Synthesis and Characterization of new seven-membered heterocyclic derivatives compounds

(Oxazepines)

تحضير وتشخيص بعض المشتقات لمركبات جديدة ذات حلقات سباعية (الاوكسازيبينات)

A Dissertation

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By

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قال تعالى

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

يَرْفَعِ اللَّهُ الَّذِينَ آمَنُوا مِنْكُمْ
وَالَّذِينَ أُوتُوا الْعِلْمَ دَرَجَاتٍ

صَدَقَ اللَّهِ الْعَظِيمِ

المجادلة (11)

شكر وتقدير

قال تعالى (وَمنْ يّشْـكْر فُـأّنِمَاّ يّشْـكْر لَنّفْسَـهِ)

وقال رسوله الكريم (صلى الله عليه واله)

من لم يشكر الناس لا يشكر الله عز وجل

الحمد لله الذي جعل الشكر مفتاحا لذكره والصلاه والسلام على خير خلقه نبيه الصادق الامين واله الطيبين الطاهرين نحمد الله عز وجل الذي وفقنا في اتمام هذا البحث العلمي والذي الهمنا الصحه والعافيه والعزيمه

فالحمد لله حمدا كثيرا

و أنا على مشارف نهاية رحلة بحثي هذا لا يسعني إلا أن أتقدم بعظيم امتناني الى الأستاذ المشرف الدكتور (زياد عمران موسى)

لدعمه و مساندته لي طيلة فترة البحث والتي كان لها الأثر الكبير في التخفيف من صعوبات ومشقات البحث . كذلك أجد من الواجب أن اتقدم بخالص تقديري الى عمادة كلية العلوم و رئاسة قسم الكيمياء

وختاما

لا بد لنا ونحن نخطو خطواتنا الاخيرة في الحياة الجامعية من وقفه نعود الى اعوام قضيناها في الجامعة مع اساتذتنا الكرام الذين قدمو لنا الكثير باذلين بذلك جهودا كبيرفي بناءً جيل الغد لتبعث الامه من جديد وقبل ان نمضي نقدم اسمى ايات الشكر ولامتنان والتقدير والمحبه الى الذين حملو اقدس رساله في الحياه الى الذين مهدو لنا طريق العلم والمعرفه الى جميع اساتذتنا الافاضل اساتذه قسم الكيمياء

الأهداء

بسمً الله والحمد والشكر لله رب العالمين بعد مسيرة دراسية حملت في طياتها الكثير من الصعوبات والمشقة والتعب اليوم نقطف ثمرها و الحمد لله الذي بتوفيقه وتسهيل منه جل في علاه أكملت مسيرتي العلمية وانتهت دراسة البكالوريوس لتفتح معي ان شاء الله افاق حياة أخرى اهدي تخرجي و نجاحي الى الذين لا يجزيهم مني كلام فلهم اهدي ما حصدت، ولا انسى من بأيديهم تكللت مساعي الإبداع إلى من كان لي سنداً وعوناً عند الشدائد طوال عمري، إلى الرجل الأبرز في حياتي الى الرجل الذي كان له الدور الأكبر في وصولي إلى هذه المرحلة)والدي الحبيب(وإلى من جعل المولى)عز وجل (الجنه تحت قدميها ووقرها في كتابه والى الشفاه التي اكثرت لي الدعاء) امي الحبيبه (وجميع من وقف معي من عائلتي والى من وقف معي مشجعا لاكمال هذه المسيره)زوجي العزيز(والىً الانسان الذي علمني معنى الالتزام والاخلاص والتفاني في العمل الى الدكتور المشرف) زياد عمران موسى (كما اتفضل بجزيل الشكر الى من تطيب الاوقات برفقتهم جميع أصدقائي الذين وقفوا معي وفقكم الله

Introduction:

Chemistry of 7-membered heterocyclic ring systems in recent years gained considerable attention due to the wide range of biological activities of these systems. For the same reason, the natural products containing the seven rings brought the attention of the researchers and the focus was on the heterocyclic rings containing N, O, and S as hetero atoms and the fused rings system containing the benzo derivatives.

Imines are organic compounds containing an azomethine group and identified by the general formula (R1R2C=NR3) where R1,R2 and R3 are alkyl, aryl, cyclo alkyl or heterocyclic groups, They originally prepared by the German scientist Hugo Schiff in 1864 from the condensation of amino group in primary amines and amino acids with the carbonyl group in aldehydes or ketones, and therefor are known as Schiff bases, The importance of imines is owing to their uses as key intermediates for organic synthesis , organometallic ligands , corrosion inhibitors , analytical reagents , growth controlling agent . Most imines and their organometallic compounds exhibit significant biological activities , and medical uses such as anti-inflammatory.

Oxazepines

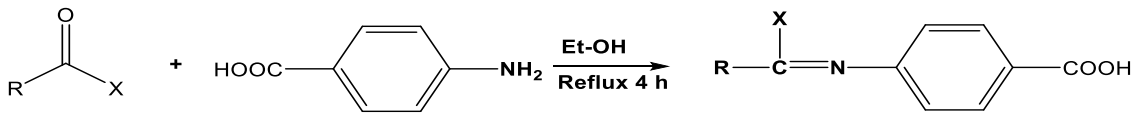
Oxazepines are class of seven-membered heterocyclic ring compounds containing an oxygen atom at position 1 and a nitrogen atom in one of the three locations (2,3 or 4) in the heptane ring , they may contain carbonyl groups and double bonds so they are known as unsaturated and non-aromatic . Oxazepine is an unsaturated, seven membered containing heteroatoms and oxygen in the position 1 and nitrogen in position 3 in addition to five carbon atoms. It is synthesized by the pericyclic cycloaddition of Schiff bases with anhydrides.

Most of the Oxazepines exhibit a wide range of biological activities and pharmaceutical applications such as anticonvulsant, anti-tumor and Colorectal Adenocarcinoma ,anti-bacterial , antioxidant and anti-inflammatory , beside their uses as corrosion inhibitors ,and liquid crystal components.

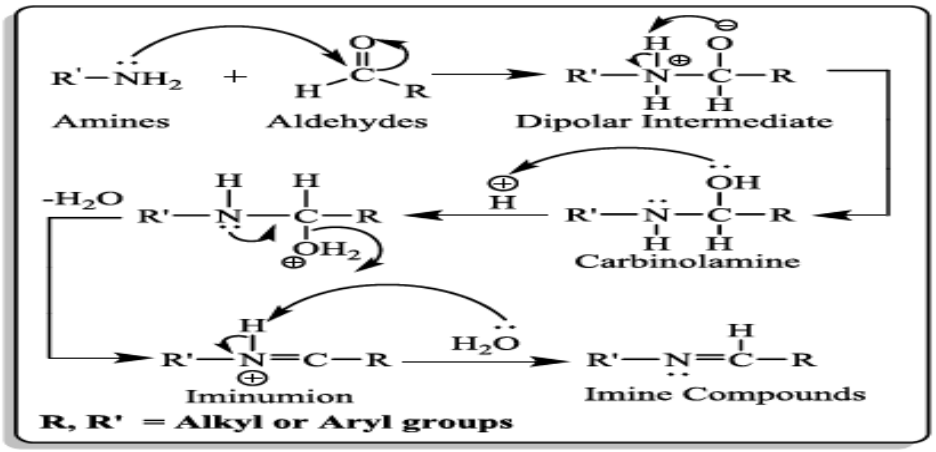
Synthesis of compounds

General procedure for synthesis of imines compounds[A].

A mixture of *p-aminobenzoic acid* (0.01 mol) and benzaldehyde (0.01 mol) in absolute ethanol (25 mL) with A few drops of glacial acetic acid as a catalyst was placed in round bottom flask (100mL) with stirring. The reaction mixture was refluxed for 4hr and then left to cool down to room temperature, whereby, a solid product [A] was obtained. The solvent was removed by filteration and the residual solid was recrystallized twice from absolute ethanol. The reaction pathway for the formation of Imine compounds [A] is depicted by
scheme (1).



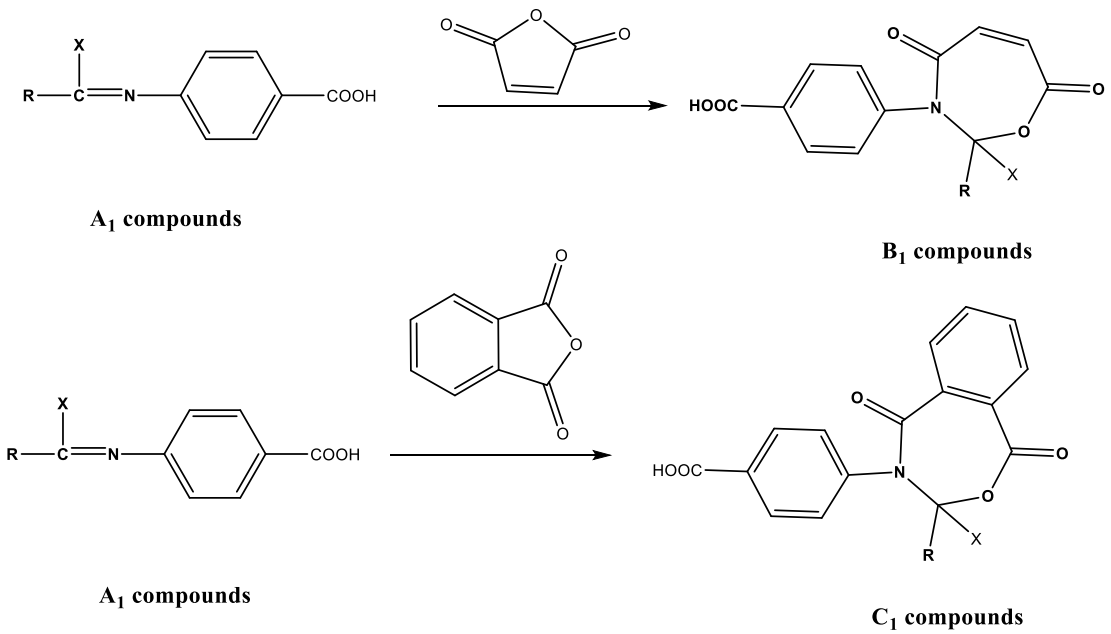
Scheme 1: synthesis of imine compounds [A]



Scheme 2: Mechanism of reaction synthesis of imine

General procedure of synthesis of oxazepine:

It was prepared by using 0.01mol, 0.98g of maleic and 0.01 mol 0.148g of phathaleic anhydride respectively, and 0.01 mol of Schiff bases(A) in abs. EtOH with stirring.). Then, the mixture of reaction have refluxed. Finally, filtration of solution and collected the precipitate. Physical properties of synthesized oxazepine



Scheme 3: synthesis of oxazepine [B] and [C] compounds

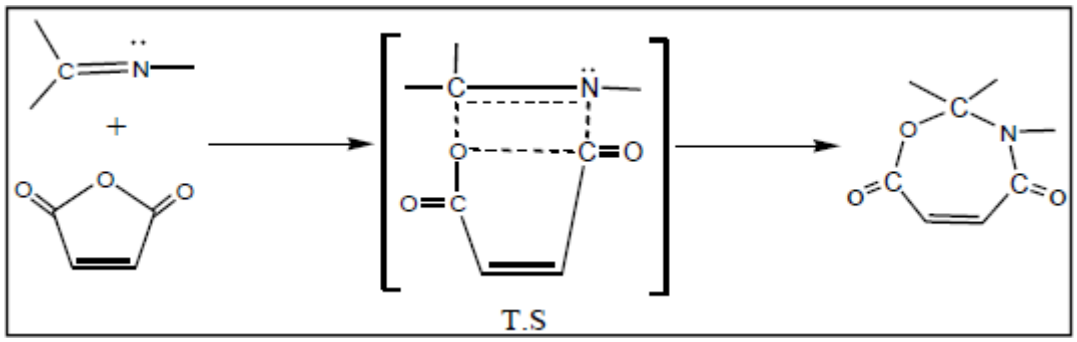
Results and dissection:

Target oxazepine compounds [**B**] and [**C**] were synthesized according to the route presented in Scheme 3. Imines [A] have been synthesized as precursors for oxazepine compounds by reaction of aromatic carbonyl compounds and aromatic amines using absolute ethanol as the solvent.

FT-IR spectrum of imine derivative [A] showed disappearance of the absorption around 1675cm-1 attributed to the υ(C=O) of carbonyl group ,also disappearance of the doublet absorption band around (3390 cm-

1,3270 cm-1) attributed to the asymmetric and symmetric stretching vibrations of (-NH2) group ,respectively and appearance of strong absorption band at (1610) cm-1 attributed to the stretching vibration of exocyclic imine group (C=N) and strong absorption band at (1703) cm-1 attributed to the stretching vibration of (C=O) of carboxylic acid .

1,3-Oxazepine derivatives [B], [C] have been prepared by using a pericyclic reaction type [2-5] cyclo addition reaction between imine group in compounds [A] as two membered component and maleic and phthalic anhydrides as five membered components to give seven - membered 1,3-oxazepine ring. [2-5] cycloaddition reaction is a concerted process proceeds via a single cyclic transition state and thus there is no intermediate in the process .Mechanism of 1,3-oxazepine ring formation has been shown in the following scheme:



FT-IR spectrum of 1,3-oxazepine derivative [B] showed disappearance of the strong band at1610cm-1 attributed to the stretching vibration of exocyclic imine group (C=N) and appearance of two strong absorption bands at1695 cm-1 and1626 cm-1 attributed to the υ(C=O) for lactone and lactam structures inside1,3-oxazepine ring ,respectively.

FT-IR spectrum of 1,3-oxazepine derivative [C] showed disappearance of the strong band at1610cm-1 attributed to the stretching vibration of exocyclic imine group (C=N) and appearance of two strong absorption bands at1724 cm-1 and1693 cm-1 attributed to the υ(C=O) for lactone and lactam structures inside1,3-oxazepine ring ,respectively.

These compounds were characterized by FTIR in Table 1, as flow:-

Comp. No.	$\upsilon_{(C-H)}$ arom. cm-1	$\upsilon_{(C-H)}$ aliph. cm-1	$\upsilon_{(C=O)}$ cm-1 lacton lactam	$\upsilon_{(C=N)}$ cm-1	$\upsilon_{(C=C)}$ cm-1	$\upsilon_{(C-N)}$ Lacton cm-1	$\upsilon_{(C-O)}$ Lacton cm-1
A	3041	2912	---	1610	1429	---	---
B	3000	2993	1695 1626	---	1427	1222	1161
C	3066	2999	1724 1693	---	1423	1267	1159

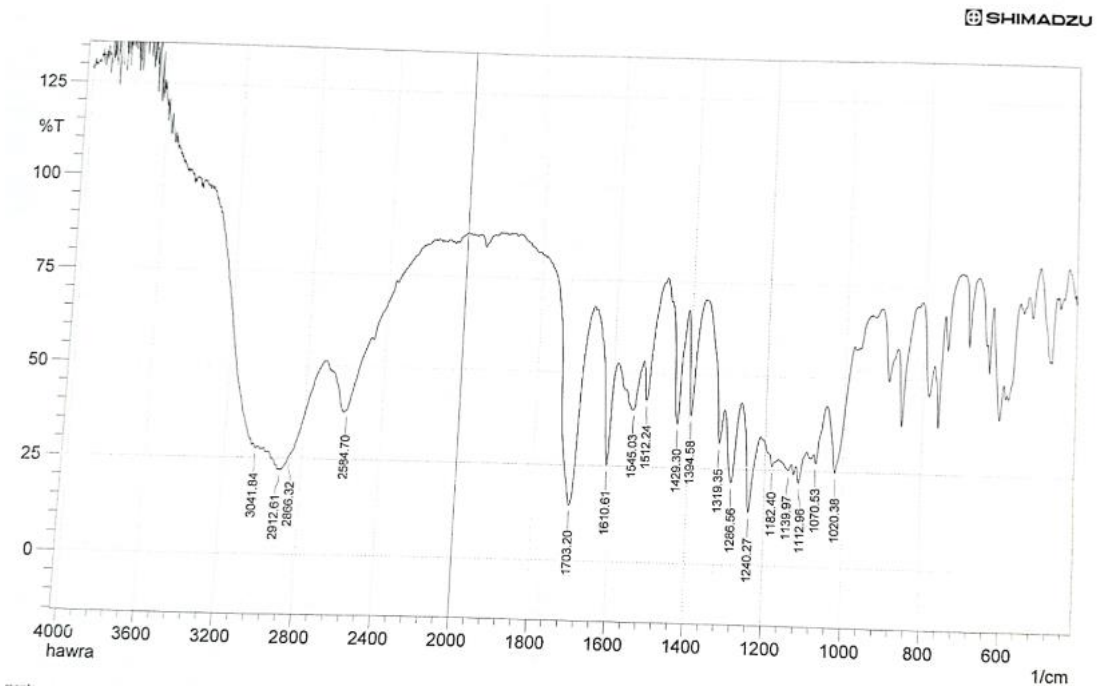


Figure 1: FT-IR spectrum of imine compound A

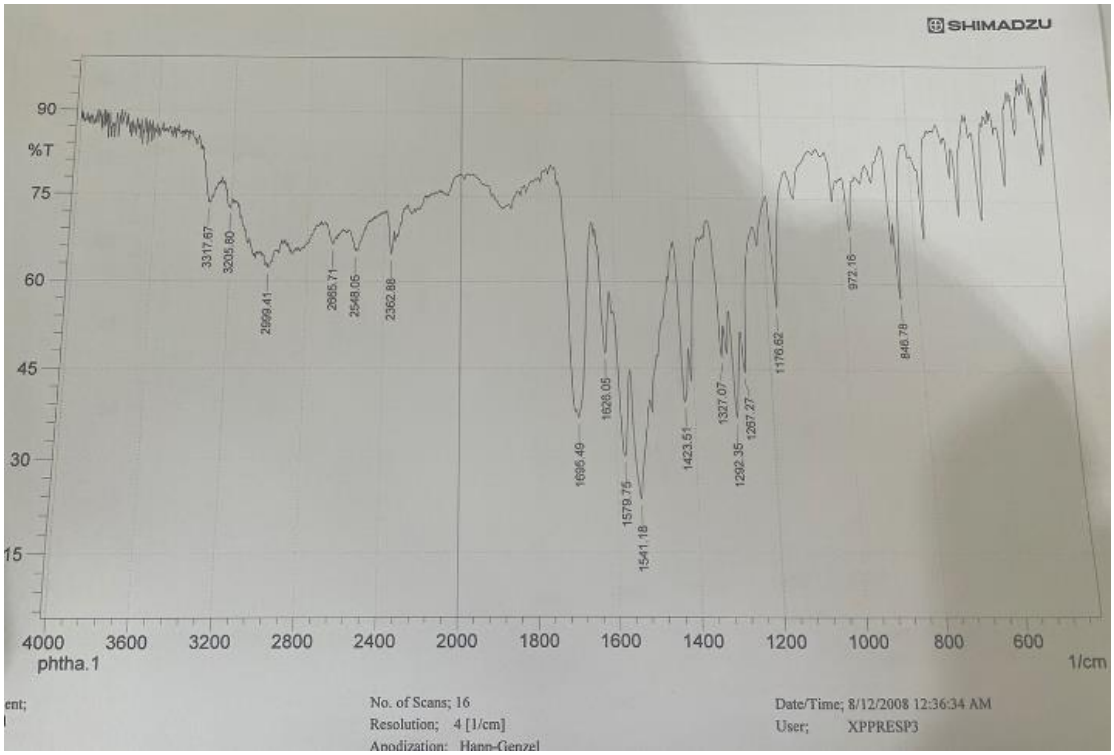


Figure 4: FT- IR spectrum for oxazepine compound B

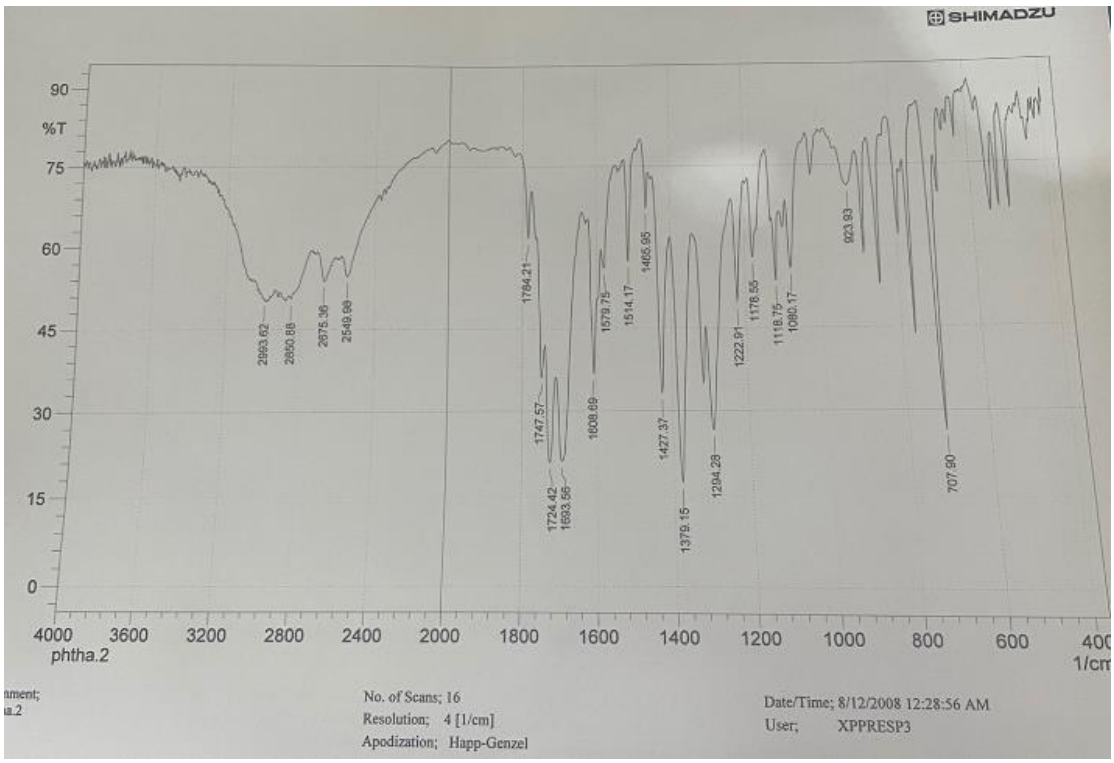


Figure 7: FT-IR spectrum for oxazepine compound C

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