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Research Article

ADVANCING SUSTAINABLE PRACTICE IN AN UG INORGANIC CHEMISTRY EXPERIMENT

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ABSTRACT

Aims: The research investigated opportunities to advance sustainable practice within the context of an undergraduate inorganic chemistry experiment. **Place and Duration of Study:** Dept of Pure and Applied Chemistry, University of Strathclyde, between October 2023 and April 2024. **Methodology:** A synthetic inorganic experiment taught to level 3 undergraduate students was assessed against 5 different green chemistry principles. The practical chosen for study in this research was a N-heterocyclic carbene (NHC) complex of copper (I) chloride which was synthesized in three steps. **Results:** Step 1 and step 3 of the synthesis was improved, and the modified methods led to increased sustainable practice in terms of: reduced quantities of resources, reduced solvents, green solvents, reduced waste and reduced energy consumption. **Conclusion:** The new laboratory synthesis improved sustainable practice by increased performance against 5 green chemistry principles. The educational experience of students has been maintained whilst improving sustainable practice within the synthetic chemistry module in the undergraduate chemistry programme. When reviewing experiments within chemistry curricula, staff should be encouraged to review potential improvements in synthetic mechanisms to enhance sustainable practice.

Keywords: Sustainable laboratory practice, chemical education research.

INTRODUCTION

Green chemistry, also known as sustainable chemistry, is expressed by the Environmental Protection Agency as ''the design of chemical products that reduce or eliminate the use of hazardous substances'', with the central focus to promote sustainability in the environmental, social and economic aspects of chemical science [1]. In its essence, green chemistry drives sustainable chemical approaches and resources, whilst preserving innovative scientific research and efficiency of chemical production, to ensure a sustainable future for the next generations [2]. A framework developed by Anastas and Warner [3], aimed to assist chemists in making greener chemicals, processes and products is guided by 12 green chemistry principles which are still used today.

The integration of green and sustainable chemistry principles into undergraduate teaching laboratories is a key aspect of modern chemistry education [4]. This can be achieved through the incorporation of sustainable and life cycle assessment concepts in chemistry laboratories [5-10]. Sustainable inorganic chemistry experiments have been previously published [11,12] highlighting the potential for inorganic chemistry experiments to contribute to a more sustainable world by addressing the challenges of resource utilization, waste generation and energy consumption.

This research project explored the potential impact of developing more sustainable processes within the context of an undergraduate chemistry experiment. The practical chosen for study in this research was the preparation of a N-heterocyclic carbene (NHC) complex of copper (I) chloride. The experiment is a key fundamental inorganic experiment as NHCs are used in chemical catalysis as they can efficiently encourage carbon-carbon bond formation. Moreover, the practical allows students to explore and understand molecular orbital theory, carbene molecules, spin states, influence of substituent's, and cyclic complexes. In this work, an NHC complex was synthesized by reacting an imidazolium salt with copper (I) oxide (deprotonation of the imidazolium occurred in-situ).

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METHODOLOGY OF THE CURRENT STUDENT EXPERIMENT

N-heterocyclic carbenes (NHCs) are used frequently in coordination chemistry and transition metal catalysis as these ligands can be beneficial due to their electronic, stability and selectivity properties. Three different NHCs were used in this research study, namely IPr, IXy and IMes (Figure 1). The NHCs can be safely stored in an undergraduate laboratory in their imidazolium salts forms as they are non-air-sensitive [13].

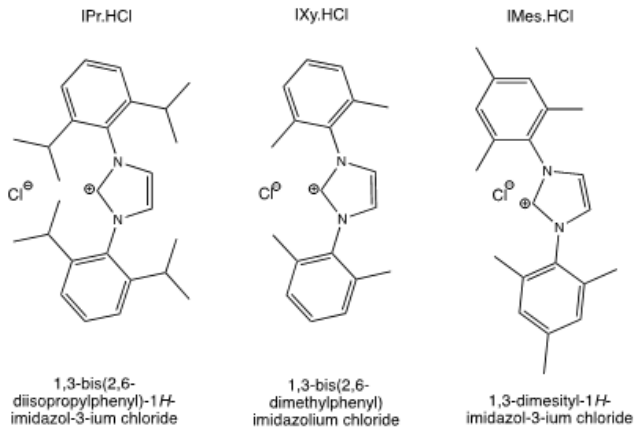

Figure 1: IPr, IXy, IMes imidazolium salt precursors to N-heterocyclic carbenes.

STEP 1: Preparation of Glyoxal-bis (2,6-dimethylphenyl) diimine. The first step of the reaction scheme was as follows:2,6-dimethylaniline (5cm^3), 40% glyoxal solution (3cm^3), isopropanol (30cm^3), and formic acid (5 drops) were combined and stirred (24h). The product was

isolated by filtration and air dried. The resultant bright yellow powder product was glyoxal-bis (2,6-dimethylphenyl) diimine (IXy.HCl). The reaction scheme is illustrated in Figure 2.A product mass of 4.1 g (77% yield) was achieved, and the product identify was confirmed by ATR-FTIR spectroscopy.

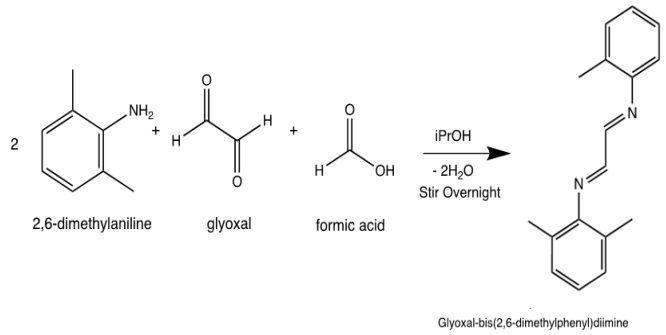

Figure 2: Reaction Scheme for STEP 1 - Preparation of Glyoxal-bis (2,6-dimethylphenyl) diimine.

STEP 2: Preparation of 1,3-bis-(2,6-dimethylphenyl) imidazolium chloride: In the second step of the student experiment, the diimine produced in step 1 was used to prepare the imidazolium chloride salt, IXy.HCl: glyoxal-bis (2,6-dimethylphenyl) diimine (2.5g) and formaldehyde (0.28g) were suspended in ethyl acetate (80cm^3) and refluxed. Chlorotrimethylsilane (1.2cm^3) and ethyl acetate (2cm^3) were added, then the mixture was refluxed (1.5h). The product was isolated by filtration and dried *in vacuo*. The final beige colored product was 1,3-bis-(2,6-dimethylphenyl) imidazolium chloride. The reaction scheme is illustrated in Figure 3. A product mass of 2.2 g (76% yield) was achieved with product identify confirmation by ATR-FTIR.

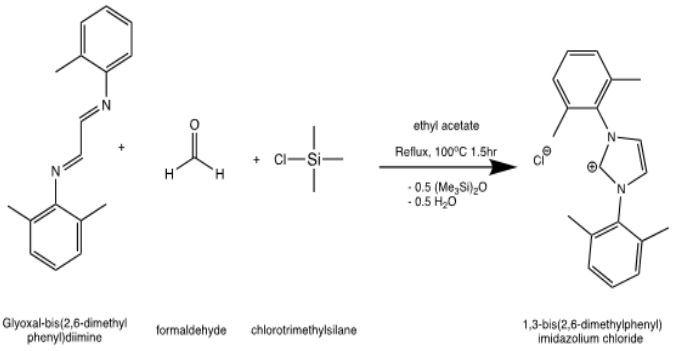

Figure 3: Reaction Scheme for STEP 2 - Preparation of 1,3-bis-(2,6-dimethylphenyl) imidazolium chloride.

STEP 3: Preparation of 1,3-bis (2,6-dimethylphenyl) imidazol-2-ylidene) copper(I) chloride: In the final step of the synthesis 1,3-bis(2,6-dimethylphenyl) imidazolium chloride (0.75 g, 2.4 mM) and copper(I) oxide (0.25g, 1.7mM) were suspended in tetrahydrofuran (40 cm^3) and refluxed for 2h. The orange solution was isolated by filtration, and its volume reduced *in vacuo* (~ 5cm^3). The crystalline product, (1,3-bis(2,6-dimethylphenyl)imidazol-2-ylidene) copper(I) chloride, was isolated by filtration and air dried; see Figure 4 for reaction scheme. The final product was obtained and identified by ATR-FTIR, with a final product mass of 0.33 g, indicating a 51% yield for step 3 of the student experiment.

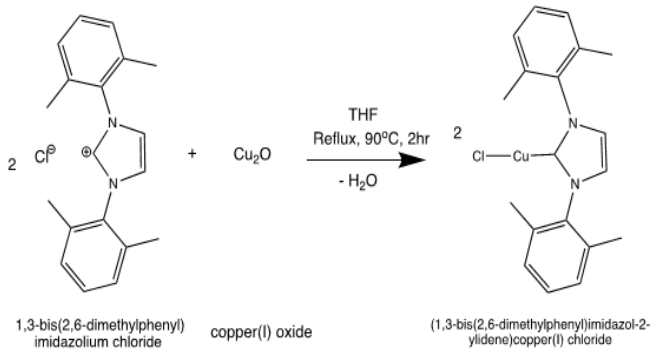

Figure 4: Reaction Scheme for STEP 3 - Preparation of 1,3-bis(2,6-dimethylphenyl)imidazol-2-ylidene)copper(I) chloride.

RESULTS AND DISCUSSION

In line with the 12 principles of green chemistry [3], this research study aimed to increase sustainable practice in the 3 steps used to conduct the NHC experiment. More specifically, the selected principles listed in Table 1 were used to drive forward sustainable practice in the student experiment.

Table 1: The selected green chemistry principles used to improve sustainability of the NHC student experiment.

Green Chemistry Principle	Title	Short Explanation
2	Atom Economy	Synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product.
3	Less Hazardous Chemical Syntheses	Wherever practicable, synthetic methods should be designed to use and generate substances that possess little or no toxicity to human health and the environment.
5	Safer Solvents and Auxiliaries	The use of auxiliary substances (e.g., solvents, separation agents, etc.) should be made unnecessary wherever possible and innocuous when used.
6	Design for Energy Efficiency	Energy requirements of chemical processes should be recognized for their environmental and economic impacts and should be minimized. If possible, synthetic methods should be conducted at ambient temperature and pressure.
12	Inherently Safer Chemistry for Accident Prevention	Substances and the form of a substance used in a chemical process should be chosen to minimize the potential for chemical accidents, including releases, explosions, and fires.

Review and Assessment of Sustainable Practices in STEP 1

In step 1 of the experiment, electrical energy was required to operate a hot plate stirrer which ran continuously for a period of 24h. To reduce energy consumption, the experiment was repeated using a reduced heated stir time of 3h. As shown in Table 2,a reduction of heated stir time from 24 to 3h resulted in a 28% reduction in product mass, with the yield falling from 78 to 56%. To proceed to step 2 of the current experiment a minimum quantity of 2.5 g of diimine is required. It was therefore concluded that the more sustainable stir time of 3 h could be used within the first step of the experiment as it

produced sufficient quantity of product for students to progress to the second step.

Table 2: Results from STEP1: comparing the impact of different heated stir times.

	Mass of Final Product / g			Yield / %		
	Expt. 1	**Expt. 2**	**Mean**	**Expt. 1**	**Expt. 2**	**Mean**
24 h Stir	4.138	4.099	4.119	78.3	77.5	77.9
3 h Stir	2.790	3.128	2.959	52.8	56.2	54.5

Review and Assessment of Sustainable Practices in an Inorganic Year 3 Experiment: STEP 2

The second step of the student experiment was thought to be relatively sustainable in terms of practice, however a reduction in energy, and volumes of solvents, were investigated to assess possible advancements in sustainable practice. While the reflux temperature used in this step was slightly higher (by 10ºC) than used in the following step of the procedure, it was only required for 1.5h to produce a product yield of 2.2g.Lower reflux temperatures were explored, however this led to product yields less than 60% and masses close to 1g. Since students are required to recover a minimum of 0.75g of product to progress to the final stage of the synthesis, it was concluded that lowering the reflux temperature was not suitable as it may lead to students not being able to collect enough product to progress to the final stage of the experiment.

This synthetic step also used ethyl acetate and acetone; both are classified as green solvents, so no alternative solvents were investigated. Instead, solvent volumes used were reduced to investigate the impact on product mass. Lower solvent volumes also led to lower product yields < 60%, leading to low product mass which would compromise the student's progress to the final stage of the experiment. In conclusion the second step of the student experiment was deemed to be sustainably progressive as written, and no modifications were suggested for this part of the student experiment.

Review and Assessment of Sustainable Practices in an Inorganic Year 3 Experiment: STEP 3

In the third and final step of the student experiment, opportunities to explore advanced sustainable practices using reduced quantities of reagents to conserve cost, hazards and waste were explored. In the original synthesis protocol, 0.75 g (2.4mmol) of 1,3-bis (2,6-dimethylphenyl) imidazolium chloride, (IXy.HCl) was added to 0.25 g (1.7 mmol) in 40 cm^3 of THF. Here different approaches were used with reagent quantities reduced by a factor of 10 (referred to herein as microscale reactions).

Approach 1 – A micro scale reaction using water as the solvent and a commercially available reagent, 1,3-bis(2,6-diisopropylphenyl) imidazolium chloride (IPr.HCl) with copper (I) oxide.

Approach 2 – (i) A weak base approach previously published [14] was used to produce the NHC product. In this reaction THF was replaced with potassium carbonate and acetone. Copper (I) oxide was replaced with copper chloride and three different reagents were investigated using micro scale quantities of reagents.
(ii)The weak base microscale approach was used with mechanochemical synthesis [15].

Investigation of Micro-Scale Approach 1.

In the first approach to improving sustainable practice in the third step of the student experiment0.102g of 1,3-bis(2,6-diisopropylphenyl) imidazolium chloride (0.24 mmol, IPr.HCl) and 0.023 g of copper(I) oxide (0.17mmol) were added to 1 cm^3 of deionized water. The product was isolated by filtration and its volume reduced to 1 cm^3*in vacuo*; see Figure 5.

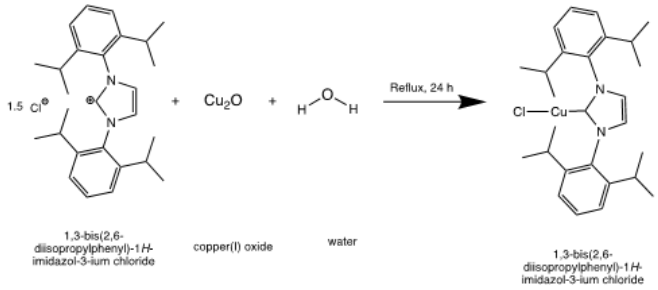

Figure 5: Reaction schematic of micro-scale approach 1 using a green solvent.

The crystalline product (0.057 g), a white solid isolated by filtration and air dried, was analysed by ^{1}H NMR. The spectrum indicated that multiple species were present in the collected solid, including the desired neutral heteroleptic product, however, unreacted (IPr.HCl) and the homoleptic cation, $[Cu(IPr)_2]^+$ were also identified in the final solid. In conclusion although approach 1 used 10 times less reagent quantities, a greener solvent, and a commercially available reagent, it required a longer reaction time (24h reflux vs 2h), and higher temperature (100°C vs 90°C for THF) resulting in greater energy consumption. Moreover, considering the unreliability of the final product, micro-scale approach 1 was eliminated as an alternative third step of the experiment.

Investigation of Micro scale Approach 2 (i)Using a Weak Base Method.

Micro scale apparatus, and lower quantities of reagents were used to synthesize the M-NHC product using three reagents:

- 1,3-bis(2,6-dimethylphenyl) imidazolium chloride; the IXy.HCl product obtained from the second step of the student experiment
- Commercially available 1,3-bis(2,6-diisopropylphenyl) – IPr.HCl
- Commercially available 1,3-bis(2,4,6-trimethylphenyl) – IMes.HCl

All three reagents IXy.HCl, IPr.HCl, or IMes.HCL were used in the weak base method using a 1:1 ratio of reagent: CuCl and the masses used were approximately 10 times lower than those used in the original student experiment.

First the IXy.HCl reagent synthesized in step 2 of the experiment was used(0.075g, 0.24 mmol) with copper(I) chloride (0.032 g, 0.24 mmol) and potassium carbonate (0.332 g, 0.24 mmol). Reagents were suspended in acetone (1 cm^3) and refluxed for 1 h. The reaction mixture was filtered through silica/cotton wool, and the solvent volume was reduced to approximately 1 cm^3*in vacuo*. The solid was filtered, isolated and dried producing an off-white solid powder. Addition of *n*-hexane resulted in precipitation of solids, which were isolated by filtration, and dried *in vacuo*. The expected product, (1,3-bis(2,6-dimethylphenyl)imidazol-2-ylidene)copper(I) chloride, was isolated as an off-white powder with a mass of 0.021 g. The same

procedure was then repeated for IPr.HCl(0.102 g, 0.24 mmol), and IMes. HCl (0.082 g, 0.24 mmol), with product masses of 0.064 or 0.060 g. ^{1}H NMR spectral analysis confirmed that the reaction using IPr.HCl had successfully produced the pure heteroleptic product, [Cu(IPr)Cl], with a yield of 54.6%. However, the reaction with IMes. HCl resulted in a mixture of both [Cu(IMes)Cl] and $[Cu(Mes)_2]^+$ and the IXy.HClreaction produced the homoleptic cation, $[Cu(IXy)_2]^+$, as confirmed by x-ray crystallographic analyses.

To improve the product yield and purity of the micro-scale reaction products, the molar equivalent of CuCl was increased (0.48 mmol) to give a 2:1 ratio with reagents. All three imidazolium ligands reacted successfully with copper(I)chloride in a 1:2 ratio, producing yields of the expected product between 53.7 and 94.1 %, and proton NMR was used to confirm the product's identity and purity (see Table 3).

Table 3: Micro-scale Results from Synthesizing N-Heterocyclic Carbenes with Three Different Carbene Ligands (IPr, IXy and IMes) in 1:2 ratio with copper(I) chloride via Weak-Base Route

Type of Ligand Used	Final Mass of Product / g	Yield/ %	1H NMR Data
IXy.HCl	0.055 0.085	60.8 94.1	(400 MHz, $CDCl_3$): δ2.184 (s, 12H, CH_3), 7.122 (s, 2H, C=CH), 7.229 (d, 4H, meta-CH, $^3J_{HH}$ = 7.6Hz), 7.336 (t, 2H, para-CH, $^3J_{HH}$ = 7.6 Hz)
IPr.HCl	0.063	53.7	(400 MHz, $CDCl_3$): δ1.255 (dd, 24H, CH_3,$^4J_{HH}$ = 6.8Hz), 2.566 (q, 4H, CH-CH_3, $^3J_{HH}$ = 6.9Hz), 7.128 (s, 2H, C=CH), 7.305 (d, 4H, meta-CH, $^3J_{HH}$ = 7.6Hz), 7.489 (t, 2H, para-CH, $^3J_{HH}$ = 7.8Hz)
IMes.HCl	0.056	57.7	(400 MHz, $CDCl_3$): δ 2.128 (s, 12H, ortho-CH_3), 2.370 (s, 6H, para-CH_3), 7.023 (s, 4H, meta-CH), 7.074 (s, 2H, C=CH)

Investigation of Micro scale Approach 2 (ii)Using a Weak Base Method and Mechanochemical Synthesis

To further enhance sustainable practice within the final step of the student experiment, the weak base approach using the Ipr.HCl ligand was investigated with a mechanochemical synthesis approach to drive the reaction and eliminate the need for reflux; thus, eliminating the need for a solvent and reducing energy consumption. In this procedure, IPr.HCl (0.204g, 0.48 mmol), copper(I) chloride (0.065g, 0.48 mmol) and potassium carbonate (0.199g, 1.44 mmol) were ground with a mortar and pestle (30 min). The fine green powder, see Figure 6, was suspended in dichloromethane (1 cm^3), and filtered through silica/ cotton wool. The solvent was removed *in vacuo*, then *n*-hexane (3 cm^3) was added to form a precipitate, which was isolated by filtration, and dried *in vacuo*. The expected final product, (1,3-bis(2,6-diisopropylphenyl)-2,3-dihydro-1*H*-imidazol-2-yl)copper(II)chloride, was a fine white powder.

Figure 6: Mechanochemical synthetic approach to eliminate use of solvent and reflux during step 3 of the student reaction

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The mass of the final product was 0.104 g, but ^{1}H NMR analysis of the product identified multiple species present in the power including unreacted IPr.HCl, as well as the cationic species $[Cu(IPr)_2]^+$. This indicated that the mechanochemical synthesis route was not able to provide a pure product. It was also postulated that this method would likely lead to disengagement and disinterest of students due to the need for grinding reagents by hand for 30 min. This method was therefore not taken forward and no further progression of mechanochemical synthesis was considered.

CONCLUSIONS

This study was undertaken to assess improvements in sustainable practice in an UG chemistry experiment to synthesis the M-NHC product1,3-bis(2,6-diisopropylphenyl)-2,3-dihydro-1*H*-imidazol-2-yl) copper(II) chloride. The experiment was conducted over 3 steps and each step was considered in turn to advance sustainable practice in the student experiment. In the first step of the experiment, the stir time was successfully reduced from 24h to 3h, whilst still attaining a sufficient yield of 54.5%, and mass of product at 2.959 g. Although the quantity of product produced was approximately 50% lower than compared to the original synthesis, there was sufficient product to allow a student to proceed to step 2 of the reaction. The reduction in heated stir times may seem to have little impact from an energy perspective, however considering the experiment is undertaken by over 120 students each academic year, the cumulative saving in energy was thought to be useful.

In step 2 of the experiment, no further net positive sustainable practice was achieved as this step already used green solvents, short reaction times and the material produced in step 1 was used as a reagent; mapping onto green chemistry principles 2 and 3.Various approaches were used to study the third and final step of the student experiment (see Figure 7). The most viable route to increasing sustainable practice was by implementing a weak base route which involved replacement of THF with green solvents, reduced reflux times and micro-scale quantities of reactants; mapping onto green chemistry principles 3, 5, 6 and 12.

Overall, a more sustainable practical chemistry experiment was created with no compromise on product purity or on student experience and education. This study therefore represents opportunities to improve sustainable practice within a chemistry programme. The outcome of this short study will have an immediate impact as the modified experiment will be implemented from this coming academic year onwards. This study confirms the work of Bru [16] and suggests that simple solutions can be used to improve sustainable practice in UG experiments.

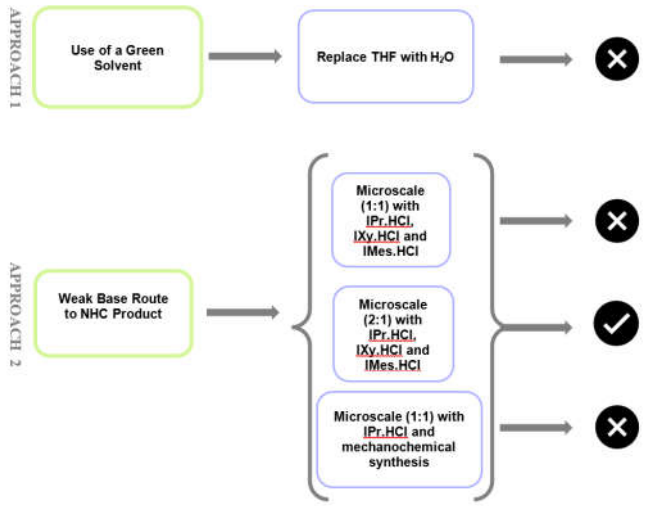

Figure 7: Micro-scale approaches used in STEP 3 of the experiment.

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Competing interests

Authors have declared that no competing interests exist.

Authors' Contributions

Gibson van Milcreated the research project, supervised the work, and wrote the manuscript. Dodds supervised the laboratory work and provided suggestions on experiment modification. Magowan undertook the literature survey, undertook the practical work, and wrote a project thesis from which the paper was constructed. All authors have read and approved drafts of the manuscript.

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