2-Arylhydrazono-3-oxopropanals in Heterocyclic Synthesis: Synthesis of Arylazopyrazole, Arylazoisoxazole and Dialkylpyridazine-5,6-dicarboxylate Derivatives. New One-step Synthesis of Arylazopyrimidines.

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A novel synthesis of arylpyrazole, isoxazole, dialkyl 1,6-dihydropyridazine 5,6-dicarboxylate derivatives and a new one-step synthesis of azolopyrimidines under microwave-assisted conditions are reported.

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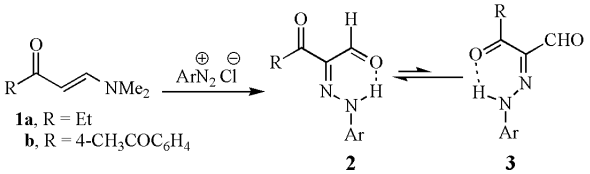
Some time ago an easy synthesis of 2-arylhydrazonopropanals has been reported from our laboratories [1-3]. Since that time we have been involved in investigations aimed at exploring synthetic potentialities of this class of compounds [1-5]. In a continuation to this work we report the synthesis of 2-arylhydrazonals **2a-h** *via* coupling **1a,b** with aromatic diazonium salts. The reactivity of **2a-h** toward nitrogen nucleophiles by microwave heating "green technology" [6,7] in the absence of solvent is reported. Results are compared with those obtained from conventional heating utilizing procedures similar to those reported earlier [1-5,8-11]. Moreover further examples of the novel 1,6-dihydropyridazine-5,6-dicarboxylate *via* reacting 2-arylhydrazonals with dimethyl acetylenedicarboxylate and triphenylphosphine [4] is reported. Thus, **2a-h** were obtained in 50-80% yields *via* coupling **1a,b** with aromatic diazonium salts. ^{1}H-NMR of the products indicated that they exist at least in DMSO solution as mixtures of the anti form **2** and syn form **3**. The anti form generally predominated (Figure 1).



2a, Ar = Ph; R = Et;
b, Ar = 4-$CH_3C_6H_4$; R = Et;
c, Ar = 4-$NO_2C_6H_4$; R = Et;
d, Ar = 4-$OCH_3C_6H_4$; R = Et;
e, Ar = Ph; R = 4-$CH_3COC_6H_4$;
f, Ar = 4-$NO_2C_6H_4$; R = 4-$CH_3COC_6H_4$;
g, Ar = 4-$CH_3OC_6H_4$; R = 4-$CH_3COC_6H_4$;
h, Ar = 2-$CH_3OC_6H_4$; R = 4-$CH_3COC_6H_4$;

Figure 1

Compounds **2a-h** reacted with phenylhydrazine in refluxing ethanol for one hour to yield the phenylhydrazones **4a-h**. Phenylhydrazones **4b,d,f** could be also obtained on heating of **2b,d,f** and phenylhydrazine in a microwave oven for 5-10 minutes at full power. Products of microwave reaction were found to be more pure in crude form and to be formed in better yields. Reacting **2a,c** with hydrazine hydrate also afforded the hydrazones **4i,j**. While hydrazones of structure similar to **4** were reported earlier to cyclize readily into pyrazoles [2], cyclization of **4a-d** proceeded with difficulty. Only after long reflux in pyridine 4-8 hours, could **4c,g** be cyclized into **5a,b**. However, the hydrazones **4i,j**, on the other hand, cyclized into **5c,d** on reflux in pyridine for 4 hours.

The reaction of **2a-d** with hydroxylamine hydrochloride in ethanolic sodium acetate has afforded, similar to earlier reports on arylhydrazones [2,5], oximes **6a-d**. Compounds **6a,b** were also obtained on treatment of **2a,b** with hydroxylamine hydrochloride and sodium carbonate in a microwave oven at full power (*cf*. Table 1). Compounds **6a-d** cyclized into isoxazoles **7a-d** on reflux in acetic anhydride. In contrast to this **2c** afforded the nitrile **8** on treatment with hydroxylamine in acetic acid and in the presence of ammonium acetate in a microwave oven. It is believed that the initially formed oxime is acylated to yield **9** under these conditions and readily then underwent a thermal pericyclic elimination of acetic acid *via* a six membered transition state (Figure 2).

Compound **2a** condensed with 5-amino-1*H*-1,2,4-triazole **10a** to yield **11a** whose structure was established by single crystal X-ray diffraction (Figure 3). Similarly, condensation of aminopyrazoles **10b-d** with **2b,c** afforded the pyrazolo[1,5-*a*]pyrimidines **11b-d**. It is believed that **10a-d** initially condense with **2** to yield **12** which then cyclises into **11** (Figure 4).

The reaction of **2a,c** with 2-aminobenzimidazole (**13**) afforded a product that was assigned to structure **14** rather than **15** based on NOE difference that revealed that the ethyl function and benzimidazole H are spatially proximal. The ethylpyridazine carboxylate **16** could be readily obtained *via* condensing **2c** with diethylmalonate in ethanolic piperidine (Figure 5).

In a previous work [4] it has been reported that the reaction of 2-arylhydrazonals with dimethylacetylene dicarboxylate

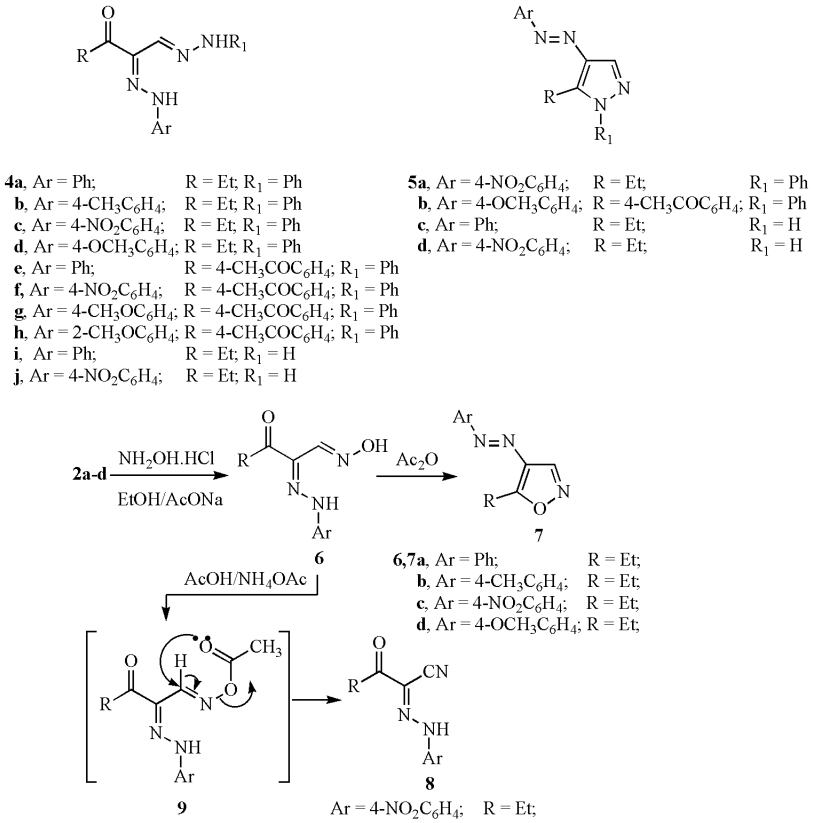


Figure 2

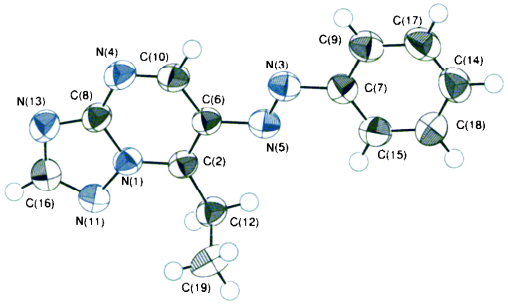


Figure 3. Molecular structure of **11a** with atoms labeling scheme.

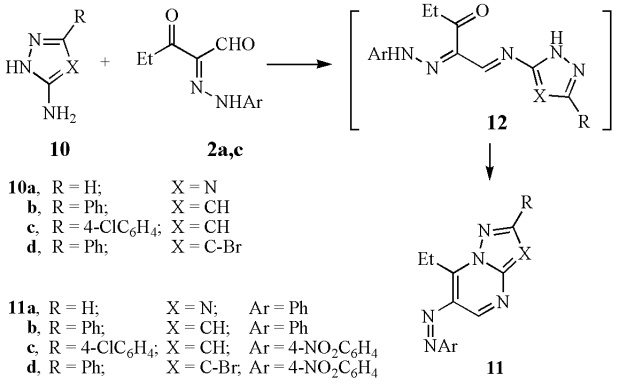


Figure 4

(DMAD) and triphenylphosphine affords dihydropyridazines. Although alternative structures were also possible no conclusive evidence for the proposed structure was offered. Also no mechanism to account for formation of the reaction product has been presented. In the present study, a facile one-pot synthesis of dimethyl 1,6-dihydropyridazine-5,6-dicarboxylates **18** in high yield utilizing the 3-oxo-2-(arylhydrazono)pentanal **2a-d** or 3-(4-acetylphenyl)-3-oxo-2-(arylhydrazono)-propionaldehyde **2e-g** as precursors for this ring system is reported. Thus, compounds **2a-d** reacted with DMAD in the presence of tripheylphosphine at room temperature in dichloromethane solution to yield a product for which structures **18-20** seemed possible. Structures **19,20** could be readily ruled out based on ^{1}H NMR that revealed the absence of signals either for NH or ring CH_2 (Figure 6).

Thus, the structure **18** was established as the reaction product. Compound **18** is assumed to be formed *via* initial addition of the ylide "formed by adding triphenyl phosphine to the acetylenedicarboxylate" to hydrazone **2** yielding **17** and then elimination of triphenylphosphine oxide to

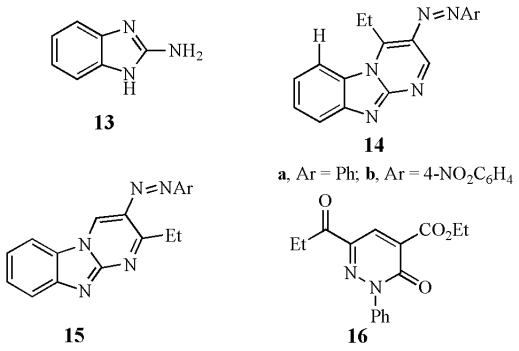


Figure 5

Table 1
Comparison Between Reaction Times and Yields Obtained from Conventional and Microwave Heating

Compd	Conventional Δ Yield (%)	Conventional Δ Time (min.)	Microwave Δ Yield (%)	Microwave Δ Time (min.)
4b	71	60	89	10
4d	70	60	90	5
4f	71	60	82	10
6a	70	240	86	10
6b	60	240	85	5
11a	65	360	97	2
11b	79	360	99	2
14a	60	360	95	2

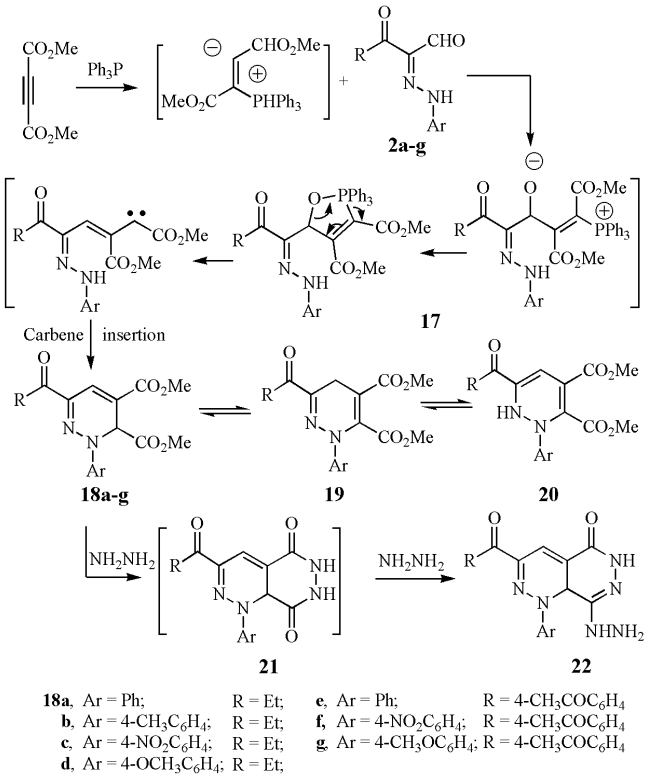


Figure 6

yield **18**. Similarly the arylhydrazones **2e-g** reacted with DMAD in the presence of triphenylphosphine to yield the pyridazine dicarboxylate derivatives **18e-g**. Compound **18a** reacted with hydrazine hydrate to afford **22** most likely *via* intermediacy of **21** (Figure 6).

EXPERIMENTAL

All melting points were measured on a Gallenkamp electrothermal melting point apparatus and are uncorrected. Microwave oven SJO 390W. IR spectra were recorded as KBr pellets on a Pye Unicam SP 3-300 Spectrophotometer. ^{1}H NMR spectra were recorded in hexadeuterated dimethylsulfoxide (DMSO-d_6) or deuteriochloroform ($CDCl_3$) at 200 or 300 MHz on a Varian Gemini NMR spectrometer using tetramethylsilane (TMS) as an internal reference and results are expressed as δ values. Mass spectra were performed on a Shimadzu GCMS-QP 1000 Ex mass spectrometer at 70 eV. Elemental analyses were carried out at the Microanalytical center of Cairo University.

Preparation of Compounds **2a-h**.

General Procedure.

A cold solution of aryldiazonium salt (10 mmol) was prepared by adding a solution of sodium nitrite (10 mmol into H_2O) to a cold solution of the aromatic amine hydrochloride or heterocyclic amine derivatives with stirring. The resulting solution of the aryldiazonium salt was added to a cold solution of 1-dimethylaminopent-1-en-3-one (**1a**) (1.27 g, 10 mmol) or 1-(4-acetylphenyl)-3-dimethylaminopropenone (**1b**) in ethanol (50 ml) containing sodium acetate (5 g). The reaction mixture was stirred at room temperature for 30 min. The solid product, so formed, was collected by filtration, washed with water and crystallized from the proper solvent.

3-Oxo-2-(phenylhydrazono)pentanal (**2a**).

This compound was obtained in 70 % yield; mp 93 ºC; red crystals from dilute ethanol, IR (KBr): ν 3500(br NH), 1680(CO aldehyde), 1648 cm^{-1} (CO ketone); ^{1}H NMR (d_6-DMSO): δ = 1.1 (t, 3H, CH_3), 2.9(q, 2H, CH_2), 7.3-7.4(m, 3H, Ar-H) 7.6(d, 2H, Ar-H), 9.9, 9.5(s, 1H, CHO), 14.1, 14.5(s, 1H, NH); MS (EI, 70 EV): *m/z* 203(32.6%) [M-1]$^+$.

Anal. Calcd. for $C_{11}H_{12}N_2O_2$ (204.23): C, 64.69; H, 5.92; N, 13.72 %. Found: C, 64.80; H, 5.89; N, 13.60.

3-Oxo-2-(*p*-tolylhydrazono)pentanal (**2b**).

This compound was obtained in 72 % yield, mp 133 ºC; orange crystals from ethanol, ^{1}H NMR (d_6-DMSO): δ = 1.1 (t, 3H, CH_3), 2.3 (s, 3H, CH_3), 3.0 (q, 2H, CH_2), 7.3-8.6 (m, 4H, Ar-H), 9.6, 9.9 (s, 1H, CHO), 14.5, 15.0(s, 1H, NH); MS (EI, 70 EV): *m/z* 218 (87.2%) (M$^+$).

Anal. Calcd. for $C_{12}H_{14}N_2O_2$ (218.25): C, 66.04; H, 6.47; N, 12.84 %. Found: C, 66.00; H, 6.49; N, 13.00.

3-Oxo-2-(4-Nitrophenylhydrazono)pentanal (**2c**).

This compound was obtained in 72 % yield, mp 125 ºC; red crystals from ethanol, ^{1}H NMR (d_6-DMSO): δ = 1.1 (t, 3H, CH_3),

2.9 (q, 2H, CH_2), 6.7-7.9 (m, 4H, Ar-H), 9.2, 9.8 (s, 1H, CHO), 13.9, 14.5 (s, 1H, NH); MS (EI, 70 EV): *m/z* 249 (34.1%) (M^+).

Anal. Calcd. for $C_{11}H_{11}N_3O_4$ (249.22): C, 53.01; H, 4.45; N, 16.86 %. Found: C, 53.20; H, 4.50; N, 16.75.

3-Oxo-2-(4-Methoxyphenylhydrazono)pentanal (**2d**).

This compound was obtained in 72 % yield, mp 120 ºC; red crystals from ethanol, ^1H NMR (d_6-DMSO): δ = 1.09 (t, 3H, CH_3), 2.8 (q, 2H, CH_2), 3.7 (s, 3H, OCH_3), 7.06 (d, 2H, Ar-H), 7.6(d, 2H, Ar-H), 9.4, 9.9(s, 1H, CHO), 14.3, 14.7 (s, 1H, NH); MS (EI, 70 EV): *m/z* 234 (15.2%) (M^+).

Anal. Calcd. for $C_{12}H_{14}N_2O_3$ (234.25): C, 61.53; H, 6.02; N, 11.96 %. Found: C, 61.35; H, 6.09; N, 11.77.

3-(4-Acetylphenyl)-3-oxo-2-(Phenylhydrazono)propionaldehyde (**2e**).

This compound was obtained in 70 % yield; mp 153 ºC; yellow crystals from dilute ethanol, IR (KBr): ν 3118 (NH), 1660, 1641 cm^{-1} (CO); ^1H NMR ($CDCl_3$): δ = 2.6 (s, 3H, CH_3), 6.4-7.9 (m, 9H, Ar-H), 9.5, 10.0 (s, 1H, CHO), 13.2, 14.2 (s, 1H, NH); MS (EI, 70 EV): *m/z* 293 (32.9%.) $[M-1]^+$.

Anal. Calcd. for $C_{17}H_{14}N_2O_3$ (294.31): C, 69.38; H, 4.79; N, 9.52 %. Found: C, 69.19; H, 4.69; N, 9.42.

3-(4-Acetylphenyl)-3-oxo-2-(4-nitrophenylhydrazono)propionaldehyde (**2f**).

This compound was obtained in 72 % yield, mp 149 ºC; red crystals from ethanol/dioxan (1:1), ^1H NMR (d_6-DMSO): δ = 2.6 (s, 3H, CH_3), 6.7-7.9 (m, 8H, Ar-H), 9.6, 10.1 (s, 1H, CHO), 12.9, 14.0 (s, 1H, NH); MS (EI, 70 EV): *m/z* 339 (16.5%) (M^+).

Anal. Calcd. for $C_{17}H_{13}N_3O_5$ (339.30): C, 60.18; H, 3.86; N, 12.38 %. Found: C, 60.21; H, 3.78; N, 12.39.

3-(4-Acetylphenyl)-2-(4-methoxyphenylhydrazono)-3-oxopropionaldehyde (**2g**).

This compound was obtained in 70 % yield, mp 136 ºC; red crystals from methanol, IR (KBr): ν 3424(NH), 1714, 1676 cm^{-1} (CO); ^1H NMR (d_6-DMSO): δ = 2.6 (s, 3H, CH_3), 3.8 (s, 3H, OCH_3), 7.0 (d, 2H, Ar-H), 7.4 (d, 2H, Ar-H), 7.9 (d, 2H, Ar-H), 8.1 (d, 2H, Ar-H), 9.6, 10.0 (s, 1H, CHO), 13.2, 14.4 (s, 1H, NH); MS (EI, 70 EV): *m/z* 324(17.1%) (M^+).

Anal. Calcd. for $C_{18}H_{16}N_2O_4$ (324.33): C, 66.66; H, 4.97; N, 8.64 %. Found: C, 66.56; H, 4.91; N, 8.68.

3-(4-Acetylphenyl)-2-(2-methoxyphenylhydrazono)-3-oxo-propionadehyde (**2h**).

This compound was obtained in 85 % yield, mp 139 ºC; orange crystals from ethanol/dioxan (1:1), ^1H NMR (d_6-DMSO): δ = 2.6 (s, 3H, CH_3), 3.7 (s, 3H, OCH_3), 6.3-8.1 (m, 8H, Ar-H), 9.6, 10.0 (s, 1H, CHO), 13.2, 14.3 (s, 1H, NH); MS (EI, 70 EV): *m/z* 324 (47%) (M^+).

Anal. Calcd. for $C_{18}H_{16}N_2O_4$ (324.33): C, 66.66; H, 4.97; N, 8.64 %. (Found: C, 66.65; H, 4.92; N, 8.55.

Preparation of Compounds **4a-j**.

General Procedures.

Method A, Thermal Reaction.

A mixture of 2-arylhydrazonopentanals (**2a-d**) or arylhydrazonopropanal (**2e-h**) (10 mmol) with phenylhydrazine (1.08 g, 10 mmol) or hydrazine hydrochloride (1.04 g, 10 mmol) was refluxed in ethanol for 1 h. The solid product obtained was collected by filtration and crystallized from the proper solvent.

Method B, Microwave Heating.

A mixture of 2-arylhydrazonopentanals (**2b,d**) or arylhydrazonopropanal (**2f**) (10 mmol) with phenylhydrazine (1.08 g, 10 mmol) was heated in a domestic microwave oven at full power for 10 minutes. The resulting product was collected by filtration, washed with ethanol and crystallized from the proper solvent (mp mixed mp and TLC).

1, 2-Bis-(phenylhydrazono)pentan-3-one (**4a**).

This compound was obtained in 70 % yield, mp 236 ºC; red crystals from ethanol, IR (KBr): ν 3255(NH), 1620 cm^{-1} (CO); ^1H NMR (d_6-DMSO): δ = 1.08 (t, 3H, CH_3), 3.1 (q, 2H, CH_2), 7.1-7.4 (m, 10H, Ar-H), 8.2 (s, 1H, H-1), 10.8 (s, 1H, NH), 13.1 (s, 1H, NH); MS (EI, 70 EV): *m/z* 294(62.9%) (M^+).

Anal. Calcd. for $C_{17}H_{18}N_4O$ (294.36): C, 69.37; H, 6.16; N, 19.03%. (Found: C, 69.41; H, 6.20; N, 19.01.

1-(Phenylhydrazono)-2-(*p*-tolylhydrazono)pentan-3-one (**4b**).

This compound was obtained in 71 % yield by Method A after 60 min. reflux while Method B yielded 89% after heating for 10 min in a domestic microwave oven at full power. Mp 244 ºC; dark orange crystals from ethanol/dioxan (1:1), ^1H NMR (d_6-DMSO): δ = 1.1 (t, 3H, CH_3), 2.3 (s, 3H, CH_3), 2.9 (q, 2H, CH_2), 6.8-7.3 (m, 9H, Ar-H), 8.2 (s, 1H, H-1), 10.7 (s, 1H, NH), 13.1 (s, 1H, NH). MS (EI, 70 EV): *m/z* 308(38.2%) (M^+).

Anal. Calcd. for $C_{18}H_{20}N_4O$ (308.38): C, 70.11; H, 6.54; N, 18.17%. Found: C, 70.00; H, 6.49; N, 17.98.

1-(Phenylhydrazono)-2-(4-nitrophenylhydrazono)pentan-3-one (**4c**).

This compound was obtained in 65 % yield, mp 131 ºC; orange crystals from ethanol, ^1H NMR (d_6-DMSO): δ = 1.2 (t, 3H, CH_3), 2.9 (q, 2H, CH_2), 6.8-7.3 (m, 9H, Ar-H), 8.2 (s, 1H, H-1), 10.7 (s, 1H, NH), 13.2 (s, 1H, NH); MS (EI, 70 EV): *m/z* 339 (M^+).

Anal. Calcd. for $C_{17}H_{17}N_5O_3$ (339.35): C, 60.17; H, 5.05; N, 20.64%. Found: C, 60.25; H, 5.00; N, 20.79.

1-(Phenylhydrazono)-2-(4-methoxyphenylhydrazono)pentan-3-one (**4d**).

This compound was obtained in 70 % yield by Method A, after 60 min. reflux while Method B yielded 90% after heating for 5 min in a domestic microwave oven at full power. Mp 230 ºC; red crystals from ethanol/dioxan (1:1), ^1H NMR (d_6-DMSO): δ = 1.1 (t, 3H, CH_3), 2.9 (q, 2H, CH_2), 3.7 (s, 3H, OCH_3), 6.8-7.3 (m, 9H, Ar-H), 8.2 (s, 1H, H-1), 10.7 (s, 1H, NH), 13.2 (s, 1H, NH); ^{13}C NMR: δ 9.4 (*C*H3), 29.4 (*C*H_2), 56.1 (O*C*H_3), 112.7, 115.8, 116.5, 120.6, 130.1, 132.0, 132.3, 156.4 (phenyl carbon), 136.9 (*C*-1), 144.5 (*C*-2); MS (EI, 70 EV): *m/z* 325 (34.2%) $[M+1]^+$.

Anal. Calcd. for $C_{18}H_{20}N_4O_2$ (324.38): C, 66.65; H, 6.21; N, 17.27%. Found: C, 66.58; H, 6.30; N, 17.32.

1-(4-Acetylphenyl)-2,3-bis-(phenylhydrazono)propan-l-one (**4e**).

This compound was obtained in 69 % yield, mp 239 ºC; orange crystals from ethanol/dioxan (1:1), IR (KBr): ν 3263 (NH), 1620 cm^{-1} (CO); ^1H NMR (d_6-DMSO): δ = 2.6 (s,3H,CH_3), 7-7.4 (m, 14H, Ar-H), 8.4 (s, 1H, H-3), 9.5 (s, 1H, NH), 11.0 (s, 1H, NH); MS (EI, 70 EV): *m/z* 384 (14.2%) (M^+).

Anal. Calcd. for $C_{23}H_{20}N_4O_2$ (384.44): C, 71.86; H, 5.24; N, 14.57%. Found C, 71.80; H, 5.32; N, 14.60.

1-(4-Acetylphenyl)-2-(4-nitrophenylhydrazono)-3-(phenylhydrazono)propan-1-one (**4f**).

This compound was obtained in 71 % yield by Method A, after 60 min. reflux while Method B yielded 82% after heating for 10 min in a domestic microwave oven at full power. Mp 210 ºC; dark red crystals ethanol, ^{1}H NMR (d_6-DMSO): δ = 2.6 (s, 3H, CH_3), 7.1-8.3 (m, 13H, Ar-H), 8.3 (s, 1H, H-3), 11.2 (s, 1H, NH), 13.4 (s, 1H, NH); MS (EI, 70 EV): *m/z* 429 (M^+).

Anal. Calcd. for $C_{23}H_{19}N_5O_4$ (429.43): C, 64.33; H, 4.46; N, 16.31%. Found: C, 64.24; H, 4.42; N, 16.23.

1-(4-Acetylphenyl)-2-(4-methoxyphenylhydrazono)-3-(phenylhydrazono)propan-l-one (**4g**).

This compound was obtained in 70 % yield, mp 175 ºC; red crystals from ethanol/dioxan (1:1), ^{1}H NMR (d_6-DMSO): δ = 2.6 (s, 3H, CH_3), 3.7 (s, 3H, OCH3), 7.01-8.0 (m, 13H, Ar-H), 8.5 (s, 1H, H-3), 9.5 (s, 1H, NH), 11.0 (s, 1H, NH). MS (EI, 70 EV): *m/z* 414 (M^+).

Anal. Calcd. for $C_{24}H_{22}N_4O_3$ (414.46): C, 69.55; H, 5.35; N, 13.52 %. Found: C, 69.72; H, 5.29; N, 13.50.

1-(4-Acetylphenyl)-2-(2-methoxyphenylhydrazono)-3-(phenylhydrazono)propan-l-one (**4h**).

This compound was obtained in 70 % yield, mp 188 ºC; dark orange crystals from ethanol, ^{1}H NMR (d_6-DMSO): δ = 2.6 (s, 3H, CH_3), 4.0 (s, 3H, OCH3), 6.9-8.4 (m, 13H, Ar-H), 8.3(s, 1H, H-3), 10.9 (s, 1H, NH), 13.3 (s, 1H, NH); MS (EI, 70 EV): *m/z* 415 $(M+1)^+$.

Anal. Calcd. for $C_{24}H_{22}N_4O_3$ (414.46): C, 69.55; H, 5.35; N, 13.52 %. Found: C, 69.49; H, 5.25; N, 13.49.

1-Hydrazono-2-(phenylhydrazono)pentan-3-one (**4i**).

This compound was obtained in 77 % yield, mp 101 ºC; orange crystals from ethanol, ^{1}H NMR (d_6-DMSO): δ = 1.07 (t, 3H, CH_3), 2.44 (q, 2H, CH_2), 6.4-7.1 (m, 7H, Ar-H, NH_2), 8.3 (s, 1H, H-1), 12.6 (br s, 1H, NH); MS (EI, 70 EV): *m/z* 218 (M^+).

Anal. Calcd. for $C_{11}H_{14}N_4O$(218.26): C, 60.53; H, 6.47; N, 25.67 %. Found: C, 60.60; H, 6.52; N, 25.58.

1-Hydrazono-2-(4-nitro-phenylhydrazono)pentan-3-one (**4j**).

This compound was obtained in 65 % yield, mp 150 ºC; red crystals from ethanol, ^{1}H NMR (d_6-DMSO): δ = 1.2 (t, 3H, CH_3), 2.42 (q, 2H, CH_2), 6.7-7.9 (m, 7H,Ar-H, NH_2), 8.1 (s, 1H, H-1), 13.6 (br s,1H, NH); MS (EI, 70 EV): *m/z* 263 (M^+).

Anal. Calcd. for $C_{11}H_{13}N_5O_3$ (263.25): C, 50.19; H, 4.98; N, 26.60 %. Found: C, 50.22; H, 5.05; N, 26.65.

Preparation of Pyrazole Derivatives **5a-d**.

General Procedure.

A solution of compounds **4c**,**g**,**i,j** (10 mmol) in pyridine (10 ml) were refluxed for 4-8 hours. The solid products obtained were collected by filtration and crystallized from ethanol to afford **5a-d** respectively.

5-Ethyl-4-(4-nitrophenylazo)-1-phenylpyrazole (**5a**).

This compound was obtained in 70 % yield, mp 153-157 ºC; dark red crystals from ethanol, ^{1}H NMR (d_6-DMSO): δ = 1.3 (t, 3H, CH_3), 3.1 (q, 2H, CH_2), 7.4-7.5 (m, 5H, Ar-H), 7.9 (d, 2H, Ar-H), 8.09 (s, 1H, H-3), 8.3 (d, 2H, Ar-H); MS (EI, 70 EV): *m/z* 321 (M^+).

Anal. Calcd. for $C_{17}H_{15}N_5O_2$ (321.34): C, 63.54; H, 4.70; N, 21.79%. Found: C, 63.47; H, 4.77; N, 21.88.

5-(4-Acetylphenyl)-4-(4-methoxyphenylazo)-1-phenylpyrazole (**5b**).

This compound was obtained in 60 % yield, mp 206 ºC; pale brown crystals from ethanol, IR (KBr): ν 1681 cm^{-1} (CO); ^{1}H NMR (d_6-DMSO): δ = 2.6 (s, 3H, CH_3), 3.7(s, 3H, OCH_3), 6.8-7.9 (m, 13H, Ar-H), 7.5 (s, 1H, H-3); MS (EI, 70 EV): *m/z* 397 $[M+1]^+$.

Anal. Calcd. for $C_{24}H_{20}N_4O_2$ (396.45): C, 72.71; H, 5.08; N, 14.13%. Found: C, 72.66; H, 5.14; N, 14.24.

3-Ethyl-4-(phenylazo)pyrazole (**5c**).

This compound was obtained in 70 % yield, mp 90 ºC; brown crystals from ethanol, IR (KBr): ν 3398 cm^{-1} (NH); ^{1}H NMR (d_6-DMSO): δ = 1.3 (t, 3H, CH_3), 2.99 (q, 2H, CH_2), 7.4-7.7 (m, 5H, Ar-H), 7.75 (s, 1H, H-5), 13.19 (br s, 1H, NH); MS (EI, 70 EV): *m/z* 200 (M^+).

Anal. Calcd. for $C_{11}H_{12}N_4$ (200.24): C, 65.98; H, 6.04; N, 27.98%. Found: C, 66.01; H, 6.09; N, 27.85.

3-Ethyl-4-(4-nitrophenylazo)pyrazole (5d).

This compound was obtained in 75 % yield, mp 115 ºC; dark brown crystals from ethanol, ^{1}H NMR (d_6-DMSO): δ = 1.4 (t, 3H, CH_3), 3.1 (q, 2H, CH_2), 7.4-7.7 (m, 5H, Ar-H), 7.9 (s, 1H, H-5),13.3 (br s,1H, NH); MS (EI, 70 EV): *m/z* 245 (M^+).

Anal. Calcd. for $C_{11}H_{11}N_5O_2$ (245.24): C, 53.87; H, 4.52; N, 28.56%. Found: C, 54.00; H, 4.41; N, 28.44.

Preparation of Compounds **6a-d**.

General Procedures.

Method A, Thermal Reaction.

A warm solution of hydroxylamine hydrochloride (0.69 g, 10 mmol) and sodium carbonate (1.26 g, 12 mmol) in (10 ml) water were added to a stirred solution of the arylhydrazonopentanals (**2a-d**) (10 mmol) in ethanol (4 ml) The reaction mixture was stirred at room temperature for 4 h. The oximes soon separated as semisolid crystals that were solidified by cooling in crushed ice. The solid product, so formed, was collected by filtration and crystallized from the proper solvent.

Method B, Microwave Heating.

A mixture of hydroxylamine hydrochloride (0.69 g, 10 mmol), sodium carbonate (1.26 g, 12 mmol) and arylhydrazonopentanals (**2a,b**) (10 mmol) was placed in the microwave oven and heated for 5 to 10 min at full power. The resulting product was washed with ethanol and crystallized from the proper solvent.

3-Oxo-2-phenylhydrazonopentanal-l-oxime (**6a**).

This compound was obtained in 70 % yield by Method A, after 240 min. reflux while Method B yielded 86% after heating for 10 min in a domestic microwave oven at full power; mp 180 ºC; red crystals from dilute ethanol; IR (KBr): ν 3240 (OH), 3210 cm^{-1} (NH); ^{1}H NMR (d_6-DMSO): δ = 1.06 (t, 3H, CH_3), 2.9 (q, 2H, CH_2), 7.3-7.4 (m, 5H, Ar-H), 8.3 (s, 1H, H-1), 9.92 (s, 1H, NH), 9.99 (s, 1H, oxime-H); MS (EI, 70 EV): *m/z* 219(M^+).

Anal. Calcd. for $C_{11}H_{13}N_3O_2$ (219.24): C, 60.26; H, 5.98; N, 19.17%. Found: C, 60.09; H, 5.99; N, 19.30.

3-Oxo -2-(*p*-tolylhydrazono)pentanal-l-oxime (**6b**).

This compound was obtained in 60 % yield by Method A, after 240 min. reflux while Method B yielded 85% after heating for 5 min in a domestic microwave oven at full power; mp 199 ºC; orange crystals from ethanol; IR (KBr): ν 3385 (OH), 3145 (NH), 1650 cm^{-1} (CO); ^1H NMR (d_6-DMSO): δ = 1.06 (t, 3H, CH_3), 2.3 (s, 3H, CH_3), 2.9 (q, 2H, CH_2), 7.22 (s, 4H, Ar-H), 8.3 (s, 1H, H-1), 11.8 (s, 1H, NH), 12.5 (s, 1H, oxime-H); MS (EI, 70 EV): *m/z* 233(M^+).

Anal. Calcd. for $C_{12}H_{15}N_3O_2$ (233.27): C, 61.79; H, 6.48; N, 18.01%. Found: C, 61.80; H, 6.38; N, 17.89.

2-(4-Nitrophenylhydrazono)-3-oxopentanal-l-oxime (**6c**).

This compound was obtained in 60 % yield, mp 163 ºC; red crystals dilute AcOH, ^1H NMR (d_6-DMSO): δ = 1.07 (t, 3H, CH_3), 2.9 (q, 2H, CH_2), 6.7-7.9 (m, 4H, Ar-H), 8.1 (s, 1H, H-1),10.9 (s, 1H, NH), 11.6 (s, 1H, oxime-H); MS (EI, 70 EV): *m/z* 264(M^+).

Anal. Calcd. for $C_{11}H_{12}N_4O_4$ (264.24): C, 50.00; H, 4.58; N, 21.20%. Found: C, 49.81; H, 4.49; N, 21.00.

2-(4-Methoxyphenylhydrazono)-3-oxopentanal-l-oxime (**6d**).

This compound was obtained in 60 % yield, mp 120 ºC; yellow green crystals from ethanol, ^1H NMR (d_6-DMSO): δ = 1.06 (t, 3H, CH_3),2.9 (q, 2H, CH_2), 3.7 (s, 3H, OCH_3), 6.99 (d, 2H, Ar-H), 7.3 (d, 2H, Ar-H), 8.3 (s, 1H, H-1), 11.8 (s, 1H, NH), 12.5 (s, 1H, oxime-H); MS (EI, 70 EV): *m/z* 249(M^+).

Anal. Calcd. for $C_{12}H_{15}N_3O_3$ (249.27): C, 57.82; H, 6.07; N, 16.86%. Found: C, 57.90; H, 5.97; N, 16.76.

Preparation of Isoxazole Derivatives **7a-d**.

General Procedure.

Each of oximes **6a-d** (10 mmol) was refluxed in acetic anhydride (10 ml) for 4 h, and then left to cool at room temperature. The solid product separated as pale yellow crystals that were collected by filtration and recrystallized from the proper solvent.

5-Ethyl-4-(phenylazo)isoxazole (**7a**).

This compound was obtained in 69 % yield, mp 73 ºC; pale red crystals from AcOH, ^1H NMR (d_6-DMSO): δ = 1.2 (t, 3H, CH_3), 2.4 (q, 2H, CH_2), 7.1-8.3 (m, 5H, Ar-H), 8.12 (s, 1H,isoxazolyl-H); MS (EI, 70 EV): *m/z* 201 (M^+).

Anal. Calcd. for $C_{11}H_{11}N_3O$ (201.23): C, 65.66; H, 5.51; N, 20.88%. Found: C, 65.46; H, 5.53; N, 21.00.

5-Ethyl-4-(4-methylphenylazo)isoxazole (**7b**).

This compound was obtained in 67 % yield, mp 81 ºC; yellow crystals from dilute AcOH, ^1H NMR (d_6-DMSO): δ = 1.13 (t, 3H, CH_3), 2.4 (s,3H,CH_3), 3.1 (q, 2H, CH_2), 7.4 (d, 2H, Ar-H), 7.9 (d, 2H, Ar-H), 8.55 (s, 1H,isoxazolyl H); MS (EI, 70 EV): *m/z* 215 (M^+).

Anal. Calcd. for $C_{12}H_{13}N_3O$ (215.25): C, 66.96; H, 6.09; N, 19.52%. Found: C, 66.76; H, 6.10; N, 19.70.

5-Ethyl-4-(4-nitrophenylazo)isoxazole (**7c**).

This compound was obtained in 75 % yield, mp 131 ºC; dark brown crystals from AcOH, ^1H NMR (d_6-DMSO): δ = 1.15 (t, 3H, CH_3), 3.13 (q, 2H, CH_2), 8.3 (d, 2H, Ar-H), 8.7 (d, 2H, Ar-H), 8.73 (s, 1H, isoxazolyl-H); ^{13}C NMR: δ =8.1 (CH_3), 33.5 (CH_2), 119.6 (*C*-4), 120.6, 126.3, 138.4, 143.3 (phenyl carbon), 147.5 (*C*-3), 148.9 (*C*-5); MS (EI, 70 EV): *m/z* 246 (M^+).

Anal. Calcd. for $C_{11}H_{10}N_4O_3$ (246.22): C, 53.66; H, 4.09; N, 22.75%. Found: C, 53.72; H, 3.99; N, 22.90.

5-Ethyl-4-(4-methoxyphenylazo)isoxazole (**7d**).

This compound was obtained in 72 % yield, mp 95 ºC; pale brown crystals from AcOH, ^1H NMR (d_6-DMSO): δ = 1.2 (t, 3H, CH_3), 2.6 (q, 2H, CH_2), 3.7 (S, 3H, OCH_3), 7.2 (d, 2H, Ar-H), 7.5 (d, 2H, Ar-H), 8.1 (s, 1H,isoxazolyl-H); MS (EI, 70 EV): *m/z* 231 (M^+).

Anal. Calcd. for $C_{12}H_{13}N_3O_2$ (231.25): C, 62.33; H, 5.67; N, 18.17%. Found: C, 62.13; H, 5.76; N, 18.20.

2-[(4-Nitrophenyl)hydrazono]-3-oxo-pentanenitrile (**8**).

Mixture of hydroxylamine hydrochloride (0.69 g, 10 mmol), ammonium acetate (0.77 g, 10 mmol) and arylhydrazonopentanal **2c** (10 mmol) was placed in the microwave oven and heated for 10 min at full power. The resulting product was washed with ethanol and crystallized from ethanol. This compound was obtained in 95 % yield, mp 212 ºC; dark brown crystals from ethanol, ^1H NMR (d_6-DMSO): δ = 1.3 (t, 3H, CH_3), 2.4 (q, 2H, CH_2), 7.5 (d, 2H, Ar-H),7.6 (d, 2H, Ar-H), 11.2 (s,1H,NH); ^{13}C NMR: δ = 8.9 (CH_3), 29.8 (CH_2), 116.9 (*C*N), 115.4, 126.5, 133.7, 143.2 (phenyl carbon), 148.6 (*C*-2), 198.9 (*C*O); MS (EI, 70 EV): *m/z* 247[M+1)]$^+$.

Anal. Calcd. for $C_{11}H_{10}N_4O_3$ (246.22): C, 53.66; H, 4.10; N, 22.75%. Found: C, 53.61; H, 4.00; N, 22.69.

Preparation of Pyrimidine Derivatives **11a-d**, and Pyrimido[1,2-*a*]-benzimidazole Derivatives **14a,b**.

General Procedures.

Method A, Thermal Reaction.

One of the 2-arylhydrazonopentanals **2a,c** (10 mmol) in ethanol (30 ml) was treated with one of the heterocyclic amines **10a-d, 13** (10 mmol). The mixture was heated under reflux for 4-6 h and allowed to cool at room temperature. The solid product was collected by filtration and crystallized from the proper solvent.

Method B, Microwave Heating.

A mixture of arylhydrazonopentanal **2a** (10 mmol) with one of the heterocyclic amines **10a**, **13** (10 mmol) was placed in the microwave oven and heated for 2 min at full power. The resulting product was washed with ethanol and crystallized from the proper solvent.

7-Ethyl-6-phenylazo-1,2,4-triazolo[1,5-*a*]pyrimidine (**11a**).

From a mixture of **2a** and **10a** after 360 min by Method A, reflux yielded 65% while Method B yielded 97% after heating for 2 min in a domestic microwave oven; mp 149 ºC; orange crystals from ethanol, ^1H NMR (d_6-DMSO): δ = 1.4 (t, 3H, CH_3), 3.7 (q, 2H, CH_2), 7.6-7.9 (m, 5H, Ar-H), 8.8 (s, 1H, H-2), 9.2 (s, 1H, H-5); MS (EI, 70 EV): *m/z* 252 (M^+).

Anal. Calcd. for $C_{13}H_{12}N_6$ (252.28): C, 61.89; H, 4.79; N, 33.31%. Found: C, 61.79; H, 4.81; N, 33.41.

2-Phenyl-6-phenylazo-7-ethylpyrazolol[1,5-*a*]pyrimidine (**11b**).

From a mixture of **2a** and **10b** after 360 min. reflux by Method A yielded 79% while Method B yielded 99% after heating for 2 min in domestic microwave oven. Mp 182 ºC; orange crystals from ethanol, ^1H NMR (d_6-DMSO): δ = 1.4 (t, 3H, CH_3), 3.8 (q, 2H, CH_2), 7.3 (s, 1H, H-3), 7.3-7.4 (m, 10H, Ar-H), 8.9 (s, 1H, H-5); MS (EI, 70 EV): *m/z* 327 (M^+).

Anal. Calcd. for $C_{20}H_{17}N_5$ (327.39): C, 73.37; H, 5.23; N, 21.39%. Found: C, 73.19; H, 5.31; N, 21.20.

2-(4-Chlorophenyl)-6-(4-nitrophenylazo)-7-ethylpyrazolol[1,5-*a*]pyrimidine (**11c**).

This compound was obtained in 80 % yield, from a mixture of **2c** and **10c**, after 4-6 h reflux; mp >300 ºC; dark red crystals from ethanol/DMF (2:1), ^{1}H NMR (d_6-DMSO): δ = 1.2 (t, 3H, CH_3), 2.59 (q, 2H, CH_2),6.5 (s, 1H, H-3), 7.3-8.5 (m, 8H, Ar-H), 9.3 (s, 1H, H-5); MS (EI, 70 EV): *m/z* 406 (M^+).

Anal. Calcd. for $C_{20}H_{15}ClN_6O_2$ (406.83): C, 59.05; H, 3.72; N, 20.66%. Found: C, 59.20; H, 3.69; N, 20.74.

2-Phenyl-3-bromo-6-(4-nitrophenylazo)-7-ethylpyrazolol[1,5-*a*]-pyrimidine (**11d**).

This compound was obtained in 85 % yield, from a mixture of **2c** and **10d** after 4-6 h reflux; mp 194 ºC; dark brown crystals from ethanol, ^{1}H NMR (d_6-DMSO): δ = 1.2 (t, 3H, CH_3), 2.5 (q, 2H, CH_2), 7.3-8.2 (m, 9H, Ar-H), 9.26 (s, 1H, H-5); MS (EI, 70 EV): *m/z* 453 $[M+2]^+$.

Anal. Calcd. for $C_{20}H_{15}BrN_6O_2$ (451.28): C, 53.23; H, 3.35; N, 18.62%. Found: C, 53.16; H, 3.45 N, 18.53.

3-Phenylazo-4-ethylpyrimido[1,2-*a*]benzimidazole (**14a**).

This compound was obtained in 60 % yield by Method A, after 360 min. reflux from a mixture of **2a** and **13**, while Method B yielded 95% after heating for 2 min in a domestic microwave oven at full power; mp 231 ºC; brown crystals from methanol, ^{1}H NMR (d_6-DMSO): δ = 1.2 (t, 3H, CH_3), 2.6 (q, 2H, CH_2), 7.2-7.7 (m, 9H, Ar-H), 9.2 (s, 1H, H-2); MS (EI, 70 EV): *m/z* 301 (M^+).

Anal. Calcd. for $C_{18}H_{15}N_5$ (301.35): C, 71.74; H, 5.02; N, 23.24%. Found: C, 71.87; H, 4.99; N, 23.05.

3-(4-Nitrophenylazo-4-ethylpyrimido[1,2-*a*]benzimidazole (**14b**).

This compound was obtained in 72 % yield, from a mixture of **2c** and **13** after reflux for 360 min. mp 185 ºC; brown crystals from ethanol, ^{1}H NMR (d_6-DMSO): δ = 1.2 (t, 3H, CH_3), 2.6 (q, 2H, CH_2), 7.4 (d, 2H, Ar-H), 7.7 (d, 2H, Ar-H), 8.2-8.3 (m, 4H, Ar-H), 9.3 (s, 1H, H-2); MS (EI, 70 EV): *m/z* 346 (M^+).

Anal. Calcd. for $C_{18}H_{14}N_6O_2$ (346.35): C, 62.42; H, 4.07; N, 24.26%. Found: C, 62.33; H, 3.99; N, 24.30.

Ethyl-2-(4-nitrophenyl)-3oxo-6-propionyl-2,3-dihydropyridazine-4-carboxylate (**16**).

To a solution of 3-oxo-2-(4-nitrophenylhydrazono)pentanal (**2c**) (10 mmol) in ethanol (30 ml), diethylmalonate (1.6 g, 10 mmol) and piperidine (12 mmol) was added. The mixture was refluxed for 6 h, then left to cool at room temperature. The solid product, so formed, was collected by filtration and recrystallized from ethanol. This compound was obtained in 85 % yield, mp 106 ºC; dark red crystals from dilute ethanol, ^{1}H NMR (d_6-DMSO): δ = 1.07 (t, 3H, CH_3), 1.4 (t, 3H, CH_3), 2.4 (q, 2H, CH_2), 4.2 (q, 2H, CH_2), 7.3 (s, 1H, H-5), 7.9-8.1 (m, 4H, Ar-H); MS (EI, 70 EV): *m/z* 346 $(M+1)^+$.

Anal. Calcd. for $C_{16}H_{15}N_3O_6$ (345.31): C, 55.65; H, 4.38; N, 12.17%. Found: C, 55.56; H, 4.29; N, 12.21.

Preparation of 2,3-Dihydropyridazines Derivatives **18a-g**.

General Procedure.

To a magnetically stirred solution of Ph_3P (2.6 g, 10 mmol) and each of 2-arylhydrazonopentanals (**2a-d**) or 2-arylhydrazonopropanals (**2e-g**) (10 mmol) in (CH_2Cl_2) (10 ml) was added drop wise a solution of dimethyl acetylenedicarboxylate (1.4 g, 10 mmol). The mixture was left at room temperature overnight, and then treated with ethanol and the solid product was collected by filtration and crystallized from the proper solvent.

Dimethyl-2-phenyl-6-propionyl-2, 3-dihydropyridazine-3,4-dicarboxylate (**18a**).

This compound was obtained in 92 % yield, mp 114 ºC; red crystals from methanol/ethanol, IR (KBr): ν 1744, 1716 (CO ester), 1618 cm^{-1} (CO); ^{1}H NMR (d_6-DMSO): δ = 1.1 (t, 3H, CH_3), 2.8 (q, 2H, CH_2), 3.6 (s, 3H, OCH_3), 3.8 (s, 3H, OCH_3), 6.1 (s, 1H, NCH), 7.4 (s, 1H, H-5), 7.2-7.6 (m, 5H, Ar-H); MS (EI, 70 EV): *m/z* 271(M^+-59).

Anal. Calcd. for $C_{17}H_{18}N_2O_5$ (330.34): C, 61.81; H, 5.49; N, 8.48%. Found: C, 61.93; H, 5.45; N, 8.35.

Dimethyl-2-*p*-tolyl-6-propionyl-2,3-dihydropyridazine-3,4-dicarboxylate (**18b**).

This compound was obtained in 81 % yield, mp 258 ºC; red crystals from ethanol, ^{1}H NMR (d_6-DMSO): δ = 1.07 (t, 3H, CH_3), 2.3 (s, 3H, CH_3), 2.4 (q, 2H, CH_2), 3.67 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 6.2 (s,1H, NCH), 6.3-6.8 (m, 4H, Ar-H), 7.5 (s, 1H, H-5); MS (EI, 70 EV): *m/z* 344 (M^+).

Anal. Calcd. for $C_{18}H_{20}N_2O_5$ (344.36): C, 62.78; H, 5.85; N, 8.13%. Found: C, 62.59; H, 5.76; N, 8.33.

Dimethyl-2(4-nitrophenyl)-6-propionyl-2,3-dihydropyridazine-3,4-dicarboxylate (**18c**).

This compound was obtained in 95 % yield, mp 211 ºC; red crystals from methanol, ^{1}H NMR (d_6-DMSO): δ = 1.07 (t, 3H, CH_3), 2.4 (q, 2H, CH_2), 3.6 (s, 3H, OCH_3), 3.7 (s, 3H, OCH_3), 6.2 (s, 1H, NCH), 7.4 (s, 1H, H-5), 6.7-7.9 (m, 4H, Ar-H); MS (EI, 70 EV): *m/z* 375(M^+).

Anal. Calcd. for $C_{17}H_{17}N_3O_7$ (375.33): C, 54.40; H, 4.57; N, 11.20%. Found: C, 54.21; H, 4.66; N, 11.30.

Dimethyl-2-(4-methoxyphenyl)-6-propionyl-2,3-dihydropyridazine-3,4-dicarboxylate (**18d**).

This compound was obtained in 90 % yield, mp 113 ºC; red crystals from ethanol, ^{1}H NMR (d_6-DMSO): δ = 1.18 (t, 3H, CH_3), 2.9 (q, 2H, CH_2), 3.7 (s, 3H, OCH_3), 3.8 (s, 3H, OCH_3), 6.05 (s, 1H, NCH), 7.6 (s, 1H, H-5), 6.9-7.4 (m, 4H, Ar-H); MS (EI, 70 EV): *m/z* 361 $[M+1]^+$.

Anal. Calcd. for $C_{18}H_{20}N_2O_6$ (360.36): C, 59.99; H, 5.59; N, 7.77%. Found: C, 60.10; H, 5.49; N, 7.95.

Dimethyl-6-(4-acetylbenzoyl)-2-phenyl-2,3-dihydropyridazine-3,4-dicarboxylate (**18e**).

This compound was obtained in 82 % yield, mp 165 ºC; red crystals from dioxan, IR (KBr): ν 1744, 1715(CO ester), 1615 cm^{-1} (CO); ^{1}H NMR (d_6-DMSO): δ = 2.6 (s, 3H, CH_3), 3.6 (s, 3H, OCH_3), 3.7 (s,3H, OCH_3), 6.2 (s, 1H, NCH), 6.4-7.9 (m, 9H, Ar-H), 8.11 (s, 1H, H-5); MS (EI, 70 EV): *m/z* 420 (M^+).

Anal. Calcd. for $C_{23}H_{20}N_2O_6$ (420.42): C, 65.71; H, 4.79; N, 6.66%. Found: C, 65.70; H, 4.71; N, 6.56.

Dimethyl-6-(4-acetylbenzoyl)-2-(4-nitrophenyl)-2,3-dihydropyridazine-3,4-dicarboxylate (**18f**).

This compound was obtained in 82 % yield, mp 170 ºC; red crystals from methanol, ^{1}H NMR (d_6-DMSO): δ = 2.6 (s, 3H,

CH_3), 3.6 (s, 3H, OCH_3), 3.7 (s, 3H, OCH_3), 6.2 (s, 1H, NCH), 6.6-8.05 (m, 8H, Ar-H), 8.11 (s, 1H, H-5); MS (EI, 70 EV): *m/z* 466 $[M+1]^+$.

Anal. Calcd. for $C_{23}H_{19}N_3O_8$ (465.42): C, 59.36; H, 4.11; N, 9.03%. Found: C, 59.54; H, 4.08; N, 8.89.

Dimethyl-6-(4-acetylbenzoyl)-2-(4-methoxyphenyl)2,3-dihydropyridazine-3,4-dicarboxylate (**18g**).

This compound was obtained in 79 % yield, mp 147 ºC; dark red crystals from dilute methanol, ^1H NMR (d_6-DMSO): δ = 2.6 (s, 3H, CH_3), 3.6 (s, 3H, OCH_3), 3.71 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 6.2(s, 1H, NCH), 6.9 (d, 2H, Ar-H), 7.5 (d, 2H, Ar-H), 7.6 (s, 1H, H-5), 7.9 (d, 2H, Ar-H), 8.1 (d, 2H, Ar-H); MS (EI, 70 EV): *m/z* 450 (M^+).

Anal. Calcd. for $C_{24}H_{21}N_2O_7$ (449.44): C, 64.14; H, 4.71; N, 6.23 %. Found: C, 63.99; H, 4.69; N, 6.31.

8-Hydrazino-1-phenyl-3-propionyl-6,8a-dihydro-1*H*-pyridazino[4,5-*c*]pyridazin-5-one (**22**).

A mixture of compound **18a** (10 mmol) in EtOH (30 ml) was treated with hydrazine hydrate (20 mmol). The mixture was heated under reflux for 1 h and allowed to cool to r.t. The solid product was collected by filtration and crystallized from EtOH. This compound was obtained in 90 % yield, mp 177 ºC; pale yellow crystals from ethanol/dioxan (1:1), IR (KBr): ν 3420, 3330, 2918 (NH, NH_2), 1679 (ring CO), 1614 cm^{-1} (CO); ^1H NMR (d_6-DMSO): δ = 1.06 (t, 3H, CH_3), 2.4 (q, 2H, CH_2), 5.7 (s, 1H, NCH), 6.7 (s, 1H, H-4), 7-7.4 (m, 7H, Ar-H, NH_2), 9.2 (br s, 1H, NH), 9.9 (br s, 1H, NH); MS (EI, 70 EV): *m/z* 312(M^+).

Anal. Calcd. for $C_{15}H_{16}N_6O_2$ (312.33): C, 57.68; H, 5.16; N, 26.91%. Found: C, 57.62; H, 5.10; N, 26.85.

REFERENCES AND NOTES

[1] F. Al-Omran, M. M. Abdel-Khalik, A. Abuel-Khair and M. H. Elnagdi, *OPPI*, **29**(3) 285 (1997).

[2] K. M. Al-Zaydi, E. A. Hafez, and M. H. Elnagdi, *J. Chem. Research (S)*, 154 (2000); (M) 510 (2000).

[3] H. Bahbehani, M. M. Abdel-Khalik, and M. H. Elnagdi, *OPPI*, **31**, 551 (1999).

[4] M. M. Abdel-Khalik, S. M. Agamy and M. H. Elnagdi. *Synthesis,* 1861 (2001).

[5] N. A. Al-Awadi, M. H. Elnagdi, Y. A. Ibrahim, K. Kaul and A. Kumar; *Tetrahedron*, **57**, 1609 (2001).

[6] A. S. Matlack in "Introduction to Green Chemistry" Marcel Dekker Inc., New York, Basel, (2001).

[7] J. Clark and D. MacQuarrie in "Handbook of Green Chemistry and Technology" Blackwell Science Ltd., Paris, (2002).

[8] M. M. Abdel-Khalik, S. M. Agamy and M. H. Elnagdi. *Z. Naturforsch.,* **55b**, 1211 (2000).

[9] A. A. Elassar and A. A. Elkhair, *Tetrahedron*, **59**, 8463 (2003).

[10] A. Almazroa, M. H. Elnagdi, and A .M. SalahEl-Din *J. Heterocyclic Chem.,* **41**, 267 (2004).

[11] M. A. Al-Shiekh, A. M. Salah El-Din, E. A. Hafez, and M. H. Elnagdi, *J. Chem. Research* **3**, 174 (2004).