Courtney Riddles, 2010-2013

Courtney Riddles came to my research in the Fall semester of 2010 and expressed interest in doing some research when she took my CHM 375 Inorganic Chemistry class. She also enrolled at first in my research courses CHM 399 and CHM 499 and worked in my research laboratory for almost three years.

Courtney received the project to prepare in larger amounts two cyanoxime ligands shown in Figure 1 and prepare their Ag(I) complexes. These were intended for further antimicrobial studies including making polymeric composites with embedded in them AgL and investigate their effect on biofilm formation.

Along the way new interesting findings emerged. Thus crystal structures of both metal-free cyanoximes revealed the formation of diastereomeric mixture for H(PiPCO), and different polymorph for the H(MCO) ligands. Structures of both are presented in Figure 2.

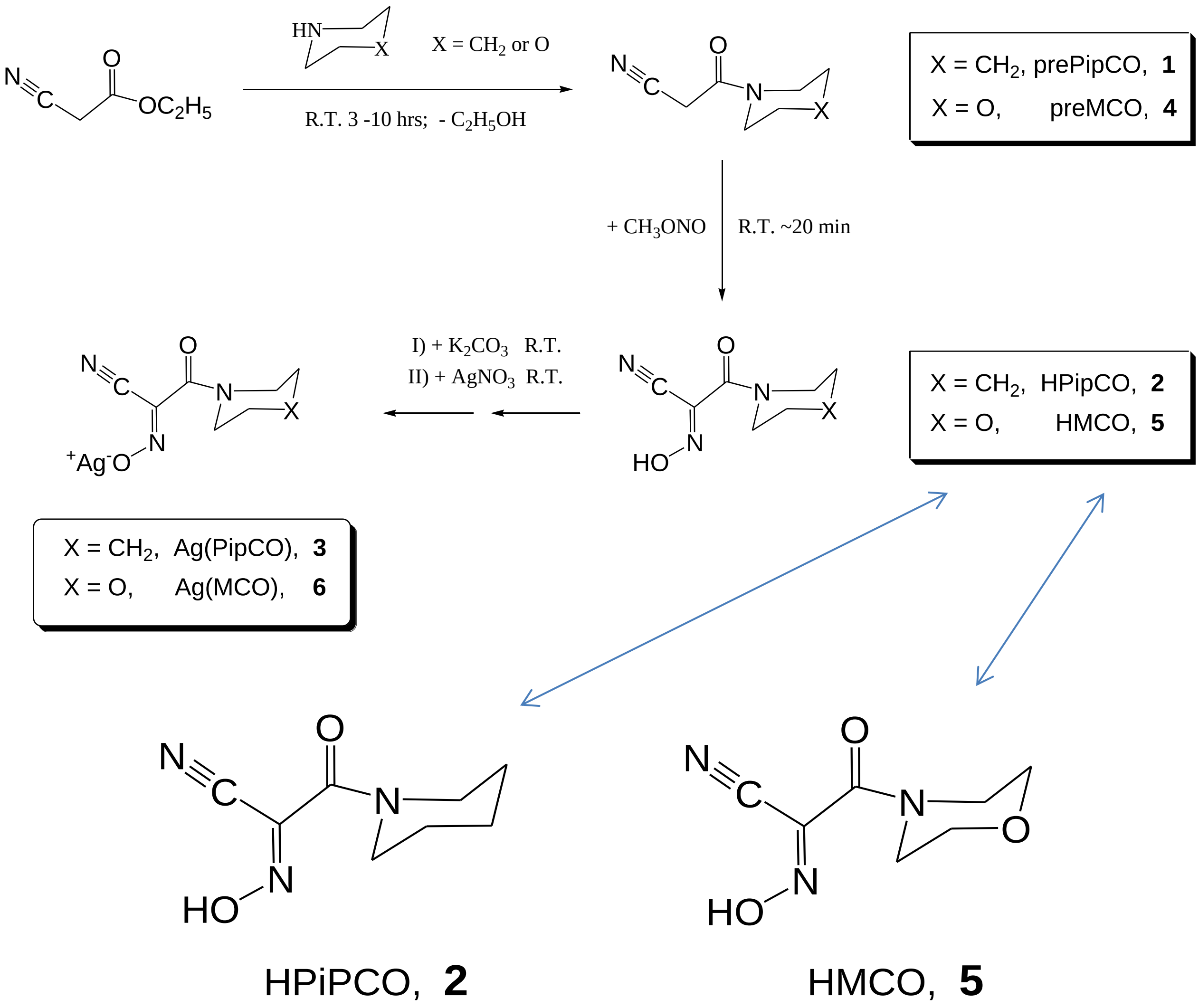


Figure 1. **Room temperature $^{13}C\{^1H\}$ NMR spectrum of H(DECO) in dmso-d_6 showing two non-equivalent ethyl groups of the amide fragment.**

Also, she conducted first systematic investigation of solvatochromism phenomenon for both these cyanoximes. It turned out that they, depending on the nature of the solvent, may show up in solutions as yellow or pink colors. There is a remarkably large for these *n*→π* transitions in the *nitroso*-chromophore energy gap shown in Figure 3.

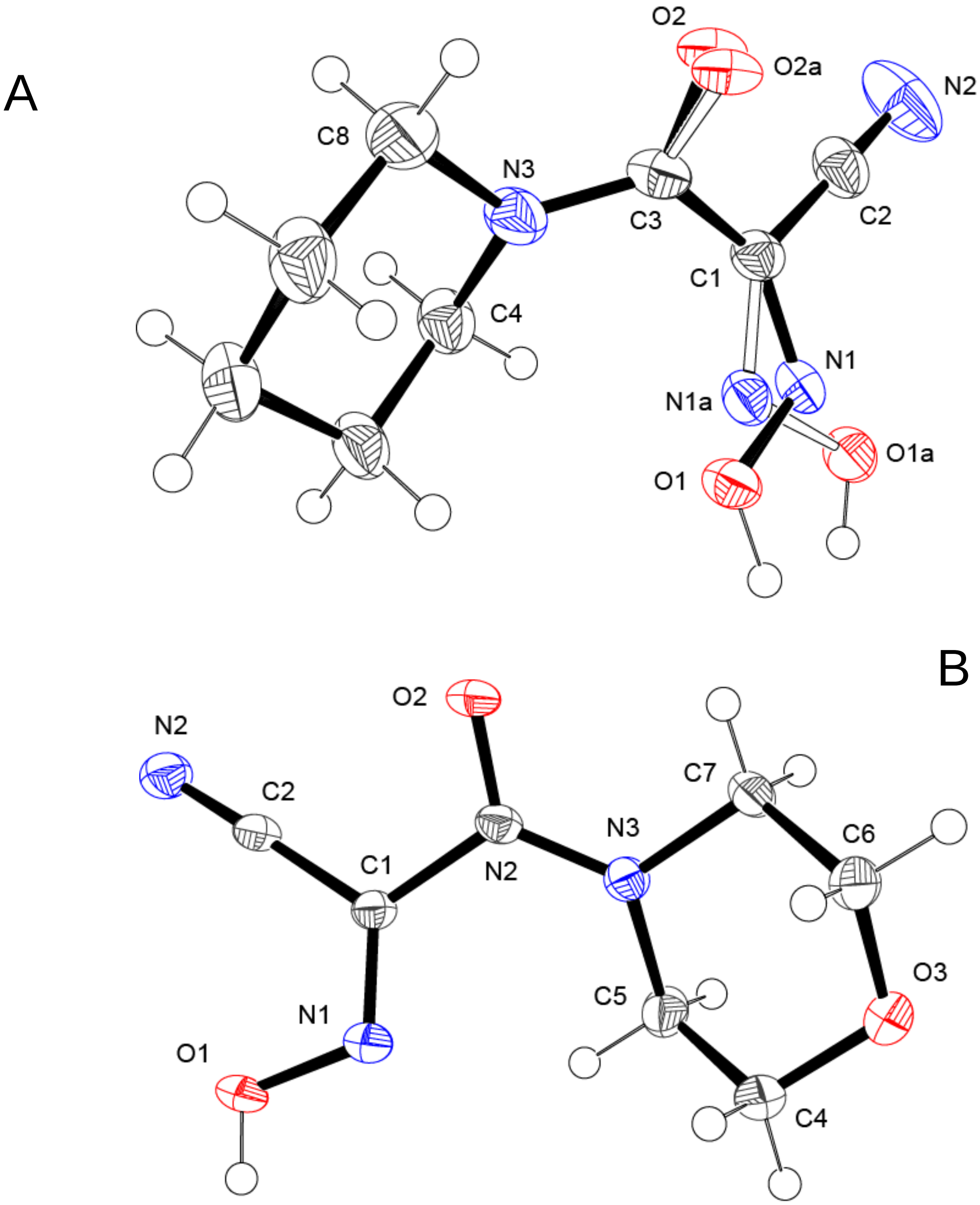


Figure 2. Molecular structures and numbering schemes for HPiPCO (A, two diastereomers - syn and anti - are shown), and HMCO (B); an ORTEP drawing at 50% thermal ellipsoids probability.

The reaction between $AgNO_3$ and deprotonated with K_2CO_3 cyanoximes in aqueous solutions leads to the formation of stoichiometric 1:1 complexes of AgL composition. Both Ag(PiPCO) and Ag(MCO) represent yellow powders somewhat sensitive to light in wet conditions (Figure

4). However, being thoroughly dry complexes are visible light stable for many months! Nevertheless, Courtney investigated stability of those two AgL to UV-radiation that is commonly used for sterilization purposes in biomedical practice and also for curing polymeric composites that are used in dental practice (400 nm curing light). These studies were conducted using the diffusion-reflectance spectroscopy (SDR) at time intervals. Results are displayed in Figures 5 and 6.

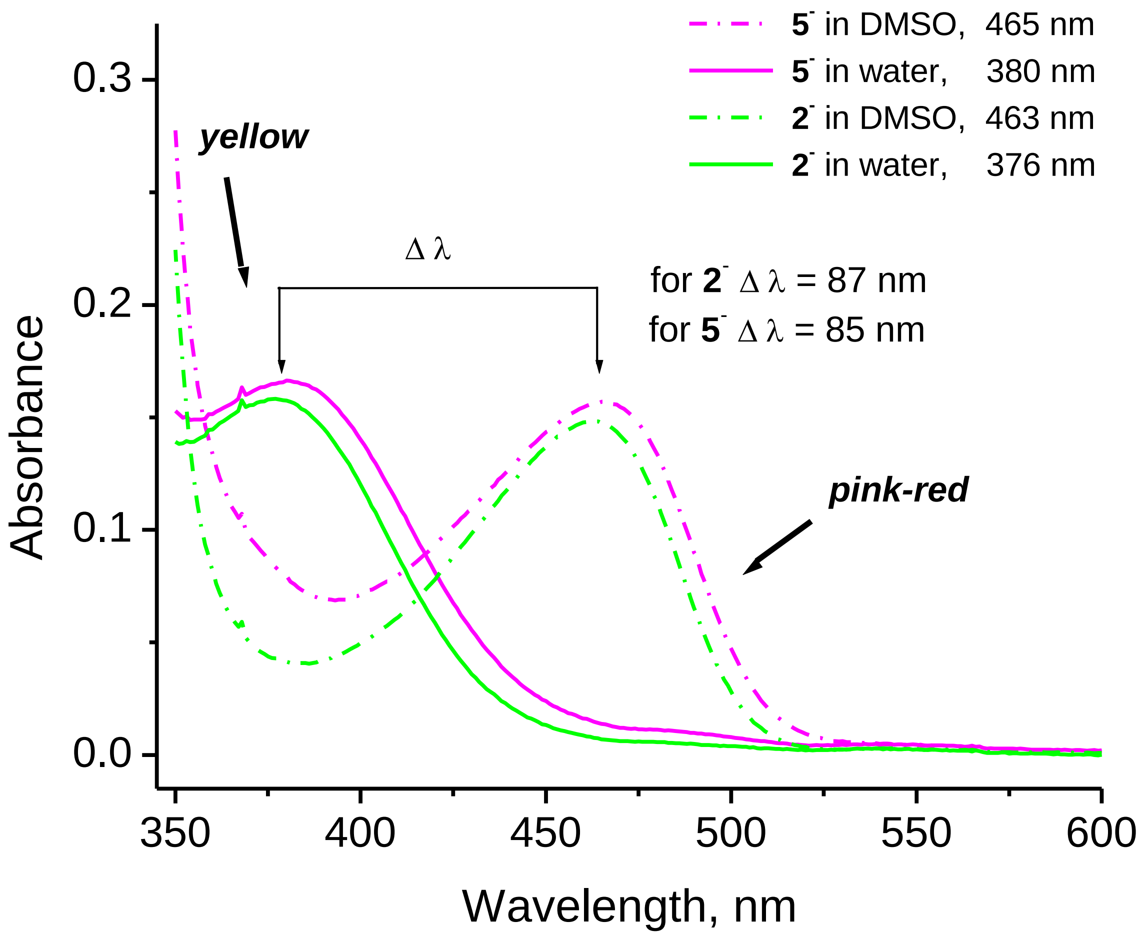


Figure 3. Visible spectra of isomolar solutions (5 mM) of cyanoxime anions of 2^- (green) and 5^- (pink) in water, and DMSO. For recording these spectra initial cyanoximes were deprotonated with one drop of $N(C_4H_9)_4OH$ solution; 1 cm cuvette, T=296 K.

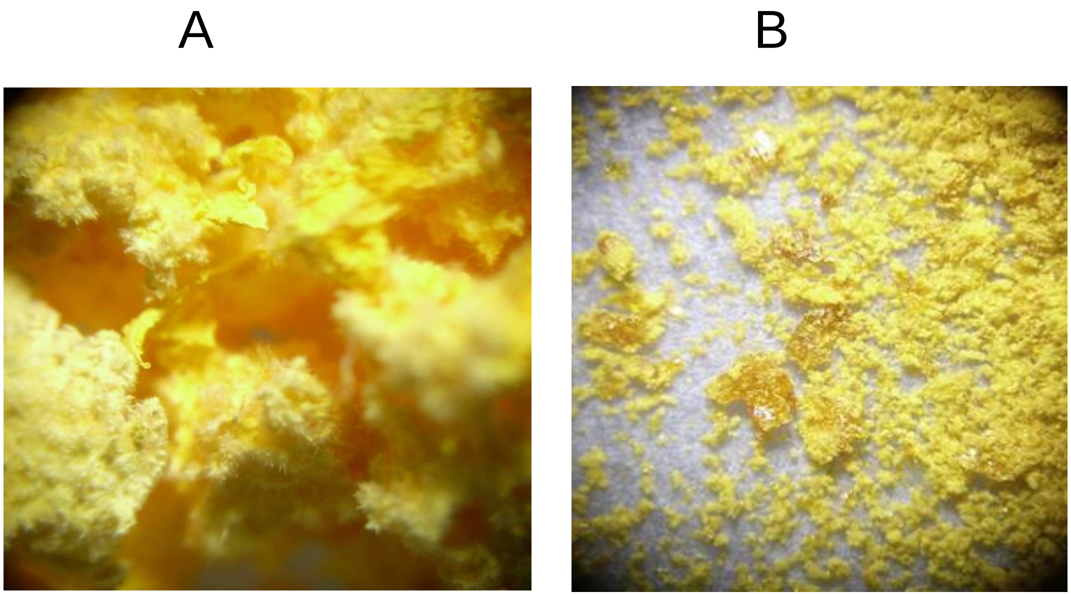


Figure 4. **Actual photographs of dry, powdery 6, Ag(MCO) (A) and 3, Ag(PiPCO) (B) under the microscope at 40x magnification.**

The light sensitivity of both AgL compounds was assessed by using the initial rate of photo-decomposition process as explained in Figure 7. Thus, Ag(PipCO) is by far more stable towards UV-light than its analog Ag(MCO).

Finally, both silver(I) cyanoximates were added to the light-curable acrylate polymeric composites, that are typically used in dental practice, and antimicrobial properties of these systems were investigated. Results clearly evidenced powerful effect as compared with control samples of polymers without addition of Ag(I) complexes (Figures 8 and 9).

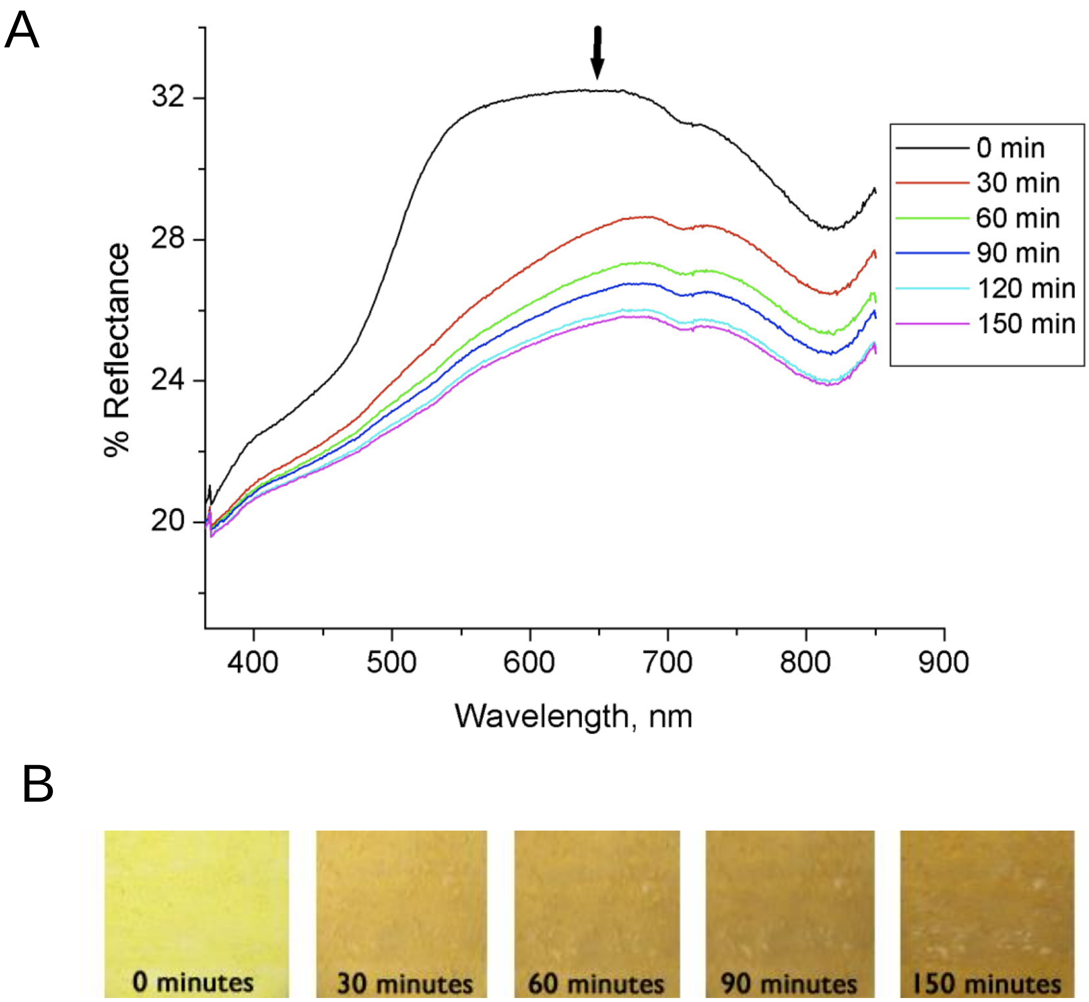


Figure 5. Diffusion reflectance spectra changes for the sample of Ag(PiPCO), 3, with time of exposure to UV-light (A); an arrow points on a significant samples reflectance decrease due to darkening. Actual photographs of samples over time (B).

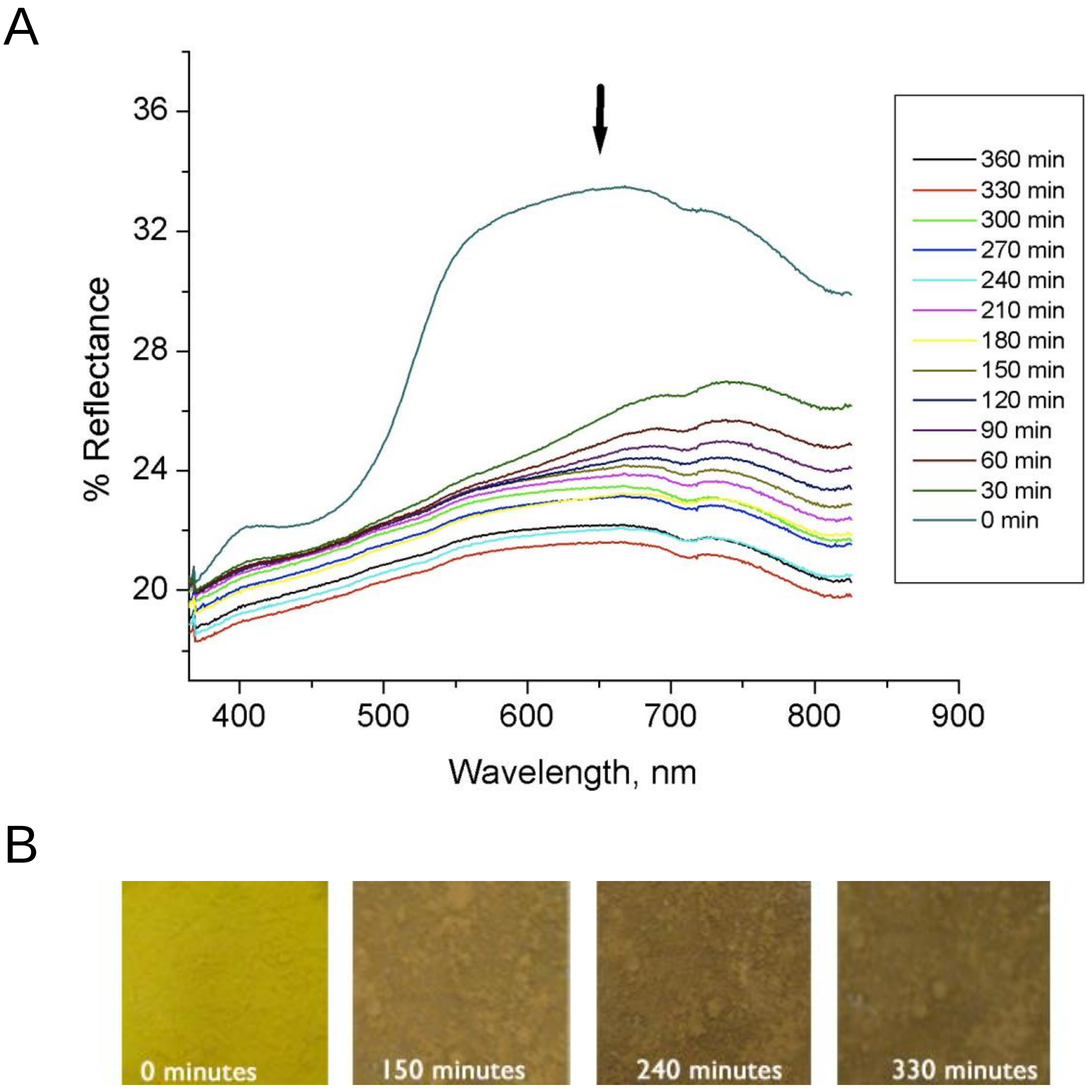


Figure 6. Spectroscopic changes of the Ag(MCO), 6, sample reflectance over time of exposure to UV-light (A); actual photographs of samples over time (B).

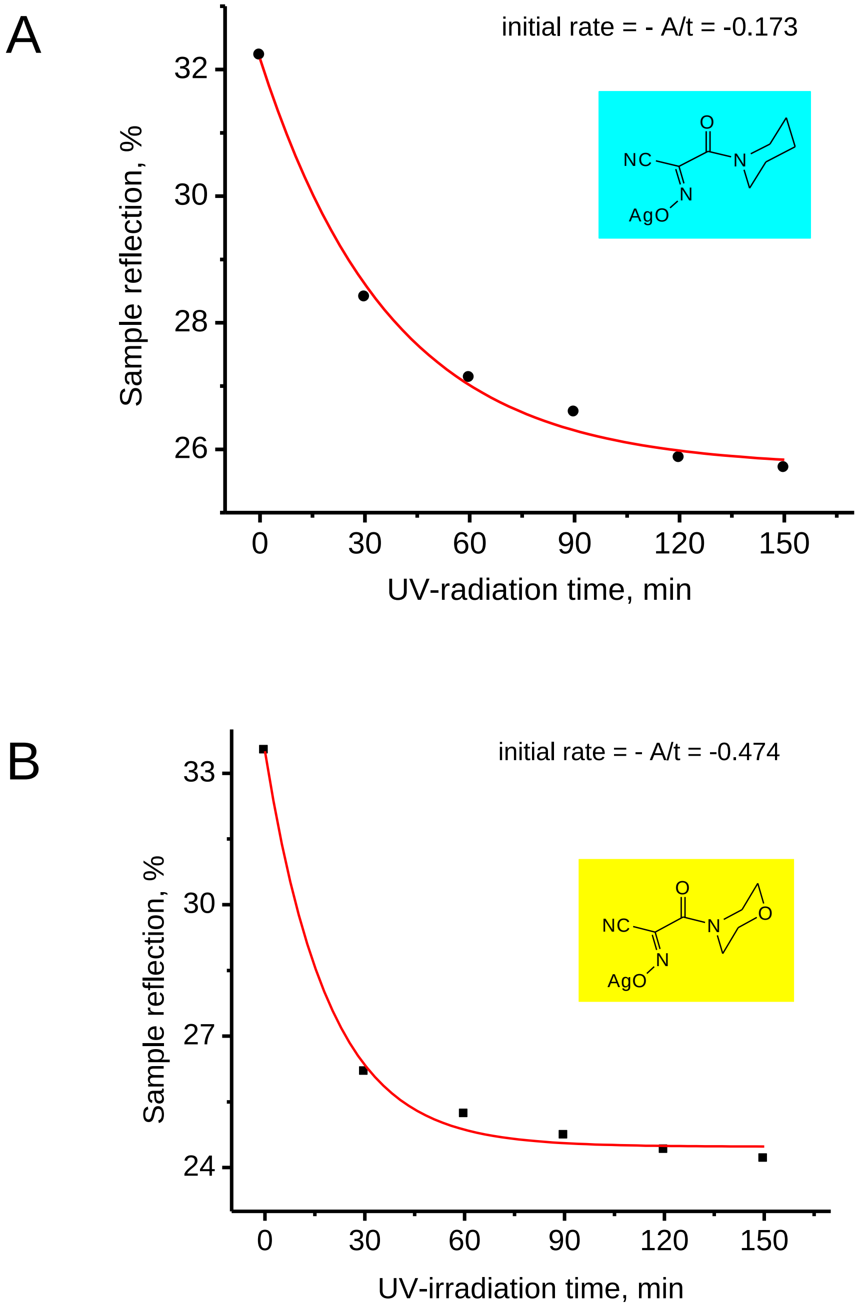


Figure 7. **Time dependence of AgL samples reflectance change upon irradiation with the UV-light source. A – Ag(PiPCO) with data fit the best to a monoexponential decay function $y = y_0 + A\,e^{(-x/t)}$ with the following parameters: $y_0 = 25.72 \pm 0.21$; $A = 6.45 \pm 0.29$; $t = 37.34 \pm 4.55$; $\chi^2 = 0.05669$ and $R^2 = 0.9943$. B – Ag(MCO), best fit to a monoexponential decay function $y = y_0 + A\,e^{(-x/t)}$ with the following parameters: $y_0 = 24.48 \pm 0.17$; $A = 9.02 \pm 0.34$; $t = 19.03 \pm 2.24$; $\chi^2 = 0.09001$ and $R^2 = 0.99577$.**

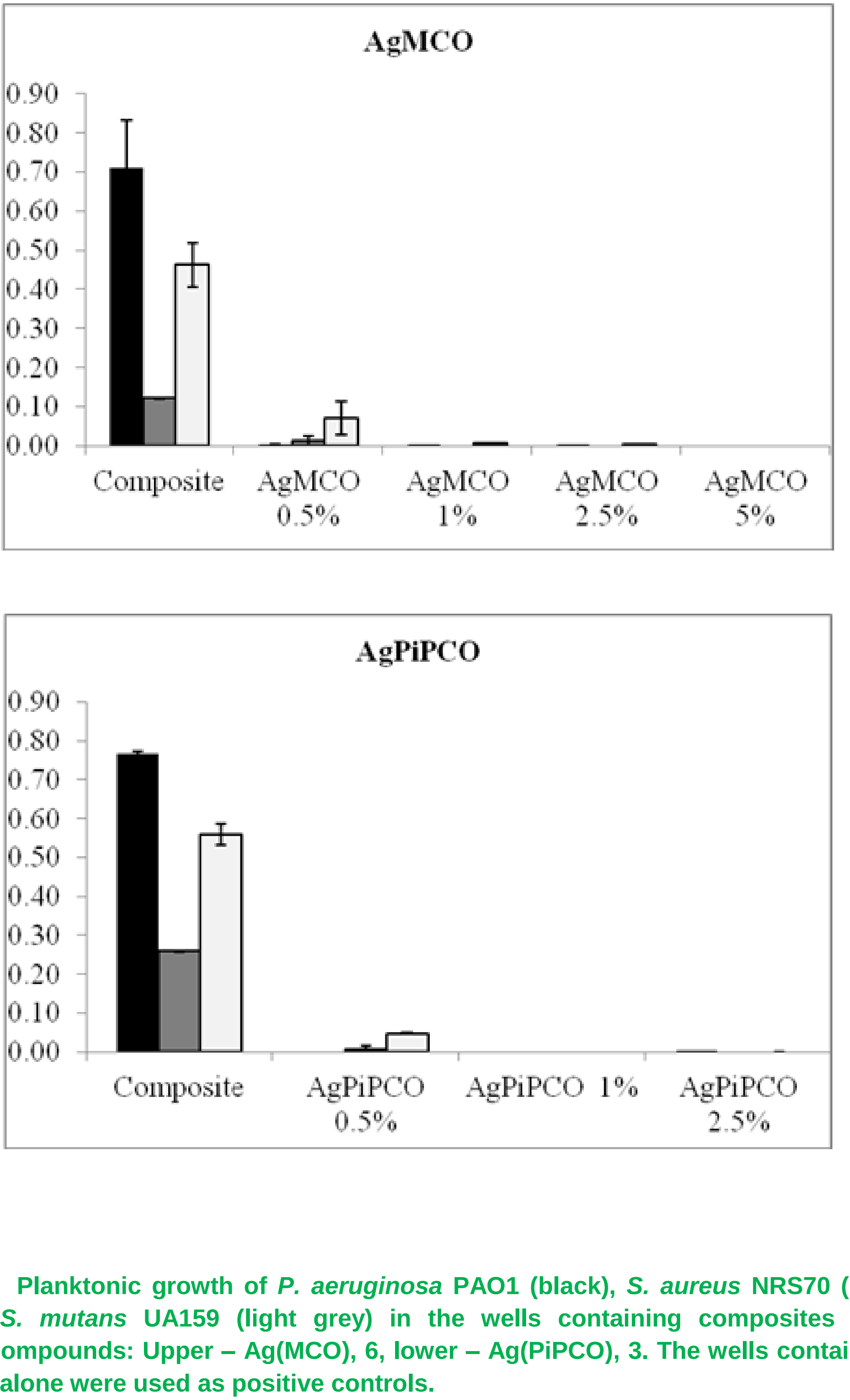
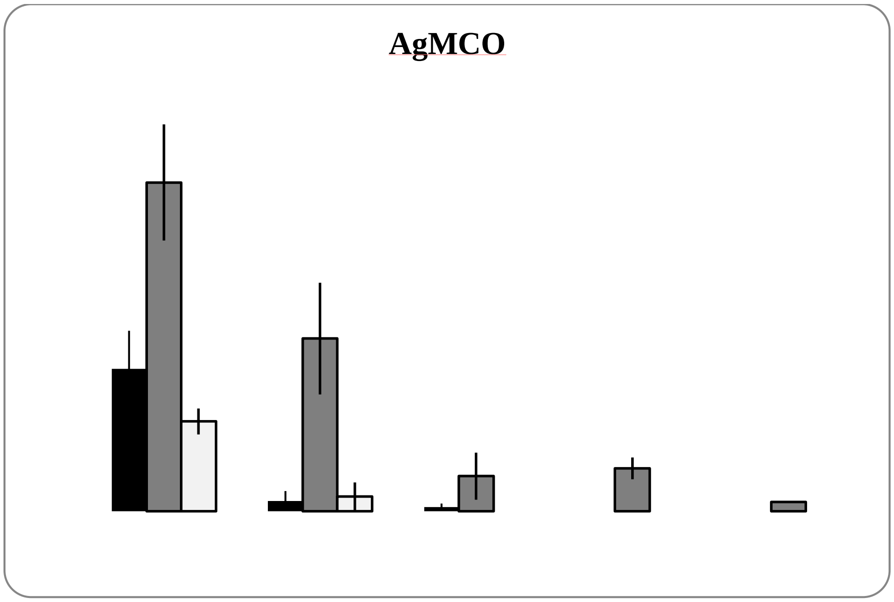


Figure 8. **Planktonic growth of *P. aeruginosa* PAO1 (black), *S. aureus* NRS70 (dark grey), and *S. mutans* UA159 (light grey) in the wells containing composites with embedded compounds: Upper – Ag(MCO), 6, lower – Ag(PiPCO), 3. The wells containing composites alone were used as positive controls.**



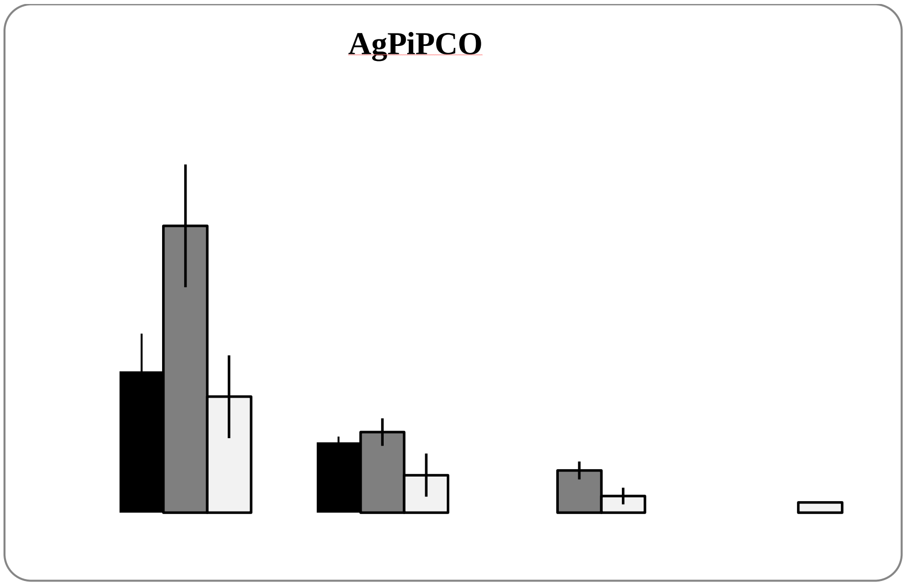


Figure 9. Biofilm growth of *P. aeruginosa* PAO1 (black), *S. aureus* NRS70 (dark grey), and *S. mutans* UA159 (light grey) in the wells containing composites with embedded compounds: Upper – Ag(MCO), 6, lower – Ag(PiPCO), 3. The wells containing composites alone were used as positive controls.

One major peer-reviewed paper was published with Courtney being the first author!

Riddles, C.N.; Whited, M.; Lotlikar, S.R.; Still, K.; Patrauchan, M; Silchenko, S.; Gerasimchuk, N. “Synthesis and characterization of two cyanoxime ligands, their precursors, and light insensitive antimicrobial silver(I) cyanoximates.” *Inorganica Chimica Acta*. **2014**, *412*, 94-103.

This paper received a very good citations and downloading statistics from the Elsevier portal.

Poster presentation of Courtney Riddles at Missouri State University undergraduate research conference in April.