

Synthesis of New Schiff's Bases Derived from 4-Phthalimidyl Acetophenone

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Abstract

Eight new Schiff's bases were prepared in three steps. The first step includes synthesis of phthalamic acid from the reaction between phthalic anhydride with p-amino acetophenone which in turn fused in the second step to form the corresponding phthalimide. The third step involved condensation of the prepared phthalimide with different primary aromatic amines to form new Schiff's bases. These compounds were characterized by FT-IR, $^1\text{H-NMR}$ and $^{13}\text{C-NMR}$ spectroscopy. Most of the synthesized compounds have been screened for their antimicrobial activities by using agar cup plate method against two types of bacteria. The results showed that the new Schiff's bases exhibit good to moderate antibacterial activity.

Keywords: Schiff's bases, amic acid, imide, biological activity.

Introduction

The chemistry of the carbon –nitrogen double bond plays a vital role in progresses of chemistry Science[1]. Schiff's bases can be synthesized from an aromatic amines and carbonyl compounds by nucleophilic addition forming a hemiaminal followed by dehydration to generate imine. They are well known intermediates for the preparation of azeidines, thiazolidinones, oxadiazelines and many other derivatives [2,3]. They have been used as analgesic, anthelmintic, antitubercular, plant growth regulator, antiviral and antitumor [4,5]. In this work a series of new Schiff's bases derived from 4-phthalimidyl acetophenone were prepared, characterized and their antimicrobial activity were studied.

Experimental

Melting points were determined in Gallen Kamp melting point apparatus and were uncorrected. FTIR spectra were recorded on SHIMADZU FTIR - 8400 Fourier Transform Infrared spectrophotometer as KBr disc. $^1\text{H-NMR}$ and C^{13}NMR spectra were recorded on Bruker spectrospro ultra shield magnets 300 MHz instrument using tetramethyl silane (TMS) as an internal standard and DMSO-d_6 as a solvent in Ahl-Albate University in Jordan.

1.Preparation Of Phthalamic Acid (1) [6]

(0.01 mol) 1.4g of phthalic anhydride was dissolved in (10 mL) of acetone in a suitable

round bottomed flask fitted with dropping funnel. The dropping funnel was supplied with (0.01 mol) 1.37 g of p-amino acetophenone dissolved in (10 mL) of acetone then this solution was added to the mixture dropwise with stirring for 1 hr at room temperature. The formed precipitate was filtered off then recrystallized from ethanol.

2.Preparation of Phthalimide (2) [7]

(0.01 mol) of amic acid (1) was placed in a wide dry pyrex tube which was immersed in an oil bath and provided with a thermometer. The oil bath was heated until fusion of amic acid then thermometer was maintained at ten –degrees above the melting point of amic acid for 45 min. The resulted fused material was cooled. The formed solid was recrystallized from hexane.

Table (1) lists physical properties and FT-IR spectral data of compounds (1) and (2).

Preparation of Schiff's Bases (3-10) [2]

A mixture of phthalimide (2) (0.0006 mol) and substituted aniline (0.0006 mol) was dissolved in absolute ethanol (10 mL) and few drops of glacial acetic acid were added. The mixture was refluxed for 4hrs on water bath then was poured into crushed ice with stirring. The separated solid was filtered, then recrystallized from suitable solvent.

Table (2) lists physical properties and FT-IR spectral data of Schiff's bases (3-10).

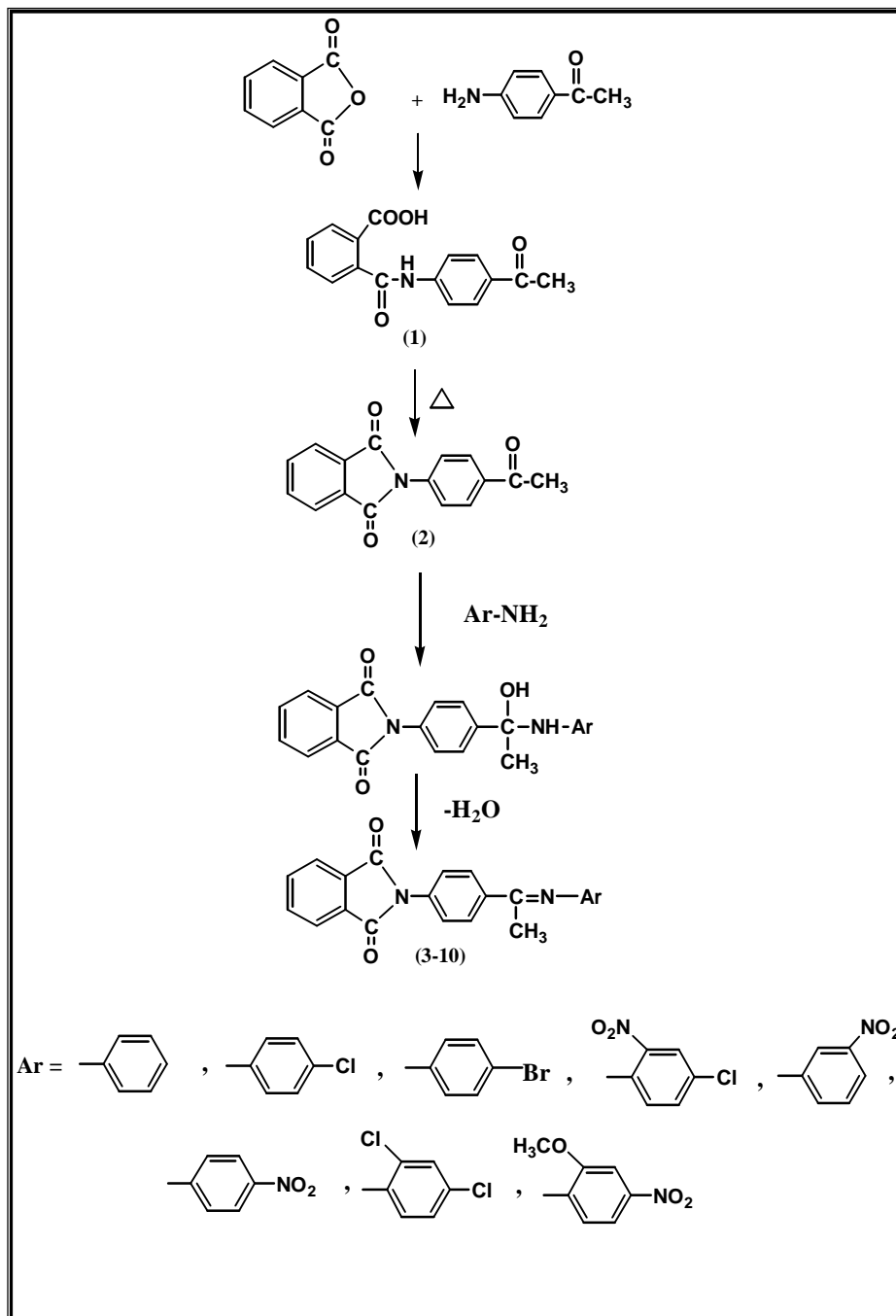
4. Biological Activity [8]

Most of the synthesized compounds were tested for their biological activity by the agar cup plate method. The organism used were *staphylococcus aureus* as gram positive bacteria and *Pseudomonas aeruginosa* as gram negative bacteria and dimethyl sulphoxide was used as sample solution. Using sterilized cork borer cups were scooped out of agar medium contained in a Petri dish which was previously inoculated with the microorganisms. The test compound solution

(0.1 mL) was added in the cups and the Petri dishes were subsequently incubated at 37 °C for 48 hrs. Zones of inhibition produced by each compound was measured in mm and the results are listed in Table (5).

Results and Discussion

New eight Schiff's bases were synthesized from the reaction of phthalimide (2) with substituted anilines as shown in Scheme (1). These Schiff's bases possess good biological activities.



Scheme (1).

The first step includes synthesis of phthalamic acid from the reaction between phthalic anhydride and p-amino acetophenone. The second step includes synthesis of phthalimides via fusion of phthalamic acid, then the prepared imide was introduced in reaction with substituted anilines in the third step to form Schiff's bases.

The % Yield of the prepared Schiff's bases were in the range {30-93} % it was noticeable presence of electron withdrawing constituents in aromatic ring caused increasing of yield percent of the prepared compounds .

These compounds were identified by FT-IR, $^1\text{H-NMR}$ and $^{13}\text{C-NMR}$ spectroscopy.

FT-IR spectrum of compound (1) showed clear absorption bands at (3326) Cm^{-1} , (3047) Cm^{-1} , (1704) Cm^{-1} , (1674) Cm^{-1} , (1589) Cm^{-1} and (1326) Cm^{-1} due to $\nu(\text{N-H})$, $\nu(\text{C-H})$ aromatic, $\nu(\text{C=O})$ ketone and $\nu(\text{C=O})$ amide, $\nu(\text{C=C})$ aromatic and $\nu(\text{C-N})$ respectively .

FT-IR spectrum of compound (2) showed clear absorption bands at (3055) Cm^{-1} , (1712) Cm^{-1} , (1596-1681) Cm^{-1} and (1380) Cm^{-1} due to $\nu(\text{C-H})$ aromatic, $\nu(\text{C=O})$ ketone and imide, $\nu(\text{C=C})$ aromatic and $\nu(\text{C-N})$ respectively [9,10] .

While FT-IR spectra of Schiff's bases (3-10) showed clear absorption bands at (3047-3093) Cm^{-1} , (1704-1712) Cm^{-1} , (1504-1625) Cm^{-1} , (1596-1643) Cm^{-1} and (1350-1388) Cm^{-1} due to $\nu(\text{C-H})$ aromatic, $\nu(\text{C=O})$ ketone and imide , $\nu(\text{C=C})$ aromatic, $\nu(\text{C=N})$ and $\nu(\text{C-N})$ respectively .

FT-IR spectra of compounds (3) ,(6) and (7) showed clear absorption bands at (1087) Cm^{-1} , (1041) Cm^{-1} and (1087) Cm^{-1} due to $\nu(\text{C-Cl})$ [9,10].

Finally, FT-IR spectra of compounds (3), (6) and (9) showed clear absorption bands at (1388-1450) Cm^{-1} , (1350-1488) Cm^{-1} and (1388-1481) Cm^{-1} due to $\nu(\text{NO}_2)$.

$^1\text{H-NMR}$ spectra of compound (1) showed singlet signal at 2.3 ppm due to CH_3 group, multiplet signals at (6.5-8.1) ppm due to aromatic protons and NH group and singlet signal at 10.6 ppm due to OH carboxylic. While $^1\text{H-NMR}$ spectra of compound (2) showed singlet signal at 2.5 ppm due to CH_3 group and multiplet signals at (7.6-8.1) ppm due to aromatic protons .

$^1\text{H-NMR}$ spectra of compounds (3), (4) and (6) showed singlet signal at 2.5 ppm due to CH_3 group and multiplet signals at (6.2-8.1) ppm due to aromatic protons.

Finally $^1\text{H-NMR}$ spectra of compound (9) showed singlet signal at 2.5 ppm due to CH_3 group, singlet signal at (3.8) ppm due to OCH_3 group and multiplet signals at (6.3-8.1) ppm due to aromatic protons [9,10] .

$^{13}\text{C-NMR}$ spectra of compound (1) showed signal at 27 ppm due to CH_3 , signals at (112-136) ppm due to aromatic carbons , signals at (167-169) ppm due to C=O imide and signals at (195-197) ppm due to C=O ketone.

$^{13}\text{C-NMR}$ spectra of compound (2) showed signal at 27 ppm due to CH_3 , signals at (124-136) ppm due to aromatic carbons, signal at (136) ppm due to C=N , signal at (167) ppm due to C=O imide and signal at (197) ppm due to C=O ketone.

While $^{13}\text{C-NMR}$ spectra of compounds (3), (4) and (6) showed signal at (27) ppm due to CH_3 group, signals at (107-136) ppm due to aromatic carbons, signals at (145-150) ppm due to C=N and signal at (167) ppm due to C=O imide .

Finally, $^{13}\text{C-NMR}$ spectra of compound (9) showed signal at (27) ppm due to CH_3 group, signal at (56) ppm due to OCH_3 , signals at (106-135) ppm due to aromatic carbons, signal at (146) ppm due to C=N and signal at (167) ppm due to C=O imide [9,10].

Biological activity [11,12]

The prepared phthalimide (2) and the prepared Schiff's bases (3-9) showed different biological activities against two types of bacteria gram positive and gram negative bacteria including *staphylococcus aureus* and *Pseudomonas aeruginosa* .The test results showed that all Schiff's bases are inactive against *staphylococcus aureus* except compound (3) which showed very high activity against this bacteria .

While the Schiff's bases (3,4,6,8,9) showed moderate activity against *Pseudomonas* except compound (5) which was highly active and compounds (2,10) which are slightly active against this bacteria.

All these result are shown in Table (5).

Table (1)
Physical properties and FT-IR spectral data of compounds (1) and (2).

Compd. No.	Compound structure	M.P. °C	Yield %	Color	Major FTIR Absorptions Cm^{-1}						
					ν O-H	ν N-H	ν C=O Amide	ν C=O Ketone	ν C=C Aromatic	ν C=O Imide	ν C-N
1		218-219	76	Yellow	3240	3326	1674	1704	1589	—	1326
2		238-240	75	Yellow	—	—	—	1712	1681 1596	1712	1380

Table (2)
Physical properties and FT-IR spectral data of Schiff's bases (3-10).

Compd. No.	Compound Structure	M.P. °C	Yield %	Color	Major FTIR Absorptions Cm^{-1}			
					ν C=O Imide	ν C-N	ν C=N	Other
3		146-148	66	Orange	1712	1388	1643	ν C-NO2 1450 1388 ν C-Cl 1087
4		112-114	71	Yellow	1712	1350	1620	ν C-NO2 1488 1355
5		220-222	50	Off White	1712	1388	1604	ν C-Cl 1087
6		170-172	70	Gray	1712	1388	1610	ν C-NO2 1390 1310
7		68-70	93	Off White	1712	1388	1604	ν C-Cl 1041
8		165-166	30	Off White	1712	1380	1596	—
9		138-140	75	Yellow	1712	1388	1627	ν C-NO2 1481 1388
10		218-220	66	Gray	1712	1388	1625	—

Table (3)
¹H-NMR spectral data for some of the prepared compounds.

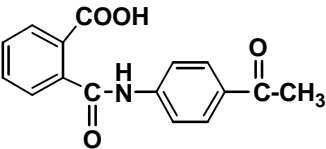
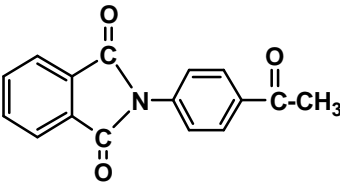
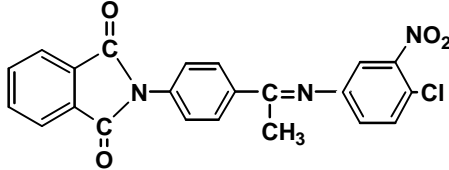
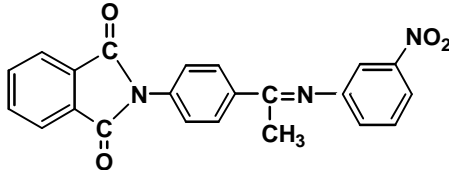
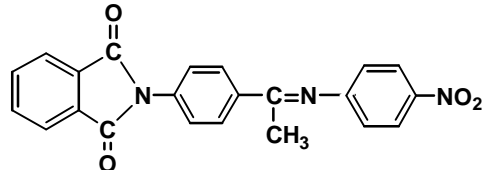
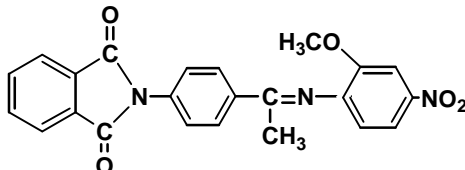
Compd. No.	Compound structure	¹ H-NMR spectral data
1		$\delta = 6.5-8.1$ ppm, $\delta = 2.3$ ppm <u>CH₃</u> Aromatic protons and N-H, 10.6 ppm OH carboxylic
2		$\delta = 7.1-8.1$ ppm, $\delta = 2.5$ ppm <u>CH₃</u> Aromatic protons.
3		$\delta = 7-8.1$ ppm, $\delta = 2.5$ ppm <u>CH₃</u> . Aromatic protons.
4		$\delta = 7.2-8.1$ ppm, $\delta = 2.5$ ppm <u>CH₃</u> Aromatic protons.
6		$\delta = 6.2-8.1$ ppm, $\delta = 2.5$ ppm <u>CH₃</u> Aromatic protons.
9		$\delta = 6.3-8.1$ ppm, $\delta = 2.5$ ppm <u>CH₃</u> Aromatic protons, $\delta = 3.8$ ppm <u>OCH₃</u>

Table (4)
¹³C-NMR spectral for some of the prepared compounds.

Compd. No.	Compound structure	¹³ C-NMR spectral data
1		$\delta = (112-136) \text{ ppm}$, $\delta = 27 \text{ ppm CH}_3$ Aromatic carbons, $\delta = 167-169 \text{ ppm C=O Imide}$ $\delta = 195-197 \text{ ppm C=O Ketone}$
2		$\delta = (124-136) \text{ ppm}$, $\delta = 27 \text{ ppm CH}_3$ Aromatic carbons, $\delta = 167 \text{ ppm C=O Imide}$ $\delta = 197 \text{ ppm C=O Ketone}$
3		$\delta = 7 \text{ ppm CH}_3$, $\delta = (118-136) \text{ ppm}$ Aromatic carbons, $\delta = 145 \text{ ppm C=N}$, $\delta = 167 \text{ ppm C=O imide}$
4		$\delta = 27 \text{ ppm CH}_3$, $\delta = (107-130) \text{ ppm}$ Aromatic carbons, $\delta = 149, 150 \text{ ppm C=N}$, $\delta = 167 \text{ ppm C=O imide}$
6		$\delta = 27 \text{ ppm CH}_3$, $\delta = (112-136) \text{ ppm}$ Aromatic carbons, $\delta = 149 \text{ ppm C=N}$, $\delta = 167 \text{ ppm C=O imide}$
9		$\delta = 27 \text{ ppm CH}_3$ $\delta = 56 \text{ ppm OCH}_3$, $\delta = (106-135) \text{ ppm}$ aromatic carbons 146 ppm C=N $\delta = 167 \text{ ppm C=O imide}$

Table (5)
Antimicrobial activity of the prepared compounds.

Compd. No.	Gram positive bacteria	Gram negative bacteria
	<i>S.aureus</i>	<i>aerugenos Pseudomonas</i>
2	-	-
3	++++	++
4	-	++
5	-	+++
6	-	++
7	-	+
8	-	++
9	-	++
10	-	-

Key to symbols : Inhibition zone < 6= - Inactive

Slightly active 10= +

Moderately active 11-13=++

Highly active 15=+++

Very high activity 20=++++

References

- [1] H.J. Yang ,W.H. Sun, Z. Long and Z.Ma, "The rapid synthesis of Schiff's bases without solvent under microwave irradiation", *Chin. Chem. Lett.*, Vol. 13, No.1, 2002, pp-3-6.
- [2] J. J. Vora, S. B. Vasava, K. C. Parmar, S.K.Chauhan and S.S.Sharma, "Synthesis , Spectral and microbial studies of some Novel Schiff's bases derivatives of 4-methyl pyridine-2 - amine ", *Journal of chemistry*, Vol.6, No.4, 2009, pp-1205-1210.
- [3] M. N .Ibrahim and S. A .Sharif, "Synthesis, Characterization and use of Schiff's bases as fluorimetric analytical reagents", *E.J.Chem.*, Vol.4, No.4, 2007, pp-531-535.
- [4] N. A. Salim, "Synthesis and characterization of Novelazole heterocycles based on 2, 5-Disubstituted thiazole", *Turk J.Chem.*, Vol.32, 2008, pp-229-235.
- [5] E. M. Hodnett and W.J. Dunn, "Structure – antitumor activity correlation of some Schiff's bases", *J. Med. Chem.*, Vol.13, No.4, 1970, pp-768-770.
- [6] S. A. Mahdi, "Synthesis, identification and biological Activity study of N-(substituted benzothiazole-2-yl) maleimides and N-substituted sulfonamide maleimides substituted with different heterocyclics", 2008, MSc., thesis University of Baghdad.
- [7] M.A. Yassien, "Synthesis and Characterization of Several N-Substituted Isoimides and Studing Indetials their ability for Chain growth and Condensation polymerization", 2007, MSc., thesis University of Baghdad.
- [8] S. Bairagi, A. Bhosale and M.Ndeodhar," Design, synthesis and evaluation of Schiff's bases of 4-chloro-3- coumarin aldehyde as antimicrobial agent", *E .J. Chem* , Vol.6, No.3, 2009, pp-759-762.
- [9] R.M.Silverstein and G.C. Bassler "spectrometric identification of organic compounds", 4th Edition 1981, John and sons, New Yourk.

- [10] D. H. Williams, and Felming; Translated by Sarkess J. Y. Sarkess ; "*Spectroscopic methods in organic chemistry*", 1st Edition. Baghdad University, 1986, New Yourk.
- [11] H. Vahidi, M. Kamalinejad and N. Sedaghati," Antimicrobial Properties *Croccus sativus L.*", *Iranian Journal of Pharmaceutical Research*, Vol. 1, 2002, pp-33-35.
- [12] A. S. Jain, S.J. Surana, S.B. Gokhale, A. U. Tatiya and R. C. Bothara, "Antimicrobial Properties of *Eranthemum roseum* (Vahl) R.Br.", *Iranian Journal of Pharmaceutical Research*, Vol.6, No. 2, 2007 , pp- 131-133.

الخلاصة

تم تحضير ثمانية من قواعد شيف جديدة مشتقة من 4-فتال ايميديل اسيتوفينون بثلاث خطوات:
تضمنت الخطوة الأولى تحضير حامض الفتال اميك من تفاعل انهيدريد الفتاليك مع بارا امينو اسيتوفينون والذي بدوره صهر في الخطوة الثانية للحصول على الفتال ايميد المقابل .
أما الخطوة الثالثة فقد تضمنت تكاثف الفتال ايميد المحضر مع أمينات اروماتية أولية مختلفة للحصول على قواعد شيف جديدة. تم تشخيص المركبات المحضرة بمطيافية FT-IR و $^1\text{H-NMR}$ و $^{13}\text{C-NMR}$. كما ودرست الفعالية البيولوجية لهذه المركبات بإتباع طريقة الحفر تجاه نوعين من البكتريا وقد أظهرت المركبات فعالية واضحة نحو أحد نوعي البكتريا قيد الدراسة.