

Synthesis of Azetidinones from 2-Imino-Benzal-4,6-Diaryl Pyrimidines and 2-Imino-Benzal-4,6-Diaryl-5,6-Dihydro Pyrimidines and Evaluation of Their Antimicrobial Activity

MRS. ANJALI M. RAHATGAONKAR

Department of Chemistry
Institute of Science, Nagpur-440 001, India

N-(2-amino-4,6-diaryl pyrimidine)-4-phenyl-2-azetidinones were prepared from 2-iminobenzal-4,6-diaryl pyrimidines by condensing it with acetyl chloride and triethylamine in benzene.

INTRODUCTION

In continuation of our work¹ on the 2-amino-diaryl-pyrimidines and 2-amino-diaryl-dihydro pyrimidines, the nuclei of prime importance, we now report the synthesis and antimicrobial activity of N-(2-amino-4,6-diaryl pyrimido)-4-phenyl azetidinones (3) and N-(2-amino-4,6-diaryl-5,6-dihydro pyrimido)-4-phenyl azetidinones (4).

Literature survey reveals that the azetidinones and their corresponding derivatives have been synthesized by a number of workers²⁻⁴ with different starting material. The biological activity of the β -lactam antibiotics is generally believed to be associated with the chemical reactivity of their β -lactam ring⁵. Azetidinones have been known to exhibit interesting biological activities like anti-inflammatory, sedative, hypnotic and anti-convulsant⁶. This promoted us to synthesise different azetidinones from above said important starting materials (1) and (2).

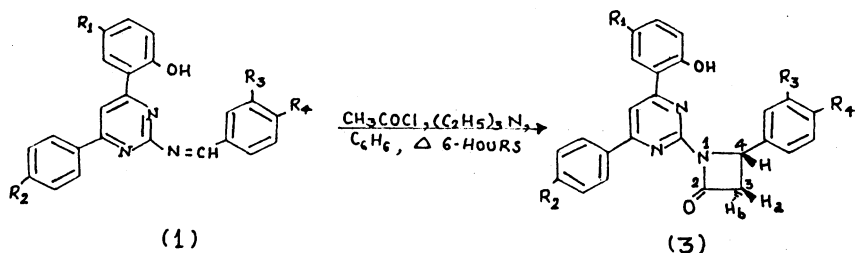
The synthesized compounds were tested for antimicrobial activities by using DMF as solvent against *E. coli*, *B. subtilis*, *K. pneumoniae*, *S. aureus*. At 100 μ g/mL compound (3e) was found to show comparable zone of inhibition with penicillin and it was measured in mm.

EXPERIMENTAL

All the melting points are uncorrected and taken in open capillaries. The IR spectra (KBr) were recorded on Magna IR 550 Series-II spectrometer. The ¹H NMR spectra were recorded on AC-Brucker 300 MHz spectrophotometer using 5 mm tubes.

General Procedure

Preparation of *N*-[4-(2-hydroxy-5-methyl-phenyl)-6-phenyl pyrimido]-4-phenyl 2-azetidinone (3a): (Scheme I; Table-I): A mixture of compound (1) (0.01 mol), acetylchloride (0.01 mol), triethylamine (2 mL) and benzene (10 mL) was taken in RB flask. The reaction mixture was refluxed for 6 h on water-bath. Solvent was evaporated to dryness. The sticky mass was triturated with solvent ether. The resulting powdery mass was recrystallized from ethanol (yield 70%).

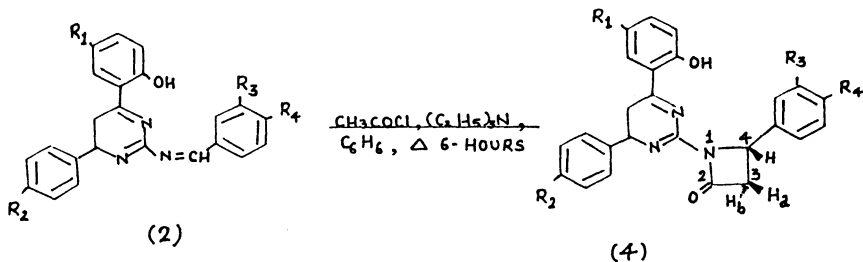


Scheme-I

Compound (3a): NMR (CDCl₃ + DMSO-d₆): δ (1.2–1.3, t, 1H, C₃—H), δ (3.2, q, 1H, CHb), δ (3.5, q, 1H, CHa), δ (2.3, s, 3H, Ar—CH₃), δ (7.2–8.2, m, 13H, Ar—H), δ (9.1, s, 1H, Ar—OH).

IR (KBr) ν cm⁻¹: 3370 ν (Ar—OH), 2677 (CH₂), 1662 ν (C=O) lactam, 1620 ν (C=N).

Preparation of *N*-[4-(2-hydroxy-5-methyl, phenyl)-5,6-dihydro-6-phenyl pyrimido]-4-phenyl-2-azetidinones (4a) (Scheme-II; Table-I): To the solution of compound (2) (0.01 mol), acetyl chloride (0.01 mol), triethylamine (2 mL) and benzene (20 mL) were added. The reaction mixture was refluxed for 6 h on water-bath. Solvent was evaporated and the sticky mass was triturated with solvent ether. Further it was recrystallized from ethanol to get white crystalline compound (yield: 70%).



Scheme-II

Compound (4a): NMR (CDCl₃ + DMSO-d₆): δ (1.2–1.3, t, 1H, C₃—H), δ (3.2, s, 1H, CHb), δ (3.8, q, 1H, CHa), δ (2.3, s, 3H, Ar—CH₃), δ (6.9–7.9, m, 15H, Ar—H), δ (10.1, 1H, Ar—OH).

IR (KBr) ν cm⁻¹: 3370 (Ar—OH), 2677 (CH₂), 1660 ν (C=O), 1620 ν (C=N).

TABLE-1 CHARACTERISATION DATA OF VARIOUS COMPOUNDS PREPARED

Comp. No.	R ₁	R ₂	R ₃	R ₄	m.p. (°C)	Yield (%)	m.f.	% Analysis		
								C	H	N
3a	CH ₃	H	H	H	236	80	C ₂₆ H ₂₁ N ₃ O ₂	76.6	5.1	9.2
3b	CH ₃	H	NO ₂	H	220	70	C ₂₆ H ₂₀ N ₄ O ₆	75.0	4.2	10.1
3c	CH ₃	H	H	OCH ₃	225	90	C ₂₇ H ₂₃ N ₃ O ₃	77.0	5.2	9.6
3d	CH ₃	H	H	OH	198	60	C ₂₆ H ₂₁ N ₃ O ₃	72.0	4.9	10.2
3e	Cl	H	H	H	190	85	C ₂₅ H ₁₈ N ₃ O ₂ Cl	72.2	3.1	9.2
3f	Cl	H	NO ₂	H	205	72	C ₂₅ H ₁₇ N ₄ O ₄ Cl	73.1	3.1	10.2
3g	Cl	H	H	OCH ₃	235	92	C ₂₆ H ₂₀ N ₃ O ₃ Cl	75.2	4.6	9.2
3h	Cl	H	H	OH	210	70	C ₂₅ H ₁₈ N ₃ O ₃ Cl	72.0	3.9	9.8
4a	CH ₃	H	H	H	202	70	C ₂₆ H ₂₃ N ₃ O ₂	70.0	5.2	9.9
4b	CH ₃	H	NO ₂	H	190	60	C ₂₆ H ₂₂ N ₄ O ₄	76.0	5.1	10.2
4c	CH ₃	H	H	OCH ₃	210	80	C ₂₇ H ₂₅ N ₃ O ₃	76.0	6.1	9.2
4d	CH ₃	H	H	OH	220	65	C ₂₆ H ₂₃ N ₃ O ₃	75.1	5.1	10.1
4e	CH ₃	OCH ₃	H	H	229	80	C ₂₇ H ₂₅ N ₃ O ₃	76.1	5.9	9.1
4f	CH ₃	OCH ₃	NO ₂	H	240	70	C ₂₇ H ₂₄ N ₄ O ₄	78.2	6.3	10.9
4g	CH ₃	OCH ₃	H	OCH ₃	220	95	C ₂₈ H ₂₇ N ₃ O ₄	78.9	6.9	9.3
4h	CH ₃	OCH ₃	H	OH	240	70	C ₂₇ H ₂₅ N ₃ O ₄	77.1	6.3	9.1
4i	Cl	H	H	H	215	90	C ₂₅ H ₂₀ N ₃ O ₂ Cl	72.1	4.9	8.9
4j	Cl	H	NO ₂	H	205	70	C ₂₅ H ₁₉ N ₄ O ₄ Cl	73.2	3.9	10.6
4k	Cl	H	H	OCH ₃	209	95	C ₂₆ H ₂₂ N ₃ O ₃ Cl	75.9	5.1	9.1
4l	Cl	H	H	OH	212	60	C ₂₅ H ₂₀ N ₃ O ₃ Cl	73.1	4.7	9.6
4m	Cl	OCH ₃	H	H	220	90	C ₂₆ H ₂₂ N ₃ O ₃ Cl	75.1	5.3	9.1
4n	Cl	OCH ₃	NO ₂	H	198	70	C ₂₆ H ₂₁ N ₄ O ₅ Cl	77.3	5.1	10.6
4o	Cl	OCH ₃	H	OCH ₃	218	95	C ₂₇ H ₂₄ N ₃ O ₄ Cl	76.0	6.9	9.1
4p	Cl	OCH ₃	H	OH	216	60	C ₂₆ H ₂₂ N ₃ O ₃ Cl	74.0	5.6	9.3

ACKNOWLEDGEMENTS

The authors are thankful to UGC for Research Grant; Government Medical College, Microbiology Dept., Nagpur for carrying out antimicrobial activity; and National Cancer Institute, Maryland, USA for anticancer activity. The authors are also thankful to RSIC Nagpur for carrying out IR spectra and Central Instrumentation Centre Laboratory, Chandigarh.

REFERENCES

1. Mrs. Anjali M. Rahatgaonkar and B.J. Ghiya, *Asian J. Chem.*, **10**, 958 (1998).
2. R.H. Udipi M. Jeesson and A.R. Bhatt, *Indian J. Heterocyclic Chem.*, **6**, 99 (1996).
3. R.H. Udipi, N. Kasinath and A.R. Bhatt, *Indian J. Heterocyclic Chem.*, **7**, 221 (1998).
4. P. Berheim, *Science*, **92**, 204 (1940).
5. M.S. Manhas and A.K. Bose, *Beta Lactams: Natural and Synthetic, Part 1*, Wiley-Interscience, New York, p. 187 (1971).
6. M. Tandon, P. Kumar, P. Tandon, T.N. Bhalla and J.P. Bharathwal, *Acta Pharm. Jugosl.*, **B3**, 93 (1963).

(Received: 20 February 1999; Accepted: 21 May 1999)

AJC-1727