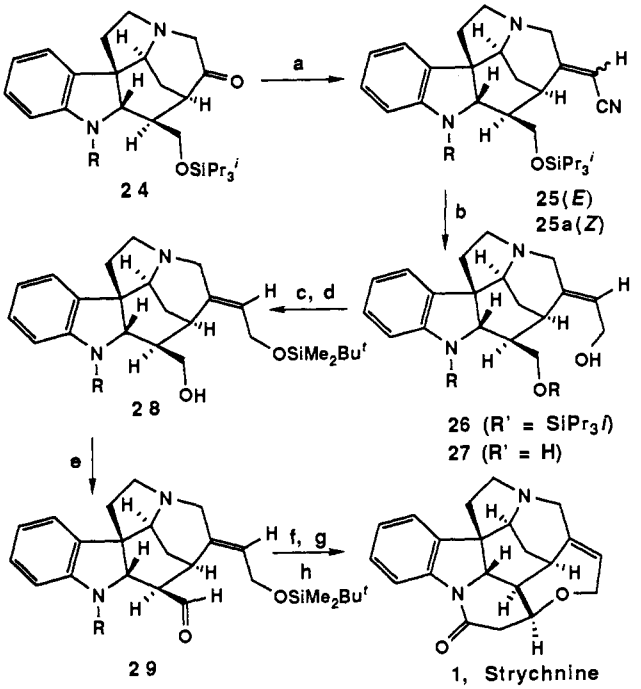
Scheme VI[a,b]



[a] R = $SO_2C_6H_4OMe$-*p*. [b] (a) $(EtO)_2P(O)CH_2CN$/KHMDS/THF at 25 °C (72%). (b) DIBAL/CH_2Cl_2 H_3O^+ workup. $NaBH_4$/MeOH (31%). (c) 2 N HCl/MeOH (81%). (d) TBDMSOTf/DBU/CH_2Cl_2, -20 °C (60%). (e) SO_3·C_5H_5N/DMSO/Et_3N (70%). (f) py/HF (60%). (g) Na/anthracenide/DME (85%). (h) $CH_2(CO_2H)_2$/NaOAc/Ac_2O (70%).

ketal hydrolysis proceeded, as expected, to give the furanoside relay compound **2**.

At this stage we decided that **2** might be more readily available from degradation of strychnine (**1**), allowing examination of the final stages with substantially more material.[7]

The Wieland–Gumlich aldehyde (W-G A) **20**[8] was treated with *p*-$MeOC_6H_4SO_2Cl$/py (70%) followed by catalytic osmylation[9] to give the rearranged glycoside derivative **22** (70–80%) (X-ray). Reduction ($LiBH_4$) of **22** gave the tetrol **23** (43–56%), which was cleaved (H_5IO_6) to give the relay compound **2** (55–61%). Using this sequence **2** is available in gram quantities in three steps from **21**, Scheme V.

Treatment of **2** with TIPSOTf/DBU/CH_2Cl_2 from 0 °C to 25 °C gave the ketone **24** (69%). When **24** was treated with $(EtO)_2P(O)CH_2CN$/KHMDS/THF at 25 °C, it was cleanly transformed into **25** (72%) as a mixture of geometrical isomers, 3:2, with the desired *E* isomer in excess. The stereoisomers **25**/**25a** were readily separated, and the desired *E* isomer was reduced with DIBAL followed by $NaBH_4$ to give **26** (31% for two steps). The *Z* isomer could be converted into a mixture of the *E* and *Z* stereoisomers by irradiation (tungsten) in benzene. In this way we could obtain (*E*)-**25** in 52% yield after one cycle. Desilylation (2 N HCl/MeOH, 16 h) gave the diol **27** (81%), which was identical with the material made by DIBAL reduction (90%) of **21**. Selective protection of the allylic hydroxyl (TBDMSOTf/DBU/CH_2Cl_2/-20 °C) followed by oxidation (SO_3·C_5H_5N/DMSO/Et_3N) gave the aldehyde **29** (42% for two steps). Desilylation (py/HF) of **29** gave the protected W-G A **21** (60%), which was deprotected (Na/anthracenide)[10] to give **20** (85%). Since Robinson[11] has converted **20** into strychnine by treatment with $CH_2(CO_2H)_2$/NaOAc/Ac_2O (70%), this completes the second synthesis of strychnine, and the first of the W-G A, Scheme VI.

Acknowledgment. The National Institutes of Health (GM 32718) are thanked for their financial support of this research. Dr. John C. Huffman (Molecular Structure Center, Indiana University, Bloomington, IN 47415) and Dr. Vince Lynch (UT, Austin) are thanked for the X-ray structure determination of compounds **10a**, **16a**, **19**, and **22**, respectively. L.M. thanks the Fulbright Commission for a fellowship.

Supplementary Material Available: Details of the X-ray structure determination of **10a**, **16a**, and **19**, including tables of fractional coordinates, isotropic thermal parameters, anisotropic thermal parameters, bond lengths, and bond angles and spectral details for compounds **2**, **4–6**, **7a** (R = R' = H), **8–10**, **10a,b**, **11–13**, **15**, **16**, **16a**, **17**, **18**, **18a**, **19**, **21–25**, **25a**, and **26–29** (66 pages). Ordering information is given on any current masthead page.

(7) It is amusing to note that strychnine is less expensive than tryptamine!

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Enantioselectivity in FAB Mass Spectrometry

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Received July 1, 1991
Revised Manuscript Received January 7, 1992

Enantioselective complexation is a very important aspect of the field of molecular recognition. Modified crown ethers in particular have played fundamental roles as synthetic hosts in this field.[1] Cram and Lehn showed that chiral crown ethers involving 1,1-dinaphthyl units[2] or tartaric acid derivatives,[3] respectively, exhibited a high degree of enantioselectivity toward organic ammonium ions in solution. Many workers have continued to investigate enantiomeric selectivity with other types of modified crown compounds.[1,4-6] These selectivities are based upon different association constants, rate constants, calorimetric data, etc. To date, various detection methods of such diastereomeric complexes and their applications have been extensively developed with a variety of methods, such as NMR,[6,7] UV,[8] HPLC,[9] and others.[10] However, the application or the applicability of fast atom bombardment mass spectrometry (FABMS) to this has been virtually unknown.[11-14] We report here the first observation concerning

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Chart I

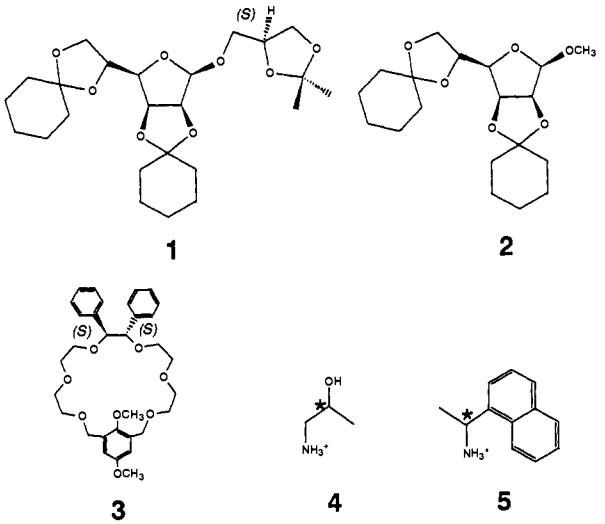

Table I. $[I(M + A)^+/I(R + A)^+]$ and $[I(M + A_R)^+/I(M + A_S)^+]$ Values

M		A^+ 4	A^+ 5	R
1	*R*	1.2	1.6 ± 0.03[b]	12C4
	S	1.2	1.3 ± 0.08[b]	
	R/*S*	1.0[a]	1.2[a]	
2	*R*	0.74	0.71 ± 0.03[b]	12C4
	S	0.74	0.65 ± 0.03[b]	
	R/*S*	1.0[a]	ca. 1.0[a]	
3	*R*	1.7	0.90 ± 0.03[b]	15C5
	S	1.7	0.74 ± 0.03[b]	
	R/*S*	1.0[a]	1.2[a]	

[a] $[I(M + A_R)^+/I(M + A_S)^+]$ value. [b] Standard deviation (n = 5).

enantioselectivity of a modified carbohydrate derivative toward enantiomeric alkylammonium ions by FABMS.

A host carbohydrate **1** was designed and synthesized for observing enantioselectivity toward organic cations (Chart I). The key features are as follows: (1) use of the β-D-mannofuranose skeleton,[15] (2) *O*-alkyl modification of the hydroxy groups to promote selectivity for capturing cations,[15,16] (3) introduction of cyclohexylidene units as potential steric barriers, and (4) addition of another oxygen-containing dioxolane unit for increasing complexation ability.

Table I shows the relative FABMS peak intensities, $[I(M + A)^+/I(R + A)^+]$, of the relevant diastereomeric adduct ions. Here, the internal standard technique is employed for quantitative comparisons,[15,17] and the internal reference compound (R) is carefully chosen so that $[I(M + A)^+/I(R + A)^+]$ values are kept nearly constant during prolonged scan times (10–50 scans).

The relative peak intensity of the adduct ion between **1** and (*R*)-**5** is 20% higher than that between **1** and the enantiomeric (*S*)-**5** (Figure 1).[18] Since the pair of (*R*)- and (*S*)-alkylammonium ions is of equivalent hydrophobicity, it is reasonable

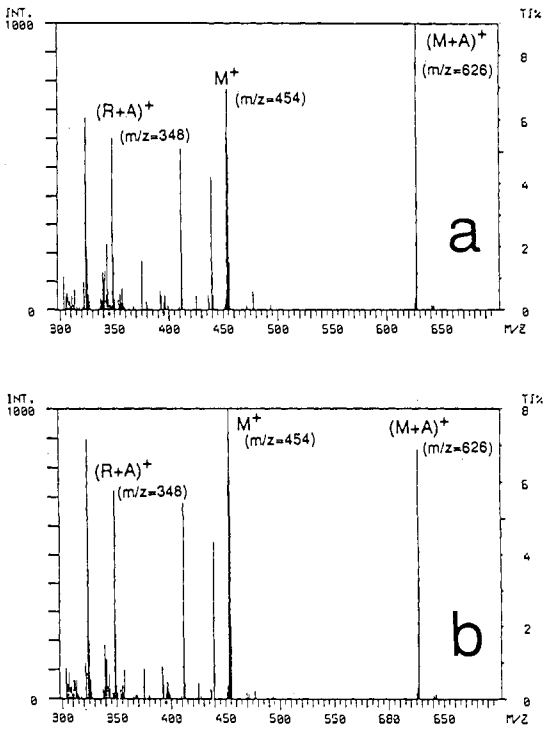

Figure 1. Quantitative FAB mass spectra for a mixture of **1**, 12C4, and an enantiomer of **5** with NBA matrix: (a) (*R*)-**5**; (b) (*S*)-**5**.

to assume that such different relative peak intensities under the same conditions reflect the different stabilities of the diastereomeric ions.[12,19] The peak intensity may be affected by fragmentation (decomposition). However, we cannot clearly detect any different decomposition patterns in conventional (EBE-type) FABMS/MS (MI and CAD) spectra for these two diastereomeric adduct ions.[20]

A similar value is obtained for another pair (**3**–**5** set) involving a modified crown ether.[21] In the case of lesser steric requirements for such complexations (**1**–**4**, **2**–**4**, **3**–**4**, **2**–**5** sets), the value of $[I(M + A_R)^+/I(M + A_S)^+]$ is almost unity. Therefore, when more severe steric hindrance and sterically different complementarity for the diastereomeric set is expected, the quantity goes up to 1.2 (**1**–**5**, **3**–**5** sets). These findings suggest that FABMS, which may reflect certain gas-phase phenomena,[12,15] can detect the different stabilities of these diastereomeric ions only if there exists different intermolecular complementarity which provides energetically different interactions. This is consistent with the fact that charge–dipole and related interactions in the gas phase in the absence of solvent effects are larger than those in the solution phase.[19,22] The present enantioselectivity in FABMS proves that the modified carbohydrate possesses the ability to capture organic ions in terms of multisite charge–dipole interactions at a particular complexation site.

Acknowledgment. This work was partially supported by a grant-in-aid for scientific research from the Ministry of Education, Science, and Culture, Japan. We are grateful to Dr. Takeshi Kinoshita and Miss Terumi Watanabe (Analytical and Metabolic Research Laboratories, Sankyo Co., Ltd.) for measuring FABMS/MS spectra.

Supplementary Material Available: Listings and details of additional spectral data for **1** (3 pages). Ordering information is given on any current masthead page.

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(20) We thank a reviewer for his suggestion of taking FABMS/MS spectra. The FABMS/MS(MI) data are nearly the same: $a(A)^+/a(M + 1)^+$ = 6.0 (*R*-pair) and 5.7 (*S*-pair); *a* denotes area intensity.

(21) In the case of the azophenolic derivative of the **3**–**5** set, enantioselectivity could not be detected by UV methods (in EtOH).[8]

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