EurJOC
European Journal of Organic Chemistry

A Journal of ChemPubSoc Europe

Accepted Article

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To be cited as: *Eur. J. Org. Chem.* 10.1002/ejoc.201801448

Link to VoR: http://dx.doi.org/10.1002/ejoc.201801448

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10.1002/ejoc.201801448

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Chiral tetraaryl- and tetraalkynylborates as chiral solvating agents for tetraalkylammonium salts

Eiji Tayama*[a] and Takeshi Sugawara[b]

Abstract: The application of tetra-carbon-substituted chiral borate sodium salts ($NaBR^*_4$) as NMR chiral solvating agents for various tetraalkylammonium salts (R_4NX) has been successfully demonstrated. Ion exchange between R_4NX and $NaBR^*_4$ proceeded in excellent yields and provided the corresponding diastereomeric salts ($R_4NBR^*_4$). The ee values of the R_4NX salts were determined by ^1H NMR analysis of $R_4NBR^*_4$. Two types of chiral borates, tetraaryl- and tetraalkynylborates with optically active 1,1'-binaphthyl components were used. At the beginning of this research, we investigated the efficacy of a known chiral tetraarylborate developed by Pommerening et al. for R_4NX. To expand the possibility of further structural design of the chiral borate, we designed chiral tetraalkynylborates as a new structure. Their synthesis and application are also described.

Introduction

The enantiomeric excess (ee) of a chiral compound must be determined to judge the success or failure of an asymmetric synthesis. The most standard and widely applicable, reliable method is HPLC analysis using a chiral column (chiral HPLC) with a UV/Vis detector; however, this method requires a UV-active substituent, such as an aryl moiety, in the compound. Frequently, the UV-active substituent is introduced by further synthetic transformations of the chiral compounds. Consequently, developments of chiral solvating agents such as chiral acids, metal complexes, and cyclic receptors have been studied to allow the determination of ee by NMR analysis, even in the absence of a UV-active substituent.[1,2]

In our previous works on tetraalkylammonium salts (R_4NX), such as N-chiral ammonium salts **2**,[3] **3**,[4] and azetidine-2-carboxylic acid derived-ammonium salt (1*R*,2*R*)-**4**[5] (Figure 1), we had difficulties to determine their ees. Fortunately, some N-chiral ammonium salt derivatives could be evaluated by chiral HPLC with trifluoroacetic acid and diethylamine as additives in the mobile phase. However, these conditions were ineffective for less polar R_4NX salts without hydroxy groups, such as (1*R*,2*R*)-**4**, because the interactions between R_4NX and the chiral stationary phase of the column would be decreased by the presence of the additives. Furthermore, no chiral solvating agents applicable for R_4NX species had been developed at that time, and therefore we considered developing an efficient way to determine the ee of an R_4NX species. In 2017, Pommerening et al. reported chiral sodium tetraarylborate (*S*)-**1a** as an asymmetric catalyst (Figure 2).[6] Their work inspired us, and we found that ion exchange of triflate salt (1*R*,2*R*)-**4** with sodium tetraphenylborate ($NaBPh_4$) in THF gave (1*R*,2*R*)-**4-BPh$_4$** in an almost quantitative yield (Figure 1).[5,7] Additionally, (*S*)-**1a** has a remarkable advantage over well-known phenoxide-type chiral borates, such as bis(1,1'-binaphthalene-2,2'-dioxy)borate.[8] Tetra-carbon-substituted (*S*)-**1a** is less polar and more chemically stable, which allows chromatographic purification. As shown in Figure 1 (this work), when the chiral borate was subjected to ion exchange, the resulting tetraalkylammonium borate ($R_4NBR^*_4$) forms a diastereomeric salt. The ees of the starting R_4NX and its precursor amine, R_3N, were determined by NMR analysis.[9] Thus, we decided to investigate the ability of (*S*)-**1a** as a chiral solvating agent for R_4NX. To facilitate the further structural design of chiral borates and its preparation, we designed chiral tetraalkynylborates **1b**–**d** as a new structure (Figure 2). The synthesis and application of these species as chiral solvating agents were demonstrated.

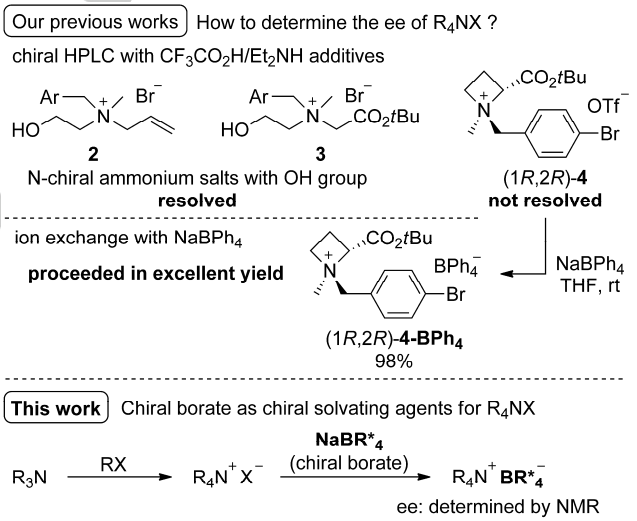

Figure 1. Determination of the ee of R_4NX by NMR analysis

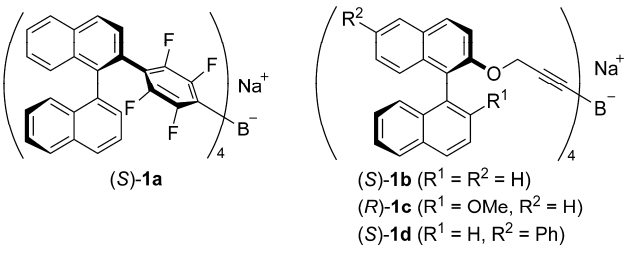

Figure 2. Chiral borates: (*S*)-**1a** developed by Pommerening et al. (ref. 6a) and our designed (*S*)-**1b**, (*R*)-**1c**, and (*S*)-**1d**.

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Results and Discussion

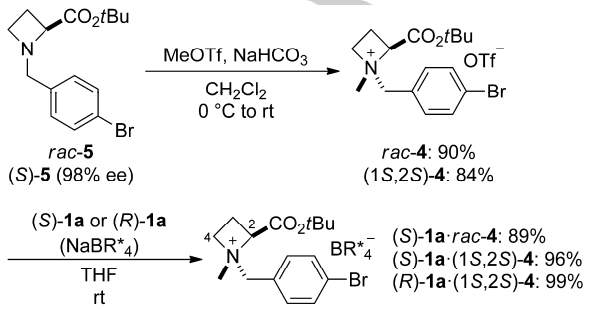
First, we selected chiral borate **1a** and investigated its efficacy as a chiral solvating agent using ammonium salts **4** as model compounds (Scheme 1). Diastereomerically pure ammonium salts *rac*-**4** and (1*S*,2*S*)-**4** were prepared by *N*-quaternization of precursor tertiary amine **5** with methyl triflate (MeOTf).[5] Ion exchange of **4** with a slight excess (1.1 to 1.3 equivalents) of (*S*)-**1a** or (*R*)-**1a** in THF proceeded smoothly. Evaporation and chromatographic purification provided ammonium chiral borate salts **1a**·**4** in excellent yields.

^{1}H NMR analysis of (S)-**1a**·*rac*-**4** in chloroform-*d* ($CDCl_3$) was conducted, and a portion of the spectrum[10] (δ 4.40–2.35) is shown as (i) in Figure 3. Clearly resolved signals from 2-H and 4-H, as in *rac*-**4**, were observed with almost baseline separation. To assign each diastereomer, ^{1}H NMR analyses of (*S*)-**1a**·(1*S*,2*S*)-**4** and (*R*)-**1a**·(1*S*,2*S*)-**4** were also conducted. Their partial spectra are shown as (ii) and (iii), respectively. Only one diastereomer was detected. The chemical shifts were slightly different (0.02-0.03 ppm). Small amounts of impurities such as H_2O or solvents might be affected to move the chemical shifts. In fact, when ^{1}H NMR analysis of (*S*)-**1a**·*rac*-**4** was carried out in acetone-d_6 (iv), the chemical shifts were not resolved and almost the same with those of triflate salt *rac*-**4**.[11] A polar solvent would disrupt the cation-anion interactions and break the asymmetry around the ammonium cation.

To clarify that chiral borate **1a** is a useful chiral solvating agent for R_4NX, we attempted an anion exchange of *rac*-**4** with a commercially available chiral anion, such as D-camphor-10-sulfonic acid sodium salt (D-**6**) (Scheme 2). Ion exchanged D-**6**·*rac*-**4** was not obtained, and 90% of *rac*-**4** was recovered. To the best our knowledge, previous examples of ion exchanges between R_4NX and a sulfonate anion (RSO_3^-) are usually performed under the following combinations: (i) an ammonium hydroxide (R_4NOH) and a sulfonic acid (RSO_3H) or (ii) R_4NX and silver sulfonate (RSO_3Ag).[12] The use of **1a** offers a great advantage in ion exchange with R_4NX because the reaction proceeds in excellent yields under mild and simple conditions.

We next investigated the efficacy of **1a** as a chiral solvating agent towards standard amino acid esters, such as valine, that do not have a UV-active substituent (Scheme 3). Ammonium salts *rac*-**9a-OTf** and *rac*-**9a-I** were prepared from DL-valine *tert*-butyl ester (*rac*-**7a**) via *N*-methylations [stepwise via *rac*-**8a** (path a) or directly (path b)]. Anion exchange of the triflate and iodide salts with (*S*)-**1a** under the same conditions provided (*S*)-**1a**·*rac*-**9a** in good yields.

^{1}H NMR analysis of (*S*)-**1a**·*rac*-**9a** was conducted, and a portion of the spectrum (δ 2.85–0.60) is shown in Figure 4, (i). Baseline-separated chemical shifts from 2-H, $N(CH_3)_3$, and 4-H were observed. Similarly, the spectrum (ii) derived from (*S*)-**1a**·(*S*)-**9a**, prepared by ion exchange between (*S*)-**1a** and (*S*)-**9a-OTf**[13] (97% yield), showed one diastereomer. To demonstrate that our method enables the determination of amino acid-derived ammonium salts such as **9a** and its precursor amines, **7a** and **8a**, we prepared the 50% ee mixture of (*S*)-**9a-OTf**.[13] Anion exchange with (*S*)-**1a** (98% yield) followed by ^{1}H NMR analysis afforded spectrum (iii). Integral values for the chemical shifts of 2-H, $N(CH_3)_3$, and 4-H of the enantiomers showed ratios of approximately 3/1. To check kinds of anions are not affected for the resolution, ^{1}H NMR analysis of (*S*)-**1a**·*rac*-**9** derived from iodide salt *rac*-**9a-I** was conducted (iv). These results were in agreement with spectrum (i) derived from *rac*-**9a-OTf**.



Scheme 1. Preparation of tetraalkylammonium chiral borate salts **1a**·**4**.

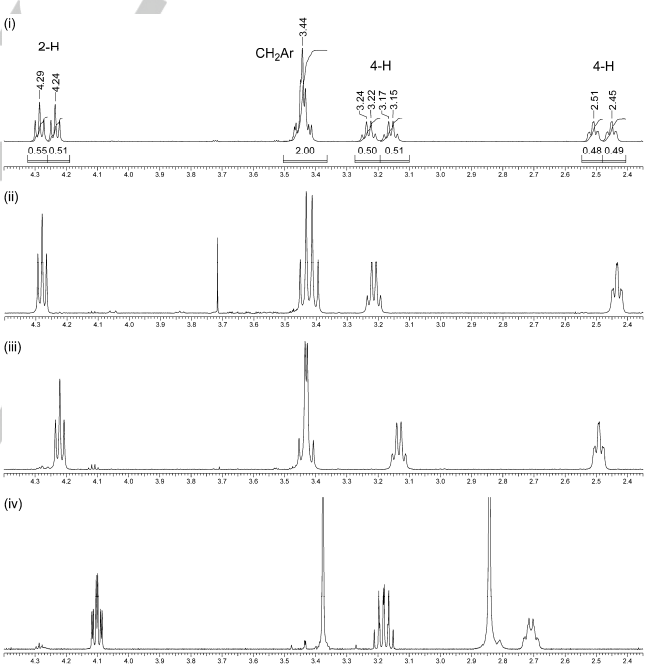
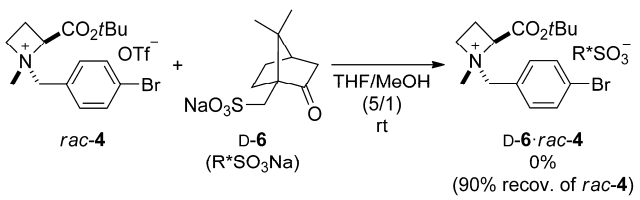
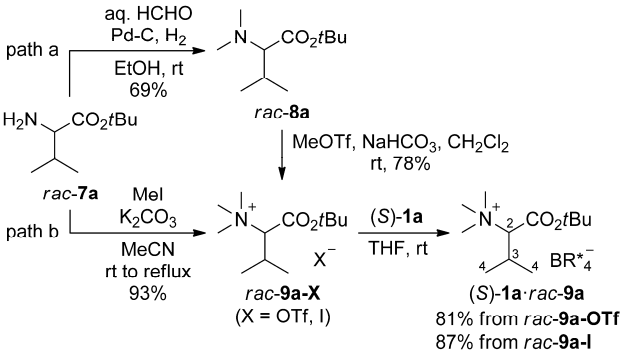


Figure 3. Partial 700 MHz ^{1}H NMR spectra of **1a**·**4** at 20 °C, (i) (*S*)-**1a**·*rac*-**4** in $CDCl_3$, (ii) (*S*)-**1a**·(1*S*,2*S*)-**4** in $CDCl_3$, (iii) (*R*)-**1a**·(1*S*,2*S*)-**4** in $CDCl_3$, and (iv) (*S*)-**1a**·*rac*-**4** in acetone-d_6.



Scheme 2. Attempted ion exchange between *rac*-**4** and D-**6**.



Scheme 3. Preparation of (*S*)-**1a**·*rac*-**9a**

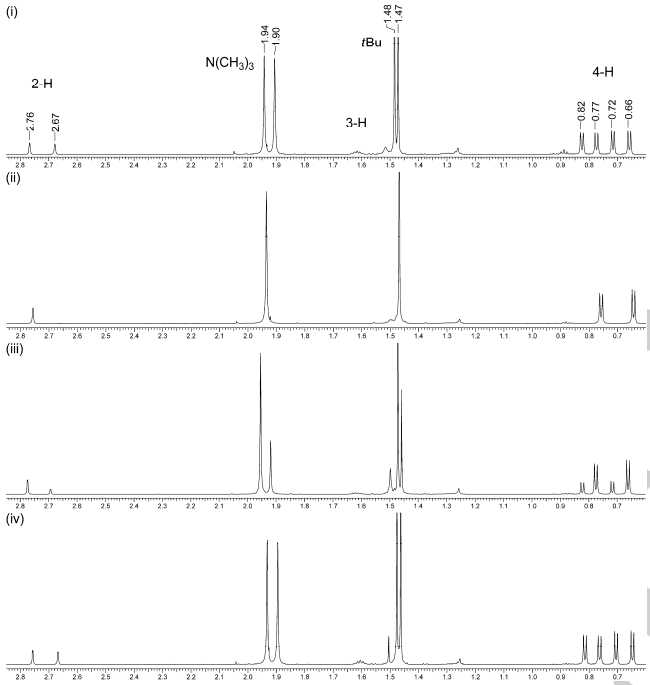
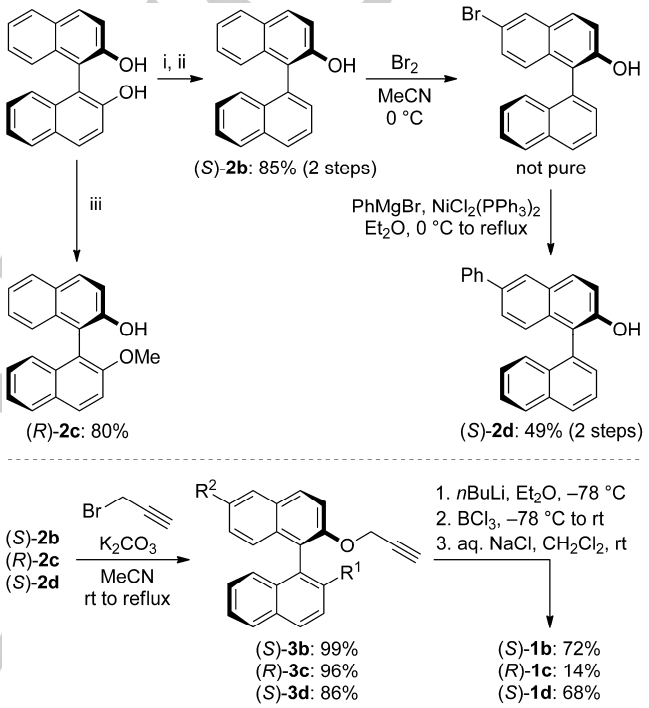


Figure 4. Partial 700 MHz ^{1}H NMR spectra of (*S*)-**1a**·**9a** in $CDCl_3$ at 20 °C. Derived from: (i) *rac*-**9a-OTf**, (ii) (*S*)-**9a-OTf**, (iii) (*S*)-**9a-OTf** (50% ee), (iv) *rac*-**9a-I**.

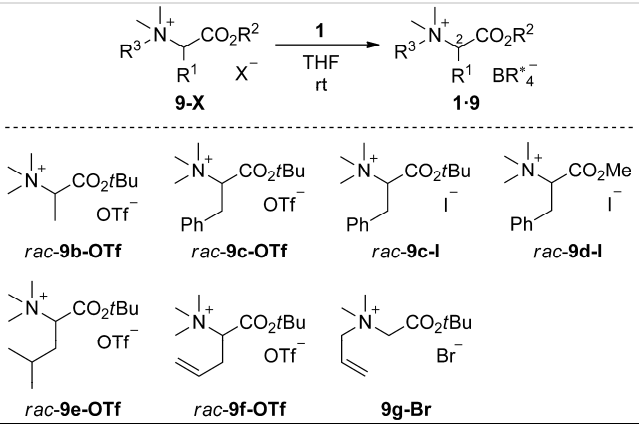
Since chiral borate **1a** was found to act as a chiral solvating agent, we decided to investigate the ability of chiral tetraalkynylborates **1b**–**d** prepared from [1,1'-binaphthalen]-2-ol derivatives **2b**–**d** via *O*-propargylation into **3b**–**d** (Scheme 4). These synthetic routes do not require the use of expensive tetrafluorobenzene linker such as (*S*)-**1a**.[6a,6b] (*S*)-**2b**[14] and 2'-methoxy derivative (*R*)-**2c**[15] were prepared by known methods. We next examined a substitution at the 6-position, as in (*S*)-**2b**. Treatment of (*S*)-**2b** with Br_2 in MeCN, which has been reported for the synthesis of analogous compounds,[16] gave the desired 6-bromo derivative as the main product. However, the pure compound could not be obtained. Thus, the product was coupled with PhMgBr. Careful chromatographic purification of the coupled product afforded pure 6-phenyl derivative (*S*)-**2d** in 49% yield from (*S*)-**2b**. *O*-Propargylation of monophenol **2b**–**d** into **3b**–**d** proceeded in good yields. Lithiation of **3b**–**d** with *n*BuLi in Et_2O, treatment with BCl_3, followed by brine treatment afforded target chiral borates **1b**–**d**. (*S*)-**1b** and (*S*)-**1d** were obtained in 72% and 68% yields, respectively. On the other hand, the yield of (*R*)-**1c** was only 14% with recovery of (*R*)-**3c**. The 2'-OMe substituent would inhibit tetra-substitution of the boron atom because of steric repulsion.[17] By treatment with brine, the hydrolysis of the mono-, di-, and tri-substituted derivatives would regenerate (*R*)-**3c**. Although the synthetic route to (*S*)-**2d** should be optimized, we started to investigate the efficacies of (*S*)-**1b** and (*S*)-**1d** as chiral solvating agents.



Scheme 4. Preparation of chiral tetraalkynylborates **1b**–**d**. (i) Tf_2O, *i*Pr_2NEt, CH_2Cl_2, 0 °C to rt, without purification. (ii) Pd-C, H_2 (1 atm), *i*Pr_2NEt, EtOH, rt. (iii) MeI, K_2CO_3, acetone, rt to reflux.

To define the substrate scope and limitations of chiral borates (*S*)-**1a**, **1b** and **1d**, we prepared various amino acid-derived ammonium salts *rac*-**9b**–**g-X** and examined their resolution. Representative resolved chemical shifts are shown in Table 1. ^{1}H NMR analysis of (*S*)-**1a**·*rac*-**9b** derived from (*S*)-**1a** and alanine derivative *rac*-**9b-OTf** afforded baseline-separated chemical shifts such as 2-H (δ 2.94 & 2.84, q) and 3-H (δ 0.90 & 0.71, d) (Entry 1). The use of (*S*)-**1b** instead of (*S*)-**1a** also provided baseline-separated chemical shifts for 3-H (δ 0.47 & 0.41, d) (Entry 2). Although the peak separation value (ΔΔδ) for 3-H was smaller than those of (*S*)-**1a** [(*S*)-**1a**: ΔΔδ = 0.19, (*S*)-**1b**: ΔΔδ = 0.06], (*S*)-**1b** also acts as a chiral solvating agent for R_4NX. The same experiment with (*S*)-**1d** showed almost the same result (Entry 3). To clarify the efficacy of (*S*)-**1** as a chiral solvating agent, we examined this resolution for phenylalanine-,

Table 1. ^{1}H NMR analysis of (*S*)-**1**·*rac*-**9** in $CDCl_3$ at 20 °C and their representative separated chemical shifts[a]

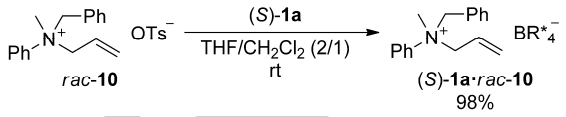


Entry	9-X	(*S*)-1	Yield[b] [%]	Representative separated chemical shifts δ (splitting pattern)	
1[c]	**9b-OTf**	**1a**	90	2.94, 2.84 (q)	0.90, 0.71 (d)
2	**9b-OTf**	**1b**	96	0.47, 0.41 (d)	
3	**9b-OTf**	**1d**	87	2.73, 2.68 (q)	0.50, 0.42 (d)
4	**9c-OTf**	**1b**	99	2.58, 2.40 (dd)	
5[d]	**9c-I**	**1b**	92	2.58, 2.40 (dd)	
6[e]	**9d-I**	**1b**	88	3.32, 3.22 (dd)	2.71, 2.65 (s)
7	**9e-OTf**	**1b**	93	0.76, 0.70 (ddd)	
8	**9e-OTf**	**1a**	91	3.05, 2.99 (dd)	1.06, 0.98 (ddd)
9	**9f-OTf**	**1b**	96	not clearly resolved	
10	**9f-OTf**	**1a**	90	2.96, 2.88 (dd)	
11[d]	**9g-Br**	**1a**	93	not clearly resolved	

[a] Unless otherwise noted, the reactions were performed in THF and the products were analyzed by 700 MHz NMR. [b] Isolated yield. [c] Analyzed by 400 MHz NMR. [d] Performed in THF/CH_2Cl_2 (10/1). [e] Performed in THF/MeOH (4/1).

leucine-, triflate-, iodide-, *tert*-butyl-, and methyl ester-derived ammonium salts (Entries 4–10). The use of (*S*)-**1b** was applicable in many cases; however, by comparing Entry 7 to Entry 8 and Entry 9 to Entry 10, it was found that (*S*)-**1a** is a more efficient chiral solvating agent than (*S*)-**1b** for various types of R_4NX. In the resolution of the α-allylglycine derivative *rac*-**9f-OTf**, (*S*)-**1b** did not provide any separated chemical shifts (Entry 9). In contrast, the use of (*S*)-**1a** provided baseline-separated chemical shifts for 2-H (δ 2.96, 2.88, dd) (Entry 10). Additionally, we tried an asymmetric recognition of the methylene protons (α or allylic) as seen in glycine-derived ammonium salt **9g-Br** using (*S*)-**1a** as a chiral solvating agent (Entry 11). However, the methylene protons did not separate.

Finally, we examined the resolution of N-chiral ammonium salt *rac*-**10** with (*S*)-**1a** (Scheme 5). Their anion exchange was carried out in THF/CH_2Cl_2 (2/1) to dissolve the starting salts and, the exchange provided corresponding ammonium borate salt (*S*)-**1a**·*rac*-**10** in 98% yield. The partial ^{1}H NMR spectrum (δ 4.05–3.15) showed approximately 50/50 separation of the allylic and benzylic methylene protons (Figure 5).



Scheme 5. Preparation of (*S*)-**1a**·*rac*-**10**.

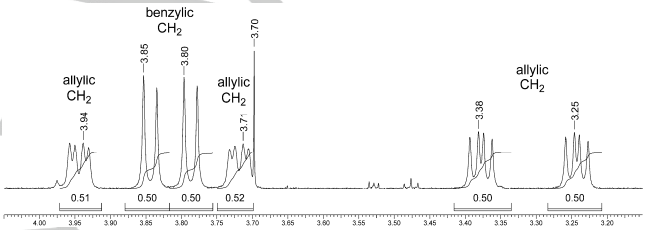


Figure 5. Partial 700 MHz ^{1}H NMR spectrum of (*S*)-**1a**·*rac*-**10** in $CDCl_3$ at 20 °C.

Conclusions

In conclusion, we successfully demonstrated that tetra-carbon-substituted chiral borate **1** is a useful chiral solvating agent for various types of tetraalkylammonium salts R_4NX, as observed by ^{1}H NMR analysis. This method enables the determination of the ees of R_4NX salts and their precursor amines, R_3N. The procedure is quite simple, can be performed under mild conditions, and applicable for typical counter anions, such as triflate (OTf), iodide (I), bromide (Br), and tosylate (OTs). While the exact reason is unclear at present, chiral tetraarylborate **1a**, developed by Pommerening et al.,[6a] is much more effective for resolving chemical shifts than our designed chiral tetraalkynylborate **1b**. The rigid structure of **1a** or its tetrafluorobenzene component might have positive effects. However, **1b** is easy to prepare and further functionalize, such as into **1d**.

Further studies on chiral borates **1** are necessary, e.g., chromatographic separation or fractional crystallization of diastereomeric salts, determination of absolute stereochemistry of R_4NX by single-crystal X-ray diffraction, and the scope and limitations of structural design. These studies will expand the applications of **1** for various areas of chemistry.

Experimental Section

General: Specific rotations were recorded on a JASCO polarimeter P–1010. Infrared spectra (IR) were recorded on a Perkin Elmer Spectrum GX FT-IR or a JASCO FT/IR-4600 spectrometer. ^{1}H, ^{13}C and ^{11}B NMR spectra were measured on Varian spectrometers (^{1}H: 700 MHz, ^{13}C: 175 MHz; ^{1}H: 400 MHz, ^{13}C: 100 MHz) or a Bruker spectrometer (^{1}H: 400 MHz, ^{13}C: 100 MHz, ^{11}B: 128 MHz). Me_4Si (δ 0 ppm) was used as an internal standard in $CDCl_3$ for ^{1}H NMR, and $CDCl_3$ (δ 77.00 ppm) was used for ^{13}C NMR. The residual protons (δ 2.05 ppm) were used as an internal standard in acetone-d_6 for ^{1}H NMR, and acetone-d_6 (δ 29.92 ppm) was used for ^{13}C NMR. Me_4Si (δ 0 ppm) was used as an internal standard in DMSO-d_6 for ^{1}H NMR, and DMSO-d_6 (δ 39.51 ppm) was used for ^{13}C NMR. Boron trifluoride diethyl etherate ($BF_3{\cdot}OEt_2$) was used as an external standard (δ 0 ppm) for ^{11}B NMR. The splitting patterns are denoted as follows: s, singlet; d, doublet; t, triplet; q, quartet; sept, septet; m, multiplet; and br, broad peak. High-resolution mass spectra (ESI, APCI, positive, and negative) were measured on a Thermo Fisher Scientific LC/FT-MS spectrometer. Reactions involving air- or moisture-sensitive compounds were conducted in appropriate round-bottomed flasks with a magnetic stirring bar under an argon (Ar) atmosphere. Anhydrous tetrahydrofuran (THF) was purchased from KANTO Chemical Co., Inc., Japan. Anhydrous diethyl ether (Et_2O) was obtained by distillation from sodium benzophenone prior to use. A 1 M BCl_3 *n*-heptane solution was purchased from Sigma-Aldrich. (*S*)- and (*R*)-sodium tetrakis(2-[2,3,5,6-tetrafluorophenyl]-1,1′-binaphthalene)borate [(*S*)-**1a** and (*R*)-**1a**] were prepared according to the literature.[6a-b, 18] D-Camphor-10-sulfonic acid sodium salt (D-**6**) was purchased from FUJIFILM Wako Pure Chemical Corporation. For thin layer chromatography (TLC) analysis throughout this work, Merck TLC plates (silica gel 60 F_{254}) were used. The products were purified by preparative column chromatography on silica gel (60N, spherical neutral) purchased from KANTO Chemical Co., Inc., Japan.

(*S*)-[1,1'-Binaphthalen]-2-ol [(*S*)-2b][14, 19]: A solution of (*R*)-1,1'-bi-2-naphthol (1.43 g, 5.00 mmol) and *N*,*N*-diisopropylethylamine (0.87 mL, 5.0 mmol) in CH_2Cl_2 (25 mL) was treated with Tf_2O (0.84 mL, 5.0 mmol) at 0 °C and the mixture was stirred for 1 h at room temperature under an Ar atmosphere. The resulting mixture was diluted with H_2O and extracted with CH_2Cl_2. The combined extracts were washed with brine, dried over Na_2SO_4, and evaporated. A mixture of the residue, *N*,*N*-diisopropylethylamine (1.74 mL, 10.0 mmol), and Pd-C (loading: 10 wt.%, 0.16 g) in EtOH (25 mL) was stirred for 12 h at room temperature under a H_2 atmosphere. The resulting mixture was filtered through a pad of Celite and the filtrate was evaporated. The residue was purified by chromatography on silica gel (*n*-hexane/CH_2Cl_2 = 1.5/1 to 1/1 as the eluent) to afford (*S*)-**2b** (1.15 g, 85% yield) as colorless crystals. M.p. 169-170 °C. $[\alpha]^{23}_{589}$ = −121.6 (*c* = 1.0, $CHCl_3$). IR (KBr): ν_{max} = 3542, 3054, 1618, 1591, 1513, 1503, 1468, 1435, 1383, 1346, 1335, 1303, 1291, 1270, 1254, 1229, 1188, 1165, 1143, 1125, 1075, 1013, 971, 937, 819, 804, 788, 780, 753, 723 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (d, *J* = 8.0 Hz, 1H, ArH), 7.96 (d, *J* = 8.0 Hz, 1H, ArH), 7.89 (d, *J* = 8.8 Hz, 1H, ArH), 7.85 (d, *J* = 8.0 Hz, 1H, ArH), 7.63 (dd, *J* = 8.4, 6.8 Hz, 1H, ArH), 7.55-7.47 (m, 2H, ArH), 7.38 (d, *J* = 8.8 Hz, 1H, ArH), 7.36-7.28 (m, 3H, ArH), 7.22 (ddd, *J* = 7.5, 7.5, 1.4 Hz, 1H, ArH), 7.09 (d, *J* = 8.4 Hz, 1H, ArH), 4.91 (s, 1H, OH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.9, 134.1, 133.8, 132.8, 131.4, 129.8, 129.6, 129.2, 128.9, 128.4, 128.0, 126.8, 126.52, 126.51, 126.0, 125.7, 124.9, 123.3, 118.7, 117.4 ppm.

(*S*)-2-(Prop-2-yn-1-yloxy)-1,1'-binaphthalene [(*S*)-3b]: A mixture of (*S*)-**2b** (135 mg, 0.50 mmol) and K_2CO_3 (69 mg, 0.50 mmol) in MeCN (2.5 mL) was stirred for 30 min at room temperature under an Ar atmosphere. The mixture was treated with propargyl bromide (49 μL, 0.65 mmol) and refluxed for 14 h. The resulting mixture was cooled to room temperature and filtered. The filtrate was evaporated and the residue was purified by chromatography on silica gel (*n*-hexane/CH_2Cl_2 = 2/1 as the eluent) to afford (*S*)-**3b** (152 mg, 99% yield) as colorless crystals. M.p. 110-111 °C. $[\alpha]^{23}_{589}$ = +38.1 (*c* = 1.0, $CHCl_3$). IR (KBr): ν_{max} = 3296, 3052, 2919, 2869, 1620, 1592, 1506, 1472, 1452, 1433, 1366, 1323, 1275, 1261, 1247, 1230, 1152, 1135, 1079, 1056, 1041, 1015, 919, 905, 862, 805, 781, 741 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98 (d, *J* = 9.2 Hz, 1H, ArH), 7.95 (d, *J* = 8.0 Hz, 1H, ArH), 7.93 (d, *J* = 8.0 Hz, 1H, ArH), 7.88 (d, *J* = 8.4 Hz, 1H, ArH), 7.61 (dd, *J* = 8.0, 7.0 Hz, 1H, ArH), 7.57 (d, *J* = 8.8 Hz, 1H, ArH), 7.48-7.43 (m, 2H, ArH), 7.36-7.31 (m, 1H, ArH), 7.35 (ddd, *J* = 8.0, 7.0, 1.6 Hz, 1H, ArH), 7.30-7.20 (m, 2H, ArH), 7.16 (dddd, *J* = 8.8, 1.6, 0.8, 0.8 Hz, 1H, ArH), 4.57 (d, *J* = 2.4 Hz, 2H, CH_2), 2.39 (t, *J* = 2.4 Hz, 1H, C≡CH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.6, 134.2, 134.0, 133.6, 132.8, 129.6, 129.2, 128.5, 128.2, 127.9, 127.8, 126.4, 126.2, 125.9, 125.71, 125.70, 125.5, 124.8, 124.1, 115.8, 79.0, 75.4, 57.1 ppm. HRMS (APCI): calcd. for $C_{23}H_{16}O$ $[M]^+$ 308.1196, found 308.1190.

(*S*)-Sodium tetrakis(3-([1,1'-binaphthalen]-2-yloxy)prop-1-yn-1-yl)borate [(*S*)-1b]: A suspension of (*S*)-**3b** (851 mg, 2.76 mmol) in Et_2O (28 mL) was treated with a 1.6 M *n*BuLi hexane solution (1.6 mL, 2.6 mmol) at –78 °C under an Ar atmosphere and stirred for 1 h at the same temperature. The resulting mixture was treated with a 1 M BCl_3 *n*-heptane solution (0.58 mL, 0.58 mmol) at –78 °C. The mixture was allowed to warm to room temperature and stirred for 17 h. The resulting mixture was quenched with H_2O, treated with a small amount of brine, and extracted with CH_2Cl_2. The combined organic extracts were evaporated and the residue was dissolved in CH_2Cl_2 (28 mL). The solution was treated with brine (28 mL) and the two phase mixture was stirred for 2 days at room temperature. The CH_2Cl_2 layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined extracts were dried over Na_2SO_4. Evaporation of the solvent and purification of the residue by chromatography on silica gel (CH_2Cl_2 only followed by CH_2Cl_2/MeOH = 20/1, 10/1, to 5/1 as the eluent) afforded (*S*)-**1b** (603 mg) as a white solid. The obtained (*S*)-**1b** included H_2O (9 wt.%) and CH_2Cl_2 (4 wt.%) determined by ^{1}H NMR analysis. Calculated yield of (*S*)-**1b** was 72%. M.p. 147-150 °C. $[\alpha]^{26}_{589}$ +55.0 (*c* = 1.0, $CHCl_3$). IR (KBr): ν_{max} = 3057, 3008, 2925, 2863, 1621, 1591, 1506, 1470, 1459, 1433, 1370, 1326, 1274, 1217, 1147, 1134, 1081, 1034, 1011, 949, 896, 863, 805, 781, 749 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.83-7.71 (m, 16H, ArH), 7.48 (d, *J* = 9.2 Hz, 4H, ArH), 7.43 (dd, *J* = 7.8, 7.8 Hz, 4H, ArH), 7.37-7.25 (m, 12H, ArH), 7.25-7.04 (m, 16H, ArH), 4.38 (d, *J* = 16.0 Hz, 4H, OCH_2), 4.34 (d, *J* = 16.0 Hz, 4H, OCH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.1, 133.9, 133.4, 132.5, 129.51, 129.48, 128.4, 128.1, 127.9, 127.8, 126.3, 126.1, 125.9, 125.8, 125.6, 124.00, 123.98, 116.4, 102.9-100.2 (br m), 88.4-87.6 (br m), 59.8 ppm. ^{11}B NMR (128 MHz, $CDCl_3$): δ = –33.6 ppm. HRMS (ESI): calcd. for $C_{92}H_{60}BO_4$ $[M - Na]^-$ 1239.4590, found 1239.4572.

(*R*)-2'-Methoxy-[1,1'-binaphthalen]-2-ol [(*R*)-2c][15]: A mixture of (*R*)-1,1'-bi-2-naphthol (715 mg, 2.50 mmol) and K_2CO_3 (416 mg, 3.01 mmol) in acetone (25 mL) was stirred for 1 h at room temperature under an Ar atmosphere. The mixture was treated with MeI (156 μL, 2.51 mmol) and refluxed for 17 h. The resulting mixture was cooled to room temperature and filtered. The filtrate was evaporated and the residue was purified by chromatography on silica gel (*n*-hexane/CH_2Cl_2 = 1/1 to 1/2 as the eluent) to obtain (*R*)-**2c** (669 mg, 89% yield) as colorless crystals. M.p. 82-84 °C. $[\alpha]^{22}_{589}$ –44.0 (*c* = 1.0, $CHCl_3$). IR (KBr): ν_{max} = 3488, 3429, 3056, 2938, 2838, 1619, 1592, 1507, 1462, 1431, 1379, 1361, 1331, 1264, 1247, 1206, 1174, 1146, 1128, 1082, 1054, 1019, 972, 938, 904, 863, 813, 774, 750, 708 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99 (d, *J* = 8.8 Hz, 1H, ArH), 7.87 (d, *J* = 8.8 Hz, 1H, ArH), 7.86 (ddd, *J* = 8.4, 0.6, 0.6 Hz, 1H, ArH), 7.83 (ddd, *J* = 8.0, 0.6, 0.6 Hz, 1H, ArH), 7.41 (d, *J* = 8.8 Hz, 1H, ArH), 7.34 (ddd, *J* = 8.4, 6.8, 1.2 Hz, 1H, ArH), 7.33 (d, *J* = 8.8 Hz, 1H, ArH), 7.28 (ddd, *J* = 8.0, 6.8, 1.2 Hz, 1H, ArH), 7.25 (ddd, *J* =

8.4, 6.8, 1.2 Hz, 1H, ArH), 7.22-7.14 (m, 2H, ArH), 7.03 (dddd, *J* = 8.4, 1.2, 0.6, 0.6 Hz, 1H, ArH), 4.94 (s, 1H, OH), 3.74 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.9, 151.2, 134.0, 133.7, 131.0, 129.7, 129.3, 129.1, 128.1, 127.3, 126.4, 124.9, 124.8, 124.1, 123.2, 117.4, 115.3, 114.9, 113.7, 56.6 ppm. HRMS (ESI): calcd. for $C_{21}H_{15}O_2$ $[M - H]^-$ 299.1078, found 299.1074.

(*R*)-2-Methoxy-2'-(prop-2-yn-1-yloxy)-1,1'-binaphthalene [(*R*)-3c]: Prepared in 96% yield (777 mg) from (*R*)-**2c** (720 mg, 2.40 mmol) by the same procedure with (*S*)-**3b**. Colorless crystals. M.p. 155-156 °C. $[\alpha]^{23}_{589}$ +38.8 (*c* = 1.0, $CHCl_3$). IR (KBr): ν_{max} = 3294, 3056, 3021, 2962, 2935, 2874, 2839, 1619, 1590, 1507, 1460, 1429, 1355, 1323, 1264, 1252, 1218, 1177, 1148, 1133, 1089, 1059, 1046, 1020, 964, 931, 910, 892, 866, 809, 780, 755, 705 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.98 (d, *J* = 8.8 Hz, 1H, ArH), 7.97 (d, *J* = 8.8 Hz, 1H, ArH), 7.87 (ddd, *J* = 8.1, 1.2, 1.2 Hz, 1H, ArH), 7.86 (ddd, *J* = 8.1, 1.2, 1.2 Hz, 1H, ArH), 7.57 (d, *J* = 9.2 Hz, 1H, ArH), 7.45 (d, *J* = 8.8 Hz, 1H, ArH), 7.34 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H, ArH), 7.31 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H, ArH), 7.21 (ddd, *J* = 8.8, 6.8, 1.2 Hz, 1H, ArH), 7.20 (ddd, *J* = 8.8, 6.8, 1.2 Hz, 1H, ArH), 7.14-7.09 (m, 2H, ArH), 4.61 (dd, *J* = 16.3, 2.4 Hz, 1H, OCH_2), 4.55 (dd, *J* = 16.3, 2.4 Hz, 1H, OCH_2), 3.77 (s, 3H, OCH_3), 2.37 (dd, *J* = 2.4, 2.4 Hz, 1H, C≡CH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.9, 153.1, 134.0, 133.9, 129.8, 129.5, 129.2, 129.1, 127.9, 127.8, 126.3, 125.4, 125.3, 124.0, 123.5, 121.2, 119.0, 116.2, 114.0, 79.3, 75.1, 57.2, 56.8 ppm. HRMS (APCI) calcd. for $C_{24}H_{19}O_2$ $[M + H]^+$ 339.1380, found 339.1373.

(*R*)-Sodium tetrakis(3-((2'-methoxy-[1,1'-binaphthalen]-2-yl)oxy)prop-1-yn-1-yl)borate [(*R*)-1c]: Prepared from (*R*)-**3c** (263 mg, 0.777 mmol) and a 1 M BCl_3 *n*-heptane solution (0.16 mL, 0.16 mmol) by the same procedure with (*S*)-**1b**. The obtained (*R*)-**1c** (31.4 mg) included H_2O (3 wt.%) and CH_2Cl_2 (1 wt.%) determined by ^1H NMR analysis. Calculated yield of (*R*)-**1c** was 14%. Pale yellow solid. M.p. 153-156 °C. $[\alpha]^{26}_{589}$ +29.8 (*c* = 1.0, $CHCl_3$). IR (KBr): ν_{max} = 3057, 3006, 2931, 2856, 2840, 1719, 1621, 1592, 1507, 1474, 1463, 1431, 1402, 1356, 1328, 1272, 1262, 1250, 1218, 1178, 1147, 1133, 1087, 1059, 1014, 955, 903, 862, 810, 775, 749, 707 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.86-7.72 (m, 16H, ArH), 7.53 (d, *J* = 8.6 Hz, 4H, ArH), 7.30 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 4H, ArH), 7.26-7.16 (m, 12H, ArH), 7.07-6.99 (m, 8H, ArH), 6.94 (d, *J* = 8.6 Hz, 4H, ArH), 4.47 (d, *J* = 15.2 Hz, 4H, OCH_2), 4.43 (d, *J* = 15.2 Hz, 4H, OCH_2), 3.48 (s, 12H, OCH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.6, 153.6, 133.7, 133.6, 129.60, 129.55, 129.4, 129.1, 128.0, 127.9, 126.4, 126.3, 125.3, 125.1, 123.9, 123.6, 120.1, 119.1, 116.7, 114.5, 104.0-100.5 (br m), 88.4-87.6 (br m), 59.7, 57.0 ppm. ^{11}B NMR (128 MHz, $CDCl_3$): δ = –33.5 ppm. HRMS (ESI): calcd. for $C_{96}H_{68}BO_8$ $[M - Na]^-$ 1359.5013, found 1359.5012.

(*S*)-6-Phenyl-[1,1'-binaphthalen]-2-ol [(*S*)-2d]: (Step 1) A solution of (*S*)-**2a** (1.21 g, 4.48 mmol) in MeCN (22 mL) was treated with Br_2 (0.46 mL, 9.0 mmol) at 0 °C and the mixture was stirred for 2 h at the same temperature. The resulting mixture was quenched with saturated aq. Na_2SO_3 and extracted with EtOAc. The combined extracts were washed with saturated aq. $NaHCO_3$ followed by brine, dried over Na_2SO_4, and evaporated. The residue was purified by chromatography on silica gel (*n*-hexane/CH_2Cl_2 = 3/1 to 1/1 as the eluent) to afford 6-bromo-[1,1'-binaphthalen]-2-ol with impurities (1.55 g) as a white solid. This product was not pure and used in next step without further purification. (Step 2) A solution of the solid (1.55 g) and $NiCl_2(PPh_3)_2$ (0.14 g, 0.21 mmol) in Et_2O (9 mL) was treated with a ca. 1 M PhMgBr Et_2O solution (13.5 mL, 13.5 mmol, prepared from PhBr and Mg) at 0 °C under an Ar atmosphere. The mixture was refluxed for 12 h, quenched with saturated aq. NH_4Cl at 0 °C, and extracted with EtOAc. The combined extracts were washed with brine, dried over Na_2SO_4, and evaporated. Careful chromatographic purification of the residue on silica gel (*n*-hexane/CH_2Cl_2 = 2/1 to 1/1 as the eluent) afforded pure (*S*)-**2d** (117 mg, 8% yield) as a white solid and a mixture of (*S*)-**2d** and impurities as a white solid. To obtain more pure (*S*)-**2d**, the mixture was purified by 2nd and 3rd chromatography under the same conditions. The combined yield (1st to 3rd) of pure (*S*)-**2d** was 49% (762 mg). M.p. 51-55 °C. $[\alpha]^{22}_{589}$ –198.4 (*c* = 1.0, $CHCl_3$). IR (KBr): ν_{max} = 3513, 3435, 3057, 1622, 1596, 1494, 1473, 1446, 1420, 1384, 1361, 1312, 1287, 1256, 1231, 1197, 1150, 1130, 1076, 1018, 973, 940, 890, 831, 802, 779, 758, 735, 699 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.06 (d, *J* = 2.0 Hz, 1H, ArH), 8.04 (d, *J* = 8.4 Hz, 1H, ArH), 7.99 (d, *J* = 8.4 Hz, 1H, ArH), 7.96 (d, *J* = 8.4 Hz, 1H, ArH), 7.70-7.64 (m, 3H, ArH), 7.59-7.48 (m, 3H, ArH), 7.48-7.41 (m, 3H, ArH), 7.39-7.31 (m, 3H, ArH), 7.17 (d, *J* = 8.4 Hz, 1H, ArH), 4.93 (s, 1H, OH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.1, 141.0, 136.1, 134.2, 133.1, 132.8, 131.3, 130.2, 129.6, 129.3, 129.2, 128.8, 128.5, 127.2, 127.1, 126.9, 126.6, 126.2, 126.0, 125.9, 125.8, 125.5, 118.7, 117.9 ppm. HRMS (ESI): calcd. for $C_{26}H_{17}O$ $[M - H]^-$ 345.1285, found 345.1280.

(*S*)-6-Phenyl-2-(prop-2-yn-1-yloxy)-1,1'-binaphthalene [(*S*)-3d]: Prepared in 86% yield (339 mg) from (*S*)-**2d** (354 mg, 1.02 mmol) by the same procedure with (*S*)-**3b**. White solid. M.p 52-55 °C. $[\alpha]^{21}_{589}$ –66.7 (*c* = 1.0, $CHCl_3$). IR (KBr): ν_{max} = 3286, 3058, 2953, 2926, 2871, 1623, 1593, 1493, 1475, 1446, 1370, 1359, 1333, 1276, 1222, 1190, 1159, 1141, 1086, 1058, 1035, 1016, 935, 889, 832, 798, 778, 759, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.08 (d, *J* = 2.0 Hz, 1H, ArH), 8.03 (d, *J* = 8.4 Hz, 1H, ArH), 7.96 (d, *J* = 8.4 Hz, 1H, ArH), 7.94 (d, *J* = 8.4 Hz, 1H, ArH), 7.69-7.57 (m, 4H, ArH), 7.52-7.41 (m, 5H, ArH), 7.38 (d, *J* = 8.4 Hz, 1H, ArH), 7.34 (tt, *J* = 7.4, 1.2 Hz, 1H, ArH), 7.29 (ddd, *J* = 8.4, 7.4, 1.2 Hz, 1H, ArH), 7.24 (d, *J* = 8.4 Hz, 1H, ArH), 4.58 (d, *J* = 2.4 Hz, 2H, OCH_2), 2.39 (t, *J* = 2.4 Hz, 1H, C≡CH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.7, 140.9, 136.8, 133.9, 133.7, 133.4, 132.8, 129.9, 129.6, 128.8, 128.6, 128.2, 127.9, 127.23, 127.19, 126.3, 126.2, 126.1, 126.0, 125.8, 125.7, 125.5, 124.8, 116.3, 79.0, 75.4, 57.1 ppm. HRMS (APCI): calcd. for $C_{29}H_{21}O$ $[M + H]^+$ 385.1587, found 385.1576.

(*S*)-Sodium tetrakis(3-((6-phenyl-[1,1'-binaphthalen]-2-yl)oxy)prop-1-yn-1-yl)borate [(*S*)-1d]: Prepared from (*S*)-**3d** (302 mg, 0.785 mmol) and a 1 M BCl_3 *n*-heptane solution (0.14 mL, 0.14 mmol) by the same procedure with (*S*)-**1b**. The obtained (*S*)-**1d** (156 mg) included H_2O (2 wt.%) and CH_2Cl_2 (2 wt.%) determined by ^1H NMR analysis. Calculated yield of (*S*)-**1d** was 68%. Pale yellow solid. M.p. 180-182 °C. $[\alpha]^{24}_{589}$ –55.3 (*c* = 1.0, $CHCl_3$). IR (KBr): ν_{max} = 3055, 2864, 1621, 1592, 1492, 1473, 1444, 1359, 1331, 1274, 1218, 1187, 1140, 1083, 1026, 1011, 950, 888, 831, 799, 777, 758, 697 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.86 (d, *J* = 1.4 Hz, 4H, ArH), 7.73-7.63 (m, 12H, Ar), 7.58-7.50 (m, 8H, ArH), 7.45-7.33 (m, 20H, ArH), 7.30 (tt, *J* = 7.2, 1.4 Hz, 4H, ArH), 7.26-7.19 (m, 8H, ArH), 7.17 (d, *J* = 8.4 Hz, 4H, ArH), 7.09 (d, *J* = 9.2 Hz, 4H, ArH), 7.05 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 4H, ArH), 4.25 (d, *J* = 15.2 Hz, 4H, OCH_2), 4.20 (d, *J* = 15.2 Hz, 4H, OCH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.1, 140.7, 136.7, 133.9, 133.5, 133.1, 132.5, 129.9, 129.7, 128.8, 128.4, 128.2, 127.9, 127.2, 126.2, 126.14, 126.08, 125.93, 125.88, 125.6, 124.0, 116.8, 102.2-101.5 (br m), 88.4-87.6 (br m), 59.8 ppm. ^{11}B NMR (128 MHz, $CDCl_3$): δ = –33.6 ppm. HRMS (ESI): calcd. for $C_{116}H_{76}BO_4$ $[M - Na]^-$ 1543.5842, found 1543.5827.

1-(4-Bromobenzyl)-2-(*tert*-butoxycarbonyl)-1-methylazetidin-1-ium trifluoromethanesulfonate (*rac*-4): (Step 1) A mixture of 4-bromobenzylamine (253 μL, 2.00 mmol), *tert*-butyl 2,4-dibromobutanoate[5] (604 mg, 2.00 mmol), and K_2CO_3 (0.83 g, 6.0 mmol) in MeCN (10 mL) was refluxed for 4 h. The resulting mixture was cooled to room temperature followed by filtered. The filtrate was evaporated and the residue was purified by chromatography on silica gel (*n*-hexane/EtOAc = 6/1 to 4/1 as the eluent) to obtain *tert*-butyl 1-(4-bromobenzyl)azetidine-2-carboxylate (*rac*-**5**) (334 mg, 51% yield) as colorless crystals, m.p. 34-36 °C. Spectroscopic data: see (*S*)-**5**. (Step 2) A mixture of *rac*-**5** (334 mg, 1.02 mmol) and $NaHCO_3$ (0.26 g, 3.1 mmol)

in CH_2Cl_2 (5 mL) was treated with MeOTf (139 μL, 1.23 mmol) at 0 °C and stirred for 2 h at room temperature. The resulting mixture was evaporated to ca. 1/2 to 1/3 volume and the residue was purified by chromatography on silica gel (CH_2Cl_2/MeOH = 20/1 to 10/1 as the eluent) to obtain *rac*-**4** (449 mg, 90% yield) as a white solid, m.p. 142-145 °C. Spectroscopic data: see (1*S*,2*S*)-**4**.

(1*S*,2*S*)-1-(4-Bromobenzyl)-2-(*tert*-butoxycarbonyl)-1-methylazetidin-1-ium trifluoromethanesulfonate [(1*S*,2*S*)-4][5]: (Step 1) A solution of L-azetidine-2-carboxylic acid (490 mg, 4.85 mmol) and NaOH (388 mg, 9.70 mmol) in H_2O (4.9 mL) was treated with benzyl chloroformate (0.73 mL, 5.1 mmol) at 0 °C. After stirring for 1 h at 0 °C and for 1 h at room temperature, the resulting aqueous mixture was washed with Et_2O. The aqueous solution was acidified with 4 M aq. HCl and extracted with EtOAc. The combined organic extracts were washed with H_2O followed by brine, dried over Na_2SO_4, and evaporated. A solution of the residue in CH_2Cl_2 (10 mL) was treated with H_2SO_4 (0.05 mL) and isobutene (excess) at room temperature. The resulting solution was stirred for 11 h at room temperature. The resulting mixture was treated with saturated aq. $NaHCO_3$ and extracted with EtOAc. The combined extracts were washed with brine, dried over Na_2SO_4, and evaporated. Purification of the residue by chromatography on silica gel (*n*-hexane/EtOAc = 4/1 to 3/1 as the eluent) gave (*S*)-1-benzyl 2-*tert*-butyl azetidine-1,2-dicarboxylate (1.02 g, 72% yield) as a colorless oil. (Step 2) A mixture of (*S*)-1-benzyl 2-*tert*-butyl azetidine-1,2-dicarboxylate (242 mg, 0.831 mmol) and Pd-C (loading: 10 wt.%, 18 mg) in EtOAc (4.2 mL) was stirred for 2 h at room temperature under a H_2 atmosphere. The resulting mixture was filtered through a pad of Celite and the filtrate was evaporated. A mixture of the residue, 4-bromobenzyl chloride (171 mg, 0.832 mmol), and $NaHCO_3$ (0.21 g, 2.5 mmol) in MeCN (4.2 mL) was refluxed for 4 h. The resulting mixture was cooled to room temperature and filtered. The filtrate was evaporated and the residue was purified by chromatography on silica gel (*n*-hexane/EtOAc = 7/1 to 4/1 as the eluent) to give (*S*)-*tert*-butyl 1-(4-bromobenzyl)azetidine-2-carboxylate [(*S*)-**5**] (215 mg, 79% yield) as colorless crystals, m.p. 33-35 °C. $[\alpha]^{22}_{589}$ = –58.6 (*c* = 1.0, EtOH). 98% ee [determined by HPLC analysis: Daicel Chiralpak AD-H column (25 cm), *n*-hexane/EtOH = 95/5 as the eluent, flow rate = 0.50 mL/min, t_R = 8.6 min (1.1%) for (*R*) and 9.3 min (98.9%) for (*S*)]. IR (film): ν_{max} = 3002, 2974, 2931, 2829, 1734, 1591, 1485, 1452, 1400, 1391, 1365, 1294, 1239, 1154, 1095, 1068, 1011, 979, 940, 845, 814, 791, 744, 682 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.42 (ddd, *J* = 8.6, 2.2, 2.2 Hz, 2H, ArH), 7.19 (ddd, *J* = 8.6, 2.2, 2.2 Hz, 2H, ArH), 3.77 (d, *J* = 12.8 Hz, 1H, CH_2Ar), 3.60 (ddd, *J* = 8.4, 8.2, 0.6 Hz, 1H, 2-H), 3.49 (d, *J* = 12.8 Hz, 1H, CH_2Ar), 3.27 (dddd, *J* = 8.2, 6.6, 2.5, 0.6 Hz, 1H, 4-H), 2.86 (ddd, *J* = 9.2, 8.0, 6.6 Hz, 1H, 4-H), 2.31 (dddd, *J* = 10.5, 9.2, 8.4, 8.2 Hz, 1H, 3-H), 2.16 (dddd, *J* = 10.5, 8.2, 8.0, 2.5 Hz, 1H, 3-H), 1.41 (s, 9H, *t*Bu) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.8, 136.5, 131.3, 130.7, 121.0, 80.8, 65.2, 61.8, 50.7, 28.0, 21.4 ppm. HRMS (ESI): calcd. for $C_{15}H_{21}BrNO_2$ $[M + H]^+$ 326.0750, found 326.0737. (Step 3) A mixture of (*S*)-**5** (161 mg, 0.494 mmol) and $NaHCO_3$ (0.13 g, 1.5 mmol) in CH_2Cl_2 (2.5 mL) was treated with MeOTf (67 μL, 0.59 mmol) at 0 °C and stirred for 2 h at room temperature. The resulting mixture was purified by chromatography on silica gel (CH_2Cl_2/MeOH = 20/1 to 10/1 as the eluent) to obtain (1*S*,2*S*)-**4** (203 mg, 84% yield) as a colorless gum. $[\alpha]^{21}_{589}$ = –23.3 (*c* = 1.0, EtOH). IR (KBr): ν_{max} = 3049, 2983, 2935, 1736, 1595, 1492, 1468, 1412, 1396, 1371, 1325, 1263, 1225, 1155, 1074, 1031, 1013, 979, 936, 885, 829, 787, 757, 725 cm^{-1}. ^1H NMR (400 MHz, acetone-d_6): δ = 7.72 (d, *J* = 8.8 Hz, 2H, ArH), 7.69 (d, *J* = 8.8 Hz, 2H, ArH), 5.72 (dd, *J* = 9.8, 9.8 Hz, 1H, 2-H), 4.92-4.80 (m, 1H, 4-H), 4.86 (s, 2H, CH_2Ar), 4.07 (ddd, *J* = 9.8, 9.8, 3.6 Hz, 1H, 4-H), 3.34 (s, 3H, NCH_3), 3.15 (dddd, *J* = 12.0, 9.8, 9.8, 9.8 Hz, 1H, 3-H), 2.78-2.65 (m, 1H, 3-H), 1.44 (s, 9H, *t*Bu) ppm. ^{13}C NMR (100 MHz, acetone-d_6): δ = 164.5, 135.3, 133.3, 128.5, 125.6, 122.3 (q, *J* = 320 Hz), 85.9, 71.7, 67.9, 62.9, 45.5, 27.9, 19.3 ppm. HRMS (ESI): calcd. for $C_{16}H_{23}BrNO_2$ $[M – OTf]^+$ 340.0907, found 340.0893.

Representative procedure for preparation of (*S*)-1a·*rac*-4: A mixture of (*S*)-**1a** (36 mg, 0.022mmol) and *rac*-**4** (9.8 mg, 0.020 mmol) in THF (2.0 mL) was stirred for 2 days at room temperature. The resulting mixture was evaporated and the residue was purified by chromatography on silica gel (*n*-hexane/CH_2Cl_2 = 1/1 followed by CH_2Cl_2/MeOH = 20/1 to 10/1 as the eluent) to obtain (*S*)-**1a**·*rac*-**4** (34.7 mg, 89% yield) as a white solid.

***tert*-Butyl 2-amino-3-methylbutanoate (*rac*-7a):** (Step 1) A solution of DL-valine (630 mg, 5.38 mmol) and NaOH (430 mg, 10.8 mmol) in H_2O (5.4 mL) was treated with benzyl chloroformate (0.83 mL, 5.9 mmol) at 0 °C. After stirring for 0.5 h at 0 °C and for 3 h at room temperature, the resulting aqueous mixture was washed with toluene. The aqueous solution was acidified with 4 M aq. HCl and extracted with EtOAc. The combined organic extracts were washed with H_2O followed by brine, dried over Na_2SO_4, and evaporated to obtain crude *N*-carbobenzoxy-DL-valine (1.12 g, 83% yield) as a white solid. (Step 2) A solution of the crude *N*-carbobenzoxy-DL-valine (762 mg, 3.03 mmol) in CH_2Cl_2 (6 mL) was treated with H_2SO_4 (0.06 mL) and isobutene (excess) at room temperature. The resulting solution was stirred for 2 days at room temperature. The resulting mixture was treated with saturated aq. $NaHCO_3$ and extracted with EtOAc. The combined extracts were washed with brine, dried over Na_2SO_4, and evaporated. Purification of the residue by chromatography on silica gel (*n*-hexane/EtOAc = 10/1 to 5/1 as the eluent) gave *tert*-butyl 2-(((benzyloxy)carbonyl)amino)-3-methylbutanoate (827 mg, 89% yield) as a colorless oil. (Step 3) A mixture of *tert*-butyl 2-(((benzyloxy)carbonyl)amino)-3-methylbutanoate (316 mg, 1.03 mmol) and Pd-C (loading: 10 wt.%, 22 mg) in EtOAc (5 mL) was stirred for overnight at room temperature under a H_2 atmosphere. The resulting mixture was filtered through a pad of Celite and the filtrate was evaporated to obtain *rac*-**7a** (143 mg, 80% yield) as a colorless oil. The product was pure without purification. IR (film): ν_{max} = 3386, 3320, 2966, 2933, 2874, 1727, 1600, 1466, 1391, 1368, 1339, 1282, 1251, 1154, 1048, 974, 958, 911, 851, 777, 748 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.17 (d, *J* = 4.8 Hz, 1H, 2-H), 2.00 (sept d, *J* = 6.8, 4.8 Hz, 1H, 3-H), 1.47 (s, 9H, *t*Bu), 1.43 (br, 2H, NH_2), 0.97 (d, *J* = 6.8 Hz, 3H, 4-H), 0.90 (d, *J* = 6.8 Hz, 3H, 4-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.8, 80.7, 60.3, 32.1, 28.0, 19.2, 17.0 ppm. HRMS (ESI): calcd. for $C_9H_{20}NO_2$ $[M + H]^+$ 174.1489, found 174.1486.

***tert*-Butyl 2-(dimethylamino)-3-methylbutanoate (*rac*-8a):** A mixture of *rac*-**7a** (143 mg, 0.825 mmol), Pd-C (loading: 10 wt.%, 19 mg), and 37 wt.% aq. HCHO (0.82 mL, 11 mmol) in EtOH (4.1 mL) was stirred for overnight at room temperature under a H_2 atmosphere. The resulting mixture was filtered through a pad of Celite and the filtrate was evaporated. Purification of the residue by chromatography on silica gel (*n*-hexane/EtOAc = 8/1 as the eluent) gave *rac*-**8a** (95.1 mg, 57% yield) as a colorless oil. IR (film): ν_{max} = 2967, 2935, 2871, 2831, 2787, 1723, 1469, 1454, 1389, 1367, 1347, 1290, 1272, 1248, 1215, 1147, 1124, 1040, 976, 928, 912, 859, 830, 791, 740 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.60 (d, *J* = 10.4 Hz, 1H, 2-H), 2.32 (s, 6H, $N(CH_3)_2$), 1.97 (d sept, *J* = 10.4, 6.6 Hz, 1H, 3-H), 1.48 (s, 9H, *t*Bu), 0.96 (d, *J* = 6.6 Hz, 3H, 4-H), 0.90 (d, *J* = 6.6 Hz, 3H, 4-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.1, 80.5, 75.0, 41.3, 28.3, 27.4, 19.5, 19.3 ppm. HRMS (ESI): calcd. for $C_{11}H_{24}NO_2$ $[M + H]^+$ 202.1802, found 202.1798.

1-(*tert*-Butoxy)-*N*,*N*,*N*,3-tetramethyl-1-oxobutan-2-aminium trifluoromethanesulfonate [*rac*-9a·OTf]: A mixture of *rac*-**8a** (95.1 mg, 0.472 mmol) and $NaHCO_3$ (120 mg, 1.43 mmol) in CH_2Cl_2 (2.4 mL) was treated with MeOTf (64 μL, 0.57 mmol) at room temperature and stirred for 3 h. The resulting mixture was evaporated to ca. 1/2 to 1/3 volume and the residue was purified by chromatography on silica gel (CH_2Cl_2/MeOH = 20/1 to 10/1 as the eluent) to obtain *rac*-**9a·OTf** (135 mg, 78% yield) as a white gum. IR (KBr): ν_{max} = 3034, 2984, 2946, 1730,

1634, 1498, 1481, 1421, 1397, 1372, 1297, 1263, 1223, 1160, 1029, 977, 963, 930, 894, 848, 798, 755, 715 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.97 (d, *J* = 1.6 Hz, 1H, 2-H), 3.37 (s, 9H, $N(CH_3)_3$), 2.54-2.41 (m, 1H, 3-H), 1.55 (s, 9H, *t*Bu), 1.29 (d, *J* = 7.2 Hz, 3H, 4-H), 1.10 (d, *J* = 6.8 Hz, 3H, 4-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.3, 120.6 (q, *J* = 318 Hz), 85.6, 78.9, 52.2, 27.9, 26.5, 23.1, 19.0 ppm. HRMS (ESI): calcd. for $C_{12}H_{26}NO_2$ $[M - OTf]^+$ 216.1958, found 216.1949.

1-(*tert*-Butoxy)-*N*,*N*,*N*,3-tetramethyl-1-oxobutan-2-aminium iodide [*rac*-9a-I]: A mixture of *rac*-**7a** (50 mg, 0.29 mmol), MeI (90 μL, 1.4 mmol), and K_2CO_3 (0.20 g, 1.4 mmol) in MeCN (1.5 mL) was stirred for 2 h at room temperature and refluxed for 1 h. The mixture was cooled to room temperature and filtered. The filtrate was evaporated and the residue was purified by chromatography on silica gel (CH_2Cl_2/MeOH = 10/1 to 5/1 as the eluent) to afford *rac*-**9a-I** (92.8 mg, 93% yield) as a pale yellow gum. IR (KBr): ν_{max} = 3053, 3009, 2971, 2938, 1736, 1541, 1492, 1474, 1456, 1412, 1393, 1369, 1312, 1286, 1249, 1210, 1148, 1133, 971, 957, 930, 892, 846, 794, 727, 708 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 4.22 (d, *J* = 1.6 Hz, 1H, 2-H), 3.62 (s, 9H, $N(CH_3)_3$), 2.74-2.61 (m, 1H, 3-H), 1.56 (s, 9H, *t*Bu), 1.33 (d, *J* = 7.2 Hz, 3H, 4-H), 1.11 (d, *J* = 6.8 Hz, 3H, 4-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.0, 85.5, 78.8, 52.8, 27.9, 26.4, 23.1, 19.1 ppm. HRMS (ESI): calcd. for $C_{12}H_{26}NO_2$ $[M - I]^+$ 216.1958, found 216.1947.

Representative procedure for preparation of (*S*)-1b·*rac*-9b (Table 1, Entry 2): A mixture of (*S*)-**1b** (20 mg, 0.016 mmol) and *rac*-**9b-OTf** (5.2 mg, 0.015 mmol) in THF (1.5 mL) was stirred for 48 h at room temperature. The resulting mixture was evaporated and the residue was purified by chromatography on silica gel (*n*-hexane/CH_2Cl_2 = 1/1 followed by CH_2Cl_2/MeOH = 20/1 to 10/1 as the eluent) to obtain (*S*)-**1b**·*rac*-**9b** (20.5 mg, 96% yield) as a white gum.

Preparation of (*S*)-1a·*rac*-10: A mixture of (*S*)-**1a** (34 mg, 0.021 mmol) and *rac*-**10** (7.0 mg, 0.017 mmol) in THF (1.1 mL) and CH_2Cl_2 (0.6 mL) was stirred for 3.5 days at room temperature. The resulting mixture was evaporated and the residue was purified by chromatography on silica gel (*n*-hexane/CH_2Cl_2 = 1/1 followed by CH_2Cl_2/MeOH = 20/1 to 10/1 as the eluent) to obtain (*S*)-**1a**·*rac*-**10** (31.2 mg, 98% yield) as a white gum.

Conflict of interest

The authors declare no conflict of interest.

Keywords: ammonium salts • amino acids • chiral borates • chiral anions • chiral resolution

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10.1002/ejoc.201801448

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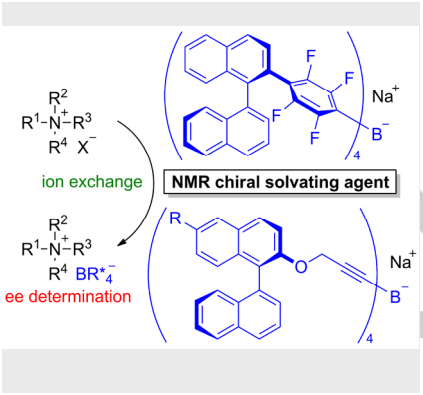
Layout 1:

FULL PAPER

Tetra-carbon-substituted chiral borate sodium salts ($NaBR^*_4$) act as chiral solvating agents for various tetraalkylammonium salts (R_4NX). The ees of R_4NX species could be determined by ^1H NMR analysis of ion exchanged diastereomeric tetraalkylammonium borate salts.



Chiral Resolution

Eiji Tayama, Takeshi Sugawara*

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Chiral tetraaryl- and tetraalkynylborates as chiral solvating agents for tetraalkylammonium salts