Synthesis and Characterization of some Barbituric acid Derivatives

Jasim Ali Abdullah

Department of Chemistry
College of Education for Pure Science
University of Mosul, Mosul, Iraq.

***Abstract*- Barbituric acid (BA) derivatives (chalcones) (1 and 2) were prepared from the reaction of □-methylcinnamaldehyde or terephthalatedehyde with barbituric acid in the presence of acetic acid through the well-known reaction Knoevenagel, which were converted to chalcone epoxides (3 and 4) by the reaction of chalcones (1 and 2) with hydrogen peroxide. The resulting epoxides (3 and 4) were reacted with hydrazine, urea and thiourea through a Michael addition reaction or a Claisen reaction and then cyclization to give five- and six- heterocyclic compounds that contain in their structure the hydroxyl group (3a-c and 4a-c). These compounds were characterized by TLC, melting point and spectroscopic methods such as FTIR, CHNS, ^{1}H-NMR, ^{13}C- NMR, GC-mass and HRMS.**

***Keywords*: BA, Barbituric acid, Chalcones, epoxide Heterocyclic, six membered ring.**

1 Introduction:

Barbituric acid (BA) calls a pyrimidines play an essential role in chemistry and biological systems. BA is one of the most important derivatives of pyrimidines[1]. The BA moiety is present in different synthetic compounds such as pharmaceutical and industrial applications[2]. Owing to various pharmaceutical and biological activities of 2,4,6-trioxohexahydro-pyrimidine and its derivatives, they have been applied extensively in medicine and bioorganic researches[3]. BA is a strong acid in aqueous medium and has an active methylene group can be involved in Knoevenagel type condensation reaction[4], [5]. BA is a cyclic amide used as the parent compound to produce barbiturates that act as central nervous system depressants[6]. BA itself does not give sedative and hypnotic effects but the substituted derivatives with alkyl or aryl group at position 5 provide effects[7]. The BA derivatives have special place in pharmaceutical chemistry. They have broad biological spectrum ranging from classical applications in medical treatments as anticonvulsant, sedative, antispasmodic, hypnotic and local anesthetic drugs[8]. They have been also found useful in anti- osteoporosis, anti-tumor, anti-cancer treatments and as central nervous system depressants[9] . Due to the applications of barbiturates exploration of new routes for the synthesis of these compounds is axiomatic Exploration of novel protocols for the synthesis of desirable organic compounds is a growing trend in organic synthesis[10].

Different synthetic routes have been reported for the synthesis of 5-arylidine barbituric acid derivatives by using many methods such as infra-red promoted, microwave irradiation, ionic liquid mediated condensation, and uses variety of catalysts and grinding method. these methods are suffering by limitation of longer reaction time, effluent pollution bis-addition and self-condensation, lower yields etc [11].

Herein, BA reacted with □□Methylcinnamaldehyde or terephthalaldehyde by Knoevenagel type condensation reaction to form three compounds same as chalcone, there converted to chalcone epoxides by reacted with hydrogen peroxide. These epoxides compounds can be reacted with any other compounds have hydrogen active to form cyclic or heterocyclic compounds. These compounds can also play as pharmaceutical and biological activities.

2 Result and Discussion:

Before starting to explain the compounds In ^{1}H NMR spectrum table (4) we noticed some peaks are constant in all compounds approximately such as CH_3 and CH for compounds (1,3,3a-c) appeared that (δ 2.12-2.47 ppm, s, for CH_3), (δ3.02-5.15ppm, for CH cyclic and (δ 8.35-8.69 ppm, s, for CH in compounds (1 and 2)) these peaks conjugated with carbonyl group. In other hands, we saw constant peaks in compounds (1, 3, 3a-c) nearly that (δ 5.78-6.25 ppm, s, for CH_3-C=*CH-) because this group doesn't fall under influence reaction [12]. (δ 9.46-11.58 ppm,s,br, NH_{free}) NH is free for cyclic Barbituric acid also it was constant peaks ,because it is repeated in all compounds. In all of compounds in H aromatic ring we noticed multi peaks in (1, 3, 3a-c) compounds while, in (2, 4, 4a-c) appeared singlet peaks in the last compounds because the substitution on the aromatic ring is in *para* , *para* 4H ring are equivalents. Also in ^{13}C-NMR table (5). ^{13}C-NMR spectrum appeared that a major peaks at

(δ16.11,134.97,150.92ppm, for $^{*}CH_3$-$^{*}C$=$^{*}C$-H) (131.48,152.34 ppm, $^{*}C$=$^{*}CH$.) for compound (1) the other peaks in table (5);

2.1 Synthesis of chalcone compounds (1and 2)

Chalcone compounds (1 and 2) was prepared by condensation of □□methylcinnamaldehyde or terepthalaldehyde with BA by Knoevenagel type condensation reaction. chalcones, which have been prepared in the following scheme (1) and table (1) included chemical and physical properties of these compounds with melting point[13].

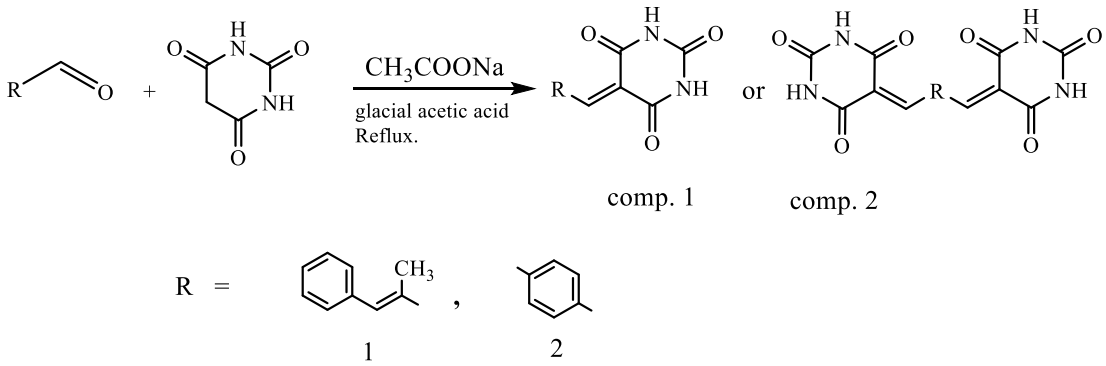


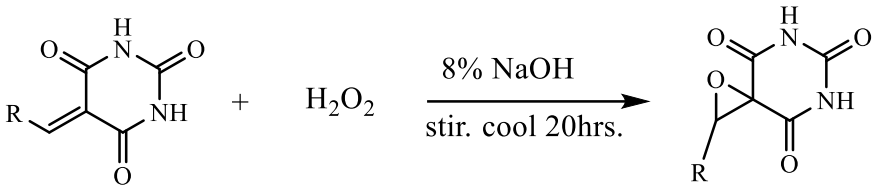
Table (1): physical properties and other characteristics for synthesis chalcones (1 and 2).

Comp. No.	m.p ^{0}C	color	Solvent	Rf	Time	M.F	M.W	Yield %
1	277-279	Deep yellow	Abs. EtOH	0.5	12 min.	$C_{14}H_{12}N_2O_3$	256	90
2	290-292	Pale yellow	Dioxane	0.4	9 min.	$C_{16}H_{12}N_4O_6$	354	87

In the FT-IR spectrum table (3) there are three major peaks; which are depending on the different substitution groups appeared in the chalcone compounds (1and 2), and its relative carbonyl group (C=O isolated), (C=O conjugated), (C=C) It is worth noting that in the infrared spectrum (FT-IR) it is noted that the carbonyl (C=O conjugated) groups[14][15] in all the aforementioned unsaturated ketone compounds possess stretching frequencies less than their natural frequencies, due to its succession with the double bond (olefin), which works to decrease the value of the force constant and thus lower frequencies. The carbonyl groups stretch for these compounds, and the rest of the absorbance are shown in Table (3). These compounds contain (C=$O_{conj.}$) conjugated with (C=C), (C=$O_{unconj.}$) and (C=CH.), (C=C-C=C), (NH) and (C=$O_{Ba.}$) for Barbituric acid constant; there are six different peaks which are appeared at (1726, 1677 cm^{-1}) for (C=$O_{unconj.}$) for compounds (1 and 2) respectively, (1662, 1658 cm^{-1}) for (C=$O_{conj.}$) respectively, (C=O_{Ba}) at (1626,1677 cm^{-1}) it same with (C=O_{uncoj}) because, it isn't under the same effect[16]. (C=C-C=C), (C=C) at (1620, 1605 cm^{-1}) and (NH) appeared peak at (3314, 3240 cm^{-1}). ^{1}H-NMR spectrum chart table (4) appeared that: (δ8.35-8.69ppm, s, CH1=C), at (δ5.88ppm, s, CH2=C for compound (1)), at (δ 10.96-11.58 ppm, s.br, N-H(1)) while, at (δ1 0.96ppm, for compound(2)), δ7.17-7.51ppm (m, 5H) m, Ar-H. for compound(1)); while, (δ7.42 ppm,(s, 4H) s, Ar-H for compound(2)). In ^{1} ^{3}C-NMR spectrum table (5) appeared that constant peaks It was mentioned earlier such as δ16.11,134.97,150.92ppm for CH_3-C=CH and δ131.48,152.34ppm for C=CH this peak disappeared in other compounds. δ160.32, δ171.89 for C=O(2) , C=O(4) and C=O(6) respectively. Multi peaks appeared at δ123.84-137.22ppm for Ar-C in compound (1). Compound (2) δ146.47,115.04ppm for C=CH this peak also disappeared in other compounds. δ154.17, δ160.04 for C=O(2) , C=O(4) and C=O(6) respectively. Two peaks appeared at δ129.32-134.88 for Ar-C in compound (2).

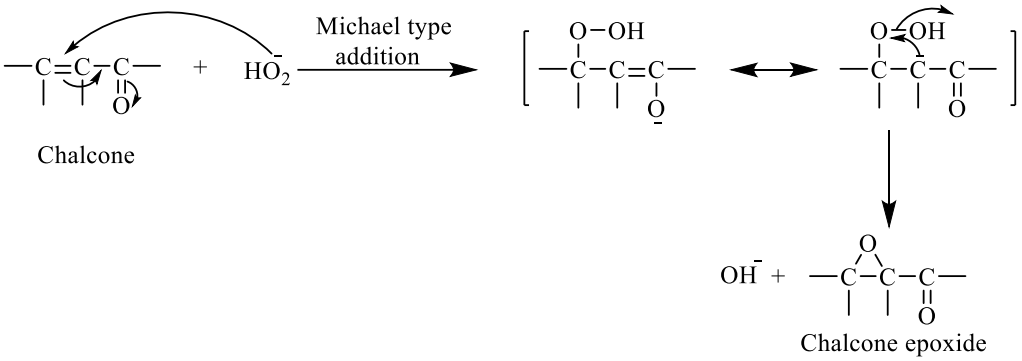
2.2 Synthesis of chalcone epoxides compounds (3 and 4).

Compounds (3 and 4) were synthesized from react of (1, 2) compounds of chalcones with hydrogen peroxide (H_2O_2). According to the Synthetic and Mechanism scheme (2).



comp. 3 and 4

Mechanism:

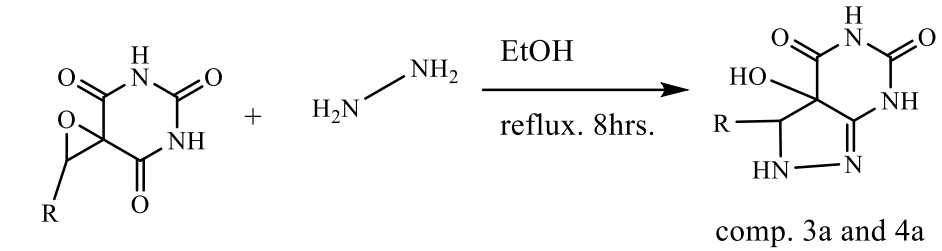


Scheme (2)

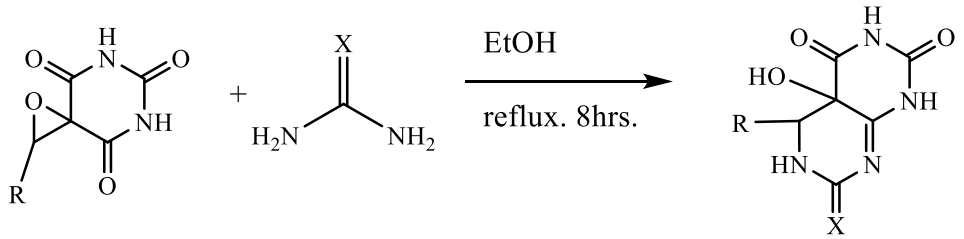
Compound (1) differentiated with compound (2) in conjugated with carbonyl group [16]. The carbon (2) without carbonyl group has high positive charge than other therefore, these compounds reacted with the anion (HO^-_2) via Michael addition due to the chalcone epoxides (3 and 4).In the FTIR for compounds table (3), peaks of carbonyl appeared in high value because, $C=O_{conj.}$ Converted to $C=O_{unconj.}$ due to the formation of the oxirane ring and (C=C) disappearance [14]. The FTIR spectrum gave strong absorption peaks at a range of frequencies (1673-1678 cm^{-1}) for carbonyl group. (1605- 1635 cm^{-1}) for (C=C), (902-905 cm^{-1}) for C-O-C the other peaks in table (3). ^{1}H-NMR spectrum chart table (4) appeared that: (δ3.50-3.60ppm, s, CH cyclic), at (δ5.98ppm, s, CH2=C) for compound (3), at (δ10.48-10.51ppm, s,br, N-H free), at (δ7.26-7.51 (m, 5H)ppm, m, Ar-H.) at (δ7.41ppm (s, 4H), Ar-H.). In ^{13}C-NMR spectrum table (5) appeared δ10.24,135.57,108.48ppm for CH_3-C=CH, at δ57.99,84.37 for C-O, CH-O, at162.01,169.42 C=O(2) , C=O(4) and C=O(6) respectively. Multi peaks appeared at δ120.78-134.90ppm for Ar-C in compound (3). Compound (4) δ123.84-138.32ppm for C-O, CH-O, at δ154.93,169.42 for C=O(2) , C=O(4) and C=O(6) respectively[17]. Two peaks appeared at δ123.84-138.32 for Ar-C in compound (4).

2.3 Synthesis of compounds (3_{a-c} and 4_{a-c}).

These compounds were synthesized from react of (3 and 4) with hydrazine hydrate, urea and thiourea. According to the Synthetic and Mechanism scheme (3).

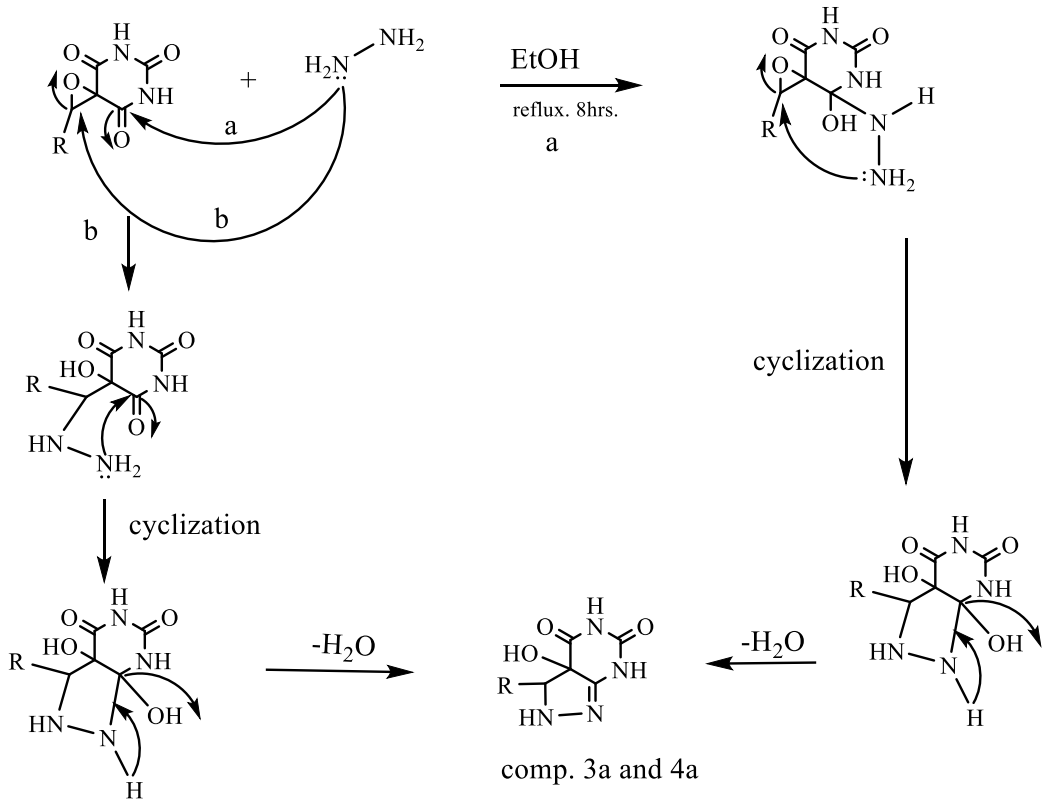


comp. 3a and 4a



X= O , S comp. 3b,c and 4b,c

Mechanism:



comp. 3a and 4a

Scheme (3)

The reaction was divided into two divisions (a and b). Division (a) consists a nucleophile of nitrogen hydrazine hydrate with lone pair of electron attack the carbon of carbonyl [18]. It similar to claisen condensation and the reaction continue to attack the carbon epoxide for cyclization[19]. This reaction dependent on hydroxyl group formation. It must be on the most substitution carbon and the hydroxyl group is nearly from carbonyl group which due to hydrogen bonding (H.B) [20], [21]. This production will be more stable. Then the intermediate compound formation loss (H_2O) molecule to form the product. Compound also formed in division (b) by attacking with lone pair of nitrogen to carbon of epoxide, the reaction is similar to Michael addition reaction [22] [23]. and then was cyclized after attacking the carbon of carbonyl and loss a hydrate molecule. In the two divisions reaction the required compound was formed and equals due to high yield. This reaction applies to other compounds when the compounds (3 and 4) reacted with urea and thiourea [24].

These compounds were studied and characterized by their melting points table (2). FT-IR,^{1}HNMR, ^{13}CNMRspectra, GC-Mass, EI, HRMS, CHNS and checked by T.L.C.

The FT-IR spectrum of these compounds table (3) shown that disappearance of one of (C=O) group at (1673-1698 cm^{-1}) and its appeared new peak at (1572-1598 cm^{-1}) which is relative to the (C=N) one of the carbonyl group is constant it is between two nitrogen in the barbituric acid because it is not under reaction that is called (BA) it is appeared in the range at (1696-1725 cm^{-1}) while the other carbonyl is decrease because hydrogen bonding formed with hydroxyl group as formation and its appeared in range peak at (1630-1650 cm^{-1}) which is relative to (C=O) (H. B)[25] [26]. (C=C) appeared at (1589-1620 cm^{-1}) and OH group appeared at (3195-3501 cm^{-1}) and N-H appeared in the range (3125-3446 cm^{-1}). ^{1}H-NMR spectrum chart table (4) for compounds (3_{a-c} and 4_{a-c}) appeared that: (δ2.12-2.42ppm, s, CH for CH_3 which is relative to the compounds (3_{a-c}), (δ5.78- 6.25ppm, s, CH for CH2=C for compound (3_{a-c}))[27]. at (δ3.02-5.15ppm, s, CH_{cyclic}) for compounds (3_{a-c} and 4_{a-c}) , at (δ10.58, 8.76ppm, s,br, N-$H_{pyraz.}$) for compounds (3_a and 4_a), at (δ9.32-10.74,ppm, s,br, N-H_{pyrim}) for compounds (3_{b-c} and 4_{b-c}) it is relative to pyrimidine ring formation, at (δ5.60- 8.82ppm, s,br, N-$H_{conj.}$) for N-H conjugated with C=N to compounds (3_{a-c} and 4_{a-c}), at (δ10.86- 11.49ppm, s,br, N-H_{free}) for barbituric acid ring,it isn't under reaction, at (δ2.98-4.11,ppm, s,br, O-H) for compounds (3_{a-c} and 4_{a-c}), at δ7.17-7.52 (m, 5H) ppm for compound (3_{a-c})); and (δ7.19- 7.59ppm, s, Ar-H) for compounds (4_{a-c}) [28]. In ^{13}CNMR spectrum table (5) appeared Many peaks remain within their rates no need to mention that [29]–[31]. We mention the important peaks, at range (δ95.05-110.61ppm, C for *C-OH); (δ48.08-66.11ppm, C for *CH-NH); (δ154.02-168.89ppm, C for C=N); (δ149.01-164.99ppm, C=O2), (δ169.42-179.77ppm, C, for C=O6) ; (δ162.01 and 165.83ppm, C for $C=O_{new}$ for Compounds 3_b and 4_b) and at (δ179.43 and 189.33ppm, C, for C=S for compounds 3_c and 4_c)[32], [33]. GC-Mass, EI and HRMS spectrum table (6) appeared the exactly molecular weight and the elemental analysis (CHNS) gives acceptable results in table (7). All spectroscopic measurements confirmed the validity of all compounds, including what was presented to the figures of some of them.

Table (2): physical properties and other characteristics for the synthesis Schiff base derivatives (3,4)

Comp. No.	m.p ^{0}C	color	Solvent	Rf	Time	M.F	M.W	Yield %
3	212-214	white	Abs. EtOH	0.5	6 min.	$C_{14}H_{12}N_2O_4$	272	85
4	225-228	white	Abs. EtOH	0.6	5 min.	$C_{16}H_{10}N_4O_8$	386	87
3a	267-269	red crystal	EtOH	0.4	5 min.	$C_{14}H_{14}N_4O_3$	286	83
3b	256-258	white	EtOH	0.4	3 min.	$C_{15}H_{14}N_4O_4$	314	89
3c	243-245	pale yellow	Dioxane	0.5	3 min.	$C_{15}H_{14}N_4O_3S$	330	78
4a	260-261	red	Dioxane	0.5	5 min.	$C_{16}H_{14}N_8O_6$	414	85
4b	253-255	white crystal	EtOH	0.5	3 min.	$C_{18}H_{14}N_8O_8$	470	84
4c	277-279	yellow	EtOH-Benzene	0.6	4 min.	$C_{18}H_{14}N_8O_6S_2$	502	90

Table (3): IR Spectral of compounds (1 – 4c)

Comp. No.	IR (KBr), ν (cm^{-1})								U.V ($CHCl_3$) λmax (nm)
	C=O unconj. C=O conj.	C=O BA C=O new	C=O H.B C=S	C=C-C=C C=C	C-O-C	C=N	N-H_{BA}	OH	
1	1726, 1662	1726, ——	_____	1620, ——	_____	____	3314		422
2	1677, 1658	1677, ——	_____	—— 1605	_____	____	3240	—	431
3	1673, 1673	1673, ——	_____	—— 1635	902	____	3465		373
4	1698, 1698	1698	_____	——, ——	905	____	3507	—	394
3a	——	1725, ——	1650, ——	_____, 1620	_____	1584	3422	3476	385
3b	——	1725, 1725	1630, ——	_____, 1598	_____	1587	3161	3441	391
3c	_____	1715, ——	1641, 1572	_____ 1589	_____	1572	3358	3501	397
4a	_____	1696, ——	1630, ——	_____	_____	1598	3125	3195	405
4b	_____	1696, 1696	1643, ——	_____	_____	1596	3446	3446	417
4c	_____	1678, ——	1647, 1518	_____	_____	1590	3327	3432	423

Table (4): ^{1}H-NMR data of compounds (1 – 4c)

Comp. No.	CH_3	CH1=C, CH_{cyclic}	CH2=C	NH_{pyraz}	$NH_{pyrim.}$	$NH_{conj.}$	NH_{free}	OH	Ar-H
1	s, 2.47	s, 8.35, ——	s, 5.88	_____	_____	_____	s.br, 10.96, 11.58	____	7.17-7.51 (m, 5H)
2	——	s, 8.69, ——	_____	_____	_____	_____	s.br, 10.96	____	7.42 (s, 4H)
3	s, 2.22	—— s, 3.50	5.98	_____	——	_____	s.br, 10.48	____	7.26-7.51 (m, 5H)
4	——	—— s, 3.60	_____	_____	_____	_____	s.br, 10.51	____	7.41 (s, 4H)
3a	s, 2.42	—— s, 3.02	s, 6.18	s.br,10.58		s.br, 8.82	s.br, 11.37	s,br. 3.51	7.17-7.52 (m, 5H)
3b	s, 2.33	—— s, 4.33	s, 6.25	_____	s.br, 9.92	s.br, 5.60	s.br, 11.22	s,br. 2.98	7.17-7.52 (m, 5H)
3c	s, 2.12	—— s, 4.33	s, 5.78	_____	s.br, 9.68	s.br, 8.42	s.br, 11.15	s,br. 3.10	7.17-7.52 (m, 5H)
4a	——	—— s, 3.57	_____	s.br,8.76	_____	s.br, 5.88	s.br, 10.86	s,br. 2.79	7.58 (s, 4H)
4b	——	——	_____	_____	s.br, 9.32	s.br,	s.br,	s,br.	7.59 (s,

		s, 4.76				6.10	11.49	3.42		4H)
4c	——	—— s, 5.15	_____	_____	s.br, 10.74	s.br, 5.73	s.br, 11.43	s,br. 4.11	7.19	(s, 4H)

Table (5): ^{13}C-NMR data of compounds (1- 4c)

Comp. No.	*C=*CH	*CH$_3$-*C=*C-H	*C-O, *CH-O	*C-OH, *CH-NH	*C=N	Ar-C	*C=O(2) *C=O(4) C=O(6) *	*C=O$_{new}$	*C=S
1	131.48,152.34	16.11,134.97,150.92	_____	_____	_____	123.84 - 137.22	160.32 171.89 171.89	_____	_____
2	146.47,115.04	_____	_____	_____	_____	129.32 - 134.88	154.17 166.02 166.02	_____	_____
3	_____	10.24,135.57,108.48	57.99, 84.37	_____	_____	120.78 - 134.90	162.01 169.42 169.42	_____	_____
4	_____	_____	80.95, 55.53	_____	_____	123.84 - 138.32	154.93 169.42 169.42	_____	_____
3a	_____	10.24,134.90,120.05	_____	95.05 57.99	162.01	121.78 - 135.57	156.38 —— 169.42	_____	_____
3b	_____	10.24,134.90,121.78	_____	102.22 57.99	158.99	120.05 - 135.57	149.01 —— 169.42	162.01	_____
3c	_____	10.24,134.90,121.78	_____	106.24 64.67	162.33	120.05 - 135.57	153.31 —— 171.67	_____	179.43
4a	_____	_____	_____	96.87 48.08	154.02	122.52 - 139.97	152.50 —— 176.01	_____	_____
4b	_____	_____	_____	104.99 54.88	161.02	126.53 - 136.26	154.23 —— 179.77	165.83	_____
4c	_____	_____	_____	110.61 66.11	168.89	124.73 - 142.01	164.99 —— 175.21	_____	189.33

Table (6): GC-Mass, EI and HRMS spectrum of compounds (1-4)

Comp. NO.	m/z	%	m/z	%	m/z	%	m/z	%	m/z	%	HRMS Calc.	HRMS Meas.
1	257	16	256	75	199	23	188	25	171	19	256.13228	257.14353
	121	33	89	15	77	17	56	100				
2	355	6	354	34	188	20	121	33	91	22	354.12172	355.12952
	78	14	44	13								
3	273	13	272	75	334	90	277	17	235	20	272.153541	273.160817*
	219	21	193	35	116	50	67	78	56	100		
4	387	14	386	64	363	77	346	20	266	30	386.143704	387.150981*
	222	35	172	96	88	45	56	100				
3a	287	12	286	81	230	62	83	53	77	16	286.106138	287.103767*
	69	16	56	100								
3b	315	7	314	42	217	40	123	41	119	14	314.101044	315.107680*
	91	11	83	22	77	14	56	100				
3c	331	17	330	100	305	11	228	6	203	27	330.079209	331.085836*
	172	14	167	10	131	10	111	11	104	25		
	97	29	84	28	77	15	56	73				
4a	415	24	414	69	371	73	329	28	238	41	414.104168	415.101902*
	203	15	144	47	130	49	101	15	77	22		
	56	100										
4b	471	10	470	32	235	35	203	85	139	10	470.093007	471.100625*
	119	9	84	19	56	65						
4c	503	10	502	60	429	31	355	18	203	32	502.048319	503.056133*
	116	24	84	15	77	10	56	100				

* = $[M+H]^+$ = Calculated Molecular Ion Mass or Measured Molecular Ion Mass for some compounds.

Table (7): Element analysis (CHNS) of compounds (1-4)

Comp. No.	$C_{theo.}$	$C_{prac.}$	$H_{theo.}$	$H_{prac.}$	$N_{theo.}$	$N_{prac.}$	$S_{prac.}$	$S_{prac.}$	M.F	Mol. Mass
1	65.62	65.732	4.72	5.682	10.93	10.975			$C_{14}H_{12}N_2O_3$	256.26
2	54.24	54.273	2.85	2.811	15.81	15.853			$C_{16}H_{12}N_4O_6$	354.28
3	61.76	61.813	4.44	4.487	10.29	10.376			$C_{14}H_{12}N_2O_4$	272.26
4	49.75	49.654	2.61	2.691	14.50	14.564			$C_{16}H_{10}N_4O_8$	386.28
3a	58.74	58.832	4.93	4.955	19.57	19.581			$C_{14}H_{14}N_4O_3$	286.29
3b	57.32	57.421	4.49	4.512	17.83	17.841			$C_{15}H_{14}N_4O_4$	314.30
3c	54.54	54.545	4.27	4.313	16.96	16.982	9.70	9.811	$C_{15}H_{14}N_4O_3S$	330.36
4a	46.38	46.395	3.41	3.512	27.04	27.063			$C_{16}H_{14}N_8O_6$	414.34
4b	45.96	45.971	3.00	3.120	23.82	23.852			$C_{18}H_{14}N_8O_8$	470.36
4c	43.03	43.044	2.81	2.831	22.30	22.325	12.76	12.779	$C_{18}H_{14}N_8O_6S_2$	502.48

3 Conclusions

The Knoevenagel method has been used in this work to synthesis of chalcone from aldehydes and BA, this method more importantly to reduction of environmental impacts relative to prepare epoxides which easy reaction to give high yields of five and six membered ring compounds derived from BA. Characteristics of the final product including FTIR ^{1}HNMR, ^{13}C-NMR ,GC-Mass, HRMs, CHNS indicate the configuration of the required compounds.

4 Experimental:

Melting point were determined on a Stuat melting apparatas SM30. Infrared spectra were recorded on a Bruker, FT-IR Spectrophotometer Tensor 27, Germany, and a biotech Engineering, FT-IR-600, U.K., using KBr discs. Alpha Bruker/ATR Diamond. Ultra-Violet spectra were recorded on Shimadzu UV – 1650 pc, UV-Visible spectrophotometer, Japan, using chloroform as a solvent. ^{1}HNMR and ^{13}CNMR spectra were recorded on Bruker AC 250, Bruker ARX 300, Bruker ARX 500. For ^{1}H-NMR characterization, ^{13}C- NMR, All ^{1}H-NMR spectra presented in this work were collected in $CDCl_3$ or in DMSO-d6 solution. All chemical shifts are given in ppm. using TMS as internal references.

Multiplicities are given as follow: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad signal. Mass spectrometry MS were recorded on AMD MS40, varian MAT CH7, MAT 731 (EI, 70ev), intecta AMD 402 (EI, 70ev and CI), finnigan MAT 95 (CI, 200ev). High Resolution Mass Spectrometry (HRMS). Were recorded on Varian MAT 311, Intecta AMD 402. Elemental Analysis were recorded on LECO CHNS-932, Thermoquest Flash EA 1112. To ensure the purity of the resulting compounds used technique. Thin layer chromatography (TLC) was carried out, the presence of iodine as an aspect of the spot.

4.1 Synthesis of chalcones: 5-(2-methyl-3-phenylallylidene) pyrimidine -2,4,6- (*1H,3H,5H*) -trione (1)[34].

A mixture of □□methylcinnamaldehyde (0.01 mol.) and Barbituric acid (1.28 g 0.01 mol.) in glacial acetic acid (10 mL) with catalytic amount of sodium acetate (1gm) in glacial acetic acid (5 mL) was refluxed for 2 hours. The reaction mixture was allowed to cool. The solid that separated was filtered, dried & recrystallized from proper solvent.

4.2Synthesis of: 5,5'-(1,4-phenylene bis (methanylylidene)) bis (pyrimidine-2,4,6 (1H,3H,5H) -trione) (2) [34] .

A mixture of terephthalaldehyde (0.01 mol.) and Barbituric acid (2.56 g 0.0 2 mol.) in glacial acetic acid (20 mL) with catalytic amount of sodium acetate (2gm) in glacial acetic acid (10 mL) was refluxed for 2 hours. The reaction mixture was allowed to cool. The solid that separated was filtered, dried and recrystallized from proper solvent.

4.3 Synthesis of chalcone epoxides: 2-(1-phenylprop-1-en-2-yl)-1-oxa-5,7-diazaspiro[2.5]octane-4,6,8-trione (3), and 2,2'-(1,4-phenylene) bis (1-oxa-5,7-diazaspiro[2.5]octane-4,6,8-trione) (4)[35].

In a round bottom flask (250 mL) equipped with a magnetic stirrer, (0.1mol.) of chalcone was dissolved in (40 mL) acetone, (15 mL) of methanol and (15 mL) of (8%) sodium hydroxide, then (15 mL) of (30%) hydrogen peroxide was added. the solution was stirred sometimes for a period of time. Then the flask was leaved with its contents in the refrigerator for (20) hours. The precipitate filtered and recrystallized by ethanol to give a white crystalline precipitate.

4.4 Synthesis of heterocyclic compounds from chalcone epoxides (3a-c and 4a-c). General procedure[17]:

A mixture of compounds (3 or 4) (0.01 mol.) and active hydrogen compounds such as, hydrazine hydrate, urea and thiourea (0.0 1 mol.) or (0.02 mol. For compounds 4) in (20 mL) ethanol was refluxed for 8 hours. The reaction mixture was allowed to cool. The solid that separated was filtered, dried and recrystallized from proper solvent.

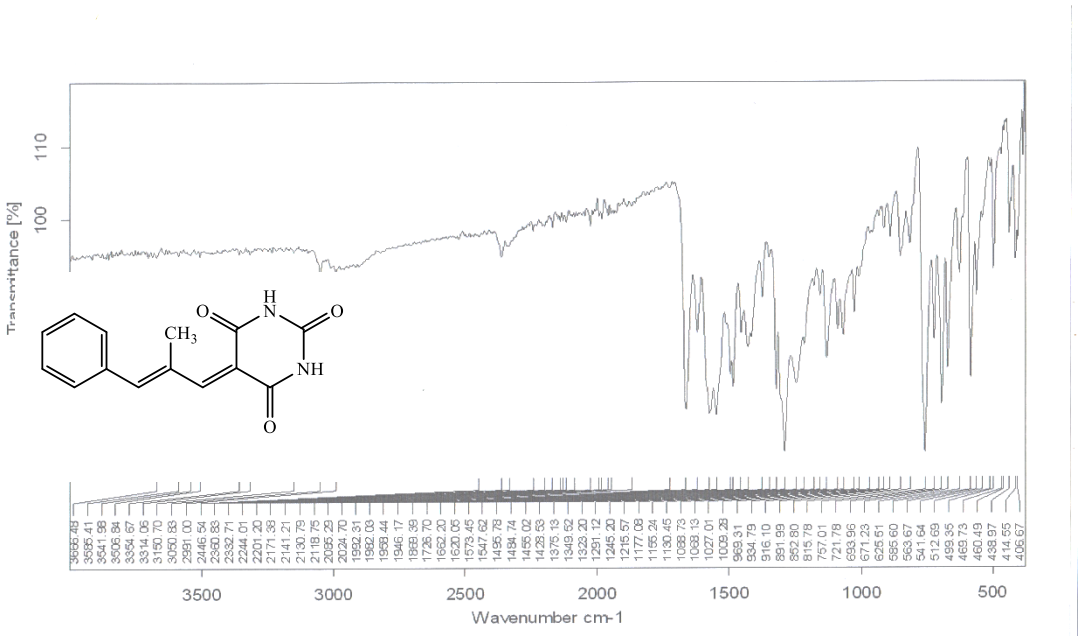


Figure (1): FT-IR for compound (1)

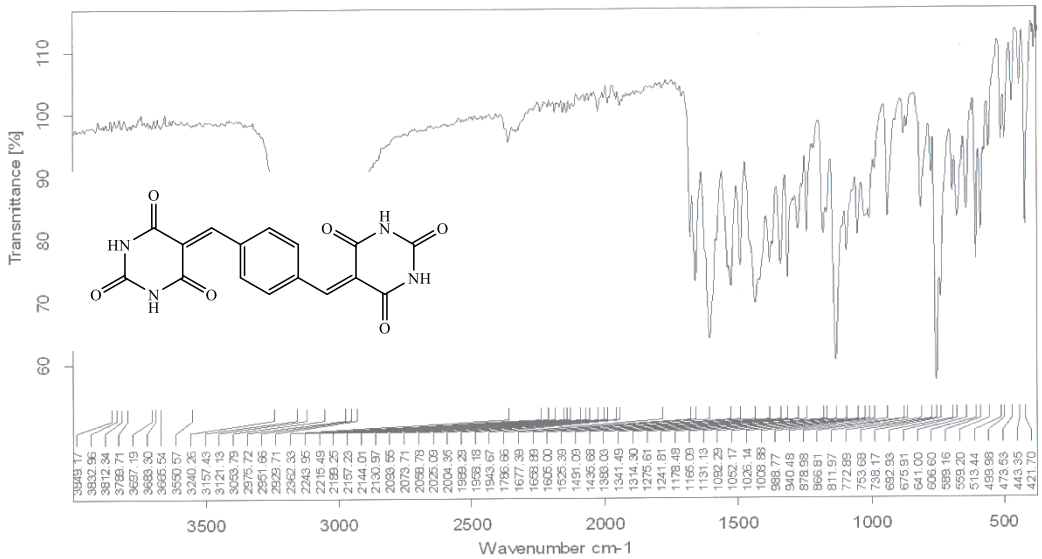


Figure (2): FT-IR for compound (2)

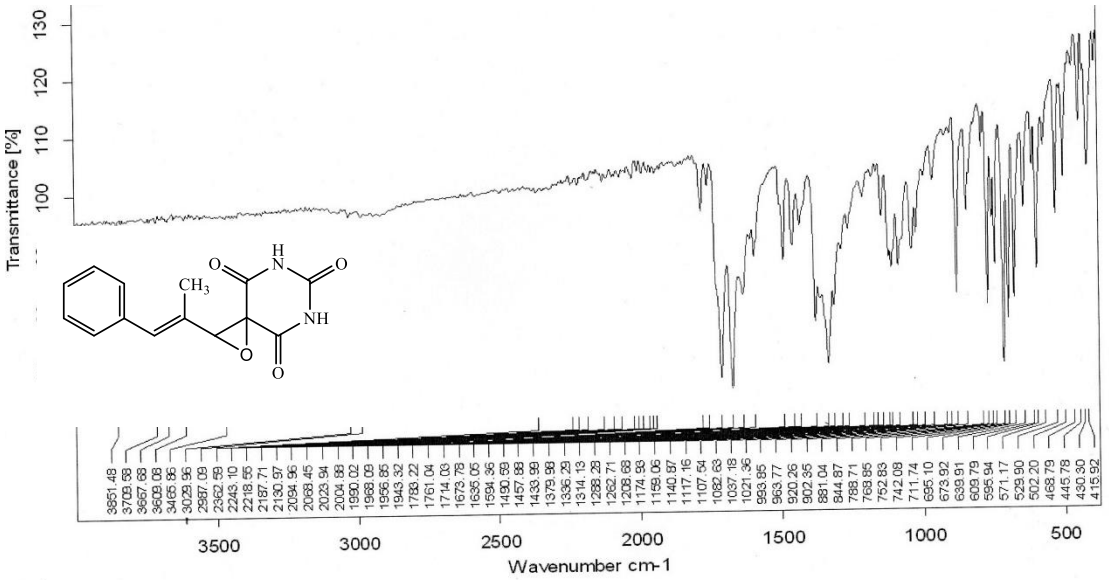


Figure (3): FT-IR for compound (3)

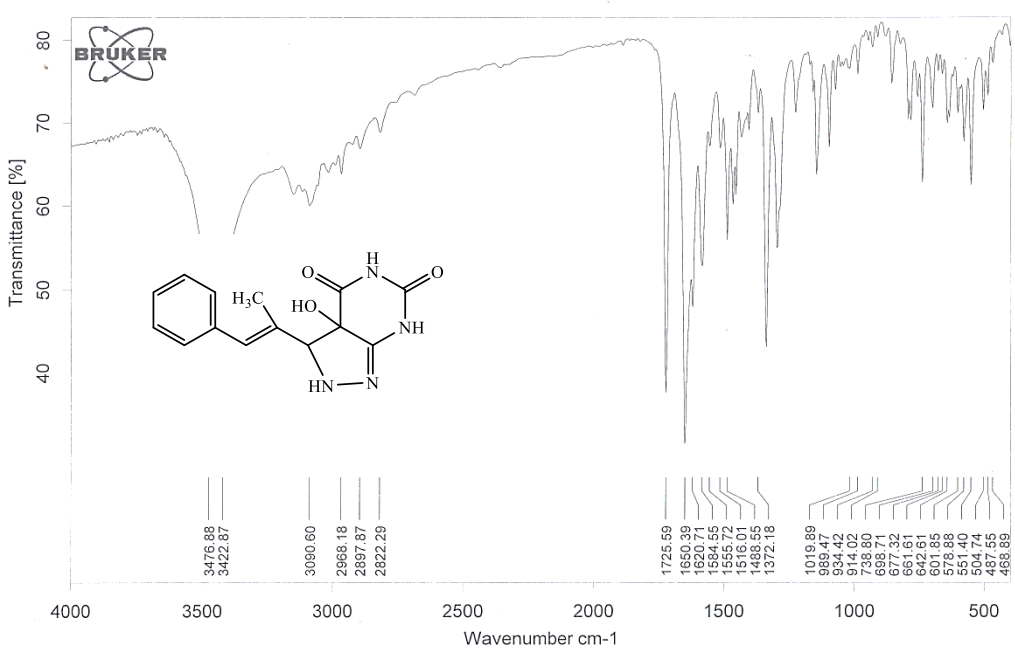


Figure (4): FT-IR for compound (3a)

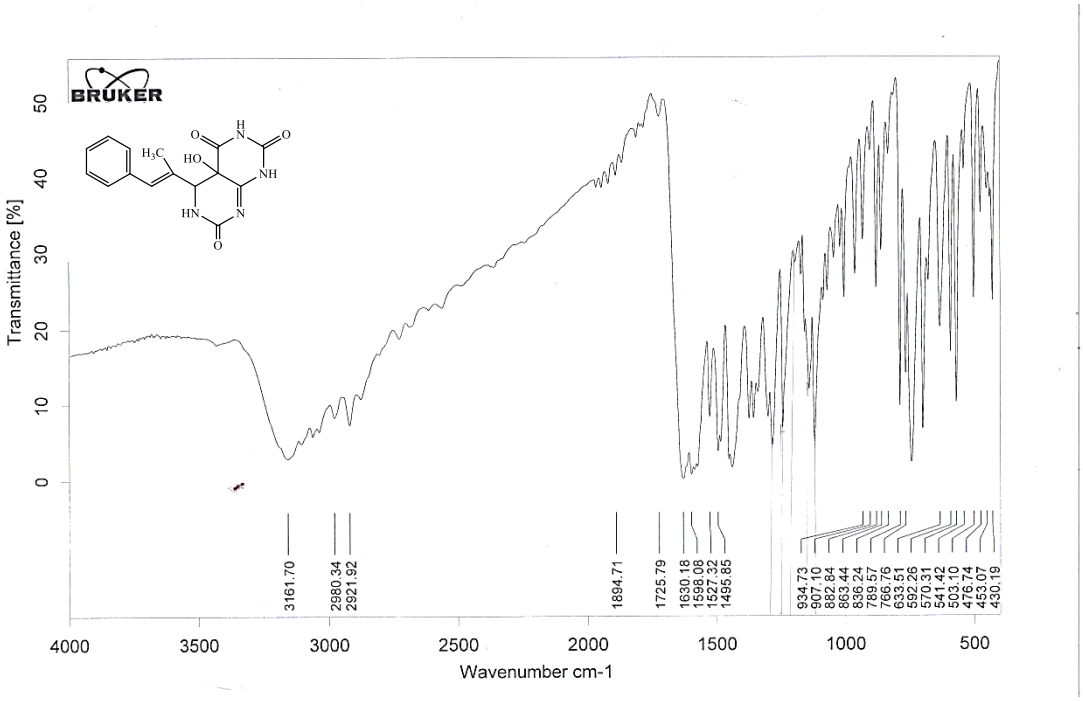


Figure (5): FT-IR R for compound (3b)

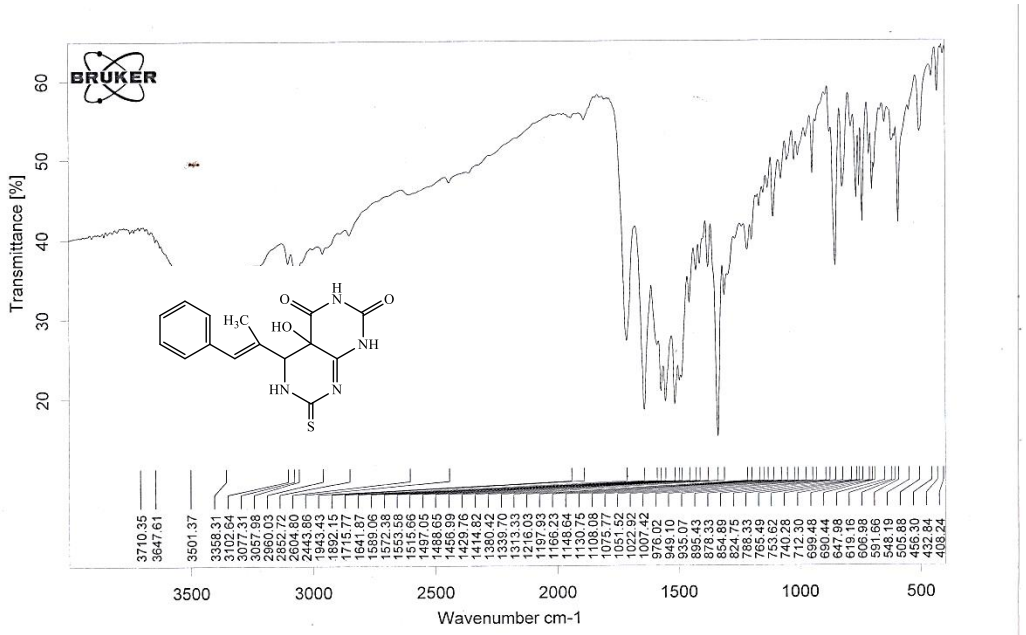


Figure (6): ^{1}H-NMR for compound (3c)

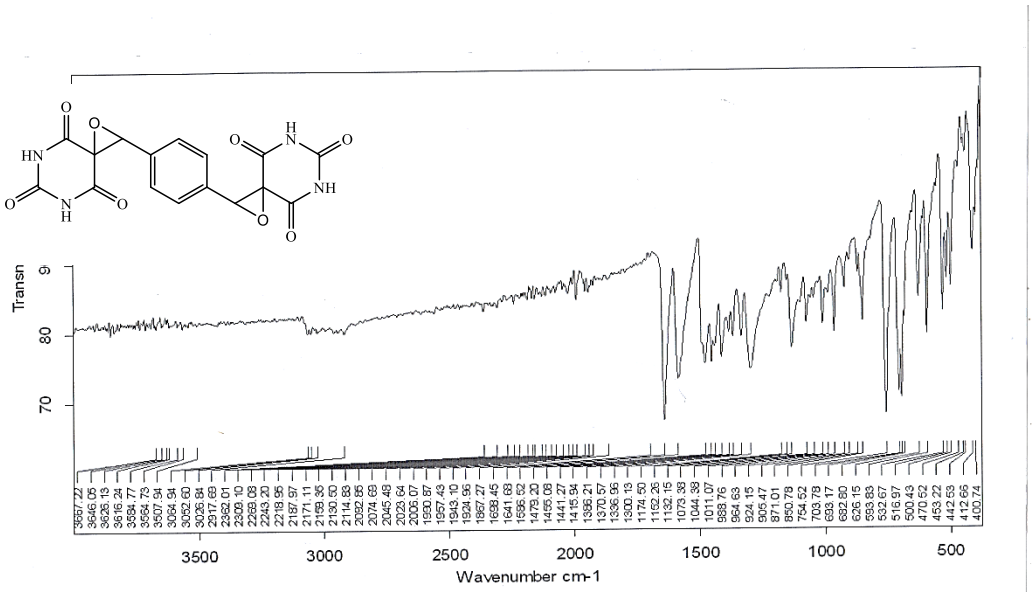


Figure (7): FT-IR for compound (4)

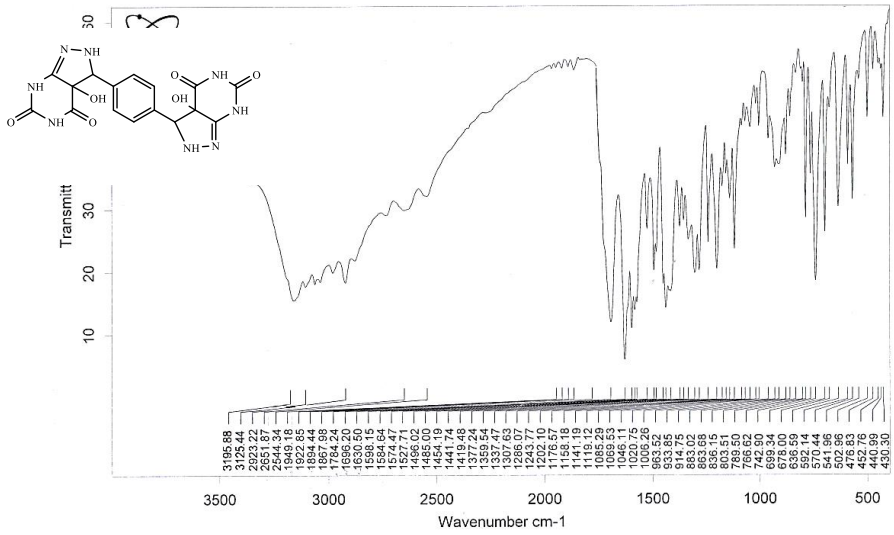
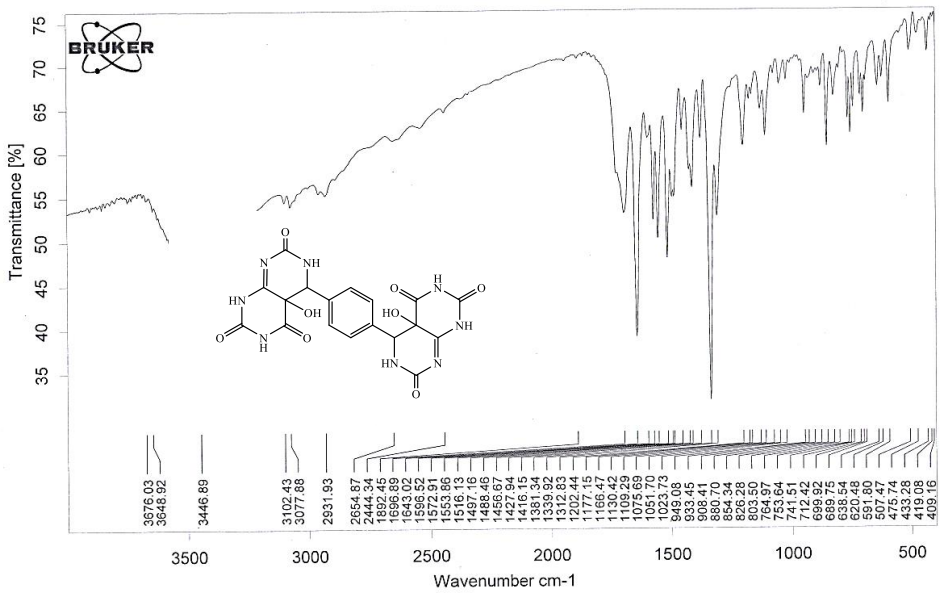


Figure (8): FT-IR for compound (4a)

Figure (9): FT-IR for compound (4b)



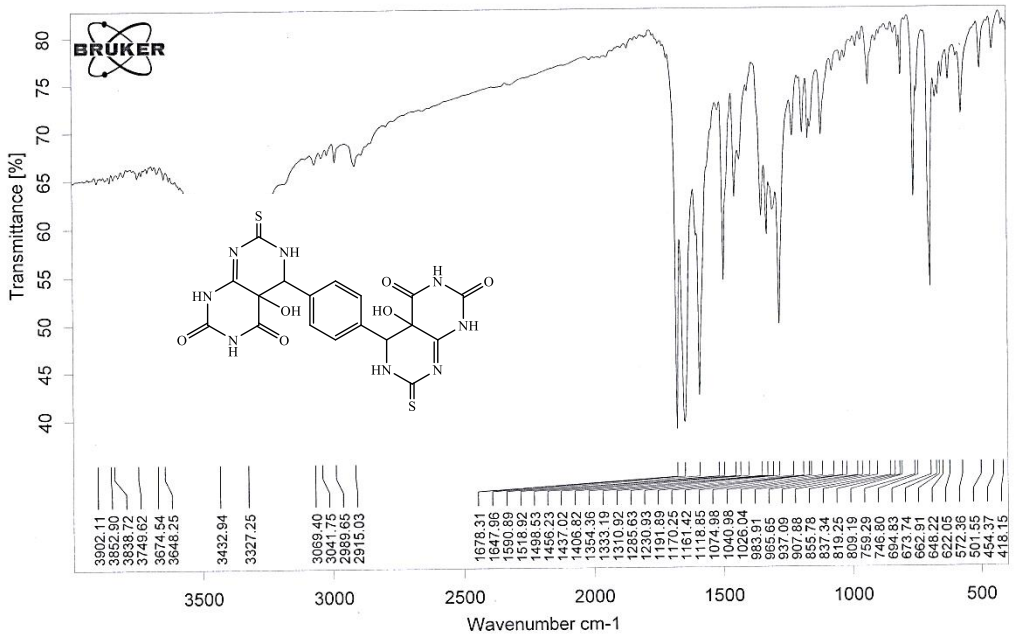


Figure (10): FT-IR for compound (4c)

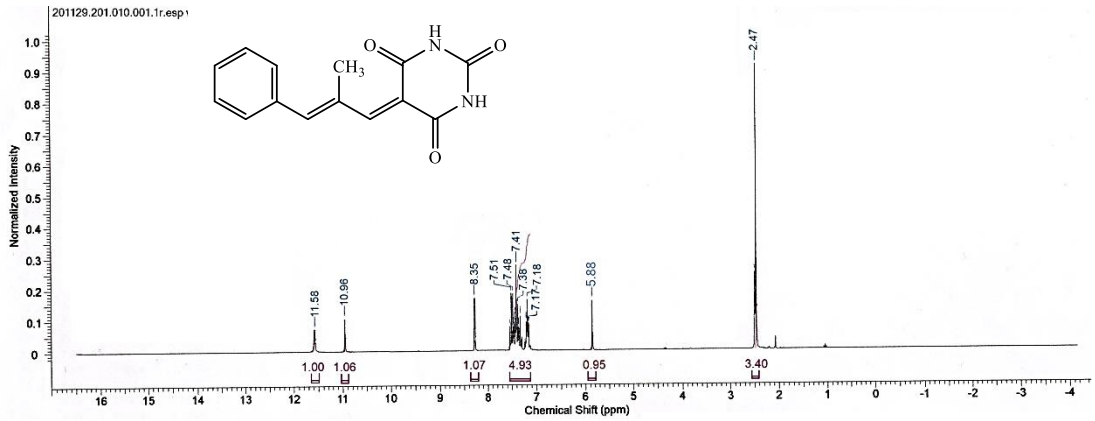


Figure (11): ^{1}H-NMR for compound (1)

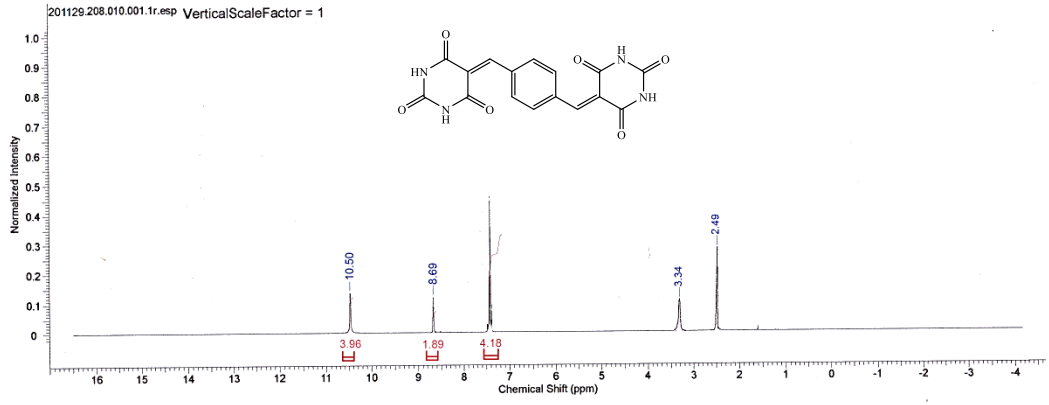


Figure (12): ^{1}H-NMR for compound (2)

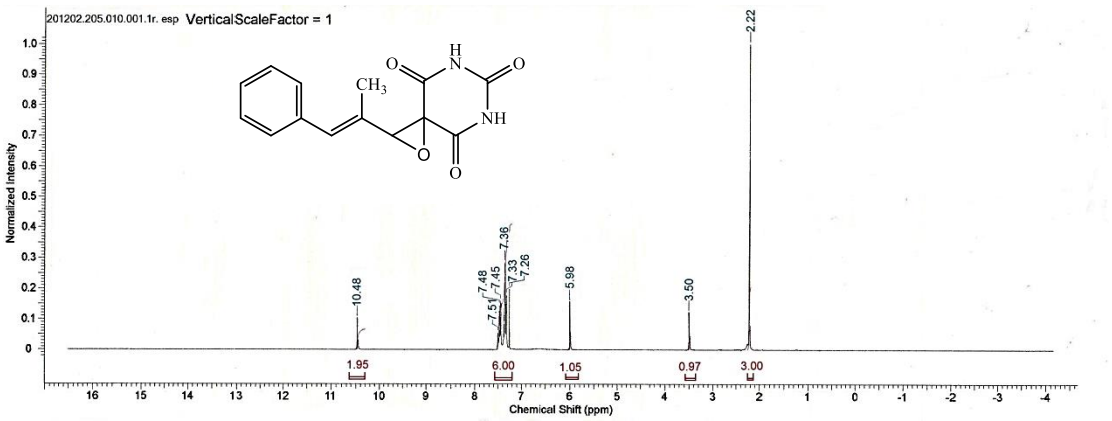


Figure (13): ^{1}H-NMR for compound (3)

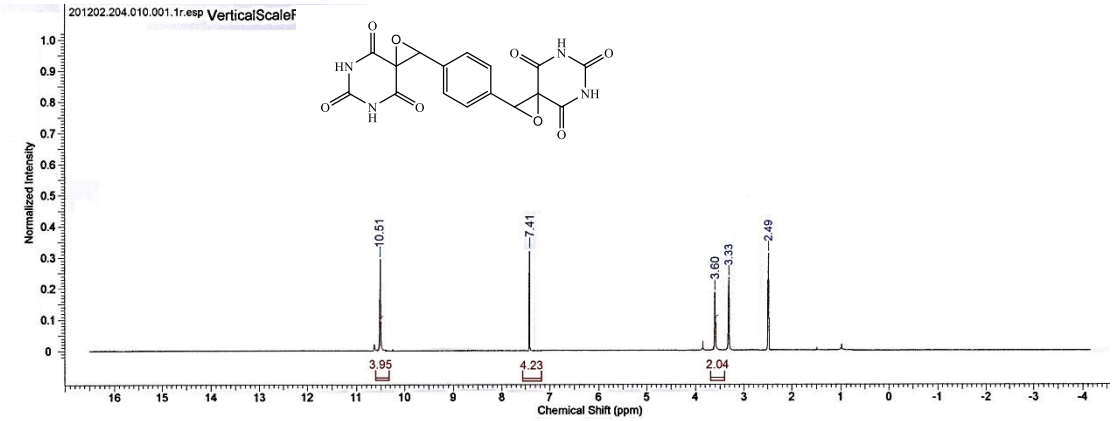


Figure (14): ^{1}H-NMR for compound (4)

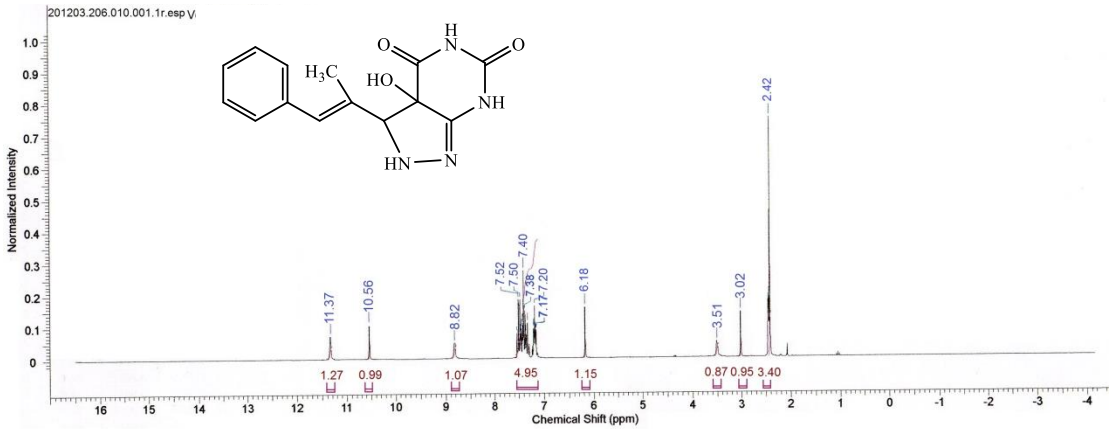


Figure (15): ^{1}H-NMR for compound (3a)

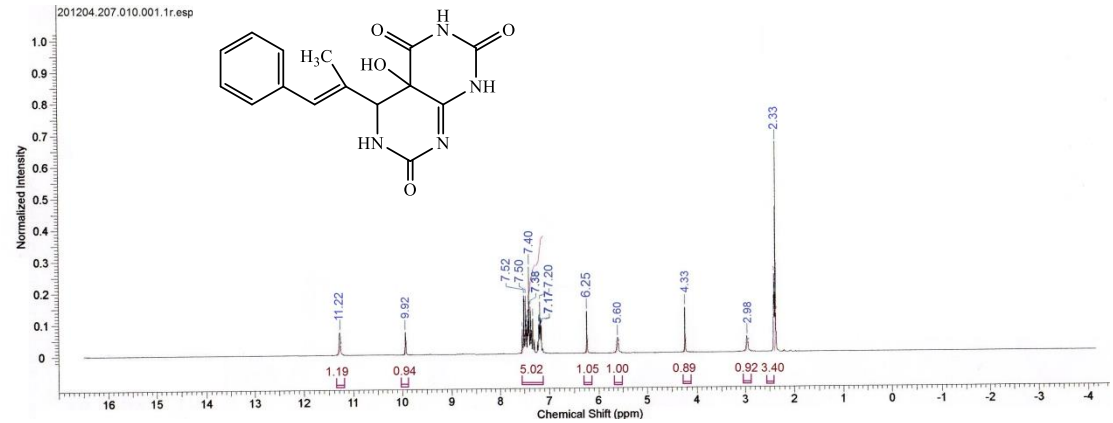


Figure (16): ^{1}H-NMR for compound (3b)

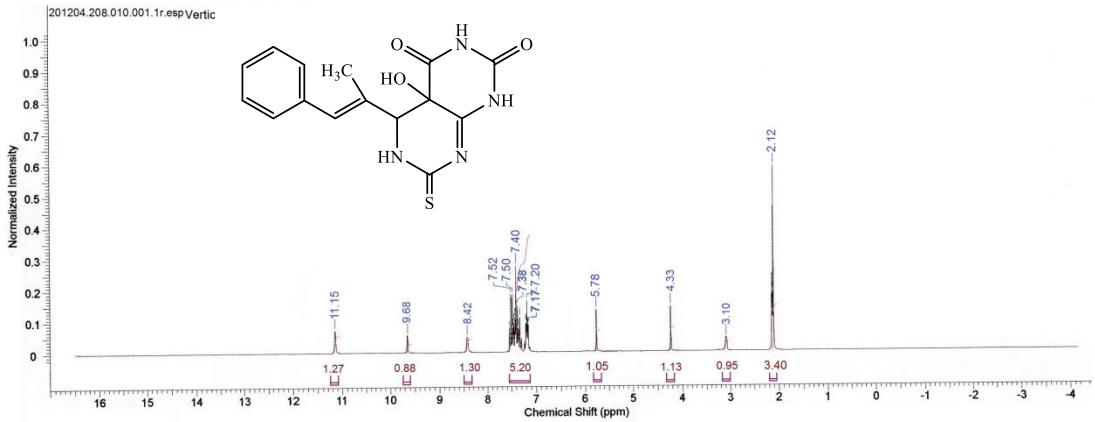


Figure (17): ^{1}H-NMR for compound (3c)

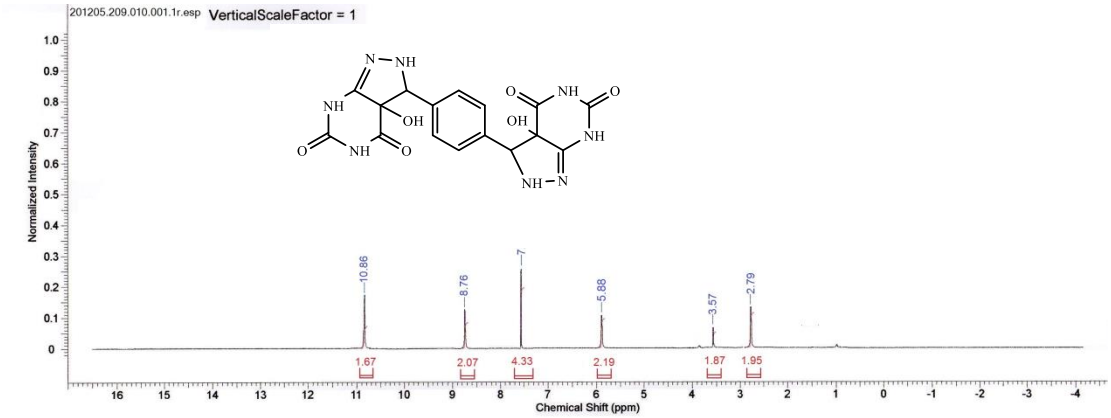


Figure (18): ^{1}H-NMR for compound (4a)

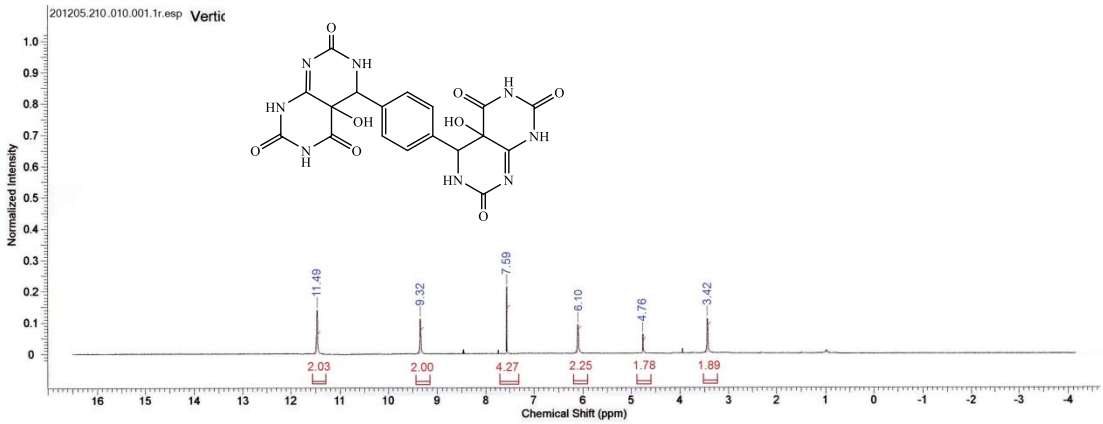


Figure (19): ^{1}H-NMR for compound (4b)

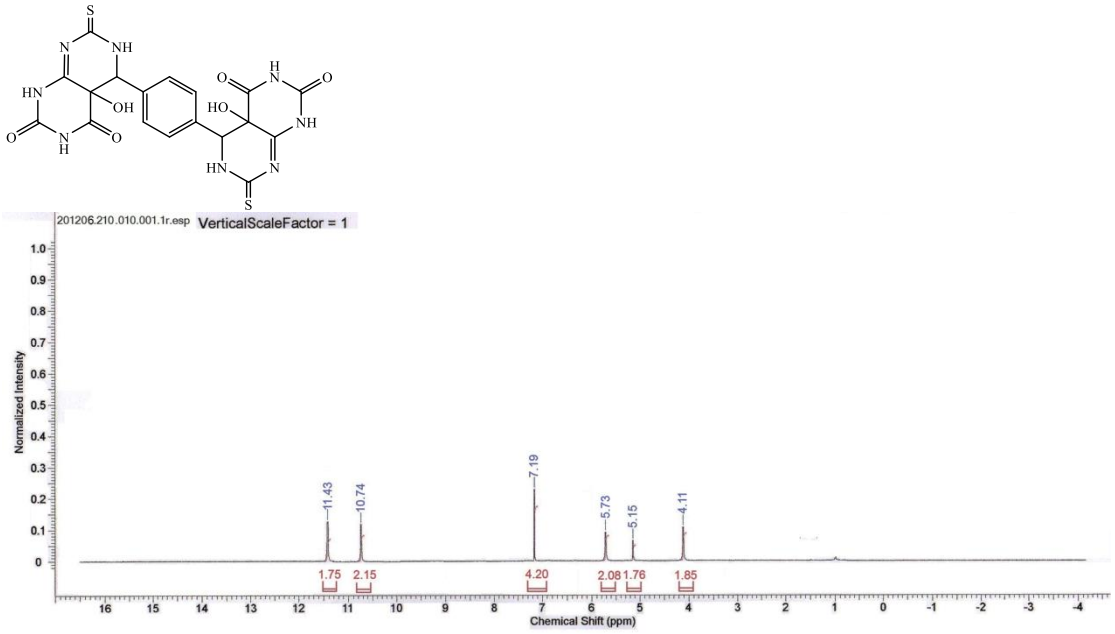


Figure (20): ^{1}H-NMR for compound (4c)

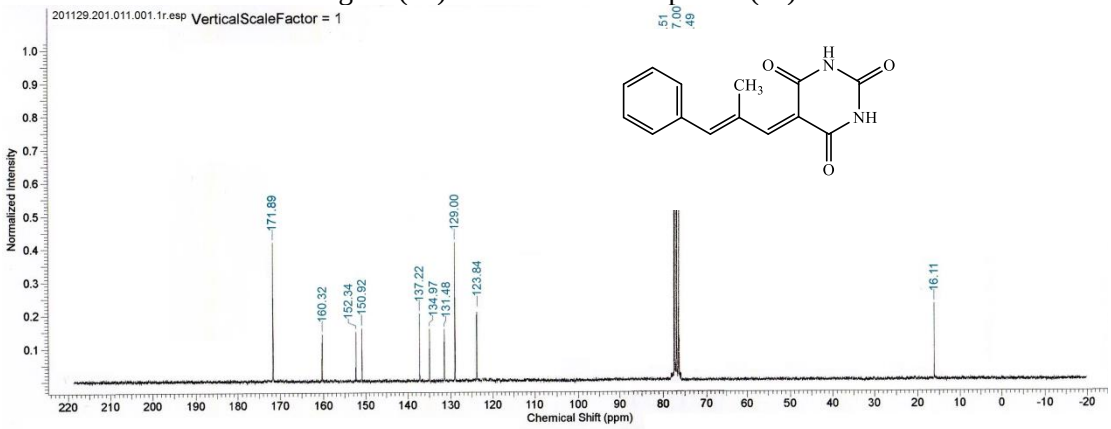


Figure (21): ^{13}C-NMR for compound (1)

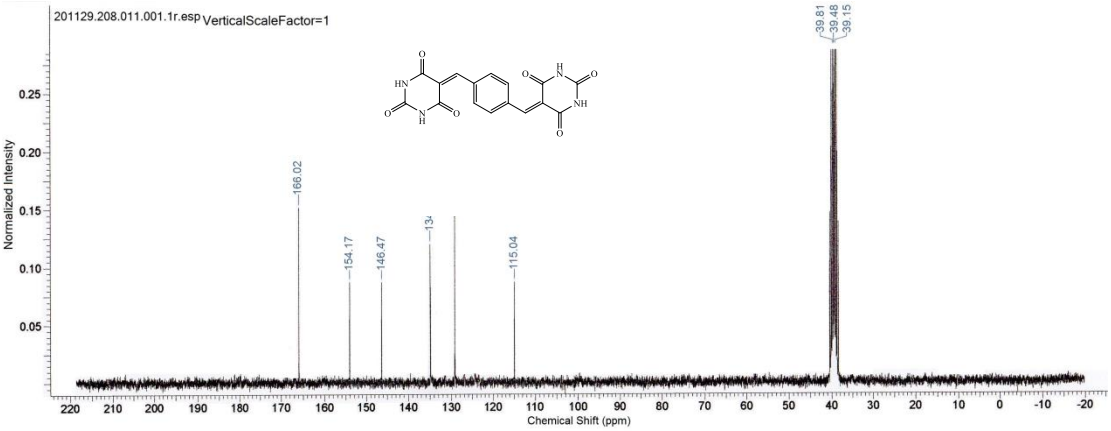


Figure (22): ^{13}C-NMR for compound (2)

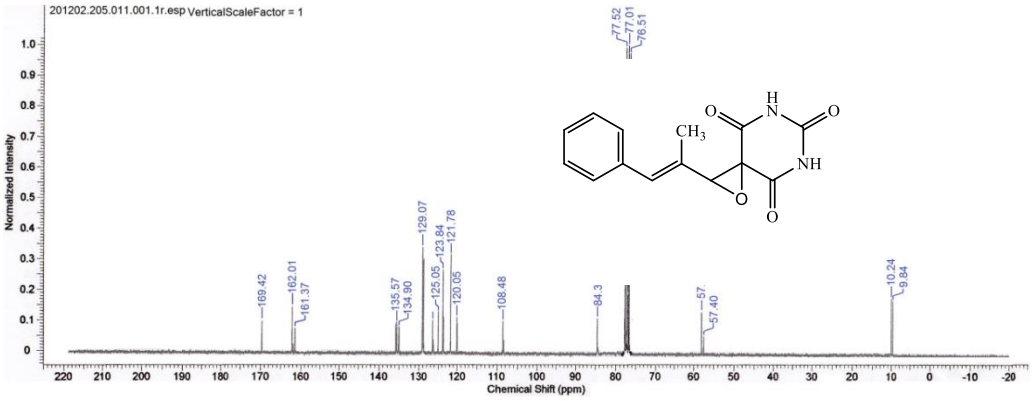


Figure (23): ^{13}C-NMR for compound (3)

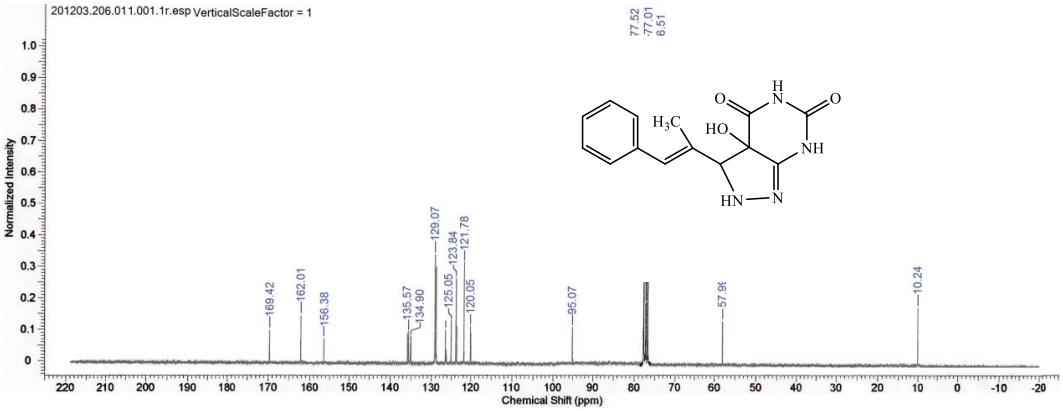


Figure (24): ^{13}C-NMR for compound (3a)

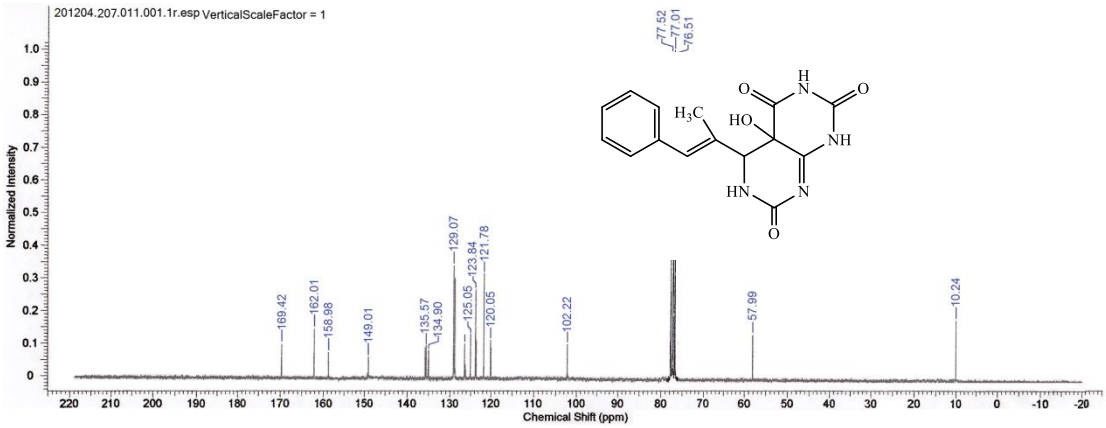


Figure (25): ^{13}C-NMR for compound (3b)

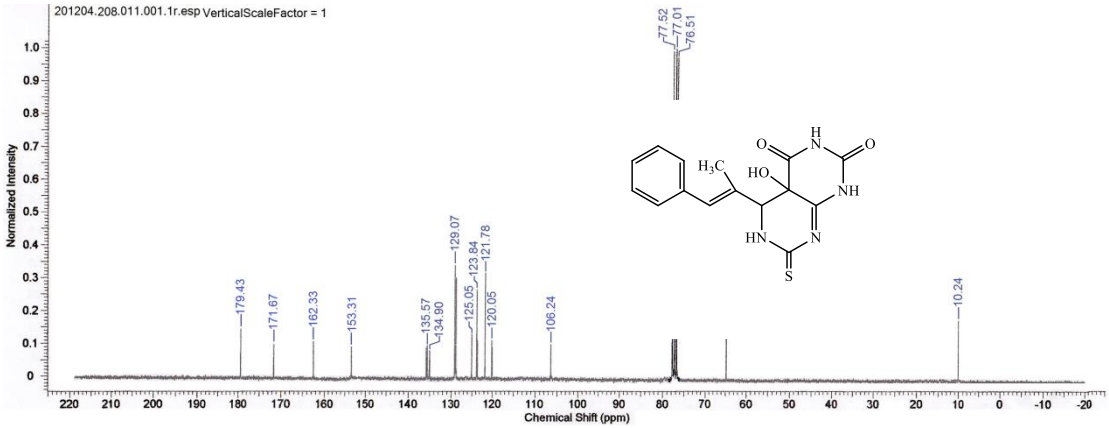


Figure (26): ^{13}C-NMR for compound (3c)

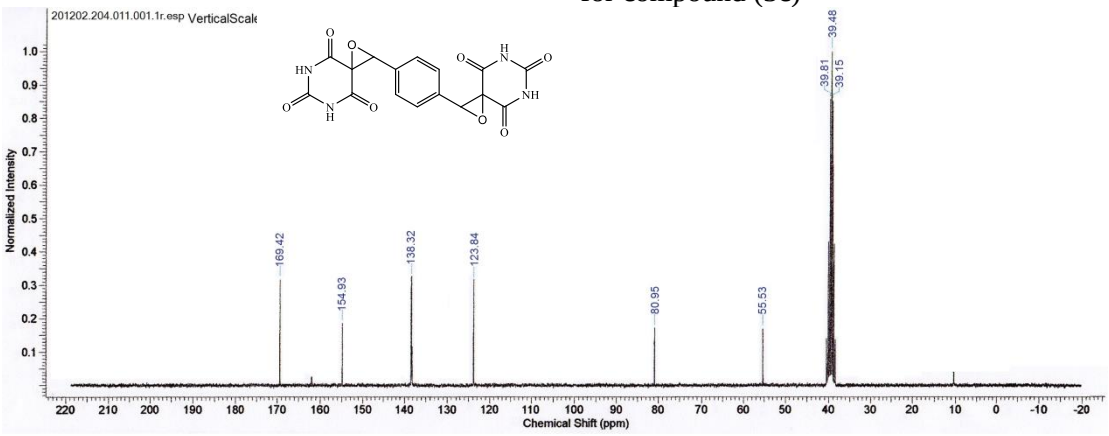


Figure (27): ^{13}C-NMR for compound (4)

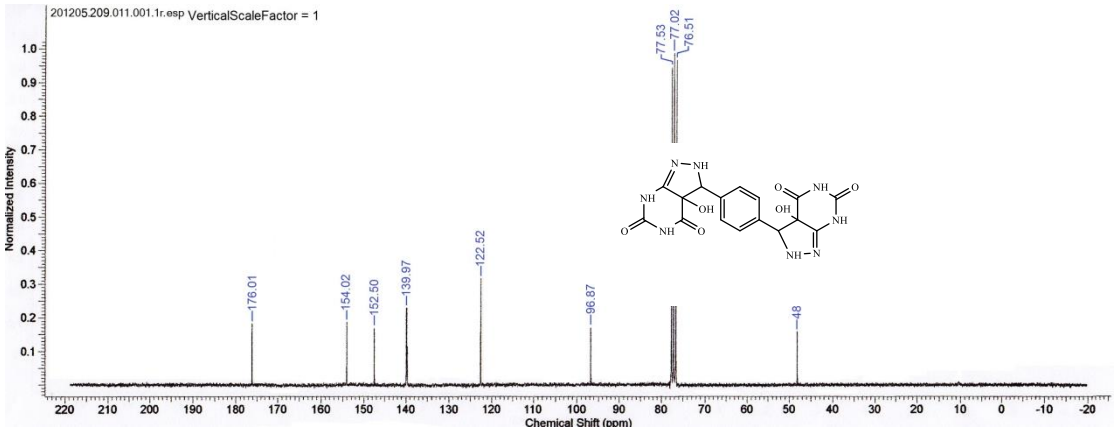


Figure (28): ^{13}C-NMR for compound (4a)

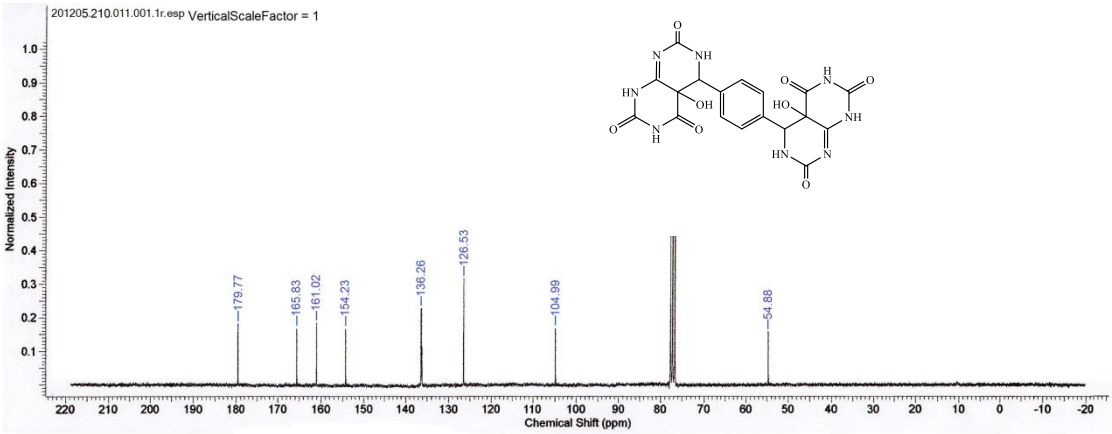


Figure (29): ^{13}C-NMR for compound (4b)

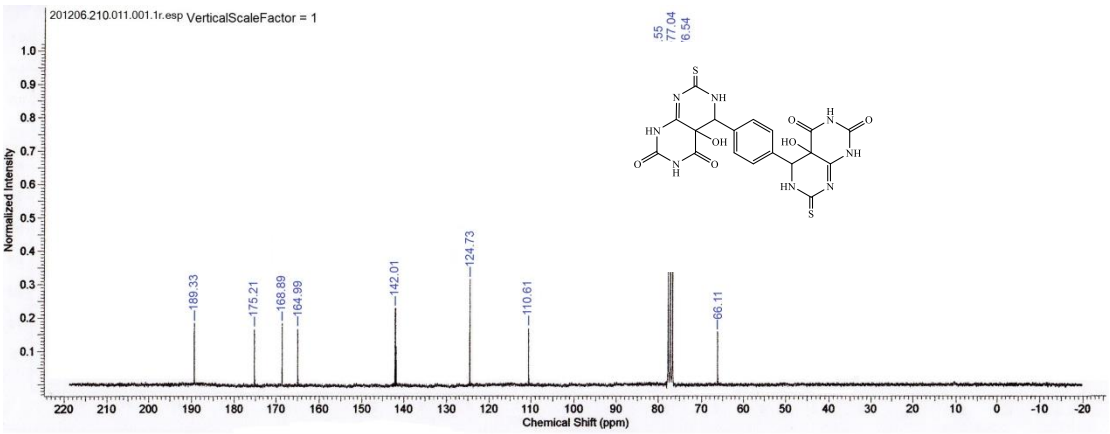


Figure (30): ^{13}C-NMR for compound (4c)

Acknowledgment
We want to thank the president of the university of Mosul Dr. Kossay AL-Ahmady.

REFERENCES:

[1] D. Best, D. J. Burns, and H. W. Lam, "Direct Synthesis of 5-Aryl Barbituric Acids by Rhodium(II)-Catalyzed Reactions of Arenes with Diazo Compounds," *Angew. Chemie*, vol. 127, no. 25, pp. 7518–7521, 2015, doi: 10.1002/ange.201502324.

[2] N. Seyyedi, F. Shirini, M. Safarpoor, and N. Langarudi, "RSC Advances catalysts for the synthesis of barbituric and," *RSC Adv.*, vol. 6, pp. 44630–44640, 2016, doi: 10.1039/C6RA05878G.

[3] J. Khalafy, M. Ezzati, P. Madadi, A. P. Marjani, and H. Y. Asl, "Synthesis of Some 5-[2-Aryl-2-oxoethyl]-1,3-dimethylpyrimidine-2,4,6-trione Derivatives by a One-pot, Three-component Reaction," *South African J. Chem.*, vol. 70, no. 24, pp. 132–136, 2017, doi: 10.17159/0379-4350/2017/v70a19.

[4] N. R. Dighore, P. L. Anandgaonker, S. T. Gaikwad, and A. S. Rajbhoj, "Solvent free green synthesis of 5-arylidine barbituric acid derivatives catalyzed by copper oxide nanoparticles.," *Res. J. Chem. Sci.*, vol. 4, no. 7, pp. 93–98, 2014, [Online]. Available: http://www.isca.in/rjcs/Archives/v4/i7/14.ISCA-RJCS-2014-114.pdf.

[5] B. M. Uttam, "Organic Chemistry : An Indian Journal A Solvent Free Green Protocol for Synthesis of 5-Arylidine Barbituric Acid," *Org Chem Ind J.*, vol. 12, no. 3, p. 102, 2016.

[6] M. P. Parmar, R. M. Vala, and H. M. Patel, "Importance of Hybrid Catalysts toward the Synthesis of 5 H - Pyrano [2 , 3 - d] pyrimidine-2-ones / 2 , 4-diones (Thiones)," 2023, doi: 10.1021/acsomega.2c05349.

[7] Y. Hosseini, S. Rastgar, A. Zerrin Heren, Orhan Büyükgüngör, and N. N. Pesyan, "One-pot new barbituric acid derivatives derived from the reaction of barbituric acids with BrCN and ketones," *J. Chinese Chem. Soc.*, vol. 58, no. 3, pp. 309–318, 2011, doi: 10.1002/jccs.201190031.

[8] R. Haggam, "Heterocyclization of barbituric acid : Synthesis of novel condensed pyrimidines," vol. 3, no. 4, pp. 692–698, 2015.

[9] S. Pozo, S. Vera, M. Oiarbide, and C. Palomo, "Catalytic Asymmetric Synthesis of Quaternary Barbituric Acids," pp. 15308–15311, 2018, doi: 10.1021/jacs.7b09124.

[10] D. Tsiourvas, Z. Sideratou, A. A. Haralabakopoulos, G. Pistolis, and C. M. Paleos, "Molecular recognition of amphiphilic di(dodecyl)barbituric acid with long-chain alkylated adenine and thymine derivatives," *J. Phys. Chem.*, vol. 100, no. 33, pp. 14087–14092, 1996, doi: 10.1021/jp9603344.

[11] M. Gholami, S. Nasseri, A. Mesdaghinia, F. Vaezi, A. Mahvi, and K. Naddaffi, "Ar ch of ch of," vol. 30, no. 1, pp. 73–80, 2001.

[12] J. A. Abdullah, R. K. Yhya, and H. T. S. A. S. Toohi, "Synthesis of some Imidazolidinone compounds under phase transfer conditions and photo cleavages studies of molecular for these compounds," *Egypt. J. Chem.*, vol. 64, no. 12, pp. 6959–6966, 2021, doi: 10.21608/EJCHEM.2021.79805.3924.

[13] S. Kumar *et al.*, "Synthesis, molecular docking and biological evaluation of bis-pyrimidine Schiff base derivatives," *Chem. Cent. J.*, vol. 11, no. 1, pp. 1–16, 2017, doi: 10.1186/s13065-017-0322-0.

[14] J. T. Li, X. F. Liu, Y. Yin, and C. Du, "Synthesis of 2,3-epoxy-1-phenyl-3-aryl-1-propanone by combination of phase transfer catalyst and ultrasound irradiation," *Org. Commun.*, vol. 2, no. 1, pp. 1–6, 2009.

[15] S. T. Ha and Y. W. Low, "Synthesis and phase transition behaviours of new chalcone derivatives," *J. Chem.*,

vol. 2013, 2013, doi: 10.1155/2013/943723.
[16] S. N. Kegeler, "Organocatalyzed Synthesis of Epoxides from Chalcones Utilizing Amino Acids," 2018, [Online]. Available: https://scholarworks.wmich.edu/masters_theses.
[17] M. Salem, "Some reactions of chalcone epoxides: Part II," *Indian J. Chem. Sect. B*, vol. 16, no. August 1978, pp. 693–696, 1978.
[18] I. K. Ho and R. A. Harris, "Mechanism of action of barbiturates.," *Annu. Rev. Pharmacol. Toxicol.*, vol. 21, pp. 83–111, 1981, doi: 10.1146/annurev.pa.21.040181.000503.
[19] S. Nisa and M. Yusuf, "Novel 1,3,4-bisthiadiazoline derivatives: Syntheses, in-vitro antimicrobial and antioxidant studies," *J. Saudi Chem. Soc.*, vol. 25, no. 2, p. 101195, 2021, doi: 10.1016/j.jscs.2020.101195.
[20] M. Kidwai, R. Thakur, and R. Mohan, "Ecofriendly synthesis of novel antifungal (thio) barbituric acid derivatives," *Acta Chim. Slov.*, vol. 52, no. 1, pp. 88–92, 2005.
[21] Y. Deng, S. Yin, X. Jing, and Y. Zheng, "Design, synthesis, and antiviral activities evaluation of novel quinazoline derivatives containing sulfonamide moiety," *Heterocycl. Commun.*, vol. 29, no. 1, pp. 1–8, 2023, doi: 10.1515/hc-2022-0160.
[22] A. Habib, S. Riaz, I. Ahmad, D. Najaf Iqbal, and S. Kamal, "C-Ni bond functionalization in the reaction of binuclear cyclometallated Ni(II) complexes with chlorophosphines," *J. Saudi Chem. Soc.*, vol. 25, no. 2, p. 101178, 2021, doi: 10.1016/j.jscs.2020.101178.
[23] H. T. S. A. S. Toohi, M. A. Rabeea, J. A. Abdullah, and R. F. Muslim, "Synthesis and characterization activated carbon using a mix (asphalt-polypropylene waste) for novel azo dye (HNDA) adsorption," *Carbon Lett.*, vol. 31, no. 5, pp. 837–849, 2021, doi: 10.1007/s42823-020-00185-3.
[24] N. Hazerei et al, "A p p l ied C hemical R esearch Synthesis of Pyrazolopyranopyrimidine and Dihydropyrano [2 , 3- c] pyrazole Derivatives using Vitamin D as an Efficient Catalyst under Green Condition," 2023.
[25] N. Al-Jaeed, S. Lahsasni, H. A. Ghabbour, and N. N. E. El-Sayed, "Crystal structure of N,N-dimethyl-N′-(2-methyl-4-oxo-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-d]pyrimidin-3(4H)-yl)formimidamide, C14H18N4OS," *Zeitschrift fur Krist. - New Cryst. Struct.*, vol. 232, no. 2, pp. 217–219, 2017, doi: 10.1515/ncrs-2016-0212.
[26] J. A. Abdullah and M. A. Rabeaa, "Grinding-Assisted Synthesis of Some Heterocyclic Compounds JA," *Asian J. Chem.*, vol. 32, no. 7, pp. 1713–1718, 2020.
[27] J. Li *et al.*, "Design , synthesis , and anticancer activity," pp. 4–13, 2023.
[28] M. M. Ghorab, A. M. Soliman, M. S. Alsaid, and A. A. Askar, "Synthesis, antimicrobial activity and docking study of some novel 4-(4,4-dimethyl-2,6-dioxocyclohexylidene)methylamino derivatives carrying biologically active sulfonamide moiety," *Arab. J. Chem.*, vol. 13, no. 1, pp. 545–556, 2020, doi: 10.1016/j.arabjc.2017.05.022.
[29] K. M. Hello, J. K. Shneine, and A. A. Numan, "synthesis and biological activity of some barbituric acid derivatives via Schiff´ s bases," *Iraqi J Sci*, vol. 50, no. September, pp. 423–430, 2009.
[30] S. Shaygan, H. Pasdar, N. Foroughifar, M. Davallo, and F. Motiee, "Cobalt (II) complexes with Schiffbase ligands derived from terephthalaldehyde and ortho-substituted anilines: Synthesis, characterization and antibacterial activity," *Appl. Sci.*, vol. 8, no. 3, 2018, doi: 10.3390/app8030385.
[31] J. A. Abdullah, B. J. M. Aldahham, M. A. Rabeea, F. A. Asmary, H. M. Alhajri, and M. A. Islam, "Synthesis, characterization and in-silico assessment of novel thiazolidinone derivatives for cyclin-dependent kinases-2 inhibitors," *J. Mol. Struct.*, vol. 1223, 2021, doi: 10.1016/j.molstruc.2020.129311.
[32] F. A. Pokatilov, H. V. Akamova, and V. N. Kizhnyaev, "Synthesis and properties of tetrazole-containing polyelectrolytes based on chitosan, starch, and arabinogalactan," *E-Polymers*, vol. 22, no. 1, pp. 203–213, 2022, doi: 10.1515/epoly-2022-0026.
[33] N. A. Salamou *et al.*, "Synthesis, characterization, and antibacterial activity of a new poly azo compound containing N-arylsuccinimid and dibenzobarrelene moieties," *Heterocycl. Commun.*, vol. 29, no. 1, 2023, doi: 10.1515/hc-2022-0157.
[34] M. A. Sattar, M. K. Khatun, T. K. Sarkar, and S. M. Al-reza, "Ecofriendly Synthesis of Bioactive 2-thiobarbituric Acid Derivatives," vol. 2, no. 3, pp. 83–86, 2017, doi: 10.11648/j.ijbc.20170203.11.
[35] V. A. Dixit *et al.*, "Design and synthesis of novel Y-shaped barbituric acid derivatives as PPARγ activators," *Eur. J. Med. Chem.*, vol. 108, pp. 423–435, 2016, doi: 10.1016/j.ejmech.2015.11.030.