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Novel Dechlorane Analogues and Possible Sources in Peregrine Falcon Eggs and Shark Livers from the Western North Atlantic Regions

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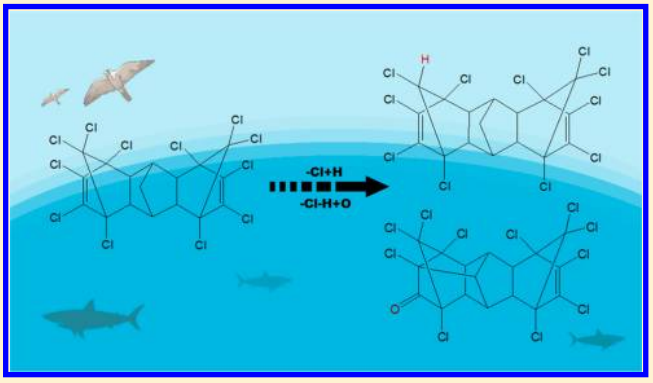
Supporting Information

ABSTRACT: During the investigation of dechlorane-related chemicals in North American wildlife, two unknown polychlorinated compounds (referred to as U1 and U2) were discovered. After extensive sample cleanup, structural information on U1 and U2 was characterized by gas chromatography (GC) coupled with single quadrupole mass spectrometer (MS) or GC-quadrupole time-of-flight (QToF) MS. Mass spectral evidence suggests that both U1 and U2 are structurally related to Dechlorane 603 (Dec603; $C_{17}H_8Cl_{12}$), an analogue of the chlorinated flame retardant Dechlorane Plus. From the results we suspect U1 ($C_{17}H_9Cl_{11}$) to be a monohydro analogue of Dec603 (i.e., one chlorine atom in Dec603 is replaced by a hydrogen atom). U1 may be formed via the degradation of Dec603's stereoisomers or present as an impurity in commercial Dec603 products. Mass spectral characterization of U2 ($C_{17}H_7OCl_{11}$) suggests it is a carbonylic derivative of Dec603, likely formed via metabolic transformation of Dec603 or its photoisomer. Semiquantitative measurement revealed that U1 and U2 were present at estimated median concentrations of 49 ng/g lipid weight (lw) and 59 ng/g lw in peregrine falcon (*Falco peregrinus*) eggs, from the mid-Atlantic region of the United States, and 4.6 and 3.0 ng/g lw in shortfin mako shark (*Isurus oxyrinchus*) livers from the western North Atlantic Ocean, respectively. Our results demonstrate the occurrence of these two novel Dec603-related chemicals in both terrestrial and aquatic ecosystems.



INTRODUCTION

Dechlorane Plus (DP, $C_{18}H_{12}Cl_{12}$) is a chlorinated flame retardant produced by the Diels−Alder reaction of two equivalents of hexachlorocyclopentadiene (HCCPD) and one equivalent of 1,5-cyclooctadiene.[1] The technical DP mixture contains two stereoisomers, *syn*-DP and *anti*-DP.[1] Since the first report of DP isomers on their environmental occurrence in the North American Great Lakes air,[2] this chlorinated flame retardant has been discovered in various environmental compartments, including air, water, sediment, and biota,[3−7] and raised broad concerns due to their persistent, bioaccumulative, and toxic characteristics.[8,9]

Recent studies also reported a suite of chemicals structurally resembling DP isomers (collectively referred to as dechlorane-related chemicals) in technical mixtures and environmental samples. Several major dechlorane-related chemicals, including Dechlorane 602 (Dec602, $C_{14}H_4Cl_{12}O$), Dechlorane 603 (Dec603, $C_{17}H_8Cl_{12}$), and Dechlorane 604 (Dec604, $C_{13}H_4Br_4Cl_6$), are formed by using various dienophile starting materials in the Diels−Alder reactions.[10] These chemicals are used as flame retardants in different applications, particularly as alternatives to DP isomers when DP does not meet the specific voltage leakage and thermal standards in certain applications.[1]

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In addition to these major dechlorane analogues, other related chemicals were also reported in the environment. Some of them are impurities present in side reactions or incomplete synthesis of DP, such as 4-vinylcyclohexene DP (VCH-DP) and 1,3- and 1,5-Dechlorane Plus monoadducts (DPMA).[11] The others are dechlorination products of DP isomers, such as monodechlorinated and didechlorinated DP (Cl_{11}-DP and Cl_{10}-DP)[12,13] or debromination products of Dec604, such as Br-Dec604 and Br_2-Dec604.[14] Several dechlorane-related analogues, including Dec602, Dec603, and Dec604 Component B (Dec604CB), were frequently detected in air, sediment, and fish from the Great Lakes of North America, fish from the St. Lawrence River (Canada), Illinois (U.S.) rivers, and Liaodong Bay (China), Franciscana dolphins (*Pontoporia blainvillei*) from Brazil, bottlenose dolphins (*Tursiops truncatus*) and common dolphins (*Delphinus delphis*) from Southern European waters, bobcats (*Lynx rufus*) from the midwestern U.S., and peregrine falcon (*Falco peregrinus*) eggs from Canada and Spain.[10,12,15−19] These findings demonstrate global distribution of dechlorane-related chemicals and their substantial bioaccumulation potencies.[1]

We recently determined a suite of known dechlorane analogues in peregrine falcon eggs from the mid-Atlantic United States (U.S.) and livers of shortfin mako sharks (*Isurus oxyrinchus*) from the western North Atlantic Ocean. During the instrumental analysis using gas chromatography-single quadrupole mass spectrometry under electron-capture negative ionization or electron impact mode (GC-ECNIqMS or GC-EIqMS), two unknown peaks were frequently detected in egg or liver extracts. Mass spectral analyses suggest that the two unknowns are polychlorinated and their fragmentation patterns partially resemble those of major dechlorane analogues. However, neither of the two unknown peaks fully matches with any known dechlorane analogues on both the retention time and mass fragmentation patterns. We suspected these peaks represent novel dechlorane analogues or the derivatives related to known dechlorane analogues. Therefore, the present study was subsequently undertaken to (1) characterize these two novel dechlorane-related substances using different mass spectrometers and ionization sources and discuss their potential sources and (2) estimate their concentrations in peregrine falcon eggs and shortfin mako shark livers and compare them with other major dechlorane analogues found in these two species. Our results broaden the current knowledge on the environmental occurrence, fate, and bioaccumulation of the dechlorane family of flame retardants.

MATERIALS AND METHODS

Chemicals and Reagents. Reference standards of dechlorane analogues, including Dec601, Dec602, Dec603, Dec604, Dec604CB, *anti*-Cl_{11}-DP, *anti*-Cl_{10}-DP, Chlordene Plus (Cplus), and *anti*- and *syn*-DP, were purchased from Wellington Laboratories (Guelph, ON, Canada). Surrogate standard 4′-fluoro-2,3,3′,4,5,6-hexabromodiphenyl ether (FBDE-160) and internal standard 3′-fluoro-2,2′,4,4′,5,6′-hexabromodiphenyl ether (FBDE-154) were also purchased from Wellington Laboratories. Styrene divinylbenzene beads (3% cross-linkage, 40−80 μm bead size, ≤2000 MW limit) and isolute silica sorbent were purchased from Bio-Rad (Hercules, CA) and Biotage Inc. (Charlotte, NC), respectively. Solvents used were high performance liquid chromatography (HPLC) grade (Fisher Scientific, Hanover Park, IL).

Samples. Addled peregrine falcon (*Falco peregrinus*) eggs (n = 15) were collected during the period from 2013 to 2014 from the Chesapeake Bay, United States (U.S.) by avian ecologists from the Center for Conservation Biology, The College of William and Mary. Shortfin mako sharks (n = 25) were sampled by scientists from the Cape Canaveral Scientific Inc. using hooked gear from offshore waters ranging from southern Maine to New York from 2008 to 2014. Liver tissues were removed from each shark. For qualitative characterization of unknown dechlorane analogues, a composite per species was prepared by pooling and homogenizing an aliquot of each individual samples with approximately equal weights, whereas semiquantitative measurements were conducted on individual samples.

Sample Treatment. Approximately 15 g of peregrine falcon egg composite and 1.2 g of shark liver composite were extracted and processed in five and three replicates (3 and 0.4 g each), respectively. Each replicate was ground with diatomaceous earth and subjected to pressurized fluid extraction (Dionex ASE 350 Accelerated Solvent Extractor, Thermo Scientific, Sunnyvale, CA) with dichloromethane (DCM) at 100 °C and 1500 psi. The extract was dehydrated by passing through sodium sulfate and then purified with gel permeation chromatography (GPC, length 40 cm, diameter 1.5 cm) packed with 6 g of styrene divinylbenzene beads in a mixture of hexane and DCM (HEX/DCM, 1:1, v/v). After the first fraction was eluted with 30 mL of HEX/DCM (1:1, v/v) and discarded, the second fraction was eluted with 60 mL of HEX/DCM (1:1, v/v) and then concentrated for further cleanup through a 2 g isolute silica solid phase extraction (SPE) cartridge. After the cartridge was preconditioned with 10 mL of HEX, the sample was loaded and the cartridge was washed with 3 mL of HEX. Target compounds were then eluted out with 11 mL of a HEX/DCM mixture (6:4, v/v). The final extracts of five replicates of falcon egg composite or three replicates of shark liver composite were combined by species and fractionated through a 7 g silica gel column (250 × 11 mm i.d.) in order to further remove other potential interferences (e.g., dechlorane analogues and other chlorinated substances) from the fraction containing two unknown chemicals for better mass spectral characterization. After the combined extract was loaded, the silica gel column was eluted with 30 mL of HEX, 30 mL of HEX/DCM (8:2, v/v), and followed by 30 mL of HEX/DCM (1:1, v/v). The eluent was collected into nine fractions (10 mL of each fraction). The two unknown analytes were found to be present in fractions 5−7 only. These three fractions were combined, concentrated under nitrogen, and transferred to a GC vial.

To estimate the concentrations of the two unknown compounds (referred to as U1 and U2), approximately 0.5−1 g of individual peregrine egg or 0.2−0.5 g of individual shark liver was ground with diatomaceous earth, spiked with surrogate standard, and then extracted with ASE. A procedural blank was processed along with each set of seven samples. After running the mixture through sodium sulfate to remove moisture, the extract was gravimetrically tested for lipid content by using 10% of the extract. The remaining extract was cleaned through GPC and then SPE, using the same procedures (except the cleanup through a 7 g silica gel column) that were applied to composite samples as mentioned before. The final extract was concentrated to around 200 μL and spiked with internal standard FBDE-154.

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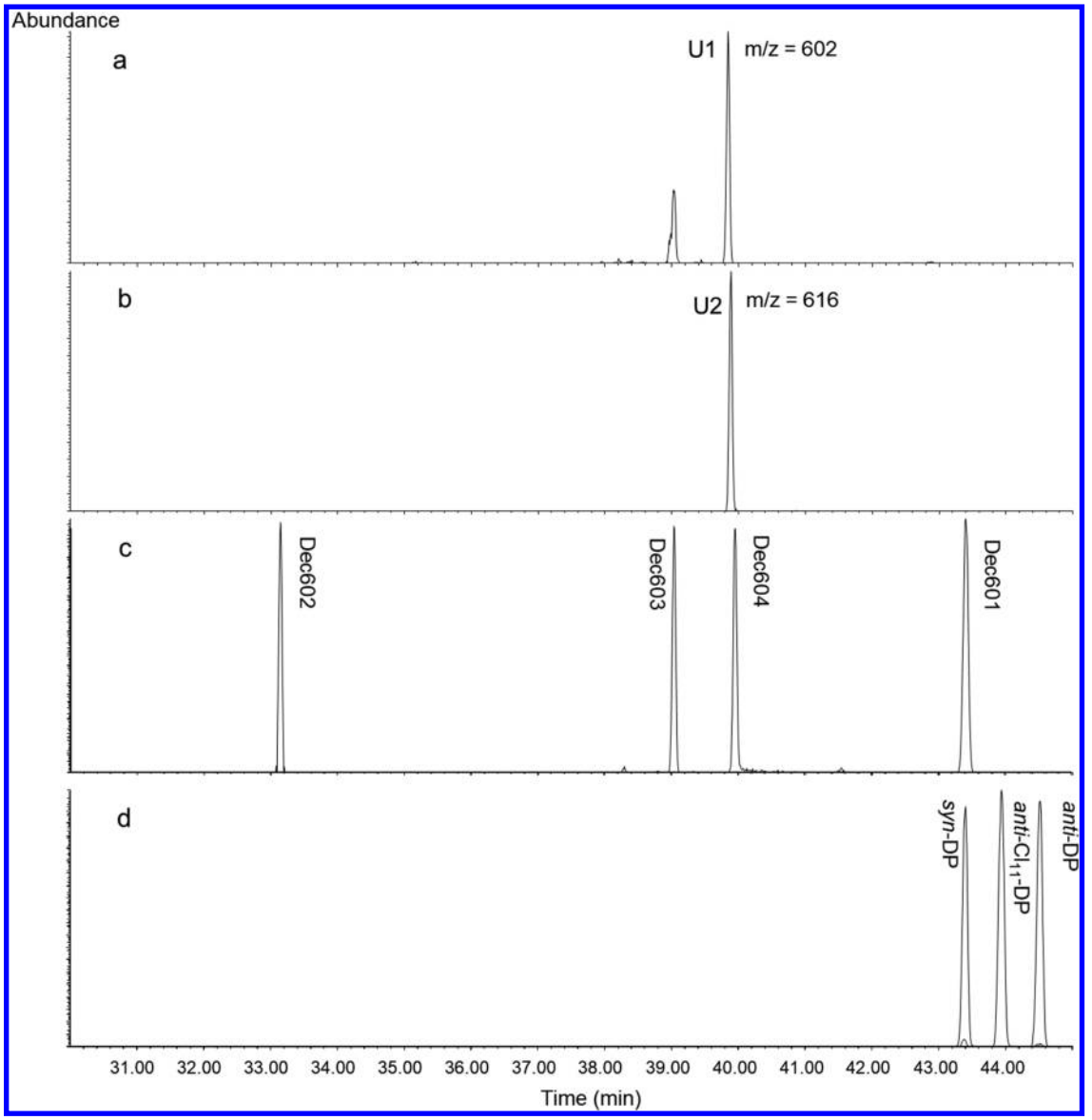

Figure 1. Gas chromatography-quadrupole mass spectrometry (electron-capture negative ionization mode) mass chromatograms of: (a and b) U1 and U2 in peregrine falcon egg composite extract; (b) a mixture of dechlorane analogue reference standards, including Dec601, Dec602, Dec603, and Dec604; and (d) a reference standard mixture of *syn*-DP, *anti*-DP, and *anti*-Cl_{11}-DP. It is noted that the first eluting peak on Figure 1a represents a fragment ion of Dec603 at m/z 602.

Instrumental Analysis. Characterization of U1 and U2 in composite extracts was first conducted on an Agilent 7890B GC (Agilent Technologies, Palo Alto, CA) coupled with an Agilent 5977A low resolution, single quadrupole mass analyzer in both ECNI and EI ionization modes. The GC was equipped with a 30 m HP-5MS column (0.25 mm i.d., 0.25 μm, J &W Scientific, Agilent Tech.). The GC injector was operated in a pulsed-splitless mode and held at 260 °C. Initial oven temperature was held at 80 °C for 3 min, ramped to 150 °C at 10 °C/min, and finally increased to 300 °C at 5 °C/min (held for 10 min). Full scan (scan range 30−950 m/z) mass spectra were generated for the unknown analytes under EI (ion source 230 °C) or ECNI (ion source 200 °C) modes. The heated transfer line temperature and quadrupole temperature were set as 280 and 150 °C, respectively.

To gain in-depth structural information on U1 and U2, we also analyzed the composites using a system of Agilent 7890B GC coupled with a Waters Xevo G2-XS quadrupole time-of-flight mass spectrometer equipped with atmospheric pressure ionization for GC (GC-APCI-HRqToFMS) (Waters Corp., Milford, MA). The mass resolution is around 20000 fwhm (full width at half-maximum) at m/z 600. The APCI source temperature was set at 125 °C, and the cone gas flow and corona current were 175 L/h and 3.0 μA, respectively. The GC injector was operated in splitless mode at 280 °C. GC separation was conducted with a 15 m DB-5HT column (0.25 mm i.d., 0.1 μm film thickness, J &W Scientific, Agilent Tech.) with oven temperature held initially at 120 °C for 1 min, ramped to 245 °C at 20 °C/min, increased to 280 °C at 10 °C/min, and finally increased to 320 °C at 40 °C/min (held for 3 min). Temperatures of the transfer line and source were set as 330 and 125 °C, respectively. Full scan (scan range 100−1000 m/z) and tandem MS spectra (collision energy ramped from 10 to 40 eV) were gained for the two unknown peaks. The ions passing through Q1 in the tandem MS experiment were m/z 601.8 and 615.8 for U1 and U2, respectively.

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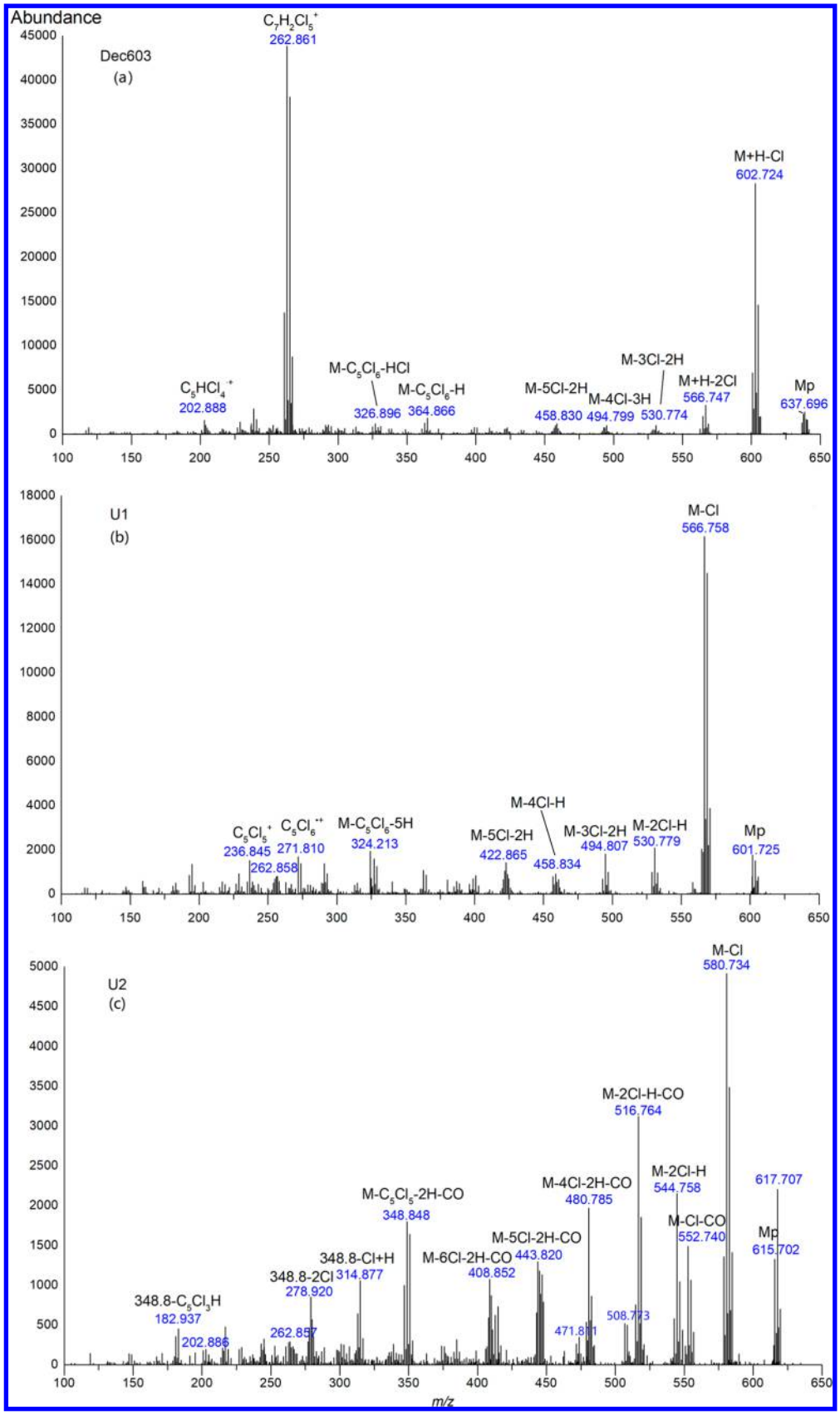

Figure 2. Atmospheric pressure GC source (positive) quadrupole time-of-flight tandem mass spectra of Dec603 in the reference standard (a) and U1 and U2 in the peregrine falcon egg composite extract (b and c).

Concentrations of U1 and U2, along with other major dechlorane analogues, were estimated or quantitatively determined in individual egg or liver samples based on GC-ECNIqMS, following the same GC program and MS

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parameters aforementioned. Concentrations of U1 and U2 were estimated using the response factor for Dec603, given that U1 and U2 were suggested to be structurally related to Dec603 (see Results and Discussion). Therefore, the characteristic ion of Dec603 (m/z 638) was employed to estimate U1 and U2 concentrations in peregrine egg and shark liver extracts. Other dechlorane analogues were quantitatively determined in the samples based on their respective reference standards and characteristic ions for quantification (summarized in Table S1).[20]

Quality Assurance/Control and Data Analysis. The analytical precision and accuracy values for U1 and U2 were assessed through spiking experiments using other dechlorane analogues (i.e., Dec601, Dec602, Dec603, Dec604, Dec604CB, *anti*-Cl_{11}-DP, *anti*-Cl_{10}-DP, Cplus, and *syn*- and *anti*-DP) as alternatives, given that the reference standards of U1 and U2 are not available. Commercial chicken eggs purchased from a local supermarket were spiked with 20 ng each of these dechlorane analogues and processed in five replicates with the same procedures as the treatment of peregrine eggs or shark livers. The mean (±standard deviation or SD) recoveries of the spiked dechlorane analogues ranged from 83.6 ± 9.2% to 95.0 ± 8.4%. No residues were detected in any procedural blanks for U1 and U2 as well as other known dechlorane analogues. Surrogate standard FBDE-160 was used to adjust for the loss of target analytes throughout sample treatments and its mean (±SD) recoveries were 82.3 ± 9.0% in peregrine eggs and 80.1 ± 10.7% in shark livers. Concentration data of dechlorane analogues, including U1 and U2, were reported after the correction with surrogate recovery. The limit of quantification (LOQ), estimated as an analyte response ten times the standard deviation of the noise during GC-ECNIqMS analysis, ranged from 0.4 to 0.8 ng/g lipid weight (lw) for major dechlorane analogues of interest (Table S1).[20] The LOQ for Dec603 (i.e., 0.6 ng/g lw) was used to represent that for U1 or U2, assuming they have similar ECNI response factors. Spearman's correlation analyses were employed to determine concentration correlations between dechlorane analogues (PASW Statistics 18.0, IBM Inc.).

RESULTS AND DISCUSSION

Extensive mass spectral analyses revealed the presence of the two unknown substances (U1 and U2) in both peregrine egg and shark liver composites. These two analytes coeluted with each other during GC-ECNIqMS analysis and had retention times very close to that of Dec604 and approximately 0.5 min after that of Dec603 (Figure 1). Thorough cleanup and separation procedures as described in the Materials and Methods section efficiently reduced the interferences and increased the sensitivities of U1 and U2 relative to noise during GC-MS analyses by removal of bulk lipids and other potential interference compounds. This facilitated the acquisition of high quality mass spectra. The GC-ECNIqMS analyses revealed that U1 and U2 exhibit fragmentation patterns similar to those of main dechlorane analogues such as Dec603, but their molecular ions are different from any of the known dechlorane analogues. We inferred they are structurally related to Dec603 according to the mass spectral evidence shown below.

Mass Spectral Characterization of U1. The compound U1 is suspected to be a monohydro analogue of Dec603 or its stereoisomers (referred to as Cl_{11}-Dec603). The mass spectrum gained from GC-ECNIqMS analysis reveals a dominance of the ion cluster centered at m/z 602 amu. This ion cluster appears to represent U1's molecular ion (M), as essentially no ions are observed above m/z 602 to the maximum m/z 950 (Figure S1). In contrast with the abundance of the molecular ion cluster under ECNI mode, the GC-EIqMS analysis reveals a low abundance of the molecular ion (Figure S2). The EIqMS analyses of reference standards of Dec602, Dec603, and Dec604 all reveal a low abundance of their molecular ions. This is because as Diels–Alder adducts, dechlorane analogues can be easily dissociated through the retro-Diels–Alder (RDA) reaction under EI ionization.[21] The GC-APCI-HRqToFMS analysis determined the exact mass of the molecular ion to be 601.725 amu, which corresponds to an elemental composition of $^{12}C_{17}{}^{1}H_{9}{}^{35}Cl_{11}$ and is 0.003 amu from the theoretical monoisotopic mass with an error of 4.98 ppm (Figure S3). The same level of mass accuracy was also determined for the exact masses of other major ions in the cluster (e.g., M+2 and M+4).

Compared with the elemental composition of Dec603 ($C_{17}H_8Cl_{12}$), U1 ($C_{17}H_9Cl_{11}$) was suggested to be a monohydro analogue of Dec603 or its stereoisomers, possessing a molecular structure similar to that of Dec603 except that a chlorine atom in Dec603 or its stereoisomer is replaced by a hydrogen atom. Indeed, high similarities in fragmentation patterns were observed between U1 and Dec603 under ECNI, EI, or APCI-HRqToFMS modes (Figures S1, S2, and 2, respectively). A sequential loss of chlorine atoms was observed in the ECNI mass spectra of U1 and Dec603, which consistently produced fragment ion clusters of M-Cl+H, M-2Cl, M-3Cl+H, M-4Cl, and M-5Cl. The relative abundances of these ion clusters in the EI spectrum are also similar between U1 and Dec603. Given that dechlorane-related chemicals are produced by Diels–Alder reactions with HCCPD, the RDA dissociation represents one of the most characteristic fragmentation patterns for major dechlorane analogues, which usually produces chlorinated cyclopentadiene ions.[17] For example, the ECNI analyses of U1 and Dec603 produce a common fragment ion at m/z 236.8, which corresponds to the RDA product ion $C_5Cl_5^-$. The ion cluster of $C_5Cl_5^+$ is also observed in the EI mass spectrum of U1 and Dec603. Similarly, during GC-APCI-HRqToFMS analyses, the RDP product ions $C_5Cl_6^{\bullet+}$ (m/z 271.810) and $C_5Cl_5^+$ (m/z 236.845) are both observed in U1's and Dec603's mass spectra (Figure 2). Other ions that characterize the GC-APCI-HRqToFMS fragmentation of Dec603, such as M-Cl, M-3Cl-2H, M-5Cl-2H, M-C_5Cl_6-nH, are also observed in U1's mass spectrum (Figure 2). This mass spectral evidence, along with the elemental composition, collectively suggests that U1 is a monohydro analogue of Dec603.

However, it is noted that a major discrepancy in the mass spectral characteristics between U1 and Dec603 is the relative abundance of the ion cluster $C_7H_2Cl_5^+$ in their GC-APCI-HRqToFMS spectra (centered at m/z 262.858 and m/z 262.861, respectively) (Figure 2). This ion cluster may be formed via RDA decomposition into hexachloronorbornadiene ($C_7H_2Cl_6$), followed by loss of a chlorine atom. The relative abundance of RDA fragments depends on the pertinent critical energy compared with critical energies of competing fragmentations.[21] The difference in the relative abundance of $C_7H_2Cl_5^+$ between U1 and Dec603 is likely due to their differences in the critical energy distributions during GC-APCI-HRqToFMS fragmentation.

Given that the chlorine substitution pattern is not clear for U1, one of its possible structures is described in Figure 3 and

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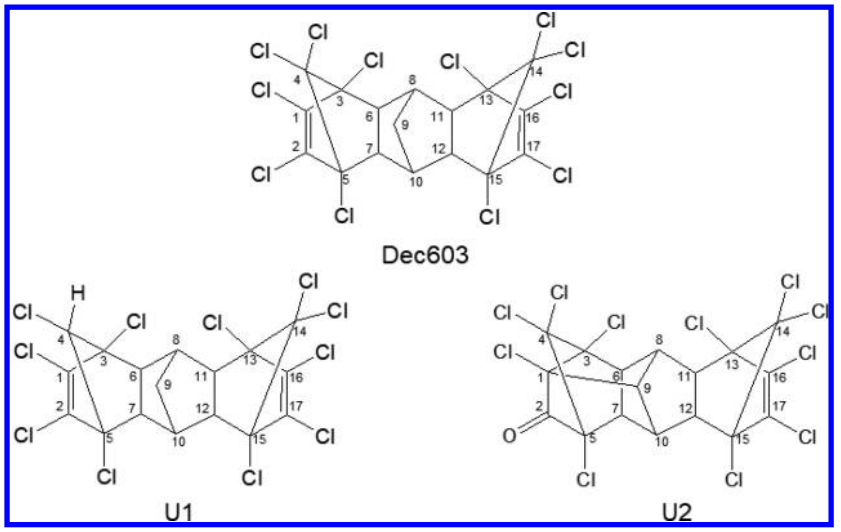

Figure 3. Chemical structure of Dec603 and possible structures for U1 and U2. Given that the exact substitution patterns remain unknown for U1 and U2, the structures presented here are used as an example to discuss their structural characteristics.

used as an example to interpret U1's possible GC-APCI-HRqToFMS fragmentation pathways (Figure S4). Compared with Dec603, which contains two bridging carbons (referred to as carbon 4 and 14, Figure 3) each being substituted with two chlorine atoms and a third bridging carbon (carbon 9) without chlorine substitution, this possible U1 congener has a chlorine atom on one bridging carbon (e.g., carbon 4) replaced by a hydrogen atom. Hydrodechlorination on bridging carbons also occurs in aldrin[22,23] and DP.[24] The U1's predominant fragment ion cluster (i.e., M-Cl, centered at m/z 566.758) during GC-APCI-HRqToFMS analysis is very likely formed via loss of a chlorine atom at the bridging carbon 14 (or at another carbon from the same side, i.e. carbon 13, 15, 16, or 17) instead of any other carbon numbered 1−5. Otherwise, possible RDA dissociation of the fragment ion cluster M-Cl could result in the formation of $C_5Cl_4H^+$ (theoretical m/z 202.888) and $C_5Cl_4H_2^{\bullet+}$ (theoretical m/z 203.880). However, these two ions are not observed in U1's GC-APCI-HRqToFMS mass spectrum. Instead, possible RDA dissociations of the molecular ion M and M-Cl likely produce ions that include $C_5Cl_6^{\bullet+}$ (m/z 271.810) and $C_5Cl_5^+$ (m/z 236.845), which are all observed in U1's mass spectrum. This further supports the plausibility of the proposed structure for U1 as described in Figure 3.

The possibility of the existence of multiple possible stereoisomers for U1 merits attention. This is largely due to the complexity of the steric structures of Dec603 and its possible stereoisomers. The Dec603 standard produced by Wellington Laboratories (also used in our study) represents the most favorable product for the Diel-Alder reactions, which exhibits as an "*exo*" structure, i.e., both dichlorovinylic groups on the same side as the bridging carbon in the central norbornane (the structure of Wellington Dec603 is provided in Figure S5). Additional stereoisomers may also likely be produced during the reactions, including the "*endo*" isomers, i.e., two dichlorovinylic groups on the different sides relative to the bridging carbon in the central norbornane. We would like to point out that U1 has a longer retention time than that of Dec603 during GC-EIqMS analyses, even though the former contains one less chlorine atom. The GC elution order for polychlorinated chemicals follows a typical pattern that the higher the degree of chlorination the slower they elute.[25] However, steric structures may substantially affect the pattern. Brazeau et al. indicates that the *endo* protonated species of DP or its dechlorinated products usually elute slower than their *exo* counterparts.[24] For example, *anti-endo*-Cl_{11}-DP is eluted later than *anti-exo*-Cl_{11}-DP. We acknowledge that additional analytical work (e.g., use of nuclear magnetic resonance spectroscopy or X-ray diffraction) to better elucidate U1's steric structure and substitution patterns is needed. However, the limitation in available sample masses prevented us from these additional analyses in the present study.

Possible Sources of U1. As a monohydro derivative of Dec603, U1 could be formed as a degradation product of Dec603 or present as an impurity in commercial Dec603 products. The hydrodechlorination is often observed in chemical or biological degradation of polychlorinated compounds, including norbornene derivatives such as aldrin, dieldrin, mirex, and DP.[22,23,26,27] Aldrin and dieldrin have similar structures and could be described as monoadducts of Dec603, where HCCPD has only been added to one side of norbornadiene. Both of these chemicals have been shown to dehalogenate in the presence of superoxide ion ($O_2^{-\bullet}$), which is known to be involved in biological oxidations.[22] As a dimer of HCCPD, mirex has been well demonstrated to undergo environmental degradation which yields monohydro and dihydromirex isomers via successive exchanges of its chlorine atoms with hydrogen.[28,29] Similarly, photoirradiation can degrade DP isomers into a series of dechlorination products, including the [-1Cl+1H], [-2Cl+2H], [-3Cl+3H], and [-4Cl +4H] species.[30] DP isomers could also be dechlorinated into Cl_{11}-DP by sewage sludge microorganisms during anaerobic digestion[27] or through hepatic dechlorination as reported in northern snakehead (*Channa argus*).[31] These studies suggest the likelihood of the transformation of Dec603 stereoisomers into their monohydro derivatives via either environmental degradation or metabolic transformation or a combination of the two pathways.

U1 could also be present as an impurity in technical Dec603 products. Dec603 is synthesized by the Diels−Alder reaction of HCCPD with bicyclo[2.2.1]-2,5-heptadiene.[32] HCCPD contains many lower chlorinated impurities, such as octachlorocyclopentene, hexachloro-1,3-butadiene, tetrachloroethane, and pentachlorobenzene.[33] Pentachloro-impurities in the

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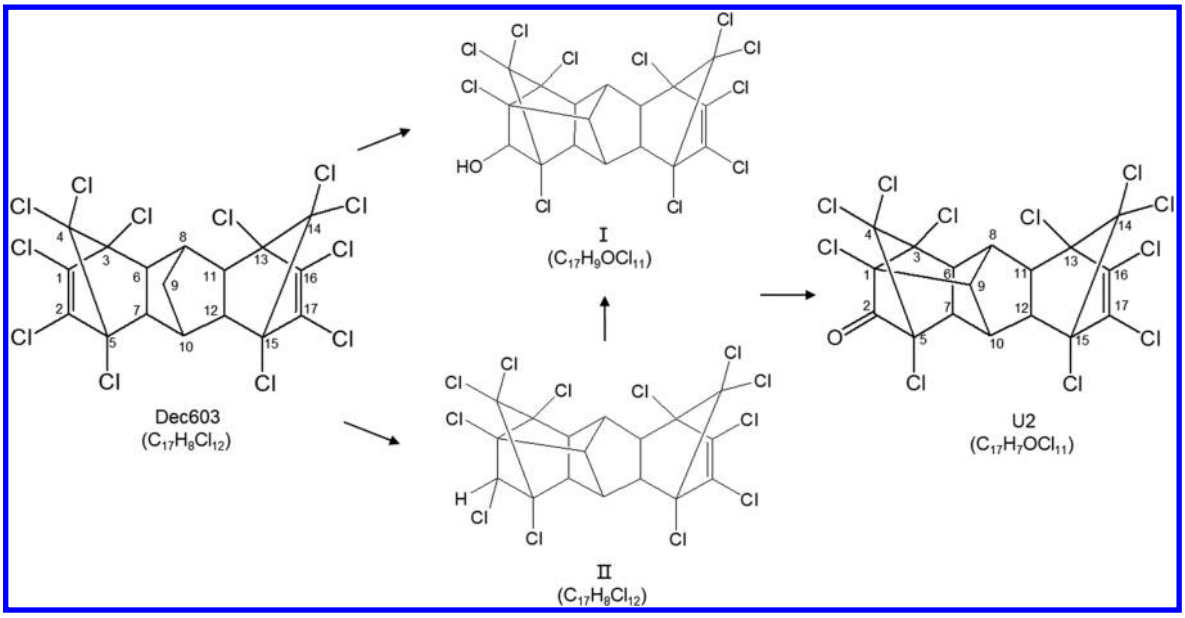

Figure 4. Possible transformation pathways from Dec603 to U2.

HCCPD reagent could result in the formation of chemicals containing 11 chlorine atoms during the Diels–Alder production of Dec603. Previous studies indicated the presence of VCH-DP as an impurity in technical DP products,[34] likely arising from the Diels–Alder reactions with 4-vinylcyclohexene (VCH) which may exist as an impurity in 1,5-cyclooctadiene, a starting material for DP production.[11] This evidence indirectly suggests the possibility of U1 as an impurity formed during the in the Diels–Alder production of Dec603.

Mass Spectral Characterization of U2. We suggest U2 might be a carbonylic derivative of Dec603, based on the mass spectral characterization and literature information from other structurally related chemicals. The ECNIqMS analysis indicates that the dominant ion cluster centered at m/z 616 amu represents the molecular ion of U2, as essentially no ions are observed above m/z 616 to the maximum m/z 950 amu. The APCI-HRqToFMS analysis reveals that the elemental composition of U2 is $C_{17}H_7OCl_{11}$ since the exact mass of $^{12}C_{17}{}^{1}H_7{}^{16}O_1{}^{35}Cl_{11}$ is 615.701 and is 0.002 amu from the theoretical monoisotopic mass with an error of 3.25 ppm (Figure S6). One of the possible structures of U2 is described in Figure 3 and used as an example to interpret U1's fragmentation pathways (Figure S7). Partial similarity in fragmentation patterns was observed between U2 and Dec603 under the ECNIqMS, EIqMS, and APCI-HRqToFMS modes. The formation of M-2Cl and M-Cl+H as well as the sequential loss of chlorine atoms from these two major fragment ions is observed in the ECNI analyses of both U2 and Dec603 (Figure S1). Possible RDA fragments such as $C_5Cl_5^-$ and $C_5Cl_6^{\bullet -}$ under ECNI mode; $C_5Cl_5^+$, $C_5Cl_6^{\bullet +}$, and $C_7H_2Cl_5^+$ under EI mode; or $C_7H_2Cl_5^+$ (m/z 262.857) and $C_5Cl_4H^+$ (m/z 202.886) under GC-APCI-HRqToFMS mode are commonly observed in U2's mass spectra, suggesting it resembles other major dechloranes in the formation pathway (i.e., Diels–Alder reactions). However, compared with the GC-APCI-HRqToFMS mass spectrum of Dec603, a unique fragmentation pattern for U2 is the transition from the ion cluster at m/z 580.734, corresponding to an element composition of $C_{17}H_7OCl_{10}$, to the ion cluster at m/z 552.740, corresponding to an element composition of $C_{16}H_7Cl_{10}$, with a mass difference of 27.994 amu. This fragmentation may represent the loss of a carbonyl group, suggesting the existence of a C=O group in U2's structure. The loss of a carbonyl group during GC-APCI-HRqToFMS analysis is also observed from m/z 544.758 (M-H-2Cl) to m/z 516.764, from m/z 508.773 (M-2H-4Cl) to m/z 480.785, or from m/z 471.811 (M-2H-5Cl) to m/z 443.820 (Figure 2). Therefore, based on this mass spectral evidence, we suggest that U2 represents a carbonylic derivative of Dec603.

Possible Sources of U2. The presence of a carbonyl group in the chemical structure of U2 has not been reported for any derivative of Dec601, Dec602, Dec603, Dec604, or DP. However, the transformation into a carbonylic derivative has been reported for other related chemicals. For example, environmental and metabolic transformation of dieldrin has been reported to form a variety of possible products, including photodieldren and its carbonylic metabolite keto-photodieldrin.[35] Bridged keto-photodieldrin is mainly found in the urine and kidneys of male rats after being dosed with high levels of dieldrin.[36,37] It was also found as a major metabolite in bluegill fish (*Lepomis macrochirus*) following dieldrin exposure.[38] Given the partial similarity between Dec603 and dieldrin in their molecular structures, we hypothesize that Dec603 follows metabolic pathways similar to those reported for dieldrin for the formation of U2. The potential metabolic pathways are interpreted below by using a possible U2 structure (see Figure 3) as an example.

During metabolic transformation, possible sites of attack in the molecule of Dec603 are the vinyl carbon atoms substituted with two chlorine atoms (e.g., carbon 1 and 2, Figure 4). We suggest that the Dec603 molecule is subjected to dechlorination and then hydroxylation at one of the vinyl carbons, followed by a structural rearrangement to form a hydroxylated and "caged" structure (e.g., between carbon 1 and 9, compound **I** in Figure 4). Further oxidation of this hydroxylated intermediate (compound **I**) will likely form U2. Matthews and Matsumura have speculated a metabolite of hydroxylated and "caged" structure as an intermediate during dieldrin metabolism, and the intermediate was further oxidized to keto-photodieldrin.[39] Another possible pathway to produce

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U2 is through a bridged isomer of Dec603 (i.e., compound **II** in Figure 4), which may be produced via photodegradation of Dec603. Photodieldrin has been reported as a main photo-induced isomerization product of dieldrin (see their structures in Figure S8), suggesting the likelihood of photo isomerization of Dec603 in the environment. Rat exposure studies demonstrate keto-photodieldrin as one of the principal metabolites of photodieldrin in urine.[40−42] On the basis of these studies, we suggest that other than the direct metabolism of Dec603, compound **I** may also be produced from metabolic transformation of Dec603's photoisomer (compound **II**), followed by oxidation to form U2. Therefore, we hypothesize that U2 is a metabolic transformation product of Dec603 or its photo intermediate.

The fact that studies on the environmental and metabolic transformation of major dechlorane analogues remain very limited merits emphasis. The above hypothesis is merely based on the structural characterization of U2 and the similarity between Dec603 and dieldrin in their molecular structures. No direct evidence is available to support our hypothesis, which requires future *in vitro* and *in vivo* studies to verify. The knowledge gap in the environmental and biological transformation of major dechlorane analogues may not only prevent us from a better understanding of the fate of these persistent and bioaccumulative substances but also result in an underestimation of the exposure of fish/wildlife to dechloranes and their derivatives.

Estimation of U1 and U2 Concentrations. Concentrations of U1 and U2 were estimated in 15 peregrine falcon eggs from the Chesapeake Bay and 25 shortfin mako shark livers from the western North Atlantic Ocean (Table 1 and Table S2 in Supporting Information). U1 and U2 were detected in all 15 peregrine eggs with estimated concentrations ranging from 18 to 143 ng/g lw (median: 49 ng/g lw) and 25 to 302 ng/g lw (median: 59 ng/g lw), respectively. Concentrations of U1 and U2 in peregrine eggs were comparable to those of Dec602 (median: 73.6 ng/g lw) and Dec603 (median 36.6 ng/g lw) but much higher than the concentrations of other dechlorane analogues detected in the same samples (Tables 1 and S2). U1 and U2 were also detected in 24 and 22 out of the 26 shark livers, with concentrations ranging from <LOQ to 560 ng/g lw (median: 4.6 ng/g lw) and <LOQ to 420 ng/g lw (median: 3.0 ng/g lw), respectively. These concentrations were comparable to those of Dec602 (median: 6.5 ng/g lw) but were 1 order of magnitude greater than those of any other dechlorane analogues in shark livers, including Dec603 (median: 0.8 ng/g lw).

Table 1. Detection Frequencies (DF) and Concentrations (ng/g lipid weight) of U1, U2, and Other Dechlorane Analogues in Peregrine Falcon Eggs (n = 15) and Shortfin Mako Shark Livers (n = 25)

	peregrine falcon eggs (n = 15)			shortfin mako shark livers (n = 25)		
	DF	median	range	DF	median	range
lipid %		6.3	5.5−7.2		61	30−96
U1	100	49	18−143	96	4.6	<LOQ[a]-550
U2	100	59	25−302	88	3.0	<LOQ-420
Dec603	100	36.6	21.9−145	84	0.8	<LOQ-187
Dec602	100	73.6	23.3−247	100	6.5	<LOQ-82.6
Dec604	100	0.5	0.2−2.3	0	nd[b]	nd
anti-DP	100	7.7	3.4−170	72	0.4	<LOQ-14.4
syn-DP	100	3.7	1.2−52.6	64	0.2	<LOQ-9.5
anti-Cl_{11}-DP	87	0.3	<LOQ-1	12	<LOQ	<LOQ-4.4
anti-Cl_{10}-DP	80	0.3	<LOQ-4.3	0	nd	nd

[a]LOQ = limit of quantification. [b]nd = not detectable.

Statistical analysis revealed significant correlations between the concentrations of U1 and U2 (r_s = 0.96, p < 0.001) in peregrine eggs (Table S3). Concentrations of U1 or U2 were also significantly correlated with those of Dec602, Dec603, and Dec604 (p < 0.001 in all cases, Table S3). However, no significant correlation was found between U1 (or U2) and any of the DP isomers or derivatives, including *anti*-Cl_{11}-DP, *anti*-Cl_{10}-D, *syn*-DP, and *anti*-DP. In shortfin mako shark livers, U1 and U2 were also statistically correlated between each other (r_s = 0.89, p < 0.001) and with several other dechlorane analogues, such as Dec603, *syn*-DP, and *anti*-DP (Table S3). These results clearly suggest that U1 and U2 are closely related to major dechlorane analogues (particularly Dec603), suggesting they may share common sources. However, the interanalogue relationship also varies between peregrine falcon eggs and mako shark livers, likely due to influences by species-specific exposure sources, food web transfer, and metabolism.

Frequent detection of U1 and U2 in peregrine eggs and shark livers demonstrate that these two novel Dec603 derivatives are present in both terrestrial and aquatic ecosystems. Bioaccumulation of the derivatives of dechlorane-related chemicals has been reported in few studies. Shen et al. determined that both Dec602 and its monohydro derivative are present in approximately equal concentrations in Arctic beluga whale (*Delphinapterus leucas*) blubber, Great lakes whitefish (*Coregonus clupeaformis*), and lake trout (*Salvelinus namaycush*).[17] Suspected mono and di-dechlorinated products of Dec603 were also reported in the nontarget screening of one peregrine falcon egg from Southern Germany.[43] Cl_{11}-DP was also frequently detected in peregrine falcon eggs from Canada and Spain.[16] These studies suggest that possible monohydro and dihydro derivatives of dechlorane analogues possess considerable bioaccumulation potential, sometimes even comparable with their parent chemicals. This increases the overall risk of fish and wildlife exposure to dechlorane analogues collectively as a major group of chlorinated flame retardants.

Since the first report of *syn*- and *anti*-DP isomers in 2006,[2] an increasing number of dechlorane-related chemicals have been discovered in environmental samples. The Diels−Alder reactions for the production of dechlorane analogues could form a very complex mixture of products with different structures and chlorination patterns, which are either produced on purpose or as impurities in commercial products. The possible stereoisomers for these major dechloranes and their derivatives as well as potential degradation or metabolism further increase complexity in the group of dechlorane-related chemicals. In addition to the known dechlorane analogues (including U1 and U2) found in this study, it is very likely that other related chemicals are also present in the environment and organisms. However, the exploration of additional novel analogues and derivatives will require substantial analytical efforts and more authentic analytical standards.[44] As Hites and

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Jobst pointed out,[44] the most important aspect in the identification of new chemicals is their environmental significance and reproducibility. Therefore, for a better elucidation of the environmental relevance of dechlorane-related chemicals, more efforts are needed to investigate their sources, environmental behavior, and potential toxicity to wildlife and humans.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.est.8b06214.

Characteristic ions for GC-MS(ECNI) analysis; concentrations of U1, U2, and other dechlorane analogues; Spearman's correlation coefficients; electron-capture negative ionization (scan range m/z 30-950 amu) single quadrupole mass spectra; isotopic distribution of the molecular ion clusters of U1 and U2; representative molecular structures of the major fragments of U1 and U2 and possible fragmentation pathways; chemical structure of the Wellington Dec603 reference standard; chemical structures of dieldrin, its photo isomer photodieldrin, and their metabolite ketophotodieldrin (PDF)

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