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Maleimide-functionalized poly(2-ethyl-2-oxazoline): synthesis and reactivity†

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Poly(2-ethyl-2-oxazoline)s ($PEtOx_{23}$ – M_n = 2300 g mol^{-1}, $Đ$ = 1.07; $PEtOx_{46}$ – M_n = 4400 g mol^{-1}, $Đ$ = 1.06) end-functionalized with a maleimide moiety were prepared from azide-terminated $PEtOx_x$-N_3 *via* copper-catalyzed azide–alkyne cycloaddition (CuAAC) with an alkyne-bearing maleimide (MI). The latter has been synthesized in a three-step procedure, including protection of the maleimide double bond prior to the modification of PEtOx. $PEtOx_x$-MI was characterized by NMR (^{1}H, ^{13}C), SEC, FT-IR, and MALDI-ToF MS and, after deprotection of the maleimide, used in nitrile imine-mediated tetrazole-ene cycloaddition (NITEC) processes for covalent attachment to silicon surfaces in a grafting-to approach.

Introduction

Both the manipulation and the understanding of soft materials at the nanoscale are improving significantly[1] and the field of nanotechnology in conjunction with soft matter and/or functional polymers, surfaces, nanoparticles, and hybrid materials is of interest regarding applications in biomedicine[2–5] and optoelectronics.[6–8] Ideally, such materials are synthesized in high yields and using straightforward chemistry.[9,10] In case of low-yield and unspecific reactions ill-defined materials are obtained, which might be of limited functionality or contain significant amounts of unwanted byproducts.[11] Monomers featuring additional (protected) functional groups which are unaffected by the polymerization method of choice are arguably the most important cornerstone for the preparation of polymeric materials with precisely controlled architecture, functionality, and addressability.[12–14] Hereby, the respective polymerization technique of choice and its tolerance towards the presence of functional groups limits the range of accessible monomers. In that respect, the development of controlled radical polymerizations with their most important representatives atom-transfer radical polymerization (ATRP),[15,16] reversible addition–fragmentation transfer polymerization (RAFT),[17,18] and nitroxide-mediated polymerization (NMP)[19,20] was a very significant step forward to overcome some of the limitations of traditional living ionic techniques.[12]

However, some functional monomers typically cannot be polymerized in a controlled manner due to potential side reactions (*e.g.* recombination reactions between the desired functional group and the active polymer chain leading to termination, cross-linking, or branching). In that case, post-polymerization modification represents an elegant alternative to introduce functionalities that are not compatible with polymerization strategies and in this way many interesting macromolecular architectures such as end- and sidechain functionalized linear polymers, block copolymers, star polymers or graft copolymers can be prepared.[9,10,12,13,21]

Post-polymerization modifications and, in general, polymer/material science have been strongly influenced by the introduction of click chemistry.[22–28] For an overview on click chemistry with regard to polymer modifications[9,11,13,29,30] or reactions beyond classical click chemistry[12,31–33] the reader is directed to recent review articles. Thereby, a conscious use of the term "click chemistry" is required with regard to the specifics of polymer synthesis and a clear distinction from merely "efficient" and "successful" polymer analogous reactions needs to be made.[34]

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In the current study, well-defined poly(2-ethyl-2-oxazoline)s (PEtOx) with a terminal maleimide functionality were prepared and used for surface modification. Therefore, azide-terminated $PEtOx_x$-N_3 was synthesized *via* cationic ring-opening polymerization (CROP),[35,36] followed by the conjugation with an alkyne-functionalized maleimide (MI) *via* copper catalyzed azide–alkyne cycloaddition (CuAAC).[28,37–40] The maleimide functionality of MI and, respective, $PEtOx_x$-MI had to be protected and, thus, its deprotection procedure was also investigated. Selected Diels–Alder reactions (DA) fulfill the click criteria and especially reactions of certain dienes with maleimide containing materials renders them an appropriate tool for polymer post-polymerization functionalization,[33,41–45] protein conjugation, or the synthesis of block copolymers. In that respect, only few examples for hydrophilic maleimide-functionalized polymeric materials have been reported so far. Prominent examples are poly(ethylene oxide) (PEO)[46,47] or poly(ethylene glycol) methacrylate (PEGMA).[48,49]

After the characterization *via* NMR, SEC, FT-IR, and MALDI-ToF MS, $PEtOx_x$-MI was used for surface functionalization in light-induced nitrile imine-mediated tetrazole-ene cycloaddition (NITEC) processes.[50–54] Furthermore, poly(2-oxazoline)s (POx) coated surfaces open up promising alternatives to PEGylated surfaces for biomedical applications *e.g.* as antifouling coatings or for DNA binding and release.[55–57] In "grafting to" approaches POx have already been attached to glass substrates using photoimmobilization,[58–62] but the herein presented NITEC strategy offers several benefits like high selectivity, bio-orthogonality, and fast reaction times.[52,63,64]

Experimental section

Materials

Acetonitrile (ACN) was purified using a Solvent Purification System (SPS, Innovative Technology, PM-400-3-MD) equipped with two activated alumina columns. 2-Ethyl-2-oxazoline (EtOx) and methyl tosylate (Aldrich) were distilled over barium oxide under reduced pressure before polymerization and stored under argon. *N*-(3-Dimethylaminopropyl)-*N*′-ethylcarbodiimide hydrochloride (EDC-HCl), 4-dimethylaminopyridine (DMAP) and prop-2-yn-1-ol were purchased from Sigma-Aldrich. All other chemicals were used as received if not otherwise mentioned. 4-Maleimidobutyric acid[65] and compound **1**[66] were synthesized as reported in the literature.

Instruments

Nuclear Magnetic Resonance (NMR) proton and carbon spectroscopy (^1H and ^{13}C) were measured on a 250 MHz or a 300 MHz Bruker AC spectrometer at 298 K using the residual solvent resonance as an internal standard. The chemical shifts are given in ppm.

Size-Exclusion Chromatography (SEC) measurements were performed on a Shimadzu system equipped with a SCL-10A system controller, a LC-10AD pump, a RID-10A refractive index detector and a PSS-SDV-linear S column at 40 °C using a chloroform, triethylamine and 2-propanol (94 : 4 : 2) mixture as eluent at a flow rate of 1 mL min^{-1}. The system was calibrated with polystyrene (100–100 000 g mol^{-1}) standards.

Fourier Transform Infrared Spectroscopy (FT-IR) was performed on a FT-IR spectrometer FT-IR Affinity-1 from Shimadzu and measured in the range of 4000–600 cm^{-1}.

For the measurements of the Matrix-Assisted Laser Desorption/Ionization (MALDI) spectra, an Ultraflex III ToF/ToF instrument (Bruker Daltonics, Bremen, Germany) was used. The instrument is equipped with a Nd-YAG laser and a collision cell. All spectra were measured in positive and reflector mode. The instrument was calibrated prior to each measurement with an external PMMA standard from PSS. For the MALDI-ToF-MS sample preparation, separate solutions of polymer (10 mg mL^{-1} in chloroform), *trans*-2-[3-(4-*tert*-butylphenyl)-2-methyl-2-propenylidene] (DCTB) (30 mg mL^{-1} in chloroform), or 2,5-dihydroxybenzoic acid (DHB) and doping of sodium chloride (NaCl), (100 mg mL^{-1} in acetone) were prepared and mixed following the dried droplet spotting technique. 0.5 μL of the mixture was spotted onto the target plate.

Elemental Analyses were carried out on a EuroVector EuroEA3000 elemental analyzer.

For crystal structure determination intensity data were collected on a Nonius KappaCCD diffractometer, using graphite-monochromated Mo-K_α radiation. Data were corrected for Lorentz and polarization effects; absorption was taken into account on a semi-empirical basis using multiple-scans.[67–69] The structure was solved by direct methods (SHELXS)[70] and refined by full-matrix least squares techniques against F_o^2 (SHELXL-97).[70] All hydrogen atoms were located by difference Fourier synthesis and refined isotropically.

The polymerizations were performed in a Biotage Initiator Sixty microwave synthesizer equipped with a non-invasive FT-IR sensor (accuracy: 2%) in capped vials.

X-Ray Photoelectron Spectroscopy (XPS) was performed in a K-Alpha+ spectrometer (ThermoFisher Scientific, East Grinstead, UK) using a microfocused, monochromated Al Kα X-ray source (400 μm spot size). The K-Alpha charge compensation system was employed during analysis, using electrons of 8 eV energy, and low-energy argon ions to prevent any localized charge build-up. The kinetic energy of the electrons was measured by a 180° hemispherical energy analyzer operated in the constant analyzer energy mode (CAE) at 50 eV pass energy for elemental spectra. Data acquisition and processing using the Thermo Avantage software is described elsewhere.[71] The spectra were fitted with one or more Voigt profiles (BE uncertainty: ±0.2 eV) and Scofield sensitivity factors were applied for quantification.[72] All spectra were referenced to the C 1s peak (C–C, C–H) at 285.0 eV binding energy controlled by means of the well-known photoelectron peaks of Cu, Ag and Au respectively.

Synthesis

Synthesis of $PEtOx_x$-N_3. Methyl tosylate and 2-ethyl-2-oxazoline (EtOx) were dissolved in acetonitrile (ACN) in microwave vials at different monomer to initiator ratios ([M]/[I]) at a monomer

concentration of 4 M and capped under inert conditions in a glove box. The capped vials were placed in a microwave synthesizer at 140 °C. The polymerization was terminated *via* the addition of dry sodium azide under inert conditions. The reaction solution was diluted with chloroform and the organic layers were washed with brine and dried over sodium sulfate. Afterwards, the polymers were obtained by evaporation of the solvent under reduced pressure. After dissolving the residue in a few mL of chloroform the product was precipitated in cold diethyl ether, filtered off and dried *in vacuo*.

^{1}H NMR (300 MHz, $CDCl_3$, δ): 3.6–3.2 (br, –N–CH_2–CH_2–), 2.5–2.2 (br, CO–CH_2–CH_3), 1.2–1.0 (br, CO–CH_2–CH_3) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$, δ): 175–173 (*C*=O), 50–42 (–N–*C*H_2–*C*H_2–), 27–25 (CO–*C*H_2–CH_3), 10–8 (CO–CH_2–*C*H_3) ppm.

PEtOx$_{23}$-N$_3$: SEC ($CHCl_3$/*i*-PrOH/Et_3N): M_n = 1900 g mol^{-1}, $Đ$ = 1.10 (PS-calibration), MS (MALDI-ToF MS, DCTB/NaCl): M_n = 1915 g mol^{-1}, $Đ$ = 1.08, yield: 56%.

PEtOx$_{46}$-N$_3$: SEC ($CHCl_3$/*i*-PrOH/Et_3N): M_n = 4200 g mol^{-1}; $Đ$ = 1.05 (PS-calibration), MS (MALDI-ToF MS, DCTB/NaCl): M_n = 4636 g mol^{-1}, $Đ$ = 1.03, yield: 75%.

FT-IR: ν [cm^{-1}] = 2976 and 2932 (CH), 2100 (N_3), 1627 (C=O), 1429 (CH_2/CH_3), 1371 (CH_3), 1194 (C–N).

Synthesis of 2-propynyl-4-(1,3-dioxo-3a,4,7,7a-tetrahydro-1*H*-4,7-epoxyisoindol-2(3*H*)-yl)butanoate (2). 1, prop-2-yn-1-ol (1.2 eq.), EDC-HCl (3 eq.) and DMAP (0.15 eq.) were dissolved in dichloromethane (0.1 M solution) and stirred at room temperature for 24 h. Afterwards, the mixture was filtered and the clear solution was washed five times with water. The organic phase was dried over sodium sulfate and the solvent was removed under reduced pressure. Subsequently, the crude product was purified *via* column chromatography (silica gel 60, $CHCl_3$: ethyl acetate 7 : 1). **2** was obtained as white crystals. Yield: 47% (of theory).

^{1}H NMR (300 MHz, $CDCl_3$, δ): 6.51 (s, 2 H, 2 C*H*), 5.26 (s, 2 H, 2 C*H*), 4.67 (d, 2H, OCH_2), 3.55 (t, 2H, CH_2), 2.84 (s, 2 H, 2 C*H*), 2.45 (t, 1H, C≡C*H*), 2.35 (t, 2 H, CH_2), 1.93 (m, 2 H, CH_2) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$, δ): 176.96 (O–*C*=O), 172.51 (N–*C*=O), 137.21 (*C*=*C*), 81.52 (C_{furan}–O), 75.56 (CH_2–*C*≡C–H), 52.67 (O–*C*H_2), 47.99 (*C*H–*C*H), 38.73 (N–*C*H_2), 31.63 (*C*H_2–C=O), 23.37 (*C*H_2) ppm.

FT-IR: ν [cm^{-1}] = 3282 (≡CH), 3015 (=CH), 2987 and 2937 (CH), 2361 (C≡C), 1739 (O–C=O), 1689 (N–C=O), 1445 (CH_2/CH_3), 1396 (CH_3), 1154 (C–O–C).

MS (MALDI-ToF MS, DHB): *m*/*z* calculated for $[C_{15}H_{15}NO_5]^{Na+}$: 312.08; found: 312.08 $[M + Na]^+$.

EA: 62.46% C, 5.62% H, 5.15% N, (calc.: 62.28% C, 5.23% H, 4.84% N).

Crystal data: $C_{15}H_{15}NO_5$, M_r = 289.28 g mol^{-1}, colourless prism, size 0.046 × 0.042 × 0.040 mm^3, monoclinic, space group *C*2/*c*, *a* = 28.1106(7), *b* = 5.8720(2), *c* = 21.0927(6) Å, β = 130.543(1)°, *V* = 2645.79(13) Å^3, *T* = −140 °C, *Z* = 8, ρ_{calcd} = 1.452 g cm^{-3}, μ(Mo-K$_\alpha$) = 1.1 cm^{-1}, multi-scan, transmin: 0.6986, transmax: 0.7456, *F*(000) = 1216, 9256 reflections in *h*(−36/36), *k*(−7/7), *l*(−25/27), measured in the range 2.54° ≤ Θ ≤ 27.49°, completeness Θ_{max} = 99.3%, 3026 independent reflections, R_{int} = 0.0334, 2663 reflections with $F_o > 4\sigma(F_o)$, 250 parameters, 0 restraints, $R1_{obs}$ = 0.0379, wR_{obs}^2 = 0.0925, $R1_{all}$ = 0.0448, wR_{all}^2 = 0.0968, GOOF = 1.057, largest difference peak and hole: 0.330/−0.208 e Å^{-3}.

Synthesis of PEtOx$_x$-MI *via* CuAAC. 2 (2.5 eq.) and PEtOx$_x$-N_3 (500 mg) were dissolved in 10 mL THF. Copper bromide (CuBr, 2.5 eq.) and *N*,*N*,*N*′,*N*″,*N*‴-pentamethyldiethylenetriamine (PMDETA, 2.5 eq.) were added and stirred for 1 hour at 50 °C. Afterwards, the reaction solution was allowed to stir at room temperature overnight. The copper was removed *via* a short aluminum oxide (AlOx) column and the solvent was evaporated under reduced pressure. The residue was dissolved in 10 mL dichloromethane and subsequently the polymer was precipitated in cold diethyl ether, filtered off and dried *in vacuo*.

^{1}H NMR (300 MHz, $CDCl_3$, δ): 6.51 (s, 2 C*H*), 3.75 (t, CH_2), 3.6–3.3 (br, –N–CH_2–CH_2–), 2.85 (s, 2 C*H*), 2.5–2.2 (br, CO–CH_2–CH_3), 1.86 (m, CH_2), 1.2–1.0 (br, CO–CH_2–CH_3) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$, δ): 176–172 (*C*=O), 136.24 (*C*=*C*), 80.66 (C_{furan}–O), 48–43 (–N–*C*H_2–*C*H_2–), 26–24 (CO–*C*H_2–CH_3), 22.40 (–*C*H_2–), 10–8 (CO–CH_2–*C*H_3) ppm.

FT-IR: ν [cm^{-1}] = 2980 and 2939 (CH), 1740 (O–C=O), 1635 (N–C=O), 1426 (CH_2/CH_3), 1374 (CH_3), 1201 (C–N).

PEtOx$_{23}$-MI: SEC ($CHCl_3$/*i*-PrOH/Et_3N): M_n = 2250 g mol^{-1}, $Đ$ = 1.07 (PS-calibration), MS (MALDI-ToF MS, DCTB/NaCl): M_n = 2727 g mol^{-1}, $Đ$ = 1.04, yield: 22%;

PEtOx$_{46}$-MI: SEC ($CHCl_3$/*i*-PrOH/Et_3N): M_n = 4350 g mol^{-1}, $Đ$ = 1.06 (PS-calibration), MS (MALDI-ToF MS, DCTB/NaCl): M_n = 4764 g mol^{-1}, $Đ$ = 1.02, yield: 73%.

Deprotection procedure of PEtOx$_x$-MI

20 mg of PEtOx$_x$-MI were dissolved in 500 µL of deuterated dimethylformamide and the resulting solution was heated to 130 °C for different reaction times. After the desired reaction time the degree of cleavage was determined by ^{1}H NMR spectroscopy (300 MHz, DMF-d_6). Alternatively, PEtOx$_x$-MI was deprotected in the bulk at 100 °C *in vacuo* prior to photografting experiments.

Functionalization of silicon wafers with tetrazole (Sur 1)

Silicon wafers were functionalized with tetrazole (**Sur 1**) according to previous reports.[73]

Polymer photografting onto silicon wafers (Sur 2)

A tetrazole functionalized silicon wafer (**Sur 1**) was immersed in a solution of deprotected PEtOx$_x$-MI in dry dichloromethane (c = 6 mg mL^{-1}). The solution was degassed with an argon stream for 10 min, while cooled in an ice bath and the surface was irradiated with an Arimed B6 lamp for 24 h. The surface **Sur 2** was removed from the solution and washed extensively with dichloromethane. X-ray photoelectron spectroscopy (XPS) was performed before and subsequently to the photo-ligation of deprotected PEtOx$_x$-MI onto the tetrazole surface. The results are summarized in Fig. 4 and the full table of atomic percents (at%) is given in the ESI.†

Results and discussion

Maleimide-functionalized poly(2-ethyl-2-oxazoline)s (PEtOx$_x$-MI) with two different chain lengths was prepared *via* copper catalyzed azide–alkyne cycloaddition (CuAAC). Azide-functionalized poly(2-ethyl-2-oxazoline)s (PEtOx$_x$-N$_3$) of different molar mass and with narrow molecular weight distributions ($Đ$ < 1.2) were synthesized according to literature[36,74–76] (Scheme 1) and combined with an alkyne-functionalized maleimide, which has been synthesized in a three-step procedure (Fig. 1A).

The protection of the maleimide double bond using furan was necessary to make it less prone against nucleophilic attack.[66] In that respect, the actual PEtOx$_x$-MI can be achieved *via* a subsequent deprotection step (Scheme 1). Besides the characterization (NMR: Fig. 1C, FT-IR: Fig. S1,† MALDI: Fig. S2,† EA) the compound could be crystallized und enabled X-ray structure analysis (Fig. 1B for the respective crystal structure image).

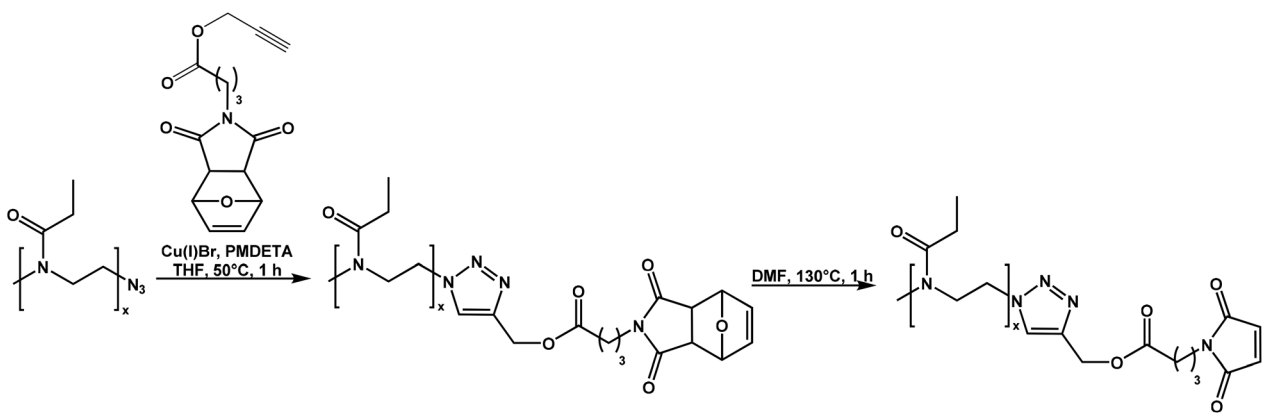
The following CuAAC between the maleimide and PEtOx$_x$-N$_3$ was carried out using copper(I) bromide (CuBr) and *N*,*N*,*N*′,*N*″,*N*‴-pentamethyldiethylenetriamine (PMDETA) as a catalyst-ligand system.[38,40] The temperature was set to 50 °C for one hour to prevent the retro Diels–Alder (retro-DA) reaction with respect to the maleimide-furan Diels–Alder (DA) adduct and afterwards stirred at ambient temperature overnight to ensure full conversion. For purification, copper was removed by a short aluminum oxide (AlOx) column and the final polymer was isolated by precipitation in cold diethyl ether. Characterization was carried out using SEC, NMR (Fig. 2), MALDI (Fig. S3†), and FT-IR (Fig. S4†).

An increase of the molar mass for both PEtOx$_{23}$-MI and PEtOx$_{46}$-MI by comparison of the respective SEC traces was observed (see Table 1 for detailed information).

The NMR spectrum shows resonances associated with the PEtOx backbone peak at 3.5, 2.3 and 1.2 ppm as well as the furan protection group at 6.5 ppm. The degree of functionalization of PEtOx$_x$-MI was determined to be nearly quantitative within the range of the error of the method (NMR). Subsequently, the deprotection procedure of PEtOx$_x$-MI was investigated in detail. The polymer was dissolved in deuterated dimethylformamide (DMF-d_6) and heated to 130 °C for different reaction times in an oil bath. The same approach was carried out for the pristine maleimide for comparison. The resonance at 6.5 ppm was used to determine the degree of functionalization by comparing it to the signal in the range of 2.3 ppm of the PEtOx$_x$-MI. The disappearance of the furan resonance was observed, showing clearly the deprotection of the maleimide with time (Fig. 3). The degree of cleavage was determined and illustrated in a deprotection *vs.* time plot showing close to 50% of cleavage after only five minutes and complete deprotection within one hour under these conditions for all systems investigated.

Subsequently, the reactivity of the terminal maleimide was investigated by immobilization of the deprotected PEtOx$_x$-MI on a tetrazole functionalized silicon wafer (**Sur 1**) *via* photochemical NITEC reaction (**Sur 2**, Fig. 4). The tetrazole functionalization was carried out according to a previous report.[73] For the NITEC reaction the tetrazole surface (**Sur 1**) was immersed in a degassed and dry solution of polymer in dichloromethane and exposed to UV-irradiation for 24 h using an Arimed B6 lamp. Unreacted material was removed from the surface by extensive washing with solvent, and subsequently the surface was dried in an argon stream and analyzed *via* X-ray photoelectron spectroscopy (XPS). The surface with immobilized PEtOx$_x$-MI (**Sur 2**) was compared to a neat tetrazole functionalized silicon wafer (**Sur 1**) and the data is shown in Fig. 4.

The XPS signals at 286.6 eV and 288.4 eV correspond to C–O, C–N and amide carbons and increase from 3.4 at% to 6.3 at% and 0.9 at% to 3.0 at% for the functionalization with PEtOx$_{46}$-MI.[54] The increase in the signal at 400.3 eV from 1.7 at% to 3.1 at% additionally indicates the presence of amide nitrogen atoms on the surface. A further proof for the formation of a PEtOx layer on the surface is the decrease in signals for silicon and oxygen as evident from Table S3.†



Scheme 1 Synthesis of PEtOx$_x$-MI *via* CuAAC and subsequent deprotection.

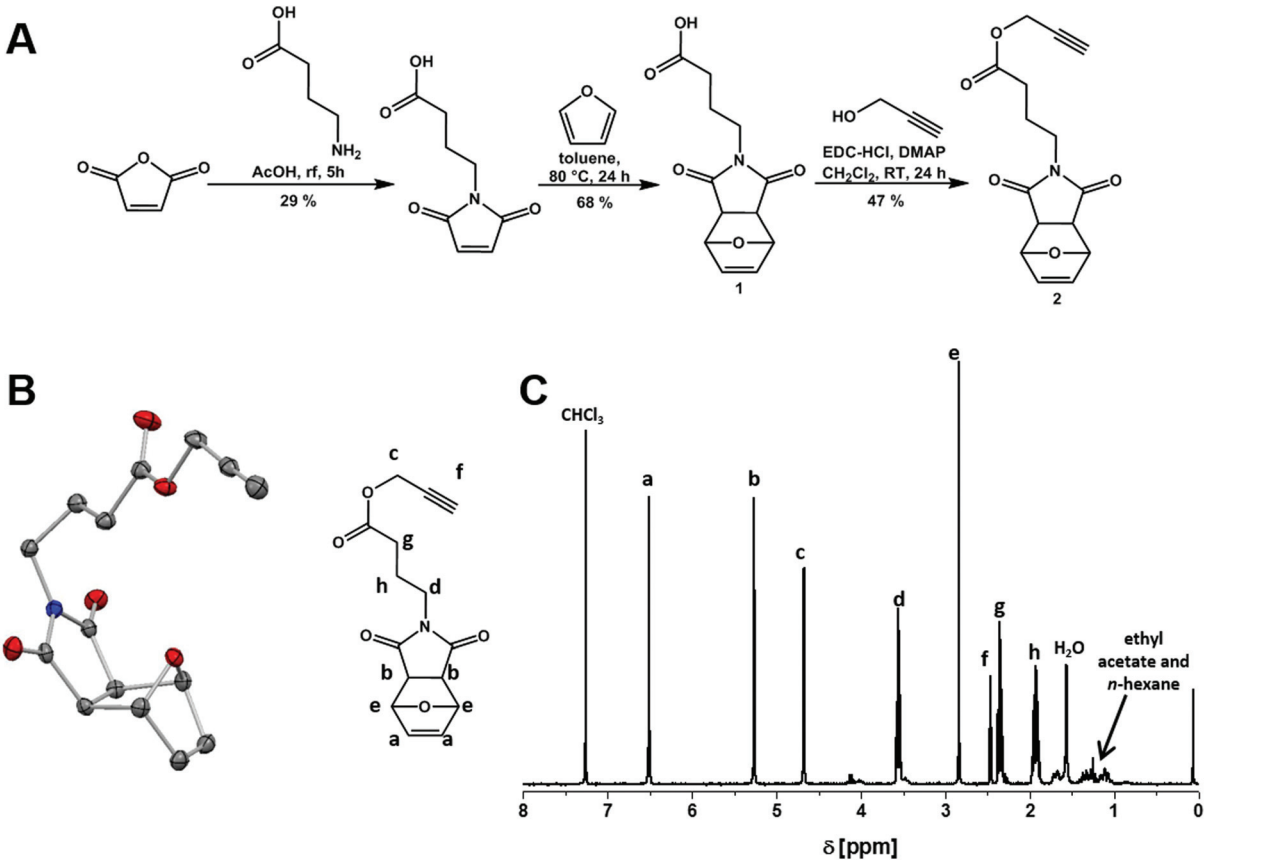


Fig. 1 Synthetic strategy for the preparation of the alkyne-functionalized maleimide (A), including the molecule structure (B, 50% probability level, hydrogens omitted, dark grey: carbon, blue: nitrogen, red: oxygen), and a ^{1}H-NMR (300 MHz, $CDCl_3$) spectrum of the alkyne-functionalized maleimide (C).

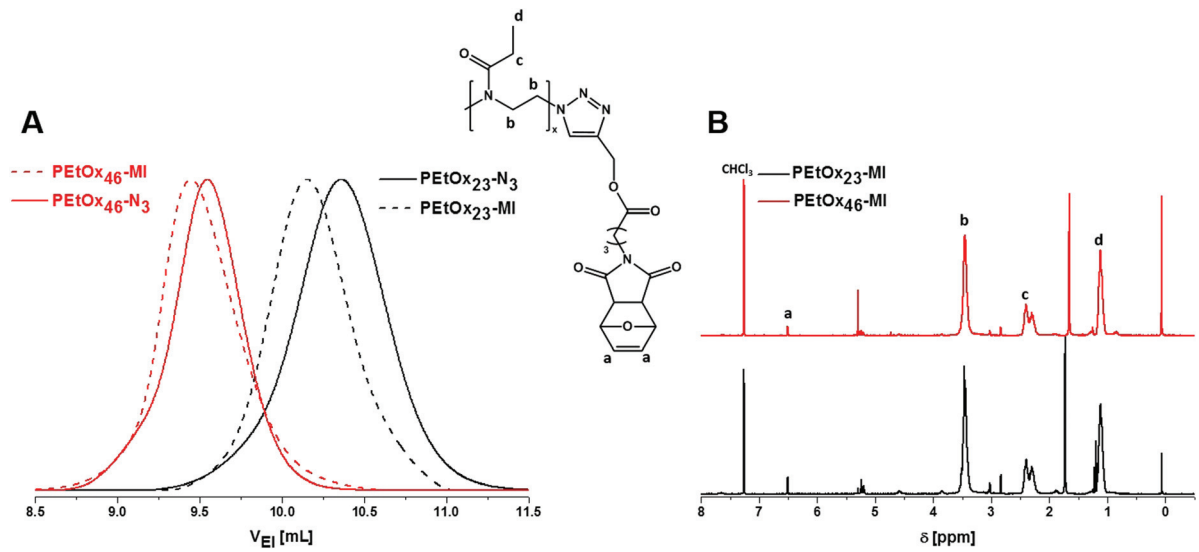


Fig. 2 Comparison of the SEC traces for $PEtOx_x$-N_3 (straight line)/$PEtOx_x$-MI (dashed line) (A) and characterization *via* NMR spectroscopy (300 MHz, $CDCl_3$) for a degree of polymerization of: 23 (black traces) and 46 (red traces, B).

Table 1 Characterization of $PEtOx_x$-N_3 and $PEtOx_x$-MI *via* SEC and MALDI-ToF MS

Polymer	M_n [a] [g mol^{-1}]	$Đ$ [a]	M_n [b] [g mol^{-1}]	$Đ$ [b]
$PEtOx_{23}$-N_3	1900	1.10	1900	1.08
$PEtOx_{46}$-N_3	4200	1.05	4600	1.03
$PEtOx_{23}$-MI	2300	1.07	2700	1.04
$PEtOx_{46}$-MI	4400	1.06	4800	1.02

[a] SEC ($CHCl_3$/*i*-PrOH/Et_3N) (PS-calib). [b] MS (MALDI-ToF, DCTB/NaCl) (PMMA calib).

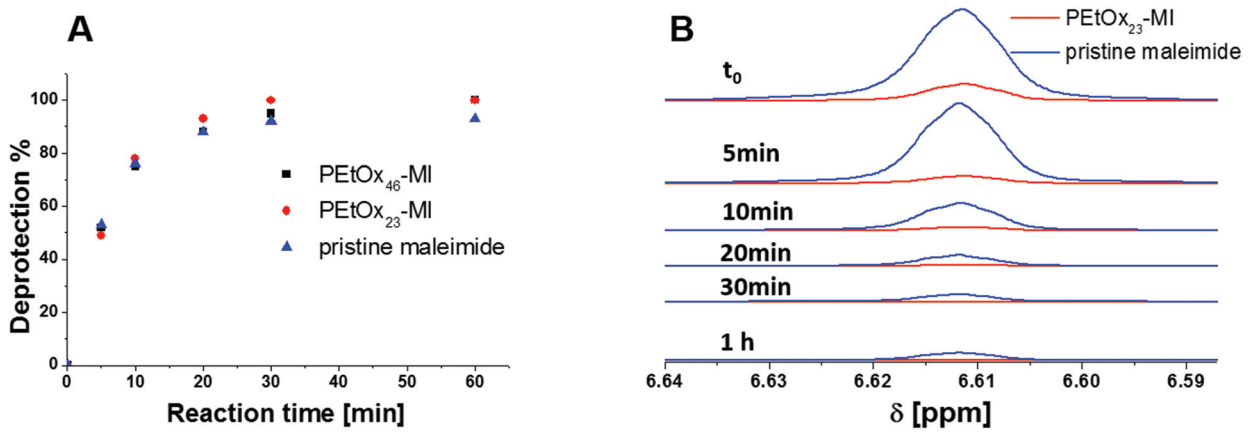


Fig. 3 Time dependent deprotection of $PEtOx_{23}$-MI (red line) and the pristine maleimide (blue line, A) and comparison of the respective ^{1}H-NMR spectra (300 MHz, DMF-d_6) at different reaction times (B).

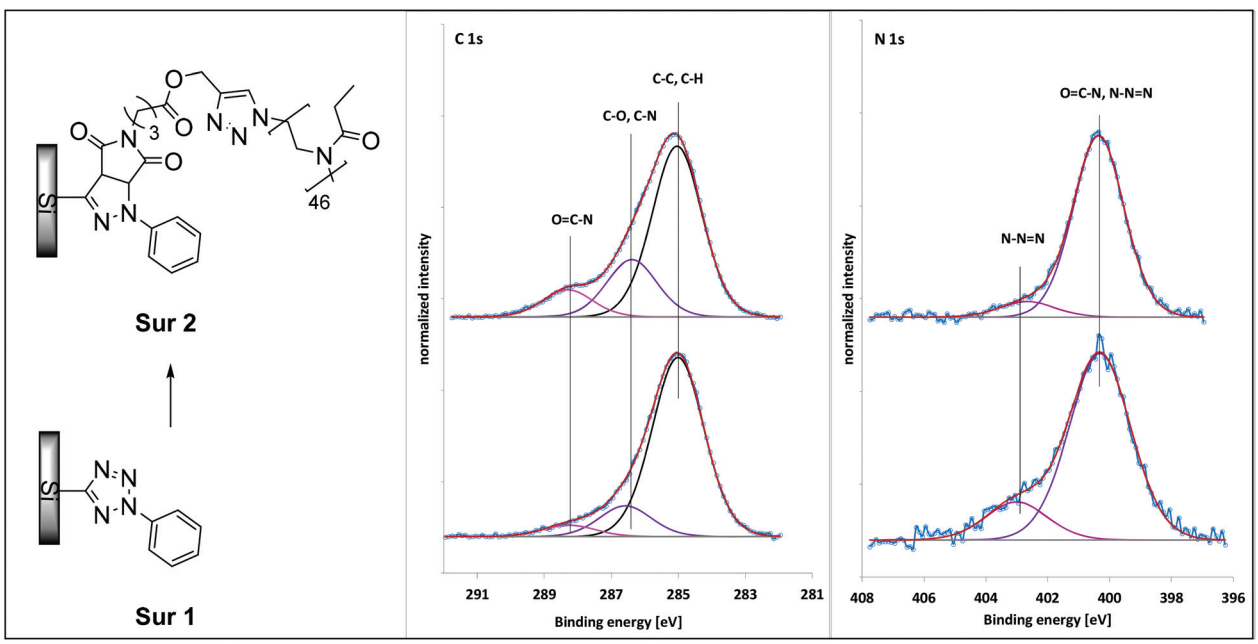


Fig. 4 XPS characterization of the $PEtOx_{46}$-MI functionalized silicon wafer (**Sur 2**) in comparison to the tetrazole functionalized silicon wafer (**Sur 1**).

Conclusions

In summary, the preparation and the reactivity of maleimide-functionalized PEtOx$_x$-MI is presented, starting from PEtOx$_x$-N$_3$ and an alkyne-functionalized maleimide. Two degrees of polymerization (23 and 46) for PEtOx$_x$ were chosen and the covalent attachment of the maleimide functionality was realized using a CuAAC approach. Due to its high reactivity the maleimide had to be protected with furan prior to the coupling and we could show that complete deprotection within one hour at 130 °C can be achieved afterwards. PEtOx$_x$-MI was subsequently immobilized on a tetrazole functionalized silicon wafer *via* a photochemical NITEC reaction and this was confirmed by XPS analysis. Such surfaces might be of interest for layer-by-layer approaches or where control over cell adhesion on surfaces is desired – in both cases the deprotection of PEtOx$_x$ to linear PEI would be necessary, as we have recently demonstrated for SiO$_2$@P(EtOx-*stat*-EI) hybrid nanoparticles.[77] As an alternative strategy, in case of hydrophobic poly(2-oxazoline)s a maleimide endgroup has been introduced *via* direct endcapping very recently by Luxenhofer *et al.*[78] These materials were then used to modify elastin-like proteins.

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