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Halogen bond mediated self-assembly of polymer-resorcinarene complexes

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A new supramolecular system based on halogen bonded macromolecular substances is presented. Binding and complex formation between a halogen bond acceptor N-benzyl ammonium resorcinarene bromide and a library of polymeric halogen bond donors based on iodotetrafluorophenoxy functionality is shown. The complex formation was confirmed in liquid state by dynamic light scattering and transmission electron microscopy. Spectroscopic measurements in solid state confirm the halogen bonding. In particular, the study shows that both homopolymers and polyethylene glycol block copolymers act as effective halogen bond donors leading to polymer architecture dependent complex morphologies.

Self-assembly of macromolecules has been employed for a long time to produce tailored bottom-up structures for diverse applications.^[1–3] Formation of these well-defined assemblies, like vesicles^[3] and micelles,^[4] rely not only on solubility differences of blocks in copolymers, but also on non-covalent interactions such as electrostatic

binding.^[5,6] In addition to these frequently applied interactions, halogen bonding (XB) has recently gained more interest within supramolecular chemistry research.^[7–11] Halogen bonding is a noncovalent directional interaction between a halogen (XB donor) and a Lewis base (XB acceptor).^[8,11] The interaction most commonly occurs between a halogen atom, like iodine, incorporated in an organic compound and a Lewis base such as a neutral amine group or a charged anion. The bond strength can be tuned by changing the halogen ($I > Br > Cl$), as the σ -holes in the halogens are different in positivity.^[11] Moreover, by modifying the hybridization of the carbon atoms linked to the XB binding site and by covalently adding electron-withdrawing moieties to the structure, σ -hole magnitude can be further increased.^[12] For example, haloarenes are known to be effective in this kind of strengthening.^[13] Halogen bonding has been studied widely with cavitands^[14–17] and in macromolecular systems^[18–26]. With the cavitands focus in halogen bonding has been among forming capsules,^[14] networks^[16] and ribbons^[17]. Polymers, on the other hand, have been studied with small molecules^[23–25] and macromolecules^[18–22] yielding materials with added functionality^[18,24] as well as controlled morphology^[20] and orientation^[23,25]. Overall, properties of XB provide a versatile toolbox for many fields of supramolecular self-assembly, like material science^[8,9] and medicine^[27,28].

In this study, we show halogen bonding between a macrocyclic compound, *N*-benzyl ammonium resorcinarene bromide (NARBr) **R1**, and linear iodine functionalized polymers **P1-P4** (**Scheme 1**). These polymers were chosen as they are known to be effective XB donors when bound with linear polymers comprising an amine XB acceptor site.^[19] Here, we demonstrate that the XB acceptor can be replaced with a macrocyclic compound having an anionic XB acceptor site. Unlike in the many previous polymeric XB system,^[19,20,22–24] we have used an anionic XB acceptor as they are generally considered to have enhanced halogen bonding^[29] in comparison to the neutral XB

acceptor species. Overall, macrocycles are interesting compounds for supramolecular chemistry as besides having a large structural variation, they are capable in molecular recognition and complex formation.^[30] The particular resorcinarene XB acceptor was chosen based on previous research, which shows that it acts as a sufficient XB acceptor both in solid and liquid state.^[16] Self-assembly of the selected compounds leads into spherical complexes held together by the interaction between the XB donor iodine and XB acceptor bromide. Notably, all of the polymers were capable in complex formation in contrast to the previously reported results.^[19] Architecture and size of the XB assemblies observed in this study can be modified in solution state by changing the polymer composition from homopolymer (**P1-P2**) to block copolymer with a polyethylene glycol (PEG) block (**P3-P4**), and by varying the molecular weight of the polymers. Homopolymer (**P5**) with pentafluorophenoxy functionality instead of iodotetrafluorophenoxy groups was used as a control compound.

Halogen bonding between the XB donor polymers **P1-P4** and XB acceptor resorcinarene **R1** was first studied in solution state by mixing the XB donor and the XB acceptor in 1:1 binding group ratio (**R1** has four binding groups and the polymers have n binding groups depending on the number of repeating units) in dimethyl sulfoxide (DMSO) and dialyzing the mixture against water. Complex formation was evident already with the naked eye and the formation of colloidal particles was clearly observed (Figure 1a and S2-S4). Self-assembly of the complexes was further verified by turbidity measurements revealing a clear difference in the optical density (OD) of the polymer-resorcinarene assemblies in comparison to the components alone and the control mixture **P5-R1** without halogen bonds (Figure 1b). Polymers **P2** and **P4** showed slightly lower OD, which can be because of the smaller sized assemblies observed both in dynamic light scattering (DLS) (Figure 1c) and transmission electron microscopy (TEM) (Figure 1e) analysis. The dialyzed solution state samples were studied by DLS to define the

hydrodynamic diameters, D_h , of the assemblies (Figure 1d and S2-S4). Comparison of the data in Figure 1c shows that the length of the iodine-containing block had an effect on the complex size as the shorter blocks yielded larger assemblies, but with the longer iodine functionalized blocks (**P2** and **P4**) the complex diameter was well below 300 nm. Additionally, polydispersity index (PDI) values for all assemblies were low indicating relatively uniform assembly size (Figure 1c).^[31]

Complex formation was also studied also in lower resorcinarene concentration. Optical density measurements revealed that the complexation occurs already at the 0.5:1 **R1:P1** binding group ratio (Figure S5a), and based on the DLS data, the dialysis yielded assemblies in the same size range and with similar polymer block length dependencies as with the 1:1 binding group ratio (Figure S5b). Complexation was shown to work also with a monofunctional bromide compound tetrabutylammonium bromide (TBABr). The OD values are slightly lower than with **R1** but they clearly show complex formation (Figure S6a). DLS data indicates that the complexes are in the same size range as with the resorcinarene XB acceptor and the PDI values are relatively low (Figure S6b). Hence, the polymers can most probably be complexed with large variety of bromide salts making the system highly versatile.

To further study the solution state XB assemblies, TEM imaging was employed. Overall, the images showed spherical assemblies for all of the different combinations (Figure 1e and S1-S4). In contrast to a previous report,^[19] a PEG stabilizing block was not needed to obtain organized structures as also the homopolymers **P1** and **P2** mixed with **R1** formed clearly outlined individual spherical complexes. Anions are commonly regarded as more effective XB acceptors than neutral species,^[29] which might lead to the enhanced binding observed here. Additionally, in agreement with the DLS measurements, the assembly sizes varied depending on the block lengths of the XB donor polymers. The longer iodine containing blocks, **P2** and **P4**, yielded smaller assemblies around 200 nm

in diameter. Overall, DLS-based hydrodynamic diameters and TEM analysis -based Feret diameters (D_F) were well in line with each other. For **P2** and **P4** the PDI values in DLS and standard deviations in TEM image analysis are small and inferior compared to ones obtained with **P1** and **P3**, thus indicating that more controlled assemblies are gained with longer XB donor blocks. Additional observation from the TEM images was that the block copolymer -based assemblies tend to aggregate, and in addition, they had less pronounced outline, which could be due to core-shell formation where the PEG-block is on the outer shell and the XB components are in the inner core. Clustered structures have been observed also previously for halogen bonded assemblies containing PEG-based polymers, which yielded in their case wormlike structures.^[19] The control polymer **P5** did not show any well-ordered assemblies with the XB acceptor **R1** (Figure S7) implying that iodine plays a key role in the XB based self-assembly. Moreover, the pristine compounds **P1**, **P2**, **P3**, **P4** and **R1** alone showed no ordered structures (Figure S8-S12) confirming that both donor and acceptor are needed to produce spherical assemblies with reduced size.

To confirm the halogen bonding, further measurements were carried out in solid state. Raman spectroscopy was employed to monitor the vibrational changes upon XB interaction. As in many previous studies,^[18,23,32,33] XB-sensitive C–I stretching frequency is interrogated and upon complex formation the band at approximately 202 cm^{-1} is expected to shift to lower energies. As seen in Figure 2a, already at 1:1 acceptor:donor ratio for the **P1-R1** complex, a redshift from the original peak ($203.0 \pm 0.3 \text{ cm}^{-1}$) to lower energies was clear. Moreover, when NARBr **R1** concentration was further increased, the shift became even more prominent by first showing a bimodal peak at 5:1 (**R1:P1**) ratio and eventually a complete shift to lower energies with the ratio of 9:1 (Figure 2a and 2b). This redshift is an indication of C–I bond lengthening as a result of charge transfer^[33], and similar shifts confirming the XB have been observed also

1 previously both experimentally and computationally.^[32] In addition, the same behavior
2 is observed for the other XB donor homopolymer **P2** (Figure S13), and as expected, no
3 peak at the aforementioned position is seen for the control compound **P5** (Figure S21).
4 For the pristine block copolymers **P3** and **P4**, the C–I peak was observed at lower
5 wavelengths, 200.8 ± 1.3 and 201.2 ± 0.7 cm^{-1} respectively, which could be because of
6 slight intramolecular bonding with the PEG ether functionality. However, an addition of
7 the XB acceptor **R1** shifted the peak to lower energies confirming that also the block
8 copolymers are active XB donor compounds (Figure S14-S15). For the original Raman
9 spectra, see Figure S16-S21.

10 Halogen bonding between the resorcinarene and the different polymers was further
11 confirmed with Fourier transform infrared spectroscopy (FTIR) measurements. As seen
12 in Figure 2c, multiple transitions at 700-1600 cm^{-1} region can be observed. Peaks at
13 1000-1250 cm^{-1} region are related to the C–F stretching vibrations, and peak shifts and
14 intensity increases around this area are generally considered as an indication of halogen
15 bonding.^[23,25,33] When spectra of the pure **P1** is compared to the spectra of **P1-R1**
16 mixture (1:1 binding group ratio) one can observe such changes at **P1** peaks 1035 and
17 1265 cm^{-1} , which both shift to lower wavelengths and higher intensities. In addition,
18 other peaks, like 1096 cm^{-1} , show similar shifts but the interpretation is elusive as the
19 peaks overlap with the **R1** based peaks. These shifts were most pronounced for **P1**, but
20 also the other homopolymer **P2** showed similar shifts indicating halogen bonding
21 (Figure S22b). For the block copolymers, shifts were alike but less pronounced (Figure
22 S22c-S22d), which is well in agreement with the Raman spectroscopy results. In
23 addition, samples with higher **R1** concentration (5:1 acceptor:donor ratio) were
24 prepared, but opposite to Raman measurements, peaks originating from the polymers
25 were too weak to provide additional information. For the control compound **P5** samples
26 no clear shift indicating XB was observed (Figure S22e).

In conclusion, herein we have shown that all the iodotetrafluorophenoxy functionalized polymers can complex with the bromide anion of the macrocycle via halogen bonding. This was first confirmed in solution state with turbidity, DLS and TEM measurements. XB donor polymer length was shown to play a role in the size control of the assemblies. Based on the TEM images the produced polymer-resorcinarene complexes were spherical and in addition, block-copolymer-based complexes tended to aggregated. Moreover, the XB interaction was confirmed in solid state where Raman spectroscopy showed shifts in the C–I peak demonstrating halogen bonding especially for the homopolymers. Solid state XB was additionally verified with FTIR measurements where C–F peak shifts strongly, indicating halogen bonding. Although self-assembly systems of cavitands and polymers have been widely reported halogen bonded systems are still largely unexplored.^[34] In the future studies, this XB-based system could be further explored in several ways, for example, by adding a guest molecule to the macrocycle to increase the overall functionality^[35,36] or by using a more gradual solvent switch to prospectively achieve more diverse morphologies^[1,20].

Supporting Information

Supporting Information including materials and methods, additional TEM images and DLS results, Raman and FTIR spectroscopy is available from the Wiley Online Library.

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Conflict of Interest

The authors declare no conflict of interest.

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Scheme 1. Structures of the XB donor polymers **P1-P4**, the control polymer **P5** and the XB acceptor resorcinarene **R1**.

Figure 1. Sample characterization after dialysis from DMSO to water. a) Image of the dialyzed samples showing increased turbidity for the **P1-R1** mixture in comparison to pristine **P1** and **R1**. b) Optical density measurements showing noticeably higher OD for the polymer-resorcinarene mixtures in comparison to control mixture **P5-R1** and pristine compounds. Average values of three measurements together with standard deviations are presented. c) Hydrodynamic diameter (solid columns) and polydispersity index values (patterned columns) from DLS measurements for the XB acceptor-donor mixtures. Average values of three measurements together with standard deviations are presented. d) Intensity-average size distribution for the **P1-R1** assemblies together with autocorrelation curve, hydrodynamic diameter and polydispersity index e) TEM images of the XB acceptor-donor mixtures together with image analysis -based Feret diameters.

Figure 2. Spectroscopy data for **R1:P1** complexation. a) Raman spectra of the area related to C–I stretching peak. b) Raman peak values plotted against binding group ratio. Average values of three measurements together with standard deviations are presented. c) FTIR spectra of **R1**, **R1:P1** (1:1 binding group ratio) and **P1** showing XB related peak shift.

A new supramolecular system based on halogen bonded macromolecules yields tunable complexes. Both homopolymers and block copolymers are effective halogen bond donors when combined with a macrocyclic anionic halogen bond acceptor. By varying the polymer architecture different liquid state assembly morphologies are obtained. Spectroscopic measurements confirm the halogen bonding.

Keyword Halogen bonding

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