

Medical Science Sample

Case Report

Acute Appendicitis Masquerading as Distal Intestinal Obstruction Syndrome in Adult

Cystic Fibrosis

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~~Overshadowed by Sino-pulmonary infections,~~With the improved life expectancy in ~~c~~Cystic ~~f~~Fibrosis (CF) patients, there has been an increase in ~~commonly affects~~gastrointestinal ~~organs~~manifestations because of secretory and motility dysfunction. Infrequently, these changes ~~can~~ result in ~~d~~Distal ~~i~~ntestinal ~~O~~bststruction ~~s~~ndrome (DIOS), an ~~more and more increasingly~~ diagnosed gastrointestinal ~~condition~~entity in adult ~~Cystic Fibrosis~~CF patients. We present ~~the~~a case ~~of a~~ 22-year-old ~~man~~le who presented to our hospital with right lower quadrant abdominal pain, ~~with~~Despite the suspicion of acute appendicitis, ~~the patient and~~was subsequently diagnosed ~~as with~~ DIOS. Our case highlights the importance ~~of considering~~ DIOS as ~~a~~ differential diagnosis ~~of for~~ right lower quadrant abdominal pain in CF patients, especially ~~for~~ by physicians working at community hospitals ~~that which~~ may not have a ~~CF~~Cystic Fibrosis care program available.

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1. Introduction

Cystic ~~F~~ibrosis (CF) is a genetic disease ~~of that affects~~ multiple organs. ~~With~~Because of ~~advancements~~ing in the ~~managem~~enting of CF ~~patients~~, patients ~~can~~ now ~~often survive~~ ~~become to~~ adulthood [1]. ~~However, the i~~Improved life expectancy among adult CF patients has ~~given~~riseled to ~~an increase in~~ extrapulmonary, notably gastrointestinal, manifestations, which ~~did not happen~~was previously ~~uncommon~~Distal ~~i~~ntestinal ~~o~~bststruction ~~S~~ndrome (DIOS) continues to be a rising complication in adult CF patients, presenting ~~as with~~ acute abdominal pain ~~like and mimicking~~ an acute abdominal ~~emergency~~.

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2. Case Report

A 22-year-old Turkish-origin ~~man~~le with a past medical history of ~~Cystic Fibrosis~~CF presented with a one-day history of right lower quadrant abdominal pain. He described ~~a~~sharp periumbilical pain that continued to worsen, which then shifted to ~~the~~ right lower quadrant ~~of the~~ abdomen. Prior to the onset of the abdominal pain, he reported ~~experiencing~~ nausea and anorexia for three days. His last bowel movement was two days prior to admission. ~~The patient was also diagnosed with CF~~Cystic Fibrosis at the age of four, and ~~the~~his disease progressed to exocrine

~~pancreatic~~ insufficiency, which was being treated with ~~pancreatic enzymes~~. Upon reviewing the patient's past history, it was noted that he had several episodes of pneumo~~n~~ia, for which he was appropriately treated with antibiotics. ~~N~~otably, no history of constipation or recurrent abdominal discomfort was reported prior ~~to this~~. At home, the patient was prescribed ~~a~~lbuterol inhalation~~er~~ as needed, ~~d~~ornase ~~a~~lfa inhalation~~er~~, ~~a~~ztreonam lysine nebulization, 500 mg ~~a~~zithromycin three times a week, ~~I~~ansoprazole, ~~I~~umacaftor-ivacaftor twice a day, ~~I~~ipase-protease-amylase capsule three times a day, and a multivitamin capsule once a day. ~~The patient was also diagnosed with Cystic Fibrosis at the age of four and his disease progressed to exocrine pancreas insufficiency, which was being treated with pancreatic enzymes.~~ On abdominal examination, he ~~was found to have had~~ diminished bowel sounds and ~~tenderness on right lower quadrant with~~ equivocal rebound tenderness ~~on the right lower quadrant~~. Laboratory analysis showed leukocytosis (~~white blood cell count~~, WBC 13.0 mm/K³; ~~n~~Neutrophils count, 62%) with a normal differential. He had no electrolyte imbalances. Computed ~~t~~omography (~~CT~~) of the ~~a~~Abdomen revealed thickening, ~~and~~ edema around the termi~~n~~al ileum, ~~inflammatory changes in the a~~ colon ~~with inflammatory changes~~, free fluid in the right paracolic gutter adjacent to the cecum, ~~an~~ appendix measuring 5.3×4.6 mm, and reactive lymph nodes (Figures 1 and 2).

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Commented [A8]: Please consider specifying the dosage and form of intake for all drugs to ensure consistency.

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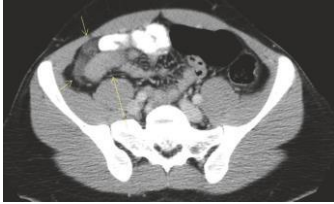


FIGURE 1: Axial abdominal computed tomography scan depicting thickening around the terminal ileum and colon (yellow arrows) along with extraluminal fluid and reactive lymph nodes.

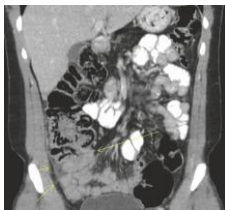


FIGURE 2: Coronal view computed tomography scan with showing thickening of the ileum with a distended appendix (yellow arrows).

measuring 5.34.6 mm, and reactive lymph nodes (Figures 1 and 2). Due to extraluminal fluid and cecal wall edema with inflammation, early acute appendicitis could not be excluded as a possible diagnosis. Surgical intervention was performed, which revealed a ruptured microperforation of a cecal diverticulum and a distended appendix in chronic adhesions, for which he required an appendectomy and partial cecectomy with an intact ileocecal valve (IC valve) valve. Postoperatively, he was diagnosed with DIOS and was subsequently started on Polyethylene glycol. The patient made an unremarkable recovery and was discharged. He was followed up in the outpatient clinic without and did not have any recurrence of any symptoms.

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Commented [A11]: Please consider elaborating on how/why this diagnosis was made postoperatively, or how DIOS was distinguished from appendicitis, as this is unclear here.

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3. Discussion

~~Due to the improved life expectancy of CF patients, DIOS is now being increasingly diagnosed in adult patients with CF. Distal Intestinal Obstruction Syndrome (DIOS) was called a Meconium Ileus equivalent in the past, described by the collection of viscid fecal material within the lumen combined with sticky mucoid intestinal content adherent to the intestinal wall of the terminal ileum and cecum [1].~~ Perez-Aguilar et al. reported ~~a that the~~ prevalence of ~~DIOS was~~ 19.5% (mean age 20.6 years) among 46 CF patients in a retrospective analysis, while Dray et al. ~~conducted a cross-sectional study~~ reporting a 15.8% (mean age 28.9 years) prevalence ~~in among~~ 171 CF patients ~~in a cross-sectional study~~ [2, 3]. ~~Despite the~~ ~~Though there continues to be a~~ limited assessment ~~of on~~ the prevalence of DIOS in adult CF patients, DIOS is ~~considered more~~ common among adults ~~compared to than among~~ children ~~due to because of increased~~ disease progression.

~~Distal Intestinal Obstruction Syndrome (DIOS), previously known as was called a Meconium Ileus equivalent, in the past, described is characterized by the collection of viscid fecal material within the lumen combined with sticky mucoid intestinal content adherent to the intestinal wall of the terminal ileum and cecum [1].~~ Defective intestinal chloride and water secretions into the gut, luminal acidity, and loss of bile salt all contribute to the

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development of DIOS [1]. These patients characteristically present with right lower quadrant pain, nausea, abdominal distension, and failure to pass stools or flatus [1, 3]. In some patients, a palpable right lower quadrant mass ~~can may be appreciated present~~ that may be confirmed on abdominal ~~radiography X-ray~~ [1]. Though abdominal ~~X-rays areradiography is~~ recommended to aid in the diagnosis of DIOS, ~~they areit is~~ inadequate in differentiating ileus from other causes of abdominal pathologies that may present in ~~Cystic FibrosisCF~~ patients [4]. Due to ~~the proximity of~~ the anatomical ~~locationsproximity~~, as well as the overlapping clinical presentations, appendicitis and intussusception may mimic DIOS. ~~This which~~ further leads to diagnostic uncertainty. ~~Overlap of several intra-abdominal pathologies in CF increases the risk of misdiagnosis, especially with acute appendicitis,~~ as these patient's underlying pathologies may be masked ~~in CF patients~~ with pulmonary infections' ~~using~~ antibiotics, ~~as seen in our case~~ [5, 6].

Osmotic laxatives are the cornerstone of bowel regimens for the treatment of DIOS. The most commonly prescribed ~~laxative is p~~Polyethylene Glycol, (PEG)-administerrated at a dose of 20–40 ml/~~kKg/hH~~, ~~up twitho~~ a maximum of 1 ~~H/kg/h~~ for a total of 8 hours, ~~resulting in aachieving~~ fecal effluent consisting of clear fluid, along with ~~the~~ resolution of abdominal pain and constipation [1, 6]. If the diagnosis remains unclear, and thus, requires surgical intervention, ~~ICileoeecal~~ valve resection should be considered to prevent the ~~development and~~ recurrence of intestinal obstruction sequelae ~~and growth~~, especially in adolescents [7].

With the increase in immigration of foreigners ~~intothrough~~ America, inner-city and community hospitals may not be ~~sufficiently~~ equipped with a ~~Cystic FibrosisCF~~ care center; ~~moreover, nor may~~ these hospitals ~~may not~~ have programs in provision, with expertise available to other clinicians involved in patient care. ~~Therefore, our case highlights the significance of considering DIOS as a differential diagnosis in CF patients presenting with right lower quadrant abdominal pain, particularly in hospitals without a CF care program available.~~

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

All authors contributed to the revision and approval of the manuscript.

References

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~~3.~~ X. Dray, T. Bienvenu, N. Desmazes-Dufeu, et al, "Distal intestinal obstruction syndrome in adults with cystic fibrosis," [Clinical Gastroenterology and Hepatology](#)~~Clin Gastroenterol Hepatol~~, vol. 2, no. 6, pp. 498–503, 2004.

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~~4.~~ K. Nassenstein, B. Schwerger, M. Kammer, J. Status, T. Lauenstein, and J. Barkhausen, "Distal intestinal obstruction syndrome in the early postoperative period after lung transplantation in a patient with cystic fibrosis: morphological findings on computed tomography," *Gut*, vol. 54, no. 11, pp. 1662–1663, 2005.

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~~5.~~ Y. Al Abed, Y. W. Hameed, J. W. Roy, J., and A.P.S. & Kumar, A. P. S. (2007). "Appendicitis in an adult patient with cystic fibrosis: a diagnostic challenge," *Gut*, vol. 56, no. (12), pp. 1799–1800, 2007.

~~5.~~

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~~7.~~ J. M. Abraham and C. J. Taylor, "Cystic Fibrosis & disorders of the large intestine: DIOS, constipation, and colorectal cancer," *Journal of Cystic Fibrosis*, supplement 2, pp. S40–S49, 2017.

7. A. Mentessidou, I. Loukou, G. Kampourglou, A. et al, "Long-term intestinal obstruction sequelae and growth in children with cystic fibrosis operated for meconium ileus: expectancies and surprises," [Journal of Pediatric Surgery](#), vol. 2018; 53, no. (8, pp.) 1504–1508 2018.

Life Sciences Sample

Case Report

Methylmalonic Acidemia with Novel *MUT* Gene Mutations

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A 5-year-old boy presented with poor weight gain and recurrent episodes of fever, feeding problems, and lethargy, since from the age of 11 months, and poor weight gain. He was admitted to our hospital and evaluated for metabolic disorders; subsequently, he causes and was diagnosed with methylmalonic acidemia (MMA). He was treated with vitamin B12 and carnitine supplements and has been followed-up for the last 3 years. Mutation analysis by next generation sequencing (NGS), supplemented with Sanger sequencing, revealed two novel mutations in exon 5 and 3 of variants in the *MUT* gene responsible for the methylmalonic acidemia MMA in exon 5 and exon 3. Recently, he developed dystonic movements, including orofacial dyskinesia. With advent of NGS, judicious use of Thus, next generation sequencing NGS along with Sanger sequencing can help in identification of causative possibly pathogenic mutations responsible for various clinical conditions and can help in early diagnosis and appropriate treatment of the conditions.

1. Case Presentation

A 5-year-old boy. The child presented for the first time at the age of 11 months, presented with recurrent complaints of fever, vomiting, poor feeding, and lethargy since the age of 11 months. On examination We observed that the patient he had pallor and tachypnea and was drowsy. Laboratory tests Further evaluation suggested that the patient had was suggestive of high anion-gap metabolic acidosis with ketonuria (urine ketones 3+) and with normal electrolytes, blood sugar (94 mg/dL), vitamin B12, and homocysteine levels. Plasma ammonia and plasma lactate were was 118 units; and plasma lactate was 2.9 units, respectively. Transcranial magnetic stimulation TMS results were as normal, but gas chromatography mass spectrometry analysis of but urine GCMS revealed elevated 3-OH propionic acid [12.39 retention time (RT)] as well as and elevated methyl malonic acid levels [16.92 RT, Suppl Figure 1, in Supplementary Material available online at <https://doi.org/10.1155/2017/8984951>]. Since then, this patient child was on a low-protein diet, and carnitine, biotin, thiamine, and vitamin B12 injections; he Child was thereafter admitted to the hospital on seven multiple occasions (7 times) with acute decompensation and managed as per protocol. Mutational analysis was sent for methylmalonic acidemia (MMA) which showed a single heterozygous missense variant c.976 A>G (p.Arg326Gly) in exon 5 of the *MUT* gene (genomic coordinates: chr 6: 49421405); as a variant of uncertain significance. Chromosomal microarray analysis done did not reveal any major deletion or duplication that which could disrupt the gene. Since exon 3 and exon 6 were not adequately covered by next generation sequencing (NGS), further evaluation by Sanger sequencing for targeted exons was performed done, and a second 2nd

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Commented [A 6]: The significance of the recent developments in the patient's etiology is unclear; this sentence also breaks the flow of this abstract-like

Commented [A7]: The main text for a case report usually begins with a Background/Introduction section that provides readers with relevant background

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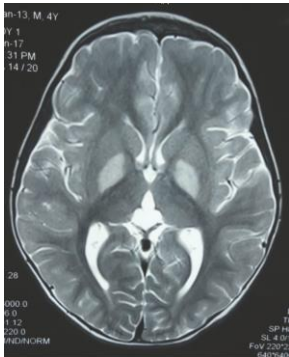
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mutation in exon 3 c.753 G>A (p.=) was identified. The variants were ~~predicted as found to be~~ damaging ~~by the on-SIFT database score (Suppl data), and as They were also predicted to be~~ deleterious ~~by on-Polyphen-2 and Mutation-Taster, but they were and absent not found~~ in the ExAC database. ~~Brain magnetic resonance image MRI brain of the patient (done at from~~ the age of ~~four~~ 4 years) ~~was showing~~ multifocal cystic encephalomalacic changes with surrounding gliosis in deep white matter predominantly in frontoparietal regions (Figure 1). ~~During In the latest admission of the patient to the hospital, we observed -child was found to~~ have fresh neurological findings in the form of perioral tremors, generalized hypertonia, and generalized dystonia with clonus with exaggerated deep tendon reflexes. ~~The patient He~~ was treated with intravenous dextrose and sodium bicarbonate and was continued on carnitine and ~~injection of~~ vitamin B12 ~~injections~~. Plasma ammonia ~~and plasma lactate were was~~ 18 units and lactate level was 4.9 units, ~~respectively~~. ~~Brain magnetic resonance image MRI brain of the patient was repeated, and~~ revealed bilateral basal ganglia hyperintensities, suggestive of metabolic stroke. After the subsidence of acute crisis, he was discharged on carnitine, ~~injection of~~ vitamin B12, ~~injections~~, and trihexyphenidyl. ~~His p~~Parents were counseled regarding ~~the~~ prognosis and for prenatal diagnosis ~~for next~~ subsequent pregnancies.

2. Discussion

MMA presents with lethargy, acidosis, hypoglycemia/hyperglycemia, ketosis, and recurrent episodes. MMA ~~due to MUT gene mutations~~ usually leads to severe phenotypes ~~due to MUT gene mutations~~, and around 35–40% of cases are due to ~~novel~~ mutations [1, 2]. ~~There can be M~~missense or nonsense mutations, deletions, insertions, ~~and so on in the~~ MUT gene and so on can leading to a clinical phenotype.



~~FIGURE 1: The MRI brain -magnetic resonance image of the -5-year-old~~ FIGURE 1: The MRI brain -magnetic resonance image of the -5-year-old ~~boy child with -MUT-related -methylmalonic acidemia MMA showing -predominant~~ boy child with -MUT-related -methylmalonic acidemia MMA showing -predominant ~~frontoparietal -abnormalities -in -the~~ frontoparietal -abnormalities -in -the form of encephalomalacia and gliosis.

The advent of NGS technology has enabled better characterization of mutations in several populations. However, Sanger sequencing remains a useful adjunct in molecular testing ~~in of~~ these cases. ~~It is required to find mutations when there is a strong clinical suspicion for them.~~ It is required to find mutations when there is a strong clinical suspicion for them. ~~Sometimes in NGS, due to because of~~ incomplete coverage of the exons ~~by NGS, Sanger~~ sequencing is required to find mutations, if there is strong clinical suspicion. In this study, by

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In academic writing, the results should be clearly presented and not left at the assumption of the readers

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using both the techniques. ~~By careful use of both techniques, we could find~~ the two *MUT* variants responsible for MMA in the patient. ~~the clinical condition. Previously, in a Saudi study on 60 patients of MMA patients,~~ nonsense, missense, and frameshift mutations were detected across the *MUT* gene [3]. Another study in 43 Chinese patients identified 8 recurrent mutations and 10 novel mutations in the *MUT* gene [4]. A previous Indian study in 15 patients with ~~of~~ clinically diagnosed MMA identified one novel exon 12 mutation in the *MUT* gene with predicted pathogenicity. ~~In this case~~ Here, we identified two novel variants, one in exon 3 and another in exon 5 of the *MUT* gene, ~~and both~~ were labelled as variants of unknown significance (VUS). The exon 3 variant is a synonymous variant, and a different nucleotide change c.753 G>C (p.Lys251Asn) has been reported earlier in ClinVar. Some synonymous variants can also affect ~~the~~ splicing or protein function and lead to clinical phenotypes. The identified exon 5 variant is ~~novel~~ew, but ~~another~~ close variant c.977 G>A (p.Arg326Lys) has been reported in ClinVar. The variants were found to be deleterious on bioinformatic analysis and were ~~absent not found in~~ the ExAC database. Both variants identified in the present case ~~could be responsible for possibly explain the phenotype of~~ MMA phenotype in the child. *MUT*-related MMA has poor prognosis in most cases. Specialized diet and supplements may not improve the outcomes, even if MMA is diagnosed early. Early recognition and appropriate treatment of acute crises are necessary. Metabolic stroke can sometimes occur in the absence of acute metabolic decompensation; ~~thus, so~~ meticulous neurological examination at ~~every each~~ visit is ~~important~~useful. The treatment options for MMA for therapy include early liver transplantation [5]; ~~and possibly~~ gene therapy ~~could also be used~~ in the future. Genetic counseling and prenatal diagnosis ~~could~~ help the ~~se~~ families of the patients in making reproductive decisions in the future.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

Acknowledgments

The authors would like to acknowledge Dhiti Omics Technologies Pvt Ltd for assistance ~~help~~ in mutation analysis.

References

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Physical Science Sample

Structural Prediction prediction of Bisbis(di-p-anisole)-1,4-azabutadiene-bis[triphenylphosphine]ruthenium(II) complex Using using ³¹P NMR Spectroscopy spectroscopy

Author Details

Abstract¹

~~In this study, The present paper reports the use of ³¹P NMR spectroscopy to predict the isomer structures of [bis-4-methoxy-phenyl-[3-(4-methoxy-phenyl)-allylidene]-amino]-bis[triphenylphosphine]ruthenium(II) complex, also known as bis(di-p-anisole)-1,4-azabutadiene-bis[triphenylphosphine]ruthenium(II) complex, was synthesized using: The complexation reaction was carried out (di-p-anisole)-1,4-azabutadiene (compound 1), triphenylphosphine, and ruthenium chloride in 2:2:1 ratio under refluxing conditions of (di-p-anisole)-1,4-azabutadiene (compound 1), triphenylphosphine (PPh₃), and ruthenium chloride in the ratio of 2:2:1 for five 5 hours. The formation of the In addition, ruthenium(II) complex were was confirmed by also characterized using FTIR and UV-Vis spectroscopic analyse to support the formation of ruthenium(II) complexes. ³¹P NMR spectroscopy pic study on ruthenium(II) complexes suggested indicated the presence of that there are three isomers present after the complexation reaction.~~

~~Keywords: ³¹P NMR spectroscopy; FTIR spectroscopy; UV-Vis spectroscopy; Ru complex; Isomers; Structure prediction~~

¹ NMR, nuclear magnetic resonance; FTIR, Fourier transform infrared; UV-Vis, ultraviolet-visible

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1. Introduction

Nuclear magnetic resonance (NMR) spectroscopy is an essential instrument-analytical tool in the field of chemistry as it can help determine-elucidate the structure of a molecule, identify-detect the presence of impurities in a sample, and determine the rates-of formation and-as-well-as degradation of a compound. Even in 1970s, NMR has been used as early as in the 1970s already been used to determine-detect the cancer formation which was identified to be offered a simple, fast, and low-cost method to-for this purpose identify-cancer formation [1-3].

For inorganic chemists commonly use, using of ^{31}P NMR spectroscopy to identify the structures of a complexes containing phosphine ligands is very common [4, 5]. For example, the well-known examples is the use of ^{31}P NMR spectroscopy to determine the mechanism of Wilkinson hydrogenation was determined by ^{31}P NMR spectroscopy, mechanism-based on by identifying the coupling patterns among the phosphine ligands as well as those and also the coupling constants between the phosphine ligands as well as and the rhodium(I) metal centre [6].

In As part of our long-term research interest on the synthesis of in-ruthenium(II) complexes-synthesis, we used the (di-*p*-anisole)-1,4-azabutadiene (**1**) and triphenylphosphine (PPh_3) as the ligands to-for reaction react with ruthenium trichloride under reflux conditions. The structures of the products- resulting complexes were formed, were checked-identified by using ^{31}P NMR spectroscopy, FTIR spectroscopy, and UV-Vis spectroscopy and the results found in the spectra are worth to be discussed in the present communication. For inorganic chemist, using of ^{31}P NMR to identify the structure of a complex containing phosphine ligands is very common [4, 5]. The well-known examples is the use of ^{31}P NMR spectroscopy to determine the Wilkinson hydrogenation mechanism by identifying the coupling patterns among phosphine ligands and also the coupling constants between phosphine ligands as well as rhodium(I) metal centre [6].

2. Methodology

The ruthenium complexes were characterized using UV/Vis, FTIR, and ^{31}P NMR spectroscopy. The IR spectra were recorded using on a Thermo Scientific Nicolet iS10 spectrophotometer in-using KBr disc. The ^1H NMR spectrum for-of compound **1** and ^{31}P NMR spectrum for-of the ruthenium(II) complexes were recorded using on a JEOL JNM-ECA 500 spectrometer with TMS as an the internal standard. The absorption spectra was/were recorded with-on a Jasco V-630 UV-Vis spectrophotometer.

2.1. Preparation of (4-Methoxy-phenyl)-[3-(4-methoxy-phenyl)-allylidene]-amine or (di-*p*-Anisole)-1,4-azabutadiene (**1**)

4-Methoxycinnamaldehyde (1.62 g, 10.00 mmol) was dissolved in 10 mL of ethanol, and followed by the addition of 4-methoxyaniline (1.23 g, 10.00 mmol) which was then added to solution. The reaction mixture was stirred and to obtain a resulted in green-yellow solid, which. The solid was filtered, washed with 5 mL of ethanol, and dried *in vacuo*. The solid was purified by dissolving it in DCM and then layered with hexane via slow diffusion to yield compound **1**. Yield: 2.368 g (88.7%); IR (KBr, cm^{-1}): 3036 (C-H stretching), 1627 (C=N- stretching), 1601 (C=C stretching, aliphatic), 1575 and 1468 (C=C stretching, aromatic), and 1110 (OCH_3 stretching); ^1H NMR (500 MHz, CDCl_3): δ : 8.25 (d, 1H, Hz, -CH=N-), 7.47 (d, 2H, Hz-), 7.18 (d, 2H, Hz-), 7.05 (t, 1H, Hz, H-C α), 6.99 (m, 1H, H-C β), 6.90 (d, 4H, Hz-), 3.83 (s, 3H, OCH_3), and 3.81 (s, 3H, OCH_3); UV-Vis (DCM, /nm): 273, 373; Anal. Calc. for $\text{C}_{17}\text{H}_{17}\text{O}_2\text{N}$ (%): C, 76.38; H, 6.41; N, 5.24; Found (%): C, 76.75; H, 6.31; N, 5.05.

2.2. Preparation of [Bis(4-methoxy-phenyl)-[3-(4-methoxy-phenyl)-allylidene]-amino]-bis[triphenylphosphate]ruthenium(II) or Bis(di-*p*-anisole)-1,4-azabutadiene]-bis[triphenylphosphine]ruthenium(II) Complexes

For the synthesis of bis(di-*p*-anisole)-1,4-azabutadiene-bis[triphenylphosphine]ruthenium(II) complex, $\text{RuCl}_3 \cdot x\text{H}_2\text{O}$ (2.070 g, 1.0 mmol) and PPh_3 (0.525 g, 2.0 mmol) were added to a round-bottom flask containing 10 mL ethanol, and the mixture was then refluxed. Compound **1** (0.316 g, 2.0 mmol) was then added to the round-bottom flask, and the mixture was refluxed again. The resulting pale-maroon solids were was formed, filtered and washed with hexane, and the precipitate was dried *in vacuo*: IR (KBr, cm^{-1}): 3034 (C-H stretching), 1661 (C=N), 1576 (-merged IR band of-for aliphatic and aromatic C=C stretching from aliphatic and aromatic), 1469 (C=C stretching of aromatic ring), and 654 (Ru-C), and 577

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(Ru-N): ^31P NMR (202.5 MHz, CDCl_3) δ : 49.7 (d, 1P, Hz), 47.4 (d, 1P, Hz), 41.7 (d, 1P, Hz), 39.7 (d, 1P, Hz), 35.1 (s, $\text{Ph}_3\text{P}=\text{O}$), and 29.9 (s, 1P); UV-Vis (DCM) (λ): 321 and 382.

On the other hand, the binding of compound **1** to the ruthenium(II) metal center was confirmed using FTIR and UV-Vis spectroscopies. Comparing the IR spectra between of compound **1** and the ruthenium complexes (Figure 4) reveals that the vibrations of C=N and C=C stretching bands are shifted with respect to those in **1**, thereby confirming the binding of **1** to the ruthenium(II) metal center. The C=N stretching band is blue-shifted from 1627 cm^{-1} in the spectrum of compound **1** to 1661 cm^{-1} in the spectrum of the ruthenium complex [97, 108]. In contrast, whereas the C=C stretching IR band appears at 1601 cm^{-1} in the spectrum of compound **1** but it is not clearly shown in the spectrum of the complex, because the IR bands of aliphatic and aromatic C=C bands for aliphatic and aromatic were merging into one a single broad IR band centered at 1576 cm^{-1} . Nevertheless, the two additional IR peaks are present at 577 and 654 cm^{-1} in the fingerprint region of the spectrum at 577 and 654 cm^{-1} , indicating the formation of the respective Ru-N and Ru-C bonds [49].

Figure 4: IR spectra of (a) compound **1** and (b) ruthenium(II) complexes.

The complexation of compound **1** to the ruthenium(II) metal center is further supported by the UV-Vis data spectra as shown in Figure 5. For the case of compound **1**, two absorption bands were observed at 273 and 372 nm, which are assigned to the transitions of the benzene ring and imine group [210], respectively. After the complexation, both the absorption bands undergo significant bathochromic shifts to 321 and 382 nm, respectively, thereby confirming the significant shifts of these two absorption bands have proven compound **1** was successfully bound to the ruthenium(II) metal center via the nitrogen atom from the C=N group and the carbon atom from the aliphatic C=C group in the C=C-N moiety.

Figure 5: UV-Vis spectra of (a) compound **1** and (b) ruthenium(II) complex.

3. Results and Discussion

Characterization of the ruthenium complexes was done using UV-Vis, FTIR, and ^31P NMR spectroscopy. The IR spectra was found by Thermo Scientific Nicolet iS10 in KBr disc. ^1H NMR spectrum for compound **1** and ^31P NMR spectrum for ruthenium(II) complexes obtained through JEOL JNM-ECA 500 spectrometer with TMS as an internal standard. The absorption spectra recorded with Jasco V-630 spectrophotometer.

Once the complexation was confirmed, as discussed above, the ^31P NMR spectrum of the ruthenium complex (Fig. 3) was analyzed for its detailed structural elucidation. The ^31P NMR spectrum of the product shows appearance of two pairs of doublets and one singlet, indicating in the ^31P NMR spectrum for ruthenium complexes (Figure 1) indicate the formation of that there are three isomers (1:1:1 ratio) present as a result of the complexation reaction with the ratio of 1:1:1.

Figure 3: ^31P NMR spectrum for ruthenium(II) complexes.

The singlet at 29.88 ppm reveals that the two PPh_3 units are magnetically equivalent in the ruthenium(II) complex. There can be three possible structures based on this singlet. In the first case, the two PPh_3 units are either located at the axial positions of an octahedron and are trans to each other (Figure 24(a) [117], while in the other two cases, they are located on the or located at equatorial plane, which is only trans only to either one of the C atoms from the C=C bond (Fig. 4(b)) or the N atom from the N=C bond (Figure 24(bc)).

Figure 24: Postulated structures of (a) *trans*- and (b) and (c) *cis*-[bis(*di-p*-anisole)-1,4-azabutadiene]-bis(triphenylphosphine)ruthenium(II).

Meanwhile, the pair of doublets at 41.84 and 39.74 ppm with a coupling constant of 21 Hz is assigned to a *cis*-isomer of the ruthenium(II) complex as shown in Figure 35(a). Lastly, the other pair of doublets at 49.80 and 47.36 ppm with a coupling constant of 38 Hz is assigned to a *trans*-ruthenium(II)

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complex shown in (Figure Fig. 35(b)). It is evident that the difference in the coupling constants between of the ruthenium(II) complexes arises in Figures 3(a) and 3(b) is due owing to the positions of the PPh₃ ligands. The doublet with a smaller coupling constant (t, namely, 21 Hz) is assigned to the cis-isomer because both the PPh₃ ligands are in the equatorial plane. The presence of doublets originate because the for the PPh₃ ligands in the complex is shown in Figure 3(a) because both PPh₃ ligands are trans to different atoms, that is, (nitrogen and carbon) atoms. For In the ruthenium(II) complex shown in as shown in Figure Fig. 35(b), the two PPh₃ ligands are located at the axial positions and are trans to each other. The Lastly, the single peak observed at 35.14 ppm is attributed to the presence of the triphenylphosphine oxide [128].

Figure Fig. 35: Postulated structures of (a) *cis*- and (b) *trans*-[bis(di-*p*-anisole)-1,4-azabutadiene]-bis[triphenylphosphine]ruthenium(II).

On the other hand, the binding of compound 1 to ruthenium(II) metal centre can be confirmed using FTIR and UV-Vis spectroscopy. Comparing the IR spectra between compound 1 and ruthenium complexes (Figure 4), the vibrations of C=N and C=C stretching bands have been shifted after binding to ruthenium(II) metal centre. For C=N stretching band, it shifted from 1627 cm⁻¹ in compound 1 to 1661 cm⁻¹ in ruthenium complex [9, 10], whereas for C=C stretching, the IR band appears at 1601 cm⁻¹ in compound 1 but it is not clearly shown in the complex because the IR bands of C=C bands for aliphatic and aromatic were merging into one board IR band centred at 1576 cm⁻¹. Nevertheless two additional IR peaks are present in the finger print region at 577 and 654 cm⁻¹ indicating the formation of respective Ru-N and Ru-C bonds [11].

Figure 4: IR spectra of compound 1 (a) and ruthenium(II) complexes (b).

The complexation of compound 1 to ruthenium(II) metal centre can be further supported by the UV-vis data as shown in Figure 5. For compound 1, two absorption bands were observed at 273 and 372 nm which are assigned to transition of the benzene ring and transition of the imine group [12], respectively. After the complexation, both absorption bands shifts to 321 and 382 nm, respectively. Significant shifts of these two absorption bands have proven compound 1 was successfully bound to ruthenium(II) metal centre via the nitrogen atom from C=N group and carbon atom from C=C aliphatic group in C=C-C=N moiety. The bathochromic shift of these two absorption bands was due to the backbonding of electrons from Ru to the antibonding orbitals of C=C-C=N moiety in compound 1. This, in turn, has weakened the bond in C=C-C=N [13].

Figure 5: UV-Vis spectra of compound 1 (a) and ruthenium (II) complex (b).

In addition, the data from IR and UV-Vis revealed that the successful binding of compound 1 has bound to the ruthenium(II) metal centre was confirmed from the IR and UV-Vis spectral data.

4. Conclusion

The ³¹P NMR spectra revealed the evidence from ³¹P NMR spectrum has shown the presence of three isomers of the bis(di-*p*-anisole)-1,4-azabutadiene-bis[triphenylphosphine]ruthenium(II) complex in the 1:1:1 ratio of 1:1:1. [Two of the three isomers are those shown in Fig. 5, i.e., one *cis* and one *trans* isomer, while the third isomer could be any one of those shown in Fig. 4. In addition, the data from IR and UV-Vis revealed that compound 1 has bound to ruthenium(II) metal centre.]

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15.

HIGHLIGHTS

- Three isomers were detected for a phosphine-bearing Ru complex using ³¹P NMR.
- Formation of Ru-N and Ru-C bonds were confirmed by FTIR spectroscopy.
- At least one cis isomer and one trans isomer of the complex were formed.

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