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Preparation, investigation, theoretical study and biological activity of 2-[4-acetyl phenoxy) N-(4-substitutent phenyl)] acetoamide derivatives

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ABSTRACT

We have prepare a number of 2-[4-acetyl phnoxy) N-(4-substitutent phenyl)] acetoamide from reaction α-chloro acetoamide-N-(P-substitute phenyl) with p- acetyl phenol in the presence of sodium and absolute ethanol. All products, have been characterized by IR and theoretical study. The anti bacterial activity of prepared compounds was described. The in vitro anti bacterial activity of the compounds was determined against pathogenic gram negative Escherichia coli and gram positive Staphylococcus aureus bacteria. Anti bacterial results indicated that the compounds possessed a broad spectrum of activity.

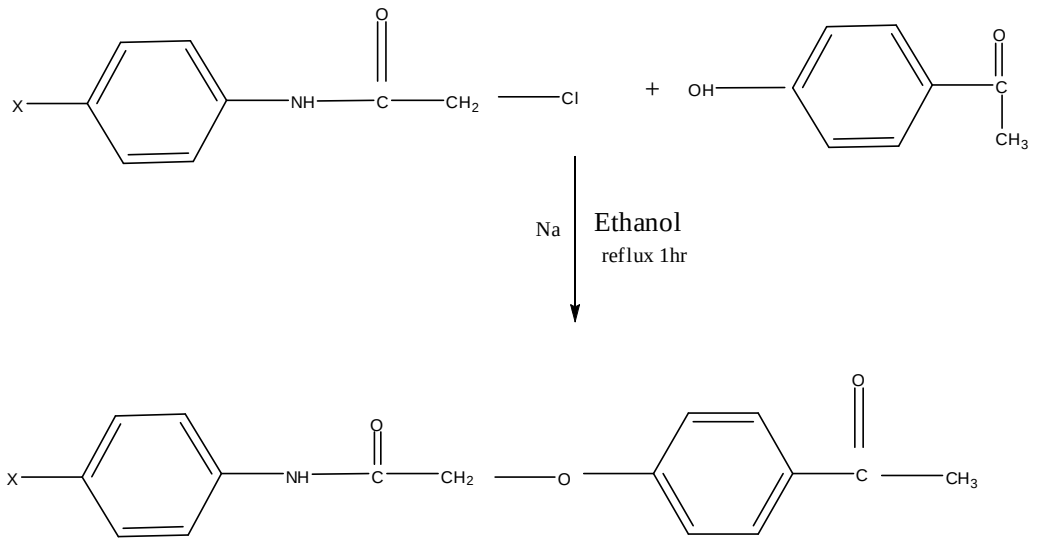
INTRODUCTION

α-chloro acetoamide-N-(P-substitute phenyl) were prepared , characterized and theoretical studied have been described in pervious papers[1-10].

Phenoxy compound derivatives are wildly used in many fields including pharmaceutical industry due to their biological properties such as herbicide[11] drug [12] and antibacterial [13-16].

Alhazam[5] was prepared α-chloro acetoamide-N-(P- substituent) phenyl from condensation p-substituent aniline with PPh_3/CCl_4. To continuation of our work on α-chloro acetoamide-N-(P- substituent), we repore here in this paper , the preparation , characterization , theoretical study and biological activity of 2 [(acetyl phenoxy) –N- (4-sub.Phenyl)] acetoamide derivatives as shown in Scheme 1.

General procedure of preparation :
Six new compounds (1-6) were synthesis in this study based on the solution of (0.8 g) sodium in 15 mL absolute ethanol was mixed with 0.033 mL from p-acetyl phenol. 0.048 mol from α-chloro aceamide-N-(p-substitutent)phenyl was added for above solution step by step with stirring . At end , the solution was heated under reflux for 1hr. After cooling and filteraion , the compound was washed with water and recrystalized from methanol[4]. To obtain the six compounds as described in table 1.



X= H (1); X= CH_3 (2); X= OMe (3); X= Cl (4); X= NMe_2 (5); X= NO_2 (6).

Scheme 1: The synthesis of (1 – 6) compounds

Table 1: Characterization of (1- 6) compounds

Com. No.	X	Molecular weight	Molecular Formula	Mp ^oC	Yield
1	H	269	$C_{16}H_{18}NO_3$	212-214	60%
2	CH_3	283	$C_{17}H_{17}NO_3$	210-211	60%
3	OCH_3	299	$C_{17}H_{17}NO_4$	222-223	55%
4	Cl	203	$C_{16}H_{14}NO_3Cl$	199-200	60%
5	NMe_2	312	$C_{18}H_{20}N_2O_4$	325-227	60%
6	NO_2	314	$C_{16}H_4N_2O_4$	182-183	60%

Physical Measurements:
IR spectra were recorded on a SHAIDZU 8400 Ft-IR spectrophotometer . Melting point were measured on a Gall en Kamp melting point apparatus and were uncorrected.

Theoretical Calculation :
All theoretical computations were performed IVPC. The AM_1 semi-empirical method in program Hyperchem 6.01 were utilized to compute the properties of compounds.
Charge density (q_N) and heat of formation (ΔH). Chem. Draw prog. 4.5 was used to compute theoretical ^{13}C chemical shifts.

Determination of the biological activity of the prepared compounds:
Different concentrations were used to determine the biological activity of each prepared compounds (3 - 6), against strains of pathogenic gram positive and gram negative bacteria which are (*Staphylococcus aureus* and *Escherichia coli*), using a filter disk assay .The biological activity was defined as the clear zone of growth inhibition [23].

RESULTS AND DISCUSSION

^{13}C NMR :
Prepared compounds (1 to 6) are characterized depending on the additive method by using CS-Chem. Draw program. The a viable table for chemical shifts of ^{13}C NMR [14-16] are also utilized in the characterization . The values of peaks position are shown in Table 2.

FT-IR spectra :
In the examination of IR spectra for these compounds, references [20-22] were utilized .

The spectra of these compounds show that all compounds have common peak such as $(N-H)_{st}$ at 3255-3190 Cm^{-1} , $(C=O)_{st}$ at 1690-1650 Cm^{-1} , $(C-H\ Aromaic)_{st}$ at 3066-3100 Cm^{-1} , CH strecting in CH_2 a 2933-3930 Cm^{-1} , $(C-O-C)_{st}$ a 1165.8-1200 Cm^{-1} , $(C-N)_{st}$ at 1250-1260 Cm^{-1} .

The substitution on benzene ring such as:
NO_2 asy stretching at 1537 Cm^{-1} , NO_2 sym stretching at 1300 Cm^{-1} ,C-Cl stretching at 830 Cm^{-1} And C-Br stretching at 700 Cm^{-1} .

Electronic Properties :
Some molecular information about these compounds (1-6) such as charge density (q_{N-H}) dipole moment (μ) , heat formation (ΔH) ,vibration frequency for υNH and C=O were calculated by AM_1 molecular orbital semiemperical method for geometry optimized which are presented in Table 3.

Table 2 : Bands ^{13}C NMR spectra of these compounds

X	CH_3	C=O	C_4	$C_{3,5}$	$C_{2,6}$	C_1	CH_2	C=O	C_1	$C_{2,6}$	$C_{3,5}$	C_4	X
+1	26.6	197	129	129.8	114.2	162.5	66.6	167.6	136.5	112.6	128.9	128	
CH_3	26.6	197	129	129.8	114.2	162.5	66.6	167.2	136.5	112.6	129.2	136	21.3
OCH_3	26.6	197	129	129.8	114.2	162.5	66.6	167.2	130.6	121.5	114.5	155.9	55.6
Cl	26.6	197	129	129.8	114.2	162.5	66.6	167.2	136.2	122.6	129	133.3	
NMe_2	26.6	197	129	129.8	114.2	162.5	66.6	167.2	128	120.4	113	155	40.2
NO_2	26.6	197	129	129.8	114.2	162.5	66.6	167.2	144.6	109.9	124.1	143.6	

Table 3 : Electronic properties of (1 – 6) compounds

X	H	CH_3	OCH_3	Cl	NMe_2	NO_2
ΔH	-37	-30	-50	-20	-55	-50.1
μ	4.4	5.4	4.4	4.8	5.0	5.2
$\upsilon_{C=O}$	1690	1655	1726	1690	1698	1700
υ_{NH}	3250	3225	3216	3200	3190	3210
q_{NH}	-0.2918	-0.2992	-0.2992	-0.2991	-0.2994	0.2982

The biological activity of the compounds :-
The results of antibacterial activity of the prepared compounds (3 - 6) were shown in table (4). The prepared compounds in this study were shown very effective against gram negative strain (***Escherichia coli***) but less active against gram positive strain **(*Staphylococcus aureus***). It has been postulated that cell membrane of (***Escherichia coli***) contains many condensed fat layers compared with (***Staphylococcus aureus***) [24]. An antimicrobial is a substance that kills or inhibits the growth of microorganisms such as bacteria, fungi, or protozoans, as well as destroying viruses. Antimicrobial drugs either kill microbes (microbicidal) or prevent the growth of microbes (microbistatic) [25].

Some N-phenyl acetamide derivatives of *N, N*-substituted acetamides have been found to possess significant antimicrobial activity and antitoxic [26 - 29]**.** Based on the structural data some common features can be deduced in all the pharmacological divergent classes [30- 31].

A basic nitrogen which may be part of heteroaromatic ring or cyclic/acyclic system intended to interact electrostatically with the appropriate target [32- 36].

Table 4 : The anti bacterial activity of the prepared compounds against pathogenic (G+) and (G-) bacterial strains.

Bacteria Extracts & conc. (mg\ml.)		*S. aureus* (Pathogenic)	*E. coli* (Pathogenic)
3	100	---	---
	50	---	20
	25	---	25
4	100	20	30
	50	20	20
	25	25	30
5	100	10	30
	50	10	20
	25	---	20
6	100	---	---
	50	---	---
	25	---	---

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