Pergamon

Tetrahedron Letters 40 (1999) 8079–8084

TETRAHEDRON
LETTERS

Complexation of alkali metal and tetramethylammonium ions with polyacids. pH-Metry consequences

Soad Aous,[a] Yves Petillot,[b] Claude Bosso,[c] Maurice Vincens,[a] Eric Forest[b] and
Michel Vidal[a,*]

[a]*LEDSS IV, Université Joseph Fourier, BP 53X, 38 041 Grenoble Cedex, France*
[b]*Institut de Biologie Structurale, CEA-CNRS, 41 Av. des Martyrs, 38 027 Grenoble Cedex 1, France*
[c]*Centre de Recherche sur les Macromolécules Végétales. CNRS BP 53X, 38 041 Grenoble Cedex, France*

Received 4 May 1999; accepted 11 August 1999

Abstract

Mass Spectrometry (MS) enables the study of alkali metal and tetramethylammonium (TMA) complexes which are formed during potentiometric titrations. Their formation and their evolution as a function of pH are confirmed by means of ^{23}Na NMR spectroscopy. This is a common phenomenon which calls the principle of pH-metric titration of polyacids into question.

Literature shows a large heterogeneity in the pKa values of polyaminoacids together with explanations to justify this diversity.[1a] However, the formation of alkali complexes during titrations is frequently invoked.[1b,c] It was postulated in potentiometry that this complex formation could be avoided by replacement of the alkali metal ions by the TMA ion. Even though pH-metry is common practice in chemistry, surprisingly, such an hypothesis has not yet been verified, neither has the one which previously admitted that polyacid titrations are interpreted by a succession of Brønsted equilibra:

$$H_nL + m\,H_2O \rightleftharpoons m\,H_3O^+ + H_{n-m}L^{m-}$$

We identified by MS the alkali metal or TMA complex cations which were formed at different pH values and we evaluated their stability. A ^{23}Na NMR spectroscopy study allowed us to confirm the formation and the evolution of the alkali complexes in solution with the variation of the ion/ligand ratio.

1. Identification of complexes by MS: FAB[14] and ESIMS[14] methods

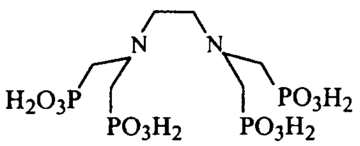
We studied three acids: EDTMP,[13] OTMP[10–13] and DOTA[13] in FAB[12] and ESIMS,[12] by carefully controlling the temperature and the accelerating voltage.[2] FAB and positive ESIMS, gave the same

---

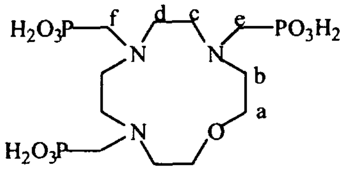
[*] Corresponding author. Fax: 33 (0)4.76.51.43.82; e-mail: michel.vidal@ujf-grenoble.fr

0040-4039/99/$ - see front matter
PII: S0040-4039(99)01536-1

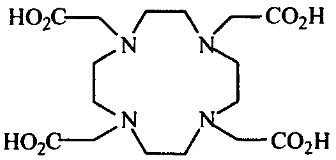
results, which were coherent for the three considered acids in the presence of alkali metal ions and TMA.



EDTMP



OTMP



DOTA

We present here the results acquired with EDTMP (LH_8), and K^+ ions or TMA.

- A solution I of the ligand (10^{-3} M), without electrolyte (pH 1.16) displays only the molecular peak $[LH_8+H]^+$.
- When KOH was added to solution I until pH 1.5 (solution II) the corresponding mass spectrum displayed four main peaks: $[LH_8+H^+]^+$, $[LH_8K]^+$, $[LH_7K_2]^+$ and $[LH_6K_3]^+$ (Fig. 1). The same spectrum is obtained by addition of an equivalent of electrolyte (KCl) to solution I giving solution III which differed from solution II only in peak intensities. Further addition of KOH to solution II caused an evolution of the spectra towards the species in which H^+ were progressively substituted by K^+ until the $[LK_8H]^+$ species appeared. This evolution was correlated with a decrease until disappearance of the first observed peaks, $[LH_9]^+$, $[LH_8K]^+$, $[LH_7K_2]^+$, etc...

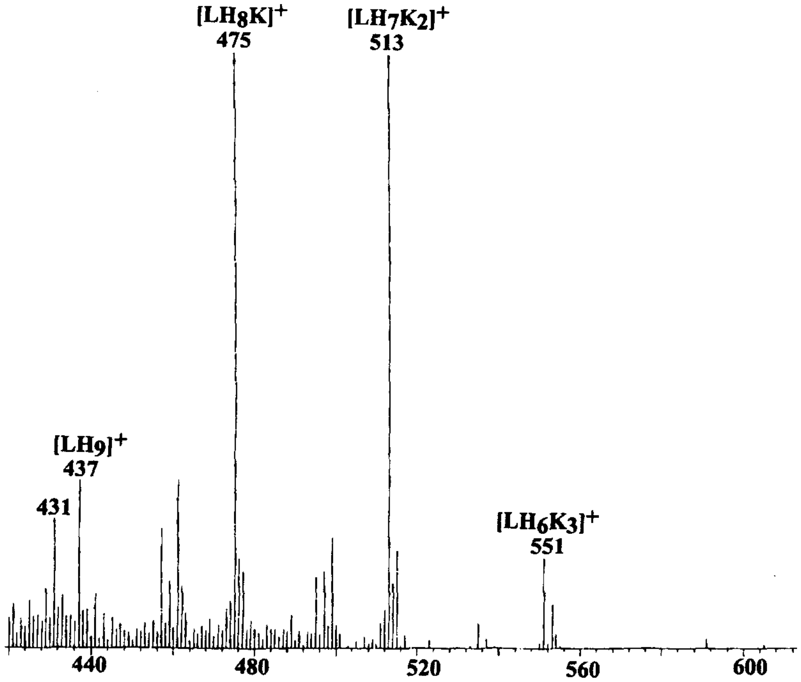


Figure 1. FAB mass spectrum of solution II

- Simultaneous introduction of Na^+ and K^+ ions resulted in spectra showing the association of the ligand with one type of ion $[LH_8Na]^+$, $[LH_8K]^+$, $[LH_7Na_2]^+$, $[LH_7K_2]^+$... and mixed complexes $[LH_7NaK]^+$, $[LH_6Na_2K]^+$...
- Addition of tetramethylammonium hydroxide to solution I resulting in solution IV, showed peaks

corresponding to $[LH_{n-m+1}(TMA)_m]^+$ (Fig. 2). The simultaneous addition of alkali metal ions and TMA also indicated the formation of mixed complexes.

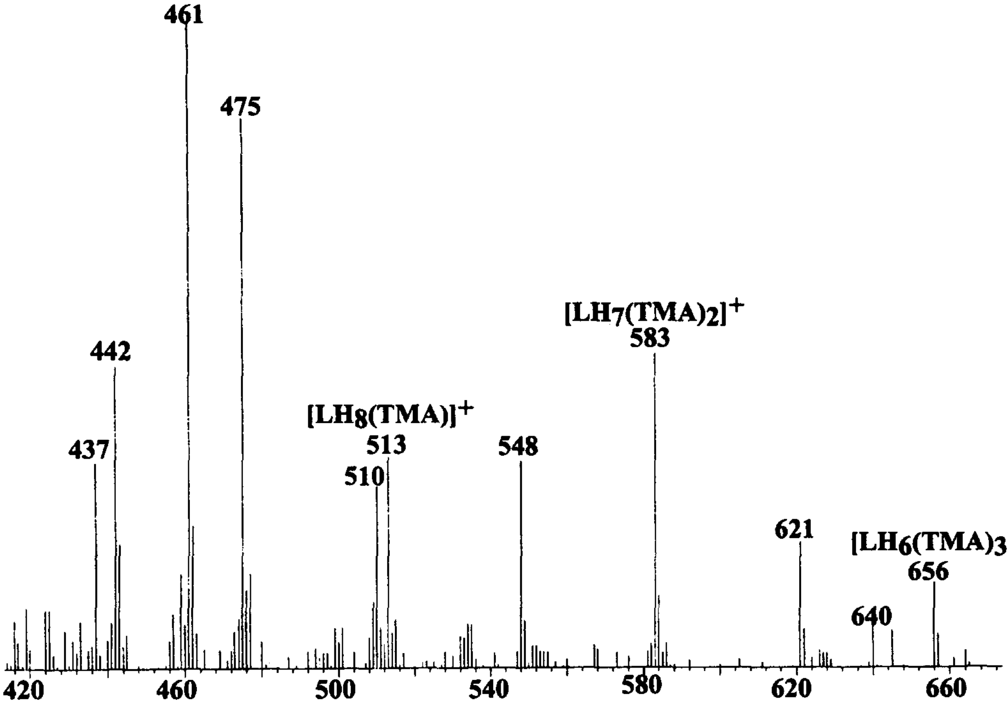


Figure 2. FAB mass spectrum of solution IV

- K^+ ions diffused by a calomel electrode were also trapped by the solution of ligand.

2. Results observed in negative ESIMS

The ESIMS analyses of mixtures of the ligand with KCl adjusted to pH 7.5 by addition of KOH, permitted observation of the formation of: $[LH_7]^-$, $[LH_6]^{2-}$, $[LH_6K]^-$ and $[LH_5K]^{2-}$ anions (Fig. 3).

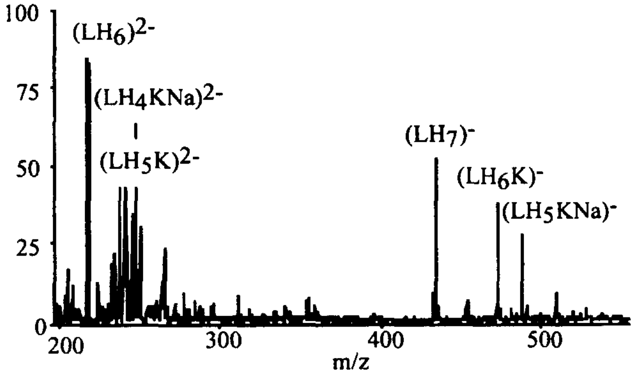


Figure 3. ESIMS mass spectrum in the negative mode of a mixture of LH_8–KCl

3. The determination of complex stability by ESMS

We evaluated the stability of complexes formed according to the method described by Gall et al.[3] by plotting the peak intensity of the $[LH_8Na]^+$ complex versus the orifice voltage (OR) of the mass spectrometer and by comparing the maximum of each resulting curve to a reference complex,[2d,4] NaDOTA (complexing constant $\beta_{1,1,0}$ is about of 10^4).[5,6]

Fig. 4 compares the I=f(OR) diagrams for the NaEDTMP, NaOTMP and NaDOTA metal complexes. The following features were worth noting: for the three complexes, the ionic current intensity was very high. The maxima were located in the same zone of OR value (within 100 and 130 volts). This demonstrated that in a gaseous phase, the three complexes were very stable and NaOTMP and NaDOTA exhibited comparable stability, higher than NaEDTMP. If the hierarchy of stability in the aqueous phase is of the same order as in the gaseous phase, which is admitted when the vaporization/ionization temperature is low, the stability constant of NaEDTMP and NaOTMP in the aqueous solution is thus close to $10.^4$

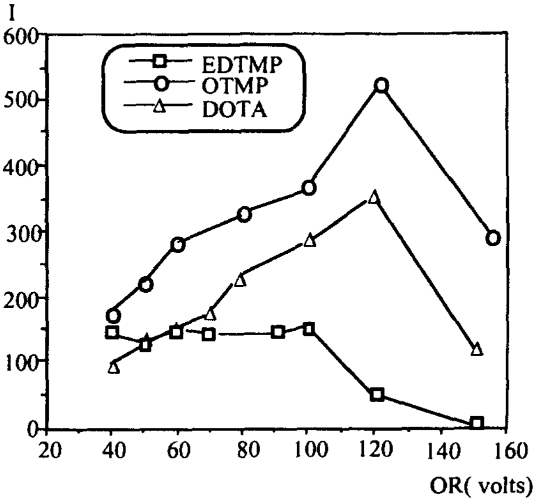


Figure 4. I=f(OR) diagrams of sodium complexes of EDTMP, OTMP and DOTA

4. ^{23}Na NMR spectroscopy studies

The importance of MS observations and their consequences in pH-metry, reconsidering the titration principle itself, required the use of a different analytical approach in order to confirm them. Recently, ^{23}Na NMR spectroscopy studies were employed to prove the formation of mononuclear alkali metal complexes[7,8] (chemical shift and width versus height of peaks were studied). As our results from MS studies on Na^+ and K^+ ions were similar, we chose, for technical reasons, to study the ^{23}Na NMR spectroscopy of these complexes.

In a preliminary study, we verified that δ_{Na} and $\Delta\nu_{1/2}$ of Na^+ ion were practically independent of Na^+ concentration and pH in water solution ($\Delta\delta$ <4 Hz and $\Delta\nu_{1/2}$=0.1 Hz for 8 mol Na^+ ions added per mol of the initial Na^+ ion).

Addition of NaOH to a solution of EDTMP (10^{-2} M) induced a down field shift of the ^{23}Na NMR spectrum together with broadening of the signal (Fig. 5). The δ_{Na} and $\Delta\nu_{1/2}$ depended on the amount of NaOH added. We observed an increase of δ_{Na} and $\Delta\nu_{1/2}$ values until 8 mol of NaOH were added per mol of EDTMP: $\Delta\delta_{max}=29.4$ Hz and $\Delta\Delta\nu_{1/2\ max}$ ≈24 Hz. Beyond this, δ_{Na} and $\Delta\nu_{1/2}$ remained constant or slightly decreased which was attributed to coalescence phenomenon.

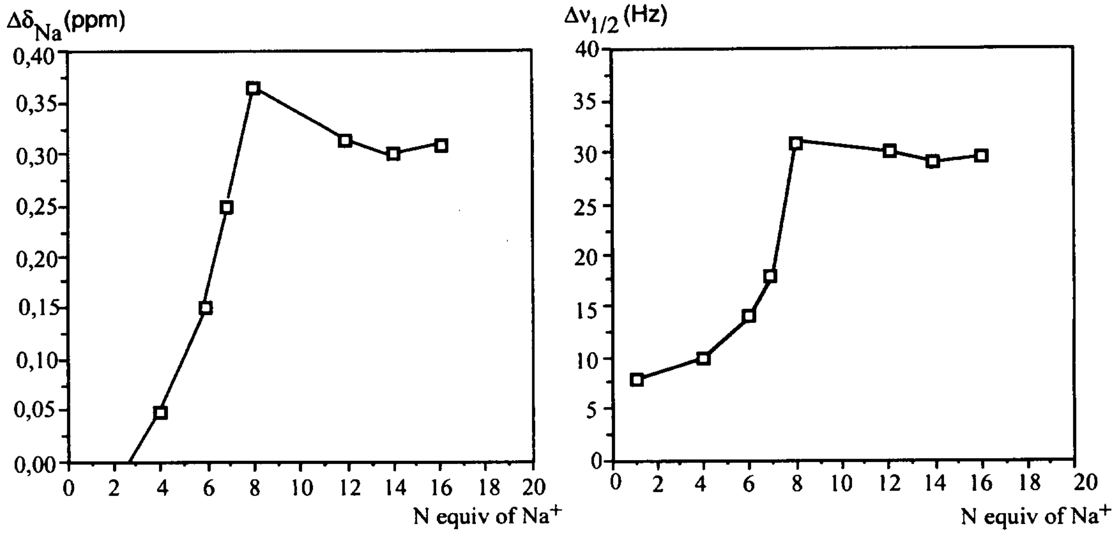


Figure 5. $\Delta\delta_{Na}$ and $\Delta\nu_{1/2}$ during addition of NaOH to EDTMP solution

In conclusion, our results which seem valid for other series of acids,[9] calls into question the principle of pH-metric titration of polyacids. The cations M^+ issued from the base or from the electrolyte were either free or complexed in solution; consequently the titration is that of a mixture of LH_n acid and $LH_{n-m}M_m$ complexes, the proportions of which depend on their stability, the concentration of the electrolyte and the progress of the titration.

References

1. (a) Wagener, J. M.; Jarvis, N. V. *S. Afr. J. Chem.* **1995**, *48*, 85. (b) Geraldes, C. F. G. C.; Sherry, A. D.; Cacheris, W. P. *Inorg. Chem.* **1989**, *28*, 3336. (c) Rizkalla, E. N.; Choppin, G. R. *Inorg. Chem.* **1983**, *22*, 1478.
2. (a) Colton, R.; Mitchell, S.; Traeger, J. C. *Inorg. Chim. Acta.* **1995**, *231*, 87. (b) Rigault, A. M.; Gervais, A. D.; Baxter, P. N. W.; Van Dorsselaer, A.; Lehn, J. M. *Inorg. Chem.* **1996**, *35*, 2307. (c) Bitsch, F.; Hegy, G.; Dietrich-Buchecker, C.; Leize, E.; Sauvage, J. P.; Van Dorsselaer, A. *New J. Chem.* **1994**, *18*, 801. (d) Fauvelle, F.; Jaquinod, M.; Pétillot, Y.; Forest, E. *European Mass Spectrometry* **1996**, *2*, 381.
3. Gall, L. N.; Smirnov, I. V.; Chuprikov, A. V.; Yu Shadrin, A.; Shkurov, V. A. *Dokl. Akad. Nauk. 3*, **1992**, *325*, 514.
4. Shadrin, A. Yu; Shkurov, V. A.; Smirnov, I. V.; Chuprikov, A. V. *Zh. Obshch. Khim.* **1992**, *62*, 5, 1178.
5. (a) Delgado, R.; Frausto da Silva, J. J. R. *Talanta* **1982**, *29*, 815. (b) Stetter, H.; Frank, W.; Mertens, R. *Tetrahedron* **1981**, *37*, 767.
6. ESMS (OR=30 V) shows that, at pH ≤7, NaDOTA is very preponderant over the other complexes Na_xDOTA which accredits this value determined by potentiometry.
7. (a) Israëli, Y.; Detellier, C. *J. Phys. Chem. B* **1997**, *101*, 1897. (b) Blixt, J.; Detellier, C. *J. Am. Chem. Soc.* **1995**, *117*, 8536. (c) Tsukube, H.; Shinoda, S.; Mizutani, Y.; Okano, M.; Takagi, K.; Hori, K. *Tetrahedron* **1997**, *53*, 10, 3487.
8. Sherry, A. D.; Ren, J.; Huskens, J.; Brücher, E.; Toth, E.; Geraldes, C. F. G. C.; Castro, M. M. C. A.; Cacheris, W. P. *Inorg. Chem.* **1996**, *35*, 4604.
9. Caprioli, R. M. *Anal. Chem.* **1983**, *55*, 2387.
10. Synthesis of OTMP: 90 mg of formaldehyde at 37% in water was added to a mixture of 0.5 mmol of 10-oxa-1,4,7-triazacyclododecan, 355 μL of water heated to reflux, 130 μL of HCl 37% and 4 mmol of H_3PO_3.[11] The mixture was kept at reflux for 12 h. Water (25 mL) was added then evaporated, this treatment was repeated seven times. The solid was recrystallized in water–methanol. Yield: 66%. NMR ^1H (D_2O,TMSPA) 3.93 (m, 4H, H_a); 3.77 (m, 4H, H_b); 3.63 (m, 4H,

H_c); 3.14 (m, 4H, H_d); 3.52 (d, 4H, H_e J=12.4); 3.01 (d, 2H, H_f J=10.9). NMR ^{13}C (D_2O, TMSPA) 67.30 (C_a), 58.23 (C_b), 57.05 (C_c), 53.32 (C_d), 54.87 (d, C_e $^1J_{CP}$=143.2), 53.20 (d, C_f $^1J_{CP}$=149.9). NMR ^{31}P (D_2O, TMSPA, H_3PO_4) 11.83 (2P), 6.78 (1P). SM FAB (glycerol): molecular peak 456.

11. Mollier, H.; Naïni, A.; Dumont, C.; Audo, D.; Serratrice, G.; Vincens, M.; Vidal, M.; Grand, S.; Lebas, J. F. *Bull. Soc. Chim. Fr.* **1992**, *129*, 376.
12. Conditions of analysis. ESIMS: API III+ (Perkin–Elmer Sciex) triple quadrupole mass spectrometer with an electrospray source. Solution was introduced by means of a syringe pump on a VALCO-C14WI injector with a 1 µL internal loop, the solvent used for infusion consisting of MeOH:H_2O (20:80) FAB: NERMAG R 10-10C. Matrix: mixture of solution:glycerol (50:50). NMR: Bruker AM300 working at 79.39 MHz in ^{23}Na. Solvent D_2O.
13. EDTMP: acid ethylenediaminetetramethylenephosphonique; DOTA: acid 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetique; OTMP: acid 1-oxa-4,7,10-triazacyclododecane-4,7,10-trimethylenephosphonique.
14. ESIMS: electrospray ionisation mass spectrometry, FAB: fast atom bombardment.