

STUDENT 5

THE GAS PHASE ACIDITIES OF PHOSPHOLIPIDS: EXPERIMENT AND THEORY

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Electrospray ionisation mass spectrometry has emerged over the last ten years as the most efficient methodology for lipidomic analysis and has dramatically accelerated progress in the field.¹⁻³ Negative ion electrospray mass spectrometry, in particular, has been shown to be a powerful method for the detection of acidic phospholipids in complex lipid extracts. While absolute quantitation of these species continues to require laborious separation procedures, comparison of ESI-MS lipid profiles of crude lipid extracts is gaining popularity as a means to rapidly identify relative differences in phospholipid abundances between samples.¹ This methodology has been recently been dubbed “shotgun lipidomics”.³ While such experiments are extremely useful in highlighting gross differences in lipid profiles their usefulness for quantitation can be limited by the differing ionisation efficiencies of the phospholipid headgroups. Difficulties in understanding the underlying cause of such differences are exacerbated by the dearth of thermochemical data available for lipids in the gas phase.

We have measured the tandem mass spectra of a range of proton bound phospholipid dimers containing different headgroup combinations. Analysis of these data using the kinetic method provides a sequence for the gas phase acidities of $PE \cong PA < PG < PS < PI$. These data are, for the most part, supported by quantum chemical calculations that provide best estimates of gas phase acidities for these phospholipid headgroups: $\Delta H_{\text{acid}}(PE) = 1390 \text{ kJ mol}^{-1}$, $\Delta H_{\text{acid}}(PA) = 1388 \text{ kJ mol}^{-1}$, $\Delta H_{\text{acid}}(PG) = 1339 \text{ kJ mol}^{-1}$, $\Delta H_{\text{acid}}(PS) = 1318 \text{ kJ mol}^{-1}$ and $\Delta H_{\text{acid}}(PI) = 1329 \text{ kJ mol}^{-1}$. The relative importance of these gas phase data and established solution phase ionisation constants⁴ to the electrospray ionisation efficiencies of phospholipid mixtures and the consequences for the shotgun approach to lipidomics will be discussed.

References:

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4. Marsh, D., *CRC Handbook of Lipid Bilayers*; CRC Press: Boca Raton, 1990.