Xanthine Quartets on Au(111)

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As a non-canonical secondary formation of DNA sequences, DNA quadruplexes have sparked tremendous interest in the biological and medical societies, due to their paramount importance in homologous recombination, DNA replication, transcriptional regulation, chromosome stability, and high therapeutic potentials. Albeit ample speculation on a possibility of various quadruplexes, the only one whose presence has been explicitly confirmed is the guanine (G)-quadruplex, composed of stacking G-quartets with monovalent cations coordinated in between.

Xanthine (3,7-dihydro-purine-2,6-dione, X) is a purine base ubiquitously distributed in most human body tissues and fluids as well as in other organisms. As an intermediate in nucleic acid degradation, xanthine can be generated *in vivo* from guanine by deamination. Very promisingly, recent results based on mass spectroscopy, nuclear magnetic resonance spectroscopy and quantum chemical computations proposed that xanthine and its derivatives have the potential to be an alternative candidate to form stable quartets, while molecular dynamics simulations further suggested that the high degree of structural and energetic compatibility of X-quartet may lead to new quadruplexes by replacing G-quartets with X-quartets. However, definitive experimental evidence, confirming the existence of the X-quartets, has been still lacking. Considering that xanthine is one of the original nucleobases in prebiotic Earth and found abundant in meteorites from outer space,19 the conformation of X-oligomer and the chirality of X-networks must be extraordinarily intriguing for understanding prebiotic synthesis of nucleic acid, which is fundamental to origin of life.

In this work, X-quartet has been fabricated and visualized for the first time. Based on *in situ* thermodynamic investigation and the calculated stabilization energies, the quartet network is confirmed to be the most stable phase of xanthine on Au(111). Importantly, in contrast to guanine, it is revealed that the formation of the X-quartet is not dependent on the participation of metal atoms. Moreover, the quartets are homochiral, composed by either of the two xanthine enantiomers. Interestingly, both the quartet itself and the 2-D assembly of the quartets prefer homochirality. This work demonstrates a potential for xanthine to construct quartets hence artificial new DNA quadruplexes, which may find various applications in genetic regulation and antitumor therapy, meanwhile indicates that homochiral X-based oligo-nucleotides might have been prevailing at early stages of life.

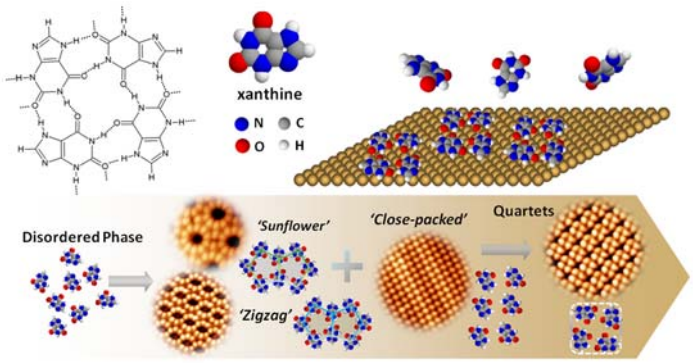

Illustration of a xanthine quartet and the thermodynamic transformation of xanthine on Au(111)