Tetrahedron Letters, Vol. 33, No. 27, pp. 3825-3828, 1992
Printed in Great Britain

0040-4039/92 $5.00 + .00
Pergamon Press Ltd

Estimation of Cation Binding Properties in Crown and Lariat Ether Complexes using Fast Atom Bombardment Mass Spectrometry

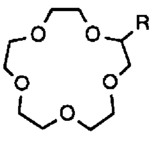
Toshio Takahashi*, Akira Uchiyama, Kaoru Yamada,
Bert C. Lynn,[†] and George W. Gokel[†#*]
Lion Corporation, 7-13-12, Hirai, Edogawa-ku, Tokyo 132, Japan and
[†]Department of Chemistry, University of Miami
Coral Gables, Florida 33124 U.S.A.

Abstract: The complexation behavior of crown and lariat ethers with alkali metal ions has been assessed by means of FAB-mass spectrometry and shown to correlate semi-quantitatively with findings obtained in the solution phase.

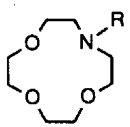
The fascinating recent report of Dearden and coworkers[1] that mass spectral methods may be used to characterize crown ether complexes and reactions in the gas phase, prompts us to disclose our own related efforts. Their basic findings were that in the gas phase, cations prefer to be within the crown ether hole and that when sandwich complexation occurs, it is between macrocycles and cations in which the latter is larger than the former. In the broadest sense, we confirm their finding for the 15-crown-5 system, and show that when a lariat ether[2] sidearm is present, sandwich complexation is not required even when the aforementioned size differential exists.

Since fast atom bombardment (FAB) mass spectrometry provides a rapid means for investigating complexation between crown ethers and metal ions in solutions,[3-5] we applied the FAB-MS method to the analysis of lariat ether complexation in a matrix solution. Under normal electron impact conditions, gas phase samples are ionized by the electron beam which results in ionization of the parent and/or production of fragments. In the FAB technique, the energy in the incident beam causes desorption of the substrate (complex) from a solution matrix and far fewer fragments are generally observed once the system reaches the gas phase. The advantage of this technique for the exploration of complexation is that the complexes tend to retain their integrity in the gas phase and can thus be observed directly.

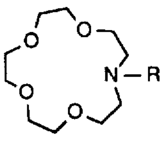
The FAB technique is known to produce results that correlate with solution chemistry. Because so little sample is required in this technique,[6] we thought to apply it to the assessment of cation binding strengths[7] in the large and multi-ring macrocycles such as those recently developed to serve as cation-conducting channels.[8] Sandwich complexation by crown ethers that possess cavity sizes smaller than the cation to which they bind are well known in solution and have been studied in the report noted above. Lariat ethers have the ability to provide a bound cation with three-dimensional solvation without requiring a sandwich structure.[9] As models for these more complex systems, we evaluated Na^+ stability constants for the N-pivot lariat ethers in the FAB matrix by determining the peak intensity of the [crown•Na]$^+$ relative to that of the free ligand [crown•H]$^+$. We have thus assessed the binding of carbon- and nitrogen-pivot lariat ethers by using the FAB technique. The compounds studied are summarized below.



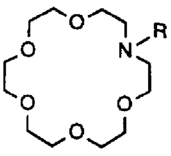
1, R = H
2, R = MOEOMe
3, R = MOEOPr
4, R = MOEOEOMe
5, R = MOEOEOEMPh



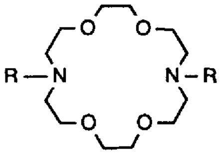
6, R = 4-Ph-OMe
7, R = MMMOH
8, R = 2-Ph-OMe



9, R = H
10, R = Me
11, R = Pr
12, R = MPh
13, R = MCOO-t-Bu



14, R = H
15, R = MPh
16, R = EOEOEOMe
17, R = EOEOMe
18, R = EOMe



19, R = H
20, R = CH_2Ph
21, R = 2-MeOPh
22, R = EOMe

The first compound studied was 15-crown-5, a non-lariat crown ether. In this case, no sidearm involvement is possible in complexation so a comparison with sidearm samples can be made. A 1:1 mixture of 15-crown-5 and KCl was studied. The most intense peak in the spectrum was observed at m/z = 259 [15-crown-5•K]$^+$. A second ion peak at m/z = 479, consistent with the formulation [(15-crown-5)$_2$•K]$^+$, was also observed. The spectrum suggests that the 2:1 complex of 15-crown-5 with KCl was formed in the matrix.[9]

The FAB spectra of 15-membered-ring carbon-pivot lariat ether mixtures with KCl show the corresponding [(crown)$_2$•K]$^+$ peaks along with [crown•K]$^+$ peaks are observed but they are less intense than those observed for the 15-crown-5/KCl mixture. The relative abundance of the [(C-lariat)$_2$•K]$^+$ peaks are listed in the Table. The data indicate that the relative intensity of the [(C-lariat)$_2$•K]$^+$ peak decreases with increasing sidearm length. For 1:1 mixtures of the 15-membered-ring derivatives with NaCl, the compounds with short sidearms gave weak [(C-lariat)$_2$•Na]$^+$ peaks and the FAB spectra or derivatives having longer sidearms showed no [(C-lariat)$_2$•Na]$^+$ (see Table). The data suggest that formation of the 2:1 complexes becomes less favorable as cation size is decreased. In addition, in the case of the mixtures with NaCl, the relative abundance of the [(C-lariat)$_2$•Na]$^+$ peak correlates (for the two examples studied) with sidearm length. The relative abundance of [(crown)$_2$•metal]$^+$ peak in the FAB spectra of 12-membered and 15-membered-ring N-pivot lariat ethers are also summarized in Table I.

Table. Relative intensities of [(crown)$_2$•M]$^+$/[crown•M]$^+$

Cpd. No.	C/N Pivot	Ring Size	Sidearm	Ratio A[a] for K$^+$	Ratio A[a] for Na$^+$	B[b]	Ratio log K$_S$ (Na$^+$)[c]
1	N/A	15	H	9.7	–	–	3.24
2	C	15	$CH_2OCH_2CH_2OCH_3$	5.0	1.3	–	3.01
3	C	15	$CH_2OCH_2CH_2OBu$	0.6	0.1	–	3.09
4	C	15	$CH_2O(CH_2CH_2O)_2CH_3$	0.3	0	–	3.13
5	C	15	$CH_2O(CH_2CH_2O)_3CH_2Ph$	0.2	0	–	3.51
6	N	12	C_6H_4–4–OCH_3	1.9	1.7	0.52	1.18
7	N	12	$CH_2CH_2CH_2OH$	1.0	0.5	0.95	2.35
8	N	12	C_6H_4–2–OCH_3	1.0	0.4	1.52	2.75
9	N	15	H	3.5	0.7	1.02	1.70
10	N	15	CH_3	1.0	0.3	2.63	3.39
11	N	15	$CH_2CH_2CH_2CH_3$	0.7	0	2.66	3.02
12	N	15	$CH_2C_6H_5$	0.5	0	2.11	2.77
13	N	15	CH_2CO–O–*t*-Bu	0.5	0	4.16	4.20
14	N	18	H	–	–	0.81	2.69
15	N	18	$CH_2C_6H_5$	–	–	3.57	3.41
16	N	18	$(CH_2CH_2O)_3CH_3$	–	–	3.87	4.28
17	N	18	$(CH_2CH_2O)_2CH_3$	–	–	5.16	4.33
18	N	18	$CH_2CH_2OCH_3$	–	–	8.30	4.58
19	N	18	H	–	–	0.38	1.50
20	N	18	$CH_2C_6H_5$	–	–	2.33	2.72
21	N	18	C_6H_4–2-OCH_3	–	–	2.60	3.65
22	N	18	$CH_2CH_2OCH_3$	–	–	6.48	4.75

a. Ratio A is 100[(crown)$_2$•M$^+$/[crown•M]$^+$. b. Ratio b is [crown•Na]$^+$/[crown•H]$^+$. c. Binding constants (log K$_S$) were determined in anhydrous methanol at 25.0 °C.

The [(N-lariat)$_2$•metal]$^+$ peaks of N-pivot lariat ethers were much less intense than those observed for C-pivot lariat ether mixtures. The data suggest that the presence of the sidearms decreases 2:1 complex formation in solution. Furthermore, for 12-membered-ring lariat ethers, [(N-lariat)$_2$•Na]$^+$ peaks decrease in the order (log K$_S$ in CH_3OH): **6** (1.38) > **7** (2.35) > **8** (2.75). Note that as the steric accessibility of the sidearm donor group increases, the tendency for the system to form 2:1 complexes diminishes. As expected from solution studies, 18-membered-ring N-pivot lariat ethers and BiBLEs (bibracchial, *i.e.*, two armed lariat ethers) showed no peak attributable to

[(BiBLE)$_2$•K]$^+$ indicating that the 2:1 complex with KCl is not formed in the matrix.

From these data, it can be seen that there is a good correlation between the peak intensity of [crown•Na]$^+$ relative to [crown•H]$^+$ and the sodium binding constant in anhydrous methanol. The intensity of [crown•Na]$^+$/[crown•H]$^+$ increases with an increase in the solution sodium binding constant. These results demonstrate that FAB mass spectrometry can be used for estimating the stability constants of lariat ether complexes and therefore semi-quantitatively, the effect of the sidearm on complexation in solution.

The sensitive FAB technique may readily be applied to the study of complexation interactions as observed in the mass spectrometer that correlate with solution phase observations. We have applied these to a number of model systems and extension of the technique to the study of far more complex structures is underway and will be reported in due course.

References

* Address correspondence to either author.

We gratefully acknowledge partial support of this work by a grant (GM 36262) from the NIH.

1. Zhang, H.; Chu, I.-H.; Leming, S.; Dearden, D.V.; *J. Am. Chem. Soc.* **1991**, *113*, 7415.
2. (a) Dishong, D.M.; Diamond, C.J.; Cinoman, M.I.; Gokel, G.W.; *J. Am. Chem. Soc.* **1983**, *105*, 586. (b) Schultz, R.A.; Dishong, D.M.; Gokel, G.W.; *J. Am. Chem. Soc.* **1982**, *104*, 625. (c) Schultz, R.A.; White, B.D.; Dishong, D.M.; Arnold, K.A.; Gokel, G.W.; *J. Am. Chem. Soc.* **1985**, *107*, 6659. (d) Gatto, V.J.; Gokel, G.W.; *J. Am. Chem. Soc.* **1984**, 106, 8241.
3. (a) Johnstone, R.A.W.; Lewis, I.A.S.; *J. C. S. Chem. Commun.* **1984**, 1268. (b) Johnstone, R.A.W.; Lewis, I.A.S.; *Int. J. Mass Spectrom.* **1983**, *46*, 451. (c) Johnstone, R.A.W.; Lewis, I.A.S.; Rose, M.E.; *Tetrahedron* **1983**, *39*, 1597.
4. Bonas, G.; Boss, C.; Vegnon, M.R.; *Rapid Commun. Mass Spectrom.* **1988**, *2*, 88.
5. Yamada, K.; Matsutani, S.; Uchiyama, A.; Takahashi, T.; *J. Incl. Phenom.* **1991**, *11*, 49.
6. FAB spectra were acquired on a JEOL DX 303 by using a 6-8 KeV Xe primary beam and a *m*-nitrobenzyl alcohol matrix. The spectra reported herein were peak averaged over 4 scans using a DA 5000 data system. The compounds reported in this paper were prepared as previously described.[2] In a typical experiment, *m*-nitrobenzyl alcohol (1 µL), 1 µL of a 50mM lariat ether solution (CHCl$_3$), and 1 µL of a 50 mM aqueous solution of metal chloride were carefully mixed on the FAB probe. Binding constants for the lariat ethers were determined potentiometrically in anhydrous methanol as previously described.[2]
7. Inoue, Y. and Gokel, G.W. (Eds.), *Cation Binding by Macrocycles*, Marcel Dekker, New York, 1990.
8. Nakano, A.; Xie, Q.; Mallén, J.V.; Echegoyen, L.; Gokel, G.W.; *J. Am. Chem. Soc.* **1990**, *112*, 1287.
9. Gandour, R.D.; Fronczek, F.R.; Gatto, V.J.; Minganti, C.; Schultz, R.A.; White, B.D.; Arnold, K.A.; Mazzocchi, D.; Miller, S.R.; Gokel, G.W.; *J. Am. Chem. Soc.* **1986**, *108*, 4078.

(Received in USA 4 March 1992)