



Using microwave and ultrasound to synthesis of substituted bis-acyl hydrazone derivatives



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Abstract

In this paper, some new bis-acyl hydrazone derivatives (**4a-f**) were prepared through the reaction of carboxylic acid hydrazides with 1,4-diacetylbenzene using classical methods, microwave and ultrasound irradiation methods. These compounds are obtained through a series of reactions where some carboxylic acids react with ethanol first in the presence of concentrated sulfuric acid to give the corresponding esters (**2a-f**), which when treatment with aqueous hydrazine give carboxylic acid hydrazides (**3a-f**). Thus, the results proved that the use of microwave and ultrasound techniques is much better than the classical methods, as it gave a higher yield, shorter reaction time, and the absence of the use of solvents. All newly synthesized compounds were confirmed by IR, (¹H & ¹³C) NMR spectral analysis and the corresponding reactions were monitored by TLC using the reported eluent.

Keywords: bis-acyl hydrazone, acid hydrazide, 1,4-diacetylbenzene, Microwave, ultrasound technique

1. Introduction

Imine group (-C=N-) included in hydrazones is considered an essential moiety of functional group and are a special type of compounds in the Schiff bases family. Hydrazones were synthesized by condensation of aldehydes or ketones with hydrazine or hydrazine derivatives and it plays an essential role in biological systems such as mechanism of transformation reaction and racemization [1]. Schiff bases are also known to be highly effective in synergistic effects on insecticides and plant growth regulators [2,3]. Similarly, a number of bis-hydrazones of acyl, aryl, and heteroaryl compounds have been studied because of their ability to possess a wide spectrum of biological properties such as antibacterial [4], antiviral [5], antifungal [6], anticancer [7] anti- and anti-protozoal [8]. The hydrazones

are very interesting compounds and they are considered as intermediate compounds in synthesizing different heterocyclic compounds [9]. Some bis-hydrazone possess a good activity as antioxidant [10]. Keeping in view the importance of bis-hydrazones, we here in the study the synthesis, characterization of some new bis-acylhydrazone derivatives based on microwave and ultrasound technique.

2. Experimental

Chemicals and solvents used are commercially available, Merck, Fluka and BDH. Melting points were determined in open capillaries tube on Stuart SMP10 Melting point apparatus. The purity of the compounds was confirmed by TLC using silica gel (0.5mm thickness,) and visualized in iodine carboxylic acids (2a-f). These compounds were prepared according to the procedure described in the literature [11], and gave the following physical properties as shown in table 1.

Purification of the products was carried out by means of the methodology reported for each product [11]. The IR spectra were recorded in potassium bromide on Shimadzu FTIR-8400S. ¹H and ¹³C-NMR spectra were carried out by: Bruker, model ultra-shield 400 MHz, origin: Switzerland and are reported in ppm (δ) DMSO-d₆ was used as a solvent with TMS as an internal standard. The ester of

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Receive Date: 31 May 2021, Revise Date: 16 June 2021, Accept Date: 20 June 2021

DOI: [10.21608/ejchem.2021.78532.3842](https://doi.org/10.21608/ejchem.2021.78532.3842)

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Synthesis of 4-substituted benzohydrazide (3a-f).

A mixture of (0.2 moles) of esters (2a-f) and (0.4 moles) (20ml) Hydrazine hydrate were refluxed in 40ml of absolute ethanol for 4hrs. The resultant mixture was concentrated, cooled, to give precipitate of carboxylic acid hydrazides (3a-f). The compounds purity was checked by TLC technique, The Physical data are recorded in Table 2.

The mixture was refluxed with stirred for about (3hrs.), and then solvent was evaporating. The resulting solid was dried, and recrystallized from suitable solvents. These compounds purity was checked by TLC technique (monitored by TLC, ethyl acetate/hexane, 4:1). The Physical data are recorded in Table 3.

Synthesis of substituted bis-acyl hydrazone (4a-f):**Conventional Method (A) [13]**

Dissolved (0.002 moles) of hydrazides (3a-f), 1,4-diacetylbenzene (0.001mole) in absolute ethanol (50 ml), with 5 drops of glacial acetic acid was added.

Table 1: The Physical data for compounds.(2a-f)

Comp. No.	X	M.p.(°C) (Let.) [12]*	Yield %	Color	Crystallization solvent
2a	4- Cl	74-75 (73-75)*	94	white	aq, ethanol
2b	4- Br	Oily B.P.35 (oily BP.31)*	89	colourless	methanol
2c	4-NO ₂	54-56 (55-58)*	95	yellow	methanol
2d	4-CH ₃	Oily B..P232 (oily BP.232)*	88	colourless	chloroform
2e	4- OH	117-118 (115-118)*	90	white	ethanol
2f	4-OCH ₃	Oily B..P262 (oily BP.263)*	92	colourless	ethanol

Table 2. The Physical data for compounds.(3a-f)

Comp. No.	X	M.p.(°C) (Let.) *[12]	Yield %	Color	Crystallization solvent
3a	4- Cl	161-163 (162-166)*	88	yellow	acetone
3b	4- Br	165-167 (166-167)*	84	white	ethanol
3c	4-NO ₂	221-223 (218-220)*	73	Pale yellow	methanol
3d	4-CH ₃	114-117 (116-118)*	88	white	methanol
3e	4- OH	261-263 (264-266)*	65	white	ethanol
3f	4-OCH ₃	135-137 (136-140)*	86	brown	ethanol

Table 3: The Physical data for compounds.(4a-f)

Comp. No.	X	M.p. (°C) (Lit. *)	Yield % (methods)			Color	Crystallizati on solvent
			A	B	C		
4a	4-Cl	217-219	69	84	88	Pale yellow	methanol
4b	4-Br	239-241	71	81	84	Pale orange	aq.ethanol
4c	4- NO ₂	258-259 (257)*	80	90	93	Pale yellow	ethanol
4d	4-CH ₃	235-237	65	82	88	white	ethanol
4e	4- OH	288-290 (289)*	74	82	84	white	acetone
4f	4-OCH ₃	241-243	68	83	86	brown	methanol

*

[13] By Conventional Method

Method (B)(Microwave irradiation):[14]

A mixture of hydrazides (3a-f) (0.002 moles) and 1,4-diacetylbenzene (0.001 mole), was thoroughly ground with a pestle in a mortar at room temperature, then transferred to small beaker . Microwave irradiation was applied on the reaction mixture at 50% microwave power level (800 watts) for interval of time specified during 8 min. after completion of the reaction, the reaction mixture was cooled to room temperature, washed with water and recrystallized from a suitable solvent,

Method (C) (Ultrasound Technique)[15]

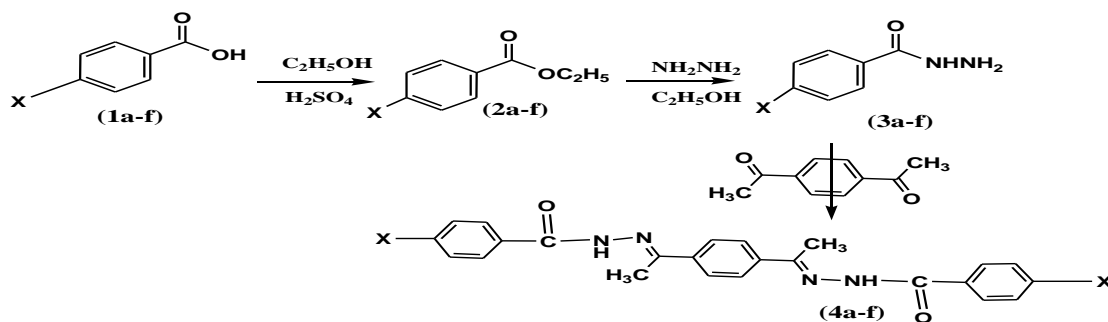
A mixture of hydrazides (3a-f) (0.001mole), 1,4-diacetylbenzene (0.002 moles) dioxane (30 mL) containing triethylamine (0.2 g,2 mmosl) was irradiated by an ultrasonic generator in a water-bath at 50–60 °C for 30 min . (monitored by TLC). On completion of the reaction the formed precipitate was isolated by filtration, washed with ethanol, dried and recrystallized a suitable solvent to give pure compounds (5a–f). The Physical data are recorded in Table 3.

3. Results and Discussion

The present work involves the synthesis of some new bis-acylhydrazone derivatives using different methods like, classical, ultrasound, and microwave irradiation methods. We found that the three methods give the same output, but the practical methods proved that the ultrasound method is the best in terms

of the amount of product and the shorter reaction time, also the microwave irradiation gave relatively better results than the traditional methods. The targeted substituted bis-acyl hydrazone (4a-f) were prepared as shown in Scheme 1.

The structures of compounds (4a-f) have been identified based on their FT-IR, ¹H-NMR, and ¹³C-NMR. The FT-I R spectra were characterized by the presence at the range (3168-3189 cm⁻¹) due to (NH), the range (1632-1672 cm⁻¹) refer to (C=O) amide groups besides at the range (1602-1627 cm⁻¹) due to (C=N) bands also at the range (3075-3085 cm⁻¹) for (CH aromatic) bands. The assignment of the vibration ν (cm⁻¹) of the IR absorption bands spectra was illustrated in Table 4. Whereas the chemical shifts that appeared in the ¹H-NMR show signals due to exhibition of protons of (CH₃C=N) as singlet at the range (2.31-2.59 ppm) and at the range (10.59-11.21 ppm) in addition the other obtained values for compounds (4a-f) are listed in Table (5) and gave good agreements with those published in literature for similar compounds [13,16] In the ¹³C-NMR spectra of compounds (4a-f) showed different signals for all carbon atoms which mentioned in the table 5, The most important of these signals at the range δ (13.6-15.27 ppm) assigned to CH₃, δ (167.85 – 168.9 ppm), due to (-C=N-NH). The carbons atom of carbonyl group were appeared at the range δ (162.9 -164.1 ppm) while the signals of the carbon of aromatic ring (Ar-C) all signals appears. All the carbon atoms in structures of titled compounds which gave additional support to the results. As shown in Table 5 . These data gave approval for what was mentioned in the scientific references for similar compounds [17, 18].



Scheme 1: Synthesis of compounds (4a-f)

Table 4: The FT-IR data of compounds (4a-f).

Comp. No.	FT-IR $\nu(\text{cm}^{-1})$				
	C=N	C=O	NH	C-H-Ar	Others
4a	1608	1665	3168	3075	741(C-Cl)
4b	1616	1648	3174	3080	--
4c	1602	1671	3189	3085	1535(Asymmetrical) 1348(Symmetrical)
4d	1627	1643	3177	3079	
4e	1618	1632	3169	3079	3332(OH phenolic)
4f	1625	1672	3181	3077	

Table 5: The ^1H & ^{13}C -NMR data of compounds (4a-f).

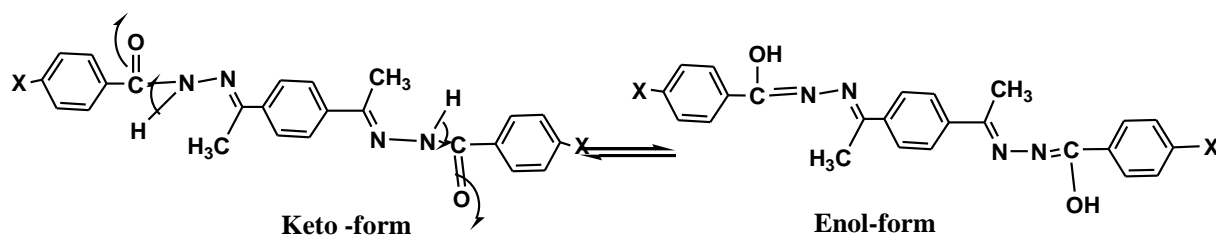
Comp. No.	^1H -NMR $\delta(\text{ppm})$ DMSO- $_6$		^{13}C -NMR $\delta(\text{ppm})$ DMSO- $_6$	
	4a	2.31(s,6H,(CH ₃ C=N)),6.72(s,4H,ArH), 7.62-8.21(m,8H,ArH),10.92(s,2H,2NH).		14.6(CH ₃)128.8,129.1,129.4,132.4,136.1,137. 8, 162.9(C=O),168.1(-C=N-NH).
4b	2.33(s,6H,(CH ₃ C=N)),6.66 (s,4H,ArH), 7.68-8.01(m,8H,ArH),11.04(s,2H,2NH).		15.27CH ₃),126.75,128.9,129.4,129.75,132.01, 133.4,162.9,168.55(-C=N-NH).	
4c	2.35(s,6H,(CH ₃ C=N)),7.68(s,4H,ArH), 8.1-8.29(m,8H,ArH),11.21(s,2H,2NH).		13.95(CH ₃),122.1,128.6,128.9,129.5,136.4141 .1,151.5,162.99,(C=O),167.85(-C=NNH).	
4d	2.34(s,6H,(CH ₃ C=N)),1.93(s,3H,CH ₃),6.78(s,4H,ArH) ,6.99-8.1(m,8H,ArH),11.01(s,2H,2NH). 11.01(s,2H,2NH).		13.6(CH ₃),24.65,127.7,129.2,129.8,131.4,135. 9141.45,159.8,163.2,(C=O),167.89(-C=N- NH).	
4e	2.38(s,6H,(CH ₃ C=N)),6.868(s,4H,ArH),7.79- 7.98(m,8H,ArH),10.11(s,2H,2OH),10.59(s,2H,2NH)		15.21(CH ₃).56.1,117.2,125.9,128.3,129.4,129. 8136,4,161.8,163.2(C=O),168.5(-C=NNH).	
4f	2.59(s,6H,(CH ₃ C=N)),3.45(s,3H,OCH ₃),6.58(s,4H,Ar H),6.98-7.89 (m,8H,ArH),11.19(s,2H,2NH).		13.8(CH ₃),55.6,115.2,126.3,127.6,128.8,129.3 ,129.9,136.2,164.1(C=O),168.9(-C=N-NH).	

(s)singlet (m):multiplet

The bis-acylhydrazone compounds (4a-f) can exist in keto-enol form where these compounds suffer undergo deprotonation from enolised amide oxygen

The FT-IR spectrum disclosed the presence of C=O at the range (1632-1672 cm^{-1}) bands with no

absorbance at the in a site that resembles a hydroxyl group. This is further supported by ^1H NMR spectrum which shows no absorbance at the site of OH group i.e. the keto form was predominate as shown in scheme 2.



Scheme 2 ; Tautomeric forms of the compounds(4a-f)

4. Conclusions

We conclude that the experience of green methods (microwave and ultrasound technology) is a favourite because it provides many advantages over conventional methods as, the less solvent are used with higher yields, shorter reaction time and the environment friendly.

Acknowledgments

The authors acknowledge and thank the Department of Chemistry, College of Science University of Mosul for their support to complete this research ,

Conflicts of Interest

There are no conflicts to declare

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