Supplementary Material (ESI) for Chemical Communications

[5C+1N] Annulation: A Novel Synthetic Strategy for Functionalized 2,3-Dihydro-4-pyridones

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Electronic supplementary information (ESI)

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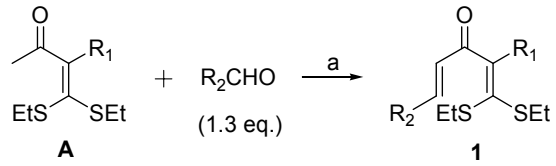
I. General

All reagents were purchased from commercial sources and used without treatment, unless otherwise indicated. The products were purified by column chromatography over silica gel. ^{1}H NMR and ^{13}C NMR spectra were recorded at 25ºC on a Varian 500 MHz and 125 MHz, respectively, and TMS as internal standard. IR spectra (KBr) were recorded on a Magna-560 FTIR spectrophotometer in the range of 400~4000 cm^{-1}. Elemental analyses were measured on a PE-2400 analyzer (Perkin-Elmer). Mass spectra were recorded on Agilient 1100 LCMsD mass spectrometer.

II. Preparation of Substrates:

Synthesis of α-alkenoyl ketene-(*S,S*)-acetals **1**. These compounds were synthesized *via* the Claisen-Schmidt condensation of α-acyl ketene-(*S,S*)-acetals with aldehydes.



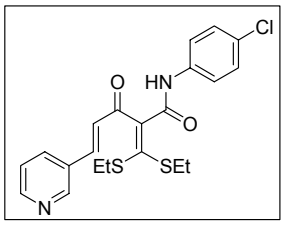
Key: (a) NaH (2.0 eq.), DMSO, 0~70ºC, 1.0~2.0 h.

Entry	A	R_1	R_2	Product	Y (%)[a]
1	$\mathbf{A_1}$	4-ClC_6H_4NHCO	3-pyridyl	**1g**	93
2	$\mathbf{A_2}$	C_6H_5CO	4-ClC_6H_4	**1l**	95

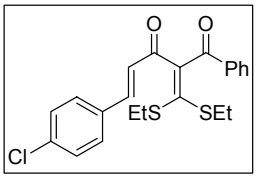
[a] Isolated yields.

Typical procedure for the preparation of **1** (with **1g** as an example): To a solution of α-acyl ketene-(*S,S*)-acetals $\mathbf{A_1}$ (1670 mg, 5.0 mmol) and 3-Pyridinecarboxaldehyde (0.62 mL, 6.5 mmol) in DMSO (6.0 mL) at 0 ºC was added NaH (240 mg, 10.0 mmol) in one portion. The reaction mixture was stirred at 0 ºC for 10 min, then heated and kept at 70 ºC for 0.5 h. After the starting material $\mathbf{A_1}$ was consumed as indicated by TLC, the resulting mixture was then allowed to cool down to room temperature and poured onto ice-water (250 mL) under stirring. The precipitated solid was collected by filtration, washed with water (3 × 30 mL), and dried in *vacuo* to afford the product **1g** (2013 mg, 93%) as a yellow solid.

The spectra and analysis data of other compounds **1** have been reported in our previous paper: Bi, X.; Dong, D.; Liu, Q.; Pan, W.; Zhao, L.; Li, B. *J. Am. Chem. Soc.* 2005, **127**, 4578.



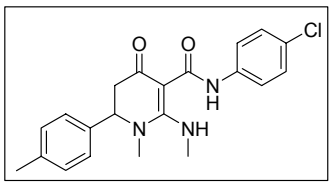
(*E*)-2-[Bis(ethylthio)methylene]-*N*-(4'-chlorophenyl)-3-oxo-5-(pyridin-3'-yl)pent-4-enamide (1d): Yellowish solid, m.p. 170-171 °C, ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.31 (t, J = 7.5 Hz, 6H), 2.98 (q, J = 7.5 Hz, 4H), 7.16 (d, J = 16.0 Hz, 1H), 7.29 (d, J = 8.5 Hz, 2H), 7.33-7.36 (m, 1H), 7.57 (d, J = 8.5 Hz, 2H), 7.64 (d, J = 16.0 Hz, 1H), 7.86 (d, J = 8.0 Hz, 1H), 8.62 (d, J = 3.5 Hz, 1H), 8.78 (s, 1H), 8.92 (br s, 1H). IR (KBr, cm^{-1}) 3292, 1666, 1627, 1595, 1547, 1332, 1157, 829.



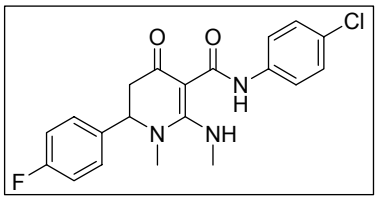
(*E*)-2-[Bis(ethylthio)methylene]-5-(4'-chlorophenyl)-1-phenylpent-4-ene-1,3-dione (1h): Yellowish solid, m.p. 144-145 °C, ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.04 (br s, 3H), 1.32 (br s, 3H), 2.73 (br s, 2H), 2.94 (br s, 2H), 6.96 (d, J = 15.5 Hz, 1H), 7.33 (d, J = 8.0 Hz, 2H), 7.44-7.48 (m, 4H), 7.56-7.59 (m, 1H), 7.68 (d, J = 15.5 Hz, 1H), 7.97 (d, J = 8.5 Hz, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 193.35, 187.74, 148.63, 144.95, 143.66, 137.21, 136.50, 133.61, 133.16, 129.68, 129.65, 129.17, 128.64, 125.52, 29.86, 28.58, 14.92, 14.44. IR (KBr, cm^{-1}) 1668, 1599, 1444, 1330, 1185, 824.

III. Synthesis and analytical data of dihydro-4-pyridones **2**, **3** and **4**.

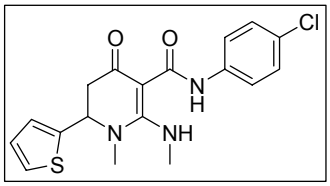
General procedure for the cyclization of α-alkenoyl ketene-(*S*,*S*)-acetals **1** with amines (preparation of **2a1** as an example): To a solution of α-alkenoyl ketene-(*S*,*S*)-acetal **1a** (900 mg, 2.0 mmol) in DMF (5 mL) was added methylamine (aq., 30%) (0.63 mL, 6.0 mmol) in one portion at room temperature. The reaction mixture was stirred for 36 h at room temperature and then poured into saturated sodium chloride aqueous (50 mL) which was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phase was washed with water (3 × 30 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was purified by flash chromatography (silica gel, diethylether : acetone = 6 : 1) to give **2a1** (620 mg, 81%).



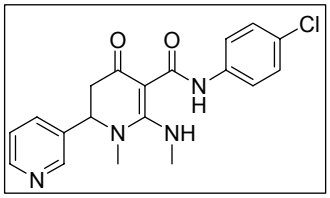
***N*-(4'-Chlorophenyl)-1-methyl-2-(methylamino)-4-oxo-6-(4'-methylphenyl)-1,4,5,6-tetrahydropyridine-3-carboxamide (2a1):** White solid, m.p. 181-183 °C, ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.33 (s, 3H), 2.80 (dd, J = 5.5, 16.0 Hz, 1H), 2.94-3.10 (m, 7H), 4.46 (dd, J = 5.5, 11.5 Hz, 1H), 7.16 (s, 4H), 7.22 (d, J = 7.5 Hz, 2H), 7.51 (d, J = 7.5 Hz, 2H), 11.32 (br s, 1H), 12.48 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 187.98, 167.76, 137.91, 137.88, 135.71, 129.63, 128.60, 127.65, 126.29, 121.84, 92.75, 61.14, 41.41, 40.76, 32.95, 21.05. IR (KBr, cm^{-1}) 2973, 1636, 1568, 1521, 1490, 1401, 1090, 825. ES-MS (*m/z*): 384.0 $[(M + 1)]^+$. Anal. Calcd for $C_{21}H_{22}ClN_3O_2$: C, 65.71; H, 5.78; N, 10.95; Found C, 65.89; H, 5.71; N, 10.99.



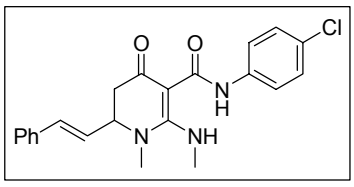
***N*-(4'-Chlorophenyl)-6-(4'-fluorophenyl)-1-methyl-2-(methylamino)-4-oxo-1,4,5,6-tetrahydro pyridine-3-carboxamide (2b1):** White solid, m.p. 152-153 °C, ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.75 (dd, J = 5.5, 16.0 Hz, 1H), 3.03-3.07 (m, 4H), 3.10 (s, 3H), 3.46 (dd, J = 5.5, 10.0 Hz, 1H), 7.02-7.06 (m, 2H), 7.18-7.29 (m, 4H), 7.51 (d, J = 8.5 Hz, 2H), 11.37 (br s, 1H), 12.43 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 187.86, 170.03, 167.69, 148.25, 147.44, 137.84, 132.55, 128.61, 127.68, 121.85, 119.85, 108.47, 106.78, 101.31, 92.68, 61.14, 41.22, 40.84, 32.94. IR (KBr, cm^{-1}) 2974, 1645, 1564, 1520, 1489, 1401, 1257, 1030, 833.



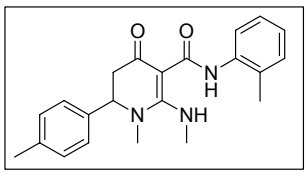
***N*-(4'-Chlorophenyl)-1-methyl-2-(methylamino)-4-oxo-6-(thiophen-2-yl)-1,4,5,6-tetrahydropy ridine-3-carboxamide (2c1):** White solid, m.p. 160-161 °C, ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.82 (d, J = 16.0 Hz, 1H), 3.04 (s, 3H), 3.15-3.19 (m, 4H), 4.46 (s, 1H), 6.93 (s, 2H), 7.21 (d, J = 7.5 Hz, 2H), 7.50 (d, J = 7.5 Hz, 2H), 11.33 (br s, 1H), 12.41 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 188.13, 169.48, 167.74, 143.03, 137.77, 128.60, 127.74, 127.14, 25.20, 124.92, 121.85, 92.77, 57.60, 41.06, 39.77, 32.44. IR (KBr, cm^{-1}) 2970, 1644, 1568, 1538, 1490, 1402, 1379, 1323, 1223, 1153, 1009, 816, 699. ES-MS (*m/z*): 376.1 $[(M + 1)]^{+}$. Anal. Calcd for $C_{18}H_{18}ClN_3O_2S$: C, 57.52; H, 4.83; N, 11.18; Found: C, 57.77; H, 4.95; N, 11.14.



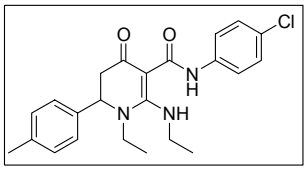
***N*-(4'-Chlorophenyl)-1-methyl-2-(methylamino)-4-oxo-6-(pyridin-3-yl)-1,4,5,6-tetrahydropyr idine-3-carboxamide (2d1):** White solid, m.p. 143-145 °C, ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.74 (dd, J = 3.5, 16.0 Hz, 1H), 3.06 (s, 3H), 3.12-3.15 (m, 4H), 4.49 (dd, J = 3.5, 11.5 Hz, 1H), 7.20 (d, J = 8.5 Hz, 2H), 7.27 (s, 1H), 7.47 (d, J = 8.5 Hz, 2H), 7.57 (d, J = 7.5 Hz, 1H), 8.55 (s, 1H), 11.40 (br s, 1H), 12.33 (s, 1H). IR (KBr, cm^{-1}) 3440, 2972, 1636, 1568, 1522, 1490, 1401, 1317, 1091, 828.



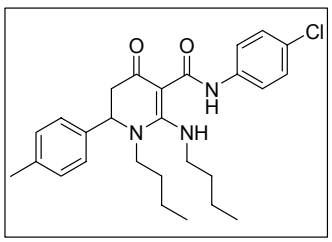
(*E*)-*N*-(4'-Chlorophenyl)-1-methyl-2-(methylamino)-4-oxo-6-styryl-1,4,5,6-tetrahydropyridine-3-carboxamide (2e1): White solid, m.p. 132-133 °C, ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.54 (dd, J = 4.0, 16.0 Hz, 1H), 2.95-3.06 (m, 4H), 3.20 (s, 3H), 4.01 (m, 1H), 6.26 (dd, J = 7.0, 16.0 Hz, 1H), 6.56 (d, J = 16.0 Hz, 1H), 7.23-7.37 (m, 7H), 7.53 (d, J = 8.5 Hz, 2H), 11.30 (br s, 1H), 12.53 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 188.02, 169.14, 167.89, 137.83, 135.70, 132.84, 128.68, 128.63, 128.30, 127.74, 126.64, 125.80, 121.95, 92.22, 60.38, 40.72, 39.76, 32.92. IR (KBr, cm^{-1}) 3466, 2969, 1636, 1567, 1521, 1490, 1401, 1247, 1090, 829. ES-MS (*m/z*): 418.0 $[(M + 23)]^+$. Anal. Calcd for $C_{22}H_{22}ClN_3O_2$: C, 66.75; H, 5.60; N, 10.61; Found: C, 66.52; H, 5.91; N, 10.70.



1-Methyl-2-(methylamino)-4-oxo-*N*-(*o*-tolyl)-6-(*p*-tolyl)-1,4,5,6-tetrahydropyridine-3-carboxamide (2f1): White solid, m.p. 136-137 °C,^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.34 (s, 3H), 2.80 (dd, J = 6.5, 16.0 Hz, 1H), 3.01-3.09 (m, 7H), 4.47 (dd, J = 1.0, 6.5 Hz, 1H), 6.96-6.99 (m, 1H), 7.15-7.18 (m, 6H), 8.04 (d, J = 7.5 Hz, 1H), 11.49 (br s, 1H), 12.22 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 187.86, 170.23, 167.74, 137.77, 137.53, 135.81, 130.11, 129.54, 128.64, 126.30, 126.06, 123.20, 122.12, 92.96, 61.07, 41.30, 40.73, 32.87, 21.01, 18.58. IR (KBr, cm^{-1}) 3446, 2970, 1645, 1570, 1524, 1456, 1403, 1253, 1153, 820.

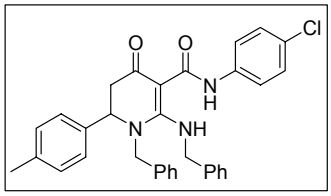


***N*-(4'-Chlorophenyl)-1-ethyl-2-(ethylamino)-4-oxo-6-(*p*-tolyl)-1,4,5,6-tetrahydropyridine-3-carboxamide (2a2):** White solid, m.p. 149-151 °C, ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.34 (t, J = 7.0 Hz, 3H), 1.40 (t, J = 7.0 Hz, 3H), 2.32 (s, 3H), 2.79 (dd, J = 3.5, 16.0 Hz, 1H), 3.18 (dd, J = 6.0, 16.0 Hz, 1H), 3.39-3.47 (m, 3H), 3.52-3.58 (m, 3H), 4.47 (dd, J = 3.5, 6.0 Hz, 1H), 7.11-7.15 (m, 4H), 7.1 (d, J = 9.0 Hz, 2H), 7.49 (d, J = 9.0 Hz, 2H), 11.37 (br s, 1H), 12.45 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 188.47, 168.40, 167.89, 137.93, 137.37, 136.39, 129.38, 128.56, 127.53, 125.98, 121.89, 93.19, 56.77, 47.88, 41.54, 39.89, 20.97, 15.51, 13.58. IR (KBr, cm^{-1}) 3448, 2975, 1646, 1569, 1532, 1490, 1456, 1401, 1246, 1141, 828. ES-MS (*m/z*): 434.3 $[(M + 23)]^+$. Anal. Calcd for $C_{23}H_{26}ClN_3O_2$: C, 67.06; H, 6.36; N, 10.20; Found: C, 67.38; H, 6.38; N, 10.42.

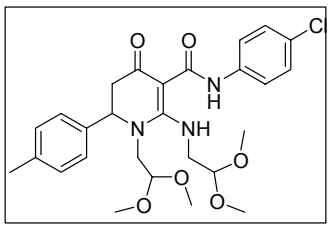


1-Butyl-2-(butylamino)-*N*-(4'-chlorophenyl)-4-oxo-6-(*p*-tolyl)-1,4,5,6-tetrahydropyridine-3-ca

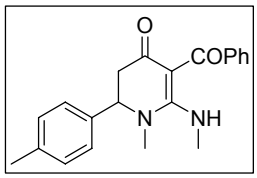
rboxamide (2a3): White solid, m.p. 119-120 °C, ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.94-0.98 (m, 6H), 1.33-1.50 (m, 4H), 1.71-1.75 (m, 4H), 2.31 (s, 3H), 2.77 (dd, J = 2.5, 16.5 Hz, 1H), 3.16 (dd, J = 6.0, 16.5 Hz, 1H), 3.30-3.35 (m, 4H), 4.48 (dd, J = 2.5, 6.0 Hz, 1H), 7.13 (s, 4H), 7.21 (d, J = 8.5 Hz, 2H), 7.49 (d, J = 8.5 Hz, 2H), 11.42 (br s, 1H), 12.48 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 188.33, 168.40, 167.89, 137.93, 137.37, 136.39, 129.38, 128.56, 127.53, 125.95, 121.84, 93.12, 57.27, 53.36, 46.64, 40.14, 32.18, 30.62, 20.97, 20.15, 20.10, 13.79, 13.65. IR (KBr, cm^{-1}) 3433, 2958, 2872, 1646, 1568, 1532, 1490, 1307, 1092, 829. ES-MS (*m/z*): 468.5 $[(M + 1)]^+$. Anal. Calcd for $C_{27}H_{34}ClN_3O_2$: C, 69.29; H, 7.32; N, 8.98; Found: C, 69.50; H, 7.33; N, 8.95.



1-Benzyl-2-(benzylamino)-*N*-(4'-chlorophenyl)-4-oxo-6-(4'-methyl)-1,4,5,6-tetrahydropyridin e-3-carboxamide (2a4): White solid, m.p. 185-186 °C, ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.33 (s, 3H), 2.60 (d, J = 16.5 Hz, 1H), 2.89 (dd, J = 6.0, 16.5 Hz, 1H), 4.35 (d, J = 15.0 Hz, 1H), 4.47 (d, J = 6.0 Hz, 1H), 4.60 (dd, J = 5.5, 16.5 Hz, 1H), 4.72 (dd, J = 6.5, 16.5 Hz, 1H), 4.91 (d, J = 15.5 Hz, 1H), 7.07-7.12 (m, 4H), 7.23 (d, J = 8.5 Hz, 2H), 7.28-7.38 (m, 10H), 7.52 (d, J = 9.0 Hz, 2H), 12.12 (br s, 1H), 12.50 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 188.73, 169.07, 167.76, 137.76, 137.53, 137.08, 136.17, 135.92, 129.54, 129.19, 128.96, 128.63, 128.43, 127.88, 127.79, 127.49, 126.89, 126.08, 121.90, 94.00, 56.85, 49.84, 40.58, 21.02. IR (KBr, cm^{-1}) 3446, 3028, 1644, 1568, 1529, 1490, 1452, 1400, 1304, 1245, 1091, 829, 733, 696. ES-MS (*m/z*): 558.2 $[(M + 23)]^+$.

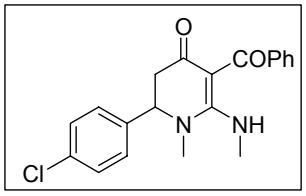


***N*-(4-Chlorophenyl)-1-(2',2'-dimethoxyethyl)-2-(2',2'-dimethoxyethylamino)-4-oxo-6-(*p*-tolyl) -1,4,5,6-tetrahydropyridine-3-carboxamide (2a5):** Colorless semisolid. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.29 (s, 3H), 2.78 (dd, J = 2.5, 16.5 Hz, 1H), 3.24 (dd, J = 6.5, 16.5 Hz, 1H), 3.24 (dd, J = 6.5, 16.5 Hz, 1H), 3.35 (s, 3H), 3.40 (s, 6H), 3.43-3.56 (m, 3H), 3.47 (s, 3H), 3.70 (dd, J = 5.0, 15.0 Hz, 1H), 4.53-4.58 (m, 2H), 4.68 (d, J = 3.0 Hz, 1H), 7.10-7.14 (m, 4H), 7.20 (d, J = 9.0 Hz, 2H), 7.52 (d, J = 9.0 Hz, 2H), 10.92 (br s, 1H), 12.31 (s, 1H). IR (KBr, cm^{-1}) 3430, 2981, 1654, 1555, 1501, 1468, 1299, 1003, 821.

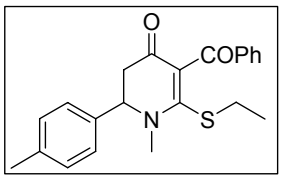


5-Benzoyl-1-methyl-6-(methylamino)-2-(*p*-tolyl)-2,3-dihydropyridin-4(*1H*)-one (2g): White

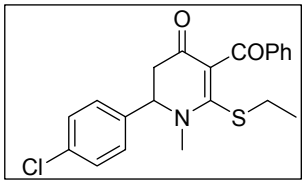
solid, m.p. 198-200 °C, ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.37 (s, 3H), 2.80 (dd, J = 5.0, 17.0 Hz, 1H), 2.96 (dd, J = 5.0, 17.0 Hz, 1H), 3.07 (s, 3H), 3.19 (s, 3H), 4.61 (dd, J = 5.0, 5.0 Hz, 1H), 7.20-7.33 (m, 9H), 10.52 (br s, 1H). IR (KBr, cm^{-1}) 3351, 3249, 1625, 1593, 1558, 1499, 1401, 1147, 824, 729.



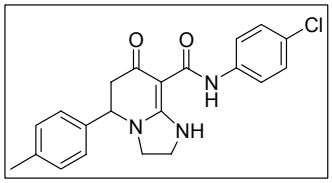
5-Benzoyl-2-(4'-chlorophenyl)-1-methyl-6-(methylamino)-2,3-dihydropyridin-4(*1H*)-one (2h): White solid, m.p. 214-215 °C, ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.79 (dd, J = 3.5, 17.0 Hz, 1H), 3.00 (dd, J = 3.5, 17.0 Hz, 1H), 3.08 (s, 3H), 3.21 (s, 3H), 4.59 (t, J = 3.5 Hz, 1H), 7.20 (d, J = 7.5 Hz, 2H), 7.24 (d, J = 7.5 Hz, 2H), 7.30-7.36 (m, 3H), 7.40 (d, J = 8.0 Hz, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 195.28, 188.32, 168.20, 142.61, 137.33, 133.81, 130.08, 128.99, 127.92, 127.85, 127.54, 101.94, 60.97, 41.05, 40.36, 32.47. IR (KBr, cm^{-1}) 3350, 1618, 1593, 1558, 1500, 1399, 1289, 1148, 1091, 833, 724. ES-MS (*m/z*): 355.2 $[(M + 1)]^+$.



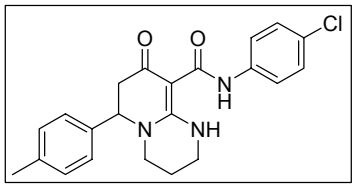
5-benzoyl-6-(ethylthio)-1-methyl-2-(*p*-tolyl)-2,3-dihydropyridin-4(*1H*)-one (3g): Colorless semisolid. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.11 (t, J = 7.0 Hz, 3H), 2.36 (s, 3H), 2.73 (q, J = 7.0 Hz, 2H), 2.83 (dd, J = 4.0, 16.0 Hz, 1H), 3.15 (dd, J = 6.5, 16.0 Hz, 1H), 3.41 (s, 3H), 4.75 (dd, J = 4.0, 6.0 Hz, 1H), 7.20 (s, 4H), 7.27-7.30 (m, 2H), 7.41-7.45 (m, 1H), 7.63 (d, J = 7.5 Hz, 2H). IR (KBr, cm^{-1}) 2925, 1668, 1623, 1521, 1362, 1312, 1075, 815.



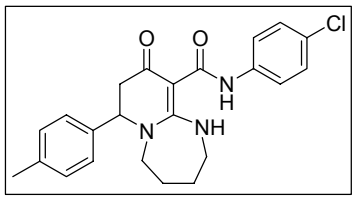
5-Benzoyl-2-(4'-chlorophenyl)-6-(ethylthio)-1-methyl-2,3-dihydropyridin-4(*1H*)-one (3h): White solid, m.p. 92-93 °C, ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.14 (t, J = 7.5 Hz, 3H), 2.69-2.81 (m, 3H), 3.21 (dd, J = 6.5, 16.0 Hz, 1H), 3.44 (s, 3H), 4.76 (dd, J = 3.5, 6.5 Hz, 1H), 7.26 (d, J = 8.0 Hz, 2H), 7.30-7.34 (m, 2H), 7.39 (d, J = 8.0 Hz, 2H), 7.44-7.47 (m, 1H), 7.62 (d, J = 7.0 Hz, 2H). IR (KBr, cm^{-1}) 1646, 1521, 1455. ES-MS (*m/z*): 386.4 $[(M + 1)]^+$.



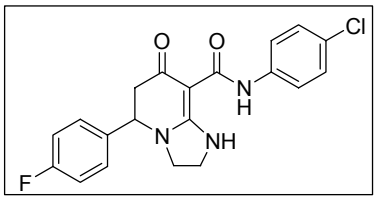
***N*-(4'-Chlorophenyl)-7-oxo-5-(4'-methylphenyl)-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridine -8-carboxamid (4a):** White solid, d.p. 222-224 °C, ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.37 (s, 3H), 2.77-2.88 (m, 2H), 3.11-3.14 (m, 1H), 3.37-3.39 (m, 1H), 3.68-3.76 (m, 2H), 4.37 (dd, *J* = 5.5, 11.0 Hz, 1H), 7.21 (s, 4H), 7.25 (d, *J* = 8.5 Hz, 2H), 7.57 (d, *J* = 8.5 Hz, 2H), 9.49 (br s, 1H), 11.94 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 187.86, 167.08, 166.28, 138.56, 137.91, 135.38, 129.77, 128.58, 127.39, 126.76, 121.25, 88.49, 59.07, 47.67, 44.54, 43.05, 21.06. IR (KBr, cm^{-1}) 3446, 1646, 1557, 1539, 1490, 1457, 1298, 824. ES-MS (*m/z*): 382.2 $[(M + 1)]^+$. Anal. Calcd for $C_{21}H_{20}ClN_3O_2$: C, 66.05; H, 5.28; N, 11.00; Found: C, 66.41; H, 5.03; N, 11.10.



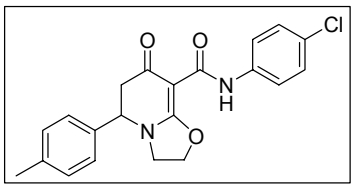
***N*-(4'-Chlorophenyl)-8-oxo-6-p-tolyl-2,3,4,6,7,8-hexahydro-*1H*-pyrido[1,2-a]pyrimidine-9-car boxamide (4b):** White solid, m.p. 165-166 °C,^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.93-2.07 (m, 2H), 2.33 (s, 3H), 2.61 (dd, *J* = 3.5, 16.0 Hz, 1H), 3.16 (dd, *J* = 7.5, 16.0 Hz, 1H), 3.25-3.48 (m, 4H), 4.43 (dd, *J* = 3.5, 7.5 Hz, 1H), 7.10-7.16 (m, 4H), 7.22 (d, *J* = 8.5 Hz, 2H), 7.52 (d, *J* = 8.5 Hz, 2H), 11.79 (br s, 1H), 12.70 (s, 1H). IR (KBr, cm^{-1}) 3450, 2968, 1636, 1560, 1522, 1399, 1326, 1153, 1093, 825.



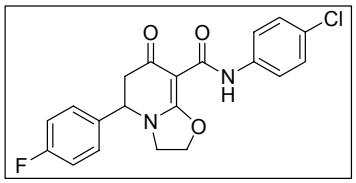
***N*-(4'-Chlorophenyl)-9-oxo-7-(4'-methylphenyl)-1,2,3,4,5,7,8,9-octahydropyrido[1,2-a][1,3]di azepine-10-carboxamide (4c):** White solid, m.p. 158-159 °C, ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.65-1.90 (m, 4H), 2.34 (s, 3H), 2.73 (dd, *J* = 6.5, 16.0 Hz, 1H), 2.98 (dd, *J* = 5.5, 16.0 Hz, 1H), 3.01-3.60 (m, 4H), 4.48 (dd, *J* = 5.5, 6.5 Hz, 1H), 7.12-7.27 (m, 6H), 7.53 (d, *J* = 9.0 Hz, 2H), 11.58 (s, 1H), 12.57 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 187.29, 169.28, 167.81, 138.02, 137.95, 137.60, 136.32, 129.63, 129.58, 128.84, 128.60, 127.63, 127.59, 126.49, 121.82, 121.13, 91.77, 62.44, 54.28, 44.93, 42.52, 26.31, 25.73, 21.08. IR (KBr, cm^{-1}) 2945, 1635, 1567, 1516, 1490, 1445, 1371, 1139, 1092, 826.



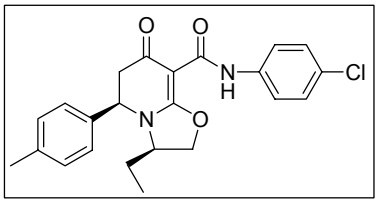
***N*-(4-Chlorophenyl)-5-(4-fluorophenyl)-7-oxo-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridine-8-carboxamide (4d):** White solid, d.p. 227-229 °C, ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.80-2.82 (m, 2H), 3.16 (dd, *J* = 10.0, 20.0 Hz, 1H), 3.34-3.38 (m, 1H), 3.75 (dd, *J* = 10.0, 20.0 Hz, 1H), 3.77-3.80 (m, 1H), 4.41 (dd, *J* = 10.0, 10.0 Hz, 1H), 7.08-7.12 (m, 2H), 7.25 (d, *J* = 8.5 Hz, 2H), 7.31-7.34 (m, 2H), 7.56 (d, *J* = 8.5 Hz, 2H), 9.56 (br s, 1H), 11.89 (s, 1H). IR (KBr, cm^{-1}) 3314, 2980, 1650, 1558, 1510, 1490, 1366, 1298, 1223, 841, 775.



***N*-(4'-Chlorophenyl)-7-oxo-5-(4-methylphenyl)-3,5,6,7-tetrahydro-*2H*-oxazolo[3,2-a]pyridine-8-carboxamide (4e):** White solid, m.p. 187-189 °C, ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.17 (s, 3H), 2.37-2.96 (m, 2H), 3.33-3.39 (m, H), 3.47-3.51 (m, 1H), 4.55 (dd, *J* = 7.5, 10.5 Hz, 1H), 4.67-4.73 (m, 1H), 4.83-4.88 (m, 1H), 7.21-7.24 (m, 6H), 7.64 (d, *J* = 8.5 Hz, 2H), 11.51 (s, 1H). IR (KBr, cm^{-1}) 3447, 3029, 1668, 1582, 1533, 1476, 1131, 917, 824. ES-MS (*m/z*): 405.2 $[(M + 23)]^+$. Anal. Calcd for $C_{21}H_{19}ClN_2O_3$: C, 65.88; H, 5.00; N, 7.32; Found: C, 66.02; H, 5.05; N, 7.41.

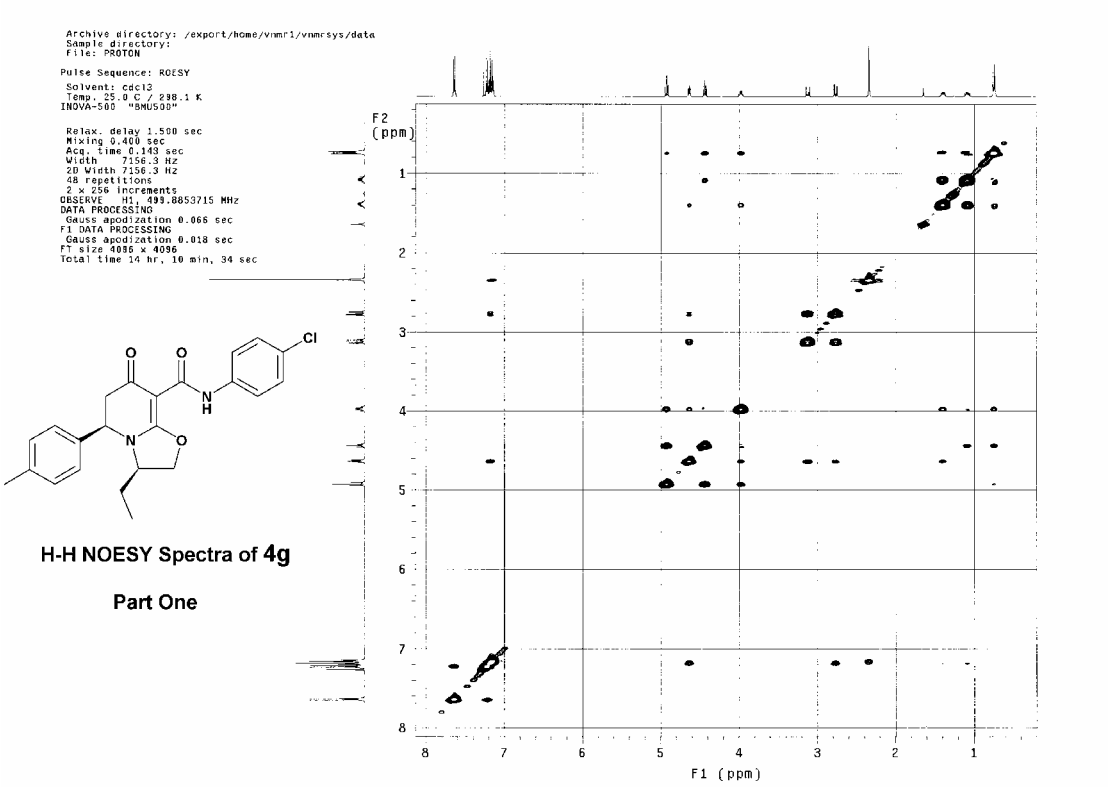


***N*-(4'-Chlorophenyl)-5-(4'-fluorophenyl)-7-oxo-3,5,6,7-tetrahydro-*2H*-oxazolo[3,2-a]pyridine-8-carboxamide (4f):** White solid, m.p.169-170 °C,^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.90 (d, *J* = 7.5 Hz, 2H), 3.33-3.47 (m, 2H), 4.57 (dd, *J* = 8.5, 17.0 Hz, 1H), 4.68-4.88 (m, 2H), 7.09-7.12 (m, 2H), 7.22-7.32 (m, 4H), 7.63 (d, *J* = 9.0 Hz, 2H), 11.48 (s, 1H). IR (KBr, cm^{-1}) 3031, 1662, 1599, 1550, 1484, 1321, 1125, 821.



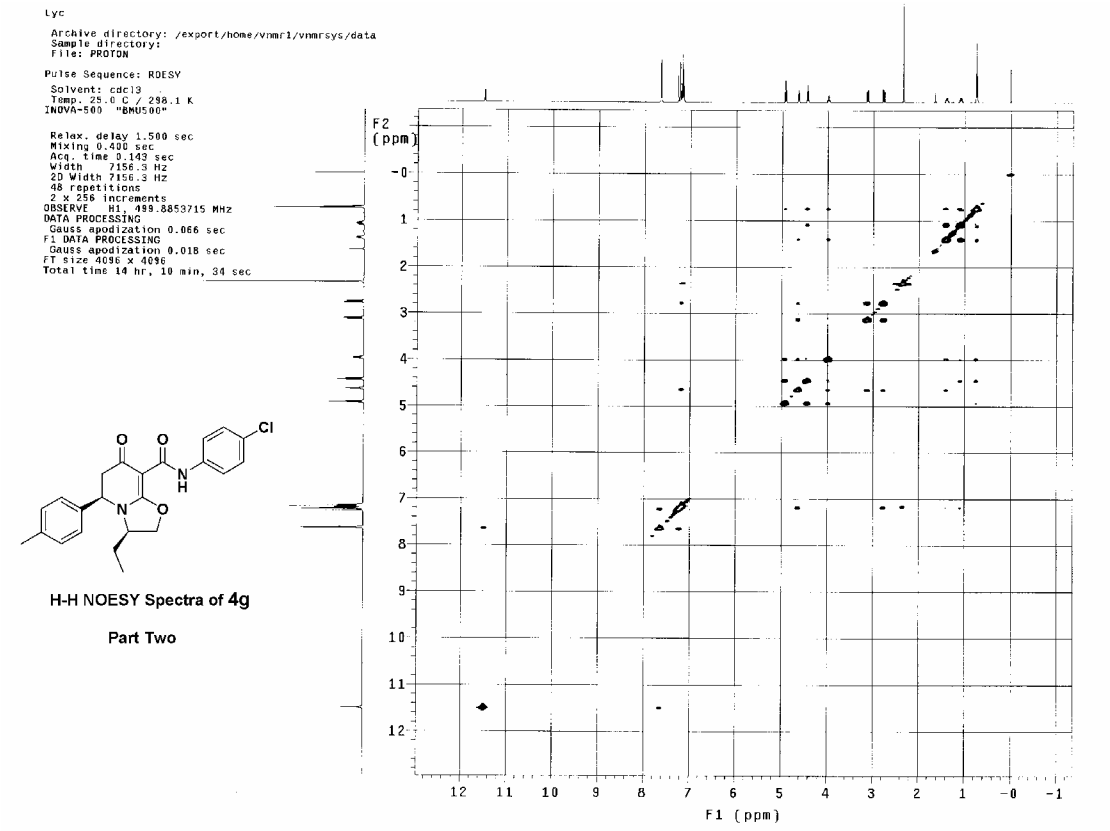
(3*R*,5*R*)-8-Benzoyl-3-ethyl-5-(4'-methylphenyl)-2,3,5,6-tetrahydrooxazolo[3,2-a]pyridin-7-one (4g): White solid, m.p. 145-146 °C,^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.74 (t, *J* = 7.5 Hz, 3H), 1.04-1.10 (m, 1H), 1.37-1.41 (m, 1H), 2.33 (s, 3H), 2.75 (dd, *J* = 5.0, 16.5 Hz, 1H), 3.13 (dd, *J* = 7.0, 16.5 Hz, 1H), 3.95-4.00 (m, 1H), 4.44 (dd, *J* = 9.0, 18.0 Hz, 1H), 4.63 (dd, *J* = 5.0, 7.0 Hz, 1H),

4.93 (dd, J = 9.0, 18.0 Hz, 1H), 4.63 (dd, J = 5.0, 7.0 Hz, 1H), 4.93 (dd, J = 9.0, 18.0 Hz, 1H), 7.13-7.23 (m, 6H), 7.64 (d, J = 8.0 Hz, 1H), 11.51 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 188.84, 171.89, 162.48, 138.90, 138.15, 135.12, 129.81, 128.51, 127.18, 126.23, 120.98, 90.53, 74.81, 60.80, 55.23, 43.26, 25.38, 21.04, 9.16. IR (KBr, cm^{-1}) 3025, 2942, 1666, 1559, 1533, 1489, 1450, 1137, 829. ES-MS (*m/z*): 411.1 $[(M + 1)]^+$. Anal. Calcd for $C_{23}H_{23}ClN_2O_3$: C, 67.23; H, 5.64; N, 6.82; Found: C, 67.66; H, 5.73; N, 6.78.



H-H NOESY Spectra of 4g

Part One



H-H NOESY Spectra of 4g

Part Two