efficiency of the treatment: the carbamate band at 1739 cm^{-1} has well disappeared (*Figure 1B*). The water contact angle of 72.7° was indicative of a more hydrophilic surface, as compared to the starting material (*Table 6*). From the N/C × 100 atomic ratios, given by the XPS spectra (*Table 2*, entries 3 and 4), we calculated a percentage of derivatization within 72–78%§. The fine structure of the C_{1s} peak (*Figure 3*) showed an important *C*-N contribution at 285.5 eV, and the disappearance of the carbamate contribution. Accordingly, in the SIMS spectrum, the peak at *m/z* 121 was also missing. Thus all the spectroscopic data are consistent with the complete deprotection of PEEK-$NHCO_2Ph$ to give the fully aminated surface called PEEK-NH_2.

The PEEK-NH_2 film could be further functionalized by reaction with 1,3-propanesultone in toluene (*Scheme 2*,

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† We considered a theoretical monomer unit consisting of [(PEEK-OH + PEEK-NH_2)$_x$ + (PEEK-$NHCOCH_2Cl$)$_y$], i.e. [($C_{19}O_3$ + $C_{19}O_2N$)$_x$ + ($C_{21}O_3NCl$)$_y$], where $x + y = 1$. For $x = 0.89$ and $y = 0.11$, the calculated Cl/C × 100 atomic ratio was 0.11/19.22 × 100 = 0.572 (experimental value = 0.55).

‡ We considered a theoretical monomer unit consisting of [(PEEK-OH)$_x$ + (PEEK-$NHCO_2Ph$)$_y$], i.e. [($C_{19}O_3$)$_x$ + ($C_{26}O_4N$)$_y$], where $x + y = 1$. For $x = 0.25$ and $y = 0.75$, the calculated N/C × 100 atomic ratio was 0.75/24.25 × 100 = 3.093 (experimental value = 3.099).

§ We considered a theoretical monomer unit consisting of [(PEEK-OH)$_x$ + (PEEK-NH_2)$_y$], i.e. [($C_{19}O_3$)$_x$ + ($C_{19}O_2N$)$_y$], where $x + y = 1$. For $x = 0.22$ and $y = 0.78$, the calculated N/C × 100 atomic ratio was 0.78/19 × 100 = 4.10 (experimental value = 4.058).

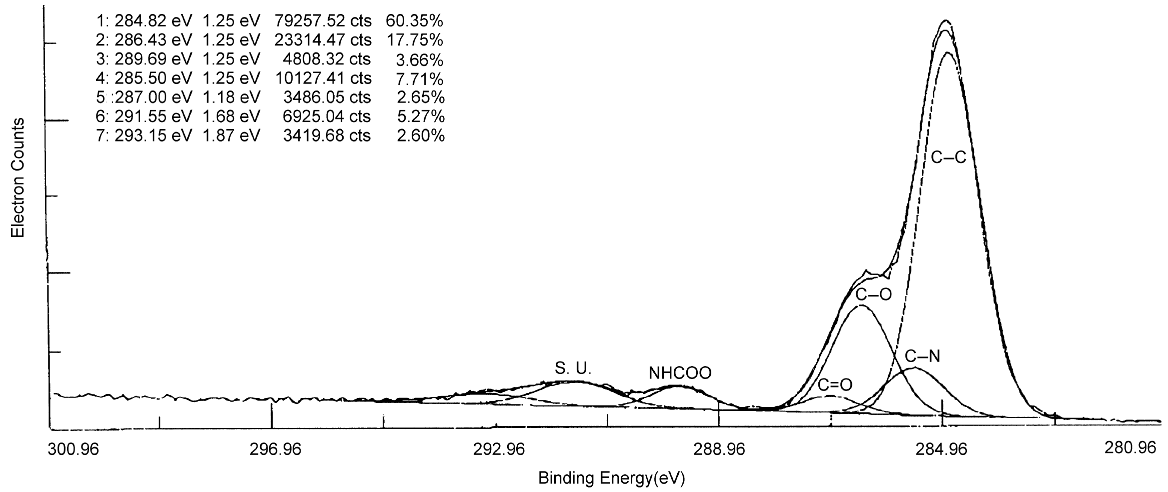


Figure 2 XPS analysis of PEEK-$NHCO_2Ph$ film; detailed C_{1s} peak

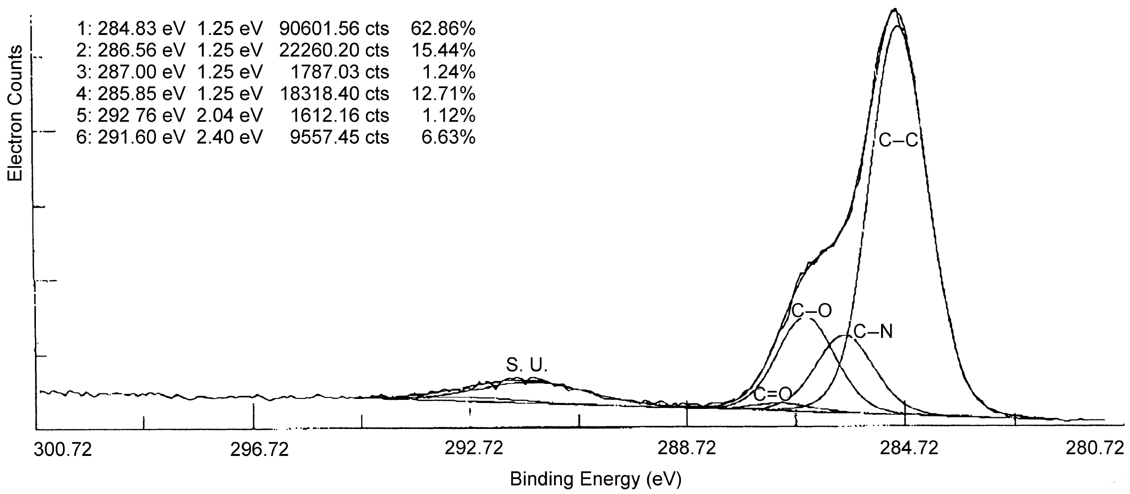


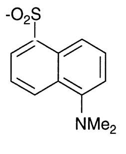
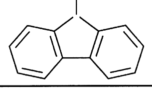
Figure 3 XPS analysis of PEEK-NH_2 film; detailed C_{1s} peak

Table 3). The resulting PEEK-SO_3H was analysed by XPS; depending on the experimental conditions (temperature and duration of the treatment), the amount of grafted sultones varied within 9–25%. The best result was obtained after 10 h of reaction at 80°C (entry 2, *Table 3*, *Figure 4*)¶. However, in all cases, surface erosion occurred (i.e. progressive dissolution of the modified interface), as evidenced by the diminution of the N/C × 100 atomic ratios. In those experiments, the PEEK-OH blank samples showed a relatively important adsorption of the sultone reagent, and some amine contamination.

Indirect amination of the PEEK-OH film

We envisaged fixing glycinamide and glutamine on the PEEK-OH surface using their primary amide function as a nucleophilic anchorage point. For that purpose, their respective amine function has to be protected. The selected protecting groups were trifluoroacetyl[28], 5-dimethylamino-1-naphthalenesulfonyl (dansyl)[30], and 9-fluorenylmethoxycarbonyl (FMOC)[31]. They are classical masking groups in peptide synthesis; moreover, they will provide useful spectroscopic tags for the analysis of the corresponding modified polymer surfaces (XPS, fluorescence, SIMS).

Table 4 Fixation of glycimamide and glutamide derivatives on 4,4′ dimethoxy benzhydrol

Entry	n	X	R	Yield **5**	Yield **6**	Yield **7**
1	0	H	-$COCF_3$	a, 38% $^{(a)}$	<10%$^{(b)}$	NE*
2	2	COOH	-$COCF_3$	b, $^{(c)}$	54%$^{(b)}$	NE
3	0	H		c, 65% $^{(a)}$	90%$^{(b)}$	NE
4	2	COOH	-CO_2CH_2 	d, 94% $^{(b)}$	93%$^{(b)}$	100%$^{(b)}$

(a) isolated after column chromatography; (b) crude; (c) commercially available product

*Non Evaluated

The N′-protected glycinamides **5a** and **5c**, and the *N*′-protected glutamines **5b** and **5d** were prepared using conventional methods (see Experimental section; *Scheme 3*, *Table 4*). Their reactivity, in homogeneous solution,

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¶ We considered a theoretical monomer unit consisting of $[(\text{PEEK-OH})_x + (\text{PEEK-NH}_2)_y + (\text{PEEK-SO}_3\text{H})_z]$, i.e. $[(C_{19}O_3)_x + (C_{19}O_2N)_y + (C_{22}O_5NS)_z]$, where $x + y + z = 1$. For $(x + y) = 0.75$ and $z = 0.25$, the calculated S/C × 100 atomic ratio was 0.25/19.75 × 100 = 1.266 (experimental value = 1.296).

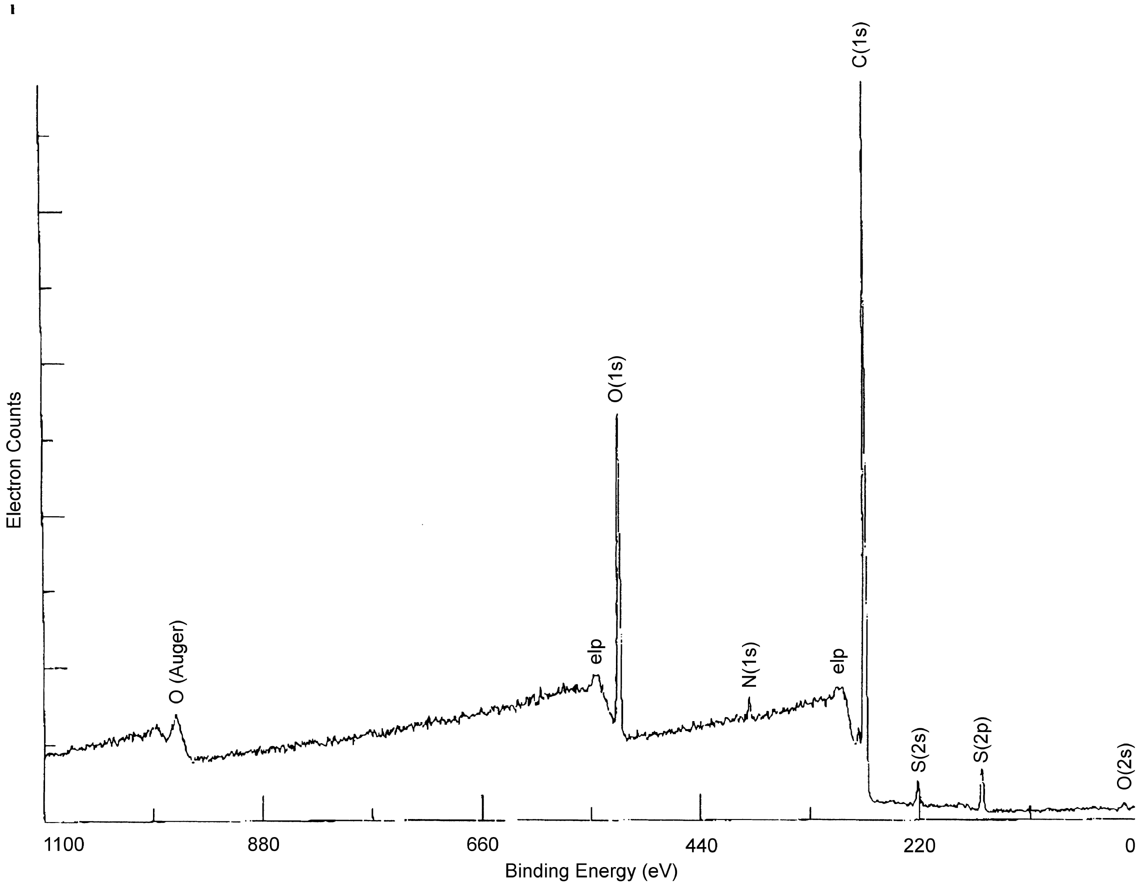
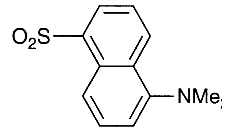
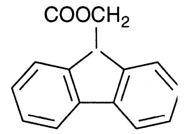


Figure 4 XPS analysis of PEEK-SO$_3$H film; general spectrum

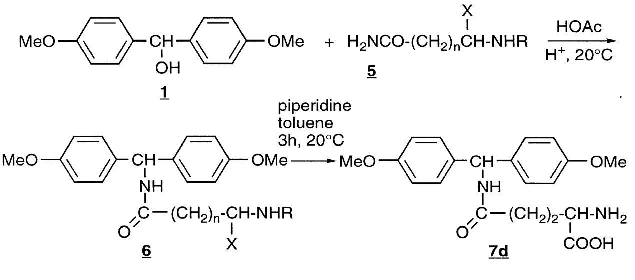
Table 5 XPS analysis of PEEK-OH films coupled to (N-protected) amino-amide derivatives **5**

Entry	PEEK-OH[a]	PEEK-NHCO-(CH$_2$)$_n$-CH(X)NHR			Conc. of **5**	N/C × 100			% of modified polymer units
		n	X	R		Blank	Sample	Corrected	
1	84%	0	H		1% **5c**	3.063	5.533	2.470	16
2	88%			(PEEK-dansyl)	2% **5c**	0.489	2.107	1.618	11
3	88%				4% **5c**	0.232	0.456	0.224	2
4	82%	2	CO$_2$H		1% **5d**	0	1.568	—	18
5	75%			(PEEK-FMOC)	1% **5d**	0	2.044	—	24
6	—	2	CO$_2$H	H (PEEK-glutamine)	(from entry 5)	0	2.672	—	26

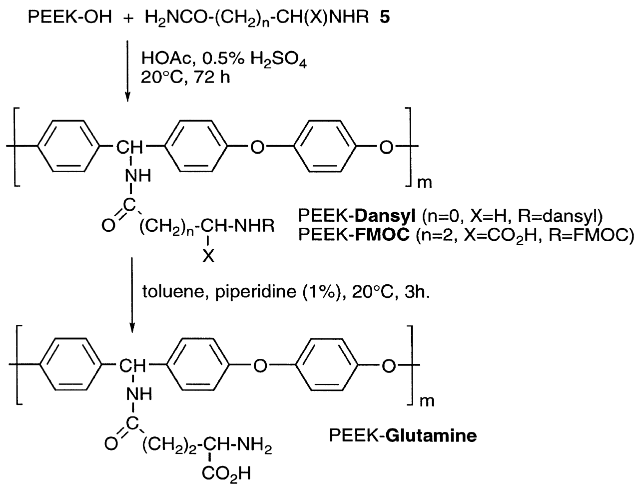
[a] Percentage of reduction

towards 4,4′-dimethoxybenzhydrol **1** was first investigated; the reactions were conducted in acetic acid, at room temperature, with sulfuric acid as catalyst[21]. High yields of coupling (products **6c** and **6d**) were obtained with compounds **5c** and **5d** (*Scheme 3*, *Table 4*); these amides were thus selected for the anchorage on the polymer film. Deprotection of **6d** with piperidine[22,31] was considered under various conditions (see experimental section); the FMOC cleavage was quantitative.

PEEK-OH film samples were immersed during 72 h into different solutions of *N*′-(dansyl) glycinamide **5c** in acetic acid containing 0.5% of H$_2$SO$_4$. The solution with 1% of



Scheme 3 Fixation of glycinamide and glutamine derivatives on 4,4′-dimethoxybenzhydrol



Scheme 4 Preparation of PEEK-glutamine

Table 6 Water contact angles

	Sample	θw
1	PEEK-OH (75%)	75.8° (± 0.9)
2	PEEK-NHCO$_2$Ph (from PEEK-OH 82%)	78.8° (± 1.1)
3	PEEK-NH$_2$ (from PEEK-NHCO$_2$Ph)	72.7° (± 1.2)
4	PEEK-FMOC (from PEEK-OH 75%)	81.2° (± 0.8)
5	PEEK-glutamine (from PEEK-FMOC)	75.7° (± 1.5)

reagent was homogeneous, while the solution with 2% and 4% of **5c** were cloudy and unhomogeneous, respectively. Blank samples were prepared by similarly treating PEEK-OH, but omitting the acid catalyst. After rinsing as usual, the various samples were analysed by XPS (*Scheme 4*, *Table 5*). The corrected percentages of modified polymer units[‖] were respectively 16%, 11% and 2%, for samples treated with increasing concentrations of **5c**. The unfavourable effect of heterogeneous reactive solutions on the surface chemistry has been previously pointed out[8]. In these experiments, the blank samples showed an important contribution of the adsorption of the lipophilic reagent **5c**. The presence of dansyl motifs on the polymer surface (samples of entry 2, 11% of derivatization) was qualitatively confirmed by fluorescence spectroscopy[32,33]. The typical emission was observed at 460 nm, for the excitation at 337 nm. Due to the moderate yield of **5c** grafting, we did not studied the deprotection step on the PEEK-Dansyl samples.

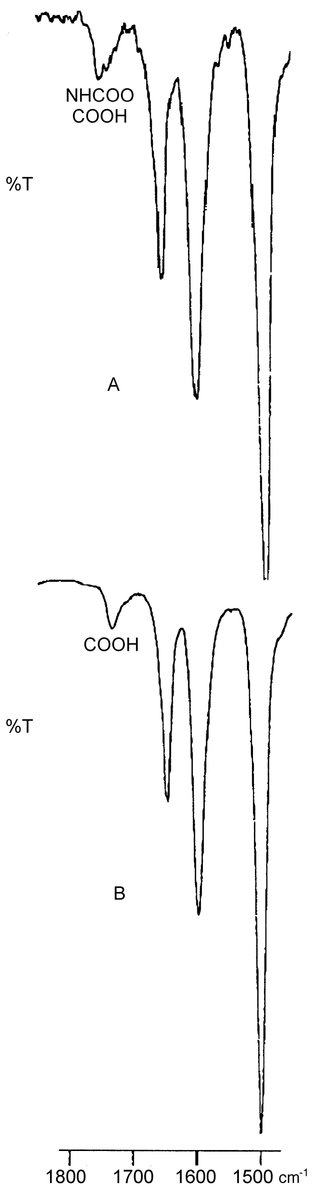


Figure 5 MIR spectrum of PEEK-FMOC and PEEK-glutamine films. (A) PEEK-FMOC film; (B) PEEK-glutamine film

The *N*′-(9-fluorenylmethoxycarbonyl)-(L)-glutamine **5d** was similarly fixed on PEEK-OH samples to furnish PEEK-FMOC (*Scheme 4*, *Table 5*). In this case, the blank samples did not contain nitrogen atoms (XPS analysis); the more hydrophilic reagent **5d** (presence of the CO$_2$H group) was not adsorbed. From the N/C × 100 atomic ratios of PEEK-FMOC samples, we concluded[**] that the surface derivatization was within 18–24%. The water contact angle value of 81.2° (*Table 6*) was consistent with the grafting of lipophilic fluorenyl motifs. The presence of these groups was further qualitatively confirmed by SIMS; the spectrum of positive ions revealed peaks at *m*/*z* 165 and 179, typical of the fluorenyl- and 9-fluorenylmethylene cations. The FMOC group could not be detected by SIMS on the blank samples; this confirmed the XPS analyses. The MIR spectrum of PEEK-FMOC (*Figure 5A*) showed clearly a broad band centred at 1714 cm^{-1}, corresponding to the absorption of the carbamate and carboxyl functions. The amide function gave a band at 1650 cm^{-1}, just near the PEEK carbonyl band due to the benzophenone motifs of the bulk. In the XPS analysis (*Figure 6*), the C$_{1s}$ fine structure also clearly showed the carbamate and carboxyl functions (*C*=O contribution at 289.65 eV), and the amide function (*C*=O contribution at 288.55 eV); the contribution of the *C*–N bonds appeared at 285.32 eV.

The deprotection step was conducted by treatment of PEEK-FMOC with piperidine[22,31]. Using piperidine as solvent and reagent, we recovered a polymer film the surface of which was similar (XPS analysis) to the one of the blank sample (PEEK-OH immersed in piperidine); we

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[‖] We considered a theoretical monomer unit consisting of [(PEEK-OH)$_x$ + (PEEK-dansyl)$_y$], i.e. [(C$_{19}$O$_3$)$_x$ + (C$_{33}$O$_5$N$_3$S)$_y$], where $x + y = 1$. For $x = 0.83$ and $y = 0.17$, the calculated N/C × 100 atomic ratio was 0.51/21.38 × 100 = 2.38 (experimental value = 2.47).

[**] We considered a theoretical monomer unit consisting of [(PEEK-OH)$_x$ + (PEEK-FMOC)$_y$], i.e. [(C$_{19}$O$_3$)$_x$ + (C$_{39}$O$_7$N$_2$)$_y$], where $x + y = 1$. For $x = 0.76$ and $y = 0.24$, the calculated N/C × 100 atomic ratio was 0.48/23.8 × 100 = 2.017 (experimental value = 2.044).

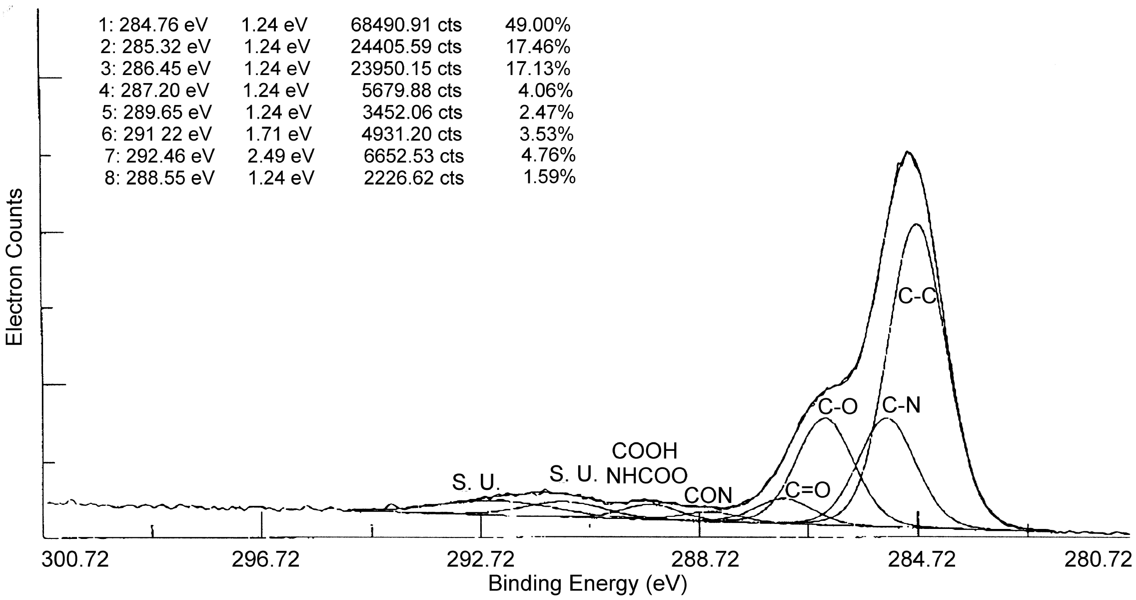

Figure 6 XPS analysis of PEEK-FMOC film; detailed C_{1s} peak

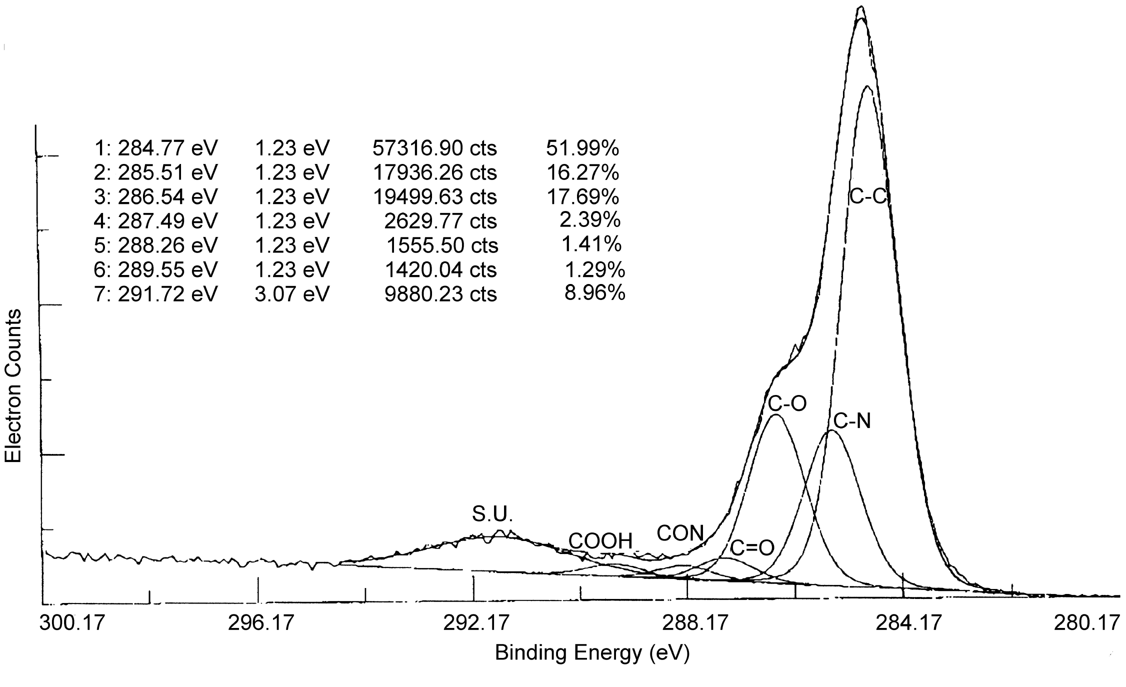

Figure 7 XPS analysis of PEEK-glutamine film; detailed C_{1s} peak

concluded that the modified interface was soluble in neat piperidine. Therefore, we immersed the PEEK-FMOC film into a diluted solution of piperidine in toluene, during 3 h at room temperature (*Scheme 4*, *Table 5*). After rinsing, the XPS analysis of the PEEK-glutamine film gave a N/C × 100 atomic ratio of 2.672, corresponding to 26% of modified polymer units††. The fine structure of the C_{1s} peak (*Figure 7*) revealed a significant diminution of the C=O contribution at 289.6 eV due to the disappearence of the carbamate function, but the remaining of the carboxyl function (2.5% in PEEK-FMOC and 1.3% in PEEK-glutamine). The amide contribution was visible at 288.26 eV (1.4%). A typical fragment of glutamine was found in the SIMS spectrum (negative mode) at *m*/*z* 89 ($C_3H_7NO_2$). The MIR spectrum (*Figure 5B*) showed the carboxyl band at 1742 cm^{-1}. The water contact angle of PEEK-glutamine was 75.7° (*Table 6*), a value significantly lower than the value measured for the PEEK-FMOC precursor.

CONCLUSION

In this paper we have further illustrated the usefulness of PEEK-OH as a key intermediate for the designed grafting of various chemical motifs on the PEEK surface by wet chemistry. The surface hydroxyl groups of PEEK-OH could be quantitatively replaced by amine functions in two steps, involving the substitution with phenylcarbamate and the

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††We considered a theoretical monomer unit consisting of [(PEEK-OH)$_x$ + (PEEK-glutamine)$_y$], i.e. [$(C_{19}O_3)_x$ + $(C_{24}O_5N_2)_y$], where $x + y = 1$. For $x = 0.74$ and $y = 0.26$, the calculated N/C × 100 atomic ratio was 0.52/20.3 × 100 = 2.561 (experimental value = 2.672).

basic hydrolysis of the PEEK-$NHCO_2Ph$ intermediate. This procedure led to the PEEK-NH_2 film displaying amine functions directly fixed on the polymer backbone. The level of functionalization was high, corresponding to about 70–80% of the monomer units analysed by the XPS technique (50–100 Å depth).

The grafting of glutamine also proceeded in two steps, involving the PEEK-OH substitution by N'-FMOC protected glutamine and the deprotection with piperidine. The PEEK-glutamine film displayed α-amino acid motifs fixed on the polymer backbone via a short spacer-arm. The level of functionalization was medium, corresponding to about 25% of the monomer units analysed by the XPS technique.

Finally, we could prepare a PEEK film (PEEK-SO_3H) displaying sulfonic acid motifs on its surface; this resulted from the nucleophilic opening of 1,3-propane sultone by PEEK-NH_2. Our procedure constitutes a valuable alternative to the direct sulfonation of PEEK samples with concentrated sulfuric acid. Indeed, it is well established that such treatment leads to the polymer dissolution[34,35].

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