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Synthesis and Characterization of Some New Uracil Derivatives and their Biological Activity

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ABSTRACT

This research includes the synthesis of thirty derivatives of uracil. Nucleophilic substitution reaction (thiol, alkylthio, hydrazino, thioacid,.. etc) of 4-chlorouracil afforded the corresponding derivatives. The 4-(2`-thiol-1` ,3`,4`-oxadiazole-5`-thiomethyl) uracil (12), ( N` - phenyl – 2` - thio -1` ,3`,4`-triazole-5`-methyl)-(2,6-dihydroxy-4-pyrimidinyl) sulphide (14) and 5-(2`,6`-dihydroxy-4`-pyrimidinyl thioacetamido)-1,3,4-thiadiazole-2-thiol (15), were synthesized by treatment of 4-thioacetichydrazide uracil (11) with carbon disulfide in the presence of a base or phenylisothiocyanate in the presence of base. Mannich bases of alkynyl thio derivativeis (3a & 10) were synthesized by the reaction of paraformaldehyde and secondary amine in the presence of CuCl ($19_{a,b}$ & $20_{a,b}$).

These compounds were characterized by spectroscopic methods (IR & UV), by their elemental analysis (C,H,N) and R_f values.

Biological activity of the synthesized compounds was determined.

Keywords: 4-chloro uracil, 2,6-dihydroxy-4-pyrimidinyl thioacetic acid, Biological activity.

INTRODUCTION

Pyrimidines are among those molecules that make life possible as being some of the building of nucleic acids (DNA & RNA)[1]. Pyrimidines are an interesting class of heterocycles which possess numerous biological and pharmacological effects. The pyrimidine ring system is found in many pharmaceuticals, herbicides and fungicides[2].

Various analogues of thiopyrimidines, aminothiopyrimidines, and hydroxy thiopyrimidines have been synthesized due to their interesting biological activities such as anti-bacterial, anti-fungal and anti-viral activities. They also showed significant chemotherapeutical activities[3].

In this paper, we report new results regarding a selective nucleophilic substitution reaction at 4-chlorouracil or by cyclization of the uracil derivatives to obtain new thirty derivatives of uracil by different routes. The resulting uracil derivatives were characterized by spectroscopic methods (IR

and UV), by their elemental analysis (C,H,N) and determination of R_f values by using two systems.

Finally, the biological activity of the synthesized compounds was determined using: Staphylococcus, Klebsiella sp, Candida, Escherichia coli, Pseudomonas, Streptococcus, Salmonella and Proteus.

EXPERIMENTAL

Melting points were determined on an electrothermal melting point apparatus. IR Spectra were recorded using the KBr disc on Unicam sp3-1000-spectrophotometer. The UV and visible absorption were determined in ethanol 95% using Hitachi U2000 spectrophotometer. Elemental analysis (C,H,N) were performed on an elemental analysis system. Chromatography paper chromatograms were developed by the ascending technique, the solvent system being: [Propanol (6) : conc. ammonium (3) ; water (1)], and [1-pentanol (5): acetic acid (2): water (3)]

4-Mercapto uracil (2)

The mixture of 4-chloro uracil (0.003 mol, 0.75gm) in ethanol (20ml), and thiourea (0.004 mol, 0.35gm) in ethanol (15ml), was refluxed for three hours with stirring. The excess of ethanol was removed, and then a concentrated solution of sodium carbonate in water was added; on cooling, the product was formed, recrystalized from aqueous ethanol yielded the compound (2) as yellow precipitate (Yield 70%, m.p. 235 $^{\circ}$C (decomp.). physical properties (Table 1).

4-Alkylthio Uracil (3a-c)

4-Mercaptouracil (0.001 mol, 0.144 gm), was dissolved in crushed ethanol (15ml), and crushed potassium hydroxide (0.001 mol, 0.04gm), was added to the solution, alkyl halide (0.001 mol) was added dropwise to the mixture which refluxed for two hours, the solution was acidified with hydrochloric acid until the product was obtained, filtered off and recrystalized from suitable solvent (Table 1).

Also the method was used for alkylation N^1, N^3 and SH of compound (2) by using three moles of alkyl halide, yielded the pyrimidine (3c) as yellow needles (yield 75%, m.p. 68-70 °C), Physical properties (Table 1).

4-Hydrazinouracil (4)

4-chlorouracil (0.005 mol, 1gm) was dissolved in methanol (95%) (15 ml), and hydrazine hydrate (0.005 mol, 0.35 gm) was added slowly with stirring to the solution, the whole was refluxed for three hours on steam bath. On cooling, the product was collected as a yellow precipitate, recrystallized from ethanol to give the compound (4). Physical properties (Table 1).

Schiff's Bases (5a-e)

Schiff's bases were prepared from (0.001 mol, 0.2gm) of compound (4) with aldehyde or ketone (0.001 mol) in ethanol (15ml). The resulting mixture was refluxed for three hours, and then cooled. The product was filtered off and recrystallized from ethanol, The Physical properties (Table 1).

Preparation of 4-(3',5'-Dioxo-2',3',4',5'-tetrahydropyrazol) uracil and 4-(3',5'-Dimethyl pyrazol) uracil (6,7).
A mixture of compound (4) (0.0015 mol, 0.21gm) and ethylmalonate or acetylacetone (0.0015 mol, 0.24 gm or 0.15 gm) was refluxed in dioxane (20ml) for five hours. The reaction mixture was allowed to cool, poured into cold water (60 ml). The solid product so produced was filtered off and recrystallized from ethanol to produce compound (6) and (7) respectively (yield 61%), Physical properties (Table 1).

2,6-Dihydroxy-4-pyrimidinylthioacetic acid (8)
Compound (1) (0.01 mol, 2gm) was dissolved in ethanol (15 ml), and a solution of mercaptoacetic acid (0.01 mol, 0.92 gm) in aqueous sodium hydroxide (10%) (10ml) was added gradually. The resulting mixture was refluxed for four hours, then cooled and acidified with concentrated hydrochloric acid until the yellow precipitate was formed, filtered off, dried and recrystallized from aqueous ethanol to obtain compound (8), Physical properties (Table 1).

Ethyl (2,6-Dihydroxy-4-pyrimidinyl) thioacetate & Propynyl (2,6-dihydroxy-4-pyrimidinyl) thioacetate (9,10)
The solution of compound (8) (0.005 mol, 1gm) in excess of thionyl chloride (10 ml), was refluxed gently on a water bath with stirring for three hours. The excess of thionyl chloride was removed under vacuum to give the corresponding acid chloride. Ethanol or propargayl alcohol was added (6 ml) and refluxed for two hours, the mixture was extracted with (10 ml) of benzene or chloroform, then (15 ml) of sodium carbonate solution, dried over anhydrous magnesium sulfate, filtered off and removed the solvent to give the compound (9) or (10) respectively, Physical properties (Table 1).

4-Thio acetic hydrazide Uracil (11)
The solution of compound (8) (0.002 mol, 0.4 gm) in thionyl chloride (6ml) was refluxed for three hours, and the excess of thionyl chloride was removed under vacuum to give acid chloride, pyridine (8ml) was added, then hydrazine hydrate (1ml) added dropwise to the mixture with cooling and stirring, left the stirring overnight at room temperature. The mixture was refluxed for two hours at 80 °C, and then cooled, the excess of pyridine was removed under vacuum, and the hydrazine derivative (11) was obtained, physical properties (Table 1).

4-(2`-Thio-1`,3`,4`-oxadiazol-5`-thiomethyl) Uracil (12)
Hydrazide compound (11) (0.01 mol, 1.8 gm) was dissolved in ethanol 95% (50 ml), sodium carbonate (0.01 mol) was added in (1 ml) of water. After a solution was occurred slightly then carbon disulphide (0.01 mol, 0.76 gm) was added and the mixture refluxed for three hours, after the mixture was concentrated by evaporating the excess of ethanol under vacuum to a small volume. A precipitate was obtained by adding the solution to ice containing hydrochloric acid, the solid was filtered off and dried, recrystallized from benzene yielded compound (12) (yield 45%, m.p. 225°C decomp.), physical properties (Table 1).

1-(4`-Uracil thioacetyl)-4-phenylthiosemicarazide (13)
To a solution of compound (11) (0.01 mol, 1.8 gm) in ethanol (30 ml), phenylisothiocyanate (0.01 mol, 0.27 gm) was added, and the reaction mixture was refluxed for one hour, the excess of the solvent was removed under vacuum. The product was extracted with ethylacetate and dried over anhydrous sodium sulphate to give compound (13) as oil in a good yield.

N'-Phenyl-2'-thio-1',3',4'-triazole-5-methyl-(2,6-dihydroxy-4-pyrimidyl) sulphide (14)
The mixture of compound (13) (0.015 mol, 3.53 gm) in 2N sodium hydroxide (20 ml) was refluxed for three hours, cooled and acidified with hydrochloric acid (10%) to give the compound (14), recrystallized from ethanol (yield 80%, m.p. 178-181 °C), (Table 1).

5-[2',6'-Dihydroxy-4-pyrimidinyl thioacetamido]-1,3,4-thiadiazol-2-thiol (15)
A solution of compound (8) (0.005 mol, 1 gm) in excess of thionyl chloride (8 ml) was heated under reflux on water bath with stirring for three hours, then the excess of thionyl chloride was removed under vacuum to give the acid chloride derivative. Then a solution of 5-Amino-1,3,4-thiadiazole-2-thiol (0.011 mol, 1.33 gm) in tetrahydrofuran, (50 ml) and triethyl amine (0.015 mol, 0.15 gm) was added, the resulting mixture was refluxed with stirring for four hours. Filtered off and the filtrate was concentrated to a small volume by evaporating the excess of the solvent, acidified with concentrated hydrochloric acid to give the precipitate which was filtered off and recrystallized from ethanol, physical properties (Table 1).

General procedure for preparation of compounds (16,17 & 18)
A solution of compound (12 or 14 or 15) (0.001 mol, 2.02 gm) and tri ethyl amine (0.01 mol, 1.091 gm) in ethanol (50 ml), was heated slightly, and alkyl halide (propargyl bromide, benzyl bromide or 2,4-dinitrochloro benzene) (0.01 mol, 1.19 gm) was added, the heating was continous for four hours. Cooled, the precipitate was formed after addition of ice-water, filtered off and recrystallized from ethanol, physical properties (Table 1).

General procedure for preparation of Mannich bases compounds (19 & 20)
The mixture of acetylenic derivative (3a or 10) (0.002 mol) and paraformaldehyde (0.002 mol, 0.06 gm) in isopropyl alcohol (15 ml) was heated slightly, cuprous chloride (0.07 gm) was added and appropriate secondary amine(diethyl amine, dicyclohexyl amine or morphine) (0.002 mol) was added, the resulting mixture was refluxed for three hours then filtered off. The filtrate was poured onto crushed ice and extracted by chloroform, dried over anhydrous magnesium sulphate, filtered and the solvent was removed to obtain the product (19 & 20) physical properties (Table 1), (Scheme 3).

Table (1): Physical properties, yield, molecular formula and elemental analysis of the synthesized compounds.

Co. No	Molecular weight & Molecular Formula	Yield %	m.p. °C	Crystallization solvent	colour	C,H,N C/(F)
1	($C_4H_3N_2O_2Cl$) 146.53	90	300 dec.	EtOH+H_2O	White	
2	($C_4H_4N_2O_2S$) 144.15	70	235 dec.	EtOH+H_2O	Yellow	
3a	($C_7H_6N_2O_2S$) 182.20	41	oil	Benzene	Red	46.15 (46.03) 3.29 (3.16) 15.38 (13.01)
3b	($C_{10}H_5N_3O_3Cl_2$) 318.14	60	150 dec.	EtOH	Red	37.7 (37.29) 1.57 (1.14) 13.20 (13.01)
3c	($C_{22}H_{10}N_8O_{14}S$) 642.43	75	68-70	EtOH	Yellow	
4	($C_4H_6N_4O_2$) 142.12	51	270 dec.	EtOH	White	
5a	($C_9H_8N_4O_3$) 220.18	80	240 dec.	EtOH	Brown	
5b	($C_{11}H_{10}N_4O_3$) 246.22	75	231 dec.	EtOH	Orange	
5c	(C12H9N5O3) 271	80	188-190	EtOH	Red	53.13 (53.02) 3.32 (3.21) 25.83 (25.24)
5d	($C_9H_{12}N_4O_2$) 208	75	115-118	EtOH	Red	
5e	($C_{14}H_{10}N_4O_3$) 282	60	150 dec.	EtOH	Black	
6	(C7H6N4O4) 210	60	120 dec.	Chloroform	Gray	40.0 (39.25) 2.85 (2.54) 26.6 (26.13)
7	($C_9H_{10}N_4O_2$) 206	60	110 dec.	Benzene	Gray	
8	(C6H6N2O4S) 202	85	190 dec.	EtOH	Yellow	35.64 (35.12) 2.97 (2.53) 13.86 (13.49)
9	($C_8H_{10}N_2O_4S$) 230	80	>300 dec.	EtOH	Brown	
10	(C9H8N2O4S) 240	40	oil	chloroform	Brown	45.0 (44.64) 3.33 (3.06) 11.6 (11.19)
11	(C6H8N4O3S) 188	60	Oil	chloroform	Red	33.33 (33.01) 3.7 (3.21) 25.9 (25.34)
12	(C7H6N4O3S2) 260	45	225 dec.	Benzene	Yellow	32.5 (32.21) 2.32 (2.16) 21.7 (21.36)
13	($C_{13}H_{13}N_5O_3S_2$) 353	90	150 dec.	EtOH	Brown	
14	(C13H11N5O2S2)333	80	179-181	EtOH	Green	46.84 (46.42) 3.30 (3.12) 21.02 (20.89)
15	(C8H7O3N5S3) 317	82	Oil	Chloroform	Black	30.6 (30.26) 2.18 (2.03) 20.43 (20.13)
16a	($C_{14}H_{12}N_4O_3S_2$)348	62	290 dec.	Methanol	Yellow	
16b	($C_{13}H_8N_6O_7S_2$)424	66	210 dec.	Methanol	Yellow	
17	($C_{16}H_{13}N_5O_2S_2$)371	60	Oil	EtOH	Brown	
18	($C_{11}H_9N_5O_3S_3$)335	50	Oil	Chloroform	Black	
19a	($C_{10}H_{13}N_3O_2S$)239	40	Oil	Benzene	Red	
19b	($C_{12}H_{15}N_3O_3S$)281	50	Oil	Chloroform	Dark brown	
20a	($C_{12}H_{15}N_3O_4S$)297	40	Oil	Chloroform		
20b	($C_{22}H_{31}N_3O_4S$)433.5	42	Oil	Benzene		

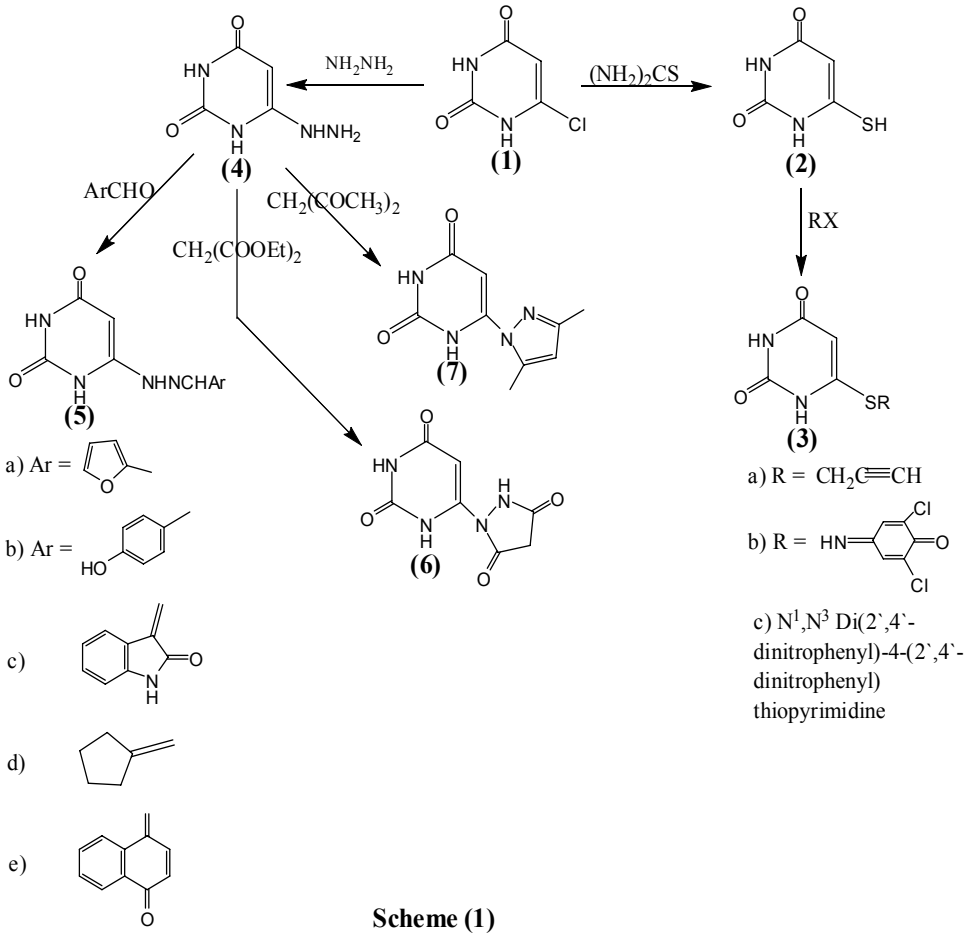
Table (2): Spectral data for synthesized compounds (IR cm^{-1}), (λ nm).

Co. No.	γ - OH	γ N-H	γ C=N	γ C=O	γ C=C arom	γ C-H aliph.	γ C-S	γ other	λ max EtOH (95%), 10^{-3}			
1	3600	3350	1640	1710	1590	--	--	γ C-Cl 760	247	303	354	
2	3620	3250	1650	1710	1500	--	780	γ S-H 2250	255	280	370	
3a	3500	3200	1600	1700	1500	2850	780	γ C≡CH 3200-3250	244	295	303	372
3b									246	372	383	
3c									245	260	280	372
4	3650	3350	1650	1700	1570	--	--	γ NH_2 3365	344	371	454	
5a	3510	3250	1650	1640	1620	2850	--	γ C-O 1150	245	319	372	381
5b	3600	3200	1680	1710	1550	--	--	γ C-H Ar 3100				
5c	3600	3220	1600	1700	1600	--	--	C-H Ar 3100	244	267	374	413
5d	3600	3200	1600	1700	--	2850	--	--				
5e									242	373	382	419
6									241	299	333	373
7									243	267	323	372
8									244	304	354	371
9									240	300	349	370
10	3500	3200	1600	1710	1550	2850 , 2900	790	γ C≡C 2100, C≡CH 3250	210	250	272	371
11									242	310	340	371
12	3600	3200	1620	1690	1600	2950	780	C-O-C 1100, SH 2250	244	267	310	329
13									246	300	312	372
14	3500	3150	1600	1610	1550	2900	780	γ C-H Ar 3100, SH 2250	246	325	372	383
15	3600	3200	1600	1700	1500	2850	780	γ C=OAmide 1680	244	268	300	370
16a	3600	3150	1600	1650	1610	2850	780	γ C-O-C 1150 CH Ar 3000	245	260	320	340
16b	3600	3150	1600	1680	1600	2900	780	γ c-o-c 1150, NO_2 1560				
17	3600	3200	1610	1640	1550	2880	780	γ C≡C 2150, C-H 3000, C≡CH 3500	245	267	311	373
18	3500	3150	1620	1720	1490	2900	780	γ C≡C 2100	246	250	312	371
19a									209	242	269	
19b									208	244	301	389
20a									210	250	272	371
20b									215	248	280	370

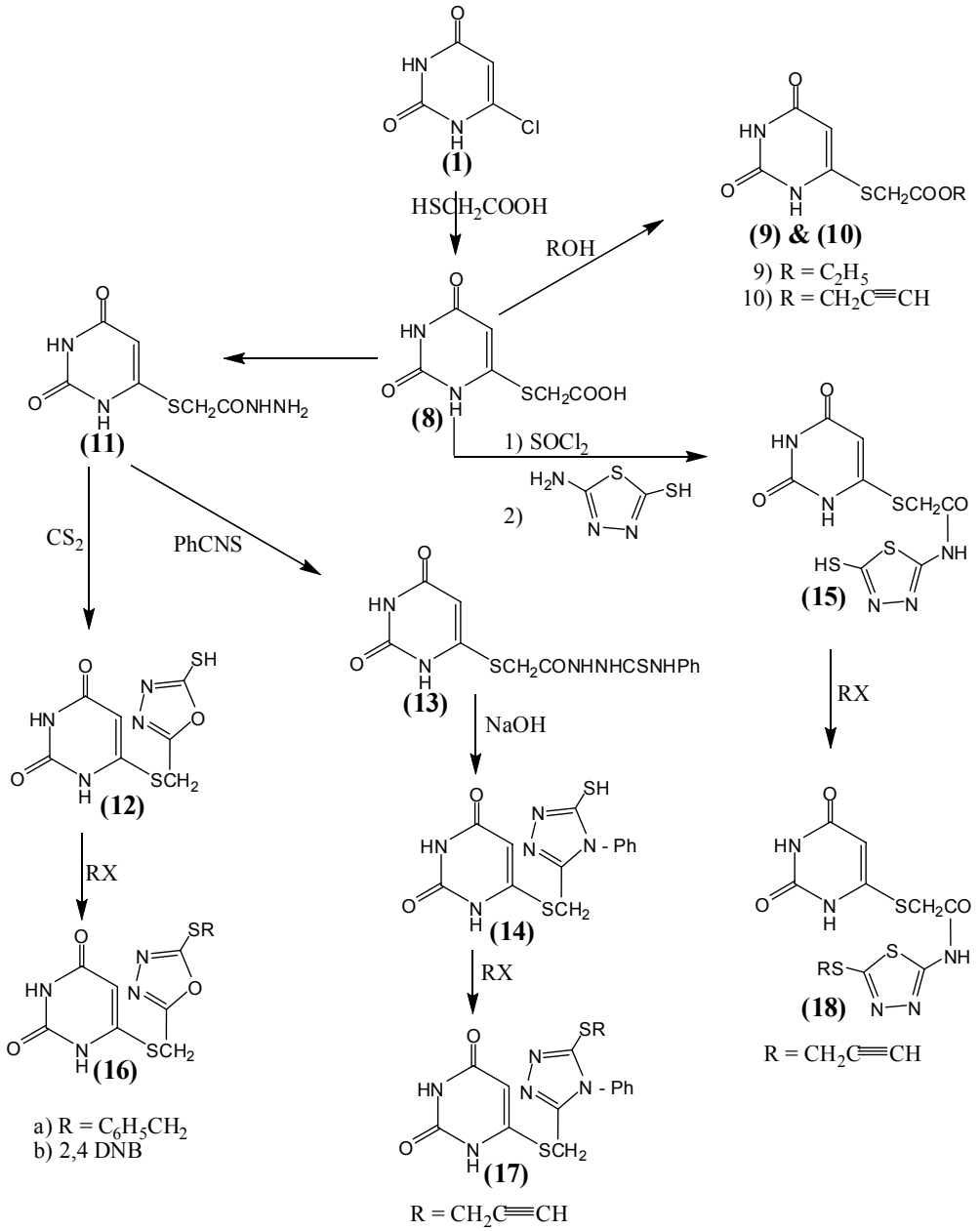
Table (3): Chromatographic behaviour of the synthesized compounds.

Compound No.	R_f value in system (1)	R_f value in system (2)
1	0.68	0.67
2	0.73	0.75
3a	0.45	0.59
3c	0.54	0.5
4	0.57	0.49
5a	0.56	0.57
5b	0.58	0.60
5c	0.59	0.67
6	0.98	0.92
7	0.95	0.89
8	0.41	0.46
9	0.32	0.35
10	0.73	0.70
11	0.51	0.47
12	0.44	0.41
13	0.31	0.36
14	0.45	0.42
15	0.97	0.99
16a	0.40	0.37
16b	0.38	0.35
17	0.82	0.85
18	0.42	0.45
19a	0.79	0.61
19b	0.66	0.58
20a	0.73	0.70
20b	0.60	0.62

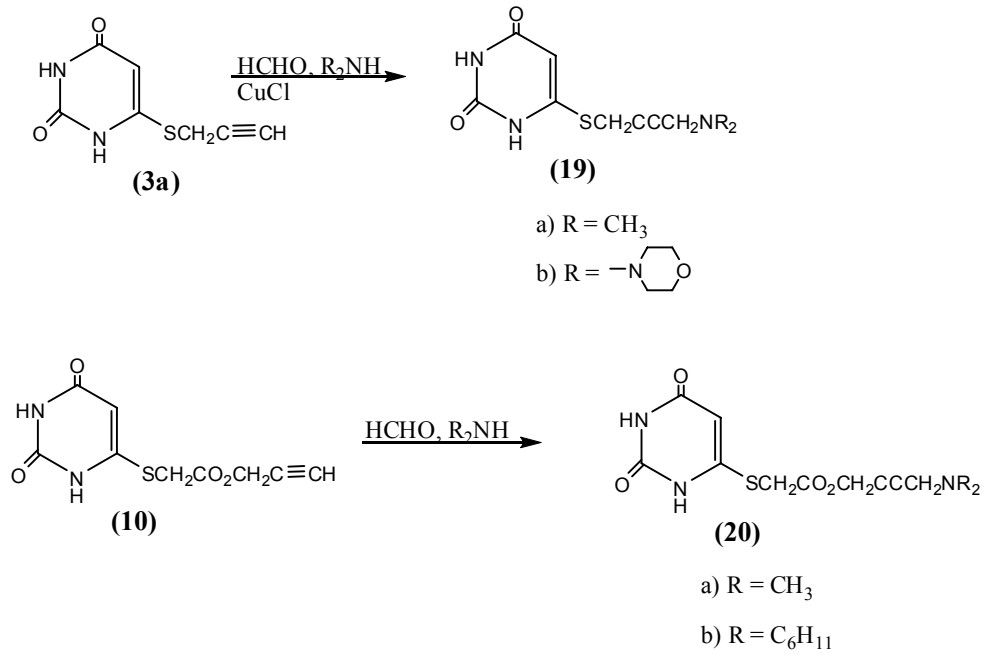
System (1) : Water : ammonia : propanol (1 : 3 : 6)
System (2) : Water : acetic acid : 1-pentanol (3 : 2 : 6)


NH2NH2
(NH2)2CS
ArCHO
CH2(COCH3)2
CH2(COOEt)2
RX
(1)
(2)
(3)
(4)
(5)
(6)
(7)
a) Ar =
b) Ar =
c)
d)
e)
a) R = CH2C≡CH
b) R =
c) N1,N3 Di(2`,4`-dinitrophenyl)-4-(2`,4`-dinitrophenyl) thiopyrimidine

Scheme (1)


(1)
HSCH2COOH
ROH
(9) & (10)
9) R = C2H5
10) R = CH2C≡CH
(8)
(11)
1) SOCl2
2)
CS2
PhCNS
(15)
(13)
NaOH
RX
(12)
(14)
(18)
R = CH2C≡CH
(16)
a) R = C6H5CH2
b) 2,4 DNB
(17)
R = CH2C≡CH

Scheme (2)



Scheme (3)

RESULTS AND DISCUSSION

The anti-bacterial, anti-viral and anti-cancer activities of various thio, amino and hydroxy pyrimidines have been studied by many workers. In addition, various fused pyrimidines have been reported[4].

The present work describes the synthesis of some new 4-substituted uracil and also the synthesis of its triazole, oxadiazole and thiadiazole derivatives.

The chloropyrimidines are of a great preparative importance. Thus, 4-chlorouracil[5] was used as starting material, and the replacement of an active chlorine atom in position (4) of uracil by nucleophilic groups (mercapto, thioalkyl, hydrazino, thioacid,…. Etc.) is normally a convenient rout to obtain 4-substituted uracil derivatives[6].

As shown in scheme 1 heating under reflux a solution of 4-chlorouracil (1) in ethanol with thiourea yield the corresponding 4-mercaptouracil (2)[7]. Its structure was confirmed by physical properties (Table 1), IR spectrum & UV spectrum (Table 2), showed the presence of SH- group stretching (2250-2650 cm^{-1}) and the absence of the stretching band at (760 cm^{-1}) due to C-Cl and R_f values (Table 3).

Thiols behaved as strong nucleophile, therefore undergo the alkylation easily with alkyl halides as SN^2 mechanism to give the corresponding sulphides[8,9]. Alkylation of compound (2) with equivalent amount of alkyl halides in potassium hydroxide, while cooling, the mixture after acidification yielded the corresponding 4-alkyl thiouracil (3), but, using propagyl bromide in the presence of triethyl amine in ethanol resulted in the formation of 4-

alkynyl thiouracil (3a). The structure was confirmed by physical properties & C,H,N (table 1) and the IR spectrum (Table 2) showed the presence of ($\equiv CH$) stretching absorption at (3200 cm^{-1}) and ($C \equiv C$) weak stretching absorption at (2100 cm^{-1}) also disappearance of stretching band at (2550 – 2650 cm^{-1}) due to SH group, the UV spectrum (Table 2) and R_f values (Table 3), also the structure of (3_b) was confirmed by physical properties & C,H,N (Table 1), spectral data (Table 2) and R_f values (Table 3).

Treatment of compound (2) with three moles (excess) of 2,4-dinitrochlorobenzene as active aryl halide lead to the formation of the corresponding N^1,N^3-di(2,4-dinitrophenyl)-4-(2',4'-dinitrophenyl thio) pyrimidine (3c) physical properties (Table 1). IR spectrum, UV spectrum (Table 2) and R_f values (Table 3) of compound (3a-c) are in agreement with assigned structures, (c.f. Experimental and Scheme 1).

The 4-hydrazino uracil (4) was obtained by refluxing compound (1) with equimolar of hydrazine hydarate in ethanolic solution. The structure of compound (4) was identified by IR & UV (Table 2) and R_f values (Table 3). While the reaction of compound (4) with equimolar of selected aromatic or heterocyclic aldehydes or ketone (α-furfural, p-hydroxy benzaldehyde, Isatin, cyclopentanone and 1,4-benzoquinone) in ethanol afforded the corresponding Schiff`s bases (5a-e) and their structures were confirmed by physical properties, C,H,N (Table 1) spectra data (Table 2) and R_f values (Table 3).

Recently, there has been a great deal of interest in the synthesis of Uracil derivatives possessing various functional groups by cyclization or by substitution reactions. Refluxing compound (4) with dicarbonyl derivatives (diethylmalonate or acetyl acetone) in dioxane yielded the corresponding compounds (6 and 7) respectively, which have a new ring system[10]. The spectroscopic data is in agreement with the signed structures 6 & 7 physical properties and C,H,N (c.f. Experimental and Scheme 1)

Uracil thiocarboxylic acid and their esters can be synthesized by nucleophilic attack to 4-chlorouracil with a mercaptoacetic acid in alkaline solution by using potassium hydroxide in ethanol and refluxing for four hours to give the thio acid (8). Its structure was confirmed by physical properties C,H,N (Table 1), IR & UV spectra (Table 2) and R_f values (Table 3), (Scheme 2)

The importance of synthesizing new acetylenic ester arises from their potential biological activity. Uracil thio acid (8) was treated with thionyl chloride to the corresponding acid chloride which was the reactive reactant in the synthesis of esters (9 &10) or the acid hydrazide (11) by using ethanol or propargyl alcohol or hydrazine hydrate, their physical properties and C,H,N (Table 1) and spectra data (Table 2) and R_f values (Table 3).

Treatment of the approprative acid hydrazide derivative (11) with carbon disulphide in alkaline medium caused cyclization by internucleophilic attack to give the corresponding oxadiazole derivatives (12)[11]. The structure was identified by physical properties C,H,N (Table 1) and spectra data (Table 2) and R_f values (Table 3). While the refluxing of the acid hydrazide (11) with phenylisothiocyanate in ethanol gave the compound (13) and the cyclization was occurred in alkaline solution (2N-NaOH) to give the triazole derivative (14), also the structure was confirmed, physical properties, C,H,N (Table 1), spectra data (Table 2) and R_f values (Table 3).

But the thiadiazole derivatives (16) was synthesized[12] by refluxing the acid chloride derivative of uracil (8) with 2-amino-3H-1,2,4-thiadiazole-2-thiol (15) in the presence of triethyl amine in tetrahydrofuran (THF) for four hours to give the compound (16), its

structure was confirmed by physical properties C,H,N (Table 1), spectra data (Table 2) and R_f values (Table 3).

The alkylation of compounds (12,14,15) with an equivalent amount of halide (2,4-dinitro chloro benzene, benzyl chloride and propargyl) in the presence of triethyl amine in ethanol resulted the compounds ($16_{a,b}$, 17,18). The structure were identified by physical properties (Table 1), spectra data (Table 2) showed the presence of C-S-C stretching absorption band at 780 cm^{-1} and disappearance of the stretching band of 2250-2660 cm^{-1} due to SH group.

Consequently the alkynyl derivatives (3_a, 10) which were heated under reflux with paraformaldehyde, appropriate secondary amine (N,N-dimethyl amine, morpholine and N,N-dicyclohexylamine) and catalytic amount of cuprous chloride to increase the nucleophilicity of acetylenic linkage in the isopropyl alcohol were used as solvent to give the corresponding Mannich bases ($19_{a,b}$ and $20_{a,b}$), (Scheme 3) the structures were confirmed by physical properties (Table 1); spectra data (Table 2) showed the presence of $-CH_2-$ stretching absorption band at 2850-2900 cm^{-1} and disappearance of the stretching band at 3300 cm^{-1} due to $C\equiv C$-H and R_f values (Table 3).

Finally, the antimicrobial activity of the synthesized compounds were tested in vitro against eight species of bacterio (Escherichia coli, proteus, sp, Salmonella, SPP, Pseudomonas aeruginosa, Strepto coccus, Klebsiella SP, Staphylococcus, and Candida albieans) by using agar diffusion method[13,14.15]. The results are shown in the following Table 4.

Table (4): Effects of some new compounds on the growth of bacteria (zone of inhibition in mm.).

Co. No.	E. Coli	Prolcus SP	Salmonella	Pseud.	stre	kleb	Staphylo	Candida
2	-	-	-	-	-	++	-	+
3b	+++++	++++	+++	+++++	+++++	+	-	-
3c	++++	++++	++++	++	++++	-	-	-
5c	+++++	++	+++++	++++	+++++	++++	++	+
7	-	-	-	-	-	+++	-	+
8	+++++	++	++	++	++	-	-	-
9a	-	-	-	-	-	++	±	±
11	++	+++	+++	++++	+++++	-	-	-
12	++	++	++	±	+	+++	-	-
13	+	++	++	++	++++	++++	++	±
14	++	+	+++	+	+	++	-	-
15	-	-	±	-	-	-	-	±
16a	±	+	-	-	-	++	-	-
17	++	+++	+	+	++	+++	-	±
18	-	+++	++	-	+	++	-	-

0-3 mm 2(-) , 6-9 mm (±), 10-14 mm = +, 15-18 mm =(++),19-21 mm =(+++),
22-28 mm =(++++), and 29-35 mm =(+++++)

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تحضير وتشخيص بعض مستشقات اليوراسيل الجديدة وفعاليتها البيولوجيه

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ملخص:

في هذا البحث تم تحضير وتشخيص حوالي ثلاثين مشتق جديد لليوراسيل ومنها:
تفاعلات الاستبدال النيوكليوفيلية (ثيول، ثيوالكيل، هيدرازينو، حامض ثيوخليك) للمركب 4-كلورو يوراسيل تعطي المشتقات المقابله (2، 3$_{c-a}$، 4، 5$_{e-a}$، 6، 7، 8)، وكذلك المركبات 4-(˝2-ثايول-1`،3`،4`- اوكسادايازول-5'-ثايومثيل) يوراسيل(12) وكبريتيد(ن'-فينيل-2'-ثايول- 1`،3`،4`- ثرايازول –5`- مثيل) (6,2- ثنائي هيدروكسيل - ˝4- بريميديل) 14 وايضا 5-(˝6،˝2- ثنائي هيدروكسيل-˝4- بريميديل ثايواسيتاميد)-4,3,1– ثايوديازول -2- ثايول (15)، ثم تحضيرها بمعاملة المشتق4- ثايوخليك هيدرازيد يوراسيل (11) مع ثاني كبريتيد الكاربون او فنيل ايزوسيانات بوجود القاعدة.
تم تحضير قواعد مانيخ (19$_{a}$ و $_{b}$) و (20$_{b}$ ،$_{a}$) للمشتقات الاستيلينية (3$_{a}$ و 10).
اثبتت الصيغ التركيبية لهذه المركبات باستخدام الاجهزه الطيفيه (IR, UV) والتحليل الدقيق للعناصر (C,H,N) وقياس قيم R_f، ثم تم تعيين فعاليتها البيولوجية.