

Studying arsenate thioester formation with Arsenic-75 nuclear magnetic resonance spectroscopy

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Introduction: There is a revival of arsenic in modern medicine since arsenic trioxide at low doses induces leukaemia cells to undergo apoptosis and at higher doses causes blood flow to solid tumors to shut down [1]. Arsenic-75 NMR was used as a probe of arsenate interactions in solution. The line width at half-height of the ⁷⁵As NMR signal was studied systematically as a function of solution pH. The study of the interaction of arsenate with mono and dithiol compounds (like cysteine and 1,2-dithiol-3-propanol) was undertaken in order to follow arsenate thioester formation. ⁷⁵As has a spin of 3/2, 100% natural abundance and a receptivity of 143 relative to ¹³C. Despite a favourable natural abundance and receptivity, arsenic NMR spectra are difficult to obtain as a result of the large quadrupole moment of the ⁷⁵As nucleus ($Q = 0.3 \times 10^{-24} \text{ cm}^2$), which tends to produce broad lines owing to quadrupolar relaxation. For a quadrupolar nucleus with spin I , under extreme narrowing conditions, line widths are given by

$$\Delta\nu_{1/2} = \frac{3\pi(2I+3)}{10I^2(2I-1)} \frac{[e^2 q_{zz} Q]^2}{h^2} (1 + \eta^2/3) \tau_c$$

where e is the charge of the electron, q is the electric field gradient at the nucleus, with q_{zz} as its largest component, η is the asymmetry parameter for q , and τ_c is the isotropic tumbling correlation time (1-10 ps for nonviscous liquids). Since ⁷⁵As has a large Q and a low spin value of 3/2, it has a large line width in any asymmetric environment [2-4].

Experimental: The spectra were measured as aqueous solutions in non-spinning 2 ml cylindrical vials containing an internal capillary of a KAsF₆ standard using a Varian 400 MHz spectrometer and a Bruker broadband probe. All arsenicals were used in 1 molar concentrations. The probe was taken out and tuned to 68.488 MHz after each sample change.

Results and Discussion: Figs. 1 and 2 show ⁷⁵As-NMR spectra of the used standard and an exemplary sample system with arsenate, dithiol and internal standard.

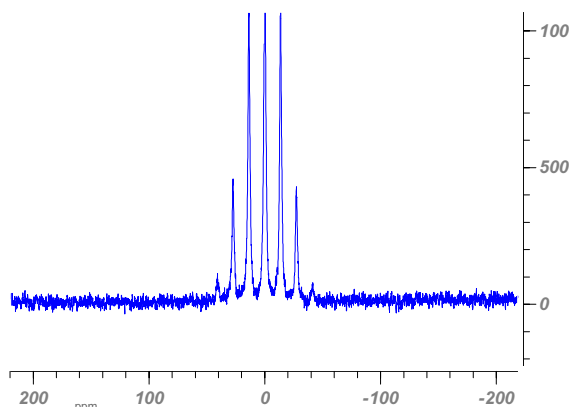


Fig. 1: ⁷⁵As-NMR spectrum of [AsF₆]⁻ at pH=7, used as standard for all further experiments

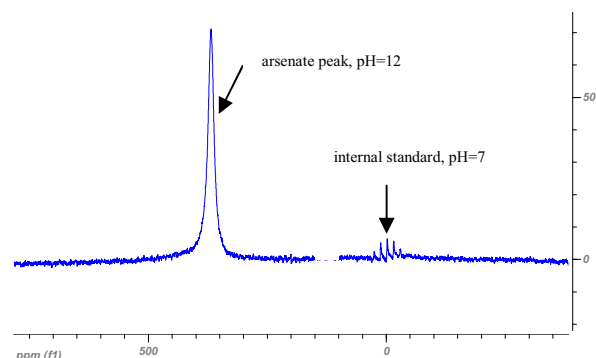


Fig. 2: ⁷⁵As-NMR spectrum of arsenate after addition of an equimolar amount of 1,2-dithiol-3-propanol, pH=12

A linear correlation between the amount of added thiol and the line width was observed, whereas changes in chemical shift were not registered. The signal line width strongly depends on the symmetry of the chemical environment of a species. This is why one can conclude that arsenic thioesters are formed under these conditions and the high symmetry of the AsO₄³⁻ is lost. We also tried to obtain spectra of various non-symmetric organic and inorganic arsenic species in aqueous solution, e.g. AsI₃ or cacodylic acid, but the signals were too broad to be observed.

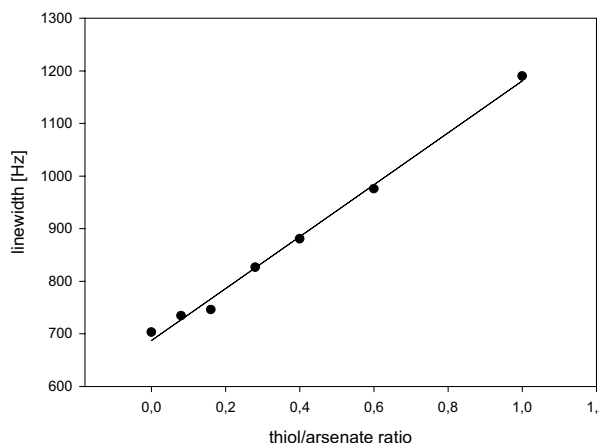


Fig. 3: Linear dependency of line width and symmetry loss by arsenate-thiol complexation with 1,2-dithiol-3-propanol at pH=12

Conclusion: Keeping in mind the limitations of quadrupolar relaxation induced line broadening in unsymmetrical chemical environments, ⁷⁵As NMR is a very promising probe to follow arsenate interactions with various thiols in solution.

References:

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