of MO theory clearly cannot make quantitiative predictions for reactions that will undoubtably involve differential solvation of the various species studied. Nevertheless, MO theory can be quite useful for identifying those instances where competing reaction paths might be of similar energies and suggesting what changes in reaction design might be successful in changing the relative importance of the different pathways.

Acknowledgment. This work was supported in part by grants from the City University of New York PSC-CUNY Research Award Program CA-37359 from the National Cancer Institute, DHHS, and CH-272 from the American Cancer Society.

Registry No. 1, 50-46-4; **2a**, 96649-31-9; **2b**, 96649-32-0; **2c**, 96649-33-1; **3a**, 96666-24-9; **3b**, 96666-25-0; **3c**, 96666-26-1.

Regiospecific A,B Capping onto β-Cyclodextrin. Characteristic Remote Substituent Effect on ^{13}C NMR Chemical Shift and Specific Taka-amylase Hydrolysis

Iwao Tabushi* and Tatsuya Nabeshima

Department of Synthetic Chemistry, Kyoto University, Sakyo-ku, Kyoto, 606 Japan

Kahee Fujita,† Atsuo Matsunaga,† and Taiji Imoto†

Faculty of Pharmaceutical Sciences, Kyushu University, Maedashi, Fukuoka, 812 Japan

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A,B-regiospecific (97% A,B and 3% A,C) capping of β-cyclodextrin was first achieved by the use of *m*-benzenedisulfonyl chloride. The A,B regiochemistry is ascertained by a remarkable effect of a remote substituent of ring A on the high-field ^{13}C NMR chemical shift of ring B. Further support for the A,B structure is obtained by its specific hydrolysis to disubstituted fragmental sugars catalyzed by Taka-amylase. The novel cap was converted to a series of A,B-disubstituted β-cyclodextrins—diiodo, dideoxy, bis(butylsulfenyl), bis(phenylsulfenyl), and bis((*p*-*tert*-butylphenyl)sulfenyl). Characteristic remote chemical shifts in 100-MHz ^{13}C NMR were observed for these A,B derivatives, the C_6, C_4, and C_1 shifts of which were extremely useful for the differentiation of an A,B regioisomer from other regioisomers. Noteworthy is the remarkable chemical shift difference thus produced between C_6, C_4, and C_1 on the A ring and C_6, C_4, and C_1 on the B ring, providing an interesting possibility of spectroscopic determination of clockwise and counterclockwise A,B structure.

A basic principle showing how enzyme activity develops may be given by eq 1. For preparation of an artificial

(enzyme activity) = (guest recognition)[1] + (multifunctional catalysis) + (local environment) (1)

multifunctional catalyst having certain specific enzymic activity, specific three-dimensional arrangement of two (or more) functional groupings is necessary and important. The geometrical arrangement may be classified into the limiting conformations, *E*, *R*, and *Z*, shown in Figure 1.

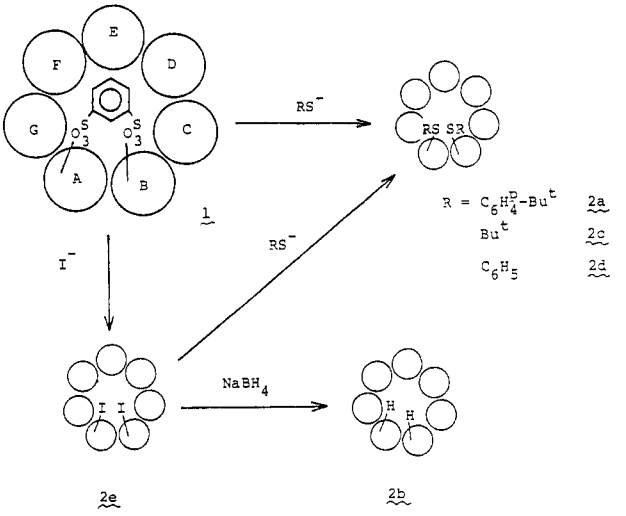
Disubstituted β-cyclodextrins have been used successfully as artificial enzymes.[2] The cyclodextrin cavity provides an effective recognition site as well as an appropriate local environment and the functional groups provide an effective catalytic site. Disubstituted β-cyclodextrins were conveniently prepared through regiospecific bifunctionalization at A,C[3a,c] or A,D[3] positions (see Scheme I), which are close to the *R* and *E* regiochemistry, respectively.

We now report that regiospecific A,B bifunctionalization is achieved in good preparative yield by use of *m*-benzenedisulfonyl chloride as the capping reagent. The A,B cap should be a good starting material for the preparation of a variety of artificial enzymes each of which has functional groups on the primary rim in the *Z* regiochemistry.

Results and Discussions

The A,B cap, **1**, was prepared from *m*-benzenedisulfonyl chloride and dry β-CD in dry pyridine. Practically pure **1** was obtained in 40% preparative yield. Precaution must be taken not to use too much (≫30 mol %) of the A,B capping reagent, which easily leads to the formation of double caps and a triple cap in a nearly statistical ratio. When an appropriate amount of the capping reagent is used, the A,B capping is found to be a convenient and efficient procedure.

Scheme I. A,B Regiospecific Functionalization of β-Cyclodextrin



†Responsible for Taka-amylase-catalyzed hydrolysis.

(1) (a) Tabushi, I. *Tetrahedron*, **1984**, *40*, 269. (b) Tabushi, I. *Acc. Chem. Res.* **1982**, *15*, 66. (c) Bender, M. L.; Komiyama, M. "Cyclodextrin Chemistry"; Springer-verlag: New York, 1978.

(2) (a) Breslow, R.; Doherty, J. B.; Guillot, G.; Lipey, C. *J. Am. Chem. Soc.* **1978**, *100*, 3227. (b) Breslow, R.; Bovy, P.; Hersh, C. L. *Ibid.* **1980**, *102*, 2115. (c) Tabushi, I; Kuroda, Y.; Mochizuki, A. *Ibid.* **1980**, *102*, 1152. (d) Tabushi, I.; Kuroda, Y. *Ibid.* **1984**, *106*, 4580.

(3) (a) Tabushi, I.; Kuroda, Y.; Yokota, K.; Yuan, L. C. *J. Am. Chem. Soc.* **1981**, *103*, 711. (b) Tabushi, I.; Yuan, L. C. *Ibid.* **1981**, *103*, 3574. (c) Tabushi, I.; Yamamura, K.; Nabeshima, T. *Ibid.* **1984**, *106*, 5267.

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Table I. ^{13}C NMR Chemical Shifts ($CDCl_3$, Me_4Si) of β-Cyclodextrin Derivatives (JEOL JNM GX 400)

	C_1	C_4	C_2	C_3, C_5	C_6
per Si β-CD	102.647	82.094	75.003	72.192 71.949	61.997

	C_1, C_1'	C_2, C_2'	C_3, C_3', C_5	C_4	C_4'	C_5'	C_6'	other C atoms 1	other C atoms 2
per Si A,B (t-BuS)$_2$CD (**3c**)	102.2–103.2	74.5–75.4	71.3–72.7	81.5–82.5	86.09 86.24	69.95 70.13	61.6–62.3	41.42 41.71	31.06 31.23
per Si A,D (t-BuS)$_2$CD (**4c**)	102.2–103.4	74.6–75.3	71.3–72.6	81.6–82.4	86.45	70.10 70.14	61.5–62.3	41.48	31.15 31.17
per Si A,B Me_2CD (**3b**)	102.0–103.8	74.2–75.4	71.5–72.7	81.5–83.0	89.7–90.7	66.4–67.5	61.4–62.6		
per Si A,D Me_2CD (**4b**)	101.7–104.0	74.2–75.5	71.1–72.8	81.6–83.0	89.7–90.3	66.3–67.1	61.3–62.7		

	C_1	C_4	C_2	C_3, C_5	C_6
β-CD[a]	102.969	82.586	74.074	73.448 73.066	60.959

	C_1, C_1'	C_2, C_2', C_3, C_3', C_5	C_4'	C_5'	C_6	C_6'	other C atoms 1	other C atoms 2
A,B (t-BuS)$_2$CD[a] (**2c**)	102.4–103.4	72.8–74.3	82.0–82.8	85.08 85.62	71.41 71.58	60.5–61.2	42.32 42.52	31.80 31.92
A,D (t-BuS)$_2$CD[a] (**6a**)	102.2–103.6	73.0–74.3	81.9–82.8	86.10	71.91	60.4–61.2	42.51	31.82

[a] Measured in Me_2SO-d_6 (Me_4Si, external).

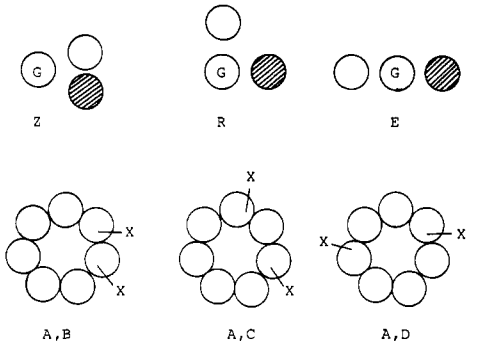
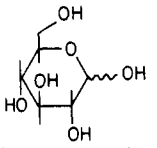


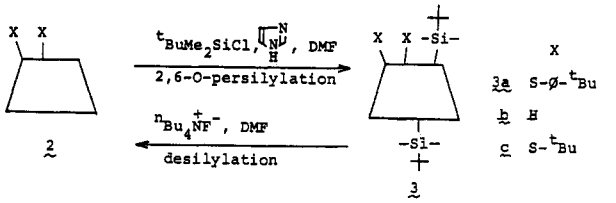
Figure 1. Limiting geometrical arrangement of functional groupings in enzyme active sites and CDs. *Former notation* (those accepted in Chemical Abstracts) for glucose rings of β-cyclodextrin is for a view from the secondary side. However, a view from the primary side is more convenient to draw a detailed glucose structure; this usually depicts a primary OH as a top and secondary OH as a bottom.



Therefore a *new notation system* is adopted in which the glucoses are named A, B, C, D, E, F, and G rings, respectively, counterclockwise and viewed from the primary hydroxyl side. A systematic nomenclature becomes necessary since A,B and B,A (or A,G) regioisomers have now been prepared and characterized by us, where A and B are different. Abbreviations: G for a guest molecule bound to enzymes; A, R, and E are for zusammen, rechtwinkelig, and entgegen, respectively.

The cap structure is supported by IR (1370 and 1160 cm^{-1} for sulfonate, 815, 685 cm^{-1} for *m*-phenylene), TLC (R_f 0.48, SiO_2, *n*-PrOH–AcOEt–H_2O–NH_3 (aqueous) = 5:3:3:1, anisaldehyde detection as well as UV detection), and 400-MHz ^1H NMR. The substitution at the primary position is ascertained for a series of cyclodextrin derivatives obtained from the present cap by use of the ^1H and ^{13}C NMR (see Table I). The skeletal structure is ascertained also by 100-MHz ^{13}C NMR and mass spectra after

Scheme II



chemical conversion to other cyclodextrin derivatives (vide infra). Regiochemistry of disubstituted β-cyclodextrin is usually very difficult to determine.[4] A,B regiochemistry was determined after conversion to the corresponding dideoxy or disulfenyl derivatives.

Conversion of **1** to the corresponding dideoxy derivative **2b**[3a] was carried out via the $NaBH_4$ reduction of the corresponding diiodide **2e**[3a] and to bis((*p*-*tert*-butylphenyl)-sulfenyl) **2a**, bis(*tert*-butylsulfenyl) **2c**, or bis(phenylsulfenyl) derivative **2d** directly or via **2e** (Scheme I).

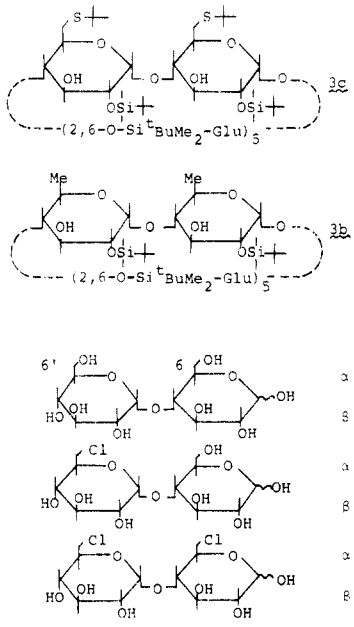
Like other cyclodextrins, the present cyclodextrin derivatives are not easily obtained in pure states through single column chromatography. Efficiency of chromatographic separation becomes high when these cyclodextrins are persilylated. Thus, silylation[5,6b] of **2a**, **2b**, and **2c** was carried out with *t*-$BuMe_2SiCl$ in DMF at 80 °C to give the corresponding persilylated compounds, **3a**, **3b**, and **3c**, respectively (Scheme II). Pure regioisomers of the silylated compounds were readily and effectively obtained through column chromatography (silica gel, eluted by chloroform). The persilylated products were very soluble in aprotic solvents, such as hexane, AcOEt, Et_2O, or $CHCl_3$, slightly soluble in alcohol, and insoluble in H_2O. They readily decompose under acidic conditions, but are quite stable under basic conditions. ^1H NMR spectra and elemental analysis clearly indicated that five primary C_6 and seven secondary C_2 hydroxyl groups of the cyclodextrin derivatives were silylated by the reaction with *t*-$BuMe_2SiCl$. A,B-disubstituted cyclodextrin derivatives **2a–c** were obtained by desilylation of the purified per-

(4) Boger, J., Brenner, D. G.; Knowles, J. R. *J. Am. Chem. Soc.* **1979**, *101*, 7630. Regiochemistry of disubstituted β-cyclodextrins can not be determined well by their information.

(5) Wife, R. L.; Reed, D. E.; Leworthy, D. P.; Barnett, D. M.; Regan, P. D.; Volger, H. C. First International Symposium on Cyclodextrins, Budapest, 1981, p 301.

(6) (a) Treatment of the silylated β-CDs with tetra-*n*-butylammonium fluoride in DMF at room temperature gave the corresponding desilylated compounds. (b) Michalski, T. J.; Kendler, A.; Bender, M. L. *J. Inclusion Phenom.* **1983**, *1*, 125.

Table II. Substituent Effect on ^{13}C NMR Schemical Shift (ppm)[a]



	C_{6A}	C_{6B}[1]
3c	30.00	30.23
3b	17.74	17.91

	C_6'	C_6[2]
α	61.7	62.0
β		61.8
α	45.4	62.1
β		61.9
α		46.1
β	45.6	45.6

[a] (1) Chemical shifts of C_{6A} and C_{6B} may be the opposite of that shown in $CDCl_3$. (2) In D_2O. See ref 16.

silylated compounds (Scheme II). The desilylation[6] proceeded smoothly, giving pure A,B-disubstituted β-CD's quantitatively. The purity was checked by NMR spectra and HPLC analysis. The skeletal structure of a series of the cyclodextrin derivatives is ascertained by 100-MHz ^{13}C NMR (see Table I) and mass spectra. ^{13}C NMR chemical shifts observed for a series of A,B-disubstituted β-CD demonstrate two characteristics supporting the skeletal structure (see Table I): (i) Carbon atoms on the A and B ring experience remarkable remote substituent effects (vide infra). (ii) Carbon atoms on other rings behave normally as cyclodextrin units. 100-MHz ^{13}C NMR and enzyme-catalyzed hydrolysis are the most powerful tools for determination of A,B regiochemistry. Most useful in the ^{13}C NMR is the remote (A ⇄ B) ^{13}C chemical shift. The chemical shifts were appreciably affected by the remote *tert*-butylsulfenyl or any other substituent on the A (or B) ring for the C_1, C_4, and C_6 positions of B (or A) ring of prim,prim-A,B-disubstituted β-cyclodextrins, respectively. ^{13}C NMR chemical shift was reported as a useful tool for structure determination of cyclodextrin derivatives only in simple cases.[3a,4,5,6b,7] In the present example, 25- or 50-MHz ^{13}C NMR (by using 100- and 200-MHz NMR apparatus, respectively) are not useful for the remote chemical shift study. However, by use of a 400-MHz NMR apparatus (JEOL JNM FX 400) satisfactory analysis of a ^{13}C chemical shift becomes possible (see Tables I and II). Evidently, ^{13}C chemical shifts of C_1, C_4, and C_6 on the glucose ring bearing substituent X_B are remarkably affected by the substituent X_A on A ring (hereafter, carbons

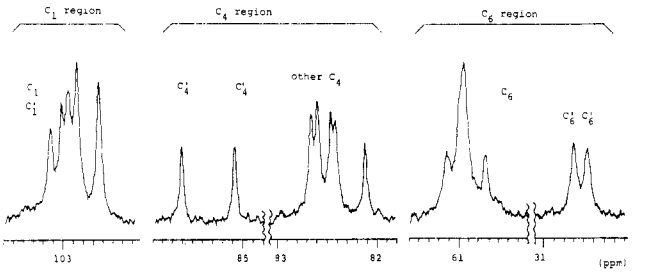


Figure 2. 100-MHZ ^{13}C NMR spectrum (C_1, C_4, C_6) of A,B-(*t*-BuS)$_2$-CD (**2c**) (in Me_2SO-d_6, Me_4Si).

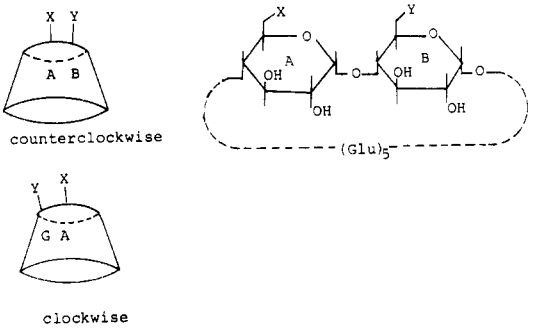


Figure 3. Pseudoenantiomers of unsymmetrically A,B-disubstituted cyclodextrin. Clockwise and counterclockwise orientations.

Table III. Influence of a Substituent at One Glucose Ring on ^{13}C NMR Chemical Shifts of Another Substituted Ring

	A,B-(*t*-BuS)$_2$CD (**2c**)	A,D-(*t*-BuS)$_2$CD (**6a**)
C_1	−0.04 ± 0.11[a]	0.01 ± 0.03[a]
C_4	−0.62 ± 0.27	0.13 ± 0.0
C_6	−0.08 ± 0.07	0.08 ± 0.0

[a] C_{1A} and C_{1B} (or C_{1D}) are assigned tentatively by a additivity rule.[17]

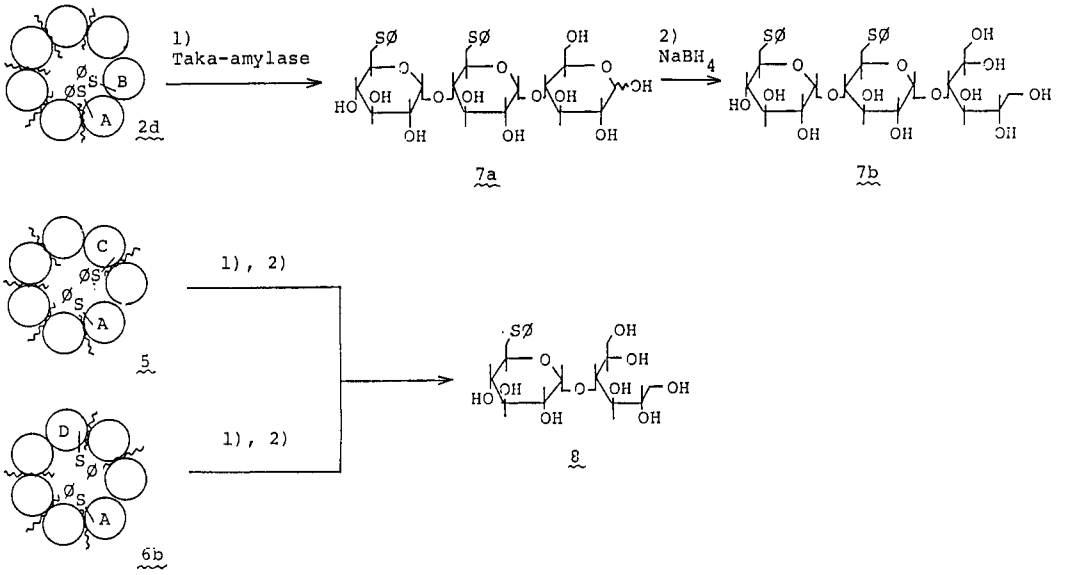
of glucose rings bearing a substituent are designated by C′$_i$), while the C_1, C_4, and C_6 ^{13}C shifts on other rings are only slightly affected by X_A. As a result, a clear chemical shift difference of 0.54 ppm between C′$_4$ on A ring and B ring for *tert*-butylsulfenyl is now observed for prim,prim-A,B-bis(*tert*-butylsulfenyl)-β-CD (see Figure 2 and Table III). While for A,D-(*t*-BuS)$_2$-CD (**4c**), the splitting of the C′$_4$ absorption was practically nonexistent within the precision of the digital resolution limit (0.00607 ppm for the present apparatus, see Table I). Similar trends are also observed for C′$_5$, C′$_6$, and also for other substituents. For A,C regioisomers, the ^{13}C NMR spectra are very similar to the corresponding A,D isomers. In conclusion remote substituent effects on the ^{13}C NMR chemical shift by use of high-field NMR are very useful to determine the A,B regiochemistry except for extremely crowded derivatives. The remarkable remote chemical shifts observed for the present A,B isomers are in the same order of magnitude as the chemical shifts observed for C_6 of prim,prim-disubstituted maltose (Table II), again strongly supporting the A,B regiochemistry.

The regiochemistry is further supported by our Taka-amylase-catalyzed hydrolysis of A,B-bis(phenylsulfenyl)-β-CD (**2d**), followed by the $NaBH_4$ reduction to give **7b** as one of the major products (see Scheme III). The structure of **7b** was supported by FAB mass and NMR spectra. FAB MS indicates that **7b** is a disubstituted reduced trisaccharide[8] (*m/e* 713 ([M + Na]$^+$, 0.59%), 690

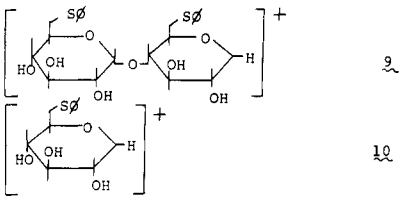
(7) (a) Tabushi, I.; Kuroda, Y.; Shimokawa, K. *J. Am. Chem. Soc.* **1979**, *101*, 1614. (b) Takeo, K.; Hirose, K.; Kuge, T. *Chem. Lett.* **1973**, 1233. (c) Bergern, R. J.; Meeley, M. P.; Mochida, Y. *Bioorg. Chem.* **1976**, *5*, 121. (d) Harada, A.; Furue, M.; Nozakura, S. *Macromolecules* **1976**, *9*, 701. (e) Siegel, B.; Pinter, A.; Breslow, R. *J. Am. Chem. Soc.* **1977**, *99*, 2309. (f) Gagnair, D.; Mancier, D.; Vincendon, M. *Org. Magn. Reson.* **1978**, *11*, 344. (g) Boger, J.; Corcoran, R. J.; Lehn, J.-M. *Helv. Chim. Acta* **1978**, *61*, 2190. (h) Szejtli, J.; Liptàk, A.; Jodàl, I.; Fügedi, P.; Nànasi, P.; Neszmélyi, A. *Starch/Staerkè* **1980**, *32*, 165. (i) Tabushi, I.; Yuan, L. C.; Shimikawa, K.; Yokota, K.; Mizutani, T.; Kuroda, Y. *Tetrahedron Lett.* **1981**, *22*, 2273. (j) Ueno, A.; Breslow, R. *Ibid.* **1982**, *23*, 3451. (k) Czarnik, A. W.; Breslow, R. *Carbohydr. Res.* **1984**, *128*, 133.

(8) (a) Omichi, K.; Matsushima, Y. *J. Biochem.* **1978**, *84*, 835. (b) Melton, L. D.; Slessor, K. N. *Can. J. Chem.* **1973**, *51*, 327.

Scheme III



(M+, 0.17), 509 (9, 2.8), 255 (10, 37)). The 400-MHz ^1H NMR spectrum also indicates the presence of two phenyl groups and 10 hydroxyl groups. Moreover, the 100-MHz ^{13}C NMR spectrum is consistent with the proposed structure containing a sugar alcohol[9] part and two substituents on the A and B rings (see Experimental Section).



Compound 8 was not obtained as one of the major products (the ratio of 8 to **7b** was less than 7/100 by HPLC analysis) in the reduction of **7a**. On the other hand, A,C- and A,D-bis(phenylsulfenyl)-β-CDs (**5** and **6**) were converted to 8 as one of the major products in a similar treatment (the observed ratios of 8 to the corresponding triose are more than 100/1.8 and 100/1.9, respectively, by HPLC analysis). The present results on the Taka-amylase hydrolysis also suggest a possibility of convenient structural determination of the regioisomers including clockwise/counterclockwise isomerism.

The A, B regiochemistry is also supported by comparison with the known A,C and A,D regioisomers.[3] The qualitative as well as quantitative analysis of the regiochemistry are also conveniently made by HPLC by using A,C- and A,D-bis((*p-tert*-butylphenyl)sulfenyl)-B-CDs relevantly prepared[3c] and observed retention volume (11.6, 13.0, and 15.2 min for the A,B, A,D, and A,C isomer, respectively; CH_3CN/H_2O = 3.5/1, 2.0 mL/min, 900 psi carbohydrate column[3c]). The observed regioselectivity of the present A,B capping was; AB:AC:AD = 97:3:negligible, which is satisfactorily high for the regiospecific preparation of A,B-disubstituted β-cyclodextrin in a large quantity.

The present A,B-regiospecific capping is compared with recently reported procedures[10] for random preparation of the regioisomers in Table IV. A much higher preparative yield and also a simpler isolation procedure (see Table IV) are advantages of the present capping reaction over random functionalization. Thus, the novel regiospecific A,B difunctionalization of β-cyclodextrin at the primary positions is concluded to be a versatile preparative procedure. Application of the technique to preparation of a variety of artificial enzymes is now in progress in our group.

Experimental Section

Instruments and Apparatus. ^1H NMR spectra were recorded on a JEOL PMX-60, a JEOL FX 100, or a JEOL JNM-GX 400 spectrometer. ^{13}C NMR spectra were recorded on JEOL FX 100 or JEOL JNM-GX 400. The chemical shifts are given in δ values from Me_4Si in $CDCl_3$. in Me_2SO-d_6, ^{13}C NMR spectra were obtained with a coaxial dual cell. The inner tube (5φ) contained 1% Me_4Si in $CDCl_3$, which was used as external standard by taking the chemical shift of the central peak of $CDCl_3$ from Me_4Si as 77.02 ppm. The outer tube (10φ) contained a Me_2SO-d_6 solution of a cyclodextrin derivatives. IR spectra were obtained by using a Hitachi Model 260-50 spectrophotometer. Electronic absorption spectra were measured with a Union Giken high-sensitivity spectrophotometer SM 401. FAB mass spectral data were provided at the Faculty of Pharmaceutical Sciences, Kyushu University. Elemental analyses were performed by the Microanalytical Laboratory of Kyoto University. Thin-layer chromatography (TLC) was carried out on 0.25-mm E. Merck precoated silica gel plates (60F-254). Spot detection was carried out by UV light and/or staining with 0.45% anisaldehyde in MeOH–AcOH–H_2SO_4 (860:90:45, V/V).[11] E. Merck silica gel-60 (70–230 mesh) was used for silica gel column chromatography. E. Merck Lobar Prepacked column (LiChroprep RP-8 (40–63 μm) prepacked column, size B (310-25)) was used for reversed-phase column chromatography. High-performance liquid chromatography (HPLC) was performed analytically on a Waters Model 6000 instrument with a carbohydrate analysis column (3.9 mm × 30 cm, Waters p/n 84038), or on a Hitachi 635A with a TSK GEL LS-410 ODS SIL column (4 × 300 nm, 5 μm), made in Toyo Soda Japan.

Materials. Commercially available β-cyclodextrin (Ando Kasei Industry) was used after recrystallization from water and was dried in vacuo (<0.1 mmHg) at 80–90 °C at least for 12 h by using a liquid N_2 trap and/or a P_2O_5 trap. Pyridine (Nakarai Chemicals Co. Ltd.) was purified by refluxing over KOH for 12 h, then over extremely anhydrous BaO[3c] at least 12 h, and finally distilled just before use.[12] Dimethylformamide was kept standing over CaH_2 overnight and then distilled under reduced pressure before use.[13]

(9) Kieboom, A. P. G.; Toorn, J. M. van der; Bekkum, H. van *Recl. Trav. Chim. Pays-Bas* **1977**, *86*, 35.
(10) Fujita, K.; Matsunaga, A.; Imoto, T. *J. Am. Chem. Soc.* **1984**, *106*, 5740.
(11) "Handbook of Chromatography"; Zweig, G., Sherma, J., Eds.; CRC Press: Cranwood Parkway, 1972; Vol. 1, p 127.
(12) Riddick, J. A.; Bunger, W. B. In "Techniques of Chemistry: Organic Solvent"; Weissberger, A., Ed.; Wiley-Interscience: New York, 1970; Vol. 2, p 826.

Table IV. Comparison of Random Difuctionalization and Regiospecific Difunctionalization

functionalization procedure	yield of A,B isomer, % based on modifying reagent used	yield of A,B isomer, % based on β-CD used	products in column chromatography[c]	relative mole ratio
			mono-T_s-CD	63
tosylation[a] (random)	7.6 (1.7)[b]	9.0 (7.3)[b]	di-Ts-CD[d]	26.0 (total), 3 isomers
			A,B	8.3
			A,C	9.1
			A,D	8.6
			tri-T_s-CD	7.6 (total), 5 isomers
			A,B,C	
			A,B,E	
			A,C,E	
			A,B,D	
			A,B,F	
			tetra-T_s-CD	2.6 (total), 5 isomers
			A,B,C,D	
			A,B,C,F	
			A,B,D,F	
			A,B,C,E	
			A,B,D,E	
present capping (regiospecific)			monocap	91 (total)
			A,B	88
	40	13	A,C	3
			double cap	ca. 9 (total), 2 isomers
			A,B;C,D	
			A,B;D,E	

[a] Mole ratio of the modifying reagent to β-cyclodextrin was 1.7:1. [b] Mesitylenesulfonation of α-cyclodextrin reported in ref 10. 8.7 equiv of the sulfonyl chloride was used probably due to wetness of the solvent used. [c] Amounts of the other products, which are not listed in this column, were negligible. [d] In the case of mesitylenesulfonation in ref 10, mole ratio of AB:AC:AD was 7.3:9.1:13.6 for α-CD.

Imidazole was purified by recrystallization from benzene and then dried in vacuo.[14] *tert*-Butyl mercaptan (Wako Pure Chemical Industries, Ltd.), sodium *m*-benzenedisulfonate (Wako or Tokyo Kasei Kogyo Co., Ltd.), and *p*-*tert*-butylthiophenol (Tokyo Kasei) were used without further purification. Taka-amylase was purchased from Sigma Chemical Company. *m*-Benzenedisulfonyl chloride was prepared by treatment of sodium *m*-benzenedisulfonate with PCl_5 according to the reported procedure:[15] IR (KBr) 1375 (SO_2Cl), 1165 (SO_2Cl), 800, 675 cm^{-1}; mp 60–61 °C (lit.[15] mp 63 °C).

***m*-Benzenedisulfonyl Capped Cyclodextrin (1).** Dry β-cyclodextrin (50 g, 44 mmol) was dissolved in 1 L of dry pyridine. To this solution was added dropwise 3.6 g (13 mmol) of *m*-benzenedisulfonyl chloride dissolved in 100 mL of dry pyridine at 25 °C with stirring. After the addition was complete, the solvent was evaporated from the resultant yellow solution in vacuo below 25 °C by using a rotary flash evaporator. Pale brown residue remained and was further dried overnight under reduced pressure (<0.1 mmHg) below 25 °C by using a liquid N_2 trap to give 86.1 g of dry crude product. The crude cap (10 g) was treated with 100 mL of EtOH–H_2O (2:3) at ca. 35 °C and the solution, after elimination of a tiny amount of insoluble powder, was added dropwise to 1 L of CH_3CN–H_2O (6:1) with stirring. White precipitates formed were filtered off by suction and the filtrate was evaporated to dryness in vacuo below 30 °C. The resultant residue was dissolved in 30 mL of 20% aqueous EtOH and the solution was stirred for 1 h at room temperature with 20 mL of anion exchange resins (IRA-400, Cl form). The resins were removed by filtration, and then the solvent was evaporated in vacuo below 30 °C. The pale brown residue thus obtained was dried in vacuo (<0.1 mmHg) overnight to give 0.9 g of practically pure *m*-benzenedisulfonyl capped β-CD. For further purification, silica gel column chromatography was applied by using CH_3CN–H_2O (6:1) as an eluent: IR (KBr) 1370, 1160, 815, 685 cm^{-1}; ^1H NMR (Me_2SO-d_6) 2.80–4.72 (m, 61 H), 4.72–4.98 (m, 7 H), 7.92–8.42 (m, 4 H).

2,6-*O*-Dodecakis(*tert*-butyldimethylsilyl)-A,B-bis((*p*-*tert*-butylphenyl)sulfenyl)-β-cyclodextrin (3a). A mixture of dry A,B-bis((*p*-*tert*-butylphenyl)sulfenyl)-β-CD (765 mg, 0.535 mmol), *tert*-butyldimethylsilyl chloride (1.3 g, 11.3 mmol), dry imidazole (1.2 g, 17.6 mmol), and dry DMF (30 mL) was heated at 90 °C for 24 h under argon. After cooling to room temperature, the solvent was evaporated from the reaction mixture in vacuo. The crude product was purified by repeated silica gel column chromatography (at least twice) by using $CHCl_3$ as an eluent to give 246 mg of 2,6-*O*-persilylated A,B-disulfenyl β-CD: IR(KBr) 3460 (br), 1255, 1045, 860, 840, 785 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ −0.12–0.06 (m, MeSiO–C_6, 30 H), 0.11–0.21 (m, MeSiO–C_2, 42 H), 0.79–0.89 (m, *t*-BuSiO–C_6, 45 H), 0.89–0.98 (m, *t*-BuSiO–C_2, 63 H), 1.175, 1.277 (s, *t*-Bu adjacent to benzene, 18 H), 3.14–4.21 (m, 49 H), 4.42–4.55 (m, C_3–OH, 7 H), 4.81–4.93 (m, C_1–H, 7 H), 7.10–7.36 (m, aromatic 8 H); UV (hexane) λ_{max} 257 nm (ε 21 700). Anal. Calcd for $C_{134}H_{262}O_{33}S_2Si_{12}$: C, 57.43; H, 9.42. Found: C, 57.32; H, 9.67.[17]

A,B-Bis((*p*-*tert*-butylphenyl)sulfenyl)-β-cyclodextrin (2a). Sodium methoxide (650 mg, 0.12 mmol) was mixed with 2.0 g (0.12 mmol) of *p*-*tert*-butylthiophenol dissolved in 20 mL of absolute MeOH under argon. From the clear solution thus formed a white powder of sodium *p*-*tert*-butylthiophenolate was obtained by evaporation of the solvent in vacuo. To the sodium salt were added *m*-benzenedisulfonyl-capped β-cyclodextrin (1.01 g, 0.755 mmol) and 40 mL of dry DMF. The resultant solution was heated at 80 °C for 10 h under nitrogen. After cooling to room temperature, the precipitated *m*-benzenedisulfonic acid disodium salt was filtered off and the filtrate was concentrated to dryness in vacuo. To the pale brown residue were added 50 mL of H_2O and concentrated HCl until the pH of the solution became below 2. The resultant turbid mixture was shaken with Et_2O (70 mL × 4). The aqueous layer and the insoluble product were combined and EtOH was added until the suspension became homogeneous. The solution was concentrated to 20 mL, and then EtOH (40 mL) was added to give pale brown precipitates. The precipitates were collected by suction filtration and dried at 80 °C in vacuo overnight to give 765 mg (0.565 mmol) of A,B-bis((*p*-*tert*-butylphenyl)-

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sulfenyl)-β-CD (**2a**): IR (KBr) 1150, 1080, 1030, 945, 825, 755 cm^{-1}; ^1H NMR (400 MHz, Me_2SO-d_6) δ 1.134 (s, *t*-Bu, 9 H), 1.231 (s, *t*-Bu, 9 H) 3.13–3.93 (m), 4.46–4.56 (m, prim OH, 5 H), 4.81–4.94 (m, C_1-H, 7 H), 5.71–5.96 (m, sec-OH, 14 H), 7.16–7.32 (m, aromatic, 8 H).[17]

2,6-*O*-Dodecakis(*tert*-butyldimethylsilyl)-A,B-bis(*tert*-butylsulfenyl)-β-cyclodextrin (3c). Bis-(*tert*-butylsulfenyl)-β-cyclodextrin (**2c**) was treated with *tert*-butyldimethylsilyl chloride and dry imidazole dissolved in dry DMF similarly to that of **2a**. Purification was achieved by repeated (at least twice) silica gel column chromatography by using $CHCl_3$ as an eluent: IR (KBr) 3460 (br), 2960, 2940, 2900, 2860, 1475, 1365, 1260 ($SiCH_3$), 1160, 1140, 1095, 1045, 860, 840, 785 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.01–0.08 (m, MeSiO–C_6, 30 H), 0.12–0.19 (m, MeSiO–C_2, 42 H), 0.84–0.89 (m, *t*-BuSiO–C_6, 45 H), 0.89–0.96 (m, *t*-BuSiO–C_2, 63 H), 1.315 (s, *t*-BuS, 9 H), 1.337 (s, *t*-BuS, 9 H), 2.83–4.13 (m, 42 H), 4.41–4.57 (m, HO–C_3, 7 H), 4.82–4.91 (m, C_1–H, 7 H). Anal. Calcd for $C_{122}H_{254}O_{33}S_2Si_{12}$: C, 54.63; H, 9.54. Found: C, 54.61; H, 9.67.[17]

Amylolysis of Bis(phenylsulfenyl)-β-cyclodextrin with Taka-amylase. To a solution of A,D-bis(phenylsulfenyl)-β-cyclodextrin (**6b**) (25 mg, 1.9×10^{-5} mol) in 0.3 mL of dimethyl sulfoxide was added 2.7 mL of 0.2 N sodium acetate buffer (pH 5.5) containing 0.01 M calcium chloride and 25 mg of Taka-amylase. After the mixture was incubated at 40 °C for 10 days, the enzyme was denaturated by the addition of 1.0 mL of 3 N aqueous ammonia. The supernatant obtained by centrifugation of the mixture was evaporated to dryness in vacuo. To the resultant residue were added 4 mL of a 1% aqueous $NaBH_4$ mixture and the mixture was stirred overnight at room temperature. The reaction mixture was acidified to pH 3–4 by the addition of 2 N hydrochloric acid and then filtered by using a membrane filter (Toyo, Membrane Filter 0.45-μm type NC). The crude product in the filtrate was purified by reversed-phase column chromatography by using a gradient elution (from 0–30% aqueous ethanol with 300 mL of water and 300 mL of 30% aqueous ethanol to give **8** (9 mg, 2.1×10^{-5} mol, 54%). A,C-bis(phenylsulfenyl)-β-cyclodextrin (**5**) (25 mg, 1.9×10^5 mol) was hydrolyzed with the amylase, followed by the reduction with a similar procedure to that of the A,D isomer to give 10 mg (2.3×10^{-5} mol, 60%) of **8**. A,B-Bis(phenylsulfenyl)-β-cyclodextrin (**2d**) (110 mg, 8.35×10^{-5} mol) was treated with Taka-amylase at 40 °C for 12 days. After the usual workup, in a similar way to the reaction of **5** or **6b**, the residue obtained by evaporation of the supernatant was dissolved in 30 mL of 10% aqueous ethanol and purified by reversed-phase column chromatography with a gradient elution (from 20% to 50% aqueous ethanol using 400 mL of 20% aqueous ethanol and 400 mL of 50% aqueous ethanol), giving hydrolyzed compound **7a** (42 mg, 6.1×10^{-5} mol, 73%). **7a** was reduced as described above, giving **7b** (38 mg, 5.5×10^{-5} mol) after the usual chromatographic separation with a gradient elution (from 15% to 50% aqueous ethanol using 300 mL of 15% aqueous ethanol and 300 mL of 50% aqueous ethanol). **7a**: FAB MS, *m/e* (relative intensity) 711 ($[M + Na]^+$, 0.82%), 688 (M^+, 0.68), 509 (**9**, 4.6), 255 (**10**, 57). **7b**: ^1H NMR (400 MHz, Me_2SO-d_6) δ 2.93–3.58 (m), 3.63–3.78 (m, 5 H), 3.98–4.07 (m, 1 H), 4.40–4.52 (m, OH, 4 H), 4.547 (d, J = 5.1 Hz, OH, 1 H), 4.892 (d, J = 3.7 Hz, $C_{1'}H$ or $C_{1''}H$, 1 H), 5.032 (d, J = 5.1 Hz, OH, 1 H), 5.099 (d, J = 3.7 Hz, $C_{1'}H$ or $C_{1''}H$, 1 H), 5.234 (d, J = 5.9 Hz, 1 H), 5.580 (d, J = 6.4 Hz, OH, 1 H), 5.633 (d, J = 2.9 Hz, OH, 1 H), 5.671 (d, J = 6.1 Hz, OH, 1 H), 7.09–7.39 (m, aromatic 10 H); ^{13}C NMR (100 MHz, Me_2SO-d_6) δ 35.04, 35.13 ($C_{6'}$, $C_{6''}$), 62.57, 62.80 (C_1, C), 67.10, 67.18, 69.34, 69.99, 71.44, 71.57, 71.86, 72.37, 72.45, 72.72 (C_2, $C_{2'}$, $C_{2''}$, C_3, $C_{3'}$, $C_{3''}$, $C_{4''}$, C_5, $C_{5'}$, $C_{5''}$), 82.68, 83.38 (C_4, $C_{4'}$), 100.19, 101.16 ($C_{1'}$, $C_{1''}$), 125.24, 125.29, 127.76, 128.02, 128.66, 128.80, 137.08 (aromatic C); FAB MS, *m/e* (relative intensity) 713 ($[M + Na]^+$, 0.59%), 690 (M^+, 0.17), 509 (**9**, 2.8), 255 (**10**, 37). **8**: ^1H NMR (100 MHz, Me_2SO-d_6) δ 2.9–4.1 (m), 4.2–4.7 (m, OH, 5 H), 4.7–5.1 (m, OH, $C_{1'}H$, 2 H), 5.20 (d, J = 6 Hz, OH, 1 H), 5.48 (d, J = 6 Hz, OH, 1 H), 7.0–7.5 (m, aromatic 5 H); ^{13}C NMR (25 MHz, MeSO-d_6) δ 35.1 ($C_{6'}$), 62.5, 62.8 (C_1, C_6), 70.1, 71.1, 71.3, 72.0, 72.3, 72.8 (other C atoms), 83.4 (C_4), 1 00.6 ($C_{1'}$), 125.2, 127.7, 128.8, 137.4 (aromatic C atoms); FAB MS, *m/e* (relative intensity) 475 ($[M + K]^+$, 0.63%), 459 ($[M + Na]^+$, 6.5), 437 ($[M + H]^+$, 0.14), 255 (**10**, 12).

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Registry No. **1**, 96761-39-6; **2a**, 80781-23-3; **2b**, 95475-29-9; **2c**, 96761-40-9; **2d**, 95475-68-6; **2e**, 96761-41-0; **3a**, 96791-14-9; **3b**, 96791-15-0; **3c**, 96791-16-1; **5**, 95475-67-5; **6b**, 95475-66-4; **7a**, 96761-42-1; **7b**, 95475-30-2; **8**, 96761-43-2; β-cyclodextrin, 7585-39-9; *m*-benzenedisulfonyl chloride, 585-47-7; *p-tert*-butylthiophenol, 2396-68-1; sodium *p-tert*-butylthiophenolate, 54166-35-7; Taka-amylase, 9001-19-8.

Composite Parameter Method: Application to Calculated Stabilization Energies of Strained and Unsaturated Molecules

Marvin Charton*

Chemistry Department, School of Liberal Arts and Sciences, Pratt Institute, Brooklyn, New York 11205

Arthur Greenberg* and Tyler A. Stevenson

Department of Chemical Engineering and Chemistry, New Jersey Institute of Technology, Newark, New Jersey 07102

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Ab initio molecular orbital calculations at the 4-31G level have been employed to obtain methyl stabilization energies of monosubstituted ethylenes, ethynes, cyclopropanes, and benzenes. A technique called the composite parameter method is developed and applied to correlations between methyl stabilization energies of the four classes of substituted hydrocarbons. The technique establishes the consistency and utility of the data set and also shows that the pattern of stabilization energies in ethynes is markedly different from those of the other three molecular classes.

There is a dearth of thermochemical data for substituted strained molecules (e.g., cyclopropanes)[1,2] and even for unsaturated molecules such as acetylenes.[3] Thus, for the present at least, attempts to investigate thermochemical

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