Microwave Assisted Synthesis of Potassium Hydrotris (3,5-dimethyl-1H-pyrazol-1-yl)borate (KTp*)

Dr. Hussain Ibrahim Alarabi ***Dr. Hamid Aboagila Alqamoudy***
Department of Chemistry - Faculty of Science, Zawia
Zawia University

Abstract :

Microwave-assisted synthesis of the scorpionate ligand, potassium hydrotris(3,5-dimethyl-1H-pyrazol-1-yl)borate (KTp), by the reaction of potassium tetrahydroborate (KBH_4) with 3,5-dimethylpyrazole (Pz*) has been investigated. All reaction parameters, including temperature, time and power, have been investigated and optimized. The reaction conditions were varied and the product was monitored by infrared spectroscopy. The microwave method has been compared with the classical reflux method. The microwave method has been found to give higher reaction yield and consume less time.*

Keywords :

Microwave; scorpionate; tris(pyrazolyl) borate; ligand.

1. Introduction:

The use of microwave technology in organic synthesis has become common but its application in other fields such as coordination chemistry and materials science is not quite as developed. This synthetic technique is based on the observation that some reactions proceed much faster and with higher yields under microwave irradiation as compared to conventional heating. In many cases, reactions that normally require many hours at reflux temperature under classical conditions can be completed within several minutes or even seconds in a microwave oven. Until the mid-1980s, microwave heating had been used in the chemical laboratory only in some drying procedures. In 1985 and 1986, the first publications describing the use of microwave ovens for chemical digestions and chemical synthesis appeared in the literature.[1,2] Since the appearance of those two articles, microwave heating has been one of the most rapidly advancing areas of chemistry and hundreds of papers on this topic appear each year[3,4]. The technology has advanced to the point where a number of manufacturers have been making specialized ovens and vessels for a variety of chemical procedures.

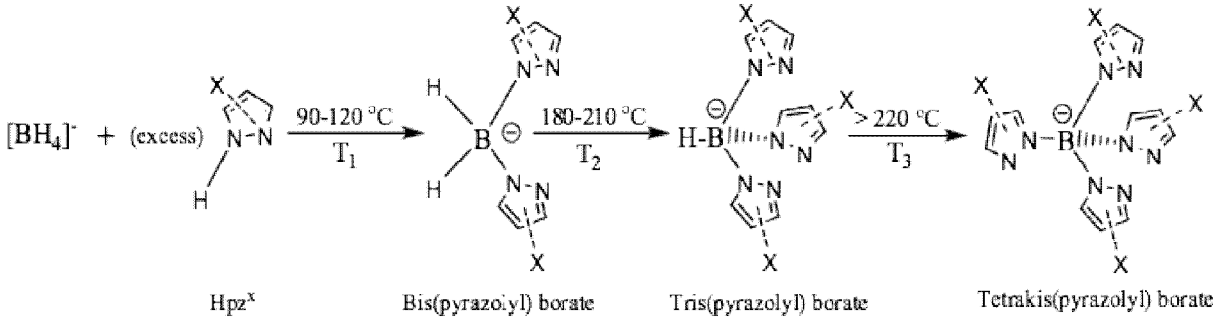
Recent simplifications of microwave reaction enhancement techniques have increased safety and practical utility of the microwave oven for their use in organic laboratories. Recent improvements in controlling reactions have been made possible by microwave equipment for synthesis. These equipments have new tools, such as simultaneous external cooling of the reaction mixture. The reaction vessel is cooled from the

outside by compressed air or with the aid of a cooling fluid while being irradiated by microwaves. This allows a higher level of microwave power to be directly administered to the reaction mixture but will prevent overheating by continuously removing heat. Microwave instruments dedicated to synthesis offer temperature and pressure sensors, built-in magnetic stirring, power control, software operation and sophisticated safety controls. An environmentally friendly method is an important feature of microwave assisted organic synthesis chemistry, since it requires no solvent (dry media synthesis) or very little solvent as an energy transfer medium [5].

Pyrazole-derived ligands, known collectively as poly (pyrazolyl) ligands, are derived from two or more N-deprotonated pyrazole rings bound to a main group atom through one of the ring nitrogens.[6] The basic skeleton of the ligand involves pyrazole units bonded to a main group apex via the nitrogen atoms at the dis- placement of hydrogen.[7] Tris(pyrazolyl) borate (Tp^x) ligands, known as scorpionates, have attracted considerable attention and proven to be extremely popular ligands since their introduction by Trofimenko in 1967.[8-10] They constitute one of the most widely used group of ligands in chemistry. In fact, complexes of tris(pyrazolyl) borates are now known for most of the elements in the periodic table.[11] Because Tp ligands are versatile and readily prepared, they have been used by many ongoing research projects[12,13]. Tris(pyrazolyl) borate ligands have a wide range of applications because of their ease of synthesis, ease of functionalization, and the steric protection which they afford to transition metal centers.[14-21] Their applications include biomedical applications[22], enzyme modeling[23], C-H bond activation[24,25], metal ion

extraction[26], ring-opening polymerization of lactides[15,27], and polymerization of olefins[28].

Synthesis of poly(pyrazolyl) borate ligands can be efficiently performed by heating tetrahydroborate ion in excess molten pyrazole[29-32]. As depicted in scheme 1, the degree of pyrazole substitution on the central boron is controlled by temperature adjustment, thus successively giving access to bis-, tris- and tetrakis-(pyrazolyl) borate.



Scheme 1. Synthesis of poly(pyrazolyl)borate.

After completion of the reaction, excess pyrazole is either distilled off, sublimed in vacuo, or washed away with an appropriate solvent and the residue can be directly used for the synthesis of complexes or it can be isolated as a salt.

In this work, we report the investigation of the use of microwave in the synthesis of the scorpionate ligand, potassium hydrotris(3,5-dimethyl-1H-pyrazol-1-yl)borate (KTp*), by the reaction of potassium tetrahydroborate (KBH_4) with 3,5-dimethylpyrazole (Pz*)

2. Experimental:

2.1.Chemicals and Materials:

Hydrazine sulphate, 2,4-pentanedione, ether, petroleum ether, sodium chloride, anhydrous potassium carbonate and potassium tetraborohydrate were of analytical grade and were used without further purification, table (1).

Table 1. List of chemicals used in the research

Chemicals	Company
KBH_4	Rledel-dehaen AG seelze-Hannover
2-4pentanedione	Avocado Research chem.calsLtd
Hydrazinium Sulphate	BDH chemicals Ltd poole England
Toluene	Riedel-edhaen or Avonchem
N-hexane, $CHCl_3$, MeOH, Toluene, Ether, Acetone	Breckland scientific supplies - BDH chemicals Ltd poole England - Fluka - Fisher Chemicals
petroleum ether (60-80°C)	Eurostar Scientific Limited

2.2. Instruments:

Microwave assisted syntheses were carried out in a Milestone microwave extraction system (start E). Infrared spectra were recorded on an IR spectrometer Varian 660. ^{13}C NMR and ^{1}H NMR spectra were

recorded on a Bruker at 400 MHz spectrometer. Chemical shifts are reported in ppm relative to tetramethylsilane (TMS).

2.3. Syntheses:

2.3.1. Synthesis of 3,5-dimethylpyrazole (Hpz) (1):*

Acetyl acetone 10.2mL (9.94g, 0.09mole) was added dropwise to a stirred solution of hydrazine sulphate (33g, 0.25mole) (200ml, 2.5M NaOH) at 15^0C. The mixture was stirred at room temperature for 1 hour. After that, 100ml of water was added and the mixture was stirred to dissolve inorganic salts. The mixture was transferred to a 500mL separatory funnel and shaked with 50ml of ether. The layers were separated and the aqueous layer was extracted with 20ml of ether. The combined ethereal extracts were washed with saturated sodium chloride solution and drayed with over anhydrous potassium carbonate. The ether was removed by evaporation. The resulting white precipitate was collected (18.12g). Recrystallization of the product was carried out in petroleum ether (60-80°C). Yellow-white crystalline solid was obtained, (75% yield). (m.p: 107-108°C). IR (cm^{-1}): ν(NH) 3200, ν(CH) 2873, 2928, 3036; ^{1}H NMR ($CDCl_3$): δ 10.50 (1H, NH), δ 5.82 (1H, CH), δ 2.28 (6H, CH_3); ^{13}C NMR ($CDCl_3$): 144.23 (C1,3), 103.93 (C2), 12.14 (C4,5).

2.3.2. Synthesis of Potassium Hydrotris(3,5-dimethyl-1H-pyrazol-1-yl)borate (KTp) (2):*

Two methods were used in the synthesis of KTp* (***2***):

Method A (*conventional****):***

A mixture of 3,5-dimethylpyrazole (9.13g, 94.97mmol) and potassium tetrahydroborate (1.30g, 24.10mmol) was heated gradually to 210^{o}C in a 50mL flask by a electromantle. The mixture was kept at this temperature, for 90 minutes, until the di-hydrogen evolution was complete. The mixture was cooled to 100^{o}C and hot toluene (50mL) was added. The product was filtered and washed several times with hot toluene to remove the excess pyrazole. The product was isolated as a white powder. (yield: 73 %); m.p: >380°C ; IR (cm^{-1}): ν(BH) 2436, ν(CH) 2862, 2925, 2960; ^{1}H NMR (DMSO): δ 2.05 (9H, CH_3), δ 3.17 (9H, CH_3), δ 5.53 (3H, CH), δ 8.53 (1H, BH); ^{13}C NMR (DMSO): δ 12.4 (C4), 13.7(C5), 103.2 (C2),141.9 (C1), 144.6 (C3).

Method B (*microwave****):***

A powder mixture of potassium tetrahydroborate (0.07g, 1.29mmole) and 3,5-dimethylpyrazole (0.5g, 5.20mmole) was placed in a glass tube. The tube was put in a TFM vessel on the rotating balance plate inside the microwave. The microwave programs A and B, shown in tables (2) and (3), respectively, were run to completion. The rotor was cooled to room temperature. The product was washed several times with toluene and collected by filtration. The product was isolated as a white powder. (Yield: 90 %); m.p: >380°C; IR (cm^{-1}): ν(BH) 2436, ν(CH) 2862, 2925, 2960.

Table 2. *Microwave program A*

No.	Step	Time	Temperature	Microwave power
1	Heating	2 minutes	200°C	1000 Watt
2	Reaction	3 minutes	200°C	1000 Watt
3	Cooling	5 minutes		
Stirring speed: 60%.				

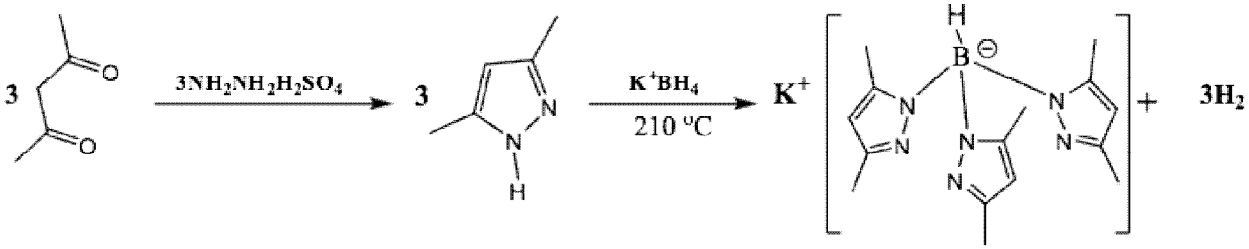
Table 3. *Microwave program B*

No.	Step	Time	Temperature	Microwave power
1	Heating	4 minutes	100°C	900 Watt
2	Reaction	13.5 minutes	100°C	900 Watt
3	Cooling	5 minutes		
Stirring speed: 60%				

3. Results and Discussion:

3.1. Synthesis and Characterization of Potassium Hydrotris(3,5-dimethyl-1H-pyrazol-1-yl)borate (KTp) (2):*

The ligand Potssium Hydrotris(3,5-dimethyl-1H-pyrazol-1-yl)borate (KTp*) (KTp*) **2** was prepared according to the method outlined in scheme (2). Acetylacetone was converted to the pyrazole **1** by reaction with hydrazinium sulphate by a classical reflux method. The pyrazole was reacted with KBH_4 by using the microwave method developed in this work and the classical reflux method. FT-IR, ^{1}H and ^{13}C NMR spectroscopy were used to confirm the identity of the products.



1 **2**

Scheme 2. Synthesis of KTp **(2)***

Infrared spectroscopy was used in the characterization of compounds **1** and **2** synthesized in this work. The IR spectrum of compound **1** (Hpz*) shows a band at 3200cm^{-1} that was assigned to the stretching vibration frequency, $\nu_{(N-H)}$, of N-H. The bands at 2873 and 2928cm^{-1} can be attributed to the stretching vibrations of the aliphatic C-H group. The aromatic C-H group stretching frequency, $\nu_{(C-H)}$, occurs at 3036cm^{-1}.

In compound **2** (KTp*)**,** the IR spectrum, figure 1, shows a band at 2436cm^{-1} that was assigned to the stretching vibration, $\nu_{(B-H)}$, of the B-H group. The C=N group stretching frequency, $\nu_{(C=N)}$, occurs at 1537cm^{-1}, and the C-N group stretching frequency, $\nu_{(C-N)}$, occurs at 1028cm^{-1}. There is a band due to the N-N group stretching frequency, $\nu_{(N-N)}$ at 978cm^{-1}. The bands at 2862, 2925 and 2960cm^{-1} can be attributed to the stretching vibrations of the aliphatic and aromatic C-H groups.

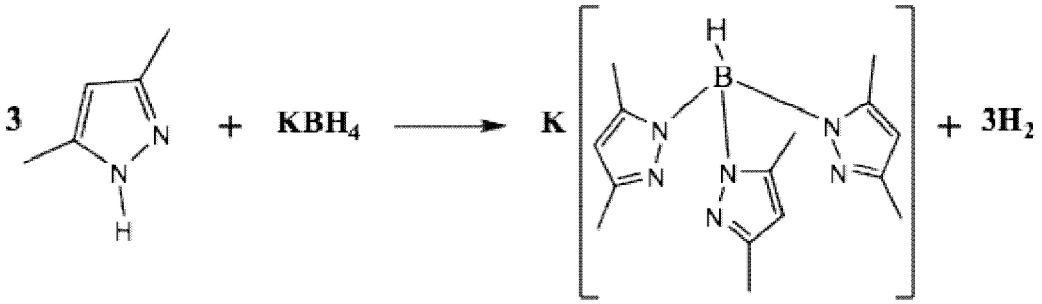
The NMR spectrum of 3,5-dimethylpyrazole (Hpz*) **1** was recorded in $CDCl_3$. The ^{1}H NMR shows one singlet at 2.28ppm (6H) assigned to the methyl protons of the pyrazole ring, a singlet at 5.82ppm (1H) assigned to the C-H proton of the pyrazole ring, and a singlet at 10.50ppm (1H) assigned to N-H proton. The ^{13}C NMR shows a peak at 12.14ppm assigned to the methyl carbons, a peak at 144.45ppm assigned the quaternary carbons, and a peak at 103.93ppm assigned to the C-H carbon of the pyrazole ring.

The NMR spectra of compound **2** (KTp*) has been recorded in DMSO. The ^{1}H NMR shows two singlets at 2.08ppm (9H) and 3.36ppm (9H) assigned to the pyrazole rings methyl protons, a singlet at 5.53ppm (3H) assigned to the C-H protons of the pyrazole rings and a singlet at 8.53ppm (1H) assigned to the B-H proton. The ^{13}C NMR shows two peaks

at 12.45 and 13.68ppm assigned to the methyl carbons of the pyrazole rings, two peaks at 141.95 and 144.63ppm assigned to the quaternary carbons, and a peak at 103.17ppm assigned to the C-H carbon of the pyrazole rings. In 3,5-dimethylpyrazole, the two sets of methyl group protons are equivalent and give a single peak. However, because of the linkages of one of the N atoms in each pyrazole ring with the boron atom in the KTp* ligand, the symmetry of the pyrazole ring is reduced. Therefore, the methyl groups show two resonances in the ^{1}H NMR of KTp*.

3.2. Investigation of the use of Microwave in the Synthesis of Potassium Hydrotris(3,5-dimethyl-1H-pyrazol-1-yl)borate (KTp) (2):*

Tris(pyrazolyl) borate ligands are prepared by the reaction of pyrazoles Hpz with metal tetrahydroborate MBH_4 (M= K or Na) in a 4:1 molar ratio in a solvent by classic reflux method or by heating the solid mixture without a solvent. After completion of the reaction, excess Hpz is either removed by sublimation or washed off with toluene. For example, potassium tris(3,5-dimethyelpyrazolyl) hydroborate has been prepared by the reaction of the pyrazole (3,5-dimethyelpyrazole) Hpz* with potassium tetrahydroborate KBH_4 in a 4:1 molar ratio:



In the present work, the use of microwave technology in the synthesis of potassium tris(3,5-dimethyelpyrazolyl) hydroborate (KTp*) (**2**) has been thoroughly investigated. Three parameters, which affect

microwave synthesis, have been studied. These parameters are energy, temperature and time. They must be controlled to fit with each other and to reach the optimum reaction conditions and give the highest reaction yield. With these parameters varied, the reaction product was identified by infrared spectroscopy.

In the first attempt to synthesize **2**, high energy (1000Watt), high temperature (200^{o}C) and short reaction time were used. The parameters used at 1000watt are shown in table 4.

Table 4. *The parameters used at 1000watt in the synthesis of* ***2***

No.	Step	Time	Temperature	Microwave power
1	Heating	2 minutes	200°C	1000 Watt
2	Reaction	3 minutes	200°C	1000 Watt
3	Cooling	5 minutes		

The result was excellent, and the reaction was completed in a high yield. This was shown by the measured IR spectrum of the product shown in figure 1.

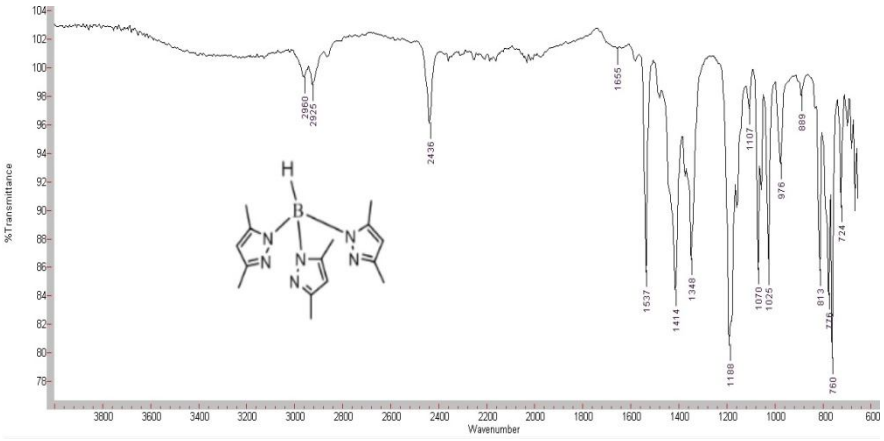


Figure 1. *Infrared spectrum of* ***2*** *synthesized at 1000 and 900watt*

The energy and temperature in this first attempt were very high and caused some concern regarding the microwave and the safety in the laboratory because the reaction is accompanied by the release of the flammable hydrogen gas. Hence, several attempts were made to reach completion of the reaction and obtain a high reaction yield while reducing the energy and temperature and increasing reaction time. The most prominent attempts that have been made can be summarized as follows:

- At 600watt, the reaction did not occur regardless of how much the temperature and time were increased.
- At 700watt, the reaction did occur but did not go to completion and there were a noticeable amount of unreacted pyrazole and KBH_4 in all attempts. Table **5** shows the parameters used at 700watt.

***Table 5**. The parameters used at 700watt*

No.	Step	Time	Temperature	Microwave power
1	Heating	2 minutes	200°C	700 Watt
2	Reaction	3 minutes	200°C	700 Watt
3	Cooling	5 minutes		

The measured IR spectrum, figure **2**, revealed that there are two bands in the B-H stretching region at 2437 and 2362cm^{-1}.

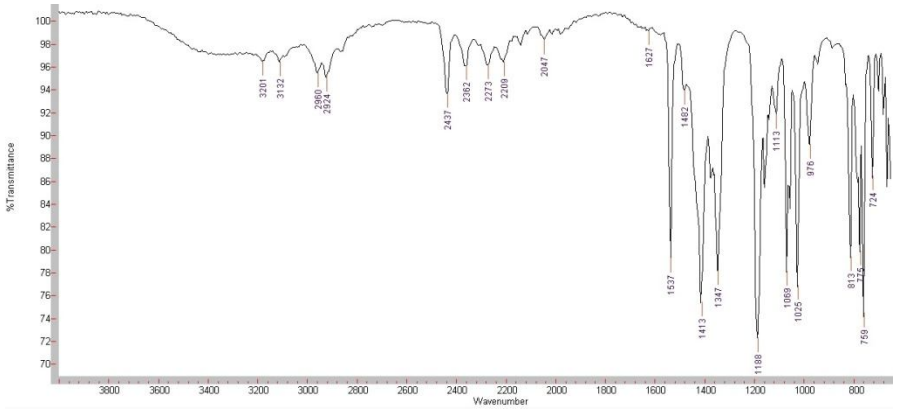
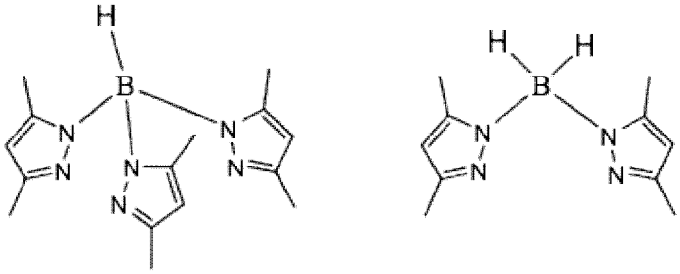


Figure 2. *Infrared spectrum of the product synthesized at 700watt*

This indicated that the product contained bis(pyrazolyl)borate and probably the intended tris(pyrazolyl)borate, in other words, the reaction did not go to completion.



Tris(pyrazolyl)borate Bis(pyrazolyl)borate

There are also bands at 2273, 2209 and 1113cm^{-1}, which indicate the presence of unreacted KBH_4 and bands at 3201 and 3132cm^{-1}, which indicate the presence of unreacted pyrazole. In conclusion, at 700watt the reaction product was a mixture of bis(pyrazolyl)borate, the intended tris(pyrazolyl)borate, unreacted pyrazole and unreacted KBH_4.

At 800 watt, the reaction was completed in all attempts, but the percent yield was low. Table **6** shows the parameters used at 800watt.

Table 6. *The parameters used at 800watt*

No.	Step	Time	Temperature	Microwave power
1	Heating	4minutes	100°C	800 Watt
2	Reaction	6 minutes	100°C	800 Watt
3	Cooling	5 minutes		

In all attempts, the yield was low, and contained some unreacted KBH_4. This was shown by the measured IR spectrum of the product (figure 3). The presence of only one peak in the B-H stretching region, at 2436cm^{-1}, indicated the formation of tris(pyrazolyl) borate.

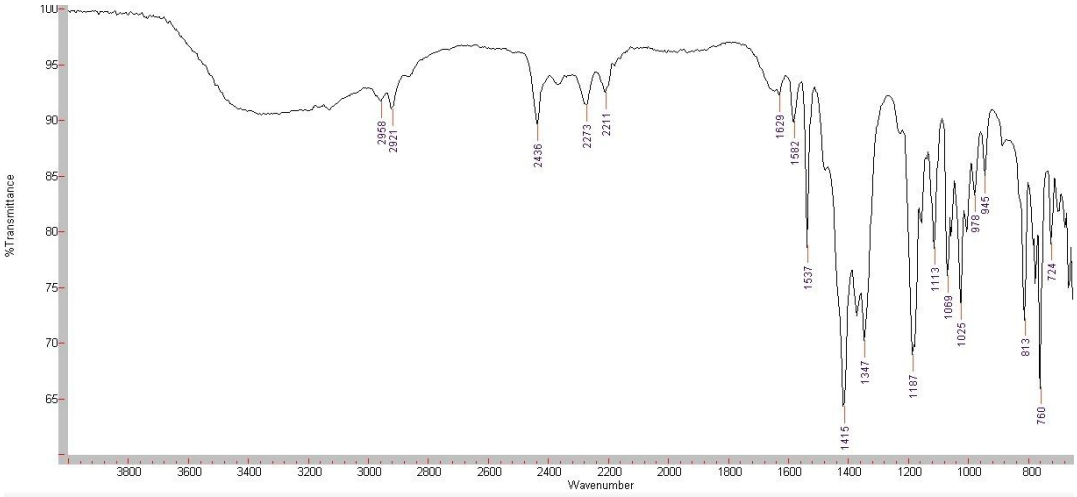


Figure 3*. Infrared spectrum of the product synthesized At 800watt*

At 900watt, the reaction was completed, the reaction yield was high. Tables (7), (8), (9) and (10) show the parameters used at 900watt.

Table** 7. The parameters used at 900watt in the synthsis of **2

No.	Step	Time	Temperature	Microwave power
1	Heating	4 minutes	110°C	900 Watt
2	Reaction	12 minutes	110°C	900 Watt
3	Cooling	5 minutes		

***Table 8**. The parameters used at 900watt*

No.	Step	Time	Temperature	Microwave power
1	Heating	4 minutes	100°C	900 Watt
2	Reaction	13.5 minutes	100°C	900 Watt
3	Cooling	5 minutes		

***Table 9**. The parameters used at 900watt*

No.	Step	Time	Temperature	Microwave power
1	Heating	4 minutes	100°C	900 Watt
2	Reaction	12.5 minutes	100°C	900 Watt
3	Cooling	5 minutes		

Table 10. *The parameters used at 900watt in the synthesis of 2*

No.	Step	Time	Temperature	Microwave power
1	Heating	4 minutes	80°C	900 Watt
2	Reaction	13.5 minutes	80°C	900 Watt
3	Cooling	5 minutes		

The effect of reaction time and temperature was investigated by varying these parameters. When the temperature was above 80°C, small amount of dark yellow material were observed on the edges of the reaction mixture which indicated some decomposition of the product. Therefore, the optimum temperature was set at 80°C. At 80°C, the reaction time was set at 13 minutes because the reaction was not completed when the time was decreased to less than 12 minutes.

One major disadvantage of the use of microwave in the synthesis of **2** is that the total weight of the reaction mixture must not exceed one gram. This means that the ligand has to be synthesized in small portions. One attempt was made to increase the amount of reaction mixture to above 1.0g. When 1.0g of pyrazole was mixed with 0.14g of KBH_4, giving a total weight of 1.14g, a black material was obtained and the glass tube containing the reaction mixture was broken. It was clear that the amount of hydrogen gas released was too high and caused an expulsion. As a result, it was decided to maintain the reaction mixture's total weight bellow 1.0g. The amounts pyrazole and KBH_4 were set at 0.5g and 0.07g, respectively.

4.Conclusion:

The synthetic and characterization results obtained in this work, lead to the conclusion that the (KTp*) ligand **2** can be synthesized in the solid form using microwave assisted synthesis instead of the classical reflux method in a 1:4 ratio between KBH_4 and 3,5-dimethylpyrazole **1** (Hpz*). The microwave method was easier than the classical method. The microwave assisted synthesis of the ligand gives higher percentage yield, and saves reaction time and solvent. One major disadvantage of the use of microwave in the synthesis of **2**, is that the total weight of the reaction mixture must not exceed one gram. This means that the ligand has to be synthesized in small portions.

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