Enantioseparation of 1[\(\beta\)]'-bi-2-naphthol benzoates using high performance liquid chromatography

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Abstract: The enantiomeric separations of 2'-hydroxy-1[\(\beta\)]'-binaphthyl-2-yl benzoate, HNB1[\(\beta\)]', 1[\(\beta\)]=binaphthyl-2[\(\beta\)]=diyl dibenzoate, BNDB and 2'-methoxy-1[\(\beta\)]'-binaphthyl-2-yl benzoate, MBNB were studied on Chirex[\(S\)]'-LEU & S[\(S\)]'-NEA cellulose triis 35-dimethylphenylcarbamate, Chiralcel OD-H and amylose triis 35-dimethylphenylcarbamate, Chiralpak AD-H columns respectively using high performance liquid chromatography. The effects of mobile phase, column temperature and compound structures on the enantioseparations were discussed. The Chiralpak AD-H exhibited stronger capability of enantioseparation in comparison with those of Chirex[\(S\)]'-LEU & S[\(S\)]'-NEA and Chiralcel OD-H for 1[\(\beta\)]'-bi-2-naphthol benzoates. When using the mobile phase of n-hexane/2-propanol 40/60 v/v the chiral selectivities of HNB1, BNDB and MBNB were 1.76, 1.74 and 1.40 respectively. Moreover, in comparison with that of 1[\(\beta\)]'-bi-2-naphthol, the mechanisms of the enantioseparation of 1[\(\beta\)]'-bi-2-naphthol benzoates related to the substituted groups at 2-position the elution orders and thermodynamic parameters were also discussed.

Key words: high performance liquid chromatography, HPLC enantioseparation, chiral stationary phase, 1[\(\beta\)]'-bi-2-naphthol benzoates

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拆分研究,不仅可以准确测定它们的对映体纯度,而

单一的

甲酰氯反应合成,所有样品均经硅胶柱纯化、红外光

外消旋化合物由厦门大学化学化工学院陈安齐教授

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石油醚

乙醇溶液的圆二色光谱图

处,

对应的圆

二氯乙

微孔膜过滤,超声波脱气后使用。

色 谱 第

卷

1.1

1.2

BN

MBNB

2 MBNB

Fig. 2 Circular dichromism spectra of

MBNB in ethanol solution

1.3

Chirex® S'-LEU & S'-NEA

Fig. 1 Structures of 1,3'-bi-2-naphthol and

1,3'-bi-2-naphthol benzoates

BN > HBNB > BNDB = MBNB

10ATVP

SPD-M10AVP

Phenomenex

Pirkle

Chirex® S'-LEU & S'-NEA

Chiralcel OD-H

Chiralpak AD-H

Daicel

Chiralcel OD-H

Chiralpak AD-H

Jasco

J-810

R-BN

R-BN

BN

MBNB

MBNB

Chiralpak AD-H

HBNB
Chiralcel OD-H and Chiralpak AD-H columns were tested. The flow rate was 0.75 mL/min. The mobile phase consisted of a 0.5% diethylamine solution in methanol/water (90/10). The enantiomers were separated using an injection of 10 µL of a 1 mg/mL solution of the racemic mixture. The separation was complete, but the resolution was not high enough to separate the racemic peaks. A 0.5% diethylamine solution in methanol/water (85/15) was used instead, and the separation was improved. The enantiomers were separated using an injection of 10 µL of a 1 mg/mL solution of the racemic mixture. The separation was complete, and the resolution was high enough to separate the racemic peaks.

2.1 Chiralcel S*-LEU & S*-NEA

Table 1: Data of enantiomeric separations of 1,3-bi-2-naphthol and its derivatives on a Chiralcel S*-LEU & S*-NEA column

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Composition</th>
<th>k₁</th>
<th>k₂</th>
<th>α</th>
<th>Rₛ</th>
</tr>
</thead>
<tbody>
<tr>
<td>BN</td>
<td>82/16/2</td>
<td>1.19</td>
<td>1.56</td>
<td>1.31</td>
<td>4.26</td>
</tr>
<tr>
<td>HBNB</td>
<td>94/6/0.05</td>
<td>4.49</td>
<td>8.26</td>
<td>1.84</td>
<td>6.00</td>
</tr>
<tr>
<td>BNDB</td>
<td>94/6/0.05</td>
<td>2.70</td>
<td>3.02</td>
<td>1.12</td>
<td>1.11</td>
</tr>
<tr>
<td>MBNB</td>
<td>94/6/0.05</td>
<td>3.09</td>
<td>3.09</td>
<td>1.00</td>
<td>–</td>
</tr>
</tbody>
</table>

* MP: mobile phase; n-hexane/1,2-dichloroethane/ethanol v/v/v. ** n-hexane/ethanol v/v.

Fig. 3: Chromatograms of racemic 1,3-bi-2-naphthol and 1,3-bi-2-naphthol benzoates on a Chiralcel S*-LEU & S*-NEA column.

Mobile phases: n-hexane/1,2-dichloroethane/ethanol v/v/v. a. 82/16/2 for BN b. 94/6/0.05 for HBNB c. 94/6/0.05 for BNDB d. n-hexane/ethanol v/v for MBNB e. 95/5 for BNNB.

2.2 Chiralcel OD-H

Chiralcel OJ and Chiralcel OD-H columns were tested. The flow rate was 0.5 mL/min. The mobile phase consisted of a 0.5% diethylamine solution in methanol/water (90/10). The enantiomers were separated using an injection of 10 µL of a 1 mg/mL solution of the racemic mixture. The separation was complete, but the resolution was not high enough to separate the racemic peaks. A 0.5% diethylamine solution in methanol/water (85/15) was used instead, and the separation was improved. The enantiomers were separated using an injection of 10 µL of a 1 mg/mL solution of the racemic mixture. The separation was complete, and the resolution was high enough to separate the racemic peaks.

HBNB > BN > BNDB > HBNB > BNDB > 90/10 v/v/v v/v/v. ** n-hexane/ethanol v/v.
### Table 2 Data of enantioseparations of 1[3']-bi-2-naphthol and 1[3']-bi-2-naphthol benzoates on a Chiracel OD-H column

<table>
<thead>
<tr>
<th>Solute</th>
<th>MP I °</th>
<th>Composition</th>
<th>(k_1)</th>
<th>(k_2)</th>
<th>(\alpha)</th>
<th>(R_s)</th>
<th>MP II °</th>
<th>Composition</th>
<th>(k_1)</th>
<th>(k_2)</th>
<th>(\alpha)</th>
<th>(R_s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BN</td>
<td>85/15</td>
<td>1.45</td>
<td>1.64</td>
<td>1.13</td>
<td>1.47</td>
<td></td>
<td>90/10</td>
<td>3.54</td>
<td>4.08</td>
<td>1.15</td>
<td>1.51</td>
<td></td>
</tr>
<tr>
<td>HNB</td>
<td>85/15</td>
<td>0.83</td>
<td>1.08</td>
<td>1.30</td>
<td>2.43</td>
<td></td>
<td>90/10</td>
<td>1.51</td>
<td>1.68</td>
<td>1.11</td>
<td>1.23</td>
<td></td>
</tr>
<tr>
<td>BNDB</td>
<td>85/15</td>
<td>0.72</td>
<td>0.72</td>
<td>1.00</td>
<td>-</td>
<td></td>
<td>90/10</td>
<td>1.19</td>
<td>1.19</td>
<td>1.00</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>MBNB</td>
<td>95/5</td>
<td>1.15</td>
<td>1.22</td>
<td>1.06</td>
<td>0.66</td>
<td></td>
<td>95/5</td>
<td>1.68</td>
<td>1.68</td>
<td>1.00</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>MBNB</td>
<td>95/5</td>
<td>0.68</td>
<td>0.68</td>
<td>1.00</td>
<td>-</td>
<td></td>
<td>90/10</td>
<td>1.13</td>
<td>1.31</td>
<td>1.16</td>
<td>1.69</td>
<td></td>
</tr>
</tbody>
</table>

* MP: mobile phases; I: n-hexane/ethanol v/v; II: n-hexane/2-propanol v/v.

#### Fig. 4 Chromatograms of racemic 1[3']-bi-2-naphthol and 1[3']-bi-2-naphthol benzoates on a Chiracel OD-H column

Mobile phases: a. 85/15 for BN b. 85/15 for HNB c. 95/5 for BNDB. n-hexane/2-propanol v/v.

#### Fig. 5 Influences of alcohols in mobile phases on retention factors \(k_2\) and separation factors \(\alpha\) of racemic 1[3']-bi-2-naphthol and 1[3']-bi-2-naphthol benzoates

Mobile phases a and b. n-hexane/ethanol; c and d. n-hexane/2-propanol.
4.96...手性固定相的螺旋沟槽大小和立体环境，引起色谱保留机理和手性识别位点发生变化所致。图6给出了联萘对映体在...图给出了联萘二酚和联萘二酚苯甲酸酯对映体在柱上的拆分色谱图。图6

图6 Chromatograms of racemic 1H-‘-bi-2-naphthol and 1H-‘-bi-2-naphthol benzoates on a Chiralpak AD-H column
Mobile phases n-hexane/2-propanol 40/60 v/v for upper figures n-hexane/ethanol 40/60 v/v for lower figures.

2.4...手性拆分驱动形式不仅与溶质的性质有关，而且与醇类极性调节剂的性质有关。...
结论

对于羟基联萘苯甲酸酯、联萘二苯甲酸酯和甲氧基联萘苯甲酸酯对映体，在手性柱上呈现最好的拆分效果。采用正己烷-乙醇或正己烷-异丙醇流动相，它们均能得到很好的基线分离。

在手性柱上，联萘对映体中的萘羟基对其手性拆分有重要的影响；在手性柱上，除了萘羟基的氢键作用外，手性固定相的螺旋沟槽的包夹作用也会影响联萘对映体的手性拆分；在手性柱上，改变醇类调节剂可能会影响联萘对映体的出峰顺序和手性拆分驱动形式。

参考文献:
3. Liu X Ding J Gao L X. Chinese Journal of Chromatography 2005 23 146
7. Ruan Y Ao X Chen A Q et al. Journal of Xiamen University Natural Science 2002 4 217
8. Weng W Fan W Zhu Q et al. Journal of Instrumental Analysis 2008 7 21
15. Wang T Chen Y Vailaya A. J Chromatogr A 2000 902 345