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Synthesis and Biological Activity of Thiazole, 4-Thiazolidine, Azetidinone Having Tetrahydrocarbazole Moiety

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Some new thiazole, 4-oxo-thiazolidine, azetidinone have been synthesized and evaluated for their antimicrobial activity. Structural assignments of these compounds have been made on the basis of elemental analyses and IR spectral data.

Key Words: Thiazole, 4-Thiazolidine, Azetidinone, Tetrahydrocarbazole, Synthesis, Biological activity.

INTRODUCTION

In continuation of our work on the synthesis of biologically active heterocycles[1-3], we contemplated to synthesize 2-amino-4-(tetrahydrocarbazol-9-yl) thiazole, 2-(phenyl)-3-(tetrahydrocarbazolylacetamidyl)-4-oxo-thiazolidine and 9-[α-(2-phenyl-3-chloro-4-oxo-1-azetidinylamino)-acetyl]-9H-tetrahydrocarbaz ole **(Scheme-1).** Early workers[4-6] have synthesized various thiazoles, 4-oxo-thiazolidine and azetidinone. All the synthesized compounds **2, 5** and **6** were screened for antimicrobial activity[7,8] against *Escherichia coli, Staphylococcus aureus, Salmonella typhi, Aspergillus niger* and *Penicillum oxaliocum.* The compounds were tested at 100 μg/mL concentration in DMF.

EXPERIMENTAL

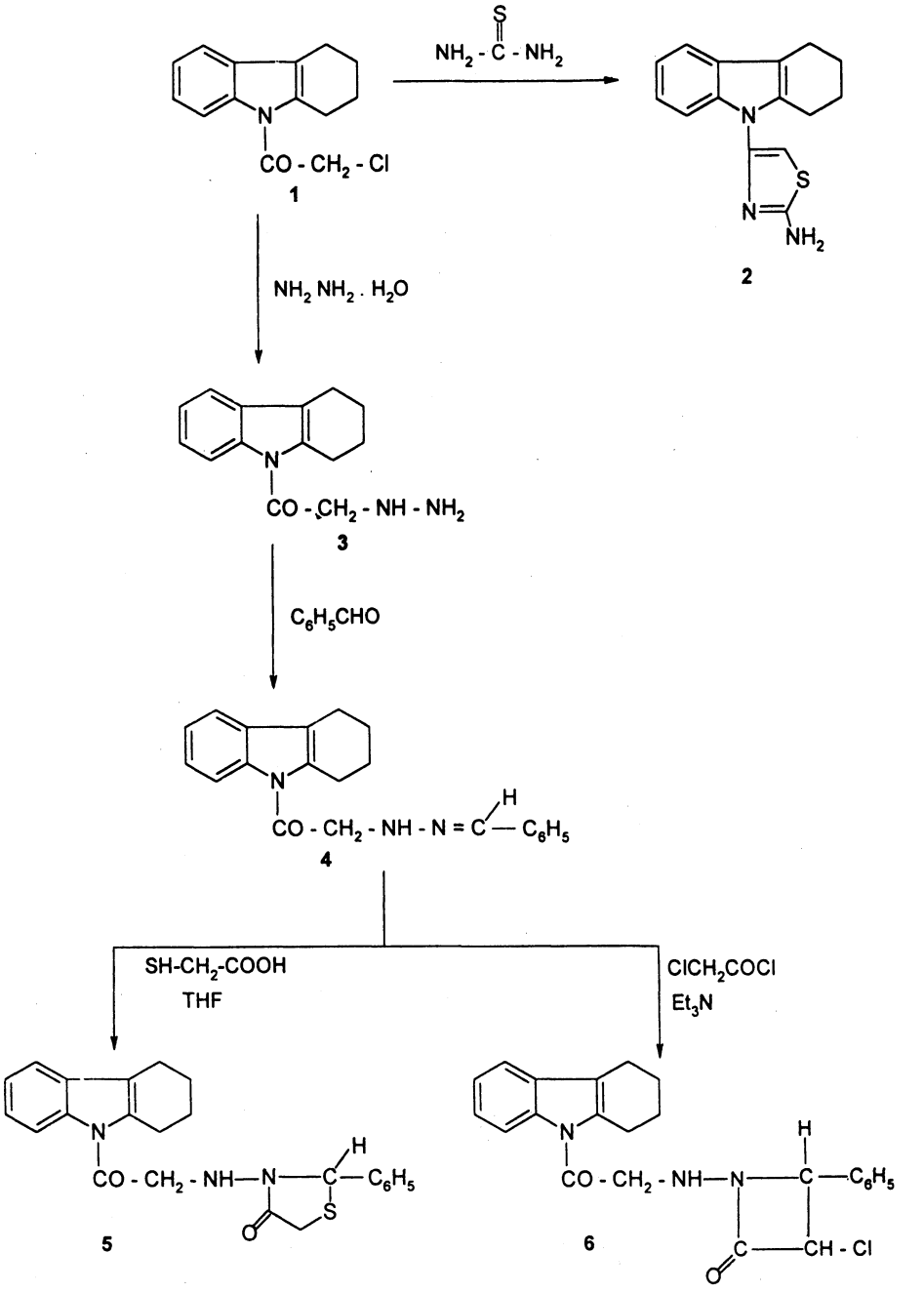
All melting points were taken in open capillary tubes and are uncorrected. Purity of the compounds was checked by TLC on silica gel-G plates. IR spectra in KBr discs were recorded on Bruker IFS 66V FT-IR spectrophotometer. Elemental analyses of the synthesized compounds were carried out using Hereaus-CHN-rapid analyzer.

Synthesis

N_9-(Chloroacetyl)-1,2,3,4-tetrahydrocarbazole (1): Tetrahydrocarbazole (0.02 mol, 3.5 g) and chloroacetyl chloride (0.02 mol, 2.5 g) in benzene (50 mL) were refluxed for 4 h. The excess of solvent was distilled off and the residue kept under reduced pressure. The solid thus separated was filtered and crystallized from ethanol to give compound **(1).**

2-Amino-4-(tetrahydrocarbazol-9-yl)thiazole (2): A mixture of N_9-(chloroacetyl)-tetrahydrocarbazole **(1)** (0.01 mol, 2.5 g) and thiourea (0.01 mol, 1 g) in ethanol was refluxed for 5 h. The product was filtered off and washed

with sodium carbonate solution. It was then crystallized from ethanol to get compound **(2)**.



Scheme-1

Tetrahydrocarbazol-9-acetyl hydrazine (3): A mixture of N_9-(chloroacetyl)-tetrahydrocarbazole **(1)** (0.01 mol, 2.5 g) and hydrazine hydrate (0.04 mol, 2 mL) in absolute ethanol was refluxed for 5 h. The solution was poured into ice-cold water. The resulting solid was filtered, dried and crystallized from ethanol to give compound **(3)**.

N_9-(Phenylidenehydrazidomethyl) tetrahydrocarbazole (4): A solution of tetrahydrocarbazol-9-acetyl hydrazine **(3)** (0.01 mol, 2.5 g) in chloroform (50 mL), benzaldehyde (0.01 mol, 11 mL) and 4–5 drops of glacial acetic acid was refluxed on a water bath for about 8 h, cooled and evaporated to obtain a residue which was crystallized from ethanol to give compound **(4)**.

2-Phenyl-3-(N_9-tetrahydrocarbazolylacetamidyl)-4-oxo-thiazolidine (5): A mixture of N_9-(phenylidenehydrazidomethyl) tetrahydrocarbazole **(4)** (0.01 mol, 3.3 g) in tetrahydrofuran (30 mL) and mercaptoacetic acid (0.01 mol, 2 mL) with a pinch of anhydrous zinc chloride was refluxed for about 10 h on a water bath. The separated solid was filtered and recrystallized from ethanol to give compound **(5)**.

9-[α-(2-Phenyl-3-chloro-4-oxo-1-azetidinylamino)acetyl]-9H-tetrahydrocarbazole (6): To a well stirred solution of N_9-(phenylidenehydrazidomethyl) tetrahydrocarbazole **(4)** (0.01 mol, 3.3 g), triethylamine (0.02 mol, 2 mL) in dry 1,4-dioxane (25 mL) was added chloroacetylchloride (0.02 mol, 3 mL) dropwise at room temperature. The reaction mixture was stirred for 1 h and refluxed for 2 h. On removal of dioxane under reduced pressure, a solid was obtained which was crystallized from ethanol to give compound **(6)**.

TABLE-1
PHYSICAL DATA AND CHARACTERIZATION OF SYNTHESIZED COMPOUNDS

Compd. No.	m.f. (m.w.)	m.p. (°C)	Yield (%)	Analysis % Found (Calcd.) C	H	N	IR (cm^{-1})
1.	$C_{14}H_{14}NOCl$ (247.5)	141	70	67.18 (67.87)	5.27 (5.65)	5.34 (5.65)	1713 ν(C=O) and 714 ν(C—Cl)
2.	$C_{15}H_{15}N_3S$ (269)	169	61	66.42 (66.91)	5.13 (5.57)	15.26 (15.61)	3341 ν(NH_2), 1610 ν(C=N) and 630 ν(C—S—C)
3.	$C_{14}H_{17}N_3O$ (243)	64	52	68.34 (69.13)	6.16 (6.99)	17.04 (17.28)	3398 ν(NH_2), 1679 ν(C=O) and 1466 ν(C—N)
4.	$C_{21}H_{21}N_3O$ (331)	108	56	75.87 (76.13)	6.09 (6.34)	12.31 (12.68)	1661 ν(C=O) and 1621 ν(—CH=N—)
5.	$C_{23}H_{23}N_3OS$ (389)	181	48	70.32 (70.95)	5.14 (5.91)	10.23 (10.79)	1700 ν(C=O) and 699 ν(C—S—C)
6.	$C_{23}H_{22}N_3O_2Cl$ (407.5)	139	35	67.54 (67.73)	5.12 (5.39)	9.82 (10.30)	1702 ν(C=O), 1647 ν(CO—NH) and 737 ν(C—Cl)

RESULTS AND DISCUSSION

Amongst the compounds tested against *S. aureus*, compound **5** showed high activity, compound **2** showed moderate activity whereas compound **6** exhibited less activity.

Compound **2** showed moderate activity against *S. typhi*. Compounds **5** and **6** reported moderate activity and compound **2** displayed very good activity against *A. niger*.

Compounds **2, 5** and **6** exhibited less activity against *P. oxaliocum*.

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