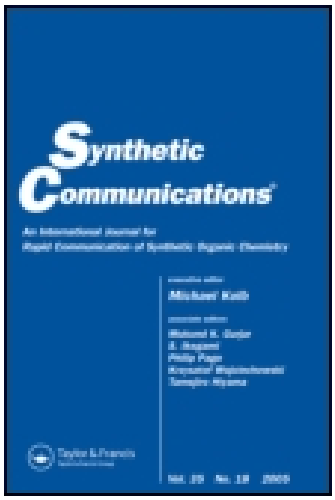

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A FACILE SYNTHESIS OF ETHYL-2-METHYL-5-ARYL-5H-CHROMENO-[3,4-c]PYRIDINE-1-CARBOXYLATES

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A FACILE SYNTHESIS OF ETHYL-2-METHYL-5-ARYL-5H-CHROMENO-[3,4-c]PYRIDINE-1-CARBOXYLATES

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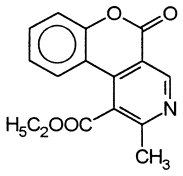
ABSTRACT

Flav-4-ones on reaction with DMF/$POCl_3$ gave 4-chloro- 2-aryl-2H-chromene-3-carbaldehydes which on reaction with ethyl-3-aminocrotonate give under Hantszch reaction conditions ethyl-2-methyl-5-aryl-5H-chromeno[3,4-c]pyridine-1-carboxylates in good yields.

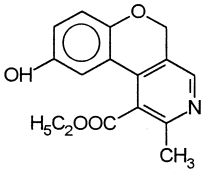
Several flavanones, substituted chromanones and chromenes show a variety of biological activities such as anticancer,[1] gastroprotective,[2] coronary vasodilator[3] and diuretic.[4] In view of the potential bioactivity shown by these heterocyclics, in the present study several new pyridyl fused aryl substituted chromenes (**6a–g**) are synthesised by a modification of the Hantszch reaction[5] starting from 4-chloro-2-aryl-2H-chromene-3-carbaldehydes (**5a–g**). Hantszch synthesis involves the reaction of aromatic or α,β-unsaturated aldehydes with NH_3 in ethyl acetoacetate or ethyl-3-aminocrotonate to give dihydropyridines and pyridines.[6–12] Earlier, we reported the synthesis of ethyl-2-methyl-5-oxo-[1]benzopyrano-[3,4-c]-pyridine-1-carboxylates[13] (**1**) and

*Corresponding author.

ethyl-2-methyl-5H-chromeno[3,4-c]pyridine-1-carboxylates.[14] One of these compounds, ethyl-9-hydroxy-2-methyl-5H-chromeno[3,4-c]pyridine-1-carboxylate (**2**) showed high activity in antituberculosis screening.[15] Since more lipophilic analogs of the new bioactive structure are expected to show



(1)



(2)

enhanced antituberculor activity, we planned the synthesis of aryl substituted analogues of ethyl-2-methyl-5H-chromeno-[3H]-pyridine-1-carboxylates (**6a–g**). Their synthesis and characterization is described in this paper.

2′-Hydroxy chalcones **3a–g** were obtained by the base catalyzed condensation of o-hydroxy acetophenones with substituted benzaldehydes.[16] These were cyclised to the corresponding flav-4-ones (**4a–g**) by heating in EtOH/HCl. The flavan-4-ones (**4a–g**) on reaction with DMF/$POCl_3$ (Vilsmeier-Haack reaction)[17] gave 4-chloro-2-aryl-2H-chromene-3-carbaldehydes (**5a–g**) in 85% yields.

An equimolar solution of 4-chloro-2-aryl-2H-chromene-3-carbaldehyde (**5a**) and ethyl-3-aminocrotonate in acetic acid was stirred at room temperature for 24 h. The acetic acid was distilled off and the reaction mixture poured onto ice. The crude product was purified using column chromatography to give ethyl-2-methyl-5-(4′-methylphenyl)-5H-chromene-[3,4-c]-pyridine-1-carboxylate (**6a**) in 70% yield. The ^{1}H NMR spectrum of **6a** showed a signal pattern characteristic of a pyridyl ring fused to 3, 4 position of the chromene rather than the alternative 1,4-dihydropyridyl substituted chromenes (**7a–g**). Similarly **6b–g** were obtained from the reaction of ethyl-3-aminocrotonate with **5b–g** respectively.

The reaction of aromatic aldehydes and α,β-unsaturated carbonyl compounds with ethyl-3-aminocrotonate generally gives dihydropyridines and pyridines.[6–9] Michael reaction of **5a–g** with ethyl-3-aminocrotonate followed by an intramolecular condensation of the carbonyl and amino group leads to the formation of the fused dihydropyridyl moiety (**11a–g**) which by loss of HCl gives aromatised and fused pyridine ring **6a–g** as shown in Scheme 2.

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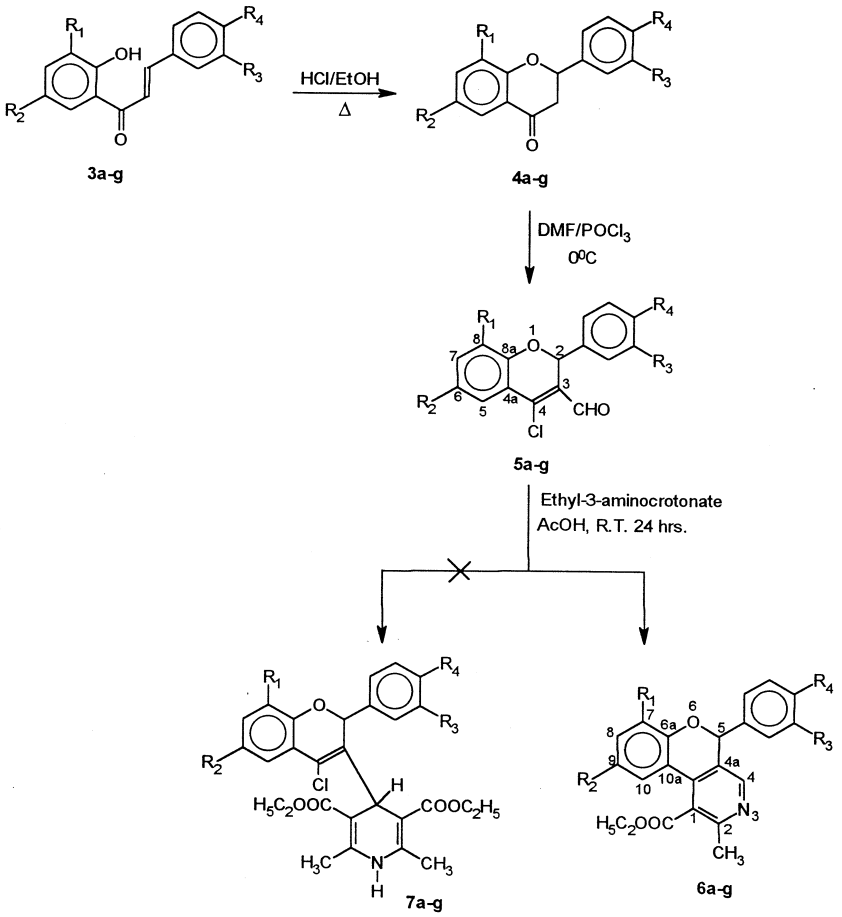


a) $R_1=R_2=R_3=H$; $R_4=CH_3$

b) $R_1=R_3=R_4=H$; $R_2=Cl$

c) $R_1=R_3=H$; $R_2=Cl$; $R_4=OCH_3$

d) $R_1=H$; $R_2=Cl$; $R_3=R_4=OCH_3$

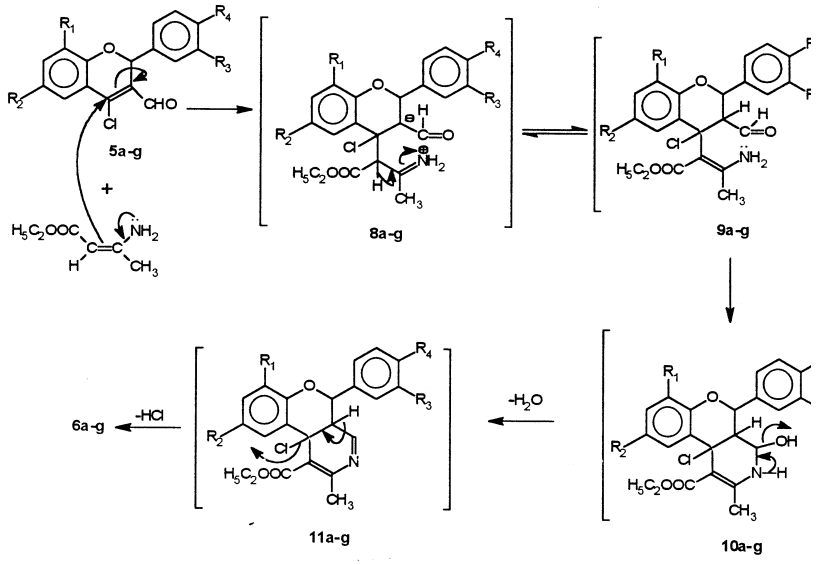
e) $R_1=R_3=H$; $R_2=Cl$; $R_4=CH_3$

f) $R_2=R_3=H$; $R_1=Cl$; $R_4=CH_3$

g) $R_2=R_3=H$; $R_1=R_4=Cl$

Scheme 1.

Mechanism :



a) R_1=R_2=R_3=H; R_4=CH_3

b) R_1=R_3=R_4=H; R_2=Cl

c) R_1=R_3=H; R_2=Cl; R_4=OCH_3

d) R_1=H; R_2=Cl; R_3= R_4=OCH_3

e) R_1=R_3=H; R_2=Cl; R_4=CH_3

f) R_2=R_3=H; R_1=Cl; R_4=CH_3

g) R_2=R_3=H; R_1= R_4=Cl

Scheme 2.

EXPERIMENTAL

Melting points were determined in sulfuric acid bath and are uncorrected IR spectra were recorded on FT-IR Perkin-Elmer 1605 spectrophotometer and ^{1}H NMR (200 MHz) and ^{13}C NMR (50.3 MHz, $CDCl_3$) were recorded on a Varian Gemini 200 spectrometer using TMS as internal standard (Chemical shifts in δ ppm). Mass spectra were recorded on as VG

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micro mass 7070H instrument. UV spectra were recorded on as Shimadzu UV-Visible Spectrophotometer (Model No. UV-1601). Elemental analysis were done on a Elementar Vario EL instrument.

General procedure for the synthesis of 4-chloro-2-aryl-2H-chromene-3-carbaldehydes (5a–g): To Flav-4-ones (**4a–g**) (10 mmoles) in dry dimethyl formamide (50 mmoles) a freshly distilled dry phosphorus oxychloride (9 mmoles) was added with constant stirring at 0°C. The reaction mixture was kept overnight and then poured on to crushed ice. The yellow compound (**4a–g**) that separated was filtered, washed with water the product on chromatography over silicagel by eluting with pet.ether gave **4a–g** in 85% yield. These were recrystallised from methanol to give yellow crystals.

4-Chloro-2-(4-methyl phenyl)-2H-3-chromene carbaldehyde (5a): m.p. 98°C. IR (KBr): 1603 (C=C). 1667 cm^{-1} (CHO). UV (MeOH): 210 nm (log ε 4.2), 292 nm (log ε 4.0) and 307 nm (log ε 4.0). ^{1}H NMR: δ 2.22 (4′-CH_3), 6.25 (s, H-2), 6.68 (bd, J = 10 Hz, H-8), 6.95 (m, H-7), 7.0 (d, J = 10 Hz, H-3′, 5′), 7.10 (d, J = 10 Hz, H2′, 6′), 7.30 (m, H-6), 7.65 (bd, J = 10 Hz, H-5), and 10.22 (s, 3-CHO). ^{13}C NMR: δ 21.0 (C-4′-CH_3), 74.9 (C-2), 117.5 (C-8), 120.0 (C-4a) 122.0 (C-6), 126.2 (C-3, C-7), 126.5 (C-2′, 6′), 129.2 (C-3′, 5′), 134.0 (C-5), 135.0 (C-4′), 138.5 (C-1′), 143.5 (C-4), 155.0 (C-8a), and 188.0 (CHO). MS: m/z 284 M^+ (25), 286 (8), 270 (24), 256 (100), 220 (20), and 206 (20). Anal. Calcd. for $C_{17}H_{13}ClO_2$: C, 71.74, H, 4.62. Found: C, 71.71, H, 4.60%.

4,6-Dichloro-2-phenyl-2H-3-chromene carbaldehyde (5b): m.p. 114°C. IR (KBr): 1606 (C=C), 1662 cm^{-1} (CHO). UV (MeOH): 207 nm (log ε 4.8), 297 nm (log ε 4.4) and 367 nm (log ε 3.9). ^{1}H NMR: δ 6.45 (s, H-2), 6.83 (d, J = 10 Hz, H-8), 7.25 (m, H-7, 2′, 3′, 4′, 5′ and 6′), 7.68 (d, J = 2 Hz, H-5), and 10.26 (s, CHO). ^{13}C NMR: δ 26.0 (C-7), 75.3 (C-2), 118.5 (C-8), 121.5 (C-4a), 126.5 (C-2′, 6′), 127.0 (C-3), 127.5 (C-6), 128.5 (C-3′, 5′), 129.0 (C-4′), 134.0 (C-5), 137.8 (C-1[1]), 142.0 (C-4), and 153.8 (C-8a). MS: m/z 304 M^+ (40), 306 (26), 274 (100), 276 (66), 238 (10), 227 (5), and 176 (20). Anal. Calcd. for $C_{16}H_{10}Cl_2O_2$: C, 62.97, H, 3.31. Found: C, 62.98, H, 3.30%.

4,6-Dichloro-2-(4-methoxy phenyl)-2H-3-chromene carbaldehyde (5c): m.p. 126°C. IR (KBr): 1601 (C=C). 1660 cm^{-1} (CHO). UV (MeOH): 204 nm (log ε 4.2), 296 nm (log ε 4.6) and 374 nm (log ε 4.2). ^{1}H NMR: δ 3.79 (4′-OCH_3), 6.30 (s, H-2), 6.80 (d, J = 10 Hz, H-8), 6.75 (d, J = 10 Hz, H-3′, 5′), 7.20 (d, J = 10 Hz, H-7′, 6′), 7.30 (dd, J = 10, 2 Hz, H-7), 7.70 (d, J = 2 Hz, H-8), and 10.28 (s, CHO). ^{13}C NMR: δ 55.2 (4′-OCH_3), 75.0 (C-2), 114.0 (C-3′, 5′), 118.7 (C-8), 121.5 (C-4a), 126.0 (C-7), 127.0 (C-3), 127.5 (C-6), 128.5 (C-2′, 6′), 130.0 (C-1′), 134.1 (C-5), 142.0 (C-4), 153.8 (C-8a), and 160.3 (C-4′). MS: m/z 333 M^+ (10), 335 (6), 304 (100), 306 (66), 298 (20), 227 (10), and 163 (10). Anal. Calcd. for $C_{17}H_{12}Cl_2O_3$: C, 60.90, H, 3.60. Found: C, 60.92, H, 3.61%.

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4,6-Dichloro-2-(3,4-dimethoxyphenyl)-2H-3-chromenecarbaldehyde (5d): m.p. 122°C. IR (KBr): 1604 (C=C), 1666 cm^{-1} (CHO). UV (MeOH): 211 nm (log ε 5.0), 234 nm (log ε 4.0), 294 nm (log ε 4.6) and 371 nm (log ε 4.1). ^{1}H NMR: δ 3.78 (s, OCH_3), 6.28 (s, H-2), 6.65–6.82 (m, 4H, H-2′, 5′, 6, and H-8), 7.25 (dd, J = 10 Hz, H-7), 7.68 (d, J = 2 Hz, H-5), and 10.28 (s, CHO). ^{13}C NMR: δ 55.6 (OCH_3), 55.7 (OCH_3), 75.0 (C-2), 110.5 (C-2′), 110.7 (C-5′), 118.5 (C-8), 119.0 (C-6′), 121.5 (C-4a), 125.8 (C-7), 127.0 (C-3), 127.5 (C-6), 130.0 (C-1′), 134.0 (C-5), 141.8 (C-4), 149.0 (C-4′), 149.5 (C-3′), and 153.5 (C-8a). MS: m/z 362 M^+ (30), 344 (20), 334 (100), 336 (66), 281 (20), and 279 (20). Anal. Calcd. for $C_{18}H_{14}Cl_2O_4$: C, 59.21, H, 3.87. Found: C, 59.20, H, 3.86%.

4,6-Dichloro-2-(4-methyl phenyl)-2H-3-chromenecarbaldehyde (5e): m.p. 113°C. IR (KBr): 1600 (C=C). 1658 cm^{-1} (CHO). UV (MeOH): 206 nm (log ε 4.8), 297 nm (log ε 4.4) and 375 nm (log ε 4.0). ^{1}H NMR: δ 6.25 (s, H-2), 6.82 (d, J = 10 Hz, H-8), 7.08 (m, 4-H, H-3′, 5′, 2′, and 6′), 7.30 (dd, J = 10, 2 Hz, H-7), 7.68 (d, J = 2 Hz, H-5), and 10.25 (s, CHO). ^{13}C NMR: δ 20.9 (CH_3), 75.0 (C-2), 118.6 (C-8), 121.0 (C-4a), 126.0 (C-7), 126.5 (C-2′, 6′), 127.0 (C-3), 127.5 (C-6), 129.0 (C-3′, 5′), 134.0 (C-5), 134.3 (C-4′), 138.6 (C-1′), 142.0 (C-4), and 153.8 (C-8a). MS: m/z 317 M^+ (21), 319 (14), 288 (100), 290 (66), 238 (5), and 189 (10). Anal. Calcd. for $C_{17}H_{12}Cl_2O_2$: C, 63.96, H, 3.78. Found: C, 63.97, H, 3.79%.

4,8-Dichloro-2-(4-methyl phenyl)-2H-3-chromenecarbaldehyde (5f): m.p. 153°C. IR (KBr): 1599 (C=C). 1660 cm^{-1} (CHO). UV (MeOH): 209 nm (log ε 4.8), 306 nm (log ε 4.6) and 362 nm (log ε 4.1). ^{1}H NMR: δ 2.30 (s, 4′-CH_3), 6.50 (s, H-2), 6.96 (dd, J = 10, 10 Hz, H-6), 7.08 (d, J = 10 Hz, H-3′, 5′), 7.20 (d, J = 10 Hz, H-2′, 6′), 7.42 (dd, J = 10, 2 Hz, H-7), 7.63 (dd, J = 10, 2 Hz, H-5), and 10.32 (s, 3-CHO). ^{13}C NMR: δ 21.0 (4′-CH_3), 75.2 (C-2), 120.2 (C-6), 120.5 (C-4a), 122.5 (C-8), 125.0 (C-7), 126.5 (C-2′, 6′), 128.0 (C-3), 129.2 (C-3′, 5′), 134.2 (C-4′), 134.5 (C-5), 138.5 (C-1′), 142.8 (C-4), and 151.0 (C-8a). MS: m/z 318 M^+ (18), 320 (12), 303 (15), 289 (100), 291 (80), 253 (10), 255 (10), 239 (15), and 189 (20). Anal. Calcd. for $C_{17}H_{12}Cl_2O_2$: C, 63.96, H, 3.78. Found: C, 63.97, H, 3.79%.

4,8-Dichloro-2-(4-chloro phenyl)-2H-3-chromenecarbaldehyde (5g): m.p. 125°C. IR (KBr): 1602 (C=C) 1662 cm^{-1} (CHO). UV (MeOH): 207 nm (log ε 4.7), 306 nm (log ε 3.4), and 360 nm (log ε 3.9). ^{1}H NMR: δ 6.50 (s, H-2), 7.02 (dd, J = 10, 10 Hz, H-6) 7.25 (m, H-2′, 3′, 5′, and 6′), 7.47 (dd, J = 10, 2 Hz, H-7), 7.65 (dd, J = 10, 2 Hz, H-5), and 10.35 (s, CHO). ^{13}C NMR: δ 74.8 (C-2), 120.0 (C-4a), 122.7 (C-6), 122.8 (C-8), 125.0 (C-7), 127.9 (C-3), 134.5 (C-5), 135.0 (C-4′), 136.2 (C-1′), 143.5 (C-4), 151.0 (C-8a), and 188.0 (CHO). MS: m/z 330 M^+ (30), 340 (25), 309

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(100), 311 (90), 275 (15), 239 (25), and 176 (25). Anal. Calcd. for $C_{16}H_9Cl_2O_2$: C, 56.58, H, 2.66. Found: C, 56.59, H, 2.67%.

General procedure for the synthesis of ethyl-2-methyl-5-aryl-5H-chromene[3,4-c]pyridine-1-carboxylates (6a–g): 4-Chloro-2-aryl-2H-chromene-3-carbaldehyde (**5a–g**) (3 mmoles) and ethyl-3-amino crotonate (3 mmoles) were dissolved in acetic acid (10 ml) and kept in constant stirring at room temperature for 48 hours. The acetic acid was distilled off under reduced pressure. Then the reaction mixture was poured on to crushed ice. Pale yellow solid separated out. It was filtered and washed with water and chromatographed over silica gel by eluting with pet either: chloroform 8:2 to give **6a–g** which were recrystallised methanol to give pale yellow crystals. **6a–g** were obtained in 70% yield.

Ethyl-2-methyl-5-(4-methyl phenyl)-5H-chromene[3,4-c]pyridine-1-carboxylate (6a): m.p. 102°C. IR (KBr): 1719 cm^{-1} (ester carbonyl). UV (MeOH): 210 nm (log ε 4.5), 275 nm (log ε 4.7), and 333 nm (log ε 4.7). ^{1}H NMR: δ 1.34 (t, J = 8 Hz, CH_3), 2.37 (s, CH_3), 2.87 (s, CH_3), 4.32 (q, J = 8 Hz, OCH_2), 6.23 (s, H-5), 6.90 (dd, J = 10, 2 Hz, H-7), 7.2 (m, H-8, H-9, 2′, 3′, 5′, 6 aromatic), 7.62 (s, H-4), and 8.32 (dd, J = 10, 2 Hz, H-10). ^{13}C NMR: δ 14.0 (CH_3), 21.0 (CH_3 of 4′-CH_3), 25.0 (C-2 CH_3), 61.0 (OCH_2), 78.9 (C-5), 117.2 (C-7), 122.0 (C-9), 122.1 (C-10b), 124.0 (C-1), 125.1 (C-8), 125.5 (C-4a), 127.8 (C-2′, 6′), 129.0 (C-3′, 5′), 132.0 (C-10), 135.8 (C-4′), 136.0 (C-4), 138.5 (C-1′), 150.0 (C-10a), 155.8 (C-2), 159.5 (C-6a), and 166.4 (C=O). MS: m/z 359 M^+ (80), 358 (40), 330 (15), 268 (100), and 240 (20). Anal. Calcd. for $C_{23}H_{21}NO_3$: C, 76.85, H, 5.88, N, 3.90. Found: C, 76.86, H, 5.89, N, 3.91%.

Ethyl-9-chloro-2-methyl-5-phenyl-5H-chromene[3,4-c]pyridine-1-carboxylate (6b): m.p. 136°C. IR (KBr): 1718 cm^{-1} (ester carbonyl). UV (MeOH): 228 nm (log ε 4.7), 299 nm (log ε 4.3), and 342 nm (log ε 4.3). ^{1}H NMR: δ 1.33 (t, J = 8 Hz, CH_3), 2.87 (s, CH_3-2), 4.30 (q, J = 8 Hz, OCH_3), 6.22 (s, H-5), 6.85 (q, J = 10 Hz, H-7), 7.22 (dd, J = 10, 2.5 Hz, H-8), 7.32 (m, H5, H-2′, 3′, 4′, 5′, 6′), 7.60 (s, H-4), and 8.32 (d, J = 2.5 Hz, H-10). ^{13}C NMR: δ 14.1 (CH_3), 25.0 (CH_3-2), 61.0 (OCH_2), 79.0 (C-5), 118.8 (C-7), 123.2 (C-10b), 124.8 (C-1), 125.0 (C-8), 125.5 (C-4a), 127.8 (C-9), 128.0 (C-2′, 6′), 128.2 (C-3′, 5′), 128.5 (C-4′), 132 (C-10), 136.1 (C-4), 138.5 (C-1′), 148.5 (C-10a), 154.5 (C-2), 160.0 (C-6a), and 166.0 (C=O). MS: m/z 379 M^+ (80), 381 (26), 350 (10), 302 (100), 304 (33), 274 (20), 228 (15), and 69 (40). Anal. Calcd. for $C_{22}H_{18}ClNO_3$: C, 69.58, H, 4.79, N, 3.69. Found: C, 69.57, H, 4.78, N, 3.68%.

Ethyl-9-chloro-2-methyl-5-(4-methoxy phenyl)-5H-chromene[3,4-c]pyridine-1-carboxylate (6c): m.p. 158°C. IR (KBr): 1710 cm^{-1} (ester carbonyl). UV (MeOH): 205 nm (log ε 4.5), 230 nm (log ε 4.5), 277 nm (log ε 4.0) and 344 nm (log ε 4.0). ^{1}H NMR: δ 1.35 (t, J = 8 Hz, CH_3), 2.88 (s, CH_3-2),

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3.80 (s, OCH_3-4′), 4.33 (q, J = 8 Hz, OCH_2), 6.22 (s, H-5), 6.85 (d, 2H, J = 10 Hz, H-3′, 5′), 6.82 (d, J = 10 Hz, H-7), 7.2 (d, J = 10 Hz, 2H, H-2′, 6′), 7.26 (dd, J = 10 Hz, H-8), 7.63 (H-4) and 8.25 (d, J = 2.5 Hz, H-10). ^{13}C NMR: δ 14.2 (CH_3), 25.0 (CH_3-2), 55.3 (OCH_3-4′), 61.2 (OCH_2), 79.0 (C-5), 114.2 (C-3′, 5′), 119.0 (C-7), 123.5 (C-10b), 124.5 (C-1), 125.0 (C-8), 126.0 (C-4a), 127.0 (C-9), 129.2 (C-2′, 6′), 130.5 (C-1′), 132.0 (C-10), 136.1 (C-4), 149.0 (C-10a), 154.2 (C-2), 160.0 (C-6a), 160.3 (C-4′), and 166.5 (C=O). MS: m/z 409 M^+ (100), 408 (40), 380 (20), 302 (50), and 274 (20). Anal. Calcd. for $C_{23}H_{20}ClNO_4$: C, 67.41, H, 4.93, N, 3.42. Found: C, 67.40, H, 4.92, N, 3.41%.

Ethyl-9-chloro-2-methyl-5-(3,4-dimethoxy phenyl)-5H-chromene[3,4-c] pyridine-1-carboxylate (6d): m.p. 172°C. IR (KBr): 1711 cm^{-1} (ester carbonyl). UV (MeOH): 208 nm (log ε 4.6), 229 nm (log ε 4.4), 279 nm (log ε 4.0) and 343 nm (log ε 3.8). ^{1}H NMR: δ 1.37 (t, J = 8 Hz, CH_3), 2.88 (s, CH_3-2), 3.80 (s, OCH_3), 3.85 (s, OCH_3), 4.32 (q, J = 8 Hz, OCH_2), 6.20 (s, H-5), 6.80 (m, 4H, H-7, 2′, 5′, 6′), 7.25 (dd, H-8), 7.62 (s, H-4), and 8.28 (d, J = 2 Hz, H-10). ^{13}C NMR: δ 14.0 (CH_3), 25.0 (CH_3-2), 56.0 (OCH_3), 56.1 (OCH_3), 61.2 (OCH_2), 79.0 (C-5), 111.0 (C-5′), 111.1 (C-2′), 119.0 (C-7), 121.0 (C-6′), 123.8 (C-10b), 124.5 (C-1), 125.0 (C-8), 126.0 (C-4a), 127.0 (C-9), 131.0 (C-1′), 132.0 (C-10), 136.0 (C-4), 148.5 (C-10a), 149.4 (C-3′), 149.5 (C-4′), 154.0 (C-2), 160.0 (C-6a), and 166.0 (C=O). MS: m/z 439 M^+ (40), 441 (13), 408 (20), 364 (20), 335 (60), 337 (40), 302 (20), and 149 (100). Anal. Calcd. for $C_{24}H_{22}ClNO_5$: C, 65.51, H, 5.03, N, 3.18. Found: C, 65.53, H, 5.04, N, 3.17%.

Ethyl-9-chloro-2-methyl-5-(4-methyl phenyl)-5H-chromene[3,4-c]pyridine-1-carboxylate (6e): m.p. 149°C. IR (KBr): 1718 cm^{-1} (ester carbonyl). UV (MeOH): 276 nm (log ε 4.3), 299 nm (log ε 4.3), and 334 nm (log ε 4.4). ^{1}H NMR: δ 1.35 (t, J = 8 Hz, CH_3), 2.38 (s, CH_3), 2.87 (s, CH_3), 4.32 (q, J = 8 Hz, OCH_2), 6.22 (s, H-5), 6.84 (d, J = 10 Hz, H-7), 7.20 (m, 5H, H-8, H-2′, 3′, 5′, 6′), 7.63 (s, H-4), and 8.25 (d, J = 2.5 Hz, H-10). ^{13}C NMR: δ 14.0 (CH_3), 21.0 (CH_3-4′), 24.9 (CH_3-2), 61.2 (OCH_2), 79.0 (C-5), 119.0 (C-7), 123.5 (C-10b), 124.8 (C-1), 125.0 (C-8), 126.0 (C-4a), 127.5 (C-9), 128.0 (C-2′, 6′), 129.5 (C-3′, 5′), 130.0 (C-10), 135.5 (C-4′), 136.0 (C-4), 138.6 (C-1′), 148.8 (C-10a), 154.2 (C-2), 160.0 (C-6a), and 166.1 (C=O). MS: m/z 393 M^+ (100), 392 (30), 302 (90), 304 (30), 274 (25), 256 (5), and 228 (20). Anal. Calcd. for $C_{23}H_{20}ClNO_3$: C, 70.13, H, 5.10, N, 3.56. Found: C, 70.14, H, 5.12, N, 3.55%.

Ethyl-7-chloro-2-methyl-5-(4-methyl phenyl)-5H-chromene[3,4-c]pyridine-1-carboxylate (6f): m.p. 182°C. IR (KBr): 1721 cm^{-1} (ester carbonyl). UV (MeOH): 276 nm (log ε 3.9), 304 nm (log ε 4.0), and 333 nm (log ε 4.0). ^{1}H NMR: δ 1.38 (t, J = 8 Hz, CH_3), 2.32 (s, CH_3), 2.88 (s, CH_3), 4.32 (q, J = 8 Hz, OCH_3), 6.35 (s, H-5), 6.96 (dd, J = 10, 10 Hz, H-9), 7.15 (A_2,

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B_2, 2′, 3′, 5′, 6′ aromatic J = 10 Hz), 7.35 (dd, J = 10, 2 Hz, H-8), 7.75 (s, H-4), and 8.20 (dd, J = 10, 2 Hz, H-10). ^{13}C NMR: δ 14.0 (CH_3), 21.0 (CH_3 of 4′-CH_3), 25.0 (C-2CH_3), 61.2 (OCH_2), 79.0 (C-5), 122.5 (C-9), 122.7 (C-10b), 124.0 (C-8), 124.8 (C-8), 125.2 (C-7), 125.5 (C-4a), 127.8 (C-2′, 6′), 129.5 (C-3′, 5′), 132.5 (C-10), 135.5 (C-4′), 136.5 (C-4), 138.8 (C-1′), 149.2 (C-10a), 152.0 (C-2), 160.2 (C-6a), and 166.5 (C=O). MS: m/z 394 M^+ (100), 396 (33), 393 (40), 378 (30), 364 (20), 302 (90), 304 (20), and 274 (30). Anal. Calcd. for $C_{23}H_{20}ClNO_3$: C, 70.13, H, 5.11, N, 3.56. Found: C, 70.14, H, 5.12, N, 3.57%.

Ethyl-7-chloro-2-methyl-5-(4-chlorophenyl)-5H-chromene[3,4-c]pyridine-1-carboxylate (6g): m.p. 131°C. IR (KBr): 1728 cm^{-1} (ester carbonyl). UV (MeOH): 277 nm (log ε 4.2), 304 nm (log ε 4.3), and 332 nm (log ε 4.2). ^{1}H NMR: δ 1.40 (t, J = 8 Hz, CH_3), 2.90 (s, CH_3, C-2), 4.36 (q, J = 8 Hz, OCH_3), 6.38 (s, H-5), 7.00 (dd, J = 10, 10 Hz, H-9), 7.30 (m, 5H, H-2′, 6′, 3′, 5′, and H-8), 7.78 (s, H-4), and 8.20 (dd, J = 10, 2 Hz, H-10). ^{13}C NMR: δ 14.3 (CH_3), 25.0 (C-2 CH_3), 61.3 (OCH_2), 78.5 (C-5), 122.2 (C-9), 122.4 (C-10b), 124.0 (C-1), 124.2 (C-8), 124.6 (C-7), 129.0 (C-2′, 6′), 129.2 (C-3′, 5′), 132.5 (C-10), 135.0 (C-4′), 136.5 (C-4), 137.1 (C-1′), 149.2 (C-10a), 151.5 (C-2), 160.5 (C-6a), and 166.0 (C=O). MS: m/z 413 M^+ (80), 415 (52), 380 (10), 302 (100), 304 (33), 274 (15), and 228 (5). Anal. Calcd. for $C_{22}H_{17}Cl_2NO_3$: C, 63.77, H, 4.13, N, 3.38. Found: C, 63.78, H, 4.14, N, 3.40%.

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