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Microwave-Assisted Synthesis and Characterization of Cyclometalated Iridium Complexes

by Alexis R Burnette, Thomas N Rohrabaugh Jr, and Ryan M O'Donnell

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Alexis R Burnette
Arizona State University

Thomas N Rohrabaugh Jr and Ryan M O'Donnell
Sensors and Electron Devices Directorate, CCDC Army Research Laboratory

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14. ABSTRACT
Microwave-assisted organic synthesis (MAOS) has gained popularity as a replacement for traditional methods of heating reaction vessels using sand or oil baths and hot plates. MAOS is advantageous due to the use of pressurized vessels that allow for superheating of solvents above their boiling points and the homogeneous distribution of heat within reaction vessels. The application of MAOS and automated column chromatography to the syntheses of cyclometalated iridium chromophores is described in detail for $[Ir(pbt)_2Cl]_2$ and $[Ir(pbt)_2(acac)]$, where pbt is 2-phenylbenzothiazole and acac is acetylacetonate. The reaction time was reduced to 5%–10% of the time required for reported literature procedures by employing MAOS. These results were found to be generally applicable to the general class of [Ir(C^N)2Cl]2 and [Ir(C^N)2(LX)] complexes, where C^N represents a cyclometalating ligand and LX an ancillary ligand. These reduced reaction times result in time and energy savings and allow for high-throughput chemical syntheses when combined with the use of an autosampler. Implementation of automated column chromatography resulted in the rapid, efficient purification of the target chromophores from crude product. Chemical characterization of the materials produced using MAOS demonstrate that the products are identical to those obtained using traditional methods.

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1. Introduction

Since the late 1980s, microwave-assisted organic synthesis (MAOS) has become a useful method of obtaining desired chemical products with high yields.[1] Classic methods of heating reaction vessels traditionally used sand or oil baths and hot plates. While initial attempts to employ microwave radiation for reaction heating used modified, domestic microwave ovens, several instrument companies (Anton Paar, Biotage, CEM, etc.) now manufacture dedicated microwave reactors for chemical synthesis with enhanced safety features.

Under traditional reaction conditions, the boiling point of the solvent used limits the maximum temperature. Reflux conditions are commonly used in organic synthesis to achieve the maximum possible reaction temperature by boiling the reaction solvent but require condensers to cool and condense the solvent vapors back into their liquid form to avoid solvent loss. While air-cooling with a Vigreux condenser may work for certain solvents, most reflux condensers use flowing, chilled water that introduces laboratory hazards such as flooding due to disconnection of supply tubing.[1,2] Furthermore, the common practice of flowing, chilled water poses a challenge to sustainability efforts with flow rates on the order of 1–4 L per minute.[3] Modern microwave reactors do not require water or other flowing liquids, which mitigates laboratory risk and environmental impact.

One benefit of MAOS is the ability to superheat the reaction solvent in a contained environment. The use of sealed, pressure-tolerant reaction vials in the microwave reactor allows for reaction temperatures higher than the boiling point of the solvent, which leads to faster reaction times. The reaction time reduction is a result of the Arrhenius law (Eq. 1), which states that the rate constant increases exponentially with the increase in reaction temperature.[4]

Equation 1 represents the Arrhenius law:

$$k = Ae^{-\frac{E_a}{RT}} \tag{1}$$

k = rate constant

A = pre-exponential factor

E_α = activation energy

R = gas constant

T = reaction temperature

The result is a doubling of the reaction rate for every 10 °C increase in temperature. Therefore, just by slightly increasing the temperature, a reaction could be

completed in half the time. Furthermore, unlike the thermal transfer processes required when heating reaction flasks with sand or oil baths, microwaves are able to penetrate the reaction vessel and are absorbed directly by the reaction solvent. This results in more-efficient, rapid heating of the reaction solvent volume with a more homogeneous distribution. This facilitates a more efficient and energy-saving approach to chemical synthesis. Thus, microwave reactors support sustainable chemistry efforts by minimizing the reaction time required for each synthetic step and do not require flowing refrigerants to contain refluxing solvent.

Note all of the modern microwave reactors manufacturers offer have optional autosampler attachments. The use of an autosampler permits the unattended operation of sequential reactions for increased sample throughput.

Transition metal chromophores (TMCs) have found broad application in photoredox catalysis,[5] photodynamic therapy,[6,7] organic light-emitting diodes,[8,9] and nonlinear optical (NLO) applications.[10–12] Interest in the NLO properties of these materials has increased recently with reports of both two-photon absorption and reverse saturable absorption (RSA).[10] These compounds generally exhibit large intersystem crossing quantum yields, long-lived excited states, moderate-to-high photoluminescence quantum yields, substantial photostability, and synthetic tunability through rational ligand design.[13] Second- and third-row d^6 TMCs, such as Ru^{II} or Ir^{III}, are of particular importance due to their large spin-orbit coupling constants and the prevalence of metal-to-ligand charge transfer excited states.[8] However, conventional TMC syntheses rely heavily upon reflux conditions with syntheses requiring several hours, days, or even weeks of reaction time.[14–17]

The US Army is interested in the development of NLO materials capable of absorbing light across the visible spectrum in both their ground and excited states in its pursuit of RSA materials.[12,18] The use of MAOS and automated column chromatography greatly enhance the efficiency of the materials development process compared with traditional synthetic chemistry techniques. This report describes the current standard operating procedures (SOPs) of the US Army Combat Capabilities Development Command (CCDC) Army Research Laboratory's (ARL's) Laser Protection Team (LPT) for developing new cyclometalated iridium complexes. The synthesis of $[Ir^{III}(pbt)_2(acac)]^0$, where pbt is 2-phenylbenzothiazole and acac is acetylacetonate, is described in the following to highlight the advantages of MAOS and automated column chromatography.

We demonstrate reduction of the reaction time for generation of the μ-chloro-bridged Ir dimer from greater than 24 h, required for a traditional reflux,[16] down to 90 min in the microwave. Similarly, synthesis of the acac complex can be performed in 30 min using microwave protocols as opposed to less than 12 h

required for reflux conditions.[15] These decreased reaction times were accomplished through judicious choice of reaction solvent and temperature. Although only the results for the $[Ir(pbt)_2Cl]_2$ and $[Ir(pbt)_2(acac)]$ complexes are presented, we have found these methods to be generally applicable to related $[Ir(C^N)_2Cl]_2$ and $[Ir(C^N)_2(LX)]$ complexes in our laboratories, where C^N represents a cyclometalating ligand and LX an ancillary ligand.

2. Materials and Methods

2.1 Materials

Iridium(III) chloride hydrate (53% metal content) was purchased from Pressure Chemical Co. All other reagents, chemicals, and solvents were purchased from Sigma-Aldrich at a minimum of American Chemical Society reagent–grade quality and used as-received. Figure 1 depicts the structure of the pbt cyclometalating ligand. Similar C^N cyclometalating ligands can be purchased or synthesized to incorporate different functional groups, such as methoxy, trifluoromethyl, nitro, and other substituents.

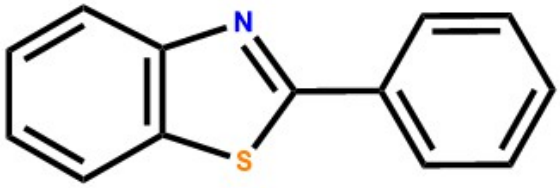

Fig. 1 Structure of pbt ligand

2.2 Instrumentation

The Anton Paar Monowave 450 microwave reactor equipped with a MAS 24 autosampler was used to perform all syntheses. The Monowave 450 requires the use of glass reaction vials specific to the reactor with G30 vials used in these experiments.

A vacuum oven held at 70 °C was used to remove residual solvent from powders after each synthetic step for a minimum duration of 2 h.

The Buchi Reveleris X2 flash chromatography system was used in place of traditional column chromatography as a method of improving the efficiency and speed of product purification. FlashPure EcoFlex 25-g silica columns were used for separations. This chromatography system uses pressurized solvent flow with fine-tuned binary solvent mixture gradients to reduce the amount of solvent required for separations. The system employed identifies fractions of interest via

an integrated UV-visible spectrometer. It can readily identify normally undetected impurities, which leads to enhanced purity of the final product.

A rotary evaporator, commonly referred to as a rotovap, was used to remove liquid solvent from product fractions.

Other standard laboratory equipment used included beakers, Büchner funnels, filter paper, glass vials for storage, Pasteur pipettes, round bottom flasks, and thin layer chromatography (TLC) plates with fluorescent indicator.

Proton (H-1) nuclear magnetic resonance (NMR) spectra were measured on a Bruker 600 MHz Avance NMR spectrometer, referenced to the internal residual solvent peak, and processed using Mnova software.

2.3 Synthesis of Cyclometalated Iridium Dimer: $[Ir(pbt)_2Cl]_2$

2.3.1 Using the Microwave Reactor

1) Add the cyclometalating ligand, pbt, and iridium chloride, $IrCl_3 \bullet xH_2O$ ($x \approx 3$), into a G30 Anton Paar reaction vial in a 2:1 molar ratio.
2) Add 10–15 mL of 3:1 volume-to-volume percent (v/v) 2-methoxyethanol/water solvent mixture to the vial.
3) Place a stir bar in the vial and securely attach the cap and rubber septum. Ensure a proper seal exists between all parts of the reaction vessel.
4) Place the reaction vial in the Monowave 450 carousel, select the appropriate vial position on the instrument monitor, and press Insert on the display.
5) Name the reaction and include the associated notebook and page numbers for reference.
6) Select a microwave method (e.g., “Iridium dimer synthesis”) or create one if needed. The “Iridium dimer synthesis” method is as follows:
    6.1) Step 1: Heat contents to 150 °C as fast as possible.
    6.2) Step 2: Hold for 90 min at 150 °C.
    6.3) Step 3: Cool to 45 °C.
    6.4) Stirrer speed is held at 600 rpm for the entire reaction.
7) Select the appropriate vial type (e.g., glass vial G30) and press OK.
8) After confirming the correct method for synthesis, press OK.

9) Press Start and the automated carousel will perform the experiments in the order specified in the Task List.

10) View the reaction using the integrated camera as it begins.

    10.1) This can be important to confirm that the stir bar spins properly and to ensure there are no visible issues.

    10.2) The camera can be used at any point to take pictures and video of the vial during the reaction process.

11) Once the reaction is complete, the automated robot arm will return the vial to the carousel and move down the Task List to the next experiment until all are completed.

12) Remove the reaction vial from the carousel and proceed to purification.

Synthesis using the microwave reactor method is shown in Fig. 2.

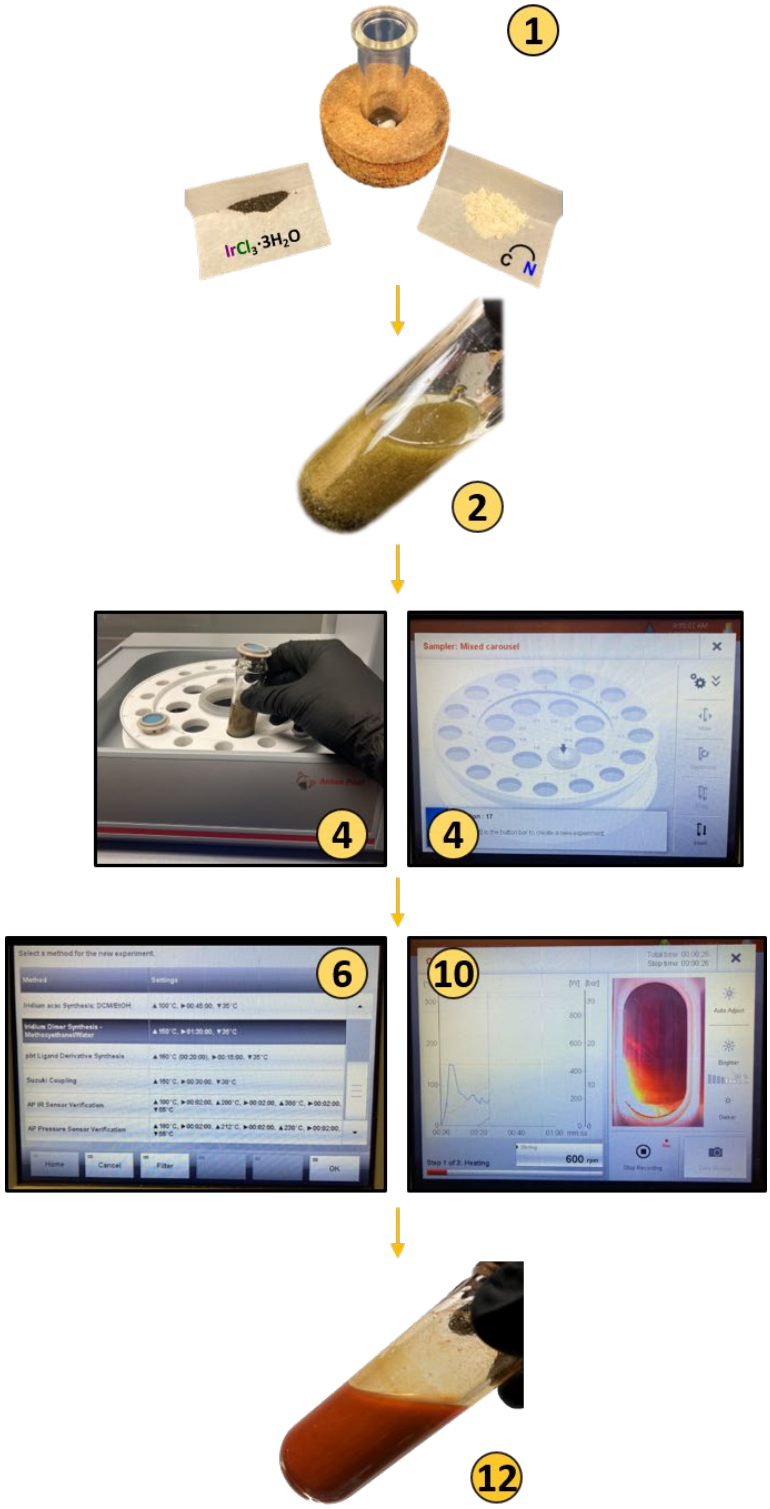

Fig. 2 Synthetic procedure with numbers corresponding to the reaction steps

2.3.2 Purification of Cyclometalated Iridium Dimer

Caution: Perform these steps inside a fume hood to avoid releasing any harmful fumes (e.g., hydrogen chloride [HCl] vapors) into the workspace.

1) Add crude product to a beaker with a stir bar.
2) Add 15 mL of 1-M HCl (aqueous) to aid precipitation of the material.
3) Allow the mixture to stir for 10–15 min until a considerable amount of precipitate forms.
4) Pour the slurry onto a Büchner funnel with filter paper to capture the precipitate. *Be sure to pour directly onto the filter paper so that none of the product goes through the funnel.*
5) Wash the filtered product with a sequence of 1-M HCl (aqueous), water, and hexanes (~10–25 mL each) until filtrate liquid runs clear.
    5.1) Colored filtrate liquid may indicate the presence of impurities, such as unreacted ligand in the product, or unanticipated solubility of the product.
    5.2) If colored filtrate is observed, repeat the washing process until the filtrate runs clear. Avoid overuse of hexanes, as it may dissolve the product and reduce overall yield.
6) Once the colored, powder product has dried on the Büchner funnel, carefully transfer the material into a tared storage vial.
7) Dry vial containing product for at least 2 h (or overnight) in a vacuum oven at 70 °C. *This step is important to remove any residual solvent from the dimer product.*
8) Once the product is dry, reweigh the vial to determine the amount of product synthesized (weighing by difference technique) and calculate the percent yield.

The chemical structure of the cyclometalated iridium dimer is shown in Fig. 3.

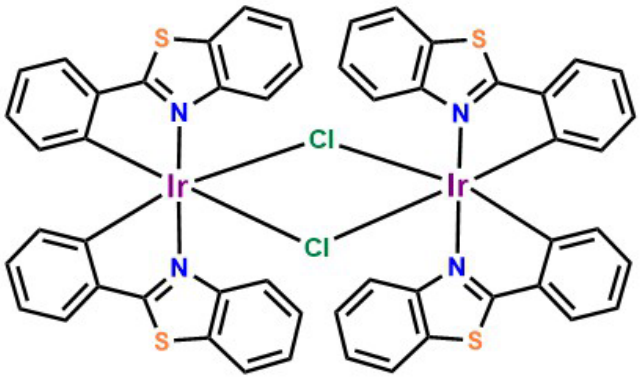

Fig. 3 Chemical structure of $[Ir(pbt)_2Cl]_2$

2.3.3 Thin Layer Chromatography (TLC) Test

1) The TLC test is used to assess the purity of the dimer and confirm that the starting materials, such as the pbt ligand, were fully reacted during the course of the synthesis or removed during the work-up. *The TLC test should be performed prior to using the dimer for subsequent syntheses.*

2) Place a TLC plate with fluorescent indicator on the lab bench and prepare a developing chamber with a small amount of eluent, such as a mixture of dichloromethane (DCM) or ethyl acetate with hexanes. *A favorable eluent mixture for these types of syntheses is 80:20 (v/v) DCM/hexanes.*

3) Collect a small amount of each starting material and product dimer dissolved in DCM. Gently spot each material on the plate adjacent to each other with a microcapillary tube and generate a co-spot that contains all of the materials.

4) Lower the plate into the developing chamber and allow the solvent to travel up the plate.

5) Remove the TLC plate when the solvent line reaches approximately 2/3 to the top of the plate. *If the solvent line rises to the top of the plate, this could skew results and the test should be repeated.*

6) View results under a UV light using shortwave (254 nm) and/or longwave (365 nm) irradiation.

7) The calculation of retention factors (Rfs) can be used to analyze and compare each component on the TLC plate. A ruler is used to determine the distance that each spot traveled and to compare with the solvent front, or the distance that the eluent traveled, using Eq. 2. *Note that Rf values are specific to eluent composition and stationary phase.*

7.1) The Rf values for the free ligand, iridium dimer, and iridium acac complex should all be different, as shown in Fig. 4. If two components, for instance free ligand and iridium acac complex, exhibit identical Rf values, either the sample is impure or the two species are co-eluting. Changing the eluent mixture can aid in separating co-eluting materials or provide further support that the sample is impure.

7.2) To account for differences in elution flow across the plate and aid in visualization, a co-spot that contains all materials (free ligand, iridium dimer, and iridium acac complex) is typically included, as seen in Fig. 4.

8) The cyclometalated iridium dimer is considered pure when only one spot appears on the TLC and no starting materials are observed.

$$Rf = \frac{distance\ spot\ moved}{distance\ eluent\ moved} \tag{2}$$

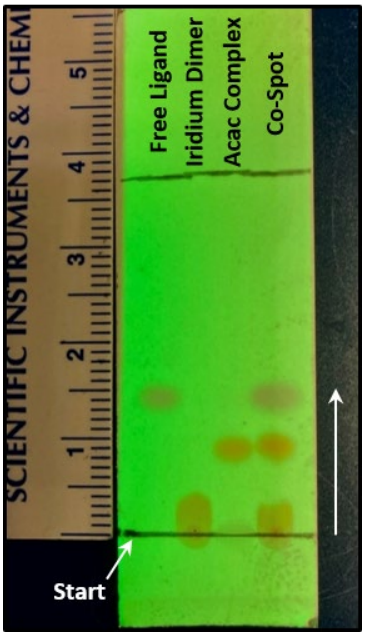

Fig. 4 TLC plate illuminated with shortwave UV light (254 nm) to show specified components. White arrow on the right indicates the direction of the eluent flow during development. Eluent was a (80:20, v/v) DCM/hexanes mixture.

2.4 Synthesis of acac Complexes: [Ir(pbt)$_2$(acac)]

2.4.1 Microwave Procedure

The synthesis of the cyclometalated iridium acac complex (Fig. 5) and related complexes with other ancillary ligands is similar to the dimer synthesis in the microwave reactor.

1) Place approximately 0.1 mmol of [Ir(pbt)$_2$Cl]$_2$ dimer into a G30 Anton Paar reaction vial with 0.2 mL of tetrabutylammonium hydroxide (TBAOH) (1.0 M in methanol, 2 equivalents) and 0.2 mL of acac (20 equivalents), both delivered by syringe.
    1.1) The amount of dimer used is determined by available material and desired amount of acac complex.
    1.2) It may be helpful to start with minimal dimer to confirm appropriate reaction conditions before scaling up.
2) Add 10–15 mL of 2-ethoxyethanol to the vial.
3) Place a stir bar in the vial and securely attach the cap and rubber septum. Ensure a proper seal exists between all parts of the reaction vessel.
4) Place the reaction vial in the Monowave 450 carousel, select the appropriate vial position on the instrument monitor, and press Insert on the display.
5) Name the reaction and include the associated notebook and page numbers for reference.
6) Select a microwave method (e.g., acac synthesis) or create one if needed. The acac synthesis method is as follows:
    6.1) Step 1: Heat contents to 150 °C as fast as possible.
    6.2) Step 2: Hold for 30 min at 150 °C.
    6.3) Step 3: Cool to 45 °C.
    6.4) Stirrer speed is held at 600 rpm for the entire reaction.
7) Select the appropriate vial type (e.g., glass vial G30) and press OK.
8) After confirming the correct method for synthesis, press OK.
9) Press Start and the automated carousel will perform the experiments in the order specified in the Task List.

10) (Optional) View the reaction using the integrated camera.

11) Once the reaction is complete, the automated robot arm will return the vial to the carousel and move down the Task List to the next experiment until all are completed.

12) Remove the reaction vial from the carousel and proceed to purification.

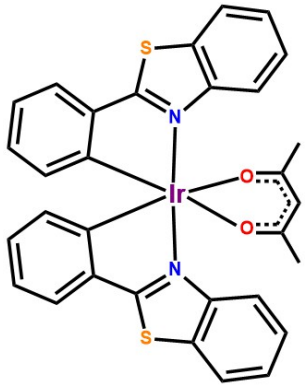

Fig. 5 Chemical structure of [Ir(pbt)$_2$(acac)]

2.4.2 Purification of acac complexes

1) Combine 150 mL of water with crude product in a beaker. Add a stir bar and allow product to precipitate.

2) Pour precipitate over a Büchner funnel and use vacuum filtration to remove the water.

3) Wash the filter cake with water, ethanol, and hexanes to remove the reaction solvent, unreacted acac, and other impurities.

4) Dissolve filter cake in DCM and filter once more into a clean side arm filter flask to separate out any insoluble particles.

5) Transfer organic extracts to a round bottom flask and reduce solvent volume with a rotovap.

6) Proceed to column chromatography to further purify, if necessary.

2.4.3 Flash Column Chromatography:

The Reveleris X2 System is used to collect pure fractions of the desired cyclometalated iridium acac complex (Fig. 6). This system collects samples based on absorbance signals greater than the threshold intensity as measured at specific wavelengths with the built-in UV-visible spectrometer.

1) Load crude product onto silica gel and place in solid sample loader attachment.

2) Insert prepacked silica column cartridge.

3) Perform automated flash column chromatography on crude material using a binary mixture of hexanes and DCM as eluent. *The mixture is ramped from 0% to 100% DCM linearly over the chromatograph run.*

4) Waste eluent is automatically diverted by the system to a waste container.

5) Fractions with absorbance values exceeding the preset intensity threshold are collected into test tubes.

6) Perform TLC tests to determine which fractions contain the desired [Ir(pbt)$_2$(acac)] product. *Many fractions should be tested, and only the purest/identical samples should be chosen for recovery.*

7) Combine the fractions suspected to contain pure [Ir(pbt)$_2$(acac)] in a round-bottom flask and remove solvent via rotovap.

8) Place powder product in a storage vial and set in a 70 °C vacuum oven for at least 2 h to remove any residual solvent.

9) Once dried, weigh final product and calculate yield.

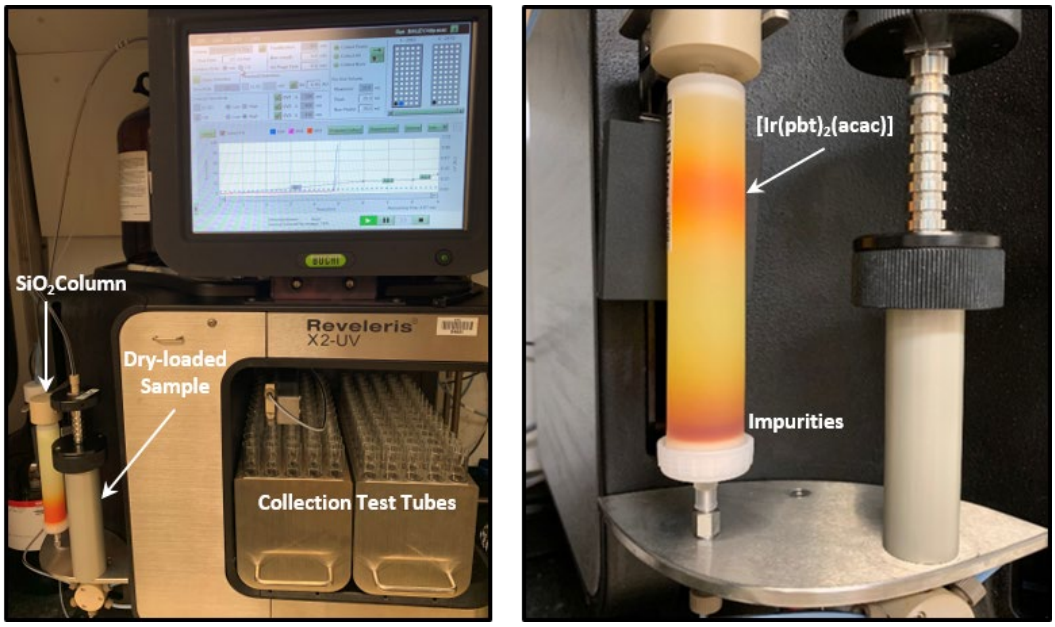

Fig. 6 (left) Reveleris running a column chromatography process. (right) Close-up of silica column showing the bright orange band associated with pure [Ir(pbt)$_2$(acac)].

3. Results and Discussion

The synthesis of $[Ir(pbt)_2Cl]_2$ and $[Ir(pbt)_2(acac)]$ using MAOS was described in detail. Using MAOS, the time required for synthesis was reduced to 5%–10% of the time required for traditional methods, resulting in significant time and energy savings. Implementation of automated column chromatography also provides faster, more efficient, and more reproducible sample purification than traditional techniques. A recent report on the use of 1,2-dimethoxyethane as a solvent, in lieu of 2-ethoxyethanol, for the synthesis of $[Ir(ppy)_2(acac)]$ and related chromophores described cleaner reaction products that did not require column chromatographic purification.[19] This promising result is currently being investigated in our labs to further increase the efficiency and speed of novel chromophore syntheses. The chemical characterization of the $[Ir(pbt)_2(acac)]$ chromophore is provided in the following to demonstrate that the product obtained is identical to material reported in the literature. Thus, no unforeseen chemical reactions occurred during the use of MAOS compared with the use of traditional synthetic methods (e.g., refluxing conditions).

After synthesis is complete, chemical characterization is a critical part of the procedure used to determine the quality and chemical identity of the synthetic product. This step is important because it confirms whether the desired product has been successfully synthesized and if there are any impurities present in the product. The primary techniques used for chemical characterization are TLC, NMR, and X-ray crystallography.

TLC is an important qualitative test used during synthesis to ensure all starting materials have reacted or been removed during purification and the generation of product. Photographs of a TLC plate developed using an eluent of 80:20 (v/v) dichloromethane to hexanes mixture is shown in Figs. 4 and 7. The TLC spots for pbt ("Free Ligand"), $[Ir(pbt)_2Cl]_2$ ("Iridium Dimer"), and $[Ir(pbt)_2(acac)]$ ("Acac Complex") are shown along with a "Co-spot" that contains a mixture of all three components along with their corresponding Rf values. Not shown in Figs. 4 and 7 is the free acac ligand that exhibits an Rf of approximately 0.95 in 80:20 (v/v) DCM/hexanes eluent. We have found the qualitative ordering of the starting materials and products depicted in Figs. 4 and 7 to be characteristic of this class of materials that aids in the synthesis of novel chromophores with unknown Rf values.

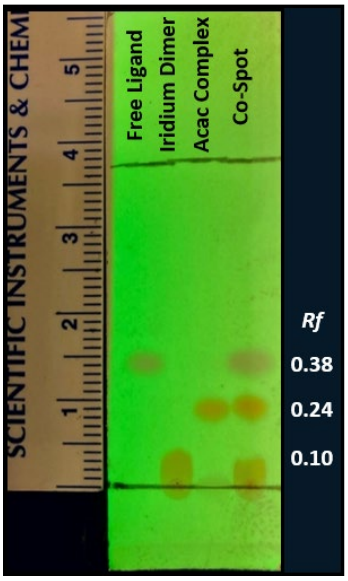

Fig. 7 TLC plate illuminated with shortwave UV light (254 nm) to show specified components. White text on the right indicates the calculated Rf of the specified components. Eluent was a (80:20, v/v) DCM/hexanes mixture.

TLC provides critical information regarding the completion of reactions and qualitative purity of the product. For instance, the observation of free cyclometalating ligand in the Iridium Dimer channel shown in Fig. 7 would indicate that the reaction had not gone to completion or that excess ligand remained in the crude product. Either longer reaction times would be required or further purification would be necessary. Similarly, the presence of free acac ligand or iridium dimer in the Acac Complex channel on the TLC plate would indicate an incomplete reaction or necessitate further purification of the crude product. Pure product is indicated by the presence of a single spot on the TLC plate, while impurities would appear as multiple spots within a vertical channel. However, the presence of a single spot does not guarantee purity, as impurities could co-elute, requiring the choice of a different solvent mixture for TLC development, or they may simply not be observed. Therefore, further chemical analysis is required.

NMR spectroscopy is an effective method for determining the structures of chemical compounds and assessing the purity of a sample. By analyzing the chemical shifts, δ(ppm); examining peak splitting patterns, termed multiplicity; and integrating the NMR signals, certain compounds can be suggested to be present in the sample. The chemical shifts of the signals correspond to three regions of interest for $[Ir(pbt)_2(acac)]$ and $[Ir(C^N)_2(acac)]$ chromophores in general: the aromatic region (~6–9 ppm), acac methine proton peak (~4.5 – 5.5 ppm), and aliphatic region (~1–3 ppm). The number of protons present in the NMR spectra, obtained through signal integration, and their multiplicity should match those expected for a

proposed structure. The presence of additional NMR signals not associated with the chromophore of interest are typically attributable to residual solvent, which can be determined by comparison to known values,[20] or indicates the presence of impurities such as unreacted free ligand, which must be removed from the sample.

The H-1 NMR spectrum of [Ir(pbt)$_2$(acac)] dissolved in deuterated chloroform is provided in Fig. 8. The measured signals are δ 8.10 (m, 2H), 7.90 (m, 2H), 7.65 (dd, 2H, J = 7.8, 0.6 Hz), 7.43 (m, 4H), 6.85 (td, 2H, J = 7.2, 0.6 Hz), 6.63 (td, 2H, J = 7.2, 1.2 Hz), 6.41 (d, 2H, J = 7.2 Hz), 5.13 (s, 1H), and 1.76 (s, 6H). Thus, all 23 of the predicted protons for the [Ir(pbt)$_2$(acac)] structure shown in Figs. 5 and 8 were observed and accounted for. The 16 aromatic protons observed between approximately 6 and 8 ppm were attributed to the pbt cyclometalating ligand. The singular proton observed at 5.13 ppm corresponds to the methine proton of the acac ligand. Finally, the six protons observed in the aliphatic region are assigned to the methyl groups of the acac ligand. These results are in accordance with the literature values reported for [Ir(pbt)$_2$(acac)] measured in deuterated dimethylsulfoxide.

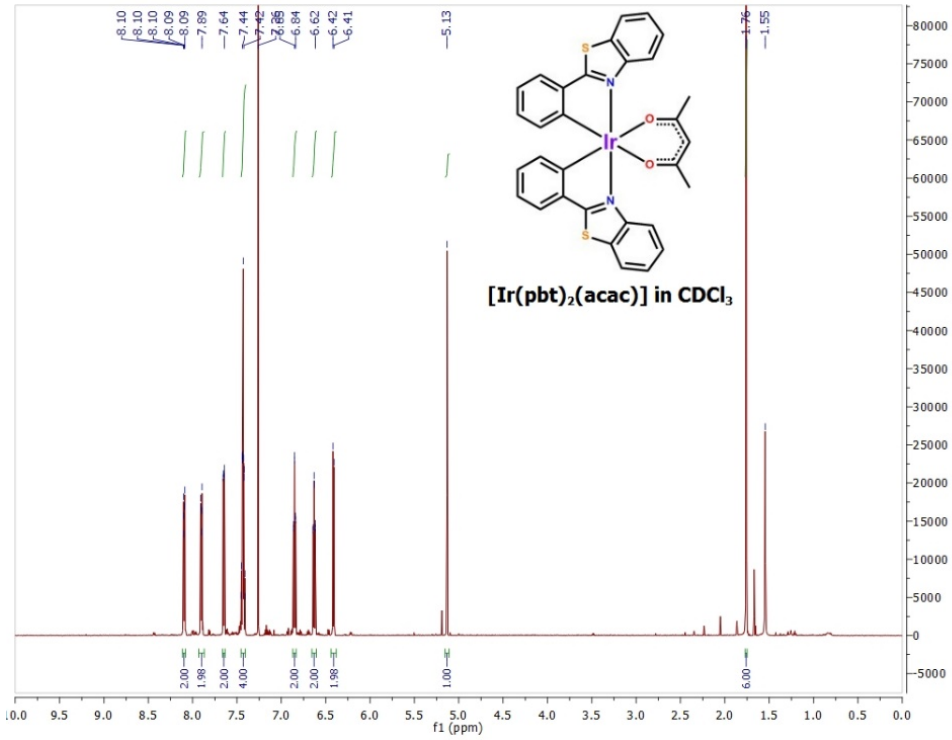

Fig. 8 H-1 NMR data for [Ir(pbt)$_2$(acac)] complex in deuterated chloroform

Structural determination by X-ray crystallography provides one of the most significant forms of analysis to confirm the structural identity of a complex. Since this method identifies atomic positions in a crystal of the sample, it can definitively confirm if the desired cyclometalated iridium acac chromophore has been synthesized or not. Crystal structures provide information such as bond lengths,

bond angles, and torsion angles that are unique to each structure. Generally, if a crystal structure has been previously reported, a comparison of the newly obtained crystal to the reported unit cell may be sufficient for structural confirmation. This avoids the time-intensive process of rigorously determining the full crystal structure. As the crystal structure of [Ir(pbt)$_2$(acac)] had been previously reported and catalogued in the Cambridge Crystallographic Data Centre database, we reproduce the reported crystal structure in Fig. 9.[21] The X-ray crystallographic data confirms the predicted structure shown in Fig. 5 and is consistent with the H-1 NMR spectra shown in Fig. 8.

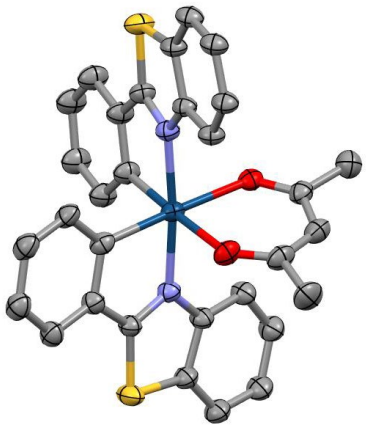

Fig. 9 X-ray crystallographic structure of [Ir(pbt)$_2$(acac)] depicted at the 50% ellipsoid probability level with hydrogens omitted for clarity. (Adapted with permission from Cole JM et al. © 2013 American Chemical Society.[21])

Obtaining a crystal for analysis can be difficult and time-consuming, as crystal growth is a tricky process that can take days or even years to find suitable growth conditions. It is recommended to try multiple conditions using a variety of solvents and temperature environments (such as at room temperature versus in the refrigerator). Once a crystal has formed, caution must be taken as to not damage it. Additionally, not all grown crystals will be suitable for crystallographic analysis due to small size, twinning, cracking, and other potential issues. For cyclometalated iridium complexes like the ones mentioned, the authors have found success growing crystals suitable for X-ray crystallographic characterization by either layering ethanol on top of, or via vapor diffusion of *n*-hexane into, a concentrated dichloromethane solution containing the chromophore.

4. Conclusion

Synthesis of $[Ir(pbt)_2Cl]_2$ and $[Ir(pbt)_2(acac)]$ using MAOS has been detailed and is representative of related $[Ir(C^N)_2Cl]_2$ and $[Ir(C^N)_2(acac)]$ chromophores. The SOP developed uses modern microwave protocols to access elevated temperatures for reduced reaction times and requires less reaction solvent than traditional methods. Reaction time for the preparation of μ-chloro-bridged iridium dimers has been reduced from more than 24 h to 90 min. Similarly, reaction times for the generation of acac complexes have been reduced from more than 12 h to 30 min. These reduced reaction times result in energy savings and allow for high-throughput chemical syntheses when combined with the use of an autosampler. The implementation of automated column chromatography results in the rapid, efficient purification of the target chromophores. Furthermore, the structural identity of the material synthesized using the MAOS SOP was demonstrated to be identical to material synthesized using traditional reflux methods. These protocols enhance the development process of novel RSA chromophores by the ARL LPT by increasing the synthetic throughput and efficiency of the syntheses while simultaneously reducing the environmental impact by minimizing power consumption and solvent requirements.

5. References

1. Council NR. Prudent practices in the laboratory: handling and management of chemical hazards, updated version. Washington (DC): The National Academies Press; 2011. p. 360.

2. Baum EW, O'Callaghan I, Cinninger L, Esteb JJ, Wilson AM. Static fluid condensers for the containment of refluxing solvent. ACS Sustain Chem Eng. 2013;1(12):1502–1505.

3. Grist M, Perkins D, Barber DM. Introducing a novel and highly efficient water-saving condenser. ACS Sustain Chem Eng. 2013;1(12):1498–1501.

4. Kremsner JM, Stadler A. A chemist's guide to microwave synthesis. Graz (Austria): Anton Paar; 2018.

5. Prier CK, Rankic DA, MacMillan DWC. Visible light photoredox catalysis with transition metal complexes: applications in organic synthesis. Chem Rev. 2013;113(7):5322–5363.

6. Monro S, Colón KL, Yin H, Roque J, Konda P, Gujar S, Thummel RP, Lilge L, Cameron CG, McFarland SA. Transition metal complexes and photodynamic therapy from a tumor-centered approach: challenges, opportunities, and highlights from the development of TLD1433. Chem Rev. 2019;119(2):797–828.

7. White JK, Schmehl RH, Turro C. An overview of photosubstitution reactions of Ru(II) imine complexes and their application in photobiology and photodynamic therapy. Inorganica Chim Acta. 2017;454:7–20.

8. Longhi E, De Cola L. Iridium(III) Complexes for OLED application. In: iridium(III) in optoelectronic and photonics applications. Hoboken (NJ): John Wiley & Sons Inc; 2017. p. 205–274.

9. O'Donnell RM, Moore AE, Shi J, Ensley TR, Ferry MJ, Bambha NK, Shensky WM. Iridium complexes containing nitro-derivatized isoquinoline ligands for photonic applications. Proceedings of SPIE. 2019 Feb;10915.

10. Kim K-Y, Farley RT, Schanze KS. An iridium(III) complex that exhibits dual mechanism nonlinear absorption. J Phys Chem B. 2006;110(35):17302–17304.

11. Shensky WM, Ferry MJ, O'Donnell RM, Ensley TR, Shi J. Nonlinear optical characterization of multinuclear iridium compounds containing tricycloquinazoline. Appl Opt. 2017;56(3):B179–B183.

12. Ferry M, O'Donnell R, Bambha N, Ensley T, Shensky W, Shi J. Reverse saturable absorption (RSA) in fluorinated iridium derivatives. Proceedings of SPIE. 2017;10360.

13. Balzani V, Ceroni P, Juris A. Photochemistry and photophysics: concepts, research, applications. Hoboken (NJ): Wiley; 2014.

14. Sun Y, Machala ML, Castellano FN, Controlled microwave synthesis of RuII synthons and chromophores relevant to solar energy conversion. Inorganica Chim Acta. 2010;363(1):283–287.

15. Lamansky S, Djurovich P, Murphy D, Abdel-Razzaq F, Kwong R, Tsyba I, Bortz M, Mui B, Bau R, Thompson ME. Synthesis and characterization of phosphorescent cyclometalated iridium complexes. Inorgc Chem. 2001;40(7):1704–1711.

16. Laskar IR, Chen T-M. Tuning of wavelengths: synthesis and photophysical studies of iridium complexes and their applications in organic light emitting devices. Chem Mater. 2004;16(1):111–117.

17. O'Donnell RM, Grusenmeyer TA, Stewart DJ, Ensley TR, Shensky WM, Haley JE, Shi J. Photodriven oxygen removal via chromophore-mediated singlet oxygen sensitization and chemical capture. Inorg Chem. 2017;56(15):9273–9280.

18. Shensky WM, O'Donnell RM, Shi J, Lee S, Ferry MJ, Bambha NK. In broadband excited-state absorption in metal dithiolene complexes. Proceedings of SPIE Photonics West; 2019 Feb 2–7; San Francisco, CA.

19. Sanner RD, Cherepy NJ, Pham HQ, Young VG. Phosphorescent heteroleptic iridium(III) cyclometallates: improved syntheses of acac complexes and quantum chemical studies of their excited state properties. Polyhedron. 2020;176:114256.

20. Fulmer GR, Miller AJM, Sherden NH, Gottlieb HE, Nudelman A, Stoltz BM, Bercaw JE, Goldberg KI. NMR chemical shifts of trace impurities: common laboratory solvents, organics, and gases in deuterated solvents relevant to the organometallic chemist. Organometallics. 2010;29(9):2176–2179.

21. Cole JM, Bowes KF, Clark IP, Low KS, Zeidler A, Parker AW, Laskar IR, Chen TM. Material profiling for photocrystallography: relating single-crystal photophysical and structural properties of luminescent bis-cyclometalated iridium-based complexes. Crystal Growth and Design. 2013;13(5):1826–1837.

List of Symbols, Abbreviations, and Acronyms

acac	acetylacetonate
ARL	Army Research Laboratory
CCDC	US Army Combat Capabilities Development Command
DCM	dichloromethane
H-1	proton
HCl	hydrogen chloride
Ir	iridium
LPT	Laser Protection Team
MAOS	microwave-assisted organic synthesis
NLO	nonlinear optics
NMR	nuclear magnetic resonance
pbt	2-phenylbenzothiazole ligand
Rf	retention factor
ppm	parts per million
RSA	reverse saturable absorption
rotovap	rotary evaporator
SOP	standard operating procedure
TBAOH	tetrabutylammonium hydroxide
TLC	thin layer chromatography
TMC	transition metal chromophores
UV	ultraviolet
v/v	volume/volume %

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