Experimental and Therotical Spectral Study of 4-amino-2-hydroxy-6-phenylpyrimidine-5-carbonitrile

J.S.Aher[1*], A.V.Kardel[1], M.R.Gaware[2], D.D.Lokhande[3]

1Organic Chemistry Research Centre, Department of Chemistry, K.R.T. Arts, B.H. Commerce and A.M. Science College, Shivaji Nagar, Gangapur Road Nashik 422 002, (MS), India
2Department of Chemistry, Arts, Commerce and Science College, Nandgaon, Dist. Nashik, (MS)
3Department of Chemistry, KPG Arts, Commerce and Science College Igatpuri, Nashik (MS), India
Affiliated to Savitribai Phule Pune University (Formerly University of Pune), M.S., India
Corresponding Author Email: js_aher@rediffmail.com

ABSTRACT

4-amino-2-hydroxy-6-phenylpyrimidine-5-carbonitrile was synthesized from the benzaldehyde,malanonitrile and urea followed by characterization using IR spectroscopic technique. Quantum chemical calculations were performed to optimize geometry of the title compound by density functional theory method at B3LYP level and 6-311++G (d, p) as basis set. Fundamental vibrational frequencies were calculated theoretically by DFT and HF method and compared with experimental data. The small difference between observed and scaled theoretical frequencies were recorded. Absorption maxima (λmax) is calculated with the help of HOMO-LUMO energy gap. Small energy gap implies an electron density transfer from HOMO to LUMO and implies the reactivity of the title compound.

Keywords: DFT study, HOMO-LUMO, IR spectrum, 4-amino-2-hydroxy-6-phenylpyrimidine-5-carbonitrile, vibrational frequencies.

INTRODUCTION

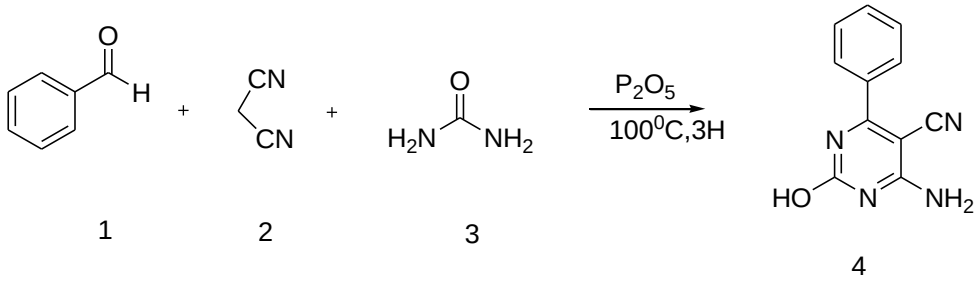
Nitrogen heterocyclic compounds are of special interest, as they constitute an important class of natural and non-natural products, many of which exhibit useful biological activities.[1] Pyrimidines, being an integral part of DNA and RNA impart diverse pharmacological activities. The biological and synthetic significance places this scaffold at a prestigious position in medicinal chemistry research [2] Heterocyclic molecules are of biological interest due to their potential physical and chemical properties [3]. Among these, the pyrimidine compounds occupy a unique position in pharmaceutical chemistry, as they are components of nucleic acids. The important pyrimidine compounds have diverse applications as bactericidal [2] fungicidal [4], analgesics [5], anti-inflammatory [6] and anti tumor agents [7]. Nowadays, the one-step methods involving three-component condensation using different reagents and catalysts are popular in synthetic organic chemistry for the synthesis of heterocyclic compounds. These single step methods are more convenient as compared with two-step strategies as they require shorter reaction times, product isolation easy and give higher yields and recoveries of the product. Peter Russell and George H. Hitchings prepared 2, 4, 6- triaminopyrimidines by refluxing malononitrile with guanidine in alcohol [12]. Biginelli reported one-step synthesis of 3, 4-dihydro pyrimidones by three- component condensation of aldehydes, ethyl acetoacetate and urea [13] in alcoholic medium using strong mineral acid. These compounds possess several pharmaceutical properties like antibacterial, antiviral, anti-inflammatory, anti-

hypertensive. Although a number of papers have been reported concerning the synthesis of pyrimidine derivatives [8, 9], few one-pot syntheses [10, 11] have been published using aromatic aldehydes, cyano ethyl acetate and thiourea. . Ab initio and Density Functional Theory (DFT) methods have become a powerful tool to investigate molecular structure and vibrational spectra in most of the chemical studies. Traditional ab initio methods have been used for many years and there is number of evidence of computational data from which researchers can choose a proper theory level that predicts the physical and chemical properties of the system under consideration [14]. DFT methods can produce good optimization of the chemical system [15]. N Sundaraganesan et al. [16] reported the optimized geometry and vibrational frequencies, of 4-amino-2-hydroxy-6-phenylpyrimidine-5-carbonitrile by HF and density functional B3LYP method with the 6-311G (d, p) basis set. S Chandra et al. reported IR and HOMO-LUMO energy gap of 4-amino-2-hydroxy-6-phenylpyrimidine-5-carbonitrile experimentally and theoretically, by DFT method at B3LYP level using 6-311++ G (d, p) basis set. Literature survey reveals that, optimization and vibrational frequencies for 4-amino-2-hydroxy-6-phenylpyrimidine-5-carbonitrile have not been reported so far. Therefore, the 4-amino-2-hydroxy-6-phenylpyrimidine-5-carbonitrile synthesized by the reported method. The optimized geometries and vibrational frequencies of the title compound was carried out by density functional theory method at B3LYP level using 6-311++G (d, p) basis set.These frequencies were analysed and compared with the experimental data. HOMO and LUMO energy have been used to calculate absorption maxima of the molecule.

EXPERIMENTAL WORK (SYNTHESIS OF 4-AMINO-2-HYDROXY-6-PHENYLPYRIMIDINE-5-CARBONITRILE)

4-amino-2-hydroxy-6-phenylpyrimidine-5-carbonitrile was synthesized from aldehyde (1),malanonitrile (2) and urea (3) in presence of phosphorus pentoxide following scheme-1 one pot efficient procedure .The solid product obtained was purified by crystallisation using ethyl alcohol

Synthesis



1 2 3 4

Scheme-1

MATERIALS AND METHOD

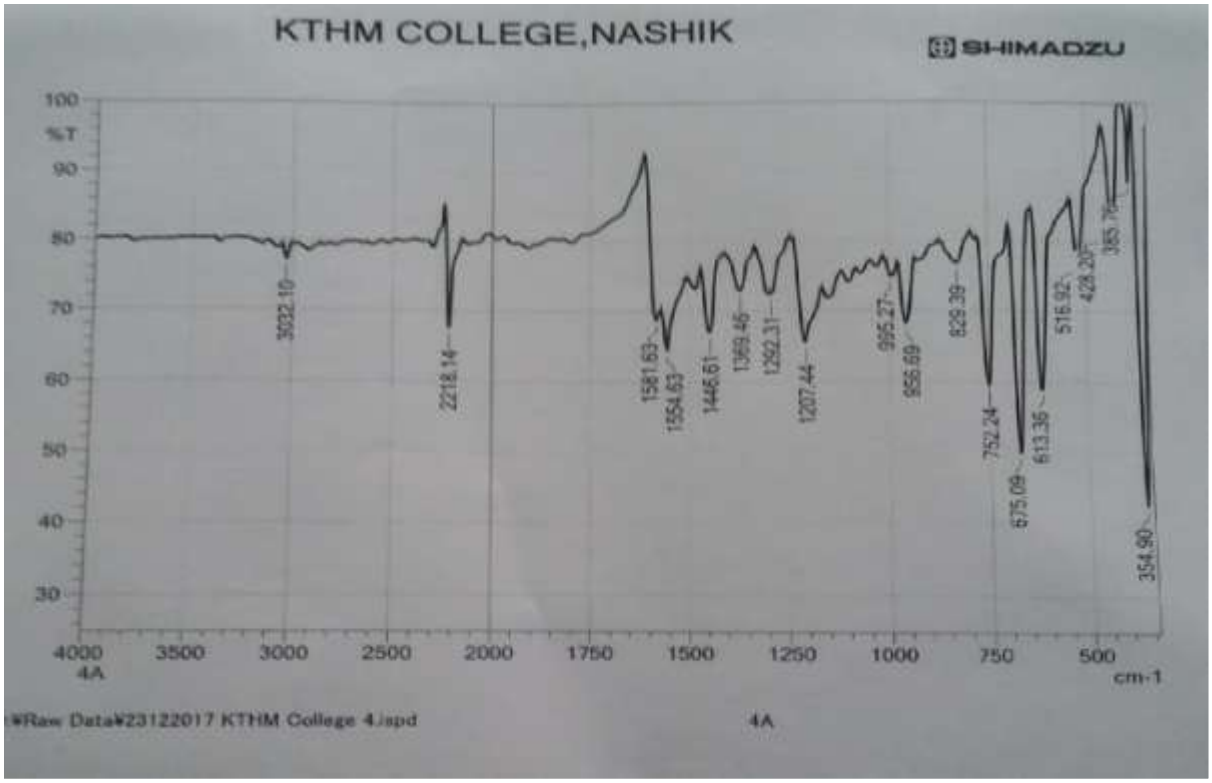
The reagents required for the synthesis of 4-amino-2-hydroxy-6-phenylpyrimidine-5-carbonitrile were analytical grade purchased from Sigma Aldrich and S.D. Fine chemicals and were used without further purification. IR spectrum was recorded as KBr pellets on a Shimadzu FTIR-408 spectrophotometer

Computational Details: Computational calculations were performed on an lenovo Core i3 personal computer using the Gaussian 09W program[19] package without any constraint on the geometry. Geometries of the compound was optimized by DFT/B3LYP at 6-311++G (d, p) basis set to confirm the structure as minima. The vibrational frequency assignments and other parameters were made using Gauss View 5.0 molecular visualization program.

Spectral Data: The spectral data of the compound is shown below. The experimental IR and theoretical IR spectrum are shown in figure 1.

Experimental and computed (scaled) selected fundamental vibrations of 4-amino-2-hydroxy-6-phenylpyrimidine-5-carbonitrile.

Selected normal mode	Calculated IR frequencies cm^{-1} (Scaled)	IR intensities (km) mol	Experimental IR frequencies cm^{-1}	Assignments
66	3995	183.56	3800	O-H str.
65	3817	88.43	3851	N-H str. (1^o amine) (Asym)
64	3687	129.19	3032	N-H str. (1^o amine) (Sym)
63	3247	2.44	3250	Ar-H str. (sym)
58	2459	45.27	2218	C≡N str. (sym)
54	1706	350.40	1581	Ar. C=C str.
51	1554	476.19	1555	C-O str.
50	1409	2.02	1446	Ar-H (ip) bending



(b) IR Spectrum by DFT/B3LYP at 6-311++G (d, p)

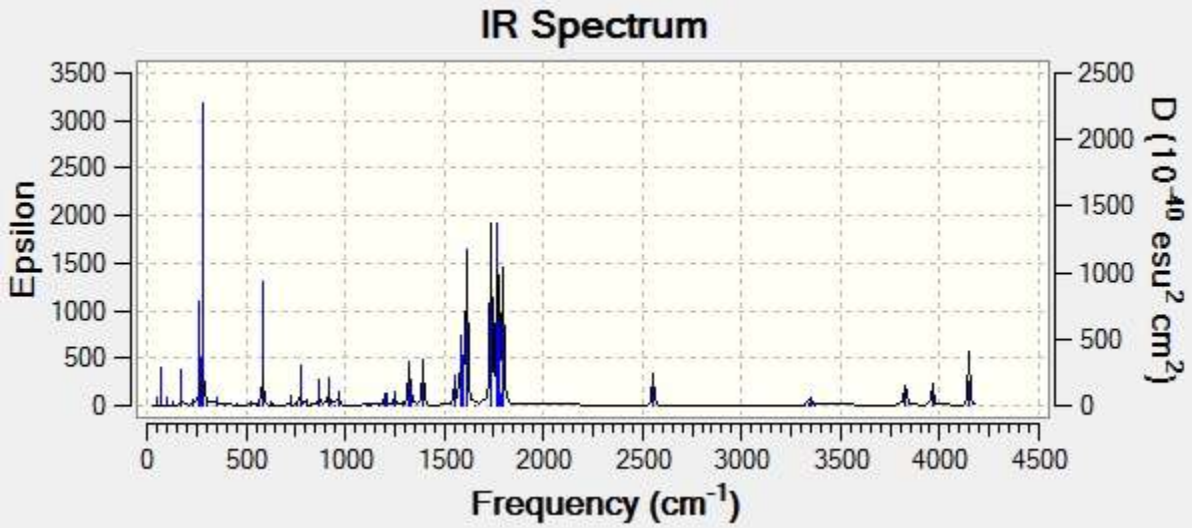
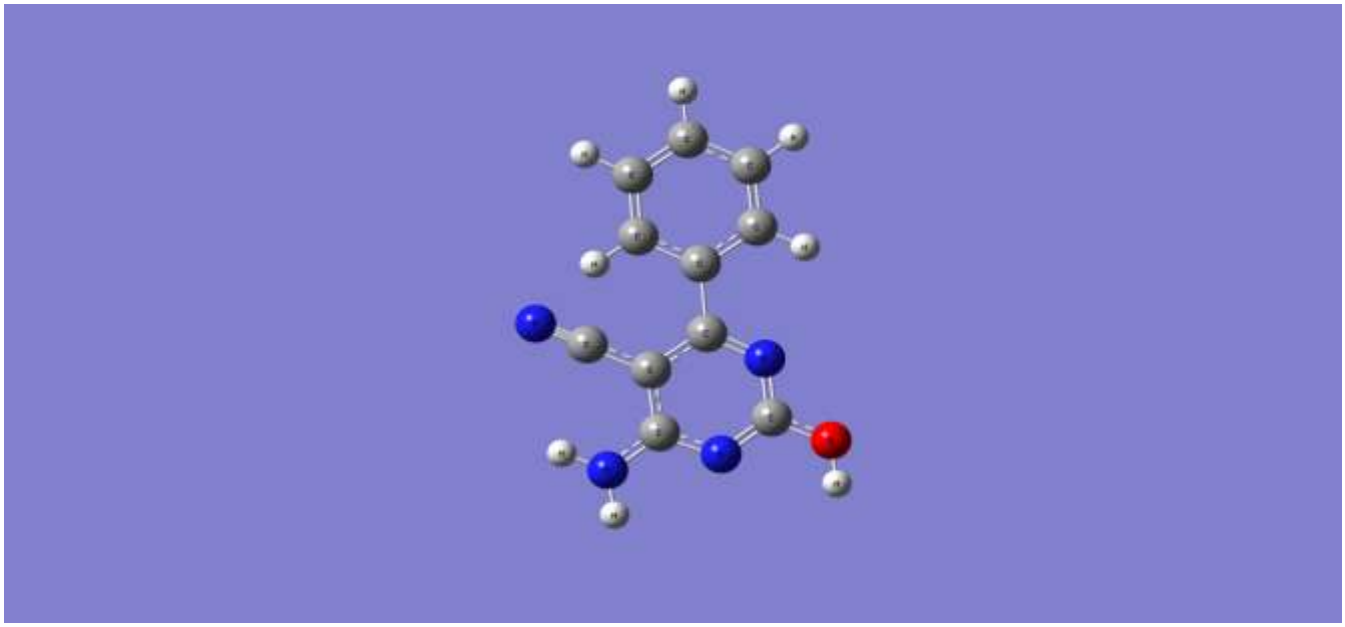


Fig. 1-IR spectrum (Experimental and Theoretical) of 4-amino-2-hydroxy-6-phenylpyrimidine-5-carbonitrile.

Optimized molecule of 4-amino-2-hydroxy-6-phenylpyrimidine-5-carbonitrile.



RESULT AND DISCUSSION

During the progress of reaction, the activated malononitrile is likely to be formed via a Knoevenagel condensation reaction of aromatic aldehydes and malononitrile. These further reacted with urea to form desired product. In the presence of phosphorus pentoxide, reaction proceeds smoothly giving desired products in short time and in a quantitative yield. The formation of the product takes place when aryl aldehydes were reacted with malononitrile to form arylmethylene malononitrile, which subsequently reacted with urea to form desired product. Phosphorus pentoxide is inexpensive reagent and has tendency to absorb water molecules. The latter property of phosphorus pentoxide enhances the rate of reaction, as one water molecules are formed during the progress of the reaction.Therefore isolation of product was much easier.These results introduce another important application of phosphorus pentoxide in organic synthesis.

CONCLUSION

4-amino-2-hydroxy-6-phenylpyrimidine-5-carbonitrile was synthesized and characterised by the IR spectroscopy.The optimized geometries were computed by DFT/ B3LYP at different basis sets using Gaussian 09W package and Gauss view A-5.0. Vibrational assignments were examined by DFT and HF methods of computation and the values predicted by DFT/B3LYP at 6-311++G (d, p) were found to be nearly in good agreement with the experimental values of the title compound.

ACKNOWLEDGEMENTS

Authors are very thankful to Maratha Vidya Prasarak Samaj Nashik for providing infrastructure, Principal, K.R.T. Arts B. H. Commerce and A.M. Science College, Gangapur Road, Nashik-422 002, (MS), India for providing the research facilities.

REFERENCES

[1] Ghorab MM, Heiba MI, Hassan AA, Abd Eiaziz AB, El-Gazzar MG. Antimicrobial evaluation of novel pyrrole, pyrazole, pyrimidine and pyrrolo[2,3-*d*]pyrimidine derivatives bearing sulphonamide moiety. J Am Sci.2011;7(1):1063-72.

[2] Kappe CO. Biologically active dihydropyrimidones of the Biginelli-type – a literature survey. Eur J Med Chem. 2000;35(12):1043-52. [1] Brown, R.C. D. Recent developments in solid phase organic synthesis. J. Chem. Soc. Perkin Trans 1, 1998, 3293-320.

[3] Pershin, N. G.; Sherbakova, L. I.; Zykova, T. N.; Sakolova, V. N. Antibacterial activity of pyrimidine and pyrrolo-(3,2-d)-pyrimidine derivatives. Pharmacol. Taksiko., 1972, 35, 466-71

[4] Metolcsy, G. Structure-activity correlations and mode of action of some selected types of antifungal compounds. World Rev. Pest Contr. 1971, 10, 50-59; [Chem. Abstr. 1972, 76, 82031s].

[5] Regnier, G. L.; Canevar, R. J.; Canevar, J. C.; Douarec, L.; Halstop, S.; Daussy, J. Triphenylpropylpiperazine derivatives as new potent analgetic substances. J. Med. Chem., 1972, 15, 295301

[6] Winter, C. A.; Fisley, E. A.; Nuss, G. W. Carrageenin-induced edema in hind paw of the rat as an assay for anti-inflammatory drugs. Proc. Soc. Exp. Biol. Med., 1962, 111, 544-47.

[7] Suguira, A. F.; Schmid, M.M.; Brown, F.G. Effect of compounds on a spectrum of rat tumors. Cancer Chemother. Rep. Part 2, 1973, 3(1), 231-38.

[8] Mojtahedi, M. M.; Saidi, M. R.; Shirzi, J. S.; Bolourtchian, M. Microwave promoted efficient synthesis of substituted uracils and thiouracils under solvent-free conditions. Synth. Commun., 2002,32, 851-55

[9] Ma, Y.; Qian, C.; Wang, L.; Yang, M. Lanthanide Triflate catalysed biginelli reaction. One-pot synthesis of dihydropyrimidinones under solvent free conditions. Org. Chem., 2000, 65, 3864-68

[10] Kambe, S.; Salto, K. H.; A one pot synthesis of 4-oxo-2-thioxopyrimidine derivatives by the ternary condensation of ethyl cyanoacetate, aldehydes, and thiourea. Synthesis, 1979, 4, 287-89.

[11] Ji-Tai, Li.; Zhi-Ping Han, Lin.; Jun-Fen Li.; Tong-Shuang, One-pot synthesis of 4-oxo-2-thioxohexahydropyrimidines catalyzed by potassium carbonate under ultrasound. Synth. Commun.,2004, 34,2623-31

[12] Russell, Hitchings, H.G. Some 2,4,6-triamino-S-alkyl and SBenzylpyrimidines. J. Am. Chem. Soc., 1952, 74, 3443-44.

[13] Biginelli, P. Aldehyde-urea derivatives of aceto- and oxaloacetic acids. Gazz. Chim. Ital., 1893, 23, 360-413

[14] W. J. Here, L. D. Burke, A. J. Shusterman and W. J. Pietro, "Experiments in Computational Chemistry", Wave-Function, Inc, CA, 1993.

[15] R. G. Parr and W, Yang "Density Functional Theory of Atoms and Molecules", Oxford Univ. Press, 1989.
[16] N. Sundaraganesan, B. Dominic Joshua, C. Meganathan and S. Sebastian; Indian Journal of Chemistry, June 2008, Vol.47A, 821-829