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Synthesis of 2-Amino Dihydropyrimidines, Their Thiocarbamide Derivatives and Study of Their Antimicrobial Activity

P.B. HEDA and B.J. GHIYA*
Chemistry Department
Institute of Science, Nagpur-440 001, India

Various substituted acetophenones (I) were prepared by Fries migration of substituted phenyl acetates. (I) on Claisen-Schmidt condensation with substituted aromatic aldehydes in presence of 40% NaOH gave different substituted chalcones (II). (II) on cyclocondensation with guanidine carbonate in ethylene glycol gave 2-amino-5,6-dihydro pyrimidines (III). (III) on reaction with phenyl isothiocyanate in benzene gave respective thiocarbamide derivatives (IV). Structures of compounds (III) and (IV) were confirmed on the basis of elemental analysis, chemical properties and IR, NMR and mass spectra. Antimicrobial activities of some of the synthesised compounds was also studied.

INTRODUCTION

Pyrimidine is a basic nucleus in DNA and RNA and has been associated with a number of biological activities[1]. Substituted pyrimidines and their derivatives are also well known to have a number of biological, antimicrobial and pharmaceutical activities[2]. Many pyrimidine derivatives have been found to be active against different forms of cancer[3]. Earlier workers have reported synthesis of some substituted 5,6-dihydropyrimidine derivative using urea and acrylic esters[4]. Therefore, it was thought interesting to sythesise substituted 5,6-dihydropyrimidines from chalcone and their thiocarbamide derivatives and study their antimicrobial activities and anticancer activities. 2-Amino-4,6-(sub.)-diphenyl-5-6-dihydro pyrimidine (III) was prepared by cyclocondensation of substituted chalcone with guanidine carbonate in ethylene glycol. (III) was then treated with phenyl isothiocyanate in benzene to get 1-phenyl-3-(4,6-(sub)-diphenyl-5,6-dihydropyrimidine-2-yl) thiourea (IV). Some of the synthesised compounds were screened for antimicrobial activity, m.p., yield etc. (Tables 1, 2).

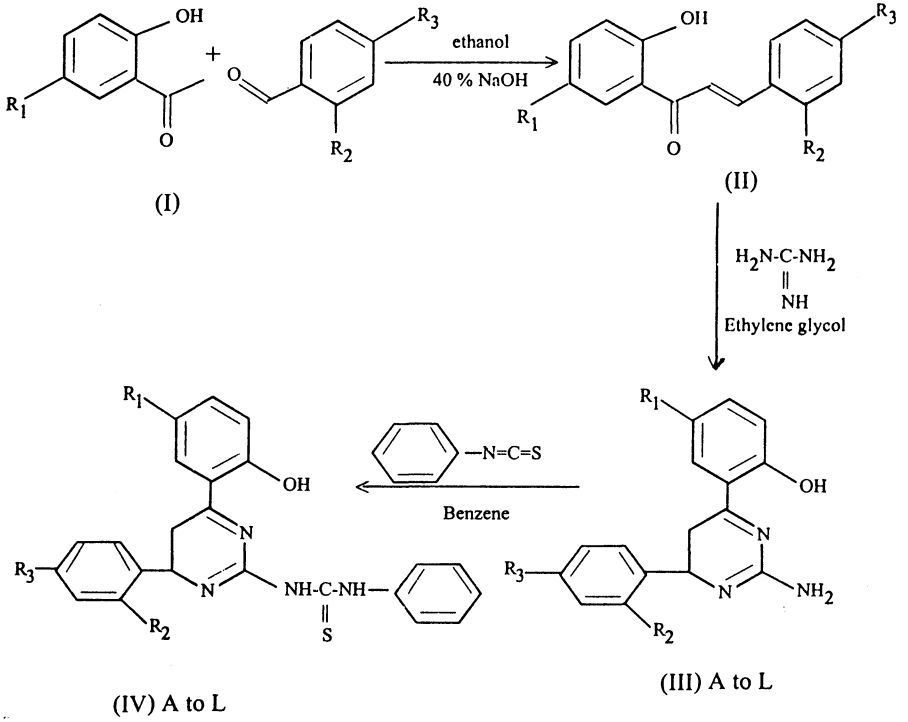
TABLE-1

S. No.	Compd.	R_1	R_2	R_3	Mol. formula	% N		Yield %	m.p. (°C)
						Calcd.	Found		
1.	IIIA	H	H	H	$C_{16}H_{15}N_3O$	15.85	15.78	50	165
2.	IIIB	H	H	OCH_3	$C_{17}H_{17}N_3O_2$	14.25	14.15	50	190
3.	IIIC	H	Cl	H	$C_{16}N_{14}N_3OCl$	14.00	13.90	50	180
4.	IIID	H	H	$N(CH_3)_2$	$C_{18}H_{20}N_4O$	18.18	18.05	50	210
5.	IIIE	CH_3	H	H	$C_{17}H_{17}N_3O$	15.05	14.95	50	179
6.	IIIF	CH_3	H	OCH_3	$C_{18}H_{19}N_3O_2$	13.59	13.38	50	220
7.	IIIG	CH_3	Cl	H	$C_{17}H_{16}N_3OCl$	13.44	13.35	50	185
8.	IIIH	CH_3	H	$N(CH_3)_2$	$C_{19}H_{22}N_4O$	17.39	17.30	50	230
9.	IIII	Cl	H	H	$C_{16}H_{14}N_3OCl$	14.00	13.90	50	198
10.	IIIJ	Cl	H	OCH_3	$C_{17}H_{16}N_3O_2Cl$	12.74	12.65	50	200
11.	IIIK	Cl	Cl	H	$C_{16}H_{13}N_3OCl_2$	12.57	12.25	50	205
12.	IIIL	Cl	H	$N(CH_3)_2$	$C_{18}H_{19}N_4OCl$	16.35	16.15	50	210

TABLE-2

S. No.	Compd.	R_1	R_2	R_3	Mol. formula	% N		Yield %	m.p. (°C)
						Calcd.	Found		
1.	IVA	H	H	H	$C_{23}H_{20}N_4OS$	14.00	13.90	80	170
2.	IVB	H	H	OCH_3	$C_{24}H_{22}N_4O_2S$	13.02	13.00	80	195
3.	IVC	H	Cl	H	$C_{23}H_{19}N_4OSCl$	12.88	12.75	80	192
4.	IVD	H	H	$N(CH_3)_2$	$C_{25}H_{25}N_5OS$	15.80	15.70	80	218
5.	IVE	CH_3	H	H	$C_{24}H_{22}N_4OS$	13.52	13.20	80	165
6.	IVF	CH_3	H	OCH_3	$C_{25}H_{24}N_4O_2S$	12.61	12.45	80	212
7.	IVG	CH_3	Cl	H	$C_{24}H_{21}N_4OSCl$	12.48	12.25	80	195
8.	IVH	CH_3	H	$N(CH_3)_2$	$C_{26}H_{27}N_5OS$	15.31	15.15	80	242
9.	IVI	Cl	H	H	$C_{23}H_{19}N_4OSCl$	12.88	12.68	80	200
10.	IVJ	Cl	H	OCH_3	$C_{24}H_{21}N_4O_2SCl$	12.05	12.00	80	195
11.	IVK	Cl	Cl	H	$C_{23}H_{18}N_4OSCl_2$	11.94	11.75	80	212
12.	IVL	Cl	H	$N(CH_3)_2$	$C_{25}H_{24}N_5OSCl$	14.65	14.28	80	218

Scheme 1



EXPERIMENTAL

The structures of these compounds were established by elemental analysis, chemical properties and spectral analysis. All melting points were taken in open capillaries and are uncorrected. Purity of compounds was checked by TLC on silica gel-G. IR spectra were recorded on Perkin-Elmer spectrophotometer, mass spectra on Jeol D-300 (EI/CI) spectrophotometer and ^{1}H NMR spectra on Brucker AC 300F NMR spectrometer at 300 MHz.[5]

The chalcones used for the synthesis of 2-amino-5,6-dihydropyrimidines (III) were synthesised by Claisen-Schmidt condensation of substituted acetophenones and substituted aromatic aldehydes.

(1) Preparation of 2-amino-4,6(sub) diphenyl 5,6-dihydropyrimidine (III)

(II) (0.01 mol), guanidine carbonate (0.01 mol) and ethylene glycol (25 mL) were refluxed for 3 h. The reaction mixture was cooled and kept overnight. It was then poured in water. The product formed was filtered, washed with water, dried and crystallised from rectified spirit to get (III).

IIIJ IR (cm^{-1}): 3464 ν(OH), 3349 ν(NH_2), 2925 ν(CH_2), 1230 ν(OCH_3), 588 ν(C—Cl). ^{1}H NMR: δ 3.85 (s, OCH_3), 6.7 (s, CH_2), 7–8 (m, 8H, ArH), 14 (s, OH). Mass m/z = 329.

(2) Preparation of 1-phenyl-3-(4,6-(sub)-diphenyl-5-6-dihydropyrimidine-2-yl) thiocarbamide (IV)

III (0.01 mol) was dissolved in dry benzene (50 mL) and phenyl isothiocyanate (0.01 mol) was added to it. The reaction mixture was refluxed for 1 h. It was allowed to cool when crystalline solid separated out. It was filtered, washed with benzene and crystallised from ethanol to get crystalline solid (IV).

IVJ IR (cm^{-1}): 3471 ν(OH), 3352 ν(—NH), 2930 ν(CH_2), 1644 ν(NH), 1050 ν(C=S), 748 (mono sub benzene), 589 ν(C—Cl). ^1H NMR: δ 3.85 (s, OCH_3), 6.7 (s, CH_2), 7–8 (m, 8H, ArH), 14 (s, OH). Mass m/z = 465.

Note: The NMR is similar to 2-amino dihydropyrimidine as the thiourea derivative seems to undergo cleavage during NMR determination.

Antimicrobial activity

The antimicrobial activity of some of the synthesised dihydropyrimidines and their thiocarbamide derivatives was determined by agar well technique. Various strains used for testing antimicrobial activitity were *Sal. typhi*, *E. coli*, *S. aureus*, and *P. aeruginosa*. Penicillin was used as standard for comparison. The tested compounds showed less activity than penicillin.

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REFERENCES

1. R.N. Goyal, R. Bhushan and A. Agarwal, *J. Indian Chem. Soc.*, **62,** 229 (1985).
2. B.R. Desai, S.R. Modi and H.B. Naik, *Orient J. Chem.*, **9,** 262 (1993).
3. C. Cheng, *Prog. Med. Chem.*, **6,** 67 (1969).
4. Fisher and Roeder, *Ber.*, **34,** 3751 (1901).
5. B.J. Ghiya and M.G. Marathey, *J. Indian Chem. Soc.*, **37,** 739 (1960).

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