SEPARATION OF 2-PHENYLBUTYROPHENONE ON **DAICEL'S NEWEST IMMOBILIZED CHIRAL STATIONARY PHASE CHIRALPAK® IJ**

APPLICATION NOTE

INTRODUCTION

Coated polysaccharide chiral stationary phases (CSPs) have been utilized for the separation of a vast assortment of chiral molecules. While these phases work extremely well, they are limited in the range of solvents that they can safely utilize. With the introduction of more resilient immobilized versions of these coated polysaccharide phases, Daicel Corporation has provided the analytical chemist with a broader spectrum of solvents for screening, thus increasing the potential for achieving a chiral resolution. The newest immobilized phase being introduced is CHIRALPAK® IJ, the immobilized version of CHIRALCEL® OJ. CHIRALPAK® IJ is a cellulose polymer derivatized with tris(4-methylphenylbenzoate) moieties.

As previously stated, the access to an expanded range of solvents for screening provides an increased potential of finding separations for molecules that were previously not resolved, or poorly resolved on their corresponding coated phases. 2-Phenylbutyrophenone is one such example presented in this application note. 2-Phenylbutyrophenone is a key starting material in the synthesis of Tamoxifen, a critical estrogen modulator used in the treatment of breast cancer. Not previously separated on CHIRALCEL® OJ under normal phase conditions, the ability of the immobilized CHIRALPAK® IJ to withstand dichloromethane (DCM) yielded a baseline resolution.

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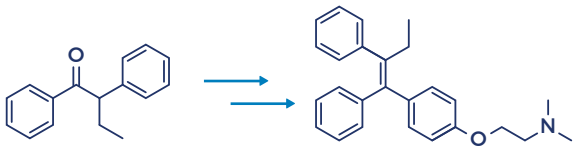
SYNTHESIS OF A CRITICAL ESTROGEN MODULATOR



2-PHENYLBUTYROPHENONE TAMOXIFEN

EXPERIMENTAL

CHROMATOGRAPHIC CONDITIONS FOR THE SCREENING OF 2-PHENYLBUTYROPHENONE

CHIRALCEL® OJ-H (5 µm) - (4.6 mm I.D. X 150 mm)	
MOBILE PHASE	n-Hex/EtOH = 50:50 v/v n-Hex/IPA = 50:50 v/v
FLOW RATE	1.0 ml/min
DETECTION	UV, 225 nm, ref 450 nm
TEMPERATURE	25°C
SAMPLE	1.0 mg/ml in EtOH
INJECT. VOL.	5.0 µl

CHIRALPAK® IJ (5 µm) - (4.6 mm I.D. X 150 mm)	
MOBILE PHASE	n-Hex/DCM = 80:20 v/v n-Hex/EtOAc = 80:20 v/v n-Hex/THF = 80:20 v/v n-Hex/MtBE = 80:20 v/v
FLOW RATE	1.0 ml/min
DETECTION	UV, 280 nm, ref 450 nm
TEMPERATURE	25°C
SAMPLE	1.0 mg/ml in EtOH
INJECT. VOL.	5.0 µl

EXPERIMENTAL CONTINUED

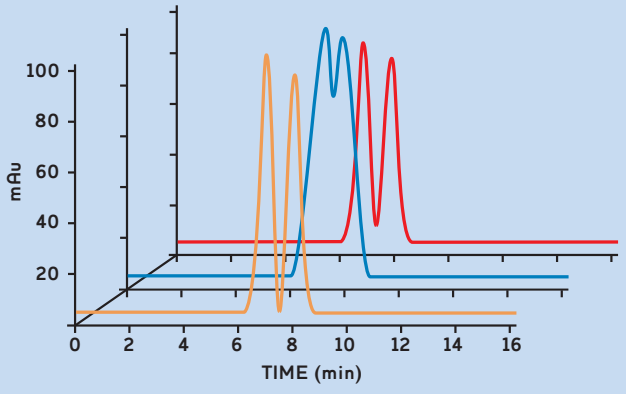
CHROMATOGRAPHIC CONDITIONS FOR THE OPTIMIZATION OF 2-PHENYLBUTYROPHENONE

CHIRALCEL® OJ-H (5 µm) - (4.6 mm I.D. X 150 mm)	
MOBILE PHASE	n-Hex/EtOH = 85:15 v/v n-Hex/IPA = 70:30 v/v
FLOW RATE	1.0 ml/min
DETECTION	UV, 225 nm, ref 450 nm
TEMPERATURE	25°C
SAMPLE	1.0 mg/ml in EtOH
INJECT. VOL.	5.0 µl

CHIRALPAK® IJ (5 µm) - (4.6 mm I.D. X 150 mm)	
MOBILE PHASE	n-Hex/DCM = 94:6 v/v
FLOW RATE	1.0 ml/min
DETECTION	UV, 280 nm, ref 450 nm
TEMPERATURE	25°C
SAMPLE	1.0 mg/ml in EtOH
INJECT. VOL.	5.0 µl

FIGURE 1:

BASELINE SEPARATION OF 2-PHENYLBUTYROPHENONE



— CHIRALPAK® IJ with n-Hex/DCM = 94:6 v/v
— CHIRALPAK® OJ-H with n-Hex/EtOH = 85:15 v/v
— CHIRALPAK® OJ-H with n-Hex/IPA = 70:30 v/v

DISCUSSION

2-Phenylbutyrophenone screened on the conditions in the table above (Chromatographic Conditions for the Screening of 2-Phenylbutyrophenone) which yielded partial separations on CHIRALCEL® OJ-H for both n-Hex/EtOH and n-Hex/IPA conditions, as well as a partial separation on CHIRALPAK® IJ with n-Hex/DCM. In order to maintain similar analysis times, the optimization of n-Hex/EtOH conditions did not go above 85/15, which was not sufficient to produce a baseline resolution. Optimization of n-Hex/IPA on CHIRALCEL® OJ-H yielded a near baseline separation, however the optimization was again limited to maintain similar retention times. The optimization of the extended range conditions (n-Hex/DCM) on CHIRALPAK® IJ achieved a robust, quantifiable baseline separation. This previously unreported chiral separation will allow for the accurate assessment of this critical starting material's purity.

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