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Benzosiloxaboroles: Silicon Benzoxaborole Congeners with Improved Lewis Acidity, High Diol Affinity, and Potent Bioactivity

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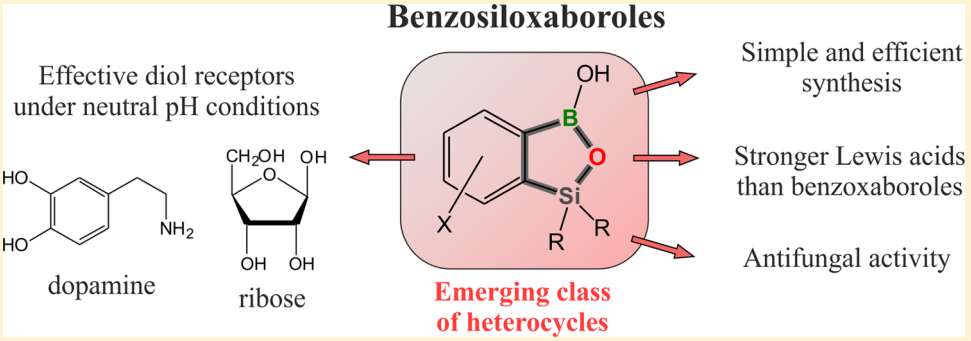
Supporting Information

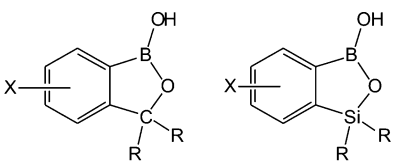


ABSTRACT: The synthesis and physicochemical properties of benzosiloxaboroles, the silicon analogues of an important class of heterocyclic compounds—benzoxaboroles—is presented. They were prepared by halogen−lithium exchange reactions of (2-bromophenyl)boronates with *n*-BuLi followed by the silylation or boronation of (2-lithiophenyl)dimethylsilanes. The cyclization of the resulting 2-(dimethylsilyl)phenylboronates apparently occurs through intramolecular dehydrogenative cyclization reaction in the presence of water. Unlike the case for benzosiloxaborole, the formation of its analogue containing a thiophene ring is thermodynamically unfavorable, which was confirmed by theoretical calculations. The presence of a B−O−Si linkage results in increased Lewis acidity with respect to the analogous benzoxaboroles. The acidity is strongly enhanced by fluorination or introduction of phenyl groups at the silicon atom. Selected compounds show good antifungal activity, and thus they are potential small-molecule therapeutic agents. They can also serve as effective receptors for biologically relevant diols under neutral pH conditions.

INTRODUCTION

1,3-Dihydro-1-hydroxy-2,1-benzoxaborole (**I**) and its derivatives were synthesized and characterized in 1957 (Chart 1).[1] However, only recently has great attention been paid to this group of heterocyclic compounds. Apart from their use as organoboron partners for Suzuki−Miyaura cross-coupling,[2] benzoxaboroles have been successfully employed in medicinal chemistry.[3−5] Their superior diol-binding properties under neutral aqueous conditions have been extensively exploited for applications in sugar sensing[6] and column chromatography for separation of the nucleosides or glycoproteins.[7] These boron heterocycles emerged as novel small-molecule therapeutic agents possessing very good antibacterial,[8] antifungal,[9] and anti-inflammatory[10] bioactivity and concomitant low toxicity. For instance, 5-fluoro- and 5-chloro-1,3-dihydro-2,1-benzoxaborole (referred to as AN2690 and AN2718, respectively) were identified as potent antifungal agents against infection of the nails (dermatophytic onychomycosis).[11] Other benzoxaboroles are also effective against other important human diseases, including human African trypanosomiasis (HAT, known as sleeping sickness),[12] malaria,[13] and some liver dysfunctions.[14] Recent intensive efforts have resulted in the

Chart 1. General Structures of 1-Hydroxybenzoxaborole and 1-Hydroxybenzosiloxaborole



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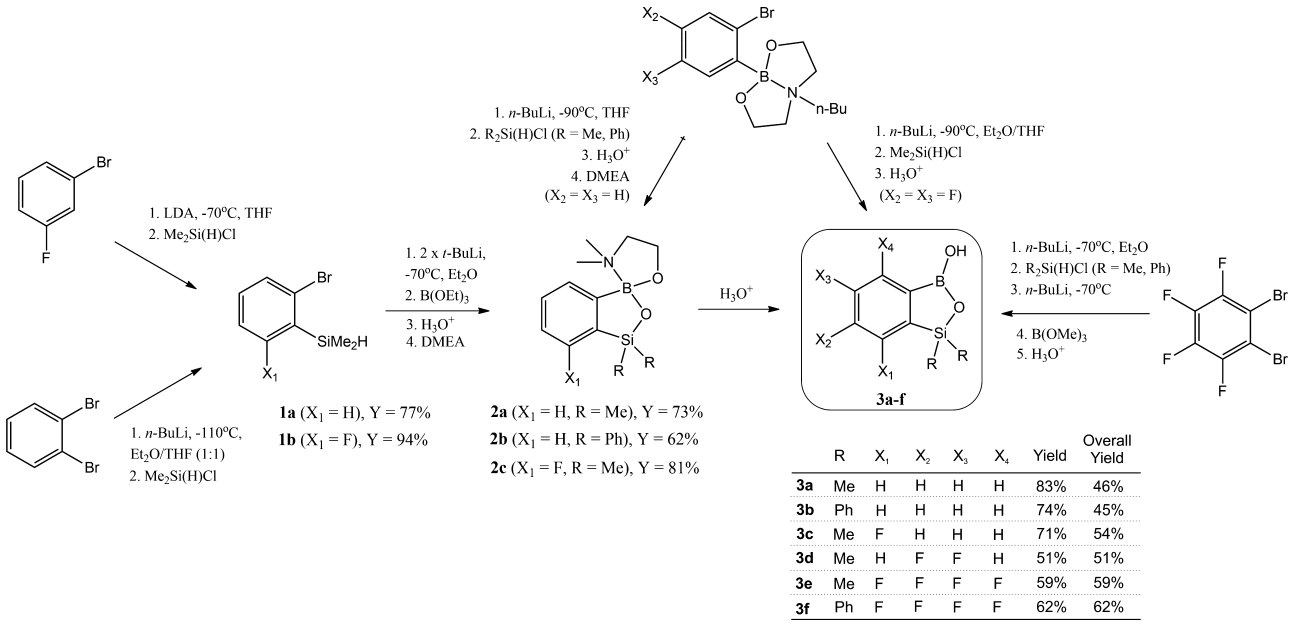
Scheme 1. Synthesis of Benzosiloxaboroles 3a–f



	R	X_1	X_2	X_3	X_4	Yield	Overall Yield
3a	Me	H	H	H	H	83%	46%
3b	Ph	H	H	H	H	74%	45%
3c	Me	F	H	H	H	71%	54%
3d	Me	H	F	F	H	51%	51%
3e	Me	F	F	F	F	59%	59%
3f	Ph	F	F	F	F	62%	62%

preparation of over 6000 benzoxaborole derivatives. However, there are only a few examples of related systems where the five-membered boraheterocycle is fused with a benzene ring. These include benziodoxaboroles[15] with a hypervalent iodine atom as a part of the borole ring, benzophosphoxaborole featuring a B–O–O–C peroxo moiety in the pinacol ring,[16] and benzoxadiboroles—cyclic semianhydrides of 1,2-phenylenediboronic acids—investigated by us in detail recently.[17] To extend chemistry to this rapidly growing area, we have turned our attention to silicon-based analogues of benzoxaboroles—benzosiloxaboroles (**II**). Herein, we report on their preparation and physicochemical characterization, including an evaluation of Lewis acidity. Specifically, the latter point is relevant to further studies on the bioanalytical applications and biological activity of these compounds.

RESULTS AND DISCUSSION

Synthesis. Two general approaches for the preparation of benzosiloxaboroles were elaborated. The first method involved the addition of $R_2Si(H)Cl$ (R = Me, Ph) to 2-(2′-lithiophenyl)-butyl-1,3,6,2-dioxazaborocan or its fluorinated analogue (both generated by Br/Li exchange reactions as described previously[17,18]) at −90 °C (Scheme 1). Alternatively, (2-bromophenyl)dimethylsilane (**1a**) and its fluorinated derivative **1b** were subjected to Br/Li exchange reactions followed by boronation. The resultant (2-(diorganosilyl)phenyl)boronates were hydrolyzed with dilute acid to give the final benzosiloxaboroles with concomitant evolution of dihydrogen. The isolation of pure siloxaboroles **3a–c** from hydrolyzed reaction mixtures was aided by the precipitation of the respective chelate complexes **2a–c** with 2-(*N*,*N*-dimethylamino)ethanol (DMAE). The formation of complex **2a** was confirmed by X-ray diffraction (Figure S54a, Supporting Information). Complexes **2a–c** can be then deprotected with dilute acid to recover the sufficiently pure products **3a–c** in good yields. 5,6-Difluorobenzosiloxaborole **3d** was obtained without the need for the isolation of an intermediate DMAE complex. 4,5,6,7-Tetrafluorobenzosiloxaboroles **3e,f** were accessible via a simple one-pot synthesis from 1,2-dibromo-3,4,5,6-tetrafluorobenzene, which implies that intermediate (2-bromo-3,4,5,6-tetrafluorophenyl)diorganosilanes were not isolated prior to the Br/Li exchange and boronation. The overall reaction yields for all studied benzosiloxaboroles were in the range 42–62%, and their structures were confirmed by multinuclear (^{1}H, ^{13}C, ^{11}B, ^{19}F) NMR spectroscopy. The ^{29}Si{^{1}H} NMR spectra were recorded for **3a,c,e** showing resonances at 22.3–23.0 ppm: i.e., in the range observed for many C_3SiO-type compounds (ca. 0–50 ppm).[19] The downfield shift with respect to the signal for the compound $(Me_3SiO)_3B$ also featuring a B–O–Si linkage (^{29}Si 12.3 ppm[20]) may be due to the strain of the five-membered silaheterocycle.

The formation of the siloxaborole heterocycle apparently occurs via an intramolecular dehydrogenative condensation in the presence of water. It was already demonstrated that the Si–H bond in arylsilanes can be activated due to an interaction with the Lewis acidic boron-based group located at the ortho position of the aromatic ring.[21] The formation of the Si–H···B bridge makes the silicon atom more susceptible to coordination with a water molecule. Thus, the elimination of H_2 can be interpreted in terms of an attack of the proton from the oxonium moiety on the hydrido ligand at the pentacoordinate silicon center according to the mechanism proposed for hydrolysis and alcoholysis of 2-(dimesitylboryl)(dimethylsilyl)-benzene.[22] However, the intramolecular cyclization leading to 5-mesityl-2,2-dimethyl-3,4-benzo-1,2,5-oxasilaboracyclopentene was a minor pathway, as it required the cleavage of a relatively inert B–mesityl bond. Hence, a dimeric species featuring the Si–O–Si linkage was formed as a major product. In contrast, the condensation of BOH and SiOH moieties is apparently favored.

It seems that the close vicinity of these groups is crucial for the formation of the siloxaborole heterocycle. This was confirmed by theoretical calculations (B3LYP/aug-cc-pVDZ), which indicate that the dehydrative cyclization leading to **3a,e** is thermodynamically favored (Table 1). A similar effect is observed for the corresponding benzoxaboroles. However, this is in contrast with the case for the thiophene-based analogue **4** (Scheme 2), where boron and silicon atoms are

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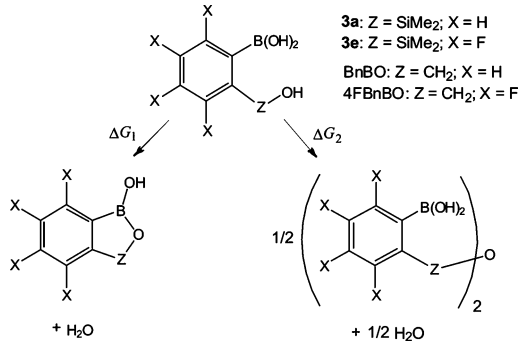
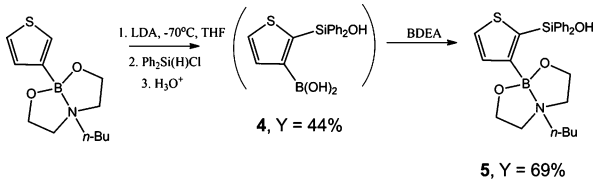
Table 1. Results of Quantum-Chemical Calculations (B3LYP/aug-cc-pVDZ) of Dehydrative Cyclization versus Dimerization in Selected Benzoxaboroles snd Benzosiloxaboroles[a]



	3a	3e	4	BnBO	4FBnBO
ΔG_1	−23.7	−29.3	10.0	−28.3	−31.2
ΔG_2	2.1	3.8	−19.4	25.2	27.0

[a] ΔG values are given in kJ/mol.

Scheme 2. Synthesis of 2-[(Hydroxy)diphenylsilyl]thiophene-3-boronic Acid 4 and Its BDEA Ester 5



more separated due to a wider angle between C−B and C−Si vectors. Thus, the cyclization through the formation of a B−O−Si linkage is disfavored in this case, as it would introduce a remarkable strain to the resulting structure. On the basis of the calculations, **4** tends to form a diboronic acid via formation of a siloxane linkage, but it could not be isolated in a well-defined form. However, we obtained its crystalline complex **5** with *N*-butyldiethanolamine (BDEA) featuring a (hydroxyl)-diphenylsilyl group (for details on its crystal structure see the Supporting Information).

The chemical integrity of siloxaborole ring in D_2O solutions was studied by performing ^1H and ^{19}F NMR analyses of **3c** over a wide range of pH (Figure 1). The ^{19}F NMR spectrum of **3c** under acidic conditions exhibits a signal at −104.3 ppm corresponding to the neutral form of **3c**. In pure D_2O the major peak at −104.3 ppm is accompanied by a less intense resonance at −106.3 ppm, which indicates that **3c** coexists in the equilibrium with its anionic form (**3c**·OH^-) in a proportion of 5:1. The ^1H NMR spectrum features broad signals of aromatic and methyl hydrogen atoms. Under weakly basic conditions (D_2O/$NaHCO_3$), the anionic form strongly prevails. In D_2O/NaOH a single ^{19}F NMR resonance of **3c**·OH^- at −105.7 ppm is observed and, accordingly, well-resolved resonances appear in the ^1H NMR spectrum. The presence of a tetracoordinate boron atom is supported by a single ^{11}B NMR resonance at 5.4 ppm. It is worth noting that no changes in the spectra were observed when the samples were analyzed after a few days, which indicates that the studied compound is quite stable in aqueous solutions over a wide range of pH.

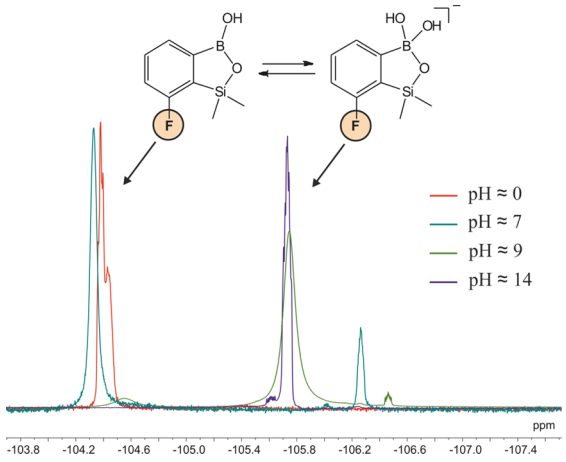
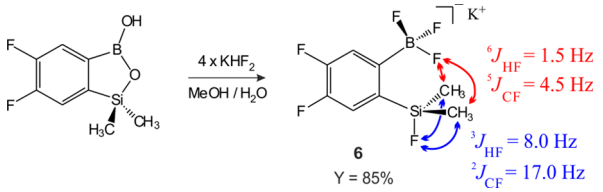


Figure 1. Superimposed ^{19}F NMR spectra of **3c** in D_2O solutions under varying pH conditions.

Cleavage of Siloxaborole Ring. It was reported that ortho-silylated phenylboranes act as bidentate Lewis acids capable of binding the fluoride anion through the formation of a B−F−Si bridge, which is driven by the high thermodynamic strength of B−F and Si−F bonds.[23] This has prompted us to investigate the interaction between the selected benzosiloxaborole **3d** and aqueous KHF_2 as a source of F^-. Specifically, it was interesting to check whether the B−O−Si linkage will be cleaved upon the addition of KHF_2. Indeed, we found that both the boron and silicon atoms were effectively fluorinated to give the fluoroborate salt [2-(FMe_2Si)-4,5-$F_2C_6H_2BF_3$]K (**6**) as the sole product in good yield (Scheme 3). The $^{29}Si\{^1H\}$ NMR

Scheme 3. Cleavage of Siloxaborole Ring in 3d with KHF_2



spectrum of **6** in acetone-d_6 shows a doublet ($^1J_{SiF}$ = 267.0 Hz) at 18.0 ppm: i.e., in the range expected for a tetracoordinate silicon atom. It is noticeable that in the ^1H NMR spectrum of **6** the signal of methyl groups appears as a doublet of quartets due to a vicinal coupling ($^3J_{HF}$ = 8.0 Hz) with the Si-bound fluorine and an apparent through-space coupling ($^6J_{HF}$ = 1.5 Hz) with the B-bound fluorine atoms. Accordingly, a doublet of quartets ($^2J_{CF}$ = 17.0 Hz, $^5J_{CF}$ = 4.5 Hz) of the methyl carbon at −0.1 ppm is observed in the ^{13}C NMR spectrum. This may suggest that the preferred conformation features intramolecular (Si)C−H···F−B contacts. It should be stressed that there is no evidence for the formation of a Si···F−B bridge even at lower temperature (−50 °C). However, the signal of BF_3^- fluorine atoms in the ^{19}F NMR spectrum becomes broad and loses its quartet structure, which may point to the partially restricted rotation of the trifluoroborate group around the C−B bond at a lower temperature. The crystal structure of **6** features the presence of two molecules in the asymmetric part of the unit cell, which differ mainly in the conformation of the $SiMe_2F$ group (Figure S55 in the Supporting Information). The first conformer supports the structure formulation based upon NMR studies with one of the fluorine atoms from the BF_3^-

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group interacting with Si-bound methyl groups ($d_{C16\cdots F2}$ = 3.135(1) Å, $d_{H16B\cdots F9}$ = 2.51 Å; $d_{C15\cdots F2}$ = 3.202(1) Å, $d_{H15C\cdots F9}$ = 2.60 Å). In the second conformer the $SiMe_2F$ group is twisted around the C−Si bond with the fluorine atom facing the BF_3^- group, which provides a stronger coordination to the potassium cation.

Crystal Structure of 3e. An analysis of the crystal structure of **3e** (Figure 2) shows that the B−C bond length is slightly

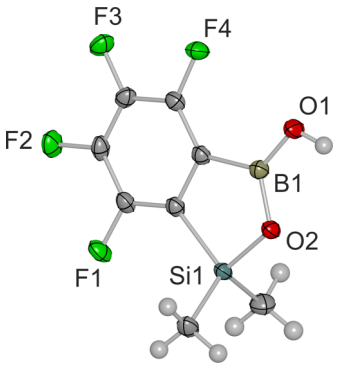

Figure 2. Molecular structure of **3e**.

longer than that in 1,3-dihydro-1-hydroxy-2,1-benzoxaborole (BnBO; 1.581(2) Å versus 1.496÷1.550 Å), whereas B−O bond lengths are slightly shorter (endocyclic, 1.388(2) Å versus 1.401−1.412 Å; exocyclic, 1.337(2) Å versus 1.348÷1.372 Å).[24] Such a discrepancy can be attributed to longer Si−O versus C−O bond lengths. This also leads to an increase in the endocyclic C−B−O bond angle (111.7(1)° in **3e**, 108.0−110.5° in BnBO), which partially alleviates the oxaborole ring strain. The increase of the endocyclic bond angle on the B atom can also be attributed to the known *gem*-dimethyl effect.[25] This is also consistent with the effect of two methyl groups at the 3-position observed for 1,3-dihydro-1-hydroxy-3,3-dimethyl-2,1-benzoxaborole (3,3-dMe-BnOB).[26] The basic structural motif in **3e** is based on centrosymmetric H-bonded dimers ($d_{O1\cdots O2}$ = 2.774(1) Å, $d_{H1\cdots O2}$ = 1.94 Å) resembling those typical of benzoxaboroles.[3]

Acidity of Benzosiloxaboroles. We have measured the pK_a values for all studied systems (**3a−f**, **4**) in water/methanol solution (1/1) and compared them with those reported for the related benzoxaboroles BnOB and 3,3-dMe-BnOB (Table 2). The pK_a of **3a** is 7.9: i.e., it is lower than that reported for 3,3-diMe-BnOB (pK_a = 8.3).[26] Apparently, the boron atom in **3a** is less saturated by the endocyclic oxygen lone pairs in comparison with 3,3-diMe-BnOB, which is likely due to the competition with the distinctive Si−O bond conjugation effect. On the other hand, **3a** is less acidic than BnOB (pK_a = 7.2),[6b,26] which could be attributed to a positive inductive effect of methyl groups. In addition, the endocyclic C−B−O angle is slightly larger than that in BnOB, which in turn disfavors ionization in aqueous solutions (i.e., acceptance of the hydroxide anion). Conversely, the introduction of electron-withdrawing phenyl groups at the silicon atom significantly increases the acidity (**3b**: pK_a = 6.8). The same effect is observed when fluorine substituents are attached to the benzene ring, as the pK_a values for mono- (**3c**), di- (**3d**), and tetrafluorinated (**3e**) derivatives are equal to 7.2, 6.8 and 4.7, respectively. Cumulation of these two effects in **3f** results in the most acidic (pK_a = 4.2) oxaborole system known to date. This is (also quantitatively) in line with our recent observations regarding a strong acidifying effect (by 3.0 pK_a units) of ring perfluorination in 1,2-phenylenediboronic acid.[17] However, it should be stressed that the formation of a siloxaborole heterocycle is crucial for the acidity enhancement. The pK_a of boronated thienylsilanol **4** was estimated to be 9.2: i.e., it is higher by 2.4 pK_a units with respect to the related compound **3b** and is comparable to the value reported for phenylboronic acid (pK_a = 8.8).[27]

Interaction of Benzosiloxaboroles with Diols. Considering the strong interest in organoboranes as receptors for biologically relevant molecules, we have determined the association constants K_s of two selected derivatives (**3c,d**) with target compounds including dopamine, monosaccharides, and adenosine and its monophosphate (AMP). For this purpose, the method proposed by Springsteen and Wang, utilizing Alizarin Red S (ARS) as a fluorescent probe, was used.[28] The results are given in Table 3. Usually **3c** exhibits a higher affinity toward all examined compounds, including ARS. Different K_s values for compounds of comparable acidity can be explained on the basis of the binding mechanism presented by Tomsho and Benkovic.[29] According to this report, related benzoxaboroles bind ARS most readily in their neutral form (while one hydroxyl group of ARS is deprotonated). Under conditions used in our studies (pH 7.0), benzosiloxaboroles **3c,d** remain in their neutral forms in amounts of ca. 60% and 40%, respectively. Although the general trend of K_s change as a function of boron atom acidity was consistent with Tomsho and Benkovic theory, the extent of the observed differences was much greater than could be expected. Moreover, the very high affinity of benzosiloxaboroles toward dopamine is surprising. Taking into account the reactivity of neutral benzosiloxaborole with catecholates, the affinity toward dopamine should be lower than that for ARS (the influence of the amine moiety seems to be insignificant, since the K_s values for both benzosiloxaborole−2-phenylethylamine (PEA) complexes are very low in comparison to those for dopamine complexes). Therefore, the mechanism of interactions between benzosiloxaboroles and diols (in particular catechols) should be further elucidated. Finally, the great differences in the affinities of benzosiloxaborole **3c,d** to ribose and related compounds (adenosine and

Table 3. Stability Constants (K_s, M^{-1}) of Complexes Formed between 3c,d and Biologically Relevant Target Compounds

	ARS	dopamine	ribose	adenosine	AMP	sorbitol
3c	7770	13700	4830	2030	4960	822
3d	4480	11600	214	214	289	680
	PEA	fructose	glucose	glucosamine		galactose
3c	362	582	45.9	711		36.3
3d	29.6	287	13.1	33.1		19.7

Table 2. Acidities (pK_a Values) of Benzosiloxaboroles Studied

	BnOB[24]	3,3-diMe-BnOB[23]	**3a**	**3b**	**3c**	**3d**	**3e**	**3f**	**4**
pK_a	7.2	8.3	7.9	6.8	7.2	6.8	4.7	4.2	9.2

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AMP) should be emphasized. This is not consistent with results reported for complexes of benzoxaboroles with AMP derivatives.[26] Therefore, the binding mechanism of ribose and its derivatives by benzosiloxaboroles seems to be significantly different from that observed for benzoxaboroles. On the other hand, the effect of increased acidity of boron atom (**3d** vs **3c**) on the binding of nitrogen-containing species (i.e., glucosamine, PEA) is related to electron donor−acceptor interactions. Upon binding hydroxyl anion, the boron atom loses its ability to bind an electron-donating nitrogen atom.

In addition, the ^{1}H NMR spectrum of an equimolar mixture of **3c** and adenosine in DMSO-d_6 revealed that complexation products exist in the equilibrium with substrates, which is manifested by the broadening of the peaks from the ribose fragment (Figures S44 and S45 in the Supporting Information). A more detailed examination of the interaction of siloxaboroles with diols will be given in due course.

Biological Activity. Further investigation has been undertaken in order to estimate the antimicrobial potency of the obtained compounds. Three (**3c−e**) of the six compounds were investigated, as the solubilities of the remaining compounds were too low. A total of 14 bacterial and 7 yeast standard strains were used in this step of the study. Minimal inhibitory concentration (MIC) and minimal bactericidal concentration (MBC) were evaluated according to CLSI and EUCAST recommendations.[30] All tested fluoro-substituted compounds showed the highest activity against bacteria from *Staphylococcus* genus: MIC range 25−100 mg/L (Table S2 in the Supporting Information). However, MBCs for tested compounds against all bacterial strains were high—over 400 mg/L. Thus, the analyzed compounds should be considered as bacteriostatic rather than bactericidal agents. On the basis of the methodology[31] it has also been proven that compounds **3c−e** were probably actively removed from Gram-negative rods by the cell wall efflux systems. On the other hand, the studied compounds (especially **3d**) are significantly more active against yeast strains than against bacteria (MIC range 0.78−200 mg/L, Table 4), which indicates their potential as antifungal agents.

Table 4. Antifungal Activity of Selected Benzosiloxaboroles

	MIC (mg/L)		
yeast strain	**3c**	**3d**	**3e**
C. albicans ATCC 90028	50	50	200
C. parapsilosis ATCC 22019	100	100	50
C. krusei ATCC 6258	50	50	200
C. quilliermondii IBA 155	12.5	6.25	50
C. tropicalis IBA 171	50	0.78	1.56
S. cerevisiae ATCC 9763	6.25	3.13	25
S. cerevisiae IBA 198	3.13	1.56	50

CONCLUSIONS

In a summary, a series of 1,3-dihydro-1,1-diorgano-1,2,3-benzosiloxaboroles was prepared using two general synthetic strategies. Irrespective of the used method, the introduction of the $SiHR_2$ group to the aromatic ring is straightforward. Furthermore, the ortho assistance of the boronic group enables the rapid hydrolytic cleavage of the Si−H bond under mild conditions. Thus, benzosiloxaboroles with diverse substitution patterns are readily accessible. On the basis of a comparison between **3a** and 3,3-diMe-BnOB, these boraheterocycles seem to be stronger Lewis acids than their nonsilicon counterparts. This can be explained by the Si−O conjugation weakening the B−O back-bonding. In addition, the Lewis acidity of benzosiloxaboroles is greatly enhanced by the fluorination of the benzene ring and by the replacement of methyl with phenyl groups at the silicon atom. Under neutral pH conditions, both studied benzosiloxaboroles **3c,d** very strongly bind dopamine. However, **3c** is a much more effective receptor for sugars and related compounds. Specifically, high K_s values were determined for the complexation of ribose and AMP. Moreover, initial screenings revealed that benzosiloxaboroles (especially **3d**) show promising antifungal activity. Hence, the potential applications of these compounds in bioanalytical and medicinal chemistry should be considered. Further work on structure−property relationships for this group of compounds is currently in progress. Specifically, it is aimed at the design of systems which could be employed as selective sensors for important bioanalytes or potent antimicrobial agents.

EXPERIMENTAL SECTION

General Comments. Solvents used for reactions were dried by heating to reflux with sodium/benzophenone and distilled under argon. Starting materials, including halogenated benzenes, trialkylborates, chlorodiorganosilanes $R_2(H)SiCl$ (R = Me, Ph), DMAE, and BDEA, were used as received without further purification. In the ^{13}C NMR spectra the resonances of boron-bound carbon atoms were not observed in most cases as a result of their broadening by a quadrupolar boron nucleus. ^{1}H, ^{13}C, and ^{29}Si NMR chemical shifts are given relative to TMS using residual solvent resonances. ^{11}B and ^{19}F NMR chemical shifts are given relative to $BF_3{\cdot}Et_2O$ and $CFCl_3$, respectively.

Synthesis. *1-Bromo-2-(dimethylsilyl)benzene (**1a**).* *n*-BuLi in hexane (2.5 M; 20.8 mL, 0.052 mol of *n*-BuLi) was added dropwise to a stirred solution of 1,2-dibromobenzene (11.8 g, 0.05 mol) in THF/Et_2O (1/1, 150 mL) at −110 °C over 1 h. The resulting white slurry was stirred for 15 min, followed by a slow addition of $Me_2(H)SiCl$ (5.4 mL, 0.052 mol) in Et_2O (5 mL). The resulting mixture was warmed to −80 °C and stirred for 15 min. The cooling bath was removed and the mixture was slowly warmed to room temperature. The resultant suspension was filtered under argon and concentrated. The oily residue was distilled under reduced pressure (bp 83−88 °C/2 Torr) to give **1a** in 77% (8.7 g) yield. ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ 7.55 (dd, J = 8.0, 1.0 Hz, 1H, Ph), 7.49 (dd, J = 7.0, 2.0 Hz, 1H, Ph), 7.30 (td, J = 7.0, 1.0 Hz, 1H, Ph), 7.24 (td, J = 8.0, 2.0 Hz, 1H, Ph), 4.55 (sp, J = 4.0 Hz, 1H, SiH), 0.46 (d, 6H, J = 4.0 Hz, $SiMe_2$) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6 MHz): δ 139.3 (Ph), 136.6 (Ph), 132.4 (Ph), 131.1 (Ph), 130.8 (Ph), 126.6 (Ph), −3.6 ($SiH(CH_3)_2$) ppm. Anal. Calcd for $C_8H_{10}BrSi$ (214.15): C, 44.87, H, 4.71. Found: C, 44.75, H, 4.63.

*1-Bromo-3-fluoro-2-(dimethylsilyl)benzene (**1b**).* A solution of 1-bromo-3-fluorobenzene (1.75 g, 10 mmol) in THF (10 mL) was added to a stirred solution of LDA (10 mmol) freshly prepared from *n*-BuLi (10 M, 1.0 mL, 10 mmol) in THF (30 mL) at −78 °C. The resultant white solution was stirred for 1 h to give a colorless precipitate. The electrophile $SiHMe_2Cl$ (0.95 g, 10 mmol) was then added to the stirred mixture to give a colorless solution, which was stirred for 1 h and then hydrolyzed with H_2O (100 mL). Dilute aqueous H_2SO_4 was added until the pH was slightly acidic. Et_2O (50 mL) was next added and the mixture was stirred for 10 min. The organic phase was separated and the aqueous phase extracted with Et_2O (20 mL). The combined organic solutions were dried over $MgSO_4$ and evaporated to give a residue which was distilled under reduced pressure (bp 60−63 °C/1 Torr) to give **1b** as a colorless liquid. Yield: 2.18 g (94%). ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ 7.34 (dd, J = 8.0, 0.5 Hz, 1H), 7.19 (td, J = 8.0, 6.5 Hz, 1H), 6.95 (td, J = 8.0, 1.0 Hz, 1H), 4.75 (sp, J = 4.0 Hz, 1H, $SiH(CH_3)_2$), 0.45 (d, J = 4.0 Hz, 6H, $SiH(CH_3)_2$). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6 MHz): δ 167.1 (d, J = 246.0 Hz), 132.1 (d, J = 10.0 Hz), 130.3 (d, J = 12.0 Hz), 128.9 (d, J = 3.0 Hz), 125.9 (d, J = 31.0 Hz), 114.0 (d, J = 27.0 Hz), −3.2

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ppm. Anal. Calcd for C_8H_9BrFSi (232.15): C, 41.39, H, 3.91. Found: C, 41.20, H, 3.68.

*3-[2-(N,N-Dimethylamino)ethanolato]-1,3-dihydro-1,1-dimethyl-1,2,3-benzosiloxaborole (**2a**). Method A.* A solution of 2-(2′-bromophenyl)-6-butyl-1,3,6,2-dioxazaborocan (16.2 g, 0.05 mol) in THF (40 mL) was added to a solution of *n*-BuLi (10 M solution in hexanes, 5.2 ml, 0.052 mol) in THF (150 mL) at −90 °C. During the addition the reaction mixture was warmed to −80 °C. After 20 min of stirring it was again cooled to −90 °C. Then $Me_2(H)SiCl$ was slowly added (5.4 mL, 0.052 mol) and a thick slurry was formed. It was warmed to −30 °C, quenched with 1.5 M aqueous H_2SO_4 to reach a pH of ca. 4−5, and stirred at room temperature until evolution of H_2 ceased. The aqueous phase was separated followed by the extraction with Et_2O (3 × 20 mL). The extracts were added to the organic phase, which was concentrated under reduced pressure. Then a solution of DMAE (5.1 mL, 0.051 mol) in Et_2O (10 mL) was added, resulting in precipitation of a white solid. It was filtered and washed with hexane (10 mL). Drying in vacuo afforded **2a** as a white powder. Mp: 131−135 °C. Yield: 6.8 g (55%). ^{1}H NMR ($CDCl_3$, 300.2 MHz): δ 7.55 (broad, 2H, Ph), 7.33 (broad, 2H, Ph), 4.2 (broad, 2H, OCH_2), 3.2 (broad, 2H, CH_2N), 2.5 (broad, 6H, NMe_2), 0.35 (broad, 6H, $SiMe_2$) ppm. ^{11}B NMR ($CDCl_3$, 96.3 MHz): δ 10.8 ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz): δ 148.7 (Ph), 131.0 (Ph), 130.0 (Ph), 128.3 (Ph), 127.3 (Ph), 59.8 (CH_2O), 58.6 (CH_2N), 45.8 ($N(CH_3)_2$), 1.0 ($Si(CH_3)_2$) ppm. HRMS (EI): calcdfor $C_{12}H_{20}BNO_2Si$ $[M]^+$ 249.1356, found 249.1364.

Method B. A solution of **1a** (2.15, 0.01 mol) in Et_2O (5 mL) was slowly added to a stirred solution of *t*-BuLi (1.7 M, 12.5 mL, 0.021 mol) in Et_2O (50 mL) at −70 °C. The lithiate was stirred for 30 min at −50 °C. Then it was cooled to −70 °C and $B(OEt)_3$ (2.4 mL, 0.014 mol) was added dropwise. The reaction mixture was hydrolyzed with H_2SO_4 (1.5 M). The workup was carried out as described for method A. Yield: 1.8 g (73%). Mp: 133−135 °C.

*3-[2-(N,N-Dimethylamino)ethanolato]-1,3-dihydro-1,1-diphenyl-1,2,3-benzosiloxaborole (**2b**).* This compound was prepared as described for **2a** (method A) using $Ph_2Si(H)Cl$ instead of $Me_2(H)SiCl$. Mp: 154−158 °C. Yield: 2.2 g (62%). ^{1}H NMR ($CDCl_3$, 300.2 MHz): δ 7.68 (m, 6H, Ph), 7.34 (m, 8H, Ph), 4.2 (broad, 2H, OCH_2), 3.2 (broad, 2H, CH_2N), 2.4 (broad, 6H, NMe_2) ppm. ^{11}B NMR ($CDCl_3$, 96.3 MHz): δ 11.2 ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz): δ 144.85 (broad, Ph), 136.66 (broad, Ph), 135.0 (Ph), 134.3 (Ph), 131.8 (Ph), 131.1 (Ph), 129.6 (Ph), 128.8 (Ph), 127.7 (Ph), 127.6 (Ph), 59.9 (broad, CH_2O), 58.8 (broad, CH_2N), 46.0 (broad, $N(CH_3)_2$) ppm. HRMS (EI): calcd for $C_{22}H_{24}BNO_2Si$ $[M]^+$ 373.1669, found 373.1660.

*3-[2-(N,N-Dimethylamino)ethanolato]-7-fluoro-1,3-dihydro-1,1-dimethyl-1,2,3-benzosiloxaborole (**2c**).* The product was prepared as described for **2a** (method B) starting with **1b** (2.32 g, 10 mmol), as colorless crystals. Yield: 2.16 g (81%). Mp: 168−169 °C. ^{1}H NMR (acetone-d_6, 400.2 MHz): δ 7.30 (m, 2H, Ph), 6.84 (td, J = 7.0, 1.5 Hz, 1H), 3.95 (broad, 2H, CH_2O), 3.18 (broad, 2H, CH_2N), 2.52 (broad, 6H, $N(CH_3)_2$), 0.27 (s, 6H, $Si(CH_3)_2$). $^{13}C\{^1H\}$ NMR (acetone-d_6, 100.6 MHz): δ 165.5 (d, J = 241.0 Hz, Ph), 133.8 (d, J = 31.0 Hz, Ph), 131.5 (d, J = 6.0 Hz, Ph), 128.2 (Ph), 113.3 (d, J = 25.0 Hz, Ph), 60.2 (CH_2O), 59.0 (CH_2N), 45.8 ($N(CH_3)_2$), 1.2 ($Si(CH_3)_2$) ppm. ^{19}F NMR (acetone-d_6, 376.5 MHz): δ −103.54. ^{11}B NMR (acetone-d_6, 96.3 MHz) δ 11.4 ppm. HRMS (EI): calcd for $C_{12}H_{19}BFNO_2Si$ $[M]^+$ 267.1262, found 267.1256.

*1,3-Dihydro-3-hydroxy-1,1-dimethyl-1,2,3-benzosiloxaborole (**3a**).* **2a** (2.5 g, 0.01 mol) was dissolved in Et_2O (20 mL), and H_2SO_4 (1.5 M) was added dropwise to reach pH 2. The reaction mixture was refluxed for 30 min. After the mixture was cooled to room temperature, the water phase was separated and washed with Et_2O (4 × 5 mL). The organic phases were combined and concentrated under reduced pressure to give **3a** as a colorless viscous oil. Yield: 1.5 g (83%). ^{1}H NMR ($CDCl_3$, 400.1 MHz): δ 7.85 (m, 1H, Ph), 7.63 (m, 1H, Ph), 7.49 (m, 2H, Ph), 6.03 (broad, 1H, B−OH), 0.46 (s, 6H, $Si(CH_3)_2$) ppm. ^{11}B NMR ($CDCl_3$, 96.3 MHz): δ 30.9 ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz): δ 149.9 (Ph), 131.7 (Ph), 130.9 (Ph), 130.5 (Ph), 129.8 (Ph), −0.4 ($Si(CH_3)_2$) ppm. $^{29}Si\{^1H\}$ NMR ($CDCl_3$, 99.3 MHz): δ 22.3 ppm. HRMS (EI): calcd for $C_{16}H_{20}B_2O_3Si_2$ $[M]^+$ 338.1137 (diboroxane formed upon dehydration), found 338.1143.

*1,3-Dihydro-3-hydroxy-1,1-diphenyl-1,2,3-benzosiloxaborole (**3b**).* This compound was prepared as described for **3a**. A crystalline solid was obtained. Mp: 163−165 °C. Yield: 2.23 g (74%). ^{1}H NMR ($CDCl_3$, 300.2 MHz): δ 7.89 (m, 1H, Ph), 7.80 (m, 1H, Ph), 7.67 (dd, J = 8.0, 1.5 Hz, 4H, $SiPh_2$), 7.54 (m, 2H, Ph), 7.40 (m, 6H, $SiPh_2$), 5.07 (broad, 1H, OH) ppm. ^{11}B NMR ($CDCl_3$, 96.3 MHz): δ 32.4 ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz): δ 146.8 (Ph), 134.9 (Ph), 132.5 (Ph), 131.9 (Ph), 131.6 (Ph), 131.2 (Ph), 130.8 (Ph), 130.1 (Ph), 128.1 (Ph), 127.6 (Ph) ppm. HRMS (EI): calcd for $C_{18}H_{15}BO_2Si$ $[M]^+$ 302.0934, found 302.0939.

*7-Fluoro-1,3-dihydro-3-hydroxy-1,1-dimethyl-1,2,3-benzosiloxaborole (**3c**).* This compound was prepared as described for **3a**, starting with **2c** (2.67 g, 10 mmol). The product was isolated as a white crystalline solid. Yield: 1.39 g (71%). Mp: 109−110 °C. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 7.63 (dd, J = 7.0, 2.5 Hz, 1H, Ph), 7.48 (m, 1H, Ph), 7.10 (t, J = 7.0 Hz, 1H, Ph), 6.47 (br, 1H, B−OH), 0.52 (s, 6H, $Si(CH_3)_2$). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 164.7 (d, J = 245.0 Hz, Ph), 143.2 (br, Ph), 134.5 (d, J = 30.5 Hz, Ph), 132.7 (d, J = 7.0 Hz, Ph), 127.5 (d, J = 3.0 Hz, Ph), 117.2 (d, J = 24.5 Hz, Ph), −0.7 ($Si(CH_3)_2$) ppm. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −104.70 ppm. ^{11}B NMR ($CDCl_3$, 96.3 MHz): δ 29.9 ppm. $^{29}Si\{^1H\}$ NMR ($CDCl_3$, 99.3 MHz): δ 22.4 ppm. ^{19}F NMR (376.5 MHz, D_2O + HCl, pH ∼0): δ −104.35 (**3c**) ppm. ^{19}F NMR (376.5 MHz, D_2O, pH ∼7): δ −104.33 (**3c**, 85%), −106.26 (**3c**·OH^-, 15%) ppm. ^{19}F NMR (376.5 MHz, D_2O + $NaHCO_3$, pH ∼9): δ −104.55 (**3c**, 7%), −105.75 (**3c**·OH^-, 93%) ppm. ^{19}F NMR (376.5 MHz, D_2O + NaOH, pH ∼14): δ −105.72 (**3c**·OH^-) ppm. HRMS (EI): calcd for $C_8H_{10}BFO_2Si$ $[M]^+$ 196.0527, found 196.0533.

*5,6-Difluoro-1,3-dihydro-3-hydroxy-1,1-dimethyl-1,2,3-benzsiloxaborole (**3d**).* A solution of 2-(2′-bromo-4′,5′-difluorophenyl)-6-butyl-1,3,6,2-dioxazaborocan[17b] (3.66 g, 10 mmol) in THF (15 mL) was added to a previously prepared solution of *n*-BuLi (10 M solution in hexanes, 1.10 mL, 11 mmol) in Et_2O (80 mL) at −90 °C. After 20 min of stirring $Me_2(H)SiCl$ (1.3 mL, 12 mmol) was slowly added to the resulting grayish suspension and a clear colorless solution was formed. This was then warmed gradually to −20 °C, which resulted in a white, thick slurry. It was quenched with H_2SO_4 (1.5 M) to pH 4 and stirred at room temperature until hydrogen evolution ceased. The water phase was separated followed by extraction with Et_2O (2 × 20 mL). The extracts were added to the organic phase, which was concentrated under reduced pressure, to give a white waxy residue. It was crystallized from hexane (20 mL) to give **3d** as a white powder. Mp: 69−71 °C. Yield: 1.1 g (51%). ^{1}H NMR (300.2 MHz, $CDCl_3$): δ 7.62 (dd, J = 10.0, 7.5 Hz, 1H, Ph), 7.38 (dd, J = 10.0, 7.5 Hz, 1H, Ph), 0.47 (s, 6H, $Si(CH_3)_2$) ppm. ^{11}B NMR ($CDCl_3$, 96.3 MHz): δ 30.3 ppm. ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 153.0 (dd, J = 256.0, 13.0 Hz, Ph), 152.1 (dd, J = 256.0, 13.0 Hz, Ph), 147.0 (Ph), 120.1 (d, J = 14.5 Hz, Ph), 119.0 (d, J = 15.1 Hz, Ph), −0.7 ($Si(CH_3)_2$) ppm. ^{19}F NMR ($CDCl_3$, 375.5 MHz): δ −134.12 (ddd, J = 17.0, 11.5, 8.5 Hz), −135.90 to −136.14 (m) ppm. HRMS (EI): calcd for $C_8H_9BF_2O_2Si$ $[M]^+$ 214.0433, found 214.0425.

*4,5,6,7-Tetrafluoro-1,3-dihydro-3-hydroxy-1,1-dimethyl-1,2,3-benzosiloxaborole (**3e**).* 1,2-Dibromo-3,4,5,6-tetrafluorobenzene (6.2 g, 0.02 mol) was dissolved in Et_2O (50 mL) and cooled to −70 °C. Then *n*-BuLi (2.8 M solution in hexanes, 7 mL, 0.02 mol) was added dropwise and the reaction mixture turned green. Subsequently, $Me_2(H)SiCl$ was added (2.2 mL, 0.02 mol) followed by the addition of another portion of *n*-BuLi (2.8 M, 7 mL, 0.02 mol) and THF (5 mL). After 30 min of stirring at −60 °C, $B(OMe)_3$ (2.2 mL, 0.02 mol) was added and the reaction mixture was warmed to −30 °C, quenched with 1.5 M aqueous H_2SO_4 to reach the pH 2−3, and stirred at room temperature until evolution of H_2 ceased. The aqueous phase was separated followed by extraction with Et_2O (2 × 20 mL). The extracts were added to the organic phase, which was concentrated under reduced pressure. Then hexane (20 mL) was added and a white solid precipitated. It was filtered, washed with hexane (2 × 5 mL), and dried in vacuo to give **3e**. Mp: 112−115 °C. Yield: 2.95 g (59%). ^{1}H NMR

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($CDCl_3$, 300.2 MHz): δ 5.17 (broad, 1H, B−OH), 0.53 (s, 6H, $Si(CH_3)_2$) ppm. ^{11}B NMR ($CDCl_3$, 96.3 MHz): δ 28.8 ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz): δ 149.8 (ddd, J = 254.0, 9.5, 3.0 Hz, Ph), 148.1 (ddd, J = 245.0, 9.5, 2.0 Hz, Ph), 143.3 (dddd, J = 75.0, 19.0, 13.0, 2.5 Hz, Ph), 140.8 (dddd, J = 71.0, 19.0, 13.0, 2.5 Hz, Ph), 130.4 (d, J = 30 Hz, Ph), −1.0 ($Si(CH_3)_2$) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz): δ −128.0 (ddd, J = 24.0, 21.5, 5.5 Hz, 1F), −131.5 (td, J = 21.5, 5.5 Hz, 1F), −149.0 (ddd, J = 24.0, 18.0, 5.5 Hz, 1F), −151.3 (ddd, J = 21.5, 18.0, 5.5 Hz, 1F) ppm. $^{29}Si\{^1H\}$ NMR ($CDCl_3$, 99.3 MHz): δ 23.0 ppm. HRMS (EI): calcd for $C_8H_7BF_4O_2Si$ $[M]^+$ 250.0245, found 250.0235.

*4,5,6,7-Tetrafluoro-1,3-dihydro-3-hydroxy-1,1-diphenyl-1,2,3-benzsiloxaborole (**3f**).* This compound was prepared as described for **3e** using $Ph_2(H)SiCl$ instead of $Me_2(H)SiCl$. The obtained crude product was contaminated with the byproduct *n*-$BuB(OH)_2$. It was purified by recrystallization from $CHCl_3$/hexane (10 mL, 1/1) to afford a white crystalline solid. Mp: 82−84 °C. Yield: 2.2 g (62%). ^1H NMR ($CDCl_3$, 300.2 MHz): δ 7.68 (m, 4H, Ph), 7.51 (m, 2H, Ph), 7.43 (m, 4H, Ph), ppm. ^{11}B NMR ($CDCl_3$, 96.3 MHz): δ 29.1 ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz): δ 150.0 (dd, J = 256.0, 8.0 Hz, Ph), 148.5 (dd, J = 246.5, 7.5 Hz, Ph), 143.8 (dddd, J = 18.5, 15.5, 12.5, 2.5 Hz, Ph), 141.2 (dddd, J = 19.0, 15.5, 12.5, 2.0 Hz, Ph), 134.6 (d, J = 0.5 Hz, $SiPh_2$), 131.6 ($SiPh_2$), 130.0 ($SiPh_2$), 128.4 ($SiPh_2$), 128.3 (d, J = 12.5 Hz, Ph) ppm. ^{19}F NMR ($CDCl_3$, 282.4 MHz): δ −124.56 (ddd, J = 23.5, 21.0, 6.0 Hz, 1F), −130.85 (td, J = 21.0, 7.5 Hz, 1F), −147.71 (ddd, J = 23.5, 18.0, 7.5 Hz, 1F), −150.08 (ddd, J = 21.5, 18.0, 6.0 Hz, 1F) ppm. HRMS (EI): calcd for $C_{18}H_{11}BF_4O_2Si$ $[M]^+$ 374.0558, found 374.0572.

*2-[(Hydroxy)diphenylsilyl]thiophene-3-boronic Acid (**4**).* A solution of 6-butyl-2-[3′-thienyl]-1,3,6,2-dioxazaborocan (1.75 g, 0.03 mol) in THF (10 mL) was added to a stirred solution of LDA (0.031 mol) freshly prepared from *n*-BuLi (10 M, 3.1 mL, 0.031 mol) in THF (50 mL) at −78 °C. The resultant colorless solution was stirred for 1 h to give a colorless precipitate. The electrophile $Ph_2(H)SiCl$ (7.94 g, 0.032 mol) was then added to the stirred mixture to give a colorless solution, which was warmed to −30 °C, quenched with 1.5 M aqueous H_2SO_4 to reach a pH of ca. 4−5, and stirred at room temperature until evolution of H_2 ceased. The aqueous phase was separated, followed by extraction with Et_2O (3 × 20 mL). The extracts were added to the organic phase, which was concentrated under reduced pressure to give the product as a viscous oil. Yield: 4.31 g (44%). ^1H NMR ($CDCl_3$, 300.2 MHz): δ 7.70−7.60 (m, 4H, Ph), 7.49−7.31 (m, 8H, Ph, Th), 2.32 (broad, 2H, B−OH) ppm. ^{11}B NMR ($CDCl_3$, 96.3 MHz): δ 29.0 ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz): δ 135.0 (Ph), 131.8 (Th), 131.3 (Th), 130.0 (Ph), 129.7 (Ph), 127.9 (Ph), 127.7 (Th) ppm. Anal. Calcd for $C_{16}H_{15}BO_3SSi$ (326.25): C, 58.90, H, 4.63. Found: C, 58.59, H, 4.91.

*6-Butyl-2-[2′-((hydroxy)diphenylsilyl)-3′-thienyl]-1,3,6,2-dioxazaborocan (**5**).* A solution of *N*-butyldiethanolamine (0.58 g, 0.005 mol) in diethyl ether (5 mL) was added to a stirred solution of **4** (1.53 g, 0.005 mol) in Et_2O (10 mL). A white crystalline precipitate was formed, and the resulting suspension was stirred for 1 h at room temperature. The crystalline product was collected by filtration, washed with Et_2O (2 × 5 mL), and dried to give **5**. Yield: 1.18 g (69%, 1.55 g). Mp: 105−108 °C. ^1H NMR ($CDCl_3$, 300.2 MHz): δ 7.71 (dd, J = 8.0, 1.5 Hz, 4H, Ph), 7.56 (d, J = 4.5 Hz, 1H, Th), 7.40 (d, J = 4.5 Hz, 1H, Th), 7.46−7.32 (m, 6H, Ph), 4.19−3.93 (m, 4H, CH_2O), 2.77 (m, 2H, CH_2N), 2.66 (broad, 2H, H_2O, SiOH), 2.34 (m, 2H, CH_2N), 2.07 (m, 2H, $NCH_2CH_2CH_2CH_3$), 1.19 (m, 2H, $NCH_2CH_2CH_2CH_3$), 1.04 (m, 2H, $NCH_2CH_2CH_2CH_3$), 0.82 (t, J = 7.0 Hz, 3H, $NCH_2CH_2CH_2CH_3$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz): δ 135.5 (Th), 135.4 (Th), 135.0 (Ph), 129.9 (Ph), 129.2 (Ph), 127.8, 127.4 (Th), 59.6 (CH_2O), 56.0 (CH_2N), 54.5 ($NCH_2CH_2CH_2CH_3$), 29.1 ($NCH_2CH_2CH_2CH_3$), 20.5 ($NCH_2CH_2CH_2CH_3$), 14.0 ($NCH_2CH_2CH_2CH_3$) ppm. ^{11}B NMR ($CDCl_3$, 96.3 MHz): δ 11.1 ppm. Anal. Calcd for $C_{24}H_{30}BNO_3SSi$ (451.46): C, 63.85, H, 6.70. Found: C, 63.61, H, 6.44.

*Potassium [2-(Fluorodimethylsilyl)phenyl]trifluoroborate (**6**).* A saturated aqueous solution of KHF_2 (0.117 g, 1.5 mmol) was added to a stirred solution of **3d** (0.064 g, 0.3 mmol) in MeOH (1 mL) at room temperature. After ca. 5 min a white solid precipitated; it was filtered off, washed with diethyl ether (2 × 1 mL), and dried in vacuo to give the title compound. Mp: 303−305 °C. Yield: 0.075 g (85%). ^1H NMR (acetone-d_6, 300.2 MHz): δ 7.40−7.30 (m, 2H), 0.41 (dq, J = 8.0, 1.5 Hz, 6H, $Si(CH_3)_2$) ppm. ^{11}B NMR (acetone-d_6, 96.3 MHz): δ 2.9 (q, J = 50 Hz) ppm. $^{13}C\{^1H\}$ NMR (acetone-d_6, 100.6 MHz): δ 150.4 (dd, J = 247.0, 11.5 Hz, Ph), 148.1 (dd, J = 243.0, 12.5 Hz, Ph), 136.4 (d, J = 14.5 Hz, Ph), 120.5 (dd, J = 12.5, 8.0 Hz, Ph), 119.8 (d, J = 11.5 Hz, Ph), −0.1 (dq, J = 17.0, 4.5 Hz, $Si(CH_3)_2$) ppm. ^{19}F NMR (acetone-d_6, 282.4 MHz): δ −136 (m, 3F, BF_3K), −143.3 (m, 1F, Ph), −147.6 (m, 1F, Ph), −157.3 (sp, J = 8.0 Hz, 1F, $SiF(CH_3)_2$) ppm. $^{29}Si\{^1H\}$ NMR (acetone-d_6, 99.3 MHz): δ 18.0 (d, J = 267.0 Hz). ^1H NMR (acetone-d_6, 300.2 MHz, T = −50 °C): δ 7.37−7.27 (m, 2H), 0.37 (m, 6H, $Si(CH_3)_2$) ppm. ^{19}F NMR (acetone-d_6, 282.4 MHz, T = −50 °C): δ −135.9 (broad, 3F, BF_3K), −142.6 (m, 1F, Ph), −146.6 (m, 1F, Ph), −157.3 (sp, J = 8.0 Hz, 1F, $SiF(CH_3)_2$) ppm. $^{29}Si\{^1H\}$ NMR (acetone-d_6, 99.3 MHz, T = −50 °C): δ 18.5 (d, J = 266.0 Hz) ppm. Anal. Calcd for $C_8H_8BF_6KSi$ (296.13): C, 32.45, H, 2.72. Found: C, 32.22, H, 2.61.

Structural Measurement and Refinement Details. A single crystal of **3e** was measured at 100 K on a SuperNova diffractometer equipped with an Atlas detector (Cu Kα radiation, λ = 1.54184 Å). X-ray diffraction data sets for single crystals of **2a**, **5**, and **6** were collected at 100 K on a SuperNova diffractometer equipped with an Eos CCD detector (Mo Kα radiation, λ = 0.71073 Å). Data reduction and analysis were carried out with the CrysAlisPro program.[32] All structures were solved by direct methods using SHELXS-97 and refined using SHELXL-2013.[33] All non-hydrogen atoms were refined anisotropically. CCDC depository numbers: 1047174 (**2a**), 1047175 (**3e**), 1047176 (**5**), 1400000 (**6**).

*Crystal data for **2a**:* $C_{12}H_{20}BNO_2Si$, M_r = 249.19 au; triclinic; $P\bar{1}$; a = 8.853(1) Å, b = 8.961(1) Å, c = 17.416(1) Å, α = 77.09(1)°, β = 89.02(1)°, γ = 86.32(1)°, V = 1344.0(2) Å^3; d_{calc} = 1.231 g cm^{-3}; μ = 0.16 mm^{-1}; Z = 4; $F(000)$ = 536; number of collected/unique reflections (R_{int} = 6.3%) 20831/7336, $R[F]/R_w[F]$ ($I \geq 3\sigma(I)$) = 6.5%/14.0%, $\Delta\varrho_{res}$(min/max) = +0.69/−0.45 e Å^{-3}.

*Crystal data for **3e**:* $C_8H_7BF_4O_2Si$, M_r = 250.04 au; triclinic; $P\bar{1}$; a = 7.059(1) Å, b = 8.246(1) Å, c = 9.243(1) Å, α = 85.36(1)°, β = 86.53(1)°, γ = 85.64(1)°, V = 533.9(1) Å^3; d_{calc} = 1.555 g cm^{-3}; μ = 2.37 mm^{-1}; Z = 2; $F(000)$ = 252; number of collected/unique reflections (R_{int} = 1.9%) 6978/2208, $R[F]/R_w[F]$ ($I \geq 3\sigma(I)$) = 3.4%/9.7%, $\Delta\varrho_{res}$(min/max) = −0.36/+0.46 e Å^{-3}.

*Crystal data for **5**:* $C_{24}H_{30}BNO_3SSi$, M_r = 451.45 au; orthorhombic; $P2_12_12_1$; a = 11.393(1) Å, b = 12.124(1) Å, c = 16.833(1) Å, V = 2325.0(1) Å^3; d_{calc} = 1.290 g cm^{-3}; μ = 0.22 mm^{-1}; Z = 4; $F(000)$ = 960; number of collected/unique reflections (R_{int} = 3.4%) = 46116/9589, $R[F]/R_w[F]$ ($I \geq 3\sigma(I)$) = 3.3%/8.6%, $\Delta\varrho_{res}$(min/max) = +0.36/−0.21 e Å^{-3}.

*Crystal data for **6**:* 2•$C_8H_8BF_6KSi$, M_r = 296.16 au; orthorhombic; $P2_12_12_1$; a = 7.0742(1) Å, b = 10.7508(2) Å, c = 15.0965(4) Å, V = 1136.15 (4) Å^3; d_{calc} = 1.731 g cm^{-3}; μ = 0.62 mm^{-1}; Z = 2; $F(000)$ = 592; number of collected/unique reflections (R_{int} = 2.1%) 25149/9326, $R[F]/R_w[F]$ ($I \geq 3\sigma(I)$) = 2.5%/6.5%, $\Delta\varrho_{res}$(min/max) = +0.53/−0.27 e Å^{-3}.

Computational Methods. All geometry optimizations and frequency calculations were carried out with the GAUSSIAN09 suite of programs[34] and B3LYP functional[35] using aug-cc-pVDZ[36] basis sets. The minima were confirmed by vibrational frequency calculations within the harmonic approximation (no imaginary frequencies). In optimization processes no symmetry constraints were applied.

Determination of Stability Constants of Complexes Formed between Organoboron Derivatives (OB) and Selected Target Compounds (TC). Fluorescence measurements were taken with a Synergy Mx Microplate Reader (BioTek Instruments Inc.). pH Measurements were performed using an MA 234 pH/Ion Analyzer (Mettler Toledo). Three stock solutions have been prepared. Solution A contained 90 μM ARS in 0.01 M HEPES buffer, while solutions B and C contained 4.5 mM of compounds **3c**,**d**, respectively, both in 0.01 M HEPES buffer. The pH of all solutions was adjusted to 7.0 using 3 M NaOH. Solution D was prepared by 10-fold dilution of solution A with an appropriate volume of solution B adequate to

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obtain a 50-fold molar equivalent of **3c** with respect to ARS. Solution E was prepared in the same manner, except for the use of solution C instead of B, and the molar excess of **3d** was 100-fold. Both solutions were diluted with 0.01 M HEPES buffer, and the pH was adjusted to 7.0. Solutions D and E were mixed with different volumes of 9 μM ARS (0.01 M HEPES buffer, pH 7.0) to obtain a series of solutions with a fixed concentration of ARS and various concentrations of OB (i.e., various molar ratios of OB to ARS). The fluorescence spectra were taken after assessing an optimal excitation wavelength for both solutions D and E, i.e., 468 and 440 nm, respectively. The maximum fluorescence intensities were plotted against the concentration of both OBs (Figures S63 and S64 in the Supporting Information) in order to assess the optimal concentration of OBs (0.45 and 0.72 mM for **3c,d**, respectively) during further studies. The stability constants of OB-ARS complexes K_1 have been calculated according to the Benesi–Hildebrand method by dividing an intercept by a slope in the $1/\Delta F$ vs $1/C_{BC}$ plot (Figure S65 in the Supporting Information). Every point taken into calculations was an average of measurements made for four individual solutions. The stability constants of OB-TC complexes K_s were determined by the titration of an OB-ARS complex solution with a chosen TC. Solutions F and G containing 0.45 and 0.72 mM of compounds **3c,d**, respectively, 9 μM ARS, and a portion of TC were obtained. The added portions of TC were tuned to reduce the fluorescence intensity to the level of 25–35% of the value obtained for an original solution. The series of solutions with fixed OB and ARS concentration and a range of TC concentrations were prepared by mixing solutions D and E with solutions F and G in various ratios, respectively. The fluorescence spectra were recorded as described above for determination of K_1 constants. As previously, each point taken for calculations was an average of four individual measurements. The K_s values were calculated by plotting $[TC_0]/P$ vs Q, where $[TC_0]$ is the total concentration of TC, Q is a quotient of concentrations of free and bound ARS (calculated from fluorescence data), and P is defined by the equation

$$P = [L_0] - \frac{1}{K_1 Q} - \frac{[I_0]}{1 + Q}$$

where $[L_0]$ is the total OB concentration, $[I_0]$ is the total ARS concentration, and K_1 is the stability constant of the OB-ARS complex. K_s is calculated by dividing K_1 by the slope of the plot $[TC]_0/P$ vs Q (Figure S51 in the Supporting Information).

■ ASSOCIATED CONTENT

Supporting Information

Figures, a table, and CIF files giving details of X-ray crystallographic, computational, and solution multinuclear NMR studies, acidity constant measurements, interactions with selected bioanalytes, and antimicrobial activity. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.organomet.5b00265.

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Notes

The authors declare no competing financial interest.

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