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**ALKYLHETEROAROMATIC-CARBONITRILES AS BUILDING
BLOCKS IN HETEROCYCLIC SYNTHESIS: SYNTHESIS OF ETHYL
1-SUBSTITUTED-5-CYANO-4-METHYL-6-OXOPYRIDINE-3-CARBOXY
LATES; VERSATILE PRECURSORS FOR POLYFUNCTIONALLY
SUBSTITUTED ISOQUINOLINES AND PYRIDO[3,4-C]PYRIDINE**

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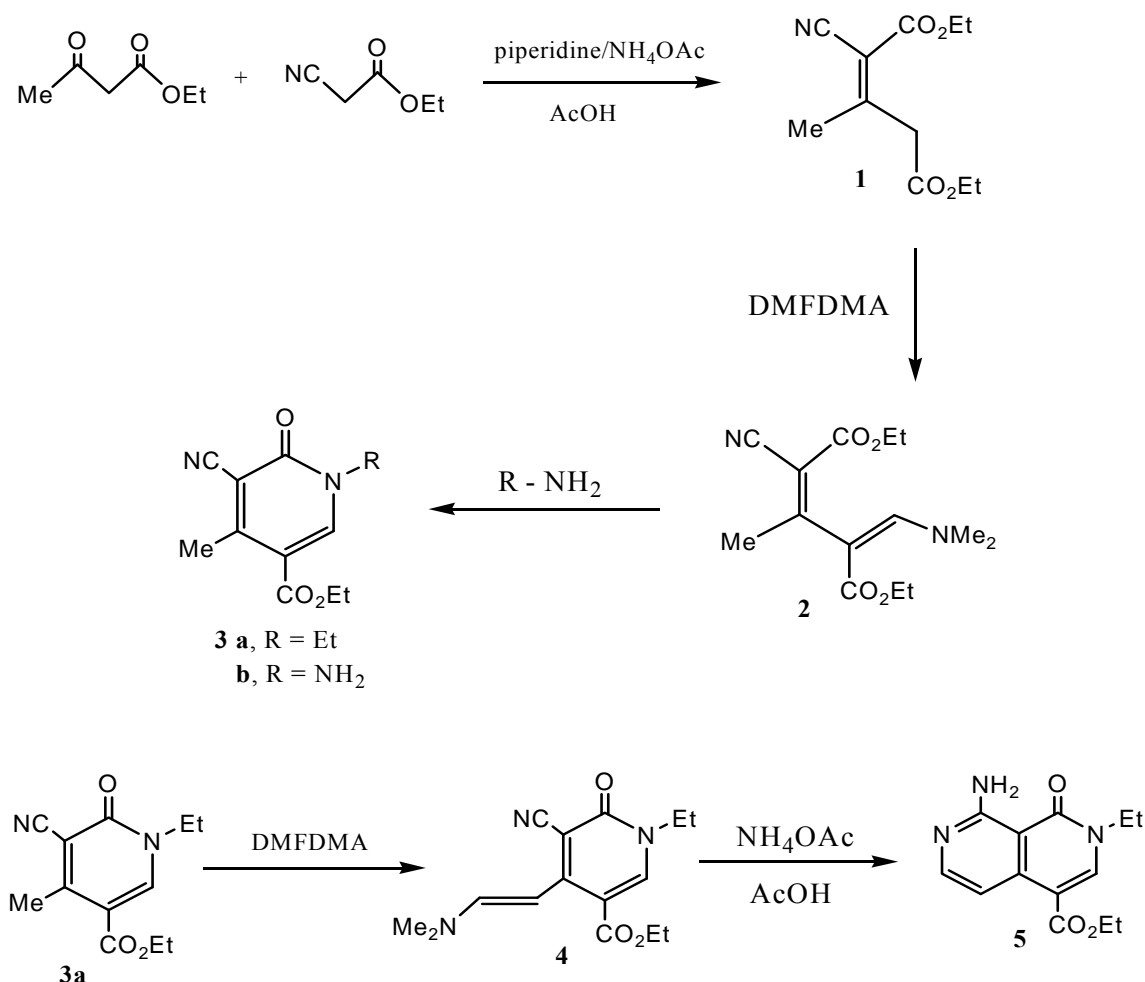
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Abstract – The title compounds were prepared *via* reacting diethyl 2-cyano-4-dimethylamino-methylene-3-methylpent-2-enedioic acid **2** with hydrazine hydrate and with ethyl amine. The formed pyridones **3a** condensed with dimethylformamide dimethyl acetal to yield the corresponding enamine **4** that could be cyclised into the pyrido[3,4-*c*]pyridine **5** by reflux in acetic acid in presence of ammonium acetate. The reaction of **3a** with elemental sulfur afforded the thienopyridine **6** that reacted readily with electron poor olefins and acetylenes to yield isoquinolines **8**, **10** and **11**. Compound **3a** reacted with benzylidene-malononitrile to yield the isoquinoline **14**.

Alkyl heteroaromatic carbonitriles have been extensively utilized as precursors to benzofused heterocycles.¹⁻³ Whereas we have explored potentialities of alkylpyridazinylcarbonitriles as precursors to phthalazines⁴⁻⁷ and cinnolines,⁸ Elnagdi *et al.*^{9, 10} and Dopp *et al.*^{11, 12} have reported on utility of 4-alkyl-coumarinylcarbonitriles as precursors to benzocoumarines. Only very recently Alzaidi *et al.*¹³ and Al-Mousawy *et al.*¹⁴ have reported on the utility of 3-aryloxy-4-methyl-2,6-dioxypyridine-5-carbonitriles as precursors to isoquinolines and pyridopyridazines. In conjunction to our interest in chemistry of alkylazinyllcarbonitriles we report here an efficient synthesis of ethyl 1-substituted-5-cyano-4-methyl-6-oxopyridine-3-carboxylates and their utility for synthesis of polyfunctionally substituted isoquinolines and pyrido[3,4-*c*]pyridines.

Condensing ethyl cyanoacetate with ethyl acetoacetate in refluxing toluene in presence of ammonium acetate following literature procedure¹⁵ has afforded (*Z*)-diethyl 2-cyano-3-methylpent-2-enedioate **1**. However, the product was highly impure, and consequently we

have stirred a mixture of ethyl cyanoacetate and acetoacetic ester in ethanol in presence of potassium carbonate and the product, so formed, proved identical with the product obtained *via* literature procedure, but was formed in better yield and higher purity that enabled its utility as such for next steps (**Scheme 1**).

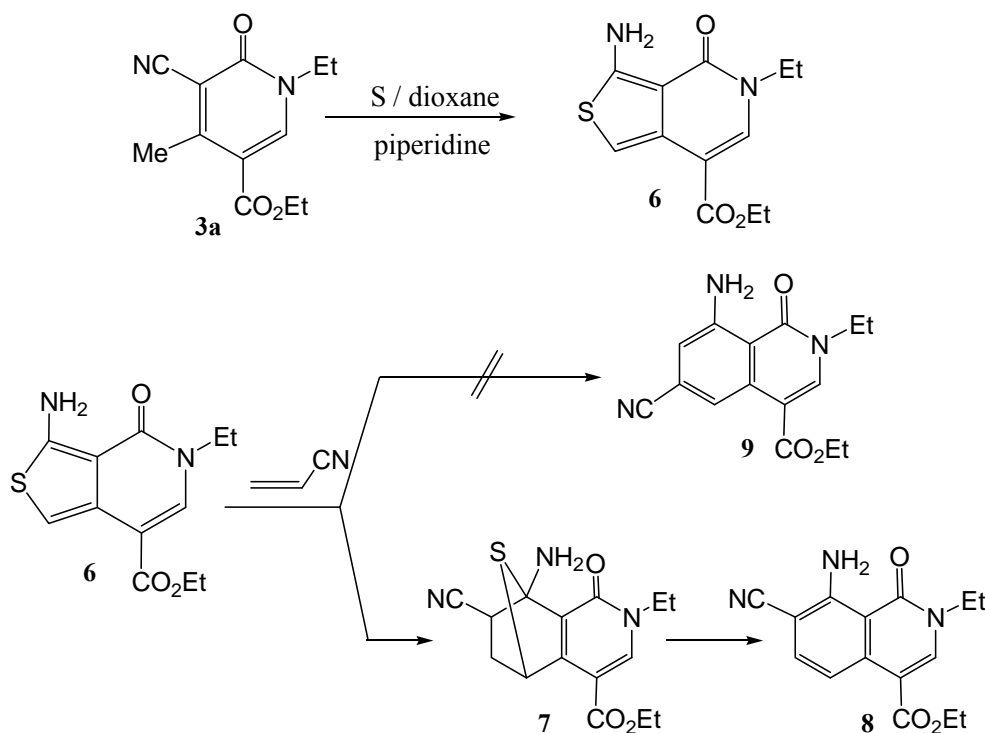


Scheme 1

Compound **1** condensed with dimethylformamide dimethyl acetal (DMFDMA) to yield pent-2-endioic acid ester **2** in a good yield (68% yield). The latter reacted with ethylamine in refluxing ethanol to yield the targeted pyridone **3 a** in 52% yield. The reaction of **2** with hydrazine hydrate afforded the N-aminopyridone **3 b** in 65% yield. The methyl function in **3 a** condensed with DMFDMA to yield an enamine **4** (46% yield) that was assigned as *trans* structure based on presence of two olefinic protons at 5.31 and 6.12 ppm with $J = 14.6 \text{ Hz}$; typical for *trans* olefinic protons. Compound **4** cyclized readily upon reflux in acetic acid in presence of ammonium acetate to yield pyridopyridone **5** in 27% yield (**Scheme 1**).

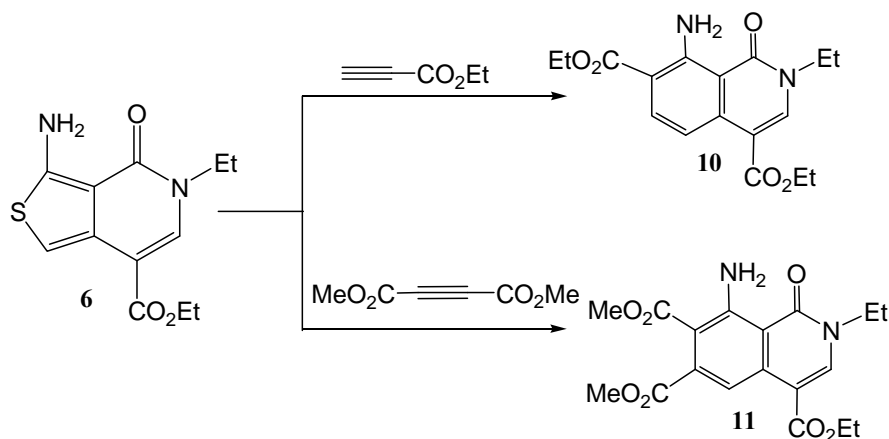
Typical to alkylazinylnitriles compound **3 a** reacted with elemental sulfur in dioxane in presence of piperidine to yield the thienopyridone **6**. Compound **6** reacted with acrylonitrile to yield

product of 4 + 2 cycloaddition with hydrogen sulfide elimination. In theory both **8** and **9** can be formed. However $^1\text{H-NMR}$ revealed protons at 7.15 and 7.64 with $J = 8.4$ Hz typical for H-5 and H-6 isoquinoline protons. Thus structure **8** was established for this product (**Scheme 2**).



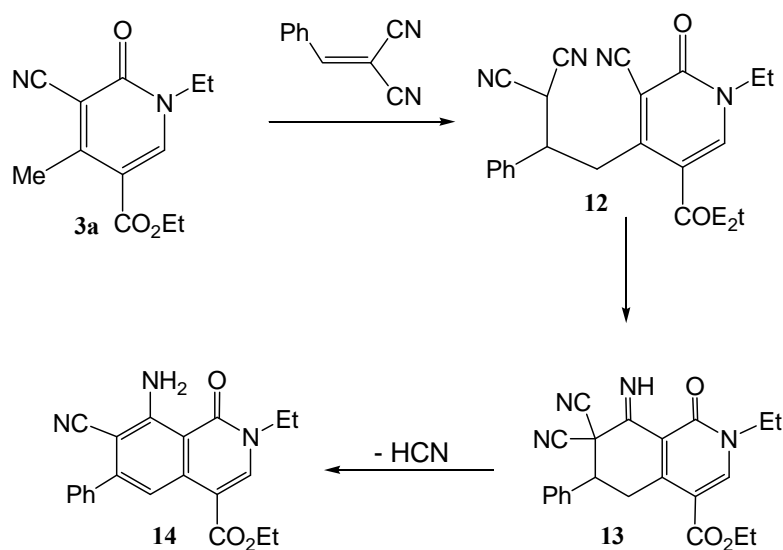
Scheme 2

Similar to its behavior toward acrylonitrile compound **6** reacted with ethyl propiolate and dimethyl acetylenedicarboxylate to yield **10** and **11** respectively. It is of value report that o-protons in **10** showed coupling value of 8.3 Hz typical for such protons (**Scheme 3**).



Scheme 3

Compound **3a** reacted with benzylidene-malononitrile to yield the isoquinoline **14**; that was formed, most likely, *via* **12** and **13** and hydrogen cyanide elimination (**Scheme 4**).



Scheme 4

In conclusion we have developed an easy approach to alkyl pyridinylcarbonitriles and could reveal that these are versatile precursors to polyfunctionally substituted isoquinolines.

EXPERIMENTAL

Melting points were recorded on Gallenkamp apparatus and are uncorrected. Infrared spectra (KBr) were determined on a Perkin-Elmer 2000 FT-IR system. NMR measurements were determined on a Bruker DPX spectrometer, at 600 MHz for ^1H NMR and 125 MHz for ^{13}C NMR, in DMSO- d_6 as solvent 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.

Reaction of ethyl acetoacetate with ethyl cyanoacetate:

Method A: A mixture of ethyl acetoacetate (1.30 g, 10.0 mmol), ethyl cyanoacetate (1.13 g, 10.0 mmol), 0.5 g of acetic acid, 0.2 g of ammonium acetate, and 0.02 g of piperidine was dissolved in 25 mL dry benzene.¹⁵ The mixture was refluxed in a flask fitted by azeotropic water separator on an oil bath at 160°C till removing 0.5 mL water were separated. The product was cooled to rt and washed with saturated NaCl solution then with distilled water. The product was obtained by vacuum distillation under 0.3 pressure to give ~ 0.62 g (bp_{0.3} 120°C, yield: 38%).

Method B: A mixture of ethyl acetoacetate (1.30 g, 10.0 mmol), ethyl cyanoacetate (1.13 g, 10.0 mmol), and 0.5 g of K_2CO_3 anhydrous dissolved in 50 mL absolute EtOH. The mixture was stirred overnight. The product was washed by water, extracted with chloroform and then dried by anhydrous sodium sulphate. The pure product was obtained by evaporation of CHCl_3 and proved

identical with the purified product obtained by method A.

(Z)-Diethyl 2-cyano-3-methylpent-2-enedioate (1)

This compound was obtained as a yellow oil (yield: 68%); IR(KBr): $\nu = 1610.3$ (C=C), 1680 (C=O), 1686 (C=O), 2190.29 (CN) cm^{-1} , $^1\text{H NMR}$ (DMSO- d_6): $\delta = 1.13$ (t, $J = 7.0$ Hz, $J = 7.2$ Hz, 6H, two ester CH_3), 2.32 (s, 3H, CH_3), 3.37 (s, 2H, CH_2), 3.95 (q, 2H, $J = 7.0$ Hz, CH_2), 4.24 (q, 2H, $J = 7.2$ Hz, CH_2); $^{13}\text{C NMR}$ (DMSO- d_6): $\delta = 13.7$ (CH_3 of $\text{CO}_2\text{C}_2\text{H}_5$), 14.2 (CH_3 of $\text{CO}_2\text{C}_2\text{H}_5$), 15.4 (CH_3), 38.8 (CH_2), 58.1 (O- CH_2), 60.6 (O- CH_2), 97.2 ($=\text{C}(\text{CN})$), 116.8 (CN), 165.2 ($=\text{C}(\text{CH}_3)$), 169.6 (C=O), 170.1 (C=O); MS, m/z (%), 225.1 (M^+ , 98), 151.0 (100), 123.0 (84). Anal. Calcd for $\text{C}_{11}\text{H}_{15}\text{NO}_4$: C, 58.66; H, 6.71; N, 6.22. Found: C, 58.61; H, 6.69; N, 6.19.

Reaction of 1 with *N,N*-dimethylformamide dimethyl acetal (DMFDMA):

A mixture of **1** (2.25 g, 10.0 mmol), and dimethylformamide dimethyl acetal (2.40 g, 20.0 mmol) was dissolved in 25 mL dry xylene. The mixture was refluxed for 5 h, and then cooled to rt then treated with petroleum ether. The solid product, so formed, was collected by filtration and recrystallized from EtOH to give **2**.

Diethyl 2-Cyano-4-dimethylaminomethylene-3-methyl-pent-2-enedioate (2)

This compound was obtained as pale green solid (yield: 68%); IR(KBr): $\nu = 1608$ (C=C), 1675 (C=O), 1682 (C=O), 2192.3 (CN) cm^{-1} , $^1\text{H NMR}$ (DMSO- d_6): $\delta = 1.2$ (t, 6H, $J = 7.1$ Hz, $J = 7.2$ Hz, two ester CH_3), 2.32 (s, 3H, CH_3), 3.23 (s, 6H, $\text{N}(\text{CH}_3)_2$), 4.04 (q, $J = 7.1$ Hz, $J = 7.2$ Hz, 4H, 2 O- CH_2), 7.28 (s, 1H, CH); $^{13}\text{C NMR}$ (DMSO- d_6): $\delta = 13.3$ (aliphatic, CH_3), 13.9 (CH_3 of $\text{CO}_2\text{C}_2\text{H}_5$), 14.1 (CH_3 of $\text{CO}_2\text{C}_2\text{H}_5$), 45.2 (2 N- CH_3), 59.0 (O- CH_2), 59.6 (O- CH_2), 98.1 ($=\text{C}(\text{CN})$), 102.1 (C, B to enamine N), 116.4 (CN), 147.7 (C, α to enamine N), 164.8 (C=O), 166.7 (C=O), 167.0 ($=\text{C}-\text{CH}_3$); MS, m/z (%), 280.2 (M^+ , 98), 235.1 (48), 119.1 (42). Anal. Calcd for $\text{C}_{14}\text{H}_{20}\text{N}_2\text{O}_4$: C, 59.99; H, 7.19; N, 9.99. Found: C, 59.97; H, 7.16; N, 9.92.

Reaction of 2 with ethylamine and with hydrazine:

A mixture of **2** (2.80 g, 10.0 mmol), and 10.0 mmol of ethylamine (70 wt. % solution in water) or hydrazine hydrate (80 wt. % solution in water) in 25 mL of EtOH was refluxed for 6 h. The solid crude product, so formed, was collected by filtration and purified by recrystallization from EtOH to give **3a** and **3b**, respectively.

Ethyl 5-cyano-1-ethyl-4-methyl-6-oxo-1,6-dihydro-pyridine-3-carboxylate (3a)

This compound was obtained as a brown solid (yield: 52%); IR(KBr): $\nu = 1611$ (C=C), 1668 (C=O), 1675 (C=O), 2188.1 (CN) cm^{-1} , $^1\text{H NMR}$ (DMSO- d_6): $\delta = 1.04$ (t, 3H, $J = 7.0$ Hz, amide CH_3), 1.19

(t, 3H, $J = 7.2$ Hz, ester CH₃), 1.82 (s, 3H, CH₃), 3.87 (q, 2H, $J = 7.0$ Hz, N-CH₂), 4.11 (q, 2H, $J = 7.2$ Hz, O-CH₂), 8.51 (s, 1H, pyridine CH); ¹³C NMR (DMSO-*d*₆): $\delta = 12.0$ (aliphatic, CH₃), 13.4 (CH₃, ester CH₃), 13.8 (CH₃, ester CH₃), 41.2 (CH₂, N-CH₂), 61.3 (CH₂, O-CH₂), 102.5 (C, C₅, pyridone), 115.4 (=C(CN)), 118.7 (CN), 139.4 (CH, C₆, pyridone), 159.2 (C=O, amide), 163.7 (C=O, ester), 164.6 (C, pyridone C-4); MS, *m/z* (%), 234.1 (M⁺, 98), 188.1 (54). Anal. Calcd for C₁₂H₁₄N₂O₃: C, 61.53; H, 6.02; N, 11.96. Found: C, 61.49; H, 5.97; N, 11.92.

Ethyl 1-amino-5-cyano-4-methyl-6-oxo-1,6-dihydro-pyridine-3-carboxylate (3b)

This compound was obtained as a pale brown solid (yield: 65%); IR(KBr): $\nu = 1609$ (C=C), 1665 (C=O), 1671 (C=O), 2184.1 (CN), 3425 (br., NH₂) cm⁻¹, ¹H NMR (DMSO-*d*₆): $\delta = 1.19$ (t, 3H, $J = 7.1$ Hz, ester CH₃), 2.46 (s, 3H, CH₃), 4.13 (q, 2H, $J = 7.1$ Hz, O-CH₂), 4.67 (s, 2H, NH₂), 8.26 (s, 1H, pyridine CH); ¹³C NMR (DMSO-*d*₆): $\delta = 12.7$ (CH₃, pyridine-CH₃), 13.4 (CH₃, ester CH₃), 60.8 (CH₂, O-CH₂), 100.4 (C, pyridine C-5), 116.3 (=C(CN)), 118.6 (CN), 132.0 (CH, pyridone C-6), 158.4 (C=O, amide), 164.2 (C=O, ester), 167.3 (C, pyridone C-4); MS, *m/z* (%), 221.1 (M⁺, 100), 176 (64). Anal. Calcd for C₁₀H₁₁N₃O₃: C, 54.29; H, 5.01; N, 19.00. Found: C, 54.24; H, 4.96; N, 18.95.

Reaction of 3a with dimethylformamide dimethylacetal:

A mixture of **3a** (2.34 g, 10.0 mmol) and (1.8 g, 15.0 mmol) of dimethylformamide dimethyl acetal was dissolved in 25 mL of dry xylene and was refluxed for 6 h, then treated with petroleum ether. The solid product, so formed, was collected by filtration and recrystallized from EtOH to give **4**.

(E)-Ethyl 5-cyano-4-(2-(dimethylamino)vinyl)-1-ethyl-6-oxo-1,6-dihydropyridine-3-carboxylate (4)

This compound was obtained as a brown solid (yield: 46%); IR(KBr): $\nu = 1610$ (C=C), 1664 (C=O), 1690 (C=O), 2187 (CN) cm⁻¹, ¹H NMR (DMSO-*d*₆): $\delta = 1.32$ (t, 3H, $J = 7.0$ Hz, amide CH₃), 1.68 (t, 3H, $J = 7.1$ Hz, ester CH₃), 2.73 (s, 6H, (CH₃)₂N), 3.24 (q, 2H, $J = 7.0$ Hz, N-CH₂), 4.22 (q, 2H, $J = 7.1$ Hz, O-CH₂), 5.31 (d, 1H, $J = 14$ Hz, enamine H), 6.72 (d, 1H, $J = 14$ Hz, enamine H), 8.02 (s, 1H, pyridone C-6); ¹³C NMR (DMSO-*d*₆): $\delta = 13.3$ (CH₃, amide CH₃), 13.5 (CH₃, ester CH₃), 38.6 (CH₃, two CH₃, (CH₃)₂N), 41.0 (CH₂, N-CH₂), 60.7 (CH₂, O-CH₂), 99.8 (=C(CN)), 104 (CH enamine), 116.3 (C, pyridone C-5), 118.4 (CN), 130.1 (CH, pyridone C-6), 142.0 (CH, =CH-N enamine), 161.4 (C=O, amide), 164.9 (C=O, ester), 169.8 (C, pyridone C-4); MS, *m/z* (%), 289.1 (M⁺, 100), 260.1 (19). Anal. Calcd for C₁₅H₁₉N₃O₃: C, 62.27; H, 6.62; N, 14.52. Found: C, 62.23; H, 6.59; N, 14.47.

Cyclization of enamine 4 in the presence of NH₄OAc:

A mixture of enamine **4** (2.89 g, 10.0 mmol), 1 g of ammonium acetate, and 25 mL of glacial acetic acid was refluxed for 5 h, then the crude solid product was neutralized by aqueous sodium carbonate and then the pure product was separated by long column chromatography through silica gel by using 1:3 EtOAc : n-hexane to yield **5**.

Synthesis of Ethyl 8-amino-2-ethyl-1-oxo-1,2-dihydro-[2,7]naphthyridine-4-carboxylate (5)

This compound was obtained as a brown solid (yield: 27%); IR(KBr): $\nu = 1609$ (C=C), 1669 (C=O), 1694 (C=O), 3345 (br. NH₂) cm⁻¹, ¹H NMR (DMSO-*d*₆): $\delta = 1.29$ (t, 3H, *J* = 7.0 Hz, amide CH₃), 1.38 (t, 3H, *J* = 7.1 Hz, ester CH₃), 3.06 (q, 2H, *J* = 7.0 Hz, N-CH₂), 4.26 (q, 2H, *J* = 7.1 Hz, O-CH₂), 5.76 (s, 2H, NH₂), 7.29 (d, 1H, *J* = 8 Hz, aromatic H), 8.32 (d, 1H, *J* = 8 Hz, aromatic H), 8.56 (s, 1H, aromatic H); ¹³C NMR (DMSO-*d*₆): $\delta = 13.1$ (CH₃, amide CH₃), 13.2 (CH₃, ester CH₃), 40.4 (CH₂, N-CH₂), 59.7 (CH₂, O-CH₂), 110.3, 112.4, 116.2, 134.7, 148.6, 149.2 (aromatic C), 163.0 (C, C=O), 165.2 (C, C-NH₂), 165.7 (C=O, ester); MS, *m/z* (%), 261.2 (M⁺, 100), 232.2 (32). Anal. Calcd for C₁₃H₁₅N₃O₃: C, 59.76; H, 5.79; N, 16.08. Found: C, 59.73; H, 5.75; N, 16.02.

Reaction of 3a with elemental sulfur:

A mixture of **3a** (2.34 g, 10.0 mmol), and 0.5 g of elemental sulfur, 0.2 g of piperidine was dissolved in 25 mL dioxane and then was refluxed for 5 h, the reaction was followed by TLC. The solvent was removed under vacuum and then triturated with water. The solid product, so formed, was purified by crystallization from EtOH to give **(6)**.

Ethyl 3-amino-5-ethyl-4-oxo-4,5-dihydro-thieno[3,4-*c*]pyridine-7-carboxylate (6)

This compound was obtained as a yellow solid (yield: 55%); IR(KBr): $\nu = 1610$ (C=C), 1664 (C=O, amide), 1690 (C=O, ester), 3350 (br. NH₂) cm⁻¹, ¹H NMR (DMSO-*d*₆): $\delta = 1.24$ (t, 3H, *J* = 7.0 Hz, amide CH₃), 1.33 (t, 3H, *J* = 7.1 Hz, ester CH₃), 3.08 (q, 2H, *J* = 7.0 Hz, N-CH₂), 4.14 (q, 2H, *J* = 7.1 Hz, O-CH₂), 5.96 (s, 2H, NH₂), 6.84 (s, 1H, thiophene H), 8.37 (s, 1H, pyridone H); ¹³C NMR (DMSO-*d*₆): $\delta = 13.8$ (CH₃, amide CH₃), 14.4 (CH₃, ester CH₃), 40.6 (CH₂, N-CH₂), 59.2 (CH₂, O-CH₂), 106.1 (C, pyridone C-5), 123.6 (CH, thiophene CH), 132.8, 133.2, 138.6, 140.5 (aromatic C), 163.2 (C=O, amide), 166.7 (C=O, ester); MS, *m/z* (%), 266.1 (M⁺, 100), 237.1 (21). Anal. Calcd for C₁₂H₁₄N₂O₃S: C, 54.12; H, 5.30; N, 10.52; S, 12.04. Found: C, 54.07; H, 5.24; N, 10.45; S, 11.99.

Cycloaddition reactions of thienopyridine 6 with acrylonitrile, ethyl acrylate, and with dimethyl acetylenedicarboxylate

A mixture of thienopyridine derivative **6** (2.66 g, 10.0 mmol) and 10.0 mmol of acrylonitrile, ethylacrylate or dimethyl acetylenedicarboxylate was dissolved in 25 mL dioxane and then was

refluxed for 8 h, the reaction progress was followed by TLC, then the crude product was collected by filtration and purified by recrystallization from EtOH to give pure product **8**, **10** and **11**, respectively.

Ethyl 8-amino-7-cyano-2-ethyl-1-oxo-1,2-dihydro-isoquinoline-4-carboxylate (8)

This compound was obtained as a pale brown solid (yield: 26%); IR(KBr): $\nu = 1608$ (C=C), 1669 (C=O, amide), 1688 (C=O, ester), 2210 (CN), 3300 (br. NH₂) cm⁻¹, ¹H NMR (DMSO-*d*₆): $\delta = 2.03$ (t, 3H, $J = 7.0$ Hz, amide CH₃), 2.33 (t, 3H, $J = 7.2$ Hz, ester CH₃), 3.98 (m, 4H, $J = 7.0$ Hz, $J = 7.2$ Hz, two overlapped CH₂), 5.04 (s, 2H, NH₂), 7.05 (d, 1H, $J = 8.4$ Hz, benzene H), 7.67 (d, 1H, $J = 8.4$ Hz, benzene H), 7.93 (s, 1H, pyridone H); ¹³C NMR (DMSO-*d*₆): $\delta = 13.1$ (CH₃, amide CH₃), 13.4 (CH₃, ester CH₃), 41.2 (CH₂, N-CH₂), 61.7 (CH₂, O-CH₂), 99.2 (C(CN)), 115.8 (C, pyridone C-5), 117.4 (CN), 118.6, 119.0, 128.2, 137.7, 140.5, 149.7, 150.3 (aromatic C,s), 162.6 (C=O, amide), 165.4 (C=O, ester); MS, *m/z* (%), 285.1 (M⁺, 100), 240.1 (29). Anal. Calcd for C₁₅H₁₅N₃O₃: C, 63.15; H, 5.30; N, 14.73. Found: C, 63.11; H, 5.26; N, 14.67.

Diethyl 8-amino-2-ethyl-1-oxo-1,2-dihydroisoquinoline-4,7-dicarboxylate (10)

This compound was obtained as a dark brown solid (yield: 35%); IR(KBr): $\nu = 1605$ (C=C), 1662 (C=O, amide), 1685 (C=O, ester), 1697 (C=O, ester), 3340 (br., NH₂) cm⁻¹, ¹H NMR (DMSO-*d*₆): $\delta = 1.43$ (t, 3H, $J = 7.0$ Hz, amide CH₃), 2.31 (m, 6H, CH₃ and ester CH₃, $J = 7.1$ Hz), 3.08 (m, 4H, two CH₂, $J = 7.0$ Hz), 3.21 (q, 2H, $J = 7.1$ Hz, CH₂), 5.30 (s, 2H, NH₂), 7.16 (d, 1H, $J = 8.3$ Hz, benzene H), 7.87 (d, 1H, $J = 8.3$ Hz, benzene H), 8.47 (s, 1H, Pyridone H); ¹³C NMR (DMSO-*d*₆): $\delta = 13.6$ (CH₃, amide CH₃), 13.8 (CH₃, ester CH₃), 14.0 (CH₃, ester CH₃), 40.2 (CH₂, N-CH₂), 59.1 (CH₂, O-CH₂), 61.3 (CH₂, O-CH₂), 115.4 (C, pyridone C-5), 116.4, 116.9, 118.2, 128.4, 134.6, 139.3, 147.7 (aromatic C), 162.8 (C=O, amide), 165.4 (C=O, ester), 168.6 (C=O, ester); MS, *m/z* (%), 332.1 (M⁺, 100), 258.1 (35). Anal. Calcd for C₁₇H₂₀N₂O₅: C, 61.44; H, 6.07; N, 8.43. Found: C, 61.42; H, 6.01; N, 8.36.

Ethyl 6,7-dimethyl 8-amino-2-ethyl-1-oxo-1,2-dihydroisoquinoline-4,6,7-tricarboxylate (11)

This compound was obtained as a dark brown solid (% yield = 24); IR(KBr): $\nu = 1600$ (C=C), 1667 (C=O, amide), 1678 (C=O, ester), 1685 (C=O, ester), 1688 (C=O, ester), 3340 (br., NH₂) cm⁻¹, ¹H NMR (DMSO-*d*₆): $\delta = 1.20$ (t, 3H, $J = 7.0$ Hz, amide CH₃), 1.32 (t, 3H, $J = 7.2$ Hz, ester CH₃), 3.68 (s, 6H, two CH₃), 3.94 (q, 2H, $J = 7.0$ Hz, N-CH₂), 4.26 (q, 2H, $J = 7.2$ Hz, O-CH₂), 5.13 (s, 2H, NH₂), 7.84 (s, 1H, aromatic H), 8.63 (s, 1H, pyridone H); ¹³C NMR (DMSO-*d*₆): $\delta = 13.5$ (CH₃, amide CH₃), 14.8 (CH₃, ester CH₃), 41.9 (CH₂, N-CH₂), 54.2 (CH₃, two ester CH₃), 61.3 (CH₂, O-CH₂), 116.4 (C, pyridone C-5), 118.2, 118.5, 124.6, 128.0, 136.6, 139.3, 148.2 (aromatic C), 162.9 (C=O, amide), 166.1 (C=O, ester), 168.4 (C=O, ester), 168.6 (C=O, ester); MS, *m/z* (%),

376.1 (M^+ , 100), 213.1 (14). Anal. Calcd for $C_{18}H_{20}N_2O_7$: C, 57.44; H, 5.36; N, 7.44. Found: C, 57.40; H, 5.31; N, 7.36.

Reaction of 3a with benzylidene-malononitrile:

A mixture of pyridone **3a** (2.34 g, 10.0 mmol), and (1.54 g, 10.0 mmol) of benzylidenemalononitrile, 25 mL of EtOH in the presence of piperidine was refluxed for 4 h, then the crude product formed upon cooling was collected by filtration and purified by recrystallization from EtOH to give pure product **14**.

Ethyl 8-amino-7-cyano-2-ethyl-1-oxo-6-phenyl-1, 2-dihydroisoquinoline-4-carboxylate (14)

This compound was obtained as a brown solid (yield: 68%); IR(KBr): $\nu = 1600$ (C=C), 1668 (C=O), 1684 (C=O), 2191 (CN), 3350 (br., NH_2) cm^{-1} , 1H NMR (DMSO- d_6): $\delta = 1.21$ (t, 3H, $J = 7.0$ Hz, amide CH_3), 1.65 (t, 3H, $J = 7.1$ Hz, ester CH_3), 3.87 (q, 2H, $J = 7.0$ Hz, N- CH_2), 4.29 (q, 2H, $J = 7.1$ Hz, O- CH_2), 5.37 (s, 1H, NH_2), 7.65 (m, 6H, aromatic), 8.37 (s, 1H, pyridone C-6); ^{13}C NMR (DMSO- d_6): $\delta = 13.2$ (CH_3 , amide CH_3), 13.7 (CH_3 , ester CH_3), 40.2 (CH_2 , N- CH_2), 62.3 (CH_2 , O- CH_2), 100.4 ($=C(CN)$), 115.1 (C, pyridone C-5), 115.7 (CH, aromatic), 117.4 (CN), 118.6, 126.4, 132.2, 135.7, 138.6, 142.2, 149.6 (aromatic C), 163.2 (C=O, amide), 168.8 (C=O, ester); MS, m/z (%), 361.2 (M^+ , 98), 77.1 (34). Anal. Calcd for $C_{21}H_{19}N_3O_3$: C, 69.79; H, 5.30; N, 11.63. Found: C, 69.76; H, 5.26; N, 11.57.

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