Gas-phase interactions of di- and tri-organotins with glycine and cysteine

Jean-Yves Salpin, Latifa Latrous, Violette Haldys, Jeanine Tortajada, Catarina Correia

Gas-phase interaction of di- and tri-organotins with glycine and cysteine

Jean-Yves Salpin[1,2], Latifa Latrous[3], Violette Haldys[1,2], Jeanine Tortajada[1,2], Catarina Correia[1,2]

1. Laboratoire Analyse et Modélisation pour la Biologie et l'Environnement (LAMBE), University of Evry val d'Essonne – Evry – France
2. CNRS – UMR 8587
3. Laboratoire de Chimie-Analytique et Electrochimie – Faculté des Sciences de Tunis – Tunis – Tunisia

OVERVIEW

- First detailed gas-phase study dealing with the interaction taking place between di- and tri-organotin(IV) compounds and two amino acids: glycine and cysteine.
- Combination of MS/MS studies (including labeling experiments) and Density Functional Theory calculations.

INTRODUCTION

- The exponential increase of the industrial, agricultural and biological applications of organotins (OTCs) has led to their accumulation in biological systems.[1] These compounds are generally very toxic, and depending on the nature and the number of the organic groups bound to the Sn cation, show specific effects to different organisms even at very low concentrations.[2] Organotins have also emerged as potentially biologically active compounds [3], and it is noticeable that organotins compounds occupy an important place in cancer chemotherapy reports.[4] However, their mechanisms of action are still not well understood. Since amino acids (AA) and peptides are efficient biological metal ion binders, their interaction with organotin cations may play an important role in these mechanisms. In order to clarify the OTC/peptide interaction, various studies were carried out in solution. To the best of our knowledge, the interaction of OTCs with aminoacids or peptides has not been explored in detail by mass spectrometry so far, though such gas-phase studies could provide useful insights about their intrinsic reactivity. In this context, the gas-phase interactions of organotins R_2SnCl_2 and R_3SnCl (R=Me, n-Bu, Ph) with glycine and cysteine have been investigated by combining mass spectrometry and theoretical calculations.

METHODOLOGY

Experimental

- Experiments performed on a QSTAR Pulsar-i mass spectrometer (AB Sciex) fitted with a nanospray source.
- 10^{-4}M/5.10^{-4}M glycine/OTC mixtures in methanol/water solutions (50/50 v:v) nanosprayed (20-50 nL.min^{-1}) using borosilicate emitters (Proxeon) (capillary voltage: 900V).
- MS/MS experiments with N_2 as collision gas. Laboratory frame collision energies ranging from 8 to 25 eV ("pulse off" mode).

Computational

- Density functional theory (DFT) calculations were carried out using the B3LYP hybrid functional, as implemented in the Gaussian 09 suite of programs.
- Optimization with the 6-31+G(d,p) basis set, without any symmetry constraint. Use of the Def2-SVP effective core potential and basis set for Sn.[5]
- Harmonic vibrational frequencies were computed at the same level.

CONCLUSION

- The gas-phase reactivity of organotins towards glycine and cysteine is markedly different from that observed with alkali or transition metal ions.
- Di-organotins appear much more reactive than tri-organotins.
- Theoretical calculations are under progress in order to describe the potential energy surfaces associated with the main dissociation channels.

REFERENCES

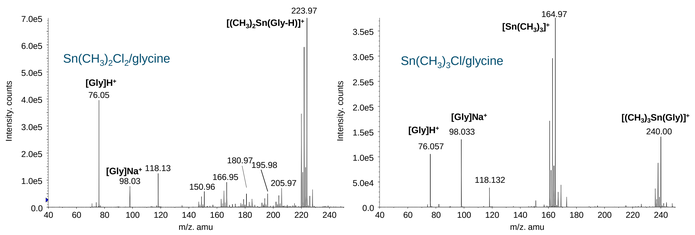
[1] J.T. Byrd, M.O. Andrae, *Science* 218 (1982) 565.
[2] M. Hoch, *Appl. Geochem.* 16 (2001) 719.
[3] L. Pellerto, L. Nagy, *Coord. Chem. Rev.* 224 (2002) 111.
[4] S. Tabassum, C. Pettinari, J. *Organomet. Chem.* 691 (2006) 1761.
[5] B. Metz, H. Stoll, M. Dolg, *J. Chem. Phys.* 113 (2000) 2563.
[6] L. Rodriguez-Santiago, M. Sodupe, J. Tortajada, *J. Phys. Chem. A* 105 (2001) 5340.
[7] F. Rogalewicz, Y. Hoppilliard , G. Ohanessian, *Int. J. Mass Spectrom.* 206 (2001) 45.

Contact: jean-yves.salpin@univ-evry.fr

60th ASMS Conference on Mass Spectrometry
Vancouver, BC, Canada – May 20 - 24, 2012

RESULTS

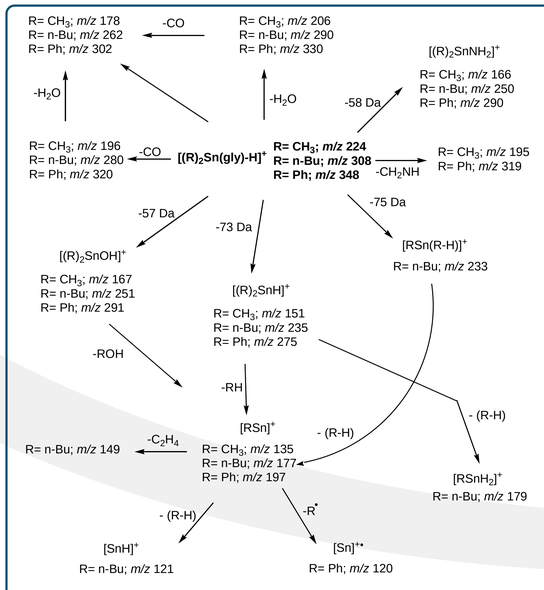
Nano-ESI spectra



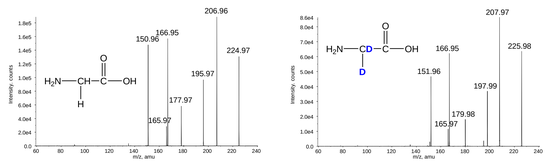
- Nano-ESI spectra remarkably simple in spite of the strong tendency to hydrolysis of organotins in aqueous solution.
- Interaction between di-organotins and AAs results in the formation of $[(R)_2Sn(AA\text{-}H)]^+$ ions while tri-organotins give rise to $[(R)_3Sn(AA)]^+$ species.
- Sn-containing ions easily recognizable. Isotopic profiles confirm the lack of chloride atom(s).
- No doubly-charged species were detected.

Reactivity of $[(R)_2Sn(AA\text{-}H)]^+$ complexes

- MS/MS spectra of $[(R)_2Sn(AA\text{-}H)]^+$ complexes are particularly informative. For each amino acid, the three $[(R)_2Sn(AA\text{-}H)]^+$ complexes share several common fragmentations.
- Some dissociation processes, such as loss of water, carbon monoxide or 46 Da, are similar to those observed with other metal cations such as Ni(I) [6] or Zn(II). [7]
- Other fragment ions are specific of organotins, and several dissociation routes are characteristic of a given organic substituent.

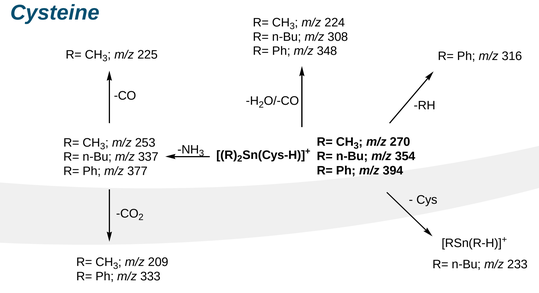


Glycine	Precursor ion	Product ions			
	$[(CH_3)_2Sn(Gly\text{-}H)]^+$	$-H_2O$	-CO	$-CO, H_2O$	$[(CH_3)_2SnH]^+$
Not labeled	*m/z* 223.98	*m/z* 205.96	*m/z* 195.98	*m/z* 177.97	*m/z* 150.97
1-^{13}C	*m/z* 224.97	*m/z* 205.96	*m/z* 195.97	*m/z* 177.97	*m/z* 150.97
2,2-d_2	*m/z* 225.98	*m/z* 207.97	*m/z* 197.99	*m/z* 179.98	*m/z* 151.96



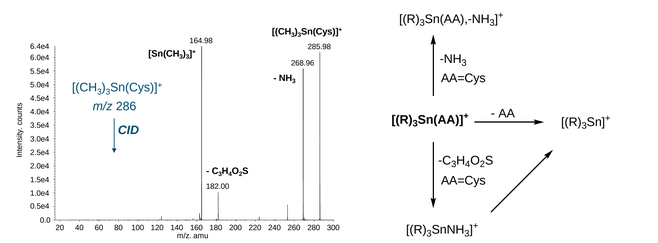
- The use of labeled amino acids gives useful insights about the dissociation processes. For example, formation of the $[(R)_2SnH]^+$ ion involves the migration of one C_α hydrogen of glycine.

Cysteine



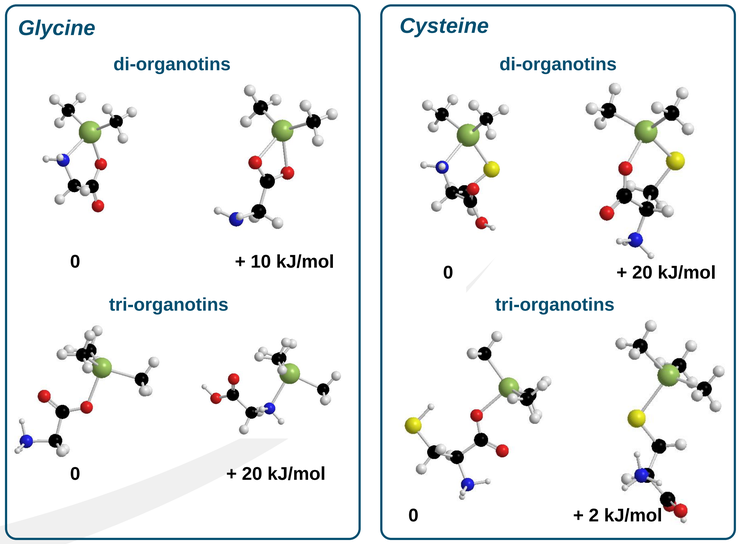
- The behaviors upon collision of the cysteine and glycine complexes are sensibly different, suggesting a different coordination scheme.

Reactivity of $[(R)_3Sn(AA)]^+$ complexes



- Unimolecular reactivity rather simple compared with that of di-organotin complexes. With glycine, only intact elimination of the aminoacid is observed.

Computational study



- Interaction of di- and tri-organotins leads to bi- and monodentate species, respectively. The $(R)_3Sn^+$ moiety is only slightly tetrahedral.
- The binding scheme of glycine and cysteine is clearly different. As expected, tin exhibits a strong affinity for sulfur.
- For di-organotins, the most stable forms are obtained from neutral aminoacids, while $(R)_3Sn^+$ ions strongly stabilize zwitterionic forms.
- For a given system, relative energies do not vary with the nature of R.