Table I. Spin-Lattice Relaxation Times, Nuclear Overhauser Enhancements, and Rotational Correlation Times for Aqueous Ammonium-N_{15} Ion

T, °C	$T_{1,obsd}$, s	η	$T_{1,dd}$, s	τ_c, ps
3.3	35.2	-4.80	36.2	1.41
21	44	-4.67	46.5	1.10
21[a]	46.4	-4.78	47.9	1.07
36	59.5	-4.26	69	0.74
48	78.5	-4.66	83	0.62
80	86.2	-4.16	102	0.50
21	409[b]	-0.57	544	1.50

[a] For 0.7 M NH_4NO_3 in 0.5 M HCl. [b] For ND_4^+ in DCl/D_2O.

in contrast to previous studies at higher temperature, where spin-rotation relaxation is dominant.[6,11] The correction is slightly larger for ND_4^+, owing to diffusional effects and chemical exchange with incompletely deuterated solvent. The rotational correlation time for the ammonium ion was then calculated according to eq 2, with $\langle r_{NH}^{-3}\rangle^{-1/3} = 1.03$ Å[13] $= \langle r_{ND}^{-3}\rangle^{-1/3}$, and

$$\frac{1}{T_{1,dd}} = 4\,\frac{\frac{2}{3}I(I+1)\gamma_N^2\gamma_{H\text{ or }D}^2\hbar^2}{r_{NH\text{ or }ND}^6}\,\tau_c \qquad (2)$$

the values are listed in Table I. Since τ_c is independent of concentration, we may conclude that ion pairing does not contribute to the observed values, which are characteristic of solvated NH_4^+.

The correlation times in Table I are indeed ca. 10^{-12} s, which is shorter than the 9×10^{-12} s for H_2O in liquid water[14] and remarkably close to the 0.2×10^{-12} s for CH_4 in liquid methane.[15] So rapid a rotation is perhaps surprising, inasmuch as the protons of NH_4^+ are hydrogen-bonded to solvating water molecules, and rotation requires breaking and remaking those hydrogen bonds. There are reasons to suppose that those hydrogen bonds are both strong and directional: In the gas phase, the enthalpy of hydration of NH_4^+ is 10.6-20.6 kcal/mol per water molecule,[16a] and hydrogen bonding is estimated[16b] to contribute up to 20 kcal/mol to the binding of crown ethers to ammonium ions. Also, it has long been known[17] that NH_4^+ fits into the H_2O lattice, and NH_4Br in 18-crown-6 shows protons in directional hydrogen bonds.[18] Moreover, according to MO calculations on $NH_4^+{\cdot}OH_2$,[19] 5.5 kcal/mol is required to create even one bifurcated hydrogen bond, where the H_2O is located midway between two NH protons. Finally, according to a simple electrostatic model,[20] with 11%[21] of a positive charge on each H interacting with water dipoles in a medium of dielectric constant 1, the barrier to rotation of NH_4^+ is >6 kcal/mol. Yet any such barrier would reduce the rate of rotation to a value well below what we observe.

Nor can the protons be tunneling[22] through such a barrier, since the τ_c for $^{15}ND_4^+$, given in Table I, shows that rotation of this ion is retarded only by a factor of $\sim 2^{1/2}$. This is the classical value for k_H/k_D due to the increased moment of inertia. (For comparison with a process known to involve tunneling, the inversion rate of ND_3 is only 1/14 that of NH_3.[23])

Therefore we conclude that there is no substantial barrier to rotation of aqueous NH_4^+. By comparing the observed τ_c with the value expected for a free rotor of this moment of inertia, we estimate that this barrier is only 1.6 kcal/mol. On the other hand, from the temperature dependence of the correlation times in Table I, an apparent activation E_A of 2.76 ± 0.32 kcal/mol and a $\log_{10} A$ of 14.04 ± 0.23 can be calculated. We cannot exclude the possiblity that the discrepancy between these two estimates of the barrier is due to a slight increase of the apparent E_A, owing to the temperature dependence of density.[24] However, the experimentally determined τ_c is characteristic of the average environment of the NH_4^+ ion, averaged over a long time ($T_1 \sim 10^2$ s). If any appreciable fraction (>10%) of the ions are in "disordered" environments—temporarily desolvated or with bifurcated hydrogen bonds—that favor rotation, these can dominate the average. Then the observed E_A would represent the temperature dependence of this fraction. Moreover, since the observed log A is too large for a free rotor of this moment of inertia ($\log_{10} A = 13.1$), we conclude that 1.6 kcal/mol is a better estimate of the barrier to rotation.

So low a barrier might have been anticipated: Bifurcated hydrogen bonds are quite common in crystals.[25] Also, the enthalpy of hydration of NH_4^+, corrected for hydrophobic effects, lies on the plot vs. $1/r$ for hydration of alkali-metal ions.[26] We conclude that solvation of aqueous ammonium ion may involve hydrogen bonds, but these are not strong and directional.

Acknowledgment. We are grateful to Dr. John Wright for modifying the NT200 spectrometer to allow gated deuterium decoupling. This research was supported by National Science Foundation Grant CHE 81-16800.

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Molecular Recognition through the Exact Placement of Functional Groups on Rigid Matrices via a Template Approach[1]

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Received August 20, 1985

Molecular recognition of polymers prepared by imprinting with templates has been intensively studied in recent years.[2,3] In this way progress has been made in building specific binding sites into polymers as models of biological receptors and enzymes. Imprinting during the preparation of cross-linked polymers in most cases has been used for the preparation of chiral cavities containing functional groups. The selectivity observed in racemic resolution then is a result of the combination of the exact cavity-shape fitting

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(1) Enzyme-Analogue Built Polymers. 20. For Part 19, see: Wulff, G.; Poll, H.-G.; Minarik, M. *J. Liquid Chromatogr.*, in press.

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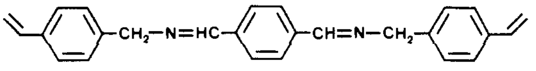
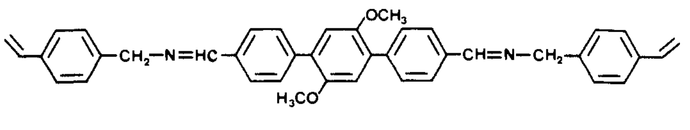
0002-7863/86/1508-1089$01.50/0

Table I.[a] Selectivity of Polymers with Each of the Two Amino Groups in a Defined Distance

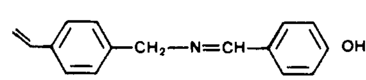
Monomer 1



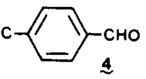
Monomer 2



	Splitting Percentage	Distance r of groups (nm)	Apparent Binding Constants of 4	5	6	Selectivity
Polymer A-1 from 1	84%	0.72	1.38	0.20	0.20	$\alpha_{4,5}$ = 4.60 $\alpha_{4,6}$ = 5.37
Polymer A-2 from 2	91%	1.56	0.42	0.30	0.59	$\alpha_{6,5}$ = 1.69 $\alpha_{6,4}$ = 1.81
Polymer A-3 from 3	~90%	—	0.18	0.12	0.14	—



3



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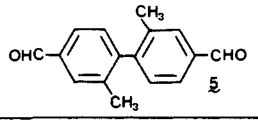

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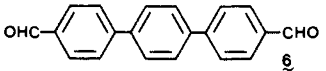
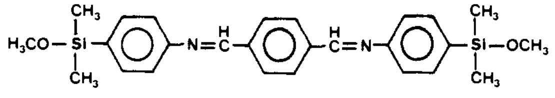


6

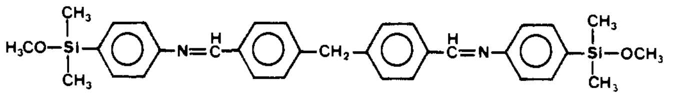
[a] For details, see text and eq 1. The distance of groups was determined from molecule models, assuming the most probable conformation. Equilibration in acetonitrile containing 2.5% water and 10 μmol/L toluenesulfonic acid.

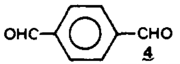
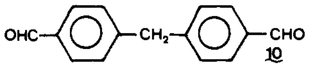
Table II.[a] Selectivity of Modified Silicas with Each of the Two Amino Groups in a Defined Distance

Monomer 7



Monomer 8



	Splitting Percentage	Distance r of groups (nm)	Apparent Binding Constants of  4	 10	Selectivity α′
Silica modified with 7	>95%	0.72	4.91	2.58	1.74
Silica modified with 8	>95%	1.05	9.07	13.77	1.67
Silica modified with 9 (at random)	—	—	2.26	2.05	—

Monomer 9 $H_2N-(CH_2)_3-Si(OCH_3)_3$

[a] For details see ref 8 and Table I.

and the exactness of the arrangement of the functional groups. It was of interest whether the arrangement of the functional groups alone can cause selectivity due to the distinct distance of two functional groups. The question is whether a two-dimensional information transfer instead of a three-dimensional one will be sufficient to bring about selectivity.

This paper reports on investigations to introduce two amino groups with the aid of a template in a distinct distance into cross-linked polymers.[4] Furthermore it reports on a significant broadening of the concept by using for the first time a similar imprinting procedure on the surface of silica through the formation of siloxane bonds. With this method it was possible to locate two functional groups on a more or less plane surface of silica (see Figure 1) and to investigate only the selectivity caused by distance accuracy.

For polymer imprinting as template monomers the bis(azomethines) **1**[4a] and **2**[5] were used. They were radically copolymerized with ethylene glycol dimethacrylate in the presence of inert solvent to macroreticular polymers.[6] The dialdehyde templates could be split off under mild conditions. The mean distance of the remaining amino groups should be 0.72 nm in the case of **1** and 1.56 nm in the case of **2** as template monomer. For

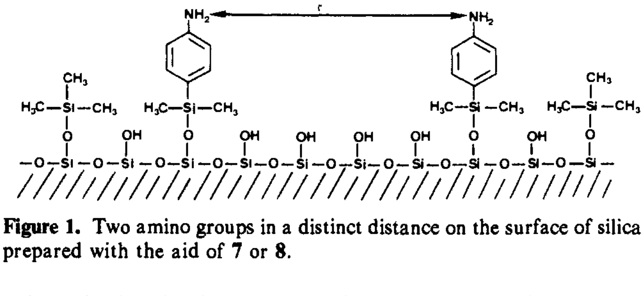


Figure 1. Two amino groups in a distinct distance on the surface of silica prepared with the aid of **7** or **8**.

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(4) Earlier work in this direction had shown that selectivity, due to the distance of two functional groups, is difficult to achieve. See: (a) Wulff, G.; Lauer, M.; Disse, B. *Chem. Ber.* **1979**, *112*, 2854–2865. (b) Lauer, M. Doctoral Thesis, University of Bonn, 1978.

(5) All new compounds gave spectral properties and analytical data consistent with the assigned structure. Details of their preparation and properties will be published elsewhere.

(6) Polymers were prepared as described earlier (see ref 2b and 2c).

comparison purposes a polymer with randomly distributed amino groups was prepared from **3**.

To investigate the distance accuracy both polymers were equilibrated with an equimolar mixture of the three dialdehydes **4**, **5**, and **6**, requiring for a two-point binding a distance of the amino groups in the polymer of 0.72, 1.14, and 1.56 nm, respectively. With other distances only a one-point binding is expected.

In Table I the apparent binding constants obtained under the conditions used are given. Polymers A-1 and A-2 showed the highest uptake for the dialdehyde with the same distance of the functional groups as the template. The selectivity was calculated as the selectivity factor α and corrected for the different nonspecific adsorption to the polymer with statistically distributed amino groups; e.g.,

$$\alpha'_{4,5} = \frac{K_4/K_{4\,\mathrm{stat}}}{K_5/K_{5\,\mathrm{stat}}} \qquad (1)$$

where K_4 = apparent binding constant for substance **4** on P A-1 or P A-2 and $K_{4\,\mathrm{stat}}$ = apparent binding constant for substance **4** on P A-3.

The observed selectivity is astonishingly high in the case of P A-1 with $\alpha'_{4,6} = 5.37$. Even a distance difference of only 0.42 nm (4.2 Å) shows a selectivity of $\alpha'_{4,5} = 4.60$. The polymer prepared from **2** with larger distance between the groups (1.56 nm) was less selective but still showed $\alpha'_{6,5} = 1.69$ and $\alpha'_{6,4} = 1.81$ which indicates a strong preference for its own template. This shows that the functional groups at the polymer remain in a given position since distances of 0.42 nm can be clearly recognized by the added dialdehydes.[7]

Aside from a selective two-point binding, the foregoing example might contain some shape selectivity as well. To avoid any shape selectivity, two amino groups were attached to the surface of silica at a distinct distance from one another using the template monomers **7** and **8**.[5] In this case the attachment to the surface occurs by condensation through siloxane bonds between the methoxy silane groups of **7** and **8** and the silanol groups on the surface of the silica.[8] Most of the remaining silanol groups were afterwards blocked by reaction with hexamethyldisilazane to avoid nonspecific adsorption. The templates could be split off to more than 95% (see Figure 1). In this case the position of the two amino groups should not be changed by chain mobility, swelling, or shrinking as in a polymer. The distance can only be altered by conformational changes within the functional group part.

The selectivity was determined by equilibration with an equimolar mixture of the two template dialdehydes **4** and **10** (see Table II). Both silicas showed a significant difference in binding preferring their own templates with α-values of 1.74 and 1.67. So only by the distance selectivity and with differences of only 0.33 nm (between **4** and **10**) could selectivity be obtained.

Imprinting on the surface of silica is thus a further extension of the original imprinting method.[2,3] The method appears to be applicable for a wide range of examples, some of them have already been verified.[9]

Acknowledgment. We thank "Fonds der Chemischen Industrie" and the "Minister für Wissenschaft und Forschung des Landes Nordrhein-Westfalen" for financial support.

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(7) For related work using diketals for the introduction of each two diol groupings, see: Shea, K. J.; Dougherty, T. K. *J. Am. Chem. Soc.*, following paper in this issue. We are grateful to professor Shea for an exchange of information prior to publication.

(8) Wide-pore silica Fractosil 500, Merck, Darmstadt) was used. An amount of monomers **7** and **8** was used that would be expected to cover around 20% of the surface (2×10^{-5} and 9×10^{-6} mol/g, respectively) and to attain site isolation of each two groups. Condensation was effected by boiling in xylene for 40 h, similar to methods for binding substances via one siloxane group (see, e.g., Evans, M. B.; Dale, A. D.; Little, C. J. *Chromatographia* **1980**, *13*, 5. Practically all monomer had been taken up by a two-point binding. After this time an excess of hexamethyldisilazane was added and again refluxed for 20 h.

(9) Wulff, G.; Heide, B., unpublished results.

Molecular Recognition on Synthetic Amorphous Surfaces. The Influence of Functional Group Positioning on the Effectiveness of Molecular Recognition

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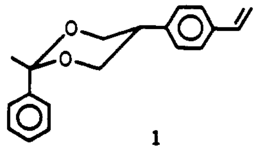
The template synthesis method is used to prepare macroreticular polymers containing sites of organic functional groups. The spatial relationship of the functional groups at each site is determined, in part, by the spacer used to introduce the functionality and by the mobility of functional groups on the polymer surface. Sites prepared by this method have been shown to exhibit molecular recognition. The technique employed for the construction of these sites was developed by Wulff[1] and co-workers and has also been applied by ourselves[2] and others[3] for the preparation of selectively functionalized network polymers. This paper reports the results of an investigation of how molecular recognition is influenced by the *initial positioning of the functional groups at the binding site.*

The system chosen for study is outlined in Scheme I. Aromatic ketones are used for spacer or template molecules. Ketals **1**–**3**[4] (1–2 mol %), prepared from 2-(*p*-vinylphenyl)-1,3-propanediol,[5]



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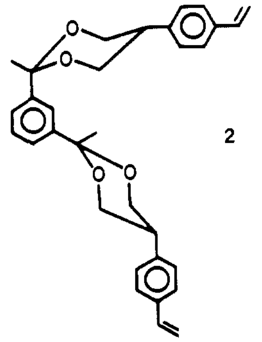
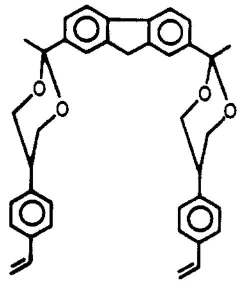


2



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(4) Single stereoisomers (cis) of the bis-ketal template assemblies were used for these experiments. Their stereochemistry was assigned on the basis of NMR and X-ray crystallographic studies of model 1,3-dioxanes; Shea, K. J.; Dougherty, T. K. *J. Org. Chem.* **1985**, *50*, 4439.

(5) All new compounds gave spectral properties and analytical data consistent with the assigned structure.