International Journal of Recent Research and Review, Vol. XI, Issue 1, March 2018
ISSN 2277 – 8322

Synthesis and Characterization of Some Pyrazole , Pyrazoline and Pyrazolidine Derivatives

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***Abstract*- An efficient and practical synthesis of some pyrazole, pyrazolineand pyrazolidine derivatives was achieved throughof benzilic acid hydrazide with acetyl acetone, benzoyl acetone, ethyl or methyl aceto acetate and diethyl malonate respectively, also reaction of hydrazidewith acetonyl acetone to give a compound. The structures of the prepared compounds were confirmed by the available physical and spectral methods.**

***Keywords* - Benzilic acid hydrazide, Pyrazoline, pyrazole derivatives, pyrazolidine biological activity**

I. INTRODUCTION

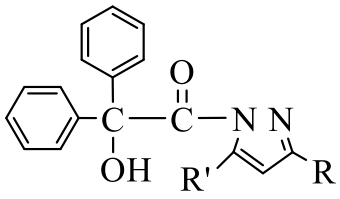
Pyrazole, pyrazolidine, pyrazoline and its derivatives are the subject of many research studies due to their wide spread potential biological activities. Literature survey revealed thatthese derivatives possess diverse pharmacological activitiesare important compounds with multiple uses as well as their different biological properties. It was found that pyrazole and some of its derivatives could be used as a stabilizer or emitter in the UV [1] machine. It could also be used in the preparation of the ionic ion [2], as well as an inhibitor of the enzymes. [3] The biological efficiency of these compounds was characterized by its use in various fields, As an anti-inflammatory [4], analgesic [5], potent antifungal agent against Candida strains [6],anti-inflammatory, antioxidant and antimicrobial [7, 8] antibacterial and antitubercular activities [8].Also pyrazoline and pyrazolidine derivatives represent attractive synthetic targets due to their extensive applications in the chemical and medicinal industries[9].

II. EXPERIMENTAL SETUP

Melting points were measured on Electrothermal 9300 (uncorrected). FTIR spectra were recovered using KBr disk Fourier-Transform, Tensor Co. Brucker, 2003, Germany. UV spectra were performed on Shimadzu UV-VIS Recording UN-160 Spectrophotometer using chloroform as a solvent. ^{1}HNMR spectra were obtained from Brucker (400 MHz) Swiss, using $CDCl_3$, as solvent, TMS as internal standard.

A. Preparation of 1-Benziloyl-3,5-dialkylpyrazole (2a-2b)[10]:

To a mixture of benzylic acid hydrazide (1) (0.001 mole) and (0.001 mole) of acetyl acetone or benzoyl acetone in (30ml)of ethanol ,the (5ml)of acetic acid was added, then it was refluxed for (4hrs.)The solvent was evaporate under reduce presser and poured on crushed ice , the solid product filtered and wash with cold water , and recrystallized from ethanol to give the product (2a and 2b),the physical properties are shown in table I.



B. Preparation of N-[Benziloyl-3-methyl-5-oxo-2-pyrazoline(3) by two methods:

method (A) [11]

Dissolved (0.001 mole, 0.24 gm) of benzilic acid hydrazide, ethyl acetoacetate (0.001mole) in absolute

ethanol (30ml)and (1ml) of concentrated hydrochloric acid was added. The mixture was refluxed for (8hrs) and then solvent was evaporate. The solid precipitate was filtered off and recrystallized from ethanol to give the product as white crystal (m.p. 111-113 ^{o} C. Yield 95%).

method (B)[12]

The mixture of (0.001 mole,0.24 gm) of benzilic acid hydrazide , methyl acetoacetate (0.001mole)were heating for about one hour, then(30ml) of absolute ethanol was added ,The mixture was refluxed for (2hrs.), then solvent was evaporate. Solid product was formed, and recrystallized from ethanol to give the product as white crystal(m.p. 110-112^{o} C. Yield 53%).

C. Preparation of 2-Benziloylpyrazolidine-3,5-dion (4)[12].

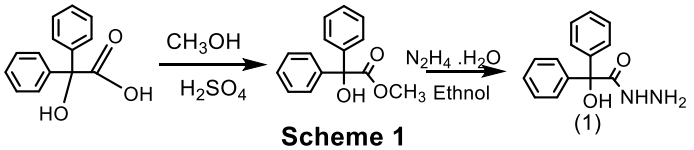
A mixture of(0.001moel) benzylic acid hydrazide ,(0.001 mole) of diethylmalonate were dissolve in (20ml.)of absolute ethanol then the mixture was refluxed for (2hrs.), the mixture was ,then distilled under a reduced pressure, cooled, The resulting solid was filtered, dried and recrystallized from aqueous ethanol to give the corresponding compound (4) as a white crystal,(m.p. 173-175 ^{o} C. Yield 83%).

*D. Preparation of N-(Hydroxydiphenylacetamide)-2,5-dimethyl pyrrole(F14): (5)[*13]

Dissolved (0.001 mole) of benzilic acid hydrazide, acetonyl acetone (0.001mole)in absolute ethanol (20ml)and (1ml) of glacial acetic acid was added. The mixture was refluxed for (4hrs) and then solvent was evaporate and poured on crushed ice . The solid precipitate was filtered off and wash with cold water, recrystallized from methanol to give the product as powder brown (m.p. 183-185 ^{o} C. Yield 73%).

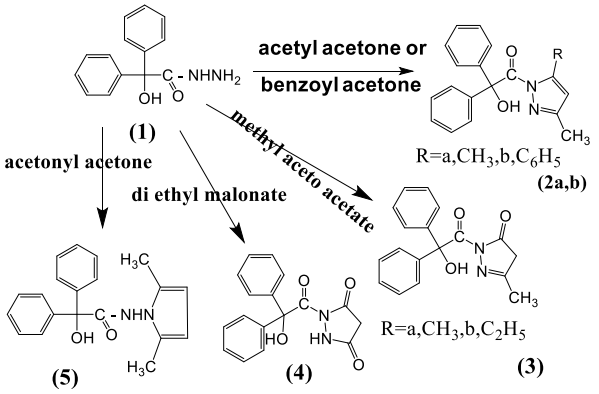
III.RESULTS AND DISSCUSIONS

Keeping in view the biological activity and medical importance of pyrazole , pyrazoline and pyrazolidine compounds Benzilic acid hydrazide (1)was prepeardusing the reported method[13], starting frombenzilic acid which on usual esterification to methyl benzilate then convertd to acid hydrazide (1) as shown in scheme 1.



Scheme 1

We have synthesized some derivatives of pyrazole , pyrazoline and pyrazolidine starting from benzylic acid hydrazide which readily undergo reaction with carbonyl compounds such asacetyl acetone , benzoyl acetone,ethyl acetoacetate, methyl acetoacetate, diethylmalonate and acetonyl acetone to synthesized some new pyrazole , pyrazoline and pyrazolidine derivatives[14].



Scheme 2

The structure of target compounds was confirmed by physical properties which are listed in table I.While the spectral data are listed in table II.

The FT-IR spectra for compound (2a and 2b) manifests a strong absorption band and at (1621 ,1647cm^{-1})due to stretching vibration of C=N group and at(1653.1676cm^{-1}) due to carbonyl amide group in compounds(2a and 2b)respectively. While the U.V. spectra shows a maximum absorption at wavelength at (224, 260 nm) which indicated a blue shift and at wavelength at (340, 348 nm) which indicated a red shift for compounds (2a and 2b) respectively. Compound (3) shows a strong absorption band at (1601^{-1}) due to stretching vibration of C=N group, at (1653.1676cm^{-1}) due to carbonyl amide group and at(1653.1676cm^{-1}) due to

cyclic carbonyl in compound (3) while the U.V. spectrum shows a maximum absorption at wavelength at (258 -260 nm) which indicated a blue shift and at wavelength at (304-312nm) which indicated a red shift for compound(3).

The compound (4) appear strong absorption bands inFT-IR spectrum at (1632,1649cm^{-1}) due to stretching vibration of two carbonyl group ,in addition at (3257cm^{-1}) for NH group in this compound While the U.V. spectrum shows a maximum absorption at wavelength at (224 -246nm) which indicated a blue shift and at wavelength at (315-322nm) which indicated a red shift for compound(4). Compound (5) shows a strong absorption band at (1658^{-1}) due to stretching vibration of C=C group, and at (3292cm^{-1}) due to NH group in compound (5) while the U.V. spectrum shows a maximum absorption at wavelength at (250 -259 nm) which indicated a blue shift and at wavelength at (314 -320 nm) which indicated a red shift for compound (5).

The ^{1}H-NMR spectrum for compounds (2a and 2b) shows singlet band at δ (2.117,2.260ppm)(3H)for CH_3 group,broad band atδ (5.868,5.276ppm)(1H)for OH group.Alsothe aromatic part showed multiplet in the range(6.505-7.695ppm) and in the range(6.689-7.693ppm),while ^{13}C-NMR Spectrumshowed the carbon signal of CH_3 group ,the carbon signal of carbon carbonyl group appeared at δ values 163.69,159.371 and other carbons signal are appeared at δ values for compounds (2a and 2b) as shown in table III.

The ^{1}H-NMR spectra for compound (3) in (DMSO-d_6) in ppm showed significant peaks as the following. .singlet at (2.49ppm) due to CH_3group,multipletpeak at (3.346ppm)for CH_2 group compound(3),also theproton of (OH)group was appeared in (4.696ppm).In addition the aromatic part showed multiplet in the range(7.089-7.401ppm) due to aromatic protons .Finally^{13}C-NMR Spectra showed peaks for the carbon signal appeared at δ values as shown in table IV. The ^{1}H-NMR spectra for compound (4)showed significant peaks as the following, multiplet peak at (3.054ppm) for CH_2group, singlet peak at (5.875ppm)due to OH group and the NH group in compound (4)appeared at(10.215ppm) for one proton,Finally^{13}C-NMR Spectra showed peaks for the carbon signal appeared at δ values as shown in table IV.

The ^{1}H-NMR spectra for compound (5) in (DMSO-d_6) in ppm showed significant peaks as the following. Two peaks as singlet at (2.15ppm)due to two methyl group,Two peaks as broad at (5.55ppm)due to two CH group,also the proton of (OH)group was appeared in (6.41ppm),While the NH group was appeared in (6.99ppm).In addition the aromatic part showed multiplet in the range (7.27-7.392ppm) due to aromatic protons . Finally ^{13}C-NMR Spectra showed peaks for the carbon signal appeared at δ values as shown: 10.34.85.11,106.7.119.98,127.55,128.35,129.32,130.14,130.35,141`,11,166.25,171.06.

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Table I
Physical properties for compounds (2a&2b)

Comp. No.	**R**	**R'**	**m.p °C**	**Yield %**	**Color**
2a	CH_3	CH_3	148-150	44	White
2b	CH_3	Ph	176-179	58	White

Table II
UV and IR Spectra data for compounds (2a&2b)

Comp. No..	UV $CHCl_3$	IR. $\upsilon(cm^{-1}, KBr)$		
		C=O	C=N	OH
2a	224,340	1653	1621	3392
2b	260,348	1676	1647	3419

Table III
^{1}H-NMR^{13}C-NMRspectrum data for compounds 2a & 2b

Comp. No.	^{1}H-NMR δ (ppm)	^{13}C-NMR δ (ppm)
2a	2.117 (s, 3H, CH_3), 2.260(s,3H,CH_3), 5.276(s,1H,CH), 5.317(s,1H,OH), 6.505-7.695(m,10H, ArH).	14.468, 16.030, 84.474,111.082, 127.184, 127.217, 127.316, 127.332, 127.390, 127.447, 127.488, 127.583, 127.612, 127.661, 127.702, 142.422, 143.536, 153.457, 163.690
2b	2.007(s,3H,CH_3), 5.868(s,1H,CH), 5.002(s,1H,OH), 6.689-7.963(m, 15H,ArH)	13.112, 82.45, 112.351, 127.145, 127.192, 127.215, 127.451, 127.527, 127.63, 128.885, 131.301, 142.13, 149.351, 159.371

Table IV

^{13}C-NMRto carbon signal for compounds (3,4)

Comp. No.	^{13}C-NMR δ (ppm)
3	16,333,81.65,127.75,127.8, 128.01,128.8, 128.14,128.20,128.26,128,32,15 4,98,166.85, 170.09
4	41.54,85.25,126.93,127.25, 127.51,128.03, 129.32 141,03,165.87,170.83