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Synthesis and Antibacterial Activity of 6-(5'-Substituted-2'-benzofuryl)-4-aryl-4*H*-2-oxopyrimidines

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Various 2-acetyl-5-substituted benzofurans and their subsequent transformation into benzofuran analogues of α, β, unsaturated ketenes by reaction with various 5-substituted-5-hydroxyl benzaldehydes have been synthesized. These benzofuran analogues of α, β, unsaturated ketones are further modified chemically into different nitrogen heterocyclic systems. In present studies, the synthesis of oxopyrimidines coupled with various benzofurans was reported. The structures of these compounds were established on the basis of elemental analysis and spectral studies. Screening of antibacterial activity of synthesized oxopyrimidines were also carried out by qualitative methods.

Key Words: α, β-Unsaturated ketones, Benzofuran, Oxopyrimidines.

INTRODUCTION

Pyrimidine is the most important member of all the diazines, as this ring system occurs widely in living organisms. Uracil, thymine and cytosine are the pyrimidine bases of nucleic acids. The chemistry of pyrimidine[1,2] has been widely studied.

Pyrimidines have occupied an unique place in the field of medicinal chemistry. Some antibacterial[3,4] and antimalarial[5,6] drugs are pyrimidine derivatives. Certain pyrimidine derivatives are known to display analgesic[7], sedative, antiphlogistic[7], antifilarial[8], antileishmonial[9,10], antitumor[11], antifungal[12], antiviral[13] and insecticidal[14] activities. Also a number of oxopyrimidines were reported as potential anti HIV agents[15-17]. Various efforts are being made to synthesize potential compounds containing benzofuran moiety linked with pyrimidine and pyridine, which posses useful biological activities[18-20]. Benzofurans coupled with single or more than one nitrogen heterocycles are reported to be useful antihypertensive agents[21].

Keeping in view the biological importance and chemotherapeutic properties of oxopyrimidine and benzofuran derivatives, the attempt has been made to synthesize some new oxopyrimidine derivatives linked to benzofuran.

EXPERIMENTAL

The melting points were recorded using hot paraffin bath and are uncorrected. Chemicals used were AR grade. IR spectra were recorded on Perkin-Elmer spectro-

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photometer in the range 4000-400 cm^{-1} in Nujol mull and as KBr pellets. PMR spectra were recorded with TMS an internal standard using $CDCl_3$ and DMSO-d_6 as solvent.

Synthesis of 6-(5'-substituted-2'-benzofuryl)-4-aryl-4*H*-2-oxopyrimidines: A suspension of 1-(5'-substituted-2'-benzofuryl)-3-aryl-2-propene-1-one and urea into 1:1 molar ratios were dissolved in ethyl alcohol. An alcoholic potash was added, refluxed for 8 h. Further cooling and acidifying the reaction mixture gave the desired products. The yields (%) is 40-65 (Table-1).

TABLE-1

Substituents		m.p. (ºC)	Yield (%)	m.f.	m.w.	N (%)		Antimicrobial activity (zone of inhibition)	
R	R'					Calcd.	Found.	*E. coli* (gram -ve)	*S. aureus* (gram +ve)
H	H	234	52	$C_{18}H_{14}N_2O_2$	290.0	9.65	9.47	10	15
H	OH	237	56	$C_{18}H_{14}N_2O_3$	306.0	10.92	10.58	8	–
H	CH_3	155	55	$C_{19}H_{16}N_2O_2$	304.0	9.21	8.94	8	17
H	Cl	282	48	$C_{18}H_{13}N_2O_2Cl$	324.5	8.62	8.73	9	22
H	OCH_3	222	55	$C_{19}H_{16}N_2O_3$	320.0	8.75	8.68	8	8
H	Furyl	268	45	$C_{16}H_{12}N_2O_3$	280.0	10.00	10.50	10	40
H	Thiophenyl	145	48	$C_{16}H_{12}N_2O_2S$	296.0	9.45	9.70	8	10
CH_3	H	156	60	$C_{19}H_{16}N_2O_2$	304.0	9.21	8.90	8	20
CH_3	OH	217	55	$C_{19}H_{16}N_2O_3$	320.0	8.75	8.50	10	11
CH_3	CH_3	172	58	$C_{20}H_{18}N_2O_2$	318.0	8.8	8.70	8	30
CH_3	Cl	215	52	$C_{19}H_{15}N_2O_2Cl$	338.5	8.27	8.30	8	24
CH_3	OCH_3	1741	66	$C_{20}H_{18}N_2O_3$	334.0	8.38	8.15	9	9
CH_3	Furyl	179	51	$C_{17}H_{14}N_2O_3$	294.0	9.85	9.21	10	20
CH_3	Thiophenyl	167	54	$C_{17}H_{14}N_2O_2S$	310.0	9.03	8.80	10	10
Cl	H	253	60	$C_{18}H_{13}N_2O_2Cl$	324.5	8.62	8.50	10	8
Cl	OH	97	64	$C_{18}H_{13}N_2O_3Cl$	340.5	8.22	8.10	10	20
Cl	CH_3	167	65	$C_{19}H_{15}N_2O_2Cl$	338.5	8.27	8.40	8	22
Cl	Cl	238	50	$C_{18}H_{12}N_2O_2Cl_2$	359.0	7.79	7.80	9	12
Cl	OCH_3	175	58	$C_{19}H_{15}N_2O_3Cl$	354.5	6.59	6.40	10	16
Cl	Furyl	166	52	$C_{16}H_{11}N_2O_3Cl$	314.5	8.3	6.20	12	8
Cl	Thiophenyl	158	54	$C_{16}H_{11}N_2O_2SCl$	330.5	8.47	8.50	8	8
OCH_3	H	144	70	$C_{19}H_{16}N_2O_3$	320.0	8.45	8.60	8	14
OCH_3	OH	202	62	$C_{19}H_{16}N_2O_4$	336.0	8.33	8.50	8	14
OCH_3	CH_3	231	65	$C_{20}H_{18}N_2O_3$	334.0	8.38	8.40	10	8
OCH_3	Cl	194	58	$C_{19}H_{15}N_2O_3Cl$	354.5	7.84	7.60	8	8
OCH_3	OCH_3	186	65	$C_{20}H_{18}N_2O_4$	350.0	8.00	8.10	9	20
OCH_3	Furyl	238	53	$C_{17}H_{14}N_2O_4$	310.0	9.05	9.00	10	30
OCH_3	Thiophenyl	217	65	$C_{17}H_{14}N_2O_3S$	326.0	8.58	8.40	8	12

Drug substance: zone of inhibition. Standard streptomycine: 10 mm. Standard griseofluevin: 9 mm. Control of $CHCl_3$: 7 mm.

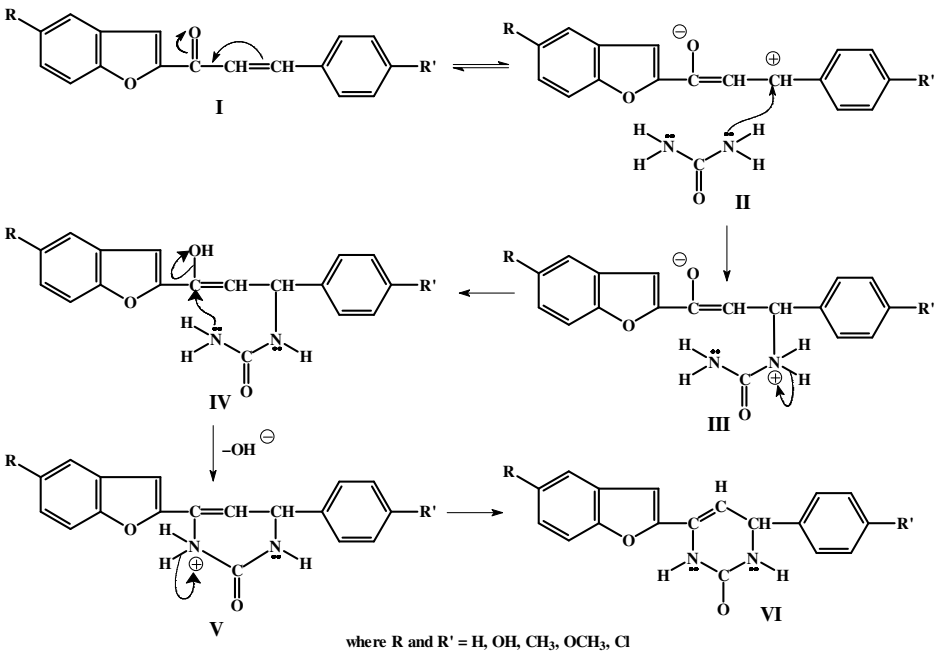
The products were purified by recrystallization from suitable solvents. The purity of the compounds were checked by TLC and structures were confirmed by elemental and spectral analysis (IR and NMR).

Screening of antibacterial activity of synthesized oxopyrimidines were carried out by qualitative methods and it is found that these compounds show moderate activity (Table-1).

RESULTS AND DISCUSSION

Synthesis of 6-(5'-methoxy-2'-benezofuryl)-4-(4-methoxy phenyl)-4*H*)-2-oxopyrimidine: To a solution of 1-(5'-methoxy-2'-benzofuryl)-3-(4-methoxyphenyl) -2-propene-1-one (0.01 mol, 3.5 g) and urea (0.01 mole, 1.12 g) in 50 mL ethyl alcohol taken in round bottom flask, alcoholic potassium hydroxide (50 % solution, 10 mL) was added to it. The reaction mixture was refluxed for 8 h. Further, it was cooled and poured into ice-cold water. It is carefully neutralized by acetic acid. The solid product thus obtained was filtered, washed with water and dried. Recrystallization from ethyl alcohol gave a pure compound (m.p. 186 ºC, yield 65 %) m.f. $C_{20}H_{18}N_2O_4$. Elemental analysis (%) found (calcd.) N, 8.10 (8.00). IR (KBr, ν_{max}, cm^{-1}): 3400 (-OH), 3200 (-NH), 3065 (AR-H), 2933, 2837 (-CH_3), 1664 (-C=O), 1251 (C-O-C). PMR δ (6.8-7.8, 8H, m, Ar-H); (6.7, 1H, S, NH_d), (4.8, 1H, d, Ha); (3.82, 3H, S, CH_3); (3.7, 3H, S, CH_3Ar); (3.29, 1H, d, NH_c); (1.27, 1H, t, H_b).

the other compounds (**VI_1 VI_{28}**) were prepared by extending the above reaction to other substituted α, β. Unsaturated ketones (**I_1 I_{28}**) and can be explain by the following reaction (**Scheme-I**).



Scheme-I

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REFERENCES

1. D.J. Brown, *Rev. Pure Appl. Chem*., **3**, 115 (1953).
2. D.J. Brown, The pyrimidines, Ed. A. Weissberger, Interscience, New York, pp. 183-210 (1962).
3. W.O. Foye, Principle of Medicinal Chemistry, Lea and Febiger, Philadelphia (1981).
4. G.N. Pershin, L.I. Sherbakova, T.N. Zykova and V.N. Sakolva, *Farmakol and Taksikol*, **35**, 466 (1972); *Chem. Abstr.*, **77**, 155580z (1972).
5. E.A. Steck, The Chemotherapy of protozoan Diseases; Walter Reed, Army Institute of Research Washington D.C. (1971).
6. P.E. Thompson and L.M. Werbal, Antimalerial Agents, Chemistry and Pharmacology, Academic Press, New Yark (1970).
7. S. Senda, H. Funimura and H. Izumi, *Japan Kokai*, JP 6824 (1968); *Chem. Abstr.*, **70**, 78001r (1969).
8. R.E. Howells, J. Tinsly, F. Devaney and G. Smith, *Acta Tropia*, **38**, 289 (1982); *Chem. Abstr.*, **96**, 384K (1982).
9. V.J. Ram, *Prakt Chem.*, **331**, 893 (1989).
10. V.J. Ram, N. Haque and P.Y. Guru, *Eur. J. Med. Chem.*, **27**, 851 (1992).
11. K. Saguria, A.F. Schmid, M.M. Schimid and F.G. Brown, *Cancer Chemother Res.*, **2**, 231 (1973).
12. G. Matolesy, *Word Rev. Contr.*, **10**, 50 (1971).
13. F.L. Mercer, L.F. Lindhorst and B. Commoner, *Science*, **117**, 558 (1953).
14. G.C. Cheng, *Prog. Med. Chem*., **6**, 67 (1969).
15. R. Vig, C. Mao, T.K. Venkatachalam, L. Tuel, Ahlgreen, E.A. Suldeck and F.M. Uekum, *Bio. Med. Chem. Lett.*, **8**, 1461 (1998).
16. E.A. Sudbeck, C. Mao, R. Vig, T.K. Venkatachalam, L. Tuel-Ahlgren and Fatih M. Uckun, *Antimicrob. Agent Chemother.*, **42**, 3225 (1998).
17. E. Nizi, M. Botta, F. Corelli, F. Manetti, F. Messina and G. Maga *Tetrahedron Lett*., **39**, 3307 (1998).
18. P.I. Abramenko, V.G. Zhiryankov and K. Ponomareva, *Khim. Getevotsiki Soedin*, **6**, 796 (1974).
19. P.I. Abramonko and V.G. Ziryankov, *Kim. Geterosiki Soedin*, 1357 (1976); *Chem. Abstr.*, **86**, 56729 (1977).
20. R.A. Abramovitch and M.N. Inbasekaran, *Tetrahedron Lett*., **18**, 1109 (1977).
21. B.C. Ross, European Patent, EP 514,192 (1992); *Chem. Abstr.*, **119**, 9554 (1993).

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