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Novel Synthesis of Some New Hydrazide- Hydrazones Containing Benzilic Acid Unit

Salim J. Mohammed, FatinG. Zuhair

Department of Chemistry, College of Science, University of Mosul, Iraq

Email:dr_salimjasim@yahoo.com

***Abstract*- A series of new hydrazones, namely of 2-hydroxy-2,2-diphenyl-N-(aryl methylene) aceto hydrazide (4a-g) and 2-hydroxy-N(1-alkylalkyllidene)-2,2-diphenyl aceto hydrazide (5a-f) derivatives were synthesized by the reaction of benzilic acid hydrazide (3) with substituted aromatic aldehydes and substituted ketones respectively . The synthesized hydrazones were characterized on the bases of their physical properties and spectroscopic data. Some of these compounds were tested for biological activities as antibacterial and antifungal agents and showed a significance to moderate activity.**

***Keywords*-Heterocyclic, hydrazones, benzilic acid, biological activity**

I. INTRODUCTION

Hydrazones are the condensation products of hydrazine derivatives with carbonyl compounds, they contain an acyclic group >C=N-N< . It is long since hydrazones and their derivatives, due to their high complexion ability. In general attends aroylhydrazone compounds by condensation of aldehydes or ketones, with carboxylic acid hydrazides or hydrazine and its derivatives, these were interested by many researchers in the preparation of these compounds through a variety of methods of preparation[1-4]. The remarkable biological activity of acid hydrazides and their corresponding aroylhydrazones and the dependence of their activity on the mode of organic synthesis.Aroylhydrazones have been demonstrated to possess antitubercular [5-7]antibacterial [8-10] and anticonvulsant [11-13] activities.

In previous and continuing our studies the effects of our attention to the great importance of these compounds, so our attention was focused on the follow-up study of these particular compounds derived from benzilic acid hydrazide.

II. EXPERIMENTAL SETUP

Melting points were measurement in open capillary type on Stuart melting pointSMP30.The IR spectra using KBr disk were recorded on FTIR-600 Bio Tec. Engineering Management Co.Ltd.(UK) using KBr discs.^{1}H-NMRand ^{13}C-NMR spectra were recorded on JEOLEEA400MHZFT-NMR.UV spectra were determined on a shimadzu UV/Vis -1650 pc Spectrometer using chloroform as a solvent. The methyl benzilate (2) was prepared by the usual esterfication method, benzilic acid hydrazide (3)was prepared using reported method[11]starting from methyl benzilate.

A. Preparation of 2-hydroxy-2,2-diphenyl-N-(aryl methylene) aceto hydrazide[14,15](F$_4$a-g)

Dissolved (0.001 mole,0.24 gm) of benzilic acid hydrazide, substituted aldehydes or thiophene-2-carboxyaldehyde(0.001mole)in absolute ethanol (30ml).The mixture was refluxed for six hours and then solvent was evaporate. The solid precipitate was filtered off and recrystallized from suitable solvent. Physical and spectral data are listed in tables (I andIII).Table I Shows the physical constants for compounds (4a-g).

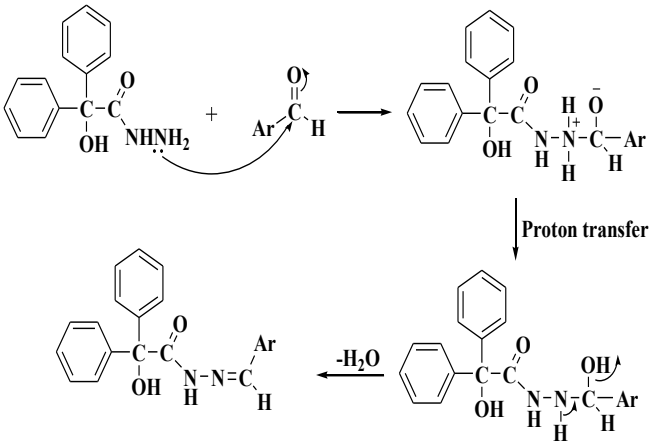
B. Preparation of2-hydroxy-N(1-alkylalkyllidene)- 2,2-diphenylacetohydrazide[16] (F$_5$a-f)

Dissolved (0.001 mole, 0.24 gm) of benzilic acid hydrazide , substituted ketones(0.001mole)in absolute ethanol (30ml), (1ml) of glacial acetic acid was added. The mixture was refluxed for four hours, then solvent was

evaporate. The mixture was added to crushed ice and stirrer magnetically. The resulting solid was dried, and recrystallized from suitable solvent. Physical and spectral data are listed in (Table II and IV).Table II shows the physical constants for compounds (5a-f).

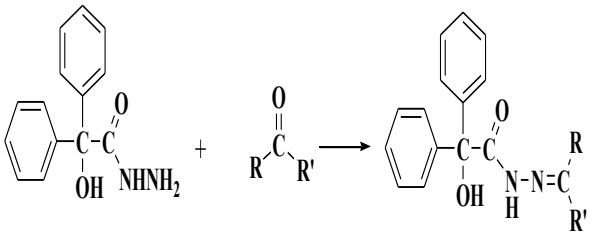
III. RESULTS AND DISSCUSION

In the present work, the synthesis of some substituted hydrazones from benzilic acid hydrazide, thus benzilic acid (1) was converted to methyl benzilate (2) by reaction with methanol. The ester was treated with hydrazine hydrate in ethanol to afford benzilic acid hydrazide (3) [17]. We have synthesized various new hydrazones (4a-g) and (5-f) by condensation. The acid hydrazide (3) with a variety of aromatic aldehydes and ketones are shown in scheme 1 and 2.



(4a- g)

Scheme 1



(3) (5a-f)

Scheme 2

The structures of the target compounds (4a-g) and (5a-f) were elucidated using UV, IR, ^{1}H-NMR and ^{13}C-NMR. The IR spectra for compounds (4a-g) showed the following stretching bands; (1597-1618cm^{-1}) due to the (C=N) bond, (3025-3061cm^{-1}, (3250-3255cm^{-1}) for the (O-H) bond, (1640-1655 cm^{-1}) stretching for (C=O amide) group and (3211-3309 cm^{-1}) due to (NH) group, while the compounds(5a-f) showed the following stretching -bands;(1597-1649cm $^{-1}$) stretching for (C=N)bond, (1662-1687 cm^{-1}) stretching for (C=O amide) group,(3057-3062cm $^{-1}$) due to (ArCH) and(3302-3363 cm^{-1}) due to (NH) group .

The ^{1}H-NMR spectra for compounds (4a-g)in (DMSO-d_6) which showed singlet bands in the range(8.941-9.92ppm) due to N=CH group also singlet bands at the range (10.942-11.944ppm) due to NH group, in addition the multiplet peaks for aromatic parts . The UV spectrum showed λ_{max} ($CHCl_3$) in the range (320-348nm) due to ($\pi \rightarrow \pi^*$) and (n- π^*) transition (Table III).

^{13}C-NMR Spectra showed peaks for compound (4a)at the following data (14.92, 22.15, 83.253, 127.255,127.148,128.252,129.534,143.423,153.551,165.251).Also, compound(4c) showed data at (15.355, 41.984, 82.118, 125.923, 127.526, 127.493, 127.537, 128.818, 133.114, 142.520, 163.159, 165.228) while compound(4f) appeared at δ values(12.526, 82.443, 108.155, 113.059, 127.348, 128.552, 139.988, 143.143, 152.137, 164.049)

While, the IR spectrum for compounds (5a-f) showed absorption bands in the region (1662-1678cm^{-1}) stretching for (C=O amide) group, at (1597-1649 cm^{-1}) stretching group for (C=N) group , (at (3302-3363cm^{-1}) due to (NH)group and at (3033 cm $^{-1}$ -3062 cm $^{-1}$) stretching for ArCH part. The UV spectra of hydrazones (5a-f) Shows in chloroform as solvent intense maxima at (256-324 nm) which belonged to (π - π^*) an (n- π^*) transition.

The^{1}H-NMR of compounds(5a-f)showed significant peaks as the following .singlet at range(2.372-2.593 ppm)for CH_3group, also singlet peak at (10.235 –10.742 ppm) due to NH group ,in addition the aromatic bands showed multipletpeaks and others peaks for groups in synthesized compounds(Table IV).

^{13}C-NMR Spectra Showed peaks for hydrazone (5a) were found (14.92, 22.15, 83.253, 127.255, 127.148, 128.252, 129.534, 143.423, 153.551, 165.251) ,while compound(5c) showed data 15.355, 41.984, 82.118, 125.923, 127.526, 127.493, 127.537, 128.818, 133.114, 142.520, 163.159, 165.228) and compound(5f) appeared at δ values (12.526, 82.443, 108.155, 113.059, 127.348, 128.552, 139.988, 143.143, 152.137, 164.049)which gave additional support to the results.

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TABLE I

Physical data for compounds (4a-g)

Comp. No.	Ar	Molecular formula	M.P °C	Yield %	Color	Cryst. solvent
4a	3-MeO-4-OH-C_6H_3	$C_{22}H_{20}N_2O_4$	123-125	48	pale yellow	EtOH+ H_2O
4b	4-MeO-C_6H_4	$C_{22}H_{20}N_2O_3$	173-175	74	white	MeOH
4c	2-BrC_6H_4	$C_{21}H_{17}N_2O_2Br$	153-155	67	yellow	EtOH
4d	Thiophene-2-yl	$C_{19}H_{16}N_2O_2S$	168-170	70	brown	EtOH
4e	Piperonyl	$C_{22}H_{18}N_2O_4$	194-196	50	light brown	EtOH
4f	4-CHO-C_6H_4	$C_{22}H_{18}N_2O_3$	317-319	73	white	MeOH
4g*	C_6H_4(Bis)	$C_{36}H_{31}N_5O_4$	317-318	43	white	DMSO

*Benzaldehyde (0.002mole, 0.49gm) from hydrazide

TABLE II

Physical data for compounds (5a-f)

Compd. No.	R	R'	Molecular formula	M.P °C	Yield %	Color
5a	CH_3	CH_3	$C_{17}H_{18}N_2O_4$	189-190	91	white
5b	n-butyl	n-butyl	$C_{23}H_{30}N_2O_4$	124-127	63	white
5c	phCH_2	CH_3	$C_{23}H_{22}N_2O_2$	155-156	56	pale yellow
5d	Butane-1-yl	CH_3	$C_{19}H_{19}N_2O_2$	86-88	54	dark yellow
5e	pentyl	CH_3	$C_{20}H_{22}N_2O_2$	113-115	86	dark yellow
5f	Furan-2-yl	CH_3	$C_{20}H_{18}N_2O_3$	118-120	93	yellow

Table III
Spectral data for compounds (4a-g)

Comp. No.	I.R. υ (cm^{-1}, KBr)				U.V.($CHCl_3$) λmax(nm)	^{1}H-NMR δ (ppm)
	N-H	C=N	C=O	ArCH		DMSO-d_6
4a	3215	1610	1640	3054	326	δ 3.89 (S, 3H, OCH_3), δ 3.874 (S, 1H, OH), δ 4.9 (S, 1H,phenolic OH),δ 6.95-8.1(m, 2H, ArH), δ 7.279-7.378 (m, 6H, ArH), δ 7.42-7.485 (m, 4H, ArH), δ 9.92 (S, 1H, N=CH), δ 11.42 (S, 1H, NH).
4b	3230	1604	1645	3030	322	δ 3.870 (S, 3H, OCH_3), δ 3.874 (S, 1H, OH), δ 6.988-8.018(m, 2H, ArH), δ 7.284-7.375 (m, 6H, ArH), δ 7.438-7.458 (m, 4H, ArH), δ 9.883 (S, 1H, N=CH), δ 11.378 (S, 1H, NH).
4c	3205	1597	1660	3025	340	δ 3.728 (S, 3H, OH), δ 7.291-7.442 (m, 9H, ArH), δ 7.374-7.461 (m, 3H, ArH), δ 7.674 (d, 1H, ArH), δ 7.937 (d, 1H,ArH), δ 8.941 (S, 1H, N=CH), δ 11.923 (S, 1H, NH).
4d	3211	1601	1649	3062	340	δ 4.657 (S, 1H, OH), δ 6.558 (d, 1H, H3, Thiophene-2-yl), δ 7.442-7.521 (m, 10H, Ar-H), δ 8.991 (S, 1H, N=CH), 10.742 (S, 1H, NH)
4e	3286	1593	1678	3082	336	δ 4.612 (S, 1H, OH), δ 6.576 (d, 1H, H3, Piperonyl), δ 7.433-7.512 (m, 10H, Ar-H), δ 9.841 (S, 1H, N=CH),10.754 (S, 1H, NH)
4f	3286	1597	1665-1725	3059	320	δ 3.728 (S, 3H, OH), δ 7.291-7.442 (m, 9H, ArH), δ 7.374-7.461 (m, 3H, ArH), δ 7.674 (d, 1H, ArH), δ 7.937 (d, 1H,ArH), δ 8.954 (S, 1H, N=CH), δ 11.923 (S, 1H, NH).
*4g	3309	1618	1651	3060	348	δ 3.711(S, 3H, OH), δ 7.296-7.467 (m, 9H, ArH), δ 7.381-7.467 (m, 3H, ArH), δ 7.687 (d, 1H, ArH), δ 7.945 (d, 1H,ArH), δ 8.954 (S, 1H, N=CH), δ 11.944 (S, 1H, NH).

TABLE IV
Spectral data for compounds (5a-f)

Comp. No.	I.R. υ (cm^{-1}, KBr)				U.V.($CHCl_3$) λmax(nm)	^{1}H-NMR δ (ppm)
	N-H	C=N	C=O	ArCH		DMSO-d_6
5a	3323	1649	1675	3059	258	2.372 (S, 3H, CH3), 2.593 (S, 3H, CH3), 4.623 (S, 1H, OH), 7.335-7.556 (m, 6H, ArH), 7.705-7.974 (m, 4H, ArH), 10.542 (S, 1H, NH)
5b	3302	1638	1662	3062	256	δ 3.749 (d, 2H, CH_2), δ 4.798 (S, 1H, OH), δ 7.162-7.194 (m, 5H, phenyl group), δ 7.387-7.656 (m, 10H, ArH), 10.245 (S, 1H, NH)
5c	3363	1637	1684	3057	266	δ 2.145 (S, 3H, CH_3), δ 3.758 (d, 2H, CH2), δ 4.898 (S, 1H, OH), δ 7.165-7.195 (m, 5H, phenyl group), δ 7.287-7.656 (m, 10H, ArH), 10.235 (S, 1H, NH)
5d	3329	1633	1687	3060	268	δ 2.264 (S, 3H, CH_3), δ 4.647 (S, 1H, OH), δ 6.549 (d, 1H, H_2), δ 7.439-7.511 (m, 10H, Ar-H), 10.739 (S, 1H, NH)
5e	3321	1630	1666	3059	302	δ 2.155 (S, 3H, CH_3), δ 3.768 (d, 2H, CH_2), δ 4.889 (S, 1H, OH), δ 7.167-7.198 (m, 5H, phenyl group), δ 7.278-7.656 (m, 10H, ArH), 10.245 (S, 1H, NH)
5f	3332	1597	1667	3055	324	δ 2.269 (S, 3H, CH_3), δ 4.657 (S, 1H, OH), δ 6.558 (d, 1H, H3, furan), δ 7.442-7.521 (m, 10H, Ar-H), 10.742 (S, 1H, NH)