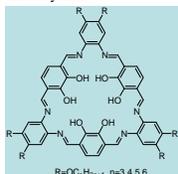


Mass Spectrometric Studies of Conjugated Schiff-Base Macrocycles

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Objectives

Investigate comparatively ESI and MALDI mass spectrometry for the characterization of novel conjugated Schiff-base macrocycles.



Scheme 1: Structure of conjugated Schiff-base macrocycles

Methods

The ESI-MS experiments were carried out on Bruker Esquire-LC and Micromass LCT. The MALDI-MS was performed on Bruker Biflex IV.

Stock solutions of the synthesized macrocycle samples were normally prepared in CH_2Cl_2 or CHCl_3 .

For ESI-MS, the working solutions were made by the dilution of stock solutions with methanol. The cationization reagents included NaOAc, KOAc, RbI and CsOAc. For evaluation of the alkali metal cation selectivities, solution containing single macrocycle with multiple metal cations were analyzed.

MS/MS spectra of the protonated and metalated macrocycles were measured on Bruker Esquire-LC. LCT was used to measure the accurate masses of fragment ions formed with in-source CID.

Several different matrices including dithranol and anthracene as well as different cationization reagents were tested for MALDI-MS.

Results and Discussion

ESI-MS

ESI-MS of the macrocycles with different peripheral alkoxy chains in chloroform/methanol generated mainly the protonated ion (see Fig. 1a).

The metal cationized adducts were formed with the addition of alkali metal salt to the macrocycles (see Figs. 1b & c). The conjugated Schiff-base macrocycles showed very high metal ion affinities to alkali metals.

The competitive metal complexation suggested the following order of binding, $\text{Cs}^+ > \text{Rb}^+ > \text{Na}^+$ (Fig. 2). This order follows the cation size except Rb.

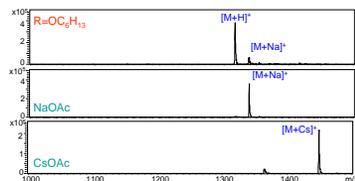


Fig. 1: ESI-MS of macrocycles with and without cationizing reagents

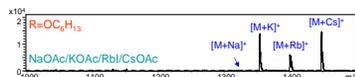


Fig. 2: Alkali metal complexation of macrocycles

Fragmentation Study

Fragmentation of protonated and metalated macrocycles was investigated using a series of macrocycles with different peripheral alkoxy chains and different metal cations.

MS/MS spectra of protonated macrocycles produced four major fragments, a, b, c and d as seen in Fig. 3. The MS/MS data are summarized in Table 1. Same neutral losses were found for macrocycles with different peripheral alkoxy chains. The proposed fragmentation pattern in Scheme 2 was supported by accurate mass measurements on the fragments listed in Table 2. The C=N bond cleavages are responsible for the fragmentations.

MS/MS spectra of alkali metal macrocycle complexes showed two extra fragmentation channels, e and f (Figs. 4 & 5) in addition to the four channels of protonated ions. Table 3 summarizes the MS/MS data of sodiated macrocycles. Same neutral losses were found for cationized macrocycles with different peripheral alkoxy chains and macrocycle complexes with different cations. The fragmentation channel f involves the rearrangement and fragmentation of peripheral group R. Two channels for c and d are closed for (M+Cs)⁺ (Fig. 6) and (M+Rb)⁺. Rb isotopes were used to confirm that the metal cations are included in the fragments.

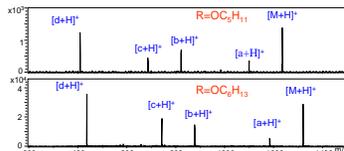


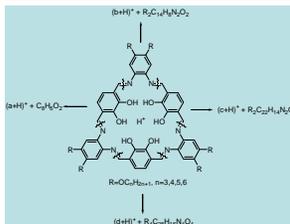
Fig. 3: MS/MS spectra of protonated macrocycles, [M+H]⁺

Table 1: MS/MS data for protonated macrocycles, [M+H]⁺

| R | OC ₂ H ₁₃ | OC ₂ H ₁₁ | OC ₂ H ₉ | OC ₂ H ₇ | Neutral Loss |
|------------------|---------------------------------|---------------------------------|--------------------------------|--------------------------------|--|
| M+H ⁺ | 1316 | 1232 | 1148 | 1064 | |
| a+H ⁺ | 1182 | 1098 | 1014 | 930 | C ₂ H ₂ O ₂ |
| b+H ⁺ | 877.8 | 821.6 | 765.5 | 709.6 | R ₂ C ₂₈ H ₁₀ N ₂ O ₂ |
| c+H ⁺ | 743.7 | 687.6 | 631.5 | 575.4 | R ₂ C ₂₀ H ₁₀ N ₂ O ₁ |
| d+H ⁺ | 439.5 | 411.4 | 383.3 | 355.3 | R ₂ C ₂₀ H ₁₀ N ₂ O ₁ |

Table 2: High-resolution accurate mass data for some ions of protonated macrocycle (R=OC₂H₁₃)

| Ion | Elemental Composition | Calculated Value | Observed Value | Error (ppm) |
|------------------|---|------------------|----------------|-------------|
| M+H ⁺ | C ₇₈ H ₁₃₃ N ₆ O ₁₂ | 1315.7634 | 1315.7682 | 3.42 |
| a+H ⁺ | C ₇₆ H ₁₂₇ N ₆ O ₁₀ | 1181.7268 | | |
| b+H ⁺ | C ₅₂ H ₆₉ N ₂ O ₈ | 877.5117 | 877.5123 | 0.68 |
| c+H ⁺ | C ₄₄ H ₆₃ N ₂ O ₆ | 743.4748 | 743.4730 | -2.15 |
| d+H ⁺ | C ₂₈ H ₂₉ N ₂ O ₄ | 439.2601 | 439.2601 | 0.87 |



Scheme 2: Proposed fragmentation pattern for protonated macrocycles

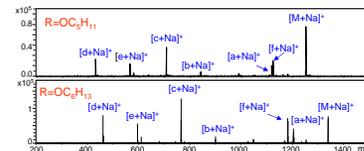


Fig. 4: MS/MS spectra of macrocycle complex with sodium, [M+Na]⁺

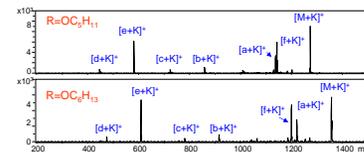
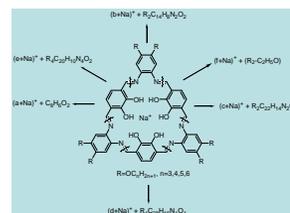


Fig. 5: MS/MS spectra of macrocycle complex with potassium, [M+K]⁺

Table 3: MS/MS data for sodiated macrocycle, [M+Na]⁺

| R | OC ₂ H ₁₃ | OC ₂ H ₁₁ | OC ₂ H ₉ | OC ₂ H ₇ | Neutral Loss |
|-------------------|---------------------------------|---------------------------------|--------------------------------|--------------------------------|--|
| M+Na ⁺ | 1338 | 1254 | 1170 | 1086 | |
| a+Na ⁺ | 1204 | 1120 | 1036 | 952 | C ₂ H ₂ O ₂ |
| b+Na ⁺ | 899.8 | 843.8 | 787.8 | 731.6 | R ₂ C ₂₈ H ₁₀ N ₂ O ₂ |
| c+Na ⁺ | 765.8 | 709.8 | 653.8 | 597.5 | R ₂ C ₂₀ H ₁₀ N ₂ O ₁ |
| d+Na ⁺ | 461.5 | 433.5 | 405.5 | 377.3 | R ₂ C ₂₀ H ₁₀ N ₂ O ₁ |
| e+Na ⁺ | 595.6 | 567.5 | 539.5 | 511.4 | R ₂ C ₂₀ H ₁₀ N ₂ O ₂ |
| f+Na ⁺ | 1182 | 1126 | 1070 | 1014 | (R ₂ -C ₂ H ₂ O) |



Scheme 3: Proposed fragmentation pattern of sodiated macrocycles

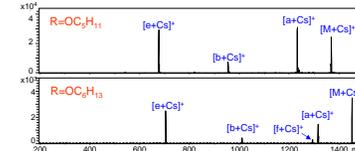


Fig. 6: MS/MS spectra of macrocycle complex with cesium, [M+Cs]⁺

MALDI-MS

Metal cationized macrocycle was the base peak with LDI-MS (neat macrocycle) and protonated ion was the dominant peak with MALDI using a matrix like dithranol (see Fig. 7). Addition of alkali metal salts (NaOAc, KOAc, CsOAc) to the macrocycles caused multiple metalation of the macrocycles (see Fig. 8).

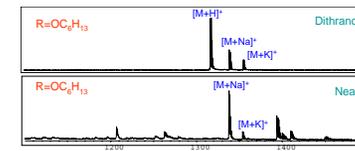


Fig. 7: LDI-MS and MALDI-MS of macrocycles

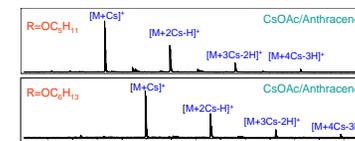


Fig. 8: MALDI-MS of macrocycles using CsOAc as cationization reagent

Conclusions

Both ESI and MALDI-MS produced molecular ions for the characterization of Schiff-base macrocycles. Metal complexation was very efficient.

Fragmentation patterns of protonated and metalated macrocycles were proposed. The differences in fragmentation suggested a binding difference of different cations in macrocycles.