

Preparation and Identification of Macrocycles of Oxazepine Compounds

Nagham . Mahmood .Aljamali

Chem. Dept, College of Education , Univ. Kufa , IRAQ.

E-mail :Dr.Nagham _mj@yahoo . Com

Abstract:

A new type of macrocycles of oxazepine compounds have been prepared in this article , the macrocycles has been linked with (maleic anhydride, phthalic anhydride ,3- nitro phthalic anhydride)to produce new type which are macrocycles oxazepine.

Macrocycles oxazepine have been investigated by several techniques ((Uv-Visble),(C.H.N)-analyzer (FT-IR)-spectra ,H-NMR spectra ,Melting points).

Keyword : macro cycle , oxazepine , macro compounds , cyclization .

الخلاصة :

تم في هذا البحث تحضير نوع جديد لحلقات عيانية للأوكسازيبين و ذلك من مفاعلة الحلقة العيانية مع أحد الأنهيدريدات (أنهيدريد المالك ، أنهيدريد الفيثالك ، 3-تايترو أنهيدريد الفيثالك) لإنتاج حلقات الأوكسازيبين العيانية والتي تم إستخدام عدة تقنيات لتشخيصها تمثلت بطيف الأشعة فوق البنفسجية -المرئية ،الأشعة تحت الحمراء ، التحليل الدقيق للعناصر وطيف الرنين النووي المغناطيسي ودرجات الانصهار.

كلمات مفتاحية: حلقات كبيرة ، ، أوكسازيبين ، حلقات عيانية ، الغلق الحلقي .

Introduction :

Diethyl malonate is important class of compounds in several field of organic chemistry such as alkylation of acetoxy halide,incorporation with heterocyclic compounds to produce pharmaceutical compounds which have a wide range of pharmacological properties,for this reason,many methods have been reported for the preparation of these compounds in the last years have several applications.

In this work,the compound have been synthesized from combination of two compounds[Zhong,et.al.2004.,Clemons,et.al.2004.,Kucukguzel,etal.2004]by cyclocondensation or cyclization of same compound to produce hetero cycles including heteroatom containing nitrogen& sulphur atoms,for this reason their biological activity highly efficient [Maradiya. H.2002 .,Marione. M ,et al .2002 Varanda s.L,et al .2005] & low poisonous.

Since the discovery of the biological importance [Ikizler .A ,et al .2000 Xuezhang .L,et al.2002.,Wujec.M,et al.2004]of these compounds,the aim of many researcher was to synthesize many different substituted& various uses in many studies[Onkol.T,et al.2004.,Zamani.K,et al.2004] .

Experimental:

-All chemicals used were supplied from Merck & BDH-chemical company .

-All measurements were carried out by :

1 –Melting points : electro thermal 9300 ,melting point engineering(digital), LTD,U.K

2 – FT.IR spectra : fourrier transform infrared shimadzu 8300–(FT.IR) , KBr disc was performed.

3 – (C.H.N)– Elemental analyses were carried out by means of micro analytical unit of 1180 C. H. N elemental analyzer ., And The (¹H-NMR)- spectra were obtained in DMSO solution using (Bruker, Ultra Shield 3000 MKZ, Switzerland) .

Synthesis of 4-Propanoat -6-methyl-hydro pyridazinone (4) from (1-3):

The compound (4) was synthesized by reaction between (0.01mole, 1.6g) diethylmalonate& acetyl methyl chloride with refluxed for (2hrs) until the precipitate

formed, after cooling, the precipitate was filtered off, then (0.01 mole, 2.1 g) of this precipitate was condensed with (0.01 mole, 0.32 g) of hydrazine in presence of absolute ethanol with reflux for (2hrs), after cooling, the precipitate was filtered off & recrystallized with absolute ethanol for twice to yield 86% from compound (4).

Synthesis of : 3,4-pyrazolone-6-methyl hydropyridazine (5): and : 3,4-thiazepanone -6-methyl –hydropyridazine (6):

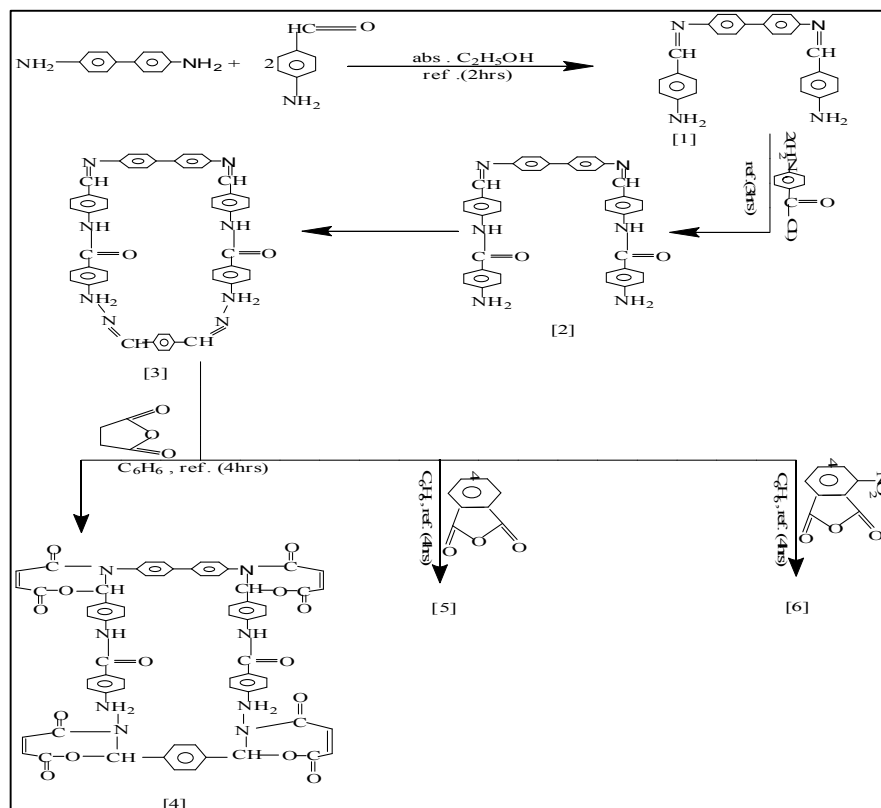
Condensation reaction by refluxing mixture of (0.01 mole, 1.8 g) of compound (4) with one of (0.01 mole, 0.32 g) of hydrazine, (0.01 mole, 0.7 g) of mercapto amino ethylene respectively, were react for (4hrs), after cooling, the precipitate was filtered off & recrystallized for twice with absolute ethanol to give 84%, 87% of compounds (5), (6) respectively.

Synthesis of 3-propanoate –hydro thiophen -2-one (7): and 2,3-thiazepinone –dihydrothiophen (8):

(0.01 mole, 1.6 g) of diethyl malonate was condensed with (0.01 mole, 0.9 g) of mercapto ethylene chloride in presence of ethanol with refluxing for (2hrs), the precipitate was filtered off, then (0.01 mole, 2.2 g) of this precipitate was cyclized upon heating in refluxing for (4hrs), after cooling, the precipitate was filtered off & dried, recrystallized from absolute ethanol for twice to yield 85% of compound (7).

The compound (8) was synthesized by refluxing between (0.01 mole, 1.7 g) of compound (4) & (0.01 mole, 0.7 g) of mercapto amino ethylene for (4hrs), after cooling, the precipitate was filtered & dried, recrystallized from absolute ethanol for twice to yield 87%.

Reaction Scheme:



Results & Discussion :

All synthesized compounds (1-8) have been characterized by their melting points, TLC technique and spectroscopic techniques (FT-IR-spectra, (C.H.N) analysis, & H-NMR-spectra) :

The spectra of compounds (1-8) showed : disappearance of frequency such as thiol group (SH) in compound (3), ester group (COOC_2H_5) in compounds (3,4,7) and appearance new bands such as $\{(\text{CH}_2\text{-S})$, (NH-CO) , (C=N) endo cycle $\}$ in compounds (5-8) , while in H-NMR-spectra, disappearance of signals and peaks such as proton of thiol group (SH) in compound (3) , proton of ethyl group in ester (COOC_2H_5) in compounds (3,4,7) and appearance new peaks such as signals due to protons of $\{(\text{CH}_2\text{-S})$, (NH-CO) , (NH) endo cycle $\}$ in compounds (5-8) , these changes in position of peaks are evidence of synthesized compounds (1-8) , the details:

Compound (4): absorption band appeared at $(1678)\text{cm}^{-1}$ due to carbonyl of amide (CO-NH) [Silver Stein R M, et al.2007] , other band appeared at $(1588)\text{cm}^{-1}$ due to (C=N) endocyclic ., singlet signal at δ 9.8 for one proton of amide (1H, Singlet, NH-CO) [Silver Stein R M, et al.2007] , signals at δ 10.43, 10.55 for protons of ethyl group of ester (2H, 3H ; Triplet, multiplet ; COOC_2H_5) , singlet signal at δ 2.38 for three protons of methyl group (3H, Singlet, $-\text{CH}_3$) , signals at δ 2.9 for protons of (2H, 2H , triplet, $\text{CH}_2\text{-CH}_2\text{-}$) in cycle.

Compound (5) : absorption band appeared at $(1681)\text{cm}^{-1}$ due to carbonyl group of amide (CO-NH) , two bands appeared at $(1577$, $1488)\text{cm}^{-1}$ due to (C=N) endocyclic

[Silver Stein R M, et al.2007], other bands appeared at $(3345)\text{cm}^{-1}$ due to (-NH) of amide in cycle ., singlet signal at δ 9.8 for one proton of amide (1H, singlet, NH-CO), singlet signal at δ 7.82 for one proton of (1H, singlet, NH-N=) in cycle , signals at δ 3.45, δ 2.9 for protons of (1H-triplet , 2H-doublet , $\text{CH}_2\text{-CH-}$) [Silver Stein R M, et al.2007], in cycle & singlet signal at δ 2.87 for three protons of methyl group (3H, singlet, CH_3).

Compound (6) : absorption band appeared at $(1686)\text{cm}^{-1}$ due to carbonyl group of amide (CO-NH) , two bands appeared at $(651$, $1438)\text{cm}^{-1}$ due to (C-S) & (S-CH_2) (Silver Stein R M, et al.2007) respectively of endocyclic , other bands appeared at $(1595$, $1460)\text{cm}^{-1}$ due to (C=N) endocyclic [Silver Stein R M, et al.2007]., singlet signal at δ 9.9 for one proton of amide (1H, singlet, NH-CO) , signal at δ 3.95 for protons of $(\text{CH}_2\text{-CH-})$ in cycle .

Compound (7) : absorption band appeared at $(1730)\text{cm}^{-1}$ due to carbonyl group of ester (COOC_2H_5) [Silver Stein R M, et al.2007], two bands appeared at $(1436$, $1629)\text{cm}^{-1}$ due to (S-CH_2) , (S-CO) endocyclic [Silver Stein R M, et al.2007], respectively ., signals at δ 3.98 for protons of $(\text{S-CH}_2\text{CH}_2\text{-})$, signals at δ 10.36 for protons of ethyl group of ester (COOC_2H_5) .

Compound (8) : absorption band appeared at $(1660)\text{cm}^{-1}$ due to carbonyl group of amide (CO-NH) , & two bands appeared at $(663$, $1486)\text{cm}^{-1}$ due to (C-S) & (S-CH_2) [Silver Stein R M, et al.2007] endocyclic , respectively ., singlet signal at δ 9.72 for proton of amide (1H, singlet, NH-CO) , signal at δ 3.80 for protons of (2H, 2H; triplet, $\text{S-CH}_2\text{CH}_2\text{-N}$) in first cycle , & signal at δ 3.10 for protons of (2H, 2H; triplet, $\text{SCH}_2\text{CH}_2\text{-}$) [Silver Stein R M, et al.2007], in second cycle .

Other data of functional groups and other peaks shown in the following in table {1,2}, fig. {1-10} . these changes in position of bands are evidence of synthesized compounds (1-8) .

It was found from compared the calculated data with found data of these compounds in (C.H.N)–Analysis , the results were compactable , the data of analysis,M.F , and melting points are listed in table {2}.

These reactions followed by TLC technique through appearance of one spot, which indicates to formation of compounds (1-8) .

Acknowledgement :

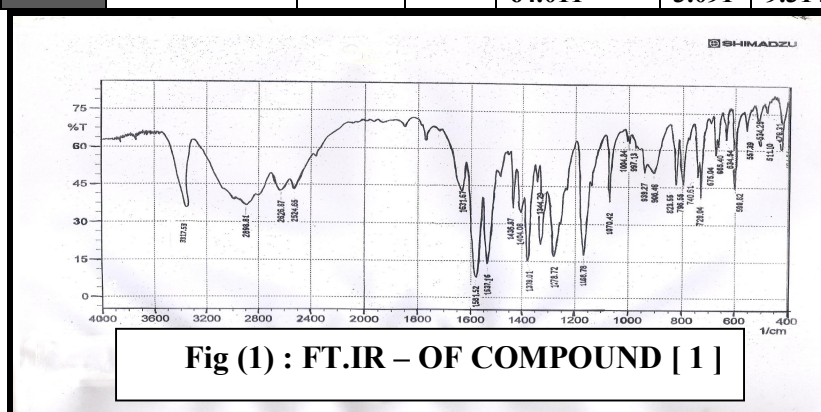
I would like to express my thanks to Mr .Ahmad for providing (C.H.N) element analytical , H.NMR-spectrum & melting points(digital).And express my thanks to ((Zaidan Company of Chemical)) in Jordan for supplied some materials .

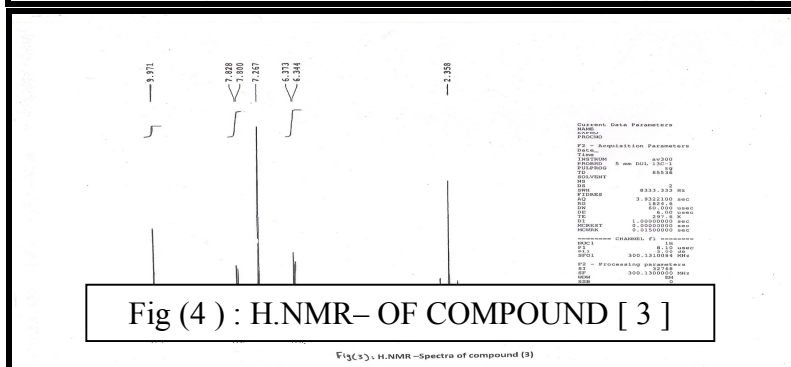
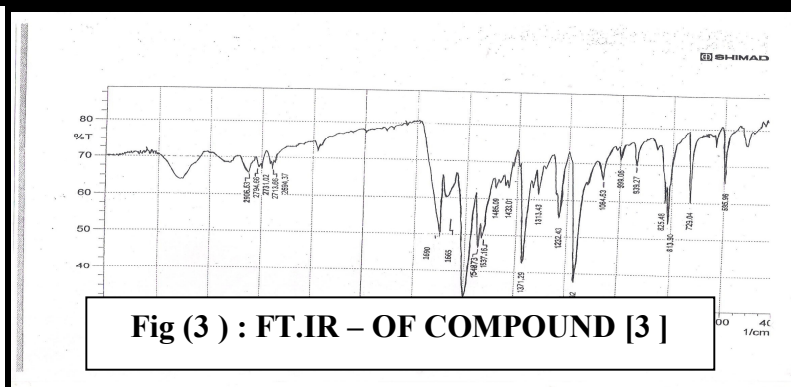
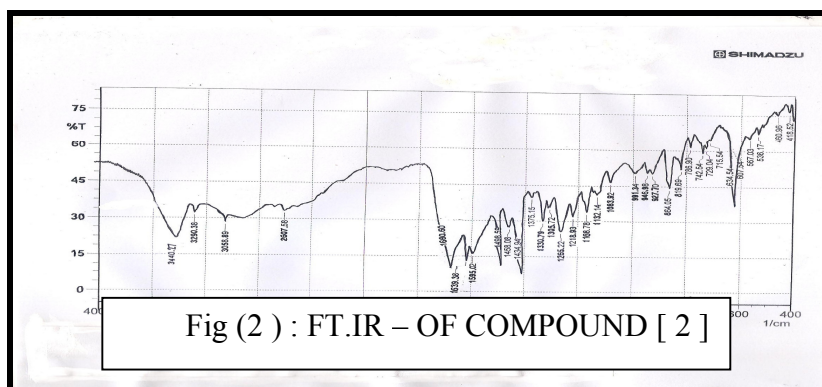
Table (1).FT-IR data (cm⁻¹) of compounds [3-6].

Comp. no	(C=N) Imine group	(C=O)str. Lactam(amide)	(C-O-C)	Others
[1]	1631	----	----	(-NH ₂):3317
[2]	1639	----	----	(-NH ₂):3440
[3]	1611	----	----	
[4]	----	1690 1665	1232	
[5]	----	1700 1675	1230	
[6]	----	1705 1670	1240	(C-NO ₂): 1330,1535

Table (2) : Melting points , M.F , $\lambda_{\max}$ & (C.H.N) Analysis of compounds.

Comp. No	M.F	m.p (°C)	$\lambda_{\max}$ (nm)	Calc./found C%	H%	N%
1	C ₂₆ H ₂₂ N ₄	152	315			
2	C ₄₀ H ₃₂ N ₆ O ₂	168	340			
3	C ₄₈ H ₃₄ N ₆ O ₂	210	375			
4	C ₆₄ H ₄₂ N ₆ O ₁₄	228	395	68.694 68.608	3.756 3.761	7.513 7.490
5	C ₈₀ H ₅₀ N ₆ O ₁₄	235	410	72.837 72.793	3.793 3.738	6.373 6.384
6	C ₈₀ H ₄₆ N ₁₀ O ₂₂	248	420	64.085 64.011	3.070 3.091	9.345 9.314





References:

- Akine .S, Hashimoto .D, Saiki .T, Nabeshima .T ., (2004)., Tetrahedron Lett ,45, 4225-4227., Cited by IVSL OF IRAQ*.
- Amanda .J., Joseph .K.H ,Federico .E ,Yan .A and Mark J., (2005., J.Org . Chem, 70,7936-7946.
- Beckmann .U, Brooker . S ., (2003)., Coord . Rev, 245,17-29 .
- Beer.P,D., Gale .P.A ., (2001)., Angew .Chem. Int.Ed, 40,486-516.
- Eldeen .Z.M.,Eur. (1982)..J.Med. Chem .,5,479.
- Fahad.A.H.and Obaid .H., (2001)..Iraqi journal of chemistry ,27,3 .
- Ismail .E.G., (1999).,Turk.J.Chem.,23,67.
- Jarrahpour.A,Motamedifar.M and Paskhir . K., (2004)..Molecule, 9,875,1420.
- Leroy.C., (2003)..Annu.Rep.Porg.Chem.,Sect.A, 99,289-347.
- Mustafa .Y, Askin. K and Basaran .D .,(2007).. J. Serb . Chem .Soc,72 ,3 , 215 –224.
- Naghham .M . Al Jamali ., (2004)..J .AL- Qadisiah for pur Science .,9,4,257-267.
- Naghham .M . Aljamali ., (2010)..J. Al –Qadisiah . 15 ,1,33-39.
- Naghham .M, Al-Jamali ., (2010). , J. Babylon .,3,18,925-942.
- Rajaa.A., (2008)..M.Sc.Thesis ,University of Kufa.

- Shirakawa .S., Yamamoto .K., Kitamura .M., Ooi .T., Maruoka .K., (2005),Angew . Chem . Int.Ed, 44,625-628.
- ilverstin. R.M. , (1996)., "Spectrometric Identification of Organic Compound " , 6th Ed .John Wiley and Sons Inc .
- Vigato . P.A Tamburini .S ., (2004)..Coord . Chem .Rev , 248,1717-2128.