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Cyclization of Multi Components Reactions and (Preparation, Investigation, Thermal Curves)

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Abstract

Many cyclic compounds were formatted via multi components reactions and cyclization reaction through many steps with (various conditions , various starting materials , various components), in first step , aromatic amine derivative were reacted with ammonium thiocyanate in cyclization reaction to yield 2-aminobenzothiazole derivative , which reacted with formaldehyde and benzaldehyde as a multi components reaction ., then the resulting compounds cyclized with (semicarbazide , ortho-phenyl diamine , ortho-thiol aniline , ortho- amino phenol). Investigation of compounds carried out through many techniques (FT.IR , H.NMR , Mass) – Spectra , Thermal studies

Keywords: Multi Components , Cyclization, Heterocyclic ,Oxadiazole, Imidazole, Thiazole, Oxazole.

Introduction

A heterocyclic compounds are a cyclic compound which have at least two different elements or more as members of its structure. Heterocyclic chemistry is the branch of synthetic chemistry dealing with the preparation[(1-3)] , characterization ,uses[(4-6)], applications[(7-9)] of these compounds that include all of the nucleic acids, drugs, cellulose and many natural and industrial dyes[(10-12)].

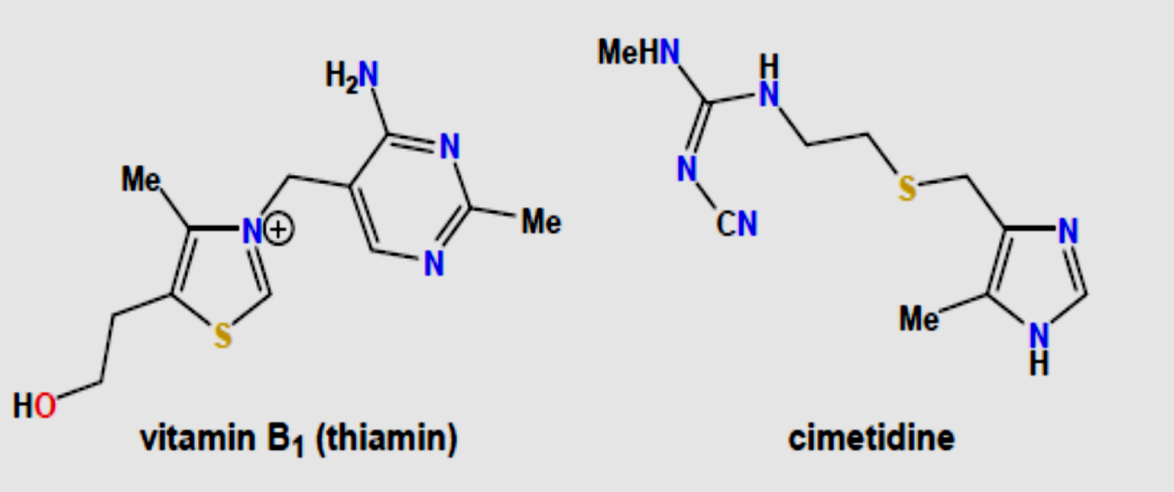


Fig.(1): Heterocycle compounds as a drugs

Heterocyclic derivatives have a wide range of uses[13-15] and applications[16-19] in pharmaceutical chemistry[20-24],which involved many[25-28] of the biochemical material essential to bio- molecules like vitamins ,nucleic acids, the chemical materials[29-31] that carry the genetic information controlling inheritance, include a long chains of heterocyclic units held together by other types[32-36] of substances . Many naturally occurring dyes , pigments, vitamins, and antibiotics are heterocyclic compounds[37-40].

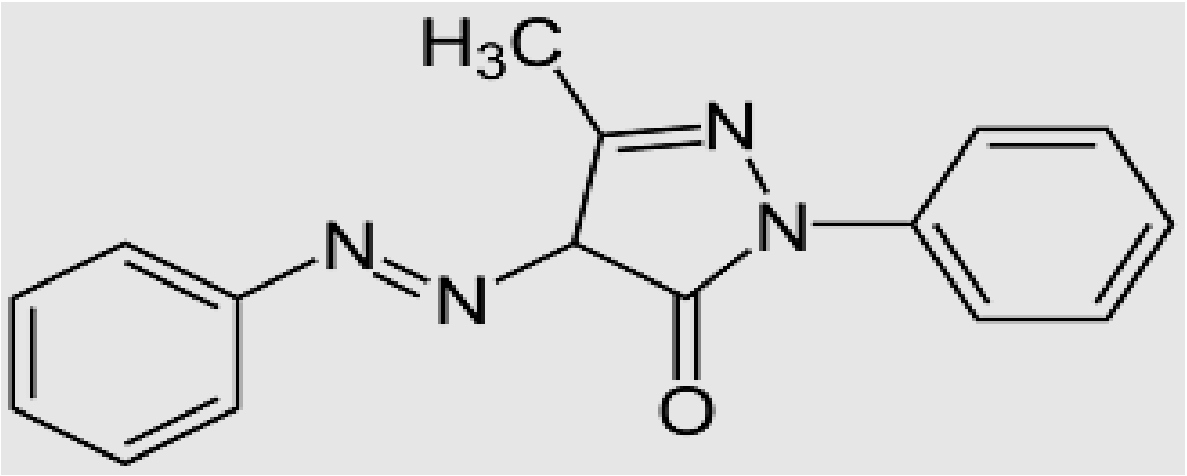


Fig.(2): Heterocyclic compound as a dye

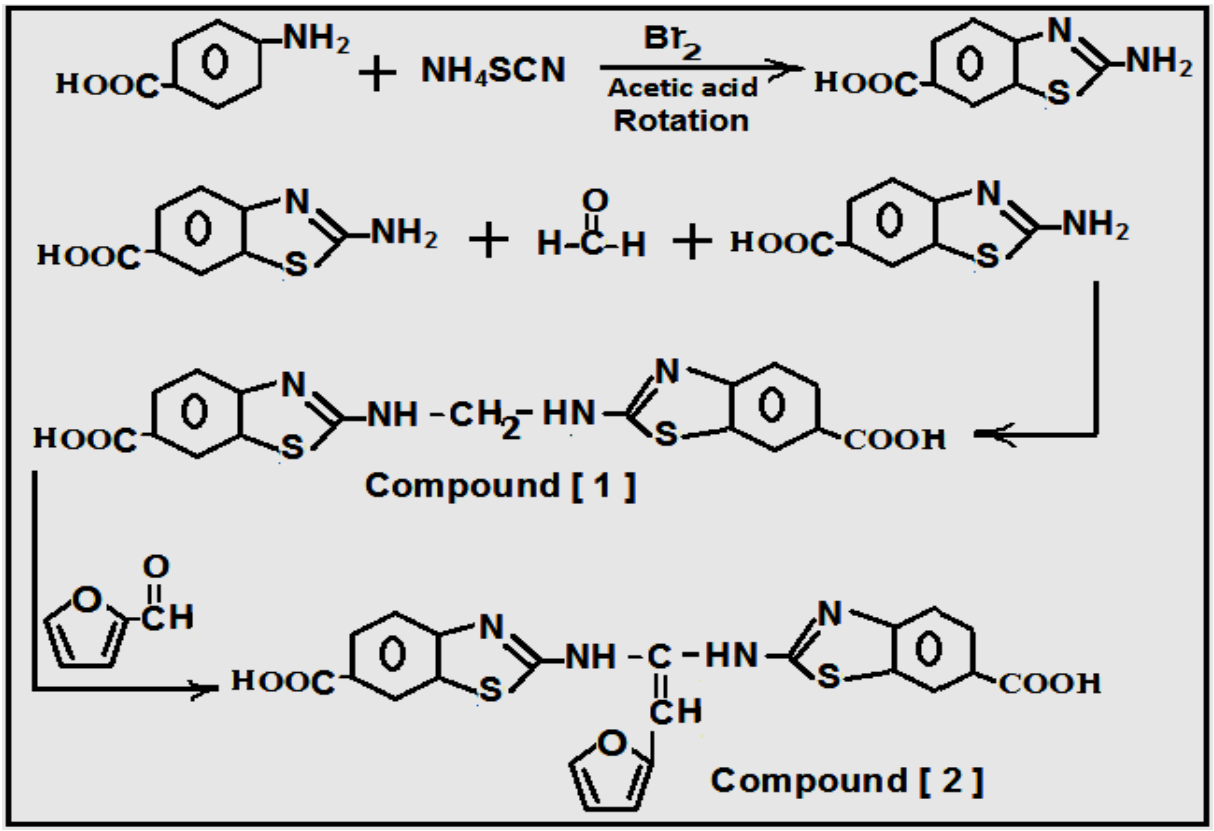
Experimental Part

Allcompounds were investigation through : FT-IR spectra (FT-IR 8300 Shimadzu) in the range (400-4000) cm^{-1} asKBr discs ., 1H.NMR– Spectra in DMSO–solvent., Mass spectra, thermal studying , solubility test , physical properties :

Procedures

Synthesis of Compounds {1 , 2 }

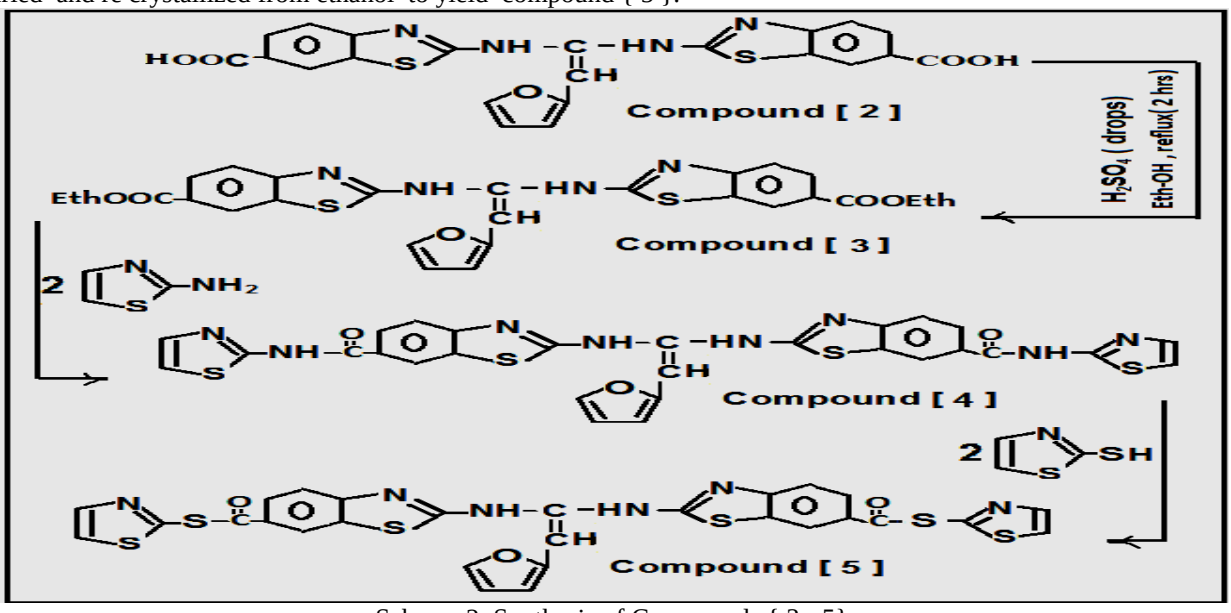
p-Amino benzoic acid (0.1mole) reacted with ammonium thiocyanate (0.1mole) with (7 ml) of (Br_2) drop by drop with (5ml) of glacial acetic acid with rotation for (3hrs) at (10 C°)according to literatures[21 ,23],the resulting compound (0.2 mole) reacted with (0.1 m0le) of formaldehyde with rotation for (4 hrs) in acid medium (3 ml) (HCl or H_2SO_4) to give compound{ 1 }.,which dissolved in (5 % NaOH) solution then reacted with furfural at room temperature and rotation for (5 hrs) , then filtered , dried and re crystallized from ethanol to yield compound { 2 }.



Scheme.1: Synthesis of Compounds { 1 , 2}

Synthesis of Compounds{ 3- 5}:

Compound { 2 }(0.01mole) refluxed with ethanol and (3 ml) (H_2SO_4) for (2 hrs) to give compound {3} as ester , which (0.1 mole) refluxed with (0.2 mole) of 2-aminothiazole for (2 hrs) in ethanol as a solvent , then filtered , dried and re crystallized from ethanol to yield compound { 4 }., while compound { 2} (0.1 mole) refluxed with (0.2 mole) of 2-mercaptothiazole for (3 hrs) in ethanol as a solvent according to procedures[38, 40] , then filtered , dried and re crystallized from ethanol to yield compound { 5 }.



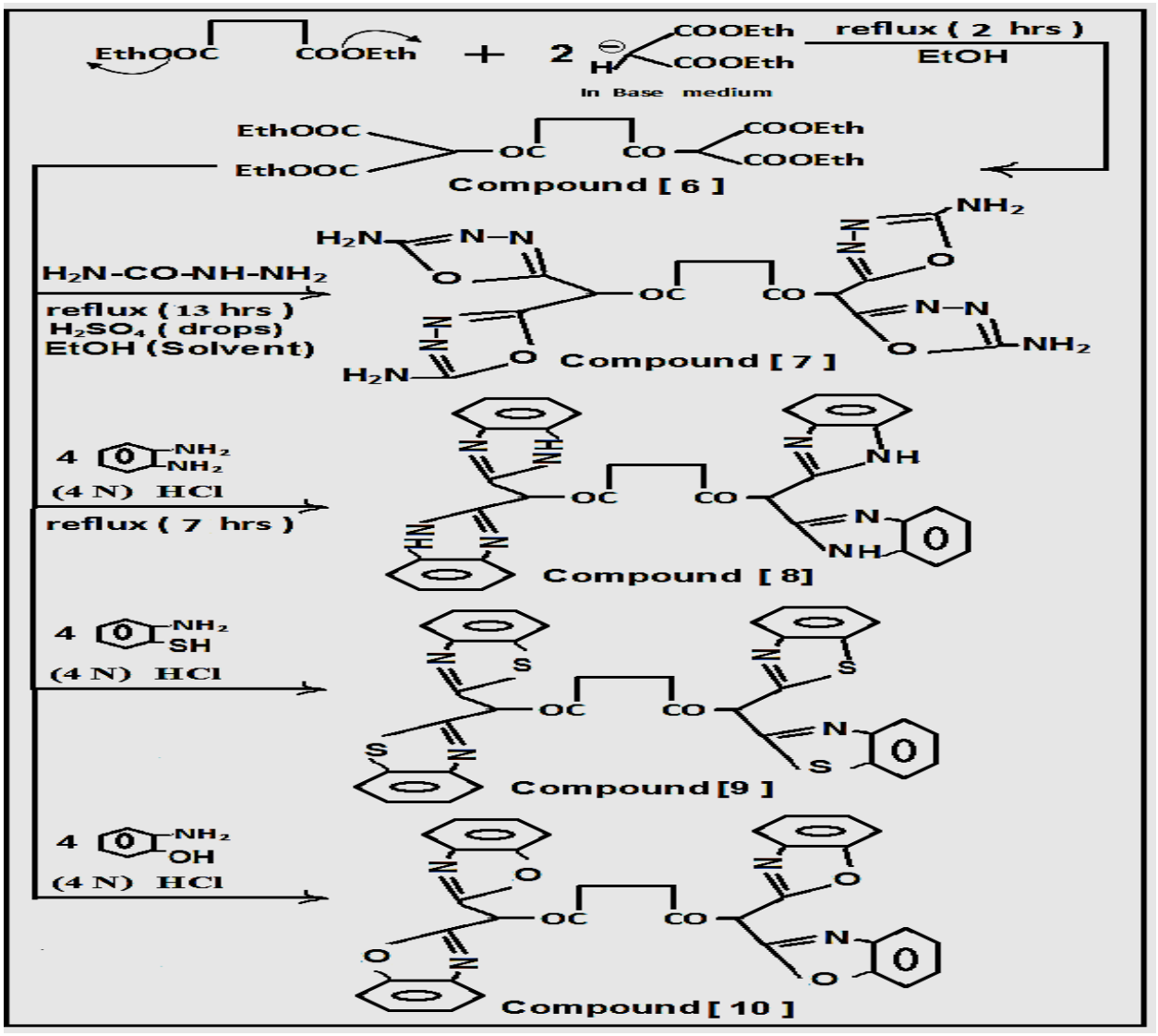
Scheme.2: Synthesis of Compounds { 3 - 5}

Synthesis of Compounds{ 6 , 7 }:

Diethyl malonate (0.2 mole) dissolved in base medium then refluxed with (0.1 mole) of diethylsuccinatewith ethanol for (2 hrs) to give compound {6} as ester , which (0.1 mole) refluxed with (0.2 mole) of semicarbazide for (13 hrs) in ethanol as a solvent and (3 ml of H_2SO_4)according to procedures[21, 23], then filtered , dried and re crystallized from ethanol to yield compound { 7 }.

Synthesis of Compounds{ 8 - 10 }:

Compound { 6} (0.1 mole) refluxed with (0.4mole) of ortho-phenyl diamine for (7hrs) with (4 N of HCl) , then filtered , dried and re crystallized from ethanol to yield compound { 8 }., while compound { 6} (0.1 mole) refluxed with (0.4 mole) of ortho-thiol aniline for (9 hrs) with (4 N of HCl) , then filtered , dried and re crystallized from ethanol to yield compound { 9 }.,compound { 6} (0.1 mole) refluxed with (0.4 mole) of ortho-hydroxy aniline for (9hrs) with (4 N of HCl) according to procedures[21, 23] , then filtered , dried and re crystallized from ethanol to yield compound { 10 }.,



Scheme.3: Synthesis of Compounds { 6- 10}

Results and Discussion

Our compounds characterized with many spectral methods like (FT.IR ,H.NMR ,Mass) spectra and with thermal studies:

Spectral Investigation

FT.IR- Spectra of Compounds: It appeared many absorption bands appeared at (C=N) Endocycle: 1641., (C-S) endocycle of benzothiazole : 734 ., (-CO-O-) carbonyl of carboxyl group : 1719 ., (NH)Amine group :3270 ., (OH) hydroxyl of carboxyl group: 3120 in compound { 1} , while other bands appeared at (C=N) Endocycle: 1649., (C-S) endocycle of benzothiazole : 728 ., (-CO-O-) carbonyl of carboxyl group : 1714 ., (NH)Amine group :3276 .,(OH) hydroxyl of carboxyl group: 3135 ., (CH=C): 3100in compound {2} ., other bands appeared at (C=N) Endocycle: 1650., (C-S) endocycle of benzothiazole : 717 ., (-CO-O-) carbonyl of ester group : 1722 ., (NH)Amine group :3262 ., (CH=C): 3097in compound { 3 }., but compound {4} appeared bands at (C=N) Endocycle: 1643., (C-S) endocycle of benzothiazole : 729 ., (NH)Amine group :3273 ., (CH=C): 3096 ., (-NH-CO) amine of amide : 3204 ., (CO-N) carbonyl of amide : 1689 ., while compound { 5} gave bands at (C=N) Endocycle: 1637., (C-S) endocycle of benzothiazole : 711 ., (NH)Amine group :3264 ., (CH=C): 3104 .,(CO-S) carbonyl : 1694 ., other bands at (-CO-O-) carbonyl of ester group : 1724 .,(-CO-CH_2-) carbonyl of ketone : 1708 ., (CH-) aliphatic : 2967 in compound {6} , the spectrum of compound { 7} appeared bands at (-CO-CH_2-) carbonyl of ketone : 1713 ., (CH-) aliphatic : 2985 ., (NH_2) amine group: (3245 , 3266) .,(C=N) Endocycle of oxadiazole: 1663 ., but bands at (-CO-CH_2-) carbonyl of ketone : 1711 ., (CH-) aliphatic : 2918 ., (NH) amine : 3210 .,(C=N) Endocycle of imidazole: 1656 due to compound {8 } ., while appearance of bands at (-CO-CH_2-) carbonyl of ketone : 1709 ., (CH-) aliphatic : 2923 .,(C=N) Endocycle of thiazole: 1642 ., (C-S) endocycle of benzothiazole : 753 due to compound { 9} ., the compound {10} gave bands at (-CO-CH_2-) carbonyl of ketone : 1716 ., (CH-) aliphatic : 2900 .,(C=N) Endocycle of oxazole: 1642 .,all bands abstracted in Table (1) .

Table (1): FT.IR- data (cm^{-1}) of Compounds { 1-10 }

Compounds	Other Groups
{ 1 }	(C=N) Endocycle: 1641., (C-S)endocycle of benzothiazole : 734 ., (-CO-O-) carbonyl of carboxyl group : 1719 ., (NH)Amine group :3270 ., (OH) hydroxyl of carboxyl group: 3120 .
{ 2 }	(C=N) Endocycle: 1649., (C-S) endocycle of benzothiazole : 728 ., (-CO-O-) carbonyl of carboxyl group : 1714 ., (NH)Amine group :3276 ., (OH) hydroxyl of carboxyl group: 3135 ., (CH=C): 3100 .
{ 3 }	(C=N) Endocycle: 1650., (C-S) endocycle of benzothiazole : 717 ., (-CO-O-) carbonyl of ester group : 1722 ., (NH)Amine group :3262 ., (CH=C): 3097 .
{4}	(C=N) Endocycle: 1643., (C-S) endocycle of benzothiazole : 729 ., (NH)Amine group :3273 ., (CH=C): 3096 ., (-NH-CO) amine of amide : 3204 ., (CO-N) carbonyl of amide : 1689 .
{5}	(C=N) Endocycle: 1637., (C-S) endocycle of benzothiazole : 711 ., (NH)Amine group :3264 ., (CH=C): 3104 .,(CO-S) carbonyl : 1694 .
{6}	(-CO-O-) carbonyl of ester group : 1724 .,(-CO-CH_2-) carbonyl of ketone : 1708 ., (CH-) aliphatic : 2967 .
{7}	(-CO-CH_2-) carbonyl of ketone : 1713 ., (CH-) aliphatic : 2985 ., (NH_2) amine group: (3245 , 3266) .,(C=N) Endocycle of oxadiazole: 1663 .
{8}	(-CO-CH_2-) carbonyl of ketone : 1711 ., (CH-) aliphatic : 2918 ., (NH) amine : 3210 .,(C=N) Endocycle of imidazole: 1656 .
{9}	(-CO-CH_2-) carbonyl of ketone : 1709 ., (CH-) aliphatic : 2923 .,(C=N) Endocycle of thiazole: 1642 ., (C-S) endocycle of benzothiazole : 753.
{10}	(-CO-CH_2-) carbonyl of ketone : 1716 ., (CH-) aliphatic : 2900 .,(C=N) Endocycle of oxazole: 1642 .

^{1}H.NMR- Spectra of Compounds

It appeared peaks at δ DMSO-d6(solvent): 2.50 ., (N-CH_2-N-) Protons : 1.92 ., (NH-): 5.12 ., Protons of Phenyl ring : (6.84-7.89)., (-COOH)proton of carboxyl group of acid : 13.42 in compound { 1 } ., while it gave signals at(NH-): 5.32 ., Protons of Phenyl ring : (6.67-7.99)., (-COOH)proton of carboxyl group of acid : 13.26 ., (C=CH) :2.41 in compound { 2 } ., (., (NH-): 5.48 ., Protons of Phenyl ring : (6.84-7.72)., (-COO-Eth)protons of ethyl group :(3.03 , 3.27) ., (C=CH) :2.29 in compound { 3} .,(NH-): 5.31 ., Protons of Phenyl ring and heterocycles: (6.96-7.64)., (-CO-NH)proton of amide group :10.03 ., (C=CH) :2.10 in compound {4} ., (NH-): 5.62 ., Protons of Phenyl ring and heterocycles: (6.75-7.83) ., (C=CH) :2.19 in compound {5} ., (CO-CH_2-

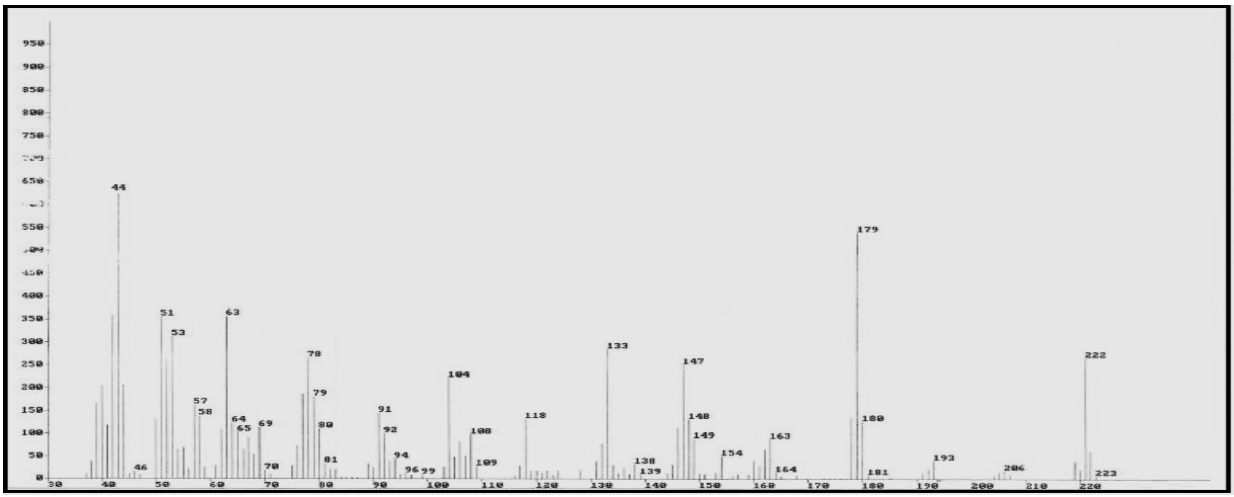
CH_2-CO) : (2.00 , 2.09 , 2.25) ., (COOEth): (3.05 – 3.37) in compound { 6} .,(CO-CH_2-CH_2-CO): (2.08 , 2.11 , 2.19) ., (NH_2) : 5.67 in compound { 7} ., (CO-CH_2-CH_2-CO) : (2.06 , 2.17 , 2.29) ., (NH) : 5.23 ., Protons of Phenyl ring : (6.96-7.64) in compound { 8} .,(CO-CH_2-CH_2-CO) : (2.13 , 2.18 , 2.21) .,Protons of Phenyl ring : (6.80-7.52) in compound { 9} ., (CO-CH_2-CH_2-CO) : (2.09 , 2.17 , 2.24) .,Protons of Phenyl ring : (6.98-7.87) in compound { 10} which give (CO-CH_2-CH_2-CO) : (2.09 , 2.17 , 2.24) .,Protons of Phenyl ring : (6.98-7.87). evidences for preparation of our compounds ., and other peaks abstracted in table (2)

Table (2): H.NMR-data (δ - ppm) of Compounds{ 1 – 10 }

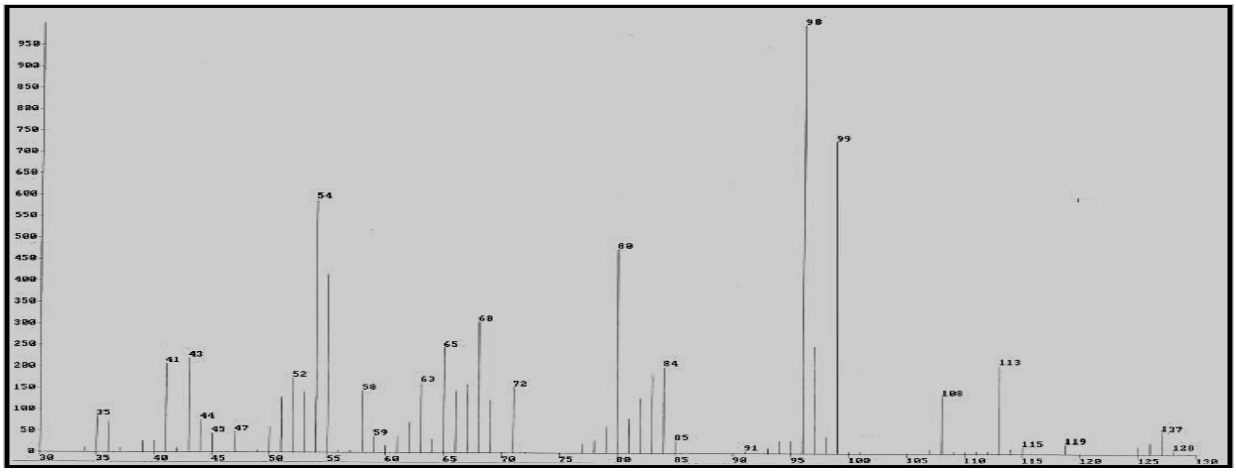
Compounds	Other groups
{ 1 }	DMSO-d6(solvent): 2.50 ., (N-CH_2-N-) Protons : 1.92 ., (NH-): 5.12 ., Protons of Phenyl ring : (6.84-7.89)., (-COOH)proton of carboxyl group of acid : 13.42 .
{ 2 }	DMSO-d6(solvent): 2.50 ., (NH-): 5.32 ., Protons of Phenyl ring : (6.67-7.99)., (-COOH)proton of carboxyl group of acid : 13.26 ., (C=CH) :2.41 .
{ 3 }	DMSO-d6(solvent): 2.50 ., (NH-): 5.48 ., Protons of Phenyl ring : (6.84-7.72)., (-COO-Eth)protons of ethyl group :(3.03 , 3.27) ., (C=CH) :2.29 .
{4}	DMSO-d6(solvent): 2.50 ., (NH-): 5.31 ., Protons of Phenyl ring and heterocycles: (6.96-7.64)., (-CO-NH)proton of amide group :10.03 ., (C=CH) :2.10 .
{5}	DMSO-d6(solvent): 2.50 ., (NH-): 5.62 ., Protons of Phenyl ring and heterocycles: (6.75-7.83) ., (C=CH) :2.19 .
{6}	DMSO-d6(solvent): 2.50 ., (CO-CH_2-CH_2-CO) : (2.00 , 2.09 , 2.25) ., (COOEth): (3.05 – 3.37).
{7}	DMSO-d6(solvent): 2.50 .,(CO-CH_2-CH_2-CO): (2.08 , 2.11 , 2.19) ., (NH_2) : 5.67 .
{8}	DMSO-d6(solvent): 2.50 ., (CO-CH_2-CH_2-CO) : (2.06 , 2.17 , 2.29) ., (NH) : 5.23 ., Protons of Phenyl ring : (6.96-7.64).
{9}	DMSO-d6(solvent): 2.50 ., (CO-CH_2-CH_2-CO) : (2.13 , 2.18 , 2.21) .,Protons of Phenyl ring : (6.80-7.52).
{10}	DMSO-d6(solvent): 2.50 ., (CO-CH_2-CH_2-CO) : (2.09 , 2.17 , 2.24) .,Protons of Phenyl ring : (6.98-7.87).

The Mass Spectra of Compounds

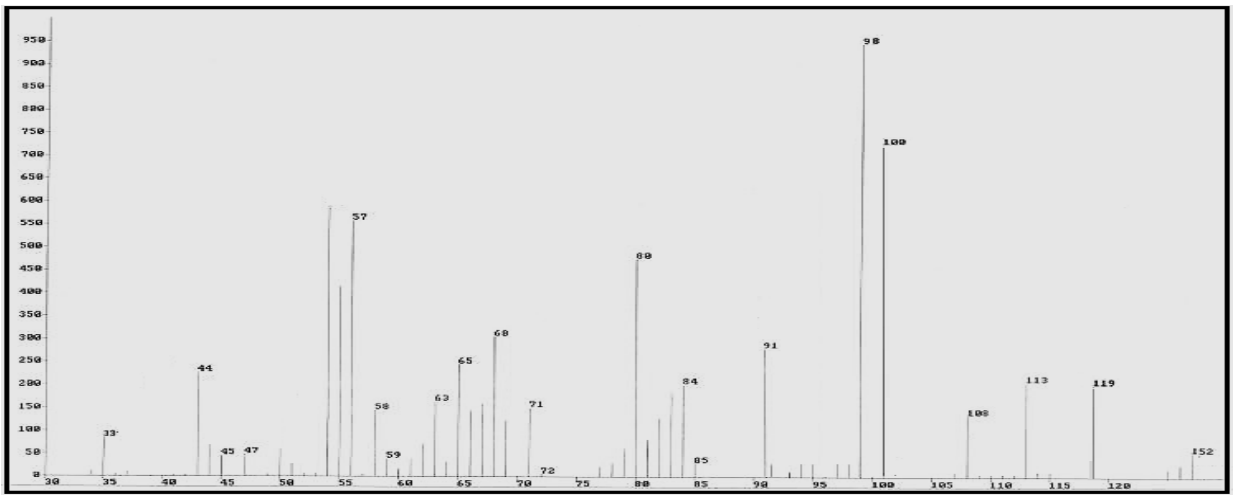
There spectra showed good results for formatted compounds and appeared good evidence for their fragments in figures(3-5):



Fig(3): Mass Spectra of Compound { 5 }



Fig(4): Mass Spectra of Compound { 8}



Fig(5): Mass Spectra of Compound{ 10}

Thermal – Curves of Compounds

The compounds studied through thermal analysis which appeared stability against different temperatures in figures (6- 10) :

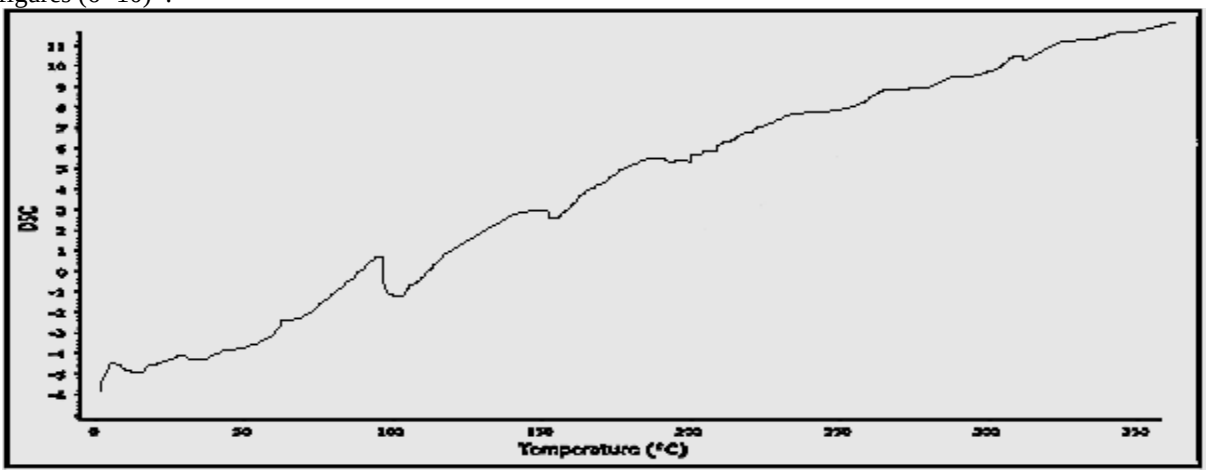


Fig (6) : Thermal Curve of Compound{4}

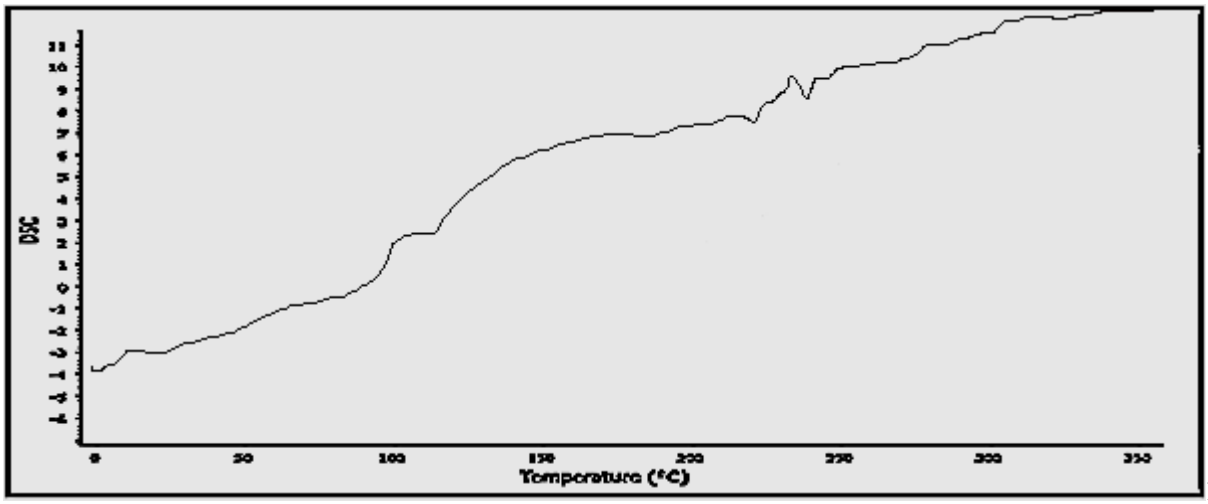


Fig (7) : Thermal Curve of Compound{5}

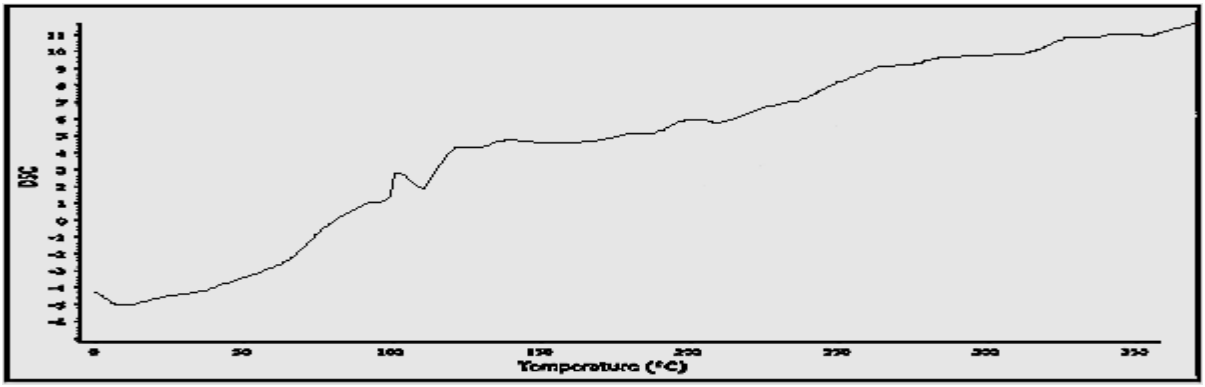


Fig (8) : Thermal Curve of Compound{8}

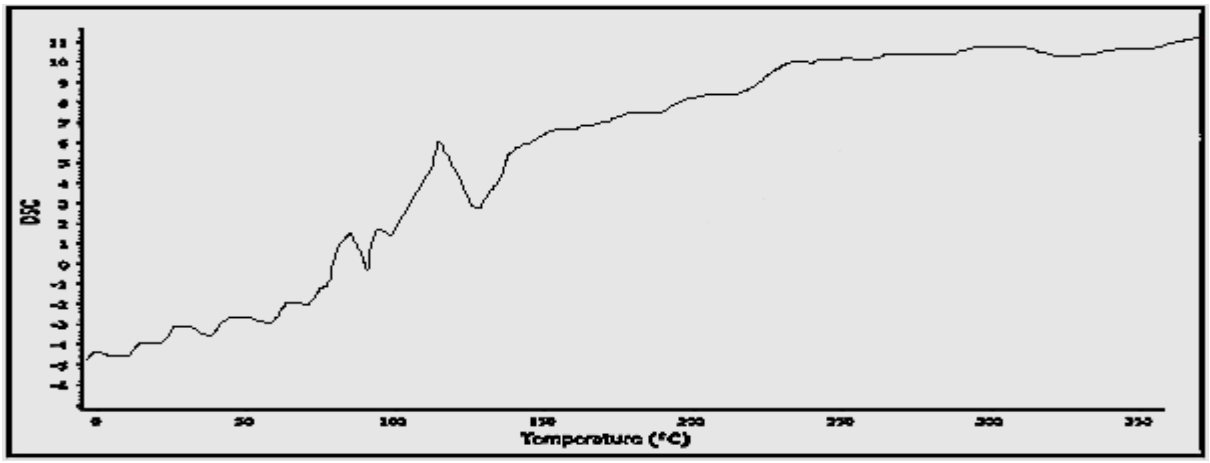


Fig (9) : Thermal Curve of Compound{9}

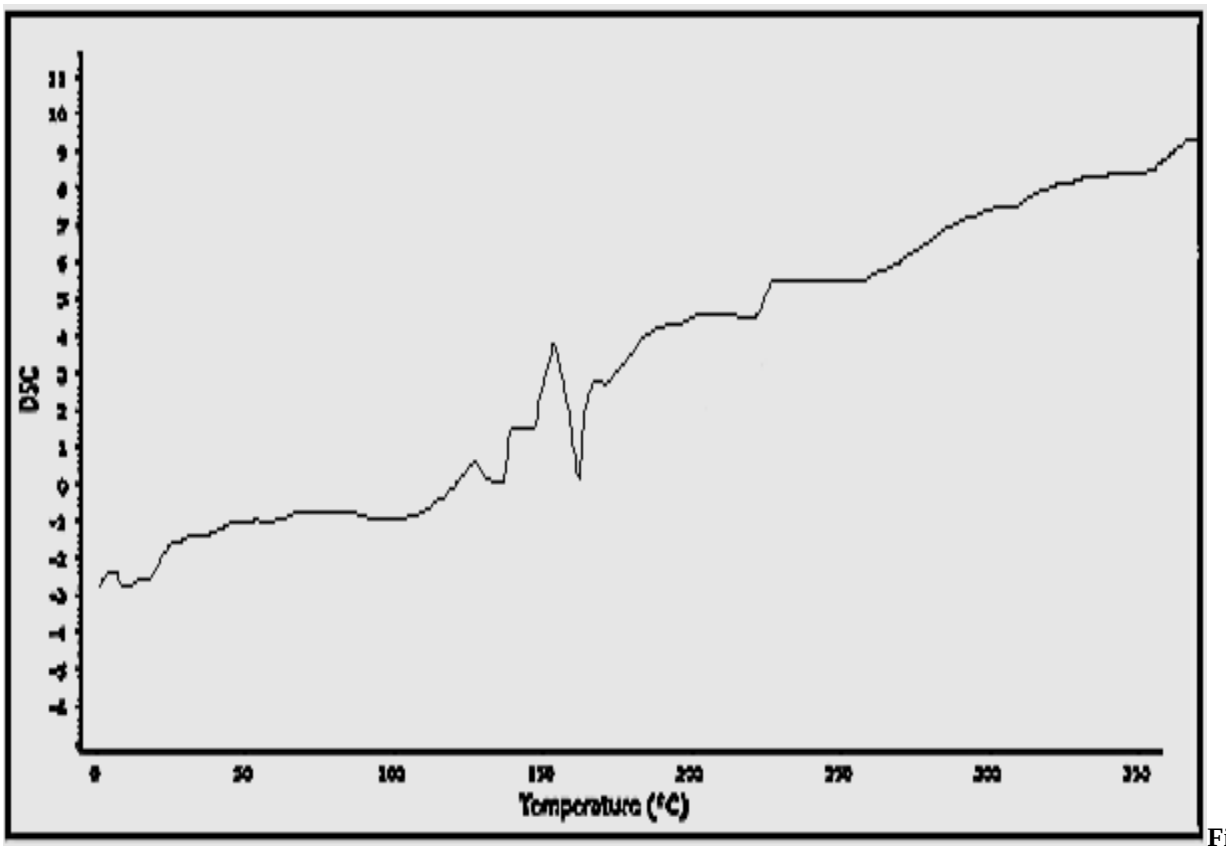


Fig (10): Thermal Curve of Compound{10}

Solubility of Compounds in Organic Solvents

Test of the solubility of compounds screened with several organic solvents according to (type of solvent , polarity of solvents , activity of functional groups) in compounds, the results abstracted in Table (3).

Table (3) : Behavior of compounds in Solvents

Compounds	Solvents					
	C_2H_5OH	Methanol	Chloroform	Acetone	Benzene	Toluene
(1)	+	+	-	-	-	-
(2)	+	+	-	-	-	-
(3)	+	+	-	-	-	-
(4)	+	+	-	-	-	-
(5)	+	+	-	-	-	-
(6)	+	+	-	-	-	-
(7)	+	+	-	-	-	-
(8)	+	+	-	-	-	-
(9)	+	+	-	-	-	-
(10)	+	+	-	-	-	-

Physical and Chemical Properties of Compound {1 – 10 }

The Results In Table (4) Appeared Properties And Characterization Like: [(R_f) Of TLC- Technique For Following The Reactions ,Type Of Solvent Which Was Used In TLC – Plate , Yield From Reactions %], All Data Are Abstracted In Table (4):

Table(4): Some Physical and Chemical Properties for compounds {1 – 10 }

Compounds	Yield %	R_f	Solvents of (TLC) (1:2)
(1)	72	0.4	Ethanol : Benzene
(2)	70	0.70	Ethanol : Benzene
(3)	64	0.70	Ethanol : Benzene
(4)	78	0.70	Ethanol : Benzene
(5)	74	0.68	Ethanol : Benzene
(6)	68	0.66	Ethanol : Benzene
(7)	70	0.70	Ethanol : Benzene
(8)	74	0.62	Ethanol : Benzene
(9)	72	068	Ethanol : Benzene
(10)	76	0.64	Ethanol : Benzene

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