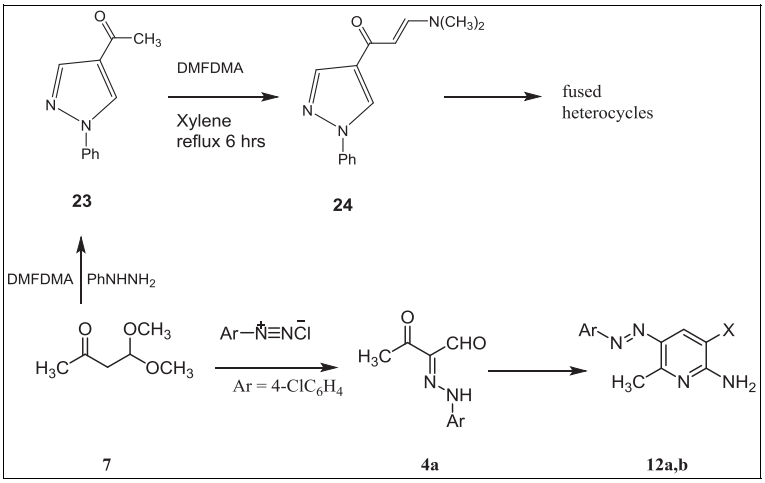
Acetylacetaldehyde Dimethyl Acetal as Versatile Precursors for the Synthesis of Arylazonicotinic Acid Derivatives: Green Multicomponent Syntheses of Bioactive Poly-Heteroaromatic Compounds

Huwaida M. E. Hassaneen and Ismail A. Abdelhamid*

Chemistry Department, Faculty of Science, Cairo University, Giza 12613, Egypt
*E-mail: ismail_shafy@yahoo.com
Received January 29, 2016
DOI 10.1002/jhet.2673
Published online 00 Month 2016 in Wiley Online Library (wileyonlinelibrary.com).



A simple and efficient one-pot synthesis of interesting arylhydrazonals could be achieved *via* coupling of acetylacetaldehyde dimethyl acetal with aromatic diazonium salts. Dimroth type rearrangement was observed during the reaction of the arylhydrazonals with malononitrile or ethyl cyanoacetate leading to the formation of arylazonicotinic acid derivatives. The reaction of arylhydrazonals with malononitrile and aldehydes in the presence of DABCO afforded 4-styryl-1,2-dihydropyridine-3-carbonitrile whose structure was established by X-ray crystallography. Pyrazolyl-enaminone was accomplished and used as a scaffold to synthesize bioactive fused heterocyclic compounds such as 1,2,4-triazolo[1,5-*a*]pyrimidine **28**, benzo [4,5]imidazo[1,2-*a*]pyrimidine **30** and pyrazole[1,5-*a*]pyrimidine derivatives **32**.

J. Heterocyclic Chem., **00,** 00 (2016).

INTRODUCTION

Functionally substituted 2-arylhydrazonals are versatile reagents, and their chemistry has recently received considerable interest [1–8]. In previous work from Elnagdi's laboratories [1,9–15] the 2-arylhydrazonals were prepared through condensation of methylketones **1** with dimethylformamide dimethylacetal (DMFDMA) **2** followed by coupling reaction of the formed enamines with aromatic diazonium salts. Although, this process is the most extensively utilized route for the preparation of 2-arylhydrazonals, it is energy consuming, quite expensive, multistage and environmentally non-friendly process. Trials to prepare the arylhydrazonal **4** through the reaction of arylhydrazones **5** with formaldehyde in ethanol gives compound **6** as side product[16]. In our contribution 2-arylhydrazonals **4** were prepared in excellent yields with good purity through the direct coupling of acetoacetaldehyde dimethylacetale **7** in aqueous media with aromatic diazonium salts (cf. Fig. 1). The reactivity of 2-arylhydrazonals of type **4** toward both electrophilic [1,17–19] and nucleophilic [20,21] reagents has been explored. We also report on the utility of the commercially available, inexpensive acetylacetaldehyde dimethyl acetal **7** as precursor to poly-substituted heteroaromatics of potential biological activity (Fig. 1).

RESULTS AND DISCUSSIONS

Coupling of acetylacetaldehyde dimethyl acetal **7** in aqueous media with aromatic diazonium salts afforded **4a** in excellent yield with good purity. The reaction of **4a** with ethyl cyanoacetate in the presence of an excess amount of ammonium acetate and a few drops of acetic acid afforded ethyl 2-amino-6-methyl-5-arylazonicotinate **12a**. The pathway of this reaction may involve initial condensation of **4a** with ethyl cyanoacetate to yield the hydrazono-enone **8** that then cyclized to generate the pyran-imine **10**. In the presence of a high concentration of ammonium acetate, pyran-imine **10** undergoes a Dimroth type rearrangement to yield **11** that then cyclized *via* elimination of water to yield **12a** (Scheme 1).

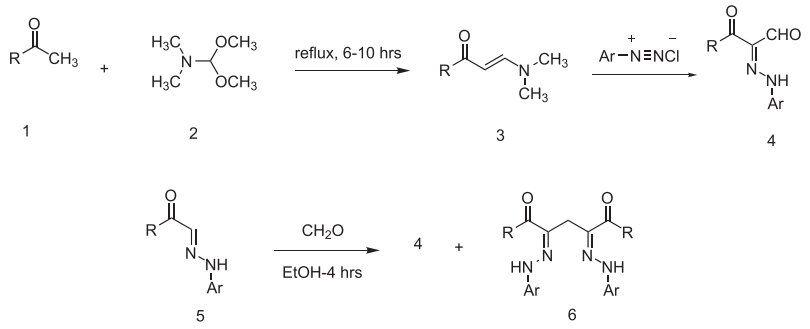
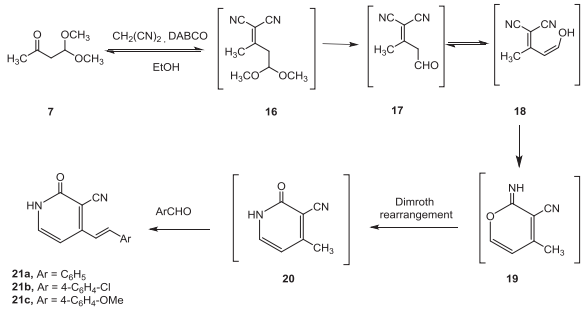


Figure 1. The synthetic strategies of 2-arylhydrazonals.

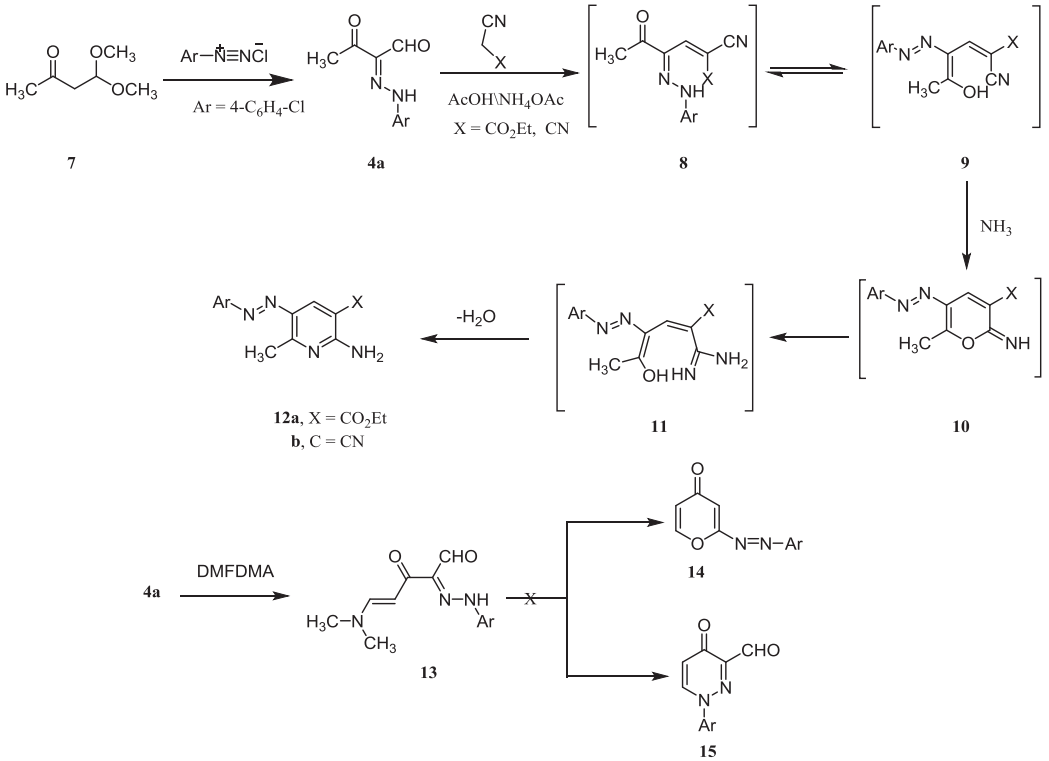
Similarly, reaction of **4a** with malononitrile in the presence of an excess amount of ammonium acetate and a few drops of acetic acid afforded **12b** (Scheme 1). Formation of **12a,b** is believed to follow the well-established previously published route [22]. The structures of products **12a,b** were confirmed based on their spectral and elemental analyses (see Experimental). Furthermore, the condensation of arylhydrazonal **4a** with DMFDMA afforded the hydrazonal-enaminone **13**. Trials to affect further cyclization of **13** into **14** or **15** did not succeed (Scheme 1).

A novel multicomponent synthesis of pyridine **21a–c** could be achieved *via* heating a mixture of **7**, malononitrile and aromatic aldehyde in the presence of DABCO. It is believed that acetoacetaldehyde dimethylacetale **7** initially

Scheme 2. Multicomponent synthesis of pyridine-2-one.



Scheme 1. Synthesis of arylazonicotinic acid derivatives.



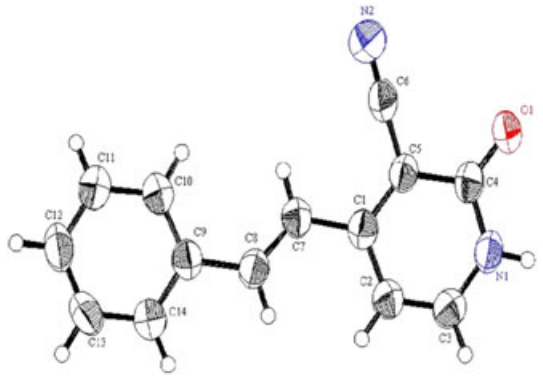
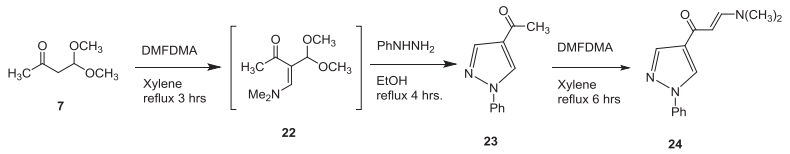


Figure 2. X-ray crystal structure of compound **21a**. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

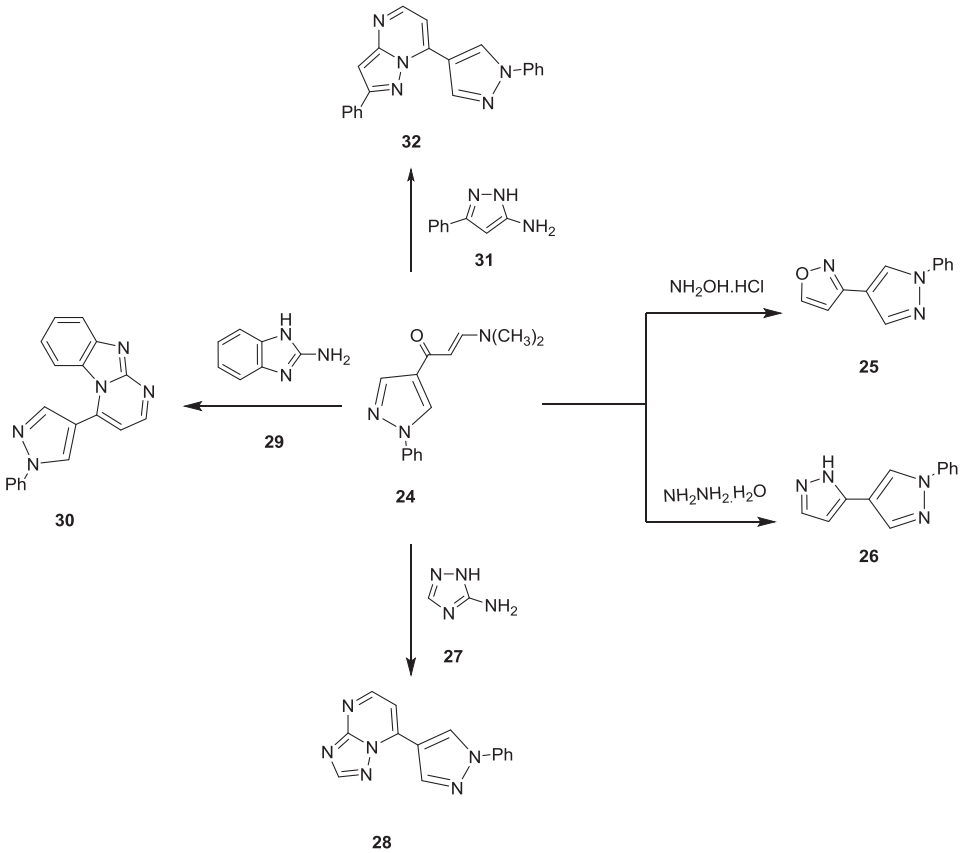
condensed with malononitrile to yield non-isolable product **16** that hydrolyzes into **17** followed by isomerization and cyclization to generate the pyran-2-imine **19**. Compound **19** underwent Dimroth rearrangement to yield **20** that then condensed subsequently with aromatic aldehydes to afford (*E*)-2-oxo-4-styryl-1,2-dihydropyridine-3-carbonitrile. The structure of **21a** was established *via* x-ray crystallography (CCDC 983759) (Scheme 2 and Fig. 2).

Condensation of compound **7** with DMFDMA in refluxing xylene afforded enaminone **22** that then reacted with phenylhydrazine to give 4-acetylprazole **23**. Further condensation of **23** with DMFDMA in xylene leads to the formation of 3-[(*E*)-3-*N*,*N*-dimethylamino)acryloyl]-1-phenyl-1*H*-pyrazole **24**. It is noteworthy to mention that compound **24** has not been reported hitherto. The structure of the enaminone **24** was confirmed by its elemental analysis and spectral data. For example, the ^{1}H NMR spectrum displayed two singlet at $\delta = 2.83$ and 3.09 ppm characteristic for the —N(CH$_3$)$_2$ group, two doublets at $\delta = 5.63$ and 7.86 ppm with coupling constant $J = 12$ Hz, assignable to the two olefinic protons (Scheme 3).

Scheme 3. Synthesis of 4-acetyl pyrazole.



Scheme 4. Reactivity of enaminone of 4-acetylpyrazole.



The pyrazolyl enaminone **24** can be used as scaffold for synthesis of a diversity of other heterocycles (Scheme 4). Thus treatment of enaminone **24** with hydroxylamine hydrochloride or hydrazine hydrate in refluxing ethanol resulted in formation of 3-(1*H*-pyrazol-4-yl)isoxazole **25** and 3,4′-bipyrazole derivatives **26**, respectively (Scheme 4). The reactivity of enaminone **24** toward some heterocyclic amines was also examined. Thus, reaction of **24** with 3-amino-1,2,4-triazole **27** in acetic acid under reflux afforded the respective 1,2,4-triazolo[1,5-*a*]pyrimidine derivative **28**. Similar reaction of **24** with 2-aminobenzimidazole **29** and 5-amino-3-phenyl-pyrazole **31** under the same reaction conditions yielded the respective benzimidazo[1,2-*a*]pyrimidine and pyrazole[1,5-*a*] pyrimidine derivatives **30** and **32**. The reaction of heterocyclic amines with enaminone proceeded first via Michael-type addition of exocyclic amino group of each amine used to the activated double bond of **24** with concurrent elimination of dimethyl amine and dehydrative cyclization [15,23,24]. The ^{1}H NMR spectrum of each product **28**, **30**, and **32** revealed two doublets signals in the regions at δ = 7.89–8.06 and 8.48–8.62 ppm assignable to the two vicinal protons of pyrimidine ring residue [25].

CONCLUSION

In conclusion, we have developed a simple and efficient method for the synthesis of 2-arylhydrazonals and acetylpyrazole utilizing acetoacetaldehyde dimethylacetale as starting material. The synthetic utility of these compounds as building blocks for novel arylazonicotinic acid as well as other functionally substituted heterocycles has also been investigated. These new classes of compounds are interesting both in their own right as unusual molecules and for their potential pharmacological and biological activities.

EXPERIMENTAL

General. Melting points are reported uncorrected and were determined with a Sanyo (Gallaenkamp) instrument. Infrared spectra were recorded using KBr pellets and a Jasco FT-IR 6300 instrument, and absorption bands are reported in cm^{-1}. ^{1}H- and ^{13}C NMR spectra were determined by using a Bruker DPX instrument at 400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR and either $CDCl_3$ or DMSO-d_6 solutions with TMS as internal standards. Chemical shifts are reported in δ (ppm). Mass spectra and accurate mass were measured using a GCMS DFS Thermo spectrometer with the EI (70 EV) mode. X-ray crystallographic structure determinations were performed by using Rigaku Rapid II and Bruker X8 Prospector single crystal X-ray Diffractometers. All reactions were monitored by using TLC with 1:1 ethyl acetate-petroleum ether as eluent and run the starting materials were completely consumed.

Synthesis of (E)-2-(2-(4-chlorophenyl)hydrazono)-3-oxobutanal 4a. A cold solution of aromatic diazonium salt (10 mmol) was prepared by adding a solution of sodium nitrite (10 mmol) to cold solution of 4-chloroaniline hydrochloride (10 mmol) with stirring. The resulting solution of diazonium salt was added to cold solution of **7** (1.32 g, 10 mmol), containing sodium acetate (0.5 g). The reaction mixture was stirred at rt for 30 min; the solid product formed was washed with water and crystallized from ethanol.

Yellow crystals, (88%), mp 137–139°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.50 (s, 3H, CH_3), 7.41–7.44 (m, 4H, Ar—H), 10.11 (s, 1H, CHO), 14.62 (br., 1H, NH, D_2O exchangeable). ^{13}C NMR (100 MHz, $CDCl_3$): 24.6, 117.5, 125.6, 129.8, 131.8, 139.6, 189.9, 197.0. MS, m/z (%) = 226 (M + 2, 12), 225 (M + 1, 13), 224 (M+, 45), 181 (10), 127 (100), 111 (30), 75 (10); *Anal*. Calcd for $C_{10}H_9ClN_2O_2$ (224.64): C, 53.47; H, 4.04; N, 12.47. Found: C, 53.36; H, 3.93; N, 12.33%.

General synthetic procedure, exemplified by ethyl 2-amino-6-methyl-5-p-chlorophenyl-azonicotinate 12a,b. A reaction mixture of 2-arylhydrazonal **4a** (2.24 g, 10 mmol), active methylenenitrile derivatives (ethyl cyanoacetate or malononitrile) (10 mmol), and ammonium acetate (3 g) in acetic acid (10 mL) was stirred at reflux for 30 min. The mixture was cooled to r.t. and then poured into ice-water. The crude product was collected by filtration and crystallized from ethanol.

Ethyl (E)-2-amino-5-((4-chlorophenyl)diazenyl)-6-methylnicotinate 12a. Brown solid (80%), mp 202–204°C. IR (KBr): 3345, 3310 (NH_2); 1700 (CO). ^{1}H NMR (400 MHz, DMSO-d6): δ 1.24 (t, 3H, *J* = 7.2 Hz, CH_3), 2.51 (s, 3H, CH_3), 4.29 (q, 2H, *J* = 7.2 Hz, CH_2), 7.32 (br., 2H, NH_2, D_2O exchangeable) 7.41 (d, 2H, *J* = 8.2 Hz, Ar—H), 7.77 (d, 2H, *J* = 8.2 Hz, Ar—H), 8.20 (s, 1H, Pyridine-H). ^{13}C NMR (100 MHz, DMSO-d6): δ 14.4, 24.96, 62.3, 115.6, 128.2, 129.3, 130.1, 133.9, 140.2, 141.8, 156.5, 162.9, 194.6. MS, m/z (%) = 320 (M + 2, 8), 319 (M + 1, 36), 318 (M+, 97), 277 (25), 248 (100), 207 (15), 111 (72), 75 (18); *Anal.* Calcd for $C_{15}H_{15}ClN_4O_2$ (318.76): C, 56.52; H, 4.74; N, 17.58. Found: C, 56.39; H, 4.59; N, 17.39%.

2-Amino-5-((4-chlorophenyl)diazenyl)-6-methylnicotinonitrile 12b. Brown solid (84%), mp 195–197°C. IR (KBr): 3342, 3275 (NH_2); 2201 (CN). ^{1}H NMR (400 MHz, DMSO-d6): δ 2.51 (s, 3H, CH_3), 7.51 (br., 2H, NH_2, D_2O exchangeable) 7.61 (d, 2H, *J* = 8.2 Hz, Ar—H), 7.79 (d, 2H, *J* = 8.2 Hz, Ar—H), 8.65 (s, 1H, Pyridine-H). ^{13}C NMR (100 MHz, DMSO-d6): δ 25.1, 114.0,

127.9, 128.4, 129.5, 134.3, 136.6, 139.7, 141.7, 156.8. MS, m/z (%) = 273 (M + 2, 8), 272 (M + 1, 33), 271 (M +, 100), 230 (10), 225 (100), 196 (8), 111 (45), 75 (15); *Anal*. Calcd for $C_{13}H_{10}ClN_5$ (271.71): C, 57.47; H, 3.71; N, 25.78 Found: C, 57.39; H, 3.65; N, 25.71%.

Synthesis of 2-(2-(4-chlorophenyl)hydrazono)-5-(dimethylamino)-3-oxopent-4-enal 13. A reaction mixture of hydrazonal **4a** (2.24 g, 10 mmol) and DMFDMA (2.64, 20 mmol) in toluene (5 mL) was heated under reflux for 8 h. The solid product that formed was collected and crystallized from ethanol. The reaction gave dark yellow crystal, yield (70%); mp 173–175°C. IR (KBr): 3322 (NH); 1660, 1698 (2CO). ^{1}H NMR (400 MHz, DMSO-d6): δ 2.64 (s, 3H, CH_3), 3.03 (s, 3H, CH_3), 6.26 (d, 1H, *J* = 12 Hz, CH), 7.07–7.65 (m, 4H, Ar—H), 7.73 (d, 1H, *J* = 12 Hz, CH), 8.89 (s, 1H, CHO), 10.32 (br., 1H, NH, D_2O exchangeable). ^{13}C NMR (100 MHz, DMSO-d6): δ 30.1, 36.2, 113.3, 118.7, 121.2, 125.8, 129.0, 129.7, 154.4, 162.8, 196.2. MS, m/z (%) = 279 (M^+, 10), 237 (35), 182 (80), 140 (100), 127 (93), 111 (55), 75 (25); *Anal*. Calcd for $C_{13}H_{14}ClN_3O_2$ (279.72): C, 55.82; H, 5.04; N, 15.02. Found: C, 55.65; H, 4.89; N, 14.86%.

Synthesis of 2-oxo-4-styryl-1,2-dihydropyridine-3-carbonitrile derivatives 21a–c. A mixture of 4,4-dimethoxybutan-2-one **7** (1.32 g, 10 mmol), aromatic aldehydes (10 mmol), and malononitrile (0.66 g, 10 mmol) in EtOH (25 mL) in the presence of DABCO (20%) was stirred at reflux for 3–4 h, cooled, and then poured into ice-water. The formed solid was collected by filtration and recrystallized from proper solvents.

(E)-2-oxo-4-styryl-1,2-dihydropyridine-3-carbonitrile 21a. Faint yellow crystals, (78%); mp. 299–300°C. IR (KBr): 3221 (NH); 2221 (CN); 1675 (CO). ^{1}H NMR (400 MHz, DMSO-d_6): δ = 4.49 (br., 1H, NH, D_2O exchangeable) 5.15 (d, 1H, *J* = 4 Hz, pyridine-H), 7.23 (d, 1H, *J* = 16 Hz, CH=), 7.47–7.75 (m, 5H, Ph—H), 7.62 (d, 1H, *J* = 16 Hz, CH=), 8.96 (d, 1H, *J* = 4 Hz, pyridine-H). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 105.7, 112.5, 114.3, 123.2, 127.8, 128.2, 129.2, 130.8, 135.0, 142.3, 157.4, 160.2, MS, m/z (%) = 222 (M+, 60), 196 (100), 178 (20), 166 (10), 117 (5), 77 (10), 66 (15); *Anal*. Calcd. for $C_{14}H_{10}N_2O$ (222.24): C, 75.66; H, 4.54; N, 12.60. Found: C, 75.53; H, 4.49; N, 12.54%.

(E)-4-(4-chlorostyryl)-2-oxo-4-styryl-1,2-dihydropyridine-3-carbonitrile 21b. Yellow crystals, (78%); mp. 310–312°C. IR (KBr): 3223 (NH); 2220 (CN); 1675 (CO). ^{1}H NMR (400 MHz, DMSO-d_6): δ = 4.49 (br., 1H, NH, D_2O exchangeable) 5.35 (d, 1H, *J* = 4 Hz, pyridine-H), 7.23 (d, 1H, *J* = 16 Hz, CH=), 7.43 (d, 2H, *J* = 8.4 Hz, Ar—H) 7.72 (d, 2H, *J* = 8.4 Hz, Ar—H), 7.62 (d, 1H, *J* = 16 Hz, CH=), 8.90 (d, 1H, *J* = 4 Hz, pyridine-H). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 105.7, 112.5, 114.3, 123.2, 127.8, 128.2, 129.2, 130.8, 135.0, 142.3, 157.4, 160.2, MS, m/z (%) = 258 (M + 2, 6), 257 (M + 1, 16), 256 (M+, 55), 220 (20), 196 (100), 178 (20), 166 (10), 117 (5), 77 (10), 66 (15); *Anal*. Calcd. for $C_{14}H_9ClN_2O$ (256.69): C, 65.51; H, 3.53; N, 10.91. Found: C, 65.47; H, 3.49; N, 10.88%.

B:(E)-4-(4-methoxystyryl)-2-oxo-1,2-dihydropyridine-3-carbonitrile 21c. **17c**. Yellow crystals, (78%); mp. 289–290°C. IR (KBr): 3226 (NH); 2219 (CN); 1670 (CO). ^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.53 (s, 3H, CH_3O) 4.52 (br., 1H, NH, D_2O exchangeable) 5.15 (d, 1H, *J* = 4 Hz, pyridine-H), 7.23 (d, 1H, *J* = 16 Hz, CH=), 7.47–7.75 (m, 4H, Ph—H), 7.62 (d, 1H, *J* = 16 Hz, CH=), 8.88 (d, 1H, *J* = 4 Hz, pyridine-H). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 53.2, 105.3, 112.5, 114.3, 115.2, 123.2, 127.8, 130.8, 135.0, 142.3, 158.2, 159.4, 162.3, MS, m/z (%) = 252 (M+, 62), 221 (45), 196 (100), 178 (22), 166 (11), 117 (8), 77 (15), 66 (18); *Anal*. Calcd. for $C_{15}H_{12}N_2O_2$ (252.27): C, 71.42; H, 4.79; N, 11.10. Found: C, 71.36; H, 4.76; N, 11.08%.

Synthesis of 1-(1-phenyl-1H-pyrazol-4-yl)ethan-1-one 23. A mixture of 4,4-dimethoxybutan-2-one **7** (1.32 g, 10 mmol) and DMFDMA (1.19 g, 10 mmol) in xylene (25 mL) was reflux for 3 h, cooled and then poured into ice-water. The formed yellowish oil was extracted by dichloromethane then refluxed with phenylhydrazine (1.08 g, 10 mmol) in ethanol (25 mL) for 3 h, cooled, and then poured into ice-water. The formed product was collected by filtration and recrystallized from EtOH to give faint yellow crystals, (78%); mp. 125–126°C. IR (KBr): 1689 (CO). ^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.49 (s, 3H, CH_3), 7.37–7.92 (m, 5H, Ph—H), 8.17 (s, 1H, pyrazole-H), 9.18 (s, 1H, pyrazole-H). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 28.4, 119.5, 125.8, 127.8, 130.1, 131.5, 139.4, 141.6, 192.2, MS, m/z (%) = 186 (M+, 45), 171 (100), 116 (20), 77 (25); *Anal*. Calcd. for $C_{11}H_{10}N_2O$ (186.21): C, 70.95; H, 5.41; N, 15.04. Found: C, 71.04; H, 5.33; N, 15.18%.

Synthesis of (E)-3-(dimethylamino)-1-(1-phenyl-1H-pyrazol-4-yl)prop-2-en-1-one 24. A mixture of 4-acetyl-1-phenyl-1*H*-pyrazole **23** (0.93 g, 5 mmol) and DMFDMA (3 mL) was refluxed for 6 h in xylene (30 mL). The solid that precipitated was collected and crystallized from EtOH to yield yellow crystals, (78%); mp. 142–144°C. IR (KBr): 1659 (CO). ^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.83 (s, 3H, CH_3), 3.09 (s, 3H, CH_3), 5.63 (d, 1H, *J* = 16 Hz, —CH=) 7.38–7.96 (m, 5H, Ph—H), 7.86 (d, 1H, *J* = 16 Hz, =CH—) 8.17 (s, 1H, pyrazole-H), 8.98 (s, 1H, pyrazole-H). MS, m/z (%) = 241 (M+, 38), 186 (19), 185 (25), 170 (100), 116 (20), 75 (35); *Anal*. Calcd. for $C_{14}H_{15}N_3O$ (241.29): C, 69.69; H, 6.27; N, 17.41. Found: C, 69.65; H, 6.19; N, 17.36%.

Synthesis of 3-(1-phenyl-1H-pyrazol-4-yl)isoxazole 25. To a solution of **24** (1.2 g, 5 mmol) in absolute ethanol was added hydroxylamine hydrochloride (0.35 g, 5 mmol) and

anhydrous potassium carbonate (0.5 g, 5 mmol). The reaction mixture was refluxed for 6 h. The precipitate formed upon cooling was filtered off and crystallized from ethanol to yield yellow crystals, (80%); mp. 150–152°C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 6.79 (d, 1H, *J* = 10 Hz, isoxazole-H), 7.18 (d, 1H, *J* = 10 Hz, isoxazole-H), 7.38–7.92 (m, 5H, Ph—H), 8.12 (s, 1H, pyrazole-H), 8.68 (s, 1H, pyrazole-H). MS, m/z (%) = 211 (M+, 55), 167 (100), 166 (53), 115 (22), 70 (30); *Anal*. Calcd. for $C_{12}H_9N_3O$ (211.22): C, 68.24; H, 4.29; N, 19.89. Found: C, 68.19; H, 4.23; N, 19.81%.

Synthesis of 1′-phenyl-1′H,2H-3,4′-bipyrazole 26. To a solution of **24** (1.2 g, 5 mmol) in absolute ethanol was added hydrazine hydrate (5 mL, 10 mmol). The reaction mixture was refluxed for 5 h. The precipitate formed upon cooling was filtered off and crystallized from ethanol to give pale yellow crystals, (80%), mp. 185–187°C. IR (KBr): 3295 (NH). ^{1}H NMR (400 MHz, DMSO-d_6): δ = 6.93 (d, 1H, *J* = 10 Hz, pyrazole-H), 7.23–7.82 (m, 5H, Ph—H), 7.88 (d, 1H, *J* = 10 Hz, pyrazole-H), 8.13 (s, 1H, pyrazole-H), 8.58 (s, 1H, pyrazole-H), 10.24 (s, 1H, NH, D_2O exchangeable), MS, m/z (%) = 211 (M + 1, 14), 210 (M+, 100), 170 (75), 166 (53), 115 (31), 75 (55), 70 (50); *Anal*. Calcd. for $C_{12}H_{10}N_4$ (210.23): C, 68.56; H, 4.79; N, 26.65. Found: C, 68.51; H, 4.71; N, 26.59%.

General method for synthesis of compounds 28, **30**, and **32**. To a solution of **24** (1.2 g, 5 mmol) in acetic acid (25 mL) was added the appropriate heterocyclic amine (**27**, **29**, and **31**) (5 mmol). The reaction mixture was refluxed for 5 h then cooled. The solid that formed was collected and crystallized from proper solvents.

7-(1-Phenyl-1H-pyrazol-4-yl)-[1,2,4]triazolo[1,5-a]pyrimidine 28. Yellow crystals, (76%), mp. 173–175°C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.23–7.92 (m, 5H, Ph—H), 8.06 (d, 1H, *J* = 6 Hz, pyrimidine-H), 8.17 (s, 1H, pyrazole-H), 8.38 (s, 1H, pyrazole-H), 8.59 (d, 1H, *J* = 6 Hz, pyrimidine-H), 8.76 (s, 1H, triazole-H), MS, m/z (%) = 263 (M + 1, 19), 262 (M+, 32), 216 (100), 170 (60), 165 (53), 111 (31), 75 (55), 70 (50); *Anal*. Calcd. for $C_{14}H_{10}N_6$ (262.27): C, 64.11; H, 3.84; N, 32.04. Found: C, 64.05; H, 4.06; N, 32.12%.

4-(1-Phenyl-1H-pyrazol-4-yl)benzo[4,5]imidazo[1,2-a] pyrimidine 30. Pale yellow crystals, (73%), mp. 165–167°C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.33–7.86 (m, 9H, Ar—H), 7.89 (d, 1H, *J* = 6 Hz, pyrimidine-H), 8.17 (s, 1H, pyrazole-H), 8.36 (s, 1H, pyrazole-H), 8.48 (d, 1H, *J* = 6 Hz, pyrimidine-H), 8.91 (s, 1H, triazole-H), MS, m/z (%) = 312 (M + 1, 19), 311 (M+, 32), 236 (11), 195 (100), 170 (55), 165 (50), 111 (31), 75 (55), 70 (50); *Anal*. Calcd. for $C_{19}H_{13}N_5$ (311.34): C, 73.30; H, 4.21; N, 22.49. Found: C, 73.26; H, 4.19; N, 22.47%.

2-Phenyl-7-(1-phenyl-1H-pyrazol-4-yl)pyrazolo[1,5-a] pyrimidine 32. Yellow crystals, (78%), mp. 195–197°C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.38–7.87 (m, 10H, Ar—H), 7.92 (d, 1H, *J* = 6 Hz, pyrimidine-H), 8.12 (s, 1H, pyrazole-H), 8.33 (s, 1H, pyrazole-H), 8.62 (d, 1H, *J* = 6 Hz, pyrimidine-H), 8.96 (s, 1H, triazole-H), MS, m/z (%) = 338 (M + 1, 30), 337 (M+, 54), 262 (100), 170 (60), 165 (53), 111 (31), 75 (55), 70 (50); *Anal*. Calcd. for $C_{21}H_{15}N_5$ (337.38): C, 74.76; H, 4.48; N, 20.76. Found: C, 74.69; H, 4.43; N, 20.71%.

Acknowledgments. The authors express deep sense of gratitude to the Prof. M. H. Elnagdi for his keen interest and constant encouragement.

REFERENCES AND NOTES

[1] Makhseed, S.; Hassaneen, H. M. E.; Elnagdi, M. H. Zeitschrift Für Naturforsch B 2007, 62, 529.
[2] Hassaneen, H. M.; Elwan, N. M.; Hassaneen, H. M. Synth Commun 2006, 32, 3047.
[3] Elwan, N. M.; Hassaneen, H. M.; Hassaneen, H. M. Heteroat Chem 2002, 13, 585.
[4] Hassaneen, H. M.; Abdallah, T. A.; Abdelhadi, H. A.; Hassaneen, H. M. E.; Pagni, R. M. Heteroat Chem 2003, 14, 491.
[5] Hassaneen, H. M. E.; Hassaneen, H. M.; Elnagdi, M. H. Zeitschrift Für Naturforsch B 2004, 59, 1132.
[6] Abdelhamid, I. A.; Nasra, M. A.; Elnagdi, M. H. Synlett 2009 3237.
[7] Al-awadi, N. A.; Ibrahim, M. R.; Abdelhamid, I. A.; Elnagdi, M. H. Tetrahydron 2008, 64, 8202.
[8] Abdelhamid, I. A.; Darwish, E. S.; Nasra, M. A.; Abdel-gallil, F. M.; Fleita, D. H. Arkivoc 2008, 2008, 117.
[9] Mohamed Al-Mousawi, S. Curr Org Chem 2016, 15, 3503.
[10] Al-Shiekh, M. A.; Salah El-Din, A. M.; Hafez, E. A.; Elnagdi, M. H. J Heterocycl Chem 2004, 41, 647.
[11] Abdallah, S. O.; Metwally, N. H.; Anwar, H. F.; Elnagdi, M. H. J Heterocycl Chem 2005, 42, 781.
[12] Al-Omran, F.; Khalik, M. M. A.; Abou-Elkhair, A.; Elnagdi, M. H. Synthesis (Stuttg) 1997, 1997, 91.
[13] Al-Awadi, N. A.; Elnagdi, M. H.; Ibrahim, Y. A.; Kaul, K.; Kumar, A. Tetrahedron 2001, 57, 1609.
[14] Almazroa, S.; Elnagdi, M. H.; El-Din, A. M. S. J Heterocycl Chem 2004, 41, 267.
[15] Ghozlan, S. A. S.; Abdelhamid, I. A.; Gaber, H.; Elnagdi, M. H. J Chem Res 2004 789.
[16] Al-Mousawi, S. M.; Moustafa, M. S.; Elnagdi, M. H. Heterocycles 2008, 75, 2201.
[17] AL-Saleh, B.; Makhseed, S.; Hassaneen, H. M.; Elnagdi, M. H. Synthesis (Stuttg) 2006, 2006, 59.
[18] Hassaneen, H. M. E.; Awad, E. M.; Hassaneen, H. M. Zeitschrift Für Naturforsch B 2007, 62, 111.
[19] Hassaneen, H. M. E. Synth Commun 2007, 37, 3579.
[20] Hassaneen, H. M. E. Arkivoc 2007, 2007, 154.
[21] Hassaneen, H. M. E.; Pagni, R. M. Zeitschrift Für Naturforsch B 2010, 65, 1491.
[22] Al-Mousawi, S. M.; Moustafa, M. S.; Abdelhamid, I. A.; Elnagdi, M. H. Tetrahedron Lett 2011, 52, 202.
[23] Abdelhamid, I. A.; Ghozlan, S. A. S.; Kolshorn, H.; Meier, H.; Elnagdi, M. H. Heterocycles 2007, 71, 2627.
[24] Ghozlan, S. A. S.; Abdelhamid, I. A.; Elnagdi, M. H.; Gaber, H. M. J Heterocycl Chem 2005, 42, 1185.
[25] Ho, Y.-W. J Chinese Chem Soc 2007, 54, 1075.