Microwave-Assisted Synthesis of Molybdenum Hexacarbonyl Complexes with Pyridine-Based Ligands

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Abstract

Literature suggests that the substituted derivatives of molybdenum hexacarbonyl with pyridine ligands show anti-cancer properties and are stable under atmospheric conditions. However, the reaction of molybdenum hexacarbonyl and pyridine ligands typically lasts for over 20 hours with the yield less than 50% and is thus highly inefficient. Microwave-assisted synthesis has been developed recently and proves effective in other reaction involving organometallics. This work investigates the effectiveness of microwave-assisted synthesis of molybdenum hexacarbonyl with pyridine-based ligands. Since the pyridine ligands involved are not commercially available, this project also targets at the synthesis of these ligands. The pyridine-based ligands are structurally similar to chalcones, or 1,3-diaryl-2-propen-1-ones. Hence they may share similar properties and the project adopted the preparation method of chalcones for the synthesis of pyridine ligands. Problems due to impurity arised in the preparation of these ligands, and two-solvent recrystallisation was found to be effective in removing the impurities.

1. Introduction

Molybdenum hexacarbonyl and its substitutional derivatives show both air stability and water stability. The naphthalenyl group of the pyridine ligands shown in **Fig. (1)** is biologically active. Literature suggests that pyridine-based ligands exhibit potential anti-cancer properties. Hence, the end product through the substitution of one or several carbonyl groups with these pyridine ligands has potential medical applications.

Molybdenum hexacarbonyl is noteworthy as a water-stable and air-stable derivative of a metal at its zero-oxidation state. $Mo(CO)_6$ demonstrates an octahedral geometry, which is comprised of six rod-like CO ligands attached to the central Mo atom. The compound is useful as reagent in several processes by ligand exchange. Replacement of the carbonyl ligands affords a large number of different molybdenum complexes which have found use in organic synthesis.

Pyridine is a basic heterocyclic organic compound. It is structurally related to benzene, with one methine group (=CH−) replaced by a nitrogen atom. The nitrogen centre of pyridine features a lone pair of electrons. Pyridine tends to enter nucleophilic substitution of the ring by strong organometallic bases. Pyridine and its derivatives are widely used as ligands in coordination chemistry. A ligand is an ion or a molecule that binds to a central metal atom.

Chalcone is an aromatic ketone and an enone that forms the central core for a variety of important biological compounds. Chalcones are abundant in edible plants and are known to be biologically active. Their pyridine-based analogues display an array of medicinal properties,

including anti-inflammatory, cytotoxic, and anticancer activities. Chalcones are usually prepared via aldol condensation of aldehyde and ketone.

In previous attempts to synthesize molybdenum carbonyl complexes, methods which involve high temperature or long reaction time are generally used. These methods also require a number of steps which must be carried out under an inert atmosphere and involve potentially hazardous reagents. For example, an early method of synthesizing $[CpMo(CO_3)]_2$ requires the reaction between $Mo(CO)_6$ vapour and cyclopentadiene at 250 °C, which gives a yield of 30%. The previous synthesis of $[Mo_2(\mu\text{-}O_2CMe)_4]$ also involves heating for 20h, which gives a 37% yield.

Microwave synthesis is a newly-developed method which is intended to increase the rate of reaction. Previous research succeeded in accelerating reactions and increasing their yield utilising a modified domestic microwave oven. Compared to conventional heating which usually involves the use of a furnace or a bath and heats the surface of the sample via convection or conduction, microwave-assisted heating is able to heat the object throughout its volume. Hence, its benefits include reaction rate acceleration, milder reaction conditions, and higher chemical yield.

Reactions of group 6 carbonyl complexes, most notably $Mo(CO)_{6,}$ with a range of mono, bi, and tridentate ligands have been carried out in a modified conventional microwave oven. These reactions, which produces various tetracarbonyl complexes, are generally carried out without an inert atmosphere, with results of high yield and short reaction time. For example, the reaction between $Mo(CO)_6$ and dicyclopentadiene through microwave-assisted synthesis gives a yield of 94% and takes 1h of heating.

There lack sufficient investigations on the pyridine chalcones at which this project aims, including their general properties and method of synthesis. They are structurally related to the chalcones, or 1,3-diaryl-2-propen-1-ones, as shown in **Fig. (2).**. This suggests that the two compounds may have similar properties.

This project thus aims to investigate the efficiency and effectiveness of microwave-assisted synthesis in the reaction between the pyridine chalcones and molybdenum hexacarbonyl, and to obtain an optimized condition for this reaction. In addition, this project also aims at developing a preparation method for the pyridine chalcones.

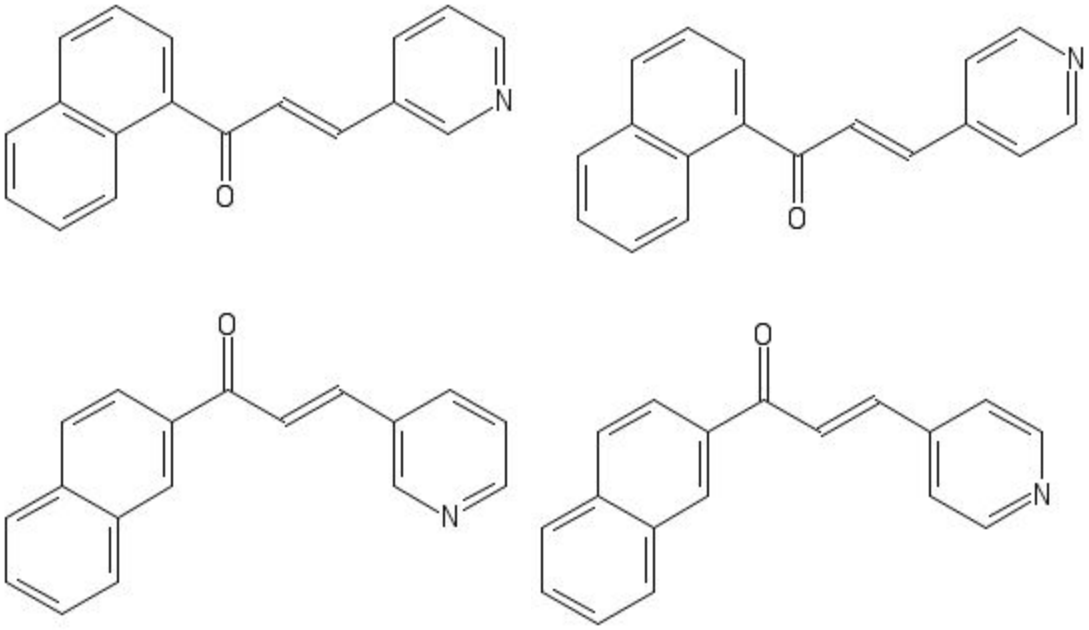

Fig. (1). Pyridine chalcones

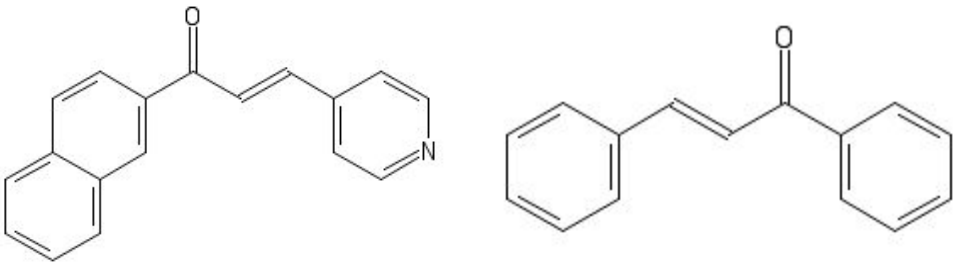

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Fig. (2) 1. 1-Naphthalen-1-yl-3-pyridin-4-ylprop-2-en-1-ne
2. 1,3-diaryl-2-propen-1-one

2. Solution Design and Procedure

Materials required for this project inlude:
1-Acetonaphthone
2-Acetonaphthone
3-Pyridinecarboxaldehyde
4-Pyridinecarboxaldehyde
Molybdenum hexacarbonyl

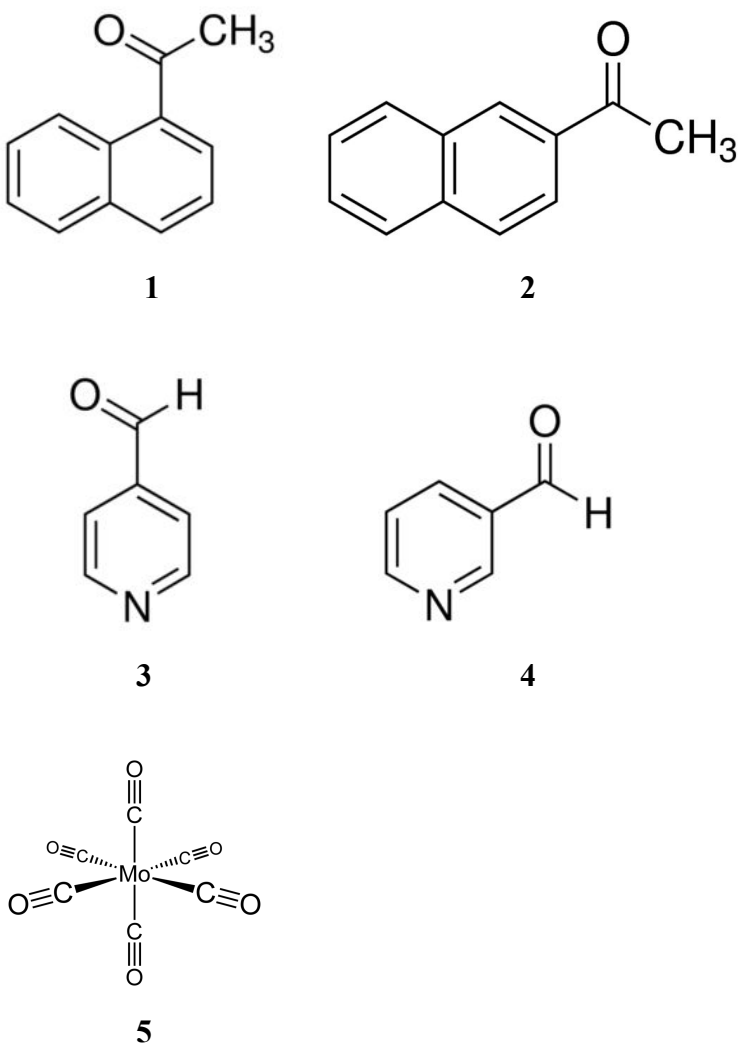


Fig. (3). 1, 1-Acetonaphthone
2, 2-acetonaphthone
3, 3-pyridinecarboxaldehyde
4, 4-pyridinecarboxaldehyde
5, molybdenum hexacarbonyl

Before embarking on the microwave-assisted synthesis of molybdenum carbonyl complex, it is necessary for preparing the pyridine chalcones as they are not commercially available. These pyridine chalcones used for the microwave-assisted synthesis are similar to chalcones, or 1,3-diaryl-2-propen-1-ones, thus they may share similar properties. The method to synthesize chalcones using aldol condensation is likely to be feasible for the synthesis of our project's target pyridine chalcones.

0.751g of 2-acetonaphthone was added to a stirred solution sodium hydroxide pellet dissolved in 12 mL of water and 80 mL of 85% ethanol. The mixture was stirred at ambient temperature for 15 minutes. 0.415mL of 4-pyridinecarboxaldehyde was added via microlitre pipette. The reaction mixture was stirred until all reactants dissolved and give a pale yellow solution. The reaction mixture was stirred using at ambient temperature for 18 hours.

The product mixture gave a dark orange solution without significant precipitate. 10 mL of deionized water was added to the mixture and a suspension of fine powdery solids was produced. The precipitate, **Sample 1**, formed was collected by suction filtration on a Buchner funnel and air-dried.

0.671mL of 1-acetonaphthone was added to a stirred solution sodium hydroxide pellet dissolved in 15 mL of water and 70 mL of 85% ethanol. The mixture was stirred at ambient temperature for 15 minutes. 0.415mL of 4-pyridinecarboxaldehyde was added to the mixture. The reaction mixture was stirred until all reactants dissolved and give a dark yellow solution. The reaction mixture was stirred using at ambient temperature for 18 hours.

The product mixture gave a dark brown solution without significant precipitate. 10 mL of deionized water was added to the mixture and orange precipitate forms. The precipitate, **Sample 2**, was collected by gravitational filtration.

0.751g of 2-acetonaphthone was added to a stirred solution sodium hydroxide pellet dissolved in 15 mL of water and 55mL of 85% ethanol. The mixture was stirred at ambient temperature for 15 minutes. 0.415mL of 3-pyridinecarboxaldehyde was added via microlitre pipette. The reaction mixture was stirred until all reactants dissolved and give a yellow solution. The reaction mixture was stirred at ambient temperature for 18 hours.

The product mixture gave a dark red solution without significant precipitate. 10 mL of deionized water was added to the mixture and a suspension of fine powdery solids form. The precipitate, **Sample 3**, was collected by suction filtration.

0.671mL of 1-acetonaphthone was added to a stirred solution sodium hydroxide pellet dissolved in 10mL of water and 25 mL of 85% ethanol. The mixture was stirred at ambient temperature for 15 minutes. 0.415mL of 3-pyridinecarboxaldehyde was added to the mixture. The reaction mixture was stirred until all reactants dissolved and gave a yellow solution. The reaction mixture was stirred using at ambient temperature for 18 hours.

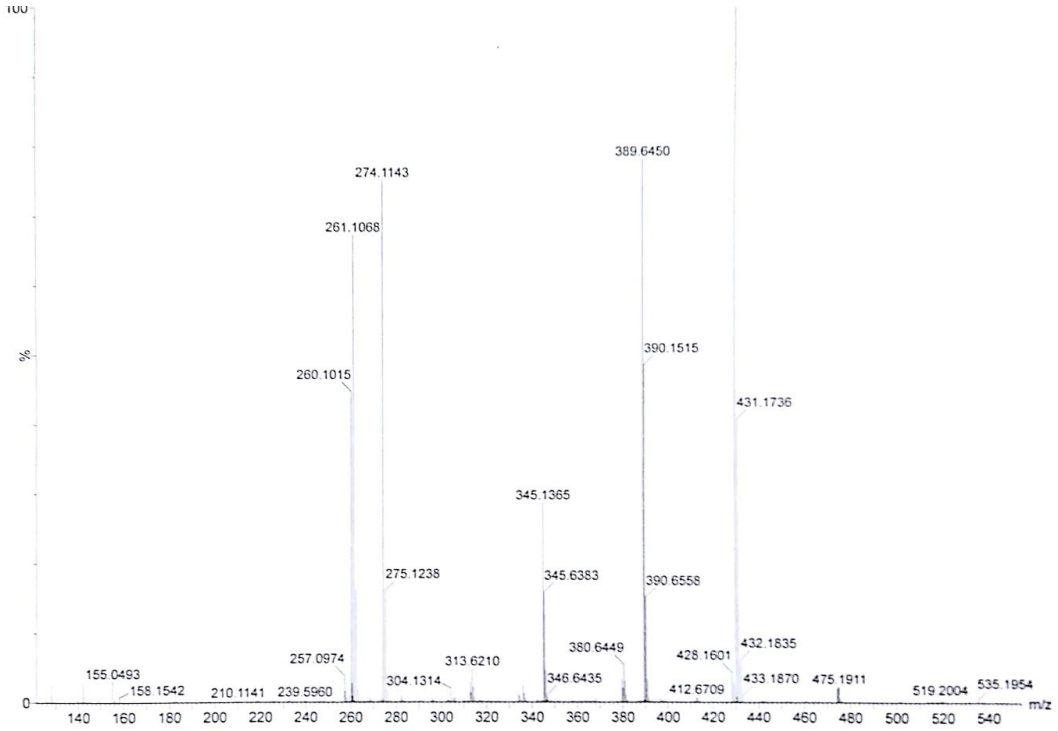
The product mixture gave a dark red solution without significant precipitate. 10 mL of deionized water was added to the mixture and brown precipitate forms. The precipitate, **Sample 4**, was collected by gravitational filtration.

Melting point tests were conducted to determine the melting point ranges of the samples. The results are as tabulated in **Fig. (3)**. Mass spectrum tests were conducted to examine the purity of the product. The results are tabulated in **Fig. (4)**.

Sample number	1	2	3	4
Start of melting /℃	130.0	156.0	131.5	145.0
End of melting/℃	144.0	168.0	145.0	155.0
Melting point range/℃	14.0	12.0	13.5	10.0

Fig. (4). Melting point test results of the samples.

Results of both tests concur on the presence of impurities.



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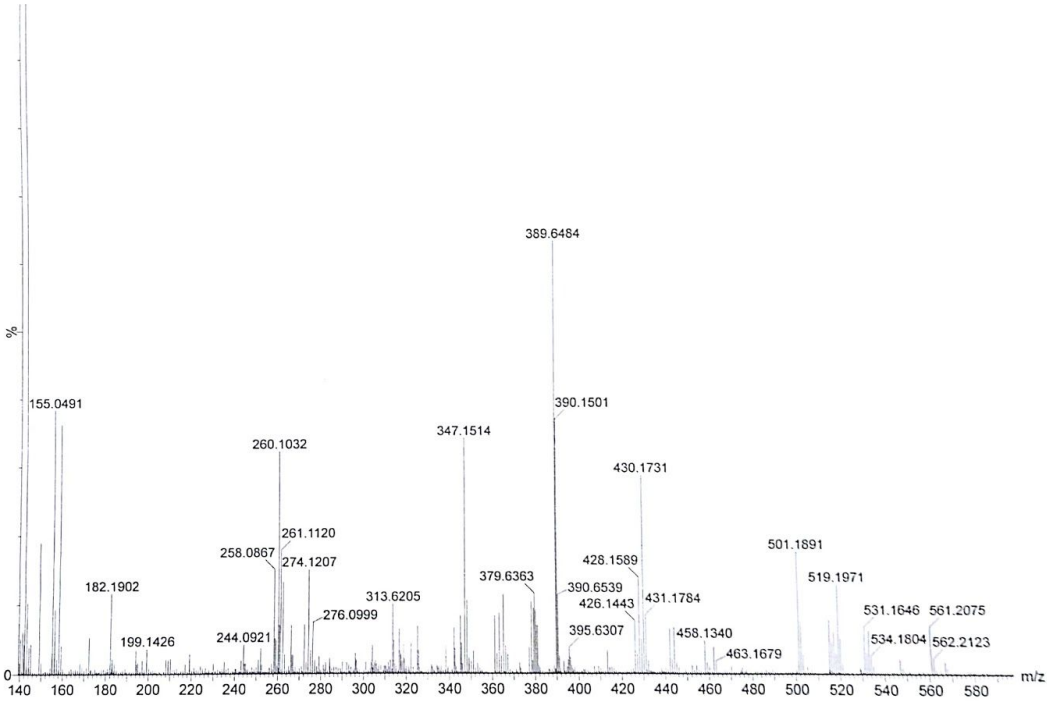

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Fig. (5). 1, Mass spectrum result of **Sample 1**
2, Mass spectrum result of **Sample 2**

3. Results and Discussion

The purity of the starting materials is necessary to the success of the microwave-assisted synthesis which follows. In order to improve the purity, several methods have been attempted to remove the existing impurities. **Sample 2** was selected to run the recrystallisation.

Method A: 0.33g of solids from **Sample 2** was added to 130 mL of deionized water which was heated to 90℃ on a hot plate. The solids proved insoluble in water, hence it is impossible to carry out recrystallization using water.

Method B: A portion of the solids from **Sample 2** was completely dissolved in ethanol by adding 85% ethanol drop by drop. The mixture is heated to 75 degree Celsius to evaporate the solvent and the temperature was maintained for 2 hours. A precipitate is produced. Decomposition Is suspected as the precipitate obtained was black in colour and appeared sticky and sludge-like.

Method C: A portion of the solids from **Sample 2** are dissolved in minimum amount of 85% ethanol in a beaker by adding the solvent drop by drop. The beaker is covered using a piece of

parafilm with a small opening with a radius of approximately 5 mm. The solution was kept in the fridge to ensure a low rate of evaporation. Recrystallisation occurred and solids were formed. The precipitate was undesirable as they appeared oil-like and sticky.

Method D: A portion of the solids from **Sample 2** were dissolved in minimum amount of 85% ethanol by adding the solvent drop by drop. Deionized water is added to the solution until a suspension of fine powdery solids is produced. The precipitate is collected by suction filtration on a Buchner funnel.

Melting point tests and mass spectrum analyses were conducted to determine the purity of **Sample 2** after recrystallisation.

	Before recrystallisation	After recrystallisation using **Method D**
Start of melting/℃	156.0	154.0
End of melting/℃	168.0	160.0
Melting point range/℃	12.0	6.0

Fig. (6). Melting point test results before and after recrystallisation

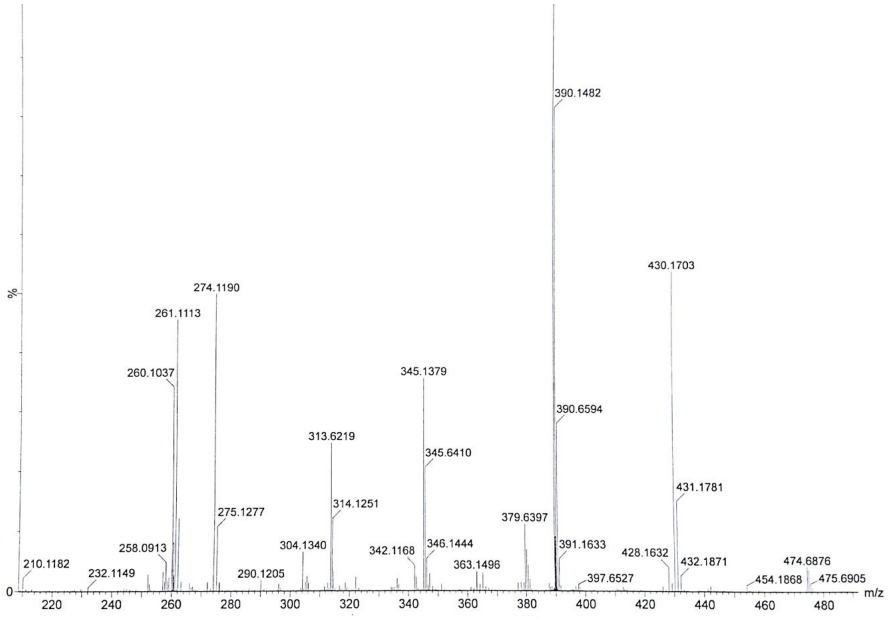

Fig. (7). Mass spectrum result of Sample 2 after recrystallisation

The melting point range of Sample 2 decreases after purification. Nearly all minor peaks in the mass spectrum graph before recrystallisation are not present in the second graph. It is therefore certain that purification via two-solvent recrystallisation is effective.

The two-solvent recrystallisation is also used for the purification of the other samples. Due to the limit of time and limit of apparatus, only the melting point test of recrystallisation of Sample 1 is carried out. The results are consistent with that of Sample 2, as the melting point range decreases from 14.0 ℃ to 4.0 ℃.

4. Conclusion

Time limitation restricts the project from investigating the microwave-assisted synthesis of molybdenum carbonyl complexes. However, studying the preparation and purification of pyridine chalcones is necessary, as it ensures the accuracy of any following experiments.

The reaction of aldol condensation between acetonaphthone and pyridinecarboxaldehyde in a solution containing base produces the target pyridine chalcone. The solids can be precipitated by adding water to the solution and obtained by suction filtration via a Buchner funnel. Two-solvent recrystallisation with water and ethanol as the two solvents can be used to purify the solids obtained.

The pyridine chalcones produced using the method above can be used for further investigations regarding microwave-assisted synthesis.

5. Acknowledgement

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6. References

Sahu, N. K., Balbhadra, S. S., Choudhary, J., & Kohli, D. V. (2012). Exploring Pharmacological Significance of Chalcone Scaffold: A Review. Current Medicinal Chemistry, 19(2), 209-225. doi:10.2174/092986712803414132

Kromer, L., Coelho, A. C., Bento, I., Marques, A. R., & Romão, C. C. (2014). The effect of specific modifications of the amine ligands on the solubility, stability, CO release to myoglobin and whole blood, cell toxicity and haemolytic index of [Mo(CO)4(NR3)2] complexes. Journal of Organometallic Chemistry, 760, 89-100. doi:10.1016/j.jorganchem.2013.12.009

Ardon, M., Hogarth, G., & Oscroft, D. T. (2004). Organometallic chemistry in a conventional microwave oven: The facile synthesis of group 6 carbonyl complexes. Journal of Organometallic Chemistry, 689(15), 2429-2435. doi:10.1016/j.jorganchem.2004.04.030

Ahmad, M. R., Sastry, V. G., Bano, N., & Anwar, S. (2016). Synthesis of novel chalcone derivatives by conventional and microwave irradiation methods and their pharmacological activities. Arabian Journal of Chemistry, 9. doi:10.1016/j.arabjc.2011.09.002

Marradi, M. (2005). Molybdenum Hexacarbonyl [Mo(CO)6]. Synlett, (7), 1195-1196. doi:10.1055/s-2005-865206

Rohrmann, E., Jones, R. G., & Shonle, H. A. (1944). The Use of Chalcones in the Synthesis of Medicinal Intermediates. Journal of the American Chemical Society, 66(11), 1856-1857. doi:10.1021/ja01239a012

"Hexacarbonylmolybdenum (CHEBI:30508)". Chemical Entities of Biological Interest (ChEBI). UK: European Bioinformatics Institute.

Faller, J. W. (2001). Hexacarbonylmolybdenum. Encyclopedia of Reagents for Organic Synthesis. doi:10.1002/047084289x.rh004

Toda, F., Tanaka, K., & Hamai, K. (2010). ChemInform Abstract: Aldol Condensations in the Absence of Solvent: Acceleration of the Reaction and Enhancement of the Stereoselectivity. ChemInform, 22(8). doi:10.1002/chin.199108095