A High-efficiency Preparation, Properties and Structure of (*R*,*S*)- and (*S*,*S*)-Pyrrolidine-2-carboxylic Acid 3,5-Dioxa-4-boracyclohepta[2,1-*a*;3,4-*a*′]dinaphthalen-4-yl Esters

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A highly-efficient preparative procedure for (*R*,*S*)- and (*S*,*S*)-pyrrolidine-2-carboxylic acid 3,5-dioxa-4-boracyclohepta[2,1-*a*;3,4-*a*′]dinaphthalen-4-yl esters [namely (*R*,*S*)-BNBAP and (*S*,*S*)-BNBAP] is described and the crystal structure of (*R*,*S*)-BNBAP was obtained. The data indicate that (*R*,*S*)-BNBAP is a spirocyclic inner borate salt with almost normal tetrahedral configuration. This structural form may be the basic reason for their high chemical, optical and thermodynamic stability.

Keywords chiral inner borate salt, preparation, property, crystal structure

Introduction

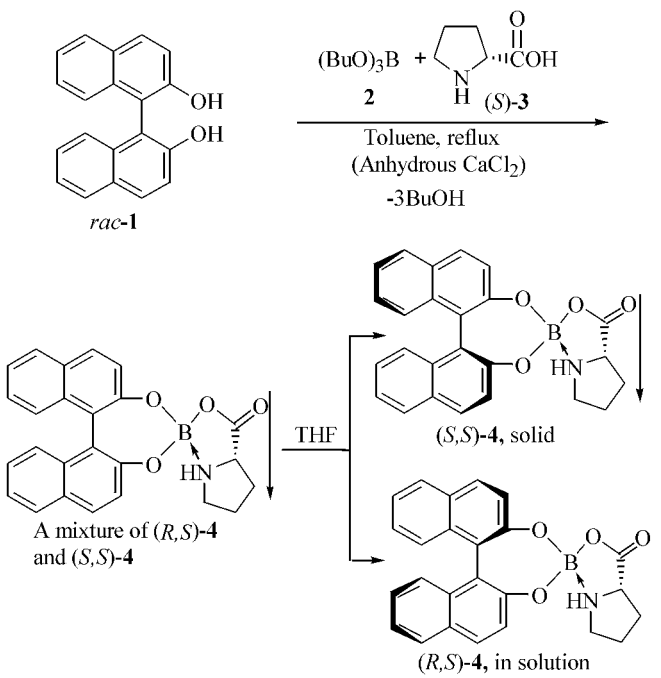
(*R*,*S*)- and (*S*,*S*)-pyrrolidine-2-carboxylic acid 3,5-dioxa-4-boracyclohepta[2,1-*a*;3,4-*a*′]dinaphthalen-4-yl esters, namely (*S*)- and (*R*)-1,1′-bi-2-naphtholboric acid (*S*)-proline anhydrides [(*R*,*S*)-BNBAP and (*S*,*S*)- BNBAP], are intermediates in the preparation of versatile chiral auxiliaries enantiopure 1,1′-bi-2-naphthols.[1] Recently, it was observed that they could catalyze a number of asymmetric reactions.[2] Therefore, it is important to develop a more convenient procedure to prepare. Previously, it was suggested[1] that (*R*,*S*)-BNBAP and (*S*,*S*)-BNBAP might be boron compounds with a N→B coordinate bond; however, this view has not been demonstrated by crystal structure analysis. In the present paper, we report our rapid preparation, the properties of (*R*,*S*)-BNBAP and (*S*,*S*)-BNBAP, and the crystal structure of (*R*,*S*)-BNBAP.

Results and discussion

Preparation and properties of (*R*,*S*)- BNBAP *and* (*S*,*S*)-BNBAP

In our preceding articles,[1] the preparation of (*R*,*S*)-BNBAP and (*S*,*S*)-BNBAP was reported via diastereomeric separation using $BH_3 \cdot SMe_2$ or H_3BO_3 as the boron resource. In those preparations, the starting material borane and the reaction intermediates were all susceptible to moisture and it took about 8 h for highly-efficient reaction of 1,1′-bi-2-naphthol with boric acid. Undoubtedly, it would influence preparative efficiency. In consideration of the fact that the stability for alkyl borates to hydrolysis increases with the increase of the size of alkyl group, and the esterification activity of boron compounds decreases in the order of borane (including haloborane), borate ester and boric acid, we examined the reactions of racemic 1,1′-bi-2-naphthol, butyl borates and (*S*)-proline, and found a high-efficiency preparative method for (*R*,*S*)-BNBAP and (*S*,*S*)-BNBAP as shown in Scheme 1.

Scheme 1



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Racemic 1,1′-bi-2-naphthol (**1**) was refluxed with *n*-butyl borate (or *i*-butyl borate or *s*-butyl borate) (**2**) in toluene for 3 h to give a homogeneous solution. The resulting alcohol in the course of the reaction was removed by absorption of anhydrous $CaCl_2$ charged in a Soxhlet apparatus or a dropping funnel with pressure-equalization arm. After the reaction solution was cooled to about 60 ℃, solid (*S*)-proline (**3**) in a 1∶1 molar ratio was directly added with constant stirring, followed by refluxing the mixture for an additional 2 h, and then cooled to room temperature to give a large amount of white precipitate. The solid was separated and stirred in THF at room temperature for 0.5—1 h, and indissoluble (*S*,*S*)-BNBAP [(*S*,*S*)-**4**] was obtained almost quantitatively. The crude (*S*,*S*)-**4** was treated successively with water and methanol to provide pure (*S*,*S*)-**4**, which could be directly applied to asymmetric reactions (for example, asymmetric reduction of carbonyl compounds *etc*.). The THF mother liquor removed from (*S*,*S*)-**4** was evaporated to dryness to give a crude product enriched with (*R*,*S*)-BNBAP [(*R*,*S*)-**4**]. After washing or crystallizing in methanol, pure (*R*,*S*)-**4** was obtained.

In fact, the process above can be further simplified. An equimolar mixture of *rac*-**1**, a butyl borate and (*S*)-proline was allowed to reflux in dry toluene for 3 h, a solid mixture of both desired products precipitated, almost quantitatively. After treatment according to the same procedure as described above, (*S*,*S*)-**4** and (*R*,*S*)-**4** were obtained in almost same yields. Thus, two desired products were prepared conveniently.

Alternately, if *rac*-**1** was replaced by enantiopure (*S*)- or (*R*)-1,1′-bi-2-naphthol in the above reaction, (*S*,*S*)-**4** and (*R*,*S*)-**4** could be directly obtained in toluene as a white precipitate, respectively. Their IR and ^{1}H NMR spectra were the same as those of the products obtained from diastereomeric separation.

(*S*,*S*)-**4** and (*R*,*S*)-**4** are white solid with high thermodynamic and optical stability. No melting or decomposition was observed up to 290 ℃, and no mutarotation occurred when they were refluxed in toluene for 8 h. They have strong resistance to oxidation, hydrolysis and acidolysis. After treatment with 2 mol·L^{-1} HCl at ambient temperature for 24 h, (*S*,*S*)-**4** and (*R*,*S*)-**4** were recovered almost quantitatively. The solubility of (*S*,*S*)-**4** and (*R*,*S*)-**4** in a number of solvents was considerably different. (*S*,*S*)-**4** was hardly soluble in many common solvents such as H_2O, ROH (R = Me, Et, *i*-Pr), $CHCl_3$, CH_3CN, THF, Et_2O, C_6H_6, $C_6H_5CH_3$ *etc*., while (*R*,*S*)-**4** is soluble in CH_3CN, $CHCl_3$, ROH (R = Me, Et), CH_3COOEt, *etc*., and is very soluble in THF. This difference in solubility is the basis for efficient separation of (*S*,*S*)-**4** and (*R*,*S*)-**4**.

Crystal structure of (*R*,*S*)-**4**

The sample of (*R*,*S*)-**4** obtained above was dissolved in $CH_3COOC_2H_5$ and evaporated slowly to give the single crystals suitable for structure analysis. Crystal structure and the parameters of (*R*,*S*)-**4** were shown in Fig. 1 and Tables 1—3, respectively.

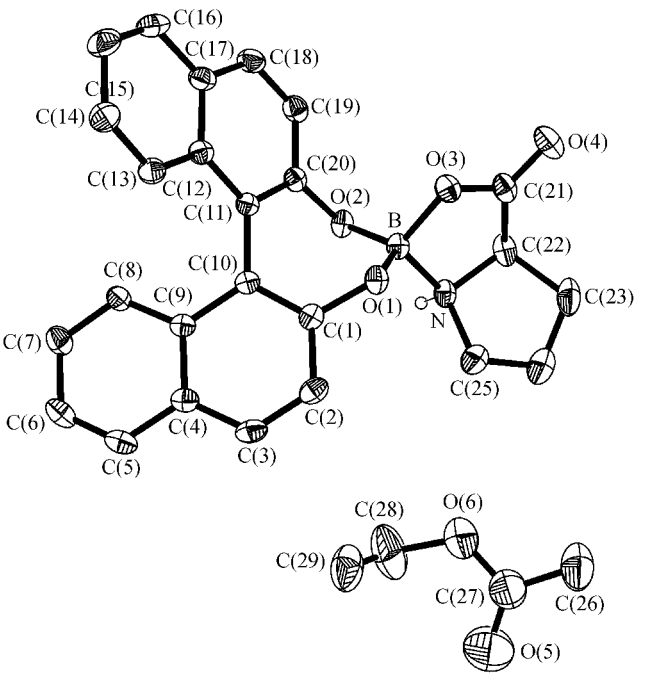

Fig. 1 Molecular structure of (*R*, *S*)-BNBAP · 0.75$CH_3COOC_2H_5$. Only the hydrogen atom on nitrogen atom was shown, other hydrogen atoms were omitted for clarity.

It could be seen that our preceding suggestion was in good conformity with the structure. It had a spirocyclic structure, in which the boron atom existed in tetracoordinated form. Distance between the boron and the nitrogen of the pyrrolidine ring is 0.1604 (4) nm, which is a little longer than that of N—B bond calculated (0.157 nm), indicating that a strong coordinate bond formed between the two atoms, resulting in partial positive charge on the nitrogen and partial negative charge on the boron, *i*.*e*., (*R*,*S*)-**4** is a spirocyclic inner borate salt. On the other hand, the B—O bonds in (*R*,*S*)-**4** were obviously shortened as compared with other tetracoordinated boron compounds[3] containing three B—O bonds, implying that there is a strong back-coordination of the lone pair electrons of the oxygen atoms to the boron atom, which not only provides higher charge density at the boron atom and enlarges difference in electron density between the atoms (*i*.*e*., it enhances ionic nature for the inner salt), but also makes the boron spirocyclic framework more tightly. In addition, it can be seen from the selected bond angles [(109.6 ± 4.5)°, except deviation of angles O(3)-B-N and O(2)-B-O(1) from 109.5° is slightly large] that the boron atom is almost located in the middle of a normal tetrahedron. This configuration of the inner borate salt can be the inherent cause of their strong resistance to oxidation, hydrolysis and acidolysis.

Table 1 Non-hydrogen atom coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($nm^2 \times 10$) for (R,S)-BNBAP

Atom	x	y	z	U_{eq}[a]	Atom	x	y	z	U_{eq}[a]
B	-95(3)	133(3)	4597(2)	48(1)	C(12)	440(2)	818(3)	1667(2)	49(1)
N	-37(2)	2152(3)	5633(2)	54(1)	C(13)	1424(3)	51(4)	132(2)	54(1)
O(1)	978(2)	376(2)	4557(1)	52(1)	C(14)	1232(3)	-599(4)	419(2)	69(1)
O(2)	-327(2)	2532(2)	51(1)	3881(1)	C(15)	64(4)	-497(5)	-211(2)	80(1)
O(3)	-1166(2)	265(2)	4547(2)	58(1)	C(16)	-913(3)	187(5)	97(2)	71(1)
O(4)	-2846(2)	-65(4)	5241(2)	88(1)	C(17)	-767(3)	838(4)	1043(2)	57(1)
O(5)	5469(8)	2932(17)	9411(5)	233(6)	C(18)	-1789(3)	1496(5)	1399(2)	66(1)
O(6)	3944(4)	2744(8)	8129(4)	127(2)	C(19)	-1628(3)	2043(4)	2312(2)	61(1)
C(1)	1997(2)	961(3)	4223(2)	46(1)	C(20)	-433(2)	2020(3)	2937(2)	48(1)
C(2)	3178(3)	850(4)	4854(2)	58(1)	C(21)	-1872(3)	583(3)	5209(2)	60(1)
C(3)	4228(3)	1383(4)	4579(2)	61(1)	C(22)	-1284(3)	808(4)	5896(2)	65(1)
C(4)	4143(2)	2131(4)	3680(2)	53(1)	C(23)	-950(5)	1325(7)	6995(3)	101(2)
C(5)	5208(3)	2824(4)	3408(3)	66(1)	C(24)	351(5)	1832(6)	7345(3)	94(1)
C(6)	5114(3)	3615(5)	2569(3)	71(1)	C(25)	946(3)	1639(5)	6480(2)	121(3)

[a] U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

Table 2 Hydrogen coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($nm^2 \times 10$) for (R,S)-BNBAP

Atom	x	y	z	U_{eq}[a]	Atom	x	y	z	U_{eq}[a]
H(0A)	32	3182	5557	64	H(23A)	-1509	1818	7362	121
H(2A)	3241	406	5468	70	H(23B)	-1017	223	7061	121
H(3A)	5010	1251	4990	73	H(24A)	770	1204	7887	112
H(5A)	5992	2728	3821	80	H(24B)	379	2894	7552	112
H(6A)	5824	4072	2415	88	H(25A)	1171	576	6404	89
H(7A)	3869	4300	1341	82	H(25B)	1697	2265	6543	89
H(8A)	2122	3162	1719	64	H(26A)	4017	1320	10176	197
H(13A)	2219	-7	1723	65	H(26B)	3522	543	9159	197
H(14A)	1888	-1116	220	82	H(26C)	2829	1983	9467	197
H(15A)	-48	-896	-841	96	H(28A)	3927	4276	6998	214
H(16A)	-1696	228	-323	86	H(28B)	4984	4652	7916	214
H(18A)	-2580	1546	991	79	H(29A)	5813	3675	6675	181
H(19A)	-2313	2442	2536	74	H(29B)	5036	2168	6707	181
H(22A)	-1816	2725	5816	78	H(29C)	6104	2611	7598	181

[a] U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

Table 3 Selected bond lengths (nm) and bond angles (°) for (R,S)-BNBAP

B—O(2)	0.1453(3)	O(4)—C(21)	0.1206(4)	O(2)-B-O(1)	115.1(2)	C(1)-O(1)-B	120.5(2)
B—O(1)	0.1441(3)	C(1)—C(10)	0.1376	O(2)-B-O(3)	113.7(2)	C(20)-O(2)-B	113.6(2)
B—O(3)	0.1478	C(10)—C(11)	0.1486(3)	O(1)-B-O(3)	105.5	C(21)-O(3)-B	113.0(2)
B—N	0.1604(4)	C(11)—C(20)	0.1382	O(2)-B-N	105.8(2)	O(4)-C(21)-O(3)	123.7(3)
N—C(25)	0.1492(4)	C(19)—C(20)	0.1408(4)	O(1)-B-N	114.1(2)	C(10)-C(1)-O(1)	121.4(2)
N—C(22)	0.1502(4)	C(21)—C(22)	0.1491(5)	O(3)-B-N	102.1(2)	O(1)-C(1)-C(2)	117.0(2)
O(1)—C(1)	0.138(3)	C(22)—C(23)	0.1561(5)	C(25)-N-C(22)	106.3(2)	C(20)-C(11)-C(10)	119.3(2)
O(2)—C(20)	0.1374(3)	C(11)—C(12)	0.1434(4)	C(25)-N-B	118.2(2)	O(3)-C(21)-C(22)	111.2(2)
O(3)—C(21)	0.1342(3)	C(9)—C(10)	0.1440(4)	C(22)-N-B	105.0(2)	O(4)-C(21)-C(22)	125.1(3)

Conclusions

(S,R)- and (S,S)-pyrrolidine-2-carboxylic acid 3,5-dioxa-4-boracyclohepta[2,1-a;3,4-a']dinaphthalen-4-yl esters can be conveniently prepared via "one pot" reaction of racemic or enantiopure 1,1′-bi-2-naphthol, a butyl borate and (S)-proline in toluene. These preparative methods possess some obvious advantages such as simple operational procedure, short period for preparation and high efficiency. Crystal structure analysis for (R,S)-pyrrolidine-2-carboxylic acid 3,5-dioxa-4-boracyclohepta[2,1-a;3,4-a′]dinaphthalen-4-yl ester indicated that it

was a spirocyclic inner borate salt with almost normal tetrahedron configuration. This structural form determines highly thermodynamic, chemical and optical stability for the chiral boron compound.

Experimental

General

(*S*)-Proline was purchased from Wuhan University Bio-chemical Co. and was dried previous to use. Racemic 1, 1′-bi-2-naphthol was produced in Beijing Xizhong Chemical Factory and recrystallized from diethyl ether, m.p. 218—220 ℃; IR (KBr) ν: 3507, 3436 (O—H) cm^{-1}. *n*-Butyl borate, *i*-butyl borate and *s*-butyl borate were synthesized according to the literatures.[4] Toluene was used in analytical grade.

IR spectra were recorded on a Testscan Shimadzu FTIR 8000 or a Nicolet 170 SX FT-IR spectrophotometer in KBr. ^{1}H NMR spectra were performed on a Varian Mercury VX 300 and all chemical shifts were reported as δ values relative to Me_4Si. Optical rotations were measured on a Perkin-Elmer 241 Mc polarimeter. Melting points were determined on a VEB Wagetechnik Rapio PHMK 05 instrument and were not corrected.

Preparation of (*S*,*R*)-**4** *and* (*S*,*S*)-**4** *via diastereomeric separation*

Racemic 1,1′-bi-2-naphthol (5.72 g, 20 mmol), *i*-butyl borate (4.80 g, 20 mmol) and dried (*S*)-proline (2.50 g, 21.7 mmol) were allowed to mix in dry toluene (130 mL) and refluxed with constant stirring for 3 h to precipitate a large amount of white solid. The isobutanol liberated in the reaction was absorbed by anhydrous calcium chloride (*ca*. 15 g) charged in a Soxhlet extractor (or a dropping funnel with pressure-equalization arm). The reaction mixture was cooled to room temperature. The white solid was separated by filtration, washed successively with a novel toluene and diethyl ether, and then dried under reduced pressure to give a mixture (7.70 g) of (*S*,*S*)-**4** and (*R*,*S*)-**4** in 94% yield. The solid was extracted by using 80 mL of THF with stirring for 1 h at ambient temperature. The indissoluble solid was filtered and washed successively with a fresh THF, H_2O and CH_3OH, dried under reduced pressure, offered (*S*,*S*)-**4** (4.55 g). It did not melt at up to 295 ℃. After the recrystallization from acetonitrile, its IR, ^{1}H NMR and mass spectra were the same as those reported.[1] The mother liquor removed from (*S*,*S*)-**4** was evaporated to dryness to obtain the yellowish solid residue enriched with (*R*,*S*)-**4** (4.60 g). The residue was treated with CH_3OH and recrystallized from ethyl acetate to give a 1∶0.75 solvate of (*R*,*S*)-**4** and ethyl acetate. ^{1}H NMR (DMSO-d_6) δ: 1.16 (t, *J* = 7.2 Hz, 2.25H, C**H**$_3$CH$_2$O), 1.73—2.25 [m, 6.25H, CH_2CH_2 + CH_3COO (s, 1.97, 2.25H)], 3.08—3.21 (m, 1 H, NC**H**H), 3.36—3.48 (m, 1 H, NCH**H**), 4.01 (q, *J* = 7.2 Hz, 1.5H, OCH_2CH_3), 4.52—4.58 (m, 1H, NCHCOO), 7.08 (t, *J* = 9.0 Hz, 2H, 2H-Binap[5]), 7.19—7.27 (m, 3H, 3H-Binap), 7.35 (t, *J* = 7.8 Hz, 2H, 2H-Binap), 7.44 (d, *J* = 9.3 Hz, 1H, H-Binap), 7.96 (d, *J* = 9.3 Hz, 2H, 2H-Binap), 7.99 (d, *J* = 8.7 Hz, 2H, 2H-Binap), 8.44 (q, *J* = 6.6 Hz, 1H, NH); IR (KBr) ν: 3205 (N—H), 3056 (Ar—H), 2978 (C—H), 1773 (C = O, prolinate), 1734 (C = O, acetate), 1337 (B—O), 1240 (Ar—O), 1210 (N→B), 1021 (C—O) cm^{-1}.

In the above reaction, almost the same results were obtained when *i*-butyl borate was replaced by *n*-butyl borate or *s*-butyl borate.

Direct preparation of (*S*,*R*)-**4** *and* (*R*,*S*)-**4** *from enantiopure* 1,1′-*bi*-2-*naphthol*

Similar to the procedure described above, a mixture of either enantiopure 1,1′-bi-2-naphthol, butyl borate and (*S*)-proline was allowed to reflux in toluene to give almost pure (*S*,*S*)-**4** or (*R*,*S*)-**4** in more than 90% yield.

X-*Ray crystal structure analysis for* (*R*,*S*)-**4**

Single crystal suitable for X-ray crystal structure analysis was obtained by slow evaporation of ethyl acetate solution of (*R*,*S*)-**4**. A colorless crystal of (*R*,*S*)-**4**·$0.75CH_3COOC_2H_5$ having the dimension of 2.0 mm × 1.2 mm × 0.7 mm was mounted on a glass fiber. X-Ray crystallographic data collection and cell refinement were performed on an Enraf-Nonius CAD4 four-circle diffractometer using graphite monochromated Mo Kα (λ = 0.071073 nm) radiation at temperature 293(2) K. All programs used for structure solutions and refinements were included in the SHELXTL (Sheldrick, 1997) package. A total of 2696 unique reflections were collected, of which 2413 reflections had $I > 2\sigma(I)$ and were used in the structure solution and refinements. The corrections for Lp factors and empirical absorption were applied to the intensity data. The structure was solved by direct methods and refined on F^2 using a full-matrix least-squares technique. The non-hydrogen atoms were refined by a full-matrix least-squares, anisotropically, and hydrogen atoms were included but not refined. Cell dimensions were obtained by the least-squares refinement of well centered 25 reflections in the θ range of 1.49°—26.01°. The intensities of three representative reflections were measured after every 300 reflections. The final cycle of full-matrix least-squares refinement was based on 2413 observed reflections and 335 variable parameters. Convergence with unweighted and weighted agreement factors was achieved at $R = 0.054$ and $R_w = 0.136$ ($w = 1/[s^2(F_o^2) + (0.1018P)^2 + 0.0401P]$, where $P = (F_o^2 + 2F_c^2)/3$). The residual density had largest diffraction peak 279 e·nm^{-3} and minimum trough at −206 e·nm^{-3}.

Crystal data for (*R*,*S*)-**4**·$0.75CH_3COOC_2H_5$: empirical formula, $C_{28}H_{26}BNO_{5.5}$; formula weight, 475.31;

calculated density (D), 1.220 Mg/m^3; volume, 1.2935(4) nm^3; crystal system, monoclinic; space group, $P2_1$; Z = 2; unit cell dimensions: a = 1.0843(2) nm, b = 0.87247 (17) nm, c = 1.3961 (3) nm, β = 101.67°; absorption coefficient (μ), 0.084 mm^{-1}; limiting indices, $0 \leqslant h \leqslant 13$, $0 \leqslant k \leqslant 10$, $-17 \leqslant l \leqslant 16$; F(000), 500; GOF, 1.069.

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5 2H-Binap represents two protons of binaphthalene ring.

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