

Synthesis of ^{13}C -labeled mixed halogenated PXDDs (X=Cl, Br)

R. Luijk, G. Zwick, K. Hedwig, L. Stieglitz

Kernforschungszentrum Karlsruhe, P.O. Box 3640, D-76021 Karlsruhe, Germany

1. Introduction

The central objective of this study was the synthesis of ^{13}C -labeled mixed brominated chlorinated dibenzo-p-dioxins. Pure components or eventually a mixture of these labeled compounds will enable the quantification of their native analogues in fly ash samples from waste incineration processes.

Due to the toxicity and high cost price of the dibenzo-p-dioxin standards (starting compounds) the synthesis of mixed bromochlorodioxins has to be conducted on a microgram scale. Furthermore, the synthesis has to be directed towards mono- and dibrominated compounds because of their occurrence in MWI fly ashes. Four methods will be tested for the synthesis of mixed brominated chlorinated dibenzo-p-dioxins.

- (1) Bromination of polychlorodibenzo-p-dioxins by Br_2 ¹⁾
- (2) Partial exchange of bromine in polybromodibenzo-p-dioxins by CuCl_2/HCl in a gas-solid phase reaction on a model fly ash system²⁾
- (3) Partial exchange of bromine in polybromodibenzo-p-dioxins by CuCl_2/KCl in a solid phase reaction on a model fly ash system
- (4) Bromination of polychlorodibenzo-p-dioxins by FeBr_3 in a heterogeneous system³⁾

These methods will be evaluated with unlabeled starting materials. The results of synthesis methods (1) and (2) are presented in this paper. Methods (3) and (4) will be tested in the near future. The best method will be used in the synthesis of ^{13}C labeled compounds.

2. Experimental

The experimental details of methods (1) and (2) are described in literature^{1,2)}. Method (1) was applied to two solutions. Solution I contained 2,7-dichloro- and 2,3,7-trichlorodibenzo-p-dioxin, and solution II contained 1,2,3,4-tetrachloro-, 1,2,3,7,8-pentachloro-, 1,2,3,4,7,8-hexachloro- and 1,2,3,4,6,7,8-heptachlorodibenzo-p-dioxin, respectively. The starting amount was 2.5 μg for each isomer in solution I and 1.25 μg for each isomer in solution II. The electrophilic aromatic bromination (E.A.B.) of polychlorodibenzo-p-dioxin precursors was conducted in CHCl_3 at room

temperature (24 h) and under reflux conditions at 61 C (2 h). A solvent exchange procedure on a 1 g Alox column was conducted to remove original solvents n-nonane and toluene. Method (2) was applied to 2,3,7,8-tetrabromodioxin. A solvent exchange on a 20 g Alox column was conducted to remove n-nonane. The starting compound 2,3,7,8-Br₄DD (0.5 µg/g) and the catalyst CuCl₂ (0.5 wt%) were impregnated on a Mg-silicate carrier by pore volume impregnation from a solution in methanol. The exchange reactions were performed in a fixed bed vertical tube reactor. The sample size was 2 g. A flow of nitrogen (50 mL/min) containing 5 vol. % HCl was passed through the fixed bed. The reaction time was 5, 10 and 15 min at 300 C, respectively, and 10 min at 275 C (all experiments as single experiments).

Analysis of mixed bromochlorodibenzo-p-dioxins was performed with HR-GC/MSD (HP 5890-5970 series); SIM-mode, DB-5 (30 m, i.d. 0.32 mm, d_f 0.25 µm), on column injection (1 µL, pressure 0.6 bar), T-program 80 C (4 min) $\xrightarrow{30^{\circ}\text{C}/\text{min}}$ 200 C (0 min) $\xrightarrow{5^{\circ}\text{C}/\text{min}}$ 300 C (20 min). The samples were also analyzed with HR-GC/AED (HP 5921A-5890 series) under similar conditions; DB-5 (30 m, i.d. 0.32 mm, d_f 0.25 µm), split splitless injection (1 µL, iso-octane), T-program 80 C (2 min) $\xrightarrow{30^{\circ}\text{C}/\text{min}}$ 200 C (0 min) $\xrightarrow{5^{\circ}\text{C}/\text{min}}$ 300 C (20 min). Emissions lines of Br and Cl were measured at 478.550 and 479.454 nm, respectively.

3. Results and discussion

Method (1) Bromination of polychlorodibenzo-p-dioxins by Br₂

The results of the bromination of two standard solutions (solution I contained 2,7-dichloro- and 2,3,7-trichlorodibenzo-p-dioxin, solution II contained 1,2,3,4-tetrachloro-, 1,2,3,7,8-pentachloro-, 1,2,3,4,7,8-hexachloro- and 1,2,3,4,6,7,8-heptachlorodibenzo-p-dioxin, respectively) are shown in Figs. 1(a) and 1(b). These figures show the chromatograms of the reaction products of E.A.B. at 61 C (2 h). At room temperature only negligible amounts of brominated products were observed for solution I, while solution II showed no brominated products at all. At 61 C mono- to tetrabrominated products were observed in solution I and mono- to tribrominated products in solution II. Table I shows the different products of E.A.B. with their absolute yields in ng and nmole and their relative yields to the starting materials. Two analysis methods were applied, GC-MSD and GC-AED. The latter one is assumed to furnish more reliable data, because unlike GC-MSD, no discrimination between the products is expected to occur in the detector part. GC-AED offers an appropriate means to verify response factors applied for mixed bromochloro compounds in the GC-MSD analysis.

After stirring for 2h at 60 C di- to tetrachlorodibenzo-p-dioxin were disappeared almost completely. The higher chlorinated starting materials showed little reactivity. Obviously, the reactivity is related to the number of chlorine substituents in the starting compound. Chlorine substituents exercise a deactivating influence on electrophilic aromatic bromination.

(a)

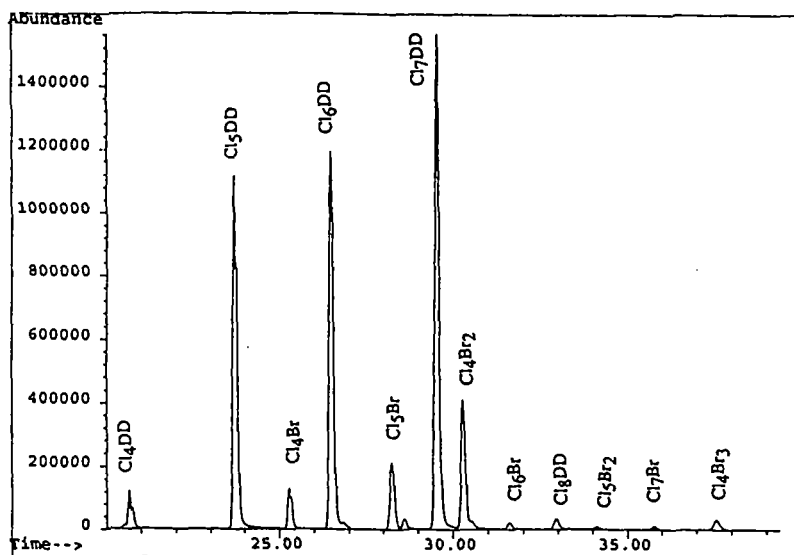
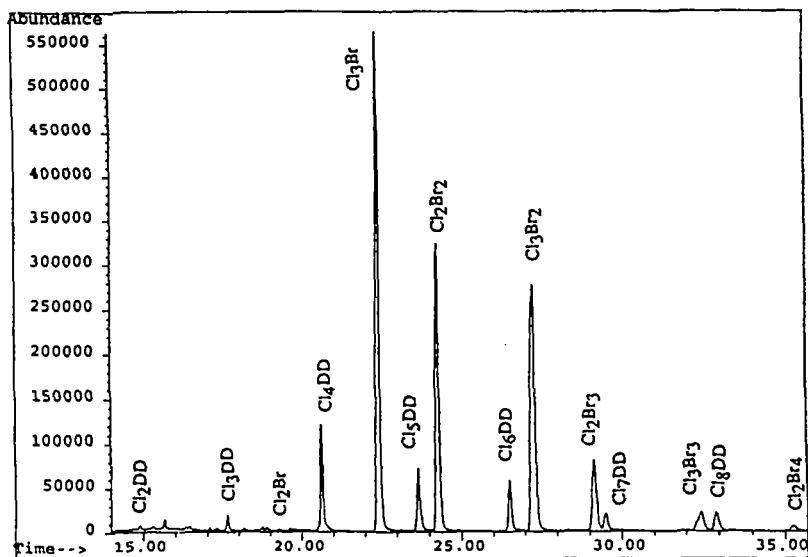


Figure 1. GC/MS Total Ion Currents (TICs) of E.A.B. experiments at 61 C, 2h of (a) solution I (2,7-Cl₂DD and 2,3,7-Cl₃DD) and (b) solution II (1,2,3,4-Cl₄DD, 1,2,3,7,8-Cl₅DD, 1,2,3,4,7,8-Cl₆DD and 1,2,3,4,6,7,8-Cl₇DD)

ANA

Table I. The results of E.A.B. experiments of di- to heptachlorodibenzo-p-dioxin at 61 C, 2h

					GC/MS				GC/AED
					yield				yield
	Mw		ng	nmole	%		ng	nmole	%
Cl ₂ DD	252		2	0,00	0,17		77	0,31	6,55
Cl ₂ BrDD	332		1	0,00	0,06		n.d.		
Cl ₂ Br ₂ DD	410		443	1,08	23,17		313	0,76	16,37
Cl ₂ Br ₃ DD	490		202	0,41	8,84		472	0,96	20,66
Cl ₂ Br ₄ DD	568		32	0,06	1,21		360	0,63	13,59
		total	680	1,56	33,46		1222	2,67	57,18
Cl ₃ DD	286		8	0,03	0,68		83	0,29	7,1
Cl ₃ BrDD	366		670	1,83	44,56		402	1,10	26,9
Cl ₃ Br ₂ DD	446		326	0,73	17,79		502	1,13	27,5
Cl ₃ Br ₃ DD	524		146	0,28	6,78		197	0,38	9,2
		total	1150	2,87	69,81		1184	2,89	70,35
Cl ₄ DD	322		10	0,03	0,84				
Cl ₄ BrDD	400		91	0,23	6,17				
Cl ₄ Br ₂ DD	480		472	0,98	26,57		266	0,55	14,91
Cl ₄ Br ₃ DD	558		163	0,29	7,92				
		total	1681	3,50	41,5				
Cl ₅ DD	368		861	2,34	72,51				
Cl ₅ BrDD	436		222	0,51	15,78				
Cl ₅ Br ₂ DD	514		40	0,08	2,41				
		total	1123	2,93	90,70				
Cl ₆ DD	390		1230	3,15	103,58				
Cl ₆ BrDD	470		20	0,04	1,40				
Cl ₆ Br ₂ DD	548		3	0,00	0,18				
		total	1253	3,20	105,16				
Cl ₇ DD	426		1573	3,69	132,46				
Cl ₇ BrDD	504		41	0,08	2,92				
		total	1614	3,77	135,38				

Moreover, a discrimination between lateral and non-lateral positions is assumed due to the charge density distribution in the aromatic ring. Therefore, 1,2,3,4-Cl₄DD is expected to undergo electrophilic bromination more easily than 2,3,7,8-Cl₄DD. The main E.A.B. products of the di- tri- and tetrachlorodibenzo-p-dioxin precursors are Cl₂Br₂DD, Cl₃BrDD and Cl₄Br₂DD, respectively. The overall yields including unreacted starting material vary from 40% to 135%. The low overall yields for the reaction of di- to tetrachlorodibenzo-p-dioxin were also observed in the E.A.B. experiments at 25 C. Therefore, it is concluded that the solvent exchange procedure on a micro Alox column (1 g) gives rise to substantial losses of starting materials.

A general trend is observed in the comparison of GC/MS and GC/AED data. Within the series of $\text{Cl}_2\text{Br}_x\text{DD}$ and $\text{Cl}_3\text{Br}_x\text{DD}$ ($x=1-4$) the yield of higher brominated compounds ($x>3$) is underestimated in the GC/MS analysis where response factors of 1 (relative to nearest eluting PCDD standard) were applied. The response of a quadropool mass spectrometer decreases rapidly in the higher mass range (400-800 amu). Therefore, GC/AED offers a useful technique to calculate relative response factors for mixed bromochlorodibenzo-p-dioxins. Unfortunately, in this experiment the yield of the higher brominated compounds was too low to calculate reliable response factors.

The mass chromatograms of the brominated products of 2,7-dichlorodibenzo-p-dioxin reveal a selective route of bromination. According to the available literature a selectivity for the lateral 2,3,7,8-positions is postulated. The predicted products are 2,7- Cl_2 -3-BrDD, 2,7- Cl_2 -3,8-Br₂DD. Further isomer-specific assignment of the products is difficult to obtain. Steric and electronic influences of bromine and chlorine substituents have to be taken into consideration.

Method (2) Partial exchange of bromine in polybromodibenzo-p-dioxins by CuCl_2/HCl in a gas-solid phase reaction on a model fly ash system

The results of the bromine-chlorine exchange reaction in 2,3,7,8-Br₄DD at 275 C and 300 C are shown in Fig. 2. The overall recovery of the exchange products and the unreacted starting material was about 30% in all experiments. The quantification of starting material and reaction products was performed with ¹³C-labeled PCDD standards. For the mixed halogenated compounds relative response factors were estimated from the relative response of tetrachloro- versus tetrabromodibenzo-p-dioxin ($\text{Cl}_4\text{DD} = 1$, $\text{Cl}_3\text{BrDD} = 0.75$, $\text{Cl}_2\text{Br}_2\text{DD} = 0.5$, $\text{ClBr}_3\text{DD} = 0.35$, $\text{Br}_4\text{DD} = 0.25$).

Increasing the reaction time at 300 C from 5 to 10 and 15 minutes resulted in a shift towards the more chlorinated products. Decreasing the temperature to 275 C resulted in a slower exchange rate.

The mass chromatograms of the exchange products showed single peaks for all exchange products. Only for 2,3,7,8-substituted dibromo-dichlorodibenzo-p-dioxin there is more than one isomer possible. However, according to the retention index calculation method of Donnelly *et al.*⁴⁾ only a small distinction of 3 Retention Index (RI) units between 2,3-Br₂-7,8-Cl₂-dibenzo-p-dioxin and 2,7-Br₂-3,8-Cl₂-dibenzo-p-dioxin is calculated. No distinction is calculated between 2,7-Br₂-3,8-Cl₂-dibenzo-p-dioxin and 2,8-Br₂-3,7-Cl₂-dibenzo-p-dioxin. Therefore, it is not clear whether a selective route of substitution is followed.

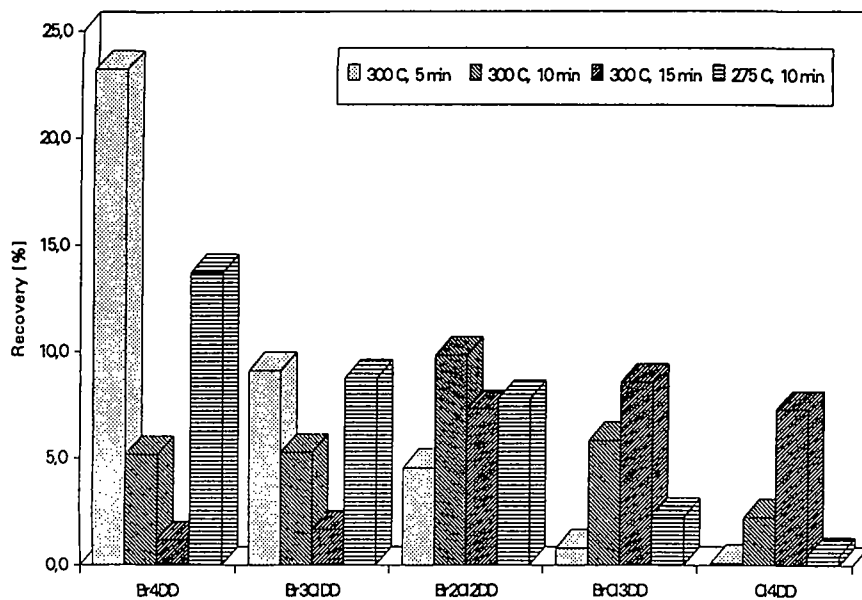


Figure 2. The bromine-chlorine exchange in 2,3,7,8-Br₄DD (yield in %)

4. References

- 1) Kende A.S., J.J. Wade, D. Ridge, A. Poland (1974) *J. Org. Chem.* 39, 931-937
- 2) Luijk R., C. Dorland, P. Smit, J. Jansen, H.A.J. Govers (1994) *Chemosphere* 28, 1299-1309
- 3) Nestrick T.J., L.L. Lamparski., T.L. Peters (1989) *Chemosphere* 18, 1761-1770
- 4) Donnelly J.R., W.D. Munslow, A.H. Grange, T.L. Pettit, R.D. Simmons, K.S. Kumar, G.W. Sovocool (1991) *Biol. Mass Spectrom.* 20, 329-337