Synthesis and characterization of some New 2- and 6- substituted of 5- Acetyl - 4- (P- phenyl) Pyrimidine and substituted thieno [2, 3- d] Pyrimidine

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Abstract

The series of new pyrimidines derivatives 2- and 6- Substituted of 5 - Acetyl - 4 - (P- phenyl) Pyrimidine and Substituted thieno [2, 3- d] Pyrimidine are synthesis by the reaction between some substituted of benzaldehydes with ethyl aceto acetate in the present of ethanol as a solvent to give the products (3e-h), when react alkyl halide with (3e-h) in ethanol obtain new Pyrimidine derivatives (4e-h) heating them with phosphorous oxy chloride in dioxane to form (5e-h) which reacts with thiourea in ethanol to produce (6e-h) these compounds reacting with chloro acetic acid to form new Substituted thieno [2,3-d] Pyrimidine (8e-h).

All the synthesized compounds of new pyrimidines derivatives are identified by the physical properties by it's melting points, colors and the yields are characterized by the elemental (CHN) analysis, IR, UV Spectrum

Key words: Ethyl aceto acetate, substituted of benzaldehydes, new pyrimidines derivatives, IR, UV Spectrum.

Introduction:

The Pyrimidines derivatives are an interesting class of heterocycles which possess acyclic structure with two Nitrogen atoms in the ring and numerous biological, pharmacological effects[(1)]. Most of the sugar, vitamins. alkaloids, which are Nitrogenous bases occurring in many antibiotics,such as pencillin, are the Pyrimidines derivatives[(21)], anticancer[(18)], anti schizophrenia [(7)] ,and antihypertensive [(13)] activity anti viral[(14)], anti titumer[(3)],anti inflammatory [(17)], anti microbial [(20)]and anti fungal[(2)] anti histaminic [(19)] ,and analgesic, malaria, Alzheimers disease, Parkinson's diseas, [(5)] and anti oxidant properties [(6)]. Pyrimidine nucleus occurs in a wide range of compounds having biologic activity and the majority of thieno[2, 3- d]pyrimidine have been synthesied from thiophenes [(8, 9)] and, therefore, it was decided to synthesise some new pyrimidines derivatives ,The pyrimidines ring is fused to various heterocyclic, such as : (purines) in nucleic acids, pyrrolo pyrimidines, pyrido pyrimidines, pteridines. quinazolines, tri azolo Pyrimidines, pyrazolopyrimidines and furopyrimidines)which are agro chemicals, and veterinary products [(4, 15 ,16)] ; fused pyrimidines continues to attract considerable attention because of their great practical usefulness, primarily, due to a very wide spectrumof biological activity[(12)] Thienopyrimidines occupy a special position among these compounds, along with some other pyrimidines systems co ntaining an annulated fiven- membered heterocyclic ring. Thienopyrimidines are structural analogs of biogenic purines and can be considerable as potential nucleic acid anti metabolites[(10)] Aromatic and heteroaromatic compounds, bearing an O-aminoester group, are useful substrates for the preparation of various condensed pyrimidines heterocyclic system[(11)].

Aim of the Study:

Synthesis and Characterization of Some New **2-** and 6-were Substituted of **5** - Acetyl **- 4** - (P-phenyl) Pyrimidine as well as thieno **[2, 3- d]** Pyrimidine.

Materials and Methods:

All melting points were measured in Celsius degrees on an electrothermal 9100 melting point apparatus . Fourier Transform Infrared spectra for synthesized compounds were recorded using the KBr disc technique on A JASCO 440 FTIR spectrophotometer. The elementals (CHN) analysis were performed using an Exeter CE -440 elemental analyzer and the UV spectrum was recorded on a shimadzu mini -1240 spectrophotometer .

The general procedures for preparation:

Method I: Preparation of Compounds (3e-h)

A mixture of substituted aldehydes (0.01mole) ethyl aceto acetate (0.01mole) thiourea (0.01mole) and potassium carbonate (0.01mole)in ethanol was heated under reflux for 6hrs .The solid precipitated during the reaction was collected by adding stirred water acidified with acetic acid .The deposited precipitate was collected, washed with water and recrystallized from ethanol to give the products[(22)]

Method II: Preparation of Compounds (4e-h)

A mixture of (3e-h) (0.01mole) alkyl halide or alkenyl halide and potassium carbonate(0.01mole) in ethanol 40ml was heated under reflux for 5hrs ,allowed to cool and diluted with water. the solid product was filtered off and recrystallized from ethanol [(22)]

Method III : Preparation of Compounds (5e-h)

A solution of (4e-h) 0.01mole in dioxane 40ml was heated with phosphorous oxy chloride 20ml. under reflux for 4hrs .The reaction mixture was cooled and poured in to ice water and the solid formed was collected dried and recrystallized from chloroform or ethanol [(22)]

Method IV: Preparation of Compounds (6e-h)

Amixture of (5e-h) 0.01mole and thiourea 0.01mole in ethanol was heated under reflux for 6hrs .The reaction mixture was left to cool ,the solid formed was filtered and recrystallized from ethanol to give the products [(22)]

Method V: Preparation of Compounds (8e-h)

A mixture of compounds (6e-d) 0.01mole ,chloro acetic acid 0.01mole and sodium ethoxide (0.012mole) in ethanol 30ml was heated under refluxed for 3hrs . The reaction mixture allowed to cool and then was filtered off and recrystallized from ethanol or chloroform to give the products[(22)].

Results:

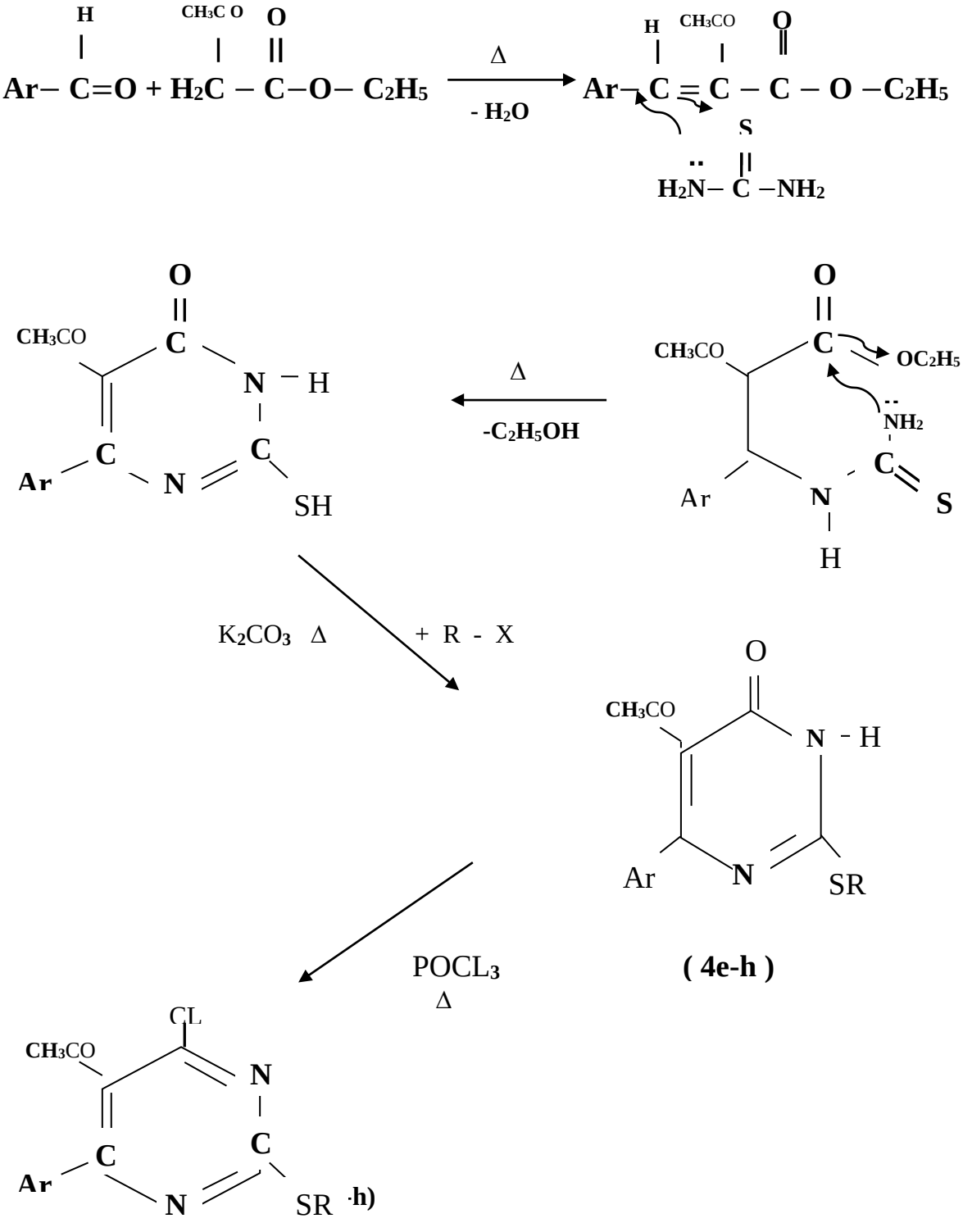
The pyrimidines derivatives(3e-h) were synthesized by the reaction between a substituted benzaldehydes (1e-h) with ethyl aceto acetate and potassium carbonate in the present of ethanol as a solvent to give the intermediate compounds and the cyclo condensation of compounds (2e-h) with thiourea in ethanol yield the products compounds (3e-h). The pyrimidines derivatives (3e-h) were identified by it's melting points (234-235°C),(242-243°C),(168. 2°C), 304°C decompose corresponding, while the yields of these compounds are : 46.96%, 60.13%, 64.24 %, 61.86% . The synthetic pathway of the products are shown in Scheme (I)

The Substituted thieno [2, 3- d] Pyrimidine (8e-h) were identified by it's melting points (245-246°C), (250-251°C) ,(274-275°C), (289-290°C) corresponding, while the yields of these compounds are: 71%, 65%, 77%, 70% .The synthetic pathway of the products are shown in Scheme (II).

Table(1): Physical properties for the synthesized Compounds (3e- h) and (8.e-h)

Compounds NO	Ar	M.Formula M.weight g/mole	Yield % color	M.P C°	C/F				
					C%	H%	N%	O% F%	S% CL%
3e	C_6H_5F	$C_{12}H_9N_2SO_2F$ 263	46.96 white	234-235	54.75 54.70	3.42 3.40	10.64 10.60	12.11 12.10 7.22 7.20	12.16 12.10 - -
3f	$C_6H_5NO_2$	$C_{12}H_9N_3SO_4$ 291	60.13 white	242-243	49.48 49.42	3.09 3.07	14.43 14.40	21.99 21.90	10.99 10.80
3g	$C_6H_5N(CH_3)_2$	$C_{14}H_{15}N_3SO_2$ 289	64.24 white	168.2	53.87 53.82	2.85 2.83	17.10 17.11	13.06 13.04	13.06 13.04
3h	C_6H_5CL	$C_{12}H_{11}N_2SOCL$ 266.5	61.86 white	304 decompose	54.03 54.10	4.12 4.10	10.50 10.55	6.003 6.004 - -	12.007 12.006 13.32 13.30
8e	C_6H_5F	$C_{15}H_{11}O_2N_2S_2F$ 334	71 white	245-246	53.89 53.80	3.29 3.30	8.38 8.32	9.58 9.50 5.68 5.60	19.16 19.18 -
8f	$C_6H_5NO_2$	$C_{15}H_{11}O_4N_3S_2$ 329	65 White	250-251	54.71 54.65	3.34 3.30	12.76 12.70	19.45 19.44 -	19.45 19.40
8g	$C_6H_5N(CH_3)_2$	$C_{17}H_{17}O_2N_3S_2$ 359	77 White	274-275	56.82 56.80	4.73 4.70	11.69 11.60	8.91 8.90 -	17.82 17.80 -
8h	C_6H_5CL	$C_{15}H_{11}O_2N_2S_2CL$ 350.5	70 White	289-290	51.35 51.33	3.13 3.10	7.98 7.90	9.12 9.10 -	18.25 18.20 10.12 10.10

(Scheme -I-)


Ar– C=O + H2C – C–O– C2H5
Δ
- H2O
Ar–C ≡ C – C – O –C2H5
H2N– C –NH2
CH3CO
OC2H5
NH2
Ar
SH
K2CO3 Δ
+ R - X
POCL3
Δ
(4e-h)
CL
SR

Scheme(II)

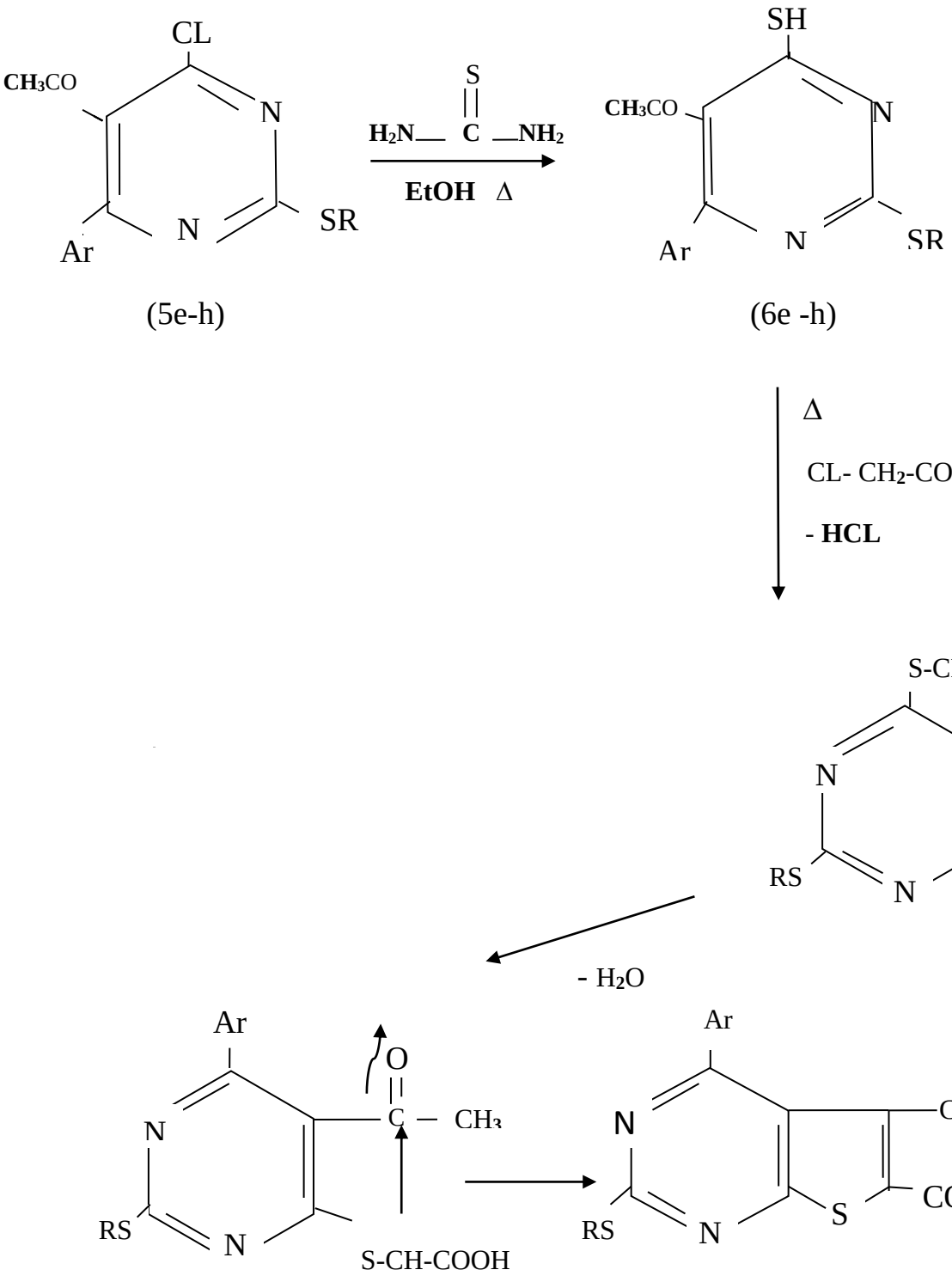

CL
CH3CO
N
N
SR
Ar
S
H2N C NH2
EtOH Δ
SH
CH3CO
N
N
SR
Ar
(5e-h)
(6e -h)
Δ
CL- CH2-COOH
- HCL
S-CH2-COOH
COCH3
N
RS
N
Ar
- H2O
Ar
O
C
CH3
N
RS
N
S-CH-COOH
Ar
CH3
N
RS
N
S
COOH

Table (2) : The **structure** and the **IUPAC** name of the chemical substituent's

Compounds NO	The structure of the substituent's	the IUPAC name of the substituent's	R
1e	P- F-C_6H_5-CHO	Para -floro benzaldehyde	-
1f	P-NO_2-C_6H_5 -CHO	Para -nitro benzaldehyde	-
1g	P- N.N $(CH_3)_2$ -C_6H_5-CHO	Para - N, N di methyl benzaldehyde	-
1h	m -CL-C_6H_5-CHO	Meta chloro benzaldehyde	-
3e	P- F -C_6H_5	Para -floro phenyl	-
3f	p - NO_2 - C_6H_5	Para -nitro phenyl	-
3g	P- N, N $(CH_3)_2$ - C_6H_5	Para - N, N di methyl phenyl	-
3h	m - CL - C_6H_5	Para -chloro phenyl	-
(4e-8e)	CH_3- cl	Chloro methane	CH_3-
(4f-8f)	CH_3- cl	Chloro methane	CH_3-
(4g-8g)	CH_3 - CH_2 -cl	Chloro ethane	CH_3 - CH_2 -
(4h-8h)	CH_2 =CH - CH_2 - cl	Chloro propane	**CH_2 =CH- CH_2-**

FTIR Analysis of compounds (3e - h) :

The IR spectrum of compounds (3e -h) showed characteristic absorptions bands at (3447 - 3112) cm^{-1} for (-NH) stretching bands, the main absorptions bands are observed at (1672-1637) cm^{-1} for (C = N), but showed (C= C) stretching vibration band (1561- 1422) cm^{-1} and the appearanced a strong bands at (1705- 1680) cm^{-1} of (C= O) pyrimidinone , appearanced band observed the substituted benzene ring at (3087- 3004) cm^{-1} scribed to the stretching aromatic(C-H) .The bands were observed at (2947- 2861) cm^{-1} for the(C- H) aliphatic and strong band (C= S) at (1250 - 1110) cm^{-1}**,** the appearanced a strong bands at (1169) cm^{-1} for Fluoride, while appearance a strong band at (1554) cm^{-1} for Nitro group and the absorptions band for chloride at(1087) cm^{-1}**. T**he selected FTIR data are listed in Table (3)

FTIR Analysis of compounds (8e-h) :

The IR spectrum of compounds (8e -h) showed characteristic absorptions bands at (1630-1670) cm^{-1} for (C = N), but showed (C= C) stretching vibration band at (1550-1590) cm^{-1} and appearance bands observed the substituted benzene ring at (3002-3150) cm^{-1} scribed to the stretching aromatic(C-H) and the bands observed at (2856-2990) cm^{-1} for the(C- H) aliphatic and strong band (CS) at (890 - 980) cm^{-1} while the strong band observed for(COOH) at (3450-3500) cm^{-1}. The selected FTIR data are listed in Table (3)

Table (3): The FTIR absorptions of the Prepared Compounds (3e - h) and (8e-h).

Compounds No	- NH	C_{Aryl} - H	C_{Ali} - H	C = C C= N	C= O COOH	C= S - S C	C- F C- NO_2 C- CL
3e	3112	3030- 3006	2932- 2891	1561 1653	1700- 1680 -	1190 -	1169 - -
3f	3446	3016	2933- 2890	1422 1637	1705- 1698 -	1230 -	- 1554 -
3g	3447- 3181	3087- 3013	2932- 2889	1559 1637	1700- 1680 -	1250 -	-
3h	3444- 3181	3079- 3004	2947- 2861	1556 1672	1700 -	1110 -	- - 1087
8e	-	3100 - 3050	2990- 2893	1590 1670	- 3450	- 895	1160 - -
8f	-	3090- 3049	2980- 2856	1590 1657	- 3500	- 980	- 1560 -
8g	-	3070- 3002	2909- 2870	1564 1630	-- 3456	- 890	- -
8h	-	3150- 3008	-2870 2982	1550 1654	- 3466	- 899	- 1085

The UV spectrums of compounds (3e-h):

The selected VU data are listed in Table (3), The appearance of two big bands in the compounds (3e , 3g, 3h) the absorptions of these compounds at (282 - 217) nm indicated the presence of achromophoric group in (C = S) or (C = C) or (C= N) from (Л → Л*) and (n → Л*) and the last band is in the visible absorption.

Table (4): the UV absorptions of some prepared compounds (3e- h) .

Compounds No	ƛ nm	ε	A
3e	222 266	82090 20820	0.8209 0.2082
3f	219 282	41900 38870	0.4190 0.3887
3g	217 281	56960 35910	0.5696 0.3591
3h	230 293	66790 31650	0.6679 0.3165

A = ε . C . L A = absorbance ε = Molarities absorbance
C = the concentrate molarities L = length of cell

References:

1- Ali Yosif, T. Atto Amir , (2002), synthesis of New piperazine Derivatives containing1,3,4 - Oxadiazole or 1,2,4- Trizaole ring, Iraq Journal of chemistry(202)

2- AL- Douh, M . H, O, Hasnah ,A . Shafida . (2010) . Synthesis, spectroscopic and crystal structure studies of N,N -Bis (2- hydroxy -3- methoxybenzylidene) diaminobenzen derivatives, university of Aden Journal of Natural and Applid Sciences, vol 12, 325 .

3-Baraldi P.G,. Pavani M. G, . Nunez M, (2002), Anti microbial and antitumor activity of N - hetero imine 1, 2 ,3 - di thiazoles and their transformation - intrazolo - imidazol - and pyrioazolo pyrimidines Broog, medicinal chemistry . 10, 449, 456.

4- Brown D. J. ,(1984) Pyrimidines and their Benzo derivatives in Comprehensive Hetero cyclic chemistry, Pergamon Press, oxford, vol 3 , 443.

5- Bruno O, Brullo C,. Schenone S,. Ranise A,. Bondavalli F. E . Barocelli, (2002) .Progressin in SH - [I]benzo pyran [4 ,3-d] pyrimidine -5- amino series : 2- methoxy derivatives effective as anti platelet agents with analgesic activity, farmaco, 57, 753 -758

6- Bruno - O- , Brullo C. ,.Schenone S, (2002) ,progress in 5H-[1] Benzopyrano [4, 3 - d] pyridine -5-amine series : 2-methoxy derivatives effective as antiplatelet agents with analgesic activity, farmco,57,753-758

7- Chiyun J, Clark, G.w and .Borsotti G, Eur. patent (1989), Chemistry Abstract 330, 381, ,109 (25), 1188, 485.

8- Chowdhury A .Z .M .S, . matin M . M and . Anwar M .N ,(1997) synthesis and anti microbialactivites of fused pyrimidines, part II, sci 21, 79- 83 chemistry Abstract, 130 ,237, 520.

9- Clark J, M.S . Shahhet ,(1993), synthesis of Thino [2 ,3-d] pyrimidines from 4,6 - Dichloro pyrimidine-5- carbaldehydes , journal of Hetrocyclic Chemistry, unversity of Ioannina, 1065 -

10- EL- Gaby M.S.A.E.A,.Ahdel- Hamide S.G,.Ghorab M.M and .EL- Syayed S.M, (1999) Synthesis and anticancer activity in vitro of some new pyrimidines, Acta .pharm.49, 149-158.

11- Ellis G.P, Synthesis of fused Heterocyclic in the Chemistry of Heterocyclic Compounds, (2002), Wiley, New York, Vol 47, 226.

12- Katritzky A .R, (2006) Advances in Heterocyclic Chemistry , Vol 92, 83 -126

13-.Kumar A, . Taju B.P,, .Gurtu S,J . -sinha N and . shanker K,indian,(1988) , chemistry Abstract Journal .chemistry 27B (1), 109 (15) ,128915 P

14- Nasr M .N and. Gineinah M . M, (2002) . pyridio [2,3 -d] pyrimidines and pyrimido [5`, 4`: 5,6] pyrido [2, 3 - d] pyrimidines as new antiviral agents, synthesis and biological activity, Arch . phaem . 335 ,289 - 295

15- Petrie C.R.,.Cottam,. Mckerman H. B, . Robins P.A and. Revankar K. K G.R, (1985) Synthesis and biological activity of 6- azacadeguomycin and certian 2, 4, 6 tri ubstituted pyrazolo [3,4 -d] pyrimidine ribonucleosides, Journal medicinal chemistry, 28, 1010 -1016

16- Roth B and . cheng C, (2002) Progress in medicinal Chemistry, Elsevier Bio medical Press, New York vol 9 .

17- Sekkina M. M, (1985) Theoretical chemistry. Acta, , 96 ,19

18- Shish00 G . J, . shirsath V.S, . Rathod I ,S, . Petorvanu M, (2001) New pyrrolo - pyrimidine derivatives with anti fungal or anti bacterial properties, Ann .pharm . .59 ,139 - 140

19- Shishoo C. J,. Shirsath V.S,. Rathod I.S(2001). Synthesis and anti histaminic activity of some condensed 2- (substituted) aryl amino ethyl pyrimidine - 4 - (3) ones, Arzneimforsch 51, 221- 231.

20- Simon D, R. Daniel, B. Detlef , D. Bodo .(2007), selective Nucleophilic Substitution Reaction in 2,4, 6- Trisulfanyl- substituted Pyrimidine -5- carbonitriles by secondary Amines, journal Heterocyclic chemistry, institute for pharmazie, pharmazeutische chemic, 757

21- Sondhi S.M, .Johar M,. Rajrarnshi S, (2001) .Anti Cancer anti inflammatory,Australian journal chemistry 54 ,69 - 74

22- Wermuth C. G, G . Schlewer, J.J . Bourguignon, G. Maghioros, M.. J.Boucht, C.Morie, J.P.Worms and K.Biziere, (1989), synthesis and characterization of fused heterocyclic compounds, Journal Medicinal Chemistry, 32, 528.

تخليق وتشخيص بعض مستبدلات البيريميدين الجديدة 2 , 6, 5- اسيتيل – 4- (بارا – فينيل) بيريميدين وكذلك مستبدلات الثيانو [2, 3- d] بيريميدين

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الملخص

سلسلة مشتقات البيريميدين الجديدة 2 , 6, 5- اسيتيل - 4 - (بارا - فينيل) بيريميدين وكذلك مستبدلات الثيانو [2, 3- d] بيريميدين تم تخليقها بواسطة التفاعل بين بعض مستبدلات البنزالدهيد مع ايثيل اسيتو اسيتات وذلك في وجود الايثانول كمذيب لتعطي الناتج (3e-h) وعند تفاعلها مع الكيل الهاليد في وجود الايثانول تم الحصول على مشتقات البيريميدين الجديدة (4e-h) وعند تسخينها مع الاوكسي فوسفو كلورايد في وجود الداي اوكسان تتكون المركبات (5e-h) وعند تفاعلها مع الثيوريا في وجود الايثانول تم الحصول على (6e-h) هده المركبات تتفاعل مع محلول كلورو حمض الخليك لنحصل على مستبدلات الثيانو [2, 3- d] بيريميدين (8e-h).

وقد خضعت المركبات التي تم تخليقها لدراسة خواصها الفيزيائية مثل تعيين درجات الانصهار وتحديد ألوانها وكذلك المردود المئوي % (الحصيلة) كما تم تشخيصها من خلال تحليل العناصر CHN ودراسة أطياف الأشعة فوق البنفسجية UV والأشعة تحت الحمراء IR.

الكلمات المفتاحية: إيثيل اسبتو اسيتات، مستبدلات البنزالدهيد، مشتقات البيريميدين الجديدة، أطياف الأشعة فوق الحمراء IR، أطياف الأشعة فوق البنفسجية UV.