APPLICATION NOTE

The Chiral Separation of the Stereoisomers of Permethrin

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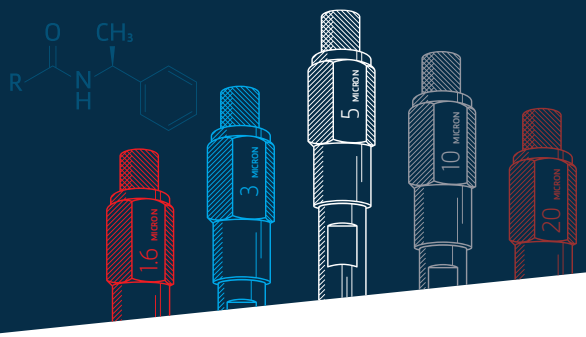

DAICEL Chiral Technologies

INTRODUCTION

Permethrin is a commonly used insecticide and insect repellant, and is often prescribed as a medication to treat scabies and head lice. The structure of permethrin is such that it contains two chiral centers, adjacent to each other on the dimethyl cyclopropane moiety (Figure 1). This gives rise to a mixture of 4 stereoisomers, or more specifically, two pairs of enantiomers.

Although several reports are present in the literature demonstrating partial resolution, those reports were unable to fully resolve all 4 isomers of the permethrin mixture. This is important to note, especially for permethrin's applications as an insecticide. As awareness of the downstream effects of chiral pesticides and insecticides within the agricultural industry continues to rise, being able to accurately quantify all 4 isomers is crucial to ensure its safe application.

Presented in this note is the first reported normal phase high performance liquid chromatography (HPLC) separation of all 4 isomers of permethrin. CHIRALPAK® IG and CHIRALPAK® IJ separately are capable of resolving two or three of the isomers. However when coupled, baseline resolution of all 4 stereoisomers can be achieved.

EXPERIMENTAL

Chromatographic Conditions for the Separation of Permethrin			
Column	CHIRALPAK® IG-3 (250 mm x 4.6 mm i.d., 3 µm) Part #: 87525	CHIRALPAK® IJ-3 (250 mm x 4.6 mm i.d., 3 µm) Part #: 90525	Coupled IG-3 and IJ-3
Mobile Phase	95-5-0.1 = Hex-EtOH-DEA		90-10-0.1 = Hex-EtOH-DEA
Flow Rate	1.0 ml/min		
Detection	UV 280 nm ref. 450 nm		
Temperature	25°C		
Sample	1.0 mg/ml in EtOH		
Injection Volume	5 µl		10 µl

Permethrin and Diethylamine (DEA) were purchased from Sigma Aldrich and used as-is. The solvents used were all purchased from Pharmco, were HPLC-grade or higher, and were used as-is. Specifically the hexanes (Hex) contained 95% n-hexane. The ethanol (EtOH) was reagent alcohol, which contains 90% EtOH, 5% methanol, and 5% isopropanol (v/v/v). Initial screening and optimization were performed on an Agilent 1200 equipped with a quaternary mixing pump and utilized a DAD.

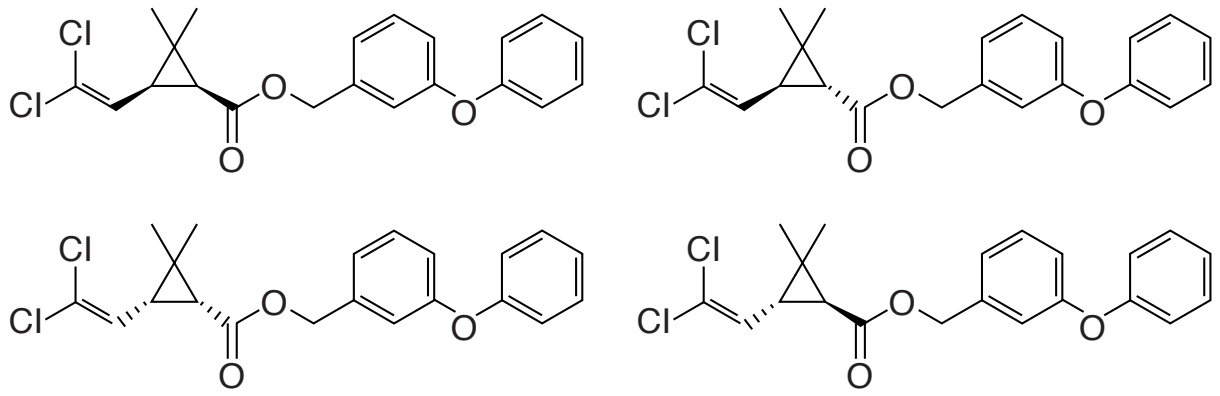

Figure 1: Four stereoisomers of Permethrin

RESULTS AND CONCLUSIONS

Permethrin was screened on Daicel's immobilized library of polysaccharide-based chiral stationary phases (CSPs) with starting conditions of 90-10-0.1 = Hex-EtOH-DEA. From this, partial separations showing three peaks were observed on both CHIRALPAK® IG-3 and IJ-3 (150 mm x 4.6 mm i.d., 3 µm). In an attempt to optimize, the mobile phase strength was reduced to 95-5-0.1 = Hex-EtOH-DEA to improve the compounds retention, and the column length increased to 250 mm for additional resolution. This resulted in the blue and orange traces in Figure 2, blue for IG-3 and orange for IJ-3.

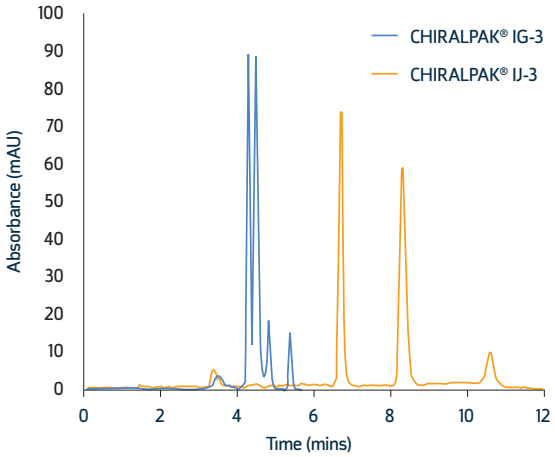

Figure 2: Separation of Permethrin on CHIRALPAK® IG-3 and CHIRALPAK® IJ-3 Individually

As can be seen, IG is able to resolve well the two minor isomers in the mixture, however the major isomers coelute. IJ is able to resolve the two major isomers from each other, however one of the minor isomers coelutes with the second major isomer peak.

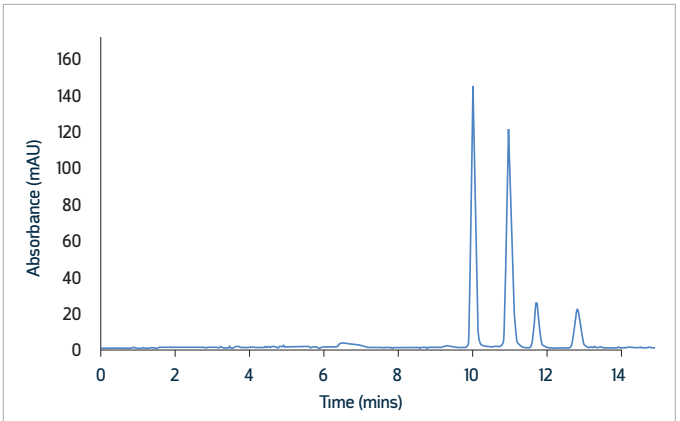

Figure 3: Separation of Permethrin on CHIRALPAK® IG-3 coupled with CHIRALPAK® IJ-3

With IG and IJ each performing better in some aspect of separating the permethrin mixture, the hypothesis was that the unique performance of each column coupled together could result in baseline separation of the complete mixture. This indeed was achieved, with a separation baseline enough to return to the original screening conditions of 90-10-0.1 = Hex-EtOH-DEA to help shorten the excessive retention. This optimization resulted in the separation shown in Figure 3. This separation was achieved by placing IJ-3 first in series with IG-3 second. A similar result is achieved when IG-3 is placed first in series with IJ-3 second. Despite the coupling of two 3 µm columns, the system pressure never exceeded 130 bar.

With this new method available for the separation of all stereoisomers of Permethrin, a more accurate and reliable quantification can be performed. This is especially important with the increasing focus on environmental and biological impacts of insecticides and pesticides both domestically and internationally.