Boronic Acids Mediate Glycoside Transport through a Liquid Organic Membrane via Reversible Formation of Trigonal Boronate Esters

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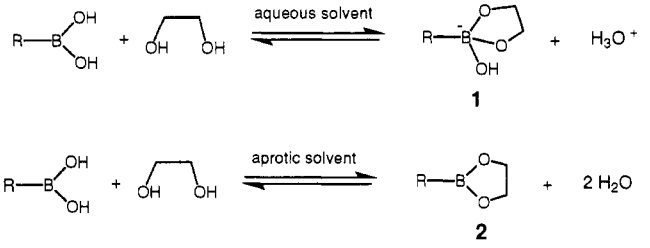
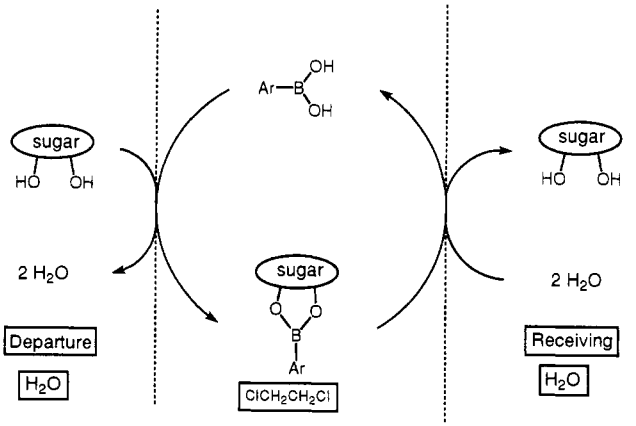
The ability of phenylboronic acid and 3-(1-adamantylcarboxamido)phenylboronic acid to mediate the transport of *p*-nitrophenyl β-D-glucopyranoside (glucoside), *p*-nitrophenyl β-D-galactopyranoside (galactoside), *p*-nitrophenyl β-D-mannopyranoside (mannoside), and *p*-nitrophenyl β-D-xylopyranoside (xyloside) through a liquid dichloroethane membrane in the presence and absence of trioctylmethylammonium chloride was determined. In the absence of the lipophilic ammonium cation, the boronic acids transported significant amounts of galactoside, suggesting that transport was mediated by reversible formation of a trigonal boronate ester. Extraction and transport experiments as a function of pH provided confirming evidence for this transport mechanism. The apparent order of diol selectivity for the trigonal boronate transport pathway was observed to be *cis*-α,γ-diol > *cis*-α,β-diol ≈ *trans*-α,γ-diol ≫ *trans*-α,β-diol. Uphill transport of galactoside was achieved by including boric acid in the receiving phase and lipophilic boronic acid in the organic layer, representing a functionally biomimetic example of active transport driven by group translocation.

The molecular recognition of saccharides is currently an active area of biological and chemical research. Recently there have been a number of reports of relatively small, artificial receptors designed to bind saccharides via noncovalent forces.[1] Using a slightly different approach, our research group,[2] along with others, has chosen to utilize the well-known covalent complexation of saccharides with boronic acids as a basis for developing molecular receptors for saccharide transport[3] and chemosensing.[4] In aqueous solution, saccharide compounds combine reversibly with boronic acids to form anionic tetrahedral boronate adducts, **1**, as the predominant complex. With arylboronic acids, significant amounts of **1** are usually observed at neutral pH.[5] In the presence of tetralkylammonium cations, lipophilic ion pairs can form which allow the saccharides to be extracted from aqueous solution and transported through liquid organic membranes.[2,3] All the transport systems reported thus far have operated via this tetrahedral boronate pathway. The alternative complexation of boronic acids with saccharides to form neutral trigonal boronate esters, **2**, is generally considered unfavorable in aqueous environments. Nonetheless, we report here that under certain conditions boronic acids can mediate transport of saccharide derivatives through a liquid organic membrane via the reversible trigonal boronate pathway described in Scheme 1.



Scheme 1



Results and Discussion

We have examined the ability of phenylboronic acid, **3**, and the more lipophilic 3-(1-adamantylcarboxamido)-phenylboronic acid, **4**, to mediate the transport of *p*-nitrophenyl β-D-glucopyranoside (glucoside), *p*-nitrophenyl β-D-galactopyranoside (galactoside), *p*-nitrophenyl β-D-mannopyranoside (mannoside), and *p*-nitrophenyl β-D-xylopyranoside (xyloside) through a liquid dichloroethane membrane, in the presence and absence of trioctylmethyl-

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(2) (a) Paugam, M.-F.; Smith, B. D. *Tetrahedron Lett.* **1993**, *34*, 3723-3726. (b) Paugam, M.-F.; Morin, G. T.; Smith, B. D. *Tetrahedron Lett.* **1993**, *34*, 7841-7844.

(3) (a) Shinbo, T.; Nishimura, K.; Yamaguchi, T.; Sugiura, M. *J. Chem. Soc., Chem. Commun.* **1986**, 349-351. (b) Grotjohn, B. F.; Czarnik, A. W. *Tetrahedron Lett.* **1989**, *30*, 2325-2328. Mohler, L. K.; Czarnik, A. W. *J. Am. Chem. Soc.* **1993**, *115*, 2998-2999.

(4) (a) Murakami, H.; Nagasaki, T.; Hamachi, I.; Shinkai, S. *Tetrahedron Lett.* **1993**, *34*, 6273-6276 and references cited therein. (b) Yoon, J.; Czarnik, A. W. *J. Am. Chem. Soc.* **1992**, *114*, 5874-75. (c) Nagai, Y.; Kobayashi, K.; Toi, H.; Aoyama, Y. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 2965-2971.

(5) Pizer, R.; Tihal, C. *Inorg. Chem.* **1992**, *31*, 3243-3247.

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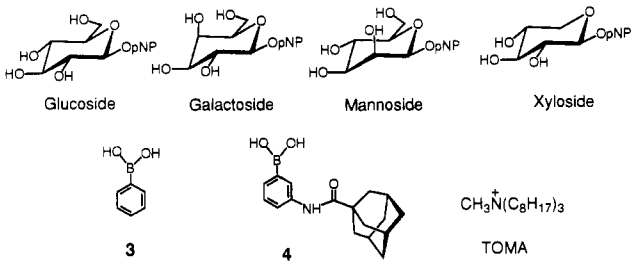
ammonium (TOMA) chloride. The transport rates were determined by standard U tube experiments where an aqueous departure phase is separated from an aqueous receiving phase by a dichloroethane layer.[6] The downhill (passive diffusion) transport experiments began with glycoside only in the departure phase, whereas the uphill (active) transport experiments began with equal amounts of glycoside in each aqueous phase.



It is worth emphasizing why we chose to study the transport of glycosides rather than reducing sugars which is perhaps a more practical research goal. In neutral aqueous solution, reducing sugars exist as an equilibrium mixture of pyranose, furanose, and open-chain isomers (the cyclic structures, of course, have the added possibility of epimerization at the anomeric position). In acidic or alkaline solutions, aldose–ketose isomerization reactions are known to occur.[7] Complexation with borate and boronates has been shown to bias all of these isomeric interconversions; the base-catalyzed aldose–ketose pseudoequilibrium is moved toward the ketose isomer,[8-10] hexoses and pentoses form borate complexes only in their furanose forms,[11] and mutarotation to favor a *cis*-1,2-diol is usually observed.[11,12] Thus, any study on the transport of reducing sugars is significantly complicated by the uncertainty of the structure(s) of the transported species. In contrast, *p*-nitrophenyl glycosides are locked in a single configuration and the structures of their corresponding boronate complexes can be confidently predicted from well-established precedence.[8-13] As well, the *p*-nitrophenyl glycoside chromophore allowed transport rates to be easily determined via UV absorption (λ_{max} 302 nm, ϵ = 9800 M^{-1} cm^{-1}).

Table 1 shows the rates of downhill glycoside transport for various carrier combinations. For each downhill experiment, the carrier combination was preequilibrated between the three layers before the glycoside was introduced into the departure phase. After a short induction period, the initial rates of glycoside appearance in the receiving phase were determined. The glycoside transport rates determined at pH 7.4 in the absence of any carrier were defined as the rates of background diffusion (entry 1). In the presence of a 3–TOMA admixture, the transport of glucoside, galactoside, and mannoside were enhanced by factors of 10, 18, and 18, respectively (entry 4). On the basis of the previous studies, these transport enhancements can be attributed to the formation of a lipophilic ion pair comprised of anionic tetrahedral boronate–glycoside adduct and TOMA.[2,3] Xyloside with one less hydroxyl is more lipophilic than the other glycosides examined and so displayed a higher rate of background diffusion (entry 1). No carrier system was found which significantly enhanced its downhill transport. The stability of a tetrahedral boronate–diol adduct is known to be strongly dependent on the structure of the diol component, and the usual order of stability for cyclic diols is *cis*-α,β-diol > *cis*-α,γ-diol > *trans*-α,γ-diol ≫ *trans*-α,β-diol.[8-13] Figure 1 shows the most likely tetrahedral boronate–glycoside structures predicted from this correlation. Xyloside with only *trans*-α,β-diols is predicted to not form a boronate complex.[14]

The observation that **3** alone was unable to significantly facilitate glucoside and mannoside transport (entry 3) is in agreement with the assignment of a tetrahedral boronate–TOMA ion pair pathway as the major transport mechanism for these glycosides. We were interested to find, however, that **3** alone enhanced galactoside transport by a factor of 12 (entry 3). This result suggested that, depending on the experimental conditions, galactoside can be transported by boronic acids via two different pathways.

Table 1. Rates of Downhill *p*-Nitrophenyl β-D-Glycoside Transport

		rate[a] (rel rate in parentheses) ● 15%			
entry	carrier[b]	glucoside	galactoside	mannoside	xyloside
1	none	2.5 (1.0)	3.5 (1.0)	2.5 (1.0)	44 (1.0)
2	TOMA	3.0 (1.2)	6.0 (1.6)	6.5 (2.4)	79 (1.8)
3	**3**	4.0 (1.6)	46 (12)	6.0 (2.1)	24 (0.5)
4	**3**-TOMA	25 (10)	66 (18)	48 (18)	75 (1.7)
5	**4**	8.0 (3.2)	55 (15)	9.5 (3.5)	–
6	**4**-TOMA	42 (17)	58 (16)	45 (17)	–

[a] Rate (10^{-8} M min^{-1}) that glycoside initially appeared in the receiving phase. [b] Aqueous phases contained sodium phosphate, 10 mM, pH 7.4.

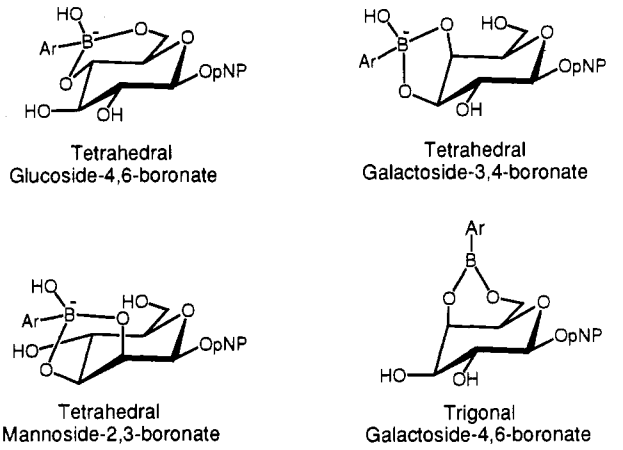


Figure 1. Most likely tetrahedral and trigonal boronate structures of transported glycosides.

(6) (a) *Liquid Membranes: Chemical Applications*; Araki, T., Tsukube, H., Eds.; CRC Press: Boca Raton, 1990. (b) Fyles, T. M. In *Inclusion Aspects of Membrane Chemistry*; Osa, T., Atwood, J. L., Eds.; Kluwer: Boston, 1991; Chapter 2.

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(9) (a) Acree, T. E. *Adv. Chem. Ser.* **1973**, *117*, 208–219. (b) Foster, A. B. *Adv. Carbohydr. Chem.* **1957**, *12*, 81–115.

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(13) (a) van Duin, M.; Peters, J. A.; Kieboom, A. P. G.; Bekkum, H. V. *Tetrahedron* **1985**, *41*, 3411–3421. van Duin, M.; Peters, J. A.; Kieboom, A. P. G.; Bekkum, H. V. *Tetrahedron* **1984**, *40*, 2901–2911. (b) Lorand, J. P.; Edwards, J. O. *J. Org. Chem.* **1959**, *24*, 769–774.

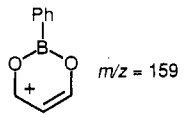
(14) β-Xylosides are known to form *cis*-2,4-boronates; however, these structures force all the ring substituents to be axially oriented.[8] Under the conditions of the transport it is not surprising such a strained complex is not detected.

Table 2. Extraction of *p*-Nitrophenyl β-D-Glycopyranosides into Dichloroethane[a]

entry	carrier	pH[b]	% glycoside extracted		
			glucoside	galactoside	mannoside
7	3	water	0.2	2.2	0.2
8	3	7.4	0.1	2.5	0.2
9	3-TOMA	7.4	2.0	6.6	3.4
10	4	7.4	0.3	6.3	0.8
11	4-TOMA	7.4	2.6	8.6	5.2
12	3	12.4	0.1	0.1	0.2
13	3-TOMA	12.4	21	27	24

[a] Starting solutions were 1.36 mM glycoside and 1 mM carrier, reproducibility ± 10%. [b] Buffer was 10 mM sodium phosphate.

One pathway involves a tetrahedral boronate–TOMA ion pair and the other a neutral trigonal boronate formed by reversible condensation of the galactoside with the boronic acid (Scheme 1). Further evidence in favor of this rationalization included the following observations: (i) **3** was able to extract galactoside from neutral aqueous solution into dichloroethane in measurable amounts (Table 2, entries 7 and 8). The more lipophilic **4** not only increased galactoside extraction and transport but was also able to extract and slightly enhance glucoside and mannoside transport (entries 5 and 10).[15] NMR and mass spectral studies of the extracted galactoside–boronate complexes were strongly in favor of a trigonal, *cis*-4:6-boronate (Figure 1). The EI mass spectrum of the galactoside–**3** extract showed a base line fragment at $m/z = 159$, assigned to the six-membered boronate fragment **5**. Fragments expected



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for a five-membered boronate were not observed.[8,16] The galactoside–**4** complex was extracted in sufficient amount to allow characterization by NMR. The ^1H NMR showed a major and a minor complex. ^{13}C NMR proved the major complex to be the cis-4:6 adduct.[17] (ii) Extraction of galactoside with 3–TOMA was more effective than **3** alone (entry 9 vs 8), particularly at alkaline pH where tetrahedral boronate is favored (entry 12 vs 13, pK_a of **3** is 8.86, while the "apparent pK_a" for the equilibrium to form its corresponding boronate **1** is somewhat more acidic depending on diol structure[4b]). (iii) The pH profile of galactoside transport mediated by **3** is shown in Figure 2. Transport was observed to be a maximum at neutral pH, where apparently the extraction and subsequent transport of the trigonal galactoside boronate adduct is optimal.[18]

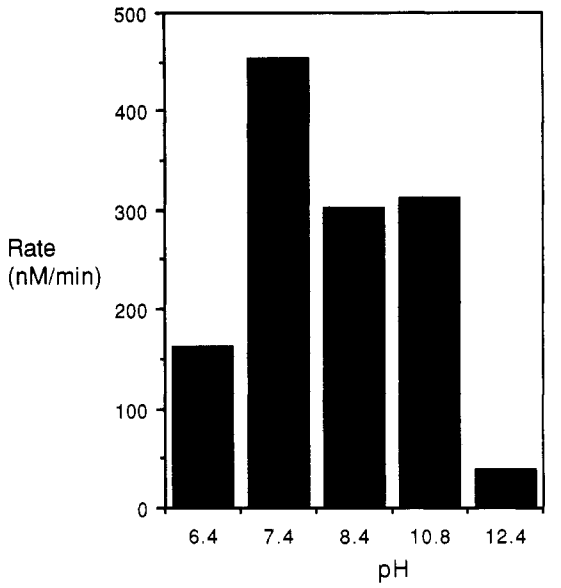

Figure 2. pH profile of downhill galactoside transported by **3**, 10 mM sodium phosphate.

Table 3. Rates of Uphill *p*-Nitrophenyl β-D-Glycopyranoside Transport

entry	carrier[b]	rate[a] (nM min^{-1})	
		glucoside	galactoside
14	3-TOMA	+100	+100
15	3	<+1	−11

[a] Rate that glycoside concentration initially changed in the receiving phase. [b] Departure phase was 10 mM sodium phosphate, pH 12.4. Receiving phase was 10 mM sodium phosphate, pH 7.4.

At higher pH, the amount of trigonal boronate is diminished as it is converted into tetrahedral boronate, which in the absence of TOMA is not transported. At pH values below neutral, 3–galactoside complexation of any type, trigonal or tetrahedral, becomes unfavored.[5] (iv) With 3–TOMA as the transport system, strong uphill transport in the direction of an alkaline to neutral pH gradient was achieved for glucoside and galactoside (Table 3, entry 14), in agreement with the original observations of Shinbo concerning the effects of pH on uphill transport mediated by a tetrahedral boronate.[3a] With **3** alone as the carrier, no transport was observed for glucoside, whereas weak uphill transport in the direction of neutral to alkaline pH was observed for galactoside (entry 15). This latter result is essentially an experimental artifact. The equilibrium equations shown in Scheme 1 are pH independent; thus, uphill transport driven by a pH gradient is not predicted. However, as noted in point iii, initial trigonal transport from a neutral aqueous phase is faster than transport from a basic aqueous phase because of the differences in the amount of available trigonal carrier. Since the uphill experiment was started by a sudden increase of the receiving phase pH from neutral to basic, the system responded with a net movement of trigonal carrier (some of it complexed with galactoside) toward the basic phase.

Transport mediated by the reversible formation of trigonal boronates has hitherto not been reported. Trigonal boronates are usually hydrolytically unstable and thus a minor presence in an aqueous environment; however, recent work by Shinkai on the extraction of hexoses with lipophilic arylboronic acids has produced examples where

(15) In anhydrous conditions, *trans*-4,6-glucopyranoside and *cis*-2,3- and *trans*-4,6-mannopyranoside boronates are the trigonal arylboronate esters formed.[8]

(16) Reinhold, V. N.; Wirtz-Peitz, F.; Biemann, K. *Carbohydr. Res.* **1974**, *37*, 203–221.

(17) It is possible that the enhanced ability of galactoside to form trigonal boronate esters is not due entirely to the extra stability of its cis-4,6 adduct. The galactoside contains a *cis*-3,4,6-triol which, in principle, allows interconversion between 4,6 and 3,4 adducts without the boronate actually dissociating from the galactoside. This adds a favorable entropic contribution to galactoside–boronate binding which is unavailable to the other glycosides examined.

(18) This statement presumes the rate-determining step for transport is diffusion from the departure phase into the organic layer. In this situation, transport rates increase with extraction as long as the kinetics of dissociation are not rate determining,[6] a point that will be elaborated in a future paper. Morin, G. T.; Hughes, M. P.; Paugam, M.-F.; Smith, B. D. Manuscript in preparation.

the extracted species are trigonal boronates.[19] Literature evidence in favor of trigonal boronates existing in small amounts in aqueous solution comes from complexation studies of polyols with boric acid, where the analogous trigonal borate esters have been identified via NMR methods.[20] Our observation that the extracted galactoside–boronate complexes are the cyclic six-membered, trigonal cis-4,6 monoadducts is in agreement with literature precedence that they are more stable than the 5-membered cis-3,4 analogues.[8,17,21] In addition, the fact that mannoside was hardly transported by **3** is evidence against a 5-membered cis-α,β adduct forming in large amounts under these transport conditions.[15] It has been previously reported that ribonucleosides are also not transported through similar liquid organic membranes by **3** alone.[2a,3b]

As a final note, one of the goals of our research is to develop artificial, but functionally biomimetic, uphill saccharide transport systems. Besides the pH-driven strategy described above, we have previously demonstrated uphill saccharide transport systems mediated by a boronic acid and driven by an anion gradient[2a] and a cation gradient.[2b] An alternative biotic method of concentrating ions and small molecules into cells is the strategy of group translocation. A well-known example is the phosphoenol pyruvate-dependent phosphotransferase system (PTS) where transported sugars are phosphorylated on the intracellular face of bacterial membranes, producing anionic derivatives that have little propensity for back-transport.[22] The use of group translocation (also known as reaction pumping) to achieve uphill transport in abiotic systems has been reported by Fyles who utilized a combination of lipophilic and hydrophilic ionophores to affect uphill transport of metal cations.[23,24] We reasoned that a combination of lipophilic and hydrophilic boron acids could be used in a similar manner. Accordingly, we transformed the transport system described in Scheme 1 into a method of driving galactoside transport uphill via group translocation. The experiment began with equal concentrations of galactoside in each aqueous phase (pH 10.1), excess boric acid as the hydrophilic complexation agent in the receiving phase, and **3** as the lipophilic transporting agent in the organic layer. Figure 3 shows that uphill galactoside transport was achieved in the direction of the boric acid-containing receiving phase. Apparently, the galactoside was transported across the membrane according to Scheme 1 and was trapped in the receiving phase as a highly water-soluble borate complex. Control experiments showed that in the absence of **3** the rate of uphill galactoside transport was approximately three times lower, that in the absence of boric acid no uphill transport was observed, and that when galactoside was replaced with glucoside no uphill transport was observed. Thus, in this active transport system, the free energy of galctoside–borate complexation is the energy source driving galactoside transport against its concentration gradient.

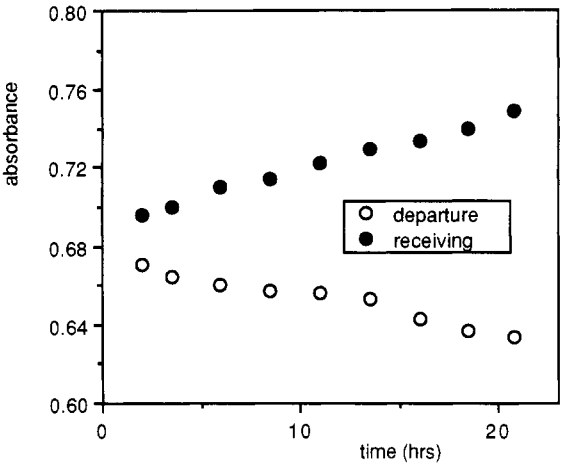

Figure 3. Change in galactoside absorbance in the departure phase (0.5 M sodium carbonate, pH 10.1) and receiving phase (0.4 M sodium carbonate, 0.1 M boric acid, pH 10.1), with **3** as the carrier (experiment reproduced four times, see text for a summary of controls).

In summary, we have shown that boronic acids can mediate selective glycoside transport through a liquid organic membrane by forming a reversible trigonal boronate ester with a glycoside diol. The apparent order of diol selectivity for the trigonal boronate transport pathway was observed to be *cis*-α,γ-diol > *cis*-α,β-diol $\approx$ *trans*-α,γ-diol $\gg$ *trans*-α,β-diol,[17] which differs from the selectivity of the tetrahedral boronate pathway. Extraction of a glycoside as its trigonal boronate ester and its subsequent transport through an organic layer is maximal when the aqueous phase is at neutral pH and is enhanced by increasing the lipophilicity of the boronic acid.[18]

Experimental Section

General. All *p*-nitrophenyl β-D-glycopyranosides were purchased from Sigma and used without further purification. Phenylboronic acid, **3**, and trioctylmethylammonium chloride (TOMA, Aliquat-336) were purchased from Aldrich.

3-(1-Adamantylcarboxamido)phenylboronic acid, 4. A solution of (3-aminophenyl)boronic acid (0.923 g, 6.74 mmol) and 1-adamantanecarbonyl chloride (1.34 g, 6.74 mmol) in pyridine (22 mL) was heated for 20 h at 105 °C under a nitrogen atmosphere. The reaction mixture was quenched with 10% H_2SO_4 and extracted with ethyl acetate. The organic layer was dried over $MgSO_4$ and removed under reduced pressure. The crude product was purified by flash column chromatography (hexane:ethyl acetate (2:1)) to yield **4** (0.375 g, 19%) in its anhydride form: mp 224–229 °C; R_f = 0.15 (hexane:ethyl acetate (2:1)); ^{1}H NMR (slightly wet acetone-d_6, 300 MHz) δ 1.76 (br s, 6H), 2.02 (br s, 6H), 2.08 (s, 3H), 7.16 (s, 2H), 7.25 (t, 1H, J = 7.8 Hz), 7.53 (d, 1H, J = 8.1 Hz), 7.83 (d, 1H, J = 8.1 Hz), 7.96 (s, 1H), 8.43 (s, 1H) ppm; ^{13}C NMR (acetone-d_6, 125 MHz) δ 28.1, 36.4, 39.2, 41.5, 122.6, 125.2, 128.3, 128.7, 129.6, 176.5 ppm; MS (positive-ion FAB with glycerol matrix) m/z 356 (M + 57, trigonal boronate–glycerol adduct + H), exact mass 356.2032, calcd for $C_{17}H_{23}O_3NB$ 356.2033. Anal. Calcd for $C_{51}H_{60}O_6N_3B_3$: C, 72.62; H, 7.17; N, 4.98. Found: C, 72.42; H, 7.04; N, 5.14.

Downhill Transport. A solution of boronic acid (1 mM, with or without 1 mM TOMA) in dichloroethane (7 mL) was shaken in a separatory funnel with an equal volume of the appropriate buffer solution. After the layers were separated, the organic phase was placed in the bottom of a U tube apparatus (1.20-cm internal diameter, 10 cm high, 2.5 cm between each arm) equipped with a "spectral" stir bar (Fisher) and a magnetic stirrer. Half of the aqueous phase was carefully added to the departure arm of the U tube and the other half to the receiving arm. The organic layer was stirred at the same rate for every experiment (470 ± 15 rpm as determined by a stroboscope), and

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(23) Fyles, T. M.; Hansen, S. P. *Can. J. Chem.* **1988**, *66*, 1445.
(24) For another example of artificial active glucose transport driven by group translocation see: Broun, G.; Thoma, D.; Slegny, E. *J. Membr. Biol.* **1972**, *8*, 313–318.

the U tube was clamped at the same position relative to the magnetic stirrer. To begin the experiment, 150 μL of the appropriate *p*-nitrophenyl β-D-glycopyranoside (33 mM) in water was added to the departure arm. Every 30 min a 1-mL aliquot was removed from the receiving arm, its absorbance at 302 nm quickly determined, and the aliquot returned to the receiving arm. All transport runs were reproduced at least in duplicate. The reproducibility of observed rate constants was always less than 20% and usually less than 10%.

Uphill Transport. By use of a procedure similar to the downhill transport experiments, a dichloroethane solution (7 mL, 1 mM) of **3** (with or without 1 mM TOMA) was shaken with an aqueous glycoside solution (7 mL, 0.06 mM, pH 7.4). The organic layer was placed in the bottom of the U tube and the glycoside solution added in equal volumes to the departure and receiving arms. The pH in the departure arm was then increased to pH 12.4 by carefully adding concentrated sodium hydroxide. The glycoside concentrations in both phases were monitored via their absorbance at 302 nm.

Extractions. A solution of glycoside (1.36 mM) in the appropriate buffer solution (4 mL) was shaken vigorously with a solution of the boronic acid (1 mM, with or without 1 mM TOMA) in dichloroethane (4 mL), and the two layers were clarified by centrifugation. The mannoside extractions were conducted with half the volumes. The amount of glycoside in the organic layer was determined from its UV absorption at 302 nm. Repetition of the extractions indicated a reproducibility of ±10%.

Characterization of Galactoside Extraction Products. The organic layer resulting from extraction of galactoside with **3** was examined by mass spectroscopy. The FAB spectrum showed a parent ion at m/z = 388 corresponding to trigonal monoadduct. In the EI spectrum, the parent ion was absent and a base line fragment at m/z = 159, assigned to fragment **3**, was observed.[8,16] The extraction of galactoside with **4** was repeated with chloroform, and the organic layers were examined by mass and NMR spectroscopy. The FAB spectrum showed a parent ion at m/z = 564 corresponding to trigonal monoboronate, whereas the EI spectrum only showed a base line fragment at m/z = 135 corresponding to adamantyl cation. ^{1}H NMR of a $CDCl_3$ extract showed it to contain a major and a minor component.[17] Upon standing, some of the major component precipitated and was reexamined by ^{1}H and ^{13}C NMR in acetone-d_6. It was found to be identical to a sample prepared by condensation of the galactoside with **4** under Dean–Stark conditions. Comparison of its ^{13}C NMR spectrum with that of the galactoside alone showed the galactoside-**4** adduct to be the trigonal *cis*-4,6-boronate shown in Figure 1. Particularly diagnostic was the 3 ppm downfield shift of the galactoside C-6 carbon upon complexation. *p-Nitrophenyl β-D-galactoside 4,6-(3-(1-adamantylcarboxamido)-phenylboronate)*: ^{1}H NMR (300 MHz, acetone-d_6) δ 1.74 (br s, 6H), 1.99 (br s, 6H), 2.07 (s, 3H), 3.86 (s, 2H), 4.19 (dd, 1H, J = 12.3, 1.2 Hz), 4.32 (br s, 1H), 4.39 (dd, 1H, J = 12.3, 2.1 Hz), 4.43 (s, 1H), 4.56 (s, 1H), 4.80 (br s, 1H), 5.32 (d, 1H, J = 7.2 Hz), 7.21 (t, 1H, J = 8.3 Hz), 7.25 (d, 2H, J = 9.3 Hz), 7.53 (d, 1H, J = 7.5 Hz), 7.78 (s, 1H), 7.93 (d, 1H, J = 8.1 Hz), 8.18 (d, 2H, J = 9.1 Hz), 8.47 (s, 1H) ppm; ^{13}C NMR (acetone-d_6, 125 MHz) δ 28.1, 37.2, 39.7, 42.2, 65.3, 69.9, 71.4, 71.7, 101.4, 117.4, 123.6, 126.3, 126.4, 128.4, 129.1, 129.8, 139.7, 143.3, 163.4, 176.4 ppm.

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