Group : Organic Chemistry (ORC) and Analytical Chemistry (WFSR)
Project : **Synthesis, purification and structure elucidation of pesticide metabolites to establish human pesticide exposure**
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Introduction

Recently on Dutch television we could see a report on pesticide exposure of people working in or living close to bulb fields, where pesticides are sprayed (https://zembla.bnnvara.nl/nieuws/omwonenden-bollenvelden-hoger-blootgesteld-aan-bestrijdingsmiddelen). Human exposure can in principle be assessed by measuring pesticide residues in human urine. Unfortunately, since pesticides are metabolized quite rapidly, the original parent compounds are difficult to detect and are often very low in concentration. Recently we identified new metabolites of pesticides that can be monitored more readily in humans. Most pesticide metabolites, however, are not commercially available as reference standards. This hampers not only analytical confirmation of the identity of pesticide metabolites but also their quantification and the consecutive risk analysis based on urine concentrations.

We have found a number of possible chlorine-containing pesticide metabolites at presumably low concentrations in urine. Among the observed pesticides are organophosphorous (examples chlorpyrifos-methyl, pirimiphos-methyl) and neonicotinoid types (examples imidacloprid, thiamethoxam). Some metabolites of these pesticides are thought to be potentially neurotoxic [1,2]. A known metabolite of the neurotoxic organophosphorous pesticide chlorpyrifos-methyl is desmethyl-chlorpyrifos-methyl. Recently, EFSA (European Food Safety Authority) has been reviewing maximum residue levels for this compound [3] and stated that the desmethyl-chlorpyrifos-methyl metabolite should also be measured. Nitro-group containing neonicotinoids, such as imidacloprid, are primarily neurotoxic for insects (much less toxic for vertebrates). The imidacloprid desnitro-metabolite (or guanidine), however, binds by far better to the vertebrate nicotinic acid receptor than its parent [2], indicating a much higher potential toxicity for vertebrates than its parent.
Organophosphorous pesticides can be demethylated at the phosphate through controlled hydrolysis reactions [4]. Nitro-groups on neonicotinoiden have been reported to be removed by using an iron-powder reduction step [5].

Goals

The final aim of this project is to synthesize and purify pesticide metabolites so that they can used as standards in high-resolution liquid chromatography (LC) orbitrap mass spectrometry (MS) analysis to identify and quantify amounts present in urine biomonitoring.

Topics to be studied

Organic synthesis/purification of demethylation metabolites of organophosphorous pesticides and of desnitro-neonicotinoiden from parent compounds. Structure elucidation of purified reaction products. Using the purified metabolites in the LC-orbitrap-MS analysis.

Techniques to be used

Organic synthesis, purification, preparative LC-MS, 2D-NMR, LC-orbitrap-MS

Information

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