Asian Journal of Chemistry Vol. 8, No. 1 (1996) 177–179

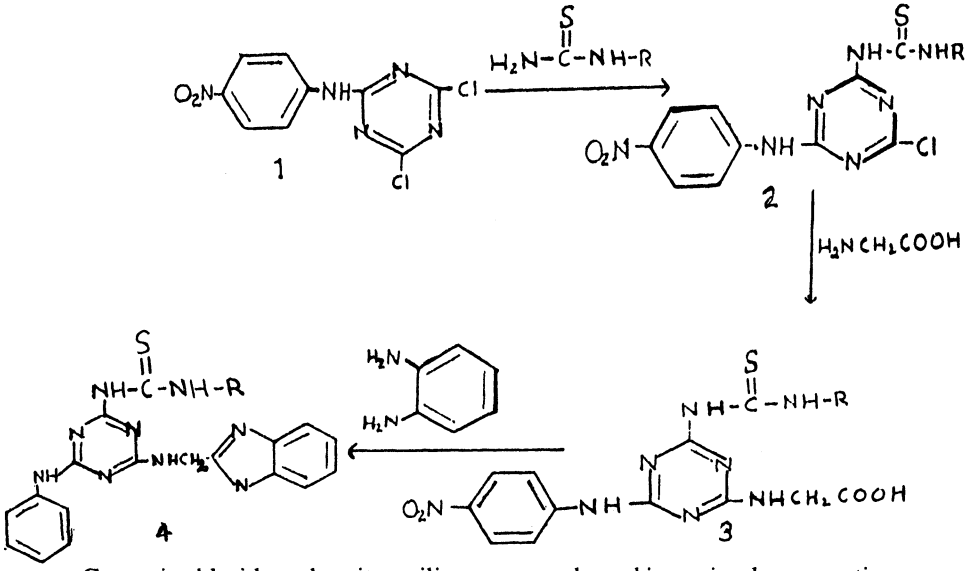
NOTE

Study and Synthesis of Benzimidazole Derivatives as Antibacterial Agents

C.P. SINGH*, S. KUMAR and S.S. NAYAL
Research Division, Department of Chemistry
Sahu Jain College, Najibabad-246 763, India

In the present note, the authors describe the preparation of benzimidazole derivatives and studied their antibacterial properties.

Benzimidazole derivatives possess a wide range of biological activities, such as antibacterial[1], antifungal, anithelmintic[2] etc. S-triazines have been found to be active against African sleeping sickness, malaria and cancer[3]. Triazinylthiourea derivatives are reported to be bactericidal agents[4]. Thiourea derivatives possess various therapeutic activities[5]. Prompted by the pharmacological importance of benzimidazoles, we have pre- pared 2-(4′-nitroanilino)-4-(arylthioureido)-6-(benzimidazol-2′-yl-methyl-amino)-S-triazine derivatives (4a–j).



Cyanuric chloride and *p*-nitroaniline were condensed in equimolar proportions. The intermediate (1) so obtained was reacted with various arylthioureas to get the corresponding intermediates (2), which were further condensed with aminoacetic acid to give the corresponding intermediates (3). They were conden-

sed with *o*-phenylenediamine to get the corresponding S-triazine derivatives (4a–j). Structures of the compounds were established by elemental and spectral data (Table-1).

TABLE-1
ANALYTICAL AND PHYSICAL DATA OF COMPOUNDS 4a–j

Compd. No.	R	m.p. (°C)	Yield %	Mol. formula	Analysis: Found/Reqd.		
					C	H	N
4a	C_6H_5-	242	53	$C_{24}H_{20}O_2N_{10}S$	54.64 (54.68)	3.82 (3.90)	27.29 (27.34)
4b	*o*-$CH_3C_6H_4$-	239	54	$C_{25}H_{22}O_2N_{10}S$	57.01 (57.03)	4.12 (4.18)	26.56 (26.61)
4c	*m*-$CH_3C_6H_4$-	140	60	$C_{25}H_{22}O_2N_{10}S$	56.98 (57.03)	4.14 (4.18)	26.51 (26.61)
4d	*p*-$CH_3C_6H_4$-	>300	50	$C_{25}H_{22}O_2N_{10}S$	56.99 (57.03)	4.13 (4.18)	26.53 (26.61)
4e	*o*-ClC_6H_4-	298	52	$C_{24}H_{19}O_2N_{10}SCl$	52.63 (52.69)	3.41 (3.47)	25.54 (25.62)
4f	*m*-ClC_6H_4-	240	48	$C_{24}H_{19}O_2N_{10}SCl$	52.65 (52.69)	3.44 (3.47)	25.52 (25.62)
4g	*p*-ClC_6H_4-	242	46	$C_{24}H_{19}O_2N_{10}SCl$	52.64 (52.69)	3.45 (3.47)	25.53 (25.62)
4h	*o*-$NO_2C_6H_4$-	280	45	$C_{24}H_{19}O_2N_{11}S$	51.69 (51.70)	3.40 (3.41)	27.60 (27.64)
4i	*m*-$NO_2C_6H_4$-	284	58	$C_{24}H_{19}O_4N_{11}S$	51.66 (51.70)	3.38 (3.41)	27.62 (27.64)
4j	*p*-$NO_2C_6H_4$-	>300	51	$C_{24}H_{19}O_4N_{11}S$	51.67 (51.70)	3.37 (3.41)	27.66 (27.64)

Infrared spectra (KBr) were recorded on a Perkin-Elmer spectrophotometer. Melting points were determined in open capillaries. Purity of the compounds was checked by TLC.

2-(4′-Nitroanilino)-4,6-dichloro-S-triazine (1)

It was prepared according to the reported method[6].

2-(4′-Nitroanilino)-4-(arylthioureido)-6-chloro-S-triazine (2)

A stirred solution of (1) (5.72 g, 0.01 mole) in acetone at 35°C, was added to a solution of arylthiourea (0.01 mole) in acetone over a period of 0.5 h. The temperature was gradually raised to 45°C during 2 h with stirring and maintaining a neutral pH. It was then poured on to crushed ice, and the resulting solid was dried and crystallised from alcohol (75–90%); melting points of the intermediates (2): R = C_6H_5, 201°C; *o*-$CH_3C_6H_4$, 219°C; *m*-$CH_3C_6H_4$, 260°C; *p*-$CH_3C_6H_4$, 224°C; *o*-ClC_6H_4, 245°C; *m*-ClC_6H_4, 207°C; *p*-ClC_6H_4, 204°C; *o*-$NO_2C_6H_4$, 170°C; *m*-$NO_2C_6H_4$, 177°C; *p*-$NO_2C_6H_4$, 201°C.

2-(4-Nitroanilino)-4-(arylthioureido)-6-(acetic acid-2′-yl-amino)-S-Triazine (3)

General method: The mixture of (2) (0.015 mole) and aminoacetic acid (1.55 g, 0.0207 mole) in 10.4 mL sodium carbonate (0.414 mole) solution was refluxed for 3 h on an oil bath. It was then acidified with hydrochloric acid to obtain the acid, which was dried and crystallised from alcohol (60–70%); melting points of the intermediates (3): R = C_6H_5, 190°C; *o*-$CH_3C_6H_4$, 177°C; *m*-$CH_3C_6H_4$, 150°C(d); *p*-$CH_3C_6H_4$, 160°C(d); *o*-ClC_6H_4, 126°C; *m*-ClC_6H_4, 185°C; *p*-ClC_6H_4, 200°C(d); *o*-$NO_2C_6H_4$, 101°C; *m*-$NO_2C_6H_4$, 111°C; *p*-$NO_2C_6H_4$, 160°C(d).

General method for the preparation of 2-(4′-nitroanilino)-4-(arylthioureido)-6-(benzimidazol-2′-yl-methyl-amino)-S-triazine (4a–j): The mixture of (3) (0.01 mole) and *o*-phenylenediamine (0.76 g, 0.007 mole) in 20 mL 4N hydrochloric acid was refluxed for 8 h on a water bath. It was then rendered alkaline with liquor ammonia and the resulting solid was dried and crystallised from alcohol (Table-1). ν_{max} (cm^{-1}): 830–820, ν (C_3N_3), 1480–1475, ν(C—N, thiourea), 1660–1650, ν(C—N, conjugative cyclic), and 3990–3400, ν(NH).

Antibacterial activity

The compounds were screened for antibacterial activity against *S. aureus* and *E. coli* at a concentration of 10 mg mL^{-1} using agar diffusion method[7]. Amongst the compounds (Table-1) tested, compound number 4a showed maximum activity (zone of inhibition 2.5 and 3 mm) and compound number 4 f showed minimum activity (zone of inhibition 1 and 0.5 mm) against *S. aureus* and *E. coli* respectively.

ACKNOWLEDGEMENT

The authors wish to express their cordial gratitude to Dr. A.N. Singh (Principal) and Dr. Shyam Singh, Scientist-F, Medicinal Chemistry Division, CDRI, Lucknow for testing of antibacterial activity.

REFERENCES

1. F.E. King and R.M. Acheson, *J. Chem. Soc.*, 1401 (1949).
2. V.K. Agarwal and S. Sharma, *Indian J. Chem.*, **22B**, 781 (1983).
3. S.H. Buckley and C.P. Rhoads, *Cancer Research*, **10**, 207 (1950).
4. Toyoma Chemical Industry Co. Ltd., *Chem. Abstr.*, **64**, 11281 (1966).
5. N.P. Buv-Hoi, *Int. J. Leprosy*, **22**, 16 (1954).
6. R.L. Mayer, *Chem. Abstr.*, **36**, 5199 (1942).
7. P.S. Desai and K.R. Desai, *J. Indian Chem. Soc.*, **67**, 688 (1990).
8. M.C. Bryant, Antibiotics and Their Laboratory Control, Butterworth, London, p. 26 (1968).

(*Received*: 29 July 1995; *Accepted*: 13 September 1995) AJC-1013