# Synthesis of Heterocyclic Derivatives of Alkyl 2-(Cyanomethyl)-4-methyl-3-quinolinecarboxylates



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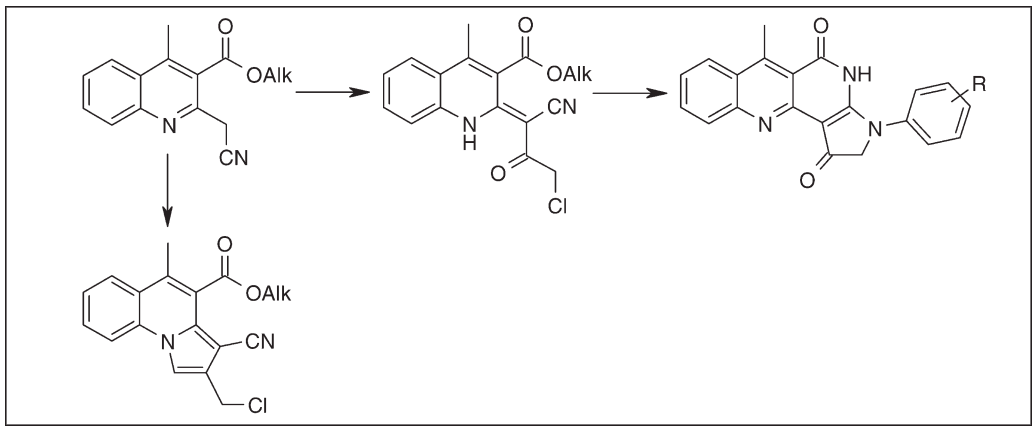


The article reports reactions of a series of known alkyl 2-(cyanomethyl)-4-methyl-3-quinolinecarboxylates. In the course of the present study the synthesis of new heterocyclic derivatives of alkyl 2-(cyanomethyl)-4-methyl-3-quinolinecarboxylates was achieved.

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## INTRODUCTION

Quinolineacetonitrile core is found in many biologically potent compounds. In this context, many synthetic routes to quinilineacetonitriles were developed [1–9]. Synthetic interest in these compounds has been stimulated by two factors: (i) the chemical activity of the nitrile unit in addition reactions and (ii) the chemical activity of the methylene group in electrophilic substitution reaction. The mentioned groups have been used in many step-by-step domino-type syntheses leading to a number of structurally diverse heterocyclic compounds [10]. Besides quinolineacetonitriles other hetarylacetonitriles belong to a little investigated class of compounds with considerable synthetic potential. This work was undertaken to prepare novel hetarylacetonitriles and investigate their chemical properties.

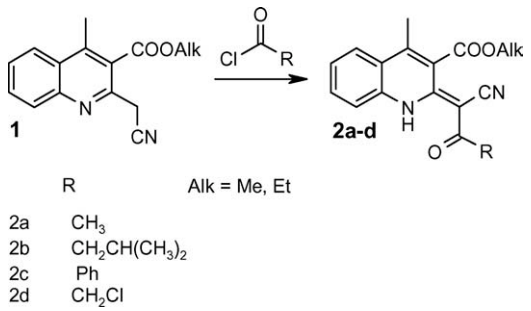
In our recent paper, we described the synthesis and chemical properties of some 2-chloromethyl-4-methyl-3-quinolinecarboxylates and alkyl 2-(cyanomethyl)-4-methyl-3-quinolinecarboxylates [11]. These compounds bear four selectively addressable reactive groups, such as ester, nitrile, methylene group, and the ring nitrogen. Here, we investigate the reactivity of these groups toward different electrophilic and nucleophilic reagents.

## RESULTS AND DISCUSSION

Methylene group of arylacetonitriles is known to readily react with anhydrides and chloroanhydrides of carboxylic acids [12–16]. We carried out this reaction with alkyl-2-chloromethyl-4-methyl-3-quinolinecarboxylates using chlorides of aliphatic and aromatic carboxylic acids as acylating agents (Scheme 1). The reaction proceed quickly under mild conditions giving products **2** in 69–94% isolated yields. $^1$H-NMR spectra of compounds **2** display singlets of NH protons near 16.5 ppm. The considerable low-field chemical shift is indicative of a strong intramolecular hydrogen bonding of NH-proton with carbonyl oxygen.

As shown in Scheme 2, the active chlorine of ethyl 2-(3-chloro-1-cyano-2-oxopropyl)-4-methylquinolino-3-carboxylate **2d** is readily substituted with sulfide anion giving rise to the corresponding thioether **3**. Interestingly, similar reaction of compound **2d** with aromatic amines does not yield the substitution product. The expected secondary amine **5′** (Scheme 2) underwent an intramolecular addition reaction with nitrile moiety followed by an intramolecular acylation. Thus, the derivatives of the new heterocyclic system benzo[β]pyrrolo[2,3-h]naphthyridine **5a–c** were obtained by a domino-type process reaction depicted in Scheme 2.

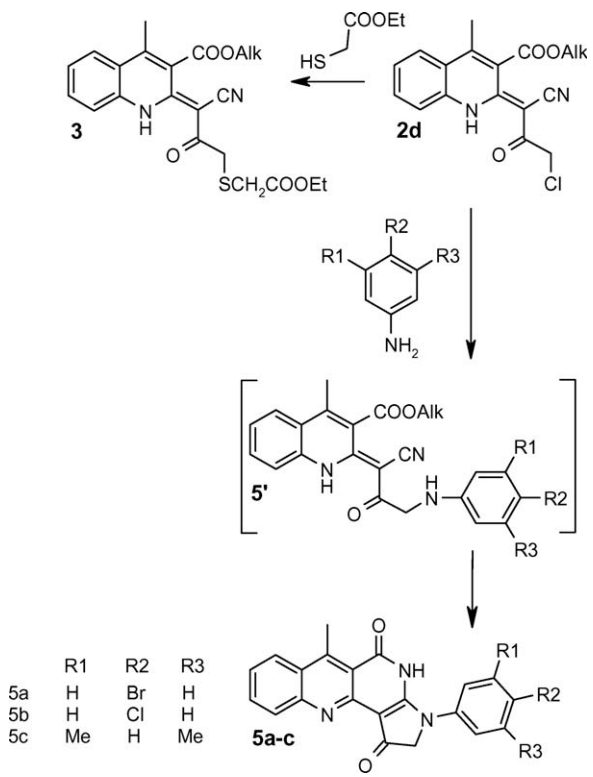
**Scheme 1**



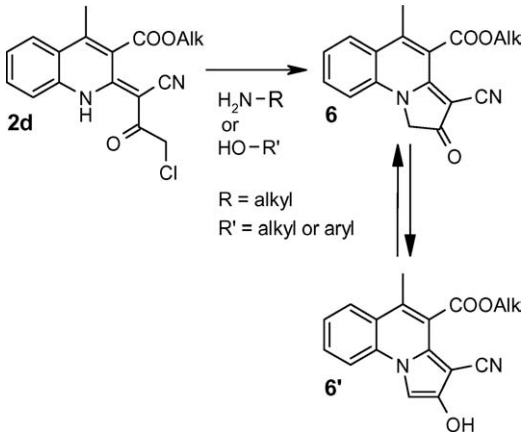

The structure and purity of compounds **5** were fully confirmed by means of NMR and IR spectroscopy and LCMS analysis. Signals pertaining to nitrile and ester groups are absent in the IR spectra of **5a–c.** In $^1$H-NMR spectra of **5a–c**, the signal of methyl group in position 4 of the quinoline ring is low-field shifted by 1 ppm compared with the corresponding proton signal in compounds **2**. The latter effect is the result of magnetic field of conformationally restricted amide oxygen with respect to the methyl group in **5**.

All attempts to substitute the chlorine atom of **2d** by reactions with aliphatic amines or alcohols were unsuccessful. As shown in Scheme 3, the reaction only leads to the product of intramolecular alkylation **6**. Most probably, O- and N-nucleophiles act as bases with respect to NH-proton of compound **2d**.

**Scheme 2**




**Scheme 3**



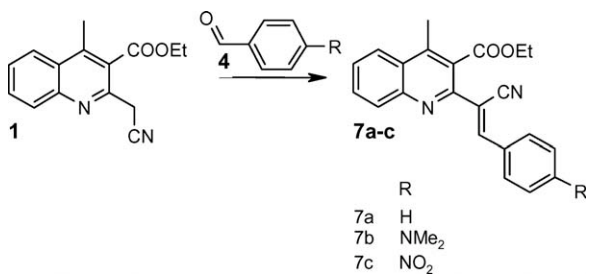

As appears from $^1$H-NMR spectrum of compound **6** recorded in DMSO-d6, keto-enol tautomeric equilibrium is shifted to the enol form (60%).

The attempts to use quinoline **1** in Knovenagel condensation with various aldehydes in the presence of bases such as morpholine or pyrimidine were unsuccessful. Therefore, we have optimized the reaction conditions for obtaining the Knoevenagel adducts **7** (Scheme 4). The condensation proceeded successfully in pyridine in the presence of chlorotrimethylsilan affording compounds **7** in exclusively Z-isomeric form in nearly quantitative yields.

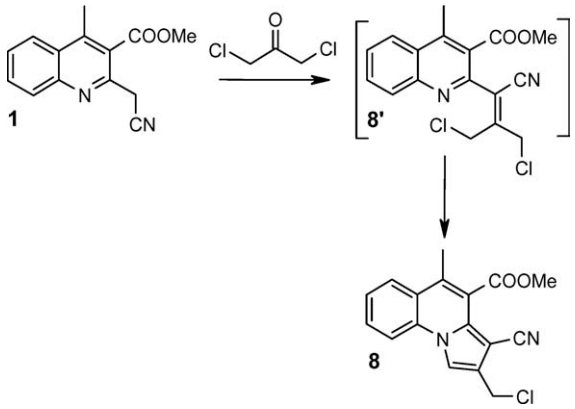
The quinoline nitrogen is easily alkylated [17–19]. An intramolecular alkylation of the quinoline nitrogen securing the quinoline aromatic system is the most preferred reaction of this type. Thus, a condensation of **1** and 1,3-dichloro-2-propanone under Knoevenagel conditions gives rise to a novel derivative of pyrrolo[1,2-a]quinoline **8** (Scheme 5). No open chain Knoevenagel adduct **8′** was isolated. The structure of **8** was proved by single crystal X-ray analysis (Fig. 1).

We investigated the chemical reactivity of chlorine atom in compound **8** toward nucleophilic agents, such as benzylamine. As shown in Scheme 6, the reaction of **8** with benzylamine yields open chain secondary amine **9**. All attempts at the subsequent intramolecular cyclization reaction of **9** to obtain tricyclic derivative **10** were hitherto unsuccessful.

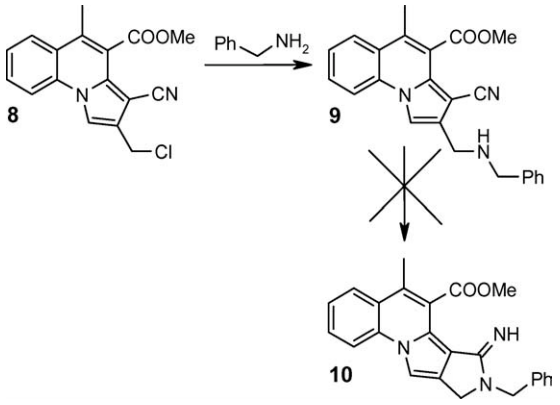
**Scheme 4**



**Scheme 5**




**Scheme 6**




All starting materials were purchased from commercial sources and used without additional purification. Commercial DMF was additionally dried by distillation over $P_2O_5$ under reduced pressure. Melting points were determined in open capillary tubes in a Thiele apparatus and uncorrected. $^1$H and $^{13}$C-NMR spectra were recorded on a Varian UNITY*plus* 400 spectrometer (400 MHz for $^1$H and 100 MHz for $^{13}$C) in DMSO-$d_6$ solutions. Chemical shifts (δ) are given in ppm with TMS as internal standard. LC/MS analyses were performed on an Agilent 1100 instrument. The structure and purity of all compounds were confirmed by $^1$H- and $^{13}$C-NMR, LC/MS, and elemental analysis.

## EXPERIMENTAL

**General procedure for the acylation of 1.** Cyanomethyl quinolin **1** (1 g., 4 mmol) and pyridine (4.2 mmol) were dissolved in 4 mL of 1,4-dioxane. Then, an acid chloranhydride (4.2 mmol) was added drop wise to the stirred solution at room temperature. The reaction mixture was stirred at 50°C for 1 h. The solvent was removed under reduced pressure, and the residue was triturated with water (10 mL). The precipitated solid was filtered, washed with water, and dried in vacuum to give pure derivatives **2a–c**. Compounds **2** could additionally be purified by recrystallization from EtOH.

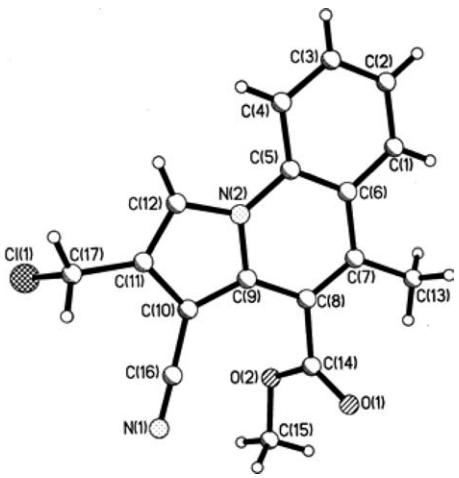



**Figure 1.** X-ray molecular structure of methyl 2-(chloromethyl)-3-cyano-5-methyl-pyrrolo[1,2-a]quinoline-4-carboxylat **8**.

***2-(1-Cyano-2-oxopropyl)-4-methyl-3-quinolinecarboxylic acid, methyl ester (2a).*** Yield 94%. M.p. 199°C (EtOH). $^1$H-NMR: δ = 2.33 (s, 3H, $\underline{CH_3}CO$), 2.55 (s, 3H, 4-$CH_3$), 3.90 (s, 3H, $COO\underline{CH_3}$), 7.56 (t, 1H, $J$ = 7.5 Hz), 7.76 (d, 1H, $J$ = 8 Hz), 7.81(t, 1H, $J$ = 7 Hz), 8.06(d, 1H, $J$ = 7.5 Hz), 16.5 (s, 1H, NH). $^{13}$C-NMR: δ = 16.6 ($CH_3$), 28.2 ($CH_3$), 53 ($OCH_3$), 76.1 (COCHCN), 119.3 (CN), 120.1, 122.1, 123.2, 125.1, 126.5, 133.6, 135.2, 148.1, 150.2, 166.0 (COO), 195.5 (CO). Anal. Calcd. for $C_{16}H_{14}N_2O_3$: C, 68.07, H, 5.00, N, 9.45. Found: C, 68.11, H, 5.06, N, 9.47. Ms: m/z 283, 284 ($M^+$.).

***2-(1-Cyano-4-methyl-2-oxopentyl)-4-methyl-3-quinolinecarboxylic acid, methyl ester (2b).*** Yield 89%. M.p. 190°C (EtOH). $^1$H-NMR: δ = 0.94 (d, 6H, $J$ = 6.5 Hz, $(\underline{CH_3})_2CH$), 2.16 (m, 1H, $J$ = 6.5 Hz, $(CH_3)_2\underline{CH}$), 2.55 (d, 2H, $J$ = 7 Hz, $\underline{CH_2}CH$), 2.58 (s, 3H, 4-$CH_3$), 3.91 (s, 3H, $COO\underline{CH_3}$), 7.58 (t, 1H, $J$ = 7.25 Hz), 7.83 (w.s, 2H), 8.1 (d, 1H, $J$ = 8 Hz), 16.5 (s, 1H, NH). $^{13}$C-NMR: δ = 17.0 ($CH_3$), 22.9 (($CH_3$)$_2$), 26.1 ($CH_2$), 53.3 ($OCH_3$), 76.2 (COCHCN), 119.3 (CN), 120.1, 122.0, 123.1, 125.8, 126.8, 134.1, 135.5, 148.4, 149.8, 166.1(COO), 195.5 (CO). Anal. Calcd. for $C_{19}H_{20}N_2O_3$ : C, 70.35, H, 6.21, N, 8.64. Found: C, 70.46, H, 6.30, N, 8.66. Ms: m/z 325, 326 ($M^+$.).

***2-(1-Cyano-2-oxo-2-phenylethyl)-4-methyl-3-quinolinecarboxylic acid, methyl ester (2c).*** Yield 88%. M.p. 263°C (EtOH). $^1$H-NMR: δ = 2.63 (s, 3H, 4-$CH_3$), 3.91 (s, 3H, $COO\underline{CH_3}$), 7.56 (w.s, 2H,), 7.76 (d, 1H, $J$ = 8 Hz), 7.81(t, 1H, $J$ = 7 Hz), 7.91 (w.s, 4H), 8.06(d, 1H, $J$ = 7.5 Hz), 16.5 (s, 1H, NH). $^{13}$C-NMR: δ = 16.2 ($CH_3$), 27.0 ($OCH_3$), 53.1 (COCHCN), 116.2, 124.1, 125.8, 126.5, 128.0, 129.5, 130.1, 130.9, 131.3, 134.8, 145.2, 147.1, 168.2. Anal. Calcd. for $C_{21}H_{16}N_2O_3$: C, 73.24, H, 4.68, N, 8.13. Found: C, 73.45, H, 4.58, N, 8.10. Ms: m/z 345, 346 ($M^+$).

***2-(3-Chloro-1-cyano-2-oxopropyl)-4-methyl-3-quinolinecarboxylic acid, ethyl ester (2d).*** Cyanomethylquinolin **1** (1 g., 4 mmol) and pyridin (4.2 mmol) were dissolved in 5 mL of 1,4-dioxane. The solution was cooled on an ice bath to ca. 5°C. Then, chloroacetylchloride (4.2 mmol) was added drop wise to the stirred solution. The reaction mixture was stirred at room

temperature for 3 h. The precipitated solid was filtered, washed with water, and dried in vacuum to give pure **2d**. Yield 69%. M.p. 180°C (EtOH). $^1$H-NMR: δ = 1.34 (t, 3H, *J* = 7 Hz, $OCH_2\underline{CH_3}$), 2.63 (s, 3H, 4-$CH_3$), 4.41 (k, 2H, *J* = 7 Hz, $O\underline{CH_2}CH_3$), 4.59 (d, 2H, *J* = 2.5 Hz, $COCH_2Cl$), 7.63 (t, 1H, *J* = 7.5 Hz), 7.88 (m, 2H, *J* = 7.5 Hz), 8.14 (d, 1H, *J* = 7.5 Hz), 16.5 (s, 1H, NH). $^{13}$C-NMR: δ = 14.0($OCH_2\underline{CH_3}$), 16.7 ($O\underline{CH_2}CH_3$), 47.1, 62.6, 74.3, 118.7(CN), 119.6, 122.9, 123.4, 125.8, 127.0, 133.9, 134.9, 148.9, 149.3, 165.3 (COO), 188.9(CO). Anal. Calcd. for $C_{17}H_{15}ClN_2O_3$ :C, 61.73, H, 4.57, Cl, 10.72, N, 8,47. Found: C, 61.90, H, 4.63, Cl, 10.65, N, 8,44. Ms: m/z 333, 334 ($M^+$).

**General procedure for Knoevenagel reaction of 1 with 4.** Cyanomethylquinoline **1** (1 g., 4 mmol) and benzaldehyde (4.2 mmol) were dissolved in 5 mL of pyridine. Then TMS-Cl (0.86 g, 8.2 mmol) was poured carefully in one portion to the solution. The reaction mixture was heated at 50–55°C for 1 h and then left overnight at room temperature. The precipitated solid was filtered, washed with water, and dried in vacuum to give pure compounds **7a–c**. Compounds **7** could be additionally purified by recrystallization from EtOH.

***2-{(Z)-1-Cyano-2-phenyletenyl}-4-methyl-3-quinolinecarboxylic acid, ethyl ester (7a).*** Yield 80%. M.p. 95°C (EtOH). $^1$H-NMR: δ = 1.29 (t, 3H, *J* = 6.5 Hz, $OCH_2\underline{CH_3}$), 2.77 (s, 3H, 4-$CH_3$), 4.39 (k, 2H, *J* = 6.5 Hz, $O\underline{CH_2}CH_3$), 7.56 (m, 3H), 7.76 (t, 1H, *J* = 7.5 Hz), 7.92 (m, 4H), 8.10 (d, 1H, *J* = 8 Hz), 8.26 (d, 1H, *J* = 8 Hz). $^{13}$C-NMR: δ = 14.2, 16.0, 62.5, 110.6, 117.7, 125.4, 126.0, 126.6, 128.7, 129.6, 129.7, 130.0, 131.9, 132.0, 133.3, 145.1, 146.7, 149.2, 149.6, 167.5(CO). Anal. Calcd. for $C_{22}H_{18}N_2O_2$: C, 77.17, H, 5.30, N, 8.18. Found: C, 77.06, H, 5.24, N, 8.13. Ms: m/z 343, 344($M^+$.).

***2-{(Z)-1-Cyano-2-[4-(dimethylamino)phenyletenyl]}-4-methyl-3-quinolinecarboxylic acid, ethyl ester (7b).*** Yield 85%. M.p. 158°C (EtOH). $^1$H-NMR: δ = 1.27 (t, 3H, *J* = 6.5 Hz, $OCH_2\underline{CH_3}$), 2.71 (s, 3H, 4-$CH_3$), 3.04 (s, 6H, $(Me)_2N$), 4.37 (k, 2H, *J* = 6.5 Hz, $O\underline{CH_2}CH_3$), 6.82 (d, 2H, *J* = 8 Hz), 7.70 (m, 2H), 7.87 (d, 3H, *J* = 7.5 Hz), 8.05 (d, 1H, *J* = 8 Hz), 8.21 (d, 1H, *J* = 8 Hz). $^{13}$C-NMR: δ = 14.3 ($OCH_2\underline{CH_3}$), 15.9 ($O\underline{CH_2}CH_3$), 62.3, 102.1, 112.1, 119.2, 120.5, 125.3, 126.1, 128.0, 129.8, 132.1, 144.4, 146.8, 149.3, 150.5, 152.8, 167.9(CO). Anal. Calcd. for $C_{24}H_{23}N_3O_2$: C, 74.78, H, 6.01, N, 10.90. Found: C, 74.87, H, 6.09, N, 10.79. Ms: m/z 386, 387 ($M^+$.).

***2-{(Z)-1-Cyano-2-[4-nitrophenyl]etenyl]}-4-methyl-3-quinolinecarboxylic acid, ethyl ester (7c).*** Yield 89%. M.p. 204°C (EtOH). $^1$H-NMR: δ = 1.29 (t, 3H, *J* = 6.5 Hz, $OCH_2\underline{CH_3}$), 2.77 (s, 3H, 4-$CH_3$), 4.39 (k, 2H, *J* = 6.5 Hz, $O\underline{CH_2}CH_3$), 7,79 (t, 1H, *J* = 7.5 Hz), 7.93 (t, 1H, *J* = 7.5 Hz), 8.08 (s, 1H), 8.12(d, 1H, *J* = 8 Hz), 8.16 (d, 2H, *J* = 8 Hz), 8.28(d, 1H, *J* = 8 Hz), 8.39(d, 2H, *J* = 8 Hz). $^{13}$C-NMR: δ = 14.2, 15.9, 62.6, 114.4, 116.9, 124.1, 124.6, 125.4, 125.9, 126.8, 128.9, 130.1, 130.2, 132.0, 139.3, 145.5, 146.7, 146.8, 148.9, 167.3 (CO). Anal. Calcd. for $C_{22}H_{17}N_3O_4$: C, 68.16, H, 4.38, N, 10.85. Found: C, 68.05, H, 4.25, N, 10.78. Ms: m/z 388, 389 ($M^+$.).

**General procedure for the preparation of benzo[β]-pyrrolo[2,3-h]-naphthyridines 5a–c.** Quinoline **2d** (1g., 3 mmol) and aniline (12 mmol) were dissolved in a minimal volume of dimethylformamide at room temperature with the aid of sonication. The mixture was kept for 5 days at room temperature and then heated at 50°C for 2 h. Upon cooling to room temperature a solid precipitate was formed. The precipitated solid was filtered, washed with water, and dried in vacuum to give pure **5a–c**.

***3-(4-Bromophenyl)-6-methyl-2,3-dihydro-1H-benzo[β]-pyrrolo[2,3-h]-1,6-naphthiridine-1,5(11H)-dione (5a).*** Yield 38%. M.p. >300°C. $^1$H-NMR (TFA): δ = 3.60 (s, 3H, $CH_3$), 7.46 (w.s, 2H), 7.88 (w.s, 2H), 8.04 (w.s, 1H), 8.31 (w.s, 2H), 8.71 (w.s, 1H). $^{13}$C-NMR (TFA): δ = 16.9, 71.4, 91.0, 110.9, 113.2, 115.4, 117.7, 119.2, 125.35, 125.8, 126.6, 127.3, 129.0, 131.4, 134.2, 136.8, 138.5, 143.8, 163.3, 168.5, 191.6. Anal. Calcd. for $C_{21}H_{14}BrN_3O_2$: C, 60.02, H, 3.36, N, 10,00. Found: C, 60.10, H, 3.41, N, 9.91. Ms: m/z 421 ($M^+$).

***3-(4-Chlorophenyl)-6-methyl-2,3-dihydro-1H-benzo[β]-pyrrolo[2,3-h]-1,6-naphthiridine-1,5(11H)-dione (5b).*** Yield 35%. M.p. >300°C. $^1$H-NMR (TFA): δ = 3.45 (s, 3H, $CH_3$), 7.46 (w.s, 2H), 7.52 (w.s, 2H), 7.85 (w.s, 1H), 8.17 (w.s, 2H), 8.47 (w.s, 1H). $^{13}$C-NMR (TFA): δ = 17.0, 111.1, 113.3, 115.6, 117.9, 126.7, 127.4, 129.2, 131.2, 137.9, 138.6, 163.3, 168.6, 191.8. Anal. Calcd. for $C_{21}H_{14}ClN_3O_2$: C, 67.12, H, 3.75, Cl, 9.43, N, 11.18. Found: C, 67.16, H, 3.80, Cl, 9.42, N, 11.15. Ms: m/z 376, 377 ($M^+$).

***3-(3,5-Dimethylphenyl)-6-methyl-2,3-dihydro-1H-benzo[β]-pyrrolo[2,3-h]-1,6-naphthiridine-1,5(11H)-dione (5c).*** Yield 36%. M.p. >300°C. $^1$H-NMR (TFA): δ = 2.33 (s, 6H, $CH_3$), 3.45 (s, 3H, $CH_3$), 6.95 (w.s, 2H), 7.18 (w.s, 1H), 7.83 (w.s, 1H), 8.20 (w.s, 2H), 8.51 (w.s, 1H). $^{13}$C-NMR (TFA): δ = 17.0, 19.5, 111.2, 113.4, 115.5, 118.0, 119.1, 122.3, 126.1, 127.5, 129.2, 132.8, 138.7, 142.2, 163.3, 168.4, 191.0. Anal. Calcd. for $C_{23}H_{19}N_3O_2$: C, 74.78, H, 5.18, N, 11.37. Found: C, 74.75, H, 5.16, N, 11.30. Ms: m/z 370, 371 ($M^+$).

***2-{1-Cyano-3-[(2-etoxy-2-oxoethyl)thio]-2-oxopropyl}--4-methyl-3-quinolinecarboxylic acid, ethyl ester (3).*** Quinoline **2d** (1g., 3 mmol) and ethyl ester of mercaptoacetic acid (0.28 g, 3 mmol) were dissolved in 4 mL of DMF. Then, triethylamine (3.1 mmol, 0.43 mL) was added to the solution. The reaction mixture was stirred for 24 h at room temperature. The solvent was removed under reduced pressure. The solid residue was triturated with water (5 mL), filtered, and recrystallized from *i*-PrOH to yield compound **3**. Yield 94%. M.p. 123°C. $^1$H-NMR: δ = 1.18 (t, 3H, *J* = 7 Hz), 1.34 (t, 3H, *J* = 7 Hz), 2.62 (s, 3H), 3.48 (s, 2H), 3.78 (s, 2H), 4.09 (k, 2H, *J* = 7 Hz), 4.40 (k, 2H, *J* = 7 Hz), 7.61 (t, 1H, *J* = 8,5 Hz), 7.87 (w.s., 2H), 8.13 (d, 1H, *J* = 8.5 Hz), 16.5 (s, 1H, —NH). $^{13}$C-NMR: δ = 14.0($OCH_2\underline{CH_3}$), 14.4, 16.7, 33.7, 61.3, 62.5($O\underline{CH_2}CH_3$), 75.0, 119.4, 119.5, 122.9, 123.5, 125.9, 126.8, 133.8, 135.0, 148.5, 149.7, 165.4, 170.0, 192.8. Anal. Calcd. for $C_{21}H_{22}N_2O_5S$: C, 60.85, H, 5.35, N, 6.76. Found: C, 60.79, H, 5.34, N, 6.72. Ms: m/z 415, 417 ($M^+$.).

***3-Cyano-2-hydroxy-5-methylpyrrolo[1,2-α]quinoline-4-carboxylic acid, ethyl ester (6).*** Cyanomethylquinoline **1** (1 g., 4 mmol) and pyridine (4.2 mmol) were dissolved in 5 mL of 1,4-dioxane. Chloroacetylchloride (4.2 mmol) was added drop wise to the stirred solution cooled on an ice bath. The reaction mixture was stirred at 50°C for 4 h. The solvent was removed under reduced pressure and the residue was triturated with water (10 mL). The precipitated solid was filtered and washed with water to give **6**. Yield 95%. M.p. 206°C. $^1$H-NMR: (enol-form; 60%) δ = 1.34 (t, 3H, *J* = 6.5 Hz, $OCH_2\underline{CH_3}$), 4.41 (k, 2H, *J* = 6.5 Hz, $O\underline{CH_2}CH_3$), 7.55 (t, 1H, *J* = 8 Hz), 7.75 (t, 2H), 8.05 (d, 1H, *J* = 8 Hz), 8.26 (d, 1H, *J* = 8 Hz), 10.36 (s, 1H, OH); (keton-form; 40%) δ = 1.34 (t, 3H, *J* = 6.5 Hz,

$OCH_2\underline{CH_3}$), 2.61 (s, 3H, 4-$CH_3$), 4.41 (k, 2H, $J$ = 6.5 Hz, $O\underline{CH_2}CH_3$), 4.85 (s, 2H), 7.50 (t, 1H, $J$ = 8 Hz), 7.59 (d, 1H, $J$ = 8 Hz), 7.83 (t, 1H, $J$ = 8 Hz), 8.10 (d, 1H, $J$ = 8 Hz). $^{13}$C-NMR: (enol-form; 60%) δ = 14.0($OCH_2\underline{CH_3}$), 20.3, 60.0($O\underline{CH_2}CH_3$), 91.6, 104.9, 111.2, 119.5, 119.6, 125.3, 125.9, 128.8, 129.9, 139.8, 141.7, 144.6, 146.2, 162.7; (keton-form; 40%) δ = 14.0($OCH_2\underline{CH_3}$), 20.3, 52.2, 62.2, 80.75, 111.5, 113.8, 115.3, 122.8, 124.9, 126.1, 130.2, 139.6, 152.0, 167.1, 178.8, 187.9. Anal. Calcd. for $C_{17}H_{14}N_2O_3$: C, 69.38, H, 4.79, N, 9.52. Found: C, 69.35, H, 4.77, N, 9.56. Ms: m/z 295, 296 ($M^+$.).

***2-(Chloromethyl)-3-cyano-5-methylpyrrolo[1,2-α]quinoline-4-carboxylic acid, methyl ester (8).*** Cyanomethylquinolin **1** (1 g., 4 mmol) and 1,3-dichloro-2-propanone (0.52 g, 4.1 mmol) were dissolved in 3 mL of DMF. Chlorotrimethylsilane (0.9 g, 8.2 mmol) was added to the solution, and reaction mixture was stirred at 56°C for 16 h. The precipitated solid was filtered and recrystallized from *i*-PrOH to give **8**. Yield 66%. M.p. 187°C. $^1$H-NMR: δ = 3.95 (s, 3H, $OCH_3$), 4.95 (s, 2H, $CH_2Cl$), 7.58 (t, 1H, $J$ = 8 Hz), 7.76 (t, 1H, $J$ = 8 Hz), 8.05 (d, 1H, $J$ = 8 Hz), 8.32 (d, 1H, $J$ = 8 Hz), 8.58 (s, 1H). $^{13}$C-NMR: δ = 20.3, 38.2, 51.3 (OMe), 91.4, 114.5, 115.4, 119.3, 123.0, 125.2, 125.3, 125.9, 128.5, 130.0, 141.5, 142.8, 145.9, 162.5. Anal. Calcd. for $C_{17}H_{13}ClN_2O_2$: C, 65.29, H, 4.19, Cl, 11.34, N, 8.96. Found: C, 65.18, H, 4.19, Cl, 11.36; N, 8.99. Ms: m/z 313, 314 ($M^+$).

***3-Cyano-5-methyl-2-[[(phenylmethyl)amino]methyl]pyrrolo[1,2-α]quinoline-4-carboxylic acid, methyl ester (9).*** Compound **8** (1 g, 3.2 mmol) and benzylamine (0.72 g, 6.7 mmol) were dissolved in 7 mL of DMF. The reaction mixture was stirred at 100°C for 6 h. The solvent was removed under reduced pressure, and the residue was triturated with water (10 mL). The precipitated solid was filtered and recrystallized from *i*-PrOH to give **9**. Yield 72%. M.p. 153°C. $^1$H-NMR : δ = 3.92 (s, 3H, $OCH_3$), 3.94 (s, 2H), 3.97 (s, 2H), 7.26 (t, 1H, $J$ = 7.5 Hz), 7.34 (t, 2H, $J$ = 7.5 Hz), 7.45 (d, 2H, $J$ = 7.5 Hz), 7.58 (t, 1H, $J$ = 8 Hz), 7.76 (t, 1H, $J$ = 8 Hz), 8.05 (d, 1H, $J$ = 8 Hz), 8.32 (d, 1H, $J$ = 8 Hz), 8.58 (s, 1H). $^{13}$C-NMR: δ = 20.3, 41.0, 51.4 (OMe), 56.0, 94.7, 115.3, 116.5, 118.6, 122.5, 123.0, 125.3, 126.1, 126.5, 126.9, 127.0, 127.8, 130.4, 135.6, 143.3, 143.8, 147.4, 162.5. Anal. Calcd. for $C_{24}H_{21}N_3O_2$: C, 75.18, H, 5.52, N, 10.96. Found: C, 75.13, H, 5.55, N, 10.85. Ms: m/z 384 ($M^+$.).

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