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NOTE

Antimicrobial Study of Phenyl Substituted 4-Oxoacids

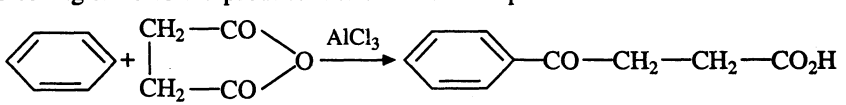
G. SIKKANDAR
Research and Post-Graduate Department of Chemistry
Jamal Mohamed College, Tiruchirapalli-620 020, India

Phenyl substituted 4-oxoacids were prepared by Friedel-Craft's reaction between substituted benzene with succinic anhydride in presence of anhydrous aluminium chloride. These compounds were tested *in vitro* for their antibacterial activity against gram positive bacteria (*S. aureus* and *S. subtilis*) and gram negative bacteria (*E. coli* and *P. aeruginosa*). The MIC values were determined by using serial dilution method.

4-Oxoacids are not only useful in the synthesis of several carbocyclic and heterocyclic compounds but they also find application as biologically active compounds[1]. The Friedel-Craft's reaction of succinic anhydride with toluene, xylene and mesitylene were reported to give the corresponding phenyl substituted 4-oxo-4-phenylbutanoic acids[2]. Aromatic ethers like anisole and phenetole were condensed with succinic anhyride to get the corresponding 4-oxoacids[3]. Literature survey reveals that there is little work on the antimicrobial study of these compounds. The title compounds were prepared and screened for their antibacterial activity against some gram positive (*S. aureus* and *B. subtilis*) and some gram negative (*E. coli* and *P. aeruginosa*) pathogens.

Preparation of 4-oxoacids

A mixture of sodium dried benzene (2.25 mol), succinic anhydride (0.34 mol) and powdered anhydrous aluminium chloride (0.75 mol) was refluxed for 1 h with continued stirring. It was added with water and ice-cold conc. HCl and the mixture was then steam distilled to separate unreacted benzene. After cooling in freezing mixture the product was obtained and purified[4].



benzene I — Succinic anhydride — 4-oxo-4-phenylbutanoic acid IIa

The Friedel-Craft's reaction of succinic anhydride with toluene, anisole, phenetole, chlorobenzene and bromobenzene yielded corresponding *p*-phenyl substituted compounds[5, 6]. However-4-oxo-4-(3-nitrophenyl) butanoic acid was prepared by the nitration of the unsubstituted 4-oxoacid. All the compounds were characterised by their melting points and spectral data.

Antimicrobial Study

The bacterial species used for screening are known pathogens. *S. aureus* causes suppurative and invasive lesions leading to pus formation. *E. coli* causes gastro-intestinal infections and secondary infection of wounds. *P aeruginosa* causes suppurative wounds and urinary tract infections and *B. subtilis* is responsible for urinary tract infections[7, 8].

The graded dilutions of the test compounds in 2.5% DMSO were prepared and the antibacterial activity was assayed using serial dilution method[9]. The minimum inhibitory concentrations (MIC) were recorded at the end of an incubation period of 24 ± 2 h. The minimum concentration able to prevent any detectable growth of the microorganism is given in Table-1.

TABLE-1
MIC VALUES IN MOLAR CONCENTRATION

Compound	Substitutent	*S. aureus*	*B. subtilis*	*E. coli*	*P. aeruginosa*
IIa	H	1.50	1.70	2.20	2.30
IIb	*p*-CH_3	2.24	2.20	2.60	2.68
IIc	*p*-OCH_3	2.28	2.32	2.72	2.72
IId	*p*-OC_2H_5	2.36	2.40	2.86	2.80
IIe	*p*-Cl	0.62	0.64	1.32	1.30
IIf	*p*-Br	0.58	0.54	1.24	1.24
IIg	*m*-NO_2	0.12	0.18	0.24	0.16

The results show that all the compounds are antimicrobially active at a definite concentration. The activity of the compounds follows the order

$$NO_2 > Br > Cl > H > CH_3 > OCH_3 > OC_2H_5$$

It is obvious that the inhibitory action gets enhanced with the introduction of nitro, chloro and bromo groups in the phenyl ring. However the compounds with ethoxy, methoxy and methyl substituents are lesser active compared to unsubstituted parent 4-oxoacid. The present study proves that the title compounds may find application for therapeutic purposes in human diseases provided they are nontoxic to human body.

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