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AB initio Calculations and FT-IR and FT RAMAN SPECTRA of 2-chloro 4 methylpyrimidine

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ABSTRACT: FT-IR spectrum of 2-chloro 4 methylpyrimidine in the region 400-4000 cm^{-1} has been recorded in KBr pellet technique with a Bruker IFS-66 Fourier transform spectrometer. FT-Raman spectrum in powder form has been recorded in the region 50-4000 cm^{-1} on a Bruker IFS 66 optical bench with an FRA 106 Raman module attachment interfaced to a microcomputer. Geometry and vibrational wave numbers were calculated using ab-initio calculations with HF method. The results were compared with experimental values. The observed FT-IR and FT-Raman vibrational frequencies were analyzed and assigned to different normal modes of the molecule. Most of the modes have wave numbers in the expected range and the error obtained was, in general, very low. Using PEDs, the contributions were determined for different modes to each wave number. From the PED, it is apparent that the frequency corresponding to C=N stretching contains 88% contribution from the C=N stretching force constant and it mixes with C-CN stretching mode to the extent of 12%.

KEYWORDS: spectra, methylpyrimidine, Raman, wave, spectrometer, module, contributions

I. INTRODUCTION

The vibrational spectrum and structure spectrum of methylpyrimidine's derivatives are important because of the involvement in bioactivities and applications in pharma, agricultural & other domains [1-3]. The medicinal value of heterocyclic compounds helps in the attraction of 2-amino methylpyrimidine derivatives [4, 5].

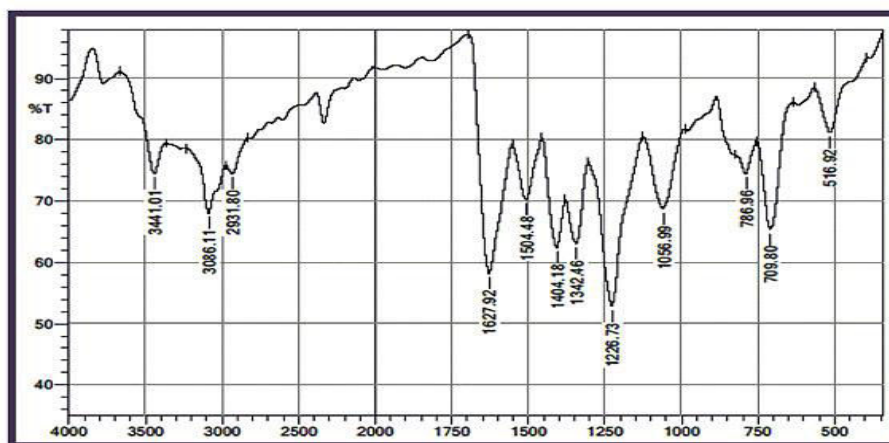
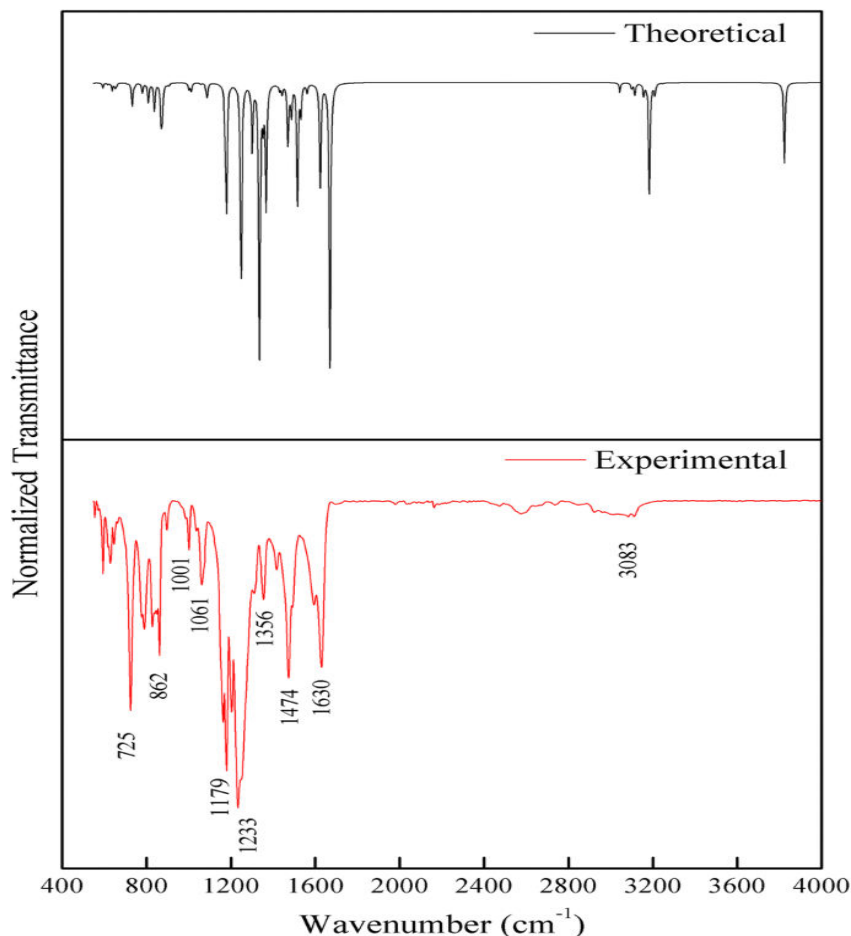


Figure 3: ¹FT-IR spectrum of the title compound

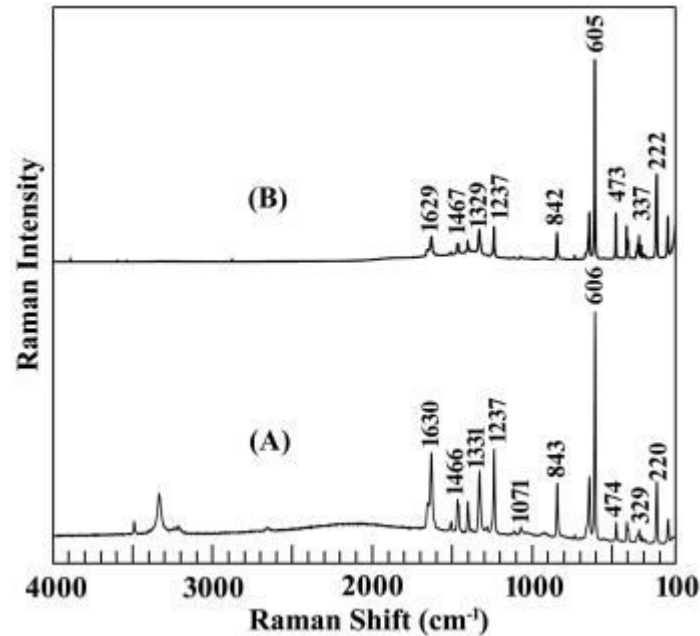
Methylpyrimidine is mixed with ethanol to make it not suitable for drinking. For synthesizing DNA[6], sulfamethylpyrimidine (a drug against various infections of Bacteria and virus), antihistaminic drugs tripeleennamine & mepyramine, water repellents, herbicides and killing bacteria. The Ring formation is found in some chemical compounds even though it's not from methylpyrimidine synthesis.



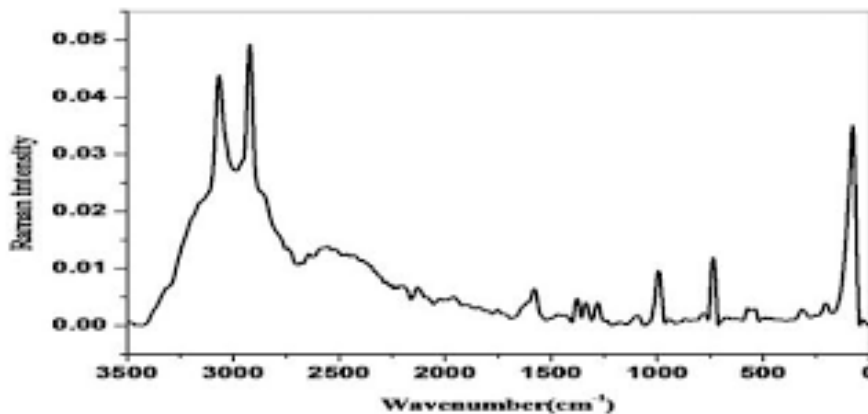
It includes Vitamin B niacin & pyridoxine, isoniazid antituberculosis drug, nicotine and plants which contains nitrogen[7]. From Coal Tar Methylpyrimidine is produced which is the by product of gasification of the coal. The spike in requirement of Methylpyrimidine resulted in synthesizing from acetaldehyde and ammonia in more affordable methods which yields 20,000 tons per year. A hetero aromatic compound which is miscible with water & organic solvents [8]. Crystalline hydrochloride salt is formed when its mixed with HCl which melts at 145-147 °C [9]. During organic reactions, methylpyrimidine behaves both as a "tertiary amine (protonation, alkylation, acylation, and N-oxidation at the nitrogen atom) and also as aromatic compound"(undergoing nucleophilic substitutions). It is electron deficient due to the presence of electronegative nitrogen in the methylpyrimidine ring. So it undergoes soon an electrophilic aromatic replacement reactions which depicts a benzene derivatives; the unbound reactions will not look for protons (prorogated methylpyrimidine is always electron-deficient). Methylpyrimidine inclines to nucleophilic substitution metalation of the ring by strong organ metallic bases not like Benzene [10-11]. Three chemical clusters are noted for the reactivity of methylpyrimidine. Methylpyrimidine enunciates aromatic properties during electrophilic substitution with electrophiles. The capability of methylpyrimidine and its derivatives to oxidize, which helps in forming the amine oxides (N-oxides), which is of the nature of tertiary amines [12]. Lone pair of electrons because of methylpyrimidine`s nitrogen center which is not part of aromatic ring, having the chemical properties of tertiary amines. By donating its pair of electrons to a Lewis acid as in the sulfur trioxide methylpyrimidine complex it can perform as a Lewis base. The complexes forming with transition of metals ions make methylpyrimidine a weak ligand [13]. The geometry of isomeric methylpyrimidines was examined by X-ray crystallography [14], microwave spectroscopy [15] and surface-enhanced Raman spectroscopy [16]. DFT vibrational studies of 5-bromo-2-nitromethylpyrimidine [17], pyridinium complexes [18], and 2-chloro 4 methylpyrimidine [19] were stated. Tautomerization and rotamerization of amino methylpyrimidines has been described [20].

II. DISCUSSION

PASS analysis of the title compound predicts activities the top four activities Taurine dehydrogenase inhibitor, CDP-glycerol glycerophosphotransferase inhibitor, Membrane integrity agonist, Leukopoiesis stimulant with probability to be active (Pa) value were 0.857, 0.829, 0.824 and 0.785 respectively.



High resolution crystal structure of the corresponding inhibitors triclinic ternary complex (6ADH), glycerol-3-phosphate cytidyltransferase (1COZ), beta1 adrenergic receptor (2Y02) and antimicrobial peptidase lysostaphin (4LXC), were downloaded from the protein data bank website and these receptors are used as target for docking study. PatchDock is a very efficient algorithm for protein–small ligand and protein–protein docking and is a geometry-based molecular docking algorithm. [19,20] It is aimed at finding docking transformations that yield good molecular shape complementarity. The algorithm was verified on enzyme–inhibitor and antibody–antigen complexes from benchmark 0.0, where it successfully found near-native solutions for most of the cases. [1,2] The PatchDock algorithm divides the Connolly dot surface representation of the molecules into concave, convex and flat patches. Then, complementary patches are matched in order to generate candidate transformations. Each candidate transformation is further evaluated by a scoring function that considers both geometric fit and atomic desolvation energy.

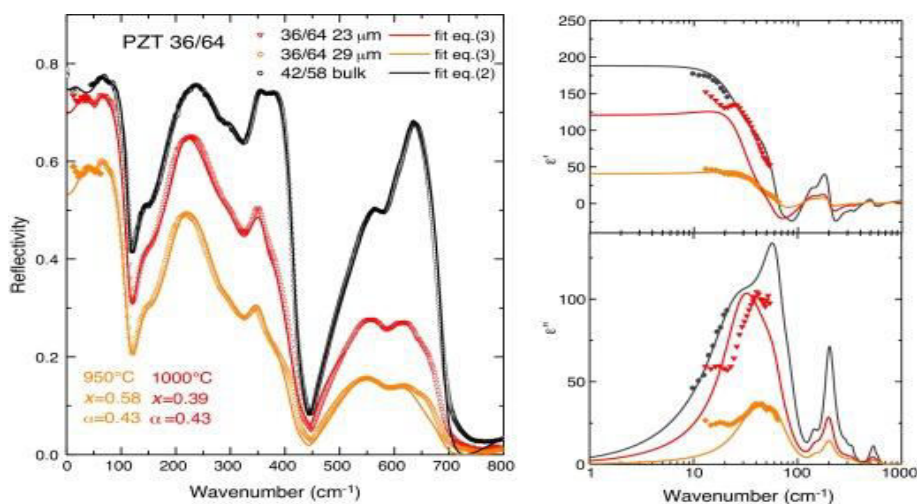


Finally, an RMSD (root mean square deviation) clustering is applied to the candidate solutions to discard redundant solutions. The main reason behind PatchDock's high efficiency is its fast transformational search, which is driven by local feature matching rather than brute force searching of the six-dimensional transformation space. [17,18] The ligand title molecule and proteins retrieved from protein data bank are in PDB format submitted to the PatchDock

Server.PatchDock Server, a web page is generated to show the predicted solutions, downloading and viewing the solutions. The detailed ligand-receptor interactions are viewed using Discovery Studio Visualizer 4.0 software. The ligand binds at the active site of the substrate by weak non-covalent interactions. In the case of ligand with triclinic ternary complex interactions are detailed. Amino acids Glu107 forms H-bond π -alkyl and π -anion interaction with pyridine ring, Gly108 forms H-bond with NH₂ group and Val186, Lys185 forms alkyl interaction with methyl group of the title compound.[3,4]

III. RESULTS

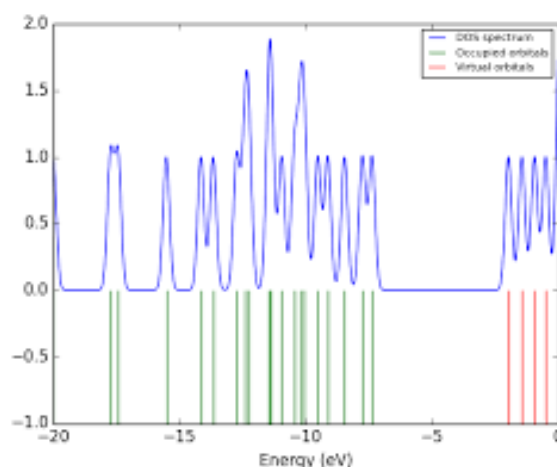
The improved geometric parameters of title compound were deciphered and equated with the before announced experimental values for a comparable compound.



The FT-IR and FT-Raman spectra of 2-chloro 4 methylpyrimidine were recorded and vibrational modes were allotted with the guide of the trial and figured vibrational wave numbers and their TEDs. The second-order perturbation theory investigation of fock network, ESP, energy gap, polarizability and first hyper polarizability counts were performed on x2-chloro 4 methylpyrimidine ($x=2C, 3C, 4C$). [15,16] As indicated by the computed outcomes of ESP, the normal greatest negative electrostatic potential estimation of x2-chloro 4 methylpyrimidine ($x=2C, 3C, 4C$), increment all together in 2-chloro 4 methylpyrimidine.[5,6] Low estimation of HOMO LUMO energy gap proposes the likelihood of intra-molecular charge move in the molecule. This assumes a vital part in the huge increment of β value, which is an additive property to show non-linear optical movement. The NBO investigation uncovers hyper conjugative cooperation, ICT and adjustment of molecule. The examination of NBO estimations of x2-chloro 4 methylpyrimidine ($x=2C, 3C, 4C$) proposes the pharmaceutical properties of 2-chloro 4 methylpyrimidine was more noteworthy than the others. The molecular docking experiments demonstrates that the docked ligand, title compound compound steady complex with pyridine inhibitor and gives a binding affinity value of - 4.75 Kcal/mol and this outcome recommends that the compound may show inhibitory action against cyclin-subordinate kinase 2 (CDK2). It is believed that the results of the current theoretical investigations could support the development of clinical applications.[7,8]

IV. CONCLUSIONS

This study reports the molecular structure and spectroscopic (FT-IR, FT-Raman, UV-Vis, ¹H and ¹³C NMR) investigations of 2-chloro 4 methylpyrimidine. The quantum computational calculations were performed by density functional theory (DFT) method using the B3LYP/6-311++G(d,p) basis set. The vibrational wavenumbers and NMR chemical shifts were matched well with the experimental data. [13,14] The title molecules exhibited two kinds of dimers such as J and H- type dimers. The Mulliken atomic charge distribution for neutral, anionic, and cationic states was performed to predict Fukui function and global softness of the molecules. From the molecular electrostatic potential (MEP) map the reactive sites were identified and the reactivity of the title compounds was examined through the HOMO-LUMO energy gap.[9,10]



Natural Bonding Orbital (NBO) analysis revealed that the presence of stabilization interactions within the title molecules. In addition, the molecular docking studies carried out for title molecules to determine protein ligand interaction to confirm the inhibition activity against *Mycobacterium tuberculosis*. Additionally, the non-linear optical property was also calculated for title molecules.[11,12]

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