Diastereoisomer- and Enantiomer-specific Profiles of Hexabromocyclododecane in the Atmosphere of an Urban City in South China

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Hexabromocyclododecanes (HBCDs) are ubiquitous contaminants in the environment, but little is known on the occurrence and distribution of HBCDs in the background atmosphere of urban environments. In this study, air samples were collected from four sites in the city of Guangzhou, a typical fast developing metropolitan of South China, for quantifying the concentration levels, diasteroisomer profiles, gas-particle distribution and enantiomeric fractions of HBCDs. The results showed that the measured mean atmospheric HBCD concentrations ranged from 0.69 to 3.09 pg/m³, which were similar to those reported from remote or urban sites of the U.S., but were significantly lower than those of Europe. The analysis on diastereoisomer profiles indicated that α-HBCD (59–68%) was the dominant isomer and β-HBCD was a minor isomer in all air samples, which appeared to be different from commercial products. A large variable percentage of HBCDs (69.1–97.3%) are existed in the particle phase, suggesting that long-range tansport of HBCDs might be occur in some environmental conditions. The results of enantiomeric fractions indicated that β- and γ-HBCD were racemic mixtures in the tested air samples and that (−)-α-HBCD was slightly enriched in the typical urban site, implying that the HBCDs in these studied sites might be a mixture of emissions from both local sources and soil-air exchange.

Introduction

Hexabromocyclododecane (HBCD), the third most produced brominated flame retardant (BFR), mainly used as additive BFR in building materials for thermal insulation, as well as in upholstery textiles and electrical household equipment (*1*). Since the production and use of penta- and octabromodiphenyl ethers has been banned in Europe, HBCDs might be an alternative for polybrominated diphenyl ethers (PBDEs) in some applications (*2*). Recent studies indicated that HBCDs are ubiquitous organic contaminants and share the major characteristics of persistent organic pollutants (POPs): persistency, bioaccumulation, long-range transport, and toxicity (*3*). They have been included on the OSPAR (The Convention for the Protection of the Marine Environment of the North-East Atlantic, OSPAR) list of chemicals for priority action (*4*). Although there are not any restrictions on the production or use of HBCDs, the increasing HBCDs concentration levels in environmental compartments have raised scientific concerns about their environmental behavior, toxicity, and risk assessment (*3, 5*).

The commercial HBCDs mainly consist of α-HBCD, β-HBCD, and γ-HBCD. The total concentrations of these diastereoisomers can be determined by gas chromatography (GC) with electron capture detection (ECD) or mass chromatography (MS). However, these techniques can not separately measure individual isomers due to thermal rearrangement at temperatures above 160 °C and thermal decompositions at temperature above 240 °C (*6–8*). Liquid chromatography coupled to mass spectrometry (LC-MS) or tandem mass spectrometry (LC-MS/MS) are currently preferred for separation and quantification of the diastereoisomers (*9*). The detailed information regarding analytical methodologies for determination of HBCDs in various environmental matrixes could be found in recent reviews (*3, 5, 10*).

Recent studies on HBCDs in the atmosphere from remote sites in Sweden and Finland and biota samples from Eastern Greenland and Svalbard (*3*) suggest that HBCDs could undergo long-range transport from western Europe and eastern North America to Arctic regions. However, the long-range transport route of HBCDs via the atmosphere still remains unclear. Many prior studies did not address the partition between the gas and the particulate phase even though it is an important process affecting the deposition and transport of HBCDs. Majority of the prior research mainly focused on the high exposure area such as HBCD and styrene manufacturing sites (*11*). The only available data for background locations have been reported in Scandinavian countries (*12, 13*) and the United States (*14*). Statistical data (*15*) indicated that Asian countries consumed 23% of the global HBCD production in 2001, and HBCD consumption is still growing. Limited data on HBCDs have been reported by Ueno et al. (*16*) for skipjack tuna and Isobe et al. (*17*) for small cetaceans. To our knowledge, no prior study reported the diastereoisomers and enantiomers of atmospheric HBCDs in Asia.

The purpose of this study was to investigate the atmospheric HBCDs through intensive sampling in an economically fast growing city, Guangzhou, South China (Figure 1). Guangzhou is the capital of Guangdong Province and is the largest metropolitan area in southern China. Furthermore, the distribution of the α-, β-, and γ-HBCD diastereomers, partition between gas- and particulate-phase, and enantiomeric fractions were also investigated in this study.

Experimental Section

Sampling Information. Four sampling sites were chosen to encompass a range of aerosol types and potential BFR sources (See Figure S1, Supporting Information). The detailed information in sampling sites was described in ref *18*. In brief, two industrial sites (Ind-1, Ind-2), one typical urban site (U-1), and a city background site on the top of the Baiyun mountain in Guangzhou (B-1) were included in this study.

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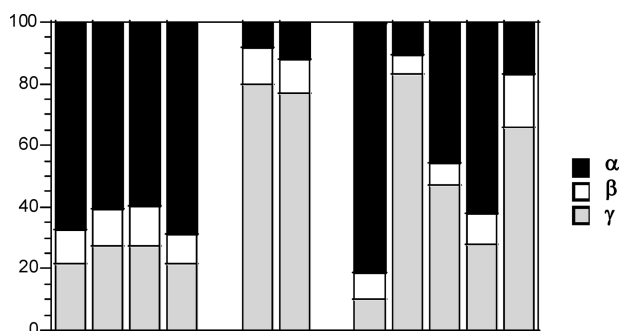**FIGURE 1. The comparison diastereoisomers profile in Guangzhou with commercial product and those reported in the United States.**

TABLE 1. The Total HBCDs Concentrations and Frequency of Detection at Four Sample Sites in Guangzhou

	mean	median	range	frequency of detection
U-1	3.09	3.21	2.20–3.92	16/16
B-1	1.67	1.61	1.14–2.25	16/16
Ind-1	0.69	0.68	0.28–1.18	16/16
Ind-2	0.89	0.66	0.40–1.78	13/16

Samplers were deployed on top of high buildings with heights of 15, 10, and 25 m at Ind-1, Ind-2, and U-1, respectively.

A sampler was installed outside a radar station at B-1. Thirty-two pairs of samples were collected simultaneously from the four sites during June 15–30, 2004. Air volumes of 417–952 m³ were drawn at 0.3–0.7 m³/min for 24 h through 20.3−25.4 cm GFF glass fiber filters (Whatman, Maidstone, England), and subsequently through 6.5 cm in diameter- 7.5 cm in thickness (a density of 0.030 g/cm³) polyurethane foam (PUF) plugs using a high-volume air sampler (Tianhong Intelligent Instrument Plant of Wuhan, China).

Materials. Native and $^{13}C_{12}$-labeled α-, β-, γ- HBCD were purchased from Cambridge Isotope Laboratories (Andover, MA) and used as received. All of the solvents used for the extraction and cleanup were redistilled using a glass system. Neutral silica gel (80–100 mesh) and alumina (100–200 mesh) were Soxhlet extracted with a mixture of 1:1 methylene chloride:methanol for 72 h prior to use. Sodium sulfate was baked at 450 °C and stored in sealed containers. The HPLC-grade methanol and acetonitrile were obtained from Merck (Darmstadt, Germany). Ammonium acetate was from JT Baker (Phillipsburg, NJ). Commercial HBCD (including high-melting and low-melting products) were received as a gift from one of the biggest HBCD manufacturing plants in China (Qingdao Haida Chemical Co., Qingdao, China).

Sample Preparation and Cleanup. Before use, GFFs were baked at 450 °C for 12 h to remove any organic contaminant, and PUF plugs were Soxhlet extracted for 48 h with each of following solvents: methanol and 1:1 acetone-hexane. The sample extraction and cleanup procedures were used which has been described in ref *18*. Briefly, the PUF plugs and GFF filters were spiked with PCB 209 and ^{13}C-PCB 141 and were Soxhlet extracted with a mixture of acetone:hexane (1:1) for 72 h. Activated copper granules were added during extraction for removing elemental sulfur. Concentrated extracts were cleaned and fractionated on acid/ basic multilayer silica gel columns with 70 mL of methylene chloride:hexane (1:1). The final extracts were concentrated to 200 µL under a gentle nitrogen stream and a known amount of internal standard (^{13}C-PCB 208) was added. After finishing PBDEs analysis by GC-MS, the extracts were further cleaned up on acidified silica and eluted with a mixture of methylene chloride and hexane, which is helpful for decreasing matrix effects. For determination of HBCD diastereomers, the solvent was exchanged to methanol for LC-MS/MS analysis. $^{13}C_{12}$-labeled α-, β-, and γ- HBCD were added as internal standards for diasteroisomer and enantioisomer determination.

Chemical Analysis. An Agilent 1100 series liquid chromatograph (Agilent Technologies, Palo Alto, CA) coupled to an Applied Biosystems/Sciex API 4000 triple quadrupole mass spectrometer (Applied Biosystems, Foster City, CA) was used. Injection volume was 10 µL and the flow rate was 0.5 mL/min. The mass spectrometer was operated in electrospray ionization negative ion mode with multiple reaction monitoring (MRM). The $(M-H)^- \rightarrow Br^-$ transition at m/z 640.6 → 79 and 652.6 → 79 was monitored for the three native and $^{13}C_{12}$-labeled HBCD isomers, respectively. MS/MS optimized parameters for three HBCD isomers were described in ref *29* in detail.

For the separation of HBCD diastereoisomers, a Zorbax SB-C18 reversed-phase column (4.6 × 250 mm, 5 µm, Agilent) was used. The gradient mobile phase consists of methanol (A)/ acetonitrile (B)/water with 10 mM ammonium acetate in water (C). Flow rate was set at 0.5 mL/min. The gradient program started at an initial composition of 80:10:10 A/B/C (V/V) and was ramped to 50:40:10 A/B/C in 18 min, followed to 30:70 A/B at 23 min, and was held for 7 min, then returned to 80:10:10 A/B/C in 8 min. The column was equilibrated for a further 6 min.

For the separation of HBCD enantiomers, a Luna 3u C18(2) reversed-phase column (4.6 × 150 mm, 3 µm, Phenomenix) coupled to a chiral NUCLEODEX beta-PM column (Macherey-Nagel GmbH and Co, Düren, Germany) LC (4.0 × 200 mm, 5 µm) were used. The gradient mobile phase consists of methanol (A)/ acetonitrile (B)/water with 10 mM ammonium acetate in water (C). Flow rate was set at 0.4 mL/min. The gradient program started at an initial composition of 30:60:10 A/B/C (V/V) and was ramped to 25:65:10 A/B/C in 20 min, followed to 30:70 A/B at 30 min, and was held for 5 min, then return to 30:60:10 A/B/C in 7 min. The examples of chromatographic separation of HBCD diastereoisomers and enantiomers can be seen in Figure S2, Supporting Information.

The enantiomeric signatures were expressed as enantiomer fractions (EFs), calculated as the peak areas of the enantiomeric pairs by the following formula:

$$EF = \frac{(+A)}{(-)A + (+)A} \quad (1)$$

Considering the matrix effect and mass response, $^{13}C_{12}$-labeled α-, β-, and γ-HBCD were added as internal standard for both quantification and correction of EF values, which is described in ref *29*.

For confirming the elution order, enantiomerically pure α-, β-, γ- HBCDs were prepared using chiral NUCLEODEX beta-PM column which was used in ref *19*, then the optical rotation of each individual was measured to determine their elution order. The individual enantiomer fractions were then run on the C18 (achiral)/cyclodextrin (chiral) LC-MS/MS system to determine the elution order and further used to determine the atmospheric samples. The enantiomer fractions of HBCDs in gas-phase were not determined due to their low concentrations.

QA/QC. Field blanks were prepared by loading a PUF plug and GFF filter to the sampler for 24 h at each site during the sampling period with no air drawing through. The procedural blanks were analyzed sequentially with the samples. No analyte was detected in either the field blanks or the procedural blanks. The recoveries from 18 spiking experiments (α-, β-, γ- HBCDs at three concentration levels of 1, 4, and 10 ng were spiked into nine clean GFF filters and nine PUF plugs) and ranged from 65.5 to 80.7%, 61.2 to 68.6%,
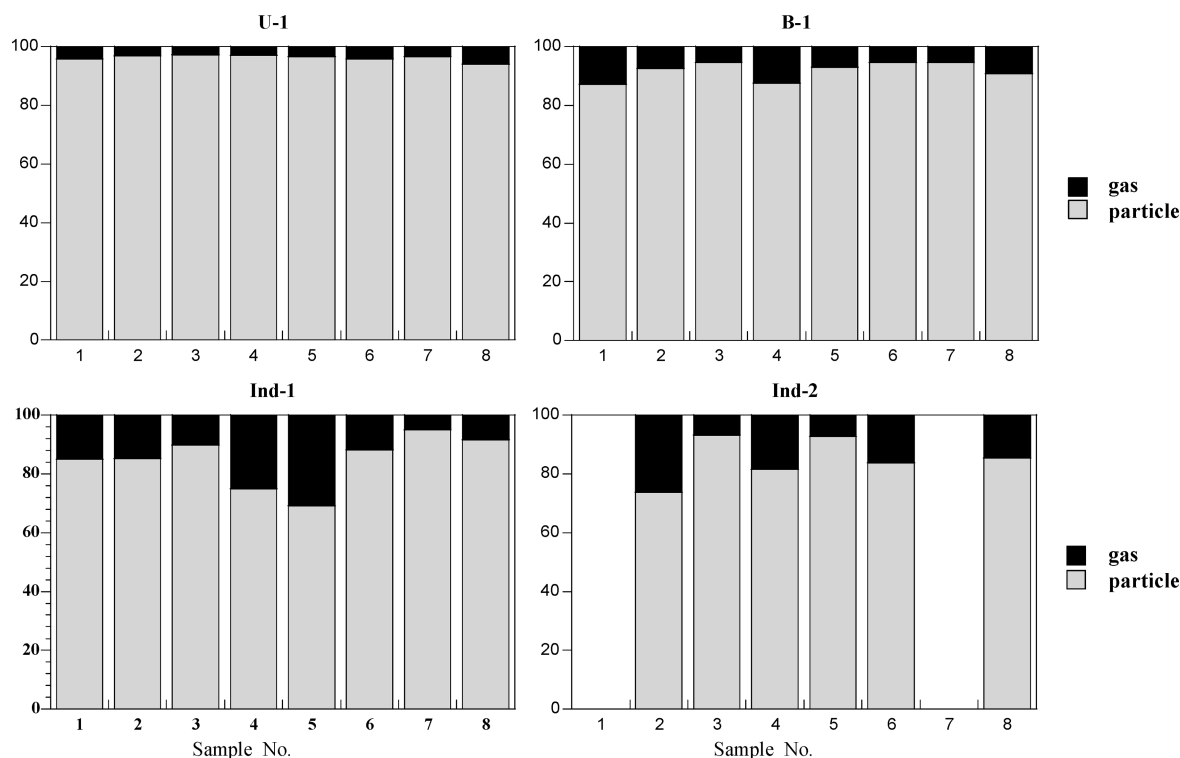
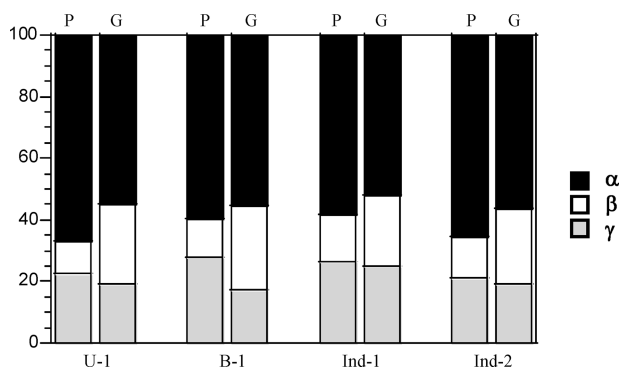FIGURE 2. Relative distribution of total HBCDs between the gas- and particle-phase at the four sampling sites.

FIGURE 3. The diastereoisomers profile in gas- and particle-phase in Guangzhou.

and 70.% to 79.3%, respectively. All the samples were analyzed in triplicate by both LC-MS/MS and chiral LC-MS/MS. Reported concentrations were not surrogate recovery corrected.

Results and Discussion

Concentration Levels and Distribution. All the α-, β-, and γ-HBCD in gas- and particle-phase of the four sampling sites were determined by LC-MS/MS. The detection frequency of three diastereoisomers in U-1, B-1, and Ind-1 were 100%, whereas three samples (including two gas- and one particle-phase) in Ind-2 were below the detection limit. The sum concentrations of total HBCDs (ΣHBCDs) including gas- and particle-phase were summarized in Table 1. As shown in Table 1, the mean (median) values of atmospheric ΣHBCDs in the four sites are 3.09 (3.21), 1.67 (1.61), 0.69 (0.68), and 0.89 (0.66) pg/m³ for U-1, B-1, Ind-1, and Ind-2, respectively. The HBCD concentrations of in U-1 were substantially higher than those in Ind-1 and Ind-2, suggesting that urban areas are the source of this compound.

It was also consistent with the BSEF technical report about HBCD applications, which is mainly used as flame retardant

in building materials and upholstery textiles (*15*). The mean and median concentrations of HBCDs for the B-1 samples were generally higher than those at the Ind-1 and Ind-2 sites, even though B-1 was chosen as the background site in our study. It may be the result of recently increased construction activities for residential houses around the Baiyun mountain area. However, relatively high PBDE concentrations in Ind-1 and Ind-2 were reported in our previous study (*18*). This is likely because the two sites are close to a large industrial park that included heavy users of electronic/electrical equipment, plastics, textile, polyurethane foam, and auto-mobile manufacturing, which are large consumers of BFRs but not HBCD users. Table S1 in the Supporting Information summarizes the currently available atmospheric HBCDs data in background, rural/remote, and working environments at plants producing extruded polystyrene foam using HBCDs as flame retardant. Our HBCD concentration data (0.7–3.1 pg/m³) were similar to those (0.6–4.5 pg/m³) of the five U.S. sites (urban, semiurban, agricultural, and remote) from Lake Michigan through the Midwest to the Gulf of Mexico (*14*). The reported European atmospheric HBCD concentrations ranged from 2 to 280 pg/m (*3*) from remote sites in North Sweden and Finland, and 76–610 pg/m³ from urban air in Stockholm, Sweden (*13*). Notably, up to 150 μg/m³ of HBCDs were detected from the plants manufacturing extruded polystyrene foam flame retarded with HBCDs in Norway. The much higher concentration levels of HBCDs in European background atmosphere could be due to the fact that HBCDs were used to replace the penta- and octa-BDE products in Europe much earlier than in North America and Asia (*15*). In 2001, the market consumptions for HBCD were about 9500, 3500, and 2800 tons for Europe, Asia, and North America, respectively.

Diastereoisomers Profiles. The diastereoisomer profiles in four sampling site were shown in Figure 1. The detailed concentrations of α-, β-, and γ-HBCD in the gas- and particle-phase are summarized in Table S2 of the Supporting Information. The profiles of commercial products in China (low-melting point and high-melting point products), and

TABLE 2. Enantiomer Fractions for α-, β- and γ-HBCD in the Particle-Phase in Guangzhou

location	α-HBCD		β-HBCD		γ-HBCD	
	EF	SE	EF	SE	EF	SE
U-1	0.413	0.008	0.517	0.007	0.507	0.015
B-1	0.472	0.019	0.490	0.010	0.516	0.008
Ind-1	0.482	0.015	0.476	0.011	0.540	0.011
Ind-2	0.493	0.007	0.507	0.022	0.520	0.006
commercial product						
LMP[a]	0.483	0.007	0.497	0.007	0.522	0.006
HMP[b]	0.487	0.010	0.511	0.004	0.518	0.007

[a] Low-melting point product. [b] High-melting point product.

those reported from the United States were also included in Figure 1. As indicated in Figure 1, the diastereoisomers profiles of HBCDs in our sampling sites were different from those of commercial HBCDs. All the air samples were dominated by α-HBCD (59–68%), whereas γ-HBCD (77–80%) was the dominant isomer in commercial products. β-HBCD was detected in the smallest amounts for all cases. Hoh and Hites (15) reported variable profiles in the background air samples from the United States, with three of the seven samples dominated by γ-HBCD, one had approximately equal amounts of α-HBCD and γ-HBCD, and three were dominated by α-HBCD. Thomsen et al. (20) found that the γ-HBCD was the dominated isomer in the working environment from the plant manufacturing extruded polystyrene foam. Furthermore, the HBCDs diastereoisomer profiles have also been analyzed in various biota and sediment samples (3, 21). α-HBCD and γ-HBCD are usually the dominant isomer in the most biota and sediment samples, respectively. However, concentrations of α-HBCD in some sediments were also much higher than those of γ-HBCD (22). To date, it is still unclear whether the variable diastereoisomer profile of HBCDs is caused by thermal isomerization during the processing of HBCDs or by stereoisomer-specific environmental processes (3). The previous study indicated that γ-HBCD might be converted to α-HBCD above 160 °C, and incorporating HBCD into plastic sometimes requires this temperature (23, 24). Therefore, the dominant isomer can be converted from γ-HBCD to α-HBCD during this process. Apparently, for a better understanding of the sources of HBCD isomers, more air samples should be further investigated.

Gas-Particle Distribution. Table S2 in the Supporting Information showed the particle- and gas-phase concentrations (pg/m³) of HBCDs at all the four sampling sites. The relative distributions of the total HBCDs and each diastereoisomers between the gas- and particle-phase were shown in Figures 2 and 3. As shown in Figure 2, the HBCDs presented in the particle phase are 95.0–97.3%, 87.2–94.7%, 69.1–95.1%, and 73.8–93.2% for U-1, B-1, Ind-1, and Ind-2, respectively. It is obviously indicated that the variety of gas- and particle-phase distribution fall into narrow range, suggesting that U-1 samples appeared to be closer to equilibrium than at other sites. These results were similar to those of PBDE partitioning between gas- and particle-phase in our previous study on the same four sampling sites (18). It might be due to the fact that U-1 located in a highly populated area with heavy traffic flows and TSP in this site should be enriched with soot-type particulates, which have a strong tendency to adsorb and/or absorb HBCDs (18). For Ind-1 and Ind-2 sites, the variable distribution of HBCDs seems implied that some fresh HBCDs may continue to emit into the atmosphere from local sources so that an equilibrium state could not be established. For gas-particle distribution on each diastereoisomers, the similar trend in all the sites was observed that the percentage of β-HBCD in gas phase is higher than those in particle phase (Figure 3), whereas the percentage of α- and γ-HBCD in gas phase is lower than those in particle

phase. The average relative abundances of three diastereoisomers in gas- and particle-phases are 55/25/20 and 62/13/25, respectively. This might be caused by slightly different physicochemical properties of three diastereoeoisomers. We do not have data about octanol/air (K_{oa}) partition coefficient of three HBCD diastereoisomers, but Hayward (25) reported that the Log K_{ow} of α-, β-, and γ-HBCD are 5.47, 5.07, and 5.12, respectively.

Gas-particle distribution is an important process affecting the deposition, transport and subsequent fate of HBCD. It is intuitive that low volatility (4.7×10^{-7} mmHg) and low water solubility (3.4 µg/L) allow HBCDs to be primarily sorbed to environmental solids such as atmospheric particulate matter (16, 26). Thus, it is difficult for long-range transport and tends to deposit near point sources (27). However, Remberger et al. (13) detected HBCDs in remote background air sample from Sweden and Finland, and suggested long-range atmospheric transport potential of this compound. Our result indicated that a large percentage of HBCDs (69.1–97.3%) can be sorbed to atmospheric particulate matter and that long-range transport of HBCDs would occur under certain environmental conditions.

Enantiomer Fractions of HBCD Diastereoisomers. The enantiomers of α-, β-, and γ-HBCD were determinated by LC-MS/MS using the method described in experimental section. Before the determination, it was assumed the HBCD standards are racemic mixtures, with an EF value of 0.50. Indeed, the calculated EF values based on the response areas for α-, β-, and γ-HBCD, are 0.487 ± 0.011, 0.490 ± 0.007, and 0.510 ± 0.005 ($n = 6$), respectively. The slight deviation of EF values for chiral organic contaminants were often founded no matter whether GC-MS or LC-MS/MS were used for determination. It might be related to the enantiomeric purity of the standard (28). They might be also derived from the unequal response of the enantiomers when LC-MS/MS was used for analysis. Marvin et al. (29) examined the potential influences of column bleed and mobile phase on EF values of HBCDs. Their result confirmed that mobile phase could affect the response of enantiomers. Dodder et al. (30) also observed that the response of the mass spectrometer between the elution of the two enantiomers was changed due to the extracted matrix component. In our study, we also found that mobile phase compositions would affect both the chromatographic separation and sensitivity of diastereoisomers. The EF values in the recovery experiments of this study are 0.493 ± 0.012, 0.489 ± 0.009, and 0.502 ± 0.008 ($n = 6$) for α-, β-, and γ-HBCD, respectively, suggesting that no enantiomeric fractionation occurred during the sample preparation and cleanup.

Table 2 summarized the EF values for α-, β- and γ-HBCD in the particle-phase. The EF values of HBCDs in gas-phase were not determined due to low concentration levels in all the samples. Statistic analysis was conducted using SPSS software and the comparison of EF values between HBCDs in air samples and commercial products (including low-melt pointing and high-melt pointing product) was conducted

using independent-samples *t* test. As shown in Table 2, the mean EF values of β- and γ-HBCD in four sample sites range from 0.476 to 0.517, and 0.507 to 0.540, respectively, whereas the EF values of the two commercial products obtained in the Chinese manufacturing plant are 0.497–0.511, and 0.518–0.512 for β- and γ-HBCD. Statistic analysis indicated that the slight shift of both EF values was not significantly different ($P > 0.05$). It appeared that no stereoselective transformation existed for these two diastereoisomers in our study. However, the EF values of α-HBCD in four sites presented variable data, with ranging from 0.417 to 0.493. EF value of α-HBCD in U-1 is 0.413 ($P < 0.05$), suggesting that HBCDs in soils might be partially contributed to the atmospheric concentration. It should be mentioned that, for sample U-1, α-HBCD had experienced enantioselective reduction, whereas β- and γ-HBCD had shown racemic distribution. These two contradictory phenomena could be explained as follow. First, the α-HBCD in U-1 site is the highest concentrations in all air samples. It is known that higher concentration levels often result in elevated biotransformation rates and thus an EF different from racemic 0.50. This is consistent with Janák et al. (*31*) and Bidleman et al. (*32*). Second, the results of gas-particle distribution quantified in this study indicated that HBCDs in U-1 sites get closer equilibrium between gas- and particle- phase, and some HBCDs in soils near U-1 sites might contribute to the atmospheric HBCDs (*33*). Variable distribution patterns in Ind-1 and Ind-2 sites implied that HBCDs might be emitted directly into the atmosphere from local sources. Several prior studies (*30, 34, 35*) have reported the selective accumulation of different HBCD enantiomers in marine fish herring, predatory birds, and dolphins. To our knowledge, this is the first report of the enantiomer fractions for HBCDs in air samples. Chiral signatures in organic comtaminat has been successfully used in several previous studies for assessment of source apportionment and long-range transport in many studies. Future studies on chiral HBCDs in air and sediment are needed for understanding the source and fate of this high volume BFR product.

Acknowledgments

Supporting Information Available

Table SI, atmospheric HBCDs concentrations in the literature; Table S2, particle- and gas-phase concentrations (pg/m³) of HBCDs in the Guangzhou; Figure S1, map of air sampling sites; Figure S2, chromatographic separation of HBCD diastereoisomers and enantiomers in a standard mixture and air samples. This material is available free of charge via the Internet at http://pubs.acs.org.

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ES7027857