

A Rapid Synthesis of ^{13}C -Labelled Internal Standards for the Analysis of Brominated Dibenzo-p-dioxins and Dibenzofurans and Mixed Brominated/Chlorinated Dibenzo-p-Dioxins

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Abstract

$^{13}\text{C}_{12}$ -labelled mono- and dibromodibenzo-p-dioxin and mono-, di- and tribromodibenzofuran isomers were photochemically synthesized from commercially available $^{13}\text{C}_{12}$ -2,3,7-tribromodibenzo-p-dioxin and 2,3,7,8-tetrabromodibenzofuran. *n*-alkane solutions of these compounds were irradiated for several minutes using UV light, which resulted in the formation of one or two predominant isomers for each of the homologue groups listed above. $^{13}\text{C}_{12}$ -2,3,7,8-tetrabromodibenzo-p-dioxin was also irradiated in carbon tetrachloride. In this case Br/Cl exchange took place to yield all three 2,3,7,8 substituted mixed halogenated dibenzo-p-dioxins (Br_3ClDD , $\text{Br}_2\text{Cl}_2\text{DD}$, BrCl_3DD) as well as 2,3,7,8- Cl_4DD . No byproducts were detected for any of the syntheses nor was a cleanup of the resulting mixtures necessary.

Introduction

There is a growing interest in brominated and mixed halogenated dibenzo-p-dioxins (DDs) and dibenzofurans (DFs) in the environment. Appropriate internal standards are a prerequisite for the reliable analysis of these compounds. Stable isotopes, usually ^{13}C labelled compounds, are currently the preferred internal standards in DD/DF analysis using mass spectrometer detection. At the time of this study there were $^{13}\text{C}_{12}$ standards commercially available for Br_3DD , Br_4DF , Br_4DD , Br_5DF , Br_5DD and Br_6DD . As part of an effort to develop an analytical method for BrDD/DFs , we decided to synthesize standards for the remaining lower brominated homologues. This experience was then expanded to the synthesis of 2,3,7,8-substituted mixed halogenated DDs.

Only one previous synthesis of $^{13}\text{C}_{12}$ -mono- to tribrominated DDs was encountered in the literature¹. A high temperature (240°C) bromination of $^{13}\text{C}_{12}$ -dibenzo-p-dioxin with iron(III)bromide was employed. This procedure is not isomer specific and results in mixtures of about three halogenation levels. On the other hand, syntheses leading to distinct isomers like condensation reactions of phenols and catechols or cyclizations of halogenated diphenyl ethers are laborious and cumbersome.

A rapid, easily executed synthesis producing small quantities (several μg) was desired, and hence a photochemical synthesis was developed. Photochemically induced bromine/hydrogen exchange has been postulated for the photodegradation of brominated DDs and DFs in the environment and has also been observed in the laboratory. The mechanism is trivial. Homolytic cleavage of the Ar-Br bond is followed by the abstraction of a hydrogen atom from the solvent. In mixed brominated/chlorinated aromatics the bromine atom is exclusively replaced ^{2,3}. Since there was also an immediate need for the three ¹³C-labelled mixed brominated/chlorinated 2,3,7,8-*X*₄DDs and no reports of the synthesis of these compounds were found in the literature, a photochemically induced halogen/halogen exchange in the presence of CCl_4 was also tested.

Experimental

¹²C₁₂-2,3,7,8-Br₄DD/F, ¹²C₁₂-2,3,7,8-Cl₄DD, ¹²C₁₂-2-Br-3,7,8-Cl₃DD, ¹²C₁₂-2,3-Br₂-7,8-Cl₂DD, ¹²C₁₂-2,3,7-Br₃DD, ¹³C₁₂-2,3,7,8-Br₄DD/F and ¹³C₁₂-2,3,7-Br₃DD (special manufacture) were obtained from Cambridge Isotope Laboratories, Woburn, MA. The following ¹²C₁₂ native standards had been synthesized previously in our laboratory: Br₁DF (substitution pattern unknown), 2,8-Br₂DF, 2-BrDD, 2,3-Br₂DD, 2,7/2,8-Br₂DD (~1:1 mix) and 2,3,7-Br₃-8-CIDD. A Br₃DF-standard was not available.

A Rayonett Photochemical Reactor RPR-100 (Southern New England Ultraviolet Co.) equipped with two (180° geometry) low-pressure mercury lamps coated with white phosphorus RPR 3000 A was used for irradiation. The emission spectrum of these lamps resembles a Gaussian bell curve ($\lambda_{\text{max}} = 300 \text{ nm}$, 10% intensity at 340 nm) showing no distinct lines. A special irradiation vessel made from pyrex glass allowed the use of chemical filter solutions (salts of lead and mercury) with cut-off points at 310 nm (filter A) and 320 nm (filter B) respectively.

(1) *Br₃DD*. A solution of 13 μg of ¹³C₁₂-2,3,7-Br₃DD in toluene was transferred to the irradiation vessel and evaporated to dryness by applying a gentle stream of nitrogen. 0.2 ml of n-hexane was added and again evaporated to dryness to remove any residues of toluene. Then 1.0 ml of n-hexane was added, the solution was sonified in an ultra sonic bath for 10 min and then irradiated at room temperature without chemical filter in the merry-go-round for 6.5 min. Sub samples of 30 μl were isolated and after reduction in volume to 10 μl directly injected into the GC (full scan) to monitor the progress of the reaction. When the reaction was complete the contents of the irradiation vessel were transferred to a 5 ml volumetric flask and made up to volume with toluene.

(2) *Br₄DF*. A solution of 11.2 μg of ¹³C₁₂-2,3,7,8-Br₄DF in n-nonane was transferred to the irradiation vessel and concentrated to 1.0 ml with the help of nitrogen. After sonification (10 min) the solution was irradiated for 18 min at room temperature in the middle of the photoreactor without the merry-go-round while protected by filter B. The workup was as described above.

(3) *Br₄DF*. A solution of 11.2 μg of ¹³C₁₂-2,3,7,8-Br₄DF was treated as described above and irradiated for 50 min at room temperature. Filter A was applied.

(4) *Br₄DD*. A solution of 22.5 μg of ¹³C₁₂-2,3,7,8-Br₄DD in n-nonane was evaporated to dryness. The residue was redissolved in about 1 ml of CCl_4 and again evaporated to dryness to remove any residues of nonane. The residue was again redissolved in 1.0 ml of CCl_4 , sonified and irradiated in the middle of the photoreactor at room temperature for 25 min. Filter A was applied. Then the CCl_4 was again evaporated, the residue redissolved in toluene and transferred to a 5 ml volumetric flask.

Results and Discussion

The major products of each experiment are listed in Table 1. One predominant and, in the case of the dibenzofurans, a number of minor isomers were synthesized for each of the desired homologue groups with yields better than 50%. No irregularities in the mass spectra (100-600 amu) were observed and no $^{12}\text{C}_{12}$ -contamination was detected (< 0.2 %). The reactions were very easy to conduct.

Table 1 Product yields of reactions (1) - (4)

	<u>yield (mol%)</u>					Σ
	DD	Br ₁ DD	Br ₂ DD	Br ₃ DD		
Reaction (1)	~5	33	34	0		72
	DF	Br ₁ DF	Br ₂ DF	Br ₃ DF	Br ₄ DF	
Reaction (2)	0	0	~5	31	44	80
Reaction (3)	~5	23	44	0	0	72
	Cl ₄ DD	BrCl ₃ DD	Br ₂ Cl ₂ DD	Br ₃ ClDD	Br ₄ DD	
Reaction (4)	7	8	12	14	9	50

It was not necessary to remove reagents from the products as no reagent but light was used. No byproducts were detectable in the products of reactions 1-3 using gas chromatography and a mass selective detector in scan mode (100-600 amu) except contaminants that were present in the starting material. Higher hydrocarbons that were found in the nonane solution of the purchased Br₄DD liquid standard are probably the reason for the small amounts (< 5%) of reduction products observed following irradiation of Br₄DD in CCl₄. Br₃DD, Br₂ClDD, BrCl₂DD and Cl₃DD arising from Br/H exchange were identified from their mass spectra. If desired, this finding could be used to prepare these reduction products by irradiating Br₄DD in a suitable mixture of n-hexane and CCl₄. However, the yield per single compound would probably be low.

On the other hand, there must have been some polar byproducts as the yield of dibenzofuran from Br₄DF or Cl₄DD from Br₄DD following prolonged irradiation was low.

While there are likely polar byproducts arising from e.g. ring fission and subsequent degradation, they could at most account for 20-50% since the total yield of identified products was 50-80%. Furthermore, due to their polar character these byproducts would be removed during the working up of real samples. For these reasons a clean up step - the

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most laborious step in many synthetic procedures - was not necessary. The resulting mixtures could be used directly as internal standards.

It was found that light of about 320 nm is necessary for the reactions. A repetition of experiment 2 with a filter solution with a cut off point at about 340 nm resulted in no measurable conversion of Br₄DF within one hour.

The Br/H exchange could not be stopped at one level of bromination. However, since the rate constant for the debromination of Br₄DF is higher than the rate constant for the debromination of Br₃DF, and this one is higher than the one for Br₂DF, and so on³⁾, only two products could be detected at the same time in reasonable amounts. Br₄DF for instance had completely disappeared when Br₁DF began to form. Therefore, the reaction was optimized in such a way that two levels of bromination each were formed in about equal amounts: Reaction 1 giving Br₂DD and Br₁DD; reaction 2 giving Br₄DF and Br₃DF; and reaction 3 giving Br₂DF and Br₁DF. These solutions could now be mixed as desired. Because the Br/H exchange induced by UV-light was even faster in the dibenzofuran series than in the dibenzodioxin series, chemical filters were used to shift the spectrum in the reaction vessel to even longer wavelengths. The resulting irradiation times were more convenient and made the reaction more reproducible.

The Br/Cl exchange in CCl₄ differs somewhat from the Br/H exchange described above. Since there is no stabilizing effect during the reaction by the loss of bromine atoms the reaction could not be optimized in the same way. Substitution of bromine by chlorine even seemed to accelerate the further debromination rather than to hinder it. The product distribution was broader, which meant that it was not possible to prepare e.g. only Br₂Cl₂DD and Br₃ClDD in equal amounts with no BrCl₃DD and Br₄DD. Considerable amounts of Cl₄DD formed before the Br₄DD had disappeared (see Tab. 1). Since side reactions are taking place it is easiest to prepare Br₃ClDD and most difficult to prepare BrCl₃DD with good yields. The conditions given for experiment 4 are a compromise between overall yield and equal distribution of the three mixed halogenated X₄DDs.

Product identification

The following isomers were identified as main products by the help of two columns (XTI-5 and SP-2331) and a retention index system^{4,5)}: 2-BrDD; 2,7/2,8-Br₂DD (1:1); 2/3-BrDF (19:1); 2,8/2,7/3,7-Br₂DF (25:10:1); 2,3,8/2,3,7-Br₃DF (5:1); 2-Br-3,7,8-Cl₃DD; 2,3-Br₂-7,8-Cl₂DD, 2,3,7-Br₃-8-ClDD.

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