in a strongly reduced overlap of the π electrons with the cationic center. Thus, the interplay of electronic and steric effects produces a slight deshielding of the absorptions for the carbocationic center and indicates an overall destabilizing effect of the trimethylsilyl group in **2**.

The geometry of the perpendicular conformer of the 2-silylallyl cation was optimized by keeping the Si–C2–C1 bond angle constant at 120° as otherwise it collapsed into a geometry resembling the 3-silyl-2-propenyl cation. The geometry obtained with a constricted Si–C2–C1 bond angle was used for the IGLO calculation. The cationic center of the perpendicular form of the allyl cation is at δ ^{13}C 362.0, deshielded from the planar form by 133.2 ppm. On the other hand, the corresponding difference for **10** and **5** is 67.9 ppm. The relatively shielded cationic absorption for **10** implies hyperconjugative stabilization by the β-Si substituent in the favorable perpendicular conformation.

The present study shows that β-silyl substitution in allylic cations does not result in stabilization. However, it decreases the rotational barrier due to β-silyl stabilization in the intermediate perpendicular allyl cation. The slight destabilizing effect observed in the present study could be inferred to arise from a neighboring silicon-induced anisotropic effect or from the trimethylsilyl group induced twisted π system. The lack of stabilization in carbocation **2** rules out the importance of the electron-releasing inductive effect as a significant contributing factor for β-silyl stabilization. Similar conclusions were reached recently by Kresge and Tobin on the hydrolysis of β-(trimethylsilyl)vinyl ethers.[9]

Experimental Section

Diethyl ether was freshly distilled from Na–benzophenone ketyl. 2-Adamantanone, 1-(trimethylsilyl)vinyl bromide, vinyl bromide, and *tert*-butyllithium were obtained from Aldrich and used as received. [1-(Trimethylsilyl)vinyl]lithium and vinyllithium were prepared following literature procedures.[6] GC/MS analyses were performed on a Finnigan-Mat/Incos-50 mass spectrometer equipped with a Varian 3400 gas chromatograph. ^{1}H and ^{13}C NMR spectra were obtained on a Varian VXR-200, Unity-300, or a Bruker-360 instrument equipped with a variable-temperature probe. ^{1}H and ^{13}C NMR chemical shifts for the cations are referenced to external capillary tetramethylsilane. Melting points are uncorrected.

2-[1-(Trimethylsilyl)vinyl]-2-adamantanol. 2-(Trimethylsilyl)vinyl bromide (2.86 g, 15.96 mmol) dissolved in 50 mL of ether was placed in an oven-dried 250-mL 3-necked round-bottomed flask, equipped with a magnetic stirrer, a rubber septum, and a nitrogen inlet. The flask was cooled to −78 °C in a dry ice/acetone bath, and excess *tert*-butyllithium (1.7 M in pentane, 14.1 mL, 23.9 mmol) was added dropwise through the addition funnel. The contents were warmed to 0 °C, stirred for 30 min, and recooled to −78 °C. Adamantanone (2 g, 13.3 mmol) dissolved in about 50 mL of ether was added dropwise to the contents and stirred for 30 min. The contents were warmed to room temperature, poured into 100 mL of water, and extracted with ether (2 × 50 mL). The organic layers were washed with saturated sodium bicarbonate (2 × 20 mL) and dried ($MgSO_4$), and the solvents were rotary evaporated. Compound **1** was obtained as a white solid (2.5 g, 75%) after recrystallization from pentane at −78 °C: mp 79.8 °C; MS (m/z) 250 (0.4, M^+), 235 (21), 160 (42.5), 151 (57.6), 127 (23.9), 75 (100); ^{1}H NMR δ 5.90 (d, 1 H, J = 1.63 Hz, Z-vinylic H), 5.62 (d, 1 H, J = 1.9 Hz, E-vinylic H), 2.32 (d, 2 H, J = 11.5 Hz, C6-H), 1.5–2.15 (m, 13 H), 0.2 (s, 9 H, $Si(CH_3)_3$); ^{13}C NMR δ 155.9 (C1′), 125.8 (C2′), 78.0 (C2), 37.7 (C6), 36.1 (C1, C3), 35.1 (C4, C9), 33.0 (C8, C10), 27.7 (C5), 27.2 (C7), −1.1 ($Si(CH_3)_3$).

2-Vinyl-2-adamantanol. Using the above procedure, vinyllithium prepared from vinyl bromide (0.86 g, 8 mmol) and *tert*-butyllithium (9.4 mL, 16 mmol), was allowed to react with 2-adamantanone (1 g, 6.7 mmol). 2-Vinyl-2-adamantanol (**3**) (0.95 g, 83%) was obtained as colorless crystals upon recrystallization from pentane at −78 °C: mp 53.6 °C; MS (m/z) 178 (100, M^+), 163 (22.2), 149 (26.3), 135 (40.2), 121 (22.5), 109 (24.9), 91 (30.4); ^{1}H NMR δ 6.28 (m, 1 H, C1′-H), 5.16 (d, 1 H, J = 11 Hz, C2′ E-H), 5.35 (d, J = 18 Hz, C2′ Z-H), 2.2 (d, 2 H, J = 12.8 Hz, C6-H), 1.4–1.9 (m, 13 H); ^{13}C NMR δ 144.7 (C1′), 113.5 (C2′), 74.1 (C2), 37.9 (C6), 37.8 (C1, C3), 34.6 (C4, C9), 32.7 (C8, C10), 27.3 (C5), 27.1 (C7).

Preparation of Carbocations. FSO_3H was doubly distilled. The precursor alcohols (50 mg) were suspended in SO_2ClF in 5-mm NMR tubes and were treated with 5-fold excess of FSO_3H in SO_2ClF solution at −120 °C (liquid-nitrogen/pentane bath). The dissolution of the cations in SO_2ClF was achieved by efficient mixing with a vortex stirrer.

Acknowledgment. Support of our work by the National Institutes of Health is gratefully acknowledged. We are grateful to Professor W. Kutzelnigg and Dr. M. Schindler for providing a copy of their IGLO program.

---

[9] Kresge, A. J.; Tobin, J. B. *J. Phys. Org. Chem.* **1991**, *4*, 587.

Binding Constants as a Probe of the Microenvironment in Polymer-Supported Reagents

Spiro D. Alexandratos,* Corinne E. Grady, Paul Merda, and Paul T. Kaiser

Contribution from the Department of Chemistry, University of Tennessee, Knoxville, Tennessee 37996.
Received September 23, 1991

Abstract: A procedure is developed for quantifying the degree to which a ligand–substrate interaction is affected by the microenvironment surrounding the polymer-supported ligand. The binding constants between a series of substrates (such as substituted benzoic acids, anilines, phenols, etc.) and a ligand covalently bound to different polymer matrices are calculated through the Langmuir isotherms. The binding constants across different matrices quantify the effect of the microenvironment on each ligand–substrate interaction. A linear correlation of the binding constants with the substituent Hammett σ constants yields a slope that is a measure of the interaction's sensitivity to electron density changes within a given matrix; comparing the slopes across different matrices provides a measure of how the polymeric microenvironment influences that sensitivity. Matrix flexibility is thus found to have a major impact on the ligand–substrate interaction.

Introduction

Polymer-supported reagents have been designed with ionic and molecular recognition for application to such areas as chromatographic separations and optical resolutions.[1] As biomimetic polymers, they have been used for selective organic transformations.[2] Ligand–substrate binding is considered to be a function of the electrostatic interactions at the active site. The degree to which the polymer matrix on which ligands are covalently bound

---

[1] *Syntheses and Separations Using Functional Polymers*; Sherrington, D. C., Hodge, P., Eds.; John Wiley: New York, 1988.

[2] Breslow, R. *Chem. Soc. Rev.* **1972**, *1*, 553. *Biomimetic Polymers*; Gebelein, C. G., Ed.; Plenum Press: New York, 1990.

influences the recognition process still needs to be addressed quantitatively. Previous studies suggest that effects from the matrix can be superimposed on ionic and molecular interactions.[3-8] Differences in a polymer's microenvironment from bulk solution have been studied with fluorescence spectroscopy.[9,10] Such differences have been used in hydrophobic interaction chromatography for the separation of proteins.[11]

A method of analysis is required to determine the extent to which the ligand–substrate interaction depends upon the microenvironment surrounding the polymer-supported ligand. We report that molecular binding studies within a Hammett-type correlation may be used as a probe of the polymeric microenvironment. The procedure developed for quantifying matrix effects on the ligand's microenvironment is as follows: (1) synthesize polymer-supported reagents with a given ligand bonded onto different matrices; (2) choose a series of aromatic substrates with a common functional group and vary the electron density at that functional group by varying the substituents on the aromatic ring; (3) calculate Langmuir isotherms and binding constants[12] for each substrate (a comparison of binding constants across different matrices quantifies the effect of the microenvironment on each ligand–substrate interaction); and (4) correlate the binding constants with the substituent σ constants. With a given matrix, the slope is a measure of the interaction's sensitivity to electron density changes, and a comparison of slopes across different matrices provides a measure of how the polymeric microenvironment influences that sensitivity.

Experimental Section

The general procedure for the synthesis of copolymer beads via suspension polymerization has been published.[13] The copolymers were crosslinked with 2% and 15% divinylbenzene (technical grade DVB, Dow Chemical Co.). The copolymer for the partially functionalized 2% DVB amine resin was prepared from a vinylbenzyl chloride (Dow)/styrene (Aldrich) monomer solution in a 40:60 weight ratio in order to ensure a uniform distribution of the ligands throughout the matrix.

The general procedure for the amination reaction with dimethylamine has been published.[14] A reaction time of 17 h was used in the present case, rather than 4 h, in order to ensure complete reaction of the highly crosslinked and partially functionalized polymer supports. The total capacity of each resin was determined by successive 1-L elutions of H_2O, 1 N HCl, H_2O, 1 N NaOH, H_2O, 1 N HCl, H_2O, and 1 N $NaNO_3$. The chloride content of the last elution was determined by Mohr titration. In this manner, the fully functionalized 2% and 15% DVB polymers were determined to have capacities of 5.15 and 3.91 mequiv/g, respectively, while the 40% functionalized polymer had a capacity of 2.19 mequiv/g. All capacities are referenced to the dry weight of the polymer. The presence of quaternary amine sites on these polymers (arising through a secondary crosslinking reaction) was evaluated by 1-L elutions of H_2O, 1 N NaOH, H_2O, and 1 N $NaNO_3$ and titrating the last eluent for hydroxide ions with 0.1 N H_2SO_4. The quaternary site capacity for each polymer, in the order listed above, is 0.30, 0.00, and 0.00 mequiv/g. Only the dimethylamine ligand is thus present to complex the molecular substrates.

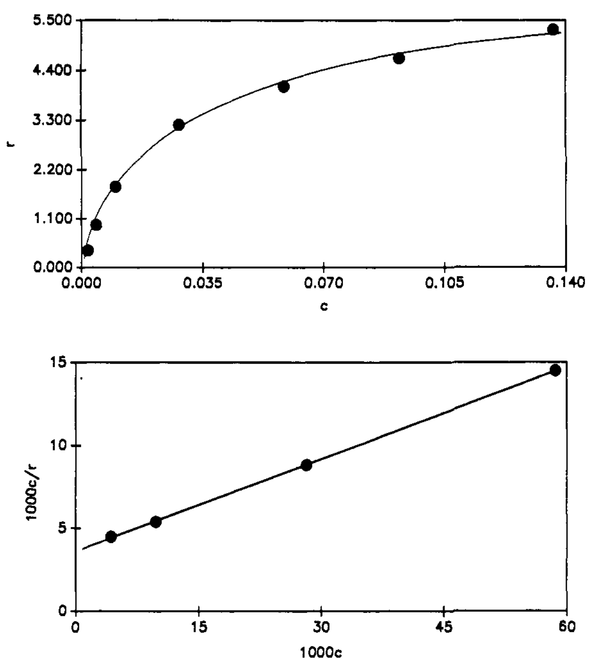

Figure 1. Adsorption isotherm of the 2% DVB amine polymer interacting with benzoic acid (a, top); y-reciprocal plot of the 2% DVB amine polymer interacting with benzoic acid (b, bottom).

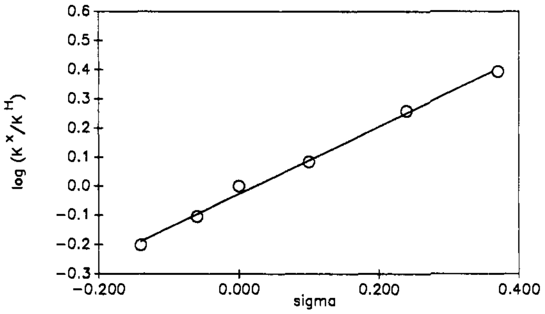

Figure 2. Hammett plot of binding constant ratios for the 2% DVB amine polymer/ArCOOH interaction.

Table I. Binding Constants (M^{-1}) for the Polymer-Supported Dimethylamine Ligands and Substituted Benzoic Acids

polymer		substituted ArCOOH					
%DVB	%fn[a]	p-CH_3	m-CH_3	H	m-CH_3O	p-Cl	m-Cl
2	100	32.13	40.17	51.07	61.94	92.56	126.19
15	100	15.39		19.41		43.11	67.99
2	40	32.20		38.01		68.55	97.85

[a] Percent functionalization.

The substrates are a series of benzoic acids with substituents (p-CH_3, m-CH_3, H, m-CH_3O, p-Cl, and m-Cl) used to adjust the hydrogen-bonding ability of the functional group. The tendency of each substituent to act as an electron donor or withdrawer is quantified by its Hammett σ constant[15] (−0.14, −0.06, 0, 0.10, 0.24, and 0.37 for the substituents in the order listed above).

The current procedure for quantifying the extent of molecular complexation by the polymeric reagents expands on one which has been published[16] in order to yield a complete isotherm plot. All points in the isotherm plots used Buchner-dried (rather than vacuum-dried) polymer beads. Methanol is the preferred solvent[17] in which to carry out these studies; the water in the polymers was thus exchanged with methanol prior to contact with the substrate solutions. The polymer beads were weighed on a Mettler analytical balance. A representative sample whose Buchner-dry weight was known was oven-dried at 110 °C, and the dry to wet weight ratio was then used to determine the dry weights of all

---

(3) Warshawsky, A. *Isr. J. Chem.* **1979**, *18*, 318.

(4) Green, B. R.; Hancock, R. D. *Hydrometallurgy* **1981**, *6*, 353.

(5) Schwachula, G.; Popov, G. *Pure Appl. Chem.* **1982**, *54*, 2103.

(6) Xu, W. Y.; Smid, J. *J. Am. Chem. Soc.* **1984**, *106*, 3790.

(7) Winston, A.; Kirchner, D. G.; Rosthauser, J. W. *Gov. Rep. Announce. Index (U.S.)* **1980**, *80*, 2348.

(8) Shambhu, M. B.; Theodorakis, M. C.; Digenis, G. A. *J. Polym. Sci., Polym. Chem. Ed.* **1977**, *15*, 525.

(9) Mikes, F.; Labsky, L.; Strop, P.; Kralichek, J. *Polym. Sci. Technol.* **1985**, *30*, 265.

(10) Peterson, K. A.; Zimmt, M. B.; Fayer, M. D.; Jeng, Y. H.; Frank, C. W. *Macromolecules* **1989**, *22*, 874.

(11) Shaltiel, S. In *Affinity Chromatography and Biological Recognition*; Chaiken, I. M., Wilchek, M., Parikh, I., Eds.; Academic Press: Orlando, FL, 1983.

(12) Connors, K. A. *Binding Constants: The Measurement of Molecular Complex Stability*; John Wiley: New York, 1987.

(13) Tomoi, M.; Ford, W. T. *J. Am. Chem. Soc.* **1981**, *103*, 3821.

(14) Alexandratos, S. D.; Quillen, D. R.; Bates, M. E. *Macromolecules* **1987**, *20*, 1191.

(15) Hammett, L. P. *Physical Organic Chemistry*, 2nd ed.; McGraw-Hill: New York, 1970. Hansch, C.; Leo, A.; Unger, S. H.; Kim, K. H.; Nikaitani, D.; Lien, E. J. *J. Med. Chem.* **1973**, *16*, 1207.

(16) Alexandratos, S. D.; Kaiser, P. T.; Grady, C. E. *Solvent Extr. Ion Exch.* **1991**, *9*, 309.

(17) Alexandratos, S. D.; Kaiser, P. T. *Ind. Eng. Chem. Res.* **1990**, *29*, 1306.

samples for calculation of the final substrate capacities. A 17-h contact time ensured that all samples had attained equilibrium. The amount of ArCOOH complexed by the polymers was determined potentiometrically (Corning pH/ion meter 150) and was in accord with values obtained colorimetrically. Repeat runs showed a precision of ±2%.

Results

The effect of a polymer's overall polarity (as set by the percent substitution) and rigidity (as controlled by the crosslink level) on the interaction between a dimethylamine ligand on polystyrene and a carboxylic acid group was investigated. The adsorption isotherm for the benzoic acid interaction with the fully functionalized 2% DVB amine polymer is given in Figure 1a. The saturation capacity for all of the aromatic acids is 4.8 mequiv/g. The binding constant was calculated from the y-reciprocal plot[12] (Figure 1b) with lower and upper limits of 20% and 80% saturation, respectively, as recommended by Deranleau.[18] The linearity of all plots (correlation coefficients 0.99 or greater) confirms the assumption of 1:1 complex formation inherent to the y-reciprocal calculation. Binding constants from these plots were consistent with those calculated from Scatchard and double-reciprocal plots.

The binding constants from the interaction with fully functionalized 2% DVB polymer are found to increase with increasing substrate ability to hydrogen bond with the amine lone pair (Table I). Correlating the data within a Hammett-type relationship through the relative ratios of the binding constants (substituted acids, K^X, to benzoic acid, K^H) in Figure 2 yields eq 1, where the slope now quantifies the interaction's sensitivity to electron density changes at the active site.

$$\log (K^X/K^H) = 1.159\sigma - 0.027 \qquad (1)$$

The polymer's flexibility is found to be critical to maximizing the ligand–substrate interaction: as indicated in Table I, the binding is approximately 50% weaker in the more highly crosslinked polymer. The 15% DVB matrix also shows a 12% increase in sensitivity to electron density changes (eq 2) relative to that with a flexible 2% DVB matrix.

$$\log (K^X/K^H) = 1.296\sigma + 0.045 \qquad (2)$$

Decreasing the polarity of a flexible matrix by decreasing its percent substitution to 40% results in a milder increase in binding constants relative to the fully functionalized polymer (Table I), with increasing σ values. The Hammett plot yields eq 3. A comparison of the slopes shows a 15% decrease in reaction sensitivity with the less polar network (cf. eq 1).

$$\log (K^X/K^H) = 0.980\sigma + 0.038 \qquad (3)$$

Discussion

While the ligand–substrate interaction is an important factor in determining the binding constant, the polymeric microenvironment plays an equally critical role in the overall value. Decreasing matrix flexibility decreases the binding between the ligand and the substrate with a 12% increase in sensitivity to changes in the active site electron density relative to the flexible 2% DVB matrix. The lower binding is not due to the lower capacity and polarity of the 15% DVB polymer since decreasing the polarity of the microenvironment at a flexible crosslink level leads to a 15% decrease in reaction sensitivity. Decreasing the degree of substitution decreases the polymer's polarity as measured by its ability to sorb low-polarity solvents such as dioxane (the dielectric constant for dioxane is 2.209, while it is 2.284 for benzene, 7.6 for tetrahydrofuran, and 20.1 for 1-propanol).[19] A comparison of the polarities of different polymers based on their swelling ratios (mL swollen polymer/mL dry polymer) is thus possible at a constant crosslink level. Comparing 2% DVB-crosslinked, 100%-substituted polystyrene with 40%-substituted and unsubstituted polystyrene shows swelling ratios in dioxane of 1.19, 1.76, and 3.10 mL/mL, respectively; the increased sorption of a nonpolar solvent with decreasing degree of substitution points to a decrease in the polymer's overall polarity.

Weaker substrate binding with decreasing matrix flexibility may be due to steric effects within the matrix: at higher crosslink levels, the polymer chains lose their ability to adopt new equilibrium conformations as proximate ligands bind substrates, and this could result in longer ligand–substrate distances (hence, lower binding constants) in order to minimize steric crowding. This is supported by the lower saturation capacity of the 15% DVB polymer (56% of maximum) relative to the 2% DVB polymer (94% of maximum). Matrix flexibility can thus change the values of the binding constants quite dramatically, and this can have implications in cases where extrapolations are made from soluble analogues to polymer-supported reagents and catalysts.

Studies are in progress with styrene–acrylonitrile, styrene–methacrylonitrile, and styrene–methyl methacrylate copolymers. Direct comparisons to small-molecule analogues are also in progress following the Benesi–Hildebrand treatment.

Acknowledgment. We are grateful to the Department of Energy, Office of Basic Energy Sciences, for its continuing support of this research through Grant DE-FG05-86ER13591. The vinylbenzyl chloride was a generous gift of the Dow Chemical Company.

Registry No. $HO_2CC_6H_4$-p-CH_3, 99-94-5; $HO_2CC_6H_4$-m-CH_3, 99-04-7; $PhCO_2H$, 65-85-0; $MeOC_6H_4$-m-CO_2H, 586-38-9; ClC_6H_4-p-CO_2H, 74-11-3; ClC_6H_4-m-CO_2H, 535-80-8.

---

(18) Deranleau, D. A. *J. Am. Chem. Soc.* **1969**, *91*, 4044.

(19) *Handbook of Chemistry and Physics*, 71st ed.; Lide, D. R., Ed.; CRC Press: Boca Raton, FL, 1991; Chapter 8, p 44.