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NOTE

Synthesis and Antimicrobial Activity of Some Halo Derivatives of Thiophene

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Some halo derivatives of thiophene were synthesised from thiophene and screened for their antimicrobial activity against *Escherichia coli, Bacillus subtilis, Colletorichum capsici* and *Candida albicans.*

Key Words: Synthesis, Antimicrobial activity, Thiophene.

The remarkable fact is that the chemical and physical properties of thiophene and benzene are nearly similar, therefore their biochemistry[1] and pharmacology[2] affect all organisms equally. We have worked on the synthesis of thiophene derivatives **(Ia–Ig)** and on their antimicrobial activity.

(Ia) 2-Chlorothiophene and (Ib) 2,5-Dichlorothiophene: At 50°C chlorine is bubbled in 0.125 mol (10.5 g) thiophene for 5 min; after chlorine addition is complete the temperature is raised to 80°C and a vigorous stream of nitrogen gas is bubbled for 10 min and 14 g of KOH pellets are added cautiously over a period of 30 min. 10 g NaOH is added and the mixture boiled under reflux for 3 h, mixture is filtered and the filtrate is charged to an efficient fractionating column. 2-Chloro thiophene is collected at 128–138°C and 2,5-dichlorothiophene at 161–162°C (yield 72%).

(Ia) ***2-Chlorothiophene*:** b.p. 128–138°C; Refractive index $^{n}D^{20}$ 1.5, UV λ_{max} 236 mμ; IR (cm^{-1}) (KBr) ν(C—H) 3076, ν(C—S—C) 1256, δ(C—H) 540.

(Ib) ***2,5-Dichlorothiophene*:** b.p. 161–162°C; $^{n}D^{20}$ 1.85, UV λ_{max} 236 mμ; IR (cm^{-1}) ν(C—H) 3081, ν(C—S—C) 1261, δ(C—H) 556 .

(Ic) 2-Bromothiophene and (Id) 2,5-Dibromothiophene: 0.125 mol (10.5 g) thiophene is mixed with 100 mL of acetic acid, cooled to 10°C and 0.079 mol (6.312 g) bromine is dissolved in 100 mL of acetic acid, cooled to 10°C and added slowly to thiophene acetic acid solution and the mixture stirred until the solution is light brown in colour. The mixture is warmed to 80°C and 10 g of KOH pellets is added to the well stirred mixture over a period of 1–2 h; the mixture is boiled for 6–8 h and distilled in a fractionating column. The 2-bromothiophene is collected at 149–152°C and 2,5-dibromo-thiophene at 210–212°C (yield 62%).

(Ic) ***2-Bromothiophene*:** b.p. 149–152°C; $^{n}D^{20}$ 1.58, UV λ_{max} 236 mμ; IR (cm^{-1}) ν(C—H) 3066, ν(C—S—C) 1249, δ(C—H) 525.

(Id) ***2,5-Dibromothiophene*:** b.p. 210–212°C; $^{n}D^{20}$ 1.63, UV λ_{max} 252 mμ; IR (cm^{-1}) ν(C—H) 3072, ν(C—S—C) 1253, δ(C—H) 535.

(Ie) 2,3-Dibromothiophene: 0.012 mol (2.378 g) of 4,5-dibromothiophene carboxylic acid, 1.083 g mercuric acetate and 100 mL glacial acetic acid are mixed and heated with stirring for 4 h at reflux temperature, cooled and filtered. The solid

is then transferred to a flask and boiled under reflux for 1 h with excess of aqueous sodium chloride (20%) and then treated with 10 mL of conc. HCl. The mixture is steam distilled. 2,3-Dibromo thiophene is collected in the distillate, dried and fractionated (yield 69%).

(If) 3-Bromothiophene: 0.23 mol (5.71 g) of 2,3-dibromothiophene, 1.2 g magnesium, 25 mL of ether and 1 mL of ethyl bromide are mixed, a few crystal of iodine are added and the mixture is boiled for 6 h and 200 mL of water is added—slowly at first, then rapidly. The ether layer is decanted, dried and the ether distilled off. The product 3-bromothiophene distils at 155–157°C (yield 63%).

b.p. 155–157°C; $^{n}D^{20}$ 1.5861, UV λ_{max} 236 mμ; IR cm^{-1} ν(C—H) 3069, ν(C—S—C) 1246, δ(C—H) 525.

(Ig) 2-Iodothiophene: 0.17 mol (14.2 g) of thiophene and 20 mL benzene are mixed and the mixture vigorously stirred, cooled to 0°C in an ice bath; 0.014 mol (2.8 g) mercuric oxide and 0.01 mol (1.26 g) iodine are added alternately in small amount during the period of 15–20 min; the yellow mercuric oxide changes to crimson mercuric iodide; the mixture is filtered by suction and the residue is washed with three 25 mL portions of ether. The ether and benzene are removed by distillation and residue is fractionally distilled; 2-iodothiophene distils at 73°C.

Antimicrobial Activity: The activity was determined using paper disc plate method[3] by measuring the inhibition zones in mm. All the compounds **(Ia–g)** were screened *in vitro* for their antimicrobial activity against bacteria and the fungal details have been cited in Table-1. Compounds **1b** and **1d** showed high and others moderate antimicrobial activity.

TABLE-1
COMPARABLE ANTIMICROBIAL ACTIVITY OF (Ia–g) WITH KNOWN CHOSEN STANDARD DRUGS

Standard Drugs	Comp.	Antibacterial activity		Antifungal activity	
		E. coli	*B. subtilis*	*C. capsici*	*C. albicans*
	Ia	(18)	(15)	(16)	(20)
	Ib	(20)	(24)	(20)	(25)
	Ic	(15)	(10)	(23)	(11)
	Id	(25)	(26)	(25)	(16)
	Ie	(20)	(16)	(17)	(14)
	If	(16)	(14)	(18)	(18)
	Ig	(21)	(16)	(19)	(16)
Norfloxacin		27	25	20	25
Ampicillin		22	23	24	18
Chloramphenicol		20	27	25	20

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