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A SIMPLE METHOD FOR CHIRAL RESOLUTION OF 1，1’-BI-2-NAPHTHOL

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Abstract： An improved method for preparing enantiomerically pure 1，1’-bi-2-naphthols is described. 1，1’-bi-2-naphthol boric anhydride was generated from the reaction of racemic 1，1’-bi-2-naphthol and boric anhydride. Its two diastereoisomers could be efficiently separated in THF using（L）-proline as the resolving agent. Treatment in three successive steps yielded 79% and 74% enantiomerically pure（S）- and（R）-1，1’-bi-2-naphthol respectively.

Key words： 1，1’-bi-2-naphthol，chiral resolution
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INTRODUCTION

C_2 chiral 1，1’-bi-2-naphthol 1 occupies a position of prime importance in a wide range of enantioselective reactions. It plays an important role in asymmetric syntheses with very high enantiomeric purity. Relevant literature reports several methods for the preparation of optically active 1，1’-bi-2-naphthol. Chromatography separation using a chiral stationary phase has been developed rapidly in recent years. But the intrinsic feature of chromatography obstructs its further application for large-scale preparation，so that the fractional crystallization by chiral resolution is still the most preferred approach for the time being. It can yield enantiomers with high enantiomeric purity and can be carried out on a synthetic scale as well. The crystallization method is laborious，expensive and low in yield. Recently，Shan Zi-xing reported a relatively simple and convenient method for the resolution of racemic 1，1’-bi-2-naphthol via a cyclic borate ester together with an alkaloid or amino acid as the resolving agent. In this method，the pivotal borate should be generated from the reaction of racemic 1，1’-bi-2-naphthol with borane dimethyl sulfide complex，$H_3B \cdot SMe_2$，synthesis of which is complicated and expensive. If this special complex can be replaced by a common boron compound，the resolving procedure will become inexpensive and much easier to handle. Here we report an improved process for optical resolution of racemic 1，1’-bi-2-naphthol. Briefly，racemic 1，1’-bi-2-naphthol reacts with boric anhydride to generate 1，1’-bi-2-naphthol boric anhydride. When（L）-proline was used as resolving agent，the two diastereomers could be efficiently separated in THF. Treatment in three successive steps yielded 79% and 74% enantiomerically pure（S）-and（R）-1，1’-bi-2-naphthol respectively.

EXPERIMENTAL DETAILS

The 5.72 g（20 mmol）racemic 1，1’-bi-2-naphthol was refluxed with 1.53 g（22 mmol）specially pretreated boric anhydride in 120 ml toluene for 6 hours. The 5.27g of powdery white solid obtained was 87% 1，1’-bi-2-naphtholboric anhydride 2. It did not melt at up to 300 ℃. Fig.1 is the IR spectra of 1，1’-bi-2-naphtholboric anhydride. The position and relative intensity of the absorbing peaks were as follows（KBr，cm^{-1}）：1618 m，1596 m，1509 m，1470（naphthalene ring framework）ms，1359（$v^{as}_{B\text{-}O}$）s，1306（$v_{B\text{-}O\text{-}B}$）vvs，1221（$v^{as}_{C\text{-}O}$）s，817 vs，751（$\delta_{C\text{-}H}$）vs.

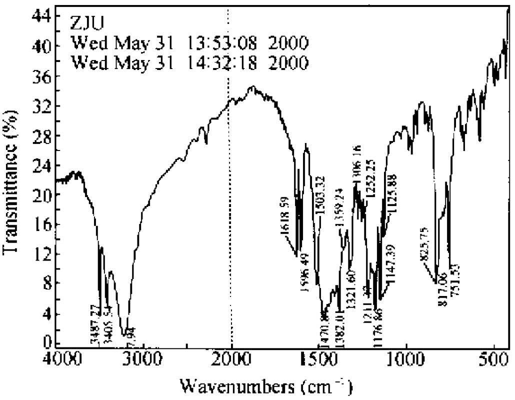

Fig. 1 **FT-IR spectra of** 1, 1'**-bi-2-naphtholboric anhydride** 2

Three grams (5 mmol) 1, 1'-bi-2-naphtholboric anhydride 2 (prepared as stated above) was mixed with 1.15g (10 mmol) (L)-proline 3 in 50 ml dried tetrahedrofuran. The mixture was refluxed for 3 hours to yield a great quantity of white solid precipitate. After cooling down to room temperature, the solid precipitate was filtered out, washed successively with tetrahydrofuran and diethyl ether, and dried under vacuum to yield 90% pure 2.16g 1, 1'-bi-2-naphtholboric acid (L)-proline derivative 4A (based on $C_{25}H_{20}BNO_4 \cdot C_4H_8O$). It did not melt at up to 260 ℃. Fig. 2 is the IR spectra of 4A. The relative intensity of IR absorbing peaks were as follows (KBr, cm^{-1}): 1749 s, 1742 ($v^{as}_{C\text{-}O}$) ms, 1622 m, 1586 m, 1506 m, 1472 (naphthalene ring framework) m, 1369 m, 1334 ($v^{as}_{B\text{-}O}$) ms, 1251 ($v^{as}_{\text{naphthalene ring-O-B}}$) vs, 1234 ($v^{as}_{N \rightarrow B}$) s, 1078 ($v^{s}_{B\text{-}O}$) vs, 1050 ($v^{s}_{\text{Naphthalene ring-O-B}}$) s, 1022 ($v^{s}_{C\text{-}O}$) vs, 824 ms, 752 ($\delta_{\text{binaphthyl-H}}$) s.

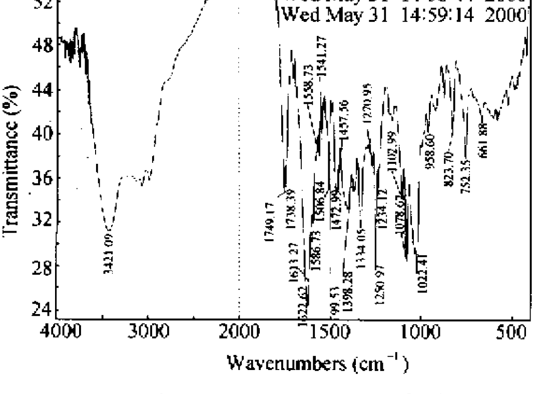

Fig. 2 **FT-IR spectra of** 4A

The solid 4A was treated successively with 30 ml 2mol/L NaOH and 30 ml 2mol/L HCl at room temperature with stirring, followed by addition of 30 ml diethyl ether to produce a two-phase solution. The organic layer was separated and the water layer was extracted with diethyl ether (8ml × 2). The organic phase combined with the extract were washed with saturated brine, dried over anhydrous sodium sulfate, filtered, and evaporated to dryness. Finally 1.22 g of (S)-(−)-1, 1'-bi-2-naphthol was obtained, melt point 206 – 208℃, $[\alpha]^{25}_{D} = -33.1$ (c = 1, THF), 94% ee ($[\alpha]^{25}_{D} = -35.2$, 100% ee), overall yield 79%.

The mother liquor with 4A removed was evaporated to dryness to give a yellowish solid residue, which was then washed with a small amount of benzene and dried under vacuum to yield 2.04 g of 4B. It did not melt at up to 260 ℃. The IR spectra of 4B resembled that of 4A in shape. The crude 4B was then subjected to the same procedure as that for 4A until 1.06 g (R)–(+)–1, 1'-bi-2-naphthol was finally obtained, melt point 206 – 208 ℃, $[\alpha]^{25}_{D} = +26.4$ (c = 1, THF), 75% ee, overall yield 74%.

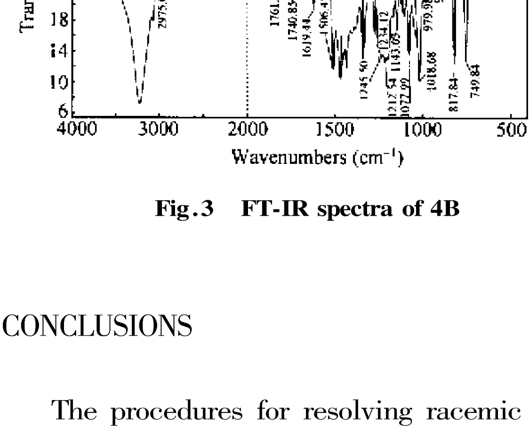

Fig. 3 **FT-IR spectra of 4B**

CONCLUSIONS

The procedures for resolving racemic 1, 1'-bi-2-naphthol can be expressed as follows:

Racemic 1, 1'-bi-2-naphthol (1) reacted

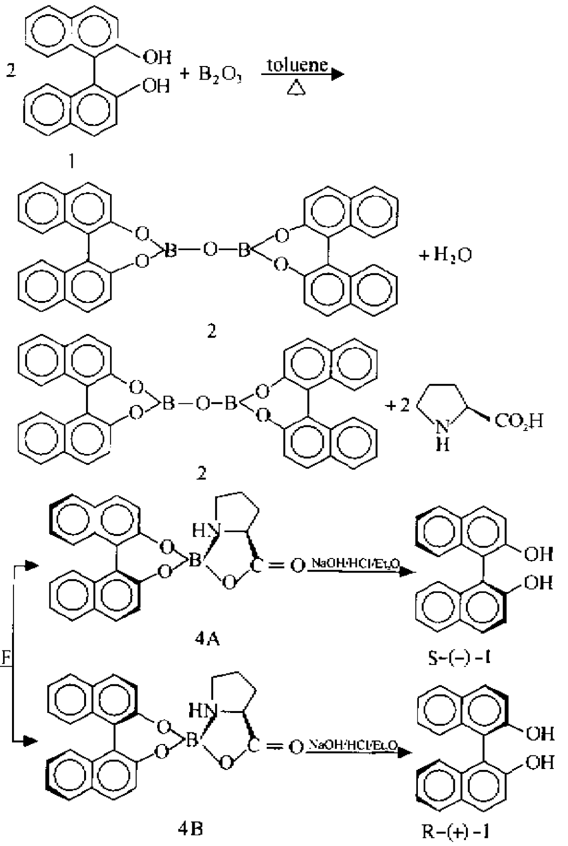

Fig.4 Schematic representation for resolving racemic 1，1'-bi-2-naphthol

with boric anhydride in toluene after being refluxed for 6 h. The resulting water should be continuously removed during the course of the reaction. The reacted mixture was cooled down to room temperature and filtered. The solid was washed successively with freshly dried toluene and diethyl ether， dried under vacuum to give 1，1'-bi-2-naphtholboric anhydried 2， which was allowed to reflux with （L）-proline 3 in tetrahydrofuran for 3 h to produce a white precipitate of （S）-1，1'-bi-2-naphtholboric acid （L）-proline anhydride 4A. The precipitate 4A was filtered out， and the filtrate was evaporated to give solid （R）-1，1'-bi-2-naphtholboric acid （L）-proline anhydride 4B. 4A and 4B were separately dissolved in dilute NaOH and followed by treatment with dilute HCl and diethyl ether， to yield （S）-（ – ）- and （R）-（ + ）-1，1'-bi-2-naphthol from the corresponding organic phase respectively. After further kinetic crystallization in benzene， enantiomercially pure （S）-（ – ） and （R）-（ + ）-1，1'-bi-2-naphthol of over 95% ee were obtained.

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