Synthesis of boronic esters derived from boronic and diboronic acids and tartrate derivatives

Ma. Gabriela Montiel Schneider [ab], Sandra D. Mandolesi [a] and Liliana C. Koll [ab]

[a] *Instituto de Química del Sur (INQUISUR), Departamento de Química, Universidad Nacional del Sur, Avenida Alem 1253, 8000 Bahía Blanca, Argentina.*
[b] CONICET, Argentina. E-mail: gabriela.montiel@uns.edu,ar; sdmando@criba.edu.ar; lckoll@criba.edu.ar

---

Abstract:

We present here the synthesis of some new boronic esters derived from phenyl boronic acid, 9-anthracene boronic acid, 1,4-phenyldiboronic acid, 1,4-naphtalene diboronic acid and 9,10-anthracene diboronic acid using tartaric acid, dimethyl tartrate and dibenzyl tartrate as diols. They have obtained by simple dehydrating techniques and can be useful in asymmetric synthesis.

Keywords: boronic acids, boronic eters, tartaric acid derivates.

Introduction

Boronic acid and their esters are highly valuable compounds which have found extensive applications in organic and medicinal chemistry. Moreover, they can be used as protecting groups in carbohydrate chemistry, [1] general substrates in the Suzuki coupling, [2] chiral derivatizing agents [3] and glucose-selective fluorescence sensor.[4]

Boronic acids, which are not found in nature, are the products of the second oxidation of boranes. They are an attractive class of synthetic intermediates, because of their unique properties as mild organic Lewis acids, together with their stability and ease of handling. However, because they are solids that tend to exists as mixtures of oligomeric anhydrides, especially the six-member boroxines (**Figure 1**), the corresponding boronic esters are often preferred as synthetic intermediates. Besides, by losing the capability of the hydroxyl group, boronic esters are less polar and easy to handle.

The synthesis of boronic esters from boronic acids and alcohols is an equilibrium which can be driven to the boronate product removing the water produced in the reaction by distillation with a Dean-Stark apparatus or by using dehydrating agents like CaH_2, $MgSO_4$ or molecular sieves. One of the first reports on the formation of boronic esters from diols and polyols was made by Kuivila and co-workers, who described the preparation of several esters of phenylboronic acid by reaction of the latter with sugars like mannitol and sorbitol, and 1,2-diols like cathecol and pinacol. [5] Tartrate boronic ester derivatives have been widely used in asymmetric synthesis as chiral Lewis acid catalysis.

Some examples are allylations of aldehydes, [6] cyclopropanations of olefins, [7] hydroboronations of alkynes, [8] ketones reductions, [9] aldol reactions, [10] additions of imines[11] and Diels-Alder reactions.[12]

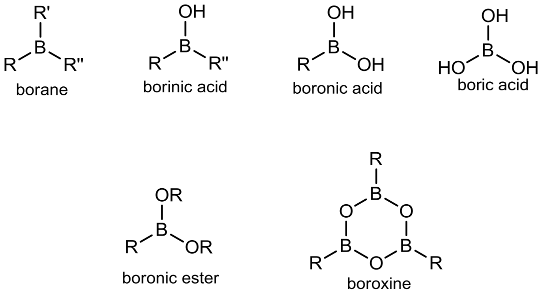
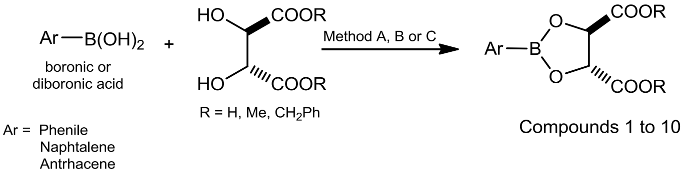


Figure 1. Oxygenated organoboron compounds

Results and Discussions

Taking into account the wide use of boronic ester tartrate derivatives, we were interested in the synthesis of some new boronic esters, starting from the corresponding boronic acids. The boronic acids subject of this work are phenyl and 9-anthracene boronic acid; 1,4-phenyl-, 1,4-naphtalene- and 9,10-anthracene-diboronic acid. The reactions of these substrates with (L)-tartaric acid, dimethyl-(L)-tartrate and dibenzyl-(L)-tartrate afforded the desired products, in almost all cases (**Scheme 1**). Results are summarized in **Table 1**.



Scheme 1. Synthesis of boronic ester tartrate derivatives

Three methods were performed. Method A: room temperature, molecular sieves, toluene, 2 to 5h reaction time; Method B: reflux, toluene, 20h reaction time; Method C: reflux, CaH_2, THF, 1 to 3h reaction time. Method B cannot be performed whith tartatic acid since the high temperatures achieve in this method can destroyed the reactive.

Table 1 . Synthesis of aryl- mono- and di-boronic esters of tartaric acid, dimethyl and dibenzyl- (L)- tartrate

Entry	Boronic acid	Diol	Method	Yield (%)[a]	Compound	^{11}B (ppm)
1	Phenylboronic acid	(L)-tartaric acid	C	100	1	29,0
2	Phenylboronic acid	Dimethyl-(L)-tartrate	A and B	100	2	31,9
3	Phenylboronic acid	Dibenzyl-(L)-tartrate	A	100	3	31,4
4	1,4-phenyldiboronic acid	(L)-tartaric acid	A	100	4	33,4
5	1,4-phenyldiboronic acid	(L)-tartaric acid	C	-----	-----	
6	1,4-phenyldiboronic acid	Dimethyl-(L)-tartrate	A	73	5	31,6
7	1,4-phenyldiboronic acid	Dimethyl-(L)-tartrate	B	70	5	
8	1,4-phenyldiboronic acid	Dibenzyl-(L)-tartrate	A	-----	-----	-----
9	1,4-phenyldiboronic acid	Dibenzyl-(L)-tartrate	B	83	6	40,8
10	1,4-naphtalenediboronic acid	(L)-tartaric acid	C	-----	-----	-----
11	1,4-naphtalenediboronic acid	Dimethyl-(L)-tartrate	A	55	7	32,0
12	1,4-naphtalenediboronic acid	Dibenzyl-(L)-tartrate	A	72	8	30,7
13	9-anthraceneboronic acid	(L)-tartaric acid	C	-----	-----	-----
14	9-anthraceneboronic acid	Dimethyl-(L)-tartrate	A	78	9	34,7
15	9,10-anthracendiboronic acid	(L)-tartaric acid	C	-----	-----	-----
16	9,10-anthracendiboronic acid	Dimethyl-(L)-tartrate	A	-----	-----	-----
17	9,10-anthracendiboronic acid	Dimethyl-(L)-tartrate	B	73	10	34,8
18	9,10-anthracendiboronic acid	Dibenzyl-(L)-tartrate	A	-----	-----	-----

[a] Calculates by ^{1}H-NMR.

The formation of the boronic esters is easily detectable by ^{1}H-NMR since the methine signal of the diols (which appears at 4 – 4,5 ppm) shift to 5 ppm and in ^{13}C-NMR move from 71.0 ppm (right of the chloroform signal) to 76.8 ppm (left of the chloroform signal), as it is shown in **Figure 1**, for the reaction of Entry 7 in Table 1.

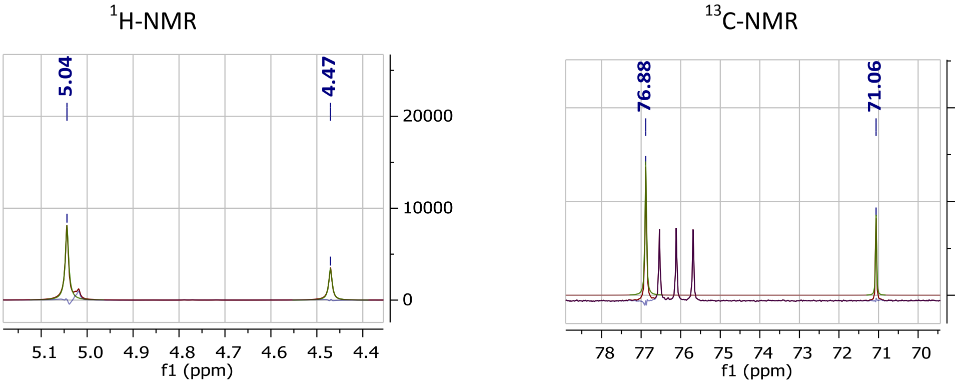


Figure 2. ^{1}H and ^{13}C-NMR showing the shift of the methines from diols to boronic esters

The structures of the new boronic ester tartrate derivatives is shown below. (**Figure 3**).

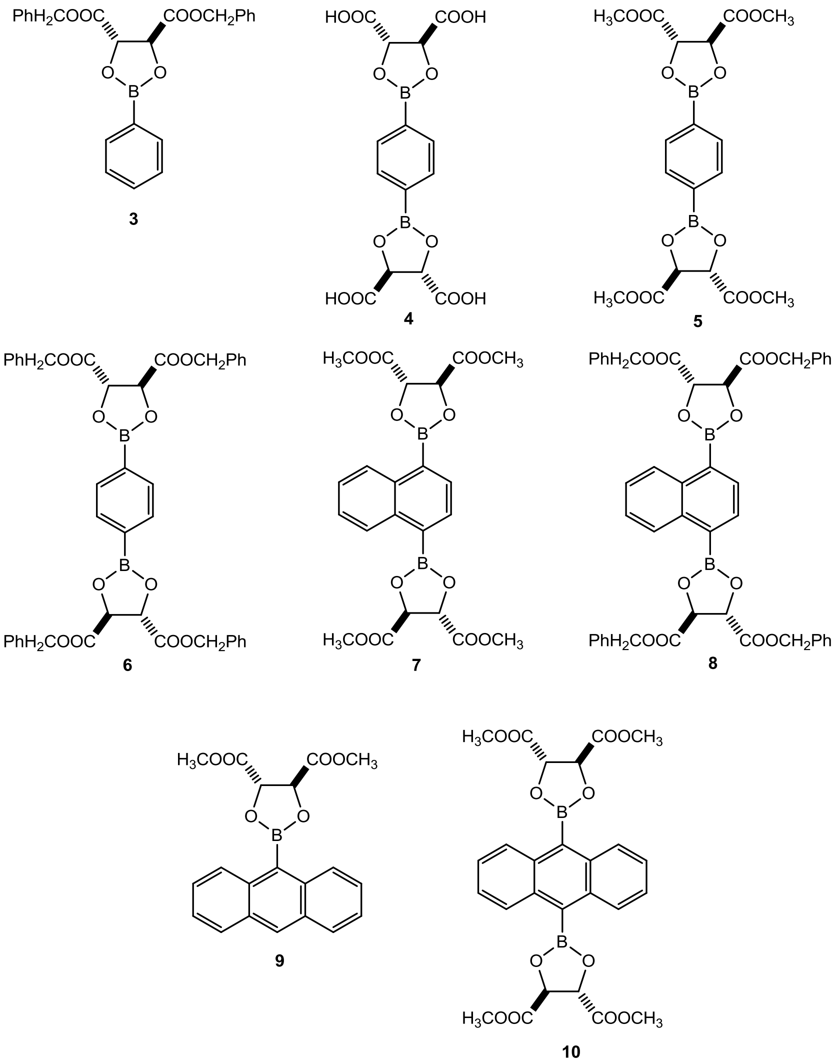


Figure 3. New boronic esters tartrate derivatives

Conclusions

The synthesis and characterization of some new boronic ester tartrate derivates was achieved using simple dehidrating techniques. To our knowledge, only the synthesis of dimethyl 2-phenyl-1,3,2-dioxaborolane-4,5-dicarboxylate and 2-phenyl-1,3,2-dioxaborolane-4,5-dicarboxylic acid (compound 1 and 2; Entry 1 and 2 in Table 1), have already been reported previously.[13]

As these new boronic esters synthesized in this work could be important tools in asymmetric synthesis, further studies with these compounds will be made and the results will be informed opportunely.

Acknowledgments

This work was supported by grants from ANPCyT (Capital Federal, Argentina), CONICET (Buenos Aires, Argentina) and Universidad Nacional del Sur (Bahía Blanca, Argentina). A fellowship from CONICET to MGMS is acknowledged.

Experimental section

General methods

Unless otherwise noted, all reagents were purchased from commercial suppliers and used without purification. All reactions were carried out under an inert atmosphere. Boronic acids were synthesized according to literature procedures.[14] 1,4-dibromo naphthalene, [15] 9,10-dibromo anthracene[16] and dibenzyl-(L)-tartrate were synthesized following the reference method.[17] Toluene was dried with $CaCl_2$, and then fractionally distilled (108-109°C) in inert atmosphere from sodium. Dry THF was achieved by distillation from sodium benzophenone.

General procedures

All the reactions were carried out following the same procedure. One experiment is described in detail in order to illustrate the methods used.

Method A

In a two necked round-bottom flask 150 mg (1,2 mmol) of phenyl boronic acid, 213 mg (1,2 mmol) of dimethyl-(L)-tartrate and 1,6 g of activated molecular sieves were added in 7 ml of toluene. The reaction was stirred at room temperature. After 2 hours the mixture was filtered and the solvent evaporated under vacuum.

Method B

In a two necked round-bottom flask adapted with a Dean-Stark apparatus 200 mg (1,2 mmol) of 1,4-phenyldiboronic acid, 797 mg (2,4 mmol) of dibenzyl-(L)-tartrate were added in 7 ml of toluene. The reaction was heated until no more formation of water was detected. Then the reaction was allowed to cool at room temperature and the solvent was evaporated under vacuum.

Method C

In a two necked round-bottom flask 100 mg (0,6 mmol) of 1,4 phenyldiboronic acid, 181 mg (1,2 mmol) of (L)-tartaric acid and 100 mg (2,4 mmol) of CaH_2 were added in 5 ml of THF. After 1 hour the reaction was filtered and the solvent evaporated under vacuum.

References

1- James T.D.; Sandanayake, S. ; Shinkai, S. *Angew. Chem., Int. Ed. Engl.* **1996**, 35, 1910-1922.
2- Miyaura, R.; Suzuki, A. *Chem Rew.* **1995**, 95, 2457-2483.
3- Morandi, S.; Caselli, E.; Forni, A.; Bucciarelli, M.;Torre, G.; Prati, F. *Tetrahedron: Asymmetry* **2005**, 16, 2918-2926.
4- Karnati, V.V.; Gao, X.; Gao, S.; Wang, W.; Ni, S.; Sankar, S.;Wang, B. *Bioorg. Med. Chem. Lett*. **2002**, 12, 3373-3377.
5- Kuivila, H.G.; Keough, A.H.; Soboczenski, E.J.; *J. Org. Chem.* **1954**, *8*,780–783.
6- a) Roush, W. R.; Hoong, L. K.; Palmer, M. A. J.; Park, J. C. *J. Org. Chem.* **1990**, 55, 4109–4117; b) Roush, W. R.; Adam, M. A.; Walts, A. E.; Harris, D. J. *J. Am. Chem.Soc.* **1986**, 108, 3422–3434; c) Roush, W. R.; Walts, A. E.; Hoong, L. K. *J. Am.Chem. Soc.* **1985**, 107, 8186–8190
7- a) Llewellyn, D. B.; Arndtsen, B. A. *Tetrahedron: Asymmetry* **2005**, 16, 1789–1799; Luithle, J. E. A.; Pietruszka, J. *J. Org. Chem.* **2000**, 65, 9194–9200; b)Luithle, J. E. A.; Pietruszka, J. *Eur. J. Org. Chem.* ***2000***, 2557–2562; c) Luithle, J. E. A.; Pietruszka, J. *J. Org. Chem.* **1999**, 64, 8287–8297; d) Nakayama, K.; Rainier, J.D. *Tetrahedron* **1990**, 46, 4165–4170.
8- Luithle, J. E. A.; Pietruszka, J.; Witt, A. *Chem. Commun*. **1998**, 2651–2652.
9- Eagon, S.; Kim, J.; Yan, K.; Haddenham, D.; Singaram, B. *Tetrahedron Lett*. **2007**, 48, 9025–9029; (b) Cordes, D. B.; Kwong, T. J.; Morgan, K. A.; Singaram, B. *Tetrahedron Lett*. **2006**, 47, 349–351.
10- (a) Furuta, K.; Maruyama, T.; Yamamoto, H. *J. Am. Chem. Soc*. **1991**, 113, 1041–1042; (b) Boldrini, G. P.; Lodi, L.; Tagliavini, E.; Trombini, C.; Umani-Ronchi, A. *J.Organomet. Chem*. **1987**, 336, 23–28.
11- Yim, H. K.; Wong, H. N. C. *J. Org. Chem.* **2004**, 69, 2892–2895.
12- Ishihara, K.; Gao, Q.; Yamamoto, H. *J. Am. Chem. Soc*. **1993**, 115, 10412–10413.
13- Suri, J.T.;Vu, T.; Hernandez, A.; Congdon J.; Singaram, B. *Tetrahedron Lett*. **2002**, 3649-3652.
14- a) Lemmonier, J.F.; Guénée, L.; Beuchat, C.; Wesolowski, T.A.; Mukherjee, P.; Waldeck, D.H.; Gogick, K.A.; Petoud, S.; Piguet, C. *J. Am. Chem. Soc*. **2011**, 133, 16219-16234. b) Zhang, F.J.; Cortez, C.; Harvey, G. *J. Org. Chem.* **2000**, 65, 3952-3960. C) Kim. S.K.; Yang, B.; Ma, Y.; Lee, J.H.; Park, J.W. *J.Mater.Chem*. **2008**, 18, 3376-3384.
15- Cakmak, O.; Demirtas, I.; Balaydin, H.T. *Tetrahedron*, **2002**, 58, 5603-5609.
16- Clarke, H.T.; Murray, T.F. *Org. Synth*. **1941**, Coll. Vol. 1, 207-208
17- Furuta, K.; Gao, Q.Z.; Yamamoto, H.; *Org. Synth*. **1998**, Coll. Vol. 9, 722-726.