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Synthesis of Novel thiazolidinone Oxazepens derivatives from Schiff's base

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Abstract:

A new thiazolidinone and oxazepens compounds drived from azo compounds were synthesized. Thiazolidinone compounds prepaerd by added of α-Mercapto acetic acid to different synthesized Schiff bases respectivey in benzene as a solvent. Oxazepens derivatives were prepared by added of maleic anhydride to a solution of Schiff's base in dry benzene and then the mixture was refluxed two hours. On other hand, Schiff's bases prepared by the reaction of 4-methylbenzohydrazide with different appropriate aldehydes in absolute ethanol. All Schiff bases derivatives were characterized on the basis of their microanalysis IR, ^{1}HNMR spectral data.

Keywards: Schiff bases, thiazolidinone, Oxazepene, Malic anhydride, Cycloaddition Reaction.

الخلاصة :

تم تصنيع مركبات جديدة من ثيازوليدينون وأوكسازيبينز مشتقة من مركبات الآزو. مركبات ثيازوليدينون prepaerd بإضافة حامض الأسيتيك ألفا ميركابتو إلى قواعد شف المركبة المختلفة في البنزين كمذيب. تم تقشير مشتقات Oxazepens مسبقًا بإضافة أنهيدريد المالئيك إلى محلول من قاعدة شف في بنزين جاف ثم تمت تصعيد الخليط لمدة ساعتين. من ناحية أخرى ، تم تحضير قواعد شف بتفاعل 4 ميثيل بنزوهيدرازيد مع الألدهيدات المختلفة المناسبة في الإيثانول المطلق. تم تمييز جميع مشتقات قواعد شيف على أساس البيانات الطيفية الخاصة بهم من التحليل الدقيق- IR و 1HNMR.

Introduction:

In recent decades, a big wave has emerged that is interested in studying and synthesis of heterocyclic compounds this because of the important biological properties of these compounds [1]. One of these compounds is 1, 3-oxazepine rings was based on limited classical type of reaction is a per cyclic reactions [2, 3] are used to synthesis of 1, 3-oxazepine ring derivatives [4, 5].

Some oxazepine derivatives showed biological activities against various types of bacteria [6, 7] and some of them act as inhibitors of some enzymes action [8]. On other hand, thiazolidinone derivatives exhibit diverse pharmacological activities like anti-inflammatory[9], analgesic[10], antiviral, antimicrobial[11, 12], antimycobacterial[13], anti-fungal activities[14, 15]. Based on the above observation it is worthwhile to prepare newer compounds of thiazolidinone derivatives for their anticonvulsant activity [16].

Experiment

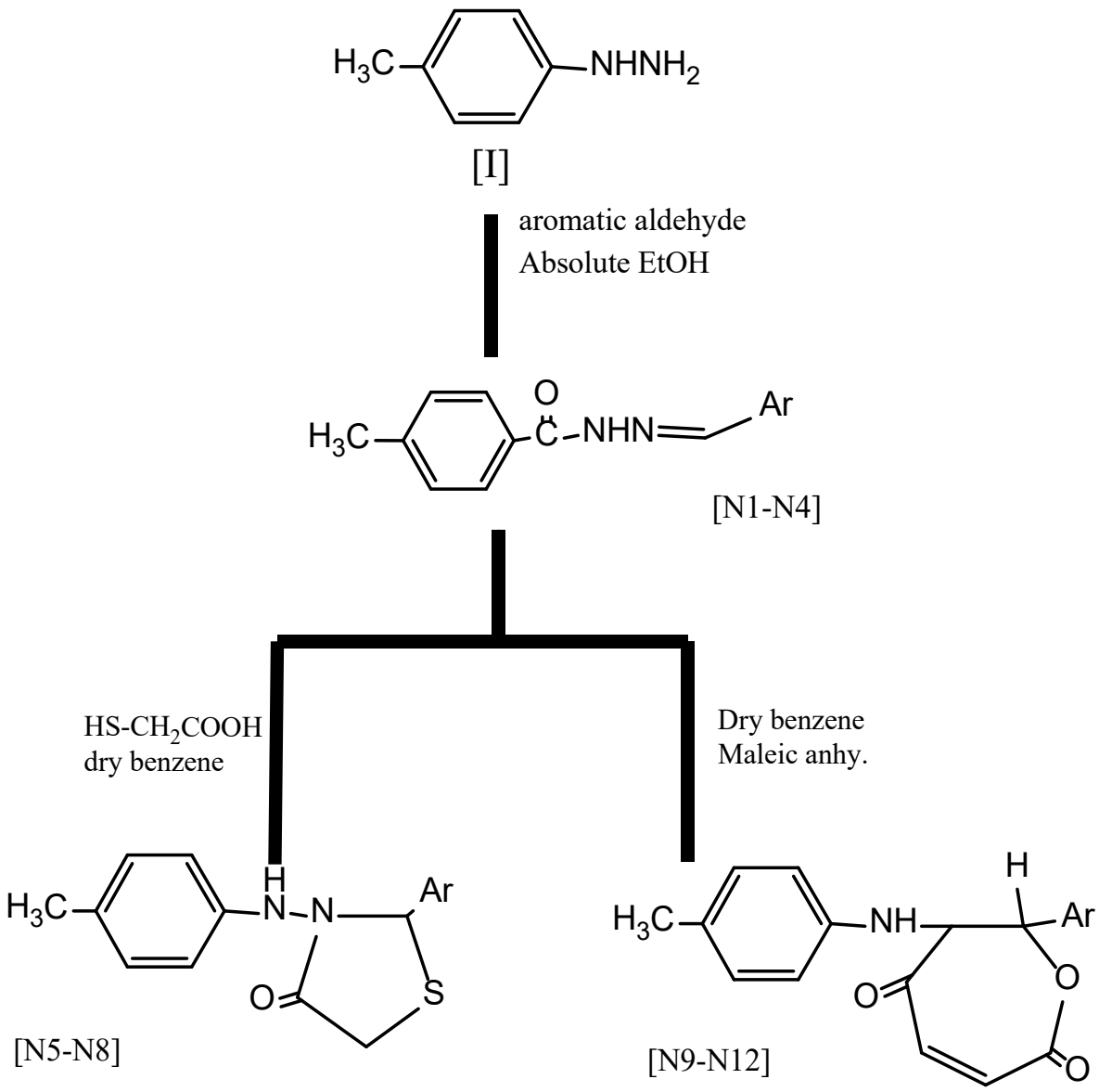
(1) All chemicals used were supplied from Merck, Fluka and BDH-chemical Company.
(2) Melting points were recorded using Gallen Kamp melting point apparatus and are uncorrected.
(3) FI-IR spectra: Fourrier transform infrared shimadzu (8300) (FI-IR), KBr disc was performed by Al- Nahrain University Iraq.
(4) HNMR spectra: in center Lab-Institute of Earth and Environmental Science, Al-byat University Jordan.

Experimental section

1.1. Synthesis of Schiff's bases compounds [N1-N4] prepared [17, 18] by addition of appropriate aldehyde (0.001 mol) to a solution of compound 4-methylbenzohydrazide [I] (0.15g, 0.001mol) in absolute ethanol (20ml). The mixture was refluxed for 4-5 hours and cooled; the formed precipitate was filtered and recrystallized from ethanol.

1.2. Synthesis of thiazolidinone derivatives [N5-N8] to a stirred solution of Schiff's base (0.000055mol) in (5ml) dry benzene α-Mercapto acetic acid (0.051g, 0.000055mol) in (15ml) dry benzene was added drop wise. The reaction mixture was refluxed for about 10 hours, then the mixture was left at room temperature for 24 hours and extra solvent was evaporated and neutralized by a solution of 10% sodium bicarbonate, the pale yellow solid was filtered off and recrystallized from benzene [19, 20].

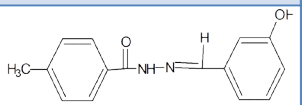
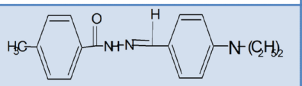
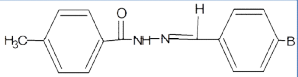
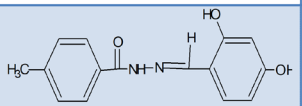
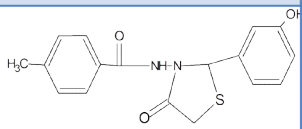
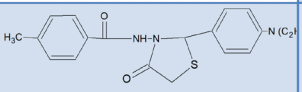
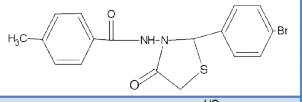
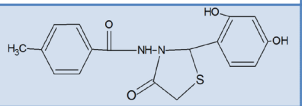
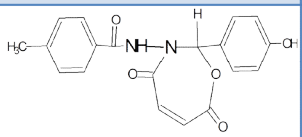
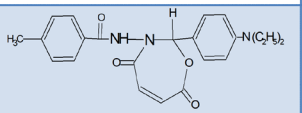
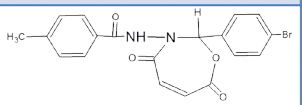
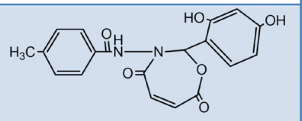
1.3. Synthesis of oxazepine derivatives (N9-N12) A mixture of (0.1g) from malice and phthalic anhydrid respectively in benzene was stirring with heating for five minuet, then (0.2 g) from prepared Schiff bases was dissolved in (5ml) of benzene and added gradually to anhydride solution and refluxing for 4 hours at (70-80 ° C). The mixture was cold and the precipitate recrystilized from benzene [21, 22]. The physical properties of compounds (N1-N12) are listed in table (1-1).



Ar: Ph-OH, Ph-$N(C_2H_5)_2$, Ph-Br, Ph-$(OH)_2$

Scheme I

Table(1): The physical properties of compounds [N1-N12]

Comp. No.	Molecular formula	Melting Point	Color	Solvent	Yield (%)
N1		83-85	Pale yellow	Ethanol/Water	87
N2		155-157	Bright yellow	Ethanol/Water	94
N3		180-182	White	Ethanol/Water	96
N4		194-196	orange	Dry Benzene	81
N5		152-154	Bright yellow	Dry Benzene	76
N6		200 deco.	orange	Dry Benzene	91
N7		131-133	Pale yellow	Ethanol	58
N8		106-108	yellow	Ethanol	52
N9		210-212	brown	Ethanol	69
N10		106-108	Red	Ethanol	52
N11		175-177	yellow	Ethanol	58
N12		186-188	Pale brown	Ethanol	53

Results and Discussion:

Schiff bases prepared by mixing an equals moles of amine and aldehyde in acetic acid, the oxygen of carbonyl compounds will attack to proton of acetic acid to give HO^{+}=C ion and, then the Oxygen carbon double bond will break and a carbocation with full charge form. The Neucleuphil attacks the electrophil and a water molecule eliminates [23, 24].

FT-IR spectrum of azoaldehyde derivatives [N1-N4] showed the following

characteristic absorption bands respectively: 3211.3, 3224.8, 3284.5 and 3213.2 cm^{-1} for v(N-H str.), bands at 3099.4 , 3050.0 , 3030.0 and 3037.7 cm^{-1} attributed to the v(C-H str.) aromatic. Bands at 1568.05, 1598.9, 1600.8 and 1618.2 cm^{-1} for v (C=N str.), bands of v (C=O str.) amide appear at 1649.0, 1662.5, 1662.5 and 1618.2 cm^{-1}. Band at 3290 cm^{-1} attributed to stretching vibration of v (OH str.) of compound [N1] , 746 cm^{-1} for v(C-Br str.) for [N3] and broad band at 3382 cm^{-1} for v(OH str.) of [N4].

The ^{1}H.NMR spectrum of compound [N1] absorption δ 8, 72 (s, 1H, N=CH) and δ 8, 22 (s, 1H, NH) and δ 6.9-7.7 (m, 8H, aromatic) δ 5.2 (s 1H, OH) and δ 2.33 (s, 3H, CH_3).

^{1}H.NMR spectrum of compound [N2] absorption δ 9, 01 (s, 1H, N=CH) and δ 8, 06 (s, 1H, NH) and δ 7.2-8.03 (m, 8H, aromatic) δ 3.3(q, 4H, CH2) δ 2.6 (s, 3H, CH_3).and δ 1.9 (t, 3H, CH_3).

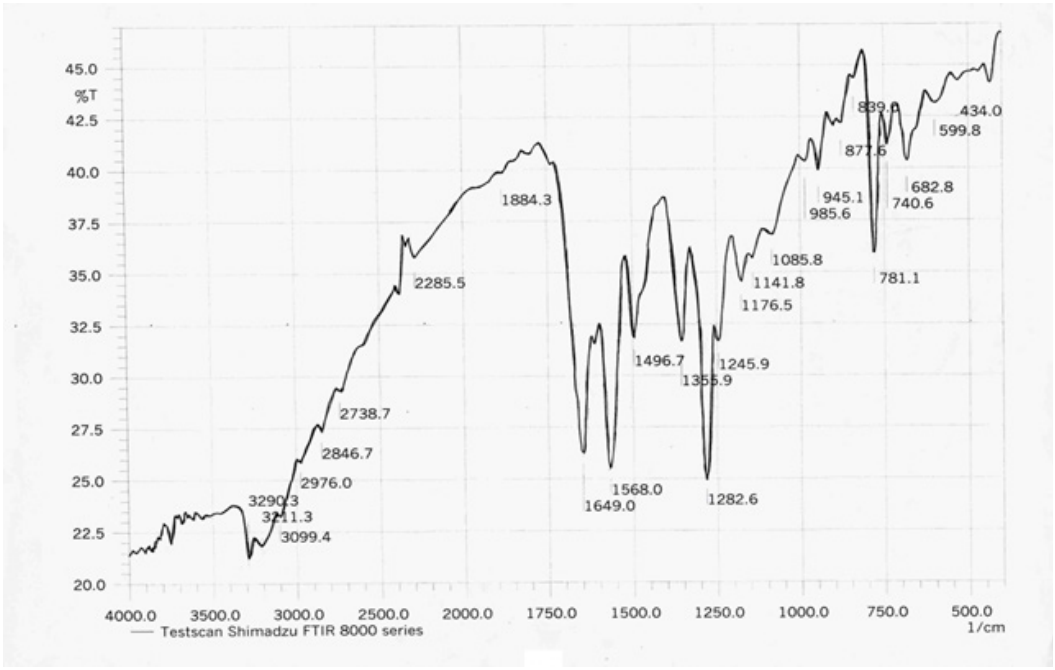
FT.IR spectrum of compounds [N4-N8] showed the following absorption bands respectively assigning the proposed structure: for υ (C=O str.) amide 1650, 1670.2, 1658.7 and1650 cm^{-1}, bands υ(C=O str.) carbonyl of thiazoldninone at: 1712.7, 1710.7, 1691.5 and 1708.8 cm^{-1} respectively. Bands of υ (N-H str.) for [N2 and N3] respectively 3232.5and 3041.5 cm^{-1} on other hand both compound [N1 and N4] υ (N-H str.) overlap with OH. Bands v (C-H str.) aromatic in plane appear 3055.0 and (2923.9-2850.6) cm^{-1} for [N6 and N7] respectively. Absorption bands at 764, 740, 744 and 748 were due to v (C-S-C str.). Broad band's at 3400 and 3244 cm^{-1} due to v (OH str.) for [N5 and N8] respectively.

The ^{1}H.NMR spectrum of compound [N7] absorption: δ ∧. 0 (s,1H,NH), δ 7.2-7.8 (m, 8H , aromatic) , δ 5.3 (s, 1H ,CH ring), δ 2.50 (s, 3H, CH_3) and δ 4.2 (s, 2H, CH_2 ring).

The FT- IR spectra of the title synthesized compound [N9-N12] showed the following absorption bands respectively: for υ(C=O str.) cyclic

1710.7, 1660, 1739.7 and 1678 cm^{-1}, υ(N- H str.) for compound [N9] overlap with (OH str.), for compound [N10 -N12] bands of v(N-H str.) respectively: 3205.5, 3180 and 3200 cm^{-1}. Bands of v(C=O amide) [N10-N12] appear respectively: 1645.2, 1647.1 and 1651 cm^{-1}.

The ^{1}H.NMR spectrum of compound [N11] absorption: δ 8. 8 (s,1H,NH), δ 7.3-7.7 (m, 8H , aromatic) , δ 7.5 (s, 1H ,CH ring), δ 2.7 (s, 3H, CH_3) and absorbs δ 5.9-6.2 (d*d, 2H, HC=CH ring). The FTIR and HNMR charts of the synthesized compounds [N1-N12] shown below [fig 1-16].



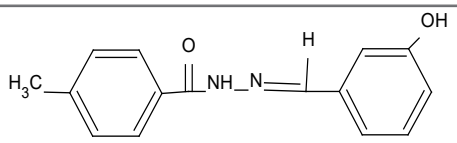
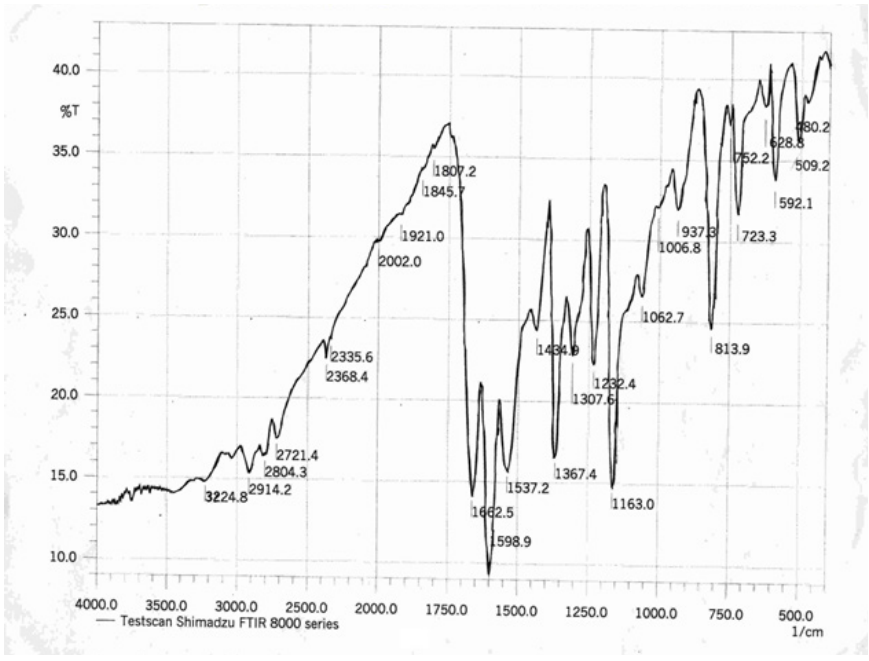


Figure (1) N'-(3-hydroxybenzylidene)-4-methylbenzohydrazide
Compound N1



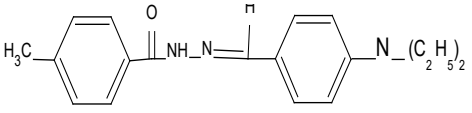
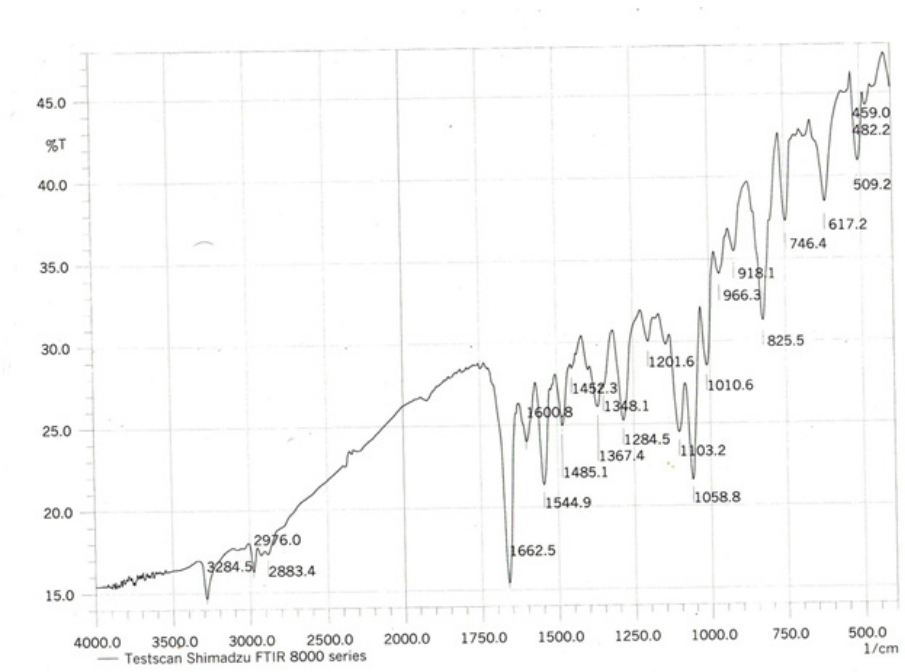


Figure (2) N'-[4-(diethyl amino) benzylidene]-4-methylbenzohydrazide
Compound N2



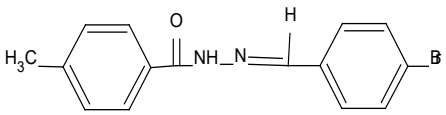
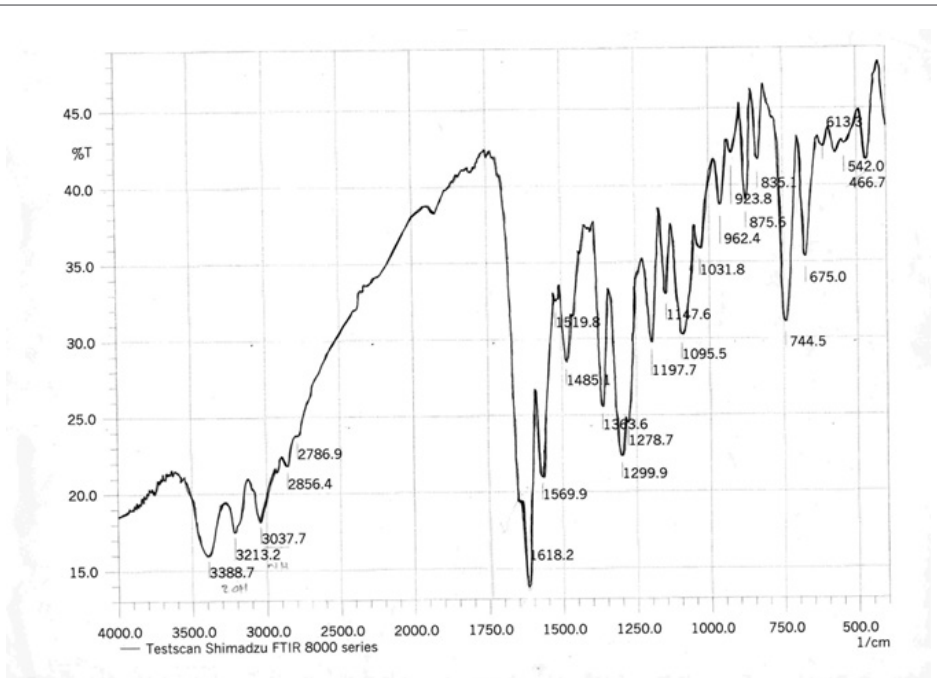


Figure (3) N'-(4-bromobenzylidene)-4-methylbenzohydrazide Compound N3



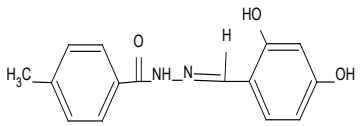
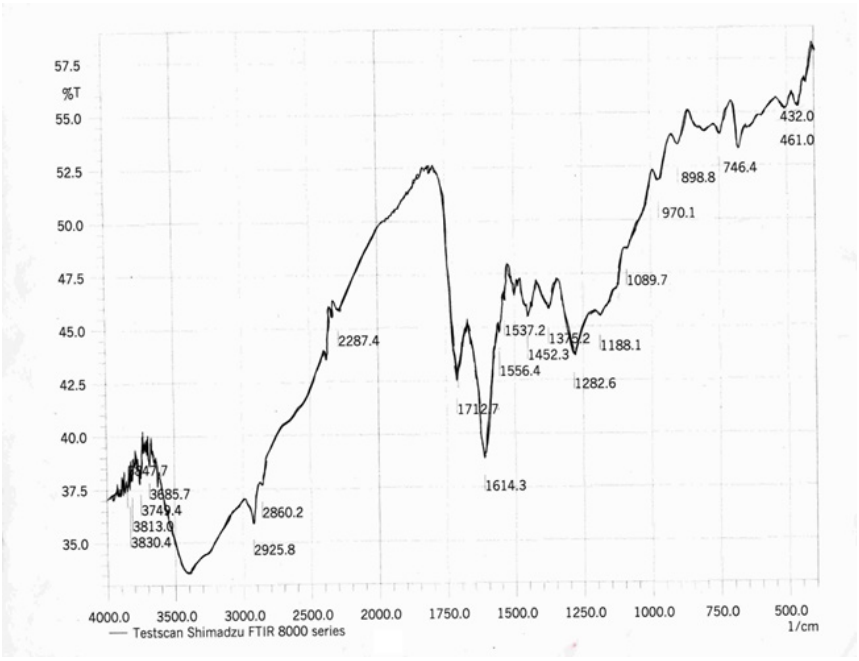


Figure (4) N'-[(2, 4-dihydroxybenzylidene)-4-methylbenzohydrazide Compound N4



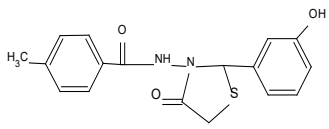
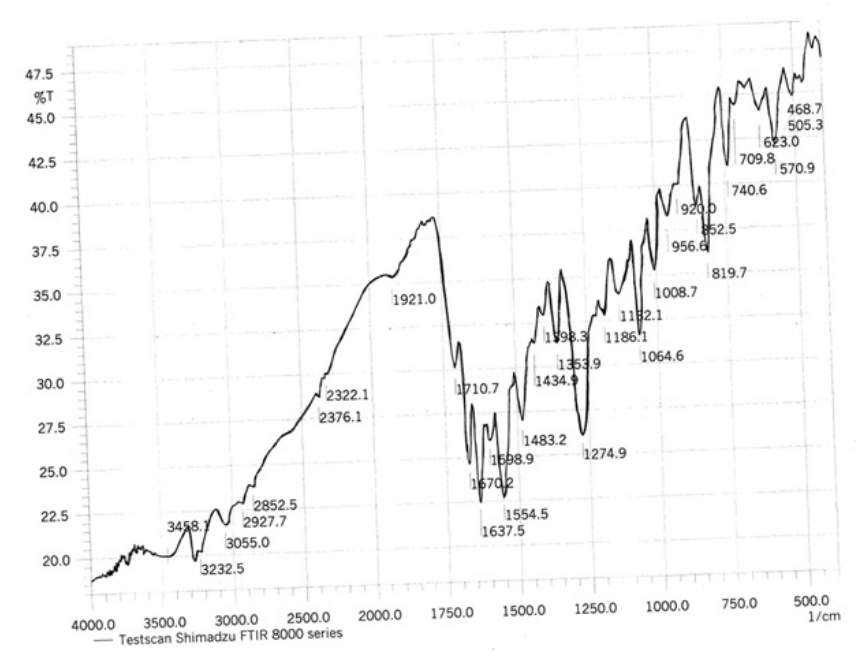


Figure (5)
N-[2-(4-hydroxy phenyl)-4-oxo-1, 3-thiazolidin-3-yl]-4-methyl benzamide
Compound N5



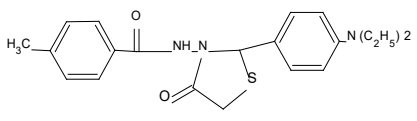
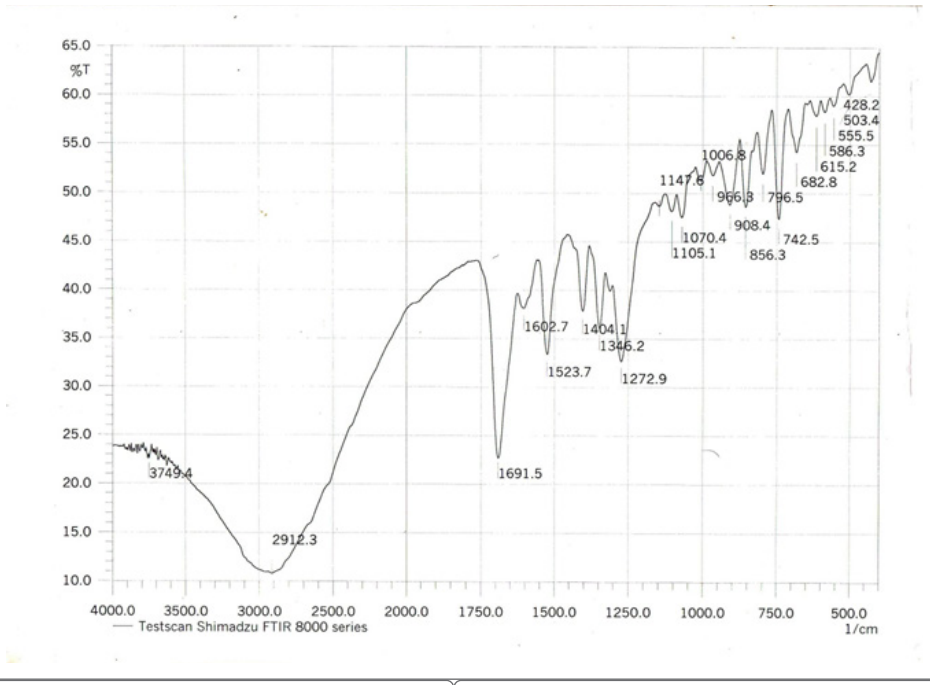


Figure (6) N-{2-[4-(diethylamino) phenyl]-4-oxo-1, 3-thiazolidin-3-yl}-4-methylbenzamide
Compound N6



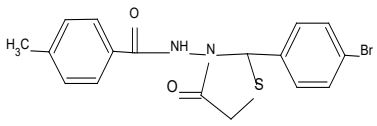
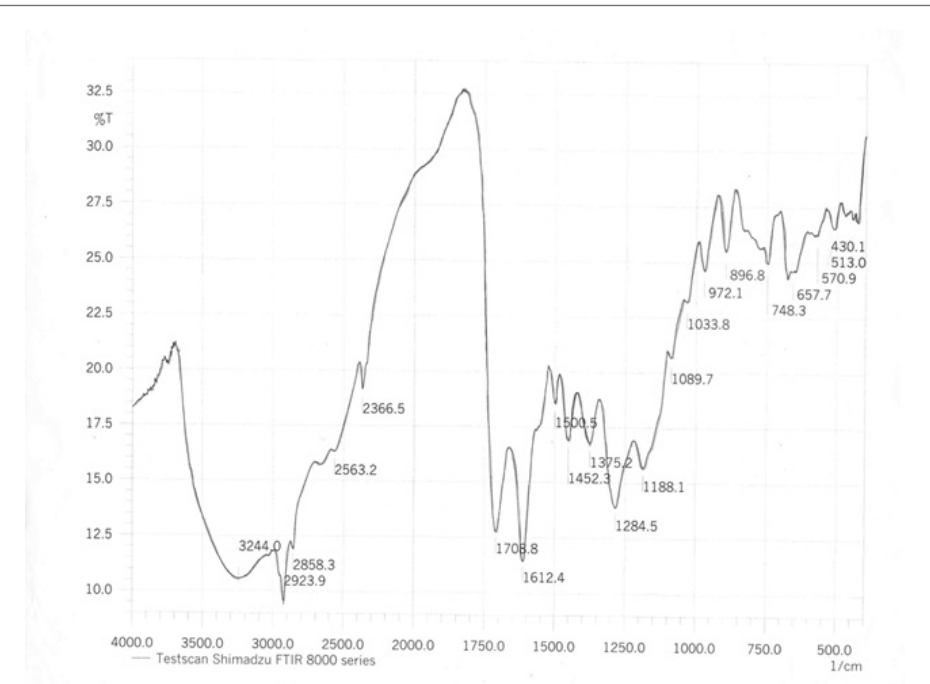


Figure (7) N -[2-(4-bromophenyl)-4-oxo-1, 3-thiazolidin-3-yl]-4-methylbenzamide
Compound N7



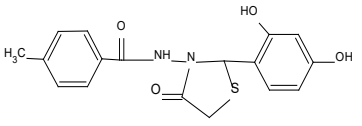
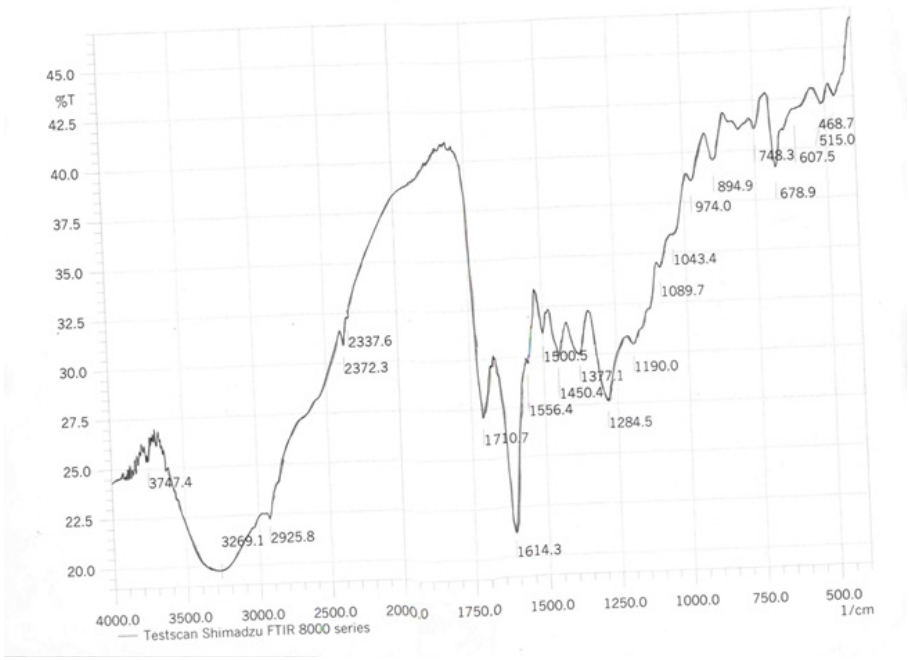


Figure (8) N-[2-(2, 4-dihydroxyphenyl)-4-oxo-1, 3-thiazolidin-3-yl]-4-methylbenzamide
Compound N8



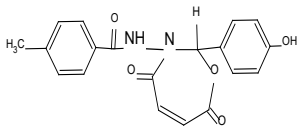
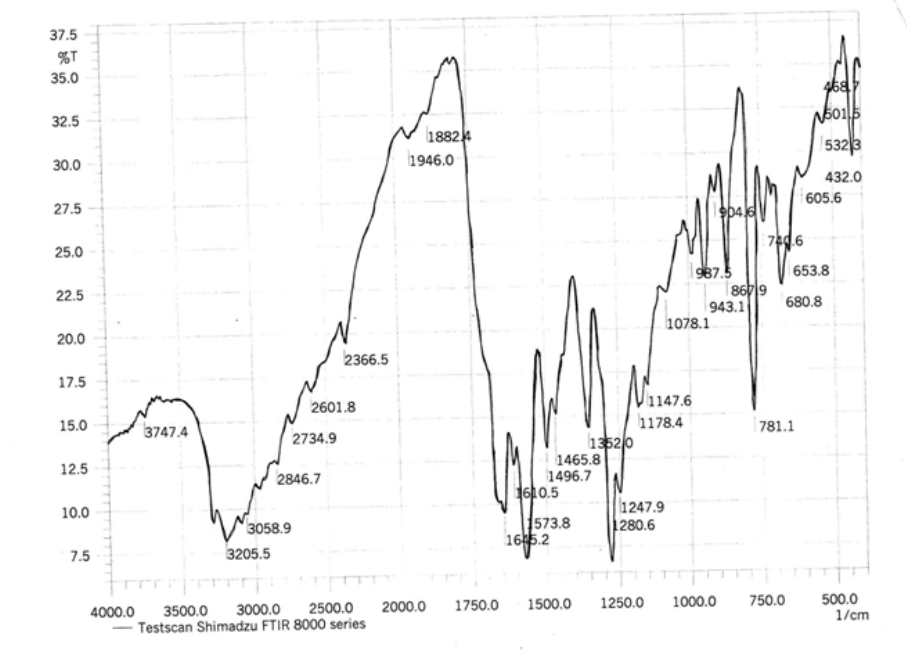


Figure (9) N-[2-(4-hydroxyphenyl)-4, 7-dioxo-4, 7-dihydro-1, 3-oxazepin-3(2H)-yl]-4-methylbenzamide Compound N9



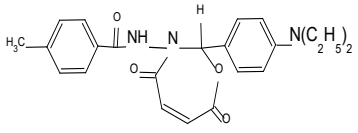
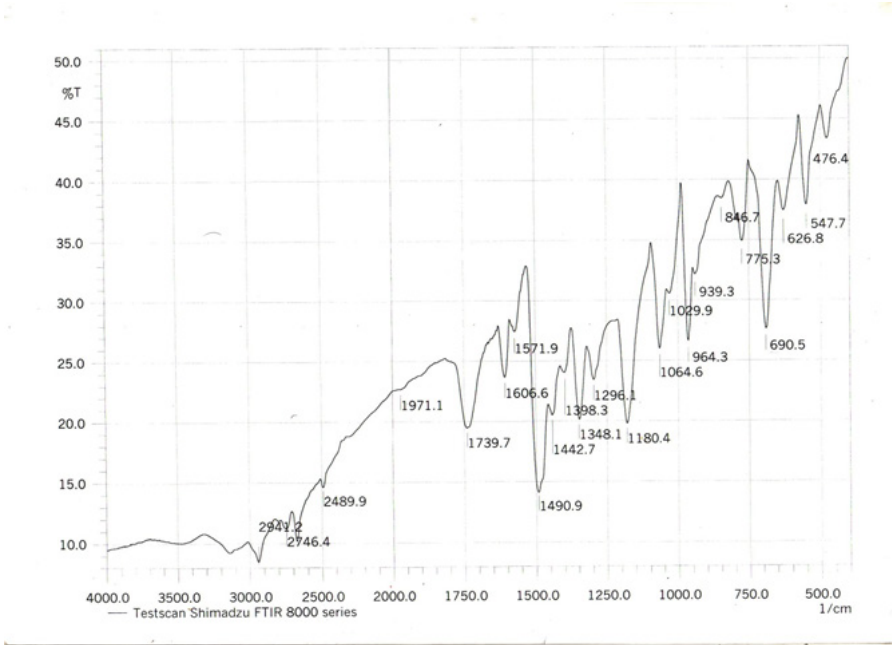


Figure (10) N-[2-[4-(diethylamino) phenyl]-4, 7-dioxo-4, 7-dihydro-1, 3-oxazepin-3(2H)-yl]-4-methylbenzamide Compound N10



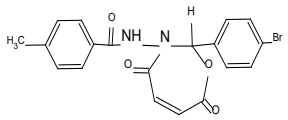
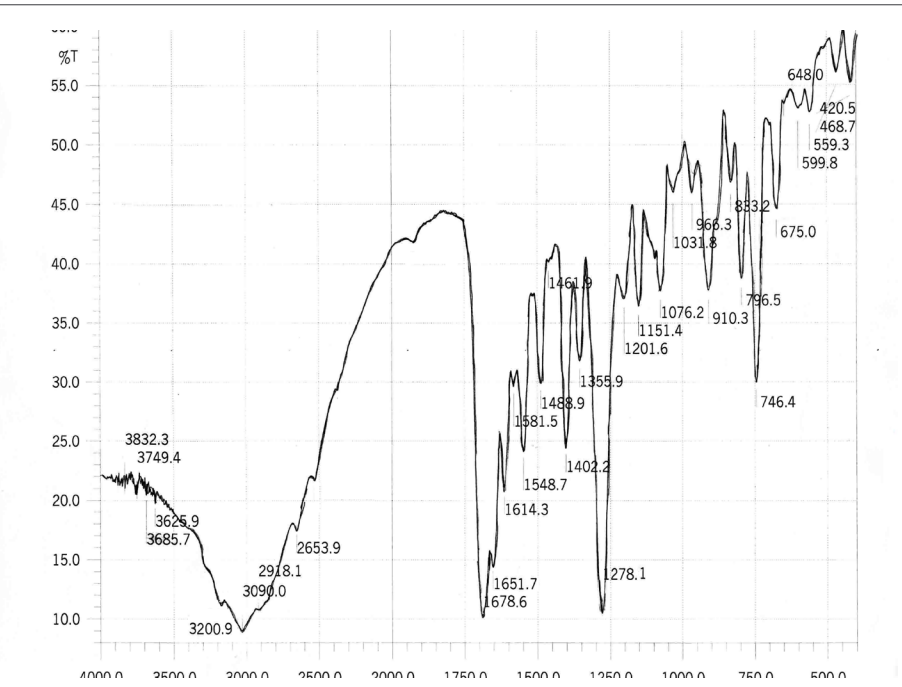


Figure (11) N-[2-(4-bromophenyl)-4, 7-dioxo-4, 7-dihydro-1, 3-oxazepin-3(2H)-yl]-4-methylbenzamide
Compound N11



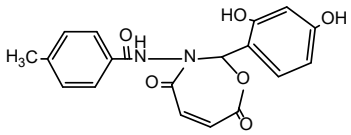
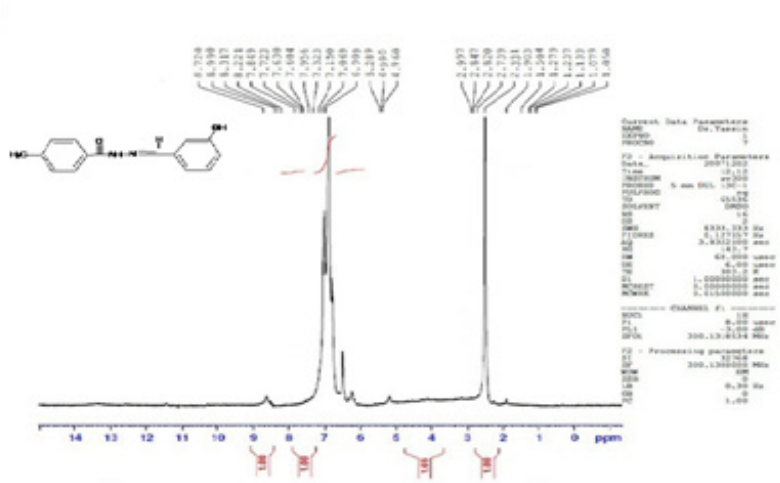
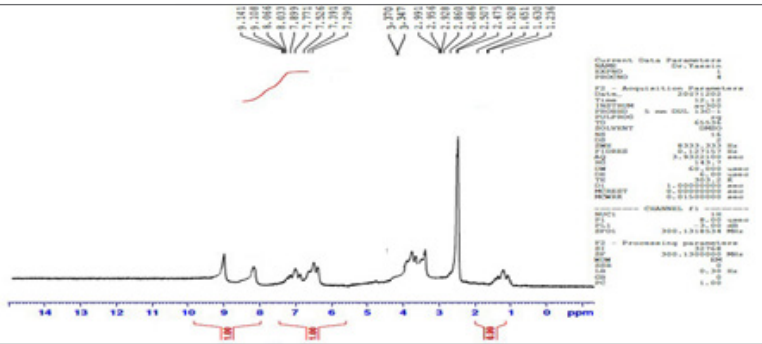


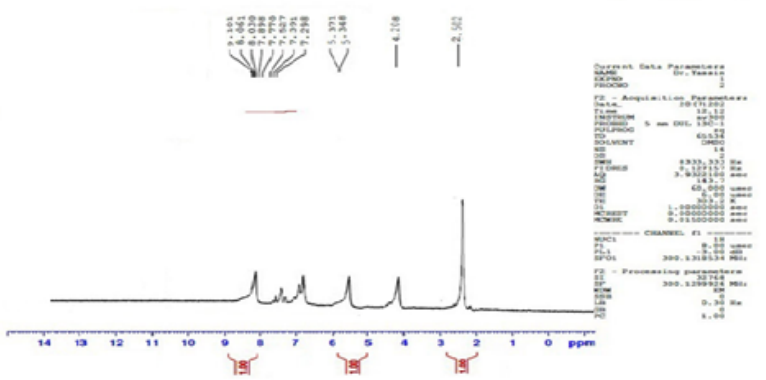
Figure (12) N-[2-(2,4-dihydroxyphenyl)-4, 7-dioxo-4, 7-dihydro-1, 3-oxazepin-3(2H)-yl]-4-methylbenzamide
Compound N12



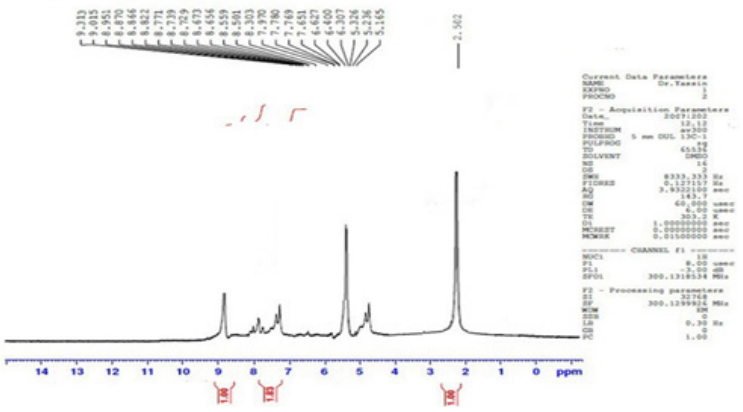
(Fig 13)
1-HNMR for compound N1



(Fig 14)
1-HNMR for compound N2



(Fig 15)
1-HNMR for compound N7



(Fig 16)
1-HNMR for compound N12

Conclusions

New 4- methyl-[N-(4-oxo-2-aryl-1, 3-thiazolidine-3-yl)] benzohydrazide and N- (4, 7-dioxo-2-aryl-1, 3-oxazepin-3(2H)-yl)-4-methylbenzamide derivatives were synthesized in two steps starting from N-arylidene-4-methylbenzohydrazide in dry benzene with different reagents.

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