Aminomethylene ketones and enamines in heterocyclic synthesis: synthesis of functionally substituted pyridine, pyrazole, fused pyrimidine and fused [1,5]diazocine derivatives

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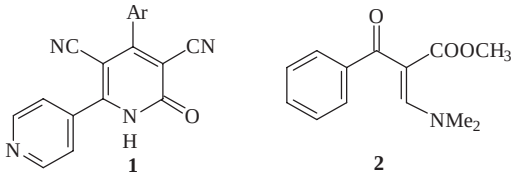
Methyl 2-benzoyl-3-dimethylaminopropenoate (**2**) and 2-(benzimidazo-2-yl)-3-dimethylaminoacrylonitrile (**27**) were condensed with various type of reagents under different conditions to afford new acyclic, cyclic and fused heterocyclic derivatives.

Keywords: aminomethylene ketones, enamines, heterocyclic synthesis

The pyridine nucleus is a major component of a variety of natural products and drugs.[1-3] Previously we found a convenient method of synthesising various functionally substituted pyridines[4,5] such as compound **1** (Scheme 1). Furthermore several pharmacological studies have also pointed out the value of thieno[2,3-*b*]pyridine,[6] pyrazolo[1,5-*a*] pyrimidine,[7] pyrimido[1,2-*a*]pyrimidine[8] and pyrido[1,2-*a*] pyrimidine as biologically active nuclei. These findings focused on incorporating of compounds **2** and **27** with several reagents in the hope of obtaining new compounds of enhance biological and pharmacological activities.

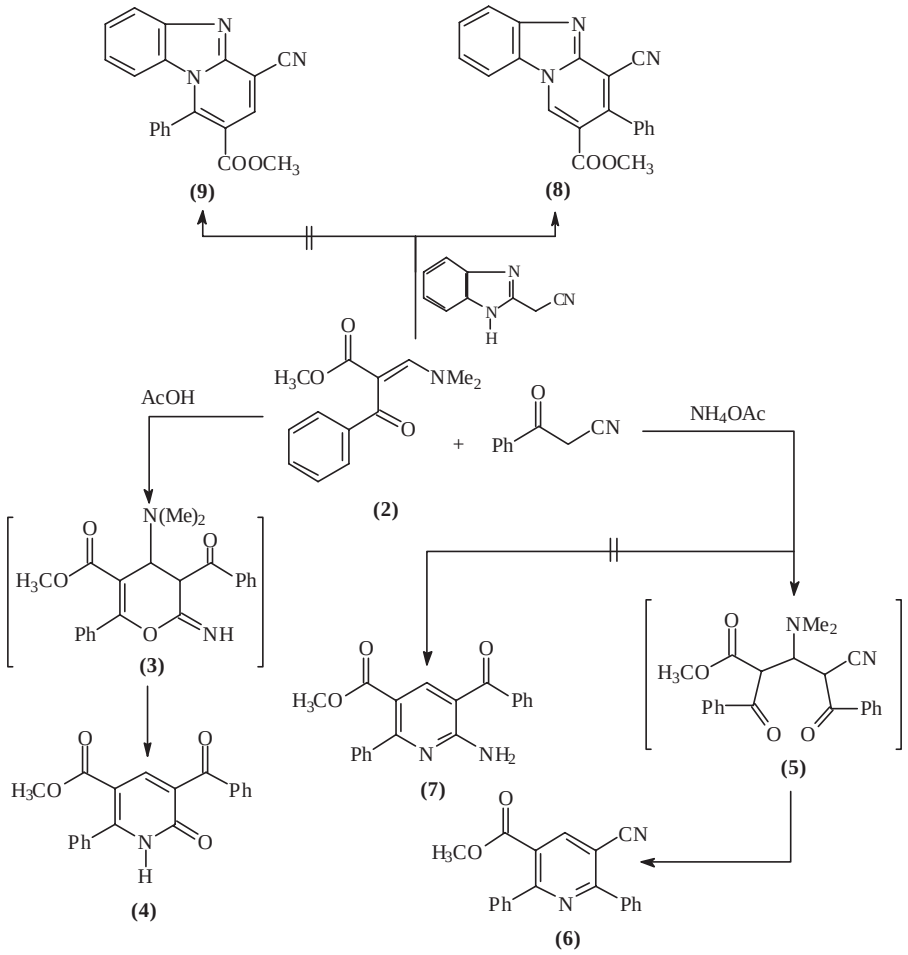


1 **2**

Scheme 1

Results and discussion

In conjunction with our interest in developing efficient synthesis of azoles, azines and azoloazines as potential



Scheme 2

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pharmaceuticals, agrochemicals or dye intermediate.[9-12] We report here on the utility of methyl 2-benzoyl-3-dimethylaminopropenoate (**2)** and compound **27** in synthesising of some pyridines, pyrazoles, pyrimidines, thieno[2,3-*b*]pyridines, pyrazolo[1,5-*a*]pyrimidines and dibenzimidazo[1,2-*a*:1',2'-*e*][1,5]diazocine.

Compound **2** was prepared via reaction of acetophenone with dimethylcarbonate followed by treatment of the non-isolable product by dimethylformamide dimethylsulfate.[13] The structure of compound **2** was confirmed on the bases of elemental analysis and spectral data. The reactivity of enaminone carboxylate **2** towards some active methylenes was investigated. Thus, treatment of **2** with benzoylacetonitrile in refluxing acetic acid afforded the pyridone derivative **4**. Formation of **4** is assumed to proceed *via* initial addition of active methylene reagent across the double bond in **2** yielding the Michael adduct followed by intra molecular cyclisation to give the non-isolable intermediate pyranimine **3** which underwent Dimroth type rearrangement.

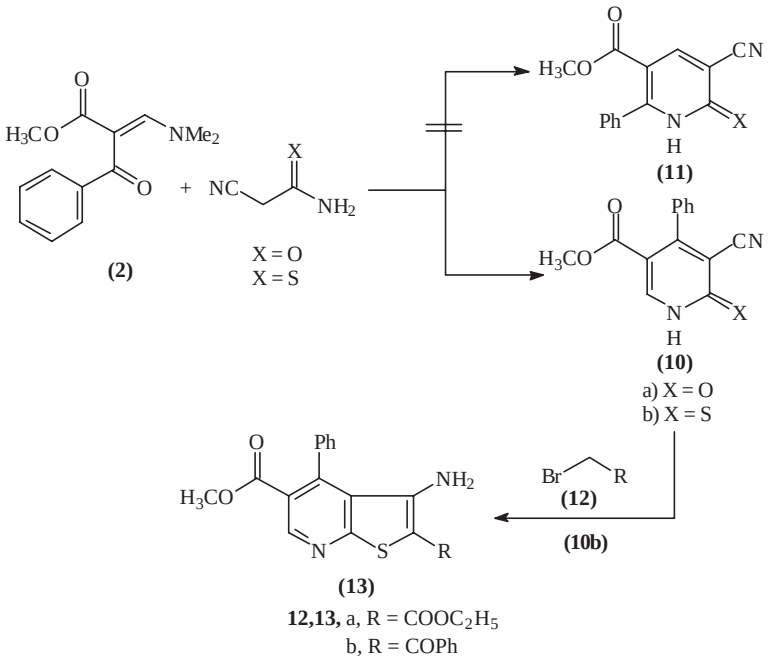
On the other hand, when the previous reaction was carried out in the presence of NH_4OAc the product was identified as methyl 2,6-diphenyl-5-cyanopyridine-3-carboxlate **6** not compound **7** via the intermediate **5**. The structure of **6** was established based on the spectral data. Thus, the IR showed the presence of cyano group at ν 2213 cm^{-1} and ^1H NMR revealed the absence of the NH_2 signal. In a similar manner (benzimidazo-2-yl) acetonitrile reacted with **2** to yield **8** not **9**. Structure **8** was confirmed on the basis of elemental analysis, IR and in particular ^1H NMR spectrum, the later have revealed the presence of H-6 pyridine signal at low field (δ = 8.5 ppm) (Scheme 2). Also, compound **2** reacted with cyanoacetamide and cyanothioacetamide[14] in refluxing ethanol in the presence of sodium ethoxide to give a high yield of products for which structures **10** not **11**. Structure **10** was assigned on the basis of spectral data. Thus, the IR spectra showed the presence of NH and CN absorptions at ν 3320 and 2217 cm^{-1} respectively. Also the ^1H NMR revealed the H-2 pyridine signal at 8.13 ppm. It was reported that, thieno[2,3]pyridines possess good antibacterial[6] and antihypertensive[15] this, prompted us to synthesise **13a,b** via reaction of **10b** with α-alkyl halides **12a,b** in refluxing pyridine to afford **13a,b** (Scheme 3).

Compound **2** reacted with C-nucleophiles in which *N*,*N*-dimethylamino group is substituted.[16] Thus, 5,5-dimethylcyclohexane-1,3-dione and 3-methyl-1*H*-pryazol-5-one were condensed with **2** in refluxing AcOH to give acyclic products which were formulated as methyl 2-benzoyl-3-(5,5-dimethyl-1,3-dioxocyclohexan-2-yl)propenoate **14** and methyl 2-benzoyl-3-(3-methyl-5-oxo-1*H*-pyrazol-4-yl)propenoate **16** not **15** and **17** respectively. Structures **15** and **17** were ruled out based on elemental analysis, IR and ^1H NMR spectra which showed the presence of $-COOCH_3$ signal at δ 3.85 ppm. Trials for cyclisation of both **14** and **16** were unsuccessful.

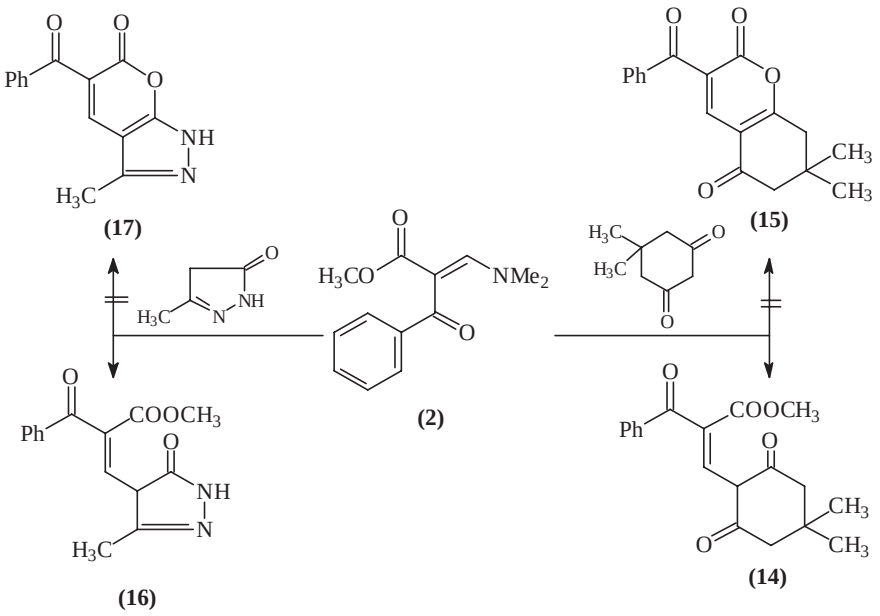
The reactivity of the enaminone **2** towards certain nitrogen nucleophiles was also investigated. Thus, treatment of **2** with hydrazines **18** in refluxing EtOH gave **19** based on the elemental and spectral data in particular ^1H NMR which revealed resonance at approximately 8.69 ppm corresponding to H-5 pyrazole beside the expected signals. Also, compound **2** reacted with guanidine hydrochloride in refluxing ethanolic sodium ethoxide solution yielding 2-aminopyrimidine derivative **20** (Scheme 5).

The aforementioned results, prompted us to investigate the reactivity of **2** towards some heterocyclic amines. Thus, compound **2** reacted with 5-aminopyrazole derivatives **21a–c** in refluxing EtOH to afford an excellent yield of single product identified as pyrazolo[1,5-*a*] pyrimidines **22a–c**, similar reaction was previously reported.[17-19] The structure **22** was confirmed by elemental and spectral data. Thus, the ^1H NMR showed the presence of $COOCH_3$ at 3.69 ppm and H-6 pyrimidine at 8.98 ppm. But the condensation of **2** with 2-aminopyridine[16] in refluxing AcOH gave 3-benzoylpyrido[1,2-*a*]pyrimidine-4-one **(24)** in a good yield via the intermediate **23**. The structure of **24** was confirmed based on the ^1H NMR which showed the absence of $COOCH_3$ and the presence of H-4 pyridmidine at δ 8.91 ppm. Also, the mass spectrum revealed a molecular ion peak at *m/z* 250 (47 %) corresponding to the molecular formula $C_{15}H_{10}N_2O_2$. Similarly, 2-aminobenzoimidazole and 2-aminopyrimidine derivative[8] were condensed with **2** to give **25** and **26** respectively (Scheme 6).

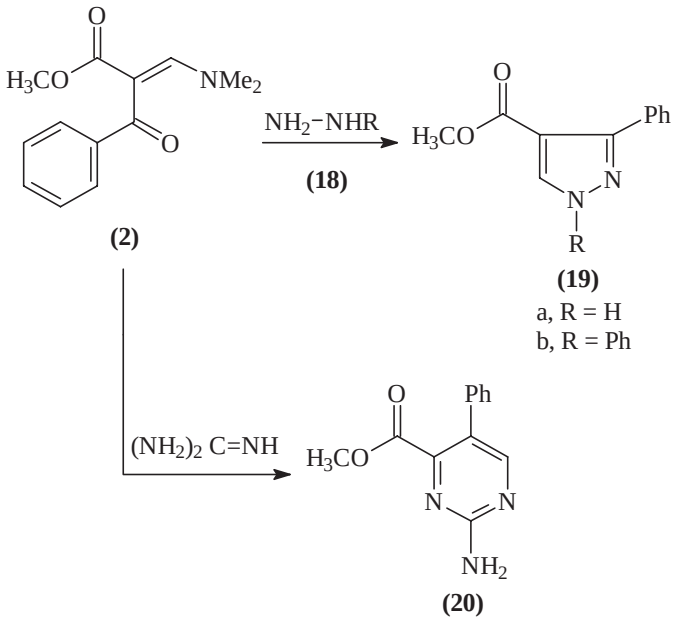
We report here the reactivity of enamine **27**[20,21] in [4+2] cycloaddition reactions. Thus, the enamine **27** reacted with



Scheme 3



Scheme 4



Scheme 5

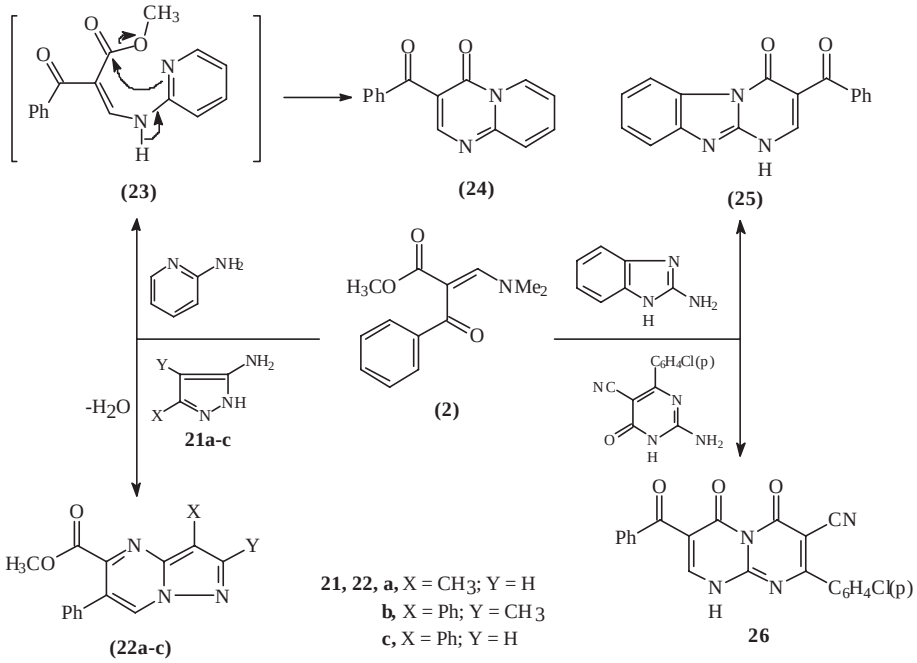
ethyl propionate or dimethyl acetylenedicarboxylate in refluxing dimethylformamide to afford benzimidazo[1,2-a] pyridines (**28a,b**). It was assumed that the reaction proceed *via* the 4+2 cycloaddition followed by loss of dimethylamine. Also, **27** reacted with hippuric acid[22] to yield **30**. Compound **30** was believed to be formed via the non-isolable **29** which in turn transforms into **30** under reaction conditions (Scheme 7).

Finally, compound **27** reacted with 5-amino-3-methylpyrazole **31** in refluxing AcOH yielding unexpected product which was formulated as dibenzimidazo[1,2-a:1', 2'-e][1,5]diazocine-3,7-dicarbonitrile[23-25] (**32**) due to the dimerisation of **27** this indicates that 5-aminopyrazole is not involved in the reaction, where compound **33** was not isolated. On the other hand, **32** was obtained by heating **27** in AcOH. The structure of **32** was established based on spectral data. Thus, the IR*(*KBr) revealed the absence of absorption NH and the presence of CN at ν 2225 cm^{-1} and the mass spectrum showed a molecular ion peak at *m/z* 334 (100 %) corresponding to the molecular formula $C_{20}H_{10}N_6$. Also, its ^{1}H NMR spectrum showed in addition to the expected signals, singlet at δ 8.13 ppm attributed to H-2, H-6 1,5-diazocine derivative (Scheme 7).

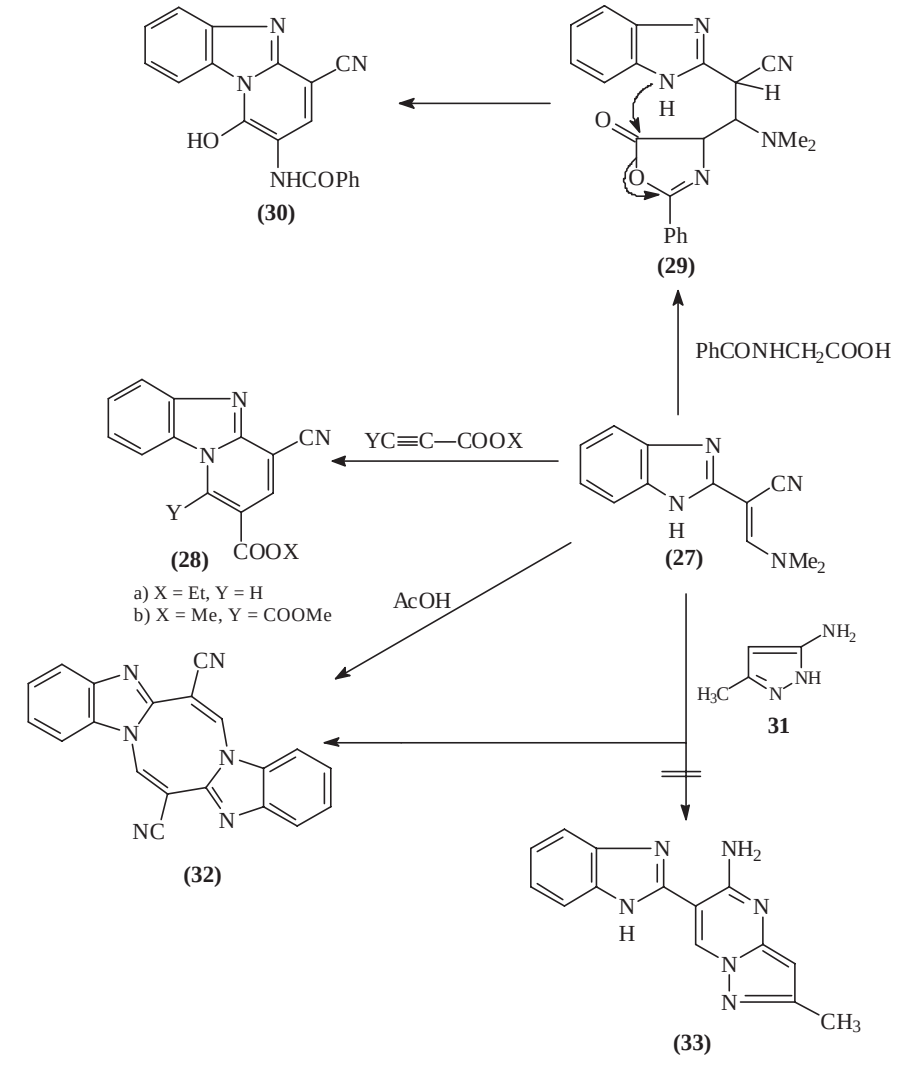
Experimental

Melting points were uncorrected, determined in glass capillary tubes on a MEL-TEMP II melting point apparatus. IR spectra were recorded with a Shimadzu FTR-8201 PC spectrophotometer. ^{1}H NMR were obtained on a varian Gemini (200 MHz) spectrometer using DMSO d_6 and/or $CDCl_3$-d_1 as a solvent and TMS as an internal reference. Mass spectra were performed on a Shimadzu G cmS -QP 1000EX spectrometer using direct inlet system and EI-QI MS LRUPL. Microanalysis was performed by the Microanalytical Unit at Cairo University. Thin layer chromatography was carried out on 5 × 20 cm plates coated with silica gel GF 254 type 60, mesh size 50–250.

2-Benzoyl-3-dimethylaminopropenoate **(2)**: Prepared according to lit.[10] Yield (70 %), m.p. 70 °C, pale orange crystals from EtOH;



Scheme 6



Scheme 7

IR (KBr) ν_{max}/ cm^{-1}: 1715 (C=O ester.) 1665 (C=O); ^1H NMR ($CDCl_3$) δppm = 2.33 (s, 6H, NMe_2) 3.78 (s, 3H, OCH_3), 7.21–8.10 (m, 6H, H–Ar + H-3); ms: *m/z* = 232 (M^+, 48 %). Anal calcd. for $C_{13}H_{15}NO_3$: C, 66.93; H, 6.43; N, 6.00. Found: C, 67.10; H, 6.50; N, 5.90 %.

Preparation of ***4*** *and* ***8*** *(general procedure):* A mixture of compound **2** (0.01 mol) and benzoylacetonitrile or (benzoimidazo-2-yl)acetonitrile (0.01 mol) was heated and stirred at 80–90 °C in glacial acetic acid (5ml) for 2h upon cooling, the separated product was filtered washed with saturated solution of sodium hydrogen carbonate and water, dried and recrystallised from EtOH as yellow crystals.

Methyl 5-benzoyl-6-oxo-2-phenyl-1H-pyridine-3-carboxylate **(4)**: Yield (48 %), m.p. 275 °C; IR (KBr) ν_{max}/ cm^{-1}: 3230 (NH), 1710 (C=O) 1665 (C=O); ^1H NMR (DMSO-d_6) δppm = 3.71 (s, 3H, -OCH_3), 6.31 (s, 1H, H-4 pyridine), 7.41–7.88 (m, 10H, H–Ar), 8.97 (s, 1H, NH); ms: *m/z* = 333 (M^+, 93 %). Anal calcd. for $C_{20}H_{15}NO_4$: C, 72.07; H, 4.50; N, 4.20. Found: C, 72.10; H, 4.30; N, 4.40 %.

Methyl 4-cyano-3-phenylbenzimidazo [1,2-a]pyridine-2-carboxylate **(8)**: Yield (80 %), m.p. 290 °C, yellow crystals; IR (KBr) ν_{max}/ cm^{-1}: 2213 (CN), 1715 (C=O, ester); ^1H NMR (DMSO-d_6) δppm = 3.72 (s, 3H, –OCH_3), 7.13–7.75 (m, 8H, H–Ar), 7.98 (d, 1H, *J* = 8Hz, H-9 Ar), 8.47 (s, 1H, H-6 pyridine); ms: *m/z* = 327 (M^+, 100 %). Anal calcd. for $C_{20}H_{13}N_3O_2$: C, 73.39; H, 4.00; N, 12.54. Found: C, 73.40; H, 4.10; N, 12.70 %.

Methyl 5-cyano-2,6-diphenylpyridine-3-carboxylate **(6)**: To a solution of enaminone **2** (0.01 mol) and ammonium acetate (1 g) in ACOH (5 ml), benzoylacetonitrile (0.01 mol) was added. The reaction mixture was heated under reflux for 1 h. the solvent was removed in vacuum, the residual solid was crystallised from methanol, as colourless crystals.

Yield (65 %), m.p. 145 °C; IR (KBr) ν_{max}/ cm^{-1}: 2213 (CN), 1715 (CO ester); ^1H NMR ($CDCl_3$) δppm = 3.77 (s, 3H, OCH_3), 7.48–7.66 (m, 8H, H–Ar), 8.07 (d, 2H, H–Ar), 8.47 (s, 1H, H-4 pyridine); ms: *m/z* = 314 (M^+, 39.9 %). Anal calcd. for $C_{20}H_{14}N_2O_2$: C, 76.43; H, 4.45; N, 8.91. Found: C, 76.40; H, 4.30; N, 9.00 %.

Methyl 5-cyano-1,6-dihydro-6-oxo(thioxo)-4-phenylpyridine-3-carboxylate **(10a,b)**: *General procedure:* A mixture of compound **2** (0.01 mol) and cyanoacetamide or cyanothioacetamide (0.01 mol) in sodium ethoxide solution (20 ml) [prepared from 0.3 g sodium metal in (20 ml) absolute ethanol]. The reaction mixture was refluxed for 2–3 h, then poured into ice cooled water and neutralisation with HCl (10 %). The solid produced so formed was collected by filtration and recrystallised from EtOH.

Methyl 5–cyano-1, 6-dihydro-6-oxo-4-phenylpyridine-3-carboxylate **(10a)**: Yield (63 %), m.p. 240 °C, orange crystals; IR (KBr) ν_{max}/ cm^{-1}: 3320 (NH), 2217 (CN), 1713 (C=O); ^1H NMR (DMSO-d_6) δppm = 3.76 (s, 3H, OCH_3), 7.36–7.94 (m, 5H, H–Ar), 7.99 (s, 1H, H-2 pyridine), 9.82 (br, 1H, NH); ms: *m/z* = 254 (M^+, 14.3 %). Anal calcd. for $C_{14}H_{10}N_2O_3$: C, 66.14; H, 3.92; N, 11.02. Found: C, 66.20; H, 3.90; N, 11.10 %.

Methyl 5-cyano-1, 6-dihydro-4-phenyl-6-thioxopyridine-3-carboxylate **(10b)**: Yield (73 %), m.p. 280 °C, deep brown powder; IR (KBr) ν_{max}/ cm^{-1}:3310 (NH), 2217 (CN), 1710 (C=O); ^1H NMR (DMSO-d_6) δppm = 3.78 (s, 3H, OCH_3), 7.41–7.86 (m, 5H, H–Ar), 8.13 (s, 1H, H-2 pyridine), 9.91 (br, 1H, NH); ms: *m/z* = 270 (M^+, 35 %). Anal calcd. for $C_{14}H_{10}N_2O_2S$: C, 62.21; H,3.73; N, 10.36. Found: C, 62.20.; H, 3.60; N, 10.30 %.

Preparation of **(13a, b)**: To a suspension of **10b** (0.01 mol) in pyridine (10 ml), was added alkyl halides **12** (0.01 mol). The mixture was stirred with heating under reflux for 2–3 h., then allowed to cool and neutralisation with HCl (10 %). The solid product so formed, was collected by filtration and recrystalised from DMF.

Ethyl 3-amino-5-methoxycarbonyl-4-phenylthieno[2,3-b]pyridine-3-carboxylate **(13a)**: Yield (52 %), m.p. 292 °C, yellowish green crystals; IR (KBr) ν_{max}/ cm^{-1}: 3430 (NH_2), 1725 (C=O), 1705 (C=O); ^1H NMR (DMSO-d_6) δppm = 1.29 (t, 3H, CH_3), 3.73 (s, 3H, OCH_3), 4.31 (q, 2H, CH_2), 5.63 (s, 2H, NH_2), 7.31–7.81 (m, 5H, H–Ar), 8.31 (s, 1H, H-6 pyridine); ms: *m/z* = 356 (M^+, 34 %). Anal calcd. for $C_{18}H_{16}N_2O_4S$: C, 60.67; H, 4.52; N, 7.86; S,8.99. Found: C, 60.70; H, 4.50; N, 7.90; S,8.90 %.

Methyl 3-amino-2-benzoyl-4-phenylthieno [2,3-b]pyridine-5-carboxylate **(13b)**: Yield (64 %), m.p. 305 °C, green powder; IR (KBr) ν_{max}/ cm^{-1}: 3455 (NH_2), 1725 (C=O), 1662 (C=O); ^1H NMR (DMSO-d_6) δppm = 3.72 (s, 3H, OCH_3), 6.1 (br, 2H, NH_2), 7.41–7.89 (m, 10H, H–Ar), 8.10 (s, 1H, H-6 pyridine). Anal calcd. for $C_{22}H_{16}N_2O_3S$: C, 68.04; H, 4.12; N, 7.21; S, 8.24. Found: C, 68.20; H, 4.30; N, 7.10; S, 8.30 %.

Preparation of **14** *and* **16**, *General procedure*: To a solution of 1,2-dihydro-3-methylpyrazolone or dimedone (0.01 mol) in acetic acid (5 ml), compound **2** (0.01 mol) was added and the mixture was heated under reflux for 5–6 h. The reaction was followed by TLC (chloroform/methanol, 15:1 as solvent). After reaction was completed, acetic acid was evaporated *in vacuo* and the solid residue was crystallised from EtOH.

Methyl 2-benzoyl-3-(5,5-dimethyl-1,3-dioxocyclohexan-2-yl) propenoate **(14)**: Yield (53 %), m.p. 265 °C, orange powder; IR (KBr) ν_{max}/ cm^{-1}: 2985 (CH, aliph), 1720 (C=O), 1669 (C=O); ^1H NMR ($CDCl_3$) δppm = 0.96 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 2.14 (s, 2H, CH_2), 2.20 (s, 2H, CH_2), 2.46 (d, 1H, H-2), 3.74 (s, 3H, OCH_3), 7.25–7.45 (m, 6H, H–Ar + H-olifinic); ms: *m/z* = 328 (M^+, 100 %). Anal calcd. for $C_{19}H_{20}O_5$: C, 69.51; H, 6.09. Found: C, 69.60; H, 6.10 %.

Methyl 2-benzoyl-3-(1,2-dihydro-3-methyl-5-oxopyrazol-4-yl)-propenoate **(16)**: Yield (69 %), m.p. 310 °C, orange red powder; IR (KBr) ν_{max}/ cm^{-1}: 3230 (NH), 1713 (C=O); ^1H NMR ($CDCl_3$) δppm = 2.10 (d, 1H, H-4 pyrazol), 3.10 (s, 3H, CH_3), 3.85 (s, 3H, OCH_3), 7.25–7.73 (m, 6H, H–Ar + H-olifinic), 8.35 (br, 1H, NH). Anal calcd. for $C_{15}H_{14}N_2O_4$: C, 62.93; H, 4.89; N, 9.79. Found: C, 62.90; H, 4.90; N, 9.80 %.

Preparation of **19a, b, 20** *and* **22a–c**, *General procedure*: To a solution of **2** (0.01 mol) in ethanol (10 ml) was added to a suitable hydrazines or heterocyclic aromatic amines (0.01 mol). The reaction mixture was refluxed for 5–10 h. then, left to cool at room temperature. The product so formed was collected by filtration and crystallised from ethanol.

Methyl 1-H-3-phenylpyrazole-4-carboxylate **(19a)**: Yield (73 %), m.p. 122 °C, colourless powder; IR (KBr) ν_{max}/ cm^{-1}: 3310 (NH), 1710 (C=O, ester); ^1H NMR ($CDCl_3$) δppm = 3.95 (s, 3H, OCH_3) 7.41–7.98 (m, 5H, H–Ar), 8.69 (s, 1H, H-5 pyrazole), 8.98 (br, 1H, NH); ms: *m/z* = 202 (M^+, 69 %).Anal calcd. for $C_{11}H_{10}N_2O_2$: C, 65.33; H, 4.98; N, 13.85. Found: C, 65.40; H, 4.70; N, 13.80 %.

Methyl 1,3-diphenyl pyrazole-4-carboxylate **(19b)**: Yield (75 %), m.p. 135 °C, colourless powder; IR (KBr) ν_{max}/ cm^{-1}: 1715 (C=O, ester); ^1H NMR ($CDCl_3$) δppm = 3.74 (s, 3H, OCH_3) 7.30–7.63 (m, 10H, H–Ar), 8.17 (s, 1H, H-5 pyrazole); ms: *m/z* = 278 (M^+ 69 %). Anal calcd. for $C_{17}H_{14}N_2O_2$: C, 73.38; H, 5.03; N, 10.07. Found: C, 73.40; H, 5.10; N, 10.10 %.

Methyl 6-amino-3-phenylpyrimidine-2-carboxylate **(20)**: Yield (75 %), m.p. 135 °C, pale yellow; IR (KBr) ν_{max}/ cm^{-1}: 3415 (NH_2), 1715 (C=O, ester); ^1H NMR ($CDCl_3$) δppm = 3.74 (s, 3H, OCH_3) 6.53 (br, 2H, NH_2), 7.30–7.63 (m, 5H, H–Ar), 8.17 (s, 1H, H-6 pyrimidine); ms: *m/z* = 229 (M^+ 69 %). Anal calcd. for $C_{12}H_{11}N_3O_2$: C, 62.87; H, 4.83; N, 18.33. Found: C, 62.60; H, 4.60; N, 18.20 %.

Methyl 3-methyl-6-phenylpyrazolo[1,5-a]pyrimidine-5-carboxylate **(22)**: Yield (80 %), m.p. 160 °C, colourless powder; IR (KBr) ν_{max}/ cm^{-1}: 1720 (C=O, ester); ^1H NMR ($CDCl_3$) δppm = 2.56 (s, 3H, CH_3), 3.69 (s, 3H, OCH_3), 7.49–7.71 (m, 6H, H–Ar + H-3 pyrazole), 8.96 (s, 1H, H-6 pyrimidine); ms: *m/z* = 267 (M^+, 100 %). Anal calcd. for $C_{15}H_{13}N_3O_2$: C, 67.41; H, 4.86; N, 15.73. Found: C, 67.40; H, 4.70; N, 15.80 %.

Methyl 2-methyl-3,6-diphenylpyrazolo[1,5-a]pyrimidine-5-carboxylate **(22b)**: Yield (65 %), m.p. 198 °C. pale yellow; IR (KBr) ν_{max}/ cm^{-1}: 1718 (C=O, ester); ^1H NMR ($CDCl_3$) δppm = 2.56 (s, 3H, CH_3), 3.69 (s, 3H, OCH_3), 7.43–7.71 (m, 10H, H–Ar), 8.98 (s, 1H, H-6 pyrimidine); ms: *m/z* = 343 (M^+, 96 %). Anal calcd. for $C_{21}H_{17}N_3O_2$: C, 73.46; H, 4.96; N, 12.24. Found: C, 73.50; H, 4.90; N, 12.40 %.

Methyl 3,6-diphenyl[1,5-a]pyrimidine-5-carboxylate **(22c)**: Yield (38 %), m.p. 169 °C, pale yellow; IR (KBr) ν_{max}/ cm^{-1}: 1715 (C=O, ester); ^1H NMR ($CDCl_3$) δppm = 3.74 (s, 3H, OCH_3), 7.34–7.78 (m, 11H, H–Ar + H-3-pyrazole), 8.98 (s, 1H, H-6 pyrimidine); ms: *m/z* = 329 (M^+, 63 %). Anal calcd. for $C_{20}H_{15}N_3O_2$: C, 72.94; H, 4.55; N, 12.76. Found: C, 72.70; H, 4.30; N, 12.70 %.

The preparation of **24–26**, *general procedure*: To a solution of a heterocyclic amines (0.018 mole) in acetic acid (5 ml), compound **2** was added and the mixture was heated under reflux for 3–7 h. The reaction was followed by TLC. After reaction was completed, acetic acid was evaporated *in vacuo* and the solid residue was recrystallised from an appropriate solvent.

3-Benzoylpyrido[1,2-a]pyrimidine-4-one **(24)**: This compound was prepared from 2-aminopyridine, 3 h of reflux, yield (38 %), m.p. 125 °C, orange crystals from petroleum ether; IR (KBr) ν_{max}/ cm^{-1}: 1689 (C=O), 1663 (C=O); ^1H NMR ($CDCl_3$) δppm = 7.46–7.98 (m, 8H, H–Ar+ H pyridine), 8.21 (d, 1H, *J* = 8.0 Hz, H-6 pyridine), 8.91 (s, 1H, H-4 pyrimidine); ms: *m/z* = 250 (M^+, 47 %). Anal calcd. for $C_{15}H_{10}N_2O_2$: C, 72.00; H, 4.00; N, 11.20. Found: C, 72.10; H, 4.10; N, 11.30 %.

3-Benzoyl-1H-benzoimidazo[1,2-a]pyrimidine-4-one **(25):** This compound was prepared from 2-aminobenzoimidazole, 5 h of reflux, yield (55 %), m.p. > 310 °C, buff powder from EtOH/DMF; IR (KBr) ν_{max}/ cm^{-1}: 3310 (NH), 1695 (C=O), 1663 (C=O); ^{1}H NMR (DMSO-d_6) δppm = 7.43–7.78 (m, 9H, H–Ar), 8.31 (s, 1H, NH), 8.58 (s, 1H, H-6 pyrimidine); ms: *m/z* = 289 (M^+, 46.3 %). Anal calcd. for $C_{17}H_{11}N_3O_2$: C, 70.58; H, 3.80; N, 14.53. Found: C, 70.70; H, 3.70; N, 14.60 %.

3-Benzoyl-1H-4,6-dioxo-8-(p-chlorophenyl)pyrimidio[[1,2-a] pyrimidine-7-carbonitrile **(26)**: This compound was prepared from 2-amino-4-(p-chlorophenyl)-6-oxopyrimidine-5-carbonitrile, 7 h of reflux, yield (39 %), m.p. 305 °C, buff powder from EtOH; IR (KBr) ν_{max}/ cm^{-1}: 3210 (NH), 2215 (CN), 1688 (C=O), 1662 (C=O); ^{1}H NMR ($CDCl_3$) δppm = 7.31–7.84 (m, 9H, H–Ar), 8.31 (s, 1H, H-6 pyrimidine), 8.93 (s, 1H, NH); ms: *m/z* = 402 (M^+, 5.9 %). Anal calcd. for $C_{21}H_{11}Cl N_4O_3$: C, 62.60; H, 2.73; Cl, 8.81; N, 13.91. Found: C, 62.60; H, 2.80; Cl, 9.00 N, 14.00 %.

The preparation of **28a,b**, *general procedure*: A mixture of each ethyl propionate, dimethyl actylene dicarboxylate (0.01 mol) and compound **27** (0.01 mol) was refluxed in dimethylformamide (5 ml) for 1–2 h. The solvent was removed then left to cool at room temperature. The target compounds separated as solid that were collected by filtration and recrystallised from ethanol.

Ethyl 4-cyanobenzimidazo[1,2-a]pyridine-2-carboxylate **(28a)**: Yield (45 %), m.p. 223 °C, pale orange; IR (KBr) ν_{max}/ cm^{-1}: 2210 (CN), 1710 (C=O); ^{1}H NMR ($CDCl_3$) δppm = 1.39 (t, 3H, CH_3), 4.42 (q, 2H, CH_2), 7.49–7.65 (m, 2H, H–Ar), 7.90 (d, 1H, *J* = 9.0 Hz, H–7 Ar), 8.49 (s, 1H, H-4 pyridine), 8.58 (d, 1H, *J* = 9.0 Hz, H–9 Ar), 9.90 (s, 1H, H-2 pyridine); Anal calcd. for $C_{15}H_{11}N_3O_2$: C, 67.92; H, 4.15; N, 15.84. Found: C, 67.70; H, 4.20; N, 15.90 %.

Dimethyl 4-cyanobenzimidazo[1,2-a]pyridine-1,2-dicarboxylate **(28b)**: Yield (54 %), m.p. 202 °C, deep yellow; IR (KBr) ν_{max}/ cm^{-1}: 2215 (CN), 1728 (C=O, ester); ^{1}H NMR ($CDCl_3$) δppm = 4.0 (s, 3H, OCH_3), 4.25 (s, 3H, OCH_3), 7.25 (s, 1H, H-4 pyridine), 7.48 (d, 1H, H-7 Ar), 7.67 (m, 2H, H-8,9 Ar), 8.09 (d, 1H, *J* = 9.0 Hz, H-9 Ar); ms, *m/z* = 309 (M^+, 100 %). Anal calcd. for $C_{16}H_{11}N_3O_4$: C, 62.13; H, 3.55; N, 13.59. Found: C, 62.20; H, 3.60; N, 13.50 %.

2-Benzoylamino-1-hydroxybenzimidazo[1,2-a]pyridine-4-carbonitrile **(30)**: A solution of **27** and hippuric acid (0.01 mol) in acetic anhydride (20 ml) was heated under reflux for 3 h. The reaction mixture was concentrated under reduced pressure. The formed solid product was filtered off and crystallised from dioxane to yield pale yellow crystals.

Yield (62 %), m.p. 302 °C, pale brown; IR (KBr) ν_{max}/ cm^{-1}: 3410 (OH), 2217 (CN), 1689 (C=O); ^{1}H NMR (DMSO-d_6) δppm = 7.31 (s, 1H, H-4 pyridine), 7.65–7.98 (m, 8H, H–Ar), 8.31 (d, 1H, *J* = 9.0 Hz, H–9 Ar), 8.69 (s, 1H, NH), 11.40 (s, 1H, OH); ms, *m/z* = 328 (M^+, 35 %). Anal calcd. for $C_{19}H_{12}N_4O_2$: C, 69.51; H, 3.65; N, 17.07. Found: C, 69.70; H, 3.40; N, 17.20 %.

Dibenzoimidazo[1,2-a:1',2'-e][1,5]diazocine-3,7-dicarbonitrile **(32)**: A solution of compound **27** (0.5g) was heated under reflux in acetic acid (5 ml) for 1 h. or stirred at room temperature for 6 h. The solvent was removed under reduced pressure and the solid residue was crystallised from dioxane to give yellowish green powder. Yield (85 %), m.p. 350 °C, orange crystals; IR (KBr) ν_{max}/ cm^{-1}: 2225 (CN), 1631 (C=O); ^{1}H NMR (DMSO-d_6) δppm = 7.34–7.71 (m, 8H, H–Ar), 8.13 (s, 2H, H-2 ,H-6[1,5] diazocine); ms, *m/z* = 334 (M^+, 100 %). Anal calcd. for $C_{20}H_{10}N_6$: C, 71.81; H, 3.01; N, 25.14. Found: C, 71.90; H, 3.00; N,25.20 %.

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