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Trophodynamics of Emerging Brominated Flame Retardants in the Aquatic Food Web of Lake Taihu: Relationship with Organism Metabolism across Trophic Levels

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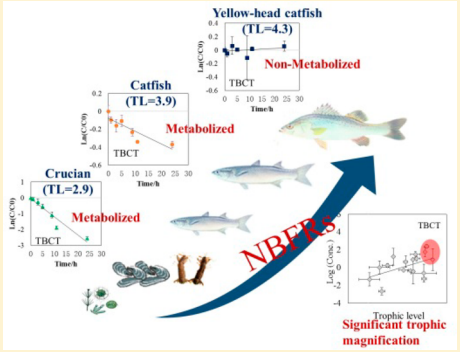
Supporting Information

ABSTRACT: Despite the increasing use and discharge of novel brominated flame retardants, little information is available about their trophodynamics in the aquatic food web, and their subsequent relationships to compound metabolism. In this study, concentrations of 2,4,6-tribromophenyl allyl ether (ATE), 1,2-dibromo-4-(1,2-dibromoethyl)cyclohexane (TBECH), tetrabromo-*o*-chlorotoluene (TBCT), pentabromobenzyl acrylate (PBBA), 1,2-bis(2,4,6-tribromophenoxy)ethane (BTBPE), bis(2-ethylhexyl)-3,4,5,6-tetrabromo-phthalate (TBPH), and decabromodiphenyl ethane (DBDPE) were measured in 17 species, including plankton, invertebrates, and fish from Lake Taihu, South China. Trophodynamics of the compounds were assessed, and metabolic rates were measured in the liver microsomes of crucian (trophic level [TL]: 2.93), catfish (TL: 3.86), and yellow-head catfish (TL: 4.3). Significantly positive relationships were found between trophic levels and lipid-normalized concentrations of ATE, BTBPE, and TBPH; their trophic magnification factors (TMFs) were 2.85, 2.83, and 2.42, respectively. Consistently, the three chemicals were resistant to metabolism in all fish microsomes. No significant relationship was observed for βTBECH (p = 0.116), and DBDPE underwent trophic dilution in the food web (TMFs = 0.37, p = 0.021). Moreover, these two chemicals showed steady metabolism with incubation time in all fish microsomes. TBCT and PBBA exhibited significant trophic magnifications in the food web (TMF = 4.56, 2.01). Though different metabolic rates were observed for the two compounds among the tested fish species, TBCT and PBBA both showed metabolic resistance in high-trophic-level fish. These results indicated that metabolism of organisms at high trophic levels plays an important role in the assessment of trophic magnification potentials of these flame retardant chemicals.



INTRODUCTION

Brominated flame retardants (BFRs) including various organobromine compounds are a major group of chemical flame retardants added to textiles, plastics, electronics, clothing and building materials to reduce their flammability. Strict regulations have been imposed on the use of BFRs, and the most frequently used BFRs, polybrominated diphenyl ethers (PBDEs), have been banned and added to the Persistent Organic Pollutants list of the Stockholm Convention.[1] Restrictions on PBDEs usages have resulted in the emergence of a number of alternative "novel" BFRs (NBFRs) to meet the flammability standard. Thus, NBFRs, such as 1,2-bis(2,4,6-tribromophenoxy)ethane (BTBPE), bis(2-ethylhexyl)-3,4,5,6-tetrabromo-phthalate (TBPH), decabromodiphenyl ethane (DBDPE), 2,4,6-tribromophenyl allyl ether (ATE), 1,2-dibromo-4-(1,2-dibromoethyl) cyclohexane (TBECH), tetrabromo-*o*-chlorotoluene (TBCT), and pentabromobenzyl acrylate (PBBA) are produced and used in increasing amounts.[2] Wide environmental occurrences,[3−11] long-range atmospheric transportations,[12,13] and potential toxicity[14,15] have been reported for these chemicals, which deserve more attention with respect to their environmental risks.

Characterization of trophic transfer is a vital criterion for assessing the ecological risk of NBFRs. Because of their high lipophilicity (log K_{OW}: 4.4−11.1),[2] NBFRs are bioaccumulative in aquatic biota; this finding has been supported by numerous reports on the occurrences of these compounds in invertebrates and fish from both freshwater and marine environments.[6,16,17] NBFRs have also been detected in highly trophic marine organisms such as seabirds, whales, and seals.[10,18−20] While most studies have focused on the accumulated levels of NBFRs in the aquatic biota, only one study has explored the trophodynamics of DBDPE in the aquatic food web, and found that DBDPE underwent significant trophic magnification in Lake Winnipeg, Canada.[21] The results suggested that most of the emerging NBFRs might

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exhibit a high trophic magnification potential in the aquatic environment. However, little quantitative information is available about the trophodynamics of most NBFRs in aquatic food webs.

Recent studies have reported that metabolic rate is an important factor influencing the trophic magnification factor (TMF) of various compounds.[22−24] Significant correlations have been observed between TMF and the model-derived or laboratory-measured metabolic rates of numerous chemicals.[22,23] The highest TMF values were always found for compounds that are slowly metabolized by animals and are moderately hydrophobic.[22,23] In these studies, one group of organisms (e.g., rainbow trout or weever) was chosen for measuring the metabolic rates;[22,23] however, species-specific differences in the metabolism of xenobiotics among various fish species have been reported.[25,26] Moreover, it has been suggested that the decreasing biotransformation capacity with increasing trophic levels contributes to the biomagnification of organochlorines in the aquatic food web.[27] NBFRs are a group of compounds widely found in aquatic biotas and exhibit diverse metabolic behaviors in organisms. BTBPE can be metabolized to lower-brominated congeners and OH-metabolites in rats,[28,29] and monohydroxy-TBECH was identified as the major metabolite of TBECH in *in vitro* rat and human liver microsomal assays.[30,31] In contrast, TBPH was resistant to metabolism in human and rat subcellular fractions and fish species.[26,32] Thus, the diverse metabolism and high trophic magnification potentials of NBFRs make them suitable for exploring the relationships between trophic transfer behaviors and metabolic rates in biota occupying different trophic levels.

In this study, 8 NBFRs, namely ATE, αTBECH, βTBECH, PBBA, TBCT, BTBPE, TBPH, and DBDPE, shown in Figure S1 in the Supporting Information (SI), were selected due to the high production volume,[2] frequent environmental occurrences,[3−11] and wide range of log K_{OW} (4.4−11.1).[2] The target compounds were measured in 17 organisms including plankton, 4 invertebrates, and 12 species of the aquatic food web from Lake Taihu. Trophic transfer behaviors of these chemicals were determined on the basis of the trophic levels estimated using stable isotopes. Then, microsomes of three fish species including yellow-head catfish, catfish, and crucian with trophic levels ranging from 2.93 to 4.3 were extracted and used to measure the metabolic rates of the target compounds. The relationships between trophic magnification potentials of NBFRs and metabolic rates in the biotas occupying different trophic levels were assessed. The result of this study fills in the data gap on the occurrence and trophodynamics of NBFRs, and also helps to explore the effects of metabolic capabilities in organisms with different trophic levels on trophodynamics of the chemicals in the aquatic food web.

MATERIALS AND METHODS

Chemicals and Reagents. ATE, αTBECH, βTBECH, TBCT, PBBA, BTBPE, and ^{13}C-labeled BDE209 were purchased from Wellington Laboratories Inc. (Guelph, ON, Canada, purity >98%). TBPH, benzo[*a*]pyrene (B[*a*]P), perylene-d_{14}, and DBDPE were obtained from AccuStandard (New Haven, CT, purity >98%). 6′-MeO-BDE17 (purity >98%) was synthesized in the Department of Biology and Chemistry, City University of Hong Kong.[33] Dichloromethane (DCM), *n*-hexane, water, acetone, acetonitrile, and methanol of pesticide residue grade were purchased from Fisher Chemicals (Fair Lawn, NJ). Monopotassium phosphate, dipotassium phosphate, ethylene diamine tetraacetic acid, glycerol, and sucrose were purchased from Beijing Chemicals. Granular anhydrous sodium sulfate and aluminum oxide (200−300 mesh) were purchased from Sinopharm Chemical Reagent Co., Ltd. (Shanghai, China). The NADPH-regenerating system was purchased from Promega (Madison, WI). Distilled water was prepared using a Milli-Q Synthesis water purification system (Millipore, Bedford, MA).

Sample Collection. Lake Taihu, the third largest freshwater lake in China, is located in the southeast region of China, with an approximate area of 2338 km^2 and a maximum depth of 1.9 m. Components of the aquatic food web from Lake Taihu were collected in August 2014 and May 2015. The food web included primary producers (seston/plankton) (n = 6), four invertebrates species including freshwater mussel (*Anodonta*) (n = 6), clam (*Lamellibranchia*) (n = 6), crayfish (*Procambarus clarkii*) (n = 6), and snail (*Bellamya purificata*) (n = 6), 12 fish species including ricefield eel (*Monopterus albus*) (n = 6), blunt-snout bream (*Megalobrama amblycephala*) (n = 2), whitebait (*Hemisalanx prognathous*) (n = 5), crucian (*Carassius auratus*), carp (*Carassius cuvieri*) (n = 3), pipefish (*Tylosurus crocodilus*) (n = 3), silver fish (*Protosalanx hyalocranius*) (n = 6), whitefish (*Alburnus*) (n = 6), catfish (*Silurus asotus*) (n = 6), redfin culter (*Cultrichthys erythropterus*) (n = 7), wolfish (*Anarrhichtys Ocellaus*) (n = 3), and yellow-head catfish (*Pelteobagrus fulvidraco*) (n = 6). A detailed description of collected samples is provided in Table 1 and S1. The whole bodies of seston/plankton, soft tissues of invertebrates, and muscles of fishes were stored at −20 °C prior to the chemical and isotope analysis.

Microsome Preparation. Crucian, catfish, and yellow-head catfish were selected because these fish species occupy relatively wide ranges of trophic levels, and the size of these fish is suitable for the extractions of liver tissues. Fresh liver tissues of three fish species including crucian, catfish, and yellow-head catfish were used for assessing the intrinsic clearance rates of NBFRs. The liver microsomes of crucian, catfish, and yellow-head catfish were prepared according to Dyer's method.[34] In brief, approximately 5 g of tissue was homogenized in 10 mL of the buffer (25 mM PBS, 1.25 mM EDTA, 1 mM DTT, 10% (v/v) glycerol; pH = 7.4). Homogenates were centrifuged at 10,000*g* (4 °C) for 15 min, and then the resulting supernatant was further centrifuged at 100,000*g* (4 °C) for 60 min. The microsomal fraction was suspended in 10 mL of the buffer (50 mM PBS, 1 mM EDTA, 20% (v/v) glycerol; pH = 7.4), and stored in liquid nitrogen until use.

***In Vitro* Microsomal Incubations.** For the *in vitro* incubations of fish microsomes, reactions were performed in triplicate experiments in separate glass vials at 25 °C by using our previously reported methods.[22] The reliability of the *in vitro* assays is easily influenced by the high variability in enzyme viability and metabolic capacity between different batches. The incorporation of B[*a*]P benchmarking was found to substantially reduce the variabilities between batches,[22] and thus applied in the *in vitro* incubations. In brief, the reaction mixtures (200 μL) contained liver microsomes (1 mg/mL protein, final concentration), substrates (0.5 μM for both target compounds and B[*a*]P, 1% v/v of DMSO), and an NADPH regenerating system (NADP 6.5 mM, glucose 6-phosphate 16.5 mM, $MgCl_2$ 16.5 mM, and glucose 6-phosphate dehydrogenase 2 U/mL). The reaction was terminated by adding 200 μL of ice-cold acetone after 0, 1, 3, 5, 9, 11, and 24 h. Protein concentrations were determined using the Bradford method, and heat-inactivated microsomes were used as the negative controls.

Sample Preparations. The biological samples were first freeze-dried, and then approximately 0.5−2 g of the dried samples was spiked with the surrogate standards (6′-MeO-BDE17 and C^{13}-BDE209) and Soxhlet-extracted with a mixture

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Table 1. Mean Biological Parameters and Concentrations of Target NBFRs (pg/g wet weight) in Organisms Collected from Lake Taihu[a]

Species	TL	*n*	ATE	βTBECH	TBCT	PBBA	BTBPE	TBPH	DBDPE
Plankton/seston	2.00 ± 0.27	6	46.6 ± 12.0 (31.4−61.8)	43.2 ± 3.9 (<MDL-41.1)	11.1 ± 4.3 (4.8−17.8)	8.8 ± 6.2 (<MDL-15.0)	<MDL	143 ± 90.2 (<MDL-270)	3570 ± 1930 (1270−5580)
Freshwater mussel	1.08 ± 0.53	6	13.7 ± 7.4 (<MDL-23.4)	385 ± 348 (<MDL-1010)	2.1 ± 4.6 (<MDL-11.5)	12.1 ± 13.6 (<MDL-35.3)	<MDL	51.0 ± 43.8 (<MDL-43.1)	9310 ± 5600 (751−11900)
Clam	1.71 ± 0.17	6	24.5 ± 13.9 (<MDL-46.3)	83.2 ± 25.8 (<MDL-125)	<MDL	7.3 ± 7.9 (<MDL-20.0)	<MDL	76.2 ± 98.9 (<MDL-251)	689 ± 697 (217−2060)
Crayfish	1.59 ± 0.53	6	21.3 ± 16.6 (<MDL-54.6)	348 ± 273 (<MDL-795)	16.8 ± 11.2 (<MDL-33.5)	<MDL	<MDL	<MDL	6270 ± 5210 (2340−13200)
Snail	3.16 ± 0.15	6	1030 ± 106 (883−1190)	148 ± 38.6 (86.7−180)	<MDL	146 ± 42.6 (78.9−200)	776 ± 396 (106−1230)	507 ± 445 (<MDL-1280)	284 ± 213 (<MDL-612)
Ricefield eel	2.82 ± 0.23	6	13.9 ± 13.1 (<MDL-36.7)	877 ± 506 (441−1550)	<MDL	18.8 ± 13.4 (<MDL-40.6)	62.1 ± 25.4 (<MDL-113)	1100 ± 766 (<MDL-2540)	682 ± 361 (408−1290)
Blunt-snout bream	3.30 ± 0.04	2	169 ± 43.6 (138−200)	<MDL	76.0 ± 18.2 (63.1−88.9)	<MDL	47.0 ± 20.1 (<MDL-61.2)	2130 ± 101 (2050−2200)	118 ± 24.7 (100−135)
Whitebait	2.29 ± 0.05	5	361 ± 46.5 (282−400)	<MDL	295 ± 370 (<MDL-890)	25.7 ± 15.9 (<MDL-52.5)	63.1 ± 14.5 (<MDL-77.5)	1370 ± 1850 (188−4610)	80.6 ± 38.1 (<MDL-127)
Crucian	2.93 ± 0.10	6	108 ± 58.5 (36.9−167)	<MDL	83.1 ± 62.7(<MDL-155)	14.8 ± 1.1 (<MDL-8.5)	87.5 ± 62.7 (<MDL-161)	211 ± 135 (98.7−394)	58.0 ± 24.9 (<MDL-93.7)
Carp	3.42 ± 0.25	3	416 ± 77.6 (202−68.2)	42.5 ± 47.4 (<MDL-83.6)	310 ± 236 (156−582)	23.2 ± 31.0 (<MDL-69.5)	<MDL	245 ± 192 (<MDL-437)	337 ± 78.0 (282−392)
Pipefish	3.48 ± 0.18	3	621 ± 34.6 (583−651)	<MDL	198 ± 97.8 (91.8−284)	93.8 ± 17.7 (79.9−114)	<MDL	664 ± 311 (384−998)	928 ± 700 (210−1600)
Silver fish	3.31 ± 0.07	6	213 ± 162 (127−543)	20.5 ± 48.7 (<MDL-120)	84.1 ± 130 (<MDL-264)	31.5 ± 21.4 (<MDL-57.9)	<MDL	77.6 ± 6.7 (<MDL-77.4)	75.8 ± 129 (<MDL-304)
Whitefish	3.85 ± 0.65	6	1230 ± 1230 (235−3030)	102 ± 152 (<MDL-374)	67.9 ± 163 (<MDL-400)	100 ± 23.5 (72.3−135)	261 ± 194 (<MDL-506)	3320 ± 5730 (<MDL-14900)	1450 ± 1670 (559−4820)
Catfish	3.86 ± 0.12	5	416 ± 77.6 (335−543)	<MDL	<MDL	103 ± 88.2 (30.4−247)	235 ± 253 (<MDL-670)	713 ± 480 (386−1538)	922 ± 25.1 (904−939)
Redfin culter	3.90 ± 0.03	7	692 ± 256 (379−1010)	<MDL	1220 ± 1970 (120−5590)	51.0 ± 46.9 (<MDL-139)	225 ± 293 (<MDL-740)	1830 ± 1450 (<MDL-4540)	516 ± 322 (242−1180)
Wolffish	3.99 ± 0.11	3	437 ± 59.9 (383−501)	2550 ± 1090 (1600−3740)	2920 ± 1610 (1960−4780)	<MDL	189 ± 147 (<MDL-349)	1040 ± 186 (897−1250)	1010 ± 112 (878−1080)
Yellow-head catfish	4.30 ± 0.06	6	294 ± 169 (154−605)	<MDL	930 ± 1080 (<MDL −2540)	183 ± 81.2 (97.2−297)	700 ± 729 (219−2110)	1230 ± 400 (844−1910)	<MDL

[a]Concentrations were expressed as mean ± SD (range). <MDL: concentrations below the detection limits. αTBECH was only detected in Silver fish with concentrations of 134 ± 208 pg/g ww (ND-407 pg/g ww).

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of dichloromethane and hexane (3:1) for 24 h. Aliquot of the extract was rotated to dryness, and the lipid amounts were determined gravimetrically. The rest extract was redissolved in 4 mL of hexane and passed through a glass column containing 8 g of 5% H_2O-deactivated active Al_2O_3. This column was eluted with 15 mL of hexane and 10 mL of dichloromethane. The eluent was concentrated to 50 μL in hexane and analyzed by gas chromatography-electron capture negative ionization mass spectrometry (GC-ECNI-MS).

For the incubation samples, the incubation mixture in each vials was added with 1 mL of water and surrogate standards, and extracted three times with 1 mL of hexane. The aquatic fraction was loaded onto a Pasteur pipe filled with sodium sulfate to remove moisture and then eluted using 1 mL of hexane and 1 mL of DCM. Combined with the organic fraction, the eluate was concentrated to 50 μL in hexane before analysis by GC-ENCI-MS.

Instrumental Analysis. Identification and quantification of the target NBFRs were performed by using GC-ECNI-MS (Shimadzu QP 2010 Ultra, Japan). A splitless injector was used, and the injection volume was 1 μL. The injection temperature, the interface temperature, and the ion source temperature were 290, 320, and 260 °C, respectively. For the analysis of ATE, αTBECH, βTBECH, TBCT, PBBA, BTBPE, and TBPH, separation was achieved on an HP-5 capillary column (30 m × 0.25 mm × 0.25 μm film thickness, Agilent, USA). The carrier gas was helium at a constant flow rate of 2 mL/min. The column oven temperature was programmed to increase from 120 °C (2 min) to 310 °C (5 min) at a rate of 8 °C/min. For the DBDPE analysis, the separation was achieved on a VF-5MS capillary column (15 m × 0.25 mm × 0.25 μm film thickness, Agilent, USA). The carrier gas was helium at a constant flow rate of 5 mL/min. The column oven temperature was programmed to increase from 120 °C (2 min) to 310 °C (5 min) at a rate of 30 °C/min. The target compounds were analyzed through selected ion monitoring (SIM) for m/z ^{79}Br- and ^{81}Br- except for ^{13}C-BDE209, of which the monitored ions were m/z 494.6 and 498.6 (Figure S2).

Identification and quantification of B[a]P were performed by GC-MS in EI mode. The separation was achieved on a HP-5MS capillary column (30 m × 0.25 mm × 0.25 μm film thickness, Agilent, USA). A splitless injector was used, and the injection volume was 1 μL. The source temperature was 250 °C. The injection temperature was 250 °C. The carrier gas was helium at a constant flow rate of 2 mL/min. The column oven temperature was programmed to increase from 70 °C (2 min) to 220 °C (3 min) at a rate of 20 °C/min, then to 300 °C (5 min) at a rate of 20 °C/min. Monitoring fragment ions were m/z 252 and 126 for B[a]P, and m/z 264 and 260 for perylene-d_{14}.

Quantitation and Quality Assurance Quality Control (QA/QC). All equipment was rinsed with acetone and hexane before use. Six replicate spiked samples and one matrix sample were analyzed to determine the general recovery rates. The absolute recoveries for the spiked samples were 76.2 ± 7.8%, 82.5 ± 2.3%, 75.8 ± 2.6%, 69.9 ± 1.8%, 79.5 ± 4.5%, 75.5 ± 3.1%, 74.5 ± 3.5%, and 71.1 ± 1.2% for ATE, αTBECH, βTBECH, TBCT, PBBA, BTBPE, TBPH, and DBDPE, respectively. Good separations of all target compounds were achieved in the GC-MS analysis, as shown in Figure S2. The isotopic anions of bromine were monitored in the ECNI-MS analysis for identification and quantitation of target NBFRs. The chromatography of 14 PBDEs and 8 MeO-PBDEs, widely detected with high abundances in biotas, were compared to that of target NBFRs, and coelution of these brominated compounds were not observed in the GC-MS analysis. To automatically correct for the losses of analytes during extraction or sample preparation and to compensate for the variations in the instrumental response from injection to injection, the quantification of the analytes was achieved using a surrogate standard method with calibration against standard solutions. ATE, αTBECH, βTBECH, TBCT, PBBA, BTBPE, and TBPH were quantified relative to 6′-MeO-BDE17 due to its similar ionization, nondetection in environmental samples and comparable recovery rate compared to the target NBFRs. DBDPE was quantified relative to ^{13}C-BDE209. Reproducibility of target chemicals were examined by duplicate analysis, and the relative standard deviation of concentrations of NBFRs were within 20% (n = 10). The recovery of 6′-MeO-BDE17 and ^{13}C-BDE209 in all of the analyzed samples was 72.4 ± 27.1% and 73.3 ± 19.6% (n = 88), respectively. A procedural blank was analyzed in each batch of six samples to check for interfering peaks and to correct the sample values. All target NBFRs, except for αTBECH, were detected in the blank samples. For compounds with detectable blank contamination, the method detection limits (MDLs) were set at three times the standard deviation of the procedural blanks. For compounds not detected in the blank samples, MDLs were based on a signal-to-noise ratio of 3. The MDLs were 4.2, 1.6, 48, 4.1, 8.3, 43, 75, and 68 pg/g ww for ATE, αTBECH, βTBECH, TBCT, PBBA, BTBPE, TBPH, and DBDPE, respectively.

Stable Isotope Analysis. Samples of plankton/seston, invertebrates, and fishes were homogenized and then freeze-dried. All of the samples were extracted using methanol for 12 h to remove isotopically lighter lipids. After drying at 70 °C for 12 h, 0.3 mg of the samples was packed into Sn capsules and analyzed with an elemental analyzer (Thermo Flash 2000, MA,) interfaced with an isotope ratio mass spectrometer (Thermo Delta V). The stable nitrogen and carbon isotope ratios were expressed as follows:

$$\delta x = (R_{samp}/R_{ref} - 1) \times 1000(‰) \quad (1)$$

where δx (‰, per thousands) is the isotope composition of the sample relative to the reference material, and R_{samp} and R_{ref} are the absolute isotope ratio in the sample and the reference material, respectively. Atmospheric air and Vienna Pee Dee Belimnite (VPDB) were used as the reference materials for δ^{15}N and δ^{13}C, respectively.

Data Analysis. Trophic magnification factors (TMFs) were calculated using the following equations on the basis of the relationships between trophic levels and logarithmic concentrations of the individual organisms. In this study, trophic levels were estimated by assuming that seston/plankton represented a trophic level of 2.0 and the enrichment factor of δ^{15}N was set as 3.8 according to a previous study on Lake Taihu.[35] The trophic positions of the aquatic organisms were calculated using the following equation.

$$TL_{consumer} = 2 + (\delta^{15}N_{consumer} - \delta^{15}N_{plankton})/3.8 \quad (2)$$

The relationships between log-transformed NBFRs concentrations and trophic positions of the biota are shown in eq 3, and TMFs were calculated using eq 4.

$$\log \text{NBFRs concentration (lipid corrected)} = a + b\text{TL} \quad (3)$$

$$\text{TMFs} = 10^b \quad (4)$$

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Correlations between NBFRs concentrations and trophic levels were examined using Spearman's correlation test, and when the p value was less than 0.05, the linear regression between NBFRs concentrations and trophic levels was considered to be statistically significant. In this study, when more than 50% of the samples were below the MDLs, the chemicals were not included in the TMF calculations. In the case of concentration less than the detection limits, ProUCL values ranging from 0 to values close to MDLs were generated based on the distribution of all samples (U.S. EPA, ProUCL 5.1).

The intrinsic clearance rates of the substrates were determined by measuring the first-order rate constant for metabolism of the substrate at a low concentration.[36,37] The depletion data followed first-order kinetics, and was expressed as follows.

$$\ln C_t = \ln C_0 - K \cdot t \quad (5)$$

where t is the incubation time; C_0 and C_t are the substrate concentrations in the incubation media at time zero and time t, respectively; and K is the apparent first-order biotransformation rate constant (h^{-1}). The *in vitro* intrinsic clearance values (CL, mL/h/mg protein) were calculated as follows.

$$\mathrm{CL} = \frac{K}{C_{\mathrm{protein}}} \quad (6)$$

where C_{protein} is the protein concentration (mg protein/mL) of the incubation mixtures.

RESULTS AND DISCUSSION

Levels and Profiles. The target eight NBFRs, namely ATE, αTBECH, βTBECH, TBCT, PBBA, BTBPE, TBPH, and DBDPE, were all detected in the biota samples from Lake Taihu (Table1). αTBECH was only detected in silver fish (134 ± 208 pg/g ww), and the average concentrations of the other NBFRs in all of the biotas were 346 ± 363, 276 ± 628, 366 ± 744, 49.7 ± 54.9, 161 ± 234, 870 ± 906, and 1550 ± 2550 pg/g ww for ATE, βTBECH, TBCT, PBBA, BTBPE, TBPH, and DBDPE, respectively. The highest concentrations of ATE (1230 ± 1230 pg/g ww), βTBECH (2550 ± 1090 pg/g ww), TBCT (2920 ± 1610 pg/g ww), PBBA (183 ± 81.2 pg/g ww), and TBPH (3320 ± 5730 pg/g ww) were detected in fish species, and those of BTBPE (776 ± 396 pg/g ww) and DBDPE (9310 ± 5600 pg/g ww) were detected in snail and freshwater mussel, respectively. To compare the levels of the other detected NBFRs with those reported by previous studies, concentrations calculated using lipid-based results were used. TBPH and ATE were only reported in marine mammals. Concentrations of TBPH and ATE were 0.04−3859 ng/g lw and 5400−9100 pg/g ww in beluga blubber from Hong Kong,[38] and seal blubber from Greenland, respectively, and the levels were higher than those in fish (TBPH: 2.2−110 ng/g lw, ATE: 13.9−1230 pg/g ww) in this study. BTBPE was detected with a relatively high frequency (75%) and concentrations of 5.7 ± 4.9 ng/g lw in the fish from Lake Taihu, and these levels were higher than those of the fish from Lake Winnipeg (0.13−0.95 ng/g lw),[6] and of trout from Lake Ontario (0.5−2.5 ng/g lw).[17] Concentrations of α/βTBECH were ND-5.93 ng/g lw in lake trout from Lake Erie,[39] which were within the concentrations ranges of these compounds in this study (ND-22.2 ng/g lw). Concentrations of TBCT in carp in this study (8.2−24.8 ng/g lw) was comparable to that in the same species (ND-30 ng/g lw) from streams and lakes across the state of Illinois, USA.[40] DBDPE was detected in all of the target species except for yellow-head catfish with detected concentrations ranging from 3.1 to 64.8 ng/g lw, which were comparable to the reported values for fish collected from Dongjiang River, South China (35−68 ng/g lw), and a pond in an e-waste site in South China (ND-338 ng/g lw).[41,42]

As shown in Figure 1, the profiles of the target NBFRs varied steadily with increasing trophic levels of organisms in Lake Taihu. In the plankton/seston, DBDPE was the predominant compound, accounting for 93% of the total NBFR concentrations. In the invertebrates, the average percentages of DBDPE decreased to 69%, and the proportions of βTBECH and ATE increased to 5.9% and 9.7%, respectively. In fish, the profiles of NBFRs differed considerably as compared to those of the plankton/seston and invertebrates occupying low trophic levels. TBPH was the predominant NBFRs in fish with a contribution of 12.8%−83.5% to the total concentrations, followed by ATE (0.5%−40.9%), DBDPE (1%−38.5%), and TBCT (0.18%−35.8%). Among the eight target NBFRs, only BTBPE and DBDPE were simultaneously reported in plankton and fish from Lake Winnipeg, Canada, and Pearly River Delta, South China.[6,10] Similar concentration ratios between the two compounds (DBDPE/BTBPE) were found in the results of both this study (0.4−5.7) and previous studies (0.3−2.9). The profile variations of ATE, βTBECH, TBCT, PBBA, BTBPE, TBPH, and DBDPE in organisms with increasing trophic levels could be attributed to the different trophic magnification potentials of the compounds.

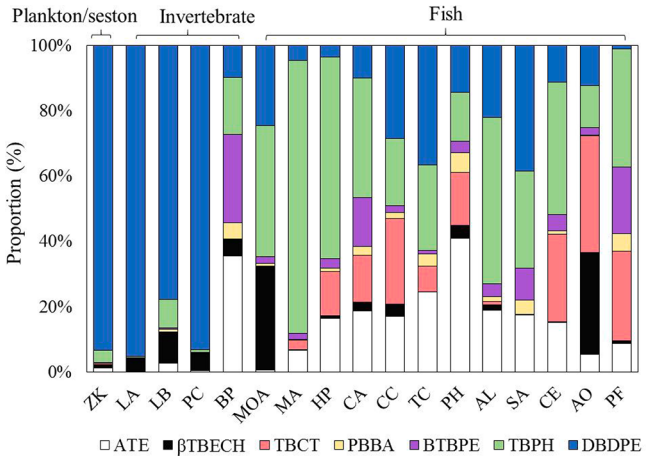

Figure 1. Profiles of target NBFRs in collected organisms collected from Lake Taihu.

Trophodynamics. The stable carbon and nitrogen isotope values for organisms from Lake Taihu are shown in Figure 2 and Table S1. δ^{13}C and δ^{15}N were in the range of −30.4 to −19.4‰ and 10 to 22.2‰, respectively. A statistically significant correlation was observed between stable carbon and nitrogen isotope values (r^2 = 0.7935, p < 0.001), and δ^{15}N showed a stepwise enrichment with increasing trophic levels of the biotas. The δ^{15}N enrichment factor was used to build an isotopic food web model to estimate the trophic levels of all of the species (eqs 1 and 2). The trophic levels were estimated to be 1.08−3.16, 2.0 ± 0.27, and 2.29−4.3 for the invertebrates, plankton/seston, and fish in Lake Taihu, respectively. The estimated trophic levels in this study were consistent with those of previous studies on the trophodynamics of pharmaceutically active compounds, polychlorinated biphenyls, and bisphenol analogues in Lake Taihu.[43−46] In particular, the trophic levels of

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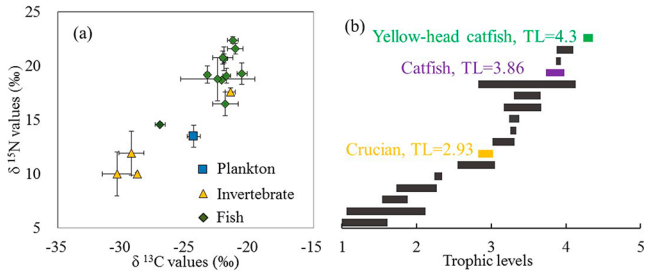

Figure 2. Stable carbon and nitrogen isotopes of organisms from Lake Taihu (a), and estimated trophic levels for each species (b). Liver microsomes of yellow-head catfish (TL = 4.3), catfish (TL = 3.86), and crucian (TL = 2.93) were extracted for metabolic tests.

snail and crucian were 3.16 ± 0.15 and 2.93 ± 0.51, respectively, which were comparable to those reported for the two species previously (2.7 and 3.01),[43,47] The trophic levels of some fish species (carp: 3.42 ± 0.25, catfish: 3.86 ± 0.12, and yellow-head catfish: 4.30 ± 0.06) were also consistent with those reported by previous studies in Lake Taihu (carp: 3.7, catfish: 3.78−3.8, and yellow-head catfish: 4.5).[44,46]

A regression analysis was conducted between lipid-normalized concentrations of the NBFRs (log-transformed) and trophic levels (Figure 3) and the statistical results of this regression analysis are presented in Table 2. Among the target NBFRs, significantly positive relationships were found between trophic levels and lipid-normalized concentrations of ATE (p = 0.005), BTBPE (p = 0.007), TBPH (p = 0.004), PBBA (p = 0.015), and TBCT (p = 0.044). No significant relationship was observed for βTBECH (p = 0.116). TMFs were 2.85, 2.83, 2.42, 2.01, and 4.56 for ATE, BTBPE, TBPH, PBBA, and TBCT, respectively, suggesting that these compounds exhibited significant trophic magnifications in the aquatic food web, and βTBECH exhibited a relatively low biomagnification potential (TMFs = 0.39). To the best of our knowledge, this is the first report on the trophodynamics of ATE, βTBECH, TBCT, PBBA, and TBPH. While no significant correlation was observed for BTBPE in the aquatic food web in Lake Winnipeg, Canada (TMFs = 1.86, p = 0.28),[21] the compound showed high biogmagnification potentials in a laboratory feeding study of juvenile rainbow trout (Oncorhynchus mykiss) (BMF = 2.3).[48] Lipid equivalent concentrations of DBDPE decreased significantly with increasing trophic levels (p = 0.012), and TMFs of DBDPE was 0.37, suggesting that this compound underwent trophic dilution in the food web in Lake Taihu. These results are different from those reported for the compounds in the food web in Lake Winnipeg, in which DBDPE was observed to undergo significant trophic magnification with a TMFs of 8.6 (p = 0.001).[21] Although it is not possible to specifically compare the trophodynamic differences between food webs in various locations, a reasonable cause may be that the food web used in Law's estimation of TMFs only included one zooplankton, and six fish species, and the food web length was only approximately 1.6.[21] Moreover, trophodynamic studies ideally includes individual species that range over at least 3 TLs to achieve the objective of quantifying the trophic magnification potentials of a chemical.[49]

In general, substances with log K_{OW} of approximately 5−8 easily exhibit significant trophic magnification in the aquatic food web. In this study, ATE, PBBA, BTBPE, and TBCT with estimated log K_{OW} values of 5.09−7.88 exhibited significantly high trophic magnification potentials, and TBECH and DBDPE with log K_{OW} values of 4.37 and 11.1,[2] respectively, exhibited

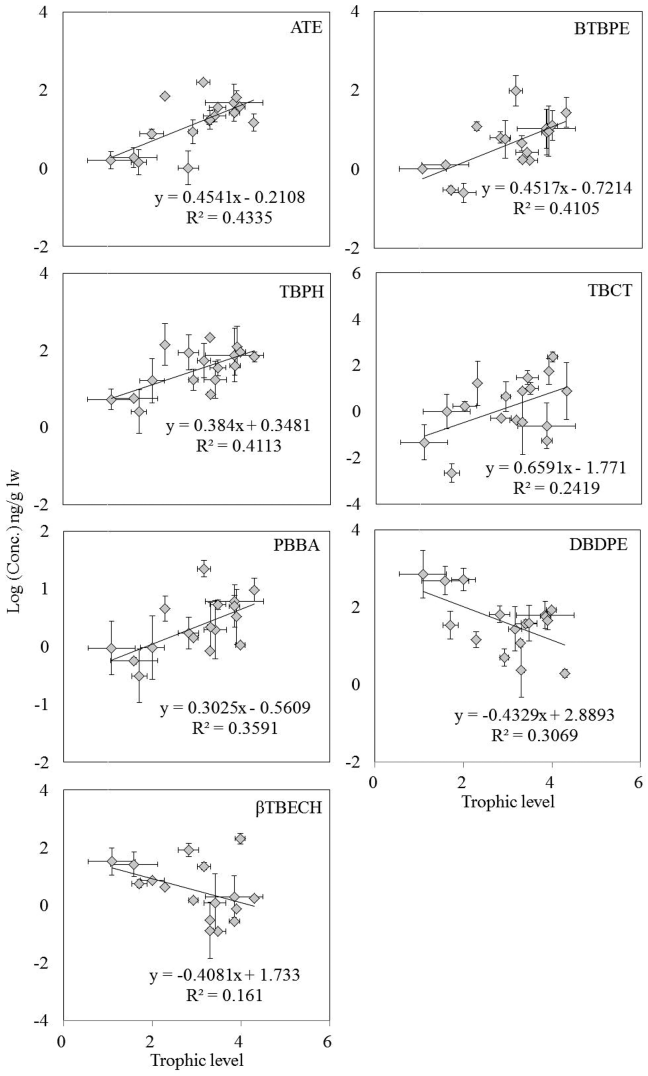

Figure 3. Relationship between concentrations of NBFRs (ng/g lw) and trophic levels of organisms in Lake Taihu, South China.

low TMFs. These results are consistent with the fact that log K_{OW} is an important factor influencing trophodynamics. One exception of the target NBFRs was TBPH, with a log K_{OW} of 10.08;[2] it exhibited significant trophic magnification in the food web possibly due to its high resistance to metabolism. It has been reported that log K_{OW} and metabolic rate both contribute to the trophic magnification potentials of compounds in the aquatic ecosystem.[22,23] For compounds with log K_{OW} about 10, their resistances to metabolism would also lead to the high trophic magnification potentials.[23] Some previous studies have reported the extremely low metabolic rates of TBPH to metabolism in the liver S9 fraction of fat-head minnow (CL = 9×10^{-6} mL/h/mg protein), carp (CL = 9×10^{-5} mL/h/mg protein), mouse (CL = 4×10^{-5} mL/h/mg protein), and human (CL ≈ 0), and the possible reason could be that the fully brominated phenyl ring of TBPH may exhibit steric hindrance when binding to metabolic enzymes.[26,32] Previous investigations of the trophic transfer of PAHs and PBDEs in Lake Taihu provided an opportunity to compare the TMFs of NBFRs with those of other chemicals. TMFs of ATE, TBCT, PBBA, and TBPH were comparable with those of PBDEs (1.97, 2.95, and 1.87 for BDE47, BDE100, and BDE154, respectively) with the same range of log K_{OW} (5.95−7.9),[45] but higher than

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Table 2. Parameters of Regression Analysis between Logarithm of Concentration and Trophic Levels, and *in Vitro* Intrinsic Clearance Values (mL/h/mg protein) of Target NBFRs[a]

	Trophodynamics		Crucian (TL = 2.93)			Carp (TL = 3.86)			Yellow-head catfish (TL = 4.3)		
Chemicals	Slope	TMFs	CL	r^2	$CL/CL_{B[a]P}$	CL	r^2	$CL/CL_{B[a]P}$	CL	r^2	$CL/CL_{B[a]P}$
ATE	0.4541	2.85	0.0038	0.1106	0.05	0.01	0.5251	0.14	0.0011	0.0066	0.01
BTBPE	0.4517	2.83	0.0058	0.5473	0.08	0.0046	0.608	0.06	0.007	0.2786	0.05
TBPH	0.3840	2.42	0.0014	0.1093	0.02	−0.0067	0.8948	−0.09	0.0091	0.4083	0.06
PBBA	0.3025	2.01	0.1224	0.77	1.59	−0.0244	0.343	−0.33	−0.0047	0.3149	−0.03
TBCT	0.6591	4.56	0.1141	0.9243	1.48	0.0145	0.7821	0.2	−0.0022	0.0852	−0.02
DBDPE	−0.4329	0.37	0.1051	0.7918	1.37	0.0727	0.8716	0.43	0.1616	0.7213	1.1
βTBECH	−0.4081	0.39	0.0112	0.7878	0.15	0.0274	0.8948	0.38	0.0136	0.7609	0.1
αTBECH	–	–	0.006	0.8288	0.08	0.0232	0.8531	0.32	0.0119	0.7488	0.08

[a]The values underlined represent statistically significant correlation ($p < 0.05$). r^2 is the coefficient value of regression between $\ln(C_t/C_0)$ and time in the microsomal incubations of NBFRs. The depletion curve of $CL_{B[a]P}$ in each specie is shown in Figure S3.

those of similar hydrophobic PAHs (TMFs: 0.91−1.9) in the Lake Taihu food web.[50] The different TMFs for these chemicals with similar log K_{OW} indicated that other factors, e.g., metabolism, could affect the trophic magnification potentials of compounds. Recent studies have demonstrated that metabolic rates of a chemical is another vital factor influencing the trophic magnification potentials; for instance, a compound that is slowly metabolized by animals exhibits the highest TMFs in the environment.[21,22] Therefore, metabolic rates of the target compounds in organisms along the trophic levels in the food web were further assessed.

Metabolic Rates. A substrate depletion approach has been established for the measurement of the *in vitro* intrinsic clearance rates for various chemicals.[22,24] Microsomes of crucian, catfish, and yellow-head catfish occupying increasing trophic levels in the food web (2.93, 3.86, and 4.3, respectively, Figure 2B) were used to obtain the intrinsic metabolic rates of the eight target NBFRs. The biotransformation of all of the target compounds followed the first-order kinetics in the liver microsomes of the three fish species (Figure 4). B[*a*]P was used as a benchmark compound to normalize the variations occurring across different batches of analyses,[22] and the depletion of B[*a*]P in the three species is shown in the SI, Figure S3. A summary of the *in vitro* metabolic rates for the eight compounds is presented in Table 2. ATE, BTBPE, and TBPH showed no significant metabolism after 24 h of incubations with the liver microsomes of the three species. DBDPE, αTBECH, and βTBECH underwent steady metabolism, and the CL of these compounds relative to that of B[*a*]P was determined to be 0.08−1.37. The results suggested that DBDPE is metabolized at a rapid rate similar to that of B[*a*]P. Different metabolic rates among the tested fish species were observed for TBCT and PBBA. TBCT exhibited relatively high metabolic rates when incubated with the liver microsomes of crucian and catfish ($CL/CL_{B[a]P}$ = 1.48 and 0.2, respectively), but no significant decline was found in the incubation with yellow-head catfish microsomes. Steady metabolism was observed for PBBA only in incubations with crucian microsomes ($CL/CL_{B[a]P}$ = 1.59). To the best of our knowledge, no information is available about the *in vitro* intrinsic clearance of NBFRs in fish. It is interesting to note that most of the NBFRs were resistant to the metabolism in fish occupying high trophic levels in the food web, and some compounds exhibited significant clearance in the microsomes of low-trophic-level fish (Table 2).

The *in vitro* metabolic rates of seven NBFRs in organisms at high trophic levels were found to be consistent with their trophodynamics in the aquatic food web (Table 2). Compounds showing no significant metabolism in the three fish species

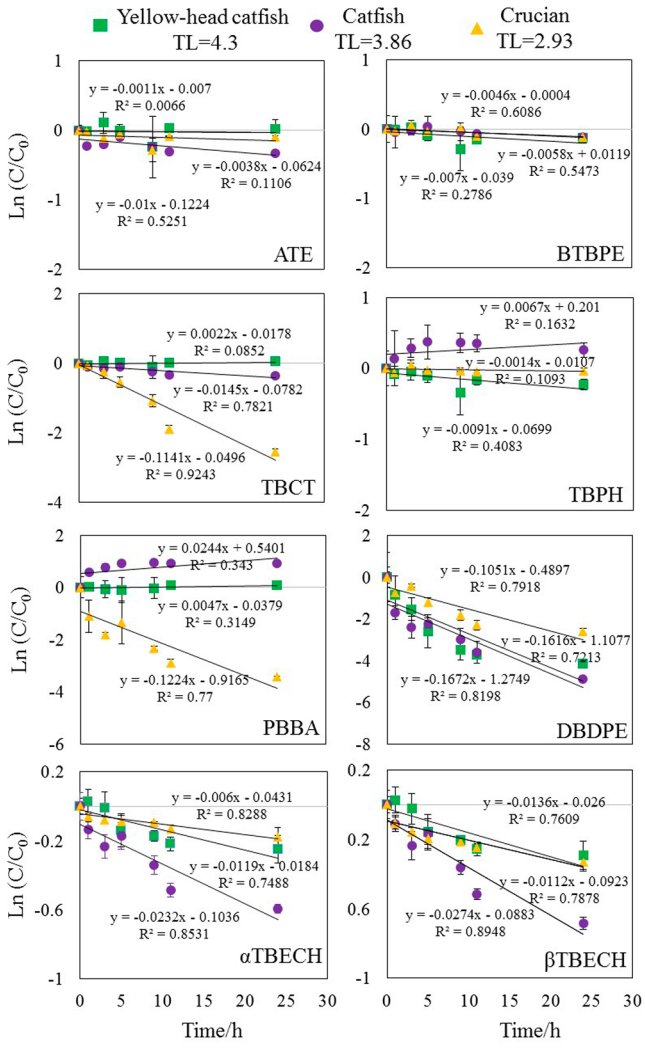

Figure 4. Concentrations of target NBFRs with incubation time in the incubations with liver microsomes of yellow-head catfish (green square), catfish (purple rectangle), and crucian (yellow triangle).

(ATE, BTBPE, and TBPH) exhibited significantly trophic magnifications (TMFs = 2.85, 2.83 and 2.42, respectively, $p < 0.05$). Compounds with rapid metabolic rates in the three fish species (DBDPE and βTBECH) underwent trophic dilution (TMFs = 0.37, $p < 0.05$) or did not biomagnify (TMFs = 0.39, $p > 0.05$) in the food web of Lake Taihu. Moreover, we could predict that αTBECH would not show a high trophic magnification in the

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aquatic food web on the basis of its measured metabolic rates. For TBCT and PBBA, though relatively low concentrations of the compounds in fish at low trophic levels (catfish and crucian) led to the less significant correlations of TMFs than those of ATE, BTBPE, and TBPH, the metabolic resistance of TBCT and PBBA in high-trophic-level fish (yellow-head catfish) resulted in the high trophic magnification potentials of the compounds. Therefore, metabolism of chemicals in the top-level organisms plays a more important role in the assessment of the trophic magnification potentials. In the previous studies, the decreased chemical elimination efficiency of organisms occupying increasing trophic levels was also reported on the basis of theoretical derivations together with experimental data, and the relationship resulted in the trophic-level differences in the bioconcentrations and biomagnifications of chemicals.[27,51] The results of this study are consistent with the hypothesis of previous studies, suggesting that decreased metabolism capacities in organisms occupying increasing trophic levels contribute to the trophic magnifications of the chemicals. In addition, measurement of metabolic rates of organisms at high trophic levels provided a more accurate trophic magnification assessment.

In summary, this study clarified the trophodynamic behaviors of NBFRs in the aquatic food web from Lake Taihu. The *in vitro* intrinsic clearance values of the target chemicals among three fish species with different trophic levels were assessed. Though the metabolic capacity of NBFRs varied among the three fish species, metabolic rates of organisms at high trophic levels were found to be consistent with their respective trophic transfer behaviors. Our results suggested that metabolism of organisms at high trophic levels plays an important role in the assessment of trophic magnification potentials of chemicals.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.est.7b06588.

Figures, and a table addressing (1) structures of target NBFRs; (2) GC-MS chromatogram of standards of NBFRs; (3) substrate depletion curves for B[a]P in three fish species; (4) descriptions of the biotas collected from Lake Taihu (PDF)

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Notes

The authors declare no competing financial interest.

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