Synthesis of Novel Amphiphilic Azobenzenes and X-ray Scattering Studies of their Langmuir Monolayers

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SUPPORTING INFORMATION:

Synthesis:

As 4,4'-diamino-azobenzene (**1**) is commercial available at reasonable cost, the alkylation of this compound appeared an attractive route to the target molecules. However all our attempts of direct alkylation of this material failed to give the desired compounds in acceptable yields.

In the literature many different approaches to direct alkylation of aniline and anilide type compounds are found.[1-5] A number of these methods, outlined in Scheme S1, were applied in our initial attempts at synthesizing the target molecules. In our hands they all failed to give the desired product in an appreciable yield. None of the methods produce dialkylated 4,4'-diaminoazobenzene and only method a) and c) produce moderate yields of the monoalkylated product.
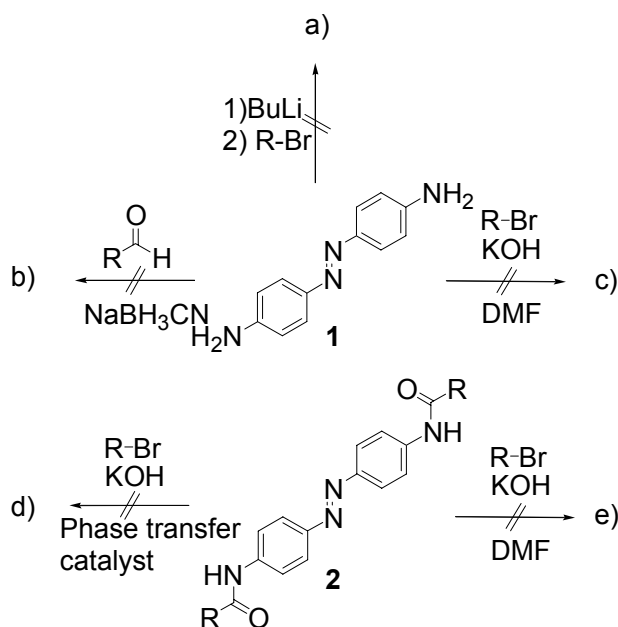
Scheme S1. Attempted methods of alkylation. Route a) See Ref. 1, b) see Ref. 2, c) see Ref. 3, d) see Ref. 4, and e) see Ref. 5.

The successful method presented here is based on the results of Blevins and Blanchard, who have shown that **1** can be acylated in high yields using acid chlorides.[6] From the literature it is also known that symmetric azobenzenes can be prepared by reduction of the nitrobenzenes with Lithium Aluminum Hydride[7] in an aprotic medium. This combined with the acylations reported by Blevins and Blanchard lead us to the acylation-reduction procedure presented in Scheme 1 (main text). This approach has been applied successfully for the preparation of the derivatives listed in Table 1 (main text), *e.g.*, the N,N'-dialkylation of **1** to **3a** is done in two steps with an overall yield of 46 %.

The acylations described below apply to most acid chlorides and anhydrides, the only difference being the solvent used for recrystallization. For the reduction of the amides **2** and **4** a large surplus of reductant and long reaction times are necessary. The daylong reaction time can be substituted with a minimum of 4 hours at reflux temperature; these are harsh conditions and will not be endured by all substitution patterns. The NMR spectra of the tetra substituted species show a significant signal broadening due to hindered rotation of the bonds near the aromatic core. The tetra alkylated and dialkylated/diacylated compounds have melting points near ambient temperatures and in our hands their purification has only been possible by flash chromatography using graduated elution with heptane/ethyl acetate. Crystallization of **5a** was observed in a pentane solution at -25$^{\text{o}}$C.

When followed by MALDI-TOF MS and TLC all the reactions, both acylations and reductions, have quantitative conversion. The reason that the overall yield reported is only low to moderate is found in the cis-trans isomerism of the azobenzene moiety. The

starting material and the products contain a percentage (1-10%) of the *cis* isomer identified by ^{1}H-NMR, *e.g.* (CDCl$_3$) δ 8.83 (s, 2H), δ 7.55 (d, 4H, J=8.9Hz) and δ 6.88 (d, 4H, J=8.8Hz) in the aromatic region of the spectrum of the crude product in the synthesis of compound **2b**. The pure products are isolated by careful chromatography, where a significant amount of the product is discarded as the *cis*-isomer is regarded as an impurity. If the compounds **2-5** are to be used as intermediates in further synthetic steps the *cis*-impurity can be ignored and the materials obtained in excellent yields.

Experimentals:

MALDI-TOF MS experiments were performed on a Bruker Daltronix Flex system without matrix. ESI-TOF was done on a Micromass quadrupole-TOF setup from acetonitrile/methanol mixtures. 1H NMR (300 MHz) and 13C NMR (75 MHz) spectra were recorded on a Varian instrument. Samples were prepared using CDCl3 purchased from Cambridge Isotope Labs. Microanalyses were performed at the Microanalytical Laboratory at the Department of Chemistry, University of Copenhagen.

Flash column chromatography was done using silica 60 (0.063-0.200 mm.) from Merck and dry column vacuum chromatography was performed using silica 60 (0.015-0.040 mm.) from Merck.

N,N'-didodecanoyl-4,4'-diamino-azobenzene (**2a**):

   The compound was prepared according of the procedure described by Blanchard,[9] with the following modifications. In a 500 ml round bottom flask 0.85 g (4 mmol) of 4,4'-diamino-azobenzene was dissolved in 150 ml THF (distilled from Na/benzophenone). While stirring 2.06 g (16 mmol) ethyl diisopropylamine (Anhydroscan) was added,

followed by 3.17 g (16 mmol) of dodecanoyl chloride. The reaction mixture was stirred 1 hour at room temp, and the reaction was quenched with 150 ml 2 M HCl (aq.). The yellow solid was collected by filtration and washed with three portions of 50 ml CH_2Cl_2 to remove unreacted and mono acylated material. Recrystallization from 1.5 l of toluene afforded the pure product as a paper like light yellow solid, yield 1.53 g (66.3 %). Optimization of the reaction conditions showed that addition of dichloromethane to the solvent of recrystallization reduced the volume needed and afforded an increase of the yield up to 15 %.

^{1}H NMR (CDCl$_3$ with TFA): δ 8.34 (s, 2H), δ 7.91 (d, 4H), δ 7.70 (d, 4H), δ 2.51 (t, 4H), δ 1.73 (m, 4H), δ 1.26 (m, 32H), δ 0.88 (t, 6H). MS; Direct inlet: 576 m/z (M$^+$). MALDI-TOF: m/z 577 (M+H$^+$) and 599 (M+Na$^+$). Anal. Calcd. for $C_{36}H_{56}N_4O_2$: C, 74.96; H, 9.78; N,9.71. Found: C, 73.90; H, 9.90; N, 9.50.

N,N'-di(2-(2-(2-methoxy-ethoxy)-ethoxy)-acetyl)-4,4'-diamino-azobenzene (**2b**):

4-4'-Diamino-azobenzene (**1**) 0.85 g (4 mmol) and ethyl diisopropylamine (Anhydroscan) 2.06 g (16 mmol) was dissolved in 150 ml THF (distilled from Na/benzophenone), after 5 min. of stirring 2-(2-(2-Methoxy-ethoxy)-ethoxy)-acetyl chloride 3.8 g (19 mmol) was added and the reaction mixture was stirred overnight. 250 ml of ethyl acetate was added and the reaction was poured onto 200 ml of water. The organic phase was separated, washed with brine and dried over sodium sulphate. The product was isolated as orange needles by flash column chromatography with a graduated elution from heptane to ethyl acetate, in a yield of 0.765 g (40 %).

^{1}H-NMR (CDCl$_3$): δ 8.97 (s, 2H), δ 7.91 (d, 4H, J=8.9Hz), δ 7.79 (d, 4H, J=8.9Hz), δ 4.14 (s, 1H), δ 3.79 (m, 4H), δ 3.73 (m, 1H), δ 3.60 (m, 4H), δ 3.38 (s, 6H). ^{13}C-NMR (CDCl$_3$): δ 168.3, δ 149.1, δ 139.7, δ 123.6, δ 120.0, δ 71.65, δ 71.13, δ 70.65, δ 70.22, δ 70.00, δ 58.91. MS; MALDI-TOF: m/z 555 (M+Na$^+$) and 571 (M+K$^+$). UV-vis λ$_{max}$ (nm (log ε)) (MeCN): 443 (3.37) (sh), 356 (4.40), 247 (4.23). Anal. Calcd. for C$_{26}$H$_{36}$N$_4$O$_8$: C, 58.63; H, 6.81; N,10.25. Found: C, 57.69; H, 6.92; N, 10.25.

N,N'-diacetyl-N,N'-didodecyl- 4,4'-diamino-azobenzene (**4a**):

To a solution of 0.35 g (1 mmol) of N,N'-didodecyl-4,4'-diamino-azobenzene (**3a**) in 20 ml of methylene chloride was added first 0.5 g (4 mmol) of dry ethyl diisopropylamine (Anhydroscan), then 0.314 g (4 mmol) of acetyl chloride with stirring in a nitrogen atmosphere. The reaction was monitored with TLC and upon completion, after approximately 4 hours, was poured onto 50 ml of 10 % aqueous potassium carbonate. The product was extracted with two 50 ml portions of ether, washed with water and dried over sodium sulfate. The solvent was removed in vacuum and the product was isolated as small dark yellow needles in a yield of 0.17 g (27 %) by flash chromatography using petrol ether as eluent.

^{1}H-NMR (CDCl$_3$): δ 7.96 (d, 4H, J=8.6Hz), δ 7.32 (d, 4H, J=8.6Hz), δ 3.73 (m, 4H), δ 1.91 (s, 6H), δ 1.52 (m, 4H), δ 1.22 (s, 36H), δ 0.85 (t, 6H, J=6.7Hz). MS; MALDI-TOF: m/z 633 (M+H$^+$).

trans-N,N'-didodecyl-N,N'-di(2-(2-(2-methoxy-ethoxy)ethoxy)-acetyl)-4,4'-diamino-azobenzene (**4b**):

   The compound was prepared from N,N'-didodecyl-4,4'-diamino-azobenzene (**3a**) by acylation with 2-(2-(2-methoxyethoxy)ethoxy)acetyl chloride. To a mixture of 80 ml ether and 80 ml methylene chloride was added 1.0 g (1.8 mmol) N,N'-didodecyl-4,4'-diamino-azobenzene (**3a**), 0.93 g (7.2 mmol) of ethyl diisopropylamine. To the stirred solution 1.41 g (7.2 mmol) 2-(2-(2-methoxyethoxy)ethoxy)acetyl chloride was added and stirring was continued for 2.5 hours. The reaction mixture was quenched with 150 ml 10% K_2CO_3 and the product extracted with 150 ml ether. The organic phase was washed twice with 10% K_2CO_3, twice with NH_4CL and twice with water and then dried over Na_2SO_4. The crude product was evaporated onto silica (grain 0.015-0.040 mm.) and purified with dry column vacuum chromatography, using graduated elution starting from pure ether going to 3:1 ether/THF.

   The product was isolated as an orange viscose oil, yield 1.22 g (77 %).

   1H NMR ($CDCl_3$): δ 7.97 (d, 4H), δ 7.25 (d, 4H), δ 3.95 (t, 4H), δ 3.73 (t, 4H), δ 3.61 (m, 12H), δ 3.50 (m, 4H), δ 3.34 (s, 6H), δ 1.51 (m, 4H), δ 1.23 (m, 36H), δ 0.87 (t, 6H). MS; MALDI-TOF: m/z 869 (M +H^+), m/z 891 (M+Na^+). UV-vis λ_{max} (nm (log ε)) (MeCN): 440 (3.03), 340 (4.41), 232 (4.29). Anal. Calcd. for $C_{50}H_{84}N_4O_8$: C, 69.09; H, 9.74; N,6.45. Found: C, 68.90; H, 9.87; N, 6.20.

trans-N,N'-didodecyl-N,N'-di(monosuccinoyl)-4,4'-diamino-azobenzene (**4c**):

   The compound was prepared from N,N'-didodecyl-4,4'-diamino-azobenzene (**3a**) by reaction with succinic anhydride. N,N'-didodecyl-4,4'-diaminoazobenzene (3a), 0.8 g

(1.5 mmol), was dissolved in a mixture of 50 ml. ether and 50 ml. of methylene chloride. To this 8.9 g (85 mmol) succinic anhydride and 2.5 g (26 mmol) sodium propionate was added followed by 50 ml. of chloroform. The reaction mixture was brought to reflux and the reflux was maintained for 9 h. The reaction was monitored by TLC (ether). After completion the reaction was poured onto 200 ml of NH_4Cl(aq.) (200 g/l). The organic phase was separated and the solvent was removed by evaporation. The crude product was dissolved in 250 ml ether and washed several times with 0.1 M NaOH. The phases were separated and the aqueous phase was extracted with 150 ml ether. The combined organic phase was washed twice with 0.1 M HCl and twice with water. The product was extracted from the organic phase with 0.5 M NaOH. The alkaline phase was washed twice with ether and was carefully neutralized with HCl. The product was then extracted with two portions of ether, and the organic phase was dried over Na_2SO_4 and the solvent is removed in vacuo. The product is a yellow to orange very viscous oil, almost a wax. Yield 189 mg (15%). If further purification is necessary dry column vacuum chromatography can be used with graduated elution going from pure petrol ether bp. <50°C over pure ether to pure THF.

^{1}H NMR (CDCl$_3$): δ 7.99 (d, 4H), δ 7.36 (d, 4H), δ 3.75 (t, 4H), δ 2.65 (t, 4H), δ 2.4 (m, 4H), δ 1.52 (m, 4H), δ 1.23 (m, 36H), δ 0.86 (t, 6H). MS; MALDI-TOF: m/z 749 (M +H$^+$), m/z 771 (M+Na$^+$), m/z 787(M+K$^+$). UV-vis λ_{max} (nm (log ε)) (MeCN): 435 (2.56) , 347 (3.79) (sh). Anal. Calcd. for $C_{44}H_{68}N_4O_6$: C, 70.55; H, 9.15; N,7.48. Found: C, 69.90; H, 9.18; N, 7.25.

N,N'-didodecyl-4,4'-diamino-azobenzene (**3a**):

The compound was prepared from dodecanoic acid N,N'-didodecanoyl-4,4'-diamino-azobenzene (**2a**) by reduction with lithium aluminium hydride. 5 g (8.7 mmol) of N,N'-didodecanoyl-4,4'-diamino-azobenzene (**2a**) was dissolved in a 2:5 mixture of THF/toluene (500 ml). While stirring 7 pellets of 0.65 g each, a total of 4.55 g (120 mmol) $LiAlH_4$, was added and the reaction mixture was heated to reflux. Reflux temperature was maintained for 4 hours. The reaction mixture was cooled to 0°C and quenched with 250 ml NH_4Cl (aq.) (200 g/l). The product was extracted with two portions of 250 ml ether. The organic phase was washed with three portions of water and filtered through a silica plug. The solvent was evaporated and the crude product was recrystallized from methylene chloride to yield 3.3 g (70 %) of yellow, needle shaped crystals.

^1H NMR ($CDCl_3$): δ 7.74 (d, 4H), δ 6.63 (d, 4H), δ 3.96 (t, 2H), δ 3.17 (q, 4H), δ 1.65 (m, 4H), δ 1.2-1.5 (m, 36H), δ 0.89 (t, 6H). ^{13}C NMR ($CDCl_3$): δ 149.9, δ 144.8, δ 124.2, δ 112.1, δ 43.70, δ 31.83, δ 29.57, δ 29.54, δ 29.51, δ 29.49, δ 29.41, δ 29.34, δ 29.26, δ 27.07, δ 14.03. MS; MALDI-TOF: m/z 549 (M +H$^+$). High-Res ESI-TOF: Calculated for $C_{36}H_{60}N_4^+$: m/z 549.482, experimentally found: 549.437. UV-vis λ_{max} (nm (log ε)) (MeCN): 436 (3.27).

N,N'-diethyl N,N'-didodecyl 4,4'-diamino-azobenzene (**5a**):

The compound was prepared from acetic acid N,N'-diacetyl-N,N'-didodecyl- 4,4'-diamino-azobenzene (**4a**) by reduction with $LiAlH_4$ in THF. 100 mg (0.17 mmol) of acetic acid N,N'-diacetyl-N,N'-didodecyl- 4,4'-diamino-azobenzene (**4a**) was dissolved

in 20 ml of THF (distilled from Na/benzophenone) and a 0.65 g (20 mmol) LiAlH$_4$ tablet was added while stirring. The stirring was continued at ambient temperatures for 76 hours. The reaction was quenched with 50 ml of water and the THF was removed in vacuum. The product was extracted with 100 ml ether and washed with ammonium chloride and brine. The solvent was removed in vacuum and the crude product purified by flash chromatography using graduated elution from pentane to ethyl acetate. The product was isolated as small needles in an overall yield of 60 mg (58%).

^{1}H-NMR (CDCl$_3$): δ 7.76 (d, 4H), δ 6.69 (d, 4H), δ 3.43 (q, 4H), δ 3.31 (t, 4H), δ 1.62 (m, 4H), δ 1.32 (m, 4H), δ 1.27 (s, 32H), δ 1.20 (t, 6H), δ 0.88 (t, 6H). MS; MALDI-TOF: m/z 605 (M$^+$). UV-vis λ$_{max}$ (nm (log ε)) (MeCN): 459 (4.42), 479 (4.400) (sh), 430 (4.33) (sh), 327 (3.63), 256 (3.97). Anal. Calcd. for C$_{40}$H$_{68}$N$_4$: C, 79.41; H, 11.33; N,9.26. Found: C, 78.66; H, 11.66; N, 9.09.

Langmuir isotherms:

a)

b)
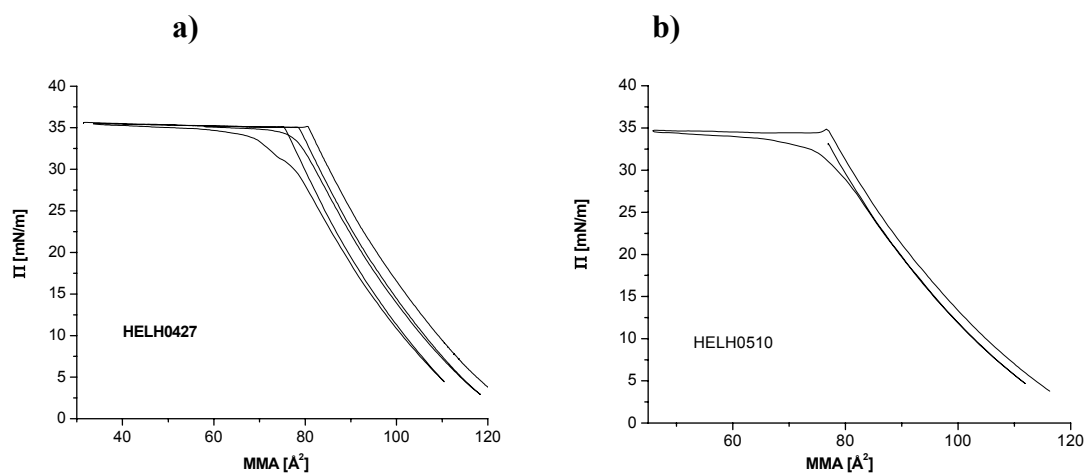
Figure S1: Surface pressure-molecular area isotherms recorded during several compression-expansion cycles (compression rate: 6-12 Å^2/molecule min; barrier speed: 12-25 mm/min) for compound **4b** when spread on a pure water subphase. Isotherms recorded at a) 20 ^{o}C and b) 3.3 ^{o}C respectively.

a)   b)
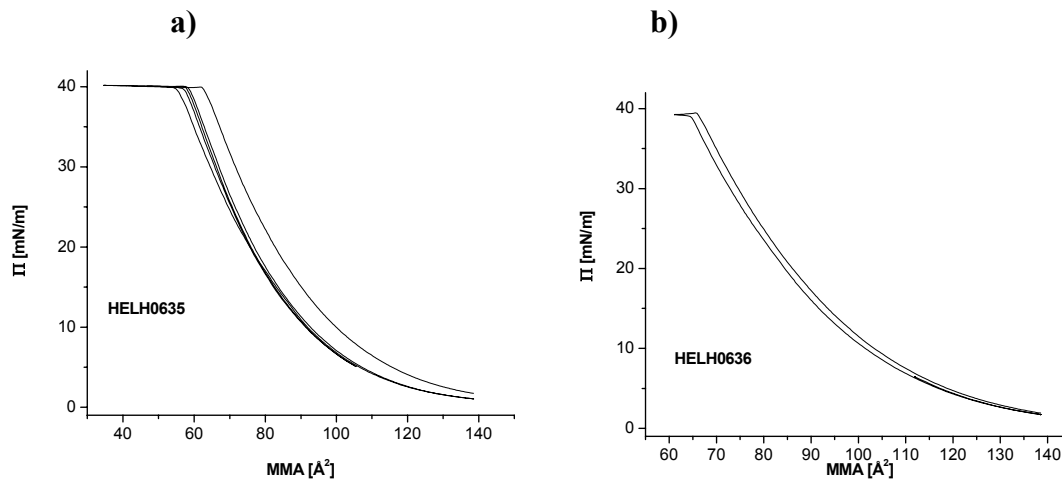
Figure S2: Surface pressure-molecular area isotherms recorded at 20.5 ^{o}C during several compression-expansion cycles (compression rate: 5-8 Å^{2}/molecule min ; barrier speed: 10-16 mm/min) for compound **4c** when spread on a) a pure water subphase and b) an alkaline (pH=11) water subphase.

a) HELH0675

b) HELH0724
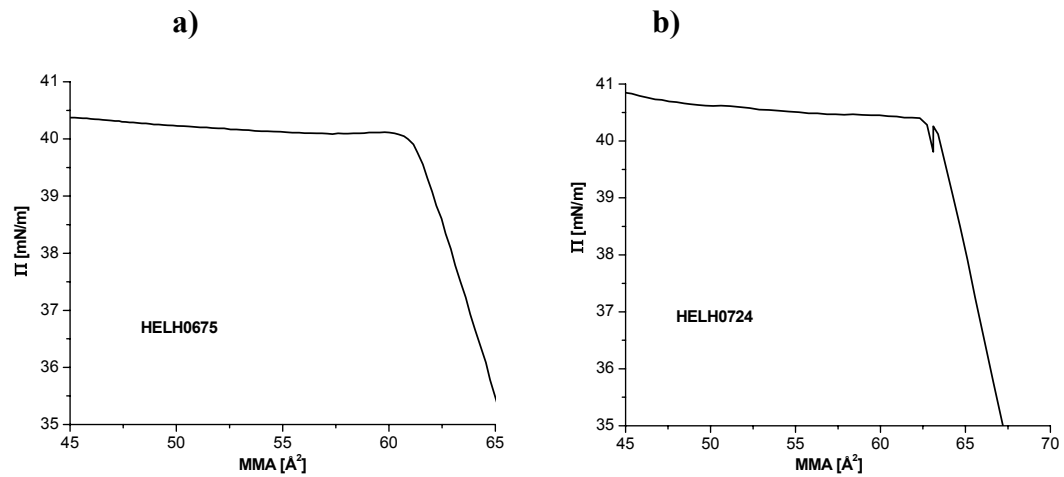
Figure S3: Compression isotherms showing the transition point for compound **4c** on alkaline (pH=11) water subphase at a) 20.5 ^{o}C and b) 3.3 ^{o}C

Figure S4:

X-ray reflectivity curves and the resulting electron density profiles for Langmuir films of compound **4b** on pure water at 3.3 °C and various mMa values.

Left: Normalized X-ray reflectivities $R(Q_z)/R_F(Q_z)$ (linear and logarithmic plots).

The points are the measured data and the smooth curves are fitted $R(Q_z)/R_F(Q_z)$, each corresponding to one of the inverted[8] $\rho(z)$ curves on the *right*.

It is apparent that the scatter in the $\rho(z)$ curves (resulting from variation of the control parameters of the inversion[8]) is small. This scatter, together with the ($\sim$ 3%) uncertainty on the mMA, gives rise to the uncertainties quoted in tables S1 and S2.

Right: Electron density profiles $\rho(z)$ *vs. z. z* is set to zero at the air-film interface, taken as the point where $\rho(z) = 0.5\rho_{water}$ (red broken line). The interface to water ($z = z_w$, defined as the point where the electron density is 3% above that of bulk water) is indicated by a solid blue line (uncertainty indicated by dotted lines). Combined with the molecular areas deduced from the Langmuir isotherms ($\sim$ 3% accuracy) these data give a quantitative account of the total electron density normal to the water surface: By multiplication of the profiles by the mMa, and subsequent integration, the depth $z = z_N$ at which the integrated electron density corresponds to all $N=476$ electrons of the molecule is obtained:

$mMA \cdot \int_{-\infty}^{+z_N} \rho(z)dz \equiv N = 476.$ z_N is marked by a solid black line (uncertainty indicated by dotted lines). Key parameters are summarized in

Table S1. Vertical dashed blue line indicates $\rho_{water} = 0.334$ electrons/Å^3.

Figure S5:

X-ray reflectivity curves and the resulting electron density profiles for Langmuir films of compound **4c** on KOH (*aq.*), *pH* = 11 at 20.5 °C and various mMa values.

Left: Normalized X-ray reflectivities $R(Q_z)/R_F(Q_z)$ (linear and logarithmic plots).

Right: Electron density profiles $\rho(z)$ *vs. z*. The depth $z = z_N$ corresponds to $N=444$ electrons of the **4c** molecule and two K$^+$ ions:

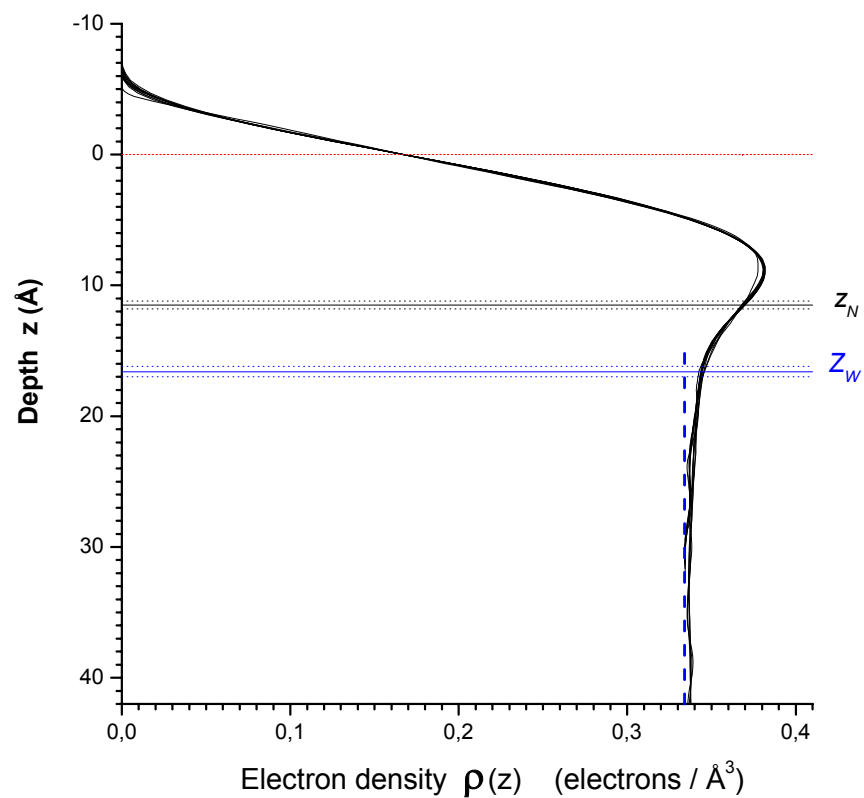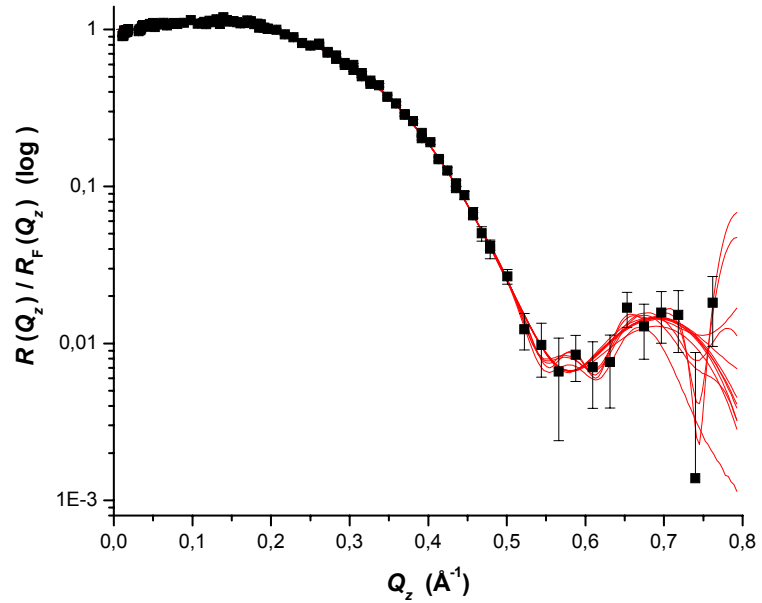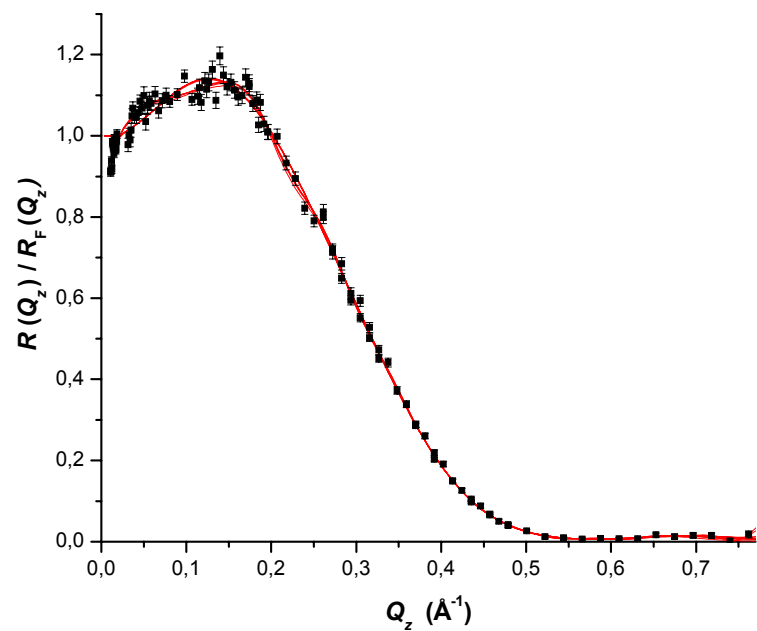$mMA \cdot \int_{-\infty}^{+z_N} \rho(z)dz \equiv N = 444.$ For details, see Figure S4.

Figure S4a:
Compound **4b** on pure water at 3.3 °C and mMa = 116 Å^2/molecule**.**
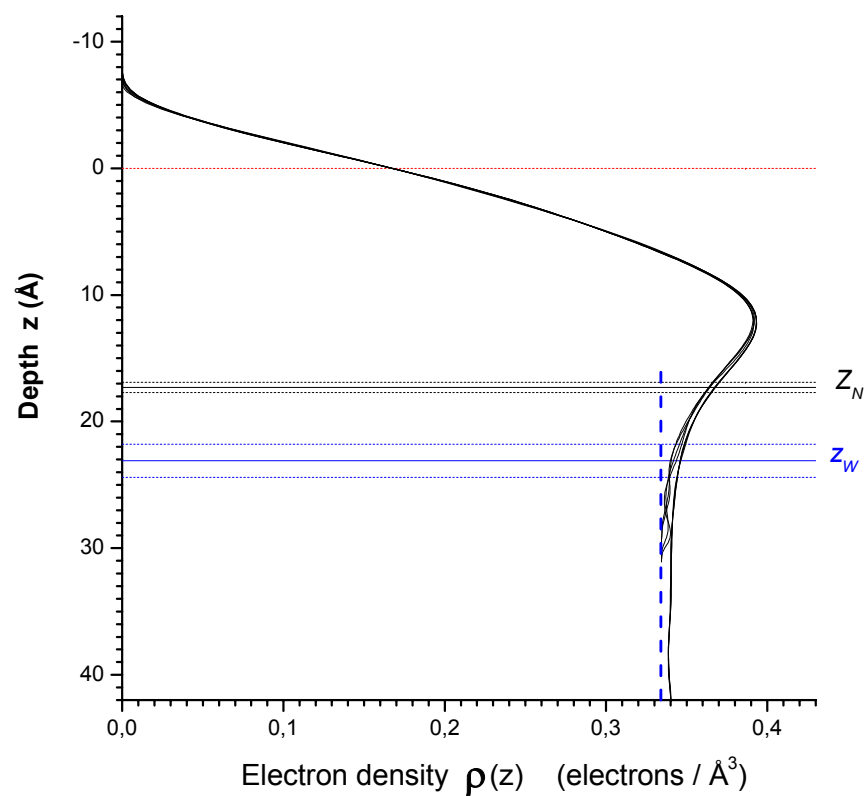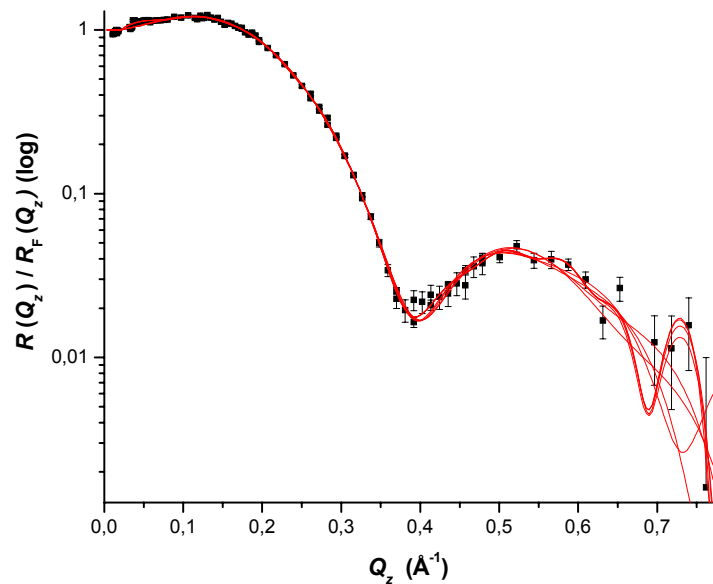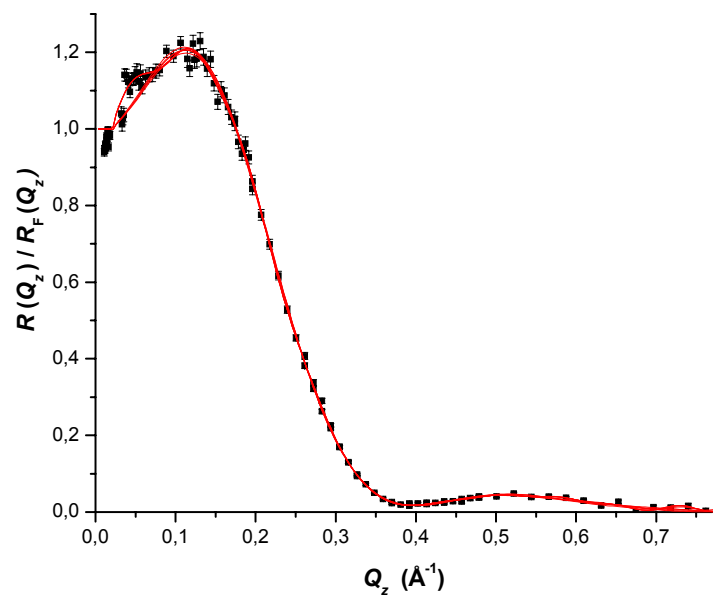
Figure S4b:
Compound **4b** on pure water at 3.3 °C and mMa = 77 Å²/molecule.
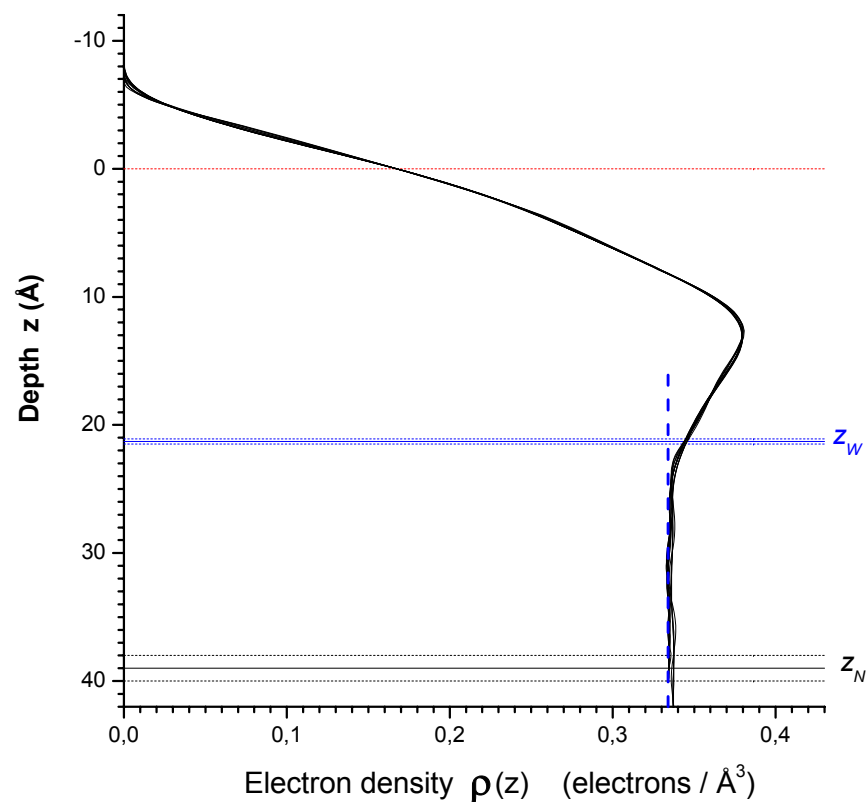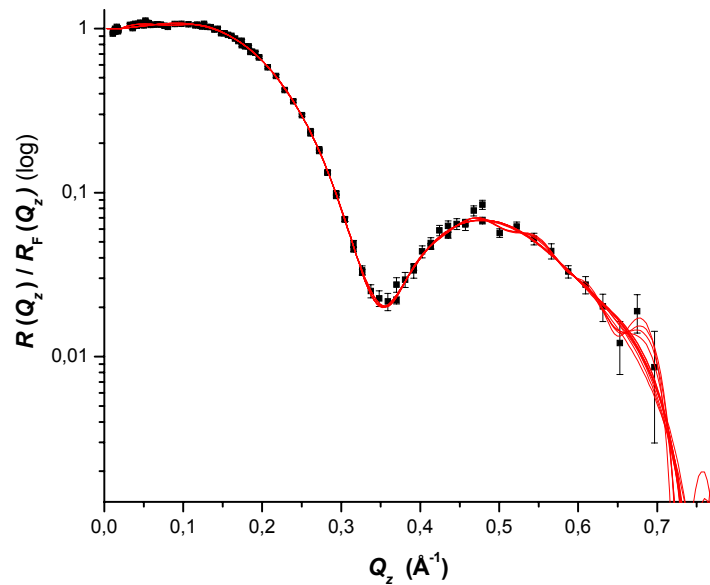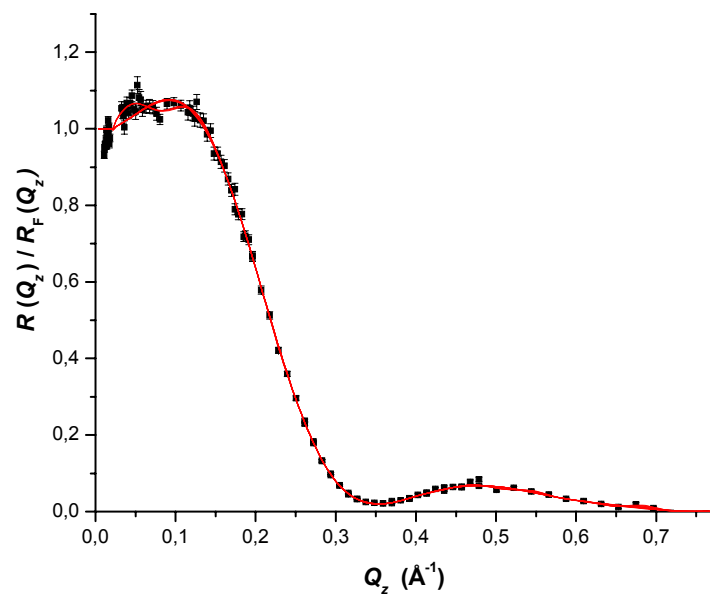
Figure S4c:
Compound **4b** on pure water at 3.3 °C and mMa = 36 Å^2/molecule**.**
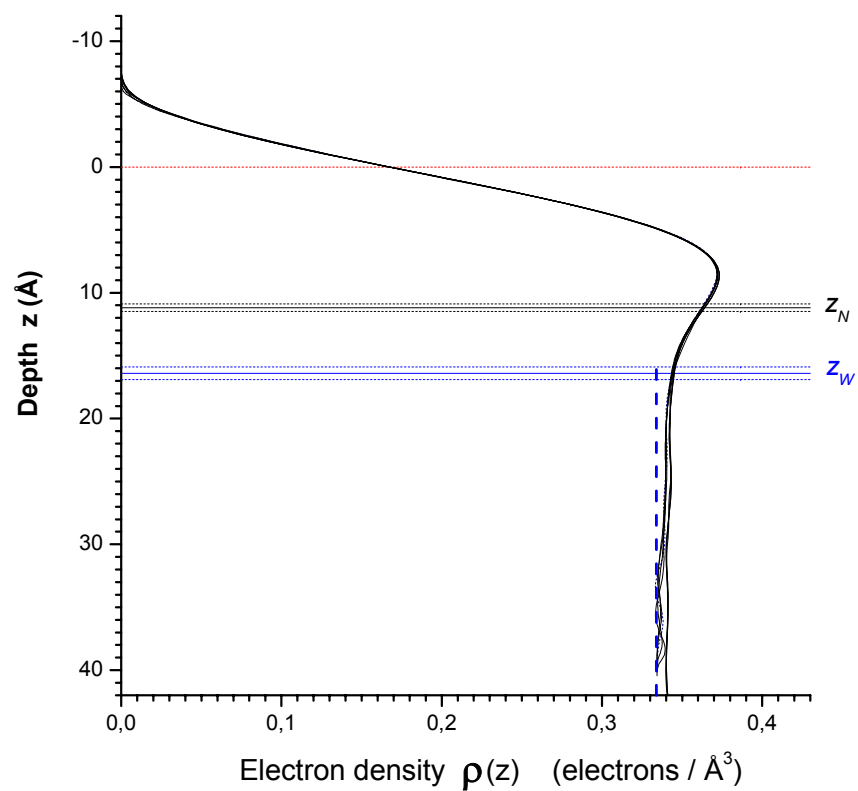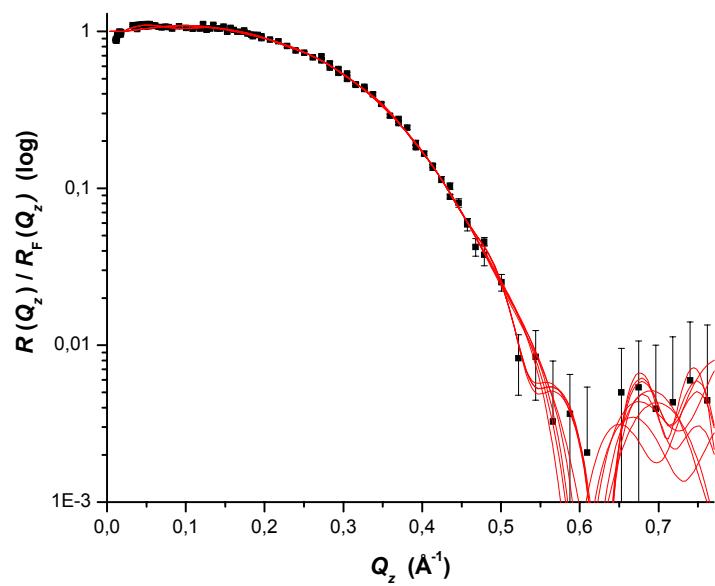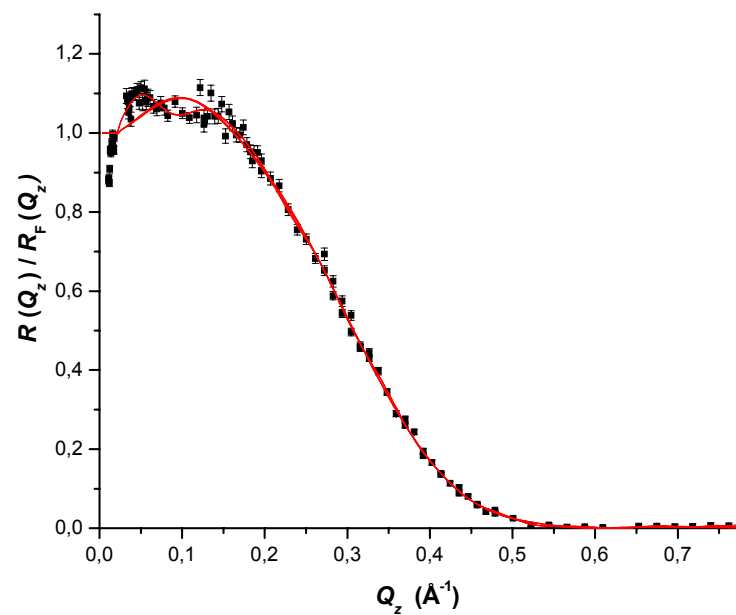
Figure S5a:
Compound **4c** on KOH(aq) pH= 11 at 20.5 °C and mMa = 112 Å^2/molecule**.**
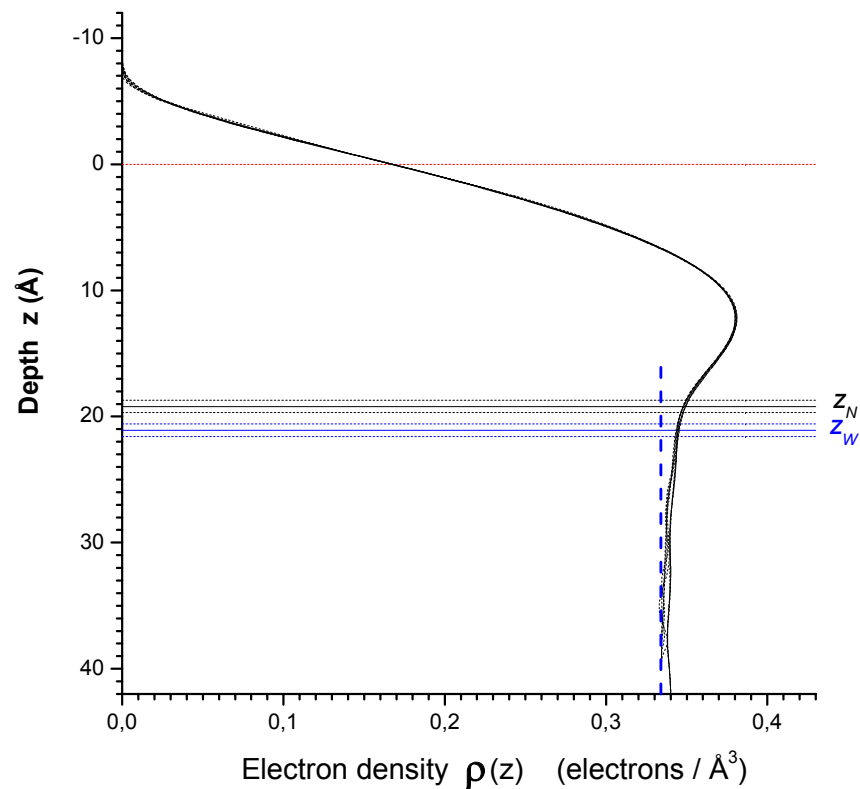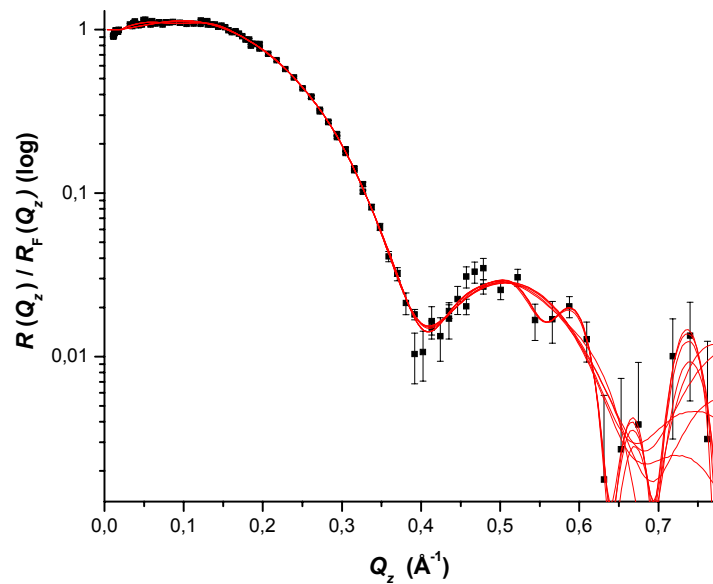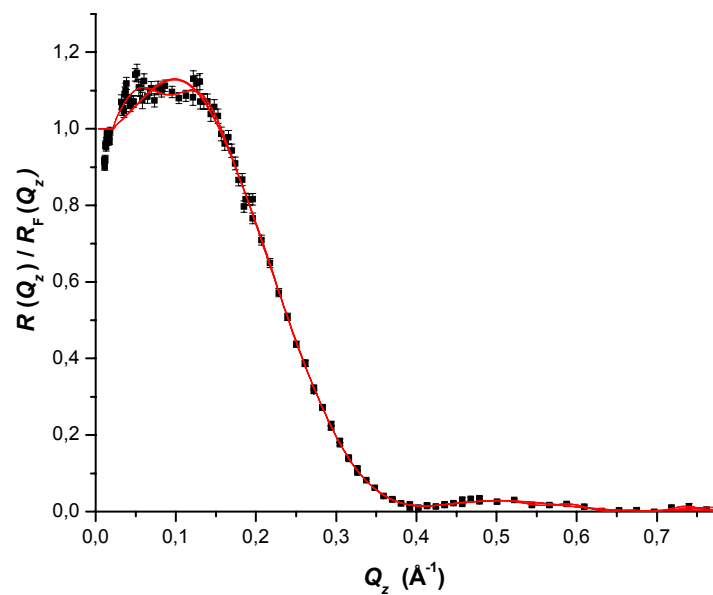
Figure S5b:
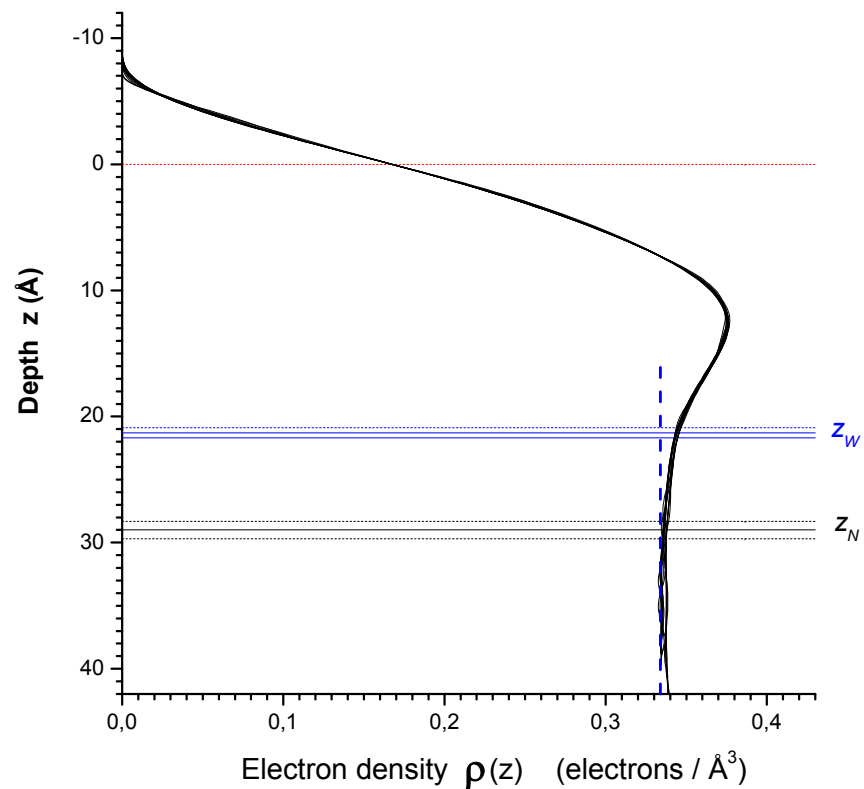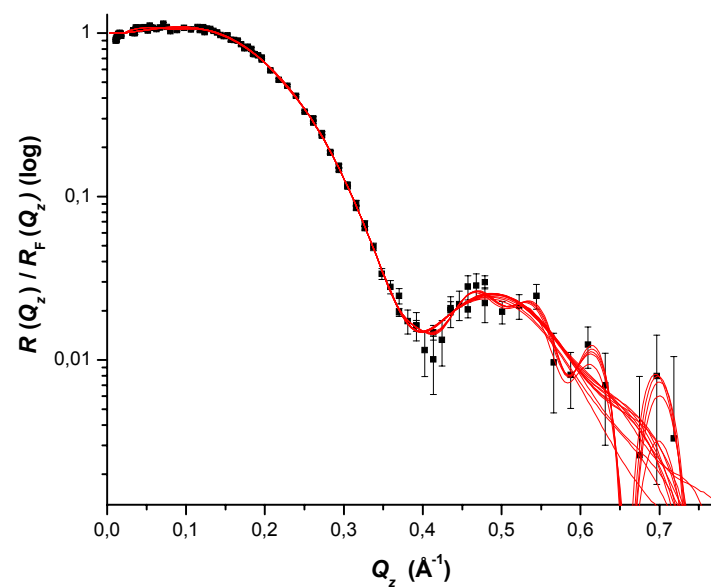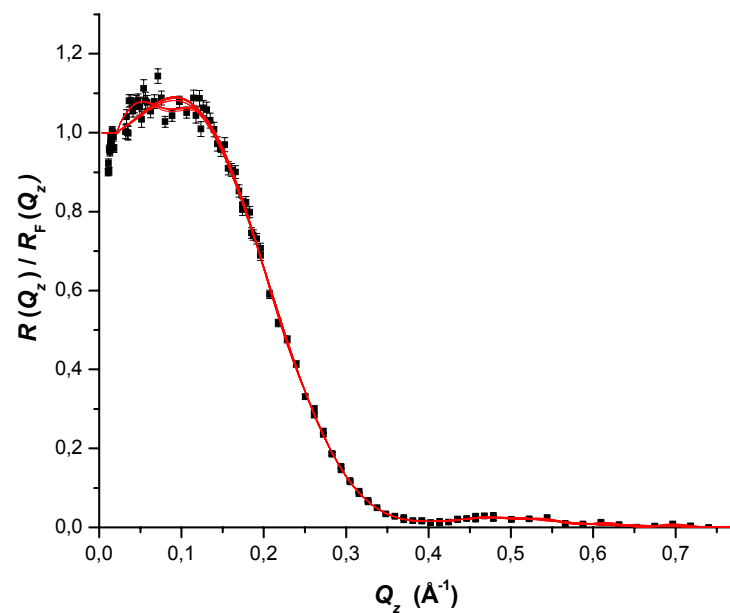Compound **4c** on KOH(aq) pH= 11 at 20.5 °C and mMa = 66 Å^2/molecule**.**

Figure S5c:
Compound **4c** on KOH(aq) pH= 11 at 20.5 °C and mMa = 44 Å^2/molecule**.**

X-ray reflectometry and structure analysis:

Table S1 (identical to Table 2 in manuscript): Summary of key parameters for the Langmuir film of **4b** at 3.3 °C.

MMA (Å^2/molecule)	Air-film interface[1] (Å)	Estimated depth z_w of the film-water[2] interface (Å)	Depth z_N where N electrons are accounted for[3] (Å)	Electron surplus[4]	Estimated water content in the monolayer[5]: n(water)/MMa
116±3	$z \equiv 0$	16.6±0.4	11.5±0.3	210±24	21±2
77±2	$z \equiv 0$	23.1±1.3	17.3±0.4	157±37	16±4
35.6±1	$z \equiv 0$	21.3±0.2	39±1	-212±7	n/a

1) Defined as the point where $\rho = 0.5\rho_{\text{water}}$

2) Defined as the point where $\rho = 1.03\rho_{\text{water}}$.

3) Based on integration of the electron density profiles: $\text{MMA} \cdot \int_{-\infty}^{+zN} \rho(z)dz \equiv N = 476$ electrons per **4b** molecule.

4) Being the integral $\text{MMA} \cdot \int_{zN}^{zw} \rho(z)dz$ between the lines z_N and z_w (Figure S4).

5) Being the electron surplus divided by the 10 electrons of a water molecule.

Table S2 (identical to Table 3 in manuscript): Summary of key parameters for the Langmuir film of **4c** at 20.5 °C, subphase of KOH(aq) pH = 11.

MMA (Å^2/molecule)	Air-film interface[1] (Å)	Estimated depth z_w of the film-water[2] interface (Å)	Depth z_N where N electrons are accounted for[3] (Å)	Electron surplus[4]	Estimated water content in the monolayer[5]: n(water)/MMa
112±3	$z \equiv 0$	16.4±0.5	11.2±0.3	204±24	20±2
66±2	$z \equiv 0$	21.1±0.5	19.2±0.5	45±17	4±2
44±1	$z \equiv 0$	21.3±0.4	29.0±0.7	-116±10	n/a

1) Defined as the point where $\rho = 0.5\rho_{\text{water}}$

2) Defined as the point where $\rho = 1.03\rho_{\text{water}}$.

3) Based on integration of the electron density profiles:

$\text{MMA} \cdot \int_{-\infty}^{+zN} \rho(z)dz \equiv N = 408 + 36 = 444$ electrons for each **4c** molecule (including two K^+ ions).

4) Being the integral $\text{MMA} \cdot \int_{zN}^{zw} \rho(z)dz$ between the lines z_N and z_w (Figure S5).

5) Being the electron surplus divided by the 10 electrons of a water molecule.

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See also note 14 of the main text.