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Functionalization of pyridyl ketones using deprotolithiation-*in situ* zincation

Madani Hedidi,[a,b,c] William Erb,[a,*] Frédéric Lassagne,[a] Yury S. Halauko,[d,*] Oleg A. Ivashkevich,[d] Vadim E. Matulis,[e] Thierry Roisnel,[f] Ghenia Bentabed-Ababsa[b,*] and Florence Mongin[a]

[a] *Chimie et Photonique Moléculaires, Institut des Sciences Chimiques de Rennes, UMR 6226, Université de Rennes 1 - CNRS, Bâtiment 10A, Case 1003, Campus de Beaulieu, CS74205, 35042 Rennes Cedex, France*
[b] *Laboratoire de Synthèse Organique Appliquée, Faculté des Sciences, Université d'Oran 1 Ahmed Ben Bella, BP 1524 El M'Naouer, 31000 Oran, Algeria.*
[c] *Present address: Département de Chimie, Faculté des Sciences, Université Hassiba Benbouali de Chlef, Hay Es-Salem, RN 19, 02000 Chlef, Algeria.*
[d] *UNESCO Chair of Belarusian State University, 14 Leningradskaya Str., Minsk 220030, Belarus.*
[e] *Research Institute for Physico-Chemical Problems of Belarusian State University, 14 Leningradskaya Str., Minsk 220030, Belarus.*
[f] *Centre de DIFfractométrie X, Institut des Sciences Chimiques de Rennes, UMR 6226, Université de Rennes 1 - CNRS, Bâtiment 10B, Campus de Beaulieu, CS 74205, 35042 Rennes Cedex, France*

william.erb@univ-rennes1.fr, hys@tut.by, badri_sofi@yahoo.fr

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1. General Procedures

All the reactions were performed under an argon atmosphere. THF was distilled over sodium/benzophenone. Column chromatography separations were achieved on silica gel (40-63 μm). Melting points were measured on a Kofler apparatus. IR spectra were taken on a Perkin-Elmer Spectrum 100 spectrometer. ^{1}H and ^{13}C Nuclear Magnetic Resonance (NMR) spectra were recorded on a Bruker Avance III spectrometer at 300 MHz and 75 MHz, respectively, except in the case of compound **2'm** for which a Bruker Avance I at 500 MHz and 125 MHz was used. ^{1}H chemical shifts (δ) are given in ppm relative to the solvent residual peak and ^{13}C chemical shifts are relative to the central peak of the solvent signal.[1] 3-Benzoyl-2-fluoropyridine (**1d**),[2] 3-benzoyl-2-chloropyridine (**1e**),[2] 3-benzoyl-2-methoxypyridine (**1i**),[2] 4-azafluorenone (**1j**),[3] 4-azaxanthone (**1k**)[4] and 4-azathioxanthone (**1l**)[5] have been prepared as described previously.

2. Experimental Procedures and Compound Characterizations

General procedure 1: A stirred cooled (0 °C) solution of LiTMP prepared at 0 °C in THF (6 mL) from 2,2,6,6-tetramethylpiperidine (1.7 mL, 10 mmol) and BuLi (1.6 M hexanes solution, 10 mmol) was treated with TMEDA (0.77 mL, 5.0 mmol) and CuCl (495 mg, 5.0 mmol). The mixture was stirred for 15 min at 0 °C before introduction of the required substrate (5.0 mmol). After 2 h at 25 °C, a solution of the required aroyl chloride (10 mmol) in THF (3 mL) was added. The mixture was stirred at 40 °C overnight before addition of a 1M aqueous solution of NaOH (20 mL) and extraction with Et_2O (2 x 20 mL). After washing the organic phase with an aqueous saturated solution of NH_4Cl (10 mL) and drying over anhydrous Na_2SO_4, the solvent was evaporated under reduced pressure, and the product was isolated after purification by flash chromatography on silica gel (the eluent is given in the product description).

2-Chloro-3-(2-chlorobenzoyl)pyridine (1f). The general procedure 1 using 2-chlorobenzoyl chloride (0.88 g) gave **1f** (eluent: heptane-AcOEt 90:10) in 57% yield as a yellow powder: mp 68-70 °C; IR (ATR): 660, 739, 751, 769, 780, 816, 924, 1053, 1061, 1079, 1128, 1245, 1301, 1396, 1435, 1558, 1574, 1587, 1678, 3060 cm^{-1}. The other analyses are as described previously.[3]

2-Chloro-3-(2-methoxybenzoyl)pyridine (1g). The general procedure 1 using 2-methoxybenzoyl chloride (0.74 mL) gave **1g** (eluent: heptane-AcOEt 80:20 to 70:30) in 58% yield as an orange oil: IR (ATR): 672, 726, 755, 909, 924, 1020, 1077, 1112, 1127, 1161, 1250, 1307, 1397, 1436, 1464, 1485, 1567, 1597, 1652, 2246, 2841, 2945 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.59 (s, 3H), 6.91 (dd, 1H, *J* = 8.4 and 0.9 Hz), 7.05 (td, 1H, *J* = 7.5 and 1.0 Hz), 7.30 (dd, 1H, *J* = 7.5 and 4.8 Hz), 7.53 (ddd, 1H, *J* = 7.8, 7.2 and 1.8 Hz), 7.73 (dd, 1H, *J* = 7.5 and 2.1 Hz), 7.77 (dd, 1H, *J* = 7.8 and 1.8 Hz), 8.43 (dd, 1H, *J* = 5.1 and 2.1 Hz); ^{13}C NMR ($CDCl_3$) δ 55.7 (CH_3), 111.8 (CH), 120.9 (CH), 122.2 (CH), 126.5 (C), 131.2 (CH), 135.1 (CH), 137.5 (C), 137.6 (CH), 147.3 (C), 150.0 (CH), 159.3 (C), 192.7 (C). The ^{1}H NMR data are as described previously.[4]

2-Chloro-3-cinnamoylpyridine (1h). The general procedure 1 using cinnamoyl chloride (1.67 g) gave **1h** (eluent: heptane-AcOEt 80:20) in 47% yield as a beige powder: mp 74-76 °C; ^{1}H NMR ($CDCl_3$) δ 7.17 (d, 1H, *J* = 16 Hz), 7.38 (dd, 1H, *J* = 7.5 and 4.8 Hz), 7.40-7.45 (m, 3H), 7.51 (d, 1H, *J* = 16 Hz), 7.56-7.60 (m, 2H), 7.83 (dd, 1H, *J* = 7.5 and 1.8 Hz), 8.53 (dd, 1H, *J* = 4.8 and 2.1 Hz); ^{13}C NMR ($CDCl_3$) δ 122.5 (CH), 125.5 (CH), 128.8 (2CH), 129.1 (2CH), 131.3 (CH), 134.1 (C), 135.5 (C), 138.4 (CH), 147.0 (CH), 147.8 (C), 151.1 (CH), 191.9 (C). The ^{1}H NMR data are as described previously.[6]

2-Benzoyl-3-iodopyridine (2a). To a stirred mixture of 2-benzoylpyridine (**1a**, 0.18 g, 1.0 mmol) and $ZnCl_2 \cdot TMEDA$[7] (0.26 g, 1.0 mmol) in THF (3 mL) at -30 °C was added dropwise a solution of LiTMP (prepared by adding BuLi (about 1.6 M hexanes solution, 1.5 mmol) to a stirred, cooled (0 °C) solution of 2,2,6,6-tetramethylpiperidine (0.25 mL, 1.5 mmol) in THF (3 mL) and stirring for 5 min) cooled at -30 °C. After 15 min at -30 °C, a solution of I_2 (0.38 g, 1.5 mmol) in THF (5 mL) was introduced, and the mixture was stirred overnight before addition of an aqueous saturated solution of $Na_2S_2O_3$ (5 mL) and extraction with AcOEt (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by chromatography over silica gel (eluent: heptane-AcOEt 80:20) to afford **2a** in 50% yield as a yellow powder: mp 98-100 °C; IR (ATR): 666, 702, 739, 795, 939, 1011, 1064, 1165, 1287, 1316, 1416, 1450, 1595, 1674, 3056 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.16 (dd, 1H, *J* = 8.1 and 4.8 Hz), 7.44-7.50 (m, 2H), 7.61 (tt, 1H, *J* = 7.4 and 1.4 Hz), 7.81-7.86 (m, 2H), 8.26 (dd, 1H, *J* = 8.1 and 1.2 Hz), 8.63 (dd, 1H, *J* = 4.5 and 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 89.8 (C), 125.6 (CH), 128.8 (2CH), 130.6 (2CH), 134.1 (CH), 134.8 (C), 147.3 (CH), 148.1 (CH), 159.2 (C), 194.3 (C); HRMS (ESI): calcd for $C_{12}H_8INNaO$ ($[M+Na]^+$) 331.9548, found 331.9546.

General procedure 2: To a stirred mixture of the required ketone (1.0 mmol) and $ZnCl_2 \cdot TMEDA$[7] (0.26 g, 1.0 mmol) in THF (3 mL) at -55 °C was added dropwise a solution of LiTMP (prepared by adding BuLi (about 1.6 M hexanes solution, 1.5 mmol) to a stirred, cooled (0 °C) solution of 2,2,6,6-tetramethylpiperidine (0.25 mL, 1.5 mmol) in THF (3 mL) and stirring for 5 min) cooled at -55 °C. After 15 min at -55 °C, a solution of I_2 (0.38 g, 1.5 mmol) in THF (5 mL) was introduced, and the mixture was stirred overnight before addition of an aqueous saturated solution of $Na_2S_2O_3$ (5 mL) and extraction with AcOEt (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by chromatography over silica gel (the eluent is given in the product description).

3-Benzoyl-4-iodopyridine (2c). The general procedure 2 using 3-benzoylpyridine (**1c**, 0.18 g), but performed at -70 °C instead of -55 °C, gave **2c** (eluent: heptane-AcOEt 80:20) in 37% yield as a yellow powder: mp 136-138 °C; IR (ATR): 656, 705, 731, 918, 938, 1156, 1259, 1290, 1317, 1393, 1449, 1538, 1558, 1580, 1667, 2928, 3063 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.46-7.53 (m, 2H), 7.65 (tt, 1H, *J* = 7.4 and 2.7 Hz), 7.78-7.84 (m, 2H), 7.91 (d, 1H, *J* = 5.4 Hz), 8.31 (d, 1H, *J* = 5.4 Hz), 8.45 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 104.4 (C), 129.0 (2CH), 130.5 (2CH), 134.4 (CH), 134.9 (CH), 135.4 (C), 140.5 (C), 148.2 (CH), 150.7 (CH), 195.1 (C); HRMS (ESI): calcd for $C_{12}H_8INNaO$ ($[M+Na]^+$) 331.9548, found 331.9545.

3-Benzoyl-2-fluoro-4-iodopyridine (2d). The general procedure 2 using 3-benzoyl-2-fluoropyridine (**1d**, 0.20 g) gave **2d** (eluent: heptane-AcOEt 80:20) in 63% yield as a yellowish powder: mp 144 °C; IR (ATR): 660, 684, 827, 877, 926, 1171, 1230, 1271, 1316, 1391, 1442, 1449, 1539, 1574, 1669, 3084 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.46-7.53 (m, 2H), 7.65 (tt, 1H, *J* = 7.4 and 1.4 Hz), 7.75 (dd, 1H, *J* = 5.4 and 1.1 Hz), 7.79-7.83 (m, 2H), 7.97 (dd, 1H, *J* = 5.1 and 0.9 Hz); ^{13}C NMR ($CDCl_3$) δ 107.3 (d, C, *J* = 3.6 Hz), 127.9 (d, C, *J* = 36 Hz), 129.2 (2CH), 129.9 (2CH), 132.3 (d, CH, *J* = 4.5 Hz), 134.8 (C), 134.8 (CH), 148.4 (d, CH, *J* = 15 Hz), 158.8 (d, C, *J* = 241 Hz), 191.6 (d, C, *J* = 3.5 Hz); HRMS (ESI): calcd for $C_{12}H_7FINNaO$ ($[M+Na]^+$) 349.9454, found 349.9455.

3-Benzoyl-2-chloro-4-iodopyridine (2e).[8] The general procedure 2 using 3-benzoyl-2-chloropyridine (**1e**, 0.22 g) gave **2e** (eluent: heptane-AcOEt 80:20) in 73% yield as a yellow powder: mp 130-132 °C; IR (ATR): 657, 684, 725, 799, 827, 923, 1162, 1195, 1217, 1266, 1313, 1360, 1428, 1449, 1528, 1547, 1581, 1595, 1668, 2927, 3062 cm^{-1}; ^1H NMR ($CDCl_3$) δ

7.47-7.54 (m, 2H), 7.65 (tt, 1H, *J* = 7.4 and 1.4 Hz), 7.79-7.84 (m, 3H), 8.11 (d, 1H, *J* = 5.4 Hz); ^{13}C NMR ($CDCl_3$) δ 105.3 (C), 129.3 (2CH), 129.9 (2CH), 133.2 (CH), 134.0 (C), 134.8 (CH), 140.0 (C), 146.9 (C), 149.8 (CH), 193.1 (C).

2-Chloro-3-(2-chlorobenzoyl)-4-iodopyridine (2f). The general procedure 2 using 2-chloro-3-(2-chlorobenzoyl)pyridine (**1f**, 0.25 g) gave **2f** (eluent: heptane-AcOEt 80:20) in 78% yield as a yellowish powder: mp 112-114 °C; IR (ATR): 682, 732, 745, 761, 789, 829, 923, 1054, 1162, 1196, 1214, 1252, 1282, 1359, 1429, 1466, 1529, 1546, 1586, 1667, 1683, 3066 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.38 (ddd, 1H, *J* = 7.8, 6.6 and 1.8 Hz), 7.47-7.56 (m, 2H), 7.78 (d, 1H, *J* = 5.1 Hz), 7.80 (ddd, 1H, *J* = 8.1, 1.8 and 0.6 Hz), 8.07 (d, 1H, *J* = 5.1 Hz); ^{13}C NMR ($CDCl_3$) δ 105.4 (C), 127.3 (CH), 132.0 (CH), 132.9 (CH), 133.2 (C), 133.5 (CH), 134.5 (CH), 134.7 (C), 140.8 (C), 146.9 (C), 149.7 (CH), 191.4 (C); HRMS (ESI): calcd for $C_{12}H_6{}^{35}Cl_2INNaO$ ($[M+Na]^+$) 399.8769, found 399.8769.

2-Chloro-4-iodo-3-(2-methoxybenzoyl)pyridine (2g). The general procedure 2 using 2-chloro-3-(2-methoxybenzoyl)pyridine (**1g**, 0.25 g) gave **2g** (eluent: heptane-AcOEt 70:30) in 70% yield as a yellow powder: mp 162-164 °C; IR (ATR): 693, 712, 747, 786, 835, 925, 1014, 1045, 1090, 1114, 1160, 1177, 1199, 1215, 1251, 1294, 1366, 1434, 1465, 1482, 1532, 1550, 1575, 1595, 1651, 1940, 2840, 2944 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.62 (s, 3H), 6.95 (dd, 1H, *J* = 8.4 and 0.9 Hz), 7.11 (ddd, 1H, *J* = 8.1, 7.2 and 0.9 Hz), 7.60 (ddd, 1H, *J* = 9.0, 7.2 and 0.9 Hz), 7.74 (d, 1H, *J* = 5.1 Hz), 8.01 (d, 1H, *J* = 5.4 Hz), 8.06 (dd, 1H, *J* = 7.8 and 1.8 Hz); ^{13}C NMR ($CDCl_3$) δ 56.0 (CH_3), 103.6 (C), 112.3 (CH), 121.3 (CH), 123.7 (C), 132.1 (CH), 132.8 (CH), 136.4 (CH), 143.5 (C), 145.9 (C), 148.3 (CH), 160.2 (C), 191.3 (C); HRMS (ESI): calcd for $C_{13}H_9{}^{35}ClINNaO_2$ ($[M+Na]^+$) 395.9264, found 395.9260.

2-Chloro-3-cinnamoyl-4-iodopyridine (2h). The general procedure 2 using 2-chloro-3-cinnamoylpyridine (**1h**, 0.24 g) gave **2h** (eluent: heptane-AcOEt 80:20) in 27% yield as a yellow powder: mp 118-120 °C; IR (ATR): 680, 700, 733, 748, 765, 975, 1037, 1110, 1138, 1198, 1269, 1330, 1363, 1429, 1449, 1528, 1548, 1575, 1595, 1619, 1649, 2925, 3063 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.95 (d, 1H, *J* = 16 Hz), 7.32 (d, 1H, *J* = 16 Hz), 7.38-7.49 (m, 3H), 7.55-7.59 (m, 2H), 7.80 (d, 1H, *J* = 5.1 Hz), 8.10 (d, 1H, *J* = 5.1 Hz); ^{13}C NMR ($CDCl_3$) δ 105.5 (C), 124.9 (CH), 129.0 (2CH), 129.3 (2CH), 131.7 (CH), 133.4 (CH), 134.0 (C), 140.2 (C), 146.9 (C), 148.5 (CH), 149.8 (CH), 193.2 (C); HRMS (ESI): calcd for $C_{14}H_9{}^{35}ClINNaO$ ($[M+Na]^+$) 391.9315, found 391.9316.

3-Benzoyl-4-iodo-2-methoxypyridine (2i). The general procedure 2 using 3-benzoyl-2-methoxypyridine (**1i**, 0.21 g) gave **2i** (eluent: heptane-AcOEt 80:20) in 88% yield as a yellow powder: mp 144-146 °C; IR (ATR): 660, 685, 707, 730, 803, 847, 926, 1015, 1234, 1274, 1301, 1313, 1372, 1455, 1552, 1668, 2948 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.82 (s, 3H), 7.39 (d, 1H, *J* = 5.4 Hz), 7.45 (tt, 2H, *J* = 7.5 and 1.7 Hz), 7.59 (tt, 1H, *J* = 7.4 and 1.4 Hz), 7.78-7.83 (m, 2H), 7.86 (d, 1H, *J* = 5.4 Hz); ^{13}C NMR ($CDCl_3$) δ 54.2 (CH_3), 104.9 (C), 127.0 (CH), 128.6 (C), 128.9 (2CH), 129.7 (2CH), 134.1 (CH), 135.1 (C), 147.5 (CH), 160.5 (C), 194.5 (C); HRMS (ESI): calcd for $C_{13}H_{10}INNaO_2$ ($[M+Na]^+$) 361.9654, found 361.9651.

1-Iodo-4-azafluorenone (2j). The general procedure 2 using 4-azafluorenone (**1j**, 0.18 g) gave **2j** (eluent: heptane-AcOEt 80:20) in 33% yield as a yellow powder: mp 184 °C; IR (ATR): 669, 749, 805, 915, 1042, 1171, 1265, 1341, 1379, 1442, 1550, 1717 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.47 (td, 1H, *J* = 7.2 and 1.2 Hz), 7.61-7.67 (m, 2H), 7.76 (ddd, 1H, *J* = 7.2, 1.2 and 0.6 Hz), 7.87 (dt, 1H, *J* = 7.5 and 0.9 Hz), 8.14 (d, 1H, *J* = 5.4 Hz); ^{13}C NMR ($CDCl_3$) δ 102.4 (C), 121.3 (CH), 124.5 (CH), 129.4 (C), 131.7 (CH), 134.6 (CH), 135.0 (C), 135.7 (CH), 141.3 (C), 152.7 (CH), 166.2 (C), 190.1 (C); HRMS (ESI): calcd for $C_{12}H_6INNaO$

([M+Na]$^+$) 329.9392, found 329.9394. ***1,5-Diiodo-4-azafluorenone (2j')*** was also isolated in 20% yield as a yellowish powder: mp 244 °C; IR (ATR): 659, 693, 761, 783, 824, 924, 1054, 1102, 1164, 1266, 1338, 1369, 1454, 1543, 1556, 1713, 2854, 2924 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.13 (dd, 1H, *J* = 7.8 and 7.2 Hz), 7.70 (d, 1H, *J* = 5.4 Hz), 7.76 (dd, 1H, *J* = 7.5 and 1.1 Hz), 8.07 (dd, 1H, *J* = 7.8 and 2.0 Hz), 8.30 (d, 1H, *J* = 5.4 Hz); ^{13}C NMR ($CDCl_3$) δ 86.8 (C), 102.3 (C), 124.1 (CH), 129.6 (C), 132.2 (CH), 134.8 (CH), 137.1 (C), 141.4 (C), 147.5 (CH), 151.8 (CH), 165.8 (C), 188.7 (C); HRMS (ESI): calcd for $C_{12}H_5I_2NNaO$ ([M+Na]$^+$) 455.8358, found 455.8360.

1-Iodo-4-azaxanthone (2k). The general procedure 2 using 4-azaxanthone (**1k**, 0.20 g) gave **2k** (eluent: CH_2Cl_2-heptane 80:20) in 60% yield as a yellow powder: mp 190-192 °C; IR (ATR): 728, 742, 761, 835, 922, 1085, 1115, 1183, 1219, 1248, 1274, 1318, 1346, 1367, 1443, 1464, 1537, 1557, 1612, 1659, 1724, 1978, 2925 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.40 (ddd, 1H, *J* = 8.1, 6.9 and 1.1 Hz), 7.52 (dq, 1H, *J* = 8.4 and 0.6 Hz), 7.74 (ddd, 1H, *J* = 8.7, 6.9 and 1.5 Hz), 8.01 (d, 1H, *J* = 5.1 Hz), 8.17 (d, 1H, *J* = 4.8 Hz), 8.26 (ddd, 1H, *J* = 8.1, 1.8 and 0.6 Hz); ^{13}C NMR ($CDCl_3$) δ 106.6 (C), 116.0 (C), 118.3 (CH), 121.0 (C), 125.1 (CH), 127.2 (CH), 135.6 (CH), 135.8 (CH), 152.3 (CH), 154.3 (C), 160.2 (C), 176.1 (C); HRMS (ESI): calcd for $C_{12}H_6INNaO_2$ ([M+Na]$^+$) 345.9341, found 345.9343. ***1,6-Diiodo-4-azaxanthone (2k')*** was also isolated in 10% yield as a yellow powder: mp 262-264 °C; IR (ATR): 734, 768, 920, 1019, 1101, 1266, 1369, 1428, 1444, 1538, 1655, 1722, 2924 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.20 (t, 1H, *J* = 7.8 Hz), 8.07 (d, 1H, *J* = 4.8 Hz), 8.21-8.25 (m, 2H), 8.29 (dd, 1H, *J* = 7.2 and 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 85.2 (C), 106.9 (C), 115.7 (C), 121.8 (C), 126.5 (CH), 127.7 (CH), 136.1 (CH), 145.6 (CH), 152.7 (CH), 153.5 (C), 160.2 (C), 175.9 (C); HRMS (ESI): calcd for $C_{12}H_5I_2NNaO_2$ ([M+Na]$^+$) 471.8307, found 471.8306.

1-Iodo-4-azathioxanthone (2l). The general procedure 2 using 4-azathioxanthone (**1l**, 0.21 g) gave **2l** (eluent: CH_2Cl_2) in 60% yield as a yellow powder: mp 184-186 °C; IR (ATR): 697, 724, 802, 922, 1079, 1166, 1232, 1301, 1319, 1348, 1412, 1433, 1521, 1542, 1588, 1643, 1945, 2234, 2929, 3087 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.51 (ddd, 1H, *J* = 8.4, 6.9 and 1.2 Hz), 7.57 (ddd, 1H, *J* = 8.1, 1.5 and 0.6 Hz), 7.66 (ddd, 1H, *J* = 8.4, 6.9 and 1.5 Hz), 8.11 (d, 1H, *J* = 4.8 Hz), 8.17 (d, 1H, *J* = 5.1 Hz), 8.52 (ddd, 1H, *J* = 8.1, 1.5 and 0.6 Hz); ^{13}C NMR ($CDCl_3$) δ 107.4 (C), 125.3 (C), 125.9 (CH), 127.1 (CH), 128.9 (C), 130.4 (CH), 133.0 (CH), 135.2 (C), 136.8 (CH), 151.0 (CH), 159.7 (C), 179.8 (C); HRMS (ESI): calcd for $C_{12}H_6INNaOS$ ([M+Na]$^+$) 361.9112, found 361.9115.

1-Iodo-9-xanthone (2m). The general procedure 2 using 9-xanthone (**1m**, 0.20 g) gave **2m** (eluent: heptane-CH_2Cl_2 100:0 to 80:20) in 72% yield as a pale yellow powder: mp 176 °C (lit.[9] 172-173.5 °C); IR (ATR): 663, 752, 777, 849, 903, 931, 1108, 1147, 1161, 1234, 1255, 1297, 1328, 1346, 1421, 1443, 1466, 1554, 1590, 1612, 1661, 3065 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.27 (dd, 1H, *J* = 8.4 and 7.8 Hz), 7.36 (ddd, 1H, *J* = 8.1, 7.2 and 0.9 Hz), 7.41 (dm, 1H, *J* = 9.0 Hz), 7.48 (dd, 1H, *J* = 8.4 and 1.2 Hz), 7.70 (ddd, 1H, *J* = 8.7, 7.2 and 1.8 Hz), 8.00 (dd, 1H, *J* = 7.6 and 1.1 Hz), 8.31 (ddd, 1H, *J* = 8.1, 1.8 and 0.5 Hz); ^{13}C NMR ($CDCl_3$) δ 91.3 (C), 117.7 (CH), 119.1 (CH), 120.1 (C), 121.3 (C), 124.3 (CH), 127.3 (CH), 134.7 (CH), 135.0 (CH), 138.6 (CH), 154.9 (C), 156.8 (C), 175.4 (C). These data are similar to those reported previously.[9]

1-Iodo-9-fluorenone (2n). The general procedure 2 using 9-fluorenone (**1n**, 0.18 g) gave **2n** (eluent: heptane-AcOEt 90:10) in 52% yield as a yellow powder: mp 148 °C (lit.[10] 147-148.5 °C); IR (ATR): 733, 747, 784, 792, 918, 1056, 1085, 1126, 1149, 1186, 1257, 1281, 1295, 1437, 1563, 1588, 1606, 1715, 3048 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.15 (dd, 1H, *J* = 8.1 and 7.5 Hz), 7.33 (ddd, 1H, *J* = 10.2, 7.5 and 4.8 Hz), 7.49-7.56 (m, 3H), 7.68-7.74 (m, 2H); ^{13}C

NMR ($CDCl_3$) δ 91.6 (C), 120.1 (CH), 120.2 (CH), 124.7 (CH), 129.8 (CH), 134.0 (C), 134.1 (C), 135.0 (CH), 135.1 (CH), 140.6 (CH), 142.0 (C), 147.2 (C), 191.8 (C). ***9'-Hydroxy-1,9'-bi-9-fluorenone (2n')*** was also isolated in 35% yield as a yellow powder: mp 222-224 °C (lit.[11] 222-224 °C); IR (ATR): 686, 728, 753, 771, 803, 909, 958, 1066, 1102, 1139, 1195, 1265, 1284, 1427, 1451, 1469, 1572, 1592, 1607, 1683, 2245, 3060, 3302 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.47 (dd, 1H, *J* = 8.1 and 0.9 Hz), 7.11 (dd, 1H, *J* = 8.1 and 7.5 Hz), 7.28 (td, 2H, *J* = 7.5 and 0.9 Hz), 7.33-7.42 (m, 4H), 7.47-7.57 (m, 4H), 7.70 (d, 2H, *J* = 7.2 Hz), 7.78 (d, 1H, *J* = 7.2 Hz), 7.94 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 85.5 (C), 119.9 (CH), 120.3 (2CH), 120.3 (CH), 124.7 (2CH), 125.3 (CH), 128.4 (CH), 128.4 (2CH), 129.2 (2CH), 129.6 (CH), 132.1 (C), 133.4 (C), 135.5 (CH), 136.0 (CH), 139.9 (2C), 144.3 (C), 146.8 (C), 148.8 (C), 149.5 (2C), 198.2 (C).

2-Benzoyl-5-iodothiophene (2o). The general procedure 2 using 2-benzoylthiophene (**1o**, 0.19 g) gave **2o** (eluent: heptane-AcOEt 80:20) in 80% yield as a whitish powder: mp 129-131 °C (lit.[12] 132-133 °C); IR (ATR): 685, 696, 714, 783, 812, 857, 927, 952, 1066, 1138, 1213, 1297, 1316, 1378, 1405, 1443, 1516, 1575, 1595, 1613, 3054, 3228 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.27 (d, 1H, *J* = 3.9 Hz), 7.33 (d, 1H, *J* = 3.9 Hz), 7.46-7.53 (m, 2H), 7.57-7.63 (m, 1H), 7.80-7.85 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 86.0 (C), 128.6 (2CH), 129.1 (2CH), 132.6 (CH), 135.7 (CH), 137.6 (C), 138.1 (CH), 149.5 (C), 186.7 (C). These data are as described previously.[12]

1-(2-Pyridyl)-9-xanthone (2'm). To a stirred mixture of 9-xanthone (**1m**, 0.19 g, 1.0 mmol) and $ZnCl_2$·TMEDA[7] (0.25 g, 1.0 mmol) in THF (3 mL) at -55 °C was added dropwise a solution of LiTMP (prepared by adding BuLi (about 1.6 M hexanes solution, 1.5 mmol) to a stirred, cooled (0 °C) solution of 2,2,6,6-tetramethylpiperidine (0.25 mL, 1.5 mmol) in THF (3 mL) and stirring for 5 min) cooled at -55 °C. After 15 min at -55 °C, 2-chloropyridine (0.55 g, 4.8 mmol), palladium(II) chloride (14 mg, 80 μmol), and 1,1'-diphenylphosphinoferrocene (44 mg, 80 μmol) were added to the reaction mixture, and the latter was heated at THF reflux for 16 h. After addition of water (0.5 mL) and EtOAc (50 mL), and drying over anhydrous Na_2SO_4, the solvent was evaporated under reduced pressure. The coupled product was isolated by purification by chromatography over silica gel (eluent: heptane-AcOEt 60:40 to 50:50) to afford **2'm** in 76% yield as a light grey powder: mp 183-184 °C; IR (ATR): 631, 672, 725, 750, 760, 786, 925, 1235, 1301, 1333, 1349, 1431, 1463, 1488, 1569, 1589, 1599, 1615, 1652, 2962, 3065 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.28-7.35 (m, 3H), 7.40 (d, 1H, *J* = 7.8 Hz), 7.48 (d, 1H, *J* = 8.4 Hz), 7.58 (dd, 1H, *J* = 8.4 and 0.7 Hz), 7.69 (td, 1H, *J* = 7.8 and 1.5 Hz), 7.74 (t, 1H, *J* = 7.9 Hz), 7.77 (td, 1H, *J* = 7.7 and 1.7 Hz), 8.16 (dd, 1H, *J* = 8.0 and 1.4 Hz), 8.69 (d, 1H, *J* = 4.6 Hz); ^{13}C NMR ($CDCl_3$) δ 117.7 (CH), 118.7 (CH), 119.6 (C), 122.2 (CH), 122.7 (C), 123.7 (CH), 124.0 (CH), 126.5 (CH), 127.0 (CH), 133.9 (CH), 134.8 (CH), 135.6 (CH), 142.7 (C), 148.9 (CH), 155.6 (C), 157.1 (C), 159.9 (C), 176.9 (C).

4-Benzoyl-3-iodopyridine (2b). To a stirred mixture of 4-benzoylpyridine (**1b**, 0.18 g, 1.0 mmol) and $ZnCl_2$·TMEDA[7] (0.26 g, 1.0 mmol) in THF (3 mL) at -30 °C was added dropwise a solution of LiTMP (prepared by adding BuLi (about 1.6 M hexanes solution, 2.0 mmol) to a stirred, cooled (0 °C) solution of 2,2,6,6-tetramethylpiperidine (0.33 mL, 2.0 mmol) in THF (3 mL) and stirring for 5 min) cooled at -30 °C. After 15 min at -30 °C, a solution of I_2 (0.51 g, 2.0 mmol) in THF (5 mL) was added, and the mixture was stirred overnight before addition of an aqueous saturated solution of $Na_2S_2O_3$ (5 mL) and extraction with AcOEt (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by chromatography over silica gel (eluent: heptane-AcOEt 80:20) to afford **2b** in 45% yield as a yellow powder: mp 92-94 °C; IR (ATR): 683, 701, 728, 835, 938, 1011, 1082, 1175, 1262, 1281, 1316, 1394, 1448, 1580,

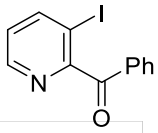
1595, 1669, 3058 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.19 (dd, 1H, *J* = 4.8 and 0.6 Hz), 7.41-7.48 (m, 2H), 7.61 (tt, 1H, *J* = 7.4 and 1.4 Hz), 7.72-7.76 (m, 2H), 8.61 (d, 1H, *J* = 4.8 Hz), 8.97 (d, 1H, *J* = 0.9 Hz); ^{13}C NMR ($CDCl_3$) δ 91.0 (C), 122.3 (CH), 128.9 (2CH), 130.2 (2CH), 134.0 (C), 134.4 (CH), 148.6 (CH), 151.3 (C), 157.7 (CH), 194.7 (C); HRMS (ESI): calcd for $C_{12}H_8INNaO$ ($[M+Na]^+$) 331.9548, found 331.9546. ***4-Benzoyl-3,5-diiodopyridine (2b')*** was also isolated in 10% yield as a yellowish powder: mp 148 °C; IR (ATR): 683, 704, 728, 796, 934, 1037, 1174, 1202, 1270, 1314, 1389, 1450, 1499, 1580, 1595, 1672, 3059 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.52 (td, 2H, *J* = 7.7 and 0.9 Hz), 7.68 (tt, 1H, *J* = 7.5 and 1.7 Hz), 7.79-7.83 (m, 2H), 8.91 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 90.7 (2C), 129.5 (2CH), 130.2 (2CH), 132.3 (C), 135.0 (CH), 155.4 (C), 156.3 (2CH), 194.8 (C); HRMS (ESI): calcd for $C_{12}H_7I_2NNaO$ ($[M+Na]^+$) 457.9888, found 457.9888.

2-Amino-4-phenylpyrido[3,2-*d*]pyrimidine (3a). A mixture of CuI (20 mg, 0.10 mmol), guanidine hydrochloride (0.19 g, 2.0 mmol), K_3PO_4 (0.88 g, 4.0 mmol), 2-benzoyl-3-iodopyridine (**2a**, 0.31 g, 1.0 mmol) and DMSO (0.5 mL) was degased and heated under argon at 110 °C for 24 h. After filtration over celite (washing using AcOEt) and removal of the solvents, the crude product is purified by chromatography over silica gel (eluent: heptane-AcOEt-NEt_3 80:18:2) to afford **3a** in 77% yield as a yellowish powder: mp 140-142 °C; IR (ATR): 695, 739, 765, 804, 1124, 1231, 1344, 1376, 1422, 1458, 1548, 1583, 1601, 1628, 3060, 3171, 3313, 3477 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.67 (br s, 2H), 7.51-7.58 (m, 4H), 7.91 (dd, 1H, *J* = 8.7 and 1.7 Hz), 8.16-8.20 (m, 2H), 8.71 (dd, 1H, *J* = 3.9 and 1.7 Hz); ^{13}C NMR ($CDCl_3$) δ 127.9 (CH), 128.2 (2CH), 130.6 (CH), 131.2 (2CH), 133.8 (CH), 135.5 (C), 136.2 (C), 146.9 (CH), 149.5 (C), 159.9 (C), 169.4 (C); HRMS (ESI): calcd for $C_{13}H_{10}N_4Na$ ($[M+Na]^+$) 245.0803, found 245.0800.

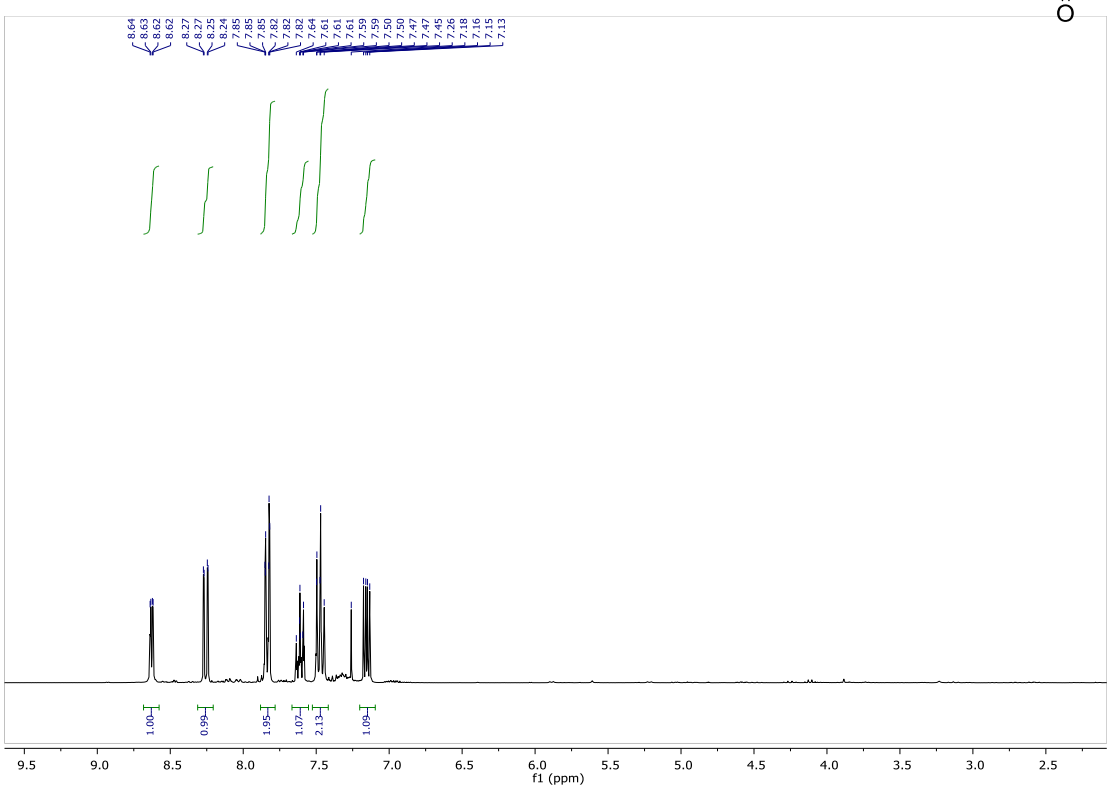
5-Phenylbenzo[*f*][1,7]naphthyridine (4a). A mixture containing 2-benzoyl-3-iodopyridine (**2a**, 0.15 g, 0.50 mmol), 2-aminophenylboronic acid hydrochloride (0.17 g, 1.0 mmol), K_2CO_3 (0.55 g, 4.0 mmol), EtOH (0.5 mL), H_2O (1 mL) and toluene (5 mL) was degased for 30 min. $Pd(PPh_3)_4$ (58 mg, 50 μmol) was then added, and the mixture was heated at reflux under argon for 24 h. After filtration over celite (washing using AcOEt), drying over Na_2SO_4 and removal of the solvents, the crude product was purified by chromatography over silica gel (eluent: heptane-AcOEt 90:10) to afford **4a** in 68% yield as a white powder: mp 134-136 °C (lit.[13] 133-135 °C); ^1H NMR ($CDCl_3$) δ 7.49-7.60 (m, 3H), 7.73 (ddd, 1H, *J* = 8.4, 7.2 and 1.5 Hz), 7.77 (dd, 1H, *J* = 8.4 and 4.2 Hz), 7.82 (ddd, 1H, *J* = 8.4, 6.9 and 1.5 Hz), 8.10-8.14 (m, 2H), 8.32 (dd, 1H, *J* = 8.1 and 1.5 Hz), 8.56 (dd, 1H, *J* = 8.1 and 1.2 Hz), 8.99 (dd, 1H, *J* = 8.4 and 1.5 Hz), 9.09 (dd, 1H, *J* = 4.5 and 1.7 Hz). These data are similar to those previously reported.[13]

3. ^{1}H- and ^{13}C-NMR Spectra

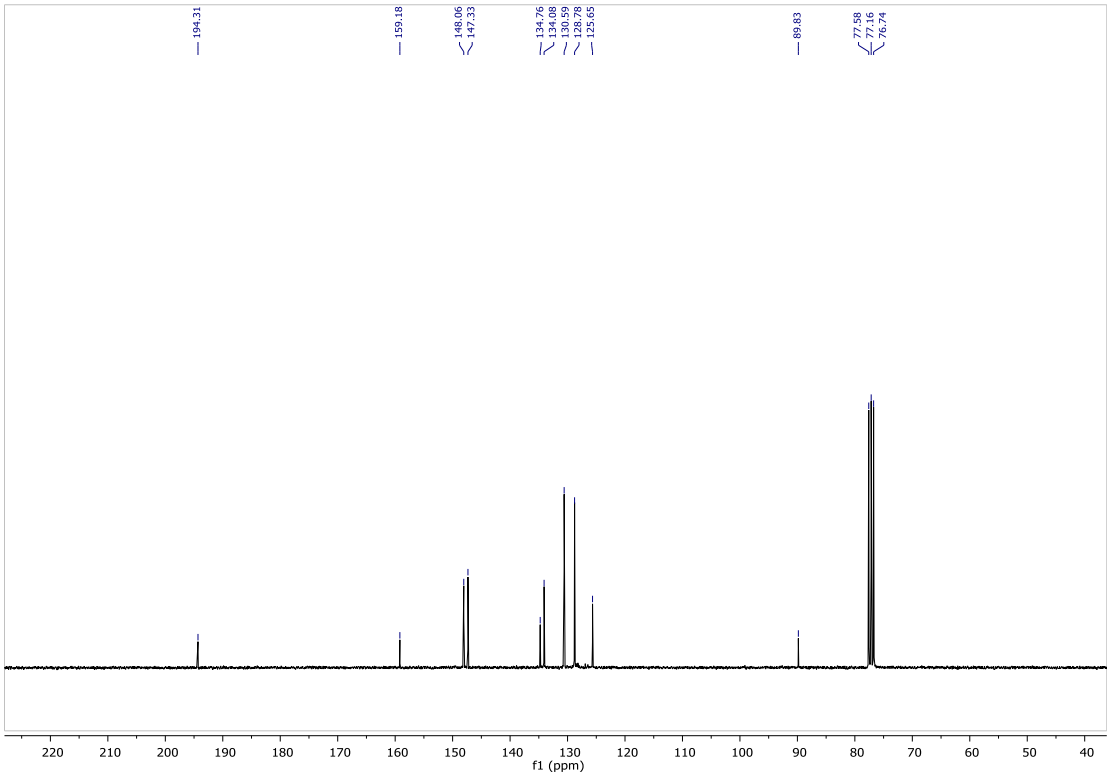
2-Benzoyl-3-iodopyridine (2a).



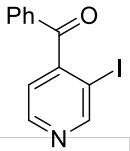
^{1}H – 300 MHz – $CDCl_3$



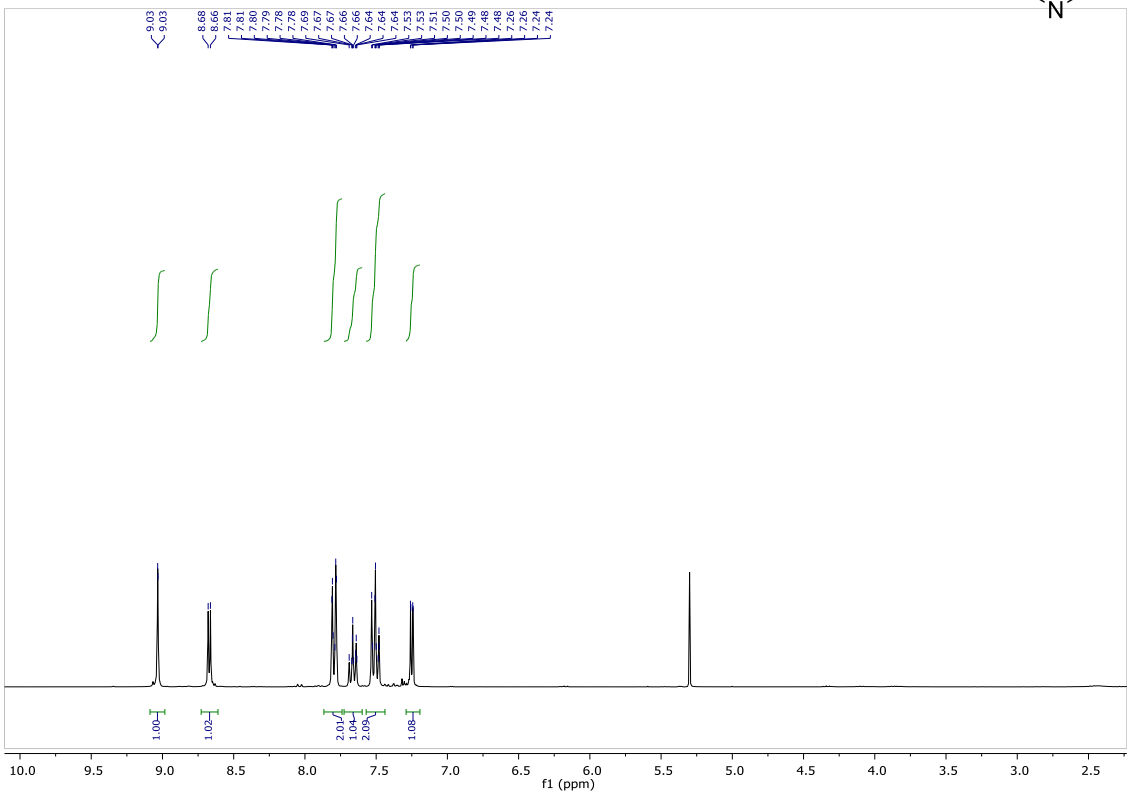
^{13}C – 75 MHz – $CDCl_3$



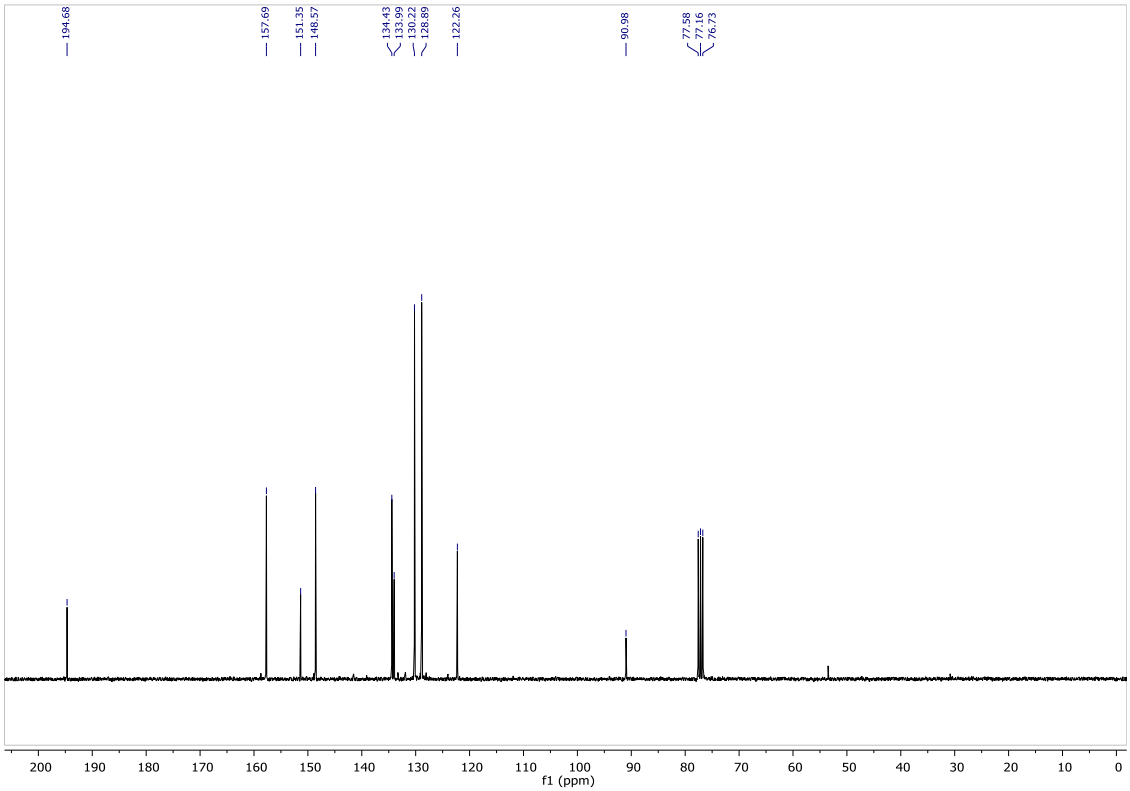
4-Benzoyl-3-iodopyridine (2b).



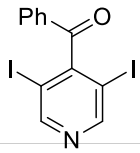
^{1}H – 300 MHz – $CDCl_3$



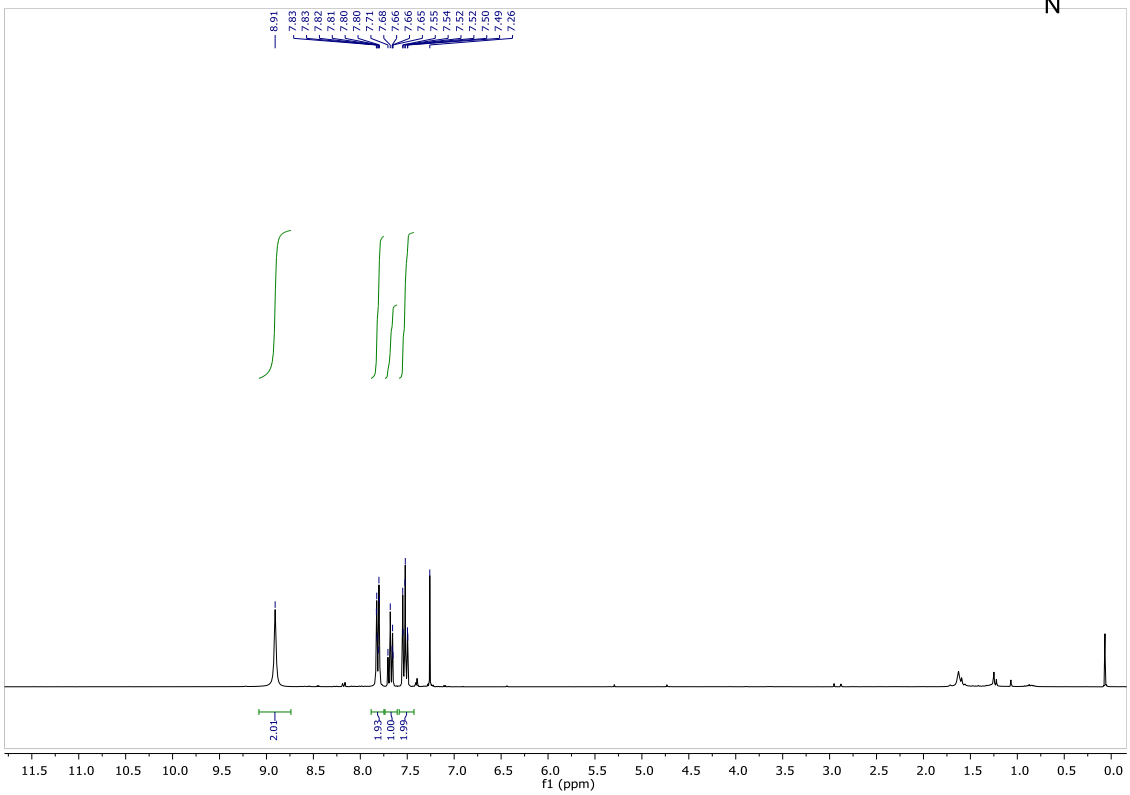
^{13}C – 75 MHz – $CDCl_3$



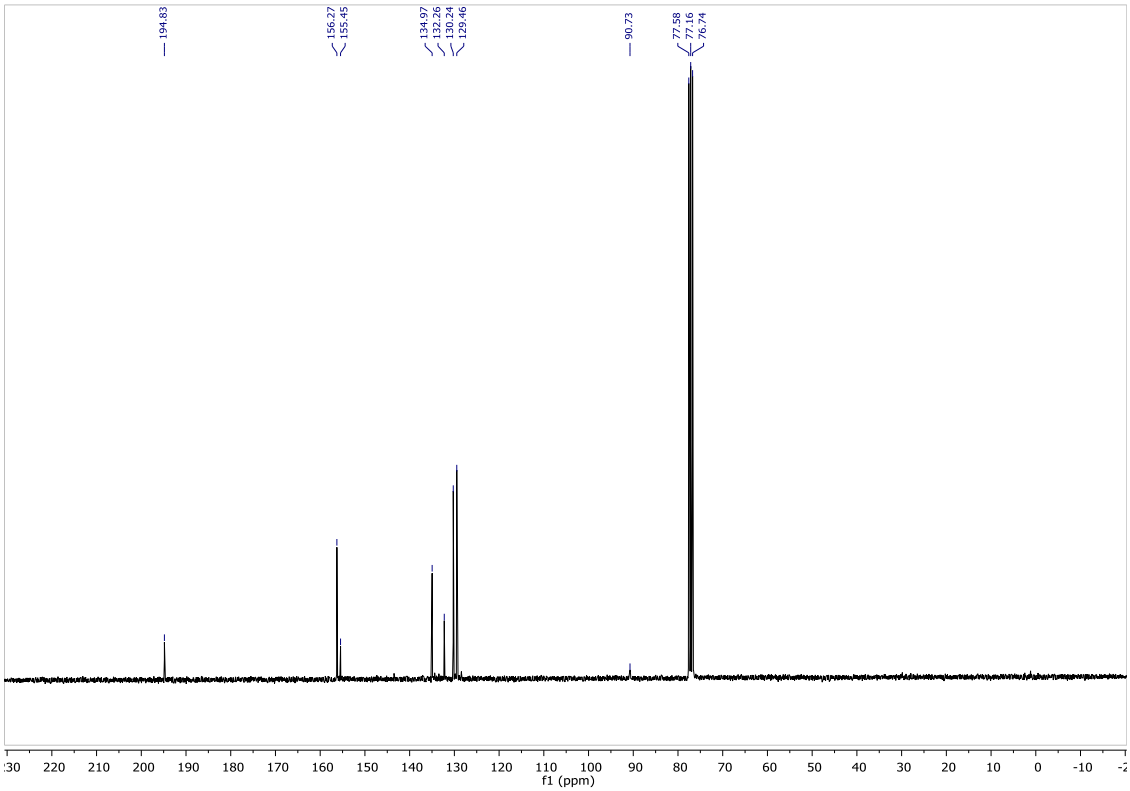
4-Benzoyl-3,5-diiodopyridine (2b').



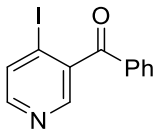
^{1}H – 300 MHz – $CDCl_3$



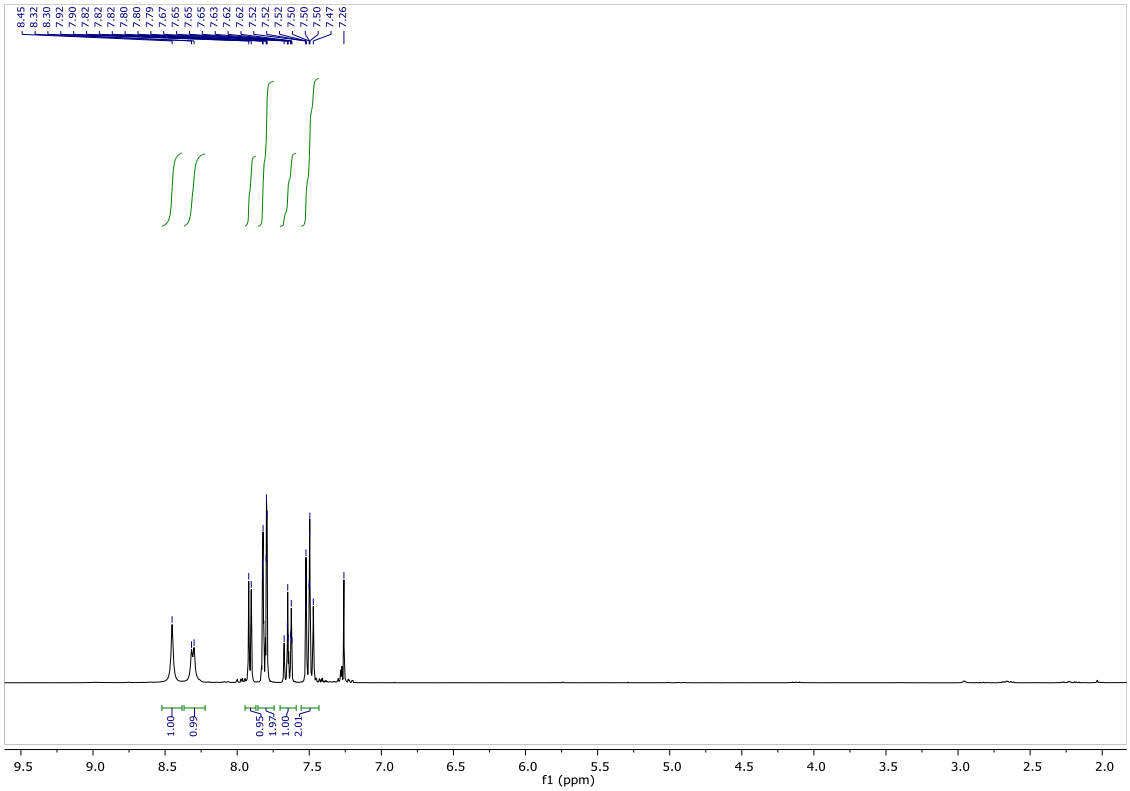
^{13}C – 75 MHz – $CDCl_3$



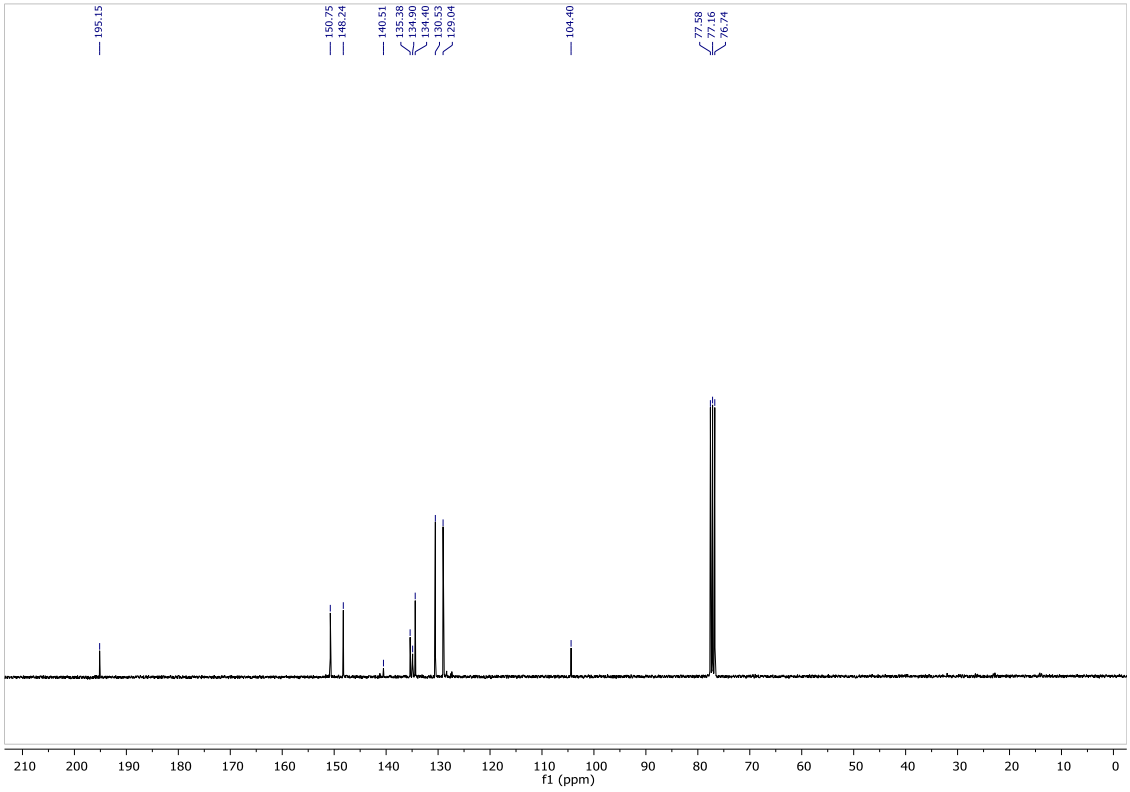
3-Benzoyl-4-iodopyridine (2c).



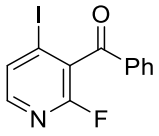
^{1}H – 300 MHz – $CDCl_3$



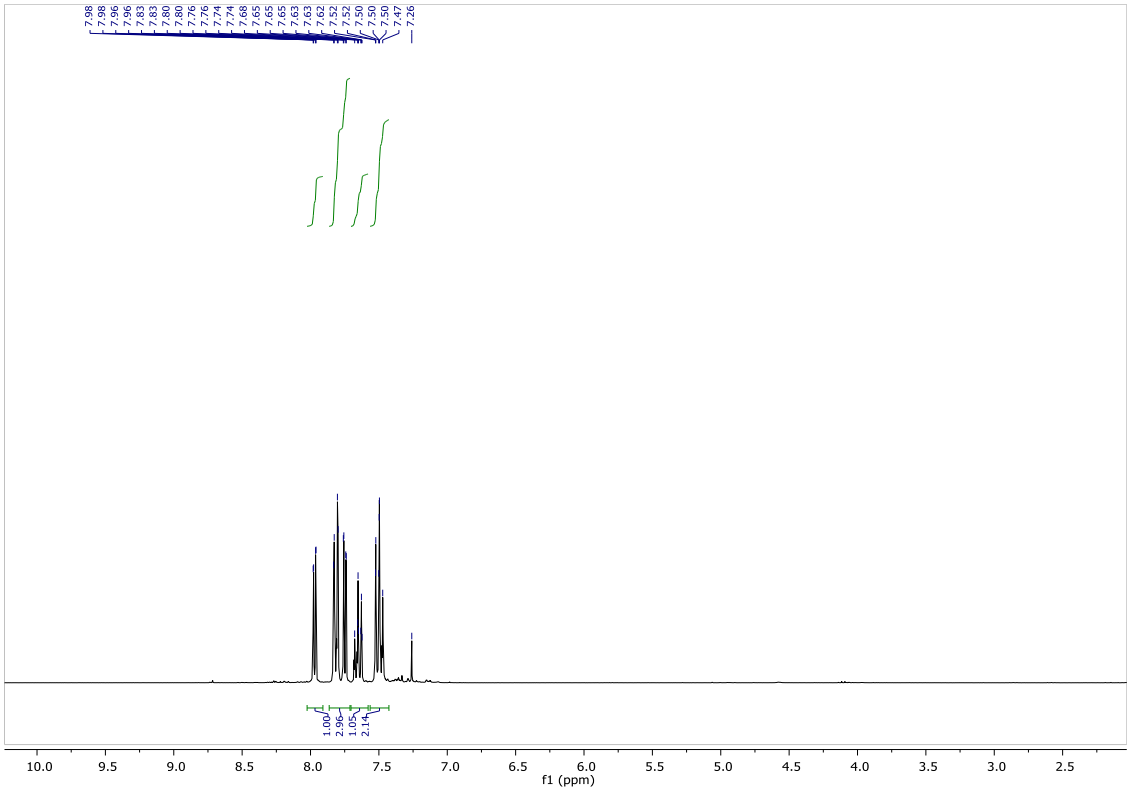
^{13}C – 75 MHz – $CDCl_3$



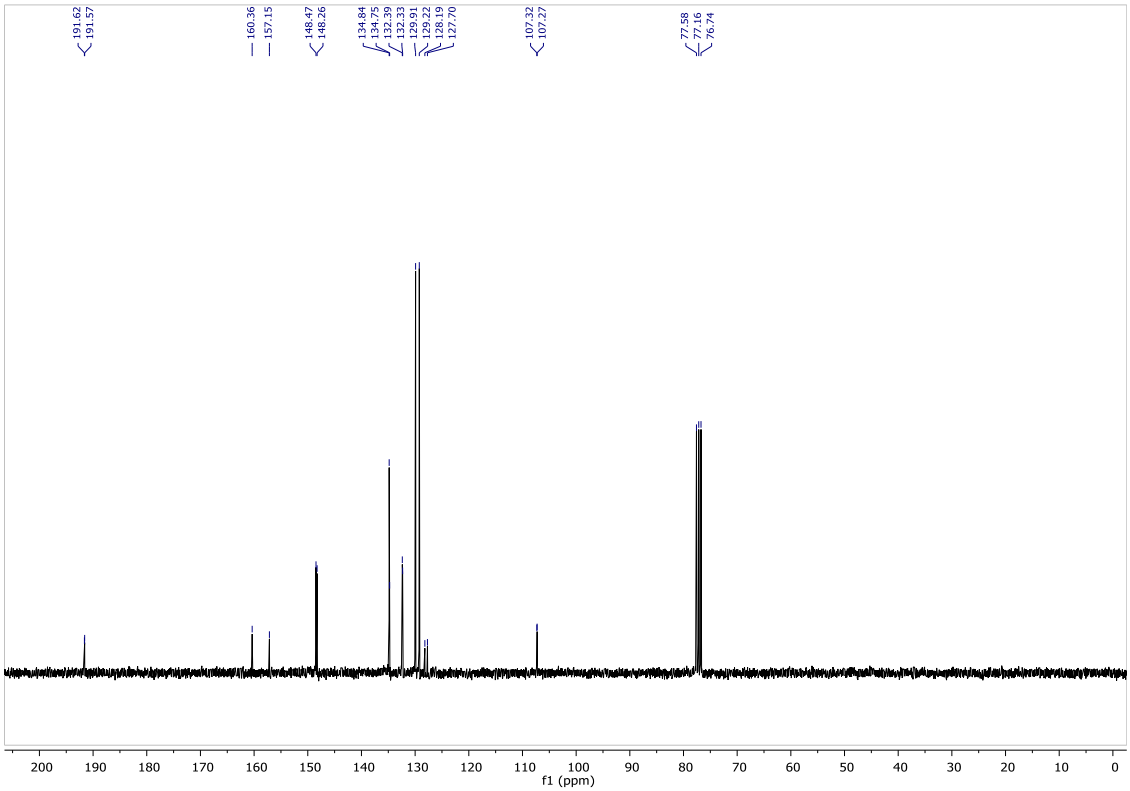
3-Benzoyl-2-fluoro-4-iodopyridine (2d).



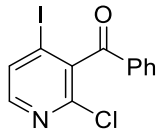
^{1}H – 300 MHz – $CDCl_3$



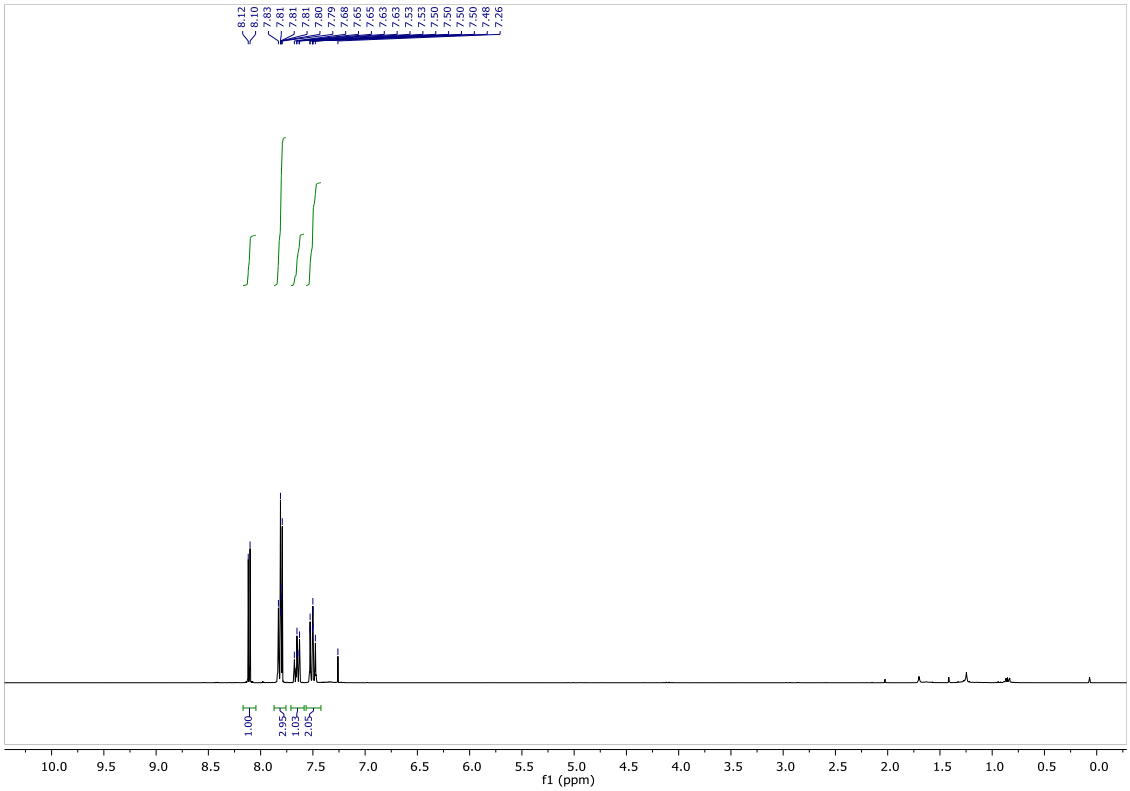
^{13}C – 75 MHz – $CDCl_3$



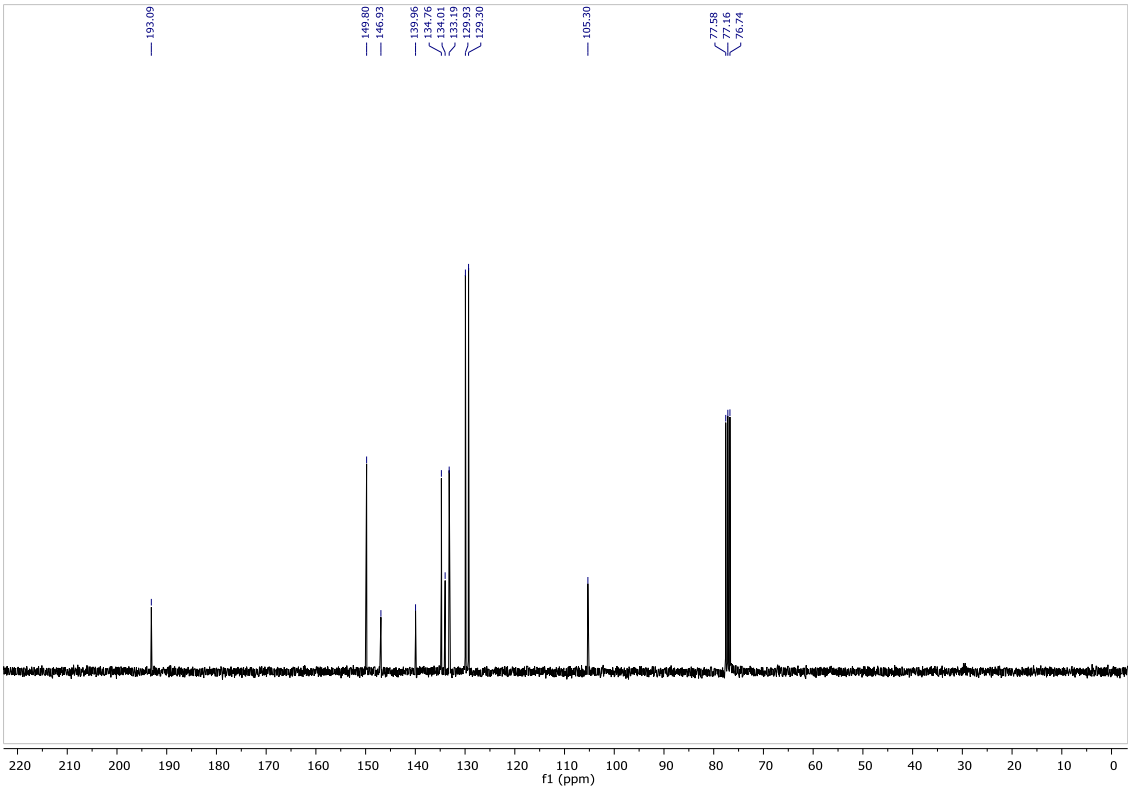
3-Benzoyl-2-chloro-4-iodopyridine (2e).



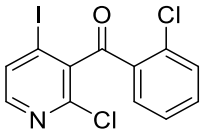
^{1}H – 300 MHz – $CDCl_3$



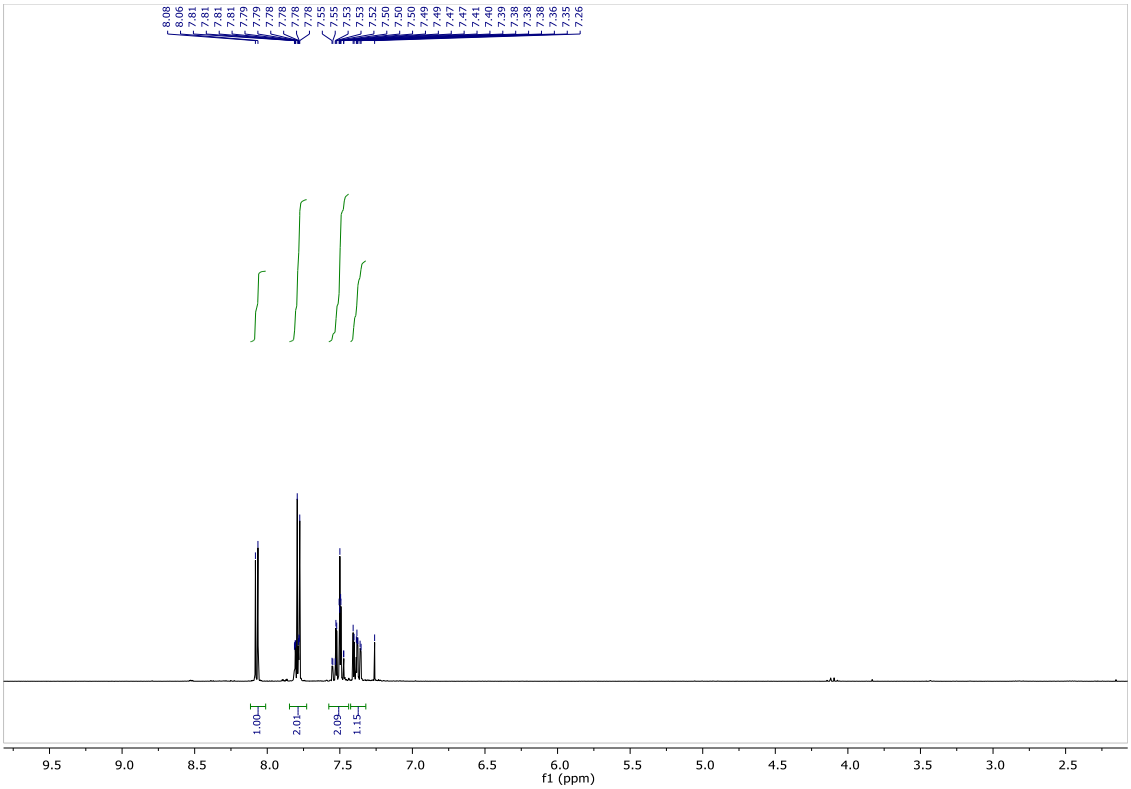
^{13}C – 75 MHz – $CDCl_3$



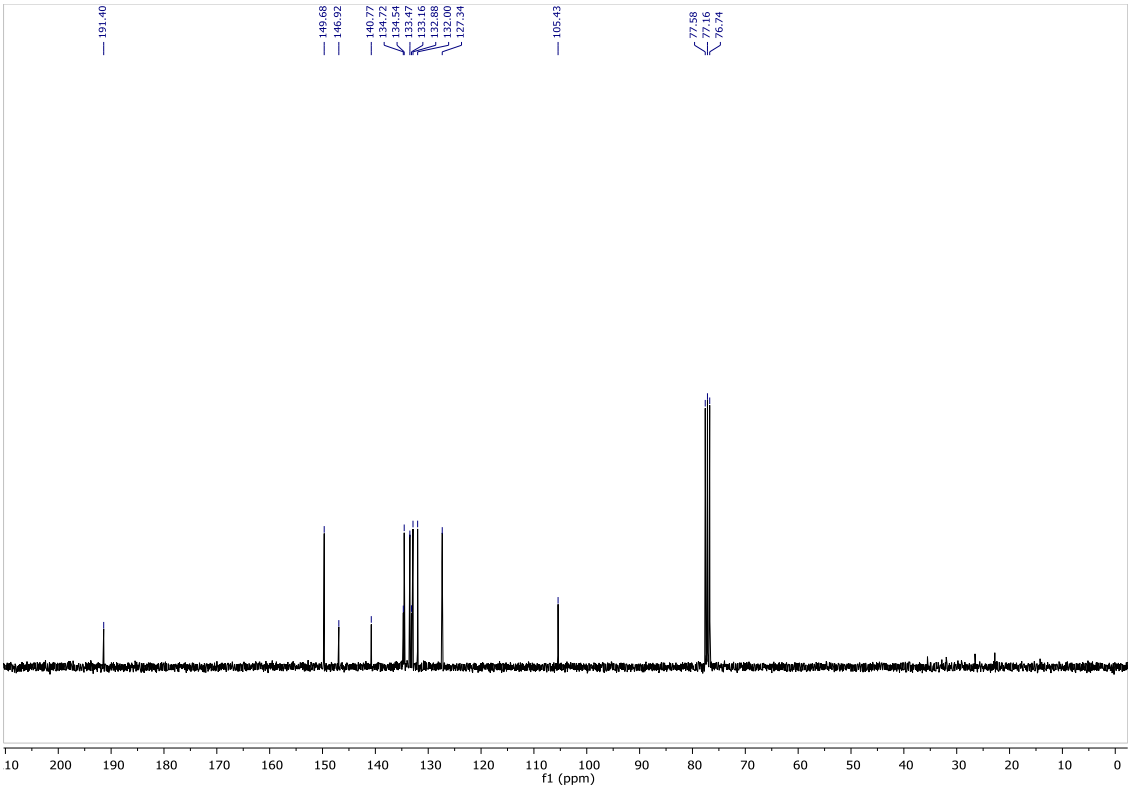
2-Chloro-3-(2-chlorobenzoyl)-4-iodopyridine (2f).



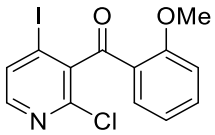
^{1}H – 300 MHz – $CDCl_3$



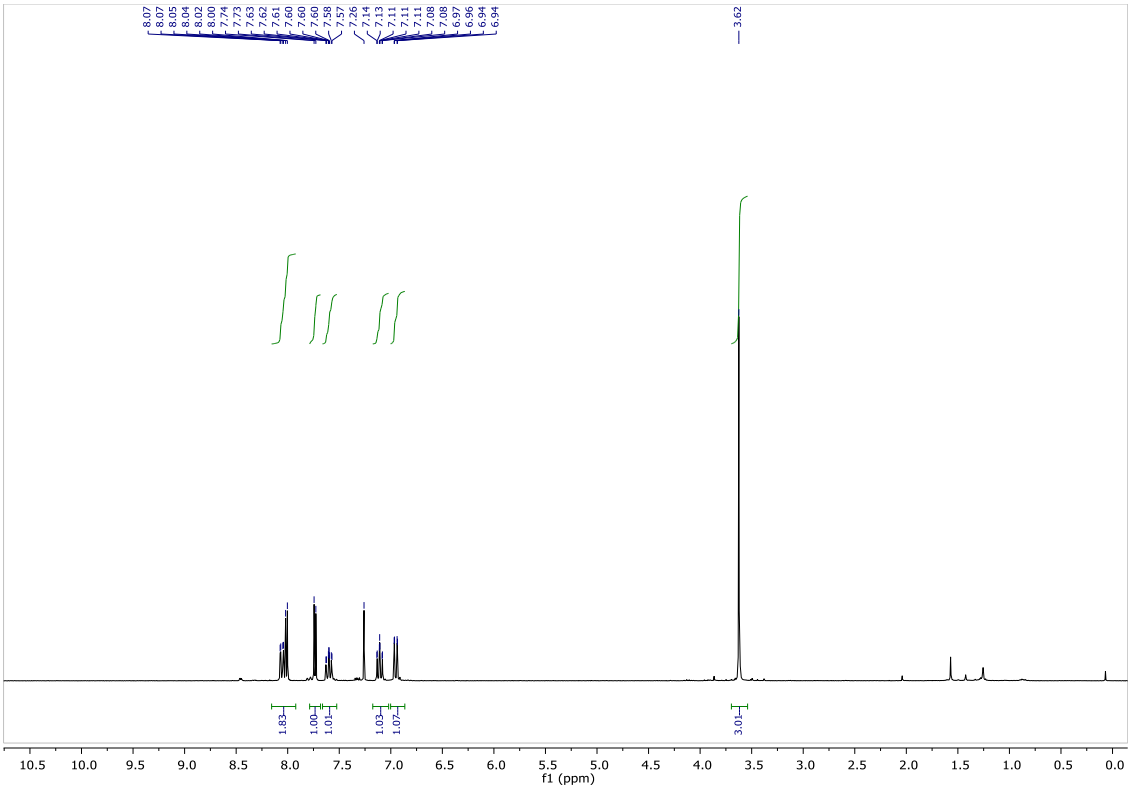
^{13}C – 75 MHz – $CDCl_3$



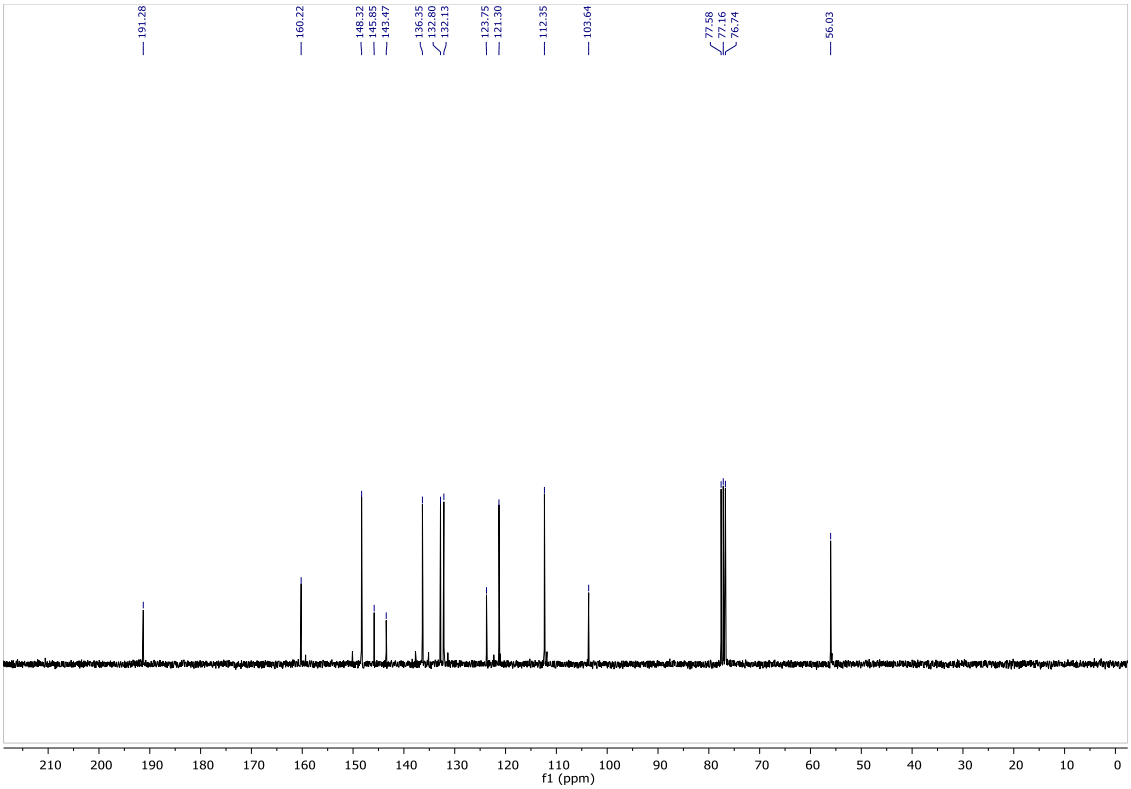
2-Chloro-4-iodo-3-(2-methoxybenzoyl)pyridine (2g).



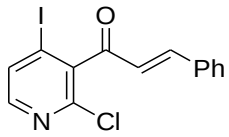
^{1}H – 300 MHz – $CDCl_3$



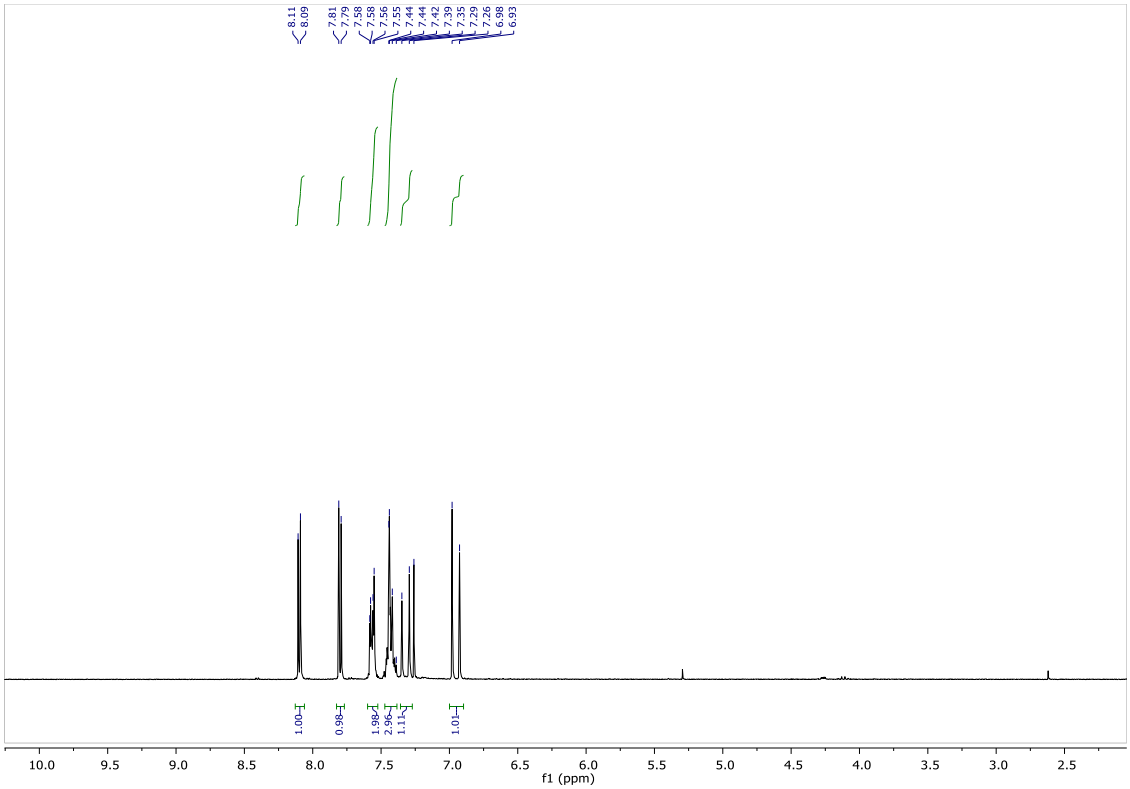
^{13}C – 75 MHz – $CDCl_3$



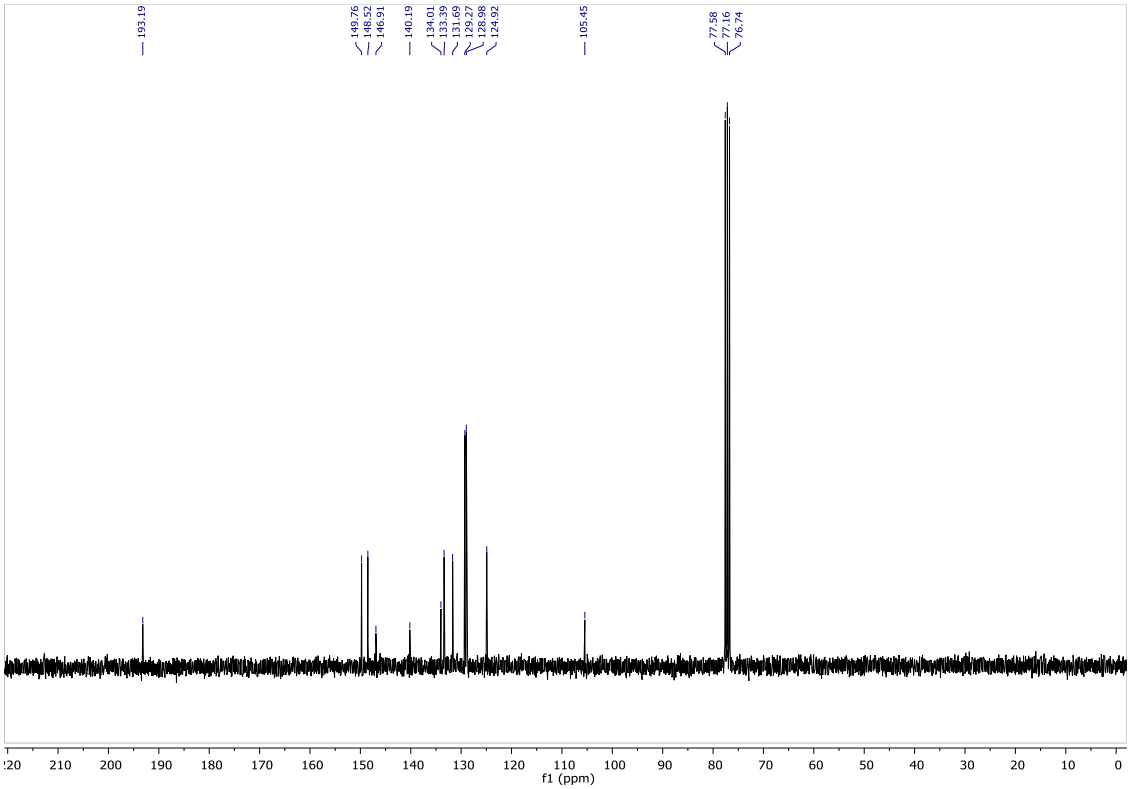
2-Chloro-3-cinnamoyl-4-iodopyridine (2h).



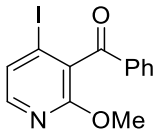
^{1}H – 300 MHz – $CDCl_3$



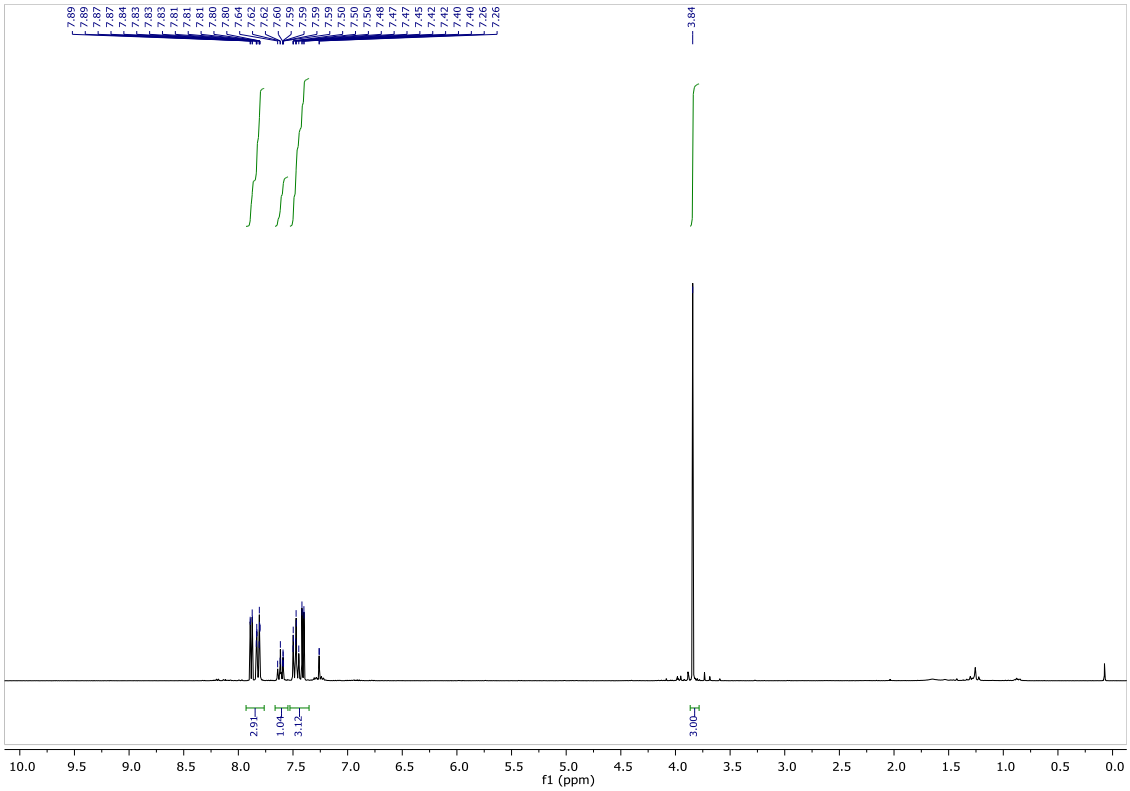
^{13}C – 75 MHz – $CDCl_3$



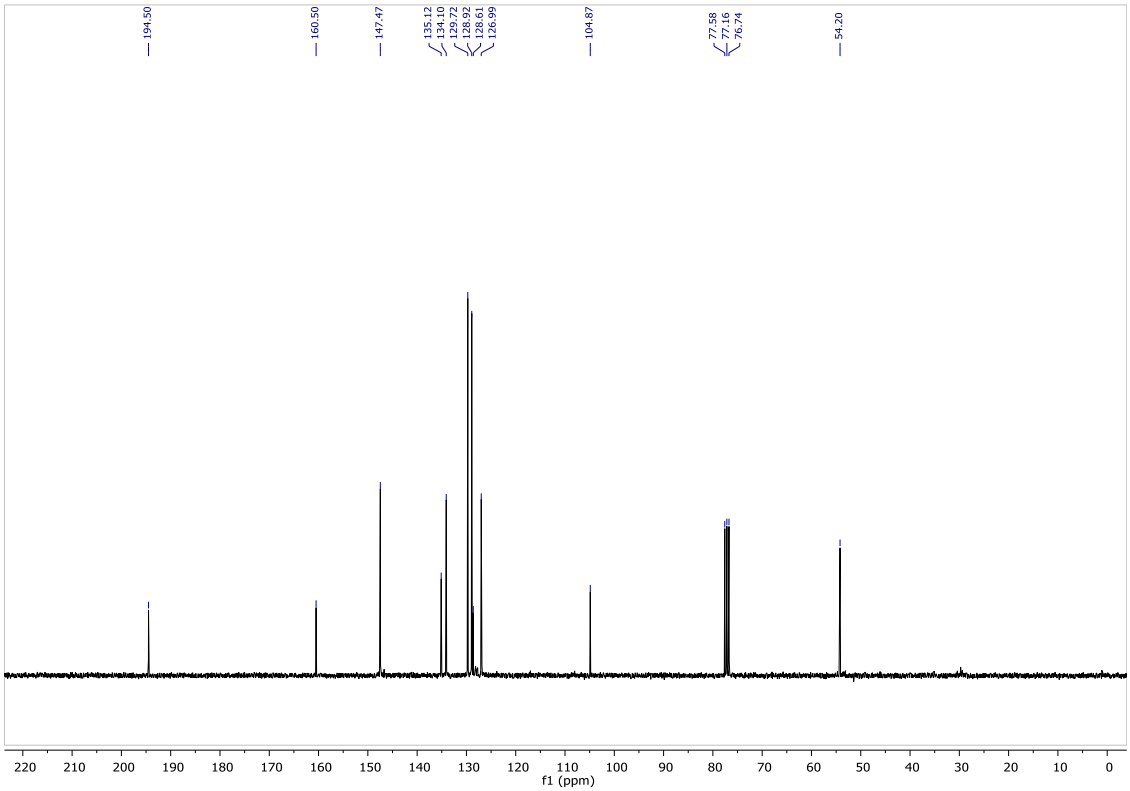
3-Benzoyl-4-iodo-2-methoxypyridine (2i).



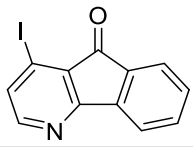
^{1}H – 300 MHz – $CDCl_3$



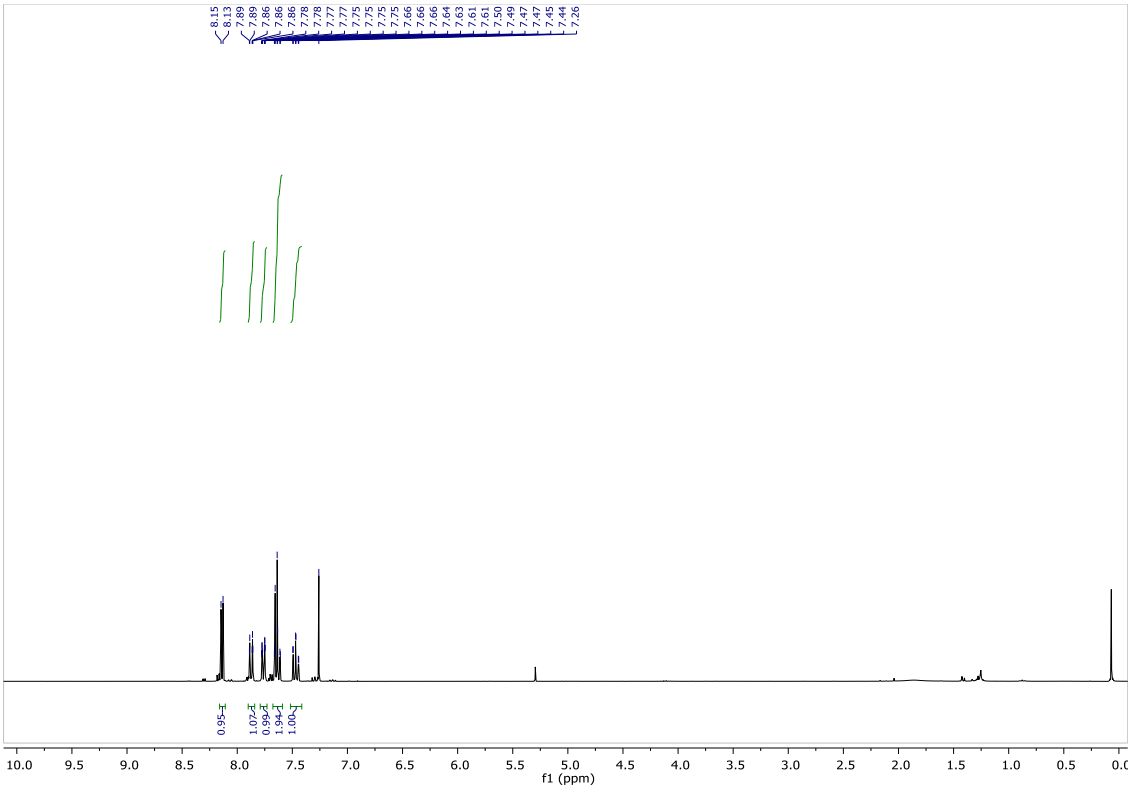
^{13}C – 75 MHz – $CDCl_3$



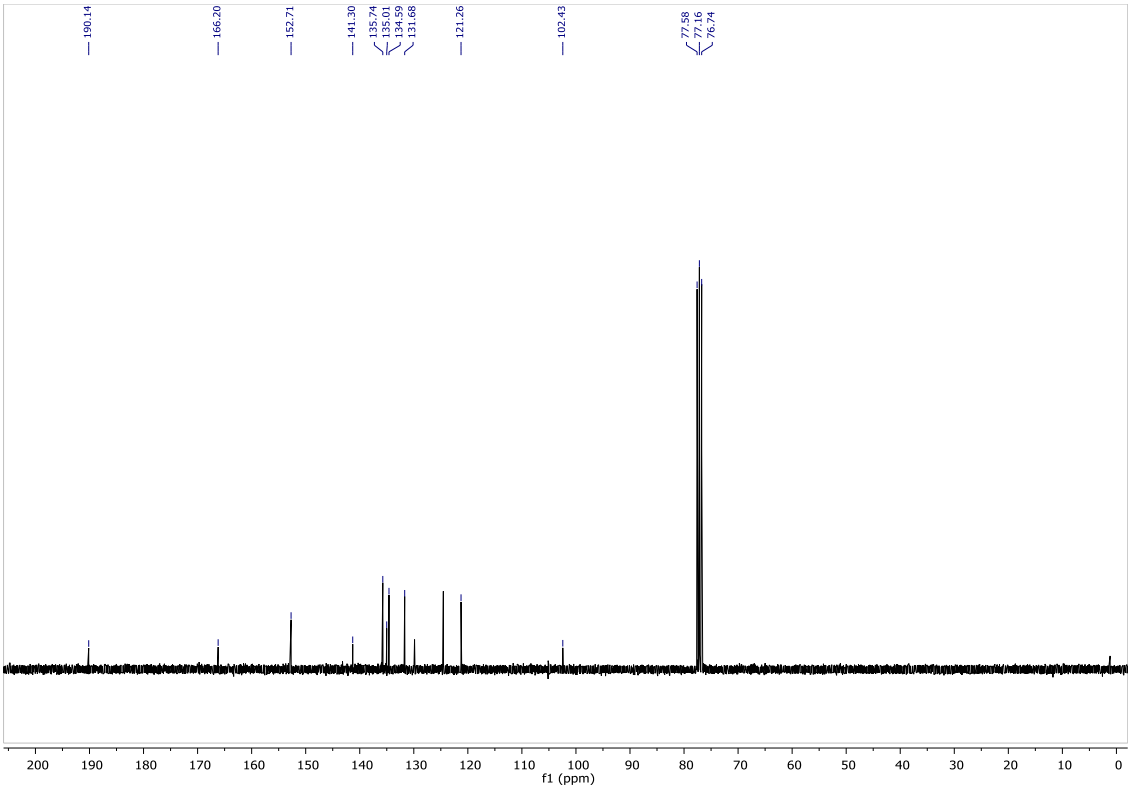
1-Iodo-4-azafluorenone (2j).



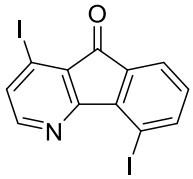
^{1}H – 300 MHz – $CDCl_3$



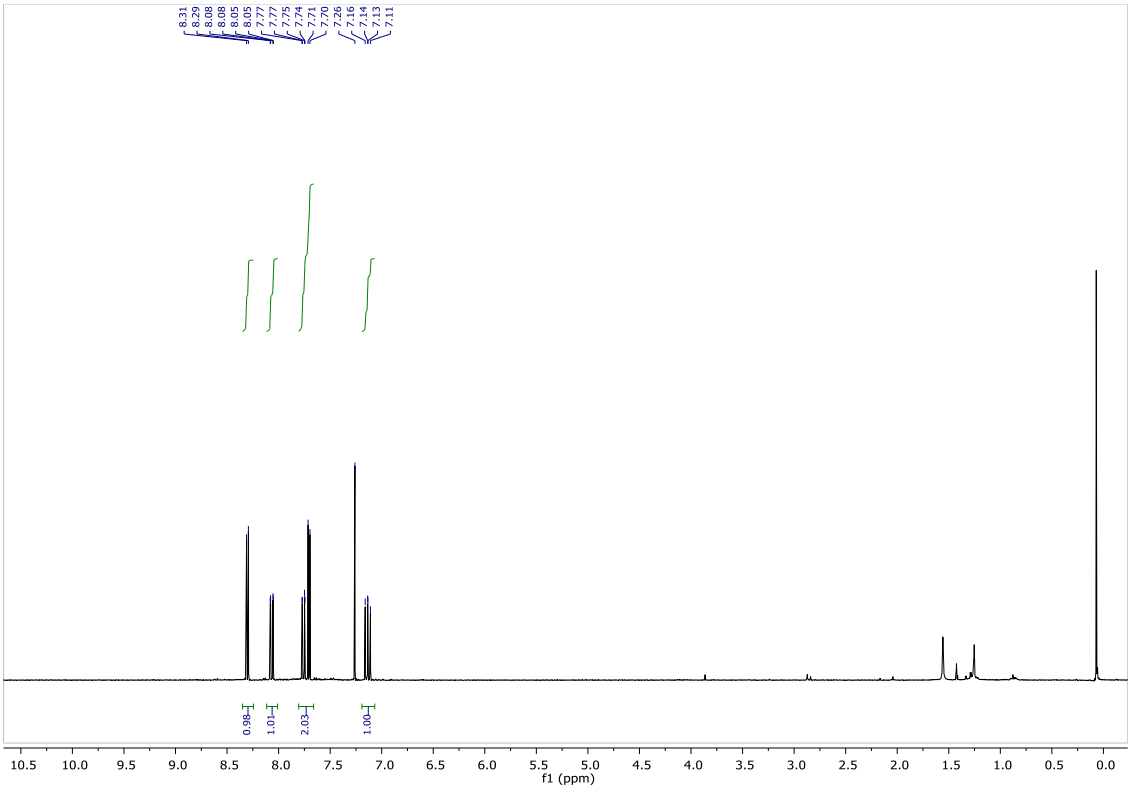
^{13}C – 75 MHz – $CDCl_3$



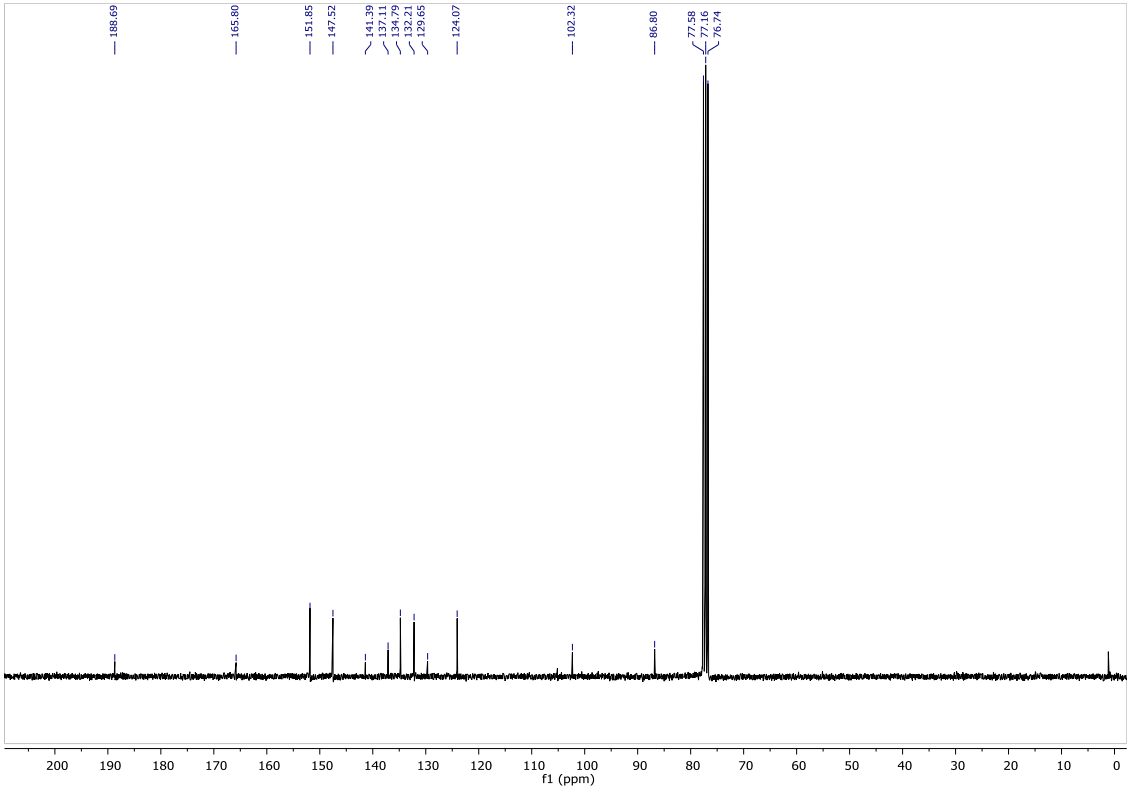
1,5-Diiodo-4-azafluorenone (2j').



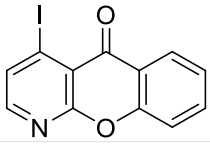
^{1}H – 300 MHz – $CDCl_3$



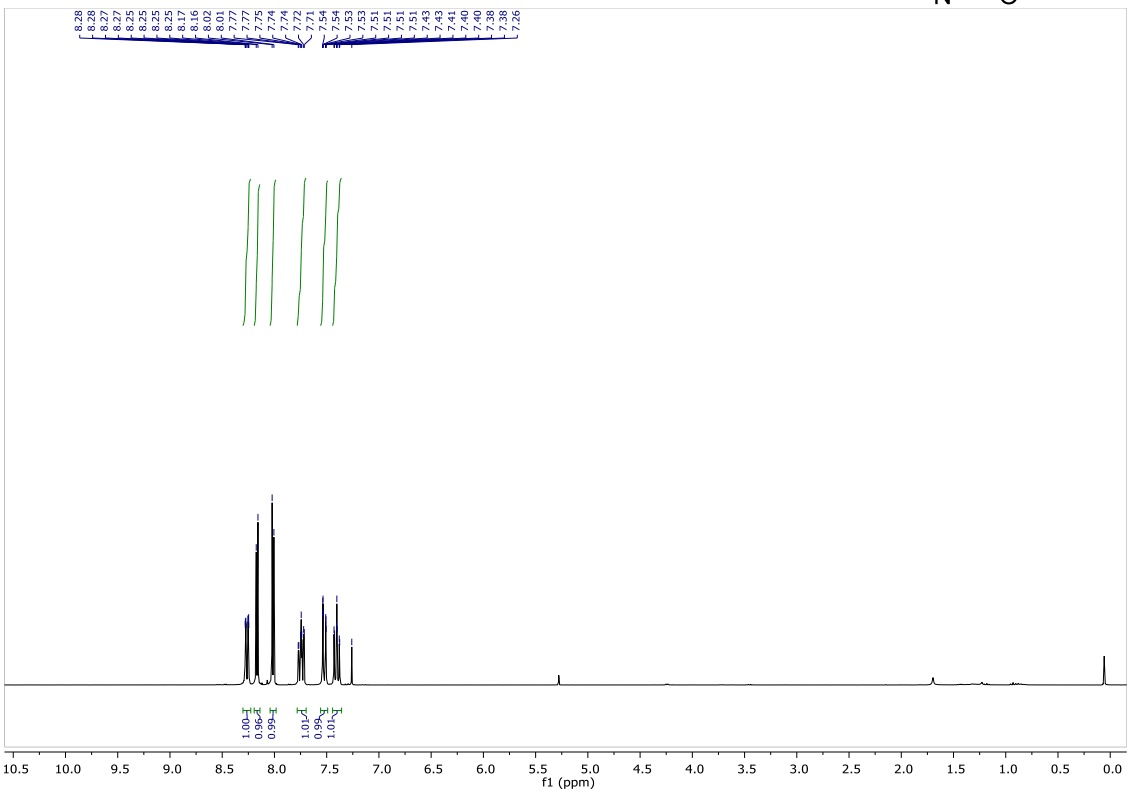
^{13}C – 75 MHz – $CDCl_3$



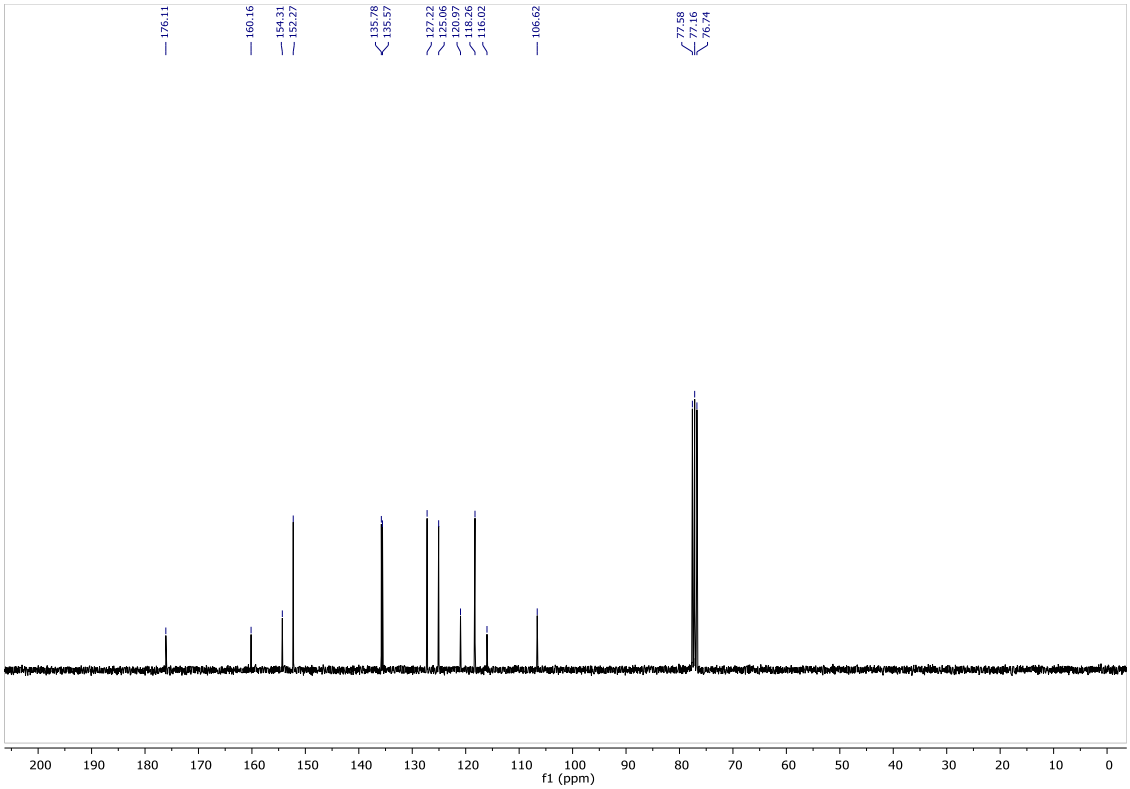
1-Iodo-4-azaxanthone (2k).



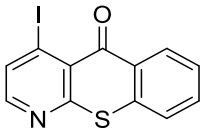
^{1}H – 300 MHz – $CDCl_3$



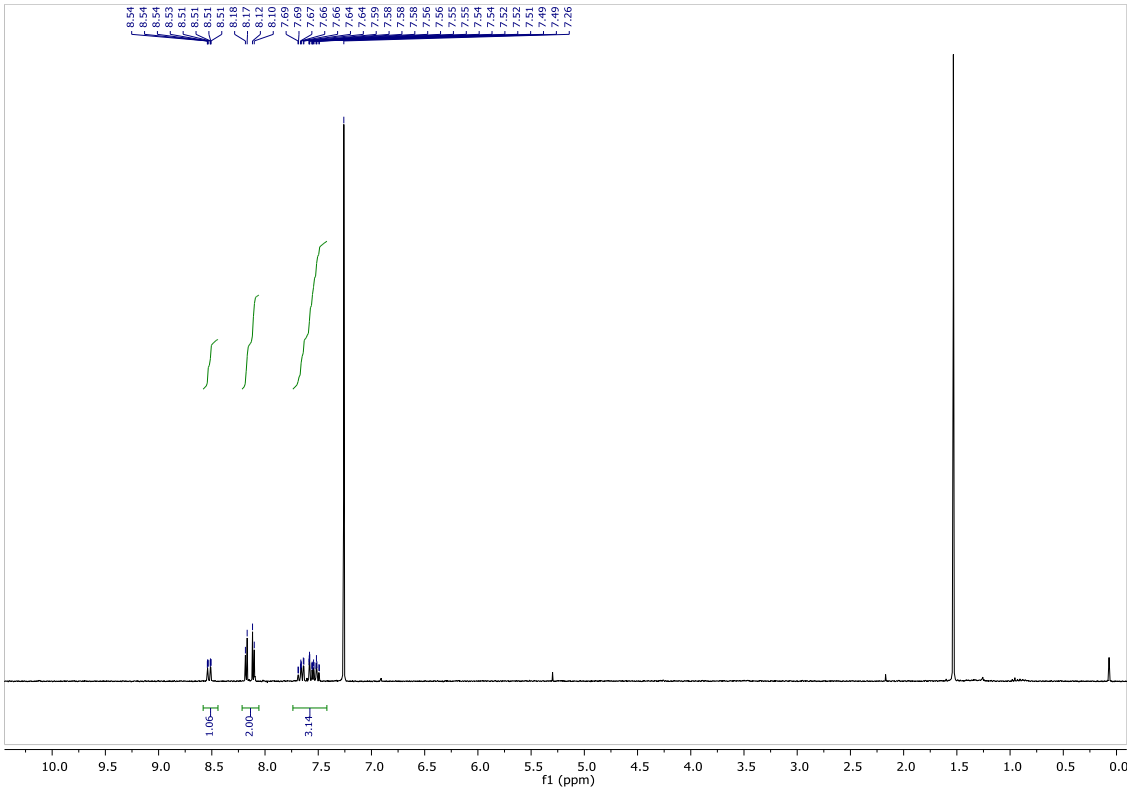
^{13}C – 75 MHz – $CDCl_3$



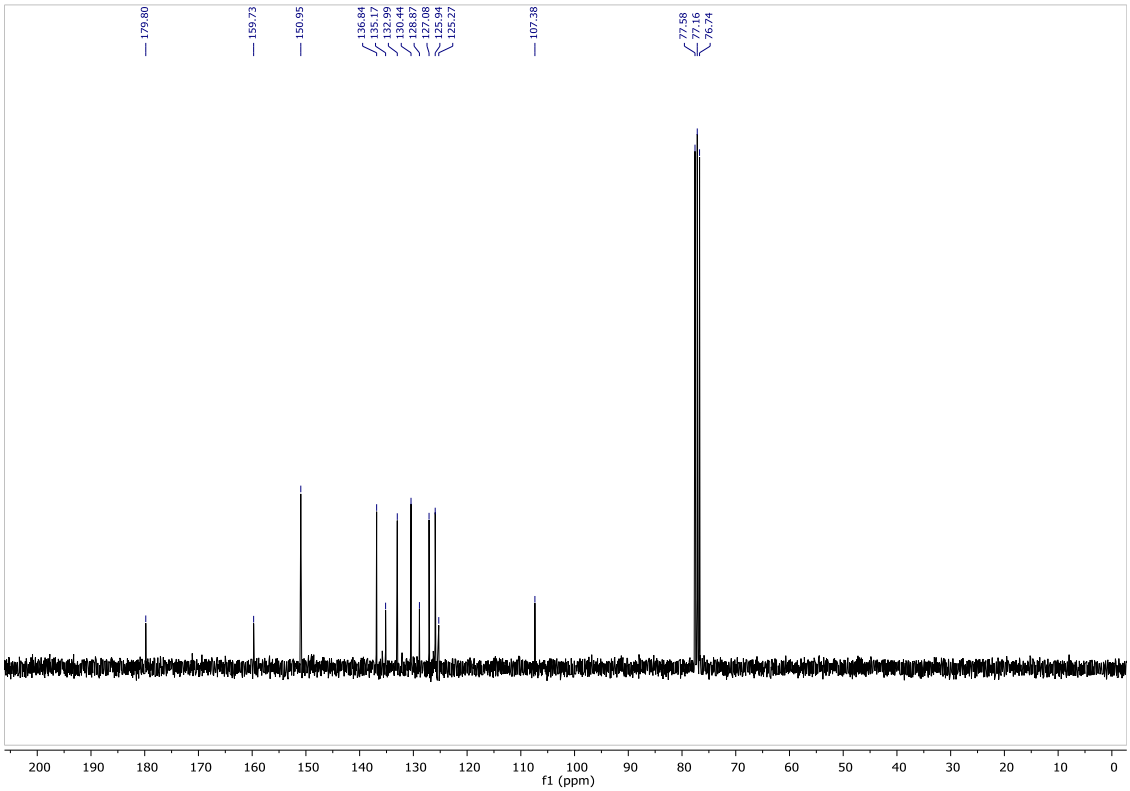
1-Iodo-4-azathioxanthone (2l).



^{1}H – 300 MHz – $CDCl_3$

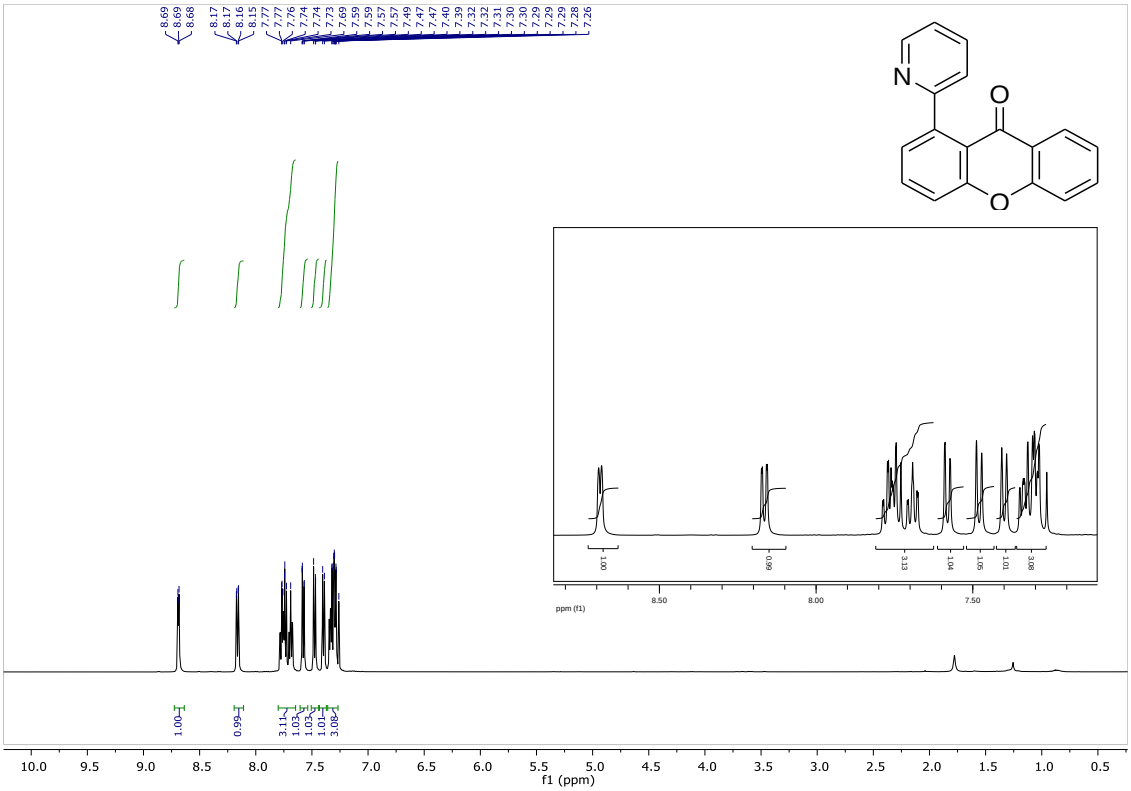


^{13}C – 75 MHz – $CDCl_3$

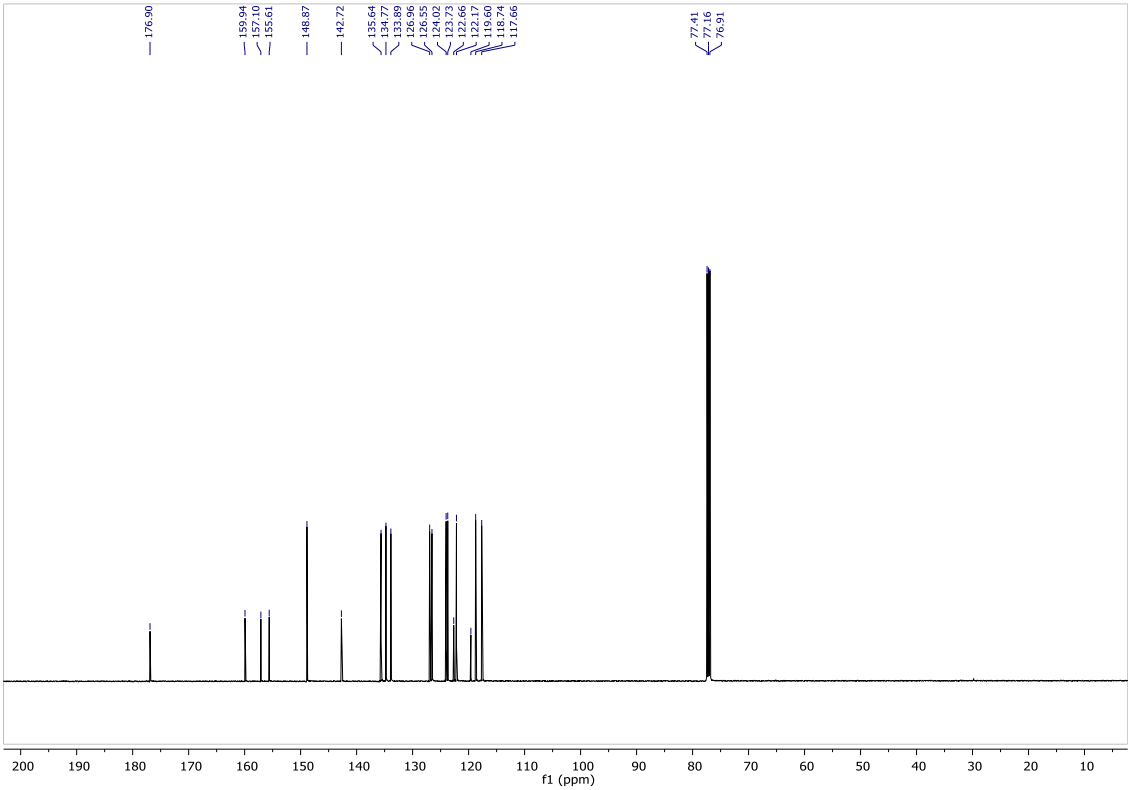


1-(2-Pyridyl)xanthone (2'm).

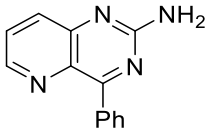
^{1}H – 500 MHz – $CDCl_3$



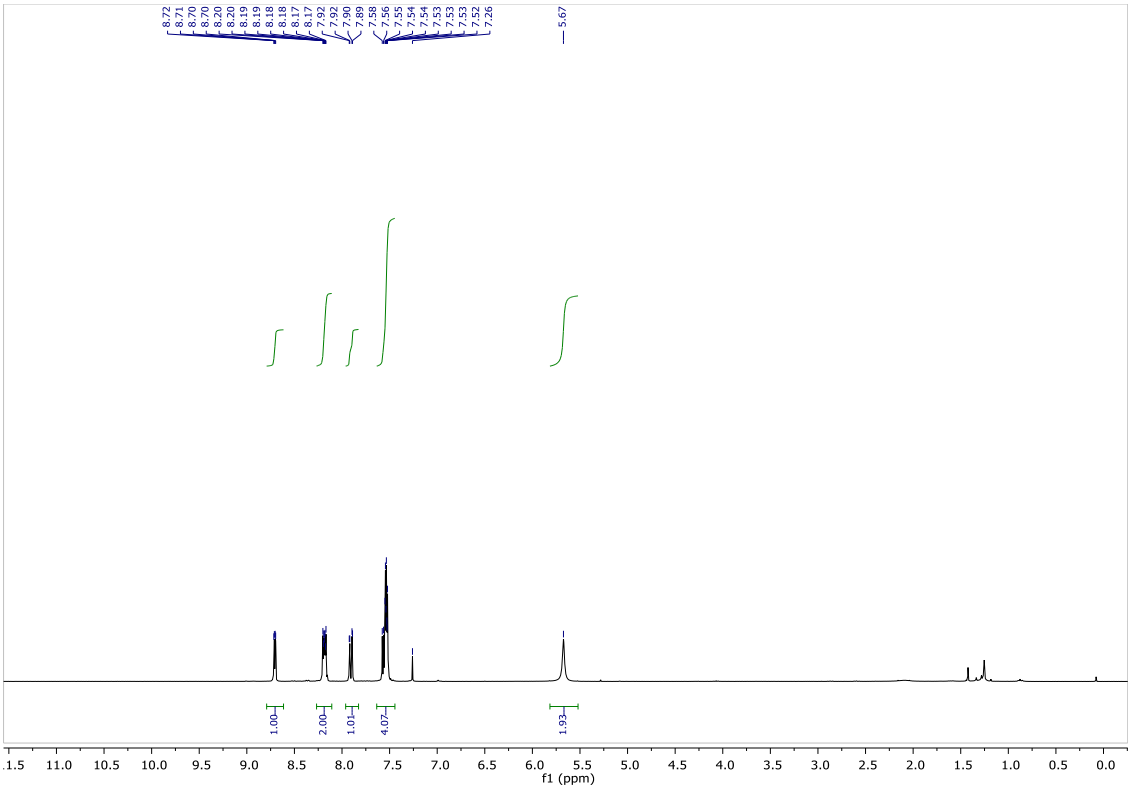
^{13}C – 125 MHz – $CDCl_3$



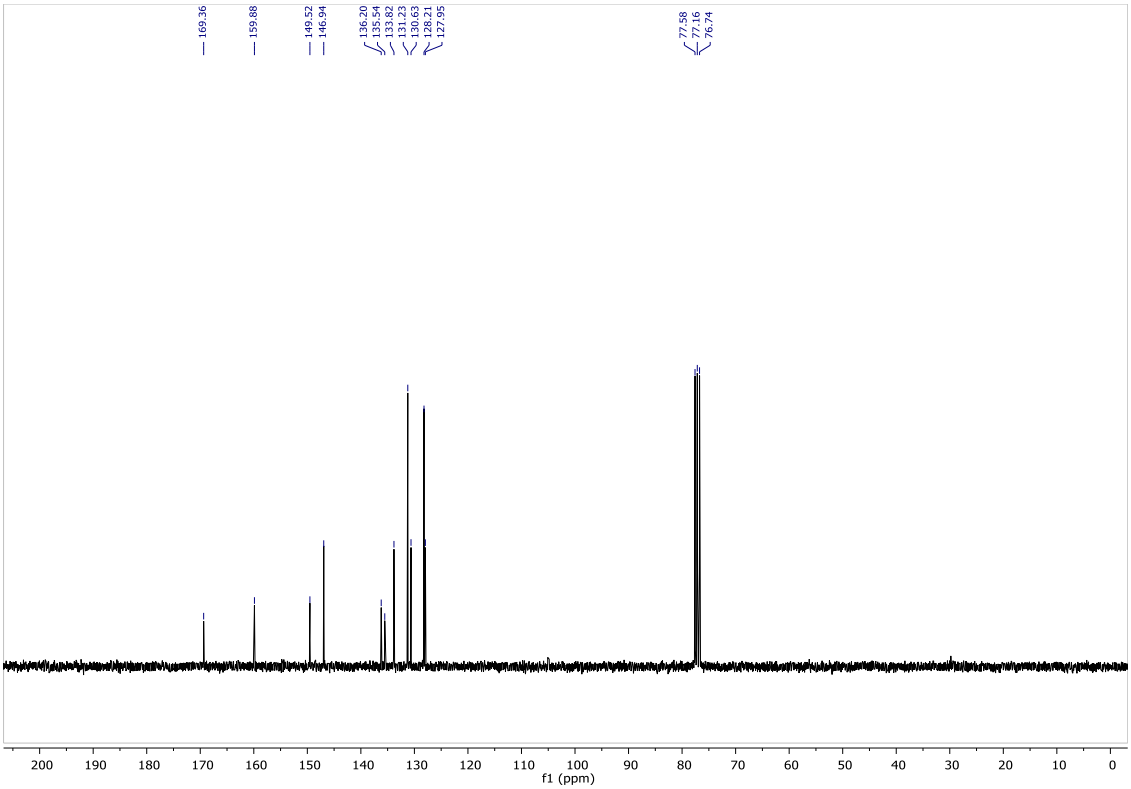
2-Amino-4-phenylpyrido[3,2-*d*]pyrimidine (3a).



^{1}H – 300 MHz – $CDCl_3$



^{13}C – 75 MHz – $CDCl_3$



4. Crystal Data

Crystallography. The samples were studied with monochromatized Mo-Kα radiation (λ = 0.71073 Å). X-ray diffraction data were collected by using D8 VENTURE Bruker AXS diffractometer (**2j'**, **2k'**) or APEXII Bruker-AXS diffractometer (**2n'**). For **2j'** and **2n'**, the structure was solved by direct methods using the SIR97 program,[14] and then refined with full-matrix least-square methods based on F^2 (SHELX-97)[15] with the aid of the WINGX program.[16] For **2k'**, the structure was solved by direct methods using the SHELXT program,[17] and then refined with full-matrix least-square methods based on F^2 (SHELXL-2014).[18] All non-hydrogen atoms were refined with anisotropic atomic displacement parameters. Except oxygen- or nitrogen-linked hydrogen atom that was introduced in the structural model through Fourier difference maps analysis, H atoms were finally included in their calculated positions. Molecular diagrams were generated by ORTEP-3 (version 2.02).[19]

Crystal data for 2j' (CCDC 1475309): $C_{12}H_5I_2NO$, M = 432.97, T = 150 K, monoclinic, P $2_1/c$, a = 17.4324(15), b = 4.1685(4), c = 15.7648(16) Å, β = 95.635(4) °, V = 1140.04(19) Å^3, Z = 4, d = 2.523 g cm^{-3}, μ = 5.492 mm^{-1}. A final refinement on F^2 with 2610 unique intensities and 145 parameters converged at $\omega R(F^2)$ = 0.1039 ($R(F)$ = 0.0428) for 2404 observed reflections with $I > 2\sigma(I)$.

Crystal data for 2k' (CCDC 1475009): $C_{12}H_5I_2NO_2$, M = 448.97, T = 150(2) K, monoclinic, P $2_1/c$, a = 4.3887(3), b = 23.7759(18), c = 11.1283(9) Å, β = 92.847(3) °, V = 1159.75(15) Å^3, Z = 4, d = 2.571 g cm^{-3}, μ = 5.410 mm^{-1}. A final refinement on F^2 with 2656 unique intensities and 154 parameters converged at $\omega R(F^2)$ = 0.0501 ($R(F)$ = 0.0225) for 2463 observed reflections with $I > 2\sigma(I)$.

Crystal data for 2n' (CCDC 1475010): $C_{26}H_{16}O_2$, M = 360.39, T = 150(2) K, monoclinic, P $2_1/c$, a = 8.1791(3), b = 15.1330(9), c = 14.8514(10) Å, β = 100.614(2) °, V = 1806.77(18) Å^3, Z = 4, d = 1.325 g cm^{-3}, μ = 0.083 mm^{-1}. A final refinement on F^2 with 4140 unique intensities and 256 parameters converged at $\omega R(F^2)$ = 0.1243 ($R(F)$ = 0.0541) for 2969 observed reflections with $I > 2\sigma(I)$.

5. Literature

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