March 2010 ISSN: 0974 - 7516 Volume 6 Issue 1

Trade Science Inc.

Organic CHEMISTRY

An Indian Journal

Full Paper

OCAIJ, 6(1), 2010 [66-69]

# Synthesis, spectral and microbial studies of 3-{4-[2-methyl-4-(4-methoxybenzylidene)-5-oxo-imidazol- 1-yl]phenyl}-2-(substituted phenyl)-1,3-thiazolidin- 4-one

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*Received: 21st January, 2010 ; Accepted: 31st January, 2010*

## ABSTRACT

3-{4-[2-methyl-4-(4-methoxybenzylidene)-5-oxo-imidazol- 1-yl]phenyl}-2-(substituted phenyl)-1,3-thiazolidin- 4-one have been prepared by the refluxation for 8 hours of 4-(4-methoxybenzylidene)-1-{4-[(stituted-benzylidene)amino]phenyl}-2-methyl-imidazol-5-one with thioglycolic acid and anhydrous zinc chloride in presence of ethanol. the intermidiate 4-(4-methoxybenzylidene)-1-{4-[(stitutedbenzylidene) amino]phenyl}-2-methyl-imidazol-5-one synthesized by the condensation of 1-(4-aminophenyl)-4-(4-methoxybenzylidene)-2-methyl-imidazol-5-one with various aldehydes.



## KEYWORDS

Stitutedbenzylidene;
Benzaldehyde;
Recrystallization;
Oxazolone.

## INTRODUCTION

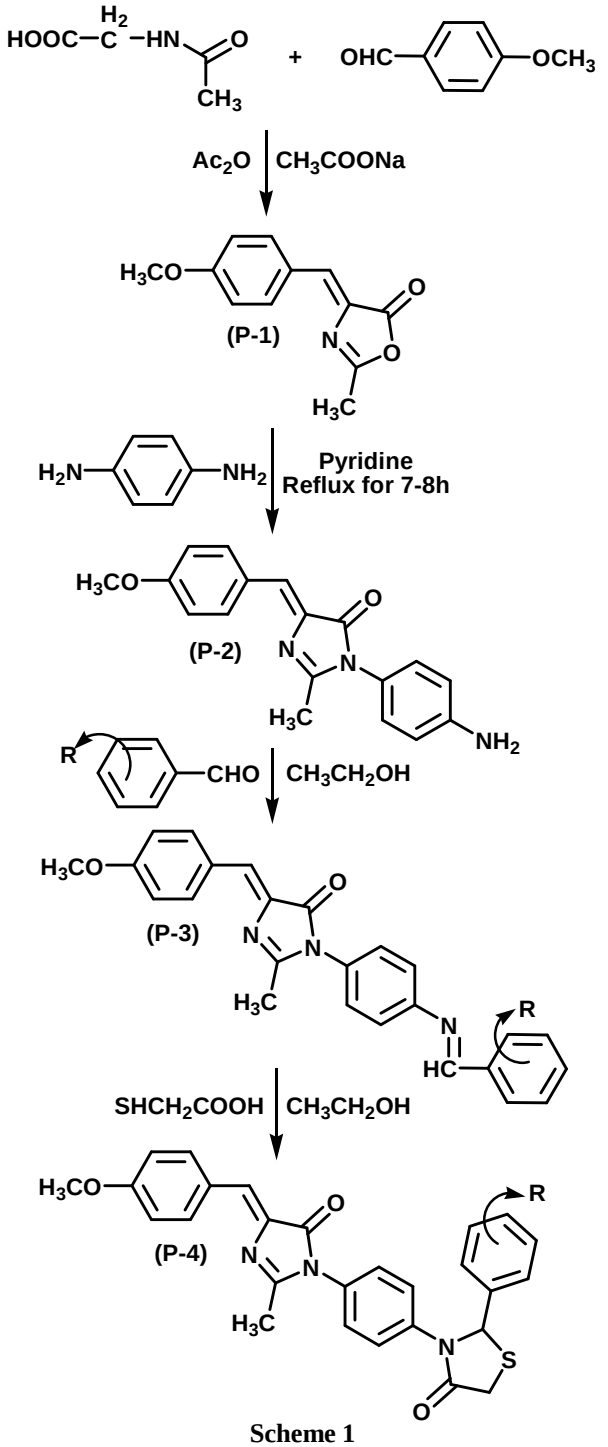
Numerous reports have appeared in literature, which highlight the chemistry and uses of 4-thiazolidinones derivatives. F.C.Brown reviewed the chemistry of 4-thiazolidinones in depth in 1961[1]. The chemistry and importance of 4-thiozolidinone have been reviewed in depth by Newkome[2] and Singh[3].

4-Thiazolidinone and its derivatives are known to possess a variety of Physiological properties viz. analgesic, local[4] and spiral[5] anesthetic, CNS stimulant[6], hypnotics[7], antibacterial[8], antifungal[9], antitubercular[10], anticancer and anti-HIV[11].

From the literature, we found that several 4-thiazolidinones are known to display antimicrobial and therapeutic activies. 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 decieded to synthesis3-{4-[2-methyl-4-(4-methoxybenzy lidene)-5-oxo-imidazol-1-yl]phenyl}-2-(substituted phenyl) -1,3-thiazolidin- 4-one.

## 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 $^{13}$C-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.




Scheme 1

## Preparation of 4-(4-methoxybenzylidene)-2-methyl-1,3-oxazol-5-one (P-1)

In a 500ml conical flask equipped with a reflux condenser a mixture of 4-methoxy benzaldehyde (50.394g, 0.37M), acetyl glycine (29g, 0.25M), acetic anhydride (63.5g, 0.62M) and anhydrous sodium acetate (15g, 0.183M) 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 25ml of ice-cold alcohol and then finaly wash with 25ml of boiling water, dry at 100°C. The yield of almost pure oxazolone was 78 %, m.p.193°C.

Found: C(66.32%) H(5.09%) N(6.42%), Calcd. for $C_{12}H_{11}NO_3$: C(66.35%) H(5.10%) N(6.45%).

## Preparation of 1-(4-aminophenyl)-4-(4-methoxy benzylidene)-2-methyl-imidazol-5-one (P-2)

In a 250ml conical flask (equipped with a reflux condenser) a mixture of 4-(4-methoxybenzylidene)-2-methyl-1,3-oxazol-5-one (21.722g, 0.1M), benzene-1,4-diamine (10.81g, 0.1M), 25ml pyridine and about one pellet of KOH was placed and was heated on sand bath for 7-8hours. 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 72 % and the product melts at 184°C.

Found: C(70.32%) H(5.55%) N(13.64%), Calcd. for $C_{18}H_{17}N_3O_2$: C(70.34%) H(5.58%) N(13.67%).

IR (KBr); ($cm^{-1}$): 3360 (>N-H), 3095 (= CH-), 2910 (-CH Stretch), 1720 (>C = O imidazolone), 1605 (>C = N-), 1505 (>C = C<), 1375 (-$CH_3$ bend), 1250 (C-O), 1150(C-N).

## Preparation of 4-(4-methoxybenzylidene)-1-{4-[(substitutedbenzylidene) amino] phenyl}-2-methyl-imidazol-5-one (P-3)

In a 250ml flask (equipped with reflux condenser) a mixture of 1-(4-aminophenyl)-4-(4-methoxybenzylidene)-2-methyl-imidazol-5-one (3.073g 0.01M), substituted benzaldehyde (0.01M) and absolute alcohol (30ml) were placed and 1 to 2 drops of hydrochloric acid was added and then, the mixture was heated on water bath for 6 hours and then cooled and the precipitates were filtered off and re-crystallized from absolute alcohol.

IR (KBr); **(P-3c)** ($cm^{-1}$): 3095 (= CH-), 2930 (-CH Stretch), 1690 (>C = O imidazolone), 1610 (>C = N-), 1500 (>C = C<), 1420 (-$CH_3$ bend), 1250 (C-O), 1150 (C-N).

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**TABLE 1 : Physical constant of 3-{4-[2-methyl-4-(4-methoxybenzylidene)-5-oxo-imidazol- 1-yl]phenyl}- 2-(substituted phenyl)-1,3-thiazolidin- 4-one**

| No. | Sub. No. | R | Mole. For. | Mole.Wt. (g/m) | Yield(%) | M.P.°C | Carbon(%) | | Hydrogen(%) | | Nitrogen(%) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Found | Required | Found | Required | Found | Required |
| 1 | P-4a | 4-Cl | $C_{27}H_{22}ClN_3O_3S$ | 503.99988 | 58 | 208 | 64.32 | 64.34 | 4.38 | 4.40 | 8.31 | 8.34 |
| 2 | P-4b | 2-Cl | $C_{27}H_{22}ClN_3O_3S$ | 503.99988 | 54 | 218 | 64.31 | 64.34 | 4.39 | 4.40 | 8.32 | 8.34 |
| 3 | P-4c | 3-$OCH_3$, 4-$OCH_3$ | $C_{29}H_{27}N_3O_5S$ | 529.60678 | 60 | 230 | 65.75 | 65.77 | 5.11 | 5.14 | 7.91 | 7.93 |
| 4 | P-4d | H | $C_{27}H_{23}N_3O_3S$ | 469.55482 | 58 | 240 | 69.04 | 69.06 | 4.92 | 4.94 | 8.92 | 8.95 |
| 5 | P-4e | 2-OH | $C_{27}H_{23}N_3O_4S$ | 485.55422 | 55 | 149 | 66.76 | 66.79 | 4.75 | 4.77 | 8.16 | 8.65 |
| 6 | P-4f | 3-$OCH_3$, 4-OH | $C_{28}H_{25}N_3O_5S$ | 515.5802 | 62 | 185 | 65.21 | 65.23 | 4.86 | 4.89 | 8.12 | 8.15 |
| 7 | P-4g | 4-OH | $C_{27}H_{23}N_3O_4S$ | 485.5542 | 54 | 181 | 66.76 | 66.79 | 4.75 | 4.77 | 8.62 | 8.65 |
| 8 | P-4h | 4-$N(CH_3)_2$ | $C_{29}H_{28}N_4O_3S$ | 512.62262 | 59 | 205 | 67.92 | 67.95 | 5.50 | 5.51 | 10.91 | 10.93 |
| 9 | P-4i | 4-$OCH_3$ | $C_{28}H_{25}N_3O_4S$ | 499.580 | 56 | 203 | 67.30 | 67.32 | 5.01 | 5.04 | 8.40 | 8.41 |
| 10 | P-4j | 3-$NO_2$ | $C_{27}H_{22}N_4O_5S$ | 514.55238 | 52 | 132 | 63.01 | 63.02 | 4.31 | 4.31 | 10.86 | 10.89 |

**TABLE 2 : Antimicrobial activities of 3-{4-[2-methyl-4-(4-methoxybenzylidene)-5-oxo-imidazol- 1-yl]phenyl}-2-(substituted phenyl)-1,3-thiazolidin- 4-one**

| Sr. No. | Comp. No. | R | Zone of inhibitions in mm | | |
|---|---|---|---|---|---|
| | | | *E.coli* | *S. aureus* | *C. albicans* |
| 1 | P-4a | - 4-Cl | 17 | 18 | 20 |
| 2 | P-4b | - 2-Cl | 16 | 14 | 18 |
| 3 | P-4c | - 3-$OCH_3$, -4-$OCH_3$ | NA | 16 | 16 |
| 4 | P-4d | - -H | 15 | 14 | 15 |
| 5 | P-4e | - 2-OH | 16 | 15 | 16 |
| 6 | P-4f | - 3-$OCH_3$, -4-OH | 18 | 18 | 17 |
| 7 | P-4g | - 4-OH | 15 | 16 | 15 |
| 8 | P-4h | - 4-$N(CH_3)_2$ | 14 | 15 | 16 |
| 9 | P-4i | - 4-$OCH_3$ | 15 | 14 | 15 |
| 10 | P-4j | - 3- $NO_2$ | 13 | 14 | 14 |
| 11 | Penicillin | - | 18 | 20 | - |
| 12 | Kanamycine | - | 19 | 24 | - |
| 13 | Baycor 25 w.p | - | - | - | 24 |
| 14 | Amphotericine | - | - | - | 21 |

NMR: **(P-3j)**: 2.490, singlate (3H) (-$CH_3$), 3.416, singlate (3H) (-$OCH_3$), 5.783, singlate (1H) (= CH-vinylic), 5.857, singlate (1H) (-Ar-CH = N-), 7.062-7.917, multiplate (12H) (Ar-H).

## Preparation of 3-{4-[2-methyl-4-(4-methoxybenzylidene)-5-oxo-imidazol-1-yl] phenyl} -2-(substituted phenyl)-1,3-thiazolidin- 4-one (P-4)

A solution of compound 4-(4-methoxybenzylidene)-1-{4-[(substituted benzylidene) amino] phenyl}-2-methyl-imidazol-5-one (0.01M), thiogly- colic acid (0.92g, 0.01M) and anhydrous zinc chloride (2g) in absolute ethanol (60 ml) was refluxed for 8 hours, concentrated, cooled and poured into crushed ice, and then filtered. The product obtained was purified by re-crystallization from acetone.

IR (KBr); **(P-4f)**: ($cm^{-1}$): 3300 (-OH), 3090 (= CH-), 2930 (-CH), 1710 (>C = O imidazolone), 1600 (>C = N-), 1500(>C = C<), 1470 (-$CH_2$ bend.), 1350 (-$CH_3$ bend), 1250 (C-O-), 1150 (C-N), 700 (C-S-C Stretch.).

NMR: **(P-4h)**: 1.162, singlate (2H) (>$CH_2$), 1.810, singlate (6H) (-$N(CH_3)_2$), 2.490, singlate (3H) (-$CH_3$), 2.530, triplet (1H) (>CH-N<), 3.440, singlate (3H) (-$OCH_3$), 5.717, singlate (1H) (= CH-vinylic), 7.001-7.435, multiplate (12H) ( Ar-H).

## ACKNOWLEDGEMENTS

The authors are thankful to the Sheth L.H.Science College, Mansa for providing research facilities. One of the author Pankaj S.Patel is thankful to UGC. Ganeshkhind, Pune, for Teacher Research Fellowship.

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