Derivatisation of 4-nonylphenol and bisphenol A with halogenated anhydrides

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Abstract The aim of this work is to synthesize and characterise the halogenated derivatives of the endocrine disrupting compounds (EDCs) 4-nonylphenol (4-NP) and bisphenol A (BPA). Characterisation was performed after gas chromatographic (GC) separation on-line coupled to mass spectrometric (MS) detector and a Fourier Transform Infrared (FTIR) spectroscopic detector. Further structure elucidation was done applying Nuclear Magnetic Resonance spectroscopy (NMR).

Two different approaches for the preparation of derivatives were evaluated. At first trifluoroacetyl derivatives were synthesized by the reaction of trifluoroacetic acid (TFA) anhydride and the EDCs in acetonitrile at a temperature of 50°C for 30 minutes. In a second step the 4-NP was derivatised using trichloroacetic acid anhydride and triethylamine in diethyl ether at 20°C for 30 minutes.

After synthesis the halogenated NP and BPA derivatives were characterised applying GC/MS, GC/FTIR and NMR. Three indices for a successful derivatisation were observed: EI-GC/MS proved a complete derivatisation presenting a characteristic fragmentation pattern for each derivative. The IR spectra obtained by GC/FTIR after derivatisation and separation confirmed the loss of the phenolic O-H stretching vibration at 3,600 cm⁻¹ while typical absorptions for halogenated compounds now were observed. The NMR-spectra contained the predicted resonance signals.

Keywords Characterisation; endocrine disrupting compounds; halogenated derivatives; synthesis

Introduction

4-NP and BPA are compounds which belong to the group of anthropogenic EDCs. These compounds, also known as xenoestrogens (Gülden et al., 1997), are synthetic chemicals produced with large production volumes. While 4-NP is a biodegradation product of nonylphenol polyethoxylates (NPEOs) (Lee and Peart, 1995) used as surfactants while BPA is applied in the production of polymer compounds like epoxy- and phenolic resins and polycarbonates or as precursor for flame-retardants or co-reactant in the production of thermals papers. After use these compounds reach waste water treatment plants (WWTP) with waste water discharges. The EDCs are eliminated incomplete during the waste water treatment process. So they were discharged with the effluents into the rivers and surface waters serving for drinking water treatment. Estrogenic responses in fish exposed to WWTP-effluents were observed (Purdom et al., 1994). To monitor their complete elimination it is necessary to apply sensitive and selective analytical method for the determination of these compounds present in very low concentration levels. GC on-line adapted to different detectors has proved to be suitable for the sensitive and selective determination of volatile substances. Derivatisation of 4-NP and BPA using halogenated groups (Croley and Lynn, 1998; Rinken, 2002) is quite useful to improve volatility. Before these derivatives can be applied in analytical determination procedures it was necessary to characterise them and their behaviour under analytical conditions by analytical techniques such as GC/MS and GC/FTIR. To ensure purity structure was also elucidated by NMR.
Methods

Chemicals

Trifluoroacetic acid (TFA) anhydride ((CF$_3$CO)$_2$O) was of “analytical reagent grade” (Sigma Aldrich, Taukirchen, Germany), trichloroacetic acid anhydride was purchased with a purity > 98% from Fluka Chemie GmbH (Taufkirchen, Germany). The blend of 4-NP was of “technical grade” (purity > 98%) and was also purchased from Fluka Chemie AG. Bisphenol A was a gift from Dow GmbH (Stade, Germany) and was of technical purity. Acetonitrile, acetone, diethyl ether and n-hexane were of “Residue Analysis” purity grade from LGC Promochem GmbH (Wesel, Germany). Sodium sulfate (Na$_2$SO$_4$) from Merck (Darmstadt, Germany) used for organic solvent drying was activated at a temperature of 450°C for 8 hours. Dimethylsulfoxide-d$_6$ (DMSO-d$_6$) and chloroform-d (CDCl$_3$), both deuterated up to 99.9% were used as NMR-solvents and were purchased from Sigma Aldrich. Nitrogen gas (N$_2$) for the gentle evaporation of organic solvents and helium gas (He) used as carrier gas in GC separations were of 99.999% purity (Linde, Germany).

Derivatisation

**Trifluoroacetylation.** NP and BPA were dissolved in acetone (100 µg/mL). 1 mL of this solution was put into a reclosable glass tube and was evaporated to dryness. The residue was dissolved in 200 µL acetonitrile and 50 µL TFA anhydride was added. The glass tubes were closed and heated for 30 minutes at 60°C. The reaction was stopped by evaporating until dryness with nitrogen gas at a temperature of 60°C. The derivatised residues were reconstituted in 1 ml hexane and were ready for analyses.

**Trichloroacetylation.** The evaporated residue of the NP solution was dissolved in 1 ml diethyl ether. After addition of 50 µL triethylamine and 300 µL TFA anhydride the glass tubes were closed and the reaction takes place in 30 minutes at room temperature. 1 mL of water was added and the derivatives were extracted by shaking three times applying 1mL of hexane. The organic layer was dried over sodium sulfate and concentrated to 1 ml. This solution was used for the different characterisation steps.

**Gas chromatography-mass spectrometry.** A Finnigan MAT GCQ GC (San Jose, USA) equipped with an ion trap MS was used for GC/MS analysis. The MS was tuned with perfluorotributylamine (PFTBA) using the autotune program. The GCQ was equipped with an A 200 S auto sampler (Finnigan MAT. San Jose, USA). The GC separation was performed on a fused silica capillary column (Valcobond VB-5; film thickness 0.25 µm; 60 m × 0.25 mm I.D. (VICI, Gig Harbor, USA)). The GC/MS conditions used for analysis were as follows: carrier gas, helium; linear velocity, 40 cm/s; injector temperature, 250°C; transfer line temperature, 275°C; ion source temperature, 150°C. For analysis 2 µl split injections (1:10) were carried out by auto sampler. The GC temperature program conditions were as follows: initial oven temperature 80°C, held for 3 min, heated to 280°C by a temperature ramp of 10°C/min and hold for 7 minutes. The positive EI full scan data were acquired under the following conditions: mass range (m/z 30 to 1,000), scan time, 1.76 s, solvent delay, 8 min, electron energy 70 eV, emission current, 250 µA and electron multiplier voltage, 1100 V.

**Gas chromatography – Fourier transform infrared spectroscopy.** A PE 8420 GC equipped with a PE 1700x GC/FTIR Interface and a PE 1740 FTIR spectrometer all from Perkin Elmer (Rodgau-Jügesheim, Germany) was used for IR analysis. The GC conditions were as follows: carrier gas, helium; gas pressure linear, 110 KPa, injector temperature, 250°C; transfer line temperature, 200°C. For analysis 2 µL split injections (1:10) were carried out manually. The GC temperature program conditions were: initial oven temperature 40°C,
held for 4 min, heated to 280°C by a temperature ramp of 10°C/min and hold for 25 minutes. The infrared spectra were recorded at a scan speed of 2.0 cm/s at a resolution of 8 cm⁻¹ and a scan range from 4,000 to 700 cm⁻¹.

**Nuclear magnetic resonance spectroscopy.** 1H- 13C- and 19F-NMR results were recorded in CDCl₃ or DMSO(d₆) on a Varian Inova-400 spectrometer (Varian Inc., Palo Alto, USA) at 100, 375 or 400 MHz, respectively. Chemical shifts (d) are given in ppm relative to the internal standard tetramethylsilane (TMS).

**Results and discussion**

**Gas chromatography/mass spectrometry**

The mass spectra of the halogenated NP and BPA are shown in Figure 1. The molecular ion ([M⁺]) of NP-TFA is detected at m/z 316. There is also a fragmentation of the alkyl chain because of the difference of m/z 14 observed for the fragments. For BPA-bis-TFA only a fragmentation of a CH₃-group from the molecule ion at m/z 420 could be observed. The NP-TClA derivative shows the same fragmentation of the alkyl chain as the trifluoro derivative; in addition, however, signals of the not halogenated NP were observed. The relative abundances of the ³⁵Cl/³⁷Cl isotope fragments are characteristic for this compound. The specific fragment ions which can be used for quantification are shown in Table 1.

**Gas chromatography/infrared spectroscopy (GC/FTIR)**

In the GC/FTIR spectra of the halogenated derivatives no absorption at 3,600 cm⁻¹ could be observed. At this IR region normally the stretching vibration of the phenolic OH-group leads to an absorption. So a substitution reaction at the phenolic group has taken place. In Table 1 the typical absorptions observed for the halogenated substances are presented.

![Figure 1](https://iwaponline.com/wst/article-pdf/50/5/115/420113/115.pdf)

**Table 1** Specific fragment ions and IR absorptions for the halogenated NP and BPA

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Fragment ions m/z</th>
<th>Absorption cm⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonylphenoltrifluoroacetate (NP-TFA)</td>
<td>203, 231, 245</td>
<td>1100–1250, 1800</td>
</tr>
<tr>
<td>Nonylphenoltrichloroacetate (NP-TClA)</td>
<td>405, 420</td>
<td>750, 1750</td>
</tr>
<tr>
<td>Bisphenol-A-bis-(trifluoroacetate) (BPA-bis-TFA)</td>
<td>230, 244, 258</td>
<td>1100–1250, 1800</td>
</tr>
</tbody>
</table>
Nuclear magnetic resonance spectroscopy (NMR)

$^1$H, $^{13}$C and $^{19}$F-NMR chemical shifts in ppm relative to the TMS standard are given in Table 2. For positions of atoms cf. Figure 2.

Conclusions

With this work it could be confirmed that 4-NP and BPA reacted with halogenated acetic acid anhydrides resulting in halogenated acetyl derivatives. The presented mass-spectra, infrared-spectra and the results of the NMR spectroscopy show that the structure of the derivatives is the same as the predicted structures. This derivatisation would now be used in analytical methods for the determination of 4-nonylphenol and bisphenol A.

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References


