

Gas-Phase Host-Guest Chemistry of Carcerands and Hemicarcerands

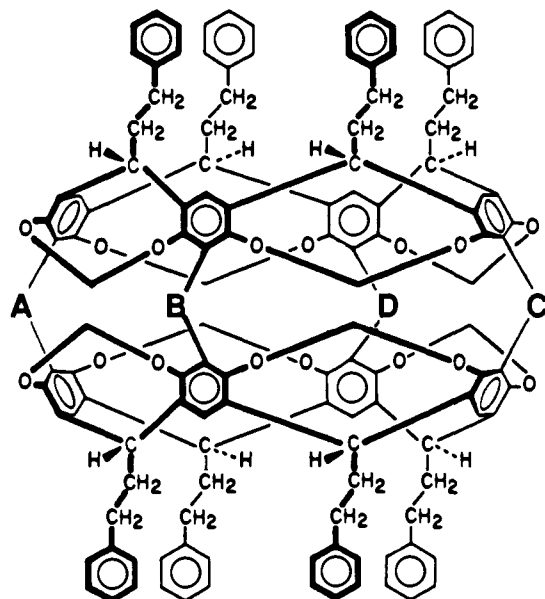
Lydia M. Nuwaysir,¹ John A. Castoro, Cathy Liub-Chii Yang,² and Charles L. Wilkins*

Contribution from the Department of Chemistry, University of California, Riverside, Riverside, California 92521. Received November 7, 1991

Abstract: Gas-phase host-guest chemistry of two hemicarcerands and one carcerand, having masses of approximately 2000 Da and with successively more restricted access to their interior phases (because they possess two, three, and four bridging $-\text{O}-\text{CH}_2-\text{O}-$ groups, respectively), are studied by laser desorption Fourier transform mass spectrometry (LD-FTMS). Gas-phase reactions of the hemicarcerands with dimethylacetamide and of a triply-bridged hemicarcerand with α -pyrone are reported, and it is shown that the laser desorption behavior and gas-phase reactivities are in qualitative agreement with the expected effects of steric requirements of the guests.

Introduction

A topic of great interest in recent years is the synthesis of molecules (hosts) capable of encapsulating smaller molecules (guests) within open interior cavities containing portals allowing the smaller guest species to enter and depart.³⁻¹² Such molecules have served as models of molecular recognition in biological systems and have provided better understanding of the nature of hydrophobic and van der Waals interactions in aqueous solutions. Recently, Cram and co-workers synthesized a series of host compounds, with the general structure 1, collectively categorized



1a, A = C = $-\text{OCH}_2\text{O}-$; 1b, A = B = C = $-\text{OCH}_2\text{O}-$; 1c, A = B = C = D = $-\text{OCH}_2\text{O}-$

as carcerands or hemicarcerands, depending upon the number of bridging $-\text{O}-\text{CH}_2-\text{O}-$ bonds (A-D) contained in any particular structure.¹³⁻¹⁸ These carcerands are non-collapsible molecular cells which can retain guest molecules within their interiors. Once formed, the host/guest complex (carceplex) often maintains its structural integrity in the gaseous, liquid, and solid states. For hemicarcerands, the phenomenon of constrictive binding (i.e. the effect of steric repulsions which must be overcome for dissociation of a hemicarceplex) has been introduced as a key concept in understanding the solution phase guest capture and release chemistry of these molecules.¹⁹ A recent elegant paper discussing the chemistry of the α -pyrone hemicarceplex derived from 1b describes the interior as a "new phase of matter" and suggests unique chemical consequences of confining reactive guests within this phase.¹⁸ Not surprisingly, the gas-phase host-guest chemistry of carcerands and hemicarcerands, some of which is reported here, has been relatively unexplored. This is due in large measure to the non-volatility of these polar compounds, which have molecular masses in excess of 2000 Da. However, it is possible to use the well-established technique of laser desorption Fourier transform mass spectrometry (LD-FTMS)²⁰ to study host-guest chemistry of even such non-volatile materials in the gas phase. Such studies parallel similar gas-phase triple quadrupole²¹ and laser desorption FTMS²² investigations of crown ether host-guest complexation, albeit with significantly different constraints. Here we report results of LD-FTMS investigations of a series of closely related molecular species which includes two hemicarcerands (1a and 1b) and a carcerand (1c) and their corresponding hemicarceplexes and carceplexes with a variety of guests.²³ Within this series the number of bridge groups increases from two (AC) to three (ABC) to four (ABCD), with concurrently increasing constraints on guest

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ingress and egress. The general structure should be understood to indicate that hydrogen atoms are located at the termini where the B or D linkages are not present.

Experimental Section

Studies were performed using a 7-T Nicolet FTMS-2000 Fourier transform mass spectrometer equipped with an automatic solids probe and a differentially-pumped dual-cell with the cubic source and analyzer regions separated by a 2-mm conductance limit. The FTMS is interfaced to a Tachisto 215 CO₂ laser for desorption and ionization and a Lambda Physik EMG 201-MS excimer laser operating at 308 nm for photo-dissociation. The CO₂ laser is directed into the mass spectrometer through a ZnSe window in the source flange and is focused to ~1 mm² spot size on the tip of the solids probe by an off-axis paraboloid mirror mounted on the source cell assembly. The laser delivers approximately 10⁶–10⁸ W/cm² per 80 ± 40 ns pulse. The excimer laser energy is approximately 180 mJ at the output coupler and the unfocused beam is directed through a quartz window in the analyzer flange into the analyzer cell.

Spectra were obtained in the direct mode under broadband excitation and observation conditions. Ions were excited via a 200-Vpp chirp excitation covering a band width of 2.6 MHz, 500 kHz, or 200 kHz, and both source and analyzer cell detection was employed. 64K or 128K data transients were collected, augmented by one level of zero filling, and analyzed by fast Fourier transformation to obtain magnitude mode spectra. No apodization or signal averaging was employed. Trapping voltages were 1.6 V, and delays between laser desorption and ion excitation were generally a few seconds unless otherwise noted. For photo-dissociation experiments, ions were allowed to transfer to the analyzer cell through the 2-mm conductance limit by grounding the central trapping plate for a period of several hundred microseconds to a few milliseconds, prior to triggering the excimer laser.

Carcerand and hemicarcerand samples were obtained from Cram's laboratory at the University of California, Los Angeles. Hemicarcerand and hemicarceplex samples were estimated to be at least 99.8% pure¹⁹ and the carcerand host-guest complexes to be at least 99.7% pure.^{14,17} Dimethylacetamide, α -pyrone, dichloromethane, chloroform, and tetrachloroethane were purchased from commercial sources and used without further purification. Samples were dissolved in suitable solvents and either deposited onto a stainless steel probe tip previously coated with a thin layer of NaCl or mixed with a saturated solution of NaCl prior to sample deposition and solvent evaporation. A leak valve was used to introduce neutral reactants for ion-molecule reaction studies.

Results and Discussion

As mentioned above, LD-FTMS is an appropriate tool for investigation of gas-phase chemistry of substances as non-volatile as the compounds discussed here. Typically, use of a pulsed carbon dioxide laser for desorption results in formation of abundant molecular ion species (in the present study, sodium-cationized), which can be trapped in the FTMS dual-cell for variable periods under computer control.²⁴ Thus, it is possible to introduce neutral reagents and explore the time-dependence of any ion-molecule reactions which are observed. Because sodium chloride was added to all samples prior to laser desorption, all of the laser desorption FTMS spectra recorded in the present study were comprised exclusively of sodium-attached ions, consistent with the well-known high affinity of alkali cations for oxygen-containing compounds and the ubiquitous observation of alkali-cationized species for virtually all heteroatom-containing substances subjected to LD-FTMS. Although the present study provides no direct evidence of the locations of the complexed sodium atoms, there is no reason to expect that they reside within the hemicarcerand or carcerand cavities, given the ready availability of numerous easily-accessible oxygens around the ring peripheries.

Hemicarcerand **1a**, the most open of the three host compounds studied, was prepared in dimethylacetamide (DMA), and its FAB mass spectrum showed no evidence of ions corresponding to the expected host-guest complex. On examination by LD-FTMS, using a delay of 100 ms between the laser desorption event and detection of the resulting ions in the source region of the dual cell, only sodium-attached host molecular ions were observed. When the delay was systematically increased in a series of experiments focussing the laser on fresh portions of the same probe sample,

sodium-attached ions with the mass of the expected **1a**-DMA complex were detected. For delays of 300 ms, 1.3 s, and 15.3 s the abundance of the complex ions relative to the sodium-attached host ions changed from 8% to 50% to 150%, consistent with a gas-phase reaction of the desorbed host ions with neutral dimethylacetamide released from the probe sample during and following the desorption process. This behavior is completely consistent with the observation that such hemicarceplexes lose their guests with facility upon heating in solution.¹⁹ In a second set of experiments, intended to investigate the premise that the complex was forming due to gas-phase reaction of host molecular ions with guest neutrals, the desorbed sodium-cationized hemicarcerand ions were immediately transferred to the analyzer cell and detected following a 15-s delay. No host-guest complex ions were detected. Because the transfer procedure involves use of the z-axis motion of the ions to effect their partition between source and analyzer regions, they can be efficiently transferred to the analyzer under conditions where relatively few neutrals are transferred. In a second experiment, the source cell was pressurized to ca. 10⁻⁷ Torr with dimethylacetamide, prior to laser desorption. After laser desorption and following a 10-s delay, sodium-attached **1a** (multiplet centered on m/z 2017.2), **1a**-DMA (m/z 2104.3), **1a**-2DMA (m/z 2191.5) were detected in the ratio of 1:1.2:2 (i.e. there was virtually complete conversion to host-guest complex forms).

The hemicarcerand **1b** is of interest in light of the recent report of the reactions of the α -pyrone hemicarceplex to form incarcerated cyclobutadiene in solution.¹⁸ When the same hemicarceplex is subjected to LD-FTMS, sodium-attached **1b** and sodium-attached **1b**- α -pyrone carceplex ions are observed in a ratio of 4:3. When the empty hemicarcerand is desorbed in the presence of a 10⁻⁷-Torr pressure of α -pyrone and allowed to react for 10 s prior to detection, carceplex ions with a relative abundance of about 20% are observed. Longer reaction times (up to 30 s) result in no change in the ratio of host to host-guest ions. When **1b** is desorbed into a similar static pressure of DMA, sodium-attached ions of the **1b**-DMA complex are observed in 50% relative abundance following a 1-s reaction delay and become the predominant species after a 15-s reaction delay, with a **1b**-2DMA complex also being observed under the latter conditions. In that case, sodium-attached ions of **1b**, **1b**-DMA, and **1b**-2DMA are observed in the ratio of 2:6:1. Thus, the more closed hemicarcerand **1b** reacts with DMA in the gas phase in a similar manner to the AC hemicarcerand **1a**.

Finally, the isolated and purified carceplexes of the ABCD carcerand **1c**^{14,17} with DMA, dimethylformamide (DMF), and dimethyl sulfoxide (DMSO) were examined by LD-FTMS. Figure 1 shows the positive ion LD mass spectra of these three compounds. Sodium-attached host ions, in addition to the expected sodium-attached host-guest ions, are observed for all three carceplexes. The high relative abundances of carceplex ions provide further evidence that the guests are indeed trapped within the host's interior, in accord with the ample NMR, spectroscopic, and (for the DMA carceplex) X-ray structure¹⁷ evidence provided earlier.^{14,17} Were this not so, it would be expected that laser desorption would liberate the guests with ease, as is the case for the hemicarceplexes of the much more open compound **1a**. Furthermore, the structures of these carceplexes, in contrast to the hemicarcerands, lack portals sufficiently large to permit guest egress, dictating that liberation of guests can only occur by ring-opening processes. The portals of **1b** (which is essentially **1c** with one bridge ruptured) are believed to be slot-shaped,¹⁹ facilitating escape of DMF and DMA because their shapes are roughly complementary to the portal, while the roughly tetrahedral guest, DMSO, cannot so easily escape from **1c** with one bridge ruptured. In addition, the relative ratios of carcerand to carceplex suggest that larger guests can facilitate ring opening, perhaps through release of steric strain. Consequently, the DMA carceplex ion is observed in low relative abundance and the DMF carceplex in roughly equal abundance, and the DMSO carceplex ions predominate in the LD mass spectra. These observations are consistent with the expected more ready release of larger guests

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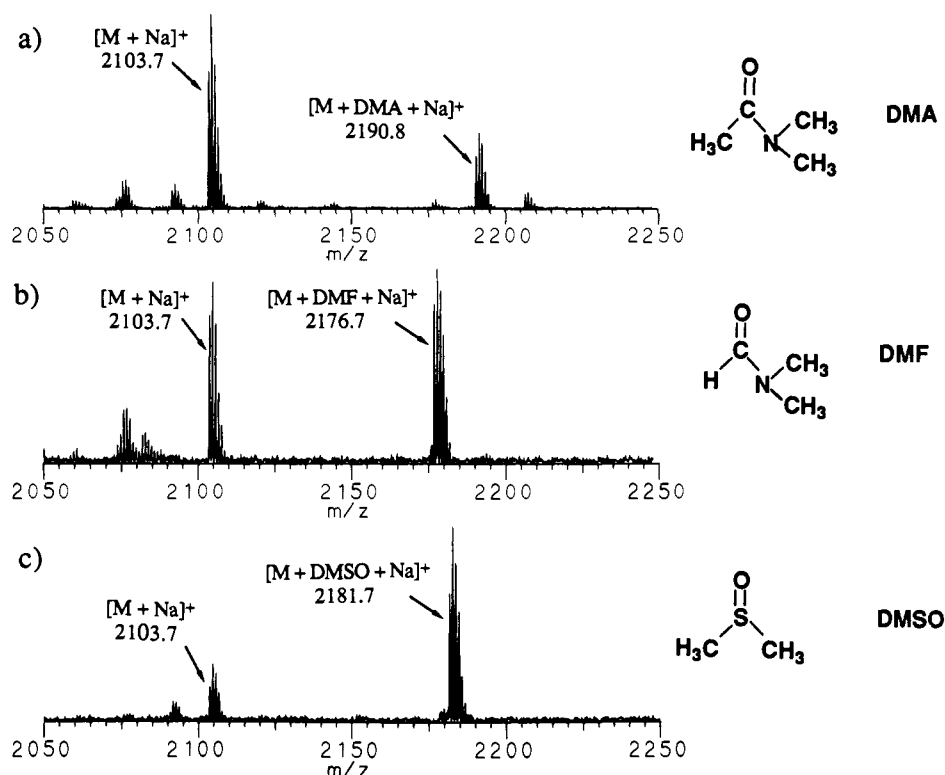


Figure 1. Laser desorption Fourier transform mass spectra of carceplexes of carcerand **1c** with (a) dimethylacetamide, (b) dimethylformamide, and (c) dimethyl sulfoxide.

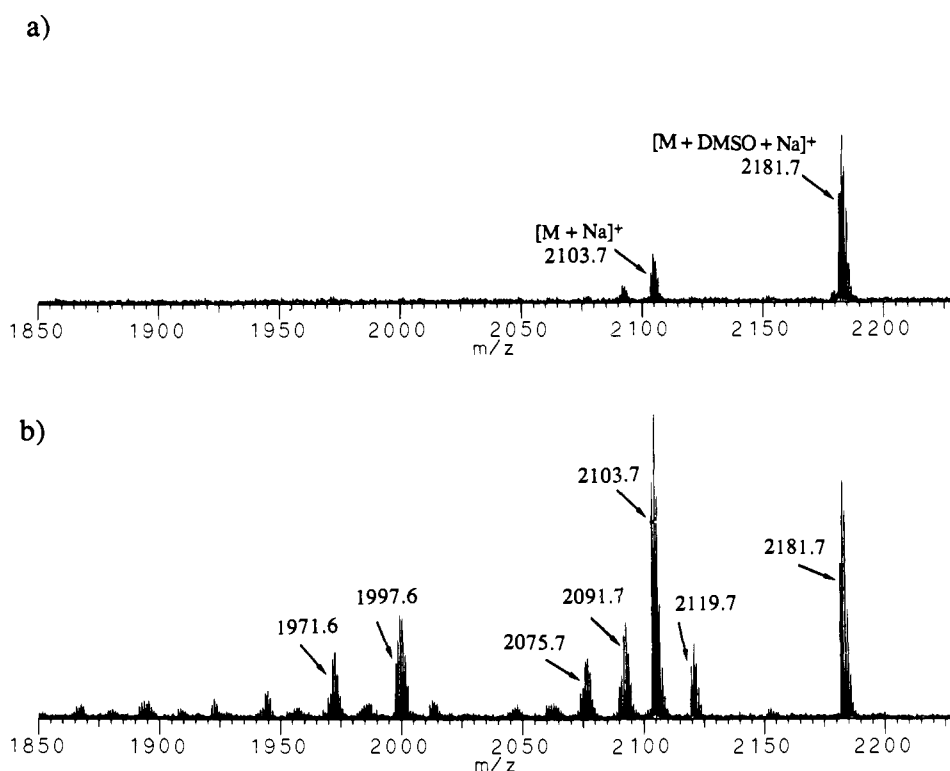


Figure 2. Photodissociation of DMSO carceplex with **1c**: (a) CO_2 laser desorption, eject all ions with $m/z < 2090$; (b) same as (a) followed by 308-nm excimer laser photodissociation and measurement of the resulting photodissociation mass spectrum. Spectra a and b are plotted with the same absolute abundance scale.

under LD-FTMS conditions. Photodissociation FTMS spectra of all three carceplexes provide further support for this interpretation. For example, Figure 2 contains spectra of the DMSO complex comparing the CO_2 LD spectrum (Figure 2a) with the spectrum (Figure 2b) obtained by 308-nm photodissociation of the trapped sodium-carceplex ions following laser desorption.²⁴ Note that the absolute abundance of sodium carcerand ions relative

to sodium carceplex ions increases significantly from the original ratio, prior to photodissociation. The change in this ratio could result either from release of the guests (to yield $[M + Na]^+$), other fragmentations of the sodium carceplex (decreasing its abundance), or both. Interestingly, when the relative abundances of the fragment ions are added to that of the remaining sodium carceplex ions, the ratio of that sum to the relative abundance of the $[M$

+ Na]⁺ ions is about 2, suggesting sodium carceplex ions as the major precursor of fragments. Furthermore, the presence of fragment ions, indicative of rupture of bridging -O-CH₂-O- groups (e.g. *m/z* 2119.7 [M - OCH₂O - O]⁺), which could only derive from the sodium carceplex, support this interpretation. Obviously loss of all or portions of the pendant ethylphenyl groups, which are also observed (e.g. *m/z* 1971.6 [M - PhCH₂CH₂ - O + Na]⁺ and *m/z* 1997.6 [M - PhCH₂CH₂ - H + Na]⁺), could occur from either the sodium carcerand or the sodium carceplex precursors. However, taken as a whole, the photodissociation results suggest ring opening to release incarcerated guests is taking place.

Conclusions

Under the laser desorption conditions employed in the present study, carceplexes **1c** with incarcerated dimethylformamide, dimethylacetamide, and dimethyl sulfoxide are sufficiently stable to retain at least some of the guest species in the resulting sodium-attached ions. Furthermore, the degree of guest retention parallels the size order, with the smallest guest being retained most, as expected. It appears that the larger guests lower the barrier to ring opening due to release of steric strain associated with their incarceration. Because of the requirement that the carcerand ring open to permit egress of incarcerated guests, the abundant ions with *m/z* 2103.7 [M + Na]⁺ appearing in both the laser desorption and the LD-photodissociation spectra of all three carceplexes must be either ring-opened species or ring-closed species which opened to allow guest departure and subsequently re-cyclized.

When the doubly-bridged hemicarceplex **1a**-DMA is subjected to the same laser desorption conditions, only free hemicarcerand sodium-attached ions are observed. This behavior parallels that

observed upon heating the compound in solution and is not unexpected, due to the relative size of its portals, which permit free egress of guest molecules. Equally important, gas-phase formation of the hemicarceplex also is facile, due to the ease with which neutral solvent can effect entry and the ability of the hemicarceplex interior to serve as a molecular receptor. In fact, under appropriate conditions the hemicarcerand can be converted almost quantitatively to **1a**-DMA. However, a significant amount of the triply-bridged hemicarcerand- α -pyrone host-guest complex derived from **1b** survives laser desorption, and although the parent hemicarcerand also can be shown to form complexes with guests in the gas phase, these reactions appear somewhat less facile than the corresponding reactions of **1a**, consistent with the more restricted access of potential guests to the hemicarcerand's inner phase. Thus, for the triply-bridged hemicarcerand, the more bulky α -pyrone complexes to the extent of about 20%, while DMA complexes with about 78% of the hemicarcerand ions. In summary, the gas-phase chemistry of these substances is consistent with that observed in solution. Finally, the ability to produce and retain substantial amounts of hemicarceplex ions under FTMS trapping conditions raises the intriguing possibility of pursuing gas-phase studies of incarcerated guest chemistry similar to those carried out in solution. This is a prospect we hope to explore.

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The Role of Deuterium in Optical Activity: The CD Spectrum of (*S,S*)-Dideuteriooxirane

Sara Ben-Tzur,[†] Anat Basil,[†] Aharon Gedanken,^{*,†} Jeffrey A. Moore,[‡] and John M. Schwab^{*,†}

Contribution from the Department of Chemistry, Bar-Ilan University, Ramat Gan 59100, Israel, and Department of Medicinal Chemistry and Pharmacognosy, School of Pharmacy and Pharmaceutical Sciences, Purdue University, West Lafayette, Indiana 47907.

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Abstract: The circular dichroism of (*S,S*)-[2,3-²H₂]oxirane has been investigated in the gas phase over the 1800–1500-Å region. While the absorption spectrum reveals only two allowed transitions, the CD spectrum shows a third transition which is magnetic dipole allowed and electric dipole forbidden. The CD sign of the first excited state complies with a quadrant rule which was formulated for the oxirane chromophore. This consignate behavior is contrary to the role of deuterium in carbonyl compounds, where an antiocant behavior is observed.

The circular dichroism of the oxirane chromophore has recently been the subject of many experimental¹⁻⁵ and theoretical studies.^{2,6,7} The interest in oxirane is in part due to its role as a building block for asymmetric synthesis.⁸ Optically active oxiranes can be synthesized from naturally occurring chiral compounds.^{9,10} Its small size and its rigid skeleton make the oxirane moiety an ideal candidate for ab initio calculations of its rotatory strength.^{2,6}

The absorption of oxirane was first reported by Liu and Duncan¹¹ and by Lowrey and Watanabe.¹² In both of these studies all the sharp features were assigned as members of Rydberg or valence transitions. These assignments were later questioned

in an extensive study by Basch et al.¹³ They measured the absorption of gaseous oxirane, a solid film of oxirane, and a

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[†] Bar-Ilan University.

[‡] Purdue University.