JOC The Journal of Organic Chemistry

ARTICLE

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Three-Step Synthesis of Ethyl Canthinone-3-carboxylates from Ethyl 4-Bromo-6-methoxy-1,5-naphthyridine-3-carboxylate via a Pd-Catalyzed Suzuki−Miyaura Coupling and a Cu-Catalyzed Amidation Reaction

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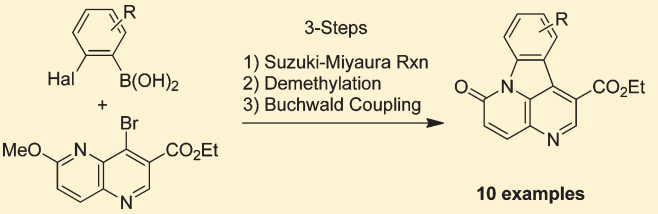
Supporting Information

ABSTRACT: Ethyl canthin-6-one-1-carboxylate (**1b**) and nine analogues **1c**−**k** were prepared from readily prepared ethyl 4-bromo-6-methoxy-1,5-naphthyridine-3-carboxylate (**2b**) via a three-step non-classical approach that focused on construction of the central pyrrole (ring B) using Pd-catalyzed Suzuki−Miyaura coupling followed by Cu-catalyzed C−N coupling. Furthermore, treatment of the ethyl canthinone-1-carboxylate **1b** with NaOH in DCM/MeOH (9:1) gave the canthin-6-one-1-carboxylic acid (**6**) in high yield. All compounds are fully characterized.

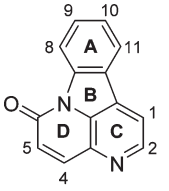


1. INTRODUCTION

Canthin-6-one (**1**, Figure 1) (6*H*-indolo[3,2,1-*de*][1,5]naphthyridin-6-one), first isolated in 1952 by Haynes,[1] is the parent of the >120-member canthinone alkaloid family, which includes over 40 naturally occurring analogues.[2] Selected canthin-6-one alkaloids have interesting biological properties including antiparasitic activity against *Trypanosoma cruzi* (Chagas disease)[3] and *Plasmodium falciparum* (malaria),[4] antibacterial,[5] and antifungal[6] properties. Furthermore, some canthinones are cytotoxic against several strains of cancer cells[4a,b,7] and act as vasodilators since they can inhibit cAMP phosphodiesterase,[8] and 1-methoxycanthinone is a potent anti-HIV agent.[7f]

Owing to this broad range of biological activity there is continued demand for syntheses that provide functionalized canthinones efficiently. Canthinones bearing carboxylate groups are of particular value since modification of the carboxylate group can lead to a wide variety of other functionalities. We note that there are several reports on the preparation of canthinone-2-carboxylates,[9] but only two reports on canthinone-5-carboxylates[10] and one report each on canthinone-1,2-dicarboxylates[11] and 1,2,5-tricarboxylates.[9c] No specific routes to canthinone-1-carboxylates have been reported, and we therefore considered preparing a series of this class of canthinones.

The "classical" approach to synthesize canthinones relies on the sequential construction of rings C and D starting from indoles or construction of the D ring starting from β-carbolines.[9b−d,g,10a,11,12] Recently, we demonstrated both a rapid one-pot and stepwise non-classical convergent synthesis of canthinones **1a** (R^1 = H) that required access to available 4-bromo-6-methoxy-1,5-naphthyridine (**2a**) (R^1 = H), 4-bromo-5,6-dihydro-1,5-naphthyrid-6-one



Canthin-6-one (**1**)

Figure 1. Structure and chemical numbering of canthin-6-one.

(**3a**) (R^1 = H), and 2-haloarylboronic acids.[13] The synthesis involved construction of ring B via transition-metal-catalyzed intermolecular C−C and intramolecular C−N bond formation. By varying the 2-haloarylboronic acids the construction of analogues bearing substitution on ring A was achieved (Scheme 1).

Here we disclose our successes related to the preparation of 10 new canthinone-1-carboxylates including the first examples of aza-canthinone analogues starting from ethyl 4-bromo-6-methoxy-1,5-naphthyridine-3-carboxylate **2b** (R^1 = CO_2Et) via the stepwise protocol.

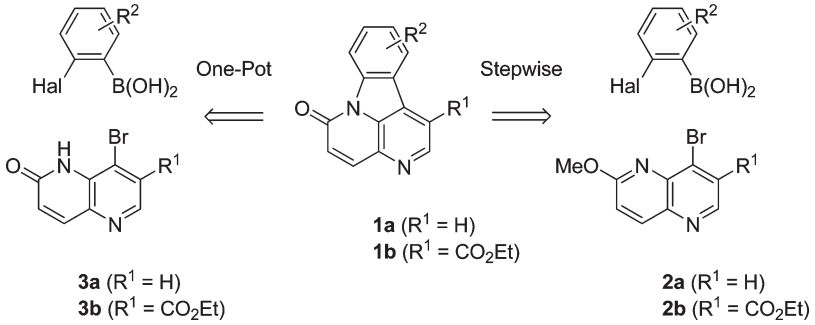
2. RESULTS AND DISCUSSION

The stepwise synthesis of the desired ethyl canthinone-1-carboxylate **1b** (R^1 = CO_2Et) (ethyl 6-oxo-6*H*-indolo[3,2,1-*de*]-[1,5]naphthyridine-1-carboxylate) required the known ethyl 4-bromo-6-methoxy-1,5-naphthyridine-3-carboxylate (**2b**), which

Received: April 21, 2011
Published: May 12, 2011

   dx.doi.org/10.1021/jo200824b | *J. Org. Chem.* 2011, 76, 5113–5122

Scheme 1. One-Pot and Stepwise Routes to Canthinones via Naphthyridines and Naphthyridones



can be prepared in multigram quantities (3−5 g) in three steps from commercially available 6-methoxypyridin-3-amine.[14] Attempts to access the one-pot procedure required access to the unknown ethyl 4-bromo-6-oxo-5,6-dihydro-1,5-naphthyridine-3-carboxylate (**3b**); however, this route could not be realized because a clean demethylation of the bromonaphthyridine **2b** using either TMSCl/NaI in MeCN, aq HBr in dioxane at reflux, or BBr_3 in DCM 0 to ca. 20 °C failed.

2.1. Suzuki−Miyaura Coupling Reactions of the Bromonaphthyridines 2b. With ethyl 4-bromo-6-methoxy-1,5-naphthyridine-3-carboxylate (**2b**) in hand the stepwise synthetic protocol was followed. As such, the Suzuki−Miyaura coupling of a variety 2-haloarylboronic acids (1.8 equiv) with the bromonaphthyridine **2b** using Pd(dppf)Cl_2·DCM (5 mol %) as catalyst and K_2CO_3 (2 equiv) as base in aqueous dioxane/H_2O (3:1) heated to reflux for ca. 2 h gave 8-(2-haloaryl)-2-methoxynaphthyridines **4a**−**l** in high yields (Table 1).

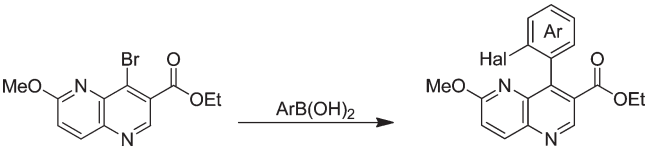
Typically the reactions came to completion with only a minimal quantity of biphenyl byproduct present (by TLC). The ethyl 4-(2-haloaryl)-6-methoxy-1,5-naphthyridine-3-carboxylates **4a**−**l** were isolated by dry flash chromatography (hexane/*t*-BuOMe, 4:1) as viscous yellow oils that were in nearly all cases crystallized from pentane. Furthermore, electron impact (EI) mass spectrometry of these naphthyridines indicated only very weak or nonvisible parent ions owing to a very facile fragmentation of the 2-halogen on the 4-aryl substituent, leading to the m/z (M^+ − Hal) ion as the base peak.

The Suzuki−Miyaura coupling also tolerated the use of the heterocyclic 2-chloropyrid-3-ylboronic acid (entry 13) and 3-chloropyrid-4-ylboronic acid pinacol ester (entry 14), which afforded the corresponding pyridylnaphthyridines **4k** and **4l** in 64% and 62% yields, respectively, with no sign of bipyridyl byproducts. Sterically demanding 2,6-disubstituted arylboronic acids, however, led to the quantitative recovery of the starting bromonaphthyridine **2b** (entries 11 and 12).

2.2. Demethylation of 4-Aryl-6-methoxy-1,5-naphthyridines 4. Demethylation of the ethyl 4-(2-haloaryl)-6-methoxy-1,5-naphthyridine-3-carboxylates **4a**−**l** to afford the desired ethyl 4-(2-haloaryl)-6-oxo-5,6-dihydro-1,5-naphthyridine-3-carboxylates **5a**−**l** was achieved using TMSCl/NaI[15] in MeCN heated to reflux for about 1−2 h (Table 2).

Earlier attempted demethylations using aqueous HCl in dioxane at reflux that had previously worked well for the nonester analogues,[13] and BBr_3 resulted in complex reaction mixtures (TLC). Interestingly, the TMSCl/NaI demethylation conditions were selective and differentiated between the naphthyridine and anisidine methoxy groups (entry 7). The naphthyridones **5a**−**l**

Table 1. Reaction of Bromonaphthyridine 2b (1.2 mmol) with ArB(OH)$_2$ (1.8 equiv) in the Presence of K_2CO_3 (2 equiv), Pd(dppf)Cl_2·DCM (5 mol %) in Dioxane/H_2O (3:1) Heated at Reflux for 2 h



2b **4**

entry	ArB(OH)$_2$	yield of **4** (%)
1	2-BrC_6H_4B(OH)$_2$	**4a** (98)
2	2-ClC_6H_4B(OH)$_2$	**4b** (90)
3	2,3-$Cl_2C_6H_3$B(OH)$_2$	**4c** (99)
4	2,4-$Cl_2C_6H_3$B(OH)$_2$	**4d** (86)
5	2-Cl-4-$F_3CC_6H_3$B(OH)$_2$	**4e** (92)
6	2-Cl-4-MeC_6H_3B(OH)$_2$)	**4f** (84)
7	2-Cl-4-MeOC_6H_3B(OH)$_2$	**4g** (90)
8	2-Cl-4-FC_6H_3B(OH)$_2$	**4h** (89)
9	2,5-$Cl_2C_6H_3$B(OH)$_2$	**4i** (92)
10	2-Cl-5-$F_3CC_6H_3$B(OH)$_2$	**4j** (92)
11	2-Cl-6-FC_6H_3B(OH)$_2$	[a]
12	2-Cl-6-MeOC_6H_3B(OH)$_2$	[a]
13	2-Cl-Pyrid-3-ylB(OH)$_2$	**4k** (64)
14	3-Cl-Pyrid-4-ylB(OR)$_2$[b]	**4l** (62)

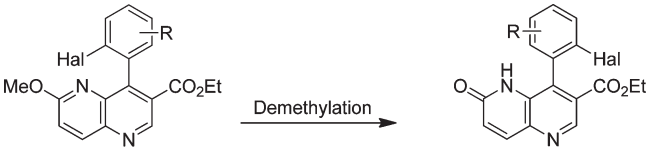
[a] No reaction; starting bromonaphthyridine **2b** recovered. [b] 3-Cl-Pyrid-4-ylB(OR)$_2$ = pinacol ester.

were isolated using dry flash chromatography (*t*-BuOMe, 100%) and recrystallized from the same solvent. ^{1}H NMR spectroscopy of the products showed the absence of the naphthyridine methoxy signals (ca. 3.7 ppm) and the formation of a broad exchangeable signal at 8.0−8.6 ppm attributed to the naphthyridone amide NH. The presence of the amide was also supported by FTIR spectroscopy, which showed new amide carbonyl stretching frequencies ν(NH-C═O) 1659−1697 cm^{-1}. With the naphthyridones **5a**−**l** accessible, formation of the central B ring could be pursued via a copper-catalyzed Buchwald cyclization.

2.3. Synthesis of Ethyl Canthinone-1-carboxylate 1b and Its Analogues. Treating ethyl 4-(2-bromophenyl)-6-oxo-5,6-dihydro-1,5-naphthyridine-3-carboxylate (**5a**) with our typical Buchwald conditions [CuI (5 mol %), DMEDA (10 mol %),

dx.doi.org/10.1021/jo200824b |*J. Org. Chem.* 2011, 76, 5113–5122

Table 2. Demethylation of Naphthyridines 4 (0.5 mmol) with TMSCl (5 equiv) and NaI (3 equiv) in MeCN (1 mL) at Reflux for 1−2 h To Give Naphthyridones 5

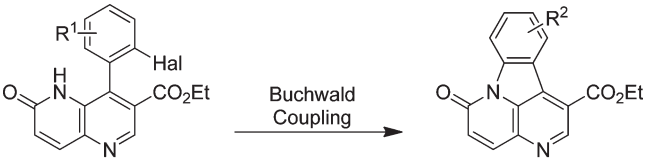


4a-l **5a-l**

entry	Hal	R	yield of **5** (%)
1	Br	H	**5a** (70)
2	Cl	H	**5b** (81)
3	Cl	3-Cl	**5c** (92)
4	Cl	4-Cl	**5d** (83)
5	Cl	4-F_3C	**5e** (80)
6	Cl	4-Me	**5f** (74)
7	Cl	4-MeO	**5g** (89)
8	Cl	4-F	**5h** (98)
9	Cl	5-Cl	**5i** (97)
10	Cl	5-F_3C	**5j** (92)
11	Cl	3-aza	**5k** (83)
12	Cl	4-aza	**5l** (67)

Cs_2CO_3 (2 equiv), water (2 equiv) in refluxing dioxane, 1 h][13] gave the ethyl canthinone-1-carboxylate **1b** in 85% yield (Table 3, entry 1). However, these conditions were not successful with the 2-chlorophenyl analogue **5b** that gave only traces of product even after 24 h (entry 2). The reaction could, however, be driven to completion when additional CuI/DMEDA (a total of 30 mol % with respect to CuI) was added to the reaction mixture, affording after 18 h the canthinone **1b** in moderate yield (48%) (entry 3). By premixing various ratios of CuI and DMEDA in dioxane/H_2O (1 mL), we found that a ratio of CuI (10 mol %)/DMEDA (60 mol %) added to the reaction mixture of starting material and base in dioxane/H_2O (1 mL) significantly improved the product yield and shortened the reaction time, affording the desired canthinone **1b** in 84% yield in only 9 h (entry 4). Further increases in the ratio of CuI/DMEDA, 1:8 and 1:10, did not improve the yields but did shorten the reaction times further, 82%/3.5 h and 83%/3 h, respectively. Keeping the ratio of CuI/DMEDA at 1:6 and reducing the quantity of CuI (5 mol %) led to a very slow reaction that gave only traces of product after 24 h (TLC). In a further attempt to improve the cyclization, DMEDA was replaced with the ligand *trans-N,N′*-dimethyl-1,2-cyclohexanediamine (DMCDA), which was known to be particularly effective for C−N coupling of chloro-substituted substrates.[16] As such, when a dioxane/H_2O (1 mL) solution of the 2-chlorophenyl analogue **5b** (R^1 = H) and Cs_2CO_3 (2 equiv) was treated with a premix of CuI (10 mol %)/DMCDA (60 mol %) and heated to reflux for 2 h, the cyclization was completed, affording the canthinone **1b** in 74% yield (entry 5). These conditions also worked well for most of the remaining 2-chlorophenyl derivatives (entries 8−10, 15, and 16). The exceptions were the 2,3-dichlorophenyl analogue **5c** (R^1 = 3-Cl) (entries 6 and 7), which gave no reaction even with 30 mol % CuI, and the 2-chloro-4-methoxyphenyl, 2-chloro-4-fluorophenyl, 2-chloropyrid-3-yl, and 3-chloropyrid-4-yl analogues, **5g** (R^1 = 4-MeO), **5h** (R^1 = 4-F), **5k** (R^1 = 3-aza), and **5l** (R^1 = 4-aza), which required a CuI catalyst loading of at least 20 mol % to reach completion (entries 11−14 and 17−20) (Table 3). Worthy of note was the cyclization of the two pyridyl analogues **5k** and **5l** that afforded, to the best of our knowledge, the first azacanthinones **1j** and **1k** in 69% and 56% yields, respectively (entries 18 and 20). The failure to cyclize the 2,3-dichlorophenyl analogue **5c** was surprising since the analogous non-ester-substituted canthinone was readily prepared.[13] This anomaly is now under further investigation.

Table 3. Cyclization of Naphthyridones 5 (0.13 mmol) with CuI, Ligand, Cs_2CO_3 (2 equiv), and Water (2 equiv) in Refluxing Dioxane (2 mL) To Give Canthin-6-ones 1

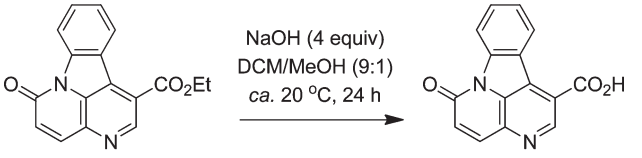


5a-l **1b-k**

entry	Hal	CuI (mol %)	ligand (mol %)	time (h)	R^2	yield of **1** (%)
1	Br	5	DMEDA (10)	1	H	**1b** (85)
2	Cl	5	DMEDA (10)	24	H	[a]
3	Cl	30	DMEDA (60)	18	H	**1b** (48)
4	Cl	10	DMEDA (60)	9	H	**1b** (84)
5	Cl	10	DMCDA (60)	2	H	**1b** (74)
6	Cl	10	DMCDA (60)	24	8-Cl	[b]
7	Cl	30	DMCDA (180)	24	8-Cl	[b]
8	Cl	10	DMCDA (60)	4	9-Cl	**1c** (85)
9	Cl	10	DMCDA (60)	1	9-F_3C	**1d** (90)
10	Cl	10	DMCDA (60)	12	9-Me	**1e** (80)
11	Cl	10	DMCDA (60)	24	9-MeO	[a]
12	Cl	20	DMCDA (120)	24	9-MeO	**1f** (73)
13	Cl	10	DMCDA (60)	24	9-F	[a]
14	Cl	20	DMCDA (120)	24	9-F	**1g** (70)
15	Cl	10	DMCDA (60)	1.5	10-Cl	**1h** (89)
16	Cl	10	DMCDA (60)	4.3	10-F_3C	**1i** (95)
17	Cl	10	DMCDA (60)	24	8-aza	[a]
18	Cl	20	DMCDA (120)	4	8-aza	**1j** (69)
19	Cl	10	DMCDA (60)	24	9-aza	[a]
20	Cl	20	DMCDA (120)	4	9-aza	**1k** (56)

[a] Incomplete reaction. [b] No reaction; starting material recovered even after 24 h.

Scheme 2. Hydrolysis of Ethyl Canthinone-1-carboxylate 1b



1b **6** (99%)

Having demonstrated a route to the ethyl canthinone-1-carboxylates **1b**−**k**, we showed that the ester group of the ethyl

dx.doi.org/10.1021/jo200824b |*J. Org. Chem.* 2011, 76, 5113–5122

canthinone-1-carboxylate **1b** could be readily hydrolyzed (Scheme 2). Treating a DCM/MeOH (9:1) solution of the ethyl canthinone-1-carboxylate **1b** with NaOH (4 equiv) at ca. 20 °C for 24 h[17] afforded a precipitate assumed to be the sodium carboxylate. Acidification of the reaction mixture using 10% HCl followed by extraction with EtOAc afforded the orange canthinone-1-carboxylic acid **6** (6-oxo-6*H*-indolo[3,2,1-*de*][1,5]naphthyrid-ine-1-carboxylic acid) in excellent yield.

3. CONCLUSION

Starting from the known ethyl 4-bromo-6-methoxy-1,5-naphthyridine-3-carboxylate (**2b**), a series of eight ethyl canthinone-1-carboxylates **1b**−**i** were prepared bearing various substituents on the A ring, together with the 8-aza and 9-aza analogues **1j** and **1k** that constitute two members of previously unknown ring systems. The synthetic route that was used involved three key steps: first the Suzuki−Miyaura arylation of the 4-bromonaphthyridine **2b** to afford the ethyl 4-(2-haloaryl)-6-methoxy-1,5-naphthyridine-3-carboxylates **4a**−**l**, then the TMSCl/NaI mediated demethylation to afford the ethyl 4-(2-haloaryl)-6-oxo-5,6-dihydro-1,5-naphthyridine-3-carboxylates **5a**−**l**, and finally the copper-catalyzed Buchwald cyclization to afford the target ethyl canthinone-1-carboxylates **1b**−**k**. The biological properties of these compounds are now being studied.

4. EXPERIMENTAL SECTION

4.1. General Procedures. DCM was freshly distilled from CaH_2 under argon. Reactions were protected from atmospheric moisture by $CaCl_2$ drying tubes. Anhydrous Na_2SO_4 was used for drying organic extracts, and all volatiles were removed under reduced pressure. All reaction mixtures and column eluents were monitored by TLC using commercial glass backed thin layer chromatography (TLC) plates (Kieselgel 60 F_{254}). The plates were observed under UV light at 254 and 365 nm. The technique of dry flash chromatography[18] was used throughout for all non-TLC scale chromatographic separations using silica gel 60 (less than 0.063 mm). Melting points were determined using a hotstage microscope apparatus. Solvents used for recrystallization are indicated after the melting point. UV spectra were obtained using a UV−vis spectrophotometer and inflections are identified by the abbreviation "inf". IR spectra were recorded on a FTIR-NIR spectrometer with a Ge ATR accessory and strong, medium, and weak peaks are represented by s, m, and w, respectively. ^1H and ^{13}C NMR spectra were recorded either at 300 and 75 MHz, respectively or at 500 and 125 MHz, respectively. DEPT 135 or APT NMR studies identified quaternary and tertiary carbons, which are indicated by (s) and (d) notations, respectively. Deuterated solvents were used for homonuclear lock, and the signals are referenced to the deuterated solvent peaks. Low resolution (EI) mass spectra were recorded on a GC−MS with direct inlet probe. Ethyl 4-bromo-6-methoxy-1,5-naphthyridine-3-carboxylate (**2b**) was prepared according to literature procedures.[14]

4.2. Ethyl 4-(2-Bromophenyl)-6-methoxy-1,5-naphthyridine-3-carboxylate (4a) (Typical Procedure; See Table 1, Entry 1). Ethyl 4-bromo-6-methoxy-1,5-naphthyridine-3-carboxylate (**2b**) (310 mg, 1 mmol), K_2CO_3 (279 mg, 2 equiv), Pd(dppf)Cl_2·DCM (41 mg, 0.05 mmol), and 2-bromophenylboronic acid (264 mg, 1.8 mmol) were dissolved in dioxane/H_2O (3:1) (2 mL). The stirred mixture was heated to reflux (preheated oil bath) and refluxed for 2 h until the reaction was finished (TLC), before it was allowed to cool to ca. 20 °C. It was diluted (DCM, 20 mL), dried (Na_2SO_4), filtered, and adsorbed onto silica gel. Dry flash chromatography (hexane/*t*-BuOMe, 4:1) gave the title compound **4a** (378 mg, 98%) as colorless cubes, mp 80−81 °C (DCM/pentane), R_f 0.60 (hexane/*t*-BuOMe, 8:2); (found: C, 55.7; H, 3.8; N, 7.3. $C_{18}H_{15}BrN_2O_3$ requires C, 55.8; H, 3.9; N, 7.2); λ_{max} (DCM)/nm 231 (log ε 4.01), 264 (3.14), 333 (3.36); ν_{max}/cm^{-1} 1703s, 1612 m, 1498 m, 1402 m, 1338 m, 1255 m, 1110 m, 840 m, 748s; δ_H (500 MHz; CD_2Cl_2) 9.28 (1H, s, Ar *H*), 8.27 (1H, d, *J* = 9.0, Ar *H*), 7.69 (1H, d, *J* = 7.9, Ar *H*), 7.40 (1H, ddd, *J* = 7.4, 7.4, 1.3, Ar *H*), 7.30 (1H, ddd, *J* = 8.5, 7.6, 1.7, Ar *H*), 7.21 (1H, dd, *J* = 7.6, 1.6, Ar *H*), 7.17 (1H, d, *J* = 9.2, Ar *H*), 4.15 (2H, q, *J* = 7.1, O*CH*$_2$), 3.70 (3H, s, O*CH*$_3$), 1.05 (3H, t, *J* = 7.1, *CH*$_3$); δ_C (125 MHz; CD_2Cl_2) 166.0 (s), 162.7 (s), 148.5 (d), 147.3 (s), 144.3 (s), 140.4 (d), 140.0 (s), 138.5 (s), 132.2 (d), 130.9 (d), 129.4 (d), 126.9 (d), 126.3 (s), 123.2 (s), 118.3 (d), 61.8 (O*CH*$_2$), 54.0 (O*CH*$_3$), 13.9 (*CH*$_3$); *m*/*z* (EI) 307 (M^+ − Br, 100%), 279 (75), 247 (8), 236 (12), 191 (14), 164 (12).

*4.2.1. 4-(2-Chlorophenyl)-6-methoxy-1,5-naphthyridine-3-carboxylate (**4b**).* (307 mg, 90%) as colorless plates, mp 67−69 °C (pentane), R_f 0.60 (hexane/*t*-BuOMe, 8:2); (found: C, 63.2; H, 4.4; N, 8.1. $C_{18}H_{15}ClN_2O_3$ requires C, 63.1; H, 4.4; N, 8.2); λ_{max} (DCM)/nm 236 (log ε 4.03), 261 (3.63), 270 (3.61), 282 inf (3.49), 327 (3.49), 339 (3.46); ν_{max}/cm^{-1} 2992w, 2941w, 1705s (C═O), 1612 m, 1562w, 1501 m, 1479w, 1464w, 1433w, 1402s, 1366 m, 1339s, 1321s, 1290 m, 1261s, 1256 m, 1223 m, 1206 m, 1180w, 1134 m, 1113 m, 1059w, 1034s, 1018 m, 999w, 932w, 868w, 843s, 812w, 775 m, 760 m; δ_H (500 MHz; CD_2Cl_2) 9.28 (1H, s, Ar *H*), 8.27 (1H, d, *J* = 9.0, Ar *H*), 7.50 (1H, dd, *J* = 7.7, 1.4, Ar *H*), 7.39 (1H, ddd, *J* = 7.5, 7.5, 1.8, Ar *H*), 7.36 (1H, ddd, *J* = 7.5, 7.5, 1.5, Ar *H*), 7.24 (1H, dd, *J* = 7.3, 1.9, Ar *H*), 7.17 (1H, d, *J* = 9.2, Ar *H*), 4.15 (2H, q, *J* = 7.1, O*CH*$_2$), 3.70 (3H, s, O*CH*$_3$), 1.05 (3H, t, *J* = 7.2, *CH*$_3$); δ_C (125 MHz; CD_2Cl_2) 166.1 (s), 162.8 (s), 148.5 (d), 145.8 (s), 144.2 (s), 140.4 (d), 140.1 (s), 136.3 (s), 133.3 (s), 131.1 (d), 129.4 (d), 129.1 (d), 126.6 (s), 126.3 (d), 118.3 (d), 61.8 (O*CH*$_2$), 54.0 (O*CH*$_3$), 13.9 (*CH*$_3$); *m*/*z* (EI) 308 (MH^+ − Cl, 20%), 307 (M^+ − Cl, 100), 280 (14), 279 (68), 264 (17), 247 (12), 236 (8), 226 (7), 219 (8), 201 (5), 191 (10), 165 (5), 164 (11), 113 (5).

*4.2.2. Ethyl 4-(2,3-Dichlorophenyl)-6-methoxy-1,5-naphthyridine-3-carboxylate (**4c**).* (373 mg, 99%) as colorless cubes, mp 107−108 °C (pentane), R_f 0.30 (hexane/*t*-BuOMe, 8:2); (found: C, 57.5; H, 3.9; N, 7.3. $C_{18}H_{14}Cl_2N_2O_3$ requires C, 57.3; H, 3.7; N, 7.4); λ_{max} (DCM)/nm 232 (log ε 3.94), 261 (3.32), 269 (3.28), 327 (3.27), 339 (3.25); ν_{max}/cm^{-1} 3046w (Ar CH), 2990w, 2941w, 1713s (C═O), 1612 m, 1499s, 1479w, 1450w, 1402 m, 1371w, 1339 m, 1323s, 1277 m, 1261 m, 1225 m, 1180w, 1144 m, 1117 m, 1038 m, 1018 m, 991w, 941w, 848 m, 816 m, 789 m, 773w; δ_H (300 MHz; CD_2Cl_2) 9.30 (1H, s, Ar *H*), 8.27 (1H, d, *J* = 9.3, Ar *H*), 7.57 (1H, dd, *J* = 7.8, 1.8, Ar *H*), 7.31 (1H, dd, *J* = 7.8, 7.8, Ar *H*), 7.18 (1H, d, *J* = 9.0, Ar *H*), 7.14 (1H, dd, *J* = 7.5, 1.5, Ar *H*), 4.16 (2H, q, *J* = 7.0, O*CH*$_2$), 3.69 (3H, s, O*CH*$_3$), 1.07 (3H, t, *J* = 7.1, *CH*$_3$); δ_C (75 MHz; CD_2Cl_2) 165.7 (s), 162.9 (s), 148.6 (d), 145.4 (s), 144.4 (s), 140.4 (d), 139.9 (s), 138.8 (s), 132.8 (s), 131.7 (s), 129.9 (d), 129.2 (d), 127.1 (d), 126.0 (s), 118.6 (d), 61.9 (O*CH*$_2$), 54.0 (O*CH*$_3$), 13.9 (*CH*$_3$); *m*/*z* (EI) 378 (M^+ + 2, 0.2%), 376 (M^+, 0.2), 343 [(M^+ + 2) − Cl, 36], 341 (M^+ − Cl, 100), 333 (2), 331 (4), 315 (17), 313 (61), 298 (10), 278 (7), 270 (11), 254 (7), 225 (7), 198 (8), 189 (4), 162 (8), 126 (5), 99 (5), 63 (9).

*4.2.3. Ethyl 4-(2,4-Dichlorophenyl)-6-methoxy-1,5-naphthyridine-3-carboxylate (**4d**).* (323 mg, 86%) as colorless cubes, mp 82−83 °C (pentane), R_f 0.29 (hexane/*t*-BuOMe, 8:2); (found: C, 57.5; H, 3.7; N, 7.4. $C_{18}H_{14}Cl_2N_2O_3$ requires C, 57.3; H, 3.7; N, 7.4); λ_{max} (DCM)/nm 232 (log ε 3.66), 261 inf (2.87), 270 inf (2.76), 329 (2.95), 339 (2.93); ν_{max}/cm^{-1} 2986w, 2941w, 1712s (C═O), 1612 m, 1595w, 1570w, 1557w, 1501s, 1464 m, 1435w, 1404s, 1366 m, 1340 m, 1321s, 1281s, 1267s, 1248 m, 1225 m, 1207 m, 1180w, 1138s, 1115 m, 1099 m, 1057 m, 1034 m, 1016 m, 1001w, 932w, 866 m, 845s, 833s, 814 m, 791 m, 775 m; δ_H (300 MHz; CD_2Cl_2) 9.30 (1H, s, Ar *H*), 8.26 (1H, d, *J* = 9.0, Ar *H*), 7.55 (1H, d, *J* = 2.1, Ar *H*), 7.37 (1H, dd, *J* = 8.3, 2.1, Ar *H*), 7.25−7.20 (2H, m, Ar and Ar *H*), 4.19 (2H, q, *J* = 7.2, O*CH*$_2$), 3.72 (3H, s, O*CH*$_3$), 1.11 (3H, t, *J* = 7.1, *CH*$_3$); δ_C (75 MHz; CD_2Cl_2) 165.8 (s),

162.9 (s), 148.4 (d), 144.8 (s), 144.2 (s), 140.3 (d), 139.9 (s), 135.1 (s), 134.3 (s), 134.1 (s), 132.0 (d), 129.0 (d), 126.7 (d), 126.3 (s), 118.6 (d), 62.0 (OCH_2), 54.1 (OCH_3), 14.0 (CH_3); *m*/*z* (EI) 343 [($M^+ + 2$) − Cl, 33%], 341 (M^+ − Cl, 100), 333 (3), 331 (5), 315 (19), 313 (63), 298 (14), 278 (5), 270 (7), 253 (7), 225 (9), 198 (11), 190 (4), 163 (3), 147 (5), 124 (3), 99 (4), 80 (5).

*4.2.4. Ethyl 4-[2-Chloro-4-(trifluoromethyl)phenyl]-6-methoxy-1,5-naphthyridine-3-carboxylate (**4e**).* (377 mg, 92%) as colorless prisms, mp 90−91 °C (pentane), R_f 0.29 (hexane/*t*-BuOMe, 8:2); (found: C, 55.6; H, 3.3; N, 6.6. $C_{19}H_{14}ClF_3N_2O_3$ requires C, 55.6; H, 3.4; N, 6.8); λ_{max} (DCM)/nm 233 (log ε 3.71), 272 (2.83), 325 (2.97), 340 (2.89); ν_{max}/cm^{-1} 2986w, 2945w, 1713 m (C═O), 1612 m, 1499 m, 1472w, 1406w, 1391w, 1368w, 1343w, 1323s, 1288w, 1271 m, 1254w, 1227w, 1209w, 1177s, 1138s, 1117w, 1082 m, 1063w, 1036w, 1015w, 1003w, 934w, 897w, 868w, 843 m, 814w; δ_H (300 MHz; CD_2Cl_2) 9.33 (1H, s, Ar *H*), 8.28 (1H, d, *J* = 9.0, Ar *H*), 7.80 (1H, s, Ar *H*), 7.64 (1H, d, *J* = 8.1, Ar *H*), 7.39 (1H, d, *J* = 8.1, Ar *H*), 7.20 (1H, d, *J* = 9.0, Ar *H*), 4.17 (2H, q, *J* = 7.1, OCH_2), 3.68 (3H, s, OCH_3), 1.06 (3H, t, *J* = 7.1, CH_3); δ_C (75 MHz; CD_2Cl_2) 165.6 (s), 163.0 (s), 148.6 (d), 144.5 (s), 144.4 (s), 140.7 (s), 140.4 (d), 139.7 (s), 134.1 (s), 131.6 (d), 131.2 (q, $^2J_{CF}$ 33.2, F_3CC), 125.9 (q, $^3J_{CF}$ 3.8, F_3CC_qCH), 122.3 (q, $^3J_{CF}$ 3.8, F_3CC_qCH), 123.1 (q, $^1J_{CF}$ 269.8, F_3C), 118.8 (d), 62.0 (OCH_2), 54.1 (OCH_3), 13.8 (CH_3); *m*/*z* (EI) 411 (M^+ + H, 0.5%), 409 (M^+ − H, 1), 376 (MH^+ − Cl, 22), 375 (M^+ − Cl, 100), 365 (4), 347 (70), 332, (10), 315 (4), 304 (6), 294 (5), 287 (4), 259 (5), 232 (6), 80 (4), 64 (2).

*4.2.5. Ethyl 4-(2-Chloro-4-methylphenyl)-6-methoxy-1,5-naphthyridine-3-carboxylate (**4f**).* (299 mg, 84%) as colorless cubes, mp 69−71 °C (pentane), R_f 0.35 (hexane/*t*-BuOMe, 8:2); (found: C, 64.1; H, 4.7; N, 7.7. $C_{19}H_{17}ClN_2O_3$ requires C, 64.0; H, 4.8; N, 7.9); λ_{max} (DCM)/nm 237 (log ε 4.18), 250 inf (3.90), 258 inf (3.78), 267 inf (3.67), 329 (3.77); ν_{max}/cm^{-1} 2982w, 2943w, 2853w, 1726s (C═O), 1609 m, 1574w, 1493s, 1468w, 1433w, 1402 m, 1368 m, 1341 m, 1283 m, 1259s, 1223s, 1207 m, 1140 m, 1138 m, 1111 m, 1059w, 1038w, 1024 m, 993w, 943w, 878w, 851 m, 829 m, 818w, 772 m; δ_H (500 MHz; CD_2Cl_2) 9.25 (1H, s, Ar *H*), 8.26 (1H, d, *J* = 9.0, Ar *H*), 7.33 (1H, s, Ar *H*), 7.17 (1H, d, *J* = 9.0, Ar *H*), 7.13−7.11 (2H, m, Ar *H*), 4.17 (2H, q, *J* = 7.2, OCH_2), 3.73 (3H, s, OCH_3), 2.43 (3H, s, CH_3), 1.09 (3H, t, *J* = 7.2, CH_3); δ_C (125 MHz; CD_2Cl_2) 166.2 (s), 162.7 (s), 148.4 (d), 145.9 (s), 144.2 (s), 140.9 (d), 140.3 (s), 139.8 (s), 133.0 (s), 132.9 (C_q), 130.9 (d), 129.6 (d), 127.1 (d), 126.9 (s), 118.2 (d), 61.8 (OCH_2), 54.0 (OCH_3), 21.3 (CH_3), 14.0 (CH_3); *m*/*z* (EI) 322 (MH^+ − Cl, 19%), 321 (M^+ − Cl, 100), 311 (4), 293 (53), 278 (11), 261 (4), 250 (6), 240 (4), 233 (6), 205 (6), 178 (3), 151 (3), 138 (3), 127 (2).

*4.2.6. Ethyl 4-(2-Chloro-4-methoxyphenyl)-6-methoxy-1,5-naphthyridine-3-carboxylate (**4g**).* (335 mg, 90%) as colorless cubes, mp 97−99 °C (pentane), R_f 0.23 (hexane/*t*-BuOMe, 8:2); (found: C, 61.1; H, 4.6; N, 7.4. $C_{19}H_{17}ClN_2O_4$ requires C, 61.2; H, 4.6; N, 7.5); λ_{max} (DCM)/nm 234 (log ε 4.11), 248 inf (3.77), 259 inf (3.67), 269 inf (3.55), 288 (3.39), 326 (3.55); ν_{max}/cm^{-1} 2984w, 2943w, 2907w, 2832w, 1726s (C═O), 1609s, 1572w, 1506w, 1491s, 1464w, 1427 m, 1402 m, 1368w, 1339 m, 1310w, 1277 m, 1260s, 1236s, 1217s, 1206s, 1182w, 1136 m, 1109 m, 1043 m, 1036 m, 1018 m, 991w, 943w, 889 m, 878w, 851s, 831s, 772 m; δ_H (300 MHz; CD_2Cl_2) 9.23 (1H, s, Ar *H*), 8.25 (1H, d, *J* = 9.0, Ar *H*), 7.17 (2H, d, *J* = 8.4, Ar *H*), 7.07 (1H, d, *J* = 3.9, Ar *H*), 6.92 (1H, dd, *J* = 8.4, 3.6, Ar *H*), 4.18 (2H, q, *J* = 7.0, OCH_2), 3.87 (3H, s, OCH_3), 3.75 (3H, s, OCH_3), 1.11 (3H, t, *J* = 7.2, CH_3); δ_C (75 MHz; CD_2Cl_2) 166.2 (s), 162.7 (s), 160.3 (s), 148.2 (d), 145.7 (s), 144.0 (s), 140.4 (s), 140.2 (d), 133.9 (s), 131.9 (d), 128.0 (s), 127.1 (s), 118.3 (d), 114.4 (d), 112.4 (d), 61.8 (OCH_2), 56.0 (OCH_3), 54.0 (OCH_3), 14.0 (CH_3); *m*/*z* (EI) 338 (MH^+ − Cl, 25%), 337 (M^+ − Cl, 100), 327 (5), 309 (42), 294 (13), 277 (3), 265 (4), 251 (8), 241 (3), 221 (3), 213 (3), 178 (3), 151 (4), 99 (3).

*4.2.7. Ethyl 4-(2-Chloro-4-fluorophenyl)-6-methoxy-1,5-naphthyridine-3-carboxylate (**4h**).* (320 mg, 89%) as colorless cubes, mp 75−77 °C (pentane), R_f 0.35 (hexane/*t*-BuOMe, 8:2); (found: C, 60.1; H, 3.9; N, 7.8. $C_{18}H_{14}ClFN_2O_3$ requires C, 59.9; H, 3.9; N, 7.8); λ_{max} (DCM)/nm 233 (log ε 3.88), 261 (3.32), 271 (3.29), 325 (3.20), 339 (3.14); ν_{max}/cm^{-1} 3048w, 2986w, 1730s (C═O), 1611 m, 1572w, 1495s, 1470w, 1435w, 1402 m, 1369w, 1339 m, 1273s, 1234 m, 1213 m, 1200 m, 1182w, 1144w, 1113w, 1036w, 1016 m, 991w, 945w, 899 m, 853s, 820w, 804w, 774 m; δ_H (300 MHz; CD_2Cl_2) 9.28 (1H, s, Ar *H*), 8.26 (1H, d, *J* = 9.0, Ar *H*), 7.30−7.11 (4H, m, Ar *H*), 4.18 (2H, q, *J* = 7.1, OCH_2), 3.72 (3H, s, OCH_3), 1.10 (3H, t, *J* = 9.0, CH_3); δ_C (75 MHz; CD_2Cl_2) 165.9 (s), 164.2 (s), 161.9 (d, $^1J_{CF}$ 249.2, FC), 148.5 (d), 144.9 (s), 144.3 (s), 140.4 (d), 140.1 (s), 134.1 (d, $^3J_{CF}$ 10.6, FCCHCCl), 132.1 (d, $^4J_{CF}$ 3.8, FCCHCHC$_q$), 132.4 (d, $^3J_{CF}$ 9.1, FCCHCH), 126.6 (s), 118.5 (d), 116.5 (d, $^2J_{CF}$ 25.7, FCCH), 113.7 (d, $^2J_{CF}$ 21.9, FCCH), 61.9 (OCH_2), 54.0 (OCH_3), 14.0 (CH_3); *m*/*z* (EI) 325 (M^+ − Cl, 100%), 315 (5), 297 (55), 282 (13), 265 (7), 254 (7), 244 (7), 237 (6), 223 (3), 209 (8), 182 (11), 156 (3), 131 (5), 80 (3).

*4.2.8. Ethyl 4-(2,5-Dichlorophenyl)-6-methoxy-1,5-naphthyridine-3-carboxylate (**4i**).* (345 mg, 92%) as colorless cubes, mp 85−86 °C (pentane), R_f 0.35 (hexane/*t*-BuOMe, 8:2); (found: C, 57.3; H, 3.7; N, 7.5. $C_{18}H_{14}Cl_2N_2O_3$ requires C, 57.3; H, 3.7; N, 7.4); λ_{max} (DCM)/nm 232 (log ε 3.74), 261 inf (2.93), 268 inf (2.84), 328 inf (3.01), 340 inf (2.99); ν_{max}/cm^{-1} 2990w, 2957w, 2905w, 1711s (C═O), 1612 m, 1558w, 1497s, 1456 m, 1431w, 1402s, 1379w, 1368 m, 1339 m, 1317s, 1275 m, 1263 m, 1252 m, 1225 m, 1207 m, 1177w, 1140 m, 1128 m, 1113 m, 1094 m, 1055 m, 1032 m, 1011w, 988w, 883w, 870w, 849s, 824 m, 814 m; δ_H (500 MHz; CD_2Cl_2) 9.31 (1H, s, Ar *H*), 8.27 (1H, d, *J* = 9.0, Ar *H*), 7.45 (1H, d, *J* = 8.7, Ar *H*), 7.38 (1H, d, *J* = 8.4, Ar *H*), 7.27 (1H, s, Ar *H*), 7.19 (1H, d, *J* = 9.0, Ar *H*), 4.20 (2H, q, *J* = 6.7, OCH_2), 3.73 (3H, s, OCH_3), 1.11 (3H, t, *J* = 7.1, CH_3); δ_C (125 MHz; CD_2Cl_2) 165.7 (s), 162.9 (s), 148.5 (d), 144.5 (s), 144.4 (s), 140.4 (d), 139.8 (s), 138.0 (s), 132.1 (s), 131.9 (s), 130.9 (d), 130.3 (d), 129.3 (d), 126.1 (s), 118.7 (d), 62.0 (OCH_2), 54.1 (OCH_3), 14.0 (CH_3); *m*/*z* (EI) 343 [(M^+ + 2) − Cl, 40%], 341 (M^+ − Cl, 100), 333 (2), 331 (4), 315 (24), 313 (60), 298 (17), 278 (5), 270 (12), 253 (6), 225 (8), 198 (9), 147 (4), 99 (3), 80 (4).

*4.2.9. Ethyl 4-[2-Chloro-5-(trifluoromethyl)phenyl]-6-methoxy-1,5-naphthyridine-3-carboxylate (**4j**).* (377 mg, 92%) as colorless cubes, mp 89−90 °C (pentane), R_f 0.47 (hexane/*t*-BuOMe, 8:2); (found: C, 55.6; H, 3.1; N, 6.8. $C_{19}H_{14}ClF_3N_2O_3$ requires C, 55.6; H, 3.4; N, 6.8); λ_{max} (DCM)/nm 232 (log ε 3.70), 262 (3.02), 271 (2.98), 329 (3.00), 341 (2.99); ν_{max}/cm^{-1} 2990w, 2947w, 1724 m (C═O), 1611 m, 1574w, 1495 m, 1437w, 1400 m, 1371w, 1344 m, 1325 m, 1300w, 1287 m, 1263s, 1219 m, 1206w, 1167 m, 1148 m, 1125s, 1113 m, 1080s, 1040w, 1018 m, 989w, 928w, 876w, 845 m, 833 m, 816w, 793w; δ_H (300 MHz; CD_2Cl_2) 9.34 (1H, s, Ar *H*), 8.29 (1H, d, *J* = 9.0, Ar *H*), 7.66 (2H, s, Ar *H*), 7.56 (1H, s, Ar *H*), 7.20 (1H, d, *J* = 9.0, Ar *H*), 4.17 (2H, q, *J* = 7.5, OCH_2), 3.68 (3H, s, OCH_3), 1.06 (3H, t, *J* = 7.4, CH_3); δ_C (75 MHz; CD_2Cl_2) 165.6 (s), 163.0 (s), 148.6 (d), 144.5 (s), 144.1 (s), 140.4 (d), 139.8 (s), 137.4 (s), 129.8 (d), 127.9 (q, $^2J_{CF}$ 33.0, F_3CC), 128.9 (s), 128.4 (q, $^3J_{CF}$ 3.7, F_3CCCH), 126.3 (q, $^3J_{CF}$ 3.7, F_3CCCH), 126.0 (q, $^1J_{CF}$ 246.0, F_3C), 122.7 (s), 118.7 (d), 62.0 (OCH_2), 54.0 (OCH_3), 13.9 (CH_3); *m*/*z* (EI) 376 (MH^+ − Cl, 22%), 375 (M^+ − Cl, 100), 365 (4), 347 (70), 332 (11), 315 (4), 304 (6), 294 (5), 287 (4), 259 (5), 232 (6), 80 (4).

*4.2.10. Ethyl 3-(2-Chloropyrid-3-yl)-6-methoxy-1,5-naphthyridine-3-carboxylate (**4k**).* (220 mg, 64%) as colorless cubes, mp 120−122 °C (pentane), R_f 0.77 (*t*-BuOMe); (found: C, 59.4; H, 4.1; N, 12.3. $C_{17}H_{14}ClN_3O_3$ requires C, 59.4; H, 4.1; N, 12.2); λ_{max} (DCM)/nm 232 (log ε 3.69), 263 (3.07), 328 (3.01), 338 (3.00); ν_{max}/cm^{-1} 3044w, 2986w, 2945w, 2907w, 1722s (C═O), 1611 m, 1572w, 1557w, 1495s, 1479w, 1449w, 1429w, 1395s, 1371w, 1341 m, 1281 m, 1261 m, 1234s, 1215 m, 1179w, 1146w, 1115 m, 1074w, 1015 m, 974w, 851 m, 810 m, 773 m; δ_H (500 MHz; CD_2Cl_2) 9.38 (1H, s, Ar *H*), 8.50 (1H, br s, Ar *H*), 8.32 (1H, d, *J* = 9.0, Ar *H*), 7.66 (1H, d, *J* = 7.4 Ar *H*), 7.43−7.41 (1H, m,

dx.doi.org/10.1021/jo200824b |*J. Org. Chem.* 2011, 76, 5113–5122

Ar *H*), 7.24 (1H, d, *J* = 9.2, Ar *H*), 4.24−4.22 (2H, m, OCH_2), 3.74 (3H, s, OCH_3), 1.13 (3H, t, *J* = 7.0, CH_3); δ_C (125 MHz; CD_2Cl_2); 165.6 (s), 162.9 (s), 149.8 (s), 149.0 (d), 148.6 (d), 144.5 (s), 143.9 (s), 140.4 (d), 139.8 (s), 139.7 (d), 133.1 (s), 125.9 (s), 122.0 (d), 118.8 (d), 62.0 (OCH_2), 54.1 (OCH_3), 14.0 (CH_3); *m*/*z* (EI) 309 (MH^+ − Cl, 19%), 308 (M^+ − Cl, 100), 298 (3), 280 (69), 252 (7), 237 (4), 227 (4), 220 (3), 206 (4), 192 (5), 165 (6), 138 (3), 126 (2), 114 (2), 100 (2), 87 (2).

*4.2.11. Ethyl 4-(3-Chloropyrid-4-yl)-6-methoxy-1,5-naphthyridine-3-carboxylate (**4l**).* (213 mg, 62%) as colorless needles, mp 95−97 °C (pentane), R_f 0.77 (*t*-BuOMe); (found: C, 59.5; H, 4.3; N, 12.2. $C_{17}H_{14}ClN_3O_3$ requires C, 59.4; H, 4.1; N, 12.2); λ_{max} (DCM)/nm 229 (log ε 3.31), 249 (2.82), 261 inf (2.85), 267 (2.87), 318 (2.97), 327 (2.97); ν_{max}/cm^{-1} 2982w, 2922w, 1726 m (C═O), 1612w, 1587w, 1566w, 1499 m, 1464w, 1433w, 1402 m, 1371w, 1339 m, 1288 m, 1263 m, 1225 m, 1207w, 1180w, 1138w, 1121 m, 1096s, 1024 m, 980w, 932s, 901s, 854 m, 818w, 770w; δ_H (500 MHz; CD_2Cl_2) 9.35 (1H, s, Ar *H*), 8.70 (1H, s, Ar *H*), 8.56 (1H, s, Ar *H*), 8.28 (1H, d, *J* = 9.0, Ar *H*), 7.21−7.19 (2H, m, Ar *H*), 4.19 (3H, q, *J* = 6.6, OCH_2), 3.69 (3H, s, OCH_3), 1.09 (3H, t, *J* = 7.0, CH_3); δ_C (125 MHz; CD_2Cl_2); 165.3 (s), 163.0 (s), 149.2 (d), 148.6 (d), 147.3 (d), 144.8 (s), 144.5 (s), 143.0 (s), 140.4 (d), 139.3 (s), 131.3 (s), 125.5 (s), 125.3 (d), 118.9 (d), 62.1 (OCH_2), 54.1 (OCH_3), 13.8 (CH_3); *m*/*z* (EI) 309 (MH^+ − Cl, 19%), 308 (M^+ − Cl, 100), 298 (3), 280 (65), 252 (7), 237 (4), 227 (4), 206 (4), 192 (5), 165 (5), 138 (2), 114 (2).

4.3. Ethyl 4-(2-Bromophenyl)-6-oxo-5,6-dihydro-1,5-naphthyridine-3-carboxylate (5a) (Typical Procedure, Table 2). To a stirred solution of ethyl 4-(2-bromophenyl)-6-methoxy-1,5-naphthyridine-3-carboxylate (**4a**) (187 mg, 0.5 mmol) and NaI (255 mg, 1.5 mmol) in MeCN (1 mL) was added dropwise TMSCl (314 μL, 2.5 mmol). An orange suspension was formed in the reaction mixture, which was then refluxed for 1−2 h until the reaction was finished (TLC). The reaction was diluted with H_2O (10 mL), and $Na_2S_2O_2$ (25 mg) was added. The mixture was extracted (DCM, 15 mL), dried (Na_2SO_4), filtered, and adsorbed onto silica gel. Dry flash chromatography (*t*-BuOMe) gave the title compound **5a** (130 mg, 70%) as colorless plates, mp 201−203 °C (*t*-BuOMe), R_f 0.36 (*t*-BuOMe, 8:2); (found: C, 54.5; H, 3.9; N, 7.3. $C_{17}H_{13}BrN_2O_3$ requires C, 54.7; H, 3.5; N, 7.5); λ_{max} (DCM)/nm 233 (log ε 3.10), 349 (2.68); ν_{max}/cm^{-1} 1718 m (C═O), 1666s (NHC═O), 1317 m, 1213 m, 1141 m, 1028w, 900w, 852 m, 758 m; δ_H (500 MHz; CD_2Cl_2) 9.08 (1H, s, Ar *H*), 8.33 (1H, br s, N*H*), 8.01 (1H, d, *J* = 9.8, Ar *H*), 7.77 (1H, dd, *J* = 7.9, 1.1, Ar *H*), 7.50 (1H, ddd, *J* = 7.5, 7.6, 1.1, Ar *H*), 7.43 (1H, ddd, J 8.0, 7.6, 1.7, Ar *H*), 7.23 (1H, dd, *J* = 7.6, 1.6, Ar *H*), 6.84 (1H, d, *J* = 9.8, Ar *H*), 4.11 (2H, q, *J* = 7.1, OCH_2), 1.03 (3H, t, *J* = 7.1, CH_3); δ_C (125 MHz; CD_2Cl_2) 165.0 (s), 161.6 (s), 146.4 (d), 142.0 (d), 140.4 (s), 135.5 (s), 133.9 (d), 133.8 (s), 132.7 (s), 131.5 (d), 130.8 (d), 128.8 (d), 128.1 (d), 126.3 (s), 123.5 (s), 62.0 (CH_2), 13.9 (CH_3); *m*/*z* (EI) 373 (M^+ + 1, 1%), 372 (M^+, 2), 293 (M^+ − Br, 35), 266 (11), 220 (5), 192 (9).

*4.3.1. Ethyl 4-(2-Chlorophenyl)-6-oxo-5,6-dihydro-1,5-naphthyridine-3-carboxylate (**5b**).* (150 mg, 81%) as colorless needles, mp 130−132 °C (*t*-BuOMe), R_f 0.35 (*t*-BuOMe); (found: C, 62.2; H, 4.0; N, 8.6. $C_{17}H_{13}ClN_2O_3$ requires C, 62.1; H, 4.0; N, 8.5); λ_{max} (DCM)/nm 235 (log ε 3.89), 262 (3.51), 271 (3.50), 338 inf (3.37), 348 (3.48), 363 (3.36); ν_{max}/cm^{-1} 3036w, 2990w, 2953w, 2926w, 1715 m (C═O), 1661s (NHC═O), 1605 m, 1580w, 1487w, 1450w, 1431w, 1366 m, 1325 m, 1314 m, 1250w, 1234w, 1207 m, 1138 m, 1109 m, 1059w, 1022w, 930w, 856w, 826w, 768 m; δ_H (500 MHz; CD_2Cl_2) 9.07 (1H, s, Ar *H*), 8.45 (1H, br s, N*H*), 8.01 (1H, d, *J* = 9.8, Ar *H*), 7.59 (1H, dd, *J* = 8.1, 1.0, Ar *H*), 7.51 (1H, ddd, *J* = 7.6, 7.9, 1.8, Ar *H*), 7.46 (1H, ddd, *J* = 7.5, 7.6, 1.2, Ar *H*), 7.24 (1H, dd, *J* = 7.6, 1.6, Ar *H*), 6.84 (1H, d, *J* = 9.8, Ar *H*), 4.80 (2H, dq, *J* = 7.2, 1.6, OCH_2), 1.03 (3H, t, *J* = 7.2, CH_3); δ_C (125 MHz; CD_2Cl_2) 165.1 (s), 161.6 (s), 146.3 (d), 142.0 (d), 140.3 (s), 134.0 (s), 133.8 (s), 132.9 (s), 131.7 (s), 131.5 (d), 130.7 (d), 130.6 (d), 128.2 (d), 128.1 (d), 126.6 (s), 62.0 (OCH_2), 13.9 (CH_3); *m*/*z* (EI) 330 (M^+ + 2, 3%), 328 (M^+, 6), 293 (M^+ − Cl, 69), 265 (100), 247 (7), 219 (8), 192 (11), 164 (6), 139 (3), 113 (6), 63 (3).

*4.3.2. Ethyl 4-(2,3-Dichlorophenyl)-6-oxo-5,6-dihydro-1,5-naphthyridine-3-carboxylate (**5c**).* (166 mg, 92%) as colorless plates, mp 171.5−172.5 °C (*t*-BuOMe), R_f 0.38 (*t*-BuOMe); (found: C, 56.4; H, 3.3; N, 7.6. $C_{17}H_{12}Cl_2N_2O_3$ requires C, 56.2; H, 3.3; N, 7.7); λ_{max} (DCM)/nm 232 (log ε 3.59), 250 inf (3.01), 259 inf (2.88), 268 inf (2.75), 337 inf (3.03), 349 (3.15), 362 (3.04); ν_{max}/cm^{-1} 2978w, 2932w, 1724 m (C═O), 1665s (NHC═O), 1607w, 1578w, 1487w, 1450w, 1418w, 1395w, 1379w, 1325w, 1304 m, 1281w, 1217 m, 1144 m, 1117 m, 1098w, 1047w, 1026w, 972w, 928w, 851 m, 783 m; δ_H (500 MHz; CD_2Cl_2) 9.10 (1H, s, Ar *H*), 8.59 (1H, br s, N*H*), 8.02 (1H, d, *J* = 9.8, Ar *H*), 7.67 (1H, d, *J* = 8.0, Ar *H*), 7.41 (1H, dd, *J* = 7.8, 7.8, Ar *H*), 7.15 (1H, d, *J* = 7.6, Ar *H*), 6.84 (1H, d, *J* = 9.8, Ar *H*), 4.13 (2H, m, OCH_2), 1.05 (3H, t, *J* = 7.1, CH_3); δ_C (125 MHz; CD_2Cl_2) 164.8 (s), 161.7 (s), 146.5 (d), 142.0 (d), 140.6 (s), 134.7 (s), 134.1 (s), 133.6 (s), 132.7 (s), 132.5 (s), 132.0 (d), 129.0 (d), 128.9 (d), 128.2 (d), 126.1 (s), 62.1 (OCH_2), 13.9 (CH_3); *m*/*z* (EI) 364 (M^+ + 2, 3%), 362 (M^+, 5), 329 (20), 327 (M^+ − Cl, 63), 317 (5), 301 (36), 299 (100), 281 (6), 264 (20), 253 (7), 226 (13), 207 (7), 198 (4), 191 (6), 173 (5), 164 (8), 147 (8), 138 (6), 127 (4), 113 (7), 99 (6), 64 (5), 57 (7).

*4.3.3. Ethyl 4-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1,5-naphthyridine-3-carboxylate (**5d**).* (150 mg, 83%) as colorless plates, mp 155−156.5 °C (*t*-BuOMe), R_f 0.38 (*t*-BuOMe); (found: C, 56.4; H, 3.3; N, 7.8. $C_{17}H_{12}Cl_2N_2O_3$ requires C, 56.2; H, 3.3; N, 7.7); λ_{max} (DCM)/nm 233 (log ε 3.61), 259 inf (2.99), 268 inf (2.90), 338 inf (3.04), 349 (3.15), 362 (3.04); ν_{max}/cm^{-1} 3090w, 3032w, 2941w, 1732 m (C═O), 1707 m, 1659s (NHC═O), 1603w, 1557w, 1481w, 1447w, 1379w, 1368w, 1327 m, 1310w, 1296 m, 1206w, 1144 m, 1130 m, 1115w, 1099w, 1059w, 1030w, 1016w, 997w, 856 m, 835w, 822w, 773w, 760w; δ_H (500 MHz; CD_2Cl_2) 9.09 (1H, s, Ar *H*), 8.82 (1H, br s, N*H*), 8.02 (1H, d, *J* = 9.9, Ar *H*), 7.62 (1H, s, Ar *H*), 7.45 (1H, d, *J* = 8.2, Ar *H*), 7.19 (1H, d, *J* = 8.1, Ar *H*), 6.83 (1H, d, *J* = 9.8, Ar *H*), 4.15 (2H, q, *J* = 7.0, OCH_2), 1.10 (3H, t, *J* = 7.1, CH_3); δ_C (125 MHz; CD_2Cl_2) 164.9 (s), 161.9 (s), 146.4 (d), 142.1 (d), 140.5 (s), 136.7 (s), 134.8 (s), 133.0 (s), 132.9 (s), 131.7 (d), 130.6 (d), 130.5 (s), 128.6 (d), 128.2 (d), 126.4 (s), 62.2 (OCH_2), 14.0 (CH_3); *m*/*z* (EI) 364 (M^+ + 2, 8%), 362 (M^+, 12), 329 (29), 327 (M^+ − Cl, 82), 319 (5), 317 (7), 301 (40), 299 (100), 283 (3), 281 (8), 264 (18), 253 (10), 236 (4), 225 (18), 207 (5), 200 (4), 191 (8), 179 (3), 164 (10), 147 (11), 138 (7), 113 (8), 99 (5), 87 (4), 63 (6).

*4.3.4. Ethyl 4-[2-Chloro-4-(trifluoromethyl)phenyl]-6-oxo-5,6-dihydro-1,5-naphthyridine-3-carboxylate (**5e**).* (158 mg, 80%) as colorless cubes, mp 189−191 °C (*t*-BuOMe), R_f 0.51 (*t*-BuOMe); (found: C, 54.5; H, 3.0; N, 7.0. $C_{18}H_{12}ClF_3N_2O_3$ requires C, 54.5; H, 3.1; N, 7.1); λ_{max} (DCM)/nm 234 (log ε 4.06), 263 (3.57), 269 (3.53), 339 inf (3.56), 349 (3.66), 362 (3.54); ν_{max}/cm^{-1} 3019w, 2986w, 2941w, 2851w, 1724 m (C═O), 1665s (NHC═O), 1605 m, 1487w, 1450w, 1395 m, 1368w, 1321s, 1287w, 1204 m, 1171 m, 1134s, 1080 m, 1065 m, 1020w, 883 m, 864 m, 839 m, 800w, 775w; δ_H (300 MHz; CD_2Cl_2) 9.13 (1H, s, Ar *H*), 8.61 (1H, br s, N*H*), 8.04 (1H, d, *J* = 9.8, Ar *H*), 7.88 (1H, br s, Ar *H*), 7.73 (1H, d, *J* = 7.9, Ar *H*), 7.41 (1H, d, *J* = 7.9, Ar *H*), 6.84 (1H, d, *J* = 9.8, Ar *H*), 4.12 (2H, q, *J* = 7.1, OCH_2), 1.05 (3H, t, *J* = 7.1, CH_3); δ_C (75 MHz; CD_2Cl_2) 164.7 (s), 162.1 (s), 146.4 (d), 142.0 (d), 140.6 (s), 136.1 (s), 134.9 (s), 133.4 (q, $^2J_{CF}$ 33.5, F_3CC), 133.0 (s), 132.7 (s), 131.6 (d), 128.2 (d), 127.6 (q, $^3J_{CF}$ 3.8, F_3CCCH), 126.1 (s), 123.7 (q, $^1J_{CF}$ 272.8, F_3C), 124.9 (q, $^3J_{CF}$ 3.5, F_3CCCH), 62.3 (OCH_2), 13.8 (CH_3); *m*/*z* (EI) 398 (M^+ + 2, 3%), 396 (M^+, 8), 361 (M^+ − Cl, 50), 351 (5), 333 (100), 315 (7), 287 (7), 260 (9), 241 (4), 232 (4), 207 (4), 192 (3), 181 (3).

*4.3.5. Ethyl 4-(2-Chloro-4-methylphenyl)-6-oxo-5,6-dihydro-1,5-naphthyridine-3-carboxylate (**5f**).* (127 mg, 74%) as colorless cubes, mp 164−166 °C (*t*-BuOMe), R_f 0.40 (*t*-BuOMe); (found: C, 63.3; H, 4.4; N, 8.1. $C_{18}H_{15}ClN_2O_3$ requires C, 63.1; H, 4.4; N, 8.2); λ_{max} (DCM)/nm

234 (log ε 3.83), 261 (3.30), 268 (3.25), 339 inf (3.27), 349 (3.37), 360 (3.25); ν_{max}/cm^{-1} 2941w, 2870w, 1732 m (C═O), 1717 m, 1665s (NHC═O), 1605w, 1558w, 1541w, 1506w, 1485w, 1447w, 1395w, 1381w, 1366w, 1327w, 1310w, 1204 m, 1113 m, 1061w, 1028w, 982w, 966w, 934w, 883w, 849 m, 818 m, 802w; δ_H (300 MHz; CD_2Cl_2) 9.06 (1H, s, Ar *H*), 8.18 (1H, br s, N*H*), 8.01 (1H, d, *J* = 9.9, Ar *H*), 7.42 (1H, s, Ar *H*), 7.27 (1H, dd, *J* = 7.8, 0.6, Ar *H*), 7.12 (1H, d, *J* = 7.8, Ar *H*), 6.86 (1H, d, *J* = 9.9, Ar *H*), 4.12 (2H, q, *J* = 7.1, OC*H*$_2$), 2.45 (3H, s, C*H*$_3$), 1.06 (3H, t, *J* = 7.1, C*H*$_3$); δ_C (75 MHz; CD_2Cl_2) 165.1 (s), 161.6 (s), 146.3 (d), 142.3 (s), 142.1 (d), 140.3 (s), 134.2 (s), 133.4 (s), 133.0 (s), 131.2 (d), 130.4 (d), 129.0 (d), 128.4 (s), 128.0 (d), 126.8 (s), 62.1 (OCH$_2$), 21.3 (*C*H$_3$), 13.9 (CH$_3$); *m*/*z* (EI) 344 (M^+ + 2, 4%), 342 (M^+, 7), 307 (M^+ − Cl, 79), 297 (6), 279 (100), 261 (7), 251 (3), 233 (9), 205 (12), 192 (3), 179 (3), 152 (4), 139 (3), 126 (9), 103 (4), 89 (3), 77 (3), 63 (3).

*4.3.6. Ethyl 4-(2-Chloro-4-methoxyphenyl)-6-oxo-5,6-dihydro-1,5-naphthyridine-3-carboxylate (**5g**).* (159 mg, 89%) as colorless plates, mp 169−171 °C (*t*-BuOMe), R_f 0.23 (*t*-BuOMe); (found: C, 60.1; H, 4.1; N, 7.8. $C_{18}H_{15}ClN_2O_4$ requires C, 60.3; H, 4.2; N, 7.8); λ_{max} (DCM)/nm 240 (log ε 4.22), 259 inf (3.95), 268 inf (3.80), 286 (3.60), 341 inf (3.99), 348 (4.05), 358 inf (3.97); ν_{max}/cm^{-1} 2970w, 1736 m (C═O), 1713 m (C═O), 1662s (NHC═O), 1605 m, 1560w, 1497w, 1485w, 1450w, 1367 m, 1329 m, 1310w, 1290 m, 1227s, 1204 m, 1142 m, 1119w, 1051 m, 1038 m, 1018w, 862 m, 853 m, 812w, 775w, 764w; δ_H (300 MHz; CD_2Cl_2) 9.05 (1H, s, Ar *H*), 8.32 (1H, br s, N*H*), 8.01 (1H, d, *J* = 9.9, Ar *H*), 7.15−7.12 (2H, m, Ar *H*), 7.01 (1H, dd, *J* = 8.4, 2.4, Ar *H*), 6.84 (1H, d, *J* = 9.9, Ar *H*), 4.14 (2H, q, *J* = 7.1, OC*H*$_2$), 3.89 (3H, s, OC*H*$_3$), 1.08 (3H, t, *J* = 7.2, C*H*$_3$); δ_C (75 MHz; CD_2Cl_2) 165.2 (s), 161.8 (s), 161.6 (s), 146.3 (d), 142.0 (d), 140.2 (s), 134.5 (s), 133.9 (s), 133.3 (s), 131.4 (d), 128.0 (d), 127.1 (s), 123.2 (s), 116.1 (d), 114.3 (d), 62.0 (OCH$_2$), 56.3 (OCH$_3$), 14.0 (CH$_3$); *m*/*z* (EI) 360 (M^+ + 2, 3%), 358 (M^+, 8), 323 (M^+ − Cl, 80), 315 (2), 313 (6), 295 (100), 280 (6), 252 (9), 242 (6), 236 (6), 224 (4), 207 (6), 179 (9), 152 (4), 125 (5), 99 (5), 75 (4), 63 (3).

*4.3.7. Ethyl 4-(2-Chloro-4-fluorophenyl)-6-oxo-5,6-dihydro-1,5-naphthyridine-3-carboxylate (**5h**).* (170 mg, 98%) as colorless cubes, mp 169−170 °C (*t*-BuOMe), R_f 0.38 (*t*-BuOMe); (found: C, 59.0; H, 3.4; N, 8.0. $C_{17}H_{12}ClFN_2O_3$ requires C, 58.9; H, 3.5; N, 8.1); λ_{max} (DCM)/nm 234 (log ε 3.55), 251 inf (2.99), 259 inf (2.88), 267 inf (2.76), 339 inf (3.03), 348 (3.13), 362 (3.01); ν_{max}/cm^{-1} 3173w, 3103w, 3032w (Ar CH), 2990w, 2941w, 1715 m (C═O), 1667s (NHC═O), 1605 m, 1555w, 1493 m, 1452w, 1391 m, 1369 m, 1328 m, 1312 m, 1263w, 1217 m, 1198 m, 1134 m, 1105w, 1049w, 1024 m, 899 m, 851 m, 824w, 760 m; δ_H (500 MHz; CD_2Cl_2) 9.08 (1H, s, Ar *H*), 8.67 (1H, br s, N*H*), 8.02 (1H, d, *J* = 9.8, Ar *H*), 7.36 (1H, d, *J* = 8.5, Ar *H*), 7.23−7.20 (2H, m, Ar *H*), 6.82 (1H, d, *J* = 9.9, Ar *H*), 4.14 (2H, q, *J* = 6.9, OC*H*$_2$), 1.09 (3H, t, *J* = 7.1, C*H*$_3$); δ_C (125 MHz; CD_2Cl_2) one quaternary peak missing 165.0 (s), 163.8 (d, $^1J_{CF}$ 251.0, FC), 161.8 (s), 146.4 (d), 142.1 (d), 140.5 (s), 135.1 (d, $^3J_{CF}$ 10.8, FCCHCCl), 133.1 (d, $^4J_{CF}$ 5.4, FCCHCHC$_q$), 132.1 (d, $^3J_{CF}$ 9.0, FCCHCH), 128.1 (d), 128.0 (s), 126.7 (s), 118.2 (d, $^2J_{CF}$ 25.3, FCCH), 115.7 (d, $^2J_{CF}$ 21.7, FCCH), 62.2 (OCH$_2$), 14.0 (CH$_3$); *m*/*z* (EI) 348 (M^+ + 2, 4%), 346 (M^+, 11), 311 (M^+ − Cl, 71), 301 (6), 283 (100), 265 (14), 237 (14), 210 (21), 191 (5), 182 (10), 157 (5), 131 (10), 105 (3), 81 (3).

*4.3.8. Ethyl 4-(2,5-Dichlorophenyl)-6-oxo-5,6-dihydro-1,5-naphthyridine-3-carboxylate (**5i**).* (176 mg, 97%) as colorless cubes, mp 160−161.5 °C (*t*-BuOMe), R_f 0.57 (*t*-BuOMe); (found: C, 56.1; H, 3.3; N, 7.8. $C_{17}H_{12}Cl_2N_2O_3$ requires C, 56.2; H, 3.3; N, 7.7); λ_{max} (DCM)/nm 232 (log ε 3.70), 259 inf (2.95), 268 inf (2.82), 339 inf (3.10), 348 (3.20), 362 (3.08); ν_{max}/cm^{-1} 2959w, 2924w, 2851w, 1726 m (C═O), 1667s (NHC═O), 1607w, 1578w, 1557w, 1489w, 1470w, 1454w, 1406w, 1381 m, 1325 m, 1292w, 1207 m, 1136 m, 1103 m, 1057w, 1034w, 972w, 872w, 947 m, 818 m; δ_H (500 MHz; CD_2Cl_2) 9.11 (1H, s, Ar *H*), 8.51 (1H, br s, N*H*), 8.02 (1H, d, *J* = 9.8, Ar *H*), 7.55−7.49 (2H, m, Ar *H*), 7.26 (1H, s, Ar *H*), 6.86 (1H, d, *J* = 9.9, Ar *H*), 4.16 (2H, q, *J* = 7.0, OC*H*$_2$), 1.09 (3H, t, *J* = 7.1, C*H*$_3$); δ_C (125 MHz; CD_2Cl_2) 164.7 (s), 161.7 (s), 146.5 (d), 142.0 (d), 140.6 (s), 134.0 (s), 133.5 (s), 132.7 (s), 132.6 (s), 132.4 (s), 131.9 (d), 131.5 (d), 130.7 (d), 128.3 (d), 126.1 (s), 62.2 (OCH$_2$), 13.9 (CH$_3$); *m*/*z* (EI) 364 (M^+ + 2, 6%), 362 (M^+, 10%), 329 (42), 327 (M^+ − Cl, 87), 319 (5), 317 (9), 301 (54), 299 (100), 283 (3), 281 (7), 264 (26), 255 (9), 226 (17), 207 (4), 198 (3), 191 (6), 164 (4), 147 (4), 138 (2), 113 (2).

*4.3.9. Ethyl 4-[2-Chloro-5-(trifluoromethyl)phenyl]-6-oxo-5,6-dihydro-1,5-naphthyridine-3-carboxylate (**5j**).* (182 mg, 92%) as colorless plates, mp 201−203.5 °C (*t*-BuOMe), R_f 0.57 (*t*-BuOMe); (found: C, 54.5; H, 3.0; N, 6.9. $C_{18}H_{12}ClF_3N_2O_3$ requires C, 54.5; H, 3.1; N, 7.1); λ_{max} (DCM)/nm 232 (log ε 3.56), 263 (3.22), 270 (3.21), 283 inf (3.09), 338 inf (3.03), 348 (3.13), 362 (3.01); ν_{max}/cm^{-1} 3036w, 2967w, 1724 m (C═O), 1668s (NHC═O), 1609 m, 1578w, 1487w, 1381 m, 1327s, 1296s, 1209 m, 1169s, 1123s, 1084s, 1057w, 1034 m, 972w, 934w, 872w, 845 m, 837 m; δ_H (300 MHz; CD_2Cl_2) 9.13 (1H, s, Ar *H*), 8.70 (1H, br s, N*H*), 8.02 (1H, d, *J* = 9.9, Ar *H*), 7.80−7.75 (2H, m, Ar *H*), 7.53 (1H, d, *J* = 0.6, Ar *H*), 6.82 (1H, d, *J* = 9.6, Ar *H*), 4.12 (2H, dq, *J* = 7.2, 1.5, OC*H*$_2$), 1.03 (3H, t, *J* = 7.2, C*H*$_3$); δ_C (75 MHz; CD_2Cl_2) one quarternary carbon peak missing 164.7 (s), 162.0 (s), 146.6 (d), 142.1 (d), 140.7 (s), 138.1 (s), 132.8 (s), 132.6 (s), 131.3 (d), 130.4 (q, $^2J_{CF}$ 33.5, F$_3$CC), 128.2 (d), 128.2 (q, $^3J_{CF}$ 3.7, F$_3$CCCH), 128.0 (q, $^3J_{CF}$ 3.8, F$_3$CCCH), 127.6 (q, $^1J_{CF}$ 272.8, F$_3$C), 126.2 (s), 62.2 (OCH$_2$), 13.8 (CH$_3$); *m*/*z* (EI) 398 (M^+ + 2, 8%), 396 (M^+, 22), 361 (M^+ − Cl, 84), 353 (3), 351 (9), 333 (100), 315 (9), 313 (8), 287 (10), 264 (3), 260 (12), 241 (7), 232 (4), 226 (3), 207 (4), 192 (4), 181 (3).

*4.3.10. Ethyl 4-(2-Chloropyrid-3-yl)-6-oxo-5,6-dihydro-1,5-naphthyridine-3-carboxylate (**5k**).* (137 mg, 83%) as colorless cubes, mp 194−196 °C (*t*-BuOMe), R_f 0.09 (*t*-BuOMe); (found: C, 58.4; H, 3.7; N, 12.7. $C_{16}H_{12}ClN_3O_3$ requires C, 58.3; H, 3.7; N, 12.7); λ_{max} (DCM)/nm 217 (log ε 4.15), 348 (3.30); ν_{max}/cm^{-1} 1724 m (C═O), 1697s (NHC═O), 1602 m, 1556w, 1402w, 1384 m, 1305w, 1220 m, 1141 m, 1076 m, 1026 m, 856w; δ_H (500 MHz; CD_2Cl_2) 9.96 (1H, br s, N*H*), 9.14 (1H, s, Ar *H*), 8.62 (1H, d, 2.0, Ar *H*), 8.06 (1H, d, *J* = 9.8, Ar *H*), 7.62 (1H, d, *J* = 7.4, Ar *H*), 7.47 (1H, d, *J* = 6.2, Ar *H*), 6.79 (1H, d, *J* = 9.8, Ar *H*), 4.17 (2H, q, *J* = 6.8, OC*H*$_2$), 1.11 (3H, t, *J* = 7.2, C*H*$_3$); δ_C (125 MHz; CD_2Cl_2) 164.8 (s), 162.6 (s), 150.8 (d), 150.5 (s), 146.6 (d), 142.1 (d), 140.7 (s), 139.8 (d), 133.0 (s), 132.5 (s), 129.1 (s), 128.1 (d), 126.1 (s), 123.4 (d), 62.2 (OCH$_2$), 14.0 (CH$_3$); *m*/*z* (EI) 329 (M^+, 11%), 294 (M^+ − Cl, 95), 284 (7), 266 (100), 256 (4), 248 (6), 238 (9), 221 (10), 193 (15), 167 (11), 140 (7), 114 (8), 100 (3), 96 (4), 87 (7), 62 (6).

*4.3.11. Ethyl 4-(3-Chloropyrid-4-yl)-6-oxo-5,6-dihydro-1,5-naphthyridine-3-carboxylate (**5l**).* (110 mg, 67%) as colorless needles, mp 161−163 °C (*t*-BuOMe); R_f 0.09 (*t*-BuOMe); (found: C, 58.2; H, 3.6; N, 12.7, $C_{16}H_{12}ClN_3O_3$ requires C, 58.3; H, 3.7; N, 12.7); λ_{max} (DCM)/nm 216 (log ε 4.16), 336 (3.47); ν_{max}/cm^{-1} 1714 m (C═O), 1660s (NHC═O), 1602w, 1557w, 1371w, 1327 m, 1215 m, 1141 m, 1091w, 1018 m, 854 m; δ_H (500 MHz; CD_2Cl_2) 9.56 (1H, br s, N*H*), 9.12 (1H, s, Ar *H*), 8.77 (1H, s, Ar *H*), 8.63 (1H, br s, Ar *H*), 8.02 (1H, d, *J* = 9.8, Ar *H*), 7.19 (1H, d, *J* = 2.1, Ar *H*), 6.77 (1H, d, *J* = 9.9, Ar *H*), 4.14 (2H, q, *J* = 6.8, OC*H*$_2$), 1.07 (3H, t, *J* = 7.1, C*H*$_3$); δ_C (125 MHz; CD_2Cl_2) 164.6 (s), 162.4 (s), 150.6 (d), 148.8 (d), 146.5 (d), 142.1 (d), 140.8 (s), 140.4 (s), 132.3 (s), 131.7 (s), 131.5 (s), 128.3 (d), 125.6 (s), 125.1 (d), 62.4 (OCH$_2$), 13.8 (CH$_3$); *m*/*z* (EI) 329 (M^+, 13%), 294 (M^+ − Cl, 77), 266 (100), 233 (9), 220 (3), 193 (9), 114 (10), 100 (5).

4.4. Ethyl 6-Oxo-6*H*-indolo[3,2,1-*de*][1,5]naphthyridine-1-carboxylate (1b), (Table 3, entry 1). To a stirred solution of ethyl 4-(2-bromophenyl)-6-oxo-5,6-dihydro-1,5-naphthyridine-3-carboxylate (**5a**) (48 mg, 0.13 mmol), Cs_2CO_3 (85 mg, 0.26 mmol), CuI (2.5 mg, 0.013 mmol) in dioxane (1 mL) were added DMEDA (2.9 μL, 0.026 mmol) and H_2O (4.5 μL, 0.26 mmol). The stirred reaction

dx.doi.org/10.1021/jo200824b |*J. Org. Chem.* 2011, 76, 5113–5122

mixture was refluxed (preheated oil bath) until the reaction was complete (TLC, 1 h) and then allowed to cool to ca. 20 °C. The mixture was diluted (DCM), dried (Na_2SO_4), filtered, and adsorbed onto silica gel. Dry flash chromatography (*t*-BuOMe) gave the title compound **1b** (32 mg, 85%) as light yellow needles, mp 158−160 °C (EtOH), R_f 0.35 (*t*-BuOMe); (found: C, 70.0; H, 4.1; N, 9.5. $C_{17}H_{12}N_2O_3$ requires C, 69.9; H, 4.1; N, 9.6); λ_{max} (DCM)/nm 232 inf (log ε 3.25), 244 (3.29), 250 inf (3.28), 263 inf (3.13), 269 inf (2.99), 305 (3.07), 314 (3.06), 363 inf (2.94), 378 (3.10), 398 (3.05); ν_{max}/cm^{-1} 2957w, 2922 br m, 2853w, 1722 m (C═O), 1692s (C═O), 1665 m, 1622w, 1601w, 1582w, 1555w, 1483w, 1468w, 1441w, 1416 m, 1391 m, 1366w, 1342w, 1329w, 1294s, 1250 m, 1217 m, 1136s, 1109 m, 1094 m, 1055 m, 1016w, 930w, 910w, 893w, 874w, 854w, 839 m, 804w; δ_H (500 MHz; CD_2Cl_2) 9.32 (1H, s, Ar *H*), 8.95 (1H, d, *J* = 7.9, Ar *H*), 8.64 (1H, d, *J* = 8.2, Ar *H*), 7.98 (1H, d, *J* = 9.8, Ar *H*), 7.70−7.74 (1H, m, Ar *H*), 7.51−7.54 (1H, m, Ar *H*), 6.98 (1H, d, *J* = 9.8, Ar *H*), 4.58 (2H, q, *J* = 7.2, O*CH*$_2$), 1.53 (3H, t, *J* = 7.2, *CH*$_3$); δ_C (75 MHz; $CDCl_3$) 165.3 (s), 159.3 (s), 147.8 (d), 140.2 (s), 139.2 (d), 138.5 (s), 132.2 (s), 132.0 (d), 130.6 (d), 130.4 (s), 128.3 (d), 126.0 (d), 123.5 (s), 121.2 (s), 116.7 (d), 62.1 (O*CH*$_2$), 14.5 (*CH*$_3$); *m*/*z* (EI) 293 (M^++1, 20%), 292 (M^+, 100), 277 (7), 264 (36), 247 (60), 236 (21), 219 (26), 191 (25), 164 (22), 138 (7), 113 (4), 110 (7), 96 (8), 86 (5), 63 (4). The title compound could also be obtained microanytically pure without the use of chromatography, by filtering the dried solution through a short pad of silica, evaporation, and recrystallization.

4.5. Ethyl 9-Chloro-6-oxo-6*H*-indolo[3,2,1-*de*][1,5]naphthyridine-1-carboxylate (1c) (Typical Procedure for Entries 4−20; See Table 3). To a stirred solution of ethyl 4-(2-chlorophenyl)-6-oxo-5,6-dihydro-1,5-naphthyridine-3-carboxylate (**5b**) (43 mg, 0.13 mmol) and Cs_2CO_3 (85 mg, 0.26 mmol) in dioxane (1 mL)/ H_2O (2.4 μL, 0.13 mmol) was added a deep blue solution of CuI (2.5 mg, 0.013 mmol) and DMCDA (4 μL, 0.026 mmol) in dioxane (1 mL)/ H_2O (2.4 μL, 0.13 mmol). The stirred reaction mixture was refluxed (preheated oil bath) until the reaction was complete (TLC, 1 h) and then allowed to cool to ca. 20 °C. The mixture was diluted (DCM), dried (Na_2SO_4), filtered, and adsorbed onto silica gel. Dry flash chromatography (*t*-BuOMe) gave the title compound **1c** (28 mg, 74%) as bright yellow needles, mp 217.5−218.5 °C (EtOH), R_f 0.70 (*t*-BuOMe); (found: C, 62.5; H, 3.5; N, 8.5. $C_{17}H_{11}ClN_2O_3$ requires C, 62.5; H, 3.4; N, 8.6); λ_{max} (DCM)/nm 231 (log ε 2.30), 243 inf (3.28), 252 inf (3.30), 256 (3.32), 266 (3.27), 274 (3.18), 307 inf (3.14), 315 (3.16), 348 inf (2.96), 361 (3.09), 378 (3.26), 398 (3.21); ν_{max}/cm^{-1} 3117w, 3069w, 3042w, 2992w, 1722 m (C═O), 1692s (NC═O), 1624w, 1599w, 1555w, 1474w, 1429 m, 1414 m, 1395 m, 1366w, 1323w, 1308 m, 1288s, 1271 m, 1250w, 1217w, 1196w, 1159 m, 1105 m, 1069w, 1053 m, 1016w, 937w, 910w, 868 m, 853 m, 837s, 797 m, 766 m; δ_H (300 MHz; CD_2Cl_2) 9.39 (1H, s, Ar *H*), 8.98 (1H, d, *J* = 8.4, Ar *H*), 8.73 (1H, d, *J* = 1.8, Ar *H*), 8.05 (1H, d, *J* = 9.9, Ar *H*), 7.55 (1H, dd, *J* = 8.7, 2.1, Ar *H*), 7.04 (1H, d, *J* = 9.9, Ar *H*), 4.61 (2H, q, *J* = 7.1, O*CH*$_2$), 1.56 (3H, t, *J* = 7.2, *CH*$_3$); δ_C (125 MHz; CD_2Cl_2) 165.5 (s), 159.4 (s), 148.2 (d), 140.9 (s), 139.9 (d), 139.1 (s), 137.9 (s), 132.9 (s), 130.6 (d), 129.5 (s), 129.4 (d), 126.5 (d), 122.6 (s), 121.4 (s), 117.0 (d), 62.5 (O*CH*$_2$), 14.5 (*CH*$_3$); *m*/*z* (EI) 328 (M^+ + 2, 33%), 326 (M^+, 100), 313 (3), 311 (8), 300 (11), 298 (32), 283 (20), 281 (55), 272 (5), 270 (14), 253 (32), 247 (4), 225 (24), 198 (13), 189 (10), 174 (5), 163 (9), 138 (10), 112 (6), 99 (7), 86 (5), 63 (5).

*4.5.1. Ethyl 6-Oxo-9-(trifluoromethyl)-6H-indolo[3,2,1-de][1,5]naphthyridine-1-carboxylate (**1d**).* (42 mg, 90%) as colorless needles, mp 187.5−189 °C (EtOH), R_f 0.68 (*t*-BuOMe); (found: C, 59.9; H, 3.0; N, 7.6. $C_{18}H_{11}F_3N_2O_3$ requires C, 60.0; H, 3.1; N, 7.8); λ_{max} (DCM)/nm 230 (log ε 3.43), 243 (3.41), 251 (3.39), 265 (3.13), 274 (3.03), 298 (3.22), 307 (3.21), 365 inf (3.07), 378 (3.33), 398 (3.33); ν_{max}/cm^{-1} 2988w, 2924w, 2860w, 1717 m (C═O), 1686 m (C═O), 1608w, 1587w, 1558w, 1472w, 1420 m, 1393w, 1368w, 1337s, 1290s, 1269s, 1246w, 1221w, 1213w, 1175s, 1150s, 1126s, 1109s, 1053s, 1007w, 989w, 935w, 914w, 897 m, 878w, 837s, 814w, 807w; δ_H (500 MHz; CD_2Cl_2) 9.38 (1H, s, Ar *H*), 9.13 (1H, d, *J* = 8.4, Ar *H*), 8.94 (1H, s, Ar *H*), 8.03 (1H, d, *J* = 9.8, Ar *H*), 7.78 (1H, d, *J* = 8.4, Ar *H*), 7.03 (1H, d, *J* = 9.8, Ar *H*), 4.59 (2H, q, *J* = 7.1, O*CH*$_2$), 1.53 (3H, t, *J* = 7.1, *CH*$_3$); δ_C (125 MHz; CD_2Cl_2) 165.4 (s), 159.5 (s), 148.4 (d), 140.0 (s), 139.9 (d), 139.6 (s), 138.8 (s), 133.2 (q, $^2J_{CF}$ 32.5, F_3CC), 131.0 (d), 129.2 (d), 129.0 (s), 126.9 (s), 124.4 (q, $^1J_{CF}$ 271.3, F_3C), 122.9 (q, $^3J_{CF}$ 3.6, F_3CCCH), 122.1 (s), 114.1 (q, $^3J_{CF}$ 3.9, F_3CCCH), 62.7 (O*CH*$_2$), 14.6 (*CH*$_3$); *m*/*z* (EI) 361 (M^++1, 21%), 360 (M^+, 100), 345 (10), 332 (48), 315 (65), 304 (14), 287 (38), 259 (32), 247 (5), 232 (19), 209 (5), 180 (5), 157 (5), 144 (9), 130 (6), 87 (5), 57 (7).

*4.5.2. Ethyl 9-Methyl-6-oxo-6H-indolo[3,2,1-de][1,5]naphthyridine-1-carboxylate (**1e**).* (32 mg, 80%) as beige needles, mp 173.5−174.5 °C (EtOH), R_f 0.50 (*t*-BuOMe); (found: C, 70.6; H, 4.5; N, 9.1. $C_{18}H_{14}N_2O_3$ requires C, 70.6; H, 4.6; N, 9.2); λ_{max} (DCM)/nm 232 (log ε 3.31), 246 inf (3.37), 256 (3.41), 263 inf (3.39), 273 (3.24), 309 (3.21), 318 (3.22), 350 inf (3.01), 365 inf (3.15), 380 (3.29), 400 (3.21); ν_{max}/cm^{-1} 3078w, 2980w, 2932w, 1707s (O−C═O), 1670s (N−C═O), 1665s (C═O), 1626 m, 1605w, 1585w, 1557w, 1468w, 1429 m, 1416 m, 1395w, 1362w, 1335 m, 1287s, 1250 m, 1231 m, 1150s, 1109s, 1099 m, 1053 m, 1022w, 955w, 881w, 849 m, 837s, 802 m; δ_H (500 MHz; CD_2Cl_2) 9.28 (1H, s, Ar *H*), 8.77 (1H, d, *J* = 8.2, Ar *H*), 8.45 (1H, s, Ar *H*), 7.96 (1H, d, *J* = 9.8, Ar *H*), 7.31 (1H, d, *J* = 8.2, Ar *H*), 6.95 (1H, d, *J* = 9.6, Ar *H*), 4.56 (2H, q, *J* = 7.1, O*CH*$_2$), 2.58 (3H, s, *CH*$_3$), 1.52 (3H, t, *J* = 7.1, *CH*$_3$); δ_C (125 MHz; CD_2Cl_2) 165.8 (s), 159.7 (s), 148.1 (d), 143.7 (s), 141.0 (s), 139.6 (d), 138.8 (s), 132.8 (s), 130.7 (d), 130.6 (s), 128.1 (d), 127.4 (d), 121.6 (s), 121.1 (s), 117.2 (d), 62.4 (O*CH*$_2$), 22.5 (*CH*$_3$), 14.6 (*CH*$_3$); *m*/*z* (EI) 307 (MH^+, 62%), 297 (5), 279 (100), 261 (6), 233 (9), 205 (13), 192 (4), 179 (4), 152 (6), 127 (9), 77 (6), 57 (6).

*4.5.3. Ethyl 9-Methoxy-6-oxo-6H-indolo[3,2,1-de][1,5]naphthyridine-1-carboxylate (**1f**).* (30.5 mg, 73%) as bright colored yellow needles, mp 187−188 °C (EtOH), R_f 0.45 (*t*-BuOMe); (found: C, 67.2; H, 4.5; N, 8.6. $C_{18}H_{14}N_2O_4$ requires C, 67.1; H, 4.4; N, 8.7); λ_{max} (DCM)/nm 231 (log ε 3.36), 261 inf (3.34), 268 (3.43), 278 (3.50), 308 (3.10), 318 (3.12), 376 (3.29); ν_{max}/cm^{-1} 2976w, 2945w, 1721s (C═O), 1694 m (NC═O), 1624 m, 1608 m, 1557w, 1495 m, 1470w, 1439 m, 1418 m, 1393 m, 1369w, 1335w, 1292s, 1243s, 1186w, 1167w, 1150s, 1115 m, 1099 m, 1057 m, 1032 m, 1015w, 930w, 875w, 854w, 837s, 800w; δ_H (300 MHz; CD_2Cl_2) 9.27 (1H, s, Ar *H*), 8.82 (1H, d, *J* = 8.7, Ar *H*), 8.18 (1H, d, *J* = 2.4, Ar *H*), 7.96 (1H, d, *J* = 9.9, Ar *H*), 7.04 (1H, dd, *J* = 9.0, 2.4, Ar *H*), 6.95 (1H, d, *J* = 9.9, Ar *H*), 4.56 (2H, q, *J* = 7.1, O*CH*$_2$), 3.99 (3H, s, O*CH*$_3$), 1.52 (3H, t, *J* = 7.1, *CH*$_3$); δ_C (125 MHz; CD_2Cl_2) 165.9 (s), 163.6 (s), 159.7 (s), 148.2 (d), 142.6 (s), 139.9 (d), 138.2 (s), 133.0 (s), 130.6 (s), 130.3 (d), 129.5 (d), 120.4 (s), 116.9 (s), 114.1 (d), 101.0 (d), 62.3 (O*CH*$_2$), 56.4 (O*CH*$_3$), 14.6 (*CH*$_3$); *m*/*z* (EI) 323 (MH^+, 80%), 295 (100), 277 (5), 263 (2), 252 (8), 249 (6), 207 (7), 179 (10), 125 (5), 99 (5), 75 (5), 57 (4).

*4.5.4. Ethyl 9-Fluoro-6-oxo-6H-indolo[3,2,1-de][1,5]naphthyridine-1-carboxylate (**1g**).* (28 mg, 70%) as colorless needles, mp 203−204.5 °C (EtOH), R_f 0.75 (*t*-BuOMe); (found: C, 65.9; H, 3.5; N, 8.9. $C_{17}H_{11}FN_2O_3$ requires C, 65.8; H, 3.6; N, 9.0); λ_{max} (DCM)/nm 254 (log ε 3.60), 263 (3.58), 271 (3.52), 292 inf (3.37), 299 (3.40), 307 inf (3.34), 345 inf (306), 356 (3.22); ν_{max}/cm^{-1} 3042w, 2988w, 2918w, 1724 m (C═O), 1694s, 1628w, 1607w, 1557w, 1541w, 1522w, 1472w, 1456w, 1435w, 1422 m, 1396 m, 1331w, 1314w, 1267w, 1233 m, 1161w, 1150 m, 1117w, 1105w, 1059w, 1015w, 934w, 878w, 856 m, 843s, 831 m, 802w, 768 m; δ_H (300 MHz; CD_2Cl_2) 9.34 (1H, s, Ar *H*), 9.00 (1H, dd, $^3J_{HH}$ 8.9, $^4J_{HF}$ 5.6, Ar *H*), 8.38 (1H, dd, $^3J_{HF}$ 9.1, $^4J_{HH}$ 2.5, Ar *H*), 8.01 (1H, d, *J* = 10.0, Ar *H*), 7.26 (1H, ddd, $^3J_{HF}$ 9.0, $^3J_{HH}$ 9.0, $^4J_{HH}$ 2.5, Ar *H*), 6.99 (1H, d, *J* = 9.8, Ar *H*), 4.57 (2H, q, *J* = 7.1, O*CH*$_2$), 1.52 (3H, t, *J* = 7.2, *CH*$_3$); δ_C (75 MHz; CD_2Cl_2) 165.6 (s), 165.2 (d, $^1J_{CF}$ 250.9, FC),

dx.doi.org/10.1021/jo200824b |*J. Org. Chem.* 2011, 76, 5113–5122

159.5 (s), 148.3 (d), 141.5 (d, $^3J_{CF}$ 13.7, FCCHC$_q$, *C*-7a), 140.0 (d), 138.8 (s), 132.7 (s), 130.5 (d), 130.2 (d, $^3J_{CF}$ 10.4, FCCHCH, *C*-11), 129.8 (s), 121.3 (s), 120.4 (s), 113.9 (d, $^2J_{CF}$ 23.6, FCCH, *C*-8 or 10), 104.5 (d, $^2J_{CF}$ 28.6, FCCH, *C*-8 or 10), 62.5 (OCH_2), 14.6 (CH_3); *m*/*z* (EI) 311 ($M^+ + 1$, 20%) 310 (M^+, 75), 295 (9), 282 (42), 265 (73), 254 (18), 237 (42), 209 (37), 182 (36), 158 (10), 156 (13), 131 (11), 119 (9), 106 (8), 81 (7), 57 (9).

*4.5.5. Ethyl 10-Chloro-6-oxo-6H-indolo[3,2,1-de][1,5]naphthyridine-1-carboxylate (**1h**).* (38 mg, 89%) as light yellow needles, mp 191−193 °C (EtOH), R_f 0.70 (*t*-BuOMe); (found: C, 62.4; H, 3.3; N, 8.5. $C_{17}H_{11}ClN_2O_3$ requires C, 62.5; H, 3.4; N, 8.6); λ_{max} (DCM)/nm 399 (log ε 2.35), 381 (3.40), 306 (2.18), 228 (3.16); ν_{max}/cm^{-1} 3115w, 3051w (Ar CH), 2983w, 2947w, 2859w, 1719 m (C═O), 1679s (NC═O), 1624w, 1587w, 1557w, 1458w, 1439 m, 1402 m, 1387 m, 1366w, 1329s, 1296s, 1254s, 1225w, 1198w, 1150s, 1121 m, 1105w, 1074 m, 1049w, 1016w, 991w, 941w, 897w, 856 m, 847 m, 829 m, 806w, 766 m; δ_H (300 MHz; CD_2Cl_2) 9.33 (1H, s, Ar *H*), 8.95 (1H, d, *J* = 2.1, Ar *H*), 8.55 (1H, d, *J* = 8.7, Ar *H*), 7.99 (1H, d, *J* = 9.9, Ar *H*), 7.66 (1H, dd, *J* = 8.7, 2.1, Ar *H*), 6.98 (1H, d, *J* = 9.9, Ar *H*), 4.58 (2H, q, *J* = 7.1, OCH_2), 1.54 (3H, t, *J* = 7.2, CH_3); δ_C (75 MHz; CD_2Cl_2) 165.4 (s), 159.2 (s), 148.2 (d), 139.7 (d), 139.2 (s), 138.6 (s), 132.6 (s), 131.9 (d), 131.6 (s), 130.8 (d), 129.0 (s), 128.2 (d), 125.2 (s), 121.5 (s), 117.6 (d), 62.7 (OCH_2), 14.5 (CH_3); *m*/*z* (EI) 328 ($M^+ + 2$, 42%), 326 (M^+, 100), 300 (15), 298 (41), 283 (16), 281 (46), 272 (8), 270 (26), 253 (31), 247 (10), 225 (22), 198 (15), 190 (12), 163 (10), 149 (10), 138 (11), 126 (7), 112 (8), 99 (7), 88 (6), 63 (5).

*4.5.6. Ethyl 6-Oxo-10-(trifluoromethyl)-6H-indolo[3,2,1-de][1,5]naphthyridine-1-carboxylate (**1i**).* (44.5 mg, 95%) as beige needles, mp 188.5−190 °C (EtOH), R_f 0.70 (*t*-BuOMe); (found: C, 60.0; H, 3.0; N, 7.8. $C_{18}H_{11}F_3N_2O_3$ requires C, 60.0; H, 3.1; N, 7.8); λ_{max} (DCM)/nm 231 (log ε 3.26), 234 inf (3.24), 241 inf (3.19), 250 inf (3.14), 260 inf (3.00), 270 inf (2.86), 299 (3.03), 307 (3.03), 344 inf (2.61), 359 (2.88), 376 (3.14), 394 (3.13); ν_{max}/cm^{-1} 3119w, 3057w, 2999w, 1713 m (C═O), 1682 m (NC═O), 1628w, 1612w, 1589w, 1560w, 1474w, 1449w, 1406 m, 1393 m, 1342 m, 1323s, 1298s, 1260 m, 1219w, 1200w, 1163s, 1144s, 1123s, 1101 m, 1063 m, 1049w, 1013w, 995w, 922w, 897w, 880w, 845s, 837 m, 806w, 768 m; δ_H (500 MHz; CD_2Cl_2) 9.38 (1H, s, Ar *H*), 9.32 (1H, s, Ar *H*), 8.77 (1H, d, *J* = 8.6, Ar *H*), 8.03 (1H, d, *J* = 9.8, Ar *H*), 7.98 (1H, d, *J* = 8.5, Ar *H*), 7.01 (1H, d, *J* = 9.8, Ar *H*), 4.61 (2H, q, *J* = 7.1, OCH_2), 1.55 (3H, t, *J* = 7.1, CH_3); δ_C (125 MHz; CD_2Cl_2) 165.5 (s), 159.5 (s), 148.6 (d), 142.1 (s), 140.1 (d), 139.6 (s), 133.1 (s), 130.9 (d), 129.3 (s), 128.9 (q, $^3J_{CF}$ 3.3, F_3CCCH, *C*-9 or 11), 128.1 (q, $^2J_{CF}$ 32.5, F_3CC, *C*-10), 126.0 (q, $^3J_{CF}$ 4.2, F_3CCCH, *C*-9 or 11), 124.8 (q, $^1J_{CF}$ 272.6, F_3C), 124.3 (s), 121.8 (s), 117.3 (d), 62.9 (OCH_2), 14.5 (CH_3); *m*/*z* (EI) 361 ($M^+ + 1$, 21%), 360 (M^+, 100), 345 (11), 332 (54), 315 (70), 304 (13), 287 (34), 259 (32), 239 (4), 232 (17), 209 (7), 180 (4), 157 (5), 143 (8), 130 (5), 111 (3).

*4.5.7. Ethyl 6-Oxo-6H-pyrido[3′,2′:4,5]pyrrolo[3,2,1-de][1,5]naphthyridine-1-carboxylate (**1j**).* (26 mg, 69%) as a fine brown powder, mp (DSC) 263.6 °C (onset), peak 268.7 °C (EtOH), R_f 0.38 (MeOH/*t*-BuOMe, 1:9); (found: C, 65.6; H, 3.7; N, 14.2. $C_{16}H_{11}N_3O_3$ requires C, 65.5; H, 3.8; N, 14.3); λ_{max} (DCM)/nm 238 (log ε 4.02), 254 inf (3.95), 257 (3.98), 284 (3.79), 294 (3.82), 328 inf (3.54), 340 (3.76), 354 (3.94), 365 (3.73), 372 (3.92); ν_{max}/cm^{-1} 3078w, 2924w, 2853w, 1690s (C═O), 1672s (C═O), 1632s, 1587w, 1483w, 1462w, 1435 m, 1400 m, 1337 m, 1321w, 1298 m, 1231 m, 1190 m, 1152w, 1115 m, 1057 m, 970w, 893w, 862 m, 847 m, 824 m, 804 m; δ_H (500 MHz; CD_2Cl_2) 9.40 (1H, s, Ar *H*), 9.37 (1H, dd, *J* = 8.1, 1.8, Ar *H*), 8.82 (1H, dd, *J* = 4.8, 1.7, Ar *H*), 8.02 (1H, d, *J* = 9.8, Ar *H*), 7.54 (1H, dd, *J* = 8.1, 4.8, Ar *H*), 7.03 (1H, d, *J* = 10.0, Ar *H*), 4.58 (2H, q, *J* = 7.2, OCH_2), 1.52 (3H, t, *J* = 7.2, CH_3); δ_C (125 MHz; CD_2Cl_2) 165.6 (s), 158.2 (s), 153.3 (s), 151.7 (d), 148.2 (d), 139.8 (d), 139.6 (C_q), 137.5 (d), 131.9 (C_q), 131.8 (*C*H), 127.5 (C_q), 121.5 (d), 121.6 (s), 117.8 (s), 62.6 (OCH_2), 14.6 (CH_3); *m*/*z* (EI) 294 ($M^+ + 1$, 21%), 293 (M^+, 100), 265 (40), 248 (76), 237 (20), 220 (37), 192 (22), 165 (17), 138 (7), 114 (6), 96 (6), 87 (7), 63 (5).

*4.5.8. Ethyl 6-Oxo-6H-pyrido[4′,3′:4,5]pyrrolo[3,2,1-de][1,5]naphthyridine-1-carboxylate (**1k**).* (21 mg, 56%) as a fine bright yellow powder, mp (DSC) 206.5 °C (onset), peak 213.6 °C (EtOH), R_f 0.34 (MeOH/*t*-BuOMe, 1:9); (found: C, 65.7; H, 3.7; N, 14.2. $C_{16}H_{11}N_3O_3$ requires C, 65.5; H, 3.8; N, 14.3); λ_{max} (DCM)/nm 245 (log ε 2.98), 272 inf (2.98), 276 (2.99), 284 inf (2.97), 296 inf (2.88), 369 inf (2.52), 382 (2.76), 402 (2.77); ν_{max}/cm^{-1} 3034w, 2976w, 2918w, 1718s (C═O), 1688s (NC═O), 1624w, 1589w, 1553w, 1466w, 1427s, 1398w, 1368w, 1325 m, 1308s, 1292 m, 1265 m, 1233w, 1204w, 1179w, 1134 m, 1109w, 1059 m, 1013w, 989 m, 934w, 922w, 864 m, 851s, 806w; δ_H (500 MHz; CD_2Cl_2) 9.94 (1H, br s, Ar *H*), 9.41 (1H, s, Ar *H*), 8.82 (2H, br s, Ar *H*), 8.05 (1H, d, *J* = 10.0, Ar *H*), 7.11 (1H, d, *J* = 9.8, Ar *H*), 4.60 (2H, q, *J* = 7.2, OCH_2), 1.54 (3H, t, *J* = 7.2, CH_3); δ_C (75 MHz; CD_2Cl_2) 165.3 (s), 159.0 (s), 148.3 (d), 146.8 (d), 140.5 (s), 139.9 (d), 139.4 (d), 136.0 (s), 132.7 (s), 131.2 (d), 130.4 (s), 128.7 (s), 122.8 (s), 121.7 (d), 62.8 (OCH_2), 14.6 (CH_3); *m*/*z* (EI) 294 ($M^+ + 1$, 20%), 293 (M^+, 100), 265 (45), 248 (50), 237 (23), 220 (29), 192 (15), 165 (21), 138 (10), 110 (5), 87 (8), 63 (4).

4.6. 6-Oxo-6*H*-indolo[3,2,1-*de*][1,5]naphthyridine-1-carboxylic Acid (6). To a stirred suspension of ethyl canthin-6-one-1-carboxylate **1b** (50 mg, 0.17 mmol) in DCM/methanol (9:1, 2 mL) at ca. 20 °C was added NaOH (27.2 mg, 0.68 mmol). After 24 h a yellow precipitate was formed. The solvent was then removed in vacuo to leave a residue, which was dissolved in H_2O (5 mL), acidified using 10% HCl and extracted with EtOAc (2 × 15 mL). The combined organic phases were dried (Na_2SO_4), filtered and evaporated in vacuo to give the title compound **6** as yellow plates (44 mg, 99%), mp >300 °C (EtOH), R_f 0.20 (MeOH/*t*-BuOMe, 1:9); (found: C, 68.1; H, 3.0; N, 10.5. $C_{15}H_8N_2O_3$ requires C, 68.2; H, 3.1; N, 10.6); λ_{max} (DCM)/nm 231 inf (log ε 3.60), 247 inf (3.70), 250 (3.70), 263 (3.65), 270 (3.60), 300 (3.47), 310 inf (3.43), 361 inf (3.29), 376 (3.44), 394 (3.37); ν_{max}/cm^{-1} 3042w, 2907w, 2776w, 1730 m (C═O), 1713 m, 1688s (NC═O), 1643 m, 1632 m, 1620 m, 1591 m, 1557 m, 1470w, 1445w, 1418s, 1344w, 1329 m, 1304s, 1250s, 1217s, 1143s, 1111w, 1101w, 1047w, 1022w, 989w, 937w, 895w, 835s, 808w, 770s; δ_H (500 MHz; DMSO-d_6) OH missing 9.08 (1H, s, Ar *H*), 8.60 (1H, d, *J* = 8.1, Ar *H*), 8.36 (1H, d, *J* = 8.1, Ar *H*), 8.00 (1H, d, *J* = 9.8, Ar *H*), 7.65 (1H, t, *J* = 7.9, Ar *H*), 7.45 (1H, t, *J* = 7.6, Ar *H*), 6.95 (1H, d, *J* = 9.8, Ar *H*); δ_C (125 MHz; DMSO-d_6) 166.3 (CO_2H), 158.6 (s), 147.2 (d), 139.2 (s), 139.1 (d), 138.0 (s), 131.7 (s), 131.5 (d), 130.1 (d), 128.7 (d), 127.7 (d), 125.5 (s), 122.9 (s), 121.3 (s), 115.7 (d); *m*/*z* (EI) 264 (M^+, 100%), 247 (7), 236 (38), 219 (12), 191 (14), 164 (15), 139 (5), 132 (6), 113 (5), 104 (5), 95 (4), 88 (4), 63 (7).

■ ASSOCIATED CONTENT

Supporting Information. ^{1}H and ^{13}C NMR spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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■ ACKNOWLEDGMENT

The authors wish to thank the Cyprus Research Promotion Foundation (Grant No. ΕΠΙΧΕΙΡΗΣΕΙΣ/ΕΦΑΡΜ/0308/19) and the following organizations in Cyprus for generous donations of chemicals and glassware: The State General Laboratory, the Agricultural Research Institute, the Ministry of Agriculture,

and Biotronics Ltd. Furthermore, we thank the A. G. Leventis Foundation for helping to establish the NMR facility at the University of Cyprus.

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