ON THE SYNTHESIS OF SOME 1-(5-NITRO-2-FURYL)-3-ARYL-2-PROPEN-1-ONES.

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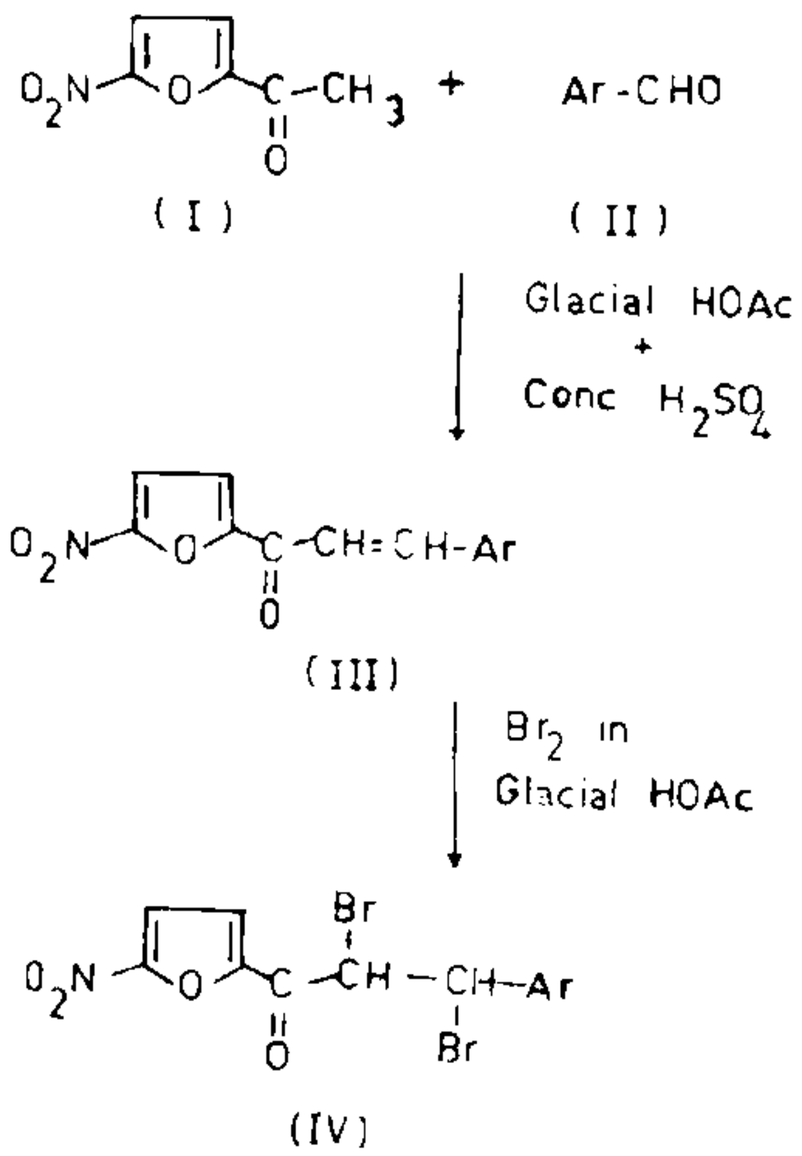
ABSTRACT

A variety of 1-(5-nitro-2-furyl)-3-aryl-2-propen-1-ones were prepared as possible antibacterial compounds. Their structures were confirmed on the basis of elemental analysis, IR, and NMR studies and by conversion into respective dibromides. The propenones were also subjected to antibacterial screening against both gram-positive and gram-negative bacteria.

INTRODUCTION

THE chemistry of chalcones has been recognized as a significant field of study for a long time because of a variety of biological activities associated with chalcones[1]. Several heterocyclic analogues have also been reported to possess bactericidal, bacteriostatic, tuberculostatic, insecticidal, antiparasitic, coronary vasodilating and choleretic activities[2-9]. Our interest in nitrofuran heterocycles[10] prompted us to synthesize and study the biological properties of chalcones carrying nitrofuran moiety. Of the two possible nitrofuryl analogues of chalcones, namely, 3-(5-nitro-2-furyl)-1-aryl-2-propen-1-ones and 1-(5-nitro-2-furyl)-3-aryl-2-propen-1-ones, a large variety of propenones of the former type are reported in literature[11-19]. However, very little work has been done on the synthesis and biological activities of the nitrofuryl propenones of the latter type[20]. In the present investigation we report the synthesis of a large number of 1-(5-nitro-2-furyl)-3-aryl-2-propen-1-ones and their dibromides and their biological activities.



Scheme 1

MATERIALS AND METHODS

5-Nitro-2-acetylfuran, obtained by nitration of 2-acetyl-furan[10], was condensed in acidic media with various substituted benzaldehydes carrying halo, methyl and methylenedioxy functions (scheme 1). Some of the substituted benzaldehydes employed for the condensation were obtained commercially and others were prepared from the corresponding aromatic amines employing the method of Beech[21, 22]. The nitrofuryl propenones (III) thus obtained were further characterized by conversion into dibromides (IV) using bromine in glacial acetic acid (scheme 1). The melting points of the new compounds were determined by capillary method and are uncorrected.

The IR spectra were obtained on a Perkin-Elmer infrared spectrophotometer. NMR spectra of some selected compounds were recorded on a 90 MHz NMR spectrometer using DMSO-d_6 as solvent and tetramethylsilane as an internal standard.

RESULTS AND DISCUSSION

The results of elemental analysis agree with theoretical values within the limits of experimental error. The physical constants and yield data are reported in tables 1 and 2. All the chalcone analogues exhibited halochromic effects with concentrated sulphuric acid. They also showed absorption bands in the region of 1665–1680 and 1610–1600 cm^{-1} characteristic of the

Table 1 *Characterization Data of* 1-(5-*Nitro*-2-*furyl*)-3-*aryl*-2-*propen*-1-*ones*

Compound No.	Ar	Yield (%) m.p.(°C)	Colour and Crystal form	Halochromism with Conc. H_2SO_4	IR(cm^{-1}) $\gamma_{C=O}$	IR(cm^{-1}) γ_{NO_2} asym. sym.
IIIa	3,4-methylene-dioxyphenyl.	87 204–6[a]	Orange micro needles	Violet	1665	1535 1365
IIIb	2-nitro-4,5-methylene-dioxyphenyl.	60 197[b]	Yellow flakes	Orange yellow	1680	1540 1380
IIIc	4-chlorophenyl	72 185[b]	Yellow needless	Pink	1660	1550 1350
IIId	2,4-dichlorophenyl	96 156–7[a]	Lemon yellow needles	Rose red	1675	1540 1360
IIIe	4-hydroxyphenyl	70 132–3[a]	Orange flakes	Orange yellow	1670	1530 1370
IIIf	4-methylphenyl	69 179[a]	Yellow stout needles	Yellowish red	1670	1545 1340
IIIg	2-bromo-4-methylphenyl	75 158[c]	Yellow micro needles	Rose red	1675	1550 1355
IIIh	2-methyl-4-bromophenyl	95 164[a]	Pale yellow needles	Dark pink	1670	1540 1380
IIIi	2-chloro-4-methylphenyl	65 142[b]	Yellow flakes	Blood red	1670	1535 1360
IIIj	2-methyl-4-chlorophenyl	69 146–7[b]	Yellow micro needles	Blood red	1665	1540 1350

Solvent of crystallization: ([a]) D.M.F. ([b]) AcOH ([c]) MeOH.

propenone moiety. Two more absorption bands in the region of 1535–1550 and 1350–1380 cm^{-1}, characteristic of the asymmetric and symmetric stretching frequencies of the nitro group were observed. In the dibromides of these propenones the stretching frequency of the carbonyl group ($\gamma_{C=O}$) was shifted to higher wave numbers indicating the loss of conjugation between carbonyl and aryl moieties on bromination. These observations are in conformity with those made by Dhar *et al.* during the infrared studies of chalocone analogues[23].

The propenones (III) were screened for their antibacterial activity against four bacteria employing the cup-plate method[24]. Chloramphenicol and dapsone (*p*-aminophenylsulphone) were used as standard drugs. The results of antibacterial screening are given in table 3. It is found that some of the propenones carrying alkyl, halo and hydroxy substituents in the aryl moiety possessed significant activity against *Aerobacter aerogenes* and *Escherichia coli*.

Table 2 *Characterization data of* 2,3-*Dibromo*-1-(5-*Nitro*-2-*furyl*)-3-*aryl*-2-*propen*-1-*ones*

Compound No.	Ar	Yield (%) m.p. (°C)	IR (cm^{-1}) $\gamma_{C=O}$	IR (cm^{-1}) γ_{NO_2} asym. sym.
IVa	3,4-methylenedioxyphenyl	70 159–61[a]	1690	1540 1360
IVb	2-nitro-4,5-methylenedioxyphenyl	69 179–81[a]	1705	1545 1350
IVc	4-chlorophenyl	89 157–58[a]	1695	1530 1350
IVd	2,4-dichlorophenyl	63 138[a]	1700	1540 1350
IVf	4-methylphenyl	67 139–41[a]	1700	1550 1340
IVg	2-bromo-4-methylphenyl	30 158[b]	1695	1560 1340
IVh	2-methyl-4-bromophenyl	57 143[a]	1700	1545 1360
IVi	2-chloro-4-methylphenyl	65 142[a]	1695	1530 1340
IVj	2-methyl-4-chlorophenyl	68 146–7[a]	1700	1540 1345

Solvent of crystallization: ([a]) HOAc ([b]) MeOH

Table 3 *Antibacterial Activity of* 1-(5-*Nitro*-2-*furyl*)-3-*aryl*-2-*propen*-1-*ones*

Compound No.	Minimum inhibitory concentration. $\mu g/ml$[a]			
	A. aer[b]	Bs[b]	Es[b]	S. au[b]
IIIa	40	100	60	100
IIIb	40	40	100	60
IIIc	40	80	140	140
IIId	20	40	40	180
IIIe	< 10	< 10	40	80
IIIf	60	40	80	120
IIIg	90	40	120	60
IIIh	100	60	140	60
IIIi	< 10	40	40	120
IIIj	< 20	< 40	< 20	160
Chloramphenicol	< 5	< 5	100	< 5
Dapsone	85	55	20	95

[a] minimum inhibitory concentration is the lowest concentration of the compound that prevents visible growth after 24 hr of incubation.

[b] A. aer: *Acrobacter aerogenes*. Bs: *Bacillus sabtilis*. Es: *Escherichia coli*. S. au: *Staphylococcus aureus*.

EXPERIMENTAL

General method for the preparation of 1-(5-*nitro*-2-*furyl*)-3-*aryl*-2-*propen*-1-*ones* (*III*):

A solution of a 5-nitro-2-acetylfuran (1.5 g, 0.01 mol) and appropriate aromatic aldehyde (0.015 mol) in glacial acetic acid (20 ml) was treated with concentrated sulphuric acid (1–2 ml). The mixture was agitated and allowed to stand at room temperature for 24 hr. The precipitated crystals of propenones (III) were collected by filtration, washed with petroleum ether (60–80°) and were recrystallized from suitable solvents. The colour, yield, melting point and other characterization data of these compounds are listed in table 1.

General method for the preparation of 2,3-*dibromo*-1-(5-*nitro*-2-*furyl*)-3-*aryl*-2-*propene*-1-*ones* (*IV*):

Propenones (III, 0.01 mol) were dissolved in glacial acetic acid (20–30 ml) by warming. The solution was cooled to room temperature and treated with a solution of bromine in glacial acetic acid (18 ml, 10% w/v), when the yellow colour of bromine persisted. The solution was allowed to stand overnight, when crystals of dibromides (IV) separated out. These crystals were collected by filtration, washed with methanol and dried. They were further recrystallized from glacial acetic acid or methanol. The colour, yield, melting point and IR data of these dibromides are listed in table

2. All the dibromides on boiling with potassium iodide in aqueous acetone regenerated the respective propenones.

Evaluation of antibacterial activity by cup-plate method

Antibacterial activity of the test compounds (III a-j) was determined against *Staphylococcus aureus*, *E. coli*, *Aerobacter aerogenes* and *Bacillus subtilis* by the cup-plate method[24]. The test compounds were dissolved in dimethylformamide and different aliquots were placed in each cup. Incubation was carried out at 30°C for 24 hr. Chloramphenicol and dapsone were used as standard drugs and solvent control was kept. Results are summarised in table 3.

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