Tetrahedron Vol. 46, No. 12, pp. 4137–4148, 1990
Printed in Great Britain

0040-4020/90 $3.00+.00

PREPARATION OF NEW QUINIC ACID BORON ESTERS IN APROTIC MEDIA

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(*Received in USA 7 December* 1989)

Summary: The syntheses, structure and reactivity of several boron derivatives of quinic acid, obtained in aprotic media, show that these boron heterocycles are useful intermediates, since they provide an alternative route to functionalize the quinic acid in a different way as when using dioxolane derivatives. Some new dioxolane derivatives of quinic acid and free quinide, as well as the lactone of quinic acid (6), were prepared in very high yields. The conformations of all new compounds were established from ^{1}H NMR measurements.

Introduction.

Many polyoxygenated carbocycles produce potent antimicrobial, antiviral and antitumoral responses, as well as growth-promoting effects[1]. Because of their pronounced biological activities and their potential as versatile chemical intermediates, polyoxygenated carbocycles have been the target of many synthetic efforts[2-4]. Quinic acid (1), a very important natural polyhydroxylated cyclohexane, is an intermediate in the shikimate pathway to aromatic aminoacids[5-7] and an important chiron in organic chemistry due to its four functionalized asymmetric carbons. Hence, it is relevant to investigate selective protection methods for these four hydroxy groups. We have been working with this molecule toward the total synthesis of enterocine[2,3] and reported the characterization of a large number of derivatives[2,3,8].

Interactions between boric acid and quinic acid have been studied by means of ^{11}B and ^{13}C NMR only in aqueous solutions[9]. In this paper we present our results for the preparation, in aprotic media, of some boron derivatives that could be relevant for the chemistry of quinic acid and of some other polyhydroxylated molecules. The new compounds were characterized by carbon-13, hydrogen-1 and boron-11 NMR, as well as by ^{1}H-^{1}H and ^{13}C-^{1}H correlation spectra. From these experiments, their conformations were fully established.

Results and Discussion.

Phenylboronic Derivatives.

Reaction of equimolar ratios of phenylboronic acid with quinic acid **1** in benzene afforded

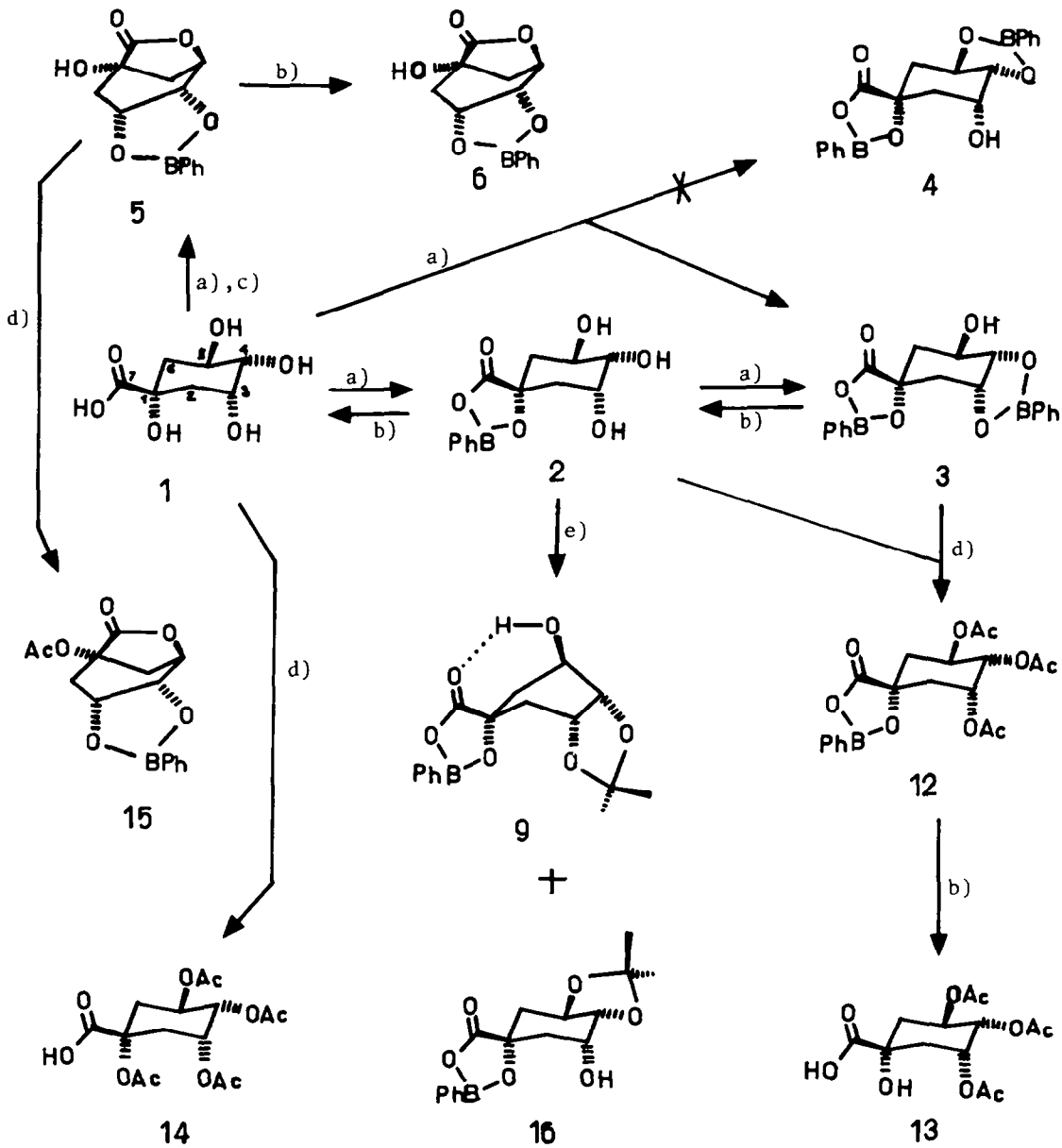
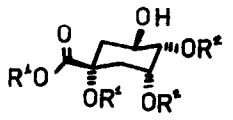
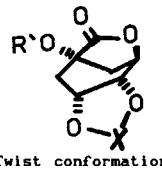


Figure 1. a) $PhB(OH)_2$; b) H_2O; c) H^+; d) Ac_2O/Py; e) 2,2-dimethoxypropane/H^+.

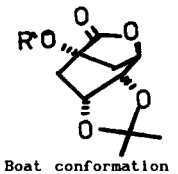
TABLE 1. ^{1}H NMR chemical shifts (ppm) and signal multiplicity.



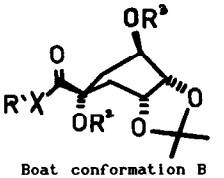
Chair conformation



Twist conformation



Boat conformation A



Boat conformation B

Compound	2α	2β	3	4	5	6α	6β	Isopropyl CH3	Isopropyl CH3	Acetyl CH3
			Chair conformation							
1[a,b,c,*]	1.7(dd)	1.6(dd)	3.8(td)	3.2(dd)	3.7(td)	1.8(dd)	1.7(dd)	-	-	-
2[a,b,d,*]	2.1(ddd)	2.2(dd)	4.4(dd)[e]	3.4(dd)	3.5(ddd)	2.2(ddd)	1.8(dd)	-	-	-
3[a,b,*]	2.2(d)	2.2(d)	4.9(td)	4.4(dd)	4.0(ddd)	1.8(dd)	1.7(dd)	-	-	-
12[f,g,h]	1.7[i](dd)	2.5[i](dd)	5.6(t)[e]	5.0(dd)	5.4(td)	2.7(dd)	2.3(dd)	-	-	2.1, 2.0
14[a,b,*]	2.6(dd)	2.5(dd)	5.4(td)	5.1(dd)	5.3(ddd)	2.3(dd)	2.4(dd)	-	-	2.0, 1.9
			Twist conformation							
5[a,f,g,*]	2.2(dd)	2.6(ddd)	4.8(ddd)	4.7(ddd)	4.9(dd)	2.3(d)	2.4(dddd)	-	-	-
6[a,b,*]	1.7(d)	1.8(ddd)	3.5(td)	3.8(ddd)	4.6(dd)	2.3(d)	2.2(ddd)	-	-	-
15[b,f,j,l]	2.2(m)	2.5(m)	4.6(m)	4.5(dd)	4.8(m)	2.4(d)	2.5(m)	-	-	-
			Boat conformation A							
7[a,c,f,*]	2.2(dd)	2.4(ddd)	4.5(ddd)	4.3(dd)	4.7(dd)	2.6(d)	2.3(ddd)	1.5	1.4	-
11[a,f,*]	2.3(dd)	2.4(ddd)	4.5(ddd)	4.3(ddd)	4.8(dd)	2.5(d)	3.0(dddd)	1.5	1.3	2.1
			Boat conformation B							
8[a,b,*]	2.0(dd)	1.6(dd)	4.3(dd)	3.9(dd)	3.7(td)	1.7(d)	1.7(d)	1.4	1.2	-
9[a,b]	k	k	4.9(d)	3.8(dd)	4.3(m)	k	k	1.41	1.26	-
10[a,b]	k	k	4.93(m)	3.87(m)	3.98(m)	k	k	1.43	1.29	-
17[c,f,h]	2.1[i](dd)	2.3[i](dd)	4.5(td)	4.1(td)	3.9(q)	2.2(ddd)	1.9(dd)	1.5	1.3	-

a) 300 MHz, b) DMSO-d6, c) from reference 4, d) aromatic protons: *o* 7.7, *m* 7.3 and *p* 7.4 ppm, e) broadened, f) CDCl3, g) aromatic protons: *o* 7.8, *m* 7.4 and *p* 7.5 ppm, h) 90 MHz, i) may be interchanged, j) aromatic protons: *o* 7.8, *m* 7.4 and *p* 7.7 ppm, k) not assigned, l) 60 MHz, m) broad, * assigned by ^{1}H-^{1}H correlation spectra.

the spiro derivative **2** in almost quantitative yields, figure 1. Reaction of compound **2** with a second equivalent of phenylboronic acid, or reaction of quinic acid with two equivalents of phenylboronic acid in benzene, gave diboronic ester **3**. The structures and conformations of **2** and **3** were established from NMR data, including correlation spectra (tables 1 and 2).

Although a remarkable selectivity in the synthesis of compound **3** is observed since no traces of ester **4** were detected, figure 1, in other cases (*vide infra*), a competition between the *cis* and *trans* derivatives does exist. Proton NMR revealed that compound **3** hydrolyzes very fast in solution to afford compound **2**, which in turn hydrolyzes slowly to quinic acid. In contrast, **2** and **3** are quite stable in the solid state. The ^{11}B NMR signals of **2** and **3** appear at δ = +9 ppm (DMSO), while a similar compound, 5-dimethyl-2-phenyl-4H-1,3, 2-dioxaborolan-4-one[10] has an absorption at +29 ppm in CCl_4. This provides evidence for coordination of DMSO to the boron atoms of **2** and **3**, which exhibit a strong Lewis acid character. Treatment of quinic acid with phenylboronic acid in toluene in the presence of traces of *p*-toluenesulfonic acid gives the lactone phenylboronic ester **5** in almost quantitative yields, figure 1. Compound **5**, the boron analogue of **7**, is stable in chloroform solutions, even allowing to exchange the OH hydrogen by a deuterium atom with D_2O. In contrast, it hydrolyzes to afford lactone **6**, by addition of water to DMSO solutions, figure 1. Lactone **6** is stable in neutral water, but it hydrolyzes when traces of base or acid are present. On the other hand, quinic acid reacts with 2,2-dimethoxypropane under acidic conditions to give the isopropylidene quinide **7**, figure 2. Alkaline hydrolysis of lactone **7** gives dioxolane **8** in almost quantitative yield, figure 2. This molecule, when reacted with one equivalent of phenylboronic acid, affords a mixture of the boradioxazolidone **9** and the diquinic boronic ester **10**. The dioxolane **8** reacts with acetic anhydride in the presence of pyridine to close again the lactone ring, thus providing the isopropylidene quinide acetate **11** in almost quantitative yields, figure 2.

Acetylation of **2** and **3**, using acetic anhydride and pyridine, afforded compound **12**, which in turn provides quinic acid triacetate **13**, after hydrolysis of the boron ester figure 1. Both **12** and **13** have the anchored chair conformation found in compound **2**, as shown by the axial coupling constant between H-4 and H-5 for **12**, and from the δ ^{13}C NMR values for **13**. Under the same acetylation conditions, quinic acid (**1**) gives the tetraacetylated derivative **14**. The tertiary hydroxyl group of **5** is resistant to acetylation at room temperature under standard reaction conditions (pyridine, Ac_2O) and the molecule readily decomposes when heated in the presence of Ac_2O. Therefore, in order to transform **5** into its acetyl derivative **15**, we were forced to initial removal of the hydroxyl hydrogen using *n*-buthyllithium in tetrahydrofuran, followed by treatment with acetyl chloride (figure 1) On the other hand, the dioxolane derivatives **9** and **16** were obtained in moderate yields by reaction of **2** with 2,2-dimethoxypropane under acid conditions, figure 1. In this case, there is a clear competition for the formation of *cis* and *trans* ketals.

TABLE 2. ^{13}C and ^{11}B NMR data[a].

Compound	C-1	C-2	C-3	C-4	C-5	C-6	C-7	Isopropyl and/or Acetyl groups	^{11}B
					Chair conformation A				
1[b,c,d,*]	74.5	37.4	69.0	74.5	66.7	40.4	175.6	- - - - -	-
2[b,c,e,*]	74.0	34.5	72.0	75.5	67.5	41.4	172.9	- - - - -	8.0[c]
3[b,c,*]	76.8	35.8	75.3	81.4	68.3	40.0	179.8	- - - - -	9.0[c]
12[f,g,h]	77.1	31.9	68.1	71.9	66.7	37.0	170.2	170.0, 21.2, 20.9, 20.6	30.0[c]
13[c,f,i]	72.0	31.8	68.7	72.0	67.3	37.6	173.8	- - - - -	-
14[b,c,*]	79.0	31.0	67.9	71.1	66.4	36.2	171.5	107.1, 28.0, 25.5	-
18[c,f]	75.7	34.5	74.6	79.2	71.6	40.4	173.2	- - - - -	9.0[c]
19[c,f]	76.3	36.7	73.3	80.2	68.1	40.4	180.5	- - - - -	9.0[c]; 25.0[g]
21[c,f]	75.6	37.8	69.8	79.1	66.5	40.9	179.3	- - - - -	4.0[c,j]
22[c,f]	76.0	38.6	70.5	79.4	66.9	42.3	179.7	- - - - -	-1.2[c,k]
					Twist conformation				
5[b,g,l,*]	70.9	41.3	73.1	73.6	75.9	34.8	178.1	- - - - -	36.0[g]
6[b,c,*]	71.4	39.2	65.4	65.1	75.7	37.2	177.5	- - - - -	-
15[f,g,m]	72.1	38.4	72.6	73.9	75.2	31.9	178.0	169.3, 20.9	36.0[g]
					Boat conformation A				
7[b,c,d,*]	71.4	37.9	71.4	72.0	75.6	34.2	178.9	109.7, 26.9, 24.2	-
11[b,g,*]	75.9	35.0	70.6	71.8	75.1	29.9	173.3	109.2, 26.8, 24.3, 169.1, 20.9	-
					Boat conformation B				
8[b,c,*]	71.9	37.3	72.7	78.4	66.6	38.1	180.6	107.1, 28.0, 25.5	-
9[b,c]	76.5	35.3	76.1 or	80.5 or	67.3 or	-	180.8 or	107.4, 26.2, 28.5 or or	-
10[b,c]	73.5	36.2	76.7	80.7	67.4	-	181.3	107.3, 26.2, 28.3	-
17[f,g,d]	77.2	35.5	71.6	80.3	67.3	36.5	177.4	108.7, 91.3, 27.3, 25.2, 30.5, 30.3	-

a) Conformations are as indicated in table 1, b) 300 MHz, c) DMSO-d6, d) reference 4, e) aromatic carbons: *o* 127.5, *m* 133.8 and *p* 130.9 ppm, f) 90 MHz, g) $CDCl_3$, h) aromatic carbons: *o* 127.5, *m* 133.7 and *p* 129.6 ppm, i) compound **13** was identified only by ^{13}C NMR, j) BF_2^+ species, k) BF_4^- species, l) aromatic carbons: *i* 132.1, *o* 128.0, *m* 135.0 and *p* 132.2 ppm, m) aromatic carbons: *i* 133.8, *o* 127.8, *m* 135.0 and *p* 138.2 ppm, * assigned by ^{13}C-^{1}H correlation spectra.

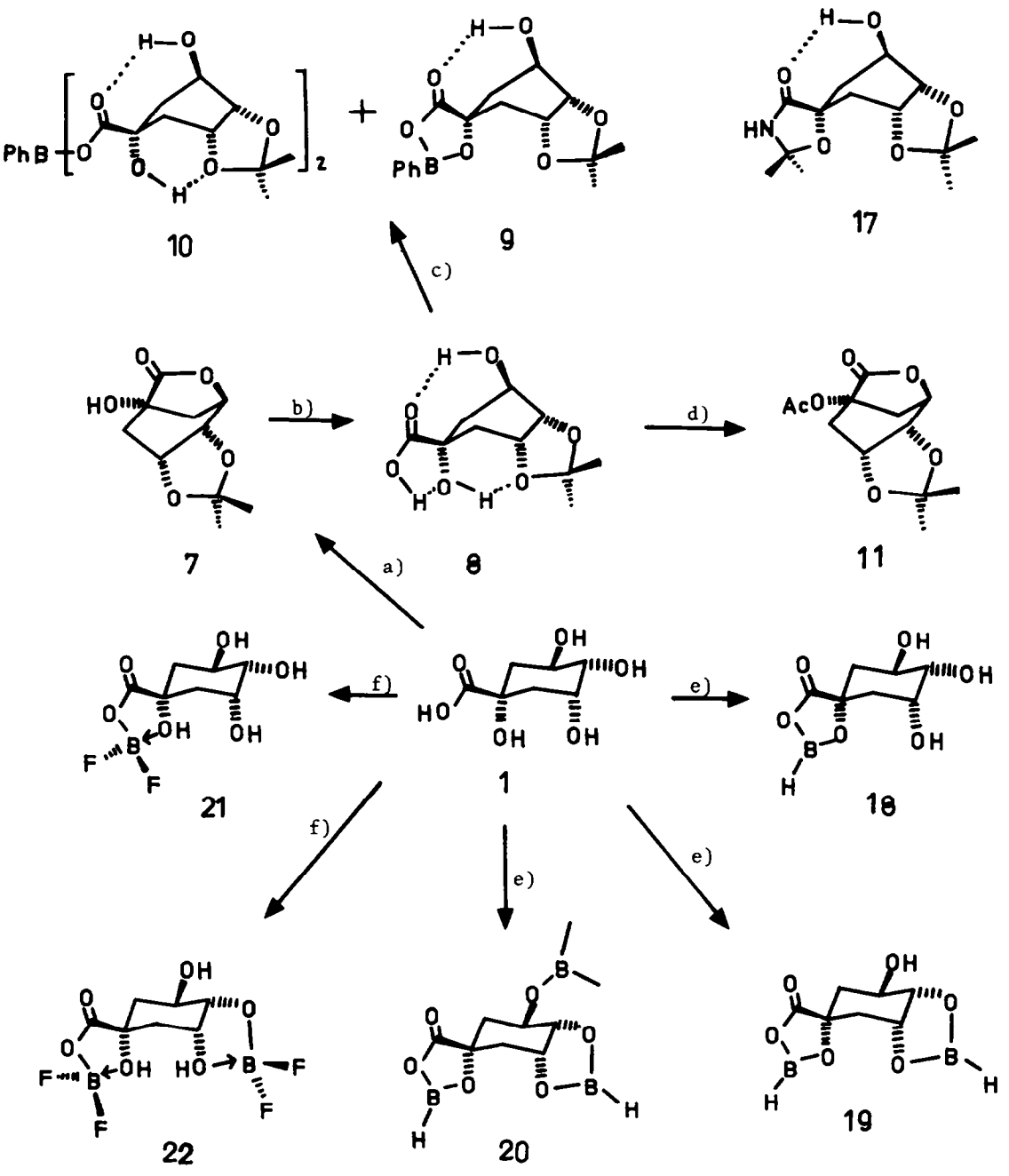


Figure 2. a) 2,2-dimethoxy propanel/H^+; b) NaOH/EtOH; c) $PhB(OH)_2$; d) Ac_2O/Py; e) BH_3-THF; f) BF_3-OEt.

A very important fact about the new compounds is to know their conformation, which appears anchored and distorted by the presence of five membered rings in all cases. The conformation can be deduced from the proton-proton coupling constants, dihedral angle calculations[11] (table 3) and carefull examination of Dreiding models. NMR and structural data were compared with that of a recently reported[8] series of quinic acid derivatives, similar kind of conformations were found in boron compounds.

Evaluation of the data of compounds **2** and **3** shows that they are in the chair conformation depicted in figure 1. Compound **2** has an axial coupling constant (J = 9.5 Hz, 174°) between H-4/H-5 and normal angles between the other protons, except for H2α/H3 (J = 3.3 Hz, 64°) thus suggesting a deformation of the chair due to a repulsion between the hydroxyl group at C-3 and one oxygen of the dioxaborolane group. Compound **3** shows large coupling constants between H-4 and H-5 (J = 7.0 Hz, 157°) and H-5 and H-6β (J = 11.6 Hz, 186°). Here the dioxolane ring junction causes a deformation that results in a very small dihedral angle (J = 7.3 Hz 12°) between H-3/H-4, although it is interesting to note that the analogue **17** has a boat conformation[8]. The conformational differences between both molecules (**3** and **17**) can be attributed to longer boron-oxygen bonds as compared to carbon-oxygen bonds. The free quinide **6** and compound **5** were found to have the twist conformation depicted in figure 1 as deduced from their small dihedral angles. Two long-range W-coupling constant were observed for **5** H-2β and H-6β and H-4 and H-6β (J = 2.4 and 1.0 Hz) while **6** has only one between H-2β and H-6β. The twist conformation is attributed to the tension of the lactone ring.

Compounds **7** and **11** show a distorted boat conformation. This is attributed to the tension created by the lactone ring and five member ring junction. The boat conformation can be deduced from the coupling constants between H-2α and H-3 (for **7** J = 3.0 Hz, 67° and for **11** J = 3.1 Hz, 66°) and between H-3 and H-2β (for **7** J = 7.0 Hz, 25° and for **11** J = 7.3 Hz, 23°). Two long-range W-coupling constants were observed between the equatorial protons H-2β and H-6β and between H-4 and H-6β for **11** (J = 2.4 and 1.4 Hz), while in the case of **7** only one is detected (J = 2 Hz) between H-2β and H-6β.

A different boat conformation is evident for compounds **8** and **17**, as deduced again from the ^{1}H-NMR data, see table 1. Here the anchored boat conformation is attributed to the tension originated by the dioxolane ring junction and by hydrogen bondings, one in compound **17** between the hydroxy group at C-5 and the carbonyl group and three for compound **8**, as illustrated in figure 2. The calculated dihedral angles based on vicinal hydrogen-hydrogen coupling constants are given in table 3.

Borane Derivatives.

Reaction of quinic acid with one equivalent of borane-THF affords the spiro boronic derivative **18**, figure 2, which shows in the ^{11}B NMR spectrum a doublet (δ = +25 ppm, J(B-H) = 170 Hz) when measured in CDCl3, and a broad signal at δ = +10 ppm when measured

TABLE 3. Coupling constants (Hz) and calculated dihedral angles based on vicinal hydrogen coupling constants (^3J)[a].

Compound	H-2β/H-3	H-2α/3	H-3/H-4	H-4/H-5	H-5/H-6β	H-5/H6α	H-2$_{gem}$	H-6$_{gem}$	H-2/H-6	H-4/H-6β
					Chair conformation					
1	3.3(49°)	3.3(64°)	2.2(61°)	7.8(164°)	7.8(148°)	4.0(44°)	13.0			
2	b	3.3(64°)	1.8(66°)	9.5(174°)	10.0(162°)	5.0(38°)	14.0	13.0	3.0[c]	
3	4.7(40°)	4.7(54°)	7.3(12°)	7.0(157°)	11.6(186°)	4.7(40°)	12.0	12.6		
12	3.3(49°)	3.3(64°)	3.3(52°)	10.0(178°)	10.0(162°)	4.7(40°)	15.0	13.0		
14	3.2(50°)	3.2(65°)	3.6(49°)	10.2(180°)	10.4(165°)	3.7(48°)	15.0	14.4		
					Twist conformation					
5	8.6(12°)	4.3(57°)	7.5(6°)	3.0(53°)	5.7(48°)	b	14.6	12.2	2.4[e]	1.0
6[d]	6.5(30°)	b	4.6(41°)	4.6(55°)	5.9(47°)	b	11.5	11.2	2.7[e]	
					Boat conformation A					
7	7.0(25°)	3.0(67°)	6.5(23°)	2.5(58°)	6.0(46°)	b	15.0	11.0	2.0[e]	
11	7.3(23°)	3.1(66°)	6.5(23°)	2.5(58°)	6.5(42°)	b	14.6	11.4	2.4[e]	1.4
					Boat conformation B					
8	6.4(29°)	4.9(53°)	4.2(43°)	5.9(44°)	5.3(50°)	5.3(36°)	14.1			
17	4.8(38°)	5.3(51°)	5.3(34°)	3.5(63°)	3.5(48°)	3.5(49°)	15.2			

a) Conformations are as indicated in table 1. Accuracy of calculated dihedral angles is ~3 degrees, b) Not resolved (smaller than 1 Hz, 80°), c) ^4J(H-2α/H-6α), d) H-3/OH J = 6.9 Hz; H-4/OH J = 4.4 Hz, e) ^4J(H-2β/H-6β).

in DMSO. Compound **18** has a very similar ^{13}C NMR spectrum to that of compound **2**. The ^{1}H NMR spectrum of **18** shows very broad signals that preclude its detailed evaluation. Quinic acid (1) affords compound **19** (δ ^{11}B NMR as a broad signal at +10 ppm in DMSO), when treated with two equivalents of borane-THF, while with an excess of borane, the reaction mixture shows an additional signal for a boric function at +18 ppm, in the ^{11}B NMR spectrum, which is attributed to **20**. Compounds **19** and **20** show similar ^{13}C NMR chemical shift to compound 3, see table 2. Evaluation of asymmetric reduction reactions of compounds **18-20** is under study in our laboratory.

Trifluoroborane Derivatives.

The reaction of quinic acid (1) with BF_3-etherate is less selective, since an equimolar ratio of reagents affords a mixture of **21** and **22**, while an excess of boron trifluoride only affords **22**, figure 2. The most acidic protons of **1** react with BF_3 to produce HF which is trapped as pyridinium salt. Structure **22** was found to be similar to that of compound 3, as deduced by comparison of their ^{13}C spectra, table 2. In **22** C-3 appears at lower fields than C-4 when compared with quinic acid, indicanting that the hydrogen of the C-3-O<u>H</u> reacted with the fluoride. The structure is further evident from the data of the ^{11}B NMR spectrum which shows two signals, one as a broad signal at δ = +4 ppm for a BF_2^+ species and the other as a sharp signal at -1.2 ppm for a BF_4^- species.

Conclusions.

Boron compounds are useful selective protecting agents of quinic acid (1) since minor modifications of reaction conditions produce different products. These boron derivatives are stable enough to be isolated and characterized. They also allow to increase the solubility of quinic acid in nonpolar solvents. The preparation of the free quinide **6**, obtained in almost quantitative yields from its boronic ester **5** is noteworthy. In general, the new boron derivatives of quinic acid, show similar conformations to those of dioxolane derivatives, however, the use of phenylboronic acid appears to be an optimal protecting route since cleaner reactions and higher yields are obtained.

Experimental.

All melting points are uncorrected. IR spectra were determined on a Nicolet MX-1 FT spectrometer. Mass spectral measurements were done using a Hewlett Packard 5985-A instrument. ^{1}H NMR and ^{13}C NMR spectra were recorded on Varian XL-300GS (300 MHz) or on Jeol FX-90 (90 MHz) spectrometers. Chemical shifts are reported in parts per million relative to Me_4Si (δ). ^{11}B NMR spectra were obtained on a Jeol FX-90 using BF_3-etherate as the external standard. (1R,3R,4R,5R) - (-) - Quinic acid [1,3,4,5-tetrahydroxycyclohexane

carboxylic acid] was purchased from Aldrich.

(1R,3R,4R,5R)-1-Carboxyl-1,7-*O,O'*-phenylboronate-1,3,4,5-tetrahydroxycyclohexane, 2.

A solution of quinic acid (1 g, 5.2 mmol) and phenylboronic acid (0.6 g, 5.2 mmol) in 150 mL of dry benzene was refluxed for 24 h in a flask provided with a Dean-Stark trap. The solvent was evaporated and a white solid (1.43 g, 99 % yield) with m.p. 145-7°C was obtained. IR (KBr) 3049(OH), 1720(COO), 1602(Ar), 1439(B-O) cm^{-1}. MS, m/e (relative intensity, %) 277(M^+-1, 12), 261(16), 146(88), 105(89).

(1R,3R,4S,5R)-1-Carboxyl-1,7:3,4-*O,O'*-*bis*-phenylboronate-1,3,4,5-tetrahydroxycyclohexane,3

The title compound was obtained using the procedure described for the preparation of compound 2, but using one equivalent of quinic acid (1 g, 5.2 mmol) and two equivalents of phenylboronic acid (1.3 g, 10.4 mmol). A white solid was obtained with m.p. 68-70°C. The yield was quantitative (1.89 g, 100%). IR (KBr) 3424(OH), 1780(COO), 1602(Ar), 1327(B-O) cm^{-1}. MS, m/e (relative intensity %) 364(M^+, 17), 346(10), 159(32), 146(100), 105(54), 77(24).

(1R,3R,4S,5R)-3,4-*O,O'*-Phenylboronate quinide, 5.

Compound 5 was obtained using catalytic amounts of p-toluensulfonic acid, quinic acid (1 g, 5.2 mmol) and phenylboronic acid (0.6 g, 5.2 mmol) following the procedure described for the preparation of 2. A white solid with m.p. 113-115°C was obtained in almost quantitative yield (1.34 g, 99%). IR (KBr) 3418(OH), 1784(COO), 1602(Ar), 1331(B-O) cm^{-1}. MS, m/e (relative intensity, %) 260(M^+, 12), 216(10), 146(100), 105(33), 77(22).

(1S,3R,4R,5R)-Quinide, 6.

Compound 5 (1 g, 5.7 mmol) was dissolved in 30 mL of water and the phenylboronic acid was extracted with hexane. Compound 6 was obtained by evaporation of the water solution in vacuo without heating. A white solid was obtained (m.p. 132-4°C) in 98 % of yield (0.97 g). IR (KBr) 3415 (OH), 1783 (COO) cm^{-1}. MS, m/e (relative intensity, %) 174 (M^+,1), 156 (2), 147 (5), 112 (27), 61 (37), 60 (100), 43 (80).

(1R,3R,4S,5R)-1-Carboxyl-3,4-*O,O'*-isopropylidene-1,3,4,5-tetrahydroxycyclohexane, 8.

A solution containing 1 g (4.7 mmol) of compound 7[8] in ethanol (20 mL) was treated with one equivalent (0.19 g, 4.7 mmol) of NaOH in ethanol (10 mL) and stirred 3 h at room temperature. The reaction mixture was neutralized with dilute HCl and the water was evaporated in vacuo. The residue was dissolved in hot acetone and filtered. The acetone was evaporated and a hygroscopic white solid obtained (m.p. 236-238°C) in 97 % (1.05 g) yield. IR (KBr) 3450(OH), 1605(COO). MS, m/e (relative intensity, %) 232(M^+, 0), 199(30), 43(100).

(1R,3R,4S,5R)-1-Carboxyl-3,4-*O,O'*-isopropylidene-1,7-*O'',O'''*-phenylboronate-1,3,4,5-tetrahydroxycyclohexane, 9 and *Bis*(-7-(1R,3R,4S,5R)-1-carboxyl-3,4-*O,O'*-isopropylidene--1,3,4,5-tetrahydroxycyclohexane)phenylboronate, 10.

Compound 8 (1 g, 3.14 mmol) was dissolved in dry benzene (200 mL) and one equivalent (0.38 g, 3.14 mmol) of phenylboronic acid was added. The reaction mixture was refluxed with a Dean Stark trap for 12 h and the solvent evaporated. This afforded a mixture of 9 and 10

which was not separated, but characterized by spectral means.

(1R,3R,4R,5R)-3,4-*O,O'*-isopropylidene quinide acetate, 11.

Compound **8** (1 g, 3.14 mmol) was dissolved in dry pyridine (10 mL) and treated with acetic anhydride (10 mL). The mixture was stirred overnight at room temperature and the volatiles were evaporated in vacuo. The solid residue was extracted with CH_2Cl_2 and the insoluble materials removed by filtration. After evaporation of the solvent, a crystalline solid (m.p. 80-2°C) was obtained in 50 % of yield (0.43 g). IR (KBr) 2992 and 2933(C-H), 1796 and 1751 (COO) cm^{-1}. MS, m/e (relative intensity, %) 256(M^+, 1), 241(100), 95(44), 43(90).

(1R,3R,4R,5R)-1-Carboxyl-1,7-*O,O'*-phenylboronate-1,3,4,5-tetrahydroxycyclohexane triacetate, 12.

The title compound can be prepared from **2** or from **3**. A solution containing 1 g (3.6 mmol of **2** or 2.7 mmol of **3**) in 4 mL of dry pyridine was treated with 4 mL of acetic anhydride and stirred overnight at room temperature. The reaction mixtures were evaporated in vacuo. In each case the residue was a yellow solid, m.p. 54-55°C, obtained in 99 % yield (1.43 and 1.07 g, respectively). IR (KBr) 1742(COO), 1602(Ar), 1300(B-O) cm^{-1}. MS, m/e (relative intensity, %) 346(10), 312(20), 43(100), 77(8).

(1R,3R,4R,5R)-(-)-Quinic acid tetraacetate, 14.

Acetylation of quinic acid (0.5 g, 2.6 mmol) following the procedure described for the preparation of compound **12**, afforded the tetracetate **14** (0.92 g, 98%), m.p. 93-4°C. IR (KBr) 1741(COO) cm^{-1}. MS, m/e (relative intensity, %) 360(M^+, 1), 240(2), 198(9), 138(14), 79(48), 43(100).

(1R,3R,4R,5R)-3,4-*O,O'*-Phenylboronate quinide acetate, 15.

To a stirred ice-cooled solution of compound **5** (0.33 g, 1.27 mmol) in 25 mL of dry THF was added an equivalent of buthyllithium (1.27 mmol). After 2 h an equivalent (0.09 mL, 1.27 mmol) of acetyl chloride was added and the stirring continued during 5 h. The solution was filtered and evaporated to give a white solid. The residue was extracted with methylene chloride to afford 0.19 g (50% yield) of **15**, m.p. 124-126°C. IR (KBr) 1793 and 1773(COO), 1602(Ar), 1377(B-O) cm^{-1}. MS, m/e (relative intensity, %) 302 (M^+, 4), 260(8), 146(100), 105(24), 77(10), 43(24).

(1R,3R,4R,5R)-1-Carboxyl-1,7-*O,O'*-hydrideboronate-1,3,4,5-tetrahydroxycyclohexane, 18.

To a stirred suspension of quinic acid (1 g, 5.2 mmol) in 50 mL of dry THF was added a 2 M (5.2 mmol) solution of borane-THF. After 5 min the solvent was evaporated. The white solid that remained decomposes at 132-134°C (1.05 g, 100%) . IR (KBr) 3390(OH), 2500(B-H), 1734(COO), 1428(B-O) cm^{-1}.

(1R,3R,4S,5R)-1-Carboxyl-1,7:3,4-*O,O',O'',O'''-bis*-hydrideboronate-1,3,4,5-tetrahydroxy cyclohexane, 19.

The same procedure used for the preparation of compound **18** was followed, but using two equivalents of the borane-THF solution (10.4 mmol). The reaction gave a solid that decomposes at 280°C (1.09 g, 99%). IR (KBr) 3331(OH), 2375(B-H), 1718(COO), 1468(B-O) cm^{-1}.

Treatment of (-)-quinic acid with Et_2O-BF_3.

To a solution containing 1 g (5.2 mmol) of quinic acid in 50 mL of dry THF was added 0.64 ml (5.2 mmol) of boron trifluoride etherate and 3.4 ml (10.4 mml) of dry pyridine. The reaction was stirred for two days at room temperature. The volatiles were evaporated and a white solid remained. The ^{13}C NMR showed the presence of three compounds that were identified as recovered **1** mixed with **21** and **22**.

(1R,3R,4S,5R)-1-Carboxyl-1,7:3,4-*O,O',O'',O'''-bis*-difluorideboronium-1,3,4,5-tetrahydroxy cyclohexane, *bis*-tetrafluoride 22.

The title compound was prepared following the procedure described above, but using 2.5 equivalents (13.0 mmol, 1.6 ml) of boron trifluoride etherate and 2.1 ml (26.0 mmol) of pyridine, compound **22** was obtained as a white solid which decomposes at 154-156°C (1.67 g, 99%). IR (KBr) 3444(OH), 1730(COO), 1112(B-F) cm^{-1}.

Acknowledgments.

We are grateful to Conacyt México for financial support and for a scholarship to C. P. T. And to Ing. L. Velasco and F. del Rio (UNAM) for mass spectra.

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