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SYNTHESIS AND CHARACTERIZATION OF 4-[2'-(5'-NITRO) IMIDAZOLYL] BENZOYL (N-ME) VALINE

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ABSTRACT

Many of the heterocyclic found to exhibit antifungal, antibacterial, cytotoxic, antineoplastic, insecticidal, anti-inflammatory, tyrosinase inhibitory and melanin production inhibitory activities.Imidazole has been drawn as promising structural units in the field of medicinal chemistry. Introduction of D-amino acids and N-methylation of amino acids like tyrosine, valine, alanine etc enhanced antimicrobial activity. Hence an attempt is made towards the sythesis of 5-nitroimidazolyl-benzoic acid derivative of N-methyl amino acids and peptide using solution phase technique of peptide synthesis. The new compounds are characterized by using IR, H^1NMR and mass spectroscopy.

KEYWORDS : Tyrosine, Valine, Alanine, Benzoic Acid, Imidazole

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INTRODUCTION

A great number of drugs are heterocyclic compounds, mostly are of synthetic origin, few have obtained from natural resources which include alkaloids, xanthines, cardiac glycosides, vitamins and several antibiotics. Heterocyclic derivatives having two nitrogen atoms oriented in, 1-3 position are endowed with wide spectrum of biological activities. Number of organo-sulphur and nitrogen containing compounds are present in living and non living system. Nitroimidazole derivatives were developed not only because of their novelty to structure but also because of novelty to action [1,2].

N-methylated amino acids are commonly found in naturally occurring peptide antibiotics. The methylation of N-atom and the hydrogen bonding pattern of peptide containing these amino acids are different from that of unmethylated peptide. The N-methylated peptide antibiotics are found to possess enhanced activity ascompared to the unmethylated forms.Therefore, an attempt is made to synthesize a new bioactive series of 5-nitroimidazole derivatives of amino acids and peptides. Biological activity studies performed on these synthetic compounds proved to give good

results [3, 4].

2. MATERIALS AND METHODS

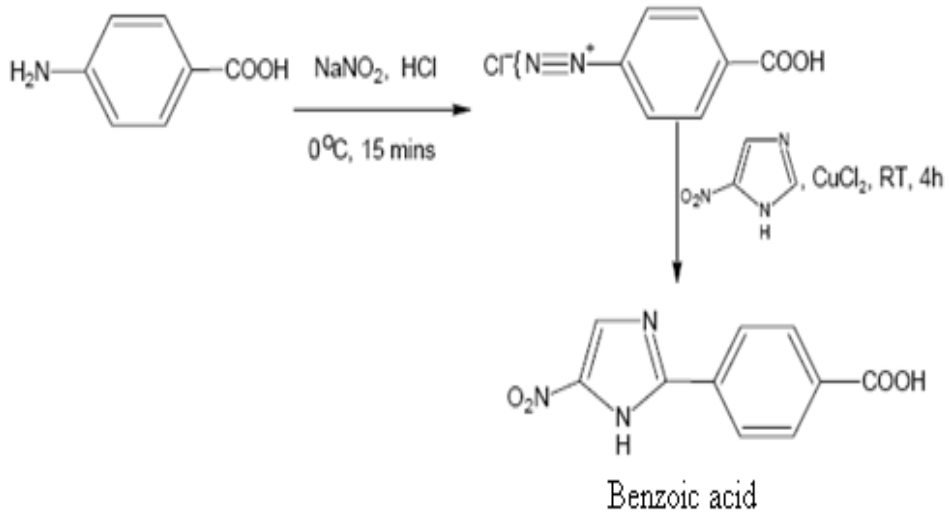
2.1 Synthesis of N-methyl amino acids methyl ester:

Amino acids were converted into the corresponding methyl ester hydrochloride using thionyl chloride and methanol. The amino end was then protected by introducing Boc-group using ditertiary butylpyrocarbonate and triethylamine to get Boc-L-amino methyl ester. N-methylation of this compound was done by treating with methyl iodide and sodium hydride (Benoition method) to get Boc-(N-Me) amino methyl ester [5].

2.2 Preparation of4-[2-(5-nitro)imidzolyl] benzoic acid :

A mixture of p-amino benzoic acid (34.25 gms, 250 mmol), dilute hydrochloric acid (15%, 120ml) and water (150ml) was heated to get a clear solution. The solution was cooled to RT and diazotized by the addition of sodium nitrite solution (30%, 48ml). The diazonium salt solution was filtered and to the filtrate, dilutes HCl (100ml) and nitroimidazole (250 mmol) and aqueous cupric chloride (5gms in 20ml of water) were added with stirring. Stirring was continued for 6 hrs and kept overnight in the refrigerator. The separated solid was collected by filtration and washed with water. The crude compound was crystallized from acetone to obtain pure of 4 [2-(5-nitro)imidazolyl] benzoic acid[6].

SCHEME-1

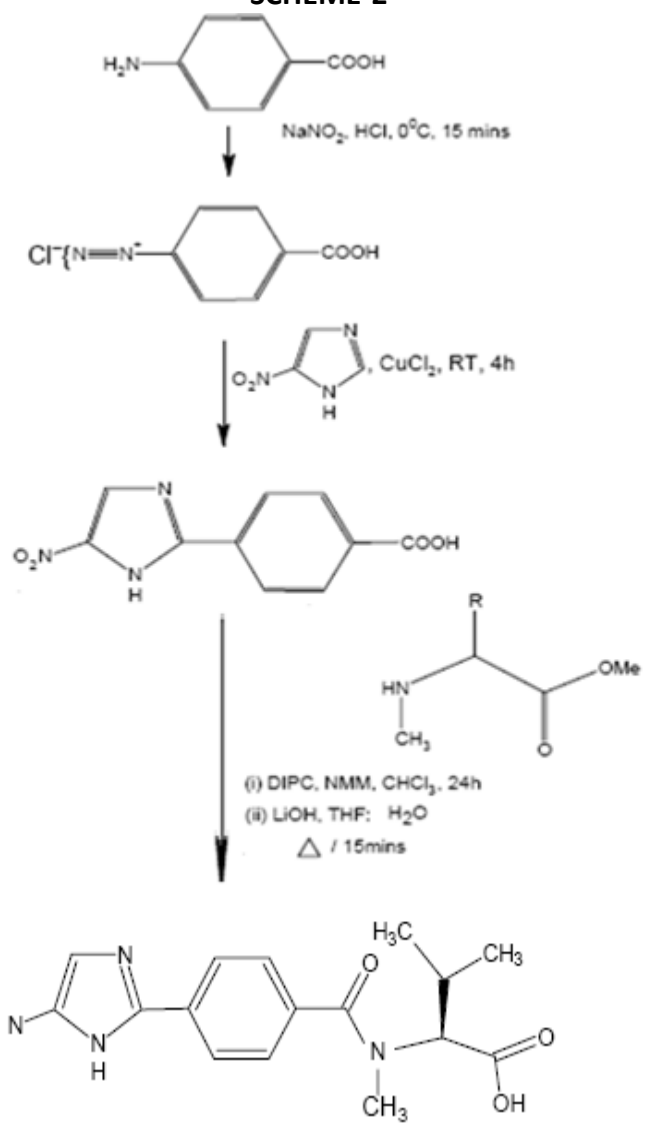


Benzoic acid

2.3 Preparation of 4-[2'-(5'-nitro) imidazolyl]benzoyl(N-Me)-aminoacid

To the (N-Me) amino acid methylester(7.0 mmol.) THF (20ml), added 4-[2'-(5'-nitro) imidazolyl] benzoic acid acid (1.631gms, 7.0 mmol.), DIPC, Et_3N (2.8ml) and stirred at room temp.for 24hr. The reaction mixture was filtered and the filtrate was concentrated under reduced pressure, residue was dissolved in $CHCl_3$, washed with 10% $NaHCO_3$ (10ml) and 5% HCl (10ml), dried over anhydrous Na_2SO_4 and evaporated under vacuum to get the title compounds. The crude product was recrystallized from $CHCl_3$ and n-hexane [8, 9].

SCHEME-2



4-[2'-(5'-nitro)imidazolyl]benzoyl(N-Me)Valine

2.4 Preliminary Analysis of the sample:

Thin-layer chromatography (TLC) was commonly used in the qualitative description of the complexity and composition of chemical mixtures.

Application of sample on TLC plates:

- The sample was applied to the chromatogram by repeated "spotting" above 1-2 cm from one end of the plate with a capillary tube.
- The most important precaution was not to apply spots below the level of the top of the solvent system in developing chamber

Developing solvent systems:

Development chamber was used for developing chromatogram. Chloroform: Methanol: Water 5:3:2 was the solvent system used for running TLC of these compounds.

Visualization of chromatogram:

After developing, the TLC plates were dried and then exposed to iodine vapours in a chamber, since chromalograms of many synthetic products were frequently observed by iodine vapors. Rf value was noted down. Purity of all the synthesized compounds including intermediates was checked by TLC on silica gel G plates. All compounds have shown only single spot indicating the completion of the reaction and thepurity of the product obtained.

$$\text{Rf value} = \frac{\text{Distance traveled by solute front}}{\text{Distance traveled by solvent front}}$$

Table.1

s.no	**Physicochemical analysis**	
1.	Mol. Formula	$C_{16}O_5N_4H_{18}$
2.	Mol. Weight	346
3.	Melting Point	120°C
4.	Physical state	Reddish Brown solid
5.	Rf.Value	0.53
6.	Solvent System	$CHCl_3$: CH_3OH : H_2O (5:3:2)

3. RESULTS AND DISCUSSION

The synthesized new amino acid derivatives further studied for characterization of IR, NMR and Mass spectra's. To study the structure-activity relationship and to optimize the structure.

^{1}HNMR (300 MHz, $CDCl_3$) δ in ppm (fig.no 1):

δ 7.7(2H, d, Aromatic-H),δ 7.6 (2H, d, Aromatic-H),δ 7.15 (1H, s, Aromatic-H),δ 6.2 (1H, br.s, NH_2) δ 4.6 (1H, m, α-H) ,δ3.8 (3H, s,-OCH_3) δ2.9 (3H, S,-NCH_3),δ1.2 (1H, m, β-H),δ0.85 (6H, d, CH_3 group of Valine)

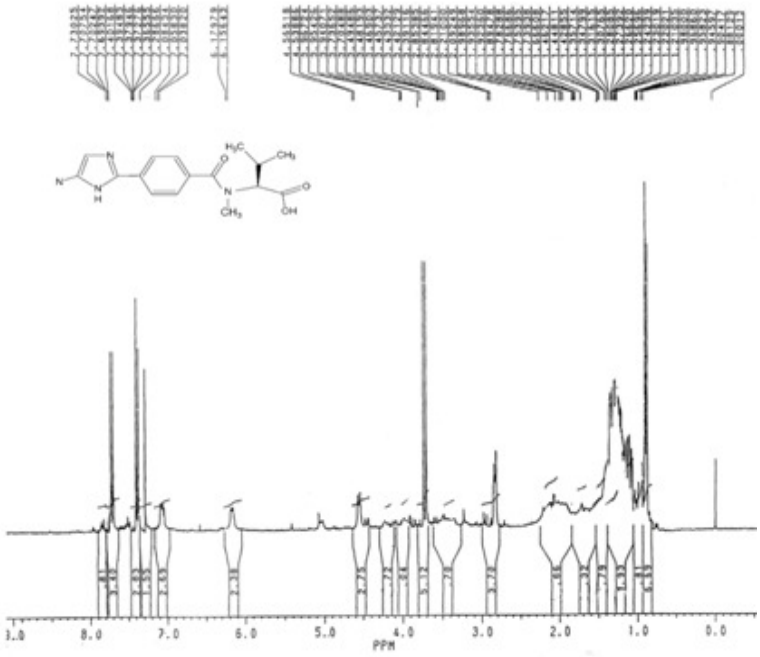


Fig. no.1: ^{1}HNMR Of 4-[2'-(5'-nitro)imidazolyl]benzoyl(N-Me)Valine

IR ($CHCl_3$) in cm-1(fig.no 2):

Peak at 3292.1 corresponds to NH and Aromatic C-H stretching, peak at 2931.1 corresponds to Aliphatic C-H stretching; peak at 2855.4 corresponds to Aliphatic C-H stretching, peak at 1701.5 corresponds to C=O (carbonyl) stretching peak at 1628.9 corresponds to C=O (amide) stretching,Peak at 1543.6 corresponds to N-H bending, peak at 1487.3 corresponds to C-H bending.

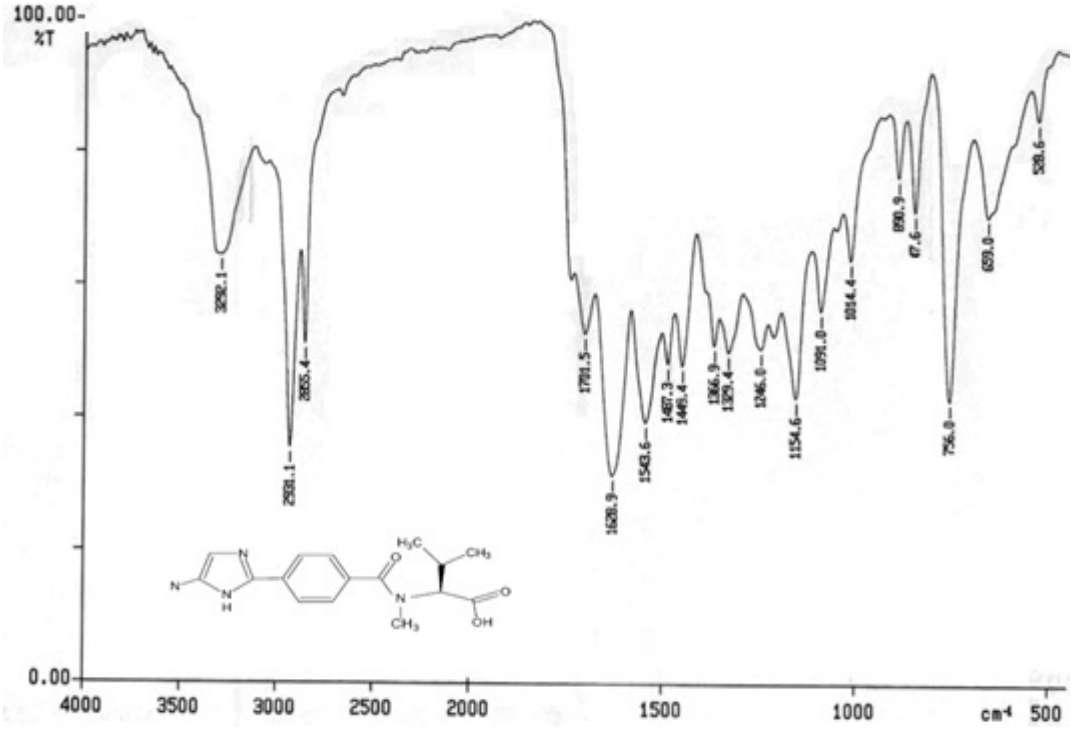


Fig. no:2 IR Spectrum of 4-[2'-(5'-nitro)imidazolyl]benzoyl(N-Me)Valine

M/z: 361 corresponds to molecular ion peak

Mass in m/z (fig.no 6):

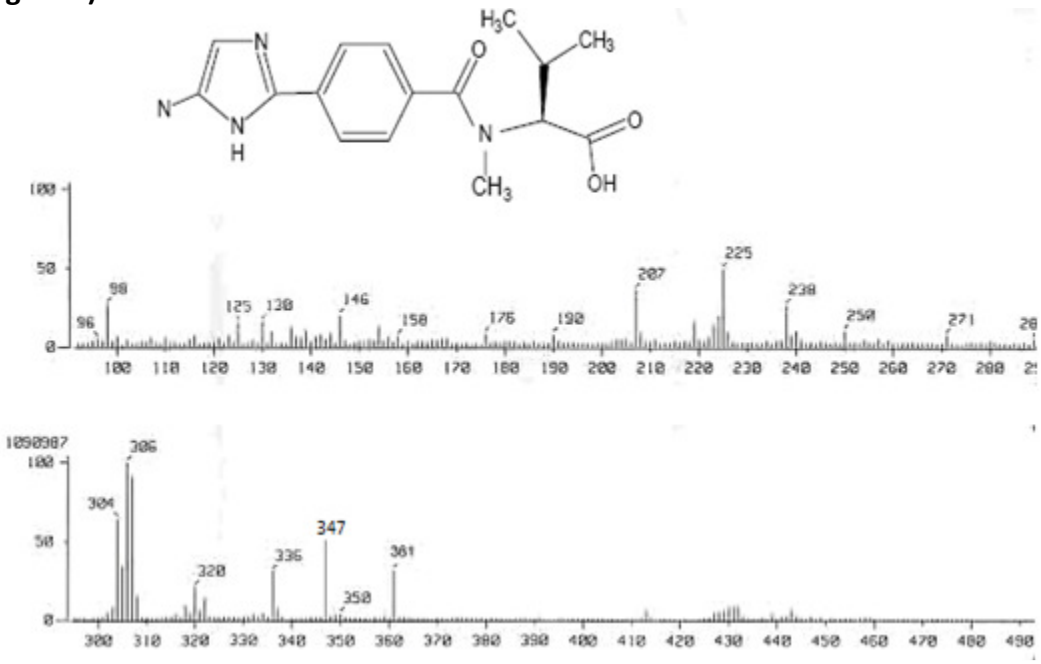


Fig.no.3: Mass spectrum of 4-[2'-(5'-nitro)imidazolyl]benzoyl(N-Me)Valine

4. CONCLUSION

The new 4-[2'-(5'-nitro) imidazolyl] benzoyl (N-Me) amino acid derivatives was synthesized and characterized by IR, NMR and Mass spectral data. By this studies find the structure-activity relationship and to optimize the structure. The synthesized amino acid derivative i.e., 4-[2'-(5'-Nitro) imidazolyl] benzoyl N-Me) valine was confirmed by physicochemical & spectral analysis.

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REFERENCES

1. Bansal RK, 'Synthesis, Reaction and Mechanism of Heterocyclic Chemistry*", Indian Journal Chemistry*, vol.12, Pg no 34-36, 1996.
2. Belagali SL, Harish K, Boja P and Himaja M., "Synthesis and biological studies of 5 (p-chlorophenyl)-furan-2-carbony peptides and 4-[2'-(5'-formyl) furyl]benzoyl peptides", *Indian Journal Chemistry*, vol.6, pg no.378-387, 1998.
3. Belagali SL and Himaja M, "Synthesis and biological activity of pyridine-3- carboxyl amino acids and peptides", *Indian Journal Heterocycle Chemistry*, vol.22, pg no.8-11, 1998.
4. Stanchev M, Tabakova S, Vedeno VG, Galovinsky E, Jung G, "Synthesis and oxazole moieties",*Arch Pharm Wheinhein,* vol.19, pg no.332 – 292, 1999.
5. Boja P, Belagali SL, Harish K, Holla BS and Gonsalves R."Synthesis and characterization of some amino acids derivatives of 3-carbethoxy-methyl-7- hydroxy-4 methyl coumarins", *Indian Journal Heterocycle Chemistry*, vol.3, pg no.263, 2000.
6. Belagali SL, Mathew T, Himaja M, Kocienski P. "A highly efficient method of N-Methylation for the amino acid derivatives" *Indian Journal Chemistry*,vol 34, pg no 45-57, 1995.
7. Benoiton NL, Akyusekli D, Chen. FM,"N,N-dialkoxycarbonyl amino acid from the sodium hydroxide mediated reaction of alkyl chloroformates with anhydrides of N-alkoxy carbonyl amino acids*",International Journal of Protein Research*,vol 45, pg no 466-470,1995.
8. Bauer AW, Kirby WM, Shersis JC, Turck M, "Antibiotic susceptibility testing by a standardized single disk method".*Indian Journal of chenistry,* vol 45,pg no493-496,1996.
9. Himaja M. Rajiv T, Geetha P, Harish K, Boja et al." hymenamide A, Unusual Biologically active Cyclic Peptide".*Boll Chim. Farmaceutico-Anno*, vol.13, pg.no168-175, 1999.

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