Synthesis and Characterization of New Phthalimides linked to Schiff’s Bases

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By

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بسم الله الرحمن الرحيم

آنزل من السماوات هAtlantae أوحى بهمراه فاحتمل السائل زيدًا وليًا وهم يوقفون عليه في النار ابتغاء ملية أو مبانٍ زيد مثله كذاكل يضرِب الله الكيك والباطل فأنى الزيد فيحصبه جفاء وأهله ما ينفع الناس

فيمضي في الأرض كذاكل يضرب الله الأمثال (17)

صدق الله العظيم

{ سورة الرعد }

« الآية 17 »
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إلى من نهلت منه العلم، وأمدني بصنع الحياة، وعلمني سبيل العطاء، إلى من يبذل نفسه وحياته من أجل، إلى القلب الدافئ (والذي الغالي).

إلى من مرت بحياتي مرور الربيع في فصول ألسن، ولكن الربيع يعود، وهي لن تعود، إلى من أيقظت في نفسي قوى الصبر، إلى من رحلت عن الدنيا وتركنت قلبي يكسره الشوق لها (أمي رحما الله).

إلى أمي، في الحياة والذين أعطوني الدعم والقوة دائماً، فأشهد بهم أزري وأقوي بهم عزيمتي.

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Abstract

The present work involved synthesis of new phthalimides linked to Schiff’s bases through different strategies. The work was divided into four main parts:

1. The first part involved synthesis of phthalimides linked to Schiff bases through phenyl sulfonamido group [5-18] Scheme(1).

Performing this part include the following steps:
   b. Dehydration of the synthesized phthalamic acid by acetic anhydride and anhydrous sodium acetate as dehydrating agent producing N-phenyl phthalimide [2].
   c. The synthesized N-phenyl phthalimide was introduced in chlorosulfonation reaction producing phthalimidyl phenyl sulfonyl chloride [3].
   d. Phthalimidyl phenyl sulfonyl chloride was treated with hydrazine hydrate producing phthalimidyl phenyl sulfonyl hydrazine [4].
   e. Reaction of compound [4] with different aromatic aldehydes and ketones producing the target compounds [5-18].

2. The second part involved synthesis of new phthalimides linked to Schiff’s bases through phenyl sulfonate moiety [20-26] Scheme(2).

Performing this part involved the following steps:
b. Reaction of compound [19] with different primary aromatic amines producing the desired compounds [20-26].

3. The third part involved synthesis of new phthalimides linked to Schiff’s bases through phenyl sulfonate moiety [28-33] Scheme(3).

This part involved the following steps:

a. Synthesis of phthalimidyl phenyl sulfonate benzaldehyde [27] via reaction of the synthesized phthalimidyl phenyl sulfonyl chloride with 4-hydroxy benzaldehyde.

b. Reaction of compound [27] with different primary aromatic amines producing the desired compounds [28-33].

4. The fourth part involved synthesis of new phthalimides linked to Schiff’s bases through methylene group [35-40].

Performing this part includes the following steps:

a. Synthesis of N-[4-phenyl phenacyl] phthalimide [34] via reaction of phthalimide potassium salt with 4-phenyl phenacyl bromide.

b. Reaction of compound [34] with different primary aromatic amines producing the desired compounds [35-40] Scheme(4).

All the synthesized compounds were characterized by FT-IR spectroscopy and $^1$H-NMR, $^{13}$C-NMR spectra for some of them.

5. Antibacterial activity for some of the synthesized imides were evaluated against two types of bacteria and the results showed that most of them have a good antibacterial activity.
Scheme (1)
N-phenyl phthalimide [2] + Chlorosulfonic acid

4-(N-phthalimidyl) phenyl sulfonyl chloride [3]

4-hydroxy acetophenone

4-[4-(N-phthalimidyl) phenyl sulfonate] acetophenone [19]

Different primary aromatic amines

4-[4'-(N-phthalimidyl) phenyl sulfonate] methyl benzylidene

R = -H, -Cl, -O2N, -Cl., -NO2
[20-26]

Scheme (2)

4-hydroxy benzaldehyde

4-[4'-N-phthalimidyl) phenyl sulfonyl] benzaldehyde [27]

Different primary aromatic amines

[28-33]

4-[4'(N-phthalimidyl) phenyl sulfonyl] benzylidene

R = H, H₃C, O₂N, Cl, Cl, CH₃, NO₂

Scheme (3)
unsubstituted Phthalimide \[\text{KOH (alcoholic)}\] phthalimide potassium salt

\[\text{4-phenyl phenacyl bromide}\]

\[\text{N-(4-phenyl phenacyl) phthalimide [34]}\]

Different primary aromatic amines

\[\text{N-phthalimidyl-4-phenyl benzylidene methane [35-40]}\]

\[R = \text{Br, HO, OH, Cl, CH}_3, \text{NO}_2\]

Scheme (4)
1-1- Schiff’s bases

A Schiff’s base is a type of chemical compounds containing carbon-nitrogen double bond $[\equiv N \equiv C]$ in which nitrogen atom connected to aryl or alkyl group, these compounds were named after Hugo Schiff \(^{(1)}\) since their synthesis was first reported by Schiff, they have the following general structure.

$$\begin{align*}
\text{R}_1 & \text{C} \equiv \text{N} \text{R}_3 \\
\text{R}_2 & \quad (\text{R}_1, \text{R}_2, \text{R}_3 \text{ are aryl or alkyl groups})
\end{align*}$$

The role of \( \text{R}_3 \) group is to stabilize the iminic Schiff’s base. Structurally a Schiff’s base (also known as imine or azomethine) is a nitrogen analogue of an aldehyde or ketone in which the carbonyl group (C=O) has been replaced by an imine or azomethine group.

Schiff’s bases of aliphatic aldehydes are unstable and readily polymerizable while those of aromatic aldehydes having an effective conjugation system are more stable\(^{(2)}\).

The most common method for preparation of Schiff’s bases involved acid-catalyzed condensation reaction of an amine and aldehyde or ketone under refluxing conditions\(^{(3,4)}\).

The first step in this reaction involved nucleophilic addition which leads to the formation of unstable carbinol amine intermediate which loses a molecule of water in the second step forming the corresponding imine.

$$\begin{align*}
\text{R}_1 \text{C} = \text{O} + \text{R}_3 \text{NH}_2 & \rightleftharpoons \text{R}_1 \overset{\ominus}{\text{O}} \text{H} \text{R}_2 \text{C} \equiv \text{N} \text{R}_3 & \rightleftharpoons \text{R}_1 \overset{\ominus}{\text{OH}} \text{H} \text{R}_2 \text{C} \equiv \text{N} \text{R}_3 + \text{H}_2 \text{O} \\
\text{Carbinol amine} & \quad \text{intermediate}
\end{align*}$$
1-2- Synthesis of Schiff’s bases

The first preparation of imines was reported in the 19th century by Schiff’s (1864). Since then a variety of methods for the synthesis of imines have been described(5).

The classical synthesis reported by Schiff’s involves condensation of carbonyl compound with an amine under azeotropic distillation(6), molecular sieves are then used to remove the formed water. In 1990s an in situ method for water elimination was developed using dehydrating solvents such as tetramethylorthosilicate or trimethylorthoformate(7,8).

In 2004, Chakraborti et al.(9) demonstrated that the efficiency of these methods is dependent on the use of highly electrophilic carbonyl compounds and strongly nucleophilic amines.

They proposed use of substances that function as Bronsted-Lowry or Lewis acids to activate the (C=O) of aldehydes, catalyze the nucleophilic attack by amines and eliminate water as the final step.

Examples of the used Bronsted-Lowry or Lewis acids include: ZnCl₂, alumina, TiCl₄, H₂SO₄, CH₃COOH and HCl(10-15).

In the 12 past years a number of innovations and new techniques have been reported, including solvent-free/ clay/microwave irradiation, solid-state synthesis, water suspension medium, NaHSO₄-SiO₂/ microwave/ solvent-free and solvent-free/CaO/microwave(16-19).

Among these innovations microwave irradiation has been extensively used due to its operational simplicity, enhanced reaction rates and selectivity(19).

In 2001 Roman and Andrei(15) synthesized twenty new Schiff’s bases with a potential biological activity resulted from the acid-catalyzed condensation of orthophenolic aldehydes with several aromatic and hetero aromatic amines in ethanol.
Yang et al. (22) performed a microwave-assisted preparation of a series of Schiff's bases via efficient condensation of salicylaldehyde and aryl amines without solvent. On the other hand, eight new Schiff's bases [2a-h] were prepared in excellent yields via the condensation of different aromatic amines and azoaldehyde [1] 2-hydroxy-3-methoxy-5-(4-methoxyphenylazo) benzaldehyde in dry dichloromethane in the presence of anhydrous MgSO₄ (23).

\[
\begin{align*}
\text{OH} & \quad \text{CHO} \\
\text{H}_2\text{SO}_4 & \quad \text{(Catalyst)} \\
\text{reflux} & \\
\end{align*}
\]

\[
R_1, R_2, R_3 = \text{H, Br, I}
\]

\[
\begin{align*}
\text{Ar =} & \\
\text{CH}_3 & \quad \text{Cl} & \quad \text{Cl} & \quad \text{Cl} & \quad \text{CO}_2\text{CH}_3 & \quad \text{CO}_2\text{CH}_3
\end{align*}
\]

In this method microwave irradiation plays an important role for promoting condensation reaction of aldehyde and amine thus reaction is performed within (0.5min.-4mins.).
Treatment of two moles of azoaldehyde [1] with one mole of 4,4'-diaminodiphenyl ether in refluxing absolute ethanol gave in excellent yields the two novel compounds [3a-b].

The new ten Schiff's bases [2a-h] and [3a-b] showed different antibacterial activities on testing against five types of bacteria.

Also several Schiff's bases [5a-d] were synthesized by Baluja et al. via condensation of sulfanilamide [4] with aromatic aldehydes.
The same team synthesized several Schiff’s bases \([7a-d]\) via refluxing 5-ethyl resacetophenone \([6]\) with aniline derivatives in methanol in the presence of anhydrous \(\text{ZnCl}_2\).

\[
\begin{align*}
\text{HO} & \quad \text{COCH}_3 \\
\text{H}_4\text{C}_2 & \\
\end{align*}
\]

\([6]\)

\[
\begin{align*}
\text{NH}_2 & \quad \text{R}_1 \\
\text{R}_2 & \\
\text{R}_3 & \\
\end{align*}
\]

\([7a-d]\)

These Schiff’s bases \([5a-d]\) and \([7a-d]\) showed good antimicrobial activity against different types of bacteria and fungi.

Since coumarin derivatives are of great interest due to their role in natural and synthetic organic chemistry and many coumarin containing products exhibit biological activity, coumarins containing a Schiff’s base are expected to have enhanced biological activities, so according to this satyanarayana and coworkers\(^{(25)}\) synthesized a series of new Schiff’s bases containing coumarin moiety by the condensation of aryl/hetero aromatic aldehydes with 2-\([(4\text{-methyl-2-oxo-2H-chromen-7-yl})\text{oxy}]\text{acetohydrazide}\) \([8]\) under conventional and microwave conditions.

\[
\begin{align*}
\text{H}_2\text{N-HN} & \quad \text{O} \\
\text{CH}_3 & \\
\end{align*}
\]

\([8]\)

\[
\begin{align*}
\text{R} & = \cdot \text{H}, \cdot \text{NO}_2, \cdot \text{Cl}, \cdot \text{OH}, \cdot \text{OCH}_3, \cdot \text{N(CH}_3)_2 \\
\end{align*}
\]

\([9a-f]\)

The synthesized compounds have been screened for antimicrobial activity.

Non classical methods including water based reaction, microwave and grindstone chemistry were used by Naqvi\(^{(26)}\) and coworkers for the preparation of Schiff’s bases \([10a-f]\) from 3-chloro-4-fluoroaniline and several benzaldehydes.
The key raw materials were allowed to react in water, under microwave irradiation and grindstone.

These methodologies constitute an energy efficient and environmentally benign greener chemistry version of the classical condensation reactions for Schiff's bases formation\(^{(27,28)}\).

Water has been proved here as a suitable (green solvent) for the synthesis of Schiff's bases and increase in %yield is in following order = Method C \(<\) Method B \(<\) Method A (grindstone) \(<\) (Microwave) \(<\) (Water based synthesis)

S. Kumar et al.\(^{(28)}\) synthesized ten Schiff's bases of sulfonamides by condensing 4-aminobenzene sulfonamide with different aromatic aldehydes in the presence of glacial acetic acid and ethanol at (50-60)\(^{\circ}\)C.

The antimicrobial activity of these compounds were examined against different Gram-positive, Gram-negative bacteria and fungal strains. The presence of azomethine and sulfonamide functional group is responsible for antimicrobial activity.

On the other hand G. Kumar et al.\(^{(29)}\) synthesized new Schiff's base via mixing a warm dilute ethanolic solution of thiocarbohydrazide with 2-amino-4-ethyl-5-hydroxy benzaldehyde under reflux for 2hrs.
Complex of Cr, Mn and Fe with this Schiff's base were prepared. The Schiff's base ligand and their complexes were tested for their antimicrobial activity against many types of bacteria and fungi. The Cr(III) Complex showed the best antimicrobial activity but the ligand alone was found to be active against the fungus *trichoderma reesei*.

Yang and Sun (30) prepared Schiff's base [9] 4-methyl-N-(3,4,5-trimethoxy benzylidene)benzene amine by three different ways.

The first one involved introducing a mixture of p-toluidine, 3,4,5-trimethoxy benzaldehyde, neutral alumina and dichloromethane into microwave oven irradiated for 4 mins.

While in the second way a solution of the two mentioned reactants in benzene was heated in reflux until no water appear then removing solvent in vaco.

The third method involved addition of anhydrous MgSO₄ to a solution of trimethoxy benzaldehyde and p-toluidine in dichloromethane followed by stirring for 2hrs. at room temperature. Comparison the results of the three methods shown in Table (1-1) indicated that microwave method is the most convenient one since it affords higher yields in shorter reaction time, clean and cheap.
Schiff’s bases have been widely used in many fields e.g. biological, inorganic, analytical drug synthesis and as bidentate ligand in the field of coordination chemistry.

The Schiff’s base complexes have been used in catalytic reactions and also have been used as fine chemicals and medical substrates. Schiff’s bases form a significant class of compounds in medicinal and pharmaceutical chemistry with several biological applications that include antibacterial, antifungal, antimalarial, antitumor, antitubercular, anti-inflammatory, antimicrobial, antiviral, and herbicidal activities.

Also Schiff’s bases are important class of ligands due to their synthetic flexibility, their selectivity and sensitivity towards the central metal atom.

The imine group present in such compounds has been shown to be critical to their biological activities.

Anticancer activities of three Schiff’s bases N-(1-phenyl-2-hydroxy-2-phenyl ethyldene)-2,4-dinitro phenyl hydrazine (PDH), N-(1-phenyl-2-hydroxy-2-phenyl ethyldene)-2-hydroxy phenyl imine (PHP) and N-(2-hydroxy benzylidine)-2-hydroxy phenyl imine (HHP) against Ehrlich
ascities carcinoma (EAC) cells in Swiss albino mice have been studied\(^{85}\).

These compounds enhanced life span, reduced average tumor weight and inhibited tumor cell growth of EAC cell bearing mice.

\[
\begin{align*}
\text{PDH} & \quad \text{PHP} \\
\text{HHH} &
\end{align*}
\]

### 1-4- Cyclic imides

Cyclic imides such as maleimide \([10]\), succininide \([11]\), phthalimide \([12]\), glutarimide \([13]\), and citraconimide \([14]\) are cyclic organic compounds, their molecules contain an imide ring and the general structure \((-\text{CO-N(R)-CO-})\)^{86}.

\[
\begin{align*}
\text{[10]} & \quad \text{[11]} & \quad \text{[12]} \\
\text{[13]} & \quad \text{[14]}
\end{align*}
\]

These cyclic imides are an important functionality which have been found to maintain significant biological activity\(^{87,88}\).
1-5- Methods for synthesis of cyclic imides

Synthesis of cyclic imides may be performed by many methods including

1-5-1- Dehydration of amic acids by using dehydrating agents

The most common method used for preparation of cyclic imides involved dehydration of amic acids by using different dehydrating agents. Amic acids are organic compounds containing both carboxyl and amide groups in their molecules and can be prepared easily with excellent yields via reaction of cyclic anhydrides with different aliphatic or aromatic amines\(^{(89-95)}\).

Treatment of amic acids with suitable dehydrating agents lead to dehydration and cyclization producing the corresponding cyclic imides as shown in Scheme (1-1).

![Scheme (1-1)](image)

The most important dehydrating agents used in dehydrating of amic acids to the corresponding imides include:

1- Acetic anhydride with anhydrous sodium acetate\(^{(96-104)}\).
2- Thionyl chloride\(^{(105-107)}\).
3- Acetyl chloride with triethyl amine\(^{(108,109)}\).
4- Phosphorus trichloride\(^{(110,111)}\).
5- Phosphorus pentaoxide\(^{(112)}\).
1-5-2- Thermal Dehydration

This method has been used for preparation of imides whenever dehydration agents failed to do so\(^\text{113,114}\).

Al-Azzawi\(^\text{115}\) applied this method successfully in the preparation of several N-substituted citraconimides in high yields (85-90\%).

Also Al-Azzawi and Al-Obaidi\(^\text{116}\) performed synthesis of several N-(hydroxy phenyl)phthalimides by depending on fusion method. Moreover Al-Azzawi and Ali\(^\text{117-120}\) synthesized a series of N-(hydroxy phenyl) maleimides and N-(hydroxy phenyl) citraconimides in high yields and purity by application of this method.

\[ \text{COOH} \text{CONH} \text{OH} \xrightarrow{\text{Fusion}} \text{CONH} \text{OH} \]
(R = H or CH\(_3\))

1-5-3- Gabriel Type Synthesis

This method involved treatment of potassium salt of unsubstituted succinimide and phthalimide with different alkyl halides producing the corresponding N-substituted imides\(^\text{121}\).

\[ \text{CONH} + \text{KOH} \xrightarrow{\text{Fusion}} \text{CONH} \]

\[ \text{CONH} \xrightarrow{\text{Br(CH$_2$)$_2$OH}} \text{CONH} \]

Scheme (1-2)
1-5-4- Diels-Alder Adducts

Maleimide and substituted maleimides can be prepared by heating maleic anhydride with cyclopentadiene to form Diels-Alder adduct [15] which was then converted to imide [15] by reaction with amine.

Heating of [16] would produce N-substituted maleimide\(^{(122)}\) as shown in Scheme (1-3)

\[
\begin{array}{c}
\text{C}_{6}H_{5} + \text{CH}_{2}=\text{CH}-\text{CH}=	ext{CH}-\text{CH}=\text{CH}-\text{CH}_{2}\text{NCHR} \\
\downarrow \\
\text{C}_{6}H_{5} \text{CH} = \text{CH} - \text{CH} = \text{CH} - \text{CH} = \text{CH} - \text{CH}_{2}\text{NCHR}
\end{array}
\]

Scheme (1-3)

1-6- Other methods used in preparation of cyclic imides

The development of simple, relatively mild, efficient and practical method for the synthesis of N-alkyl and N-arylphthalimides and succinimides was reported by Langade\(^{(123)}\).

This method was performed by using (10 mol\%) sulphamic acid catalyst. Thus a series of N-substituted phthalimides and succinimides were prepared via reaction of phthalic and succinic anhydride with primary amines in acetic acid in the presence of (10\%) sulphamic acid at (110 °C) for appropriate time.
On the other hand N-(4-nitro-2-phenoxy phenyl)methane sulfonamide or nimesulide [17] a preferential cyclo oxygenase-2 (COX-2) inhibitor is one of the well known non-steroidal anti-inflammatory drugs that has been utilized to treat pain and other inflammatory diseases.


Some of the synthesized imides showed anti-inflammatory activities when tested in rats\(^{124}\).

The prepared new imides and reaction conditions are shown in Table (1-2).
The unsubstituted cyclic imide is an important functionality which has been found to maintain significant biological activity\(^{(125-129)}\).

A series of un substituted cyclic imides were prepared from cyclic anhydrides, hydroxylamine hydrochloride and 4-N,N-dimethyl amino pyridine (DMAP) base catalyst under microwave irradiation\(^{(130)}\).

This novel microwave synthesis produced high yields of the unsubstituted cyclic imides as shown in Table (1-3).

<table>
<thead>
<tr>
<th>Comp. No.</th>
<th>Cyclic anhydrides</th>
<th>Cyclic imides</th>
<th>Reaction conditions</th>
<th>Yield(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>19</td>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
<td>110-120 ºC 10 min</td>
<td>73</td>
</tr>
<tr>
<td>20</td>
<td><img src="image3.png" alt="Image" /></td>
<td><img src="image4.png" alt="Image" /></td>
<td>110-120 ºC 15 min</td>
<td>65</td>
</tr>
<tr>
<td>21</td>
<td><img src="image5.png" alt="Image" /></td>
<td><img src="image6.png" alt="Image" /></td>
<td>110-120 ºC 15 min</td>
<td>65</td>
</tr>
<tr>
<td>22</td>
<td><img src="image7.png" alt="Image" /></td>
<td><img src="image8.png" alt="Image" /></td>
<td>110-120 ºC 15 min</td>
<td>65</td>
</tr>
<tr>
<td>23</td>
<td><img src="image9.png" alt="Image" /></td>
<td><img src="image10.png" alt="Image" /></td>
<td>110-120 ºC 20 min</td>
<td>65</td>
</tr>
<tr>
<td>24</td>
<td><img src="image11.png" alt="Image" /></td>
<td><img src="image12.png" alt="Image" /></td>
<td>110-120 ºC 20 min</td>
<td>75</td>
</tr>
</tbody>
</table>

The unsubstituted cyclic imide is an important functionality which has been found to maintain significant biological activity\(^{(125-129)}\).

A series of un substituted cyclic imides were prepared from cyclic anhydrides, hydroxylamine hydrochloride and 4-N,N-dimethyl amino pyridine (DMAP) base catalyst under microwave irradiation\(^{(130)}\).

This novel microwave synthesis produced high yields of the unsubstituted cyclic imides as shown in Table (1-3).
Table (1-3): Synthesis of unsubstituted imides using NH₂OH and DMAP

<table>
<thead>
<tr>
<th>Imides</th>
<th>Time(min)</th>
<th>Yield(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Imide 1" /></td>
<td>2.68</td>
<td>97</td>
</tr>
<tr>
<td><img src="image2" alt="Imide 2" /></td>
<td>1.82</td>
<td>96</td>
</tr>
<tr>
<td><img src="image3" alt="Imide 3" /></td>
<td>1.57</td>
<td>84</td>
</tr>
</tbody>
</table>

On the other hand Mogilaiah and Sakram(131) reported a practical and efficient method for the synthesis of 1,8-naphthyridinyl phthalimides.

Treatment of 2-amino-3-aryl-1,8-naphthyridines [25a-g] with phthalic anhydride in the presence of catalytic amount of DMF in absence of solvent under microwave irradiation afforded the corresponding N-(3-aryl-1,8-naphthyridin-2-yl) phthalimides [26a-g] Scheme (1-5) in excellent yields (92-98%) with short reaction time (3-4 min). The reaction is simple, clean, rapid and efficient.

Also a series of phthalimides possessing N-phenoxyalkyl moiety substituted at position 3 or 4 of the phenyl ring [27-35] was synthesized and evaluated for anticonvulsant activity(132).
Synthesis of these imides \([27-35]\) performed by alkylation of potassium phthalimide with appropriate phenoxyalkylbromide in the presence of \(K_2CO_3\) and triethylbenzylammonium chloride (TEBA) in acetone as shown in Scheme (1-6).

Phenoxyalkyl bromides used in the synthesis of compounds \([68-76]\) were prepared from reaction between the phenols and an excess of 1,2-dibromoethane or 1,3-dibromopropane.

\[
\text{R'} \quad \text{OH} \quad + \quad \text{Br} \quad \text{(CH}_2\text{)}_n \quad \text{Br} \quad \rightarrow \quad \text{R'} \quad \text{O} \quad \text{(CH}_2\text{)}_n \quad \text{Br} \quad \text{(R = Br)} \\
(n = 2, 3)
\]

\[
\text{C} \quad \text{O} \\
\text{N} \quad \text{K} \quad \text{+ R} \quad \text{Br} \quad \text{K}_2\text{CO}_3, \text{TEBA} \quad \text{acetone, 6 h reflux} \\
\text{C} \quad \text{O} \\
\text{N} \quad \text{R}
\]

Scheme (1-6)

<table>
<thead>
<tr>
<th>Comp. No.</th>
<th>R</th>
<th>Comp. No.</th>
<th>R</th>
</tr>
</thead>
<tbody>
<tr>
<td>27</td>
<td>((\text{CH}_2)_2\text{O} \quad \text{C(\text{CH}_3)}_3)</td>
<td>32</td>
<td>(\text{OCH}_3)</td>
</tr>
<tr>
<td>28</td>
<td>((\text{CH}_2)_2\text{O} \quad \text{Cl})</td>
<td>33</td>
<td>(\text{Cl})</td>
</tr>
<tr>
<td>29</td>
<td>((\text{CH}_2)_2\text{O} \quad \text{CH}_3)</td>
<td>34</td>
<td>(\text{C(\text{CH}_3)}_3)</td>
</tr>
<tr>
<td>30</td>
<td>(\text{Cl})</td>
<td>35</td>
<td>(\text{OCH}_3)</td>
</tr>
<tr>
<td>31</td>
<td>(\text{CF}_3)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Moreover a new series of 2-(1,3-dioxo-2,3-dihydro-1H-2-isoindolyl) ethyl-2-hydroxy-2-(substituted phenyl) acetates [39a-e] have been synthesized from the combination of N-(2-hydroxy ethyl)phthalimide [36] and substituted mandelic acids [38a-e] which resulted in both anti-inflammatory and antimicrobial activities\(^\text{(133)}\).

Among the compounds tested for anti-inflammatory activity compounds [39b] and [39e] showed significant activity and compound [39b] showed potent antibacterial and antifungal activity.
1-7- Biological Activity of Cyclic Imides

N-substituted cyclic imides represent an important class of bioactive molecules that show a wide range of pharmacological activities such as anti-inflammatory, anxiolytic, antifungal, antiviral, antibacterial, analgesic and antitumor properties\(^{(134-142)}\).

Beside these biological effects some phthalimide derivatives constitute an important class of compounds possessing diverse type of biological properties including antimicrobial\(^{(143)}\), antimalarial\(^{(143)}\), antihypertensive\(^{(144)}\), antiviral\(^{(145)}\) and herbicides\(^{(146,147)}\) activity.

Also N-phenylphthalimide and its derivatives have been widely reported to possess beneficial pharmacological effects, they have been shown to be anticonvulsant\(^{(148,149)}\), anti-inflammatory and hypolipidemic\(^{(150,151)}\).

In addition tetrachlorophthalimide has been reported to possess potent hypoglycemic activity\(^{(152-154)}\).

A series of sixteen N-phenylphthalimide derivatives [40-55] was synthesized by the reaction between phthalic anhydride and different amines in acetic acid at reflux temperature\(^{(155)}\).

The \(\alpha\)-glucosidase inhibitory activity of these compounds [40-55] in microbial and mammalian enzymes was evaluated and the results showed that N-phenylphthalimide substituted at position 3 of the benzene ring with NO\(_2\) group showed moderate \(\alpha\)-glucosidase inhibitory activity, while the presence of NO\(_2\) group at the 2- and 4-positions resulted in the most active \(\alpha\)-glucosidase inhibitor among N-phenylphthalimide derivatives.
Also a series of new cyclic imides [56a-b] and [57a-b] with a carbazole skeleton and a basic side chain at the imide nitrogen were tested in vitro for tumor cell-growth inhibition\textsuperscript{(156)}.

The results showed that compound [56a] is a superior as compared to [56b] the latter lacking the second methyl group at the aromatic scaffold.
Likewise when [57a] is compared to its methoxy derivative [57b] the latter structural modification is clearly beneficial.

![Chemical Structure](attachment:structure.png)

56a $R = CH_3$
56b $R = H$

57a $R = H$
57b $R = CH_3O$

On the other hand a series of N-substituted maleimides linked to benzothiazole moiety [58a-j] were synthesized by Al-Azzawi and Mehdi\(^{(157)}\), via reaction of maleic anhydride with different substituted-2-aminobenzothiazoles producing benzothiazol-2-yl maleamic acids followed by dehydration with acetic anhydride and sodium acetate Scheme (1-8).

Antimicrobial activity study of the synthesized maleimides [58a-j] against *Staphylococcus aureus*, *Klebsiella pneumonia* and *Candida albicans* showed that many of the prepared maleimides have good antimicrobial activity.

Also Al-Azzawi and Hassan\(^{(158)}\) synthesized a series of citraconimides linked to benzothiazole moiety [59a-k], Scheme (1-9) studying their antimicrobial activity against *Staphylococcus aureus*, *Streptococcus pyogenes*, *E.Coli*, *Pseudomonas aeruginosa* and *Candida albicans*, most of the tested citraconimides showed good antibacterial and antifungal activities.
Moreover Al-Azzawi and Al-Amerri\(^{(159)}\) synthesized a series of phthalimides [60-64] and succinimides [65-69] linked to 1,3,4-oxadiazole moiety, the new imides showed good antibacterial activity against \textit{Staphylococcus aureus} and \textit{E. Coli} bacteria.

\[
\text{Ac}_2\text{O} / \text{NaOAc} \quad \text{or Fusion}
\]

\[
\text{Ac}_2\text{O} \quad \text{NaOAc}
\]
Aim of the Work

Since both phthalimides and Schiff’s bases exhibited wide range of biological activities and have wide spectrum of biological applications the target of this work involved synthesis of new phthalimides linked to Schiff’s bases by using different strategies involving the following parts:

Part One

This part involved synthesis of phthalimides linked to Schiff’s base through phenyl sulfonamido group.

These new imides were synthesized via preparation of N-phenyl phthalamic acid which introduced subsequently in dehydration reaction producing N-phenyl phthalimide and this was treated with chloro sulfonic acid producing phthalimidyl phenyl sulfonyl chloride which in turn was treated with hydrazine hydrate producing phthalimidyl sulfonyl hydrazine which represent the main synthones introduced in reaction with different aldehydes and ketones to afford the desired new phthalimides.

Part Two

This part involved synthesis of new phthalimides linked to Schiff’s base through phenyl sulfonate moiety via reaction of phthalimidyl sulfonyl chloride with 4-hydroxy acetophenone producing phthalimidyl phenyl sulfonyl acetophenone which in turn introduced in reaction with different primary aromatic amines producing the desired new phthalimides.

Part Three

This part involved synthesis of new phthalimides linked to Schiff’s base through phenyl sulfonate moiety via reaction of phthalimidyl sulfonyl chloride with 4-hydroxy benzaldehyde producing phthalimidyl phenyl sulfonate benzaldehyde which in turn introduced in reaction with different primary aromatic amines producing the desired imides.
Part Four

This part involved synthesis of new phthalimides linked to Schiff's base through methylene group via reaction of 4-phenyl phenacyl bromide with phthalimide potassium salt producing N-(4-phenyl phenacyl) phthalimide which in turn introduced in reaction with different primary aromatic amines to afford the desired imides.
2-1- Instruments and Chemicals

2-1-1- Instruments

1. Melting points were determined on Gallenkamp capillary melting point apparatus.

2. FT-IR spectra were recorded using KBr discs on SHIMADZU FT-IR-8400 Fourier Transform Infrared Spectrophotometer, in college of science, Baghdad University and on SHIMADZU FT-IR-prestige-21 Fourier Transform Infrared Spectrophotometer, in Ibn-Sina Company.

3. $^1$H-NMR and $^{13}$C-NMR spectra were recorded on near magnetic resonance Bruker, Ultrasheild 300 MHz in Jordan, using tetra methyl silane as internal standard and DMSO-d$_6$ as solvents.

2-1-2- Chemicals

Chemicals used in this work were purchased from BDH, Merck and Fluka companies and involved the following:

<table>
<thead>
<tr>
<th>No.</th>
<th>Chemical Compounds</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Phthalic anhydride</td>
</tr>
<tr>
<td>2</td>
<td>Acetic anhydride</td>
</tr>
<tr>
<td>3</td>
<td>Different primary aromatic amines</td>
</tr>
<tr>
<td>4</td>
<td>Ethanol(abs.)</td>
</tr>
<tr>
<td>5</td>
<td>Acetic acid (glacial)</td>
</tr>
<tr>
<td>6</td>
<td>Anhydrous sodium acetate</td>
</tr>
<tr>
<td>7</td>
<td>Chlorosulfonic acid</td>
</tr>
<tr>
<td>8</td>
<td>Acetone</td>
</tr>
<tr>
<td>9</td>
<td>Hydrazine hydrate</td>
</tr>
<tr>
<td>10</td>
<td>Different aromatic aldehydes and ketones</td>
</tr>
</tbody>
</table>
The experimental chapter in this work involved the following parts:

### 2-2- Part One

This part involved synthesis of phthalimides linked to Schiff’s bases through sulfonamido group.

Performing this target involved the following steps:

1. Synthesis of N-phenyl phthalamic acid.
2. Dehydration of the prepared N-phenyl phthalamic acid producing N-phenyl phthalimide.
3. Chlorosulfonation of the prepared phthalimide producing 4-(N-phthalimidyl) phenyl sulfonyl chloride.
4. Treatment of phthalimidyl phenyl sulfonyl chloride with hydrazine hydrate producing the corresponding sulfonyl hydrazine.
5. Introducing of sulfonyl hydrazine in reaction with different aromatic aldehydes and ketones producing the desirable new phthalimide.

<table>
<thead>
<tr>
<th>No.</th>
<th>Chemical Compounds</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>Ethanol</td>
</tr>
<tr>
<td>12</td>
<td>Methanol</td>
</tr>
<tr>
<td>13</td>
<td>Hydrochloric acid</td>
</tr>
<tr>
<td>14</td>
<td>4-phenyl phenacyl bromide</td>
</tr>
<tr>
<td>15</td>
<td>Unsubstituted Phthalimide</td>
</tr>
<tr>
<td>16</td>
<td>Potassium hydroxide</td>
</tr>
<tr>
<td>17</td>
<td>Sodium hydroxide</td>
</tr>
<tr>
<td>18</td>
<td>Sodium bicarbonate</td>
</tr>
<tr>
<td>19</td>
<td>Cyclo hexane</td>
</tr>
<tr>
<td>20</td>
<td>Dioxane</td>
</tr>
</tbody>
</table>
2-2-1- Preparation of N-phenyl phthalamic acid [1]

To a solution of (0.01 mol, 1.48 g) of phthalic anhydride in 25 mL of acetone, (0.01 mol, 1mL) of aniline was added drop wise with stirring and cooling^{120,160,161,}.

Stirring was continued for two hours at room temperature the resulted precipitate was filtered, dried, recrystallized from ethanol.

The physical properties of compound [1] are listed in Table (3-1).

2-2-2- Preparation of N-phenyl phthalimide [2]

A mixture of (0.01 mol, 2.41 g) of N-phenyl phthalamic acid in 25 mL of acetic anhydride and (5 %) by weight of anhydrous sodium acetate was refluxed for two hours with stirring^{158,162,}.

The resulted homogenous solution was cooled to room temperature and pouring into crushed ice, compound [2] was obtained filtered, dried, recrystallized from acetone.

The physical properties of compound [2] are listed in Table (3-1).

2-2-3- Preparation of 4-(N-phthalimidyl) phenyl sulfonyl chloride [3]

Chlorosulfonic acid (4 mL) was added drop wise to (0.01 mol, 2.23 g) of N-phenyl phthalimide during two hours with stirring and keeping temperature at 0 °C^{162,}.

Stirring was continued for ten hours at room temperature then the resulted mixture was poured into crushed ice carefully with stirring.

The obtained precipitate was filtered, dried, recrystallized from acetone.

The physical properties of compound [3] are listed in Table (3-1).
2-2-4- Preparation of 4-(N-phthalimidyl)phenyl sulfonyl hydrazine [4]

To a solution of (0.01 mol, 3.22 g) of compound [3] in 5 mL of absolute ethanol, (0.01 mol) of hydrazine hydrate was added drop wise with stirring and keeping temperature at 0 °C.

The resulted mixture was refluxed for six hours then cooled to room temperature then pouring on crushed ice with stirring\textsuperscript{163}.

The resulted precipitate was filtered, washed with cold water, dried and finally recrystallized from ethanol.

The physical properties of compound [4] are listed in Table (3-1).

2-2-5- Preparation of Schiff’s Bases [5-18]

A mixture of 4-(N-phthalimidyl) phenyl sulfonyl hydrazine (0.01 mol, 3.17 g), aromatic aldehyde or ketone (0.01 mol) and (2-3) drops of glacial acetic acid in absolute ethanol (20 mL) was refluxed for six hours\textsuperscript{164}.

After cooling the obtained precipitate was filtered then washed with cold ethanol, dried and recrystallized from a suitable solvent.

Physical properties of compounds [5-18] are listed in Table (3-2).

2-3- Part Two

This part involved synthesis of new phthalimides linked to Schiff’s bases through phenyl sulfonate moiety.

Performing this target involved the following steps:

1. Reaction of 4-(N-phthalimidyl) phenyl sulfonyl chloride with 4-hydroxy acetophenone producing 4-(4′-(N-phthalimidyl) phenyl sulfonyl) acetophenone.

2. Introducing of the prepared phthalimidyl sulfonate acetophenone in reaction with different primary aromatic amines producing the desirable new imides.
2-3-1- Preparation of 4-(4'-(N-phthalimidyl) phenyl sulfonate) acetophenone [19]

In a three-necked flask equipped with a stirrer and thermometer a mixture of (2.04 g, 0.015 mol) of 4-hydroxy acetophenone and (3 mL) of pyridine was placed.

The flask was surrounded by a bath sufficiently cold to lower the thermometer of the mixture to 10 °C (164).

4-(N-phthalimidyl)phenyl sulfonyl chloride (0.01 mol, 3.22 g) was added in portions during 20 minutes with continuous stirring.

The mixture was refluxed for two hours on a water bath then cooled to room temperature then the reaction mixture was poured into cold water with stirring until the resulted oily layer solidified.

The solid product was filtered, washed with cold dilute HCl solution followed by dilute NaHCO₃ solution then with distilled water, dried, recrystallized from ethanol to give pale brown crystals in 70% yield and m.p.(152-154)°C.

FT-IR: 1739, 1720 cm⁻¹ ν(C=O) imide, 1674 cm⁻¹ ν(C=O) ketone, 1593 cm⁻¹ ν(C=C) aromatic, 1361 cm⁻¹ and 1176 cm⁻¹ ν(SO₂) sulfonate.

2-3-2- Preparation of 4-(4'-N-phthalimidyl) phenyl sulfonate methyl benzylidene (Schiffs base) [20-26]

In a suitable round bottomed flask (0.01 mol, 4.21 g) of compound [19] was dissolved in 20 mL of absolute ethanol then (0.01 mol) of primary aromatic amine was added followed by addition of (2-3) drops of glacial acetic acid with stirring.

The mixture was refluxed for four hours then cooled to room temperature and the obtained precipitate was filtered, dried and purified by
recrystallization from a suitable solvent.

The physical properties of Schiff's bases [20-26] are listed in Table (3-5).

2-4- Part Three

This part involved synthesis of new phthalimides linked to Schiff's bases through sulfonate moiety.

Performing this target involved the following steps:

1. Reaction of 4-(N-phthalimidyl) phenyl sulfonyl chloride with benzaldehyde producing 4-(4′-(N-phthalimidyl) phenyl sulfonate) benzaldehyde.

2. Introducing of the prepared phthalimidyl sulfonate benzaldehyde in reaction with different primary aromatic amines producing the desirable new imides.

2-4-1- Preparation of 4-(4′-N-phthalimidyl) phenyl sulfonate benzaldehyde [27]

The titled compound [27] was prepared by following the same procedure used in the preparation of compound [19] except using of 4-hydroxy benzaldehyde instead of 4-hydroxy acetophenone, recrystallized from ethanol to give pale brown crystals in 72% yield and m.p.(176-178)°C.

FT-IR: 1741 and 1718 cm⁻¹ ν(C=O) imide, 1699 cm⁻¹ ν(C=O) aldehyde, 1593 cm⁻¹ ν(C=C) aromatic and 1360, 1186 cm⁻¹ ν(SO₂) sulfonate.

2-4-2- Preparation of 4-(4′-N-phthalimidyl) phenyl sulfonate benzylidene (Schiff's bases) [28-33]

The titled compounds were prepared by following the same procedure used in the synthesis of compounds [20-26] except using of compound [27] as starting material instead of compound [19].

The physical properties of compounds [28-33] are listed in Table (3-7).
2-5- Part Four

This part involved synthesis of new phthalimides linked to Schiffs bases through methylene (-CH₂-).

Performing this target involved the following steps:

1. Preparation of phthalimide potassium salt.
2. Reaction of phthalimide potassium salt with 4-phenyl phenacyl bromide producing N-(4-phenyl phenacyl) phthalimide.
3. Introducing N-(4-phenyl phenacyl) phthalimide in reaction with different primary aromatic amines producing the desirable imides.

2-5-1- Preparation of phthalimide potassium salt

Phthalimide (0.01 mol, 1.47 g) was dissolved in 20 mL of absolute ethanol then was heated in a water bath.

The obtained clear solution was added to alcoholic potassium hydroxide solution [(0.01 mol) KOH in 25 mL absolute ethanol] with continuous stirring and cooling, then the obtained precipitate was filtered and dried.

2-5-2- Preparation of N-(4-phenyl phenacyl) phthalimide [34]

In a suitable round bottomed flask (0.01 mol, 2.75 g) of 4-phenyl phenacyl bromide was dissolved in 25 mL of absolute ethanol then (0.01 mol, 1.85 g) of phthalimide potassium salt was added gradually with stirring\(^{(164)}\).

The resulted mixture was refluxed for six hours with continuous stirring then was cooled to room temperature and the formed precipitate was filtered, washed with distilled water and dried.

The solid product was recrystallized from ethanol producing reddish brown crystals in 65% yield and m.p.(106-108)\(^\circ\)C.
FT-IR: 1774 and 1716 cm\(^{-1}\) v(C=O) imide, 1689 cm\(^{-1}\) v(C=O) ketone, 1600 cm\(^{-1}\) v(C=C) aromatic and 1392 cm\(^{-1}\) v(C-N) imide.

2-5-3- Preparation of Schiff’s Bases [35-40]

A mixture of (0.01 mol, 3.41 g) of N-(4-phenyl phenacyl) phthalimide, (0.01 mol) of primary aromatic amine in 25 mL of absolute ethanol and (2-3) drops of glacial acetic acid was refluxed for six hours with stirring.

The resulted mixture was cooled to room temperature and the precipitate was obtained, filtered, dried, recrystallized from a suitable solvent.

The Physical properties of the prepared Schiff’s bases [35-40] are listed in Table (3-9).
Results and Discussion

Among the bicyclic nitrogen heterocycles phthalimides are an interesting class of compounds with a large range of applications.

Recently phthalimide and some of its derivatives have provided to have important biological effects similar or even higher than known pharmacological molecules and so their biological activity is being a subject of biomedical research\(^{(143-151)}\).

Schiff’s bases belong to a widely used group intermediates important for production of specially chemicals like pharmaceuticals or rubber additives and also have uses in many fields including analytical, inorganic, medicinal and polymer chemistry\(^{(32-38)}\).

According to all these mentioned facts the target of the present work has been directed toward building of new molecules containing these two active moieties (phthalimide and Schiff’s base) via applying different strategies, involving the following parts:-

3-1-Part One

3-1-1- N-phenyl phthalamic acid [1]

Compound [1] was prepared via reaction of equimolar amounts of phthalic anhydride and aniline in acetone.

The reaction was carried out\(^{(159)}\) via nucleophilic attack of amino group of aniline on carbonyl group in phthalic anhydride as shown in Scheme (3-1).
The physical properties of compound [1] are listed in Table (3-1).

FT-IR spectra of compound [1] showed strong absorption bands at 3325 cm\(^{-1}\) and at 3136 cm\(^{-1}\) due to \(\nu(O-H)\) carboxylic and \(\nu(N-H)\) amide. Other absorption bands appeared at 1720 cm\(^{-1}\), 1643 cm\(^{-1}\) and 1600 cm\(^{-1}\) due to \(\nu(C=O)\) carboxylic, \(\nu(C=O)\) amide and \(\nu(C=C)\) aromatic respectively\(^{(165)}\).

\(^1\)H-NMR spectrum of this compound showed signals at \(\delta= (7.04-7.89)\) ppm due to aromatic protons and (N-H) proton and a clear signal at \(\delta= 10.33\) ppm due to (O-H) carboxylic proton while \(^{13}\)C-NMR spectrum of the same compound showed signals at \(\delta= (119.9-140)\) ppm, 167.8 ppm and 167.92 ppm due to aromatic ring carbons, (C=O) amide and (C=O) carboxyl respectively\(^{(166)}\).

3-1-2- N-phenyl phthalimide [2]

Compound [2] was prepared via dehydration of the prepared N-phenyl phthalamic acid using acetic anhydride and anhydrous sodium acetate as dehydrating agent.

Mechanism\(^{(159)}\) steps of dehydration reaction are shown in Scheme (3-2).
The physical properties of compound [2] are listed in Table (3-1) and its structure was confirmed by FT-IR, $^1$H-NMR and $^{13}$C-NMR spectral data. Thus FT-IR spectrum of compound [2] showed disappearance of $\nu$(O-H) and $\nu$(N-H) absorption bands proving success of dehydration reaction and appearance of two bands at 1735 cm$^{-1}$ and 1708 cm$^{-1}$ for asym. and sym. $\nu$(C=O) imide, absorption bands of $\nu$(C=C) aromatic and $\nu$(C-N) imide appeared at 1593 cm$^{-1}$ and 1384 cm$^{-1}$ respectively.

$^1$H-NMR spectrum of compound [2] showed disappearance of (O-H) carboxyl proton signal and appearance of two multiplet signals at
δ= (7.44-7.56) ppm and (7.89-7.97) ppm of two aromatic rings protons. 

\(^{13}\text{C}\)-NMR spectrum of the same compound showed signals at δ= (123.8-135.1) ppm and δ= 167.4 due to aromatic ring carbons and (C=O) imide respectively.

3-1-3- 4-(N-phthalimidyl) phenyl sulfonyl chloride [3]

The titled compound was prepared via treatment of N-phenyl phthalimide with chlorosulfonic acid at 0 °C.

Mechanism\(^{(157)}\) of this reaction involved electrophilic attack by chlorosulfonic acid on para position of phenyl ring in phthalimide as described in Scheme (3-3).
The physical properties of compound [3] are listed in Table (3-1).

FT-IR spectrum of compound [3] showed absorption bands at 1743 cm\(^{-1}\) and 1720 cm\(^{-1}\) due to asym. and sym. \(\nu(C=O)\) imide, also two clear absorption bands appeared at 1365 cm\(^{-1}\) and 1188 cm\(^{-1}\) due to asym. and sym. \(\nu(SO_2)\) respectively.

Other absorption bands appeared at 1585 cm\(^{-1}\) and 1300 cm\(^{-1}\) due to \(\nu(C=C)\) aromatic and \(\nu(C-N)\) imide respectively.

Compound [3] was identified also by application of Lassaigne test\(^{(164)}\), thus the positive results obtained in both tests for sulfur and chlorine gave another proofs for structure of compound [3].

**3-1-4- 4-(N-phthalimidyl) phenyl sulfonyl hydrazine [4]**

Compound [4] was prepared via treatment of phthalimidyl phenyl sulfonyl chloride with hydrazine hydrate.

The mechanism\(^{(157)}\) of this nucleophilic substitution reaction was performed by nucleophilic attack of amino group of hydrazine compound on sulfur atom in compound [3] followed by elimination of (HCl) molecule as described in Scheme (3-4).
The physical properties of compound [4] are listed in Table (3-1) and its structure was confirmed by FT-IR, \(^1\)H-NMR and \(^{13}\)C-NMR spectral data.

FT-IR spectrum of compound [4] showed two strong absorption bands at 3359 cm\(^{-1}\) and 3265 cm\(^{-1}\) to (-NH-NH\(_2\)) group and this is an excellent proof for the success of hydrazine compound formation.

Other absorption bands appeared at 1718 cm\(^{-1}\), 1710 cm\(^{-1}\), 1595 cm\(^{-1}\), 1390 cm\(^{-1}\), 1338 cm\(^{-1}\) and 1170 cm\(^{-1}\) due to asym. \(\nu(C=O)\) imide, sym. \(\nu(C=O)\) imide, \(\nu(C=C)\) aromatic, asym. \(\nu(SO_2)\), \(\nu(C-N)\) imide and sym. \(\nu(SO_2)\) respectively.
\(^1\)H-NMR spectrum of this compound showed signals at \(\delta = (3.5\) and 3.8\) ppm due to (NH\(_2\)) and (NH) of hydrazine moiety while signals of aromatic protons appeared at \(\delta = (7.39\)–7.99\) ppm.

\(^{13}\)C-NMR spectrum of compound [4] showed signals at \(\delta = (124\)–137.9\) ppm and 167 ppm due to carbons of aromatic ring and (C=O) imide respectively.

Details of FT-IR spectral data of compounds [1-4] are listed in Table (3-3).

3-1-5- N-\([4-(N\)-phthalimidyl)phenylsulfonamido\]benzylidene[5-18]

The final step in this part involved introducing of compound [4] phthalimidyl sulfonyl hydrazine in condensation reaction with different aromatic aldehydes and ketones to afford the desirable phthalimides linked to Schiff’s base through phenyl sulfonamide group.

The first step in condensation reaction between the hydrazine compound and carbonyl compounds involved nucleophilic addition\(^{167}\) of hydrazine compound to carbonyl group producing [I] which eliminate water molecule in step two to afford the desirable Schiff’s base [II] as shown in Scheme (3-5).
Physical properties of compounds [5-18] are listed in Table (3-2) and their structures are confirmed by FT-IR, $^1$H-NMR and $^{13}$C-NMR spectral data.
FT-IR spectra of compounds [5-18] showed disappearance of the two characteristic absorption bands at 3359 and 3265 cm\(^{-1}\) due to \((-\text{NH-NH}_2)\) group in hydrazine compound [4] and appearance of new clear absorption band at (1608-1658) cm\(^{-1}\) due to \(\nu(\text{C=N})\) imine. These two points are excellent proofs for the success of Schiff base formation\(^{(168)}\).

Besides FT-IR spectra of compounds [5-18] showed clear absorption bands at (1735-1743) cm\(^{-1}\) and (1706-1720) cm\(^{-1}\) due to asym. and sym. \(\nu(\text{C=O})\) imide.

Other absorptions appeared at (1573-1604) cm\(^{-1}\), (1373-1388) cm\(^{-1}\), (1157-1170) cm\(^{-1}\) and (1315-1348) cm\(^{-1}\) due to \(\nu(\text{C=C})\) aromatic, asym. \(\nu(\text{SO}_2)\), sym. \(\nu(\text{SO}_2)\) and \(\nu(\text{C-N})\) imide respectively. Moreover FT-IR spectra of Schiff bases [6,8,12,15] showed clear absorption band at (3429-3479) cm\(^{-1}\) \(\nu(\text{O-H})\) phenolic, while compound [7] showed two absorption bands at (1234 and 1126) cm\(^{-1}\) \(\nu(\text{C-O-C})\) ether and finally compound [14] showed strong absorption band at 1091 cm\(^{-1}\) due to \(\nu(\text{C-Cl})\).

All details of FT-IR spectral data of compounds [5-18] are listed in Table (3-4).

\(^1\)H-NMR spectrum of compound [5] showed signal at \(\delta= 1.4\) ppm belong to \((\text{CH}_3)\) protons, multiplet signals at \(\delta= (7.39-8.34)\) ppm due to aromatic protons and signal at \(\delta= 8.97\) ppm due to imine \((-\text{CH=N-})\) proton.

\(^1^3\)C-NMR spectrum of compound [5] showed signals at \(\delta= 24.97\) ppm, (123.8-134.4) ppm, 135.3 ppm and 159.1 ppm due to \((\text{CH}_3)\) group, aromatic ring carbons, \((\text{C=N})\) imine and \((\text{C=O})\) imide respectively.

\(^1\)H-NMR spectrum of compound [7] showed signal at \(\delta= 3.51\) ppm due to \((\text{OCH}_3)\) protons and four multiplet signals at \(\delta= (6.89-7.96)\) ppm due to aromatic protons.
\[ ^{13} \text{C-NMR spectrum of compound [7] showed signal at } \delta = 57 \text{ ppm due to (OCH}_3 \text{) group and signals at } \delta = (123.9-127.1) \text{ ppm, 135.1 ppm and 168 ppm due to aromatic carbons, (C=N) imine and (C=O) imide respectively.} \]

**Table (3-1): Physical properties of compounds [1-4]**

<table>
<thead>
<tr>
<th>Comp. No.</th>
<th>Compound structure</th>
<th>Color</th>
<th>Melting Points °C</th>
<th>Yield %</th>
<th>Recrystallization Solvent</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1" alt="Structure1" /></td>
<td>White</td>
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<td>Ethanol</td>
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<td>95</td>
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Table (3-2): Physical properties of Schiff's bases [5-18]

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<th>Yield %</th>
<th>Recrystallization Solvent</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>![Structure 5]</td>
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<td>![Structure 6]</td>
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<td>![Structure 8]</td>
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<td>![Structure 9]</td>
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<td>Ethanol</td>
</tr>
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<td>Comp. No.</td>
<td>Compound structure</td>
<td>Color</td>
<td>Melting Points °C</td>
<td>Yield %</td>
<td>Recrystallization Solvent</td>
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Table (3-3): Spectral data of compounds [1-4]

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Table (3-4): Spectral data of Schiff’s bases [5-18]

<table>
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<th>Compound structure</th>
<th>FTIR spectral data cm⁻¹</th>
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</thead>
<tbody>
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<td>Structure</td>
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Fig. No. (1): FT-IR spectrum for compound [1]
Fig. No. (2): FT-IR spectrum for compound [2]
Fig. No. (3): FT-IR spectrum for compound [3]
Fig. No. (4) : FT-IR spectrum for compound [4]
Fig. No. (5): FT-IR spectrum for compound [5]
Fig. No. (6): FT-IR spectrum for compound [6]
Fig. No. (7): FT-IR spectrum for compound [13]
Fig. No. (8) : $^1$H-NMR spectrum for compound [1]
Fig. No. (9): $^{13}$C-NMR spectrum for compound [1]
Fig. No. (10): $^1$H-NMR spectrum for compound [2]
Fig. No. (11): $^{13}$C-NMR spectrum for compound [2]
Fig. No. (12): $^1$H-NMR spectrum for compound [4]
Fig. No. (13) : $^{13}$C-NMR spectrum for compound [4]
Fig. No. (14): $^1$H-NMR spectrum for compound [5]
Fig. No. (15) : \(^{13}\)C-NMR spectrum for compound [5]
3-2-Part Two

3-2-1- 4-[4'-(N-phthalimidyl) phenyl sulfonyl] acetophenone [19]

The titled compound [19] was prepared via reaction between 4-(N-phthalimidyl) phenyl sulfonyl chloride [3] and 4-hydroxy acetophenone. This reaction represents the esterification between acid chloride (compound [3]) and substituted phenol (4-hydroxy acetophenone) and the mechanism \(^{(167)}\) was suggested via nucleophilic attack of phenolic hydroxyl group on sulfur atom in acid chloride followed by elimination of (HCl) molecule as described in Scheme (3-6).
Compound [19] was recrystallized from ethanol and was obtained as pale brown crystals in 70% yield with melting point (152-154)°C.

The major FT-IR absorptions in FT-IR spectrum of compound [19] include absorption bands at 1739 cm\(^{-1}\) and 1720 cm\(^{-1}\) due to asym. and sym. ν(C=O) imide, bands at 1674 cm\(^{-1}\), 1593 cm\(^{-1}\), 1361 cm\(^{-1}\) and 1176 cm\(^{-1}\) due to ν(C=O) ketone, ν(C=C) aromatic, asym. ν(SO\(_2\)) and sym. ν(SO\(_2\)) respectively.

\(^{1}\)H-NMR spectrum of compound [19] showed signal at δ= 2.569 ppm (CH\(_3\)) group protons and multiplet signals at (δ= 7.28-8.13) ppm due to aromatic protons, while \(^{13}\)C-NMR spectrum of the same compound showed signal at δ= 27.2 ppm due to (CH\(_3\)) group.

Signals at δ= (122.6-153) ppm due to aromatic ring carbons, signal at δ= 166.8 ppm due to (C=O) imide and signal at δ= 198 ppm due to (C=O) ketone.

Chemical test for compound [19] gave positive results in both (Iodoform test) and general test for carbonyl compounds\(^{(169)}\) and these are good additional proofs for success of compound [19] formation.

3-2-2- 4-[4’-(N-phthalimidyl) phenyl sulfonate] methyl benzylidene [20-26]

The titled Schiff’s bases [20-26] were prepared via condensation reaction of compound [19] with different primary aromatic amines.

Mechanism\(^{(167)}\) of this reaction involved nucleophilic attack of primary amine on carbonyl group in compound [19] producing addition product [I] which subsequently eliminated water molecule producing the desirable compound as shown in Scheme (3-7).
Scheme (3-7)
Physical properties of compounds [20-26] are listed in Table (3-5).

FT-IR spectra of compounds [20-26] showed disappearance of absorption band at 1674 cm\(^{-1}\) which due to \(v(C=O)\) ketone and appearance of clear strong absorption band at (1681-1690) cm\(^{-1}\) due to \(v(C=N)\) imine.

FT-IR spectra of compounds [20-26] showed bands at (1725-1743) cm\(^{-1}\), (1710-1726) cm\(^{-1}\), (1593-1595) cm\(^{-1}\), (1361-1385) cm\(^{-1}\) and (1176-1199) cm\(^{-1}\) due to asym. \(v(C=O)\) imide, sym. \(v(C=O)\) imide, \(v(C=C)\) aromatic, asym. \(v(SO_2)\) and sym. \(v(SO_2)\) respectively.

All details of FT-IR spectral data of compounds [20-26] are listed in Table (3-6).

\(^1\)H-NMR spectrum of compound [21] showed two signals at δ = 2.35 ppm and δ = 2.56 ppm due to two (CH\(_3\)) groups, while signals at δ = (7.28-8.12) ppm are due to aromatic ring protons.

\(^1\)H-NMR spectrum of the same compound showed signal at δ = 27.21 ppm due to (CH\(_3\)) group and signals at δ = (122.5-138.2) ppm due to aromatic ring carbons and signals at δ = 152.6 ppm and δ = 166.8 ppm are due to (C=N) imine and (C=O) imide respectively.

\(^1\)H-NMR spectrum of compound [24] showed signals at δ = 2.54 ppm and δ = 2.56 ppm due to two (CH\(_3\)) groups, while signals at δ = (7.28-8.12) ppm are due to aromatic ring protons.

\(^1\)H-NMR spectrum of compound [24] showed signal at δ = 27.2 ppm due to (CH\(_3\)) groups and signals at δ = (122-135) ppm due to aromatic ring carbons and signals at δ = 153 ppm and δ = 166 ppm due to (C=N) imine and (C=O) imide respectively.
Table (3-5): Physical properties of compounds [20-26]

<table>
<thead>
<tr>
<th>Comp. No.</th>
<th>Compound structure</th>
<th>Color</th>
<th>Melting Points °C</th>
<th>Yield %</th>
<th>Recrystallization Solvent</th>
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**Table (3-6): Spectral data of compounds [20-26]**

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Fig. No. (16) : FT-IR spectrum for compound [19]
Fig. No. (17): FT-IR spectrum for compound [24]
Fig. No. (18): FT-IR spectrum for compound [26]
Fig. No. (19): $^1$H-NMR spectrum for compound [19]
Fig. No. (20): $^{13}$C-NMR spectrum for compound [19]
Fig. No. (21): $^1$H-NMR spectrum for compound [21]
Fig. No. (22): $^{13}$C-NMR spectrum for compound [21]
Fig. No. (23) : $^1$H-NMR spectrum for compound [24]
Fig. No. (24): $^{13}$C-NMR spectrum for compound [24]
3-3-1- \textit{4'-(N-phthalimidyl) phenyl sulphonate} benzaldehyde [27]

Compound [27] was prepared via reaction between 4-(N-phthalimidyl) phenyl sulfonyl chloride [3] and 4-hydroxy benzaldehyde. Mechanism\textsuperscript{(167)} of reaction involved nucleophilic attack of phenolic hydroxyl group on sulfur atom in compound [3] followed by elimination of (HCl) molecule producing the desirable imides as described in Scheme (3-8).

![Scheme (3-8)](image)

Compound [27] was recrystallized from ethanol and gave pale brown crystals in 72\% yield with melting point (176-178)\textdegree C.

FT-IR spectrum of compound [27] showed absorption bands at 1741 cm\textsuperscript{-1} and 1718 cm\textsuperscript{-1} asym $\nu$(C=O) and sym. $\nu$(C=O) imide and a clear
strong absorption band at 1699 cm\(^{-1}\) \(\nu(C=O)\) aldehyde.

Other absorption bands appeared at 1593 cm\(^{-1}\), 1370 cm\(^{-1}\), 1186 cm\(^{-1}\) and 1360 cm\(^{-1}\) \(\nu(C=C)\) aromatic, asym. \(\nu(SO_2)\) and sym. \(\nu(SO_2)\) and \(\nu(C-N)\) imide respectively.

\(^1\)H-NMR spectrum of compound [27] showed signals at \(\delta = (7.37-8.13)\) ppm for aromatic protons and signal at \(\delta = 9.99\) ppm for aldehyde proton \(\ce{O=C-H}\).

\(^{13}\)C-NMR spectrum of compound [27] showed signals at \(\delta = (123.2-153.5)\) ppm due to aromatic ring carbons, signal at \(\delta = 167\) ppm due to \(\nu(C=O)\) imide and signal at \(\delta = 193\) ppm for \(\nu(C=O)\) aldehyde.

Chemical test compound [27] gave positive result in test for carbonyl compounds\(^{164}\) and this is a good additional proof for preparation of compound [27].

**3-3-2- 4-[4'-((N-phthalimidyl) phenyl sulfonate] benzylidene [28-33]**

The titled Schiff's bases [28-33] were prepared via condensation reaction of compound [27] with different primary aromatic amines.

Mechanism\(^{167}\) of this reaction involved nucleophilic attack of primary amine on carbonyl group of compound [27] producing [I] which subsequently eliminated water molecule to afford the desirable compounds as shown in Scheme (3-9).
1- \[
\text{Protonation: } \quad \text{CH}_3\text{COOH} / \text{H}^+ \quad \text{CH}_3\text{COO}^- + \text{H}^+ \]

2- \[
\text{Protonation: } \quad \text{CH}_3\text{COOH} / \text{H}^+ \quad \text{CH}_3\text{COO}^- + \text{H}^+ \]

\[\text{R} = \text{CH}_3, \text{CH}_2\text{Cl}, \text{O}_2\text{N}, \text{Cl}, \text{CH}_3, \text{NO}_2\]

Scheme (3-9)
Physical properties of compounds [28-33] are listed in Table (3-7).

FT-IR spectra of compounds [28-33] showed disappearance of absorption band at 1699 cm\(^{-1}\) \(\nu(\text{C}=\text{O})\) aldehyde and appearance of clear strong absorption band at (1620-1631) cm\(^{-1}\) due to \(\nu(\text{C}=\text{N})\) imine.

Other absorption bands appeared at (1740-1741) cm\(^{-1}\), (1720-1722) cm\(^{-1}\), (1585-1596) cm\(^{-1}\), (1365-1375) cm\(^{-1}\), (1168-1199) cm\(^{-1}\) and (1300-1355) cm\(^{-1}\) which were attributed to asym. \(\nu(\text{C}=\text{O})\) imide, sym. \(\nu(\text{C}=\text{O})\) imide, \(\nu(\text{C}=\text{C})\) aromatic, asym. \(\nu(\text{SO}_2)\), sym. (SO\(_2\)) and \(\nu(\text{C}-\text{N})\) imide respectively.

All details of FT-IR spectral data of compounds [28-33] are listed in Table (3-8).

\(^1\)H-NMR spectrum of compound [31] showed multiplet signals at \(\delta=\) (7.29-8.13) ppm for aromatic protons and clear signal at \(\delta=\) 8.58 ppm for imine proton (-N=CH\(-\)).

\(^{13}\)C-NMR spectrum of compound [31] showed signals at \(\delta=\) (122-151.7) ppm due to aromatic ring carbons, signal at \(\delta=\) 162.4 ppm for \(\nu(\text{C}=\text{N})\) and signal at \(\delta=\) 166.83 ppm for (C=O) imide.

\(^1\)H-NMR spectrum of compound [32] showed clear singlet signal at \(\delta=\) 2.08 ppm due to (CH\(_3\)) group protons, multiplet signals at \(\delta=\) (7.27-8.12) ppm for aromatic protons and singlet signal at \(\delta=\) 8.61 ppm for imine proton (-N=CH\(-\)), while \(^{13}\)C-NMR spectrum of the same compound showed signal at \(\delta=\) 31.1 ppm (CH\(_3\)) group, signals at \(\delta=\) (121.4-151.5) ppm for aromatic carbons, signal at \(\delta=\) 159 ppm (C=N) and signal at \(\delta=\) 166 ppm (C=O) imide.
Table (3-7): Physical properties of compounds [28-33]

<table>
<thead>
<tr>
<th>Comp. No.</th>
<th>Compound structure</th>
<th>Color</th>
<th>Melting Points °C</th>
<th>Yield %</th>
<th>Recrystallization Solvent</th>
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### Table (3-8): Spectral data of compounds [28-33]

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<tr>
<td>33</td>
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A1
Fig. No. (25): FT-IR spectrum for compound [27]
Fig. No. (26): FT-IR spectrum for compound [28]
Fig. No. (27): FT-IR spectrum for compound [31]
Fig. No. (28): $^1$H-NMR spectrum for compound [27]
Fig. No. (29): $^{13}$C-NMR spectrum for compound [27]
Fig. No. (30) : $^1$H-NMR spectrum for compound [31]
Fig. No. (31) : $^{13}$C-NMR spectrum for compound [31]
Fig. No. (32) : $^1$H-NMR spectrum for compound [32]
Fig. No. (33): $^{13}$C-NMR spectrum for compound [32]
3-4-Part Four

3-4-1- N-(4-phenyl phenacyl) phthalimide [34]

The titled compound was prepared via reaction of phthalimide potassium salt with 4-phenyl phenacyl bromide according to Gábral synthesis.

Unsubstituted phthalimide\(^{(170)}\) was converted to its potassium salt since the later is the stronger nucleophile which attack the electron-deficient carbon atom bonded to halogen in para phenyl phenacyl bromide as shown in Scheme (3-10).

![Scheme (3-10)](image)

Compound [34] was purified by recrystallization from ethanol and was obtained as reddish brown crystals in 65% yield with melting point (106-108)°C.

FT-IR spectrum of compound [34] showed appearance of clear absorption band at 1689 cm\(^{-1}\) due to ν(C=O) ketone.
Other absorption bands appeared at 1716 cm\(^{-1}\), 1600 cm\(^{-1}\) and 1392 cm\(^{-1}\) due to \(\nu(C=O)\) imide, \(\nu(C=C)\) aromatic and \(\nu(C-N)\) imide respectively.

\(^1\)H-NMR spectrum of compound [34] showed signal at \(\delta = 4.95\) ppm due to (-CH\(_2\)-) protons and signals at \(\delta = (7.44-8.19)\) ppm due to aromatic ring protons.

\(^{13}\)C-NMR spectrum of the same compound showed signal at \(\delta = 34.41\) ppm due to (-CH\(_2\)-) carbon and signals at \(\delta = (123.8-139.1)\) ppm, \(\delta = 145.66\) ppm and \(\delta = 191.78\) ppm due to aromatic ring carbons, (C=O) imide and (C=O) ketone respectively.

Compound [34] gave positive result in treatment with 2,4-dinitrophenyl hydrazine\(^{164}\) and this was a good proof for the formation of this compound.

**3-4-2-N-phthalimidyl-4-phenyl benzylidene methane[35-40]**

The titled compounds [35-40] were prepared via reaction between N-(4-phenyl phenacyl) phthalimide and different primary aromatic amines.

During this reaction the electron-deficient carbon of carbonyl group in compound [34] was attacked by the strong nucleophile (primary amine) producing [I] followed by elimination of water molecule\(^{167}\) producing the desirable imides [35-40] as shown in Scheme (3-11).
Scheme (3-9)
Physical properties of compounds [35-40] are listed in Table (3-9).

FT-IR spectra of compounds [35-40] showed disappearance of absorption band at 1689 cm\(^{-1}\) due to \(\nu(C=O)\) ketone and appearance of absorption band at (1620-1681) cm\(^{-1}\) due to \(\nu(C=N)\) imine.

Also all spectra showed clear absorption bands at (1697-1725) cm\(^{-1}\), (1523-1604) cm\(^{-1}\) and (1311-1396) cm\(^{-1}\) due to \(\nu(C=O)\) imide, \(\nu(C=C)\) aromatic and \(\nu(C-N)\) imide respectively.

All details of FT-IR, spectral data of compounds [35-40] are listed in Table (3-10).

\(^1\)H-NMR spectrum of compound [35] showed signal at \(\delta=5.19\) ppm due to (-CH\(_2\)-) protons and signals at \(\delta=(7.25-8.1)\) ppm due to aromatic ring protons.

\(^1^3\)C-NMR spectrum of the same compound showed signal at \(\delta=44.9\) ppm due to (-CH\(_2\)-) carbon and signals at \(\delta=(112.8-135.2)\) ppm due to aromatic ring carbons and signal at \(\delta=168\) ppm due to (C=O) ketone and (C=N) imine.
<table>
<thead>
<tr>
<th>Comp. No.</th>
<th>Compound structure</th>
<th>Color</th>
<th>Melting Points °C</th>
<th>Yield %</th>
<th>Recrystallization Solvent</th>
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Table (3-9): Physical properties of compounds [35-40]
Table (3-10): Spectral data of compounds [35-40]

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Fig. No. (34) : FT-IR spectrum for compound [34]
Fig. No. (35): FT-IR spectrum for compound [35]
Fig. No. (36): FT-IR spectrum for compound [38]
Fig. No. (37) : $^1$H-NMR spectrum for compound [34]
Fig. No. (38): $^{13}$C-NMR spectrum for compound [34]
Fig. No. (39): $^1$H-NMR spectrum for compound [35]
Fig. No. (40): $^{13}$C-NMR spectrum for compound [35]
Biological Activity

The synthesized imides in this work were expected to possess biological activity since they have two active moieties in their molecules (phthalimide and Schiff’s base), thus a preliminary evaluation of antibacterial activity for some of the new imides were tested against two types of bacteria Staphylococcus aureus (Gram-positive) and Escherichia coli (Gram-negative).

The results showed that most of the tested imides possess good antibacterial activity as shown in Table (3-11).

Table (3-11): Anti-bacterial activity for some of the Synthesized Schiff’s bases

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<tr>
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</tr>
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<td>18</td>
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</tbody>
</table>

Key to symbols =

Inactive = (-) inhibition Zone< 6 mm
Slightly active = (+) = inhibition Zone 6-9 mm
Moderately active = (++) inhibition Zone 9-12 mm
Highly active = (+++) inhibition Zone 13-17 mm
Very high activity = (++++) inhibition Zone >17 mm
Suggestions for future work

The following suggestions are found suitable for future work:

1. Synthesis of other new imides linked to Schiff’s bases by following other strategies.
2. Evaluation of antibacterial activity of all the Synthesized imides in this work against other types of bacteria and comparision the results with those of known biologically active control compounds.
3. Evaluation of antifungal activity of all Synthesized compounds in this work against different types of fungi.
4. Synthesis of new carbonyl compounds (or heterocyclic aldehydes and ketones) and new primary amines (or heterocyclic amines) then introducing them in synthesis of new imides linked to Schiff’s base.
References

References


الخلاصة

تتضمن البحث تحضير مشتقات فثال ايميد جديدة مرتبطة بقواعد شيف باستخدام طرائق تحضير مختلفة، لذلك تم تقسيم هذا البحث إلى أربعة أجزاء رئيسية:

1. الجزء الأول تضمن تحضير مشتقات فثال ايميد جديدة مرتبطة بقواعد شيف عن طريق مجموعة فنيل سلفون أميد [5-18] مخطط (1). حيث تم تحضير هذه المركبات عن طريق اتباع الخطوات التالية:
   - سحب الماء من حامض N-فنيل فثال أميد المحضر في الخطة (أ) باستخدام انيهيدريد الخليل وخلات الصوديوم اللامانية كعامل ساحب للماء لتكون الفثال ايميد المقابل [2].
   - ادخال الفثال ايميد المحضر في الخطة (ب) بتفاعل كلوروسلفنة مع حامض الكلوروسلفونيك للحصول على كلوريد سلفون فثال ايميد [3].
2. أما الجزء الثاني من البحث فيتضمن تحضير فثال ايميدات جديدة مرتبطة بقواعد شيف عن طريق مكونة الفنيل سلفونات [20-26] حيث تم تحضير هذه المركبات باتباع مايلي:
3. الجزء الثالث من البحث يتضمن تحضير فثال ايميدات جديدة مرتبطة بقواعد شيف عن طريق مكونة الفنيل سلفونات [28-33] وذلك عن طريق اتباع الخطوات التالية:
   - تفاعل المركب [27] المحضر في الخطة (أ) مع عدة أمينات أروماتية أولية معوضة سنحصل على قواعد شيف [28-33] مخطط (3).
٤. أما الجزء الاخير من البحث فيتضمن تحضير فثال ايمائد جديدة مرتبطة بقواعد شيف عن طريق مجموعة المثيلين [٣٥-٤٠] تم تحضير هذه المركبات عن طريق الخطوات التالية:

أ- تفاعل ملح البوتاسيوم للفثال ايميد مع ٤- فنيل فيناسييل برومايدين لتكوين ٤- فنيل فيناسييل فثال ايميد [٣٤].


عينت درجات الانصهار للمركبات المحضرة وشخصت طيفيا عن طريق مطيافية الابشعة تحت الحمراء FT-IR كما واستخدمت مطيافية الرنين النووي المغناطيسي بنوعية 

١١H-NMR و ١٣C-NMR في تشخيص بعض المركبات المحضره.

كذلك تضمن البحث دراسة الفعالية البيولوجية لعدد من الايمائد الجديدة المحضرة ضد انواع من البكتريا وقد اظهرت النتائج بان الايمائد الجديدة المحضرة فعالة جيدة ضد انواع البكتريا قيد الدراسة.
رسالة مقدمة إلى كلية العلوم - جامعة بغداد وهي جزء من متطلبات نيل درجة الماجستير في علوم الكيمياء / الكيمياء العضوية

قدمتها

مرؤة شوقى عبد الرزاق الجبوري

بكالوريوس علوم الكيمياء 2008

بإشراف

الدكتورة أملاء معروض العزاوي

٢٠١٢ ١٤٣٣