Ph. D. Thesis

PHYSICO CHEMICAL STUDIES OF SOME NEW HETEROCYCLIC COMPOUNDS

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NOVEMBER-2006

PHYSICO CHEMICAL STUDIES OF SOME NEW HETEROCYCLIC COMPOUNDS

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IN

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BY

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UNDER THE GUIDANCE

OF

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Statement under O.Ph.D. 7 of Saurashtra University

The work included in the thesis is my own work under the supervision of **Dr. Shipra Baluja** and leads to some contribution in chemistry subsidised by a number of references.

Date: - - 2006
Place : Rajkot.

(Nikunj S. Kachhadia)

This is to certify that the present work submitted for the Ph. D. Degree of Saurashtra University by **Nikunj S. Kachhadia** is his own work and leads to advancement in the knowledge of chemistry.

The thesis has been prepared under my supervision.

Date: - - 2006
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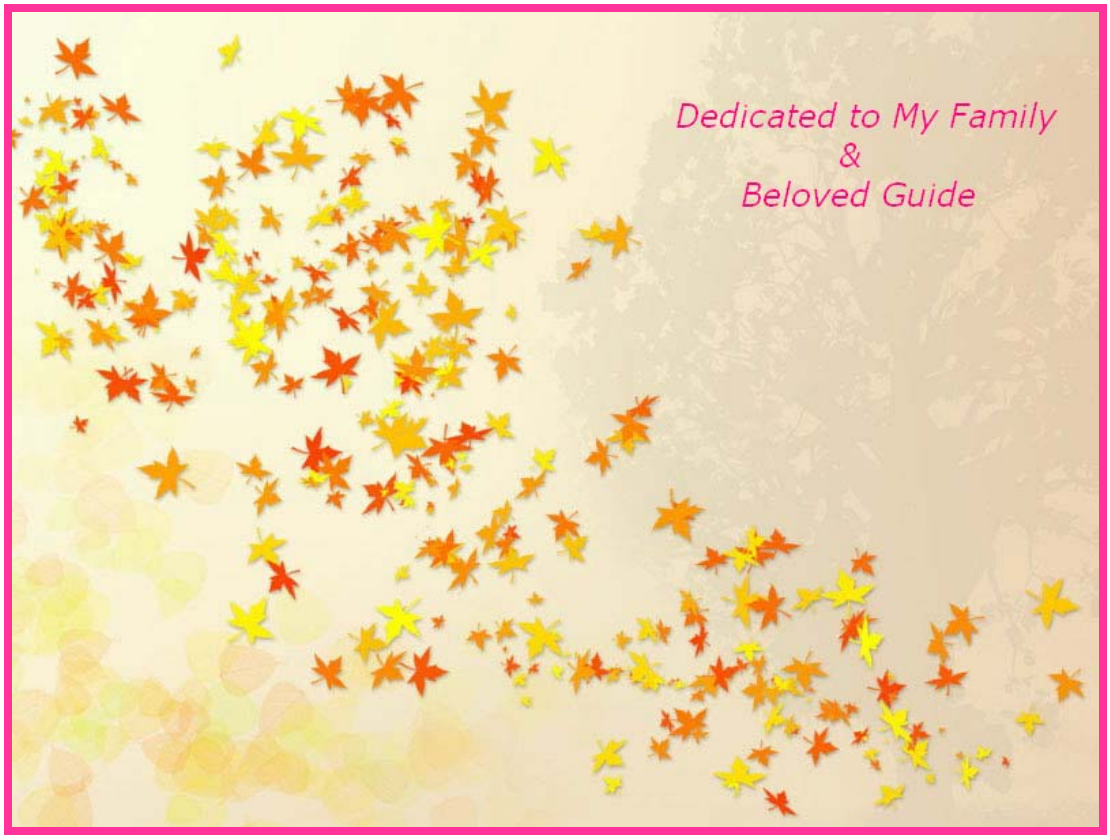
Dedicated to My Family
&
Beloved Guide

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I really very much thankful to the **Saurashtra University** for giving me valuable opportunity of being part of this prestigious institution.

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- **Nikunj S. Kachhadia**

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PHYSICO CHEMICAL STUDIES OF SOME NEW HETEROCYCLIC COMPOUNDS

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SYNOPSIS of the thesis to be submitted to the Saurashtra University for the degree of **Doctor of Philosophy** in Chemistry.

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Subject	: Chemistry
Title	: **"PHYSICO CHEMICAL STUDIES OF SOME NEW HETEROCYCLIC COMPOUNDS"**
Name of the Candidate	: **NIKUNJ S. KACHHADIA**
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Place of work	: Department of Chemistry Saurashtra University Rajkot-360 005. Gujarat (INDIA).

Summary of the work incorporated in the thesis with the title **"PHYSICO CHEMICAL STUDIES OF SOME NEW HETEROCYCLIC COMPOUNDS"** has been described as under.

The present work is divided into three parts.

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PART-1

SYNTHESIS AND CHARACTERIZATION

The chemistry of the heterocyclic compounds is as logical as that of aliphatic or aromatic compounds. The variety of heterocyclic compounds is enormous, their chemistry is complex and synthesizing them requires great skill.

This class of compounds has great applicability as drugs due to their specific chemical reactivity. Further, many natural products contain heterocyclic compounds such as alkaloids and glycosides.

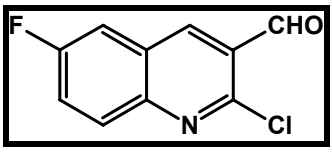
Taking in view of the applicability of heterocyclic compounds, the present work was undertaken to synthesize some new heterocycles bearing quinoline and pyrazole nucleus. All the synthesized compounds were characterized by IR, NMR and mass spectra.

Chapter-1 Synthesis of Quinoline Derivatives

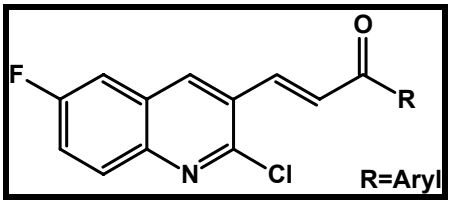
Nitrogen containing heterocyclic compounds like quinoline has received considerable attention in recent years due to their biological and pharmaceutical activities. Quinoline contains a phenyl ring fused to a pyridine ring. Quinoline is also known as benzpyridine.

The chemistry of quinoline derivatives have been of interest due to its useful application in medicine, agriculture and industry

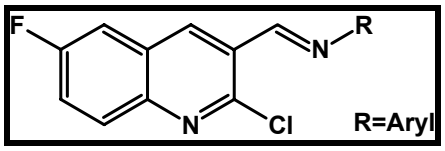
Thus the important role displayed by quinoline and its derivatives for various therapeutic and biological activities prompted us to synthesize of some schiff bases, chalcones, pyrazolines and thiopyrimidines derivatives which are mentioned in following sections.



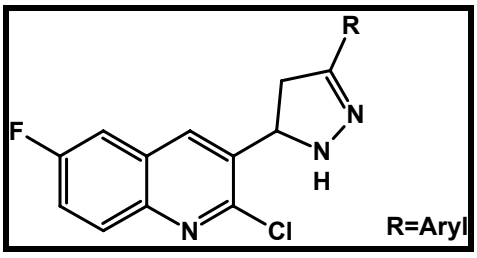
Section-I Synthesis of Chalcones



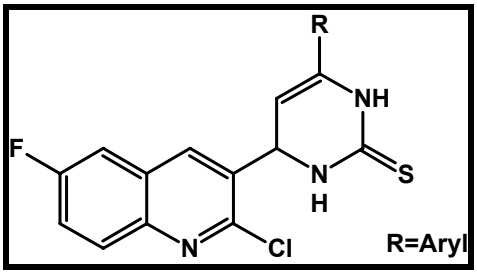
Section-II Synthesis of Schiff bases



Section-III Synthesis of Pyrazolyl Pyrazolines



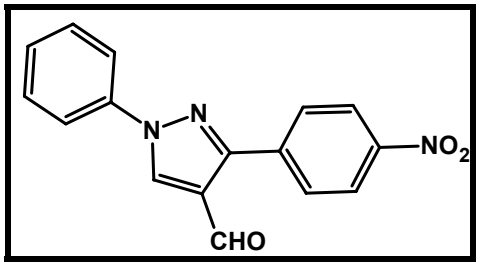
Section-IV Synthesis of Thiopyrimidine



Chapter-2 Synthesis of Pyrazoles Derivatives

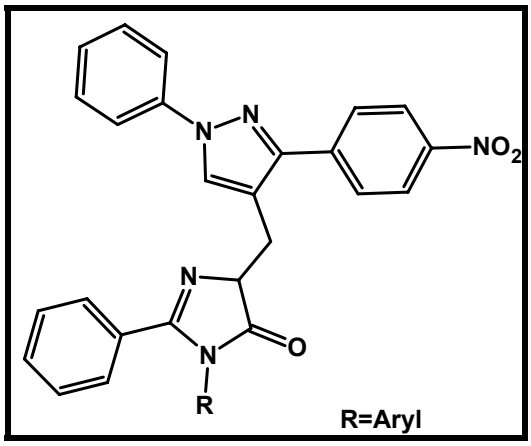
One of the most useful class in heterocyclic compounds is Pyrazole. The pyrazole ring consists of a doubly unsaturated five membered ring containing two adjacent nitrogen atoms.

The research on the chemistry of pyrazoles has been a focus of attention for chemists for a long time, due to their wide spread diversified biological activities like antitubercular, antimicrobial, hypnotics, anti-inflammatory, antitumor, plant growth regulators and are also used as herbicidal and fungicidal.



From this pyrazole moiety various imidazolinones have been synthesized as mentioned in following section.

Section-I Synthesis of Imidazolinones

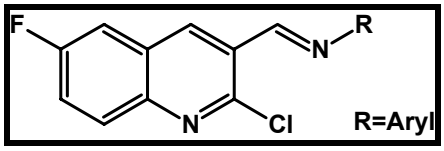


Chapter-3 Comparison of different synthesis methods

In the last few years Microwave-induced Organic Reaction Enhancement (MORE) chemistry has gained popularity as a non-conventional technique for rapid organic synthesis. Many researchers have reported the synthetic utility of MORE chemistry in routine organic synthesis. Compared to traditional processing of organic synthesis, microwave-enhanced chemistry saves significant time and very often improves conversions, clean product formation.

Ultrasound waves are known for their wide applications in various fields like life sciences, medical, cleaning, sonar, electronics, agriculture, oceanography, material science etc. Further, these waves prove to be important in synthetic organic chemistry by lowering the reaction temperature and reaction time. By using these waves, yield can be increased and one can avoid the use of phase transfer catalysts in chemical reactions.

This prompted us to synthesize various Schiff bases using the Microwave-assisted (MW) method, Ultrasound irradiation (US) and Conventional thermal (Con.) method.



PART-2

PHYSICO-CHEMICAL PROPERTIES

Chapter-1 Acoustical Properties

In this chapter, sound velocity studies of some imidazolinone derivatives of pyrazole aldehyde in dimethylformamide (DMF) and dimethylsulfoxide (DMSO) solution were done at 308.15 K with a view to understand the molecular interactions in these solutions. From these experimental data, various acoustical parameters such as isentropic compressibility, Rao's molar sound function, specific acoustical impedance, internal pressure, Vander Waals constant, free volume etc. were evaluated and results are discussed.

Chapter-2 Density and Refractive index

Refractive index is a property of the material and is extremely useful in chemical analysis. In this chapter, the refractive index of imidazolinone derivatives of pyrazole aldehyde were measured in dimethylformamide (DMF) and dimethylsulfoxide (DMSO) solutions at 308.15 K. From the refractive index measurements, the density and refractive index of synthesized compounds were determined.

Chapter-3 Conductance

The solutions of different concentrations were prepared for each imidazolinone derivatives in DMF and DMSO and the conductance of each solution was measured and equivalent conductance at infinite dilution for different compounds was evaluated.

Chapter-4 Heat of Solutions

The molar heat of solution and melting temperature of a substance can be determined from the solubility measurement at different temperatures. In the present chapter, heat of solution for all the imidazolinone derivatives was determined at different temperatures (308.15-328.15 K) in dimethylformamide (DMF) and dimethylsulfoxide (DMSO).

Chapter-5 Thermal Properties

This chapter describes the thermal properties of imidazolinone derivatives. The Thermo Gravimetric Analysis (TGA) measurements were made. From these measurements, various kinetic parameters were evaluated. Further, thermal stability of various compounds were also determined.

Chapter-6 Dissociation Constants

In the present Chapter, the dissociation constant of some Schiff bases were studied in DMF-water mixtures at 308.15K.

PART-3

BIOLOGICAL ACTIVITIES

In the present chapter, antibacterial activity of all the pyrazole and quinoline derivatives was studied against different microbes.

Signature of the Guide

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PART-I

SYNTHESIS AND CHARACTERIZATION

GENERAL INTRODUCTION

The chemistry of the heterocyclic compounds is as logical as that of aliphatic or aromatic compounds. The variety of heterocyclic compounds is enormous, their chemistry is complex and synthesizing them requires great skill.

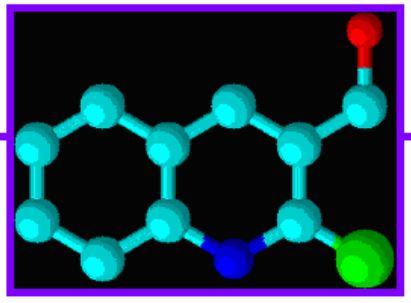
A heterocyclic compound is one which possesses acyclic structure with at least two different kinds of atoms in the ring. Among large number of heterocycles found in nature, nitrogen heterocycles are the most abundant than those containing oxygen or sulfur. The number of atoms in the heterocyclic ring can range from three to many i.e. ethylene oxide to crown ethers. Heterocyclic compounds can contain more than one ring system either heterocyclic or homocyclic.

Heterocyclic systems are encountered in many groups of organic compounds possessing great applicability in industry as well as in our life in various ways. Most of the sugars and their derivatives contain hetero atoms. Many members of the vitamin B group possess heterocyclic ring containing nitrogen.

This class of compounds has great applicability as drugs due to their specific chemical reactivity. They resemble essential metabolism and they fit biological receptors and block their normal working. Many natural products contain heterocyclic compounds such as alkaloids and glycosides. Many antibiotics including penicillin, cephalosporin, norfloxacin, streptomycin etc. also contain heterocyclic ring.

Taking in view of the applicability of heterocyclic compounds, the present work was undertaken to synthesize some new heterocycles bearing quinoline and pyrazole nucleus.

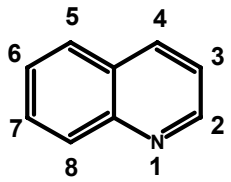
CHAPTER-1



SYNTHESIS OF QUINOLINES

INTRODUCTION

Nitrogen containing heterocyclic compounds like quinoline has received considerable attention in recent years due to their biological and pharmaceutical activities. Quinoline contains a phenyl ring fused to a pyridine ring. The numbering system for the quinoline is as follows:



Quinoline is also known as benzpyridine.

Different methods used for the synthesis of quinoline and its derivatives have been reported in literature[1-5].

These quinoline derivatives are known to have wide spectrum of therapeutic activities such as: analgesic[6,7], antiulcer[8], bactericidal[9-11], antiinflammatory[12,13], antidepressant[14], Herbicidal[15,16], anticonvulsant[17], antitumor[18,19], antidiabetic[20], antiplatlet[21-23], antiviral[24,25], antithyroid[26], antiarterioscierotics[27], antihypertensive[28], antithrombotic[29], antiallergic[30,31], antimalarial[32] etc.

Boeger et al.[33] reported pesticidal properties of some new quinoline derivatives. Synthesis and biological activity of 4-(3-aryl-2-oxo and 2-thioxo-1,3-oxazolidin-5-yl-methoxy) quinoline-2-carboxylic acids was documented by Lee and co-workers[34]. The antibacterial activity of some new quinoline derivatives have been reported by Fujita et al[35]. Beard and co-workers[36] have prepared some new N-aryl substituted tetrahydroquinolines having retinoid agonist and retinoid antagonist type biological activity. The anti-inflammatory activity of some new 5-heterocyclyquinoline was reported by Dyke and coworkers[37]. Diane and co-workers[38] reported the anticancer activity of some new quinolines. Machhi et al.[39] have prepared some new aryl-quinolinyl pyrimidinones and screened for their antibacterial activity. Shimizu et al.[40] synthesized some new quinoline carboxylic acid derivatives and reported them their antibacterial activity. The antibacterial activity of some new fluoroquinoline derivatives[41] and of 2-

quinoline derivatives[42] have also been reported. Wackernagel[43] reported some new quinoline derivatives as insecticidals whereas Michaela and co-worker[44] have reported some other quinoline derivatives as antagonist. Some new indolo quinoline derivatives are known to act as antineoplastic agent[45] whereas some are reported to be used in the treatment of autoimmune disease and allergies[46].

Ramharter et al.[47] reported In vitro activity of quinolines against Plasmodium falciparum in Gabon. Vangapandu et al.[48] reported ring-substituted quinolines as potential anti-tuberculosis agents. Joshi et al.[49] reported as novel 5-substituted amino quinoline derivatives as antimalarials. Chen et al.[50] also reported anticancer activity of certain quinoline derivatives.

Recently, the anticonvulsant activity [51] and antimicrobial activity[52] of some new quinoline derivatives have also been reported. Li et al.[53] studied antiproliferative activity of some of these derivatives.

The anti-HIV[54], anticonvulsant[55] and anti-tuberculosis activity[56] of substituted quinolines have also been documented. Warshakoon et al.[57] studied anti-obesity properties of these compounds.

Thus, the important role displayed by quinoline and its derivatives for various therapeutic and biological activities prompted us to synthesize some schiff bases, chalcones, pyrazolines and thiopyrimidines derivatives bearing quinoline nucleus in order to achieve compounds having better drug potential.

REFERENCES

(1) J. A. Moore and E. C. Capaldi; J. Org. Chem., **29**, 2860 (1964).

(2) K. Nyu, T. Kametani and T. Yamanaku; Chem. Pharma. Bull., **19**, 1321 (1971)

(3) C. K. Bradsher and T. G. Wallis; J. Org. Chem., **43**, 3817 (1978).

(4) M. Lancaster and D. J. Smith; J. Chem. Soc. Chem. Commun., **7**, 471 (1980).

(5) O. M. Cohn, B. Narine and B. Tarnowski; J. Chem. Soc., Perkin Trans, **11**, 1520 (1981).

(6) S. Mehrotra, J. P. Barthwal, T. K. Gupta and K. P. Bhargava; Ind. J. Physiol. Pharmacol., **26**, 253 (1982).

(7) F. Clemence, M. Fortin, M. O. Le and F. Delevallee; Fr. Demande FR 2 592, 879 (Cl. CO7D 401/09), Chem. Abstr., **109**, 22848d (1989).

(8) U. Minoru, K. Makoto, M. Seiji and N. Kazuyuki; JPN. Kokai Tokkyo Koho JP 60 142, 959 (Cl. CO7D 215/22), Chem. Abstr., **104**, 88454a (1986).

(9) A. Renezelti and F. Villani; Bely. BE 902, 586 (Cl. CO7D), Chem. Abstr., **104**, 2248338h (1986).

(10) Shirahata, Akira, Nakamura and Toshiyo; Chem. Abstr., **104**, 84642n (1986).

(11) S. Vurbanova and S. Chervenkov; Chem. Abstr., **107**, 77601g (1987).

(12) Jinbo, Susuma, Kohno, S. Kashima, Koichi, Suzuki, Yasuo, Kazuo and E. Mochida; Can. CA. 1 189, 078 (Cl. CO7D 215/42); Chem. Abstr.m **104**, 68761v (1986).

(13) A. Kreft, K. L. Kees, J. H. Musser and J. J. Bicksler; Chem. Abstr., **107**, 96605c (1987).

(14) J. Archibald. W. Leheup and J. Terence; Birt. UK Pat. Appl. GB 2, 182, 935, Chem. Abstr., **107**, 198110e (1987).

(15) P. Plath, N. Meyer, U. Eichenauer and H. Helmut; Ger. Offen., DE 3, 541, 722, Chem. Abstr., **107**, 96606d (1987).

(16) H. Lee and Stong; Chem. Abstr., **126**, 17876b (1997).

(17) S. J. Boigegrain, R. Keane, P. E. Verniers and J. Claude; Fr. Demande FR 2 593, 811 (Cl. CO7D 215/56), Chem. Abstr., **108**, 94413k (1988).

(18) G. J. Atwal, B. Baguley and W. A. Denny; J. Med. Chem., **31**, 1048 (1988).

(19) Sanders, G. Robert, K. Kline and L. Hurley; PCT Int. Appl. WO 01 58, 889 (Cl. CO7D 311/20), Chem. Abstr., **135**, 166941p (2001).

(20) Uragami, S. Oda and Akinori; Chem. Abstr., **5**, 113161n (1995).

(21) T. C. Wang, Y. L. Chen, C. C. Tzeng, S. S. Liou, Y. L. Chang and C. M. Teng; Heiv. Chem. Acta., **79**, 1620 (1996).

(22) M. C. Hsich, L. J. Huang, T. S. Wu, K. H. Lee, C. Teng and S. C. Kuo; Chin. Pharm. J., **50**, 277 (1998).

(23) T. C. Wang, Y. L. Chen, C. C. Tzeng, S. S. Liou, W. F. Treng, Y. L. Chang and C. M. Teng; Heiv. Chem. Acta., **81**, 1038 (1998).

(24) A. Adrian, J. M. Kelly and C. Sumvel; U. S. US 5, 306, 236 (Cl. A61K 31/435) (1996), Chem. Abstr., **125**, 25162a (1996).

(25) Tucker, J. Alan, V. A. Vaillancourt, S. J. Walter, R. K. Rene, M. E. Schnute, M. M. Cudahy, T. Suvit, S. R. Turner; PCT Int. Appl. Wo 99 32, 450 (Cl. CO7D 215/56) (1998), Chem. Abstr., **131**, 73568z (1999).

(26) I. V. Ukrainets, S. G. Taran, O. V. Gorokhova, N. A. Marusenko and A. V. Turor; Chem. Hetero. Compd., **33**, 600 (1997).

(27) G. M. Myeller, R. Angerbauer, A. brandes, M. Loeyers, C. Schmeck and D. Schmidt; Ger. Offen. DE 19, 709, 125 (Cl. CO7D 215/20) (1998); Chem. Abstr., **129**, 230650y (1998).

(28) L. Skrzypek, J. Folwarczna, W. Janies, I. Kaczmarczyksedlak, A. Masalankiewicz and M. Pyllik; Pol. J. Chem., **72**, 1127 (1998)

(29) A. Heckel, R. Soyka, W. Grell, E. Hgaksma, K. Binder and R. Zimmermann; Ger. Offen. DE 19, 727, 117 (Cl. CO7D 215/12) (1999), Chem. Abstr., **130**, 110166u (1999).

(30) T. Hidetsugu, Y. Shinobu, A. Masayoshi, S. Mitsuru and M. Osamu; Eur. Pat. Appl. EP 927, 718 (Cl. CO7D 215/38) (1997), Chem. Abstr., **131**, 73569a (1999).

(31) T. Hidetsugu, N. Shigenori, K. Nobuyuki, Y. Shinobu and A. Yasuo; Eur. Pat. Appl. EP 933, 378 (Cl. CO7H 17/02) (1999), Chem. Abstr., **131**, 116454d (1999).

(32) K. J. Raynes, P. A. Stocks and S. Ward; PCT Int. Appl. WO 00 50, 404 (Cl. CO7D 215/46), Chem. Abstr., **133**, 193087e (2000).

(33) M. Boeger, P. Maienfisch, F. Cedervaum, T. Pitterna and P. J. Nadkarni; PCT Int. Appl. WO 96 21, 652 (Cl. CO7D 231/32) (1996), Chem. Abstr., **125**, 195643s (1996).

(34) C. W. Lee, S. H. Lee, Y. S. Jung, N. S. Park and C. M. Seong; Korean J. Med. Chem., **7**, 90 (1997).

(35) M. Fujita, K. Chiba, J. Nakano, Y. Tominaga and J. I. Matsumoto; Chem. Pharm. Bull., **46**, 631 (1998).

(36) R. L. Beard, M. Teng, D. F. Colon, T. T. Duong and R. A. Chandrratna; U. S. US 5, 739, 338 (Cl. 546-153; CO7D 215/227) (1998), Chem. Abstr., **128**, 282789z (1998).

(37) H. J. Dyke and J. G. Montana; PCT Int. Appl. WO 98 20, 007 (Cl. CO7D 401/04) (1998); Chem. Abstr., **129**, 16122j (1998).

(38) H. B. Diane, D. W. Yanong, Y. Fie, Z. Nan, D. Minu and W. P. Dennis; J. Med. Chem., **44**, 822 (2001).

(39) J. Machhi, D. Patel, C. M. Desai, P. Desai and H. D. Joshi; J. Inst. Chemists, **73**, 140 (2001).

(40) S. Shimizu, T. Makino, T. Kino, H. Nagasawa, N. Ota and T. Akiba; JPN Kokiai Tokkyo Koho JP 201, 191 (Cl. CO7D 401/04) (2002), Chem. Abstr., **137**, 93736e (2002).

(41) Q. Guo, Y. Yang, J. Wang, F. Lin and Z. Zhang; Faming Zhuanli Shenquing Gongkai Shuomingshu CN 1, 306, 001 (Cl. CO7D 405/06) (2001), Chem. Abstr., **137**, 154944v (2002).

(42) Suchetak and B. Rao; Hetero. Commun., **8**, 569 (2002).

(43) M. Wackernagel; PCT Int. Appl. WO 02 46, 163 (Cl. CO7D 215/22) (2002), Chem. Abstr., **137**, 33225c (2002).

(44) J. Michaela and D. Gerd; Eur. J. Med. Chem., **38**, 661 (2003).

(45) H. Ling, H. Xichang, C. C. Ting, Niramol, Savaraj and C. C. Cheng; Eur. J. Med. Chem., **38**, 101 (2003).

(46) D. J. Best, G. Bruton and B. S. Orlek; PCT Int. Appl. WO 03 45, 922 (Cl. CO7D 215/12) (2001), Chem. Abstr., **139**, 22116h (2003).

(47) M. Ramharter, W. H. Wernsdorfer and P. G. Kremsner; Acta Tropica, **90**, 55 (2004).

(48) S. Vangapandu, M. Jain, R. Jain, S. Kaur and P. P. Singh; Bioorg. Med. Chem., **12**, 2501 (2004).

(49) A. A. Joshi, S. S. Narkhede and C.L. Viswanathan; Bioorg. Med. Chem. Lett., **15**, 73 (2005).

(50) Y. L. Chen, I. L. Chen, T. C. Wang, C. H. Han and C. C. Tzeng; Eur. J. Med. Chem., **40**, 928 (2005).

(51) Z. F. Xie, K. Y. Chai, H. R. Piao, K. C. Kwak and Z. S. Quan; Bioorg. Med. Chem. Lett., **15**, 4803 (2005).

(52) S. T. Selvi, V. Nadaraj, S. Mohan, R. Sasi and M. Hema; Bioorg. Med. Chem., 14, 3896 (2006).

(53) S. Y. Li, Y. L. Chen, C. Wang and C. C. Tzeng; Bioorg. Med. Chem.,(In Press) (2006).

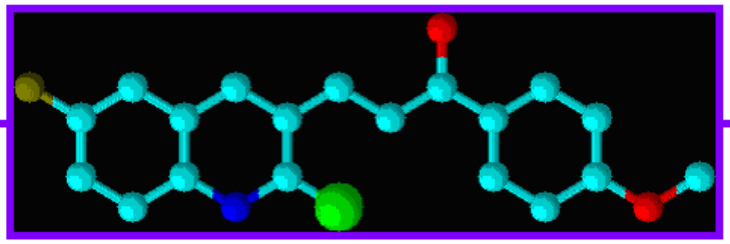
(54) V. Moret, N. D. Bosquet, P. Clayette, Y. Laras, N. Pietrancosta, A. Rolland, C. Weck, S. Marc and J. L. Kraus; Bioorg. Med. Chem. Lett., (In Press) (2006).

(55) H. G. Jin, X. Y. Sun, K. Y. Chai, H. R. Piao and Z. S. Quan; Bioorg. Med. Chem., **14**. 6868 (2006).

(56) A. Nayyar, A. Malde, E. Coutinho and Rahul Jain; Bioorg. Med. Chem., **14**, 7302 (2006).

(57) N. C. Warshakoon, J. Sheville, R. T. Bhatt, W. Ji, J. L. M. Andino, K. M. Meyers, N. Kim, J. A. Wos, C. Mitchell and J.L. Paris. Bioorg. Med. Chem. Lett., **16**, 5207 (2006).

SECTION-I



SYNTHESIS OF CHALCONES

INTRODUCTION

Chalcones are colored compounds because of the presence of the chromophore and auxochromes. They are known as benzalacetophenones or benzylidene acetophenone. Kostanecki and Tambor[1] gave the name Chalcone. The alternative names given to chalcones are phenyl styryl ketones, beanzalacetophenone, b-phenyl acrylphenone, g-oxo-a,g-diphenyl-a-propylene and a-phenyl-b-benzoethylene

The chemistry of chalcones has generated intensive scientific studies throughout the world, due to their biological and industrial applications. Chalcones are characterized by their possession of a structure in which two aromatic rings are linked by an aliphatic three carbon chain.

Different methods are available in the literature for the synthesis of chalcones[2-11]. The most convenient method is the one, that involves the Claisen-Schimidt condensation of equimolar quantities of an aryl methyl ketones with arylaldehyde in presence of alcoholic alkali[12].

Several condensing agents such as alkali of different strength[12,13] aluminium chloride[14], anhydrous boron trifluoride[15], amino acids[16], hydrochloric acid[17,18], phosphorous oxychloride[19], piperidine[20], perchloric acid[21] etc are used in the synthesis.

The chalcones have been found to be useful for the synthesis of variety of heterocyclic compounds such as cyanopyridone[23], pyridopyrimidines[24], amino pyrimidines[25], 3-cyanopyridines[26], isoxazoles[27], thiazepines[28], pyrazolines[29], oxirane[30], 1,4-oxazipines[31], 2-isothiazolidines[32], barbitone[33], oxopyrimidines[34], 1-carboxamide pyrazolines[35], 2-1H-pyrimidines[36], imine derivatives[37].

Chalcones are associated with different biological activities like cardiovascular[38], antispasmodic[39], anthelmintics[40,41], antiulcer[42,43], antiinflammatory[44-46], antiviral[47], antiallergic[48], fungicidal[49-51], bactericidal[52,53], insecticidal[54-56], antitumor[57-59], antileishmanial[60], herbicidal[61], anticancer[62,63], antitubercular[64], anti HIV[65] etc.

Mudalir and Joshi[66] reported insecticidal activity of some phenoxy chalcones. The cardiovascular activity[67] , anti tumor activity[68] and anti inflammatory activity[67, 69] of some chalcones have also been reported. Ko et

al.[70] have prepared some new chalcones for potent inhibition of platelet aggregation. Ziegler et al.[71] reported some chalcones as antiparasitic. The antimalarial activities of chalcones have also been reported by Xue et al.[72] and Dominguez et al.[73]. Seo et al.[74] have synthesized chalcones derivatives and reported them as a-glucosidase inhibitors. Larsen and co-worker[75] and Wu et al.[76] have reported anti-plasmodial activity and Boeck and et al.[77] have reported anti leishmanial activity of some chalcones. Analogs containing nitro, fluorine or bromine group respectively displayed increased selectivity against the parasites as compared with natural chalcone.

In the present chapter some chalcones were synthesized.

EXPERIMENTAL

Synthesis of (2*E*)-3-(2-chloro-6-fluoroquinolin-3-yl)-1-(4-methoxy phenyl)prop-2-en-1-one

[A] Synthesis of *N*-(4-fluorophenyl)acetamide:

A mixture of 4-fluoroaniline (1.11g, 0.01M) and acetic anhydride (1.02g, 0.01M) in absolute ethanol was refluxed in water bath for 2-3 hrs. using H_2SO_4 as catalyst. The crude product was isolated and crystallized from absolute ethanol.

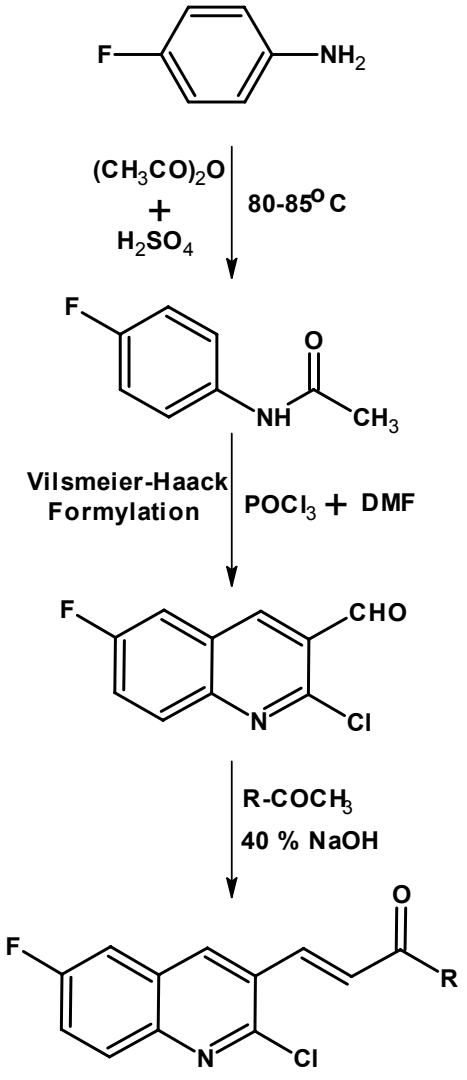
[B] Synthesis of 2-chloro-6-fluoroquinoline-3-carbaldehyde:

N-(4-fluorophenyl)acetamide (1.53g, 0.01M) was added in mixture of Vilsmeir-Haack reagent (prepared by dropwise addition of 6.5ml $POCl_3$ in ice cooled 2ml DMF) and refluxed for 27 hrs. The reaction mixture was poured into ice followed by neutralization using sodium bicarbonate. Crude product was isolated and crystallized from ethanol.

[C] Synthesis of (2*E*)-3-(2-chloro-6-fluoroquinolin-3-yl)-1-(4- methoxy phenyl)prop-2-en-1- one:

To a well stirred solution of 2-chloro-6-fluoroquinoline-3-carbaldehyde (2.09g, 0.01M) and p-methoxy-acetophenone (1.50g, 0.01M) in ethanol (25 ml), 40% NaOH added till the solution basic. The reaction mixture was stirred for 48 hrs. The contents were poured into ice, acidified, filtered and crystallized from ethanol.

REACTION SCHEME



The various physical constants such as R_f value, melting point and percentage of yield for all the synthesized chalcones are given in Table 1.1.

The characterization was done by IR, ^{1}H NMR and mass spectra.

(I) INFRA RED SPECTRA:

Instrument: SHIMADZU-FTIR-8400 Spectrophotometer

Frequency range: 4000-400cm^{-1}

Sample technique: KBr disc.

(II) ^{1}H NMR SPECTRA:

Instrument: BRUKER Spectrometer (300 MHz and 400 MHz)

Internal reference: TMS

Solvent: $CDCl_3$/DMSO

(III) MASS SPECTRA

GCMS-SHIMADZU-QP2010

All these spectra along with their tables are given in Fig.1.1 to 1.3 and Tables 1.2 to 1.3 for (2E)-3-(2-chloro-6-fluoroquinolin-3-yl)-1-(4-methoxy phenyl) prop-2-en-1-one. The proposed fragmentation of the same compound is also given in Scheme 1.1.

Table 1.1: Physical constants of chalcones.

Sr. No.	Code	R	M.F.	M. Wt. (g/mol)	Rf* Value	M.P. ^{o}C	Yield %
1.	**NVK-1A**	4-OCH_3-C_6H_4-	$C_{19}H_{13}ClFNO_2$	341	0.55	215	65
2.	**NVK-1B**	3-NO_2-C_6H_4-	$C_{18}H_{10}ClFN_2O_3$	356	0.57	209	71
3.	**NVK-1C**	2-OH-C_6H_4-	$C_{18}H_{11}ClFNO_2$	327	0.48	225	64
4.	**NVK-1D**	4-NH_2-C_6H_4-	$C_{18}H_{12}ClFN_2O$	326	0.64	198	63
5.	**NVK-1E**	4-NO_2-C_6H_4-	$C_{18}H_{10}ClFN_2O_3$	356	0.48	>300	59
6.	**NVK-1F**	3-NH_2-C_6H_4-	$C_{18}H_{12}ClFN_2O$	326	0.49	222	67
7.	**NVK-1G**	4-CH_3-C_6H_4-	$C_{19}H_{13}ClFNO$	325	0.55	217	62
8.	**NVK-1H**	4-OH-C_6H_4-	$C_{18}H_{11}ClFNO_2$	327	0.78	229	71
9.	**NVK-1I**	4-Cl-C_6H_4-	$C_{18}H_{10}Cl_2FNO$	345	0.81	245	61
10.	**NVK-1J**	4-Br-C_6H_4-	$C_{18}H_{10}BrClFNO$	390	0.88	218	57

* Acetone:Benzene: 1.5:8.5

Figure 1.1: IR spectra of (2E)-3-(2-chloro-6-fluoroquinolin-3-yl)-1-(4-methoxy phenyl) prop-2-en-1-one.

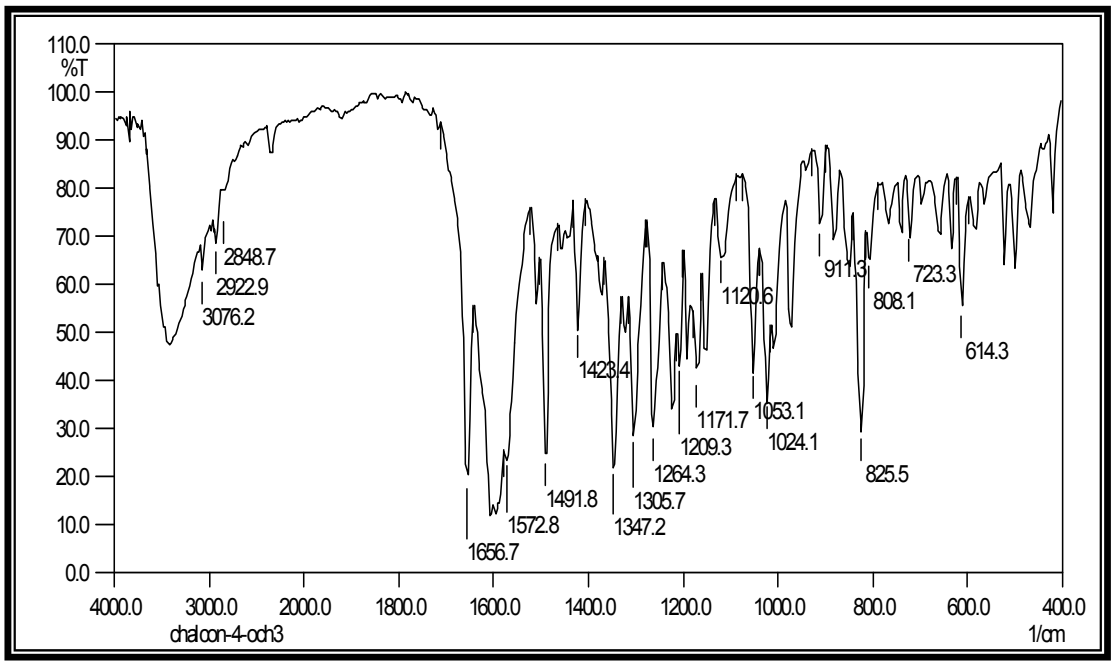
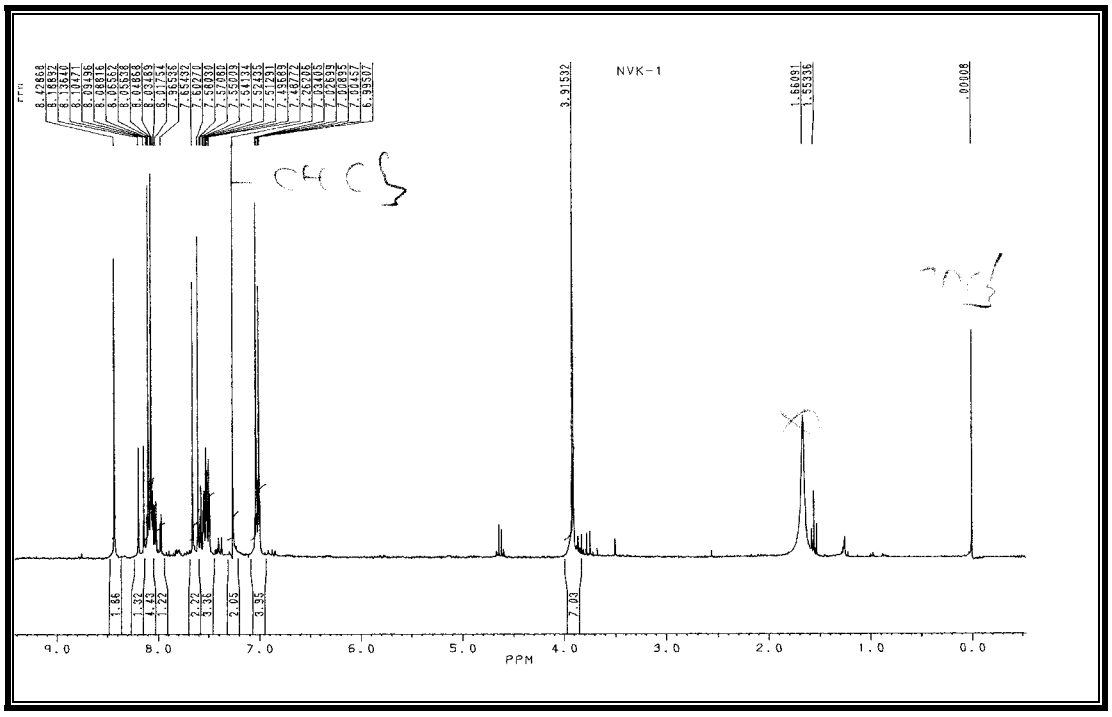


Table 1.2: IR spectral data of (2E)-3-(2-chloro-6-fluoroquinolin-3-yl)-1-(4-methoxy phenyl)prop-2-en-1-one.

Type	Vibration mode	Frequency in cm^{-1}	
		Observed	Reported
Alkane (methyl)	C-H str. (asym.)	2923	2975-5920
	C-H str. (sym.)	2849	2880-2860
	C-H def. (asym.)	1423	1470-1435
	C-H def.(sym.)	1347	1395-1370
Aromatic	C-H str.	3076	3100-3000
	C=C	1492	1585-1480
	C-H i.p. def.	1121	1125-1090
	C-H o.o.p. def.	826	860-810
quinoline moiety	C=N str.	1600	1650-1580
	C-N str.	1306	1350-1200
ether	C-O-C str. (asym.)	1264	1275-1200
	C-O-C str. (sym.)	1024	1075-1020
chalcone	C=O str.	1657	1750-1650
	C-F	1209	1400-1000
	C-Cl	723	800-600

Figure 1.2: ^{1}H NMR spectra data of (2E)-3-(2-chloro-6-fluoroquinolin-3-yl)-1-(4-methoxyphenyl)prop-2-en-1-one.



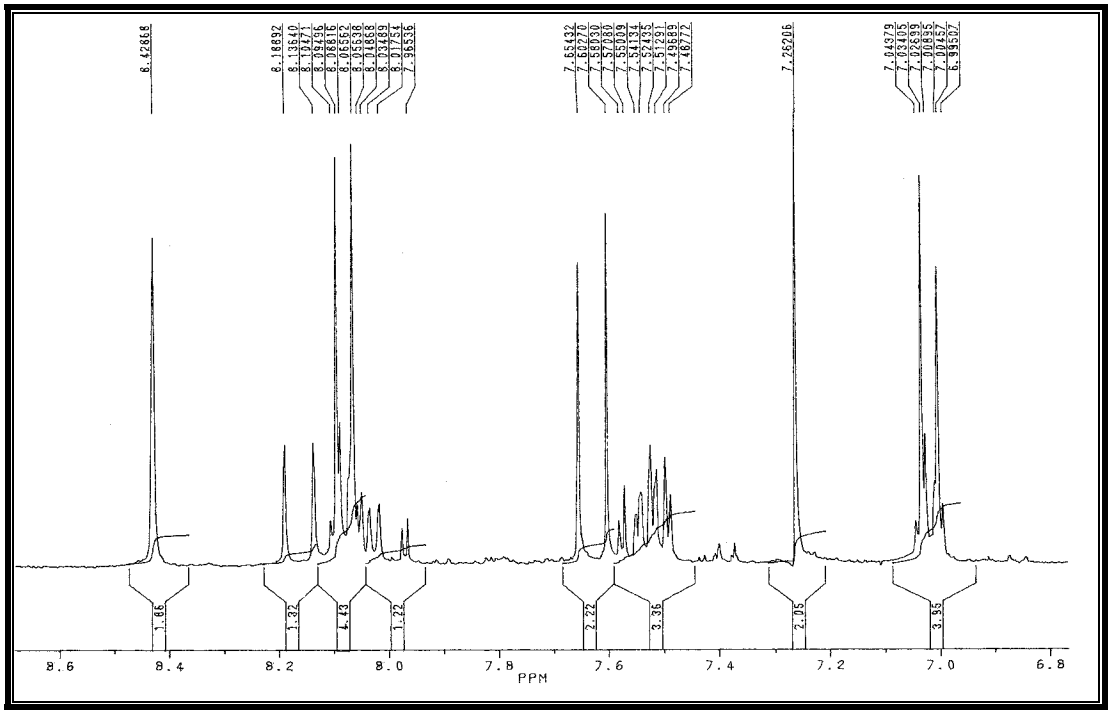
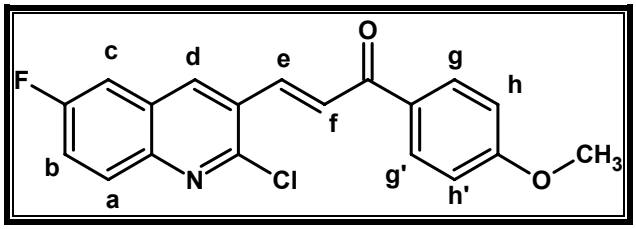
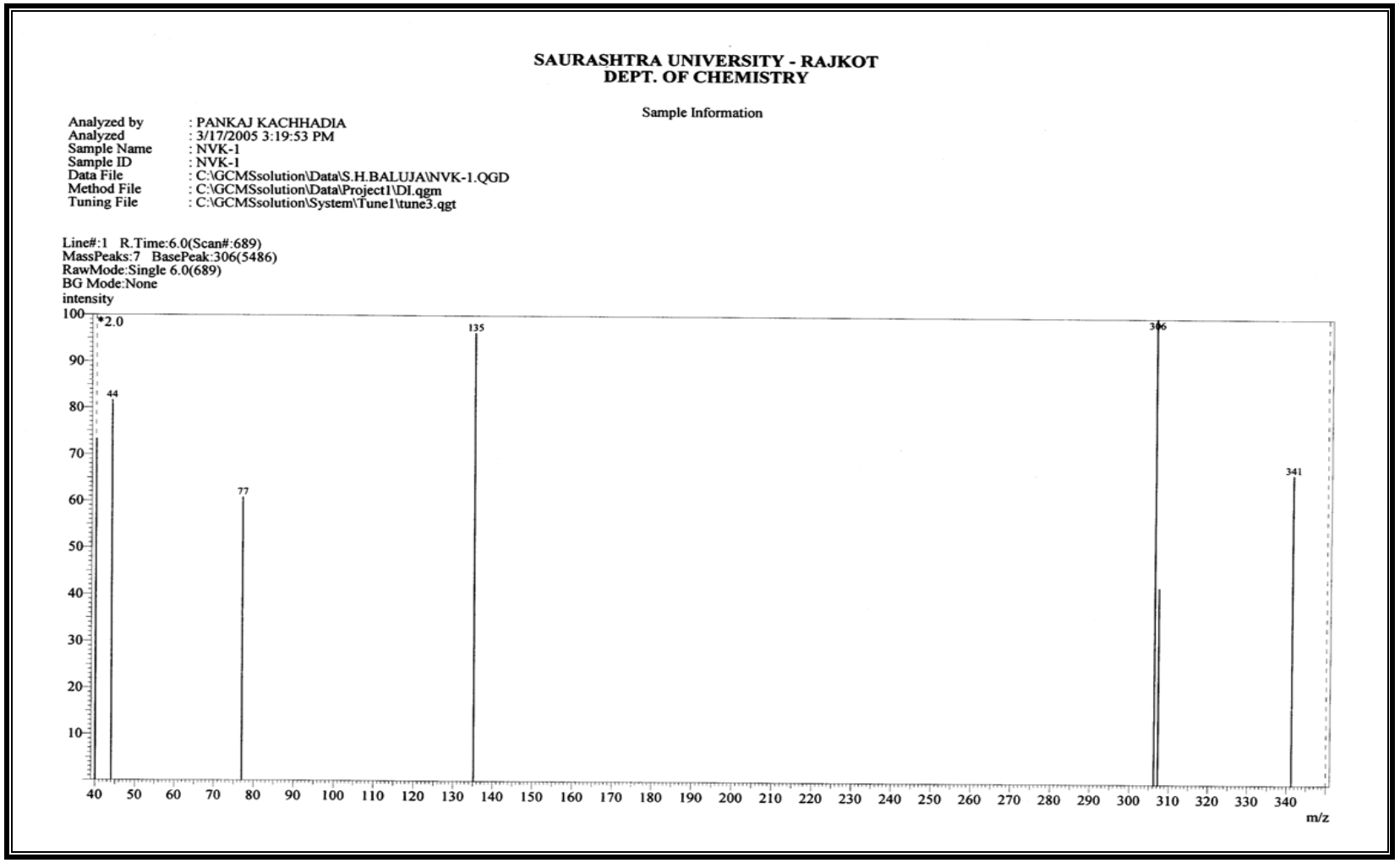


Table 1.3: ^{1}H NMR spectral data of (2E)-3-(2-chloro-6-fluoroquinolin-3-yl)-1-(4-methoxyphenyl)prop-2-en-1-one.

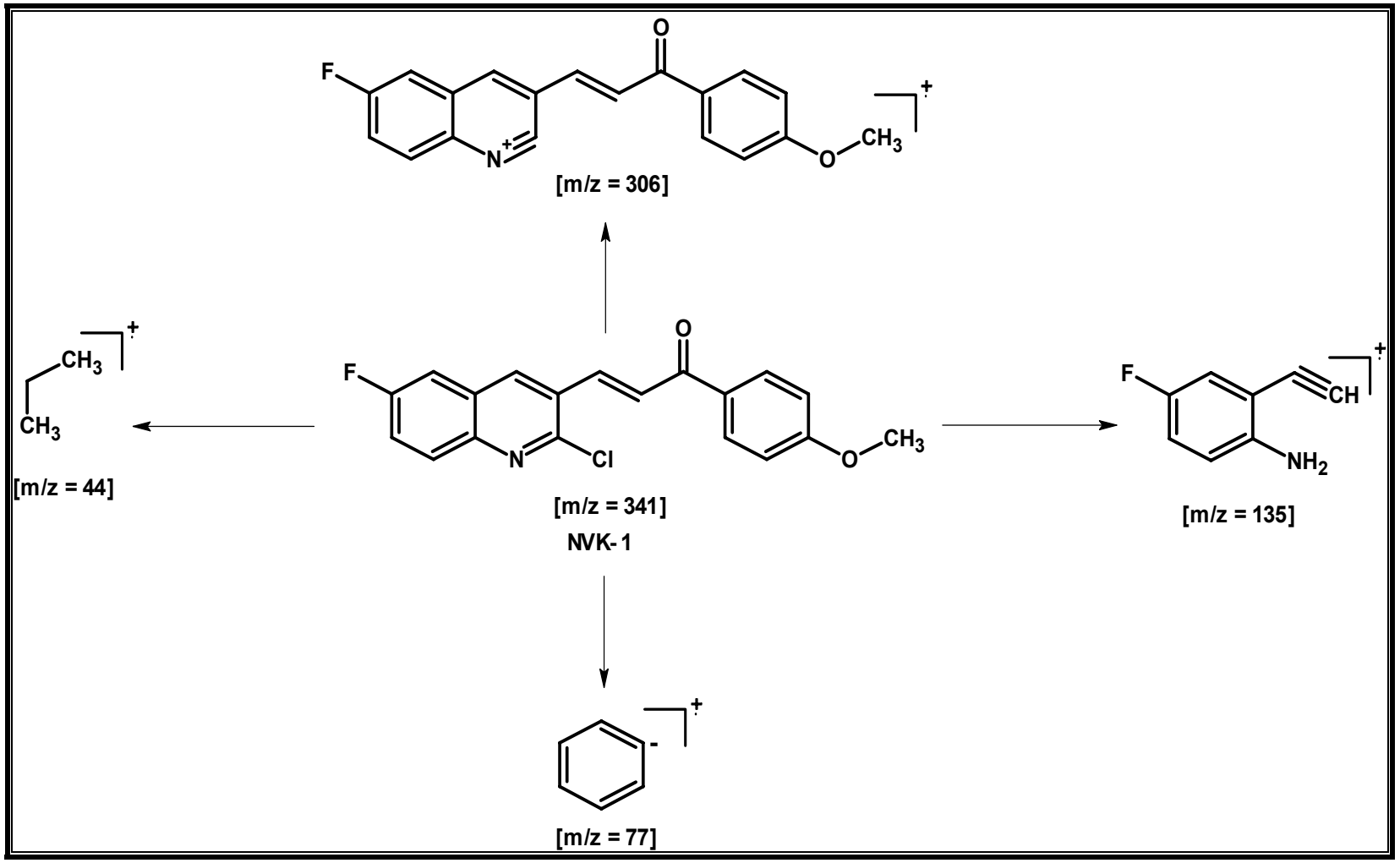


Singal No.	Signal Position (δ ppm)	Relative No. of Protons	Multiplicity	Inference	J (Hz)
1.	3.91	3H	singlet	Ar-OCH_3	-
2.	7.00-7.03	2H	doublet	Ar-H(gg')	8.9
3.	7.48-7.58	3H	multiplet	Ar-H(a)+H(b)+H(c)	-
4.	7.60-7.65	1H	doublet	=CH(e)	15.48
5.	8.06-8.09	2H	doublet	Ar-H(hh')	8.8
6.	8.13-8.18	1H	doublet	=CH(f)	15.75
7.	8.42	1H	singlet	Ar-H(d)	-

Figure 1.3: Mass spectra of (2E)-3-(2-chloro-6-fluoroquinolin-3-yl)-1-(4-methoxyphenyl)prop-2-en-1-one.



Scheme 1.1: (2E)-3-(2-chloro-6-fluoroquinolin-3-yl)-1-(4-methoxyphenyl)prop-2-en-1-one.



REFERENCES

(1) S. V. Kostanecki and J. Tambor ; Chem. Ber., **32**, 1921 (1899).

(2) H. Rupe and D. Wasserzug; Chem. Ber., **34**, 3527 (1901)

(3) D. S. Breslow and C. R. Houser; J. Am. Chem. Soc., **62**, 2385 (1940).

(4) S. A. Hermes; Chem. Abstr., **70**, 96422h (1969).

(5) P. L. Nayak and N. K. Rout ; J. Ind. Chem. Soc., **52**, 801 (1975).

(6) G. Casiraghi, G. Casnati, E. Dradi, R. Messori and G. Satori; Tetrahedron, **35**, 2061 (1979).

(7) A. Fuentes, J. M. Marinas and J. V. Sinisterra; Tetrahedron, **28**, 4541 (1987).

(8) T. Patonay, G. Toth and W. Adam; Tetrahedron, **34**, 5055 (1993).

(9) F. Severi, S. Benvenuti, L. Costantino, G. Vampa, M. Melegari and L. Antolini; Eur. J. Med. Chem., **33**, 859 (1998).

(10) S. Eddarir, N. Cotelle, Y. Bakkour and C. Rolando; Tetrahedron, **44**, 5359 (2003).

(11) S. Saravanamurugam, M. Palanichamy, B. Arabindoo and B. Murugesan; Catalysis Commun., **6**, 399 (2005).

(12) K. Kazauki, K. Htayama, S. Yokomor and T. Soki; Chem. Abstr., **85**, 5913 (1976).

(13) H. Rupe and D. Wasserzug; Chem. Ber., **34**, 3527 (1901).

(14) T. Szell ; Chem. Ber., **92**, 1672 (1959).

(15) C. Kurodo and T. Matsukuma ; Sci. Papers Inst. Phys. Chem. Res. (Tokyo), **18**, 51 (1932).

(16) D. S. Breslow and C. R. Houser ; J. Am. Chem. Soc., **62**, 2385 (1940).

(17) L. Reichel; Naturwissenschallen **32**, 215 (1944).

(18) R. B. Lyle and L. P. Paradis ; J. Am. Chem. Soc., **77**, 6667 (1955).

(19) S. A. Hermes; Chem. Abstr., **70**, 96422h (1969).

(20) A. A. Rawal and N. M. Shah ; Ind. J. Chem., **21**, 234 (1962).

(21) P. L. Cheng, P. Fournari and J. Tirouflet ; Bull. Soc. Chim. France, **6**, 102248 (1963).

(22) V. M. Vlasov ; Izu. Sib. Otd, Akad. Nauk. S. Ser. Khim. Nauk. **2**, 96 (1971); Chem. Abstr., **76**, 140411d (1972).

(23) K. Folkers, S. A. Harris; J. Am. Chem. Soc., **61**, 1245 (1939).

(24) S. W. Pfleiderer and H. Mosthafa; Syn. Org. Chem., **90B**, 738 (1957).

(25) E. C. Taylor and R.W. Morrison; J. Org. Chem., **32**, 2379 (1967).

(26) A. Sammour, Y. Akhnookh and H. Jahine; U.A.R. J. Chem., **13** 421(1970).

(27) L. S. Crawley and W. J. Fanshawe; J. Hetero. Chem., **14**, 53, (1977).

(28) K. P. Jadhav, D. B. Ingle; Ind. J. Chem., **22B**, 180 (1983).

(29) M. A. El-Hashan, M. El-Kady, M. A. Saiyed, A. A. Elsawy; Egypt. J. Chem., **27**, 715 (1985).

(30) R. A. Osisany and J. O. Oluwadiya; J. Hetero. Chem., **26**, 947 (1989).

(31) E. A. Mohamed, R. M. A. Rahman, A. A. Sayed and M. M. Ismail; Ind. J. Chem. Soc., **69**, 82 (1992).

(32) B. S. Hastak and B.J. Ghiya; Ind. J. Hetero. Chem., **2**, 133 (1992).

(33) M. R. Mahmoud, E. F. E. Awatef, M. S. Abd-El-Halim and A. M. Radwan; Ind. J. Hetero. Chem., **4**, 131 (1994).

(34) A. Khalafallah; Asian J. Chem., **8**, 951 (1996).

(35) P. S. Utale, P. B. Raghuvanshi and A. G. Doshi; Asian J. Chem., **10**, 597 (1998).

(36) P. A. Mehta and H. B. Naik; Orient. J. Chem., **14**, 159 (1998)

(37) A. Y. Deshmukh, P. B. Raghuwanshi and A. G. Doshi; Orient. J. Chem., **18**, 101 (2002).

(38) E. Marmo, A. P. Caputi and S. Cataldi; Farmaco Ed. Prat. **28**, 132 (1973).

(39) A. C. Grosscurt, H. R. Van and K. Wellinga; J. Agric. Food Chem., **27,** 406 (1979).

(40) L. Real, C. David and B. Francois; Can J. Pharm. Sci., **2**, 37 (1967).

(41) M. R. Bell; US Appl. **637**, 931 (1984); Chem. Abstr., **113**, 211828t (1990).

(42) K. Kyogoku ; Chem. Pharm. Bull., **27**, 2943 (1979).

(43) Tashio Pharmaceutical Co Ltd.; Japan, Kokai Tokkyo Koho Jp. 51, 12, 094 (Cl A 61 K 31/215): Chem. Abstr., **101**, 54722j (1984).

(44) H. Serre, J. Rey and J. P. Tarayre; Chem. Abstr., **91**, 9494a (1979).

(45) A. E. Vanstone, G. K. Maile and L. K. Nalbantoglu; Ger. Offen. DE 3, 537, 207 (Cl. 07 c 65/40), (1986); Chem. Abstr., **106**, 49778f (1987).

(46) Hsieh, Hasin, Kaw; Lee-Tai-Hua Wang, Jih-Pyang. Wang. et al.; Chem. Abstr., **128**, 225684n (1998).

(47) D. Binder, C. R. Noe, W. Holzer and B. Rosenwirth; Arch. Pharm., **318**, 48 (1985).

(48) E. T. Ogansyna et al.; Khim. Farm. Zh. **25**, 18 (1991).

(49) A. K. Padersen and G. A. Fitz Gerald; J. Pharm. Sci., **74**, 188 (1985).

(50) V. M. Gaurav and D. B. Ingle; Ind. J. Chem. **25B**, 868 (1986).

(51) B. B. Kalashnikow and J. P. Kalashnikova; Russ. J. Ger. Chem., (1998); Chem. Abstr., **130**, 296596n (1999).

(52) K. Bowden; P. A. Dal and C. K. Shah; J. Chem. Res. Synop., **12**, 2801 (1990).

(53) S. F. Nielsen, T. Boesen, M. Larsen, K. Schonning and H. Kromann; Bioorg. Med. Chem. Lett., **12**, 3047 (2004).

(54) A. C. Gross Curt, H. R. Van and K. Wellinga; J. Agric. Food. Chem. **27**, 406 (1979).

(55) S. R. Modi and H. B. Naik; Orient J. Chem., **10**, 85 (1994).

(56) M. Larsen, H. Kromann, A. Kharazmi and S. F. Nielsen; Bioorg. Med. Chem. Lett., **15**, 4858 (2005).

(57) Y. Satomi; Ind. J. Cancer, **120**, 208071 (1994).

(58) Kamei, Hideo, Koide, Tatsurou, H. Yoko and Kojima ; Cancer Biother Radio Pharm., **12**, 51 (1997).

(59) T. Andreas and K. Theodara ; PCT Int. Appl., WO 99, **54**, 278 (1999); Chem. Abstr., **131**, 28260z (1999).

(60) F. S. Nielsen and S. B. Chirstensen; J. Med. Chem., **41**, 4819 (1998).

(61) V. S. Parmar and S. C. Jain; Ind. J. Chem., Sect. B., Org. Chem. Med. Chem. **37B**, 628 (1998).

(62) G. Zongru and H. Rui; CN 1, 13, 909, Chem. Abstr., **125**, 103768 (1996).

(63) G. Achanta, A. Modzelewska, L. Feng, S. R. Khans and P. Hang; Mol. Pharmacol., (2006) (In Press).

(64) N. Lall, A. A. Hussein and J. J. M. Meyer; Fitoterapia, **77**, 230 (2006).

(65) S. Cheenpracha, C. Karalai and S. Tewtrakul; Bioorg. Med. Chem., **14**, 1710 (2006).

(66) V. R. Mudalir and V. Joshi ; Ind. J. Chem., **34 B**, 456 (1995).

(67) N. Liming, K. J. Worsencrott, M. D. Weingarten , C. Q. Meng and J. A. Sikorski; U. S. US WO 02 41336 (2002); Chem. Abstr., **139**, 85160 (2003).

(68) K. K. Srinivas, E. Hager, C. Pehit, H. Gurulingoppal, N. E. Davidson and S. R. Khan; J. Med. Chem., **46**, 2813 (2003).

(69) K. H. Huey, T. L. Ti, Y. K. Lung, C. Tsung, J. P. Wong and C. N. Lin; Bioorg. Med. Chem., **11**, 105 (2003).

(70) H. H. Ko, H. K. Hsieh, C. T. Liu, H. C. Lin, C. M. Teng and C. N. Lin; J. Pharm Pharmacol., **56**, 1333 (2004).

(71) H. L. Ziegler, H. S. Hansen, D. Staerk, S. B. Christensen and H. Hagerstrand; Antimicrob. Agents Chemother., **48**, 4067 (2004).

(72) C. X. Xue, S. Y. Cui, M. C. Liu, Z. D. Hu and B. T. Fan; Eur. J. Med. Chem., **39**, 745 (2004).

(73) J. N. Dominguez, C. Leon, J. Rodrigues, J. Gut and P. J. Rosenthal; Il Farmaco, **60**, 307 (2005).

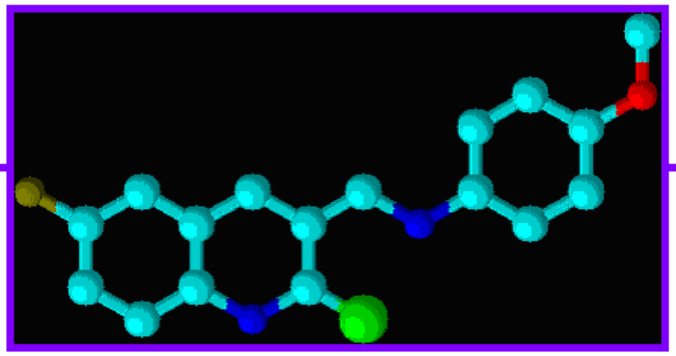
(74) W. D. Seo, J. H. Kim and K. H. Park .; Bioorg. Med. Chem., **15**, 5514 (2005).

(75) M. Larsen, H. Kromann, A. Kharazmi and S. F. Nielsen; Bioorg. Med. Chem., **15**, 4858 (2005).

(76) X. Wu, R. T. Edward and M. L. Go; Eur. J. Pharmacology, **532**, 178 (2006).

(77) P. Boeck, C. Alves and B. R. Bergmann; Bioorg. Med. Chem., **14**, 1533 (2006).

SECTION-II



SYNTHESIS OF SCHIFF BASES

INTRODUCTION

Azomethines are generally known as Schiff bases to honour Schiff, who synthesized such compounds[1]. These are the compounds containing characteristic –CH=N- group. Lots of works have been done on this class compounds due to its multi applicability. They are well known intermediate for the preparation of azetidinones, thiazolidinones, aryl acetamides and many other derivatives.

Owing to their characteristic properties like, manifestations of novel structures, thermal stabilities, abnormal magnetic properties, relevant biological properties, high synthesis flexibility, varied coordinating ability and medicinal utility, a wide range of these compounds have been synthesized and extensively studied[2-19].

Murray[20] has prepared imines by the reaction of aldehydes with amine (aromatic or aliphatic). Tabei and Saitou have reported the synthesis of some Schiff bases derived from benzaldehyde and substituted benzaldehydes with aniline[21]. Some Schiff bases from 2-hydroxy benzaldehydes were also synthesized and the effect of sunstituent on Keto-enol equilibria was also reported[22]. Some other Schiff bases have also been synthesized from various substituted benzaldehydes and their characterizations were done by using IR, NMR and mass spectra[23-25]. More et al.[26] synthesized some Schiff bases from aminothiazoles. Chang and Pan reported some Schiff bases derived from amino phenols and aromatic aldehydes[27]. A new one pot procedure for the generation of azomethine via chlorominium salt has been investigated by Anderson and co-workers[28].

Literature survey reveals that azomethines have a wide range of applications[29-34] such as corrosion inhibitor, intermediates in various reactions, in perfumery etc. Some are known to be used in many potential drugs[35] and are known to possess broad spectrum of biological activities such as antiviral[36], antifungal[37], antiparasitic[38], antibacterial[39], antiinflammatory[40] etc.

Smalders et al.[41] reported some new azomethine as potential antitumor agents. Din and Nabaweyal[42] have reported antibacterial activity of some azomethine derivatives. Khalafallah and Hasan have also suggested some styryl Schiff's bases as potential antibacterial and antifungal agents[43]. Yadav and Patil

have reported some azomethines which were screened for their antibacterial and antifungal activities[44]. Chohan et al.[45] have synthesized some azomethines and studied their antibacterial action against some gram positive and gram negative bacteria. Tilak et al.[46] have synthesized some Schiff bases and screened against carrageenin-induced edema in albino rats. The antifungal and antibacterial properties of some Schiff bases have also been reported by Pandey et al.[47] and Castellano et al.[48]. The antibacterial, antifungal, anti inflammatory and herbicidal activity of some azomethine derivatives have also been documented by Holla et al.[49,50] have documented. Selvam et al. have prepared Schiff bases from sulfonamide and its derivatives and studied their anti-HIV properties[51]. Rotheist et al.[52] have reported some new azomethines as antiparasitic agents. Adnan et al.[53] have also reported antibacterial and antifungal activities of some Schiff bases. Neslishan and Reyhan[54] have studied their antitumor activity whereas Varma[55] evaluated their antileishmanial activity. Recently, Parumal and co-workers[56] have also reported antimicrobial activity of some synthesized azomethine derivatives. Guo et.al.[57,58] have synthesized schiff bases of carboxymethyl chitosan and reported their in vitro antifungal and antioxident activity. The anti-inflammatory, analgesic and kinase (CDK-1, CDK-5, and GSK-3) inhibition activity of some azomethine derivatives have also been studied by Sondhi et al.[59]. Patole et al.[60] have reported antimycobacterial activity of Schiff base conjugates of p-amino salicyclic acid containing hydroxyl-rich side chains. Cukurovali et al.[61] have also synthesized some azomethine derivatives and investigated their antibacterial and antifungal activity. Anti-HIV activity of some other Schiff's bases have also been reported by Sriram and co-workers[62].

Thus, with an effort to capitalize the biological potential of the heterocyclic system and to provide more interesting compounds for biological study, the present work was undertaken to synthesize some azomethines bearing quinoline nucleus.

EXPERIMENTAL

Synthesis of N-[(1E)-(2-chloro-6-fluoroquinolin-3-yl)methylene]-4-methoxyaniline

[A] Synthesis of *N*-(4-fluorophenyl)acetamide:

Section-1 (A)

[B] Synthesis of 2-chloro-6-fluoroquinoline-3-carbaldehyde:

Section-1 (B)

[C] Synthesis of N-[(1E)-(2-chloro-6-fluoroquinolin-3-yl)methylene]-4-methoxyaniline:

A mixture of 2-chloro-6-fluoroquinoline-3-carbaldehyde (2.09g, 0.01M) and 4-methoxyaniline (1.23g, 0.01M) was taken in ethanol using 2-3 drops of gla. Acetic acid and the reaction mixture was refluxed for 10 hrs. The product was isolated and crystallized from absolute ethanol.

REACTION SCHEME

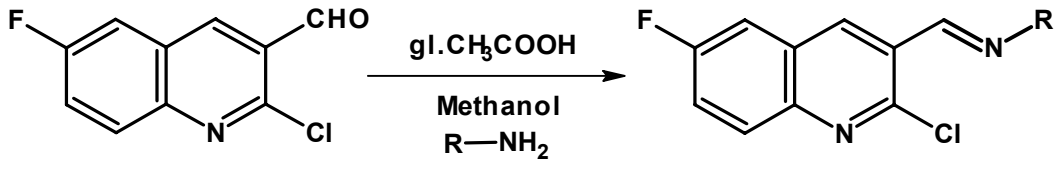


Table 2.1: Physical constants of Schiff bases.

Sr. No.	Code	R	M.F.	M. Wt. (g/mol)	Rf* Value	M.P. °C	Yield %
1.	**NVK-2A**	4-OCH_3-C_6H_4-	$C_{17}H_{12}ClFN_2O$	314	0.53	192	62
2.	**NVK-2B**	4-CH_3-C_6H_4-	$C_{17}H_{12}ClFN_2$	298	0.52	168	65
3.	**NVK-2C**	4-Cl-C_6H_4-	$C_{16}H_9Cl_2FN_2$	319	0.47	217	55
4.	**NVK-2D**	2-OCH_3-C_6H_4-	$C_{17}H_{12}ClFN_2$	298	0.34	205	59
5.	**NVK-2E**	4-NO_2-C_6H_4-	$C_{16}H_9ClFN_3O_2$	329	0.48	199	45
6.	**NVK-2F**	C_6H_5-	$C_{16}H_{10}ClFN_2$	284	0.49	188	49
7.	**NVK-2G**	$C_{10}H_7$-	$C_{20}H_{12}ClFN_2$	334	0.71	169	58
8.	**NVK-2H**	3-Cl-4-F-C_6H_3-	$C_{16}H_8Cl_2F_2N_2$	337	0.44	211	69
9.	**NVK-2I**	4-OH-C_6H_4-	$C_{16}H_{10}ClFN_2O$	300	0.69	225	45
10.	**NVK-2J**	3,4-di-Cl-C_6H_3-	$C_{16}H_8Cl_3FN_2$	353	0.33	239	48

*Acetone: Benzene: 2:8

Figure 2.1: IR spectra of N-[(1E)-(2-chloro-6-fluoroquinolin-3-yl) methylene]-4-methoxyaniline.

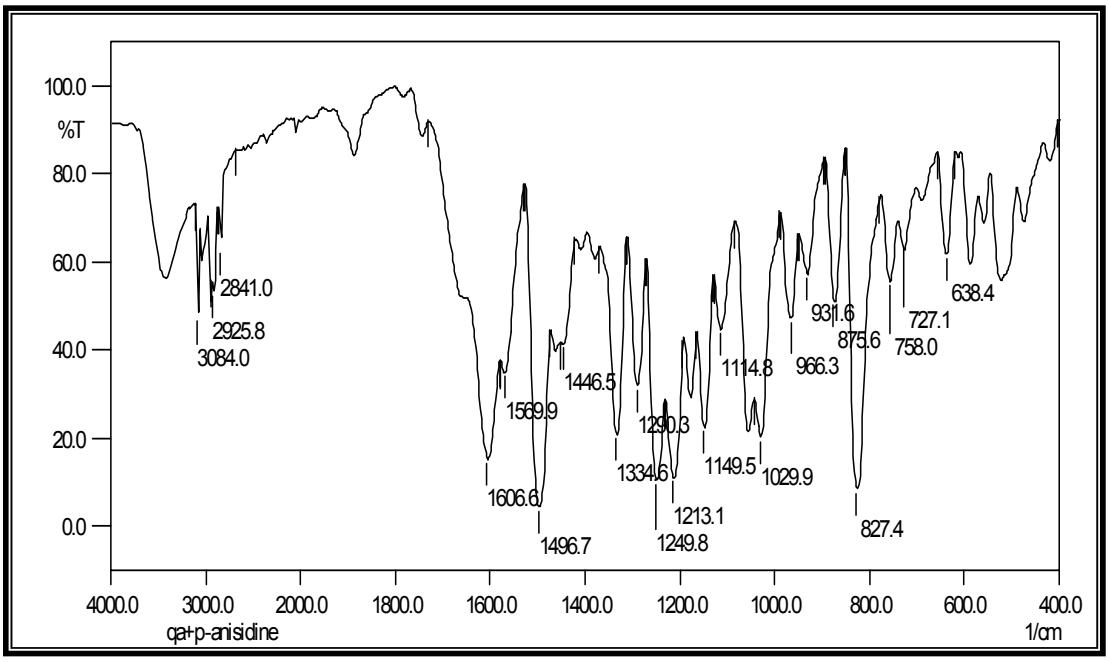
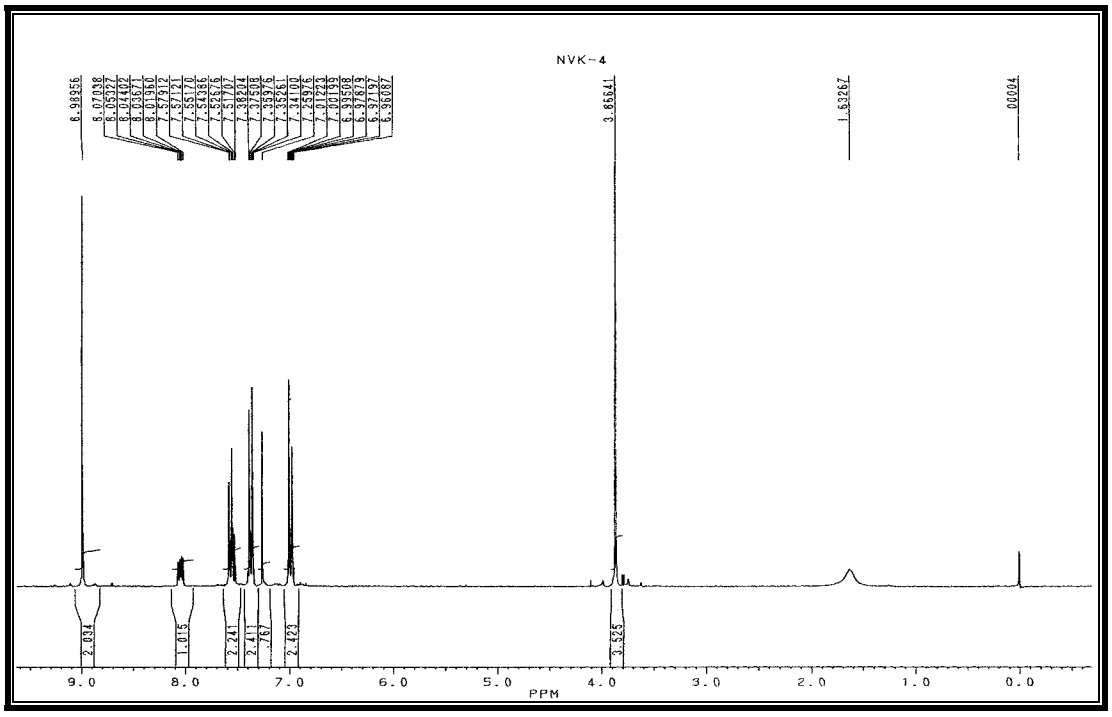


Table 2.2: IR spectral data of N-[(1E)-(2-chloro-6-fluoroquinolin-3-yl) methylene]-4-methoxyaniline.

Type	Vibration mode	Frequency in cm^{-1}	
		Observed	**Reported**
Alkane (methyl)	C-H str. (asym.)	2926	2975-5920
	C-H str. (sym.)	2841	2880-2860
	C-H def. (asym.)	1447	1470-1435
	C-H def.(sym.)	1335	1395-1370
Aromatic	C-H str.	3084	3100-3000
	C=C	1497	1585-1480
	C-H i.p. def.	1115	1125-1090
	C-H o.o.p. def.	827	860-810
azomethine	C=N str.	1607	1650-1580
	C-N str.	1290	1350-1200
ether	C-O-C str. (asym.)	1250	1275-1200
	C-O-C str. (sym.)	1030	1075-1020
	C-F	1213	1400-1000
	C-Cl	727	800-600

Figure 2.2: ^{1}H NMR spectra of N-[(1E)-(2-chloro-6-fluoroquinolin-3-yl) methylene]-4-methoxyaniline.



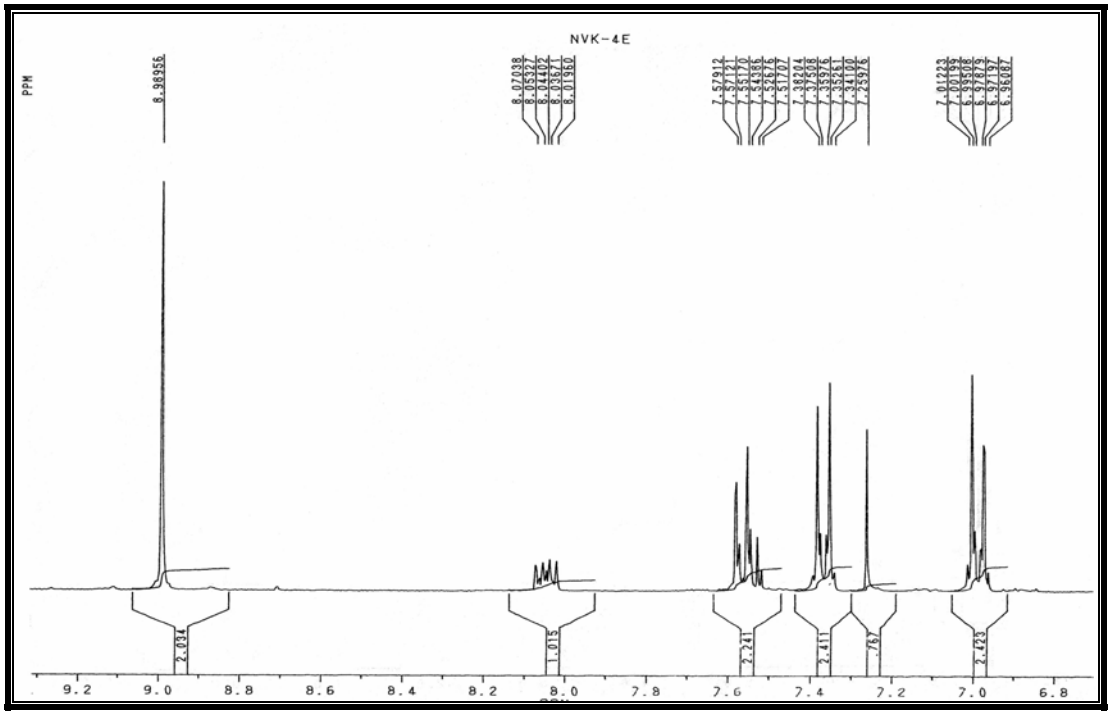
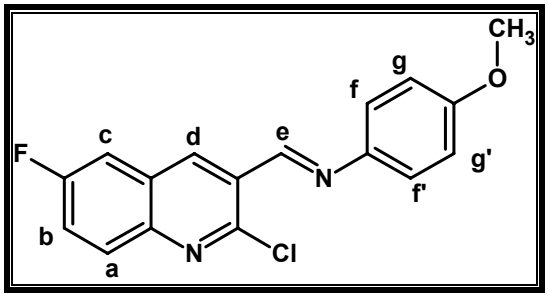
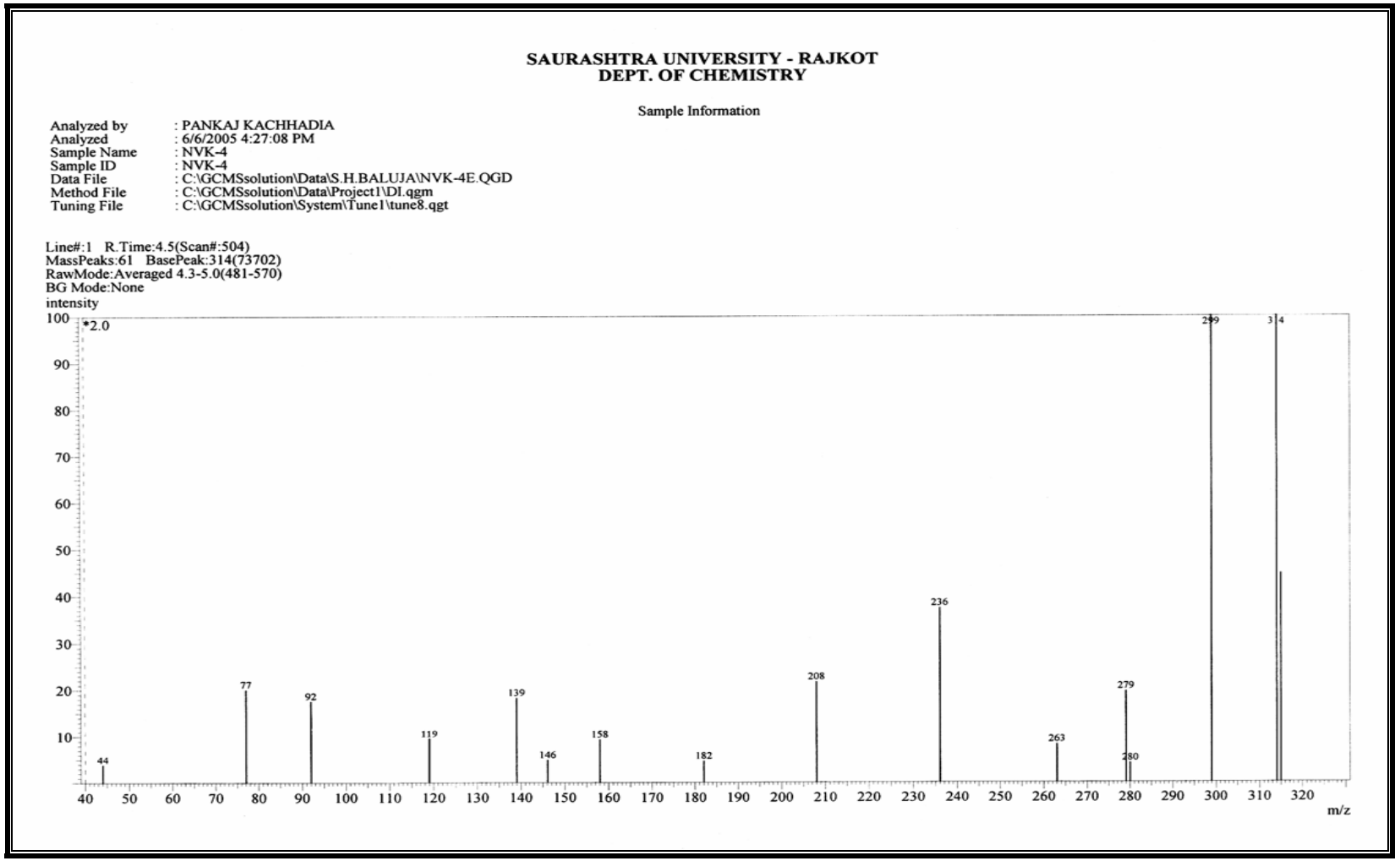


Table 2.3: ^{1}H NMR spectral data of N-[(1E)-(2-chloro-6-fluoroquinolin-3-yl) methylene]-4-methoxyaniline.

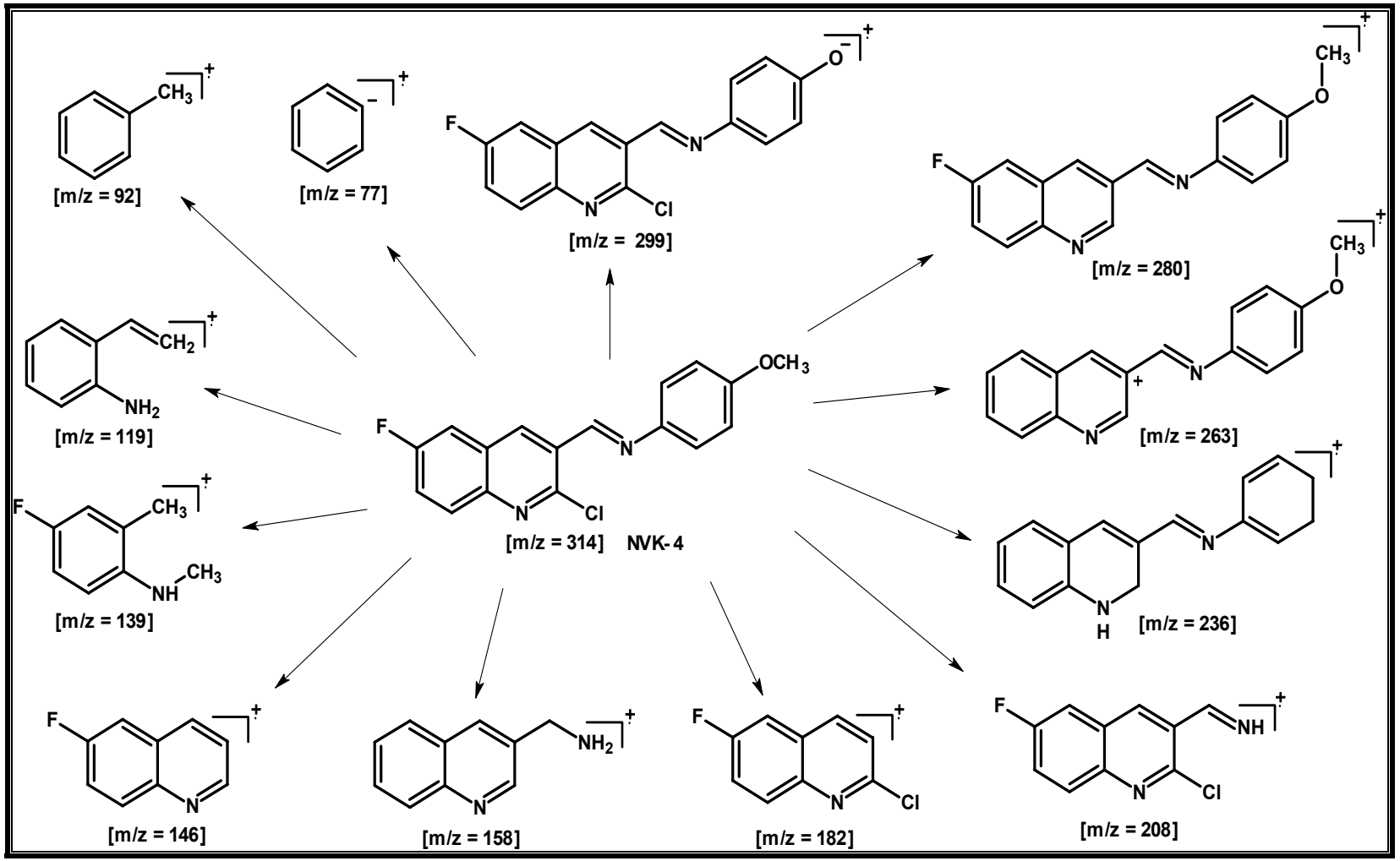


Singal No.	Signal Position (δ ppm)	Relative No. of Protons	Multiplicity	Inference	J (Hz)
1.	3.86	3H	singlet	Ar-OCH_3	-
2.	6.97-7.00	2H	doublet	Ar-H(ff')	13.06
3.	7.25	1H	singlet	Ar-H(d)	-
4.	7.35-7.38	2H	doublet	Ar-H(gg')	12.31
5.	7.51-7.57	2H	multiplet	Ar-H(a)+H(b)	-
6.	8.01-8.07	1H	quartet	Ar-H(c)	-
7.	8.98	1H	singlet	-CH(e)=N	-

Figure 2.3: Mass Spectra of N-[(1E)-(2-chloro-6-fluoroquinolin-3-yl) methylene]-4-methoxyaniline.



Scheme 2.1: N-[(1E)-(2-chloro-6-fluoroquinolin-3-yl) methylene]-4-methoxyaniline.



REFERENCES

(1) H. Schiff; Ann. Chem., **131**, 118 (1864).

(2) Strache; Ber. **21**, 2361 (1888).

(3) M. Calvin, R. H. Balies and W. K. Wilmarth; J. Am. Chem. Soc., **68**, 2254 (1946).

(4) B. M. Krasovitskii, V. B. Smelyakova and R. N. Nurmukhametov; Opti ii spek-trosk, **27**, 588 (1964).

(5) J. M. W. Scoot and W. H. Jura; Can. J. Chem., **45**, 2375 (1967).

(6) N. Castagnoli and M. Cushman; J. Org. Chem., **36**, 3404 (1971).

(7) M. Lehtinen and J. Halmekoski; Farm. Aikak., **84**, 107 (1975).

(8) S. M. E. Kousy, F. A. Ali, A. M. Donia and F. A. E. Saied; Egypt J. Pharma. Sci., **28**, 107 (1987).

(9) A. K. Varshney, P. S. Verma and S. Varsheny; Synth. React. Met. Inorg. Org. Chem., **19**, 233 (1989).

(10) R. L. Polt and M. Peterson; Tetrahedron Lett., **31**, 4985 (1990).

(11) K. Afkar and K. A. Hadi; Ind. J. Chem., **33**, 879 (1994).

(12) D. Raczynska and R. W. Taft; Bull. Chem. Soc. Jpn., **70**, 1331 (1997).

(13) R. C. Goyal, K. Arora, D. D. Agarwal and K. P. Sharma; Asian J. Chem., **12**, 919 (2000).

(14) S. K. Sridhar and A. Ramesh; Ind. J. Chem., **41**, 668 (2002).

(15) R. Mladenova, M. Ignatova, N. Manolova, T. Petrova and I. Rashkov; Eur. Poly. J., **38**, 989 (2002).

(16) B. Gandhi and S. Marjadi; Acta Cien. Ind., **XXIX**, 137 (2003).

(17) R. C. Mayur, A. Pandey and D. Sutradhar; J. Ind. Chem. Soc., **43A**, 763 (2004).

(18) M. Yyldyz, H. Unver, B. Dulger, D. Erdener, N. Ocak, A. Erdonmez and T. N. Durlu; J. Mol. Stru., **738**, 253 (2005).

(19) R. Kruszynski, M. Siwy, I. P. Czomperlik and A. Trzesowska; Inorg. Chim. Acta., **359**, 649 (2006).

(20) M. S. Murray; Chem. Rev., **26**, 297 (1940).

(21) K. Tabei and E. Saitou; Bull. Chem. Soc. Jpn., **42**, 2693 (1969).

(22) J. W. Ledbetter Jr.; J. Phys. Chem., **81**, 54 (1977).

(23) M. R. Udupa and G. Aruvamudan; Curr. Sci., **42**, 676 (1973).

(24) B. Dash, P. K. Mahapatra, D. Panda and J. M. Pattnaika; J. Ind. Chem. Soc., **61**, 1061 (1984).

(25) V. Hrust, T. Branisavljevic and N. Kallay; Anal. Chim. Acta., **343**, 135 (1997).

(26) P. G. More, R. B. Bhalvankar and S. C. Pattar, J. Ind. Chem. Soc., **78**, 474 (2001).

(27) J. Chang and S. Pan; U. S. Pat. Appl. Publ., US., **148**, 387 (2003).

(28) R. J. Anderson, S. Anderi, Batsanov, N. Belskaia, W. Paul, Groundwoqer, A. Zaytsev; Tetrahedron Lett., **45**, 943 (2004).

(29) A. Asan, S. Soylu, T. Kıyak, F. Yıldırım, S.G. Öztaş, N. Ancın and M. Kabasakaloğlu**;** Corrosion Sci.,(**In Press), (**2006).

(30) M. N. Desai and S. T. Desai; J. Electrochem. Soc., **32**, 397 (1983).
(31) Kodac; P. Fr. Pat., 983022, 18 June 195, Chem. Abstr., **49**, 2237f (1955).
(32) F. V. Well; Am. Perfumar Essent. Oil Rev., **52**, 218 (1948).
(33) Z. M. N. Nofal, M. I. El-Zahar and S. S. A. El-Karim; Molecules, **5**, 99 (2000).
(34) P. Vicini, A. Geronikaki, M. Incerti, B. Busonera, G. Poni, C. A. Cabras and P. L. Colla; Bioorg. Med. Chem., **11** , 4785 (2003).
(35) D. L. Layman, J. P. Socvill, J. F. Bartosevich and J. J. Bruce; Med. Chem., **26**, 35 (1983).
(36) Das, Arima, Lien, E. J. Trousdale and D. Melvin ; Chin. Pharm. J. (Taipet) **49** ,89 (1997).
(37) Ergenc, Nedime, Uinsoy, Nuray, Capangultate, Soruis, A. Otuk, Kiraz and Mnammer ; Arch. Pharm. **329**, 427 (1996).
(38) P.l Rathelst, N. Azos, H. E. Kashef, F. Delwasi; Eur. J. Med. Chem., **57**, 671 (2002).
(39) R. P. Pawar, N. M. Anduskary, V. B. Vibhute; J. Ind. Chem. Soc., **76**, 271(1999).
(40) A. A. Bekhil, Heshan T. V. Fahwy and A. Baraka; Eur. J. Med. Chem., **38**, 27 (2003).
(41) Smalders, R. Rene, Brunin, Dominique, Sarten and Frederic; Bull. Soc. Chim. Belg., **97**, 941 (1988) .
(42) S. E.Din and Nabaweya;Delta J. Sci., **15**, 47 (1991).
(43) A. K. Khalafallah and M. E. Hasan; Aswan Sci. Technol. Bull., **12**, 82 (1991).
(44) M. S. Yadav and S. A. Patil; Ind. J. Heterocycl. Chem., **2**, 41 (1992).
(45) Chohan, Z. Hussain, Kusuar and Somina; Chem. Pharm. Bull., **41**, 951 (1993)
(46) R. Tilak, R. Tyagi , B. Goel, K. K. Saxena, V. K. Shrivastava and A. Kumar; Ind. Drugs., **35**, 216 (1998).
(47) T. Pandey, V. P. Singh and R. V. Singh; Main Group Met. Chem., **22**, 315 (1999).
(48) S. Castellano, P. L. Colla, C. Musia and G. Stefancich; Archiv der Pharmazie, **333**, 162 (2000).
(49) B. S. Holla, B. S. Rao, K. Shridhara and P. M. Akberali; IL Farmaco, **55**, 338 (2000).
(50) B. S. Holla, K. V. Malini, B. S. Rao, B. K. Raw, N. Sarojini and S. Kumari; Eur. J. Med. Chem., **38**, 313 (2003).
(51) P. Selvam, M. Chandramohan, E. De Clercq, M. Witvrouw and C. Pannecouque; Eur. J. Pharma Sci., **14**, 313 (2001).
(52) P. Rathelst, N. Azoes, H. E. Kashef and F. Delwas; Eur. J. Med. Chem., **57**, 671 (2002).
(53) A. Adnan, H. Bekhil, T. U. Fahwy and A. Baraka; Eur. J. Med. Chem., **38**, 27 (2003).
(54) N. Demirbas and R. Ugurluogul; Turk J. Chem., **28**, 679 (2004).
(55) R. S. Varma; J. Ind. Chem. Soc., **81**, 627 (2004).
(56) P. Panneerselvam, R. R. Nair, G. Vijaylakshmi, E. H. Subramanian and S. K. Sridhar; Eur. J. Med. Chem., **40**, 225 (2005).
(57) Z. Guo, R. Chan, R. Chen, R. Xing, S. Liu, H. Yu, P. Wang, C. Li and P. Li; Carbohydrate Res., **341**, 351 (2006).
(58) Z. Guo, R. Chan, R. Chen, R. Xing, S. Liu, H. Yu, P. Wang, C. Li and P. Li; Bioorg. Med. Chem. Lett., **15**, 4600 (2005).

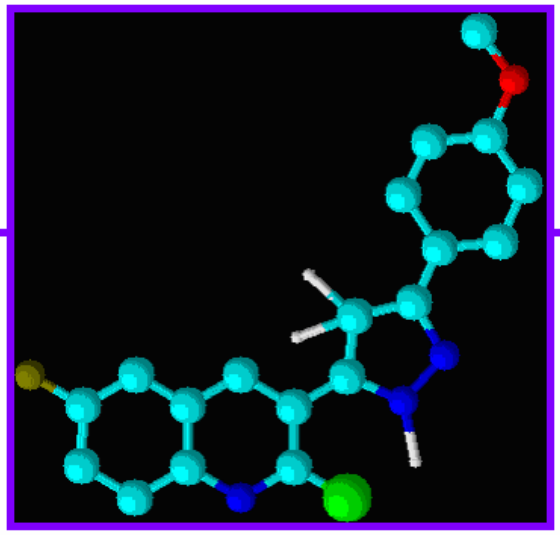
(59) S. M. Sondhi, N. Singh, A. Kumar, O. Lozach and L. Meijel; Bioorg. Med. Chem., **14**, 3758 (2006).

(60) J. Patole, D. S. Purkar, S. Padhye and C. Ratledge; Bioorg. Med. Chem., **16**, 1514(2006).

(61) A. Cukurovali, I. Yilmaz, S. Gur and C. Kazaz; Eur. J. Med. Chem., **41**, 201 (2006).

(62) D. Sriram, P. Yogeeswari, N. S. Myneedu and V. Saruswat; Bioorg. Med. Chem. Lett., **16**, 2127 (2006).

SECTION-III



SYNTHESIS OF PYRAZOLYL PYRAZOLINES

INTRODUCTION

Pyrazoline is a five membered heterocyclic system with two nitrogen atoms at the positions 1 and 2. The biodynamic behavior[1] and industrial applications[2] of pyrazolines have been studied extensively.

Various methods have been reported for the preparation of 2-pyrazoline derivatives. Hashsh et al. have synthesized pyrazolines by epoxidation of chalcones with epoxy ketones on reaction with hydrazine hydrate and phenyl hydrazine[3]. 2-pyrazolines can also be constructed by the cyclo condensation of chalcones with hydrazine hydrate[4]. Dipolar cyclo addition of nitrilimines of dimethyl fumarate, fumaronitrile and the N-aryl maleimides yielded the corresponding pyrazolines[5]. Godaliza and co-workers[6] have prepared fused pyrazolines derivatives. Few workers also reported the synthesis of 2-pyrazolines by one pot method[7,8]. Fritz et. al.[9] have synthesized some pyrazolyl pyrazolines. Paul et. al.[10] and Anshu et. al.[11] have described the microwave assisted synthesis of 2-pyrazolines. Melleller and Angew have also reported the synthesis of pyrazolines with a coupling-isomerisation sequence of halorene, propargl alcohol and methyl hydrazine[12] whereas Patel and Desai synthesized some 2-pyrazoline derivatives by the condensation of α,β-unsatured ketone and thiosemicarbazide in the presence of basic alumina and K_2CO_3[13].

From the literature survey, it was revealed that pyrazolines are better therapeutic agents. They are known to exhibit various biological activities such as antidiabetic[14], tranquilizer[15], hypoglycemic[16], diuretic[17], anticonvulsant[18,19], antineoplastic[20], cardiovascular[21], herbicidal[22], antiallergic[23], anti inflammatory[24], bactericidal[25,26], insecticidal[27], antiimplantation[28], antitumor[29], fungicidal[30], analgesic[31], antimicrobial[32] etc.

Richard and Megan [33] investigated pyrazoines bis phosphanate ester as novel anti-inflammatory and antiarthritic agents. Manna and co-worker[34] have reported 1- acetyl-5 -(2'-bromophenyl)- 4,5 -dihydro- 3-(2'-hydroxyphenyl)- 1H -pyrazolines and its derivatives as potent antiinflammatory, analgesic and antipyratic agents. Atif and coworkers[35] have patented 3-methyl-4'-(substituted phenylazo)-pyrazol-5-ones as antibacterial agent. Kucukguzel et. al.[36] have reported antimicrobial and anticonvulsant properties of some pyrazolines. Bansal and coworkers[37] have synthesized 1-acetyl-5-substituted ary-3-(b-

aminoaphthyl)-2-pyrazolines and studied their antiinflamnmatory and ulcerogenic activities. The cardiovascular[38] and vascularization propertiesagent[39] have also been reported. Matysiak and Niewiadomy [40] have synthesized some novel pyrazoline derivatives which exhibited comparable or higher activity than itraconazole and fluconazole tested under the same experimental condition. Berghot et. al[41] have studied antibacterial activities of pyrazole and pyrazoline derivatives of diazepam. Gokhan et. al.[42] have synthesized new 1,N-substituted thiocarbomoyl-3-phenyl-5-thienyl-2-pyrazoline derivatives and studied their for antidepressant, antiogenic and mammalianmonoamine oxidase (MAO)- A & B inhibitory activities. Ahn et. al[43] have synthesized cyano- pyrazoline derivatives and documented them as dipeptidyl peptidase(DP)-IVinhibitors and antidiabitic agents. Carrion et. al[44] have reported pyrazoline derivatives as antiinflammatory agents. Jeong et. al.[45] have reported pyrazole as low-density lipoprotein (LDL) antioxidant activity in the TBARS assay. Jones and co-workers[46] have synthesized 4-substituted pyrazolines and reported them as antagonists.

Recently, Chimenti et. al[47] have discovered anti helicobacter pyroli activity of some substituted diphenyl pyrazolines. The antiamoebic activity of a series of new 1,N-substituted pyrazoline analogues of thio semicarbazones were reported[48]. Ucar et. al[49] have synthesized 1-N-substituted thiocarbamoyl-3-phenyl-5-thienyl-2-pyrazolines and reported as a novel cholinesterase and selective monoamine oxidase B inhibitors for the treatment of Parkinson's and Alzeimer's disease. Prasad et. al.[50] have also synthesized some 1,3,5-triphenyl-2-pyrazolines and 3-(2''-hydroxy naphthalen-1"-yl)-1,5-diphenyl-2-pyrazolines derivatives of type(IX) and studied their antidepressant properties. Galil et. al[51] reported antiandrogenic activity of some new substituted aryl pyrazolines. Budakoh and co-workers[52] have synthesized pyrazolines possessing antiamoebic activity.

These biological properties prompted me to synthesize some pyrazoline derivatives which are reported in this chapter along with their characterization.

EXPERIMENTAL

Synthesis of 2-chloro-6-fluoro-3-[3-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-5-yl]quinoline

[A] Synthesis of *N*-(4-fluorophenyl)acetamide:

Section-1 (A)

[B] Synthesis of 2-chloro-6-fluoroquinoline-3-carbaldehyde:

Section -1 (B)

[C] Synthesis of (2*E*)-3-(2-chloro-6-fluoroquinolin-3-yl)-1-(4-methoxy phenyl)prop-2-en-1- one:

Section -1 (C)

[D] Synthesis of 2-chloro-6-fluoro-3-[3-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-5-yl]quinoline:

A mixture of (2*E*)-3-(2-chloro-6-fluoroquinolin-3-yl)-1-(4-methoxy phenyl)prop-2-en-1- one (3.41g, 0.01M) and hydrazine hydrate (0.5g, 0.01M) in 25 ml of absolute alcohol was refluxed in water bath at temp. 80-90^{o}C for 8 hrs. The reaction mixture was poured into ice. The product was isolated and crystallized from ethanol.

Similarly other substituted pyrazolines have been prepared. The physical data are recorded in Table 3.1.

REACTION SCHEME

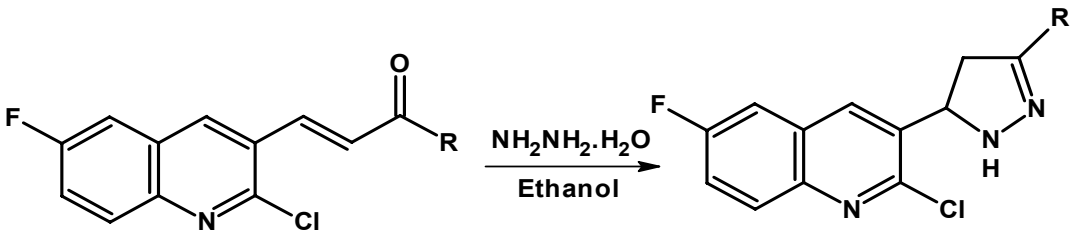


Table 3.1: Physical constants of pyrazolines.

Sr. No.	Code	R	M.F.	M. Wt. (g/mol)	Rf* Value	M.P. ^{o}C	Yield %
1.	**NVK-3A**	4-OCH_3-C_6H_4-	$C_{19}H_{15}ClFN_3O$	355	0.34	198	76
2.	**NVK-3B**	3-NO_2-C_6H_4-	$C_{18}H_{12}ClFN_4O_2$	371	0.46	165	72
3.	**NVK-3C**	2-OH-C_6H_4-	$C_{18}H_{13}ClFN_3O$	342	0.49	223	59
4.	**NVK-3D**	4-NH_2-C_6H_4-	$C_{18}H_{14}ClFN_4$	341	0.32	210	65
5.	**NVK-3E**	4-NO_2-C_6H_4-	$C_{18}H_{12}ClFN_4O_2$	371	0.41	202	69
6.	**NVK-3F**	3-NH_2-C_6H_4-	$C_{18}H_{14}ClFN_4$	341	0.43	189	64
7.	**NVK-3G**	4-CH_3-C_6H_4-	$C_{19}H_{15}ClFN_3$	340	0.33	165	66
8.	**NVK-3H**	4-OH-C_6H_4-	$C_{18}H_{13}ClFN_3O$	342	0.41	215	70
9.	**NVK-3I**	4-Cl-C_6H_4-	$C_{18}H_{12}Cl_2FN_3$	360	0.63	171	59
10.	**NVK-3J**	4-Br-C_6H_4-	$C_{18}H_{12}BrClFN_3$	405	0.43	188	66

*Acetone:Benzene: 2:8

Figure 3.1: IR spectra of 2-chloro-6-fluoro-3-[3-(4-methoxyphenyl)-4,5-dihydro -1H-pyrazol-5-yl]quinoline.

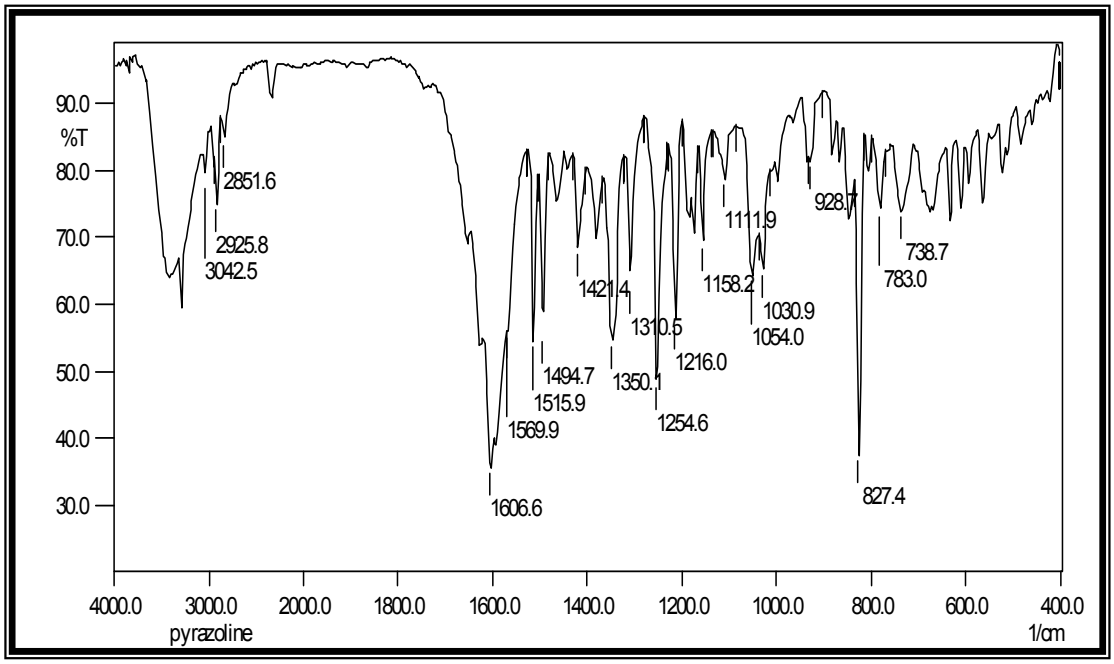
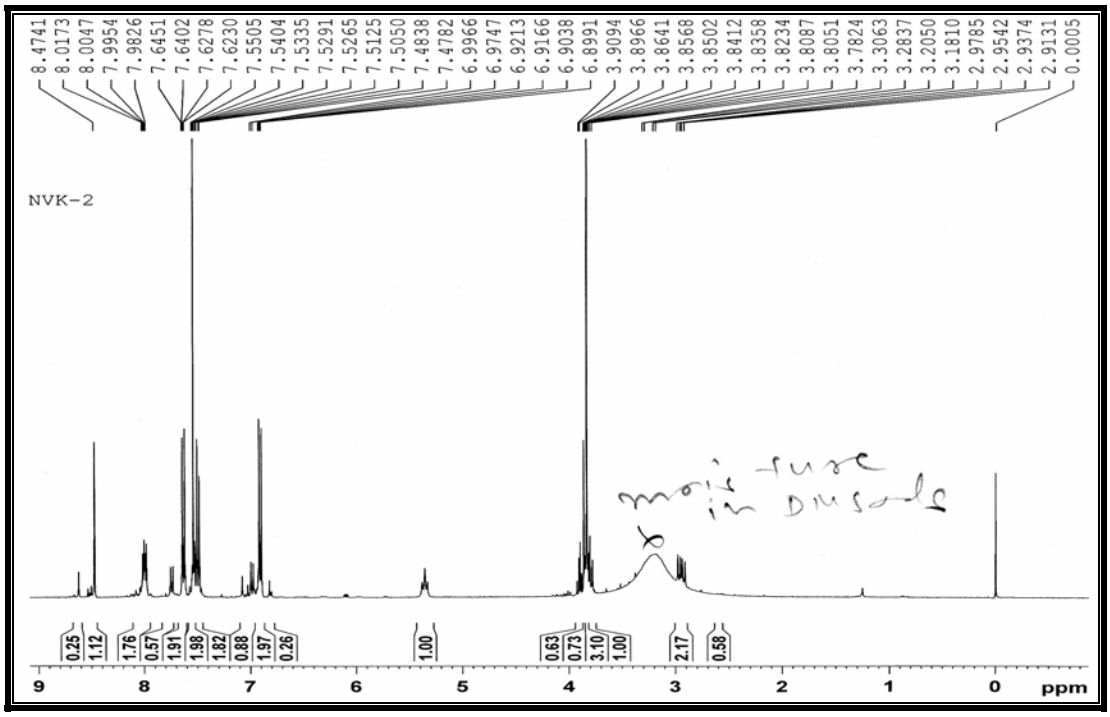


Table 3.2: IR spectral data of 2-chloro-6-fluoro-3-[3-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-5-yl]quinoline.

Type	Vibration mode	Frequency in cm^{-1}	
		Observed	Reported
Alkane (methyl)	C-H str. (asym.)	2926	2975-2850
	C-H str. (sym.)	2852	2880-2860
	C-H def. (asym.)	1421	1470-1435
	C-H def.(sym.)	1350	1395-1370
Aromatic	C-H str.	3043	3100-3000
	C=C	1516	1585-1480
	C-H i.p. def.	1031	1125-1090
	C-H o.o.p. def.	827	860-810
quinoline moiety	C=N str.	1607	1650-1580
	C-N str.	1311	1350-1200
pyrazoline	N-H str.	1255	1275-1200
	N-N	929	1150-925
	C-F	1216	1400-1000
	C-Cl	739	800-600

Figure 3.2: ^{1}H NMR spectra of 2-chloro-6-fluoro-3-[3-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-5-yl]quinoline.



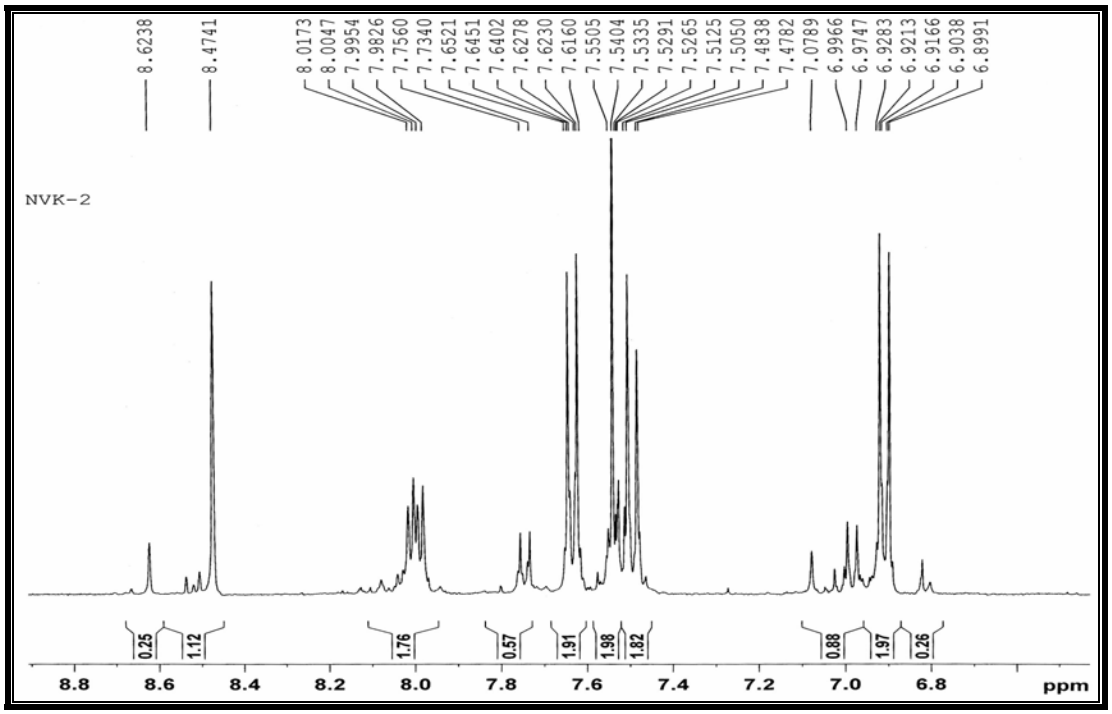
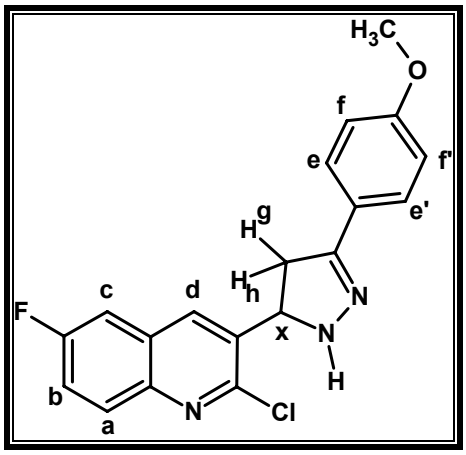
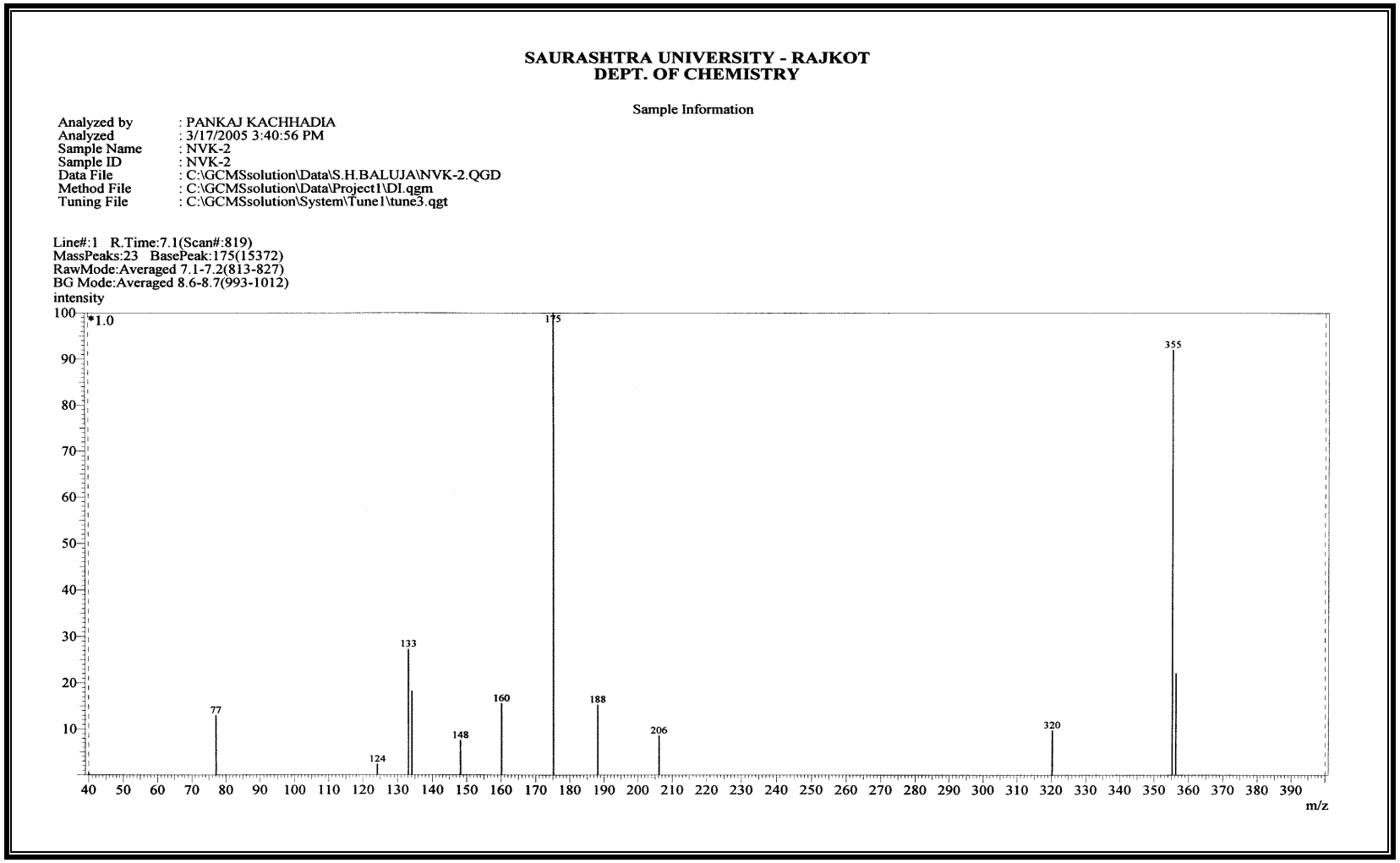


Table 3.3: ^{1}H NMR spectral data of 2-chloro-6-fluoro-3-[3-(4-methoxyphenyl)-4,5- dihydro-1H-pyrazol-5-yl]quinoline.

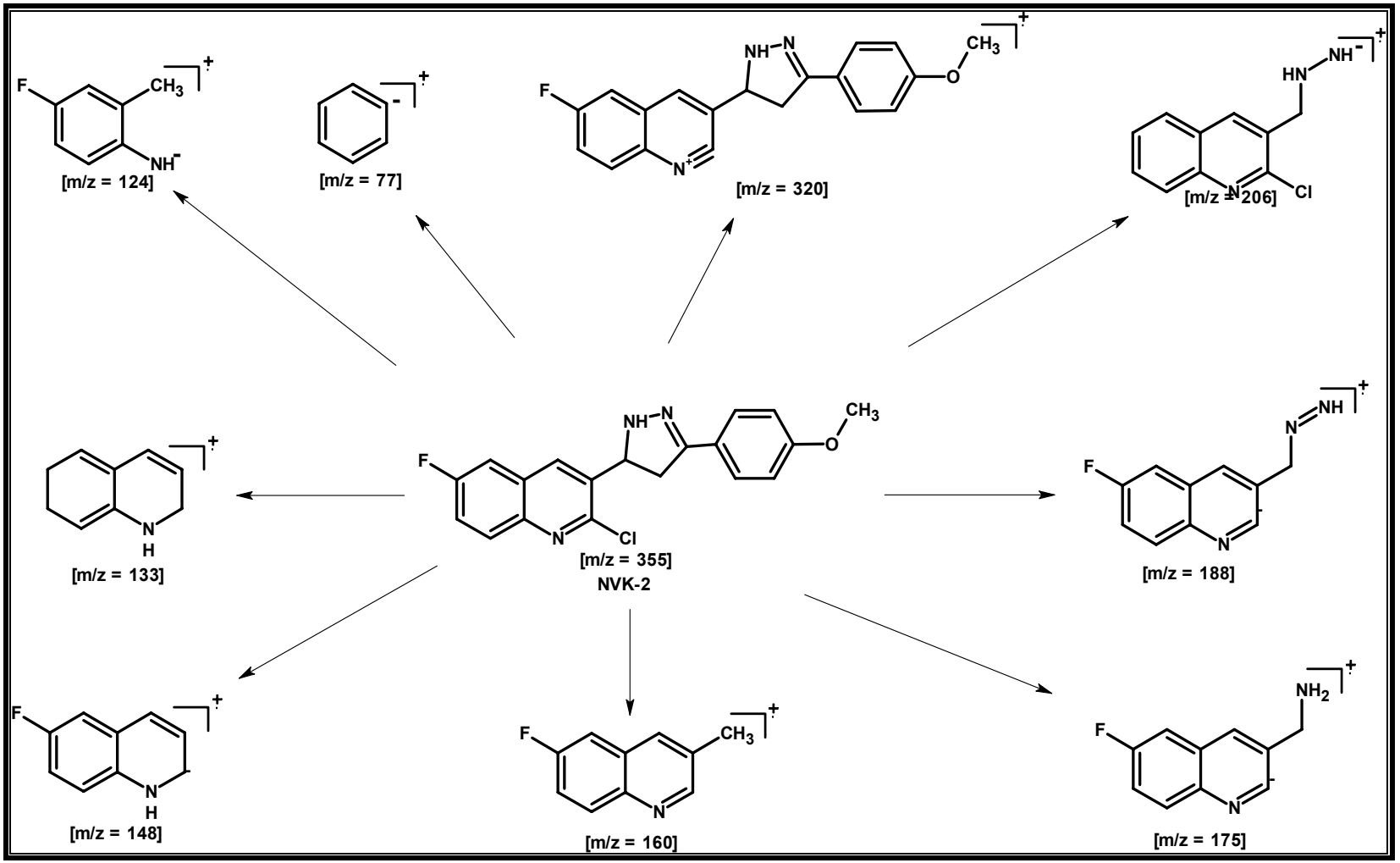


Singal No.	Signal Position (δ ppm)	Relative No. of Protons	Multiplicity	Inference	J (Hz)
1.	2.91-2.97	2H	triplet	Ar-H(g)+H(h)	-
2.	3.86	3H	singlet	Ar-OCH_3	-
3.	3.78-3.86	1H	multiplet	Ar-H(x)	-
4.	6.89-6.92	2H	doublet	Ar-H(ff')	8.88
5.	7.47-7.51	2H	multiplet	Ar-H(a)+H(b)	-
6.	7.61-7.65	2H	doublet	Ar-H(ee')	14.44
7.	7.98-8.01	1H	doublet	Ar-H(c)	13.88
8.	8.47	1H	singlet	Ar-H(d)	-

Figure 3.3: Mass Spectra of 2-chloro-6-fluoro-3-[3-(4-methoxyphenyl)- 4,5- dihydro-1H-pyrazol-5-yl]quinoline.



Scheme 3.1: 2-chloro-6-fluoro-3-[3-(4-methoxyphenyl)- 4,5- dihydro-1H-pyrazol-5-yl]quinoline.



REFERENCES

(1) J. Elguero; "In Comprehensive Heterocyclic Chemistry', Edited by A. R. Katritzky and C. W. Res., **5**, 168 (1984).

(2) R. S. Theobald; "Rodd's Chemistry of Carbon Compounds", Edited by M. F. Ansell, Vol. IV, Part C, Ch. 16 2nd Edition, (Elsenier Science Publishers B. V., Amsterdam) 59 (1998).

(3) M. A. El. Hashsh, M. El-Kady, M. A. Saiyed and A. A. Elsawy; Egypt. J. Chem., **27**, 715 (1985).

(4) A. M. Fahmy, M. Hassan, A. A. Khalf and R. A. Ahmed; Rev. Roum. Chim., **33**, 755 (1988).

(5) M. H. Hamdi, A. E. Hamad and A. H. M. Hiyam; Salter Lett., **8**, 27582 (1989).

(6) M. Gordaliza, M. Jose, M. Corral, M. A. Castro, M. L. L. Vazquez, A. S. Feliciano and A. Carpy; Bioorg. Med. Chem., **3**, 1203 (1995).

(7) W. Sebacher, G. Michl, F. Belaj, R. Brun, R. Saf and R. Weis; Tetrahedron **59**, 2811 (2003).

(8) G. Gyassi, K. Bourin, M. Lamiri and M. Soufiaoui; New J. Chem., **22**, 1545 (1998).

(9) M. Fritz, F. Rainer, E. Chritoph and A. Turberg ; PCT Int. Appl. WO 03 59, 887 (Cl. C07 D231/28) (2003); Chem. Abstr., **139**, 117441z (2003).

(10) S. Paul and R. Gupta; Ind. J. Chem., **37B**, 1279 (1998).

(11) A. Dandia, H. Taneja and C. S. Sharma; Ind. J. Hetero. Chem., **11**, 258 (1999).

(12) T. Mulleller and J. J. Angew; Chem. Int. Ed., **39**, 1253 (2000).

(13) V. M. Patel and K. R. Desai; ARKIVOC, **1**, 123 (2004).

(14) H. G. Garg and P. P. Singh; J. Chem. Soc., **2**, 1141 (1936).

(15) B. Hans, R. Rolf and R. Rudolf; US. Pat. 3, 822, 283 (1974); Chem. Abstr., **81**, 105494r (1974).

(16) K. Trena and Zolzislaw; Acta. Pol. Pharm., **36** , 227 (1979).

(17) K. Zalgislaw and A. Seffan ; Acta. Pol. Pharm., **36**, 645 (1979).

(18) Z. Brozozowsk and E. Pormarnacka; Acta. Pol. Pharm., **37**, 1378 (1980).

(19) V. K . Shrivastava, R. Chandra and A. Kumar; Ind. J. Chem., **41B**, 2371 (2002).

(20) H. M. Mokhtar and H. M. Faidallah; Pharmazie, **42**, 482 (1987).

(21) Y. Hiroyuti and O. Mocoto; Eur. Pat. Appl. Ep 295695 (Cl. C07D 401/6) (1988); Chem. Abstr., **111**, 23510 (1989).

(22) K. Wellinga and H. H. Eussen Jacobus; Eur. Pat. Ep. 269 141 (Cl C07D 231/06) (1988); Chem. Abstr., **110**, 8204 (1989).

(23) B. Roman; Pharmazie, **45**, 214 (1990).

(24) A. Kumar, R. S. Verma and B. P. Jagu; J. Ind. Chem. Soc., **67**, 120 (1990).

(25) P. Desaea; A. Nunrich; M. Carderny and G. Devaux; Eur. J. Med. Chem., **25**, 285 (1990).

(26) K. Balakrishna, R. Chimabalkar, G. Rai, R. Gururaja and S. Shenoy ; J. Ind. Coun. Chemi., **18**, 39 (2001).

(27) D. B. Reddy, T. Senshuma, B. Seehaiha and M.V. R. Reddy; Ind. J. Chem., **30B**, 46 (1991).

(28) D. B. Reddy, T. Senshuna and M. V. R. Reddy; Ind. J. Chem., **30B**, 46 (1991).

(29) W. I. Ronald and A. Adriano; Chem. Abstr., **126**, 181346f (1997).

(30) S. S. Nayal and C. P. Singh; Asian J. Chem. **11**, 207 (1999).

(31) G. Aysel, D. Seref, C. Gultaze, E. Kevser and V. Kamil; Eur. J. Med. Chem., **35**, 359 (2000).

(32) J. Panda, S. V. Srinivas, M. E. Rao; J. Ind. Chem. Soc., **79**, 770 (2002).

(33) N. Richard and M. Megan; J. Med. Chem., **36**, 134 (1993).

(34) F. Manna F. Chiments , A. Belasco, M. L. Cenicola and D'Amico; Chem. Abstr., **118**, 80902p (1993).

(35) T. Atif, E. Fatema and A. M. Abdela; Chim Pharm. J., **47**, 37 (1995).

(36) G. Kucukguzel, S. Rollas, H. Erdeniz, M. Kiraz and A. C. Ekinci; Eur. J. Med. Chem., **35**, 761 (2000).

(37) E. Bansal, V. K. Srivastava and A. Kumar; Eur. J. Med. Chem., **36**, 81 (2001).

(38) V. Malhotra, S. Pathak, R. Nath , D. Mukherjee and K. Shanker ; Ind. J. Chem., **41B**, 1310 (2002).

(39) A. J. I. Kim and D. R. Jones; PCT Int. Appl. WO 02 89, 799 (Cl. A61K31/4439) (2002); Chem. Abstr., **137**, 370086j (2002).

(40) J. Matysiak and A. Niewiadomy.; Bioorg. Med. Chem. **11**, 2285 (2003).

(41) M. A. Berghot and E. B. Moawad; Eur. J. Pharm. Sci. **20**, 173 (2003).

(42) N. Gokhan, A. Yesilada, G. Usar, K. Erol and A. A. Bilgin; Archiv per Phazmizie, **336**, 362 (2003).

(43) J. H. Ahn, H. M. Kim, S. H. Jung, S. K. Kang, K. R. Kim, S. D. Rhee, S. D. Yang, H. G. Cheon and S. S. Kim ; Bioorg. Med. Chem. Lett. **14**, 4461 (2004).

(44) M. D. Carrion, M. E. Camacho, J. Leon, V. Tapias, M. A. Gallo and A. Espinosa; Tetrahedron, **60**, 4051 (2004).

(45) T. S. Jeong, Kyung and S. Kim; Bioorg. Med. Chem. Lett., **14**, 2119 (2004).

(46) D. G. Jones, X. Liang, E. L. Stewart, R. A. Noe, L. S. Kallander, K. P. Madauss, S. P. Williams, S. K. Thompson and J. H. William; Bioorg. Med. Chem. Lett. **15**, 3203 (2005).

(47) F. Chimenti, B. Bizzarri and F. Manna ; Bioorg. Med. Chem. Lett., **15**, 603 (2005).

(48) M. Abid and A. Azam; Bioorg. Med. Chem. **13**, 2213 (2005).

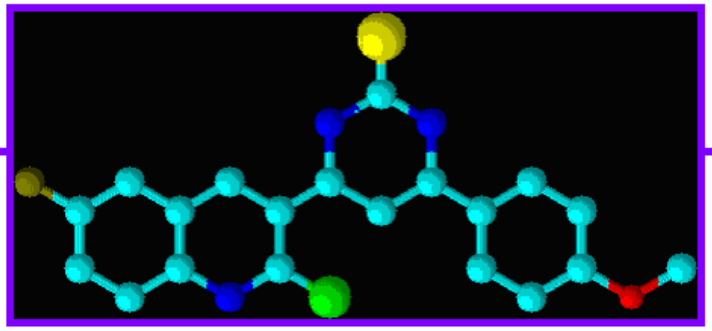
(49) G. Ucar, N. Gokhan, A. Yesilada and A. A. Bilgin; Neurosci. Lett., **382**, 327 (2005).

(50) G. Y. R. Prasad, A. L. Rao, L. Prasoona, K. Murali and P. R. Kumar; Bioorg. Med. Chem. Lett. **15**, 5030 (2005).

(51) A. E. Galil, E. Amr, N. A. A. Latif and M. M. Abdalla; Bioorg. Med. Chem. **14**, 373 (2006).

(52) A. Budakoh, M. Abid and A. Azam; Eur. J. Med. Chem., **41**, 63 (2006).

SECTION-IV



SYNTHESIS OF THIOPYRIMIDINES

INTRODUCTION

The chemistry of pyrimidines and its derivatives have been studied since past century due to their close pharmacological association with diverse pharmacological properties. Pyrimidine was first isolated by Gabriel and Colman in 1899. Though pyrimidine itself does not exist in nature but substituted pyrimidines containing pyrimidine moiety are found as a part of more complex system and are widely distributed.

The first primary synthesis of thiopyrimidine derivatives from aliphatic fragments was carried out by Frankland and Kolbs in 1848. Since then, many distinct primary synthetic methods have been devised[1-6].

By using different methods thiopyrimidine have been prepared such as: by the condensation of esters with N-methyl thiourea[7], by the condensation of β-dinitriles with thiourea and guanidine[8], by the condensation of β-aldehydronitrile with formamidine and thiourea[9]. 2-mercaptopyrimidines have been synthesized by Anderson[10] through condensation of thiourea and substituted β-ketoester in presence of sodim ethoxide. Biginnelli[11] investigated that an aromatic aldehyde with β-ketoester and urea or thiourea yield pyrimidine derivative. Jinjun[12] have prepared some new pyrimidine derivatives.

Thiopyrimidine represent one of the most active class of compounds possessing a wide spectrum of biological activities, such as antiviral and antitumor[13], antiinflammatry and analgesic[14-16], antifilarial[17], anticancer and herbicidal[18-20], antileishmanial[21,22], antineoplastic[23,24], antimicrobial[25], anti AIDS and antitumor[26], antitubercular[27], antiviral[28], antagonists[29,30], antitumor[31] and herbicidal[32].

Peesapati et al.[33] have synthesized thiopyrimidine derivatives and reported them as potent antimicrobial agent. Mahran and co-workers[34] have synthesized heterocyclic system containing thiopyrimidine nucleus as potent antimicrobial and antitumor agent. Saneyoshi and co-workers[35] have synthesized thiopyrimidine nucleosides as anticancer and antiviral agent. Daniel et al.[36] have synthesized some novel thiopyrimidine derivatives possessing anti HIV activity.

The antitumor activity[37], antimicrobial[38] and anti-herpesvirus activities[39] of some thiopyrimidine derivatives have also been reported. Shishoo et al.[40]

have reported thiopyrimidine derivatives as A2 receptor antagonists. The inhibitory activity against Human Immunodeficiency Virus (HIV) of some modified thiopyrimidine nucleosides have also been reported[41]. The antiviral activity of some thiopyrimidine have been reported by Jeong et al.[42] and Kim et al.[43] Whereas El-Fottoh et al.[44] and Saleh et al[45] have reported their anticancer and other pharmacological activities. Shigeta et al.[46] have studied the antiviral activities of 5-alkyl-2-thiopyrimidine against herpes simplex virus (HSV), varicella-zoster virus (VZV) and human cytomegalovirus (HCMV).

Recently, Wili et al.[47] reported herbicidal activity and Sondhi et al[48] reported anti-inflammatory and analgesic activity of some thiopyrimidine derivatives. Hammerland et al[49] reported Structure–activity relationship of thiopyrimidines as mGluR5 antagonists

Thus, the important role played by thiopyrimidine nucleus for various physiological activities prompted us to synthesis thiopyrimidine derivatives.

EXPERIMENTAL

4-(2-chloro-6-fluoroquinolin-3-yl)-6-(4-methoxyphenyl)-3,4-dihydropyrimidine-2(1H)-thione

[A] Synthesis of *N*-(4-fluorophenyl)acetamide:

Section-1 (A)

[B] Synthesis of 2-chloro-6-fluoroquinoline-3-carbaldehyde:

Section -1 (B)

[C] Synthesis of (2*E*)-3-(2-chloro-6-fluoroquinolin-3-yl)-1-(4- methoxy phenyl)prop-2-en-1- one:

Section -1 (C)

[D] Synthesis of 4-(2-chloro-6-fluoroquinolin-3-yl)-6-(4-methoxyphenyl)-3,4-dihydropyrimidine-2(1H)-thione:

To a well stirred solution of (2*E*)-3-(2-chloro-6-fluoroquinolin-3-yl)-1-(4-methoxyphenyl)prop-2-en-1- one (3.41g, 0.01M) and thiourea (0.76g, 0.01M) in ethanol (25 ml), add alcoholic KOH solution as catalyst. The reaction mixture was refluxed in waterbath for 12 hrs. The reaction mixture was poured into ice. The product was isolated and crystallized from ethanol.

REACTION SCHEME

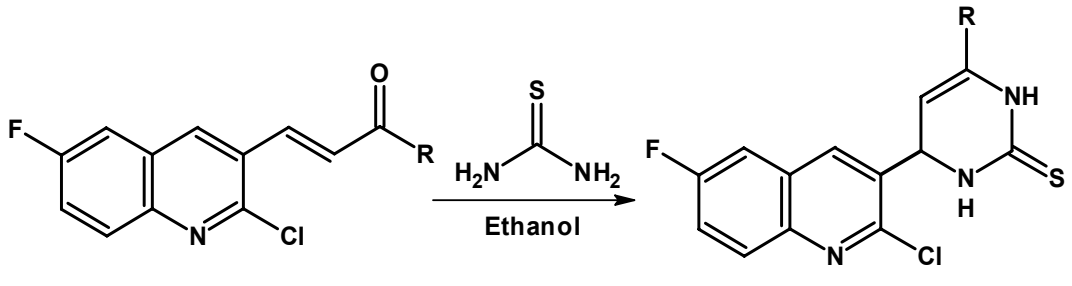


Table 4.1: Physical constants of thiopyrimidine.

Sr. No.	Code	R	M.F.	M. Wt. (g/mol)	Rf* Value	M.P. ^{o}C	Yield %
1.	**NVK-4A**	4-OCH_3-C_6H_4-	$C_{20}H_{15}ClFN_3OS$	399	0.49	169	65
2.	**NVK-4B**	3-NO_2-C_6H_4-	$C_{19}H_{12}ClFN_4O_2S$	415	0.52	175	67
3.	**NVK-4C**	2-OH-C_6H_4-	$C_{19}H_{13}ClFN_3OS$	386	0.43	205	62
4.	**NVK-4D**	4-NH_2-C_6H_4-	$C_{19}H_{14}ClFN_4OS$	385	0.49	226	56
5.	**NVK-4E**	4-NO_2-C_6H_4-	$C_{19}H_{12}ClFN_4O_2S$	415	0.43	245	59
6.	**NVK-4F**	3-NH_2-C_6H_4-	$C_{19}H_{14}ClFN_4S$	385	0.42	200	71
7.	**NVK-4G**	4-CH_3-C_6H_4-	$C_{20}H_{15}ClFN_3S$	384	0.34	192	52
8.	**NVK-4H**	4-OH-C_6H_4-	$C_{19}H_{13}ClFN_3OS$	386	0.41	185	61
9.	**NVK-4I**	4-Cl-C_6H_4-	$C_{19}H_{12}Cl_2FN_3S$	404	0.33	215	52
10.	**NVK-4J**	4-Br-C_6H_4-	$C_{19}H_{12}BrClFN_3S$	449	0.31	187	68
11.	**NVK-4K**	2-CH_3-C_6H_4-	$C_{20}H_{15}ClFN_3S$	384	0.48	185	56

* Acetone:Benzene: 1.5:8.5

Figure 4.1: IR spectra of 4-(2-chloro-6-fluoroquinolin-3-yl)-6-(4-methoxy phenyl)-3,4-dihydropyrimidine-2(1H)-thione.

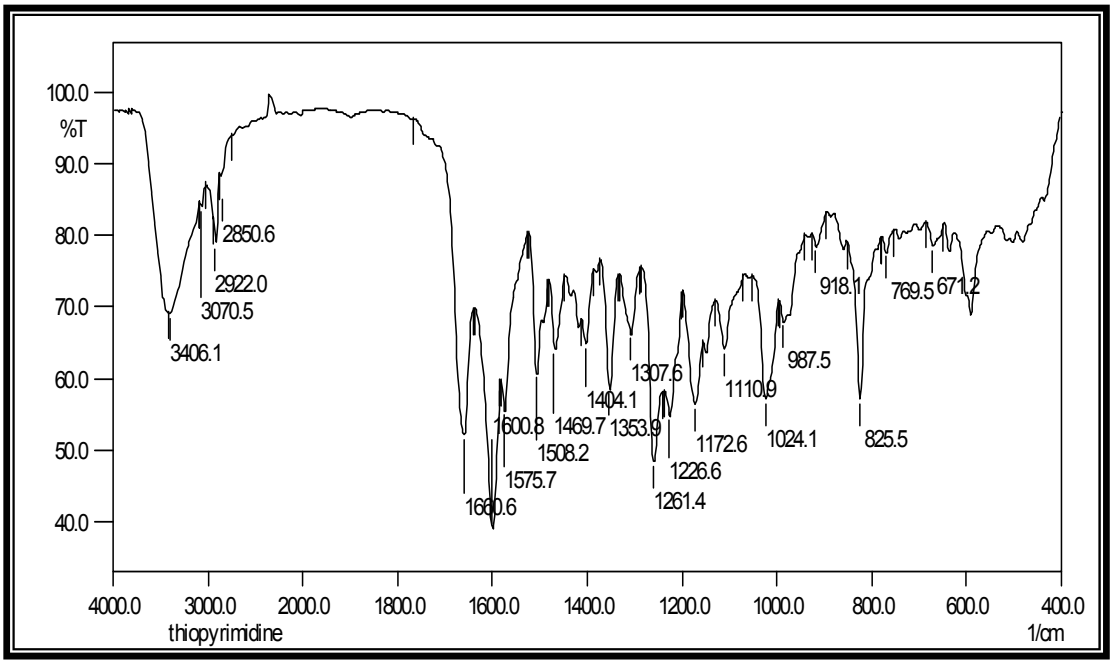
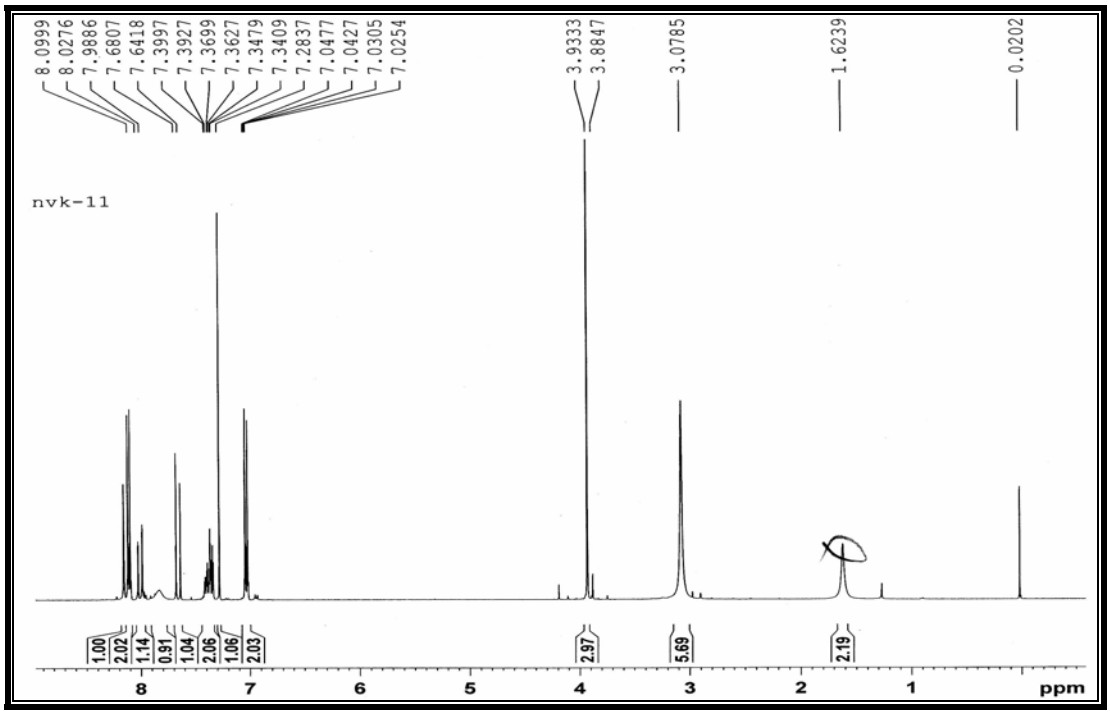


Table 4.2: IR spectra data of 4-(2-chloro-6-fluoroquinolin-3-yl)-6-(4-methoxy phenyl)-3,4-dihydropyrimidine-2(1H)-thione.

Type	Vibration mode	Frequency in cm^{-1}	
		Observed	Reported
Alkane (Methyl)	C-H str. (asym.)	2922	2975-5920
	C-H str. (sym.)	2851	2880-2860
	C-H def. (asym.)	1470	1470-1435
	C-H def.(sym.)	1354	1395-1370
Aromatic	C-H str.	3071	3100-3000
	C=C	1508	1585-1480
	C-H i.p. def.	1111	1125-1090
	C-H o.o.p. def.	826	860-810
quinoline moiety	C=N str.	1601	1650-1580
	C-N str.	1308	1350-1200
nitrongen	N-H str.	3406	3500-3310
ether	C-O-C str. (asym.)	1261	1275-1200
	C-O-C str. (sym.)	1024	1075-1020
	C=S str.	1172	1200-1050
	C-F	1227	1400-1000
	C-Cl	770	800-600

Figure 4.2: ^{1}H NMR spectra data of 4-(2-chloro-6-fluoroquinolin-3-yl)-6-(4-methoxyphenyl)-3,4-dihydropyrimidine-2(1H)-thione.



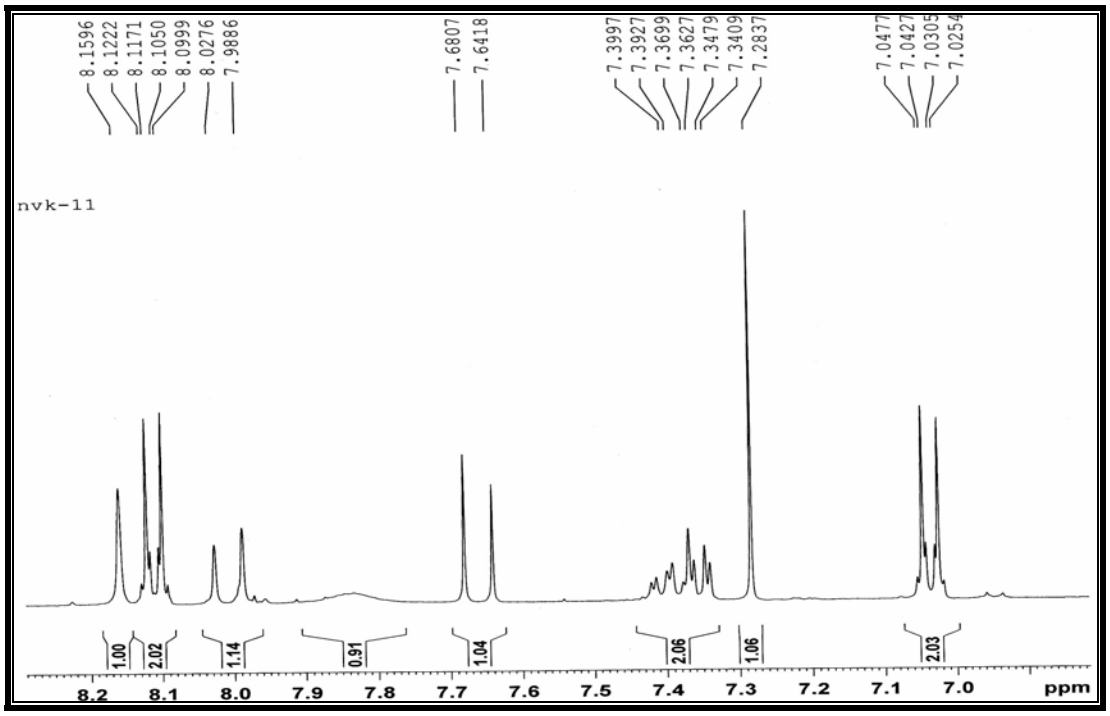
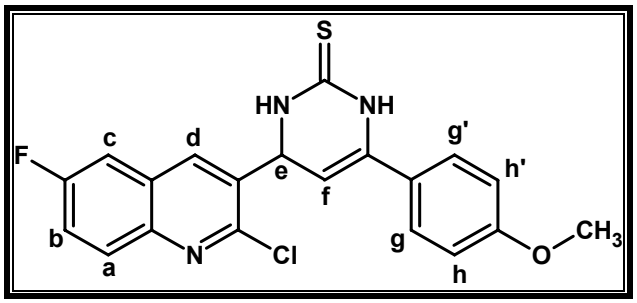
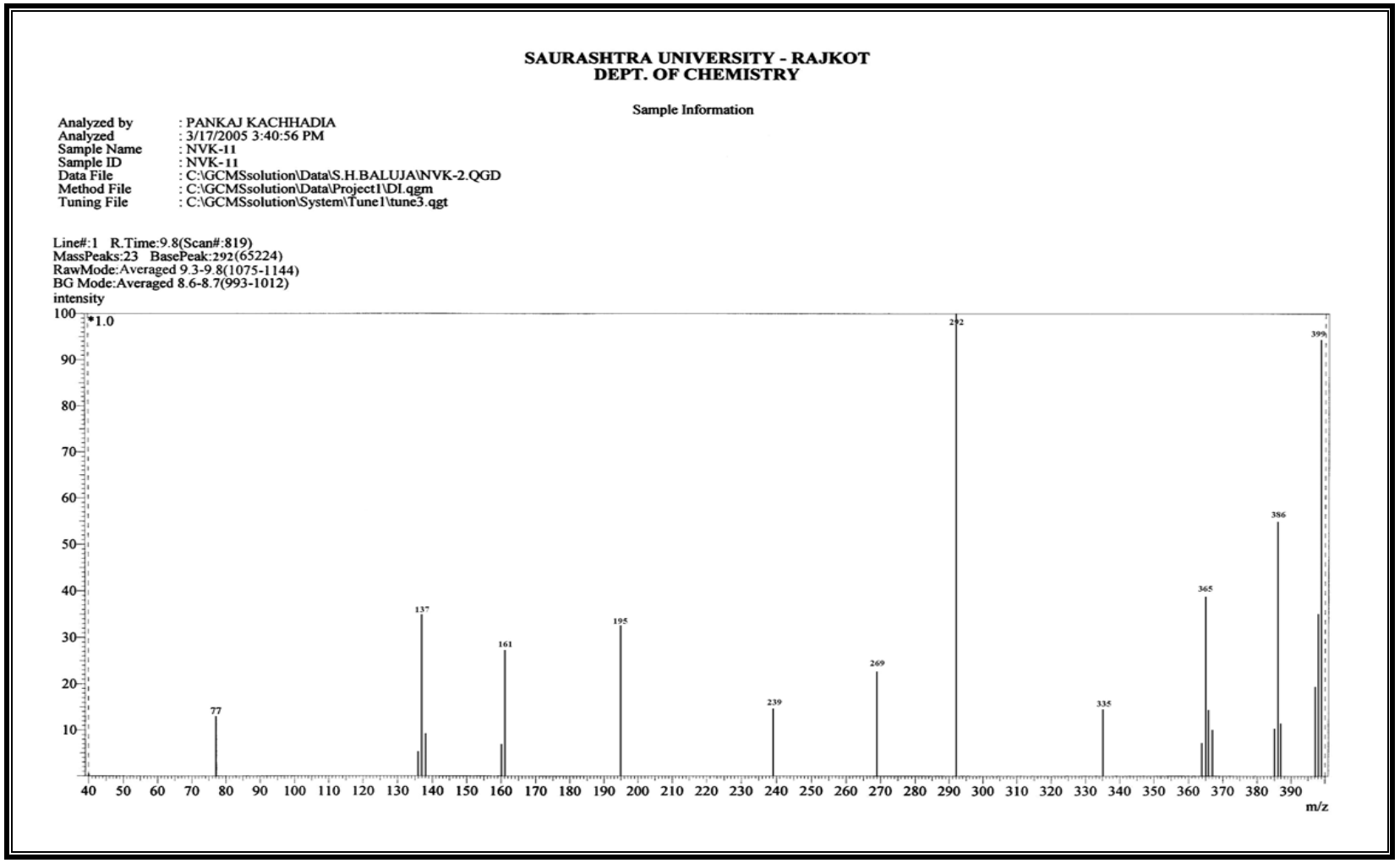


Table 4.3: ^{1}H NMR spectra data of 4-(2-chloro-6-fluoroquinolin-3-yl)-6-(4-methoxy phenyl)-3,4-dihydropyrimidine-2(1H)-thione.

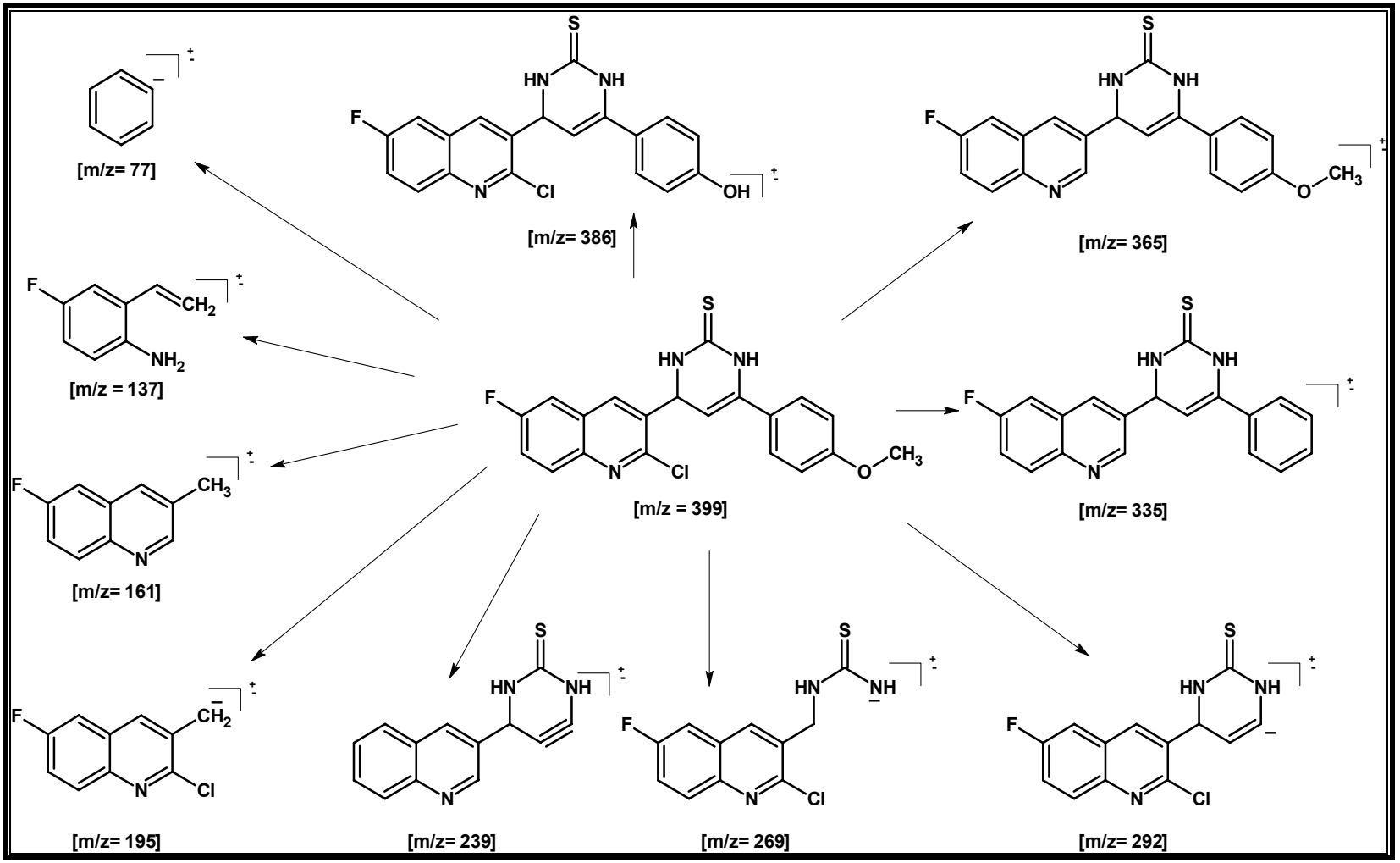


Singal No.	Signal Position (δ ppm)	Relative No. of Protons	Multiplicity	Inference	J (Hz)
1.	7.28	1H	singlet	Ar-H(f)	-
2.	3.93	3H	singlet	Ar-OCH_3	-
3.	7.02-7.04	2H	doublet	Ar-H(hh')	8.92
4.	7.34-7.39	2H	multiplet	Ar-H(b)+H(c)	-
5.	7.64-7.68	1H	doublet	Ar-H(a)	15.66
6.	7.83	1H	singlet	-NH	-
7.	7.98-8.02	1H	doublet	Ar-H(e)	15.60
8.	8.09-8.12	2H	doublet	Ar-H(gg')	8.92
9.	8.15	1H	singlet	Ar-H(d)	-

Figure 4.3: Mass Spectra of 4-(2-chloro-6-fluoroquinolin-3-yl)-6-(4-methoxyphenyl)-3,4-dihydropyrimidine-2(1H)-thione.



Scheme 4.1: Mass Spectra of 4-(2-chloro-6-fluoroquinolin-3-yl)-6-(4-methoxyphenyl)-3,4-dihydropyrimidine-2(1H)-thione.



REFERENCES

(1) H. Bredereck, F. Effenberger and H. J. Treiber; Chem. Ber, **96**, 1505 (1963).

(2) S. Inoue, A. J. Saggimoto and E. A. Nodiff; J. Org. Chem., **26**, 4504 (1961).

(3) P. Kroknke, E. Schmidt and W. Zocher; Chem. Ber., **97**, 1163 (1964).

(4) E. C. Taylor and R. W. Morrison; J. Org. Chem., **32**, 2379 (1967).

(5) D. J. Brown; Chem. Hetero. Compd., **16**, 20 (1970).

(6) H. O. Kim, Y. H. Park, H. R. Moon and L. S. Jeong; Bioorg. Med. Chem. Lett., **12**, 2403 (2002).

(7) D. J. Brown and P. Waring; Aust. J. Chem., **30**, 621 (1977).

(8) V. M. Berezovskil and A. M. Yurkevich; Zh. Ohschch. Khim., **32**, 1655 (1962).

(9) C. W. Whitehead and J. J. Traverso; J. Am. Chem. Soc., **78**, 5294 (1956).

(10) G. W. Anderson, I. F. Halverstadt, W. H. Miler and R. O. Robin; J. Am. Chem. Soc., **67**, 2197 (1945).

(11) Biginelli; Gazz. Chim. Ital., 23, 360 (1893); Atti Accad. Licel., **3**, 195 (1894).

(12) W. Jinjun, Z. Jianmin and C. Bingzi; Hauzue Tonghao, **10**, 48 (1997).

(13) K. Deo, K. Avasthi, R. Pratap and D. S. Bhakumi; Ind. J. Chem., **28B**, 237 (1898).

(14) S. Sarangam and S. Somshekara; J. Ind. Chem. Soc., **53**, 185 (1976).

(15) Z. Machan and V. Krystyna; Acta. Pol. Chem., **42B**, 516 (1985).

(16) R. P. Verma, S. M. Sondhi, N. Singhal, V. K. Sharma, R. Shukla and G. K. Patnaik; Phosphorous, Sulfur, Silicon Relat. Elem., **118**, 7 (1996).

(17) R. E. Howells, J. Tinsly, E. Devancy and G. Smith; Acta. Tropica, **38**, 289 (1982).

(18) V. J. Ram, D. A. Vanden Berghe and A. J. Vlietinck; Liebigs Ann. Chem., **797**, 112 (1987).

(19) V. J. Ram; J. Prakt. Chem., **331**, 893 (1989).

(20) V. J. Ram, N. M. Haqu and P. Y. Guru; Eur. J. Med. Chem., **27**, 851 (1992).

(21) M. Ali, A. G. Hamman and S. F. Mohmad; J. Phosphorus and Sulfur; **39**, 24 (1988).

(22) A. G. Hamman, S. M. Hussain and Z. R. Kotab; J. Phosphorus, Sulfur and Silicon, **47**, 47 (1990).

(23) C. R. Petric, H. B. Cotton and P. A. Me Kerman; J. Med. Chem., **28**, 1010 (1988).

(24) C. Hansch, P. G. Sammes and J. B. Taylor; Compre. Med. Chem., 2, 1st Ed. 323-324 (1990).

(25) V. K. Ahuwalia, R. Batia, A. Khurana and R. Kumar; Ind. J. Chem., **29B**, 1141 (1990).

(26) M. Okabe, R. C. Sun and G. Zenchoff; J. Org. Chem., **56**, 4393 (1991).

(27) M. K. Jani, B. R. Shah and N. K. Udavia; Chem. Environ. Res., **1**, 345 (1992).

(28) A. Mishra, L. M. Ojha, R. P. Tripathi, R. L. Pratap and D. S. Bhakumi; Ind. J. Hetero. Chem., **1**, 51 (1991).

(29) Nagarotham, Dhanpalam and Wong; PCT Int. Appl. WO 97, 17 969 (Cl. A61K 31/505); Chem. Abstr., **127**, 65783t (1997).

(30) K. Nicholas, P. Meghani and T. Stephen; PCT Int. Appl. WO 98, 54, 180 (Cl.CO7D 417/06) Dec. 1998; Chem. Abstr., **130**, 38394 (1999).

(31) M. Saneyoshi, Kato and Hisatoyo; JPN. Kokai Tokkyo Koho JP 10, 87, 688 (98, 87, 688), (Cl. CO7D 19/10), 7, Apr. (1998); Chem. Abstr., **128**, 183038r (1998).

(32) R. Reinhard, H. Gerhard, M. Markus, M. Olaf and A. Cryill; PCT Int. Appl. WO 99 31, 091 (Cl. CO7D 413/04); Chem. Abstr., **130**, 58844t (1999).

(33) V. Peesapati and G. Rupavani; Ind. J. Chem., **38B**, 468 (1998).

(34) M. Mahran, M. A. E. Sherbeny, El-Obaid, M. A. Abdul-Rahamn and F. A. Badria; Akexandria J. Pharm. Sci., **12**, 39 (1998).

(35) M. Saneyoshi and Wakayama; JPN Kokai, Tokkyo Koho JP 1007, 694 (9807, 694) [Cl. CO7H 19/06] 1998, Appl. 96/179, 850, 21 Jun. 1996, 8 pp (Japan); Chem. Abstr., **128**, 115201v (1998).

(36) K. Daniel, E. B. Pederson and N. B. Claus; J. Med. Chem., **41**, 191 (1998).

(37) S. A. Swalen; Ind. J. Hetero. Chem., **8**, 147 (1998).

(38) H. A. Allimony, H. A. Saad and F. A. A. El-Mariah; Ind. J. Chem., **38B**, 445 (1999).

(39) C. J. Shishoo and K. S. Jain; Ind. J. Chem., **38B**, 1052 (1999).

(40) S. Shigeta , S. Mori, T. Kira, K. Takahashi, E. Kodama, K. Konno, T. Nagata, H. Kato, T. Wakayama,N. Koike and M. Saneyoshi; Antivir. Chem. Chemother., **10**, 195 (1999).

(41) A. M. Attia, M. A. Sallam, A. A. Almehdi and M. M. Abbasi; Nucleosides Nucleotides, **18**, 2307 (1999).

(42) L. S. Jeong, Y. H. Kim, H. O. Kim, S. J. Yoo, Y. H. Park, S. H. Yeon, M. W. Chun and H. D. Kim; Nucleosides Nucleotides Nucleic Acids, **20**, 665 (2001).

(43) H. O. Kim, Y. H. Kim, H. Suh and L. S. Jeong; Bioorg. Med. Chem. Lett., **11**, 599 (2001).

(44) A. El-Fottoh, G. Hamman, A. M. Sharaf and N. A. A. El-Hafez; Ind. J. Chem., **40B**, 213 (2001).

(45) N. M. Saleh, N. M. Shieis and S. A. Mohamed; Chem. Abstr., **136**, 118422u (2002).

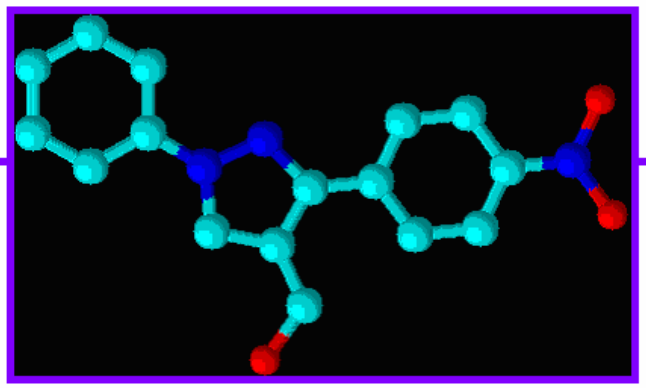
(46) S. Shigeta, S. Mori, F. Watanabe, K. Takahashi, T. Nagata, N. Koike, T. Wakayama and M. Saneyoshi; Antivir Chem Chemother., **13**, 67 (2002).

(47) P. Wili, C. Jie, W. Jun, L. Mingzhi, X. Xujian, F. Zhuanli, S. G. Shuomingshv; CN. 1, 348,985 (Cl. CO7D 239/46) 2000; Chem. Abstr., **139**, 53027 (2003).

(48) S. M. Sondhi, R. N. Goyal, A. M. Lahoti, N. Singh, R. Shukla and R. Raghubir; Bioorg. Med. Chem., **13**, 3185 (2005).

(49) L. G. Hammerland, M. Johansson, J. Malmstrom, J. P. Mattsson, A. B. E. Minidis, K. Nilsson, A. Peterson, D. Wensbo, A. Wallberg and K. Osterlund; Bioorg. Med. Chem. Lett., **16**, 2467 (2006).

CHAPTER-2



SYNTHESIS OF PYRAZOLES

INTRODUCTION

Pyrazoles are heterocyclic organic compounds having a doubly unsaturated five-member ring containing two adjacent nitrogen atoms.

Literature survey shows that synthetic pyrazole derivatives have wide applicability in the field of medicine, agriculture etc [1-5].

Knorr[6,7] first synthesized a compound 1-phenyl-3-methyl-5-pyrazoline, by the reaction of ethyl aceto acetate with phenyl hydrazine. The name pyrazole was given to such compounds, because the nucleus was derived from pyrrole by replacement of carbon by nitrogen[8].

Few workers synthesized pyrazoles as under:

Pechmann[9] has synthesized pyrazoles by the reaction of acetylenes and diazomethane. Jacobs reported the synthesis by the reaction of acetylene with diazomethane[10]. Palmey synthesized two structurally isomeric pyrazoles by the reaction of the substituted hydrazines with 1,3-dicarbonyl compounds[11]. Singh and Ojha[12] and Esribano et al.[13] synthesized pyrazoles by the reaction of ethyl aceto acetate with aryl hydrazines. Or and co workers also reported some pyrazole analogues[14]. Some pyrazole derivatives have also been reported to be synthesized by the reaction of acetonitrile derivatives with (DMF-DMA)[15]. Peruml et al.[16] have synthesized pyrazoles by the reaction of hydrazones with Vilsmeier reagent. Touzot and coworkers have reported the synthesis by the cyclo condensation of mono substituted hydrazines[17]. Boruah et al.[18] suggested one pot synthesis of pyrazoles from β-formyl enamides.

Much research has been carried out with the aim to find the therapeutic values of pyrazole moiety, since their discovery [19-24]. These derivatives were also tested for a variety of biological activities such as anthelmintic[25], herbicidal[26,27], CNS depressant[28], lipoxygenase inhibitor[29], antiulcer[30], anticancer[31], antitumor[32,33], anti-inflammatory[34,35], antiviral[36], antiepileptic[37], neurotonsin receptor[38], antimicrobial[39], neurotonsin receptor[40], immino suppressants[41,42]. Various pyrazole and its derivatives have been used in many drugs[43-45]. Pyrazole derivatives have also anti HIV[46] activity. Many of them are also known to be used as anti proliferature agent[47], protein kinase inhibitors[48] etc.

Hassan reported anti diabetic and antibacterial activity of some other pyrazoles[49]. Freddy et al. reported the biological activity of 4-5-dihydro-3-phenyl-1H-pyrazole[50]. Shimzo and co-workers have also synthesized some pyrazole derivatives and reported their herbicidal activity[51]. Rowley and Collins et al.[52] have documented pyrazole derivatives as a good dopamine D4 receptor. Some pyrimidinyl pyrazole derivatives are reported to exhibits a potent cytotoxic activity against some tumor cell lines including multidrug resistant cell lines due to the overexpression of P-glycoprotein[53]. Djuric and co-workers[54] have identified a series of bis (trifluoromethyl)pyrazoles (BTPs) as a novel inhibitor of cytokine production and even inhibit IL-2 production with a 10-fold enhancement over cyclosporine in an ex vivo assay. Devid et al.[55] have repored pyrazoles as activators of the nitrile oxide receptor and guanglate cyclase agent. Some pyrazole derivatives are also known to act as potent antiinflammatory agent.[56]. Some pyrazole derivatives are known to act as antagonist for astrogen receptor-α[57], as reverse transcriptase inhibitors for the treatment of HIV infection[58], as sodium channel blocker[59], as a neuropeptide T_5 receptor antagonists [60], as CCK1 receptor antagonist[61]. Daidone[62] et al. reported that some pyrazole derivatives with hydrazide could inhibit fibrosis. Parmar et al.[63] have synthesized pyrazole derivatives and studied their antiinvasive activity. Zhang and co-workers[64] have documented liguly potent factor Xa inhibitors with invitro anticoagulant activity of pyrazoles. Dardani et al. [65] have investigated 1-phenyl-3-toluyl-4-[ortho-1'-(N-ethyl-2'-methylpropyl amine)] phenylpyrazole as antifungal agent and showed that mycelial growth and conidial germination of fungi were blocked by the compound. Recently, Wilst et al. discovered pyrazole as potential glucocorticoid receptor ligand[66] whereas Prasanna and co-workers also reported pyrazoles as COX-2 inhibitors[67]. Some pyrazole derivatives act as COX-2 inhibitors[68] which exhibited good pharmacokinatic profile (pk), intavenous and subcutaneous (sc) dosing and demonstrated excellent in vivo efficacy in a cannine synovities model. Various other pyrazole derivatives are reported to act as cytotoxic [69] and antibacterial and antifungal agents.[70]. Recently, Gill and co-workers[71] have identified pyrazole as a novel p38 MAP kinase inhibitors. Antimalarial activity of 4-(5-trifluoromethyl-1H-pyrazol-1-yl)-chloroquine

analogues has also been evaluated in vitro against a chloroquine resistant Plasmodium falciparum clone[72].

Recently, few workers also reported antimicrobial activity[73] leishmanicidal invitro activities and cytotoxic effects[74]. Cheng et al.[75] have reported pyrazole derivatives as canine selective COX-2 inhibitors.

Due to good biological activity, some pyrazole derivatives were synthesized and are given in this chapter.

REFERENCES

(1) H. Yoji, N. Hidenori, S. Takashi and K. Takuo; JP10158107 (1998).

(2) I. Hiroyuki, I. Tsuneaki, T. Takeshi, T. Jiichi, O. Toru; JP2003286117 (2003).

(3) A. A. Bekhit and T. A. Aziem; Bioorg. Med. Chem., **12**, 1935 (2004)

(4) G. H. Elgemeie, W. A. Zaghary, K. M. Amin and T. M. Nasr; Nucleosides Nucleotides Nucleic Acids, **24**, 1227 (2005).

(5) P. Singh, K. Paul and W. Holzer; Bioorg. Med. Chem., **14**, 5061 (2006).

(6) Knorr; Ger. Pat., **26**, 429 (1883).

(7) Knorr; Ber., **16**, 2507 (1887).

(8) Knorr and Blank; Ber., **18**, 311 (1885).

(9) H. V. Pechmann; Ber., **31**, 2950 (1898).

(10) T. L. Jacobs; Hetero. Compds., **5**, 70 (1957).

(11) M. H. Palmey; Struc. Reac. Hetero. Comp., Arnold, London, 378 (1967).

(12) C. P. Singh and A. C. Ojha; J. Ind. Chem. Soc., **27**, 1172 (1980).

(13) F. G. Escribano, M. P. D. Alcantara and A. G. Senchez; Tetrahydron Lett., **29**, 6001 (1988).

(14) Y. S. Or , R. F. Clark, Q. Xie, J. McAlpine, D. N. Whittern, R. Henry and J. R. Luly ; Tetrahedron, **49,** 93 (1993).

(15) F. Al-Omran, O.Y. A. El-Hay and A. El-Khair; J. Hetero. Chem., **57,** 1617 (2000).

(16) P. T. Peruml and N. Mathivanan ; Bioorg. Med.chem. Lett., **14**, 6035 (2004).

(17) A. Touzot, M. Soufyane, H. Berber L. Toupet and C. Mirand; J. Flourine Chem., **125,** 1299 (2004).

(18) R. C. Boruah, A. Saikia, M. G. Barthakur, C. J. Saikia and U.Bora; Tetrahedren Lett., **47**, 43 (2006).

(19) M. Paintz and H. Bekemeier, J. Metzner and U. Wenzel; Agents Actions Suppl., **10**, 47 (1982).

(20) G .Palazzino , F .Melani , L. Cecchi and G .Filacchioni; Farmaco [Sci]., **41**, 566 (1986).

(21) A. X. Wang, Q. Xie, B. Lane, K. W. Mollison, G. C. Hsieh, K. Marsh, M. P. Sheets, J. R. Luly and M. J. Coghlan; Bioorg. Med. Chem. Lett., **8,** 2787 (1998).

(22) S. Rapposelli, A. Lapucci, F. Minutolo, E. Orlandini, G. Ortore, M. Pinza and A. Balsamo; Il Farmaco, **59**, 25 (2004).

(23) P. A. Brough, X. Barril, M. Beswick, B. W. Dymock, M. J. Drysdale, L. Wright, K. Grant, A. Massey, A. Surgenor and P. Workman; Bioorg. Med. Chem. Lett., **15**, 5197 (2005).

(24) L. Bhat, B. Jandeleit, T. M. Dias, T. L. Moors and M. A. Gallop; Bioorg. Med. Chem. Lett., **15**, 85 (2005).

(25) H. G. Garg and K. Nanrendrajit; J. Med. Chem., **15**, 554 (1972).

(26) M. M. El-Kerdawy, A. A. Sammour and A. A. El-Agancey; Pharmazie, **30,** 70 (1975).

(27) L. Thomas, Z. Benko and M. Gail; PCT Int. Appl. WO, **52** 926 (1998).

(28) A. I. Eid and S. Rashad; Egypt J. Pharm. Sci., **20**, 107 (1979).

(29) S. sharma and M. S. Bhatia; J. Ind. Chem. Soc., **66**, 116 (1989).

(30) I. Masazumi, M. Kazumi, N. Youich and Y. Toshihiro; Chem. Pharm. Bull., **44**, 170 (1996).

(31) S. D. Bhardwaj and V. S. Jolly; Orient. J. Chem., **12**, 185 (1996).

(32) L. Paolo, M. Stefano, S. Daniele and P. Alssandra; PCT Int. Appl. Wo (cl. Co7419104), **40**, 704 (1996).

(33) L. Paalo, M. Stefano, S. Daniele and P. Alssandra; PCT Int. Appl. WO (Cl. CO7416/04), **40**, 704 (1996).

(34) J. J. Talley, Shikarski, A. Jones, G. Matthew and C. Jaffreys; PCT Int. Appl. wo (cl. Co7D231/12), **38**, 418 (1996).

(35) J. J. Talley, Shikarski, A. Jones, G. Matthew and C. Jaffreys; PCT Int. Appl.WO (Cl. CO7D231/12), **38**, 418 (1996).

(36) L. Paolo, M. Stefano, S. Daniele and P. Alssandra; PCT Int. Appl. Wo (cl. Co7419104),**40**, 704 (1996).

(37) M. Manfred, L. H. Joachim and J. Klaus; Ger. Offen DE 19, 521, 822 (cl,co7D 231/138), Chem. Abstr., **126**, 117969j (1997).

(38) B. B. Joseph, W. Richard and A. Bentler; Eur. Pat. Appl. Ep., **95**, 9071 (1998).

(39) E. V. Pimenova, R. A. Khamatgaleev and E. V. Voronina; Khim-Farm. Zh., **32**, 272g (1998).

(40) V. Parmar, A. Kumar and A. Prasad; Bioorg Med. Chem., **7**, 1425 (1998).

(41) M. D. Treadway and W. U. Tai The; PCT Int. Appl. wo 98, 56767; Chem. Abstr., **130**, 52416n (1999).

(42) R. Christopher, H. Cai and J. Edwards; PCT Int. Appl. WO (Cl. CO7D471/00), **14**, 315 (2002).

(43) T. Ochi, K. J. Magari, A. Yonezawa, K. Matsumori and T. Fujii; Eur. J. Pharmaco., **365**, 259 (1999).

(44) P. Steffen, E. Krinn, A. Moller, W. Seeling and M. G. Rockemann; Acute Pain, **4**, 71 (2002).

(45) G. Menozzi, L. Mosti, O. Bruno, E. L. Presti, C. Musiu, S. Longu, P. L. Colla, W. Filippelli, G. Falcone and B. Piucci; Il Farmaco, **54**,41 (2003).

(46) G. J. Michael, B. Carolyn and J. Keiser; J. Med. Chem., **43**, 1034 (2000).

(47) H. Ohki, K. Hirotani, H. Naito , S. Ohsuki ,M. Minami ,A. Ejima , Y. Koiso and Y. Hashimoto; Bioorg Med. Chem. Lett., **12 ,** 3193 (2002) .

(48) Y. C. Moon; U. S. Pat. Appl. Publ.. US, **144**, 309 (2003), (Cl.,514-275; CO7D417/14) (2003).

(49) F. Allah – Hasan; Pharmazie **36**, 754 (1981).

(50) F. Havaldar and P. S. Fernandes; J. Ind.Chem. Soc., **65**, 619 (1988).

(51) S. Shimzo, K. Seigo, I. Miko, W. Hiroyuki and T. Kenji; Jpn. Kokai Tokyo Koho JP 63, 264, 584 [88, 264, 584] [cl. CO7D413112]; Chem. Abstr., **110**, 1732244 (1989).

(52) M. Rowley, I. Collins and B. Howard; J. Med. Chem.,**40**, 2374 (1997).

(53) H. Naito, M. Sugimori, I. Mitsui, Y. Nakamura, M. Iwahana, K. Hirotani, E. Kumazawa and A. Ejima; Chem. Pharm. Bull. (Tokyo), **47,** 1679 (1999).

(54) S. W. Djuric, A. Basha, H. Liu, J. R. Luly and D. J. Madar; J. Med. Chem. , **43**, 2975 (2000).

(55) L. S. David and G. B. David; J. Med. Chem., **44**, 78 (2001).

(56) K. Kawamura and K. Ando; Eur. Pat. Appl. EP (Cl. C07D405/14), **104**, 760 (2001).

(57) J. Sun, Y. R. Huang, R. William, Harringrton, S. Sheng, J. A. Katzenellenbogen and B. G. Katzenellenbogen; Endocrinology, **143**, 941 (2002).

(58) C. Romuald, M. C. Erie, Perros, Manousses, S. P. Antheny and W. Antheny; PCT Int. Appl. WO(Cl. CO7D 231/12), **04**, 424 (2002).

(59) R. N. Atkinson and M. F. Gross; PCT Int. Appl. WO(Cl. A Cl. K), **37**,274 (2003).

(60) N. Sato, T. Thakahush and T. Shibata; J. Med. Chem., **46,** 666 (2003).

(61) J. G. Breitenbucher, Clarksehon, K. Meclure, M. Hack, L. Li and N. Shankley; Bioorg. Med. Chem. Lett., **16**, 77 (2006).

(62) G. Daidone, D. Raffa, F. Plescia, B. Maggio and A. Roccaro; Arkivdoc., (**xi**) 227 (2002).

(63) V. S. Parmar, N. K. Sharma, M. Husain, A. C. Watterson and J. Kumar; Bioorg. Med. Chem., **11**, 913 (2003).

(64) Z. Zhang J. Jia, Y. Wu, W. Huang, P. Zhang, L. A. Clizbe, E. A. Goldman and U. Shinhel; Bioorg. Med. Chem. Lett., **14**, 1221 (2004).

(65) Z. Dardani, M. Beudaima, A. Sebban, A. Bahioul, S. Kitane and M. Berrader; IL Farmaco, **59**, 673 (2004).

(66) F. Wilst, T. Khiess, M. Kreizschmar and R. Bergmann; Bioorg. Med. Chem. Lett., **15,** 1303 (2005).

(67) S. Prasanna, E. Manivannan and S. C. Chaturvedi; Bioorg. Med. Chem. lett., **15**, 2097 (2005).

(68) J. Li, M. P. Lynch and L. A. Lynd ; Bioorg. Med. Chem. Lett., **13**, 1805 (2005).

(69) H. J. Park, K. Lee, S. J. Park, H. Y. Cho and K. I. Lee.; Bioorg. Med. Chem. Lett., **15**, 3307 (2005).

(70) A. R. Farghaly and H. el-kashef ; Monatshefte fur Chemie **136**, 217 (2005).

(71) A. I. Gill, M. Frederickson, A. Cleasby and S. J. Woodhead ; J. Med. Chem. **48**, 414 (2005).

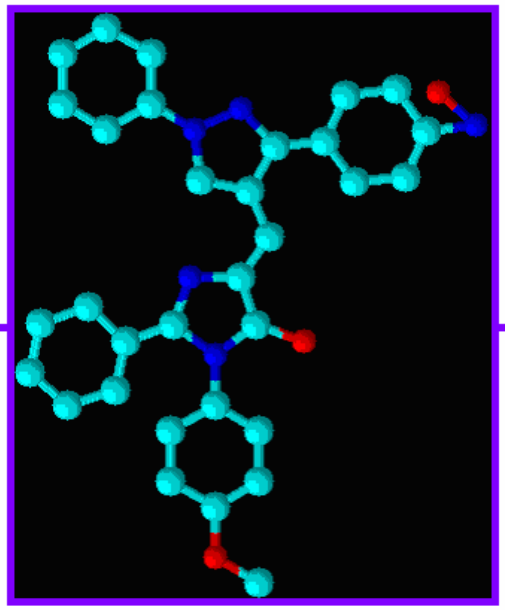
(72) A. U. Krettli, I. O. Freitas and R. P.P. Soares ; Bioorg. Med. Chem. Lett., **16**, 649 (2006).

(73) B. S. Holla , M. Mahalinga, M. Sitambaram, Karthikeyan, P. M. Akberali and N. S. Shetty; Bioorg. Med. Chem. Lett., **14**, 2040 (2006)

(74) A. M. R. Bernardino, A. O. Gomes, K. S. Chharret, A. C. Freitas and V. F. Amaral; Eur. J. Med. Chem., **41**, 80 (2006).

(75) H. Cheng, A. M. Silvia and S. B. Seibel; Bioorg. Med. Chem. Lett., **16**, 2076 (2006).

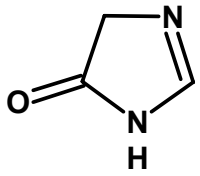
SECTION-I



SYNTHESIS OF IMIDAZOLINONES

INTRODUCTION

The five membered heterocyclic ring system 5-oxo-imidazoline have two nitrogen atom at 1 and 3-positions and a carbonyl group at 5-position.



Hoffman[1] was the first to discover 5-oxo-imidazoline by heating N'-diacetylethylene diamine in a stream of dry hydrogen chloride. Moreover, some compounds were prepared by Ladenburg[2] by the fusion of two equivalents of sodium acetate with one equivalent of ethylene diamine dihydrochloride. The synthesis of imidazolinones by aminolysis of oxazolone with amine has also been reported[3]. Takeuchi et al.[4] have synthesized imidazolinones by the reaction of azido substituted imides with triphenylphosphine or tributylphosphine, Cai et al.[5] have reported 5-imidazolinone derivatives by microwaves irradiation. Various other workers[6-10] have also reported synthesis of some new imidazolinone derivatives.

Various imidazolinones are known to exhibit a broad spectrum of biological activities such as sedative and hypnotics[11], bactericidal[12,13], antiinflammatory[14-16], antihistaminic[17], antiparkinsonian[18,19], potent CNS depressant[20,21], fungicidal[22,23], insecticidal[24], antagonists[25], hypertensive[26], antiviral[27], antitubercular[28], antimicrobial[29], antidiabatic[30], anticancer[31], anticonvulsant[32], etc.

Agrochemical activity of imidazolinones have been reported by Bascou and coworkers[33]. Kolhe and Dhingra[34] have reported anti-AIDS, antibacterial and fungicidal activity of some 5-oxo-imidazolines. Shah and co workers[35] have prepared some newimidazolines and reported anticancer and anti-HIV activity. Akyoshi et al.[36] have prepared some new imidazolinone derivatives and reported their herbicidal activity. Lucca[37] have reported imidazolinone as excellent HIV-protease inhibitors. Pilkington and Elizabeth[38] have described and studied antifungal activity of imidazolinones. Kalluraya et al.[39] have synthesized

imidazolinone derivatives and tested for their antibacterial, antiinflammatory and analagesic activities.

Griffiths and co-workers[40] had prepared imidazolinone derivatives and reported as angiotensin II antagonist losartan. Sayed[41] has synthesized imidazolinone derivatives and screened for their antibacterial and antifungal activities. Sharma and De[42] have formulated 5-oxo-imidazolines possessing potential antimicrobial activity. Peter and Vera[43] have prepared substituted imidazolinones which inhibited the abnormal cell growth in human body. Awashthi et al.[44] have synthesized some new imidazolinone derivatives and reported their antimicrobial activity. Hidayat and Preston[45] have reported ALS-inhibitory activity of imidazolinones. Ho et al.[46] have investigated some imidazolinone derivatives abolished the enzymatic activity as well as the binding affinity for the cofactor FAD (Flavin adenine dinucleotide). Solankee[47] have synthesized some imidazolinone derivatives and screened for their anticancer activity.

John and Watter[48] have also studied herbicidal activity of some imidazolinones. The antifungal[49], antireteroviral activity[50] and anti-HIV activity[51] of some other imidazolinones have also been reported. Daisuke et al.[52] have documented some new imidazolones as a telomeres inhibitors and antitumor agents. Lauter and co-workers[53] have isolated imidazoline from different methods and tested for the treatment of cytokine release. Jean et al.[54] have also tested the antileishmanial activity of some imidazolones. Hamdouchi et al.[55] have reported their potent and broad spectrum activity. Vasiliev et al.[56] have synthesized imidazolinone derivatives and reported their herbicidal activity. Jayachandran et al.[57] have also reported imidazolinones as antimicrobial agents. Moreover, Alister and Kogan[58] have documented herbicidal activity of imidazolinone derivatives. Bronson et al.[59] have reported imidazolinone derivatives as antibacterial agents.

With a view to getting better therapeutic agent, it was contemplated to synthesize some imidazolinone derivatives to enhance the overall activity of resulting compounds, which have been described in this chapter.

EXPERIMENTAL

Synthesis of N-Aryl-2-aryl-4-[1',N-phenyl-3'-p-nitrophenyl- pyrazol-4'-yl]-imidazolin-5-ones.

[A] Synthesis of N-aminophenyl-α-methyl-p-nitrophenyl azomethine:

A mixture of phenylhydrazine (1.08 g, 0.01M) and p-nitrophenyl aceto phenone (1.65 g, 0.01M) in absolute ethanol was refluxed in water bath for 2 hrs. in presence of 1 ml glacial acetic acid. The crude product was isolated and crystallised from absolute alcohol.

[B] Synthesis of 1,N-phenyl-3-p-nitrophenyl-4-formyl pyrazole:

N-Aminophenyl-a-methyl-p-nitrophenyl azomethine (2.53g, 0.01M) was added in mixture of Vilsmeir-Haack reagent (prepared by dropwise addition of 3 ml POCl3 in ice cooled 25 ml DMF). and refluxed for 5 hrs. The reaction mixture was poured into ice followed by neutralization using sodium bicarbonate. Crude product was isolated and crystallised from ethanol.

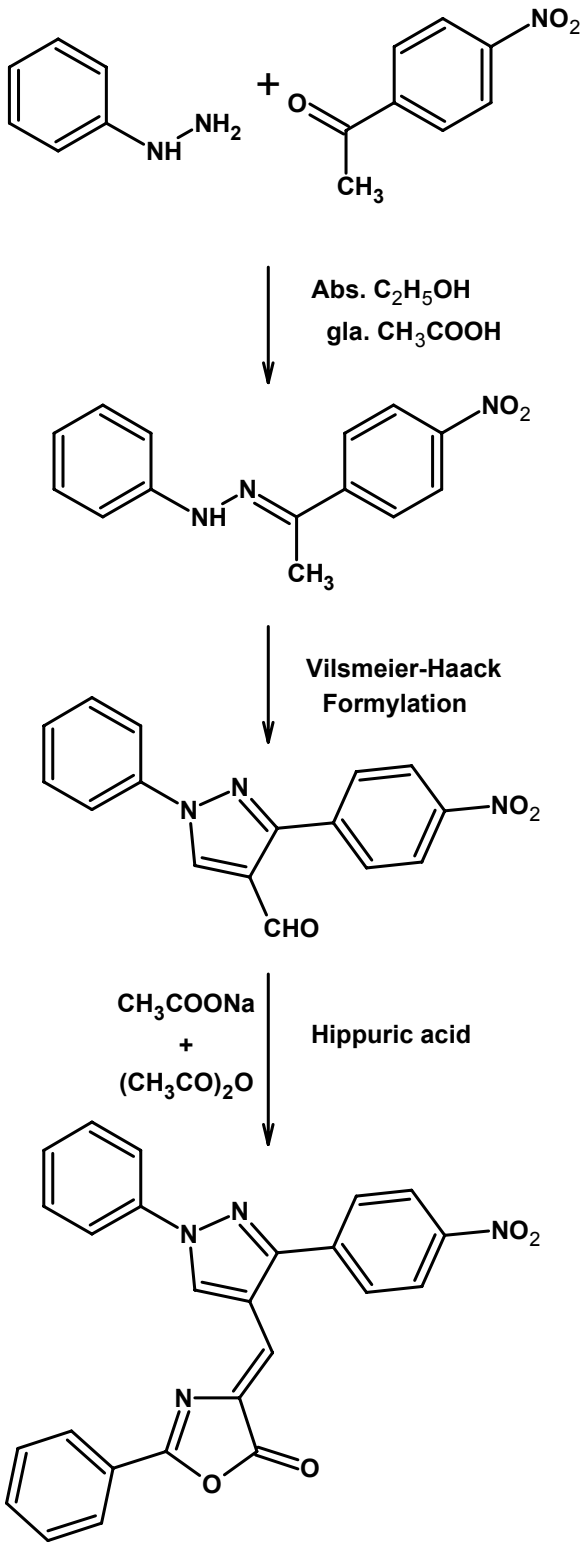
[C] (4*Z*)-4-{[3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl]methylene}-2-phenyl-1,3-oxazol-5(4*H*)-one:

A mixture of 1,N-phenyl-3-p-nitrophenyl-4-formyl pyrazole (2.93g, 0.01M), Hippuric acid (g, 0.01M), acetic anhydride (ml, 0.03M) and sodium acetate (2.0 g, 0.03) was heated on a waterbath for 4 hrs. Resulting mass was poured into water filtered and crystallized from methanol.

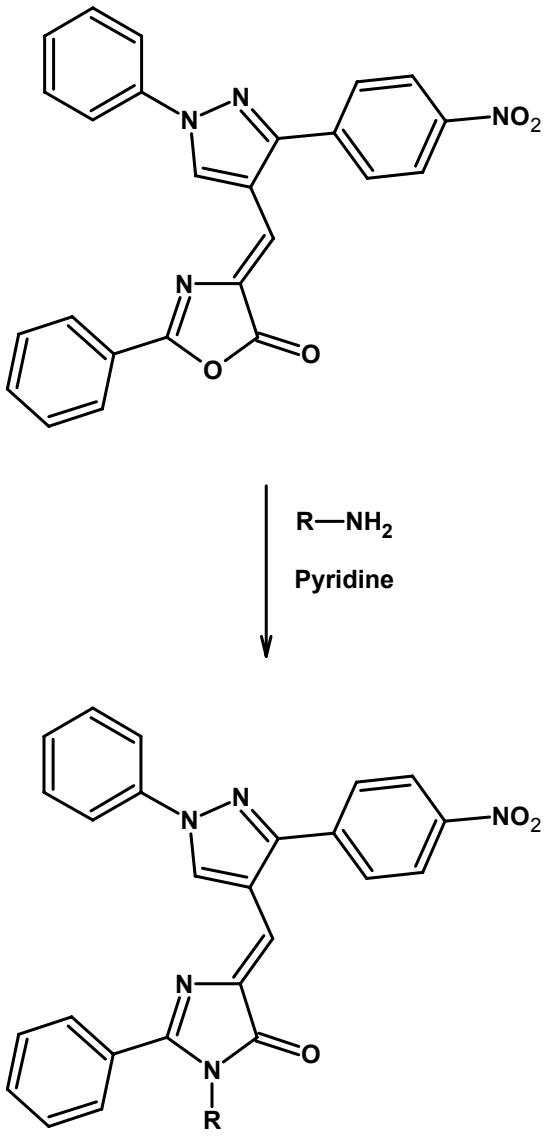
[D] Synthesis of N-Aryl-2-aryl-4-[1',N-phenyl-3'-p-nitrophenyl- pyrazol-4'-yl]-imidazolin-5-ones.

To a solution of (4*Z*)-4-{[3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl] methylene}-2-phenyl-1,3-oxazol-5(4*H*)-one (4.36g, 0.01 mol) and p-methoxy-aniline (1.23g, 0.01 mol) in dry pyridine (25 ml) was refluxed for 12 hrs. on oil bath. The content was poured on to crushed ice and neutralized with HCl, the isolated product crystallized from dioxane.

REACTION SCHEME



REACTION SCHEME



R = Aryl

Table 5.1: Physical constants of Imidazolinones.

Sr. No.	Code	R	M.F.	M. Wt. (g/mol)	Rf* Value	M.P. °C	Yield %
1.	**PAIM-1**	4-CH_3-C_6H_4-	$C_{32}H_{23}O_3N_5$	525	0.48	215	69
2.	**PAIM-2**	4-OCH_3-C_6H_4-	$C_{32}H_{23}O_4N_5$	541	0.51	205	72
3.	**PAIM-3**	2-OCH_3-C_6H_4-	$C_{32}H_{23}O_3N_5$	525	0.42	226	65
4.	**PAIM-4**	$C_{10}H_7$-	$C_{35}H_{25}O_3N_5$	564	0.47	232	67
5.	**PAIM-5**	4-F-C_6H_4-	$C_{31}H_{20}O_3N_5F$	529	0.42	198	62
6.	**PAIM-6**	4-Cl-C_6H_4-	$C_{31}H_{20}O_3N_5Cl$	546	0.43	203	65
7.	**PAIM-7**	C_6H_5-	$C_{31}H_{21}O_3N_5$	511	0.33	189	66
8.	**PAIM-8**	3-Cl-4-F-C_6H_3-	$C_{31}H_{19}O_3N_5FCl$	564	0.32	211	68
9.	**PAIM-9**	2,5-di-Cl-C_6H_3-	$C_{31}H_{19}O_3N_5Cl_2$	580	0.53	212	69

*Acetone:Benzene: 1:9

Figure 5.1: IR spectra data of N-Aryl-2-akyl-4-[1',V-phenyl-3'-p-nitrophenyl-pyrazol-4'-yl]-imidazolin-5-ones.

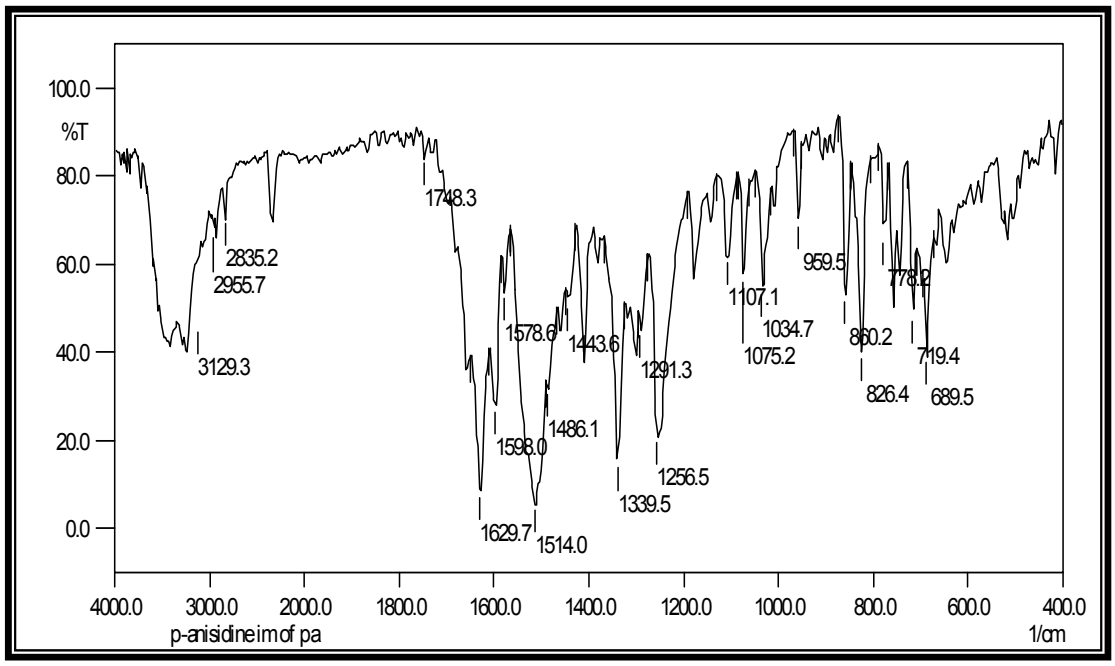
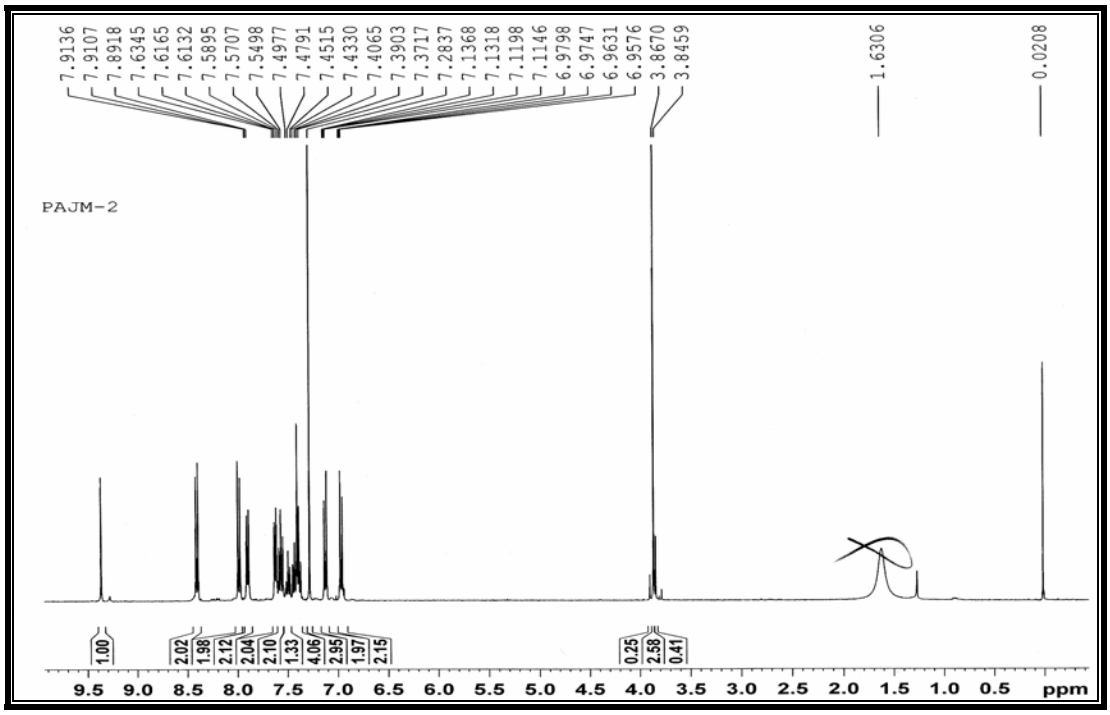


Table 5.2: IR spectral data of N-Aryl-2-akyl-4-[1',V-phenyl-3'-p-nitrophenyl-pyrazol-4'-yl]-imidazolin-5-ones.

Type	Vibration mode	Frequency in cm^{-1}	
		Observed	**Reported**
Alkane (methyl)	C-H str. (asym.)	2956	2975-5920
	C-H str. (sym.)	2835	2880-2860
	C-H def. (asym.)	1444	1470-1435
	C-H def.(sym.)	1340	1395-1370
Aromatic	C-H str.	3129	3150-3000
	C=C	1579	1585-1480
	C-H i.p. def.	1107	1125-1090
	C-H o.o.p. def.	826	860-810
Pyrazole moiety	C=N str.	1598	1650-1580
	C-N str.	1257	1350-1200
Ether	C-O-C str. (asym.)	1291	1275-1200
	C-O-C str. (sym.)	1035	1075-1020
ring	C=O str.	1748	1680-1760

Figure 5.2: ^{1}H NMR spectra data of of N-Aryl-2-aryl-4-[1',V-phenyl-3'-p-nitrophenyl- pyrazol-4'-yl]-imidazolin-5-ones.



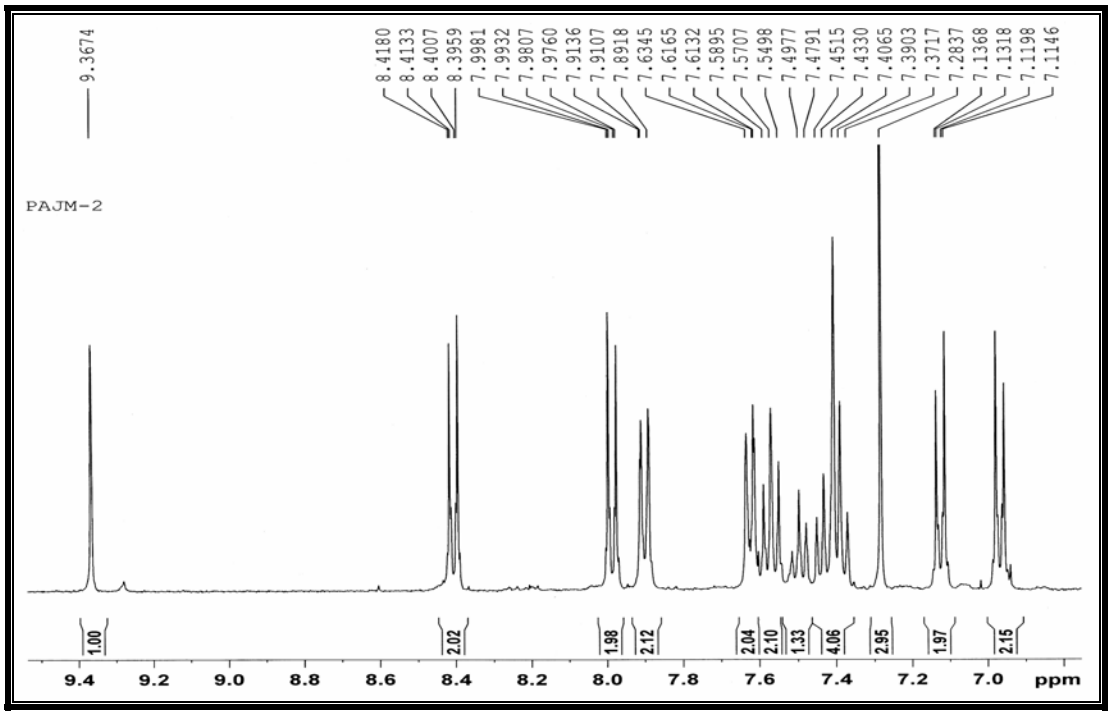
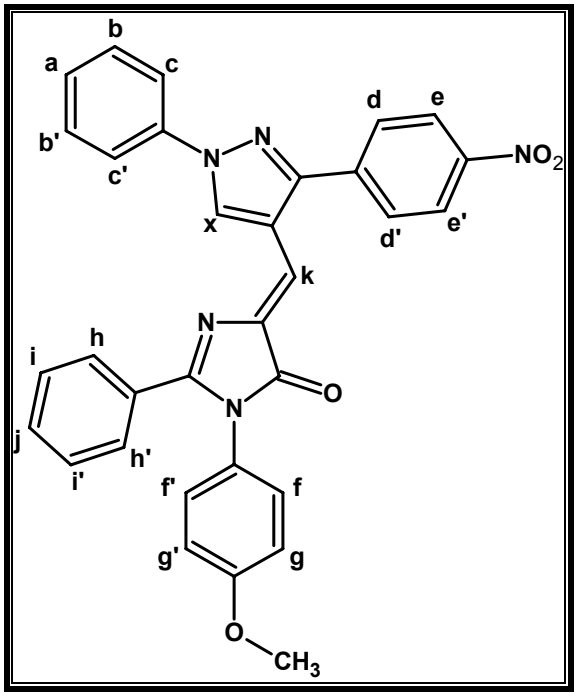
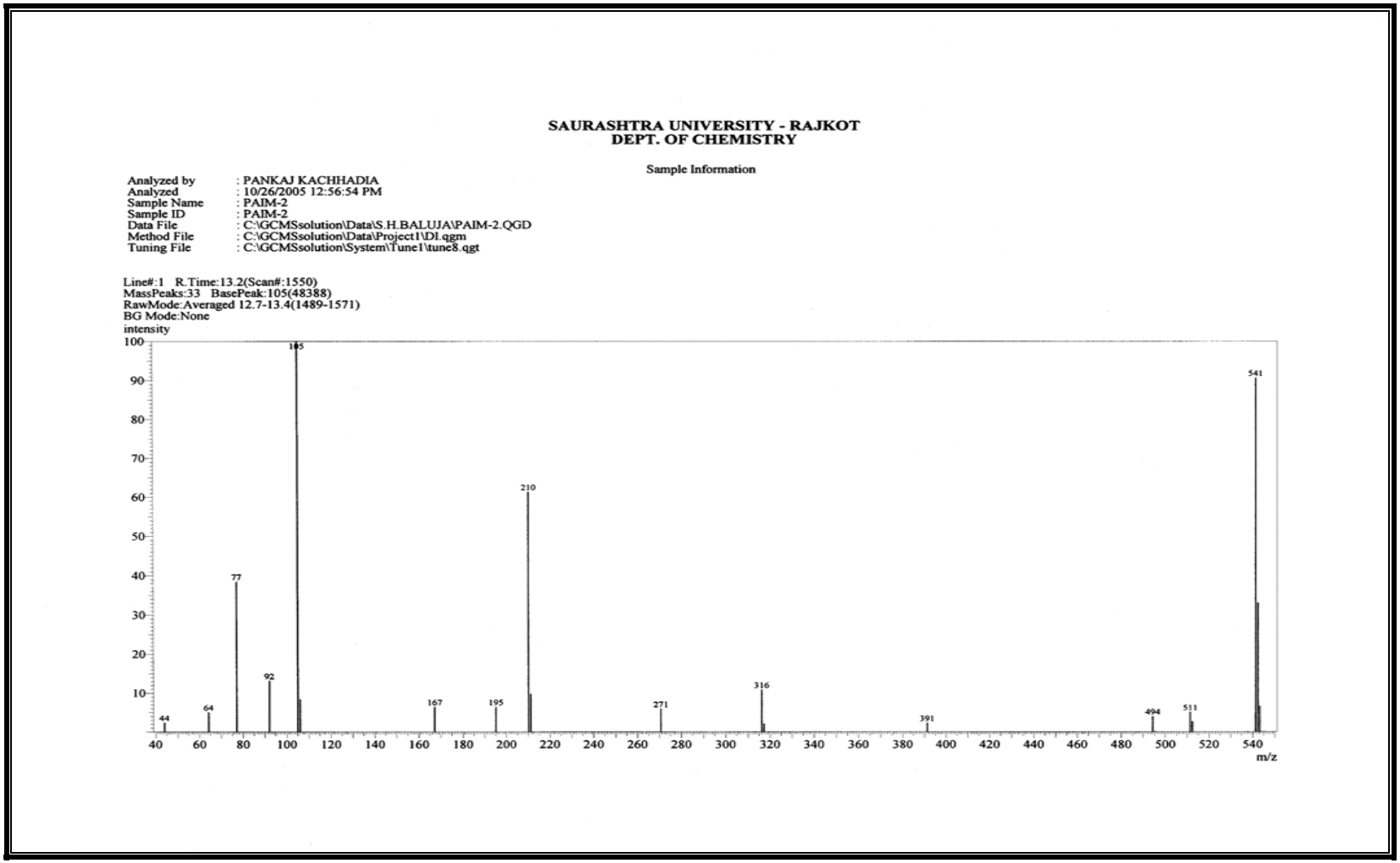


Table 5.3: ^{1}H NMR spectra data of of N-aryl-2-aryl-4-[1',V-phenyl-3'-p-nitrophenyl- pyrazol-4'-yl]-imidazolin-5-ones.

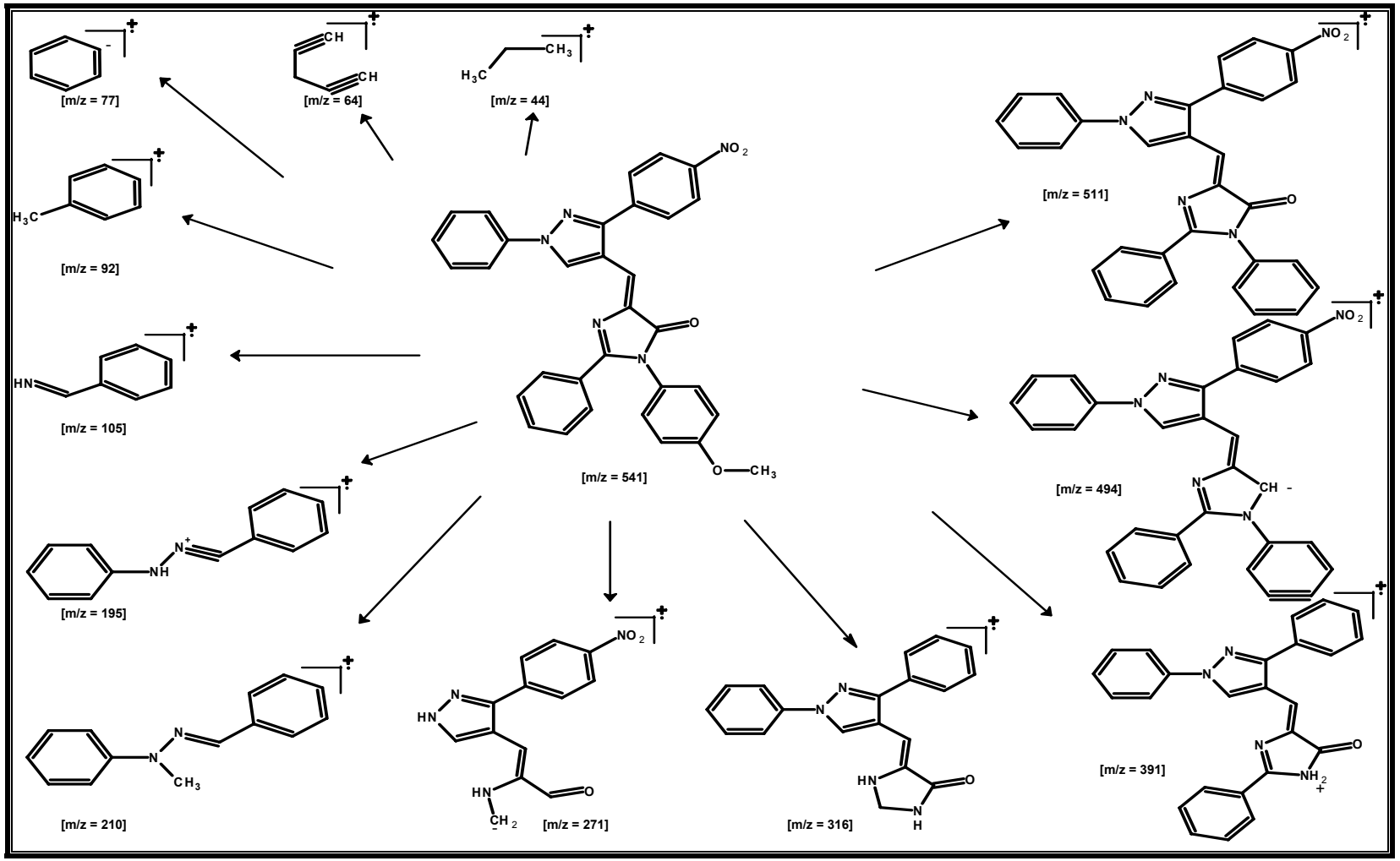


Singal No.	Signal Position (δ ppm)	Relative No. of Protons	Multiplicity	Inference	J (Hz)
1.	3.86	3H	singlet	Ar-OCH_3	-
2.	6.95-6.97	2H	d. doublet	Ar-H(gg')	8.88
3.	7.11-7.13	2H	d. doublet	Ar-H(dd')	8.88
4.	7.28	1H	singlet	Ar-H(k)	-
5.	7.37-7.45	4H	multiplet	Ar-H(hh')+H(ii')	-
6.	7.47-7.58	2H	multiplet	Ar-H(a)+H(j)	-
7.	7.61-7.63	2H	doublet	Ar-H(bb')	8.52
8.	7.89-7.91	2H	doublet	Ar-H(cc')	8.72
9.	7.97-7.99	2H	d. doublet	Ar-H(ee')	8.84
10.	8.39-8.41	2H	d. doublet	Ar-H(ff')	8.84
11.	9.36	1H	singlet	Ar-H(x)	-

Figure 5.3: Mass spectra of spectra data of N-aryl-2-aryl-4-[1',V-phenyl-3'-p- nitrophenyl- pyrazol-4'-yl]-imidazolin-5-ones.



Scheme 5.1: N-aryl-2-aryl-4-[1',V-phenyl-3'-p- nitrophenyl- pyrazol-4'-yl]-imidazolin-5-ones.



REFERENCES

(1) A. W. Hoffman; Ber., **21**, 2332 (1880).

(2) A. Ladenburg; Ber., 27, 2952 (1894).

(3) C. Granachar and G. Gulbas; Helv. Chem. Acta., **10**, 818 (1927).

(4) H. Takeuchi, S. Hagiwara & S. Eguchi; Tetrahedron, **45**, 6375 (1989).

(5) F. J. Cai, M. Q. Hug, L. Yang and D. Li; Org. Prep. Proceed Int., (1997); Chem. Abstr., **128**, 61455k (1998).

(6) H. A. Allimony, H. A. Sadd and F. A. A. E. Mariah; Ind. J. Chem., **38B**, 445 (1999).

(7) A. Saxena, N. C. Desai and K. K. Awasthi; Ind. J. Chem., **40B**, 201 (2001).

(8) D. M. Wu, Z. Ziu, Y. Yong and H. Axye; Chem. Abstr., 136, 5497 (2002).

(9) L. Varga, T. Nagy, G. Dorman and F. Darvas; Tetrahedron, **59**, 655 (2003).

(10) X. Z. Feng and D. M. Wu; Chem. Abstr., 139, 101228z (2003).

(11) M. W. Goldberg and H. H. Lehr; US, U. S. 2, 602,086 (1952); Chem. Abstr., **47**, 6987d (1953).

(12) S. A. Agripat; Neth. Appl., 6, 611,087 (1967); Chem. Abstr., **68**, 29699z (1968).

(13) K. C. Mathur and R. Sahay; J. Ind. Chem. Soc., **67**, 856 (1990).

(14) M. Verma, A. K. Chaturvedi, A. Chaudhari and S. S. Parmar; J. Phar. Sci., **63**, 1740 (1974).

(15) S. Swaroop, V. K. Saxena and S.R. Chowdhary; Ind. J. Pharma. Soc., **51**, 124 (1989).

(16) R. R. Grenshaw and G. M. Luke; Can. CA., 1, 130, 306; Chem. Abstr., **98**, 16649p (1983).

(17) S. M. Sethna and R. C. Shah; J. Ind. Chem. Sci.,**10**, 1459 (1993).

(18) K. A. Johnnes, K. Kauko, O. A. Seppo and S. Lennart; Eur. Pat. Appl. EP 58 047; Chem. Abstr., **98**, 16692m (1983).

(19) P. K. Naithani, V. K. Srivastava, J. P. Barthwal, A. K. Saxena, T. K. Gupta and K. Shanker; Ind. J. Chem., **28B**, 990 (1989).

(20) R. Agarwal, C. Chaudhary and V. S. Misra; Ind. J. Chem., **22B**, 308 (1983).

(21) E. Bousquet, G. Romeo, N.A. Santagati, T. Lancetta, A. Caruso, V. Leone, and A. Felice; IL. Farmaco., **44**, 851 (1989).

(22) M. B. Gravestock and J. F. Ryley; "Antifungal Chemotherapy in annual reports in medicinal chemistry." **19**, 127 (1984).

(23) V. K. Pandey and (Ms.) M. Tandon; Ind. J. Chem., **40B**, 527 (2001).

(24) C. R. Sharma and D. R. Shridhar; Ind. Pat., IN 154-314 (1984); Chem. Abstr., **105**, 133738 (1986).

(25) L. D. Chang; PCT Int. Appl. WO, 98 22, 208 (1998); Chem. Abstr., **129**, 41134x, (1998).

(26) H. H. Moharram, R. S. E. Amin and A. E. Dawany; J. Serb. Chem. Soc., **54**, 335 (1989).

(27) A. J. Srivastava, S. Swaroop, V. K. Saxena and P. Srivastava; Ind. J. Pharma. Sci., **51**, 23 (1989).

(28) B. S. Vashi, D. S. Mehta and V. H. Shah; Ind. J. Chem., **34B**, 802 (1995).

(29) K. K. Kataryna, E. Szymanska, M. Motyl, W. Holzer, A. Bialecka and Kasprowicze; Pharmazie, **53**, 680 (1998).

(30) K. Kawasaki, H. Kobayashi, S. Ehara and H. Sato; PCT Int. Appl. WO, 98 32, 740 (Cl. C07D 223/60) (1998); JP. Appl. 97, 110, 114 (1997); Chem. Abstr., **129**, 148945h (1998).

(31) L. J. Ho, K. J. Hyeon, S. Y. Seung, J. W. Hui and L. H. Li; Repulo. Korean Kongkue Taelo Kongbo KR, 13(486) (Cl. CO7D 403/06) (2000) ; Chem. Abstr., **136**, 134760h (2002).

(32) M. D. Shah, N. C. Desai, K. K. Awasthi, and A. K. Saxena; Ind. J. Chem., **40(B)**, 201 (2001).

(33) J. P. Bascou, G. Lacrox, J. O. Perez and C. Schmitz; PCT Int. Appl. WO, 94 01, 410, 20 Jan. (1994); Chem. Abstr., **121**, 83334c (1994).

(34) V. Kolhe and V. Dhingra; Ind. J. Hetero. Chem., **4**, 69 (1994).

(35) B. R. Shah, J. J. Bhatt, H. N. Patel and N. K. Undavia; Ind. J. Chem., **34(B)**, 201 (1995).

(36) V. Akyoshi and M. Yasuyuki; Jpn. Kokai Tokkyo Koho, JP 7 206, 829 (1995); Chem. Abstr., **123**, 283031 (1995).

(37) G. V. D. Lucca; Bioorg. Med. Chem. Lett., **7**, 495 (1997).

(38) B. L. Pilkington and R. S. Elizabeth; Brit. UK Pat. Appl. GB., 2 3,29,180; Chem. Abstr., **130**, 448172 (1999).

(39) B. Kalluraya, P. Gunaga, D. Banji and A. M. Isloor; J. Org. Chem., **64**, 8084 (1999).

(40) G. S. Griffiths, M. B. Hauck, R. Imwinkelried, J. Kohr and J. Gosteli; J. Org. Chem., **64**, 8084 (1999).

(41) A. S. E. Sayed; J. Pharma. Sci., **26**, 231 (2000).

(42) R. Sharma and B. De; Ind. J. Hetero. Chem., **9**, 185 (2000).

(43) L. J. Peter and Y. B. Vera; Eur. Pat. Appl. WO, 100, 6, 113; Chem. Abstr., **133**, 307296 (2000).

(44) K. K. Awashthi; A. K. Saxena; Ind. J. Chem., **40(B)**, 207 (2001).

(45) I. Hidayat and C. Preston; Pestiade Biochem. Physio., **71**, 190 (2001).

(46) K. J. Ho, E. J. Park, M. Y. Yoon, T. R. Han and J. D. Choi; Biochem. Biophys. Res. Commun., **282**, 1237 (2001).

(47) A. Solankee, K. Kapadiya, K. Upadhyay and J. Patel; Orient. J. Chem., **17**, 315 (2001).

(48) W. P. John and D. T. Watter; U.S. US 6, 339, 158 (Cl. 546-135;CO7D 453/02), (2002); Chem. Abstr., **136**, 85813s, (2002).

(49) A. Rossello, S. Bertini, A. Lapucci, M. Machi, A. Martinelli and S. Rapposelli; J. Med. Chem., **45**, 4903 (2002).

(50) M. L. Irene, P. Christophe, V. A. Arthur, M. Witwrouas and Z. Debyser; J. Med. Chem., **46**, 1546 (2003).

(51) D. Erickl, V. A. Arthur and H. Piet; PCT Int. Appl. WO, 02 68, 395 (Cl. C07D 235/84) (2002); Chem. Abstr., **137**, 201308c (2002).

(52) M. Daisuke, H. Koji, A. Akira, A. Hitoshi, Y. Yoshinori, A. C. Chin and M. A. Piatyszek; Chem. Abstr., **137**, 93750e (2002).

(53) S. Lauter, H. Gunther and G. Wagnewr; J. Med. Chem., **45**, 4695 (2002).

(54) M. R. Jean, C. Sabourin, N. Alvorez, R. P. Sylvie, L. B. Guillaume and L. P. Patrice; Eur. J. Med. Chem., **38**, 711 (2003).

(55) C. Hamdouchi, C. Sanchez, J. Gruber and M. Prado; J. Med. Chem., **46**, 4333 (2003).

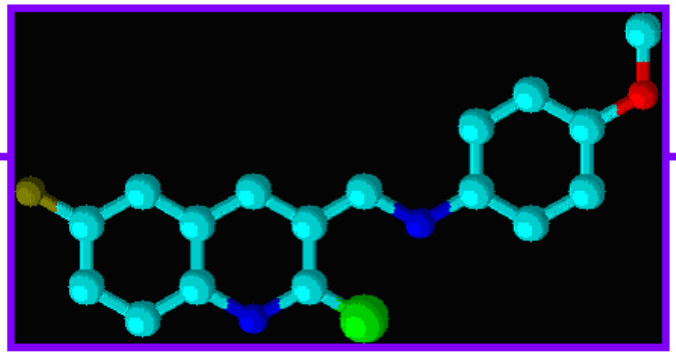
(56) A. N. Vasiliev , A. F. Lopez, J. D. Fernandez and A. J. Mocchi; Molecules, **9**, 535 (2004).

(57) E. Jayachandran, H. S. Basavaraj, G. M. Sreenivasa, L. V. G. Nargund and D. Sreenivasa Rao; Ind. J. Hetero. chem., **15**, 69 (2005).

(58) C. Alister and M. Kogan; Grop Protectien, **24**, 375 (2005).

(59) J. J. Bronson, K. L. Denbleyker, P. J. Falk and L. B. Snyder; Bioorg. Med. Chem. Lett., **16**, 3595 (2006).

CHAPTER-3



COMPARISON OF DIFFERENT METHODS USED FOR SYNTHESIS

INTRODUCTION

Developing chemical compounds with the desired biological properties is time consuming and expensive. Consequently, increasing interest is being directed towards technologies that allow more rapid synthesis and screening of chemical substances to identify compounds with functional qualities.

The research on the chemistry of schiff bases have been a focus of attention for chemists for several years due to their wide spread diversified biological activities such as antibacterial[1-3], antifungal[4-5], anti-inflammatory[6], analgesic[7], anticancer[8], anti-HIV[9] etc. This prompted us to synthesize various substituted schiff bases using the Microwave-assisted method (MW), Ultrasonic irradiation (US) and Conventional thermal method (Con.)

The microwave region of the electromagnetic spectrum lies between 1 cm and 1 m, most domestic and commercial microwave instruments operate at 2.45 GHz. When a molecule is irradiated with microwaves, it rotates to align itself with the applied field. The frequency of molecular rotation is similar to the frequency of microwave radiation and consequently the molecule continually attempts to realign itself with the changing field and energy is absorbed. It is particularly convenient that qualitatively, the larger the dielectric constant the great the coupling with microwaves. Thus, solvents such as water, methanol, DMF, ethyl acetate, acetone, chloroform, acetic acid and dichloromethane are all heated when irradiated with microwaves.

In the last few years, Microwave-induced Organic Reaction Enhancement (MORE) chemistry has gained popularity as a non-conventional technique for rapid organic synthesis[10].

Many researchers have reported the synthetic utility of MORE chemistry in routine organic synthesis[11-13]. Compared to traditional processing of organic synthesis, microwave-enhanced chemistry saves significant time and very often improves conversions, clean product formation etc. Further, it offers low cost with simplicity in processing and handling[14]. This technique has been used to promote a variety of chemical reactions such as additions, cycloadditions, substitutions, eliminations, fragmentations etc[15-21].

Recently much has been done in microwave enhanced solvent-free organic synthesis[22-34].

Further, ultrasonic waves have been used for organic synthesis[35-37]. These ultrasonic waves have frequencies greater than 20,000 cycles/sec. The ultrasound waves are known for their wide applications in various fields like life sciences, medical, cleaning, sonar, electronics, agriculture, oceanography, material science etc[38-42]. Literature survey shows that few workers synthesized some compounds using ultrasonic technique[43-54], at lower reaction temperature and in less reaction time[55].

Therefore in the present chapter, some schiff bases have been synthesized by conventional method, microwave technique and by using ultrasound waves.

The reaction scheme for the synthesis is already given in Section-I of Chapter-1 (in Part-1) in experimental part.

RESULTS AND DISCUSSIONS

The reaction time and yield of different synthesized compounds by using microwave, ultrasonic waves and conventional techniques are reported in Table 1. It is observed that using microwave and ultrasonic waves, the reaction time is reduced considerably whereas % yield increased markedly.

Further, the amount of catalyst required in these techniques is very less in comparison to conventional method.

Thus, microwave and ultrasonics proved to be better technique than conventional method.

Table 1: Comparison of %yield and reaction time of compounds synthesized by Microwave-induced method (MW), Ultrasonic irradiation (US) and Conventional thermal method (Con.) methods.

Code	Yield %			Reaction time		
	MW	US	Con.	MW min.	US hrs.	Con. hrs.
NVK-2A	74	67	62	10	2.00	12
NVK-2B	71	68	65	8	2.00	12
NVK-2C	69	62	55	9	2.15	11
NVK-2D	68	66	59	10	2.10	11
NVK-2E	71	62	45	10	2.00	12
NVK-2F	72	64	49	8	2.00	12
NVK-2G	68	65	58	8	2.00	12
NVK-2H	76	71	69	7	2.15	12
NVK-2I	66	59	45	9	2.30	12
NVK-2J	67	64	48	9	2.00	12

REFERENCES

(1) G. G. Mohamed and Z. H. A. El-Wahab; Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, **61**, 1059 (2005).

(2) R. Prabhakaran, A. Geetha, M. Thilagavathi, R. Karvembu, V. Krishnan, H. Bertagnolli and K. Natarajan; J. Inorg. Biochem., **98**, 2131 (2004).

(3) S. K. Sridhar, M. Saravanan and A. Ramesh; Eur. J. Med. Chem., **36**,615 (2001).

(4) R. Fioravanti, M. Biava, G. C. Porretta, C. Landolfi, N. Simonetti, A. Villa, E. Conte and A. P. Puglia; Eur. J. Med. Chem., **30**, 123 (1995).

(5) R. Ramesh and S. Maheswaran ; J. Inorg. Biochem., **96**, 457 (2003).

(6) A. Geronikaki, D. H. Litina and M. Amourgianou; Il Farmaco, **58**, 489 (2003).

(7) S. M. Sondhi, N. Singh, A. Kumar, O. Lozach and L. Meijer; Bioorg. Med. Chem., **14**, 3758 (2006).

(8) R. Pignatello, A. Panico, P. Mazzone, M. R. Pinizzotto, A. Garozzo and P. M. Fumeri; Eur. J. Med. Chem., **29**, 781 (1994).

(9) S. N. Pandeya, D. Sriram, G. Nath and E. De Clercq; Pharmaceutica Acta Helvetiae, **74**, 11 (1999).

(10) S. Varma; Green Chem., **1**, 43 (1999).

(11) S. Paul and R. Gupta; Ind. J. Chem., **37B**, 1279 (1998).

(12) R. Borah, D. J. Kalita and J. C. Sarma; Ind. J. Chem.; **41B**, 1032 (2002).

(13) M. Kidwai, B. Dave and R. Venkataramanan; Ind. J. Chem.; **41B**, 2414 (2002).

(14) B. L. Hayes, "Microwave Synthesis: Chemistry at the Speed of Light"; CEM Publishing: Matthews, NC, (2002).

(15) R. Gedye, F. Smith, K.Westaway, H. Ali and L. Baldisera; K. C. Can. J. Chem., **66**, 17(1987).

(16) S. Caddick, Tetrahedron; **51**,10403 (1995),

(17) A. Acosta, P. de la Cruz, P. De Miguel, E. Diez-Barra, A. de la Hoz, F. Langa, A. Loupy, M. Majdoub, N. Martín, C. Sanchez and C. Seoane; Tetrahedron Lett.; **36**, 2165 (1995).

(18) V. L. M. Sena, R. M. Srivastava, S. P. Oliveira and V. L. M. Lima; Bio. Med. Chem. Lett., **11**, 2671 (2001).

(19) A. Shaabani and A. Bazgir; Tetrahedron Lett., **45**, 2575 (2004).

(20) N. Yu. Gorobets, B. H. Yousefi, F. Belaj and C. O. Kappe; Tetrahedron, **60**, 8633 (2004).

(21) D. Simoni, M. Rossi, R. Rondanin, R. Baruchello, G. Grisolia, M. Eleopra, R. Giovannini, A. Bozzoli, S. Davalli, R. Di Fabio and D. Donati; Tetrahedron Lett., **46**, 759 (2005).

(22) S. Paul, M. Gupta, R. Gupta and A. Loupy; Tetrahedron Lett., 42, 3827 (2001).

(23) J. Jacques, V. Eynde, N. Hecq, O. Kataeva and C. O. Kappe; Tetrahedron, **57**, 1785 (2001).

(24) G. Caliendo, F. Fiorino, E. Perissutti, B. Severino, D. Scolaro, S. Gessi, E. Cattabriga, P. A. Borea and V. Santagada; Eur. J. Pharmaceu. Sci., **16**, 15 (2002).

(25) A. P. Combs , B. M. Glass and S. A. Jackson; Methods in Enzymology, **369**, 223 (2003).

(26) S. J. Song, S. J. Cho, D. K. Park, T. W. Kwon and S. A. Jenekhe; Tetrahedron Lett., **44**, 255 (2003).

(27) V. Santagada, F. Frecentese, E. Perissutti, D. Cirillo, S. Terracciano and G. Caliendo; Bioorg. Med. Chem. Lett., **14**, 4491 (2004).

(28) F. Corelli, M. Botta, A. Lossani, S. Pasquini, S. Spadari and F. Focher; Il Farmaco, **59**, 987 (2004).

(29) K. Bougrin, A. Loupy and M. Soufiaoui ; J. Photochem. Photobio. C: Photochem. Rev., **6**, 139 (2005).

(30) S. K. Samanta, I. Kylänlahti and J. Y. Kauhaluoma; Bioorg. Med. Chem. Lett., **15**, 3717 (2005).

(31) F. Mavandadi and A. Pilotti; Drug Discovery Today, **11**, 165 (2006).

(32) M. M. Heravi, G. Rajabzadeh, F. F. Bamoharram and N. Seifi; J. Mole. Cataly. A: Chemical, **256**, 238 (2006).

(33) W. Huang and G. F. Yang; Bioorg. Med. Chem., (In Press) (2006).

(34) R. Romagnoli, P. G. Baraldi, A. R. Moorman, M. A. Iaconinoto, M. D. Carrion, C. L. Cara, M. A. Tabrizi, D. Preti, F. Fruttarolo and S. P. Baker; Bioorg. Med. Chem. Lett., **16**, 5530 (2006).

(35) D. H. Bremmer. Ultrasonics Sonochemistry; **1**, s119 (1994).

(36) J. L. Luche ; C. R. Acad. Sci. Paris ; **323**, 337 (1996).

(37) F. Grieser and M. Ashokkumar; Weinheim, 120 (2004).

(38) M. M. Kamel, R. M. El-Shishtawy, B. M. Yussef and H. Mashaly; Dyes and Pigments, **65**, 103 (2005).

(39) S. M. Zhou, X. H. Zhang, X. M. Meng, X. F., S. T. Lee and S. K. Wu; J. Solid State Chem.; **178**, 399 (2005).

(40) W. Bonrath; Ultrason. Sonochem., **12**, 103 (2005).

(41) M. W. A. Kuijpers, P. D. Iedema, M. F. Kemmere and J. T. F. Keurentjes; Polymer; **45**, 6461(2004).

(42) A. Fürstner and I.Konetzki; Tetrahedron Lett., **39**, 5721(1998).

(43) K. F. Liou, P. H. Yang and Y. T. Lin; J. Organometallic Chem., **294**, 145 (1985).

(44) R. M. Savizky, N. Suzuki and J. L. Bove; Tetrahedron: Asymm., **9**, 3967 (1998).

(45) R. Katoh, H. Yakoi, S. Usuba, Y. Kakudate and S. Fujiwara; Ultrason. Sonochem., **5**, 69 (1998).

(46) A. Tuncay, B. M. Anaclerio, M. Zolodz and K. S. Suslick; Tetrehedron Lett. **40**, 599 (1999).

(47) S. F. Marcel, L. K. Jie and M. M. L. Lau; Chem. Phys. Lipids, **101**, 237 (1999).

(48) S. I. Nikitenko, P. Moisy, P. Blane and C. Madic; Comptes Rendes Chimie, **7**, 1191 (2004).

(49) W. B. Ko , J. Y. Heo , J. H. Nam and K. B. Lee; Ultrasonics, **41**, 727 (2004).

(50) W. Wei, W. Qunrong, D. Liqin, Z. Aiqing and W. Duoyuan; Ultrason. Sonochem., **12**, 411

(2005).

(51) Y. Carcenac, M. Tordeux, C. Wakselman and P. Diter; J. Fluorine Chem., **126**, 1347 (2005).

(52) V. Calvino, M. Picallo, A. J. L. Peinado, R. M. M. Aranda and C.J. D.Valle; Appl. Surface Sci., **252**, 6071 (2006).

(53) S. Zhu, Z. Zhou, D. Zhang and H. Wang; Microporous and Mesoporous Mat., **95**, 257 (2006).

(54) X. Jing, Y. Wang, D. Wu and J. Qiang; Ultrason. Sonochem., **14**, 75 (2007).

(55) A. C. Barton, S. D. Collyer, F. Davis, D. D. Gornall and K. A. Law; Biosens. Bioelectron.; **20**, 328 (2004).

PART-II

PHYSICO-CHEMICAL PROPERTIES

GENERAL INTRODUCTION

Much advancement has been made in the field of science and technology which helped people in leading a sophisticated yet luxurious life.

Several physico chemical parameters are available in the list and few of them are of much interest. It was well understood by the literature that physico chemical properties such as acoustical properties, conductivity, density, refractive index, dissociation constant etc. have contributed advancement in the physical sciences and also in daily human life. Drug macro-molecular interactions are an important phenomenon in physiological media, such as blood, membranes and intra and extra cellular fluids. Thermodynamic properties like partial molar volume and partial molar compressibility are the few sensitive indicators for understanding molecular interactions.

Refractive index is a very useful method to determine the structure and identity of unknown compounds. Thermal analysis is one the important tool for the study of thermal transformation of materials.

The study of physicochemical properties of compounds in solutions gives complete understanding of the behavior of compounds in different solvents. Literature survey shows that very little work has been reported for the study of physico chemical studies such as thermal properties, refractive index, conductance and ultrasonic of the heterocyclic compounds.

Thus, in this part of the thesis we have tried to add something in this field of science. Various physicochemical properties such as refractive index, heat of solution, conductance, thermal properties and acoustical properties for imidazolinone derivatives were determined in different solvents whereas dissociation constant for schiff bases were determined in DMF.

CHAPTER-1

ACOUSTICAL PROPERTIES

INTRODUCTION

Ultrasonic deals with study and application of high frequency sound waves usually in excess of 20 KHz (20,000 cycles per second). It works on the basis of piezoelectric effect[1-3].

Ultrasonic waves have wide range of applications in various fields[4-8] such as medicine, industry, material testing, under water ranging (depth gauges, SONAR) and cleaning (ultrasonic bath).

In medicine, it is used for various diagnosis such as pediatrics[9], vascular diseases[10], brain diseases[11], ophthalmology[12], in urology[13], in cancer cell[14] etc. It is also used to detect tumor of oral cavity[15], follow-up of wilm's tumor in the mouse[16], urethral obstruction and diverticulum of the urinary bladder[17]. Ultrasound therapy is also used in postmortem diagnosis[18]. Further, it is useful to obtain the information about bone microstructure[19], lung microstructure[20] and biological structures[21].

Ultrasonic technology is employed in food[22] and dairy industry[23]. It is also useful for investigation of wheat starch restrogadation[24], in noncontact method to monitor the doneness of bakery products[25] and for food drying process[26]. It is also applied for inactivation of micro-organisms in milk and apple cider[27], for hydrogen peroxide bleaching of cotton[28].

For the polishing of mold steel[29] and extraction of various compounds[30-33] also, ultrasonic waves have been used. These waves have also been used in animal communication (e.g. bat navigation and dog whistles).

Now a days, lots of interest has been generated on the use of ultrasound radiation in synthetic organic chemistry, which includes decrease of reaction time, increase of yield, lower reaction temperature, avoidance of phase transfer catalysis etc[34-39].

In addition to these, ultrasonic waves provide valuable information about the structure of solids[40-41]. By ultrasonic velocity measurements, the molecular interactions in pure liquid[42-45], aqueous solutions[46-48] and liquid mixtures[49-52] have also been studied. It provides a powerful, effective and reliable tool to investigate properties of solutions of polymers[53-64], carbohydrates[65-71], amino acid[72-77] etc. However, little work has been done for solid organic compounds solutions[78-82].

Thus, in the present chapter, sound velocity studies of some imidazolinone derivatives in dimethylformamide (DMF) and Dimethylsulphoxide (DMSO) solutions were done at 308.15K with a view to understand the molecular interactions in these solutions.

EXPERIMENTAL

Choice of Solvents:

N,N-Dimethylformamide (DMF) and dimethylsulphoxide (DMSO) and have been chosen as solvents in the present work. These two solvents are of industrial interest because of their wide use as solvents and solubilizing agents.

The densities, viscosities and ultrasonic velocities of solvents and solutions of different concentration were measured at 308.15 K by using pyknometer, an Ubbelohde suspended level viscometer and single frequency ultrasonic interferometer operating at 2 MHz, with the uncertainties of 0.0001 g/cm^3, $\pm$ 0.06 % and 0.01% respectively.

Density measurements:

The weight of distilled water, pure solvents and solutions of imidazolinone derivatives were measured by using pyknometer. The densities were evaluated by using following equation:

$$\rho\left(g/cm^3\right) = \frac{\left(\text{wt. of solvent or solution}\right)\left(\text{density of water}\right)}{\left(\text{wt. of water}\right)} \qquad \ldots (1.1)$$

Viscosity Measurements:

To determine the viscosity of solution, Ubbelohde viscometer[83] was used, which obeys Stoke's low[84]. The measured quantity of the distilled water / solvent / solution was placed in the viscometer, which was suspended in a thermostat at 308.15 K. The digital stopwatch, with an accuracy of $\pm$ 0.01 sec was used to determine flow time of solutions. Using the flow times (t) and known viscosity of standard water sample, the viscosity of solvent and solutions were determined according to equation:

$$\frac{\eta_1}{\eta_2} = \frac{t_1\rho_1}{t_2\rho_2} \qquad \ldots (1.2)$$

Sound velocity measurement:

Ultrasonic interferometer (Model No. F-81), Mittal Enterprise, New Delhi, working at frequency (F) of 2 MHz was used to determine sound velocity.

The solvent / solution were filled in the measuring cell with quartz crystal and then micrometer was fixed. The circulation of water from the thermostat at 308.15 K was started and test solvent / solution in the cell is allowed to thermally equilibrate. The micrometer was rotated very slowly so as to obtain a maximum or minimum of anode current (n). A number of maximum reading of anode current were counted. The total distance (d) travel by the micrometer for n=10, was read. The wave length (λ) was determined according to the equation (1.3).

$$\lambda = \frac{2d}{n} \qquad \ldots (1.3)$$

The sound velocity (U) of solvent and solutions were calculated from the wavelength and frequency (F) according to equation (1.4).

$$U = \lambda F \qquad \ldots (1.4)$$

RESULTS AND DISCUSSION

The density (ρ), viscosity (η) and sound velocity (U) of pure solvents and different imidazolinone derivatives solutions in N,N-dimethylformamide (DMF) and dimethylsulphoxide (DMSO) were calculated at 308.15 K and are given in Table 1.1.

From these measurements, various acoustical parameters like specific acoustical impendence (Z), isentropic compressibility (κ_S), intermolecular free length (L_f), Rao's molar sound function (R_m), molar compressibility (W), Vander Waals constant (b), relaxation strength (r), internal pressure (π), solvation number (S_n) etc., were evaluated using the following equations:

1. Specific acoustical impedance:

Specific acoustical impedance (Z) can be calculated as:

$$Z = U\rho \qquad \text{... (1.5)}$$

2. Isentropic compressibility:

Isentropic compressibility (κ_s) can be evaluated according to the following the equation[85]:

$$\kappa_s = \frac{1}{U^2\rho} \qquad \text{… (1.6)}$$

3. Intermolecular free path length:

Jacobson[86] proposed an equation to calculate the intermolecular free path length (L_f), which is given below:

$$L_f = K_j \kappa_s^{1/2} \qquad \text{… (1.7)}$$

where K_J is Jacobson constant (=2.0965 X 10^{-6})

4. Molar compressibility:

Molar compressibility (W) can be calculated by the following equation[87]:

$$W = \left(\frac{M}{\rho}\right)\kappa_s^{-1/7} \qquad \text{… (1.8)}$$

The apparent molecular weight (M) of the solution can be calculated according to equation (1.9):

$$M = M_1W_1 + M_2W_2 \qquad \text{… (1.9)}$$

where W_1 and W_2 are weight fractions of solvent and solute, respectively. M_1 and M_2 are the molecular weights of the solvent and compounds respectively.

5. Rao's molar sound function:

Rao's molar sound function (R_m) can be evaluated by an equation given by Bagchi et al.[88]:

$$R_m = \left(\frac{M}{\rho}\right) U^{1/3} \qquad \ldots (1.10)$$

6. Van der Waals Constant:

Van der Waals constant (b) can be calculated as follows[89]:

$$b = \frac{M}{\rho}\left\{1 - \left(\frac{RT}{MU^2}\right)\left[\sqrt{1 + \frac{MU^2}{3RT}} - 1\right]\right\} \qquad \ldots (1.11)$$

where R is the gas constant (=8.3143 JK^{-1} mol^{-1}) and T is the absolute temperature.

7. Relaxation Strength:

The relaxation strength (r) can be calculated as follows[90]:

$$r = 1 - \left[\frac{U}{U_\infty}\right]^2 \qquad \cdots (1.12)$$

where U_∞ = 1.6 x 10^5 cm/sec.

8. Relative Association (R_A):

$$R_A = \frac{\rho}{\rho_0}\left(\frac{U_0}{U}\right)^{1/3} \qquad \ldots (1.13)$$

where U, U_0 and ρ, ρ_0 are ultrasonic velocities and densities of solution and solvent respectively.

9. Internal Pressure:

Suryanarayana and Kuppuswamy[91] gave the following equation for evaluating internal pressure:

$$\pi = bRT\left[\frac{K_\eta}{U}\right]^{1/2} \frac{\rho^{2/3}}{M^{7/6}} \qquad \ldots (1.14)$$

where b is the packing factor (= 2). K is a constant (=4.28 X 10^9). The internal pressure (π) depends on temperature, density, ultrasonic velocity and specific heat at constant pressure.

10. Free Volume:

Free volume[92] can be calculated according to equation (1.15):

$$V_f = \left[\frac{MU}{K_n}\right]^{3/2} \quad \ldots (1.15)$$

The apparent molar compressibility (ϕ_K) of the solutions was calculated by the following equation:

$$\phi_K = \frac{\left(\rho_0\kappa_s - \rho\kappa_s^0\right)1000}{c\rho_0} + \frac{\kappa_s^0 M_2}{\rho_0} \quad \ldots (1.16)$$

where ρ_0 and κ_s^0 are density and isentropic compressibility of pure solvent respectively, c is the concentration of the solution and M_2 is the molecular weight of the compound.

Some of these calculated parameters are given in Tables 1.2 and 1.3.

Fig. 1.1 and 1.2 shows the variation of ultrasound velocity (U) with concentrations for all the imidazolinone derivatives in both solvents, DMF and DMSO. It is observed that ultrasonic velocity (U) increases with concentration for all the compounds. The velocity depends on intermolecular free length (L_f). The velocity increases with decreases in L_f or vice versa. Tables 1.2 and 1.3 shows that L_f decreases continuously which suggest that there is strong interaction between solvent (both DMF and DMSO) and compound molecules.

This is further supported by isentropic compressibility (κ_s) and relaxation strength (r). The variation of isentropic compressibility (κ_s) with concentration of these compounds are also shown in Fig. 1.3 and 1.4 for both solvents. It is observed from Fig. 1.3 and 1.4 and Tables 1.2 and 1.3 that both isentropic compressibility (κ_s) and relaxation strength (r) are also observed to decrease with concentration for all the compounds. The decrease of κ_s with increasing concentration might be due to aggregation of solvent molecules around solute molecules indicating thereby the presence of solute-solvent interactions. The increase of acoustical impedance (Z) (Tables 1.2 and 1.3) further confirms the solute-solvent interactions in these systems.

The correlation coefficient (γ) and correlation equations for some of the parameters are given in Table 1.4. It is observed that properties like Rao's molar sound function (R_m), molar compressibility (W) and Vander Waal's constant (b) are observed to increase linearly with concentration for all the compounds. The

linear variation of these acoustical properties indicates absence of complex formation.

The internal pressure (π) is the results of forces of attraction and repulsion between the molecules in solutions. Tables 1.2 and 1.3 shows that internal pressure decreases with concentration, which indicates the decrease in cohesive forces. Although decrease in compressibility (κ_s), intermolecular free length (L_f), relaxation strength (r) and increase of velocity (U), viscosity (η) suggest predominance of solute-solvent interactions, the decrease in internal pressure indicates the existence of solute-solute interactions also in these systems.

The free volume (V_f) of solute molecule at particular temperature and pressure depends on the internal pressure of liquid, in which it was dissolved. The decrease in molecular association causes an increase in free volume (V_f). Thus, free volume is an inverse function of internal pressure. It is evident from Table 1.2 and 1.3 that V_f increases with concentration for all the compounds in solutions. Hence, increase in free volume causes internal pressure to decreases, which indicates the solute-solute interactions. This suggests that both solute-solute and solute-solvent interactions exist in these systems.

Further, the apparent molar compressibilities (ϕ_k) of the solutions is fitted to Gucker's relation [93].

$$\phi_k = \phi^o_k + S_k \sqrt{C}$$

From the plot of ϕ_k verses $\sqrt{C}$, ϕ^o_k and S_k values are evaluated from the intercept and slope. The isentropic compressibility of all the solutions were also fitted to the following Bachem's relation[94]:

$$\kappa_s = \kappa_s^0 + AC + BC^{3/2}$$

and values of A and B were evaluated from the intercept and slope respectively. κ_s^0 is the isentropic compressibility of pure solvent. All these values of intercept and slopes are given in Table 1.5 for DMF and DMSO.

Table 1.5 shows that in DMF, A and ϕ^o_k values are negative whereas B and S_k values are positive. In DMSO also (Table 1.5) A values are negative. However, ϕ^o_k values are negative for some cases and positive for others. ϕ^o_k values are negative except for PAIM-1, PAIM-2, PAIM-8 and PAIM-9, which have low positive values. B and S_k values are also positive. The negative A and ϕ^o_k

values and positive B and S_k values suggest predominance of solute-solvent interactions.

The interactions occurring in different solutions can also be confirmed by the solvation number (S_n), which is measure of structure forming or structure breaking tendency of solute in a solution. Fig. 1.5 and 1.6 shows the variation of solvation number (S_n) with concentrations for all the compounds in the both solvents. For PAIM-2 and PAIM-6, S_n values are found increase with concentration in DMF. The increases in solvation number suggest increase in structure forming tendency of compound in a solution. However, for other compounds (except PAIM-4) at low concentration (0.01M), S_n values are higher but as concentration is increased it dropped suddenly and then it increases further with concentration. In some cases, after increasing, it becomes almost constant. This suggests that structure forming tendency decreases with concentration in most of the compounds, which may be due to dipole-dipole interactions, steric hindrance. Such interactions may cause weakening between solute and solvent molecules. This weak association is further confirmed by low relative association value (R_A), which is almost same for some compounds (Table 1.2).

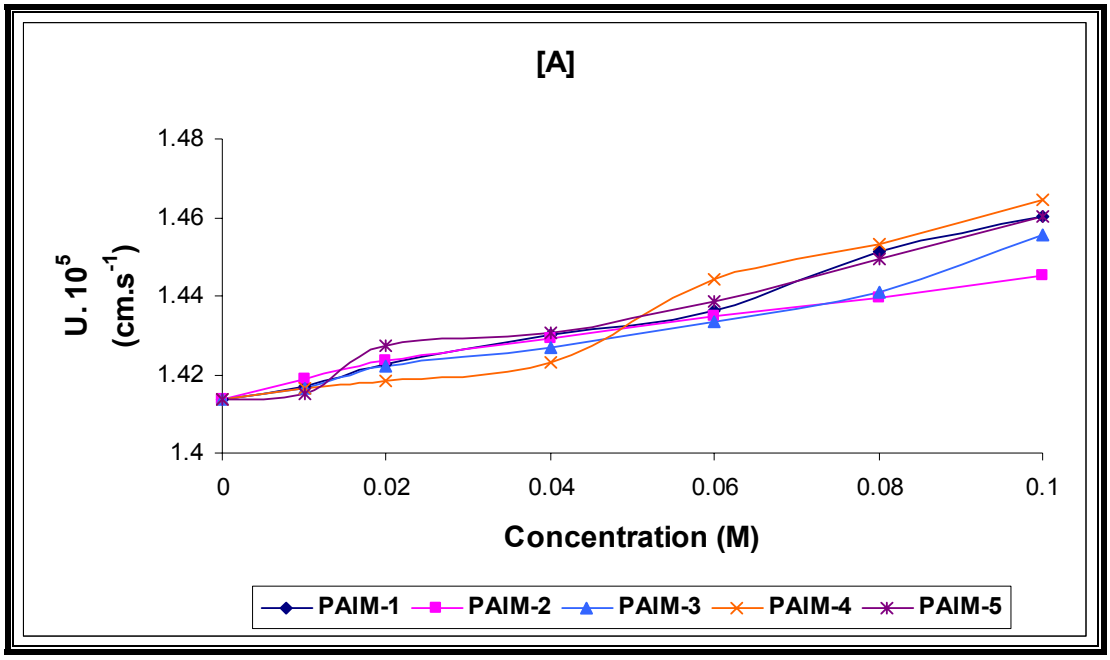
In PAIM-4 solutions, S_n values decreases with concentration suggesting thereby structure breaking tendency of this compound in DMF. The structure forming or structure breaking tendency depends on the type of solvent and types of substituent group in the compound. PAIM-4 contains bulky α-napthylamine group, which may be the reason for structure breaking tendency of PAIM-4 in DMF.

In DMSO (Fig. 1.5 and 1.6), for PAIM-5 and PAIM-6 S_n values increase with concentration. However, for other compounds at low concentration (0.00M) S_n values are higher at the beginning (except PAIM-8) but as concentration is increased, it dropped suddenly and then it increases again with concentration. Whereas in others, after increasing it becomes almost constant. In PAIM-8 solutions, S_n values decreases continuously with concentration suggesting thereby structure breaking tendency of this compound. Thus, structure forming tendency decreases with concentration in most of the compounds indicating thereby weak interactions. This weak association is further confirmed by low

relative association value (R_A), which is almost same for some compounds (Table 1.2).

Thus, it is concluded that in both DMF and DMSO solutions of studied compounds, both solute-solute and solute-solvent interactions exist.

Figure 1.1: Variation of ultrasonic velocity (U) with concentration in [A] DMF and [B] DMSO at 308.15K.



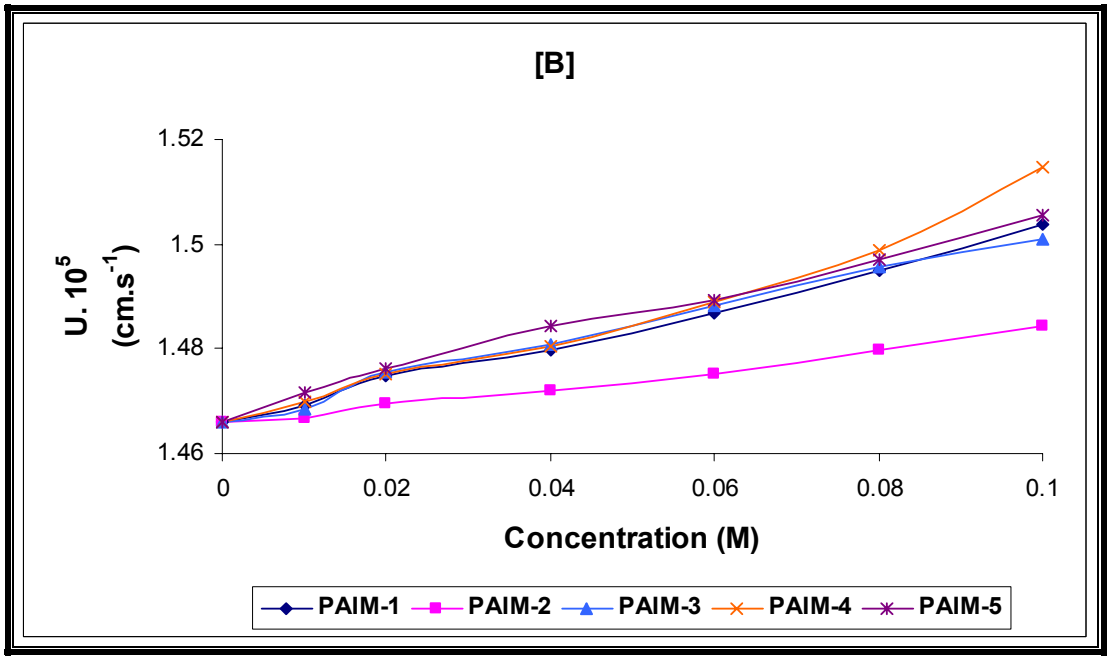
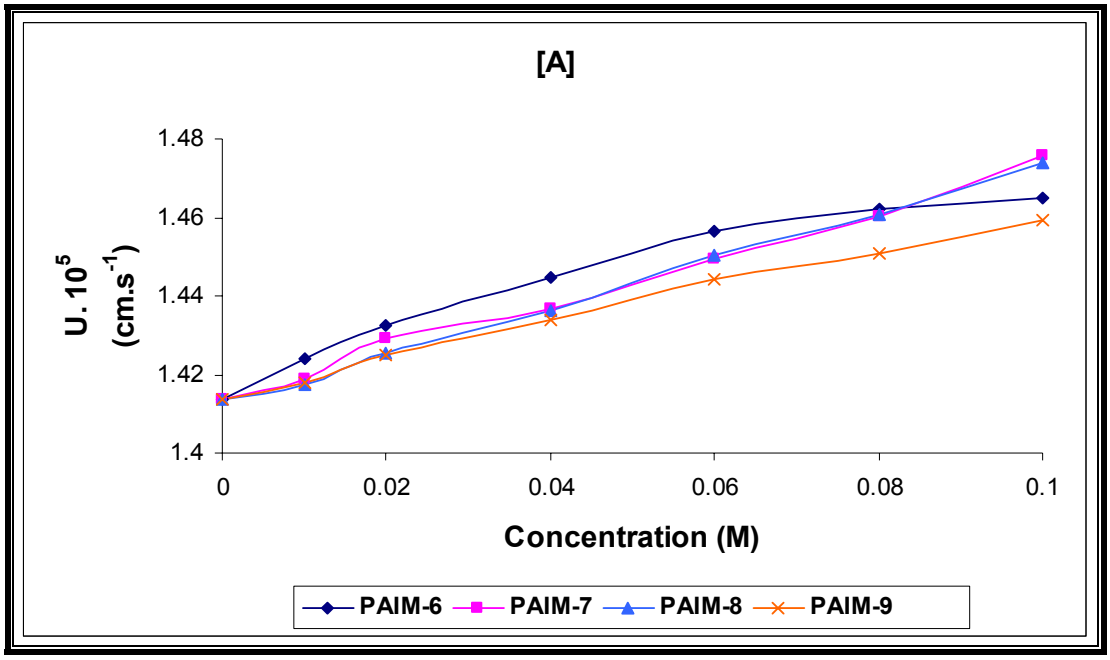


Figure 1.2: Variation of ultrasonic velocity (U) with concentration in [A] DMF and [B] DMSO at 308.15K.



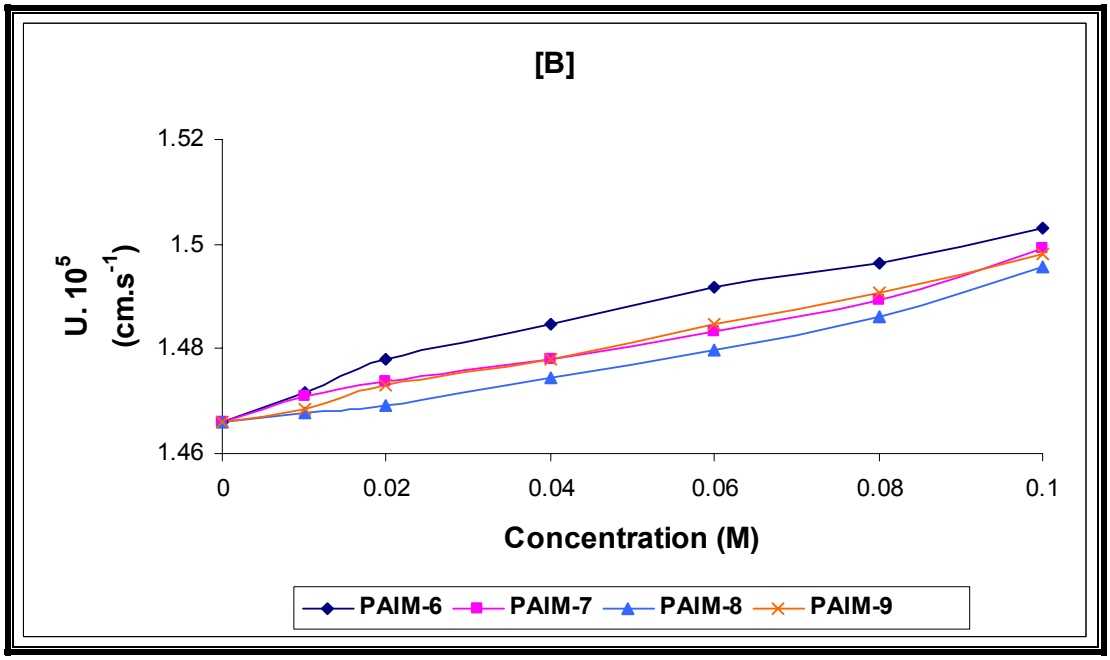
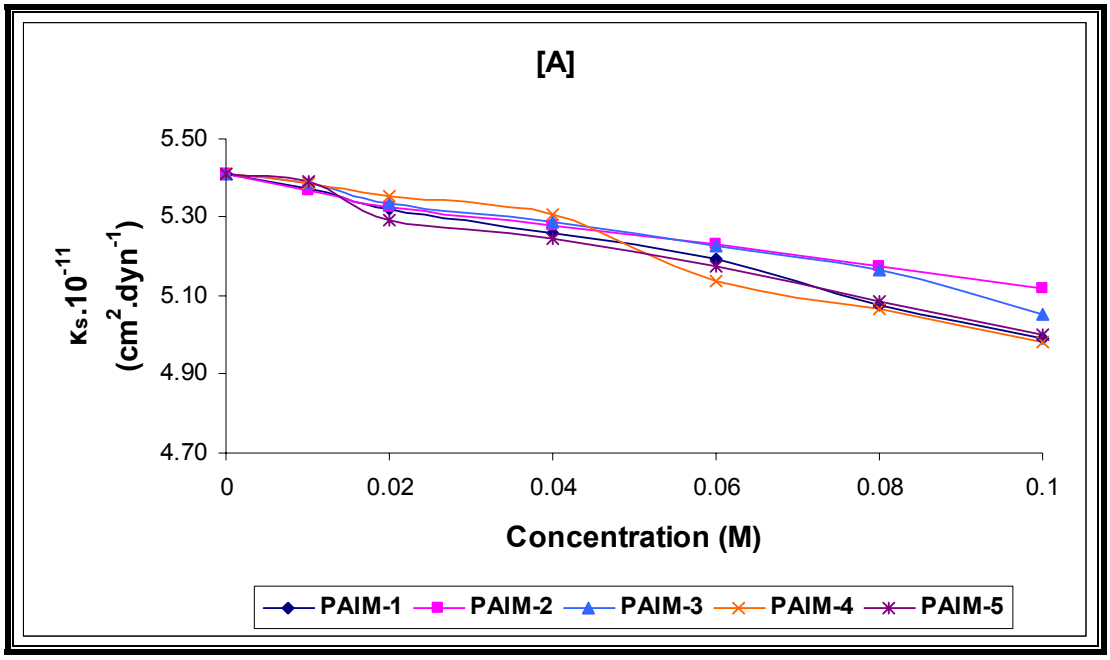


Figure 1.3: Variation of Isentropic Compressibility (κ_s) with concentration in [A] DMF and [B] DMSO at 308.15K.



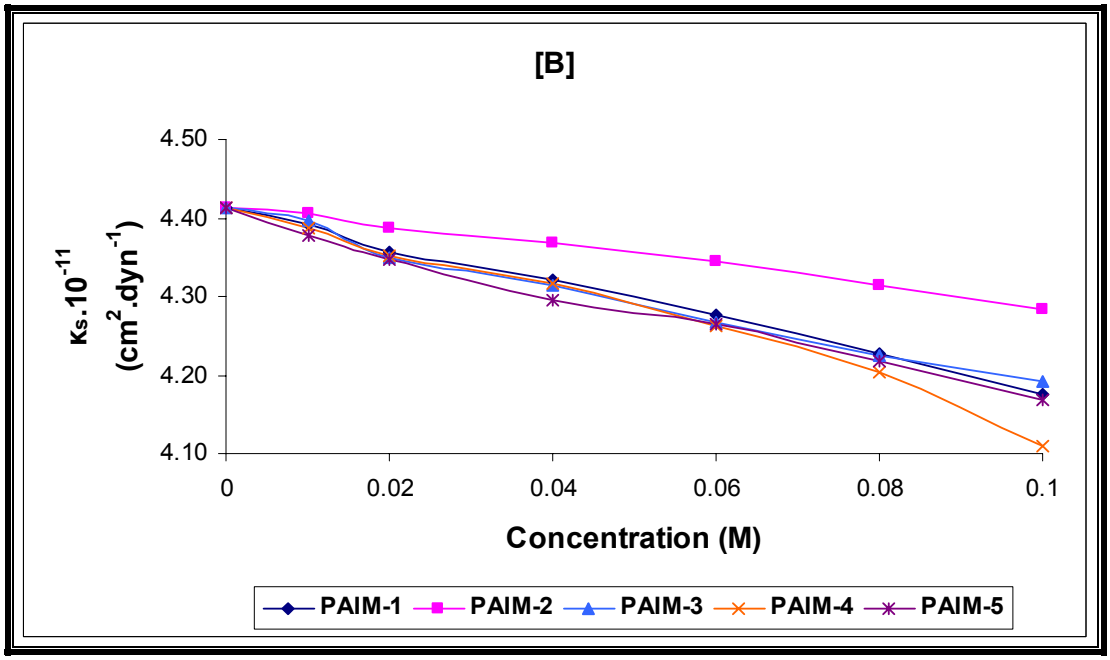
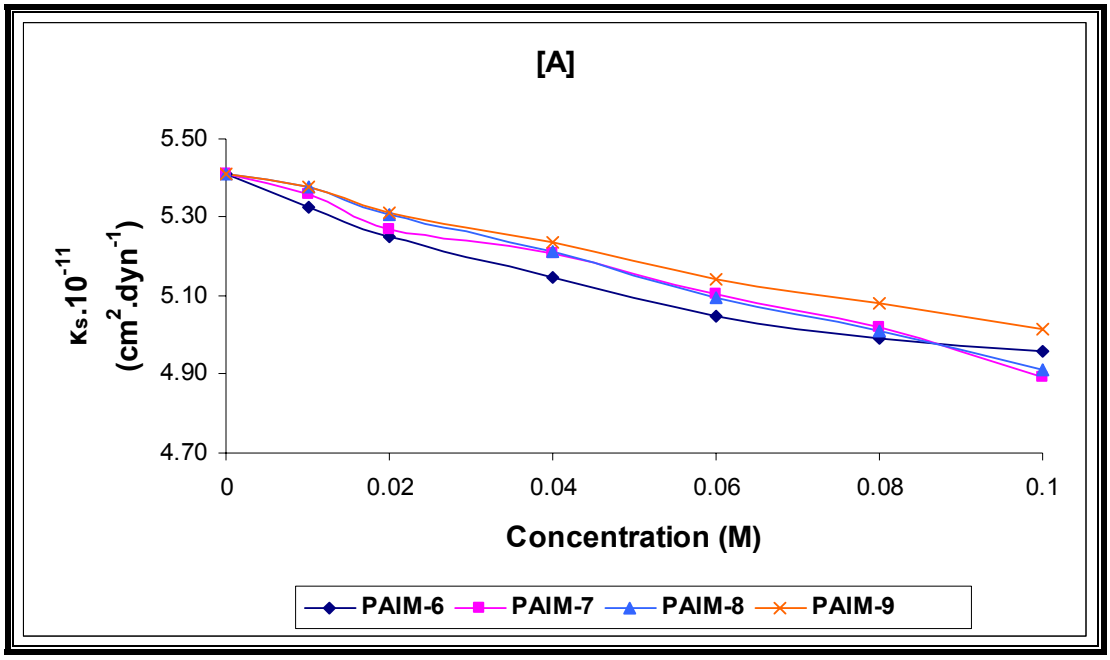


Figure 1.4: Variation of Isentropic Compressibility (κ_s) with concentration in [A] DMF and [B] DMSO at 308.15K.



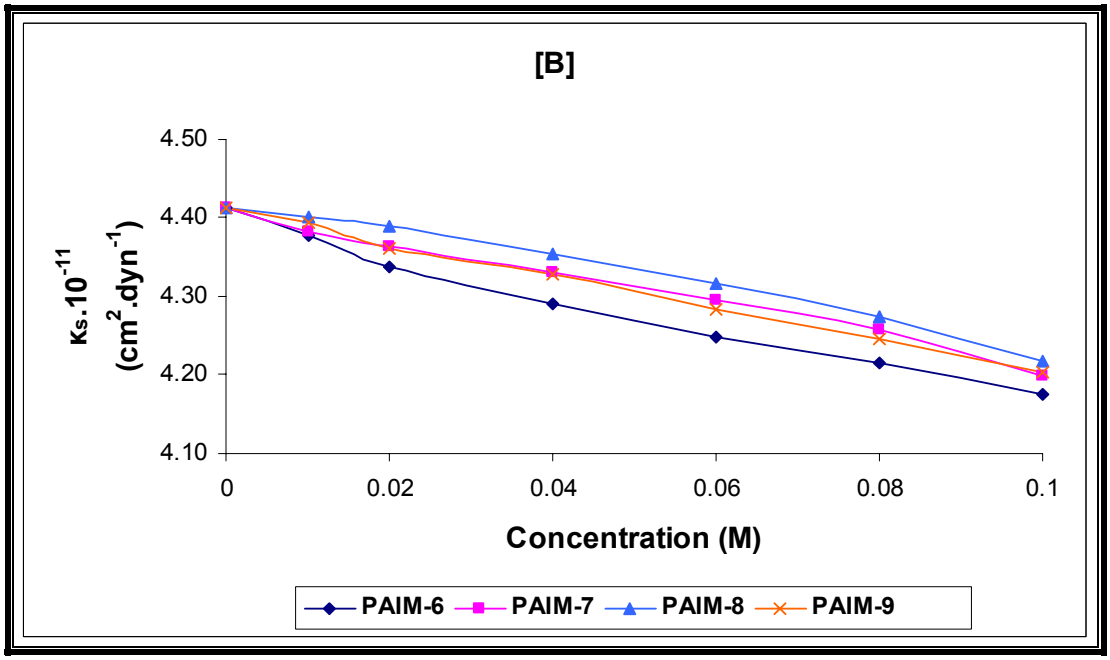
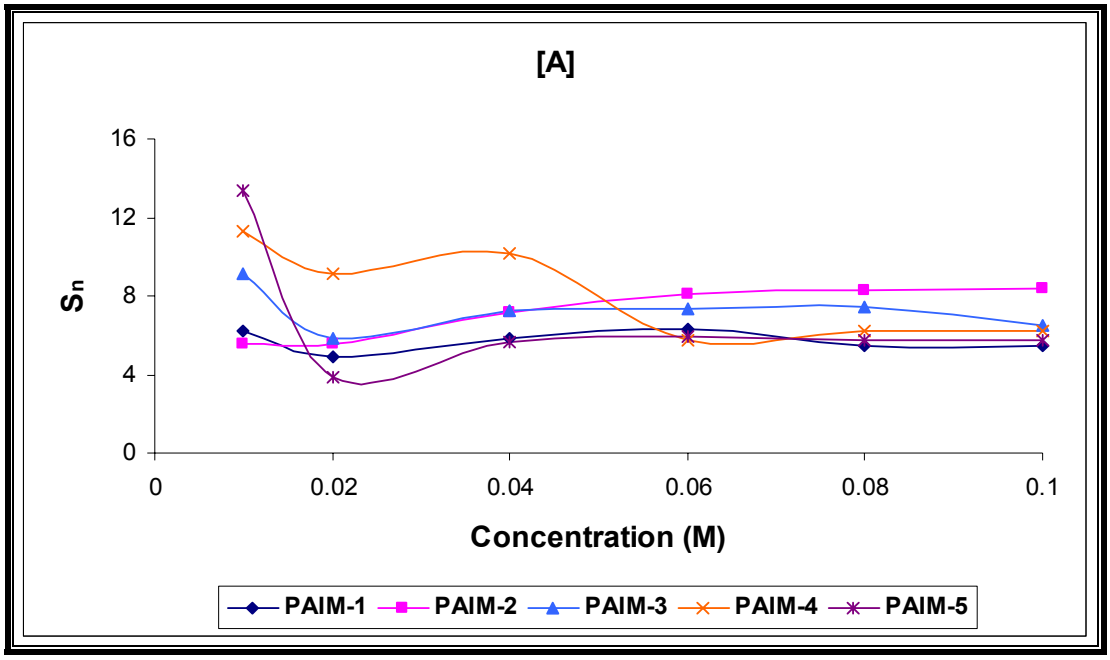


Figure 1.5: Variation of Solvation number (S_n) with concentration in [A] DMF and [B] DMSO at 308.15K.



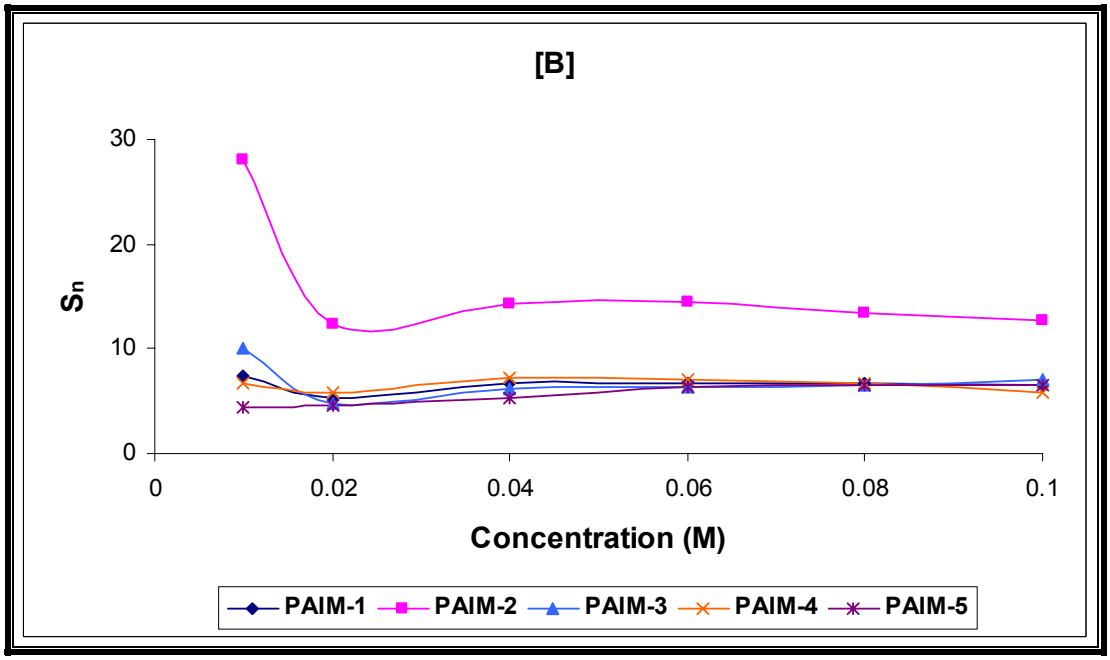
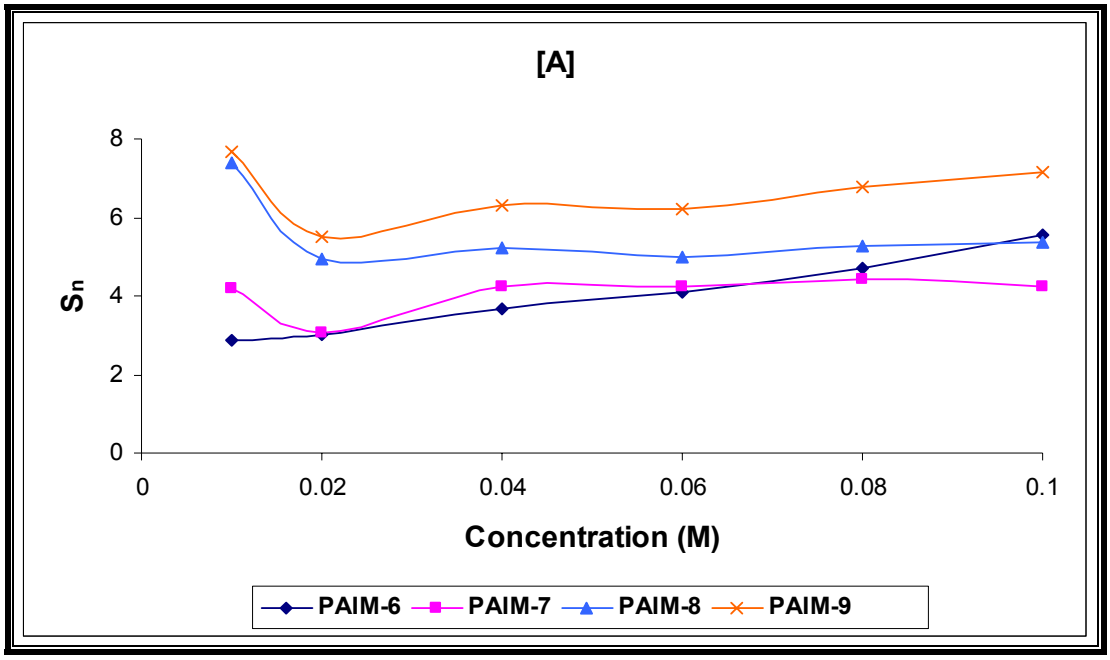


Figure 1.6: Variation of Solvation number (S_n) with concentration in [A] DMF and [B] DMSO at 308.15K.



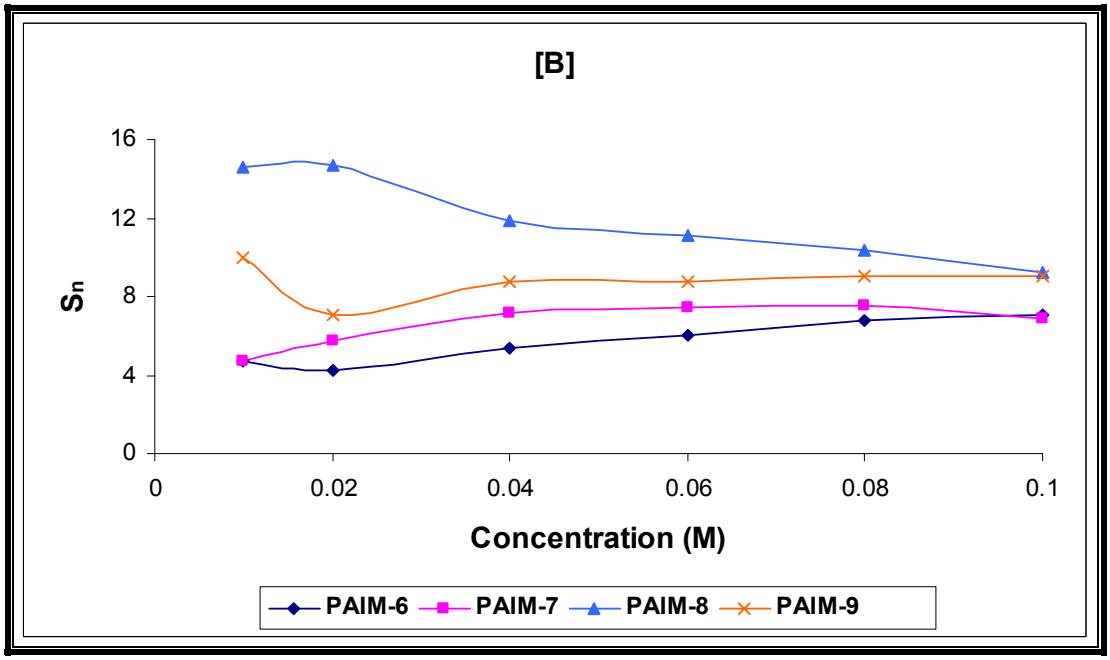


Table 1.1: The density (ρ), ultrasonic velocity (U) and viscosity (η) of Imidazolinone derivatives in DMF and DMSO at 308.15K.

Conc. (M)	Density ρ $g.cm^{-3}$	Velocity U. 10^{-5} $cm.s^{-1}$	Viscosity η.10^{3} poise	Density ρ $g.cm^{-3}$	Velocity U. 10^{-5} $cm.s^{-1}$	Viscosity η.10^{3} poise
	DMF			**DMSO**		
	PAIM -1			**PAIM -1**		
0.00	0.9249	1.4136	7.1536	1.0546	1.4660	10.6786
0.01	0.9268	1.4168	7.3048	1.0548	1.4692	10.8684
0.02	0.9285	1.4228	7.5165	1.0556	1.4748	11.0201
0.04	0.9301	1.4300	7.7198	1.0569	1.4796	11.2149
0.06	0.9328	1.4364	7.8222	1.0578	1.4868	11.3297
0.08	0.9357	1.4512	7.9827	1.0585	1.4948	11.5119
0.10	0.9393	1.4604	8.1928	1.0593	1.5036	11.6860
	PAIM -2			**PAIM -2**		
0.01	0.9254	1.4188	7.7407	1.0548	1.4668	11.4230
0.02	0.9266	1.4236	7.9298	1.0556	1.4696	11.4607
0.04	0.9277	1.4292	8.4518	1.0568	1.4720	11.7311
0.06	0.9288	1.4348	8.5310	1.0576	1.4752	11.8204
0.08	0.9325	1.4396	8.6057	1.0587	1.4796	11.9286
0.10	0.9357	1.4452	8.7669	1.0596	1.4844	12.0699
	PAIM -3			**PAIM -3**		
0.01	0.9254	1.4164	7.3723	1.0547	1.4684	10.9877
0.02	0.927	1.4220	7.5268	1.056	1.4756	11.1123
0.04	0.9292	1.4268	7.6920	1.0571	1.4808	11.3051
0.06	0.9312	1.4336	7.8630	1.0577	1.4884	11.5032
0.08	0.9327	1.4408	8.0824	1.0585	1.4956	11.7619
0.10	0.9338	1.4556	8.5520	1.0592	1.5008	12.1373

Continue…..

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Conc. (M)	Density ρ $g.cm^{-3}$	Velocity U. 10^{-5} $cm.s^{-1}$	Viscosity η.10^{3} poise	Density ρ $g.cm^{-3}$	Velocity U. 10^{-5} $cm.s^{-1}$	Viscosity η.10^{3} poise
	DMF			**DMSO**		
	PAIM -4			**PAIM -4**		
0.00	0.9249	1.4136	7.1536	1.0546	1.4660	10.6786
0.01	0.9251	1.4164	7.3415	1.055	1.4700	10.8602
0.02	0.9283	1.4184	7.5614	1.0557	1.4752	11.0263
0.04	0.9300	1.4232	7.7144	1.0572	1.4804	11.2326
0.06	0.9332	1.4440	7.9644	1.0584	1.4888	11.4098
0.08	0.9342	1.4532	8.2004	1.0593	1.4988	11.5934
0.10	0.9361	1.4644	8.2868	1.0603	1.5148	11.7999
	PAIM -5			**PAIM -5**		
0.01	0.9257	1.4152	7.8240	1.0547	1.4716	10.9877
0.02	0.9277	1.4272	8.0638	1.0554	1.4764	11.0351
0.04	0.9313	1.4304	8.4665	1.0564	1.4844	11.2105
0.06	0.9332	1.4388	8.7329	1.0572	1.4892	11.3814
0.08	0.9356	1.4496	8.9900	1.0576	1.4972	11.6108
0.10	0.9375	1.4604	9.0803	1.0585	1.5056	11.8030
	PAIM -6			**PAIM -6**		
0.01	0.9257	1.4240	7.4549	1.0548	1.4716	11.0262
0.02	0.9284	1.4324	7.5652	1.0556	1.4780	11.1080
0.04	0.9307	1.4448	7.8753	1.0569	1.4848	11.3038
0.06	0.9335	1.4564	8.0176	1.0582	1.4916	11.5746
0.08	0.9373	1.4620	8.2337	1.0594	1.4964	11.7557
0.10	0.9396	1.4648	8.4782	1.0601	1.5032	11.9872

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Conc. (M)	Density ρ $g.cm^{-3}$	Velocity U. 10^{-5} $cm.s^{-1}$	Viscosity η.10^{3} poise	Density ρ $g.cm^{-3}$	Velocity U. 10^{-5} $cm.s^{-1}$	Viscosity η.10^{3} poise
	DMF			**DMSO**		
	PAIM -7			**PAIM -7**		
0.00	0.9249	1.4136	7.1536	1.0546	1.4660	10.6786
0.01	0.9267	1.4188	7.3212	1.0549	1.4708	10.8387
0.02	0.9287	1.4292	7.4287	1.0556	1.4736	10.9424
0.04	0.9300	1.4368	7.5015	1.0568	1.4780	11.0514
0.06	0.9328	1.4492	7.7482	1.0581	1.4832	11.2413
0.08	0.9346	1.4600	7.8032	1.0592	1.4892	11.3327
0.10	0.9382	1.4756	7.9198	1.0596	1.4992	11.4330
	PAIM -8			**PAIM -8**		
0.01	0.9256	1.4176	7.7483	1.0551	1.4676	10.9261
0.02	0.9277	1.4252	8.0676	1.0556	1.4692	11.2020
0.04	0.9304	1.4360	8.2634	1.0567	1.4744	11.4350
0.06	0.9330	1.4504	8.3877	1.0581	1.4796	11.5872
0.08	0.9356	1.4608	8.5949	1.0593	1.4860	11.7623
0.10	0.9369	1.4740	8.7661	1.0599	1.4956	11.9473
	PAIM -9			**PAIM -9**		
0.01	0.9252	1.4180	7.3850	1.0555	1.4684	10.9900
0.02	0.9274	1.4248	7.5601	1.0566	1.4732	11.2092
0.04	0.9287	1.4340	7.8404	1.0576	1.4780	11.4516
0.06	0.9321	1.4444	8.1096	1.0587	1.4848	11.6665
0.08	0.9351	1.4508	8.4292	1.0596	1.4908	11.9465
0.10	0.9364	1.4592	8.6856	1.0603	1.4980	12.0950

Table1.2: Variation of acoustical parameters with concentration of imidazolinone derivatives in DMF at 308.15K.

Conc. (M)	L_f (A^o)	r	$Z .10^{-5}$ $g.cm^{-2}$	$Rm.10^{-3}$ $cm^{-8/3}.s^{-1/3}$	$W.10^{-3}$ $cm^{-1}.dyn^{-1}$	b $cm^3.mol^{-1}$	π	V_f (cm^3)	R_A
PAIM-1									
0.00	0.1542	0.2194	1.3074	4.1166	2.3144	79.0228	478.9820	0.1960	1.0000
0.01	0.1537	0.2159	1.3131	4.2553	2.3928	81.6229	465.0723	0.2007	1.0013
0.02	0.1529	0.2092	1.3211	4.3969	2.4726	84.2204	453.4569	0.2034	1.0017
0.04	0.1520	0.2012	1.3300	4.6830	2.6335	89.5511	426.3500	0.2164	1.0018
0.06	0.1511	0.1940	1.3399	4.9604	2.7901	94.7135	400.5261	0.2334	1.0032
0.08	0.1493	0.1774	1.3579	5.2441	2.9495	99.7890	378.1764	0.2498	1.0029
0.10	0.1481	0.1669	1.3718	5.5138	3.1020	104.7019	360.3942	0.2621	1.0046
PAIM-2									
0.01	0.1536	0.2137	1.3130	4.2742	2.4028	81.9479	476.5570	0.1851	0.9993
0.02	0.1530	0.2083	1.3191	4.4278	2.4892	84.7980	462.4038	0.1892	0.9995
0.04	0.1523	0.2021	1.3259	4.7368	2.6629	90.5965	440.7996	0.1914	0.9994
0.06	0.1516	0.1958	1.3326	5.0451	2.8361	96.3673	411.0275	0.2086	0.9992
0.08	0.1508	0.1904	1.3424	5.3334	2.9994	101.7605	385.9981	0.2259	1.0021
0.10	0.1500	0.1841	1.3523	5.6225	3.1630	107.1384	365.5411	0.2399	1.0042
PAIM-3									
0.01	0.1539	0.2163	1.3107	4.2615	2.3958	81.7506	466.7857	0.1979	0.9999
0.02	0.1531	0.2101	1.3182	4.4036	2.4759	84.3656	453.3518	0.2028	1.0003
0.04	0.1524	0.2048	1.3258	4.6846	2.6343	89.6484	425.7257	0.2169	1.0015
0.06	0.1515	0.1972	1.3350	4.9671	2.7934	94.9044	401.3631	0.2310	1.0021
0.08	0.1507	0.1891	1.3438	5.2520	2.9536	100.1799	380.7734	0.2428	1.0020
0.10	0.1490	0.1724	1.3592	5.5486	3.1194	105.4779	366.7280	0.2452	0.9998

Continue…..

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Conc. (M)	L_f (A^o)	r	Z .10^{-5} g.cm^{-2}	Rm.10^{-3} $cm^{-8/3}.s^{-1/3}$	W.10^{-3} $cm^{-1}.dyn^{-1}$	b $cm^3.mol^{-1}$	π	V_f (cm^3)	R_A
PAIM-4									
0.00	0.1542	0.2194	1.3074	4.1166	2.3144	79.0228	478.9820	0.1960	1.0000
0.01	0.1539	0.2163	1.3103	4.2864	2.4097	82.2286	462.7260	0.2008	0.9996
0.02	0.1534	0.2141	1.3167	4.4400	2.4971	85.1348	449.8610	0.2039	1.0025
0.04	0.1528	0.2088	1.3236	4.7693	2.6826	91.3455	417.4669	0.2216	1.0032
0.06	0.1503	0.1855	1.3475	5.1060	2.8714	97.3230	390.4225	0.2386	1.0018
0.08	0.1493	0.1751	1.3576	5.4426	3.0603	103.5193	367.2750	0.2534	1.0008
0.10	0.1480	0.1623	1.3708	5.7746	3.2467	109.5532	343.9172	0.2755	1.0003
PAIM-5									
0.01	0.1540	0.2177	1.3101	4.2619	2.3963	81.7805	480.7939	0.1810	1.0005
0.02	0.1525	0.2043	1.3240	4.4114	2.4801	84.4119	467.9142	0.1843	0.9998
0.04	0.1519	0.2008	1.3321	4.6885	2.6371	89.6480	445.5827	0.1892	1.0030
0.06	0.1508	0.1913	1.3427	4.9784	2.8001	95.0042	421.2496	0.1994	1.0030
0.08	0.1495	0.1792	1.3562	5.2664	2.9622	100.2507	399.4138	0.2101	1.0031
0.10	0.1483	0.1669	1.3691	5.5566	3.1252	105.5132	376.3731	0.2266	1.0027
PAIM-6									
0.01	0.1530	0.2079	1.3182	4.2805	2.4060	81.9678	466.6143	0.1971	0.9984
0.02	0.1519	0.1985	1.3298	4.4327	2.4919	84.7163	450.3275	0.2052	0.9994
0.04	0.1504	0.1846	1.3447	4.7465	2.6682	90.4540	423.2915	0.2168	0.9990
0.06	0.1490	0.1714	1.3595	5.0548	2.8416	96.0731	395.9151	0.2348	0.9993
0.08	0.1481	0.1651	1.3703	5.3466	3.0069	101.4900	374.8622	0.2479	1.0021
0.10	0.1477	0.1619	1.3763	5.6423	3.1739	107.0335	356.7227	0.2587	1.0039

Continue…..

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Conc. (M)	L_f (A^o)	r	$Z .10^{-5}$ $g.cm^{-2}$	$Rm.10^{-3}$ $cm^{-8/3}.s^{-1/3}$	$W.10^{-3}$ $cm^{-1}.dyn^{-1}$	b $cm^3.mol^{-1}$	π	V_f (cm^3)	R_A
PAIM-7									
0.00	0.1542	0.2194	1.3074	4.1166	2.3144	79.0228	478.9820	0.1960	1.0000
0.01	0.1535	0.2137	1.3148	4.2501	2.3897	81.4861	466.2041	0.1999	1.0007
0.02	0.1522	0.2021	1.3273	4.3872	2.4667	83.9105	451.6806	0.2073	1.0004
0.04	0.1513	0.1936	1.3362	4.6606	2.6203	88.9824	422.4349	0.2254	1.0001
0.06	0.1498	0.1796	1.3518	4.9297	2.7716	93.8495	401.1301	0.2366	1.0002
0.08	0.1485	0.1673	1.3645	5.2017	2.9244	98.7843	377.4206	0.2564	0.9997
0.10	0.1467	0.1495	1.3844	5.4658	3.0730	103.4326	357.7715	0.2746	1.0000
PAIM-8									
0.01	0.1537	0.2150	1.3121	4.2859	2.4095	82.1948	475.2721	0.1855	0.9998
0.02	0.1527	0.2066	1.3222	4.4515	2.5028	85.2185	463.1834	0.1864	1.0003
0.04	0.1514	0.1945	1.3361	4.7837	2.6898	91.3495	430.0219	0.2027	1.0007
0.06	0.1496	0.1783	1.3532	5.1187	2.8779	97.4206	399.3524	0.2225	1.0002
0.08	0.1484	0.1664	1.3667	5.4470	3.0626	103.4230	375.1530	0.2382	1.0006
0.10	0.1469	0.1513	1.3810	5.7871	3.2531	109.5528	352.4195	0.2561	0.9989
PAIM-9									
0.01	0.1537	0.2146	1.3119	4.2986	2.4165	82.4319	462.4726	0.2001	0.9993
0.02	0.1528	0.2070	1.3214	4.4734	2.5150	85.6466	445.8990	0.2069	1.0001
0.04	0.1517	0.1967	1.3318	4.8331	2.7170	92.3348	414.3268	0.2218	0.9993
0.06	0.1503	0.1850	1.3463	5.1796	2.9123	98.7164	387.6601	0.2369	1.0006
0.08	0.1494	0.1778	1.3566	5.5205	3.1047	105.0594	366.1289	0.2483	1.0023
0.10	0.1485	0.1683	1.3664	5.8746	3.3036	111.5823	345.1958	0.2627	1.0018

Table1.3: Variation of acoustical parameters with concentration of imidazolinone derivatives in DMSO at 308.15K.

Conc. (M)	L_f (A^o)	r	$Z .10^{-5}$ $g.cm^{-2}$	$Rm.10^{-3}$ $cm^{-8/3}.s^{-1/3}$	$W.10^{-3}$ $cm^{-1}.dyn^{-1}$	b $cm^3.mol^{-1}$	π	V_f (cm^3)	R_A
PAIM-1									
0.00	0.1393	0.1605	1.5460	3.9064	2.2339	74.0833	580.2555	0.1255	1.0000
0.01	0.1389	0.1568	1.5497	4.0197	2.2986	76.1779	565.9824	0.1279	0.9995
0.02	0.1384	0.1504	1.5568	4.1330	2.3631	78.2239	551.3063	0.1312	0.9990
0.04	0.1378	0.1448	1.5638	4.3542	2.4897	82.3230	522.8142	0.1389	0.9991
0.06	0.1371	0.1365	1.5727	4.5793	2.6181	86.4392	494.9934	0.1484	0.9983
0.08	0.1363	0.1272	1.5822	4.8063	2.7475	90.5615	471.1396	0.1568	0.9972
0.10	0.1355	0.1169	1.5928	5.0338	2.8770	94.6619	449.2968	0.1655	0.9960
PAIM-2									
0.01	0.1392	0.1596	1.5472	4.0255	2.3021	76.3289	579.3780	0.1187	1.0000
0.02	0.1389	0.1564	1.5513	4.1440	2.3698	78.5257	560.6900	0.1238	1.0001
0.04	0.1385	0.1536	1.5556	4.3790	2.5045	82.9337	531.5112	0.1303	1.0007
0.06	0.1382	0.1499	1.5602	4.6160	2.6400	87.3597	501.3955	0.1398	1.0008
0.08	0.1377	0.1448	1.5665	4.8524	2.7752	91.7411	474.7798	0.1493	1.0008
0.10	0.1372	0.1393	1.5729	5.0898	2.9109	96.1265	451.3386	0.1583	1.0006
PAIM-3									
0.01	0.1390	0.1577	1.5487	4.0194	2.2984	76.1853	569.1968	0.1257	0.9995
0.02	0.1383	0.1495	1.5582	4.1320	2.3627	78.1927	553.6098	0.1297	0.9992
0.04	0.1377	0.1434	1.5654	4.3545	2.4898	82.3059	524.7778	0.1374	0.9990
0.06	0.1370	0.1346	1.5743	4.5815	2.6192	86.4485	498.4611	0.1453	0.9979
0.08	0.1362	0.1262	1.5831	4.8072	2.7479	90.5615	476.1012	0.1520	0.9970
0.10	0.1357	0.1202	1.5896	5.0312	2.8758	94.6728	458.2775	0.1559	0.9965

Continue…..

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Conc. (M)	L_f (A^o)	r	$Z .10^{-5}$ $g.cm^{-2}$	$Rm.10^{-3}$ $cm^{-8/3}.s^{-1/3}$	$W.10^{-3}$ $cm^{-1}.dyn^{-1}$	b $cm^3.mol^{-1}$	π	V_f (cm^3)	R_A
PAIM-4									
0.00	0.1393	0.1605	1.5460	3.9064	2.2339	74.0833	580.2555	0.1255	1.0000
0.01	0.1389	0.1559	1.5509	4.0379	2.3089	76.5078	562.7173	0.1290	0.9995
0.02	0.1383	0.1499	1.5574	4.1693	2.3839	78.9048	545.8134	0.1329	0.9990
0.04	0.1377	0.1439	1.5651	4.4263	2.5310	83.6707	513.1970	0.1422	0.9992
0.06	0.1369	0.1342	1.5757	4.6874	2.6799	88.4385	483.2012	0.1524	0.9985
0.08	0.1350	0.1225	1.5877	4.9516	2.8305	93.2163	456.3501	0.1629	0.9971
0.10	0.1344	0.1037	1.6061	5.2224	2.9841	97.9664	431.9558	0.1739	0.9945
PAIM-5									
0.01	0.1387	0.1541	1.5521	4.0246	2.3012	76.2292	568.1955	0.1262	0.9988
0.02	0.1382	0.1485	1.5582	4.1399	2.3669	78.3273	550.5858	0.1314	0.9984
0.04	0.1374	0.1393	1.5681	4.3705	2.4984	82.5410	520.3800	0.1401	0.9976
0.06	0.1369	0.1337	1.5744	4.5987	2.6288	86.7576	493.7404	0.1485	0.9972
0.08	0.1362	0.1244	1.5834	4.8323	2.7618	91.0022	470.3091	0.1561	0.9958
0.10	0.1353	0.1145	1.5937	5.0639	2.8937	95.1852	448.5179	0.1646	0.9948
PAIM-6									
0.01	0.1387	0.1541	1.5522	4.0318	2.3053	76.3653	567.9824	0.1259	0.9989
0.02	0.1381	0.1467	1.5602	4.1557	2.3759	78.5982	549.8325	0.1310	0.9982
0.04	0.1373	0.1388	1.5693	4.3989	2.5148	83.0697	518.4728	0.1399	0.9979
0.06	0.1366	0.1309	1.5784	4.6415	2.6534	87.5189	492.2323	0.1473	0.9976
0.08	0.1361	0.1253	1.5853	4.8821	2.7910	91.9565	467.2369	0.1560	0.9977
0.10	0.1355	0.1173	1.5935	5.1273	2.9308	96.4300	445.2233	0.1639	0.9969

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Conc. (M)	L_f (A^o)	r	Z .10^{-5} g.cm^{-2}	Rm.10^{-3} $cm^{-8/3}.s^{-1/3}$	W.10^{-3} $cm^{-1}.dyn^{-1}$	b $cm^3.mol^{-1}$	π	V_f (cm^3)	R_A
PAIM-7									
0.00	0.1393	0.1605	1.5460	3.9064	2.2339	74.0833	580.2555	0.1255	1.0000
0.01	0.1388	0.1550	1.5515	4.0149	2.2957	76.0584	565.9095	0.1283	0.9992
0.02	0.1385	0.1518	1.5555	4.1200	2.3558	78.0002	551.4223	0.1319	0.9992
0.04	0.1380	0.1467	1.5620	4.3295	2.4757	81.8852	522.5358	0.1406	0.9994
0.06	0.1374	0.1407	1.5694	4.5388	2.5954	85.7431	498.2653	0.1479	0.9994
0.08	0.1368	0.1337	1.5774	4.7494	2.7157	89.6017	474.0378	0.1573	0.9991
0.10	0.1359	0.1220	1.5886	4.9682	2.8400	93.5190	451.3469	0.1673	0.9973
PAIM-8									
0.01	0.1391	0.1587	1.5485	4.0358	2.3080	76.5097	564.8399	0.1275	1.0001
0.02	0.1389	0.1568	1.5509	4.1651	2.3819	78.9315	551.0757	0.1290	1.0002
0.04	0.1383	0.1508	1.5580	4.4246	2.5303	83.7524	518.3843	0.1377	1.0001
0.06	0.1377	0.1448	1.5656	4.6822	2.6777	88.5239	487.9734	0.1477	1.0002
0.08	0.1371	0.1374	1.5741	4.9415	2.8258	93.2911	461.2044	0.1576	0.9999
0.10	0.1362	0.1262	1.5852	5.2076	2.9774	98.1059	436.7815	0.1677	0.9984
PAIM-9									
0.01	0.1390	0.1577	1.5499	4.0430	2.3122	76.6329	565.1664	0.1269	1.0003
0.02	0.1384	0.1522	1.5566	4.1808	2.3909	79.1577	548.4095	0.1302	1.0003
0.04	0.1379	0.1467	1.5631	4.4563	2.5484	84.2827	514.1080	0.1394	1.0001
0.06	0.1372	0.1388	1.5720	4.7329	2.7064	89.3783	483.1997	0.1493	0.9996
0.08	0.1366	0.1318	1.5797	5.0095	2.8644	94.4743	457.2147	0.1577	0.9991
0.10	0.1359	0.1234	1.5883	5.2885	3.0235	99.5766	431.4833	0.1689	0.9982

Table1.4: The correlation coefficient (γ) and correlation equations between some acoustical parameters and concentrations (C) of imidazolinone derivatives in DMF and DMSO at 308.15K.

Parameters	γ	Correlation equation	γ	Correlation equation	γ	Correlation equation
DMF						
	PAIM-1		**PAIM-2**		**PAIM-3**	
κ_s($cm^2.dyn^{-1}$)	0.9913	κ_s+ 4.1389C= 5.4136	0.9926	κ_s+ 2.8117C= 5.3963	0.9863	κ_s+ 3.386C= 5.416
L_f (A^o)	0.9906	L_f+ 0.1745C= 0.4476	0.9931	L_f+ 0.1179C= 0.4468	0.9854	L_f+ 0.1422C= 0.4476
Z ($g.cm^{-2}$)	0.9901	Z- 0.6299C= 1.3066	0.9943	Z- 0.4291C= 1.3085	0.9896	Z- 0.4976C= 1.3066
W ($cm^{-1}.dyn^{-1}$)	1.0000	W- 7.9005C= 2.3151	0.9998	W- 8.5016C= 2.3189	1.0000	W- 8.0181C= 2.3145
b ($cm^3.mol^{-1}$)	0.9998	b- 257.83C= 79.099	0.9997	b- 282.02C= 79.172	1.0000	b- 264.03C= 79.072
R_m ($cm^{-8/3}.s^{-1/3}$)	0.9999	R_m- 14.0220C= 4.1176	0.9997	R_m- 15.09C= 4.1255	0.9999	R_m- 14.254C= 4.1165
r	0.9864	r+ 0.5234C= 0.2209	0.9863	r+ 0.3382C= 0.2170	0.9711	r+0.4373C= 0.2207
	PAIM-4		**PAIM-5**		**PAIM-6**	
κ_s($cm^2.dyn^{-1}$)	0.9756	κ_s+ 4.5168C= 5.4359	0.9853	κ_s+ 4.0509C= 5.4092	0.9535	κ_s+ 4.5197C= 5.3626
L_f (A^o)	0.9751	L_f+ 0.1904C= 0.4484	0.9856	L_f+ 0.1707C= 0.4473	0.9556	L_f+ 0.1912C= 0.4454
Z ($g.cm^{-2}$)	0.9801	Z- 0.6641C= 1.3040	0.9895	Z- 0.6135C= 1.3074	0.9708	Z- 0.6965C= 1.3129
W ($cm^{-1}.dyn^{-1}$)	1.0000	W- 9.3230C= 2.3132	1.0000	W- 8.0901C= 2.3153	0.9998	W- 8.5932C= 2.3199
b ($cm^3.mol^{-1}$)	1.0000	b- 304.88C= 79.088	1.0000	b- 364.5C= 79.091	0.9999	b- 279.84C= 79.1440
R_m ($cm^{-8/3}.s^{-1/3}$)	0.9999	R_m- 16.581C= 4.1136	1.0000	R_m- 14.363C= 4.1181	0.9998	R_m- 15.252C= 4.1274
r	0.9631	r+0.5994C= 0.2239	0.9794	r+ 0.5136C= 0.2198	0.9425	r+ 0.5795C= 0.2126
	PAIM-7		**PAIM-8**		**PAIM-9**	
κ_s($cm^2.dyn^{-1}$)	0.9929	κ_s+ 4.9622C= 5.4013	0.9979	κ_s+ 5.0780C= 5.4138	0.9930	κ_s+ 4.0206C= 5.4027
L_f (A^o)	0.9930	L_f+ 0.2102C= 0.4470	0.9982	L_f+ 0.2149C= 0.4475	0.9936	L_f +0.1694C= 0.4470
Z ($g.cm^{-2}$)	0.9922	Z- 0.7365C= 1.3083	0.9983	Z- 0.7518C= 1.3065	0.9952	Z- 0.6040C= 1.3078
W ($cm^{-1}.dyn^{-1}$)	1.0000	W- 7.6018C= 2.3148	1.0000	W- 9.3690C= 2.3151	0.9999	W- 9.8710C= 2.3176
b ($cm^3.mol^{-1}$)	0.9999	b- 245.23C= 79.064	1.0000	b- 304.54C= 79.111	0.9999	b- 324.74C= 79.16
R_m ($cm^{-8/3}.s^{-1/3}$)	1.0000	R_m- 13.525C= 4.1170	1.0000	R_m- 16.6680C= 4.1176	0.9999	R_m- 17.537C= 4.1228
r	0.9930	r+ 0.6756C= 0.2192	0.9982	r+ 0.6886C= 0.2207	0.9940	r+ 0.5151C= 0.2184

Continue…..

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Parameters	γ	Correlation equation	γ	Correlation equation	γ	Correlation equation
DMSO						
	PAIM-1		**PAIM-2**		**PAIM-3**	
κ_s($cm^2.dyn^{-1}$)	0.9966	κ_s+ 2.3211C= 4.4116	0.9924	κ_s+ 1.2799C= 4.4159	0.9887	κ_s+ 2.2493C= 4.4075
L_f (A^o)	0.9964	L_f+ 0.1077C= 04040	0.9922	L_f+ 0.0590C= 0.4041	0.9893	L_f+ 0.1043C= 0.4038
Z ($g.cm^{-2}$)	0.9970	Z- 0.4602C= 1.5459	0.9936	Z- 0.2673C= 1.5453	0.9894	Z- 0.4450C= 1.5468
W ($cm^{-1}.dyn^{-1}$)	1.0000	W- 6.4214C= 2.2339	1.0000	W- 6.7653C= 2.2342	1.0000	W- 6.4189C= 2.2340
b ($cm^3.mol^{-1}$)	1.0000	b- 205.64C= 74.103	1.0000	b- 220.34C= 74.1130	1.0000	b- 205.80C= 74.0930
R_m ($cm^{-8/3}.s^{-1/3}$)	1.0000	R_m- 11.255C= 3.9062	1.0000	R_m- 11.8250C= 3.9068	1.0000	R_m- 11.2500C= 3.9064
r	0.9944	r+ 0.4251C= 0.1607	0.9879	r+ 0.2085C= 0.1612	0.9917	r+ 0.4110C= 0.1599
	PAIM-4		**PAIM-5**		**PAIM-6**	
κ_s($cm^2.dyn^{-1}$)	0.9831	κ_s+ 2.8581C= 4.4189	0.9925	κ_s+ 2.3426C= 4.4015	0.9822	κ_s+ 2.3070C= 4.3958
L_f (A^o)	0.9819	L_f+ 0.1313C= 0.4043	0.9929	L_f+ 0.1088C= 0.4035	0.9831	L_f+ 0.1071C= 0.4032
Z ($g.cm^{-2}$)	0.9834	Z- 0.5711C= 1.5446	0.9941	Z- 0.4584C= 1.5477	0.9873	Z- 0.4660C= 1.5486
W ($cm^{-1}.dyn^{-1}$)	1.0000	W- 7.4808C= 2.2333	1.0000	W- 6.5874C= 2.2347	1.0000	W- 6.9541C= 2.2356
b ($cm^3.mol^{-1}$)	1.0000	b- 238.70C= 74.1130	1.0000	b- 210.98C= 74.1030	1.0000	b- 223.15C= 74.1210
R_m ($cm^{-8/3}.s^{-1/3}$)	0.9999	R_m- 13.1160C= 3.9050	1.0000	R_m- 11.5540C= 3.9078	1.0000	R_m- 12.1790C= 3.9097
r	0.9723	r+ 0.5317C= 0.1622	0.9931	r+ 0.4384C= 0.1587	0.9825	r+ 0.4153= 0.1575
	PAIM-7		**PAIM-8**		**PAIM-9**	
κ_s($cm^2.dyn^{-1}$)	0.9904	κ_s+ 1.9898C= 4.4082	0.9844	κ_s+ 1.9091C= 4.4223	0.9974	κ_s+ 2.0729C= 4.4102
L_f (A^o)	0.9900	L_f+ 0.0922C= 0.4038	0.9836	L_f+ 0.0883C= 0.4044	0.9975	L_f+ 0.0960C= 0.4039
Z ($g.cm^{-2}$)	0.9932	Z- 0.4021C= 1.5465	0.9866	Z- 0.3868C= 1.5440	0.9973	Z- 0.4183C= 1.5466
W ($cm^{-1}.dyn^{-1}$)	1.0000	W- 6.0369C= 2.2344	1.0000	W- 7.4216C= 2.2335	1.0000	W- 7.8951C= 2.2332
b ($cm^3.mol^{-1}$)	1.0000	b- 194.00C= 74.1070	1.0000	b- 239.98C= 74.1150	1.0000	b- 254.98C= 74.0770
R_m ($cm^{-8/3}.s^{-1/3}$)	1.0000	R_m- 10.5690C= 3.9072	1.0000	R_m- 12.9870C= 3.9053	1.0000	R_m- 13.8190C= 3.9048
r	0.9822	r+ 0.3524C= 0.1599	0.9743	r+ 0.3326C= 0.1626	0.9975	r+ 0.3671C= 0.1607

Table 1.5: Bachem's constants A, B, ϕ^{o}_{k} and S_k of imidazolinone derivatives in DMF and DMSO at 308.15K.

COMPOUNDS	A X 10^{11} $dyn^{-1}.cm^{3}.mol^{-1}$	B X 10^{11} $dyn^{-1}.cm^{-1/2}.mol^{-3/2}$	ϕ^{o}_{k} X 10^{8} $dyn^{-1}.mol^{-1}$	S_k X 10^{8} $dyn^{-1}cm^{-3/2}.mol^{-3/2}$
DMF				
PAIM-1	-3.15	4.00	-1.42	1.50
PAIM-2	-4.95	7.27	-0.90	3.20
PAIM-3	-1.90	5.78	-1.05	3.50
PAIM-4	-1.40	10.00	-0.57	6.18
PAIM-5	-3.10	1.33	-2.20	1.50
PAIM-6	-10.80	20.00	-7.05	13.33
PAIM-7	-4.80	1.20	-3.20	2.20
PAIM-8	-5.30	5.50	-2.92	1.60
PAIM-9	-5.70	0.67	-3.70	8.13
DMSO				
PAIM-1	-1.90	1.18	0.01	1.12
PAIM-2	-0.20	3.50	1.18	1.28
PAIM-3	-2.80	1.94	-1.10	2.84
PAIM-4	-2.60	2.18	-0.33	0.30
PAIM-5	-4.00	5.58	-2.10	6.00
PAIM-6	-3.80	4.59	-2.10	5.41
PAIM-7	-3.50	6.57	-1.90	9.09
PAIM-8	-0.80	3.50	1.30	3.23
PAIM-9	-1.85	0.94	0.30	0.75

REFERENCES

(1) A. P. Cracknell; "Ultrasonics", Chapter **6**, 92 (1980). Wykenham Publishers.

(2) J. Curie and P. Curie; Compt. Rend., **91**, 294 (1880).

(3) J. Curie and P. Curie; Compt. Rend., **93**, 1137 (1881).

(4) M. K. S. Suslick; Ultrasound: It's Chemical, Physical and Biological Effects, VCH, Weinheim, (1988).

(5) T. J. Mason; Ed., Sonochemistry. The use of ultrasound in chemistry, Royal Society of Chemistry (1990).

(6) M. P. Kapoor; J. Pure Appl. Ultrason., **19**, 104 (1997).

(7) M. K. S. Suslick and G. J. Price; Ann. Rev. Mater. Sci., **29**, 295 (1999).

(8) M. Sivakumar and A. Gedanken; Synthetic Metals, **148**, 301 (2005).

(9) R. Hünig ,pediatrics today part I, publication: Pediatric Radiology, **4** ,108.116

(10) G. G. Znaiko, V. Yu. Solov'ev and V. E. Krasovskii; Biomedical Engineering, **27**, 235 (1993).

(11) A. I. Trukhanov, P. S. Kudryavtsev and D. A. Bakhtin; Biomedical Engineering, **26**, 328 (1992).

(12) N. M. Florianovich, F. E. Fridman and A. A. Chevnenko; Biomedical Engineering, **6**, 81-84.

(13) M. Falus, A. Babics, Z. Szendrői, M. Sobel and V. Szabó; International Urology and Nephrology, **2**, 379-390.

(14) K. S. Suslick; "Ultrasound: Its Chemical, Physical and Biological Effects", VCH, Weinheim, (1988).

(15) A. A. Fazylov and A. M. Dusmuratov; Biomedical Engineering, **20**, 73 (1986).

(16) E. Jouannot, J.P. Duong-Van-Huyen, K. Bourahla, P. Laugier, M. Lelievre- Pegorier and L. Bridal;Ultrasound in Medicine & Biology, **32**, 183 (2006).

(17) J. Shalev, Y. Itzchak, Hana Blau, Judith Rosenman, Z. Ben-Refael, M. Brish, S. Mashiach, D. M. Serr;Pediatric Radiology, **12**, 48-50.

(18) S. Uchigasaki, L. Oesterhelweg, A. Gehl, J.P. Sperhake, K.Puschel, S. Oshida and Nemoto; Forensic Science International,**140**, 33 (2004).

(19) M. A. Hakulinen, J. S. Day, J. Toyras, H. Weinans and J. S. Jurvelin; Phys Med Biol. **51**, 1633 (**2006).**

(20) F. Ossant, M. Lebertre, L. Pourcelot and F. Patat; Ultrasound Med Biol. **27**, 157 (2001)**.**

(21) F. I. Braginskaia and D. Floid; Biofizika., **26**, 542 (1981)

(22) J. N. Coupland and R. Saggin; Adv Food Nutr Res. **45**, 101 (2003)

(23) S. Muthukumaran, K. Yang, A. Seuren, S. Kentish, M. Ashokkumar, G.W. Stevens and F. Grieser; Separation and Purification Technology, **39**, 99 (2004).

(24) F. Lionetto, A. Maffezzoli, M.A. Ottenhof, I.A. Farhat and J.R. Mitchell; J. Food Engineering, **75**, 258 (2006).
(25) D. E. Chimenti and L. Faeth; AIP Conference Proceedings, **509**, 1849 (2000).
(26) S. de la Fuente-Banco, E. Riera-Franco de Sarabia, V.M. Acosta-Aparicio, A. Blanco-Blanco and J.A. Gallego-Juárez; Ultrasonics, In Press,(June 2006)
(27) D. J. D'Amico, T.M. Silk, J. Wu and M. Guo; J Food Prot. **69**, 556 (2006).
(28) S.I. Mistik and S. M. Yukseloglu; Ultrasonics. **43**, 811 (2005).
(29) H.Hocheng, and K.L. Kuo; International Journal of Machine Tools and Manufacture, **42**, 7 (2002).
(30) Z . Hromadkova, A. Ebringerova and P. Valachovic; Ultrason Sonochem., **9**, 37 (2002).
(31) M. Vinatoru, M. Toma, O.Radu, P. I. Filip, D. Lazurca and T. J. Mason; Ultrason Sonochem. **4**, 135 (1997).
(32) I. C. Patel and D. M. Skauen; J Pharm Sci. **58** , 1135 (1969).
(33) M. E. Ovadia and D. M. Skauen;J Pharm Sci. **54**, 1013 (1965).
(34) G. J. Price; "Current Trends in Sonochemistry", Royal Society of Chemistry, Cambridge, (1992).
(35) R. Katoh, H. Yokoi, S. Usuba, Y. Kakudate and S. Fujiwara; Ultrasonics Sonochemistry, **5**, 69 (1998).
(36) O. Krüger, Th. -L. Schulze and D. Peters; Ultrason. Sonochem., **6**, 123 (1999).
(37) Y. Zhao, X. H. Liao, J. M. Hong and J. J. Zhu; Mat. Chem. Phys., **87**, 149 (2004).
(38) M. Mexiarová, M. Kiripolský and S. Toma; Ultrason. Sonochem., **12**, 401 (2005).
(39) M. Sivakumar and A. Gedanken; Synthetic Metals, **148**, 301 (2005).
(40) S. P. Yawale, S. V. Pakade and C. S. Adagonkar, Proc. Sol. State. Sym. (BARC), 30c, 66c (1987).
(41) S. Mukherjee, C. Basu and U. S. Ghosh; J. Non-Cryst. Solids, **144**,159 (1992).
(42) S. S. Yadav, Y. P. Singh and J. Ragkumar; J. Ind. Coun. Chem., **16**, 20 (1999).
(43) S. C. Bhatt, H. Semwal, V. Lingwal, K. Singh and B. S. Semwal; J. Acous. Soc. India, **28**, 293 (2000).
(44) R. P. Varma and S. Kumar; Ind. J. Pure and apply. Phy., **38**, 96 (2000).
(45) M. Kalidoss and S. Ravi, Statistical Mechanics and its application, **312**, 59 (2002).
(46) S. Govindarajan, V. Kannappana, M. D. Naresh, K. Venkataboopathy and B. Lokanadam; J. Mol. Liq., **107**, 289 (2003).
(47) K. J. Patil and D. H. Dagade; J. Chem. Thermo., **36**, 677 (2004).
(48) S. Kamila, S. Jena and B. Bihari; J. Chem. Thermo., **37**, 820 (2005).
(49) A. Awasthi, M. Rastogi and J. P. Shukla; Fluid Phase Equilibria, **215**, 119 (2004).
(50) R. Abrahama, M. Abdulkhadar and C. V. Asokan; J. Chem.Thermo., **32**, 1 (2000).
(51) A. Dhanalakshmi and S. Sekar; J. Pure Appl. Ultrason., **21**, 97 (1999).

(52) G. L. N. Sastry; J. Acous. Soc. India, 14 ,Da-1 to Da-8 (1986).
(53) W. Li, J. Chen, J. Zhao, J. Zhang and J. Zhu; Materials Letters, **59**, 800 (2005).
(54) L. Czarnecki, A. Garbacz and M. Krystosiak; Cement and Concrete Composites, **28**, 360 (2006).
(55) M. Bradley and F. Grieser; J Colloid Interface Sci. **251**, 78 (2002).
(56) J. Li, S. Guo and X. Li; Polymer Degradation and Stability, **89**, 6 (2005).
(57) M. Mohamed and K. Koga; J. Thermal. Anal., **34**, 685 (1994).
(58) M. V. Kok; J. Tharmal. Anal., **24**, 899 (2002).
(59) K. Ramanathan and S. Ravichandran; J. Pure Appl. Ultrason., **26**,12 (2004)
(60) R. F. de Farias, C. C. Gesilva and T. A. G. Restivo, J. Serb. Chem. Soc., 70 (2005).
(61) W. R. Moore and Tidswell; Macromolec.Chem., **81**,1 (1965).
(62) J. S. Oh, J. G. Jang and Y. C. Bae; Polym., **38**, 3761 (1997).
(63) G. G. Cameroon, M. Y. Qureshi and S. C. Tavern; Polym.Int., **47**, 5 (1998).
(64) N. Somanathan, U. Arumugam and R. Balakrishnan; J. Pure Appl Ultras., **23**, 37 (2001).
(65) J. Wu, Di Chen, J. Pepe, B. E. Himberg and M. Richń; Ultrasound in Medicine & Biology, **32**, 429 (2006).
(66) K. Aeberhardt, J. Y. Laumer, P. E. Bouquerand and V. Normand; Int. J. Biol. Macromol., **36**, 275 (2005).
(67) E. Baucke, R. Behrends, K. Fuchs, R. Hagen and U. Kaatze; J. Chem. Phys. **120**, 8818 (2004).
(68) L. B. Gaïda, C.G. Dussap and J.B. Gros; Food Chemistry, **96**, 387 (2006).
(69) F. Franks, M. J. Suggetta, A. A. Ablrtts and P. A. Quickenden; J. Sol. Chem.,**1**, 131 (1972).
(70) M. V. Kaulgud, F. Zet; Physk. Chem.,**36** ,644 (1976).
(71) P. Pugazhendhi and C. V. Suryanarayana; Ind.J.Technol., **28**,644 (1990).
(72) Riyazuddeen and G.K. Bansal; Thermochimica Acta, **445**, 40 (2006).
(73) T.Fukahori, S. Nishikawa and K. Yamaguchi; J. Acoust. Soc. Am., **115**, 2325 (2004).
(74) J. I. Dunbar and R. A. Pethrick; J. Poly. Sci. Poly. Phy. Edu., **15**, 279 (1977).
(75) C. K. Rao, A. V. Rajulu, and S. V. Naidu; J. Poly Mater., **8**, 1499 (1989).
(76) S. Kalahasti, Sri Babu, A. V. Satyavati; Acustica., **71**, 77 (1990).
(77) G. Ravichandran and T. G. Nambinarayanan, Proc. Int. Conf. Ex. Ultrason., (ICEU – 99) 534 (1999)
(78) G. L. N. Sastry and B. A. Krishnamurthy; Ind. J. Pure and apply. Phy., **6**, 637 (1968).
(79) A. Dhanalakshmi, Proc. Int. Conf. Ex. Ultrason., (ICEU – 99) 477 (1999)
(80) M. Mecozzi, R. Acquistucci, A. Marina and P. C. Rill; Ultrasonic Sonochemistry, **9**, 219 (2002).
(81) C. C. Deshmukh, A. G. Doshi and P. Agrawal, Acta Ciencia Indica,XXIXC, 4 (2003).
(82) J. I. Bhat and N. S. Varaprasad, Ind. J. Pure and apply. Phy., **42**, 96 (2004).

(83) L. Ubbelhode, Inst. Pet. London **19**, 376 (1933).

(84) R. A. Robinson and R. H. Stokes, "Electrolyte Solutions", Butterworths scientific publications, London; (1955).

(85) G. L. N. Sastry and B. A. Krishnamurthy, Ind. J. Pure Apply. Phy., **6**, 637(1968).

(86) B. Jacobson, Nature (London), **173,** 772 (1954).

(87) Y. Wada, J. Phy. Soc. Jpn., **4**, 280 (1949).

(88) S. Bagchi and S. K. Nema and R. P. Singn, Eur. Polym. J., **22,** 851 (1989).

(89) P. Vigoureux, "Ultrasonics", Chapman and Hall, London (1952).

(90) G. K. Johri and R. C. Misra, Acustica, **57,**292 (1985).

(91) C. V. Suryanarayana and J. Kuppuswamy, J. Acoust. Soc. (India), **9**, 4 (1981).

(92) D. Subramanian, N. Karunanidhi and P. Aruna, J. Pure Appl. Ultrason., **21**, 5 (1999).

(93) F.T. Gucker (Jr.), Chem. Rev., **64**, 111 (1993).

(94) C. Bachem, Z. Electrochem., **41**, 570 (1935).

CHAPTER-2

DENSITY AND REFRACTIVE INDEX

INTRODUCTION

Refractive index is one of the most useful physical parameter to identify an unknown compound. Refractive Index along with density, molecular mass and specific volume is very useful in the evaluation of various thermodynamics properties of chemical materials. It is also useful for the identification of crystalline substance.

There are various other applications of refractive index also, for example, It is used for determining the percentage of sugar in fruits, juices and syrups[1], in ion exchange chromatography of inorganic and organic ionic species[2], for development and test of an integrated micro system for HPLC separation and detection[3]. Various workers used this parameter to determine film thickness[4-8] also.

Literature survey shows that refractive index of various polymer[9-11], complex refractive index[12-16], and optical fibers[17-19], solutions[20-22] and other materials[23] have been determined.

By using refractive index Fukuta et al. have been measured concentration of refrigerant/ refrigeration oil mixture[24]. Bakker et al. determined refractive index of printed and unprinted paper[25]. Strop and Brunger have been reported refractive index-base determination of detergent concentration[26]. Ali et al. studied the refractive index behavior of α-amino acids and their groups[27]. Recently Zysk et al. reported the refractive index of carcinogen-induced rat mammary tumors[28].

Much work has been done in liquid mixtures[29-44], but scantly work has been reported for the solutions, which includes solutions of organic, inorganic and polymeric materials[45-52].

In this chapter the density and refractive index of all the imidazolinone derivatives have been determined in N,N-dimethylformamide (DMF) and dimethylsulphoxide (DMSO) solutions at 308.15K.

EXPERIMENTAL

The solvents DMF and DMSO were of LR grade and are fractionally distilled by the reported method[53]. All the Schiff bases were recrystalized from methanol. For each Schiff base, a series of solutions of different concentrations were prepared in both the solvents. The density and refractive index of solutions are measured by using Pyknometer and Abbe Refrectometer respectively at 308.15 K. The results are given in Tables 2.1 and 2.2.

RESULTS AND DISCUSSION

The density of solution (ρ_{12}) is related to densities of the solvent, solute and their weight fractions g_1 and g_2 according to the equation:

$$\frac{1}{\rho_{12}} = \frac{g_1}{\rho_1} + \frac{g_2}{\rho_2} \qquad \ldots (2.1)$$

where ρ_{12} is the density of solution and ρ_1 and ρ_2 are the densities of solvent and solute respectively. Tables 2.1 and 2.2 show the experimental values of densities and refractive index for all the imidazolinone derivatives in N, N-dimethylformamide (DMF) and dimethylsulfoxide (DMSO) solutions respectively.

The density of these imidazolinone derivatives was determined from the slope of the plot of $1/g_1\rho_{12}$ verses g_2/g_1. Fig. 2.1 shows the plot of $1/g_1\rho_{12}$ verses g_2/g_1 for PAIM-1 in DMF and DMSO. The inverse of slope gives ρ_2. The densities of all the derivatives evaluated from such plots are given in Table 2.3 for both DMF and DMSO. Further, by using the following equation (2.2).

$$\rho = KM/N_A \sum \Delta V_i \qquad \ldots (2.2)$$

where ρ is the density of the compound, K is packing fraction (0.599), M is the molecular weight of the compound, N_A is the Avogadro's number and ΔV_i is the volume increment of the atoms and atomic groups present in the compound.The density of all the studied imidazolinone derivatives have been evaluated and reported in Table 2.3. The calculated volume increment ΔV_i for different atomic groups are given in Table 2.4

Comparison of densities evaluated from graphs and those calculated from eq. (2.2) showed that calculated values are different from those evaluated graphically. Also, for the same compound, density in the two solvents is different. This suggests that solvent plays an important role. In solutions molecular interactions exist which differ in different solvents. This is further confirmed by acoustical parameter which is already discussed in Chapter 1. Usually

intermolecular interactions do not affect the density but due to the presence of different substituted groups in solutes, interaction differs in different solvents which may cause change in volume thereby affecting the density of solute in a particular solvent.

The molar refraction of a pure liquid $(MRD)_1$ can be calculated by the following equation:

$$\left(MRD\right)_1 = \left[\frac{n^2 - 1}{n^2 + 1}\right]\frac{M}{\rho} \qquad \ldots (2.3)$$

where n, M and ρ are refractive index , molecular weight and density of pure liquid respectively.

For solutions, the eq. (2.4) was used to determining molar refraction.

$$\left(MRD\right)_{12} = \left[\frac{n_{12}^2 - 1}{n_{12}^2 + 1}\right]\left[\frac{X_1 M_1 + X_2 M_2}{\rho_{12}}\right] \qquad \ldots (2.4)$$

where n_{12} and ρ_{12} are refractive index and density of solution respectively. X_1 and X_2 are the mole fractions and M_1 and M_2 are the molecular weight of the solvent and solute respectively.

The plots of $(MRD)_{12}$ verses concentration for all the imidazolinone derivatives in DMF and DMSO are given in Fig. 2.2 and 2.3 respectively. It is evident from these Fig. that $(MRD)_{12}$ increase with the increase in concentration. From the values of the molar refraction of solution and pure solvent, molar refraction of solid compounds were determined by following equation:

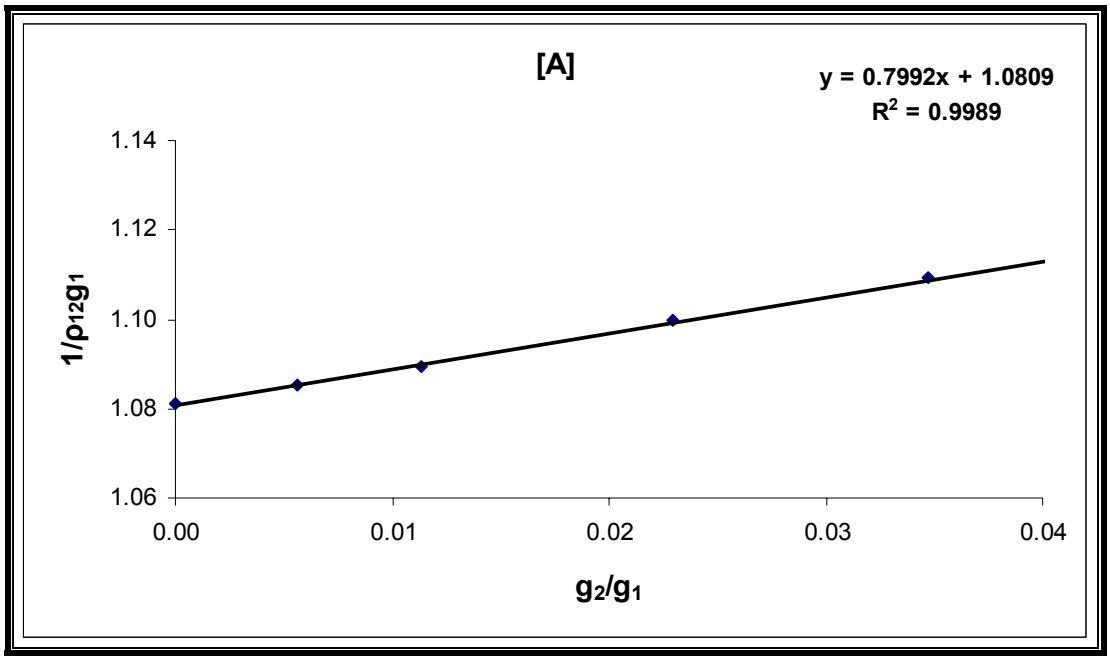
$$\left(MRD\right)_{12} = X_1\left(MRD\right)_1 + X_2\left(MRD\right)_2 \qquad \ldots (2.5)$$

From the density and molar refraction data, the refractive indexes of all the compounds were calculated from eq. (2.3). The molar refraction $(MRD)_2$ and refractive index of all the compounds are reported in Table 2.5.

It is evident from Table 2.5 that both $(MRD)_2$ and refractive index of compounds are different in each solvent. This again proves that in different solvents, intermolecular interactions are different, which affect these parameters.

In some solvents, aggregation or hydrogen bonding takes place whereas in others, breakage of bonds takes place. As refractive index and molar refraction depends not only upon atomic refraction but also upon single, double or triple bonds, these parameters are affected by the type of interactions taking place in solution. However, it is reported that bond refraction is more effective than atomic refraction. Further, bond polarity also causes change in molar refraction. Thus, type of solvent affects the Refractive Index and molar refraction of a solute.

Figure 2.1: The variation of $1/g_1\rho_{12}$ with $g_2/g1$ for PAIM-1 in [A] DMF and [B] DMSO at 308.15 K.



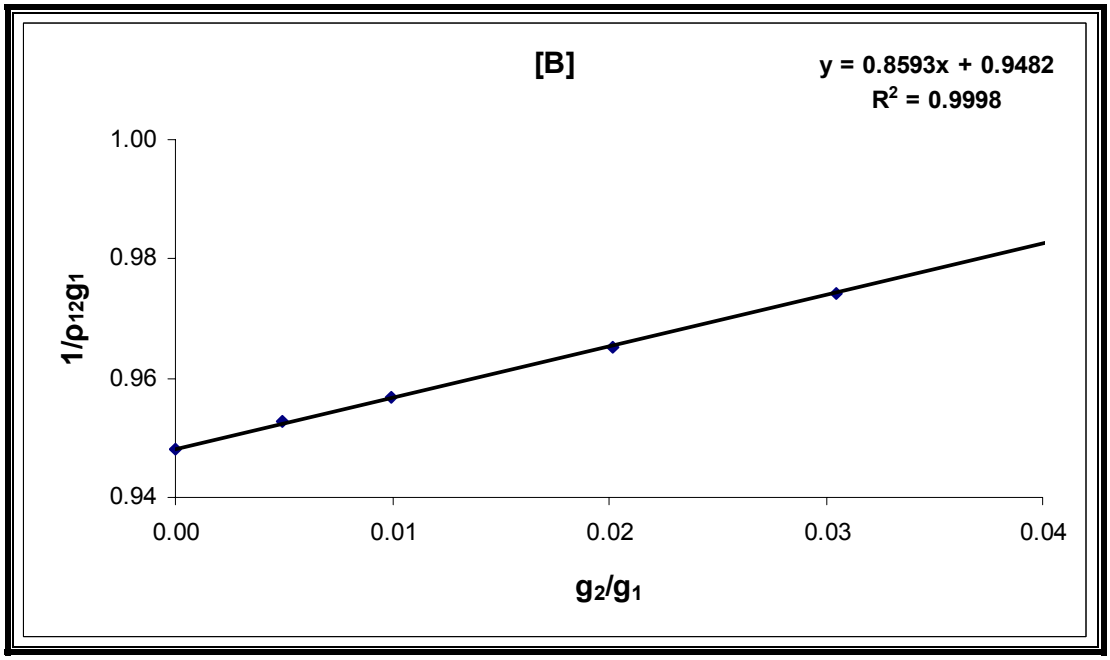
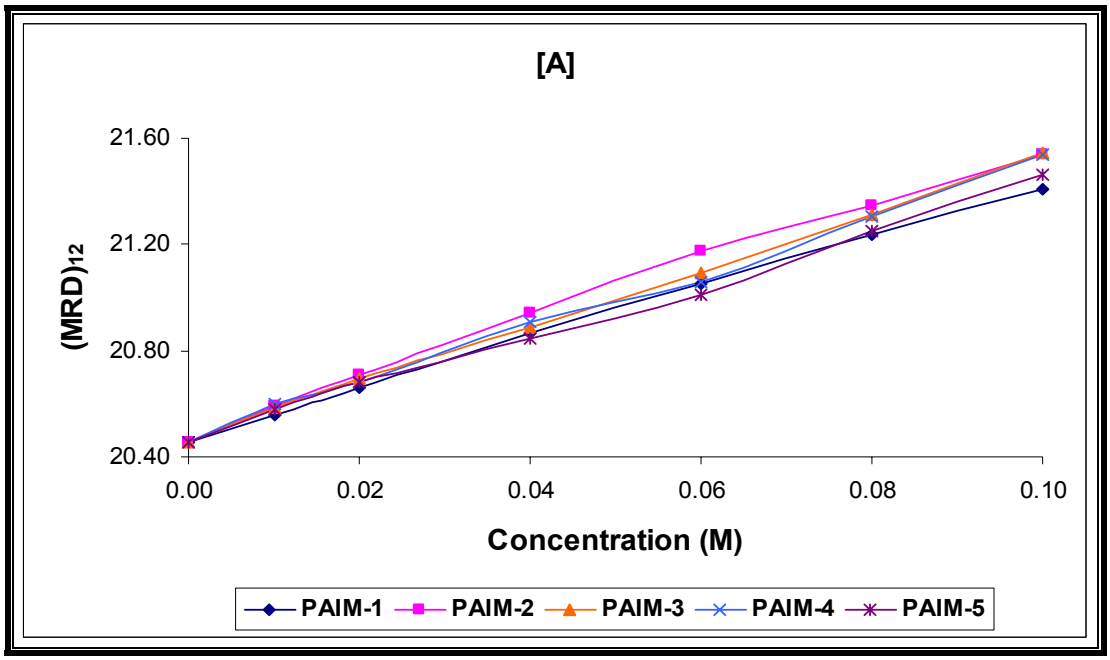


Figure 2.2: The plots of molar refraction $(MRD)_{12}$ against concentration of Imidazolinone derivatives in DMF [A] solutions at 308.15 K.



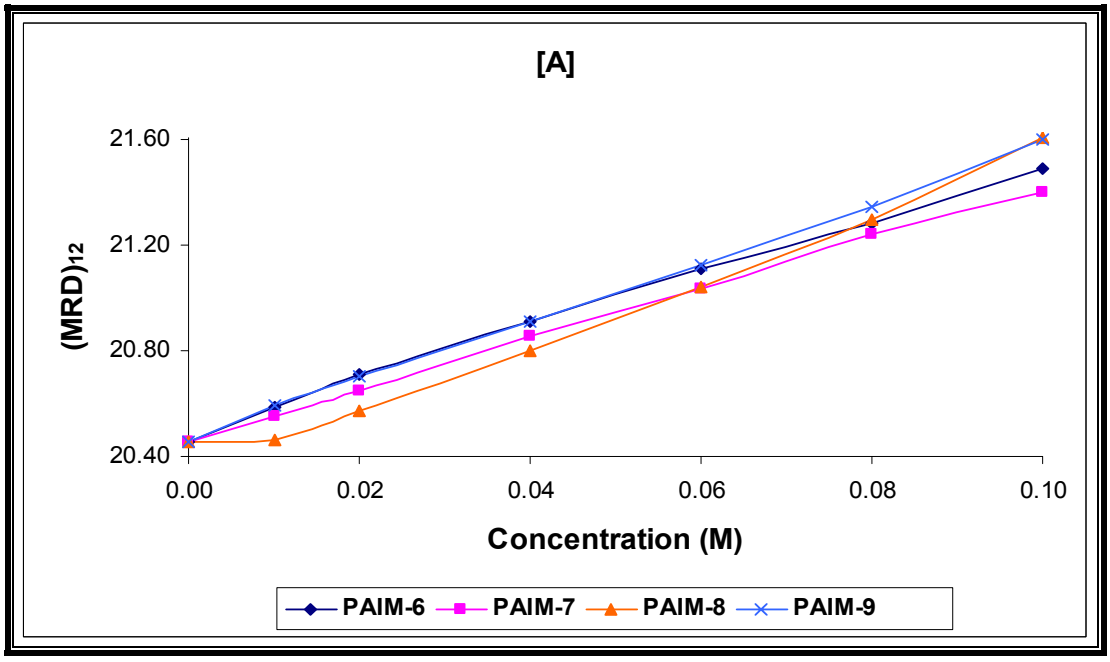
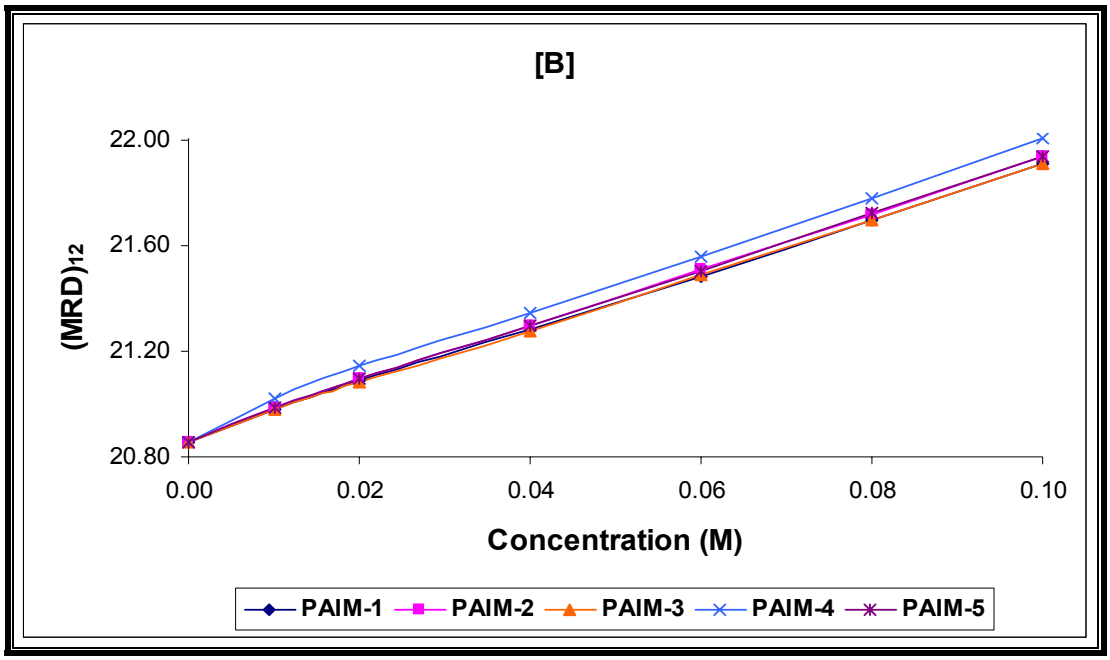


Figure 2.3: The plots of molar refraction $(MRD)_{12}$ against concentration of Imidazolinone derivatives in DMSO [B] solutions at 308.15 K.



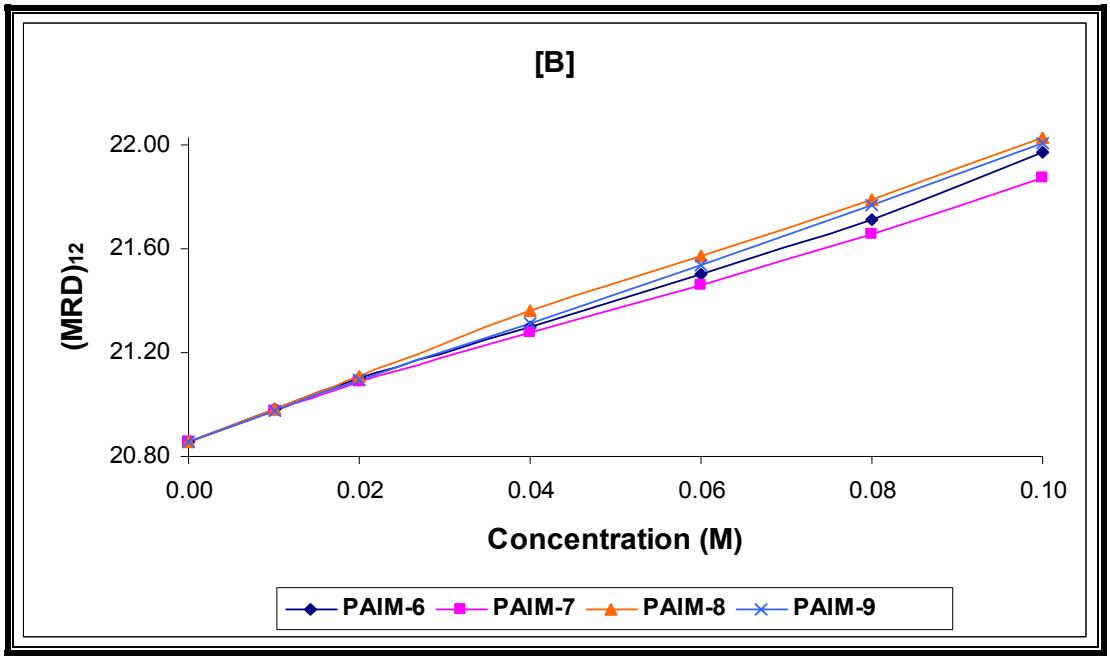


Table 2.1: The density (ρ_{12}) and refractive index (n) of imidazolinone derivatives in dimethylformamide (DMF) at 308.15K.

Conc.(M)	ρ_{12} ($g.cm^{-3}$)	g_1	g_2	n
PAIM-1				
0.00	0.9249	1.0000	0.0000	1.4310
0.01	0.9268	0.9944	0.0056	1.4320
0.02	0.9285	0.9888	0.0112	1.4330
0.04	0.9301	0.9776	0.0224	1.4340
0.06	0.9328	0.9664	0.0336	1.4350
0.08	0.9357	0.9554	0.0446	1.4360
0.10	0.9393	0.9444	0.0556	1.4370
PAIM-2				
0.01	0.9254	0.9942	0.0058	1.4320
0.02	0.9266	0.9884	0.0116	1.4330
0.04	0.9277	0.9768	0.0232	1.4340
0.06	0.9288	0.9652	0.0348	1.4350
0.08	0.9325	0.9538	0.0462	1.4360
0.10	0.9357	0.9424	0.0576	1.4370
PAIM-3				
0.01	0.9254	0.9944	0.0056	1.4320
0.02	0.9270	0.9887	0.0113	1.4330
0.04	0.9292	0.9775	0.0225	1.4340
0.06	0.9312	0.9664	0.0336	1.4350
0.08	0.9327	0.9552	0.0448	1.4360
0.10	0.9338	0.9441	0.0559	1.4370
PAIM-4				
0.01	0.9251	0.9940	0.0060	1.4320
0.02	0.9283	0.9879	0.0121	1.4330
0.04	0.9300	0.9759	0.0241	1.4340
0.06	0.9332	0.9640	0.0360	1.4340
0.08	0.9342	0.9521	0.0479	1.4350
0.10	0.9361	0.9402	0.0598	1.4360
PAIM-5				
0.01	0.9257	0.9943	0.0057	1.4320
0.02	0.9277	0.9886	0.0114	1.4330
0.04	0.9313	0.9774	0.0226	1.4340
0.06	0.9332	0.9661	0.0339	1.4340
0.08	0.9356	0.9550	0.0450	1.4360
0.10	0.9375	0.9438	0.0562	1.4370

Continue…..

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Conc.(M)	ρ_{12} ($g.cm^{-3}$)	g_1	g_2	n
PAIM-6				
0.00	0.9249	1.0000	0.0000	1.4310
0.01	0.9257	0.9941	0.0059	1.4320
0.02	0.9284	0.9883	0.0117	1.4340
0.04	0.9307	0.9767	0.0233	1.4350
0.06	0.9335	0.9651	0.0349	1.4360
0.08	0.9373	0.9537	0.0463	1.4370
0.10	0.9396	0.9422	0.0578	1.4380
PAIM-7				
0.01	0.9267	0.9945	0.0055	1.4320
0.02	0.9287	0.9890	0.0110	1.4330
0.04	0.9300	0.9781	0.0219	1.4340
0.06	0.9328	0.9673	0.0327	1.4350
0.08	0.9346	0.9564	0.0436	1.4360
0.10	0.9382	0.9458	0.0542	1.4370
PAIM-8				
0.01	0.9256	0.9939	0.0061	1.4320
0.02	0.9277	0.9878	0.0122	1.4330
0.04	0.9304	0.9757	0.0243	1.4340
0.06	0.9330	0.9636	0.0364	1.4350
0.08	0.9356	0.9516	0.0484	1.4360
0.10	0.9369	0.9396	0.0604	1.4380
PAIM-9				
0.01	0.9252	0.9938	0.0062	1.4320
0.02	0.9274	0.9876	0.0124	1.4330
0.04	0.9287	0.9752	0.0248	1.4340
0.06	0.9321	0.9629	0.0371	1.4350
0.08	0.9351	0.9507	0.0493	1.4360
0.10	0.9364	0.9384	0.0616	1.4370

Table 2.2: The density (ρ_{12}) and refractive index (n) of imidazolinone derivatives in dimethylsulphoxide (DMSO) at 308.15K.

Conc.(M)	ρ_{12} ($g.cm^{-3}$)	g_1	g_2	n
PAIM-1				
0.00	1.0546	1.0000	0.0000	1.4750
0.01	1.0548	0.9951	0.0049	1.4760
0.02	1.0556	0.9901	0.0099	1.4770
0.04	1.0569	0.9802	0.0198	1.4780
0.06	1.0578	0.9704	0.0296	1.4790
0.08	1.0585	0.9606	0.0394	1.4800
0.10	1.0593	0.9507	0.0493	1.4810
PAIM-2				
0.01	1.0548	0.9949	0.0051	1.4760
0.02	1.0556	0.9898	0.0102	1.4770
0.04	1.0568	0.9796	0.0204	1.4780
0.06	1.0576	0.9694	0.0306	1.4790
0.08	1.0587	0.9593	0.0407	1.4800
0.10	1.0596	0.9492	0.0508	1.4810
PAIM-3				
0.01	1.0547	0.9951	0.0049	1.4760
0.02	1.0560	0.9901	0.0099	1.4770
0.04	1.0571	0.9803	0.0197	1.4780
0.06	1.0577	0.9704	0.0296	1.4790
0.08	1.0585	0.9606	0.0394	1.4800
0.10	1.0592	0.9507	0.0493	1.4810
PAIM-4				
0.01	1.0550	0.9947	0.0053	1.4770
0.02	1.0557	0.9894	0.0106	1.4780
0.04	1.0572	0.9788	0.0212	1.4790
0.06	1.0584	0.9683	0.0317	1.4800
0.08	1.0593	0.9577	0.0423	1.4810
0.10	1.0603	0.9472	0.0528	1.4820
PAIM-5				
0.01	1.0547	0.9950	0.0050	1.4760
0.02	1.0554	0.9900	0.0100	1.4770
0.04	1.0564	0.9801	0.0199	1.4780
0.06	1.0572	0.9701	0.0299	1.4790
0.08	1.0576	0.9601	0.0399	1.4800
0.10	1.0585	0.9502	0.0498	1.4810

Continue…..

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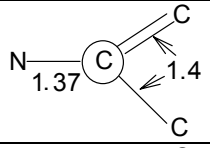
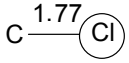
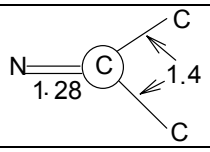
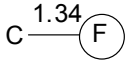
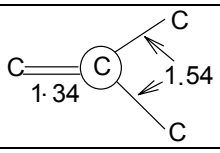
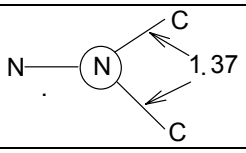
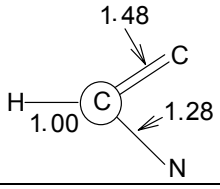
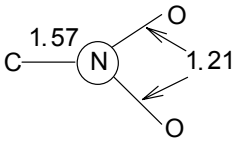
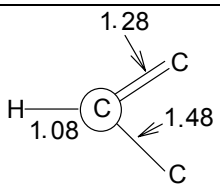
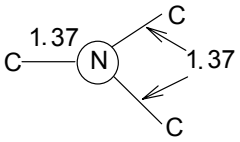
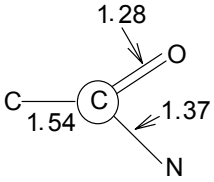
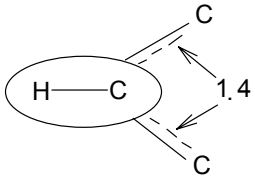
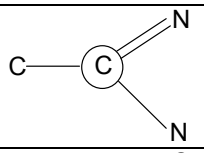
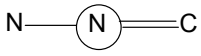
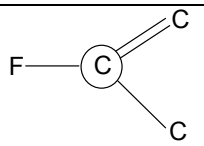
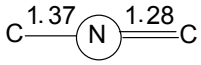
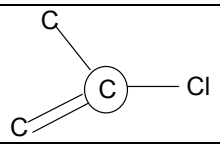
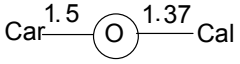
Conc.(M)	ρ_{12} ($g.cm^{-3}$)	g_1	g_2	n
PAIM-6				
0.00	1.0546	1.0000	0.0000	1.4750
0.01	1.0548	0.9949	0.0051	1.4760
0.02	1.0556	0.9897	0.0103	1.4770
0.04	1.0569	0.9795	0.0205	1.4780
0.06	1.0582	0.9692	0.0308	1.4790
0.08	1.0594	0.9590	0.0410	1.4800
0.10	1.0601	0.9488	0.0512	1.4820
PAIM-7				
0.01	1.0549	0.9952	0.0048	1.4760
0.02	1.0556	0.9904	0.0096	1.4770
0.04	1.0568	0.9807	0.0193	1.4780
0.06	1.0581	0.9711	0.0289	1.4790
0.08	1.0592	0.9616	0.0384	1.4800
0.10	1.0596	0.9520	0.0480	1.4810
PAIM-8				
0.01	1.0551	0.9946	0.0054	1.4760
0.02	1.0556	0.9893	0.0107	1.4770
0.04	1.0567	0.9786	0.0214	1.4790
0.06	1.0581	0.9679	0.0321	1.4800
0.08	1.0593	0.9573	0.0427	1.4810
0.10	1.0599	0.9466	0.0534	1.4820
PAIM-9				
0.01	1.0555	0.9945	0.0055	1.4760
0.02	1.0566	0.9891	0.0109	1.4770
0.04	1.0576	0.9782	0.0218	1.4780
0.06	1.0587	0.9673	0.0327	1.4790
0.08	1.0596	0.9565	0.0435	1.4800
0.10	1.0603	0.9456	0.0544	1.4810

Table 2.3: Experimental and calculated densities of imidazolinone derivatives in DMF and DMSO Solutions at 308.15 K.

Compounds	Density calculated from Fig. 1.1 ($g.cm^{-3}$)		Density ($g.cm^{-3}$) calculated from Eq^{n}. 2
	DMF	DMSO	
PAIM-1	1.2513	1.1637	1.2018
PAIM-2	1.1444	1.1660	1.2170
PAIM-3	1.1275	1.1596	1.2018
PAIM-4	1.1673	1.1786	1.1849
PAIM-5	1.2285	1.1410	1.2472
PAIM-6	1.2794	1.1827	1.2578
PAIM-7	1.2226	1.1801	1.1952
PAIM-8	1.1174	1.1700	1.2559
PAIM-9	1.1853	1.1680	1.2667

Table 2.4 Volume increments of some atoms and groups of atoms

Atoms or Atomic group	Volume Increments $(A^o)^3$	Atoms or Atomic group	Volume Increments $(A^o)^3$
	10.2		19.35
	7.84		9.2
	9.0		2.89
	3.61		7.46
	11.36		0.9
	14.10		14.7
	10.47		5.093
	11.40		5.62
	10.39		2.67

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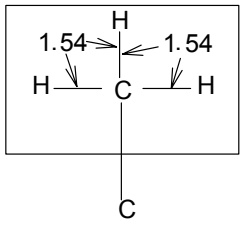
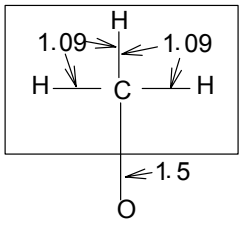
Atoms or Atomic group	Volume Increments $(A^o)^3$	Atoms or Atomic group	Volume Increments $(A^o)^3$
	23.5		26.3

Table 2.5: Molar refraction $(MRD)_2$ and refractive index (n) of Imidazolinone derivatives in DMF and DMSO at 308.15 K.

Compounds	Solvents			
	DMF		DMSO	
	$(MRD)_2$	n	$(MRD)_2$	n
PAIM-1	156	1.6660	166.5	1.6598
PAIM-2	183.75	1.7042	172	1.6626
PAIM-3	151.5	1.5643	164	1.6443
PAIM-4	164.5	1.5970	184	1.6960
PAIM-5	142	1.5728	169	1.6487
PAIM-6	181	1.7914	175.5	1.6862
PAIM-7	145.5	1.6122	167	1.6972
PAIM-8	166.25	1.5728	191.5	1.7256
PAIM-9	184.5	1.6774	183.5	1.6603

REFERENCES

(1) C.A. Zuritz, E. Muñoz Puntes, H.H. Mathey, E.H. Pérez, A. Gascón, L.A. Rubio, C.A. Carullo, R.E. Chernikoff and M.S. Cabeza; J. Food Eng., (2005)

(2) F. A. Buytenhuys; J. Chromatography, **218**, 57 (1981).

(3) D. Brennan, P. O'Brien, J. O'Brien, N. Freeman and M. Swann; Sensors and Actuators B: Chemical, **103**, 184 (2004).

(4) J. Diao and D. W. Hess; J. Phy. Chem. B., **106**, 12819 (2005).

(5) H. M. Shabana; Polymer Testing, **23**, 695 (2004).

(6) O. Nordman, N. Nordman, and N. Peyghambarian; J. Appl. Phy., **84**, 6055 (1998).

(7) S. Nair and M. Tsapatsis; Microporous and Mesoporous Materials, **58**, 81 (2003).

(8) M. Vaillancourt, D. Khatamian and M. A. Maguire; J. Nuclear Mater., **227**, 58 (1995).

(9) V. Švorčík, M. Prajer, I. Huttel, V. Rybka, V. Hnatowicz and J. Plešek; Mate. Lett., **59**, 280 (2005).

(10) A. Bello and G. M. Guzman; Eur. Poly. J., **2**, 85 (1966).

(11) D. Bosc, P. Grosso, I. Hardy, I. Assaïd, T. Batté, S. Haesaert and B. Vinouze; Optics Communications, **235**,281 (2004).

(12) J. Diao and D. W. Hess; J. Phy. Chem. B., **106**, 12800 (2005).

(13) M. Friebel, M. Meinke; J. Biomed. Opt., **10**, 64019 (2005).

(14) X. Ma , J. Q. Lu, R. S. Brock, K. M. Jacobs, P. Yang, X. H. Hu; Phys. Med. Biol., **48**, 4165(2003).

(15) E. Nichelatti; J. Opt. A: Pure. Appl. Opt., **4**, 400 (2002).

(16) J. Räty, E. Keränen and K. E. Peiponen; Meas. Sci. Technol., **9**, 95 (1998).

(17) I. Martinček, D. Káčik, I. Turek and P. Peterka; Optik – Int. J. for Light and Electron Optics, **115**, 86 (2004).

(18) I. Abe, R. E. de Góes, J. L. Fabris, H. J. Kalinowski, M. Müller, M. C. Fugihara, R. Falate, B. W. Diesel, R. C. Kamikawachi and C. L. Barbosa; Optics and Lasers in Engineering, **39**, 537 (2003).

(19) R. Michael, J. Marle, G. F. J. M. Vrensen and T. J. T. P. van den Berg; Experimental Eye Research, **77**, 93 (2003).

(20) S. D. Taylor; Fuel and Energy Abstracts, **43**,241 (2002).

(21) S. D. Taylor, J. Czarnecki and J. Masliyah; Fuel, **80**, 2013 (2001).

(22) T. Tumolo, L. Angnes and M.S. Baptista; Analytical Biochemistry, **333**, 273 (2004).

(23) A. Belendez , T. Belendez , C. Neipp , I. Pascual; Appl Opt., **41**, 6802 (2002).

(24) M. Fukuta, T. Yanagisawa , S. Miyamura and Y. Ogi; Int. J. Refrigeration, **27**, 346 (2004).

(25) J. W. P. Bakker, G. Bryntseb and H. Arwin; Thin Solid Films, **455**, 361 (2004).

(26) P Strop , AT Brunger; Protein Sci., **14**, 2207, (2005).

(27) A. Ali, S. Hyder, S. Sabir, D. Chand and A. K. Nain; J. Chem. Thermo., **38**, 136 (2006).

(28) A. M Zysk, E. J Chaney and S. A Boppart; Phys. Med. Biol., **51**, 2165 (2006).

(29) W. J. Wallace, C. S. Shephered and C. Underwood; J. Chem. Eng. Data, **13**, 11 (1968).

(30) J. Ortega and J.S. Matos; Mater. Chem. Phys., **15**, 415 (1986).

(31) J. D. Pandey, P. Jain and V. Vyas; Can. J. Chem., **72**, 63 (1994).

(32) E. Mascato, L. Mosteiro, M. M. Piñeiro, J. García, T. P. Iglesias and J. L. Legido; J. Chem. Thermodyn., **33**, 1081 (2001).

(33) A. Rodríguez, J. Canosa and J. Tojo; J. Chem. Thermodyn., **33**, 1383 (2001).

(34) A. Nagy, W. W. Szymanski, A. Czitrovszky and P. Jani; J. Aerosol Sci., **32**, 83 (2001).

(35) S. Chen, Q. Lei and W. Fang; J. Chem. Eng. Data, **47**,811 (2002).

(36) J. M. Resa, C. González, S. Ortiz de Landaluce and J. Lanz; J. Chem. Thermodyn., **34**, 995 (2002) .

(37) M. D. Pérez, S. Freire, J. J. de Llano, E. Rilo, L. Segade, O. Cabeza and E. Jiménez; Fluid Phase Equil., **212**, 331 (2003)

(38) J. M. Resa, C. González , M. Juez and S. O. de Landaluce; Fluid Phase Equil., **217**,175 (2004)

(39) J. M. Resa et al.; Fluid Phase Equil., **217**,175 (2004)

(40) S. L. Oswal, R.L. Gardas and R.P. Phalak; J. Mol. Liq; **116**,109 (2005).

(41) S. L. Oswal, R.L. Gardas and R.P. Phalak; Thermochim. Acta, **426**, 199 (2005).

(42) M. E. Taboada, H. R. Galleguillos, T. A. Graber and J. Á. Benedí; Fluid Phase Equilibria, **235**, 104 (2005).

(43) S. Minc; J. Electroanalytical Chem., **140**, 121 (1982).

(44) Z. Atik; J. Chem. Thermo., **38**, 201 (2006).

(45) J.Olivares, M.A. Díaz-García, and J.M. Cabrera; Opt. Comm., **92**, 40 (1992).

(46) D. Wright, M.A. Díaz-García, J.D. Casperson, M. De Clue, W.E. Moerner and R.J. Twieg; Appl. Phys. Lett., **73**, 1490 (1998).

(47) M.A. Díaz-García, D. Wright, J.D. Casperson, B. Smith, E. Glazer, W.E. Moerner, L.I. Sukhomlinova and R.J. Twieg; Chem. Mater., **11**,1764 (1999).

(48) E. K. Miller, M. McGehee, M.A. Díaz-García, V. Srikant, A.J. Heeger; Synth. Met., **102**, 1091

(1999).

(49) W.E. Moerner, M.A. Díaz-García, D. Wright, B.R. Smith, J. Casperson, M. Bratcher, M. DeClue, S. Siegel and R. Twieg; Polymer Preprints, **39**, 980 (1998).

(50) L. Mosteiro, E. Mascato, B. E. de Cominges, T. P. Iglesias, and J. L. Legido; J. Chem. Thermodyn., **33**, 787 (2001).

(51) M.E.Taboada, D. M.Veateliz, H R.Gallequillos and T. A.Graber; J. Chem. Eng. Data., **47**, 5 (2002).

(52) R. Mehra; Ind. Acad. Sci., **115**,147 (2003).

(53) J. A. Riddick, W. B. Bunger and T. Sakano, Organic Solvents-Physical Properties and methods of purification, Fourth Edition., Techniques of Chemistry, **II**, A Wiley-Interscience Publication, John Wiley, New York (1986).

CHAPTER-3

CONDUCTANCE

INTRODUCTION

Electrical conductance is a property of ionic solution. The conductance of electrolytic solutions depends on the concentration of the ions and also on the nature of the ions present (through their charges and mobilities. This property is useful for physico-chemical analysis. By conductometry, one can determine the dissociation constants, solubilities and rate of reactions.

Conductometry method is also useful to determine the purity of water, amount of nitrogen in biological materials etc[1], micro amounts of carbon in aqueous phase[2] and for determining of graphite in propellants[3]. Various workers used this technique to determine microgram quantities of ammonia[4], liquid film thickness in two phase flow[5], thermodynamic successive ionization constants of chloranilic acid[6], ascorbic acid in vitamin C tablet[7], carbon in uranium carbide and its solution in nitric acid[8] etc. It is also used to study enzymatic degradation of microbial biofilm[9] and streptococcus thermophilus (lactic bacteria)[10], the monomer reactivity ratios for copolymerization of itaconic acid and acrylamide[11], dye-surfactant ion pair formation in aqueous solution[12], ionic conductance of polymeric electrolytes and of polymeric composite solid electrolyres[13], the electrolyte and osmotic permeability coefficients[14], biogenic amines(cadaverine, putrescine, agmatine, histamine, tryptamine and tyramine)[15] etc. An indirect conductometric screening method has been reported for the detection of antibiotic residues in bovine kidneys[16]. Sawai et al.[17] have used this technique to investigate the growth of fungi.

Literature survey shows that conductance of various many inorganic and organic compounds have been measured in aqueous[18-31] conductance of and non-aqueous solvents[32-35].

Thus, in present work, conductance of imidazolinone derivatives are measured in N,N-dimethylformamide (DMF) and dimethylsulfoxide (DMSO) at 308.15 K. The selection of these two solvents is due to their dipolar aprotic characteristic, which avoid any proton interference with the conductivity of complex systems[36].

EXPERIMENTAL

All the solvents used were distilled prior to use. The solutions of different concentrations were prepared for each Schiff base in DMF and DMSO and the conductance of each solution was measured by using Systronics Conductivity Meter (Model No. 306) having cell constant 0.85 cm^{-1} at 308.15 K. The measured conductance was corrected by subtracting the conductance of pure solvent.

RESULTS AND DISCUSSION

The measured conductance (k) of each solution after correction was used to determine the specific conductance (κ), which is then used for the calculation of equivalent conductance (λ_c).

The equations used for calculating specific conductance (κ) and equivalent conductance (λ_c) are:

$$k = \kappa\theta \qquad \text{..... (3.1)}$$

$$\lambda_c = 1000\frac{\kappa}{C} \qquad \text{..... (3.2)}$$

where θ is the cell constant (= 0.85) and c is the concentration (g.equi./lit.) of solution.

These equivalent conductance values of all the imidazolinone derivatives in DMF and DMSO at 308.15K are reported in Tables 3.1 and 3.2 along with measured conductance (k). In DMSO, the relatively low conductivities are due to greater electro relaxation effect owing to the higher permittivity of DMSO, which contributes interionic repulsions to a larger extent[37]. It is observed that for all the systems studied, conductance increases with concentration (as also shown in Fig. 3.1 and 3.2).

The equivalent conductance (λ_c) is plotted against √C for all imidazolinone derivatives and is shown in Fig. 3.3 and 3.4. It is obvious from figures that all derivatives behave as weak electrolytes in DMF. For all the imidazolinone derivatives, the equivalent conductance increases in DMF uninterruptedly (except for PAIM-1) with decreasing concentration.

The order of λ_c in DMF is: PAIM-8 > PAIM-6 > PAIM-3 > PAIM-1 > PAIM-7 > PAIM-9 > PAIM-4 > PAIM-2 > PAIM-5. In Case of PAIM-1, as concentration decreases, λ_c increases and at 0.004M, it suddenly drops but again increases with further increases in concentration.

In DMSO, at lower concentration, λ_c is almost constant for PAIM-1, PAIM-5, PAIM-6 and PAIM-7. Then, it decreases with increasing concentration. For PAIM-2, PAIM-3 and PAIM-8, it decreases continuously (except at 0.001M for PAIM-2 and PAIM-3) with increasing concentration. However, for PAIM-4 and PAIM-9, the nature of plot is interesting. The curves increase with decreasing concentration but after reaching to a certain maximum value, it bends downwards

at very low concentration. Such behavior was also reported by Singh et al. while studying conductance of polyions[38]. It is reported that such decrease with increasing concentration is due to an increased screening of charges through counterion associations. The intramolecular coulombic interactions may also be affecting the conductance of these compounds in DMSO[39].

For weak electrolytes, it is difficult to determine λ_0. However, in the studied solutions of compounds, λ_0 values are evaluated approximately by extrapolation method. These values are compared with those determined by an alternate procedure using the following equation.

$$k = k_0 + \lambda_0 c + c\phi_{(c)} \qquad \text{..... (3.3)}$$

where k and k_0 are the electrolytic conductivity of the solutions and solvent respectively. c is the equivalent concentration and the function $\Phi_{(c)}$ denotes the effect of interionic interactions. The limiting conductivity can be determined accurately from the slope, dk/dc of plot of k verses c, provided other derivatives (dk_0/dc) and $d[c\Phi_{(c)}]/dc$ in differential form of equation (3.3) are neglected as compared to λ_0, which can be determined from differential form of equation (3.3) is

$$\frac{dk}{dc} = \frac{dk_0}{dc} + \lambda_0 + \frac{d\left[c\phi_{(c)}\right]}{dc} \qquad \text{..... (3.4)}$$

These λ_0 values are reported in Table 3.3 along with those determined by extrapolation.

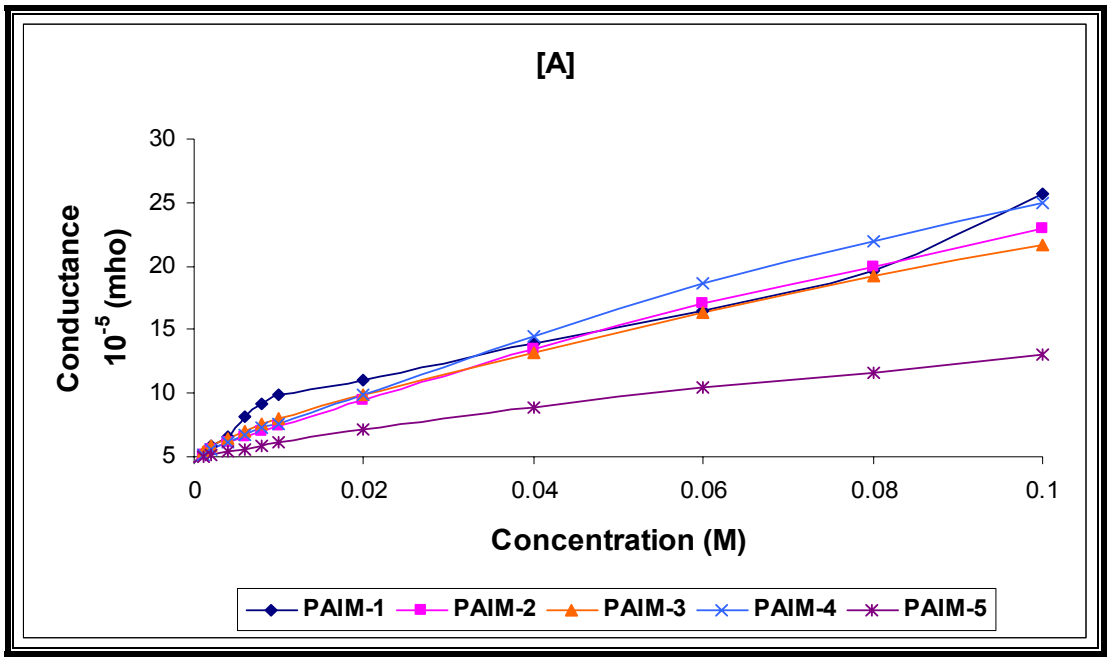
From Table 3.3, it is observed that in case of DMF, the calculated values are much different than those observed from extrapolation.

The deviation between these λ_0 values suggest the presence of interionic interactions in DMF, which should not be ignored. For PAIM-3 and PAIM-8, λ_0 values could not be evaluated due to very weak nature of compounds.

However, in DMSO, the calculated values of λ_0 from equation (3.3) are in good agreement except for PAIM-7 and PAIM-8. For PAIM-4 and PAIM-9, it could not be compared due to bending nature of λ_c vs $\sqrt{C}$ plot.

Thus, for the studied compounds, the above used method is not applicable at all in DMF solution. However, for some compounds in DMSO, it can be considered.

Figure 3.1: The variation of Conductance (κ) with concentration for imidazolinone derivatives in [A] DMF at 308.15 K.



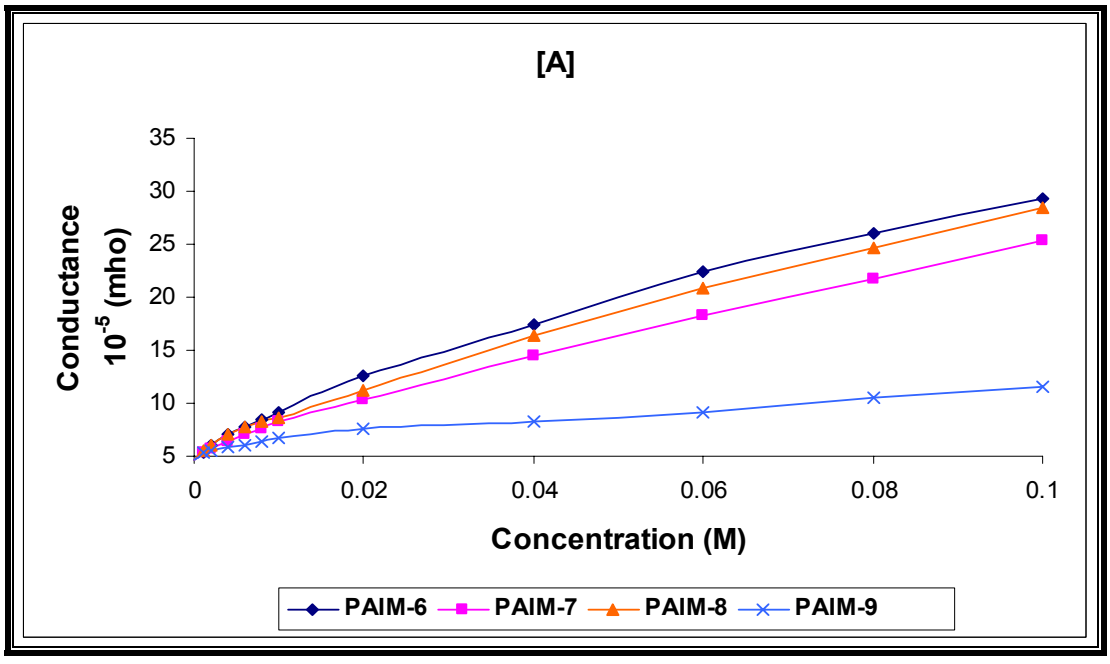
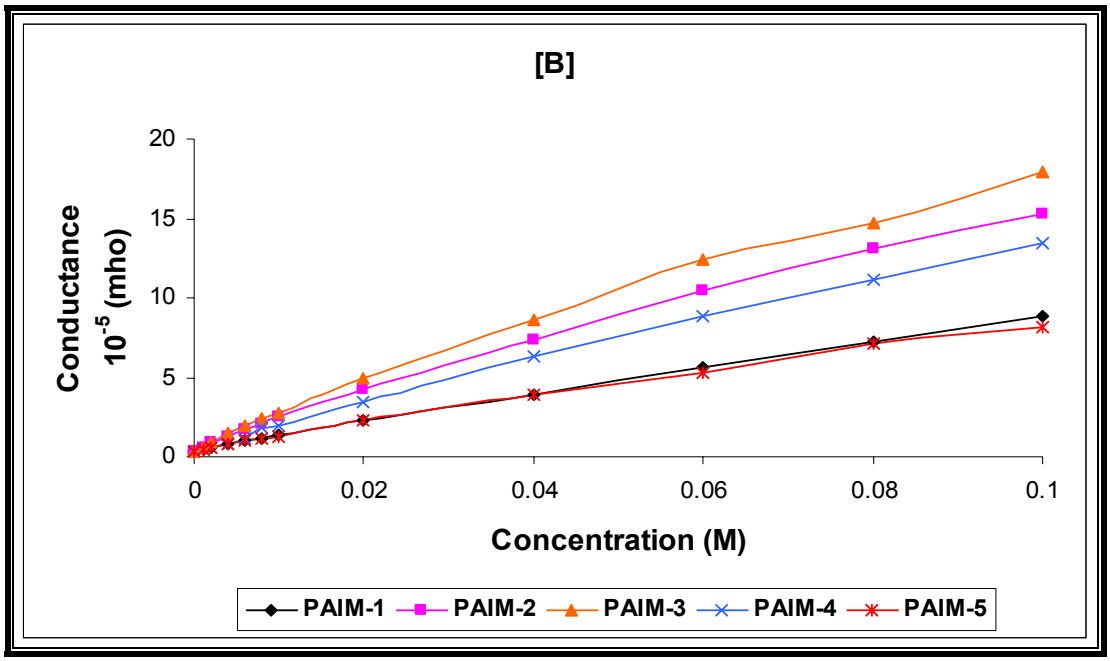


Figure 3.2: The variation of Conductance (κ) with concentration for imidazolinone derivatives in [B] DMSO at 308.15 K.



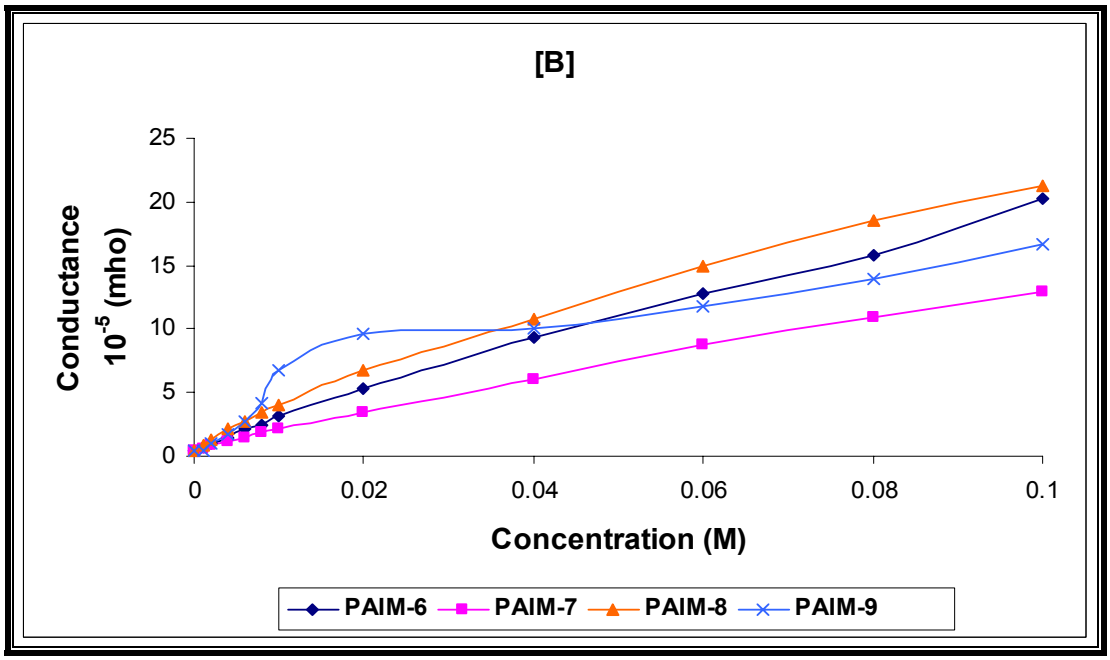
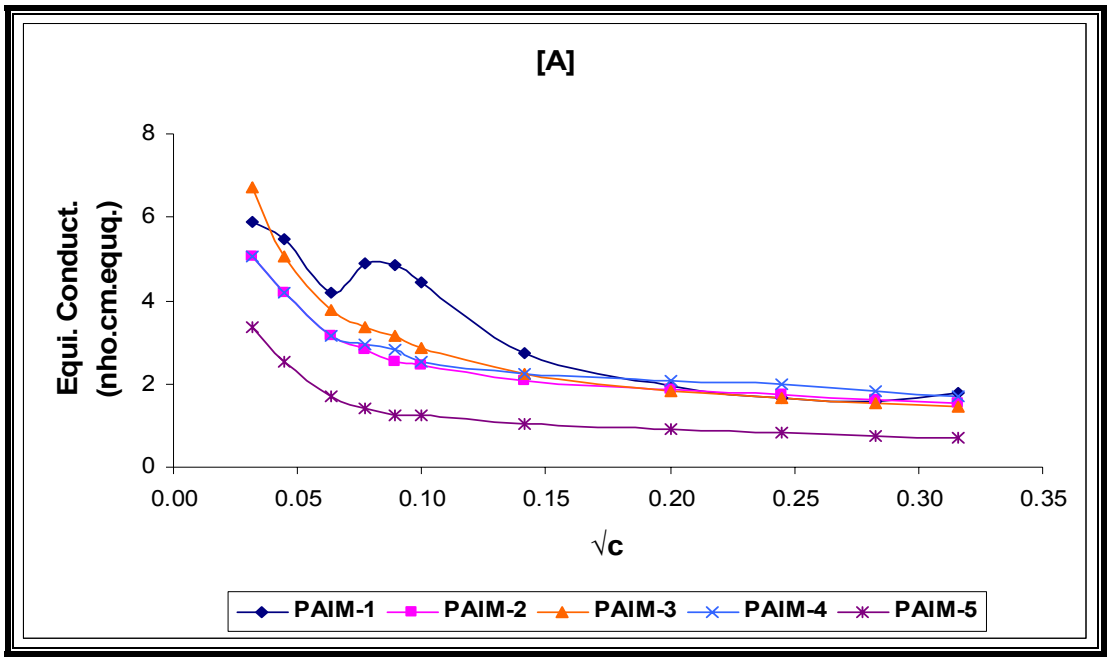


Figure 3.3: **The variation of equivalent conductance (λ_C) with √C for imidazolinone derivatives in [A] DMF at 308.15 K.**



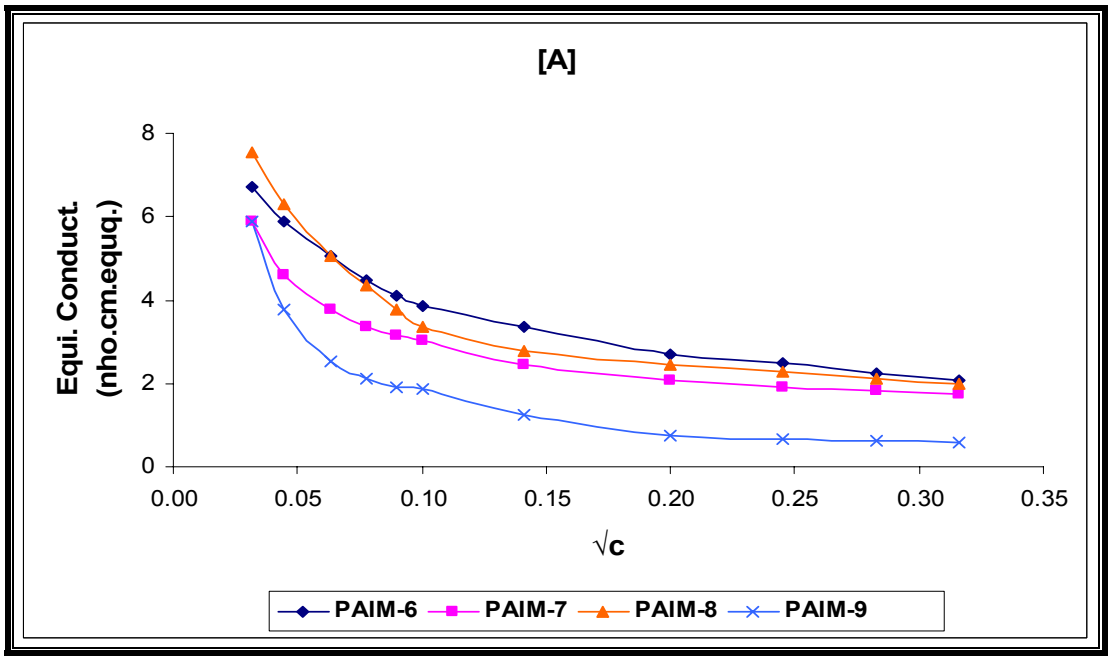
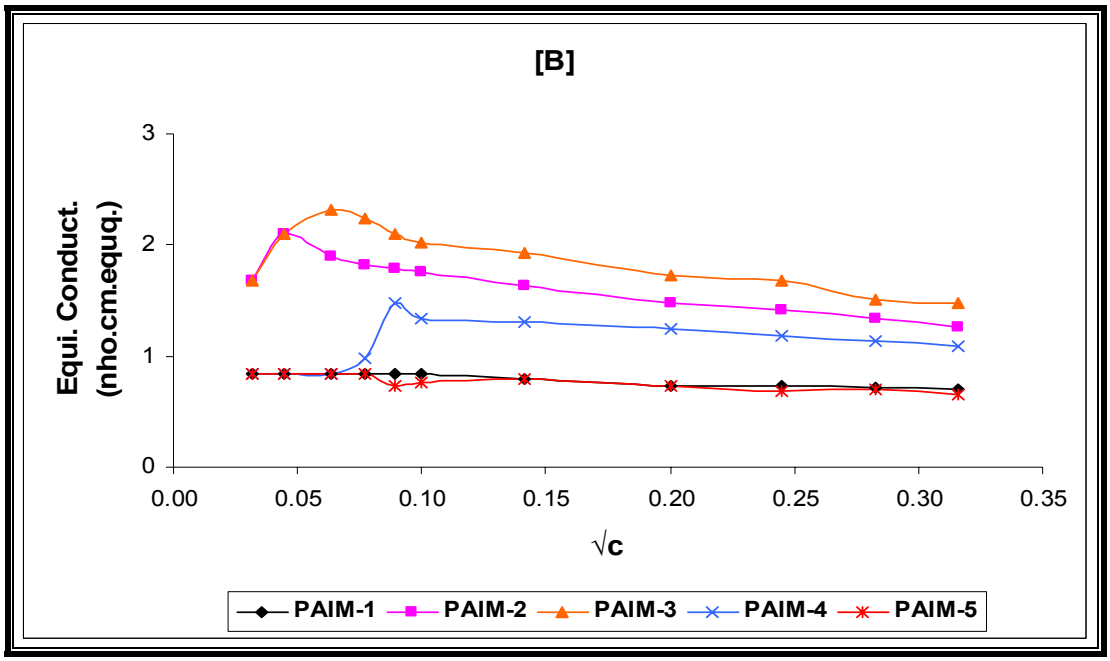


Figure 3.4: **The variation of equivalent conductance (λ_C) with $\sqrt{C}$ for imidazolinone derivatives in [A] DMSO at 308.15 K.**



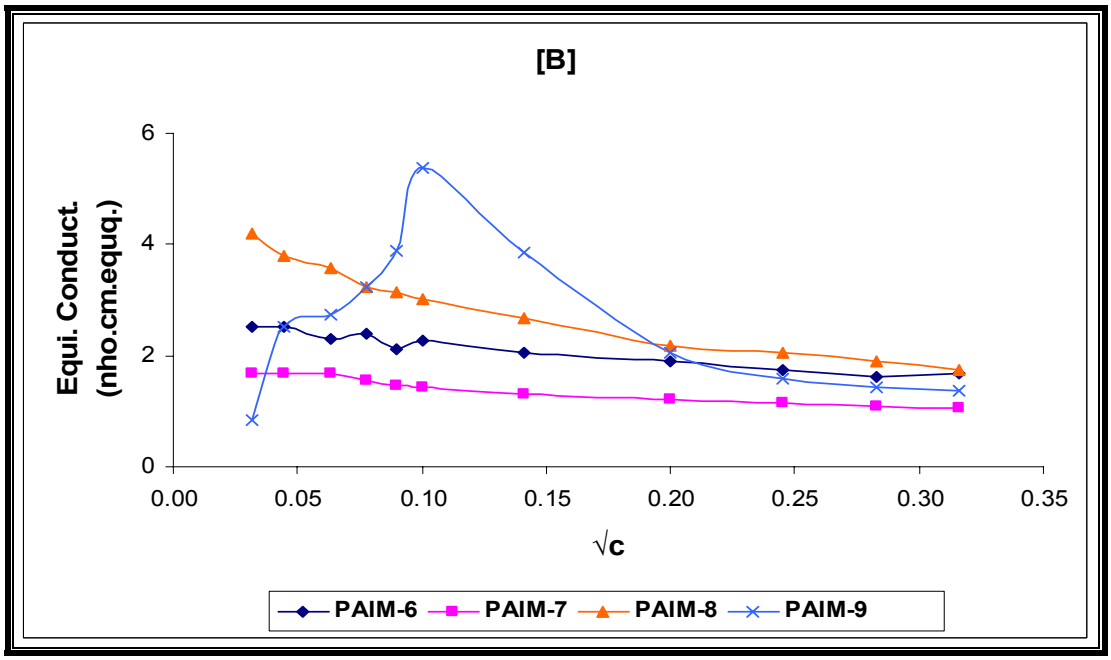


Table 3.1: The Conductance (C) and equivalent conductance (λ_C) of imidazolinone derivatives in DMF at 308.15 K.

Conc. c (g/lit)	$C.10^5$ $(\Omega)^{-1}$	λ_C (cm^2/Ω.equiv.)	$C.10^5$ $(\Omega)^{-1}$	λ_C (cm^2/Ω.equiv.)	$C.10^5$ $(\Omega)^{-1}$	λ_C (cm^2/Ω.equiv.)
	PAIM-1		**PAIM-2**		**PAIM-3**	
0.000	4.6		4.6		4.6	
0.001	5.3	5.8800	5.2	5.0400	5.4	6.7200
0.002	5.9	5.4600	5.6	4.2000	5.8	5.0400
0.004	6.6	4.2000	6.1	3.1500	6.4	3.7800
0.006	8.1	4.9000	6.6	2.8000	7.0	3.3600
0.008	9.2	4.8300	7.0	2.5200	7.6	3.1500
0.010	9.9	4.4520	7.5	2.4360	8.0	2.8560
0.020	11.1	2.7300	9.5	2.0580	9.9	2.2260
0.040	13.9	1.9530	13.5	1.8690	13.2	1.8060
0.060	16.5	1.6660	17.0	1.7360	16.3	1.6380
0.080	19.7	1.5855	20.0	1.6170	19.2	1.5330
0.100	25.7	1.7724	23.0	1.5456	21.7	1.4364
	PAIM-4		**PAIM-5**		**PAIM-6**	
0.001	5.2	5.0400	5.0	3.3600	5.4	6.7200
0.002	5.6	4.2000	5.2	2.5200	6.0	5.8800
0.004	6.1	3.1500	5.4	1.6800	7.0	5.0400
0.006	6.7	2.9400	5.6	1.4000	7.8	4.4800
0.008	7.3	2.8350	5.8	1.2600	8.5	4.0950
0.010	7.6	2.5200	6.1	1.2600	9.2	3.8640
0.020	9.9	2.2260	7.1	1.0500	12.6	3.3600
0.040	14.5	2.0790	8.9	0.9030	17.5	2.7090
0.060	18.7	1.9740	10.4	0.8120	22.5	2.5060
0.080	21.9	1.8165	11.6	0.7350	26.1	2.2575
0.100	25.0	1.7136	13.1	0.7140	29.3	2.0748
	PAIM-7		**PAIM-8**		**PAIM-9**	
0.001	5.3	5.8800	5.5	7.5600	5.3	5.8800
0.002	5.7	4.6200	6.1	6.3000	5.5	3.7800
0.004	6.4	3.7800	7.0	5.0400	5.8	2.5200
0.006	7.0	3.3600	7.7	4.3400	6.1	2.1000
0.008	7.6	3.1500	8.2	3.7800	6.4	1.8900
0.010	8.2	3.0240	8.6	3.3600	6.8	1.8480
0.020	10.4	2.4360	11.2	2.7720	7.6	1.2600
0.040	14.5	2.0790	16.3	2.4570	8.2	0.7560
0.060	18.2	1.9040	20.8	2.2680	9.2	0.6440
0.080	21.8	1.8060	24.7	2.1105	10.5	0.6195
0.100	25.4	1.7472	28.4	1.9992	11.6	0.5880

Table 3.2: The Conductance (C) and equivalent conductance (λ_C) of imidazolinone derivatives in DMSO at 308.15 K.

Conc. c (g/lit)	$C.10^5$ $(\Omega)^{-1}$	λ_C (cm^2/Ω.equiv.)	$C.10^5$ $(\Omega)^{-1}$	λ_C (cm^2/Ω.equiv.)	$C.10^5$ $(\Omega)^{-1}$	λ_C (cm^2/Ω.equiv.)
	PAIM-1		**PAIM-2**		**PAIM-3**	
0.000	0.4		0.4		0.4	
0.001	0.5	0.8400	0.6	1.6800	0.6	1.6800
0.002	0.6	0.8400	0.9	2.1000	0.9	2.1000
0.004	0.8	0.8400	1.3	1.8900	1.5	2.3100
0.006	1.0	0.8400	1.7	1.8200	2.0	2.2400
0.008	1.2	0.8400	2.1	1.7850	2.4	2.1000
0.010	1.4	0.8400	2.5	1.7640	2.8	2.0160
0.020	2.3	0.7980	4.3	1.6380	5.0	1.9320
0.040	3.9	0.7350	7.4	1.4700	8.6	1.7220
0.060	5.6	0.7280	10.5	1.4140	12.4	1.6800
0.080	7.2	0.7140	13.1	1.3335	14.7	1.5015
0.100	8.8	0.7056	15.3	1.2516	17.9	1.4700
	PAIM-4		**PAIM-5**		**PAIM-6**	
0.001	0.5	0.8400	0.5	0.8400	0.7	2.5200
0.002	0.6	0.8400	0.6	0.8400	1.0	2.5200
0.004	0.8	0.8400	0.8	0.8400	1.5	2.3100
0.006	1.1	0.9800	1.0	0.8400	2.1	2.3800
0.008	1.8	1.4700	1.1	0.7350	2.4	2.1000
0.010	2.0	1.3440	1.3	0.7560	3.1	2.2680
0.020	3.5	1.3020	2.3	0.7980	5.3	2.0580
0.040	6.3	1.2390	3.9	0.7350	9.4	1.8900
0.060	8.8	1.1760	5.3	0.6860	12.8	1.7360
0.080	11.2	1.1340	7.1	0.7035	15.8	1.6170
0.100	13.4	1.0920	8.2	0.6552	20.3	1.6716
	PAIM-7		**PAIM-8**		**PAIM-9**	
0.001	0.6	1.6800	0.9	4.2000	0.5	0.8400
0.002	0.8	1.6800	1.3	3.7800	1.0	2.5200
0.004	1.2	1.6800	2.1	3.5700	1.7	2.7300
0.006	1.5	1.5400	2.7	3.2200	2.7	3.2200
0.008	1.8	1.4700	3.4	3.1500	4.1	3.8850
0.010	2.1	1.4280	4.0	3.0240	6.8	5.3760
0.020	3.5	1.3020	6.8	2.6880	9.6	3.8640
0.040	6.1	1.1970	10.8	2.1840	10.1	2.0370
0.060	8.7	1.1620	15.0	2.0440	11.8	1.5960
0.080	10.9	1.1025	18.5	1.9005	14.0	1.4280
0.100	12.9	1.0500	21.3	1.7556	16.6	1.3608

Table 3.3: The limiting equivalent conductance (λ_0) of all the Imidazolinone derivatives in DMF and DMSO at 308.15K.

Compound Code	$\lambda_0.10^3$ $cm^2/\Omega.equiv.$ From Fig. 3.1	λ_0 $cm^2/\Omega.equiv.$ from eq.(3.4)	$\lambda_0.10^3$ $cm^2/\Omega.equiv.$ from Fig. 3.2	λ_0 $cm^2/\Omega.equiv.$ from eq.(3.4)
	DMF		DMSO	
PAIM-1	7.8	6.82	0.85	0.98
PAIM-2	6.75	2.45	2.80	2.14
PAIM-3	-	2.75	-	2.53
PAIM-4	7.15	2.41	-	1.92
PAIM-5	5.15	1.28	0.86	0.93
PAIM-6	9.1	3.95	2.80	2.71
PAIM-7	7.1	3.13	2.3	1.69
PAIM-8	-	3.03	4.8	3.78
PAIM-9	9.2	1.70	-	3.80

REFERENCES

(1) Gelb and I. Robert; Anul.Chem., **43**, 1103 (1971).

(2) W. Stuck; Microchemical Journal, **10** , 202 (1966).

(3) G. Norwitz and H. Gordan**;** Microchemical Journal, **12**, 458 (1967).

(4) F. E. Friedl; Analytical Biochemistry, **48,** 300 (1972).

(5) M. W. E. Coney; J. Phys. E: Sci. Instrum., **6**, 903 (1973).

(6) Y. Kato, K. Unoura, N. Tsunashima and A. Yamada; J. Electroanalytical Chem., **396 ,** 557 (1995).

(7) K. Grudpan, K. Kamfoo and J. Jakmunee; Talanta, **49,** 1023 (1999).

(8) M. K. Ahmed, R. Geetha, N. K. Pandey, S. Murugesan, S. B. Koganti, B. Saha, P. Sahoo and M. K. Sundararajan; Talanta, **52** , 885 (2000).

(9) C. Johansen, B. K. Bredtved and S. Moller; Methods in Enzymology, **310**, 353 (1999).

(10) D. Carminati, E. Neviani, Carminati and Neviani; J. Dairy Sci., **74,** 1472 (1991).

(11) C. Erbil, S. Özdemir and N. Uyanık; Polymer, **41**, 1391 (2000).

(12) S. Bracko and J. Span; Dyes and Pigments, **45**, 97 (2000).

(13) M. Morita, T. Fujisaki, N. Yoshimoto and M. Ishikawa; Electrochimica Acta, **46**, 1565 (2001)

(14) Stanisz, L. Koter and M. Zator; Desalination, **162**, 373 (2004)

(15) F. Kvasnicka and M. Voldrich; J. Chromatography A, **1103**, 145 (2006)

(16) A. L. Mullyniem, H. Sippla, L. Nuotia, A. Niemi and T. Henkansen; Buzalski Analyst, **127**, 1247 (2002).

(17) J. Sawai and T.Yoshikawa; Lett. Appl. Microbiol, **37**, 40 (2003).

(18) A. Apelblat; Journal of Molecular Liquids; **73-74** , 49 (1997)

(19) F. Bonino and M. Lazzari; J. Power Sources, **1,** 103 (1976).

(20) R. I. Blokhra, Y. P. Sehgal and V. P. Sharma; J. Ind. Chem. Soc., **LV,** 497 (1978).

(21) M. M. Karelson; Theor. Eksp-Khim., **15** , 80 (1979).

(22) N. K. Jha and A. Saxena; J. Ind. Chem. Soc., **LVII,** 701 (1980).

(23) H. G. Mukherjee and S. K. Datta; J. Ind. Chem. Soc., **LXII,** 67 (1985).

(24) K. Daga, S. Gaur, S. P. Ranga and R. K. Mehta; J. Ind. Chem. Soc., **LXV**, 79 (1988).

(25) M. N. Roy, D. Nandi and D. K. Hazra; J. Ind. Chem. Soc., **70,** 121 (1993).

(26) J. Ghasemi and M. Shamsipur; J. Sol. Chem., **V25,** 485(1996).

(27) D. L. Goldfarb and H. R. Corti; J. Phys. Chem., **B47,** 3358 (1997).

(28) E. Braun, Y. Eichen, U. Sivan and G. Ben-Yoseph; Nature., **391**, 775 (1998).

(29) S. P. Jauhar and S. Sandhu; Ind. J. Chem., **39A**, 392 (2000).

(30) V. K. Syal, S. Chauhan and P. K. Gupta; J. Ind. Chem. Soc., **79,** 860 (2002).

(31) M. Galloway and S. A. Soper; Electrophoresis, **23**, 3760 (2002).

(32) D. Nandi and D. K. Ha'zra; J. Ind. Chem. Soc., **80,** 21 (2003).

(33) B. P. Dey, P. K. Biswas and S. C. Lahiri; J. Ind. Chem. Soc., **80,** 271 (2003).

(34) P. Haldar and B. Das; Z. Phy. Chem., **218,** 1129 (2004).

(35) M. Abdelhedi, M. Dammak, A. Cousson and A.W. Kolsi; J. Alloys Compds, **398**, 55 (2005).

(36) M. Singh, A. Kumar, S. Easo and B. B. Prasad; Can. J. Chem., **75**, 414 (1997).

(37) M. Singh, and B. B. Prasad; J. Chem. Eng. Data., **41**, 409 (1996).

(38) Meenakhi Singh, Anil Kumar, Shirley Easo and B.B. Prasad; Can. J. Chem.; **75**, 414 (1997)

(39) B.B. Prasad, Shirley Easo and Anil Kumar; Polymer, **35**, 2874 (1994).

CHAPTER-4

HEAT OF SOLUTIONS

INTRODUCTION

When a solute is dissolved in a solvent, heat is either absorbed or evolved. Thus, dissolution of a solute in a solvent is accompanied by the heat change i.e., enthalpy change (ΔH) of the system. If the heat is absorbed i.e., the solution is cooler then ΔH is positive. If the heat is evolved i.e., the solution is warmer then ΔH is negative. The heat of solution is defined as the change in enthalpy when one mole of substance is dissolved in specified quantity of solvent at a given temperature. The heat of solution for many inorganic, organic and polymeric compounds has been reported [1-14]. Volynskaya et al. have been studied the heat of solution of amorphous polymers [15]. Meurs et al. also studied the heat of solution of some polymers [16]. Goralski et al. have been reported the heat of solution of cholesterol[17]. Yonemochi et al. studied the heat of solution of chiral drugs[18].

The molar heat of solution and melting temperature of a substance can be determined from the solubility measurements at different temperatures[19].

The thermodynamic properties of several electrolytes in different solvents have been studied by many workers[20-26]. In our laboratory, heat of solution of some organic compounds has also been determined[27, 28].

In the present work, heat of solution for some imidazolinone derivatives was determined in N,N-dimethylformamide (DMF) and Dimethylsulfoxide (DMSO) at different temperatures (308.15K to 328.15K).

EXPERIMENTAL

The solvents used for the measurements were purified and fractionally distilled prior to use by the method reported in the literature[29]. The solubility of each Schiff base was determined by transferring 25 ml of saturated solution into a pre-weighed 50 ml beaker at a definite temperature. The weight of beaker along with solution was taken and the solvent was evaporated to dryness until constant weight is obtained. This gives the weight of solute present in 25 ml saturated solution. Three replicate measurements were carried out at a particular temperature and average value of weight was determined. The experiment was repeated at other temperatures also. Subtraction of weight of solute from the weight of solution gives the weight of solvent in 25 ml saturated solution.

RESULTS AND DISCUSSION

The solubility (N_2) of Imidazolinone derivatives in DMF and DMSO are given in Tables 4.1 and 4.2 respectively. It is evident from the tables that the solubility of imidazolinone derivatives increases linearly with temperature in both the solvents. Comparison of solubility of these derivatives in DMF and DMSO shows that overall solubility is greater in DMSO than in DMF. Thus, the solvent polarity plays an important role on the solubility of studied imidazolinone derivatives.

The variation of solubility with temperature is given by;

$$\left[\frac{\ln N_2}{dT}\right]_p = \frac{\Delta H_s}{RT^2} \qquad \text{..... (4.1)}$$

where N_2 is the solubility or mole fraction, T is absolute temperature of the experiment, ΔH_s is the heat of solution and R is the gas constant. Integration of equation (4.1) between temperature limits from T and T_m gives

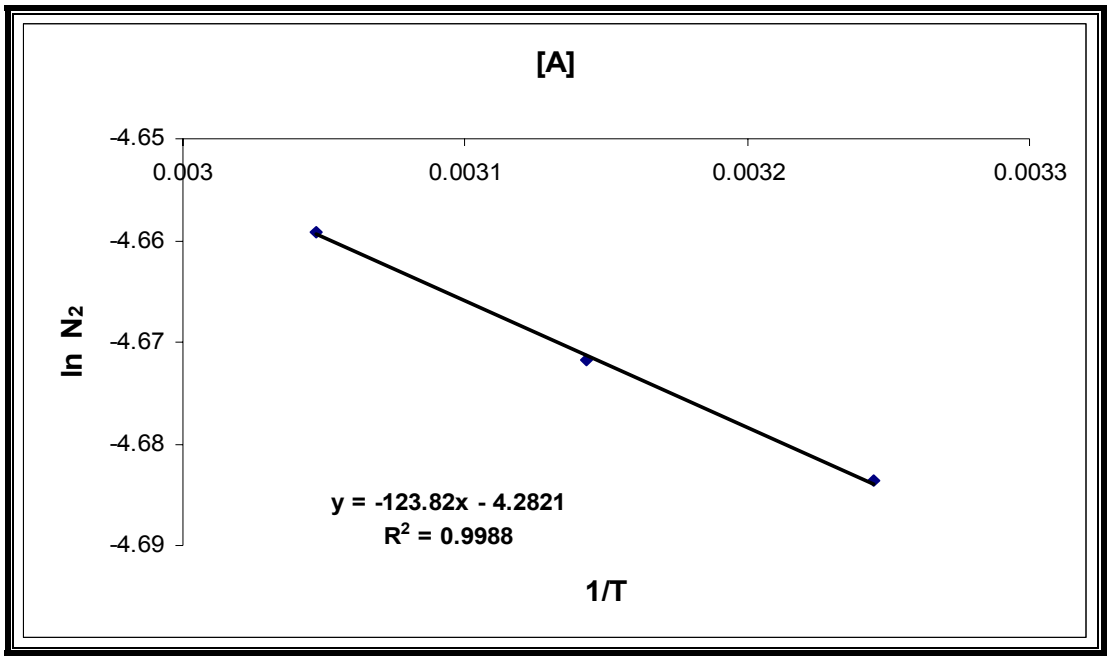
$$\ln N_2 = \frac{\left[\Delta H_s \left(T - T_m\right)\right]}{RT.T_m} \qquad \text{..... (4.2)}$$

where T = temperature of experiment and T_m = melting temperature.

Fig. 4.1 shows the variation of ln N_2 with 1/T for imidazolinone derivative (PAIM-1) in DMF [A] and DMSO [B] solutions. It is evident from the Fig. 4.1 that ln N_2 varies linearly with 1/T. The correlation coefficient γ for these plots for all the compounds in DMF and DMSO is given in Table 4.3.

From these plots and using equation (4.2), ΔH_s values are calculated and are reported in Tables 4.1 and 4.2 for DMF and DMSO respectively. It is observed that for both solvents, ΔH_s values are positive for all the compounds studied indicating thereby endothermic behavior of these compounds in both the solvents.

Figure 4.1: The variation of lnN_2 against 1/T for PAIM-1 in [A] DMF and [B] DMSO.



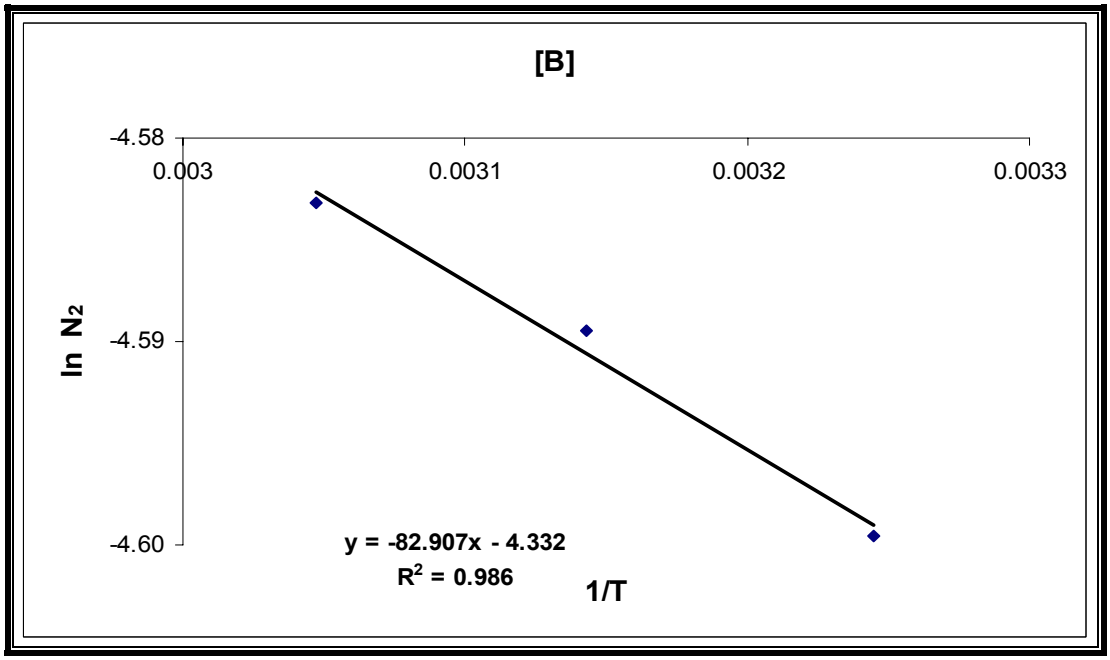


Table 4.1: The solubility (N_2) and heat of solution (ΔH_s) of imidazolinone derivatives in Dimethylformamide at different temperatures.

Temp. K	$N_2 . 10^3$	ΔH_s (k.cals/mol)	$N_2 . 10^3$	ΔH_s (k.cals/mol)	$N_2 . 10^3$	ΔH_s (k.cals/mol)
	PAIM-1		**PAIM-2**		**PAIM-3**	
308.15	9.2448	17.9109	11.5197	17.7035	14.9958	15.4772
318.15	9.3556	19.5301	11.6245	19.3809	15.0334	16.8523
328.15	9.4744	21.3452	11.7293	21.2798	15.1465	18.3656
	PAIM-4		**PAIM-5**		**PAIM-6**	
308.15	10.6579	16.4209	7.9554	19.7023	10.0131	18.3995
318.15	10.7657	17.8208	8.0802	21.6015	10.1256	20.1498
328.15	10.8706	19.3779	8.1540	23.7935	10.2245	22.1405
	PAIM-7		**PAIM-8**		**PAIM-9**	
308.15	10.5240	19.2714	2.2237	23.6950	2.9772	22.4819
318.15	10.6050	21.2427	2.3724	25.6629	3.0587	24.4872
328.15	10.6602	23.5186	2.4358	28.0433	3.1613	26.7125

Table 4.2: The solubility (N_2) and heat of solution (ΔH_s) of imidazolinone derivatives in Dimethylsulphoxide at different temperatures.

Temp. K	$N_2 . 10^3$	ΔH_s (k.cals/mol)	$N_2 . 10^3$	ΔH_s (k.cals/mol)	$N_2 . 10^3$	ΔH_s (k.cals/mol)
	PAIM-1		**PAIM-2**		**PAIM-3**	
308.15	10.0360	17.5969	12.3831	17.4168	16.1557	15.2027
318.15	10.1382	19.1943	12.4938	19.0672	16.2883	16.5304
328.15	10.2017	21.0063	12.5679	20.9493	16.3552	18.0291
	PAIM-4		**PAIM-5**		**PAIM-6**	
308.15	11.4495	16.1618	8.6891	19.3428	10.8145	18.0917
318.15	11.5661	17.5388	8.7999	21.2190	10.9371	19.8116
328.15	11.6599	19.0775	8.8918	23.3650	11.0295	21.7744
	PAIM-7		**PAIM-8**		**PAIM-9**	
308.15	11.4629	18.9097	2.5427	23.1750	3.4009	21.9676
318.15	11.5650	20.8378	2.6162	25.2475	3.4867	23.9333
328.15	11.6613	23.0537	2.6946	27.5727	3.5642	26.1558

Table 4.3: Correlation coefficient values obtained from plot of ln N_2 against 1/T.

Compounds	Correlation coefficient (γ)	
	DMF	DMSO
PAIM-1	0.9988	0.9860
PAIM-2	0.9998	0.9903
PAIM-3	0.9139	0.9707
PAIM-4	1.0000	0.9977
PAIM-5	0.9825	0.9985
PAIM-6	0.9995	0.9957
PAIM-7	0.9913	1.0000
PAIM-8	0.9521	0.9992
PAIM-9	0.9944	0.9997

REFERENCES

(1) A. W. H. Morris and J. N. Pratt; J. Appl. Phy., **16**, 517 (1965).

(2) A. K. Shukla, J. C. Ahwalia and C. N. R, Rao; J. Chem. Soc. Faraday Trans., **72**, 1288 (1976).

(3) M. Nakamura, L. G. Berterand and E. S. Friberg; C. A. **98,** 60782g (1982).

(4) H. Sigmund; J. Electrochem. Soc., **129**, 2809 (1982).

(5) E. N. Fedotova and K. I. Igumenov; C. A., **101,** 117805 m (1984).

(6) M. Pickering; J. Chem. Ed., **64**, 723 (1987).

(7) M. Khiezkowsk; Fluid Phase Equili., **42,** 269 (1988).

(8) B. Andresson and G. Olofsson; J. Sol. Chem., **18**, 1019 (1989).

(9) P. H. Parsania; Asian J. Chem., **5**,312 (1993).

(10) H. Gan, M. C. Wilding, A. Navrotsky; Cosmochimica Acta, **60,** 4131 (1996).

(11) E. S. Secco and R. A. Seccob; Phy. Chem. Chem. Phys., **1**, 5011 (1999).

(12) B. R. Deshwal and K. C. Singh; Ind. J. Chem., 42, 467 (2003).

(13) K. A. Kovnir, M. M. Shatruk, L. N. Reshetova, I. A. Presniakov, E. V. Dikarev, M. Baitinger, F. Haarmann, W. Schnelle, M. Baenitz, Y. Grin and A.V. Shevelkov; Solid State Sci., **7**, 957 (2005).

(14) O. Sklyar, T. H. Treutler, N. Vlachopoulcs and G. Wittstock; Surface Sci., **597**, 181 (2005).

(15) A. V. Volynskaya, Yu. K. Godovskii and V. S. Papkov -Polymer Science U.S.S.R., **21**, 1161 (1979).

(16) N. U. Meurs, W. T. Warmerdam and G. Somsen; Fluid Phase Equili., **46**, 263 (1989).

(17) P. Goralsk and M. Tkaczyk; Thermochimica Acta, **165**, 49 (1990).

(18) E .Yonemochi , Y. Yoshihashi, K. Terada; Pharm Res., **17**, 90 (2000).

(19) S. Glasstone; "Thermodynemics for Chemist", Litton Edu. Pub.,Inc.,New York.

(20) R. P. Held and C. M. Criss; J. Phy. Chem., **69**, 2611 (1965).

(21) Y. C. Wu and H. L. Friedman; J. Phy. Chem., **70**, 501 (1966).

(22) R. P. Held and C. M. Criss; J. Phy. Chem., 71, 2487 (1967).

(23) F. T. Vesekina, Yu. E. Kushmir, G. M. Serebrennikova; C. A., **101**, 138244 t (1984).

(24) S. Ishiguro, B. Jeliazkova, H. Ohtaki; Bull. Chem. Soc. Jpn., **58**, 1749 (1985)

(25) B. K. Kasenov, V. Bukharitsin; C. A., **112**, 12712 c (1989).

(26) E. Matteoli and L. Lepori; Fluid Phase Equili. **174**, 115 (2000).

(27) S. Baluja; Acta Cien. Ind., **30**, 163 (2004).

(28) S. Baluja; E. J. Chem., **1**, 199 (2004).

(29) J. A. Riddick, W. B. Bunger and T. Sakano; Organic Solvents- Physical Properties and Methods for purification, **4th Edition**, Techniques of Chemistry, **Vol.II**, Wiley/Interscience, Wiely, New York (1986).

CHAPTER-5

THERMAL PROPERTIES

INTRODUCTION

There are many techniques available with physical chemists and material science scientists for obtaining qualitative and quantitative informations about the composition, structure and characterization of materials. Among these techniques, thermal analysis has grown rapids recently. The importance of thermal analysis is increasing day by day because of the advancement of thermal analysis technology, relative cheapness of the equipment and the time required to achieve the desired result. Thermal analysis serves as a useful tool to follow the cource of decomposition of mixed metal precursor and the formation of stable phase at different temperature. This technique can provide the measurement of overall (global) kinetic parameters of thermally simulated reactions which permit a deeper insight in to the mechanism of high energetic compounds.

Thermal analysis has used to determine the physical and chemical properties of polymers, geological materials and coals [1-3]. Both quantitative and qualitative analysis can be carried out and one can identify and characterize the samples by qualitative investigations of their thermal behaviors. Current areas of applications include environmental measurements, composition analysis, product reliability, stability, chemical reaction and dynamic properties. Further, various reversible and non-reversible reactions[4,5], the decomposition of molecules absorbed on a surface, phase transitions etc. can also be studied.

There are various types of thermal techniques such as, Differential Scanning Calorimetry (DSC), Differential Thermal Analysis (DTA), Thermo gravimetric Analysis (TGA), Evolved Gas Detection (EGD), Evolved Gas Analysis (EGA) etc.

In these techniques, DTA and DSC are based on energy changes whereas TGA depends on weight changes. EGD and EGA techniques depend upon the evolved volatiles. The parameters measured as function of temperature in DTA, DSC, TGA and ECD are temperature difference between sample and reference coefficient of volume expansion and mass of evolved gas respectively.

In TGA technique, the mass change in a sample is recorded continuously as a function of temperature or time when it is subjected to a programmed temperature change in specific atmosphere. A derivative of thermo gravimetric curve is useful in resolving the partially over lapping steps in the multisteps

reactions involving the formation of weakly stable intermediates. By TGA, thermal stability, kinetic parameters, compositional analysis etc. can be measured.

Literature survey shows that several investigation have been carried out on the application of thermal methods in pharmaceutical industry[6-15]. Wendlandt and Collins[16] used DTA and TG technique for the characterization and identification of commercial non prescription analgesics. A number of investigators have studied the physical and chemical properties of various inorganic, organic and polymeric materials[17-34] by using thermal methods. Kinetic study of thermal decomposition of various metal complexes have also been reported by several workers[35-44]. Khraisha and Shabib reported thermal analysis of Shale oil[45]. Ihms and Brinkman reported thrmo gravimetric analysis as a polymer identification in forensic application[46]. Ruiz et al. have been studied the effect of temperature on cement paste[47]. Wendlandt[48] have applied this method (TGA) to study the thermal stability of EDTA as free acid. Further, by using this technique, the composition of binary mixtures can also be determined. One of the most important applications of thermo gravimetry is in examining the thermal stability of polymer and binding materils.

Various workers used TGA techniques as a tool in the characterization of natural rubber and styrene butadiene blends[49,50]. By using TGA, thermal properties of epoxy resins[51,52], olive wood[53], fabrics[54] and other materials have been reported.

In this chapter, thermal properties of some imidazolinone derivatives have been studied by using TGA technique.

From TGA curves, various kinetic parameters can be evaluated by several methods. In all these methods, it is assumed that thermal and diffusion barriers are negligible because small quantity of material is used. The shape of any TGA curve depends on the nature of apparatus and the way in which it is used. Further, Arrhenius equation is valid in all these methods.

The kinetic treatments are generally based on the relationship of the type:

$$dC/dt = K f(C) \qquad \ldots (5.1)$$

where C is the degree of conversion, t is time and K is rate constant. f(C) is a temperature independent function of C.

The constant K is assumed to have the Arrhenius form:

$$K = A\, e^{-E/RT} \qquad \text{... (5.2)}$$

C can also be defined as:

$$C = 1-(W/W_0) \qquad \text{... (5.3)}$$

where W_0 and W are the initial weight at t=0 and weight at any time t of the material.

Equation (7.3) can be written as:

$$(W/W_0) = (1-C) \qquad \text{... (5.4)}$$

W/ W_0 is known as residual weight fraction.

Thus, the rate of conversion is,

$$dC/dt = - (1/W_0) (dW/dt) \qquad \text{... (5.5)}$$

For homogeneous kinetics, the conversion is assumed to be of the form:

$$f (C) = (1-C)^n \qquad \text{... (5.6)}$$

where n is the order of the reaction.

Substituting the values from equation (5.2) and (5.6) in equation (5.1) gives:

$$dC/ dt = A\, e^{-E/RT} (1-C)^n$$

or $$dC/dt = (A/\beta)\, e^{-E/RT} (1-C)^n \qquad \text{... (5.7)}$$

where A is the frequency factor, β is the rate of heating and E is the energy of activation.

Various methods for single and multiple heating rates have been reported. The methods of single heating rate are as follows:

1. Freeman-Carroll [55] and Anderson-Freeman Method [56]:

At a single heating rate, Freeman and Carroll gave the following relation to analysis TGA data :

$$\ln (dC/dt)/\ln (1-C) = n\text{-}E/R\ [(1/T/(\Delta\ln(1-C)] \quad \text{... (5.8)}$$

A plot of left hand side against (1/T)/(Δln(1-C)) gives a straight line with a slope equal to -E/R and the intercept is equal to n.

Anderson and Freeman then derived the following equation by using equation (4.8):

$$(\Delta\ln[dC/dt]) = n\ (\Delta\ln(1-C)) - E/R\ \Delta(1/T) \quad \text{... (5.9)}$$

The plot of (Δln[dC/dt]) against (Δln(1-C)) for equal intervals of Δ(1/T) gives a straight line with slope equal to n and intercept -E/RΔ(1/T).

2. Sharp-Wentworth method [57]:

To analyse the TGA data for first order kinetics (n=1), Sharp and Wentworth gave the relation:

$$\log [(dC/dt)/(1-C)] = \log (A/\beta) - (E/2.303R).(1/T) \quad \text{... (5.10)}$$

The plot of log [(dC/dt)/(1-C)] against 1/T would be a straight line with slope equal to - (E/2.303R) and intercept equal to log (A/β).

3. Chatterjee Method[58]:

Based on the weight units, the following relation was developed by Chatterjee:

$$n = [\log(dW/dt)_1 - \log(dW/dt)_2] / (\log W_1 - \log W_2) \quad \text{... (5.11)}$$

where W_1 and W_2 are the sample weights.

4. Horowitz and Metzger method[59] :

In this method, the value of energy of activation E can be determined from a single TG curve by the relation:

$$\ln [\ln(1-C)^{-1}] = (E/RTs^2)\theta \quad \text{... (5.12)}$$

where $\theta = T-T_s$. T_s is the temperature at which the rate of decomposition is maximum.The frequency factor A and entropy change ΔS can be determined by the following equations:

$$\ln E - \ln (RT_s^2) = \ln A - \ln\beta - E/RT_s \quad \text{... (5.13)}$$

$$A = (k_b T / h)\, e^{\Delta S/R} \quad \text{... (5.14)}$$

where k_b is Boltzmann constant and h is Planck's constant.

EXPERIMENTAL

The Differential Scanning Calorimetry (DSC), Differential thermal analysis (DTA) and Thermo gravimetric analysis (TGA) measurements were made on the instrument “Universal V2.6D TA Instruments at the heating rate of 10°C/min in nitrogen atmosphere for all the imidazolinone derivatives.

RESULT AND DISCUSSION

The TGA thermo grams of imidazolinone derivatives are given in Fig. 5.1 to 5.5. Various thermal properties such as initial decomposition temperature (IDT), the decomposition temperature range and the maximum degradation along with the percentage weight loss and Exo / Endo transitions of imidazolinones are reported in Table 5.1.

The thermal stability can not be decided by weight loss because for all compounds, degradation is multi step process (Fig. 5.1 to 5.5). Each step is of different order. Further, the variation in the trend of thermal decomposition might be interpreted by taking into account some intermolecular interactions (structural as well as electronic) and also because of several experimental factors. However one from Table 5.1, one can say that PAIM-4 is most stable whereas PAIM-8 is less stable. This suggests that the presence of 1-napthylamine (as in PAIM-4) causes greater stability than 3-Cl-4-F-aniline (as in PAIM-8), which is less stable.

The kinetic parameters, such as order of the degradation (n), energy of activation (E), frequency factor (A) and entropy change (ΔS) for each step are reported in Tables 5.2 and 5.3.

It is evident from Tables 5.2 and 5.3 that order of reaction is quite different in different steps for different imidazolinone derivatives. For first step, order of reaction varies from 2.5 to 21. For second step also, values of n varies from 2.5 to 6.7.

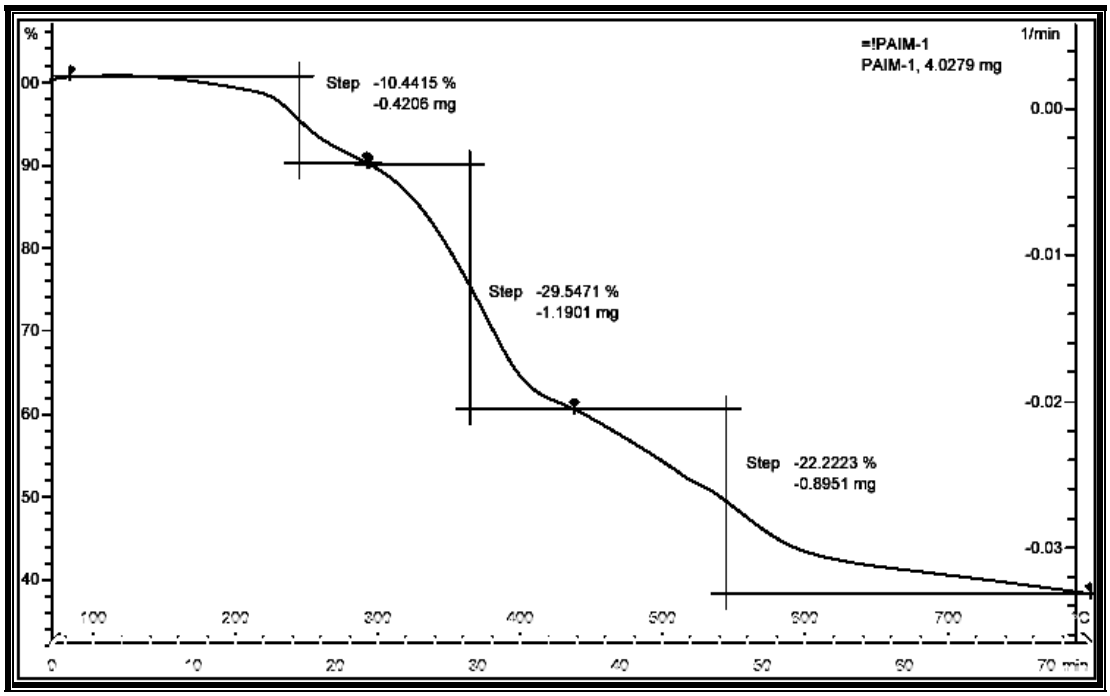
In first step, energy of activation (E) is maximum for PAIM-5 and minimum for PAIM-4. The frequency factor (A) also varies in the same order i.e., maximum for PAIM-5 and minimum for PAIM-4. In second step, energy of activation is found to be maximum for PAIM-3 and minimum for PAIM-6. The frequency factor A is also maximum for PAIM-3 and minimum for PAIM-6. Comparison of E and A values in Tables 5.2 and 5.3 shows that values of E and A are minimum for second steps of all the imidazolinone derivatives.

Further, change in entropy (ΔS^0) for all these reactions were also calculated by equation (5.14). It is observed that, change in entropy are positive

for all compounds except PAIM-4 and PAIM-9 for the first step while in second step entropy changes are negative for all the imidazolinone derivatives. The positive ΔS^0 indicates that the transition state is in less ordered state. Whereas the negative ΔS^0 values indicate that the activation complex has a more ordered or more rigid structure than the reactants and the reaction is slower than the normal[60].

Thus, the degradation in imidazolinone derivatives is multi step process with different order of reaction. Further, thermal stability depends upon the type of substituent present. It is observed that presence of 1-napthylamine (as in PAIM-4) increases the stability whereas 3-Cl-4-F-aniline (as in PAIM-8) decreases the stability.

Figure 5.1: The TGA graphs of PAIM-1 and PAIM-2.



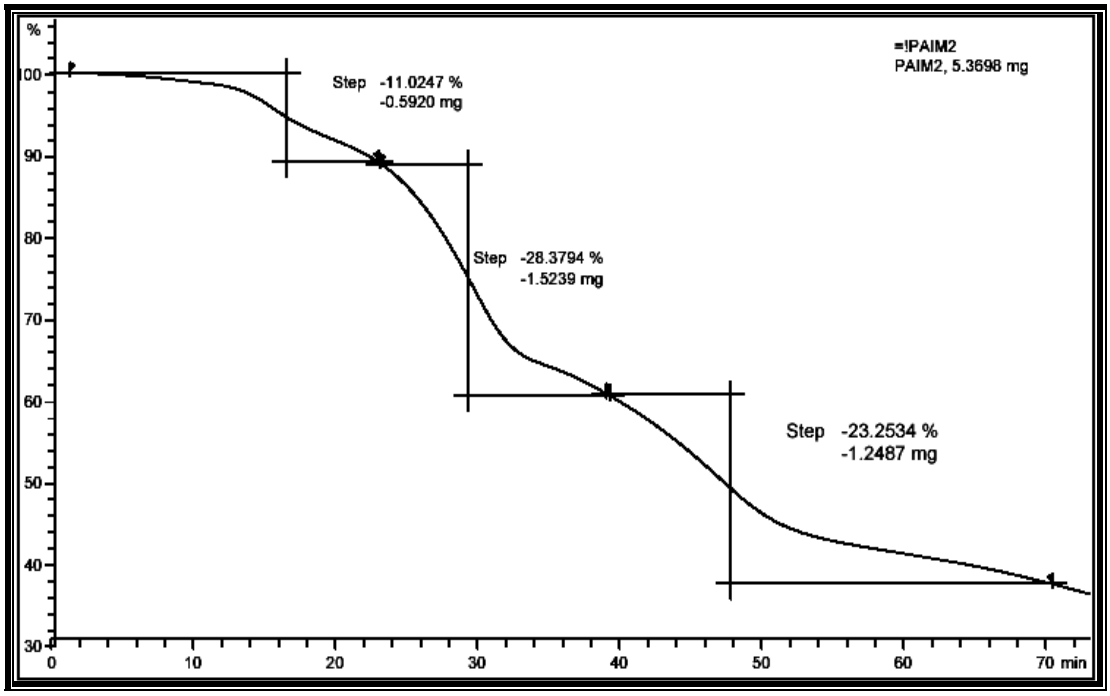
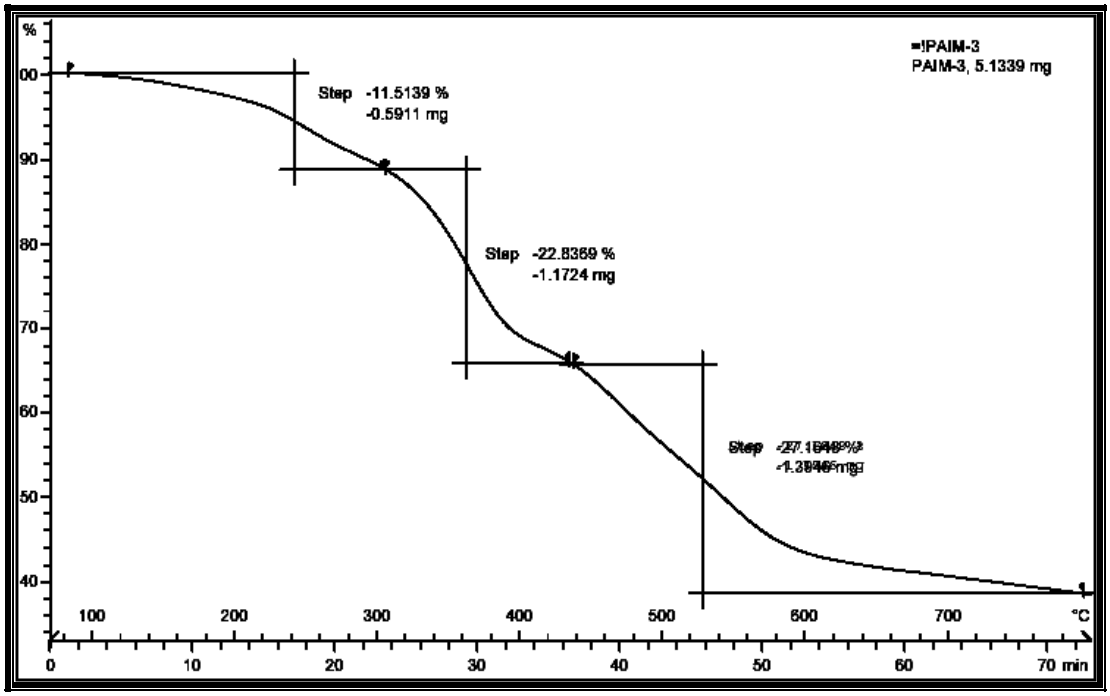


Figure 5.2: The TGA graphs of PAIM-3 and PAIM-4.



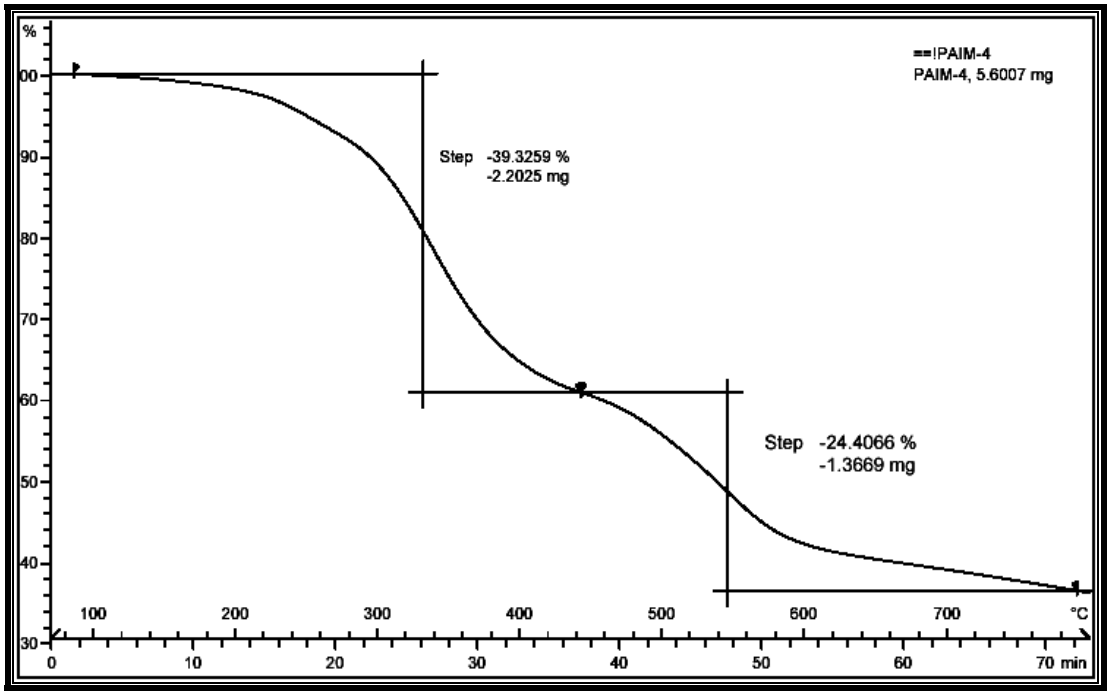
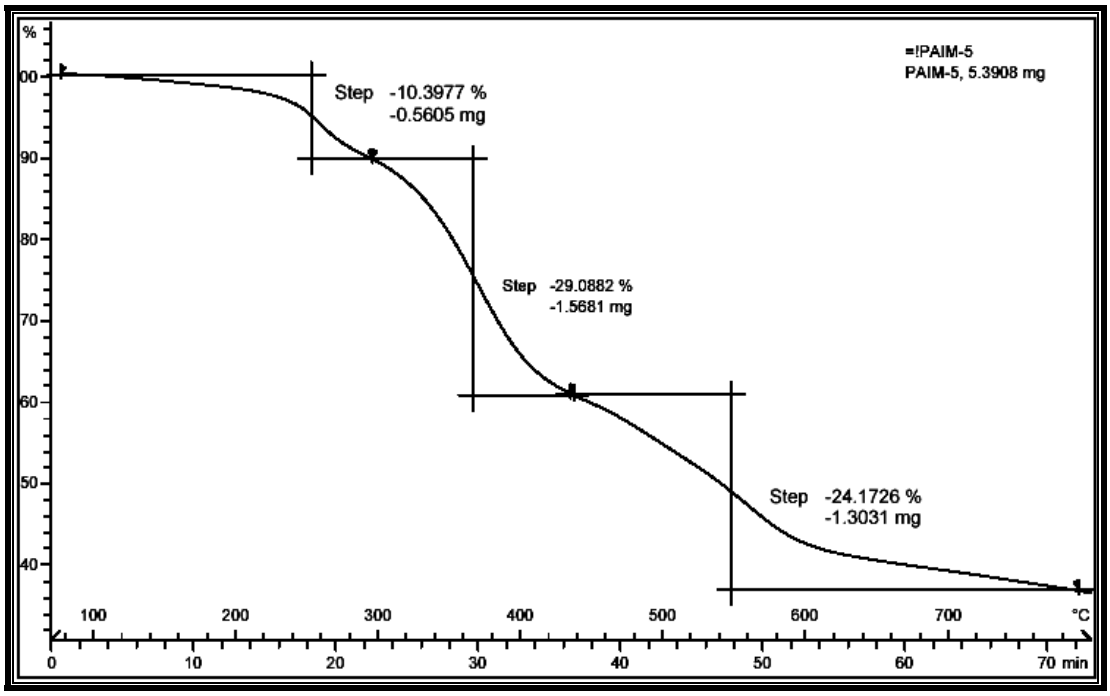


Figure 5.3: The TGA graphs of PAIM-5 and PAIM-6.



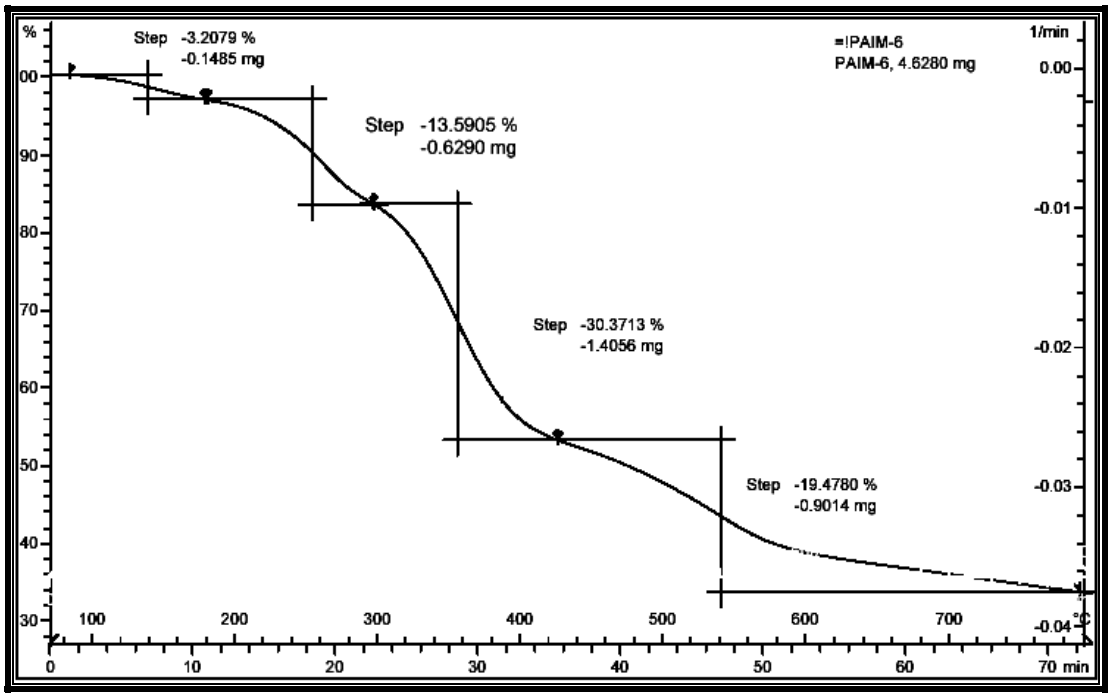
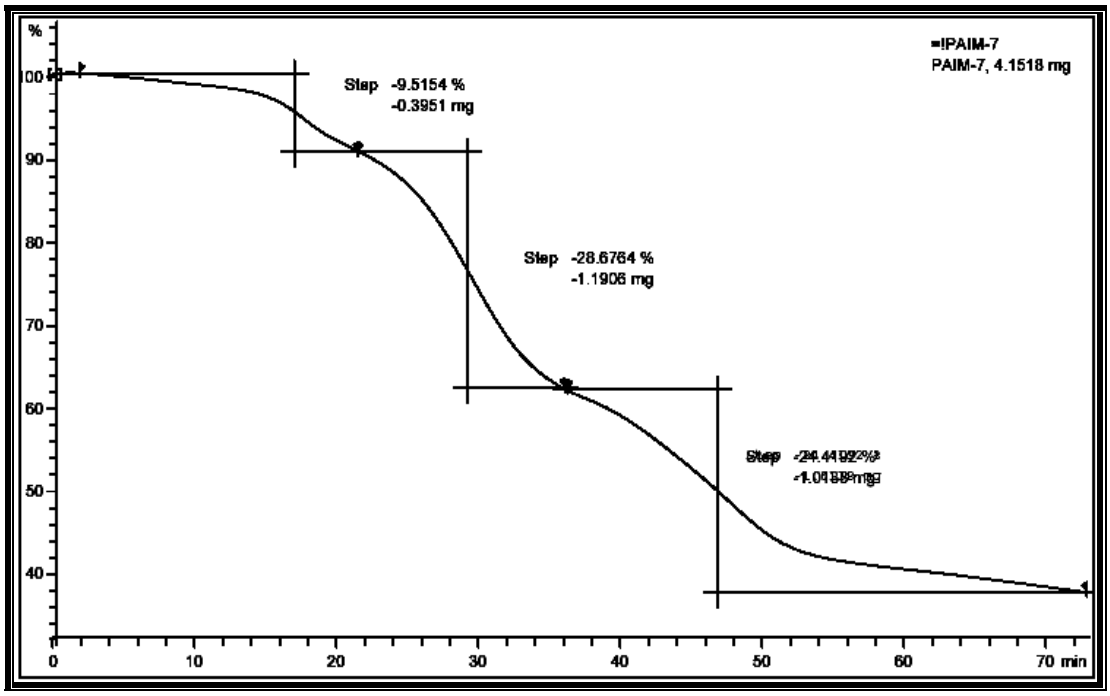


Figure 5.4: The TGA graphs of PAIM-7 and PAIM-8



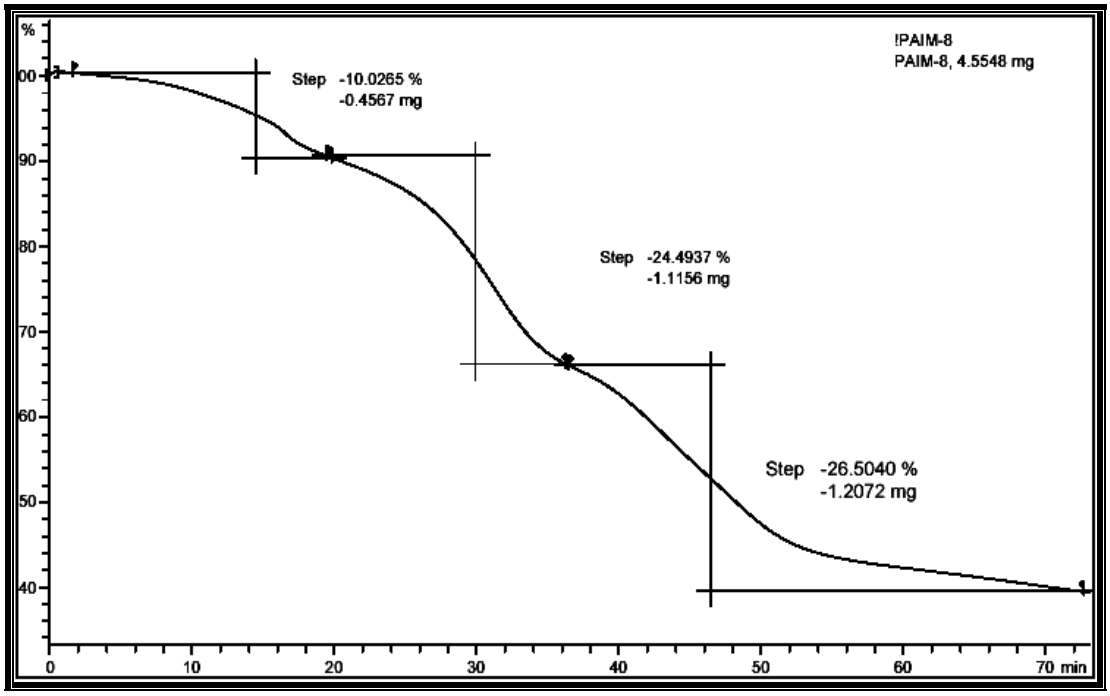


Figure 5.5: The TGA graphs of PAIM-9.

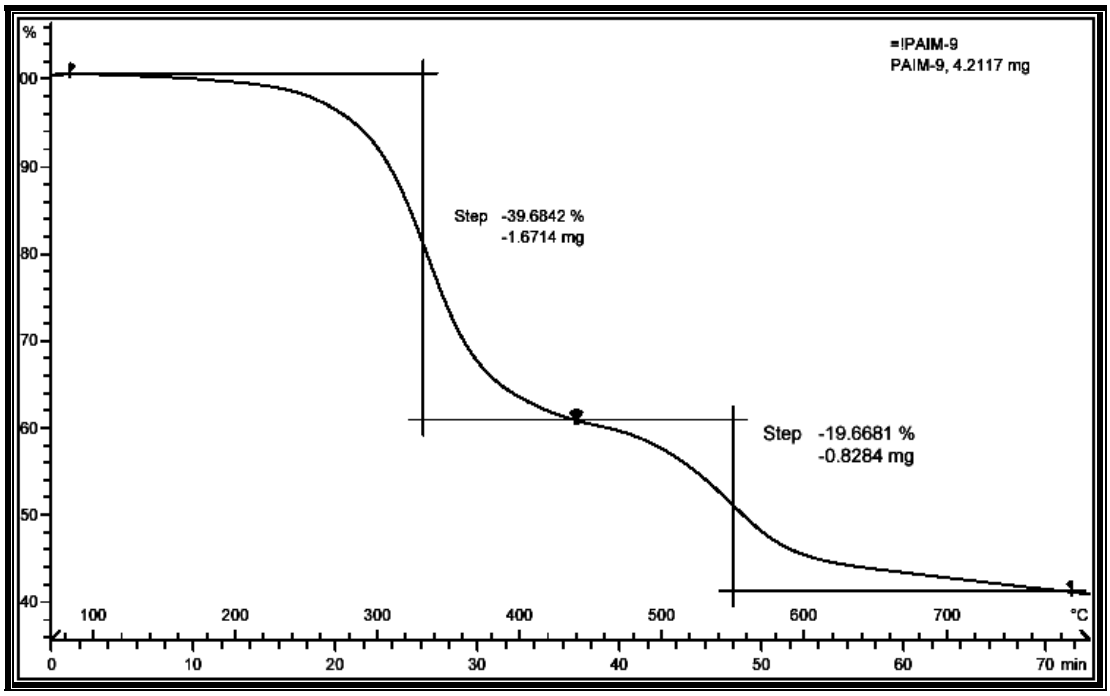


Table 5.1: TGA data for synthesized imidazolinone derivatives.

Comp. Code	Amt. (mg.)	Initial Decomp. Temp. (^oC)	Decomp. range (^oC)	% Wt. loss	Residual Wt. Loss (mg.)	Max Degradt. Temp. (^oC)
PAIM-1	4.0279	240	240 – 596	37.7891	1.5221	596
PAIM-2	5.3698	239	239 – 581	37.3425	2.0052	581
PAIM-6	5.1339	240	240 – 588	38.4844	1.9758	588
PAIM-4	5.6007	332	332 – 586	36.2675	2.0313	586
PAIM-5	5.3908	252	252 – 596	36.3415	1.9591	596
PAIM-6	4.6280	252	252 – 579	33.3523	1.6920	579
PAIM-7	4.1518	240	240 – 592	37.3890	1.5523	592
PAIM-8	4.5548	212	212 – 594	38.9758	1.7753	594
PAIM-9	4.2117	330	330 – 590	40.6477	1.7119	590

Table 5.2: The kinetic parameters for all the imidazolinone derivatives for 1st step.

Comp. code	n	E (kJ)	A (Sec^{-1})	Δs^{o} (kJ^{-1})
PAIM-1	6.00	239.83	1.54×10^{19}	269.25
PAIM-2	7.00	221.71	5.34×10^{17}	241.33
PAIM-6	5.00	232.22	4.10×10^{18}	258.27
PAIM-4	8.20	34.44	4.65	-87.37
PAIM-5	2.50	270.21	5.37×10^{21}	317.92
PAIM-6	15.00	100.96	3.61×10^{7}	46.72
PAIM-7	8.00	203.23	1.48×10^{16}	211.52
PAIM-8	21.00	87.76	1.71×10^{6}	21.21
PAIM-9	7.15	46.80	36.61	-70.27

Table 5.3: The kinetic parameters for all the imidazolinone derivatives for 2nd step.

Comp. code	n	E (kJ)	A (Sec^{-1})	Δs^{o} (kJ^{-1})
PAIM-1	6.60	44.56	26.18	-73.01
PAIM-2	6.30	61.40	415.84	-50.04
PAIM-6	2.50	119.72	6.77×10^{6}	-7.50
PAIM-4	-	-	-	-
PAIM-5	6.40	42.91	19.39	-75.53
PAIM-6	6.0	33.81	4.31	-87.95
PAIM-7	6.70	50.64	77.85	-63.89
PAIM-8	5.30	92.01	6.94×10^{4}	-7.37
PAIM-9	-	-	-	-

REFERENCES

(1) M. I. Ayad, A. Mashaly and M. M. Ayad; Thermochim. Acta, **184**, 173 (1991).

(2) R. G. J. C. Heijkants, R. V. V. Calck, T. G. V. Tienen, J. H. de Groot; Biomaterials, **26**, 4219 (2005).

(3) S. S. Guo, X. H. Sun, S. X. Wang, S. Xu, X. Z. Zhao and H. L.W. Chan; Materials Chemistry and Physics, **91**, 348 (2005).

(4) M. Niculescu, N. Vaszilcin, M. Barzescu, P. Budrugeac, E. Segal; Articol: J.Therm. Ana.Calo., **65**, 881 (2001).

(5) O. Ichinose, T. Tanaka, and N. Furuya; Electrochem., **71**, 108 (2003).

(6) G. M. Leonipoulou, K. Theodoratos and G.G. Macris; Arch. Pharm. (Athens), **30**,100 (1974).

(7) E. Domagaina and T. Slawik; Acta Pol. Pharm., **33**, 623 (1976).

(8) A. Chauvet and J. Masse; J. Trav. Soc. Pharm. Montpeller, **38**, 31 (1978).

(9) A. Radecki and M. Weolowski; J. Thermal Anal., **17**, 73 (1979).

(10) M. Weolowski; Miikrochim Acta, **1**, 199 (1980).

(11) C. R. Martinez, J. M. Sanches, J. A. P. de Ciriza and F. Marcotegni; Rev. Asoc. Esp. Farm. Hosp., **6**, 57 (1982).

(12) D. Giron; J. Pharm. Biomed. Anal. **4**, 755 (1986).

(13) S. K. Dwivedi, S. Sattari, F. Jamali and A. G. Mitchell; J. Pharma., **87**, 92 (1992).

(14) Y. A. Ribeiro, J. D. S. Oliveira, M. I. G. Leles, S. A. Juiz and M. J. Ionashiro; Thermal Anal., **46**, 1645 (1996).

(15) N. S. Fernandes, M. A. de Silva, R. A. Medes and M. Ionashiro; J. Braz. Chem. Soc., **10**, 6 (1999).

(16) W. W. Wendlant and L. W. Collins; Anal. Chim. Acta., **71,** 411 (1974).

(17) S. K. Mandal, D. S. Joardar and K. Nag; Inorg. Chem., **17,** 191 (1978).

(18) H. S. Bu, S. Z. D. Cheng and B. Wunderlich; Rapid Commun., **9**, 75 (1988).

(19) K. N. Mehrotra, M. Chauhan and R. K. Shukla; J. Ind. Chem. Soc., **69,** 587 (1992).

(20) D. M. S. Valladao, L. C. S. de Oliveira, J. N. Zuanon and M. J. Ionashiro; Thermal Anal., **46**, 1291 (1996).

(21) P. J. Bahad, N. S. Bhave and A. S. Aswar; J. Ind. Chem. Soc., **77**, 363 (2000).

(22) M. Bhattacharya, W. G. Devi and P. S. Mazumdar; J. Ind. Chem. Soc., **78,** 189 (2001).

(23) Y.Wang, C.Xu, A.Kanazawa, T.Shiono, T.Ikeda, Y.Matsuki and Y.Takeuchi; Liq. Cryst., **28**, 473 (2001).

(24) M. V. Kok; J. Thermal Anal., **24**, 899 (2002).

(25) B. Gaur, B. Lochab, V. Choudharya and I. K. Varma; J. Thermal Anal. Calorim., **71**, 467 (2003).

(26) S. B. Kanungo; J. Ind. Chem. Soc., **81**, 644 (2004).

(27) S. Dural, P. Ramadoss; Bull. Mater. Sci, **27** , 57 (2004).

(28) S. Dhanuskodi , S. Manivannan and J. Philip; J. Crys. Growth, **265**, 284 (2004).
(29) D. Devprakasam, S. Sampath and S. K. Biswas; LANGMUIR, **20**,1329 (2004).
(30) B. L. Kalra, D. K. Lewis, S. R. Singer, A. S. Raghvan; J. E. Baldwin and B. A. Hass, J. Phy. Chem., **108A**, 1155 (2004).
(31) R. F. de Farias, C. C. Gesilva and T. A. G. Restivo; J. Serb. Chem. Soc., **70** (2005).
(32) H. Kocaokutgen, M. Gür, M. S. Soylu and P. Lönnecke; Dyes and Pigments, **67**, 99 (2005).
(33) M. M. Mashaly, H. F. El-Shafiy, S. B. El-Maraghy and H. A. Habib; Spectrochim. Acta Part A: Mol. Biomole. Spectro., **61**,1853 (2005).
(34) M. M. Falcão-Rodrigues, M. Moldão-Martins and M. L. Beirão-da-Costa; Food Chem., **93**, 459 (2005).
(35) B. D. Heda and P. V. Khadikar; Chim. Belg, **89**, 331 (1980).
(36) P. C. Shrivastava, B. N. Singh, S. K. Ghosh and N. C. Ganguly; J. Thermal Anal., **31**, 1153 (1986).
(37) M. Mohamed and K. Koga; J. Thermal. Anal., **34**, 685 (1994).
(38) M. Nath, S. Goyal, G. Eng and D. Whalen; Bull. Chem. Soc. Jpn., **69**, 605 (1996).
(39) M. Khare and A. P. Mishra; J. Ind. Chem. Soc., **77**, 256 (2000).
(40) N. Chantarasiri, N. Sutivisedsa and C. Pouyvan; Chem. Mater., **37,** 2031 (2001).
(41) P. S. Mane, S. D. Salunke, S. G. Shrodkar and T. K. Chondekar; J. Ind. Chem., Soc., **79**, 661 (2002).
(42) V. M. Leovac, L. S. Vojinovic, K. M. Szeesenyl and V. I. Cesijevic; J. Serb. Chem. Soc., **68**, 919 (2003).
(43) N. T. Madun and W. Linert; J. Therm. Anal. Calori., **76**, 813 (2004).
(44) I. Kaya and M. Gul; Eur. Poly. J., **40**, 2025 (2004).
(45) Y. H. Khraisha and I. M. Shabib; Energy Conversion and Management, **43**, 229 (2002).
(46) E. C. Ihms and D. W. Brinkman; J Forensic Sci., **49**, 505 (2004).
(47) L. A. Ruiz, G. Platret, E. Massieu and A. Ehrlacher; Cement and Concrete Research, **35**, 609 (2005).
(48) W. W. Wendlandt, Anal. Chem., **32**, 848 (1960).
(49) M. T. Ramesan; Reactive and Functional Polymers, **59**, 267 (2004).
(50) M. José, F. Berridi, N. González, A. Mugica and C. Bernicot; Thermochimica Acta, **444**, 65 (2006).
(51) T. H. Ho, T. S. Leu, Y. M. Sun and J. Y. Shieh; Polymer Degradation and Stability, **91**, 2347 (2006).
(52) L. Yuan, G. Z. Liang, J. Q. Xie, J. Guo and L. Li; Polymer Degradation and Stability, **91**, 2300 (2006).
(53) N. Grioui, K. Halouani, A. Zoulalian and F. Halouani; Thermochimica Acta, **440**, 23 (2006).
(54) J. Moltó, R. Font, J. A. Conesa and I. M. Gullón; J. Anal. Appl. Pyrolysis, **76**, 124 (2006).
(55) E. S. Freeman and B. Carroll; J. Phys. Chem., **62**, 394 (1958).

(56) D. A. Anderson and E. S. Freeman; J. Polym. Sci., **54**, 253 (1961).

(57) J. H. Sharp and S. A. Wentworth; Anal Chem., **41**, 2060 (1969).

(58) P. K. Chatterjee; J. Polym. Sci., **A-3**, 4253 (1965).

(59) H. H. Horowitz and G. Metzger; Ana. Chem., **35**, 1464 (1963).

(60) A. P. Mishra, V. Tiwari, R. Singhal and S. K. Gautam; Thermons, 90 (2002)

INRODUCTION

The constants, which are used to measure the strength of acid or bases are known as dissociation constants. These constants are also known as acidity constant, ionization constant or formation constant.

The dissociation or ionization constant is determined by determining one of the species, at equilibrium. The activity or concentration of the others can be calculated from the amount of the acid or base initially introduced and the stoichiometry of the acid base equilibrium.

For the measurement of dissociation constants, various methods have been developed, such as (i) potentiometry including pH metry[1] (ii) spectrophotometry, (iii) conductometry, (iv) solubility measurements[2], (v) cryoscopy[3], (vi) measurements of the rates of acid catalyzed hydrolysis of esters[4], (vii) measurement of the relative distribution of an acid between two immiscible solvents[5] and (viii) magnetic measurements.

For the very weak acids of pK range between 11 and 14, the method of electrical conductance is useful. However, due to more time consuming[6] and contamination of carbon dioxide, this method is not widely used.

When the acid is sparingly soluble and acid strengths are very high or very low, spectrophotometer method is considered to be an ideal method but, this method is also more time consuming. It is applicable if at least one of the species at equilibrium absorbs characteristically in the ultraviolet or visible region and the relevant ionic species show absorption maxima at different wavelengths. The use of Raman spectra and nuclear magnetic constants are also known to be used for a number of acids, which are regarded as strong in aqueous solution[7].

Potentiometry is mostly used for the determination of dissociation constants of acids because it is economical in time. Further, it can be used for acids of pKa range from 2 to 11 units[6]. For this measurement, glass and calomel electrodes have been used and carbonate free potassium hydroxide is the best alkali to use as a titrant.

The potential generated by the hydrogen ions, in the solution of an acid in a given medium is measured by an electronic potentiometer assembly. The

relationship between the potential of glass electrode and the pH of the solution has the general form:

$$-\log[H^+] = pH = \frac{E_0 - E_c}{0.0591} \text{ at } 25^\circ C$$

where E_0 is the observed potential and E_c is the potential of the calomel electrode. The various terms in above equation change with time. So, this electrode cannot be used as a primary standard. However, it does provide a very convenient way of comparing the pH of a series of solutions. So, it is calibrated before and after use with a pair of known buffers, the pH of one of which must lie near to the pH region to be measured. The correctness of the results depends upon the exactness of the calibration of pH-meter. The reference solutions of known pH are preferred due to three primary reasons[8]:

1. Saturated calomel reference electrodes are not highly reproducible and this is particularly true of the small immersion type electrode.
2. The potentials of the commercial glass electrodes vary widely and the symmetry potentials may fluctuate from day to day.
3. The pH meter is usually calibrated to read directly in pH units.

For very low pK_a values, this method does not give accurate results. In such cases, more sensitive instruments should be used.

The activity of the hydrogen ions is measured directly by pH metry. So, one can get reliable values of dissociation constant by this method. However, there are certain difficulties in mixed aqueous media and nonaqueous media.

There are many applications of dissociation constants. The nature of the functional groups can be determined by simple comparison of acidity or dissociation constant of the unknown compound with those of known compounds. The dissociation or formation constant also provide useful informations about structure, tautomeric equilibria, solvent-solute interactions etc.[9].

For water-insoluble compounds, the formation constant and other thermodynamic properties are measured in purely non-aqueous organic solvent or in a mixture of two solvents, one of which may be water. A solvent mixture containing water and water-miscible organic solvent is known as mixed aqueous

medium. A number of work has been done in non-aqueous and mixed-aqueous media[10-15].

A literature survey shows that various workers studied the dissociation constant of a number of substances[16-22]. Grunwald[23] measured ionization of formic, acetic and benzoic acids by differntial potentiometry. Marshall and Grunwald[24] measured thermodynamic parameters for the ionization reactions of acetic and chloroacetic acids in aqueous ethanol. The ionization constants of various other acids in pure and mixed solvents have also been studied[25-31].

Feng and Waki[32] determined formation constant of some compounds by spectrophotometry. Allen et al. determined the acid dissociation constants of ionizable drugs by using multiwavelength spectrophotometer[33]. Spectrophotometric determination of the dissociation constants of methyl yellow in mixed protic solvents have also been reported[34]. Urquiza and Beltran[35] determined the dissociation constants of sulfonated azo dyes by capillary zone electrophoresis and spectrophotometry methods. Lachenwitzer[36] have been reported dissociation constant for bisulphate by using subtractively normalized interfacial Fourier transform infrared spectroscopy. Evagelou et al.[37] determined the dissociation constants of the cephalosporins, cefepime and cefpirome by using UV spectrometry and pH potentiometry. Kadar et al.[38] have been reported the spectrophotometric determination of dissociation constants of crown ethers.

The effect of solvent on formation constant was studied by Fedorov et al.[39]. Rengaraj et al.[40] determined the formation constant of some Schiff bases and their metal complexes. The proton-ligand dissociation constant of mercaptotriazoles was studied by Saraswathi et al.[41]. The dissociation constants of some novel polydentate ligands have also been reported[42]. Potentiometric studies on some binary and ternary complexes of copper containing dipicolinic acids and amino acids have also been reported[43].

Determination of dissociation constants of cytokinins[44], phosphinate group in phosphinic pseudopeptides[45], labile drug[46], pharmaceutical active xanthones[47], 21 amino acids[48] etc. have been reported by using capillary zone electrophoresis. Some work have been reported in Schiff bases[49-52].

In the present work, the dissociation constant of some Schiff bases are studied in DMF-water mixtures at 308.15K.

EXPERIMENTAL

The chemicals used were of B.D.H Analar grade. All solutions used for the titration are prepared using distilled water. Following are the concentrations of the solutions used for the titration.

Solutions	Concentration (M)
Nitric acid	1.0
Sodium hydroxide	0.5
Sodium nitrate	1.0
Schiff base (in DMF)	0.1

Nitric acid and sodium hydroxide were standardized by titrating with 0.1 N NaOH and 0.05 M succinic acid solution respectively.

The DMF used was of S. Merck and was purified by the reported method [53].

The buffer solutions used for the calibration of pH meter were 0.05 M potassium hydrogen phthalate and 0.01 M Borax buffer.

A systronic pH meter (Model No. EQ 664) was used for the pH determination. The systronic glass electrode and a saturated calomel electrode were used as indicator and reference electrodes respectively. Before operation, the glass electrode was immersed in 0.1 M HCl for twenty minutes. Then, it was washed thoroughly with distilled water.

Before measurement, the pH meter was calibrated with buffer solution of known pH.

Calvin Bjerrum pH titration :

The following sets of mixtures were prepared for titration:

(I) 2 ml HNO_3 (1.0M) + 4 ml water + 30 ml DMF + 4.0 ml $NaNO_3$ (1.0 M).

(ii) 2 ml HNO_3 (0.1M) + 4 ml water + 28 ml DMF + 2.0 ml ligand solution (0.1M) + 4.0 ml $NaNO_3$ (1.0 M).

Thus, total volumes (V^0) in each set = 40.0 ml and DMF: water ratio 60:40 (v/v).

The above mentioned solutions were allowed to attain a constant temperature (308.15 K) and then titrated against standard NaOH solution (0.5 M) under an inert atmosphere of nitrogen. The change in the pH of solution with each addition of alkali was recorded and is given in Tables 6.1.

THEORY

In the present work Schiff bases are of HL type. Thus, the equilibria are,

$$L + H \leftrightarrow HL$$

In general, these equations can be represented as:

$$LH_{j-1} + H \leftrightarrow LH_j$$

The thermodynamic proton-ligand stability constant (TK_j^H) is given by:

$$TK_j^H = \frac{\left[LH_j\right]}{\left\{\left[LH_{j-1}\right]\left[H\right]\right\}} \quad \text{... (6.1)}$$

TK_j^H is reciprocal of the thermodynamic dissociation constant of the acid LH_j dissociating as:

$$LH_i = LH_{i-1} + H$$

The overall thermodynamic proton-ligand stability constant β_j^H is given by:

$$T\beta_j^H = \frac{\left[LH_j\right]}{\left[L\right]\left[H\right]^j} \quad \text{... (6.2)}$$

and it refers to the reaction:

$$L + JH \leftrightarrow LH_j$$

The stoichiometric proton-ligand stability constant is given by:

$$K_j^H = \frac{\left[LH_j\right]}{\left\{\left[LH_{j-1}\right]\left[H\right]\right\}} \quad \text{... (6.3)}$$

and

$$\beta_j^H = \frac{\left[LH_j\right]}{\left[L\right]\left[H\right]^j} \quad \text{... (6.4)}$$

An inert electrolyte is used to determine the stability constant in a

particular salt medium. Sodium nitrate is mostly preferred as supporting electrolyte, because of very slight complexing tendency of nitrate ion. Generally, the competition between nitrate ion and the ligand under study is minor importance. The molar concentrations are used in place of activities.

For the determination of dissociation constants, Bjerrum[54] introduced a relation for the determination of $\bar{n}_H$, which is defined as average number of hydrogen bound to each ligand.

$$\bar{n}_H = \{K_1^H [H] + 2K_1^H K_2^H [H]^2 + ...JK_1^H K_2^H [H] ... K_j^H [H]^j\} / \{1 + K_1^H [H] + K_1^H K_2^H [H]^2.....K_1^H K_2^H.....K_j^H [H]^j \quad ... (6.5)$$

From equation (6.4), we can write

$$\bar{n}_H = \frac{\sum_{j=1}^{\eta} j\beta_j^H [H]^j}{\sum_{j=1}^{\eta} \beta_j^H [H]^j} \quad : \left(\beta_0^H = 1\right) \qquad \ldots (6.6)$$

Equation (6.6) is called Bjerrum formation function of the system.

The determination of dissociation or formation constants from experimental data comprises the following three steps: (i) evaluation of formation curve of the system (ii) calculation of stoichiometric K`s of the system by direct solution of the formation function and (iii) conversion of stoichiometric constants into thermodynamic constants.

When the system consists of a ligand, which is a conjugated base of a weak acid, the pH-metric method introduced by Bjerrum has been widely used. This method is known as "Bjerrum-Calvin pH titration technique".

In this technique, by potentiometer, the concentration of H^+ ions is measured. Thus, a large amount of data can be obtained in a short period of time. The Irving and Rossotti method[55] has some advantages, such as:

(i) This method is valid for both pure water and for the mixed solvents.

(ii) In this method, it is not necessary to convert the pH-meter reading in to stoichiometric hydrogen ion concentration.

(iii) It is not necessary to know the stoichiometric concentration of neutral salt added to maintain the ionic strength constant.

Due to these advantages, this method is used in the present work. In this method, the pH-meter is standardized using an aqueous buffer. The pH (B) is measured for two solutions: (1) A mixture containing a mineral acid, a chelating agent and a neutral electrolyte to keep ionic strength constant and (2) A mixture same as above but without the chelating agent, when titrated against an alkali solution.

After each addition of standard alkali, the pH meter reading (B) is noted using a glass electrode-saturated calomel electrode combination. For both the titrations, same initial volume of the mixture and same standard alkali is used. The titration curves obtained in the above two titrations are designated as the reagent or ligand titration curve and the acid titration curve respectively.

The possible hydrolysis reactions are ignored because (i) fresh reagent solutions were used in pH titrations, (ii) titration times were of the order of one hour, (iii) there were no observable drifts with time in the meter readings and (iv) the concentrations of the mineral acid or alkali in the solutions were small.

Usually, a pH-meter calibrated with an aqueous buffer is used for aqueous solutions only. However, for the mixed aqueous media, especially aqueous dioxane solutions, Van Uitert and Haas[56] gave a relation between the glass electrode reading B in dioxane-water medium and the stoichiometric hydrogen ion concentration of the same in mixture of varied composition and ionic strength. They reported the relation:

$$-\log\left[H^{+}\right] = B + \log f + \log U_H^0 \qquad \text{... (6.7)}$$

where f is the activity coefficient of the hydrogen ions in the solvent mixture under consideration at the same temperature and ionic strength, and U_H^0 is a correction factor at zero ionic strength, which depends only on the solvent composition and temperature. U_H^0 is taken as unity in aqueous media. The values of U_H^0 and f are reported in literature[56]. The meter reading in any aqueous dioxane solution can, therefore, be converted into hydrogen ion concentration

using equation (6.7), provided that correction factor for the appropriate solvent, salt medium, and temperature, has been determined.

Equation (6.7) can be written as:

$$1/anti\log B = [H^+]\, fU_H^0 \qquad \text{... (6.8)}$$

$$\therefore \left[H^+\right] = \frac{1}{\left[anti\log B\right]\left[fU_H^0\right]} \qquad \text{... (6.9)}$$

Substituting for $[H^+]$ in equation (6.5) we get,

$\bar{n}_H$ = $(K_1^H/f\,U^0_H)[1/\text{antilog B}] + ...+ ((JK_1^H\,K_2^H...K_J^H)/(f\,U^0_H)^J)[1/\text{antilogB}]^J$
$/(1+K_1^H/f\,U^0_H))[1/\text{antilog B}]+..+ ((K_1^HK_2^H...K_J^H)/(f\,U^0_H)J)[1/\text{antilogB}]$ ...(6.10)

$$K_j^H = fU_H^0.pK_j^H \qquad \text{... (6.11)}$$

$$\beta_j^H = fU_H^0.p\beta_j^H \qquad \text{... (6.12)}$$

The proton-ligand constant, p_{Kj}^H can be obtained by the following methods:

1. Interpolation at half $\bar{n}_H$ values:

   At the following $\bar{n}_H$ values, log K_1 and log K_2 can be determined:

$$\log K_1 = \left(\bar{n}_H\right)_{0.5} \qquad \text{… (6.13)}$$

$$\log K_2 = \left(\bar{n}_H\right)_{1.5} \qquad \text{... (6.14)}$$

2. Mid point slope method:

   For H_2L type ligands:

$$K_1K_2[L]^2 = 1$$

or
$$\log K_1K_2 = 2pL_1 \qquad \text{... (6.15)}$$

From the measured mid-point slope, D, the ratio K_1/K_2 can be calculated by eq. (6.16):

$$D = \frac{-4.606}{\left(2+\sqrt{\left(K_1/K_2\right)}\right)} \qquad \text{... (6.16)}$$

The individual values of K_1 and K_2 were obtained by using K_1/K_2 values and relation (6.15).

RESULT AND DISCUSSION

The titration curves obtained in the above two titrations are usually referred as the acid titration curve and ligand or reagent titration curve respectively. The titration curves for NVK-1 and NVK-10 schiff bases are shown in Fig. 6.1.

From these curves, the average number of protons associated with ligand (n_H) can be calculated by Irring and Rossotti equation.

$$\overline{n_H} = Y - \left\{\left(V''-V'\right)\left(N^0+E^0\right)\right\} \Big/ \left\{\left(V^0+V'\right)T_L^0\right\} \quad \ldots (6.17)$$

where Y is the number of displaceable protons per ligand molecule. For all the schiff bases, Y is taken as one. V' and V" are the volume of alkali required at the same pH for both acid and ligand titration curves respectively. V^0 is the initial volume of the test solution. N^0, E^0 and T_L^0 are the initial concentration of the alkali, acid and ligand respectively.

The values of $\overline{n_H}$ for all the schiff bases are given in Table 6.1. The general plots for the variation of $\overline{n_H}$ with B are given in Fig. 6.2 for some schiff bases.

It is evident from Table 6.1 and Fig. 6.2 that $\overline{n_H}$ values are in between zero and one. The pK_1^H values at $\overline{n_H}$ = 0.5 were evaluated for each schiff base and is given in Table 6.1.

The plots of $\log\left[\bar{n}_H \Big/ \left(\bar{n}_H - 1\right)\right]$ against B is a straight line and are shown in Fig. 6.3. From these plots, $\log pK_1^H$ values were calculated at several B by the following equation.

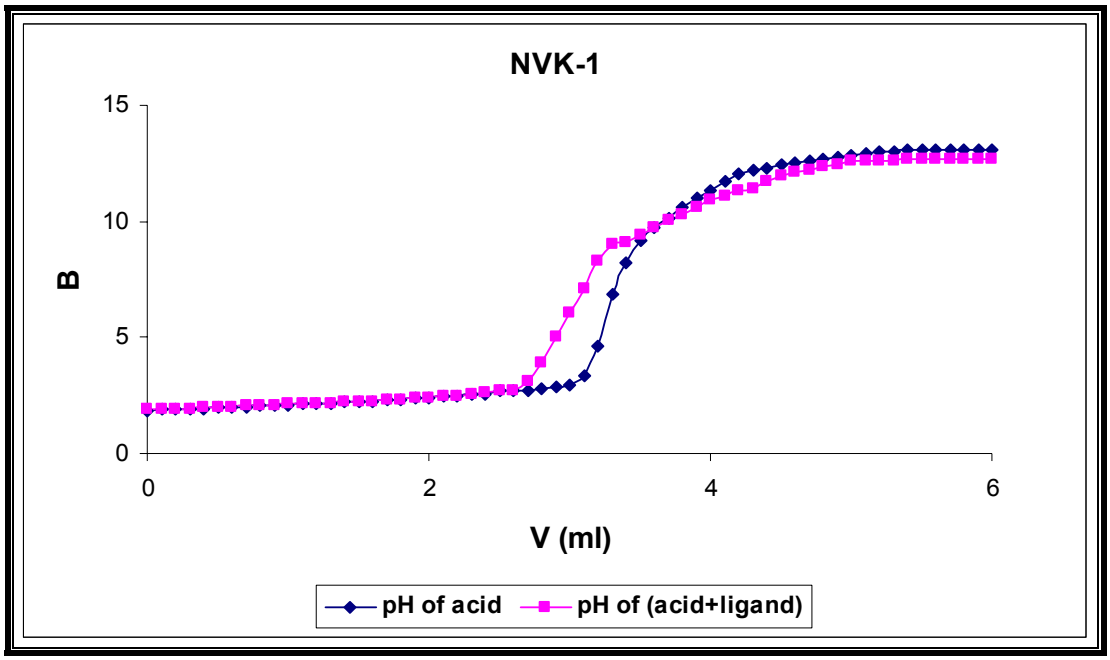
$$\log pK_1^H = B + \log\left[\bar{n}_H \Big/ \left(\bar{n}_H - 1\right)\right] \quad \ldots (6.18)$$

The average pK_1^H value is given in Table 6.1. It is evident from table that these pK_1^H values are in agreement with that obtained by the Fig. 6.2 at $\overline{n_H}$ = 0.5.

Comparison of pK_1^H values of all the schiff bases shows that, NVK-2 is more acidic whereas NVK-3 and NVK-8 are more basic than other studied schiff

bases. Both NVK-2 and NVK-3 contain methyl group. In NVK-2, it is at ortho position whereas in NVK-3 it is at para position. Thus, the presence of -CH_3 group at ortho position is found to increase the acidic character whereas the same group at para position decreases the acidity. Further, the presence of –OCH_3 and –OH groups increases the acidity as observed in NVK-1 and NVK-10 respectively. There are two –Cl groups at meta and para positions in NVK-9 which also shows high acidic character. However, when only one –Cl group is present as in NVK-6 at para position or at meta position along with fluorine group at para position as in NVK-4, the acidic character is decreased. The presence of –NH_2 group in NVK-8 cause an increase in basic character as expected.

Figure 6.1: The plot of pH (B) against volume of NaOH (V) for NVK-1 and NVK-10 at 308.15K.



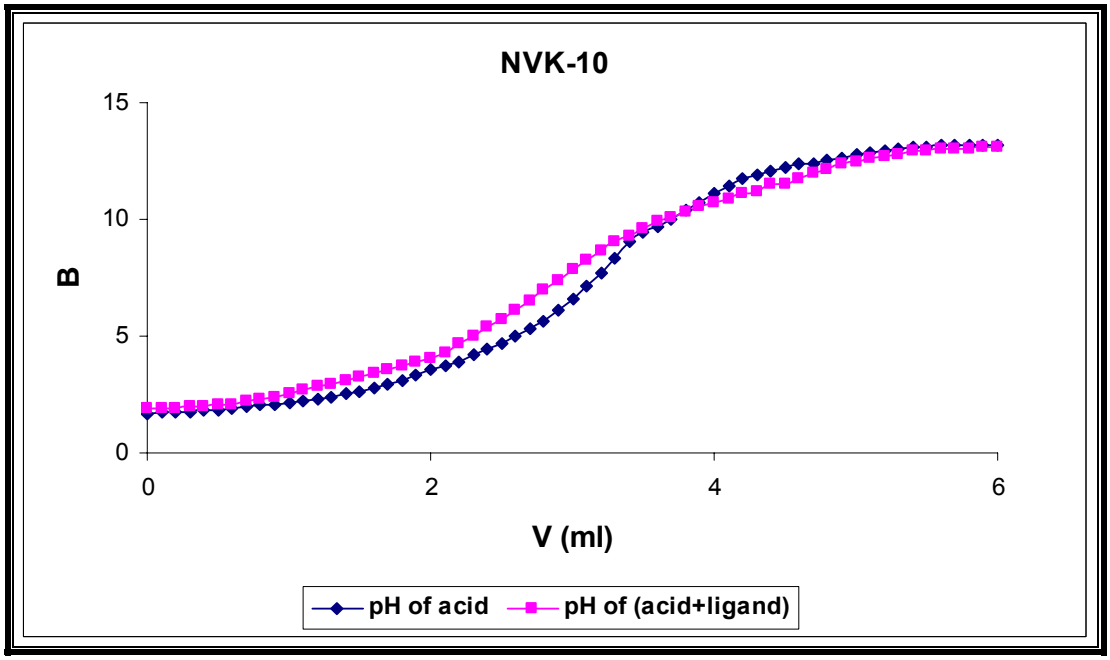
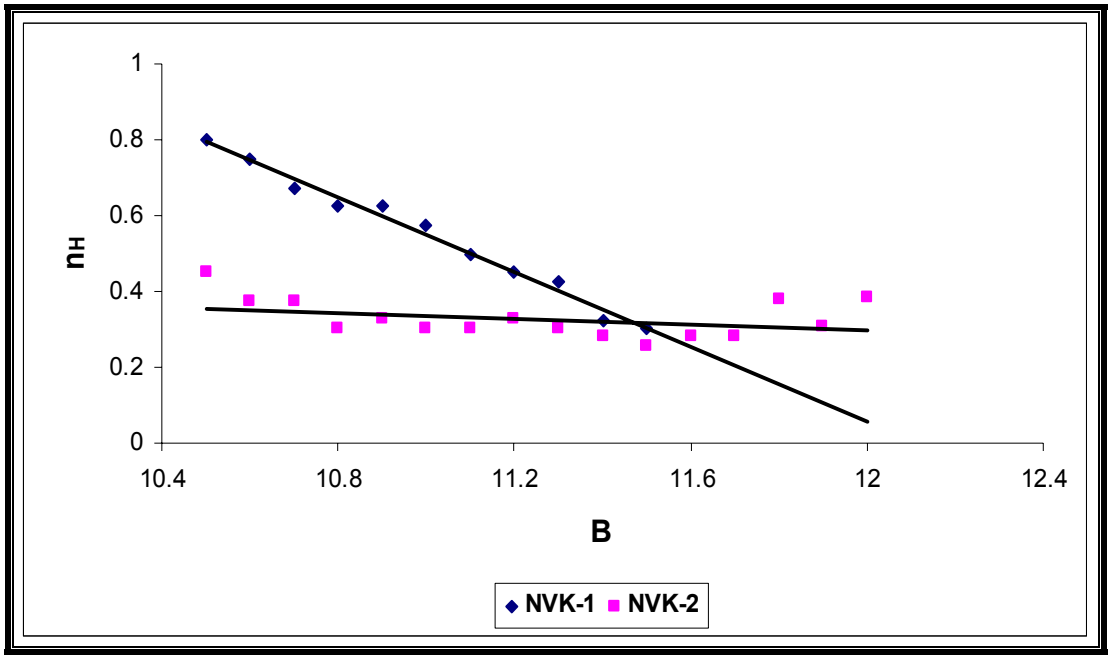


Figure 6.2: The plot of n_H against B for NVK-1, NVK-2 NVK-3 and NVK-4 at 308.15K.



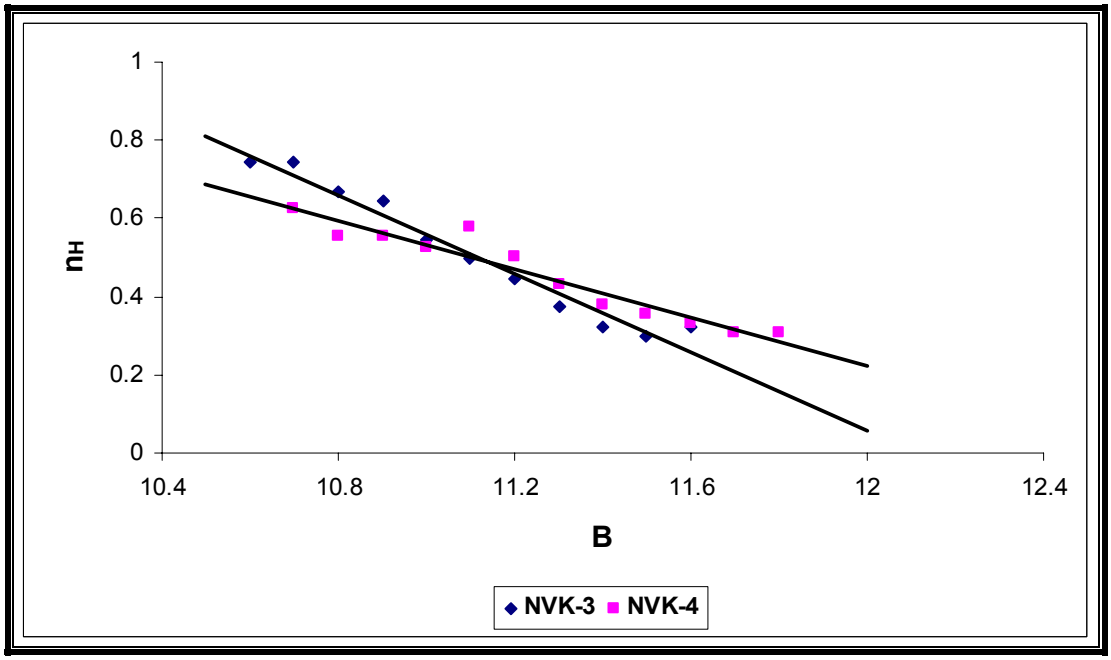
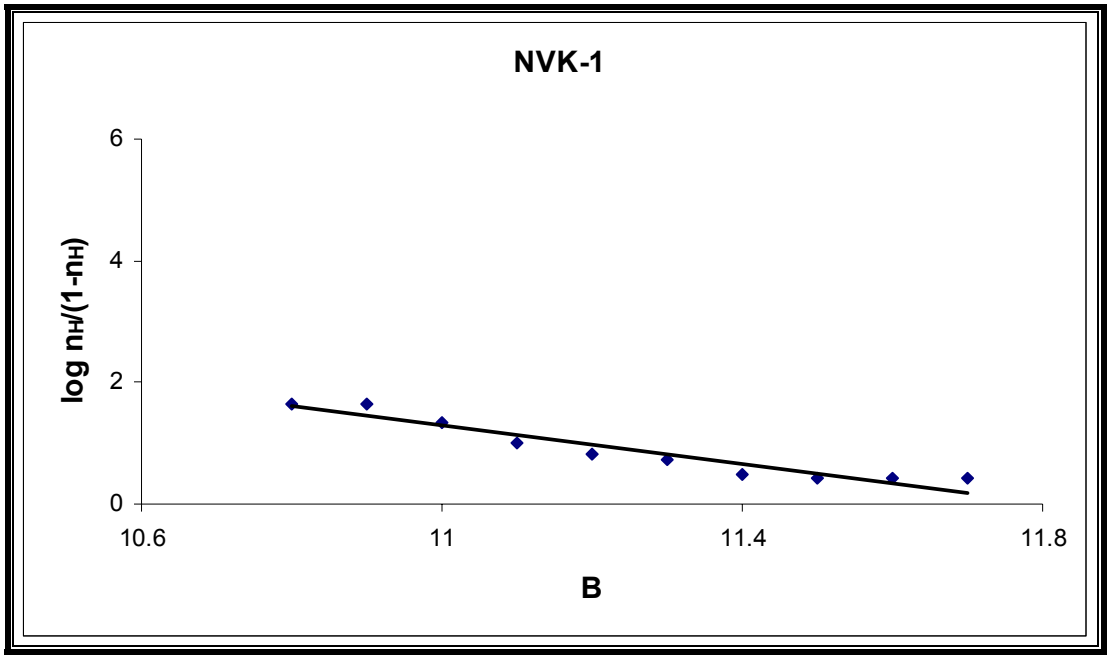


Figure 6.3: The Plot of log $n_H/(1-n_H)$ against B for NVK-1 and NVK-3 at 308.15K.



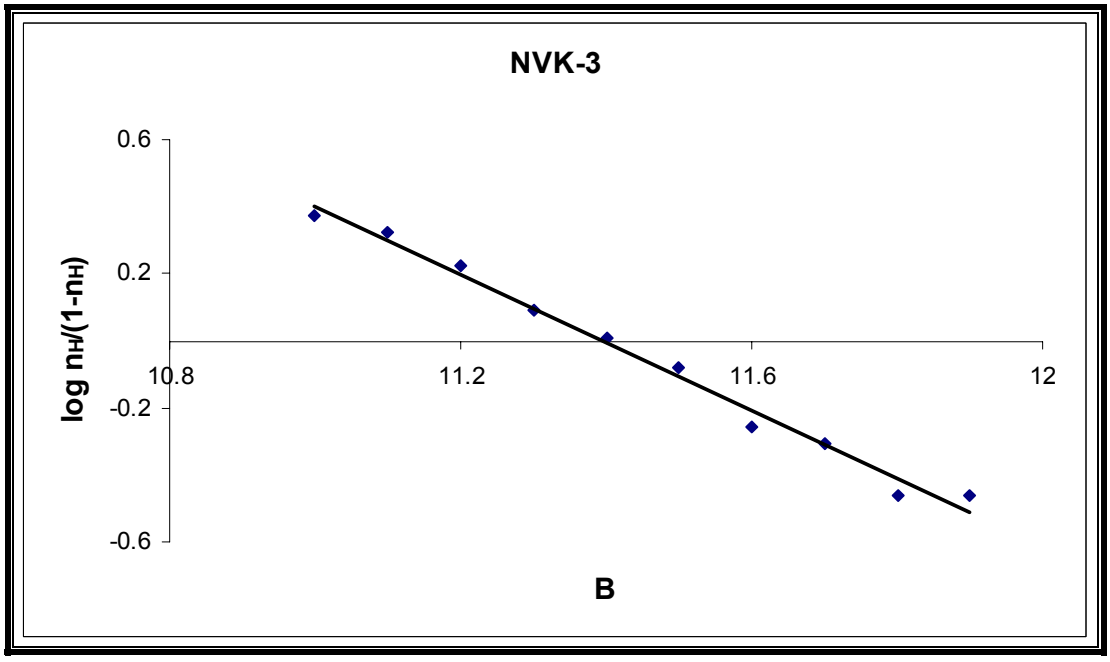


Table 6.1: The p^H(B), n_H, log $pK_1^H$and other terms for NVK schiff bases at 308.15K.

B	V'	V''	V''-V'	n_H	log $n_H/(1-n_H)$	log pK_1^H
NVK-1						
10.5	3.77	3.85	0.08	0.7989	3.9739	11.0992
10.6	3.8	3.9	0.1	0.7489	2.9818	11.0745
10.7	3.82	3.95	0.13	0.6737	2.0643	11.0148
10.8	3.82	3.97	0.15	0.6235	1.6558	11.0190
10.9	3.85	4	0.15	0.6237	1.6576	11.1195
11	3.9	4.07	0.17	0.5740	1.3476	11.1296
11.1	3.92	4.12	0.2	0.4991	0.9964	11.0984
11.2	3.95	4.17	0.22	0.4494	0.8161	11.1118
11.3	3.99	4.22	0.23	0.4249	0.7387	11.1685
11.4	4.02	4.29	0.27	0.3253	0.4822	11.0832
11.5	4.05	4.33	0.28	0.3008	0.4302	11.1337
Half-integral value= log pK_1^H= (B) $n_{H(0.5)}$= 11.10					**Ave. log pK_1^H= 11.09**	

B	V'	V''	V''-V'	n_H	log $n_H/(1-n_H)$	log pK_1^H
NVK-2						
10.5	4	4.22	0.22	0.4500	-0.0872	10.4128
10.6	4.02	4.27	0.25	0.3753	-0.2213	10.3787
10.7	4.05	4.3	0.25	0.3757	-0.2205	10.4795
10.8	4.07	4.35	0.28	0.3011	-0.3657	10.4343
10.9	4.1	4.37	0.27	0.3265	-0.3144	10.5856
11	4.12	4.4	0.28	0.3019	-0.3640	10.6360
11.1	4.15	4.43	0.28	0.3024	-0.3631	10.7369
11.2	4.2	4.47	0.27	0.3281	-0.3114	10.8886
11.3	4.24	4.52	0.28	0.3038	-0.3602	10.9398
11.4	4.28	4.57	0.29	0.2796	-0.4111	10.9889
11.5	4.3	4.6	0.3	0.2551	-0.4654	11.0346
11.6	4.34	4.63	0.29	0.2806	-0.4090	11.1910
11.7	4.38	4.67	0.29	0.2812	-0.4076	11.2924
11.8	4.45	4.7	0.25	0.3813	-0.2102	11.5898
11.9	4.47	4.75	0.28	0.3074	-0.3528	11.5472
12	4.55	4.8	0.25	0.3827	-0.2076	11.7924
Half- integral value= log pK_1^H= (B) $n_{H(0.5)}$= 11.00					**Ave. log pK_1^H= 10.93**	

Continue…..

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B	V'	V''	V''-V'	n_H	log $n_H/(1-n_H)$	log pK_1^H
NVK-3						
10.8	4.2	4.3	0.1	0.2489	0.4797	11.2797
10.9	4.22	4.35	0.13	0.3234	0.3206	11.2206
11	4.25	4.37	0.12	0.2983	0.3715	11.3715
11.1	4.27	4.4	0.13	0.3230	0.3214	11.4214
11.2	4.3	4.45	0.15	0.3725	0.2266	11.4266
11.3	4.32	4.5	0.18	0.4468	0.0929	11.3929
11.4	4.35	4.55	0.2	0.4961	0.0069	11.4069
11.5	4.37	4.59	0.22	0.5454	-0.0791	11.4209
11.6	4.4	4.66	0.26	0.6441	-0.2577	11.3423
11.7	4.42	4.69	0.27	0.6686	-0.3048	11.3952
11.8	4.44	4.74	0.3	0.7426	-0.4601	11.3399
11.9	4.47	4.77	0.3	0.7421	-0.4590	11.4410
Half- integral value= log pK_1^H= (B) $n_{H(0.5)}$= 11.40					**Ave. log pK_1^H= 11.37**	

B	V'	V''	V''-V'	n_H	log $n_H/(1-n_H)$	log pK_1^H
NVK-4						
10.7	4.25	4.4	0.15	0.6271	0.2258	10.9258
10.8	4.27	4.45	0.18	0.5527	0.0920	10.8920
10.9	4.3	4.48	0.18	0.5530	0.0925	10.9925
11	4.31	4.5	0.19	0.5283	0.0493	11.0493
11.1	4.35	4.52	0.17	0.5784	0.1372	11.2372
11.2	4.35	4.55	0.2	0.5039	0.0069	11.2069
11.3	4.37	4.6	0.23	0.4298	-0.1228	11.1772
11.4	4.4	4.65	0.25	0.3806	-0.2114	11.1886
11.5	4.42	4.68	0.26	0.3561	-0.2572	11.2428
11.6	4.45	4.72	0.27	0.3318	-0.3040	11.2960
11.7	4.47	4.75	0.28	0.3074	-0.3528	11.3472
11.8	4.5	4.78	0.28	0.3079	-0.3518	11.4482
Half- integral value= log pK_1^H= (B) $n_{H(0.5)}$= 11.08					**Ave. log pK_1^H= 11.17**	

Continue…..

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B	V'	V''	V''-V'	n_H	log $n_H/(1-n_H)$	log pK_1^H
NVK-5						
10.5	4.07	4.12	0.05	0.8752	0.8459	11.3459
10.6	4.1	4.17	0.07	0.8254	0.6746	11.2746
10.7	4.12	4.22	0.1	0.7507	0.4787	11.1787
10.8	4.15	4.25	0.1	0.7508	0.4791	11.2791
10.9	4.17	4.27	0.1	0.7510	0.4794	11.3794
11.0	4.2	4.32	0.12	0.7014	0.3708	11.3708
11.1	4.25	4.37	0.12	0.7017	0.3715	11.4715
11.2	4.27	4.47	0.2	0.5030	0.0053	11.2053
11.3	4.3	4.52	0.22	0.4537	-0.0806	11.2194
11.4	4.32	4.57	0.25	0.3795	-0.2135	11.1865
11.5	4.32	4.6	0.28	0.3051	-0.3576	11.1424
Half- integral value= log pK_1^H= (B) $n_{H(0.5)}$= 11.20					**Ave. log pK_1^H= 11.28**	

B	V'	V''	V''-V'	n_H	log $n_H/(1-n_H)$	log pK_1^H
NVK-6						
10.5	3.82	3.87	0.05	0.8745	0.8431	11.3431
10.6	3.85	3.92	0.07	0.8244	0.6716	11.2716
10.7	3.9	3.97	0.07	0.8246	0.6722	11.3722
10.8	3.95	4.05	0.1	0.7497	0.4765	11.2765
10.9	3.97	4.1	0.13	0.6748	0.3170	11.2170
11.0	4.02	4.15	0.13	0.6751	0.3177	11.3177
11.1	4.07	4.22	0.15	0.6256	0.2230	11.3230
11.2	4.1	4.27	0.17	0.5760	0.1330	11.3330
11.3	4.15	4.35	0.2	0.5017	0.0030	11.3030
11.4	4.17	4.43	0.26	0.3525	-0.2641	11.1359
11.5	4.2	4.47	0.27	0.3281	-0.3114	11.1886
11.6	4.25	4.55	0.3	0.2542	-0.4674	11.1326
Half- integral value= log pK_1^H= (B) $n_{H(0.5)}$= 11.30					**Ave. log pK_1^H= 11.27**	

Continue…..

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B	V'	V''	V''-V'	n_H	log $n_H/(1-n_H)$	log pK_1^H
NVK-7						
10.5	3.9	4	0.1	0.7494	0.4758	10.9758
10.6	3.92	4.02	0.1	0.7495	0.4761	11.0761
10.7	3.97	4.07	0.1	0.7498	0.4767	11.1767
10.8	4	4.1	0.1	0.7500	0.4771	11.2771
10.9	4.03	4.15	0.12	0.7002	0.3684	11.2684
11.0	4.07	4.2	0.13	0.6755	0.3184	11.3184
11.1	4.1	4.27	0.17	0.5760	0.1330	11.2330
11.2	4.15	4.35	0.2	0.5017	0.0030	11.2030
11.3	4.2	4.42	0.22	0.4525	-0.0828	11.2172
11.4	4.22	4.45	0.23	0.4279	-0.1262	11.2738
11.5	4.27	4.52	0.25	0.3788	-0.2148	11.2852
11.6	4.32	4.6	0.28	0.3051	-0.3576	11.2424
11.7	4.37	4.65	0.28	0.3058	-0.3560	11.3440
Half- integral value= log pK_1^H= (B) $n_{H(0.5)}$= 11.26					**Ave. log pK_1^H= 11.22**	

B	V'	V''	V''-V'	n_H	log $n_H/(1-n_H)$	log pK_1^H
NVK-8						
10.7	3.8	3.85	0.05	0.8744	0.8428	11.5428
10.8	3.82	3.88	0.06	0.8494	0.7512	11.5512
10.9	3.85	3.92	0.07	0.8244	0.6716	11.5716
11	3.87	3.95	0.08	0.7994	0.6005	11.6005
11.1	3.9	4.02	0.12	0.6993	0.3666	11.4666
11.2	3.93	4.07	0.14	0.6494	0.2678	11.4678
11.3	3.95	4.15	0.2	0.4994	-0.0010	11.2990
11.4	3.97	4.22	0.25	0.3746	-0.2226	11.1774
11.5	4	4.27	0.27	0.3250	-0.3174	11.1826
11.6	4.05	4.35	0.3	0.2509	-0.4752	11.1248
Half- integral value= log pK_1^H= (B) $n_{H(0.5)}$= 11.30					**Ave. log pK_1^H= 11.40**	

Continue…..

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B	V'	V''	V''-V'	n_H	log $n_H/(1-n_H)$	log pK_1^H
NVK-9						
10.5	4.1	4.17	0.07	0.8254	0.6746	11.1746
10.6	4.12	4.2	0.08	0.8005	0.6035	11.2035
10.7	4.15	4.25	0.1	0.7508	0.4791	11.1791
10.8	4.17	4.3	0.13	0.6763	0.3199	11.1199
10.9	4.2	4.35	0.15	0.6267	0.2250	11.1250
11.0	4.22	4.4	0.18	0.5522	0.0911	11.0911
11.1	4.25	4.45	0.2	0.5028	0.0049	11.1049
11.2	4.3	4.52	0.22	0.4537	-0.0806	11.1194
11.3	4.32	4.57	0.25	0.3795	-0.2135	11.0865
11.4	4.35	4.62	0.27	0.3303	-0.3069	11.0931
11.5	4.37	4.65	0.28	0.3058	-0.3560	11.1440
Half-integral value= log pK_1^H= (B) $n_{H(0.5)}$= 11.12					**Ave. log pK_1^H= 11.13**	

B	V'	V''	V''-V'	n_H	log $n_H/(1-n_H)$	log pK_1^H
NVK-10						
10.6	3.87	3.95	0.08	0.7994	0.6005	11.2005
10.7	3.9	3.99	0.09	0.7745	0.5358	11.2358
10.8	3.92	4.05	0.13	0.6744	0.3162	11.1162
10.9	3.95	4.1	0.15	0.6246	0.2211	11.1211
11.0	3.97	4.12	0.15	0.6247	0.2214	11.2214
11.1	4	4.2	0.2	0.5000	0.0000	11.1000
11.2	4.05	4.27	0.22	0.4506	-0.0861	11.1139
11.3	4.07	4.35	0.28	0.3011	-0.3657	10.9343
11.4	4.1	4.37	0.27	0.3265	-0.3144	11.0856
11.5	4.12	4.42	0.3	0.2520	-0.4724	11.0276
Half-integral value= log pK_1^H= (B) $n_{H(0.5)}$= 11.10					**Ave. log pK_1^H= 11.12**	

REFERENCES

(1) H. S. Harned and B. B. Owen, "The Physical Chemistry of Electrolytic Solutions", Reinhold, New York (1958).

(2) Kreb and Speakman, J. Chem. Soc., 593 (1945).

(3) R. J. Gillespie and S. Solomons, J. Chem. Soc., 1796 (1957).

(4) H. M. Dawson, G. V. Hall and A. Key, J. Chem., Soc., 2844 (1928).

(5) Farmer and Warth. J. Chem. Soc., **85**, 1713 (1904).

(6) A. S. Albert and E. P. Serjeant, "Ionization Constants of Acids and Bases",Methuen and Co., Ltd.

(7) O. Redlich and G. C. Hood, Disc. Faraday Soc., **24**, 87 (1957).

(8) R. G. Bates, "Electrometric pH determination", John Wiley and Sons, Inc.

(9) D. H. McDanial, H. C. Brown and O. Haffinger,"Dissociation constants" in Determination of organic structures by Physical methods" Editors: E. A. Brande and F. Nachod, Academic Press, Inc, N. W. (1955).

(10) B. S. Garg, M. Chaudhury and R. Dixit, Ind. Acad. Of Sci., **104**, 17 (1992).

(11) A. Gupta and B. S. Pannu, Asian J. Chem., **76,** 480 (1999).

(12) E. K. Ramaiah and K. Ram, J. Indian Chem. Soc., **74**, 90 (1997).

(13) M. A. Ghandour, E. A. Kasim, A. H. Amrallah, N. A. Abdalla and O. A. Farghly, Ind. J. Chem., **76**, 480 (1999).

(14) K. Saraswathi, S. S. Babu and Y. Sunandamma, Asian J. Chem., **12**, 313 (2000).

(15) R. V. Kinhikar and V. S. Jamode, Asian J. Chem., **6**, 174 (1994).

(16) H. S. Harned and T. R. Defell, J. Am. Chem. Soc., **63**, 3308 (1941).

(17) S. R. Jagasia and B. C. Haldar, J. Ind. Chem. Soc., **40**, 287 (1963).

(18) B. C. Patel and S. R. Patel, Ind. J. Chem., **9**, 1354 (1971).

(19) A. W. Domagala, P. K. Witold, C. A., **93**, 186461r (1981).

(20) A. Abbaspour and M. A. Kamyabi, J. Chem. Eng. Data, **46**, 623 (2001).

(21) H. S. Harned and R. S. Done, J. Am. Chem. Soc., **63**, 2579 (1941).

(22) A. Patterson and W. A. Felsing, J. Am. Chem. Soc., **64**, 1480 (1942).

(23) E. Grunwald, J. Am. Chem. Soc., **73**, 4934 (1951).

(24) H. P. Marshall and E. Grunwald, J. Am. Chem. Soc., **76**, 2000 (1954).

(25) H. S. Harned and Bridsall, J. Am. Chem. Soc., **65**, 147 (1943).

(26) M. Yasuda, Bull. Chem. Soc., (Japan) **32**, 429 (1952).

(27) M. L. Dondon and J. Paris, J. Chim. Phys., **58**, 222 (1961).

(28) L. L. Spivak, Zh. Fiz. Khim. **44**, 440 (1970).; CA. **72**, 131860g (1970).

(29) N. Y. Lyakira, T. A. Levshina, B. U. Mamzurin, L. V Shikova and V. P.Yanov Savel, Tr. Mosk. Khim. Teknol. Inst. **70**, 25 (1972); CA., **78**, 135425y (1973).

(30) C. C. Panichaiakul and E. M. Woolley, Anal. Chem., **47**, 1860 (1975).

(31) C. P. Gupta, K. G. Sharma, R. P. Mathur and R. K. Mehta, Acta Chim. Acad. Sci., **111**, 19 (1982). Sons, Inc. New york, (1962).

(32) Q. Feng and H. Waki, Polyhedran, **7**, 291 (1988).

(33) R. I. Allen, K. J. Box, J. E. A. Comer, C. Peake and K. Y. Tam; J. Pharmaceutical & Biomed. Anal., **17**, 699 (1998).

(34) J. Fan, X. Shen and J. Wang; Talanta, **49**, 843 (1999).

(35) M. P. Urquiza and J. L. Beltrán; J. Chrom. A, **917**, 331 (2001).

(36) A. Lachenwitzer, N. Li and J. Lipkowski; J. Electroanalytical Chem., **532**, 85 (2002).

(37) V. Evagelou, A. T. Kakoulidou and M. Koupparis; J. Pharmaceutical & Biomed. Anal., **31**, 1119 (2003).

(38) M. Kadar, A. Biro, K. Toth, B. Vermes and P. Huszthy; Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, **62**, 1032 (2005).

(39) U. A. Fedorov, I. D. Isqev and M. Yu. Eike, Koord. Khim., **15**, 1162 (1989).

(40) K. Rengaraj, B. Sivasankar, M. Anbu and M. Palanichamy, Ind. Acad. Sci., **104**, 707 (1992).

(41) K. Saraswathi, S. S. Babu and Y. Sunandamma, Asian J. Chem., **12**, 313 (2000).

(42) D. Cao, H. K. Lin, Z. F. Zhou, S. R. Zhu, X. C. Su and Y. T. Chen, Can. J. Chem., **79**, 455 (2001).

(43) M. M. Khalil and A. E. Attia, J. Chem. Eng. Data, **44**, 180 (1999).

(44) P. Bartak, P. Bednar, Z. Stransky, P. Bocek and R. Vespalec; J. Chrom. A, **878**, 249 (2000).

(45) D. Koval, V. Kasicka, J. Jiracek, M. Collinsova and T. A. Garrow; J. Chrom. B: Anal. Tech. Biomed. & Life Sci., **770**, 145 (2002).

(46) E. Örnskov , A. Linusson and S. Folestad; J. Pharmaceutical & Biomed. Anal., **33**, 379 (2003).

(47) X. Wu, S. Gong, T. Bo, Y. Liao and H. Liu; J. of Chrom. A, **1061**, 217 (2004).

(48) I. Zusková, A. Novotná, K. Včeláková and B.av Gaš; J. of Chroma. B, In Press, Corrected Proof, Available online 29 March 2006,

(49) M. Palanichamy and M. Anbu , Ind. Acad. Sci., **109**, 105 (1997).

(50) M. Palanichamy and M. Anbu , Ind. Acad. Sci., **111**, 105 (1999).

(51) M. B. Halli and B. Angadi, J. Ind. Chem. Soc., **79**, 464 (2002).

(52) S. S. Hussein, J. Ind. Chem. Soc., **80**, 622 (2003).

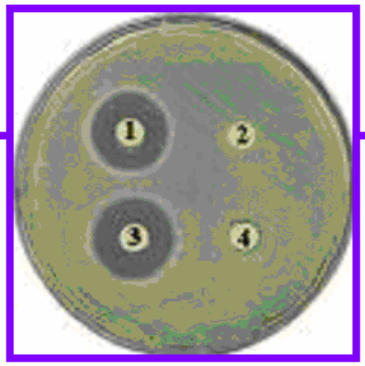
(53) J. A. Riddick, W. B. Bunger and Sakano, "Organic solvents-physical properties and methods for purification", IVth Edition, Techniques of Chemistry vol. II, A. Wiley-Interscience publication- John-Wiley, New York (1986).

(54) J. Bjerrum, Metal Ammine Formation in aqueous solution, P. Hasse and son, Copenhagen (1941).

(55) H. Irving and H. S. Rossoti, J. Chem. Soc., 2094 (1954).

(56) C. G. Van Uitert and C. G. Hass, J. Am. Chem. Soc., **75**, 451 (1953).

PART-III



BIOLOGICAL ACTIVITIES

INTRODUCTION

Biological activity spectrum of a compound represents the pharmacological effects, physiological and biochemical mechanisms of action, specific toxicity which can be revealed in compounds interaction with biological system. Further, it describes the intrinsic properties of the compound which depends on its structure.

A literature survey shows that quinoline derivatives possess various biological activities[1-5]. Further, the schiff bases have been reported to demonstrate a wide rage of pharmacological activities[6-10], which include antibacterial[11-12], antitumor[13], anti-inflammatory[14], antifungal[15], anti-HIV[16], antipyretic [17,18]etc.

With a variety of biological activity, chalcones are useful in pharmaceuticals. They are associated with biological activities like anti-inflammatory[19], antiulcer[20], fungicidal[21], antiviral[22], antitumor[23], anticancer[24], bactrericidal[25], insecticidal[26], antimalarial[27] etc., while pyrazolines are also reported to possess various biological activities like tranquilizing[28], anticonvulsant[29], herbicidal[30], antifungal[31], insecticidal[32], anti-inflammatory[33], antibacterial[34], antidiabetic[35], antidepresent[36] etc. Pyrimidine derivatives possess different biological activities such as antiviral[37], anticarcinogencic activity[38], antiinflammaroty[39], analgesic[40], antihypertensive[41], blood platelet aggregation inhibitory activity[42], anti-HIV[43] and antibacterial activity[44] etc.

Much research has been carried out with the aim to finding therapeutic values of pyrazole moiety. A large number of substituted pyrazole derivatives are prepared and tested for variety of biological activities like anthelmintic[45], CNS depressant[46], lipoxygenase inhibitor[47], antimicrobial[48], antioxidant[49], cardiovascular agent[50] and antiHIV[51] etc. Various imidazolinones are also known to exhibit a broad spectrum of biological activities such as antiparkinsonian[52], hypertensive[53], potent CNS depressant[54], antiviral[55], anticonvulsant[56], inflammatory[57,58], bactericidal[59], antitubercular[60], antimicrobial[61], anti- insecticidal[62], fungicidal[63] etc.

In this chapter, antibacterial activity of all the synthesized compounds has been studied in DMSO.

EXPERIMENTAL

The antibacterial activities of all the synthesized compounds, i.e., Schiff bases, Chalcones, imidazolinone derivatives, pyrazolines, thiopyrimidine etc. were studied in DMSO.

DMSO is a versatile non-aqueous dipolar aprotic solvent having a dielectric constant of 46.6 (25^oC) and a dipole moment of 3.9 D (25^oC). It is a highly polar but aprotic solvent, which can mix well with any liquid. It is also called a super solvent and exhibits quite interesting properties.

All the synthesized compounds were recrystallized prior to use. The solvent DMSO was also purified before use by standard method[64].

Two methods were adopted for the study: Agar disc diffusion method and Agar well diffusion method.

In Agar disc diffusion method, the concentration of compounds were less than that used in Agar well diffusion method.

For Schiff bases, chalcones and imidazolinone derivatives, Agar disc diffusion method was used.

Agar disc diffusion method[65]:

The antibacterial assay was evaluated by the method of agar disc diffusion method. The media used for the antibacterial assay were Mueller Hinton Agar No.2 and SDA media. The test strain (200 µl) was inoculated into the media (inoculums size 10^8cells/ml) when the temperature reached 40-42 °C and poured into Petri dishes (Hi-Medial). 20 µl of the test compound was impregnated in to sterile discs (7 mm, Hi-Media), allowed to dry and was introduced on the upper layer of the seeded agar plate. The plates were incubated overnight at 37 °C. The experiment was performed under strict aseptic conditions. Microbial growth was determined by measuring the diameter of zone of inhibition. For each bacterial strain controls were maintained where pure solvent was used instead of the extract. The result was obtained by measuring the zone diameter. The experiment was done three times and the mean values are presented.

Preparation of test compounds:

For all the compounds, the solutions were prepared in DMSO. These compounds were dissolved at a concentration 0.5mg/disc in DMSO.

Test microorganisms:

The bacterial strains studied are identified strains and were obtained from National Chemical Laboratory (NCL), Pune, INDIA. The investigated micro organisms are *Proteus mirabilis* NCIM2241 (PM), *Staphylococcus aureus* ATCC25923 (SA), *Bacillus cereus* ATCC11778 (BC), *E. coli* ATCC25922 (EC), *Candida tropicalis* ATCC4563 (CT), *Candida albicans* ATCC2091 (CA).

For pyrazoline and thiopyrimidine derivatives, Agar well diffusion method was used.

Agar well diffusion method[66,67]:

The antibacterial evaluation was done by agar well diffusion method using Mueller Hinton Agar No.2 as the nutrient medium. The agar well diffusion method was preferred to be used in this study since it was found to be better than the disc diffusion method as suggested by[67]. The bacterial strains were activated by inoculating a loop full of test strain in 25ml of N-broth and the same was incubated for 24h in an incubator at 37^{o} C. 0.2 ml of the activated strain was inoculated in Mueller Hinton Agar. Mueller Hinton Agar kept at 45^{o}C was then poured in the Petri dishes and allowed to solidify. After solidification of the media, 0.85 cm well was made in the plates using a sterile cork borer. Each well was filled with 0.1 ml of the test solution. The plates were incubated for 24 h at 37^{o}C. The mean value obtained for the three wells was used to calculate the zone of growth inhibition of each sample. The controls were maintained for each bacterial strain, where pure solvent (DMSO) was inoculated into the well. The inhibition zone formed by these compounds against the particular test bacterial strain determined the antibacterial activities of the synthetic compounds.

Preparation of the test compound

The synthesized test compounds were dissolved in DMSO at a concentration of 20 mg/ml.

Test microorganisms

The synthesized compounds were tested for its antibacterial activity against four Gram positive *Bacillus cereus* ATCC11778, Staphylococcus *aureus* ATCC29737, *Staphylococcus epidermidids* NCIM2493 and *Micrococcus luteus* ATCC10240, and three Gram negative bacteria viz. *Proteus mirabilis* NCIM2241, *Escherichia coli* ATCC25922 and *Klebsiella aerogenes* NICM2098 bacteria.

Microorganisms were obtained from National Chemical Laboratory (NCL), Pune, India. Microorganisms were maintained at 4°C on nutrient agar slants.

RESULTS AND DISCUSSION

Table 1: Activity of Schiff bases, Chalcones and Imidazolinone derivatives.

Comp. Code	PM	SA	BC	EC	CT	CA
NVK-1A	+	+	+	-	-	-
NVK-1B	+	+	-	-	-	-
NVK-1C	-	-	-	-	-	-
NVK-1D	-	-	-	+	-	-
NVK-1E	-	-	-	+	-	-
NVK-1F	+	-	-	-	+	-
NVK-1G	-	-	-	-	+	-
NVK-1H	-	-	-	+	-	-
NVK-1I	-	-	-	-	-	-
NVK-1J	-	-	-	-	-	-
NVK-2A	-	-	-	-	-	-
NVK-2B	-	-	-	-	+	-
NVK-2C	-	-	-	-	++	-
NVK-2D	-	-	-	-	-	-
NVK-2E	-	+	-	-	-	-
NVK-2F	-	-	-	-	-	-
NVK-2G	-	+	-	-	-	-
NVK-2H	-	-	-	-	+	-
NVK-2I	-	-	-	-	+	+
NVK-2J	-	+	+	-	-	-
PAIM-1	-	+	-	-	-	-
PAIM-2	-	-	-	-	-	-
PAIM-3	-	-	-	-	-	-
PAIM-4	-	-	+	-	-	+
PAIM-5	+	+	+	-	-	+
PAIM-6	-	-	-	-	-	-
PAIM-7	-	-	-	-	-	-
PAIM-8	-	-	-	-	-	-
PAIM-9	-		-	-	-	-
G	+++	++	++	+	-	-
Pc	+++	+++	++	++	-	-
Ns	-	-	-	-	-	+
Fu	-	-	-	-	++	++

(+) = 9-14mm (zone diameter)
(++) = 15-20mm (zone diameter)
(++) = 21-30mm (zone diameter)
Diameter of disc is 0.7cm

Table 1 shows the activity of schiff bases, chalcones and imidazolinone derivatives against different bacterial strains.

For comparison the antibacterial activity of Gentamicin (G), Piperacillin (Pc), Fluconazole (Fu) and Nystatin (Ns) were also reported.

It is evident from the Table 1 that most of these compounds do not exhibit activity against the studied bacteria. However, No.13 shows some significant activity against *Candida tropicalis* ATCC4563 (CT) as exhibited by drug Fluconazole (Fu).

The antibacterial activity of pyrazolines and thiopyrimidine derivatives which was studied by agar well diffusion method, are shown in Fig. 1-4. As it is evident from these figures that, these compounds are quite active against the studied bacteria.

PYRAZOLINES

The antibacterial activity of NVK(3A-3J) pyrazolines against Gram positive bacteria are shown in Fig. 1 while that of NVK (3A-3J) pyrazolines against Gram negative bacteria are shown in Fig. 2. *B. cereus* was the most susceptible Gram positive bacteria while *M. luteus* was the most resistant Gram negative bacterial strain. All the 10 pyrazolines showed activity against *B. cereus* but to a varied level. Maximum activity was shown by compound NVK-3E, followed by compound NVK-3G and NVK-3J. Minimum activity was shown by compound NVK-3H and NVK-3I. When *S. aureus*, the most resistant Gram positive bacteria was considered, all the ten compounds showed almost similar activity. Only compound NVK-3E, NVK-3F, NVK-3G and NVK-3J showed antibacterial activity against *M. luteus*; compound NVK-3E showed maximum activity. Compound NVK-3G showed maximum activity against *S. epidermidis* while compound NVK-3F and NVK-3I showed the least activity.

When Gram negative bacterial strains are considered, *E. coli* was the most resistant strain while *K. aerogenes* was the most susceptible strain. Compound NVK-3I did not show activity against *P. mirabilis* while compound NVK-3H did not show activity against *K. aerogenes*. Maximum activity was shown by compound NVK-3E against *K. aerogenes* followed by NVK-3A and NVK-3D; while all the compounds showed almost similar activity against *P. mirabilis*.

The obtained results showed different levels of activities against both Gram positive and Gram negative bacteria. Gram positive bacteria were found to be more susceptible than Gram negative bacteria. This could be due to the fact that the cell wall of Gram positive bacteria is less complex and lack the natural sieve effect against large molecules due to the small pores in their cell envelope[73]. Gram negative bacteria which are responsible for a large number of infectious diseases have a unique outer membrane that contains lipo polysaccharides which render them impermeable to certain antibacterial compounds[74].

Amongst the ten pyrazoline derivatives synthesized, only R is different in all the 10 compounds. It is observed that compound NVK-3E which has nitro group at para position shows the best activity. This is followed by compound NVK-3G and NVK-3J which has para methyl and para bromo groups respectively.

This differential activity of the compounds is because of the structural differences. The presence of nitro group enhances the activity. However, the methyl and bromide group attached at para position also increases the activity. The presence of nitro group at meta position decreases the activity which may be due to some steric hindrance. Other substituents are not very effective in inhibition.

A rapid and effective response to challenge pathogens is essential for the survival of all living organisms. The need for efficient agents increases with the expanding number of immunodeficient patients and with the emergence of bacterial and fungal pathogens resistant to current therapies[75].

From the above results it can be concluded that the pyrazoline derivatives which had nitro group showed best antibacterial activity provided the nitro group was at para position while the same nitro group at meta position decreased the activity. The next best was pyrazoline derivatives with methyl and bromo group at para position. Lastly, these compounds showed better antibacterial activity towards Gram positive bacteria.

THIOPYRIMIDINE

The antibacterial activity of NVK(4A-4K) pyrazolines against Gram positive bacteria are shown in Fig. 3 while that of NVK (4A-4K) pyrazolines against Gram negative bacteria are shown in Fig. 4.

All the 11 thiopyrimidines synthesized showed different activity against different bacterial strains. This may be because all the 11 compounds have different structures. Our earlier findings[76,77] suggest that there is a direct correlation between structure and antibacterial activity.

M. luteus was the most resistant Gram positive bacteria followed by *S. epidermidis*. Only 4 compounds NVK (4A-4D) showed activity against *M. luteus* while all others were inactive. Compound NVK-4B had nitro group at meta position and compound NVK-4E had same nitro group but at para position; this small structural difference resulted in inactivity. A similar effect was observed between compound NVK-4D and NVK-4F.

Only 5 compounds (NVK-4A, NVK-4B, NVK-4D, NVK-4E and NVK-4F) showed activity against *S. epidermidis*. The maximum activity was shown by compound NVK-4F which had amino group at meta position. On the other hand, 8 compounds showed activity against *B. cereus*; only compounds (NVK-4I – NVK-4K) were ineffective against this bacterial strain. Maximum activity was shown by compound NVK-4A. Only 7 compounds showed activity against *S. aureus* (Fig. 3). In this case also, maximum activity was shown by NVK-4A.

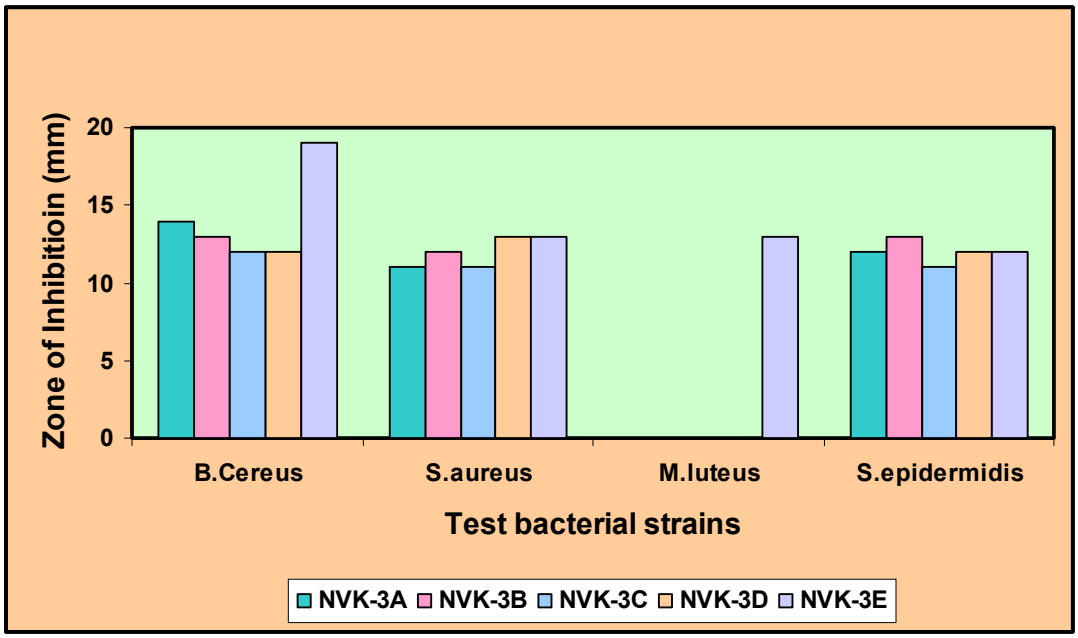
The potential of the synthesized thiopyrimidine derivatives against Gram negative bacteria are shown in Fig. 4. *E. coli* was the most resistant strain only compound NVK-4J showed some activity. The thiopyrimidine derivatives showed more activity towards *K. aerogenes* as compared to *P. mirabilis*. Maximum antibacterial activity was shown by compound NVK-4A against both these Gram negative strains.

The differential activity of the compounds against different bacterial strains is because of the differences in their structures. All the compounds have common central moiety. The compound NVK-4A, which showed maximum activity, consisted of p-methoxy benzyldehyde; while the least activity was shown by Compound NVK-4I, NVK-4J and NVK-4K. The R groups in these three

compounds were 4-Cl, 4-Br and 2-methyl which decreased the antibacterial activity.

From the above results, it can be concluded that thiopyrimidine derivative which had p-methoxy benzyldehyde showed best antibacterial activity. All the other groups in fact decreased the activity. All the eleven compounds showed better antibacterial activity towards Gram positive bacteria than Gram negative bacteria. The results also suggest that there is no universal criteria regarding the group attached, the position where it is present, in concluding whether it is a good antibacterial agent or not. The same compound may show good antibacterial activity towards one strain while it may inhibit another strain. It can only conclude that in a particular set of compounds, which structural formula is the best for a particular bacterial strain.

Figure 1: Antibacterial activity of pyrazolines against gram+ve bacterial.



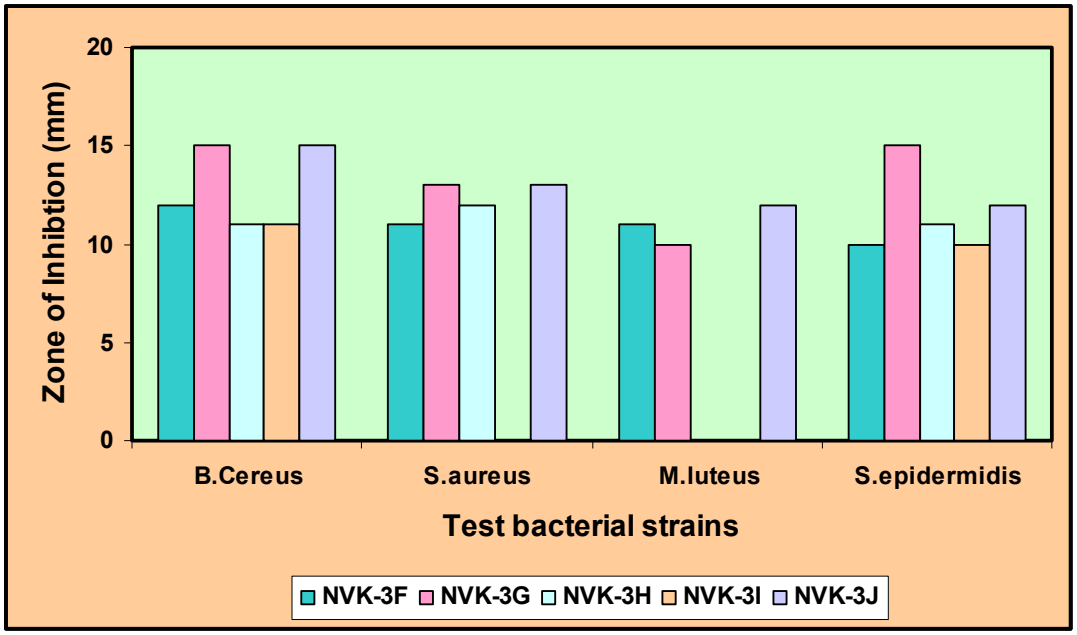
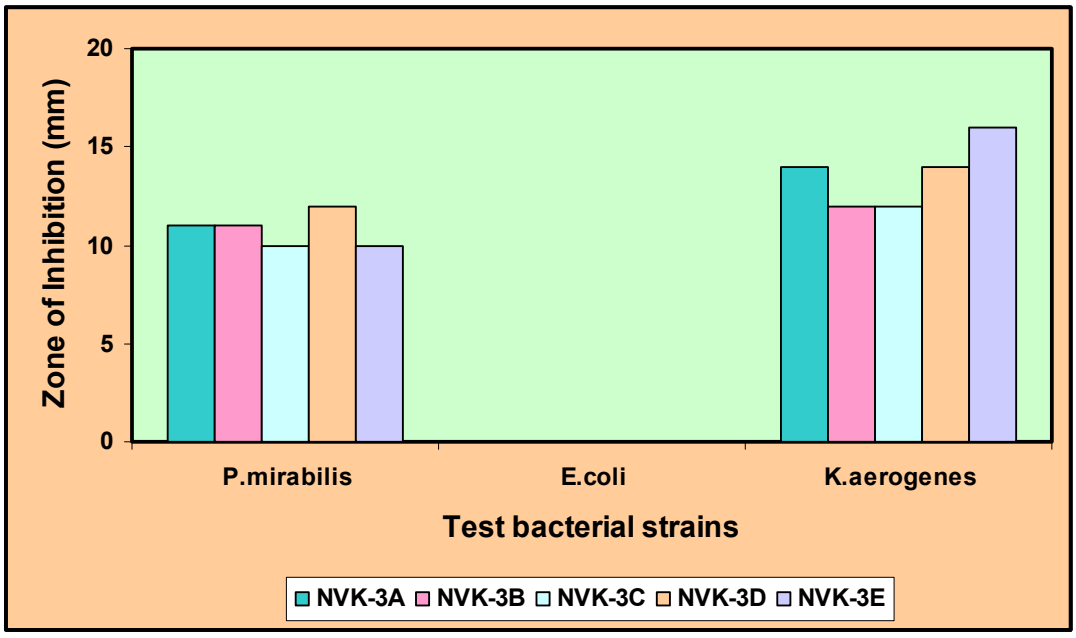


Figure 2: Antibacterial activity of pyrazolines against gram-ve bacterial.



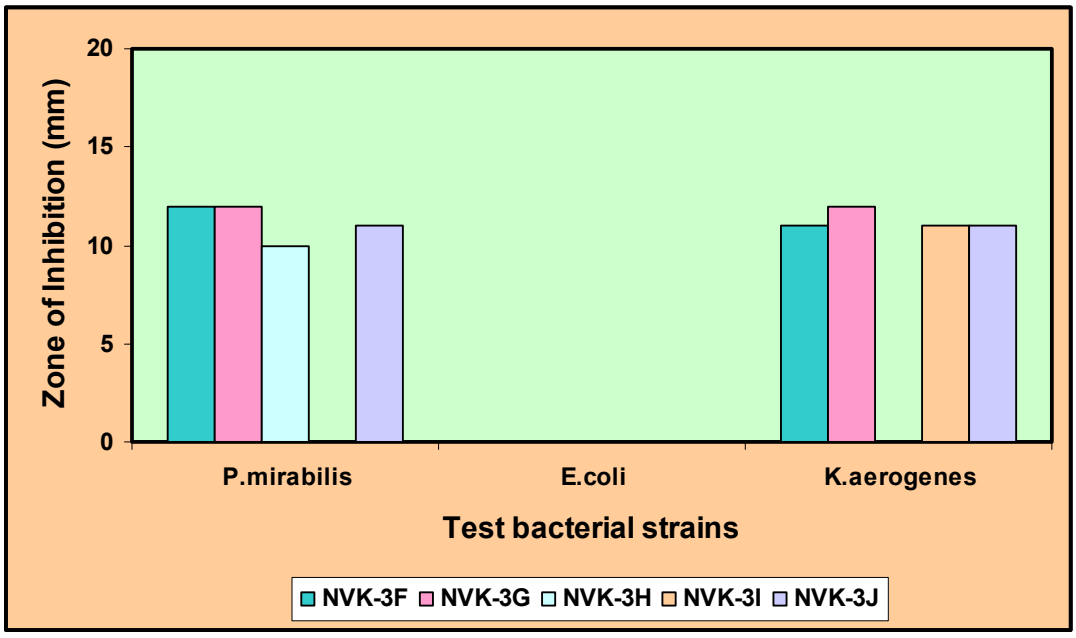
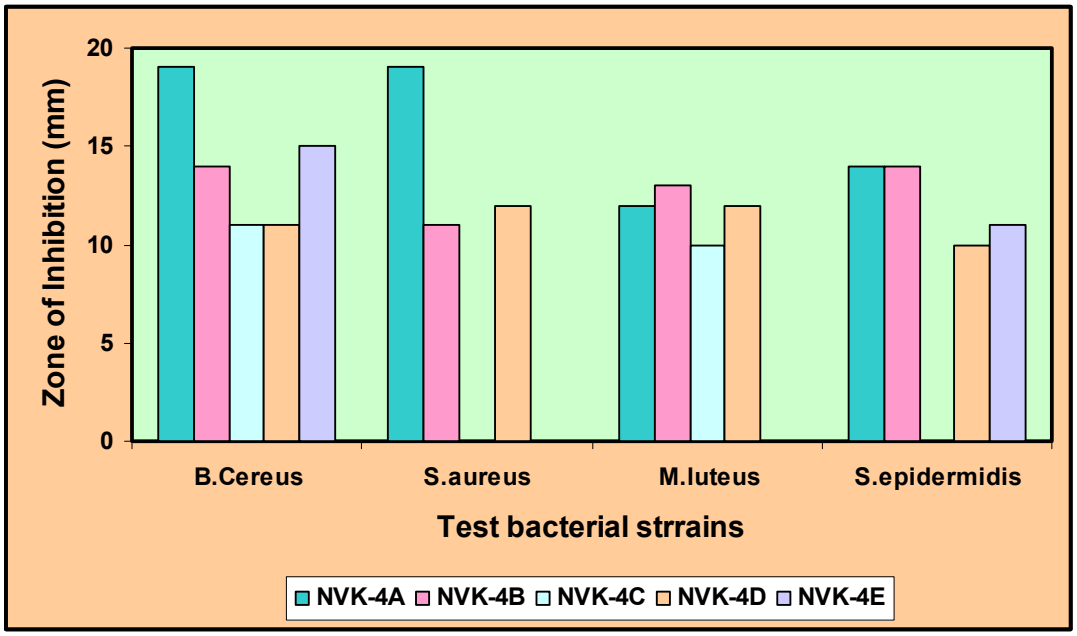


Figure 3: Antibacterial activity of thiopyrimidines against gram+ve bacterial.



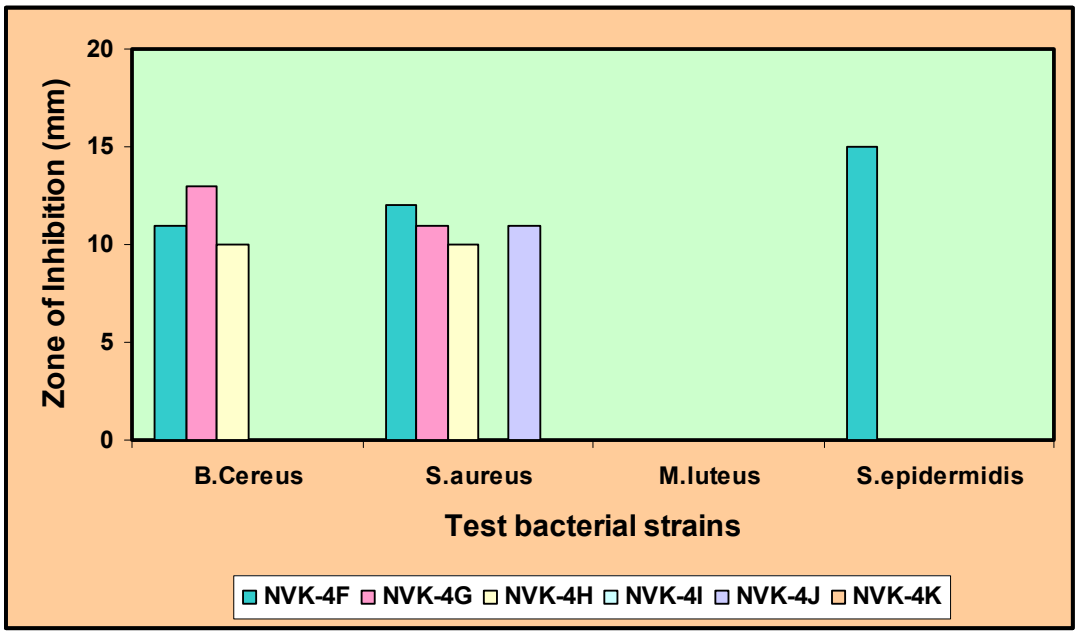
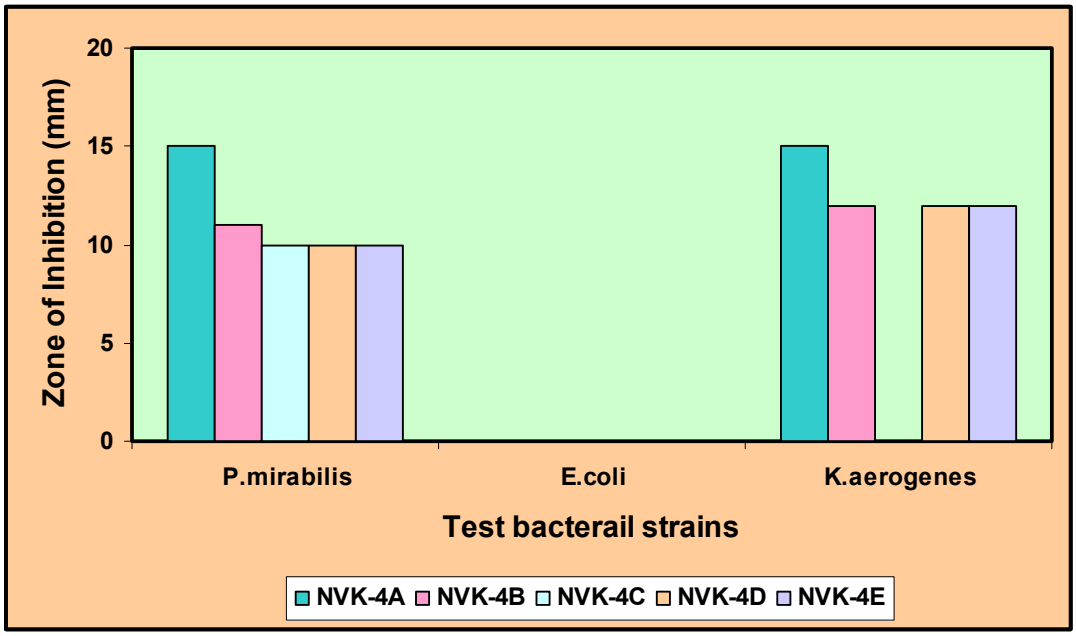
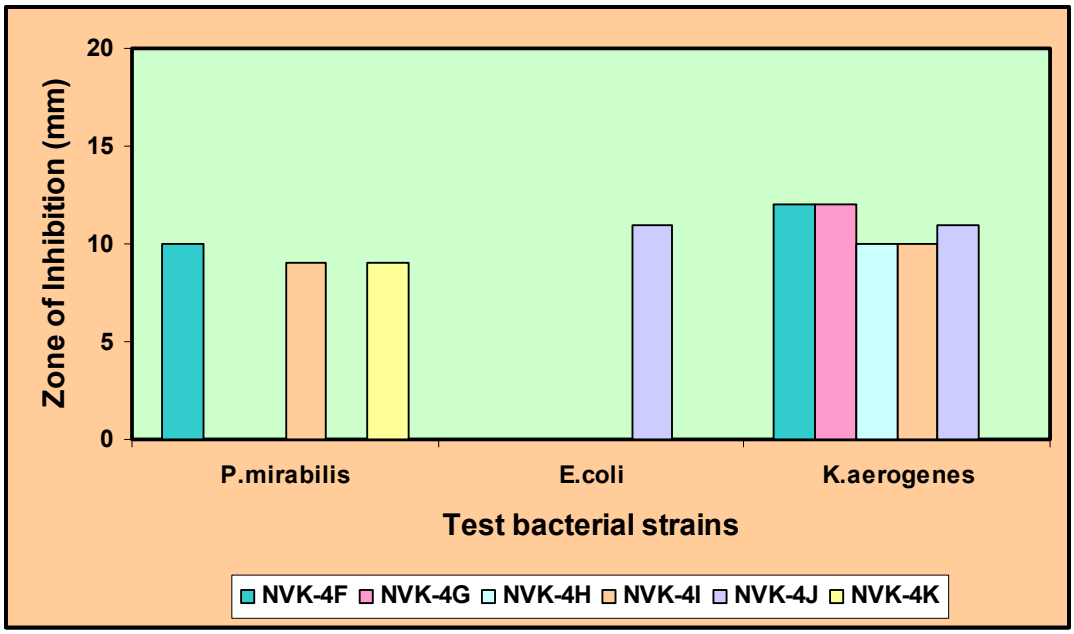


Figure 4: Antibacterial activity of thiopyrimidines against gram-ve bacterial.





REFERENCES

(1) A. Renezelti and F. Villani; Bely. BE 902, 586 (Cl. CO7D), Chem. Abstr., **104**, 2248338h (1986).

(2) Shirahata, Akira, Nakamura and Toshiyo; Chem. Abstr., **104**, 84642n (1986).

(3) S. Vurbanova and S. Chervenkov; Chem. Abstr., **107**, 77601g (1987).

(4) Jinbo, Susuma, Kohno, S. Kashima, Koichi, Suzuki, Yasuo, Kazuo and E. Mochida; Can. CA. 1 189, 078 (Cl. CO7D 215/42); Chem. Abstr.m **104**, 68761v (1986).

(5) A. Kreft, K. L. Kees, J. H. Musser and J. J. Bicksler; Chem. Abstr., **107**, 96605c (1987).

(6) B. S. Holla, B. S. Rao, K. Shridhara and P. M. Akberali; Il Farmaco, **55**, 338 (2000).

(7) R. Mladenova, M. Ignatova, N. Manolova, T. Petrova and I.Rashkov; Eur. Polym. J., **38**, 989 (2002).

(8) B. S. Holla, B. Veerendra, M. K. Shivananda and B. Poojary; Eur. J. Med. Chem., **38**, 759 (2003).

(9) P. Vicini, A. Geronikaki, M. Incerti, B. Busonera, G. Poni, C. A. Cabras and P. La Colla; Bioorg. Med. Chem., **11**, 4785 (2003).

(10) I. Kucukguzel, S. G. Kucukguzel, S. Rollas, G. O.Sanıs, O. Ozdemir, I. Bayrak, T. Altug and J. P. Stables; Il Farmaco, **59**, 893 (2004).

(11) N. S. Rao and M. G. Reddy; Bio. Met., **3**, 19 (1990).

(12) R. Shijun ; J. Med. Chem., **45**, 410 (2002)……

(13) Deliwala and Chimanlal; J. Med. Chem., **14**, 450 (1971).

(14) B. Dash, M. Patra and R. D. Patel; Proc. Ind. Acad. Sci., **19**, 894 (1980).

(15) A. K. Mittal and O. P. Singhal; J. Ind.Chem. Soc., **LIX**, 373 (1982).

(16) O. A.Hafez ; Pharmazia, **48**, 307 (1993).

(17) S. N. Pandya, D. Sriram, G. Nath and E. De. Clercq; Arzneimittelforschung., **50**, 55 (2000).

(18) Y. D.Dong, J. Y. Lan and L.V. Shan; Chin. J. Chem., **19**, 1136 (2001).

(19) H. Serre, J. Rey and J. P. Tarayre; Chem. Abstr., **91**, 9494a (1979).

(20) Tashio Pharmaceutical Ltd.; Chem. Abstr., **101**, 54722j (1984).

(21) A. K. Padersen and G. A. F. Gerald; J. Pharm. Sci., **74**, 188 (1985).

(22) D. Binder, C. R. Noe, W. Holzer and B. Rosenwirth; Arch. Pharm., **318**, 48 (1985).

(23) Y. Satomi; Ind. J. Cancer, **120**, 208071 (1994).

(24) G. Zongru and H. Rui; Chem. Abstr., **125**, 10376r (1996).

(25) S. F. Nielsen, T. Boesen, M. Larsen, K. Schonning and H. Kromann; Bioorg. Med. Chem. Lett., **12**, 3047 (2004).

(26) M. Larsen, H. Kromann, A. Kharazmi and S. F. Nielsen; Bioorg. Med. Chem. Lett., 15, 4858 (2005).

(27) A. Valla, B. Valla, D. Cartier, R. L. Guillou, R. Labia, L. Florent, S. Charne au, J. Schrevel and P. Potier; Euro. J. Med. Chem.,**12**, 385 (2005).

(28) B. Hans, R. Rolf and R. Rudolf; Chem. Abstr., **81**,105494r (1974).

(29) Z. Brozozowsk and E. Pomarnacka; Acta. Pol. Pharm., **37**, 1378 (1980).

(30) K. Wellinga, H. H. E. Jacobus; Chem. Abstr., **110**, 8204 (1989).

(31) S. S. Nayal, C.P. Singh; Asian J. Chem.; **11**, 207 (1990).

(32) D. B. Reddy, T. Senshama, B. Sechaina and M. V. R. Reddy; Ind. J. Chem., **30**, 46 (1991).

(33) E. Bansal, V. K. Srivastava and A. Kumar; Euro. J. Med. Chem., **36**, 81 (2001).

(34) M. A. Berghot and E. B. Moawad; Euro. J. Pharm. Sci., **20**, 173 (2003).

(35) J. H. Ahn, H. M. Kim, S. H. Jung, S. K. Kang, K. R. Kim, S. D. Rhee, S. D. Yang, H. G. Cheon and S. S. Kim, Bioorg. Med. Chem. Lett., **14**, 4461(2004).

(36) Y. R. Prasad, A. L. Rao, L. Prasoona, K.Murali and P. R.Kumar; Bioorg. Med. Chem Lett., **15**, 5030 (2005).

(37) W. Hentrich and W. Schepss ; Fortschr. Teerfrabenfabr. Verw. Industriezweige., **25**, 2590 (1932).

(38) D. W. Mc Kinstry and E. H. Reading; J. Franklin Inst., **237**, 422 (1944).

(39) T. Kato; Japn. Kokai. Tokkyo Koho JP., 59190974 (1984); Chem. Abstr., **102**, 132067 (1985).

(40) D. Bozing, P. Benko, L. Petocz, M. Szecsey, P. Toempe, G. Gigler and I. Gacsalyi; Eur. Pat. Appl. EP., 409233 (1991); Chem. Abstr., **114**, 247302z (1991).

(41) K. S. Atwal, B. N. Swanson, S. E. Unger, D. M. Floyd, S. Moreland, A. Hedberg and B. C. O´Reilly; J. Med. Chem., **34**, 806 (1991).

(42) Y. S. Sadanandam, M. M. Shetty and P. V. Diwan; Eur. J. Med. Chem., **27**, 87 (1992).

(43) A. Mai, M. Artico, R. Ragns and P. L. Colla; Bioorg. Med. Chem., **13**, 2065 (2005).

(44) S. Batra, S. Nag, R. pathak, M. kumar and P.K. Shukla; Bioorg. Med., Chem., **16**, 3824 (2006).

(45) H. G. Garg, N. Kaur; J. Med. Chem., **15**, 554 (1972).

(46) A. I. Eid and S. Rashad; Egypt J. Pharm. Sci., **20**, 107 (1979).

(47) S. sharma and M. S. Bhatia; J. Ind. Chem. Soc., **66**, 116 (1989).

(48) E. V. Pimenova, R. A. Khamatgaleev and E. V. Voronina; Khim-Farm. Zh., **32**, 272 (1998).

(49) V. Parmar, A. Kumar, A. Prasad; Bioorg Med. Chem. **7** , 1425 (1999).

(50) U. Schindier, K. Schoenafinger and H. Strobel; Ger. offen DE, 19, 744, 026; Chem. Abstr., **130**, 267427c (1999).

(51) J. M. Genin, B. Carolyn and J. Keiser; J. Med. Chem., **43**, 1034 (2000).

(52) M. Verma, A. K. Chaturvedi, A. Chaudhari and S. S. Parmar; J. Pharma. Sci., **63**, 1740 (1974).

(53) H. H. Moharram, R. S. El-Amin and A. El-Dawany; J. Serb. Chem. Soc., **54**, 335 (1989).

(54) E. Bousquet, G. Romeo, N.A. Santagati, T. Lancetta, A. Caruso, V. Leone, and A. Felice; Farmaco., **44**, 851 (1989).

(55) P. K. Naithani, V. K. Srivastava, J. P. Barthwal, A. K. Saxena, T. K. Gupta and K. Shanker; Ind. J. Chem., **28B**, 990 (1989).

(56) A.J. Srivastava, S. Swaroop, V. K. Saxena and P. Srivastava; Ind. J. Pharma. Sci., **51**, 23 (1989).

(57) S. M. Sethna and R. C. Shah; J. Ind. Chem. Sci., **11**, 1459 (1993).

(58) S. Swaroop, V. K. Saxena and S.R. Chowdhary; Ind. J. Pharma. Soc., **51**, 124 (1989).

(59) K. C. Mathur and R. Sahay; J. Ind. Chem. Soc., **67**, 856 (1990).

(60) B. S. Vashi, D. S. Mehta and V. H. Shah; Ind. J. Chem., **34B**, 802 (1995).

(61) K. K. Kataryna, E. Szymanska, M. Motyl, W. Holzer, A. Bialecka and Kasprowicze; Pharmazie, **53**, 680 (1998).

(62) M. D. Shah, N. C. Desai, K. K. Awasthi, and A. K. Saxena; Ind. J. Chem., **40B**, 201 (2001).

(63) V. K. Pandey and M. Tandon; Ind. J. Chem., **40B**, 527 (2001).

(64) J. A. Riddick, W. B. Bunger and T. Sakano, Organic Solvents-Physical Properties and methods of purification, Fourth Edition., Techniques of Chemistry, **II**, A Wiley-Interscience Publication, John Wiley, New York (1986).

(65) A. W. Bauer, W. M. M. Kirby, J. C. Sherris and M. Turck: Antibiotic susceptibility testing by a standardized single disk method; Am. J. Clin. Pathol., **45**, 493 (1966).

(66) C. Perez, M. Paul and P. Bazerque; *Acta Biol. Med. Exp*. **15**, 113 (1990).

(67) J. Parekh, P. Inamdhar, R. Nair, S. Baluja and S. Chanda; J. Serb. Chem. Soc. **70** (2005) 1155.

LIST OF PUBLICATIONS

(1) "Theoretical evaluation of viscosity in quaternary systems".
Shipra Baluja, Nikunj Kachhadia, Asif Solanki and Pranav Inamdar
International Journal of Physical Sciences (Inter-Disciplinary Journal), 16(2), 267-272(2004).

(2) "Thermodynamic and acoustical studies of binary mixtures of diethyl malonate at 308.15k".
Shipra Baluja, Nikunj Kachhadia, Nirmal Pandaya, Asif Solanki and Pranav Inamdar
Physics and Chemistry of Liquids, 43(3), 309-316 (2005).

(3) "Theoretical evaluation of refractive index in binary liquid mixtures"
Shipra Baluja, Nikunj Kachhadia, Nirmal Pandya and Asif Solanki
E-Journal of Chemistry, 2(7) (2005).

(4) "Theoretical evaluation of ultrasonic velocity in binary liquid mixtures of acetophenone using various approaches at 308.15k".
Shipra Baluja, Nikunj Kachhadia and Asif Solanki
E-Journal of Chemistry, 2(9) (2005).

(5) "Viscous behavior of methoxy ethanol in binary mixtures".
Shipra Baluja, Nikunj Kachhadia and Asif Solanki
E-Journal of Chemistry, 2(9) (2005).

(6) "Refractive index: Theoretical evaluation in binary liquid mixtures".
Shipra Baluja, Nikunj Kachhadia, Nirmal Pandya and Asif Solanki
International Journal of Physical Sciences (Inter-Disciplinary Journal), 18(2), 247-250 (2006).

(7) "Dissociation constants of some schiff bases"
Shipra Baluja, Nikunj Kachhadia, P. K. Kasundra and K. P. Vaishnani
International Journal of Physical Sciences (Inter-Disciplinary Journal), 18(3), 339-342 (2006).

(8) "An ultrasonic study of some drugs in solutions".
Shipra Baluja, Nikunj Kachhadia and Asif Solanki
Russian Journal of Physical Chemistry, 81(2), 1-5 (2007).

(9) "Thermodynamic studies of some 1, 2, 4-triazole derivatives in DMF and THF solutions at 308.15k".
Shipra Baluja, Nikunj Kachhadia and Asif Solanki
Physics and Chemistry of Liquids (2006) (In press).

(10) "Evaluation of biological activities of some schiff bases and metal complexes".
Shipra Baluja, Nikunj Kachhadia and Asif Solanki
Journal of Iranian Chemical Society (2006) (In Press).

LIST OF PAPERS COMMUNICATED

(1) **"Sonochemical synthesis of some schiff bases".**
Shipra Baluja, Nikunj Kachhadia and Asif Solanki
(Iranian Journal of Chemistry and Chemical Engineering)

(2) **"Synthesis and thermodynamic studies of some 1, 2, 4-triazole derivatives in DMF and THF solutions at 308.15k".**
Shipra Baluja, Nikunj Kachhadia and Asif Solanki
(Physics and Chemistry of Liquids.)

(3) **"A facile synthesis and antimicrobial activity of some 4-aryl triazole ring system".**
Shipra Baluja, Nikunj Kachhadia, Sumitra Chanda, Rajesh Chabhadiya,
Rathish Nair and Asif Solanki
(Journal of Serbian Chemical Society.)

(4) **"Synthesis of some pyrazoline derivatives by conventional, microwaves and ultrasound waves: a step to eco-friendly synthesis".**
Shipra Baluja, Nikunj Kachhadia and Asif Solanki
(Green Chemistry)

(5) "**Antibacterial studies of some metal chelates of 1,2,4- triazole schiff bases".**
Shipra Baluja, Nikunj Kachhadia, Asif Solanki, Sumitra Chanda and
Nilesh Godvani.

(6) **"Acoustical studies of binary mixtures of acetophenone at 308.15k".**
Shipra Baluja, Nikunj Kachhadia, Nirmal Pandya and Asif Solanki

(7) "**Thermal profile and decomposition kinetics of some new schiff bases".**
Shipra Baluja, Nikunj Kachhadia and Asif Solanki
(Indian J. Chem. Technology-Delhi.)

(8) **"Synthesis and thermal analysis of some 1, 2, 4-triazole derivatives".**
Shipra Baluja, Nikunj Kachhadia and Asif Solanki.

(9) **"In *vitro* antifungal activity of some new triazoles".**
Shipra Baluja, Nikunj Kachhadia, Sumitra Chanda, Parekh Jigna and Asif Solanki

(10) **"Studies on physicochemical properties of some 1,2,4- triazole derivatives".**
Shipra Baluja, Nikunj Kachhadia and Asif Solanki

(11) **"Synthesis and thermodynamic studies of some α-napthyl amine derivatives in DMF and THF solution at 313.15K"**
Shipra Baluja, Nikunj Kachhadia and Nirmal Pandya
(Indian Journal of Chemistry-A)

(12) "**Preparation, characterization and antibacterial activities of some metal complexes containing triazole schiff bases".**
Shipra Baluja, Nikunj Kachhadia, Asif Solanki, Sumitra Chanda and
Parag Ajudia
(Iranian Journal of Science)

(13) "Studies on thermodynamic properties of some imidazolinone derivatives in DMF at 308.15k".

Shipra Baluja, Nikunj Kachhadia and Asif Solanki

(Journal of Pure and Applied Ultrasonics)

(14) "Thermodynamic studies of some 1,2,4-triazole derivatives in DMF and THF at 308.15k".

Shipra Baluja, Nikunj Kachhadia and Asif Solanki

(Journal of Iranian Chemical Society)

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J. Parekh, N. Kacchadia, S. Baluja and S. Chanda

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(17) "Acoustical studies of Schiff bases in 1, 4-dioxane and dimethylformamide at 308.15 K"

Shipra Baluja, Nikunj Kachhadia and Mayur Soni

(Journal of Research in Science Teaching)

(18) "Antibacterial studies of some metal complexes of coumarin chalcones"

Shipra Baluja, Nikunj Kachhadia and Rahul Bhalodiya

(Institution of Chemists-INDIA)

(19) "Phytochemical studies of Acacia Catechu"

Shipra Baluja, Sumitra Chanda, Nikunj Kachhadia, Ratish Nair and Asif Solanki

(Journal of Iranian Chemical Society)

(20) "Density, viscosity and speed of sound of solutions of some imidazolinone derivatives in DMSO at 308.15K"

Shipra Baluja, Nikunj Kachhadia and Asif Solanki

(Journal of Iranian Chemical Society)

(21) "Acoustical properties of schiff base solutions in DMF"

Shipra Baluja, Nikunj Kachhadia and K. P. Vaishnani

(Russian Chemical Bulletin)

(22) "Thermal study of some schiff bases"

Shipra Baluja, Nikunj Kachhadia and K. P. Vaishnani

(Journal of Thermal Analysis and Calorimetry)

LIST OF PAPERS PRESENTED IN DIFFERENT CONFERENCES/SYMPOSIA

(1) "Synthesis and thermodynamic studies of some α-naphthyl amine derivatives in DMF and THF solution at 313.15K". Shipra Baluja, N. D. Pandya and N. Kachhadia, "29th International conference on solution Chemistry". Ljubljana, Slovenia, 21-25 August 2005. **(International)**

(2) "An Ultrasonic study of some drugs in solutions". Shipra Baluja, Asif Solanki and N. Kachhadia, "29th International Conference on Solution Chemistry". Ljubljana, Slovenia, 21-25 August 2005. **(International)**

(3) "In vitro Antifungal Activity of some new triazoles". Shipra Baluja, Sumitra Chanda, Jigna Parekh, Nikunj Kachhadia and Asif Solanki, "Joint International Conference on Advances in Organic Chemistry and Chemical Biology". Indian Institute of Chemical Technology, Hyderabad, Jan 11-12, 2006. **(National)**

(4) "A facile synthesis and antimicrobial activity of some 4-aryl triazole ring systems", Shipra Baluja, Sumitra Chanda, Rajesh Chabhadiya, Asif Solanki and Nikunj Kachhadia, "Joint International Conference on Advances in Organic Chemistry and Chemical Biology". Indian Institute of Chemical Technology, Hyderabad, Jan 11-12, 2006. **(National)**

(5) "Antibacterial studies of some metal chelates of 1,2,4-triazole Schiff bases", Shipra Baluja, Asif Solanki, Sumitra chanda, Nilesh Godvani and Nikunj Kachhadia, 2nd International Symposium on Drug Discovery and Process Research, K. L. E. Society's College of Pharmacy, Belgaum Feb., 10-12, 2006 **(International)**

(6) "Antibacterial study of Punica Granatum stem", Nilesh Godvani, Nikunj Kachhadia, Sumitra Chanda, Asif Solanki and Shipra Baluja, 2nd International Symposium on Drug Discovery and Process Research, K. L. E. Society's College of Pharmacy, Belgaum Feb., 10-12, 2006 **(International)**

(7) "Synthesis and antibacterial activity of some Schiff bases", Samrat Dwivedi, Shipra Baluja, Nikunj Kachhadia, Sumitra Chanda, Nirmal Pandya and Asif Solanki, 2nd International Symposium on Drug Discovery and Process Research, K. L. E. Society's College of Pharmacy, Belgaum Feb., 10-12, 2006 **(International)**

(8) "Acoustical studies of binary mixtures of acetophenone at 308.15K",Shipra Baluja, Asif Solanki , Nikunj Kachhadia, Nilesh Godvani and Anchal Kulshrestha, 2nd National Conference on Thermodynamics of Chemistry and Biological Systems, Veer Narmad South Gujarat University, Surat, 30th Octo.- 1st Nov. 2006. **(National).**

(9) " Density, viscosity and speed of sound of solutions of some imidazolinone derivatives in DMSO at 308.15K", Shipra Baluja, Nilesh Godvani, Asif Solanki and Nikunj Kachhadia, 2nd National Conference on Thermodynamics of Chemistry and Biological Systems, Veer Narmad South Gujarat University, Surat, 30th Octo.-1st Nov. 2006. **(National).**
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