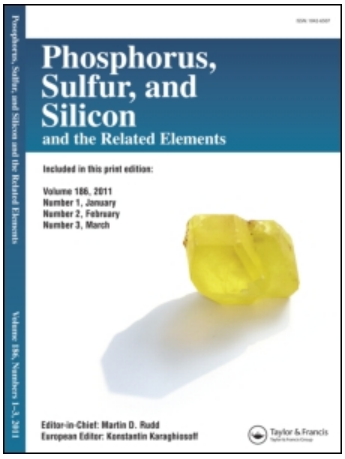

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Syntheses of 1,5-Benzothiazepines-Part XXXI: Syntheses and Antimicrobial Studies of 10-Substituted-7- (monochlorophenyl/dichlorophenyl)-*6H*-6a,7-dihydro-6-phenyl[1]benzopyrano[3,4-c]-[1,5]benzothiazepines

Umesh C. Pant[a]; A. Dandia[a]; Hem Chandra[a]; Shweta Goyal[a]; Seema Pant[b]
[a] Department of Chemistry, University of Rajasthan, [b] L.B.S. Government P.G. College, Kotputli, Jaipur, Rajasthan

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Syntheses of 1,5-Benzothiazepines-Part XXXI: Syntheses and Antimicrobial Studies of 10-Substituted-7-(monochlorophenyl/dichlorophenyl)-*6H*-6a,7-dihydro-6-phenyl[1]benzopyrano[3,4-c]-[1,5]benzothiazepines

Umesh C. Pant
A. Dandia
Hem Chandra
Shweta Goyal
Department of Chemistry, University of Rajasthan

Seema Pant
L.B.S. Government P.G. College, Kotputli, 303108, Jaipur, Rajasthan

*Two flavindogenides, 3-(2-chlorobenzylidene)-flavanone and 3-(2,4-dichlorobenzylidene)-flavanone reacted with six 5-substituted-2-aminobenzenethiols, the substituents being fluoro, chloro, bromo, methyl, methoxyl, and ethoxyl, to give respective 12 new compounds, 10-substituted-7-(2-chlorophenyl / 2,4-dichlorophenyl)-*6H-*6a,7-dihydro-6-phenyl[1]benzopyrano[3,4−c][1,5]benzothiazepines (5a–l) in 60–70% yields. The products were characterized on the basis of microanalytical data for elements and IR,* ^{1}H*, and* ^{13}C *NMR and mass spectral studies. All the synthesized compounds were evaluated for their antimicrobial activity against the bacteria,* Escherichia coli *and* GFC*, and the fungi,* Aspergillus niger*,* Aspergillus flavus*, and* Curvularia lunata*.*

Keywords α,β-unsaturated carbonyl; acidic; aminobenzene thiols; basic

INTRODUCTION

In continuation of our studies on the reactions of aminobenzenethiols with α,β-unsaturated carbonyl compounds (i) in acidic medium-ethanol/methanol containing glacial acetic acid;[1,2] ethanol saturated

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Address correspondence to Umesh C. Pant, Department of Chemistry, University of Rajasthan, Jaipur 302004, India. E-mail: ucp212001@yahoo.co.in

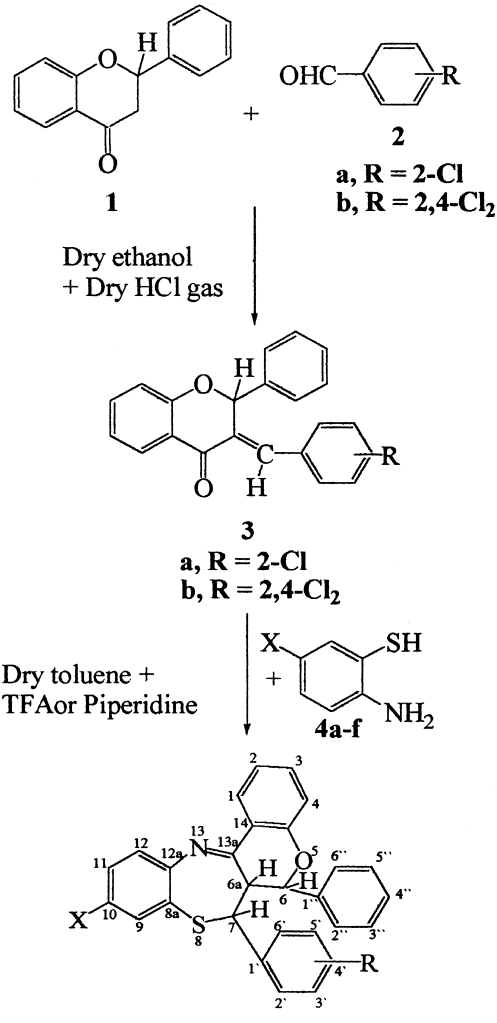
with hydrogen chloride gas;[3] toluene containing trifluoroacetic acid[4] (ii) in basic medium-pyridine;[5] toluene containing piperidine[6] and (iii) in neutral medium-anhydrous toluene;[7,8] o-xylene,[9,10] we have carried out the reactions of 5-substituted-2-aminobenzenethils with arylidene flavanones in both acidic and basic media, i.e., (i) dry toluene containing trifluoroacetic acid and (ii) dry toluene containing piperidine. Toluene was chosen as a higher boiling solvent and trifluoroacetic acid and piperidine were used to provide stronger acidic[3] and basic[6] medium, respectively. To study the effect of the acidic or basic catalyst on the yields of the final products, the reactions of 5-substituted-2-aminobenzenethiols(4a–f) with 3-(2-chlorophenyl/2,4-dichlorophenyl) benzylidene flavanones (**3a**, **b**) have been studied in the presence of acidic and basic catalyst. Chlorobenzylidene-flavanones, having one and two chlorine atoms, have been specifically chosen for the reaction with the expectation that they may exhibit antibacterial and/or antifungal activity and to evaluate as to what extent the presence of chlorine imparts antimicrobial activity and also to evaluate whether the change in percentage of chlorine in the molecule would affect the antimicrobial activity.

All the synthesised compounds 10 substituted-7-(monochlorophenyl/dichlorophenyl)-6*H*-6a,7-dihydro-6-phenyl[1]benzopyrano[3,4-c]-[1,5] benzothiazepines (**5a–l**) were, therefore, screened for their antimicrobial activity against bacteria *Escherichia coli* and *GFC* and fungus *Aspergillus flavus*, *Aspergillus niger*, and *C. lunata*.

RESULTS AND DISCUSSION

Six 5-substituted-2-aminobenzenethiols[11–15](**4a–f**), the substituents being, F, Cl, Br, CH_3, OCH_3, and OC_2H_5, and arylidene flavanone[16,17] **(3)** were prepared in the laboratory by literature methods. The flavanone **(1)** was reacted with two aldehydes, 2-chlorobenzaldehyde (**2a**) and 2,4-dichlorobenzaldehyde (**2b**) by dissolving these in ethanol and passing dry hydrogen chloride gas till the color of the reaction mixture turned blackish red and kept overnight to afford the crude product. The solid obtained was crystallized from dry ethanol to give flavindogenides, 3-(2-chlorobenzylidene)-flavanone,[16] (**3a**) and 3-(2,4-dichlorobenzylidene)-flavanone[17] (**3b**), respectively (Scheme 1).

Two flavindogenides, 3-(2-chlorobenzylidene)-flavanone (**3a**) and 3-(2,4-dichlorobenzylidene)-flavanone (**3b**) reacted with six 5-substituted-2-aminobenzenethiols (**4a–f**) in toluene with trifluoroacetic acid as acidic and piperidine as basic catalyst to give the final products, **5a–l** (Tables I & II) in 60–70% yields.



5a-l

5	X	R	5	X	R
a	F	2-Cl	**g**	F	2,4-Cl_2
b	Cl	2-Cl	**h**	Cl	2,4-Cl_2
c	Br	2-Cl	**i**	Br	2,4-Cl_2
d	CH_3	2-Cl	**j**	CH_3	2,4-Cl_2
e	OCH_3	2-Cl	**k**	OCH_3	2,4-Cl_2
f	OC_2H_5	2-Cl	**l**	OC_2H_5	2,4-Cl_2

SCHEME 1

TABLE I Physical Constants of 10-Substituted-7-(2-chlorophenyl)-6*H*-6a,7-dihydro-6-phenyl[1]benzopyrano[3,4-c][1,5]benzothiazepines (5a–f)

Compd. no.	X	R	M.P. (°C)	R_f	Yield (%) A	Yield (%) B	Mol. Formula (Mol. Weight)	Elemental analysis Found (Calcd.) (%) C	H	N
5a	F	Cl	111–112	0.78	68	62	$C_{28}H_{19}ClFNOS$ (471.5)	71.32 (71.26)	4.15 (4.02)	2.95 (2.96)
5b	Cl	Cl	112–115	0.82	64	60	$C_{28}H_{19}Cl_2NOS$ (488)	68.91 (68.85)	3.90 (3.89)	2.78 (2.86)
5c	Br	Cl	118–119	0.70	67	60	$C_{28}H_{19}BrClNOS$ (532.5)	—	—	2.55 (2.62)
5d	CH_3	Cl	117–118	0.81	62	58	$C_{29}H_{22}ClNOS$ (467.5)	—	—	2.82 (2.99)
5e	OCH_3	Cl	111–112	0.72	64	62	$C_{29}H_{22}ClNO_2S$ (483.5)	72.10 (71.97)	4.68 (4.55)	2.98 (2.89)
5f	OC_2H_5	Cl	111–113	0.70	70	66	$C_{30}H_{24}ClO_2S$ (497.5)	—	—	2.90 (2.81)

Benzylidene flavanones have exocyclic α,β-unsaturation in conjugation with cyclic carbonyl group and would thus behave as α,β-unsaturated carbonyl system. The compounds having α,β-unsaturated carbonyl system have been reported to react with 2-aminobenzenethiols in two steps, depending upon the reaction conditions.[3,8,12–14,18–22]

TABLE II Physical Constants of 10-Substituted-7-(2,4-dichlorophenyl)-6*H*-6a,7-dihydro-6-phenyl[1]benzopyrano[3,4-c][1,5] benzothiazepines(5g–l)

Compd. no.	X	R	M.P. (°C)	R_f	Yield (%) A	Yield (%) B	Mol. Formula (Mol. Weight)	Elemental analysis Found (Calcd.) (%) C	H	N
5g	F	2,4-Cl_2	99–101	0.68	68	60	$C_{28}H_{18}Cl_2FNOS$ (506)	—	—	2.68 (2.77)
5h	Cl	2,4-Cl_2	109–110	0.71	66	61	$C_{28}H_{18}Cl_3NOS$ (522.5)	—	—	2.50 (2.68)
5i	Br	2,4-Cl_2	105–107	0.70	65	63	$C_{28}H_{18}BrCl_2NOS$ (567)	—	—	2.34 (2.47)
5j	CH_3	2,4-Cl_2	98–102	0.73	69	60	$C_{29}H_{21}Cl_2NOS$ (501)	69.43 (69.32)	4.36 (4.21)	2.62 (2.79)
5k	OCH_3	2,4-Cl_2	108–110	0.72	66	58	$C_{29}H_{21}Cl_2NO_2S$ (517)	67.26 (67.18)	4.21 (4.08)	2.58 (2.70)
5l	OC_2H_5	2,4-Cl_2	102–103	0.74	68	60	$C_{30}H_{23}Cl_2NO_2S$ (532)	67.84 (67.67)	4.44 (4.35)	2.53 (2.63)

A = Acidic medium; B = Basic medium.

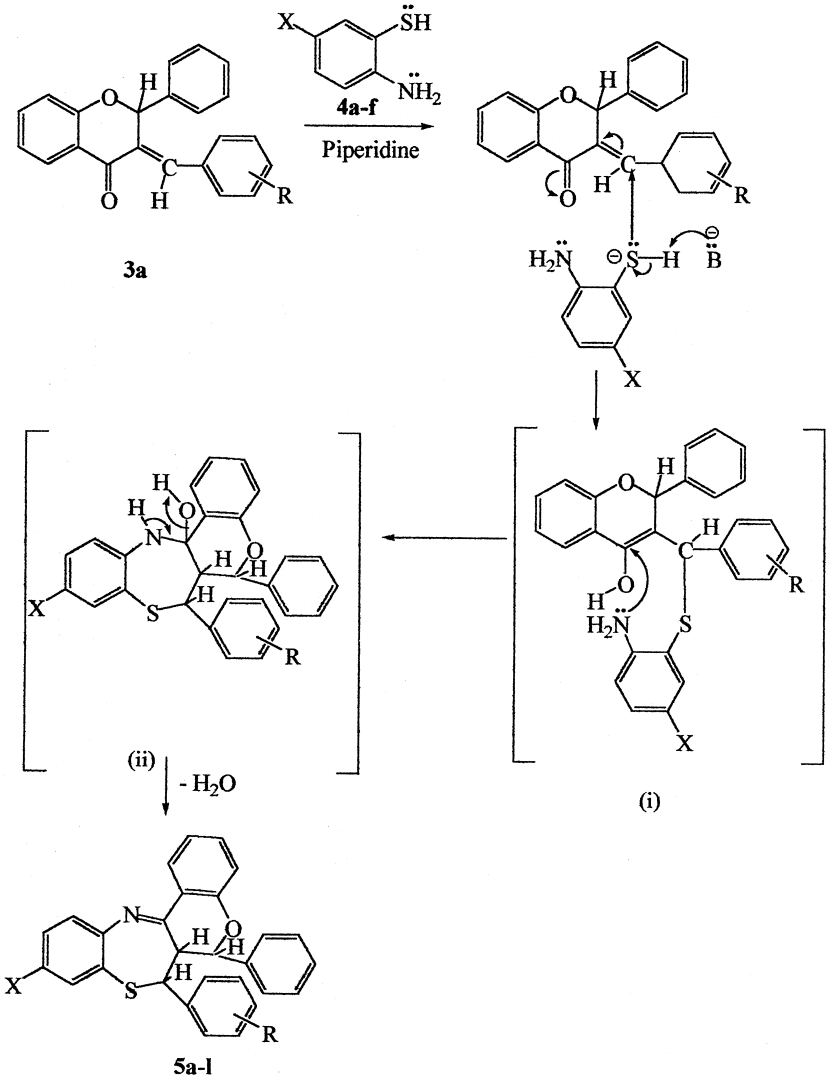
Studies by Stephens and Field[20] show that when such reactions are carried out in methanol containing a basic catalyst, a Michael adduct is obtained as an intermediate which undergoes cyclization on boiling in acidic medium, using glacial acetic acid, to give the final products. The reactions, when carried out by Levai and Bognar,[22,23] in high boiling solvent like toluene without any catalyst yielded the intermediate which cyclized on reacting further in acidic medium using glacial acetic acid. They obtained[22,23] the final products in a single step when the reactions of chalcone and aminobenzenethiols were carried out in methanol containing glacial acetic acid. Reid and Marx[21] also obtained the products in a single step when the reactions were carried out using methanol containing hydrochloric acid. The spectral evidences are reported[3,8,18–28] to support the formation of the intermediate.

These observations indicate that at first, the intermediate, a Michael adduct, is formed by the nucleophilic attack[24–28] of the sulfhydryl electrons[1] of the thiol on the β-carbon of the α,β-unsaturated carbonyl system. Benzylidene flavanones, behaving as α,β-unsaturated carbonyl systems, have electrophilic β-carbon atom, making it susceptible to nucleophilic attack by the sulfhydryl electrons of the benzenethiol. In the basic medium, the abstraction of a proton by the base increases the nucleophilicity of the sulfhyhydryl group, resulting in its attack on the β-carbon atom of the arylidene flavanone. We have carried out the reactions of 5-substituted-2-aminobenzenethiols (**4a–f**) with substituted benzylidene flavanones (**3a**, **b**) in toluene containing piperidine to obtain the final products, 10-substituted-7-(monochlorophenyl/dichlorophenyl)-6*H*-6a, 7-dihydro-6-phenyl[1]benzopyrano[3,4-c][1,5]benzothiazepines (**5a–l**) without the isolation of the intermediate. From the study of analogous reactions, as referred above,[3,8,18–28] it is evident that the intermediates (Scheme 2), are formed prior to the cyclized product.

In acidic medium, the protonation of the carbonyl group of the arylidene flavanone renders β-carbon atom electrophilic, making it susceptible to nucleophilic attack by the sulfhydryl electrons of the thiol. Thus, the reaction proceeds via the formation of Michael type adduct, leading to the formation of cyclized products (**5a–l**) by dehydrative cyclization. It is, thus, observed that the aminobenzenethiols react with α,β-unsaturated carbonyl systems to give the final products in one step, by concerted mechanism, in nearly equal yields (Tables I and II).

SPECTRAL STUDIES

In the IR spectra of the compounds, **5a–l**, the absence of characteristic carbonyl and amino group absorption signals around 1650–1685 cm[1]



SCHEME 2

and 3400–3100 cm^{-1} respectively, show that the carbonyl and amino groups are absent in the final products (**5a–l**). The presence of a strong absorption signal in the range 1612–1602 cm^{-1} which is characteristic for carbon nitrogen double bond indicate that the amino group of the thiols and carbonyl group of 3-arylidine flavanones have reacted to form carbon nitrogen double bond.

In the ^{1}H NMR spectrum of **5l**, absorption signals as a quartet at δ4.10 (J = 6 Hz) and a triplet at δ1.42 (J = 6 Hz) may be assigned to two methylene protons and three methyl protons of ethoxyl group (CH_3CH_2O—). Besides, other three protons attached to the sp^3 hybridized carbons, i.e., C-6-H, C-6a-H, and C-7-H, were expected to show absorption in the upfield region of the ^{1}H NMR spectra. In the spectra recorded at 90 MHz, these three protons showed very weak absorption signals. In ^{1}H NMR spectra recorded at 300 MHz, the signals were observed as two doublets and a double-doublet in the slightly downfield region, each integrating for one proton. Two doublets at δ4.92 (J = 1.1 Hz) and δ4.98 (J = 12.2Hz) may be assigned to C-6-H and C-7-H, because these protons are attached to sp^3 carbons which are attached with electronegative oxygen and sulphur atom, respectively. A double-doublet at δ3.68 (J_1 = 12.3, J_2 = 1.1) may be assigned to C-6a-H. Other protons of the molecule were found to show downfield absorption signals in the spectra in the region δ6.40–δ8.24 integrating for 15/16 aromatic protons (Tables III, IV). For the assignments of ^{13}C NMR signals in benzopyranobenzothiazepines, extensive studies of the ^{13}C NMR spectra of the reactants and products were made by G. Toth, A. Szollosy, A. Levai and H. Duddeck. For example, in order to assign the signals of ring D carbon atoms (Figure 1), the chemical shift data of the reference compounds, indanones[29–31] tetralones,[31,32] thiochromanones,[33] chromanone[33] and flavanone[34] were used. Similarly, to support the assignment of the ring carbons, different derivatives having different substituents were studied[35] including steric environments and the assignments of ^{13}C NMR signals of the structure. They have measured the spectra of compounds at 100, 200, and 250 MHz. Based on these data, the ^{13}C NMR signals of carbon atoms of substituted benzopyranobenzothiazepines may be summarized to appear around the values given as under.

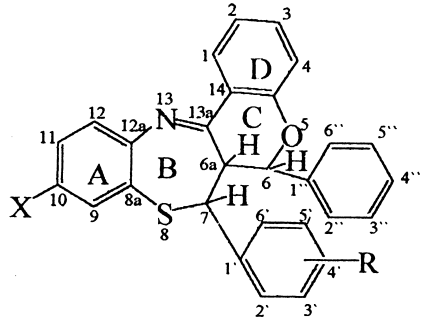


FIGURE 1 6,7,10-substituted benzopyranobenzothiazepine.

TABLE III Characteristic IR Absorptions (cm^{-1}), ^1H NMR ($CDCl_3$, δ Values in ppm, J in Hz), Signals of 10-Substituted-7-(2-chlorophenyl)-6a, 7-dihydro-6-phenyl-6*H*[1]benzopyrano[3,4-*c*][1,5]benzothaiazepines (5a–f)

Compd. no.	Aromatic ν (C—H)	Aliphatic ν(C—H)	νC=N	C-10-XH	C-6-H	C-6a-H	C-7-H	Aromatic protons (16H, m)
5a	3005	2980	1608	—	4.90 (d, J = 1.2)	3.66 (dd) (J_1 =12.3, J_2 = 1.2)	4.98 (d, J=12.3)	6.7–8.24
5b	3025	2960	1612	—	4.89 (d, J = 1.2)	3.65 (dd) (J_1 = 12.2, J_2 = 1.2)	4.97 (d, J=12.2)	6.75–8.22
5c	3000	2993	1600	—	4.91 (d, J = 1.1)	3.66 (dd) (J_1 = 12.2, J_2 = 1.1)	4.98 (d, J = 12.2)	6.74–8.25
5d	2995	2900	1605	2.41 (s, 3H)	4.90 (d, J = 1.1)	3.68 (dd) (J_1 = 12.3, J_2 = 1.1)	4.99 (d, J = 12.3)	6.44–8.20
5e	3015	2870	1608	3.80 (s, 3H)	4.92 (d, J = 1.3)	3.64 (dd) (J_1 =12.3, J_2 = 1.3)	4.97 (d, J = 12.3)	6.46–8.22
5f	3030	2965	1612	1.42 (t, 3H, J = 6) 4.10 (q, 2H, J = 6)	4.92 (d, J = 1.2)	3.66 (dd) (J_1 = 12.2, J_2 = 1.2)	4.98 (d, J = 12.2)	6.60–8.22

TABLE IV Characteristic IR Absorptions (cm^{-1}) and ^1H NMR ($CDCl_3$, δ Values in ppm, J in Hz) Signals of 10-Substituted-7-(2,4-dichlorophenyl)-6*H*-6a,7-dihydro-6-phenyl[1]benzopyrano[3,4-*c*][1,5]benzothaizepines (5g–l)

Compd. no.	Aromatic ν(C—H)	Aliphatic ν(C—H)	νC=N	C-10-XH	C-6-H	C-6a-H	C-7-H	Aromatic protons (15H, m)
5g	3030	2940	1615	—	4.91 (d, J=1.2)	3.68 (dd) ($J_1 = 12.3$, $J_2 = 1.2$)	4.98 (d, J = 12.3)	6.66–8.21
5h	3010	2925	1610	—	4.90 (d, J = 1.1)	3.66 (dd) ($J_1 = 12.1$, $J_2 = 1.1$)	4.98 (d, J = 12.1)	6.76–8.24
5i	3010	2900	1606	—	4.92 (d, J = 1.2)	3.68 (dd) ($J_1 = 12.2$, $J_2 = 1.2$)	4.97 (d, J = 12.3)	6.43–8.22
5j	3025	2912	1608	2.39 (s, 3H)	4.93 (d, J = 1.2)	3.65 (dd) ($J_1 = 12.3$, $J_2 = 1.2$)	4.98 (d, J = 12.3)	6.64–8.24
5k	3020	2910	1612	3.84 (s, 3H)	4.91 (d, J = 1.2)	3.68 (dd) ($J_1 = 12.2$, $J_2 = 1.2$)	4.96 (d, J = 12.2)	6.77–8.21
5l	3040	2930	1610	1.42 (t 3H, J = 6) 4.10 (q, 2H, J = 6)	4.92 (d, J = 1.1)	3.68 (dd) ($J_1 = 12.3$, $J_2 = 1.1$)	4.98 (d, J = 12.2)	6.40–8.24

^{13}C NMR spectrum of **5f** at 100 MHz shows signals in this pattern. Upfield absorption signals at δ21.1 and δ56.4 may be assigned to methyl (CH_3—) carbon and methylene (—CH_2—) carbon of ethoxyl group (CH_3CH_2O—). Three characteristic absorption signals in the relatively downfield region at δ76.4, δ45.3, and δ66.5 may be assigned to three sp^3 carbons, C-6, C-6a, and C-7 respectively. All the other carbons of the molecule showed absorption signals at δ118.5, 120.1, 121.8, 124.4, 125.1, 126.8, 127.2, 127.4, 127.7, 128.7, 129.4, 131.1, 131.8, 133.7, 136.2, 137.4, 137.7, 138.2, 142.7, 150.3, 155.8, 159.8, and 161.7.

In the mass spectra of the final products (**5a–l**), molecular ion peaks $[M]^+$ and $[M+2]^+$ corresponded to the calculated molecular weights of the compounds.

ANTIMICROBIAL ACTIVITY

All the synthesised compounds, **5a–l** were evaluated for their relative antibacterial and antifungal activity against the bacteria, *Escherichia coli* and *GFC* and fungi, *Aspergillus niger, Aspergillus flavus* and *Curvularia lunata* following the Plate Disc Method.[36,37] To evaluate the relative activity in the form of activity index, *Bacitracin* and *Mycostatin* were used as reference compounds in case of bacteria and fungi, respectively. Zones of inhibition, exhibited by the reference and test compounds, were measured and relative activities of the test compounds (**5a–l**) were calculated as activity index (Table V).

$$\text{Activity Index} = \frac{\text{Zone of Inhibition exhibited by test compound}}{\text{Zone of Inhibition exhibited by the reference compound}}$$

All the synthesised compounds, **5a–l**, showed moderate to good activity (activity index = 0.8–1.28) against bacteria *Escherichia coli* and *GFC* on incubation for a duration of 40 hr. Monochloro derivatives showed greater bactericidal activity than the dichloro derivatives whereas increase in the percentage of chlorine showed enhancement of antifungal activity, especially against *C. lunata* (Table V).

EXPERIMENTAL

All the recorded melting points are uncorrected. Thin layer chromatography (TLC) on silica gel G coated glass plates using benzene:methanol:aq. ammonia (7:2:1) as eluent was used for monitoring the progress of the reaction and for checking the purity of the compounds (**5a–l**). The IR spectra were taken in KBr pellets on a Perkin-Elmer Infracord 577 spectrometer. ^{13}C NMR spectra were recorded on Jeol 90 MHz FT NMR and Bruker DRX300 spectrometer using $CDCl_3$ as solvent and TMS as internal standard and mass spectra were recorded on a Jeol D-300 (EI/Cl) instrument at 70 eV. Elemental analyses were carried out at the Regional Sophisticated Instrumentation Centre, CDRI, Lucknow.

TABLE V Antimicrobial Activity of Synthesised 10-Substituted-7-(2-chlorophenyl/2,4-dichlorophenyl)-6*H*-6a,7-dihydro-6-phenyl[1]benzopyrano[3,4-c][1,5]benzothiazepines (5a–l)

Compd. no.	Bacteria		Fungi								
			A. niger			*A. flavus*			*C. lunata*		
	E. coli	*GFC*	40 hrs	72 hrs	90 hrs	40 hrs	72 hrs	90 hrs	40 hrs	72 hrs	90 hrs
5a	0.80	0.70	17	13	10	16	14	10	16	14	11
	(1.14)	(1.00)	(1.13)	(0.86)	(0.66)	(1.06)	(0.93)	(0.66)	(1.06)	(0.93)	(0.73)
5b	0.85	0.80	14	12	8	12	10	8	18	16	12
	(1.21)	(1.14)	(0.93)	(0.80)	(0.53)	(0.80)	(0.66)	(0.53)	(1.20)	(1.06)	(0.80)
5c	0.60	0.75	12	10	8	16	14	11	14	10	8
	(0.85)	(1.07)	(0.80)	(0.66)	(0.53)	(1.06)	(0.93)	(0.73)	(0.93)	(0.66)	(0.53)
5d	0.80	0.90	15	12	9	17	15	12	15	12	10
	(1.14)	(1.28)	(1.00)	(0.80)	(0.60)	(1.13)	(1.00)	(0.80)	(1.00)	(0.80)	(0.60)
5e	0.75	0.8	14	12	8	14	10	8	17	15	12
	(1.07)	(1.14)	(0.93)	(0.80	(0.53)	(0.93)	(0.66)	(0.53)	(1.13)	(1.00)	(0.80)
5f	0.90	0.60	15	13	10	18	15	10	14	11	9
	(1.28)	(0.85)	(1.00)	(0.86)	(0.66)	(1.20)	(1.00)	(0.66)	(0.93)	(0.73)	(0.60)
5g	0.70	0.80	17	15	12	16	14	11	18	15	12
	(1.00)	(1.14)	(1.13)	(1.00)	(0.80)	(1.06)	(0.93)	(0.73)	(1.20)	(1.00)	(0.80)
5h	0.80	0.90	14	10	6	20	16	11	18	15	10
	(1.14)	(1.28)	(0.93)	(0.66)	(0.40)	(1.33)	(1.06)	(0.73)	(1.20)	(1.00)	(0.66)
5I	0.60	0.70	15	13	10	12	9	7	16	12	9
	(0.85)	(1.00)	(1.00)	(0.86)	(0.66)	(0.80)	(0.60)	(0.46)	(1.06)	(0.80)	(0.60)
5j	0.80	0.60	15	12	8	16	10	8	17	15	12
	(1.14)	(0.85)	(1.00)	(0.80)	(0.53)	(1.06)	(0.66)	(0.53)	(1.13)	(1.00)	(0.80)
5k	0.70	0.70	19	16	12	18	15	12	16	12	10
	(1.00)	(1.00)	(1.26)	(1.06)	(0.80)	(1.20)	(1.00)	(0.80)	(1.06)	(0.80)	(0.66)
5l	0.70	0.90	16	14	10	14	10	8	15	10	6
	(1.00)	(1.28)	(1.06)	(0.93)	(0.66)	(0.93)	(1.00)	(0.53)	(1.00)	(0.66)	(0.40)

Values in parentheses represent activity index.

I. Preparation of 5-Substituted-2-aminobenzenethiols (4a–f)

Six 5-substituted-2-aminobenzenethiols (**4a–f**) were synthesised by following reported methods.[11–15]

II. Preparation of 3-(4-Substituted Arylidine)-flavanones (3a & 3b)

Equimolar quantities of flavanone[38,39] **(1)** in ethanol and 2-chlorobenzaldehyde **(2a)** or 2,4-dichlorobenzaldehyde **(2b)** were mixed. Dry hydrogenchloride gas was passed while heating the reaction mixture gently with stirring. The color of the reaction mixture changed from yellow to black-blackish red. On keeping it overnight, the crude-substituted arylidene flavanones were obtained which were crystallized from dry methanol. (**3a**, m.p. 137°C, reported[16] 137–138°C, yield 1.45g ,42%; **3b**, m.p. 126°C reported[16] 127–128°C, yield 1.44g, 38%).

General Procedure for the Preparation of 10-Substituted-6*H*-6a,7-dihydro-7-(monochlorophenyl/dichlorophenyl)-6-phenyl-[1]benzopyrano[3,4-*c*][1,5]benzothiazepines (5a–l)

5-Substituted-2-aminobenzenethiol (4,0.001 mol) and substituted benzylidene flavanone (3, 0.001 mol) were dissolved in dry toluene (15 mL) and mixed. Trifluoroacetic acid (5 drops) as acidic catalyst, or piperidine (10 drops) as a basic catalyst, was then added to the reaction mixtures and refluxed until color change occurred from light yellow to deep red over 6 h. The solvent was removed under reduced pressure to get a crude solid. The crude solid thus obtained, was crystallized from dry methanol to give the title compounds **(5a–l)**.

The microanalytical, spectral, and antimirobial activity data of **5a–l** are given in Tables I–V.

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