

2-Arylhydrazonopropanals as Building Blocks in Heterocyclic Chemistry: Microwave Assisted Condensation of 2-Arylhydrazonopropanals with Amines and Active Methylene Reagents

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Received: 25 July 2003; in revised form: 22 December 2003 / Accepted: 23 December 2003 / Published: 31 December 2003

Abstract: Utilization of 2-arylhydrazonopropanals for the synthesis of 2-arylhydrazonoimino propanones, 1,2,4-triazolo[4,3-a]pyrimidines, pyridopyridazine hydrazones, 3-oxaloalkanonitriles and 1,2,3-triazole derivatives by conventional heating and under microwave irradiation is described. Structural assignments are based on spectroscopic data and confirmed in some cases by X-ray crystallography.

Keywords: 2-Arylhydrazonopropanals, heterocyclic amines, active methylene compounds, microwave irradiation, X-ray structures.

Introduction

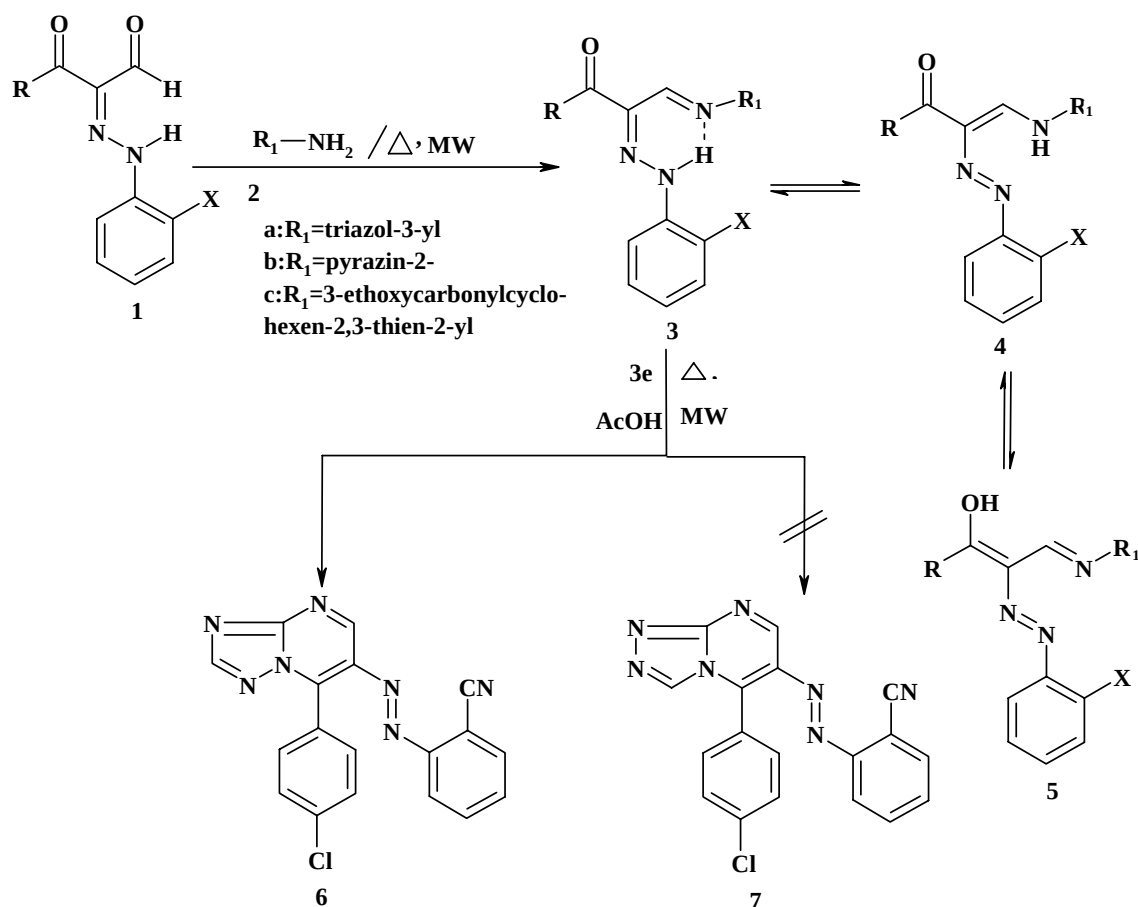
The utility of microwaves in heterocyclic synthesis is now receiving considerable attention [1-4] and enaminones have also been recently extensively utilized as precursors for the synthesis of heteroaromatics. As a part of an ongoing project, aiming to explore potential utility of microwaves as

an energy source for heterocyclic synthesis, we report here on synthesis of iminoarylhydrazonopropanone, azolopyrimidine and 3-oxaloalkanonitrile derivatives of potential interest as pharmaceuticals and photochromic dyes [5-7], and then we investigate the possibility of conducting these reactions under microwave irradiation in addition to the standard thermal conditions.

Results and Discussion

The chemistry of 2-arylhydrazonopropanals has received considerable interest in the last few years [7-14]. As part of an ongoing project in our laboratory aimed at exploring the potential utility of microwave irradiation as a source of heat for producing polyfunctionally substituted heteroaromatics, we report here on reactivity of compounds **1a-f** toward amines and some active methylene nitriles in the absence of solvent under MW irradiation in a domestic microwave oven. The yield of products obtained under the microwave heating technique (MW) and the time taken for complete the reaction are compared with those obtained by conventional heating (Δ). Thus, **1a-f** were heated with a variety of heterocyclic amines **2a-c**, hydrazine **7a** and phenylhydrazine **7b** with both conventional heating (Δ) and in a microwave oven yielding the corresponding condensation products **3a-f**, **8a-d** (Scheme 1)

Scheme 1

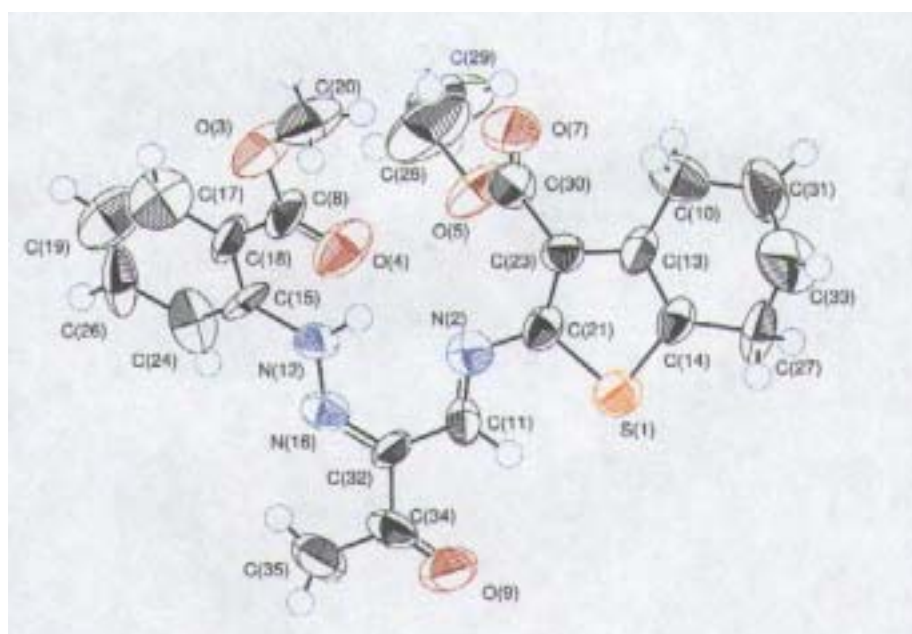


1, 3	R ₁	R	X	1, 3	R ₁	R	X
a		2-furyl	CN	e	Triazol-3-yl	C ₆ H ₄ -Cl- <i>p</i>	CN
b		CH ₃	CO ₂ Me	f	Pyrazin-2-yl	2-furyl	CO ₂ Me
c		C ₆ H ₄ -Cl- <i>p</i>	CO ₂ Me	g	Pyrazin-2-yl	C ₆ H ₄ -Cl- <i>p</i>	CN
d	Triazol-3-yl	2-furyl	CO ₂ Me				

It is noteworthy that the microwave reactions were brought to completion in a very short time compared to conventional heating. Several tautomeric forms (cf. **4**, **5**), seemed possible for the condensation products **3a-f**. An X-ray diffraction single crystal structure [15] of a representative example of the reaction products with both amines (**3b**) and with hydrazines (**8d**), established that they exist in the hydrazone form (Figures 1, 2). Compound **3b** (Figure 1) is fixed in a sterically crowded configuration to permit efficient hydrogen bonding.

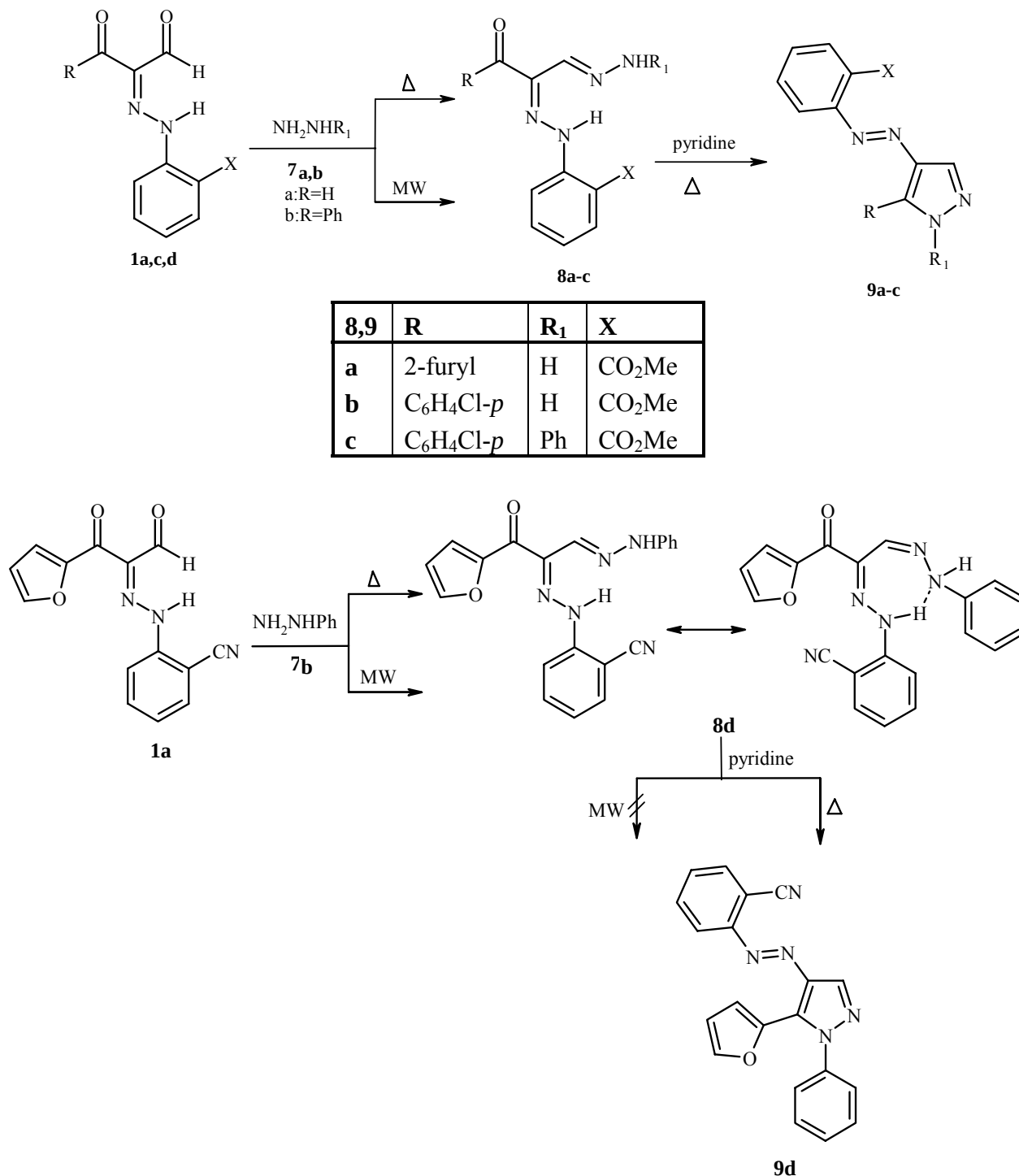
Refluxing **3e** in AcOH afforded a product that may be formulated as **6** or its isomer **7**. ¹H-NMR indicated the presence of single triazole signal at $\delta = 9.1$ ppm shifted to lower field by almost $\delta = 1.0$ ppm compared to the single triazole signal in the parent aminotriazole. Consequently the 1,2,4-triazolo[4,3-a]pyrimidine structure **6** was assigned to this reaction product (Scheme 1).

Figure 1. X-ray structure of compound **3b**.

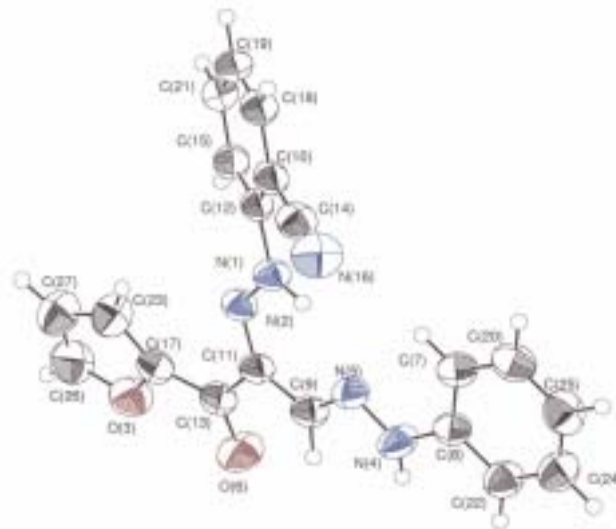
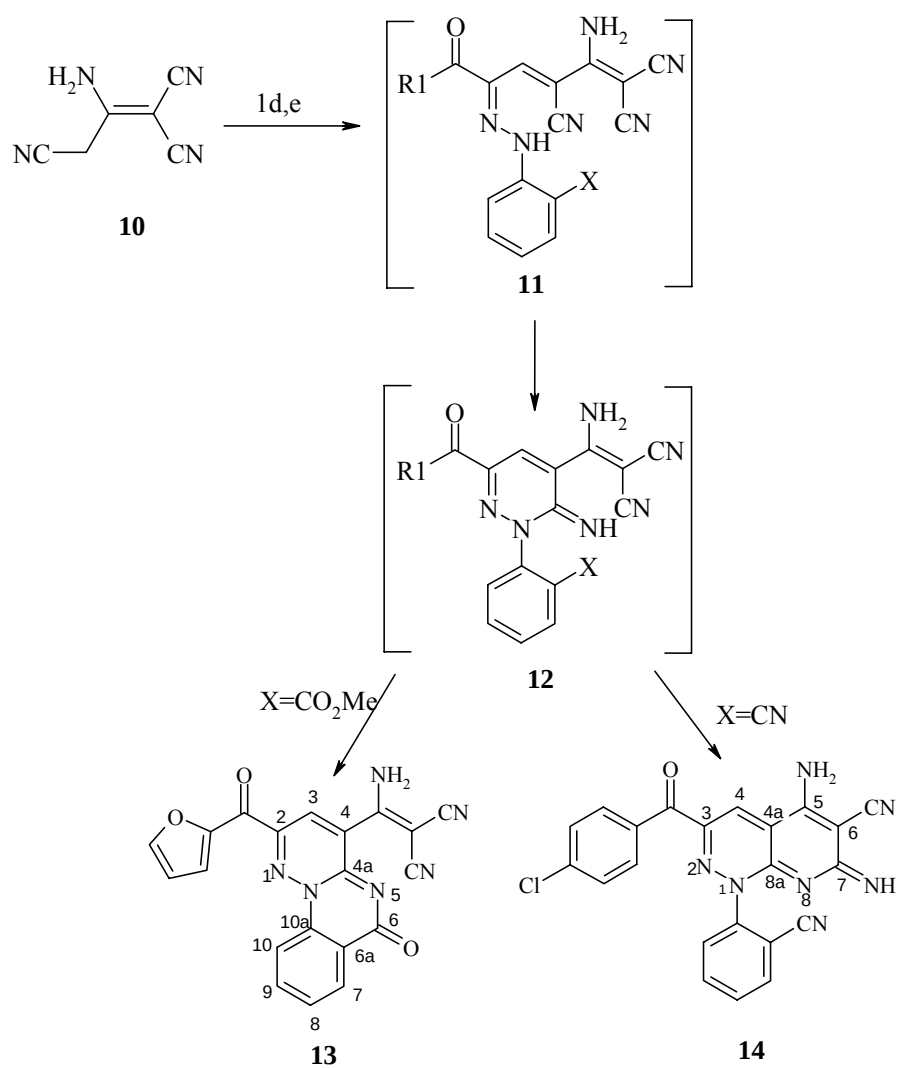


Reaction of **1a,c,d,e** with hydrazine hydrate **7a** and phenylhydrazine **7b** afforded **8a-d** both by conventional heating (Δ) and MW irradiation. On treatment of **8a-d** with pyridine using both conventional heating (Δ) and MW irradiation, **9a-d** were only obtained by conventional heating (Δ) and not by MW irradiation under a variety of conditions (Scheme 2).

Scheme 2

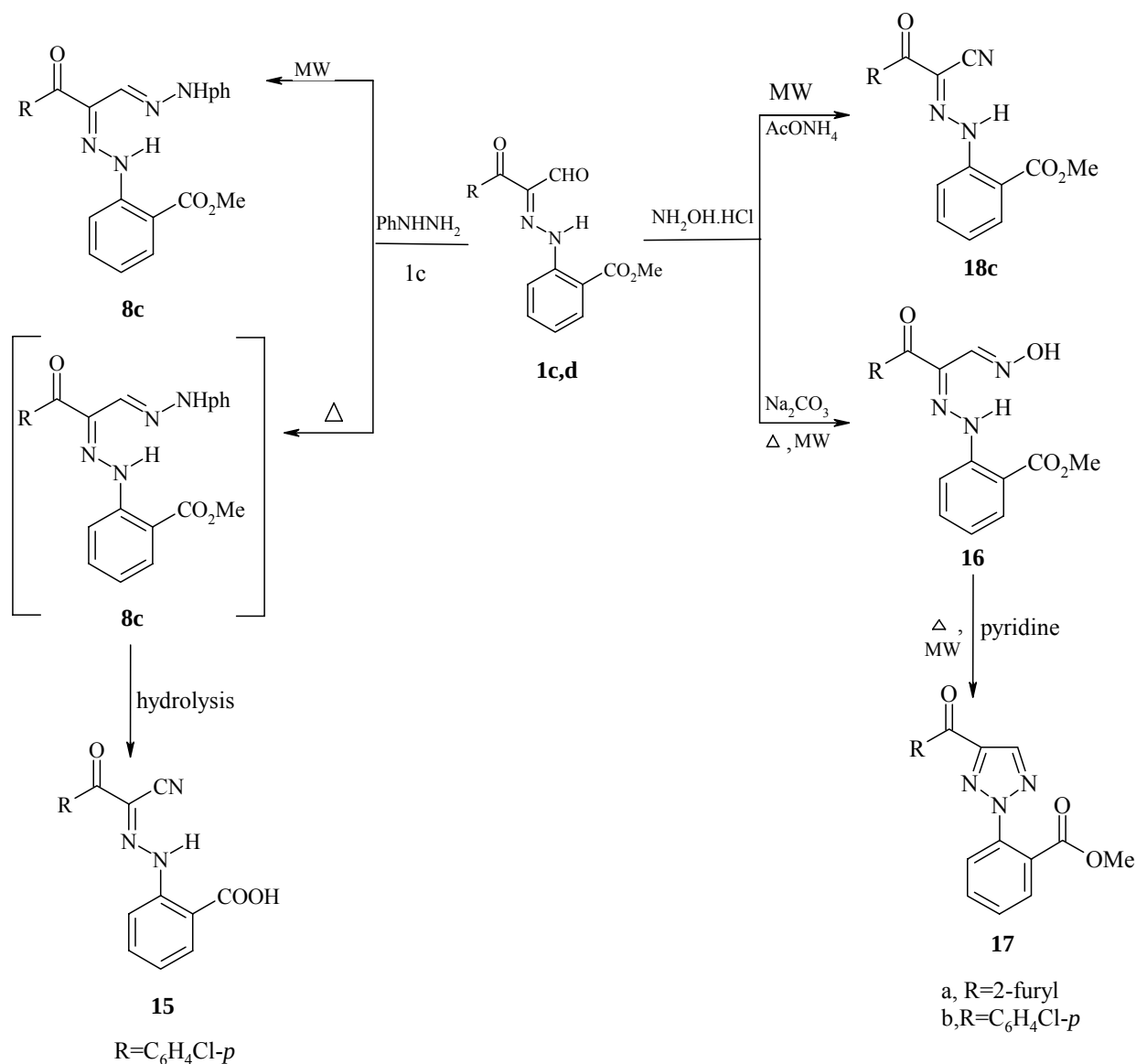


Product **8d** was recrystallized and its structure was solved by X-ray diffraction (Figure 2).

Figure 2: Molecular structure of **8d** with the atom labeling scheme.**Scheme 3**

The reaction of **1a** and **1c** with 2-amino-1,1,3-tricyanopropene (**10**) yielded the products of condensation, pyridopyridazines **13** and **14** respectively (Scheme 3). Structures **13**, **14** were established based on spectral data (IR, ^{13}C -NMR). Formation of **13**, **14** are assumed to proceed *via* intermediates **11** and **12**. Similar reactions under microwave irradiation were unsuccessful. Treatment of **1c** with phenylhydrazine by conventional heating (Δ) afforded the oxoalkanonitrile **15** most likely *via* hydrolysis of the formed phenylhydrazone intermediate **8c**, while **8c** could be also obtained *via* treatment of **1** with phenylhydrazine under MW irradiation.

Scheme 4



Reaction of **1c,d** with hydroxylamine hydrochloride in the presence of sodium carbonate under MW irradiation and conventional heating (Δ) afforded the oxime **16**, which converted into the triazole **17** on refluxing in pyridine, while reaction of **1** with hydroxylamine hydrochloride in the presence of

ammonium acetate under MW irradiation only resulted in the formation of the oxoalkanonitrile **18**. In a previous paper it was reported that treatment of 2-arylhydrazonopropanals with hydroxylamine hydrochloride by conventional heating (Δ) afforded the 3-oxoalkanonitrile [16] (Scheme 4).

Experimental

General

Melting points were measured on a Gallenkamp Electrothermal melting point apparatus and are uncorrected. The IR spectra were measured on a Nicolet Magna 520 FT IR Spectrophotometer. ^1H -NMR and ^{13}C -NMR spectra were recorded in deuterated dimethylsulfoxide (DMSO-d_6) or deuterated chloroform (CDCl_3) at 200 MHz on a Varian Gemini NMR spectrometer and a Bruker DPX 400 MHz 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. Microwave irradiation was carried out using a commercial microwave oven (SGO 390 W). Elemental analyses were carried out at the Microanalytical Center at Cairo University. All X-ray diffraction diagrams and calculations were performed using Maxus (Bruker Nonius, Delft & Macscience, Japan).

General Procedure for the Preparation of **1a-i** [8]:

A cold solution of aryldiazonium salt (0.1 mol) was prepared by adding a solution of NaNO_2 (1.5 g in 10 mL H_2O) to a cold solution of aryl amine (0.1 mol) in concentrated HCl (5 mL) with stirring as described earlier. The resulting solution of the aryldiazonium salt was then added to a cold solution of enaminones **2** in EtOH (50 mL) containing sodium acetate (0.1 mol). The mixture was stirred at r.t for 1h and the solid product formed was collected by filtration and crystallized from ethanol.

3-(4-Chlorophenyl)-2-(2-methoxycarbonylphenylhydrazono)-3-oxopropanal (1c): Yellow crystals from ethanol; m.p. 189°C ; yield 80%; IR (shows complex spectra due to H-bond between O and NH): 3022 (CH aromatic), 1711 ($\text{C}=\text{O}$ ester), 1650 ($\text{C}=\text{O}$ aldehyde), 1638 ($\text{C}=\text{O}$ ketone) and 1586 ($\text{C}=\text{N}$) cm^{-1} ; ^1H -NMR: δ = 4.05 (s, 3H, CH_3), 7.20-8.09 (m, 8H, Ar-H), 10.25 (s, 1H, CHO) and 15.69 (s, 1H, disappeared after D_2O exchange, NH) ppm; ^{13}C -NMR: δ = 52.90 (COOCH_3), 116.19, 116.40, 118.98, 128.36, 133.33, 138.75 ($\text{C}_6\text{H}_4\text{-CO}_2\text{M-o}$), 124.98, 131.59, 131.89, 134.74, 135.50 ($\text{C}_6\text{H}_4\text{-Cl-p}$), 143.54 ($\text{C}=\text{N-N}$), 166.87 (COOCH_3), 188.23 ($\text{C}=\text{O}$) and 190.49 (CHO) ppm; MS: M^+ (344); Anal. Calcd. for $\text{C}_{17}\text{H}_{13}\text{N}_2\text{O}_4\text{Cl}$ (344.76): C, 59.23; H, 3.80; N, 8.13; Found: C, 59.33; H, 3.82; N, 8.15.

General Procedure for the Preparation of **3a-g**:

Method A: A mixture of compounds **1a-e** (0.1 mol) and amines (0.1 mol) was refluxed in ethanol or dioxane (30 mL) for 2h, left to cool to room temperature and the solid was collected and crystallized from ethanol.

Method B: A mixture of compounds **1a-e** (0.1 mol) and amine (0.1 mol) and drops of ethanol were placed in the microwave oven and irradiated at 390 w for 5-15 min, left to cool to room temperature and the solid was collected and crystallized from ethanol.

2-{2-[(2-Cyanophenyl)-hydrazono]-3-furan-2-yl-3-oxo-propylideneamino}-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylic acid ethyl ester (3a**):** Dark red crystals from ethanol; m.p. 174°C; yield 93% (method A), 95% (method B); IR: 3120 (NH), 3030 (CH aromatic), 2932 (CH aliphatic), 2224 (CN), 1698 (C=O ester) and 1619 (C=O ketone) cm^{-1} ; $^1\text{H-NMR}$: δ = 1.30 (t, 3H, CH_3CH_2), 1.79, 2.79 (m, 8H, cyclohexene), 4.32 (q, 2H, CH_2CH_3), 6.57 (m, 1H, furyl H-4), 7.59, 7.76 (m, 2H, furyl H-3, H-5), 7.22, 7.63 (m, 4H, Ar-H), 8.69 (s, 1H, CH, olefinic) and 14.99 (s, 1H, NH) ppm; $^{13}\text{C-NMR}$: δ = 14.25 ($\text{CH}_3\text{CH}_2\text{O}$), 22.60, 22.86, 25.71, 26.53 (cyclohexene carbons), 60.71 ($\text{CH}_3\text{CH}_2\text{O}$), 116.81 (CN), 102.51, 125.06, 146.92, 147.05 (thienyl carbons), 122.23, 122.27, 148.32 (furyl carbons), 118.82, 124.84, 133.36, 133.82, 133.95, 135.99 ($\text{C}_6\text{H}_4\text{CN-o}$), 150.60 (C=N-N), 152.93 (HC=N), 163.39 ($\text{CO}_2\text{CH}_2\text{CH}_3$) and 177.21 (C=O) ppm; MS: M^+ (474); Anal. Calcd. for $\text{C}_{25}\text{H}_{22}\text{N}_4\text{O}_4\text{S}$ (474.54): C, 63.28; H, 4.67; N, 11.81; Found: C, 63.38; H, 4.60; N 11.89.

2-{2-[(2-Methoxycarbonyl-phenyl)-hydrazono]-3-oxo-butylideneamino}-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylic acid ethyl ester (3b**):** Dark orange crystals from ethanol; m.p. 181°C; yield 90% (method A), 99% (method B); IR: 2944 (CH aliphatic), 1695 (C=O ester) and 1600 (C=O ketone), 1508 (C=N) cm^{-1} ; $^1\text{H-NMR}$: δ = 1.07 (t, 3H, CH_3CH_2), 1.81, 2.75 (m, 8H, cyclohexene-H), 2.55 (s, 3H, CH_3), 3.85 (s, 3H, CH_3O), 4.03 (q, 2H, CH_2CH_3), 7.13-8.02 (m, 4H, Ar-H), 8.69 (s, 1H, CH olefinic) and 15.58 (s, 1H, NH) ppm; $^{13}\text{C-NMR}$: δ = 13.96 ($\text{CH}_3\text{CH}_2\text{O}$), 22.56 (CH_3CO), 23.04, 24.90, 25.51, 25.86 (cyclohexene carbons), 52.58 (COOCH_3), 116.16, 116.74, 123.63, 124.83, 131.38, 132.53 ($\text{C}_6\text{H}_4\text{CO}_2\text{Me-o}$), 134.22, 136.28, 144.52, 149.62 (thienyl carbons), 149.64 (C=N-N), 153.85 (HC=N), 163.89 ($\text{CO}_2\text{CH}_2\text{CH}_3$), 166.50 (COOCH_3) and 197.55 (C=O) ppm; MS: M^+ (455); Anal. Calcd. for $\text{C}_{23}\text{H}_{25}\text{N}_3\text{O}_5\text{S}$ (455.54): C, 60.64; H, 5.53, N, 9.22; Found: C, 60.70; H, 5.59, N, 9.15.

2-{3-(4-Chlorophenyl)-2-[(2-cyanophenyl)-hydrazono]-3-oxo-propylideneamino}-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylic acid ethyl ester (3c**):** Orange crystals from ethanol/dioxane (2:1); m.p. 189°C; yield 70% (method A), 98% (method B); IR: 3394(NH), 3000(CH aromatic), 2941(CH aliphatic), 1707 (ester C=O) and 1635 (ketone C=O) cm^{-1} ; MS: M^+ (551); Anal. Calcd. for $\text{C}_{28}\text{H}_{26}\text{N}_3\text{O}_5\text{ClS}$ (552.05): C, 60.92; H, 4.75; N, 7.61; Found: C, 60.87; H, 4.79; N, 7.70.

2(N' -{2-Furan-2-yl)-2-oxo-1-[(4H-[1,2,4]triazol-3-ylimino)-methyl]-ethylidene}-hydrazino)benzoic acid methyl ester (3d**):** Brown crystals from ethanol/dioxane; m.p. 260°C; yield 30% (method A), 40% (method B); IR (shows complex spectra due to H-bond between O in carbonyl ester group and NH hydrazone): 3490 (NH triazole), 3110 (CH aromatic), 2998 (CH aliphatic), 1697 (shows weak C=O ester), 1611(C=O ketone) and 1499 (N=N) cm^{-1} ; $^1\text{H-NMR}$ ($\text{d}_6\text{-DMSO}$) δ = 4.04 (s, 3H, CH_3O), 6.80 (m, 1H, furyl H-4), 7.3, 7.7 (m, 2H, Ar H-4, H-5), 7.5, 7.9 (d, 2H, furyl H-3, H-5), 8.02, 8.04 (d, 2H, Ar H-3, H-6), 8.12 (s, 1H, CH olefinic), 8.54 (s, 1H, 1,2,4-triazole NH), 9.35 (s, 1H, 1,2,4-triazole H-5) and

15.26 (s, 1H, NH hydrazone) ppm; ^{13}C -NMR: δ = 53.59 (COOCH_3), 113.25, 122.62, 148.58, 150.63 (furyl carbons), 116.90, 117.18, 124.86, 131.98, 133.96, 135.41 ($\text{C}_6\text{H}_4\text{-CO}_2\text{Me-o}$), 143.80 (C=N-N), 147.5 (1,2,4-triazole carbons), 155.64 (N=CH-C), 166.45 (COOCH_3) and 177.64 (C=O) ppm; MS: M^+ (366) Anal. Calcd. for $\text{C}_{17}\text{H}_{14}\text{N}_6\text{O}_4$ (366.34): C, 55.74; H, 3.85; N, 22.94; Found: C, 55.80; H, 3.89; N, 22.99.

2(*N'*-[2-(4-Chlorophenyl)-2-oxo-1-[(4H-[1,2,4]triazol-3-ylimino)-methyl]-ethylidene]-hydrazino)-benzonitrile (**3e**): Light orange crystals from dioxane; m.p. 240°C; yield 30% (method A), 35% (method B); IR: 3293 (2NH), 2227 ($\text{C}\equiv\text{N}$), 1649 (C=O), 1588 (C=N) and 1499 (N=N) cm^{-1} ; ^1H -NMR δ = 7.36-7.98 (m, 8H, Ar-H), 8.68 (s, 1H, CH olefinic), 9.35 (s, 1H, 1,2,4-triazole H-5), 14.30 (s, 1H, 1,2,4-triazole NH) and 14.82 (s, 1H, NH hydrazone) ppm; ^{13}C -NMR: δ = 116.62 (CN), 116.06, 116.09, 126.75, 126.78, 128.62, 128.77 ($\text{C}_6\text{H}_4\text{CN-o}$), 128.85, 132.63, 133.96, 135.43 ($\text{C}_6\text{H}_4\text{Cl-p}$), 136.42 (1,2,4-triazole carbons), 137.47 (C=N-N), 150.97 (HC=N) and 190.42 (C=O) ppm.; MS: M^+ (377); Anal. Calcd. for $\text{C}_{18}\text{H}_{12}\text{N}_7\text{OCl}$ (377.80): C, 57.23; H, 3.20; N, 25.95; Found: C, 57.26; H, 57.26; N, 25.90.

2-{*N'*-[2-Furan-2-yl-2-oxo-1-(pyrazin-2-yliminomethyl)-ethylidene]-hydrazino}-benzoic acid methyl ester (**3f**): Light brown crystals from ethanol/dioxane (2:1); m.p. 210°C; yield 70% (method A), 90% (method B); IR (complex due to H-bond between O and NH): 3043 (CH aromatic), 2990 (CH aliphatic), 1698 (C=O ester), 1626 (C=O ketone) and 1583 (C=N) cm^{-1} ; ^1H -NMR: δ =3.97 (s, 3H, CH_3O), 6.83 (m, 1H furyl H-4), 7.34 (m, 1H, Ar H-3), 7.60-7.61 (d, 2H, furyl H-3, H-5), 7.80 (m, 1H, Ar H-6), 7.97, 8.08 (d, 2H, Ar H-4, H-5), 8.67 (d, 2H, pyrazine H-5, H-6), 9.15 (s, 1H, CH olefinic), 9.53 (s, 1H, pyrazine H-3) and 15.93 (s, 1H, NH) ppm; MS: M^+ (377); Anal. Calcd. for $\text{C}_{19}\text{H}_{15}\text{N}_5\text{O}_4$ (377.36): C, 60.48; H, 4.01; N, 18.56; Found: C, 60.50; H, 4.25; N, 18.59.

2-{*N'*-[2-(4-Chlorophenyl)-2-oxo-1-(pyrazin-2-yliminomethyl)-ethylidene]-hydrazino}-benzonitrile (**3g**): Orange crystals from ethanol/dioxane (2:1); m.p. 255°C; yield 73% (method A), 78% (method B); IR: 3750 (NH), 3086 (CH aromatic), 2222 (CN), 1649 (C=O) and 1590 (C=N) cm^{-1} ; ^1H -NMR: δ = 7.32-7.90 (m, 8H, Ar-H), 8.45, 8.51 (m, 2H, H-5, H-6 pyrazine), 9.04 (s, 1H, CH olefinic), 9.45 (s, 1H, H-3 pyrazine) and 14.79 (s, 1H, NH) ppm; MS: M^+ (388); Anal. Calcd. for $\text{C}_{20}\text{H}_{13}\text{N}_6\text{OCl}$ (388.82): C, 61.78; H, 3.37; N, 21.61; Found: C, 61.70; H, 3.40; N, 21.20.

General Procedure for the Preparation of **6**:

Method A: Compound **3e** (0.1 mol) was refluxed in acetic acid for 2h, then left to cool at room temperature and treated with ethanol. The solid product, so formed, was collected by filtration and crystallized from ethanol.

Method B: Compound **3e** (0.1 mol) and a few drops of acetic acid were placed in the microwave oven and irradiated at 390 W for 7-20 min, then left to cool to room temperature and the solid was collected and crystallized from ethanol.

7-(4-Chlorophenyl)-6-(2-cyanophenylazo)-1,2,4-triazolo[1,5-a]pyrimidine (6): Orange crystals from ethanol; m.p. 258°C; yield 25% (method A), 30% (method B); IR: 3090 (CH aromatic), 2235 (C≡N), 1594 (C=N), 1485 (N=N) cm⁻¹; ¹H-NMR: δ= 7.46-8.02 (m, 8H, Ar-H), 9.01, 9.62 (2s, 1H, H-2, H-5); MS: M⁺ (359); Anal. Calcd. for C₁₈H₁₀N₇Cl (359.78): C, 60.09; H, 2.80; N, 27.25; Found: C, 60.24; H, 2.89; N, 27.30.

General Procedure for the Preparation of 8a-d:

Method A: A mixture of compound **1a,c,d** or **e** (0.1 mol) and hydrazine monohydrate or phenyl hydrazine (0.12 mol) was refluxed in ethanol or dioxane (30 mL) for 2 h., then left to cool to room temperature and the solid was collected and crystallized from ethanol.

Method B: Compound **1a, c, d** or **e** (0.1 mol) and hydrazine monohydrate or phenyl hydrazine (0.12 mol), and a few drops of ethanol were placed in the microwave oven and irradiated at 390 W for 1-10 min, then left to cool to room temperature and the solid was collected and crystallized from ethanol.

1-(2-Furyl)-3-hydrazono-2-(2-methoxycarbonylphenylhydrazono)-1-propanone (8a): Brown crystals from ethanol; m.p. 168°C; yield 60% (method A); IR: 3421, 3306 (NH₂), 3230 (NH), 1702 (C=O ester), 1617 (C=O ketone) and 1540 (C=N) cm⁻¹; MS: M⁺ 314; Anal. Calcd. for C₁₅H₁₄N₄O₄ (314.30): C, 57.32; H, 4.49; N, 17.83; Found: C, 57.40; H, 4.50; N, 17.89.

1-(4-Chlorophenyl)-3-hydrazono-2-(2-methoxycarbonylphenylhydrazono)-1-propanone (8b): Yellow crystals from ethanol: m.p. 204°C; yield 66% (method A), 90% (method B); IR: 3397, 3286 (NH₂), 3220 (NH), 3002 (CH aromatic), 2954 (CH aliphatic), 1699 (C=O ester), 1633 (C=O ketone) and 1580 (C=N) cm⁻¹; ¹H-NMR: δ= 3.95 (s, 3H, CH₃O), 7.54-7.92 (m, 10H, Ar-H and NH₂), 8.12 (s, 1H, CH olefinic) and 14.27 (s, 1H, NH) ppm; MS: M⁺ (358); Anal. Calcd. for C₁₇H₁₅N₄O₃Cl (358.79): C, 56.91; H, 4.21; N, 15.62; Found: C, 56.99; H, 4.25; N, 15.59.

1-(4-Chlorophenyl)-2-(2-methoxycarbonylphenylhydrazono)-3-phenylhydrazono-1-propanone (8c): Orange crystals from ethanol/dioxane(2:1): m.p. 244°C; yield 99% (method B); IR: 3273, 3178 (NH), 3178 (2 NH), 3065 (CH aromatic), 1706 (C=O ester) and 1630 (C=O ketone) cm⁻¹; ¹H-NMR: δ= 3.87 (s, 3H, CH₃O), 7.28-7.95 (m, 13H, Ar-H), 8.31 (s, 1H, CH olefinic), 10.87 (s, 1H, disappeared after D₂O exchange, NH phenylhydrazone) and 13.56 (s, 1H, disappeared after D₂O exchange, NH hydrazone); MS: M⁺ (434); Anal. Calcd. for C₂₃H₁₉N₄O₃Cl (434.89): C, 63.52; H, 4.40; N, 12.88; Found: C, 63.60; H, 4.49; N, 12.79.

2-(2-Cyanophenylhydrazono)-1-(2-furyl)-3-phenylhydrazono-1-propanone (8d): Orange crystals from ethanol: m.p. 229°C; yield 78% (method A), 80% (method B); IR: 3260, 3196 (2 NH), 3092 (CH aromatic), 2215 (C≡N), 1603 (C=O) and 1537 (C=N) cm^{-1} ; $^1\text{H-NMR}$: δ = 6.79-6.80 (m, 1H, furyl H-4), 7.26-7.63 (m, 9H, Ar-H), 7.79 (d, 1H, furyl H-3, H-5), 8.29 (s, 1H, CH olefinic), 11.06 (s, 1H, NH phenyl hydrazone) and 12.71(s, 1H, NH hydrazone); MS: M^+ (357); Anal. Calcd. for $\text{C}_{20}\text{H}_{15}\text{N}_5\text{O}_2$ (357.37): C, 67.22; H, 4.23; N, 19.60; Found: C, 67.32; H, 4.30; N, 19.58.

General Procedure for the Preparation of 9a, d.

Method A: A solution of each of compound **8a-d** (0.1 mol) in pyridine (10 mL) was refluxed for 2h., then left to cool to room temperature and the solid was collected and crystallized from ethanol.

Method B: Compounds **8a-d** (0.1 mol) and some drops of pyridine were placed in the microwave oven and irradiated at 390 W for 30 min., then left to cool to room temperature and the solid was collected and crystallized from ethanol.

3-(2-Furyl) 4-(2-methoxycarbonylphenylazo)-pyrazole (9a): Red crystals from ethanol; m.p. 160°C; yield 50% (method A); IR: 3343 (NH), 3100 (CH aromatic), 2990 (CH aliphatic), 1699 (C=O ester) and 1461 (N=N) cm^{-1} ; MS: M^+ (296); Anal. Calcd. for $\text{C}_{15}\text{H}_{12}\text{N}_4\text{O}_3$ (296.29): C, 60.81; H, 4.08; N, 18.91; Found: C, 60.89; H, 4.20; N, 18.99.

3-(4-Chlorophenyl) 4-(2-methoxycarbonylphenylazo) pyrazole (9b): Orange crystals from ethanol: m.p. 189°C; yield 50% (method A); IR: 3507 (NH), 3123 (CH aromatic), 2881 (CH aliphatic), 1745 (C=O ester) and 1498 (N=N) cm^{-1} ; $^1\text{H-NMR}$: δ = 3.83 (s, 3H, CH_3O), 7.49-8.24 (m, 8H, Ar-H), 8.48 (s, 1H, pyrazole H-5) and 9.10 (s, 1H, NH pyrazole) ppm; MS: M^+ (340); Anal. Calcd. for $\text{C}_{17}\text{H}_{13}\text{N}_4\text{O}_2\text{Cl}$ (340.77): C, 59.92; H, 3.85; N, 16.44; Found: C, 59.80; H, 3.90; N, 16.55.

3-(4-Chlorophenyl)-4-(2-methoxycarbonylphenylazo)-1-phenylpyrazole (9c): Light brown crystals from methanol: m.p. 242°C; yield 50% (method A); $^1\text{H-NMR}$: δ = 3.98 (s, 3H, CH_3), 7.36-8.18 (m, 13H, Ar-H) and 8.92 (s, 1H, pyrazole H-5) ppm; MS: M^+ (416); Anal. Calcd. for $\text{C}_{23}\text{H}_{17}\text{N}_4\text{O}_2\text{Cl}$ (416.87): C, 66.27; H, 4.11; N, 13.44; Found: C, 66.35; H, 4.29; N, 13.33.

4-(2-Cyanophenylazo)-3-(2-furyl)-1-phenylpyrazole (9d): Orange crystals from ethanol; m.p. 137°C; yield 50% (method A). IR: 3066 (CH aromatic), 2232 (C≡N) and 1495 (N=N) cm^{-1} ; MS: M^+ (339); Anal. Calcd. for $\text{C}_{20}\text{H}_{13}\text{N}_5\text{O}$ (339.36): C, 70.79; H, 3.86; N, 20.64; Found: C, 70.67; H, 3.90; N, 20.69.

General Procedure for the Preparation of **13**, **14**

Method A: A solution of compound **1a,c** (0.1 mol) in ethanol (30 mL) was treated with 2-amino-1-propene-1,1,3-tricarbonitrile (0.1mol) in the presence of few drops of piperidine and refluxed for 3h. The reaction product was washed with ethanol and dried, then recrystallized from ethanol.

Method B: Compound **1a,c** (0.1 mol) and 2-amino-1-propene-1,1,3-tricarbonitrile (0.1mol) in the presence of a few drops of piperidine were placed in the microwave oven and irradiated at 390 W for 5-10 min., then left to cool to room temperature and the solid was collected and crystallized from ethanol.

3-Amino-1-cyano-2-(2-furoyl-6-oxopyridazino[2,3-c]quinzoline-4-yl) acrylonitrile (13): Brown crystals from methanol; m.p. >300°C; yield 40%; IR: 3344 (NH₂), 2218, 2202 (2 C≡N) and 1615 (C=O) cm⁻¹; ¹H-NMR: δ= 5.49 (s, 2H, NH₂), 6.61 (m, 1H, furyl H-4), 6.65, 7.56 (m, 4H, Ar H), 7.23, 7.72 (d, 2H, furyl H-3, H-5) and 8.51 (s, 1H, H-4) ppm; ¹³C-NMR: δ= 117.2 (C≡N), 54.1 (C=C-CN), 186.6 (NH₂-C=O), 113.25, 121.62, 148.58, 150.63 (furyl carbons), 155.0 (C-2), 123.0 (C-3), 138.0 (C-4), 164.0 (C-4a), 123.3 (C-6a), 130.5 (C-7), 119.0 (C-8), 135.6 (C-9), 115.6 (C-10), 147.9 (C-10a), 177.66 (ring C=O) and 190.0 ppm (C=O); MS: M⁺ (382); Anal. Calcd. for C₂₀H₁₀N₆O₃ (382.34): C, 62.83; H, 2.64; N, 21.98; Found: C, 62.80; H, 2.70; N, 21.95.

5-Amino-3-(4-chlorobenzoyl)-6-cyano-(2-cyanophenyl)-1,7-dihydro-7-iminopyrido [2,3-c] pyridazine (14): Green crystals from ethanol; m.p. 273°C; yield 30%; IR: 3460 (NH₂), 3377 (NH), 3174 (CH aromatic), 2215, 2203 (2 C≡N) and 1632 (C=O) cm⁻¹; ¹H-NMR: δ= 5.29 (s, 2H, NH₂), 6.64-7.75 (m, 9H, Ar-H and NH) and 8.42 (s, 1H, H-4) ppm; ¹³C-NMR: δ= 116.2, 117.2 (2 C≡N), 99.6; 115.9, 119.2, 132.8, 133.6, 150.2 (C₆H₄-CN), 128.85, 132.63, 133.96, 135.40 (C₆H₄Cl-*p*), 155.0 (C-3), 123.5 (C-4), 138.0 (C-4a), 172 (C-5), 99.0 (C-6), 164.0 (C-7), 166.1 (C-8a) and 189.64 ppm (C=O); MS: (M⁺+2) (427); Anal. Calcd. for C₂₂H₁₂N₇OCl (425.84): C, 62.05; H, 2.84; N, 23.02; Found: C, 62.40; H, 2.95; N, 23.25.

2-{N-[2-(4-Chlorophenyl)-1-cyano-2-oxo-ethylidene]-hydrazino}-benzoic acid (15): Green crystals from ethanol/ dioxane (2:1); m.p.238°C; yield 35%; IR: 3449 (OH), 3305 (NH), 3057 (CH aromatic), 2220 (C≡N) and 1647 (C=O) cm⁻¹; MS (M⁺-2) (325); Anal. Calcd. for C₁₆H₁₀N₃O₃Cl (327.73): C, 58.64; H, 3.08; N, 12.82; Found: C, 58.70; H, 3.25; N, 12.77.

General Procedure for the Preparation of **16**

Method A: A warm solution of hydroxylamine hydrochloride (0.1 mol) and sodium carbonate (0.12 mol) in water (10 mL) was added to a stirred solution of the arylhydrazonopropanals **1c,d** (0.1 mol) in ethanol (10 mL). The reaction mixture was stirred at room temperature for one hour. 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 ethanol.

Method B: Compound **1c,d** (0.1 mol), hydroxylamine hydrochloride (0.1 mol), sodium carbonate (0.12 mol) and a few drops of ethanol were placed in the microwave oven and irradiated at 390 W for 5-10 min, then left to cool to room temperature and the solid was collected and crystallized from ethanol.

3-(2-Furoyl)-2-(2-methoxycarbonylphenylhydrazono)-3-oxo-propanal-1-oxime (16a): Yellow crystal from ethanol; m.p.199°C; yield 74% (method A), 82% (method B); IR (shows complex spectra due to H-bond between O ketone and NH): 3311 (br OH), 3075 (CH aromatic), 2957 (CH aliphatic), 1691 (C=O ester), 1630 (C=O ketone) and 1580 (C=N) cm^{-1} ; $^1\text{H-NMR}$: δ = 3.98 (s, 3H, CH_3O), 6.80 (m, 1H, furyl H-4), 7.29-7.77 (m, 2H, Ar H-4, H-5), 7.53, 7.90 (d, 2H, furyl H-3 and H-5), 8.02, 8.13 (d, 2H, Ar H-3, H-6), 9.63 (s, 1H, CH olefinic), 12.12 (s, 1H, NH) and 15.39 (s, 1H, OH) ppm; MS: M^+ (315); Anal. Calcd. for $\text{C}_{15}\text{H}_{13}\text{N}_3\text{O}_5$ (315.29): C, 57.14; H, 4.16; N, 13.33; Found: C, 57.20; H, 4.10; N, 13.45.

3-(4-Chlorophenyl)-2-(2-methoxycarbonylphenylhydrazono)-3-oxo-propanal-1-oxime (16b): Yellow crystals from dioxane; m.p.186°C; yield 74% (method A); IR: 3426 (br OH), 3300 (NH), 3020 (CH aromatic), 1713 (C=O ester), 1635 (C=O ketone) and 1586 (C=N) cm^{-1} ; $^1\text{H-NMR}$: δ = 4.04(s, 3H, CH_3O), 7.25-8.08 (m, 8H, Ar-H), 8.62 (s, 1H, CH olefinic), 10.25 (s, 1H, disappeared after D_2O exchange NH) and 15.69 (s, 1H, disappeared after D_2O exchange, OH) ppm; $^{13}\text{C-NMR}$: δ = 52.90 (COOCH_3), 128.35, 131.89, 134.74, 138.75 ($\text{C}_6\text{H}_4\text{-Cl-p}$), 116.18, 116.39, 124.98, 131.59, 133.32, 135.50 ($\text{C}_6\text{H}_4\text{-CO}_2\text{Me-o}$), 143.54 (C=N-OH), 166.87 (C=N-N), 188.22 (COOCH_3) and 190.49 (C=O) ppm; MS: (M^+-1) (358); Anal. Calcd. for $\text{C}_{17}\text{H}_{14}\text{N}_3\text{O}_4\text{Cl}$ (359.77): C, 56.76; H, 3.92; N, 11.68; Found: C, 56.80; H, 3.89; N, 11.63.

General Procedure for the Preparation of 17

Method A: Compound **16a** (0.1mol) was refluxed in pyridine (10 mL) for 1h, then left to cool at room temperature and treated with ethanol. The solid product, so formed, was collected by filtration and crystallized from ethanol.

Method B: Compound **16a** (0.1 mol) and drops of pyridine were placed in the microwave oven and irradiated at 390 W for 15-28 min, then left to cool to room temperature and the solid was collected and crystallized from ethanol.

4-(2-Furoyl)-2-(2-methoxycarbonylphenyl)-1,2,3-triazole (17a): Yellow crystals from ethanol; m.p.138°C; yield 56% (method A), 66% (method B); IR: 3074 (CH aromatic), 1691 (C=O ester), 1630 (C=O ketone) and 1580 (C=N) cm^{-1} ; MS: (M^++1) (298); Anal. Calcd. for $\text{C}_{15}\text{H}_{11}\text{N}_3\text{O}_4$ (297.27): C, 60.61; H, 3.73; N, 14.14; Found: C, 60.70; H, 3.69; N, 14.26.

3-(4-Chlorophenyl)-3-oxo-2-(2-methoxycarbonylphenylhydrazono)propionitrile (**18**): Compound **1c** (0.1 mol), hydroxylamine hydrochloride (0.1 mol) and ammonium acetate (0.1 mol) and a few drops of ethanol were placed in the microwave oven and irradiated at 390 W for 30 min, then left to cool to room temperature, and the solid was collected and crystallized from ethanol, giving brown crystals; m.p. 175°C; yield 40%; IR: 3230 (NH), 3070 (CH aromatic), 2222 (C≡N) and 1715 (C=O ester), 1640 (C=O ketone) cm^{-1} ; MS: ($\text{M}^+ + 1$) (342); Anal. Calcd. for $\text{C}_{17}\text{H}_{12}\text{N}_3\text{O}_3\text{Cl}$ (341.76): C, 59.75; H, 3.54; N, 12.30; Found: C, 59.85; H, 3.50; N, 12.40.

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Sample availability: Available from the corresponding author