

Nitrile Reduction Reverses the Micropollutant Uptake Selectivity of a Tetrafluoroterephthalonitrile- β -Cyclodextrin Polymer

Max J. Klemes,¹ Yuhan Ling,² Casey Ching,² Congyue Wu,² Leilei Xiao,^{1,3}
Damian E. Helbling^{2,*} and William R. Dichtel^{1,*}

¹*Department of Chemistry, Northwestern University, Evanston, IL 60208 USA*

²*School of Civil and Environmental Engineering, Cornell University, Ithaca, NY 14853 USA*

³*Department of Chemistry and Chemical Biology, Cornell University, Ithaca, NY 14853 USA*

Abstract: Organic micropollutants (MPs) are anthropogenic substances that contaminate water resources at trace concentrations. Many MPs, including per- and polyfluorinated alkyl substances (PFASs), have come under increased scrutiny because of their environmental persistence and association with various health problems. A β -cyclodextrin polymer linked with tetrafluoroterephthalonitrile (TFN-CDP) has shown promise for removing MPs from contaminated water and has a particularly high affinity towards cationic MPs. This selectivity arises from anionic groups incorporated into the crosslinker during the polymerization. Thus, the polymer does not bind many anionic MPs strongly, including anionic PFASs. To address this shortcoming, we reduced the nitrile groups in TFN-CDP to primary amines, which reverses its affinity towards charged MPs. TFN-CDP exhibits adsorption distribution coefficients ($\log K_D$ values) of 2-3 for cationic MPs and -0.5-1.5 for anionic MPs, whereas the reduced TFN-CDP exhibits $\log K_D$ values of -0.5-1.5 for cationic MPs and 2-4 for anionic MPs, with especially high affinity towards anionic PFASs. Kinetic studies of the removal of 10 anionic PFASs at environmentally relevant concentrations showed 80-98% removal of all contaminants after 30 min and was superior to commercial granular activated carbon. These findings demonstrate the scope and tunability of CD-based adsorbents derived from a single polymerization and the promise of novel adsorbents constructed from molecular receptors.

Introduction

Organic micropollutants (MPs) are chemicals present in water resources at ng L^{-1} to $\mu\text{g L}^{-1}$ concentrations as a consequence of human activities.^{1,2} Concerns about their negative effects on human health³⁻⁷ and the environment⁸⁻¹⁰ motivate the development of technologies that remove MPs more effectively.¹¹⁻¹⁶ These efforts are complicated by the broad range of physiochemical properties of MPs, including charge, size, hydrophobicity, and their diverse chemical functionality. We previously reported β -cyclodextrin (β -CD)-based polymers (CDPs) derived from nucleophilic aromatic substitution reactions with aryl-fluoride-containing crosslinkers, which have shown promise to remove MPs from water.^{11,12,14,16} For example, a CDP crosslinked by tetrafluoroterephthalonitrile (TFN), was formed as a permanently porous network (**1**, Fig 1) that rapidly removes many MPs from water,¹¹ resists fouling by natural organic matter,^{13,14} and can be regenerated.¹⁷ A study of the binding of 83 MPs under environmentally relevant concentrations revealed that **1** rapidly removes many cationic and neutral MPs, but removal of anionic MPs was variable and relatively low.¹³ This selectivity for cations was attributed to anionic phenolate groups introduced to the TFN crosslinkers during the polymerization.¹⁶ However, the inability of **1** to bind anionic micropollutants, including anionic perfluorinated alkyl substances (PFASs),^{13,16} is a major limitation to its broad utility and technological promise.

Anionic PFASs present a particular environmental problem because of their resistance to biodegradation or chemical transformation¹⁸ and correlation to negative health effects.⁶ PFASs have been used in the formulations of thousands of consumer goods¹⁹ and are present in aqueous

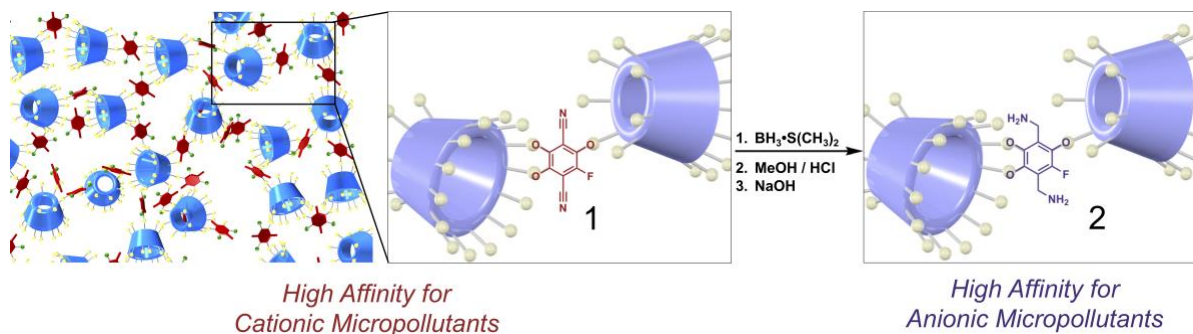


Figure 1. Post-polymerization reduction of **1** yields amine functionalized **2**, which remove anionic MPs and PFASs from water.

film-forming foam formulations used to suppress aviation fires in training scenarios.^{20,21} As a result, they have contaminated surface and ground waters near thousands of airports and military installations.^{22,23} In 2018, the Environmental Working Group reported that over 110 million people in the United States were exposed to drinking water with PFAS concentrations above 2.5 ng L⁻¹.²⁴ PFASs have been linked to cancers,³ liver damage,⁴ thyroid disease⁵ and other health problems.⁶ Contaminated water systems are typically remediated with granular activated carbon (GAC), but its modest affinity for PFASs, particularly short chain derivatives, makes it an expensive and stop-gap solution.^{25,26} In our recent reports,^{14,15} it was discovered that noncovalent interactions and the electrostatics of functional groups influence PFAS affinity to adsorbents. For example, the incorporation of more heavily fluorinated crosslinkers, as well as a lower incorporation of anionic functional groups in decafluorobiphenyl-linked CDPs were attributed to its promising perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS) removal from water. In contrast, CDPs cross-linked by epichlorohydrin exhibited inferior PFAS removal.²⁷

Based on a hypothesis that cationic CDPs would exhibit selectivity for anionic substances and PFASs relative to previous adsorbents, we reduced the nitriles of CDP **1** to primary amines. CDP **2** was synthesized from **1** (Fig 1), and this simple post-polymerization reduction transformed a polymer with low affinity for anionic MPs to a material with a high affinity for many anionic MPs, including ten anionic PFASs tested at environmentally relevant concentrations.

Results and Discussion

In a previous report,¹⁶ we described the nucleophilic aromatic substitution reaction of TFN with β -CD, providing **1** as a crosslinked polymer. The nitriles of a commercial sample of **1** were reduced to primary amines using excess $\text{BH}_3 \cdot \text{S}(\text{CH}_3)_2$ in THF at reflux for 40 hours, using conditions adapted from Mason *et al.* (Fig 1) for TFN-containing polymers of intrinsic microporosity.²⁸ After reduction, insoluble polymer **2** was subjected to an acidic workup followed by treatment with base. The reduction was characterized by FT-IR, cross-polarized magic angle spinning (CP-MAS) solid-state ^{13}C NMR, a chloranil test for amines, combustion analysis, and zeta potential measurements. FT-IR was consistent with partial reduction of the nitriles, as the spectrum of **2** shows a strongly attenuated nitrile stretch at 2238 cm^{-1} relative to that of **1** when each spectrum was normalized at the C-O stretch at 1020 cm^{-1} . The spectrum of **2** also shows an N-H bending signal at 1580 cm^{-1} (Fig 2a). In the CP-MAS ^{13}C -NMR, the nitrile carbons of **1** resonate at 94.44 ppm. This signal is attenuated in the spectrum of **2**, and a new peak is observed at 36.73 ppm (Fig S1), consistent with that of a benzylic amine carbon. The presence of amines in **2** was also verified by a positive chloranil test (Fig 2b), which is commonly used to qualitatively monitor the deprotection, capping, or coupling of amine groups in solid-phase peptide synthesis.^{29,30} In a chloranil test, acetaldehyde reacts with a primary or secondary amine forming an enamine, which then reacts with chloranil to yield a dark blue aminovinyl-quinone chromophore.³¹ In the presence of acetaldehyde and chloranil, the suspension of polymer **1** is light yellow-green, indicating the absence of amines, while the polymer **2** suspension is a dark blue-green, indicating the presence of amines (Fig 2b).

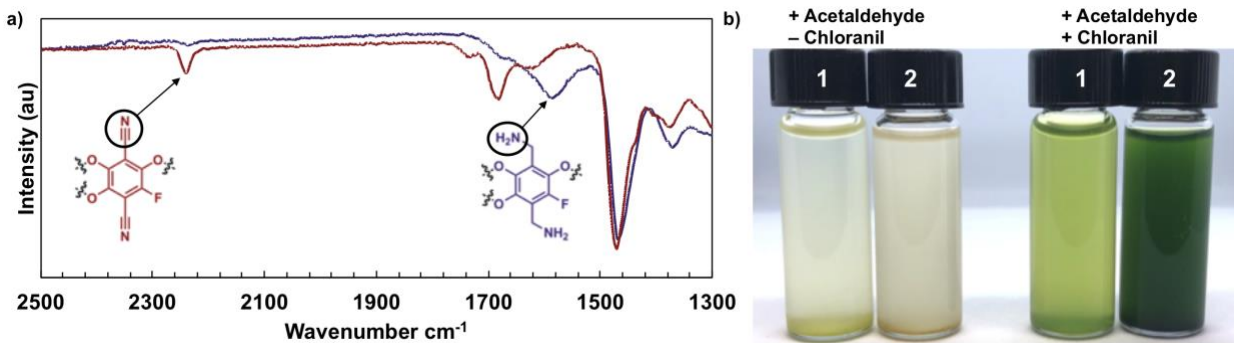


Figure 2. a) FT-IR spectra of polymers **1** (red) and **2** (purple). In the spectra of **2**, there is a significant reduction in the nitrile stretch at 2238 cm^{-1} and appearance of an N-H bend at 1580 cm^{-1} b) Chloranil test of **1** and **2**. Left two vials contain polymers **1** and **2** suspended in DMF and acetaldehyde (5%) and the right two vials contain polymers **1** and **2** suspended in DMF, acetaldehyde (5%), and chloranil (5%). The chloranil test turns blue-green in the presence of **2**, indicating the presence of amines.

Because the elemental composition of **1** and **2** in its free base form are too similar to differentiate by combustion analysis, the conversion of nitriles to amines was estimated by comparing the chloride content of each polymer following treatment with aqueous HCl. Treatment of **2** with HCl protonates its amines to the corresponding hydrochloride salts (**2**•HCl), whereas polymer **1** does not contain functional groups that are easily protonated to cationic chloride salts. The conversion of nitriles to amines was estimated from the N:Cl molar ratio in **2**•HCl of 0.72, corresponding to approximately 72% conversion of the nitrile reduction. As a control, **1** was treated with HCl as above and virtually no chloride was detected by the elemental analysis (see SI for details). Surface charges of the two polymers in neutral water were probed by zeta potential measurements. Aqueous suspensions of **1** at neutral pH have a zeta potential of $-28.9 \pm 0.7\text{ mV}$, indicating an anionic surface charge. Aqueous suspensions of **2** at neutral pH show a zeta potential of $+1.7 \pm 0.8\text{ mV}$, indicating a cationic surface charge. **2** also exhibits modest porosity with average Brunauer–Emmet–Teller surface areas of $135\text{ m}^2\text{ g}^{-1}$ when isolated as a dry solid.

As a consequence of its transformed crosslinkers, **2** has a relatively high affinity for anionic MPs, including anionic PFASs, which is the opposite selectivity observed for **1**. We measured the adsorption coefficients ($\log K_D$ values) of 91 structurally diverse MPs for **1** and **2** ($[\text{MP}]_0 = 2\text{ }\mu\text{g}$

L⁻¹; [CDP] = 25 mg L⁻¹). We found that **1** exhibited relatively high log K_D values for cationic MPs, along with neutral compounds that bind to CDs well, which is consistent with previous reports^{16,32} and observations (Fig 3).^{13,17} All 18 cationic substances exhibited log K_D values greater than 2 on polymer **1**. In contrast, 21 of 25 anionic substances and all 10 anionic PFASs exhibited relatively low log K_D values between -0.5 and 1.0 on polymer **1**. These low affinities make polymer **1** an ineffective

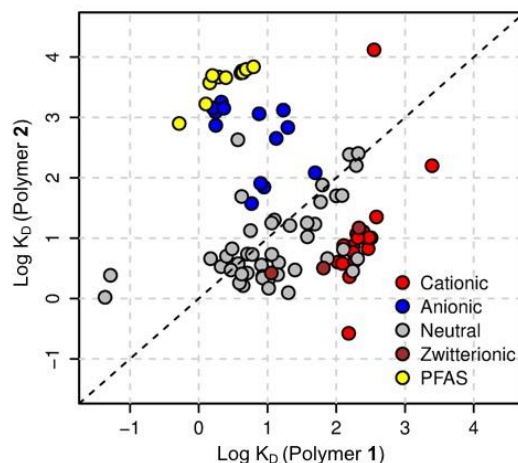


Figure 3. Affinity of 91 organic micropollutants to **2** and **1**. **2** has a higher affinity for PFAS and anionic organic micropollutants, and **1** has higher affinity for cationic and zwitterionic organic micropollutants. **1** and **2** exhibit similar affinity for most neutral organic micropollutants (25 mg L⁻¹ polymer, 2 µg L⁻¹ MPs).

adsorbent for most anionic MPs at environmentally relevant concentrations and economically reasonable doses of **1**. In contrast, polymer **2** strongly binds anionic substances, with 21 of 25 exhibiting log K_D values >2.6 and all ten anionic PFASs exhibiting log K_D values between 2.8-4.0. However, polymer **2** binds cationic MPs more weakly with log K_D values for 16 of 18 cationic MPs between -0.5-1.5. These findings demonstrate that the structure of the crosslinker plays a major role in the selectivity of CD-based adsorbents and that strategies to incorporate charged groups, either during the polymerization (phenolates),^{16,27} or by post-polymerization modification (amines), are powerful techniques to completely change the removal profiles of materials derived from a single crosslinker.

Based on the high affinity of polymer **2** for anionic PFASs, removal and uptake kinetics were also measured at environmentally relevant concentrations ([PFAS]₀ = 1 µg L⁻¹; [CDP] = 10 mg L⁻¹). Polymer **2** removes PFOA and PFOS rapidly, as the combined residual PFOA + PFOS

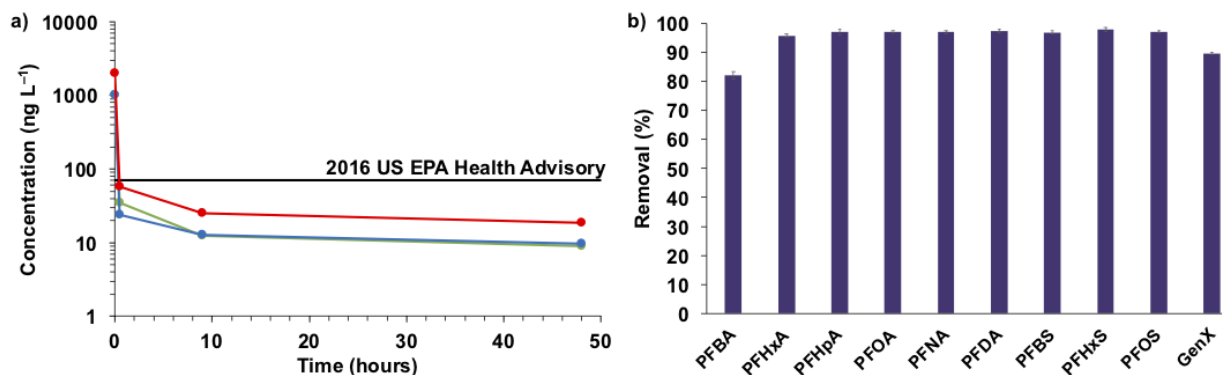


Figure 4. a) Removal of PFOA (green) PFOS (blue) and the combination of PFOA and PFOS (red) as a function of time showing that the combined concentration of PFOA + PFOS can be brought from 2000 ng L⁻¹ to below the 2016 EPA advisory limit of 70 ng L⁻¹ in 30 min and [PFAS]₀ = 1 μg L⁻¹; [CDP] = 10 mg L⁻¹. b) PFAS removal by **2** with 30 minutes of contact time; [PFAS]₀ = 1 μg L⁻¹; [CDP] = 10 mg L⁻¹.

concentration was 58 ng L⁻¹ after 30 minutes (below the 2016 EPA health advisory level of 70 ng L⁻¹ for PFOA and PFOS co-contamination) and reached an equilibrium aqueous phase concentration of approximately 25 ng L⁻¹ after 9 h (Fig 4a). Broad-spectrum PFAS removal was also evaluated across a range of PFAS chain lengths and anionic head groups (carboxylic and sulfonic acids) after 30 min of contact time ([PFAS]₀ = 1 μg L⁻¹; [CDP] = 10 mg L⁻¹). Under these conditions, 8 of 10 PFASs were removed to at least 95%, with the short, four carbon perfluorobutanoic acid (PFBA) and branched 2,3,3,3,-tetrafluoro 2-(heptafluoropropoxy)propanoate (GenX) removed to at least 80%. These two PFASs bind to β-CD with lower affinity,³³ such that their removal may rely more heavily (or even exclusively) on interactions with amine/ammonium groups in polymer **2** (Fig 4b). Benchmarking **2** against GAC (20-40 Mesh, 425-850 μm) for the removal of 10 anionic PFAS shows that **2** exhibits superior performance when compared to GAC in experiments conducted under environmentally relevant conditions after 30 min and 8 h of contact time (Fig S4). This demonstrates that **2** can outperform the leading adsorbent that is presently available for PFAS remediation. We also benchmarked **2** against powdered activated carbon (PAC, 200-950 Mesh, 10-75 μm) as a means to compare performance against a material with a similar particle size and morphology. PAC is known to

exhibit more rapid adsorption kinetics when compared to GAC, but is rarely used for PFAS remediation because its size precludes implementation in continuous-flow processes and enhances its susceptibility to fouling by natural organic matter.³⁴ In analogous experiments performed with GAC, we found that **2** performs similarly to PAC for the removal of many anionic PFASs, but outperforms PAC for the removal of PFBA (Fig S4). This is particularly exciting because only limited removal of short-chain PFASs such as PFBA has been reported with PAC or other alternative adsorbents.³⁵ Together, our findings suggest that **2** could be a viable and non-selective adsorbent for the removal of anionic PFASs regardless of their chain-length.

Conclusions

In conclusion, these findings demonstrate the promise of using polymer **2** as an adsorbent to remove anionic PFASs in contaminated ground and surface waters. The MP selectivity of a porous CDP was reversed from strongly binding cationic substances to strongly binding anionic substances through a post-polymerization reduction of its nitrile groups. The conversion of nitriles to primary amines was confirmed by spectroscopy, combustion analysis, and changes in the zeta potential. This effect likely arises from both the presence of amine groups that are partially protonated at pH 7 in water, as well as the increased pK_a of phenolates found on the crosslinkers upon reduction of the strongly electron withdrawing nitrile groups. The reduced polymer binds many anionic MPs strongly and is particularly effective at the non-selective binding of anionic PFASs. A relatively low adsorbent loading (10 mg L^{-1}) removed all anionic PFASs at environmentally relevant concentrations, outperforming the leading activated carbon adsorbents. This affinity for PFASs may arise from localizing amine groups near the CD binding sites within the network. Characterizing this effect and the nature of PFAS-polymer interactions is an important next step. More broadly, these findings demonstrate the broad tunability of CD-based

adsorbents available from a single polymerization as well as the continued promise of novel adsorbents constructed from molecular receptors.

ASSOCIATED CONTENT

Supporting Information. The Supporting Information is available along with this article at the ChemRxiv Preprint server:

Experimental procedures, Materials and Instrumentation, CP-MAS ^{13}C NMR Spectra, FT-IR Spectra, PFAS Removal by Various Adsorbents, Nitrogen Absorption Isotherm and List of Micropollutants Affinities, and Charge in Water at pH 7. (PDF)

AUTHOR INFORMATION

Corresponding Authors

WRD: wdichtel@northwestern.edu

DEH: damian.helbling@cornell.edu

Notes

Northwestern University and Cornell University have filed a patent application based on the results described in this article. D.E.H. and W.R.D. serve on the scientific advisory board and own equity and/or stock options in CycloPure, Inc., which is commercializing related cyclodextrin polymers.

Acknowledgement

The study was supported by the Center for Sustainable Polymers (CSP), a National Science Foundation (NSF) supported Center for Chemical Innovation (CHE-1413862), by the Strategic Environmental Research and Development Program (ER18-1026), and by the NSF (CHE-1541820) and by Cornell University's David R. Atkinson Center for a Sustainable Future (ACSF). This research made use of the IMSERC at Northwestern University, which has received support from the NSF (CHE-1048773); Soft and Hybrid Nanotechnology Experimental (SHyNE) Resource (NSF ECCS-1542205); the State of Illinois and International Institute for Nanotechnology (IIN). The table of contents image was created by John Beumer.

References

- (1) Richardson, S. D.; Ternes, T. A. *Anal. Chem.* **2018**, *90*, 398–428.
- (2) Carpenter, C. M. G.; Helbling, D. E. *Environ. Sci. Technol.* **2018**, *52*, 6187–6196.
- (3) Barry, V. Winqvist, A. Steenland, K. *Environ. Health Perspect.* **2013**, *121*, 1313–1318.
- (4) Gallo, V.; Leonardi, G.; Genser, B.; Lopez-Espinosa, M.-J.; Frisbee, S. J.; Karlsson, L.; Ducatman, A. M.; Fletcher, T. *Environ. Health Perspect.* **2012**, *120*, 655–660.
- (5) Melzer, D.; Rice, N.; Depledge, M. H.; Henley, W. E.; Galloway, T. S. *Environ. Health Perspect.* **2010**, *118*, 686–692.
- (6) DeWitt, J. Dietert, R. R., Ed.; *Molecular and Integrative Toxicology*; Springer International Publishing: Springer Cham Heidelberg New York Dordrecht London, 2015.
- (7) Diamanti-Kandarakis, E.; Bourguignon, J.-P.; Giudice, L. C.; Hauser, R.; Prins, G. S.; Soto, A. M.; Zoeller, R. T.; Gore, A. C. *Endocr. Rev.* **2009**, *30*, 293–342.
- (8) Vajda, A. M.; Barber, L. B.; Gray, J. L.; Lopez, E. M.; Woodling, J. D.; Norris, D. O. *Environ. Sci. Technol.* **2008**, *42*, 3407–3414.
- (9) Tetreault, G. R.; Bennett, C. J.; Shires, K.; Knight, B.; Servos, M. R.; McMaster, M. E. *Aquat. Toxicol.* **2011**, *104*, 278–290.
- (10) Gagné, F.; Bouchard, B.; André, C.; Farcy, E.; Fournier, M. *Comp. Biochem. Physiol. - C Toxicol. Pharmacol.* **2011**, *153*, 99–106.
- (11) Alsaiee, A.; Smith, B. J.; Xiao, L.; Ling, Y.; Helbling, D. E.; Dichtel, W. R. *Nature* **2016**, *529*, 190–194.
- (12) Alzate-Sánchez, D. M.; Smith, B. J.; Alsaiee, A.; Hinestroza, J. P.; Dichtel, W. R. *Chem. Mater.* **2016**, *28*, 8340–8346.
- (13) Ling, Y.; Klemes, M. J.; Xiao, L.; Alsaiee, A.; Dichtel, W. R.; Helbling, D. E. *Environ. Sci. Technol.* **2017**, *51*, 7590–7598.
- (14) Xiao, L.; Ling, Y.; Alsaiee, A.; Li, C.; Helbling, D. E.; Dichtel, W. R. *J. Am. Chem. Soc.* **2017**, *139*, 7689–7692.
- (15) Ji, W.; Xiao, L.; Ling, Y.; Ching, C.; Matsumoto, M.; Bisbey, R. P.; Helbling, D. E.; Dichtel, W. R. *J. Am. Chem. Soc.* **2018**, *140*, 12677–12681.
- (16) Klemes, M. J.; Ling, Y.; Chiapasco, M.; Alsaiee, A.; Helbling, D. E.; Dichtel, W. *Chem. Sci.* **2018**, *9*, 8883–8889.
- (17) Li, C.; Klemes, M. J.; Dichtel, W. R.; Helbling, D. E. *J. Chromatogr. A* **2018**, *1541*, 52–56.
- (18) Ahrens, L.; Bundschuh, M. *Environ. Toxicol. Chem.* **2014**, *33*, 1921–1929.
- (19) Wang, Z.; Dewitt, J. C.; Higgins, C. P.; Cousins, I. T. *Environ. Sci. Technol.* **2017**, *51*, 2508–2518.

- (20) D'Agostino, L. A.; Mabury, S. A. *Environ. Sci. Technol.* **2017**, *51*, 13603–13613.
- (21) Barzen-Hanson, K. A.; Roberts, S. C.; Choyke, S.; Oetjen, K.; McAlees, A.; Riddell, N.; McCrindle, R.; Ferguson, P. L.; Higgins, C. P.; Field, J. A. *Environ. Sci. Technol.* **2017**, *51*, 2047–2057.
- (22) Breysse, P. N. *U.S. Department of Health and Human Services: Agency for Toxic Substances and Disease Registry: Toxicological profile for Perfluoroalkyls*. 2018.
- (23) Hu, X. C.; Andrews, D. Q.; Lindstrom, A. B.; Bruton, T. A.; Schaidler, L. A.; Grandjean, P.; Lohmann, R.; Carignan, C. C.; Blum, A.; Balan, S. A.; et al. *Environ. Sci. Technol. Lett.* **2016**, *3*, 344–350.
- (24) Andrews, D. Report: Up to 110 Million Americans Could Have PFAS–Contaminated Drinking Water <https://www.ewg.org/research/report-110-million-americans-could-have-pfas-contaminated-drinking-water> (accessed Jun 2, 2019).
- (25) Sun, M.; Arevalo, E.; Strynar, M.; Lindstrom, A.; Richardson, M.; Kearns, B.; Pickett, A.; Smith, C.; Knappe, D. R. U. *Environ. Sci. Technol. Lett.* **2016**, *3*, 415–419.
- (26) Eschauzier, C.; Beerendonk, E.; Scholte-Veenendaal, P.; De Voogt, P. *Environ. Sci. Technol.* **2012**, *46*, 1708–1715.
- (27) Xiao, L.; Ching, C.; Ling, Y.; Nasiri, M.; Klemes, M. J.; Reineke, T. M.; Helbling, D. E.; Dichtel, W. R. *Chemrxiv* **2018**, Preprint.
- (28) Mason, C. R.; Maynard-Atem, L.; Heard, K. W. J.; Satilmis, B.; Budd, P. M.; Friess, K.; Lanč, M.; Bernardo, P.; Clarizia, G.; Jansen, J. C. *Macromolecules* **2014**, *47*, 1021–1029.
- (29) Vojtkovsk, T. *Pept. Res.* **1995**, *8*, 236–237.
- (30) Mařík, J.; Song, A.; Lam, K. S. *Tetrahedron Lett.* **2003**, *44*, 4319–4320.
- (31) Buckley, D.; Henbest, H. B.; Slade, P. *J. Chem. Soc.* **1957**, 4891, 4891.
- (32) Ling, Y.; Klemes, M.; Steinschneider, S.; Dichtel, W. R.; Helbling, D. E. *Water Res.* **2019**.
- (33) Weiss-Errico, M. J.; Ghiviriga, I.; O'Shea, K. E. *J. Phys. Chem. B* **2017**, *121*, 8359–8366.
- (34) Bonvin, F.; Jost, L.; Randin, L.; Bonvin, E.; Kohn, T. *Water Res.* **2016**, *90*, 90–99.
- (35) Ateia, M.; Attia, M. F.; Maroli, A.; Tharayil, N.; Alexis, F.; Whitehead, D. C.; Karanfil, T. *Environ. Sci. Technol. Lett.* **2018**, 6–11.

TOC IMAGE

