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Synthesis of Some Heterocyclic Schiff Base and Azetidinone Compounds and Their Antibacterial Activity

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As a target to synthesize various Schiff base and azetidinone derivatives, 2-amino-4-(coumarinyl-3)-thiazole has been prepared by the reactions of 3-bromo acetyl coumarin with thiourea. 3-Bromo acetyl coumarin was prepared from 3-acetyl coumarin. The resulting compound 2-amino-4-(coumarinyl-3) thiazole was treated with different aldehydes to give the Schiff base which on further reaction with chloro acetyl chloride gave the titled compounds. The structures of the compounds have been confirmed by elemental analysis and spectral analysis. The antibacterial activity of the compounds has also been screened.

Key Words: Synthesis, Schiff Base, Azetidinone, Antibacterial activity.

INTRODUCTION

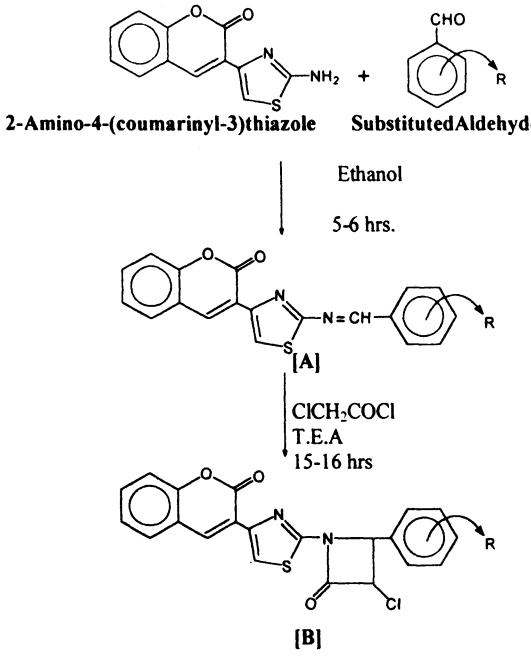
A survey of literature reveals that thiazolo coumarins possess a broad spectrum of biological importance. Thiazolo coumarin derivatives are well known biologically active compounds. Schiff bases from 2-amino-4-(coumarinyl-3) thiazole and various aldehydes are reported to have significant antibacterial activity. These derivatives have been reported as bacteriostatic[1] and fungisidic[2]. All azetidinones contain the β-lactam moiety[3, 5]. Azetdinones possess a variety of theraputic activities[6] and they were tested as antibiotic, antidepressant and sedatives. The aim of the present work is to synthesize some Schiff bases and azetidinones and test them as antibacterial drugs.

Different aldehydes were condensed with 2-amino-4-(coumarinyl-3)thiazole to yield Schiff base **[A]**. The Schiff bases **[A]** were further reacted with chloro acetyl chloride to yield azetidinones[7] **[B]**.

EXPERIMENTAL

Preparation of 2-(2′-chloro benzylide) imino-4-(coumarin-3-yl)-thiazole [Schiff base][8] [A]

2-Amino-4-(coumarinyl-3)-thiazole (0.01 mol) was taken in a Deanstark apparatus and to it 2-chloro benzaldehyde (0.01 mol) was added. The reaction mixture was refluxed for 5–6 h. During the course of the reaction the water was removed continuously. The benzene was then distilled off to get the product. The Schiff base was filtered, dried and recrystallized from absolute alcohol **(Scheme-1).** Other substituted Schiff bases were prepred in a similar manner. Data for various substituted Schiff bases are given in Table-1.



Scheme-1

TABLE–1
PHYSICAL AND ANALYTICAL DATA OF THE SCHIFF BASE [A]

No.	R	m.f. (m.w.)	Yield (%)	m.p. (°C)	% Analysis, Calcd. (Found)		
					C	H	N
BN-1	3-OH,4-OCH_3	$C_{20}H_{14}N_2O_4S$ (378.0)	82	131	63.49 (63.45)	3.70 (3.72)	7.40 (7.43)
BN-2	3:4:5$(OCH_3)_3$	$C_{22}H_{18}N_2O_5S$ (422.0)	76	123	62.55 (62.57)	4.26 (4.30)	6.63 (6.66)
BN-3	4-$N(CH_3)_2$	$C_{21}H_{17}N_3O_2S$ (375.0)	74	138	67.20 (67.18)	4.53 (4.50)	11.20 (11.19)
BN-4	2-OH	$C_{19}H_{12}N_2O_3S$ (348.0)	80	110	65.51 (65.54)	3.44 (3.48)	8.04 (8.07)
BN-5	4-Cl	$C_{19}H_{11}N_2O_2SCl$ (366.5)	71	118	62.21 (62.18)	3.00 (3.04)	7.63 (7.60)
BN-6	2-Cl	$C_{19}H_{11}N_2O_2SCl$ (366.5)	68	113	62.21 (62.24)	3.00 (3.05)	7.63 (7.67)
BN-7	2-OCH_3	$C_{20}H_{14}N_2O_3S$ (362.0)	78	112	66.29 (66.31)	3.86 (3.89)	7.73 (7.75)
BN-8	4-OCH_3	$C_{20}H_{14}N_2O_3S$ (362.0)	81	117	66.29 (66.33)	3.86 (3.87)	7.73 (7.72)
BN-9	2,4-$(Cl)_2$	$C_{19}H_{10}N_2O_2Cl_2S$ (401.0)	72	125	56.85 (56.82)	2.49 (2.46)	6.98 (6.96)
BN-10	2-NO_2	$C_{19}H_{11}N_3O_4S$ (377.0)	70	141	60.47 (60.50)	2.91 (2.94)	11.14 (11.11)

Preparation of 3″-chloro-4″-(2′-chlorophenyl)-1″-[4-(coumarin-3-yl)-thiazole-2-yl] azetidin-2″-one [B]

The 2-(2′-chloro benzylide) imino-4-(coumarin-3-yl) thiazole (0.01 mol) in benzene was taken in a 50 mL flat-bottom flask. To it chloroacetyl chloride (0.01 mol), triethylamine (0.01 mol) in benzene were added slowly. It was refluxed for 15–16 h. The triethylamine hydrochloride was removed and the benzene was distilled off to get the product **(Scheme-1).** Other substituted Schiff bases were prepared in a similar manner. Data for different substituted azetidinones are given in Table-2.

TABLE-2
PHYSICAL AND ANALYTICAL DATA OF THE AZETIDINONES [B]

No.	R	m.f. (m.w.)	Yield (%)	m.p. (°C)	% Analysis, Calcd. (Found)		
					C	H	N
BN-11	3-OH,4-OCH_3	$C_{22}H_{15}N_2O_5SCl$ (454.5)	70	107	58.08 (58.12)	3.30 (3.33)	6.16 (6.19)
BN-12	3:4:5-$(OCH_3)_3$	$C_{24}H_{19}N_2O_6SCl$ (498.5)	66	128	57.77 (57.79)	3.81 (3.83)	5.61 (5.59)
BN-13	4-$N(CH_3)_2$	$C_{23}H_{18}N_3O_3SCl$ (451.5)	60	157	61.12 (61.09)	3.98 (4.02)	9.30 (9.32)
BN-14	2-OH	$C_{21}H_{13}N_2O_4SCl$ (424.5)	69	150	59.36 (59.40)	3.06 (3.04)	6.59 (6.62)
BN-15	4-Cl	$C_{21}H_{12}N_2O_3SCl_2$ (443.0)	65	143	56.88 (56.91)	2.70 (2.73)	6.32 (6.29)
BN-16	2-Cl	$C_{21}H_{12}N_2O_2SCl_2$ (443.0)	60	153	56.88 (56.86)	2.70 (2.74)	6.32 (6.34)
BN-17	2-OCH_3	$C_{22}H_{15}N_2O_4SCl$ (438.5)	68	171	60.20 (60.23)	3.42 (3.39)	6.38 (6.40)
BN-18	4-OCH_3	$C_{22}H_{15}N_2O_4SCl$ (438.5)	71	178	60.20 (60.21)	3.42 (3.40)	6.38 (6.36)
BN-19	2,4-$(Cl)_2$	$C_{22}H_{11}N_2O_3SCl_3$ (477.5)	64	146	55.28 (55.27)	2.30 (2.32)	5.86 (5.84)
BN-20	2-NO_2	$C_{21}H_{12}N_3O_5SCl$ (453.5)	62	181	55.56 (55.54)	2.64 (2.62)	9.26 (9.29)

RESULTS AND DISCUSSION

Structures of compounds synthesized have been elucidated by elemental analysis, IR measurements. The Schiff base of above starting compound shows IR absorption park at 1660-1580 cm^{-1} ν(C=N). The azetidinone compounds were characterized by their IR absorption bands at 1760–1730 cm^{-1} ν(C=O) and 850–560 cm^{-1} ν(C—Cl).

Antibacterial Activity

This part deals with the *in-vitro* screening of newly synthesized compounds for their antimicrobial activity for filter paper disc method at a concentration of 50 μg; the species, *Staphylococcus aureus* and *Escherichia coli*, have been taken for the antibacterial activity. The compounds possess moderate to good activity against all stains in comparison with ampicillin, penicillin and tetracycline against *Escherichia coli* (Table-3).

TABLE–3
ANTIBACTERIAL ACTIVITY OF NEWLY SYNTHESISED COMPOUNDS

No.	Zone of inhibition (mm)		No.	Zone of inhibition (mm)	
	S. aureus	*E. coli*		*S. aureus*	*E. coli*
BN-1	8.0	7.0	BN-11	9.0	7.0
BN-2	9.0	10.0	BN-12	8.0	9.0
BN-3	11.0	8.0	BN-13	7.0	10.0
BN-4	9.0	10.0	BN-14	11.0	9.0
BN-5	8.0	7.0	BN-15	9.0	8.0
BN-6	7.0	9.0	BN-16	8.0	7.0
BN-7	14.0	12.0	BN-17	13.0	11.0
BN-8	13.0	12.0	BN-18	14.0	12.0
BN-9	12.0	11.0	BN-19	11.0	12.0
BN-10	7.0	6.0	BN-20	8.0	7.0

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