a single high-affinity site with an estimated association constant of 2×10^4 M^{-1}.[18,25]

The specific binding site of *rac*-Fe(5-BrEHPG)$^-$ appears to be at or near the high-affinity site for bilirubin IXα (Figure 2a). One equivalent of bilirubin IXα added to HSA ($K \approx 10^8$ M^{-1}) completely inhibits the high-affinity binding of the racemic complex (Figure 1b). Other experiments show that the specific site does not appear to be one of the common drug-binding sites, denoted site I and site II, that were identified by Sudlow et al.[27] in displacement studies using the fluorescent probes dansylamide and dansylsarcosine, respectively. The addition of a large molar excess of the structurally analogous but colorless gallium(III) complex of 5-BrEHPG to both types of HSA-probe complexes results in only small reductions of fluorescence intensity in each case ($\sim$ 20%).[18] The lack of preferential displacement of either probe removes site I and II as candidates for the high-affinity site for *rac*-Fe(5-BrEHPG)$^-$. In addition, no significant degree of tryptophan-214 fluorescence quenching, seen for some site I binding drugs,[28,29] is observed with the gallium analogue.[18]

rac-Fe(5-BrEHPG)$^-$ shares certain chemical features in common with bilirubin, such as anionic charge, hydrogen-bonding groups, and hydrophobic regions, which, while prerequisite for binding, are insufficient by themselves in directing the complex to this specific site since the meso isomer exhibits these same features yet lacks the high-affinity binding. The stereoselectivity of the binding, therefore, suggests that the unique structure of *rac*-Fe(5-BrEHPG)$^-$ may be similar to that of HSA-bound bilirubin. The conformation of bilirubin when bound is still not known despite extensive study. Although circular dichroism studies suggest that the two dipyrromethene chromophores are held in a chiral configuration at some angle relative to one another, the flexibility inherent in the central methylene gives rise to a wide range of such conformers (Figure 2c,d).[30-32] Remarkable similarity exists between *rac*-Fe(5-BrEHPG)$^-$ and extended conformations of bilirubin in terms of the relative orientation of the planar groups with respect to each other and with respect to the central anionic region (Figure 2e).[18] Such a conformation of HSA-bound bilirubin seems reasonable since it would allow the dipyrromethene units to project into different regions of the HSA molecule, as suggested by others,[34] affording noncovalent contacts with both halves that would contribute collectively to the high association constant.

This work represents the first use of rigid metal complexes to explore the shape of a protein binding site for a potentially flexible ligand. The unique stereochemistry of metal complexes makes them well suited for probing macromolecules as shown in recent applications to DNA.[5] Further studies will determine if the binding of *rac*-Fe(5-BrEHPG)$^-$ to the bilirubin site on HSA is enantiomerically specific (i.e., preferential binding of either the *RR* or *SS* isomers).

Our results also point to the feasibility of metal-containing drugs, especially for diagnosis, which mimic the chemistry of endogenous substances. The binding of *rac*-Fe(5-BrEHPG)$^-$ to the bilirubin site on HSA illustrates how simple structural features of a complex, such as the relative placement of charged, hydrogen-bonding, and hydrophobic groups, can be sufficient for its recognition by in vivo binding sites. The utility of these iron(III) complexes as hepatobiliary imaging agents[8,9] most likely stems from hepatocellular binding interactions at sites involved in the transport of bilirubin.

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Supplementary Material Available: Information on the synthesis of the complexes, binding studies, fluorescence studies, and structural comparisons and NMR spectra of the complexes (4 pages). Ordering information is given on any current masthead page.

(25) The binding data for *rac*-Fe(5-BrEHPG)$^-$, in the form of a r (moles of complex bound per mole of HSA) vs. C_{free} (unbound complex concentration) plot, was fit to the following:

$$r = (KC_{free})/(1 + KC_{free}) + PC_{free}$$

A single high affinity site with association constant K was assumed. P represents a simple partition coefficient[26] to take into account the nonsaturable, nonspecific binding noted for the meso isomer. A least-squares fit yielded $K = 2.2 \times 10^4$ m^{-1} and $P = 6.2 \times 10^3$ M^{-1}. The calculated isotherm was recast into the Scatchard format for display in Figure 1.

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A New Room Temperature Molten Salt Solvent System: Organic Cation Tetrachloroborates

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In the past decade there has been considerable interest in $AlCl_3$-containing molten salts. These melts provide novel media for fundamental studies and are also of interest in high-energy batteries and for catalytic applications.[1] Relatively few molten salt systems are liquid at or below room temperature. The properties of these systems, mainly organic chloroaluminates, have been reviewed by Hussey;[2] several other room temperature molten salts have been described recently.[3] This paper describes tetrachloroborate salts that are stable liquids at room temperature; they are products of the reaction between *n*-butylpyridinium chloride or methylethylimidazolium chloride and boron trichloride.

N-Butylpyridinium chloride (BPC) and 1-methyl-3-ethylimidazolium chloride (MEIC) were prepared as described in ref 4-6. Melts were prepared by distillation of a measured volume of BCl_3 onto a weighed amount of BPC or MEIC in a glass tube cooled with liquid nitrogen. The tube was then sealed and warmed to room temperature. The composition of such melts is uncertain by about 15%.

Conductivity cells were calibrated with standard KCl; a YSI conductivity bridge was used for specific conductance measurements. PAR equipment was used for electrochemical measurements. Raman spectra were obtained with an ISA Ramanor 2000 spectrometer, an argon ion laser, and a photon-counting system.

Both solid chlorides react exothermically with gaseous BCl_3 to form droplets of colorless, viscous melt at room temperature. The reaction with MEIC is more exothermic. When the mole ratio of BCl_3 to the organic chloride is approximately 1:1, a single phase is formed; when the ratio is 2:1, two immiscible liquid phases

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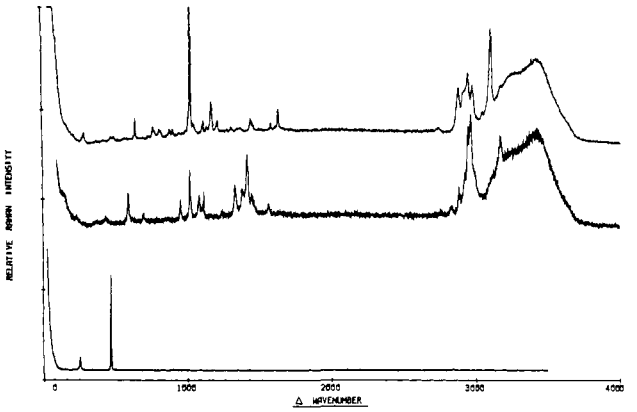

Figure 1. Raman spectra of BPC, (top), MEIC, (center) as aqueous solutions, and liquid BCl_3 (bottom).

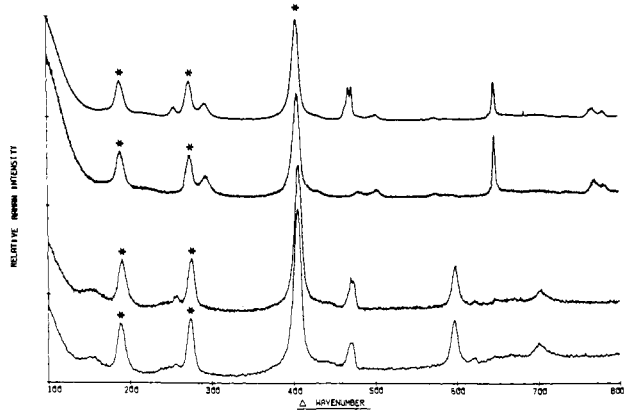

Figure 2. Raman spectra of room temperature tetrachloroborate melts: acidic BPC melt (molar ratio BCl_3:BPC = 2:1) (top); neutral BPC melt (BCl_3:BPC = 1:1) (second from top); acidic MEIC melt (BCl_3:MEIC = 2:1) (second from bottom); neutral MEIC melt (BCl_3:MEIC = 1:1) (bottom). Bands assigned to BCl_4^- are indicated by an asterisk. The composition of the neutral melt sample was nominally 1:1; however, some BCl_3 was present (peak near 470 cm^{-1}).

are formed at ~0 °C, one of which is BCl_3.

Raman spectra of aqueous solutions of BPC, MEIC and liquid BCl_3 are presented in Figure 1. Raman spectra of neutral (mole ratio BCl_3:organic chloride is approximately 1:1) and acidic (mole ratio approximately 2:1) melts prepared from BCl_3 and BPC or MEIC are presented in Figure 2. Three of the four modes of the tetrachloroborate anion are clearly seen for both the neutral and acidic melts; their positions are noted with an asterisk. The fourth mode (ν_3) is very weak and is obscured by a cation mode in the MEIC melt. The frequencies for BCl_4^- in the melts agree quite well with the tetrachloroborate frequencies reported by Bullock et al.[7] The melt frequencies and assignments are (with Bullock's frequency in parentheses) ν_1 405 (396), ν_2 188 (196), ν_3 696 (696), and ν_4 273 (275). No significant composition dependence was observed for the peak positions. In acidic melts, the spectra show the presence of dissolved BCl_3 in the melt phase; since these are saturated solutions, the intensity of the BCl_3 ν_1 peak, when compared to that of neat BCl_3, indicates that the solubility of BCl_3 in both BPC and MEIC melts is about 1 M.

Chloroaluminate melts with an excess of $AlCl_3$ are known to contain the $Al_2Cl_7^-$ ion.[8] All of the peaks in the spectra of acidic BCl_3 melts can be attributed to either the cation modes, BCl_3 modes, or BCl_4^- modes. There is no evidence for the presence of $B_2Cl_7^-$ ion in these systems, even when the melts are cooled to about 77 K.

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Table I. Properties of Tetrachloroborate Melts

composition[a]	phases[b]	liquid temp[c]	density[d]	conductivity[e]	EC window[f] Pt	EC window[f] GC
1:1 BCl_3:BPC	1	+16.5	1.28	1.6×10^{-2}	1200	3300
2:1 BCl_3:BPC	2	−18	1.26	6.1×10^{-3}	900	
1:1 BCl_3:MEIC	1	+16.5	1.29	1.6×10^{-2}	1000	3300
2:1 BCl_3:MEIC	2	−12	1.23	1.6×10^{-2}	1000	

[a] Approximate mole ratio BCl_3:organic chloride. [b] Number of liquid phases present. [c] °C (±0.5 °C). [d] g/mL (±0.05 g/mL). [e] Ω^{-1} cm^{-1} (±10%). All measured near room temperature, except for the 1:1 BPC melt which was measured at 110 °C. [f] Electrochemical window width, mV. Pt refers to platinum working electrode; GC refers to glassy carbon working electrode.

Electrochemical and physical properties of the neutral and acidic melts are collected in Table I. The electrochemical measurements were made with a quasi-reference electrode;[9] hence only the width of the electrochemical window is reported. At the anodic limit a gaseous product, probably Cl_2, is formed; the cathodic limit corresponds to cation reduction, as suggested by the intense blue for BPC,[10] or orange for MEIC,[11] color formed at both platinum and glassy carbon (GC) electrodes. There is no evidence for boron deposition from these melts.

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(Aminoalkyl)trimethylsilanes. A New Class of Monoamine Oxidase Inactivators

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Inactivators of monoamine oxidase (MAO) have been shown to exhibit antidepressant activity.[1,2] Over the last several years we have investigated the mechanisms of inactivation of MAO by cyclopropylamines,[3–13] by a cyclobutylamine,[14] and by allylamine.[15] All of the evidence from these inactivation studies supports a radical mechanism for MAO-catalyzed amine oxidation.

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