Synthesis, Characterization and Antimicrobial activities of some new Pyrazole-1-carbothioamido derivatives.

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Abstract: Some new 5-Aryl-3-[4’-(o-chlorobenzyloxy)-3’-methoxy-phenyl]-1-carbothioamide-4, 5-dihydro-1H-pyrazole derivatives were prepared. All the prepared compounds were characterized by their spectral (I.R., N. M. R., Mass) data and screened for their antimicrobial activities.

Keywords: Chalcones & Pyrazoline derivatives, Antimicrobial activities.

I. INTRODUCTION

Pyrazoline derivatives are induce with different therapeutic activities such as antimicrobial, analgesic, anthelmintic, anti-inflammatory, antitubercular, etc. These valid observations led us to synthesize some pyrazoline derivatives bearing chlorobenzyloxy derivative of some chalcones. The chemistry of chalcones containing an active keto-ethylenic linkage has been assumed important because of their versatility in the synthesis of many heterocyclic compounds. The presence of reactive α, β-unsaturated keto function in chalcones is found to be responsible for their antiallergic and anticonvulsant. Chalcones constitute an important group of natural products and some of them possess wide range of biological activity such as bactericidal, antidiabetic, analgesic, tranquilizer, etc. Pyrazoline derivative have been found to possess wide range of therapeutic activity such as diuretic, fungicidal, herbicidal and insecticidal.

Therapeutically important of Pyrazoline is used considerable interest to synthesize Pyrazoline of type-(2a-l) by the condensation of 1-(p-Methoxyphenyl)-3-[4’-(o-chlorobenzyloxy)-3’-methoxy-phenyl]-propenones of type-(1a-l) with thiosemicarbazide in order to study their biodynamic behavior. The structure of synthesized compounds were assigned based on Elemental analysis, I. R. 1H-NMR and Mass spectral data. The antimicrobial activity was assayed by using the cup-plate agar diffusion method by measuring the zone of inhibition in mm. All the compounds were screened for their antimicrobial activities against varieties of bacterial strains such Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Proteus vulgaris and fungi Aspergillus niger at 40 μg concentration. Standard drugs like Ampicillin, Amoxicillin, Norfloxacin, Benzyl penicillin and Griseofulvin were used for comparison purpose (Table-2).

II. RESULTS AND DISCUSSION

The synthesis of 1-Aryl-3-[4’-(o-chlorobenzyloxy)-3’-methoxyphenyl]-propenones (1a-l) and 3-Aryl-5-[4’-(o-chlorobenzyloxy)-3’-methoxyphenyl]-4,5-dihydro-1H-pyrazoles (2a-l) was carried out in two steps, first by the condensation of 4-[(2-chlorobenzyloxy)-3-methoxy benzaldehyde (1) with different aromatic acetophenone by Claisen-Schmidt condensation in presence of base catalyst to give chalcone derivatives (1a-l), which in next step were refluxed with thiosemicarbazide to yield pyrazoline derivatives (2a-l). (scheme-1). The formulas of the selected compounds were confirmed by the elemental analysis and their structures were determined by IR, 1H-NMR, and mass spectral data.

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A. **Antibacterial Activity**

The screening data indicated that among Carbothioamide derivatives, tested compounds 2c, 2i, 2j and 2k showed good activity against *S. aureus*. However, the compounds 2f, 2h, 2i and 2k showed substantial activity against *B. subtilis*. The compounds 2a, 2f, 2h and 2k which possess very good against *E. coli*. However, the compounds 2a, 2e, 2f and 2g showed greater degree of antibacterial activity against *P. vulgaris*. All the compounds were found to possess moderate to good activity against Gram positive and Gram negative strains.

B. **Antifungal Activity**

The screening data indicated that among Carbothioamide derivatives, tested compounds 2d, 2h, 2i and 2l exhibited good to excellent activity against *A. niger*. All other compounds exhibit mild to moderate antifungal activity against *A. niger*.

The antibacterial activity was compared with standard drug viz. Ampicillin, Amoxicillin, Norfloxacin, Penicillin and antifungal activity was compared with standard drug viz. Griseofulvin.

### III. EXPERIMENTAL SECTION

Melting points were taken in open capillar tubes are uncorrected. IR spectra (cm⁻¹) were recorded on Shimadzu-435-IR Spectrophotometer and, ¹H-NMR spectra on Bruker spectrometer (300MHz) using TMS as an internal standard, chemical shift in δ ppm.

A. **General procedure for the preparation of 1-Aryl-3-[4'-(o-chlorobenzyloxy)-3'-methoxyphenyl]-propenones (1a-l)**

Take a mixture of 4-[2-chlorobenzyl)oxy]-3-methoxy benzaldehyde (1) (0.01M) and 4-methoxy acetonone (0.01) in methanol, add a NaOH (0.002M) to the reaction mixture. The reaction mixture was magnetically stirred for 12 hrs and then left overnight. After it was pour over ice and neutralized with dil.HCl and ethanol is added for crystallization.

B. **1-Aryl-3-[4'-(o-chlorobenzyloxy)-3'-methoxyphenyl]-propenones (1a-l)**

Yield 72%, m.p. 70⁰C; IR(KBr) : ν 2951,2874,1466 (Alkane,-CH₃), 1260 (-OCH₃), 1235 (Ar-O-C) , 1672 (C=O), 1583 (C=C) ,3061,1506,1163,818 (Aromatic) cm⁻¹; ¹H-NMR (CDCl₃) : δ 3.88, (s,6H,-OCH₃), 6.86 & 7.73 (d,2H,-CH=CH₂), 5.15(s,2H,-O-CH₂), 6.96-8.03(m,11H, ArH) , Mass m/z 408.5. M.F.:C₂₅H₂₄ClN₃O₃S .

C. **General procedure for the preparation of 3-Aryl-5-[4'-(o-chlorobenzyloxy)-3'-methoxyphenyl]-4,5-dihydro-1H-pyrazoles (2a-l)**

A mixture of 1-(p-methoxyphenyl)-3-[4'-(o-chlorobenzyloxy)-3'-methoxyphenyl]-propenone (4.08g, 0.01M) in methanol (20ml) and thiosemicarbazide (0.92 g, 0.01mol) & KOH (0.025 M), was refluxed for 7-8 hrs. The product was isolated and crystallized from ethanol.

D. **3-Aryl-5-[4'-(o-chlorobenzyloxy)-3'-methoxyphenyl]-4,5-dihydro-1H-pyrazoles(2a-l)**

Yield 77%, m. p. 135⁰ C; IR(KBr) : ν 2941.26, 1452.51 (Alkane,-CH₃), 1239.59 (-OCH₃), 747.88 (-C-Cl); 1213.82 (Ar-O-C), 1679.94 (C=N), 3022.44,1503.54,1136.81,834.42 (Aromatic), 886.64 (-NH), 1597.77 (C=S) cm⁻¹; ¹H-NMR (CDCl₃) : δ 5.30 (s,2H,-O-CH₂), 6.86-8.06 (m,14H, ArH), 3.89 & 3.98 (s,6H,-OCH₃), 8.01 (s,2H,-CS-NH₂) .Mass m/z 481.5. M.F.: C₂₅H₂₄ClN₃O₃S .
Table 1

| compd no. | R          | Molecular formula | Molecular weight | M.P. ⁰C | % yield | % of N calc. | % of N found. |
|-----------|------------|-------------------|------------------|---------|---------|--------------|---------------|
| 2a        | -C₆H₅     | C₂₃H₂₃ClN₂O₂S     | 451.5            | 118     | 66      | 9.30         | 9.24          |
| 2b        | -4-NH₂-C₆H₄| C₂₃H₂₃ClN₂O₂S     | 466.5            | 123     | 65      | 12.00        | 11.84         |
| 2c        | -4-Br-C₆H₅| C₂₃H₂₃BrClN₂O₂S   | 530.5            | 137     | 70      | 7.92         | 7.90          |
| 2d        | -4-Cl-C₆H₅| C₂₃H₂₃ClN₂O₂S     | 486              | 126     | 68      | 8.64         | 8.61          |
| 2e        | -2,4-(Cl₂)-C₆H₅| C₂₃H₂₀Cl₂N₂O₂S | 520.5            | 109     | 71      | 8.07         | 8.01          |
| 2f        | -2-OH-C₆H₄| C₂₃H₂₂ClN₂O₂S     | 467.5            | 86      | 75      | 8.98         | 8.93          |
| 2g        | -3-OH-C₆H₄| C₂₃H₂₂ClN₂O₂S     | 467.5            | 90      | 60      | 8.98         | 8.92          |
| 2h        | -4-OH-C₆H₄| C₂₃H₂₂ClN₂O₂S     | 467.5            | 101     | 68      | 8.98         | 8.93          |
| 2i        | -4-OCH₃-C₆H₄| C₂₃H₂₂ClN₂O₂S | 481.5            | 135     | 77      | 8.72         | 8.70          |
| 2j        | -4-CH₃-C₆H₄| C₂₃H₂₂ClN₂O₂S     | 465.5            | 124     | 66      | 9.02         | 9.00          |
| 2k        | -3-NO₂-C₆H₄| C₂₃H₂₂ClN₂O₂S     | 496.5            | 101     | 64      | 11.28        | 11.22         |
| 2l        | -4-NO₂-C₆H₄| C₂₃H₂₂ClN₂O₂S     | 496.5            | 158     | 69      | 11.28        | 11.25         |

Table 2

![Graph showing antibacterial and antifungal activity](image)

Scheme 1

![Reaction scheme](image)

IV. CONCLUSION

The present study leads to a convenient synthetic method for the synthesis of new compounds. Which show significant antibacterial and antifungal activity. Further investigation with appropriate structural modification of the above compounds may result in therapeutically useful products.
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