Supporting information

Vilsmeier Cyclization of α-Acetyl-α-aroyl Ketene-N, S-Acetals:

Direct and Efficient Synthesis of Halogenated Pyridin-2(1H)-ones

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Contents:

1. General Considerations S2
2. Experimental procedures S2
3. Analytical data S4
4. Copies of NMR spectra for new compounds S16
1. General Considerations

All the manipulations of air-and/or moisture-sensitive compounds were carried out under a nitrogen atmosphere using standard Schlenk techniques. Reaction solvents were dried and distilled prior to use by the literature methods. $^1$H and $^{13}$C{¹H} NMR spectra were recorded on a Bruker DRX-600 spectrometer and all chemical shift values refer to $\delta$ TMS = 0.00 ppm or CDCl$_3$ ($\delta$ (¹H), 7.26 ppm; $\delta$($^{13}$C), 77.16 ppm). The HRMS analysis was achieved on Bruck microTof by using ESI method. All the melting points were uncorrected. Analytical TLC plates, Sigma-Aldrich silica gel 60F200 were viewed by UV light (254 nm). Chromatographic purifications were performed on SDZF silica gel 160.

2. Experimental procedures

(1) Typical procedure for the preparation of $\alpha$-acetyl-$\alpha$-aroyl ketene-$N, S$-acetals 1a-k

![Chemical structure](image)

K$_2$CO$_3$ (5.0 mmol) was added to a stirred solution of 1-arylbutane-1, 3-dione (5.0 mmol) in DMF (10 mL), and the mixture was stirred for 1 h at room temperature. The isothiocyanate (5.0 mmol) was then added dropwise, and the mixture was stirred for 2 h at room temperature. The bromoethane (5.0 mmol) and K$_2$CO$_3$ (5.0 mmol) was added. The reaction was quenched with 100 mL of H$_2$O after the mixture was further stirred 4 h at room temperature. The resulting mixture was extracted with dichloromethane (3×30 mL), and the combined organic phase was washed with water, dried over anhydrous MgSO$_4$, filtered, and evaporated in vacuo. The crude product was purified by silica gel chromatography (petroleum ether (30-60 °C) /diethyl ether=30:1, v/v) to give $\alpha$-acetyl-$\alpha$-aroyl ketene-$N, S$-acetals 1a-k.

(2) Typical procedure for the preparation of $\alpha$-acetyl-$N, S$-acetals 11

![Chemical structure](image)
To a stirred solution of 4-chlorobenzenamine (635 mg, 5 mmol) in dry THF (20 mL) was added n-BuLi (2.6 mL, 6 mmol) under nitrogen atmosphere over a period of 10 min at -78 °C. The reaction mixture was brought to room temperature and further stirred for 45 min. A solution of 4, 4-bis(ethylthio)but-3-en-2-one (900 mg, 5 mmol) in dry THF (10 mL) was added at 0 °C, and the reaction mixture was further stirred at room temperature for 2 h. It was refluxed for 18-20 h to complete the reaction, cooled, poured into saturated NH₄Cl solution (50 mL), and extracted with CHCl₃ (3×15 mL). The combined extracts were washed with water and brine, dried (Na₂SO₄), and evaporated to give crude product which was purified by silica gel chromatography (petroleum ether/ethyl acetate=6:1, v/v) to give 11 in 77% yield as a white solid.

(3) Typical Procedure for the Synthesis of 5-aroyl-4-halo-3-formyl pyridin-2(1H)-ones 2

The Vilsmeier reagent was prepared by adding POX₃/DMF (1.5 mmol) into icecold dry DMF (1 mL) under stirring. The mixture was then stirred for 15 min at 0 °C. To the above Vilsmeier reagent was added 1 (0.25 mmol) as a solution in DMF (1 mL). The mixture was heated to 80 °C and stirred for 4.0 h. After cooling to room temperature, the resulting mixture was poured into saturated aqueous NaCl (100 mL), which was extracted with dichloromethane (3×30 mL). The combined organic phase was washed with water, dried over anhydrous MgSO₄, filtered, and evaporated in vacuo. The crude product was purified by silica gel chromatography (petroleum ether/ethyl acetate=4:1, v/v) to give 2 as a white solid.

(4) X-ray crystallographic studies

Single crystal X-ray diffraction data of compounds (Z)-1a were recorded on a Bruker SMART APEX II diffractometer with graphite-monochromated Mo Kα radiation (λ= 0.71073 Å) at 293K. Cell parameters were obtained by global refinement of the positions of all collected reflections. Intensities were corrected for Lorentz and polarization effects and empirical absorption. The structures were solved by direct methods and refined by full-matrix least squares on F2. All non-hydrogen
atoms were refined with anisotropic temperature parameters. All hydrogen atoms on carbon atoms were generated geometrically. Structure solution and refinement were performed by using the SHELXL-97 program. The X-ray crystallographic files, in CIF format, are available from the Cambridge Crystallographic Data Centre on quoting the deposition numbers CCDC 974611 for (Z)-1a. Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

3 Analytical data

(Z)-2-(ethylthio(phenylamino)methylene)-1-p-tolylbutane-1,3-dione ((Z)-1a):
yield 85%. Yellowish crystalline solid. M.p.: 58-59 °C. ¹H NMR (600 MHz, CDCl₃) δ:
13.06 (s, 1H), 7.88 (d, J = 7.9 Hz, 2H), 7.40 (d, J = 8.0 Hz, 2H), 7.35 (t, 2H), 7.27 (d, J = 7.9 Hz, 2H), 7.21 (t, 1H), 2.43 (s, 3H), 2.21 (q, 2H), 2.07 (s, 3H), 0.88 (t, 3H). ¹³C NMR (150 MHz, CDCl₃) δ: 195.9, 194.1, 158.6, 143.9, 138.9, 137.1, 129.5 (2C), 129.4 (2C), 129.2 (2C), 125.9, 124.3 (2C), 116.3, 29.0, 28.0, 21.7, 14.0. HRMS Cacld for C₂₀H₂₁NO₂S: ([M+H]+) 340.1366; Found: 340.1366.

(Z)-2-(ethylthio(phenylamino)methylene)-1-m-tolylbutane-1,3-dione ((Z)-1b):
yield 86%. Yellowish liquid. ¹H NMR (600 MHz, CDCl₃) δ 13.07 (s, 1H), 7.80 (s, 1H), 7.76 (d, J = 7.4 Hz, 1H), 7.40 (d, J = 8.1 Hz, 2H), 7.37-7.33 (m, 4H), 7.20 (t, 1H), 2.42 (s, 3H), 2.20 (q, 2H), 2.08 (s, 3H), 0.86 (t, 3H). ¹³C NMR (150 MHz, CDCl₃) δ 196.3, 194.2, 158.9, 139.8, 138.9, 138.9, 138.5, 133.8, 129.7, 129.3 (2C), 128.5, 126.7, 126.0, 124.3 (2C), 116.4, 29.0, 28.1, 21.4, 14.0. HRMS Cacld for C₂₀H₂₁NO₂S: ([M+H]+) 340.1366; Found: 340.1380.
(Z)-2-(ethylthio(phenylamino)methylene)-1-(4-methoxyphenyl)butane-1, 3-dione ((Z)-1c): yield 84%. Yellowish crystalline solid. M.p.: 68-69 °C. $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 13.03 (s, 1 H), 7.97 (d, $J = 8.6$ Hz, 2 H), 7.40 (d, $J = 8.0$ Hz, 2 H), 7.35 (t, 2 H), 7.20 (t, 1 H), 6.96 (d, $J = 8.4$ Hz, 2 H), 3.88 (s, 3 H), 2.23 (q, 2 H), 2.07 (s, 3 H), 0.90 (t, 3 H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 195.0, 194.0, 163.7, 158.4, 139.1, 132.6, 131.8 (2 C), 129.3 (2 C), 126.0, 124.3 (2 C), 116.3, 114.0 (2 C), 55.6, 29.0, 28.0, 14.2. HRMS Calcd for C$_{20}$H$_{21}$NO$_3$S: ([M+H]$^+$) 356.1315; Found: 356.1320.

(2)-(ethylthio(phenylamino)methylene)-1-phenylbutane-1, 3-dione ((Z)-1d): yield 88%. Yellowish crystalline solid. M.p.: 66-67 °C. $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 13.08 (s, 1 H), 7.97 (d, $J = 7.3$ Hz, 2 H), 7.55 (t, 1 H), 7.46 (t, 2 H), 7.39 (d, $J = 7.8$ Hz, 2 H), 7.34 (t, 2 H), 7.20 (t, 1 H), 2.20 (q, 2 H), 2.09 (s, 3 H), 0.84 (t, 3 H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 196.1, 194.2, 159.1, 140.0, 139.0, 132.9, 129.3 (4 C), 128.7 (2 C), 126.1, 124.4 (2 C), 116.2, 29.1, 28.1, 14.0. HRMS Calcd for C$_{19}$H$_{19}$NO$_2$S: ([M+H]$^+$) 326.1210; Found: 326.1214.

(2)-(4-bromophenyl)-2-(ethylthio(phenylamino)methylene)butane-1, 3-dione ((Z)-1e): yield 90%. Yellowish crystalline solid. M.p.: 37-38 °C. $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 13.11 (s, 1 H), 7.83 (d, $J = 8.5$ Hz, 2 H), 7.60 (d, $J = 8.5$ Hz, 2 H), 7.39-7.34 (m, 4 H), 7.21 (t, 1 H), 2.20 (q, 2 H), 2.09 (s, 3 H), 0.86 (t, 3 H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 195.0, 194.0, 159.4, 138.8, 138.7, 132.0 (2 C), 130.8 (2 C), 129.3 (2 C), 128.0, 126.3, 124.4 (2 C), 115.6, 29.0, 28.2, 14.0. HRMS Calcd for C$_{19}$H$_{18}$BrNO$_2$S: ([M+H]$^+$) 404.0315; Found: 404.0311.
(Z)-2-(ethylthio(phenylamino)methylene)-1-(thiophen-2-yl)butane-1, 3-dione ((Z)-1f): yield 86%. Yellowish liquid. $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 13.02 (s, 1 H), 7.68 (t, 2 H), 7.39 (d, $J = 7.5$ Hz, 2 H), 7.35 (t, 2 H), 7.21 (t, 1 H), 7.14 (t, 1 H), 2.50 (q, 2 H), 2.14 (s, 3 H), 0.92 (t, 3 H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 193.5, 188.2, 158.8, 147.2, 138.7, 134.4, 133.4, 129.2 (2 C), 128.2, 126.1, 124.3 (2 C), 120.1, 28.7, 28.2, 14.0. HRMS Cacld for C$_{17}$H$_{17}$NO$_2$S$_2$: ([M+H]$^+$) 332.0774; Found: 332.0793.

(Z)-2-((p-toluidino)(ethylthio)methylene)-1-phenylbutane-1, 3-dione ((Z)-1g): yield 83%. Yellowish crystalline solid. M.p.: 61-62 °C.$^1$H NMR (600 MHz, CDCl$_3$) $\delta$ (Z)-1g: 13.09 (s, 1 H), 7.96 (d, $J = 7.6$ Hz, 2 H), 7.56 (t, 1 H), 7.47 (t, 2 H), 7.27 (d, $J = 7.4$ Hz, 2 H), 7.15 (d, $J = 7.9$ Hz, 2 H), 2.34 (s, 3 H), 2.20 (q, 2 H), 2.08 (s, 3 H), 0.84 (t, 3 H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 196.3, 194.0, 159.6, 140.0, 136.2, 136.0, 132.9, 129.9 (2 C), 129.3 (2 C), 128.6 (2 C), 124.3 (2 C), 115.8, 29.0, 28.1, 21.1, 14.0. (HRMS Cacld for C$_{20}$H$_{21}$NO$_2$S: ([M+H]$^+$) 340.1366; Found: 340.1370.

(Z)-2-((m-toluidino)(ethylthio)methylene)-1-phenylbutane-1, 3-dione ((Z)-1h): yield 85%. Yellowish liquid. $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 13.07 (s, 1 H), 7.97 (d, $J = 7.4$ Hz, 2 H), 7.55 (t, 1 H), 7.46 (t, 2 H), 7.21 (t, 2 H), 7.19 (s, 1 H), 7.01 (d, $J = 7.5$ Hz, 1 H), 2.34 (s, 3 H), 2.22 (q, 2 H), 2.08 (s, 3 H), 0.85 (t, 3 H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 196.2, 194.1, 159.3, 139.9, 139.3, 138.8, 132.9, 129.3 (2 C), 129.1, 128.6 (2 C), 126.9 124.9, 121.3, 116.0, 29.0, 28.1, 21.4, 14.0. HRMS Cacld for C$_{20}$H$_{21}$NO$_2$S: ([M+H]$^+$) 340.1366; Found: 340.1385.
(Z)-2-(ethylthio(4-fluorophenylamino)methylene)-1-phenylbutane-1, 3-dione ((Z)-1i): yield 75%. Yellowish liquid. $^1$H NMR (600 MHz, CDCl$_3$) δ 13.01 (s, 1 H), 7.96 (d, $J = 8.3$ Hz, 2 H), 7.56 (t, 1 H), 7.47 (t, 2 H), 7.36-7.34 (m, 2 H), 7.05 (t, 2 H), 2.20 (q, 2 H), 2.09 (s, 3 H), 0.85 (t, 3 H). $^{13}$C NMR (150 MHz, CDCl$_3$) δ 196.1, 194.4, 161.6, 160.0, 159.2, 139.9, 133.1, 129.3 (2C), 128.7 (2 C), 126.4, 126.3, 116.4, 116.3, 116.1, 29.1, 28.2, 14.0. HRMS Cacld for C$_{19}$H$_{18}$FNO$_2$S: ([M+H]$^+$) 344.1115; Found: 344.1119.

(Z)-2-((benzylamino)(ethylthio)methylene)-1-phenylbutane-1, 3-dione ((Z)-1j): yield 87%. Yellowish crystalline solid. M.p.: 61-62 °C. $^1$H NMR (600 MHz, CDCl$_3$) δ 12.16 (s, 1 H), 7.90 (d, $J = 7.9$ Hz, 2 H), 7.54 (t, 1 H), 7.44 (t, 2 H), 7.37 (t, 2 H), 7.30 (d, $J = 7.2$ Hz, 3 H), 4.77 (d, $J = 5.8$ Hz, 2 H), 2.62 (q, 2 H), 2.09 (s, 3 H), 1.00 (t, 3 H). $^{13}$C NMR (150 MHz, CDCl$_3$) δ 196.2, 193.8, 162.6, 140.3, 137.3, 132.5, 129.1 (2 C), 128.8 (2 C), 128.4 (2 C), 127.6, 126.9 (2 C), 114.35, 48.9, 30.4, 28.6, 14.2. HRMS Cacld for C$_{20}$H$_{21}$NO$_2$S: ([M+H]$^+$) 340.1366; Found: 340.1378.

(Z)-2-((o-toluidino)(ethylthio)methylene)-1-phenylbutane-1, 3-dione ((Z)-1k): yield 87%. Yellowish liquid. $^1$H NMR (600 MHz, CDCl$_3$) δ 13.08 (s, 1 H), 7.97 (d, $J = 7.4$ Hz, 2 H), 7.55 (t, 1 H), 7.46 (t, 3 H), 7.22 (d, $J = 7.3$ Hz, 1 H), 7.19-7.13 (m, 2 H), 2.37 (s, 3 H), 2.17 (q, 2 H), 2.11 (s, 3 H), 0.83 (t, 3 H). $^{13}$C NMR (150 MHz, CDCl$_3$) δ 196.2, 194.1, 160.7, 140.1, 137.6, 132.9, 132.8, 130.9, 129.3 (2 C), 128.6 (2 C), 126.6, 126.5, 125.5, 115.8, 28.9, 28.1, 18.2, 14.0. HRMS Cacld for C$_{20}$H$_{21}$NO$_2$S: ([M+H]$^+$) 340.1366; Found: 340.1382.
(Z)-4-(4-chlorophenylamino)-4-(ethylthio)but-3-en-2-one 1l: yield 76%. White crystalline solid, M.p.: 68-69 °C. $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 12.93 (s, 1 H), 7.30 (d, $J =$ 8.8 Hz, 2 H), 7.19 (d, $J =$ 8.6 Hz, 2 H), 5.26 (s, 1 H), 2.84 (q, 2 H), 2.13 (s, 3 H), 1.32 (t, 3 H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 193.4, 164.5, 137.1, 131.7, 129.2 (2 C), 126.6 (2 C), 93.1, 29.4, 26.1, 13.4. HRMS Cacld for C$_{12}$H$_{14}$ClNOS: ([M+H]$^+$) 256.0557; Found: 256.0553.

4-chloro-5-(4-methylbenzoyl)-6-oxo-1-phenyl-1,6-dihydropyridine-3-carbaldehyde 2a: yield 85%. White solid. M.p.: 160-161 °C. $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 10.14 (s, 1 H), 8.30 (s, 1 H), 7.85 (d, $J =$ 8.2 Hz, 2 H), 7.53-7.48 (m, 3 H), 7.40 (d, $J =$ 8.5 Hz, 2 H), 7.29 (d, $J =$ 8.0 Hz, 2 H), 2.43 (s, 3 H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 190.3, 185.6, 158.6, 145.8, 143.8, 143.2, 138.6, 133.1, 130.0, 129.9 (3 C), 129.8 (2 C), 129.7 (2 C), 126.3 (2 C), 114.5, 22.0. HRMS Cacld for C$_{20}$H$_{14}$ClNO$_3$: ([M+H]$^+$) 352.0735; Found: 352.0739.

4-bromo-5-(4-methylbenzoyl)-6-oxo-1-phenyl-1,6-dihydropyridine-3-carbaldehyde 2b: yield 81%. White solid. M.p.: 173-174 °C. $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 10.10 (s, 1 H), 8.26(s, 1 H), 7.85 (d, $J =$ 8.2 Hz, 2 H), 7.53-7.48 (m, 3 H), 7.40 (d, $J =$ 8.5 Hz, 2 H), 7.29 (d, $J =$ 8.0 Hz, 2 H), 2.43 (s, 3 H). $^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 191.2, 187.5, 158.2, 145.7, 143.3 (2 C), 138.6, 133.0, 132.8, 132.6, 129.8 (2 C), 129.7 (2 C), 129.6 (2 C), 126.1 (2 C), 115.0, 22.0. HRMS Cacld for C$_{20}$H$_{14}$BrNO$_3$: ([M+H]$^+$) 396.0230; Found: 396.0218.
4-chloro-5-(3-methylbenzoyl)-6-oxo-1-phenyl-1,6-dihydropyridine-3-carbaldehyde 2c: yield 82%. Yellowish solid. M.p.: 171-172 °C. \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 10.18 (s, 1 H), 8.34 (s, 1H), 7.80 (s, 1 H), 7.55 (d, \(J = 7.7\) Hz, 1 H), 7.57-7.52 (m, 3 H), 7.47 (d, \(J = 7.4\) Hz, 1 H), 7.45-7.40 (m, 3 H), 2.45 (s, 3 H). \(^13\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 190.9, 185.5, 158.5, 143.7, 143.2, 139.0, 138.6, 135.5, 135.4, 129.9, 129.7 (4 C), 128.9, 126.8, 126.2 (2 C), 114.5, 21.4. HRMS Cacld for C\(_{20}\)H\(_{14}\)ClNO\(_3\): ([M+H\(^+\)]) 352.0735; Found: 352.0730.

4-bromo-5-(3-methylbenzoyl)-6-oxo-1-phenyl-1, 6-dihydropyridine-3-carbaldehyde 2d: yield 80%. Yellowish solid. M.p.: 163-164 °C. \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 10.11 (s, 1 H), 8.27 (s, 1H), 7.78 (s, 1 H), 7.74 (d, \(J = 7.7\) Hz, 1 H), 7.53-7.49 (m, 3 H), 7.44 (d, \(J = 7.5\) Hz, 1 H), 7.42-7.38 (m, 3 H), 2.42 (s, 3 H). \(^13\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 191.8, 187.5, 158.2, 143.4, 139.0, 138.6, 135.4, 135.0, 133.1, 132.8, 129.8, 129.7 (3 C), 129.0, 126.9, 126.1 (2 C), 115.1, 21.4. HRMS Cacld for C\(_{20}\)H\(_{14}\)BrNO\(_3\): ([M+H\(^+\)]) 396.0230; Found: 396.0231.

4-chloro-5-(4-methoxybenzoyl)-6-oxo-1-phenyl-1,6-dihydropyridine-3-carbaldehyde 2e: yield 85%. Yellowish solid. M.p.: 140-141 °C. \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 10.13 (s, 1 H), 8.29 (s, 1H), 7.92 (d, \(J = 8.8\) Hz, 2 H), 7.53-7.48 (m, 3 H), 7.39 (d, \(J = 7.3\) Hz, 2 H), 6.96 (d, \(J = 8.8\) Hz, 2 H), 3.87 (s, 3 H). \(^13\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 189.3, 185.8, 165.0, 158.8, 143.9, 143.3, 138.9, 132.2 (2 C), 130.3, 130.1, 130.0 (2 C), 128.8, 126.5 (2 C), 114.8, 114.7 (2 C), 56.0. HRMS Cacld for C\(_{20}\)H\(_{14}\)ClNO\(_4\): ([M+H\(^+\)]) 368.0685; Found: 368.0680.
4-bromo-5-(4-methoxybenzoyl)-6-oxo-1-phenyl-1, 6-dihydropyridine-3-carbaldehyde 2f: yield 83%. Yellowish solid. M.p.: 96-97 °C. \( ^1 \text{H NMR} \) (600 MHz, CDCl\(_3\)) \( \delta \) 10.10 (s, 1 H), 8.26 (s, 1 H), 7.92 (d, \( J = 8.8 \) Hz, 2 H), 7.53-7.48 (m, 3 H), 7.39 (d, \( J = 7.4 \) Hz, 2 H), 6.96 (d, \( J = 8.8 \) Hz, 2 H), 3.88 (s, 3 H). \( ^1 \text{C NMR} \) (150 MHz, CDCl\(_3\)) \( \delta \) 190.0, 187.5, 164.7, 158.2, 143.3, 138.6, 133.0, 132.8, 132.0 (2 C), 129.8, 129.7 (2 C), 128.1, 126.1 (2 C), 115.0, 114.8 (2 C), 55.6. HRMS Cacld for C\(_{20}\)H\(_{14}\)BrNO\(_4\): ([M+H\(^+\)]\(^+)\) 412.0180; Found: 412.0182.

5-benzoyl-4-chloro-6-oxo-1-phenyl-1, 6-dihydropyridine-3-carbaldehyde 2g: yield 84%. Yellowish solid. M.p.: 138-139 °C. \( ^1 \text{H NMR} \) (600 MHz, CDCl\(_3\)) \( \delta \) 10.14 (s, 1 H), 8.31 (s, 1 H), 7.95 (d, \( J = 7.5 \) Hz, 2 H), 7.63 (t, 1 H), 7.52-7.49 (m, 5 H), 7.39 (d, \( J = 7.3 \) Hz, 2 H). \( ^1 \text{C NMR} \) (150 MHz, CDCl\(_3\)) \( \delta \) 190.7, 185.4, 158.5, 143.8, 143.3, 138.5, 135.4, 134.5, 129.9, 129.8 (2 C), 129.7, 129.4 (2 C), 129.1 (2 C), 126.2 (2 C), 114.5. HRMS Cacld for C\(_{19}\)H\(_{12}\)ClNO\(_3\): ([M+H\(^+\)]\(^+)\) 338.0579; Found: 338.0582.

5-benzoyl-4-bromo-6-oxo-1-phenyl-1, 6-dihydropyridine-3-carbaldehyde 2h: yield 84%. Yellowish solid. M.p.: 148-149 °C. \( ^1 \text{H NMR} \) (600 MHz, CDCl\(_3\)) \( \delta \) 10.10 (s, 1 H), 8.27 (s, 1 H), 7.96 (d, \( J = 7.4 \) Hz, 2 H), 7.63 (t, 1 H), 7.53-7.49 (m, 5 H), 7.39 (d, \( J = 7.4 \) Hz, 2 H). \( ^1 \text{C NMR} \) (150 MHz, CDCl\(_3\)) \( \delta \) 191.6, 187.4, 158.2, 143.5, 138.5, 135.0, 134.5, 133.2, 132.6, 129.9, 129.7 (2 C), 129.5 (2 C), 129.1 (2 C), 126.1 (2 C), 115.0. HRMS Cacld for C\(_{19}\)H\(_{12}\)BrNO\(_3\): ([M+H\(^+\)]\(^+)\) 382.0074; Found: 382.0081.
5-(4-bromobenzoyl)-4-chloro-6-oxo-1-phenyl-1,6-dihydropyridine-3-carboxaldehyde 2i: yield 79%. Yellowish solid. M.p.: 106-107 °C. $^1$H NMR (600 MHz, CDCl$_3$) δ 10.13 (s, 1 H), 8.31 (s, 1 H), 7.80 (d, $J = 8.5$ Hz, 2 H), 7.64 (d, $J = 8.5$ Hz, 2 H), 7.53-7.49 (m, 3 H), 7.39 (d, $J = 8.5$ Hz, 2 H). $^{13}$C NMR (150 MHz, CDCl$_3$) δ 189.5, 185.0, 158.2, 143.8, 143.4, 138.2, 134.0, 132.2 (2 C), 130.6 (2 C), 129.8, 129.7 (2 C), 129.5, 128.8, 125.9 (2 C). HRMS Calcd for C$_{19}$H$_{11}$BrClNO$_3$: ([M+H]$^+$) 415.9684; Found: 415.9681.

4-bromo-5-(4-bromobenzoyl)-6-oxo-1-phenyl-1,6-dihydropyridine-3-carboxaldehyde 2j: yield 77%. Yellowish solid. M.p.: 92-93 °C. $^1$H NMR (600 MHz, CDCl$_3$) δ 10.10 (s, 1 H), 8.28 (s, 1 H), 7.81 (d, $J = 8.5$ Hz, 2 H), 7.65 (d, $J = 8.5$ Hz, 2 H), 7.53-7.50 (m, 3 H), 7.39 (d, $J = 8.3$ Hz, 2 H). $^{13}$C NMR (150 MHz, CDCl$_3$) δ 190.7, 187.2, 158.2, 143.7, 138.6 133.8, 133.5, 132.5 (2 C), 130.8 (2 C), 130.0, 129.9, 129.8 (2 C), 126.1 (2 C), 115.1. HRMS Calcd for C$_{19}$H$_{11}$Br_{2}NO$_3$: ([M+H]$^+$) 459.9179; Found: 459.9185.

4-chloro-6-oxo-1-phenyl-5-(thiophene-2-carbonyl)-1,6-dihydropyridine-3-carboxaldehyde 2k: yield 80%. White solid. M.p.: 115-117 °C. $^1$H NMR (600 MHz, CDCl$_3$) δ 10.15 (s, 1 H), 8.31 (s, 1 H), 7.78 (d, $J = 4.9$ Hz, 1 H), 7.69 (d, $J = 3.8$ Hz, 1 H), 7.54-7.50 (m, 3 H), 7.40 (d, $J = 8.4$ Hz, 2 H), 7.16 (d, $J = 8.7$ Hz, 1 H). $^{13}$C NMR (150 MHz, CDCl$_3$) δ 185.4, 182.3, 158.4, 144.0, 143.6, 142.5, 138.5, 136.1, 135.0, 129.9, 129.7 (2 C), 129.5, 128.6, 126.2 (2 C), 114.4. HRMS Calcd for C$_{17}$H$_{10}$ClNO$_3$S: ([M+H]$^+$) 344.0143; Found: 344.0143.

4-bromo-6-oxo-1-phenyl-5-(thiophene-2-carbonyl)-1,6-dihydropyridine-3-carboxaldehyde 3a: yield 82%. Yellowish solid. M.p.: 116-117 °C. $^1$H NMR (600 MHz, CDCl$_3$) δ 10.15 (s, 1 H), 8.37 (s, 1 H), 7.79 (d, $J = 4.9$ Hz, 1 H), 7.68 (d, $J = 3.7$ Hz, 1 H), 7.53-7.49 (m, 3 H), 7.40 (d, $J = 8.4$ Hz, 2 H), 7.16 (d, $J = 8.7$ Hz, 1 H). $^{13}$C NMR (150 MHz, CDCl$_3$) δ 185.3, 182.3, 158.4, 144.0, 143.6, 142.5, 138.5, 136.1, 135.0, 129.9, 129.7 (2 C), 129.5, 128.6, 126.2 (2 C), 114.4. HRMS Calcd for C$_{17}$H$_{10}$BrClNO$_3$S: ([M+H]$^+$) 389.9534; Found: 389.9534.

4-bromo-6-oxo-1-phenyl-5-(thiophene-2-carbonyl)-1,6-dihydropyridine-3-carboxaldehyde 3b: yield 81%. Yellowish solid. M.p.: 116-117 °C. $^1$H NMR (600 MHz, CDCl$_3$) δ 10.15 (s, 1 H), 8.37 (s, 1 H), 7.79 (d, $J = 4.9$ Hz, 1 H), 7.68 (d, $J = 3.7$ Hz, 1 H), 7.53-7.49 (m, 3 H), 7.40 (d, $J = 8.4$ Hz, 2 H), 7.16 (d, $J = 8.7$ Hz, 1 H). $^{13}$C NMR (150 MHz, CDCl$_3$) δ 185.3, 182.3, 158.4, 144.0, 143.6, 142.5, 138.5, 136.1, 135.0, 129.9, 129.7 (2 C), 129.5, 128.6, 126.2 (2 C), 114.4. HRMS Calcd for C$_{17}$H$_{10}$BrClNO$_3$S: ([M+H]$^+$) 389.9534; Found: 389.9534.
**dehyde 2l:** yield 79%. White solid. M.p.: 136-137 °C. \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 10.13 (s, 1 H), 8.30 (s, 1 H), 7.80 (d, \(J = 4.8\) Hz, 1 H), 7.69 (d, \(J = 3.8\) Hz, 1 H), 7.56-7.53 (m, 3 H), 7.44 (d, \(J = 8.3\) Hz, 2 H), 7.18 (d, \(J = 8.7\) Hz, 1 H). \(^13\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 187.4, 183.4, 158.1, 143.6, 142.1, 138.5, 136.1, 135.0, 133.5, 132.4, 129.9, 129.7 (2 C), 128.6, 126.1 (2 C), 115.0. HRMS Calcd for C\(_{17}\)H\(_{10}\)BrNO\(_3\)S: ([M+H]\(^+\)) 387.9638; Found: 387.9640.

![Structure of dehyde 2l]

**5-benzoyl-4-chloro-6-oxo-1-p-tolyl-1,6-dihydropyridine-3-carbaldehyde 2m:** yield 85%. White solid. M.p.: 72-73 °C. \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 10.14 (s, 1 H), 8.30 (s, 1 H), 7.94 (d, \(J = 7.2\) Hz, 2 H), 7.63 (t, 1 H), 7.50 (t, 2 H), 7.30 (d, \(J = 8.4\) Hz, 2 H), 7.27 (d, \(J = 8.4\) Hz, 2 H), 2.41 (s, 3 H). \(^13\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 190.7, 185.5, 158.6, 143.9, 143.2, 140.1, 136.0, 135.4, 134.5, 130.2 (2 C), 129.4 (2 C), 129.0 (2 C), 125.8 (2 C), 114.3, 21.2. HRMS Calcd for C\(_{20}\)H\(_{14}\)ClNO\(_3\): ([M+H]\(^+\)) 352.0735; Found: 352.0736.

![Structure of 5-benzoyl-4-chloro-6-oxo-1-p-tolyl-1,6-dihydropyridine-3-carbaldehyde 2m]

**5-benzoyl-4-bromo-6-oxo-1-p-tolyl-1,6-dihydropyridine-3-carbaldehyde 2n:** yield 81%. White solid. M.p.: 87-88 °C. \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 10.12 (s, 1 H), 8.29 (s, 1 H), 7.98 (d, \(J = 7.8\) Hz, 2 H), 7.65 (t, 1 H), 7.52 (t, 2 H), 7.34-7.29 (m, 4 H), 2.44 (s, 3 H). \(^13\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 191.6, 187.4, 158.2, 143.5, 140.1, 135.9, 134.9, 134.4, 133.0, 132.3, 130.2 (2 C), 129.4 (2 C), 129.0 (2 C), 125.7 (2 C), 114.9, 21.7. HRMS Calcd for C\(_{20}\)H\(_{14}\)BrNO\(_3\): ([M+H]\(^+\)) 396.0230; Found: 396.0240.

![Structure of 5-benzoyl-4-bromo-6-oxo-1-p-tolyl-1,6-dihydropyridine-3-carbaldehyde 2n]

**5-benzoyl-4-chloro-6-oxo-1-m-tolyl-1,6-dihydropyridine-3-carbaldehyde 2o:** yield 82%. White solid. M.p.: 124-125 °C. \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 10.14 (s, 1 H), 8.30 (s, 1 H), 7.94 (d, \(J = 8.4\) Hz, 2 H), 7.62 (t, 1 H), 7.50 (t, 2 H), 7.39 (t, 1 H), 7.28
(d, \( J = 7.7 \) Hz, 1 H), 7.19 (t, 2 H), 2.41 (s, 3 H). \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \( \delta \) 190.7, 185.5, 158.6, 143.9, 143.3, 140.0, 138.4, 135.4, 134.5, 130.6, 129.6, 129.5, 129.4 (2 C), 129.1 (2 C), 126.7, 123.1, 114.3, 21.3. HRMS Cacld for C\(_{20}\)H\(_{14}\)ClNO:\ ([M+H]'\) 352.0735; Found: 352.0737.

5-benzoyl-4-bromo-6-oxo-1-m-tolyl-1,6-dihydropyridine-3-carbaldehyde 2p:
yield 83%. White solid. M.p.: 138-139 °C. \(^1\)H NMR (600 MHz, CDCl\(_3\)) \( \delta \) 10.10 (s, 1 H), 8.26 (s, 1 H), 7.97 (d, \( J = 8.1 \) Hz, 2 H), 7.63 (t, 1 H), 7.50 (t, 2 H), 7.40 (t, 1 H), 7.28 (d, \( J = 7.6 \) Hz, 1 H), 7.20 (t, 2 H), 2.41 (s, 3 H). \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \( \delta \) 191.6, 187.4, 158.3, 143.5, 140.0, 138.4, 135.0, 134.4, 133.1, 132.5, 130.6, 129.5, 129.4 (2 C), 129.0 (2 C), 126.2, 123.1, 114.9, 21.3. HRMS Cacld for C\(_{20}\)H\(_{14}\)BrNO:\ ([M+H]'\) 396.0230; Found: 396.0231.

5-benzoyl-4-chloro-1-(4-fluorophenyl)-6-oxo-1,6-dihydropyridine-3-carbaldehyde 2q:
yield 79%. White solid. M.p.: 148-149 °C. \(^1\)H NMR (600 MHz, CDCl\(_3\)) \( \delta \) 10.14 (s, 1 H), 8.27 (s, 1 H), 7.94 (d, \( J = 8.0 \) Hz, 2 H), 7.63 (t, 1 H), 7.50 (t, 2 H), 7.41-7.38 (m, 2 H), 7.20 (t, 2 H). \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \( \delta \) 190.5, 185.4, 163.8, 162.1, 158.5, 143.6, 143.4, 135.3, 134.6, 134.4, 129.4, 129.1 (2 C), 128.2 (2 C), 128.1, 116.9, 116.7, 114.6. HRMS Cacld for C\(_{19}\)H\(_{11}\)ClFNO:\ ([M+H]'\) 356.0485; Found: 356.0484.

5-benzoyl-4-bromo-1-(4-fluorophenyl)-6-oxo-1,6-dihydropyridine-3-carbaldehyde 2r:
yield 78%. White solid. M.p.: 128-129 °C. \(^1\)H NMR (600 MHz, CDCl\(_3\)) \( \delta \) 10.10 (s, 1 H), 8.23 (s, 1 H), 7.95 (d, \( J = 8.0 \) Hz, 2 H), 7.63 (t, 1 H), 7.50 (t, 2 H), 7.42-7.38 (m, 2 H), 7.20 (t, 2 H). \(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \( \delta \) 191.4, 187.3, 164.2, 161.2, 158.2, 143.2, 134.9, 134.5, 133.3, 132.8, 129.5 (2 C), 129.1 (2 C), 128.2, 128.1,
5-benzoyl-1-benzyl-4-chloro-6-oxo-1, 6-dihydropyridine-3-carbaldehyde 2s: yield 85%. White solid. M.p.: 129-130 °C. ¹H NMR (600 MHz, CDCl₃) δ 10.05 (s, 1 H), 8.23 (s, 1 H), 7.90 (d, J = 8.0 Hz, 2 H), 7.63 (t, 1 H), 7.49 (t, 2 H), 7.39-7.37 (m, 3 H), 7.36-7.34 (m, 2 H), 5.18 (s, 2 H). ¹³C NMR (150 MHz, CDCl₃) δ 190.7, 185.3, 159.0, 143.1, 143.0, 135.4, 134.5, 134.1, 129.4 (4 C), 129.2, 129.1 (2 C), 129.0, 128.9 (2 C), 114.5. 53.2. HRMS Cacld for C₂₀H₁₄ClNO₃: ([M+H]⁺) 399.0735; Found: 399.0741.

5-benzoyl-1-benzyl-4-bromo-6-oxo-1,6-dihydropyridine-3-carbaldehyde 2t: yield 85%. White solid. M.p.: 137-138 °C. ¹H NMR (600 MHz, CDCl₃) δ 10.00 (s, 1 H), 8.20 (s, 1 H), 7.90 (d, J = 7.3 Hz, 2 H), 7.63 (t, 1 H), 7.49 (t, 2 H), 7.39-7.35 (m, 5 H), 5.16 (s, 2 H). ¹³C NMR (150 MHz, CDCl₃) δ 191.7, 187.3, 158.7, 142.7, 135.0, 134.5, 134.1, 132.9, 131.8, 129.5 (2 C), 129.4 (2 C), 129.2, 129.1 (2 C), 128.8 (2 C), 115.1. 53.3. HRMS Cacld for C₂₀H₁₄BrNO₃: ([M+H]⁺) 396.0230; Found: 396.0237.

5-benzoyl-4-chloro-6-oxo-1-o-tolyl-1,6-dihydropyridine-3-carbaldehyde 2u: yield 77%. White solid. M.p.: 66-67 °C. ¹H NMR (600 MHz, CDCl₃) δ 10.14 (s, 1 H), 8.19 (s, 1 H), 7.93 (d, J = 8.3 Hz, 2 H), 7.63 (t, 1 H), 7.50 (t, 2 H), 7.39 (t, 1 H), 7.35 (d, J = 7.5 Hz, 2 H), 7.20 (d, J = 7.9 Hz, 1 H), 2.19 (s, 3 H). ¹³C NMR (150 MHz, CDCl₃) δ 190.5, 185.4, 158.2, 144.1, 143.5, 137.9, 135.5, 134.7, 134.5, 131.5, 130.3, 129.7, 129.3 (2 C), 129.1 (2 C), 127.6, 126.8, 114.4. 17.7. HRMS Cacld for C₂₀H₁₄ClNO₃: ([M+H]⁺) 352.0735; Found: 352.0741.
5-benzoyl-4-bromo-6-oxo-1-o-tolyl-1,6-dihydropyridine-3-carbaldehyde  

White solid. M.p.: 73-754 °C. \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 10.10 (s, 1 H), 8.16 (s, 1 H), 7.93 (d, \(J\) = 8.3 Hz, 2 H), 7.63 (t, 1 H), 7.50 (t, 2 H), 7.39 (t, 1 H), 7.35 (d, \(J\) = 7.5 Hz, 2 H), 7.20 (d, \(J\) = 7.8 Hz, 1 H), 2.19 (s, 3 H). \(^1\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 191.5, 187.4, 158.8, 143.8, 137.9, 135.1, 134.7, 134.4, 133.3, 132.5, 131.5, 130.3, 129.4 (2 C), 129.1 (2 C), 127.6, 126.8, 115.0. 17.7. HRMS Cacld for C\(_{20}\)H\(_{14}\)BrNO\(_3\): ([M+H]\(^+\)) 396.0230; Found: 396.0235.

4-chloro-1-(4-chlorophenyl)-2-oxo-1, 2-dihydropyridine-3-carbaldehyde  

Yellowish solid. M.p.: 166-167 °C. \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\): 10.27 (s, 1 H), 7.59 (d, \(J\) = 7.1 Hz, 1 H), 7.53 (d, \(J\) = 8.5 Hz, 2 H), 7.27 (d, \(J\) = 8.4 Hz, 2 H), 6.76 (d, \(J\) = 7.1 Hz, 1 H). \(^1\)C NMR (150 MHz, CDCl\(_3\)) \(\delta\) 187.4, 181.9, 144.4, 141.9, 140.7, 136.3, 135.9, 130.2 (2 C), 128.1 (2 C), 115.2. HRMS Cacld for C\(_{12}\)H\(_7\)Cl\(_2\)NO\(_2\): ([M+H]\(^+\)) 267.9927; Found: 267.9928.
4. Copies of NMR spectra for new compounds