

TABLE OF CONTENTS

Topic	Page
Dedication	i
Acknowledgement	ii
Table of contents	iii
List of tables	iv
List of figures	v
Abstract (English)	vi
Abstract (Arabic)	vii

CHAPTER ONE

1. Introduction	1
1.1. π - Deficient nitrogen- heterocyclic compounds	1
Pyrimidine derivatives .1.2	1
1.2.1. Barbiturate derivatives	2
Correlation of structure and properties of pyrimidine.1.3	5
derivative	
Solubility of pyrimidine and barbiturate .1.3.1	5
Solubility of pyrimidine .1.3.1.1	5
1.3.1.2. Solubility of barbiturates	7
Basic strength of pyrimidine and barbiturate derivatives -1.3.2	8
1.3.2.1- Basic strength of pyrimidine derivatives	8
The keto-enol tautomerism in pyrimidine derivatives -1.3.3	11
1.3.3.2- The keto-enol tautomerism of barbiturate derivatives	14
Dipole moments of pyrimidine and barbiturate -1.3.4	15
1.3.4.1- Dipole moments of pyrimidine	15
1.3.4.2- Dipole moments of barbiturate derivatives	16
Synthesis of pyrimidine and barbiturate derivatives - .1.4	16
1.4.1 - Synthesis of pyrimidine	16
1.4.2- Synthesis of barbiturate derivatives	18
Reaction of pyrimidines and Barbiturates -1.5	20
Reaction with electrophilic reagents -1.5.1	20
1.5.1.1- Addition to nitrogen	20
protonation -1.5.1.1.1	20
:Deprotonation -1.5.1.1.2	21
1.5.1.1.3- Alkylation	21

1.5.1.2- Substitution at Carbon	22
1.5.2- Reactions with oxidizing agents	26
1.5.3- Reactions with reducing agents	27
1.5.4- Reaction with nucleophilic reagents	27
1.5.5- Substitution with displacement of halogen	28
1.5.7- Photochemical reactions	29
1.6. Spectral properties of pyrimidine and barbiturates	29
derivatives	
1.6.1. Infrared spectra of barbiturates derivatives	30
Ultra-violet spectra of pyrimidine and barbiturates-1.6.2	30
derivatives	
1.6.3-Nuclear magnetic resonance of pyrimidine and	31
barbiturates	
1.6.3.1-Nuclear magnetic resonance of pyrimidine	31
1.6.3.2-Nuclear magnetic resonance of barbiturates	32
1.6.4- X- diffraction spectroscopy of barbiturates	32
1.7- The Detection and assay of barbiturates	32
1.7.1- Choice of Internal Standard and extraction technique	33
Screen method -1.7.2	34
1.7.2.1- Immunoassay Methods	34
1.7.2.2- Thin layer chromatography	34
Confirmatory methods -1.7.3	34
1.7.3.1- Spectrophotometry	34
1.7.3.2- Gas chromatography	34
1.7.4- Gas chromatography – mass spectrometry	35
1.7.5- High performance liquid chromatography	35
1.7.6- Titration method	36
Biological activity of barbiturate derivatives - 1.8	36
1.8.1- Barbiturate Development	36
1.8.2- Structure- activity relation ships	36
Toxicological characteristic of barbituric and .1.8.3	37
thiobarbituric acid	
1.9. Aim of the project	37

CHAPTER TWO

Experimental and Results .2	39
Materials .2.1	39
Chemicals .2.1.1	39
2.1.2 Solvents	39

2.1.3. Reagents	39
(Thin Layer Chromatography (TLC 2.2	39
(Infrared spectrophotometer (IR 2.3	40
2.4 Ultraviolet-visible spectrophotometer	40
2.5 General equipments	40
2.6 Methods	40
(Preparation of diethyl alkyl malonate derivatives (Ia, Ib .2.6.1	40
2.6.2. Preparation of diethyl phenyl malonate (II)	41
:(Preparation of ethane tetra carboxylic ethyl ester (III .2.6.3	42
Preparation of diethyl acetyl and benzoyl malonate (IVa, .2.6.4	43
(IVb	
:(Preparation of pyrimidine-2,4,6-trione (Va-Vf .2.6.5	44
2.6.6. Preparation of pyrimidine-2-thio-4,6-dione (VIa – VIh)	44
2.6.7.1. Investigation and characterization of the substituted	45
diethyl malonate (Ia - IVb)	
2.6.7.2 Investigation and characterization of pyrimidine-2,4,6-	46
trione and pyrimidine-2-thio-4,6-dione	
Ultraviolet-visible data measurements .2.7	47
Ultraviolet-visible scanning of the final prepared .2.7.1	47
(compounds, (solvent effect	
2.7.2. Effect of pH on the ultraviolet-visible spectra of the	47
prepared compounds	
2.8. Infrared spectral measurements	47
Infrared measurement method for studying keto-enol.2.8.1	47
phenomena	
3. Discussion	89
4.Conclusion and recommendation	113
5.REFERENCES	115

LIST OF FIGURES

Figure	Page
Scheme 2.1: Chemical structures of the prepared diethyl substituted malonate	49
Scheme 2.2: Chemical structures of the prepared 5-substituted pyrimidine -2,4,6- trione	50
Scheme 2.3: Chemical structures of the prepared 5-substituted pyrimidine -2- thio-4,6- dione	51
Fig.2.4.IR spectra of diethyl malonate	65
(Fig.2.5.IR spectra of diethyl ethyl malonate (Ia	65
(Fig.2.6.IR spectra of diethyl benzyl malonate (Ib	65
(Fig.2.7.a.IR spectra of diethyl phenyl malonate (II	66
Fig.2.7.b.IR spectra of diethyl phenyl malonate (II) (in CCl ₄	66
(Fig.2.8.IR spectra of ethane tetra ethyl carboxylic acid (III	66
(Fig.2.9.IR spectra of diethyl benzoyl malonate (IV	67
Fig.2.10.IR spectra of 5- ethyl -5- phenyl pyrimidine-2,4,6- (trione (Standard sample	67
(Fig.2.11.IR spectra of pyrimidine-2,4,6- trione (Vf	67
Fig.2.11.a.IR spectra of pyrimidine-2,4,6- trione (Vf) ((100µg/100mg	68
Fig.2.11.b.IR spectra of pyrimidine-2,4,6- trione (Vf) ((10µg/100mg	68
Fig.2.11.C.IR spectra of pyrimidine-2,4,6- trione (Vf) ((1µg/100mg	68

(Fig.2.12.IR spectra of 5-ethyl pyrimidine-2,4,6- trione (Va [Prepared mechanically]	69
(Fig.2.12.IR spectra of 5-ethyl pyrimidine-2,4,6- trione (Va [Prepared manually]	69
(Fig.2.13.IR spectra of 5-phenyl pyrimidine-2,4,6- trione (Vc [Prepared mechanically]	69
(Fig.2.13.a.IR spectra of 5-phenyl pyrimidine-2,4,6- trione (Vc [Prepared manually]	70
(Fig.2.14.IR spectra of 5-benzyl pyrimidine-2,4,6- trione (Vb	70
(Fig.2.15.IR spectra of pyrimidine-2- thio-4,6- dione (VIh	70
(Fig.2.16.IR spectra of di-(pyrimidine-2- thio-4,6- dione) (VIe	71
Fig.2.17.IR spectra of 5- benzoyl pyrimidine-2- thio-4,6- dione (VIg	71
Fig.2.18.IR spectra of 5- diethyl malonylpyrimidine-2- thio- (4,6- dione (VIId	71
(Fig.2.19.UV spectra of diethyl phenyl malonate (II	75
(Fig.2.20.UV spectra of diethyl benzyl malonate (Ib	75
(Fig.2.21.UV spectra of 5- benzyl pyrimidine-2,4,6-trione (Vb	75
Fig.2.22.UV spectra of 5- benzyl pyrimidine-2,4,6-trione (Vb) ((in ethanol	76
(Fig.2.23.UV spectra of 5- benzyl pyrimidine-2,4,6-trione (Vb (*in ethanol/ H)	76
(Fig.2.24.UV spectra of 5- benzyl pyrimidine-2,4,6-trione (Vb (in ethanol/ pH 10)	77
Fig.2.25.UV spectra of 5- phenyl pyrimidine-2,4,6-trione (Vc) ((in ethanol	77
(Fig.2.26.UV spectra of 5- phenylpyrimidine-2,4,6-trione (Vc (in ethanol/ pH 10)	78
(Fig.2.27.UV spectra of 5- phenylpyrimidine-2,4,6-trione (Vc	78

(in ethanol/ pH 13)

Fig.2.28.UV spectra of 5-ethyl-5- phenylpyrimidine-2,4,6-
(trione (standard sample) (in ether 79

Fig.2.29.UV spectra of 5-ethyl-5- phenylpyrimidine-2,4,6-
(trione (standard sample) (in ethanol 79

Fig.2.30.UV spectra of 5-ethyl-5- phenylpyrimidine-2,4,6-
(trione (standard sample) (in ethanol/ pH 10 80

Fig.2.31.UV spectra of 5-ethyl-5- phenylpyrimidine-2,4,6-
(trione (standard sample) (in ethanol/ pH 13 80

(Fig.2.32.UV spectra of pyrimidine-2-thio-4,6-dione (VIh
(in ether) 81

(Fig.2.33.UV spectra of pyrimidine-2-thio-4,6-dione (VIh
(in ethanol) 81

(Fig.2.34.UV spectra of pyrimidine-2-thio-4,6-dione (VIh
(*in ethanol/ H) 82

(Fig.2.35.UV spectra of pyrimidine-2-thio-4,6-dione (VIh
(in ethanol/ pH 10) 82

(Fig.2.36.UV spectra of pyrimidine-2-thio-4,6-dione (VIh
(in ethanol/ pH 13) 83

Fig.2.37.UV spectra of 5- phenyl pyrimidine-2-thio-4,6-dione
((VIc) (in ethanol 83

Fig.2.38.UV spectra of 5- phenyl pyrimidine-2-thio-4,6-dione
((VIc) (in ethanol/ pH 10 84

Fig.2.39.UV spectra of 5- phenyl pyrimidine-2-thio-4,6-dione
((VIc) (in ethanol/ pH 13 84

Fig.2.40.UV spectra of 5- benzyl pyrimidine-2-thio-4,6-dione
((VIb) (in ether 85

Fig.2.41.UV spectra of 5- benzyl pyrimidine-2-thio-4,6-dione
((VIb) (in ethanol 85

Fig.2.42.UV spectra of 5- benzyl pyrimidine-2-thio-4,6-dione (⁺ (VIb) (in ethanol/ H	86
Fig.2.43.UV spectra of 5- benzyl pyrimidine-2-thio-4,6-dione ((VIb) (in ethanol/ pH 10	86
Fig.2.44.UV spectra of 5- benzyl pyrimidine-2-thio-4,6-dione ((VIb) (in ethanol/ pH 13	87
Fig.2.45.UV spectra of 5- ethyl pyrimidine-2-thio-4,6-dione ((VIa) (in ethanol	87
Fig.2.46.UV spectra of 5- benzoyl pyrimidine-2-thio-4,6-dione ((VIg) (in ethanol	88
Fig.2.47.UV spectra of 5- di ethyl malonyl-2-thio-dione (VI d) ((in ethanol	88
Fig.2.48.UV spectra of di-(pyrimidine-2-thio-4,6- dione) (VIe) ((in ethanol	88

LIST OF TABLES

Table	Page
Table (1.1): Representative of disubstituted barbituric acid	4
Table (1.2): Solubility of some solid pyrimidine derivatives	6
Table (1.3): Amount of barbituric acid in undissociated form at pH 7	9
Table 2.1.a: Chemical name of the substituted diethyl malonate derivatives	52
Table 2.1.b: Chemical names of the 5-substituted pyrimidine-2,4,6-trione	52
Table 2.1.c: Chemical names of the 5-substituted pyrimidine-2-thio-4,6-dione	53
Table 2.2.a: Yield percentage, recrystallization solvent, melting or boiling point, molecular formula and molecular weight of substituted diethyl malonate	54
Table 2.2.b: Yield percentage, recrystallization solvent, melting or boiling point, molecular formula and molecular weight of the pyrimidine-2,4,6-trione	55
Table 2.2.c: Yield percentage, recrystallization solvent, melting or boiling point, molecular formula and molecular weight of the 5-substituted pyrimidine-2-thio-4,6-dione	56
Table 2.3.a: thin layer chromatography of substituted diethyl malonate derivatives	57
Table 2.3.b: thin layer chromatography of the 5-substituted pyrimidine-2,4,6-trione	57
Table 2.3.c: thin layer chromatography of the 5-substituted pyrimidine-2-thio-4,6-dione	58
Table 2.4.a: Infrared spectral data of intermediate substituted diethyl malonate derivatives	59
Table 2.4.b: Infrared spectral data of 5-substituted pyrimidine-2,4,6-trione derivatives	60
Table 2.4.c: Infrared spectral data of 5-ethyl -5-phenyl (pyrimidine-2,4,6-trione (phenobarbitone, standard sample	61

Table 2.4.d: Infrared spectral data of the 5-substituted pyrimidine-2-thio-4,6-dione	62
Table 2.4.e.i: infrared spectral study of keto-enol tautomers in (diethyl phenyl malonate (as a liquid film using CCl ₄ as solvent	63
Table 2.4.e.ii: infrared spectral study of keto-enol tautomers in (barbituric acid (using KBr disk	63
Table 2.4.f.i: infrared spectral of diethyl malonate	64
Table 2.4.f.ii: infrared spectral of urea and thio-urea	64
Table 2.5.a. ultraviolet spectral data of mono substituted diethyl malonate	72
Table 2.5.b. ultraviolet spectral data of the 5-substituted pyrimidine-2,4,6-trione derivatives	73
Table 2.5.c. ultraviolet spectral data of the 5-substituted pyrimidine-2-thio-4,6-dione	74
Table (3.1): The carbonyl stretching vibration of the coupled diethyl malonate derivatives with urea and Thiourea	105
Table (3.2): Effect of the method of preparation of alkali halides disk in compounds (Va) and (Vc) for the region 1800-1600Cm ⁻¹	108