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synthesis and spectroscopic study of some new heterocyclic compounds derived from Carbendazim

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Abstract
This work consists of the preparation of new heterocyclic compounds of five and six members starting from (ester) carbendazim (1). Reacted some compounds like ammonia derivative to the ester (1) to form compounds (2, 3 & 4). And then compounds (2&3) react with acetyl acetone to produce compounds (5 & 6) and then reacted with benzil to produce compounds (7, 8 & 9) respectively. Finally, compounds (2, 3 & 4) react with ethylchloro acetate to produce compounds (10, 11 & 12). In the other hand the ester compound (1) reacted with semicarbazid, thiosemicarbazide respectively in found phosphoryl chloride to give compounds (13&14). As shown in the Scheme (1).
Keywords: Carbendazim, Oxadiazole, Imidazole, Thiazole, Triazine, pyridazine.

تشييد ودراسة طيفية لبعض المركبات الحلقية غير المتجانسة الجديدة المشتقة من الكاربيندازيم بالطريقة الخضراء

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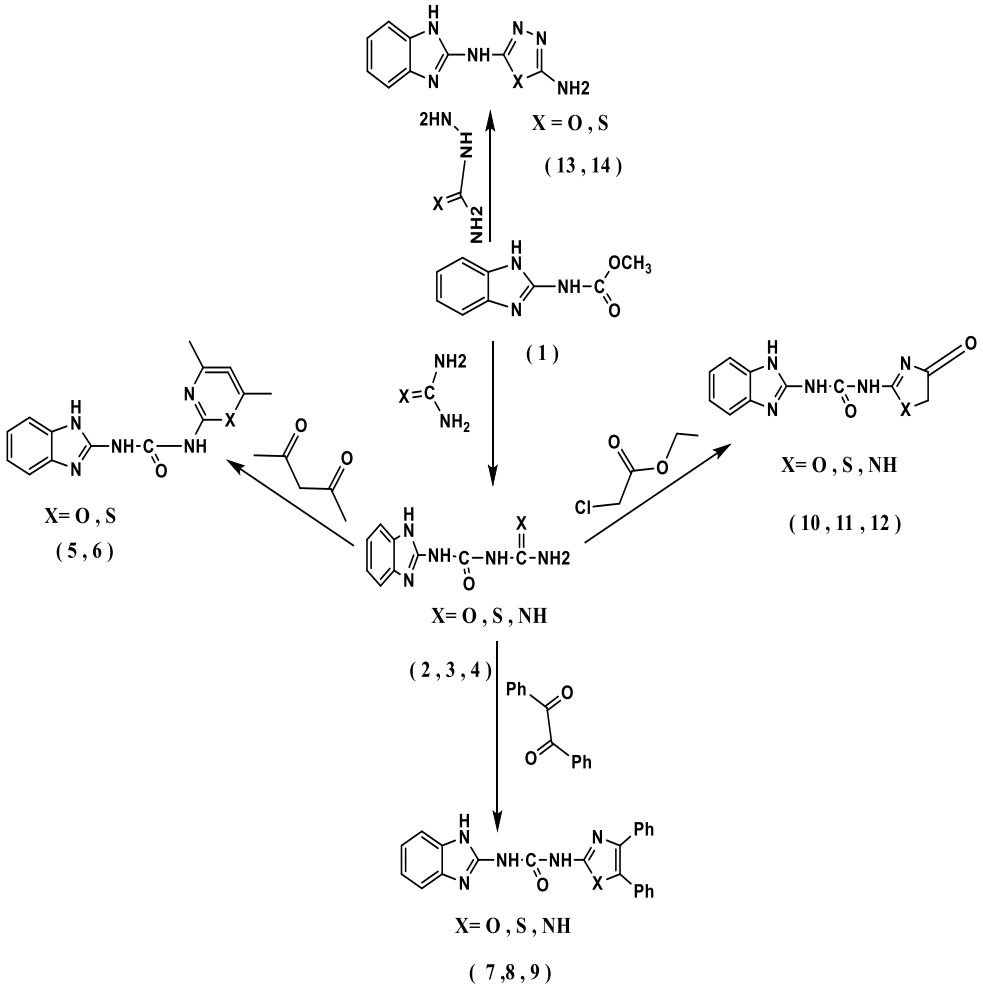
الملخص:
هذا العمل يتضمن تحضير مركبات حلقية غير متجانسة جديدة خماسية وسداسية الحلقة تبدأ من المادة الاولية كاربندازيم (1). تفاعل بعض المركبات مثل مشتقات الأمونيا مع الكاربندازيم (1) لتكوين المركبات (2، 3 و 4). ثم تتفاعل المركبات (2، 3) مع أسيتيل أستيتون لتكوين المركبات (5 و 6)، ثم تتفاعل مع بنزيل لتكوين المركبات (7، 8 و 9) على التوالي. وأخيراً، تتفاعل المركبات (2، 3 و 4) مع إيثيل كلورو أسيتات لتكوين المركبات (10، 11 و 12). ومن ناحية أخرى، يتفاعل مركب الاستر (1) مع سيميكاربازيد وثايوسيميكاربازيد على التوالي بوجود كلوريد الفوسفور لإعطاء المركبات (13 و 14). كما هو موضح في المخطط (1) .
الكلمات المفتاحية : كاربندازيم ، اوكسادايازول ، ايميدازول ، ثايازول ، ترايازين ، بيريدازين.

1.Introduction
Heterocyclic compounds constitute the largest and most varied family of organic compounds. Today there are a lot of heterocyclic compounds are known, day by day the number is increasing rapidly due to the enormous synthetic research and also their synthetic utility[1]. Heterocyclic compounds have a role in most fields of

sciences such as medicinal chemistry, biochemistry also another area of sciences[2]. Carbendazim is one compound of heterocyclic compounds, is a systemic fungicide having wide applications for controlling fungal diseases in agriculture, forestry and veterinary medicines. Carbendazim extensive and repeated use induces acute and delayed toxic effects on humans, invertebrates, aquatic life forms and soil microorganisms[3]. Carbendazim is a powder the molecular weight of 191.19 g/mol , the compound melts more than 300°C[4]. It is the active component of the extensively used fungicide - Carbendazim, a systemic benzimidazole fungicide, is applied repeatedly to control plant diseases including soil borne diseases, over a growing season. Studies were carried out under laboratory conditions to assess the effects of repeated carbendazim applications on its persistence and microbial community in soil [5]. It is a fungicide widely used for controlling fungi affecting fruits, vegetables, field crops, etc.[6]. Carbendazim [Methyl-N-benzimidazol-2-yl-carbamate] (MBC) is a light gray powder.



Scheme 1: Showed Synthesis Compounds (2-14)

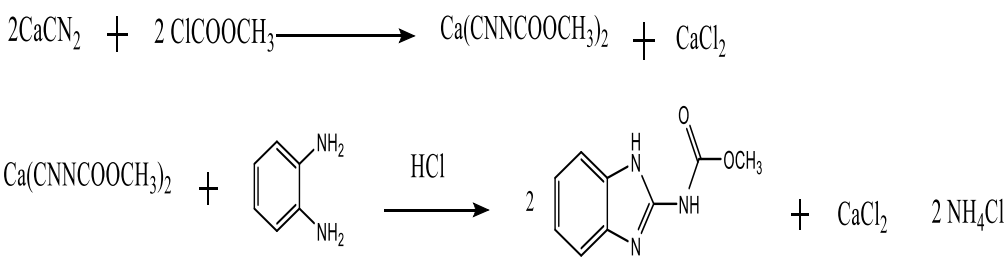
2.Experimental

2.1. Materials:

Melting points were measured on Electrothermal Gallen Kamp melting points and were uncorrected. Infrared (FT.IR.) spectra was recorded as (KBr) disk using a Brucker FT.IR. spectrophotometer. ^{1}H-NMR ^{13}C-NMR spectra was recorded using Inova 500 MHz by using DMSO - d6 as solvent, and using TMS as internal standard in University of Basrah, Iraq. And all chemicals and solvents from Fluka, Scharlau, Aldrich & BDH.

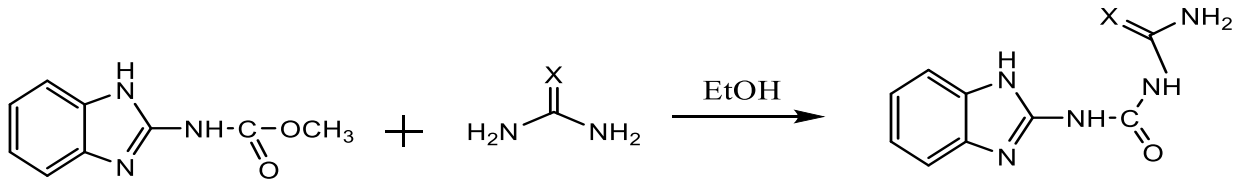
2.2. Methods:

❖ Preparation of compound Carbendazim (1)



Calcium Cyanamide will be suspended in water and will be agitated. Under stirring Methylchloroformate will be added at 35 deg C for 1 hour and maintained stirring for 2 hours. After confirming the completion of reaction, the reaction mass will be filtered and the filtrate will be mixed with Orthophenylene diamine and will be heated to 90 deg C maintaining pH 4.5 by the addition of HCl. After completion of reaction, the reaction mass will be cooled to 60 deg C and filtered, washed and dried to get carbendazim.

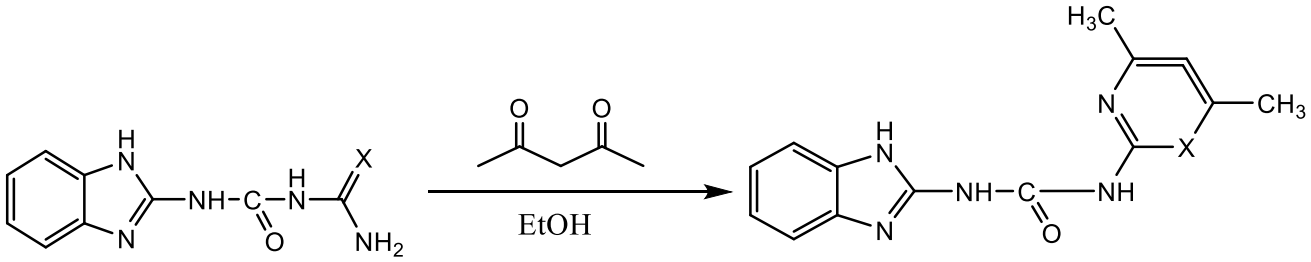
❖ Preparation of compounds (2 , 3 , 4) :



(1) X = O ⇨ 2 , X = S ⇨ 3 , X = NH ⇨ 4

Compound [2 , 3 , 4] was preparation from the reaction of compound [1] (0.00063 mol) in absolute ethanol (15 ml) with urea , thiourea , guanidine nitrate (0.00061 mol) and then added small amount of zirconyl chloride octahydrate $ZrOCl_2.8H_2O$ as a catalyst . And then the mixture was reflexed for (6 – 8) hours. After cooling and filtering, a solid product was obtained. The product was recrystallized from EtOH and dried under room temperature to give final compounds.

❖ Preparation of compounds (5 , 6) :

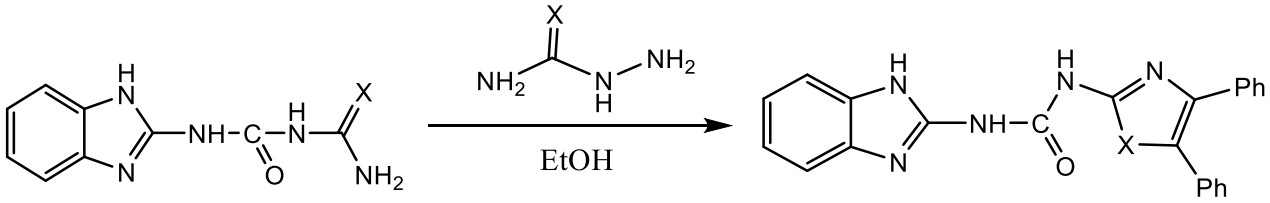


X = O ⇨ 2 ، X = S ⇨ 3

X = O ⇨ 5 ، X = S ⇨ 5

Compounds [2 , 3 ,4] (0.00012 mol) was dissolved absolute ethanol (10 ml) , acetyl acetone (0.00012 mol) was mixed to produce compounds [5 , 6]. The mixture was refluxed for 7 hours, cooled and neutralized with ammonium hydroxide solution. The precipitate was filtered and washed with water. petroleum ether (80-100) was used for recrystallization .

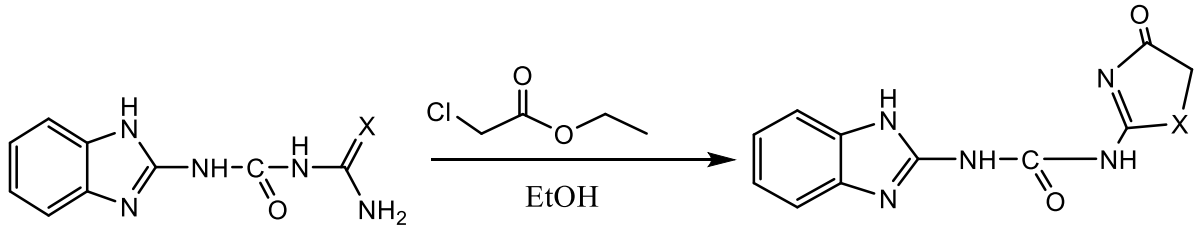
❖ Preparation of compounds (7 , 8 , 9) :



X = O ⇨ 7 ، X = S ⇨ 8 ، X = NH ⇨ 9

Compounds [2 , 3 ,4] (0.00012 mol) was dissolved absolute ethanol (10 ml) , benzyl or benzoin (0.00012 mol) was mixed to produce compounds [7 , 8 , 9]. The mixture was refluxed for 7 hours, cooled and neutralized with ammonium hydroxide solution. The precipitate was filtered and washed with water. petroleum ether (80-100) was used for recrystallization.

❖ Preparation of compounds (10, 11, 12) :

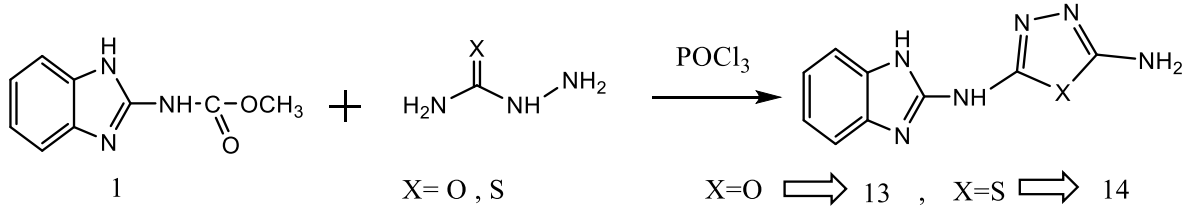


X=O ⇨ 10 ، X=S ⇨ 11 ، X=NH ⇨ 12

Compounds [2 , 3 ,4] (0.00012 mol) was dissolved absolute ethanol (10 ml) , ethyl chloroacetate (0.00012 mol) was mixed to produce compounds [10 , 11 , 12]. The mixture was refluxed for 7 hours, cooled and neutralized with ammonium

hydroxide solution. The precipitate was filtered and washed with water. petroleum ether (80-100) was used for recrystallization.

❖ Preparation of compounds (13 , 14) :



A mixture of compound [1] (0.01 mol , with semicarbazide , thiosemicarbazide (0.01 mol) and (5 ml) phosphorus oxy chloride was refluxed for 8 hrs. The cold reaction mixture was poured on crushed ice and neutralized by adding sodium hydroxide solution. The resulting solid was filtered and recrystallized from chloroform to give final product.

3-Results & Discussion:

Table 1: Physical properties of Compounds

NO.	X	m.p ℃	Color	Yield %	Molecular weight	Molecular formula
1	……..	302 – 307 dec.	white	85	191.19	$C_9H_9N_3O_2$
2	O	290 – 295 dec.	white	68	219.20	$C_9H_9N_5O_2$
3	S	185 – 190 dec.	white	70	235.27	$C_9H_9N_5OS$
4	NH	>300	white	65	218.22	$C_9H_{10}N_6O$
5	O	>300	yellow	72	283.29	$C_{14}H_{13}N_5O_2$
6	S	>300	white	56	299.35	$C_{14}H_{13}N_5OS$
7	O	290 dec.	Yellowish white	58	395.42	$C_{23}H_{17}N_5O_2$
8	S	295 dec.	Yellowish white	63	411.48	$C_{23}H_{17}N_5OS$
9	NH	175	Light brown	80	394.44	$C_{23}H_{18}N_6O$
10	O	>300	white	85	243.23	$C_{11}H_9N_5O_2$
11	S	192 – 195	Dark white	90	259.29	$C_{11}H_9N_5OS$
12	NH	185 – 190	yellow	92	242.24	$C_{11}H_{10}N_6O$

13	O	145 – 148	Dark white	86	216.20	$C_9H_8N_6O$
14	S	158 – 161	white	94	232.27	$C_{11}H_{10}N_6S$

Table 2: FT-IR of synthesized compounds

Comp. No.	Ft IR (KBr) Vcm-1			
	C=O	C=N	NH	Other
1.	1711	1621	3318	---------
2.	1711	1622	3317	---------
3.	1710	1627	3323	C=S , 1266
4.	1711	1625	3319	C-O-C ASS , 1263
5.	1710	1623	3316	C=S , 1266
6.	1710	1627	3326	---------
7.	1710	1626	3317	C-O-C ASS , 1265
8.	1710	1655	3331	C=S , 1266
9.	1626	1592	3318	----------
10.	1711	1627	3318	C-O-C ASS , 1266
11.	1711	1625	3318	C=S , 1265
12.	1745	1627	3319	----------
13.	1750	1627	3361	C-O-C ASS , 1244
14.	1756	1644	3184	C=S , 1226

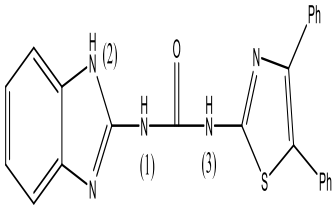
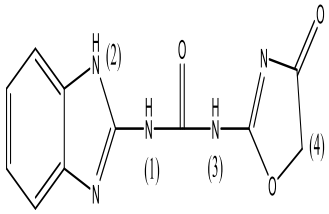
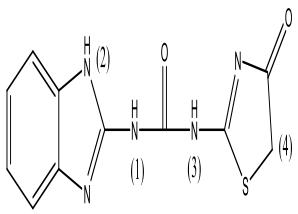
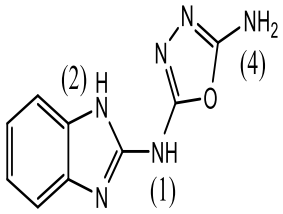
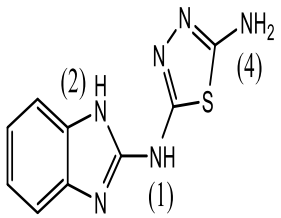
Comp. NO.	Structure	^{1}H-NMR, DMSO-d6, δ (ppm)	^{13}C-NMR, DMSO-d6, δ (ppm)
8		8.028 (1H, S, H1&H3), 8.046(1H, S, H2), 6.56 -7.93 (14H, m, aromatic protons)	111.93-136.36(C-aromatic rings); 136.04 (N-C=O); 195.30 (S-C=N); 132.70(C=N)
10		8.66 (1H, S, H1), 8.95(1H, S, H2&H3), 5.49(2H, S, H4), 7.37-7.68 (4H, m, aromatic protons	111.87-134.04(C-aromatic rings); 155.76 (N-C=O-CH_2); 153.09 (O-C=N); 148.75(C=O); 70.22(CH_2)
11		8.66 (1H, S, H1), 9.21(1H, S, H2&H3), 3.75(2H, S, H4), 7.05-7.41 (4H, m, aromatic protons	113.95-136.36(C-aromatic rings); 167.68 (N-C=O-CH_2); 155.76 (S-C=N); 148.75(NH-C=O-NH); 59.44(CH_2)
13		8.66 (1H, S, H1), 8.95(1H, S, H2), 4.55(2H, S, H3), 7.37-7.68 (4H, m, aromatic protons	111.81-129.91(C-aromatic rings); 144.25(C=N); (O-C=N); 150.96-153.08
14		9.01 (1H, S, H1), 12.68 (1H, S, H2), 4.01(3H, d, H3), 7.196-8.59 (4H, aromatic)	112.73-146.72(C-aromatic rings); 151.63(C=N); 157.73-163.50 (S-C=N)

Table 3: shows the ^{1}H-NMR & ^{13}C-NMR Spectrum of synthesized Compounds

4.Conclusions:

In this study, using simple and easy experimental methods and suitable reaction conditions, we were able to synthesize new heterocyclic compounds with both five-member and six-member ring structures. This was achieved through the reaction of esters (Carbendazim) with urea, thiourea, semicarbazide, thiosemicarbazide, and others, as depicted in Scheme (1). It is expected that these resulting compounds will have various chemical applications in the fields of pharmaceuticals and agriculture.

5.References:

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