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NOTE

Synthesis and Antibacterial Activity of Chloroacetyl Derivatives of Schiff Bases

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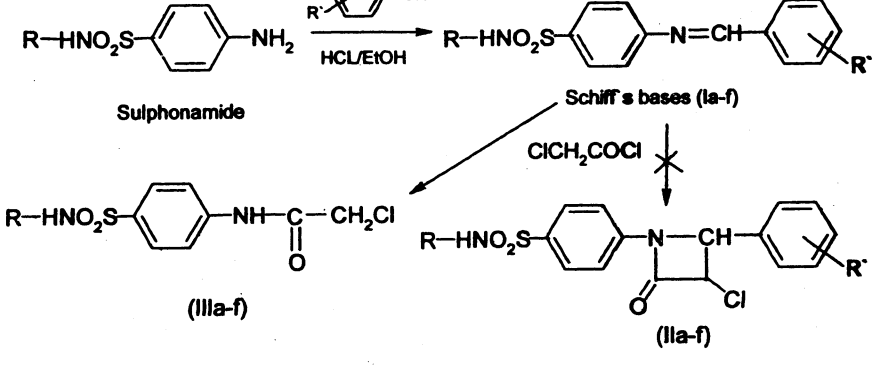
A few aromatic aldehydes were condensed with appropriate sulfa drugs to give the desired Schiff bases, which were condensed with chloroacetyl chloride in order to obtain the corresponding azetidinone derivatives. However, Schiff bases could not be converted into azetidinones; instead, chloroacetyl derivatives were obtained. The synthesized compounds were evaluated for their antibacterial activity.

Key Words: Schiff bases, Azetidinones, Sulphonamides, Antibacterial activity.

Sulphonamides are one of the least expensive antibiotics and this factor largely accounts for their greater extent of use in developing countries. They are used in urinary tract infections, meningitis, streptococcal pharyngytis, baciliary dysentery, trachoma, chancroid, malaria, toxoplasmosis, nocardiasis and conjunctivitis[1-3]. They are generally taken orally in higher doses which cause nausea, vomiting and epigastric pain[4, 5]. These studies were initiated in order to prepare the azetidinones after synthesizing the Schiff bases from sulphonamides with an aim to exploit the Schiff bases; however, the Schiff bases could not be converted into azetidinones; instead, chloroacetyl derivatives were obtained **(Scheme-1).** The structures of the synthesized compounds have been confirmed by IR and ^{1}H NMR spectral analysis.

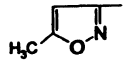
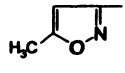


Scheme-1.

Melting points were recorded in liquid paraffin bath using open-end capillaries and are uncorrected. The IR spectra were run on Shimadzu FTIR spectrophotometer in KBr pellets. ^{1}H NMR spectra were recorded on a Bruker 300 MHz NMR spectrometer in $CDCl_3$ using TMS as internal reference. Purity of the compounds was checked by TLC on silica gel plates and spots were visualized by exposure to iodine vapours.

Synthesis of Schiff bases (1a–f): Sulphonamide (0.05 mol) was dissolved in oxygen free distilled ethanol (7 mL) and aromatic aldehyde (0.05 mol) was added to it. The solution was kept in an ice bath and stirred, conc. hydrochloric acid (0.3 mL) was added dropwise. The reaction mixture was stirred for 2 h maintaining the temperature below 5°C. The coloured product so obtained was filtered, dried and crystallized from methanol to give TLC pure compound **I.** It gave red colour with conc. sulphuric acid. **Ia:** IR (KBr, cm^{-1}): 3167 ν(N—H), 1628 ν(N=CH), 1329 and 1155 ν(SO_2 asym and sym), 1305 ν(C—N). ^{1}H NMR ($CDCl_3$) δ ppm: 3.95 (s, 3H, —OCH_3); 7.2, 7.7, 8.0 and 8.2 (d each, 2xA_2B_2, 2x *p*-disubstituted phenyl rings); 8.9 (s, aldimine). The structures, molecular formulas, yields and melting points are shown in Table-1.

TABLE-1

Compd.	R	R′	m.f.	Yield (%)	m.p. (°C)
Ia	H	4-OCH_3	$C_{14}H_{14}N_2O_3S$	80	245
Ib	H	3,4-$(OCH_3)_2$	$C_{15}H_{16}N_2O_4S$	82	222
Ic		4-OCH_3	$C_{18}H_{17}N_3O_4S$	76	156–58
Id		3,4-$(OCH_3)_2$	$C_{19}H_{19}N_3O_5S$	80	178
Ie		4-OCH_3	$C_{18}H_{16}N_4O_3S$	84	162
If		3,4-$(OCH_3)_2$	$C_{19}H_{18}N_4O_4S$	78	200–02

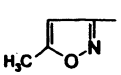
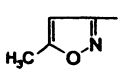
Attempted synthesis of azitidinones (IIa–f): To a well-stirred solution of compound **(I)** (0.04 mol) in dry acetone (20 mL) containing triethylamine (0.2 mL) was added chloroacetyl chloride (0.04 mol) at room temperature. The reaction mixture was stirred for 0.5 h and refluxed further for 3 h. It was filtered to remove the insoluble solid salts. The filtrate was concentrated and diluted with ice-cold water. A solid mass that separated out was filtered, dried and crystallized from methanol, which however were found to be **IIIa–f** and not the expected compounds **IIa–f.**

Compound IIIa: IR (KBr, cm^{-1}): 3203 ν(N—H), 1685 ν(C=O), 1356 and 1175 ν(SO_2 asym and sym). ^{1}H NMR ($CDCl_3$) δ ppm: 4.25 (s, 2H, —$COCH_2$—);

7.2 and 7.65 (d each, A_2B_2, ring protons). The structures, molecular formulas, yields, melting points and antibacterial activity data are shown in Table-2.

Antibacterial activity: The chloroacetyl derivatives **(IIIa–e)** were tested for antibacterial activity by agar cup-plate method[6] against the strains of *S. aureus* and *E. coli*. The testing was carried out using 100 μg/mL of sample in DMF. Sensitivity plates were seeded with bacterial innoculum of 1×10^6 CIU/mL and each cup (dia. 10 mm) was loaded with 0.1 mL of test solution. The zones of inhibition were recorded after incubation for 24 h. The activity was compared with standard drug norfloxacin. The zone of inhibition was measured in mm and reported in Table-2. Compounds showed promising activity against the tested organisms.

TABLE-2

Compd.	R	m.f.	Yield (%)	m.p. (°C)	Antibacterial activity (Zone of inhibition in mm)	
					S. aureus	*E. coli*
IIIa	H	$C_8H_9N_2O_3SCl$	56	136–38	11	16
IIIb	H	$C_8H_9N_2O_3SCl$	56	136–38	11	16
IIIc		$C_{12}H_{12}N_3O_4SCl$	62	146	12	10
IIId		$C_{12}H_{12}N_3O_4SCl$	62	146	12	10
IIIe		$C_{18}H_{11}N_4O_3SCl$	68	124–26	10	8
IIIf		$C_{12}H_{11}N_4O_3SCl$	68	124–26	10	8

Diameter of zone of inhibition of norfloxacin = 28 mm (*S. aureus*) and 26 mm (*E. coli*).

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