Preparing and Characterization of Some Heterocyclic Compounds with Studying Their Biological Activity

Muhanned A. Mahmoud
Department of Chemistry, College of Sciences for Women, University of Baghdad.
E-mail: alnemimu2006@yahoo.com.

Abstract

New compounds of (E-(1,3-bis)3-bromophenyl) prop-2-en-1-one], (E-(1-(3-Nitrophenyl-(3-(1-h-pyrrol-2-yl) prop-2-en-1-one], (E-(1-(3-Nitrophenyl-(3-(1H-pyrrol-2-yl) prop-2-en-1-one], [(E)–N,N-1,3-bis) 3-Nitrophenyl) propan-3-yl-1-ylidene) dimethan amine], (E-(1-(3-Nitrophenyl-(3-(1-H-pyrrol-2-yl) prop-2-en-1-one] and [(E-(1,3-bis)4-dimethylamino) phenyl) prop-2-en-1-one] have been synthesized. The prepared compounds have synthesized from chalcone [1] and characterized by using FT-IR, Uv/ vis and ^{1}H-NMR spectra besides, determining the melting points and Rf with the biological activity.

Keywords: Heterocyclic compounds, pyrrols, chalcones.

Introduction

Chalcones are well known intermediates for synthesizing various heterocyclic compounds. The compounds with the backbone of chalcones have been reported to possess various biological activities such as antimicrobial[1-3], anti-inflam –matory[4], antimalaria[5-6], antilies–hmanial[7], antioxidant[8] andantitubercular[9].

Chalcones are an aromatic ketone and an enone that forms the central core for a variety of important biological compounds, which are known collectively as chalcones. Aldol condensation represent an important class of carbon–double bond carbon formation reactions both in nature and in synthetic chemistry. Compounds called chalcones[10] can prepare by aldol condensation of an aromatic ketone and aldehyde.

Pyrazole also, is one of a class of organic heterocyclic compounds containing a five member aromatic ring structure composed of two nitrogen atoms and three carbon. But pyrazoline it is a class of organic heterocyclic compounds containing a five member not aromatic ring structure composed of two nitrogen atoms and three carbon[11]. In the present work we report the reaction of various substituted acetophenone with different substituted aromatic aldehyde to form chalcones [12] and then converted to pyrolles.

Experimental

Melting points were recorded with Stuart Melting point apparatus and were uncorrected. Infra red spectra (FT-IR) were recorded on Shimadzu FT-IR-8300 spectrophotometer in Ibn Sina State Company (ISSC).Uv/vis spectra were recorded on Uv/vis varian Uv-Cary-100 spectrophoto-meters in (ISSC).1H-NMR spectra were recorded on a BRUKER-400 MHz operating at 300 MHZ with tetra methyl silane as internal standard in $CDCl_3$ and DMSO-d6 as a solvent, measurements were made at Chemistry Department, AL-Baath University-Syria. Elemental Analysis (C.H.N.S.) was carried out with: Euroea Elemental Analyzer Italia by Chemical Department College of Science, Babylon University. Thin layer Chromatography (TLC) was carried out by using alumina plates percolated with silica–gel, supplied by Merck. Spots were detected with iodine vapor. The biological activity was performed by Biology Department College of Science, University of Tikrit.

1) Synthesis of 3- (2-substitutedphenyl) -1-(-3-nitrophenyl) prop-2-en-1-one (1-5)

To a stirred mixture of 3-nitro acetophenone (0.01 mol) and substituted benzaldehyde (0.01mol) in absolute ethanol (5ml) and NaOH in ethanol (30%) and continue stirring for two hours at room temperature. Allow to stand reaction mixture for 12 hours. Precipitate the reaction mixture

by addition of water, acidified with diluted HCl. Filter the product, wash with cold ethanol and allowed to afford.

2-Synthesis of (3-phenyl-4, 5-dihydro-1H-pyrazol – 5-yl)benzene (6-10).

Chalcone (1-5) (0.01mol) was dissolved in ethyl alcohol 95% (20ml) and refluxed with excess ofhydrazine hydrate for 12hrs, the reaction mixture was diluted with cold water 50ml and the white precipitate formed was filtered off and recrystallized with ethyl alcohol.

Results and Discussion

This paper reports a simple and effective method for the synthesis of chalocnes by an basic catalyzed aldol reaction we used NaOH as a convenient method. Chalcones are obtained in good to excellent yields. Our purpose was to synthesize a series of chalcones, starting from benzaldehyde and acetophenone or their substituted derivatives.

Synthesis of chalcone is a single step method. The synthesized chalcone derivatives were undergone physicochemical character ization and the obtained results are given in (Table (2)). The yields of the synthesized compounds were found to be significant. The structure of the synthesized compounds was confirmed by IR, ^{1}H-NMR, Uv/vis spectra.

All the compounds give the characteristic IR band that proved the presence of particular functional group (Table (2)) and ^{1}H-NMR, Uv/vis spectroscopy helps to find the molecular weight structures of the synthesized compounds (Table (3)). The IR band at 1778cm^{-1} suggesting the presence of (C=O) group, at 1631cm-^{1} due to (C=C) group (compound 1). The IR band at 1606 cm^{-1} indicates the presence of (C=C) group. FT-IR band at 3142cm^{-1} indicates the presence of (-OH) group (compound (2) as example). TLC, melting points, FT-IR spectroscopy for compounds (6-10) proved the presence of (C=N) group and (N-H). Also, the FT-IR band at1591cm^{-1}indicates the presence of (C=C) group. FT-IR band at 3261cm^{-1} indicates the presence of (-OH) group. The results obtained from this study confirmed that the product has formed. Henceforth viewing these characteristic properties more compounds can be synthesized and subjected to pharmacological evaluation.

UV spectrum Fig.(3) shows the transions n→л and л→л* which confirmed the presence of the un-bonded pair of electrons on nitrogen atom and aromatic system (double bond). The product (1) is also, identifiedby the 1H-NMRspectrum which shows the protons at (δ 7.5-8) ppm due to aromatic protons. Proton of (N-H) of pyrazole ring appeared at δ (8.05) Fig.(2).

The FT-IR spectrum of compound (10), shows the bands, Fig. (4), at (3250 cm^{-1}), (2924 and 2854 cm^{-1}) are attributed to υ(C-H) aromatic, and (C-H) aliphatic stretching vibrations of (C-H) group. Other characteristic bands of aromatic system is the appearance of υ(C=C) at about (1512 cm-1) besides the band at (1640 cm-1) due to (C=N).

The 1H-NMR spectrum of compound [10], shows the following characteristic chemical shifts (DMSO-d6) ppm. Protons of (CH2) of pyrazole ring appeared at (δ 4.22). Proton of (NH) group appeared at (δ 4.5). Protons of aromatic rings appeared at the range δ (7.5-8) as a multiplate peaks.

Table (1)
Physical properties of compounds [1-10].

Comp. No.	*Substituted groups*	*Molecular formula*	*Molecular weight*	*M.P/° C*	*Yield %*
1	NO_2	$C_{15}H_{10}N_2O_5$	298	120-122	80
2	OH	$C_{15}H_{11}NO_4$	269	135-137	69
3	Br	$C_{15}H_{10}NO_3Br$	332	144-147	77
4	N-Me	$C_{17}H_{16}N_2O_3$	296	141-143	73
5	Pyrrole	$C_{13}H_{10}N_2O_3$	242	125-127	70
6	NO_2	$C_{15}H_{12}N_4O_4$	312	156-158	78
7	OH	$C_{15}H_{13}N_3O_3$	283	175-177	62
8	Br	$C_{15}H_{12}N_3O_2Br$	346	170-173	74
9	N-Me	$C_{17}H_{18}N_4O_2$	310	180-182	69
10	pyrrole	$C_{13}H_{12}N_4O_2$	256	162-164	85

Table (2)
The C.H.N. analysis for some prepared compounds.

Comp. No.	M.F.	C%	H%	N%
4	$C_{17}H_{16}N_2O_3$	Cal.68.91	5.40	9.45
		Found68.92	5.43	9.42
7	$C_{15}H_{13}N_3O_3$	Cal.63.60	4.59	14.84
		Found63.58	4.55	14.90
9	$C_{17}H_{18}N_4O_2$	Cal. 65.80	5.80	18.06
		Found. 65.77	5.86	18.02
10	$C_{13}H_{12}N_4O_2$	Cal.60.93	4.68	21.87
		Found60.89	4.62	21.93

Table (3)
The Rf of the prepared compounds.

Comp. No.	R_f	Solvent
1	0.92	Dioxane
2	0.84	=
6	088	=
7	076	=
10	0.81	=

Table (٤)
FT-IR spectral data of compounds [1-5].

Comp. No.	υ(C-H) cm^{-1}	υ(C-H) aromatic cm^{-1}	υ(C=O) cm^{-1}	υ(C=C) alkene cm^{-1}	υ(C=C) aromatic cm^{-1}	Other bands cm^{-1}
1	2870	3082	1778	1631	1527, 1492	υ(NO_2) 1346- 1438 υ(C-N) 1184
2	2724	3094	1732	1627	1527,1489	υ(OH) 3444, 3468 υ(NO_2) 1364, 1427 υ(C-N) 1172
3	2730	3091	1797	1593	1546,1485	υ(NO_2) 1342- 1454 υ(C-N) 1176 υ(C-Br) 1089
4	2935, 2808	3082	1716	1647	1527, 1489	υ(N-Me) 1350 υ(NO_2) 1350- 1438 υ(C-N) 1168
5	2789	3097	1720, 1770	1616	1527, 1485	υ(N-H) 3251, 3410, 3471 υ(NO_2) 1346- 1438 υ(C-N) 1184

Table (٥)
FT-IR spectral data of compounds [6-10].

Comp.No.	υ(N-H) cm^{-1}	υ(C-H) aliphatic cm^{-1}	υ(C-H) aromatic cm^{-1}	υ(C=N) cm^{-1}	υ(C=C) cm^{-1}	Others cm^{-1}
6	3222	2854, 2944	3091	1617	1531, 1438	υ(NO_2) 1355, 1486 υ(C-N) 1180
7	3298	2856, 2926	3059	1609	1508, 1467	υ(NO_2) 1357, 1476 υ(C-N) 1180 υ(OH) 3430
8	3402	2900, 2914	3053	1599	1537, 1466	υ(NO_2) 1355, 1486 υ(C-N) 1180υ(C-Br) 1077
9	3328	2921, 2915	3077	1616	1544, 1463	υ(N-Me) 1347 υ(NO_2) 1329, 1448 υ(C-N) 1136
10	3477, 3411, 3255	2966, 2788	3087	1626	1571, 1488	υ(NO_2) 1325, 1442 υ(C-N) 1126

Microbiological Method

In this work, the antibacterial test was performed according to thedisc diffusion method. Compounds ((2), (4), (6), (8), (10)) were assayed for their antimicrobial activity in vitro against Gram-negative bacteria (*Escherichia coli*) and Gram-positive bacteria (*staphylococcus aureus*). Prepared agar and Petridishes were sterilized by autoclaving for 15min at 121C°. The agar plates were surface inoculated uniformly from the broth culture of the tested microorganisms. In the solidified medium suitably spaced apart holes were made all 6mm in diameter. These holes were filled with 100µl of the prepared compounds (1mg of the compound dissolved in 1ml of DMSO solvent), DMSO was used as a solvent. These plates were incubated at 37C° for 24h for both bacteria. The inhibition zones caused by the various compounds were examined. The results of the preliminary screening tests are listed in Table (٦).

Table (٦)
Antibacterial activities of some of the synthesized compounds.

Comp. No.	*Escherichia coli*	*Staphococcus aureus*
2	±	-
4	+	+
6	±	-
8	+	+
10	+	_

Note:(-): No inhibition, (±) = 6 - 9 mm, (+) =10 -14 mm, (++): 15-22 mm.

Conclusion: 1-For *Escherichia coli* (G-), compounds (2,6) showed moderate effect on this bacteria, while compounds (4,8,10) showed high activity againstthis bacteria.2-For *Staphylococcus aureus* (G^+), compounds (4,8) have highe effect on this bacteria except compounds (2,6,10).

Conclusion

In conclusion, we describe an efficient–procedure for the chalcones can be synthesized in good yields from aromatic aldehydes and ketones using the catalytic system NaOH/EtOH. Thus, the present method constitutes a novel synthesis of chalcones with the condition and good yields. The synthesized compounds were characterized by.

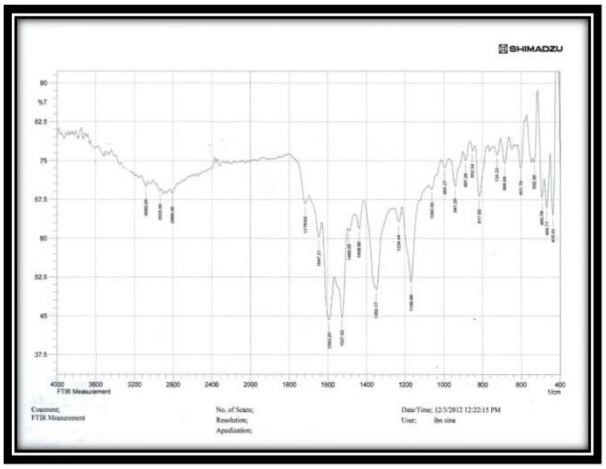


Fig.(1) FT-IR spectrum of compound (1).

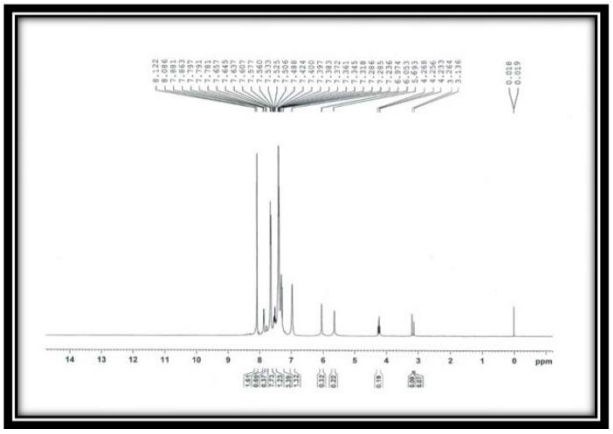


Fig.(2) H-NMR spectrum of compound (1).

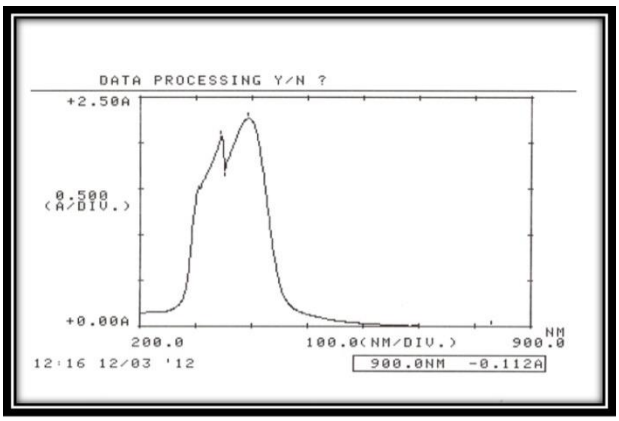


Fig.(3) UV/VIS spectrum of compound (1).

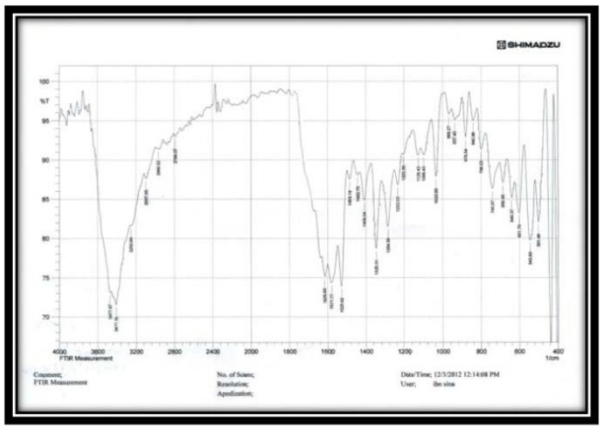


Fig.(4) FT-IR spectrum of compound (10).

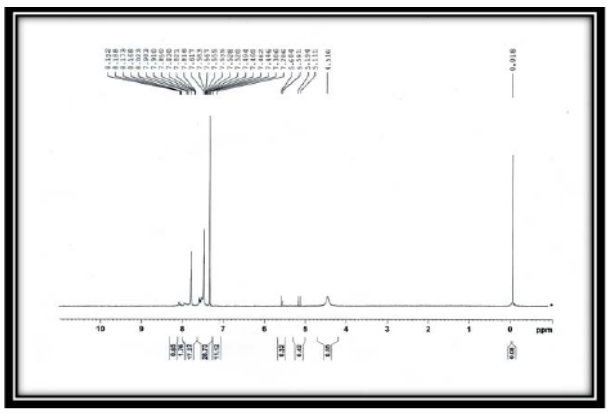
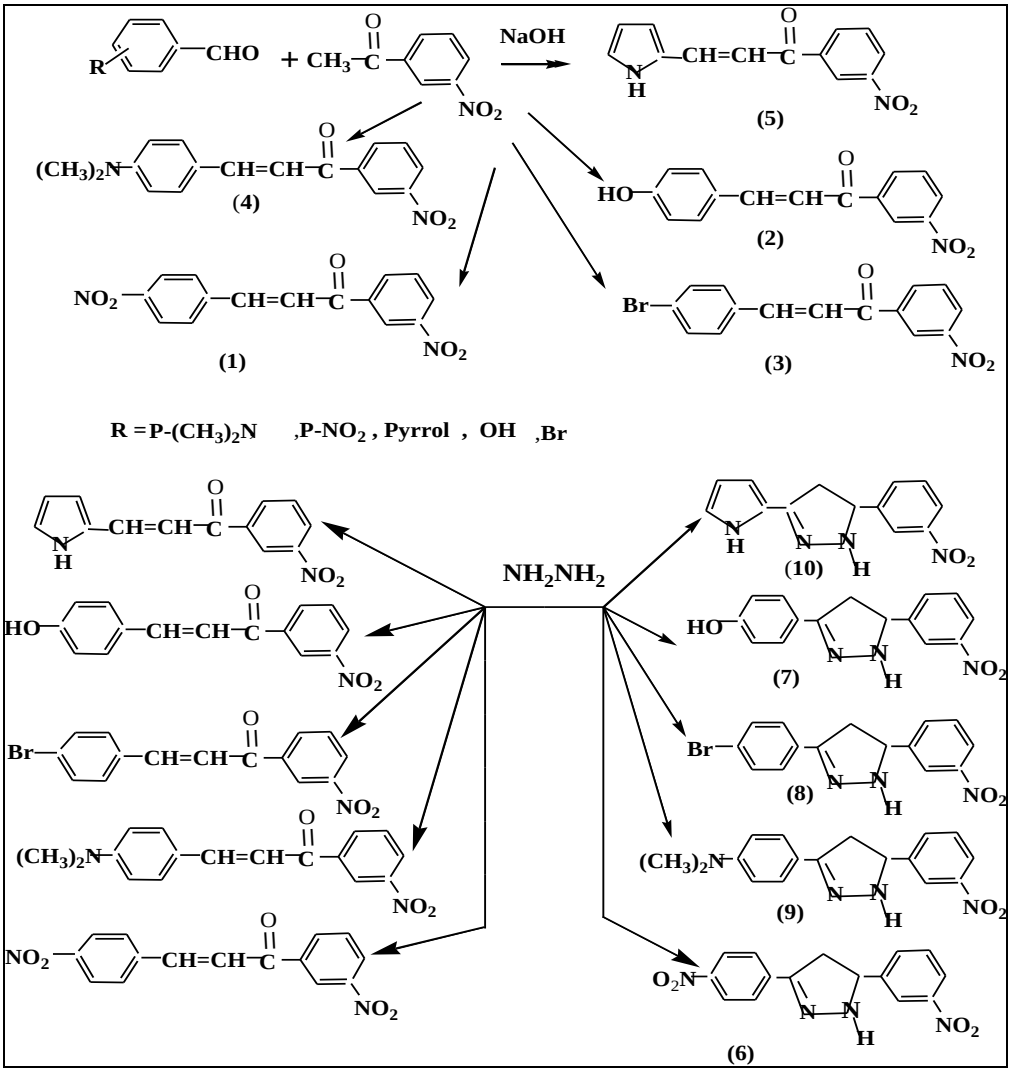


Fig.(5) 1H-NMR spectrum of compound (10).



Scheme (1) Represents the prepared compounds.

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الخلاصة

تم تحضير مركبات جديدة من (١،٣-بس) ٣-بروموفنيل) بروب-٢-ين-١-اون) و (١-(٣-نايتروفنيل ٤-(٣-١ بايرول-٢- يل) بروب-٢-ين-١-اون). و (١-(نايتروفنيل (٣-(١ بايرول-٢- يل) بروب-٢-ين-١-اون). و١،٣- بس) ٣- نايتروفنيل (بروبان-٣-يل-١-يلدين) داي ميثان امين) و(١-(٣-نايتروفنيل) (٣-(١—بايرول -٢-(بروب-٢-ين-١-اون) وكذلك (١،٣- بس) ٤- داي مثيل امينو) فنيل) بروب-٢-ين-١-اون). وقد تم تشخيص المركبات المحضرة من الجالكونات (١) باستخدام الاشعة تحت الحمراء والاشعة فوق البنفسجية وطيف الرنين النووي المغناطيسي للبروتون بجانب تحديد درجات الانصهار وتحديد نقاوة المركبات ودراسة الفعالية البايولوجية.