**Probing the redox reactivity of Alkyl-Bound Astatine-211**

Jehan Perera, Jonathan D. Burns, Lauren A. McIntash, Gabriel C. Tabacaru and Sherry J. Yennello
*University of Alabama at Birmingham in collaboration with Texas A&M University Cyclotron Institute*

Over the past year, our collaborative efforts with the Cyclotron Institute have focused on understanding the chemical behavior and redox reactivity of $^{211}$At in organic systems relevant to isotope transport and radiolabeling. Specifically, our study investigated the formation of a covalent At–carbon bond when $^{211}$At is shipped on 3-octanone-impregnated columns and evaluated strategies for recovering the isotope via selective redox reactions. The work culminated in the publication of a peer-reviewed article in Inorganic Chemistry titled **"*Probing the Redox Reactivity of Alkyl Bound Astatine: A Study on the Formation and Cleavage of a Stable At–C Bond*"**.

Initial observations showed that $^{211}$At, after being eluted from the shipped column using fresh 3-octanone, remained almost entirely in the organic phase during attempted back-extractions using both $HNO_3$ acid and NaOH, even at concentrations around ~15 M. This behavior deviated significantly from what would be expected if $^{211}$At were present as a simple ionic species such as $AtO^+$ or $At^-$. Instead, thin-layer chromatography (TLC) analyses revealed a sharp change in mobility, from a stationary spot before column loading to a fast-moving band near the solvent front after elution from the shipped column. These findings strongly suggested the formation of a neutral, lipophilic species during shipment, most likely involving a covalent At–C bond with the 3-octanone ligand.

To investigate this hypothesis, a series of experiments were conducted using both reducing and oxidizing agents to cleave the proposed At–C bond. Among the reducing agents, $NH_2OH$ was found to be the most effective, achieving approximately ~75% recovery of $^{211}$At into the aqueous phase. In contrast, $N_2H_4$ and NaOH required very high concentrations and yielded only modest recovery. Strong oxidizing agents, including ceric ammonium nitrate, $KMnO_4$, and sodium or calcium hypochlorite, were far more successful, with near-quantitative recovery (>98%) achieved at concentrations around 0.1–0.5 M. These results confirmed that redox chemistry is essential to breaking the At–C bond and enabling aqueous-phase recovery of the isotope.

Ion exchange studies and additional radio-TLC experiments confirmed the speciation of $^{211}$At after redox treatment. When recovered with $NH_2OH$, the $^{211}$At species was retained on an anion exchange resin, indicating the presence of At-. Conversely, treatment with NaOCl produced a species retained on a cation exchange resin, consistent with $At^+$. These speciation changes were also reflected in the TLC behavior: the organic-phase At–C compound showed a retention factor ($R_f$) near 0.90, while the aqueous-phase ionic species remained stationary at the baseline ($R_f = 0.00$), as expected for charged species interacting with the silica surface.

To provide molecular-level insight into the nature of the At–C species, density functional theory (DFT) calculations were carried out. The structure 4-astato-5-hydroxy-octa-3-one emerged as the most thermodynamically stable of the proposed products formed via reaction between $AtO^+$ and 3-octanone. The molecule exhibited enhanced stability due to intramolecular hydrogen bonding between the hydroxyl group and the carbonyl oxygen. Solvation modeling showed that this compound was consistently more stable in

organic solvents such as toluene or 2-octanone than in water, in agreement with the experimental observation that $^{211}$At remained in the organic phase unless redox cleavage was induced.

This work has several important implications. First, it provides the first experimental and theoretical evidence for the formation of a stable At–C bond under realistic isotope shipping conditions. Second, it demonstrates practical redox-based strategies to selectively cleave that bond and recover $^{211}$At in an ionic form, enabling further chemical manipulation or radiolabeling. Third, it highlights the amphoteric character of astatine, which can form either cationic or anionic species depending on the reaction conditions. Lastly, it offers valuable guidance for the design of transportable radiopharmaceutical intermediates, where bond stability and release conditions must be finely controlled.

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