Sudan University of Science and Technology

College of Graduate Studies

Synthesis of some Mannich base derivatives

تحضير بعض مشتقات قاعدة مانيخ

By:

Rania Ayoub Jami Mohamed Ali

(B.Sc.Chem. Honours)

A Thesis Submitted in partial fulfillment of the Degree of M.Sc.Chemistry

Supervisor:

Prof.Dr. Ahmed Elsadig Mohammed Saeed

September 2015

الايــة

(...رب أوزعني أن أشكر نعمتك التي انعمت علي وعلي والدي وأن اعمل صالحا ترضاه وأصلح لي في ذريتي اني تبت اليك واني من المسلمين)

الاحقاف الأيه 15

Dedication

This work is dedicated to …

My Family…

My Friends…

Acknowledgments

First of all thanks for Allah for everything, and my sincere thanks to my supervisor Prof. Dr. Ahmed Elsadig Mohammed Saeed for guidance during all the steps of my research.

Also to my respective family who have been my constant source of inspiration and for their support and love.

I am grateful as well to Mr.Nadir Mohamed Adam from King Abdulaziz University (Saudi Arabia) and Miss. Hadeel Hassan from Sudan University Science and Technology for their effective help.
Also to all the workers in Biochemistry lab in Africa university.
And any person helped me.

Contents

Chapter one

Chapter two

Chapter three

Chapter four

List of tables

List of figures

Abstract

Some of β-amino keto compounds were synthesized by Mannich base reaction in order to apply this reaction on different amines, ketones with benzaldehyde. These reactions were performed by three component condensation and resulted in the expected compounds.

A number of Mannich bases compounds were selected to be synthesized according to some factors which affected the reactivity and stability of these compounds, and the design and properties of Mannich bases were done by using computational program (ACD/Lab).

Experimental work based on changing the solvent and conditions was also attempted.

Elucidation of the structure of the synthesized compounds was performed using spectroscopic techniques (IR and H^1NMR) and thin layer chromatography (TLC). These spectra and chromatograms confirm the expected structure of the synthesized products. The percentage yields and melting points of all synthesized compounds were obtained.

الخلاصة

بعض مركبات البيتا كيتو الامينيه تم تحضيرها باستخدام تفاعل مانيخ وتم تطبيق التفاعل علي امينات مختلفه وكيتونات مع البنزالدهايد. هذه التفاعلات اجريت عن طريق تكاثفات ثلاثيه المكون وتم الحصول علي المركبات المطلوبه.

عدد من قواعد مانيخ تم إختيارها لتخلق وفقا لبعض العوامل التي تؤثر علي الفعالية والإستقراريه لهذه المركبات. التصميم والخواص لقواعد مانيخ تم إنجازها بواسطة البرنامج الحاسوبي تم أختيار عدد من قواعد مانيخ التي تم تحضيرها وفقا لبعض العوامل التي تؤثر علي فعاليه هذه المركبات واستقرارها .(ACD/Lab) باستخدام البرنامج الحاسوبي .

التحارب المعمليه إعتمدت علي التغيير في خواص المذيب وظروف التفاعل تم إجراءها.

تم التحقيق من شكل المركبات التي تم تخليقها بواسطه الطرق الطيفيه وكروموتوغرافيا الطبقه الرقيقة وهذة النتائج أكدت أن الشكل المقترح للمركبات المخلقه. تم حساب نسبة التحضير ودرجة الانصهار لجميع المركبات التي تم تحضيرها.

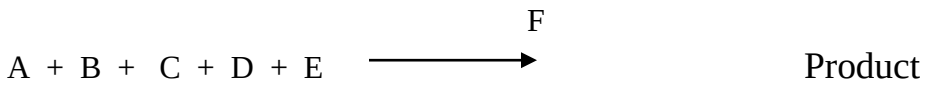
Chapter One: Introduction

1-Introduction

1.1 Multi-component reactions

1.1.1 Definition

A multi-component reaction is defined as three or more different starting materials that react to form a product. This reaction tool allows compounds to be synthesized in a few steps and the reagents are incorporated into the final product (Zhang, 2005).



This makes multi-component reactions (MCRs) highly convergent reactions, with high atom efficiency, good bond forming capabilities and higher yields in comparison to a similar multistep reaction (Agenet *et al.*, 2007). It plays an important role in combinatorial chemistry due to its ability to synthesize small drug-like molecules with several degrees of structural diversity. Multi-component reactions have been known for over 150 years. The first reaction was Strecker synthesis of α-amino cyanides in 1850 (Zhang, 2005).

A multitude of MCRs exist today, of which the isocyanide based MCRs are the most documented. Other MCRs include free-radical mediated MCRs, and it's based on organoboron compounds and metal-catalyzed MCRs. These are most frequently exploited because the isocyanide is an extraordinary functional group. It is believed to exhibit resonance between its tetravalent and divalent carbon forms. This induces the isocyanide group to undergo both electrophilic and nucleophilic reaction.The occurrence of isocyanides in natural products has also made it a useful functional group. The two most important isocyanide-based multicomponent reactions are the Passerini 3-component reaction to produce alpha-acyloxy carboxamides and the Ugi 4-component reaction, which yields the alpha-acylamino carboxamides (Quevedo, 2011).

An ideal chemical reaction should be simple to give maximum yields, utilize readily available starting materials, be a one-pot reaction and be environmentally friendly. No reaction comes close to achieving this ideality; however, multicomponent reactions are best positioned to achieve this (Agenet *et al.*, 2007).

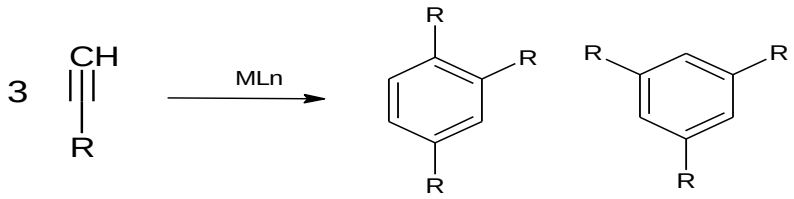
1.1.2 Types of Multi-Component reactions

There are many types of Multi-component reactions:

- Alkyne trimerisation
- Biginelli reaction
- Bucherer-Bergs reaction
- Gewald reaction
- Hantzsch pyridine synthesis
- Kabachnik-Fields reaction
- Mannich reaction
- Passerini reaction
- Pauson –Khand reaction
- Strecker aminoacid synthesis
- Ugi reaction
- Asinger reaction

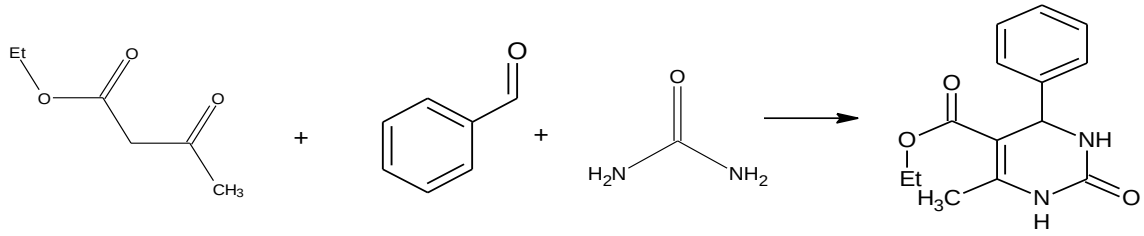
1.1.2.1 Alkyne trimerisation

An alkyne trimerisation reaction is a 2+2+2 cyclization reaction in which three alkyne molecules react to form an aromatic compound. The reaction is 'pseudo' pericyclic since it has not been observed to occur without the assistance of metal catalysis; and the metal catalyst assembles the ring stepwise via intermediates which are not directly in between (in a geometric sense) the starting material and products (Agenet *et al.*, 2007).



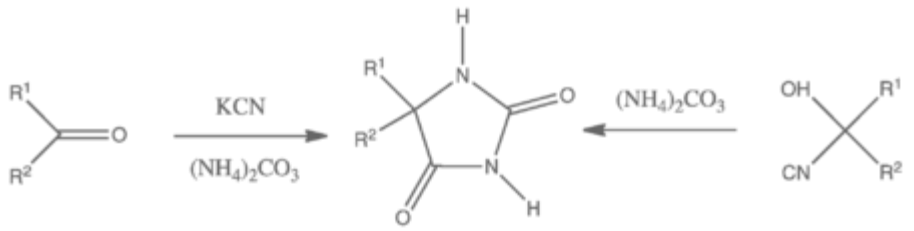
1.1.2.2 Biginelli reaction

The Biginelli reaction is a multiple-component chemical reaction that creates 3,4-dihydropyrimidin-2(1*H*)-ones from ethyl acetoacetate, an aryl aldehyde (such as benzaldehyde), and urea. It is named for the Italian chemist Pietro Biginelli (Kappe *et al.*, 2004).



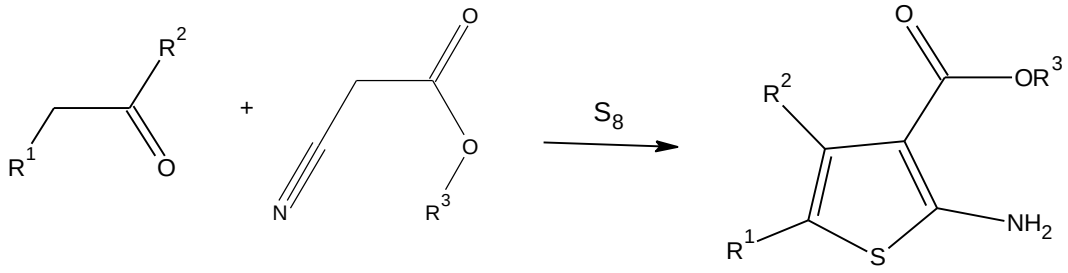
1.1.2.3 Bucherer–Bergs reaction

The Bucherer–Bergs reaction is the chemical reaction of carbonyl compounds (aldehydes or ketones) or cyanohydrins with ammonium carbonate and potassium cyanide to give hydantoins. The reaction is named after Hans Theodor Bucherer (Sabnis *et al.*, 1994).



1.1.2.4 Gewald reaction

The Gewald reaction is an organic reaction involving the condensation of a ketone (or aldehyde when R^2 = H) with a α-cyanoester in the presence of elemental sulfur and base to give a poly-substituted 2-amino-thiophene (Gewald *et al.*,1966; Sabnis *et al.*,1994).



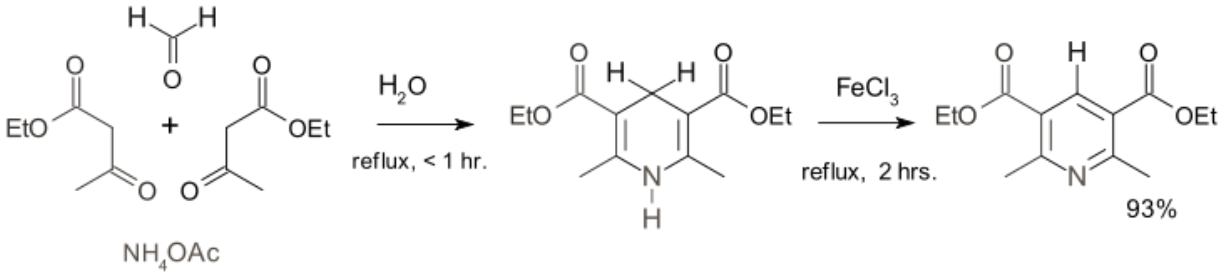
1.1.2.5 Hantzsch pyridine synthesis

The Hantzsch pyridine synthesis or Hantzsch dihydropyridine synthesis is a multi-component organic reaction between an aldehyde such as formaldehyde, 2 equivalents of a β-keto ester such as ethyl acetoacetate and a nitrogen donor such as ammonium acetate or ammonia(Jing-Jing and Xia,

2005). The initial reaction product is a dihydropyridine which can be oxidized in a subsequent step to a pyridine. The driving force for this second reaction step is aromatization. This reaction was reported in 1881 by Arthur Rudolf Hantzsch (Jacques, 2003).

A 1,4-dihydropyridine dicarboxylate is also called a 1,4-DHP compound or a Hantzsch compound. These compounds are an important class of calcium channel blockers and as such commercialized in for instance nifedipine, amlodipine or nimodipine.

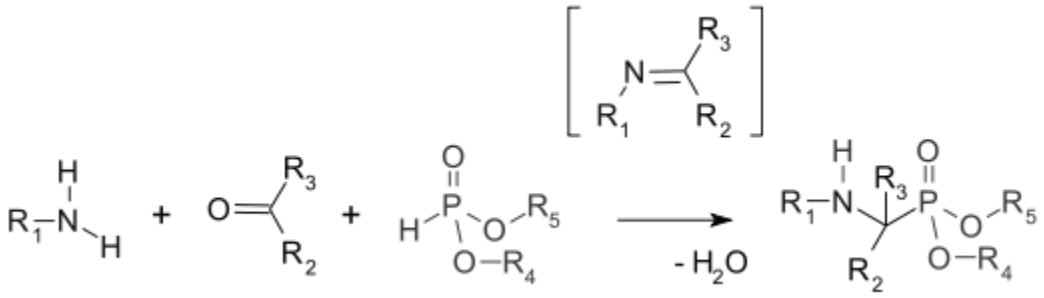
The reaction has been demonstrated to proceed in water as reaction solvent and with direct aromatization by ferric chloride or potassium permanganate in a one-pot synthesis (Jacques, 2003).



1.1.2.6 Kabachnik–Fields reaction

The Kabachnik–Fields reaction is an organic reaction forming an α-amino phosphonate from an amine, a carbonyl compound and a dialkyl

phosphonate. Aminophosphonates are synthetic targets of some importance as phosphorus analogues of α-amino acids (a bioisosteric). This multicomponent reaction was independently discovered by Martin Izrailevich Kabachnik and Ellis K. Fields in 1952 (Ellis,1952).



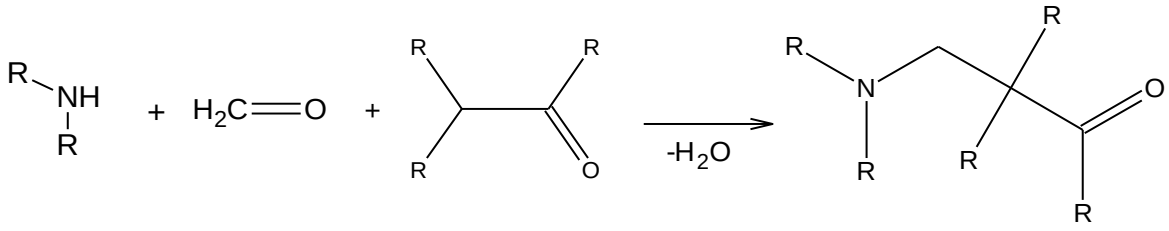
The first step in this reaction is the formation of an imine followed by an addition reaction of the phosphonate P-H bond into the C=N double bond (a Pudovik reaction). A related reaction is the Mannich reaction.

The reaction is accelerated with a combination of dehydrating reagent and Lewis acid. The carbonyl component in the reaction is usually an aldehyde and sometimes a ketone (Zefirov *et al.*, 2008).

1.1.2.7 Mannich reaction

The Mannich reaction is an organic reaction which consists of an amino alkylation of an acidic proton placed next to a carbonyl functional group by formaldehyde and a primary or secondary amine or ammonia. The final product is

a β-amino-carbonyl compound also known as a Mannich base. Reactions between aldimines and α-methylene carbonyls are also considered Mannich reactions because these imines form between amines and aldehydes. The reaction is named after chemist Carl Mannich (Krösche, 1912).



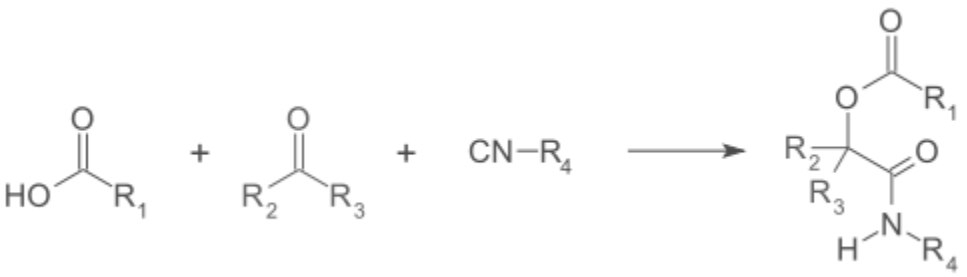
The Mannich reaction is an example of nucleophilic addition of an amine to a carbonyl group followed by dehydration to the Schiff base. The Schiff base is an electrophile which reacts in the second step in an electrophilic addition with a compound containing an acidic proton (which is, or had become an enol). The Mannich reaction is also considered a condensation reaction (Mannich, 1938).

In the Mannich reaction, primary or secondary amines or ammonia, are employed for the activation of formaldehyde. Tertiary amines lack an N–H proton to form the intermediate enamine. α-CH-acidic compounds (nucleophiles) include carbonyl compounds, nitriles, acetylenes, aliphatic nitro compounds, α-alkyl-pyridines or imines. It is also possible to use activated phenyl groups and electron-rich heterocycles such as furan,

pyrrole, and thiophene. Indole is a particularly active substrate; the reaction provides gramine derivatives (Blicke, 1936; Martens *etal.*, 1981).

1.1.2.8 Passerini reaction

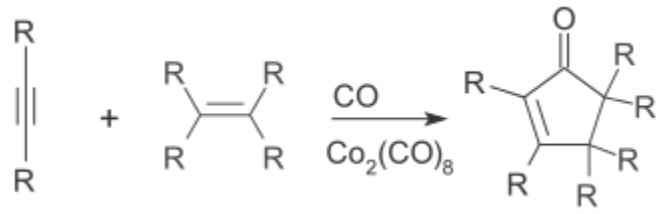
The Passerini reaction is a chemical reaction involving an isocyanide, an aldehyde (or ketone), and a carboxylic acid to form a α-acyloxy amide (Passerini *et al.*, 1931).



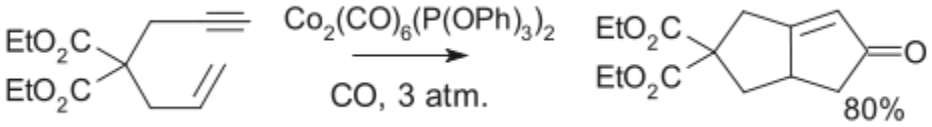
This organic reaction was discovered by Mario Passerini in 1921 in Florence, Italy. It is the first isocyanide based multi-component reaction developed, and currently plays a central role in combinatorial chemistry (Dömling *et al.*, 2000).

1.1.2.9 Pauson–Khand reaction

The Pauson–Khand reaction (or PKR or PK-type reaction) is a chemical reaction described as a [2+2+1] cycloaddition between an alkyne, an alkene and carbon monoxide to form a α,β-cyclopentenone. This reaction was originally mediated by stoichiometric amounts of dicobalt octacarbonyl, but this has since been replaced by newer and more efficient catalyst systems (Gibson *et al.*, 2003).



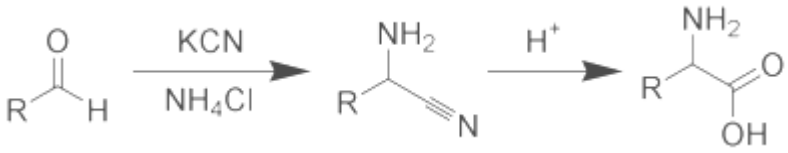
With asymmetrical alkenes or alkynes regioselectivity is always an issue, but less so with intramolecular reactions.



1.1.2.10 Strecker amino-acid synthesis

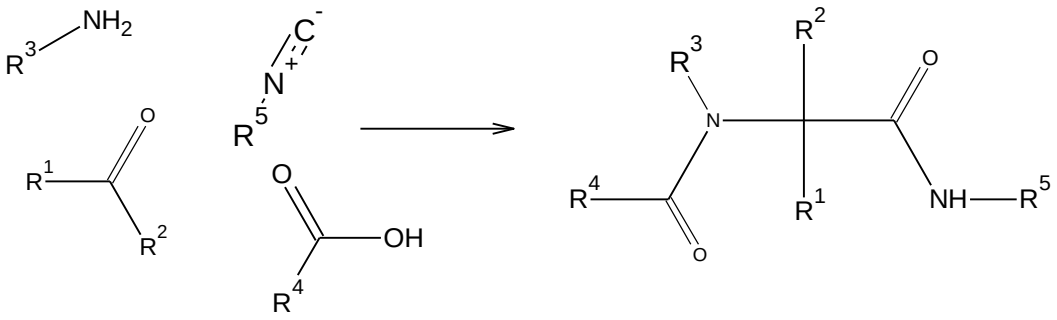
The Strecker amino-acid synthesis, devised by Adolph Strecker, is a series of chemical reactions that synthesize an amino acid from an aldehyde or ketone. The aldehyde is condensed with ammonium chloride in the presence of potassium cyanide to form an α-aminonitrile, which is

subsequently hydrolyzed to give the desired amino-acid. In the original Strecker reaction acetaldehyde, ammonia, and hydrogen cyanide combined to form after hydrolysis alanine (Strecker, 1850; Weigert *et al.*, 1975).



1.1.2.11 Ugi reaction

The Ugi reaction is a multi-component reaction in organic chemistry involving a ketone or aldehyde, an amine, an isocyanide and a carboxylic acid to form a bis-amide. The reaction is named after Ivar Karl Ugi, who first published this reaction in 1959 (Ugi *et al.*, 1959).



The Ugi reaction is exothermic and usually complete within minutes of adding the isocyanide. High concentration (0.5M - 2.0M) of reactants give the highest

yields. Polar, aprotic solvents, like DMF, work well. However, methanol and ethanol have also been used successfully. This uncatalyzed reaction has an inherent high atom economy as only a molecule of water is lost and chemical yield in general are high. Recent research has shown that the Ugi reaction is accelerated in water (Pirrung *et al.*, 2004).

1.1.3 Applications of MCRs

Multicomponent reactions are widely used in the synthesis of natural products to produce complex scaffolds. The earliest natural products synthesized were amino acids. However over time, with the development of new MCRs, more complex natural products could also be synthesized. For example, the Passerini reaction has found utility in the synthesis of azinomycin – a DNA binding and alkylating antibiotic, and eurystatin A- a natural prolyl peptidase inhibitor. The Ugi reaction has found application in the synthesis of antibiotic bicyclomycin and the synthesis of the toxin dysidenin . The Ugi reaction has also been recently exploited to synthesize 2-oxazolines, which are known to be important pharmacophores in bioactive molecules. A two step synthesis towards substituted benzoxazinones has also been reported by performing the Ugi reaction followed by an intramolecular Mitsunobu substitution. (Akul, 2011)

A part from changing substituents on the reacting components, modifications of the individual component functional groups of a MCR allows the generation of more scaffolds using almost similar reaction conditions. An example of such a modification is the replacement of the amine in the Ugi reaction with an O-benzyl hydroxamine which follows the Ugi reaction can be easily deprotected to the hydroxamic acids. These hydroxamic acids can be useful to develop enzyme inhibitors. Cyclic variations of the MCRs are also possible in which two or more components could be connected by a chain to produce heterocycles.

Multicomponent reactions are not just an integral part of synthesizing natural products, but due to their ability to produce a variety of scaffolds by simple modifications of substituents, they are being exploited for the discovery of new drugs as well. Novel inhibitors of enzymes such as serine proteases (Factor Xa) have been synthesized using MCRs. Tubulin inhibitors, which could potentially be used as anticancer agents, have also been synthesized using a van Leussen 3 component reaction. Development of new antimalarial drugs based on the chloroquine scaffold has also been researched (Werder, 2005).

A new concept to increase the potential variety in MCRs is the union of MCRs. In this combination of two or more known MCRs is done such that

the end product of one MCR acts as the starting product of the other MCR. A 7-component MCR has been developed which combines the Asinger 4-component reaction and the Ugi 4-component reaction. Clearly the utility of MCRs is gaining importance and wider acceptance from drug development to synthesis of natural products. The future requires increased utilization of the already present MCRs as well as development of novel MCRs and the union of MCRs to achieve more efficient synthesis (Kermack, 1931).

The challenge is to conduct an Multi-component reaction in such away that the network of pre-equilibrated reactions channel into the main product and do not yield side products .The result is clearly depended on the reaction conditions, solvent,temperature,catalyst,concentration ,the kind of starting materials and functional groups. Such considerations are particular importance in design compound via Multi-component reactions (Zhou *et al.*, 2011).

1.2 Mannich reaction:

The Mannich reaction is a classical method for the preparation of β-amino ketones and aldehydes (Mannich bases)(Weinheim,1998). The Mannich reaction is a very useful tool for the development and synthesis of several molecules. Also this reaction is an important carbon–carbon bond

forming reaction in organic synthesis for the preparation of various nitrogen-containing natural products and the intermediates for significant pharmaceuticals. β- amino carbonyl compounds are important nitrogen-containing compounds that can be assembled via Mannich type reactions. β - amino carbonyl moieties are found in a number of biologically active natural products (March *etal*, 1985; Mannich *et al.*, 1932).

The formation of carbon-carbon bonds is crucial to the development of organic molecules such as medicines, biodegradable plastics and natural products and a great deal of research has been focused in this area recently. Mannich reaction plays a vital role in the construction of variety of organic molecules.The products of the Mannich reaction are used for the synthesis of amino alcohols, peptides and lactams and as precursors to synthesize amino acids. β-amino ketones can be synthesized as products of three component Mannich reaction in the presence of sulfated MCM-41 as a reusable heterogeneous catalyst. The good yields under mild reaction conditions with low catalyst loading make this protocol an attractive one. Moreover there is no formation of by-products making this protocol an important addition to the methods of synthesis of natural products (Blicke, 1942).

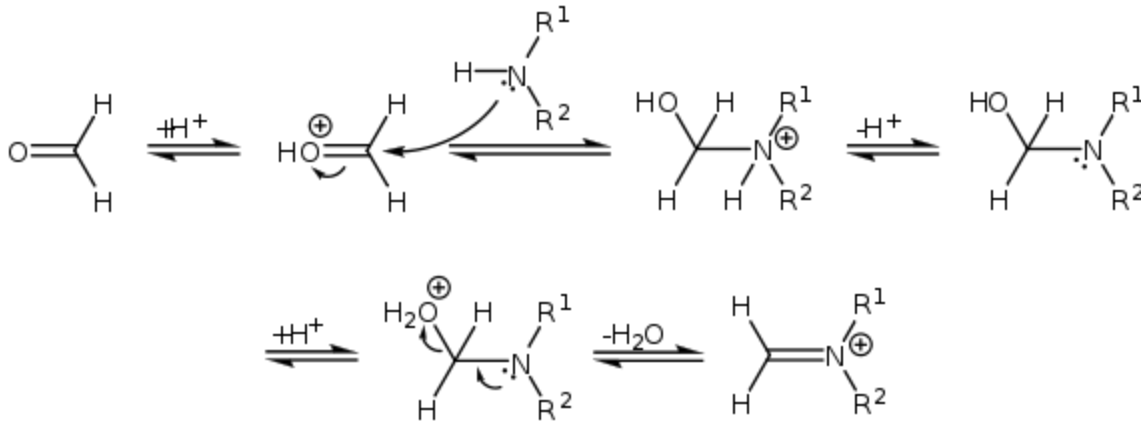
The mannich base is an end product in the Mannich reaction, which is nucleophilic addition reaction of a non-enolizable aldehyde and any primary

or secondary amine to produce resonance stabilized imine (iminium ion or imine salt).

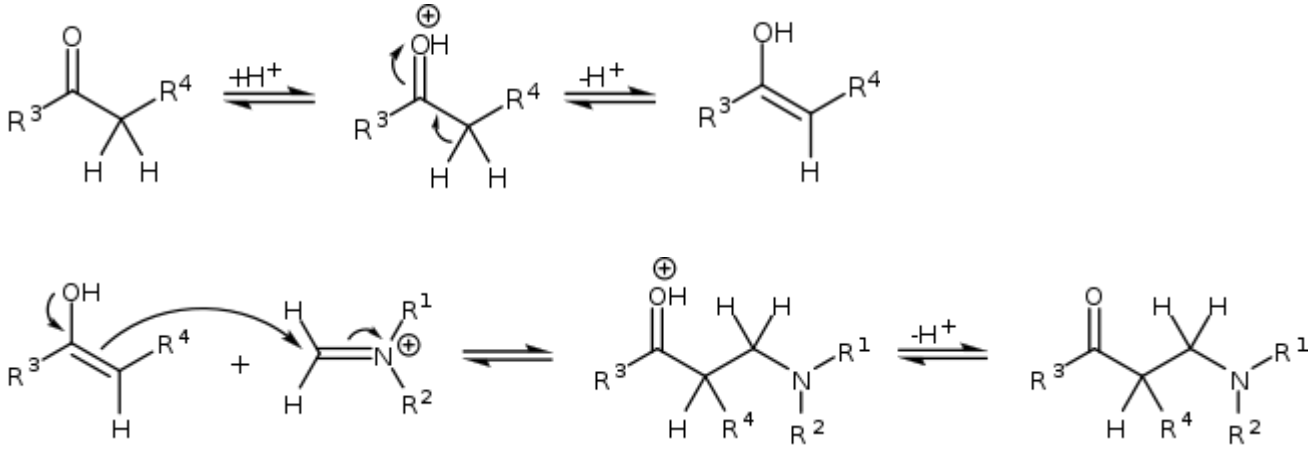
The conventional catalysts for classical Mannich reaction of aldehydes, ketones and amines involve mainly organic or mineral acids. A vast literature available for the synthesis of β-amino carbonyl compounds using Mannich reaction includes catalysts such as $HClO_4$-SiO_2 , bromo dimethylsulfonium bromide (BDMS) (Córdova *et al.*, 2013).

With primary or secondary amines, Mannich bases react with additional aldehyde and carbon acid to larger adducts $H_2N(CH_2CH_2COR)$ and $HN(CH_2CH_2COR)_2$. With multiple acidic hydrogen atoms on the carbon acid higher adducts are also possible. Ammonia can be split off in an elimination reaction to form enals and enones (Pishawikar *et al.*, 2012).

The mechanism of the Mannich reaction starts with the formation of an iminium ion from the amine and the formaldehyde.



The compound with the carbonyl functional group (in this case a ketone) can tautomerize to the enol form, after which it can attack the iminium ion (Watanabe *et al.*, 2002).



Progress has been made towards asymmetric Mannich reactions. When properly functionalized the newly formed ethylene bridge in the Mannich adduct has two prochiral centers giving rise to two diastereomeric pairs of enantiomers. The first asymmetric Mannich reaction with an unmodified aldehyde was carried with *(S)*-proline as a naturally occurring chiral catalyst (Watanabe *et al.*, 2002).

Recently, organic reactions in green solvents such as water, ethanol and their mixtures devoid of harmful organic solvents in the presence of green catalysts have attracted much attention, because these solvents are cheap, safe, and environmentally benign (RMousavi; Hazeri, 2013).

In addition, heterogeneous catalysts have gained much attention, as a result of economic and environmental benefits. They make synthetic processes clean, safe and high-yielding. The use of nano-sized inorganic solid oxides as catalysts have received much attention because of their high level of chemoselectivity, environmental compatibility, simplicity of operation and their availability at low cost. Metal oxides exhibit both Lewis acid and Lewis base character at their surface (Evin *et al.*, 1983; Mitsumori *et al.*, 2006).

The Mannich-Reaction is employed in the organic synthesis of natural compounds such as peptides, nucleotides, antibiotics, and alkaloids (e.g. tropinone). Other applications are in agro chemicals such as plant growth regulators, paint- and polymer chemistry, catalysts and main mechanism of formalin tissue crosslinking (Kumar *et al.*, 2010).

The Mannich reaction is also used in the synthesis of medicinal compounds e.g. rolitetracycline (Mannich base of tetracycline), fluoxetine (antidepressant), tramadol, and tolmetin (anti-inflammatory drug)and azacyclophanes (Rosa *et al.*, 2003; Rivera *et al.*, 2004). The

Mannich reaction and its variants are often employed to access diverse molecules, whose applications are ranging from bioactive skeletons to material science (Quevedo *et al.*, 2009; Roers *et al.*, 2001).

1.3 Cheminformatics

Chemical informatics is the application of computer technology to chemistry in all of its manifestations. Much of the current use of cheminformatics techniques is in the drug industry, but chemical informatics is now being applied to problems across the full range of chemistry. And it use mathematical and statistical methods to extract information from chemical data (Hawkins *et al.*, 2006).

Computational chemistry seeks to predict quantitatively molecular and biomolecular structures, properties, and reactivity by computational methods alone. It uses modern chemical theory to predict the speed of unknown reactions and the synthetic sequences by which complex new molecules can be made most efficiently. Computational chemistry allows chemists to explore how things work at the atomic and molecular levels and to draw conclusions that are impossible to reach by experimentation alone. Thus, computational chemistry supplements experimentally derived data.(Gardiner, 1997). Chemical information system must include registration,

computed and measured properties, chemical descriptors and inventory. The primary purpose is to be able to identify a chemical substance, find compounds similar to the target compound and determine the location of the compound. To effectively build it, an object definition of the chemical sample is paramount (Brown, 1998).

1.4 Quantitative Structure-Activity Relationship (QSAR)

QSAR is the study of the correlation between chemical structure and associated biological activity, with the ultimate goal of predicting the activity of untested chemicals based on structurally related compounds with known activity. The parentheses around the "Q" in (Q)SAR indicates that the term refers to both qualitative predictive tools. For example the structure-activity relationships (SARs) and quantitative predictive methods (quantitative structure-activity relationships (QSARs). Although the term QSAR is often used to refer to predictive models, especially computer-based models, it should be noted that QSAR is actually inclusive of a wide variety of computerized and non-computerized tools and approaches (Mary *et al.*, 2012).

The first major step in a QSPR (Quantitative structure prediction relationship) /QSAR study is the entry of the molecular structures and generation of the 3-D models. The structures are entered by sketching with

Hyper Chem. The 2-D sketch is used to generate a good, low-energy conformation with mopac using the PM3 Hamiltonian. The 3-D molecular models are needed for geometric descriptor calculation. The second major step in a QSPR/QSAR study is the generation of the molecular structure descriptors.

QSPR/QSAR methods can be used to build models that can predict properties or activities for organic compounds. To do so requires an effective way to encode the structures with calculated molecular structure descriptors. Once the models have been generated, they have predictive ability for new compounds not in the training set. The descriptors that are incorporated into the models provide an opportunity to focus on the features of the compounds that account for the property or activity of interest (Tomasz, 2010; Mary *et al.*, 2012).

1.5 Aim and Objective

β -amino carbonyl compounds are very useful in pharmaceutical and other biologically related areas of chemistry; it's used for the synthesis of amino alcohols, peptides, lactams and as precursors to optically active amino acids. One of the reactions to form these products is Mannich reaction.

Mannich bases are an amine compound having the N atom linked to the R substrate through a methylene group. The substrate may belong to a number of different classes of compounds.

This study aims to:

- Examine verity of Mannich bases compounds corresponding to their availability of synthesized them, by using chemo informatics techniques (ACD lap).
- Synthesize of several β-amino ketones (Mannich bases) through Mannich reactions.
- Characterize the structures of the targeted molecules.

Chapter Two: Materials & Methods

2. Materials and Methods

2.1 Materials

Acetophenone (120.15, 1.025-1.027)g/L, 99%, Benzaldehyde (106.12, (1.044-1.043)g/L, 99%, p-bromo acetophenone (199.06, 98%) Calcium chloride (110.99) Loba chemie, India.

Aniline (93.13, (1.02-1.025)g/L, 99%, Oxford laboratory, India).

p-amino benzoic acid (137.14, 99%), *p*-ancidine (123.15246), *p*-bromo aniline (199.06), Sulfanilamide (172.20), TECHNO PHARMCHEM, India).

All chemicals were used without further purification.

2.2 General equipment:

Melting points of the synthesized compounds were determined in open-glass capillaries on melting point apparatus. The reactions were carried out at 80 ° C with mechanical stirring using magnetic stirrer with hot plate obtained from Germany.

All the glasses used were of pyrex type.

2.3 Instruments

2.3.1 Thin layer chromatography

All reactions and purity of β-amino carbonyl compounds were monitored by thin layer chromatography (TLC) using glass plate coated with silica gel (350 mesh, 95%) obtained from sd fine-chem limited- Mumbai using 95% chloroform and 5% methanol as an eluent and the spots were visualized by iodine vapors/ultraviolet light as visualizing agents.

2.3.2 Infra-red spectroscopy

IR spectra (ν, cm^{-1}) were recorded on FTIR spectrophotometer obtained from SHIMADZU in KBr pellets.

2.3.3 ^{1}H NMR spectroscopy

^{1}H NMR spectra were recorded using DMSO as internal standard and chemical shift are in ppm.

2.4 ACD lab programmer

ACD/ChemSketch (Freeware) - Product version:12.01 (Build 38526, 26 Feb 2010) Advanced chemistry development – Copyright © 1994-2010.

2.5 Synthetic methods:

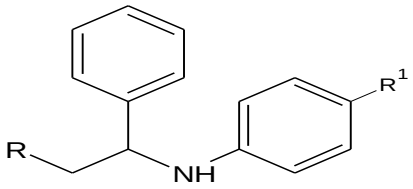
2.5.1 General method for the synthesis of β-amino p-nirto acetophenone (I - IV):

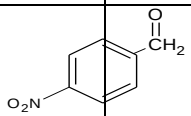
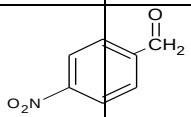
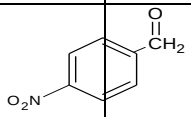
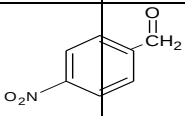
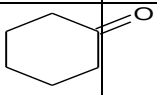
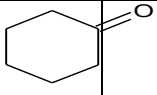
Mannich bases of acetophenone derivatives were synthesized as shown by the reaction schemes 2.1 One equivalent of calcium chloride was added to a mixture of p-amino acetophenone (5 mmole), benzaldehyde (5 mmole) and amine (5 mmole) in 5 ml ethanol. One drop of hydrochloric acid was added. The resulting mixture was stirred at 80^{o} C for 2 h. the product was filtered, washed with water, and recrystallized from ethanol.

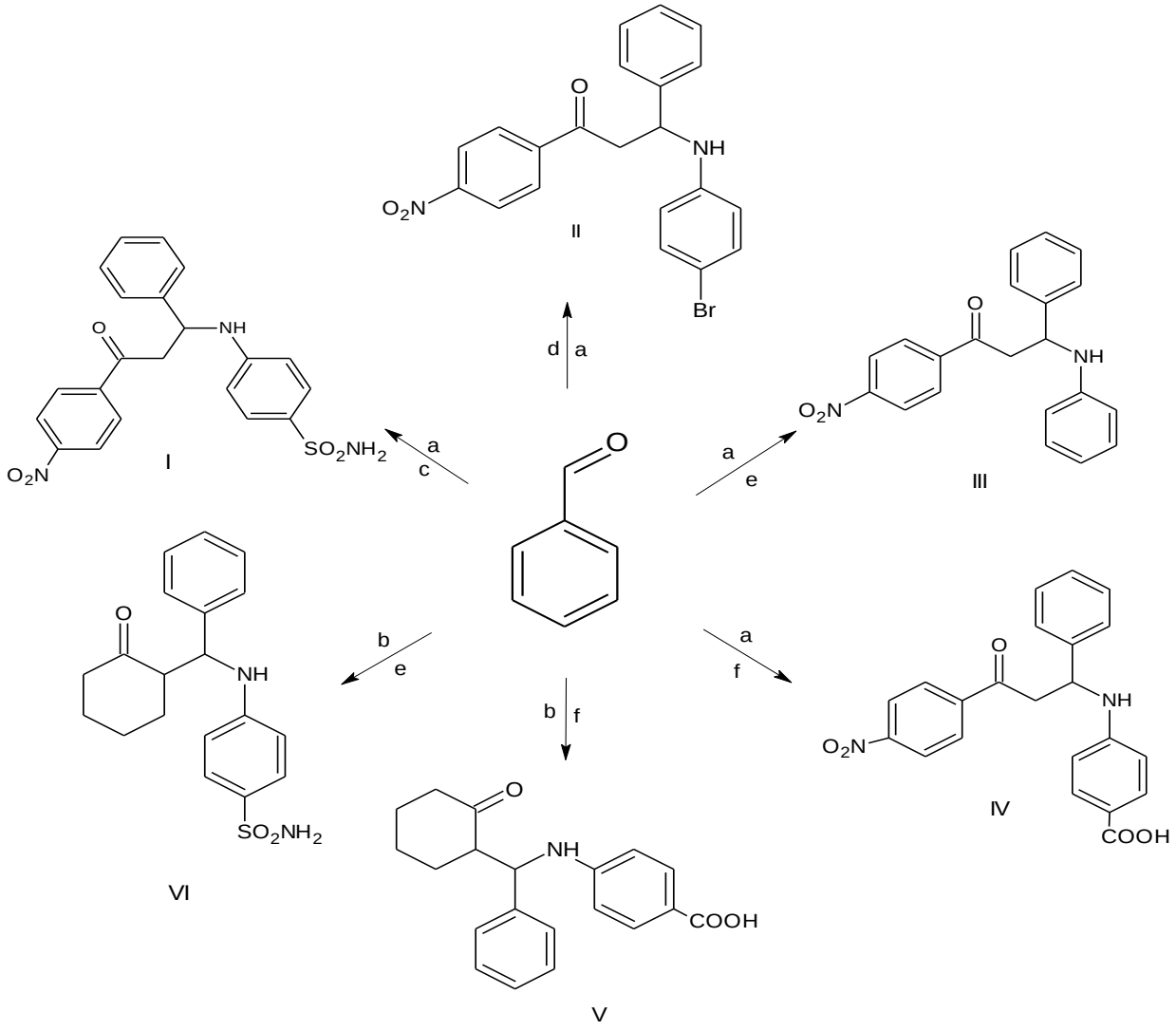
2.5.2 General method for the synthesis of β-amino cyclohexanone (V-VI):

Mannich bases of cyclohexanone derivatives were synthesized as shown by the reaction schemes 2.1 one equivalent of calcium chloride was added to a mixture of cyclohexanone (5 mmole), benzaldehyde (5 mmole) and amine (5 mmole) in 5 ml ethanol. One drop of hydrochloric acid was added. The resulting mixture was stirred at 80^{o} C for 2 h. the product was filtered, washed with water, and recrystallized from ethanol.

2.1 Chemical names of the prepared β-amino compounds (I-VI)



Compound No	R	R^1	Scientific name
I		-SO_2NH_2	4-{[3-(4-nitrophenyl)-3-oxo-1-phenylpropyl]amino} benzenesulfonamide
II		-Br	3-[(4-bromophenyl)amino]-1-(4-nitrophenyl)-3-phenylpropan-1-one
III		-H	1-(4-nitrophenyl)-3-phenyl-3-(phenylamino)propan-1-one
IV		-COOH	4-{[3-(4-nitrophenyl)-3-oxo-1-phenylpropyl]amino}benzoic acid
V		-COOH	4-{[(2-oxocyclohexyl)(phenyl)methyl]amino}benzenesulfonamide
VI		-SO_2NH_2	4-{[(2-oxocyclohexyl)(phenyl)methyl]amino} benzoic acid



2.1 Scheme show the equations of synthesized producds

Where: a= P-nitro acetophenone b= Cyclohexanone

c= Aniline d= P-bromoaniline

e= Sulphanilamide f= P-animo benzoicacid

2.6 General method of ACD/lab programmer:

There were two modes to ACD/ChemSketch, namely Structure and Draw. Structure mode was used to draw chemical molecules, while Draw mode used to create and edit graphical objects. Upon startup, the Draw Normal mode and Carbon were automatically selected. By clicking and dragging the cursor in the window, C-C bonds were created. Clicking on a carbon atom produces a branched structure. The change was made by selecting a heteroatom from the element list in the left toolbar and clicking on an atom in the structure to replace it. Radicals were made by selecting it from table which including carbon rings, carbon-based side chains and functional groups. Bond lengths and bond angle standardized by clicking on Clean Structure. The calculated properties were inserted into the ChemSketch window as a text field; on the tools menu, point to calculate, and choose the desired property. By selecting a structure and clicking on generate Name for structure, the IUPAC name was generated as a text field

underneath the structure. The value of the octanol-water partition coefficient, log P also calculated.

2.7 Trials

Some trials which involve certain reactions were curried out; results of these reactions was different according to the conditions under which they proced under. Some of these reactions give good results,while the others failed.

The reactions between p-Nitroacetophenone or hexanone as ketones with different amines and benzaldehyde acoording to mannich reaction give the following results under various conditions.

A) Mannich reaction at free solvent condition :

All the reactants and catalyst were heated under reflex at 80^0C for 2h .After that the reaction products mixture was spotted on TLC sheet for qualitative analysis, indicating that no new products had been formed.

B) Mannich reaction using water as solvent:

In this experiment water was used as a solvent and the reactants were heated and stirred under reflex at 80^0C for 2h. The reaction products mixture

was spotted on TLC sheet for qualitative analysis, indicating that no new products had been formed .

C) Mannich reaction using ethanol as solvent:

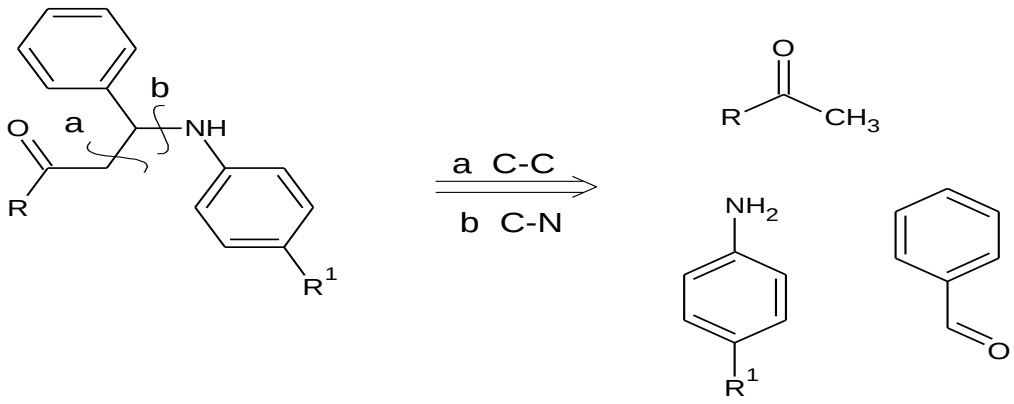
In this experiment ethanol was used as a solvent and the reactants heated were and stirred under reflex at 80^0C for 2h. After that the reaction products mixture was spotted on TLC sheet for qualitative analysis, indicating that new product were formed with low yield.

Chapter Three: Results & Dissections

3. Results and Discussion

Disconnection Approach

Disconnection of Mannich base products conform the mechanism of the reactions for all the products . According to retro synthetic analysis protocols,the disconnection occur at the bond between carbon and nitrogen atoms as well as between carbon – carbon bond giving corresponding synthons for all Mannich base products (Scheme 3.1).



Scheme 3.1 disconnection approach for β-amino compounds

From the synthetic precursor it is clearly seen that the target consist of three starting materials primary amines , aldehydes and ketones.

Besides the common alkylamines employed ever since the early work of Carl Mannich, more recent research in the synthesis of Mannich bases has been using arylamines. The aim of this study is to prepare a series of novel β

-aminoketones in one by pot three component condensation reaction of aromatic aldehyde, ketone (p-nitroacetophenone and cyclohexanone) with aromatic amine to provide β-amino carbonyl compounds. This would be an ideal Mannich type reaction and can be considered as one of the convenient C-C bond forming reaction.

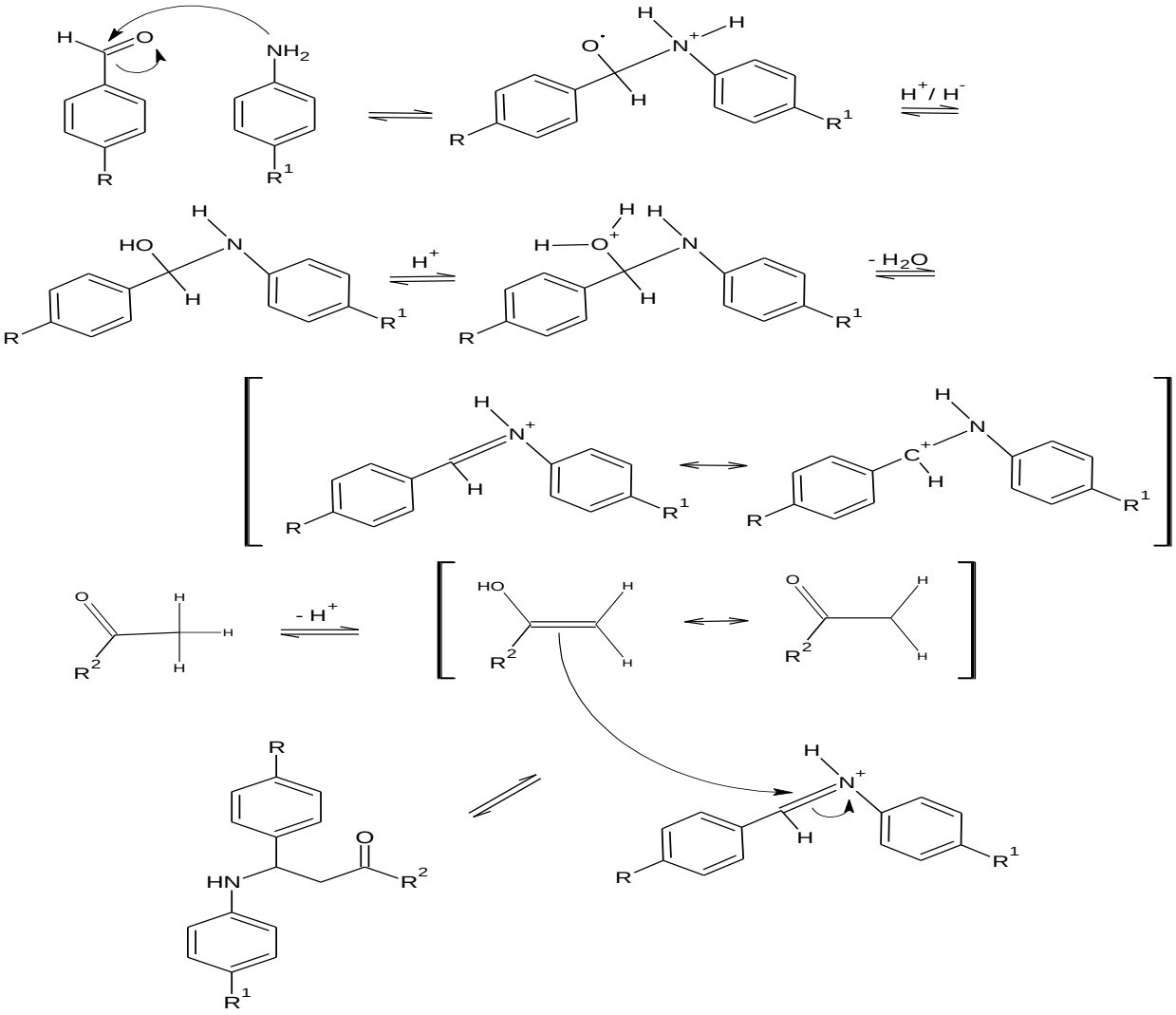
The time required for a Mannich reaction depends upon the nature of the ketone and of the amine salt and upon the boiling point of the solvent employed.

The reaction between benzalehyde and cyclohexanone with aromatic amines derivatives takes 2 hours for both Mannich basese (V) and (VI), and for the reaction between Benzaldehyde and p-nitroacetophenone with areomatic amines (I-IV) (Table 3.1).

The Mannich reaction is an example of nucleophilic addition of an amine to a carbonyl group followed by dehydration to the Schiff base. The Schiff base is an electrophile which reacts in the second step in a electrophilic addition with a compound containing an acidic proton(which is, or has become an enol). The Mannich reaction is also considered a condensation reaction. In the Mannich reaction, secondary amines are employed for the activation of benzaldehyde.

α-CH-acidic compounds (nucleophiles) include carbonyl compounds, nitriles, acetylenes, aliphatic nitro compounds, α-alkyl-pyridines or imines (Scheme 3.2).

In a number of cases the salt of the desired product precipitates when the reaction mixture is cooled. Ether facilitates separation of the product in other cases added. Occasionally the solvent is removed and crystallization of the residue brought about by washing it with acetone. Sometimes it is advantageous to liberate the basic product from its salt and purify the former by distillation, provided that the material can be distilled without decomposition.



Scheme 3.2 The mechanism of β-amino compounds

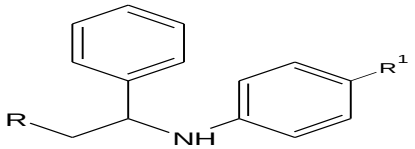


Table (3.1): Physical properties of the products:

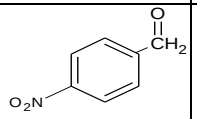
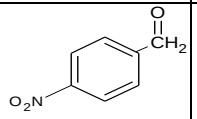
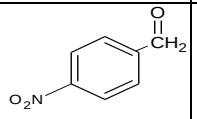
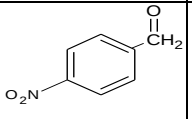
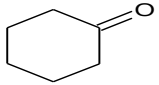
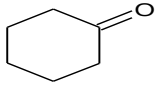
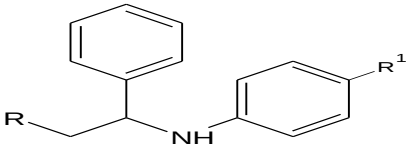
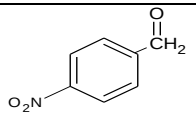
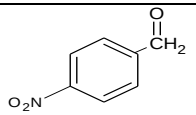
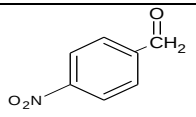
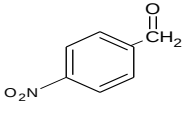
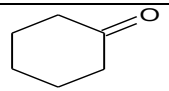
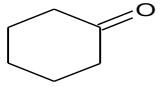
Compound No.	R	R^1	M. Formula	Formula Weight
I		$-SO_2NH_2$	$C_{21}H_{19}N_3O_5S$	425.45
II		-Br	$C_{21}H_{17}BrN_2O_3$	425.27
III		-H	$C_{21}H_{18}N_2O_3$	346.37
IV		-COOH	$C_{22}H_{18}N_2O_5$	390.38
V		-COOH	$C_{19}H_{22}N_2O_3S$	358.45
VI		$-SO_2NH_2$	$C_{20}H_{21}NO_3$	380.27

Table (3.2): The results of the products:



Compound No.	R	R^1	Yield in grams	Yield %	M.P °C	R_f
I		$-SO_2NH_2$	1.25	59	183-186	0.916
II		-Br	1.57	74	151-154	0.810
III		-H	1.09	63	157-161	0.562
IV		-COOH	1.28	66	141-144	0.423
V		-COOH	1.30	73	185-188	0.923
VI		$-SO_2NH_2$	1.17	62	156-159	0.722

*Mobile-phase :- Chloroform : Methanol (9.7:0.3)

* Solvent :- Ethanol

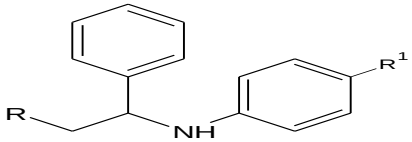


Table (3.3): Infrared absorption frequencies of the products:

Compo-und No.		R^1	C-H st-vib (Aromatic) (cm^{-1})	C-H bend (Aromatic) (cm^{-1})	C=O (cm^{-1}) Ketone	N-H str-vib (cm^{-1}) Sec-amine	N-H bend (cm^{-1})	C-H bend (Aliphatic) (cm^{-1})	S=O (cm^{-1})	N=O (cm^{-1}) Nitro	Others
I		$-SO_2NH_2$	3099.39	842.83	1687.60	3463.92	1600.81	1446.51	1334.65 1151.42	1531.73 1334.65	N-H pri-ami 3371.34
II		-Br	3070.46	852.48	1689.53	3413.77	1596.95	1488.94	-	1522.41 1346.22	C-Br 1346.22
III		-H	3055.03	848.62	1660.60	3407.98	1581.52	1446.51	-	1514.02 1330.79	-
IV		-COOH	3074.32	852.48	1662.52	3388.77	-	1423.37	-	1527.52 1342.36	O-H St-vib(acid)3250-3500
V		-COOH	3006.82	835.12	1620.09	3371.34	-	1452.30	-	-	-
VI		$-SO_2NH_2$	2958.60	837.05	1604.66	339.63	1531.37	1415.65	1332.72 1153.35	-	-

The IR spectrum of Mannich bases (I-VI) table (3.3) figures (1- 6) show the appearance of single medium to intense sharp absorption band attributed to N-H bond stretching vibration at 3371.34-3463.92 cm^{-1} region confirmed by the presence of medium and strong peak at 1531.37 -1600.81 cm^{-1} region for N-H bending frequency. Peaks at 2958.60-3099.39 cm^{-1} and 835.12 -852.48 cm^{-1} region indicate the presence of C-H stretching vibration and bending in aromatic system; strong peak at 1604.16-1687.60 cm^{-1} for C=O in ketone, is shifted to the lower value due to conjugation with aromatic system; peak at 2918-2955 cm^{-1} indicate the presence of C-H stretching vibration in aliphatic system; peak at 1415.65-1488.94 cm^{-1} indicates the presence of CH_2 bonds bending frequency. Appearance of peaks at 1332.72-1334.65 cm^{-1} and at 1151.42-1153.35 cm^{-1} region in Mannich bases (I) and (VI) table (3.3) figures (1)and (6) indicates the presence of S=O group. In Addition; sharp peaks at 1514.02-1531.73 and 1330.79-1346.22 cm^{-1} region in mannnich bases (I – IV) table (3.3) figures (1 – 4) indicate the presence of NO_2 group(symmetric and asymmetric stretching vibrations).

The common structural features of the substituted propiophenone moiety introduced in the newly synthesized arylamine Mannich bases by the initial amine (Aniline) Mannich base contributed to the facile and sure

assignment of some signals in the NMR spectra of the former substances. Di-methyl sulfoxide DMSO is used as a solvent.

The ^{1}HNMR spectrums of synthesized Mannich bases (I-VI) figures (7–12) show an intense peak at δ 2.49-2.52 ppm for the protons from the methyl group connected to the aromatic ring provides. Where as the protons of the two methylenic groups neighboring the carbonyl and the secondary amino group give three double doublets, at 3.25-3.3 ppm and 3.55-3.65 ppm respectively due to the effect of chiral center. The signal at about 12 ppm was attributed to the phenolic proton; the broad and weak signal at 4.8 to 5.1ppm is assigned for (NH) proton, thus confirming its involvement in hydrogen bond with the carbonyl group. The signals in the aromatic region of the spectra, difficult to ascribe to a particular proton because of their mingling, are presented as a multiplet; however, their number always agreed with the compound's structure.

IR and ^{1}HNMR spectroscopic techniques conform the structure of the synthesized compounds.

Chapter Four: Selection of the products

4.Selection of the compounds

In organic chemistry there is no limit to the number of possible organic reactions and mechanisms. However, certain general patterns are observed that can be used to describe many common or useful reactions. Organic reactions can be categorized based on the type of functional group involved in the reaction as a reactant and the functional group that is formed as a result of this reaction.

Several mannich base compounds have been examined, in order to select specific compounds to synthesize them. The first step was designing of 32 compounds (I –XXXII) using chemoinfomatic programmer (ACD/Lap). ACD/Labs provides sample and database files for free use with software, through the programe all the properties of the compounds have been calculated and recorded (Appendix).

4.1 Many factors are working to affect formation of the products

4.1.1 Log P

Partition coefficients are useful in estimating the distribution of drugs within the body. Hydrophobic drugs with high octanol/water partition coefficients are preferentially distributed to hydrophobic compartments such as the lipid bilayers of cells while hydrophilic drugs (low octanol/water

partition coefficients) preferentially are found in aqueous compartments such as blood serum.

The logP value of a compound, which is the logarithm of its partition coefficient between n-octanol and water $\log(c_{octanol}/c_{water})$, is a well established measure of the compound's hydrophilicity. Low hydrophilicities and therefore high logP values cause poor absorption or permeation.

So in this study compounds with high log P values were selected. Benzaldehyde derivatives with p-Nitroacetophenone or Cyclohexanone and number of aromatic amines.In state of Benzaldehyde there are number of aldehyde derivatives can be worked with like furfural , salceldehyde derivatives which have higher log P (Mannich bases VIII and X).

4.1.2 Substation effect

The effect of a substituent in the meta or para position of the benzene ring affect the rate of the reaction. Since the substitution constant and reaction constant(rho) are available , so reaction rate can be calculated. reaction constant is the same for same reaction mechanism.

The results for such calculations for the reactions have been available to becarried out (Kean, 1978).

Benzaldehyde was selected for all synthesized Mannich bases, and Aniline derivatives due to conjugation system which stabilize the nuclophilic addition.

4.1.3 Polrizability effect

The polorizability is defined as the ability of electron cloud of the molecule to distortion in the response to an external field.

External field can be due to approach of the molecule attracting regard or solvent. So this effect is very important in understanding the solvent properties and the reactivity of some compounds which may change when changing the solvent.

4.1.4 Electron withdrawing/electron donating groups

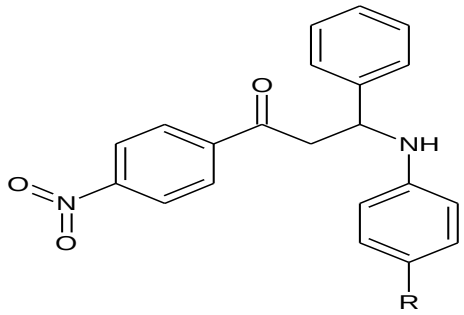
Inductive effect is ability of an atom or group to withdrow or donates electrons through the σ bond.

Strong electronegative atoms or groups have higher inductive effect. For example chlorine is more electro negative than carbon so it withdrow the bond electrons and gives higher inductive effect. Inductive effect of substituent strongly affects reactivity.

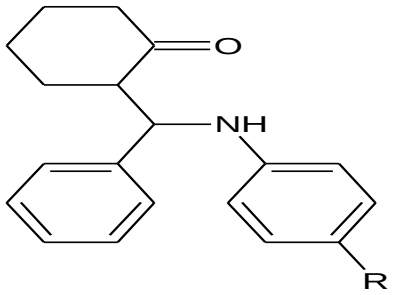
Electro-withdrowing groups enhances the reactivity and the reaction rate for this type of reactions. This idea can explain the simple formation of

the Mannich bases from p-aminoacetophenone which react as ketone than more Mannich bases resulting from reacting cyclohexanone as ketone.

4.2 Comparison of the properties of Mannich bases with some of their derivatives



R	Density	Log P	Polarizability
-H	1.261 ± 0.06 g/cm^3	4.34+/- 0.28	40.09 ± 0.5 10^{-24}cm^3
-SO_2NH_2	1.401 ± 0.06 g/cm^3	4.62+/- 0.44	44.51 ± 0.5 10^{-24}cm^3
-COOH	1.359 ± 0.06 g/cm^3	4.45+/- 0.37	42.83 ± 0.5 10^{-24}cm^3
-Br	1.462 ± 0.06 g/cm^3	5.51+/- 0.40	.13 ± 0.5 10^{-24}cm^3
-SO_3H	1.433 ± 0.06 g/cm^3	3.30+/- 0.37	43.68 ± 0.5 10^{-24}cm^3
-OCH_3	1.260 ± 0.06 g/cm^3	4.16+/- 0.37	42.73 ± 0.5 10^{-24}cm^3
-NO_2	1.366 ± 0.06 g/cm^3	4.79+/- 0.37	42.68 ± 0.5 10^{-24}cm^3



R	Density	Log P	Polarizability
-H	1.136 ± 0.06 g/cm^3	3.37+/- 0.29	15 ± 0.5 10^{-24}cm^3
-SO_2NH_2	1.304 ± 0.06 g/cm^3	1.85+/- 0.32	38.84 ± 0.5 10^{-24}cm^3
-COOH	1.251 ± 0.06 g/cm^3	3.47+/- 0.32	36.90 ± 0.5 10^{-24}cm^3
-Br	1.367 ± 0.06 g/cm^3	4.53+/- 0.40	37.20 ± 0.5 10^{-24}cm^3
-SO_3H	1.338 ± 0.06 g/cm^3	2.32+/- 0.33	38.02 ± 0.5 10^{-24}cm^3
-OCH_3	1.146 ± 0.06 g/cm^3	3.18+/- 0.31	36.80 ± 0.5 10^{-24}cm^3
-NO_2	1.258 ± 0.06 g/cm^3	3.81+/- 0.33	36.74 ± 0.5 10^{-24}cm^3

Conclusion and recommendations

Six β-aminoketo compounds were synthesized in this research, by multi-component reaction between benzaldehyde , and various aromatic amines with (P-aminoacetophenone/Cyclohexanone) ketone. The reaction followed by TLC and ethanol was chosen as the best solvent for this reaction according to the results of some trials (chanding the solvents, conditions and the reaction time). The structures of synthesized compounds were confirmed by various spectroscopic techniques (IR and H^1NMR).

The properties of the synthesized compounds were calculated by (ACD/Lab), and the percentage, Melting point and RF value were also calculated for all synthesized compounds.

Recommendations:

Benzaldehyde may be replaced by formaldehyde or any nonenolizable aldehyde to obtain another series of Mannich bases. The conditions of the reaction and the reaction time are different from reaction to another, this can be worked by following the reaction by (TLC) and IR.

Biological activity can be studied for Mannich bases. And the stability of Mannich base compounds can also take investigated.

Chapter Five: References

5. References

Agenet, N.; Buisine, O.; Slowinski, F.; Gandon, V.; Aubert, C.; Malacria, M. (2007). "Cotrimerizations of Acetylenic Compounds". *Org. React*. **68:** 1–302.

C.Mannich, M.Dannehl, ;(1938),” Uber die condensation via nitro and amino-acetophenone with formaldehyde”,*Berlin*, *Arch. Pharm*., **276:**206-211.

Córdova, A.; Watanabe, S.; Tanaka, F.; Notz, W.; Barbas Cf.;(2002)"A highly enantioselective route to either enantiomer of both alpha- and beta-amino acid derivatives",*Journal of the American Chemical Society*, **124** (9):1866–1867.

D. C. McKean,;(1978),” Individual CH bond strengths in simple organic compounds: effects of conformation and substitution”, *chem.Soc*, **7:** 399-422.

Dömling, A.; Ugi, I. ; (2000), “Multicomponent reactions with isocyanides”. *Angew. Chem. Int. Ed. Engl*. **39:** 3168–3210

F. F. Blicke,(2011) Organic Reactions, The Mannich Reaction,Inc. Published by John Wiley and Sons, Inc.

Fields, Ellis K. ; (1952), "The synthesis of esters of substituted amino phosphonic acids". *Journal of the American Chemical Society.* **74** (6): 1528–1531

Frank B.;(1998), "Chemoinformatics: What is it and How does it Impact Drug Discovery" , *Annual Reports in Medicinal Chemistry* , **33:**375-384.

Friedrich Asinger , ; (1956)"Chemiker-Treffen Salzburg: Über die einfache und ergiebige Synthese von Thiazolonen". Angewandte Chemie , **68** (11): 377

Gardiner,W.P.;(1997) ,"Statistical Analysis Methods for Chemist: A Software-base D Approach" *The Royal Society of Chemistry*: Cambridge.

Gewald, K.; Schinke, E.; Böttcher, H. Ber. 1966, synthesis of 2-aminothiophene , 99, 94-100.

Gibson ,S. E. ; (2003),Stevenazzi,A.and Angew,Homogenous catalysis with organometallic compounds, *Chem. Int. Ed*., **42:** 1800-1810

Hawkins D.M, Basak S.C, Kraker J, Geiss K.T, Witzmann FA,;(2006)," Combining Chemodescriptors and Biodescriptors in Quantitative Structure-Activity Relationship Modeling", *J Chem Inf Model.* **46**(1): 9-16.

Jean, J., Annie, M. ;(2003), "Synthesis and Aromatization of Hantzsch 1,4-Dihydropyridines under Microwave Irradiation". *An Overview*. ***8***(4): 381-391.

Jing,J. , Guan, W. ; (2005). "One-Pot Synthesis and Aromatization of 1,4-Dihydropyridines in Refluxing Water". *Synthesis,* **14:** 2379–2383.

Jürgen, M.; Heribert, O.;(1981), " Eine einfache Synthese von racemischem Cystein", *Angewandte Chemie* , **93**:680-688.

Kappe, C. O.; Stadler, A. (2004). "The Biginelli Dihydropyrimidine Synthesis". *Organic Reactions*. **63:**20-29.

Kermack, W. 0., and Muir, W. ;(1931), Attempts to Find New Antimalarials : Part VI. Derivatives of 2-/8-,*Aminoethylquinoline*, **20:**3089-3096.

Kumar G. V. S, Prasad Y. R, Mallikarjuna B. P. and Chandrashekar S. M.;(2010) *Eur. J. Med. Chem.* **45** (51):20-27.

Mannich, C., Lesser, B., and Silten, F., Ber.;(1932), *Australian journal of chemistry*, **65:**378.

Mannich, C.; Krösche, W. ; (1912). "Ueber ein Kondensationsprodukt aus Formaldehyd, Ammoniak und Antipyrin". *Archiv der Pharmazie,* **250:** 647–667.

March, Jerry (1985), Advanced Organic Chemistry: Reactions, Mechanisms, and Structure (3rd ed.), New York: Wiley.

March, Jerry ,;(1985) , Advanced Organic Chemistry: Reactions, Mechanisms, and Structure , New York: Wiley.

Mary, M., Joel, P.,Dr. Ray, K., Dr. Jonathan Chen, Dr. Jenny Tao, Dr. Edward Scollon,Christine Olinger,Dr. Patricia S., Dr. Chris R.,Dr. Kelly Mayo Dr. Yin-tak Woo,Dr. Thomas S., Dr. Edwin M.,and Dr. Sunil K.;(2012), **"**(Quantitative) Structure Activity Relationship [(Q)SAR] ", *European Commission* – Joint Research Centre .

Passerini, M.and Ragni, ; (1931) , " Sopra gli isonitrili.Gazz"*Chim. Ital*, **61:** 964–69

Pirrung, M. C.; Sarma, K. D. (2004). "Multicomponent Reactions Are Accelerated in Water". *Journal of the American Chemical Society,* **126** (2): 444–445.

Quevedo, R.; Moreno-Murillo, B. One-step synthesis of a new heterocyclophane family;(2009). *Tetrahedron Letters.* **50** (8): 936–938.

Quevedo, R.; Moreno-Murillo, B.;(2009), One-step synthesis of a new heterocyclophane family, *Tetrahedron Letters*, **50** (8):936–938.

Rivera, A.; Quevedo, R.;(2004) , "Solvent-free Mannich-type reaction as a strategy for synthesizing novel heterocalixarenes ", *Tetrahedron Letters*,**45** (45):8335–8338.

Rosa, F. A., Rebelo, R. A., Nascimento, M. G.;(2003), *Journal of the Brazilian Chemical Society* , **14:**11.

Sabnis, R.W. Barnhart, D.A. Mc Morran; (1997).*B. Bosnich Chem. Commun*. **16:**249-253.

Strecker, A. ;(1850), "Ueber die künstliche Bildung der Milchsäure und einen neuen, dem Glycocoll homologen Körper". *Annalen der Chemie und Pharmazie,* **75** (1):, 27–45

Ugi, I; Meyr, R.; Fetzer, U.; Steinbrückner, C.; (1959) , "Versuche mit Isonitrilen". *Angew. Chem*.**71** (11): 386-396.

Van de Kamp and Mosettig,; (1936),"The Mannich reaction ". *Am.Chem.. Soc.*, **58:** 15-68 .

Werder, M., Hauser, H. E. ;(2005) , *J. Med. Chem.*, **48:**60, 35; (b) Roers R and Verdine G L, ;(2001),*Tetrahedron Lett*,. **42:** 35-63

Wolfgang, ;W., Heribert , O.;(1975), "D-Penicillamin - Herstellung und Eigenschaften", *Angewandte Chemie*, **87** :372-378 .

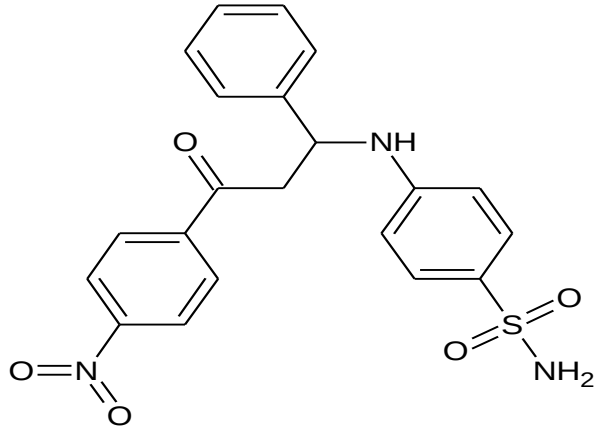
Yandong Zhang , ;(2005), "Asymmetric Multicomponent Reactions "*Institute of Organic Chemistry and Biochemistry*, Germany.

Zefirov, Nikolay S.; Elena D. Matveeva ,2008 , "Catalytic Kabachnik-Fields reaction: New horizons for old reaction" , **9:** 1–17

Appendix

Properties of some Mannich Bases products calculated by using ACD/Lab

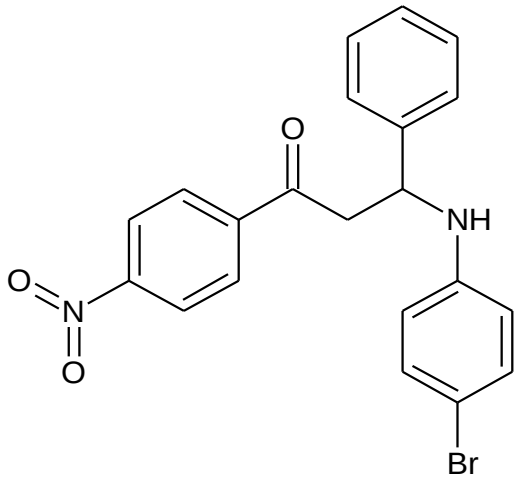
I - P.Nitroacetophenone + Sulfanilamide + Benzaldehyde :



4-{[3-(4-nitrophenyl)-3-oxo-1-phenylpropyl]amino}benzenesulfonamide

Molecular Formula	= $C_{21}H_{19}N_3O_5S$
Formula Weight	= 425.45766
Composition	= C(59.28%) H(4.50%) N(9.88%) O(18.80%) S(7.54%)
Molar Refractivity	= 112.28 ± 0.4 cm^3
Molar Volume	= 303.5 ± 3.0 cm^3
Parachor	= 867.5 ± 6.0 cm^3
Index of Refraction	= 1.661 ± 0.02
Surface Tension	= 66.7 ± 3.0 dyne/cm
Density	= 1.401 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 44.51 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 425.104541 Da
Nominal Mass	= 425 Da
Average Mass	= 425.4577 Da
M+	= 425.103992 Da
M-	= 425.105089 Da
[M+H]+	= 426.111817 Da
[M+H]-	= 426.112914 Da
[M-H]+	= 424.096167 Da
[M-H]-	= 424.097264 Da
Log P	=2.83+/- 0.37

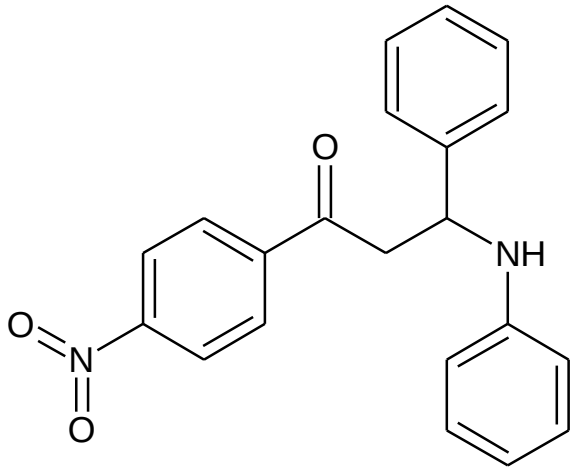
II - P-Nitro acetophenone + Benzaldehyde +P-Bromo Aniline



3-[(4-bromophenyl)amino]-1-(4-nitrophenyl)-3-phenylpropan-1-one

Molecular Formula	= $C_{21}H_{17}BrN_2O_3$
Formula Weight	= 425.27528
Composition	= C(59.31%) H(4.03%) Br(18.79%) N(6.59%) O(11.29%)
Molar Refractivity	= 108.82 ± 0.3 cm^3
Molar Volume	= 290.7 ± 3.0 cm^3
Parachor	= 803.2 ± 4.0 cm^3
Index of Refraction	= 1.671 ± 0.02
Surface Tension	= 58.2 ± 3.0 dyne/cm
Density	= 1.462 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 43.13 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 424.042247 Da
Nominal Mass	= 424 Da
Average Mass	= 425.2753 Da
M+	= 424.041699 Da
M-	= 424.042796 Da
[M+H]+	= 425.049524 Da
[M+H]-	= 425.050621 Da
[M-H]+	= 423.033874 Da
[M-H]-	= 423.034971 Da
Log P	= 5.51+/- 0.40

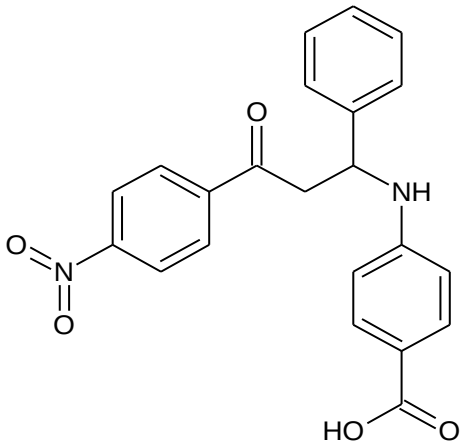
III -P.Nitroacetophenone + Aniline + Benzaldehyde :



1-(4-nitrophenyl)-3-phenyl-3-(phenylamino)propan-1-one

Molecular Formula	= $C_{21}H_{18}N_2O_3$
Formula Weight	= 346.37922
Composition	= C(72.82%) H(5.24%) N(8.09%) O(13.86%)
Molar Refractivity	= 101.12 ± 0.3 cm^3
Molar Volume	= 274.6 ± 3.0 cm^3
Parachor	= 752.7 ± 4.0 cm^3
Index of Refraction	= 1.657 ± 0.02
Surface Tension	= 56.4 ± 3.0 dyne/cm
Density	= 1.261 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 40.09 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 346.131742 Da
Nominal Mass	= 346 Da
Average Mass	= 346.3792 Da
M+	= 346.131194 Da
M-	= 346.132291 Da
[M+H]+	= 347.139019 Da
[M+H]-	= 347.140116 Da
[M-H]+	= 345.123369 Da
[M-H]-	= 345.124466 Da
Log P	= 4.34+/- 0.28

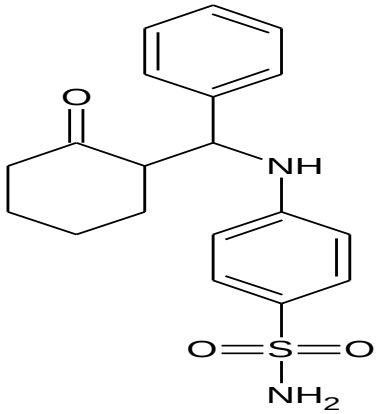
IV - P-Nitro acetophenone + Benzaldehyde +P-Amino benzoic acid



4-{[3-(4-nitrophenyl)-3-oxo-1-phenylpropyl]amino}benzoic acid

Molecular Formula	= $C_{22}H_{18}N_2O_5$
Formula Weight	= 390.38872
Composition	= C(67.69%) H(4.65%) N(7.18%) O(20.49%)
Molar Refractivity	= 108.06 ± 0.3 cm^3
Molar Volume	= 287.1 ± 3.0 cm^3
Parachor	= 814.8 ± 4.0 cm^3
Index of Refraction	= 1.676 ± 0.02
Surface Tension	= 64.8 ± 3.0 dyne/cm
Density	= 1.359 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 42.83 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 390.121572 Da
Nominal Mass	= 390 Da
Average Mass	= 390.3887 Da
M+	= 390.121023 Da
M-	= 390.12212 Da
[M+H]+	= 391.128848 Da
[M+H]-	= 391.129945 Da
[M-H]+	= 389.113198 Da
[M-H]-	= 389.114295 Da
Log P	= 4.45+/- 0.37

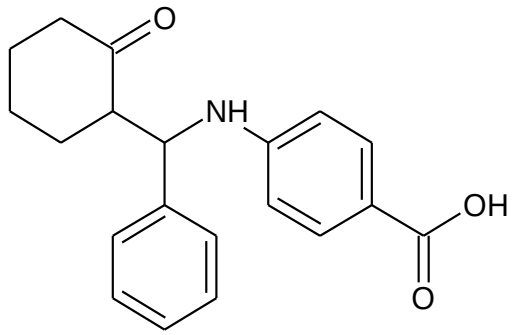
V -Cyclohexanone + Sulfanilamide + Benzaldehyde :



4-{[(2-oxocyclohexyl)(phenyl)methyl]amino}benzenesulfonamide

Molecular Formula	= $C_{19}H_{22}N_2O_3S$
Formula Weight	= 358.45458
Composition	= C(63.66%) H(6.19%) N(7.82%) O(13.39%) S(8.95%)
Molar Refractivity	= 97.99 ± 0.4 cm^3
Molar Volume	= 274.7 ± 3.0 cm^3
Parachor	= 765.4 ± 6.0 cm^3
Index of Refraction	= 1.631 ± 0.02
Surface Tension	= 60.1 ± 3.0 dyne/cm
Density	= 1.304 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 38.84 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 358.135113 Da
Nominal Mass	= 358 Da
Average Mass	= 358.4546 Da
M+	= 358.134564 Da
M-	= 358.135661 Da
[M+H]+	= 359.142389 Da
[M+H]-	= 359.143486 Da
[M-H]+	= 357.126739 Da
[M-H]-	= 357.127836 Da
LogP	=1.85+/- 0.32

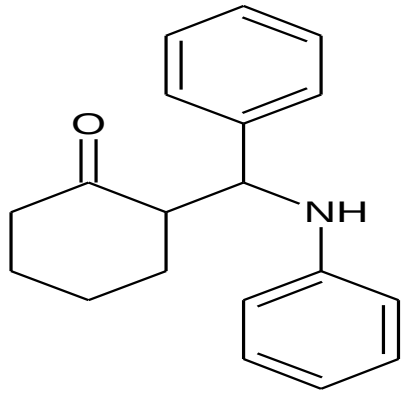
VI - Cyclohexanone + Benzaldehyde +P-Amino benzoic acid



4-{[(2-oxocyclohexyl)(phenyl)methyl]amino}benzoic acid

Molecular Formula	= $C_{20}H_{21}NO_3$
Formula Weight	= 323.38564
Composition	= C(74.28%) H(6.55%) N(4.33%) O(14.84%)
Molar Refractivity	= 93.08 ± 0.3 cm^3
Molar Volume	= 258.3 ± 3.0 cm^3
Parachor	= 718.2 ± 6.0 cm^3
Index of Refraction	= 1.639 ± 0.02
Surface Tension	= 59.7 ± 3.0 dyne/cm
Density	= 1.251 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 36.90 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 323.152144 Da
Nominal Mass	= 323 Da
Average Mass	= 323.3856 Da
M+	= 323.151595 Da
M-	= 323.152692 Da
[M+H]+	= 324.15942 Da
[M+H]-	= 324.160517 Da
[M-H]+	= 322.14377 Da
[M-H]-	= 322.144867 Da
Log P	= 3.47+/- 0.32

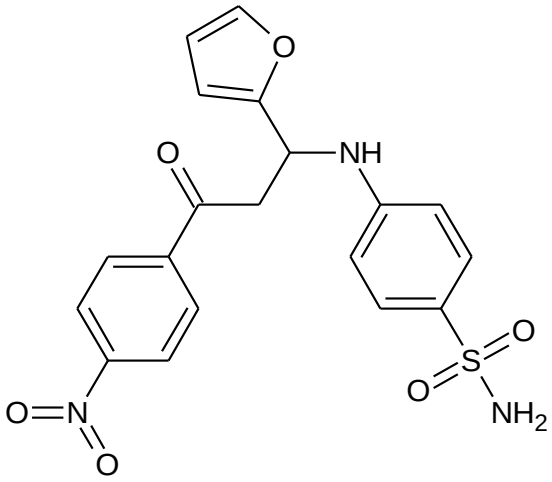
VII -Cyclohexanone + Aniline + Benzaldehyde :



2-[phenyl(phenylamino)methyl]cyclohexanone

Molecular Formula	= $C_{19}H_{21}NO$
Formula Weight	= 279.37614
Composition	= C(81.68%) H(7.58%) N(5.01%) O(5.73%)
Molar Refractivity	= 86.15 ± 0.3 cm^3
Molar Volume	= 245.8 ± 3.0 cm^3
Parachor	= 657.8 ± 6.0 cm^3
Index of Refraction	= 1.618 ± 0.02
Surface Tension	= 51.2 ± 3.0 dyne/cm
Density	= 1.136 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 34.15 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 279.162314 Da
Nominal Mass	= 279 Da
Average Mass	= 279.3761 Da
M+	= 279.161766 Da
M-	= 279.162863 Da
[M+H]+	= 280.169591 Da
[M+H]-	= 280.170688 Da
[M-H]+	= 278.153941 Da
[M-H]-	= 278.155038 Da
LogP	= 3.37+/- 0.29

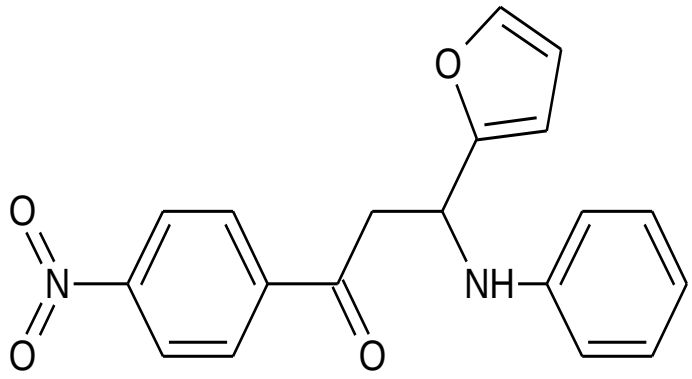
VIII -P.Nitroacetophenone + Sulfanilamide + Furfural :



4-{[1-(furan-2-yl)-3-(4-nitrophenyl)-3-oxopropyl]amino}benzenesulfonamide

Molecular Formula	= $C_{19}H_{17}N_3O_6S$
Formula Weight	= 415.41978
Composition	= C(54.93%) H(4.12%) N(10.12%) O(23.11%) S(7.72%)
Molar Refractivity	= 104.76 ± 0.4 cm^3
Molar Volume	= 286.3 ± 3.0 cm^3
Parachor	= 822.8 ± 6.0 cm^3
Index of Refraction	= 1.652 ± 0.02
Surface Tension	= 68.1 ± 3.0 dyne/cm
Density	= 1.450 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 41.53 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 415.083805 Da
Nominal Mass	= 415 Da
Average Mass	= 415.4198 Da
M+	= 415.083257 Da
M-	= 415.084354 Da
[M+H]+	= 416.091082 Da
[M+H]	= 416.092179 Da
[M-H]+	= 414.075432 Da
[M-H]-	= 414.076529 Da
LogP	= 1.99+/- 0.38

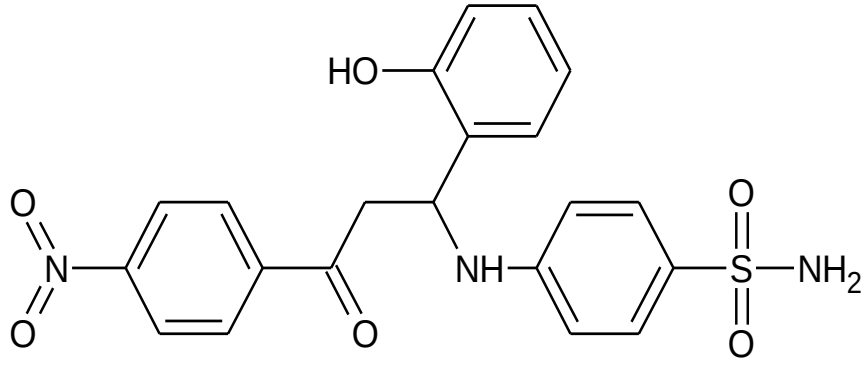
IX- P.Nitroacetophenone + Anilne + Furfural :



3-(furan-2-yl)-1-(4-nitrophenyl)-3-(phenylamino)propan-1-one

Molecular Formula	= $C_{19}H_{16}N_2O_4$
Formula Weight	= 336.34134
Composition	= C(67.85%) H(4.79%) N(8.33%) O(19.03%)
Molar Refractivity	= 93.42 ± 0.3 cm^3
Molar Volume	= 257.4 ± 3.0 cm^3
Parachor	= 706.7 ± 4.0 cm^3
Index of Refraction	= 1.646 ± 0.02
Surface Tension	= 56.8 ± 3.0 dyne/cm
Density	= 1.306 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 37.03 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 336.111007 Da
Nominal Mass	= 336 Da
Average Mass	= 336.3413 Da
M+	= 336.110458 Da
M-	= 336.111556 Da
[M+H]+	= 337.118283 Da
[M+H]-	= 337.119381 Da
[M-H]+	= 335.102633 Da
[M-H]-	= 335.103731 Da
Log P	=3.51+/- 0.30

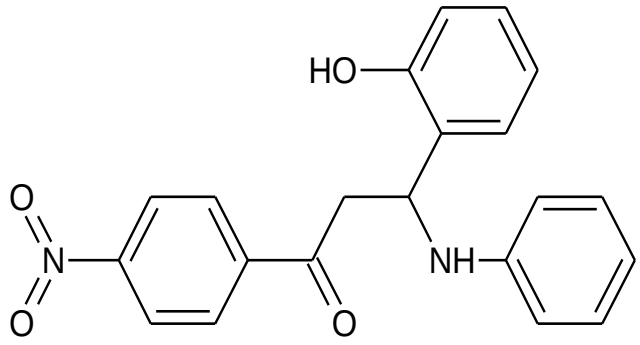
X- P.Nitroacetophenone + Sulfanilamide + Salicylaldehyde :



4-{[1-(2-hydroxyphenyl)-3-(4-nitrophenyl)-3-oxopropyl]amino}benzenesulfonamide

Molecular Formula	= $C_{21}H_{19}N_3O_6S$
Formula Weight	= 441.45706
Composition	= C(57.13%) H(4.34%) N(9.52%) O(21.75%) S(7.26%)
Molar Refractivity	= 113.81 ± 0.4 cm^3
Molar Volume	= 301.9 ± 3.0 cm^3
Parachor	= 882.7 ± 6.0 cm^3
Index of Refraction	= 1.677 ± 0.02
Surface Tension	= 73.0 ± 3.0 dyne/cm
Density	= 1.461 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 45.11 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 441.099455 Da
Nominal Mass	= 441 Da
Average Mass	= 441.4571 Da
M+	= 441.098907 Da
M-	= 441.100004 Da
[M+H]+	= 442.106732 Da
[M+H]-	= 442.107829 Da
[M-H]+	= 440.091082 Da
[M-H]-	= 440.092179 Da
Log P	= 2.09+/- 0.37

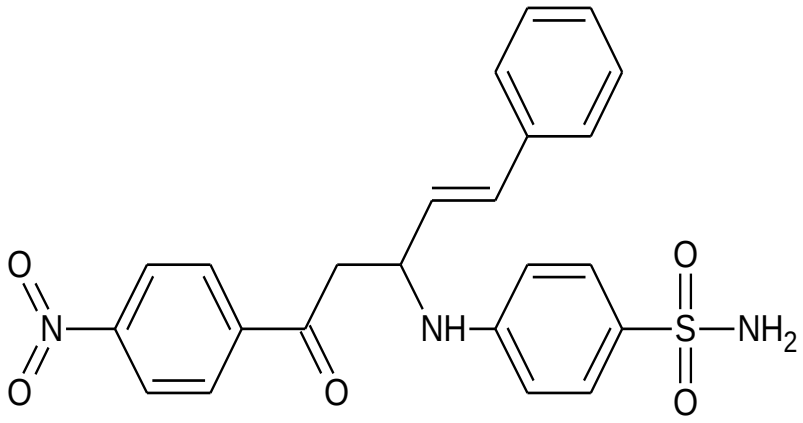
XI- P.Nitroacetophenone + Aniline + Salicylaldehyde :



3-(2-hydroxyphenyl)-1-(4-nitrophenyl)-3-(phenylamino)propan-1-one

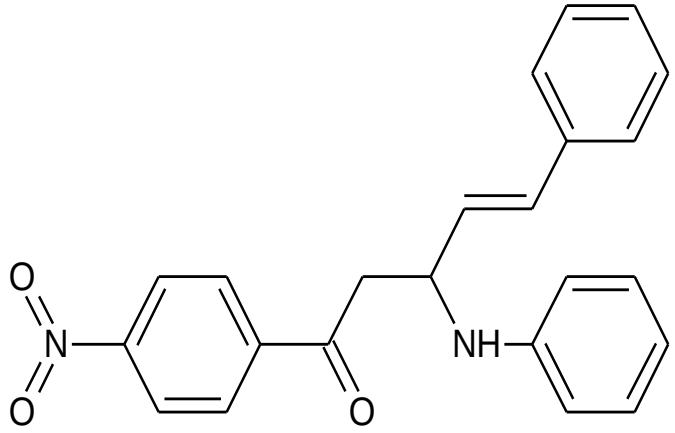
Molecular Formula	= $C_{21}H_{18}N_2O_4$
Formula Weight	= 362.37862
Composition	= C(69.60%) H(5.01%) N(7.73%) O(17.66%)
Molar Refractivity	= 103.01 ± 0.3 cm^3
Molar Volume	= 273.0 ± 3.0 cm^3
Parachor	= 767.7 ± 4.0 cm^3
Index of Refraction	= 1.678 ± 0.02
Surface Tension	= 62.5 ± 3.0 dyne/cm
Density	= 1.327 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 40.83 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 362.126657 Da
Nominal Mass	= 362 Da
Average Mass	= 362.3786 Da
M+	= 362.126108 Da
M-	= 362.127206 Da
[M+H]+	= 363.133933 Da
[M+H]-	= 363.135031 Da
[M-H]+	= 361.118283 Da
[M-H]-	= 361.119381 Da
Log P	= 3.61+/- 0.29

XII- P.Nitroacetophenone + Sulfanilamide + Cinnamaldehyde :



Molecular Formula	= $C_{23}H_{21}N_3O_5S$
Formula Weight	= 451.49494
Composition	= C(61.18%) H(4.69%) N(9.31%) O(17.72%) S(7.10%)
Molar Refractivity	= 121.45 ± 0.4 cm^3
Molar Volume	= 327.8 ± 3.0 cm^3
Parachor	= 935.3 ± 6.0 cm^3
Index of Refraction	= 1.662 ± 0.02
Surface Tension	= 66.2 ± 3.0 dyne/cm
Density	= 1.377 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 48.14 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 451.120191 Da
Nominal Mass	= 451 Da
Average Mass	= 451.4949 Da
M+	= 451.119642 Da
M-	= 451.120739 Da
[M+H]+	= 452.127467 Da
[M+H]-	= 452.128564 Da
[M-H]+	= 450.111817 Da
[M-H]-	= 450.112914 Da
Log P	=3.53+/- 0.38

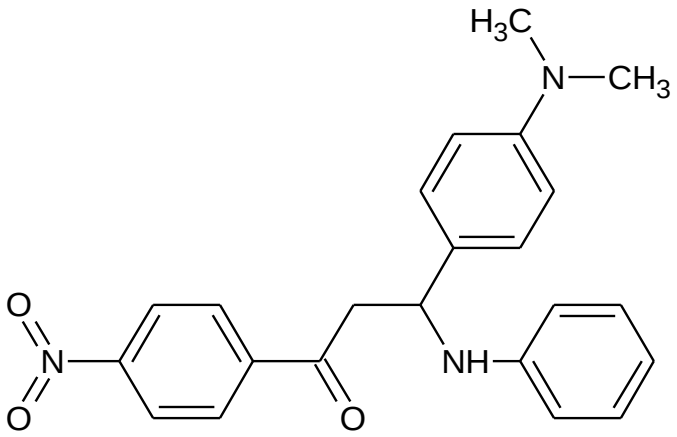
XIII- P.Nitroacetophenone + Aniline + Cinnamaldehyde :



(4*E*)-1-(4-nitrophenyl)-5-phenyl-3-(phenylamino)pent-4-en-1-one

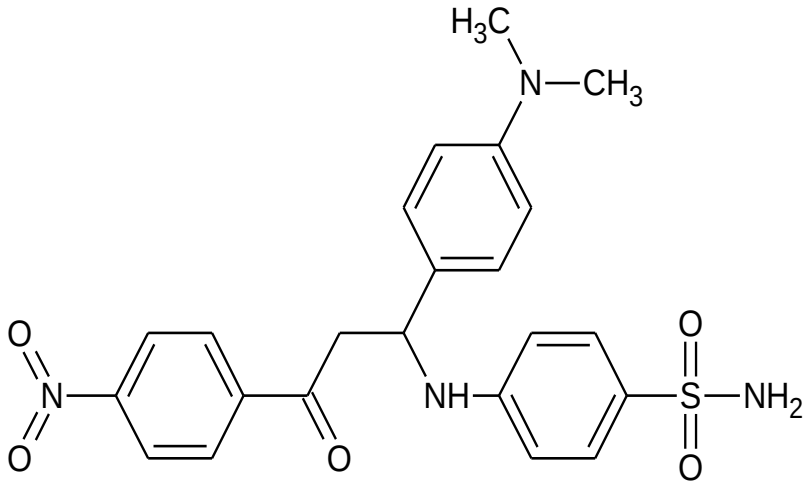
Molecular Formula	= $C_{23}H_{20}N_2O_3$
Formula Weight	= 372.4165
Composition	= C(74.18%) H(5.41%) N(7.52%) O(12.89%)
Molar Refractivity	= 112.05 ± 0.3 cm^3
Molar Volume	= 298.9 ± 3.0 cm^3
Parachor	= 817.6 ± 4.0 cm^3
Index of Refraction	= 1.673 ± 0.02
Surface Tension	= 55.9 ± 3.0 dyne/cm
Density	= 1.245 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 44.42 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 372.147393 Da
Nominal Mass	= 372 Da
Average Mass	= 372.4165 Da
M+	= 372.146844 Da
M-	= 372.147941 Da
[M+H]+	= 373.154669 Da
[M+H]-	= 373.155766 Da
[M-H]+	= 371.139019 Da
[M-H]-	= 371.140116 Da
LogP	=5.05+/- 0.37

XIV -P.Nitroacetophenone +Aniline+P-N,N-dimethylaminobenzaldehyde :



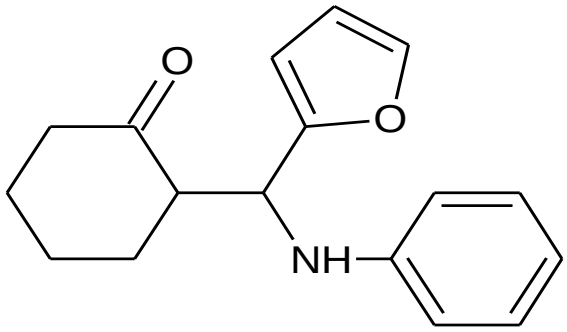
Molecular Formula	= $C_{23}H_{23}N_3O_3$
Formula Weight	= 389.44702
Composition	= C(70.93%) H(5.95%) N(10.79%) O(12.32%)
Molar Refractivity	= 115.44 ± 0.3 cm^3
Molar Volume	= 312.6 ± 3.0 cm^3
Parachor	= 854.7 ± 4.0 cm^3
Index of Refraction	= 1.660 ± 0.02
Surface Tension	= 55.9 ± 3.0 dyne/cm
Density	= 1.245 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 45.76 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 389.173942 Da
Nominal Mass	= 389 Da
Average Mass	= 389.447 Da
M+	= 389.173393 Da
M-	= 389.17449 Da
[M+H]+	= 390.181218 Da
[M+H]-	= 390.182315 Da
[M-H]+	= 388.165568 Da
[M-H]-	= 388.166665 Da
LogP	=4.45+/- 0.31

XV- P.Nitroacetophenone + Sulfanilamide +P-N,Ndimethylaminobenzaldehyde :



Molecular Formula	= $C_{23}H_{24}N_4O_5S$
Formula Weight	= 468.52546
Composition	= C(58.96%) H(5.16%) N(11.96%) O(17.07%) S(6.84%)
Molar Refractivity	= 125.41 ± 0.4 cm^3
Molar Volume	= 341.5 ± 3.0 cm^3
Parachor	= 972.2 ± 6.0 cm^3
Index of Refraction	= 1.655 ± 0.02
Surface Tension	= 65.6 ± 3.0 dyne/cm
Density	= 1.371 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 49.71 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 468.14674 Da
Nominal Mass	= 468 Da
Average Mass	= 468.5255 Da
M+	= 468.146191 Da
M-	= 468.147288 Da
[M+H]+	= 469.154016 Da
[M+H]-	= 469.155114 Da
[M-H]+	= 467.138366 Da
[M-H]-	= 467.139463 Da
LogP	=2.94+/- 0.38

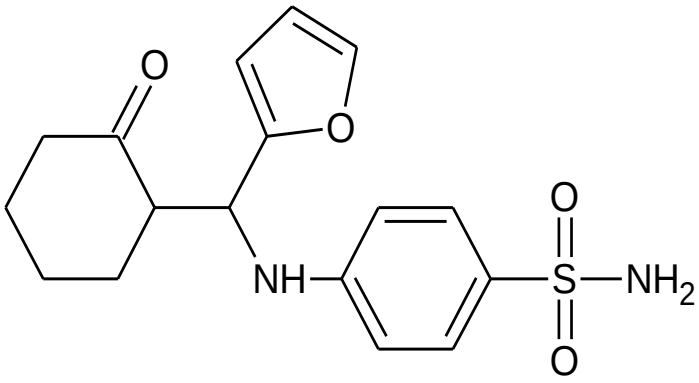
XVI- Cyclohexanone+ Aniline + Furfural :



2-[furan-2-yl(phenylamino)methyl]cyclohexanone

Molecular Formula	= $C_{17}H_{19}NO_2$
Formula Weight	= 269.33826
Composition	= C(75.81%) H(7.11%) N(5.20%) O(11.88%)
Molar Refractivity	= 78.45 ± 0.3 cm^3
Molar Volume	= 228.6 ± 3.0 cm^3
Parachor	= 613.0 ± 6.0 cm^3
Index of Refraction	= 1.602 ± 0.02
Surface Tension	= 51.6 ± 3.0 dyne/cm
Density	= 1.177 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 31.10 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 269.141579 Da
Nominal Mass	= 269 Da
Average Mass	= 269.3383 Da
M+	= 269.14103 Da
M-	= 269.142127 Da
[M+H]+	= 270.148855 Da
[M+H]-	= 270.149952 Da
[M-H]+	= 268.133205 Da
[M-H]-	= 268.134302 Da
LogP	= 2.53+/- 0.31

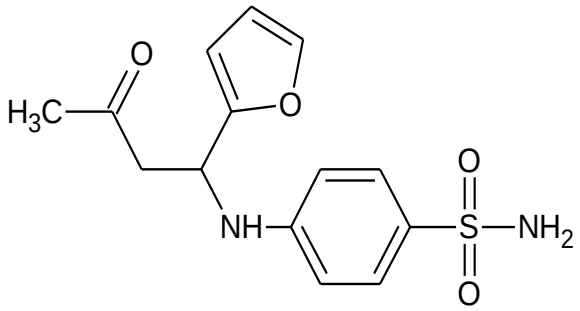
XVII- Cyclohexanone+ Sulfanilamide + Furfural :



4-{[furan-2-yl(2-oxocyclohexyl)methyl]amino}benzenesulfonamide

Molecular Formula	= $C_{17}H_{20}N_2O_4S$
Formula Weight	= 348.4167
Composition	= C(58.60%) H(5.79%) N(8.04%) O(18.37%) S(9.20%)
Molar Refractivity	= 90.47 ± 0.4 cm^3
Molar Volume	= 257.5 ± 3.0 cm^3
Parachor	= 720.6 ± 6.0 cm^3
Index of Refraction	= 1.619 ± 0.02
Surface Tension	= 61.2 ± 3.0 dyne/cm
Density	= 1.352 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 35.86 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 348.114377 Da
Nominal Mass	= 348 Da
Average Mass	= 348.4167 Da
M+	= 348.113829 Da
M-	= 348.114926 Da
[M+H]+	= 349.121654 Da
[M+H]-	= 349.122751 Da
[M-H]+	= 347.106003 Da
[M-H]-	= 347.107101 Da
LogP	= 1.01+/- 0.34

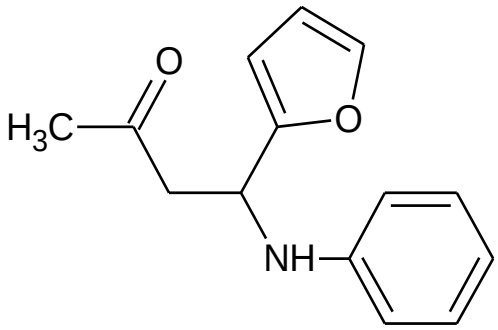
XVIII- Acetone + Sulfanilamide + Furfural :



4-{[1-(furan-2-yl)-3-oxobutyl]amino}benzenesulfonamide

Molecular Formula	= $C_{14}H_{16}N_2O_4S$
Formula Weight	= 308.35284
Composition	= C(54.53%) H(5.23%) N(9.08%) O(20.75%) S(10.40%)
Molar Refractivity	= 78.64 ± 0.4 cm^3
Molar Volume	= 228.7 ± 3.0 cm^3
Parachor	= 631.9 ± 6.0 cm^3
Index of Refraction	= 1.603 ± 0.02
Surface Tension	= 58.2 ± 3.0 dyne/cm
Density	= 1.348 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 31.17 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 308.083077 Da
Nominal Mass	= 308 Da
Average Mass	= 308.3528 Da
M+	= 308.082528 Da
M-	= 308.083626 Da
[M+H]+	= 309.090353 Da
[M+H]-	= 309.091451 Da
[M-H]+	= 307.074703 Da
[M-H]-	= 307.075801 Da
LogP	= 0.12+/- 0.28

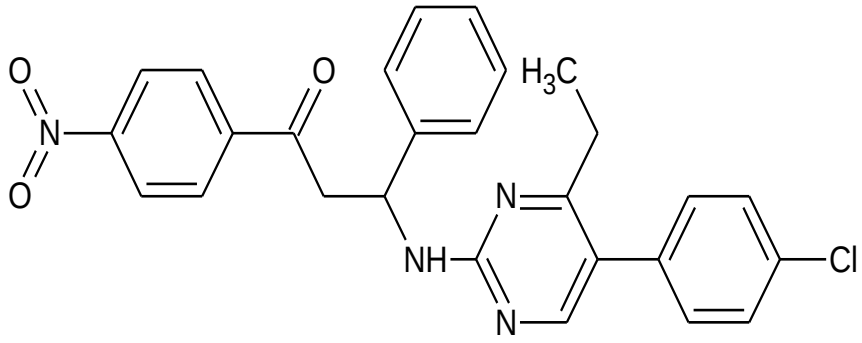
XIX- Acetone+ Aniline + Furfural :



4-(furan-2-yl)-4-(phenylamino)butan-2-one

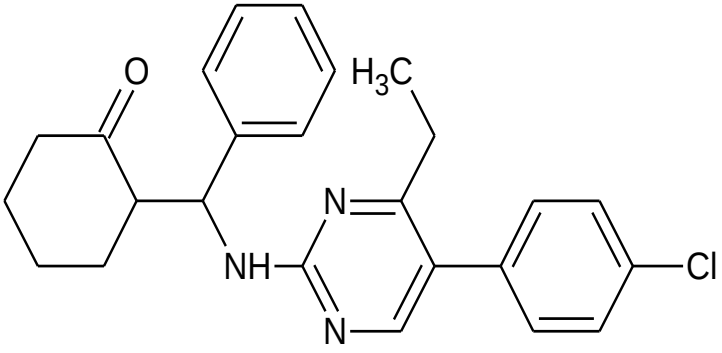
Molecular Formula	= $C_{14}H_{15}NO_2$
Formula Weight	= 229.2744
Composition	= C(73.34%) H(6.59%) N(6.11%) O(13.96%)
Molar Refractivity	= 66.58 ± 0.3 cm^3
Molar Volume	= 199.7 ± 3.0 cm^3
Parachor	= 515.3 ± 4.0 cm^3
Index of Refraction	= 1.581 ± 0.02
Surface Tension	= 44.2 ± 3.0 dyne/cm
Density	= 1.147 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 26.39 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 229.110279 Da
Nominal Mass	= 229 Da
Average Mass	= 229.2744 Da
M+	= 229.10973 Da
M-	= 229.110827 Da
[M+H]+	= 230.117555 Da
[M+H]-	= 230.118652 Da
[M-H]+	= 228.101905 Da
[M-H]-	= 228.103002 Da
LogP	= 1.64+/- 0.27

XX- P-nitro acetophenone + Benzaldehyde +Pyrimethamine



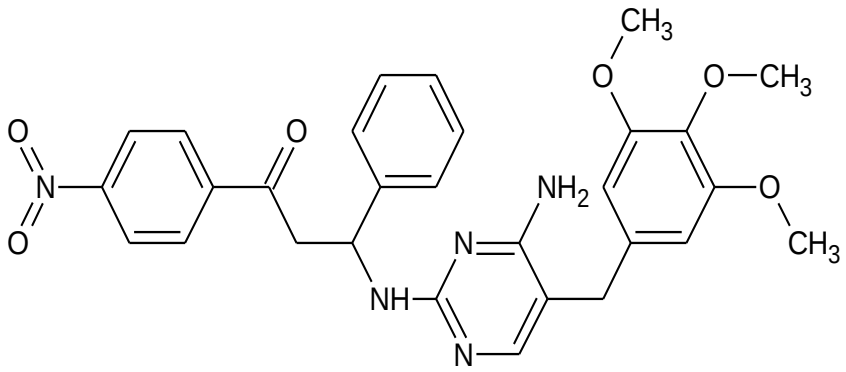
Molecular Formula	= $C_{27}H_{23}ClN_4O_3$
Formula Weight	= 486.94952
Composition	= C(66.60%) H(4.76%) Cl(7.28%) N(11.51%) O(9.86%)
Molar Refractivity	= 136.34 ± 0.3 cm^3
Molar Volume	= 371.1 ± 3.0 cm^3
Parachor	= 1026.8 ± 4.0 cm^3
Index of Refraction	= 1.656 ± 0.02
Surface Tension	= 58.6 ± 3.0 dyne/cm
Density	= 1.312 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 54.05 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 486.145868 Da
Nominal Mass	= 486 Da
Average Mass	= 486.9495 Da
M+	= 486.14532 Da
M-	= 486.146417 Da
[M+H]+	= 487.153145 Da
[M+H]-	= 487.154242 Da
[M-H]+	= 485.137495 Da
[M-H]-	= 485.138592 Da
Log P	= 6.81+/- 0.66

XXI- Cyclohexanone + Benzaldehyde +Pyrimethamine



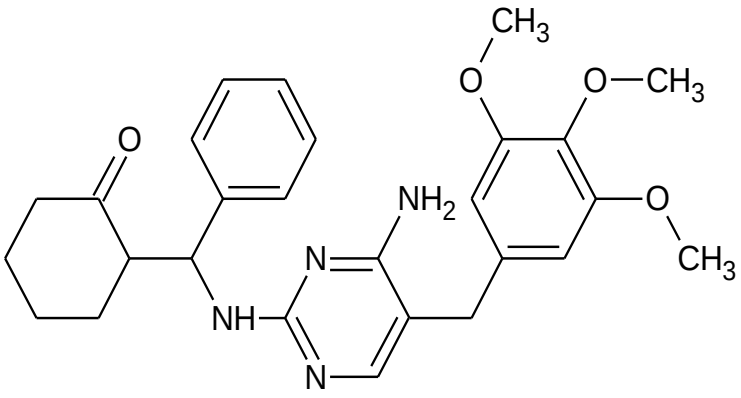
Molecular Formula	= $C_{25}H_{26}ClN_3O$
Formula Weight	= 419.94644
Composition	= C(71.50%) H(6.24%) Cl(8.44%) N(10.01%) O(3.81%)
Molar Refractivity	= 121.36 ± 0.3 cm^3
Molar Volume	= 342.3 ± 3.0 cm^3
Parachor	= 936.4 ± 6.0 cm^3
Index of Refraction	= 1.627 ± 0.02
Surface Tension	= 55.9 ± 3.0 dyne/cm
Density	= 1.226 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 48.11 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 419.17644 Da
Nominal Mass	= 419 Da
Average Mass	= 419.9464 Da
M+	= 419.175892 Da
M-	= 419.176989 Da
[M+H]+	= 420.183717 Da
[M+H]-	= 420.184814 Da
[M-H]+	= 418.168067 Da
[M-H]-	= 418.169164 Da
Log P	= 5.72+/- 0.66

XXII- P-nitro acetophenone + Benzaldehyde +Trimethoprim



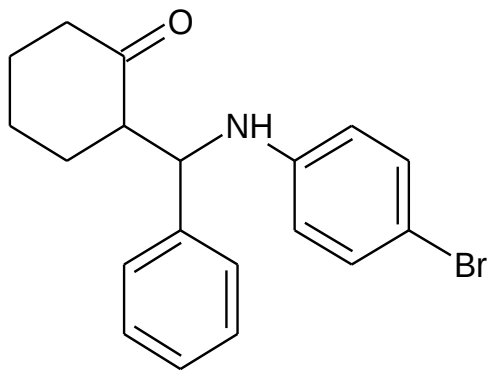
Molecular Formula	= $C_{29}H_{29}N_5O_6$
Formula Weight	= 543.57046
Composition	= C(64.08%) H(5.38%) N(12.88%) O(17.66%)
Molar Refractivity	= 150.89 ± 0.3 cm^3
Molar Volume	= 414.7 ± 3.0 cm^3
Parachor	= 1147.9 ± 4.0 cm^3
Index of Refraction	= 1.647 ± 0.02
Surface Tension	= 58.6 ± 3.0 dyne/cm
Density	= 1.310 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 59.82 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 543.211784 Da
Nominal Mass	= 543 Da
Average Mass	= 543.5705 Da
M+	= 543.211235 Da
M-	= 543.212332 Da
[M+H]+	= 544.21906 Da
[M+H]-	= 544.220157 Da
[M-H]+	= 542.20341 Da
[M-H]-	= 542.204507 Da
Log P	= 3.64+/- 0.97

XXIII- Cyclohexanone + Benzaldehyde +Trimethoprim



Molecular Formula	= $C_{27}H_{32}N_4O_4$
Formula Weight	= 476.56738
Composition	= C(68.05%) H(6.77%) N(11.76%) O(13.43%)
Molar Refractivity	= 135.91 ± 0.3 cm^3
Molar Volume	= 385.9 ± 3.0 cm^3
Parachor	= 1064.8 ± 6.0 cm^3
Index of Refraction	= 1.621 ± 0.02
Surface Tension	= 57.9 ± 3.0 dyne/cm
Density	= 1.234 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 53.88 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 476.242356 Da
Nominal Mass	= 476 Da
Average Mass	= 476.5674 Da
M+	= 476.241807 Da
M-	= 476.242904 Da
[M+H]+	= 477.249632 Da
[M+H]-	= 477.250729 Da
[M-H]+	= 475.233982 Da
[M-H]-	= 475.235079 Da
Log P	= 2.55+/- 0.97

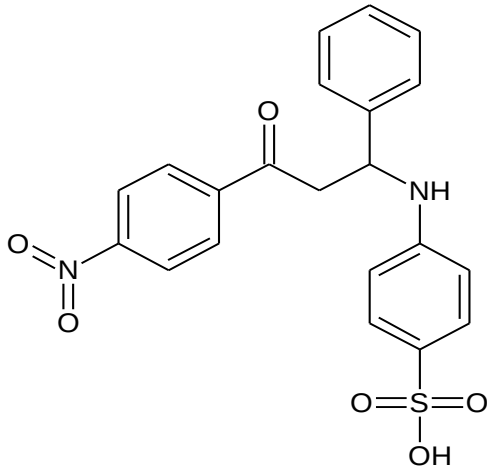
XXIV- Cyclohexanone + Benzaldehyde +P-Bromo Aniline



2-{[(4-bromophenyl)amino](phenyl)methyl}cyclohexanone

Molecular Formula	= $C_{19}H_{20}BrNO$
Formula Weight	= 358.2722
Composition	= C(63.70%) H(5.63%) Br(22.30%) N(3.91%) O(4.47%)
Molar Refractivity	= 93.84 ± 0.3 cm^3
Molar Volume	= 262.0 ± 3.0 cm^3
Parachor	= 708.8 ± 6.0 cm^3
Index of Refraction	= 1.635 ± 0.02
Surface Tension	= 53.5 ± 3.0 dyne/cm
Density	= 1.367 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 37.20 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 357.072819 Da
Nominal Mass	= 357 Da
Average Mass	= 358.2722 Da
M+	= 357.072271 Da
M-	= 357.073368 Da
[M+H]+	= 358.080096 Da
[M+H]-	= 358.081193 Da
[M-H]+	= 356.064446 Da
[M-H]-	= 356.065543 Da
Log P	= 4.53+/- 0.40

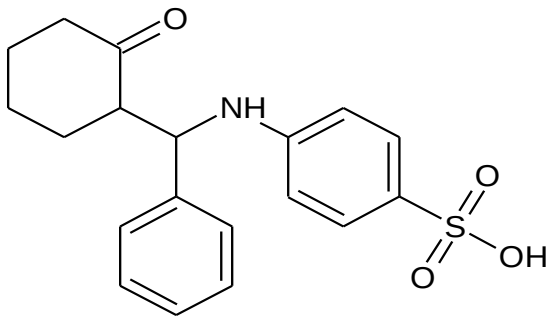
XXV- P-Nitro acetophenone + Benzaldehyde +P-Sulfanilic acid



4-{[3-(4-nitrophenyl)-3-oxo-1-phenylpropyl]amino}benzenesulfonic acid

Molecular Formula	= $C_{21}H_{18}N_2O_6S$
Formula Weight	= 426.44242
Composition	= C(59.15%) H(4.25%) N(6.57%) O(22.51%) S(7.52%)
Molar Refractivity	= 110.19 ± 0.4 cm^3
Molar Volume	= 297.3 ± 3.0 cm^3
Parachor	= 854.8 ± 6.0 cm^3
Index of Refraction	= 1.663 ± 0.02
Surface Tension	= 68.2 ± 3.0 dyne/cm
Density	= 1.433 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 43.68 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 426.088556 Da
Nominal Mass	= 426 Da
Average Mass	= 426.4424 Da
M+	= 426.088008 Da
M-	= 426.089105 Da
[M+H]+	= 427.095833 Da
[M+H]-	= 427.09693 Da
[M-H]+	= 425.080183 Da
[M-H]-	= 425.08128 Da
Log P	= 3.30+/- 0.37

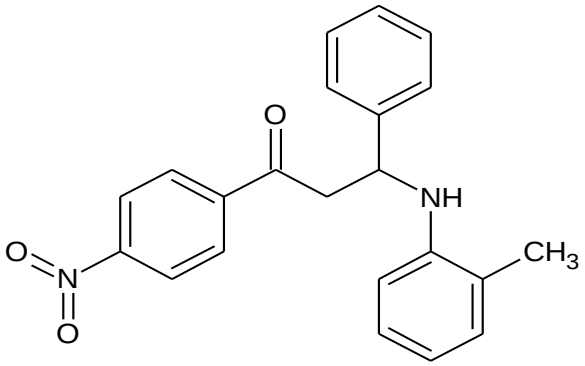
XXVI- Cyclohexanone + Benzaldehyde + P-Sulfanilic acid



4-{[(2-oxocyclohexyl)(phenyl)methyl]amino}benzenesulfonic acid

Molecular Formula	= $C_{19}H_{21}NO_4S$
Formula Weight	= 359.43934
Composition	= C(63.49%) H(5.89%) N(3.90%) O(17.80%) S(8.92%)
Molar Refractivity	= 95.90 ± 0.4 cm^3
Molar Volume	= 268.6 ± 3.0 cm^3
Parachor	= 752.7 ± 6.0 cm^3
Index of Refraction	= 1.632 ± 0.02
Surface Tension	= 61.6 ± 3.0 dyne/cm
Density	= 1.338 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 38.02 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 359.119128 Da
Nominal Mass	= 359 Da
Average Mass	= 359.4393 Da
M+	= 359.11858 Da
M-	= 359.119677 Da
[M+H]+	= 360.126405 Da
[M+H]-	= 360.127502 Da
[M-H]+	= 358.110755 Da
[M-H]-	= 358.111852 Da
Log P	= 2.32+/- 0.33

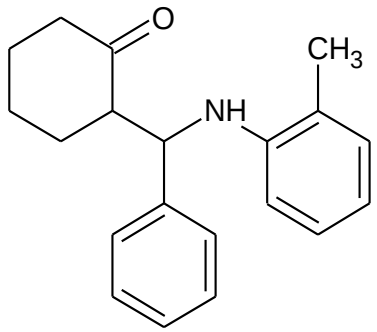
XXVII- P-Nitro acetophenone + Benzaldehyde +O-Toludine



3-[(2-methylphenyl)amino]-1-(4-nitrophenyl)-3-phenylpropan-1-one

Molecular Formula = $C_{22}H_{20}N_2O_3$
Formula Weight = 360.4058
Composition = C(73.32%) H(5.59%) N(7.77%) O(13.32%)
Molar Refractivity = 105.95 ± 0.3 cm^3
Molar Volume = 290.8 ± 3.0 cm^3
Parachor = 790.4 ± 4.0 cm^3
Index of Refraction = 1.648 ± 0.02
Surface Tension = 54.5 ± 3.0 dyne/cm
Density = 1.239 ± 0.06 g/cm^3
Dielectric Constant = Not available
Polarizability = 42.00 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass = 360.147393 Da
Nominal Mass = 360 Da
Average Mass = 360.4058 Da
M+ = 360.146844 Da
M- = 360.147941 Da
[M+H]+ = 361.154669 Da
[M+H]- = 361.155766 Da
[M-H]+ = 359.139019 Da
[M-H]- = 359.140116 Da
Log P = 4.80+/- 0.28

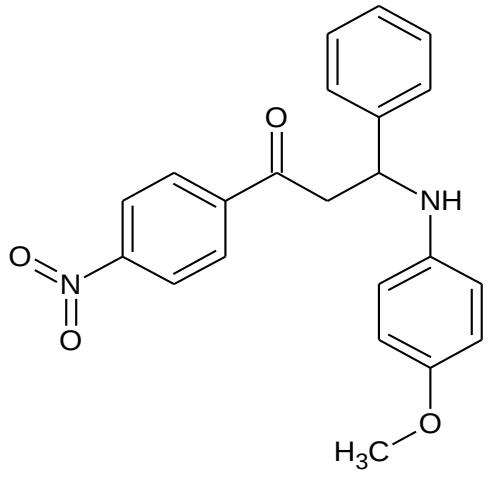
XXVIII- Cyclohexanone + Benzaldehyde + O-Toludine



2-{[(2-methylphenyl)amino](phenyl)methyl}cyclohexanone

Molecular Formula	= $C_{20}H_{23}NO$
Formula Weight	= 293.40272
Composition	= C(81.87%) H(7.90%) N(4.77%) O(5.45%)
Molar Refractivity	= 90.97 ± 0.3 cm^3
Molar Volume	= 262.1 ± 3.0 cm^3
Parachor	= 696.0 ± 6.0 cm^3
Index of Refraction	= 1.610 ± 0.02
Surface Tension	= 49.7 ± 3.0 dyne/cm
Density	= 1.119 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 36.06 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 293.177964 Da
Nominal Mass	= 293 Da
Average Mass	= 293.4027 Da
M+	= 293.177416 Da
M-	= 293.178513 Da
[M+H]+	= 294.185241 Da
[M+H]-	= 294.186338 Da
[M-H]+	= 292.169591 Da
[M-H]-	= 292.170688 Da
Log P	= 3.83+/- 0.29

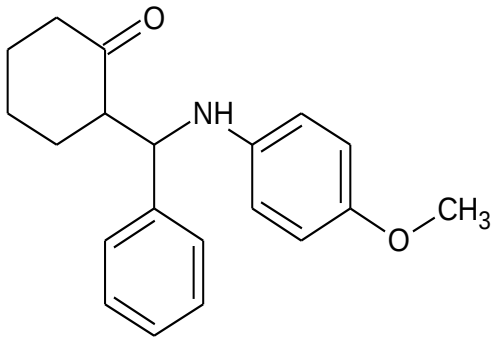
XXIX- P-Nitro acetophenone + Benzaldehyde + P- ancidine



3-[(4-methoxyphenyl)amino]-1-(4-nitrophenyl)-3-phenylpropan-1-one

Molecular Formula	= $C_{22}H_{20}N_2O_4$
Formula Weight	= 376.4052
Composition	= C(70.20%) H(5.36%) N(7.44%) O(17.00%)
Molar Refractivity	= 107.80 ± 0.3 cm^3
Molar Volume	= 298.6 ± 3.0 cm^3
Parachor	= 809.4 ± 4.0 cm^3
Index of Refraction	= 1.641 ± 0.02
Surface Tension	= 53.9 ± 3.0 dyne/cm
Density	= 1.260 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 42.73 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 376.142307 Da
Nominal Mass	= 376 Da
Average Mass	= 376.4052 Da
M+	= 376.141759 Da
M-	= 376.142856 Da
[M+H]+	= 377.149584 Da
[M+H]-	= 377.150681 Da
[M-H]+	= 375.133933 Da
[M-H]-	= 375.135031 Da
Log P	= 4.16+/- 0.37

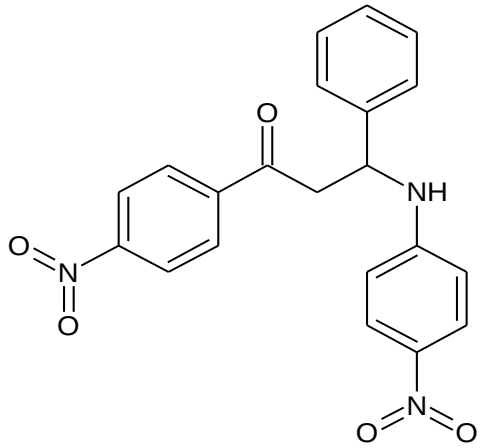
XXX- Cyclohexanone + Benzaldehyde + P- ancidine



2-{[(4-methoxyphenyl)amino](phenyl)methyl}cyclohexanone

Molecular Formula	= $C_{20}H_{23}NO_2$
Formula Weight	= 309.40212
Composition	= C(77.64%) H(7.49%) N(4.53%) O(10.34%)
Molar Refractivity	= 92.82 ± 0.3 cm^3
Molar Volume	= 269.8 ± 3.0 cm^3
Parachor	= 716.4 ± 6.0 cm^3
Index of Refraction	= 1.604 ± 0.02
Surface Tension	= 49.6 ± 3.0 dyne/cm
Density	= 1.146 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 36.80 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 309.172879 Da
Nominal Mass	= 309 Da
Average Mass	= 309.4021 Da
M+	= 309.17233 Da
M-	= 309.173428 Da
[M+H]+	= 310.180155 Da
[M+H]-	= 310.181253 Da
[M-H]+	= 308.164505 Da
[M-H]-	= 308.165603 Da
Log P	= 3.18+/- 0.31

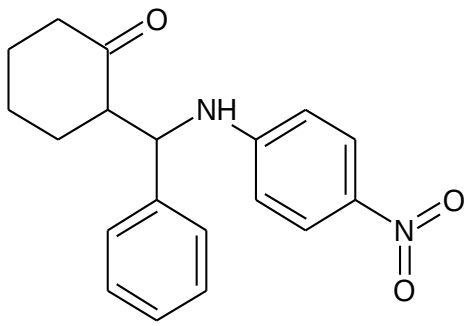
XXXI- P-Nitro acetophenone + Benzaldehyde + P- Nitro aniline



1-(4-nitrophenyl)-3-[(4-nitrophenyl)amino]-3-phenylpropan-1-one

Molecular Formula	= $C_{21}H_{17}N_3O_5$
Formula Weight	= 391.37678
Composition	= C(64.45%) H(4.38%) N(10.74%) O(20.44%)
Molar Refractivity	= 107.67 ± 0.3 cm^3
Molar Volume	= 286.4 ± 3.0 cm^3
Parachor	= 808.2 ± 4.0 cm^3
Index of Refraction	= 1.675 ± 0.02
Surface Tension	= 63.3 ± 3.0 dyne/cm
Density	= 1.366 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 42.68 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 391.116821 Da
Nominal Mass	= 391 Da
Average Mass	= 391.3768 Da
M+	= 391.116272 Da
M-	= 391.117369 Da
[M+H]+	= 392.124097 Da
[M+H]-	= 392.125194 Da
[M-H]+	= 390.108447 Da
[M-H]-	= 390.109544 Da
Log P	= 4.79+/- 0.37

XXXII- Cyclohexanone + Benzaldehyde + P- Nitro aniline



2-{[(4-nitrophenyl)amino](phenyl)methyl}cyclohexanone

Molecular Formula	= $C_{19}H_{20}N_2O_3$
Formula Weight	= 324.3737
Composition	= C(70.35%) H(6.21%) N(8.64%) O(14.80%)
Molar Refractivity	= 92.69 ± 0.3 cm^3
Molar Volume	= 257.6 ± 3.0 cm^3
Parachor	= 714.8 ± 6.0 cm^3
Index of Refraction	= 1.638 ± 0.02
Surface Tension	= 59.2 ± 3.0 dyne/cm
Density	= 1.258 ± 0.06 g/cm^3
Dielectric Constant	= Not available
Polarizability	= 36.74 ± 0.5 $10^{-24}cm^3$
Monoisotopic Mass	= 324.147393 Da
Nominal Mass	= 324 Da
Average Mass	= 324.3737 Da
M+	= 324.146844 Da
M-	= 324.147941 Da
[M+H]+	= 325.154669 Da
[M+H]-	= 325.155766 Da
[M-H]+	= 323.139019 Da
[M-H]-	= 323.140116 Da
Log P	= 3.81+/- 0.33

IR Spectra of the Mannich bases (I –IV)

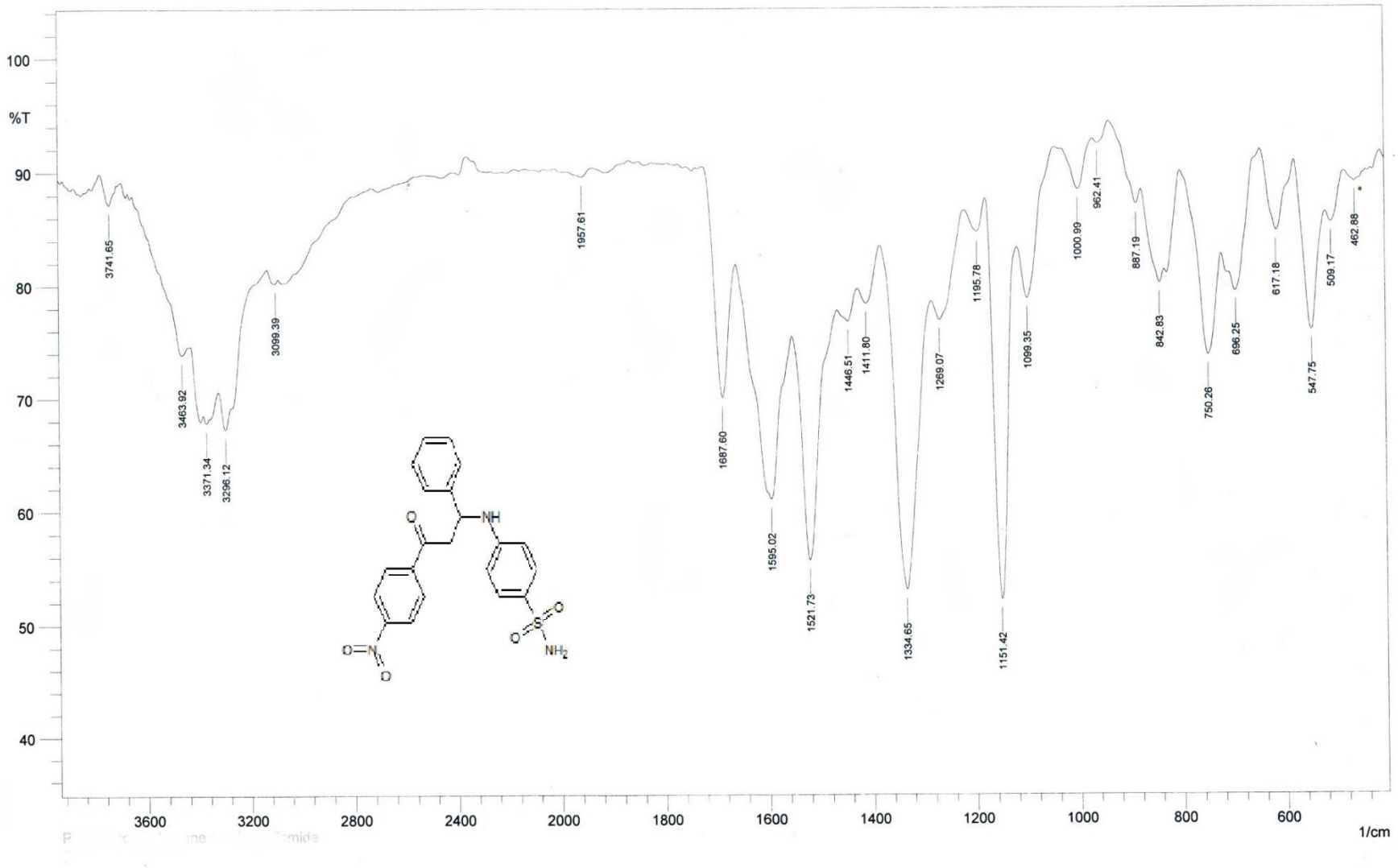


Figure 1 Mannich base (I)

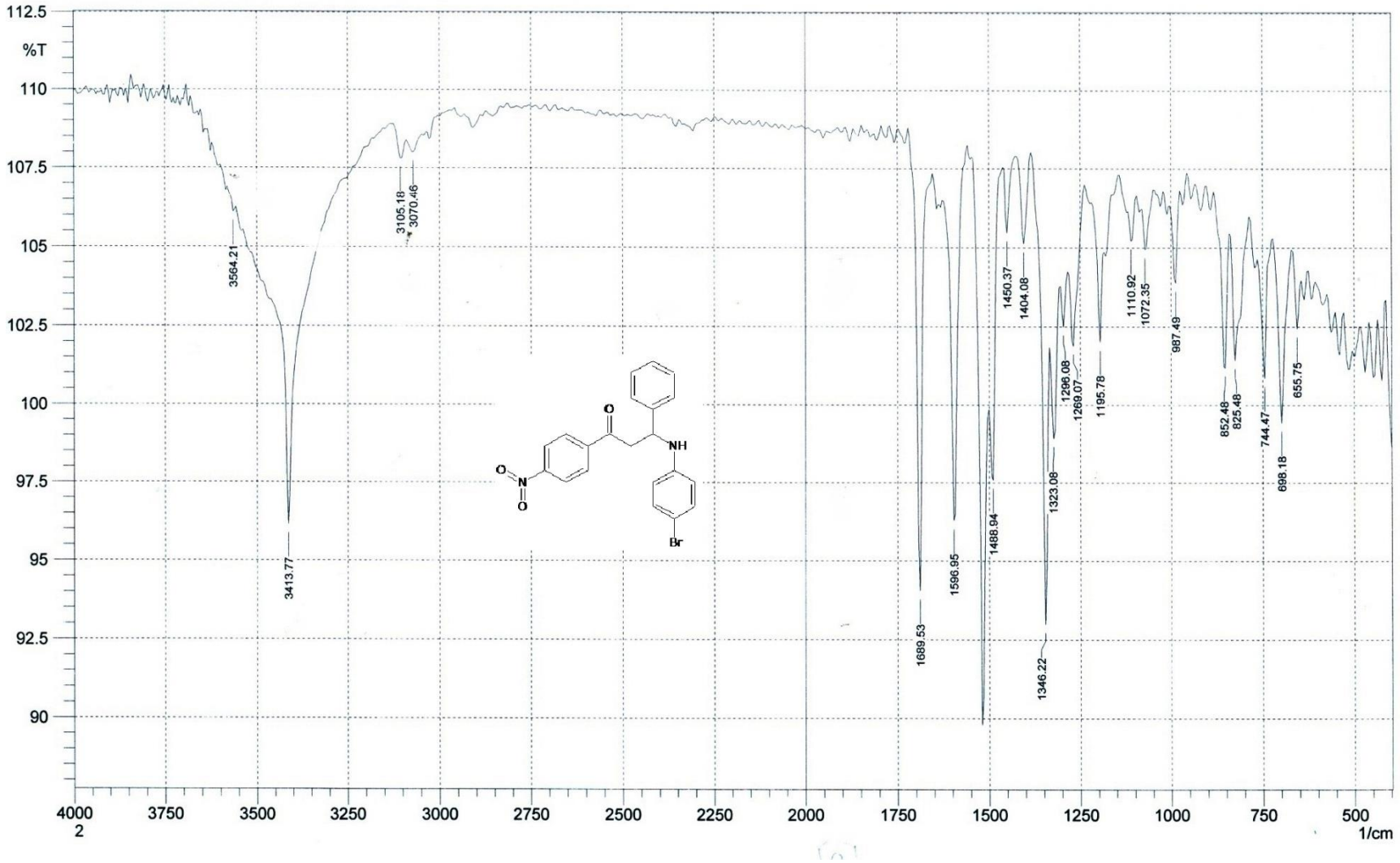


Figure 2 Mannich base (II)

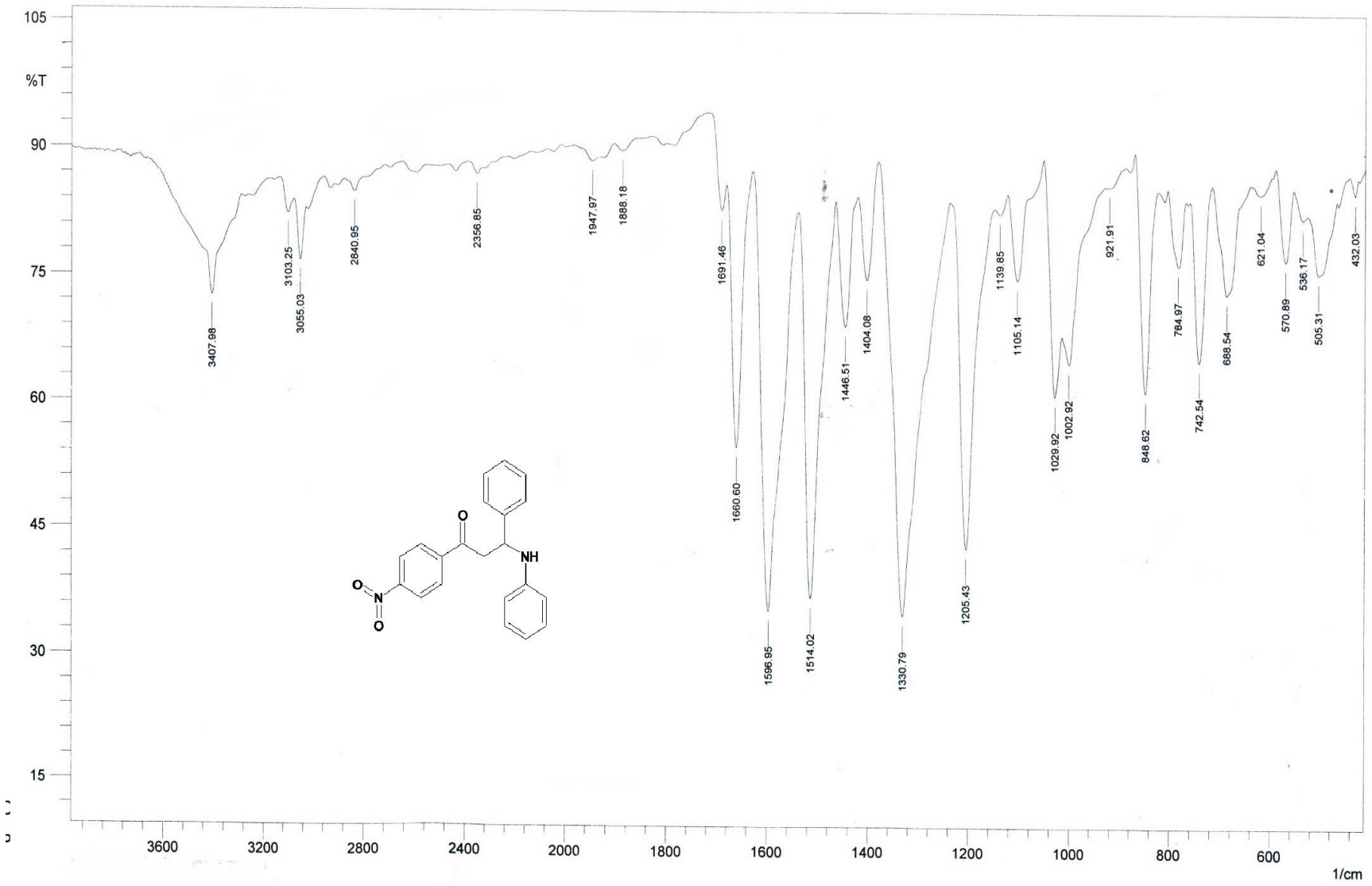


Figure 3 Mannich base (III)

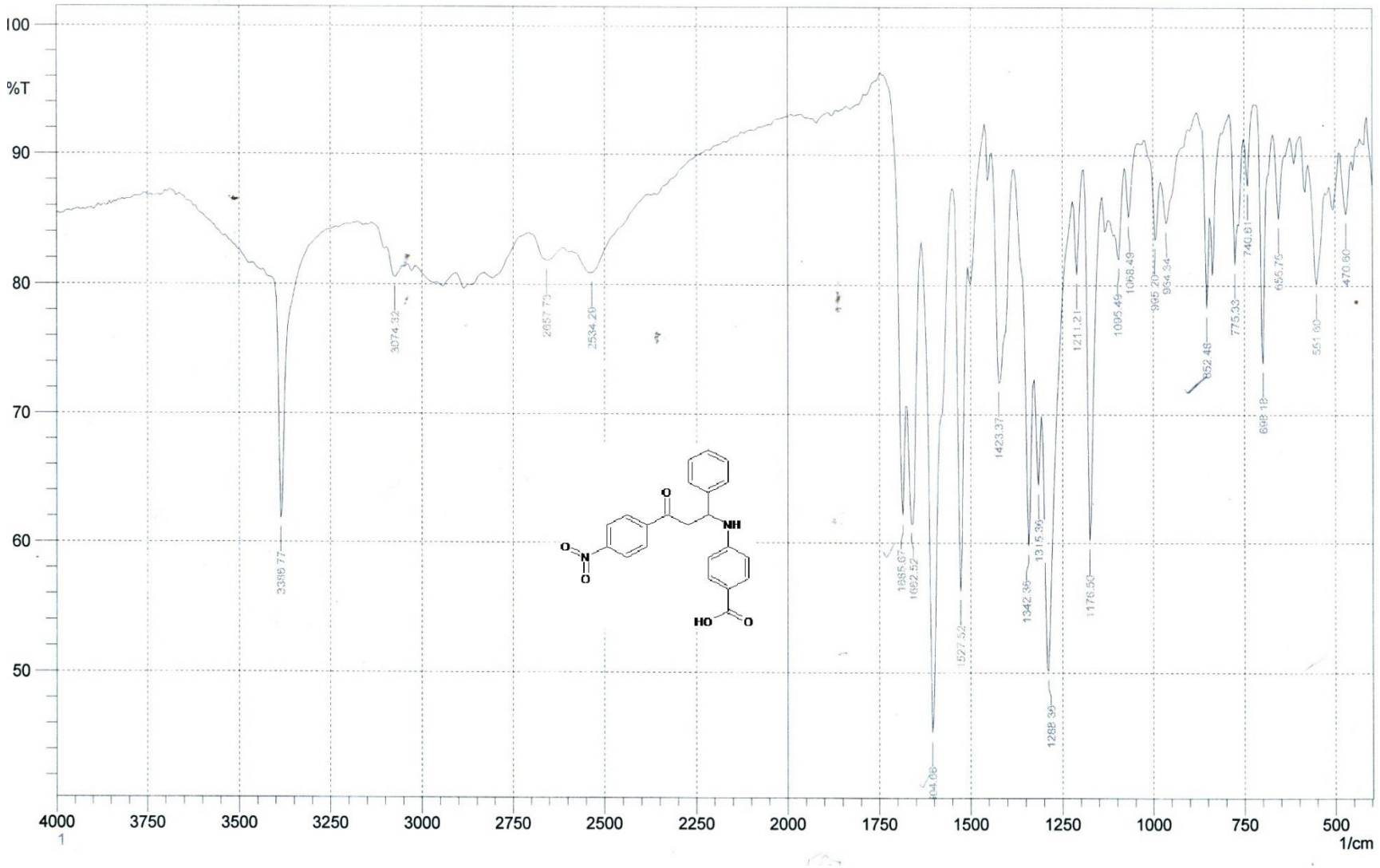


Figure 4 Mannich base (IV)

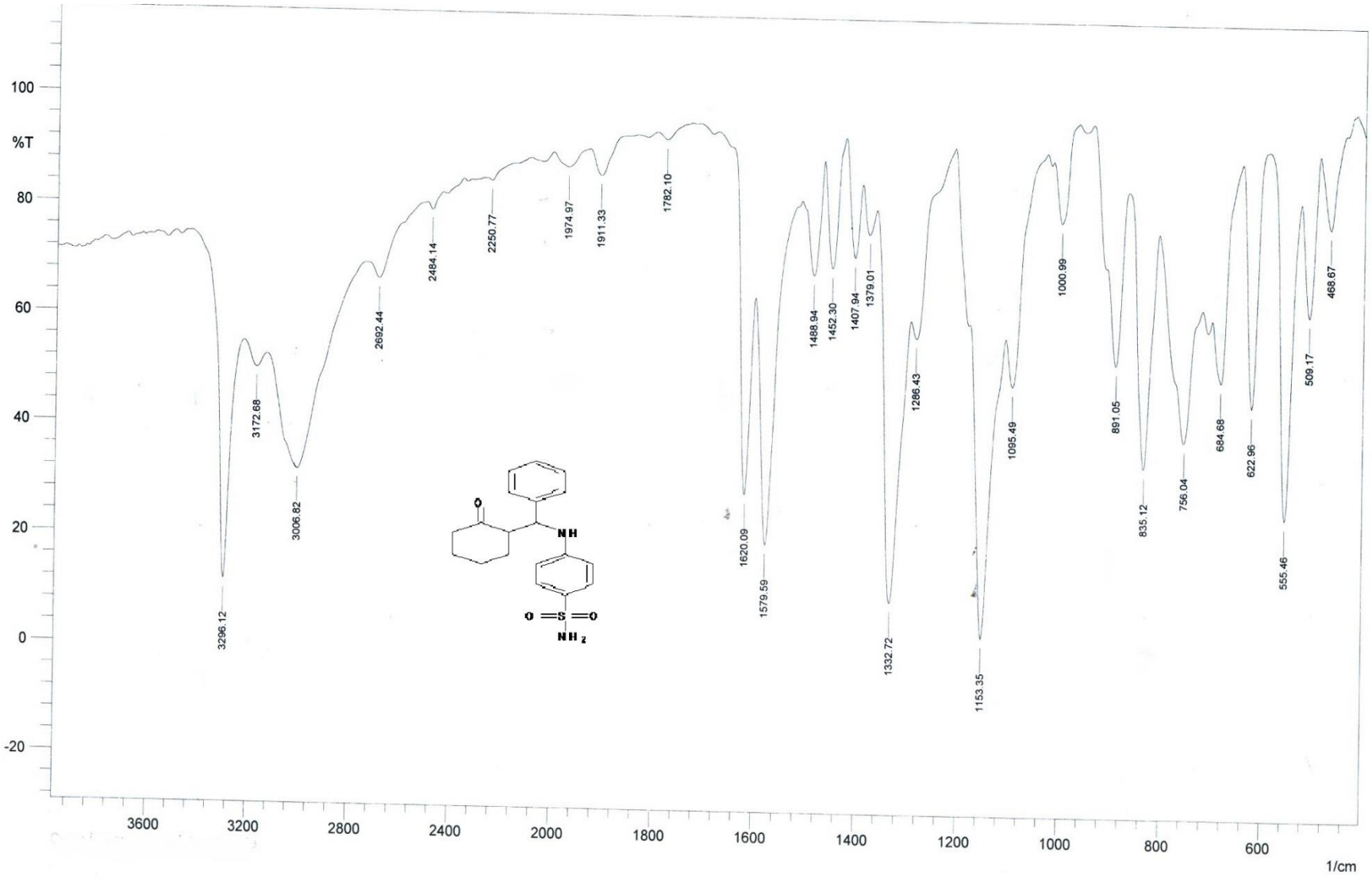


Figure 5 Mannich base (V)

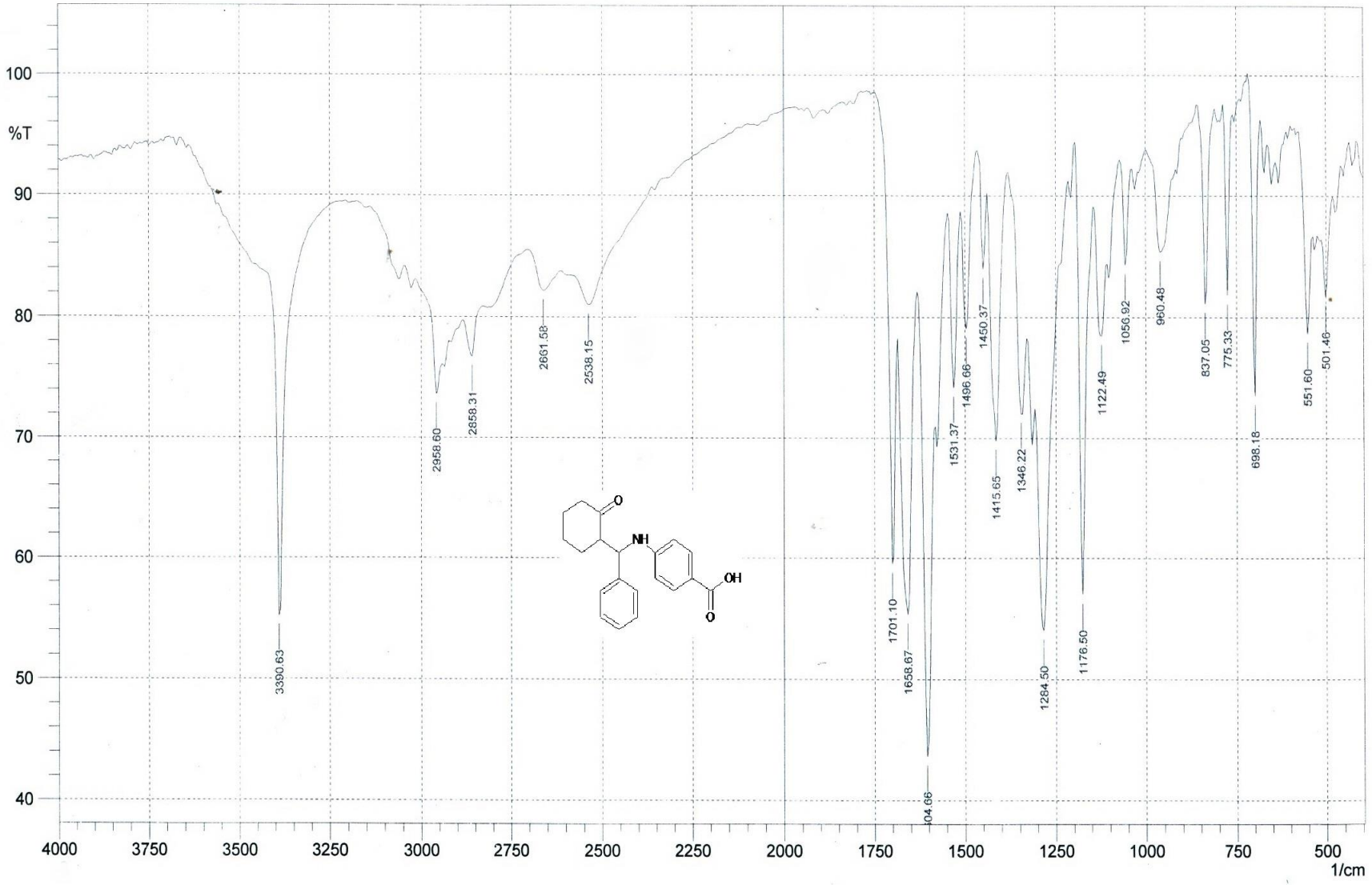


Figure 6 Mannich base (VI)

[1]HNMR spectra of the Mannich Bases (I - VI)

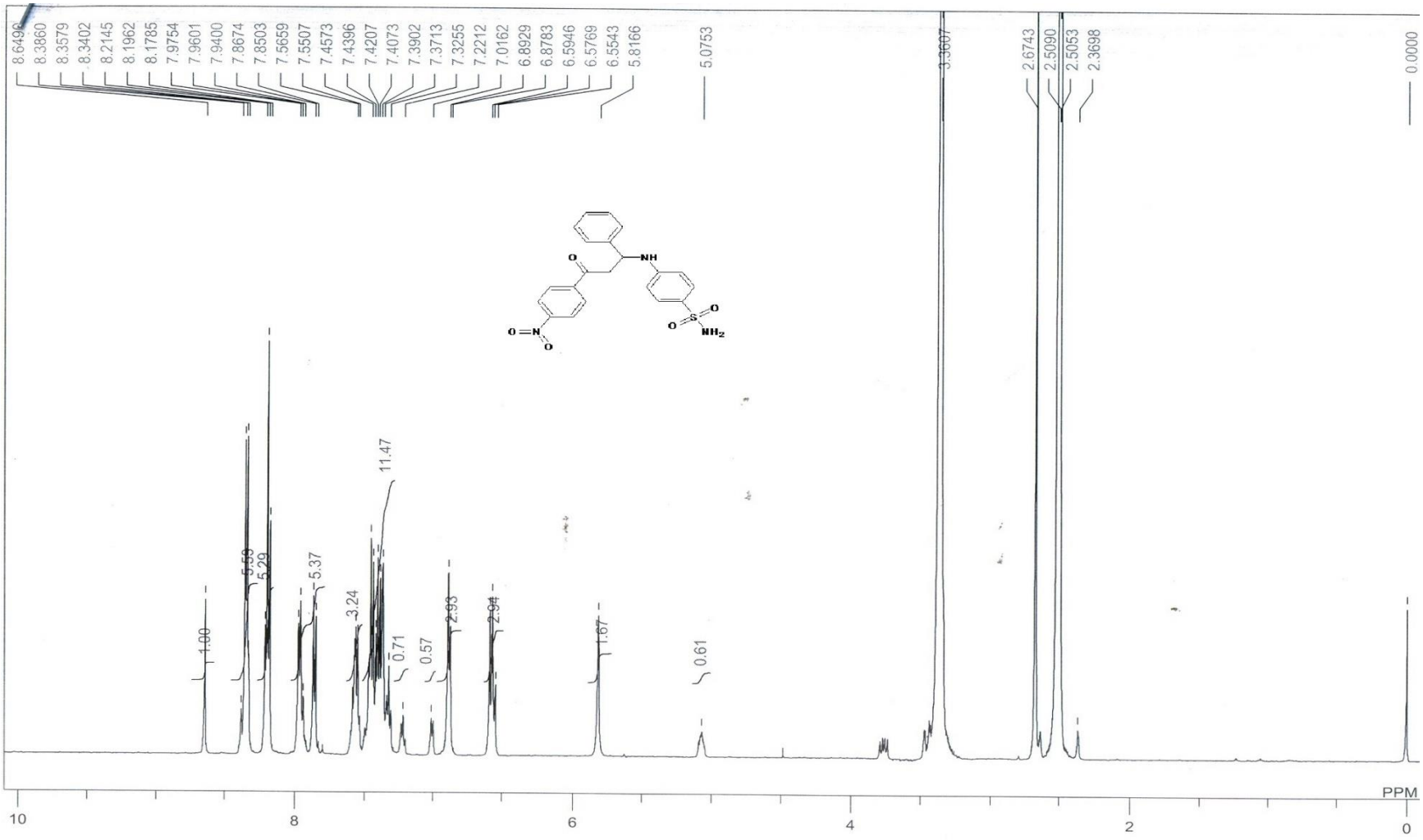


Figure 7 Mannich base (I)

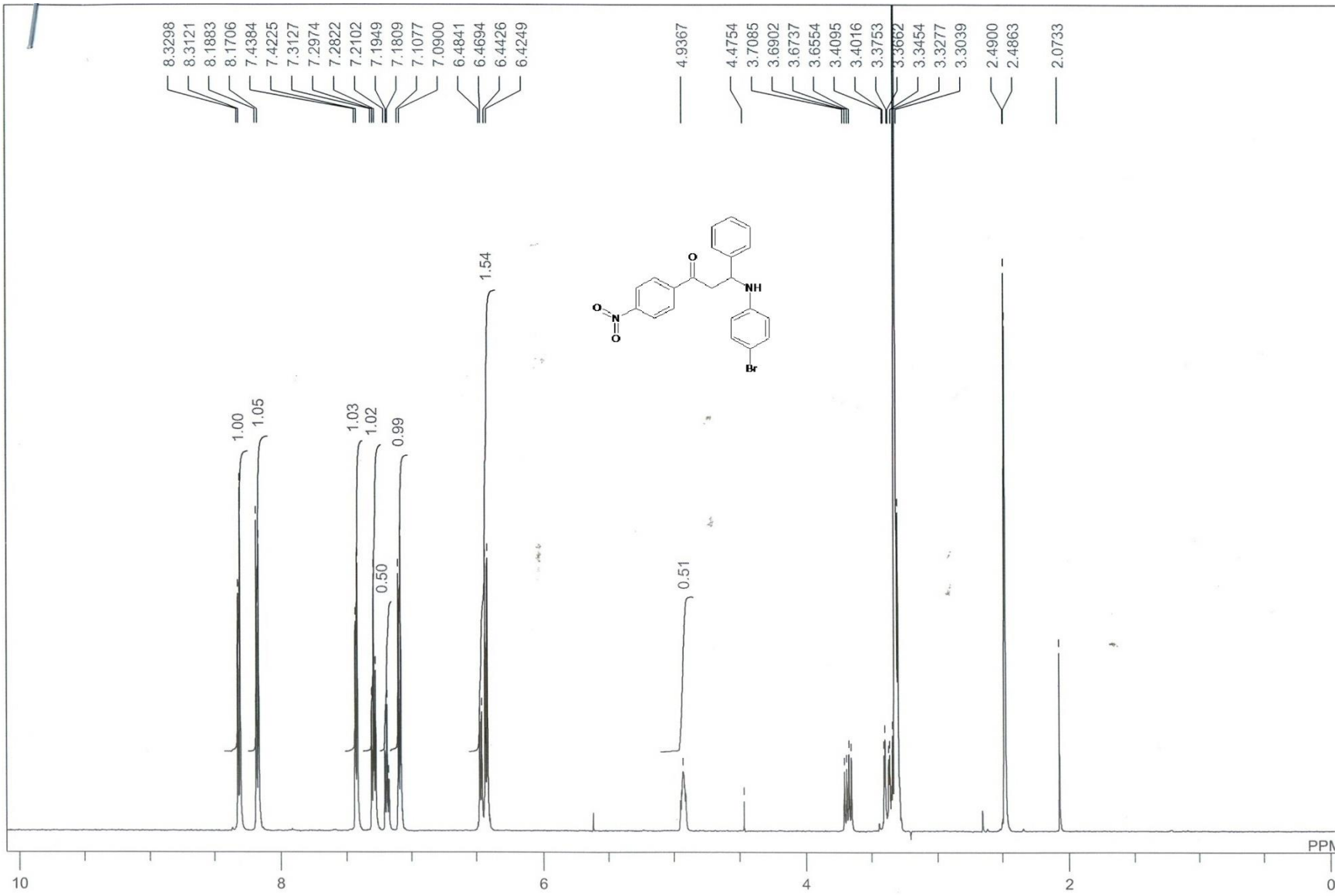


Figure 8 Mannich base (II)

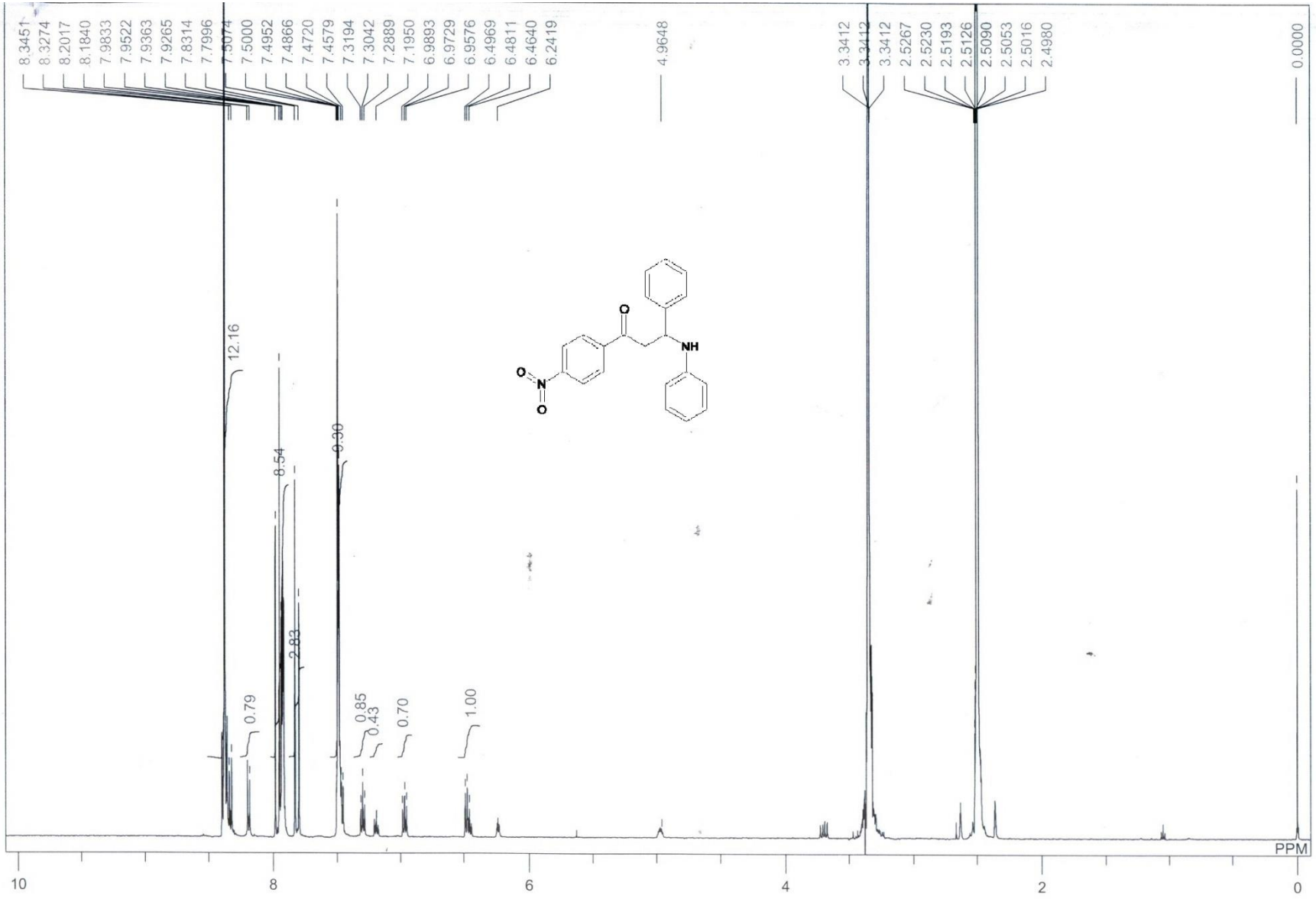


Figure 9 Mannich base (III)

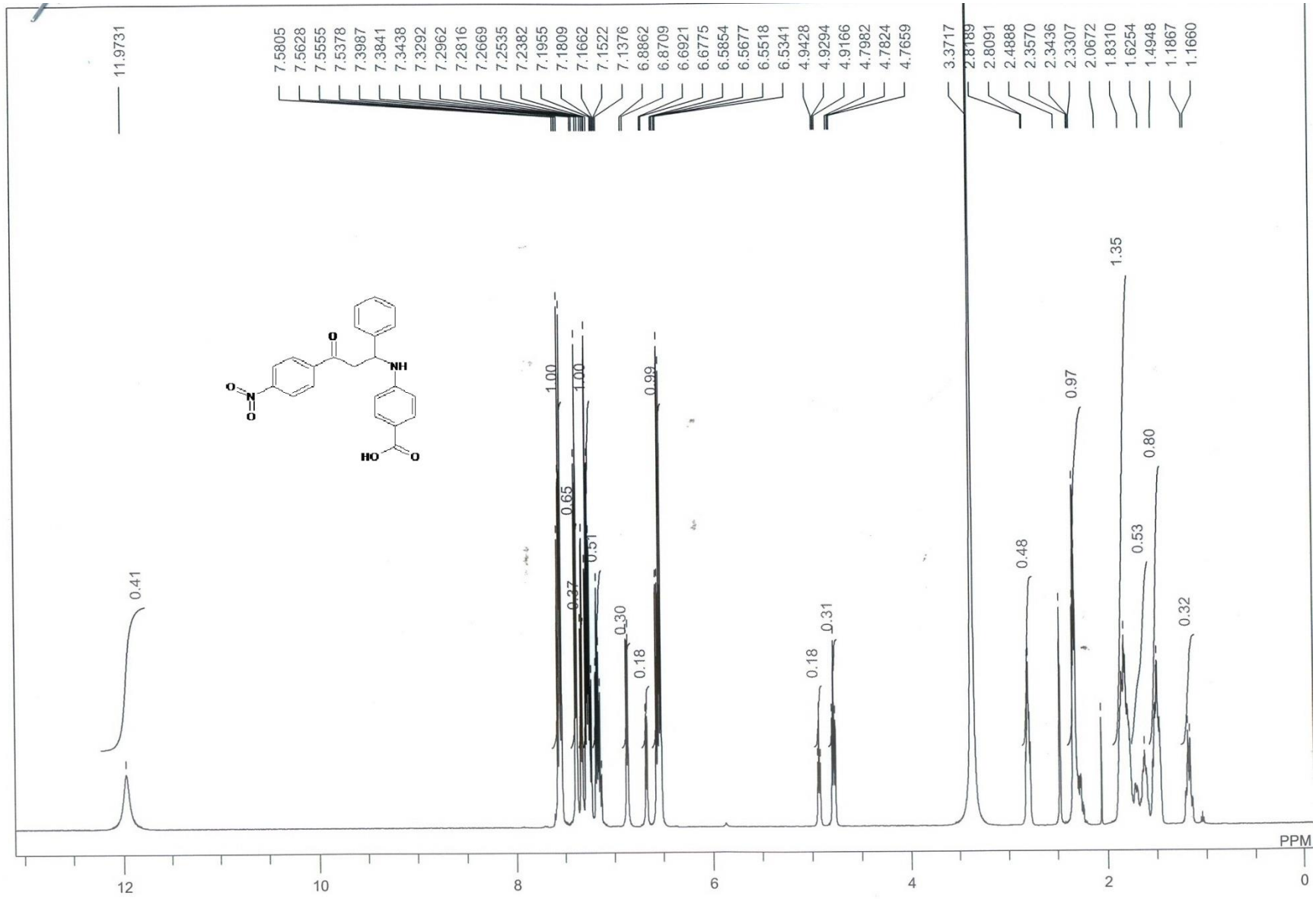


Figure 10 Mannich base (IV)

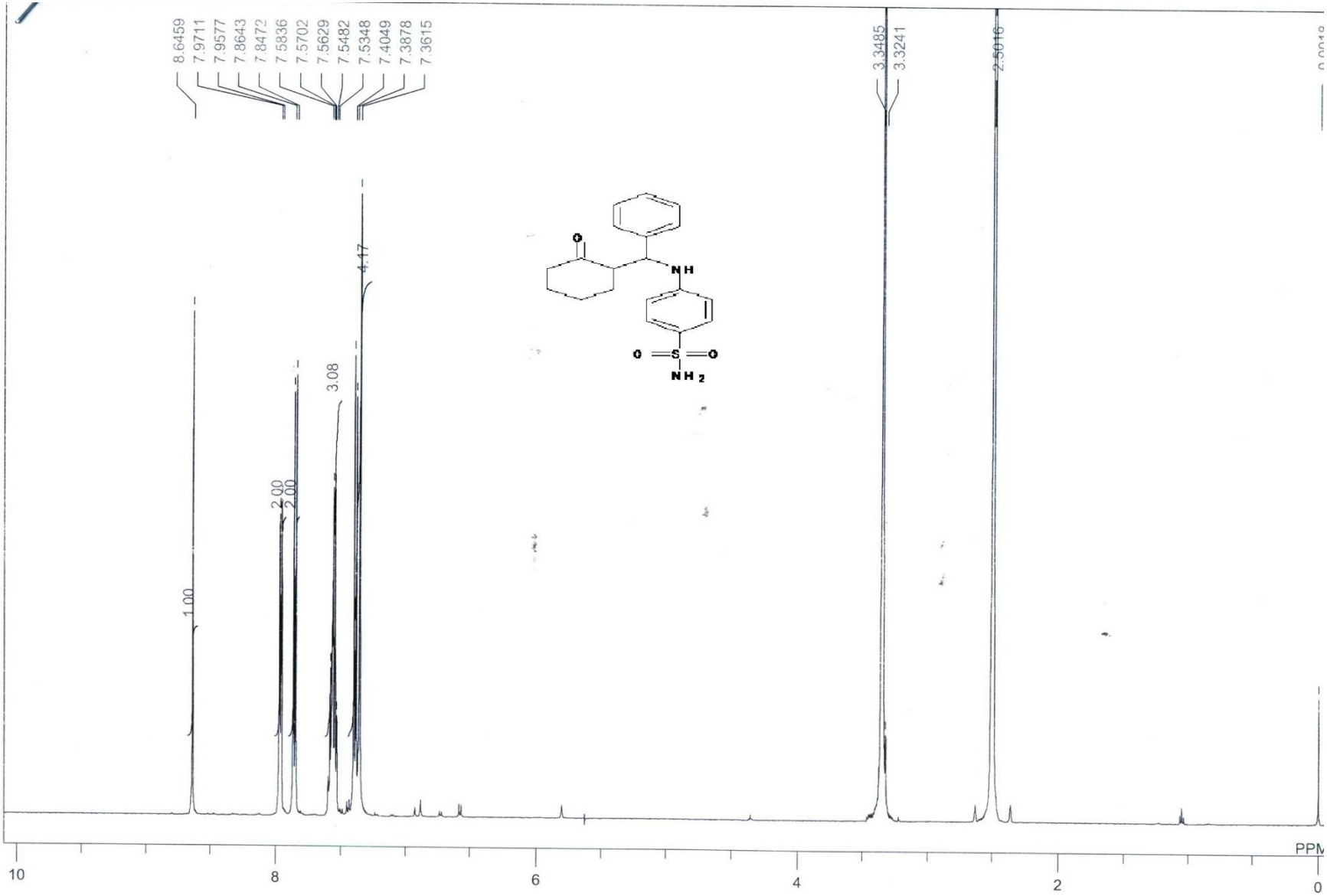


Figure 11 Mannich base (V)

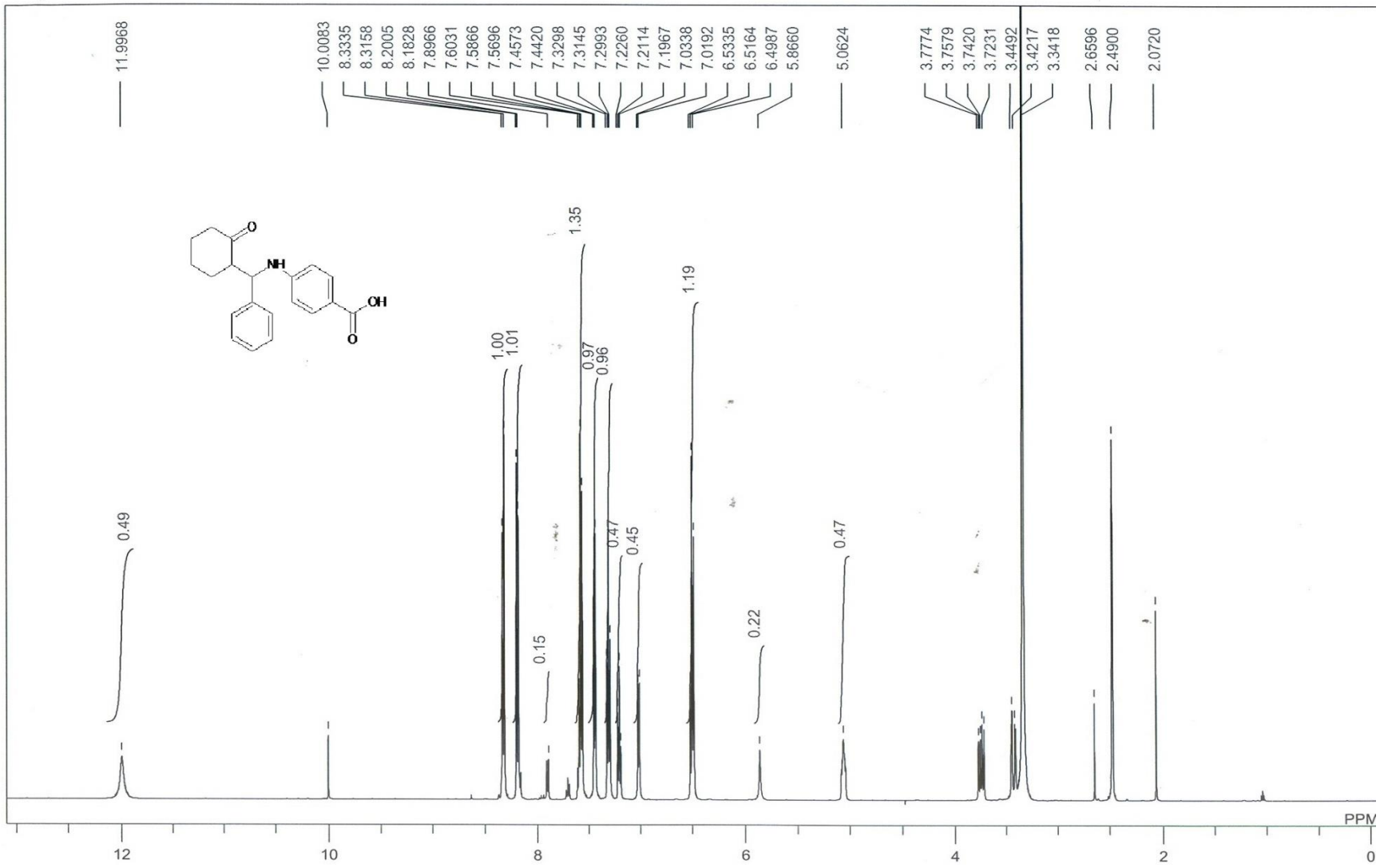


Figure 12 Mannich base (Vi)