Oxidation of L-DOPA and dopamine during gold clusters formation: NMR and computational study

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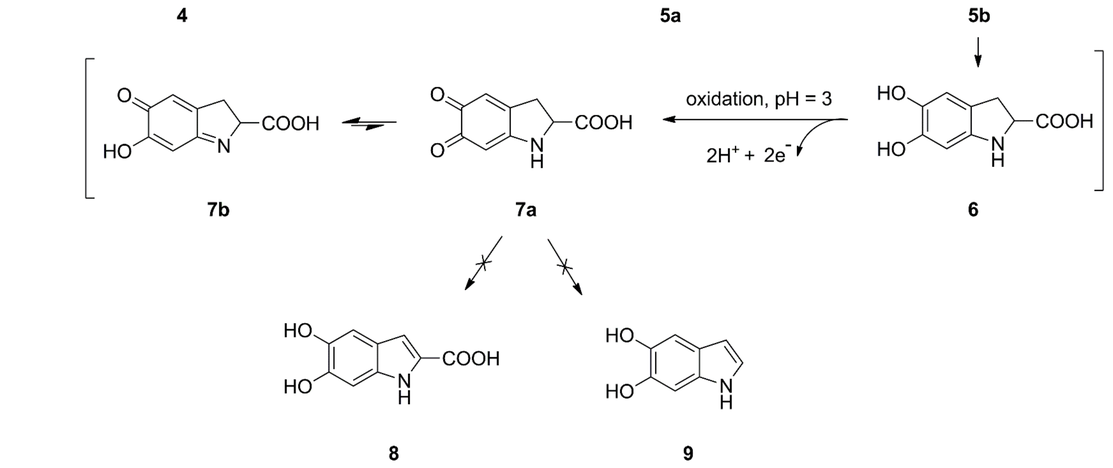
Introduction

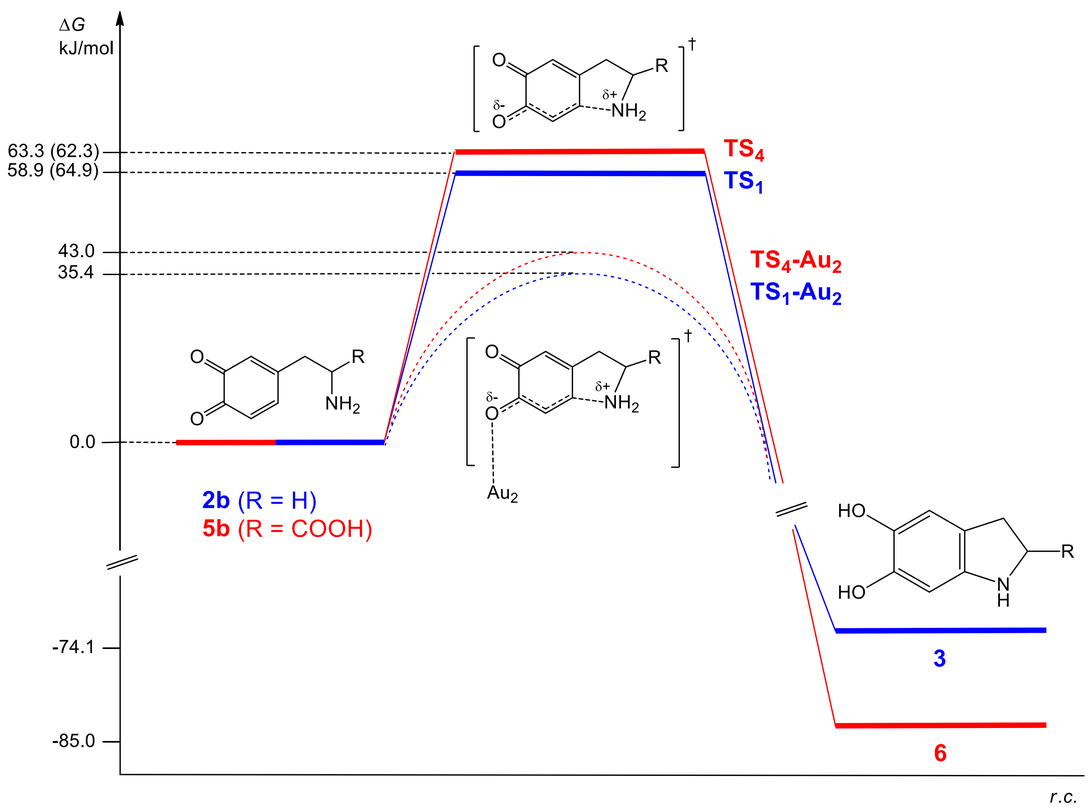
Due to their unique physical and chemical properties, gold nanoparticles (AuNPs) have been extensively used in biomedical fields, including drug delivery into the brain as they can easily penetrate through the blood-brain barrier [1]. The study employed combined NMR and computational apprach to study events at the nano-bio interface during preparation of L-DOPA/dopamine-functionalized AuNPs. During synthesis, L-DOPA/dopamine were used as both reducens and surface coating agents [2], but mechnisms of their interaction with gold clusters and nanosurface have been not yet elucidated.

Methods

AuNPs were prepared by mixing $HAuCl_4$ x $3H_2O$, spherical Aud seeds, mPEG thiol and L-DOPA or dopamine hydrochloride under vigorous stirring. The synthesized AuNPs were characterized by hydrodinamic diameter (d_H) and ζ potential using dynamic and electrophoretic light scattering (Table 1), while their shape and primary size (d) were examined by transmission electron microscopy (TEM, Figure 1). The ^1H and ^{13}C NMR spectra were obtained using a Varian INOVA 400 spectrometer (Varian, Palo Alto, CA) operating at 399.6 and 100.5 MHz, respectively. The chemical shifts are expressed in parts per million (ppm) in reference to the residual water signal. DFT calculations were performed at the M06L/6-31+G(d,p)/LANL2DZ level of theory. All computational experiments (geometry optimization, frequency calculations, solvent effects, and IRC procedures) were conducted in the Gaussian 16 software with GaussView program used for structure drawing and visualization.



Scheme 1. Oxidation and cyclization processes during the preparation of AuNPs in the presence of DOPA. Structures in squared brackets cannot be differentiate by ^1H NMR spectroscopy. All structures may exist in zwitter-ion form.



Scheme 2. Gibbs free energy diagram for intramolecular cyclization of dopaminequinone (R = H; blue line) and dopaquinone (R = COOH; red line) calculated at the SMD-M06L/6-31+G(d,p)/LANL2DZ level (solvent = water). The reactions catalyzed by Au dimer marked with dashed curves. Experimental barriers for dopaminequinone and dopaquinone are in parentheses.

Results

Table 1. Values of d_H, ζ potential and d_{TEM} for AuNPs functionalized with L-DOPA and dopamine.

Type	d_H /nm	ζ/mV[b]	d_{TEM}/nm[c]
AuNP-DOPA	126.1 ± 1.4	-32.2 ± 5.2	120.9 ± 1.3
AuNP-dopamine	137.9 ± 0.9	-33.7 ± 0.9	132.1 ± 2.3

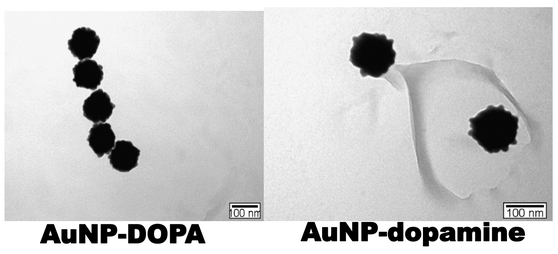


Figure 1. TEM micrographs of AuNPs.

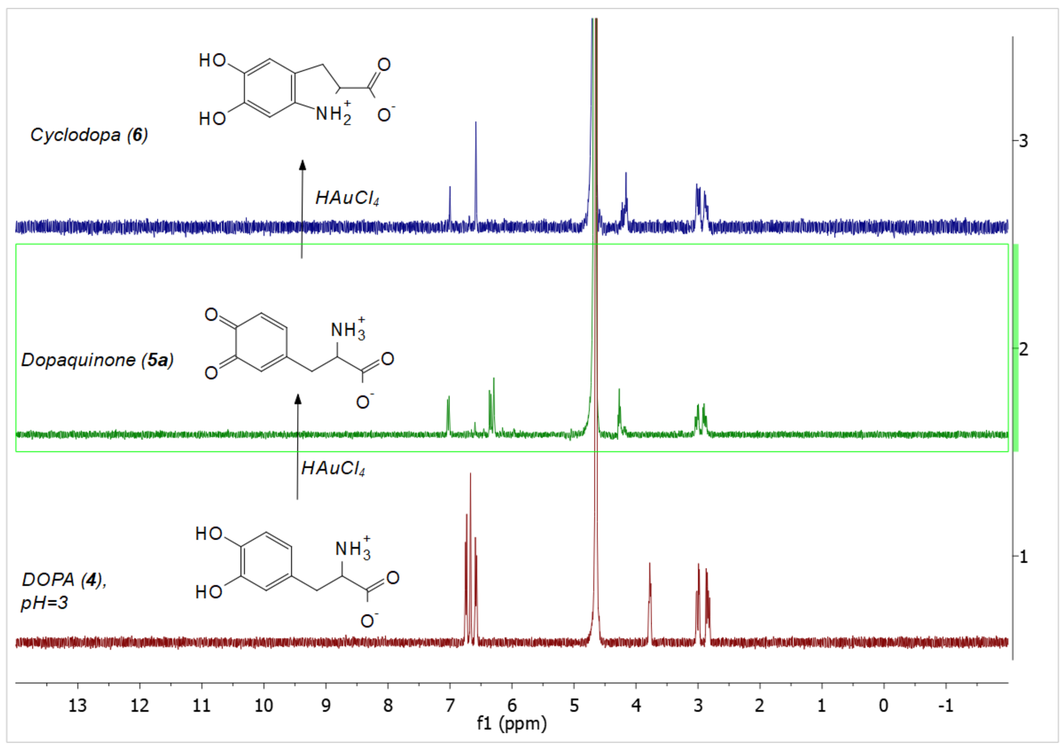


Figure 2. ^1H NMR spectra of DOPA (10 mM) and DOPA oxidation intermediates in D_2O (pH ≈ 3; $HAuCl_4$: dopamine = 4 : 1) recorded during preparation of spherical AuNPs.

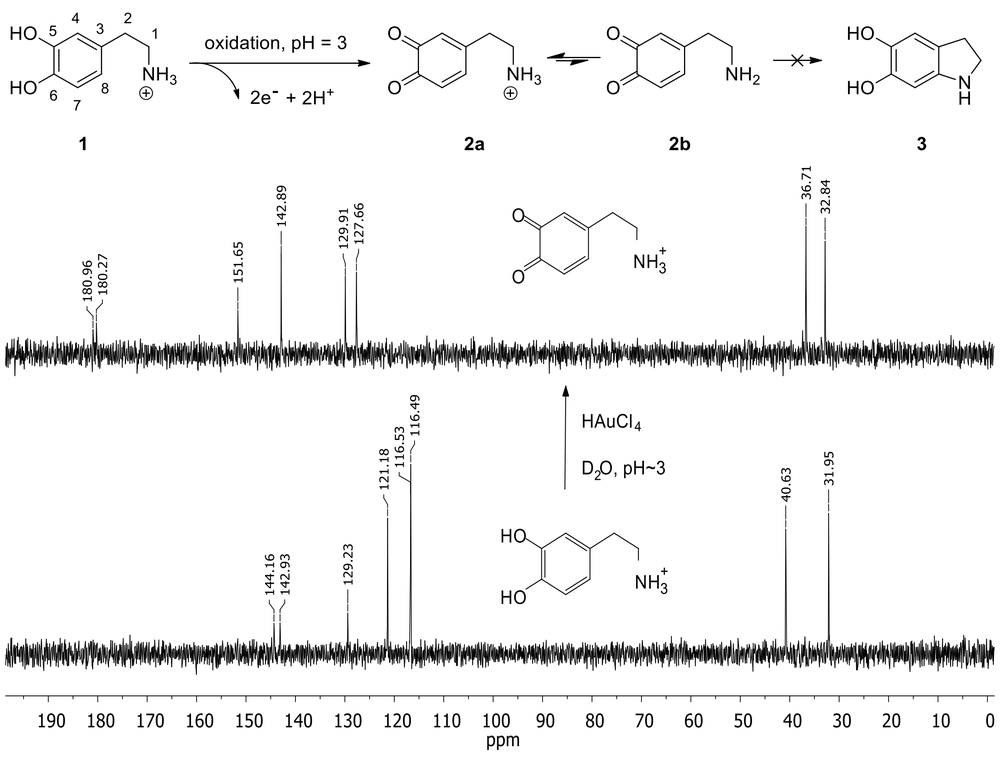


Figure 3. . ^{13}C NMR spectra of dopamine (10 mM) and dopamine oxidation intermediate (dopaminequinone) in D_2O (pH ≈ 3; $HAuCl_4$: dopamine = 4 : 1) recorded during preparation of spherical AuNPs.

Conclusion

Both dopamine and DOPA are oxidized in the course of Au cluster preparation, resulting in dopaminequineone and dopaquinone, resp. The latter undergoes intramolecular cyclization forming cyclodopa. All these intermediates are included in interactions with the AuNP surface.

References

1. Ramanathan, S. *et al., Int. J. Nanomedicine* **2018**, *13*, 5561–5576.
2. Ong et al., *ACS Appl. Mater. Interfaces* **2017**, *9*, 39259–39270.

Acknowledgement

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