Supplementary Material (ESI) for Chemical Communications

Supporting Information

A New Entry to 3-Acyl-2-aminobenzofurans: Palladium-Catalysed Cycloisomerisation of 2-(Cyanomethyl)phenyl Esters

Masahito Murai, Koji Miki, and Kouichi Ohe

Department of Energy and Hydrocarbon Chemistry, Graduate School of Engineering,

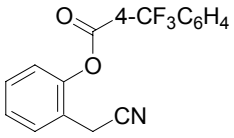
Kyoto University, Katsura, Nishikyo-ku, Kyoto 615-8510, Japan

e-mail: ohe@scl.kyoto-u.ac.jp

Table of Contents

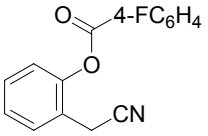
General Method. Unless otherwise noted, chemicals obtained from commercial suppliers were used without further purification. Solvents were dried by the usual methods and distilled before use. Zn powder was purified according to known methods prior to use.[1] All reactions were carried out under nitrogen atmosphere. NMR spectra were measured for solutions in $CDCl_3$ or acetone-d_6 with tetramethylsilane as an internal standard (^1H and ^{13}C): the following abbreviations are used; br: broad, s: singlet, d: doublet, t: triplet, q: quartet, m: multiplet. IR spectra were recorded with an FT-IR spectrometer. Melting points (mp) are uncorrected. Element analyses were performed at Microanalytical Center of Kyoto University. High-resolution mass spectra (HRMS) was measured with JEOL JMX-SX 102A spectrometer.

Preparation of 2-(Cyanomethyl)phenyl Esters 1

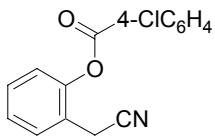


2-(Cyanomethyl)phenyl 4'-trifluoromethylbenzoate (1a): To a solution of 2-(cyanomethyl)phenol (666 mg, 5.0 mmol),[2] triethylamine (1.04 mL, 7.5 mmol), and 4-*N*,*N*-dimethylaminopyridine (6.1 mg, 0.05 mmol) in CH_2Cl_2 (20 mL) was added 4-trifluoromethylbenzoyl chloride (1.56 g, 7.5 mmol) at 0 ^oC and the mixture was stirred at room temperature for 3 h. The reaction mixture was poured into brine (20 mL), and extracted with Et_2O (20 mL x 3). The combined organic layer was dried over $MgSO_4$. The organic solvent was removed under reduced pressure and the residue was subjected to flash column chromatography on silica gel with hexane / AcOEt = 20/1 - 7/1 as eluents to afford 2-(cyanomethyl)phenyl 4'-trifluoromethylbenzoate **1a** (1.22 g, 4.0 mmol, 80% yield) as a white solid. mp 62.1-62.8 ^oC. IR (KBr): 751, 758, 771, 862, 1016, 1074, 1126, 1171, 1219, 1269, 1328, 1415, 1493, 1736 (C=O), 2259 (CN), 2945, 2981, 3062 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ3.66 (s, 2H), 7.28 (d, J = 7.6 Hz, 1H), 7.30 (t, J = 7.6 Hz, 1H), 7.41 (t, J = 7.6 Hz, 1H), 7.47 (d, J = 7.6 Hz, 1H), 7.77 (d, J = 8.0 Hz, 2H), 8.32 (d, J = 8.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ19.11, 116.7, 122.4, 122.5, 123.3 (q, J = 272.5 Hz), 125.6 (q, J = 3.3 Hz), 126.8, 129.5, 129.6, 130.5, 131.7, 135.1 (q, J = 32.3 Hz), 148.3, 163.0. Anal. calcd for $C_{16}H_{10}F_3NO_2$: C, 62.96; H, 3.30. found: C,

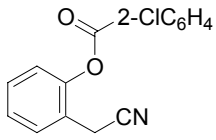
62.82; H, 3.41.



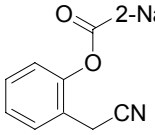
2-(Cyanomethyl)phenyl 4'-fluorobenzoate (1b): A white solid. mp 31.8-32.2 ^{o}C. IR (KBr): 756, 779, 853, 1011, 1061, 1096, 1150, 1170, 1198, 1217, 1267, 1413, 1456, 1504, 1603, 1733 (C=O), 2262 (CN), 2943, 2973 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ3.65 (s, 2H), 7.17 (d, J = 8.8 Hz, 2H), 7.26 (d, J = 7.6 Hz, 1H), 7.28 (t, J = 7.6 Hz, 1H), 7.40 (t, J = 7.6 Hz, 1H), 7.46 (d, J = 7.6 Hz, 1H), 8.22 (d, J = 8.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ19.04, 115.7, 115.9, 116.7, 122.5, 122.6, 124.7 (d, J = 3.3 Hz), 126.5, 129.4 (d, J = 8.2 Hz), 132.8 (d, J = 9.9 Hz), 148.4, 163.1, 166.1 (d, J = 255.9 Hz). Anal. calcd for $C_{15}H_{10}FNO_2$: C, 70.58; H, 3.95. found: C, 70.60; H, 3.99.



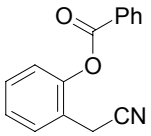
2-(Cyanomethyl)phenyl 4'-chlorobenzoate (1c): A white solid. mp 67.8-68.0 ^{o}C. IR (KBr): 759, 849, 955, 1012, 1095, 1170, 1220, 1275, 1401, 1456, 1492, 1594, 1722 (C=O), 2251 (CN), 2906, 2932 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ3.64 (s, 2H), 7.24 (d, J = 7.8 Hz, 1H), 7.28 (t, J = 7.3 Hz, 1H), 7.40 (t, J = 7.3 Hz, 1H), 7.46 (d, J = 7.8 Hz, 1H), 7.47 (d, J = 8.3 Hz, 2H), 8.13 (d, J = 8.3 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ19.00, 116.7, 122.5, 122.6, 126.6, 126.9, 129.0, 129.5, 129.6, 131.5, 140.4, 148.4, 163.4. Anal. calcd for $C_{15}H_{10}ClNO_2$: C, 66.31; H, 3.71. found: C, 66.11; H, 3.83.



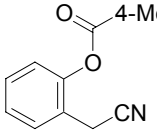
2-(Cyanomethyl)phenyl 2'-chlorobenzoate (1d): A white solid. mp 65.8-66.2 ^{o}C. IR (KBr): 756, 868, 947, 1032, 1099, 1172, 1220, 1243, 1401, 1456, 1492, 1594, 1722 (C=O), 2251 (CN), 2906, 2932 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ3.74 (s, 2H), 7.26-7.36 (m, 2H), 7.38-7.46 (m, 2H), 7.50-7.57 (m, 3H), 8.09 (d, J = 7.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ19.28, 116.9, 122.6, 122.7, 126.8, 126.9, 128.4, 129.6, 129.7, 131.5, 132.1, 133.7, 134.5, 148.5, 163.3. Anal. calcd for $C_{15}H_{10}ClNO_2$: C, 66.31; H, 3.71. found: C, 66.29; H, 3.58.



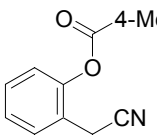
2-(Cyanomethyl)phenyl 2'-naphthoate (1e): A colorless oil. IR (neat): 761, 775, 825, 951, 1059, 1098, 1128, 1172, 1190, 1218, 1281, 1415, 1456, 1492, 1630, 1735 (C=O), 2251 (CN), 2942, 2968 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ3.70 (s, 2H), 7.28-7.32 (m, 2H), 7.42 (d, J = 7.6 Hz, 1H), 7.50 (d, J = 7.6 Hz, 1H), 7.56 (t, J = 7.6 Hz, 1H), 7.62 (t, J = 7.6 Hz, 1H), 7.89 (d, J = 8.4 Hz, 1H), 7.93 (d, J = 8.4 Hz, 1H), 7.98 (d, J = 8.4 Hz, 1H), 8.18 (d, J = 8.4 Hz, 1H), 8.81 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ19.13, 116.9, 122.7, 122.8, 125.2, 125.7, 126.6, 126.9, 127.8, 128.6, 128.9, 129.4, 129.5, 129.6, 132.2, 132.4, 135.9, 148.7, 164.5. Anal. calcd for $C_{19}H_{13}NO_2$: C, 79.28; H, 4.67. found: C, 79.43; H, 4.56.



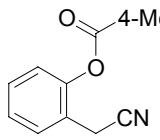
2-(Cyanomethyl)phenyl benzoate (1f): A white solid. mp 39.8-40.1 ^oC. IR (KBr): 751, 842, 1024, 1064, 1078, 1105, 1172, 1223, 1268, 1417, 1452, 1494, 1600, 1733 (C=O), 2255 (CN), 2963, 2975, 3061 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ3.65 (s, 2H), 7.23 (d, J = 8.0 Hz, 1H), 7.28 (t, J = 7.2 Hz, 1H), 7.39 (t, J = 8.0 Hz, 1H), 7.49 (t, J = 8.0 Hz, 2H), 7.52 (d, J = 8.0 Hz, 1H), 7.64 (t, J = 8.0 Hz, 1H), 8.21 (d, J = 7.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ19.05, 116.8, 122.6, 122.7, 126.5, 128.4, 128.6, 129.3, 129.4, 130.4, 133.9, 148.5, 164.1. Anal. calcd for $C_{15}H_{11}NO_2$: C, 75.94; H, 4.67. found: C, 76.18; H, 4.71.



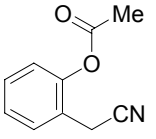
2-(Cyanomethyl)phenyl 4'-methylbenzoate (1g): A white solid. mp 44.8-45.3 ^oC. IR (KBr): 744, 837, 1019, 1072, 1103, 1170, 1221, 1269, 1417, 1457, 1493, 1610, 1735 (C=O), 2255 (CN), 2926, 2938 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ2.44 (s, 3H), 3.65 (s, 2H), 7.22-7.28 (m, 2H), 7.31 (d, J = 8.0 Hz, 2H), 7.41 (t, J = 7.6 Hz, 1H), 7.48 (t, J = 7.6 Hz, 1H), 8.10 (d, J = 8.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ18.98, 21.63, 116.9, 122.7, 122.8, 125.7, 126.4, 129.2, 129.3, 129.4, 130.2, 144.9, 148.7, 164.3. Anal. calcd for $C_{16}H_{13}NO_2$: C, 76.48; H, 5.21. found: C, 76.76; H, 5.21.



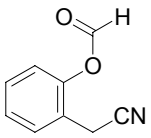
2-(Cyanomethyl)phenyl 4'-methoxybenzoate (1h): A white solid. mp 79.0-80.2 °C. IR (KBr): 753, 842, 1028, 1065, 1103, 1169, 1223, 1263, 1425, 1456, 1493, 1513, 1607, 1722 (C=O), 2245 (CN), 2842, 2929, 2959 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ3.67 (s, 2H), 3.89 (s, 3H), 7.00 (d, J = 8.4 Hz, 2H), 7.25 (d, J = 7.6 Hz, 1H), 7.29 (t, J = 7.6 Hz, 1H), 7.41 (t, J = 7.6 Hz, 1H), 7.49 (d, J = 7.6 Hz, 1H), 8.17 (d, J = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ19.09, 55.49, 114.0, 117.0, 120.7, 122.8, 122.9, 126.5, 129.4, 129.5, 132.4, 148.8, 164.0, 164.2. Anal. calcd for $C_{16}H_{13}NO_2$: C, 71.90; H, 4.90. found: C, 71.63; H, 4.89.



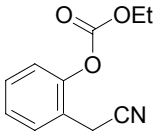
2-(Cyanomethyl)phenyl 4'-(*N*,*N*-dimethylamino)benzoate (1i): A pale yellow solid. mp 139.2-140.6 °C. IR (KBr): 761, 824, 1053, 1096, 1165, 1184, 1223, 1282, 1383, 1454, 1487, 1537, 1604, 1701 (C=O), 2247 (CN), 2826, 2925, 2960 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ3.06 (s, 6H), 3.66 (s, 2H), 6.69 (d, J = 9.2 Hz, 2H), 7.23 (d, J = 8.0 Hz, 1H), 7.26 (t, J = 8.0 Hz, 1H), 7.38 (t, J = 8.0 Hz, 1H), 7.48 (d, J = 8.0 Hz, 1H), 8.06 (d, J = 9.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ19.07, 39.94, 110.7, 114.5, 117.1, 122.8, 122.9, 126.0, 129.1, 129.2, 132.0, 148.9, 153.8, 164.4. Anal. calcd for $C_{17}H_{16}N_2O_2$: C, 72.84; H, 5.75. found: C, 72.54; H, 5.86.



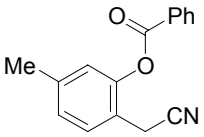
2-(Cyanomethyl)phenyl acetate (1j): A colorless oil. IR (neat): 753, 792, 830, 1011, 1095, 1171, 1202, 1370, 1417, 1456, 1492, 1588, 1768 (C=O), 2250 (CN), 2928, 2980, 3067 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ2.32 (s, 3H), 3.61 (s, 2H), 7.11 (d, J = 7.9 Hz, 1H), 7.25 (t, J = 7.9 Hz, 1H), 7.34 (t, J = 7.9Hz, 1H), 7.40 (d, J = 7.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ18.89, 20.63, 116.7, 122.2, 122.5, 126.2, 129.2, 129.3, 148.2, 168.4. Anal. calcd for $C_{13}H_9NO_2$: C, 68.56; H, 5.18. found: C, 68.39; H, 5.19.



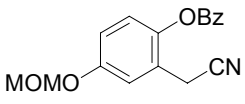
2-(Cyanomethyl)phenyl formate (1k): A colorless oil. IR (neat): 760, 830, 1085, 1116, 1172, 1215, 1415, 1457, 1493, 1589, 1740 (C=O), 2252 (CN), 2968, 3068 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ3.66 (s, 2H), 7.18 (d, J = 7.8 Hz, 1H), 7.29 (t, J = 7.8 Hz, 1H), 7.38 (t, J = 7.8 Hz, 1H), 7.47 (d, J = 7.8 Hz, 1H), 8.31 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ18.79, 116.7, 122.0, 122.1, 126.9, 129.5, 129.7, 147.4, 158.2. Anal. calcd for $C_9H_7NO_2$: C, 67.07; H, 4.38. found: C, 67.32; H, 4.64.



2-(Cyanomethyl)phenyl ethyl carbonate (1l): A colorless oil. IR (neat): 775, 897, 996, 1056, 1176, 1226, 1258, 1457, 1494, 1589, 1767 (C=O), 2251 (CN), 2986, 3068 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ1.38 (t, J = 7.31 Hz, 3H), 3.70 (s, 2H), 4.32 (q, J = 7.3 Hz, 2H), 7.28-7.30 (m, 2H), 7.36 (t, J = 7.8 Hz, 1H), 7.45 (d, J = 7.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ13.95, 18.61, 65.21, 116.7, 122.1, 122.2, 126.6, 129.3, 129.4, 148.6, 152.7. Anal. calcd for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40. found: C, 64.34; H, 5.43.



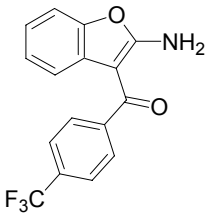
2-(Cyanomethyl)-5-methylphenyl benzoate (1m): A white solid. mp 74.0-74.6 ^oC. IR (neat): 712, 815, 892, 946, 1023, 1065, 1104, 1153, 1174, 1238, 1256, 1315, 1413, 1451, 1508, 1581, 1600, 1622, 1725 (C=O), 2247 (CN), 2857, 2920, 2970, 3032 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ2.33 (s, 3H), 3.56 (s, 2H), 7.04 (s, 1H), 7.05 (d, J = 7.3 Hz, 1H), 7.30 (d, J = 7.3 Hz, 1H), 7.47 (t, J = 7.3 Hz, 2H), 7.60 (t, J = 7.3 Hz, 1H), 8.19 (d, J = 7.3 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ18.41, 20.72, 116.9, 119.4, 123.0, 127.1, 128.5, 129.0, 129.9, 130.0, 133.7, 139.6, 148.3, 164.1. Anal. calcd for $C_{16}H_{13}NO_2$: C, 76.48; H, 5.21. found: C, 76.52; H, 5.32.



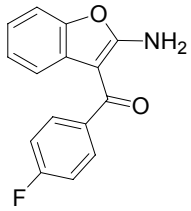
2-(cyanomethyl)-4-(methoxymethoxy)phenyl benzoate (1n): A pale yellow oil. IR (neat): 709, 804, 872, 923, 1010, 1059, 1077, 1102, 1153, 1188, 1265, 1315, 1452, 1499, 1602, 1739 (C=O), 2251 (CN), 2828, 2957, 3070 cm^{-1}. ^1H NMR (400 MHz,

$CDCl_3$): δ 3.49 (s, 3H), 3.64 (s, 2H), 5.18 (s, 2H), 7.08 (d, J = 8.3 Hz, 1H), 7.17 (s, 1H), 7.18 (d, J = 8.3 Hz, 1H), 7.53 (t, J = 7.3 Hz, 2H), 7.66 (t, J = 7.3 Hz, 1H), 8.21 (d, J = 7.3 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.26, 56.04, 94.68, 116.7, 117.0, 117.3, 123.6, 128.6, 128.7, 130.2, 130.3, 134.0, 143.0, 155.3, 164.7. Anal. calcd for $C_{17}H_{15}NO_4$: C, 68.68; H, 5.09. found: C, 68.52; H, 5.16.

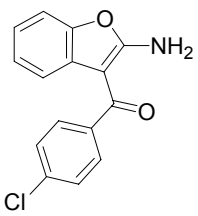
General Procedure of Palladium-Catalysed Cycloisomerisation Reactions. A flame dried Schlemk flask was charged with $Pd(OAc)_2$ (6.7 mg, 0.030 mmol), PCy_3 (16.9 mg, 0.060 mmol), zinc powder (19.6 mg, 0.30 mmol), MS4A (30 mg), and DMF (1.2 mL). After stirring at room temperature for 20 min, 2-(cyanomethyl)phenyl ester **1** (0.30 mmol) was added and the resulting mixture was stirred at 100 ^{o}C. After the time specified in Tables 1-2, the mixture was diluted with Et_2O and filtered through a short silica gel pad. The filtrate was washed with brine, and the aqueous layer was extracted with Et_2O (10 mL x 3). The combined organic layer was dried over $MgSO_4$, then filtered. The organic solvent was removed under reduced pressure and the residue was subjected to flash column chromatography on silica gel with hexane / AcOEt = 7/1 - 2/1 as eluents to afford the corresponding 3-acyl-2-aminobenzofuran **2**.



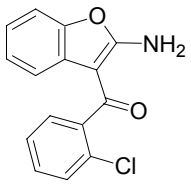
2-Amino-3-(4'-trifluoromethylbenzoyl)benzo[*b*]furan (2a): A yellow solid. mp 117.8~119.5 ^{o}C. IR (KBr): 745, 784, 854, 918, 978, 1018, 1067, 1123, 1177, 1240, 1298, 1327, 1480, 1515, 1593, 1650 (C=O), 2940, 3120, 3161, 3369 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.76 (d, J = 7.2 Hz, 1H), 7.00 (t, J = 7.6 Hz, 1H), 7.05 (t, J = 7.6 Hz, 1H), 7.20 (d, J = 7.2 Hz, 1H), 7.38 (br, 2H), 7.74 (d, J = 8.4 Hz, 2H), 7.80 (d, J = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 94.23, 110.1, 118.5, 122.2, 123.8 (q, J = 271.7 Hz), 123.9, 125.4 (q, J = 3.3 Hz), 125.6, 127.7, 132.2 (q, J = 32.2 Hz), 144.0, 149.2, 166.9, 188.8. Anal. calcd for $C_{16}H_{10}F_3NO_2$: C, 62.96; H, 3.30. found: C, 63.09; H, 3.22.



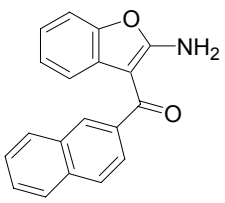
2-Amino-3-(4'-fluorobenzoyl)benzo[*b*]furan (2b): A pale yellow solid. mp 107.2-108.4 ^{o}C. IR (KBr): 745, 781, 849, 916, 977, 1021, 1095, 1153, 1177, 1240, 1298, 1336, 1478, 1509, 1599, 1644 (C=O), 2930, 3119, 3164, 3368 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ6.91 (d, J = 6.8 Hz, 1H), 7.00-7.07 (m, 2H), 7.11-7.19 (m, 4H), 7.23 (d, J = 6.8 Hz, 1H), 7.73 (d, J = 8.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ94.24, 110.1, 115.3 (d, J = 22.4 Hz), 118.7, 121.9, 123.7, 126.1, 129.9 (d, J = 8.3 Hz), 136.9 (d, J = 3.3 Hz), 149.1, 164.2 (d, J = 250.1 Hz), 166.5, 189.3. Anal. calcd for $C_{15}H_{10}FNO_2$: C, 70.58; H, 3.95. found: C, 70.67; H, 3.91.



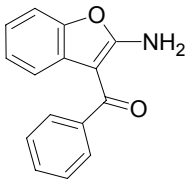
2-Amino-3-(4'-chlorobenzoyl)benzo[*b*]furan (2c): A yellow solid. mp 122.1-122.7 ^{o}C. IR (KBr): 750, 777, 840, 917, 975, 1016, 1095, 1173, 1241, 1337, 1437, 1477, 1591, 1614, 1642 (C=O), 3169, 3393 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ6.90 (d, J = 7.3 Hz, 1H), 7.03 (t, J = 7.8 Hz, 1H), 7.04 (t, J = 7.8 Hz, 1H), 7.09 (br, 2H), 7.23 (d, J = 7.3 Hz, 1H), 7.46 (d, J = 8.3 Hz, 2H), 7.66 (d, J = 8.3 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ94.23, 110.2, 118.8, 122.1, 123.9, 128.6, 129.1, 130.9, 137.0, 139.2, 149.2, 166.7, 189.2. Anal. calcd for $C_{15}H_{10}ClNO_2$: C, 66.31; H, 3.71. found: C, 66.34; H, 3.53.



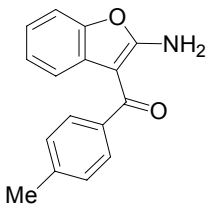
2-Amino-3-(2'-chlorobenzoyl)benzo[*b*]furan (2d): A yellow solid. mp 120.7-121.8 ^{o}C. IR (KBr): 741, 761, 851, 920, 979, 1018, 1098, 1181, 1238, 1338, 1442, 1495, 1594, 1614, 1656 (C=O), 3114, 3246, 3380 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ6.26 (d, J = 7.3 Hz, 1H), 6.94 (t, J = 7.3 Hz, 1H), 7.01 (t, J = 7.3 Hz, 1H), 7.20 (d, J = 7.3 Hz, 2H), 7.37 (br, 2H), 7.42 (m, 2H), 7.50 (d, J = 7.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ95.28, 110.0, 117.9, 122.0, 124.1, 125.8, 127.1, 127.7, 130.0, 130.3, 130.5, 140.5, 149.3, 166.3, 188.0. Anal. calcd for $C_{15}H_{10}ClNO_2$: C, 66.31; H, 3.71. found: C, 66.38; H, 3.60.



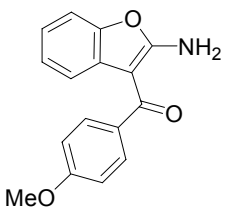
2-Amino-3-(2'-naphtoyl)benzo[*b*]furan (2e): A yellow solid. mp 47.8-49.2 ^{o}C. IR (KBr): 744, 783, 812, 915, 976, 1018, 1099 1177, 1229, 1298, 1334, 1481, 1507, 1597, 1614 1647 (C=O), 2951, 3054, 3194, 3360 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ6.85-6.94 (m, 2H), 6.95 (t, J = 6.8 Hz, 1H), 7.11 (d, J = 7.6 Hz, 1H), 7.43 (br, 2H), 7.45-7.55 (m, 2H), 7.84 (d, J = 8.0 Hz, 1H), 7.86 (t, J = 6.8 Hz, 2H), 7.92 (d, J = 8.0 Hz, 1H), 8.22 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ94.37, 109.9, 118.8, 121.7, 123.6, 124.5, 126.2, 126.4, 127.2, 127.6, 127.7, 128.1, 128.7, 132.4, 134.4, 137.9, 149.0, 166.7, 190.3 Anal. calcd for $C_{19}H_{13}NO_2$: C, 79.43; H, 4.56. found: C, 79.44; H, 4.64.



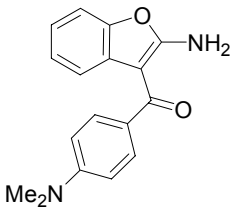
2-Amino-3-benzoylbenzo[*b*]furan (2f): A yellow solid. mp 138.9-140.3 ^{o}C. IR (KBr): 749, 762, 794, 906, 930, 974, 1017, 1104, 1173, 1185, 1243, 1300, 1338, 1437, 1481, 1596, 1618, 1645 (C=O), 2938, 3054, 3153, 3207, 3410 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ6.85 (d, J = 7.2 Hz, 1H), 6.95-7.02 (m, 2H), 7.18 (d, J = 7.2 Hz, 1H), 7.33 (br, 2H), 7.45-7.53 (m, 3H), 7.75 (d, J = 6.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ94.60, 109.8, 118.7, 121.7, 123.5, 126.1, 127.2, 128.2, 130.6, 140.8, 149.0, 166.5, 191.0. Anal. calcd for $C_{15}H_{11}NO_2$: C, 75.94; H, 4.67. found: C, 76.11; H, 4.66.



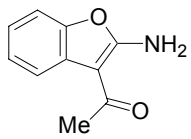
2-Amino-3-(4'-methylbenzoyl)benzo[*b*]furan (2g): A yellow solid. mp 108.6-109.2 ^{o}C. IR (KBr): 746, 776, 833, 914, 971, 1018, 1100, 1175, 1242, 1298, 1332, 1439, 1479, 1596, 1610, 1646 (C=O), 2946, 3190, 3205, 3364 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ2.42 (s, 3H), 6.98 (d, J = 8.0 Hz, 1H), 6.97-7.03 (m, 2H), 7.17-7.19 (m, 1H), 7.21 (br, 2H), 7.26 (d, J = 7.6 Hz, 2H), 7.62 (d, J = 7.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ21.51, 94.22, 109.9, 119.0, 121.7, 123.6, 126.4, 127.6, 128.9, 138.0, 141.2, 149.1, 166.6, 190.7. Anal. calcd for $C_{16}H_{13}NO_2$: C, 76.48; H, 5.21. found: C, 76.64; H, 5.20.



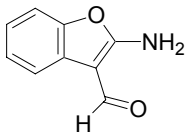
2-Amino-3-(4'-methoxybenzoyl)benzo[*b*]furan (2h): A yellow solid. mp 115.8-116.5 ^{o}C. IR (KBr): 743, 780, 844, 915, 975, 1025, 1103, 1170, 1185, 1245, 1299, 1337, 1437, 1482, 1589, 1605, 1647 (C=O), 2940, 3046, 3192, 3247, 3379 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ3.84 (s, 3H), 6.97 (d, J = 7.2 Hz, 1H), 6.95-7.02 (m, 4H), 7.18-7.21 (m, 1H), 7.27 (br, 2H), 7.74 (d, J = 7.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ55.25, 94.54, 109.8, 113.3, 118.8, 121.5, 123.4, 126.4, 129.6, 133.3, 149.0, 161.6, 166.4, 190.1. Anal. calcd for $C_{16}H_{13}NO_3$: C, 71.90; H, 4.90. found: C, 71.67; H, 4.90.



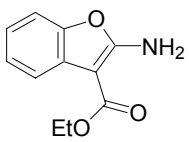
2-Amino-3-(4'-*N*,*N*-dimehylaminobenzoyl)benzo[*b*]furan (2i): A yellow solid. mp 54.2-55.8 ^{o}C. IR (KBr): 744, 780, 825, 914, 970, 1018, 1100, 1174, 1186, 1248, 1298, 1337, 1430, 1476, 1601, 1646 (C=O), 2952, 3195, 3218, 3385 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ3.05 (s, 6H), 6.71 (d, J = 7.2 Hz, 2H), 6.89 (br, 2H), 7.00-7.08 (m, 2H), 7.23-7.25 (m, 2H), 7.75 (d, J = 7.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ40.08, 94.40, 109.8, 110.7, 119.3, 121.3, 123.4, 127.0, 128.0, 130.0, 149.1, 152.5, 166.0, 190.1. Anal. calcd for $C_{17}H_{16}N_2O_2$: C, 72.84; H, 5.75. found: C, 72.54; H, 5.75.



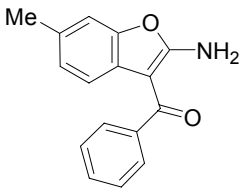
3-Acetyl-2-aminobenzo[*b*]furan (2j): A yellow solid. mp 171.2-172.3 ^{o}C. IR (KBr): 739, 753, 940, 1024, 1103, 1179, 1236, 1299, 1326, 1362, 1422, 1442, 1494, 1605, 1656 1676 (C=O), 2946, 3072, 3168, 3222, 3384 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ2.55 (s, 3H), 6.84 (br, 2H), 7.10 (t, J = 7.6 Hz, 1H), 7.25 (t, J = 7.6 Hz, 1H), 7.26 (d, J = 7.6 Hz, 1H), 7.48 (d, J = 7.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ29.52, 95.21, 110.2, 118.3, 121.6, 124.1, 126.4, 149.1, 164.8, 192.7. Anal. calcd for $C_{10}H_9NO_2$: C, 68.56; H, 5.18. found: C, 68.29; H, 5.02.



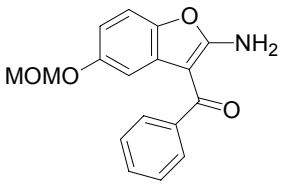
2-Amino-3-formylbenzo[*b*]furan (2k) [3]**:** A white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ6.78 (br, 2H), 6.93-7.33 (m, 3H), 7.68-7.71 (m, 1H), 9.91 (s, 1H).



2-Amino-3-ethoxycarbonylbenzo[*b*]furan (2l): A white solid. mp 69.2-69.8 °C. IR (KBr): 746, 785, 969, 1039, 1123, 1173, 1240, 1298, 1321, 1368, 1434, 1487, 1535, 1628, 1664 (C=O), 2931, 2984, 3149, 3274, 3414 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ1.42 (t, J = 7.3 Hz, 3H), 4.37 (q, J = 7.3 Hz, 2H), 6.03 (br, 2H), 7.05 (t, J = 7.8 Hz, 1H), 7.16-7.26 (m, 2H), 7.65 (d, J = 7.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ14.53, 59.66, 84.61, 109.6, 119.3, 121.4, 124.0, 126.8, 149.1, 164.5, 166.2. Anal. calcd for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40. found: C, 64.37; H, 5.49.

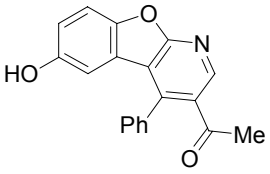


2-Amino-3-benzoyl-6-methylbenzo[*b*]furan (2m): A yellow solid. mp 123.1-123.9 °C. IR (KBr): 762, 807, 899, 937, 983, 1033, 1111, 1156, 1209, 1254, 1336, 1364, 1477, 1504, 1590, 1629, 1659 (C=O), 2859, 3177 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ2.33 (s, 3H), 6.75 (d, J = 7.8 Hz, 1H), 6.80 (d, J = 7.8 Hz, 1H), 7.01 (s, 1H), 7.18 (br, 2H), 7.42-7.56 (m, 3H), 7.69 (d, J = 7.3 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ21.15, 94.23, 110.5, 118.5, 123.5, 124.5, 127.4, 128.2, 130.7, 131.9, 140.9, 149.5, 166.5, 190.5. Anal. calcd for $C_{16}H_{13}NO_2$: C, 76.48; H, 5.21. found: C, 76.52; H, 5.32.



2-Amino-3-benzoyl-4-(methoxymethoxy)benzo[*b*]furan (2n): A yellow solid. mp 118.9-119.7 °C. IR (KBr): 756, 797, 920, 1023, 1079, 1152, 1175, 1246, 1342, 1480, 1593, 1651(C=O), 2942, 3111, 3325 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ3.40 (s, 3H), 4.98 (s, 2H), 6.55 (d, J = 2.5 Hz, 1H), 6.74 (dd, J = 2.5, 8.8 Hz, 1H), 7.06 (br, 2H), 7.11 (d, J = 8.8 Hz, 1H), 7.49 (d, J = 6.8 Hz, 1H), 7.49-7.55 (m, 1H), 7.69 (d, J = 6.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ55.78, 94.66, 95.38, 107.6, 110.2, 110.7, 127.2, 127.4, 128.3, 130.9, 140.7, 144.8, 154.0, 167.1, 190.7. Anal. calcd for $C_{17}H_{15}NO_4$: C, 68.68; H, 5.09. found: C, 68.61; H, 5.11.

Synthesis of Elbfluorene



Elbfluorene (8): To a solution of 2-amino-3-benzoyl-4-(methoxymethoxy)-benzo[*b*]furan **2n** (595 mg, 2.0 mmol), diketene (0.19 mL, 2.4 mmol) in CH_3CN (6.0 mL) were added dropwise a solution of trimethylchlorosilane (0.3 mL, 2.4 mmol) in CH_3CN (6.0 mL) at 50 ^oC over 12 h. After being stirred additionally for 2 h, the reaction mixture was poured into sat. $NaHCO_3$ aqueous solution. The aqueous layer was extracted with Et_2O (20 mL x 3). The combined organic layer was washed with brine and dried over $MgSO_4$. The organic solvent was removed under reduced pressure to afford **4** (2:1 mixture of two tautomers) as a brown oil. ^1H NMR (400 MHz, $CDCl_3$): δ2.06 (s, 3H), 2.35 (s, 3H), 3.39 (s, 6H), 3.76 (s, 2H), 5.00 (s, 4H), 5.37 (s, 1H), 6.67-6.71 (m, 2H), 6.91-6.94 (m, 2H), 7.39-7.44 (m, 2H), 7.48-7.60 (m, 8H), 7.72-7.78 (m, 4H), 10.9 (s, 1H), 11.7 (s, 1H), 13.3 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ21.75, 30.80, 50.90, 55.75, 62.53, 91.65, 94.58, 95.18, 99.84, 101.0, 107.9, 108.0, 111.8, 111.9, 113.2, 113.5, 124.8, 124.9, 127.9, 128.2, 128.3, 128.4, 128.5, 130.0, 132.0, 132.2, 133.6, 139.0, 139.3, 146.0, 146.1, 154.3, 154.4, 156.9, 158.6, 162.9, 168.5, 178.8, 191.9, 192.2, 202.0. A solution of **4** in MeOH (4 mL) was added to sodium methoxide (130 mg, 2.4 mmol), and the resulting mixture was stirred at room temperature for 8 h, then quenched by adding excess of 10% NH_4Cl aqueous solution. The aqueous layer was extracted with Et_2O (20 mL x 3). The combined organic layer was washed with brine and dried over $MgSO_4$. After the organic solvent was removed under reduced pressure**,** the resulting mixture diluted with CH_2Cl_2 (8 mL) was slowly added to pyridine (0.19 mL, 2.4 mmol) and trifluoromethanesulfonic anhydride (0.40 mL, 2.4 mmol) at -78 ^oC. After stirring for 1 h at -78 ^oC, the resulting solution was gradually warmed up to room temperature and then stirred additionally for 1 h. The solution was washed with sat. NH_4Cl aqueous solution, and the aqueous layer was extracted with Et_2O (10 mL x 3). The combined organic layer was washed with brine and dried over $MgSO_4$. The organic solvent was removed under reduced pressure and the residue was subjected to flash column chromatography on silica gel with hexane / AcOEt = 50/1 as eluents to afford **6** (555 mg, 1.12 mmol, 56% (three steps

from **2n**)) as a pale yellow oil. IR (KBr): 704, 756, 916, 1002, 1074, 1149, 1194, 1251, 1378, 1474, 1557, 1585, 1700 (C=O), 2853, 2925, 3090 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ2.15 (s, 3H), 3.41 (s, 3H), 5.02 (s, 2H), 6.86 (d, J = 2.4 Hz, 1H), 7.22-7.23 (m, 1H), 7.48-7.51 (m, 2H), 7.56 (d, J = 8.8 Hz, 1H), 7.61-7.63 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ32.03, 55.92, 95.35, 109.8, 112.9, 115.9, 118.5 (q, J = 320.7 Hz), 119.0, 121.7, 124.4, 128.5, 129.4, 130.3, 133.6, 147.1, 148.5, 151.0, 153.9, 160.3, 198.4. HRMS (FAB, $[M+H]^+$): calcd for $C_{22}H_{17}F_3NO_7S$, 496.0678; found 496.0677. To a solution of **6** (248 mg, 0.50 mmol) in THF (2 mL) was added 10% HCl aqueous solution, and the mixture was stirred at 50 ^oC for 8 h. The reaction mixture was poured into sat. $NaHCO_3$ aqueous solution, and then the aqueous layer was extracted with Et_2O (50 mL x 3). The combined organic layer was washed with brine and dried over $MgSO_4$. The organic solvent was removed under reduced pressure and the residue was subjected to flash column chromatography on silica gel with hexane / AcOEt = 10/1 as eluents to afford **7** (176 mg, 0.39 mmol, 78%) as a pale yellow solid. mp 203.4-204.8 ^oC. IR (KBr): 796, 812, 839, 903, 1023, 1134, 1168, 1218, 1293, 1375, 1421, 1497, 1588, 1699 (C=O), 3056, 3558 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ2.13 (s, 3H), 5.00 (br, 1H), 6.60 (d, J = 2.4 Hz, 1H), 7.01 (dd, J = 2.4, 8.8 Hz, 1H), 7.45-7.52 (m, 3H), 7.59-7.62 (m, 3H). ^{13}C NMR (100 MHz, d_6-acetone): δ32.08, 108.3, 113.7, 117.1, 119.4 (q, J = 320.7 Hz), 118.8, 122.6, 125.3, 129.5, 130.3, 131.0, 134.8, 148.3, 149.0, 150.4, 155.1, 161.0, 198.7. HRMS (FAB, $[M+H]^+$): calcd for $C_{20}H_{13}F_3NO_6S$, 452.0416; found 452.0412. A flame dried Schlemk flask was charged with $Pd(OAc)_2$ (2.0 mg, 0.009 mmol), dppf (5.0 mg, 0.009 mmol), **7** (135.3 mg, 0.3 mmol), triethylsilane (0.07 ml, 0.45 mmol), and DMF (1.2 mL). After stirring at 70 ^oC for 3 h, the mixture was diluted with Et_2O and filtered through a short silica gel pad. The filtrate was washed with brine, and the aqueous layer was extracted with Et_2O (10 mL x 3). The combined organic layer was dried over $MgSO_4$, and then filtered. The organic solvent was removed under reduced pressure and the residue was subjected to flash column chromatography on silica gel with hexane / acetone = 10/1 as eluents to afford elbfluorene **8** (87 mg, 0.29 mmol, 96%) as a white solid. mp 234.8-235.6 ^oC. IR (KBr): 706, 738, 835, 910, 978, 1037, 1106, 1146, 1184,

1228, 1248, 1282, 1355, 1410, 1471, 1586, 1692 (C=O), 2873, 3146 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ2.12 (s, 3H), 4.98 (br, 1H), 6.48 (d, J = 2.4 Hz, 1H), 7.00 (dd, J = 2.4, 8.8 Hz, 1H), 7.43-7.47 (m, 2H), 7.50 (d, J = 8.8 Hz, 1H), 7.58-7.62 (m, 3H), 8.75 (s, 1H). ^{13}C NMR (100 MHz, d_6-acetone): δ30.67, 108.7, 113.2, 116.1, 118.0, 123.5, 129.3, 129.9, 130.0, 132.6, 137.1, 145.9, 147.8, 149.8, 154.6, 165.1, 200.0. HRMS (FAB, $[M+H]^+$): calcd for $C_{19}H_{14}NO_3$, 304.0974; found 304.0966.

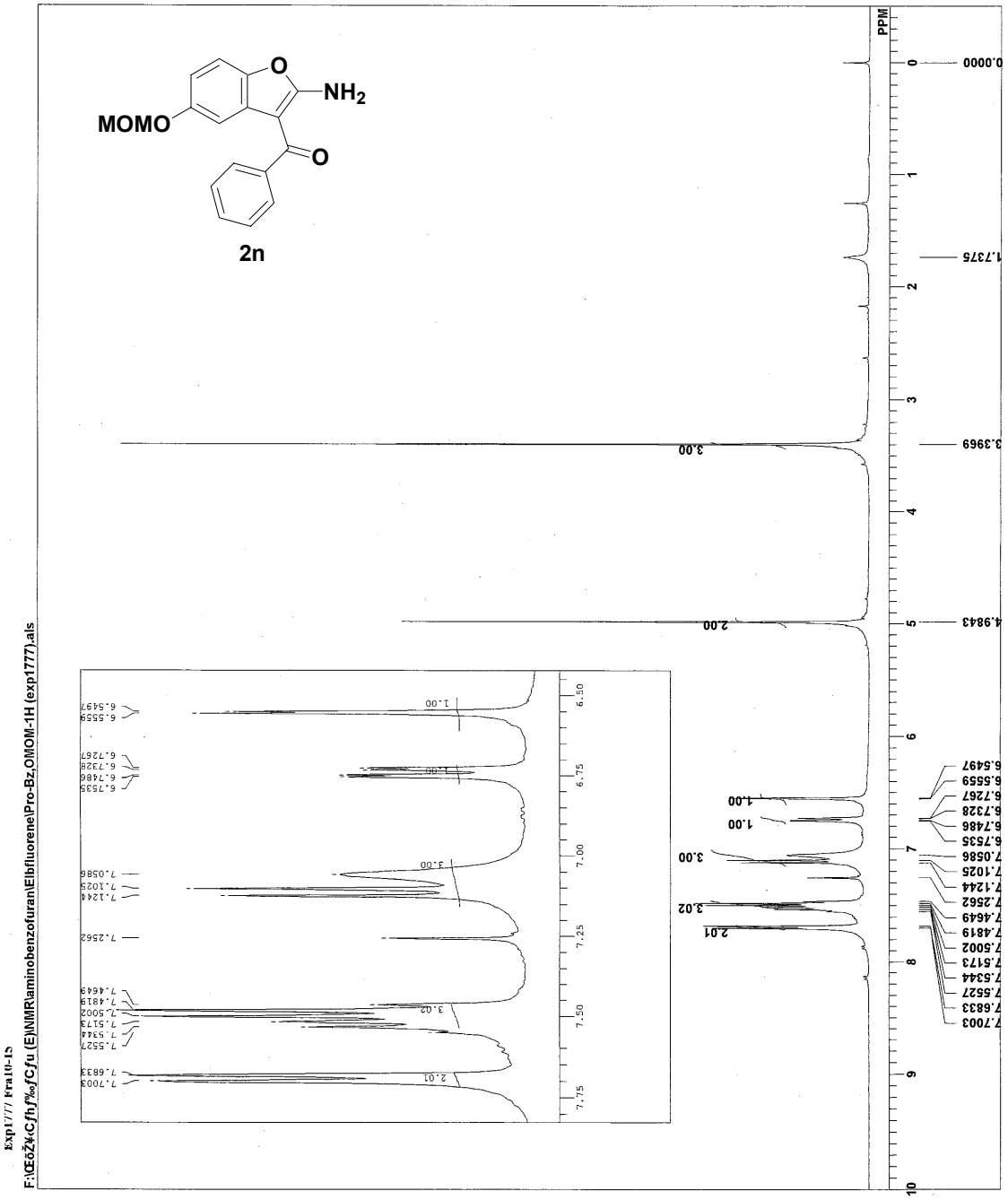
References

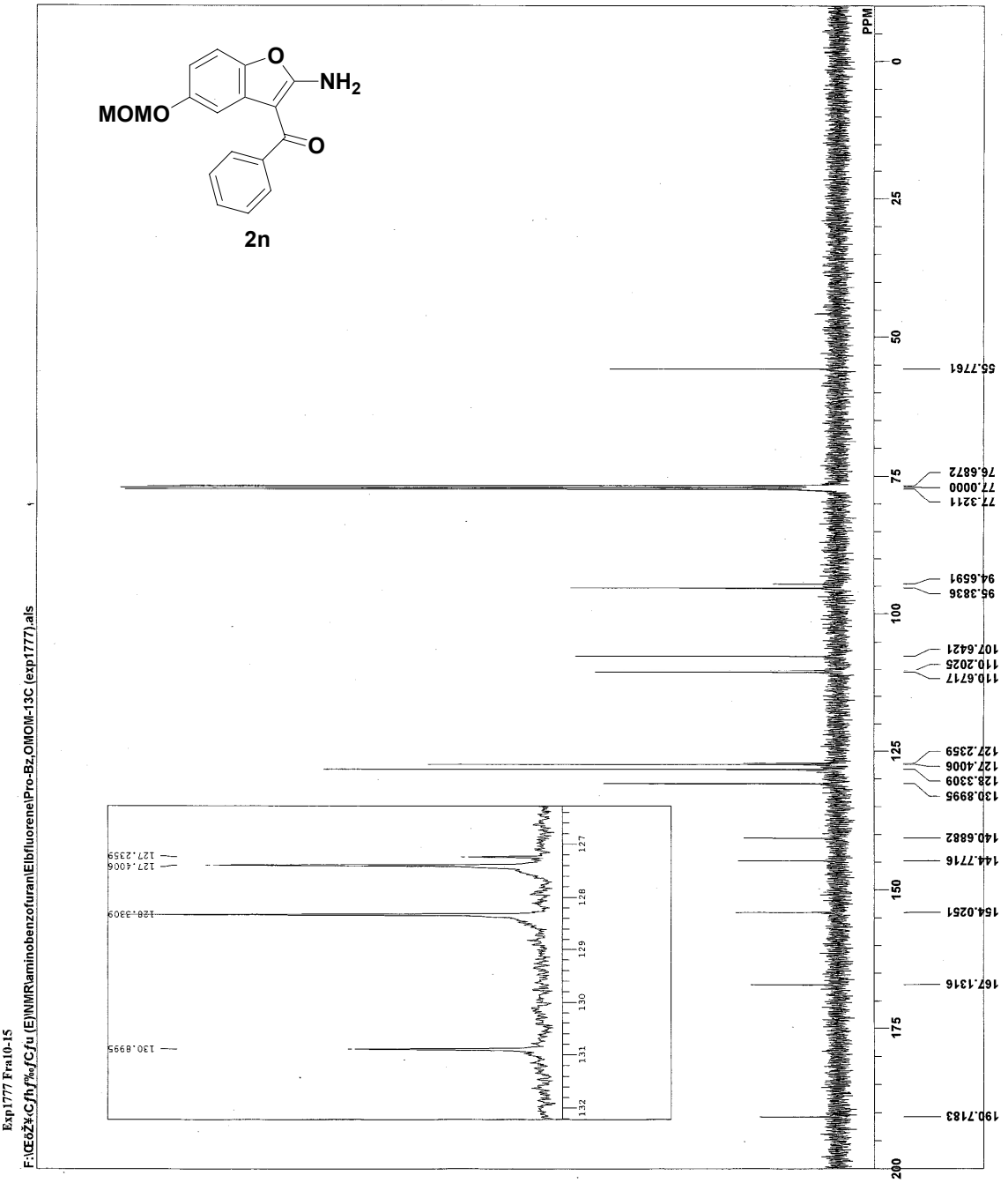
(1) Perrin, D. D.; Armarego, W. L. F. In *Purification of Laboratory Chemicals*, 4th ed.; Butterworth-Heinemann: Oxford, 1997.

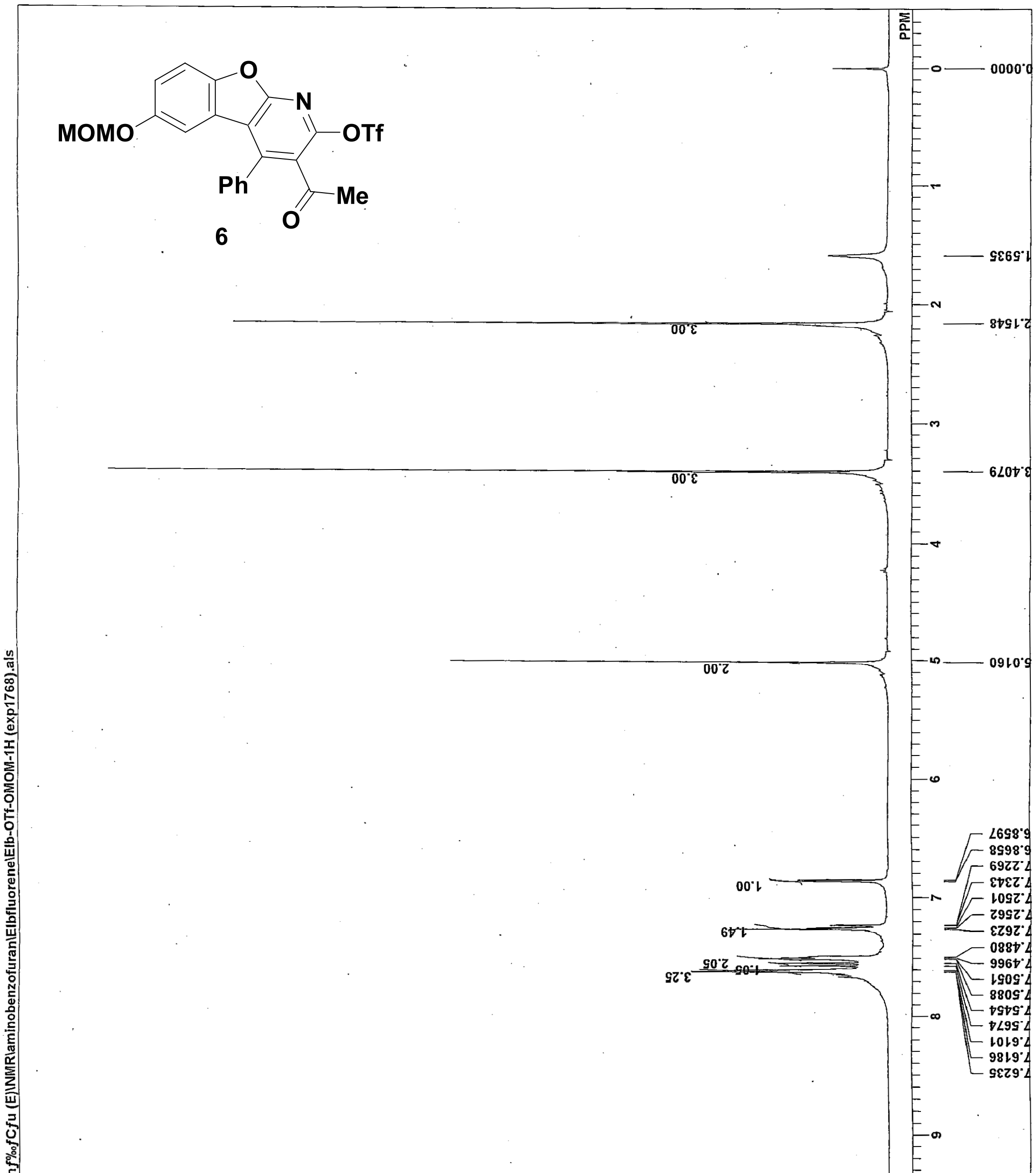
(2) Nakamura, S.; Uchiyama, M.; Ohwada, T. *J. Am. Chem. Soc.* **2003**, *125*, 5282.

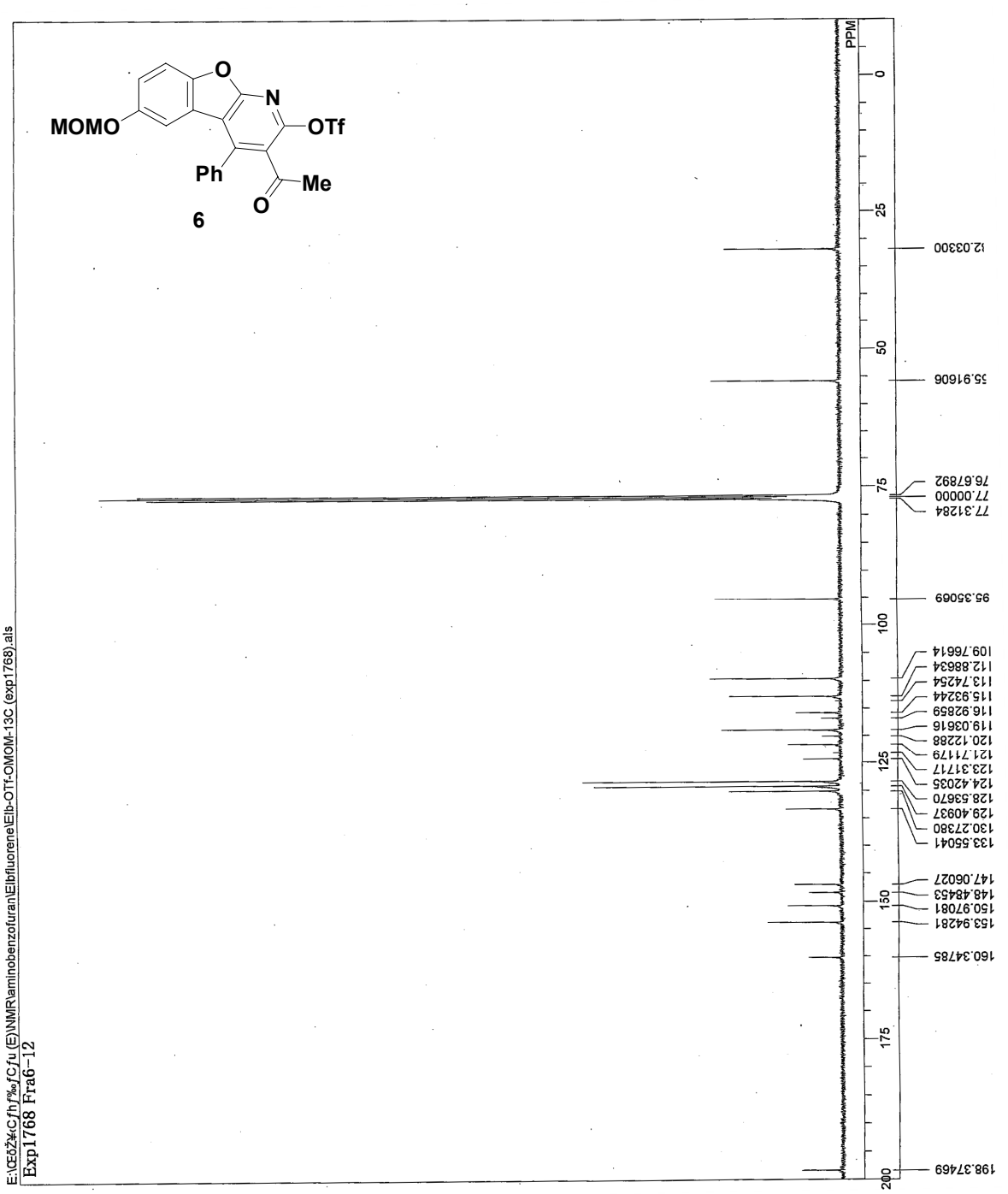
(3) Becher J.; Pluta, K.; Krake, N.; Brøndum, K.; Christensesn, N. J.; Vinader, M. V. *Synthesis* **1989**, 530.

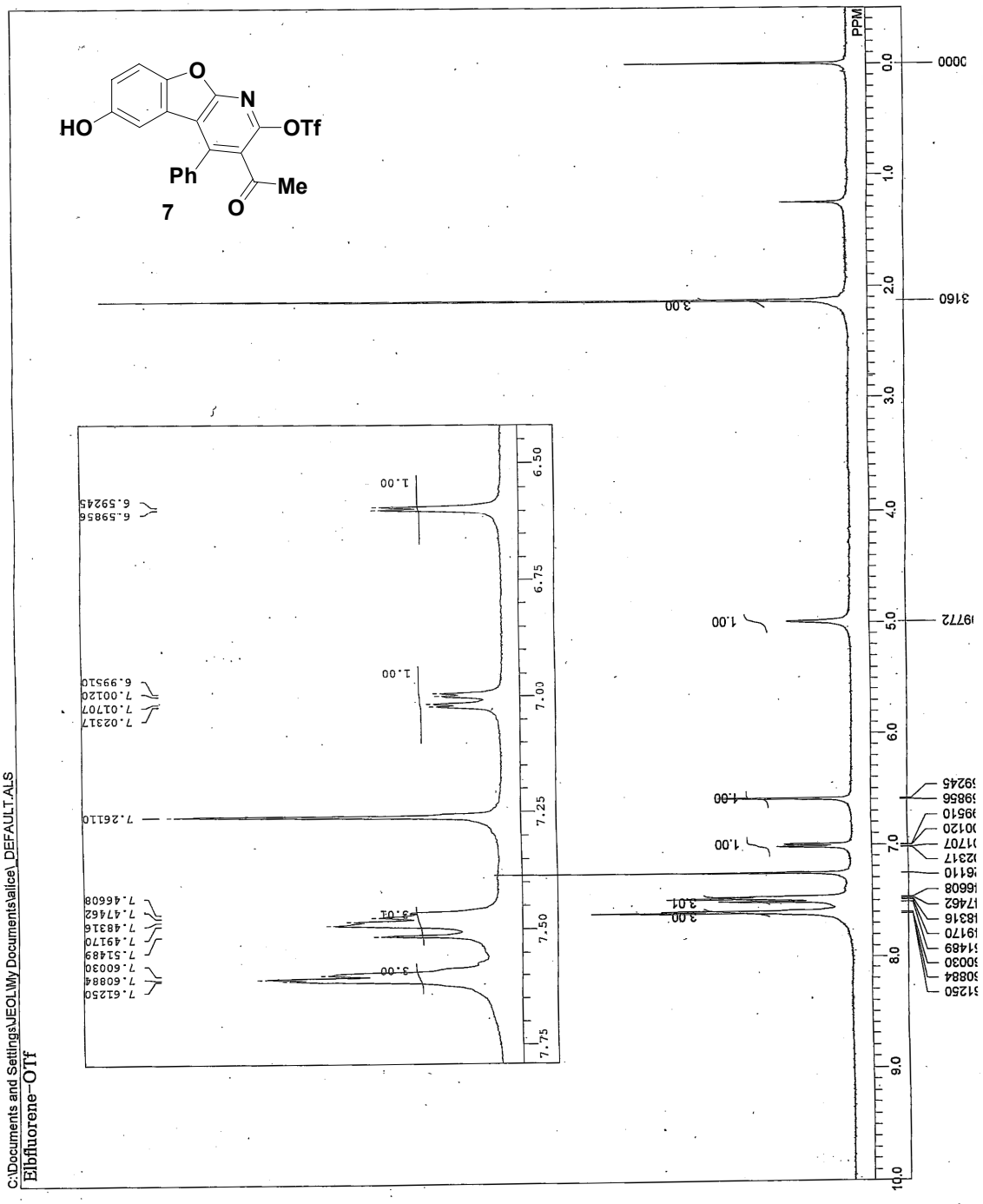
^{1}H-NMR and ^{13}C-NMR Spectra of Selected Compounds

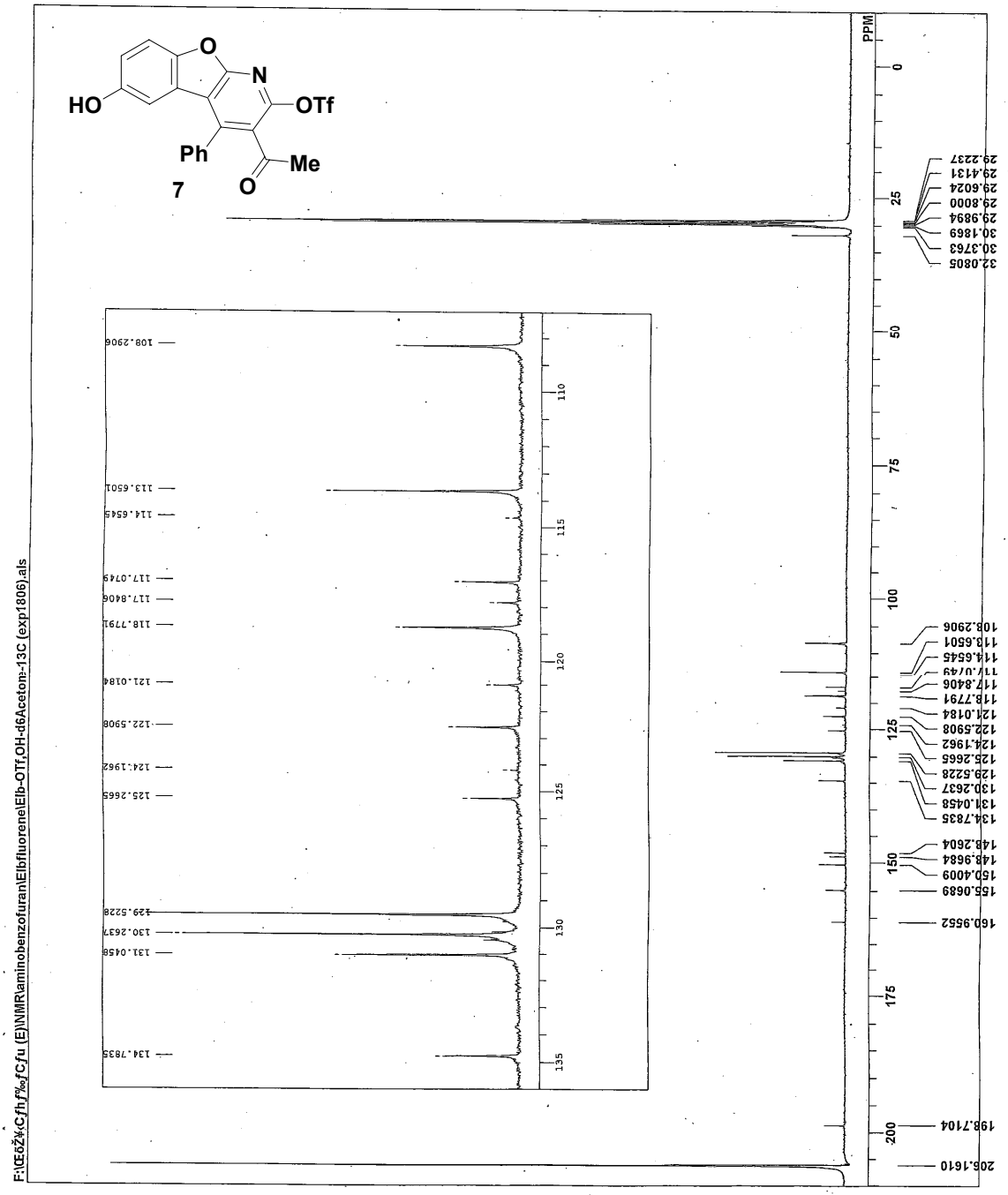


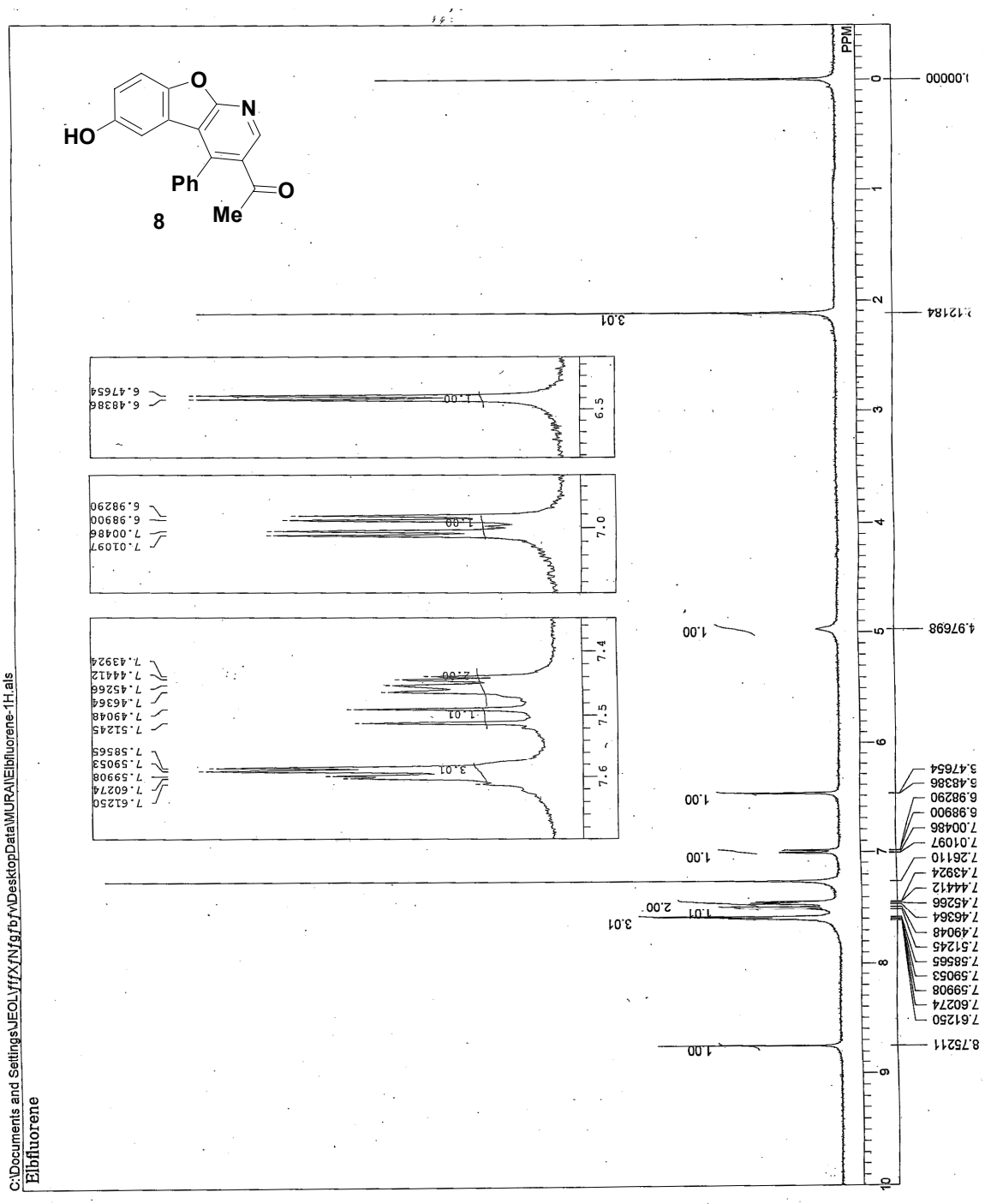

O
NH2
MOMO
O
2n
PPM
0
25
50
75
100
125
150
175
200
55.7761
76.6872
77.0000
77.3211
94.6591
95.3836
107.6421
110.2025
110.6717
127.2359
127.4006
128.3309
130.8995
140.6882
144.7716
154.0251
167.1316
190.7183
Exp1777 Fra10-15
F:\CE6Z¥:Cfh{%fCfu (E)\NMR\aminobenzofuran\Elbfluorene\Pro-Bz,OMOM-13C (exp1777).als

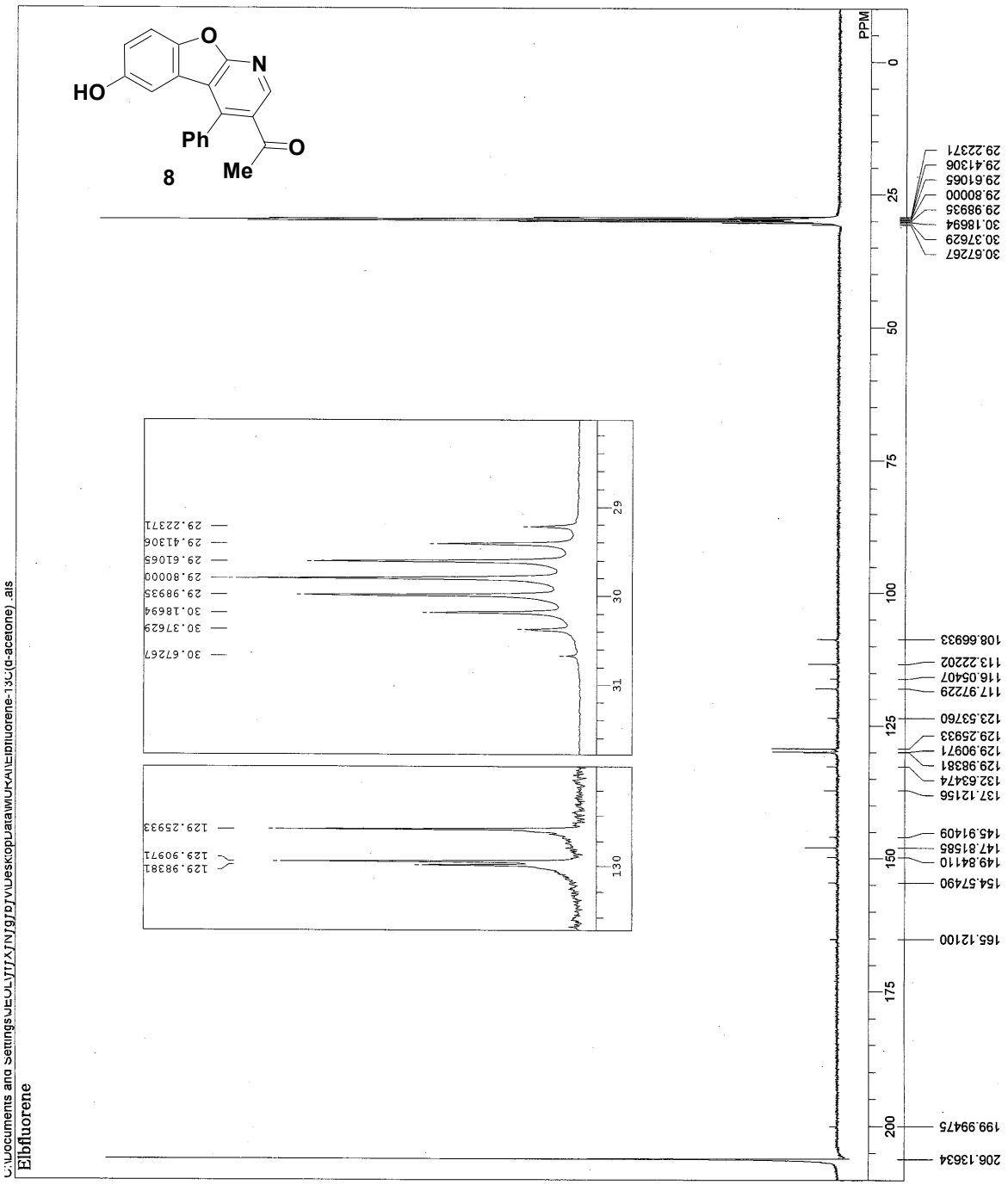

MOMO
OTf
Ph
Me
6
PPM
0.0000
1.5935
2.1548
3.4079
5.0160
3.00
3.00
2.00
1.00
1.49
2.05
3.25


MOMO
O
N
OTf
Ph
Me
O
6
PPM
0
25
50
75
100
125
150
175
200
12.03300
55.91606
76.67892
77.00000
77.31284
95.35069
109.76614
112.88634
113.74254
115.93244
116.92859
119.03616
120.12288
121.71179
123.31717
124.42035
128.53670
129.40937
130.27380
133.55041
147.06027
148.48453
150.97081
153.94281
160.34785
198.37469
E:\CE62%#C fh7‰ fC fu (E)\NMR\aminobenzofuran\E\bfluorene\E\b-OTf-OMOM-13C (exp1768).als
Exp1768 Fra6-12


HO
O
N
OTf
Ph
Me
O
7
PPM
C:\Documents and Settings\JEOL\My Documents\alice_DEFAULT.ALS
Elbfluorene-OTf


HO
O
N
OTf
Ph
Me
O
7
PPM
F:\CE6ŽŸ‹Cƒh‚f‰ƒfCƒfu (E)\NMR\aminobenzofuran\Elbfluorenel\Elb-OTf,OH-d6Aceton-13C (exp1806).als


HO
O
N
Ph
O
Me
8
PPM
C:\Documents and Settings\JEOL\fffX fN fg fb fv\Desktop\Data\MURAI\Elbfluorene-1H.als
Elbfluorene


HO
O
N
Ph
O
Me
8
PPM
0
25
50
75
100
125
150
175
200
29.22371
29.41306
29.61065
29.80000
29.98935
30.18694
30.37629
30.67267
108.66933
113.22202
116.05407
117.97229
123.53760
129.25933
129.90971
129.98381
132.63474
137.12156
145.91409
147.81585
149.84110
154.57490
165.12100
199.99475
206.13634
Elbfluorene

X-ray Crystallographic Studies of 2a. Yellow crystals of **2a** suitable for X-ray analysis were obtained by recrystallization from $CHCl_3$ / *n*-hexane. The single crystal was sealed in a Pyrex glass capillary under N_2 atmosphere and used for data collection. All measurements were made on a Rigaku RAXIS imaging plate area detector with graphite monochromated Mo-Kα radiation. Details of crystal and data collection parameters are summarized in Table 3. The positions of non-hydrogen atoms were determined by direct methods (SIR92) and subsequent Fourier syntheses (DIRDIF PATTY). An ORTEP drawing of **2a** is shown in Figure 1. Although four crystallographically independent molecules and one water molecule were included in each unit cell, only one independent molecule is shown for clarity. Thermal ellipsoids are displayed at the 50% probability level. The position of oxygen atom of water and some of the fluorine atoms of the trifluoromethyl groups had disorders. Because size and quality of the crystal was not enough, the data completeness was less than 85%. Although we tried to get another better crystal, we could not. However, the reflection parameter ratio was more than 10, and we believe that we could get sufficient reflection to just confirm the structure of the product.

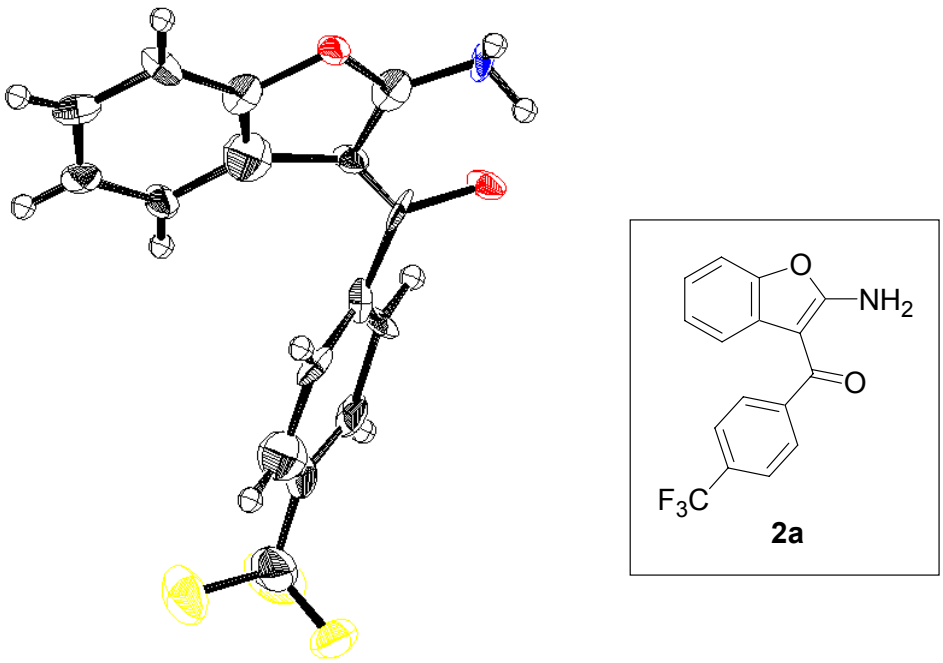


Figure 1. ORTEP drawing of **2a**.

Table 3. Summary of Crystallographic Data of **2a**

Empirical Formula: $C_{16}H_{10}F_3NO_2$
Formula weight: 305.26
Crystal system: monoclinic
Space group: P21/n (#14)
Crystal Color: yellow
lattice parameters:
a (Å) = 9.129(6), *b* (Å) = 29.139(19), *c* (Å) = 20.733(14),
V (Å ^{3}) = 5494(6), α =β = 90^o, γ = 95.000(3)^o,
Z = 16
D_{calc} (g cm^{-3}): 1.476
μ (Mo Kα) (cm^{-1}): 1.249
goodness of fit (GOF) = 1.001.
F(000) 632
Diffractometer: Rigaku RAXIS-RAPID
Radiation: MoKα (λ = 0.71070Å), Graphite Monochromated
Temp (^{o}C): 23.0
Scan Type: ω .2θ
Max. 2θ (^{o}): 55.0
No. of Reflections Mesasured total: 21191
No. of observns (*I* > 3.00σ (*I*)): 9597
Structure Solution: Direct Methods (SIR92)
Refinement: Full-Matrix Least-Squares on F
no. of variables: 829
reflection/parameter ratio: 11.58
residuals: R = 0.0786, R_{int} = 0.059, R_w = 0.1390
goodness of fit (GOF): 1.001
Max Shift/Error in Final Cycle: 0.00
Maximum peak in Final Diff Map (e (Å $^{-3}$): 1.39
Maximum peak in Final Diff Map (e (Å $^{-3}$): -1.44