JOURNAL OF CHEMICAL EDUCATION

pubs.acs.org/jchemeduc

Laboratory Experiment

Multiweek Experiments for an Inorganic Chemistry Laboratory Course: Synthesis of Nickel Complexes Supported by a Tetradentate Ligand with a N_2O_2 Donor Set

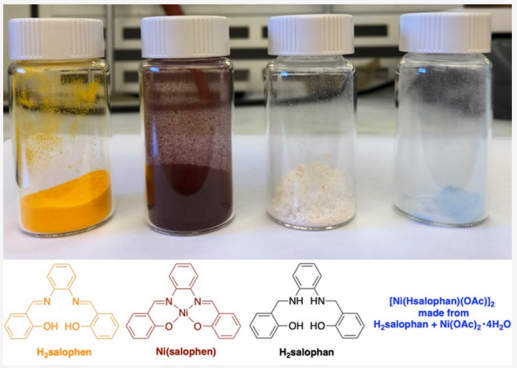
Joel D. Collett, Jeanette A. Krause, and Hairong Guan*

Cite This: *J. Chem. Educ.* 2021, 98, 592–599

Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

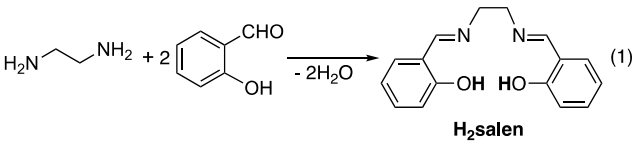
ABSTRACT: Inorganic Chemistry teaches students the concept that modifications to ligand structures, especially the donor properties, can have a drastic impact on the reactivity and stability of the metal complexes. Experiments described here reinforce this concept through the investigation of two tetradentate ligands derived from *o*-phenylenediamine and salicylaldehyde. The Schiff base ligand, H_2salophen, reacts with $Ni(OAc)_2{\cdot}4H_2O$ to yield a maroon, square planar complex, Ni(salophen). Under the same conditions, the amine-type ligand, H_2salophan, forms a light-blue compound analyzed as $[Ni(Hsalophan)(OAc)]_2$. The Ni(salophan) complex free of acetate may be produced from the reaction of H_2salophan with $Ni(OAc)_2{\cdot}4H_2O$ in the presence of NaOH but undergoes ligand dehydrogenation to yield Ni(salophen). Students conducting these experiments have the opportunity to learn synthetic techniques and various characterization methods. Most importantly, the inquiry-guided experimental design helps them develop critical thinking skills and apply acquired knowledge to solving a research problem in a laboratory course.



KEYWORDS: *Upper-Division Undergraduate, Inorganic Chemistry, Laboratory Instruction, Inquiry-Based/Discovery Learning, IR Spectroscopy, Mass Spectrometry, Molecular Properties/Structure, NMR Spectroscopy, Transition Elements, X-ray Crystallography*

INTRODUCTION

Tetradentate Schiff base ligands bearing a N_2O_2 donor set are popular building blocks for constructing metal complexes used as enzyme mimics,[1] therapeutics,[2] catalysts,[3] and novel materials.[4] *N*,*N*′-bis(salicylidene)ethylenediamine (H_2salen), arguably the best-known ligand in this class, can be readily prepared from the condensation reaction between ethylenediamine and 2 equiv of salicylaldehyde (eq 1). This synthetic strategy is applicable to a wide variety of diamines and salicylaldehyde derivatives, providing an excellent opportunity to tune the steric and electronic properties of the ligands. It is thus not surprising that the coordination chemistry of these Schiff base ligands has been continuously and extensively explored with virtually every transition metal in the periodic table.[1−4]

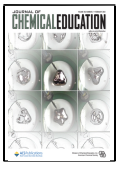


H_2salen

The imine functionalities of the Schiff base ligands are reducible to amine groups, often accomplished by using a mild reducing agent such as $NaBH_4$. The products may still serve as N_2O_2 tetradentate ligands; however, the donor properties are significantly altered. In particular, the nitrogen sites change from good π-acceptors (for imines) to pure σ-donors (for aliphatic amines). Saturation of the C═N bonds also renders the ligand backbone more flexible, which can have a profound impact on the geometry and the stability of the metal complexes. In contrast to the numerous reports on M(salen)-type complexes, transition metal complexes supported by the saturated N_2O_2 tetradentate ligands have been less frequently studied.[5]

Most undergraduate inorganic textbooks teach students how the spin state of a metal ion is influenced by ligand field and coordination geometry. Four-coordinate Ni(II) complexes, for instance, are diamagnetic ($S = 0$) with a square planar geometry when the ligands are sufficiently π-accepting, and the classical example is $[Ni(CN)_4]^{2-}$. With a weak-field ligand like chloride, $[NiCl_4]^{2-}$ is paramagnetic ($S = 1$) and adopts a tetrahedral geometry. A higher coordination number of 5 or 6 is also possible with Ni(II), largely dependent on the availability and

Received: August 25, 2020
Revised: December 9, 2020
Published: December 30, 2020



https://dx.doi.org/10.1021/acs.jchemed.0c01117
J. Chem. Educ. 2021, 98, 592−599

the properties of the supporting ligands. Five-coordinate Ni(II) complexes can be diamagnetic or paramagnetic, whereas six-coordinate Ni(II) complexes in an octahedral environment are always paramagnetic.[6] Some of these important coordination chemistry concepts can be reinforced in an inorganic laboratory course using the N_2O_2 tetradentate ligands described above. The reactivities of M(salen)-type complexes have been previously developed as laboratory course materials, although the emphasis was placed on teaching how small molecules mimic enzymes.[7] The experiments discussed herein, which were successfully implemented and refined at the University of Cincinnati in 2018−2020 (for CHEM4020L—Inorganic Chemistry Laboratory),[8] focus more on synthesis and characterization, specifically in the context of studying nickel complexes.

To discourage the practice of finding answers by simply using web search engines, *N*,*N*′-bis(salicylidene)-1,2-phenylenediamine (H_2salophen, Figure 1) is chosen over the more

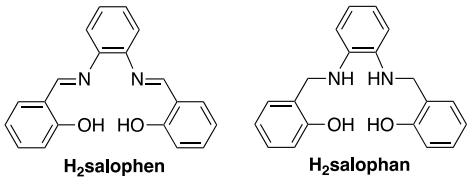


Figure 1. Structures of H_2salophen and H_2salophan.

searchable H_2salen as the starting ligand.[9] The reagents needed for the experiments are relatively inexpensive, and the time required for making each ligand or nickel complex is conveniently short (30−60 min), which, in a typical 3 h laboratory session, leaves students ample time to learn various characterization techniques. The later step of the synthesis involves a reaction of the saturated N_2O_2 tetradentate ligand (H_2salophan, Figure 1) with $Ni(OAc)_2{\cdot}4H_2O$, which leads to an open-ended project due to the ambiguity of the structure for the isolated product. Students are guided to design additional experiments and propose analytical tools to decipher what the nickel complex might look like.

LEARNING OBJECTIVES

The synthetic part of the experiments strengthens the basic techniques such as weighing, mixing, refluxing, vacuum filtration, and recrystallization that students may have already learned from general and organic chemistry laboratory courses. The analytical part of the experiments focuses on training in IR and NMR spectroscopy, complemented by mass spectrometry (MS), elemental analysis (EA), and X-ray crystallography that students are less familiar with. Additional pedagogical objectives, specifically for an upper-division laboratory course, include the following:

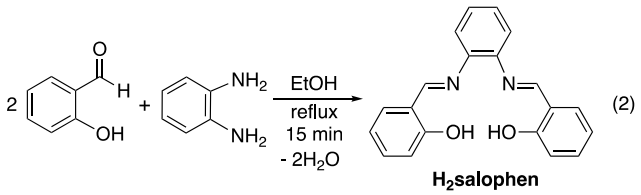
(1) enhance the understanding of ligand field theory with real-life examples;
(2) develop critical thinking skills through designing experiments;
(3) learn how to search the chemical literature and know that the literature could be wrong.

DESCRIPTION OF THE EXPERIMENTS

The experiments are divided into activities for 3 h laboratory sessions spanning 5 weeks. For the course offered at the University of Cincinnati, 12−24 students were enrolled each year, mostly chemistry or biochemistry majors with a few prepharmacy students. For a larger class or if limited by instrumentation, instructors may consider pairing students. The reagents and glassware needed for the syntheses are readily available in most chemistry laboratories or from multiple vendors at affordable prices. Each compound synthesized by our students was analyzed by IR and ^{1}H NMR spectroscopy; however, in the interest of time and cost, only one representative sample from the class was selected for $^{13}C\{^1H\}$ NMR, mass spectrometric, elemental, or X-ray crystallographic analysis. Students were provided with the experiment guide and safety data sheets (SDSs) for the chemicals to be used, typically 5 days before the scheduled laboratory session. Prior to the laboratory work, they were required to complete a prelab quiz, which was intended to test their preparation for the experiments and understanding of potential safety hazards. As assessments, a postlab assignment mainly on processing NMR data was given following the Week 2 experiments, and instructions for a combined lab report were provided following the Week 3 experiments.

Week 1: Synthesis of the H_2salophen Ligand

First, a short prelab lecture should be delivered to emphasize the importance of observing safety guidelines, appropriate ways of disposing chemical waste and used gloves, and the expectation for the multiweek experiments. Students can then proceed with the synthesis of the Schiff base ligand from salicylaldehyde and *o*-phenylenediamine (eq 2). The condensation reaction has been reported to take place in ethanol under refluxing conditions for 2−12 h[10] or at room temperature for 12 h.[11] In our students' hands, the room-temperature reaction was complete in 30 min. It is, however, recommended to perform the synthesis in refluxing ethanol for 15 min, because at room temperature both *o*-phenylenediamine and H_2salophen are poorly dissolved.[12] The orange precipitate can be collected by vacuum filtration, washed with ethanol, and dried in air. It is important to remind students that a wet product will negatively impact the subsequent steps because the amount of H_2salophen used will be overestimated. The identity and purity of the isolated product can be confirmed by ^{1}H and $^{13}C\{^1H\}$ NMR spectroscopy. For students who have not prepared an NMR sample before, a short NMR lecture is needed in class, especially on the sensitivity of the technique and the reason for using a deuterated solvent.

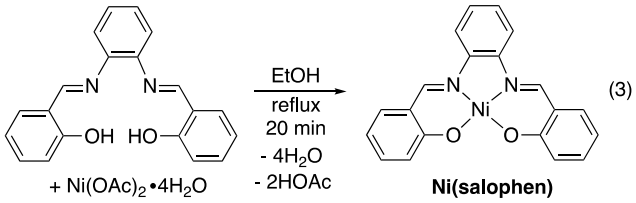


Week 2: Synthesis of the Ni(salophen) Complex

If students have not previously learned how to process raw NMR data, instructors should consider starting the second week with a tutorial on how to use MestReNova/Mnova or a vendor-specific NMR software like Topspin. The experimental part of the class involves refluxing a 1:1 mixture of H_2salophen and $Ni(OAc)_2{\cdot}4H_2O$ in ethanol (eq 3), which results in an immediate color change from orange to dark red. Reported synthetic methods for Ni(salophen) mention a reaction time of 1−2 h.[13] However, our students found that the reaction was complete in 20 min. The nickel complex can be isolated as a maroon powder following a workup procedure similar to that used for H_2salophen. As with

https://dx.doi.org/10.1021/acs.jchemed.0c01117
J. Chem. Educ. 2021, 98, 592−599

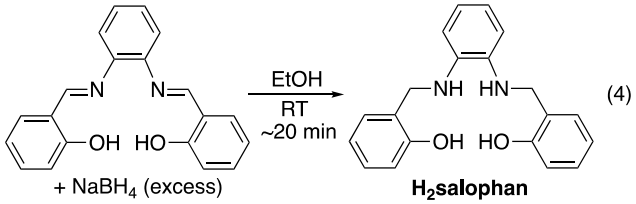
the ligand, Ni(salophen) can be analyzed by ^{1}H and $^{13}C\{^{1}H\}$ NMR spectroscopy for its identity and purity. In our experience, students understandably took longer to complete the task in Week 1. For that reason, characterization of H_2salophen by IR spectroscopy was postponed to Week 2, when the IR spectrum of the newly prepared Ni(salophen) was also recorded. This plan has an additional advantage, because students are able to immediately note the spectral change after complexation. The success of nickel coordination can be further confirmed by analyzing the NMR data of both H_2salophen and Ni(salophen), which is recommended as a postlab assignment for practicing using the NMR software.



(3)

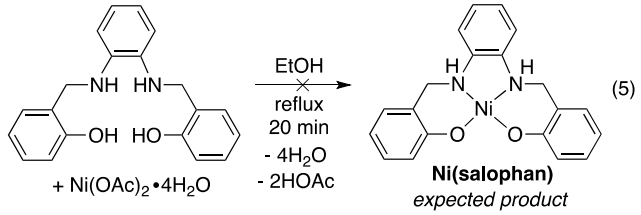
Week 3: Synthesis of the H_2salophan Ligand and the Corresponding Nickel Complex

By the third week,[14] students should be proficient with the synthetic techniques, making it feasible to complete the synthesis and characterization of a new ligand and a new nickel complex in one laboratory session. The reduction of H_2salophen to H_2salophan can be accomplished by using excess $NaBH_4$ followed by a hydrolytic workup. Most literature procedures employ methanol as the solvent for this reaction,[15] likely due to the higher solubility of $NaBH_4$ in methanol (13 g/100 mL) than in ethanol (3.16 g/100 mL).[16] However, Atwood and co-workers reported that the reduction in ethanol also occurred at a reasonably fast rate.[17] Given the lower toxicity and flammability, ethanol was chosen as the reaction medium (eq 4). The progress of the reduction can be visualized, as the product is colorless in ethanol. Typically, it takes ca. 20 min for the orange color of H_2salophen to fade completely. The desired H_2salophan ligand precipitates from the reaction mixture upon treatment with water. The solid can be collected by vacuum filtration, rinsed with distilled water and hexanes, and then air-dried at room temperature. Our characterization methods once again relied primarily on ^{1}H NMR, $^{13}C\{^{1}H\}$ NMR, and IR spectroscopy.



(4)

For comparison, complexation of $Ni(OAc)_2{\cdot}4H_2O$ with H_2salophan should be performed following the procedure identical to the one used with H_2salophen. Students are likely self-convinced that the reaction gives Ni(salophan), analogous to the formation of Ni(salophen) (eq 5). They will, however, notice something different from the Week 2 experiment: the reaction mixture turns into a green solution first but quickly forms a precipitate, which, after the typical workup steps (i.e., filtration, washing, and drying), yields a light-blue solid. Unlike Ni(salophen), the presumed "Ni(salophan)" does not dissolve in $CDCl_3$ or C_6D_6. It is only sparingly soluble in acetone and acetonitrile. While it is challenging to obtain the NMR spectra due to limited solubility in common deuterated solvents, the isolated compound can be characterized by IR spectroscopy.



(5)

Despite the lack of NMR data, the light-blue color and the paramagnetism (μ_{eff} = 3.09 μ_B, see the Supporting Information) suggested to us that the isolated nickel complex was not Ni(salophan) with a square planar geometry as shown in eq 5. Students were asked to prepare samples of this unknown compound in acetone, acetonitrile, and dimethylformamide (DMF) (all exposed to air) with the intention of growing single crystals for crystallographic analysis. In the meantime, one sample from the class was submitted for mass spectral and elemental analyses, which were expected to provide additional structural information.

After 3 weeks of experiments, students already have sufficient data to write a complete story in a lab report, which ideally should follow the format of a scientific paper (see the Supporting Information for instructions). Students should be strongly encouraged to use a chemical database such as SciFinder to search for relevant references. If a web search engine is used, they should be advised to read the primary literature.

Weeks 4 and 5: Further Investigation of the Nickel Complex Derived from H_2salophan

In actuality, when we implemented the experiments, 2 weeks elapsed after Week 3. Depending on the availability of instrumentation or the promptness of analytical services, this brief hiatus in the project may or may not be needed. We used the gap time to ask students to prepare the related Co(salophen) and Cu(salophen) complexes,[13a] but for the scope of this paper, these experiments will not be discussed. Alternatively, instructors may consider additional physical methods to characterize the compounds made in Weeks 1−3 (e.g., UV−vis spectroscopy, melting point, magnetic susceptibility, and cyclic voltammetry) while waiting for the EA and MS data or single crystals to grow.

It is important to engage students in the discussion of potential structures for the light-blue compound that they made in Week 3. Figure 2 shows several structures proposed by the students after hinting that ligands originating from $Ni(OAc)_2{\cdot}4H_2O$ may remain bound. Some students may find literature precedents supporting structures **A**[18] and **B**.[19] The latter is even more convincing because the reported color and UV−vis data match with our results. However, the EA data argue against the formulas Ni(salophan) (**A**), $Ni(salophan)(H_2O)_2$ (**B**), and $Ni(H_2salophan)(OAc)_2$ (**C**) and instead support the formula Ni(Hsalophan)(OAc) (**D**).[20] The presence of acetate can be further confirmed by the MS and IR data.

For the samples dissolved in acetone and acetonitrile, students will notice a color change from almost colorless (due to low concentrations) to orange or red in a week. This process appears to be promoted by O_2, which can be tested if gloveboxes or Schlenk lines are available to the class. The sample prepared in DMF quickly turns to green and then to dark red in less than 24 h. Students are most likely to obtain single crystals from slow evaporation of the DMF solution; the key is to use as little DMF

https://dx.doi.org/10.1021/acs.jchemed.0c01117
J. Chem. Educ. 2021, 98, 592−599

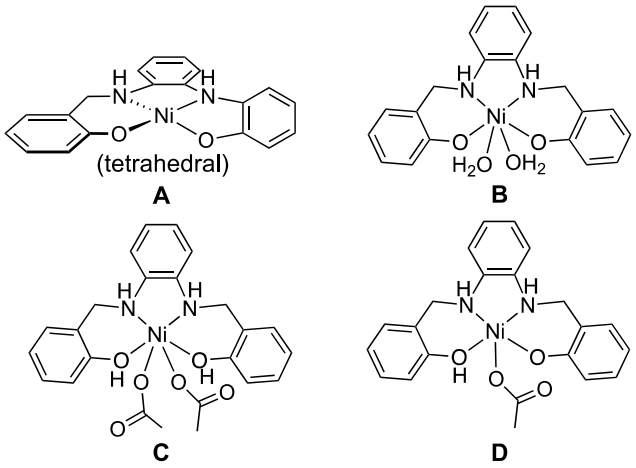


Figure 2. Potential structures for the light-blue complex synthesized from $Ni(OAc)_2{\cdot}4H_2O$ and H_2salophan (ligand coordination mode may vary).

as possible to dissolve the unknown compound. In the event that students fail to produce crystals suited for X-ray study, instructors may consider asking students to prepare a saturated solution of Ni(salophen) in hot ethanol, which yields single crystals readily upon cooling and evaporation. This back-up plan using pure Ni(salophen) to grow crystals does not shed light on the structure of the unknown compound but still gives students the opportunity to learn X-ray crystallography using their own samples.

In Week 4, students are divided into two groups: one solving the crystal structure and the other attempting another synthesis of Ni(salophan). They switch the activities in the following week. Such division may or may not be needed, depending on logistics and class size. If an X-ray diffractometer is unavailable for instructional use, the entire class can focus on the synthesis only.

In the X-ray lab, students learn various morphologies of solid samples and, under a microscope, identify crystals suitable for X-ray diffraction. Other training activities include mounting a crystal and transferring it to the goniostat of the diffractometer for data collection. Given the time constraint, a preacquired data set shall be provided to the students so that they can learn how to use the SHELX suite of programs to solve a structure (OLEX-2 may also be used for structure refinement). Crystal lattices and unit cells are often covered in the lecture-based Inorganic Chemistry course; they can be refreshed in the laboratory.

In the synthetic lab, students repeat the reaction in eq 5 except that NaOH (0.1 M in water) is also added to assist the elimination of HOAc. Students can be instructed to do so, although it is more beneficial to guide them to this path by asking them what modification to the procedures should be made in order to obtain Ni(salophan). Knowing that the unknown compound has the formula Ni(Hsalophan)(OAc), students may propose to use a base such as NaOH, Na_2CO_3, or Et_3N to remove HOAc while driving the reaction to form Ni(salophan). The inquiry-guided experimental design also leads to discussion about the amount of base used (1 or 2 equiv) and the starting materials employed (the light-blue unknown compound or H_2salophan/$Ni(OAc)_2{\cdot}4H_2O$). These variations to the procedures can of course all be tested, preferably by students working in pairs or groups. For simplicity, we had the entire class perform the synthesis using a 1:1:2 mixture of H_2salophan, $Ni(OAc)_2{\cdot}4H_2O$, and NaOH. The isolated product is no longer a light-blue solid but a rust-colored powder, which can be analyzed by both ^{1}H NMR and IR spectroscopy.

HAZARDS

Students must wear safety glasses, lab coats, and nitrile gloves while working in the laboratory. As prelab preparation, they are also required to read SDS information for the chemicals to be used. Handling some of these chemicals requires extra precaution. In particular, *o*-phenylenediamine is very toxic to aquatic life and harmful when in contact with skin or if inhaled. $CDCl_3$ is toxic if inhaled and suspected of causing cancer. $Ni(OAc)_2{\cdot}4H_2O$ is a known carcinogen and may cause an allergic skin reaction. All nickel complexes made by the students should also be treated as such, considering that the safety information regarding complexes is very limited in the literature. $NaBH_4$ should be kept in a dry place, ideally under an inert atmosphere. Special care should be taken to ensure that it does not make contact with water during storage, which may release flammable gases. Salicylaldehyde and organic solvents used in the study including EtOH, Et_2O, and hexanes are flammable and easily ignited by heat, sparks, or flames. A stock solution of NaOH is used for the final synthesis; though the concentration is relatively low (0.1 M), students should be reminded that it can be corrosive and cause skin irritation and eye damage. All X-ray equipment present hazards. Trained personnel should be present in the X-ray laboratory to ensure that students behave safely and to conduct the manipulations on the diffractometer.[21]

RESULTS AND DISCUSSION

The ^{1}H NMR spectra of H_2salophen, Ni(salophen), and H_2salophan are most informative for judging success of the

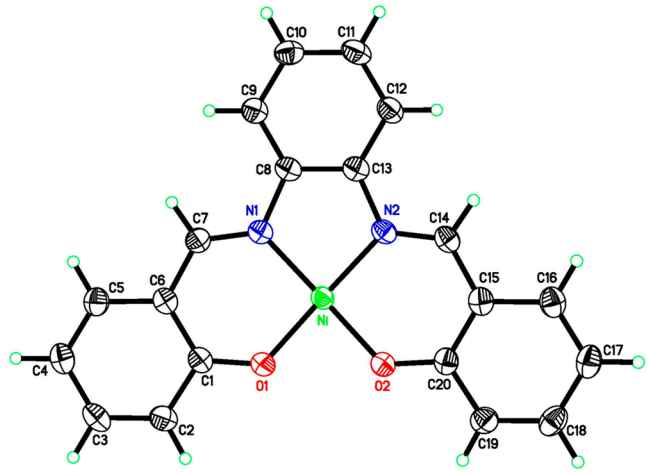


Figure 3. ORTEP drawing of Ni(salophen) at the 50% probability level.

syntheses and purity of the products. In $CDCl_3$, H_2salophen shows several aromatic resonances in the 6.90−7.40 ppm range, an imine C*H*=N resonance at 8.63 ppm, and an O*H* resonance at 13.05 ppm. The latter is shifted downfield from the O*H* resonance of a typical phenol-type compound (4−7 ppm), which can be rationalized by the presence of intramolecular hydrogen bonds (O—H···N).[11] Nevertheless, the molecule is symmetric, displaying 10 different carbon resonances as expected for the structure shown in eq 2. Students should be given reference NMR spectra of *o*-phenylenediamine and salicylaldehyde as well as the data for common NMR

https://dx.doi.org/10.1021/acs.jchemed.0c01117
J. Chem. Educ. 2021, 98, 592−599

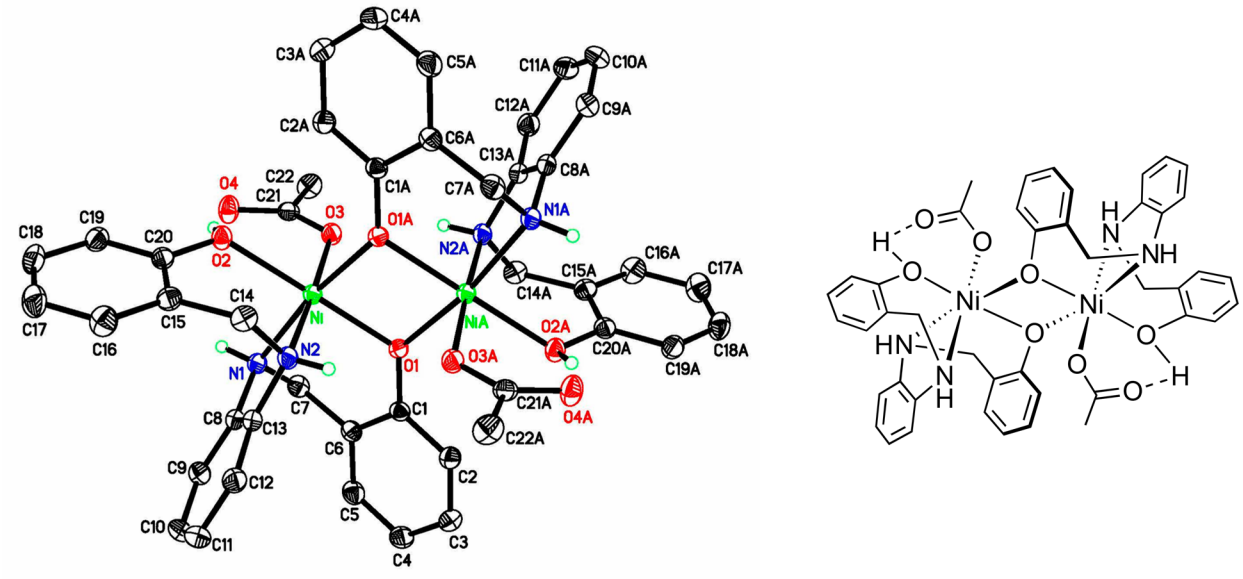


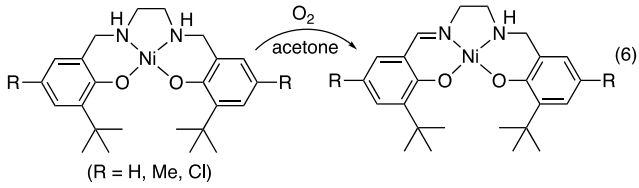
Figure 4. ORTEP drawing of [Ni(Hsalophan)(OAc)]$_2$ at the 50% probability level and the corresponding ChemDraw structure.

impurities,[22] which will help them identify the cause for an impure product. Complexation of Ni(OAc)$_2$·4H$_2$O with H$_2$salophen is evident from the ^{1}H NMR spectrum of the isolated product, where the O*H* resonance is absent, and the imine C*H*═N resonance is shifted to 8.26 ppm (in $CDCl_3$). The imine carbon resonance is also shifted upfield from 163.8 ppm in H$_2$salophen to 154.4 ppm in Ni(salophen). The remaining proton and carbon resonances are similar to those for the ligand but sufficiently different to conclude that a nickel complex is made. Reduction of H$_2$salophen to H$_2$salophan is confirmed by the disappearance of the imine C*H*═N resonance and the observation of a singlet at 4.41 ppm attributed to the C*H*$_2$—NH resonance. The O*H* and N*H* resonances of H$_2$salophan appear at 7.85 and 3.72 ppm, respectively. Students who fail to dry the product thoroughly may see significant broadening and/or slight shifting of these two resonances, which results from a rapid proton exchange with ethanol or water. The success of imine reduction is further supported by the observation of a carbon resonance at 47.9 ppm for the methylene group in H$_2$salophan.

Assigning all IR bands is unrealistic; however, when given a chart of IR frequency ranges for various vibration modes,[23] students are able to identify the more characteristic N—H, C—H, C═N, and C—O stretching bands. For example, the C═N band is located at 1609 cm^{-1} for H$_2$salophen and 1602 cm^{-1} for Ni(salophen). Due to hydrogen-bonding interactions, the O—H bands in H$_2$salophen and H$_2$salophan are too broad to be definitively assigned. In contrast, the N—H band of H$_2$salophan is observed at 3287 cm^{-1}.

According to the EA data, Ni(Hsalophan)(OAc) is the formula for the light-blue compound isolated from the reaction of H$_2$salophan with Ni(OAc)$_2$·4H$_2$O. The presence of acetate is also supported by IR spectroscopy, which shows medium-intensity bands at 1555 and 1424 cm^{-1} for the unsymmetrical and symmetrical C—O stretches, respectively.[24] Two weak bands are found in the region for O—H/N—H stretches (3213 and 3160 cm^{-1}), though on the lower end. Under MS conditions (electrospray ionization, in ethanol), this compound gives mass ions corresponding to Ni(Hsalophan) (MH^+), aggregates M_2H^+ and M_3H^+, and two acetate-containing species $[M(NiOAc)]^+$ and $[M_2(NiOAc)]^+$. These data are in agreement with structure **D** in Figure 2, its isomer involving κ^2 or free $[OAc]^-$ or with the $[Hsalophan]^-$ ligand adopting a different coordination mode, or its dimer or higher-order oligomers. The mass spectrum also reveals an ion for $[MH-2H]^+$, suggesting that the compound readily undergoes dehydrogenation.

In fact, the light-blue compound dissolved in acetone, acetonitrile, or DMF (without excluding O$_2$) changes color to red over time. The dark-red crystals grown from DMF solve as Ni(salophen) (Figure 3),[25,26] indicating that dehydrogenation or oxidation of the ligand backbone indeed has occurred. NMR analysis of the dark-red crystals further confirms the formation of Ni(salophen). The rust-colored powder isolated from the reaction of H$_2$salophan with Ni(OAc)$_2$·4H$_2$O and 2 equiv of NaOH is consistent with Ni(salophan), which is supported by the IR data (one O—H/N—H band at 3261 cm^{-1} and the lack of acetate). However, ∼50% of the students in our class obtained a material analyzed as a mixture of Ni(salophan) and Ni(salophen). In any case, the rust-colored powder is partially soluble in $CDCl_3$, and the dissolved species is confirmed as Ni(salophen). Taken together, these results suggest that both Ni(Hsalophan)(OAc) and Ni(salophan) can be readily converted to the more stable Ni(salophen), especially in the presence of O$_2$ and under heating. Students who obtained the mixture of Ni(salophan) and Ni(salophen) for the final synthesis likely had excessive heating. The related tetrahydrosalen complexes of Ni(II) have been reported to undergo partial ligand dehydrogenation with O$_2$ (eq 6),[27] in contrast to complete ligand dehydrogenation observed with the salophan-ligated complexes.



Finally, it is possible to more firmly establish the structure of the light-blue compound, provided that single crystals are grown from an acetonitrile solution evaporated under an inert atmosphere. As illustrated in Figure 4, the structure[28] features

https://dx.doi.org/10.1021/acs.jchemed.0c01117
J. Chem. Educ. 2021, 98, 592−599

a dimer of **D** with the unprotonated oxygen donor bridging two nickel centers. The protonated oxygen donor interacts with the acetate through an intramolecular hydrogen bond, which is reminiscent of the stabilizing effect of hydrogen bonds in the well-known nickel bis(dimethylglyoximate).[29] The observation of hydrogen covalently bound to the $[salophan]^{2-}$ ligand instead of the acetate can also be discussed with students through comparing the acidities of phenol-type molecules and acetic acid.

SUMMARY

The reactivity and stability of inorganic compounds are highly dependent on the donor properties and ligand flexibility, even if the same set of donor atoms are involved. This is well illustrated here for a Ni(II) system supported by a N_2O_2 tetradentate ligand. The experiments initially focus on training students in synthetic techniques and physical methods and then transition to an open-ended project that requires them to apply learned knowledge to solve a chemistry mystery. In addition to developing critical thinking skills, students also gain research-focused experience, which is typically unavailable in a course simply using procedures drawn from a laboratory manual. Furthermore, students become more critical in reading the literature, as they will find that published data could be wrong or misinterpreted. The ligands are simple and can be altered slightly if desired (e.g., using a different diamine or salicylaldehyde derivative as the starting material). Given the rich coordination chemistry of salen-type complexes, the course materials can also be expanded to semester-long experiments (e.g., studying different metal systems[7,13a,30]).

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available at https://pubs.acs.org/doi/10.1021/acs.jchemed.0c01117.

Instructions for students (PDF, DOCX)
Notes for instructors (PDF, DOCX)
Spectra and characterization data (PDF, DOCX)
NMR raw data (ZIP)
X-ray crystallographic data for Ni(salophen) (CCDC-2023070) (CIF)
X-ray crystallographic data for $[Ni(Hsalophan)(OAc)]_2 \cdot 2MeCN$ (CCDC-2043612) (CIF)

AUTHOR INFORMATION

Corresponding Author

Hairong Guan − *Department of Chemistry, University of Cincinnati, Cincinnati, Ohio 45221-0172, United States;* orcid.org/0000-0002-4858-3159; Email: hairong.guan@uc.edu

Authors

Joel D. Collett − *Department of Chemistry, University of Cincinnati, Cincinnati, Ohio 45221-0172, United States*

Jeanette A. Krause − *Department of Chemistry, University of Cincinnati, Cincinnati, Ohio 45221-0172, United States*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.jchemed.0c01117

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

The authors thank the Department of Chemistry at the University of Cincinnati and the NSF Chemical Catalysis Program (CHE-1800151) for financial support, Larry Sallans at the University of Cincinnati for assistance with mass spectrometric analysis, and the NSF MRI Program for instrumental support, which includes the purchase of two Bruker single-crystal diffractometers (CHE-0215950 and CHE-1625737) and a Bruker NEO400 MHz NMR spectrometer (CHE-1726092).

REFERENCES

(1) Erxleben, A. Transition Metal Salen Complexes in Bioinorganic and Medicinal Chemistry. *Inorg. Chim. Acta* **2018**, *472*, 40−57.

(2) (a) Muller, J. G.; Paikoff, S. J.; Rokita, S. E.; Burrows, C. J. DNA Modification Promoted by Water-Soluble Nickel(II) Salen Complexes: A Switch to DNA Alkylation. *J. Inorg. Biochem.* **1994**, *54*, 199−206. (b) Czlapinski, J. L.; Sheppard, T. L. Nucleic Acid Template-Directed Assembly of Metallosalen−DNA Conjugates. *J. Am. Chem. Soc.* **2001**, *123*, 8618−8619. (c) Giannicchi, I.; Brissos, R.; Ramos, D.; de Lapuente, J.; Lima, J. C.; Dalla Cort, A.; Rodríguez, L. Substituent Effects on the Biological Properties of Zn-Salophen Complexes. *Inorg. Chem.* **2013**, *52*, 9245−9253. (d) Majumder, S.; Pasayat, S.; Panda, A. K.; Dash, S. P.; Roy, S.; Biswas, A.; Varma, M. E.; Joshi, B. N.; Garribba, E.; Kausar, C.; Patra, S. K.; Kaminsky, W.; Crochet, A.; Dinda, R. Monomeric and Dimeric Oxidomolybdenum(V and VI) Complexes, Cytotoxicity, and DNA Interaction Studies: Molybdenum Assisted C = N Bond Cleavage of Salophen Ligands. *Inorg. Chem.* **2017**, *56*, 11190−11210.

(3) (a) Canali, L.; Sherrington, D. C. Utilisation of Homogeneous and Supported Chiral Metal(salen) Complexes in Asymmetric Catalysis. *Chem. Soc. Rev.* **1999**, *28*, 85−93. (b) Jacobsen, E. N. Asymmetric Catalysis of Epoxide Ring-Opening Reactions. *Acc. Chem. Res.* **2000**, *33*, 421−431. (c) Venkataramanan, N. S.; Kuppuraj, G.; Rajagopal, S. Metal−Salen Complexes as Efficient Catalysts for the Oxygenation of Heteroatom Containing Organic Compounds—Synthetic and Mechanistic Aspects. *Coord. Chem. Rev.* **2005**, *249*, 1249−1268. (d) Baleizão, C.; Garcia, H. Chiral Salen Complexes: An Overview to Recoverable and Reusable Homogeneous and Heterogeneous Catalysts. *Chem. Rev.* **2006**, *106*, 3987−4043.

(4) (a) Di Bella, S.; Fragalà, I.; Ledoux, I.; Marks, T. J. Role of Metal Electronic Properties in Tuning the Second-Order Nonlinear Optical Response of Coordination Complexes. A Combined Experimental and Theoretical Investigation of a Homologous Series of (*N*,*N*′-Disalicylidene-1,2-phenylenediaminato)M(II) (M = Co, Ni, Cu) Complexes. *J. Am. Chem. Soc.* **1995**, *117*, 9481−9485. (b) Wezenberg, S. J.; Kleij, A. W. Material Applications for Salen Frameworks. *Angew. Chem., Int. Ed.* **2008**, *47*, 2354−2364. (c) Gao, F.; Li, J.; Kang, F.; Zhang, Y.; Wang, X.; Ye, F.; Yang, J. Preparation and Characterization of a Poly[Ni(salen)]/Multiwalled Carbon Nanotube Composite by *in Situ* Electropolymerization as a Capacitive Material. *J. Phys. Chem. C* **2011**, *115*, 11822−11829.

(5) (a) Atwood, D. A.; Jegier, J. A.; Lindholm, N. F.; Martin, K. J.; Rutherford, D. Synthesis, Structure and Reactivity of SalanH_2-Metal Complexes. *J. Coord. Chem.* **1996**, *38*, 305−318. (b) Belaid, S.; Landreau, A.; Djebbar, S.; Benali-Baitich, O.; Bouet, G.; Bouchara, J.-P. Synthesis, Characterization and Antifungal Activity of a Series of Manganese(II) and Copper(II) Complexes with Ligands Derived from Reduced *N*,*N*′-*O*-phenylenebis(salicylideneimine). *J. Inorg. Biochem.* **2008**, *102*, 63−69. (c) Zhou, X.-F. Catalytic Oxidation and Conversion of Kraft Lignin into Phenolic Products Using Zeolite-Encapsulated Cu(II) [H_4]salen and [H_2]salen Complexes. *Environ. Prog. Sustainable Energy* **2015**, *34*, 1120−1128. (d) Reytman, L.; Braitbard, O.; Hochman, J.; Tshuva, E. Y. Highly Effective and Hydrolytically Stable Vanadium(V) Amino Phenolato Antitumor Agents. *Inorg. Chem.* **2016**, *55*, 610−618. (e) Zhao, X.; Zhang, D.; Yu, R.; Chen, S.; Zhao, D.

Tetrahydrosalen Uranyl(VI) Complexes: Crystal Structures and Solution Binding Study. *Eur. J. Inorg. Chem.* **2018**, *2018*, 1185−1191.
(6) Meyer, F.; Kozlowski, H. 6.3—Nickel. In *Comprehensive Coordination Chemistry II*; McCleverty, J. A., Meyer, T. J., Eds.; Pergamon: Oxford, 2003; pp 247−554. DOI: 10.1016/B0-08-043748-6/05084-2.
(7) (a) Appleton, T. G. Oxygen Uptake by a Cobalt(II) Complex. An Undergraduate Experiment. *J. Chem. Educ.* **1977**, *54*, 443−444. (b) Vecchio, G.; Lanza, V. Synthesis of Superoxide Dismutase (SOD) Enzyme Mimetics. A Bioinorganic Laboratory Experiment. *J. Chem. Educ.* **2009**, *86*, 1419−1421.
(8) At the University of Cincinnati, CHEM4020L is a standalone, elective laboratory course for students in their senior year fulfilling the requirements for the B.S. degree in Chemistry. The prerequisite requires a C− grade or better in CHEM4020, which is a lecture-based inorganic chemistry course.
(9) In earlier years, we implemented similar experiments with the H_2salen ligand, and found that some students would simply use Google to search for answers to prelab and postlab questions. This practice has its merit but can be dangerous for learning because of the prevalence of misinformation on the Internet. One example is the chemical structure of Ni(salen) erroneously provided on a vendor's website: https://www.sigmaaldrich.com/catalog/product/aldrich/268658?lang=en&region=US (accessed December 4, 2020).
(10) (a) Hernández-Benítez, L. J.; Jiménez-Cruz, P.; Cureño-Hernández, K. E.; Solano-Peralta, A.; Flores-Álamo, M.; Flores-Parra, A.; Garcia-Mora, I.; Castillo-Blum, S. E. $[V^{IV}O]^{2+}$ Complexes: Structure, Unusual Magnetic Properties and Cytotoxic Effect. *Inorg. Chim. Acta* **2018**, *480*, 197−206. (b) Asraf, M. A.; Ezugwu, C. I.; Zakaria, C. M.; Verpoort, F. Homogeneous Photochemical Water Oxidation with Metal Salophen Complexes in Neutral Media. *Photochem. Photobiol. Sci.* **2019**, *18*, 2782−2791. (c) Li, N.; Wang, Y.; Liu, F.; Zhao, X.; Xu, X.; An, Q.; Yun, K. Air-Stable Zirconium (IV)-Salophen Perfluorooctanesulfonate as a Highly Efficient and Reusable Catalyst for the Synthesis of 3,4-Dihydropyrimidin-2-(1H)-ones/Thiones Under Solvent-Free Conditions. *Appl. Organomet. Chem.* **2020**, *34*, No. e5454.
(11) Deng, H.; Liu, B.; Yang, C.; Li, G.; Zhuang, Y.; Li, B.; Zhu, X. Multi-Color Cell Imaging Under Identical Excitation Conditions with Salicylideneaniline Analogue-Based Fluorescent Nanoparticles. *RSC Adv.* **2014**, *4*, 62021−62029.
(12) If room temperature is preferred, students should be reminded that good mixing is the key to success for the synthesis. Otherwise, the isolated product may contain a small amount of the unreacted *o*-phenylenediamine (5%).
(13) (a) Hille, A.; Ott, I.; Kitanovic, A.; Kitanovic, I.; Alborzinia, H.; Lederer, E.; Wölfl, S.; Metzler-Nolte, N.; Schäfer, S.; Sheldrick, W. S.; Bischof, C.; Schatzschneider, U.; Gust, R. [*N*,*N*′-Bis(salicylidene)-1,2-phenylenediamine]metal Complexes with Cell Death Promoting Properties. *JBIC, J. Biol. Inorg. Chem.* **2009**, *14*, 711−725. (b) Jamshid, K. A.; Asadi, M.; Kianfar, A. H. Synthesis, Characterization and Thermal Studies of Dinuclear Adducts of Diorganotin(IV) Dichlorides with Nickel(II) Schiff-Base Complexes in Chloroform. *J. Coord. Chem.* **2009**, *62*, 1187−1198. (c) Lee, S.-Y.; Hille, A.; Frias, C.; Kater, B.; Bonitzki, B.; Wölfl, S.; Scheffler, H.; Prokop, A.; Gust, R. [Ni^{II}(3-OMe-salophene)]: A Potent Agent with Antitumor Activity. *J. Med. Chem.* **2010**, *53*, 6064−6070.
(14) If time constraints prevent full implementation of the experiments described herein, instructors may consider adopting the Weeks 1 and 2 activities only, although the benefits of working on an open-ended project will be lost.
(15) (a) Magro, A.; Crociani, L.; Prinzivalli, C.; Vigato, P. A.; Zanonato, P. L.; Tamburini, S. Coordination Ability of Free or Silica Immobilized Schiff Bases Towards Hg(II), Cd(II) and Pb(II) Ions. *Inorg. Chim. Acta* **2014**, *410*, 29−38. (b) Tayade, K.; Sahoo, S. K.; Patil, R.; Singh, N.; Attarde, S.; Kuwar, A. 2,2′-[Benzene-1,2-diylbis-(iminomethanediyl)]diphenol Derivative Bearing Two Amine and Hydroxyl Groups as Fluorescent Receptor for Zinc(II) Ion. *Spectrochim. Acta, Part A* **2014**, *126*, 312−316. (c) Dadkhah, M.; Salavati-Niasari, M.; Mir, N. Synthesis and Characterization of TiO_2 Nanoparticles by Using New Shape Controllers and Its Application in Dye Sensitized Solar Cells. *J. Ind. Eng. Chem.* **2014**, *20*, 4039−4044. (d) Ding, Z.; Yang, Y. Dioxovanadium(V) Complexes of Schiff and Tetrahydro-Schiff Bases Encapsulated in Zeolite-Y for the Aerobic Oxidation of Styrene. *Kinet. Catal.* **2017**, *58*, 290−299.
(16) Banfi, L.; Narisano, E.; Riva, R. Sodium Borohydride. In *Encyclopedia of Reagents for Organic Synthesis*; John Wiley & Sons: New York, 2001; DOI: 10.1002/047084289X.rs052.
(17) Atwood, D. A.; Benson, J.; Jegier, J. A.; Lindholm, N. F.; Martin, K. J.; Pitura, R. J.; Rutherford, D. Synthesis and Structural Characterization of Tetradentate (N_2O_2) Ligand Complexes of Zinc. *Main Group Chem.* **1995**, *1*, 99−113.
(18) Salavati-Niasari, M.; Shakouri-Arani, M.; Davar, F. Flexible Ligand Synthesis, Characterization and Catalytic Oxidation of Cyclohexane with Host (Nanocavity of Zeolite-Y)/Guest (Mn(II), Co(II), Ni(II) and Cu(II) Complexes of Tetrahydro-Salophen) Nanocomposite Materials. *Microporous Mesoporous Mater.* **2008**, *116*, 77−85.
(19) Aidyn, A.; Medzhidov, A. A.; Fatullaeva, P. A.; Tashchioglu, S.; Yalchin, B.; Saiyn, S. Oxidative Dehydrogenation in Complexes of Transition Metals (Cu(II), Co(II), Ni(II)) with N,N′-Di(2-hydroxybenzyl)diamines. *Russ. J. Coord. Chem.* **2001**, *27*, 486−492.
(20) Ni(salophan)$(H_2O)_2$, as proposed in ref 19, was prepared under conditions slightly different from ours (room temperature in methanol instead of in refluxing ethanol). We repeated the synthesis following the reported procedures. The isolated complex gave IR, MS, UV−vis, and magnetic susceptibility data identical to Ni(Hsalophan)(OAc), suggesting that the structure was misassigned.
(21) To perform the manipulations on the diffractometer, all users must undergo University of Cincinnati radiation safety and site-specific diffractometer training. Sessions are held in the Richard C. Elder X-ray Crystallography Facility.
(22) Fulmer, G. R.; Miller, A. J. M.; Sherden, N. H.; Gottlieb, H. E.; Nudelman, A.; Stoltz, B. M.; Bercaw, J. E.; Goldberg, K. I. NMR Chemical Shifts of Trace Impurities: Common Laboratory Solvents, Organics, and Gases in Deuterated Solvents Relevant to the Organometallic Chemist. *Organometallics* **2010**, *29*, 2176−2179.
(23) A useful source of IR spectrum table can be found from the Sigma-Aldrich website: *IR Spectrum Table & Chart*. https://www.sigmaaldrich.com/technical-documents/articles/biology/ir-spectrum-table.html (accessed December 4, 2020).
(24) (a) Jones, L. H.; McLaren, E. Infrared Spectra of CH_3COONa and CD_3COONa and Assignments of Vibrational Frequencies. *J. Chem. Phys.* **1954**, *22*, 1796−1800. (b) Edwards, D. A.; Hayward, R. N. Transition Metal Acetates. *Can. J. Chem.* **1968**, *46*, 3443−3446.
(25) The unit cell matches Ni(salophen) reported in the literature, although our data were collected using both Cu Kα and Mo Kα radiation and at a different temperature (150 K instead of 100 and 296 K). Students were divided into two groups: one group solved the Cu Kα data, and the other solved the Mo Kα data. They were asked to compare the results and determine whether radiation type influenced the results obtained. For references, see: (a) Chowdhury, B.; Karar, M.; Paul, S.; Joshi, M.; Choudhury, A. R.; Biswas, B. Salen Type Ligand as a Selective and Sensitive Nickel(II) Ion Chemosensor: A Combined Investigation with Experimental and Theoretical Modelling. *Sens. Actuators, B* **2018**, *276*, 560−566. (b) Ansari, R. M.; Kumar, L. M.; Bhat, B. R. Air-Stable Cobalt(II) and Nickel(II) Complexes with Schiff Base Ligand for Catalyzing Suzuki-Miyaura Cross-Coupling Reaction. *Russ. J. Coord. Chem.* **2018**, *44*, 1−8.
(26) Krause, J. A.; Al-Khasawneh, N. R.; Bain, T. R.; Beckes, A. E.; Bolender, A. J.; Brewer, B. J.; Conner, C. E.; Cox, S.; Harris, K.; Jiang, D.; Kile, A. O.; Merchant, M.; Steiger, P. M.; Strong, M.; Teal, W. P. A.; Zhang, Z.; Collett, J. D.; Guan, H. CSD entry: MUSWIJ; CCDC-2023070. *CSD Commun.* **2020**, DOI: 10.5517/ccdc.csd.cc25x5bm.
(27) Böttcher, A.; Elias, H.; Müller, L.; Paulus, H. Oxygen Activation on Ni(II)tetrahydrosalen Complexes with the Formation of Nickel-(II)dihydrosalen Complexes. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 623−625.

(28) More detailed crystallographic information can be found from the CIF file in the Supporting Information or from the Cambridge Crystallographic Data Centre (https://www.ccdc.cam.ac.uk/structures/) using the CCDC deposition number 2043612.
(29) (a) Williams, D. E.; Wohlauer, G.; Rundle, R. E. Crystal Structures of Nickel and Palladium Dimethylglyoximes. *J. Am. Chem. Soc.* **1959**, *81*, 755−756. (b) Brush, S. S. Microscopic Identification of the Crystals of Dimethylglyoxime Complexes of Cobalt(II), Iron(II), and Nickel(II). *J. Chem. Educ.* **1988**, *65*, 81.
(30) Baldwin, M. J. A Literature-Based, One-Quarter Inorganic Chemistry Laboratory Course. *J. Chem. Educ.* **2003**, *80*, 307−310.

https://dx.doi.org/10.1021/acs.jchemed.0c01117
J. Chem. Educ. 2021, 98, 592−599