approach can be extended to more remote "α,ω"-eliminations that produce unsaturated or diradical products. For benzynes **1**–**3**, the procedure involves regioselective formation of isomeric chlorophenyl anions (**1a**–**3a**) followed by measurement of the activation energies for chloride loss resulting from collisional activation (Scheme I). Barring any reverse activation energies or kinetic shifts, the measured activation energies can be directly equated with the enthalpies of bond cleavage by means of a simple thermochemical cycle to obtain heats of formation for the neutral benzyne products.[20]

m-Chlorophenyl and *p*-chlorophenyl anions (**2a** and **3a**) are readily generated from the reactions between fluoride and the corresponding (chlorophenyl)trimethylsilanes.[21] The *o*-chlorophenyl anion (**1a**) can be prepared in isomerically pure form by proton abstraction from chlorobenzene by furanide ion. The CID behavior described below, as well as the characteristic reactivity displayed by each ion, shows that they are distinct, noninterconverting structures. Proton transfer reactions of **2a** and **3a** with various reference acids indicate that the meta and para positions of chlorobenzene have similar acidities, lying between that of H_2O ($\Delta G_{acid} = 384.1 \pm 0.2$ kcal/mol)[22] and furan ($\Delta G_{acid} = 380.0 \pm 3.0$ kcal/mol).[22] Bracketing experiments with chlorobenzene and its conjugate base anion locate the gas-phase acidity of the ortho position between that of fluorobenzene ($\Delta G_{acid} = 378.9 \pm 2.0$ kcal/mol)[23] and furan. From the bracketed acidities and estimates for the entropy contributions,[24] we assign ΔH_{acid} values to the ortho, meta, and para positions of chlorobenzene to be 388 ± 2, 390 ± 2, and 390 ± 2 kcal/mol, respectively.

Each of the chlorophenyl anion isomers undergoes efficient fragmentation under single-collision conditions with argon target in the triple quadrupole analyzer to produce Cl^- as the only ionic product. Monitoring the chloride yield as a function of the center-of-mass collision energy gives an ion appearance plot from which the dissociation activation energy can be obtained using an analysis procedure that has been described previously.[19,25] Figure 1 illustrates the characteristic Cl^- appearance curves for the three isomers, along with the analytical fit for each.[26] The final average values of the CID threshold energies, E_T, for the ortho, meta, and para isomers obtained from replicate measurements are 15.7 ± 3.0, 24.2 ± 3.0, and 35.3 ± 3.0 kcal/mol, respectively, where the indicated uncertainty is at least two standard deviations.

The heats of formation of the neutral benzyne products are related to the measured chloride dissociation energies according to eq 1, where $\Delta H_{acid}(C_6H_5Cl)$ is the appropriate ortho, meta, or para acidity of chlorobenzene from this work, and the auxiliary data for HCl and C_6H_5Cl are taken from the literature.[22] The

$$\Delta H^\circ_{f,298}(C_6H_4) = (E_T + 0.6) + \Delta H_{acid}(C_6H_5Cl) - \Delta H_{acid}(HCl) + \Delta H^\circ_{f,298}(C_6H_5Cl) - \Delta H^\circ_{f,298}(HCl) \quad (1)$$

0.6 kcal/mol factor is an expansion-work term for converting the activation energies to enthalpies.[19] The final heats of formation derived in this manner are the following: $\Delta H^\circ_{f,298}$(*o*-benzyne) = 106 ± 3, $\Delta H^\circ_{f,298}$(*m*-benzyne) = 116 ± 3, and $\Delta H^\circ_{f,298}$(*p*-benzyne) = 128 ± 3 kcal/mol, where the assigned uncertainty represents the root-square sum of the component uncertainties. Adiabatic dissociation to give the ground states of the benzyne products is assumed; all three isomers are either known or predicted to be singlets.[3,10,11]

The measured heat of formation for *o*-benzyne is in excellent agreement with the recent estimates by Riveros, Ingemann, and Nibbering (105 ± 3 kcal/mol)[6] and by Guo and Grabowski (105 ± 5 kcal/mol)[7] and further confirms the claims made by these investigators that the older values in the literature (ca. 117 kcal/mol)[4,5] are too high. The quantitative accord for *o*-benzyne also supports our contention that the Cl^- dissociation reactions depicted in Scheme I occur at the thermochemical limit, i.e., with no reverse activation energy or kinetic shifts.[20] The bicyclic isomers of **2** and **3** are calculated to lie higher in energy by 32 and 77 kcal/mol, respectively.[10] Moreover, although the measured heat of formation of **3** is close to that of (*Z*)-3-hexene-1,5-diyne at 127 kcal/mol,[22] formation of this isomer as the product of Cl^- loss from **3a** at threshold by either a direct or concerted (Grob-like) fragmentation mechanism is considered unlikely in view of the substantial activation energy (>30 kcal/mol) for cyclization of the enediyne to **3**.[15] Multireference GVB calculations by Noell and Newton suggest that *m*- and *p*-benzyne (singlets) are higher in energy than the (singlet) ortho isomer by 14.5 and 23.3 kcal/mol, respectively,[10] in good agreement with the present results.

The currently accepted value for the first C–H bond energy in benzene, $DH^\circ[C_6H_5{-}H]$, is 110.9 ± 0.7 kcal/mol.[22] From the benzyne thermochemistry determined in this study we calculate the ortho, meta, and para C–H bond energies in phenyl radical to be 79 ± 3, 89 ± 3, and 101 ± 3 kcal/mol, respectively. The differences between the first and second C–H bond energies for benzene provide a quantitative measure of the extent of interaction between radical centers in the benzynes and, at the same time, expose the limitations of simple bond additivity approaches to estimating biradical thermochemistry.[27]

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Gas-Phase Molecular Recognition: Gas-Phase Crown Ether–Alkali Metal Ion Complexes and Their Reactions with Neutral Crowns

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The ability of crown ethers to selectively form complexes with alkali metal ions is well-known. The model originally proposed by Pedersen[1] and quantified by Izatt and co-workers,[2] that crowns with a given cavity size are selective for cations with radii matching that of the cavity, is now generally accepted,[3] although faults of the model have been pointed out.[4-6] Arguments against the

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"ion-in-the-hole" model are based on binding constant measurements in various solvents, and stoichiometries in condensed media. Clearly, all of these observations are influenced by the presence of solvents and counterions. In an attempt to clarify this issue and in the hope of observing gas-phase molecular recognition, we have undertaken a study of crown ether–alkali metal cation complexes in the gas phase, where neither solvents nor counterions are present, and have found strong evidence for size-dependent chemistry.

Prior work with gas-phase complexes of crown ethers includes proton transfer equilibrium measurements,[7] a study of 12-crown-4 interacting with Fe^+, Co^+, $FeCO^+$, and $CoCO^+$;[8] studies of crown–alkali metal complexes generated using fast atom bombardment (FAB) from a glycerol matrix[9,10] and using ^{252}Cf plasma desorption from a nitrocellulose matrix;[11] and a study of crown–diazonium ion complexes generated using field desorption and FAB.[12] When equimolar mixtures of alkali cations were dissolved with crowns in solution and ions were formed from the mixture using either FAB[9,10] or plasma desorption,[11] the relative crown–cation complex ion intensities, observed via conventional mass spectrometry, were found to closely parallel the relative complex stability constants in solution. These interesting results support the "ion-in-the-hole" idea, but ambiguity remains as to whether the complexes were preformed in condensed phase and then desorbed, or reflect true gas-phase chemistry.

We have generated gas-phase complexes of Li^+, Na^+, K^+, Rb^+, and Cs^+ with 12-crown-4, 15-crown-5, and 18-crown-6 using laser desorption techniques. The crown of interest (Aldrich) was dissolved in methanol, and the solution was saturated with an alkali metal salt, generally the chloride or nitrate. The solution was deposited on a stainless steel probe tip, solvent was removed, and the probe was inserted through a vacuum lock and placed immediately adjacent to the trapping cell of an Extrel FTMS-1000 ion cyclotron resonance mass spectrometer. Crown–alkali metal complex cations are observed trapped in the cell a few hundred milliseconds after the probe tip is irradiated with the focused output of an excimer-pumped dye laser (Lambda Physik LPX 205i/FL 3002). Laser pulse energies were kept less than 0.5 mJ/pulse to prevent formation of transition metal ions from the stainless steel probe material.

This method yields the desired crown–alkali metal complex cations with very little fragmentation. The observed masses correspond within experimental error to those expected for the complexes. Currently, it is unclear whether the observed complexes are preformed in condensed media and then desorbed, or formed in the gas phase after desorption.

We investigated the gas-phase reaction chemistry of crown–alkali metal complexes with neutral crown ethers introduced into the vacuum chamber through a leak valve, generally to pressures of $1-5 \times 10^{-7}$ Torr. The ionic reactants were isolated when necessary using stored-waveform inverse Fourier transform (SWIFT) techniques,[13] and products of the ion–neutral reactions were observed as a function of reaction time (up to 30 s). It should be emphasized that *this procedure unambiguously examines gas-phase processes*. Two general types of reactions were evident.

Table I. Observed Alkali Metal Cation Bound Dimers of 12-Crown-4 (**4**), 15-Crown-5 (**5**), and 18-Crown-6 (**6**)

cation	$(\mathbf{4})_2M^+$	$(\mathbf{5})_2M^+$	$(\mathbf{6})_2M^+$	$(\mathbf{4})(\mathbf{5})M^+$	$(\mathbf{5})(\mathbf{6})M^+$
Li^+	yes	no	no	no	no
Na^+	yes	yes	no	yes	no
K^+	yes	yes	no	yes	no
Rb^+	yes	yes	yes	yes	yes
Cs^+	yes	yes	yes	yes	yes

Table II. Relative Sizes of Cations and Crown Ether Cavities

cation	ionic radius,[a] Å	crown ether	cavity radius,[b] Å
Li^+	0.76	12-crown-4	0.60–0.75
Na^+	1.02	15-crown-5	0.86–0.92
K^+	1.38	18-crown-6	1.34–1.43
Rb^+	1.52		
Cs^+	1.67		

[a] Reference 17. [b] Reference 18.

First, alkali metal cations initially complexed to smaller crowns were observed in every case to transfer to larger crowns. This is consistent with expectations based on a limited number of theoretical binding affinities[14] and may reflect the increase in the number of donor atoms for the larger crowns. The exchange reactions appear to fit pseudo-first-order kinetics. Preliminary data give rate constants in the range of 10^{-11} cm^3 s^{-1} molecule^{-1}, indicating that the reactions are relatively inefficient. This is consistent with a strong orientational requirement for this reaction, probably involving a "face-to-face" approach of the complex and the accepting ligand.

The second observed reaction type involves higher mass product ions corresponding to the general stoichiometry $(crown)_2M^+$, where M = alkali metal (Table I). Cation-bound dimers have been noted in solution and characterized in solids using X-ray crystallography,[4b,15] which indicates that the cation lies between two parallel macrocyclic rings. We assume the same general structure for the gas-phase complexes and refer to them as "sandwiches", after Pedersen.[16] Both homogeneous sandwiches, where both crowns are the same, and heterogeneous sandwiches, consisting of two different crowns and a metal cation, were seen.

The pattern of sandwich formation (Table I) clearly shows that the relative sizes of the cations and macrocycle cavities (Table II) are important in determining the reactivities of these complexes. 12-Crown-4 forms sandwiches with all the alkali metal cations, all of which are too large[17] to fit within the cavity of this small ligand.[18] 15-Crown-5 forms sandwiches with all the alkali metal cations except Li^+, which is small enough to fit within the ligand cavity. 18-Crown-6 forms sandwiches only with Rb^+ and Cs^+, which have ionic radii approximately 0.1 and 0.25 Å larger, respectively, than that of the ligand cavity. The formation of $(18\text{-crown-}6)_2Rb^+$ is slow relative to that of the Cs^+ sandwich. In general, sandwich formation occurs only when the cation is larger than the ligand cavity. Mixed sandwich formation is also consistent with the "ion-in-the-hole" model: we observe $(12\text{-crown-}4)(15\text{-crown-}5)M^+$ for M = Na, K, and Rb but not for M = Li, and $(15\text{-crown-}5)(18\text{-crown-}6)M^+$ only for M = Rb or Cs.

Ligand–metal ion sandwich formation in the gas phase has been reported previously for complexes of 12-membered-ring cyclotriynes with first-row transition metal ions, and the relationship

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between ligand cavity size and cation size was offered as a possible explanation of the observed trends.[19] Sandwich formation rates were observed to decrease across the first row from Ti^+ to Fe^+, becoming much slower for the smaller ions Co^+, Ni^+, and Cu^+, which presumably fit within the ligand cavity. Valence electron count arguments were alternatively suggested. We can be confident that electronic effects are not responsible for the patterns in our data, since the alkali metal cations are closed-shell species isoelectronic with the noble gases. This suggests that the size argument may be correct for the cyclotriynes as well.

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Template-Mediated Synthesis of Metal-Complexing Polymers for Molecular Recognition

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The design of synthetic molecules capable of recognizing given chemical entities in a specific and predictable manner is of great fundamental and practical importance.[1] The principal paradigm of the molecular design of such materials involves the preorganization of binding sites of the host system (receptor) around complementary binding sites of the guest molecule (substrate).[2] Wulff and co-workers devised a novel approach to synthesizing substrate-selective polymers that consists of covalent linking of polymerizable groups around a template molecule and subsequent cross-linking polymerization of the resulting assembly.[3] The orientations of the binding sites of the template molecules sculpt the substrate-selective architecture of the templated polymers. Here we report a novel variation of this template polymerization technique to synthesize rigid macroporous polymers containing strategically distributed Cu(II)–iminodiacetate ($Cu^{II}IDA$) complexes. The resulting polymers exhibit selectivity for bisimidazole "protein analogues" that are not distinguishable by reverse-phase HPLC.

Various groups have synthesized imprinted polymers using both covalent[3] and noncovalent hydrogen bonding and electrostatic interactions[4] as the basis for recognition. Although noncovalent interactions provide polymers that exhibit faster rebinding kinetics, the recognition capabilities are limited by the weak nature of individual interactions. Due to their relative strength and selectivity, metal–ligand coordination is well-suited to molecular recognition of biological molecules, as exemplified by metal-affinity chromatographic purification of proteins.[5] We propose that very high affinity and selectivity can be achieved in polymer matrices containing metal ions strategically positioned to match the distribution of metal-coordinating groups on the surface of the molecule of interest.

Formation of the polymerizable template assembly was promoted by slow addition of 1 molar equiv of the methanolic solution of the appropriate bisimidazole derivative (**2a** or **3a**) to 2 equiv of $Cu^{II}IDA$-derivatized vinyl monomer (**1**) in methanol. Deepening of the blue coloration of the resulting solution and shifting of the 778-nm band of the $Cu^{II}IDA$ complex to 665 nm (a consequence of a ligand-to-metal charge-transfer band for copper-coordinated imidazole derivatives[6]) is indicative of complex formation. UV titration experiments suggest the stoichiometry of the Cu(II)-monomer:template complex is 2:1, with an association constant of ~8800 M^{-1}. The template assemblies were copolymerized at 60 °C with ethylene glycol dimethacrylate (EGDMA) as cross-linker and methanol as porogenic agent using azobis(isobutyronitrile) (AIBN) as initiator (Scheme I).

Scheme I

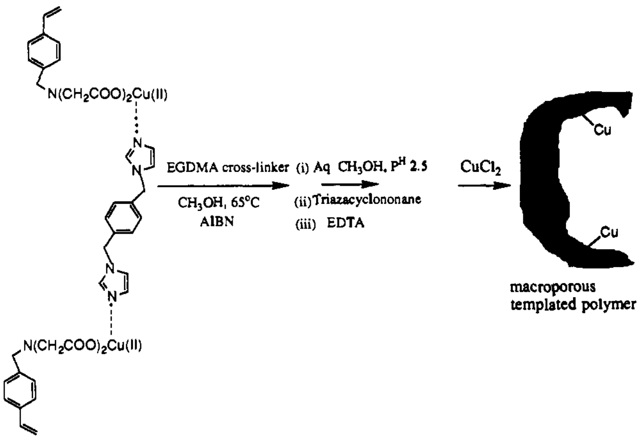
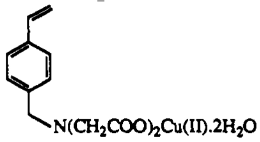


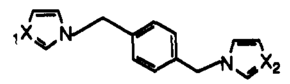
Table I. Polymerization Recipe and Workup of Templated Chelating Polymers[a]

entry	polymer	Cu(II) in polymerizatn mixture, mmol/g	template type and concn in polymerizatn mixture, mmol/g	recovery of Cu(II), mmol/g	recovery of template, mmol/g
1	P-1	0.52		0.49	
2	P-2	0.52	(**2a**) 0.26	0.47	0.26
3	P-3	0.53	(**3a**) 0.27	0.49	0.26

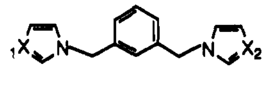
[a] Polymerization reactions were carried out in the presence of EGDMA cross-linker having a molar ratio of **1** to EGDMA of 5:95.



1



2a: $X_1 = X_2 = N$; 1,4-diimidazol-1-ylxylene
b: $X_1 = X_2 = CH$; 1,4-dipyrrol-1-ylxylene
c: $X_1 = N$, $X_2 = CH$; 1-imidazol-1-yl-4-pyrrol-1-ylxylene



3a: $X_1 = X_2 = N$; 1,3-diimidazol-1-ylxylene
b: $X_1 = X_2 = CH$; 1,3-dipyrrol-1-ylxylene

After extraction with methanol for 24 h to remove any unpolymerized and soluble contaminants (<1%), the blue macroporous polymers were treated with acidified 50% aqueous methanol (pH 2.5) at 37 °C for 36 h to remove the bisimidazole templates. A two-step procedure involving treatment with methanolic tria-

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