Conversion of some 2-arylmethylene-4-oxobutanhydrazides into pyridazinones, pyrrolones and pyrazolones

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Conversión de algunas 2-arilmetileno-4-oxobutanhidrazidas en piridazinonas, pirrolonas y pirazolonas

Conversió d'algunes 2-arilmetilen-4-oxobutanhidrazides en piridazinones, pirrolones i pirazolones

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ABSTRACT

A novel series of 2-arylmethylene-4-[4-methoxy-3-methylphenyl]-4-oxobutanhydrazides **(2a-c)** was synthesized via the reaction of 3-arylidene-5-[4-methoxy-3-methylphenyl]furan-2(3H)-ones(**1a-c)** with hydrazine hydrate. The hydrazides (2a-c) were used as starting compounds for the synthesis of a variety of heterocyclic compounds: 3(2H)-pyridazinones (3a-c), N-amino-2(3H)-pyrrolones **(7a-c)** and 1H-pyrazol-3(2H)-ones **(10a-c)** via cyclization reactions. Depending on the reaction conditions, the acylation of the hydrazides **(2a-c)** with benzoyl chloride in toluene afforded the corresponding N`-benzoyl 4-oxobutanhydrazides **(5a-b)** or 1-benzoyl-1,2-dihydro-3(4H)-pyridazinones (6a-c). The condensation of the hydrazides (**2a-c**) with various aldehydes gave the corresponding N'-arylidene-4-oxobutanhydrazides **(8a-h),** which underwent ring closure into the corresponding N-arylidenamino-2(3H)-pyrrolones (**9a-d**) upon treatment with acetic anhydride.

Keywords. Hydrazide; hydrazone; pyridazinone; pyrrolone; pyrazolone

RESUMEN:

Se sintetizó una nueva serie de 2-arilmetileno-4-[4-metoxi-3-metilfenil]-4-oxobutanhidrazidas (**2a-c**) mediante la reacción de 3-ariliden-5-[4-metoxi-3-metilfenil]furano -2(3H)-onas(**1a-c**) con hidrato de hidrazina. Las hidrazidas (**2a-c**) se utilizaron como compuestos de partida para la síntesis de una variedad de compuestos heterocíclicos: 3(2H)-piridazinonas (**3a-c**), N-amino-2(3H)-pirrolonas (**7a-c**) y 1H-pirazol-3(2H)-onas (**10a-c**) mediante reacciones de ciclación. Dependiendo de las condiciones de reacción, la acilación de las hidrazidas (**2a-c**) con cloruro de benzoílo en tolueno proporcionó las correspondientes N`-benzoil 4-oxobutanhidrazidas (**5a-b**) o 1-benzoil-1,2-dihidro-3(4H)-piridazinonas (**6a-c**). La condensación de las hidrazidas (**2a-c**) con varios aldehídos dio las correspondientes N'-ariliden-4-oxobutanhidrazidas (**8a-h**), que sufrieron cierre de anillo en las correspondientes N-arilidenamino-2(3H)-pirrolonas (**9a- d**) tras el tratamiento con anhídrido acético.

***Palabras clave*:** Hidrazida, hidrazona, piridazinona, pirrolona, pirazolona

RESUM:

Es va sintetitzar una nova sèrie de 2-arilmetilen-4-[4-metoxi-3-metilfenil]-4-oxobutanhidrazides **(2a-c**) mitjançant la reacció de 3-ariliden-5-[4-metoxi-3-metilfenil]furan -2(3H)-ones(**1a-c**) amb hidrat d'hidrazina. Les hidrazides (**2a-c**) es van utilitzar com a compostos de partida per a la síntesi de diversos compostos heterocíclics: 3(2H)-piridazinones (**3a-c**), N-amino-2(3H)-pirrolones (**7a-c**) i 1H-pirazol-3(2H)-ones (**10a-c**) mitjançant reaccions de ciclització. Depenent de les condicions de reacció, l'acilació de les hidrazides (**2a-c**) amb clorur de benzoil en toluè va donar les corresponents N`-benzoil 4-oxobutanhidrazides (**5a-b**) o 1-benzoil-1,2-dihidro-3(4H).)-piridazinones (**6a-c**). La condensació de les hidrazides (**2a-c**) amb diversos aldehids va donar els corresponents N'-ariliden-4-oxobutanhidrazides (8a-h), que van patir el tancament de l'anell en les corresponents N-arilidenamino-2(3H)-pirrolones **(9a- d)** amb tractament amb anhídrid acètic.farmacèutica, cosmètica i alimentària. Per la seva activitat biològica, l'oli essencial també es recomana per al sector agrícola com a inhibidor bac-

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tericida i insecticida, amb perspectives d'investigació i aplicació immediata.

Paraules clau: Hidrazida, hidrazona, piridazinona, pirrolona, pirazolona

1. INTRODUCTION

Hydrazides and their derivatives have been intensively synthesized for various reasons, one of which is their uses as versatile and convenient intermediates for the synthesis of wide variety of nitrogen containing heterocyclic compounds.

Some of the other reasons are their ability to make a coordination complex with transition metal and the improvement of their properties for biological and analytical applications. Moreover, they exhibit a wide spectrum of biological activities such as anti-inflammatory [1-2], antimalarial [3], antimicrobial [4], antileishmanial [5], anticonvulsant [6], antitubercular [7] and antitumor [8].

Therefore, considering that the hydrazide derivatives are important building blocks for the synthesis of various heterocycles, we have chosen to synthesize and to study the reactivity of a new series of 2-arylmethylene-4-[4-methoxy-3-methylphenyl]-4-oxobutanhydrazides.

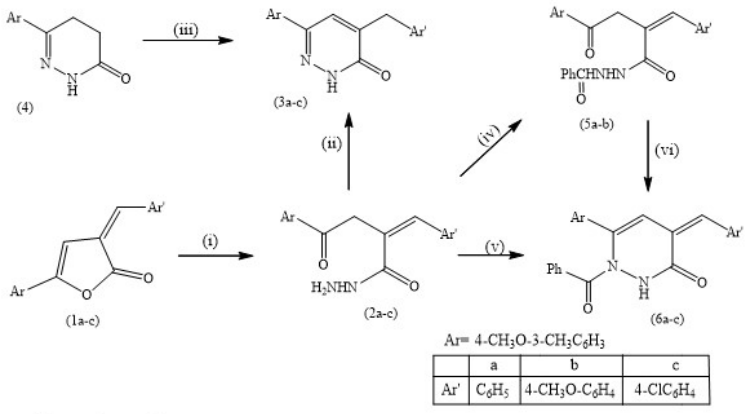
2. RESULTS AND DISCUSSION

The synthesis of the hydrazides (**2a-c**) was accomplished by the reaction of 5-[4-methoxy-3-methylphenyl]-3-substituted-2(3H)-furanones (**1a-c**) with hydrazine hydrate in cold ethanol.

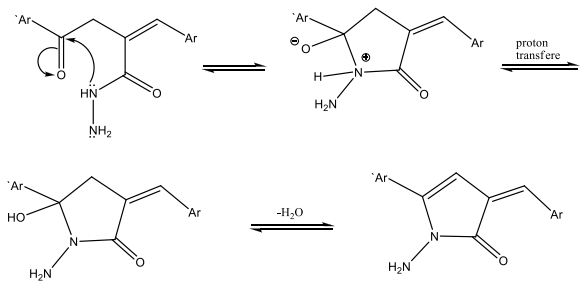
The hydrazides (**2a-c**) possess two different electrophilic centres (the carbonyl carbons and the *β*-carbon of the α,β–unsaturated carbonyl group). Therefore, various competitive pathways can operate depending on the reaction conditions. The hydrazide group is able to attack the carbonyl carbon (forming pyridazinone or pyrrolone) and the *β*-carbon of the α,β–unsaturated carbonyl group (forming pyrazole).

Thus, heating the hydrazides (**2a-c**) in refluxing benzene afforded mainly the corresponding 4-substituted-3(2H)-pyridazinones (**3a-c**). The reaction may be proceeded via intramolecular attack by the terminal nitrogen onto the carbonyl carbon yielding the hydroxy pyridazinones with subsequent dehydration providing the 3(2H)-pyridazinones (**3a-c**).

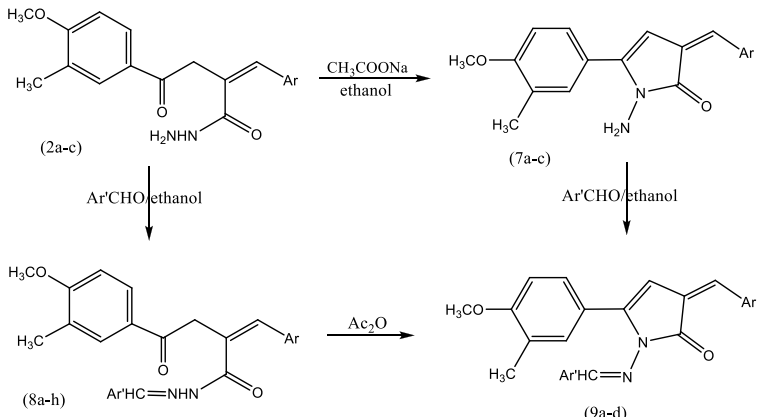
The proposed structures of pyridazinones (**3a-c**) were supported by the identity of their melting points with that of authentic samples prepared from the reaction of the corresponding 6-aryl-4,5-dihydro-3(2H)-pyridazinone (**4**) with aldehydes [9].



Scheme (1). *The formation of pyridazinone derivatives*



Scheme (2). *Proposed mechanism for the formation of compounds* (**7 a-c**)



8	Ar	Ar`
a	C_6H_5	C_6H_5
b	C_6H_5	4-ClC_6H_4
c	C_6H_5	2-HOC_6H_4
d	4-$MeOC_6H_4$	C_6H_5
e	4-$MeOC_6H_4$	4-ClC_6H_4
f	4-$MeOC_6H_4$	2-HOC_6H_4
g	4-ClC_6H_4	C_6H_5
h	4-ClC_6H_4	4-ClC_6H_4

9	Ar	Ar`
a	C_6H_5	C_6H_5
b	C_6H_5	4-ClC_6H_4
c	4-ClC_6H_4	C_6H_5
d	4-ClC_6H_4	4-ClC_6H_4

Scheme(3). *The formation of the pyrrolone derivatives*

When the hydrazides (**2a-c**) were allowed to react with benzoyl chloride in cold toluene, they afforded the corresponding N`-benzoyl hydrazides (**5a-c**); whereas, heating the hydrazides (**2a-c**) in refluxing toluene for 3hrs afforded the corresponding 4-arylidene-1-benzoyl-1,2-dihydro-3(4H)-pyridazinones (**6a-c**).

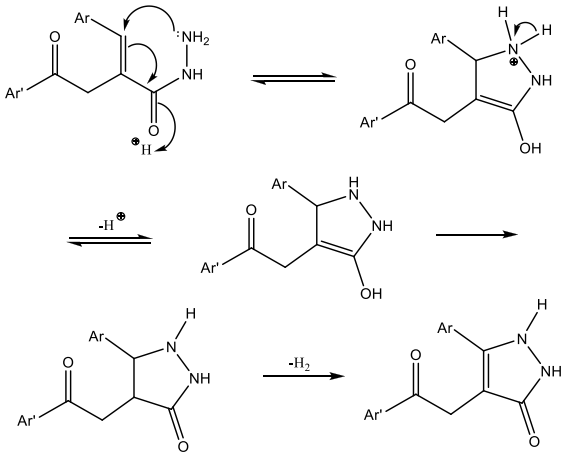
The I-R spectra of compounds (**6a-c**) revealed the absence of absorption bands characteristic for the NH_2 groups. The ^{1}H-NMR spectra of these compounds revealed the presence of singlet in the region 11.14-11.20 ppm corresponding to the NH proton of the pyridazine ring.

On the other hand, heating thehydrazides (**2a-c**) in refluxing ethanol provided mainly theN-amino-pyrrolones (**7a-c**). The formation of the N-amino-pyrrolone (**7a-c**) was assumed to proceed via the mechanism outlined in z (**2**).

The reactions of the hydrazides (**2a-c**) with aromatic aldehydes were carried out in boiling ethanol and led to the formation of the corresponding N-acylhydrazones (**8a-h**). The ^{1}H-NMR spectra of compounds (**8a-h**) revealed the appearance of new singlet signals in the upfield region (8.95-9.63 ppm) corresponding to the protons of the azomethine groups (C<u>H</u>=N).

On the other hand, on refluxing the hydrazides (**2a-c**) in ethanol in the presence of catalytic amount of HCl for 2hrs, ring closure occurred, leading to the formation of the corresponding pyrazoles (**10a-c**). The formation of the pyrazole derivatives (**10a-c**) was assumed to proceed via the intramolecular Michael addition. This behaviour is in accordance with the reported reaction of hydrazine with unsaturated carbonyl compounds.

The ^{1}H-NMR spectra of these compounds revealed the presence of singlet in the region 12.5-13.00 ppm, corresponding to the NH proton of the pyrazole ring adjacent to the keto group.



Scheme (4). *Proposed mechanism for the formation of pyrazolones* **(10a-c)**

3. EXPERIMENTAL

All melting points reported were uncorrected and determined by the open capillary tube method on a Buuchi 510 melting point apparatus. ^{1}H-NMR spectra were measured on Bruker (200 MHzw) and TMS were used as internal standard, IR spectra were recorded on a Perking Elmer 1430 ratio recording infrared spectrophotometer with CDS data station using KBr Wafer technique and mass spectra were measured on a GC-MSQP 1000EX Schimadzu at Micro analytical Laboratory, Cairo University, Cairo, Egypt. 3-Arylidene-5-[4-methoxy-3-methylphenyl]-2(3H)-furanones (**1a-c**) were prepared by us [10] from the reaction of β-[4-methoxy-3-methylbenzoylmethyl] propionic acid with aromatic aldehydes in the presence of anhydrous sodium acetate.

3.1 Formation of 2-arylidene-4-oxobutanhydrazides (2a-c)

To a solution of (0.01 mole) arylidenefuranones (**1a-c**) in ethanol (40 ml) hydrazine hydrate (0.58 ml, 0.012 mole) was added, the reaction mixture was stirred for 4hrs at room temperature and kept overnight. The resultant precipitate was filtered off and washed with diluted ethanol.

2-benzylidene-4-(4-methoxy-3-methylphenyl)-4-oxobutanehydrazide (**2a**):

Yield 81%, white powder, mp 123-124 °C. IR (KBr) υ_{max} (cm^{-1}): 3132 (NH and NH_2), 1693, 1653 (2C=O). ^{1}H-NMR (200 MHz,DMSO-d_6,): δ 2.13 (s, 3H, $\underline{CH_3}$Ar), 3.77 (s, 3H, $\underline{CH_3}$O-Ar), 4.35 (s, 2H, NH_2), 6.50-7.51(m, 10H, Ar-H, N-H and olefinic proton). MS m/z: 324 (5.4%) (M^+). Anal. calcd. for $C_{19}H_{20}N_2O_3$ (324.37): C, 70.35; H, 6.21; N, 8.64. Found: C, 70.55; H, 6.09; N, 8.70.

2-(4-methoxybenzylidene)-4-(4-methoxy-3-methylphenyl)-4-oxobutane hydrazide (**2b**):

Yield 74%, white powder, mp 144-146 °C. IR (KBr) υ_{max} (cm^{-1}): 3238, 3321 (NH and NH_2), 1695, 1646 (2C=O). ^{1}H-NMR (200 MHz, DMSO-d_6,): δ 2.13 (s, 3H, $\underline{CH_3}$Ar), 3.76 (s, 6H, 2 $\underline{CH_3}$O-Ar), 4.30 (s, 2H, NH_2), 7.46 -6.45 (m, 9H, Ar-H, NH and olefinic proton). Anal. calcd. for $C_{20}H_{22}N_2O_4$ (354.40): C, 67.78; H, 6.26; N, 7.90. Found: C, 67.98; H, 6.20; N, 7.87.

2-(4-chlorobenzylidene)-4-(4-methoxy-3-methylphenyl)-4-oxobutane hydrazide (**2c**):

Yield 79 %, white powder, mp 147-148 °C. IR (KBr) υ_{max} (cm^{-1}): 3321 (NH and NH_2), 1705, 1653 (2C=O). ^{1}H-NMR (200 MHz, DMSO-d_6,): δ 2.12 (s, 3H, $\underline{CH_3}$Ar), 3.76 (s, 3H, $\underline{CH_3}$O-Ar), 4.35 (s, 2H, NH_2), 6.55 -7.51 (m, 9H, Ar-H, NH and olefinic proton). Anal. calcd. for $C_{19}H_{19}ClN_2O_3$ (358.82): C, 63.60; H, 5.34; Cl, 9.88; N, 7.81. Found: C, 63.50; H, 5.45; Cl, 9.91; N, 7.61.

3.2 Formation of 4-Arylmethylenepyridazinones (3a-c)

A solution of the hydrazides **(2a-c)** (0.01 mole) in benzen (30 ml) was heated under reflux for 4 hrs. The solid product obtained after cooling, was filtered off, dried and crystallized from the suitable polar solvent to give white crystals of 4-aryl-6-(4-methoxy-3-methylphenyl) pyridazin-3(2H)-one (3a-c).

4-benzyl-6-(4-methoxy-3-methylphenyl)pyridazin-3(2H)-one (3a):

Yield 83 %, white crystals, mp 200-202 °C. IR (KBr) υ_{max} (cm^{-1}): 3302 (NH), 1652 (C=O). ^{1}H-NMR (200 MHz, DMSO-d_6,): δ 2.18 (s, 3H, $\underline{CH_3}$Ar), 3.86 (s, 3H, $\underline{CH_3}$O-Ar), 3.94 (s, 2H, $\underline{CH_2}$Ar), 6.84-7.51 (m, 9H, Ar-H and $\underline{CH}$ pyridazinone), 10.90 (s, 1H, NH). Anal. calcd. for $C_{19}H_{18}N_2O_2$ (306.36): C, 74.49; H, 5.92; N, 9.14. Found: C, 74.55; H, 5.80; N, 9.0.

4-methoxybenzyl-6-(4-methoxy-3-methylphenyl) pyridazin-3(2H)-one (**3b**):

Yield 81 %, white crystals, mp 186-187 °C. IR (KBr) υ_{max} (cm^{-1}): 3300 (NH), 1651 (C=O). ^{1}H-NMR (200 MHz, DMSO-d_6,): δ 2.25 (s, 3H, $\underline{CH_3}$Ar), 3.94, 3.86 (2s, 6H, $\underline{CH_3}$O-Ar), 3.99 (s, 2H, $\underline{CH_2}$Ar), 6.82-7.89 (m, 8H, Ar-H and $\underline{CH}$pyridazinone), 11.44 (s, 1H, NH). Anal. calcd. for $C_{20}H_{20}N_2O_3$ (336.38): C, 71.41; H, 5.99; N, 8.33. Found:C, 71.51; H, 5.99; N,8.45.

4-(4-chlorobenzyl)-6-(4-methoxy-3-methylphenyl) pyridazin-3(2H)-one (**3c**):

Yield 87 %, white crystals, mp 210-212 °C. IR (KBr) υ_{max} (cm^{-1}): 3431 (NH), 1659 (C=O). ^{1}H-NMR (200 MHz, DMSO-d_6,): δ 2.26 (s, 3H, $\underline{CH_3}$Ar), 3.87 (s, 3H, $\underline{CH_3}$O-Ar), 3.97 (s, 2H, $\underline{CH_2}$Ar), 6.84-7.55 (m, 9H, Ar-H, and $\underline{CH}$pyridazinone). Anal. calcd. for $C_{19}H_{17}ClN_2O_2$ (340.80): C, 66.96; H, 5.03; N, 8.22. Found: C, 66.76; H, 5.23; N, 8.52.

3.3 Formation of N`-[2-arylidene-4-(4-methoxy-3-methylphenyl)-4-oxobutanoyl] benzohydrazide (5a-c)

To a solution of the hydrazides **(2a-c)** (0.01 mole) in dry benzene (50 ml); freshly distilled benzoyl chloride (1.3ml, 0.011 mole) was added and the reaction mixture was stirred for 6 hrs. The solid that separated after cooling, was filtered off, dried and crystallized from suitable solvent to give **(5a-c)**.

N'-(2-benzylidene-4-(4-methoxy-3-methylphenyl)-4-oxobutanoyl)benzohydrazide (**5a**):

Yield 61 %, yellow powder, mp 188-190 °C. IR (KBr) υ_{max} (cm^{-1}): 3203 (NH), 1652, 1701 (2C=O). ^{1}H-NMR (200 MHz, DMSO-d_6,): δ 2.19 (s, 3H, $\underline{CH_3}$Ar), 3.82 (s, 3H, $\underline{CH_3}$O-Ar), 6.69-7.88 (m, 15H, Ar-H, NH and olefinic proton), 11.23 (s, 1H, NH). Anal. calcd for $C_{26}H_{24}N_2O_4$ (428.49): C, 72.88; H, 5.65; N, 6.54. Found: C, 67.20; H, 5.10; N, 6.55.

N'-(2-(4-methoxybenzylidene)-4-(4-methoxy-3-methylphenyl)-4oxobutanoyl)benzohydrazide (5b): Yield 46 %, yellow powder, mp 215-217 oC. IR (KBr) υmax (cm-1): 3181 (NH), 1668 (C=O). 1H-NMR (200 MHz, DMSO-d6,): δ 2.16 (s, 3H, CH3Ar), 3.79, 3.84 (2s, 6H, 2CH3O-Ar), 6.66-7.87 (m, 14H, Ar-H, NH and olefinic proton), 11.15(s, 1H, NH). Anal. calcd. for C27H26N2O5 (458.18): C, 70.73; H, 5.72; N, 6.11. Found: C, 70.89; H, 5.34; N, 6.00.

3.4 Formation of 4-arylidene-1-benzoyl-6-(4-methoxy-3-methylphenyl)-1,2-dihydro-3(4H)-pyridazinones (6a-c)

A mixture of the hydrazides **(2a-c)** (0.01 mole) and benzoyl chloride (1.ml,0.011 mole) in benzene (50 ml) was heated under reflux for 6 hrs. The solid product obtained after cooling, was filtered off, dried and crystallized from suitable solvent to give **(6a-c)**.

1-benzoyl-4-benzylidene-6-(4-methoxy-3-methylphenyl)-1,2-dihydro-3(4H)-pyridazinon (**6a**): Yield 54 %, orange powder, mp 249-250 °C. IR (KBr)

υ_{max} (cm^{-1}): 3202 (NH), 1668 (C=O). ^{1}H-NMR (200 MHz, DMSO-d_6,): δ 2.16 (s, 3H, $\underline{CH_3}$Ar), 3.79 (s, 3H, $\underline{CH_3}$O-Ar), 6.69-7.93 (m, 15H, Ar-H, pyridazine H-5 and olefinic proton), 11.20 (s, 1H, NH). Anal. calcd. for $C_{26}H_{22}N_2O_3$ (410.46): C, 76.08; H, 5.40; N, 6.82. Found: C, 67.19; H, 5.29; N, 6.50.

1-benzoyl-6-(4-methoxy-3-methylphenyl)-4-(4-methoxybenzylidene)-1,2-dihydro-3(4H)-pyridazinone (**6b**): Yield 51 %, orange powder, mp over 300°C. IR (KBr) υ_{max} (cm^{-1}): 3201 (NH), 1668 (C=O). ^{1}H-NMR (200 MHz, DMSO-d_6,): δ2.16 (s, 3H, $\underline{CH_3}$Ar), 3.79, 3.84 (2s, 6H, $\underline{2CH_3}$O-Ar), 6.65-7.86 (m, 14H, Ar-H, pyridazine H-5 and olefinic proton), 11.14 (s, 1H, NH). Anal. calcd. for $C_{27}H_{24}N_2O_4$ (440.49): C, 73.62; H, 5.49; N, 6.36. Found: C, 73.49; H, 5.30; N, 6.50.

1-benzoyl-4-(4-chlorobenzylidene)-6-(4-methoxy-3-methylphenyl)-1,2-dihydro-3(4H)-pyridazinone (**6c**): Yield 55 %, orange powder, mp 250-252 °C. IR (KBr) υ_{max} (cm^{-1}): 3186 (NH), 1694 (C=O). ^{1}H-NMR (200 MHz, DMSO-d_6,): δ 2.16 (s, 3H, $\underline{CH_3}$Ar), 3.80 (s, 3H, $\underline{CH_3}$O-Ar), 6.68-7.90(m, 14H, Ar-H, pyridazine H-5 and olefinic proton),11.20(s, 1H, NH).Anal. calcd. for $C_{26}H_{21}ClN_2O_3$ (444.91): C, 70.19; H, 4.76; N, 6.30. Found: C, 70.30; H, 4.60; N, 6.45.

3.5 Formation of 1-amino-3-arylidenepyrrolones (7a-c)

A solution of the hydrazides **(2a-c)** (0.01 mole) in ethanol (30 ml) was heated under reflux for 4 hrs. The solid product obtained after cooling, was filtered off, dried and crystallized from the suitable solvent to give orange crystals of *N*-aminopyrrolone **(7a-c)**.

1-amino-3-benzylidene-5-(4-methoxy-3-methylphenyl)-1H-pyrrol-2(3H)-one (**7a**): Yield 77 %, orange crystals, mp 213-214 °C. IR (KBr) υ_{max} (cm^{-1}): 3315 (NH), 1693 (C=O). ^{1}H-NMR (200 MHz, DMSO-d_6,): δ 2.20 (s, 3H, $\underline{CH_3}$Ar), 3.85 (s, 3H, $\underline{CH_3}$O-Ar), 5.01 (s, 2H, NH_2), 6.04 (s, 1H, $\underline{CH}$ proton of pyrrole), 6.99 -7.83 (m, 8H, Ar-H),7.22 (s, 1H, olefinic). MS: m/z: 306 (5.4%) (M^+). Anal. calcd. for $C_{19}H_{18}N_2O_2$ (306.36): C, 74.49; H, 5.92; N, 9.14. Found: C, 74.52; H, 5.62; N, 9.24.

1-amino-3-(4-methoxybenzylidene)-5-(4-methoxy-3-methylphenyl)-1H-pyrrol-2(3H)-one (**7b**): Yield 69 %, orange crystals, mp 214-215 °C. IR (KBr) υ_{max} (cm^{-1}): 3314 (NH), 1694 (C=O). ^{1}H-NMR (200 MHz, DMSO-d_6,): δ 2.08 (s, 3H, $\underline{CH_3}$Ar), 3.84, 3.82 (2s, 6H, $2\underline{CH_3}$O), 4.97 (s, 2H, NH_2), 6.37 (s, 1H, $\underline{CH}$ proton of pyrrole), 6.98- 7.80 (m,7H, Ar-H), 7.19 (s,1H, olefinic proton). Anal. calcd. for $C_{20}H_{20}N_2O_3$ (336.39): C, 71.41; H, 5.99; N, 8.33. Found: C, 71.21; H, 6.10; N, 8.03.

1-amino-3-(4-chlorobenzylidene)-5-(4-methoxy-3-methylphenyl)-1H-pyrrol-2(3H)-one (**7c**): Yield 71 %, orange crystals, mp 224-226 °C. IR (KBr) υ_{max} (cm^{-1}): 3316 (NH), 1698 (C=O). ^{1}H-NMR (200 MHz, DMSO-d_6,): δ 2.19 (s, 3H, $\underline{CH_3}$Ar), 3.84 (s,3H, $\underline{CH_3}$O-Ar), 5.01 (s,2H, NH_2), 6.38 (s,1H, $\underline{CH}$ proton of pyrrole), 6.99-7.83 (m, 7H, Ar-H),7.19 (s,1H, olefinic proton). Anal. calcd. for $C_{19}H_{17}ClN_2O_2$ (340.81): C, 66.96; H, 5.03; N, 8.22. Found: C, 66.87; H, 5.32; N, 8.01.

3.6 Formation of N'-arylidene-2-arylidene-4-(4-methoxy-3-methylphenyl)-4-oxobutanhydrazides (8a-h)

A mixture of the hydrazides **(2a-c)** (0.01 mole) and the appropriate aldehydes (0.01 mole) namely benzaldehyde, 4-chlorobenzaldehyd, salicyaldehyde in ethanol (50 ml) was heated under reflux for 4 hrs. The solid product obtained after cooling, was filtered off, dried and crystallized from the suitable solvent to give **(8a-h)**.

N',2-dibenzylidene-4-(4-methoxy-3-methylphenyl)-4-oxobutanhydrazide (**8a**): Yield 62%, white powder, mp 180-181 °C. IR (KBr) υ_{max} (cm^{-1}): 3230 (NH), 1682 (C=O). ^{1}H-NMR (200 MHz, DMSO-d_6,): δ 2.12 (s, 3H, $\underline{CH_3}$Ar), 3.74 (s, 3H, $\underline{CH_3}$O-Ar), 6.88 -7.62 (m, 14H, olefinic, NH and aromatic protons), 8.95 (s, 1H, N=$\underline{CH}$). Anal. calcd. for $C_{26}H_{24}N_2O_3$ (412.48): C, 75.71; H, 5.86; N, 6.79. Found: C, 75.41; H, 5.46; N, 6.63.

2-benzylidene-N'-(4-chlorobenzylidene)-4-(4-methoxy-3-methylphenyl)-4-oxobutan hydrazide (**8b**): Yield 64%, white powder, mp 198-199 °C. IR (KBr) υ_{max} (cm^{-1}): 3239 (NH), 1685 (C=O). ^{1}H-NMR (200 MHz, DMSO-d_6,): δ 2.12 (s, 3H, $\underline{CH_3}$Ar), 3.74 (s, 3H, $\underline{CH_3}$O-Ar), 6.88-7.65 (m, 13H, olefinic, NH and aromatic protons), 8.97 (s, 1H, N=$\underline{CH}$Ph). MS: m/z: 346 (4.2%) (M^+).Anal. calcd. for $C_{26}H_{23}ClN_2O_3$ (446.93): C, 69.87; H, 5.19; N, 6.27. Found: C, 69.97; H, 7.68; N, 6.47.

2-benzylidene-N'-(2-hydroxybenzylidene)-4-(4-methoxy-3-methylphenyl)-4-oxobutan hydrazide (**8c**): Yield 67 %, orange crystals, mp 178-180 °C. IR (KBr) υ_{max} (cm^{-1}): 3137 (NH), 1696 (C=O). ^{1}H-NMR (200 MHz, DMSO-d_6,): δ 2.19 (s, 3H, $\underline{CH_3}$Ar), 3.85 (s, 3H, $\underline{CH_3}$O-Ar), 6.72-7.87 (m, 13H, olefinic, NH and aromatic protons), 9.63 (s, 1H, N=$\underline{CH}$), 10.24 (s, 1H, OH). Anal. calcd. for $C_{26}H_{24}N_2O_4$ (428.48): C, 72.88; H, 5.65; N, 6.54. Found:C, 72.80; H, 5.40; N, 6.66.

N'-benzylidene-4-(4-methoxy-3-methylphenyl)-2-(4-methoxybenzylidene)-4-oxobutan hydrazide (**8d**): Yield 66 %, orange crystals, mp 177-178 °C. IR (KBr) υ_{max} (cm^{-1}): 1692 (C=O). ^{1}H-NMR (200 MHz, DMSO-d_6,): δ 2.20 (s, 3H, $\underline{CH_3}$Ar), 3.84, 3.85 (2s, 6H, $2\underline{CH_3}$O-Ar), 6.71, 7.29 (s, 2H, olefinic protons), 7.85 - 7.01 (m, 13H, Ar-H and NH), 9.47 (s, 1H, N=CH). Anal. calcd. for $C_{27}H_{26}N_2O_4$ (442.51): C, 73.28; H, 5.92; N, 6.33. Found: C, 73.48; H, 5.86; N, 6.53.

N'-(4-chlorobenzylidene)-4-(4-methoxy-3-methylphenyl)-2-(4-methoxybenzylidene)-4-oxobutanhydrazide (**8e**): Yield 59 %, orange crystals, mp 175-176 °C. IR (KBr) υ_{max} (cm^{-1}): 3128 (N-H), 1693 (C=O). ^{1}H-NMR (200 MHz, DMSO-d_6,): δ2.20 (s, 3H, $\underline{CH_3}$Ar), 3.84, 3.85 (2s, 6H, $2\underline{CH_3}$O-Ar), 6.72, 7.30 (2s, 2H, olefinic protons), 7.01-7.86 (m, 12H, Ar-H and NH), 9.50 (s, 1H, N=CH). Anal. calcd. for $C_{27}H_{25}ClN_2O_4$

(476.95): C, 67.99; H, 5.28; N, 5.87. Found: C, 67.78; H, 5.08; N, 5.77.

N'-(2-hydroxybenzylidene)-4-(4-methoxy-3-methylphenyl)-2-(4-methoxybenzylidene)-4-oxobutanhydrazide (**8f**): Yield 46%, orange crystals, mp 178-180 °C. IR (KBr) υ_{max} (cm^{-1}): 3217 (NH), 1673 (C=O). ^{1}H-NMR (200 MHz, DMSO-d_6,): δ2.13 (s, 3H, $\underline{CH_3}$Ar), 3.75, 3.79 (2s, 6H, 2$\underline{CH_3}$O-Ar), 6.82 -7.55 (m, 12H, olefinic, NH and aromatic protons), 9.01 (s, 1H, N=CH), 10.96 (s, 1H, OH).Anal. calcd. for $C_{27}H_{26}N_2O_5$ (458.51): C, 70.73; H, 5.72; N, 6.11. Found: C, 70.37; H, 5.55; N, 6.30.

N'-benzylidene-2-(4-chlorobenzylidene)-4-(4-methoxy-3-methylphenyl)-4-oxobutan hydrazide (**8g**): Yield 68 %, orange crystals, mp 171-173 °C. IR (KBr) υ_{max} (cm^{-1}): 3246 (NH), 1691 (C=O). ^{1}H-NMR (200 MHz, DMSO-d_6,): δ2.20 (s, 3H, $\underline{CH_3}$Ar), 3.85 (s, 3H, $\underline{CH_3}$O-Ar), 6.72, 7.31 (2s, 2H, olefinic protons), 7.03-7.90 (m, 13H, Ar-H and NH), 9.43 (s, 1H, N=CH). Anal. calcd. for $C_{26}H_{23}ClN_2O_3$ (446.93): C, 69.87;H, 5.19; N, 6.27. Found: C, 69.60; H, 5.01; N, 6.07.

N',2-bis(4-chlorobenzylidene)-4-(4-methoxy-3-methylphenyl)-4-oxobutanhydrazide (**8h**): Yield 71 %, orange crystals, mp 203-205 °C. IR (KBr) υ_{max} (cm^{-1}): 3234 (NH), 1661 (C=O). ^{1}H-NMR (200 MHz, DMSO-d_6,): δ 2.20 (s, 3H, $\underline{CH_3}$Ar), 3.85(s, 3H, $\underline{CH_3}$O-Ar), 6.38, 7.19 (2s, 2H, olefinic protons), 6.38-7.90 (m, 12H, Ar-H and NH), 9.46 (s, 1H, N=CH). Anal. calcd. for $C_{26}H_{22}Cl_2N_2O_3$ (481.37): C, 64.87; H, 4.61; N, 5.82. Found: C, 64.91; H, 4.41; N, 5.32.

3.7 Formation of 3-arylidene-1-(arylidenamino)-5-(4-methoxy-3-methylphenyl)-1H-pyrrol-2(3H)-ones (9a-d)

A mixture of the N`-acylhydrazones **(8a, 8b, 8g and/or 8h)** (0.01 mole) and distilled acetic anhydride (15 ml) was heated under reflux for 6 hrs. The product obtained after concentration and cooling, was filtered off, dried and crystallized from the proper solvent to give **(9a-d)**

3-benzylidene-1-(benzylideneamino)-5-(4-methoxy-3-methylphenyl)-1H-pyrrol-2(3H)-one (**9a**): Yield71 %, deep orange crystals, mp 168-169 °C. IR (KBr) υ_{max} (cm^{-1}): 1694 (C=O). ^{1}H-NMR (200 MHz, DMSO-d_6,): δ 2.20 (s, 3H, $\underline{CH_3}$Ar), 3.85 (s, 3H, $\underline{CH_3}$O-Ar), 6.74, 7.34 (2s, 2H, olefinic protons), 7.03-7.87 (m, 13H, Ar-H and NH), 9.45 (s, 1H, N=CH). Anal. calcd. for $C_{26}H_{22}N_2O_2$ (394.37): C, 79.16; H, 5.62; N, 7.10. Found: C, 79.40; H, 5.41; N, 7.00.

3-benzylidene-1-(4-chlorobenzylideneamino)-5-(4-methoxy-3-methylphenyl)-1H-pyrrol-2(3H)-one (**9b**): Yield76 %, deep orange crystals, mp 190-191 °C. IR (KBr) υ_{max} (cm^{-1}): 1701 (C=O). ^{1}H-NMR (200 MHz, DMSO-d_6,): δ 2.20 (s, 3H, CH_3Ar), 3.85(s, 3H, $\underline{CH_3}$O-Ar), 6.75, 7.34 (2s, 2H, olefinic protons), 7.02-7.88 (m, 12H, Ar-H and NH), 9.48(s, 1H, N=CH). Anal. calcd. for $C_{26}H_{21}ClN_2O_2$ (428.92): C, 72.81; H, 4.94; N, 6.53. Found: C, 72.60; H, 5.01; N, 6.30.

1-(benzylideneamino)-3-(4-chlorobenzylidene)-5-(4-methoxy-3-methylphenyl)-1H-pyrrol-2(3H)-one (**9c**): Yield 73 %, deep orange crystals, mp 179-180 °C. IR (KBr) υ_{max} (cm^{-1}): 1703 (C=O). ^{1}H-NMR (200 MHz, DMSO-d_6,): δ 2.20 (s, 3H, $\underline{CH_3}$Ar), 3.85 (s, 3H, $\underline{CH_3}$O-Ar), 6.73, 7.31 (2s, 2H, olefinic protons), 7.31-7.90 (m, 12H, Ar-H and NH), 9.45 (s, 1H, N=CH). Anal. calcd. for $C_{26}H_{21}ClN_2O_2$ (428.92): C, 72.81; H, 4.94; N, 6.53. Found: C, 72.99; H, 4.64; N, 6.50.

3-(4-chlorobenzylidene)-1-4-chlorobenzylideneamino)-5-(4-methoxy-3-methylphenyl)-1H-pyrrol-2(3H)-one (**9d**): Yield 81 %, orange crystals, mp 231-233 °C. IR (KBr) υ_{max} (cm^{-1}): 1706 (C=O). ^{1}H-NMR (200 MHz, DMSO-d_6,): δ 2.20 (s, 3H, $\underline{CH_3}$Ar), 3.86 (s, 3H, $\underline{CH_3}$O-Ar), 6.74, 7.32 (2s, 2H, olefinic protons), 7.03-7.91 (m, 11H, Ar-H and NH), 9.47 (s, 1H, N=CH). Anal. calcd. for $C_{26}H_{20}Cl_2N_2O_2$ (463.36): C, 67.39; H, 4.35; N, 6.05. Found: C, 67.52; H, 4.29; N, 6.20.

3.8 Formation of 5-arylpyrazolones (10a-c)

To stirred solution of (0.01 mole) of the hydrazides (**2a-c**) in ethanol (30 ml), a solution of 1N hydrochloric acid in ethanol (10 ml) was added dropwise. The reaction mixture was stirred at room temperature for 4hrs, then kept overnight. The product obtained, was filtered off, washed with ethanol and crystallized from the appropriate solvent to give the pyrazolones (**10a-c**).

4-(2-(4-methoxy-3-methylphenyl)-2-oxoethyl)-5-phenyl-1H-pyrazol-3(2H)-one (**10a**): Yield 37 %, pale yellow crystals, mp 213-214 °C. IR (KBr) υ_{max} (cm^{-1}): 3303 (NH), 1652 (C=O). ^{1}H-NMR (200 MHz, DMSO-d_6,): δ 2.19 (s, 3H, $\underline{CH_3}$Ar), 3.81 (s, 2H, CH_2),3.85 (s,3H, $\underline{CH_3}$O-Ar),7.82-6.98 (m,9H, Ar-H and NH), 12.98 (s,1H, NH). Anal. calcd. for $C_{19}H_{18}N_2O_3$ (322.36): C, 70.79; H, 5.63; N, 8.69. Found: C, 70.70; H, 5.83; N, 8.49.

4-(2-(4-methoxy-3-methylphenyl)-2-oxoethyl)-5-(4-methoxyphenyl)-1H-pyrazol-3(2H)-one (**10b**): Yield 46 %, pale yellow crystals, mp 216-217 °C. IR (KBr) υ_{max} (cm^{-1}): 3302 (NH), 1651 (C=O). ^{1}H-NMR (200 MHz, DMSO-d_6,): δ2.18 (s,3H, $\underline{CH_3}$Ar), 3.71 (s,2H, CH_2),3.81, 3.77 (2s,6H, 2$\underline{CH_3}$O-Ar),7.78-6.84 (m,8H, Ar-H and NH), 12.95 (s,1H, NH).Anal. calcd. for $C_{20}H_{20}N_2O_4$ (352.38): C, 68.17; H, 5.72; N, 7.95. Found: C, 68.32; H, 5.91; N, 7.65.

5-(4-chlorophenyl)-4-(2-(4-methoxy-3-methylphenyl)-2-oxoethyl)-1H-pyrazol-3(2H)-one (**10c**): Yield 51 %, pale yellow crystals, mp 230-231 °C. IR (KBr) υ_{max} (cm^{-1}): 3302 (NH), 1651 (C=O). ^{1}H-NMR (200 MHz, DMSO-d_6,): δ 2.18 (s, 3H, $\underline{CH_3}$Ar), 3.81 (s, 2H, CH_2), 3.84 (s, 3H, $\underline{CH_3}$O-Ar),6.98-7.87 (m, 8H, Ar-H and NH), 13.00 (s, 1H, NH).MS: *m/z*: 356.5 (19.62%) (M^+). Anal. calcd. for $C_{19}H_{17}ClN_2O_3$ (356.80): C, 63.96; H, 4.80; N, 7.85. Found: C, 63.68; H, 4.71; N, 7.66.

4. CONCLUSION

The approach of the present work was to study the reactivity of 2-arylmethylene-4-oxo-4-(4-methoxy-3-methylphenyl)butanoylhydrazides. Different heterocyclic compounds (pyridazinones, pyrroles, pyrazoles) have been synthesized from the ring closure of the hydrazides (**2a-c**) under different conditions. The treatment of hydrazides (**2a-c**) with aromatic aldehydes gave the corresponding hydrazones, which afforded the corresponding 1-arylideneaminopyrrolones on reaction with acetic anhydride.

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