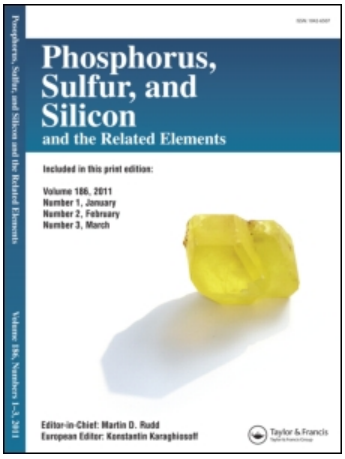


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Host-Guest Complexation Behavior of Resorcinarenes with Tetraalkylammonium Ions and *N*-Methylpyridinium Ions in Methanol: The Effect of Bulky Hydrophobic Substituents at the Extra-Annular Positions

Osamu Morikawa[a]; Hiroshi Yamaguchi[a]; Yoshiko Katsube[a]; Kazuyuki Abe[a]; Kazuhiro Kobayashi[a]; Hisatoshi Konishi[a]
[a] Department of Materials Science, Tottori University, Tottori, Japan

To cite this Article Morikawa, Osamu , Yamaguchi, Hiroshi , Katsube, Yoshiko , Abe, Kazuyuki , Kobayashi, Kazuhiro and Konishi, Hisatoshi(2006) 'Host-Guest Complexation Behavior of Resorcinarenes with Tetraalkylammonium Ions and *N*-Methylpyridinium Ions in Methanol: The Effect of Bulky Hydrophobic Substituents at the Extra-Annular Positions', Phosphorus, Sulfur, and Silicon and the Related Elements, 181: 12, 2877 — 2886
To link to this Article: DOI: 10.1080/10426500600865152
URL: http://dx.doi.org/10.1080/10426500600865152

Phosphorus, Sulfur, and Silicon, 181:2877–2886, 2006

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426500600865152

Taylor & Francis
Taylor & Francis Group

Host–Guest Complexation Behavior of Resorcinarenes with Tetraalkylammonium Ions and *N*-Methylpyridinium Ions in Methanol: The Effect of Bulky Hydrophobic Substituents at the Extra-Annular Positions

Osamu Morikawa
Hiroshi Yamaguchi
Yoshiko Katsube
Kazuyuki Abe
Kazuhiro Kobayashi
Hisatoshi Konishi
Department of Materials Science, Tottori University, Tottori, Japan

The host–guest interaction of C-methylresorcin[4]arene and its derivative having four tert-butylsulfanylmethyl groups at the extra-annular positions was studied by ^1H NMR spectroscopy in CD_3OD. Based on the association constants (Ka) and the complexation-induced NMR shifts (CIS), it was concluded that the bulky substituents create a deep cavity with a narrow entrance and improve the size and shape selectivity.

Keywords Hydrophobic interaction; molecular recognition; *N*-methylpyridinium ions; quaternary ammonium ions; resorcinarene

INTRODUCTION

The construction of host molecules with high affinity and selectivity is one of the major goals of supramolecular chemistry.[1] Calixarenes and resorcinarenes are readily available synthetic macrocyclic compounds and have been widely used as host molecules.[2,3] In order to improve their complexation properties, a variety of functionalizations has been developed.[4] Thus, the introduction of functional groups at the peripheral positions of the macrocycles has resulted in the enhancement of the internal surface area of the cavity, leading to the improved affinity

Received July 28, 2005; accepted May 4, 2006.
Address correspondence to Hisatoshi Konishi, Tottori University, Department of Materials Science, Faculty of Engineering, 4-101 Koyama-minami, Tottori, 680-8552 Japan. E-mail: konis@chem.tottori-u.ac.jp

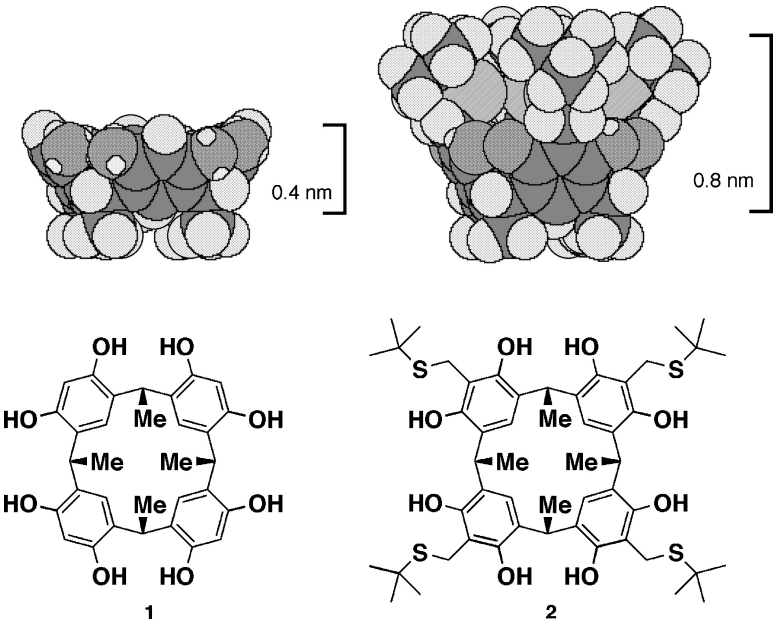


FIGURE 1 Host compounds and their space-filling model representation.

and/or selectivity derived from the interaction between the host and guest molecules.[5,6]

The resorcin[4]arenes consist of four resorcinols, which form an electron-rich cavity able to include specific guest molecules such as ammonium ions and sugars by cation-π[7,8] and CH-π[9–11] interactions. The characteristic feature of the resorcin[4]arenes is the presence of strong electron-donating OH groups, which increase the electron density of the resorcinol rings. From this point of view, we have been interested in the resorcin[4]arene derivatives bearing the OH groups.[12–14] We previously reported that the reaction of *C*-methylresorcin[4]arene (**1**) with 2-methyl-2-propanethiol and formaldehyde in acetic acid yields the resorcin[4]arene (**2**), which has eight OH groups and four *tert*-butylsulfanylmethyl substituents.[15,16] As shown in Figure 1, this compound has a deep cavity of about a 0.8-nm depth, if the substituents align vertically at the peripheral positions. On the other hand, the resorcinarene **1** has a cavity with a depth of less than 0.4 nm. To obtain insight into the effect of the bulky hydrophobic substituents on the complexation behavior, we have investigated the inclusion phenomena of **1** and **2** with tetraalkylammonium ions and pyridinium ions in methanol by ^{1}H NMR spectroscopy. These cations have been widely used as guest molecules for complexation with calixarenes and resorcinarenes.[8,17–19]

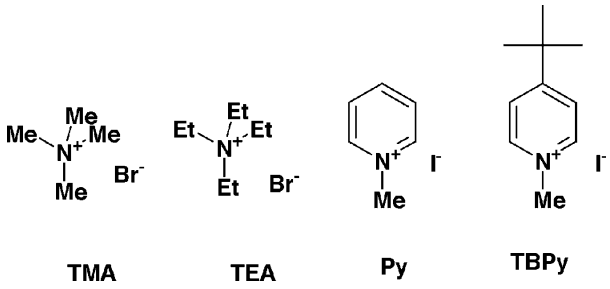


FIGURE 2 Guest compounds.

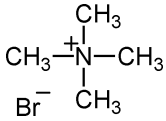
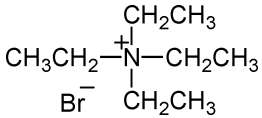
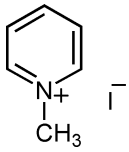
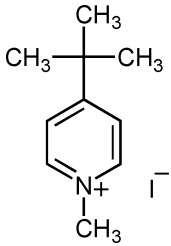
RESULTS AND DISCUSSION

The complexation behavior of hosts **1** and **2** with guests in CD_3OD was investigated by an ^1H NMR titration experiment (Job's plot). The studied guests (Figure 2) include Tetramethylammonium Bromide (**TMA**), Tetraethylammonium Bromide (**TEA**), *N*-Methylpyridinium Iodide (**Py**), and 4-*Tert*-Butyl-*N*-Methylpyridinium Iodide (**TBPy**). The general features of the NMR study are as follows. First, in all cases, except for the combination of **2** and **TEA**, large upfield shifts of the guest signals were observed in their NMR spectra. In addition, the upfield shift values, $\Delta\delta = \delta$(free guest)-δ(complexed guest), increase upon increasing the host/guest ratio. These data are consistent with the view that a guest is incorporated into the aromatic cavity of the host and subjected to the ring current effect of the aromatic rings. Second, no distinct signals ascribed to the free guest, and the host–guest species could be observed, thus indicating that the host–guest complexation equilibrium has a very fast exchange rate compared to the NMR time scale. The association constants (*Ka*) of the complexes and the complexation-induced NMR shifts (CIS) of the guest molecules are summarized in Table I.

Complexation with Tetraalkylammonium Ions

TMA is a small spherical guest molecule. The Job's plot for the complexation of host **1** and **TMA** is shown in Figure 3. The complicated data suggested the presence of a competitive complex formation with distinct stoichiometries. Indeed, it is well known that simple resorcinarenes such as **1** form 1:1[20,21] and 2:1[22,23] host–guest inclusion complexes with small quaternary ammonium ions in solid state. The 2:1 type complexes have a capsular structure in which a quaternary ammonium ion was encapsulated between the cavities of the two resorcinarene molecules.

TABLE I Complexation-Induced Shift (CIS) and Association Constants (*Ka*) Derived From NMR Titrations With Host 1 and 2 Measurements in CD_3OD at 303 K

		Host 1				Host 2	
		1:1 Complex		2:1 Complex		1:1 Complex	
Guest Compounds	Proton	CIS	K_a	CIS	K_a	CIS	K_a
	CH_3	1.32	3.1×10	2.39	3.6×10^2	1.45	2.7×10^2
	CH_3	0.95	7.0×10			ND[a]	
	CH_2	1.21					
	γ-H	2.65		4.85		3.36	
	β-H	2.66		4.51		3.24	
			1.5×10^2		6.5×10		3.3×10^2
	α-H	2.42		4.82		3.70	
	N-CH_3	1.67		2.42		2.44	
	C-CH_3	0.35				0.15	
	β-H	1.27				0.82	
			1.7×10^2				4.8×10^2
	α-H	2.40				2.39	
	N-CH_3	2.47				3.07	

[a]Not determined. See text.

The capsule structure was also stabilized by polar solvent molecules with a multiple hydrogen-bonding network. Therefore, it can be presumed that both types of complexes are present in the solution. The computational analysis of the relationship between the initial concentrations of **1** and **TMA** and the chemical shift change of TMA gave the values of $Ka_1 = 31\ M^{-1}$ and CIS $(CH_3) = 1.32$ ppm for the 1:1 complex and $Ka_2 = 360\ M^{-1}$ and CIS $(CH_3) = 2.39$ ppm for the 2:1 complex.

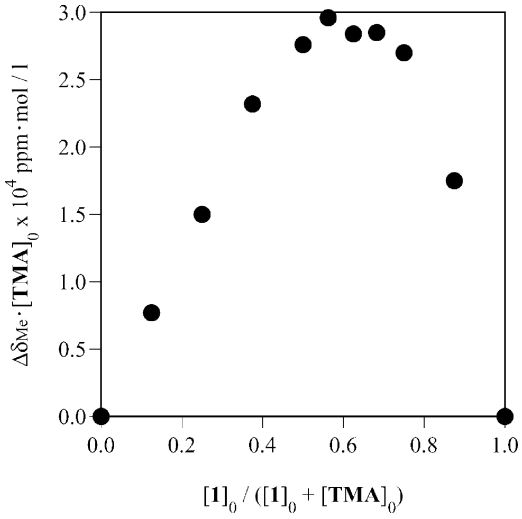


FIGURE 3 A Job's plot for the complexation of **1** and **TMA**. Total concentration: $[\mathbf{1}]_0 + [\mathbf{TMA}]_0 = 4.0 \times 10^{-3}$ mol/L.

In contrast, for host **2** with **TMA**, a 1:1 type complex formation was evidenced by the Job's plot. Thus, the values of $Ka = 270\ M^{-1}$ and $CIS(CH_3) = 1.45$ ppm are obtained using a nonlinear least-square calculation. The observed difference in **1** and **2** for **TMA** is ascribed to the hydrophobic bulky substituents at the peripheral position of the cavity, which prevent the interaction between the two resorcinarene molecules; then the formation of a 2:1 complex is unfavorable.

Next, we examined **TEA** as a guest molecule, which is spherical and larger than **TMA**. When resorcinarene **1** was used as the host molecule, the Job's plot suggested that a 1:1 complex is the predominant species. On the other hand, resorcinarene **2** produced only slight upfield shifts of the **TEA** signals. Therefore, the precise parameters for the complexation could not be calculated using our method, and it is presumed that the value of *Ka* is very small. This phenomenon is ascribed to the bulky *tert*-butyl groups, which narrow the entrance of the cavity to exclude the inclusion of a large **TEA** molecule.

Complexation with Pyridinium Ions

Py has an ellipsoidal structure and interacts with the aromatic cavity via *N*-CH_3-π and pyridinium CH-π interactions. The Job's plot for the complexation behavior of host **1** and **Py** conflicts with the formation of a single species. Thus the complexation parameters were calculated by

assuming the formation of 1:1 and 2:1 complexes, which are shown in Table I. The upfield shifts for all protons indicate that both the pyridinium moiety and the *N*-methyl group were randomly included in the cavity, although the comparison of the CIS values suggests that the cavity of **1** somewhat prefers to interact via the pyridinium CH-π. On the other hand, the Job's plot for the host **2**-**Py** complex is consistent with a 1:1 host–guest complexation. The magnitude of the CIS of **Py** is in the order of α-H > γ-H > β-H > N-CH_3. Again, this trend indicates that the pyridinium moiety is slightly preferred over the *N*-CH_3 group in the cavity of host **2**.

The guest molecule **TBPy** has a *tert*-butyl group at the γ-position. The size of the *tert*-butyl group is comparable to that of **TMA**, and then **TBPy** may enter into the cavity not from only the *N*-CH_3 end, but also the *tert*-butyl end.

For both host compounds, the Job's plots for the complexation with **TBPy** clearly indicated the formation of the 1:1 type complexes. The Job's plot for host **2**-TBPy is shown in Figure 4. In the case of host **1**, the difference in the CIS values between the *N*-CH_3 protons and the *C*-CH_3 protons is 2.12 ppm. On the other hand, in the case of host **2**, the difference is 2.92 ppm. From a comparison of these values, it can be estimated that host **2** significantly controls the alignment of the included **TBPy** molecule in the cavity. This is because the *tert*-butyl substitution

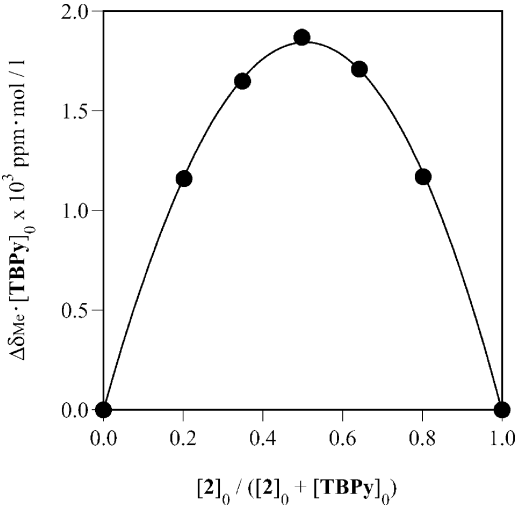


FIGURE 4 A Job's plot for the complexation of **2** and **TBPy**. Total concentration: $[\mathbf{2}]_0 + [\mathbf{TBPy}]_0 = 3.0 \times 10^{-3}$ mol/L.

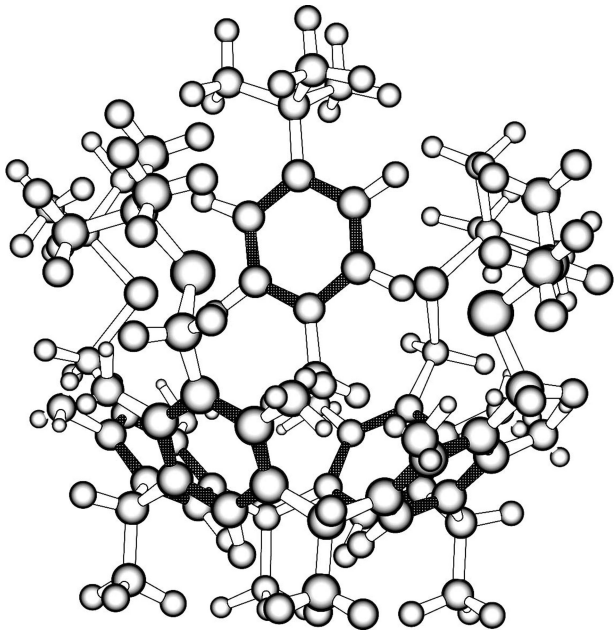


FIGURE 5 Schematic representation for the complex of resorcinarene **2** and **TBPy**. The aromatic rings are shown by the dark C–C bonds.

at the γ-position sterically prevents the pyridinium CH-π interaction with the aromatic cavity. The *Ka* value for the complex of **2** with **TBPy** was 480 M^{-1}, which is 2.8-fold greater than that of **1**. This enhancement in the *Ka* value is attributed to the hydrophobic interaction between the *tert*-butyl groups in both the host and guest molecules. The computer-generated structure for the complex of resorcinarene **2** and **TBPy** is shown in Figure 5.

CONCLUSION

The host–guest complexation behavior of resorcinarenes **1** and **2** with tetraalkylammonium ions and *N*-methylpyridinium ions was investigated by ^{1}H NMR spectroscopy in CD_3OD. The resorcinarene **2** having four *tert*-butylsulfanylmethyl groups at the extra-annular positions showed a superior size and shape selectivity than the resorcinarene **1**. It is concluded that the four bulky hydrophobic substituents at the peripheral positions create a deep hydrophobic cavity with a narrow entrance in methanol.

EXPERIMENTAL

Materials

Resorcinarene **1** was synthesized from resorcinol and acetaldehyde using a literature procedure.[24] Resorcinarene **2** was prepared by the thiomethylation of **1** in acetic acid as previously reported.[16] **Py** and **TBPy** were prepared by methylation of the corresponding pyridines with iodomethane in ethanol at an ambient temperature for 24 h in the dark.

^{1}H NMR Spectroscopy

^{1}H NMR spectra were recorded using a 270 MHz JEOL GX270 spectrometer at 30°C. CD_3OD (99.8% isotopic purity, Merck) was used as the solvent, and the residual signal of the nondeuterated fraction of its methyl group was taken as the internal reference, $\delta = 3.30$.

Determination of Parameters

The stoichiometries of the inclusion complexes were determined using the continuous variation method (Job's method).[25] This method involves running a series of ^{1}H NMR experiments that varies the host-to-guest ratios, while the total molar concentration of the host and guest ($[H]_0 + [G]_0$) remains constant. The parameters are calculated as follows. First, the upfield shifts ($\Delta\delta$) of the appropriate signals of the guest molecule were observed. Second, the $\Delta\delta \cdot [G]_0$ values were plotted versus the molar fraction of the guest ($[G]_0/\{[G]_0 + [H]_0\}$) to produce the Job's curve. The stoichiometry of the complex is obtained from the x-coordinate at the maximum in this curve. Third, the association constants (Ka) of the complexes and the complexation-induced NMR shifts (CIS) of the guest molecules were simultaneously obtained by a computer-assisted nonlinear least-square analysis.[26]

The parameters for the complexation **1-TMA** and **1-Py** were analyzed as follows. The association constants Ka_1 (1:1 complex; HG) and Ka_2 (2:1 complex; H_2G) are expressed by the following equations.

$$Ka_1 = [HG]/(([H]_0 - [HG] - 2[H_2G])([G]_0 - [HG] - [H_2G])) \quad (1)$$

$$Ka_2 = [H_2G]/(([H]_0 - [HG] - 2[H_2G])[HG]) \quad (2)$$

Eqs.(1) and (2) can be analytically solved and provide the values for [HG] and $[H_2G]$ at the given values of Ka_1, Ka_2, $[H]_0$, and $[G]_0$. The

observed $\Delta\delta$ value is expressed by Eq. (3), where CIS_1 and CIS_2 are the CIS values for the 1:1 and 2:1 complexes, respectively.

$$\Delta\delta = CIS_1([HG]/[G]_0) + CIS_2([H_2G]/[G]_0) \quad (3)$$

By using several sets of experimental data ($[H]_0$, $[G]_0$, $\Delta\delta$), together with the estimated values of Ka_1 and Ka_2, the CIS_1 and CIS_2 parameters can be calculated using the least-square method. Finally, the sum of the square of the difference between the calculated and observed chemical shift change is minimized by the systematic variation of Ka_1 and Ka_2.

REFERENCES

[1] J.-M. Lehn, *Supramolecular Chemistry: Concepts and Perspectives* (VCH, Wheinheim, 1995).
[2] V. Böhmer, *Angew. Chem., Int. Ed. Engl.*, **34,** 713 (1995).
[3] P. Timmerman, W. Verboom, and D. N. Reinhoudt, *Tetrahedron*, **52,** 2663 (1996).
[4] Z. Asfari, V. Böhmer, J. Harrowfield, and J. Vicens (Eds.), *Calixarenes 2001* (Kluwer, Dordrecht, 2001).
[5] D. J. Cram and J. M. Cram, *Container Molecules and Their Guests*, *Monographs in Supramolecular Chemistry* (The Royal Society of Chemistry, Cambridge, 1994).
[6] D. M. Rudkevich and J. Rebek, Jr., In G. J. Lumetta, R. D. Rogers, and A. S. Gopalan (Eds.), *Calixarenes for Separations*, pp. 270–282 (American Chemical Society, Washington, DC, 2000).
[7] J. C. Ma and D. A. Dougherty, *Chem. Rev.,* **97,** 1303 (1997).
[8] H.-J. Schneider, D. Guttes, and U. Schneider, *J. Am. Chem. Soc.*, **110,** 6449 (1988).
[9] K. Kobayashi, Y. Asakawa, Y. Kato, and Y. Aoyama, *J. Am. Chem. Soc.*, **114,** 10307 (1992).
[10] T. Fujimoto, R. Yanagihara, K. Kobayashi, and Y. Aoyama, *Bull. Chem. Soc. Jpn.*, **68,** 2113 (1995).
[11] M. Nishio, M. Hirota, and Y. Umezawa, *The CH/p Interaction* (Wiley-VCH, New York, 1998).
[12] H. Konishi, T. Tamura, H. Ohkubo, K. Kobayashi, and O. Morikawa, *Chem. Lett.*, 685 (1996).
[13] O. Morikawa, K. Nakanishi, M. Miyashiro, K. Kobayashi, and H. Konishi, *Synthesis*, 233 (2000).
[14] H. Konishi, O. Morikawa, K. Kobayashi, K. Abe, and A. Ohkubo, *Tetrahedron Lett.,* **44,** 7425 (2003).
[15] H. Konishi, H. Yamaguchi, M. Miyashiro, K. Kobayashi, and O. Morikawa, *Tetrahedron Lett.*, **37,** 8547 (1996).
[16] O. Morikawa, M. Miyashiro, H. Yamaguchi, K. Kobayashi, and H. Konishi, *Supramolecular Chemistry*, **11,** 67 (1999).
[17] A. Arduini, A. Pochini, and A. Secchi, *Eur. J. Org. Chem.,* 2325 (2000).
[18] K. Araki, T. Watanabe, M. Oda, H. Hayashida, M. Yasutake, and T. Shinmyouzu, *Tetrahedron Lett*., **42,** 7465 (2001).
[19] K. Araki, K. Hisaichi, T. Kanai, and S. Shinkai, *Chem. Lett*., 569 (1995).
[20] K. Murayama and K. Aoki, *Chem. Commun.,* 119 (1997).

[21] M. Mäkinen, P. Vainiotalo, M. Nissinenn, and K. Rissanen, *J. Am. Soc. Mass Spectrom.*, **14,** 143 (2003).
[22] M. Mansikkamäki, M. Nissinenn, C. A. Schalley, and K. Rissanen, *New J. Chem.*, **27,** 88 (2003).
[23] M. Mansikkamäki, M. Nissinenn, and K. Rissanen, *Chem. Comm.,* 1902 (2002).
[24] A. G. S. Högberg, *J. Org. Chem.*, **45,** 4498 (1980).
[25] C. Y. Huang, *Methods in Enzymology*, **87,** 509 (1982).
[26] K. Hirose, *J. Incl. Phenom. Macrocycl. Chem.*, **39,** 193 (2001).