α-Enones in heterocyclic synthesis, Part I. Classical synthetic and environmentally friendly synthetic approaches to alkyl and acyl azoles and azines

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The utility of 1-*N,N*-dimethylaminopent-1-en-3-one and 1-(4-acetylphenyl)-3-dimethyl aminopropenone in the synthesis of several new azolotriazine, pyrazolo[3,4-*d*]pyridazine, isoxazolo[3,4-*d*]pyridazine, azolopyrimidine and pyridine derivatives by conventional heat and also on microwave irradiation, is reported.

Keywords: fused 1,2,4-triazines, 1,2,4-triazoles, pyrazoles, isoxazoles, pyridazines, pyrimidines, microwave heating

Enaminones are versatile reagents and their chemistry has recently received considerable interest.[1] Having multiple electrophilic and nucleophilic centers, enaminones react with both electrophiles and nucleophiles.[1-3] Moreover, enaminones also undergo a variety of cycloaddition and self condensation reactions.[1,4,5]

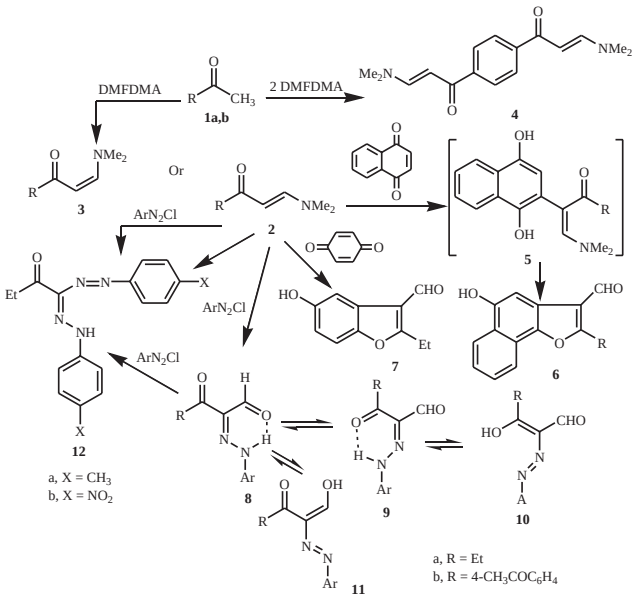
In previous work from our laboratories we have explored the chemistry of enaminones with aryl moieties.[4-11] In conjunction with this work and because of recent interest in enaminone chemistry we report here the synthesis of two enaminone derivatives with acyl moiety, and a study of their chemical behaviour, which was found to differ in some respects from previously reported behaviour. Moreover, where possible we present a comparison of the results of conventional and microwave heating. The utility of microwave heating in synthesis is now well recognised "green technology".[12,13]

Results and discussion

Heating DMFDMA with an excess of 2-butanone (**1a**) (R = Et) under reflux for 24 hours, then subsequent evaporation of excess of 2-butanone, afforded a yellow oily product of molecular formula $C_7H_{13}NO$. The ^{1}H NMR spectrum established the structure as (*E*)-1-*N,N*-dimethylaminopent-1-en-3-one **2a**, and ruled out the (*Z*)-isomer **3a**, since it showed two olefinic proton signals at δ 5.85 and 7.5 ppm with J = 16 Hz which is a typical value for *trans* coupled protons in 1,2-disubstituted olefins (Scheme 1).

Similarly, 1-(4-acetylphenyl)ethanone (1,4-diacetylbenzene) (**1b**) condensed with DMFDMA to yield a product for which the *trans* structure **2b** was assigned based on ^{1}H NMR which revealed two *trans* coupled olefinic protons (δ 5.9, 7.3 ppm, J = 14 Hz, for H-2 and H-3 respectively). The formation of 1-(4-acetylphenyl)-3-(dimethylamino)propenone **2b** using the literature[3] procedure required reflux for 6 hours and went in 65% yield, while microwave irradiation dramatically reduced the reaction time to 3 minutes with an improvement in the isolated yield (96%) (*cf.* Table 1). Condensation of **1b** with two moles of DMFDMA in dry toluene yielded the 3-dimethylamino-1-[4-(3-dimethylaminoacryloyl)phenyl] propenone **4**.

Compound **2a,b** reacted with 1,4-naphthoquinone to yield products of addition and dimethylamine elimination. These can be assigned structures **6**, formed through the intermediate Michael adducts **5**. The ^{1}H NMR of the reaction products revealed the presence of formyl signals, at δ 9.1 ppm (**6a**), 8.7 ppm (**6b**). Thus structures **6a,b** were assigned to the reaction products. Similar to its behaviour toward 1,4-naphthoquinone, compound **2a** also reacted with 1,4-benzoquinone to yield **7** (δ_{CHO} 8.9 ppm). (Scheme 1)



8	R	Ar	8	R	Ar
a	Et	C_6H_5	**e**	4-$CH_3COC_6H_4$	C_6H_5
b	Et	4-$CH_3C_6H_4$	**f**	4-$CH_3COC_6H_4$	4-$NO_2C_6H_4$
c	Et	4-$NO_2C_6H_4$	**g**	4-$CH_3COC_6H_4$	4-$CH_3OC_6H_4$
d	Et	4-$CH_3OC_6H_4$	**h**	4-$CH_3COC_6H_4$	2-$CH_3OC_6H_4$

Scheme 1

Similar to reported behaviour of enaminones, compound **2a**, coupled with aromatic diazonium chloride in the presence of ethanolic sodium acetate to yield the corresponding coupling product that are assumed to exist as an equilibrium mixture of the hydrazone structures **8** and **9** rather than the azo-enol structures **10** or **11,** based on the ^{1}H NMR spectrum. The ^{1}H NMR revealed that, at least in DMSO solution, it exists as a mixture of the *E* and *Z* hydrazone forms **8** and **9**. So, ^{1}H NMR showed two low field signals for formyl protons at δ 9.5 and δ 9.9 ppm, and the total integration of the two peaks corresponded to one proton. Consequently both were considered to be the formyl proton, the lower field signal was assigned to the *E* form which should be further deshielded with the formyl moiety, and the higher field signal was assigned for the formyl proton in *Z* form. From relative intensities of the two signals the ratio of *E* to *Z* form is calculated as 2:1. The NH hydrazone protons appears also at different fields; the lower field signal corresponds to NH of the *E* form and the higher one for NH of the *Z* form as the relative intensities of the two signals is 2:1 (Scheme 1).

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Compound **2b** also coupled readily with aromatic diazonium salts to yield a product that is assumed to exist also as an equilibrium mixture of the *E*-form **8** and *Z*-form **9** rather than potential alternative azo structures **10** or **11**, based on spectral data.

When **2a** was treated with excess of *p*-toluenediazonium chloride the bisazo compound **12a** was formed in a Japp-Klingemann type reaction which proceeds via intermediate formation of **8b**. Product **12a** was recrystallised and its structure was solved by X-ray diffraction (Fig. 1). Compound **12b** could also be prepared by coupling **8c** with *p*-nitrophenyldiazonium chloride (Scheme 1). The structure of **12b** was further proved by an alternative synthesis. Thus compound **8c** couples smoothly with *p*-nitrophenyldiazonium chloride to give the corresponding product **12b**. Compound **12b** prepared by this route was found to be identical in all respects with that prepared as described before. Note that **1a,c** afford only monocoupling products.[1]

Compounds **2a,b** coupled also with diazotised heterocyclic amines to yield azolotriazines. It has been reported that the diazotised aminopyrazole **13a** exists in equilibrium with an isolable diazobetaine **13b**. Thus our inability to isolate an acyclic hydrazone intermediate from this reaction may indicate that these reagents react via a direct 4+2 cycloaddition mechanism to the activated double bond in **2a,b**. Thus compound **2a,b** coupled with diazotised 3(5)-phenyl-5(3)-aminopyrazole **13** to yield the pyrazolo[5,1-*c*][1,2,4]triazines **15a,b** in good yields. It is thus believed that in fact **15** is formed via direct 4+2 cycloaddition (Scheme 2).

Also, coupling **2b** with diazotised 3-amino-1*H*-1,2,4-triazole and diazotised 2-aminobenzimidazole afforded the triazolo[3,4-*c*][1,2,4]triazine derivative **16** and [1,2,4]triazino[4,3-*a*]benzimidazole **17** respectively, in good yields (Scheme 2).

1,3-Dipolar cycloaddition of some nitrile imines **19** and nitrile oxides **22** to 1-*N*,*N*-dimethylaminopent-1-en-3-one (**2a**) and 1-(4-acetylphenyl)-3-dimethylaminopropenone (**2b**) was investigated. The double bond in compounds **2a,b** is electron rich and can thus undergo 1,3-dipolar cycloadditions. The reaction of nitrile imines **19a,b**, generated *in situ* by the action of triethylamine on hydrazonyl chlorides **18**, with enaminones in dry benzene afforded only one isolable product in each case. These were assigned the pyrazole structures **20a,b**. Structure **20b** could be established for the reaction product based on formation of the pyrazolo[3,4-*d*]pyridazines **21b** on reaction with hydrazine hydrate. Treatment of **2b** with nitrile oxide **22** afforded **23**, which with hydrazine hydrate formed the isoxazolo[3,4-*d*]pyridazines **24**.

Microwave irradiation was used to facilitate this cycloaddition and also to prepare the 1,3-dipole *in situ*. The cycloaddition of **19a** with **2b** under solvent-free conditions produced improved yields of **20c** and decreased the reaction times (*cf.* Experimental).

Compound **2a,b** reacted with glycine and with hippuric acid **25a,b** in refluxing acetic anhydride to yield the pyranones **28**. It is believed that **25** is first cyclised to oxazolone **26** and subsequent reaction of the latter with **2a,b** yielded **27** that rearranges to **28**. This demonstrates the general nature of the recent extension of Kepe's pyranone synthesis to reaction of hippuric acid with enaminones.[1] Attempted condensation of **28b** with hydrazine hydrate to yield the hydrazone resulted in formation of the *N*-aminopyridine derivative **29** (Scheme 3). Compound **28a** was prepared in 98% yield after 8 minutes under microwave irradiation conditions, while under thermal conditions 70% yield was obtained after refluxing for 4 hours (*cf.* Table 1).

Similar to recently reported behaviour of enaminones, aminopyrazole reacted with **2a** in refluxing ethanol yielding pyrazolo[1,5-*a*]pyrimidine **31a** via the intermediacy of acyclic **30** which could not be trapped in pure form. The ^{1}H NMR spectrum of **31a** revealed a pyrazole proton at δ 6.9 ppm and pyrimidine protons at δ 7.2 and 8.5 ppm, while its isomeric

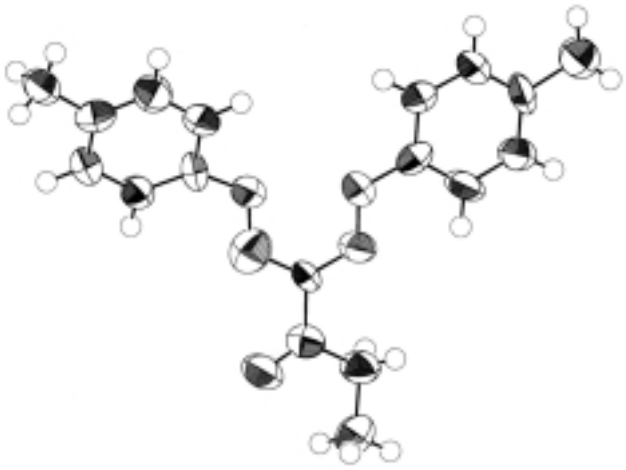
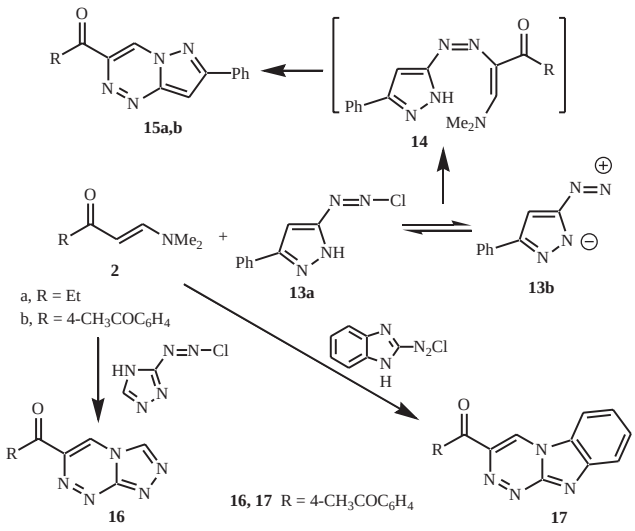
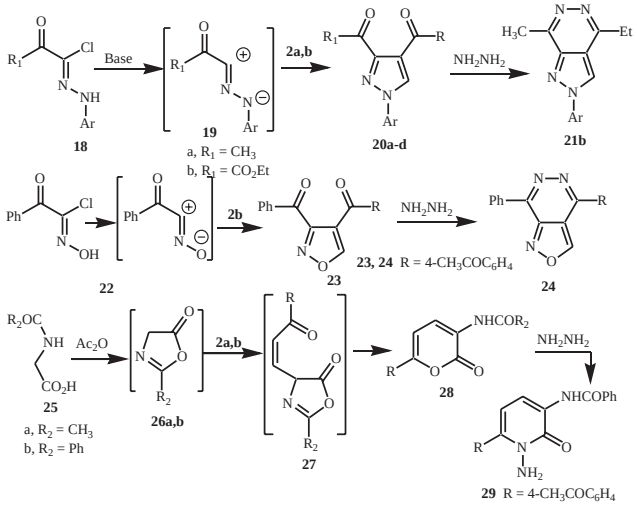


Fig. 1 Molecular structure of **12a**



Scheme 2



20	R	R_1	Ar	28	R	R_2
a	Et	CH_3	C_6H_5	**a**	Et	C_6H_5
b	Et	CH_3	4-$CH_3C_6H_4$	**b**	4-$CH_3COC_6H_4$	CH_3
c	4-$CH_3COC_6H_4$	CH_3	C_6H_5	**c**	4-$CH_3COC_6H_4$	C_6H_5
d	4-$CH_3COC_6H_4$	CO_2Et	4-$CH_3C_6H_4$			

Scheme 3

Table 1 Comparison between reaction times and yields obtained from conventional and microwave heating

	Conventional Δ		Microwave Δ	
Compd	Yield/%	Time/min	Yield/%	Time/min
2b	65	360	96	3
20a	69	480	95	10
20c	82	480	90	10
28a	70	240	98	8
31a	75	360	89	10
31b	70	30	95	20
32a	80	360	90	10
32b	80	30	93	15
33	78	360	88	10
37	70	180	93	6

structure should have shown these signals at lower field (Scheme 4). Also, compound **2a** condensed with aminotriazole to give the 7-ethyltriazolo[1,5-*a*]pyrimidine **32a** based on its ^{1}H NMR spectrum. Similarly compound **2b** condensed with aminopyrazole and aminotriazole yielding the pyrazolo[1,5-*a*]pyrimidine **31b** and triazolo[1,5-*a*]pyrimidine **32b** respectively. Compound **2a** also condensed with 2-aminobenzimidazole yielding 2-ethylpyrimido[1,2-*a*] benzimidazole **33**. Reaction of **2b** with guanidine resulted in the formation of 1-[4-(2-aminopyrimidine-4-yl) phenyl] ethanone **34** (Scheme 4). Microwave irradiation has been used to improve reaction yields of **2a,b** with different types of aminoheterocycles to produce azolopyrimidine derivatives **31a,b, 32a,b** and **33**.

Enaminone **2b** underwent self-condensation on reflux in acetic acid yielding the 1,3,5-trisubstituted benzene derivative **37**, in good yield.[4,5] The reaction takes place by condensation of three moles of the enaminone **2b** to form the intermediate **36** which loses 3 moles of dimethylamine, aromatizes and affords the final product **37.** Reflux of **2b** in acetic acid in the presence of ammonium acetate afforded the pyridine derivative **38** most likely via intermediacy of **35** (Scheme 4).[5] The self-condensation of **2b** to **37** was achieved in very high yield (93%) in 6 minutes by irradiation with microwaves.

Compound **2b** reacted with acetylacetone in acetic acid in the presence of ammonium acetate to yield **39**. The structure **39** was consistent with the elemental analysis and spectral data.

Experimental

All melting points were measured on Gallenkamp electro-thermal melting point apparatus. The microwave oven was type SJO 390 W. IR spectra were recorded as KBr pellets on a Pye Unicam SP 3-300 spectrophotometer. ^{1}H NMR spectra were recorded in deuterated dimethylsulfoxide (DMSO-d_6) or deuterated chloroform ($CDCl_3$) at 200 or 300 MHz on a Varian Gemini NMR spectrometer using tetramethylsilane (TMS) as an internal reference and shifts 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.

l-N,N-Dimethylamino-pent-1-en-3-one (**2a**)**:** A mixture of 2-butanone (**1a**) (7.21g,10mol) with dimethylformamide dimethylacetal (DMFDMA) (11.9g,10mol) was heated under reflux for 24h, then the volatile components were evaporated and the remaining oil was used without further purification. Yield (85 %); ^{1}H NMR (DMSO-d_6): δ 1.3 (t, 3H, CH_3), 3.9 (q, 2H, CH_2), 5.85 (d, 1H, H-3), 7.5 (d, 1H, H-4), MS; *m/z* 127 (M^+). $C_7H_{13}NO$ (127.17).

1-(4-Acetylphenyl)-3-dimethylamino-propenone (2b):*Procedure A:* a mixture of 1-(4-acetylphenyl)ethanone (1b) (1.27g, 10mmol) with dimethylformamide dimethylacetal (DMFDMA) (1.19g, 10 mmol) in dry toluene (50 ml) was heated under reflux for 6h, then left to cool to room temperature. The orange solid product so-formed was collected by filtration, and recrystallised from ethanol.

Procedure B: a mixture of 1-(4-acetylphenyl)ethanone(**1b**) (1.27g, 10mmol) with DMFDMA (1.19g, 10 mmol) was irradiated in a domestic microwave oven for 3 minutes. The resulting product was washed with ethanol and crystallised from ethanol to afford 96% yield. M.p. 146 °C; orange crystals. ^{1}H NMR (DMSO-d_6): δ 2.47 (s, 6H, $2CH_3$), 2.55 (s, 3H, CH_3), 5.9 (s, 1H, H-2), 7.3 (s, 1H, H-3), 7.9–8.05 (m, 4H, Ar–H). MS: *m/z* 217 (13 %, M^+). Found: C, 71.69; H, 7.01; N, 6.35. $C_{13}H_{15}NO_2$ (217.26) requires C, 71.87; H, 6.96; N, 6.45 %.

3-Dimethylamino-1-[4-(3-dimethylaminoacryloyl)phenyl]propenone (**4**): To 1-(4-acetylphenyl)-3-dimethylaminopropenone (2b)(2.17g, 10 mmol) In dry toluene was added DMFDMA (1.19g, 10mmol). The reaction mixture was then heated under reflux for 4h.The solid product, so formed, was isolated by filtration, Recrystallisation from ethanol yielded yellow crystals. Yield (75%); m.p. 265 °C; yellow crystals from ethanol, ^{1}H NMR (DMSO-d_6): δ 2.47(s, 12H, $4CH_3$), 5.8(d, 2H, H-2), 7.2(d, 2H, H-3), 8.0(m,4H, Ar–H). MS; *m/z* 273(20.1%) (M^++1). Found: C, 70.68; H, 7.32; N, 10.31. $C_{16}H_{20}N_2O_2$ (272.34) requires C, 70.56; H, 7.40; N, 10.29 %.

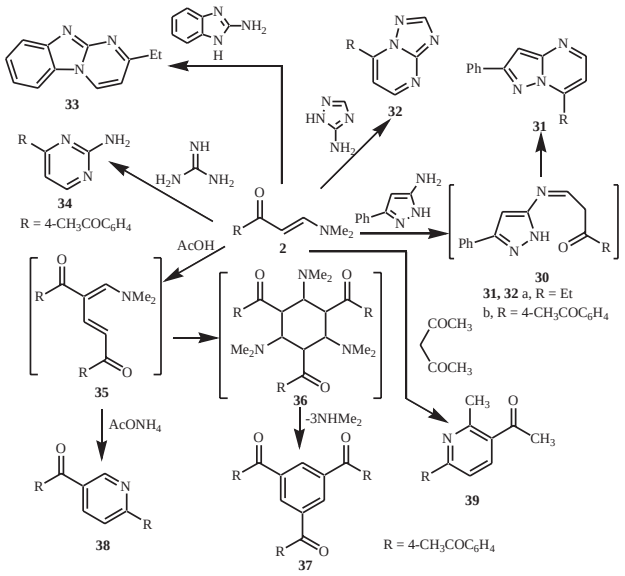
General procedure for the preparation of compounds **6a,b,7**: To a stirred solution of l-*N,N*-dimethylaminopent-1-en-3-one (**2a**) (1.27g, 10 mmol) or 1-(4-acetylphenyl)-3-dimethyaminopropenone (**2b**) (2.17g, 10 mmol) in acetic acid (30 ml), each of *p*-benzoquinone and or naphthoquinone (10 mmol) was added. Stirring was continued overnight at room temperature. The reaction mixture was evaporated *in vacuo*, and the solid product obtained was filtered off and recrystallised from a suitable solvent.

2-Ethyl-5-hydroxynaphtho[1,2-b]furan-3-carbaldehyde (**6a**): yield 85%; colourless crystals from ethanol/dioxan. ^{1}H NMR (DMSO-d_6): δ 1.2 (t, 3H, CH_3), 2.6 (q, 2H, CH_2), 6.8 (s, 1H, H-4), 7.3–7.7 (m, 4H, Ar–H), 9.1 (s, 1H, CHO), 9.5 (br s, 1H, OH). MS: *m/z* 240 (50 %, M^+). Found: C, 75.00; H, 4.99. $C_{15}H_{12}O_3$ (240.25) requires C, 4.99; H, 5.03 %.

2-(4-Acetylphenyl)-5-hydroxynaphtho[1,2-b]furan-3-carbaldehyde (**6b**): yield 70 %; m.p. 279 °C; yellow crystals from ethanol/dioxan, IR; ν_{max}/cm^{-1} 3455 br (OH), 1685, 1612 (CO) cm^{-1} ^{1}H NMR (DMSO-d_6): δ 2.6 (s, 3H, CH_3), 7.6–8.2 (m, 9H, Ar–H), 7.64 (s, 1H, H-4), 8.7 (s, 1H, CHO), 10.3 (s, 1H, OH). MS: *m/z* 330 (100 %, M^+). Found: C, 76.51; H, 4.20. $C_{21}H_{14}O_4$ (330.34) requires C, 76.36; H, 4.2 %.

2-Ethyl-5-hydroxybenzo[b]furan-3-carbaldehyde (**7**): yield 80 %; m.p. 225 °C; brown crystals from ethanol/DMF. ^{1}H NMR (DMSO-d_6): δ 1.1 (t, 3H, CH_3), 2.9 (q, 2H, CH_2), 6.8 (d, 1H, H-6), 7.4 (d, 1H, H-7), 7.9 (s, 1H, H-4), 8.9 (s, 1H, CHO), 9.4 (br s, 1H, OH). MS; *m/z* 190 (20 %, M^+). Found: C, 69.32; H, 5.30. $C_{11}H_{10}O_3$ (190.19) requires C, 69.47; H, 5.29 %.

General procedure for the preparation of compounds 8a-h, 15a,b, 16, 17: 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 diazonium salt was added to a cold solution of 1-*N,N*-dimethylaminopent-1-en-3-one (2a) (1.27 g, 10 mmol) or 1-(4-acetylphenyl)-3-dimethylaminopropenone (2b) in ethanol (50 ml) containing sodium acetate. The reaction mixture was stirred at room temperature for 30 min. The solid product so formed was washed with water and crystallised from the indicated solvent.



Scheme 4

3-Oxo-2-(phenylhydrazono)pentanal (**8a**): yield 70%; m.p. 93 °C; red crystals from dilute ethanol. IR: ν_{max}/cm^{-1} 3500 (br NH), 1680 (CO aldehyde), 1648 (CO ketone) cm^{-1} .^{1}H NMR (DMSO-d_6): 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: *m/z* 203 (33 %, M$^+$-1). Found: C, 64.80; H, 5.89; N, 13.60. $C_{11}H_{12}N_2O_2$ (204.23) requires C, 64.69; H, 5.92; N, 13.72 %.

3-Oxo-2-(p-tolylhydrazono)pentanal (**8b**): yield 72%; m.p. 133 °C; orange crystals from ethanol. ^{1}H NMR (DMSO-d_6): 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; *m/z* 218 (87 %, M$^+$); Found: C, 66.00; H, 6.49; N, 13.00. $C_{12}H_{14}N_2O_2$ (218.25) requires C, 66.04; H, 6.47; N, 12.84 %.

2-(4-Nitrophenylhydrazono)-3-oxopentanal (**8c**): yield 72 %; m.p. 125 °C; red crystals from ethanol. ^{1}H NMR (DMSO-d_6): δ 1.1 (t, 3H, CH_3), 2.9 (q, 2H, CH_2), 6.7–7.9 (m, 4H, Ar–H), 9.8, 9.2 (s, 1H, CHO), 13.9, 14.5 (s, 1H, NH). MS: *m/z* 249 (34 %, M$^+$). Found: C, 53.20; H, 4.50; N, 16.75. $C_{11}H_{11}N_3O_4$ (249.22) requires C, 53.01; H, 4.45; N, 16.86 %.

2-(4-Methoxyphenylhydrazono)-3-oxopentanal (**8d**): yield 72 %; m.p. 120 °C; red crystals from ethanol. ^{1}H NMR (DMSO-d_6): 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: *m/z* 234 (15 %, M$^+$). Found: C, 61.35; H, 6.09; N, 11.77. $C_{12}H_{14}N_2O_3$ (234.25) requires C, 61.53; H, 6.02; N, 11.96 %.

3-(4-Acetylphenyl)-2-(phenylhydrazono)-3-oxopropionaldehyde (**8e**): yield 70%; m.p. 153 °C; yellow crystals from dilute ethanol. IR; ν_{max}/cm^{-1} 3118 (NH), 1660, 1641 (CO) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 2.6 (s, 3H, CH_3), 6.4–7.9 (m, 9H, Ar–H), 9.5, 10 (s, 1H, CHO), 13.2, 14.2 ppm (s, 1H, NH). MS: *m/z* 293 (33 %, M$^+$-1); Found: C, 69.19; H, 4.69; N, 9.42. $C_{17}H_{14}N_2O_3$ (294.31) requires C, 69.38; H, 4.79; N, 9.52 %.

3-(4-Acetylphenyl)-2-(4-nitrophenylhydrazono)-3-oxopropionaldehyde (**8f**): yield 72 %; m.p. 149 °C; red crystals from ethanol/dioxan. ^{1}H NMR (DMSO-d_6): δ 2.6 (s, 3H, CH_3), 6.7–7.9 (m, 8H, Ar–H), 9.6, 10.1 (s, 1H, CHO), 12, 14(s, 1H, NH). MS; *m/z* 339(16.5%) (M$^+$); (Found: C, 60.21; H, 3.78; N, 12.39. $C_{17}H_{13}N_3O_5$ (339.30) requires C, 60.18; H, 3.86; N, 12.38 %).

3-(4-Acetylphenyl)-2-(4-methoxyphenylhydrazono)-3-oxopropionaldehyde (**8g**): yield 70 %; m.p. 136 °C; red crystals from methanol. IR: ν_{max}/cm^{-1} 3424 (NH), 1714, 1676 (CO) cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 2.6 (s, 3H, CH_3), 3.8 (s, 3H, OCH_3), 7 (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 (s, 1H, CHO), 13.2, 14.4 ppm (s, 1H, NH). MS: *m/z* 324 (17 %) (M$^+$). Found: C, 66.56; H, 4.91; N, 8.68. $C_{18}H_{16}N_2O_4$ (324.33) requires C, 66.66; H, 4.97; N, 8.64 %.

3-(4-Acetylphenyl)-2-(2-methoxyphenylhydrazono)-3-oxopropionaldehyde (**8h**): yield 85 %; m.p. 139 °C; orange crystals from ethanol/dioxan. ^{1}H NMR (DMSO-d_6): δ 2.6 (s, 3H, CH_3), 3.7 (s, 3H, OCH_3), 6.3–8(m, 8H, Ar–H) 9.6, 10(s, 1H, CHO), 13.2, 14.4(s, 1H, NH). MS; *m/z* 324 (47%) (M$^+$). Found: C, 66.65; H, 4.92; N, 8.55.$C_{18}H_{16}N_2O_4$ (324.33) requires C, 66.66; H, 4.97; N, 8.64%.

1-(7-Phenylpyrazolo[5,1-c][1,2,4]triazine-3-yl)propan-1-one (**15a**): yield 69%; m.p. 148 °C; yellow crystals from dilute ethanol. ^{1}H NMR (DMSO-d_6): δ 1.2 (t, 3H, CH_3), 2.51 (q, 2H, CH_2), 6.2 (s, 1H, H-8), 7.2–7.4 (m, 5H, Ar–H), 9.5 ppm (s, 1H, H-4). MS: *m/z* 252 (66 %) (M$^+$). Found: C, 66.81; H, 4.80; N, 22.24. $C_{14}H_{12}N_4O$ (252.27) requires C, 66.65; H, 4.79; N, 22.21 %.

1-[4-(7-Phenylpyrazolo[5,1-c][1,2,4]triazine-3-carbonyl) phenyl]ethanone (**15b**): yield 69%; m.p. 208 °C; yellow crystals from methanol/dioxan. ^{1}H NMR (DMSO-d_6): δ 2.6 (s, 3H, CH_3), 6.5 (s, 1H, H-3), 7.3–7.9 (m, 9H, Ar–H), 9.4 (s, 1H, H-7). MS: *m/z* 342 (100 %) (M$^+$). Found: C, 69.99; H, 4.09; N, 16.29. $C_{20}H_{14}N_4O_2$ (342.35) requires C, 70.17; H, 4.12; N, 16.36 %.

1-[4-[1,2,4]Triazolo[3,4-c][1,2,4]triazine-6-carbonylphenyl] ethanone (**16**): yield 70%; m.p. >300 °C; yellow crystals from ethanol/dioxan. ^{1}H NMR (DMSO-d_6): δ 2.6 (s, 3H, CH_3), 7.8–8.1 (m, 4H, Ar–H), 7.7 (s, 1H, H-5), 9.7 (s, 1H, H-4). MS: *m/z* 267 (89 %) (M$^+$) Found: C, 58.55; H, 3.31; N, 26.41. $C_{13}H_9N_5O_2$ (267.25) requires C, 58.43; H, 3.39; N, 26.21 %.

[1,2,4]triazino[4,3-a]benzimidazole-3-carbonyl)phenyl]ethanone (**17**): yield 69 %; m.p. >300 °C; orange crystals from ethanol/dioxan. ^{1}H NMR (DMSO-d_6): δ 2.6 (s, 3H, CH_3), 7.2–8 (m, 8H, Ar–H), 9.4 (s, 1H, H-4). MS; *m/z* 316 (M$^+$). Found: C, 68.46; H, 3.79; N, 17.87. $C_{18}H_{12}N_4O_2$ (316.32) requires C, 68.35; H, 3.82; N, 17.71 %.

General procedure for the preparation of formazans **12a,b**: Addition of excess of *p*-toluenediazonium salt or *p*-nitrophenyldiazonium salt to 1-*N*,*N*-dimethylaminopent-1-en-3-one (**2a**) in ethanol containg sodium acetate yielded formazan (**12a,b**) which also can be obtained by coupling of *p*-toluenediazonium salt or *p*-nitrophenyldiazonium salt with the hydrazone derivative.

1-(p-Tolyldiazo)-1-(p-tolylhydrazono)butan-2-one (**12a**): yield 70%; m.p. 133 °C; red crystals from ethanol, ^{1}H NMR (DMSO-d_6): δ 1.1 (t, 3H, CH_3), 2.3 (s, 6H, $2CH_3$), 3.0 (q, 2H, CH_2), 7.3–8.6 (m, 8H, Ar–H), 15.0 (s, 1H, NH). MS: *m/z* 307 (44 %, M$^+$-1). Found: C, 70.20; H, 6.48; N, 18.21.$C_{18}H_{20}N_4O$ (308.38) requires C, 70.11; H, 6.54; N, 18.17 %.

1-(p-Nitrophenyldiazo)-1-(p-nitrophenylhydrazono)butan-2-one (**12b**): yield 85 %; m.p. 201 °C; dark red crystals from ethanol, ^{1}H NMR (DMSO-d_6): δ 1.06(t, 3H, CH_3), 2.4(q, 2H, CH_2), 6.7–7.9 (m, 8H, Ar–H), 14.0 (s, 1H, NH). MS: *m/z* 370 (3 %, M$^+$). Found: C, 51.87; H, 3.75; N, 22.59. $C_{16}H_{14}N_6O_5$ (370.32) requires C, 51.89; H, 3.81; N, 22.69 %.

General procedure for the preparation of compounds **20a–d, 23**: *Procedure A*: To a stirred solution of the appropriate hydrazonyl halide (10 mmol) or the hydroximoyl chloride (l0 mmol) and the enaminone 1-*N*,*N*-dimethylaminopent-1-en-3-one (**2a**) (1.27 g, 10 mmol) or 1-(4-acetylphenyl)-3-dimethylaminopropenone (**2b**) (2.17g, 10 mmol) in dry benzene (20 ml), triethylamine (0.2 ml) was added portionwise over a period of 30 min. The reaction mixture was refluxed for 8h and the precipitated triethylamine hydrochloride was filtered off. The filtrate was evaporated under reduced pressure and the residue was triturated with methanol. The solid products were collected and recrystallized from a suitable solvent.

Procedure B: To a mixture of hydrazonyl halides (10 mmol) and 1-*N*,*N*-dimethylaminopent-1-en-3-one (**2a**) (1.27g, 10 mmol) or 1-(4-acetylphenyl)-3-dimethylaminopropenone (**2b**) (2.17g, 10 mmol), triethylamine (0.2 ml) was added . The mixture was irradiated in a domestic microwave oven for 10 min. The resulted product was washed with ethanol and crystallized from the indicated solvent.

1-(3-Acetyl-l-phenyl-1H-pyrazol-4-yl)propan-1-one (**20a**): Thermal heating afforded 69% yield after 8 h, while microwave heating afforded 95 % yield after 10 min. M.p. 88 °C; golden crystals from ethanol. ^{1}H NMR (DMSO-d_6): δ 1.06 (t, 3H, CH_3), 2.59 (s, 3H, CH_3), 2.89 (q, 2H, CH_2), 7.0–7.9 (m, 5H, Ar–H), 10.5 (s, 1H, H-5) MS: *m/z* 242 (21 %) (M$^+$). Found: C, 69.55; H, 5.78; N, 11.45. $C_{14}H_{14}N_2O_2$ (242.28) requires C, 69.40; H, 5.82; N, 11.56 %.

1-(3-Acetyl-1-p-tolyl-1H-pyrazol-4-yl)propan-1-one (**20b**): yield 75 %; m.p. 120 °C; yellow crystals from ethanol. ^{1}H NMR (DMSO-d_6): δ 1.1 (t, 3H, CH_3), 2.59 (s, 3H, CH_3), 2.6 (s, 3H, CH_3), 2.99 (q, 2H, CH_2), 7.0–7.9 (m, 5H, Ar–H), 10.5 (s, 1H, H-5). MS: *m/z* 256 (27 %) (M$^+$). Found: C, 70.46; H, 6.39; N, 10.83. $C_{15}H_{16}N_2O_2$ (256.30) requires C, 70.29; H, 6.29; N, 10.93 %.

1-[4-(3-Acetyl-1-phenyl-1H-pyrazole-4-carbonyl)phenyl]ethanone (**20c**): Thermal heating afforded 82 % yield after 8 h, while microwave heating afforded 90 % yield after 10 min, m.p. 162 °C; pale yellow crystals from ethanol/dioxan. ^{1}H NMR (DMSO-d_6): δ 2.59 (s, 3H, CH_3), 2.6 (s, 3H, CH_3), 7.4–8.1 (m, 9H, Ar–H), 9.08 (s, 1H, H-5). ^{13}C NMR: δ 27.6 ($\underline{C}H_3CO$), 27.7 ($\underline{C}H_3CO$), 120.3 (<u>C</u>-4), 123.1 (<u>C</u>-5), 128.7, 128.9, 129.9, 130.4, 132.5, 139.3, 140.6, 141.3 (phenyl carbons), 150.7 (<u>C</u>-3), 193.3 (<u>C</u>O), 198.2 ($\underline{C}H_3CO$), 198.3 ($CH_3\underline{C}O$). MS: *m/z* 332 (100%) (M$^+$). Found: C, 72.34; H, 4.79 N, 8.59.$C_{20}H_{16}N_2O_3$ (332.36) requires C, 72.28; H, 4.85; N, 8.43%.

Ethyl 4-(4-acetylbenzoyl)-1-p-tolyl-1H-pyrazole-3-carboxylate (**20d**): yield 79 %; m.p. 124 °C; orange crystals from ethanol. ^{1}H NMR (DMSO-d_6): δ 1.3 (t, 3H, CH_3), 2.3 (s, 3H, CH_3), 2.6 (s, 3H, CH_3), 4.2 (q, 2H, CH_2), 7.1–8.05 (m, 8H, Ar–H), 8.5 (s, 1H, H-5). MS: *m/z* 377 (100%) (M$^+$ +1). Found: C, 70.36; H, 5.41; N, 7.54. $C_{22}H_{20}N_2O_4$ (376.41) requires C, 70.20; H, 5.36; N, 7.44 %.

1-[4-(3-Benzoylisoxazole-4-carbonyl)phenyl]ethanone (**23**): yield 80 %; m.p. 120 °C; orange crystals from ethanol. IR; ν_{max}/cm^{-1} 1660, 1637 (CO), 1624 (C=N). ^{1}H NMR (DMSO-d_6): δ 2.6 (s, 3H, CH_3), 7.5–8.1 (m, 9H, Ar–H), 9.9 (s, 1H, H-5). MS; *m/z* 319 (1.2 %) (M$^+$). Found: C, 71.48; H, 4.00; N, 4.34. $C_{19}H_{13}NO_4$ (319.31) requires C, 71.47; H, 4.10; N, 4.39 %.

General procedure of the reaction of pyrazole **20a** *and isoxazole* **23** *with hydrazine hydrate*: A mixture of the pyrazole **20a** or isoxazole **23** (10 mmol) and hydrazine hydrate (10 mmol) in absolute ethanol (20 ml) was heated under reflux for 3–4h. The reaction mixture was left to cool and triturated with ethanol. The solid product was filtered off and crystallised from ethanol.

4-Ethyl-7-methyl-2-(p-tolyl)-pyrazolo[3, 4-d]pyridazine (**21**): yield 62 %; m.p. 203 °C; yellow crystals from ethanol. ^{1}H NMR (DMSO-d_6): δ 2.6 (s, 3H, CH_3), 7.2–7.9 (m, 9H, Ar–H), 9.4 (s, 1H, H-3). MS: *m/z* 251 (25 %) (M$^+$). Found: C, 71.29; H, 6.40; N, 22.01.$C_{15}H_{16}N_4$ (252.32) requires C, 71.40; H, 6.39; N, 22.20 %.

1-[4-(7-Phenylisoxazolo[3,4-d]pyridazin-4-yl)phenyl]ethanone (**24**): yield 70%, m.p. 202 °C; yellow crystals from ethanol, ^{1}H NMR

(DMSO-d_6): δ 2.6 (s, 3H, CH_3), 7.2–7.9 (m, 9H, Ar–H), 9.4 (s, 1H, H-3). MS: *m/z* 315 (75 %) (M^+). (Found: C, 72.22; H, 4.08; N, 13.45. $C_{19}H_{13}N_3O_2$ (315.33) requires C, 72.37; H, 4.16; N, 13.33 %.

General procedures for the preparation of compounds **28a-c:** *Procedure A:* a mixture of 1-*N*,*N*-dimethylaminopent-1-en-3-one (**2a**) (1.27 g, 10 mmol) or 1-(4-acetylphenyl)-3-dimethylaminopropenone (**2b**) (2.17g, 10 mmol) and glycine or hippuric acid (**25a,b**) **(**10 mmol) in dry acetic anhydride (30 ml) was refluxed for 3–4h, The solid product obtained upon cooling was isolated by filtration and recrystallised from ethanol.

Procedure B: a mixture of 1-*N*,*N*-dimethylaminopent-1-en-3-one (**2a**) (1.27 g, 10 mmol) and hippuric acid (**25b**) (1.79 g, 10 mmol) was placed in the microwave oven and irradiated for 6 min, then the reaction mixture was left to cool at room temperature. The formed solid products were collected by filtration and ecrystallised from ethanol.

N-(6-Ethyl-2-oxo-2H-pyran-3-yl)benzamide (**28a**): Thermal heating afforded 70 % yield after 4 h, while microwave heating afforded 98 % yield after 8 min. M.p. 124 °C, brown crystals from ethanol. IR: ν_{max}/cm^{-1} 3375 (NH), 1694 (ring CO), 1657 (amide CO) cm^{-1}.^{1}H NMR (DMSO-d_6): δ 1.1 (t, 3H, CH_3), 2.54 (q, 2H, CH_2), 6.3 (d, 1H, H-5), 7.50 (d, 1H, H-4), 7.57–8 (m, 5H, Ar–H), 9.5 (s, 1H, NH). ^{13}C NMR: δ 102.6 (C-5), 123.7 (C-4), 130.4 (C-3), 128.2, 129.2, 132.7, 134.3 (phenyl carbons), 160 (C-6), 162.2 (C-2), 166.3 (CO). MS: *m/z* 243 (20 %) (M^+); Found: C, 69.21; H, 5.41; N, 5.66. $C_{14}H_{13}NO_3$ (243.26) requires C, 69.13; H, 5.39; N, 5.76 %.

*N-[6-(4-Acetylphenyl)-2-oxo-2H-pyran-3-yl]acetamide (***28b**): yield 85 %, m.p. >300 °C; yellow crystals from dioxan/ethanol. IR: ν_{max}/cm^{-1} 3306 (NH), 1719 (ring CO), 1676 (amide CO) cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 1.9 (s, 3H, CH_3), 2.6 (s, 3H, CH_3), 7.3 (d, 1H, H-5), 7.4 (d, 1H, H-4), 7.8–8.1 (m, 4H, Ar–H), 6.7 (s, 1H, NH). MS; *m/z* 272 (24 %) (M^++1). Found: C, 66.32; H, 4.74; N, 5.00. $C_{15}H_{13}NO_4$ (271.27) requires C, 66.42; H, 4.83; N, 5.16 %.

N-[6-(4-Acetylphenyl)-2-oxo-2H-pyran-3-yl]benzamide (**28c**): yield 85%; m.p. 255–257 °C; orange crystals from dioxan/ethanol, ^{1}H NMR (DMSO-d_6): δ 2.6(s, 3H, CH_3), 6.7(d, 1H, H-5), 6.99(d, 1H, H-4), 7.4–7.9(m, 9H, Ar–H), 9.5(s, 1H, NH). MS; *m/z* 334(14.5%) (M^+ +1). Found: C, 72.21; H, 4.46; N, 4.05. $C_{20}H_{15}NO_4$ (333.34) requires C, 72.06; H, 4.54; N, 4.20 %.

N-[6-(4-Acetylphenyl)-1-amino-2-oxo-1,2-dihydropyridin-3-yl]benzamide (**29**): A mixture of *N*-[6-(4-acetylphenyl)-2-oxo-2*H*-pyran-3-yl]benzamide (**28c**) (10 mmol) and hydrazine hydrate (10 mmol) in ethanol was heated under reflux for 4h, then the reaction mixture was left to cool to room temperature. The formed solid product was collected by filtration and recrystallised from ethanol. Yield 84 %; m.p. 280 °C; yellow crystals from ethanol. ^{1}H NMR (DMSO-d_6): δ 2.04 (s, 2H, NH_2), 2.6 (s, 3H, CH_3), 7.16 (d, 1H, H-5), 7.35 (d, 1H, H-4), 7.5–8.2 (m, 9H,Ar–H), 9.6 (s, 1H, NH). MS: *m/z* 348 (3.4 %) (M^+ +1). Found: C, 69.30; H, 4.85; N, 12.05. $C_{20}H_{17}N_3O_3$ (347.37) requires C, 69.15; H, 4.93; N, 12.10 %.

General procedures for the preparation of compounds **31a,b, 32a,b, 33**: *Procedure A*: (i) a mixture of l-*N*,*N*-dimethylaminopent-1-en-3-one (**2a**) (1.27 g, 10 mmol) and heterocyclic amine (10 mmol) in absolute ethanol (20 ml) was heated under reflux for 6 h, then the reaction mixture was left to cool to room temperature. The formed solid products were collected by filtration, washed with ethanol, dried and recrystallized from the solvent indicated.

(ii) 1-(4-Acetylphenyl)-3-dimethylaminopropenone (**2b**) (2.17g, 10 mmol) was heated at 120 °C with aminopyrazole or aminotriazole (10 mmol) for 30 min. The reaction mixture was left to cool and triturated with ethanol. The solid product so formed was collected by filtration and recrystallised from the indicated solvent.

Procedure B: a mixture of each l-*N*,*N*-dimethylaminopent-1-en-3-one (**2a**) (1.27 g, 10 mmol) or 1-(4-acetylphenyl)-3-dimethylamino-propenone (**2b**) (2.17g, 10 mmol) and heterocyclic amine (10 mmol) was placed in the microwave oven and irradiated for 10–20 min, then the reaction mixture was washed with ethanol and left to cool at room temperature. The formed solid products were collected by filtration, and were recrystallised from the indicated solvent.

7-Ethyl-2-phenylpyrazolo[l,5-a]pyrimidine (**31a**): Thermal heating afforded 75% yield after 6 h, while microwave heating afforded 89 % yield after 10 min. M.p. 102 °C; yellow crystals from dilute ethanol. ^{1}H NMR (DMSO-d_6): δ 1.4 (t, 3H, CH_3), 3.2 (q, 2H, CH_2), 6.9 (s, 1H, H-3), 7.2 (d, 1H, H-6), 7.3–7.9 (m, 5H, Ar–H), 8.5 (d, 1H, H-5). MS: *m/z* 223 (100 %) (M^+). Found: C, 75.50; H, 5.77; N, 18.91. $C_{14}H_{13}N_3$ (223.28) requires C, 75.31; H, 5.87; N, 18.82 %.

7-(4-Acetylphenyl)-2-phenylpyrazolo[1,5-a]pyrimidine (**31b**): Thermal heating afforded 70 % yield after 30min, while microwave heating afforded 95 % yield after 20 min. M.p. 175 °C; yellow crystals from methanol. ^{1}H NMR (DMSO-d_6): δ 2.6 (s, 3H, CH_3), 7.4–7.5 (m, 9H, Ar–H), 6.7 (s, 1H, H-3), 8.5 (d, 1H, H-5), 7.6 (d, 1H, H-6). ^{13}C NMR: δ 28.1 (CH$_3$), 109.9 (C-3), 125.8, 125.87, 128.01, 128.07, 128.9, 129.0, 129.60, 129.66 (phenyl carbons), 139.3 (C-6), 139.5 (C-3a), 142.9 (C-2), 144.1 (C-5), 147.7 (C-7), 198.2 (CO). MS: *m/z* 313 (100 %) (M^+). Found: C, 76.75; H, 4.81; N, 13.33. $C_{20}H_{15}N_3O$ (313.36) requires C, 76.66; H, 4.82; N, 13.41 %.

7-Ethyl-[1,2,4]triazolo[l,5-a]pyrimidine (**32a**): Thermal heating afforded 80 % yield after 6 h, while microwave heating afforded 90 % yield after 10 min. M.p. 126 °C; yellow crystals from ethanol. ^{1}H NMR (DMSO-d_6): δ 1.3 (t, 3H, CH_3), 3.1 (q, 2H, CH_2), 7.2 (d, 1H, H-6), 8.6 (s, 1H, H-2), 8.8 (d, 1H, H-5). MS; *m/z* 148 (11 %) (M^+). Found: C, 56.83; H, 5.36; N, 37.62. $C_7H_8N_4$ (148.17) requires C, 56.74; H, 5.44; N, 37.81 %.

7-(4-Acetylphenyl)[1,2,4]triazolo[1,5-a]pyrimidine (**32b**): Thermal heating afforded 80 % yield after 30min, while microwave heating afforded 93 % yield after 15 min. M.p. 233 °C; yellow crystals from ethanol/DMF, ^{1}HNMR (DMSO-d_6): δ 2.6 (s, 3H, CH_3), 7.6 (d, 1H, H-5), 8.1 (d, 2H, Ar–H), 8.3 (d, 2H, Ar–H), 8.7 (s, 1H, H-2), 9 (d, 2H, H-6). MS; *m/z* 238(50 %) (M^+). Found: C, 65.58; H, 4.25; N, 23.41.$C_{13}H_{10}N_4O$ (238.25) requires C, 65.54; H, 4.23; N, 23.52 %.

2-Ethylpyrimido[1,2-a]benzimidazole (**33**): Thermal heating afforded 78% yield after 6 hrs, while microwave heating afforded 88% yield after 10 min. M.p. 240 °C, red crystals from ethanol. ^{1}H NMR (DMSO-d_6): δ 1.4 (t, 3H, CH_3), 2.4 (q, 2H, CH_2), 6.7–7.8 (m, 5H, Ar–H), 8.6 (d, 1H, H-4). MS: *m/z* 197 (54 %) (M^+). Found: C, 72.97; H, 5.57; N, 21.37.$C_{12}H_{11}N_3$ (197.24) requires C, 73.07; H, 5.62; N, 21.30 %.

4-(4-Acetylphenyl)-2-aminopyrimidine (**34**): A solution of guanidine carbonate (1.4g, 15 mmol) in absolute ethanol (15 ml) was added to a stirred solution of 1-(4-acetylphenyl)-3-dimethylaminopropenone (**2b**) (2.17 g, 10 mmol) in boiling absolute ethanol (10ml) and stirring was continued for 20 min. To this mixture was then added Na (0.46 g, 20 mmol) in absolute ethanol (10ml) and the reaction mixture was refluxed for 16h. The solution was allowed to cool to room temperature. The solid product so formed was collected by filtration and recrystallised from ethanol. Yield 78 %, m.p. 290 °C, magenta crystals from ethanol. ^{1}H NMR (DMSO-d_6): δ 2.6 (s, 3H, CH_3), 6.7 (br, 2H, NH_2), 7.2 (d, 1H, H-5), 8 (d, 2H, Ar–H), 8.1 (d, 2H, Ar–H), 8.3 (d, 1H, H-4). ^{13}C NMR; δ 107 (C-5), 127.6, 129.1, 138.7, 142.2 (phenyl carbons), 160 (C-6), 164.5 (C-4), 165.1 (C-2), 198 (CO). MS; *m/z* 214 (8 %) (M^+ +1). Found: C, 67.66; H, 5.30; N, 19.78. $C_{12}H_{11}N_3O$ (213.24) requires C, 67.59; H, 5.20; N, 19.70 %.

1,3,5-Tri-(4-acetylbenzoyl)benzene (**37**): 1-(4-Acetylphenyl)-3-dimethylaminopropenone (**2b**) (2.17g, 10 mmol) was refluxed in acetic acid (20 ml) for 3h. The solvent was removed and the residual solid was crystallised from acetic acid. Thermal heating afforded a 70% yield after 3 h, while microwave heating afforded a 93 % yield after 6 min. M.p. 150–154 °C; orange crystals from AcOH, ^{1}H NMR (DMSO-d_6): δ .6 (s, 9H, 3CH_3), 8.07 (s, 3H, Ar–H), 8.1 (d, 6H, Ar–H), 8.3 (d, 6H, Ar–H). MS; *m/z* 517 (15 %). (M^+ + 1). Found: C, 76.55; H, 4.59. $C_{33}H_{24}O_6$ (516.55) requires C, 76.73; H, 4.68 %.

2-(4-Acetylphenyl)-5-(4-acetylbenzoyl)pyridine (**38**): Compound **2b** (2.17g, 10mmol) and ammonium acetate (0.77g, 10 mmol) were refluxed in glacial acetic acid (30 ml) for 1h, then left to cool to room temperature. The material which separated upon cooling was isolated by filtration and recrystallised from ethanol. Yield 82 %, m.p. 188 °C, yellow crystals from ethanol. ^{1}H NMR (DMSO-d_6): δ 2.6 (s, 3H, CH_3), 2.3 (s, 3H, CH_3), 7.9–8.3 (m, 10H, Ar–H), 9 (s, 1H, H-6). MS; *m/z* 344 (31 %) (M^+ + 1). Found: C, 76.78; H, 4.89; N, 4.20. $C_{22}H_{17}NO_3$ (343.38) requires C, 76.95; H, 4.99; N, 4.08 %.

3-Acetyl-6-(4-acetylphenyl)-2-methylpyridine (**39**): A solution of 1-(4-acetylphenyl)-3-dimethylaminopropenone (**2b**) (2.17g, 10 mmol) and acetylacetone (1.79g, 10 mmol)in dry acetic anhydride (30 ml) was refluxed for 3–4h, The solid product, so formed, was collected by filtration and recrystallised from ethanol/dioxane. Yield 75%, m.p. >300 °C, pale yellow crystals from ethanol/dioxan. ^{1}H NMR (DMSO-d_6): δδ 2.4 (s, 3H, CH_3), 2.5 (s, 3H, CH_3), 2.6 (s, 3H, CH_3), 7.9 (d, 1H, H-5), 9 (d, 1H, H-4), 8.0–8.3 (m, 4H, Ar–H). MS; *m/z* 254 (26 %, M^+ +1). Found: C, 75.69; H, 5.93; N, 5.41.$C_{16}H_{15}NO_2$ (253.30) requires C, 75.87; H, 5.97; N, 5.53%.

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References

1 A.A. Elassar and A.A. Elkhair, *Tetrahedron*, 2003, **59**, 8463.
2 F. Al-Omran, M.M. Abdel-Khalik, A.A. Elkhair and M. Helnagdi, *Synthesis*, 1997, 91.

3 S.M. Al-Mousawi, M.M. Abdel-Khalik, S. El-Sheriny and M.H. Elnagdi. *J. Het. Chem.*, 2001, **38,** 155.
4 M.M. Abdel-Khalik and M.H. Elnagdi, *Synth. Commun.*, 2002, **32**, 159.
5 B. Al-Saleh, M.M. Abdel Khalik, A.M. Eltoukhy and M.H. Elnagdi,*J. Het. Chem.*, 2002, **39**, 1035.
6 S.M. Agamy, M.M. Abdel Khalik, M.H, Mohammed and M.H. Elnagdi, *Z. Naturforsch.*, 2001, **56B**, 1074.
7 F.M.A. El-Taweel and M.H. Elnagdi, *J. Het. Chem.*, 2001, **38**, 981.
8 S. Al-Mousawi, M.A. Mohammed and M.H. Elnagdi, *J. Het. Chem.*, 2001, **38**, 989.
9 M.M. Abdel Khalik, S.M. Agamy, and M.H. Elnagdi, *Z. Naturforsch.*, 2000, **55B**, 1211.
10 A.A. Hassanien, S.A.A. Ghozlan and M.H. Elnagdi, *J. Het. Chem.*, 2003, **40**, 225.
11 S. Al-Mousawi, M.M. Abdel Khalik, E. John and M.H. Elnagdi, *J. Het. Chem.*, 2003, **40**, 689.
12 A.S. Matlack in "Introduction to Green Chemistry" Marcel Dekker Inc., New York, Basel, 2001.
13 J. Clark and D. MacQuarrie in "Handbook of Green Chemistry and Technology" Blackwell Science Ltd., Paris, 2002.