

Synthesis and Antimicrobial Activity of Oxadiazole and Imidazolinone Derivatives Bearing Trimethoxybenzamide Moiety

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Among a wide variety of nitrogen heterocycles that have been explored for developing pharmaceutically important molecules, the oxadiazoles¹ and imidazolinones² have played an important role in medicinal chemistry. Furthermore, incorporation of 3,4,5-trimethoxybenzamide moiety has been found to enhance the pharmacological activity. Therefore in the present study, we have coupled it with oxadiazole and imidazolinone moieties with a view to evaluating their antimicrobial activity. 2-Aryl-5-*p*-(3',4',5'-trimethoxybenzamido)phenyl)-1,3,4-oxadiazoles (**2**) have been prepared by the cyclocondensation of 4-(3',4',5'-trimethoxybenzamido)benzoylhydrazide (**1**) with different aromatic acids. While 4-arylidene-1-*p*-(3',4',5'-trimethoxybenzamido)benzoylamino-2-methyl-5-oxo-2-imidazolinones (**3**) have been synthesised by the condensation of the latter hydrazide with azlactones. These compounds have been screened for their antimicrobial activity against different strains of bacteria and fungi

against *E. coli*. In case of *K. arogens*, the compounds bearing 2,6-dihydroxyphenyl showed accountable (18 mm) activity. The activity displayed by the compound bearing 3,5-dimethoxyphenyl against *S. pyogens* was comparable with that of displayed by known antibiotic drug norfloxacin.

The compounds with 3- and 4-chlorophenyl, 3,5-dinitrophenyl and 2-hydroxy-3-naphthyl displayed considerable (17–18 mm) activity against *A. niger*. In case of imidazolinone derivatives (**3**) the compound bearing 4-methoxyphenyl has displayed significant (21 mm) activity against *S. aureus*. The compound bearing 2-chlorophenyl was effective against *S. aureus* and *K. arogens*. The growth of *A. niger* was considerably (19 mm) inhibited by the compound bearing 4-methoxyphenyl moiety.

All other compounds showed moderate inhibition against both the bacterial and fungal strains.

Experimental

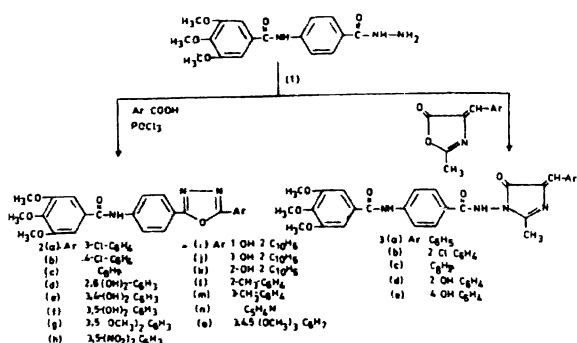
M.ps. were taken in open capillaries and are uncorrected. Ir, pmr and mass spectra were recorded on Shimadzu 435-IR spectrophotometer, Perkin-Elmer R-32 spectrometer using DMSO-*d*₆ as solvent and TMS as internal reference and on Jeol-JMS D-300 spectrometer respectively.

4-(3',4',5'-Trimethoxybenzamido)benzoylhydrazide (**1**) was prepared by known method⁴.

2-(2''-Methylphenyl)-5-*p*-(3',4',5'-trimethoxybenzamido)phenyl)-1,3,4-oxadiazole (**2**): A mixture of **1** (0.01 mol) and 2-methylbenzoic acid (0.01 mol) in phosphorous oxychloride (5 ml) was refluxed for 5–6 h. The contents were then cooled and the resulting solid was crystallised from methanol to yield **2i** (58%), m.p. 101° (Found : C, 67.35; H, 5.12; N, 9.36. C₂₅H₂₃N₃O₅ calcd. for . C, 67.41; H, 5.17; N, 9.44 %); ν_{max} (KBr) 3 300 (N–H asym.), 3 250 (N–H sym.), 1 640 (C=O), 1 610 (C=N), 1 290 (C–O–C asym.), 1 100 (C–O–C oxadiazole moiety) and 1 030 cm⁻¹ (N–N); δ 2.5 (3H, s, 2''-Ar–CH₃), 3.70 (3H, s, 4'-OCH₃), 3.83 (6H, s, 3',5'-OCH₃), 7.20 (2H, s, C₆H₂), 7.60–7.90 (9H, m, ArH), 10.40 (1H, s, CONH); *m/z* 445 (M⁺), 388, 368, 314, 249, 236, 194, 119 and 91.

Similarly, other compounds (yields 58–81%) were prepared : **2a**, m.p. 112°; **b**, 167°; **c**, 100°; **d**, 255°; **e**, 215°; **f**, 226°; **g**, 242°; **h**, 181°; **i**, 161°; **j**, 186°; **k**, 190°; **m**, 95°; **n**, 206°; **o**, 127°.

4-Arylidene-2-methyl-5-oxazolinones : These were prepared by the condensation of arylaldehydes with acetyl



Results and Discussion

All the compounds were tested for their antimicrobial activity against *S. aureus*, *S. pyogens*, *E. coli*, *K. arogens* and *A. niger* using cup-plate method³ at a concentration of 50 µg and compared with known antibiotics and antifungal drug.

In case of oxadiazole derivatives (**2**) the compound bearing 3,5-dinitrophenyl displayed promising (18 mm) activity against *S. aureus*. The maximum (17–18 mm) activity was shown by compounds bearing 3-chlorophenyl, 2,6-dihydroxyphenyl and 1-hydroxy-2-naphthyl against *S. pyogens*. The compounds having 3-chlorophenyl and 3,5-dinitrophenyl displayed significant (18–19 mm) activity

glycine in presence of sodium acetate and acetic anhydride⁵.

4-Arylidene-1-p-(3',4',5'-trimethoxybenzamido)benzoyl amino-2-methyl-5-oxo-2-imidazolines (3) : To a mixture of **1** (0.01 mol) and 4-arylidene-2-methyl-5-oxazolinone (0.02 mol), dry pyridine (20 ml) was added and the contents were refluxed for 8 h. The excess of solvent was then removed under reduced pressure and the thick slurry obtained was poured on crushed ice. The resulting solid was washed with cold water and crystallised from chloroform to yield **3a** (71%), m.p. 144° (Found : C, 65.34; H, 5.01; N, 10.81. C₂₈H₂₆N₄O₆ calcd. for : C, 65.37; H, 5.06; N, 10.89%); ν_{\max} (KBr) 3 300 (N-H asym.), 3 200 (N-H sym.), 1 710 (C=O imidazolyl), 1 650 (C=O) and 1 255 cm⁻¹ (C-O-C); δ 1.05 (3H, s, C-CH₃ imidazolinone), 3.80 (3H, s, 4'-OCH₃), 3.90 (6H, s, 3',5'-OCH₃), 7.15 (1H, s, =CH-Ar), 7.22 (2H, s, C₆H₂), 7.30-8.20 (9H, m, Ar-H-N), 8.89 (1H, s, -C-NH-N) and 10.40 (1H, s, -C-NH-).

Similarly other compounds (yields 60-69%) were

prepared : **3b**, m.p. 97°; **c**, 187°; **d**, 165° **e**, 118°.

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