Synthesis and Ultrasonic Interferometric Study of Coumarinyl Derivatives

N. R. Thakare[1], P. A. Nagpure[2], U. S. Joshi[3], S. V. Rathod[4]
[1,3,4]Department of Chemistry,[2]Department of Physics,
Shri Shivaji Science College, Amravati.(MS) INDIA.

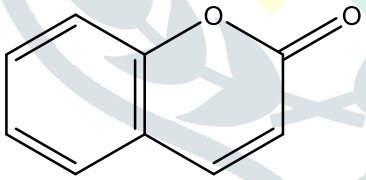
Abstract:

The Synthesis of Coumarinyl derivatives (Pyrazole) is done in greener way. Further their Ultrasonic Interferometric study has been done with the standard value of density (ρ) and viscosity (η). The value of Ultrasonic velocity (U) was determined experimentally. The molecular interaction of various synthesized Pyrazoles has been studied. By using standard relations from measured values of density (ρ), ultrasonic velocity (U) and viscosity (η), the desired acoustical and thermodynamic parameters such as adiabatic compressibility (βad), intermolecular free length (L_f), acoustic impedence (Z), relaxation time (τ), has been calculated and their wide applications in the branch of medicine and pharmacy has been studied.

Index Term- *Pyrazoles, Density, Viscosity, Ultrasonic Velocity, Molecular Interactions.*

INTRODUCTION

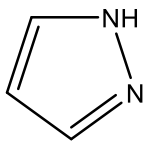
Coumarins are the best known aromatic lactones[1]. The isolation of coumarin was first reported by *Vogel*[2] in Munich in 1820. He associated the pleasant odour of the tonka bean from Guiana with that of clover, *Melilotous officinalis*, which gives rise to the characteristic aroma of new-mown hay. *Vogel* then concluded that the long colorless crystals which he discovered on slicing open tonka beans and which crystallized as glistening needles from aqueous alcohol were identical with similar crystals he obtained, albeit in much lower yield, by extracting fresh clover blossoms[3]. The name coumarin originated[4] from a Caribbean word *'coumarou'* for the tonka tree, which was known botanically at one time as *Coumarouna odorata Aubl*. Coumarin is now well accepted trivial name. The IUPAC nomenclature of the coumarin ring system is 2H-1-benzopyran-2-one. The coumarin ring system has an easy acceptability in the biological system compared to its isomeric chromones and flavones nucleus[5] and is widely distributed in nature[6-8]. An excellent account of these naturally occurring coumarins is presented by *R D H Murray* and *S A Brown*[9].



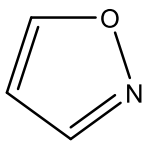
Coumarin

Coumarins can be synthesized by various methods such as, Pechmann, Perkin, Knoevenagel and Reformatsky reactions. Pechmann condensation is one of the most common procedures for the preparation of coumarin and its derivatives. This method involves the reactions between a phenol and a α-keto ester in the presence of an acid catalyst. Simple starting materials are required here to produce various substituted coumarins in good yields[10].

Pyrazole (A) is the given name to organic compounds by Knorr,[11] which is consist of a five membered ring containing adjacent nitrogen atoms. It can also be assumed as an isoxazole nucleus (B) in which -O- is replaced by –NH- group[12].



(A) Pyrazole



(B) Isoxazole

In medicine, derivatives of pyrazoles are used for:

- Analgesics
- Anti-Inflammatory Drugs
- Antipyretics
- Treating Erectile Dysfunction
- Antidiabetic (Anti-Hyperglycaemic)
- Cancer Treating Medicine
- Antifungals
- Antibacterials
- Antivirals

The pyrazole ring is found within a variety of pesticides as fungicides, insecticides & herbicides,including chlorfenapyrl, fenpyroximate, fipronil, tebufenpyrad, tolfenpyrad& tralopyril.

The characterization of given synthesize compound were known. From survey of literature it was cleared that Interferometric study of various Pyrazoles synthesized (5a-d) are not yet studied. It was therefore, thought of interest to study ultrasonic Interferrometric study of synthesized Pyrazoles (5a-d).

The Measurement of physiochemical properties such as density and ultrasonic velocity of pure components and their binary mixtures are being increasable used as tools for investigations of the properties of pure components and the nature of intermolecular interactions between the components of liquid solutions[13]. The significance reasons for the study of thermo-physical and thermodynamic properties of multi-component liquid solutions are as follows:

- They provide way for studying the physical forces acting between molecules of different species.
- The study of liquid solutions provides appearance of new phenomena, which are absent in pure liquids. The most interesting of these are the new types of phase equilibria, which are introduced by the variation in the promotion of the pure components.
- The study of thermo-physical and thermodynamic properties of liquid solutions helps in obtaining in depth knowledge about molecular interactions.

EXPERIMENTAL SECTION

O-Hydroxy acetyl coumarin (3):

4-Methyl-7-hydroxy-8-acetyl coumarin (3), m. p. 165˚C, was used as starting material which was obtained by Fries migration of 4-methyl-7-acetoxy coumarin (2) m. p. 150˚C.

7-Benzoyloxy-8-acetyl coumarin (4):

4-Methyl-7-benzoyloxy-8-acetyl coumarin (4), m. p. 198˚C, was obtained by treatment of 4-methyl-7-hydroxy-8-acetyl coumarin with benzoic acid in pyridine medium.

1-Coumaryl-3-phenylpropane-1,3-dione (5):

1-Coumaryl-3-phenylpropane-1,3-dione (5), m. p. 158˚C, was obtained by Baker-Venkatraman transformation of 4-methyl-7-benzoyloxy-8-acetyl coumarin.

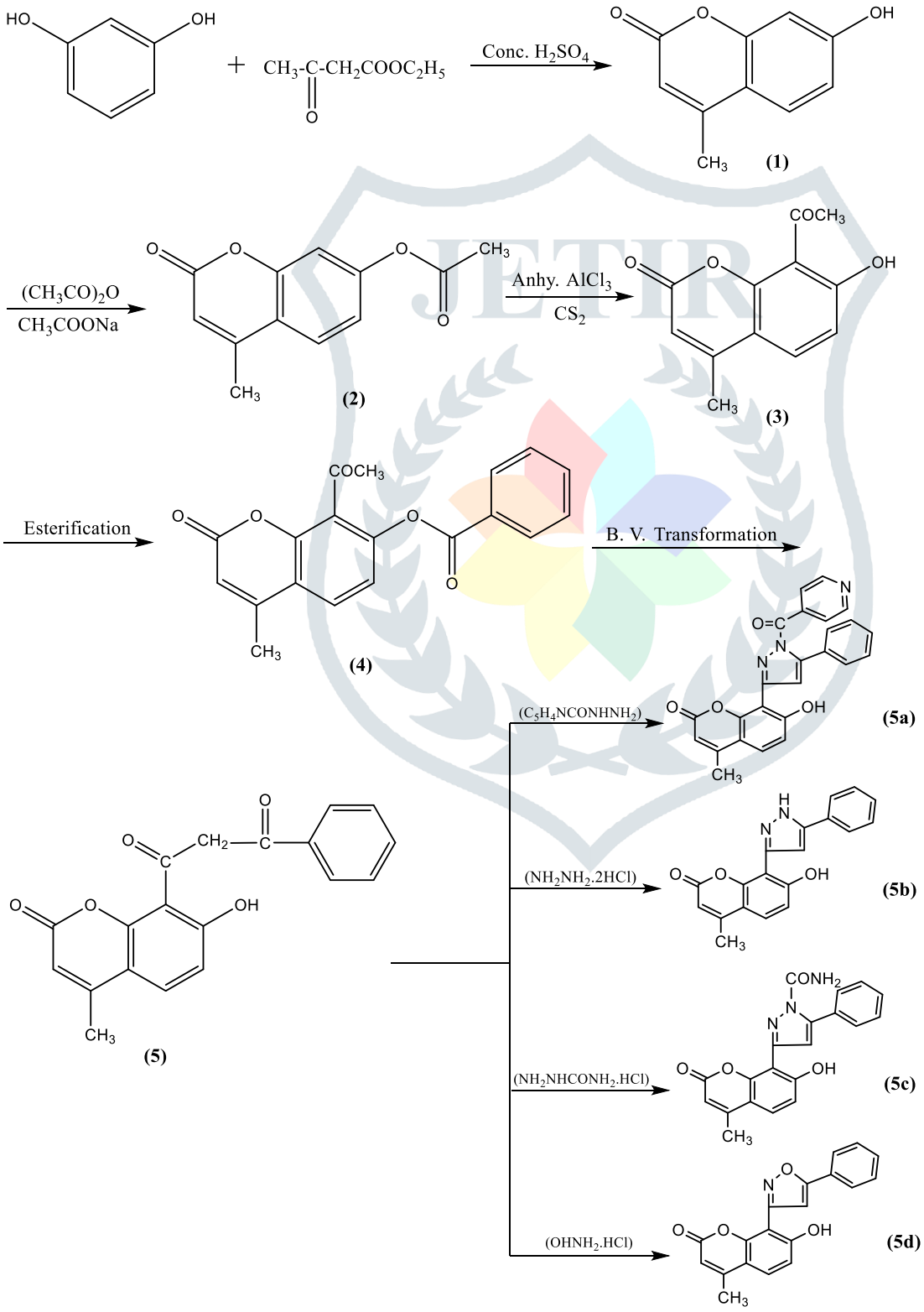
1-Pyridoyl/H/Carboxamido-3-(4-methyl-7-hydroxy-8-coumarinyl)-5-phenylpyrazoles (5a-c) & Isoxazole (5d):

1-Pyridoyl/H/Carboxamido-3-(4-methyl-7-hydroxy-8-coumarinyl)-5-phenylpyrazoles (5a-c) & Isoxazole (5d) were synthesized on refluxing 1-coumaryl-3-phenylpropane-1,3-dione (5) with isoniazide/hydrazine dihydrochloride/semicarbazide hydrochloride/hydroxylamine hydrochloride

respectively, using pyridine as a medium for 4 hrs. Thus, following Coumarinyl pyrazoles & Isoxazole were synthesized.

1. (5a)1-pyridoyl-3-(4-methyl-7-hydroxy-8-coumarinyl)-5-phenylpyrazole, **m. p.** 238˚C
2. (5b) 1-H-3-(4-methyl-7-hydroxy-8-coumarinyl)-5-phenylpyrazole, **m. p.** 275˚C
3. (5c)1-carboxamido-3-(4-methyl-7-hydroxy-8-coumarinyl)-5-phenylpyrazole, **m. p.** 267˚C
4. (5d) 7-hydroxy-4-methyl-8-(5-phenylisoxazol-3-yl)-2H-chromen-2-one, **m. p.** 440˚C

SCHEME



The all above synthesized compounds were known and their structures are confirmed by spectral analysis.

Ultrasonic Interferometric Study :

1. Unscrew the knurled cap of cell and lift it away from double walled construction of the cell. In the middle position of it pour experimental liquid and screw the knurled cap. Wipe out excess liquid overflowing from the cell.
2. Insert the cell in the heavy base socket and clamp it with the help of a screw provided on its side.
3. Connect the high frequency generator with cell by coaxial cable provided with the instrument. In ultrasonic interferometer frequency selector knob should be positioned at desired frequency (same frequency as that of liquid cell chosen).
4. Move the micrometer slowly in either clockwise or anticlockwise direction till the anode current on the ammeter on the high frequency generator shows a maximum or minimum.
5. Note the reading of micrometer corresponding to the maximum or minimum (which is sharper) in micro-ammeter. Take about 50 reading of consecutive maximum or minimum and tabulate them.
6. Take average of all differences (λ/2).
7. Once the wavelength (λ) is known the velocity (U) in the liquid can be calculated with the help of the relation[14].

RESULT AND DISCUSSION

From the standard known values of density, viscosity and experimentally determined value of ultrasonic velocity, various parameters can be calculated such as: Adiabatic Compressibility (βad), Intermolecular Free Length (L_f), Acoustic Impedance (Z) & Relaxation Time (τ) were calculated.

1) **Adiabatic Compressibility (βad):** Adiabatic compressibility depends on speed of sound and density of medium and thus was calculated by using the equation known as Newton Laplace equation:

$$\beta_{ad} = {}^{1}/_{U^2\rho} \qquad (1)$$

Where, U = Velocity & ρ = Density of given solution.

2) **Intermolecular Free Length (L_f):**

Intermolecular free length was determined by using the formula given by Jacobson.

$$L_f = K_T \beta_{ad}^{\ 1/2} \quad (\text{m}) \qquad (2)$$

Where, KT is temperature dependent constant = [(93.875+0.375T).10-8]

3) **Acoustic Impedance (Z):**

Acoustic impedance was determined from equation,

$$Z = U \times \rho \quad (\text{Kg m}^{-2}\ \text{s}^{-1}) \qquad (3)$$

4) **The Relaxation Time (τ):**

The relaxation time (τ) [18] was calculated from the relation,

$$\tau = ({}^{4}/_{3})\, \beta_{ad}\eta \quad (\text{s}) \qquad (4)$$

The standard known values of density (ρ) and viscosity (η) for the synthesized coumarinyl derivatives (Pyrazoles & Isoxazole) are 1051.09 (Kg.m^{-3}) and 1.037 (m.Pa.s) respectively at 303.15K .

Experimentally determined values of ultrasonic velocity (U) for the synthesized coumarinyl derivatives (Pyrazoles & Isoxazole) at 303.15K are represented in Table 1.

Table 1: Experimental Ultrasonic Velocity (U) for Pyrazoles & Isoxazole at 303.15K.

Sr. No.	Compound	Ultrasonic Velocity (U) (ms^{-1})
1.	1-pyridoyl-3-(4-methyl-7-hydroxy-8-coumarinyl)-5-phenylpyrazole (5a)	6×10^{2}

2.	1-H-3-(4-methyl-7-hydroxy-8-coumarinyl)-5-phenylpyrazole (5b)	5×10^{2}
3.	1-carboxamido-3-(4-methyl-7-hydroxy-8-coumarinyl)-5-phenylpyrazole (5c)	4×10^{2}
4.	7-hydroxy-4-methyl-8-(5-phenylisoxazol-3-yl)-2H-chromen-2-one (5d)	4×10^{2}

Derived parameters such as Adiabatic compressibility (β_{ad}), inter molecular free length (L_f), acoustic impedance (Z) and relaxation time (τ) for the synthesized coumarinyl derivatives (Pyrazoles & Isoxazole) at 303.15K are represented in Table 2.

Table 2: Derived parameters (β_{ad}, L_f, Z and τ) for Pyrazoles & Isoxazole at 303.15K.

Sr. No.	Compound	β_{ad} ($Kg^{-1}\ ms^{-2}$)	L_f (m)	Z ($Kg\ m^{-2}\ s^{-1}$)	T (s)
1.	1-pyridoyl-3-(4-methyl-7-hydroxy-8-coumarinyl)-5-phenylpyrazole (5a)	2.9196×10^{-3}	5.6802×10^{-8}	630654	4.0368×10^{-3}
2.	1-H-3-(4-methyl-7-hydroxy-8-coumarinyl)-5-phenylpyrazole (5b)	4.2043×10^{-3}	6.8163×10^{-8}	525545	5.8131×10^{-3}
3.	1-carboxamido-3-(4-methyl-7-hydroxy-8-coumarinyl)-5-phenylpyrazole (5c)	6.5693×10^{-3}	8.5205×10^{-8}	420436	9.0831×10^{-3}
4.	7-hydroxy-4-methyl-8-(5-phenylisoxazol-3-yl)-2H-chromen-2-one (5d)	6.5693×10^{-3}	8.5205×10^{-8}	420436	9.0831×10^{-3}

Conclusion

We have successfully synthesized the coumarinyl derivatives. Ultrasonic investigations of molecular interactions in various synthesized pyrazoles (5a-c) and isoxazole (5d) have been measured. From the experimentally determined ultrasonic velocity (U) various parameters such as Adiabatic compressibility (β_{ad}), inter molecular free length (L_f), acoustic impedance (Z) and relaxation time (τ) have been derived.

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