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Flame Retardants and Methoxylated and Hydroxylated Polybrominated Diphenyl Ethers in Two Norwegian Arctic Top Predators: Glaucous Gulls and Polar Bears

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The brominated flame retardants have been subject of a particular environmental focus in the Arctic. The present study investigated the congener patterns and levels of total hexabromocyclododecane (HBCD), polybrominated biphenyls, polybrominated diphenyl ethers (PBDEs), as well as methoxylated (MeO) and hydroxylated (OH) PBDEs in plasma samples of glaucous gulls (*Larus hyperboreus*) and polar bears (*Ursus maritimus*) from the Norwegian Arctic. The analyses revealed the presence of total HBCD (0.07–1.24 ng/g wet wt) and brominated biphenyl 101 (<0.13–0.72 ng/g wet wt) in glaucous gull samples whereas these compounds were generally found at nondetectable or transient concentrations in polar bears. Sum (Σ) concentrations of the 12 PBDEs monitored in glaucous gulls (range: 8.23–67.5 ng/g wet wt) surpassed largely those of polar bears (range: 2.65–9.72 ng/g wet wt). Two higher brominated PBDEs, BDE183 and BDE209, were detected, and thus bioaccumulated to a limited degree, in glaucous gulls with concentrations ranging from <0.03 to 0.43 ng/g wet wt and from <0.05 to 0.33 ng/g wet wt, respectively. In polar bear plasma, BDE183 was <0.04 ng/g wet wt for all animals, and BDE209 was only detected in 7% of the samples at concentrations up to 0.10 ng/g wet wt. Of the 15 MeO-PBDEs analyzed in plasma samples, 3-MeO-BDE47 was consistently dominant in glaucous gulls (ΣMeO-PBDE: 0.30–4.30 ng/g wet wt) and polar bears (ΣMeO-PBDE up to 0.17 ng/g wet wt), followed by 4′-MeO-BDE49 and 6-MeO-BDE47. The 3-OH-BDE47, 4′-OH-BDE49, and 6-OH-BDE47 congeners were also detected in glaucous gulls (ΣOH–PBDE up to 1.05 ng/g wet wt), although in polar bears 4′-OH-BDE49 was the only congener quantifiable in 13% of the samples. The presence of MeO- and OH-PBDEs in plasma of both species suggests possible dietary uptake from naturally occurring sources (e.g., marine sponges and green algae), but also metabolically derived biotransformation of PBDEs such as BDE47 could be a contributing factor. Our findings suggest that there are dissimilar biochemical mechanisms involved in PCB and PBDE metabolism and accumulation/elimination and/or OH-PBDE accumulation and retention in glaucous gulls and polar bears.

Introduction

The arctic marine ecosystem is continuously exposed to atmospheric influx of organic chemicals from remote sites of production and use. In recent years, there has been a specific environmental focus on anthropogenic organobrominated chemicals, namely, brominated flame retardants (BFRs). The BFRs that have been shown to be environmentally persistent and bioaccumulative include polybrominated diphenyl ethers (PBDEs) and hexabromocyclododecane (HBCD) isomers and to a lesser extent polybrominated biphenyls (PBBs) (*1*). These BFRs are being identified in tissues of an increasing number of seabirds and marine mammals from various locations including those from the remote Arctic (*2–5*). Retrospective analyses of archived samples have reported concentrations of PBDEs to have increased rapidly over the last 20 years in Canadian arctic marine mammals such as beluga whales (*Delphinapterus leucas*) (*6*) and ringed seals (*Phoca* hispida) (*7*).

Structural analogues to PBDEs, the methoxylated (MeO) and hydroxylated (OH) PBDEs, have also been reported in a few studies, and have been detected in blood, adipose tissues, and liver of fish, birds, and mammals, including species occupying high trophic positions, from the Baltic (*8–10*), Atlantic (*10, 11*), and Arctic environments (*5, 12*). Current understanding indicates that MeO-PBDEs found in wildlife are mostly a consequence of accumulation via natural sources in marine environments (e.g., via formation in sponges and green algae) (*9, 11*), whereas OH-PBDEs in marine organisms can be of natural origin and/or of metabolic derivation from the enzyme-mediated degradation of precursor PBDEs of environmental importance (*13*). For example, cytochrome P450 (CYP) enzyme-mediated biotransformation of PBDEs has been shown to lead to OH-PBDE formation in BDE47 dosing studies of rodents (*13, 14*). It is also possible, although not documented hitherto in any species, that MeO-PBDE residues could be sourced in part via enzyme-mediated methylation of OH-PBDEs or direct methoxylation of PBDEs (*13*). In the case of OH-PBDEs, and similar to analogous OH-PCBs (*15*), comparative variations in congener profiles and concentrations in the blood among species have been attributed to several factors such as formation via specific CYP isoenzymes and their level of catalytic activities, retention as a consequence of binding affinity for circulating proteins, and induction and protection from Phase II metabolic processes (*13*).

Several comprehensive reviews have assessed the toxicological effects of BFRs, principally PBDEs, in exposed organisms with special emphasis on their endocrine disrupting properties in humans and wildlife (*16, 17*). The state of knowledge on the potential health risks associated to PBDE

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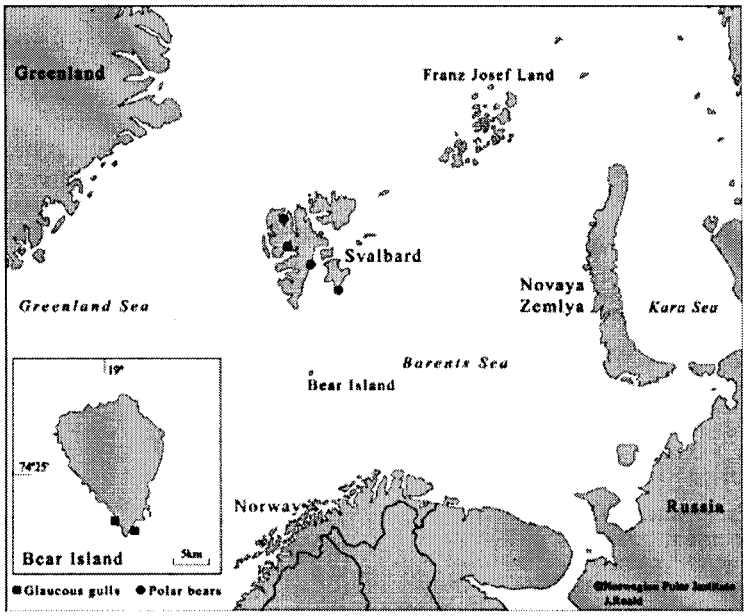

FIGURE 1. Map of the Norwegian Arctic showing sampling locations of glaucous gulls and polar bears.

exposure suggests these compounds have the propensity to disrupt thyroid hormones, cause neurological and developmental effects, and possibly cause cancer in laboratory animals. The observed endocrine and other exposure effects can also be due to OH-PBDEs. In fact, competitive bioassays in vitro have shown that thyroid-hormone-like OH-PBDEs bind to transthyretin (TTR), a principal thyroid hormone transport protein in mammals, with high affinity relative to thyroxine (T4) (*17*). The OH-PBDEs have also been shown to be agonists in vitro of estrogen receptor-mediated gene expression in human embryonic kidney cells (*18*). There is at present exceedingly little information about the biological effects and thus the toxicological potential of environmentally relevant MeO-PBDEs in laboratory animals and wildlife. Nevertheless, biological activity has been investigated for 2′-MeO-BDE68, where anti-bacterial and anti-inflammatory activity was observed in bacteria (*19*).

Glaucous gulls (*Larus hyperboreus*) feed opportunistically and utilize a wide range of food items such as eggs, chicks, fish, carrions, crustaceans, and adult birds, whereas polar bears (*Ursus maritimus*) feed almost exclusively upon ringed seals. Glaucous gulls breeding on Bear Island, in the Svalbard Archipelago (Arctic Norway), overwinter in the northeastern part of the Atlantic Ocean (*20*), whereas polar bears from Svalbard belong to a discrete population characterized by diverse home range sizes across the northern Barents Sea (*21*). Glaucous gulls and polar bears are thus apical predator species of the arctic marine food web. The Svalbard populations of these species have been documented to accumulate some of the highest levels of organochlorine (OC) contaminants relative to other circumpolar populations and species occupying lower trophic levels (*2*) and are thus vulnerable to the accumulation of other organohalogens such as BFR additives and other brominated compounds. The present study investigated the congener patterns and levels of total HBCD, PBBs, PBDEs, as well as MeO- and OH-PBDEs in plasma samples of glaucous gulls and polar bears from Svalbard in the Norwegian Arctic. Furthermore, the biotransformation ability of glaucous gulls and polar bears toward PBDEs was assessed based on PCB and OH-PCB data and MeO- and OH-PBDE formation/retention in plasma.

Experimental Section

Sample Collection. Blood samples were collected from adult male ($n = 12$) and female ($n = 15$) glaucous gulls and adult female polar bears ($n = 15$) during May–June 2004 and April 2002, respectively, from Svalbard in the Norwegian Arctic (Figure 1). A detailed description of the capture methods, morphometric measurements, sampling procedures, sample processing, and age determination of glaucous gulls and polar bears is provided by Verreault et al. (*22, 23*). Earlier studies have shown that the effect of age on the variation of OC concentrations in blood/plasma was negligible in adult male and female glaucous gulls (*24*) and adult female polar bears (*25*). Therefore, only adult individuals were included in the present study. A general qualitative assessment of the individuals at the time of sampling revealed they were all in good body condition. Both species were in heightened feeding modes in their annual cycles at the time of sampling and thus were continuously exposed to contaminants through diet. All capture and handling methods of glaucous gulls and polar bears were approved by the Norwegian Animal Research Authority (P.O. Box 8147 Dep., Oslo, NO-0033, Norway) and the Governor of Svalbard (Box 633, Longyearbyen, NO-9171, Norway).

Extraction and Cleanup. The extractable lipid content in plasma was determined by a sulfo-phospho-vanillin reaction using pure olive oil as a calibrant. Details on extraction and cleanup procedures of glaucous gull and polar bear plasma samples are given by Verreault et al. (*23*) and Sandala et al. (*26*), respectively. All contaminant analyses were carried out in the laboratories of R. J. Letcher at the Great Lakes Institute for Environmental Research, University of Windsor. Briefly, a 1.0-g plasma aliquot was spiked with internal standards, which included BDE71, 2′-OH-BDE28, CB83, CB122, and a ^{13}C-OH-PCB mixture (12 congeners), followed by acidification with 1 mL of HCl (6 M) and addition of 3 mL of 2-propanol. The denatured plasma was extracted with 6 mL of methyl-*tert*-butyl-ether (MtBE)/*n*-hexane (50:50 volume: volume (v:v)). Plasma extracts were then partitioned with a 6-mL potassium hydroxide solution (1 M in 50% ethanol), and two fractions were obtained: An aqueous fraction containing the deprotonated halogenated phenolic com-

pounds (HPCs) (e.g., OH-PCBs and OH-PBDEs) and an organic fraction containing the neutral compounds (e.g., PCBs, HBCD, PBBs, PBDEs, and MeO-PBDEs).

The aqueous fraction was acidified with H_2SO_4, and the deprotonated HPCs were back extracted with 6 mL of MtBE/*n*-hexane (50:50 v:v) then dried over Na_2SO_4 and derivatized to their MeO analogues through a methylation reaction using diazomethane. The derivatized HPCs were cleaned up on a silica gel column (5.0 g, 22% H_2SO_4 deactivated) (Grade 62, 60−200 mesh, 150 Å) (Aldrich Chemicals, Milwaukee, WI) with 50 mL of DCM/*n*-hexane (15:85 v:v). The collected fraction was finally evaporated to dryness under a gentle flow of high-purity nitrogen and reconstituted with 100 μL of isooctane for instrument determination. The organic phase was concentrated and transferred to a Florisil column (8.0 g, 1.2% H_2O deactivated) (magnesium silicate, F100−500, 60−100 mesh) (Fisher Scientific, Ottawa, ON, Canada), and the neutral target analytes were separated and cleaned up with three elutions using different solvent ratios (*23*). The fractions were concentrated and solvent exchanged to isooctane in preparation for instrument determination.

Quantification. For quantification of brominated and chlorinated neutral and derivatized HPC contaminants, appropriate fractions isolated from the sample extracts were injected automatically on a gas chromatography mass spectrometry (GC-MS) instrument (Agilent 6890; Agilent Technologies, Palo Alto, CA) operated in the negative chemical ionization (NCI) mode using methane as a buffer gas to facilitate electron capture negative ionization (GC-MS(ECNI)). The GC-MS(ECNI) analysis for brominated compounds was carried out in the selected ion-monitoring (SIM) mode using ^{79}Br and ^{81}Br anions. Detection of BFRs with GC-MS(ECNI) is a widely used approach due to its good sensitivity and selectivity for these compound classes (*27*). Compound separation was achieved using a fused silica DB-5 capillary column (30 m, 0.25 mm inside diameter (i.d.), 0.25 μm film thickness) (J & W Scientific, Folsom, CA). The exception was for BDE209 that was separated on a 15-m capillary column using the same GC conditions as for the standard GC-MS(ECNI) program to achieve minimal and consistent analytical degradation (*27*).

The brominated and chlorinated compounds were identified on the basis of their retention times on the DB-5 columns, relative to authentic standards, i.e., α-HBCD, PBBs (BB101 and BB153), PCBs (47 congeners including coelutions), OH-PCBs (12 congeners) (all from Accu-Standard, New Haven, CT), PBDEs (12 congeners), MeO-PBDEs (15 congeners), and OH-PBDEs (15 congeners). The PBDE, MeO-PBDE, and OH-PBDE congener standards were synthesized and provided by Dr. Göran Marsh (Stockholm University, Sweden) according to published procedures (*28*). As any β- and γ-HBCD residues in the samples were most likely thermally isomerized to α-HBCD and/or degraded in the GC injection port, the α-HBCD concentrations represented total HBCD. However, it is well known that the mutual ratio of the HBCD isomers changes when subjected to GC temperatures above ca. 160 °C (*27*). When at thermal equilibrium the technical HBCD mixture has been shown to be around 78% α-HBCD, 13% β-HBCD, and 9% γ-HBCD. Structural identification of mainly MeO-tetraBDEs that were detected in the neutral fractions was confirmed by reanalysis of glaucous gull and polar bear samples by monitoring the nominal mass of isotopic $[M]^-$ (*m/z* 512) and $[M + 2]^-$ (*m/z* 514) of the molecular ion cluster and $[M]^-$ (*m/z* 434) and $[M + 2]^-$ (*m/z* 436) of the $[M - Br]^-$ fragment anion. Quantification of the PBDE and OH-PBDE congeners was performed using an internal standard method based on the relative ECNI response factor (RRF) of the $^{79}Br + ^{81}Br$ anions of BDE71 and 2′-OH-BDE28 and to that of authentic congener standards in the neutral and derivatized HPC fractions, respectively. A semiquantitative approach based on an external standard method was used for total HBCD and MeO-PBDE quantification using BDE71 as a recovery surrogate. The GC-MS-(ECNI)-based determination of PCB and OH-PCB congeners in glaucous gull and polar bear plasma has been described in details elsewhere (*23, 26*).

Quality Control. Mean recoveries based on the internal standards added were on average 78 ± 5% for BDE71, 79 ± 4% for CB83 and CB122, and 91 ± 4% for 2′-OH-BDE28 and ^{13}C-OH-PCB mixture. All analyte concentrations were recovery corrected to reduce heterogeneity within and between analyte classes. Method blank samples ($n = 6$) were analyzed to monitor interferences and contamination, showing an absence of background interference for all compounds. Analytical precision was assessed by analyzing replicate extractions of glaucous gull and polar bear plasma samples and duplicate injections of authentic brominated and chlorinated standard compounds and appropriate fractions isolated from the sample extracts. The replicate extractions and duplicate injections demonstrated on average 15 and 5%, respectively, analytical variation of the compound concentrations. The method limits of quantification (MLOQs) for individual compounds were estimated based on a signal to noise ratio of 10.

Data Analyses. Because extractable lipid percentages in plasma did not correlate with concentrations of most PCBs, BFRs, MeO-PBDEs, and OH-PBDEs/-PCBs, concentrations were expressed on a wet weight basis (wet wt). The samples with contaminant concentrations below the MLOQ were assigned a value, randomly generated, between zero and the compound-specific MLOQ. However, a concentration mean for a compound was not determined if less than 60% of the samples had concentrations below the MLOQ. The differences between species and sexes of glaucous gulls in compound concentrations were investigated by general linear models using the statistical package STATISTICA (StatSoft, Tulsa, OK). Statistical significance was set at $p \leq 0.05$. Age of glaucous gulls and polar bears was excluded from further data treatments as this variable was not a significant predictor on the variation of the compounds analyzed.

Results and Discussion

Total HBCD and PBBs. Total HBCD concentrations were quantifiable in all the glaucous gull samples and in 14% of polar bear samples (Table 1). Total HBCD concentrations did not differ between male and female glaucous gulls and were generally higher than those of the minor PBDE congeners analyzed (i.e., BDE28, 66, 85, 138, 183, and 209) (Table 1). Because total HBCD was generally nonquantifiable in polar bear samples, this may indicate that the retention potential of this compound is somewhat limited in polar bear plasma compared to glaucous gulls. Studies dealing with persistent and bioaccumulative OCs (e.g., PCBs) support our findings as these classes of contaminants are generally found at lower concentrations in polar bears compared to glaucous gulls, generally by severalfolds, due to the polar bear's superior detoxification and elimination ability (*29*). Alternatively, such difference in accumulated total HBCD concentrations in plasma may be reflective of a species-specific diet and feeding rate. Nevertheless, relative to the major PBDE congeners, the generally low total HBCD concentrations in glaucous gull and polar bear samples suggest that there is a limited remote input source into the Norwegian Arctic despite the substantial use of HBCD as a BFR additive in Europe. Of the worldwide use of HBCD in 1999, that of Europe was estimated to be 56% (*30*). A recent study supporting limited deposition of HBCD in this region of the Arctic has reported concentrations in upper sediment layers of a lake on Bear Island below 0.43 ng/g dry wt (*31*). To our knowledge, neither the glaucous gull nor the polar

TABLE 1. Arithmetic Mean[a], Standard Error (SE), and Data Range of Percentage Lipid and Total HBCD, PBB, PBDE, and PCB Concentrations (ng/g wet wt) in Plasma Samples of Glaucous Gulls and Polar Bears Collected from the Norwegian Arctic

	male glaucous gulls ($n = 12$)			female glaucous gulls ($n = 15$)			female polar bears ($n = 15$)		
	% of samples > MLOQ	mean ± SE	data range	% of samples > MLOQ	mean ± SE	data range	% of samples > MLOQ	mean ± SE	data range
% lipid	100	1.54 ± 0.05	1.30–1.81	100	1.48 ± 0.07	1.03–2.02	100	1.01 ± 0.19	0.48– 3.58
Total HBCD[b]	100	0.34 ± 0.09	0.07–1.24	100	0.32 ± 0.05	0.12–0.73	14		<0.03–0.85
BB101	25		<0.13–0.72	47		<0.13–0.47	0		<0.02
BDE28	100	0.12 ± 0.01	0.05–0.20	100	0.13 ± 0.02	0.03–0.31	7		<0.01–0.06
BDE47	100	8.81 ± 1.61	4.71–24.3	100	10.6 ± 1.14	4.43–17.1	100	4.98 ± 0.46	2.63–8.79
BDE66	100	0.03 ± 0.01	0.01–0.08	100	0.07 ± 0.01	0.01–0.14	7		<0.01–0.09
BDE85	100	0.02 ± 0.01	0.01–0.07	100	0.02 ± 0.002	0.01–0.03	14		≤0.01
BDE99	100	2.53 ± 0.74	0.86–8.72	100	2.46 ± 0.35	0.91–5.94	71	0.18 ± 0.04	<0.09–0.54
BDE100	100	2.20 ± 0.53	0.88–7.0	100	2.27 ± 0.24	0.86–4.22	64	0.05 ± 0.02	<0.02–0.29
BDE138	100	0.17 ± 0.07	0.05–0.87	100	0.11 ± 0.02	0.04–0.28	0		<0.01
BDE153	100	3.77 ± 1.56	0.68–18.5	100	2.08 ± 0.26	0.90–4.83	57		<0.02–0.39
BDE154/BB153	100	2.40 ± 0.74	0.72–9.0	100	1.93 ± 0.20	0.77–3.45	100	0.12 ± 0.05	0.02–0.73
BDE183	92	0.11 ± 0.04	<0.03–0.43	100	0.09 ± 0.01	0.04–0.22	0		<0.04
BDE209	50		<0.05–0.21	36		<0.05–0.33	7		<0.06–0.10
ΣPBDE[c]	100	20.2 ± 5.08	8.43–67.5	100	19.8 ± 2.09	8.23–35.4	100	5.38 ± 0.54	2.65–9.72
ΣPCB[d]	100	1,133 ± 184	457–2,548	100	1,091 ± 146	498–2,655	100	56.9 ± 8.64	17.3–115

[a] Mean was calculated if at least 60% of the samples had concentrations of the compound >MLOQ. [b] Total HBCD: coelution of α-, β-, and γ-isomers. [c] BDE17 was <MLOQ (0.01 ng/g wet wt) in all samples. [d] ΣPCB: sum of CB28, 31, 42, 44, 49, 52, 60, 64, 66/95, 70, 74, 97, 99, 101, 105, 110, 118, 128, 129/178, 138, 141, 146, 149, 151, 153, 158, 170/190, 171/202/156, 172, 174, 177, 179, 182/187, 180, 183, 194, 195, 200, 201, 203, and 206.

bear populations of the present study are exposed to regional-sourced inputs of organohalogen contaminants during their seasonal/annual movements. To date, there has been no report on total or isomer-specific HBCD concentrations in tissue or blood samples from arctic seabirds. A recent survey in the United Kingdom has reported total HBCD concentrations (mean: 20.0 ng/g wet wt) (*32*) in liver of fish-eating cormorants (*Phalacrocorax carbo*) that were several orders of magnitude higher compared to the present glaucous gull plasma. Furthermore, there are few reports on total HBCD concentration data in marine mammals from northern locations, although they are limited to blubber and fat biopsies as the quantification matrixes (*3*).

The BB101 was detected exclusively in glaucous gulls, although less than 47% of the samples had quantifiable amounts (Table 1). Concentrations of BB101 in glaucous gull samples were comparable to those of total HBCD (Table 1). In glaucous gulls, the hexa-PBB BB153, which was quantified together with BDE154 as they were not GC resolved, were found at concentrations approximately 18-fold higher relative to polar bears (Table 1). The GC elution profile for several of the glaucous gull fractions showed marginal resolution of BDE154 and BB153, where the $^{79}Br/^{81}Br$ anion response contribution of BB153 was roughly 35%. Given that BDE154/BB153 resolution was unpredictable, combined BDE154/BB153 concentrations were reported. The relative contribution of BB153 to BDE154/BB153 concentrations was not possible to assess in polar bear samples. On the basis of present findings, the PBBs appear to be contaminants of relatively low importance in plasma of Norwegian arctic top-predators unlike their chlorinated analogues (i.e., PCBs) (*22, 23*). This may partly be explained by the fact that highly brominated PBB mixtures were used to a limited extent in Europe prior to the year 2000 (*1*). The hexa-PBB mixture (i.e., FireMaster BP-6), however, was used intensively during the early 1970s in North America (*1*).

PBDEs. All PBDE congeners monitored were detected in glaucous gull and polar bear samples with the exception of BDE17 (Table 1). The ΣPBDE concentrations in glaucous gulls were not different between sexes and were on average 73% higher than those of polar bears. In glaucous gulls, ΣPBDE concentrations were 56-fold lower than ΣPCB, whereas this difference was 11-fold in polar bears (Table 1). Important distinctions in the PBDE congener profiles existed between these two species. In female polar bears, the ΣPBDE concentration was comprised essentially of BDE47 (93%), followed by BDE99 (3%) and traces of several other minor PBDEs (Figure 2). In glaucous gull males and females a lesser proportion of BDE47 (51%) comprised the ΣPBDE concentration, with a nearly equal share of four individual penta- and hexa-BDEs, i.e., BDE99, 100, 153, and BDE154/BB153 (Figure 2). No significant difference in homologue PBDE profiles was found between male and female glaucous gulls. The major contribution of BDE47 (tetra) to the ΣPBDE concentrations in polar bear plasma and to a lesser extent in glaucous gull plasma, relative to other PBDEs, suggests that exposure and physicochemical and toxicokinetic factors highly favor the accumulation of BDE47 compared to penta- and hexa-BDEs. The domination of BDE47 in samples has also been reported in a previous PBDE assessment in fat of Svalbard polar bears (*5*). Furthermore, our results showed great consistency with studies of PCBs in polar bear fat, liver, and plasma (*22, 25, 26*) where the fingerprints were comprised of only few dominating persistent congeners (e.g., CB99, 153, 138, 180, and 170/190), as also observed in the present study for PCBs (data not shown). In contrast, analogous PCB profiles in glaucous gull tissues and plasma/blood are far more complex (*24, 33*). Polar bears are known to be metabolically efficient at transforming the most recalcitrant PCBs, thus facilitating their elimination. This has been further emphasized by studies on fat and plasma samples, including the present study (Table 2), which have been shown to contain high levels of OH-PCB (*26*) as well as methyl sulfone ($MeSO_2$) PCB metabolites (*22, 29*).

The higher brominated BDE183 (hepta) and BDE209 (deca) congeners were detected in glaucous gulls and to a lesser extent in polar bears (Table 1). However, the combined concentrations of BDE183 and BDE209 constituted <1% of those of ΣPBDE in glaucous gulls and 0.1% in polar bears (Figure 2). To our knowledge, concentrations of hepta- and deca-BDE congeners have yet not been reported in any species from the Arctic, with the exception of eggs of Swedish peregrine falcons (*Falco peregrinus*) (*34*). The BDE209 concentrations in present glaucous gulls were several orders of magnitude lower than those found in liver (range: <0.17–6.7 ng/g wet wt) of terrestrial predatory birds from the United Kingdom (*35*). The general finding of such low BDE209 levels in high trophic level vertebrates of the arctic marine food

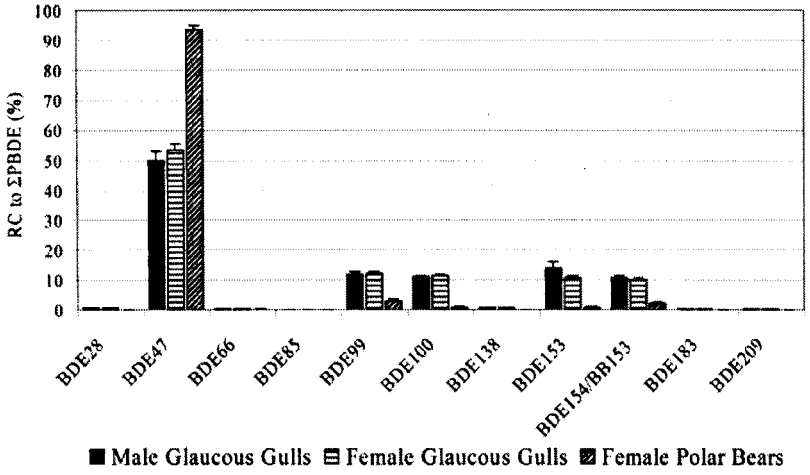

FIGURE 2. Mean (+1 standard error) relative contribution (RC) of individual PBDE congeners detected in plasma samples of glaucous gulls and polar bears to ΣPBDE.

TABLE 2. Arithmetic Mean,[a] Standard Error (SE), and Data Range of Methoxylated (MeO) PBDE and Hydroxylated (OH) PBDE and PCB Concentrations (ng/g wet wt) in Plasma Samples of Glaucous Gulls and Polar Bears Collected from the Norwegian Arctic

	male glaucous gulls (n = 12)			female glaucous gulls (n = 15)			female polar bears (n = 15)		
	% of samples > MLOQ	mean ± SE	data range	% of samples > MLOQ	mean ± SE	data range	% of samples > MLOQ	mean ± SE	data range
2′-MeO-BDE28	8		<0.02–0.13	7		≤0.02	0		<0.02
4-MeO-BDE42	33		<0.02–0.06	7		<0.02–0.04	0		<0.02
6-MeO-BDE47	92	0.05 ± 0.01	<0.02–0.17	93	0.04 ± 0.01	<0.02–0.08	27		<0.02–0.10
3-MeO-BDE47	100	0.66 ± 0.23	0.25–3.09	100	0.47 ± 0.07	0.16–1.27	13		<0.01–0.06
4′-MeO-BDE49	100	0.22 ± 0.06	0.07–0.81	100	0.17 ± 0.02	0.06–0.38	13		<0.01–0.04
6-MeO-BDE90/ 6-MeO-BDE99	50		<0.01–0.06	50		<0.01–0.02	7		<0.01–0.03
ΣMeO-PBDE[b]	100	0.95 ± 0.32	0.36–4.30	100	0.69 ± 0.10	0.30–1.75	33		NQ – 0.17
4-OH-BDE42	0		<0.09	0		<0.09	13		<0.12–0.22
6-OH-BDE47	83	0.14 ± 0.02	<0.07–0.24	73	0.14 ± 0.02	<0.07–0.26	0		<0.08
3-OH-BDE47	58		<0.07–0.50	27		<0.07–0.18	0		<0.09
4′-OH-BDE49	42		<0.08–0.54	67	0.13 ± 0.02	<0.08–0.32	13		<0.10–0.32
6′-OH-BDE49	33		<0.09–0.34	13		<0.09–0.54	0		<0.12
2′-OH-BDE68	0		<0.07	7		<0.07–0.19	0		<0.09
ΣOH-PBDE[c]	100	0.43 ± 0.07	0.12–0.79	93	0.37 ± 0.07	NQ – 1.05	13		NQ – 0.54
ΣOH-PBDE/ΣPBDE		0.03 ± 0.01	0.004–0.09		0.02 ± 0.003	NQ – 0.04			NQ – 0.08
ΣOH-PCB[d]	100	14.4 ± 3.30	3.05–37.9	100	8.46 ± 1.52	2.54–19.6	100	173 ± 27.5	4.15–394
ΣOH-PCB/ΣPCB		0.01 ± 0.002	0.005–0.02		0.01 ± 0.001	0.003–0.02		4.52 ± 1.13	0.91–16.0

[a] Mean was calculated if at least 60% of the samples had concentrations of the compound > MLOQ. [b] Following MeO-PBDE congeners were <MLOQ (range: 0.01–0.02 ng/g wet wt) in all samples: 6′-MeO-BDE17, 4′-MeO-BDE17, 5-MeO-BDE47, 6′-MeO-BDE49, 2′-MeO-BDE68, 6-MeO-BDE85, 2-MeO-BDE123, and 6-MeO-BDE137. [c] Following OH-PBDE congeners were <MLOQ (range: 0.04–0.15 ng/g wet wt) in all samples: 4′-OH-BDE17, 6′-OH-BDE17, 5-OH-BDE47, 6-OH-BDE85, 6-OH-BDE90, 6-OH-BDE99, 2-OH-BDE123, and 6-OH-BDE137. [d] ΣOH-PCB: sum of 4-OH-CB107/4′-OH-CB108, 4′-OH-CB120, 4′-OH-CB130, 3′-OH-CB138, 4′-OH-CB159, 4′-OH-CB172, 3′-OH-CB180, 4-OH-CB187, 4-OH-CB193, 4,4′-diOH-CB202, and 4′-OH-CB208. NQ = not quantifiable.

web is consistent with the physicochemical characteristics of this BFR. It has been argued that BDE209 is highly involatile and is thus a poor candidate for air-particle-associated long-range transport to the Arctic (*36*), resulting in limited bioavailability to marine wildlife. However, a study of rats that were administered a single oral dose of BDE209 has demonstrated at least 10% uptake of BDE209 (*37*). In this study, the highest concentrations were found in plasma relative to blood-rich tissues and adipose tissues. Regardless of factors influencing the degree of exposure and fate within the organism, the occurrence of BDE183 and BDE209 in glaucous gulls and polar bears clearly demonstrates that these higher brominated PBDEs are bioaccumulative, to a limited degree, in apex marine predators of the Norwegian Arctic. However, exposure to BDE183 and BDE209 in the food web of glaucous gulls and polar bears might be underestimated as a consequence of metabolic debromination. Two recent studies have shown that debromination of BDE183 and BDE209 occurs in fish leading to formation/enrichment of penta- and hexa-BDE congeners (*38*, *39*). Therefore, larger loadings of higher brominated PBDEs may be deposited in the Norwegian Arctic via atmospheric input and partially metabolized to lower brominated PBDEs in organisms (e.g., fish) of the marine food web.

MeO- and OH-PBDEs. Among the 15 MeO-PBDE and 15 OH-PBDE congeners monitored in the plasma samples, less than half of the congeners were detected in glaucous gulls and only a few in polar bears. The dominating MeO-PBDE in samples was consistently 3-MeO-BDE47, followed by 4′-MeO-BDE49 and 6-MeO-BDE47 (Table 2). In a study by Marsh et al. (*9*) 3-MeO-BDE47 has been shown to coelute with 2′-MeO-BDE66 on a DB-5-type GC column. Since we presently did not have an authentic standard for 2′-MeO-BDE66, the 3-MeO-BDE47 identified in glaucous gull neutral fractions may actually be 2′-MeO-BDE66 or a combination of 3-MeO-BDE47 and 2′-MeO-BDE66. The hydroxylated homologues 3-OH-BDE47, 4′-OH-BDE49, and 6-OH-BDE47 were also detected in glaucous gulls, although in polar bears 4′-OH-BDE49 was the only congener quantifiable in a minority of samples, in addition to 4-OH-BDE42 (Table 2). In the ECNI mass spectra of $^{79}Br/^{81}Br$ and $[M]^-/[M - Br]^-$ of the neutral fractions, a number of minor MeO-tetraBDEs were found,

although they could not be identified as authentic standards were not available. No difference between sexes of glaucous gulls was found for the concentrations and congener patterns of the MeO- and OH-PBDEs determined.

Environmental research on MeO- and OH-PBDEs has thus far provided an appreciable body of evidence suggesting that several of these compounds occur naturally in marine environments. For instance, the MeO-/OH- pairs 6-MeO-/OH-BDE47 and 2′-MeO-/OH-BDE68, all having a MeO- or OH-group in the ortho position of the diphenyl ether bond, have been isolated and structurally identified in, e.g., marine sponges, ascidians, and algae. Recent findings by Teuten et al. (*11*), who isolated 6-MeO-BDE47 and 2′-MeO-BDE68 from the blubber of North Atlantic True's beaked whales (*Mesoplodon mirus*), have confirmed the natural origin of these compounds using radiocarbon (^{14}C) analyses. Despite the fact that 2′-MeO-BDE68 is commonly detected in oceans, including the Atlantic, and biota samples (*9*, *11*), this compound was below the MLOQ in all glaucous gull and polar bear samples. Results for polar bears were in agreement with those of Wolkers et al. (*5*) who did not detect 2′-MeO-BDE68 in fat of polar bears from Svalbard. Furthermore, Malmvärn et al. (*40*) recently reported on four MeO-PBDEs (2′-MeO-BDE28, 6-MeO-BDE47, 6-MeO-BDE85, and 6-MeO-BDE137) and seven OH-PBDEs (2′-OH-BDE28, 6-OH-BDE47, 6-OH-BDE90, 6-OH-BDE99, 2-OH-BDE123, 6-OH-BDE85, and 6-OH-BDE137), which are all ortho MeO- or OH-substituted, in both red algae (*Ceramium tenuicorne*) and blue mussels (*Mytilus edulis*) from the Baltic Sea. In this study it was concluded that these compounds could not be confirmed as being sourced from production by the algae itself or by its associated microflora and/or microfauna.

To date, no study has demonstrated that metabolic formation of MeO-PBDEs occurs in animals exposed to environmentally relevant PBDEs, i.e., via methylation of OH-PBDEs (metabolically formed or accumulated from the diet) or direct methoxylation of PBDEs. Nonetheless, it has been argued that certain OH-PBDEs with an OH group in the meta or para position may be derived metabolically from PBDEs via CYP enzyme-mediated biotransformation (*9*, *13*, *28*, *40*). The state of knowledge on PCB metabolism recognizes several oxidative metabolic pathways for PCB to OH-PCB conversion, e.g., by direct insertion of an OH group in the meta position or via meta-para arene epoxide formation and subsequent epoxide hydrolase-mediated ring opening with or without a 1,2-chlorine shift (*15*). On the basis of these possible PCB transformation pathways, a portion of the meta and para OH-substituted congeners 3-OH-BDE47, 4′-OH-BDE49, and 4-OH-BDE42 detected in glaucous gull and polar bear plasma may have been derived from metabolism of the precursors BDE47 and possibly BDE49 (not determined in the present study). The metabolic formation of these meta and para OH-PBDEs is corroborated by Malmvärn et al. (*40*) who reported only findings of ortho OH-substituted PBDEs in red algae and blue mussels from the Baltic Sea. Theoretically, biotransformation mechanisms could also explain, in part, the presence of the ortho OH-substituted 6-OH-BDE47 in glaucous gull plasma. Regression analyses revealed BDE47 concentrations in glaucous gulls correlated positively with those of 6-MeO-BDE47 and 6-OH-BDE47, with nearly comparable correlation coefficients (Figure 3). The 6-MeO-BDE47 and 6-OH-BDE47 concentrations also correlated positively with other PBDE congeners analyzed. These findings suggest that a substantial proportion of 6-MeO-/OH-BDE47 retained in plasma of glaucous gulls, and possibly for polar bears, is the result of uptake from naturally produced sources and accumulation in the food chain, as their concentrations covaried in plasma with those of BDE47. However, the accumulation of 6-OH-BDE47 in plasma, assuming a portion of its burden is a result of dietary exposure,

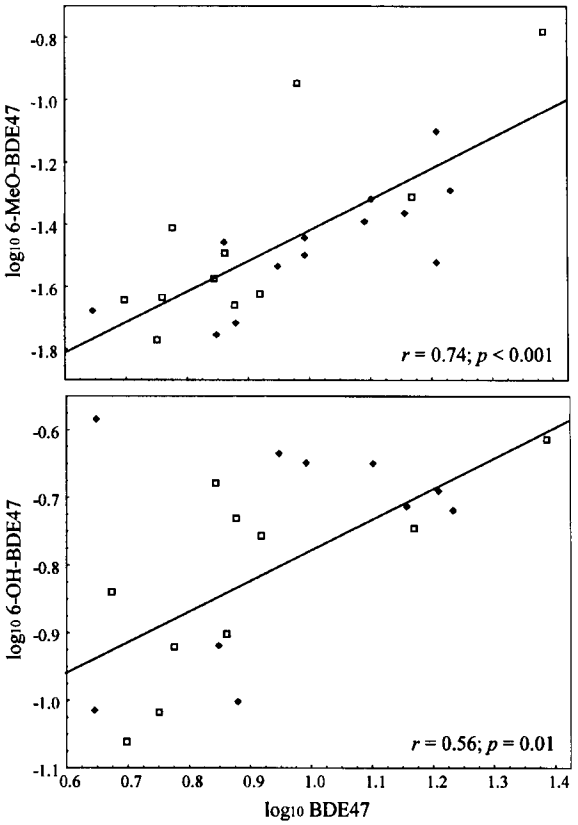

FIGURE 3. Relationships between log-transformed BDE47 and 6-MeO-BDE47 and 6-OH-BDE47 concentrations in plasma of male [□] and female [◆] glaucous gulls.

would be expected to be influenced by other essential physiological parameters. In fact, various mechanisms acting upon OH-PBDEs after absorption through the gut wall and in the liver such as conjugation, oxidation, and reduction are substantial processes that would greatly reduce the half life of the OH-PBDEs. Such processes would hypothetically result in lower or perhaps negligible OH-PBDE amounts in the circulatory system and subsequently lower in tissues following dietary exposure. However, this was not the case as plasma concentrations of 6-MeO-BDE47 and 6-OH-BDE47 were generally comparable in both species, although consistently lower than those of BDE47 (Tables 1 and 2). The octanol–water partitioning coefficients (K_{ow}) previously determined for some MeO-PBDEs have indicated their high propensity for bioaccumulation (*11*). To our knowledge, 3-OH-BDE47, 4′-OH-BDE49, and 4-OH-BDE42 have yet to be confirmed or reported as naturally occurring in any species. Therefore, metabolic formation from BDE47 and more favorable retention (and degradative protection) of these meta and para OH-substituted PBDE congeners likely contributes largely to their presence in glaucous gull and polar bear plasma. As for their MeO-analogues, i.e., 3-MeO-BDE47, 4′-MeO-BDE49, and 4-MeO-BDE42, it cannot be completely ruled out that they may be formed in vivo through methylation as a protective mechanism against toxicity. The methyl derivatives in organisms are documented to exhibit less bioactivity than the corresponding alcohols (*41*).

The formation/retention capacity of OH-PCBs between taxa has been investigated by establishing ΣOH-PCB to ΣPCB concentration ratios as for example in surveys of Bear Island glaucous gulls (*23*) and Greenland polar bears (*26*). The ΣOH-PCB to ΣPCB concentration ratios reported in plasma of Greenland polar bears (*26*) and those of the present Svalbard

polar bears (Table 2) surpassed by several orders of magnitude the ratios found in Bear Island glaucous gull plasma of the present study (Table 2) and that of Verreault et al. (*23*). These findings indicate fundamental mechanistic differences in the contributions of formation, retention, and other biochemical processes influencing OH-PCB residues between glaucous gulls and polar bears. Compared to glaucous gulls, polar bears clearly possess a unique ability to metabolically form and retain OH-PCBs. The ΣOH-PCB to ΣPCB concentration ratios in polar bears were in fact well above unity, and thus ΣOH-PCB concentrations in polar bears plasma were greater than those of ΣPCB. In contrast, ΣOH-PBDE concentrations in polar bear plasma were essentially negligible, and ΣOH-PBDE to ΣPBDE concentration ratios could mostly not be determined (Table 2). On the other hand, in glaucous gull plasma ΣOH-PBDE to ΣPBDE concentration ratios surpassed those of ΣOH-PCB to ΣPCB. Unlike OH-PCBs, it may be hypothesized that metabolically produced OH-PBDEs retained via competitive binding, or accumulated from naturally occurring sources, are rapidly conjugated in polar bears, which results in virtually nondetectable OH-PBDE amount in plasma. In general, OH-PBDEs exhibit structural similarities with the thyroid hormone T4, which has a para OH-diphenyl ether structural backbone, and several para OH-PBDE congeners that have been shown to be highly competitive with human TTR (*17*). In line with these findings, Malmberg (*42*) showed 3-OH-BDE47, 4-OH-BDE42, and 4′-OH-BDE49 had binding affinities to human TTR that were three times higher than T4 and slightly lower than T4 for 6-OH-BDE47. The present results might suggest that in polar bears meta and para OH-PCBs, but not meta and para OH-PBDEs, competitively bind and are retained by, for example, TTR interaction. Furthermore, in glaucous gulls the ortho OH-substituted 6-OH-BDE47 may competitively bind with thyroid hormone transport proteins, as well as meta and para OH-substituted PBDEs. However, because the transport of T4 in birds is primarily associated to albumin (70–75%) (*43*), other macromolecules with comparable affinity to OH-PBDEs such as TTR may be involved in the binding dynamic and retention of these compounds in the circulatory system of glaucous gulls. Therefore, based on present results, we suggest that there are dissimilar biochemical mechanisms involved in PCB and PBDE metabolism and accumulation/elimination and/or OH-PBDE accumulation and retention in glaucous gulls and polar bears. Hepatic enzyme characterizations (e.g., CYP enzymes) involved in oxidative PBDE biotransformation processes have hitherto not been investigated in glaucous gulls or polar bears to verify assumptions concerning factors affecting the congener profiles and concentrations of OH-PBDE residues. Further studies are warranted to investigate mechanisms of PBDE metabolic degradation and macromolecule binding interactions in avian and mammalian top predators.

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