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Mono- and di-phenylboronic acid receptors with fluorescence sensitivity to D-fructose

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ABSTRACT

Three monoboronic acids, namely, [3-(benzoylamindo)phenyl]boronic acid (1), [3-(nicotinamido)phenyl]boronic acid (2), and [3-(isonicotinamido)phenyl]boronic acid (3), as well as four diboronic acids, namely, [3,3′-[N,N′-(paraphthalmido)]biphenyl]diboronic acid (4), [3,3′-[N,N′-(isophthalamido)]biphenyl]diboronic acid (5), [3,3′-[N,N′-(2,6-pyridinedicarboxamido)]biphenyl]-diboronic acid (6), and [3,3′-[N,N′-(2,5-pyridinedicarboxamido)]biphenyl]diboronic acid (7), are synthesized using their corresponding acyl chlorides and 3-aminobenzeneboronic acid. All compounds are fully characterized. The crystal structure of compound 3 is determined using single-crystal X-ray diffraction analysis. Fluorescence tests are performed using a general fluorescence assay method called indicator displacement assay, which uses alizarin red S as the optical reagent to monitor the binding of the unmodified boronic acid compound with the carbohydrate. The monoboronic acids show fluorescence quenching for D-fructose in aqueous solution, whereas the diboronic acids show fluorescence enhancement in DMF solutions. The Stern–Volmer plot within the total concentration range of the compounds is linear, indicating significant sphere quenching caused by the interaction between D-fructose and boronic acid receptors.

1. Introduction

Boronic acid is a Lewis acid that reacts with a base to transform from a neutral trigonal form into an anionic tetrahedral form. Given that boronic acids strongly interact with diol-type compounds, they are attracting considerable interest as fluorescent probes for detecting saccharides. Yoon and Czarnik [1] reported the first fluorescence sensors for saccharides, i.e., anthrylboronic acids. These compounds show significant fluorescence intensity changes upon binding with saccharides. However, the binding of these compounds with saccharides only proceeds at high pH values unsuitable for physiological conditions, and such binding lacks the necessary charge change. These defects limit the application of anthrylboronic acids in actual detection [2,3]. Despite many initial successes [4–7], the application of such sensors for saccharide detection requires the development of new candidates with some favorable properties, such as biocompatibility. When a nitro group is introduced to the sensors [8], the fluorescence response of such compound is altered; further investigations into substituent effects of chemosensory devices are needed.

In boronic acid-based sensors, nitrogen near the boronic acid is important. Such sensors provide a wide pH range of measurement, particularly in human physiological conditions (pH 7.7) in saccharide determination. The amide group is not only used as hydrogen-bond donors, but also as hydrogen-bond receptors. Hydrogen bonding is a main force of molecular recognition, and thus many amide compounds are designed to be highly-selective artificial receptors, which are widely used in molecular recognition; these receptors are important units. Amide compounds are important organic synthetic intermediates, which are used in pesticides and medicine [9–13]. Boronic acid groups and amines are assembled into a molecule which not only have increased functionality, but also have with novel molecular structure. Using anthracene fluorescent reporter system as basic building block, Wang et al. [14] synthesized a series of diboronic acids compounds with different amide linkers. Biocompatible amide compounds have improved practicability. Biocompatibility means introducing an amide group which are both a hydrogen bond donor (NH–) and a hydrogen bond

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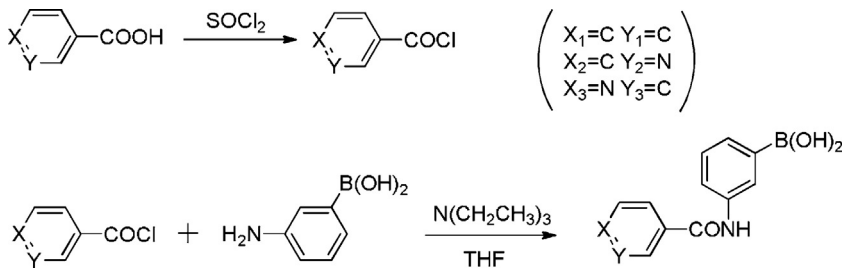

Scheme 1. Synthesis of compound 1–3.

acceptor (C=O) for its widely formed hydrogen bonds. A hydrogen bond is one of the main force of the host-guest molecule recognition and that is why so many amides are designed to be highly selective artificial receptor and widely used for molecular recognition, which has become an important class of molecular recognition units. The assembly of a boronic acid group and the amide group in the same molecule can not only to increase its functionality, but to obtain molecules having a novel structure also [15].

Boronic acid compounds are used in fluorescent sensors for carbohydrate identification [16,17]. In the present study, we designed a series of monoboronic and diboronic acids, which have amino group. We designed physiological environment to recognize D-fructose molecular [18,19].

2. Experimental

2.1. Materials

All of the chemical reagents were obtained from commercial suppliers and used without further purification. Solvents were purified and dried using standard methods prior to usage. 3-Amidophenylbronic acid, 2,6-pyridinedicarboxylic acid, and 2,5-pyridinedicarboxylic acid were purchased from a Johnson Matthey Company. Nicotinic and isonicotinic acids were obtained from Aobox Biotechnology (Beijing, China).

2.2. Synthesis

2.2.1. Synthesis of 3-(benzoylamino)phenyl boronic acid (*1*)

Benzoic acid (3 g, 25 mmol) was heated to reflux for 2 h in 15 mL sulfoxide chloride. Benzoyl chloride was obtained by distilling the excess sulfoxide chloride. 3-Amino benzene boronic acid (2.50 g, 16 mmol) was dissolved in THF (20 mL). The 3-amino benzene boronic acid solution was then added to a solution of sulfoxide chloride. The synthetic route to 3-(benzoylamino)phenyl boronic acid (**1**) is shown in Scheme 1. During the addition of triethylamine, the mixture was stirred slowly for 5 h. The yellow, sticky solid was collected by filtration and then purified by recrystallization from alcohol–water. The melting point of the purified crystals is 259.0–269.3 °C. All of the structures of the target products were characterized by FT-IR and ^{1}H NMR (Table 1).

2.2.2. Synthesis of 3-(nicotinamido)phenyl boronic acid (*2*)

The synthetic process employed is similar to that in method (**1**), except that nicotinic acid was used instead of benzoic acid. The yellow powder was collected by filtration and purified by recrystallization from alcohol–water. The synthetic route for 3-(nicotinamido)phenyl boronic acid (**2**) is shown in Scheme 1. The melting point of the obtained crystals is 195.4–198.5 °C. All of the structures of the target products were characterized by FT-IR and ^{1}H NMR (Table 1).

2.2.3. Synthesis of [3-(isonicotinamido) phenyl] boronic acid (*3*)

The synthetic process employed is similar to that in method (**1**), except that isonicotinic acid was used instead of benzoic acid. The yellow powder was collected by filtration and purified by recrystallization from alcohol–water. The synthetic route to 3-(isonicotinamido) phenyl boronic acid (**3**) is shown in Scheme 1. The melting point of the obtained crystals is 207.1–210.4 °C. All of the structures of the target products were characterized by FT-IR and ^{1}H NMR (Table 1). The XRD data for $C_{12}H_{11}BN_2O_3$(**3**)·H_2O are as follows: triclinic system, space group *P*-1; a = 4.7451(6) Å; b = 9.6977(12) Å; c = 14.2074(18) Å; α = 107.624(2)°; β = 96.207(2)°; γ = 95.620(2)°; V = 613.52(13) Å^3; Z = 2; Dc = 1.408 g cm^{-3}; $F(000)$ = 272; μ = 0.105 mm^{-1}; 3,368 reflections were measured, among which, 2,364 were unique R(int) = 0.0133, R_1 = 0.0457, $wR_2 = 0.1078[I > 2\sigma(I)]$; and GOF = 1.011.

2.2.4. Synthesis of [3,3′-[N,N′-(paraphthalmido)]biphenyl]diboronic acid (*4*)

The synthetic process employed is similar to that in method (**1**), except that terephthalic acid was used instead of benzoic acid. The white powder was collected by filtration and purified by recrystallization from DMF–water. The synthetic route to [3,3′-[N,N′-(paraphthalmido)]biphenyl]diboronic acid (**4**) is shown in Scheme 2. The melting point of the product is >300 °C. All of the structures of the target products were characterized by FT-IR and ^{1}H NMR (Table 1).

2.2.5. Synthesis of [3,3′-[N,N′-(isophthalamido)]biphenyl]diboronic acid (*5*)

The synthetic process employed is similar to that in method (**1**), except that 1,3-benzenedicarboxylic acid was used instead of benzoic acid. The white powder was collected by filtration and purified by recrystallization from DMF–water. The synthetic route to [3,3′-[N,N′-(isophthalamido)]biphenyl]diboronic acid (**5**) is shown in Scheme 3. The melting point of the product is 243.8–245.8 °C. All of the structures of the target products were characterized by FT-IR and ^{1}H NMR (Table 1).

2.2.6. Synthesis of [3,3′-[N,N′-(2,6-pyridinedicarboxamido)]biphenyl]diboronic acid) (*6*)

The synthetic process employed is similar to that in method (**1**), except that2,6-pyridinedicarboxylic acid was used instead of benzoic acid. The white powder was collected by filtration and purified by recrystallization from DMF–water. The synthetic route to [3,3′-[N,N′-(2,6-pyridinedicarboxamido)]biphenyl]diboronic acid) (**6**) is shown in Scheme 3. The melting point of this product is >300 °C. All of the structures of the target products were characterized by FT-IR and ^{1}H NMR (Table 1).