**INTRODUCTION**

Chalcones and isoxazolines have been reported to possess various biological activities such as antifungal,\(^1\) antiviral,\(^2\) anticancer\(^3\) and anti HIV\(^5\) agents. They have also been reported as good chelating agents.\(^6\)

From the literature, we found that several isoxazolines are known to display antimicrobial and therapeutic activities. Literature survey reveals scant mention of the above compounds with antimicrobial properties and hence more and more derivatives are worth tested for the possible medicinal applications. So we have decided to synthesis 5-(substitutedphenyl)-(3-[4-(2-methyl-4-(4-hydroxy benzylidene)-5-oxo-imidazol-1-yl)]phenyl)-isoxazol and study of the antimicrobial activities.

**EXPERIMENTAL**

Melting points were taken in open capillary tube and were uncorrected. IR spectra (KBr) were recorded on I.R. Spectrophotometer of Buck scientific Model No. 500 and instrument used for NMR Spectroscopy was DUL 13C-1, 300 MHz and tetramethyl silane used as internal standard. Solvent used were CDCl\(_3\) and DMSO. Purity of the compounds were checked by tlc on silica- G plates. Anti microbial activities were tested by Cup-Borer method.
Preparation of 4-(4-hydroxybenzylidene)-2-methyl-1,3-oxazol-5-one (P-1).

In a 500 ml conical flask equipped with a reflux condenser a mixture of 4-hydroxybenzaldehyde (45.184g, 0.37M), acetyl glycine (29g 0.25 M), acetic anhydride (63.5g, 0.62M) and anhydrous sodium acetate(15g 0.183 M) was placed and heated on an electric hot plate with constant shaking. As soon as the mixture has liquefied completely, transfer the flask to a water bath and heat for 2 hours. Then add 100 ml of ethanol slowly to the contents of the flask, allow the mixture to stand overnight, filter the crystalline product with solution, wash with 25 ml of ice-cold alcohol and then finally wash with 25 ml of boiling water, dry at 100 °C. The yield of almost pure oxazolone was 70 %, m.p.187°C.

Molecular Formula = C11H9NO3
Formula Weight  = 203.19406
Composition required = C(65.02%) H(4.46%) N(6.89%)
Composition found = C(65.01%) H(4.43%) N(6.88%)

Preparation of 1-(4-acetylphenyl)-4-(4-hydroxybenzylidene)-2-methyl-imidazol-5-one (P-2).

In a 250 ml conical flask equipped with a reflux condenser a mixture of 4-(4-hydroxybenzylidene)-2-methyl-1,3-oxazol-5-one(20.319g, 0.1M), 1-(4-aminophenyl)ethanone (13.51g, 0.1M), 25 ml pyridine and about one pellet of KOH was placed and was heated on sand bath for 7-8 hours. The mixture was then poured in ice. The precipitates were collected, washed with 10% HCl and re-crystallized from ethanol. The yield of the product was 73 % and the product melts at 124°C.

Molecular Formula = C19H16N2O3
Formula Weight = 320.34194
Composition required = C(71.24%) H(5.03%) N(8.74%)
Composition found = C(71.22%) H(5.01%) N(8.72%)

Preparation of 4-(4-hydroxybenzylidene)-1-[4-[3-(4-chlorophenyl)prop-2-enoyl]phenyl]-2-methyl-imidazol-5-one (P-3a)

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<th>Yield (%)</th>
<th>M.P. °C</th>
<th>Carbon (%)</th>
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Preparation of 5-(substitutedphenyl)-3-[4-(2-methyl-4-(4-hydroxybenzylidene)-5-oxo-imidazol-1-yl)]phenyl-isoxazole (P-2).

To the solution of 1-(4-acetylphenyl)-4-(4-hydroxybenzylidene)-2-methyl-imidazol-5-one, 1-(4-acetylphenyl)-4-(4-hydroxybenzylidene)-2-methyl-imidazol-5-one, and 1-(4-acetylphenyl)-4-(4-hydroxybenzylidene)-2-methyl-imidazol-5-one was added a solution of 5-(substitutedphenyl)-3-[4-(2-methyl-4-(4-hydroxybenzylidene)-5-oxo-imidazol-1-yl)]phenyl-isoxazole in ethanol. The mixture was heated on a water bath for 2 hours. The precipitate was collected, washed with 10% HCl and re-crystallized from ethanol. The yield of the product was 73 % and the product melts at 124°C.

Molecular Formula = C19H16N2O3
Formula Weight = 320.34194
Composition required = C(71.24%) H(5.03%) N(8.74%)
Composition found = C(71.22%) H(5.01%) N(8.72%)

Preparation of 4-(4-hydroxybenzylidene)-2-methyl-imidazol-5-one (P-3a)

To the solution of 4-(4-hydroxybenzylidene)-2-methyl-imidazol-5-one in ethanol, 5-(substitutedphenyl)-3-[4-(2-methyl-4-(4-hydroxybenzylidene)-5-oxo-imidazol-1-yl)]phenyl-isoxazole was added. The mixture was heated on a water bath for 2 hours. The precipitate was collected, washed with 10% HCl and re-crystallized from ethanol. The yield of the product was 73 % and the product melts at 124°C.

Molecular Formula = C19H16N2O3
Formula Weight = 320.34194
Composition required = C(71.24%) H(5.03%) N(8.74%)
Composition found = C(71.22%) H(5.01%) N(8.72%)

Acetyl glycine + 4-hydroxy benzaldehyde

\[
\text{HOOC-CH}_2\text{NH}_2\text{CONH}_2 \quad \text{Ac}_2\text{O} \quad \text{CH}_2\text{COONa}
\]

\[
\begin{array}{c}
\text{HO-} \\
\text{CHO-}
\end{array}
\]

P-1

4-(4-hydroxybenzylidene)-2-methyl-1,3-oxazol-5-one

Reflux for 7-8 hours

\[
\begin{array}{c}
\text{H}_2\text{N-} \\
\text{CO-CH}_3
\end{array}
\]

\[
\begin{array}{c}
\text{Pyridine}
\end{array}
\]

\[
\begin{array}{c}
\text{1-(4-aminophenyl)ethanone}
\end{array}
\]

P-2

1-(4-acetylphenyl)-4-(4-hydroxybenzylidene)-2-methyl imidazol-5-one

Reflux for 10 hours

\[
\begin{array}{c}
\text{R-CHO}
\end{array}
\]

\[
\begin{array}{c}
\text{Ethanol}
\end{array}
\]

P-3

4-(4-hydroxybenzylidene)-1-(4-[3-(substitutedphenyl)prop 2 enoylphenyl]-2-methyl-imidazol-5-one

Reflux for 10 hours

\[
\begin{array}{c}
\text{NH}_2\text{OH, HCl}
\end{array}
\]

\[
\begin{array}{c}
\text{Dioxane}
\end{array}
\]

P-4

5-(substitutedphenyl)-3-[4-(2-methyl-4-(4-hydroxybenzylidene)-5-oxo-imidazol-1-yl)[phenyl]-isoxazol
hydroxybenzylidene)-2-methyl-imidazol-5-one (3.203g, 0.01M) in absolute ethanol (50 ml), 4-chlorobenzaldehyde (1.40g, 0.01M) and 2 % NaOH (10 ml) were added and refluxed for 10 hours. After refluxing the reaction mixture was concentrated, cooled, filtered and neutralized with dil. HCl. The solid residue thus obtained was recrystallized with suitable solvent. The yield of the product was 62 % and the product melts at 160°C.

Molecular Formula = C_{26}H_{19}ClN_{2}O_{3}  
Formula Weight = 442.89366
Composition required = C(70.51%) H(4.32%) N(6.33%)
Composition found = C(70.50%) H(4.31%) N(6.31%)

**Preparation of 5-(4-chlorophenyl)-{3-[4-(2-methyl-4-(4-hydroxy benzylidene)-5-oxo-imidazol-1-yl)]phenyl}-isoxazol (P-4a)**

A mixture of 4-(4-hydroxybenzylidene)-1-{4-[3-(4-chlorophenyl)prop-2-enoyl]phenyl}-2-methyl-imidazol-5-one (4.428g, 0.01M) in 25ml dioxane, hydroxylamine hydrochloride (0.715g, 0.01M) and 40% potassium hydroxide (KOH) was refluxed for 10 hours. Then the reaction mixture was cooled, poured into crushed ice (100g) and neutralized with HCl. The product separated out was filtered, washed with water, dried and recrystallised from alcohol. The yield of the product was 60% and the product melts at 210°C.

Molecular Formula = C_{26}H_{18}ClN_{3}O_{3}
Formula Weight = 455.89242
Composition required = C(68.50%) H(3.98%) N(9.22%)
Composition found = C(68.48%) H(3.95%) N(9.21%)

**IR (KBr):**
3345 cm^{-1} (-OH), 3095 cm^{-1} (=CH-), 2920 cm^{-1} (-CH Stretch), P-4b 1720 cm^{-1} (>C=O imidazolone), 1605 cm^{-1} (>C=N-), 1505 cm^{-1} (>C=C<), 1370 cm^{-1} (-CH_{3} bend), 1250 cm^{-1} (C-O), 1150 cm^{-1} (C-N), 785 cm^{-1} (C-Cl).

**NMR:**
\[\delta_{2.490,}\text{ singlate (3H)} (-CH_{3})\]
\[\delta_{5.746,}\text{ singlate (1H)} (=\text{CH-vinylic})\]
\[\delta_{7.649,}\text{ complex (13H)} (\text{Ar-H})\]
\[\delta_{8.664,}\text{ singlate (1H)} (-\text{OH})\]

The short review of the antibacterial and anti fungal studies being conducted on some compounds of this series is as follows.

**Against Escherichia coli**

The maximum activity was shown by the compounds P-4a, and P-4i, the zone of inhibition are 16mm, and 15mm respectively, and the minimum activity was shown by the compounds P-4d the zone of inhibition is 11mm.

**Against S. aureus**

The maximum activity was shown by the compounds P-4c, P-4a and P-4b, the zone of inhibition are 16mm, 15mm, and 15mm and the minimum activity was shown by the compound P-4d the zone of inhibition is 10mm.

**Against Candida albicans**

The maximum activity was shown by the compounds P-4c and P-4a, the zone of inhibition are 20mm and 18mm and the minimum activity was shown by the compounds P-4j the zone of inhibition is 11mm.

**ACKNOWLEDGEMENTS**

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**REFERENCES**