

Chiral HPLC of Antifungal Compounds Utility of Chirex™ Chiral Stationary Phases

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Introduction

One of the largest groups of fungicides works by blocking C14-demethylation in sterol biosynthesis. Referred to as DMI-fungicides (DeMethylation Inhibitors), this group includes compounds in the following chemical classes: imidazoles, piperazines, pyridines, pyrimidines and triazoles. This last class, the triazoles, has the greatest number of compounds employed as fungicides, many of which are chiral.

Table 1. Triazole Fungicides

azaconazole	flusilazole	prothioconazole
bitertanol	flutriafol	simeconazole
bromuconazole	hexaconazole	tebuconazole
cyproconazole	imibenconazole	tetraconazole
difenoconazole	ipconazole	triadimefon
diniconazole	metconazole	triadimenol
epoxiconazole	myclobutanil	triticonazole
fenbuconazole	penconazole	uniconazole
fluquinconazole	propiconazole	

There are significant differences in the activity spectra of the different DMI-fungicides. Resistance to these compounds is observed in most fungal species. Typically, if resistance to one fungicide is present there will be cross-resistance to other fungicides in the same class.

In this Technical Note, simple and direct chiral HPLC methods for the resolution of two racemic antifungal triazoles are described. The separation techniques employed here can be applied to many other chiral compounds in this class.

Instrumentation & Equipment

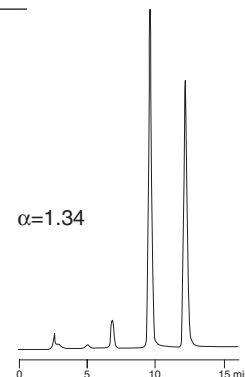
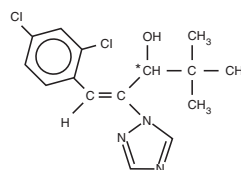
Analyses were performed using an HP 1100 LC system (Agilent Technologies, Palo Alto, CA, USA) equipped with a quaternary pump, in-line degasser, multi-wavelength detector, and autosampler. HP Chemstation software was used for the data analysis. The HPLC columns used for the analysis are Chirex™ brand (Phenomenex, Torrance, CA, USA, see Ordering Information). Standards were purchased from Sigma (St. Louis, MO), Aldrich (Milwaukee, WI), or Fluka (Ronkonkoma, NY), depending on availability.

Results & Discussion

Various Chirex™ chiral stationary phases (CSPs) were evaluated for their utility to directly resolve (without derivatization) enantiomers of two important antifungal compounds.

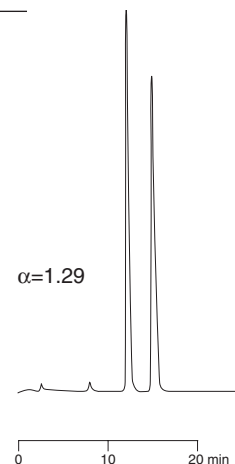
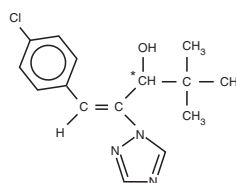
App ID 5261 Diniconazole

Column: Chirex 3020
Dimensions: 250 x 4.0mm
Order No.: 00G-3020-D0-TN
Mobile Phase: Hexane/1,2-Dichloroethane/Ethanol (100:20:1)
Flow Rate: 1.0mL/min
Conditions: UV @ 254nm



App ID 5242 Uniconazole

Column: Chirex 3020
Dimensions: 250 x 4.0mm
Order No.: 00G-3020-D0-TN
Mobile Phase: Hexane/1,2-Dichloroethane/Ethanol (100:20:1)
Flow Rate: 1.0mL/min
Conditions: UV @ 254nm



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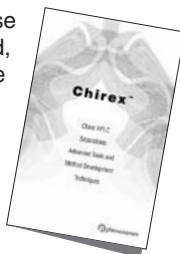
Table 2. Enantioresolution of two triazole antifungals using Chirex CSPs

Triazole Fungicide	Chirex CSP	Separation Factor (alpha)	App ID
Diniconazole	3014	1.26	13835
	3019	1.25	13836
	3020	1.34	5261
Uniconazole	3014	1.18	5240
	3019	1.21	5241
	3020	1.29	5242

References

1. Cleveland, T., J. Liq. Chromatogr. 18(4): 649-671, 1995.

If you would like more information on these columns or any specific application listed, please contact Phenomenex. Also, if you are new to chiral HPLC or are doing method development work call us today to reserve your **FREE** copy of our 70-page **Guidebook to Chiral HPLC Method Development**.



Ordering Information:

Chirex is available in a wide range of phases and column sizes, from analytical to preparative. All phases are also available in bulk (15 and 30µ particle size).

The columns discussed in this Note are listed below.

5µ Analytical Columns (mm)

Chirex Phase and Bond Linkage, 250 x 4.6mm ID

Phase	Description	Order No.
3001	(R)-PGLY and DNB Covalent Amide	00G-3001-E0-TN
3014	(S)-VAL and (R)-NEA Covalent Urea	00G-3014-E0-TN
3017	(S)-PRO and (S)-NEA Covalent Urea	00G-3017-E0-TN
3018	(S)-PRO and (R)-NEA Covalent Urea	00G-3018-E0-TN
3019	(S)-LEU and (S)-NEA Covalent Urea	00G-3019-E0-TN
3020	(S)-LEU and (R)-NEA Covalent Urea	00G-3020-E0-TN
3022	(S)-ICA and (R)-NEA Covalent Urea	00G-3022-E0-TN

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