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Research Article

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Synthesis and Characterization of 4-[2'-(5'-Nitro) Imidazolyl] Benzoyl (N-me) Phenyl alanine

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ABSTRACT

In the past two decades, a wide variety of bioactive peptides have been discovered.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.The new phenyl alanine derivatives compounds are characterized by using IR, H^1NMR and mass spectroscopy.

Key words: Tyrosine, Valine, Alanine, Benzoic Acid, Imidazole, Phenyl alanine

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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.[1, 2].

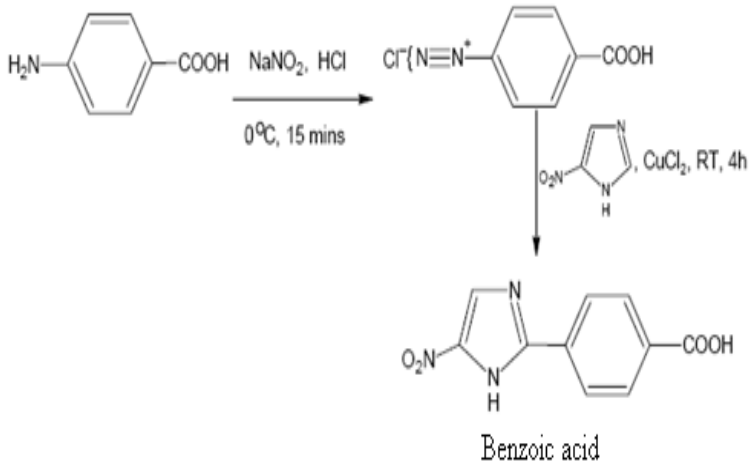
N-methylated amino acids are commonly found in naturally occurring peptide antibiotics. The methylation of N-atom and the hydrogen bonding pattern of peptide containing these amino acids are different from that of unmethylated peptide. The N-methylated peptide antibiotics are found to possess enhanced 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].

EXPERIMENTAL SECTION

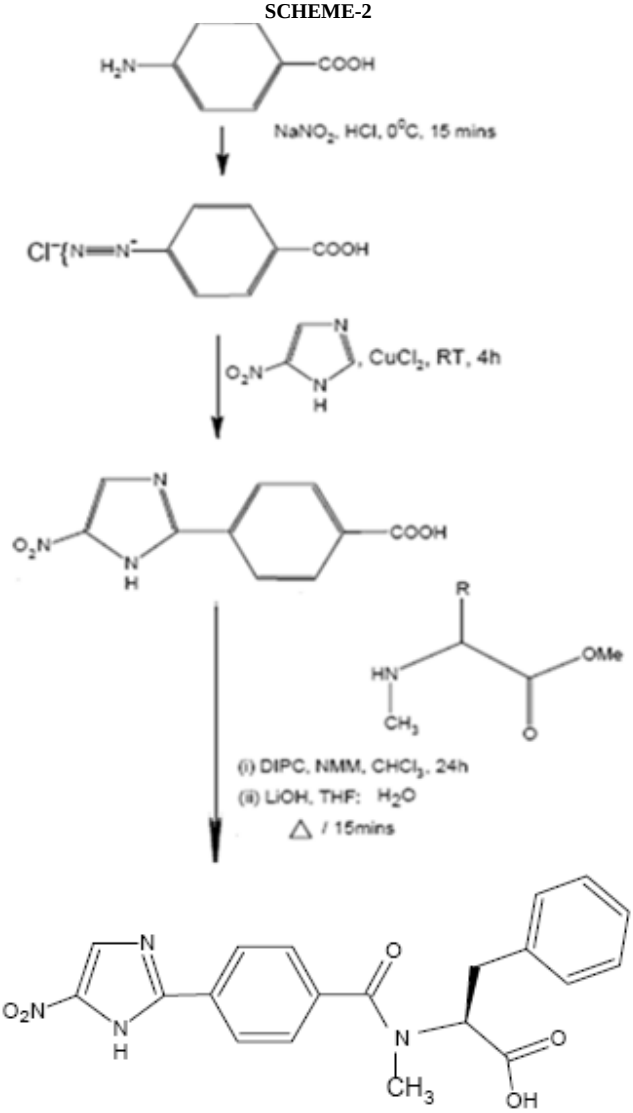
2.1 Synthesis of N-methyl amino acids methyl ester:

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].

SCHEME-1



SCHEME-2



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

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 room temperature 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].

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]**.**

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. R_f 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.

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

Table.1 Physical data of 4-[2'-(5' nitro) imidazolyl] benzoic acid

S.no	Product Name	Physical state	M.P(^{0}C)	% yield
1.	4-[2'-(5' nitro) imidazolyl]benzoic acid	Pale brown solid	256	21.49

Physicochemical analysis Table.2

S.no	**4-[2'-(5'-nitro)imidazolyl]benzoyl(N-Me)Phenyl alanine**	
1.	Mol. Formula	$C_{20}O_5N_4H_{18}$
2.	Mol. Weight	394
3.	Melting Point	173^{o}C
4.	Physical state	Sticky Brown Mass
5.	R_f.Value	0.64
6.	Solvent System	$CHCl_3$: CH_3OH : H_2O (5:3:2)

RESULTS AND DISCUSSION

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

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

δ 7.6 (1H, m, - NH)
δ 7.4 (1H, m, Aromatic-H) δ 7.1 (2H, m, Aromatic-H) δ 6.9 (2H, m, Aromatic-H)
δ 4.8 (1H, m, α-H)
δ3.8 (1H, s, $COCH_3$) δ2.9 (1H, s, -N-CH_3)
δ1.4 (2H, d, β-CH_2) δ1.2 (1H, m, γ -H) δ0.95 (6H, d, CH_3) group of phenyl alanine

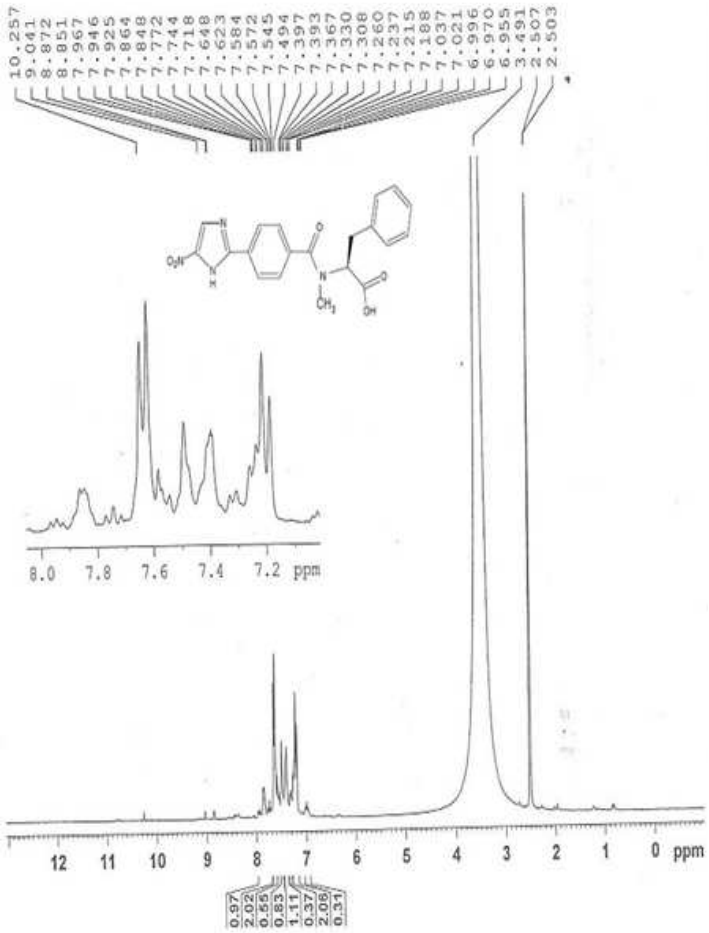


Fig.no.1

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

Peak at3448.77 corresponds to NH and Aromatic C-H stretching
Peak at 2919.63corresponds to Aliphatic C-H stretching
Peak at1645.67 corresponds to Aliphatic C-H stretching
Peak at1461.75 corresponds to C=O (carbonyl) stretching
Peak at 1410.13corresponds to C=O (amide) stretching
Peak at 1377.42 corresponds to N-H bending
Peak at 1314.98 corresponds to C-H bending.

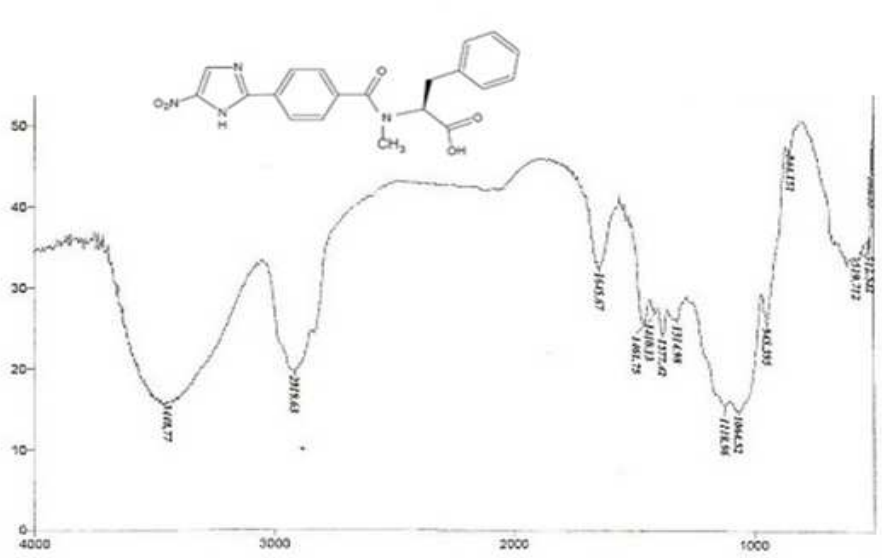


Fig.no.2

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) Phenyl alanine was confirmed by physicochemical & spectral analysis.

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