Perketals **2a**, **3a**, **4a**, **5a**, and **7a** are deprotected to the corresponding hydroperoxides (**2b**–**7b**) in high yield upon acidic solvolysis.[7] Enantiomeric excesses were determined after quantitative ketalization of the hydroperoxides with the 2-propenyl ether of (−)-*trans*-2-phenylcyclohexanol.[6] The ratio of diastereomeric perketals is easily quantified by ^{1}H NMR or RP-HPLC.[6] In all cases, the produce hydroperoxides are found to be >95% ee.

Our preliminary studies clearly show that the stereoselective synthesis of optically active dienyl hydroperoxides is possible through construction of C=C double bonds in the presence of a masked peroxide. Investigations into the application of this new transformation towards the synthesis of HPETEs and other diene hydroperoxide natural products are in progress.

Caution. Although we have not encountered any specific dangers in the course of this work, standard precautions for handling peroxides (avoidance of heat, light, or metal salts, work behind shields, use of a stabilizer[11]) should be followed whenever possible.

Acknowledgment. We thank the University of Nebraska Research Council, the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the American Cancer Society (CN-33) for financial support. We thank Chara Schryvers (Mount Marty College) for her assistance during a 1991 internship. Mass spectra were obtained by Mr. Cliff Jacoby at the Midwest Center for Mass Spectroscopy, supported by the NSF (CHE-8620177).

Supplementary Material Available: Spectroscopic and analytical data for compounds **1**, **2a**–**c**, **3a**–**c**, **4a**–**c**, **5a**–**c**, **6a**–**c**, and **7a**,**b** (10 pages). Ordering information is given on any current masthead page.

Specific Complexation with Mono- and Disaccharides That Can Be Detected by Circular Dichroism

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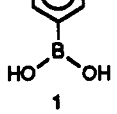
Summary: For the development of receptor molecules that can recognize sugar molecules, we newly synthesized 2,2′-dimethoxydiphenylmethane-5,5′-diboronic acid (**2**). It was shown that in the presence of **2**, D-glucose, D-maltose, D-cellobiose, and D-lactose result in a CD band at 275 nm. The results indicate that the CD spectroscopic method using **2** as a receptor molecule serves as a new sensory system for sugar molecules.

The development of receptor molecules that can precisely recognize and specifically bind guest molecules has been the focus of much recent attention.[1,2] In the design of such artificial receptor molecules, hydrogen-bonding interactions play a central role.[3-8] For example, Rebek et al.[3] synthesized model receptors that have carboxylate functions in a molecular cleft. Hamilton et al.[4] synthesized macrocyclic receptors that feature a 2,6-diaminopyridine unit as a recognition site. It was recently demonstrated that recognition through the hydrogen-bonding interactions is also effective for sugars and cyclodextrins.[9,10] However, more precise molecular recognition may be achieved through the formation of covalent bonds rather than through noncovalent interactions. It is known that boronic acids form cyclic esters with saccharides, particularly with those including *cis*-diol groups.[11] Wulff et al.[12] demonstrated that certain saccharide molecules are precisely recognized by two benzeneboronic acids immobilized in polymer matrices. In this paper, we report the specific complexation of benzeneboronic acid derivatives **1** and **2** with mono- and disaccharides. One can expect that these compounds will become CD (circular dichroism) active only when they form "specific" complexes with saccharide molecules.



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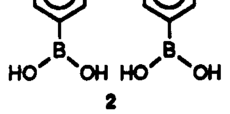

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Compounds **1** and **2** were synthesized by the treatment of *p*-bromoanisole and bis(2-methoxy-5-bromophenyl)-

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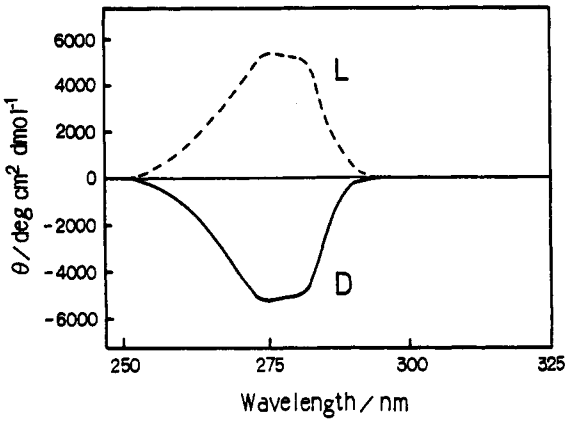


Figure 1. CD spectra for D-glucose (solid line) and L-glucose (dotted line): [glucose] = 0.10 mol dm^{-3}, [2] = 2.00 × 10^{-3} mol dm^{-3}, pH 11.3 with 0.10 mol dm^{-3} of Na_2CO_3, 25 °C.

methane, respectively, with *n*-butyllithium followed by the reaction with trimethyl borate. The products were identified on the basis of IR and NMR spectral evidence and elemental analysis.[13] A methanol solution (20 μL) containing 1 or 2 was injected into an aqueous solution (1000 μL) containing saccharide molecules (0.10 mol dm^{-3}, pH 11.3 with 0.10 mol dm^{-3} of Na_2CO_3). After 1 h, the CD spectra were measured at 25 °C.

The mixtures of saccharide molecules and 1 did not give any perceptible CD band in the UV region (above 220 nm). In the presence of 2, in contrast, certain saccharide molecules gave rise to a CD band at 275 nm (Figure 1), which was the same wavelength as the absorption maximum (λ_{max} 275 nm). Among monosaccharides tested herein,[14] only glucose (3) was CD-active.[15] As shown in Figure 1, D and L isomers afforded symmetrical CD spectra (θ_{275} −5300 for D-glucose and +5300 for L-glucose). To specify where 2 forms covalent bonds with 3 we examined methyl α-D-glucoside (4; R = CH_3, X = CH_2OH), D-xylose (4; R = H, X = H), and D-glucose-6-phosphate (4; R = H, X = $CH_2OPO_3^{2-}$) as reference compounds for 3. It was found that none of them are CD-active. The results indicate *cis*-1,2-diol and *trans*-4-OH·5-CH_2OH are essential for complexation with 2. In fact, we could construct a molecular model without any steric distortion for the cyclic complex between 2 and α-D-glucopyranose (the 1,2-diol is cis; Figure 2). The ^1H NMR spectrum of the 2·D-glucose complex also supports the structure in Figure 2.[16] On the other hand, the construction of molecular models with the cyclic structure for other monosaccharides was impossible or at least accompanied serious steric distortion. Thus, *cis*-1,2-diol and *trans*-4-OH·5-CH_2OH are prerequisites for the formation of CD-active complexes.

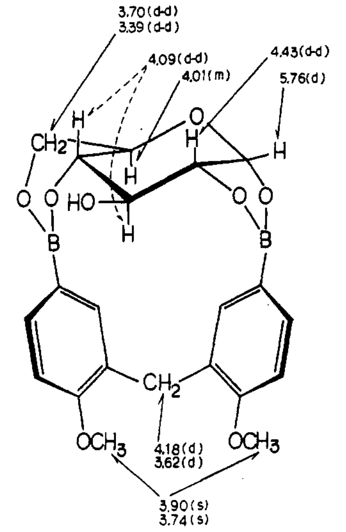
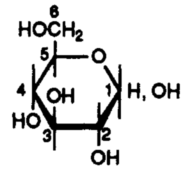


Figure 2. Structure of the 2·α-D-glucopyranose complex. The numbers indicate chemical shifts of the ^1H NMR spectrum. The splitting pattern is shown in the parentheses. One of the 3-H and 4-H protons is overlapped with HDO, so that the peak at 4.09 ppm is assigned either to 3-H or to 4-H. The J_{HH} = 3.72 Hz for 1-H and 2-H indicates that these two protons are fixed to a gauche conformation (i.e., D-glucopyranose adopts the α-form). For details of the measurement conditions, see ref 16.

Table I. Stoichiometry and Association Constants (25 °C)[a]

	CD spectra			
saccharide	λ_{max} (nm)	θ_{max} (deg cm^2 dmol^{-1})	stoichiometry	*K* (dm^3 mol^{-1})
D-glucose	275	−5300	1:1	19000
D-maltose	275	−2400	1:1	100
D-cellobiose	275	−2000	1:1	80
D-lactose	275	−1200[b]	1:1	15

[a] [2] = 2.00 × 10^{-3} mol dm^{-3}, [D-glucose] = (0.50–5.00) × 10^{-3} mol dm^{-3}, [other saccharides] = 0.01–0.1 mol dm^{-3}. [b] An upper limit of the solubility of D-lactose is 0.20 mol dm^{-3}, where 75% of D-lactose exists as the complex and θ_{obsd} = −900 deg cm^2 dmol^{-1}. The value in this table is calculated assuming the formation of the 100% complex.



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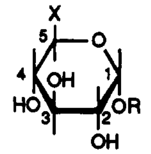

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We measured CD spectra of four disaccharides in the presence of 1 and 2.[17] Again, 1 was ineffective. In the presence of 2, on the other hand, D-maltose (5), D-cellobiose (6), and D-lactose (7) showed a negative CD band at 275 nm. The CD activity for 5 and 6 is readily explained on the basis of the prerequisites proposed for 3: the molecules have *cis*-1,2-diol and *trans*-4-OH·5-CH_2OH required for the complexation with 2. In fact, we could construct molecular models for the complexes including two covalent bonds between these diols and boronic acids. D-Lactose, which showed a relatively weak CD band, is exceptional. We consider that *cis*-3,4-diol is used for the complexation with one benzeneboronic acid moiety in 2.

From plots of θ vs [saccharide] we determined stoichiometry and association constants (*K*). The results are

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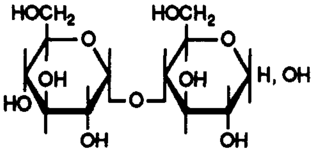
(13) 1 (isolated as boronic anhydride), mp 210–212 °C. Anal. Calcd for $C_7H_7O_2B$: C, 62.78; H, 5.23. Found: C, 62.79; H, 5.28. 2, mp 177–180 °C. Anal. Calcd for $C_{15}H_{18}O_6B_2 \cdot 0.1H_2O$: C, 56.71, H, 5.73. Found: C, 56.67: H, 5.80.

(14) D-Glucose, D–mannose, D–galactose and D–fructose were used.

(15) When the complex between 2 and D-glucose was left in a buffered (pH 11.3) solution, the CD band disappearance gradually. The θ_{max} value was about half after 1 day and one-third after 3 days. This is attributed to base-catalyzed isomerization and decomposition of D-glucose. However, the CD spectra were reproducible within the experimental error at least for 6 h after mixing.

(16) ^1H NMR ([2] = 0.010 mol dm^{-3}, [D-glucose] = 5.6 × 10^{-3} mol dm^{-3}, D_2O (containing 2 vol % DMSO-d_6, pD 11.7 with NaOD, internal standard DSS) δ 3.39 and 3.70 (2 H, d-d, 6-CH_2), 3.62 and 4.18 (2 H, d-d, $ArCH_2Ar$), 3.74 and 3.90 (3 H each, s each OCH_3), 4.01 (1 H, m, 5-CH), 4.09 (1 H, d-d, 3-CH or 4-CH, one of these two protons is overlapped with HDO), 4.43 (1 H, d-d, 2-CH), 5.76 (1 H, d, 1-CH), 6.95, 6.96, 7.13, 7.32, 7.40 (1 H, 1 H, 2 H, 1 H, 1 H, respectively, d, d, s, d, d, respectively, ArH). This spectrum is consistent with the structure proposed as in Figure 2. In addition to these peaks for the 2·D-glucose complex, those for free 2 were also observed.

(17) D-Maltose, D-cellobiose, D-lactose, and D-saccharose were used.



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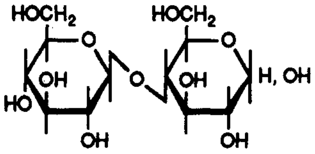

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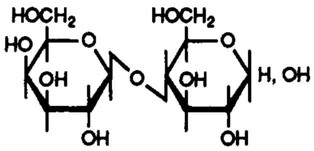

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summarized in Table I. It is seen from Table I that these saccharides from 1:1 complexes with 2 and the θ_{max} values are correlated with the K values: the larger the θ_{max}, the greater the K.

Why does only 2 afford the CD-active complexes? Compound 1 should also form complexes with saccharides, but they are all CD silent. Compound 2 can form a cyclic structure through the two-site binding (as shown in Figure 2). Conceivably, the ring structure would freeze the molecular motion of chromophoric benzene moieties in 2. This situation is favorable for the appearance of a CD band.[18] The explanation is compatible with the fact that the complexes with disaccharides, the rings of which are more flexible because of a central ether linkage, result in the smaller K values.

In conclusion, we believe that the present CD spectroscopic method serves as a new, promising sensory system for sugar molecules. Particularly, the finding that the CD spectrum is observed only when the ring-structured molecular models can be made is useful for predicting the configuration of sugar molecules.

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Supplementary Material Available: Experimental procedures for the preparation of 1 and 2 and the determination of association constants (2 pages). Ordering information is given on any current masthead page.

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$Sn(OTf)_2$-Promoted Addition of 1-Alkynes to Aldehydes

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Summary: 1-Alkynes add to aldehydes and ketones in the presence of $Sn(OTf)_2$ and an amine giving acetylenic alcohols in high yields.

The addition of metal acetylides to aldehydes is one of the most important transformations in organic synthesis, and alkali or alkali-earth metal derivatives have been generally employed for this purpose.[1] The basic nature of these reagents and the requirement of strong bases such as alkylmetals or metal amides for their generation, however, sometimes causes base-induced side reactions. In order to overcome these problems, several improved methods have been developed. For example, B,[2] Al,[3] Ce,[4] V,[5] and Mn[6] acetylides, which have been generated by transmetalation of Li, Na, or Mg acetylides, add to aldehydes and ketones. The addition reactions of Si[7] and Sn derivatives[8] were conducted in the presence of a Lewis acid or fluoride ion. 1-Haloalkynes have been added to aldehydes in the presence of $CrCl_2$.[9] Although the acetylide addition reaction can be achieved under milder conditions by these methods, the process is often not straightforward. If reactive metal acetylides could be formed from 1-alkynes with amine bases, such a method would provide a novel and useful synthetic tool. In fact, copper or palladium acetylides have been generated with amine bases,[10] although these species are not reactive enough to add to aldehydes.[11] It seemed to us that the proper selection of a metal salt in combination with an amine base might allow generation of metal acetylides that are reactive enough to add to C═O bonds. We have found

Scheme I

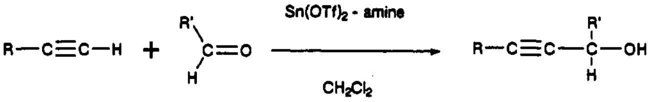

Table I. The Addition of 1-Alkynes to Aldehydes Promoted by $Sn(OTf)_2$ and Amines

R	aldehyde	method[a]	yield[b] (%)
Ph	c-C_6H_{11}	A	87, 74,[c] 70[d]
	t-BuCHO	A	81
	n-C_4H_9CHO	A	66
	PhCHO	A	66
	$PhCH_2CH_2CHO$	A	86
p-$MeOC_6H_4$	c-C_6H_{11}	A	91
PhCH═CH	c-C_6H_{11}	A	82
$PhCH_2CH_2$	*t*-BuCHO	B	64
	n-C_4H_9CHO	C	89
	$PhCH_2CH_2CHO$	C	71
n-C_5H_{11}	c-C_6H_{11}	B	76
	t-BuCHO	B	70
	$PhCH_2CH_2CHO$	C	57

[a] The reactions were carried out with $Sn(OTf)_2$ (1 mmol), amine (1 mmol), 1-alkyne (1 mmol), and aldehyde (0.33 mmol) by method A, B, or C (see text), unless otherwise noted. [b] Isolated yields are shown. All new compounds gave satisfactory ^1H NMR ^{13}C NMR, and IR spectra are elementary analyses either by HRMS or combustion. [c] The reaction was carried out with 15 mmol of the nucleophile and 5 mmol of aldehyde. [d] Two equivalents of the nucleophile was used.

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