Asian Journal of Chemistry Vol. 11, No. 4 (1999), 1427–1430

Synthesis and Biological Evaluation of 2-Imino-Benzal-4-(2′-Hydroxy Aryl)-Thiazoles and N-[4′(2″-Hydroxy Aryl) -Thiazole]-4-Aryl-2-Azetidinones.

Mrs. ANJALI MILIND RAHATGAONKAR
Chemistry Department
Institute of Science, Nagpur 440 001, India

N-[4′(2″-hydoxy aryl)-thiazole]-4-aryl-2-azetidinones were prepared by the mechanism of cycloaddition reaction of acetyl chloride to ketenes in the presence of strong base triethylamine and neutral solvent as benzene.

INTRODUCTION

Heteroyclic compounds have two nitrogen atoms or one nitrogen and one sulphur atoms oriented in 1,3-positions are involved with broad spectrum of pharmaceutical properties[1]. Thiazole derivatives have been reported to be antibacterial, antiinflammatory and antimicrobial agents[2]. Many Schiff bases, *i.e.*, imines[3,4] exhibit commendable antimicrobial and anticancer activities. In continuation of our work on heterocyclic system, in view of the powerful antibiotic activity shown by monocyclic β-lactams of azetidinones[5,6] and the fact that thiazoles and condensed products play a variety of biological activities we have been led to the synthesis of 2-iminobenzal-4-(2′-hydroxy aryl) thiazoles (2) and N-[4′(2″-hydroxy aryl)-thiazole]-4-aryl-2-azetidinones (3).

The synthesized compounds were screened for antimicrobial activity at 100 μg/concentration against the test organisms *S. aureus*, *P. aeruginosa*, *B. subtilis*, *E. coli* and *Klebsiella pneumoniae*. DMF was used as solvent and disc method for inhibition studies. Penicillin was used as a standard drug. It was found that chloro and nitro derivatives showed significant antibacterial activity. The screening reports indicate that there is still scope for further improvement if the molecule is suitably modified.

EXPERIMENTAL

IR spectra (KBr) were recorded on Magna IR 550 Series II spectrometer. The ^{1}H-NMR spectra were recorded on AC-Brucker 300 MHz spectrophotometer using 5 mm tubes. Melting points were determined in open capillaries and are uncorrected. Purity of the samples was checked by TLC by using silica-gel-G.

General Procedure

2′-hydroxy aryl thiazoles[7] (1) were prepared by known method.

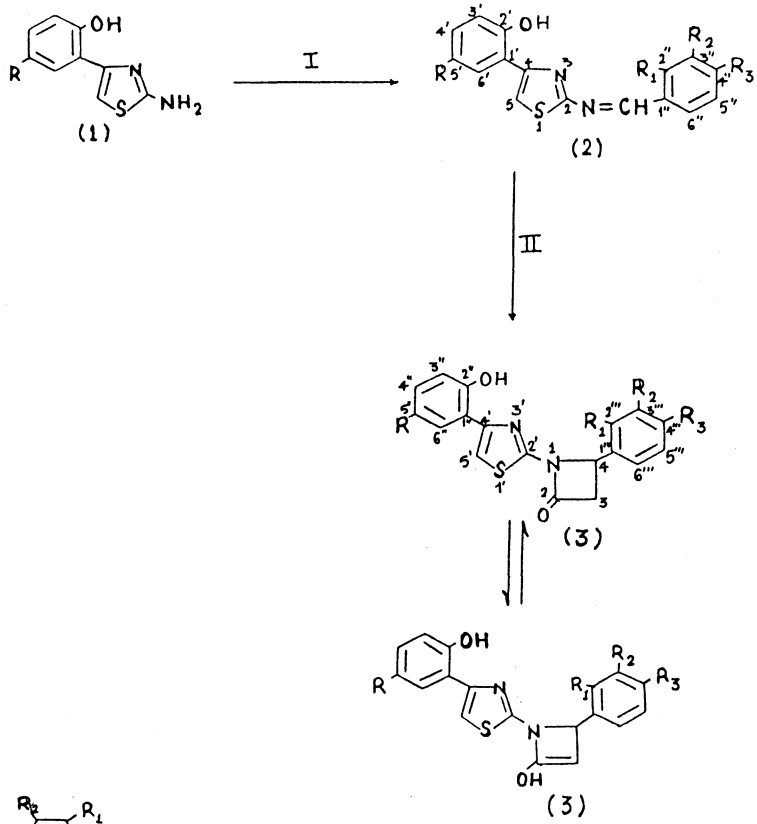
Preparation of 2-imino-(4″-methoxy benzal)-4-(2′-hydroxy-5′-chloro-phenyl)-thiazoles (2h)

A mixture of compound (1) (0.01 mol), anisaldehyde (0.01 mol), ethanol (30 mL) and 2 drops of conc H_2SO_4 was taken in round-bottomed flask. The reaction mixture was refluxed for 2 h in a water bath. The product was filtered and washed with ethanol. It was recrystallized from ethanol : dioxane (Table-1, Scheme-1).

TABLE-1
PHYSICAL CHARACTARIZATION OF COMPOUNDS

Comp. No.	R	R_1	R_2	R_3	Yield (%)	m.p. (°C)
2a	CH_3	H	H	H	80	236
2b	CH_3	H	NO_2	H	60	242
2c	CH_3	H	H	OCH_3	80	238
2d	CH_3	H	H	OH	60	205
2e	CH_3	H	OCH_3	OCH_3	50	165
2f	Cl	H	H	H	75	208
2g	Cl	H	NO_2	H	60	240
2h	Cl	H	H	OCH_3	90	220
2i	Cl	H	H	OH	50	216
2j	Cl	H	OCH_3	OCH_3	40	185
2k	H	H	H	H	90	242
2l	H	H	NO_2	H	60	196
2m	H	H	H	OCH_3	80	225
2n	H	H	H	OH	65	190
2o	H	H	OCH_3	OCH_3	40	125
3a	CH_3	H	H	H	60	225
3b	CH_3	H	NO_2	H	50	232
3c	CH_3	H	H	OCH_3	65	200
3d	CH_3	H	H	OH	45	190
3e	CH_3	H	OCH_3	OCH_3	40	140
3f	Cl	H	H	H	70	202
3g	Cl	H	NO_2	H	50	225
3h	Cl	H	H	OCH_3	75	210
3i	Cl	H	H	OH	40	212
3j	Cl	H	OCH_3	OCH_3	45	125
3k	H	H	H	H	70	239
3l	H	H	NO_2	H	60	175
3m	H	H	H	OCH_3	75	220
3n	H	H	H	OH	55	196
3o	H	H	OCH_3	OCH_3	50	145

C, H, N, analysis is found to be satisfactrily.



I R_1, R_2, R_3-CHO, Conc H_2SO_4, ethanol, Δ 2 hours

II CH_3COCl, $(C_2H_5)_3N$, and C_6H_6, Δ 6 hours

Scheme-I

NMR:- ($CDCl_3$ + DMSO-d_6): δ(3.7, S, 3H, Ar—OCH_3), δ(5.7, S, 1H,=CH), δ(6.7–7.2, m, 8H, Ar—H,), δ(8.3, S, 1H, Ar—OH)

IR: (KBr) ν_{max} cm^{-1} 3073 ν(OH), 2700 ν(—OCH_3), 1640 ν(C=N), 1109 ν(N=C—S), 819 ν(C—Cl).

Preparation of N-(4′-(2″-hydroxy-5″-chloro-phenyl) thiazole]-4-(4‴-methoxyl phenyl)-2-azetidinones (3h)

A mixture of compound (2) (0.01 mol), acetyl chloride (0.01 mol), triethylamine (2 mL), benzene (20 mL) was taken in round-bottomed flask. The reaction mixture was refluxed for 6 h in a water bath. The solvent was evaporated and sticky mass was triturated with solvent ether. It was further recrystallized from ethanol (Table-1) (Scheme-1)

NMR: ($CDCl_3$ + DMSO-d_6): δ(3.8, S, 3H, Ar—OCH_3), δ(5.7, S, 1H, C_3—H), δ(2.5, S, 1H, C_4—H), δ(6.7–7.3, m, 8H, Ar—H), δ(7.9, S, 1H, enolic —OH), δ(9.5, b, 1H, Ar—OH).

IR: (KBr): ν_{max} cm^{-1}: 3412 ν(OH), 3181 ν(enolic —OH), 2700 ν(—OCH_3), 1705 ν(β-lactam C=O), 1629 ν(C=N), 1112 ν(N=C—S), 819 ν(C—Cl),

ACKNOWLEDGEMENT

The author is thankful to RSIC Nagpur for IR, Central Instrumentation Laboratory, Chandigarh for NMR, Government Medical College, Nagpur for antimicrobial activity and National Cancer Institute, Maryland (USA) for anticancer activity. The author is also thankful to UGC for reserch grant and Dr. B.J. Ghiya for his enthusiastic cooperation.

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(*Received*: 28 April 1999; *Accepted*: 24 July 1999) AJC-1809