

Hydrolytically Stable Tricoordinate Chiral Bicyclo[4.4.0]diboronic Ester: Synthesis, Structural Characterization, and Theoretical Investigation[†]

Yan Zhou,[‡] Zixing Shan,^{*,‡} Baoshan Wang,^{*,‡} and Peng Xie[§]

Department of Chemistry, Wuhan University, Wuhan 430072, People's Republic of China, and Department of Chemistry, Central China Normal University, Wuhan 430079, People's Republic of China

Received June 26, 2006

Summary: The hydrolytically and thermally stable tricoordinate chiral bicyclo[4.4.0] diboronic ester (*R,R*)-**3c** was synthesized via a one-step reaction of a Grignard reagent with chiral spiroborate esters (*R,R,S*)-**1** and (*R,R*)-**2**. Its structure was characterized by its IR, ¹H, ¹³C, and ¹¹B NMR, and mass spectra and confirmed by X-ray analysis. Further theoretical investigation of the three possible bicyclic structures corresponding to the formula C₄₀H₃₂B₂O₄ was performed at different levels of theory. Excellent agreement with the X-ray result was obtained.

Chiral boronic esters are an important class of organoboron compounds, and they have been widely used as intermediates¹ or as protecting groups² in asymmetric synthesis. The classical preparation of organoboranes utilizes reactions of a tricoordinate trialkoxyborane or trihaloborane with a Grignard or an organolithium reagent.³ Both reactants and the product are sensitive to moisture, while hydrolytically stable chiral boronic esters⁴ exhibit great convenience in practical storage and use. The most common strategy for the preparation of hydrolytically stable boronic esters involves the conversion of tricoordinate unstable boranes to a tetracoordinate complex stabilized by an N→B bond.⁵ The preparation of enantiopure boronic esters of pinanediol was of importance in the investigation of thermodynamically and hydrolytically stable chiral boronic esters.⁶

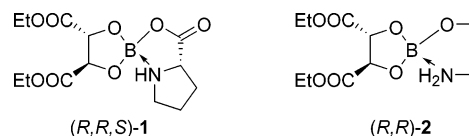


Figure 1. Chiral spiroborate esters (*R,R,S*)-**1** and (*R,R*)-**2** derived from diethyl tartrate.

Boronic esters derived from 1,2-dicyclohexylethanediol,⁷ (*R,R*)-2,3-butanediol,⁸ and tartrate acid⁹ all showed this characteristic because of unfavorable entropy of hydrolysis. However, most of these boronic esters are monocyclic, and in contrast, hydrolytically stable tricoordinate chiral fused bicyclic boronic esters are rare.¹⁰

We recently synthesized various tetracoordinate enantiopure spiroborate esters possessing an O₃BN framework via a convenient procedure.¹¹ Some of them showed highly stereoselective catalytic activity in aldol reactions¹² and in borane reductions of prochiral ketones,¹³ imines,¹⁴ and oxime ethers.¹⁵

We now report the reactions of spiroborate esters (*R,R,S*)-**1** and (*R,R*)-**2** (Figure 1) with an excess of phenylmagnesium bromide. Unexpectedly, a hydrolytically stable chiral bicyclic boronic ester composed of one unit of tetraol from phenylated tartrate and two units of phenylboronate was obtained. We report here the synthesis, structural characterization, and theoretical investigation of this new compound.

[†] Chiral Borate Esters in Asymmetric Synthesis: 6.

* To whom correspondence should be addressed. E-mail: zxshan@whu.edu.cn, wangb@chem.whu.edu.cn.

[‡] Wuhan University.

[§] Central China Normal University.

(1) For reviews, see: (a) Cragg, G. M. L.; Koch, K. R. *Chem. Soc. Rev.* **1977**, 6, 393. (b) Brown, H. C.; Jadhav, P. K.; Mandal, A. K. *Tetrahedron* **1981**, 37, 3547. (c) Deloux, L.; Srebnik, M. *Chem. Rev.* **1993**, 93, 763.

(2) (a) Reese, C. B. In *Protective Groups in Organic Chemistry*; McOmie, J. F. W., Ed.; Plenum Press: New York, 1973; p 135. (b) Wiecko, J.; Sherman, W. R. *J. Am. Chem. Soc.* **1976**, 98, 7631.

(3) For reviews, see: (a) Lappert, M. F. *Chem. Rev.* **1956**, 56, 959. (b) Gerrard, W.; Lappert, M. F. *Chem. Rev.* **1958**, 58, 8, 1081.

(4) For reviews, see: (a) Matteson, D. S.; Sadhu, K. M.; Ray, R.; Jesthi, P. K.; Peterson, M. L.; Majumdar, D.; Tsai, D. J. S.; Hurst, G. D.; Erdik, E. *J. Organomet. Chem.* **1985**, 281, 15. (b) Matteson, D. S. *Acc. Chem. Res.* **1988**, 21, 294. (c) Matteson, D. S. *Chem. Rev.* **1989**, 89, 1535. (d) Matteson, D. S. *Tetrahedron* **1989**, 45, 1859. (e) Matteson, D. S. *Tetrahedron* **1998**, 54, 10555. (g) Matteson, D. S. *J. Organomet. Chem.* **1999**, 581, 51.

(5) For N→B bond stabilized chiral boronic ester, see: (a) Mancilla, T.; Contreras, R. *J. Organomet. Chem.* **1987**, 321, 191. (b) Zhu, L.; Shabbir, S. H.; Gray, M.; Lynch, V. M.; Sorey, S.; Anslyn, E. V. *J. Am. Chem. Soc.* **2006**, 128, 1222.

(6) (a) Matteson, D. S.; Ray, R. *J. Am. Chem. Soc.* **1980**, 102, 7590. (b) Matteson, D. S.; Sadhu, K. M. *J. Am. Chem. Soc.* **1983**, 105, 2077. (c) Matteson, D. S.; Majumdar, D. *Organometallics* **1983**, 2, 1529. (d) Matteson, D. S.; Ray, R.; Rocks, R. R.; Tsai, D. J. S. *Organometallics* **1983**, 2, 1536. (e) Matteson, D. S.; Sadhu, K. M.; Peterson, M. L. *J. Am. Chem. Soc.* **1986**, 108, 810. (f) Matteson, D. S.; Beedle, E. C. *Tetrahedron Lett.* **1987**, 28, 4499. (g) Matteson, D. S.; Man, H. W. *J. Org. Chem.* **1996**, 61, 6047.

(7) Hoffmann, R. W.; Ditrich, K.; Köster, G.; Stürmer, R. *Chem. Ber.* **1989**, 122, 1783.

(8) (a) Sadhu, K. M.; Matteson, D. S.; Hurst, G. D.; Kurosky, J. M. *Organometallics* **1984**, 3, 804. (b) Tripathy, P. B.; Matteson, D. S. *Synthesis* **1990**, 200.

(9) (a) Luithe, J. E. A.; Pietruszka, J. *Liebigs Ann.* **1997**, 2297. (b) Luithe, J. E. A.; Pietruszka, J.; Witt, A. *Chem. Commun.* **1998**, 2651. (c) Luithe, J. E. A.; Pietruszka, J. *J. Org. Chem.* **1999**, 64, 8287. (d) Luithe, J. E. A.; Pietruszka, J. *J. Org. Chem.* **2000**, 65, 9194. (e) Pietruszka, J.; Schöne, N. *Angew. Chem., Int. Ed.* **2003**, 42, 5638. (f) Yim, H. K.; Wong, H. N. C. *J. Org. Chem.* **2004**, 69, 2892.

(10) (a) Bourne, E. J.; Lees, E. M.; Weigel, H. J. *Chem. Soc.* **1965**, 3798. (b) Takeuchi, M.; Chin, Y.; Imada, T.; Shinkai, S. *Chem. Commun.* **1996**, 1867. (c) Ishi-i, T.; Nakashima, K.; Shinkai, S.; Araki, K. *Tetrahedron* **1998**, 54, 8679. (d) Ishi-i, T.; Nakashima, K.; Shinkai, S.; Ikeda, A. *J. Org. Chem.* **1999**, 64, 984. (e) Kaupp, G.; Naïmi-Jamal, M. R.; Stepanenko, V. *Chem. Eur. J.* **2003**, 9, 4156.

(11) (a) Shan, Z. X.; Zhou, Y.; Liu, D. J.; Ha, W. Z. *Synth. React. Inorg. Metal-Org. Nano-Metal Chem.* **2005**, 35, 275. (b) Wang, Q. M.D. Dissertation, Wuhan University, Wuhan, 2003 (in Chinese). (c) Shan, Z. X.; Liu, S. M.; Liu, D. J. *Chin. J. Chem.* **2003**, 21, 1373. (d) Shan, Z. X.; Xiong, Y.; Li, W. Z.; Zhao, D. J. *Tetrahedron: Asymmetry* **1998**, 9, 3985. (e) Shan, Z. X.; Xiong, Y.; Zhao, D. J. *Tetrahedron* **1999**, 55, 3893.

(12) Zhou, Y.; Shan, Z. X. *Tetrahedron* **2006**, 62, 5692.

(13) (a) Liu, D. J.; Shan, Z. X.; Qin, J. G. *Chin. J. Chem.* **2004**, 22, 1336. (b) Liu, D. J.; Shan, Z. X.; Zhou, Y.; Qin, J. G. *Helv. Chim. Acta* **2004**, 87, 2310.

(14) Shan, Z. X.; Wang, Q. *Chin. J. Org. Chem.* **2005**, 25, 720.

(15) Chu, Y. B.; Shan, Z. X.; Liu, D. J.; Sun, N. N. *J. Org. Chem.* **2006**, 71, 3998.

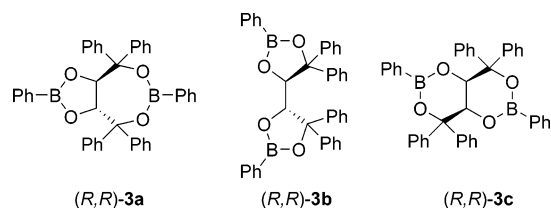


Figure 2. Three possible structures of the product **3**.

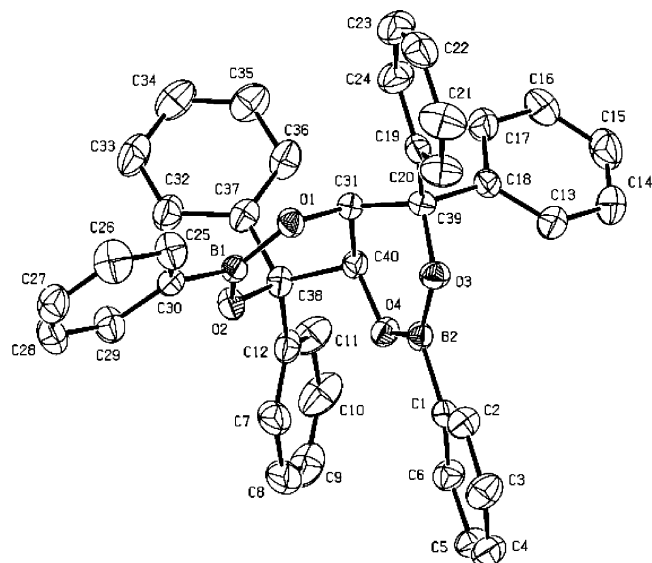


Figure 3. Molecular structure of the product **3c** (hydrogen atoms are omitted for clarity).

(*R,R,S*)-**1** and (*R,R*)-**2**, which were prepared by literature procedures,^{11a,b} were allowed to react with an excess of PhMgBr in THF at 0 °C for 1 h, then refluxed for 1.5 h, respectively. After work up and recrystallization from ethanol, white crystals were formed. From all of the available spectra (see the Supporting Information) of the final product, three candidate structures, (*R,R*)-**3a**, (*R,R*)-**3b**, and (*R,R*)-**3c**, corresponding to the formula C₄₀H₃₂B₂O₄ are proposed, although **3a** is less likely in terms of stability compared with the other two (Figure 2).

To determine the structure of the product, single-crystal X-ray diffraction was performed. As the ORTEP diagram shown in Figure 3 indicates, the product is bicyclo[4.4.0]diboronate ester **3c**.

Theoretical investigations of the three potential structures also were carried out. All calculations were performed with the GAUSSIAN 03¹⁶ programs by ab initio quantum chemistry methods.

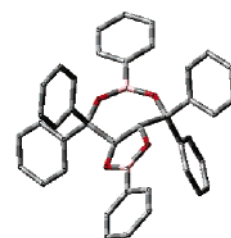
First, the geometries of **3a–3c** were fully optimized using the density functional B3LYP with the standard basis set 6-31G(d).¹⁷ Considering that the central bicyclic framework (excluding the six phenyl groups) of **3a–3c** plays the geometry-determining role, an advanced two-layer ONIOM method¹⁸ and state-of-the-art coupled cluster theory,¹⁹ i.e., CCSD(T), were employed, and the central bicyclic framework was set to be the high-layer, while the surrounding six phenyl groups were set to be the low-layer.

In terms of the enthalpy (H₂₉₈) and free energy (G₂₉₈) as shown in Table 1, **3c** is the most thermodynamically stable

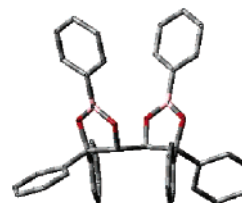
(16) Frisch, M. J.; et al. *Gaussian 03*, Revision D.01; Gaussian: Inc.: Wallingford, CT, 2004. See Supporting Information for remaining authors.

(17) (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648. (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785.

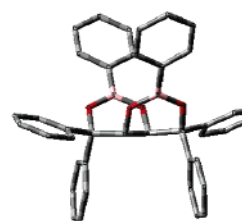
(18) Maseras, F.; Morokuma, K. *J. Comput. Chem.* **1995**, *16*, 1170.



3a



3b



3c

Figure 4. Optimized structures of the three potential products. H atoms are excluded for clarity (black: C atoms; red: O atoms; pink: B atoms).

Table 1. Comparison of the Energies of the Three Potential Structures **3a–3c** at Different Levels of Theory^a

compound	B3LYP/6-31G(d)			B3LYP/6-311+G(3df,2p)	
	ZPE	ΔH ₂₉₈	ΔG ₂₉₈	ΔH ₂₉₈	ΔG ₂₉₈
3a	0.62661	41.0	40.0	47.5	46.5
3b	0.62649	19.0	17.1	21.3	19.5
3c	0.62648	0	0	0	0

compound	ONIOM[B3LYP/6-311G(d,p): B3LYP/6-31G(d)]			ONIOM[CCSD(T)/6-311G(d,p): B3LYP/6-31G(d)]	
	ZPE	ΔH ₂₉₈	ΔG ₂₉₈	ΔH ₂₉₈	ΔG ₂₉₈
3a	0.62661	41.6	40.4	46.3	45.1
3b	0.62580	17.2	15.1	8.9	6.8
3c	0.62575	0	0	0	0

^a Energies of the enthalpies (H) and free energies (G) were calculated using the standard formula and the ab initio data²⁰ at 298.15 K and 1 atm and were given in kJ/mol relative to those of **3c**; energies of ZPE are in hartrees.

species, regardless of the level of theory. As can be seen from Table 2, the calculated geometrical parameters for **3c** are almost identical to the X-ray result. Moreover, the predicted infrared spectrum and ¹H, ¹¹B, and ¹³C NMR data of **3c** are in very good agreement with the experimental spectra (see Supporting Information).

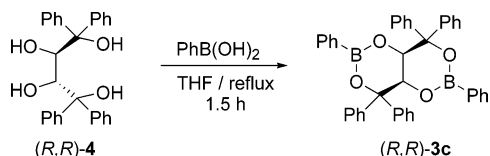
Further investigations of the molecular orbitals show that such a structure leads to significant overlap between the orbitals of the central BCO framework. As a result, a strong π–π stacking effect enhances the stability of **3c**. In the structure **3a**, the two rings are almost in a plane, and therefore, there is very little interaction between the two rings. The structure **3b** has two

(19) Pople, J. A.; Head-Gordon, M.; Raghavachari, K. *J. Chem. Phys.* **1987**, *87*, 5968.

Table 2. Selected Bond Length (Å) and Angles (deg) of the Optimized Structure of **3c in Comparison with the X-ray-Determined Values**

parameter	B3LYP/ 6-31G(d)	ONIOM	exptl
C(39)C(40)	1.531	1.530	1.532
C(31)C(39)	1.551	1.549	1.530
C(31)O(3)	1.434	1.438	1.429
O(3)B(2)	1.372	1.370	1.367
B(2)O(4)	1.374	1.373	1.361
O(4)C(40)	1.424	1.426	1.427
B(1)C(30)	1.560	1.550	1.563
C(38)C(12)	1.537	1.535	1.522
C(38)C(37)	1.543	1.542	1.532
B(1)B(2)	3.610	3.628	3.569
C(40)C(39)C(31)	110.5	110.5	110.8
C(39)C(31)O(3)	108.4	108.4	107.8
C(31)O(3)B(2)	122.2	122.4	119.3
O(4)B(2)O(3)	121.1	121.8	122.5
B(2)O(4)C(40)	120.9	121.1	122.3
O(4)C(40)C(39)	110.0	109.9	110.8

Scheme 1. Selective Condensation of the Tetraols with Phenyl Boronic Acid



five-membered rings separated by a C–C single bond, and thus the interaction between them is reduced significantly.

In the spiroborate esters (*R,R,S*)-**1** and (*R,R*)-**2**, there are several sites for the attack of PhMgBr. In the reaction, the B–O bond is easily cleaved, and two ester groups of the tartrate moiety can be diarylated, so after treatment with saturated aqueous NH₄Cl, (*R,R*)-1,1,4,4-tetraphenyl-1,2,3,4-butanetetraol, (*R,R*)-**4**, can be generated as an intermediate accompanied by phenylboronic acid. It can be estimated that the bicyclo[4.4.0]-diboronic ester **3c** is formed via an intermolecular selective 1,3-cyclocondensation between (*R,R*)-**4** and phenylboronic acid. It has been observed that the direct condensation of (*R,R*)-**4** with phenylboronic acid also furnishes (*R,R*)-**3c** in up to 94% yield (Scheme 1).

It is noteworthy that the product was stable to hydrolysis in weak acid solution. Hydrolysis did not occur when its THF (or MeOH, EtOH) solution was treated with a large excess of saturated aqueous NH₄Cl with and without external heating for more than 4 h or stirred in boiling water for 3 h. This is in sharp contrast to the previously reported 1,2-,²¹ 2,3-,²² and 1,4-cyclocondensation²³ of the cycloborate esters derived from tartaric acid. Perhaps the hydrolytic stability is due to the rigidity of the bicyclic system and the large steric effect in the

surroundings of the boron atom. However, it seems that the stronger hydrochloric acid (>1 mol/L) would destroy the structure.

In summary, reactions between Grignard reagent and tetra-coordinated spiroborate esters with a N→B bond were examined, and a hydrolytically and thermally stable chiral bicyclo[4.4.0]-diboronic ester was afforded in one step, which was confirmed by both the experimental measurements and the ab initio theoretical calculations. The stability of the tricoordinate boronic ester to hydrolysis and heat may be in relationship with the rigidity of the bicycle system and the large steric effect in the surroundings of the boron atoms.

Experimental Section

A representative procedure of the preparation of chiral bicyclic boronic ester is as follows:

(*R,R*)-3c. Phenylmagnesium bromide, which was prepared from Mg turnings (0.523 g, 21.78 mmol) and phenyl bromide (2.08 mL, 19.8 mmol) in THF (20 mL) in the conventional manner, was cooled to 0 °C, followed by careful addition of the chiral spiroborate ester (*R,R,S*)-**1** (0.987 g, 3 mmol). The mixture was stirred at 0 °C for 1 h and then was heated at reflux for 1.5 h. After it was cooled to rt, 20 mL of saturated aqueous NH₄Cl was added with stirring. The organic layer was separated, and the aqueous layer was extracted with ether (3 × 15 mL). A yellow, viscous residue was obtained after concentration of the combined extracts. Excess phenyl bromide was removed by azeotropic distillation in water, and the resulting solid residue was dissolved in hot ether, dried over Na₂SO₄, decolorized with activated charcoal, and evaporated. Then the residue was recrystallized from EtOH to give white crystals (0.6 g, 67% yield based on boron): mp 264–265 °C; [α]_D²⁵ –6.1 (*c* 0.2, CHCl₃); IR (film, cm⁻¹) ν 3019, 2947, 1601, 1437, 1328; ¹H NMR (CDCl₃, 300 MHz) δ 7.82–7.22 (m, 30H, Ar–H), 5.05 (s, 2H, CH); ¹¹B NMR (CDCl₃, 32 MHz, BF₃·OEt₂) δ 27.0; ¹³C NMR (CDCl₃, 75 MHz) δ 143.8, 142.7, 134.6, 131.5, 129.3, 128.3, 128.2, 127.9, 127.5, 126.7, 125.5, 81.3, 69.7; LC-MS (*m/z*) 600, 511, 487, 423, 339, 255, 227. Anal. Calcd (%) for C₄₀H₃₂B₂O₄: C 80.30; H 5.39; B 3.61. Found: C 80.12; H 5.35; B 3.56.

Crystal data for **3c**: C₄₀H₃₂B₂O₄, *M_w* = 598.25, triclinic, space group *P1*, *a* = 9.6051(13) Å, *b* = 9.9781(13) Å, *c* = 10.4687(14) Å, α = 111.552(2)°, β = 90.165(2)°, γ = 108.708(2)°, *V* = 875.5(2) Å³, *Z* = 1, *F*(000) = 340, *T* = 273(2) K, μ(Mo Kα) = 0.078 mm⁻¹. Of the 5740 measured reflections, 4840 were independent (*R*(int) = 0.0120). The final refinements converged at *R*1 = 0.0773 for *I* > 2σ(*I*) and *wR*2 = 0.1654 for all data.

The crystallographic information file is available as Supporting Information. These data can also be obtained (CCDC 299938), free of charge, via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K. (fax: 44-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk)).

Acknowledgment. We thank the National Natural Science Foundation of China (20372053 and 29972033) for financial support.

Supporting Information Available: The optimized structures and the calculated coordinates for **3a–3c**, molecular orbitals, calculated and experimental IR, ¹H NMR, ¹³C NMR, ¹¹B NMR for compound **3c**, full description of the experimental details, LC-MASS, ORTEP diagram, and CIF file are included and available free of charge via the Internet at <http://pubs.acs.org>.

OM060559T

(20) McQuarrie, D. A. *Statistical Thermodynamics*; Harper and Row: New York, 1973.

(21) (a) Nozaki, K.; Kobori, K.; Uemura, T.; Tsutsumi, T.; Takaya, H.; Hiyama, T. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 1109. (b) Ishihara, K.; Gao, Q.; Yamamoto, H. *J. Am. Chem. Soc.* **1993**, *115*, 10412. (c) Furuta, K.; Maruyama, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1991**, *113*, 1041.

(22) (a) Chen, Y. P.; Eltepu, L.; Wentworth, P. Jr. *Tetrahedron Lett.* **2004**, *45*, 8285. (b) Gung, B. W.; Xue, X. W.; Roush, W. R. *J. Am. Chem. Soc.* **2002**, *124*, 10692, and the references therein. (c) Nakagawa, M.; Kawate, T.; Kakikawa, T. *Tetrahedron* **1993**, *49*, 1739. (d) Kawate, T.; Nakagawa, M.; Kakikawa, T.; Hino, T. *Tetrahedron: Asymmetry* **1992**, *3*, 227.

(23) Wallace, R. H.; Zong, K. K. *J. Organomet. Chem.* **1999**, *581*, 87.