

## Using Model-Based Screening to Help Discover Unknown Environmental Contaminants

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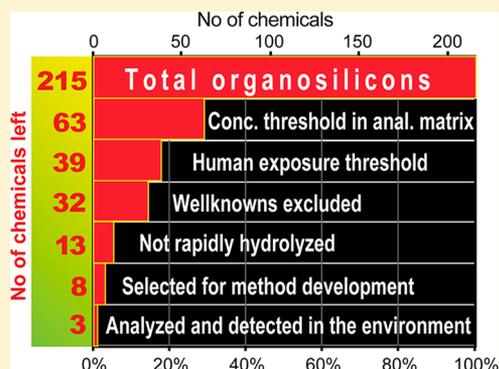
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### **S** Supporting Information

**ABSTRACT:** Of the tens of thousands of chemicals in use, only a small fraction have been analyzed in environmental samples. To effectively identify environmental contaminants, methods to prioritize chemicals for analytical method development are required. We used a high-throughput model of chemical emissions, fate, and bioaccumulation to identify chemicals likely to have high concentrations in specific environmental media, and we prioritized these for target analysis. This model-based screening was applied to 215 organosilicon chemicals culled from industrial chemical production statistics. The model-based screening prioritized several recognized organosilicon contaminants and generated hypotheses leading to the selection of three chemicals that have not previously been identified as potential environmental contaminants for target analysis. Trace analytical methods were developed, and the chemicals were analyzed in air, sewage sludge, and sediment. All three substances were found to be environmental contaminants. Phenyl-tris-(trimethylsiloxy)silane was present in all samples analyzed, with concentrations of  $\sim 50 \text{ pg m}^{-3}$  in Stockholm air and  $\sim 0.5 \text{ ng g}^{-1} \text{ dw}$  in sediment from the Stockholm archipelago. Tris(trifluoropropyl)trimethyl-cyclotrisiloxane and tetrakis(trifluoropropyl)-tetramethyl-cyclotetrasiloxane were found in sediments from Lake Mjøsa at  $\sim 1 \text{ ng g}^{-1} \text{ dw}$ . The discovery of three novel environmental contaminants shows that models can be useful for prioritizing chemicals for exploratory assessment.



### ■ INTRODUCTION

Thousands of organic chemicals are being used in industrial and household applications, and every year several hundred additional chemicals are introduced into the market. Various regulatory programs seek to protect human health and the environment from the risks that may be posed by chemicals (e.g., REACH).<sup>1</sup> Risk is a function of exposure; however, biomonitoring and monitoring data are generally lacking for exposure and risk characterization for humans and the environment for the vast majority chemicals.<sup>2,3</sup> Our knowledge of the contamination status of the environment is also limited because only a small fraction of these chemicals has been

analyzed in environmental samples. Due to the high cost of developing and applying methods for the trace analysis of chemicals in complex environmental matrixes, it is not feasible to measure all chemicals in use. Methods for prioritizing chemicals for target analysis are required, and these methods need to be evaluated.

Received: March 4, 2014

Revised: May 26, 2014

Accepted: May 28, 2014

Published: May 28, 2014

Environmental contaminants have frequently been discovered by analytical chemists who observe unknown signals during the trace analysis of environmental matrices.<sup>4–7</sup> However, this approach is biased toward identifying contaminants which are similar to known contaminants. Nontarget screening is a less biased method for contaminant discovery; typically it is based on gas or liquid chromatography coupled to mass spectrometry. It has been applied with success.<sup>8,9</sup> It is currently limited by difficulties in data processing and in assigning specific molecular structures to individual peaks.<sup>10</sup> An alternative approach that has been developed over the last 20 years is effect-directed analysis.<sup>11</sup> Starting from an adverse effect observed for a specific ecotoxicological end point, extract fractionation is used to isolate and identify the causative agent. This approach is particularly useful because it focuses on contaminants of ecotoxicological relevance, but it has proven challenging to implement<sup>12</sup> and is limited to the proper choice of end points. A common feature of the existing methods to identify new environmental contaminants is that they are limited to identifying the contaminant; they do not provide mechanistic insight into possible source/receptor relationships that could help in determining causes of the contamination or developing control strategies.

Detecting and identifying a previously undiscovered contaminant in the environment and then working backward to infer its source(s) and modes of transport has many challenges, as discussed above. An alternative is the reverse approach, starting with chemicals of interest and working forward to identify potential sources and modes of transport and—eventually—confirming their presence as a contaminant in the environment. This approach is also challenging, as predicting the sources and modes of transport of a chemical requires a quantitative understanding of the chemical and environmental properties involved.

Despite these difficulties, the theoretical screening of large numbers of chemicals to identify those with the greatest potential to be environmental exposure hazards has proven useful.<sup>13,14</sup> Initially, this approach was applied to estimate a limited number of screening criteria, such as persistence and bioaccumulation.<sup>15–17</sup> More recently, it has been extended to screening chemicals for the magnitude of potential environmental contamination and organism exposure.<sup>18,19</sup> This was made possible by the development of linked environmental fate and bioaccumulation models, together with tools that can predict physical chemical properties for large numbers of substances. The next step that made screening for actual, rather than potential, exposure possible was the development of high-throughput methods to screen chemicals for emissions.<sup>20</sup> Using these methods, a list of 12 619 discrete organic chemicals was screened for far-field exposure, yielding predicted concentrations in humans that ranged over 17 orders of magnitude.<sup>21</sup>

In this work, we explore the hypothesis that fate and exposure model-based screening methods can identify contaminants of concern and identify unknown environmental contaminants. We use high-throughput models to identify chemicals that are likely to have high concentrations in specific environmental media, including humans. The chemicals selected with this model-based screening are fed into a targeted analytical screening which concludes with the target analysis of selected compounds in environmental samples. The procedure is applied to a list of organosilicon chemicals.

## METHODS

**Model-Based Screening.** The model-based screening was conducted with the Risk Assessment IDentification And Ranking (RAIDAR) version 2.0 model.<sup>22</sup> RAIDAR couples a regional-scale multimedia environmental fate and transport mass balance model with bioaccumulation mass balance models to calculate exposures and potential risks to humans and various aquatic and terrestrial ecological receptors. RAIDAR is a steady-state model of the “Unit World” type (i.e., there is no spatial resolution of the environmental compartments air, water, soil, and sediment), which is a generic model format that has proven particularly useful for screening purposes.<sup>23</sup> The model can be used to simulate multimedia, multipathway far-field human exposures and a version of the model has been programmed in Excel to facilitate high-throughput calculations for large numbers of chemicals.<sup>21</sup>

RAIDAR requires user input of information on chemical emissions and chemical properties. To estimate emissions for large numbers of chemicals, a recently developed rapid-throughput method was employed.<sup>20</sup> The method is based upon the European Union Technical Guidance Document and uses information on chemical quantities in commerce (production and/or import rates), chemical function (use patterns), and physical chemical properties to estimate emissions to air, soil, and water for five stages of the chemical life-cycle. The chemical properties required by the model (molar mass; octanol–water partition coefficient; Henry’s law constant; degradation half-lives in air, water, soil, and sediment; and primary biotransformation half-lives in vertebrates) were either based on measurements or predictions obtained from the U.S. Environmental Protection Agency’s Estimation Program Interface Suite (EPI Suite) software program.<sup>24</sup> The integration of the chemical property estimation procedures, emissions scenarios, and the RAIDAR model to screen for chemical exposure is described in detail elsewhere.<sup>21</sup>

The chemicals to be screened were taken from a database of 12 619 organic chemicals. This list included industrial chemicals with reported production and/or import in Europe, the United States, Canada, Japan, and OECD countries. Further details of this list are given elsewhere.<sup>21</sup> To provide a manageable subset for targeted chemical screening, it was decided to focus on organosilicon chemicals. This selection was made because there was little reported research on organosilicon chemicals as environmental contaminants, which made this chemical group particularly suitable for evaluating a screening procedure for identifying unknown contaminants. All chemicals that contained silicon were extracted from the database. This yielded 287 chemicals. They were then screened and 72 substances were removed that were not discrete chemicals (e.g., technical mixtures), were inorganic (i.e., had been mistakenly classified as organic in the original database), or were quaternary amines (which are well outside of the domain of the property prediction software used, see below). This left 215 distinct organic chemicals that formed the basis for the model-based screening (see Table S1 in the Supporting Information, SI).

The screening was performed using a stepwise exclusion procedure. First, the steady-state concentrations of the chemicals were predicted using the RAIDAR model, and the chemicals were ranked according to their median concentrations in different environmental media and biota. The first filter was to set lower limits for the predicted concentrations in the environment. The purpose of this filter was to exclude

chemicals that were likely to be below the detection limits of an eventual targeted analytical screening, and for which screening would thus be pointless. Air and sediment were the matrixes selected for the targeted analytical screening (for motivation see below), and the thresholds were set to  $10^{-13}$  moles  $m^{-3}$  and  $10^{-13}$  moles  $cm^{-3}$ , respectively. The second filter was based on predicted human exposure. The purpose of this filter was to restrict the list to chemicals that higher organisms were exposed to, as such chemicals are most likely to pose an environmental risk. Humans were used as a surrogate for higher organisms in this context. The chemicals were ranked according to their predicted concentration in humans (highest concentration = rank 1), and chemicals with a human concentration rank >65 were excluded. The third filter was to exclude known environmental contaminants.

The Hydrowin model in EPI Suite provides useful information for hydrolysis reactions including “rules of thumb” and half-lives when entering chemicals one at a time; however, in “batch mode” for high-throughput screening, many chemicals cannot be treated by the model. Therefore, we did not use Hydrowin and did not include hydrolysis half-lives as RAIDAR model input for initial screening. However, some organosilicon chemicals are readily hydrolyzed,<sup>25</sup> whereby the rates are highly variable, depending on three major factors. First, for an organosilicon compound with an Si—X bond (where X = a hydrolyzable functional group), the rate of hydrolysis will depend on the polarity of the Si—X bond. For example, the hydrolysis rates generally follow the order: organohalosilanes > carboxysilanes = oximosilanes > aminosilanes = alkoxy silanes. In addition, hydrolysis rates increase with an increasing number of Si—X bonds per Si atom. Finally, the size of the nonhydrolyzable functional group attached to the Si atom also influences the hydrolysis rates. Bulky functional groups such as phenyl and *t*-butyl usually dramatically reduce the hydrolysis rates relative to a smaller group, such as methyl, while a small group such as H may increase the hydrolysis rates. On the basis of the above considerations, the organosilicon compounds were assigned to three bins according to their hydrolytical reactivity. Those chemicals in the most reactive bin were excluded.

We emphasize that the stepwise exclusion procedure was intended to prioritize chemicals for target analytical screening. This procedure can be structured in different manners, depending on the properties of potential contaminants that one wishes to prioritize.

**Targeted Analytical Screening.** The chemicals identified in the model-based screening procedure were passed on to the targeted analytical screening stage. The first step in this stage was to select a subset of the chemicals for method development in order to focus the available analytical resources. Exclusion criteria for this step included lack of availability of standards and structural similarity to known organosilicon contaminants (a conscious decision was made to focus on those chemicals with structures that were distinctly different from known organosilicon contaminants).

The second step was to test whether the chemicals could be detected using the available analytical instrumentation. Standard solutions were prepared in *n*-hexane/dichloromethane and in one case in ethyl acetate. These solutions were then analyzed using GC/MS with electron ionization employing both splitless and on-column injection. If the chemical was not detected, then it was analyzed using negative chemical ionization and/or positive chemical ionization. For several chemicals for which

none of these techniques was successful, LC/MS was tested. Standard solutions for LC/MS were prepared in methanol and acetonitrile. The fragmentation patterns using electrospray ionization were investigated with direct infusion QTOF-MS, and UHPLC/MS-MS methods were developed for the screening of environmental samples. More details on the analytical parameters used are provided in SI Table S2.

The third step was to exclude chemicals that were not stable in solution. If the chemical concentration in a standard solution (in organic solvent) decreased by an order of magnitude or more during storage for one month in the refrigerator, then it was considered unlikely that the chemical was sufficiently persistent in the environment to be a detectable contaminant, and it was excluded from further consideration.

The fourth step was target analysis of environmental samples. A tiered approach was employed in selecting samples for analysis. The guiding principle was to begin with environmental samples where the levels were expected to be highest, and—if the chemicals were found there—to proceed to samples in which lower levels were expected. Air and sewage sludge/sediment were chosen as the primary matrixes for screening: air because the modeling showed that many organosilicon chemicals are volatile and distribute preferentially into air; sewage sludge/sediment because we expected many organosilicons to be emitted to water (this is the case for a significant fraction of the known organosilicon contaminants) and the modeling showed that their hydrophobic properties would lead to their sequestration to sediment.

Initially, air samples were collected at the Bromma wastewater treatment plant (WWTP) in Stockholm. The plant serves 300 000 population equivalents and the secondary activated sludge treatment is housed in an enclosed building. Aeration of municipal wastewater in an urban environment with limited air dilution combines different factors (proximity to sources, efficient mass transfer, limited dilution) that can contribute to elevated contaminant concentrations in air. The samples were collected on 15–25 mL cartridges containing 80–140 mg of Isolute ENV+ (Biotage AB, Uppsala, Sweden) following the procedure described elsewhere.<sup>26</sup> For the second tier, extracts of air samples that had been collected for another study in Zürich during a period with a strong thermal inversion<sup>27</sup> were also subjected to GC analysis. In that study, cyclic volatile methylsiloxanes were analyzed, and the sample collection and extraction procedures were the same as used here. In a third tier effort, air samples were collected on the Stockholm University campus, which is located within the city of Stockholm, using the same method as employed at the Bromma WWTP. Sampling was done on two occasions, and in each case, duplicate samples were collected in parallel. Details about the collection of the air samples are provided in SI Table S3.

Sewage sludge was the matrix used in the first tier of the screening for hydrophobic organosilicons. Samples of digested and dewatered sludge were collected from the Bromma and Henriksdal WWTPs in Stockholm during 2013. In the second tier, surface sediment was analyzed, beginning with 4 samples collected during September 2011 on a transect from Stockholm Harbor, which is the recipient for Henriksdal and Bromma WWTP effluents for about 1 million person equivalents, through the inner Stockholm Archipelago. Sediment samples collected for other studies from two Swedish lakes<sup>28</sup> and Lakes Mjøsa and Femunden in Southern Norway<sup>29</sup> were also

analyzed. Details of the sewage sludge and sediment samples are provided in SI Table S4.

Target analysis was conducted for three chemicals; GC was used for one chemical (phenyl-tris(trimethylsiloxy)silane (M3TPh)), and LC for the other two chemicals (tris-(trifluoropropyl)trimethyl-cyclotrisiloxane (D3F), and tetrakis-(trifluoropropyl)tetramethyl-cyclotetrasiloxane (D4F)). For the air samples, the ENV+ cartridges were extracted with 3–10 fractions of 300  $\mu\text{L}$  of dichloromethane (air from the WWTP for GC analysis), 1.3 mL of *n*-hexane (air from the university for GC analysis) or  $3 \times 300 \mu\text{L}$  acetonitrile (for LC analysis). Each fraction was analyzed individually without cleanup or concentration of the extract.

For the analysis of sludge and sediment, a wet sample of 10 g (dewatered sludge) or 25 g (centrifuged sediment) was extracted with acetone (20–25 mL) and dichloromethane (1.5 mL). The acetone quantity was optimized to produce one single liquid phase, the water included. The samples were ultrasonicated for  $2 \times 15$  min. After centrifugation, the liquid phase was decanted and the sample was re-extracted with 2 mL (sludge) or 10 mL (sediment) acetone together with 5 mL dichloromethane. The extracts were combined and dichloromethane was carefully added to the single liquid phase until a dichloromethane/acetone phase formed that was distinct from the water phase. The organic phase was transferred into 250 mL flasks and cleaned up using a purge and trap technique described elsewhere.<sup>29</sup> The trap consisted of an ENV+ cartridge that was eluted with 3 fractions of 300  $\mu\text{L}$  of acetonitrile for the analysis of D3F and D4F. For the analysis of M3TPh, the combined acetonitrile fractions were quantitatively transferred to *n*-hexane (1 + 1 mL) by the addition of 1.5 mL of water.

M3TPh was analyzed by GC/MS(EI) while D3F and D4F were analyzed by UHPLC/MS-MS with electrospray ionization. Quantification was accomplished using standard addition to duplicate samples. Standard addition was done into the centrifuged sediment with a syringe after the addition of a 1.5 mL layer of dichloromethane. The instrumental methods are summarized in SI Table S5.

## RESULTS AND DISCUSSION

**Model-Based Screening.** The results of the model-based screening are summarized in the TOC art. RAIDAR predicted concentrations that ranged from  $10^{-7}$  to  $10^{-19}$  mol  $\text{m}^{-3}$  in air,  $10^{-11}$  to  $10^{-19}$  mol  $\text{cm}^{-3}$  in sediment, and  $10^{-4}$  to  $10^{-16}$  mol  $\text{m}^{-3}$  (or mmol  $\text{kg}^{-1}$  assuming a whole body density of 1000  $\text{kg}/\text{m}^3$ ) in humans for the 215 organosilicon chemicals (see SI Table S1). Of these, 52 chemicals exceeded the threshold concentration for air, and 24 the threshold concentration for sediment in the first filter. There were 13 substances common to these two groups, leaving 63 substances after the environmental concentration filter.

The human exposure filter resulted in the elimination of a further 24 chemicals. Most of these were substances with high predicted concentrations in air; only one of the eliminated chemicals had a high predicted concentration in sediment. This suggests that human exposure is correlated more strongly with concentration in sediment than with concentration in air. This can be explained by the fact that chemicals with high concentrations in sediment often possess a tendency to partition to organic matter. This tendency also fosters bioaccumulation (i.e., chemicals which partition into sediment will also partition into biota).

Seven of the chemicals that passed the second filter were known environmental contaminants, namely hexamethyldisiloxane (L2), octamethyltrisiloxane (L3), decamethyltetrasiloxane (L4), hexamethylcyclotrisiloxane (D3), octamethylcyclotetrasiloxane (D4), decamethylcyclopentasiloxane (D5), and dodecamethylcyclohexasiloxane (D6). D4, D5, and D6, three known organosilicon contaminants that have been subjected to particularly intensive regulatory assessment,<sup>30–32</sup> ranked in the top four based on concentration rankings for both predicted sediment and human concentrations. The presence of these known environmental contaminants at the top of the screened list provides some confidence about the relevance and effectiveness of the screening procedure for identifying chemicals of concern.

Of the 32 remaining chemicals, 19 were estimated to be rapidly hydrolyzed. They were removed from the chemical list. A further 7 were classified as being moderately susceptible to hydrolysis, but were retained. The chemical list after this filter is provided in Table S6.

The model-based screening procedure reduced the original list of 215 discrete chemicals to 13 chemicals that were carried through to targeted analytical screening. Redundancy in the screening procedure can be assessed using the selectiveness of each filter stage; if a filter removes only a small fraction of the chemicals passing through it, it may be possible to omit it from the screening procedure without having a large impact on the screening final outcome. The initial concentration-based filter was the most selective, removing 71% of the chemicals, followed by the reactivity filter, which removed 59% of the chemicals that passed through it (TOC art). The human exposure filters was also quite effective, removing 38% of the chemicals passing through it. The known contaminant filter was the least selective (18%), but the organosilicons were selected for this evaluation because there are few known organosilicon contaminants. Other chemical groups could have a larger fraction in this category, and then this filter could be more important. In conclusion, each filter stage in the screening procedure was useful; none was redundant.

**Targeted Analytical Screening.** Of the 13 chemicals identified by the model-based screening, eight were selected for analytical method development. The other five were not selected for a number of reasons including lack of commercial availability at the time of method development, and structural similarity to known organosilicon contaminants.<sup>26,33</sup>

Detection methods were successfully developed for five of the chemicals selected for targeted analytical screening (see SI Table S6). It is possible that a more extensive effort could have produced detection methods for the remaining three chemicals. However, it is also possible that the negative result was due to the instability of the chemicals in solution; all of the remaining three chemicals were classified as moderately susceptible to hydrolysis in the three bin categorization system.

The stability test showed that one of the five detectable chemicals was unstable in solution (see SI Table S6). This chemical was classified as moderately susceptible to hydrolysis. All of the other four chemicals were classified as less susceptible to hydrolysis.

The four detectable and stable chemicals identified by the screening procedure are shown in Figure 1. Environmental samples were screened for three of these chemicals that were compatible with our tried and proven purge and trap cleanup method for cyclic volatile methylsiloxanes, namely phenyl-tris(trimethylsiloxy)silane (M3TPh) (CAS# 2116849), tris-

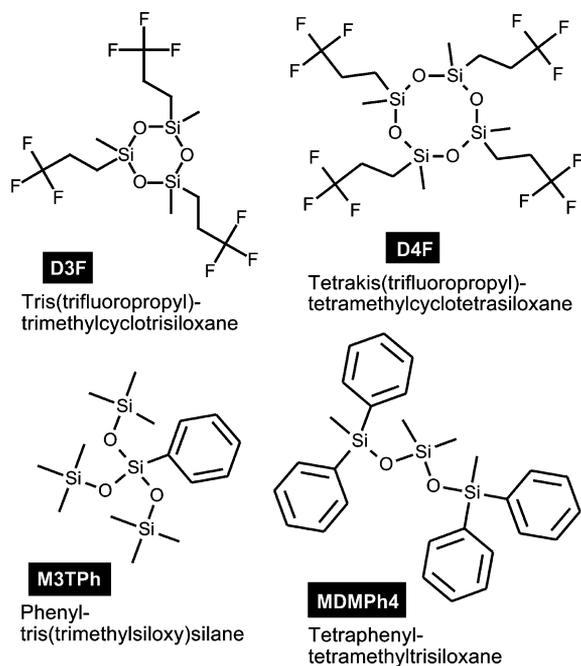


Figure 1. Substances identified for targeted analytical screening.

(trifluoropropyl)trimethyl-cyclotrisiloxane (D3F) (CAS# 2374143), and tetrakis(trifluoropropyl)tetramethyl-cyclotetrasiloxane (D4F) (CAS# 429674). The fourth chemical tetraphenyl-tetramethyl-trisiloxane (MDMPH4) (CAS# 3982829) was much less volatile and displayed poor recovery in the purge and trap cleanup step.

**M3TPh.** M3TPh was found in several matrixes. The concentrations were sufficiently high, and the analytical method was sufficiently specific that most features of the M3TPh mass spectrum were observed in full scan spectra of environmental samples. This is illustrated in SI Figure S1, which compares the mass spectra in a standard, a sewage sludge sample, and a sediment sample.

The M3TPh concentrations measured in air are given in Table 1. The concentrations were highest in the WWTP, at 5.5 ng m<sup>-3</sup>. They were a little more than an order of magnitude lower in Zürich during the inversion event and a further order of magnitude lower on the Stockholm University campus. There was good agreement between the parallel samples collected in Stockholm (difference <5%). The compound was not detected in the field blanks from the Zürich campaign. The LOQ (5 times the noise) was 0.02 ng m<sup>-3</sup>, which is 12–26 times lower than the concentrations in the Zürich samples. This indicates that the levels in these samples were not due to contamination in the field or the laboratory. In summary, the air sampling provided strong evidence that M3TPh is an atmospheric contaminant.

M3TPh was found in all sewage sludge and sediment samples (Table 1). As with the air samples, the parallel analyses of Henriksdal sludge and Beckholmen sediment gave similar concentrations (difference <15%). The mean recovery of the method was 78% (CV 8%, *n* = 7) for the sediment samples and 54% for sewage sludge. The good reproducibility and recovery provides confidence in the quality of the analytical method. No field blanks were available for the sediment samples. The least contaminated sediments provide an upper estimate for the field blank. The M3TPh contents of the Hjulstafjärden and

Table 1. Levels of Phenyl-tris(trimethylsiloxy)silane (M3TPh) in Environmental Samples

|                                  | air   | ng m <sup>-3</sup>    | ng sample <sup>-1</sup> |
|----------------------------------|---|-----------------------|-------------------------|
| Bromma WWTP                      |   | 7.4                   | 550                     |
| Zürich Kaserne 17 field blank    |   | <0.2 <sup>a</sup>     |                         |
| Zürich Kaserne 17 A              |   | 0.21                  | 1.9                     |
| Zürich Kaserne 24 field blank    |   | <0.2 <sup>a</sup>     |                         |
| Zürich Kaserne 24 A              |   | 0.49                  | 4.0                     |
| Stockholm 111201A <sup>b,c</sup> |   | 0.069                 | 4.1                     |
| Stockholm 111201B <sup>b,c</sup> |   | 0.072                 | 4.8                     |
| Stockholm 111124A <sup>b,c</sup> |   | 0.046                 | 3.2                     |
| Stockholm 111124B <sup>b,c</sup> |   | 0.044                 | 2.9                     |
|                                  | sewage sludge                               | ng g <sup>-1</sup> dw | ng sample <sup>-1</sup> |
| procedural blank                 |   | 0.21                  |                         |
| Bromma 2013                      |   | 470                   | 1400                    |
| Henriksdal A 2013 <sup>c</sup>   |   | 490                   | 1100                    |
| Henriksdal B 2013 <sup>c</sup>   |   | 530                   | 1200                    |
|                                  | sediment, transect<br>Stockholm archipelago | ng g <sup>-1</sup> dw | ng sample <sup>-1</sup> |
| Beckholmen A <sup>c</sup>        |   | 21                    | 69                      |
| Beckholmen B <sup>c</sup>        |   | 18                    | 81                      |
| Fisksätra                        |   | 3.2                   | 11                      |
| Gustavsberg                      |   | 0.38                  | 4.9                     |
| Baggensfjärden                   |   | 0.46                  | 3.9                     |
|                                  | sediment, Swedish lakes                     | ng g <sup>-1</sup> dw | ng sample <sup>-1</sup> |
| Östersjön                        |   | 1.2                   | 12                      |
| Hjulstafjärden                   |   | 0.015                 | 0.25                    |
|                                  | sediment, Norwegian lakes                   | ng g <sup>-1</sup> dw | ng sample <sup>-1</sup> |
| Mjøsa Gjøvik                     |   | 1.7                   | 13                      |
| Femunden                         |   | 0.11                  | 0.45                    |

<sup>a</sup>No peak was observed in any of the blanks. This quantity was estimated based on 5 times the noise. <sup>b</sup>The number represents the sampling date (year-month-day). <sup>c</sup>A and B denote parallel samples (air) or parallel analysis of the same sample (sludge and sediment).

Femunden samples were the lowest measured (0.25 and 0.45 ng sample<sup>-1</sup>, respectively).

The M3TPh concentrations in sewage sludge from the two Stockholm WWTPs were ~500 ng g<sup>-1</sup> dw (Table 1). The amount of M3TPh in the procedural blank was >3 orders of magnitude lower than in the samples. This indicated that M3TPh is likely being released to the aquatic environment, and led to the analysis of sediment samples.

Sediment collected at Beckholmen in Stockholm Harbor close to the outfalls of the Henriksdal and Bromma WWTPs contained 20 ng g<sup>-1</sup> dw of M3TPh. This was ~25 times lower than the concentrations measured in the sewage sludge. The M3TPh quantity in the sample exceeded the upper estimate of the M3TPh quantity in the field blank by >2 orders of magnitude, indicating that M3TPh was present in the sediment as an environmental contaminant.

A clear M3TPh concentration gradient was observed from the WWTPs along the transect through the inner Stockholm archipelago out toward the Baltic Sea. Moving from Beckholmen toward the open Baltic Sea, the M3TPh concentration decreased to 3.2 ng g<sup>-1</sup> dw at Fisksätra and further to 0.38 and 0.46 ng g<sup>-1</sup> dw at the two outer stations, Gustavsberg and Baggensfjärden. These observations indicate that M3TPh is being emitted from the Stockholm WWTPs, resulting in contamination of the recipient and a contamination plume that extends out toward the Baltic Sea.

Sediments were also analyzed from two lakes in Sweden and two lakes in Norway. In each country, one of the lakes had much higher concentrations than the other (see Table 1). In each case, the lake with the higher M3TPh concentration (Östersjön in Sweden and Mjøsa in Norway) was significantly impacted by WWTP effluent and had been shown to be contaminated with D5, a known organosilicon contaminant originating from WWTPs, while the lake with the lower M3TPh concentration (Hjulstafjärden in Sweden and Femunden in Norway) was much less impacted by WWTP effluent and had been shown to be much less contaminated with D5.<sup>28,29</sup> This is further evidence that M3TPh is an environmental contaminant in aquatic ecosystems that originates from WWTPs.

**D3F.** This chemical presented interesting analytical challenges. MS/MS analysis of standard solutions prepared in acetonitrile and analyzed using direct infusion in an acetonitrile: water (1:1, v/v) mixture produced ions corresponding to (M + 17)<sup>-</sup>. Our interpretation was that D3F was ionized after a hydrolysis reaction resulting in breakage of the ring and formation of a linear siloxanediol (D3FOH) through the addition of water (see SI Figure S2). When the same standard was chromatographed in the reversed phase column using a water/acetonitrile gradient as the mobile phase, two well-separated peaks with identical MS/MS transitions were obtained. We judged the early eluting peak to be D3FOH formed in the standard prior to analysis, while the late eluting peak was D3FOH formed via hydrolysis of D3F directly in the source. This was verified by adding water to a standard solution of D3F in acetonitrile. As the fraction of water increased, the size of the early eluting peak increased at the expense of a decreased late eluting peak (see SI Figure S3), presumably as a result of greater hydrolysis of the D3F in the standard solution prior to analysis. Moreover, when the standard in acetonitrile was subsequently analyzed using isocratic elution with acetonitrile, the size of the later eluting peak was an order of magnitude lower, which we attribute to less hydrolysis of D3F in the ion source in the near absence of water. Scanning for parents of a neutral loss of 20 (many fragments in the mass spectrum of the diol originates from the repeated loss of HF) indicated that D3FOH was the major hydrolysis product formed. D3F was quantified using the sum of the areas of the two peaks. This could result in an overestimation of the D3F concentrations, as some fraction of the D3FOH present in the environmental samples may also have been extracted. Since no standard was available for D3FOH, no response factor could be determined; it was assumed to be equal to that of D3F. This adds uncertainty to the quantification, but the D3F peak contributed on average 30% to the sum of the areas of the two peaks.

In air, D3F was only analyzed in the samples collected at Stockholm University (both 2012 and 2013). Traces of D3FOH were found ( $\sim 3\text{--}5\text{ pg m}^{-3}$ ), but similar quantities were also found in the procedural blanks ( $\sim 3\text{ pg m}^{-3}$ ). Thus, no evidence was found that D3F is an atmospheric contaminant.

The results of the targeted analytical screening of D3F + D3FOH in solid matrixes are summarized in Table 2. D3F + D3FOH were found in sewage sludge at levels ranging from 70 to 130  $\text{pg g}^{-1}\text{ dw}$ . This led to their analysis in sediment. In contrast to M3TPh, many sediment samples contained D3F + D3FOH concentrations at the low end of the observed range. Since there was no field blank, the sample with the lowest

**Table 2. Levels of Tris(trifluoropropyl)trimethylcyclotrisiloxane (D3F) and Tetrakis(trifluoropropyl)tetramethyl-cyclotetrasiloxane (D4F) in Environmental Samples**

|  | D3F + D3FOH <sup>a</sup><br>( $\text{pg g}^{-1}\text{ dw}$ ) | D4F + D4FOH <sup>a</sup><br>( $\text{pg g}^{-1}\text{ dw}$ ) |
|--|--|--|
| sewage sludge                            |  |  |
| Henriksdal 2013                          | 130  | 600  |
| Bromma 2013                              | 70   | 130  |
| sediment, transect Stockholm archipelago |  |  |
| Beckholmen                               | 19   | 300  |
| Fisksätra                                | 70   | 80   |
| Gustavsberg                              | 10   | 30   |
| Baggensfjärden                           | 30   | 50   |
| sediment, Swedish lakes                  |  |  |
| Östersjön                                | 10   | 30   |
| Runn                                     |  | 40   |
| Hjulstafjärden                           | 60   | 30   |
| sediment, Norwegian lakes                |  |  |
| Femunden                                 | 6  | 70   |
| Mjøsa (Gjøvik)                           | 1600   | 1800   |

<sup>a</sup>D3F was quantified as the sum of the areas of the D3F peak and the D3FOH peak in the chromatogram. D4F was quantified in an analogous manner.

concentration (Femunden) was used as a field blank, and samples with concentrations less than 3 times this concentration were considered below the LOD. The levels in the sediment samples collected in Stockholm Harbor ranged from  $<\text{LOD}-70\text{ pg g}^{-1}\text{ dw}$ . No gradient in concentrations was observed moving away from the harbor, but this could be due to the proximity of the measured levels to the LOD or the low method precision arising from the analytical challenges discussed above. These chemicals were detected in one of 2 sediment samples from Swedish lakes impacted by WWTPs (60  $\text{pg g}^{-1}\text{ dw}$ ). Much higher levels of D3F + D3FOH (1600  $\text{pg g}^{-1}\text{ dw}$ ) were present in Lake Mjøsa sediment. This lake has also been found to contain comparatively high levels of D5.<sup>29</sup> Taken together, the results indicate that D3F + D3FOH are contaminants in some aquatic systems. Given the evidence for relatively rapid hydrolysis of D3F in aqueous solution in the laboratory, its presence in sediment is consistent with some portion of D3F being emitted in sorbed form.

**D4F.** D4F presented analytical challenges similar to those encountered for D3F. The hydrolysis product D4FOH was formed in the ion source, in the UPLC column, and in solution, which hampered quantification. However, the ratio of the D4FOH/D4F signals was in general smaller than the ratio of the D3FOH/D3F signals, indicating that D4F was less susceptible to hydrolysis. On average, D4F accounted for 95% of the sum of the D4F and D4FOH signal.

Like D3F + D3FOH, D4F + D4FOH were not found in the air samples from Stockholm University at levels markedly above the method blank ( $\sim 2\text{ pg m}^{-3}$ ).

The results of the targeted analytical screening of D4F + D4FOH in sewage sludge and sediment are summarized in Table 2. The LOD was 90  $\text{pg g}^{-1}\text{ dw}$  based on the sample with the lowest concentration as described above. D4F + D4FOH were not detected in most of the sediment samples. However, they were clearly present in the two sewage sludge samples and two of the sediment samples. Again, comparatively high levels were detected in Lake Mjøsa (1800  $\text{pg g}^{-1}\text{ dw}$ ). This indicates

that D4F + D4FOH are also contaminants in some aquatic systems.

**Evaluation of the Overall Screening Strategy.** The combination of model-based screening and targeted analytical screening proved to be effective. Three unknown environmental contaminants were discovered. All of the chemicals that were subjected to targeted analytical screening of environmental samples based on the model-based screening were found. This high success rate was certainly to some degree fortuitous and cannot be expected in all cases. However, it does suggest that model-based screening combined with analytical prescreening is useful in guiding the search for unknown environmental contaminants.

This case study clearly illustrates that high throughput model-based screening methods for chemical fate and exposure may result in a substantial number of false positives for chemicals that are subject to hydrolysis. Environmentally relevant chemical hydrolysis databases and revised high-throughput QSPR tools to predict hydrolysis rates are needed to improve model-based screening and prioritization methods. To overcome this, we developed a set of rules for organosilicon substances. However, this approach cannot be readily applied to a broader spectrum of chemicals.

To obtain more insight into the performance of the model-based screening, the measured concentrations of the target analytes were compared with the concentrations predicted by the model. For M3TPh, the median predicted concentration in air was  $2 \text{ pg m}^{-3}$  ( $3 \times 10^{-3}$  to  $2 \times 10^3$  was the 95% uncertainty interval predicted by RAIDAR). This compares with the measured concentrations at Stockholm University (the sampling site believed to best represent regional background) of 44–72  $\text{pg m}^{-3}$ . The model median under-predicted the concentration in air by a factor of  $\sim 25$ . For sediment, the predicted median concentration was  $0.4 \text{ ng g}^{-1} \text{ dw}$  ( $5 \times 10^{-4}$  to  $3 \times 10^2$ ). This agrees well with the concentrations measured at the seaward stations in the Stockholm archipelago (0.38 and  $0.46 \text{ ng g}^{-1} \text{ dw}$ ) and in the remote lake Femunden ( $0.14 \text{ ng g}^{-1} \text{ dw}$ ), while it is higher than measured in Hjulstafjärden ( $0.015 \text{ ng g}^{-1} \text{ dw}$ ).

For D3F and D4F, the predicted median concentrations in air were 56 ( $4 \times 10^{-2}$  to  $7 \times 10^4$ ) and 0.4 ( $2 \times 10^{-3}$  to 81)  $\text{pg m}^{-3}$ , respectively. Neither was detected in the air at a LOD of  $\sim 10 \text{ pg m}^{-3}$ . In sediment, the predicted median concentrations were 36 000 ( $40$  to  $3 \times 10^7$ )  $\text{pg g}^{-1} \text{ dw}$  and 700 ( $6$  to  $8 \times 10^4$ )  $\text{pg g}^{-1} \text{ dw}$ , respectively. For D3F, the median prediction overestimates the concentrations measured in most of the sediment samples ( $6$  to  $65 \text{ pg g}^{-1} \text{ dw}$ ) by about 3 orders of magnitude (1 order of magnitude for Lake Mjøsa); however, some of the measurements are within the predicted range, including uncertainty. For D4F, the measured values in sediment from the Stockholm archipelago and Swedish lakes ( $30$ – $300 \text{ pg g}^{-1} \text{ dw}$ ) were similar to the median model prediction. The model's overestimation of the D3F concentration in sediment is in part attributable to the fact that the model did not consider hydrolysis. The analytical method development showed that D3F is particularly susceptible to hydrolysis during analysis. Thus, hydrolysis will likely be a significant loss process in the aquatic environment.

The uncertainty intervals for the model predicted concentrations of these three chemicals in air and sediment were approximately  $\pm 3$  orders of magnitude and were largely driven by uncertainty in emission rate estimates (see Arnot et al.<sup>21</sup> for a discussion of the estimation of the uncertainty interval). The

measured concentrations lie well within the uncertainty intervals of the predictions. Nevertheless, the high model uncertainty can have consequences for the results of the model-based screening. Underestimation of environmental concentrations can lead to the screening out of chemicals that have high concentrations in the environment (false negatives), while overestimation can lead to the screening in of chemicals that have nondetectable concentrations in the environment (false positives). In this work, no false positives were identified, whereby it cannot be ruled out that there were false positives after the air, sediment, and human exposure filters that were then eliminated by subsequent filters in the screening process. It is possible that the screening process did result in false negatives; however, we did not evaluate the system for this possibility. Consequently, we do not conclude that chemicals screened out in the model-based filters are not environmental contaminants. The fact that the well-known organosilicon environmental contaminants were screened in and ranked highly provides confidence in the capacity of the screening system to provide viable hypotheses for targeted testing.

This work illustrates the potential of model-based screening to assist in identifying unknown environmental contaminants. In addition, using emissions-based mechanistic models at the early stages of contaminant discovery means that additional information that they provide, for instance on sources, major chemical transport pathways, and responses to changes in emissions, is available to guide the further exploration of the contaminant issue and the eventual development of effective chemical management. We expect that model-based screening will become more useful as model uncertainty is reduced. Currently, the emissions estimates are the dominant source of model uncertainty.<sup>21</sup> Furthermore, the lack of high-throughput methods to estimate hydrolysis proved to be a particularly serious shortcoming in screening organosilicons.

Finally, we note that identifying an unknown environmental contaminant is only the first step. Much more work is required to assess a contaminant's sources, environmental behavior, and toxicity before it can be established whether it is an environmental concern.

## ■ ASSOCIATED CONTENT

### Supporting Information

Three figures (mass spectra of M3TPh, the structural formula of D3FOH and D4FOH, and chromatograms showing the elution of D3F standard solutions containing different fractions of water) and six tables (list of the 215 discrete organosilicon chemicals, analytical conditions employed when screening for detectability, details of air sampling, details of sediment sampling, instrumental methods, and list of chemicals after the reactivity filter). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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### Notes

The authors declare no competing financial interest.

## ACKNOWLEDGMENTS

This work was largely funded by the European Chemical Industry Council Long-Range Research Initiative (project ECO13). We thank the project research liaison team for their advice and support throughout the project. Additional funding was provided by the Research Council of Norway (196191). We thank Katrine Borgå and Eirik Fjeld (NIVA) for collecting the sediment samples from the Norwegian lakes, Andreas Buser (ETH Zürich) for collecting the air samples in Zürich, Markus Meili (ITM) and Per Jonsson for collecting the Stockholm sediment samples, and Cajsa Wahlberg (Stockholm Vatten) for providing access to the Bromma WWTP for air sampling.

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