Journal of Organometallic Chemistry 788 (2015) 36–41

Contents lists available at ScienceDirect

Journal of Organometallic Chemistry

journal homepage: www.elsevier.com/locate/jorganchem

Novel 2,6-disubstituted phenylboronic compounds – Synthesis, crystal structures, solution behaviour and reactivity

Agnieszka Adamczyk-Woźniak [a, *], Krzysztof Ejsmont [b], Błażej Gierczyk [c], Ewa Kaczorowska [a], Alicja Matuszewska [a], Grzegorz Schroeder [c], Andrzej Sporzyński [a], Bartosz Zarychta [b]

[a] Faculty of Chemistry, Warsaw University of Technology, Noakowskiego 3, 00-664 Warsaw, Poland
[b] Faculty of Chemistry, University of Opole, Oleska 48, 45-052 Opole, Poland
[c] Faculty of Chemistry, Adam Mickiewicz University in Poznań, Umultowska 89b, 61-614 Poznań, Poland

ARTICLE INFO

Article history:
Received 24 February 2015
Received in revised form
9 April 2015
Accepted 16 April 2015
Available online 25 April 2015

Keywords:
Boronic acids
Benzoxaboroles
Reductive amination
Tautomeric equilibria
Crystal structure

ABSTRACT

2,6-Diformylphenylboronic acid has been synthesized and characterized both in the solid state as well as in solution. In crystal, an unusual structural pattern has been found with the formation of intermolecular hydrogen bonds by $B(OH)_2$ and CHO groups as well as water molecules. In solution tautomeric equilibrium with the formation of oxaborole ring by one of the formyl groups was proved on the basis of multinuclear NMR spectroscopy. The title compound reacts with secondary mono- and diamines to form various types of substituted benzoxaboroles, which have been characterized by XRD and spectroscopic methods.

Introduction

Boronic acids are the compounds of growing interest not only for Suzuki coupling reaction [1], but also due to their wide applications in catalysis, medicine and biology [2]. A great interest has been also paid to the supramolecular systems formed by these compounds. Two hydroxyl groups can be involved in various homomeric and heteromeric hydrogen-bonded assemblies [3], as well as in condensation reaction leading to covalently bonded systems, e.g. the esters with polyols [4,5]. In addition to strong intermolecular hydrogen bonds in typical dimeric units and lateral hydrogen bonds connecting them [6,7], there are many examples of weaker inter- and intramolecular bonds formation, determining the crystal architecture. Introduction of functional groups into the ring of arylboronic acid gives further possibilities to form supramolecular assemblies in which these groups take part.

Substituents at *ortho* position of phenylboronic acids can interact with boronic group in several ways. If the substituent contains strong proton acceptor atom, intramolecular hydrogen bond can be formed. It is observed for example in case of alkoxy substituents [8]. For the *ortho*-formyl group, intramolecular hydrogen bond is also observed, and the formed seven-membered ring is essentially coplanar with the phenyl ring [9,10]. In the case of the halogen atoms at *ortho* position the formation of weak intramolecular interactions is observed [6,11,12]. The influence of acceptor atom at *ortho* position of phenylboronic acids on the geometry of the molecule was discussed recently [8].

A special group of boronic acids are those with two substituents at the *ortho* position. A variety of possible types of interactions has been found for 2,6-dialkoxyphenylboronic acids. For these compounds several polymorphs were obtained, with the examples of novel monomeric structures in addition to more common dimers or ladders [13]. A series of 2,6-difluorophenylboronic acids was also investigated. For all the investigated compounds, only one intramolecular B–O–H···F hydrogen bond is formed [11].

One of the most interesting compounds from the point of view of possible derivatization is *ortho*-formylphenylboronic acid. Depending on reaction conditions, a variety of products can be formed, including benzoxaboroles as well as amino- and imino-derivatives [14–18].

* Corresponding author. Tel.: +48 22 2346147; fax: +48 22 6282741.
E-mail address: agnieszka@ch.pw.edu.pl (A. Adamczyk-Woźniak).

http://dx.doi.org/10.1016/j.jorganchem.2015.04.026
0022-328X/

The newly obtained 2,6-diformylphenylboronic acid is a very interesting compound from the point of view of its structure as well as solution behaviour and possible derivatization.

Results and discussion

Synthesis of 2,6-diformylphenylboronic (**1**) acid and its reactions (reduction, reductive amination with morpholine and reaction with piperazine) are shown in Scheme 1.

Compound **1** was obtained from the corresponding bromide in a lithiation/boronation sequence after protecting of formyl groups. The synthesis of its pinacol ester from the same substrate was described [19], but the acid was not obtained or characterized yet. The reduction of **1** leads to hydroxymethylbenzoxaborole **2**, which was earlier synthesized by different method. Its possible structures in various solvents have been previously investigated by ^{1}H NMR [20]. Data obtained in the present work are consistent with the literature ones. Moreover, its structure was confirmed by X-ray diffraction [21]. Compound **1** in reductive amination with morpholine [17] gives the product **3** in 42% yield. Similar compound with diisopropylamino group was recently obtained with 23% yield from 7-formylbenzoxaborole, but its molecular and crystal structure was not investigated [22]. Finally, **1** reacts with piperazine to give 3-substituted bis-benzoxaborole **4** in 73% yield. For this compound ^{1}H NMR spectrum in DMSO shows two sets of signals of equal intensity, corresponding to two pairs of enantiomers, which was previously stated for the other bis-benzoxaboroles [23].

For 2-formylphenylboronic acids in solution a tautomeric equilibrium with the formation of oxaborole ring by the formyl group was previously observed. This equilibrium depends on additional substituents in phenylboronic acid [24]. In order to investigate this equilibrium, compound **1** was fully characterized by the multinuclear NMR and compared with the data for 2-formylphenylboronic acid (**5**) (Table 1). These data confirm the equilibrium between open and cyclic forms for 2,6-diformyl-phenylboronic acids (Scheme 2).

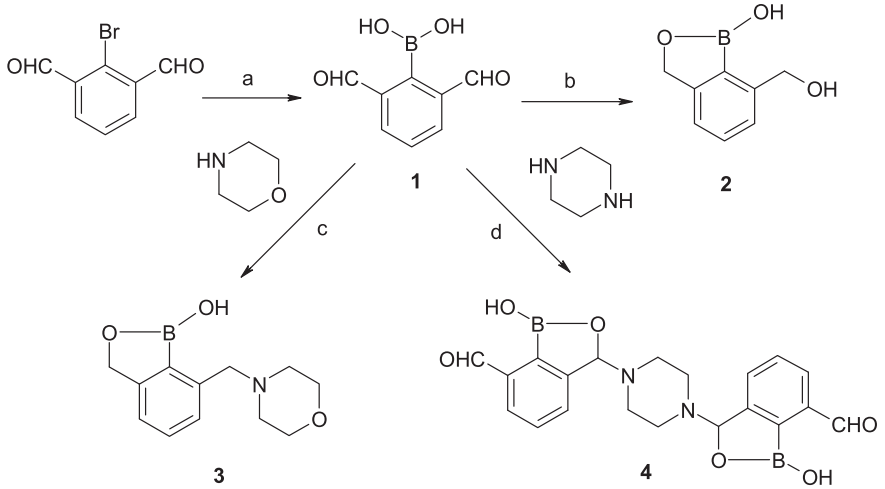
The NMR spectra indicating the presence of both open and cyclic form of **1** are shown in Fig. 1.

Equilibrium constant for this reaction can be easily determined by NMR method on the basis of the integration of the corresponding signals in ^{1}H NMR spectra [25]. The value of cyclization reaction equilibrium constant (K_{cycl}) for **1** is 1.05 ([^{2}H]$_6$-acetone, 298 K, c = 0.02 M). The concentration-dependence of tautomers ratio (K_{obs}) observed by Luliński et al. [24] has been explained by the assuming of the existence of two competitive equilibrium processes, i.e. cyclization and dimerization. Since the ratio of both tautomers of **1** is almost concentration insensitive in studied concentration range (0.02–0.5 M), this compound do not tend to dimerize in solution or the equilibrium constant of this process is very low. The determined K_{cycl} value is similar to that reported for 3-fluoro-2-formylphenylboronic acids but much higher than that for 2-formylphenylboronic acid **5** (K_{cycl} ca. 0.05; lit [24]. K_{cycl} = 0). We have not observed the formation of tricyclo form **1b** (Scheme 2). This structure is probably not formed due to unfavourable strain of the tricyclic system [20].

The ^{17}O NMR spectrum of the open (dialdehyde) form of **1** consists of two signals. The boronyl group oxygen is about 6 ppm deshielded *vs.* the corresponding atom of 2-formylphenylboronic acid. This is the result of steric interactions with a second –CHO substituent. As it has been shown in series of arylboronic acids, steric interactions are major parameter affecting the ^{17}O NMR chemical shifts of the –B(OH)$_2$ group [25]. Steric and electronic effects cause also the deshielding of aldehyde oxygen signal. Cyclization results in the appearance of new signals. The signal corresponding to free –CHO substituent overlaps with that for open tautomer. The characteristic signal assigned to B–O–C oxygen atom occurs at 153.7 ppm (shifted ca. 6 ppm downfield if comparing with cyclic form of 3-fluoro-2-formylphenylboronic acid). Signals of two –OH groups are well resolved. The signal corresponding to BOH oxygen is strongly deshielded vs. that of COH moiety, due to steric interactions and boron atom electronic effects.

Molecular and crystal structures of compounds **1** and **3** have been determined by a single crystal XRD at 100.0 K to quantify the hydrogen bonding pattern. Crystal data and structural refinements as well as selected geometric parameters and hydrogen bonds' geometry data are collected in Supplementary data (Tables S1 – S3). The molecular structures of the compounds **1** and **3** are presented in Fig. 2.

The molecule of **1** is composed with two perpendicular planes (phenyl ring and boronic group) with the angle of 90.00(23)° This conformation can be expected in the case of the *ortho*-substituent in aromatic ring unable to be hydrogen acceptor. In the case of substituent forming intramolecular hydrogen bond with B–OH group coplanar arrangement of the boronic group and the ring is observed, as mentioned above. However, there are some examples of the hydrogen acceptor at the *ortho* position which do not form



Scheme 1. Synthesis of 2,6-diformylphenylboronic acid (**1**) and its reactions. Reaction conditions: (a) 1. HC(OMe)$_3$, MeOH, H_2SO_4; 2. BuLi, Et$_2$O, THF, −78°; 3. B(OMe)$_3$, Et$_2$O, THF, −78°; 4. aq. HCl; (b) $NaBH_4$, MeOH; (c) $NaBH_4$, MeOH; (d) Et$_2$O, THF.