Synthesis and Characterization of Some New 6,6'-diphenyl-4,4'-bipyrimidine-2,2'-diol Derivatives

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Abstract

The synthesis and characterization of some novel pyrimidine derivatives has been presented. pyrimidines have been prepared from 1,6-diphenylhexa-1,5-diene-3,4-dione by treating with urea. The structure of pyrimidines has been characterized by spectral analysis by FT-IR, elemental analysis (C.H.N.) and ^{1}H NMR spectroscopy.

Keyword: pyrimidine chalcone, heterocyclic

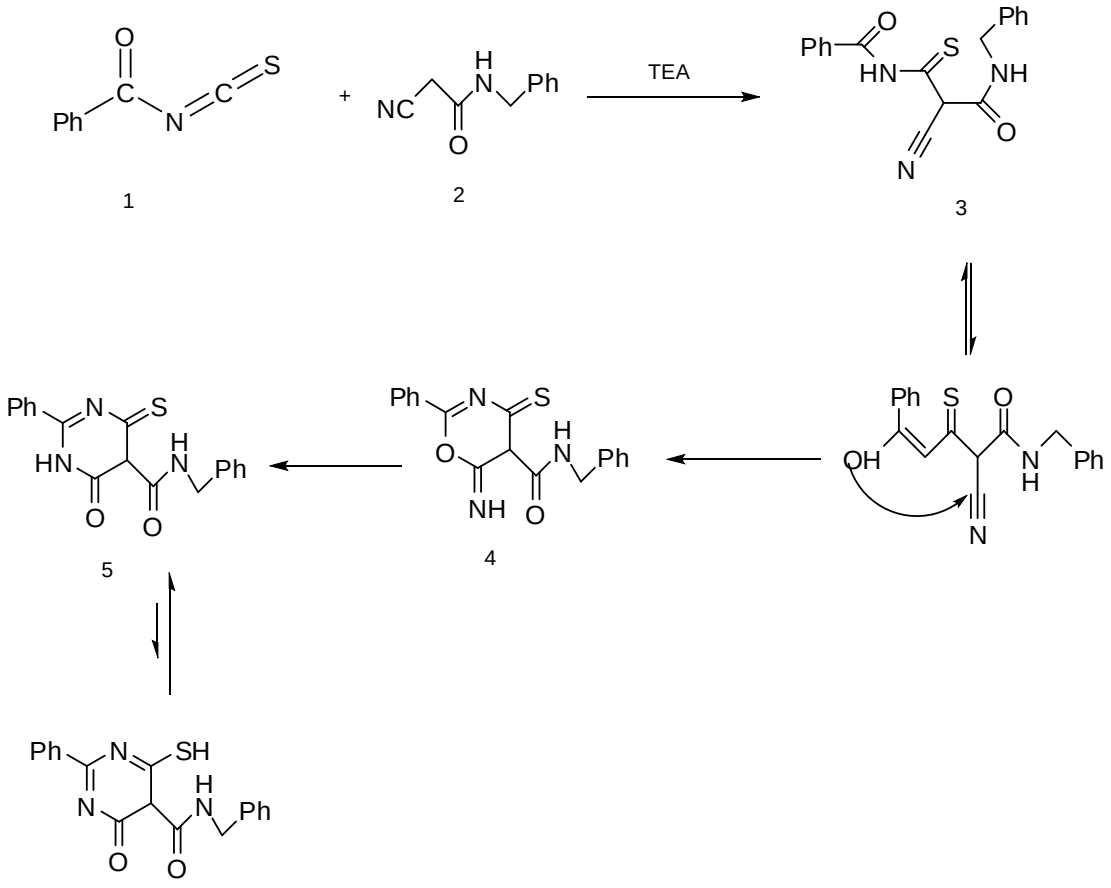
Introduction

Pyrimidine derivatives comprise adverse and interested group of drugs [1,2]. Earlier a comprehensive review of pyrimidines had been published by Brown [3]. Pyrimidines in general are extremely important for their biologicalact ivities, for example, some are antiviral agents [4]. The others, are selective cholecystokinine subtype receptor antagonists [5], anti-inflammatory [6-8], antihypertensive, diuretics, antimalarials, antithrombics, anticoagulants, antimicrobial [9-15].

As a part of a programme directed towards the synthesis of suitably functionalized heterocyclic systems of potential biological activity. [16-21]. A new synthetic route for pyrimidine thione from aroyl isothiocyanate was undertaken.

The synthetic strategy towards the synthesis of pyrimidinethione involves the addition of cyanomethylene **2** to the electrophilic carbon of heteroallene **1** to give N-[3-(benzylamino)-2-cyano-3-oxopropanethioyl]benzamide **3** followed by intramolecular cyclization via the addition of enolic form to cyano function affording N-benzyl-6-imino-2-phenyl-4-thioxo-5,6-dihydro-4H-1,3-oxazine-5-carboxamide **4** which in turn undergoes ring transformation and rearrangement to give pyrimidinethione as the final product. But on base induced addition of N-benzyl-2-cyanoacetamide to benzoyl isothiocyanate, it afforded mercapto-pyrimidine 5. The formation of **5** was potentiated by disappearance of CN group in its IR

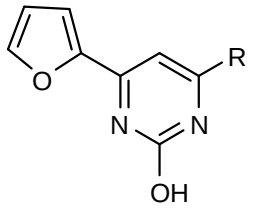
spectrum. The formation of **5** from addition of 2 to 1 may be proceeded presumably via the following mechanism:



Pyrimidine derivatives are prepared in view of the fact that a number of related compounds are known to be associated with biodynamic properties [(22)]. Pyrimidine derivatives are reported to be prepared by condensing chalcone with guanidine carbonate in methanol to give 2-Amino-dihydro pyrimidine [(23)]. Recently condensation of chalcone with guanidine nitrate is also reported [(24)].

N.Kaur et al [(25)] prepared pyrimidine deravitives by condensing chalcone and S-benzylisothiouronium chloride in piperidine. There are few reports on pyrimidine fused ring [(26)].

Bhendkar A. et. al. [(27)] reported the synthesis and antimicrobial activity of some new 4-furyl-6-(4-substituted)-2-(OH)-pyrimidine 6 by reaction of sodium nitrite and acetic acid with 2-Amino-4-furyl-6-(substituted) pyrimidine 7. All these synthesized compounds have a remarkable antimicrobial activity.



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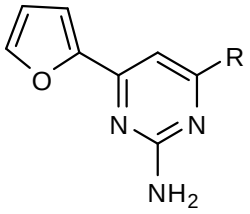

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In this work we have synthesized and characterized some of new pyrimidine Derivatives..

Experimental

General. IR spectra recorded on FT.IR SHIMADZU model 8400,. NMR spectra were acquired with a Bruker Ultra Shield (^{1}HNMR : 300 MHz) (University of AL-al-Bayt,Jordan). The chemical shifts were referenced to tetra methyl silane (TMS) as an internal reference. The elemental analysis were performed by using Euro Vector EA3000A (University of AL-al-Bayt,Jordan).

Synthesis of pyrimidine derivatives (2a-e)

General procedure. A mixture of Chalcone (**1a**–**e**) (which was prepared as mentioned in the literature) [28] (0.02mol) and urea (0.02 mol) were dissolved in ethanolic sodium hydroxide (10 ml) the mixture was reflux overnight. The precipitate obtained was filtered, washed and recrystallized from ethanol. To afford the pure products (**2a**–**e**).

6,6'-diphenyl-4,4'-bipyrimidine-2,2'-diol (2a)

Compound 2a was prepared from the reaction of 1,6-diphenylhexa-1,5-diene-3,4-dione **(1a)** with urea and gave a 73% yield with a m.p. (208-210)^{o}c. The CHN analysis for **$C_{20}H_{14}N_4O_2$** ; C, 70.17; H, 4.12; N, 16.37; Found C 70.16; H 4.11 ; N 16.37, FT-IR spectra (KBr disk) υ(cm^{-1}) 3250 (O-H stretching); 3022 (C–H stretching of Ar-H), 1616 (C=N stretching of pyrimidine), 1597 (C=C stretching of aromatic ring), 1220 (C–N stretching of pyrimidine), , **^{1}H NMR :** δ_H(DMSO) 11.83 ppm (2H, s,4) , (8.14-8.15) ppm (4H,d,3); (7.01-7.17) ppm (6H,m,1,2); 7.61 ppm (2H,s,5)

6,6'-dip-tolyl-4,4'-bipyrimidine-2,2'-diol (2b)

Compound 2b was prepared from the reaction of 1,6-dip-tolylhexa-1,5-diene-3,4-dione **(1b)** with urea gave a 75% yield with a m.p. (200-202)^{o}c. The CHN analysis for

$C_{22}H_{18}N_4O_2$; C, 71.34; H, 4.90; N, 15.13; Found C 71.32; H 4.89; N 15.12, FT-IR spectra (KBr disk) υ(cm^{-1}) 3252 (O-H stretching); 3020 (C–H stretching of aromatic ring), 2881 (C–H stretching of aliphatic), 1614 (C=N stretching of pyrimidine ring), 1596 (C=C stretching of aromatic ring), 1221 (C–N stretching of pyrimidine ring), , **^{1}H NMR :** δ_H(DMSO) 11.83 ppm (2H, s,4) , (7.37-7.39) ppm (4H,d,3); (7.07-7.07) ppm (4H,d,2); 7.61 ppm (2H,s,5) , 2.91 ppm (6H,s,1)

6,6'-bis(4-methoxyphenyl)-4,4'-bipyrimidine-2,2'-diol (2C)

Compound 2c was prepared from the reaction of 1,6-bis(4-methoxyphenyl)hexa-1,5-diene-3,4-dione **(1c)** with urea gave a 70% yield with a m.p. (198-200)^{o}c. The CHN analysis for **$C_{22}H_{18}N_4O_4$**; C, 65.66; H, 4.51; N, 13.92;Found C 65.64; H 4.51; N 13.90, FT-IR spectra (KBr disk) υ(cm^{-1}) 3250 (O-H stretching); 3021 (C–H stretching of aromatic ring), 2880 (C–H stretching of aliphatic), 1618 (C=N stretching of pyrimidine ring), 1592 (C=C stretching of aromatic ring), 1211 (C–N stretching of pyrimidine ring), **^{1}H NMR :** δ_H(DMSO) 11.83 ppm (2H, s,4) , (7.67-7.69) ppm (4H,d,3); (7.37-7.39) ppm (4H,d,2); 7.91 ppm (2H,s,5) , 3.91 ppm (6H,s,1)

6,6'-bis(4-chlorophenyl)-4,4'-bipyrimidine-2,2'-diol (2d)

Compound 2d was prepared from the reaction of 1,6-bis(4-chlorophenyl)hexa-1,5-diene-3,4-dione **(1d)** with urea gave a 79% yield with a m.p. (201-203)^{o}c. The CHN analysis for **$C_{20}H_{12}C_{l2}N_4O_2$** ; C, 58.41; H, 2.94; N, 13.62;; Found C 58.40; H 2.93; N 13.62, FT-IR spectra (KBr disk) υ(cm^{-1}) 3255 (O-H stretching); 3025 (C–H stretching of aromatic ring), 1621 (C=N stretching of pyrimidine ring), 1593 (C=C stretching of aromatic ring), 1212(C–N stretching of pyrimidine ring), **^{1}H NMR :** δ_H(DMSO) 11.83 ppm (2H, s,4) , (8.14-8.15) ppm (4H,d,3); (7.37-7.39) ppm (4H,d,2); 7.61 ppm (2H,s,5) .

6,6'-bis(4-hydroxy-3-methoxyphenyl)-4,4'-bipyrimidine-2,2'-diol (2e)

Compound 2e was prepared from the reaction of 1,6-bis(4-hydroxy-3-methoxyphenyl)hexa-1,5-diene-3,4-dione **(1e)** with urea gave a 66% yield with a m.p. (207-209)^{o}c. The CHN analysis for **$C_{22}H_{18}N_4O_6$;** C, 60.83; H, 4.18; N, 12.90; Found C 60.81; H 4.17; N 12.89, FT-IR spectra (KBr disk) υ(cm^{-1}) 3252 (OH stretching of phenol ring), 3025 (C–H stretching of aromatic ring), 2884 (C–H stretching of aliphatic), 1620 (C=N stretching

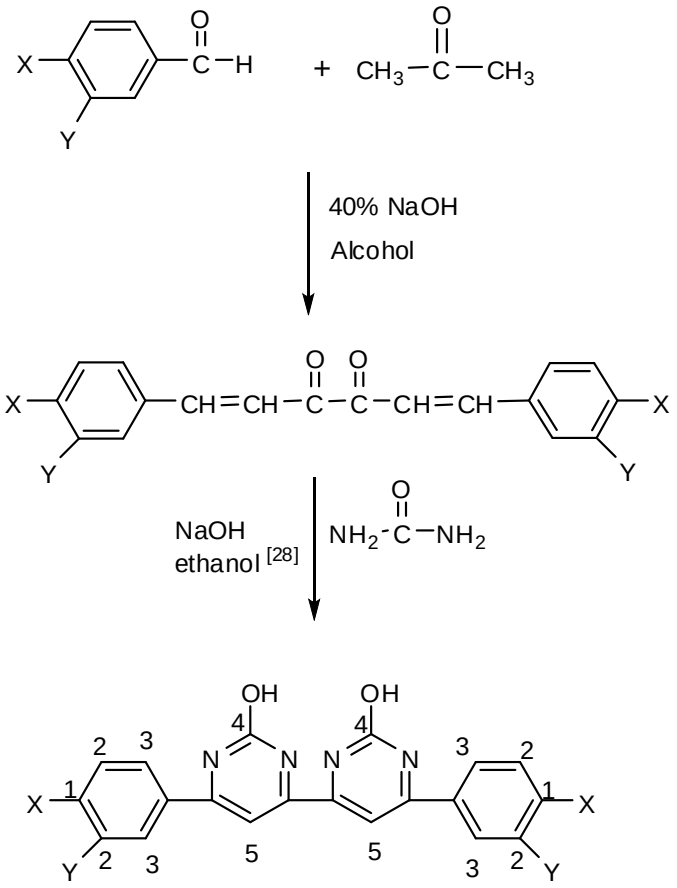
of pyrimidine ring), 1590 (C=C stretching of aromatic ring), 1215 (C–N stretching of pyrimidine ring), **^{1}H NMR :** δH(DMSO) 11.83 ppm (2H, s,4); 9.09 ppm (2H,s,1 (OH)), (7.01-7.17) ppm (6H,m,2,3); 7.61 ppm (2H,s,5) ; 3.91 ppm (6H,s,2 (OCH_3)).

Results and discussion

Treatment of chalcones derivatives **(1a-e)** with urea in boiling ethanol gave 6,6'-diphenyl-4,4'-bipyrimidine-2,2'-diol derivatives (scheme 1) in (66-79)% yield. The structures of these derivatives were characterized from their FT-IR, C.H.N and ^{1}H NMR spectra. The FT-IR spectra of 6,6'-diphenyl-4,4'-bipyrimidine-2,2'-diol compounds were characterized by the disappearance of the absorption band of chalcone that was attributed to the (C=O) stretching which appeared at (1672-1710) cm^{-1}. These fact confirmed the correct expected chemical structure of these compounds. All the IR spectra of 6,6'-diphenyl-4,4'-bipyrimidine-2,2'-diol derivatives (2a-2e) showed a band at (1614-1621) cm^{-1} which related to (C=N) stretching of pyrimidine ring , a band at (1211-1221) cm^{-1} which appeared due to (C-N) stretching of pyrimidine ring, and a band at (1590-1597) cm^{-1} which appeared due to (C=C stretching of aromatic ring). While, the C-H stretching aromatic rings showed a band within the range (3020-3025) cm^{-1} and the C-H stretching aliphatic showed a band within the range (2880-2886) cm^{-1}. The OH stretching of phenolic ring showed a band within the range (3250-3255) cm^{-1}.

The ^{1}H NMR spectra of pyrimidine derivatives are shown in figures **(1-6).**All the ^{1}H NMR spectra of pyrimidine ring were characterized [29-32] by the presence showed singlet signals within range 11.83 ppm which appeared to proton in (4) position.The proton in 5 position showed singlet signal within the range (7.61-7.91) ppm. The protons of aromatic rings in compound (2b,2c and 2d) showed doublet signals within the range (7.07-7.39) ppm which appeared to protons in (2) position because interaction with proton in (3) position, the proton in position (3) showed doublet signals within the range (7.37-8.15) ppm because interaction with proton in (2) position. While the compounds (2a) showed multiplet signals within the range (7.01-7.17) ppm which appeared to the protons in (1 and 2) positions, but the proton in (3) position showed doublet signals within the range (8.14-8.15) ppm. While the compounds (2e) showed multiplet signals within the range (7.01-7.17) ppm which appeared to the protons in (2 and 3) positions. The OCH_3 protons showed singlet signal for six protons at 3.91 ppm. The OH protons showed singlet signal for two protons in the region

δ= 9.09 ppm in compound (2e).While the CH_3 protons showed singlet signal for six protons at 2.91 ppm. While the peak of solvent (DMSO) showed singlet signal within the range 2.50 ppm.



Scheme (1)

X	Y	Compound Chalcone	Compound pyrimidine
H	H	1a	2a
CH_3	H	1b	2b
OCH_3	H	1c	2c
Cl	H	1d	2d
OH	OCH_3	1e	2e

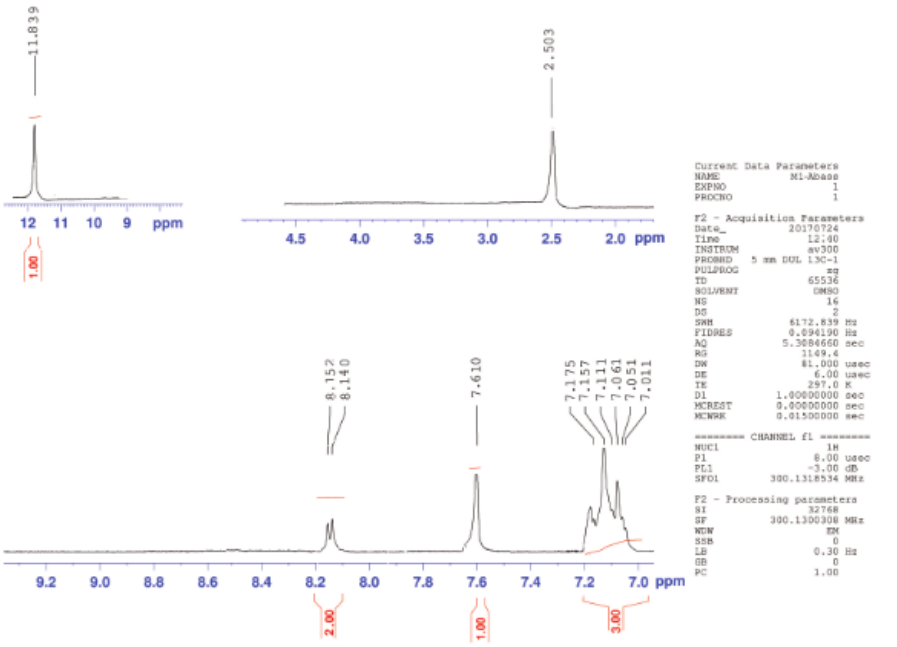


Figure (1) [1]HNMR spectra for compound (2a)

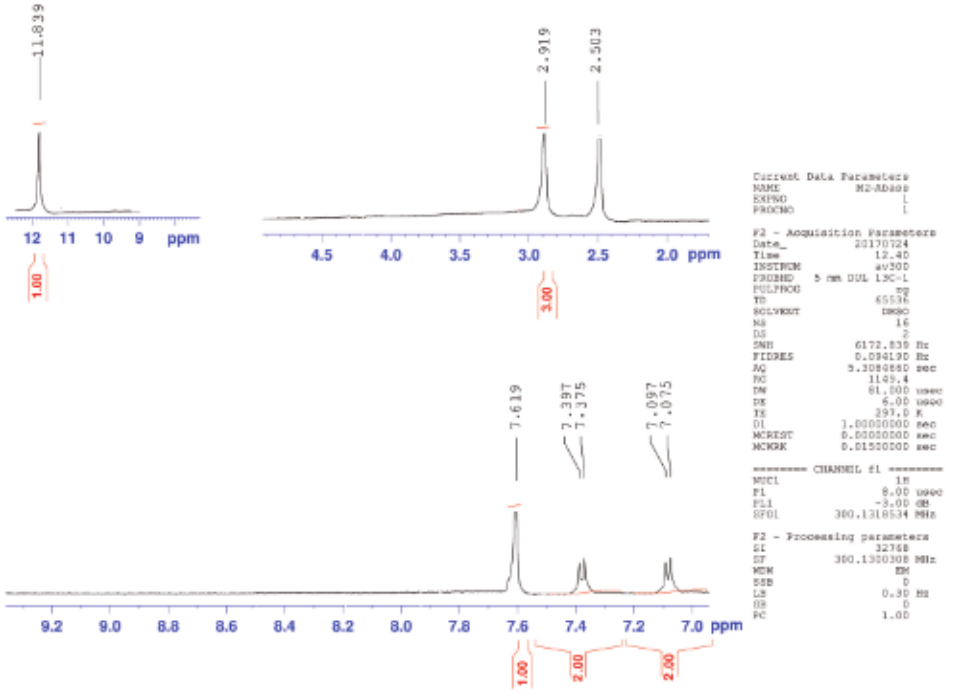


Figure (2) [1]HNMR spectra for compound (2b)

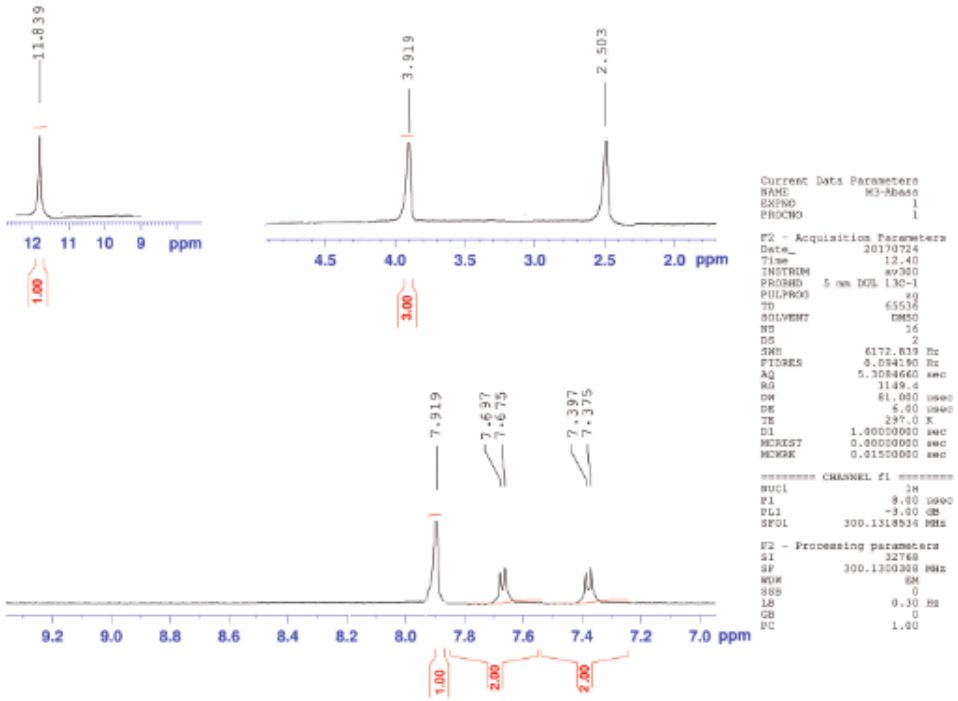


Figure (3) [1]HNMR spectra for compound (2c)

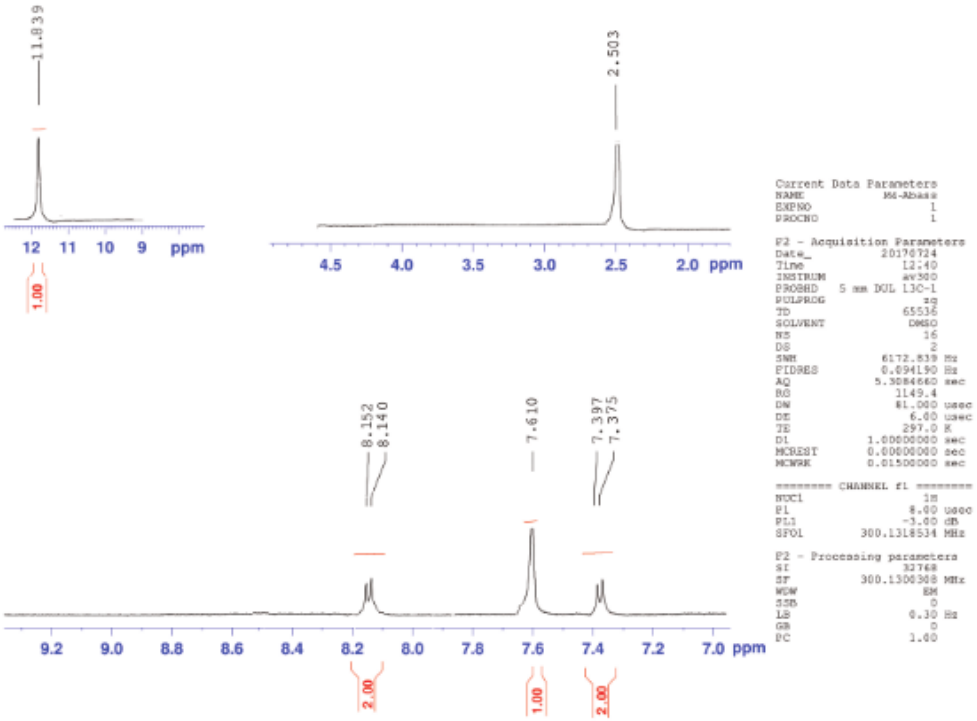


Figure (4) [1]HNMR spectra for compound (2d)

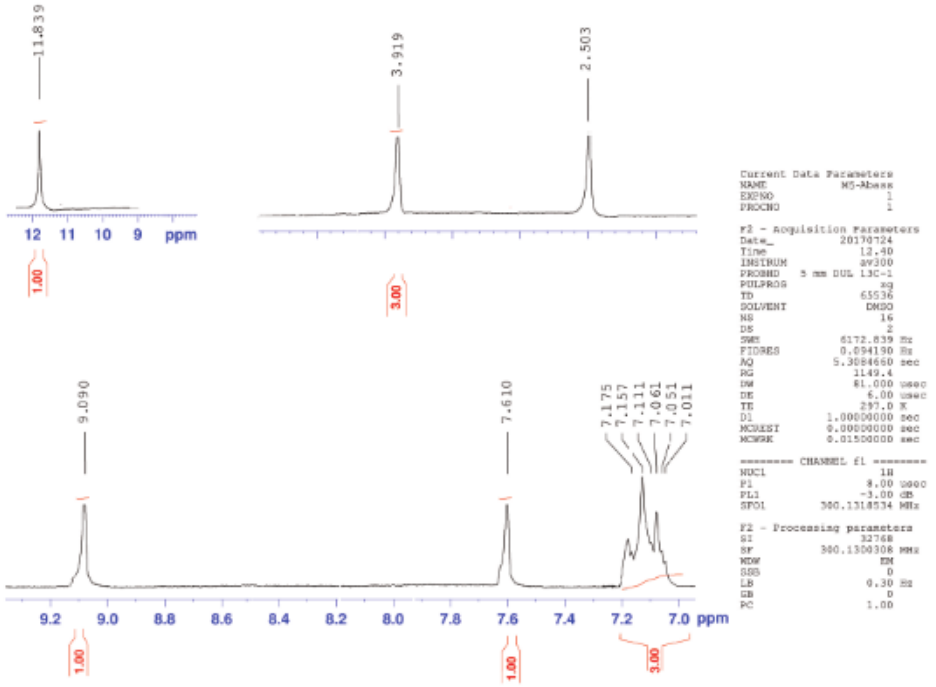


Figure (5) ^{1}HNMR spectra for compound (2e)

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تحضير وتشخيص بعض مشتقات 6,6'-diphenyl-4,4'-bipyrimidine-2,2'-diol الجديده

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الخلاصة

حضر في هذا البحث خمسة مركبات من مشتقات 6,6'-diphenyl-4,4'-bipyrimidine-2,2'-diol الجديدة من خلال تأحلق اليوريا مع مشتقات الجالكون (β,α- كيتون غير مشبع) باستخدام هيدروكسيد الصوديوم الكحولي كعامل مساعد تحت ظروف حراريه. شخصت المركبات بواسطة مطيافية الاشعة تحت الحمراء والرنين النووي المغناطيسي للبروتون وتحليل العناصر الدقيق.