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Brønsted versus Lewis Acid Type Anion Recognition by Arylboronic Acids

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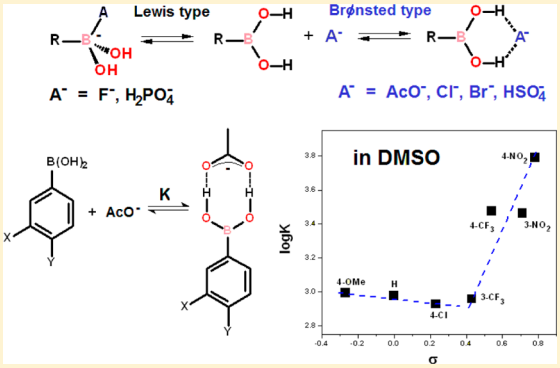
Supporting Information

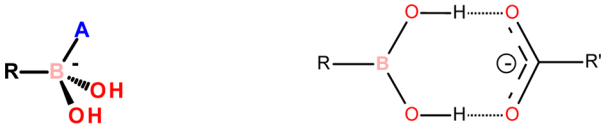
ABSTRACT: Interactions between arylboronic acids and a series of anions as tetrabutylammonium salts in DMSO and MeCN were studied by ^{1}H and ^{11}B NMR as well as spectrophotometrically. Boronic acids act as Brønsted acid type receptors through hydrogen bonding with $B(OH)_2$ hydroxyl groups toward Cl^-, Br^-, HSO_4^-, and AcO^-, but they act as Lewis acid type receptors toward F^- and $H_2PO_4^-$, which form tetrahedral adducts with the B(III) center of boronic acids, although there is also evidence for some contribution of hydrogen bonding with these anions. The Hammett plot for the binding constants of AcO^- with 3- and 4-substituted phenylboronic acids in DMSO is nonlinear, with a small negative slope for electron-donating and weakly electron-accepting substituents and a large positive slope for strongly electron-accepting substituents. 3-Nitrophenylboronic acid recognizes zwitterions of amino acids in DMSO, and its UV absorption maximum undergoes a significant red shift in the presence of acetate anions, providing a means for sensing anions optically. Arylboronic acids as Brønsted acid type receptors show relatively low sensitivity to solvent polarity and are equally or even more efficient than widely employed proton donors such as ureas or dicarboxamides.



INTRODUCTION

Acid−base properties of boronic acids are unique. In spite of the presence of proton-donor hydroxyl groups, they are known to behave as Lewis rather than Brønsted acids.[1] In line with this, anion recognition by boronic acids as well as by other organoboron compounds occurs through donation of the anion electron lone pair to the B(III) center, affording the respective tetrahedral adduct **1** (Scheme 1).[2] A large number of anion receptors based on this type of interaction, typically selective for F^-, have been reported over the past decade.[2,3] On the other hand, the proton-donor character of hydroxyl groups is clearly manifested in the hydrogen bonding of boronic acids to anionic carboxylate groups that has been observed in the crystal structures of several boronic acid complexes with carboxylate salts.[4−10] Here, the boronic acid acts as a proton-donor receptor, i.e., as a Brønsted rather than Lewis acid. The bidentate binding observed in these complexes illustrated in Scheme 1 (**2**) is reminiscent of the carboxylate complexation by ureas that is widely employed in the design of anion receptors.[11] It was noticed that ^{1}H NMR spectra of carboxylate complexes of boronic acids dissolved in DMSO contain signals in the range 8.5−10.4 ppm, which can be attributed to hydrogen-bonded protons of B-OH groups.[4] The hydrogen-bonding interaction between B-OH groups and chloride anions was also proposed as an explanation for the fluorescence quenching of a boronic acid receptor by Cl^- in dichloromethane.[12]

Scheme 1. Possible Types of Anion Binding by Boronic Acids



1 **2**

Although these examples point to a possibility of using boronic acids as proton-donor receptors for anions, there are no data regarding stability and selectivity of boronic acid−anion complexes of this type in solution. It is also not clear whether hydrogen-bonded complexation can be observed with any anion or just with some of them. In this article, we report the results of a systematic study of complex formation between arylboronic acids and anions in aprotic solvents, mostly DMSO, monitored by NMR and UV−vis spectroscopy. These results confirm the hydrogen-bonding interaction, reaction 1, for several anions, whereas with other anions, arylboronic acids act as Lewis acids. The association constants for hydrogen-bonded complexes with boronic acids are noticeably larger than those reported for usually employed bidentate hydrogen-bonding receptors such as ureas or dicarboxamides, which makes

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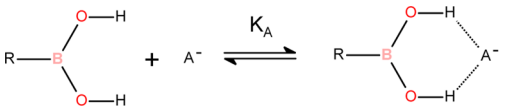
boronic acids attractive building blocks for the future design of hydrogen-bonding anion receptors.



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RESULTS AND DISCUSSION

Figure 1 shows the course of ^{1}H NMR titration of $PhB(OH)_2$ with Bu_4NAcO in DMSO-d_6. Additions of increasing amounts

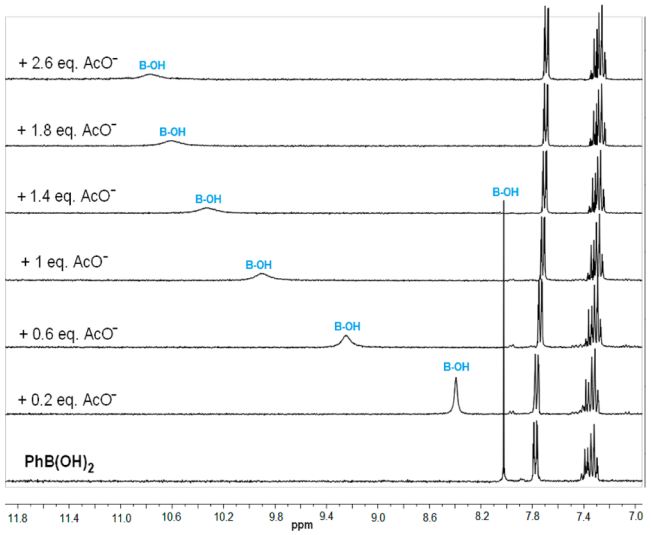

Figure 1. ^{1}H NMR titration of 5 mM phenylboronic acid by Bu_4NAcO in DMSO-d_6.

of acetate anions induce a characteristic downfield shift of the signal of B-OH protons, indicating hydrogen-bond formation of the type shown in Scheme 1 (**2**). Significant broadening of the signal may be associated with a relatively slow exchange rate between the free form and that bound to the anion phenylboronic acid. The concomitant small upfield shift of the signals of aromatic protons can be attributed to the electron-donor effect of the bound anion, also in agreement with the proposed structure (**2**) of the complex. The methyl group signal of the acetate anion undergoes a downfield shift (Table 1) by 0.14 ppm, which reflects partial proton transfer to the hydrogen-bonded anion.

The concentration dependences of chemical shifts for all host signals perfectly fit the binding isotherm for a 1:1 association process given by eq 2, where [H] and [G] are total concentrations of host and guest, respectively, K_A is the association constant, and $\Delta\delta = (\delta_{HG} - \delta_H)$ is the complexation-induced shift in the signal of a host proton.[13] The fitting of the titration plot followed by the chemical shift of the B-OH proton of phenylboronic acid to eq 2 is shown in Figure 2.

$$\delta_{obs} = \delta_H + 0.5(\Delta\delta/[H])([H] + [G] + K_A^{-1} - (([H] + [G] + K_A^{-1})^2 - 4[H][G])^{0.5}) \quad (2)$$

Similar titration plots were observed for several 3- and 4-substituted phenylboronic acids, Figure 2A. The K_A values for 4-CF_3 and 4-NO_2 phenylboronic acids were determined spectrophotometrically, as described below, since NMR titrations of these acids gave association constants with large uncertainty. Additionally, phenylboronic acid was titrated by tetramethylammonium salts of substituted benzoic acids, Figure 2B. The calculated K_A and $\Delta\delta$ values are summarized in Table 1.

The results summarized in Table 1 allow us to analyze the electronic effects of substituents in terms of the Hammett correlation, shown graphically in Figure 3. Surprisingly, the plot for substituted boronic acids (Figure 3A) is nonlinear. For the formation of a negatively charged complex, the expected positive slope is observed only for strongly electron-accepting substituents, but for electron-donating and weakly electron-accepting substituents, a small negative slope is observed. The reported Hammett ρ constants for formal acid dissociation constants (corresponding to the addition of hydroxide anions to the B(III) center) as well as for stability constants of anionic tetrahedral diol esters for arylboronic acids are about 2.[14] The slope of the line passing through the points for trifluoromethyl and nitro substituted acids is also about 2, but the deviation from this tendency for boronic acids with other substituents does not have a clear explanation. A possible reason is a

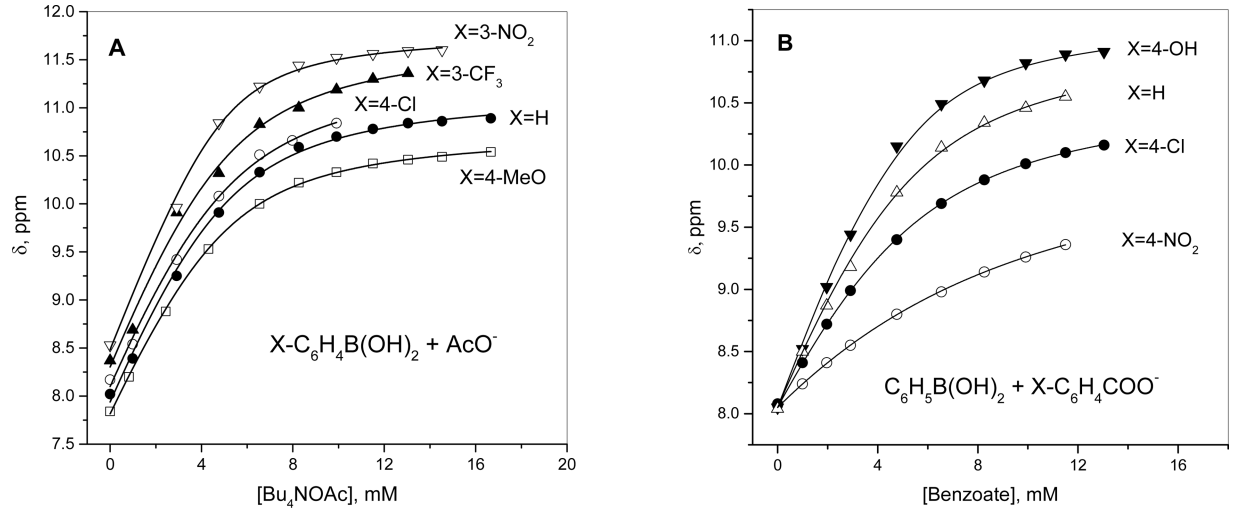

Figure 2. ^{1}H NMR titrations of (A) 5 mM substituted phenylboronic acids by Bu_4NAcO and (B) 5 mM phenylboronic acids by Me_4N salts of substituted benzoic acids in DMSO-d_6. Solid lines are fitting curves to eq 2.

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Table 1. Stability Constants (K_A) of Acetate and Benzoate Complexes of Substituted Phenylboronic Acids in DMSO-d_6

substituent			$\Delta\delta$, ppm[a]	
in boronic acid	in benzoate	K_A, M^{-1}	$-B(OH)_2$	CH_3COO^-
Titrations with Acetate				
4-MeO		990 ± 50	2.95	0.09
H		950 ± 50	3.24	0.14
4-Cl		850 ± 60	3.34	0.15
3-CF_3		910 ± 80	3.44	0.20
4-CF_3		3000 ± 100	3.10	0.22
3-NO_2		2900 ± 100	3.27	0.27
4-NO_2		6200 ± 100	3.15	0.28
Titrations with Substituted Benzoates				
H	4-OH	1300 ± 100	3.13	
H	H	720 ± 90	3.00	
H	4-Cl	490 ± 20	2.56	
H	4-NO_2	132 ± 6	2.40	

[a]Complexation-induced shifts in the signals of B-OH and CH_3 groups of acetate.

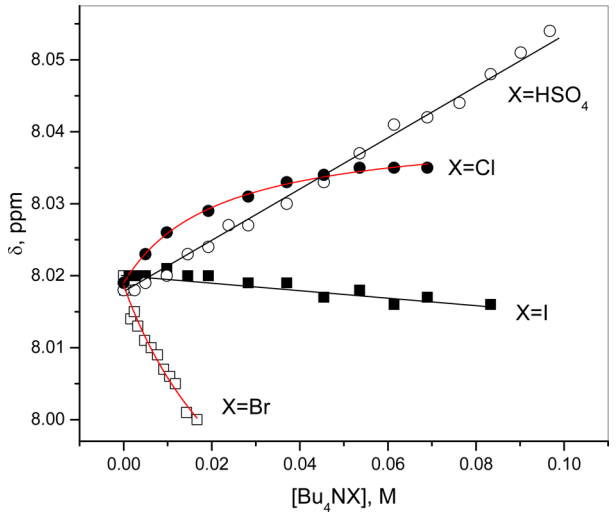

Figure 4. ^{1}H NMR titrations of 5 mM phenylboronic acid by different anions in DMSO-d_6. Solid red lines are fitting curves to eq 2.

complicated balance between free energies of complex formation and boronic acid solvation, both involving hydrogen bonding to the $B(OH)_2$ group. On the other hand, the Hammett plot for substituted benzoate anions (Figure 3B) has the expected negative slope ($\rho = -0.87 \pm 0.07$) for all types of substituents.

The complexation-induced downfield shifts in the signals of B-OH protons roughly correlate with σ values, although the dependence is not monotonic. A more regular trend is observed for complexation-induced shifts in the signals of protons of the acetate methyl group: proton donation by progressively stronger boronic acids induces stronger downfield shifts, approaching $\Delta\delta = 0.3$ ppm, observed on complete protonation of the anion.

Titrations of phenylboronic acid by tetrabutylammonium salts of other anions were performed in order to establish the selectivity of complexation. Additions of Cl^- and HSO_4^- anions caused small downfield shifts of B-OH signals, in agreement with the formation of hydrogen-bonded complexes. The respective titration plots are shown in Figure 4. The profile for HSO_4^- remains linear up to the highest employed concentration of anion and therefore the association constant cannot be calculated, but for Cl^-, the fitting to eq 2 allows one to determine the K_A value, given in Table 2. With Br^- and I^- anions, the B-OH signals shift in the opposite direction; the reason for this will be discussed later. The respective association constants are also included in Table 2.

Several reported crystal structures of hydrogen-bonding complexes of boronic acids with carboxylate anions correspond to complexes with formally neutral zwitterions of amino acids, such as, for example, the complex of phenylboronic acid with proline **3**.[5,7,8] Since free amino acids in DMSO exist predominantly as zwitterions,[15] we tested this type of interaction in solution. Figure S1 (Supporting Information) shows the ^{1}H NMR titration of 3-nitrophenylboronic acid by proline, and Figure 5 illustrates the titration plots by proline and *N*,*N*-dimethylglycine, demonstrating formation of hydrogen-bonding complexes with $K_A = 30 \pm 5$ M^{-1} for both amino acids. The strongly decreased affinity for these species, as compared to that for acetate, is a result of the much lower basicity of the carboxylate group of zwitterions. Interestingly, although the fraction of the zwitterionic form in DMSO is much higher for glycine than for *N*,*N*-dimethylglycine,[15a] interaction of glycine with phenylboronic acid in DMSO

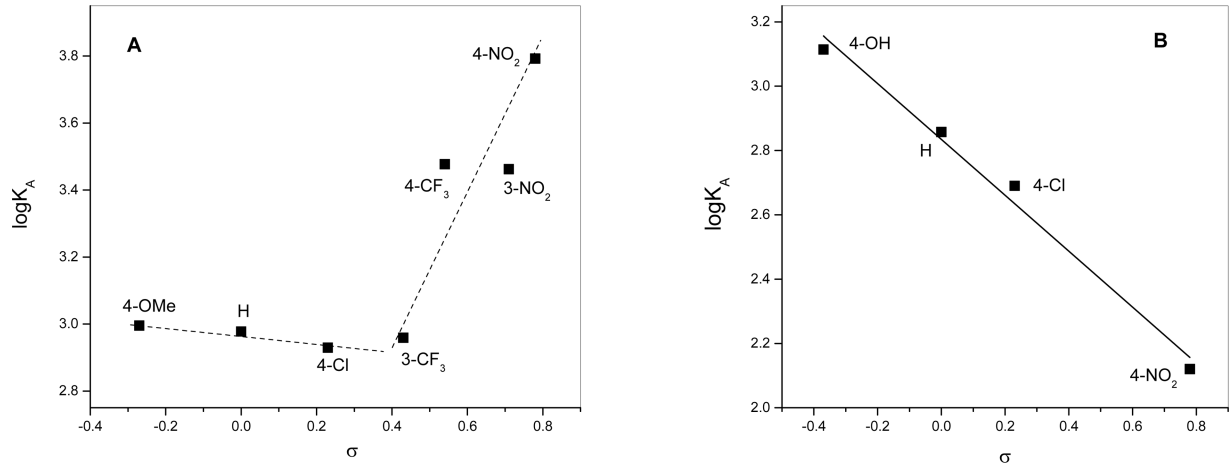

Figure 3. Hammett plots for the stability constants of hydrogen-bonded complexes of (A) substituted boronic acids X-C_6H_4-$B(OH)_2$ with acetate anions and (B) phenylboronic acid with substituted benzoate anions X-C_6H_4-CO_2^- in DMSO.

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Table 2. Stability Constants (K_A, M^{-1}) of Complexes of Phenylboronic and 3-Nitrophenylboronic Acids with Different Anions in Different Solvents and ^{11}B NMR Chemical Shifts at Saturation ($\delta(^{11}B)_{sat}$)

	$PhB(OH)_2$				$3\text{-}O_2NC_6H_4B(OH)_2$			
	DMSO		MeCN		DMSO		MeCN	$CHCl_3$
anion	log K_A[a]	$\delta(^{11}B)_{sat}$	log K_A[a]	$\delta(^{11}B)_{sat}$	log K_A[a]	$\delta(^{11}B)_{sat}$	log K_A[a]	log K_A
none		28.53				27.69		
AcO^-	2.98(2)	28.78	3.41(8)	29.13	3.46(3)[b]	27.16	3.73(2)[b]	4.01(1)[b]
$H_2PO_4^-$	2.34(6)	[c]			3.4(1)	4.78		
HSO_4^-	<0.3							
F^-	[d]	4.07					4.14	
Cl^-		1.78(7)	29.09	2.41(8)	29.92		2.74(3)	
Br^-		1.60(9)	28.86	1.72(4)				
I^-		<0.3						

[a]The number in parentheses is the standard error in the last significant digit. [b]Spectrophotometric titration. [c]Undetectable signal. [d]Not determined.

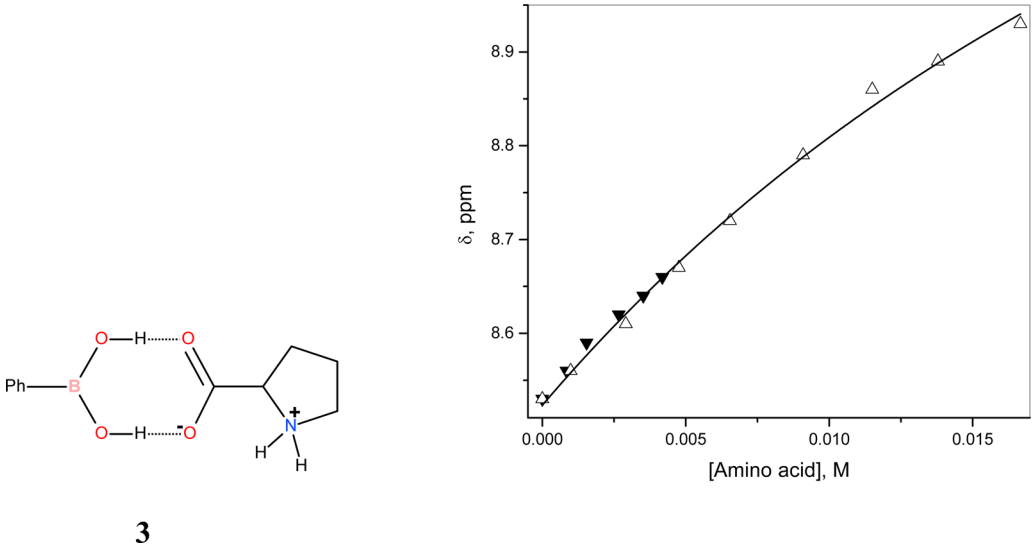

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Figure 5. ^1H NMR titrations of 5 mM 3-nitrophenylboronic acids by *N,N*-dimethylglycine (open triangles) and proline (solid triangles) in DMSO-d_6. The chemical shift of B-OH protons is used for the fitting. The solid line is the fitting curve to eq 2.

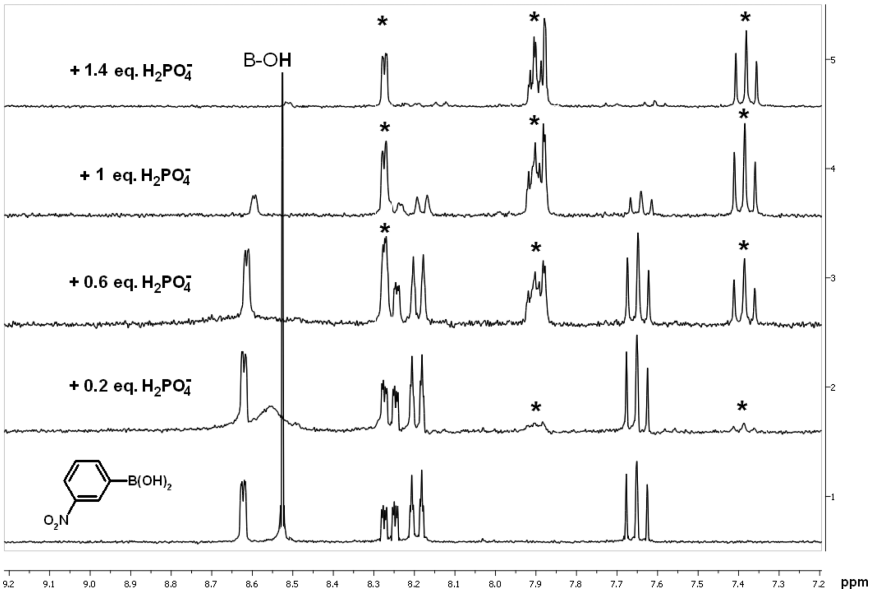

Figure 6. ^1H NMR titration of 5 mM $3\text{-}O_2NC_6H_4B(OH)_2$ by $(Bu_4N)H_2PO_4$ in DMSO-d_6.

results in the formation of a N,O chelate[16] rather than a hydrogen-bonded complex. A possible reason is that the ternary nitrogen has a lower affinity for B(III) than the primary amino group due to steric effects.

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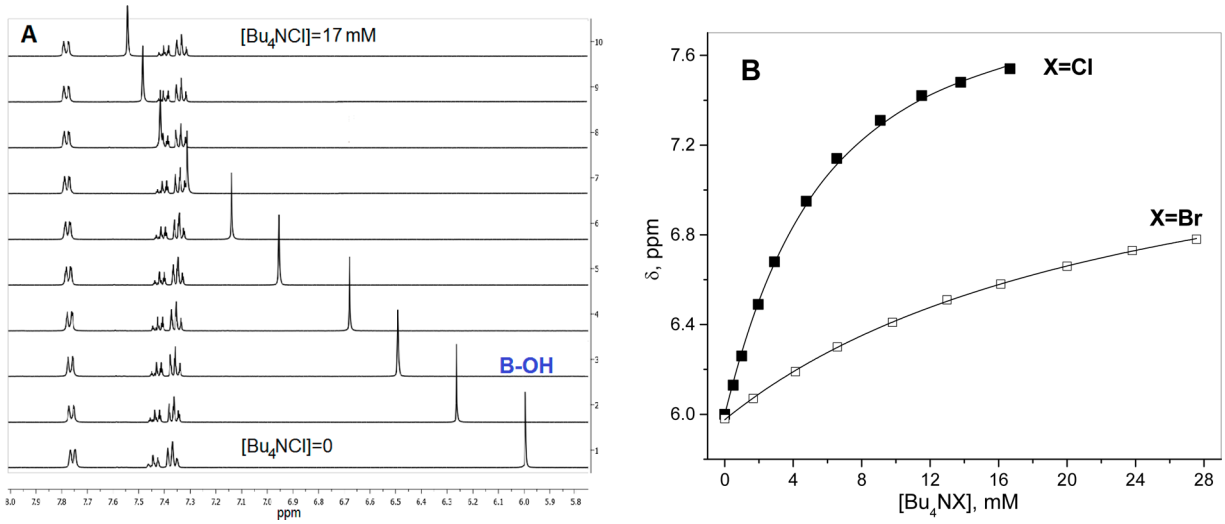

Figure 7. (A) ^{1}H NMR titration of 2.5 mM phenylboronic acid by Bu_4NCl (0−17 mM) in MeCN-d_3. (B) Titration plots of 2.5 mM phenylboronic acid in MeCN-d_3 by Cl^- and Br^-. Solid lines are fitting curves to eq 2.

Addition of $H_2PO_4^-$, even at a low concentration, caused complete disappearance of the signal of the B-OH group, but signals of aromatic protons underwent upfield shifts like that in the case of titration by acetate anions (Figure S2, Supporting Information). Fitting of these signals to eq 2 (Figure S3, Supporting Information) allowed us to calculate the association constant given in Table 2. To obtain a clearer picture with a stronger H-bonding receptor, a titration of 3-nitrophenylboronic acid by $H_2PO_4^-$ was carried out (Figure 6). After addition of 0.2 equiv of $H_2PO_4^-$, the B-OH proton signal moves slightly downfield and strongly broadens, but at higher concentrations of the anion, it again disappears completely, as in the case of phenylboronic acid. At the same time, a new set of upfield-shifted signals of aromatic protons marked with asterisks (*) appears, and their intensity grows while the intensity of the signals of free 3-nitrophenylboronic acid decreases and finally disappears completely. Such behavior reflects slow exchange, on the NMR time scale, between free and complexed components that is nontypical for hydrogen-bonded complexes. The association constant in this case can be calculated from integrated areas of signals corresponding to the free form and that bound to anion boronic acid. The respective values of K_A are given in Table 2.

A similar but more complicated picture was observed with F^- and phenylboronic acid, Figure S4 (Supporting Information). Initially, addition of anion induced a small downfield shift and broadening of the B-OH signal, but with further additions, the signal disappears completely and the second set of signals of aromatic protons starts to appear in a mode typical of a slow exchange process. The changes are complete at a 1:1 molar ratio, indicating a strong interaction, but the final spectrum still indicates the presence of a mixture of compounds. The reason for the disappearance of the ^{1}H signal of the B-OH group in the presence of F^- and $H_2PO_4^-$ is not clear, although the initially observed downfield shifts of the B-OH signals indicate at least some contribution of hydrogen bonding with these anions.

Important information about the type of anion complexes is provided by the position of the ^{11}B NMR signal. Free boronic acids with sp^2 boron have ^{11}B NMR signals around 30 ppm.[17] Formation of a hydrogen-bonded complex like **2** does not change the hybridization of the B atom, so it can change the chemical shift of ^{11}B only by small inductive and/or solvation effects. On the contrary, formation of a complex like **1** changes the hybridization of the B atom to sp^3, which has a characteristic chemical shift between 0 and 10 ppm.[17] The ^{11}B NMR spectra of phenylboronic and 3-nitrophenylboronic acids in DMSO in the absence and presence of anions are shown in Figure S5 (Supporting Information). In Table 2, the ^{11}B chemical shifts at saturation clearly show that complexes of phenylboronic acid with AcO^-, Cl^-, and Br^- are of the hydrogen-bonding type, but complexes with F^- and $H_2PO_4^-$ (with 3-nitrophenylboronic acid) are of a covalent type. Surprisingly, we were unable to detect the ^{11}B signal of phenylboronic acid at saturation with $H_2PO_4^-$ (Figure S5c), although in the case of 3-nitrophenylboronic acid, at least a low-intensity signal was clearly seen (Figure S5h).

In the less polar MeCN solvent, stability of anion complexes was, as expected, higher. During titration of phenylboronic acid by AcO^- in MeCN, the broadening of the B-OH signal was significantly stronger than that in DMSO, and the signal was already undetectable at low concentrations of added anion. The association constant given in Table 2 was determined in this case from the titration plot for a signal of an aromatic proton (Figure S6, Supporting Information). The ^{11}B chemical shift at saturation (Table 2) confirms that the complex of phenylboronic acid with AcO^- in this solvent is indeed of the hydrogen-bonded type. Figure 7A illustrates the titration of phenylboronic acid by Cl^- in MeCN-d_3, which clearly demonstrates a strong downfield shift of the signal of the B-OH proton and upfield shifts of the signals of aromatic protons. The ^{11}B chemical shift at saturation (Table 2) confirms that the complex is of the hydrogen-bonded type. Titration by Br^- shows similar characteristics. The fitting plots for both anions are shown in Figure 7B. The stability constants for AcO^- and Cl^- are ca. 3−4 times larger than those in DMSO (Table 2), but the stability constant for Br^- is only slightly larger in MeCN as compared to that in DMSO (Table 2). It is worth noting that, in MeCN solvent, addition of Br^- induces the expected downfield shift of the B-OH signal, whereas in DMSO, an upfield shift is observed (Figure 4). We believe that the reason for this discrepancy is that solvation of B-OH by strongly donating DMSO molecules induces a larger downfield shift of the signal than the complexation of B-OH with Br^-. Indeed, the

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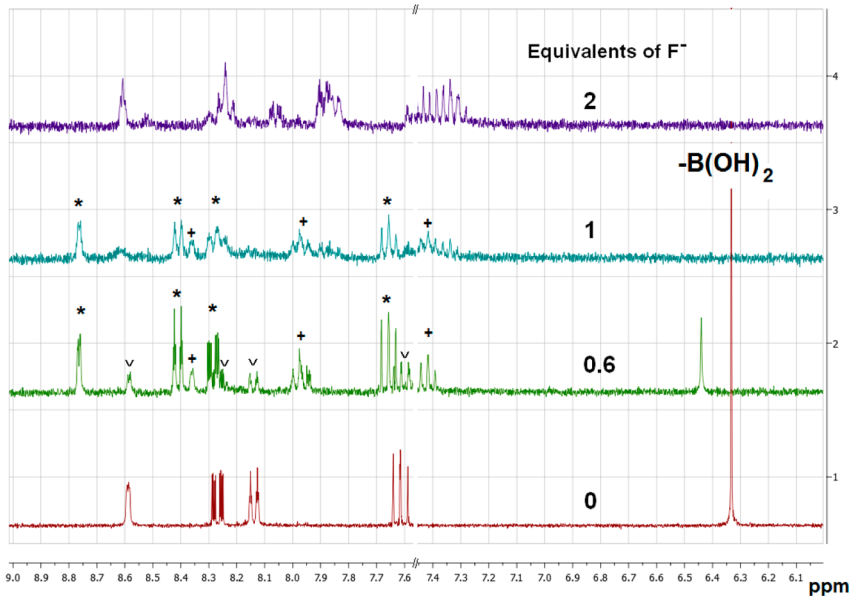

Figure 8. ^{1}H NMR titration of 5 mM 3-$O_2NC_6H_4B(OH)_2$ by $PhCH_2NMe_3F$ in MeCN-d_3. The interval between 7.45 and 7.55 ppm, which contains the signal of the phenyl group of $PhCH_2NMe_3F$, is eliminated.

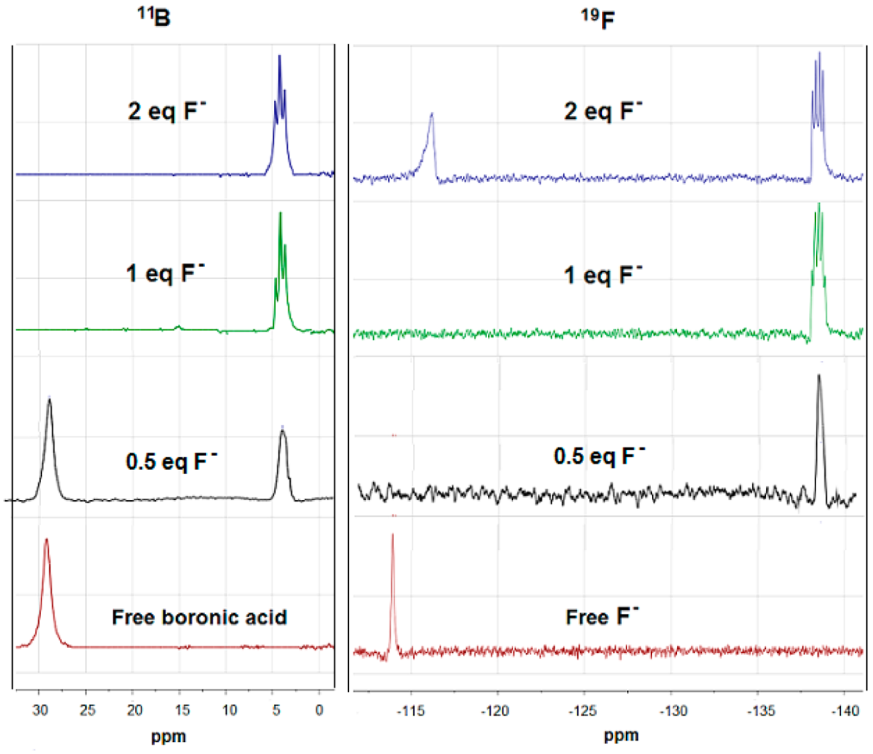

Figure 9. ^{11}B and ^{19}F NMR titrations of 20 mM 3-$O_2NC_6H_4B(OH)_2$ by $PhCH_2NMe_3F$ in MeCN-d_3.

limiting chemical shift of the proton of B-OH at saturation with Br^- in MeCN is only 7.39 ppm (calculated from the fitting of results in Figure 7B), but the chemical shift of B-OH in pure DMSO is already 8.02 ppm.

The combined results of ^{1}H and ^{11}B titrations of phenylboronic acid with F^- and $H_2PO_4^-$ anions show that the predominant type of interaction with these anions is Lewis acid type bonding, with some possible contribution of hydrogen bonding. It is also worth noting that formation of Lewis acid type adducts, on several occasions, occurs slowly on the NMR time scale, as is typical for the formation of covalent boronic acid esters.[18] To obtain additional insight on the type of interactions with fluoride anion, the system was also studied with a stronger boronic acid, 3-$O_2NC_6H_4B(OH)_2$, in the less polar MeCN solvent. The results of the ^{1}H NMR titration are shown in Figure 8.

Addition of less than 1 equiv of F^- (second from the bottom spectrum in Figure 8) induces a downfield shift of the signal of $B(OH)_2$ protons and formation of a new set of signals of aromatic protons marked with the asterisk (*), which coexists with a set of the signals of free boronic acid marked with the tick (∨). Also, a new set of lower-intensity signals marked with

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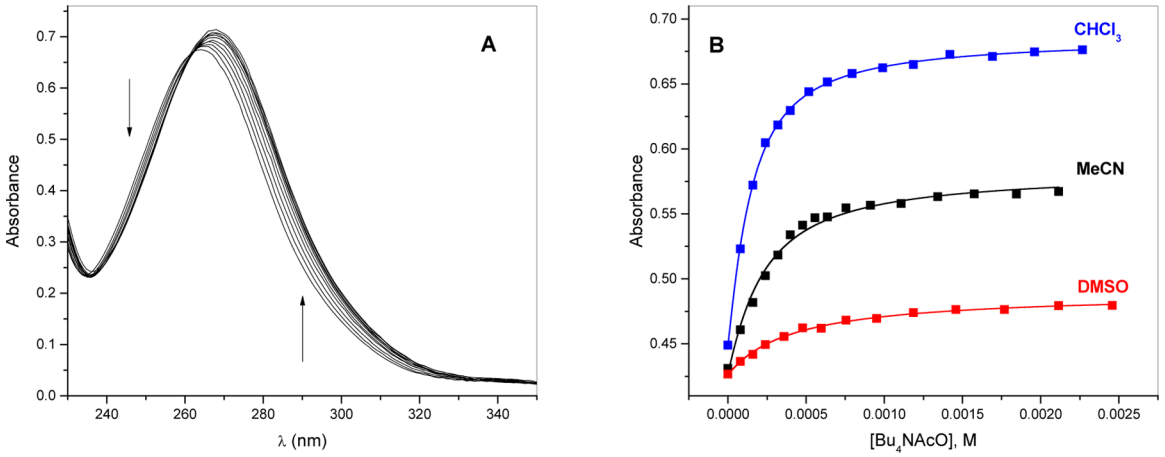
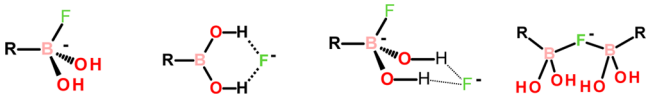


Figure 10. (A) Spectrophotometric titration of 0.1 mM 3-nitrophenylboronic acid by Bu_4NAcO in MeCN. The arrows show the direction of spectral changes on addition of increasing amounts of acetate anions. (B) Titration plots in different solvents at 290 (DMSO), 285 ($CHCl_3$), and 280 (MeCN) nm. Solid lines are the theoretical fitting curves.

+ is observed. At this step, we are most probably observing a mixture of slowly exchanging covalent and rapidly exchanging hydrogen-bonded adducts as the major components. At a 1:1 molar ratio (third spectrum), the signal of $B(OH)_2$ protons disappears, as do signals of aromatic protons of the free acid, and in the presence of the second equivalent of fluoride (the upper spectrum), again a different set of signals is observed. These results indicate an unexpectedly large number of fluoride adducts. Indeed, one can expect formation of only two types of 1:1 adducts, one covalent (**4**) and one hydrogen-bonded (**5**) and one 1:2 adduct (**6**) with both types of binding. Formation of 1:2 covalent adducts is unlikely because it would need either formation of a very rare pentacoordinate B(III) compound or binding of the second anion via OH^-/F^- exchange, which is improbable in an aprotic solvent since it needs protonation of the leaving hydroxide anion.[19] Possible types of additional species are various polymeric adducts, e.g., like **7**, resulting from the self-association of reaction components in low-polar MeCN medium at high concentrations employed for NMR measurements.



4 **5** **6** **7**

Further information was obtained from ^{11}B and ^{19}F spectra, Figure 9. According to ^{11}B results (left side of the figure), the addition of 0.5 equiv of F^- induces formation of a slowly exchanged covalent adduct with δ 4.14 ppm, most probably of the type **4**. The absence of the expected doublet structure of the signal can be attributed to broadening due to the exchange with an excess of boronic acid. Addition of 1 equiv of F^- completely transforms the boronic acid into a tetrahedral covalent adduct, as evidenced by the shift of the ^{11}B signal to 4.14 ppm, and addition of the second equivalent of the anion induces very little change in the spectrum, which means that the second fluoride anion does not interact directly with B(III). The coupling constant $J(^{11}B-^{19}F)$ = 59.02 Hz is close to other reported values for arylboronic acids,[20] but the observation of a triplet rather than a doublet signal is strange. Such multiplicity corresponds to the binding of two fluoride anions to the B(III) center, which seems improbable (see above). Most probably, this multiplicity arises due to overlapping signals of different species that are very close to each other observed in ^1H spectra, which are supposedly of the polymeric type (see above).

The ^{19}F results (right side of the figure) agree with the ^{11}B data. The added 0.5 equiv of F^- is transformed completely into a covalent adduct with δ −138.33 ppm that lacks the expected quartet structure due to exchange with excess boronic acid. In a 1:1 mixture, when free boronic acid disappears, one observes a quintet at −138.33 ppm, corresponding to a covalent adduct. The exceeding multiplicity of the signal can be explained, as in the case of the ^{11}B spectra, by overlapping signals of polymeric species. With 2 equiv of F^-, this signal converts to a quartet, as expected for a 1:1 adduct, and a new signal at −116.20 ppm appears that is close to, but does not coincide with, that of free F^- (−113.92 ppm) and may belong to the hydrogen-bonded anion. Thus, the most probable structure of the complex formed in the presence of 2 equiv of F^- is **6**.

In order to see whether arylboronic acids can be employed for optical sensing of anions via hydrogen bonding, a spectrophotometric titration of 3-nitrophenylboronic acid by acetate was performed in solvents of different polarities (DMSO, MeCN, and $CHCl_3$). In all cases, complexation was accompanied by a significant red shift of the absorption maximum, as illustrated in Figure 10A for titration in MeCN. Such red shifts are usually observed on interactions of anions with arylureas[21] and there is probably a similar origin in both cases. The fitting of the spectrophotometric titration plots to an equation similar to 2 but adopted for this type of titration[13] is shown in Figure 10B for different solvents, and the respective stability constants are given in Table 2. Evidently, the complexation-induced change in absorption is larger in less polar solvents where more tightly bound complexes are formed. Smaller, but detectable, spectrophotometric changes were observed also in titration of phenylboronic acid by AcO^- and Cl^- in MeCN. Spectrophotometrically determined association constants were reasonably close to those determined by NMR titrations.

Comparison of results obtained in different solvents (Table 2) shows that the stability of hydrogen-bonded complexes decreases in more polar solvents, as is typical for other similar systems. However, the solvent effect observed in this case, which is manifested in less than a 4-fold decrease in K_A on going from $CHCl_3$ to DMSO, is not as large as for, e.g., urea-

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based receptors for which stability constants of anion complexes are, by ca. 2 orders of magnitude, smaller in DMSO as compared to that in $CHCl_3$ (see, e.g., ref 22). We also found the binding constants of phenylboronic acid to acetate to decrease only 2- and 4-fold on addition of 1 and 3 vol % water, respectively, to DMSO.

CONCLUSIONS

The results of this study show that boronic acids act as proton-donating hydrogen-bonding receptors toward many common anions. The pronounced selectivity to acetate is a result of complementarity between anion oxygen atoms and two hydroxyls of the $B(OH)_2$ group. Surprisingly, $H_2PO_4^-$, another anion for which such complementarity could be expected, forms a Lewis type covalent adduct with boronic acids, possibly because phosphate anions have more hard character. A very hard, and isoelectronic with OH^-, fluoride anion preferably forms the covalent adduct, although there is some evidence for hydrogen bonding with this anion, too. A nonlinear Hammett plot for acetate binding with substituted arylboronic acids indicates the complex character of electronic effects in the hydrogen-bonding properties of boronic acids. Stability constants measured for phenylboronic acid and anions such as acetate or chloride in DMSO are larger than those reported for such familiar bidentate proton donors as phenylurea or *iso*-phthalamide in the same media (about 100 M^{-1} for acetate and 10 M^{-1} for chloride, see, e.g., refs 23 and 24). Finally, a significant change in absorptivity induced by anion binding makes properly substituted arylboronic acids possible candidates for the future design of neutral optical anion sensors.

EXPERIMENTAL SECTION

General Experimental Methods. Commercially available substituted phenylboronic acids, tetrabutylammonium salts of all anions besides F^-, which was used as a less hygroscopic benzyltrimethylammonium salt, and deuterated and common solvents were used as supplied. Stock solutions of tetramethylammonium salts of substituted benzoic acids were prepared by reacting the respective acid with Me_4NOH in DMSO. All titration experiments were performed at 25 °C. ^1H NMR spectra were recorded at 300 MHz. ^{11}B NMR spectra were recorded at 128.3 MHz with $Et_2O{\cdot}BF_3$ in $CDCl_3$ as the external standard using a 45° pulse, 4.82 s FID acquisition time, and 1 s acquisition delay. The sweep width was set to 423.6 ppm, and 2000 scans were performed. The ^{19}F NMR measurements were carried out at 282.3 MHz, and the signal of CF_3CO_2H at −76.55 ppm (relative to $CFCl_3$) was used as an external standard for the NMR shift.

NMR and Spectrophotometric Titrations. To a 5 mM (^1H NMR titrations) solution of a boronic acid in DMSO-d_6 or MeCN-d_3 were added portions of concentrated solutions of tetrabutylammonium salts of anions in the same solvent, and the mixture was incubated for 2 min after each addition before recording the spectrum. A similar procedure but with 0.1 mM boronic acid in common solvents was applied for spectrophotometric titrations. The observed equilibrium constants of the complex formation (K_A) were calculated from the profiles of the chemical shift or absorbance vs salt concentration by fitting to eq 2 using Origin Pro 8.5. In NMR titrations, the signals of both B-OH aromatic protons were used for fitting and the results were averaged, and in spectrophotometric titrations absorbances at several wavelengths were used for fitting and the results were averaged.

ASSOCIATED CONTENT

Supporting Information

^1H NMR titration of phenylboronic acid by $H_2PO_4^-$ and F^- in DMSO-d_6, of phenylboronic acid by AcO^- in MeCN-d_3, and of 3-nitrophenylboronic acid by proline in DMSO-d_6; ^{11}B NMR spectra. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00377.

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) (a) Hall, D. G. In *Boronic Acids: Preparation and Application in Organic Synthesis and Medicine*; Hall, D. G., Ed; Wiley-VCH: Weinheim, Germany, 2005; p 1 and references therein. (b) Lorand, J. P.; Edwards, J. O. *J. Org. Chem.* **1959**, *24*, 769.

(2) (a) Galbraith, E.; James, T. D. *Chem. Soc. Rev.* **2010**, *39*, 3831. (b) Guo, Z.; Shin, I.; Yoon, J. *Chem. Commun.* **2012**, *48*, 5956. (c) Wade, C. R.; Broomsgrove, A. E. J.; Aldridge, S.; Gabbaï, F. P. *Chem. Rev.* **2010**, *110*, 3958. (d) Peters, J. A. *Coord. Chem. Rev.* **2014**, *268*, 1.

(3) (a) Kubo, Y.; Kobayashi, A.; Ishida, T.; Misawa, Y.; James, T. D. *Chem. Commun.* **2005**, 2846. (b) Koskela, S. J. M.; Fyles, T. M.; James, T. D. *Chem. Commun.* **2005**, 945. (c) Thakur, A.; Mandal, D.; Sao, S.; Ghosh, S. *J. Organomet. Chem.* **2012**, *715*, 129. (d) Xue, M.; Wang, X.; Duan, L.; Gao, W.; Ji, L.; Tang, B. *Biosens. Bioelectron.* **2012**, *36*, 168. (e) DiCesare, N.; Lakowicz, J. R. *Anal. Biochem.* **2002**, *301*, 111. (f) Swamy, K. M. K.; Ju Lee, Y.; Lee, H. N.; Chun, J.; Kim, Y.; Kim, S.-J.; Yoon, J. *J. Org. Chem.* **2006**, *71*, 8626.

(4) Rodrıguez-Cuamatzi, P.; Arillo-Flores, O. I.; Bernal-Uruchurtu, M. I.; Höpfl, H. *Cryst. Growth Des.* **2005**, *5*, 167.

(5) Rogowska, P.; Cyranski, M. K.; Sporzynski, A.; Ciesielski, A. *Tetrahedron Lett.* **2006**, *47*, 1389.

(6) Lemmerer, A. *J. Chem. Crystallogr.* **2012**, *42*, 498.

(7) Reetz, M. T.; Huff, J.; Rudolph, J.; Toellner, K.; Deege, A.; Goddard, R. *J. Am. Chem. Soc.* **1994**, *116*, 11588.

(8) Zobetz, E.; Preisinger, A. *Monatsh. Chem.* **1989**, *120*, 291.

(9) Aakeröy, C. B.; Desper, J.; Levin, B. *CrystEngComm* **2005**, *7*, 102.

(10) Shull, B. K.; Spielvogel, D. E.; Gopalaswamy, R.; Sankar, S.; Boyle, P. D.; Head, G.; Devito, K. *J. Chem. Soc., Perkin Trans. 2* **2000**, 557.

(11) (a) Sessler, J. L.; Gale, P. A.; Cho, W. S. *Anion Receptor Chemistry*; Royal Society of Chemistry: Cambridge, 2006. (b) Amendola, V.; Bonizzoni, M.; Esteban-Gómez, D.; Fabbrizzi, L.; Licchelli, M.; Sancenón, F.; Taglietti, A. *Coord. Chem. Rev.* **2006**, *250*, 1451.

(12) Galbraith, E.; Fyles, T. M.; Marken, F.; Davidson, M. G.; James, T. D. *Inorg. Chem.* **2008**, *47*, 6236.

(13) Schneider, H.-J.; Yatsimirsky, A. K. *Principles and Methods in Supramolecular Chemistry*; John Wiley and Sons: Chichester, UK, 2000; p 144.

(14) Martínez-Aguirre, M. A.; Villamil-Ramos, R.; Guerrero-Alvarez, J. A.; Yatsimirsky, A. K. *J. Org. Chem.* **2013**, *78*, 4674.

(15) (a) Hughes, D. L.; Bergan, J. J.; Grabowski, E. J. J. *J. Org. Chem.* **1986**, *51*, 2579. (b) Headley, A. D.; Starnes, S. D. *J. Am. Chem. Soc.* **1995**, *117*, 9309.

(16) Mohler, L. K.; Czarnik, A. W. *J. Am. Chem. Soc.* **1993**, *115*, 7037.

(17) Zhu, L.; Shabbir, S. H.; Gray, M.; Lynch, V. M.; Sorey, S.; Anslyn, E. V. *J. Am. Chem. Soc.* **2006**, *128*, 1222.

(18) (a) Van Duin, M.; Peters, J. A.; Kieboom, A. P. G; Van Bekkum, H. *Tetrahedron* **1984**, *40*, 2901. (b) Pizer, R. D.; Ricatto, P. J.; Tihal, C. A. *Polyhedron* **1993**, *12*, 2137. (c) Pizer, R.; Ricatto, P. J. *Inorg. Chem.* **1994**, *33*, 2402. (d) Pizer, R.; Tihal, C. *Inorg. Chem.* **1992**, *31*, 3243.

DOI: 10.1021/acs.joc.5b00377
J. Org. Chem. 2015, 80, 4985−4993

(19) (a) Yuchi, A.; Sakurai, J.; Tatebe, A.; Hattori, H.; Wada, H. *Anal. Chim. Acta* **1999**, *387*, 189. (b) Ting, R. C.; Harwig, W.; Lo, J.; Li, Y.; Adam, M. J.; Ruth, T. J.; Perrin, D. M. *J. Org. Chem.* **2008**, *73*, 4662.
(20) Oliveira, R. A.; Silva, R. O.; Molander, G. A.; Menezes, P. H. *Magn. Reson. Chem.* **2009**, *47*, 873.
(21) Amendola, V.; Esteban-Gómez, D.; Fabbrizzi, L.; Licchelli, M. *Acc. Chem. Res.* **2006**, *39*, 343.
(22) Perez-Casas, C.; Höpfl, H.; Yatsimirsky, A. K. *J. Inclusion Phenom. Macrocyclic Chem.* **2010**, *68*, 387.
(23) Hughes, M. P.; Smith, B. D. *J. Org. Chem.* **1997**, *62*, 4492.
(24) Bühlmann, P.; Amemiya, S.; Nishizawa, S.; Xiao, K. P.; Umezawa, Y. *J. Inclusion Phenom. Mol. Recognit. Chem.* **1998**, *32*, 151.

DOI: 10.1021/acs.joc.5b00377
J. Org. Chem. 2015, 80, 4985−4993