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Research Article

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Synthesis and characterization of some new substituted malonic ester derivatives containing thiazolidone

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ABSTRACT

Some new compounds were prepared containing cycle thiazolidene from schiff bases which prepared from malonic ester with hydrazine in presence of ETOH. Then schiff bases reacted with 2-mercapto acetic acid to give thiazolidene. The prepared compounds identified by FT-IR spectroscopy, physical properties including melting point, boiling point and some of them were identified by ^{1}H-NMR and ^{13}C-NMR.

Key words: malonic ester, schiff bases, thiazolidone.

INTRODUCTION

Malonic acid and its esters are characterized by the large number of condensation products. They are important intermediates in syntheses of vitamins B1 and B6, barbiturates, non-steroidal anti-inflammatory agents, other numerous pharmaceuticals, agrochemicals and flavors & fragrances compounds.

In this work, We have documented the synthesis of some novel heterocyclic compounds prepared from cyclization of Schiff bases with different reagent like bis-4-thiazildine derivatives (10,11,12). The first member of heterocyclic compounds were synthesized by Staudinger1 in 1907 [1].

A heterocyclic compounds are one which possesses a cyclic structure with at least one or two kinds of hetero atoms in the ring. Nitrogen, oxygen and sulphur are the most common hetero atoms(2) as shown below .

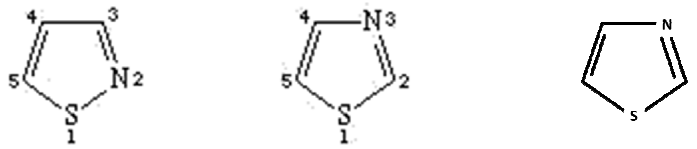


Figure -1- of heteroaromatic rings with two heteroatoms

Heterocyclic compounds have a wide range of applications. Their applications in pharmaceutics are because of their specific chemical reactivity. In most cases the chemist has specific reasons for synthesizing a particular compound, usually based on theoretical considerations, medicinal chemistry, biological mechanisms or a combination of all three. The heterocyclic compounds are very widely distributed in nature and are very essential to living organisms. They play a vital role in the metabolism of all the living cells. Also, bisheterocyclic compounds exhibit various

biological activities[3]. in this work Schiff bases (4, 5, 6) also react with two moles of mercaptoacetic acid to give bis 4-thiazildinone derivatives(13-21).

Heterocycles containing the thiazole moiety like 4-thiazolidine, as shown below ,

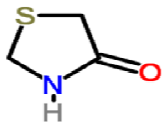


Figure -2- (4-oxothiazolidine)

The presence of reactive unsaturated ketone group in -4-thiazolidineone is responsible for their antibacterial activity [4,5,6] and antibacterial activity[7]important molecule also reported hypoglycemic activity[8] antibacterial activity[9] , antioxidant activity[10].

Bis 4-thiazildine derivatives (13-21) were reacted with two moles of poly acryloyl chloride in the presence of acetic anhydride to give poly bis (N,N-acryloyl) 4-oxathiazildine derivatives (22-30) as predict in table (1,2,3) .

EXPERIMENTAL SECTION

Instruments and chemicals :
A-instruments:
Uncorrected melting points were determined on Gallen-Kamp apparatus. Fourier transform infrared (FTIR) spectra were registered on a SHIMADZU (8300, Kyoto, Japan) infrared spectrophotometer, using KBr discs.

The 1H-NMR spectra were measured on varian EM 60 and JEOL-90 MHz spectrometers with TMS as internal reference, chemical shifts were expressed in ppm.

B-chemicals:
All chemicals in this work were supplied from BDH,Merk and Aldrich.

Table (1) : physical properties of prepared compounds

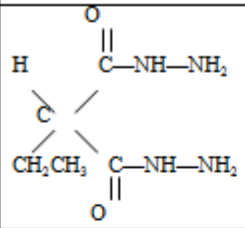
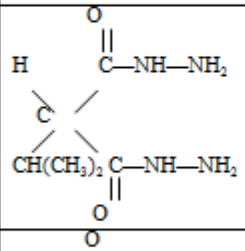
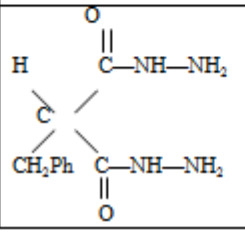
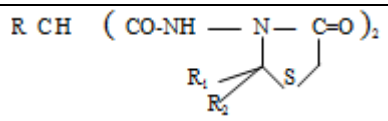
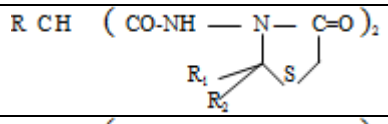
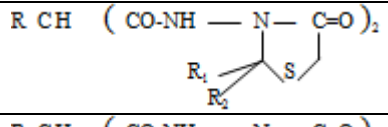
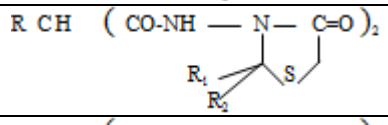
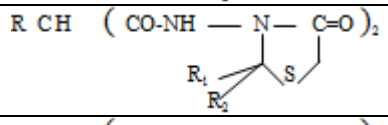
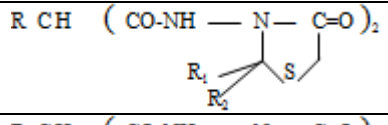
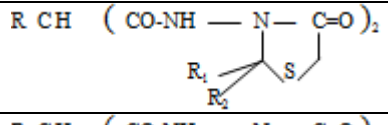
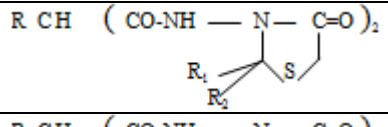
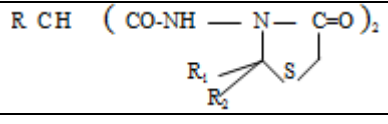
Comp. No.	Structure of Comp.	Melting point °C	Color	Yield %
1		95 -97	Gray black ppt	59 %
2		105 - 107	Gray black ppt	66 %
3		162 - 164	White ppt	60 %

Table (1) : physical properties of prepared compounds

Comp. No.	Structure of Comp.	Melting point °C	Color	Yield %
4	R H C (CO NH-N == C R_1 R_2) $_2$	177 - 179	pale White ppt.	56 %
5	R H C (CO NH-N == C R_1 R_2) $_2$	232 - 234	Yellow ppt.	60 %
6	R H C (CO NH-N == C R_1 R_2) $_2$	272 -274	Pale Yellow ppt.	55 %
7	R H C (CO NH-N == C R_1 R_2) $_2$	260 -263	pale White ppt.	48 %
8	R H C (CO NH-N == C R_1 R_2) $_2$	263-264	pale White ppt.	56 %
9	R H C (CO NH-N == C R_1 R_2) $_2$	293-294	White ppt.	58 %
10	R H C (CO NH-N == C R_1 R_2) $_2$	125 -127	White ppt.	78 %
11	R H C (CO NH-N == C R_1 R_2) $_2$	205 - 208	White ppt.	70 %
12	R H C (CO NH-N == C R_1 R_2) $_2$	233 - 235	White ppt.	54 %

Table (1) : physical properties of prepared thiazolidinone compound

Comp. No.	Structure of Comp.	Melting point °C	Color	Yield %
13		210-212	White ppt	70 %
14		215- 216	White ppt	70 %
15		218-219	White ppt	71 %
16		213-215	White ppt	77 %
17		216-217	White ppt	66 %
18		218 -220	White ppt	69 %
19		228-230	White ppt	74 %
20		270-272	White ppt	75 %
21		290 – 292	White ppt	71 %

R= CH_2 CH_3, CH
$(CH_3)_2$, CH_2Ph R1= Ph, CH_2CH_3, Ph R_2= H, H, CH_3

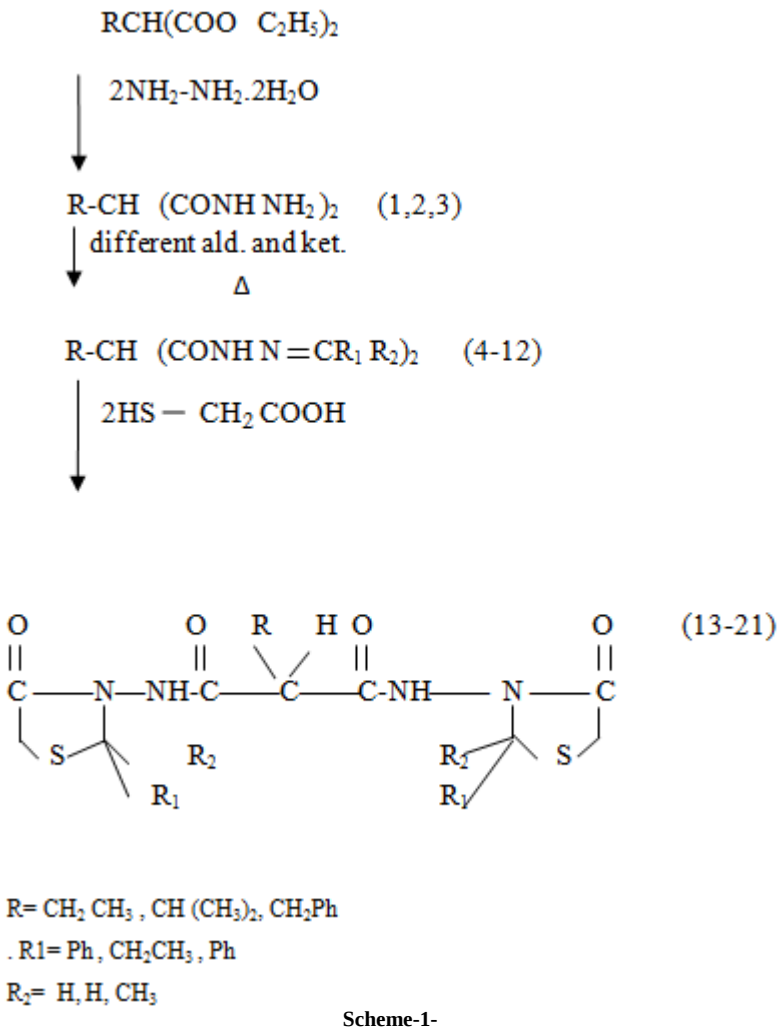
RESULTS AND DISCUSSION Synthesis of 2-alkyl malonyl hydrazide derivatives:

In round bottom flask was dissolved diethyl 2-alkyl malonate (0.01 mole) and hydrazine hydrate(0.2 mole) in 10 ml benzen. The reaction mixture was refluxed for 3 hrs. with stirring. Precipitate obtained filtered, dried and recrystallized from THF. Physical properties of compounds (1,2,3) are listed in table(1) , infrared spectral data in table (2) and solubility of product in table (3).

General method for Preparation 2- alkyl malonyl hydrazone derivatives:
In round bottom flask was placed 2-alkyl malonyl hydrazide (1,2,3) (0.10 mole) and different(aldhyde and keton) (0.20 mole) dissolved in 10 ml benzene. The reaction mixture was refluxed for 3 hrs. at 61 ^{O}C with stirring. Precipitate obtained filtered, dried and recrystallized from THF. Physical properties of compounds (4-12) are listed in table(1) , infrared spectral data in table (2) and solubility of product in table (3).

General Preparation of (4-oxothiazoldine) derivatives:
In round bottom flask was placed 2-alkyl malonyl hydrazone (4-12) (0.1mole) and Mercapto acetic acid (0.20 mole) dissolved in 10 ml benzene. The reaction mixture was refluxed for 3 hrs. at 61 ^{O}C with stirring. Precipitate obtained filtered, dried and recrystallized from THF. Physical properties of compounds (13-21) are listed in table(1) , infrared spectral data in table (2) and solubility of product in table (3) .

Main object of research to prepare of some new substituted malonic ester derivatives containing thiazolidone from alkyl malonyl as shown in schem (1),physical properties in table (1) and FTIR spectra bands in table (2).



Scheme-1-

Hydrazide compounds (1-3) appear Absorption band in (1645-1647) cm^{-1} duo to (C=O) amide , (3110-3150) cm^{-1} (-NH) , 3400 cm^{-1} (– NH_2) . Schiff basses (4-12) show disappearing of (NH_2) band (3400 cm^{-1} that indicate new band in (1510- 1658) cm^{-1} duo to (C= N) of schiff bases . compounds containing thiazolidone ring (13-21) show Absorption band in 1720 cm^{-1} (C=O thiazolidone ring) and (617 -720) cm^{-1} duo to (C-S) that indicate formation of thiazolidone ring as shown in table -4- solubility of prepare compound show in table -6 - . yield prepared compounds (48-86%) as show in table -4- . Compounds (10,16,19) in table -5- show ^{1}H NMR spectral data(δppm) for compound(10) δ 0.813 (t ,3H, CH_3 – CH_2-CH-) , (6.5-7.09) for Ph-H . δ 3.5(t,3H, CH_2- CH_3) , δ 3. 8 (t, 2H , CH-CONH) for compound (16) . δ 3.1(d , 2H, CH_2- Ph) and 8.5 (s, 1H , NH) for compound (19) .

Table (2): IR Spectral data of synthesized compounds

Comop. No.	C=O amide	C=N	- NH_2	-NH	alip - CH	C-N	= CH arom.	Other bond
1	1689	-	3589	3132	2937	1390	-	-
2	1647	-	3419	3162	2923	1320	-	-
3	1652	-	3446	3325	2937	1340	3010	-
4	1695	1627	-	3250	2960	1342	-	-
5	1645	1627	-	3200	2960	1330	-	-
6	1645	1550	-	3250	2960	1342	3015	-
7	1645	1627	-	3300	2960	1390	-	-
8	1645	1627	-	3250	2960	1320	-	-
9	1645	1627	-	3150	2960	1330	3010	-
10	1652	1560	-	3200	2980	1320	-	-
11	1652	1558	-	3200	2985	1340	-	-
12	1652	1558	-	3200	2975	1310	3020	-
13	1698	-	-	3325	2960	1390	-	720 C-S 1715 C=O thiazol ring
14	1658	-	-	3150	2995	1342	-	680 C-S 1700 C=O thiazol ring
15	1670	-	-	3200	2985	1330	3015	652 C-S 1720 C=O thiazol ring
16	1650	-	-	3225	2960	1390	-	630 C-S 1715 C=O thiazol ring
17	1655	-	-	3200	2985	1320	-	613 C-S 1700 C=O thiazol ring
18	1698	-	-	3120	2970	1340	3010	670 C-S 1720 C=O thiazol ring
19	1660	-	-	3225	2965	1310	-	700 C-S 1715 C=O thiazol ring
20	1669	-	-	3300	2985	1320	-	720 C-S 1700 C=O thiazol ring
21	1698	-	-	3200	2990	1350	3020	710 C-S 1720 C=O thiazol ring

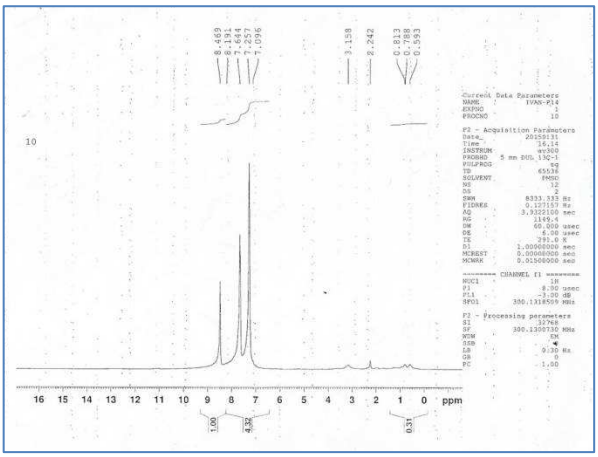
Table (3): ^{1}H NMR spectral data(δppm) for compounds(10,16,19)

Comop. No.	^{1}H NMR	^{13}C NMR
10	δ 0.813 (t ,3H, CH_3– CH_2-CH-) , 2.2 (m, 2H, CH_3– CH_2-CH-), 3.15 (t , 1H, CH_3– CH_2-CH-) ,8. 4 (S,1H , NH), 6.5 – 7.09 (Ph-H)	δ 39.7 (CH_3 – CH2- CH-) , 40.3 (CH_3 – CH_2- CH-) , 40.6 (CH_3 – CH_2- CH-) , 161.8 (O=C-NH-) , 133.7(N= CHPh), 128-132.7 (Ph) ,38.6 (C -N)
16	δ 3.5(t, 2H, CH_2- CH_3), 2.7(t ,3H, CH_2- CH_3) ,3. 8 (t, 1H , CH-CONH) , 4.3 (s, 1H , NH) , 2.86 (d,1 H , HC-$CHCH_3$) , 3.5 (d,2H , HC-CH_2CH_3) , 4.5 (s, 1 H , N HC=O) , 3.8 (d,1H, CH-C=O)	δ 39.8(CH- CH_3), 39.1(CH_2- CH_3) , 38 (-CH-$(CONH)_2$) , 46.7 (N-HC) , 39.7 (N- HC-CH_2) , 39.9 (HC-CH_3) ,40.6 (-CH-C=O), 182 (NH- C=O) , 78 .2(C-S)
19	δ 3.1(d , 2H, CH_2- Ph), 6.6-8 (m ,5H, CH_2- Ph) , 5.1 (t,1H, -CH-C=O) , 8.5 (s, 1H , NH) , 2.5 (t ,3H , CH_2-CH_3), 3.1 (d, 2 H , CH_2-CH_3).	δ 55.01(CH_2- Ph), 100 (CH_2- Ph) , 160 (CH-C=O) , 186 (N-C=O) ,160 (CH-C=O), 198 (NH- C=O) , 54.8 (C-N) , 55.09 (C-S) ,41.3 (N- CH-CH_2CH_3) , 41.4 (N- HC-CH_2CH_3) , 42.01 (N- CH-CH_2CH_3) .

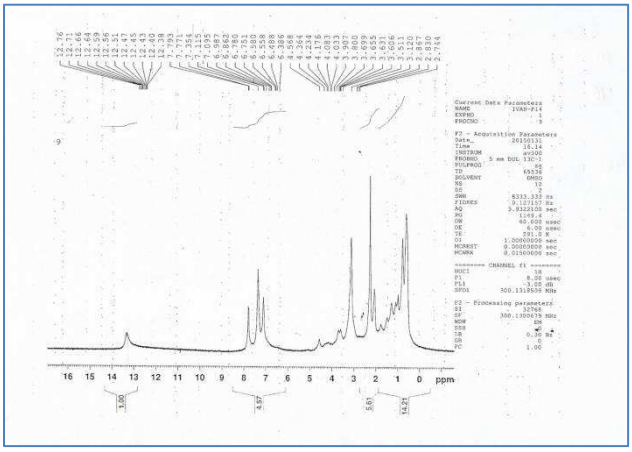
Table (4): solubility of Product

No.	Benzene	DMF	DMSO	THF	Water	CCl_4	$CHCl_3$	Acetone	EtOH
1	V.S	V.S	V.S	V.S	P.S	P.S	P.S	P.S	V.S
2	V.S	V.S	V.S	V.S	P.S	P.S	P.S	P.S	V.S
3	V.S	V.S	V.S	V.S	P.S	P.S	P.S	P.S	V.S
4	V.S	V.S	V.S	V.S	P.S	P.S	P.S	P.S	V.S
5	V.S	V.S	V.S	V.S	P.S	P.S	P.S	P.S	V.S
6	V.S	V.S	V.S	V.S	P.S	P.S	P.S	P.S	V.S
7	V.S	V.S	V.S	V.S	P.S	P.S	P.S	P.S	V.S
8	V.S	V.S	V.S	V.S	P.S	P.S	P.S	P.S	V.S
9	V.S	V.S	V.S	V.S	P.S	P.S	P.S	P.S	V.S
10	V.S	V.S	V.S	V.S	P.S	P.S	P.S	P.S	V.S
11	V.S	V.S	V.S	V.S	P.S	P.S	P.S	P.S	V.S
12	V.S	V.S	V.S	V.S	P.S	P.S	P.S	P.S	V.S
13	V.S	V.S	V.S	V.S	P.S	P.S	P.S	P.S	V.S
14	V.S	V.S	V.S	V.S	P.S	P.S	P.S	P.S	V.S
15	V.S	V.S	V.S	V.S	P.S	P.S	P.S	P.S	V.S
16	V.S	V.S	V.S	V.S	P.S	P.S	P.S	P.S	V.S
17	V.S	V.S	V.S	V.S	P.S	P.S	P.S	P.S	V.S
18	V.S	V.S	V.S	V.S	P.S	P.S	P.S	P.S	V.S
19	V.S	V.S	V.S	V.S	P.S	P.S	P.S	P.S	V.S
20	V.S	V.S	V.S	V.S	P.S	P.S	P.S	P.S	V.S
21	V.S	V.S	V.S	V.S	P.S	P.S	P.S	P.S	V.S

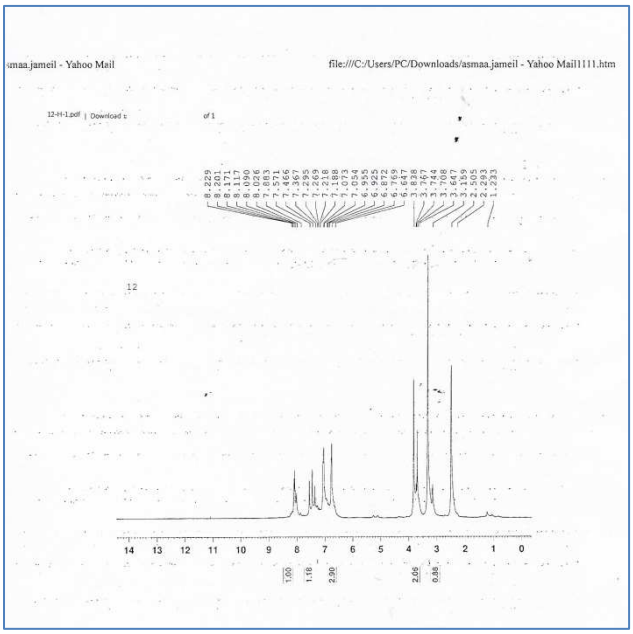
V.S=Very soluble *In.S=Insoluble* *P.S=partial soluble*



Compound No.10



Compound No.16



Compound No.19

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