Studies With Enamines: Reactivity of *N*,*N*-Dimethyl-*N*-[(*E*)-2-(4-nitrophenyl)-1-ethenyl]amine Towards Nitrilimine And Aromatic Diazonium Salts.

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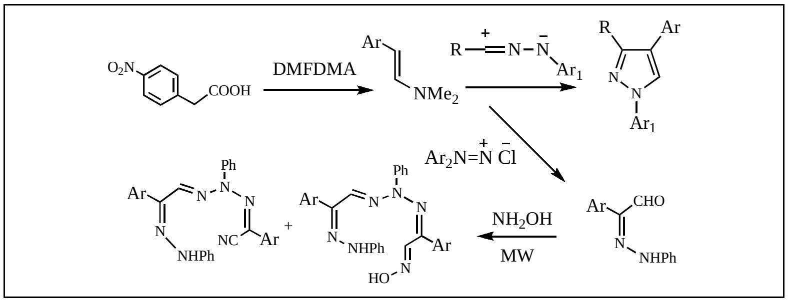

In the presence of triethylamine, cycloaddition reaction of enamine **1** with hydrazonoyl halides **2** followed by dimethylamine elimination was achieved, yielding the corresponding 1,3,4-trisubstituted pyrazoles **4**. Coupling of enamine **1** with aromatic diazonium salts afforded 2-(arylhydrazono)-2-(4-nitrophenyl)acetaldehyde **9** in good yield. Refluxing the phenyl hydrazone **9a** with chloroacetone in ethanol in the presence of triethylamine afforded 1,3,5-trisubstituted pyrazole **12a**, formed *via* intermediate **11a**. Reaction of **9a** with hydroxylamine hydrochloride in ethanol in the presence of anhydrous sodium acetate yielded oxime **13a** which was irradiated in a microwave oven in the presence of acetic acid to afford a mixture of **15a** and **16a**.

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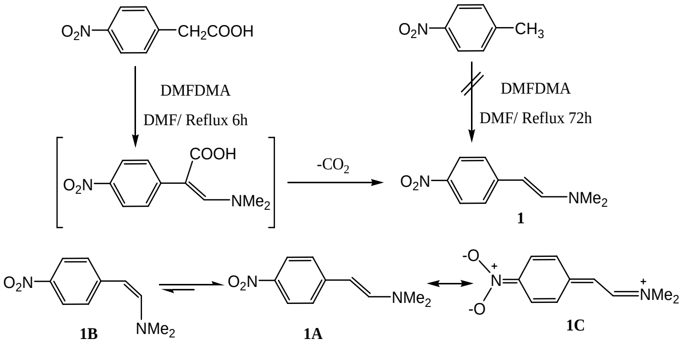
INTRODUCTION

Enamines are versatile reagents and their chemistry is receiving considerable attention [1-3]. Recently we described several efficient approaches to heteroaromatics utilizing functionally substituted enamines precursors [4-8]. In conjunction to this work and as part of a new project directed towards developing efficient routes to polysubstituted pyrazoles and 1,2,3-triazoles as potential antibacterial agents [9,10] we report here a novel synthesis of 1,3,4- and 1,3,5-trisubstituted pyrazoles.

RESULTS AND DISCUSSION

One of the main routes to enamines is condensation of dialkylamine acetals with activated methyl or methylene compounds [11-15]. The synthesis of enamines from dimethylformamide dimethylacetal (DMFDMA) with nitrotoluene has been reported [16]. However, under a variety of conditions the condensation of DMFDMA with *p*-nitrotoluene did not yield enamine **1** which was to be used as a synthetic equivalent of *p*-nitrophenylacetaldehyde. Alternatively, a procedure similar to that developed recently [17] was applied. This method involves condensation of active methylene carboxylic acids with piperidin-1-ylformamide diethylacetal, formed *in situ* from piperidine and triethylorthoformate. We condensed DMFDMA with 4-nitrophenylacetic acid in refluxing DMF and obtained enamine **1** in 80 % yield (Scheme 1).

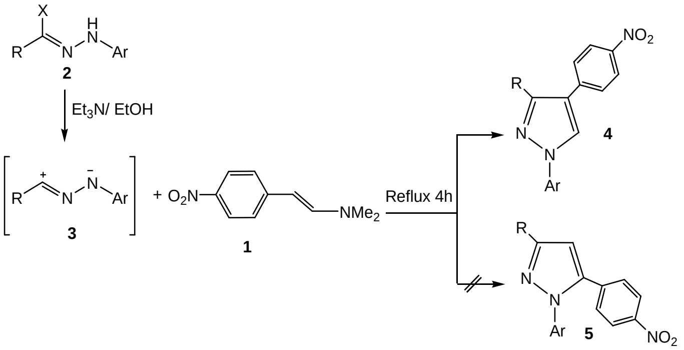
Scheme 1



It is believed that the reaction mechanism proceeds through the initial formation of a carboxylic acid intermediate which then loses CO_2. In the ^1H NMR spectrum of compound **1** the olefinic protons appear as two doublets in the region δ = 5.13 and 7.03 ppm with J = 13.5 *Hz* and the two methyl groups resonate as a singlet at 2.94 ppm. It can therefore be concluded that compound **1** exists in the *trans*-form and furthermore that the two methyl groups are magnetically equivalent probably due to a very small contribution by the resonance form **1C**. This comes in contradiction to previous reports [18,19] that prove that the two methyl signals in dimethylamino enaminones are non-equivalent.

The enamine **1**, so prepared, reacted with a variety of substituted nitrilimines **3** generated *in situ* upon treatment of hydrazonoyl halides **2** with a base to yield products of [2+3] dipolar cycloaddition with concurrent dimethylamine elimination. These products can be formulated as **4** or isomeric **5**. Structure **4** was assigned as the correct structure on the basis of its ^{1}H NMR spectrum where a resonance for H-5 appeared typically at $\delta = 8.24$ ppm [20] (Scheme 2).

Scheme 2

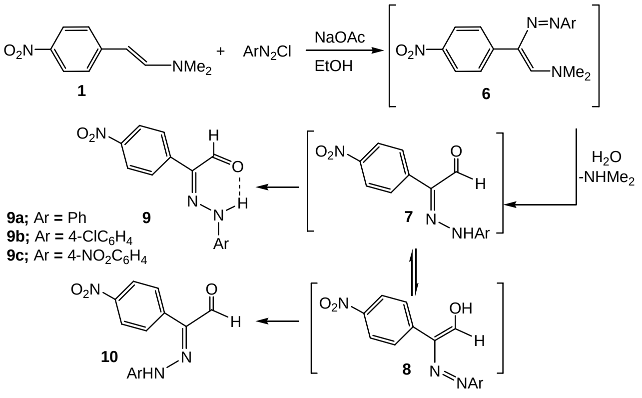


Compd. no.	R	Ar	Compd. no.	R	Ar
4a	Ph	Ph	**4f**	EtOCO	4-ClC$_6$H$_4$
4b	CH$_3$CO	Ph	**4g**	PhNHCO	Ph
4c	CH$_3$CO	4-CH$_3$C$_6$H$_4$	**4h**	PhNHCO	4-CH$_3$C$_6$H$_4$
4d	CH$_3$CO	4-NO$_2$C$_6$H$_4$	**4i**	PhCO	Ph
4e	EtOCO	Ph	**4j**	2-thenoyl	4-ClC$_6$H$_4$

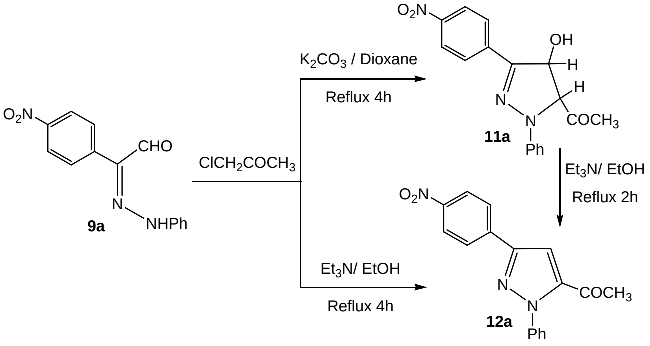
Enamine **1** exhibited typical enamine behaviour [21-23] by coupling readily with aromatic diazonium salts (Scheme 3). According to the proposed mechanism products to be expected were enazo derivative **6** or after hydrolysis and concomitant loss of dimethylamine to give hydrazonoacetaldehyde **7** or its enol tautomer **8**. After inspection of the ^{1}H NMR spectra the products were assigned the *syn* hydrazone isomer **9** or the *anti* hydrazone isomer **10**. Isomer **9** represents the most probable structure because of the single proton signal around 10.1 ppm which corresponds to the aldehydes group. This proton in the non-hydrogen bonded *anti* isomer **10** is expected at around 11 ppm. According to Al-Awadi *et al.* [24] however in tautomers analogous to **9** and **10** stereoelectronic factors were shown to outweigh possible fixation of molecules by intramolecular hydrogen bonding. We therefore only tentatively assign *syn* isomer **9** as the structure of these products.

Refluxing of **9a** with chloroacetone in dioxane in the presence of potassium carbonate gave the corresponding 4-hydroxy-4,5-dihydropyrazole derivative **11a**. Upon treatment of this compound with triethylamine in ethanol under reflux, it underwent dehydration to furnish pyrazole derivative **12a**. The latter was also prepared directly *via* refluxing of **9a** with chloroacetone in ethanol in the presence of triethylamine as a basic catalyst (Scheme 4).

Scheme 3

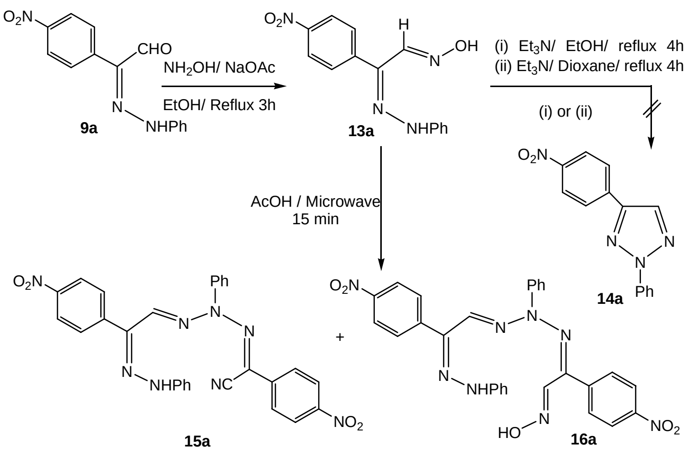


Scheme 4



The reaction of **9a** with hydroxylamine hydrochloride in ethanolic sodium acetate afforded the corresponding oxime **13a** (Scheme 5). Attempts to achieve ring closure of **13a** into the corresponding [1,2,3]triazole derivative **14a** by refluxing **13a** in ethanol or 1,4-dioxane in the presence of triethylamine according to recent report [25] failed. Irradiation of **13a** in a microwave oven in acetic acid furnished the corresponding self-condensation product **15a** and oxime **16a**.

Scheme 5



EXPERIMENTAL

Melting points were recorded on Gallenkamp apparatus and are uncorrected. Infrared spectra (KBr) were determined on a Perkin-Elmer 2000 FT-IR system. ^{1}H NMR was determined on a Bruker DPX 400 MHz superconducting spectrometer in $CDCl_3$ and DMSO-d_6 as solvents and using TMS as internal standard. Mass spectra were measured on MS 30 and MS 9 (AEI) spectrometers, with EI 70 eV. Elemental analyses were measured by means of LECO CHNS-932 Elemental Analyzer. The microwave accelerated reactions were carried out by using induced microwave convection operating at 900 W generating 2450 MHz frequency. Hydrazonoyl halides **2a-j** [26-31] were prepared by literature methods.

Synhesis of *N*,*N*-dimethyl-*N*-[(*E*)-2-(4-nitrophenyl)-1-ethenyl]amine (1). A mixture of 4-nitrophenylacetic acid (18.1 g, 0.1 mol) and DMFDMA (11.9 g, 0.1 mol) in dry DMF (50 mL) was refluxed for 4 hours, then poured into water, collected by filtration and recrystallized from ethanol to give pure **(1).** This compound was obtained in 15.36 g (80%), mp 148 °C; ir: 3051 (CH-Ar), 1631 (C=C) cm^{-1}; ^{1}H nmr ($CDCl_3$) δ 2.94 (s, 6H, $2CH_3$), 5.13 (d, 1H, *J* = 13.5 *Hz*), 7.03 (d, 1H, *J* = 13.5 *Hz*), 7.14 (d, 2H, *J* = 8 *Hz*), 8.05 (d, 2H, *J* = 8 *Hz*); ms, *m/z* (%) 192 (M$^+$, 100), 177 (10), 131 (15), 103 (20), 77 (10). Anal. Calcd. for $C_{10}H_{12}N_2O_2$: C, 62.49; H, 6.29; N, 14.57. Found: C, 62.41; H, 6.32; N, 14.54.

Synthesis of 1,3-Disubstituted-4-(4-nitrophenyl)-1*H*-pyrazole (4a-j). To a mixture of equimolar amounts of **1** and the appropriate hydrazonoyl halides **2** (1 mmol) in 20 mL dioxane were added triethylamine (0.14 mL, 1 mmol). The reaction mixture was refluxed till all of the starting materials have been disappeared (4 hours, monitored by TLC). The solvent was evaporated and the residue was treated with methanol. The solid that formed was filtered and recrystallized from appropriate solvent to give compounds **4a-j**.

1,3-Diphenyl-4-(4-nitrophenyl)-1*H*-pyrazole (4a). This compound was obtained in 0.263 g (77%), mp 162 °C [MeOH]; ir: 1595 (C=N) cm^{-1}; ^{1}H nmr ($CDCl_3$) δ 7.35-7.58 (m, 10H, Ar-H), 7.82 (d, 2H, *J* = 8 *Hz*), 8.16 (s, 1H, pyr-H), 8.20 (d, 2H, *J* = 8 *Hz*); ms, *m/z* (%) 341 (M$^+$, 100), 294 (14), 165 (20), 77 (20). Anal. Calcd. for $C_{21}H_{15}N_3O_2$: C, 73.89; H, 4.43; N, 12.31. Found: C, 73.62; H, 4.27; N, 12.25.

1-[4-(4-Nitrophenyl)-1-phenyl-1*H*-3-pyrazolyl]-1-ethanone (4b). This compound was obtained in 0.23 g (75%), mp 206 °C [EtOH]; ir: 1692 (CO), 1599 (C=N) cm^{-1}; ^{1}H nmr ($CDCl_3$) δ 2.75 (s, 3H, $COCH_3$), 7.43-7.77 (m, 5H, Ar-H), 7.82 (d, 2H, *J* = 8 *Hz*), 8.09 (s, 1H, pyr-H), 8.29 (d, 2H, *J* = 8 *Hz*); ms, *m/z* (%) 307 (M$^+$, 90), 291 (100), 244 (20), 77 (35). *Anal*. Calcd. for $C_{17}H_{13}N_3O_3$: C, 66.44; H, 4.26; N, 13.67. Found: C, 66.41; H, 4.32; N, 13.58.

1-[4-(4-Nitrophenyl)-1-(4-methylphenyl)-1*H*-3-pyrazolyl]-1-ethanone (4c). This compound was obtained in 0.25 g (78%), mp 199 °C [H_2O/EtOH]; ir: 1693 (CO), 1602 (C=N) cm^{-1}; ^{1}H nmr ($CDCl_3$) δ 2.45 (s, 3H, Ar-CH_3), 2.75 (s, 3H, $COCH_3$), 7.34 (d, 2H, *J* = 8 *Hz*), 7.68 (d, 2H, *J* = 8 *Hz*), 7.77 (d, 2H, *J* = 8 *Hz*), 8.05 (s, 1H, pyr-H), 8.26 (d, 2H, *J* = 8 *Hz*); ms, *m/z* (%) 321 (M$^+$, 100), 305 (90), 259 (20), 91 (10). Anal. Calcd. for $C_{18}H_{15}N_3O_3$: C, 67.28; H, 4.71; N, 13.08. Found: C, 67.04; H, 4.69; N, 13.31.

1-[1,4-Di(4-nitrophenyl)-1*H*-3-pyrazolyl]-1-ethanone (4d). This compound was obtained in 0.28 g (80%), mp 268 °C [H_2O/EtOH]; ir: 1695 (CO), 1596 (C=N) cm^{-1}; ^{1}H nmr ($CDCl_3$) δ 2.77 (s, 3H, $COCH_3$), 7.76 (d, 2H, *J* = 8 *Hz*), 8.03 (d, 2H, *J* = 8 *Hz*), 8.21 (d, 2H, *J* = 8 *Hz*), 8.31 (s, 1H, pyr-H), 8.47 (d, 2H, *J* = 8 *Hz*); ms, *m/z* (%) 352 (M$^+$, 90), 337 (100), 291 (20), 153 (10). Anal. Calcd. for $C_{17}H_{12}N_4O_5$: C, 57.96; H, 3.43; N, 15.90. Found: C, 58.06; H, 3.56; N, 15.93.

Ethyl 4-(4-nitrophenyl)-1-phenyl-1*H*-3-pyrazolecarboxylate (4e). This compound was obtained in 0.26 g (78%), mp 144 °C [H_2O/MeOH]; ir: 1719 (CO), 1599 (C=N) cm^{-1}; ^{1}H nmr ($CDCl_3$) δ 1.38 (t, 3H, CH_3), 4.42 (q, 2H, CH_2), 7.41-7.75 (m, 5H, Ar-H), 7.81 (d, 2H, *J* = 8 *Hz*), 8.08 (s, 1H, pyr-H), 8.28 (d, 2H, *J* = 8 *Hz*); ms, *m/z* (%) 337 (M$^+$, 100), 292 (25), 265 (40), 77 (25). Anal. Calcd. for $C_{18}H_{15}N_3O_4$: C, 64.09; H, 4.48; N, 12.46. Found: C, 64.22; H, 4.65; N, 12.20.

Ethyl 1-(4-chlorophenyl)-4-(4-nitrophenyl)-1*H*-3-pyrazolecarboxylate (4f). This compound was obtained in 0.29 g (80%), mp 160 °C [H_2O/MeOH]; ir: 1724 (CO), 1601 (C=N) cm^{-1}; ^{1}H nmr ($CDCl_3$) δ 1.37 (t, 3H, CH_3), 4.41 (q, 2H, CH_2), 7.50 (d, 2H, *J* = 8 *Hz*), 7.73 (d, 2H, *J* = 8 *Hz*), 7.75 (d, 2H, *J* = 8 *Hz*), 8.05 (s, 1H, pyr-H), 8.28 (d, 2H, *J* = 8 *Hz*); ms, *m/z* (%) 371 (M$^+$, 100), 325 (45), 299 (60), 91 (50). Anal. Calcd. for $C_{18}H_{14}ClN_3O_4$: C, 58.15; H, 3.80; N, 11.30. Found: C, 58.27; H, 4.05; N, 11.11.

4-(4-Nitrophenyl)-1-phenyl-3-phenylcarbamoyl-1*H*-pyrazole (4g). This compound was obtained in 0.29 g (75%), mp 230 °C [EtOH]; ir: 3283 (NH), 1659 (CO), 1596 (C=N) cm^{-1}; ^{1}H nmr ($CDCl_3$) δ 7.15-7.83 (m, 10H, Ar-H), 7.89 (d, 2H, *J* = 8 *Hz*), 8.13 (s, 1H, pyr-H), 8.33 (d, 2H, *J* = 8 *Hz*), 8.97 (s, 1H, NH); ms, *m/z* (%) 384 (M$^+$, 50), 292 (100), 244 (20), 77 (15). Anal. Calcd. for $C_{22}H_{16}N_4O_3$: C, 68.74; H, 4.20; N, 14.58. Found: C, 68.63; H, 4.24; N, 14.86.

1-(4-Methylphenyl)-4-(4-nitrophenyl)-3-phenylcarbamoyl-1*H*-pyrazole (4h). This compound was obtained in 0.30 g (75%), mp 225 °C [EtOH]; ir: 3271 (NH), 1655 (CO), 1597 (C=N) cm^{-1}; ^{1}H nmr ($CDCl_3$) δ 2.42 (s, 3H, Ar-CH_3), 7.15-7.71 (m, 9H, Ar-H), 7.88 (d, 2H, *J* = 8 *Hz*), 8.09 (s, 1H, pyr-H), 8.30 (d, 2H, *J* = 8 *Hz*), 8.97 (s, 1H, NH); ms, *m/z* (%) 398 (M$^+$, 50), 306 (100), 258 (20), 91 (10). Anal. Calcd. for $C_{23}H_{18}N_4O_3$: C, 69.34; H, 4.55; N, 14.06. Found: C, 69.44; H, 4.49; N, 14.30.

[4-(4-Nitrophenyl)-1-phenyl-1*H*-3-pyrazolyl](phenyl)methanone (4i). This compound was obtained in 0.29 g (78%), mp 200 °C [MeOH]; ir: 1650 (CO), 1597 (C=N) cm^{-1}; ^{1}H nmr ($CDCl_3$) δ 7.41-7.73 (m, 10H, Ar-H), 7.82 (d, 2H, *J* = 8 *Hz*), 8.20 (s, 1H, pyr-H), 8.27 (d, 2H, *J* = 8 *Hz*); ms, *m/z* (%) 369 (M$^+$, 100), 340 (20), 105 (70), 77 (70). Anal. Calcd. for $C_{22}H_{15}N_3O_3$: C, 71.54; H, 4.09; N, 11.38. Found: C, 71.79; H, 4.22; N, 11.60.

[1-(4-Chlorophenyl)-4-(4-nitrophenyl)-1*H*-3-pyrazolyl]-(2-thienyl)methanone (4j). This compound was obtained in 0.31 g (75%), mp 196 °C [EtOH]; ir: 1638 (CO), 1603 (C=N) cm^{-1}; ^{1}H nmr ($CDCl_3$) δ 7.22-7.80 (m, 7H, Ar-H), 7.83 (d, 2H, *J* = 8 *Hz*), 8.14 (s, 1H, pyr-H), 8.30 (d, 2H, *J* = 8 *Hz*); ms, *m/z* (%) 409 (M$^+$, 90), 380 (10), 111 (100), 75 (10). Anal. Calcd. for $C_{20}H_{12}ClN_3O_3S$: C, 58.61; H, 2.95; N, 10.25; S, 7.82. Found: C, 58.80; H, 2.70; N, 10.11; S, 7.61.

Synthesis of 2-(arylhydrazono)-2-(4-nitrophenyl) acetaldehyde (9a-c). To a solution of **1** (10 mmol) in ethanol (40 mL) was added sodium acetate trihydrate (1.38 g, 10 mmol), and the mixture was cooled to 0-5 °C in an ice bath. To the resulting cold solution was added portionwise a cold solution of aryldiazonium chloride, prepared by diazotizing substituted aniline (10 mmol) dissolved in hydrochloric acid (6 *M*, 6 mL) with a solution of sodium nitrite (0.7 g, 10 mmol) in water (10 mL). After complete addition of the diazonium salt, the reaction mixture was stirred for a further 30 min in an ice bath. The solid precipitate was collected by filtration, washed with water, dried and crystallized from appropriate solvent to give the respective pure **9a-c**.

2-(2-Phenylhydrazono)-2-(4-nitrophenyl)acetaldehyde (9a). This compound was obtained in 0.22 g (80%), mp 141 °C [H_2O/MeOH]; ir: 3434 (NH), 1638 (CO), 1595 (C=N) cm^{-1}; ^1H nmr ($CDCl_3$) δ 7.19-7.52 (m, 5H, Ar-H), 7.88 (d, 2H, *J* = 8 *Hz*), 8.31 (d, 2H, *J* = 8 *Hz*), 10.01 (s, 1H, CHO), 14.55 (s, 1H, NH); ms, *m/z* (%) 269 (M^+, 90), 253 (20), 105 (30), 93 (90), 77 (100). Anal. Calcd. for $C_{14}H_{11}N_3O_3$: C, 62.45; H, 4.12; N, 15.61. Found: C, 62.28; H, 4.09; N, 15.75.

2-[2-(4-Chlorophenyl)hydrazono]-2-(4-nitrophenyl)acetaldehyde (9b). This compound was obtained in 0.26 g (85%), mp 222 °C [EtOH]; ir: 3441 (NH), 1637 (CO), 1595 (C=N) cm^{-1}; ^1H nmr ($CDCl_3$) δ 7.28 (d, 2H, *J* = 7 *Hz*), 7.40 (d, 2H, *J* = 7 *Hz*) 7.87 (d, 2H, *J* = 8 *Hz*), 8.30 (d, 2H, *J* = 8 *Hz*), 10.01 (s, 1H, CHO), 14.50 (s, 1H, NH); ms, *m/z* (%) 303 (M^+, 100), 139 (25), 127 (80), 111 (65). Anal. Calcd. for $C_{14}H_{10}ClN_3O_3$: C, 55.37; H, 3.32; N, 13.84. Found: C, 55.14; H, 3.46; N, 13.85.

2-[2-(4-Nitrophenyl)hydrazono]-2-(4-nitrophenyl)acetaldehyde (9c). This compound was obtained in 0.25 g (80%), mp 268 °C [EtOH]; ir: 3466 (NH), 1632 (CO), 1603 (C=N) cm^{-1}; ^1H nmr ($CDCl_3$) δ 7.57 (d, 2H, *J* = 8 *Hz*), 7.69 (d, 2H, *J* = 8 *Hz*) 8.23 (d, 2H, *J* = 8 *Hz*), 8.39 (d, 2H, *J* = 8 *Hz*), 10.14 (s, 1H, CHO), 11.25 (s, 1H, NH); ms, *m/z* (%) 314 (M^+, 100), 138 (70), 122 (40), 108 (20). Anal. Calcd. for $C_{14}H_{10}N_4O_5$: C, 53.51; H, 3.21; N, 17.83. Found: C, 53.62; H, 3.32; N, 17.86.

Synthesis of 1-[4-hydroxy-3-(4-nitrophenyl)-1-phenyl-4,5-dihydro-1*H*-5-pyrazolyl]-1-ethanone (11a). To a solution of hydrazono-aldehyde **9a** (1 mmol) in dioxane (20 mL) containing potassium carbonate anhydrous (0.28 g, 2 mmol) was added chloroacetone (0.093 g, 1 mmol). The reaction mixture was refluxed for 4 hours, then poured into water, collected by filtration and recrystallized from ethanol to give pure **11a**. This compound was obtained in 0.23 g (70%), mp 242 °C [EtOH]; ir: 3421 (OH), 1720 (CO), 1594 (C=N) cm^{-1}; ^1H nmr (DMSO–d_6) δ 2.23 (s, 3H, $COCH_3$), 5.09 (d, 1H, *J* = 10 *Hz*), 5.97 (dd, 1H, *J* = 2 *Hz*, 8 *Hz*) 6.20 (d, 1H, *J* = 8 *Hz*), 6.89-7.32 (m, 5H, Ar-H), 8.05 (d, 2H, *J* = 8 *Hz*), 8.30 (d, 2H, *J* = 8 *Hz*); ms, *m/z* (%) 325 (M^+, 40), 307 (100), 282 (90), 104 (40), 77 (60). Anal. Calcd. for $C_{17}H_{15}N_3O_4$: C, 62.76; H, 4.65; N, 12.92. Found: C, 62.55; H, 4.61; N, 12.84.

Synthesis of 1-[3-(4-nitrophenyl)-1-phenyl-1*H*-5-pyrazolyl]-1-ethanone (12a). To a solution of hydrazono-aldehyde **9a** (1 mmol) in ethanol (20 mL) containing triethylamine (0.14 mL, 1 mmol) was added chloroacetone (0.093 g, 1 mmol). The reaction mixture was refluxed for 4 hours, then poured into water, collected by filtration and recrystallized from ethanol to give pure **12a**. This compound was obtained in 0.21 g (70%), mp 250 °C [EtOH]; ir: 1725 (CO), 1597 (C=N) cm^{-1}; ^1H nmr (DMSO–d_6) δ 2.60 (s, 3H, $COCH_3$), 6.11 (s, 1H, Pyr-H), 7.51-7.82 (m, 5H, Ar-H), 8.20 (d, 2H, *J* = 8 *Hz*), 8.34 (d, 2H, *J* = 8 *Hz*); ms, *m/z* (%) 307 (M^+, 55), 282 (100), 236 (20), 104 (25), 77 (20). Anal. Calcd. for $C_{17}H_{13}N_3O_3$: C, 66.44; H, 4.26; N, 13.67. Found: C, 66.29; H, 4.19; N, 13.81.

Synthesis of 2-(4-nitrophenyl)-2-(2-phenylhydrazono) acetaldehyde oxime (13a). To a solution of hydrazono-aldehyde **9a** (1 mmol) in ethanol (20 mL) containing sodium acetate anhydrous (0.30 g) was added hydroxylamine hydrochloride (0.07 g, 1 mmol). The reaction mixture was refluxed for 4 hours, then poured into water, collected by filtration and recrystallized from ethanol to give pure **13a**.This compound was obtained in 0.17 g (60%), mp 234 °C [EtOH]; ir: 3384 (OH), 3108 (NH), 1590 (C=N) cm^{-1}; ^1H nmr (DMSO–d_6) δ 6.23 (s, 1H, CH), 6.98-7.38 (m, 5H, Ar-H), 8.04 (d, 2H, *J* = 8 *Hz*), 8.22 (d, 2H, *J* = 8 *Hz*), 8.6 (s, 1H, NH), 12.21 (s, 1H, OH); ms, *m/z* (%) 284 (M^+, 40), 266 (100), 91 (60), 77 (25). Anal. Calcd. for $C_{14}H_{12}N_4O_3$: C, 59.15; H, 4.25; N, 19.71. Found: C, 59.12; H, 4.11; N, 19.88.

Microwave irradiation of (13a). A solution **13a** (1 mmol) in acetic acid (2 mL) was irradiated in a microwave oven for 15 min. (900 W). The solution was extracted with chloroform (3 x 10 mL). The organic extracts were dried over anhydrous magnesium sulfate, and evaporated under reduced pressure. The residue was purified through preparative thin layer chromatography [eluent: hexane / AcOEt (3:1)].

(15a). Mp 220 °C; (0.21 g, 40%); ir: 3242 (NH), 2208 (CN), 1635 (C=N) cm^{-1}; ^1H nmr ($CDCl_3$) δ 7.1 (s, 1H, CH), 7.32-8.37 (m, 18H, Ar-H), 9.10 (s, 1H, NH); ms, *m/z* (%) 532 (M^+, 40), 266 (100), 123 (30), 77 (60). Anal. Calcd. for $C_{28}H_{20}N_8O_4$: C, 63.15; H, 3.79; N, 21.04. Found: C, 63.12; H, 4.01; N, 20.88.

(16a). Mp 155 °C; (0.16 g, 30%); ir: 3444 (OH), 3130 (NH), 1639 (C=N) cm^{-1}; ^1H nmr ($CDCl_3$) δ 6.5 (s, 1H, CH), 6.8 (s, 1H, CH), 7.28-8.37 (m, 18H, Ar-H), 10.01 (s, 1H, NH), 14.56 (s, 1H, OH); ms, *m/z* (%) 550 (M^+, 50), 283 (100), 123 (10), 77 (40). Anal. Calcd. for $C_{28}H_{22}N_8O_5$: C, 61.09; H, 4.03; N, 20.35. Found: C, 61.12; H, 4.11; N, 20.18

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