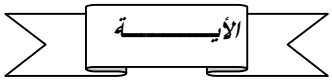

بسم الله الرحمن الرحيم

قال الله تعالى :

{ الذين يذكرون الله قياما وقعودا وعلي جنوبهم ويتفكرون في خلق السموات والأرض ربنا ما خلقت هذا باطلاً سبحانك فقنا عذاب النّار} 191.سورة آل عمران.

صدق الله العظيم

بسم الله الرحمن الرحيم

Sudan University of Science and Technology

COLLEGE OF GRADUATE STUDIES

Synthesis of Some N-Formyl Pyrazoline Derivatives

تخليق بعض مشتقات الـــ N- فورميل بارزولين

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B.Sc. (honours) Chemistry

A Thesis Submitted For The Partial Fulfillment For The Requirements Of M.Sc. Chemistry

Supervisor: Prof.Dr. Ahmed Elsadig Mohammed Saeed.

Feb.2014

Dedication:-

To my father and mother, It is one of the moments that when we should stand up and look back on the length of the travel, and we clearly see that how much your efforts support us to achieve our dreams and aims.

To my daughters, who were giving me the hope, bring me happiness and encouraged me to accomplish the best.

To my brothers, who always were standing with me.

To my husband …..

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Firstly, thank to **Allah** the beneficent, the merciful, who gave me the strength and help to complete this search.

I am immeasurably thankful to Prof.Dr.Ahmed Elsadig Mohammed Saeed, who was the best guide for me to know how to deal with the scientific tasks and how to overcome the theoretical and practical dilemmas that met me during this synthesis process. Thank you for your supervision of this research to appearing in full accuracy and credibility.

I extend my sincere thanks to Dr.Elsadig Hassan Khamis for his effective contribution through the Nuclear Magnetic Resonance Spectrometry measurements for each product in this synthesis steps.

I feel deeply grateful to the staff members, colleagues and technicians for their contributions to completion this research.

Finally, I would like to express my thanks for every one wished to me success.

Abstract:-

Synthesis of six N-formylpyrazolines was completed through applying and adjusting a reaction between their corresponding chalcones and hydrazine hydrate. While the six chalcones were synthesized via Claisen-Schmidt Condensation (CSC) reaction. The completion of the synthesis was proved by characterization of the products.

Basically the synthetic design of these compounds applied through the retrosynthetic analysis concepts and disconnection approach technique.

The structures of the chalcones and N-formylpyrazolines were identified by examining their physiochemical properties and their spectral features. The interpretation of the results demonstrated that these products have the expected structures. Whereas λ_{max} values and the observed colors of these compounds indicated of the presence of conjugated unsaturated system, IR spectrums showed existence of (C=O) in conjugation system with (C=C) in chalcones and (Aldehydic C=O), (C=N), (C-N) and (Aliphatic C-H) in N-formylpyrazoline derivatives and the aromatic rings bands served as fingerprint of these compounds and the (^{1}H, ^{13}C) -NMR spectral revealed a set of signals that confirmed their suggested structures. The agreement between the results of these different techniques investigated and removed a doubt of their final identity.

Anti-bacterial activity of all synthesized compounds was assessed by measuring their inhibition zone diameter and all of them showed an activity against Gram positive (*S.aures*) and Gram negative (*E.coli*) bacteria.

الملـــــخص:-

تم تخليق ستة من مركبات ال N- فورميل البارزولين بتطبيق وضبط التفاعل بين كل من الجالكون المقابل مع مركب الهايدرازين المائى(Hydrazine hydrate). ومركبات الجالكون الستة المستخدمة تم تخليقها كخطوة أولى من خلال تطبيق تفاعل Claisen-Schmidt Condensation إبتداءاً من كيتونات والدهيدات أروماتية. وأُثبت إكتمال عمليات التخليق بتشخيص هوية النواتج.

اعتمدت طريقة تخليق وتصميم هذه المركبات بصورة اساسية علي مفهومي ال Retrosynthesis Analysis وال Disconnection Approach Technique.

تم معرفة البنيات التركيبية للنواتج من خلال تحليل الخصائص الفيزوكيميائية والطيفية لها .وبفحص نتائج التحاليل أعلاه وجد أن المركبات الناتجة هي نفسها المركبات المتوقعة التي رسمت في مخططات التفاعل.

الألوان التي ظهرت بها هذه المركبات وقيم λ_{max} دلت علي وجـــود نظام عدم تشبع متتابع في البنيات التركيبية لهذه المركبات وطيف الأشعة تحت الحمراء لهذه المركبات برهن وجود المجموعات الوظيفية الـ (**C=O**) و(**C=C**) المتتابعة بالنسبة لمركبات الجالكونات والمجموعات (Aldehydic **C=O**) و(**C=N**) و(**C-N**) و (Aliphatic **C-H**) في مركبات الـ N- فورميل بارزولين. أما الحلقات الأروماتية لهذه المركبات فقد أظهرت حزم امتصاص مميزة و كانت بمثابة بصمة الأصبع لكل منها.أما طيف الرنين المغناطيسي بنوعيه (^{1}H-NMR و-^{13}C NMR) لهذه المركبات فقد أظهر عدد من الإشارات التي تدعم صِحت البنيات التركيبية المصممة والتوافق بين نتائج التحاليل المختلفة كان بمثابة قاطع شك في تشخيص هوية هذه المركبات.

تم فحص المقاومة البكتيرية لهذه المركبات بقياس قيم ال Inhibition Zone وأوضحت النتائج أنها مركبات نشطة ضد كل من البكتريا موجبة الجرام (*S.aures*) وسالبة الجرام (*E.coli*).

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List of Abbreviations:

CSC	Claisen-Schmidt Conensation
J	coupling constant
NMR	Nuclear Magnetic Resonance
IR	Infrared
UV	Ultraviolet
λ_{MAX}	Maximum Wavelength
IUPAC	International Union of Pure and Applied Chemistry
Z	Zusammen (German)
E	Entgegen (German)
EIMS	Electron Impact Mass Spectrometry
FABMS	Fast-Atom Bombardment Mass Spectrometry
QSAR	Quantitative Structure Activity Relationship
TLC	Thin-Layer Chromatography
Nm	Nanometer
R_F	Retention Factor
FGI	Functional Group Interconversion
str.vib	Stretching Vibration
defo.vib	Deformation Vibration
d	Doublet
Dd	Double Doublet
S	Singlet
M	Multiplet
E.coli	Escherichia coli
S.aureus	Staphylococcus aureus
Gen ^{10}	Gentamicin (10 mg /disc)
IZ	Inhibition Zone
Ppm	Part per Million
PRG	Propyleneglycol
AR	Analytical Reagent Grade
sym	symmetrical

asym	asymmetrical
g	gram
M.F	molecular formula
m.p	melting point
M.Wt	molecular weight
MIC	Minimum Inhibition Concentration
mol	mole
MW	Microwave
TClICA	TriChloroIsoCyanuric Acid
W	Watt
δ	chemical shift

Chapter One

1. Introduction:

1.1 Definition of chalcone:

Chalcone is an aromatic enone compound, which construct of two phenyl rings linked to α,β-unsaturated double bond unit and are known collectively as chalcones. This benzylidene acetophenone is the parent member of these compound derivatives (Fig 1.1) (Merck index, 2008)

Chalcone crystal structure consists of three planar moieties, including two benzene ring and carbon-carbon double bond. The dihedral angle between the two phenyl rings is 13.0(1^o) and the dihedral angle from the plane of C7/C8/C9 to the phenyl rings (C1toC6 and C10toC15) are 13.8(1^o) and 2.6(1^o) respectively, indicating that the central C7-C8-C9 fragment lies nearly in the phenyl rings plane of C10 to C15 but rather more displaced out of the other phenyl ring C1toC6. The molecule forms zigzag chain by intermolecular (C=C bond) along C axis. There is also existing of intermolecular hydrogen bonding interactions involving (C11) acting as H-bond donor via (H11) to the oxygen atom in the adjacent molecules (Wu *et a*l., 2006).

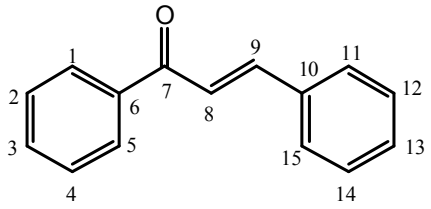


Fig (1.1): Chemical structure of chalcone

Chalcone have α,β-unsaturated system of double bonds which assume linear or nearly planar structure with two phenyl rings and they possess conjugated double bonds with completely delocalized π-electrons system on the benzene rings (Uango *et al.,* 2010). Chalcone exist as either E or Z isomers, E isomer is the most stable form, and consequently majority of chalcones are isolated as E isomer (Jain et al., 2009).

1.2 Nomenclature of chalcones:

The IUPAC approved systematic name for chalcone as 1,3-diphenyl-2-propen-1-one and it is generally thought to be cumbersome for routine

use, even for simple naturally occurring derivatives, such as the trivial name of the commonly found isoliguiritigenin which named as 1-(2`,4`-dihydroxy phenyl) -3-(4-hydroxy phenyl)-2-propen-1-one, but still the use of series systematic name and/or trivial name is wide spread. Similarly all structures are written by convention with the (A ring) to the left and has primed numbers and the (B ring) carry the non primed numbers as in (Fig 1.2) (Andersen and Markham, 2006).

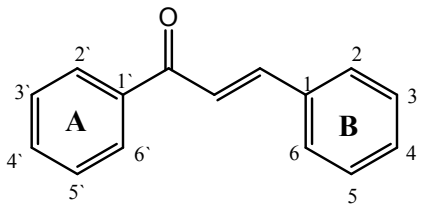


Fig 1.2 Naming system of chalcone

(Numbering of ring started separately from α,β-unsaturated carbonyl unit)

1.3 General Spectral Features of Chalcones:

1.3.1 UV Spectral Features of Chalcones:

The UV spectra of chalcones consist of two absorption bands, (Band I) which occur in range (300-380) nm and (Band II) which appear as a minor peak in the range (220-270) nm region (Wheeler *et.al.*, 1964).

In case of substituted chalcones, the substituent (*m*-NO_2, *p*-Br, *p*-Ph) of ring A and (Me, *p*-OMe, Cl, NO_2) of ring B were studied and showed a linear relationship of λ_{max} values and the substituent constants (Rongjian *et.al.*, 1992).

Most of known flavonoids showed the Band II in stronger intensity than Band I except chalcones which have relatively stronger intensity in Band I than Band II, so UV spectroscopy proved useful to distinguish between substituted chalcones and flavanones which is not possible by EI mass spectrometry due to thermal isomerizaton of chalcones (Marby *et al.*, 1970).

1.3.2 IR Spectral Features of Chalcones:

Chalcones showed the characteristic band of the α,β-unsaturated carbonyl group which usually appear in range between 1625-1650 cm^{-1} in its IR spectrum (Hegert and Kurth.,1953) and (Dhar and Gupta.,1971). The region at which other absorption bands appear depends on the type of phenyl group (aromatic ring) as well as the present substituents.

1.3.3 NMR Spectral Features of Chalcones:

In the ^{1}H-NMR of chalcone, the most important hydrogen sets are those α-hydrogen and β-hydrogen which are occur as two doublets, (J=17 Hz) in range δ (6.7-7.4) ppm (α-H) and 7.3-7.7 ppm (β-H). The other aromatic protons usually appear in range of δ (6.9-8.0) ppm depending on the type of the rings and based on electronic effects of the substituents that present on those rings. The J value (17 Hz) is clearly reveals the trans geometry for chalcones (Marby *et al*., 1970).

The ^{13}C-NMR spectrum of chalcone showed that the major carbon is carbonyl carbon which is usually occurring in range of δ (188.6-194.6) ppm (Petter *et al*., 1976). The α and β carbon atoms with respect to carbonyl group give characteristic signals in δ (116.1-128.1) ppm and (136.9-145.9) ppm respectively, which can also be readily identified by their appearance as six line multiplet in the high resonance decoupled spectrum (Sthothers,1972).

1.3.4 Mass Spectral Features of Chalcones:

The EIMS of chalcones give rise to the unusual fragment ion $[M-H]^{+}$ involving of type of intramolecular aromatic substitution reaction due to elimination of an ortho substituent (H atom) for an aromatic rings with further cyclization process to form a highly stabilizer corresponding benzopyrylium cation as basic fragmentation, this produced fragment cation undergo structural rearrangement which yield other fragments, this step always may lead to loss CO molecule (Ardanal *et al*.1991,Ardanal *et al*.,1998 ; Ronaya *et al*.,1966) and other important fragment ions can be found due to loss of H_2O and/or benzene ring (Tai *et al*. 2006).

1.4 Origin and Biosynthesis of Chalcones:

Chalcones are abundantly present in nature from ferns to higher plants and many chalcones have been isolated from various parts of plants (Zhang *et al*., 2013). Chemically chalcones are known as precursors of open chain flavonoids and isoflavonoids present in the edible plants (Detsi *et al*., 2009). These compounds are widely biosynthesized in plants and they are important for pigmentation of followers and hence act as attractant pollinators (Andersen and Markham, 2006) and the major dietary sources of chalcones are citrus fruits and apples (Barberan and Clifford, 2000).

About the biosynthesis of chalcones a lot of has been written, but a few essential points will be mentioned here. These compounds are formed by Chalcone Synthase (CHS), Catalyzes of the head-to-tail condensation of 4-coumaroyl CoA with three molecules of malonyl CoA yield naringenin

chalcone, CHS is a member of a family of closely related polyketide synthases that can utilize different starter molecules and different number of condensation reactions to yield a variety of natural products (Richard and Dixon, 1999).

1.5 Synthetic Methods of Chalcones:

Literature review reveals several methods for the synthesis of chalcones based on formation of carbon-carbon bond. Among these methods there is Claisen-Schmidt condensation reaction which it still occurs prominent position, Claisen-Schmidt condensation reaction were applied within different catalyzing agents such as sodium hydroxide (alkali medium) (Arun *et al*.,2006), sulfonic acid (Qian and Liu,2011),Iodine (Sashidhara et al.,2009), also ultrasound irradiation (Li *et al*.,2002).

Several modifications for Claisen-Schmidt condensation have been made to counter and solve some problems like toxicity reagents, long reaction time, poor yield, low selectivity and even eco-friendly procedure and the developed method that gained attention of chemists due to its advantages is the microwave radiation method (Bhuiyan *et al*., 2011).

Chalcone can also be synthesized by Wittig reaction (Xu *et al*.,1995), Suzuki reaction (Eddarir *et al*., 2003) and by Friedel crafts cyclization with cinnamoyl chloride (Dhar and Barton,1981) or by Aldol reaction under acidic medium by using HCl,BF_3,$SOCl_2$, *p*.toluene sulfonic acid (Miguel,1961 ; Hasan *et al*., 2012) but the basic Aldol reaction is unsuitable for hydroxyl substituent aromatic aldehydes because the basic species decrease the activity of aldehyde component through delocalization of corresponding anion, so if it used, it necessary to protect hydroxyl group (Jayapal *et al*., 2010). Chalcone, sometimes synthesized by debromination of corresponding α,β-dibromides (Dershowitz and Prokauer , 1961).

1.6 Quantitative Structure - Activity Relationship (*QSAR)* Studies of Chalcones:

Through the synthesis of several substituted chalcones and chalcone derivatives the QSAR studies of their pharmacological activities were achieved and a number of facts were proved. In general, the pharmacological activity of chalcone depends on the nature, number and position of the substituent(s) on both or one of the aromatic ring (A & B) (KO *et al*., 2003; Mandge *et al*., 2007; Avila *et al*., 2008; Hsieh *et al*., 2012).

1.7 Chemical Reactions of Chalcones:

1.7.1 Reduction of Chalcones:

Chalcones undergo two chemoselective reductions.1,2-reduction and 1,4-reduction , both have been carried out with different reducing agents. The obtained reduction type is highly depend on reaction condition (substrate structure, nucleophile identity and catalysis) which has been a challenging problem in organic synthesis, for example, chemoselective 1,2-reduction of chalcones were achieved (Weiliang *et al*. 2012) and also 1,4-reduction (Pingli *et al*.,2008).

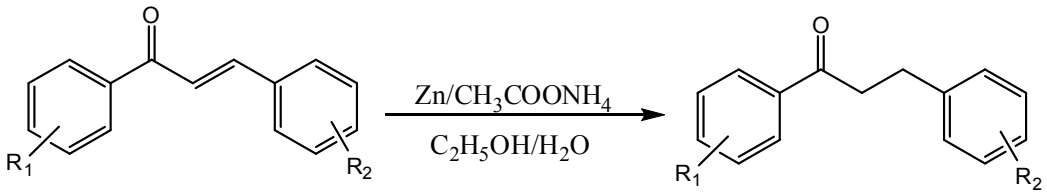


Fig (1.3): Reduction of chalcone.

1.7.2 Oxidation of Chalcones:

In bio species when chalcones converted to corresponding flavones, it is due to its oxidation process (Anderson and Markham ., 2006).

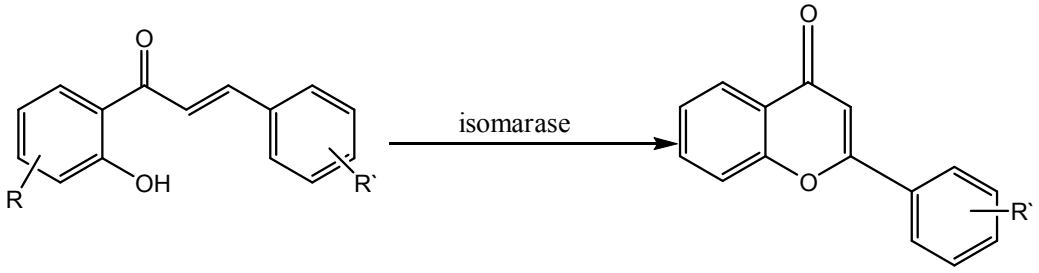


Fig (1.4): Isomaration of chalcone.

Chalcones can be oxidized by different oxidizing agents and in these reactions either the (C=O) or (C=C) group of chalcones can be attacked by an oxidant agent (AnilKumar and Sondu, 2007).

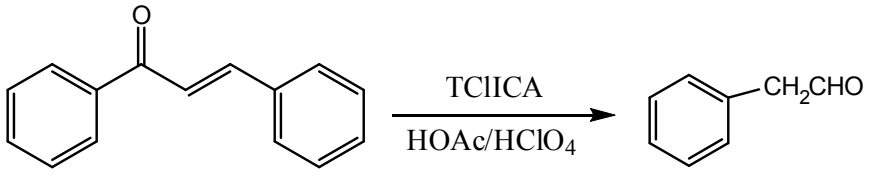
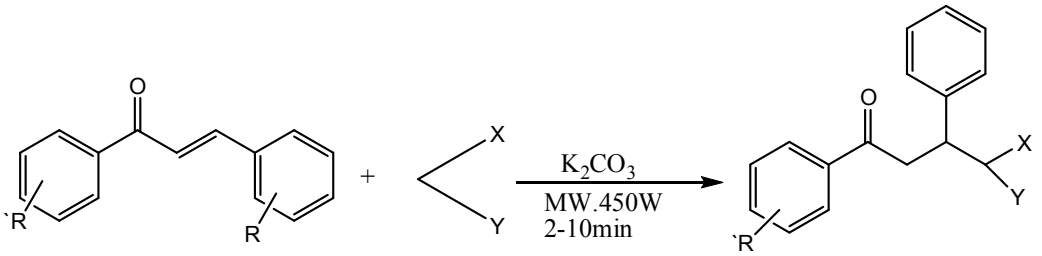


Fig (1.5): Oxidation of chalcone by TClICA .

1.7.3 Nucleophilic Addition of Chalcones:

As with α,β-unsaturated carbonyl compounds, chalcones undergo conjugate nucleophilic addition reaction for carbon-carbon bond formation and these types of reactions play major and important role in the organic synthesis field (Perlmutter, 1992) and its controlled by kinetic and thermodynamic effects (Prakash rao *et al.*, 2005 ; Deuri *et al.*, 2012).



X = COOEt Y = H, COC6H5, CN, COOEt

Fig (1.6): Reaction of chalcone with ethylacetate.

1.7.4 Cyclization Reactions of Chalcones:

Chalcones have been found to be useful for the synthesis of variety of heterocyclic compounds when it condensate with suitable nucleophilies and it can be synthon in the preparation of following compounds:

Pyrazolines and their derivatives can be synthesized by condensation of chalcones with hydrazine hydrate derivatives (Hishmat and Ocridee., 1987 ; Amir *et al.*, 2008).

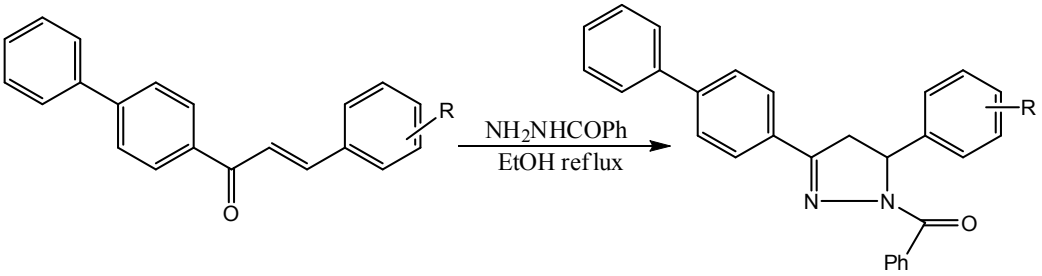


Fig (1.7): Reaction of chalcone with phenylhydrazine.

1-Carboxamide pyrazolines result from the reaction between chalcones and semicarbazide hydrochloride in ethanol (Utale *et al.*, 1998).

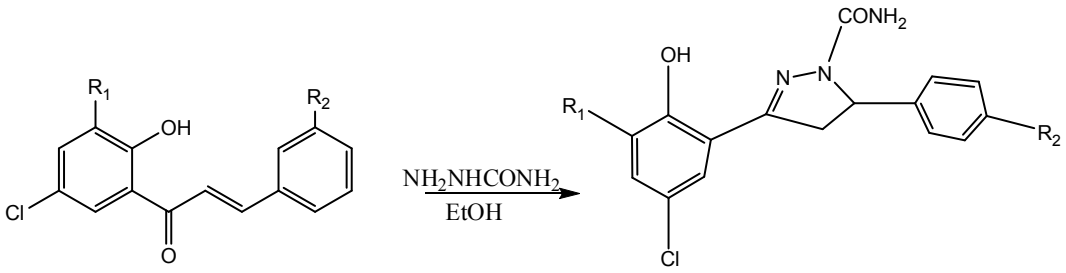


Fig (1.8): Reaction of chalcone with semicarbazide in ammonium acetate.

Chalcones on condensation with malononitrile and ammonium acetate yields 2-amino-3-cyanopyridines and (Vyas *et al.*, 2009).

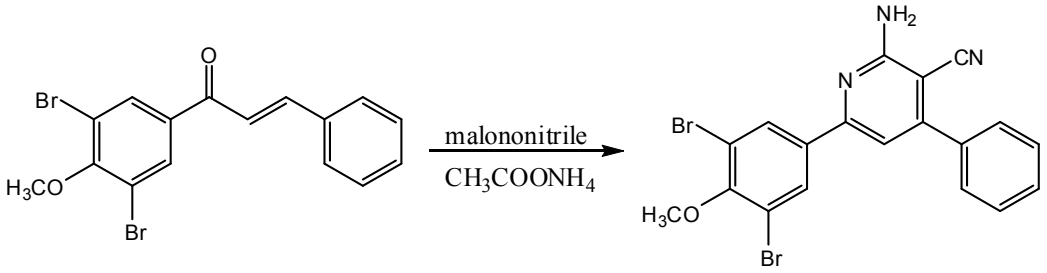


Fig (1.9): Reaction of chalcone with malononitrile in ammonium acetate.

Chalcones on reaction with thiourea in the presence of alkali/acid yield 2-thiopyrimidines (Balaji *et al*., 2010).

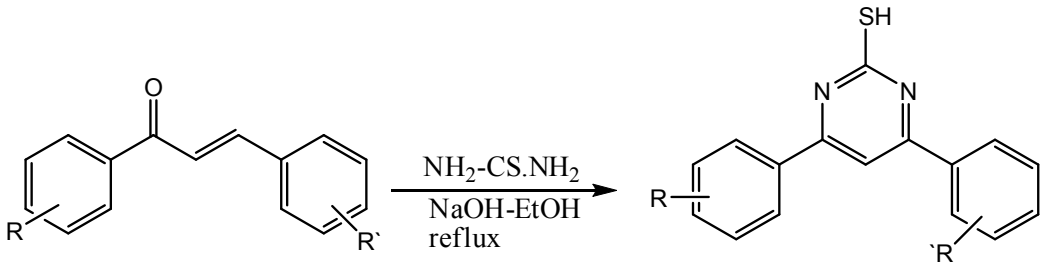


Fig (1.10): Reaction of chalcone with thiourea.

Chalcones on treatment with guanidine hydrochloride in presence of methoxide affords 2-aminopyrimidines (Jyothi *et.al,* 2012).

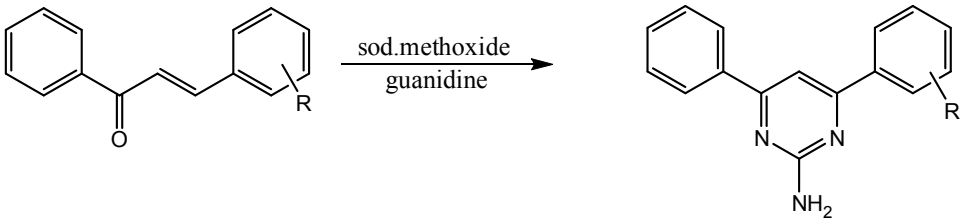


Fig (1.11): Reaction of chalcone with guanidine hydrochloride.

Chalcones on condensation with ethyl cyano acetate give cyanopyridone derivatives (Sayed *et al.,* 1983).

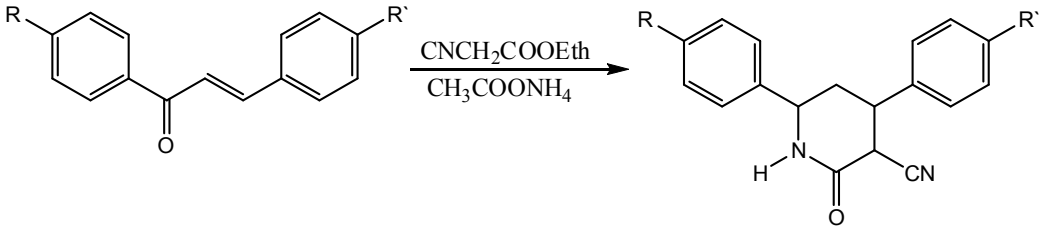


Fig (1.12): Reaction of chalcone with ethyl cyano acetate.

Chalcones when treated by malononitrile give 2-amino-3-cyanopyridine which condensed with formamide to pyridopyrimidines (Bhargava and Rajwanshi., 2013).

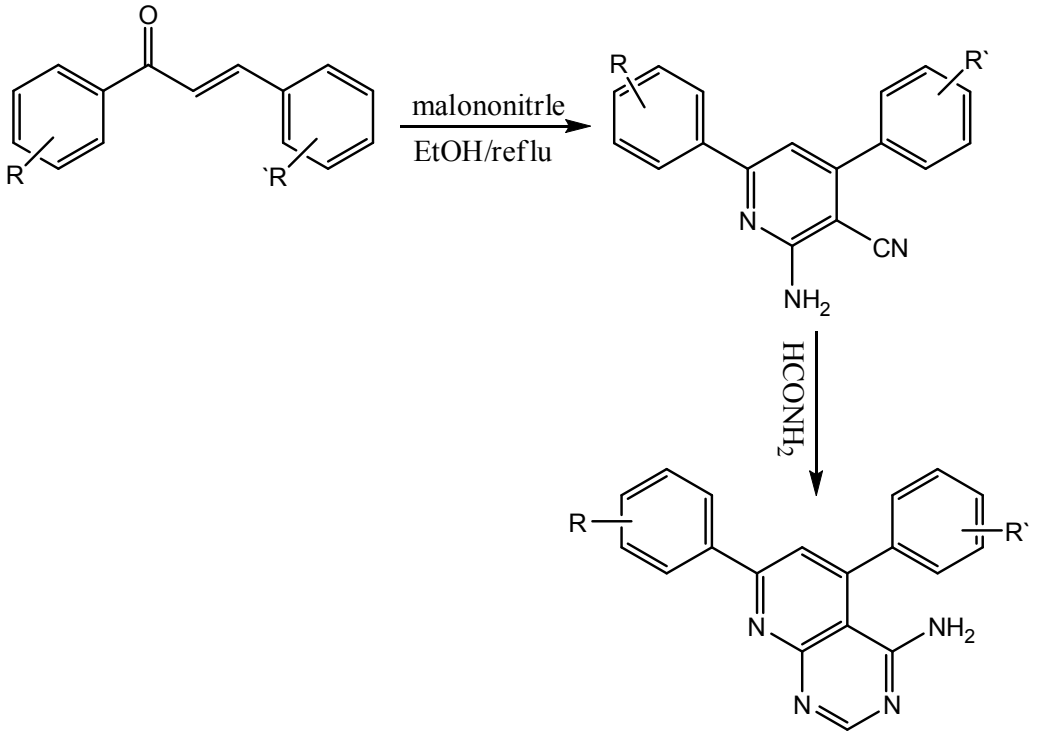


Fig (1.13): Reaction of chalcone with malononitrile and formamide.

Isoxazoles can be synthesized by reaction between chalcones and hydroxylamine hydrochloride and sodium acetate (Joshi *et al.,* 2012).

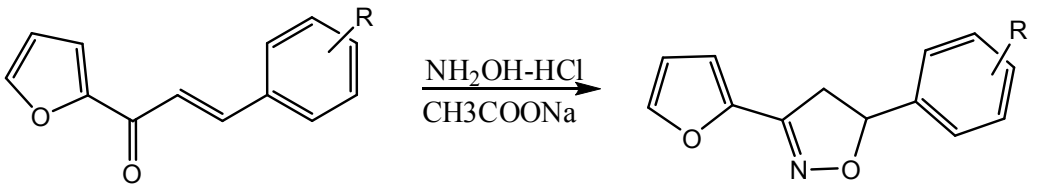


Fig (1.14): Reaction of chalcone with hydroxylamine hydrochloride.

Chalcones on treatment with urea in the presence of alkali affords 2-oxopyrimidines (Chintan *et al.,* 2012).

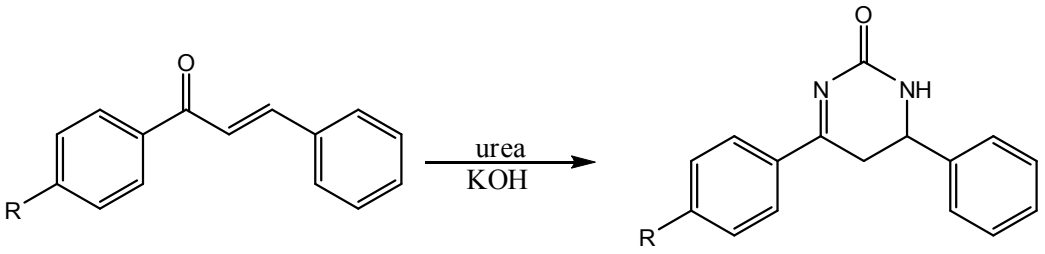


Fig (1.15): Reaction of chalcone with urea.

Chalcones react with 2-amino-ethanol (monoethanol amine) in ethanol to give 1,4-oxazipines (Pharucha and Nalk ,2000).

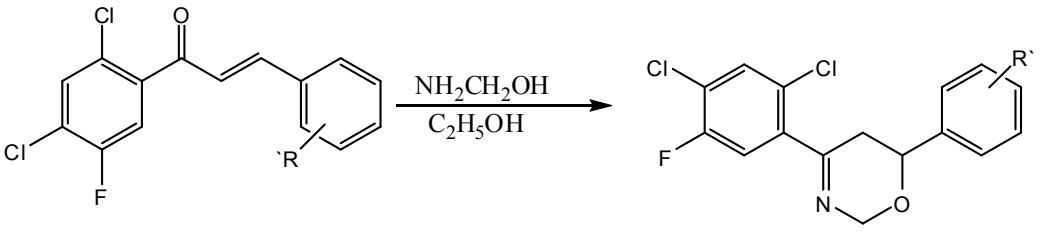


Fig (1.16): Reaction of chalcone with monoethanol amine.

Oxirane can be prepared through reaction between chalcones and hydrogen peroxide (H_2O_2) in basic medium (Helder *et al.,* 1976; Al-Sabawi, 2008).

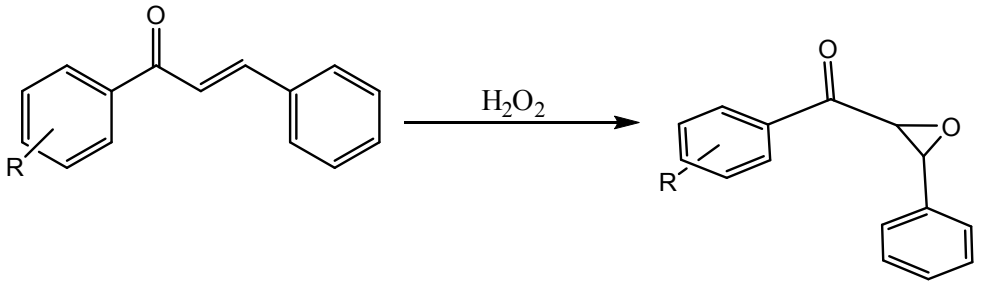


Fig (1.17): Reaction of chalcone with hydrogen peroxide.

Chalcones on reaction with barbituric acid give barbitane derivatives (Sangani et *al.,* 2006).

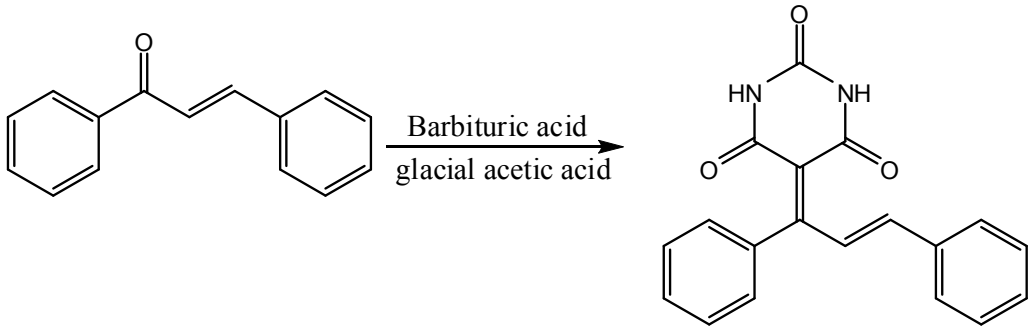


Fig (1.18): Reaction of chalcone with barbituric acid.

Chalcones when react with amines in presence of sulfuric acid as catalyst yield imine derivatives (Lonkar et *al.,* 2011).

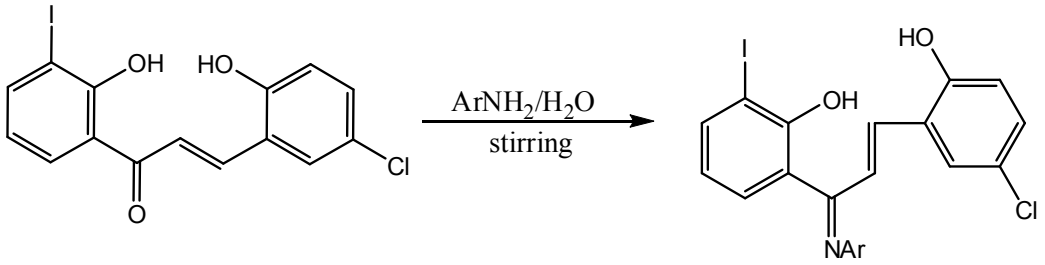


Fig (1.19): Reaction of chalcone with amine.

Chalcones on condensation with malononitrile in pyridine from 2-amino-3-cyanopyrans (Maheta et *al.,* 2012).

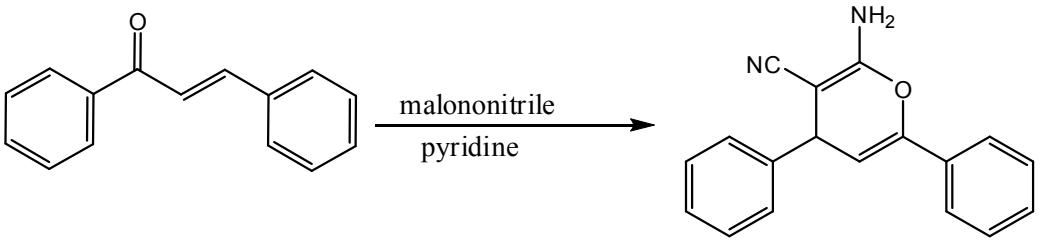


Fig (1.20): Reaction of chalcone with malononitrile in pyridine

Chalcones on reaction with 2-amino thiophenol in dry acidic methanol with drops of glacial acetic acid produces 1,5-thiazepines (EL-Bayouki, 2013).

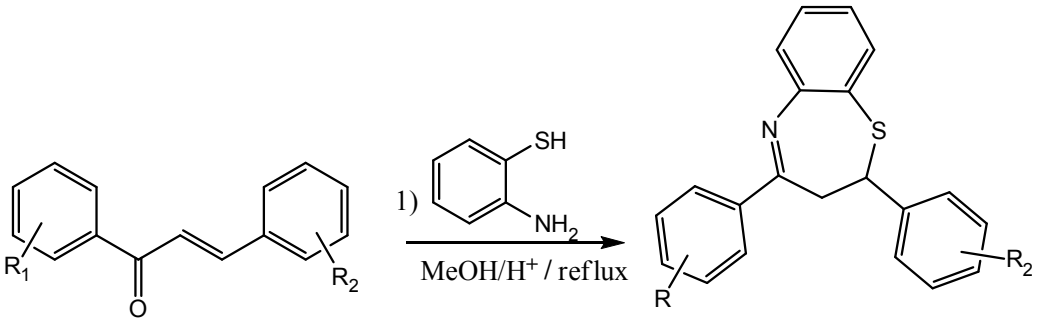


Fig (1.21): Reaction of chalcone with 2-amino thiophenol.

1.8 Importance of Chalcones:

1.8.1 Therapeutic Potential of Chalcones:

Chalcones are associated with different biological activities including, Anti-microbial(Singh *et al., 2*012),Anti-inflammatory (Hsieh *et al.,* 2000) Anti-cancer (Dias *et al.*, 2013),Anti-analgesic (Viana *et al.,*2003),Anti-ulcerative (Shigenu *et al.,*1991),Anti-malaria (Prashar *et al.*, 2012),Anti-viral (Malikarjum , 2005),Anti-leishmanial (Nielsen *et al*.,1995),Anti-oxidant (Miranda *et al*., 2000),Anti-hyperglycemic (Satyanarayana *et al.,* 2004) and Anti-tubercular (Sivakumar *et al.,* 2007).

Especial interest has been focused on the synthesis of these compounds due to their covering of a wide range of pharmacological activities, and the studies of these compounds lead to discovering new and major biological/therapeutic activities.

1.8.2 Additional Importance of Chalcones:

Chalcones and their derivatives find application as artificial sweeteners (Krbechek *et al.,* 1968), scintilator (Delcarmen *et al.,*1973), Fluorescent agent (Kamakshi *et al.,* 2010), Skin-Lightening agent, stabilizer against heat, visible-UV light and aging (Momtaz *et al.,*2008) and polymerization catalyst (Faghihi and Moghanian , 2010).

In industrial field and in chemistry and because of their relationship with flavones, aurones, aziridines (Noyce *et al.,*1995) they consider as useful in elucidation structure of natural products like Hemlock Tannin (Russell,1934), naringenin (Heller *et al* .,1980).

1.9 Pyrazoline:

Heterocyclic compounds have important moiety in organic synthesis and they exhibit a wide range of biological activities such as in 2-pyrazolines. 2-pyrazoline is one of the three practically reduced forms of pyrazole which can exist within different position of double bonds (Gupta *et al.,* 2005).

The most convenient method for synthesis of N-substituted-pyrazoline is the 1,3-dipolar cyclocondensation reaction between chalcones and hydrazine hydrate in presence of aliphatic acid (Sinloh *et.al*., 2013).

Pyrazoline is considered as therapeutic agent for anti-cancer (Hollis *et al.,* 1984), insecticidal (Grosscurt *et al.,* 1979), anti-bacterial (Barot, 1996), anti-fungal (Korgaokar *et al.,* 1996), anti-depressant (Palaska *et al.,* 2001), anti-convulsant (Siddiqui *et.al.*, 2010), anti-tumor (Wilkinson, 1992).

1.10 Aims and Objectives:

One of the reasons that make chemistry unique among science is the synthesis. Chemists make molecules newer or developer in pharmaceuticals, food additives, agriculture and all useful new molecules. And they prepare these compounds from simpler and more readily available starting materials.

This work aimed to construct some substituted five member nitrogen heterocyclic compounds (N-formylpyrazolines) and their precursors 1,3-diaryl-prop-2-en-ones as multistep synthesis concept.

The structures of resulting compounds could be proved through determination of some of their physiochemical properties and their spectralcharacteristicsby means of UV, IR, NMR, MS spectrophotometry.

Owing to the broad biological activities of these types of compounds, Anti-bacterial activity of synthesized compounds should be screened by measuring of their inhibition zone values (mm) and followed by determination of their minimum inhibition concentration (MIC).

Chapter Two

2. Materials and methods:

2.1 Materials:

Acetophenone, *p*-Bromoacetophenone, *p*-Nitroacetophenone and silica gel (G) all were obtained from Technopharm, India. Benzaldehyde, furfuraldehyde, formic acid, hydrazine hydrate, ethanol, methanol, acetone, propylenglycol and chloroform were obtained from lobachemie India and they are analytical reagent grade (AR).Potassium hydroxide and iodine were obtained from Central Drug House laboratory, India and they are (AR). Nutrient agar powder and Gentamicin-(10mg/disc) were produced from Hi Media, India.

2.2 Instruments:

2.2.1 Sensitive balance (A&D – GR- 120, Japan).

2.2.2 Magnetic Hot-plat Stirrer (Stuart-Bibby, Sterilin LTD, UK).

2.2.3 Melting points apparatus (Stuart-Scientific stone, Staffordshire, UK) and the values of melting points were uncorrected.

2.2.4 Thin-Layer chromatography was carried out by using silica gel sheets (60-GF 254 Merck – Germany) and/or precoated aluminum plates with chloroform and methanol in ratio (9.5: 0.5) respectively as mobile phase. The visualization of spots on these plates was achieved either by exposure to UV-light and/or iodine vapors.

2.2.5 Ultraviolet spectrometer (UV-Visible -1800 instrument, Shimadzu, Japan), with methanol as solvent.

2.2.6 Infrared Spectrometer (FTIR-8400 instrument, Shimadzu, Japan), with KBr disc.

2.2.7 ^{1}H-Nuclear Magnetic Resonance Spectrometer (Spect-BRUKER, 500MHz), TMS as internal standard and $CDCl_3$ as solvent.

2.2.8 ^{13}C-Nuclear Magnetic Resonance Spectrometer (Spect-BRUKER, 500MHz), $CDCl_3$ as solvent.

2.2.9 Glassware

All required glassware were Pyrex type.

2.3 General Synthetic Methods:

2.3.1 General Procedure For The synthesis of 1,3-diaryl-prop-2-en-1-ones (I-VI):

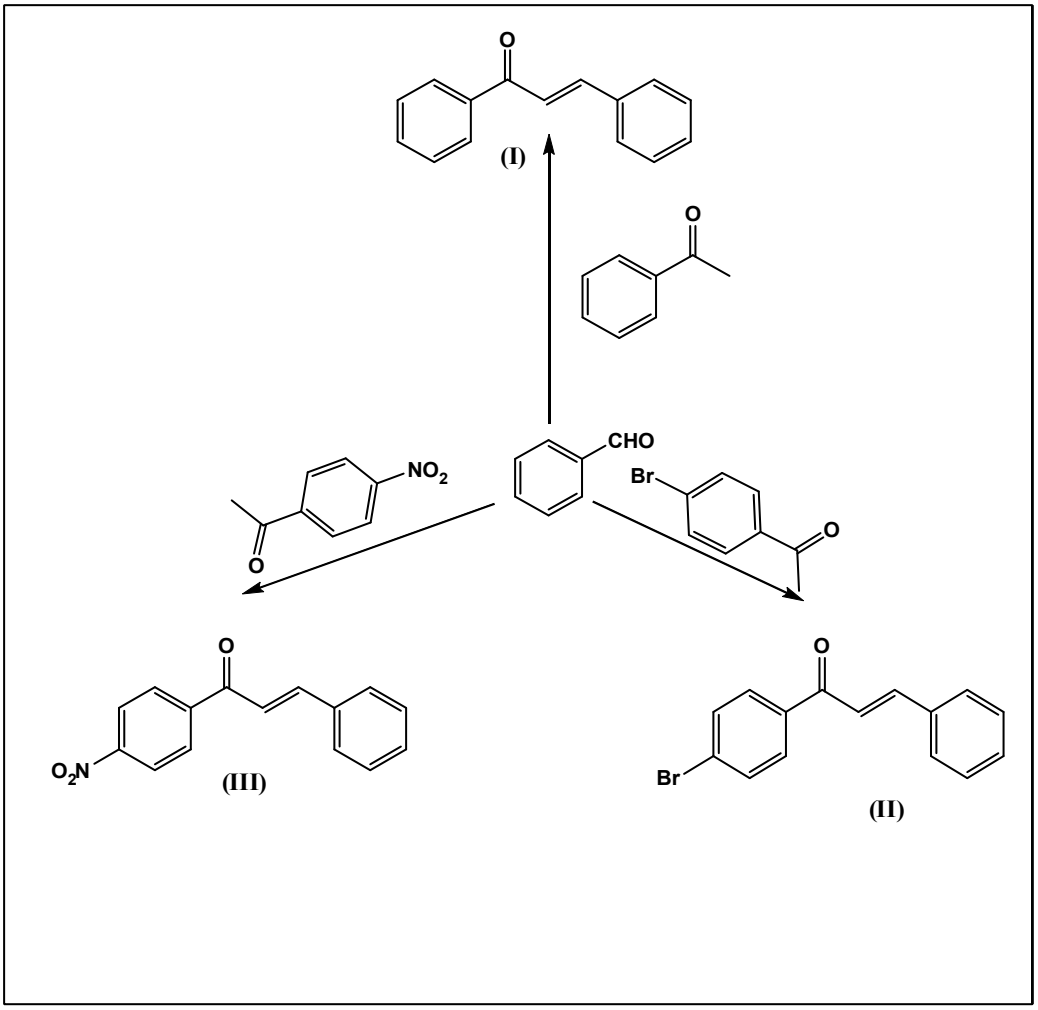
To a solution of (10mmol) of aromatic ketone (substituted or unsubstituted acetophenone), in 30ml of ethanol were added (10mmol) of aromatic aldehyde with constant stirring followed by gradual addition of (20mmol) of the potassium hydroxide. The mixture was stirred at (25-30C^{o}) for twelve hours in a magnetic hot-plate stirrer. After completion of the reaction time, the mixture was kept to stand for overnight at room temperature. The mixture was poured into crushed ice and acidified by diluted hydrochloric acid (10%) to neutral pH. The separated solid was filtered and washed with cold distilled water and recrystallized from ethanol. The yield percentage , melting point , R_f value , λ_{max} (nm) , IR , ^{1}H-NMR , ^{13}C-NMR spectra were determined and recorded (Table 2.2.a - 2.7.a).

2.3.2 General Procedure For The Synthesis of 3, 5-diaryl – 4, 5 - dihydropyrazole -1- carbaldehydes (VII-XII):

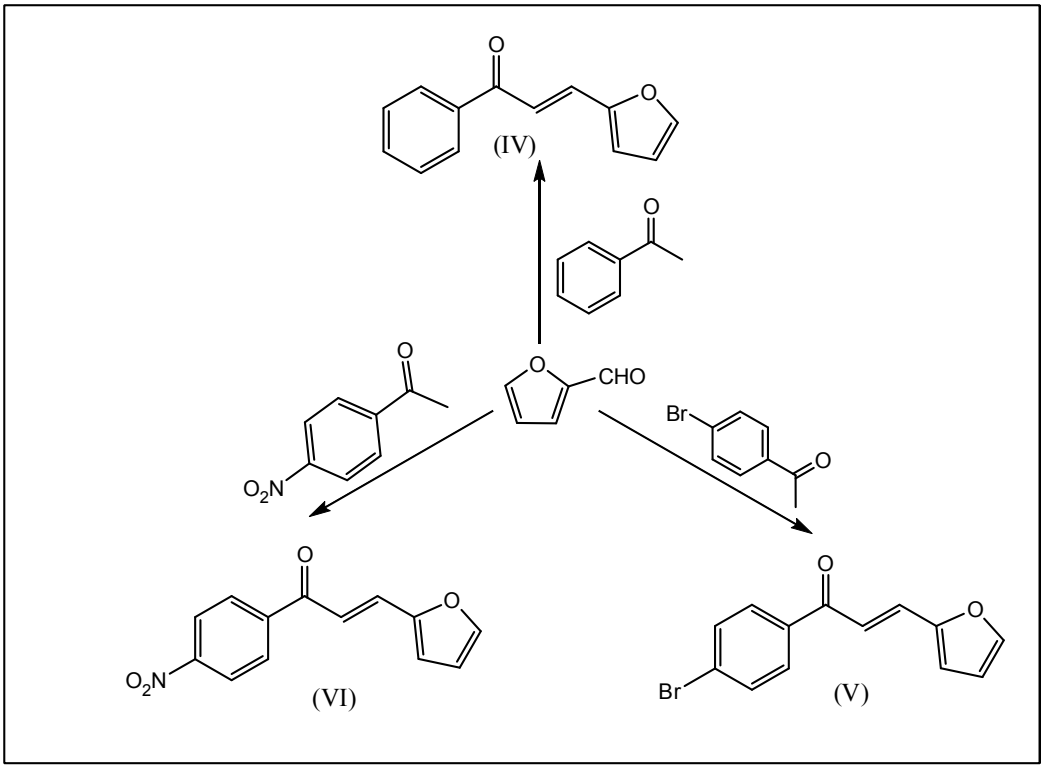
A mixture of (1.0mmol) of chalcone derivative and (4.0mmol) of hydrazine hydrate in 5ml of formic acid was refluxed for twelve hours. The reaction mixture was allowed to cool. The obtained solid was filtered and washed with cold ethanol and recrystallized from ethanol. The yield percentage, melting point, R_f value, IR, ^{1}H-NMR, ^{13}C-NMR and spectra were determined and recorded (Table 2.2.b -2.7.b).

2.3.3 Anti-bacterial Activity Test of Synthesized Compounds:

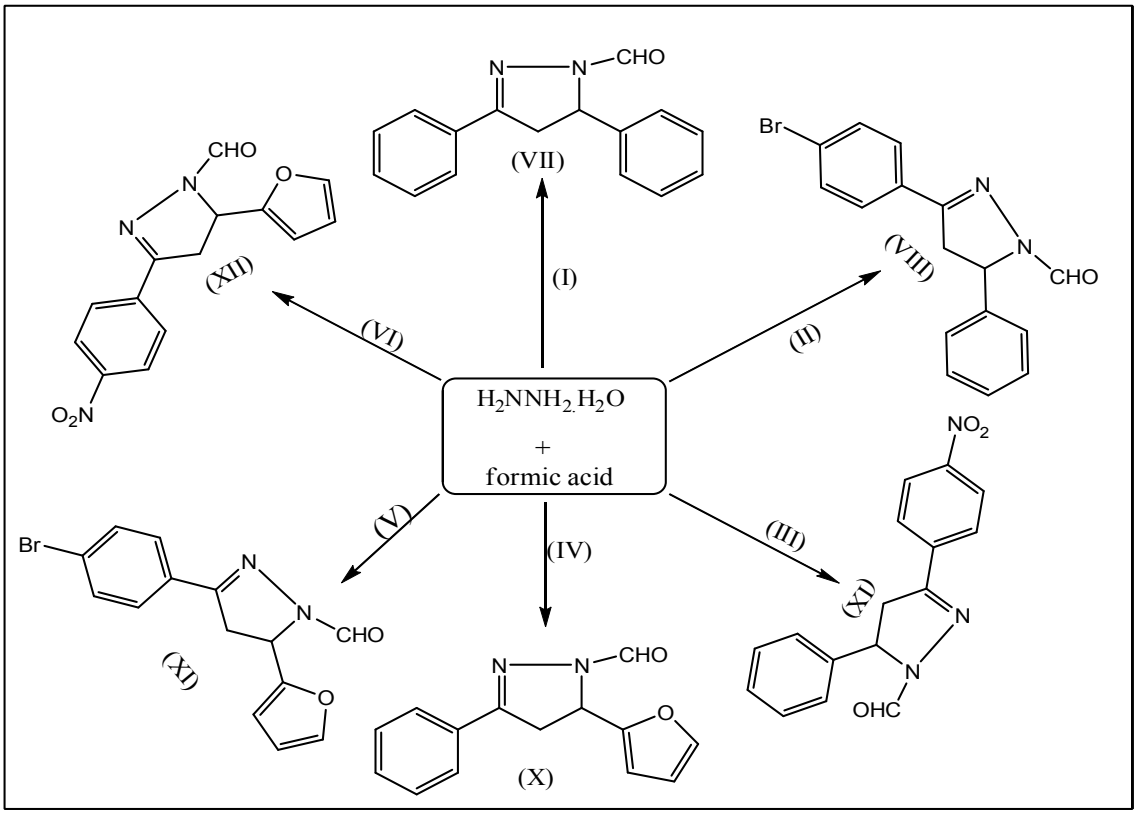
The anti-bacterial activity of the synthesized compounds was determined by using the agar diffusion method. Nutrient agar plates were prepared as directed by the manufacturer guidance then poured and left to solidify on a leveled surface. Overnight broth cultures of gram positive and gram negative bacteria were used to inoculate nutrient agar plates. After inoculation the plates were left for 5 minutes to dry. Wells (8.0 mm in diameter) were cut from the inoculated medium using a flame-sterilized cork borer, and then filled with compound solution (5µg/ml). Distilled water was used as negative control while gentamicin-10 was used as positive control. The plates were incubated at 37C° for 24 hours and the diameter of inhibition zone around each well was measured. Diameter inhibition zone was expressed in millimeters. Tests were performed in triplicate and the mean result was reported. (Table 2.8.a - 2.8.b).



Scheme (2.1): Chemical structures of the prepared 1-aryl-3-phenyl-prop-2-en-1-ones.

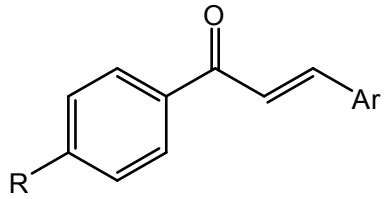


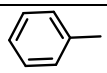
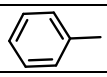
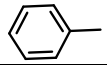
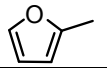
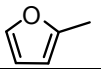
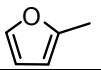
Scheme (2.2): Chemical structures of the prepared 1-aryl-3-(furan-2-yl)-prop-2-en-1-ones.



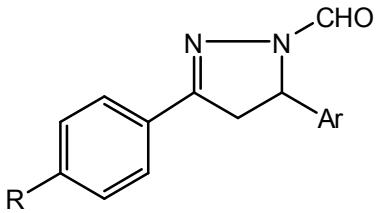
Scheme (2.3): Chemical structures of the prepared 3,5-diaryl-4,5-dihydropyrazole-1-carbaldehydes.

Table (2.1-a): Chemical names of synthesized1,3-diary-prop-2-en-1-ones.



Comp.No	R	Ar	Systematic chemical names
I	- H		1,3-diphenyl-prop-2-en-1-one
II	- Br		1-(4`-Bromophenyl)-3-phenyl-prop-2-en-1-one
III	- NO_2		1-(4`-Nitrophenyl)-3-phenyl-prop-2-en-1-one
IV	- H		1-phenyl-3-(furan-2-yl)-prop-2-en-1-one
V	- Br		1-(4`-Bromophenyl)-3-(furan-2-yl)-prop-2-en-1-one
VI	- NO_2		1-(4`-Nitrophenyl)-3-(furan-2-yl)-prop-2-en-1-one

Table(2.1-b): Chemical names of synthesized 3,5–diaryl-4,5-dihydropyrazole -1- carbaldehydes.



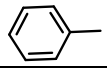
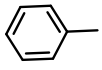
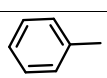
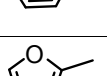
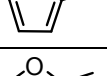
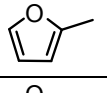
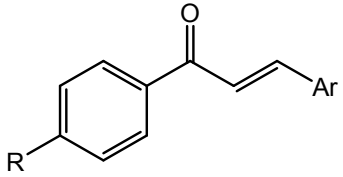
Comp.No	R	Ar	Systematic chemical names
VII	- H		3,5-diphenyl-4,5-dihydropyrazole-1-carbaldehyde
VIII	- Br		3-(4`-Bromophenyl)-5-phenyl-4,5-dihydropyrazole-1-carbaldehyde
IX	- NO_2		3-(4`-Nitrophenyl)-5-phenyl-4,5-dihydropyrazole-1-carbaldehyde
X	- H		3-phenyl-5-(furan-2-yl)-4,5-dihydropyrazole-1-carbaldehyde
XI	- Br		3-(4`-Bromophenyl)-5-(furan-2-yl)-4,5-dihydropyrazole -1- carbaldehyde
XII	- NO_2		3-(4`-Nitrophenyl)-5-(furan-2-yl)-4,5-dihydropyrazole -1- carbaldehyde

Table (2.2.a): Reaction characteristics data of synthesized 1,3-diary-prop-2-en-1-ones.



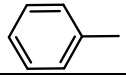
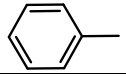
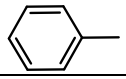
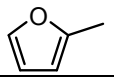
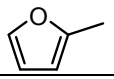
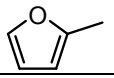
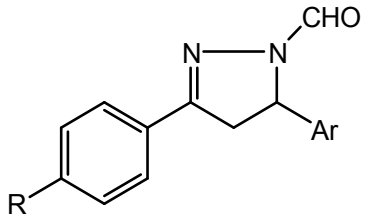
Com .No	R	Ar	M.F	M.Wt g/mol	Yield (gm)	Yield (%)	m.p (C◦) Recryst. Ethanol	Colour
I	- H		$C_{15}H_{12}O$	208.26	1.45	69.61	56-57	Pall yellow
II	- Br		$C_{15}H_{11}BrO$	287.15	2.53	88.12	115-116	Buff
III	- NO_2		$C_{15}H_{11}NO_3$	253.25	2.08	82.15	157-158	Reddish brown
IV	- H		$C_{13}H_{10}O_2$	198.22	1.57	79.21	48-49	Light brown
V	- Br		$C_{13}H_9BrO_2$	277.11	2.36	85.12	92-93	Brown
VI	- NO_2		$C_{13}H_9NO_4$	243.21	1.98	81.41	118-119	Dark brown

Table (2.2.b): Reaction characteristics data of synthesized 1,3-diaryl-4,5-dihydropyrazole-1-carbaldehy



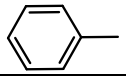
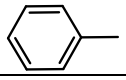
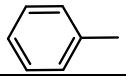
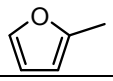
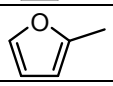
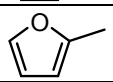
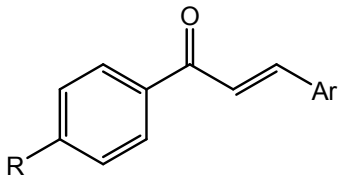
Com .No	R	Ar	M.F	M.Wt g/mol	Yield (gm)	Yield (%)	m.p (C◦) Recryst. Ethanol	Colour
VII	- H		$C_{16}H_{14}N_2O$	250.29	0.38	76.01	125-126	Light yellow
VIII	- Br		$C_{16}H_{13}BrN_2O$	329.19	0.49	74.75	147-148	Yellow
IX	- NO_2		$C_{16}H_{13}N_3O_3$	295.29	0.43	72.89	189-190	Light orange
X	- H		$C_{14}H_{12}N_2O_2$	240.26	0.47	76.63	121-122	Reddish brow
XI	- Br		$C_{14}H_{11}BrN_2O_2$	319.16	0.42	65.83	143-144	Dark brown
XII	- NO_2		$C_{14}H_{11}N_3O_4$	285.26	0.39	68.43	179-180	Very deep br

Table (2.3.a): Infrared spectral data of synthesized 1,3-diaryl-prop-2-en-1-ones.



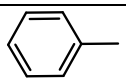
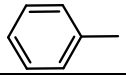
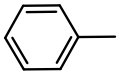
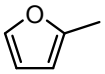
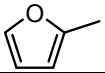
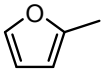
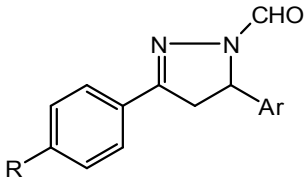
Com.No	R	Ar	C=O Str.vib Cm^{-1}	C=C Str.vib Cm^{-1}	Aromatic C=C strib.vib Cm^{-1}	Aromatic H-str.vib Cm^{-1}	Aromatic H-defo.vib Cm^{-1}
I	- H		1657	1599	1520-1447	3059	966-428
II	- Br		1659	1603	1550-1448	3059	983-462
III	- NO_2		1693	1640	1596-1448	3059	978-500
IV	- H		1678	1593	1550-1448	3059	923-460
V	- Br		1655	1595	1551-1472	3128	970-470
VI	- NO_2		1655	1596	1560-1410	3121	960-480

Table (2.3.b): Infrared spectral data of synthesized 3,5-diaryl-4,5-dihydropyrazole-1-carbaldehydes.



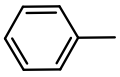
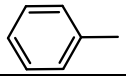
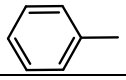
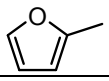
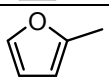
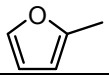
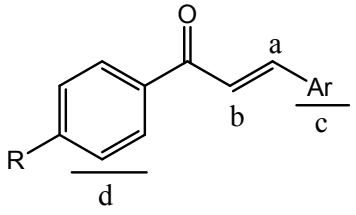
Com.No	R	Ar	C=O Str.vib Cm^{-1}	C=N Str.vib Cm^{-1}	Aromatic C=C str.vib Cm^{-1}	Aldehydic H-str.vib Cm^{-1}	Aromatic H-str.vib Cm^{-1}	Othe
VII	- H		1657	1610	1550 -1440	2922	3180	Mor benz banc in 1
VIII	- Br		1653	1600	1540-1425	2922	3192	p.Br C-N
IX	- NO_2		1650	1614	1520-1479	2914	3114	p.N 152
X	- H		1670	1616	1480	2914	3115	C-O C-N
XI	- Br		1670	1620	1520-1440	2920	3110	C-O C-N p-Br
XII	- NO_2		1670	1620	1520-1440	2920	3110	p-N 152

Table (2.4.a): ^{1}H-Nuclear Magnetic Resonance characteristic signals of synthesized 1,3-diaryl-prop-2-



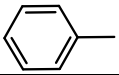
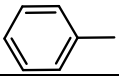
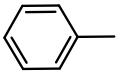
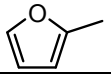
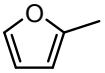
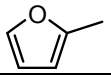
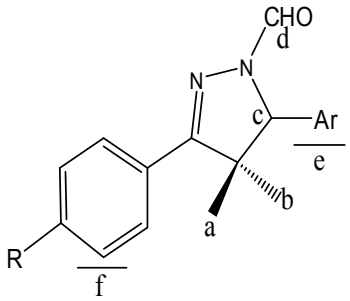
Com.No	R	Ar	Chemical shift -δ- ppm (integration, multiplicity, coupling constant)		
			a (H_β)	b (H_α)	c and d
I	- H		7.49 (1H, d, J =15)	7.24 (1H,d, J=15)	7.7(2H,d)-7.6(2H,d)-7.1(4H,t)-6.8
II	- Br		7.44 (1H, d, J =15)	7.23 (1H,d, J=15)	7.9(2H,d)-7.7(2H,t)-7.5(2H,d)-7.3
III	- NO_2		7.94 (1H, d, J =15)	7.44 (1H,d, J=15)	8.5(2H,d)-8.3(2H,d)-7.7(2H,t)-7.5
IV	- H		7.53 (1H, d, J =15)	7.37 (1H,d, J=15)	C:showed 6.75 (1H,d) , 6.54 (1H, 5.96 (1H,d), d: showed 6.90–8.05
V	- Br		7.73 (1H, d, J =15)	7.37 (1H,d, J=15)	C: showed 6.75 (1H,d), 6.53 (1H 3.74 (1H,d), d: showed , 7.28–7.9
VI	- NO_2		7.96 (1H, d, J =15)	7.54 (1H,d, J=15)	C: showed 6.83 (1H,d), 6.58 (1H 6.69 (1H,d), d: showed 7.28–8.37

Table (2.4.b): ^{1}H-Nuclear Magnetic Resonance characteristic signals of synthesized 3,5-diaryl-4,5-dihy

Carbaldehydes.



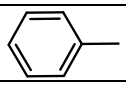
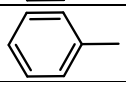
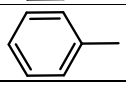
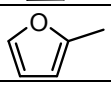
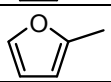
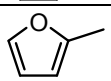
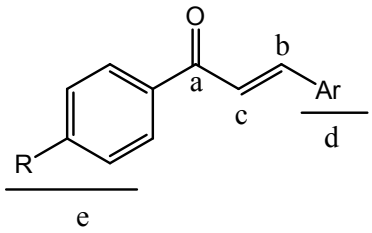
Com.No	R	Ar	Chemical shift -δ-ppm (integration, multiplicity)				
			a	B	c	d	e
VII	- H		5.57 (1H,dd)	3.84 (1H,dd)	3.26 (1H,dd)	9.00 (1H,s)	7.7(2H,d)-7.4(2H, 7.1(2H,t)-6.9(1H,d
VIII	- Br		5.46 (1H,dd)	3.70 (1H,dd)	3.11 (1H,dd)	8.88 (1H,s)	7.6(2H,d)-7.5(2H, 7.0(2H,d)
IX	- NO_2		5.50 (1H,dd)	3.95 (1H,dd)	3.23 (1H,dd)	8.32 (1H,s)	8.2(2H,d)-8.0(4H,
X	- H		5.81 (1H,dd)	3.75 (1H,dd)	3.43 (1H,dd)	8.93 (1H,s)	e: occur as 7.07 6.37(1,Hd) F: occu
XI	- Br		5.65 (1H,dd)	3.64 (1H,dd)	3.48 (1H,dd)	8.95 (1H,s)	e: occur in 7.28(1 in 7.37-8.23(4H,m
XII	- NO_2		5.81 (1H,dd)	3.53 (1H,dd)	3.43 (1H,dd)	8.93 (1H,s)	e:occur7.20(1H,d) and d: in7.07-7.49

Table (2.5.a): ^{13}C-Nuclear Magnetic Resonance characteristic signals of synthesized 1,3-diaryl-prop-2-en-1-ones.



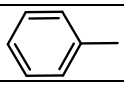
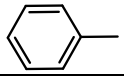
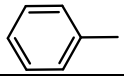
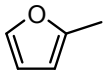
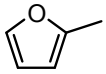
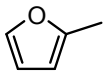
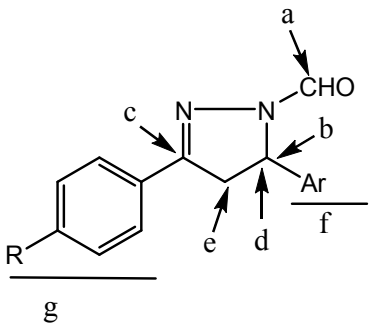
Com.No	R	Ar	Chemical shift -δ- ppm.			
			a	b	c	d and e
I	- H		206.80	146.84	122.12	132.8,131.9, 129.0 ,128.4,127.5,126.6
II	- Br		189.39	145.44	121.47	136.9, 132.2,129.7, 128.8, 129.1,126.4
III	- NO_2		189.43	152.00	124.02	131.1, 130.6, 129.4, 129.2,128.8, 128.4
IV	- H		189.80	144.97	119.32	d:showed signals in 151.0 ,132.81, 112.70, 116.73 e: showed signals in 127.66 – 130.75
V	- Br		188.62	145.15	118.62	d:showed signals in 151.0 , 136.87, 112.81, 116.73 e: showed signals in 127.80 – 131.91
VI	- NO_2		189.32	144.80	123.70	d:showed signals in 151.0 , 136.00, 112.72, 116.73 e: showed signals in 128.80 – 131.10

Table (2.5.b): ^{13}C-Nuclear Magnetic Resonance characteristic signals of synthesized 3,5-diaryl-4,5-dihydropyrazole-1- carbaldehydes



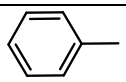
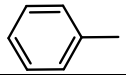
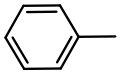
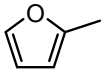
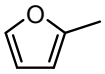
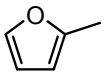
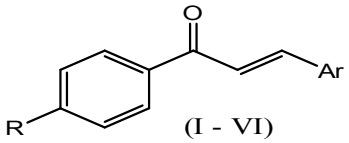
Com.No	R	Ar	Chemical shift -δ- ppm.					
			A	b	c	d	e	f and g
VII	- H		160.00	154.00	145.50	52.75	48.02	132.9, 129.0, 128.8, 128.2, 127.5, 126.9,125.6
VIII	- Br		160.11	154.74	140.40	59.23	42.51	132.09, 129.8, 129.1, 128.1, 125.6, 125.0
IX	- NO_2		161.56	159.06	141.50	58.43	38.81	133.40, 130.1, 129.7, 127.8, 125.3, 125.0
X	- H		160.12	154.60	142.82	52.21	38.33	f :showed signals in 150.77, 122.40, 111.62, 110.82 g:showed signals in 127.00 – 132.80
XI	- Br		160.11	154.90	142.43	52.60	38.35	f :showed signals in 150.68, 125.09, 108.26, 110.66 g:showed signals in 127.27 – 132.07
XII	- NO_2		160.93	154.28	142.71	52.94	38.72	f :showed signals in 151.20, 124.72, 114.30, 112.73 g :showed signals in 127.34 – 133.01

Table (2.6.a): Measured Ultraviolet absorption λ_{max} (nm) of Synthesized 1,3-diaryl-prop-2-en-1-ones.



(I - VI)

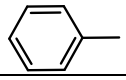
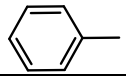
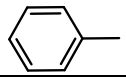
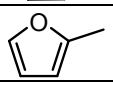
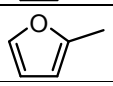
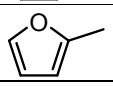
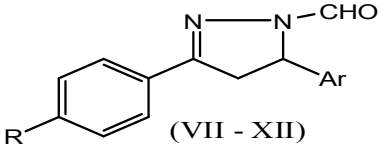
Com.No	R	Ar	Solvent	$\lambda_{max\ (nm)}$
I	- H		Methanol	298
II	- Br		Methanol	313
III	- NO_2		Methanol	343
IV	- H		Methanol	338
V	- Br		Methanol	344
VI	- NO_2		Methanol	354

Table (2.6.b): Measured Ultraviolet absorption λ_{max} (nm) of synthesized 3,5-diaryl-4,5-dihydropyrazol-1-carbaldehydes.



(VII - XII)

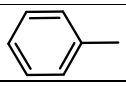
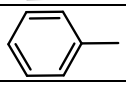
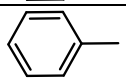
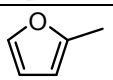
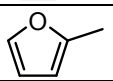
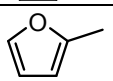
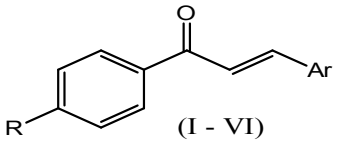
Com.No	R	Ar	Solvent	$\lambda_{max\ (nm)}$
VII	- H		Methanol	257
VIII	- Br		Methanol	295
IX	- NO_2		Methanol	290
X	- H		Methanol	278
XI	- Br		Methanol	286
XII	- NO_2		Methanol	307

Table (2.7.a): R_f values of synthesized 1,3-diaryl-prop-2-en-1-ones.



(I - VI)

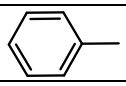
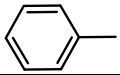
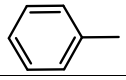
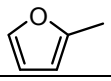
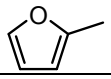
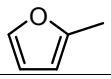
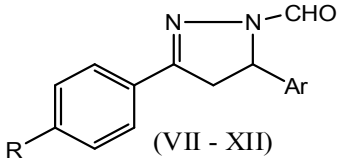
Com.No	R	Ar	Mobile phase	R_F values
I	- H		Chloroform : Methanol in (9.5:0.5)	0.91
II	- Br		Chloroform : Methanol in (9.5:0.5)	0.90
III	- NO_2		Chloroform : Methanol in (9.5:0.5)	0.74
IV	- H		Chloroform : Methanol in (9.5:0.5)	0.85
V	- Br		Chloroform : Methanol in (9.5:0.5)	0.82
VI	- NO_2		Chloroform : Methanol in (9.5:0.5)	0.84

Table (2.7.b): R_f values of synthesized 1,3-diaryl-3,4-diarylpyrazole-1-carbaldehyde



(VII - XII)

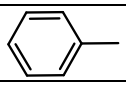
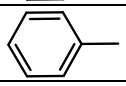
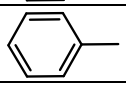
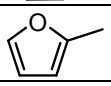
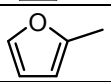
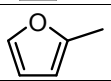
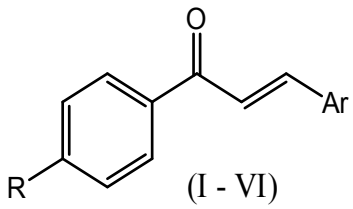
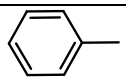
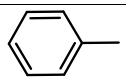
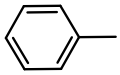
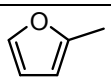
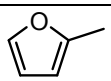
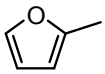
Com.No	R	Ar	Mobile phase	R_f values
VII	- H		Chloroform : Methanol in (9.5:0.5)	0.96
VIII	- Br		Chloroform : Methanol in (9.5:0.5)	0.93
IX	- NO_2		Chloroform : Methanol in (9.5:0.5)	0.98
X	- H		Chloroform : Methanol in (9.5:0.5)	0.95
XI	- Br		Chloroform : Methanol in (9.5:0.5)	0.98
XII	- NO_2		Chloroform : Methanol in (9.5:0.5)	0.97

Table (2.8.a): Mean of Inhibition zone (mm) of Antibacterial activity of synthesized 1,3-diaryl-prop-2-en-1-ones.

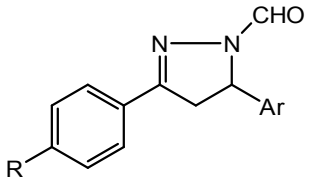


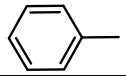
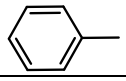
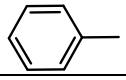
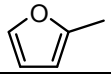
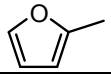
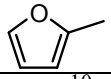
(I - VI)

Com.No	R	Ar	Mean zone of inhibition (mm)	
			E.coli	*S.aure*
I	- H		14	15
II	- Br		15	14
III	- NO_2		14	10
IV	- H		15	10
V	- Br		14	10
VI	- NO_2		15	10
Standard of control		Gen 10	25	24

*The concentration of all synthesized compounds is 5µg/ml in PRG.

Table (2.8.b): Diameter Inhibition zone of antibacterial activity of synthesized3,5-diaryl-4,5-dihydropyrazole-1-carbaldehydes.



Com.No	R	Ar	Mean zone of inhibition (mm)	
			E.coli	*S.aure*
VII	- H		11	10
VIII	- Br		13	10
IX	- NO_2		15	10
X	- H		15	13
XI	- Br		12	12
XII	- NO_2		13	13
Standard of control		Gen [10]	25	24

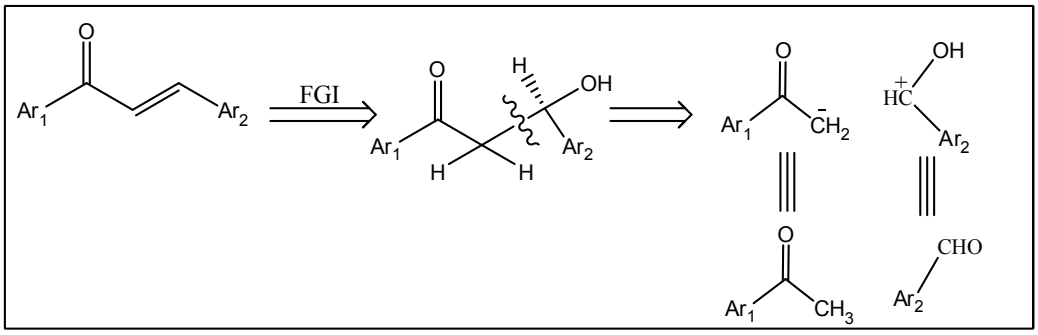
*The concentration of all synthesized compounds is 5µg/ml in PRG.

Chapter Three

3.1 Discussion:

In this work, synthesis of six chalcones and six N-formyl pyrazolines were accomplished, and in a view of the retrosynthsis analysis of these compounds it was found that the chosen reaction methods are logical synthetic way and realistic managed to prepare these compounds.

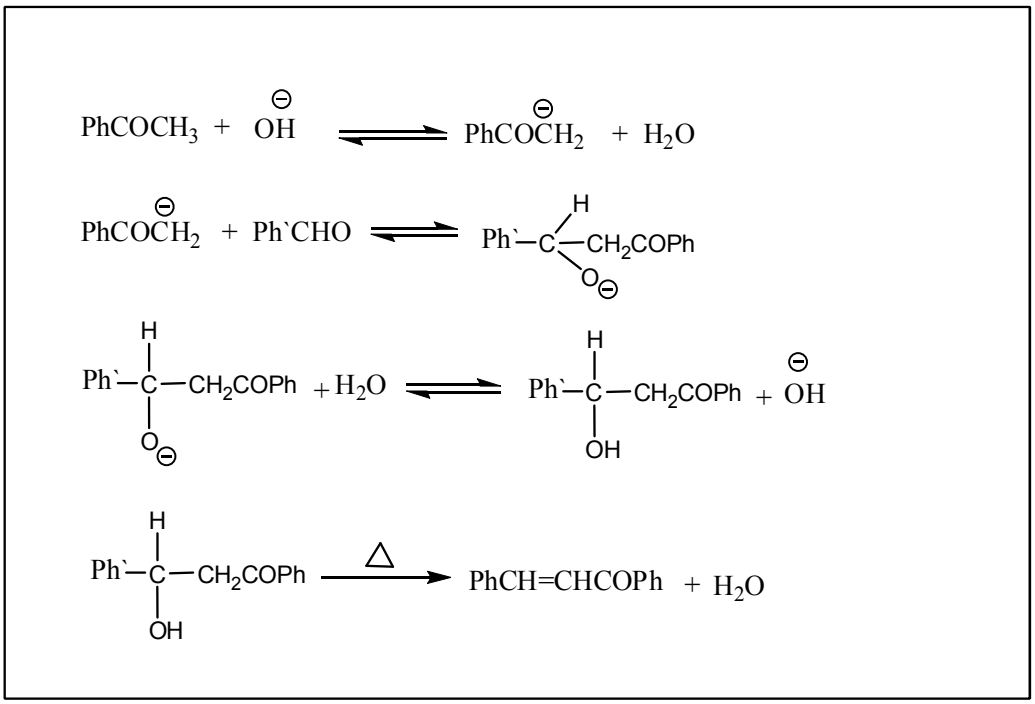
The retrosynthesis of chalcone based on FGI and suitable disconnection into perfect possible available starting materials was given in scheme (3.1).



Scheme (3.1): Retrosynthesis of chalcone.

It is obvious from the above retrosynthesis that chalcone synthesis caused by the nucleophilic addition of existing carboanion to carbonyl group of aromatic aldehyde, whereas the Adol addition species is an intermediate. Therefore the suggested synthesis way of this compound is follow the Claisen-Schmidt condensation reaction.

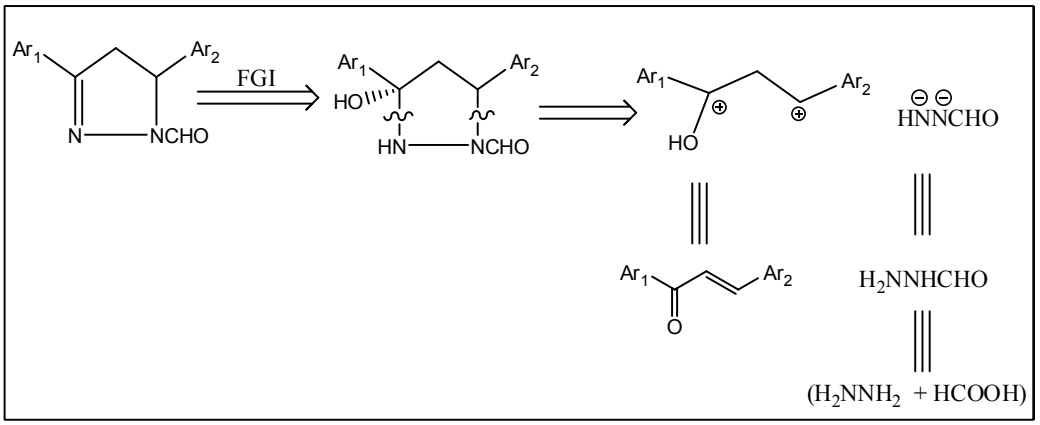
In this reaction equimolar quantities of aromatic aldehyde and acetophenone (substituted or unsubstituted) were used in the presence of an aqueous alcoholic alkali (10% - 60%), with constant stirring for twelve hours in (25 – 30C^{o}), (Arun Parik and Hanse Parik., 2006), the suggested mechanism of this reaction proved in several kinetic studies by (Coombs and Evans, 1940; Dhar and Lal, 1958; Nayak and Rout, 1975). The mechanism that has been advanced for this reaction by Nayak and Rout 1975 is illustrated bellow:



Scheme (3.2): Mechanism of chalcone formation.

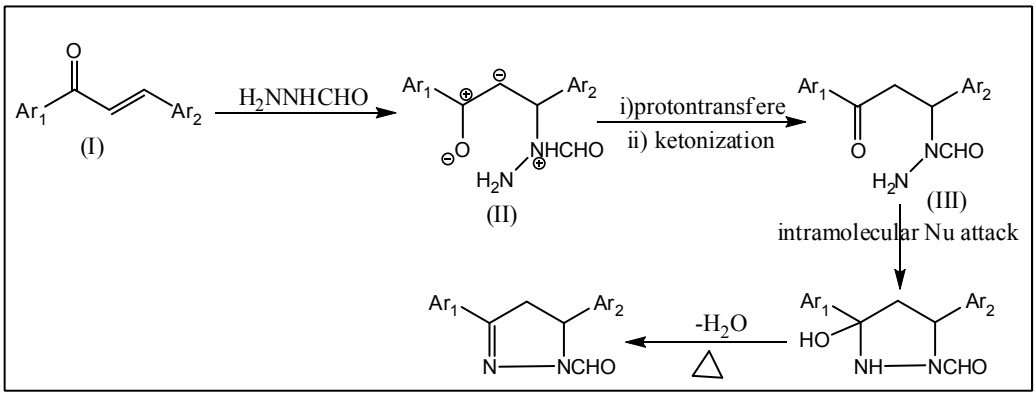
This mechanism had further studied by (Gasull *et al*., 2000) and they present that a rapid nucleophilic attack of the hydroxide anion on the carbon of methyl group of acetophenone followed by attack of acetophenate ion on the carbon atom of carbonyl group of aromatic aldehyde which is the slow step. And there is a configuration equilibrium cis-s-cis↔trans-s-trans between intermediate compounds was achieved. during this an electrophilic attack of a molecule of water on the oxygen atom bonded to C-β of the intermediate anion formed a neutral intermediate with catalyst regeneration. Followed by intermolecular hydration of neutral intermediate to give the chalcone in trans-s-trans configuration. This study of the reaction mechanism explains satisfactorily the global rate of third order reaction.

Retrosynthesis of pyrazolines according to the rational disconnections reveal that hydrazine hydrate (or it is derivatives) will produce as starting material for this synthesis scheme (3.3



Scheme (3.3): Retrosynthesis of N-formyl pyrazoline.

Refluxing of hydrazine hydrate with chalcone in formic acid will produce N-formyl pyrazoline (Rostom *et al*., 2011). The associated mechanism of this reaction was studied by (Reda *et al*., 1991) scheme (3.4).



Scheme (3.4): Mechanism of N-formyl pyrazolines formation.

Nucleophilic attack by hydrazine at the β-carbon of the chalcone forms species (II) in which the negative charge is mainly accommodated on the electronegative oxygen atom, proton transfer from the nitrogen to electronegative oxygen atom produce an intermediate enol which simultaneously turned to ketoamine, Other intermolecular nucleophilic attack by primary amino group of ketoamine on it is carbonyl carbon followed by proton transfer from nitrogen to oxygen leads to amine, then lose of water molecule yield pyrazoline.

The prepared compounds were obtained as solids and their expected structures were investigated and proved through their physiochemical and spectral studies.

Synthesized compounds occur within different colour which indicates for existence of chromophore in their structures and it is the conjugated π-bonds system.

Yield percentages of products were calculated. Chalcones were resulting in very good yield (70 – 85%) and chalcones with substituted acetophenone origin have better yield than that of unsubstituted one due to the substituent effect in stability acetophenonate ion. In pyrazolines the yield was in good range (65-76%) and their percentages basically depend on their precursor purity and stability.

R_f values of products were compared with the reactants to determine their purity and also as evidence for reaction progress and completion.

Melting points of the products were determined after recrystalization process (hot ethanol used as solvent), and melting point values were uncorrected but they were measured with high accuracy and in region within ±1degree as a difference, all these preliminary identification informations were reported in table (2.2.a and 2.2.b).

Infrared spectrum bands of products showed characteristic peaks. In chalcones, (C=O) str.vib occur in range (1655 - 1693) cm^{-1}, and (C=C) str.vib in range (1593 - 1640) cm^{-1}, these values support the presence of conjugated system.

In pyrazolines, (C=O, formyl group) str.vib occur in range (1650-1670) cm^{-1}, (C=N) str.vib in (1600 - 1620) cm^{-1} and (C-N) str.vib in range (1040 - 1070) cm^{-1}.

All compounds showed (aromatic`s H) str.vib in range (3059 - 3120) $cm^{-1}$, (aromatic`s C bonds) str.vib in range (1596 - 1410) cm^{-1}.(Br) as substituent in *para* position of phenyl group appear as medium peak in range (746 - 762) cm^{-1}, while (NO_2-) reveal two adjacent peaks for asymmetrical and symmetrical absorption in region (1344 - 1521) cm^{-1} and (1226 - 1340) cm^{-1} respectively and furyl group showed (C-O) str.vib in range (1006 - 1020) cm^{-1}.

Generally, the substitution pattern of the phenyl ring and aromatic`s H have deformation absorption occur as summation bands in range (420 - 1000) cm^{-1}, which were consider as fingerprint of these compounds. All these (IR) bands were reported in table (2.3.a and 2.3.b).

^{1}H-NMR spectrums of products confirmed their expected structures. In case of chalcones, hydrogen of β-carbon (Hβ) and hydrogen of α-carbon (Hα) showed doublet signals at δ (7.44 – 7.96) ppm and (7.24

– 7.59) ppm respectively. Hβ reveal chemical shift values more downfield than Hα due to the effect of direct link with aromatic ring (phenyl,2-furyl) where is the resonance character of these ring reduce the electron density around the β-carbon. And in other hand this carbon has partial positive charge respect to carbonyl group.

While in N-formyl pyrazolines, pyrazoline ring showed, ABX pattern signals and $H_aH_bH_x$ appear as double-doublet (dd) at δ (3.11–3.48) ppm, (3.53 – 3.95) ppm and (5.46 – 5.81) ppm respectively. While the aldehydic hydrogen occur as singlet (s) signal at δ (8.32 – 11.39) ppm.

Phenyl ring`s hydrogens occur as multiplet (m) signals at δ (6.80 – 8.44) ppm and furyl rings hydrogen showed three perfect signals for three hydrogens as doublet at δ (6.75 – 7.28) ppm, doublet-doublet at δ (6.53 – 6.87) ppm and doublet at δ (3.74 – 6.69) ppm (Table 2.4.a and 2.4.b).

^{13}C-NMR spectrums of these compounds also gave good characteristic signals. In chalcones the specific ketonoic carbon (C=O) occur at δ (188.62 – 206.80) ppm, carbon (C_α) occur at δ (118.62 – 124.02) ppm and the (C_β) occur at δ (144.80 – 152.00) ppm.

In N-formyl pyrazolines, the aldehydic carbon (C=O) occur at δ (160.00-161.56) ppm, (C-N) occur at (154.00 – 159.06) ppm, (C=N) occur at (140.40 – 145.50) ppm, methine carbon (CH) occur at (52.21 – 59.23) ppm, and methylene (CH_2) carbon occur at (38.33 – 48.03) ppm.

Phenyl ring`s carbons of these compounds occur at (125.08 – 136.92) ppm, and furyl ring`s carbon showed fine four signals at (150.6-151.00) ppm, (122.40 – 136.87) ppm, (110.66 – 116.73) ppm and (108.26 – 112.81) ppm (Table 2.5.a and 2.5.b).

λ_{max} (nm) of products were measured using methanol as solvent, and the results explain π-π* transition of conjugated system and/or π-π* transition of aromatic π bonds. Chalcones absorption occur in range (298-354) nm and pyrazolines in range (257- 307) nm (Table 2.6.a and 2.6.b).

The IR spectra, NMR spectra and λ_{max} (nm) values of these compounds were confirmed their predicted structures, and they are match together. And through the mainly inspection of their spectrums found that there is a good agreement within the values of similar compounds which mentioned in literature review.

Antibacterial sensitivity of synthesized compounds were screened against Gram positive staphylococcus aureus, *(S.aureus*), and Gram negative Escherichia Coli, (*E.coli*), by using an Nutrien Agar Diffusion Method where Nutrient Agar medium was employed as a media of

culture and Gentamicin 10mg/disc (Gen^{10}) was used as control for antibacterial activity. The Diameter Inhibition Zone values were present that synthesized compounds are active and they are more active against *E.coli* than *S.aureus* and the compounds with the furyl ring are more active than that with the phenyl ring (Table 2.8.a and 2.8.b).

Chapter Four

(4.1) Conclusion:-

The following points were concluded from this study:

- Six chalcone derivatives and their five membering nitrogen heterocyclic compounds (N-formylpyrazolines) were synthesized.
- The reaction progress was monitored with TLC technique and the products were characterized by TLC, melting point, IR, ^{1}H-NMR, ^{13}C-NMR, UV spectrometry.
- Chalcones showed characteristic str.vib IR peaks for (C=O) and (C=C) functional group. And N-formyl-pyrazolines showed str.vib peaks for (C=O), (C=N) and (C-N). While Aromatic system showed special summation bands.
- In ^{1}H-NMR spectra, chalcones showed two doublet signals for Hβ(set a) and Hα(set b)**.** And N-formyl-pyrazolines showed ABX pattern the $H_AH_BH_X$ occur as double doublet signals. While Aldehydic hydrogen occurs as singlet signal. Aromatic's hydrogens showed multiplet signals for phenyl ring and remarkable doublet ,double doublet, doublet signals occur for furyl hydrogens.
- In ^{13}C-NMR spectra, chalcones showed three different sets and characteristic three signals occur in their spectrums. But N-formyl-pyrazolines showed five sets. Aromatic's carbons showed number of signals of phenyl ring and furyl ring showed certain four signals.
- In UV spectra, chalcones and N-formyl-pyrazolines showed λ_{max} in expected range.

(4.2) Recommendations:-

- It is highly recommended that synthesized structures to be subjected to the EIMS and FABMS.
- Based upon the preliminary Anti-bacterial activity showed by the synthesized compounds, it is recommended that full Anti-microbial screening to be performed.
- In other hand studies of QSAR of this biological activity should be achieved.

Chapter Five

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Chapter Six

6. Appendices:

6.1 Appendix of IR Spectrum of Synthesized Compounds:

1. IR spectrum of (I): 1, 3-diphenyl-prop-2-en-1-one.
2. IR spectrum of (II): 1- (4`-Bromophenyl)-3-phenyl-prop-2-en-1-one.
3. IR spectrum of (V): 1- (4`-Bromophenyl)-3-(furan-2-yl)-prop-2-en-1-one.
4. IR spectrum of (VII): 3, 5-diphenyl-4,5-dihydropyrazole-1-carbaldehyde.
5. IR spectrum of (VIII): 3- (4`-Bromophenyl)-5-phenyl-4,5-dihydropyrazole-1-carbaldehyde .
6. IR spectrum of (XI): 3-(4`-Bromophenyl)-5-(furan-2-yl)-4,5-dihydropyrazole -1- carbaldehyde.

6.2 Appendix of ^{1}H-NMR Spectrum of Synthesized Compounds:

1. ^{1}H-NMR spectrum of (I): 1,3-diphenyl-prop-2-en-1-one.
2. ^{1}H-NMR spectrum of (II): 1-(4`-Bromophenyl)-3-phenyl-prop-2-en-1-one.
3. ^{1}H-NMR spectrum of (V): 1-(4`-Bromophenyl)-3-(furan-2-yl)-prop-2-en-1-one.
4. ^{1}H-NMR spectrum of (VII): 3,5-diphenyl-4,5-dihydropyrazole-1-carbaldehyde.
5. ^{1}H-NMR spectrum of (VIII): 3-(4`-Bromophenyl)-5-phenyl-4,5-dihydropyrazole -1-carbaldehyde.
6. ^{1}H-NMR spectrum of (XI): 3-(4`-Bromophenyl)-5-(furan-2-yl) 4,5-dihydropyrazole -1-carbaldehyde.

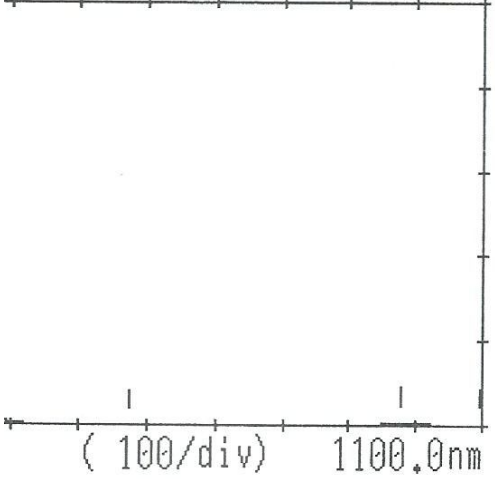
6.3 Appendix of ^{13}C-NMR Spectrum of Synthesized Compounds:

1. ^{13}C-NMR spectrum of (I): 1,3-diphenyl-prop-2-en-1-one.
2. ^{13}C-NMR spectrum of (II): 1-(4`-Bromophenyl)-3-phenyl-prop-2-en-1-one.
3. ^{13}C-NMR spectrum of (V): 1-(4`-Bromophenyl)-3-(furan-2-yl)-prop-2-en-1-one.
4. ^{13}C-NMR spectrum of (VII): 3,5-diphenyl-4,5-dihydropyrazole-1-carbaldehyde.
5. ^{13}C-NMR spectrum of (VIII): 3-(4`-Bromophenyl)-5-phenyl-4,5dihydropyrazole -1-carbaldehyde.
6. ^{13}C-NMR spectrum of (XI): 3-(4`-Bromophenyl)-5-(furan-2-yl)-4,5-dihydropyrazole-1- carbaldehyde.

6.4 Appendix of UV Spectrum of Synthesized Compounds:

1. UV spectrum of (I): 1,3-diphenyl-prop-2-en-1-one.
2. UV spectrum of (II): 1-(4`-Bromophenyl)-3-phenyl-prop-2-en-1-one.
3. UV spectrum of (V): 1-(4`-Bromophenyl)-3-(furan-2-yl)-prop-2-en-1-one.
4. UV spectrum of (VII): 3,5-diphenyl-4,5-dihydropyrazole-1-carbaldehyde.
5. UV spectrum of (VIII): 3-(4`-Bromophenyl)-5-phenyl-4,5-dihydropyrazole -1-carbaldehyde.
6. UV spectrum of (XI): 3-(4`-Bromophenyl)-5-(furan-2-yl)-4,5-dihydropyrazole -1-carbaldehyd

6:51



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Fast
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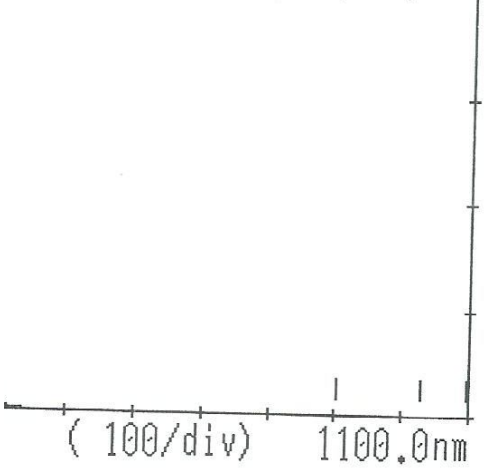

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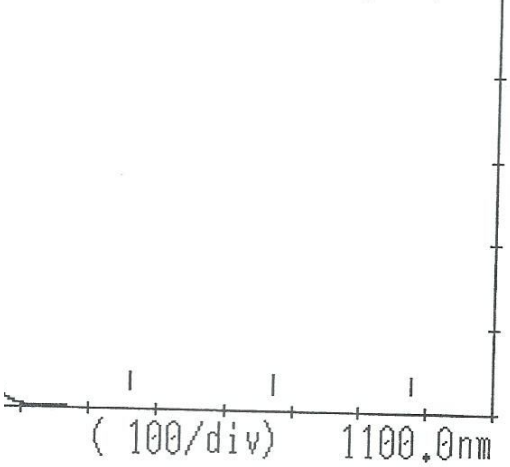

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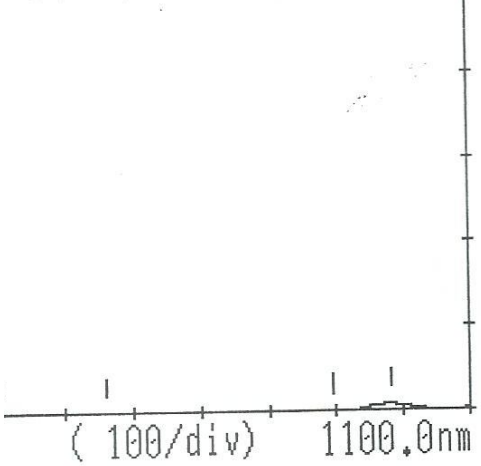
Fast
1.0



19/Sep/2013 11:34:01
Abs
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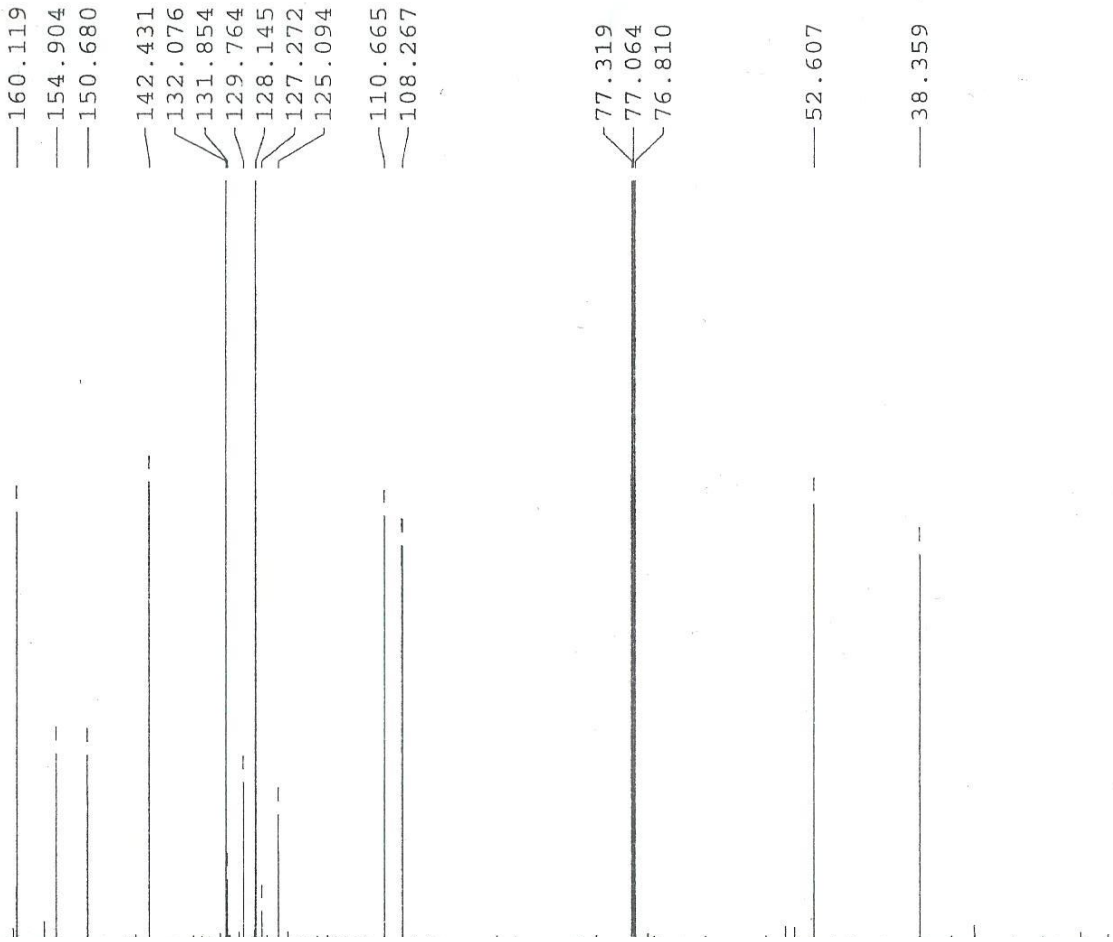
0.5
Fast
1.0

^{13}C-NMR spectrum of compound (XI):

3-(4`-Bromophenyl)-5-(furan-2-yl)-4,5-dihydropyrazole-1- carbaldehyde.



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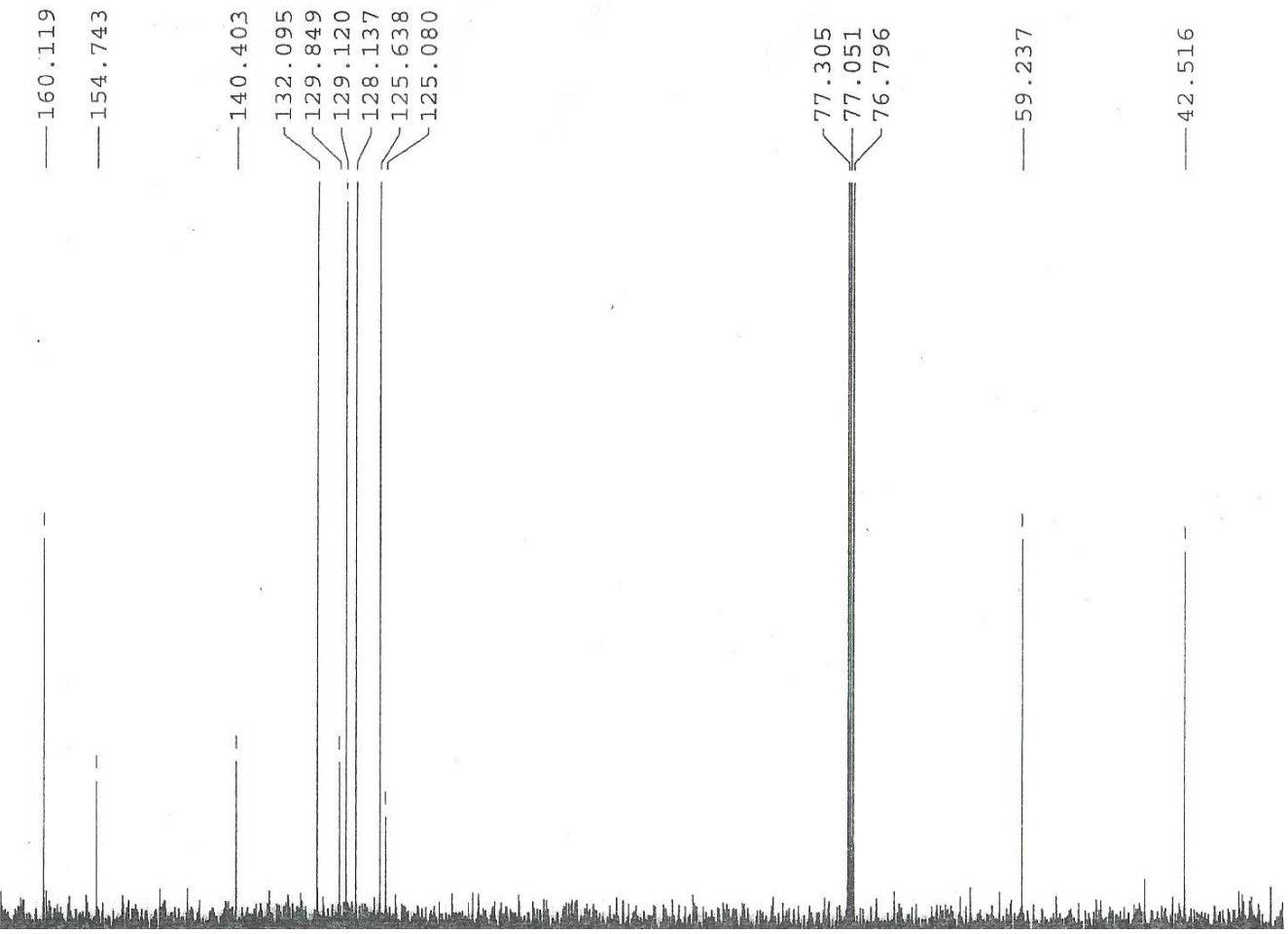
BRUKER

NAME	Dec04-2013
EXPNO	41
PROCNO	1
Date_	20131204
Time	14.26
INSTRUM	spect
PROBHD	1.7 mm PATXI 1
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	4000
DS	4
SWH	29761.904 Hz
FIDRES	0.454131 Hz
AQ	1.1010548 sec
RG	203
DW	16.800 usec
DE	6.50 usec
TE	298.0 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 usec
PL1	3.90 dB
PL1W	36.53155899 W
SFO1	125.7703643 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	6.20 dB
PL12	31.20 dB
PL13	33.20 dB
PL2W	6.44738770 W

^{13}C-NMR spectrum of compound (VIII):

3-(4`-Bromophenyl)-5-phenyl-4,5dihydropyrazole -1-carbaldehyde.



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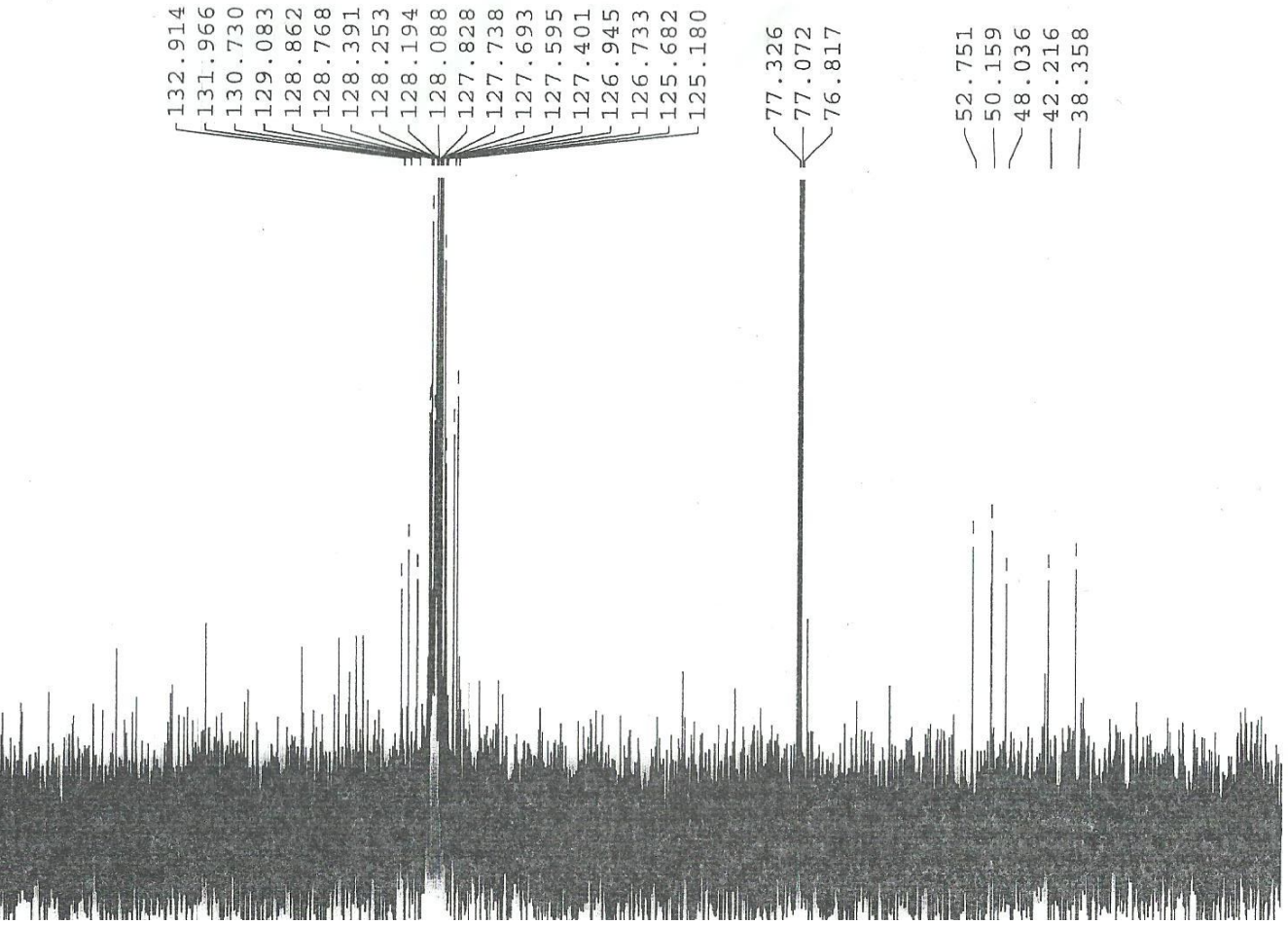
BRUKER

NAME	Dec03-2013
EXPNO	121
PROCNO	1
Date_	20131204
Time	9.34
INSTRUM	spect
PROBHD	1.7 mm PATXI 1
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	3000
DS	4
SWH	29761.904 Hz
FIDRES	0.454131 Hz
AQ	1.1010548 sec
RG	203
DW	16.800 usec
DE	6.50 usec
TE	298.0 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 usec
PL1	3.90 dB
PL1W	36.53155899 W
SFO1	125.7703643 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	6.20 dB
PL12	31.20 dB
PL13	33.20 dB
PL2W	6.44738770 W

^{13}C-NMR spectrum of compound (VII):

3,5-diphenyl-4,5-dihydropyrazole-1-carbaldehyde.



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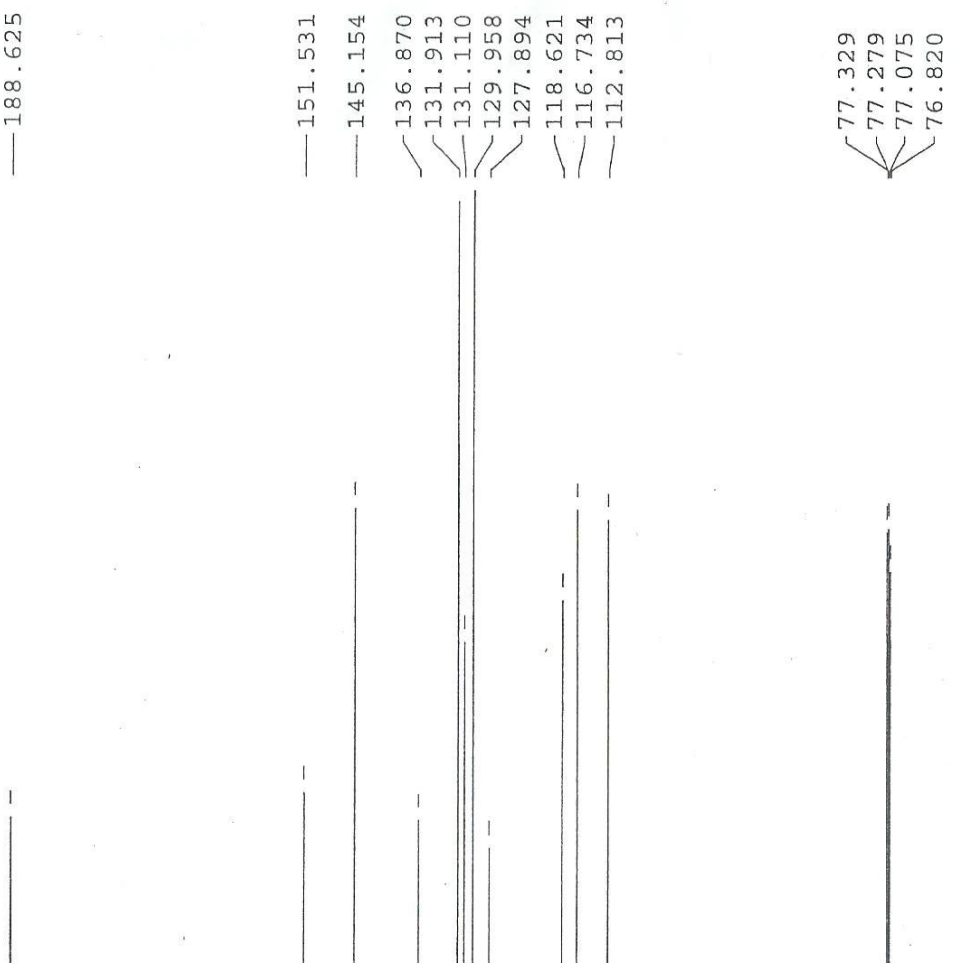
BRUKER

NAME	Dec03-2013
EXPNO	111
PROCNO	1
Date_	20131204
Time	6.49
INSTRUM	spect
PROBHD	1.7 mm PATXI 1
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	3000
DS	4
SWH	29761.904 Hz
FIDRES	0.454131 Hz
AQ	1.1010548 sec
RG	203
DW	16.800 usec
DE	6.50 usec
TE	298.0 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 usec
PL1	3.90 dB
PL1W	36.53155899 W
SFO1	125.7703643 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	6.20 dB
PL12	31.20 dB
PL13	33.20 dB
PL2W	6.44738770 W

^{13}C-NMR spectrum of compound (V):

1-(4`-Bromophenyl)-3-(furan-2-yl)-prop-2-en-1-one.



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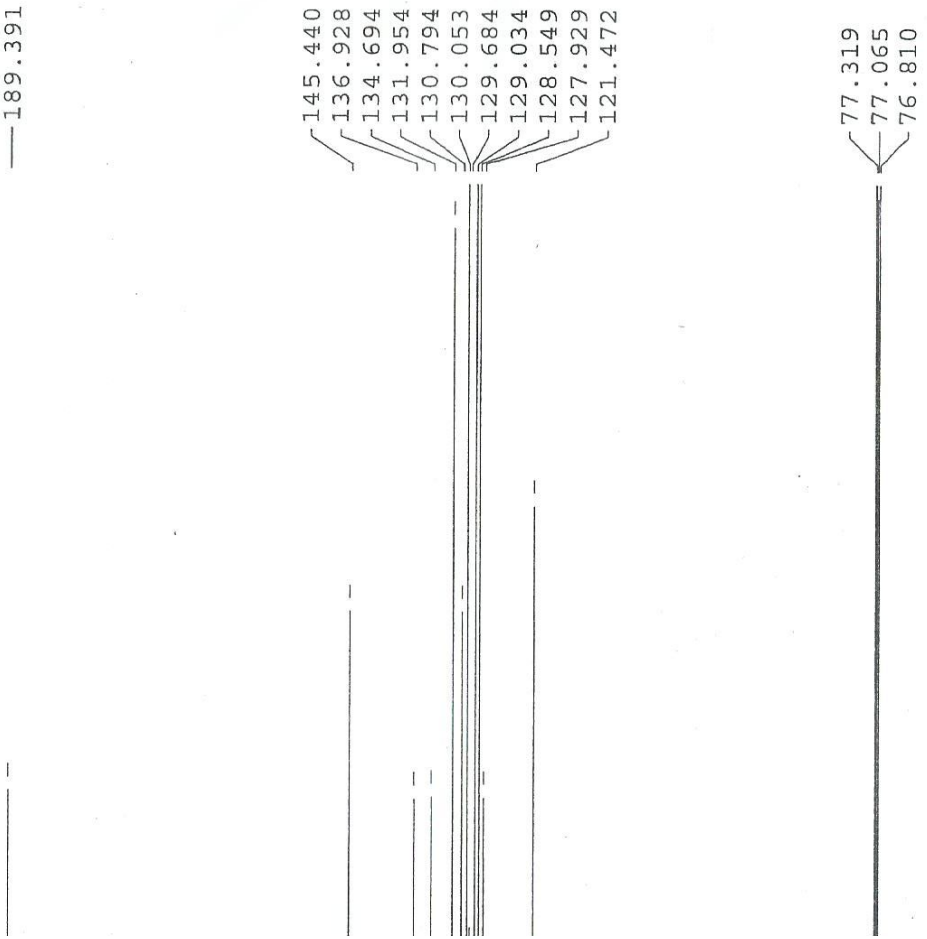
BRUKER

NAME	Dec03-2013
EXPNO	91
PROCNO	1
Date_	20131204
Time	1.21
INSTRUM	spect
PROBHD	1.7 mm PATXI 1
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	3000
DS	4
SWH	29761.904 Hz
FIDRES	0.454131 Hz
AQ	1.1010548 sec
RG	203
DW	16.800 usec
DE	6.50 usec
TE	298.0 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 usec
PL1	3.90 dB
PL1W	36.53155899 W
SFO1	125.7703643 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	6.20 dB
PL12	31.20 dB
PL13	33.20 dB
PL2W	6.44738770 W
PL12W	0.02038843 W

^{13}C-NMR spectrum of compound (II):

1-(4`-Bromophenyl)-3-phenyl-prop-2-en-1-one.



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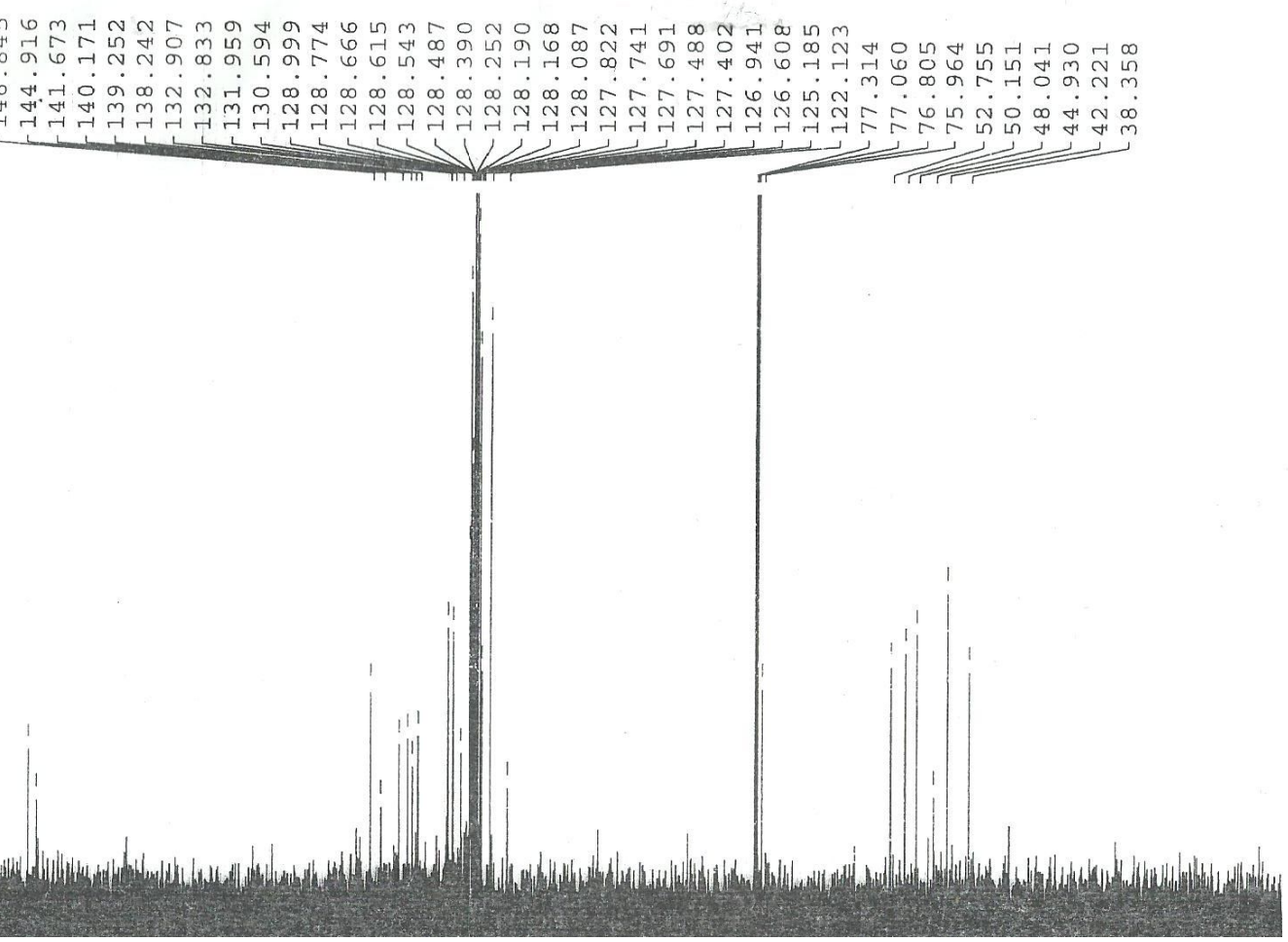
BRUKER

NAME	Dec03-2013
EXPNO	61
PROCNO	1
Date_	20131203
Time	16.14
INSTRUM	spect
PROBHD	1.7 mm PATXI 1
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	3000
DS	4
SWH	29761.904 Hz
FIDRES	0.454131 Hz
AQ	1.1010548 sec
RG	203
DW	16.800 usec
DE	6.50 usec
TE	298.0 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 usec
PL1	3.90 dB
PL1W	36.53155899 W
SFO1	125.7703643 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	6.20 dB
PL12	31.20 dB
PL13	33.20 dB

C-NMR spectrum of compound (I): 1,3-diphenyl-prop-2-en-1-one.



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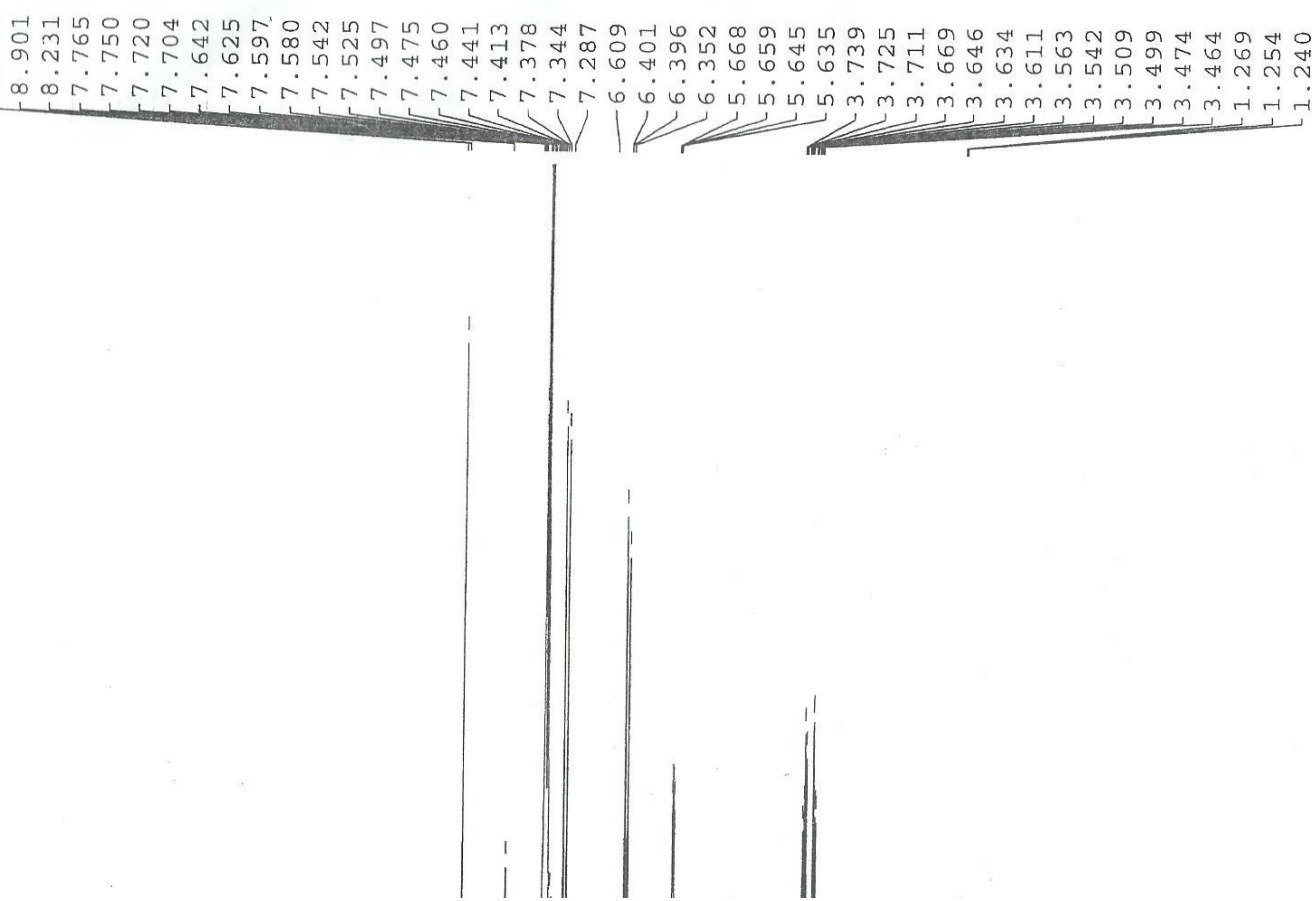
BRUKER

NAME	Dec03-2013
EXPNO	51
PROCNO	1
Date_	20131203
Time	12.52
INSTRUM	spect
PROBHD	1.7 mm PATXI 1
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	3000
DS	4
SWH	29761.904 Hz
FIDRES	0.454131 Hz
AQ	1.1010548 sec
RG	203
DW	16.800 usec
DE	6.50 usec
TE	298.0 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 usec
PL1	3.90 dB
PL1W	36.53155899 W
SFO1	125.7703643 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	6.20 dB
PL12	31.20 dB
PL13	33.20 dB
PL2W	6.44738770 W

^{1}H-NMR spectrum of compound (XI):

3-(4`-Bromophenyl)-5-(furan-2-yl)- 4,5-dihydropyrazole -1-carbaldehyde.



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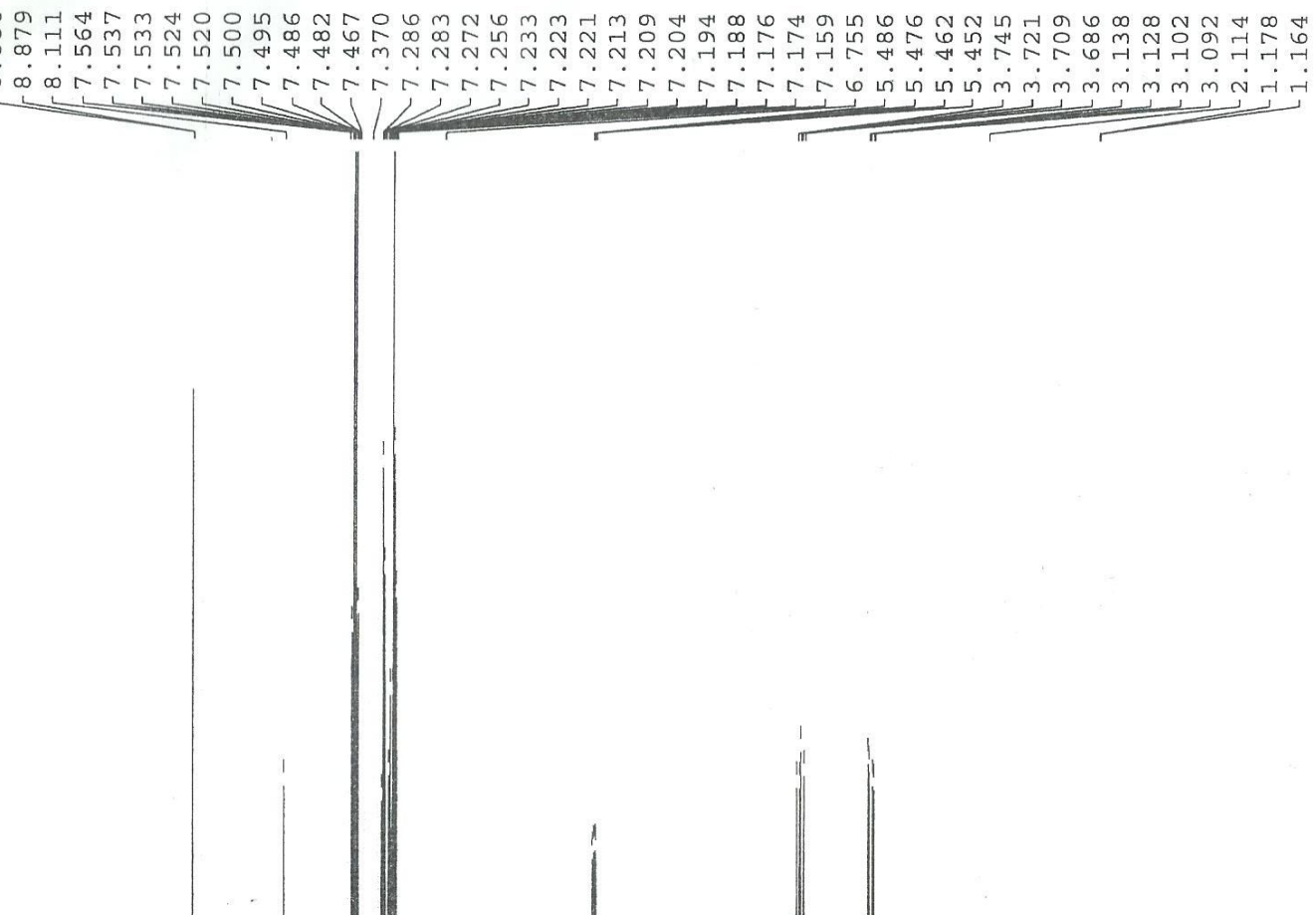
BRUKER

NAME	Dec04-2013
EXPNO	40
PROCNO	1
Date_	20131204
Time	10.21
INSTRUM	spect
PROBHD	1.7 mm PATXI 1
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	32
DS	2
SWH	10330.578 Hz
FIDRES	0.157632 Hz
AQ	3.1719923 sec
RG	203
DW	48.400 usec
DE	6.50 usec
TE	298.0 K
D1	1.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	4.50 usec
PL1	6.20 dB

H-NMR spectrum of compound (VIII):

(4`-Bromophenyl)-5-phenyl-4,5-dihydropyrazole -1-carbaldehyde.



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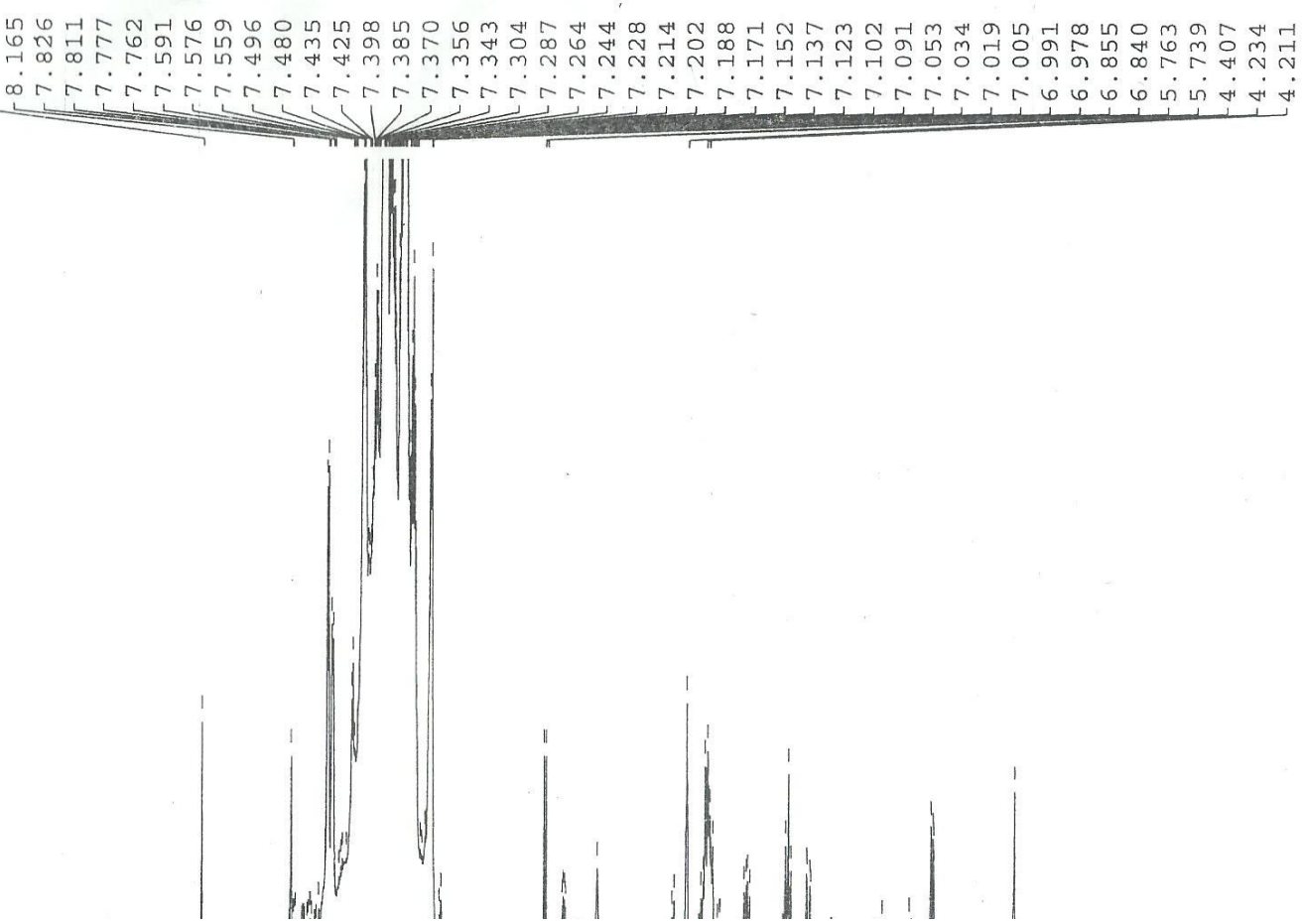
BRUKER

NAME	Dec03-2013
EXPNO	120
PROCNO	1
Date_	20131204
Time	6.55
INSTRUM	spect
PROBHD	1.7 mm PATXI 1
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	10330.578 Hz
FIDRES	0.157632 Hz
AQ	3.1719923 sec
RG	203
DW	48.400 usec
DE	6.50 usec
TE	298.0 K
D1	1.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	4.50 usec
PL1	6.20 dB
PL1W	6.44738770 W
SFO1	500.1330885 MHz

^{1}H-NMR spectrum of compound (VII):

3,5-diphenyl-4,5-dihydropyrazole-1-carbaldehyde.



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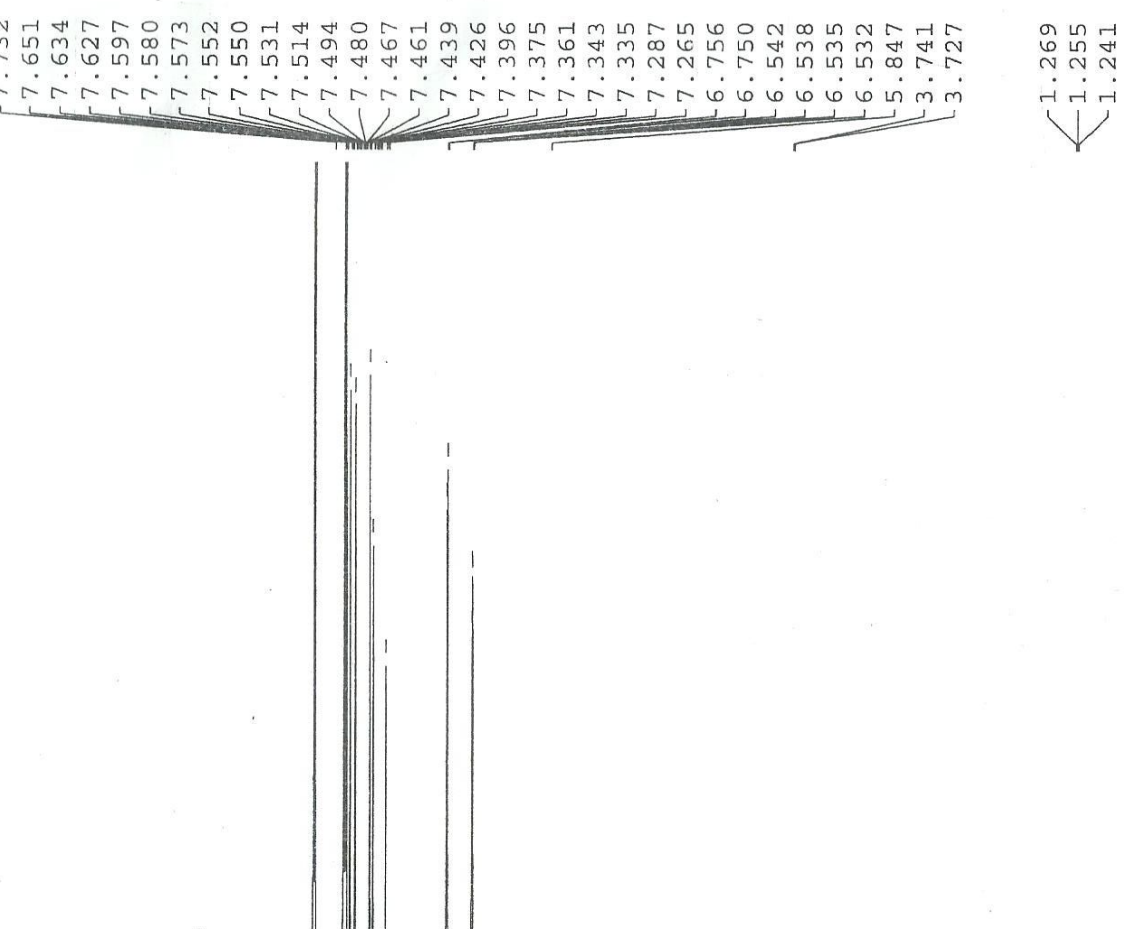
BRUKER

NAME	Dec03-2013
EXPNO	110
PROCNO	1
Date_	20131204
Time	4.10
INSTRUM	spect
PROBHD	1.7 mm PATXI 1
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	10330.578 Hz
FIDRES	0.157632 Hz
AQ	3.1719923 sec
RG	203
DW	48.400 usec
DE	6.50 usec
TE	298.0 K
D1	1.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	4.50 usec
PL1	6.20 dB
PL1W	6.44738770 W
SFO1	500.1330885 MHz

^{1}H-NMR spectrum of compound (V):

1-(4`-Bromophenyl)-3-(furan-2-yl)-prop-2-en-1-one.



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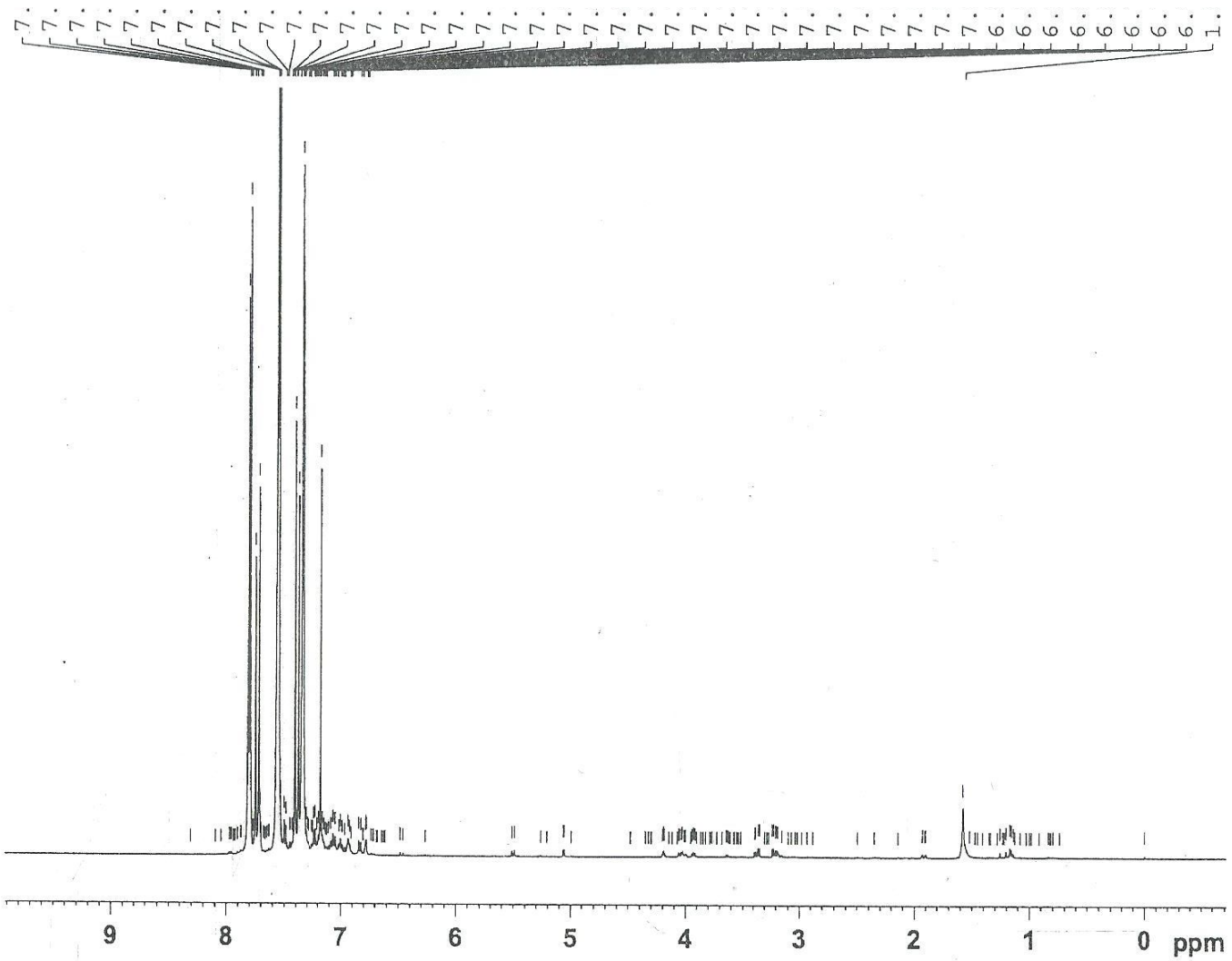
College of Pharmacy

BRUKER

NAME	Dec03-2013
EXPNO	90
PROCNO	1
Date_	20131203
Time	22.41
INSTRUM	spect
PROBHD	1.7 mm PATXI 1
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	10330.578 Hz
FIDRES	0.157632 Hz
AQ	3.1719923 sec
RG	203
DW	48.400 usec
DE	6.50 usec
TE	298.0 K
D1	1.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	4.50 usec
PL1	6.20 dB
PL1W	6.44738770 W
SFO1	500.1330885 MHz



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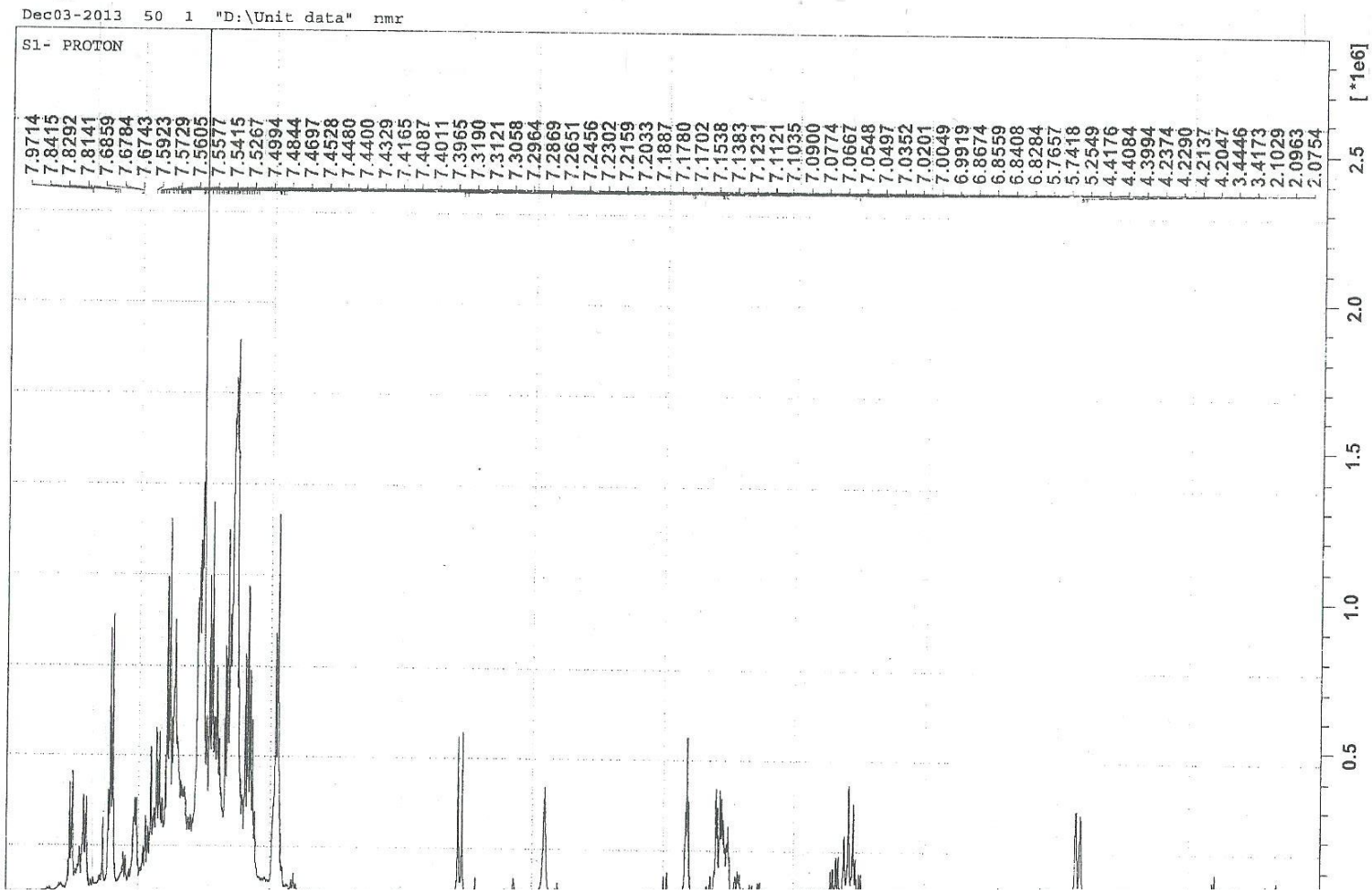
BRUKER

NAME	Dec03-2013
EXPNO	60
PROCNO	1
Date_	20131203
Time	13.34
INSTRUM	spect
PROBHD	1.7 mm PATXI 1
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	10330.578 Hz
FIDRES	0.157632 Hz
AQ	3.1719923 sec
RG	203
DW	48.400 usec
DE	6.50 usec
TE	298.0 K
D1	1.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	4.50 usec
PL1	6.20 dB
PL1W	6.44738770 W
SFO1	500.1330885 MHz
SI	32768
SF	500.1300545 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

^{1}H-NMR spectrum of compound (I): 1,3-diphenyl-prop-2-en-1-one.



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1344.29
1519.80
1870.24
3180.40
3431.13

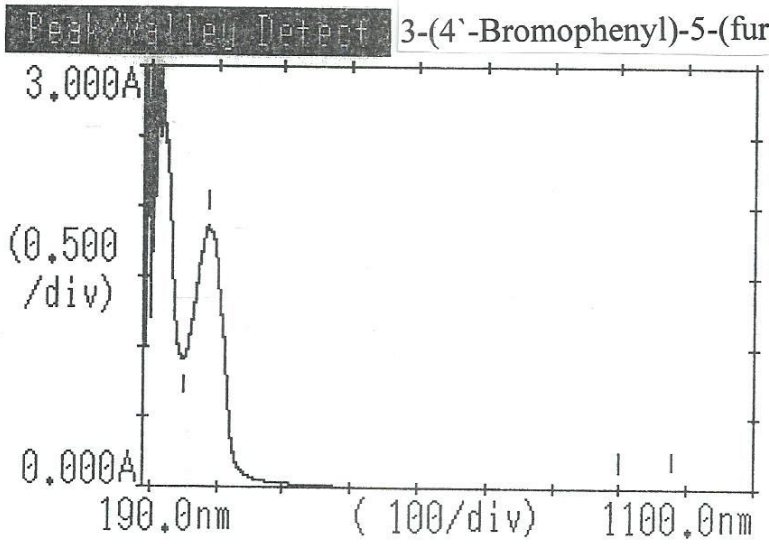
SHIMADZU
536.17
619.11
756.04
825.48
1020.27
1070.42
1128.28
1232.43
1361.65
1425.30
1652.88
2921.96
3191.97

SHIMADZU
692.40
757.97
1224.71
1367.44
1656.74
2921.96
3442.70
3732.00

SHIMADZU
472.53
590.18
663.47
742.54
817.76
970.13
1006.77
1068.49
1220.86
1284.50
1326.93
1392.51
1471.59
1550.66
1595.02
1654.81
2364.57
3128.32

UV spectrum of compound (XI):

3-(4`-Bromophenyl)-5-(furan-2-yl)-4,5-dihydropyraz



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Measure mode:	Abs
Scan range / nm:	1100.0 - 190.0
Scan pitch / nm:	0.5
Scan speed:	Fast
Slit width / nm:	1.0

Peak	
978.00	0.006
899.50	0.001
286.00	1.857
Valley	
1074.50	0.001
915.50	0.000
824.50	-0.000
249.50	0.915