On AuₙAt clusters as potential astatine carriers†

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To understand interactions between astatine atoms with gold clusters the AuₙAt and AuₙX clusters, n = 12 or 13, X = F, Cl, Br, and I, were calculated at the DFT level using basis sets with a quasi-relativistic pseudopotential and the D3 Grimme correction for the dispersion interactions. Among the studied clusters of various geometries, the interaction energy of At to the clusters is the smallest. Yet, consideration of the electron detachment from the X⁻ anion and generation of a H₂ molecule and OH⁻ anion from water shows that the formation of the astatine gold clusters is favored.

**References**

† The computations were performed using the LC-oPBE functional ‡‡ combined with the Stuttgart/Cologne Group (SDD) basis sets with quasi-relativistic pseudopotential §§ and the D3 Grimme correction ‡§ for the dispersion interactions as implemented in Gaussian 09 suite of programs. || For open-shell systems the spin contamination was checked to be small. || For more details see ESL†.

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Fig. 1 The DFT optimized\textsuperscript{a} Au\textsubscript{12}, Au\textsubscript{13} and Au\textsubscript{14} structures.

\textsuperscript{a} \& symmetry, it exhibited imaginary frequencies. Therefore, except for the slightly distorted icosahedron (Au\textsubscript{12}-3, Fig. 1), we took several other high-symmetry geometries considered before for both Au\textsubscript{12} and Au\textsubscript{13} clusters (Fig. 1).\textsuperscript{17–21}

Notice, that the non-planar Au\textsubscript{12}-1, Au\textsubscript{13}-1 and Au\textsubscript{13}-2, and Au\textsubscript{14}-1 are the most stable in the cluster of the same size (Table 1). It may seem surprising that the slightly distorted icosahedral Au\textsubscript{13}-3 structure is less stable than the most stable Au\textsubscript{13} clusters by 17.5 kcal mol\textsuperscript{−1}. However, in general, the high-symmetry (I\textsubscript{h}, D\textsubscript{6h}, D\textsubscript{3h}) Au\textsubscript{13} clusters tend to be less stable than those of lower symmetry.\textsuperscript{22} It is possible that this is a result of lack of external stabilisation forces in vacuum, while in crystals the most packed form of cluster is favorized.\textsuperscript{17,18,22} As expected,\textsuperscript{22} the planar Au\textsubscript{13}-3, Au\textsubscript{13}-4 and Au\textsubscript{14}-2 clusters are definitely the least stable (Table 1). Energetics of the quartet spin state considered for the Au\textsubscript{13} systems indicated doublets to be always significantly more stable than quartets (see ESI\textsuperscript{†}).

To model halogen–Au cluster interaction, first, we assumed that the halogen atom interacts with the cluster surface rather than is placed as one of the inner cluster atoms. In the case of planar clusters, introductory calculations indicated that the position in plane is more stable than any of the out of plane ones. Only a few, out of a multitude combinatorially possible, positions of the halogen atom on each Au cluster could be taken into account. For each halogen, the structures of those few positions were optimized. The structures fall into a few types, which however, locally are quite different. This is because in series of halogens, their electronegativities, volumes, ionization potentials, electron affinities, etc. differ a lot. The finding for all halogens were generalized, remembering that the objective of this study was to find a tendency for all halogens rather than a strict rule for a given type of cluster.

For all Au\textsubscript{14} clusters, series of similar neutral Au\textsubscript{14}X structures were optimized (Fig. 2). It appeared that the heavier the halogen the less stable the cluster (Table 2). This is not unexpected because the halogen electronegativity decreases with its mass from 3.98 for fluorine to ca. 2.2 for astatine.\textsuperscript{23} Indeed, already for the AuX molecules the interaction energies decrease monotonically from ca. −110 kcal mol\textsuperscript{−1} for fluorine to −90 kcal mol\textsuperscript{−1} for astatine. For most of the Au\textsubscript{12}X and Au\textsubscript{13}X clusters such a trend is preserved, although it is not always monotonic.

Remark, that the Au\textsubscript{12}X-3 structure is the most whereas the Au\textsubscript{13}X-4 one is the least stable. They are derived from the Au\textsubscript{12}-1 and Au\textsubscript{12}-3 clusters, respectively, which are the most and the least stable as well. However, the Au\textsubscript{13}X-1 structures are obtained from the most stable Au\textsubscript{12}-1 cluster, yet, the halogen stabilization energies in this very cluster are similar to the weakest Au\textsubscript{12}X-4 ones.

On the other hand, the most stable Au\textsubscript{13}X-3 structures are obtained from the Au\textsubscript{13}-1 clusters which are (one of two) the most stable and the least stable Au\textsubscript{13}X-5 structures are obtained from the least stable planar Au\textsubscript{12}-4 clusters. Notice however, that the Au\textsubscript{14}X-1 and Au\textsubscript{14}X-2 systems were also obtained from the most stable Au\textsubscript{13}-1 and Au\textsubscript{13}-2 clusters but yield Au\textsubscript{14}X systems which are ca. 15 kcal mol\textsuperscript{−1} less stable than Au\textsubscript{13}X-3 ones. Comparison of the geometries of the clusters shows that within the given type of the Au\textsubscript{X} clusters its structure does not vary much with the halogen. In contrast, the site the halogen is attached to the Au\textsubscript{X} molecule the interaction energies decrease monotonically from F to At atom. Finally notice, that as for the Au\textsubscript{13} clusters, the Au\textsubscript{12}X ones

\begin{table}[h]
\centering
\caption{The total energy $E$ (hartree) and energy differences $\Delta E$ (kcal mol\textsuperscript{−1}) between different Au\textsubscript{12}, Au\textsubscript{13} and Au\textsubscript{14} clusters (Fig. 1).\textsuperscript{1} Energetics for the doublet spin state of the Au\textsubscript{13} and the singlet spin state of Au\textsubscript{12} and Au\textsubscript{14} systems are presented. For Au\textsubscript{13} quartets see ESI\textsuperscript{†}}
\begin{tabular}{|c|c|c|c|}
\hline
Cluster & $E$ & $\Delta E$ & $\Delta G_{298}$ \\
\hline
Au\textsubscript{12}-1 & −1629.405910 & 0.0 & −1629.474373 \\
Au\textsubscript{12}-2 & −1629.399313 & 7.8 & −1629.462010 \\
Au\textsubscript{12}-3 & −1629.357086 & 30.7 & −1629.429677 \\
Au\textsubscript{12}-4 & −1765.181138 & 0.0 & −1765.254652 \\
Au\textsubscript{13}-1 & −1765.181104 & 0.1 & −1765.255102 \\
Au\textsubscript{13}-2 & −1765.153717 & 17.2 & −1765.227080 \\
Au\textsubscript{13}-3 & −1765.153717 & 17.2 & −1765.227080 \\
Au\textsubscript{13}-4 & −1765.129280 & 32.6 & −1765.206241 \\
Au\textsubscript{14}-1 & −1901.021432 & 0.0 & −1901.094858 \\
Au\textsubscript{14}-2 & −1900.923100 & 74.8 & −1900.980926 \\
\hline
\end{tabular}
\end{table}

Fig. 2 The DFT optimized\textsuperscript{a} Au\textsubscript{12}At and Au\textsubscript{13}At structures.
in the quartet spin state are always significantly less stable than doublets (see ESI†).

The decreasing interaction energy between halogen and gold cluster in AuX systems as the atomic number of halogen is increased would suggest that the same tendency could obey the gold clusters as a halogen carriers in water environment. In fact, in most cases the opposite is true. For example, in aqueous solutions the degree of specific adsorption on a gold surface increases in the order F– < Cl− < Br− < I−. Especially, F– has the lowest affinity and only nonspecifically or weakly specifically adsorbs on gold surface. Such an effect was observed in the case of adsorption of halides on gold electrode surfaces and aggregation of gold nanoparticles induced by halides adsorption.23 Indeed, to form an AuX cluster, the X− halide anion must be oxidized to the X0 free halogen form. As a result, the released electron is attached to water molecule and the H2 molecule and OH− anion are formed:

\[ X^- + Au_{n} + H_2O \rightarrow Au_{n}X + \frac{1}{2}H_2 + OH^- \] (1)

The energy balance of the above reaction demonstrates that the stabilization energy of the halogen atom at the Au12 and Au13 clusters in water environment tend to increase from F to At (Table 3).

In conclusion, we have computationally confirmed the higher stability of the Au12At and Au13At clusters in water environment than stability of the analogous clusters with lighter halogens. Our experimental studies already signalized a high therapeutic potential of 211At labelled gold nanoparticles functionalized with substance P and trastuzumab towards glioma cells and HER2 positive breast and ovarian cancers. These two findings open new perspectives for optimization novel 211At labelled gold nanoparticles functionalized with different biomolecules for cancer targeting therapy.

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