Electronic Supplementary Material (ESI) for Chemical Communications

Supporting Information

A Cascade Reaction of Pyrrole-2-Carbaldehyde Substituted Morita-Baylis-Hillman Adducts in the Presence of Tetrabutylammonium Hydroxide or Acetate to Construct Aza-heterocycles

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CONTENTS

General Remarks: ^{1}H NMR spectra were recorded on a Bruker AM-300 or AM-400 spectrometer for solution in $CDCl_3$ with tetramethylsilane (TMS) as internal standard; J-values are in Hz. Mass spectra were recorded with a HP-5989 instrument. All of the compounds reported in this paper gave satisfactory HRMS analytic data. Melting points were determined on a digital melting point apparatus and temperatures were uncorrected. Infrared spectra were recorded on a Perkin-Elmer PE-983 spectrometer with absorption in cm^{-1}. THF, toluene and Et_2O were distilled from sodium (Na) under argon (Ar) atmosphere. CH_3CN, 1,2-dichloroethane and dichloromethane were distilled from CaH_2 under argon (Ar) atmosphere.Commercially obtained reagents were used without further purification. All reactions were monitored by TLC with Huanghai GF254 silica gel coated plates. Flash column chromatography was carried out using aluminum oxide (basic, 200-300 mesh) at increased pressure. O-Boc-Protected Morita-Baylis-Hillman products were prepared according to the literature procedure.[1] 1H-indole-2-carbonitrile,[2a] 5-formyl-1H-pyrrole-3-carbonitrile,[2b] 4-acetyl-1H-pyrrole-2-carbaldehyde,[2c] 4-(tert-butyl)-1H-pyrrole-2-carbaldehyde[2d] were prepared according to the literature procedure.

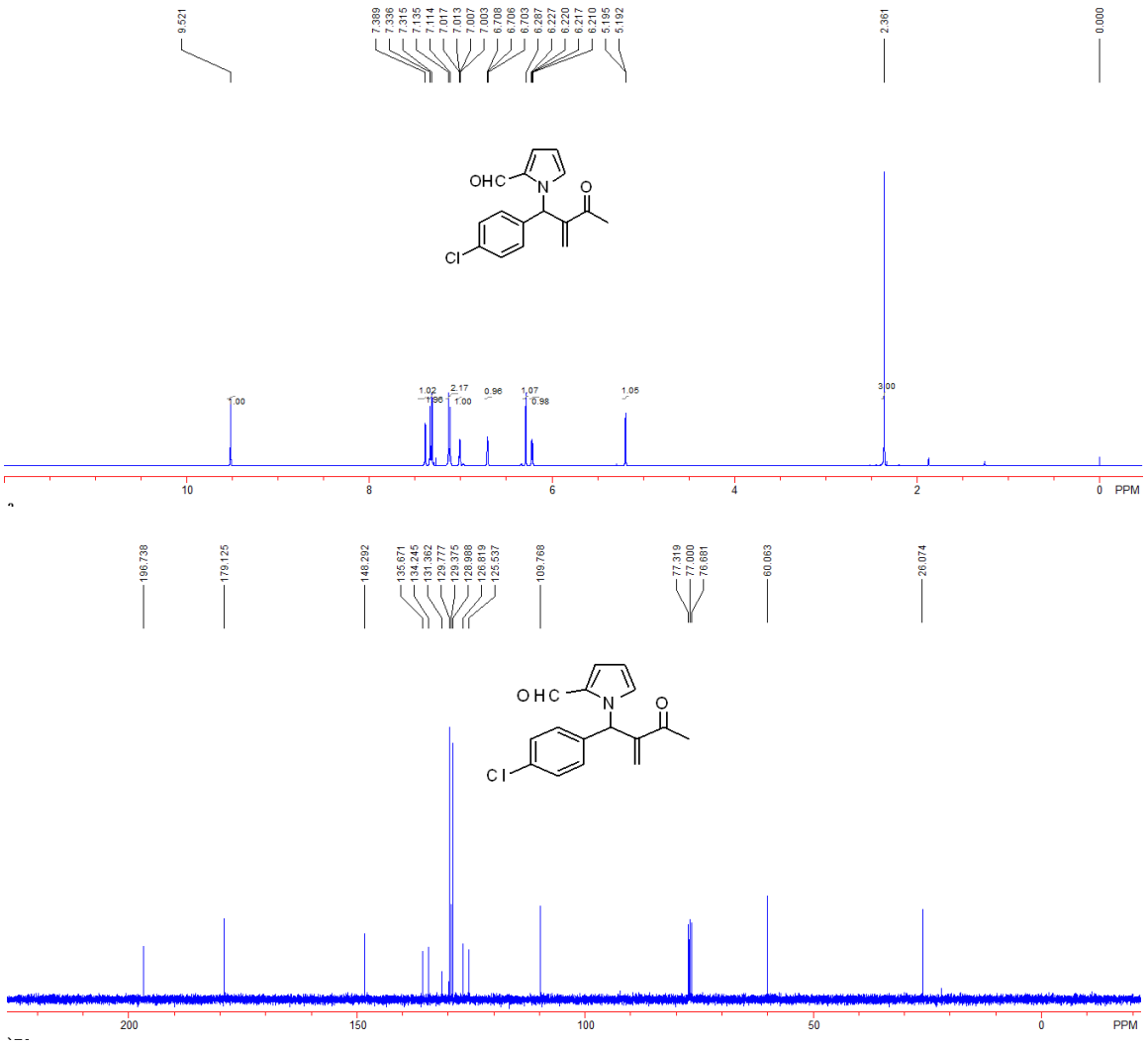
(1) (a) Pei, C. -K.; Zhang, X. -C.; Shi, M. *Eur. J. Org. Chem.* **2011**, *23*, 4479. (b) Huang, L.; Wei, Y.; Shi, M. *Org. Biomol. Chem.* **2012**, *10*, 1396.

(1) (a) Istvan, B.; Csilla, H.; Sandor, F.; Jozsef, N.; Sandor, K. WO Patent 2006010965, **2006**. (b) Anderson, H, J.; Riche, C. R.; Costello, T. G.; Loader, C. E.; Barnett, G. H. *Can. J. Chem.* **1978**, *56*, 654. (c) Elliott, L. D.; Berry, M.; Orr-Ewing, A. J.; Booker-Milburn, K. I. *J. Am. Chem. Soc.* **2007**, *129*, 3078. (d) Anderson, H, J.; Huang, C. -W. *Can. J. Chem.* **1970**, *48*, 1550.

General procedure for the synthesis of 1

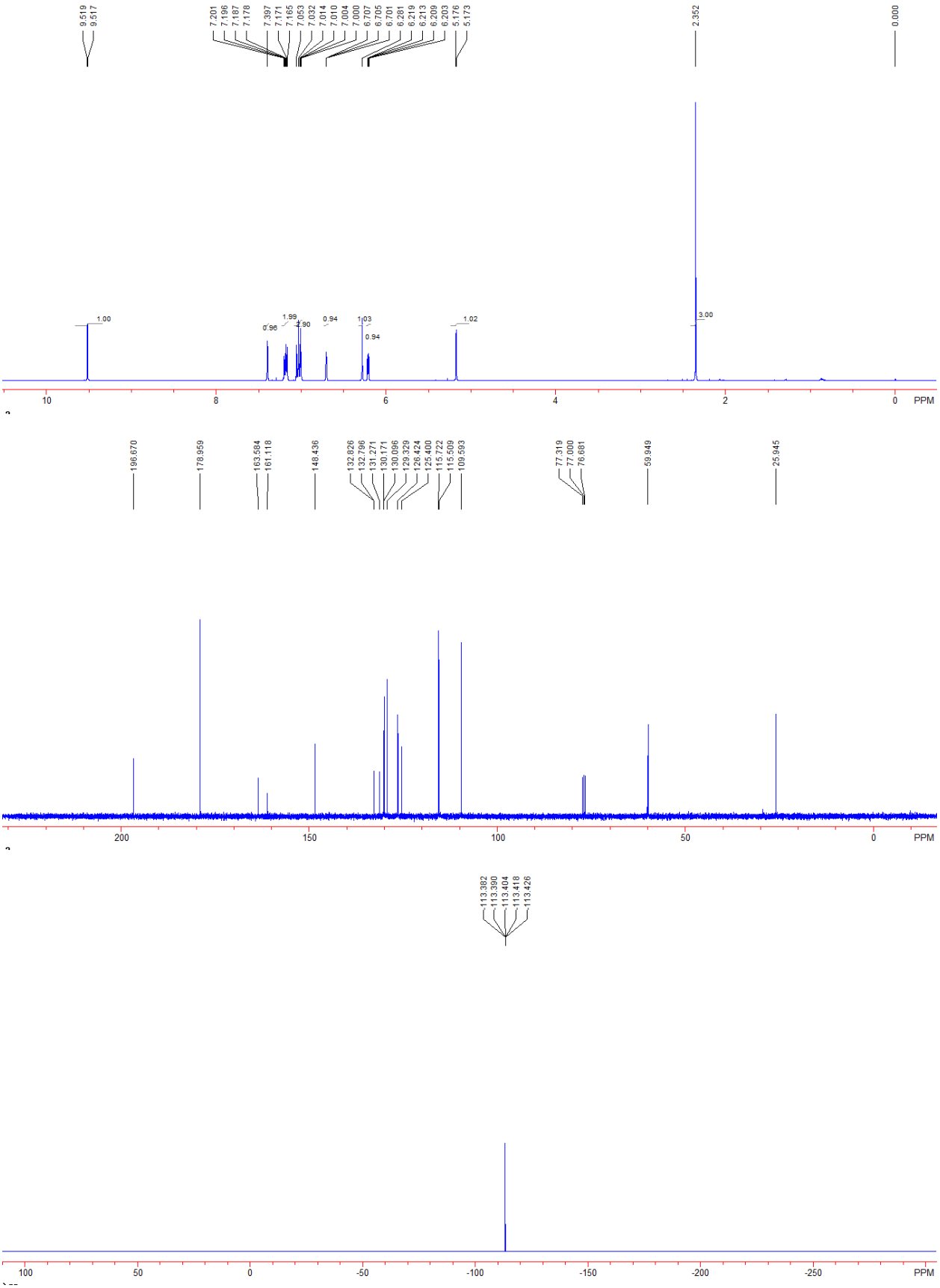
A solution of compound **A** (1.1 eq) and compound **B** (1.0 eq) in THF was stirred at room temprature for 1 h in the presence of organocatalyst DABCO (20 mol%) under argon atmosphere. After the reaction complete, the solvent was removed under reduced pressure and the residue was chromatographed on silica gel (elution with petroleum ether/EtOAc = 16/1-8/1) to provide the corresponding product **1.**

1-(1-(4-chlorophenyl)-2-methylene-3-oxobutyl)-1H-pyrrole-2-carbaldehyde 1a: 281 mg, 98% yield; a white solid, m.p. = 140-143 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.36 (s, 3H), 5.19 (d, *J* = 1.2 Hz, 1H), 6.22 (dd, *J* = 2.8 Hz, 4.0 Hz, 1H), 6.29 (s, 1H), 6.71 (t, *J* = 0.8 Hz, 1H), 7.01 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H), 7.12 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 7.39 (s, 1H), 9.52 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.1, 60.1, 109.8, 125.5, 126.8, 129.0, 129.4, 129.8, 131.4, 134.2, 135.7, 148.3, 179.1, 196.7; IR (neat) ν 2803, 2346, 1675, 1651, 1460, 1327, 1220, 1058, 956, 861, 741 cm^{-1}; MS (%) m/e 287 (6), 258 (9), 244 (25), 115 (15), 43 (100); HRMS (EI) for $C_{16}H_{14}NO_2Cl$: 287.0713; Found: 287.0716.

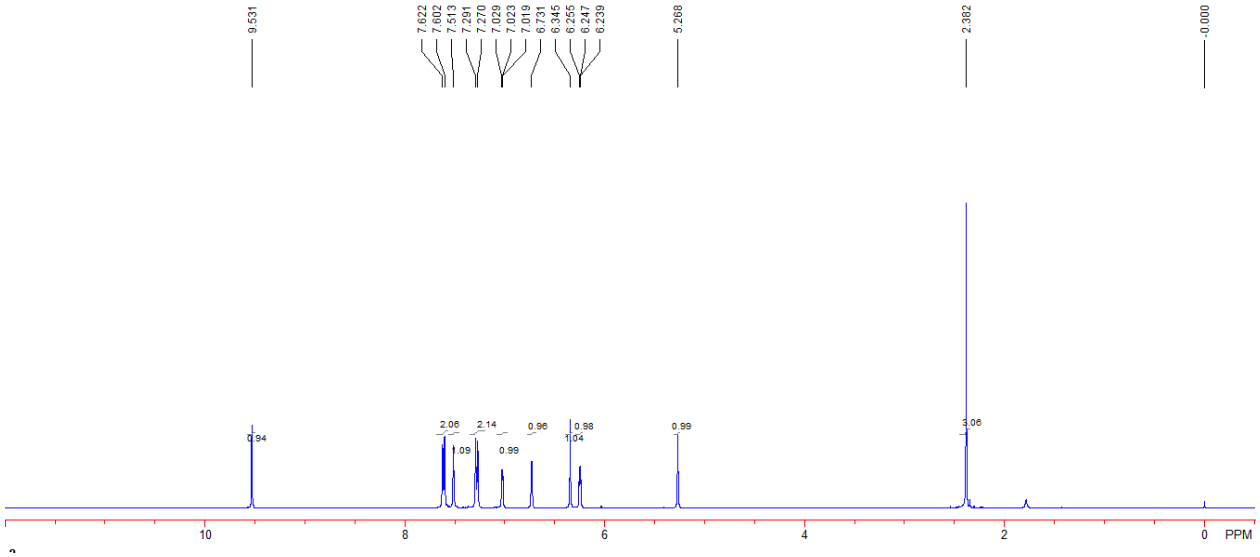


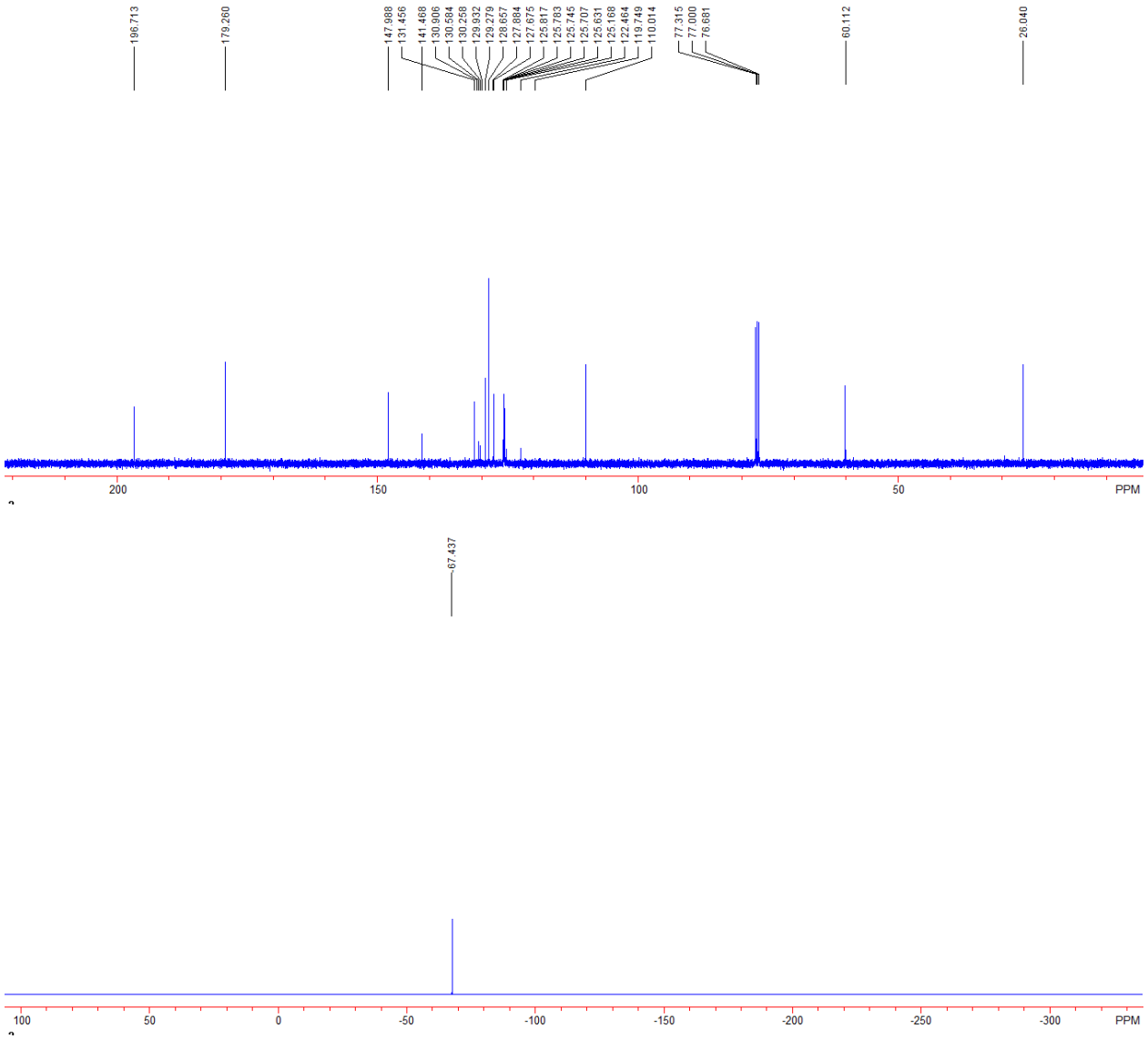
1-(1-(4-fluorophenyl)-2-methylene-3-oxobutyl)-1H-pyrrole-2-carbaldehyde 1b: 130 mg, 96% yield; a white solid, m.p. = 84-86 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.35 (s, 3H), 5.17 (d, *J* = 1.2 Hz, 1H), 6.21 (dd, *J* = 2.4 Hz, 4.0 Hz, 1H), 6.28 (s, 1H), 6.71 (t, *J* = 1.6 Hz, 1H), 7.01 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H), 7.04 (d, *J* = 8.0 Hz, 2H), 7.17-7.20 (m, 2H), 7.40 (s, 1H), 9.52 (d, *J* = 0.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.9, 59.9, 109.6, 115.6 (d, J_{C-F} = 26.3 Hz), 125.4, 126.4, 129.3, 130.1 (d, J_{C-F} = 7.5 Hz), 131.3, 132.8 (d, J_{C-F} = 3.0 Hz), 148.4, 162.4 (d, J_{C-F} = 246.6 Hz), 179.0, 196.7; ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$): δ -113.426 ~ -113.382 (m, 1F); IR (neat) ν 2924, 2806, 1678, 1652, 1505, 1417, 1322, 1218, 1029, 956, 862, 779, 744 cm^{-1}; MS (ESI) m/e

272.0 (M+H); HRMS (ESI) for $C_{16}H_{15}FNO_2$ (M+H): 272.1081; Found: 272.1089.



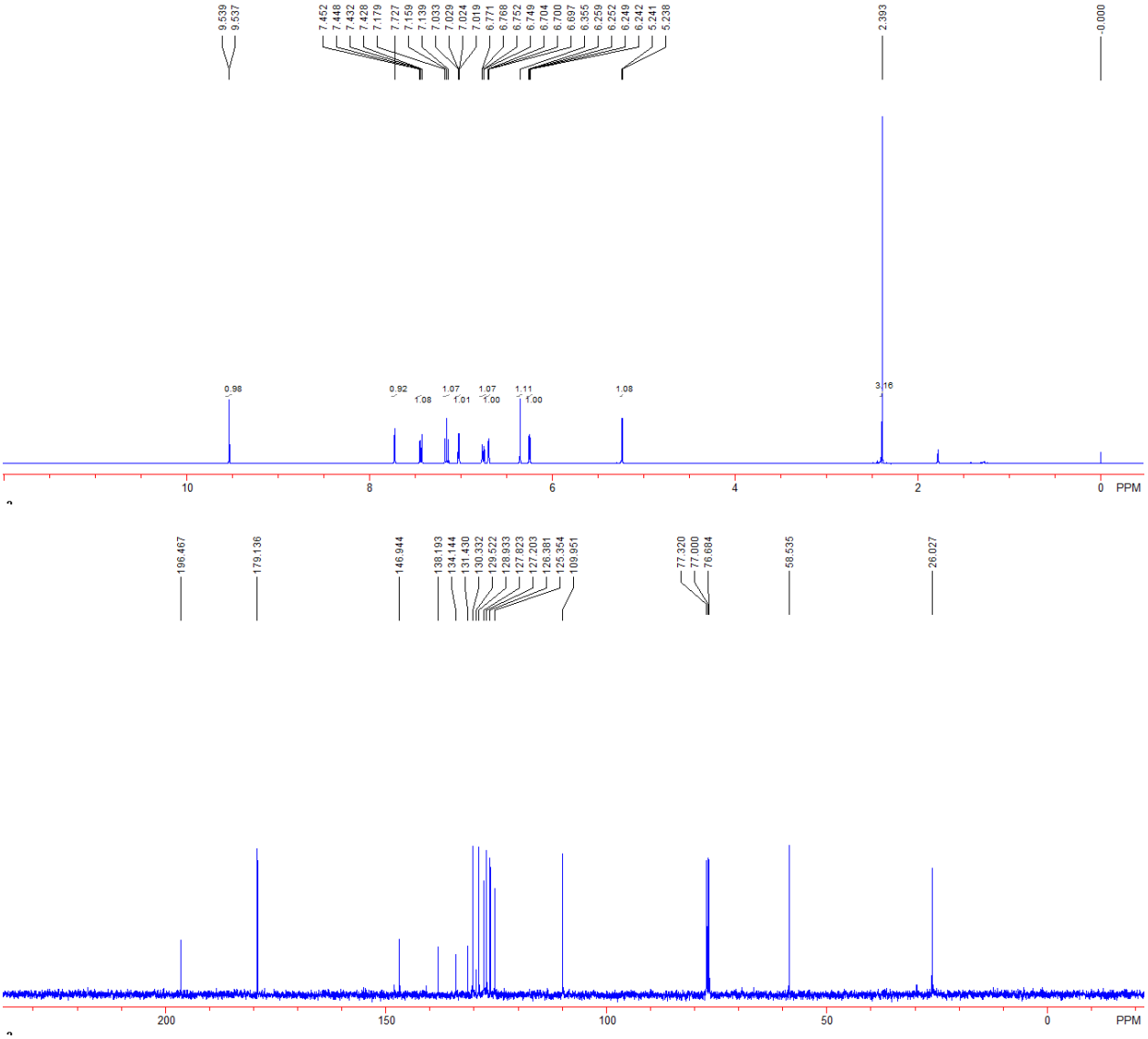
1-(2-methylene-3-oxo-1-(4-(trifluoromethyl)phenyl)butyl)-1H-pyrrole-2-carbaldehyde 1c: 161 mg, 99% yield; a white solid, m.p. = 89-92 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.38 (s, 3H), 5.27 (s, 1H), 6.25 (t, *J* = 3.2 Hz, 1H), 6.35 (s, 1H), 6.73 (s, 1H), 7.02 (t, *J* = 1.6 Hz, 1H), 7.28 (d, *J* = 8.4 Hz, 2H), 7.51 (s, 1H), 7.61 (d, *J* = 8.4 Hz, 2H), 9.53 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.0, 60.1, 110.0, 123.8 (q, $J_{C\text{-}F}$ = 271.5 Hz), 125.6, 125.8 (q, $J_{C\text{-}F}$ = 3.8 Hz), 127.7, 128.7, 129.3, 130.4 (q, $J_{C\text{-}F}$ = 32.6 Hz), 131.5, 141.5, 148.0, 179.3, 196.7; ^{19}F NMR ($CDCl_3$, 376 MHz, $CFCl_3$): δ -67.437 (s, 3F); IR (neat) ν 2925, 2854, 1681, 1654, 1469, 1417, 1323, 1221, 1109, 1065, 958, 858, 780, 747 cm^{-1}; MS (EI) *m/e* (%): 321 [M^+] (29.0), 292 (25.2), 278 (55.8), 250 (18.7), 183 (24.2), 115 (37.2), 94 (23.7), 43 (100.0); HRMS (EI) Calcd. for $C_{17}H_{14}NO_2F_3$ requires (M^+) 321.0977, Found: 321.0975.





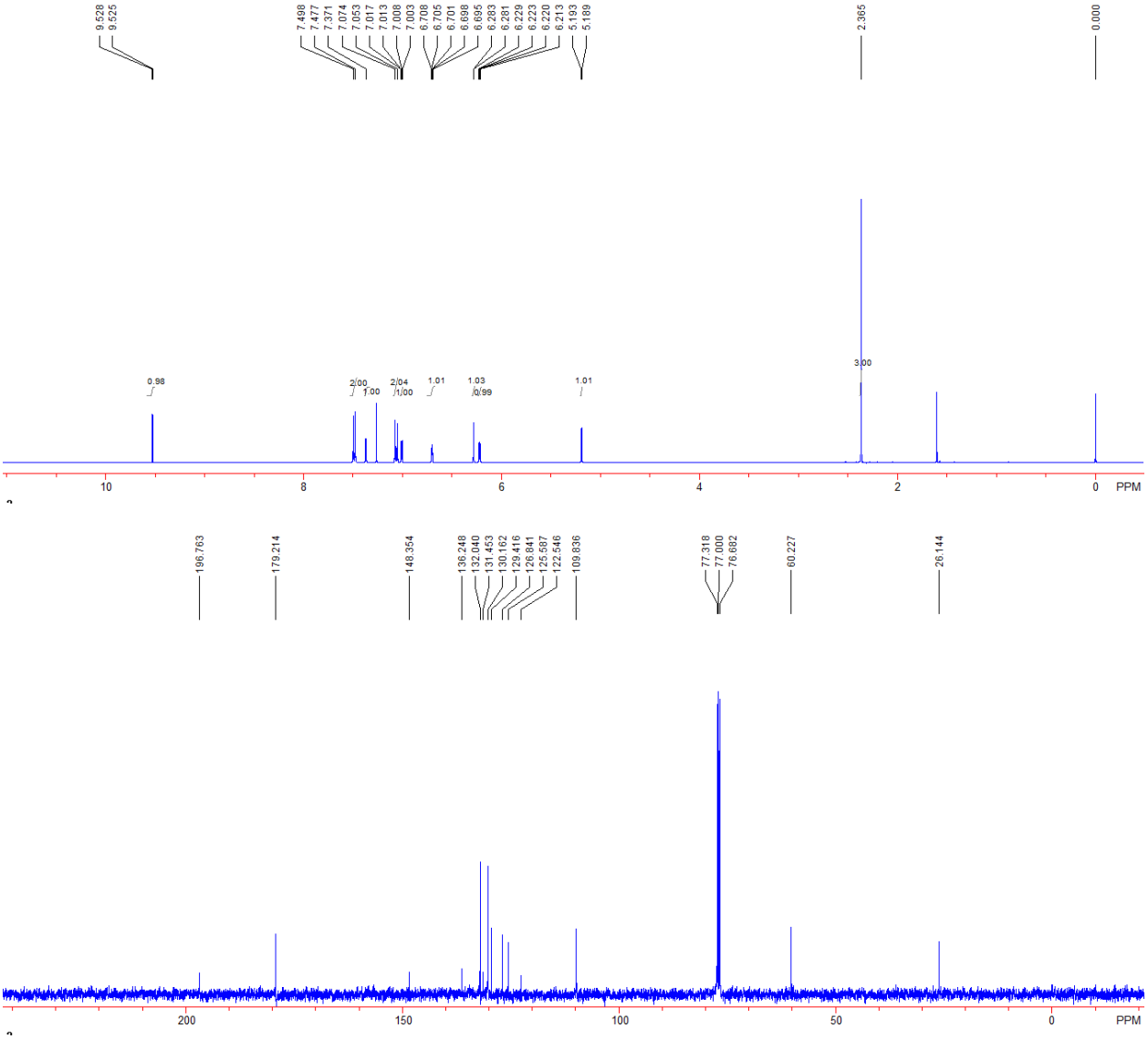
1-(1-(2,3-dichlorophenyl)-2-methylene-3-oxobutyl)-1H-pyrrole-2-carbaldehyde 1d: 91 mg, 95% yield; a white solid, m.p. = 88-91 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.39 (s, 3H), 5.24 (d, *J* = 1.2 Hz, 1H), 6.25 (dd, *J* = 2.8 Hz, 4.0 Hz, 1H), 6.36 (s, 1H), 6.70 (t, *J* = 1.2 Hz, 1H), 6.76 (dd, *J* = 1.2 Hz, 8.0 Hz, 1H), 7.03 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H), 7.16 (t, *J* = 8.0 Hz, 1H), 7.44 (dd, *J* = 1.6 Hz, 8.0 Hz, 1H), 7.73 (s, 1H), 9.54 (d, *J* = 0.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 58.5, 110.0, 125.4, 126.4, 127.2, 127.8, 128.9, 129.5, 130.3, 131.4, 134.1, 138.2, 146.9, 179.1,

196.5; IR (neat) ν 2922, 2852, 1658, 1466, 1417, 1312, 1220, 1070, 956, 873, 788, 743 cm^{-1}; MS (EI) *m/e* (%): 321 [M^+] (4.5), 286 (60.0), 280 (17.6), 278 (29.7), 149 (41.4), 113 (21.8), 94 (21.1), 43 (100.0); HRMS (EI) Calcd. for $C_{16}H_{13}NO_2Cl_2$ requires (M^+) 321.0323, Found: 321.0324.



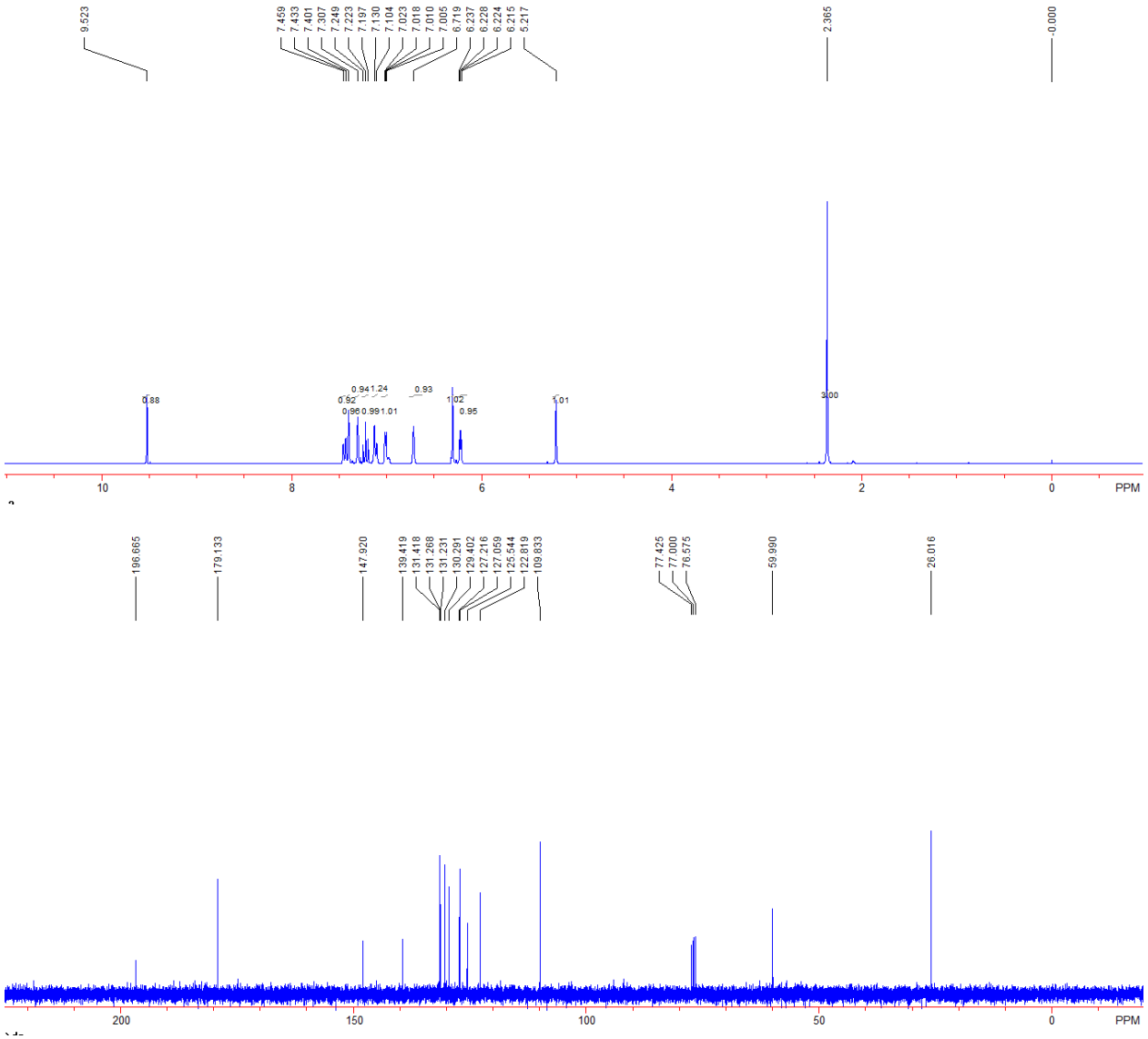
1-(1-(4-bromophenyl)-2-methylene-3-oxobutyl)-1H-pyrrole-2-carbaldehyde 1e: 140 mg, 84% yield; a white solid, m.p. = 155-157 ^oC; ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 2.37 (s, 3H), 5.19 (d, *J* = 1.6 Hz, 1H), 6.22 (dd, *J* = 2.8 Hz, 4.0 Hz, 1H), 6.28 (d, *J* = 0.8 Hz, 1H), 6.70 (dd, *J* = 1.2 Hz, 4.0 Hz, 1H), 7.01 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H), 7.06 (d, *J* = 8.4 Hz, 2H), 7.37 (s, 1H), 7.49 (d, *J* =

8.4 Hz, 2H), 9.53 (d, *J* = 1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.1, 60.2, 109.8, 122.5, 125.6, 126.8, 129.4, 130.2, 131.4, 132.0, 136.3, 148.4, 179.2, 196.8; IR (neat) ν 2924, 2853, 1681, 1650, 1469, 1322, 1217, 1075, 959, 852, 743 cm^{-1}; MS (ESI) m/e 332.0 (M+H); HRMS (ESI) for $C_{16}H_{15}BrNO$ (M+H): 332.0281; Found: 332.0293.



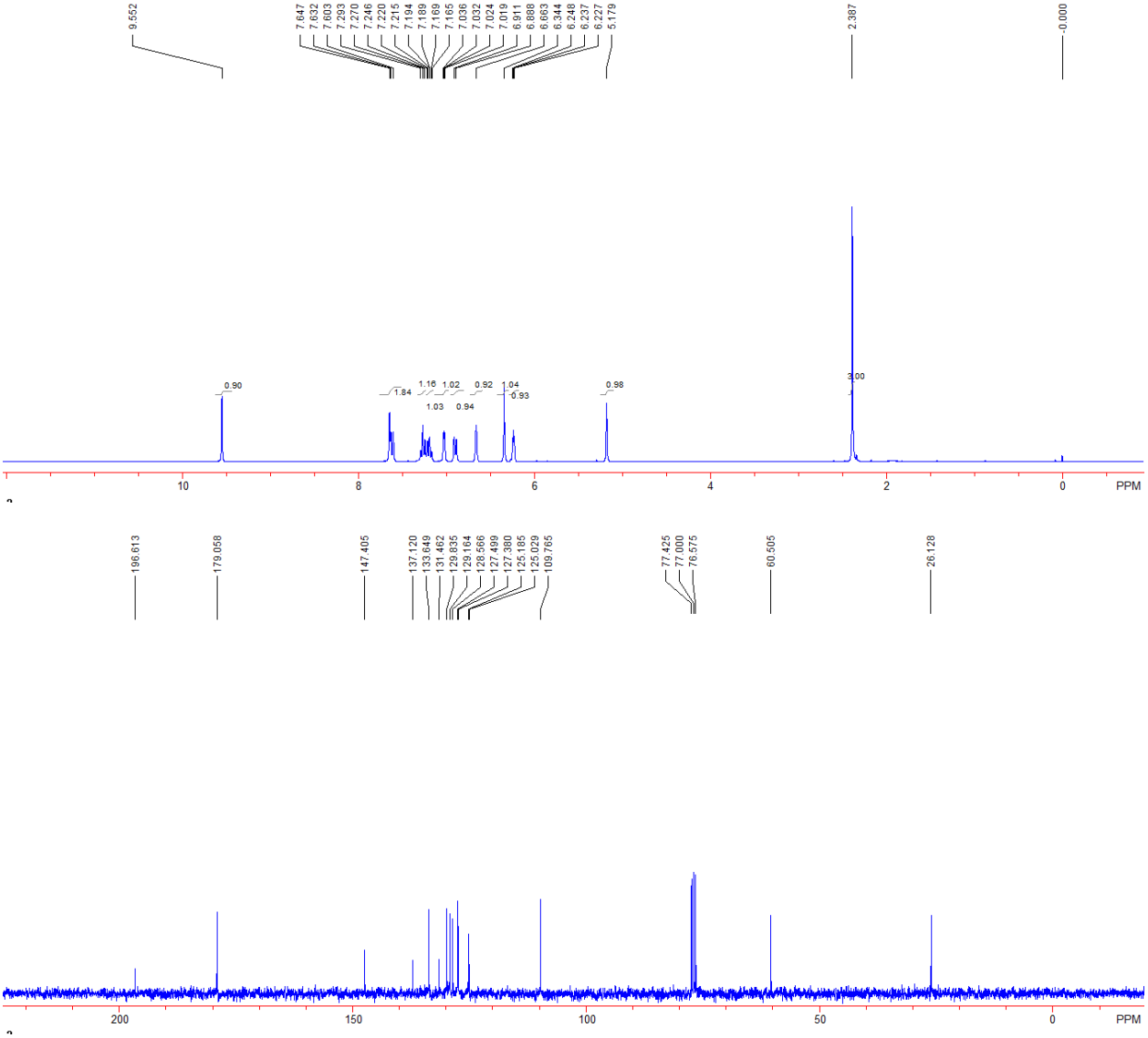
1-(1-(3-bromophenyl)-2-methylene-3-oxobutyl)-1H-pyrrole-2-carbaldehyde 1f: 180 mg, 91% yield; a white solid, m.p. = 72-75 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 2.37 (s, 3H), 5.22 (s,

1H), 6.23 (dd, *J* = 2.7 Hz, 3.9 Hz, 1H), 6.72 (s, 1H), 7.01 (dd, *J* = 1.5 Hz, 3.9 Hz, 1H), 7.12 (d, *J* = 7.8 Hz, 1H), 7.22 (t, *J* = 7.8 Hz, 1H), 7.31 (s, 1H), 7.40 (s, 1H), 7.45 (d, *J* = 7.8 Hz, 1H), 9.52 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.0, 60.0, 109.8, 122.8, 125.5, 127.1, 127.2, 129.4, 130.3, 131.2, 131.3, 131.4, 139.4, 147.9, 179.1, 196.7; IR (neat) ν 2923, 2850, 1649, 1469, 1320, 1219, 1058, 963, 863, 775, 756, 742 cm^{-1}; MS (ESI) m/e 332.0 (M+H); HRMS (ESI) for $C_{16}H_{15}BrNO_2$ (M+H): 332.0281; Found: 332.0293.

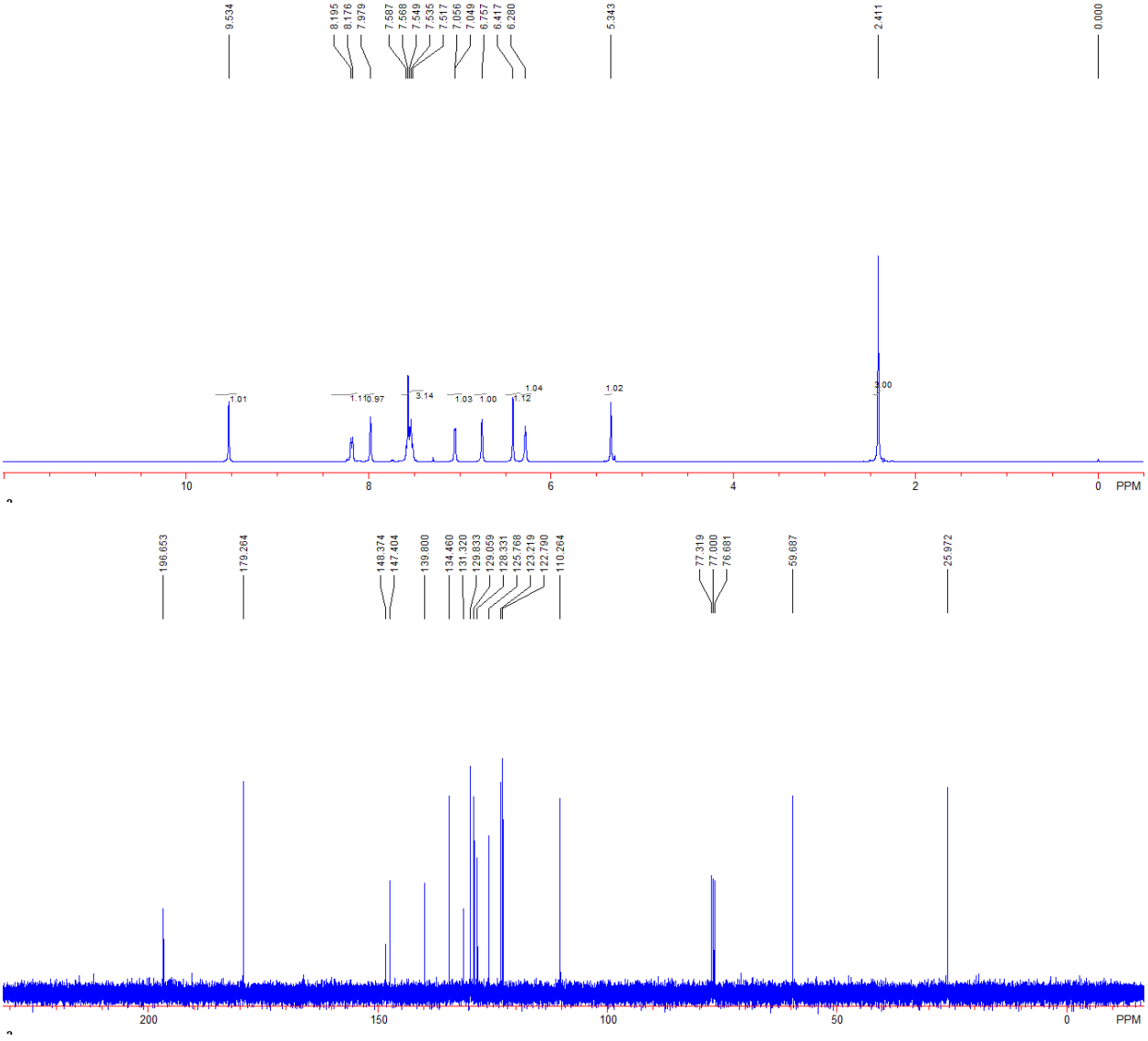


1-(1-(2-bromophenyl)-2-methylene-3-oxobutyl)-1H-pyrrole-2-carbaldehyde 1g: 200 mg, 64%

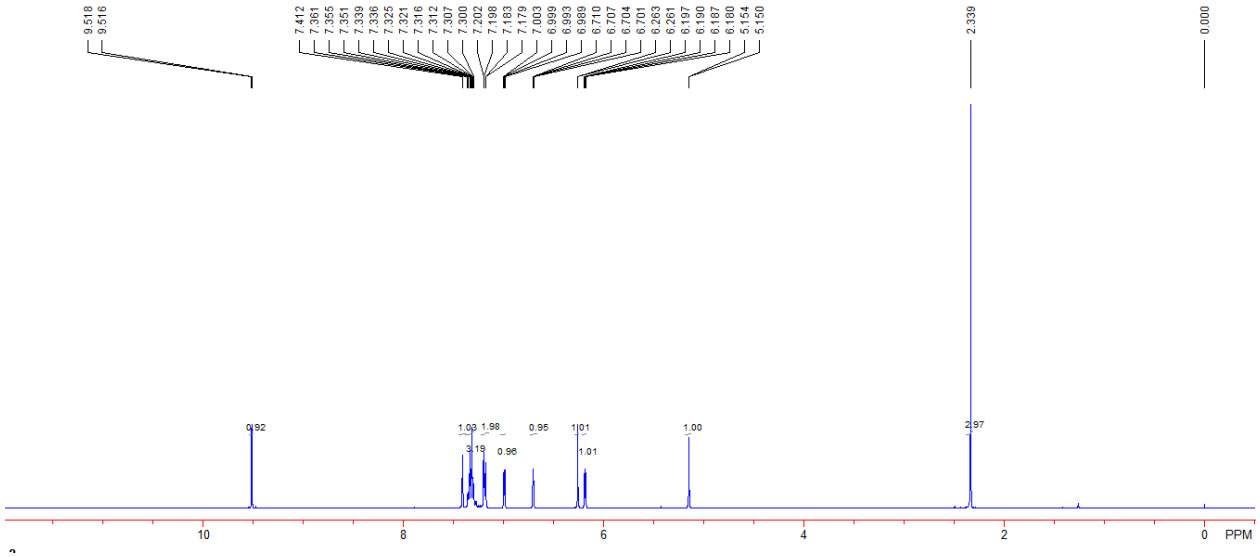
yield; a yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 2.39 (s, 3H), 5.18 (s, 1H), 6.24 (t, *J* = 3.0 Hz, 1H), 6.34(s, 1H), 6.63 (s, 1H), 6.90 (d, *J* = 6.9 Hz, 1H), 7.03 (dd, *J* = 1.2 Hz, 3.6 Hz, 1H), 7.17-7.22 (m, 1H), 7.27 (t, *J* = 6.9 Hz, 1H), 7.62 (d, *J* = 8.7 Hz, 1H), 7.65 (s, 1H), 9.55 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.1, 60.5, 109.8, 125.0, 125.2, 127.4, 127.5, 128.6, 129.2, 129.8, 131.5, 133.6, 137.1, 147.4, 179.1, 196.6; IR (neat) ν 2843, 2804, 1658, 1468, 1367, 1219, 1076, 953, 853, 744 cm^{-1}; MS (ESI) m/e 332.0 (M+H); HRMS (ESI) for $C_{16}H_{15}BrNO_2$ (M+H): 332.0281; Found: 332.0287.

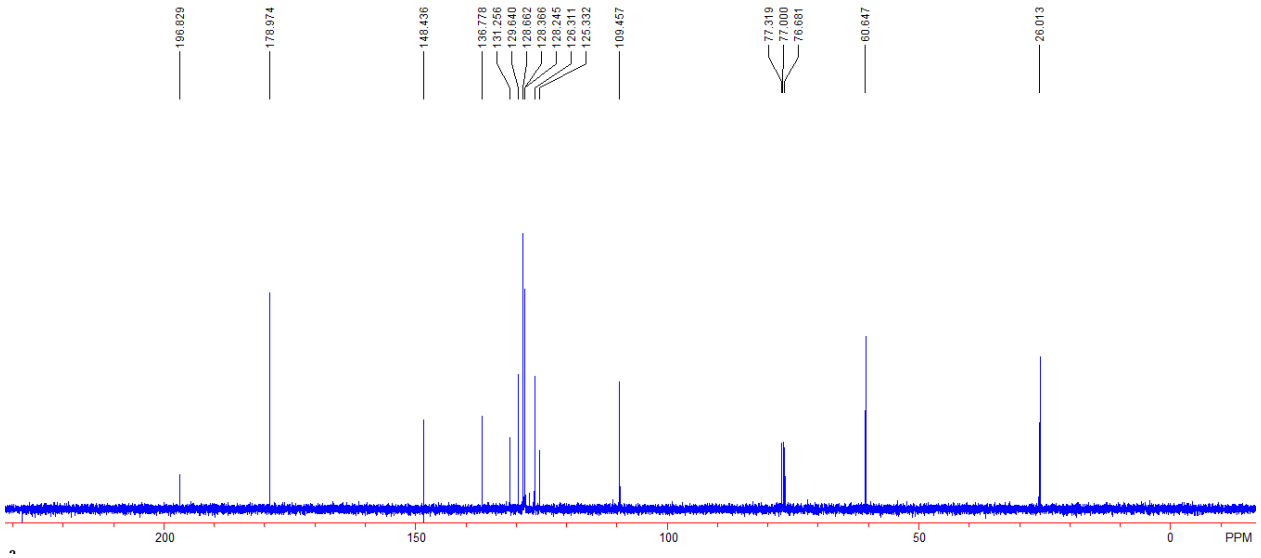


1-(2-methylene-1-(3-nitrophenyl)-3-oxobutyl)-1H-pyrrole-2-carbaldehyde 1h: 136 mg, 91% yield; a white solid, m.p. = 94-96 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.41 (s, 3H), 5.34 (s, 1H), 6.28 (s, 1H), 6.42 (s, 1H), 6.76 (s, 1H), 7.05 (d, *J* = 2.8 Hz, 1H), 7.52-7.59 (m, 3H), 7.98 (s, 1H), 8.19 (d, *J* = 7.6 Hz, 1H), 9.53 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 59.7, 110.3, 122.8, 123.2, 125.8, 128.3, 129.1, 129.8, 131.3, 134.5, 139.8, 147.4, 148.4, 179.3, 196.7; IR (neat) ν 2925, 2854, 1672, 1647, 1531, 1424, 1401, 1324, 1224, 1038, 964, 775, 726 cm^{-1}; MS (ESI) m/e 299.1 (M+H); HRMS (ESI) for $C_{16}H_{14}N_2NaO_4$ (M+Na): 321.0846; Found: 321.0858.

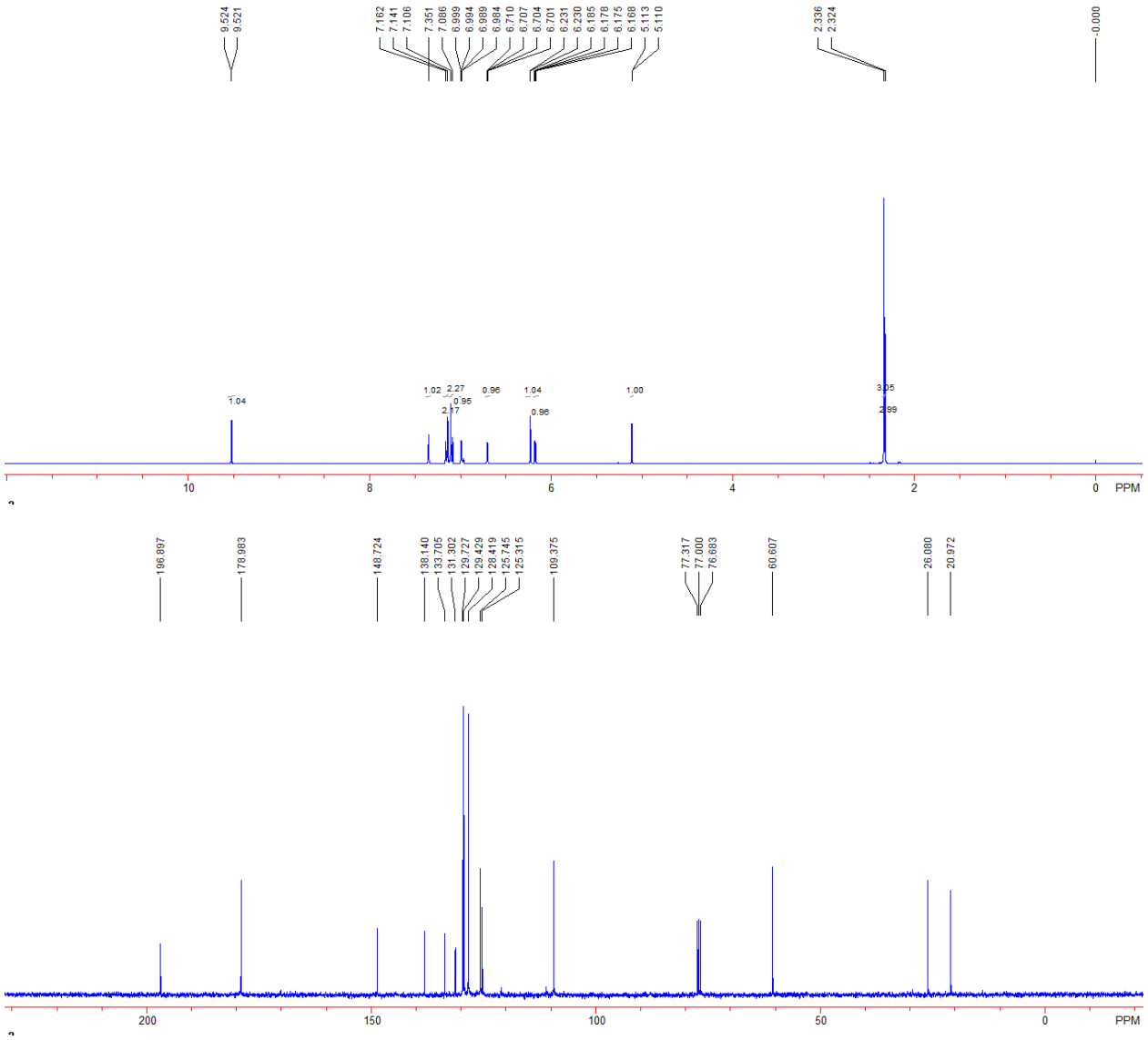


1-(2-methylene-3-oxo-1-phenylbutyl)-1H-pyrrole-2-carbaldehyde 1i: 198 mg, 76% yield; a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.34 (s, 3H), 5.15 (d, *J* = 1.6 Hz, 1H), 6.19 (dd, *J* = 2.8 Hz, 4.0 Hz, 1H), 6.26 (d, *J* = 0.8 Hz, 1H), 6.70 (dd, *J* = 1.2 Hz, 2.4 Hz, 1H), 7.00 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H), 7.19 (dd, *J* = 1.6 Hz, 7.6 Hz, 2H), 7.30-7.36 (m, 3H), 7.41 (s, 1H), 9.52 (d, *J* = 0.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 60.6, 109.5, 125.3, 126.3, 128.2, 128.4, 128.7, 129.6, 131.3, 136.8, 148.4, 179.0, 196.8; IR (neat) ν 2806, 1650, 1493, 1452, 1389, 1330, 1218, 1117, 1077, 958, 851, 755, 727 cm^{-1}; MS (ESI) m/e 254.1 (M+H); HRMS (ESI) for $C_{16}H_{16}NO_2$ (M+H): 254.1176; Found: 254.1180.



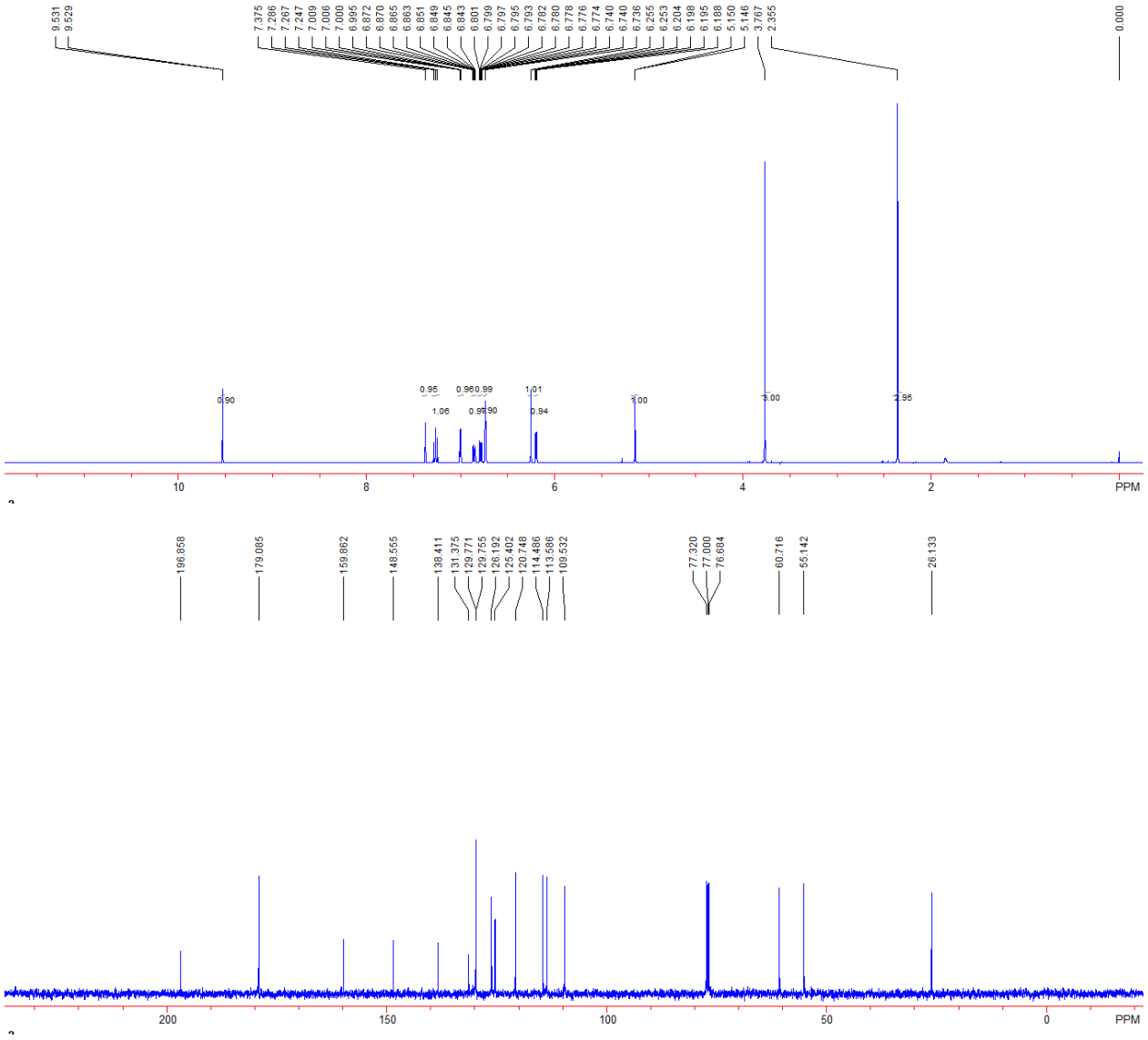


1-(2-methylene-3-oxo-1-(p-tolyl)butyl)-1H-pyrrole-2-carbaldehyde 1j: 123 mg, 84% yield; a white solid, m.p. = 115-117 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.32 (s, 3H), 2.34 (s, 3H), 5.11 (d, *J* = 1.2 Hz, 1H), 6.18 (dd, *J* = 2.8 Hz, 4.0 Hz, 1H), 6.23 (d, *J* = 0.4 Hz, 1H), 6.71 (dd, *J* = 1.2 Hz, 2.4 Hz, 1H), 6.99 (dd, *J* = 2.0 Hz, 4.0 Hz, 1H), 7.10 (d, *J* = 8.0 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.35 (s, 1H), 9.52 (d, *J* = 1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0, 26.1, 60.6, 109.4, 125.3, 125.7, 128.4, 129.4, 129.7, 131.3, 133.7, 138.1, 148.7, 179.0, 196.9; IR (neat) ν 2923, 2853, 1680, 1651, 1416, 1326, 1218, 1077, 958, 857, 777, 740 cm^{-1}; MS (ESI) m/e 268.0 (M+H); HRMS (ESI) for $C_{17}H_{17}NNaO_2$ (M+Na): 290.1152; Found: 290.1161.



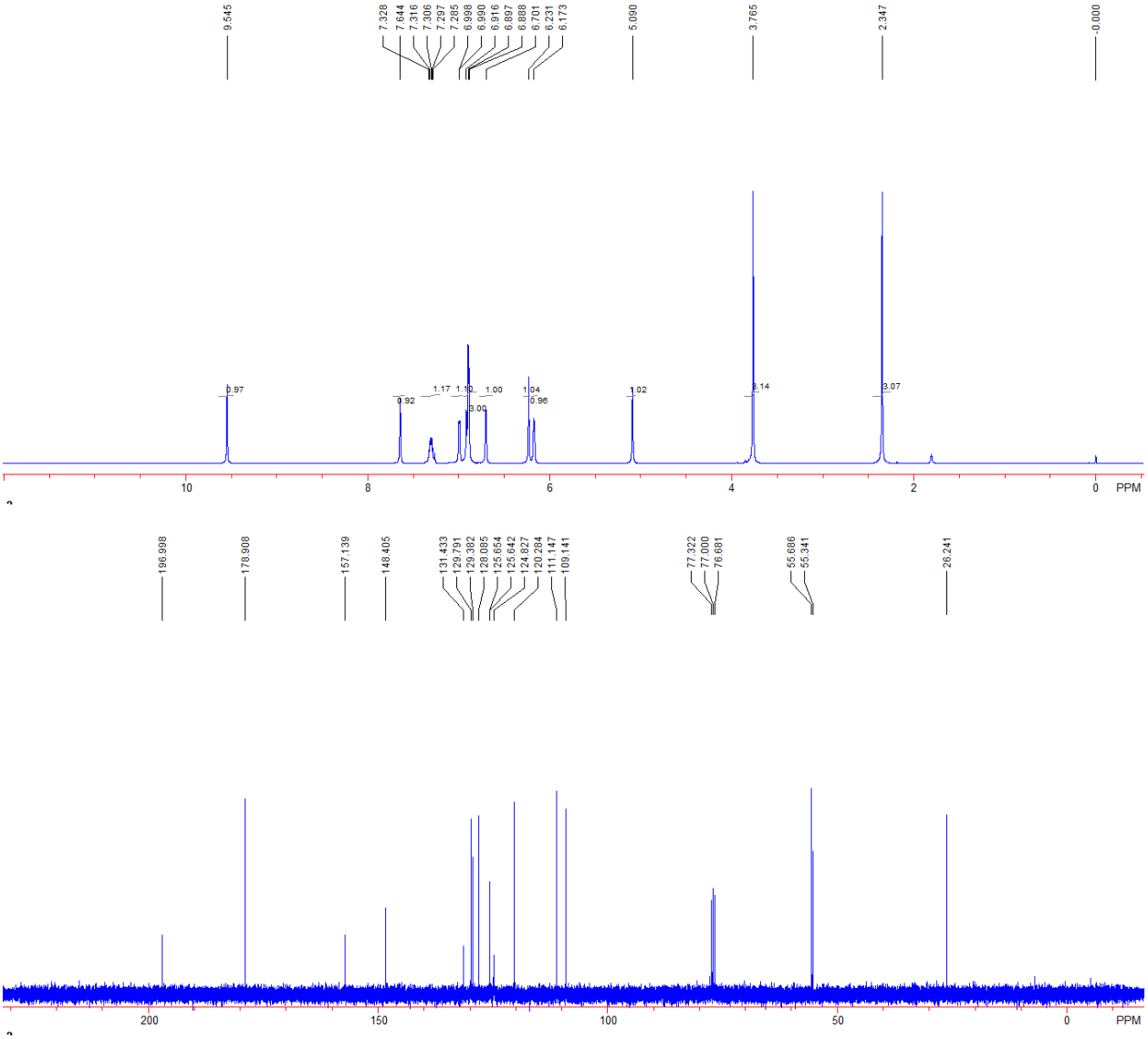
1-(1-(3-methoxyphenyl)-2-methylene-3-oxobutyl)-1H-pyrrole-2-carbaldehyde 1k: 50 mg, 88% yield; a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.36 (s, 3H), 3.77 (s, 3H), 5.15 (d, *J* = 1.6 Hz, 1H), 6.20 (dd, *J* = 2.8 Hz, 4.0 Hz, 1H), 6.25 (d, *J* = 0.8 Hz, 1H), 6.74-6.40 (m, 2H), 6.77-6.80 (m, 1H), 6.86 (ddd, *J* = 0.8 Hz, 2.4 Hz, 8.0 Hz, 1H), 7.00 (dd, *J* = 2.0 Hz, 4.0 Hz, 1H), 7.27 (t, *J* = 8.0 Hz, 1H), 7.38 (s, 1H), 9.53 (d, *J* = 0.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.1, 55.1, 60.7, 109.5, 113.6, 114.5, 120.7, 125.4, 126.2, 129.7, 129.8, 131.4, 138.4, 148.6, 159.9, 179.1, 196.9; IR

(neat) ν 2962, 2838, 1658, 1601, 1467, 1368, 1291, 1267, 1074, 959, 775, 745 cm^{-1}; MS (ESI) m/e 284.1 (M+H); HRMS (ESI) for $C_{17}H_{17}NNaO_3$ (M+Na): 306.1101; Found: 306.1111.



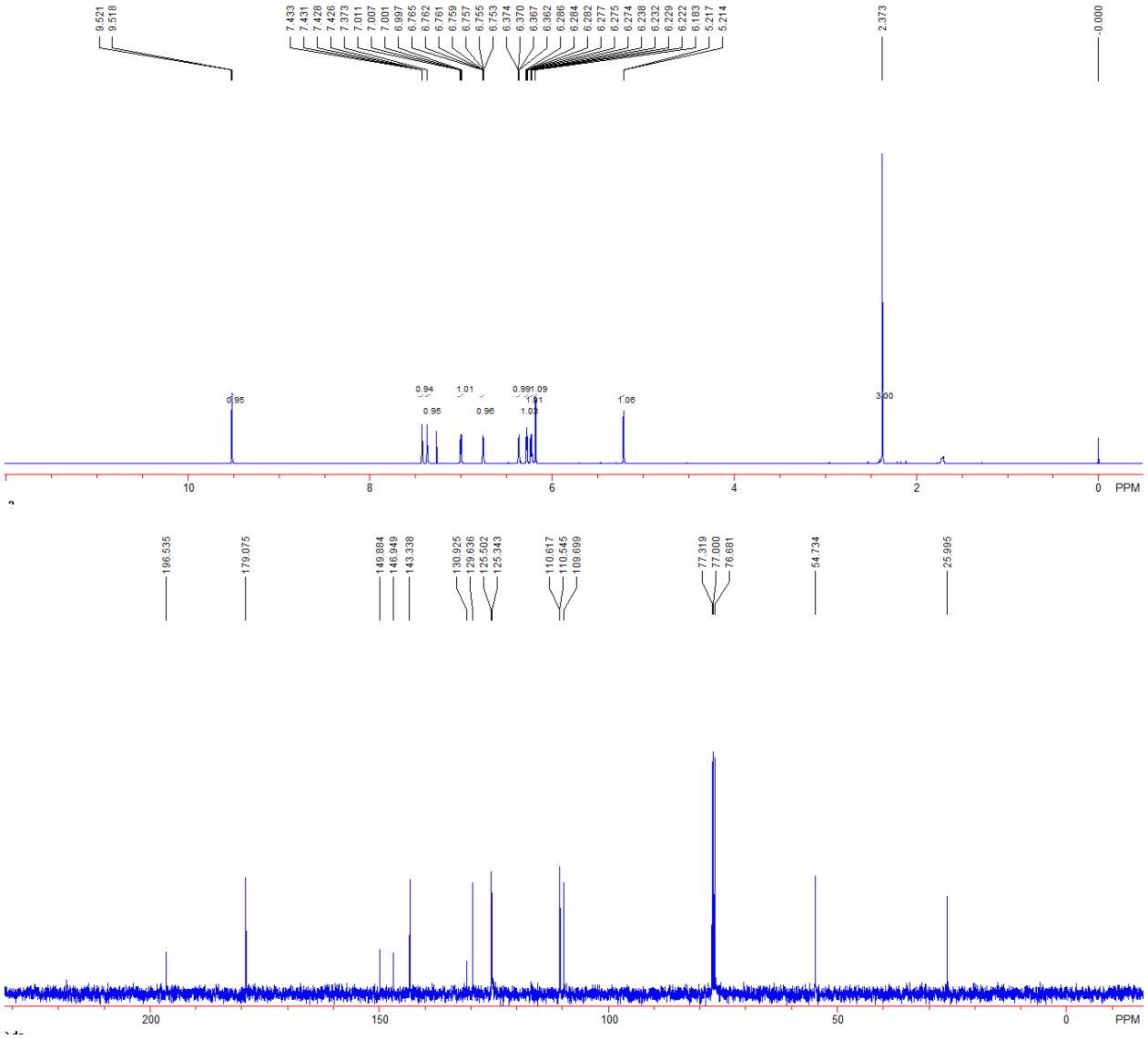
1-(1-(2-methoxyphenyl)-2-methylene-3-oxobutyl)-1H-pyrrole-2-carbaldehyde 1l: 125 mg, 88% yield; a white solid, m.p. = 128-131 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.35 (s, 3H), 3.77 (s, 3H), 5.09 (s, 1H), 6.17 (s, 1H), 6.23 (s, 1H), 6.70 (s, 1H), 6.89-6.92 (m, 3H), 6.99 (d, *J* = 3.2 Hz, 1H), 7.29-7.33 (m, 1H), 7.64 (s, 1H), 9.55 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.2, 55.3, 55.7, 109.1, 111.1, 120.3, 124.8, 125.6, 125.7, 128.1, 129.4, 129.8, 131.4, 148.4, 157.1,

178.9, 197.0; IR (neat) ν 2925, 2803, 1656, 1489, 1463, 1399, 1329, 1248, 1113, 1069, 951, 855, 773, 755 cm^{-1}; MS (ESI) m/e 284.1 (M+H); HRMS (ESI) for $C_{17}H_{17}NNaO_3$ (M+Na): 306.1101; Found: 306.1111.



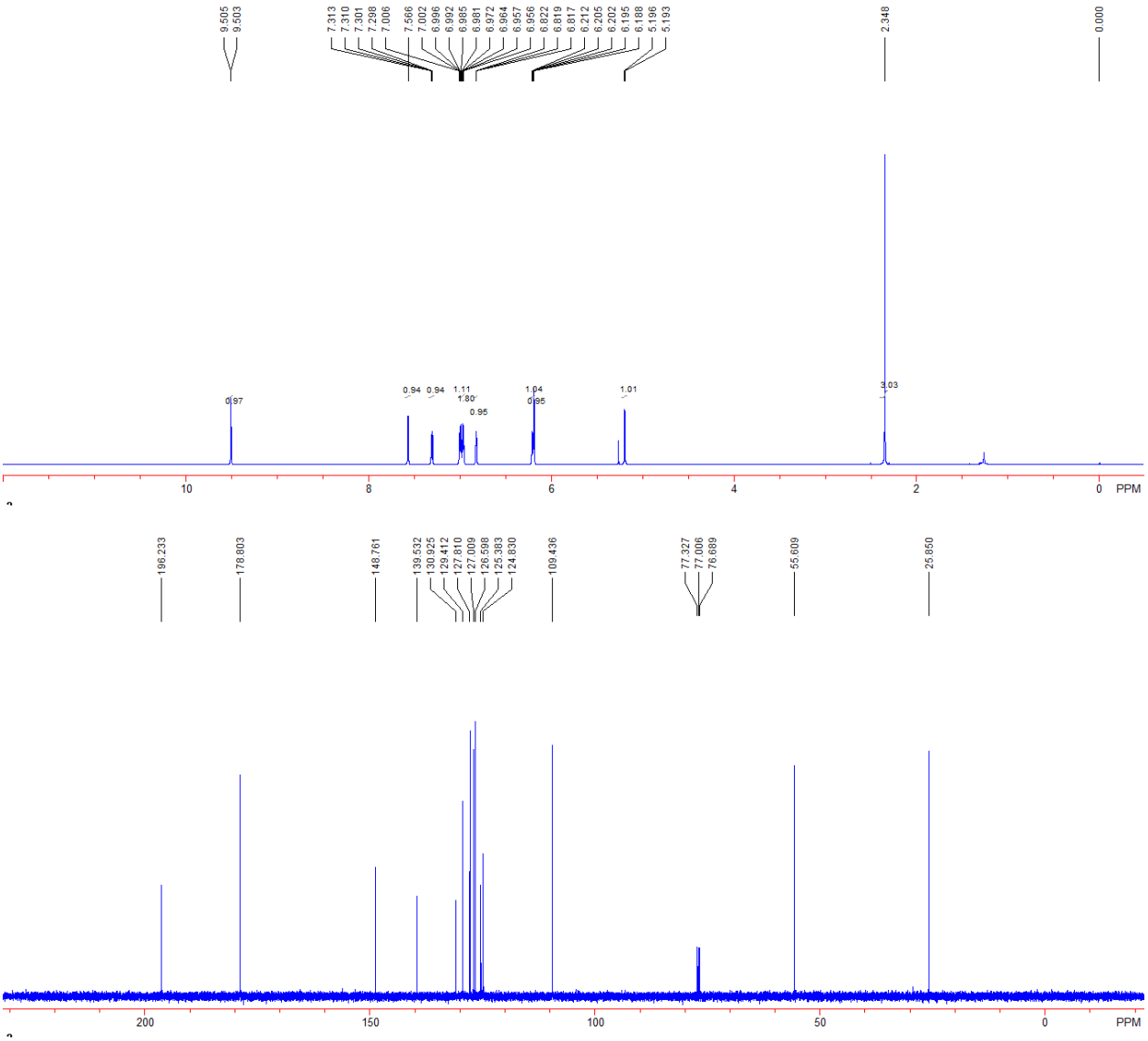
1-(1-(furan-2-yl)-2-methylene-3-oxobutyl)-1H-pyrrole-2-carbaldehyde 1m: 38 mg, 26% yield; a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.37 (s, 3H), 5.22 (d, *J* = 1.2 Hz, 1H), 6.18 (s, 1H), 6.23 (dd, *J* = 2.8 Hz, 4.0 Hz, 1H), 6.27-6.29 (m, 1H), 6.37 (dd, *J* = 1.6 Hz, 2.8 Hz, 1H), 6.75-6.77 (m, 1H), 7.00 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H), 7.37 (s, 1H), 7.43 (dd, *J* = 0.8 Hz, 2.0 Hz,

1H), 9.52 (d, J = 1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 54.7, 109.7, 110.5, 110.6, 125.3, 125.5, 129.6, 130.9, 143.3, 146.9, 149.9, 179.1, 196.5; IR (neat) ν 1656, 1468, 1400, 1368, 1317, 1276, 1116, 1014, 958, 807, 742 cm^{-1}; MS (EI) *m/e* (%): 243 [M^+] (1.8), 200 (15.5), 156 (85.6), 139 (100.0), 126 (40.2), 90 (61.1), 76 (36.6), 52 (38.2); HRMS (EI) Calcd. for $C_{14}H_{13}NO_3$ requires (M^+) 243.0895, Found: 243.0899.

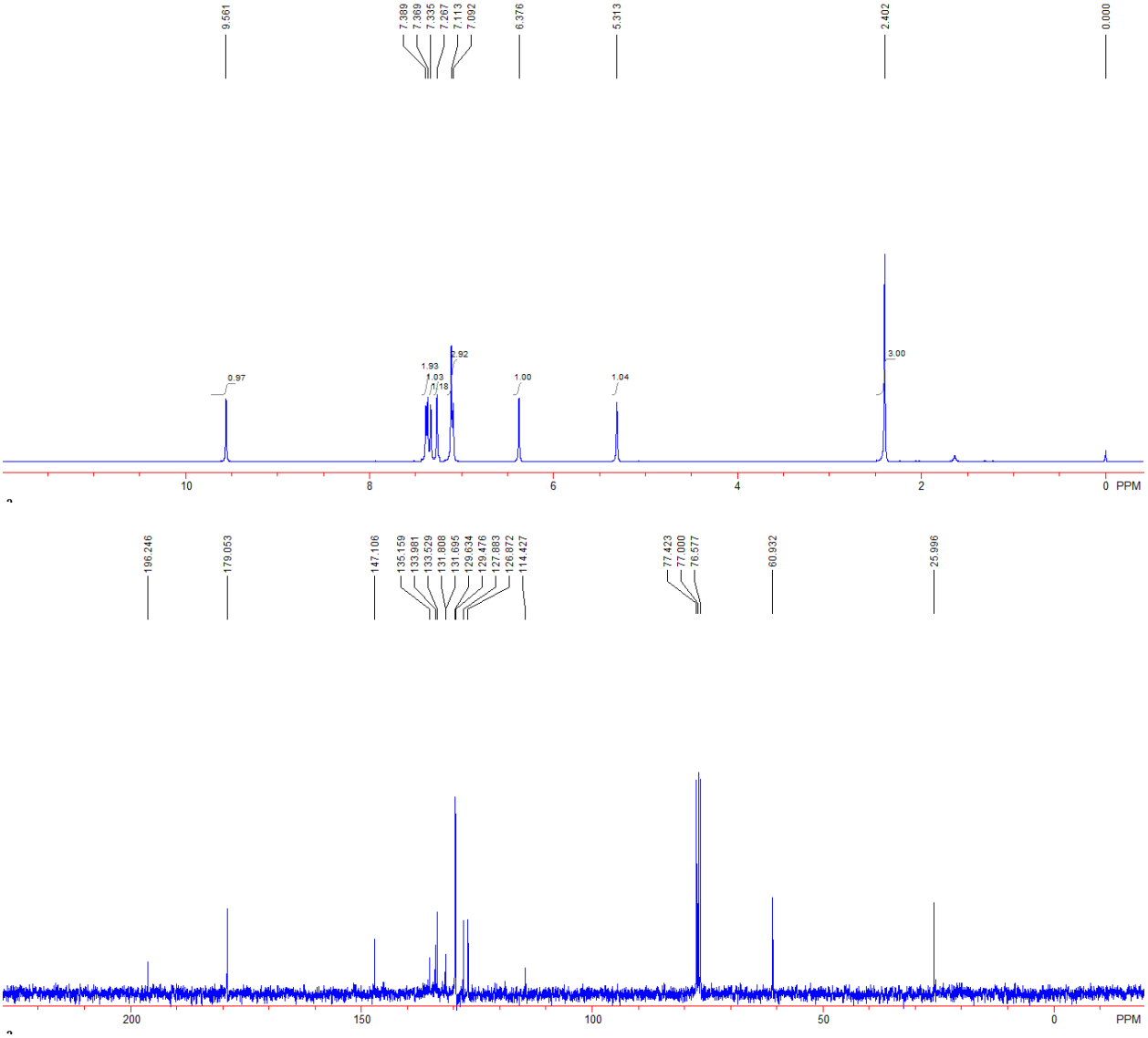


1-(2-methylene-3-oxo-1-(thiophen-2-yl)butyl)-1H-pyrrole-2-carbaldehyde 1n: 128 mg, 49% yield; a white solid, m.p. = 68-71 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.35 (s, 3H), 5.19 (d, J

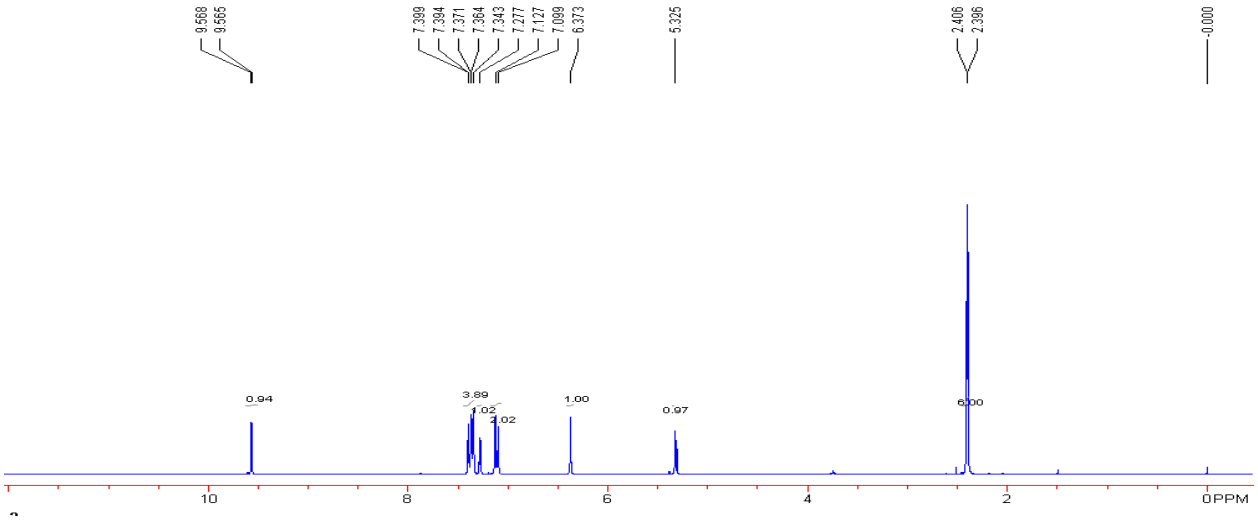
= 1.2 Hz, 1H), 6.19 (s, 1H), 6.20 (dd, *J* = 2.8 Hz, 4.0 Hz, 1H), 6.82 (t, *J* = 1.2 Hz, 1H), 6.96-6.99 (m, 2H), 7.00 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H), 7.31 (dd, *J* = 1.2 Hz, 4.8 Hz, 1H), 7.57 (s, 1H), 9.50 (d, *J* = 0.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.9, 55.6, 109.4, 124.8, 125.4, 126.6, 127.0, 127.8, 129.4, 130.9, 139.5, 148.8, 178.8, 196.2; IR (neat) ν 2924, 2805, 1654, 1467, 1391, 1315, 1218, 1033, 957, 853, 743, 708 cm^{-1}; MS (ESI) m/e 260.0 (M+H); HRMS (ESI) for $C_{14}H_{13}NNaO_2S$ (M+Na): 282.0559; Found: 282.0568.

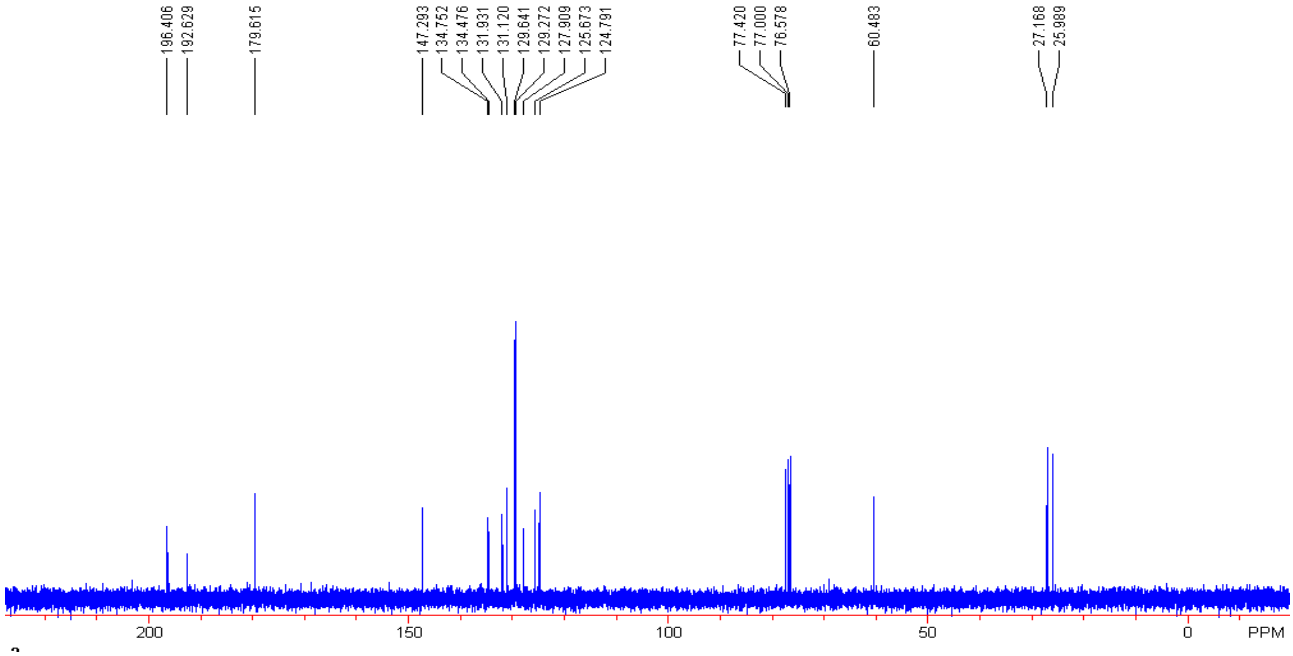


1-(1-(4-chlorophenyl)-2-methylene-3-oxobutyl)-5-formyl-1H-pyrrole-3-carbonitrile 1o: 140 mg, 99% yield; a white solid, m.p. = 76-78 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.40 (s, 3 H), 5.31 (s, 1H), 6.38 (s, 1H), 7.09-7.11 (m, 3H), 7.27 (s, 1H), 7.34 (s, 1H), 7.38 (d, *J* = 8.0 Hz, 2H), 9.56 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.0, 60.9, 114.4, 126.9, 127.9, 129.5, 129.6, 131.7, 131.8, 133.5, 134.0, 135.2, 147.1, 179.1, 196.2; IR (neat) ν 2956, 2922, 2852, 1642, 1587, 1488, 1468, 1423, 1373, 1240, 1012, 968, 853, 821, 730 cm^{-1}; MS (ESI) m/e 330.0 (M+H_2O); HRMS (ESI) for $C_{17}H_{13}ClN_2NaO_2$ (M+Na): 335.0558; Found: 335.0562.

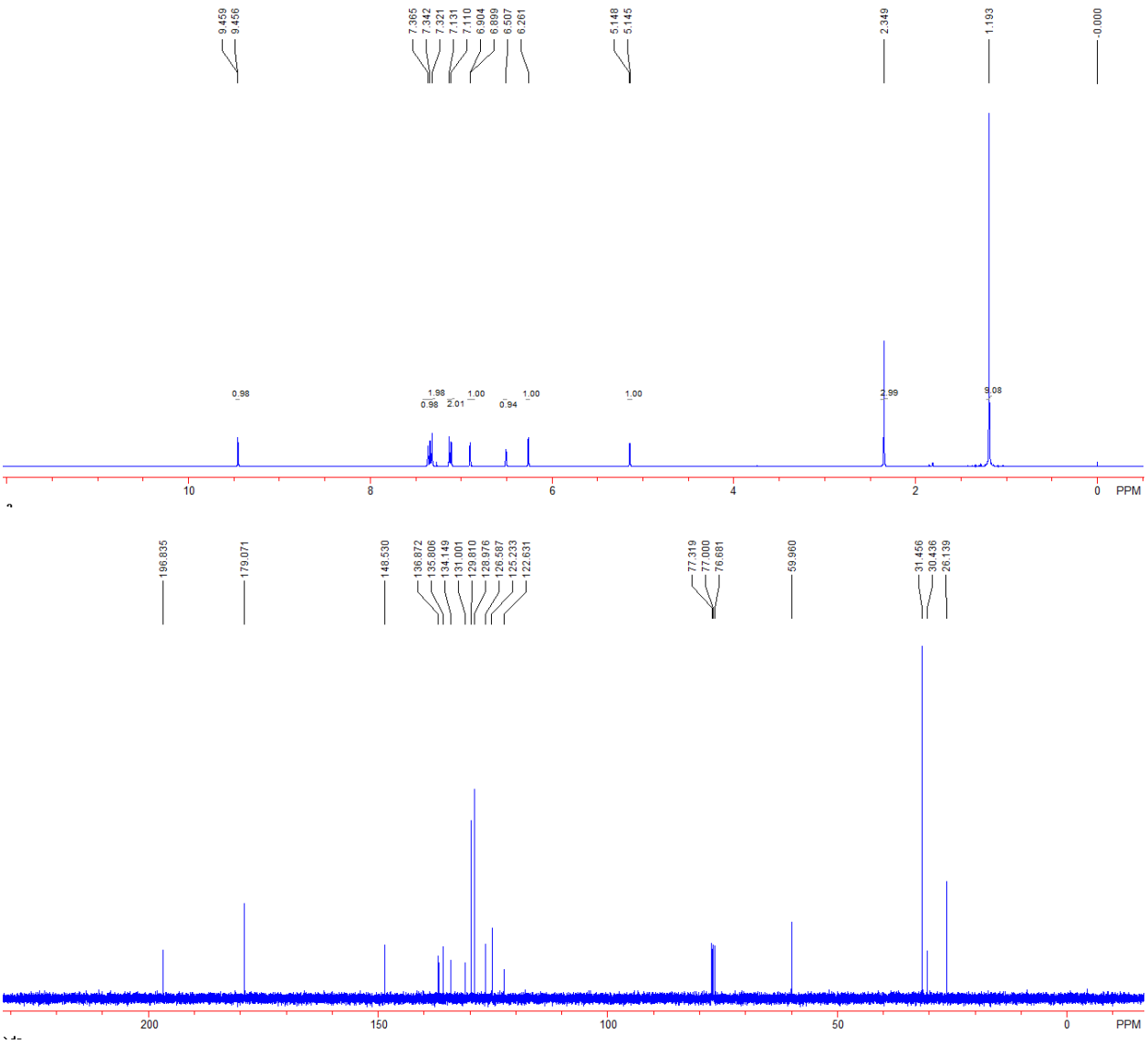


4-acetyl-1-(1-(4-chlorophenyl)-2-methylene-3-oxobutyl)-1H-pyrrole-2-carbaldehyde 1p: 181 mg, 99% yield; a white solid, m.p. = 135-137 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 2.40 (s, 3H), 2.41 (s, 3H), 5.33 (s, 1H), 6.37 (s, 1H), 7.11 (d, *J* = 8.4 Hz, 2H), 7.28 (s, 1H), 7.34-7.40 (m, 4H), 9.57 (d, *J* = 0.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.0, 27.2, 60.5, 124.8, 125.7, 127.9, 129.3, 129.6, 131.1, 131.9, 134.5, 134.8, 147.3, 179.6, 192.6, 196.4; IR (neat) ν 2925, 1662, 1536, 1486, 1372, 1214, 1098, 958, 853, 784, 758, 726 cm^{-1}; MS (ESI) m/e 352.0 (M+Na); HRMS (ESI) for $C_{18}H_{16}ClNNaO_3$ (M+Na): 352.0819; Found: 352.0725.



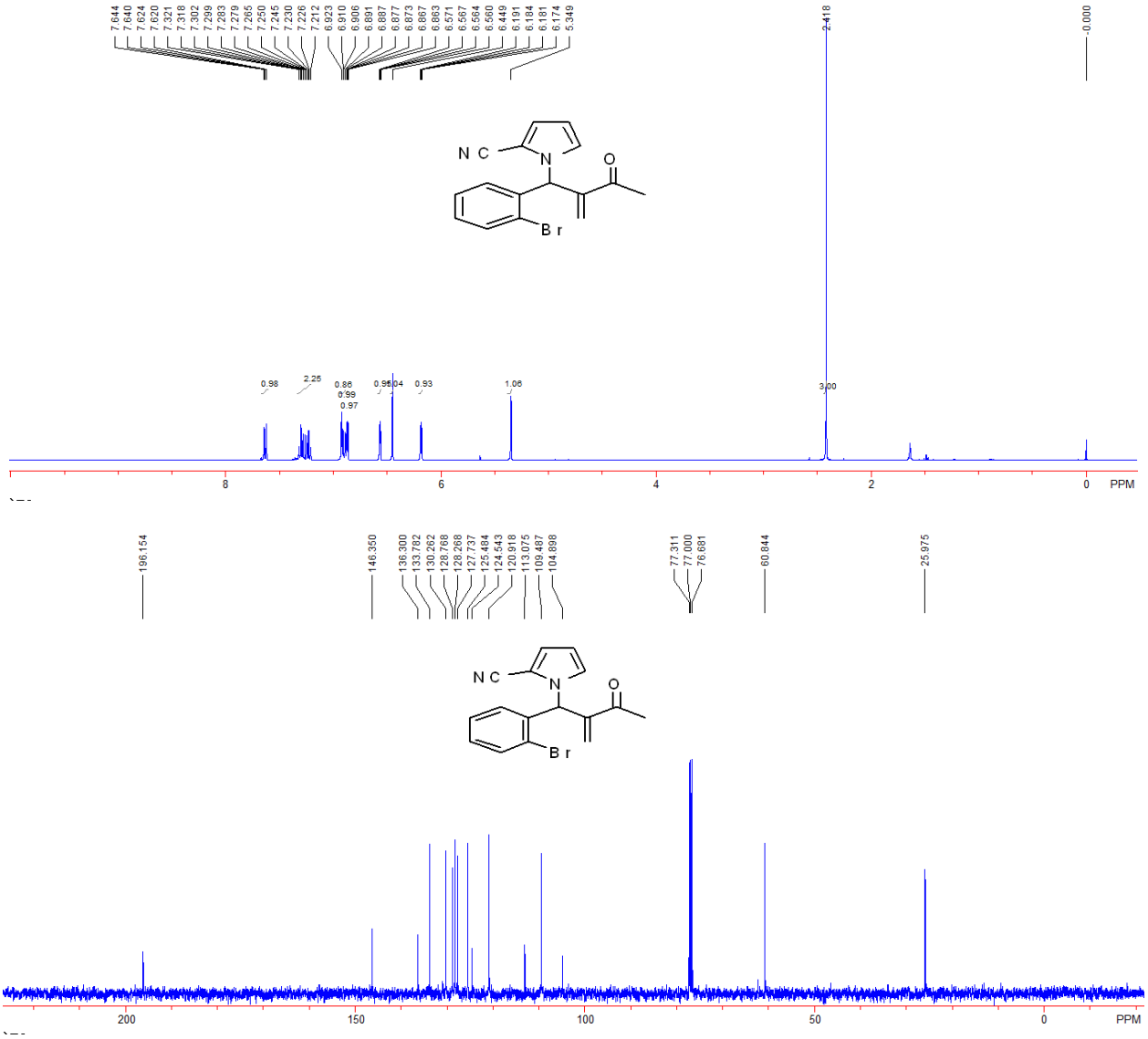


4-(tert-butyl)-1-(1-(4-chlorophenyl)-2-methylene-3-oxobutyl)-1H-pyrrole-2-carbaldehyde 1q: 170 mg, 98% yield; a white solid, m.p. = 91-94 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.19 (s, 9H), 2.35 (s, 3H), 5.15 (d, *J* = 1.2 Hz, 1H), 6.26 (s, 1H), 6.51 (s, 1H), 6.90 (d, *J* = 2.0 Hz, 1H), 7.12 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 7.37 (s, 1H), 9.46 (d, *J* = 1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.1, 30.4, 31.5, 60.0, 122.6, 125.2, 126.6, 129.0, 129.8, 131.0, 134.1, 135.8, 136.9, 148.5, 179.1, 196.8; IR (neat) ν 2958, 1688, 1656, 1489, 1394, 1361, 1228, 1088, 956, 861, 777, 731 cm^{-1}; MS (EI) *m/e* (%): 343 [M^{+}] (18.9), 330 (16.6), 328 (48.0), 302 (16.3), 300 (47.5), 136 (18.9), 115 (37.6), 43 (100.0); HRMS (EI) Calcd. for $C_{20}H_{22}NO_2Cl$ requires (M^{+}) 343.1339, Found: 343.1344.



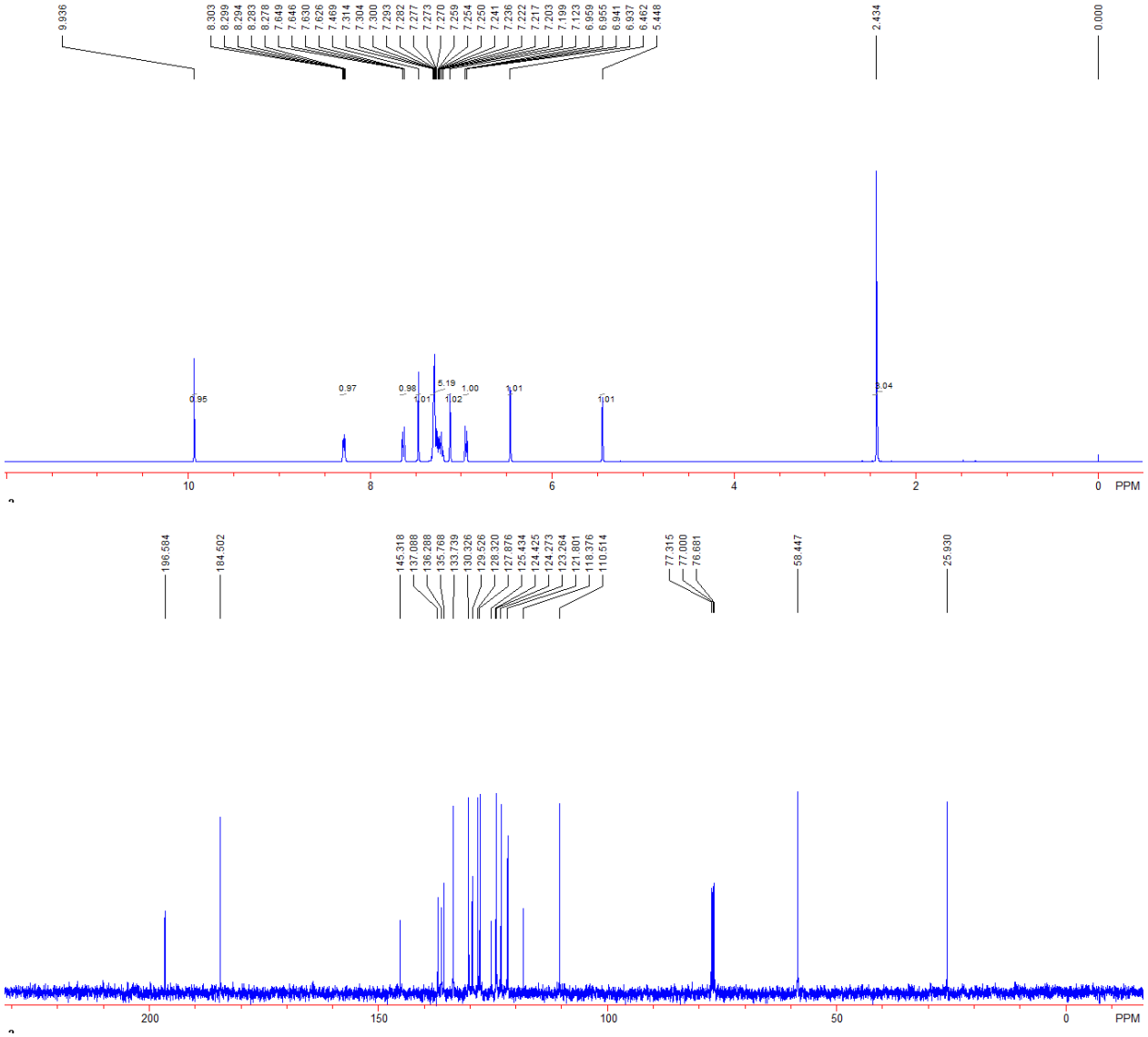
1-(1-(2-bromophenyl)-2-methylene-3-oxobutyl)-1H-pyrrole-2-carbonitrile 1r: 154 mg, 94% yield (prepared using same procedure as that of **1a**); a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.42 (s, 3H), 5.35 (s, 1H), 6.18 (dd, *J* = 2.8 Hz, 4.0 Hz, 1H), 6.45 (s, 1H), 6.57 (dd, *J* = 1.6 Hz, 2.8 Hz, 1H), 6.87 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H), 6.88-6.91 (m, 1H), 6.92 (s, 1H), 7.21-7.32 (m, 2H), 7.62-7.64 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 60.8, 104.9, 109.5, 113.0, 120.9, 124.5, 125.5, 127.7, 128.3, 128.8, 130.2, 133.8, 136.3, 146.4, 196.2; IR (neat) ν 2367, 2218, 1678, 1521, 1406, 1281, 1220, 1111, 1074, 978, 751 cm^{-1}; MS (ESI) m/e 351.2 (M+Na); HRMS (ESI)

for $C_{16}H_{13}BrN_2NaO$ (M+Na): 351.0104; Found: 351.0116.



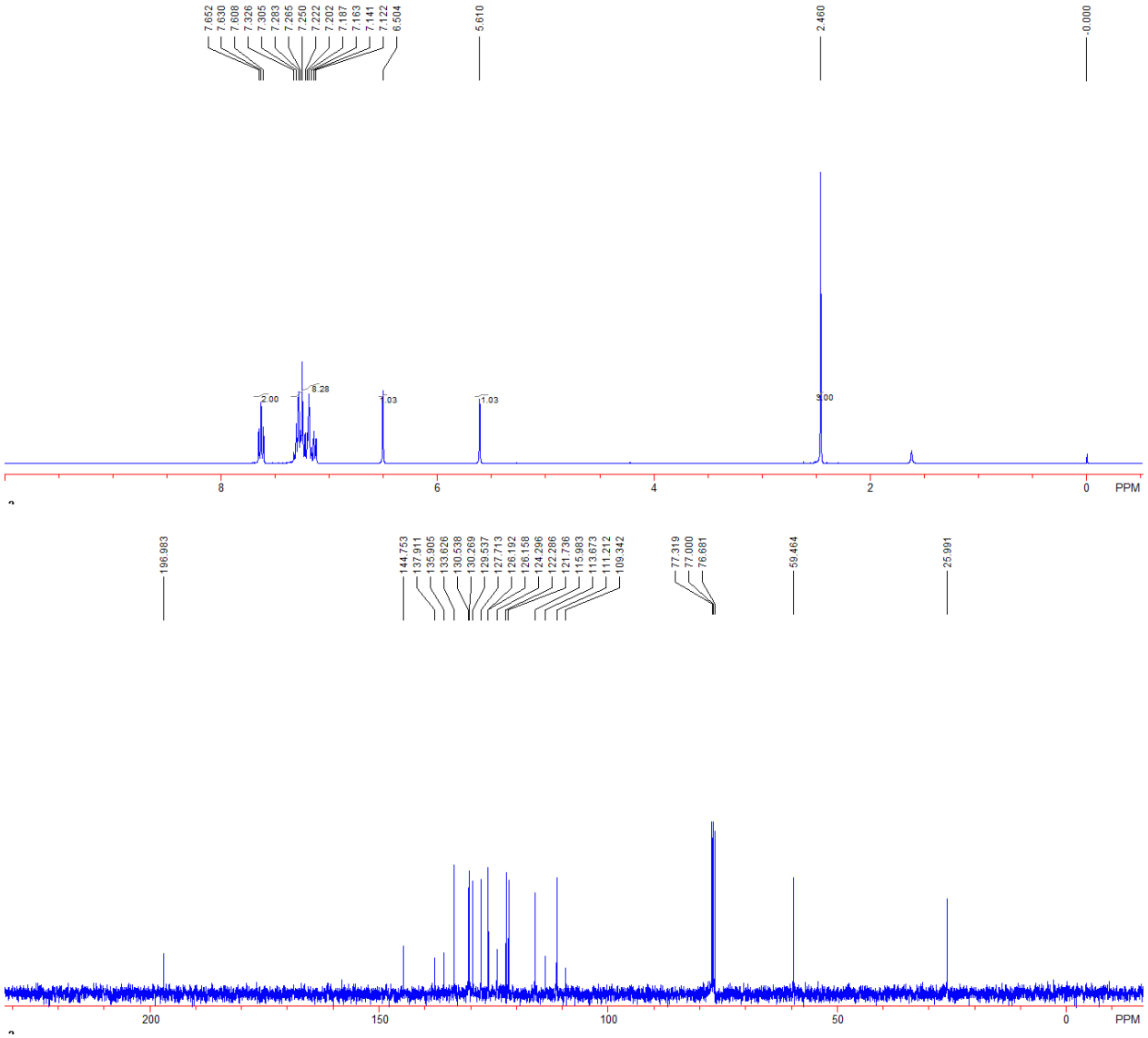
1-(1-(2-bromophenyl)-2-methylene-3-oxobutyl)-1H-indole-3-carbaldehyde 1s: 191 mg, 99% yield (prepared using the same procedure as that of **1a**); a white solid, m.p. = 149-151 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.43 (s, 3H), 5.45 (s, 1H), 6.46 (s, 1H), 6.95 (dd, *J* = 1.6 Hz, 7.2 Hz, 1H), 7.12 (s, 1H), 7.20-7.31 (m, 5H), 7.47 (s, 1H), 7.64 (dd, *J* = 1.6 Hz, 8.0 Hz, 1H), 8.28-8.30 (m, 1H), 9.94 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.9, 58.4, 110.5, 118.4, 121.8, 123.3, 124.3,

124.4, 125.4, 127.9, 128.3, 129.5, 130.3, 133.7, 135.8, 136.3, 137.1, 145.3, 184.5, 196.6; IR (neat) ν 2925, 1663, 1524, 1460, 1366, 1299, 1237, 1163, 1023, 980, 781, 745 cm^{-1}; MS (EI) *m/e* (%): 381 [M^+] (25.5), 383 (23.5), 158 (46.3), 144 (21.6), 116 (23.2), 115 (52.4), 43 (100.0), 102 (70.1); HRMS (EI) Calcd. for $C_{20}H_{16}NO_2Br$ requires (M^+) 381.0364, Found: 381.0361.



1-(1-(2-bromophenyl)-2-methylene-3-oxobutyl)-1H-indole-2-carbonitrile 1t: 121 mg, 87% yield (prepared using the same procedure as that of **1a**); a white foam; ^1H NMR (400 MHz, $CDCl_3$,

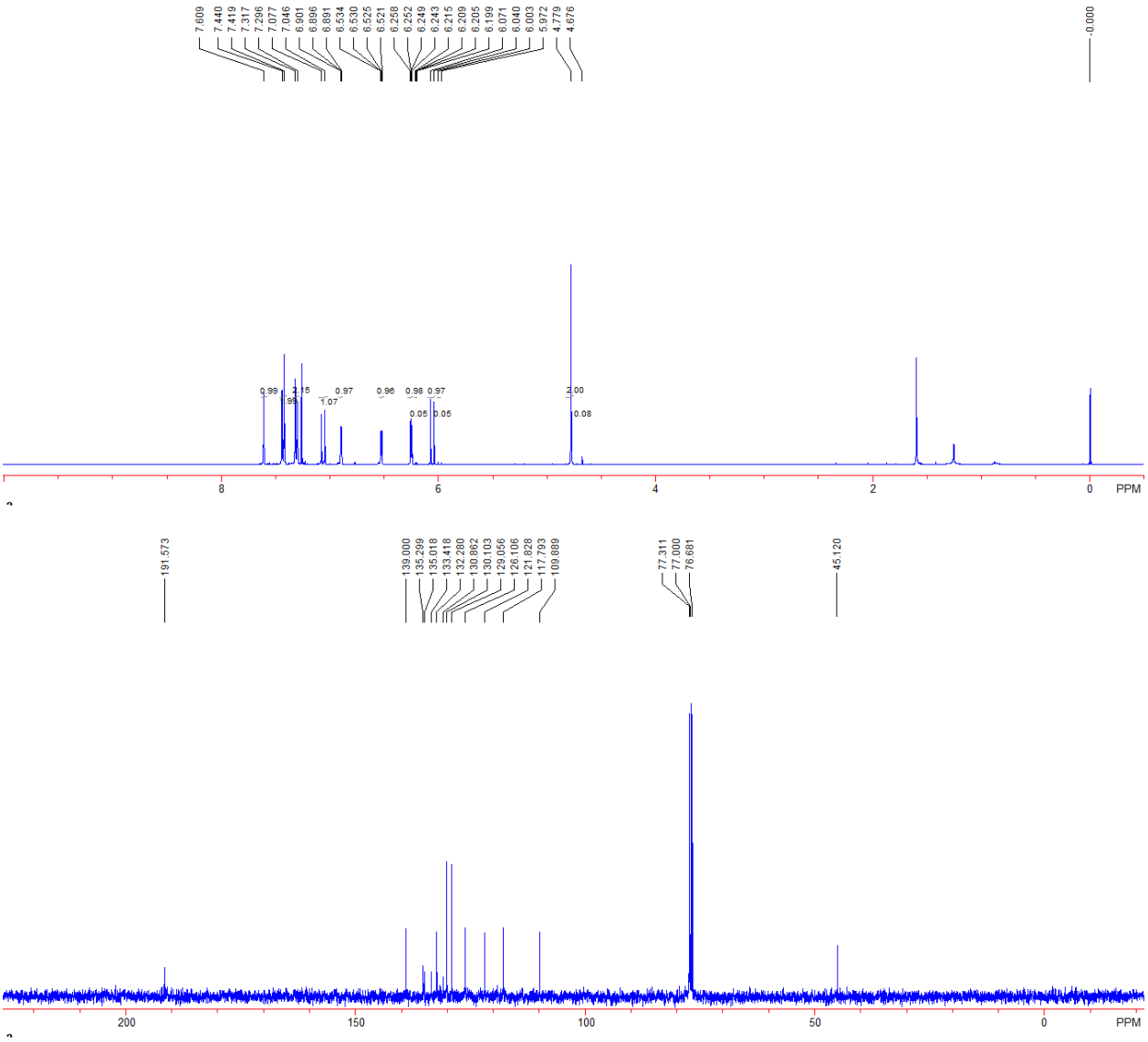
TMS) δ 2.46 (s, 3H), 5.61 (s, 1H), 6.50 (s, 1H), 6.45 (s, 1H), 7.12-7.33 (m, 8H), 7.63 (t, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 59.5, 109.3, 111.2, 113.7, 116.0, 121.7, 122.3, 124.3, 126.1, 126.2, 127.7, 129.5 130.3, 130.5, 133.6, 135.9, 137.9, 144.8, 197.0; IR (neat) ν 2220, 1678, 1442, 1402, 1362, 1317, 1244, 1116, 1025, 958, 804, 734 cm^{-1}; MS (ESI) m/e 396.0 ($M+H_2O$); HRMS (ESI) for $C_{20}H_{15}BrN_2NaO$ (M+Na): 401.0260; Found: 401.0274.



General procedure for the synthesis of 2

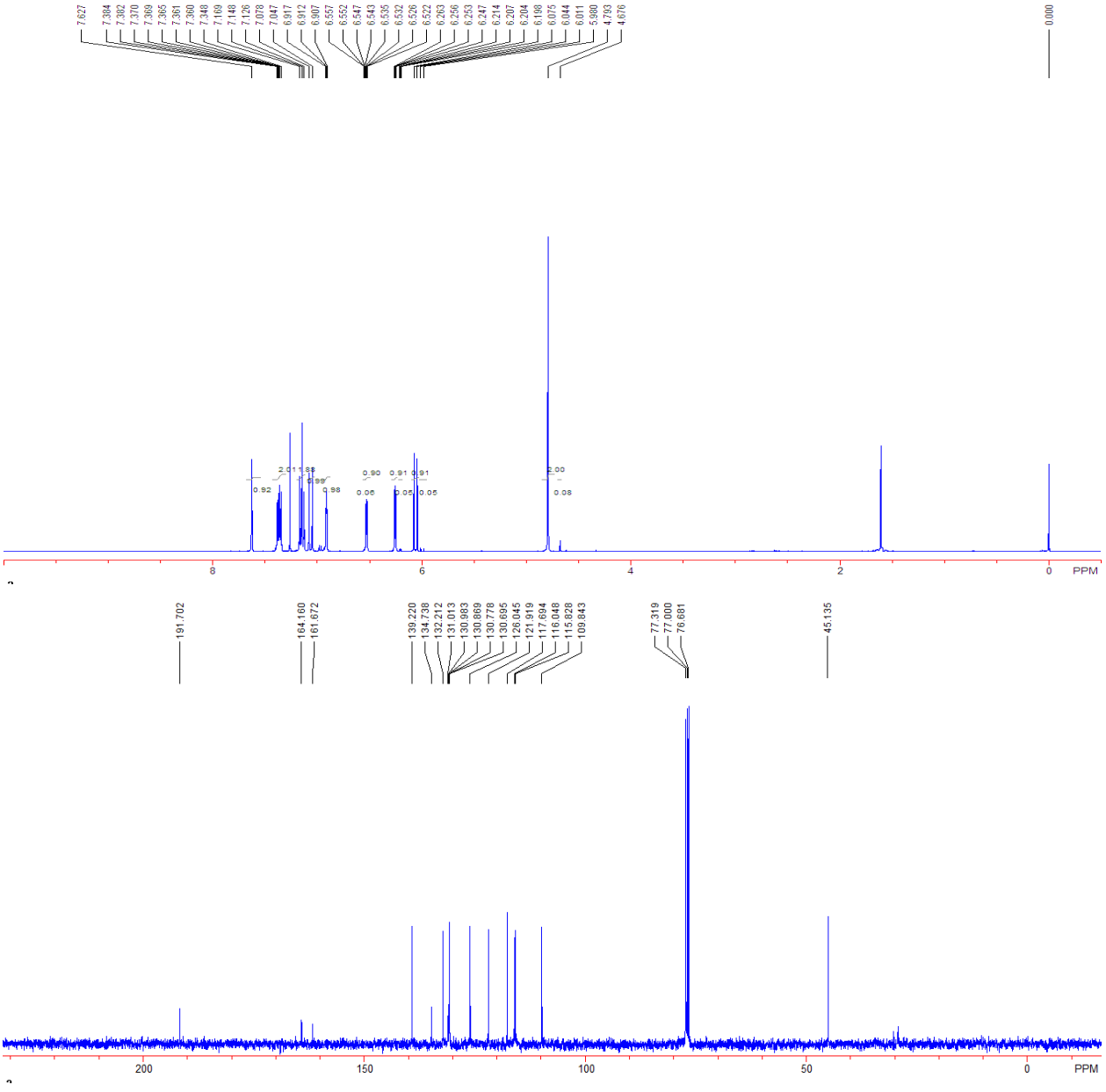
To a solution of compound **1a** (0.1 mmol, 31.0 mg) and sodium ethoxide (0.05 mmol, 3.4 mg) in THF (1.0 mL) was added tetramethylammonium hydroxide (0.02 mmol, 52 μL (10% in water)), the mixture was stirred at ambient temperature. The reaction solution was monitored by TLC. After the reaction complete, the solvent was removed under reduced pressure and the residue was chromatographed on silica gel (elution with petroleum ether/EtOAc = 8/1) to provide the corresponding product **2a**.

(E)-6-(4-chlorobenzylidene)-5H-pyrrolo[1,2-a]azepin-7(6H)-one 2a: 23 mg, 82% yield; *E*/*Z* > 20/1 (determined by crude ^{1}H NMR spectroscopy); a yellow solid, m.p. = 146-147 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 4.68 (s, 2H) (minor isomer), 4.78 (s, 2H), 5.99 (d, *J* = 12.4 Hz, 1H) (minor isomer), 6.06 (d, *J* = 12.4 Hz, 1H), 6.21 (dd, *J* = 2.4 Hz, 4.0 Hz, 1H) (minor isomer), 6.25 (dd, *J* = 2.4 Hz, 4.0 Hz, 1H), 6.53 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H), 6.90 (t, *J* = 2.0 Hz, 1H), 7.06 (d, *J* = 12.4 Hz, 1H), 7.31 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 2H), 7.61 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.1, 109.9, 117.8, 121.8, 126.1, 129.1, 130.1, 130.9, 132.3, 133.4, 135.0, 135.3, 139.0, 191.6; IR (neat) ν 2956, 2922, 2853, 1642, 1586, 1488, 1468, 1374, 1240, 1081, 956, 853, 822, 730 cm^{-1}; MS (ESI) m/e 270.0 (M+H); HRMS (ESI) for $C_{16}H_{12}ClNNaO$ (M+Na): 292.0500; Found: 292.0512.



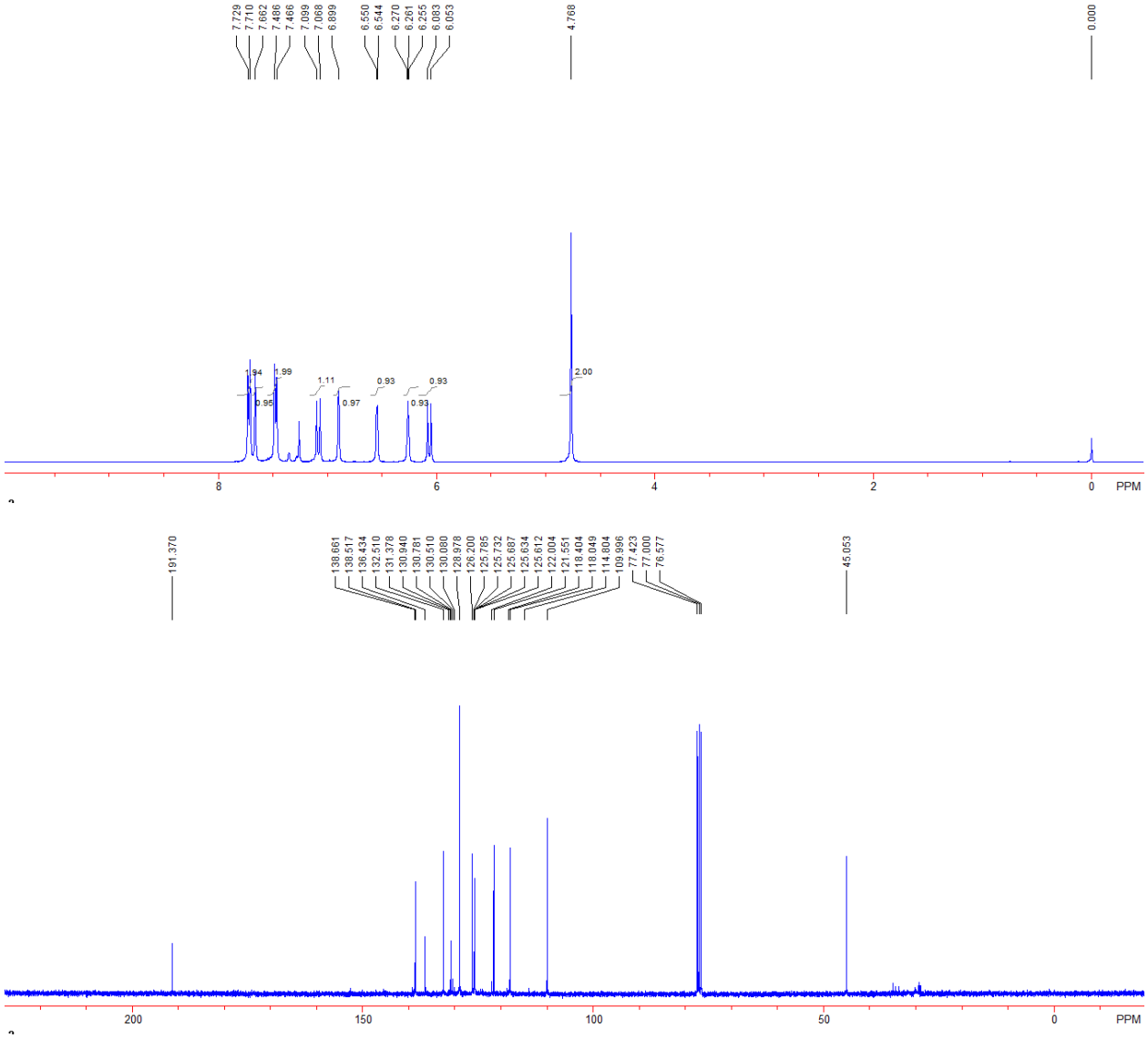
(E)-6-(4-fluorobenzylidene)-5H-pyrrolo[1,2-a]azepin-7(6H)-one 2b: 13 mg, 52% yield; *E*/*Z* > 20/1 (determined by crude ^{1}H NMR spectroscopy); a yellow solid, m.p. = 132-134 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 4.68 (s, 2H) (minor isomer), 4.79 (s, 2H), 6.00 (d, *J* = 12.4 Hz, 1H) (minor isomer), 6.06 (d, *J* = 12.4 Hz, 1H), 6.21 (dd, *J* = 2.4 Hz, 4.0 Hz, 1H) (minor isomer), 6.25 (dd, *J* = 2.4 Hz, 4.0 Hz, 1H), 6.53 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H), 6.55 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H) (minor isomer), 6.91 (t, *J* = 2.0 Hz, 1H), 7.06 (d, *J* = 12.4 Hz, 1H), 7.15 (t, *J* = 8.8 Hz, 2H), 7.35-7.38 (m, 2H), 7.63 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.1, 109.8, 115.9 (d, $J_{C\text{-}F}$ = 22.0

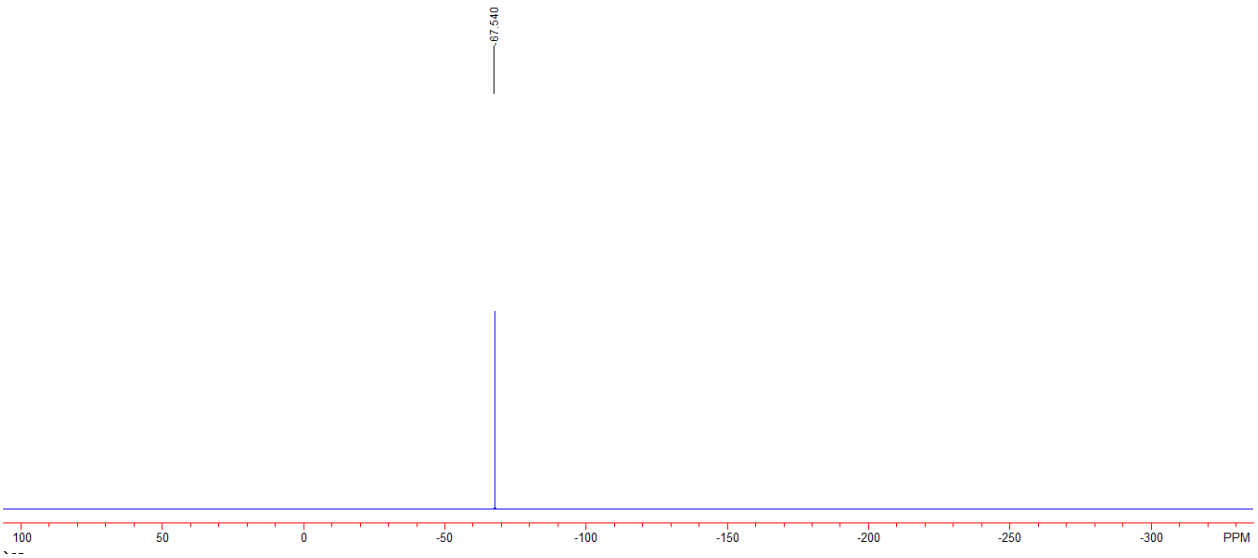
Hz), 117.7, 121.9, 126.0, 130.7 (d, J_{C-F} = 8.3 Hz), 130.9, 131.0 (d, J_{C-F} = 3.0 Hz), 132.2, 134.7, 139.2, 162.4 (d, J_{C-F} = 248.8 Hz), 191.7; ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$): δ -111.402 ~ -111.367 (m, 1F); IR (neat) ν 2918, 2850, 1653, 1602, 1508, 1471, 1390, 1327, 1265, 1225, 1066, 920, 861, 736 cm^{-1}; MS (ESI) m/e 254.0 (M+H); HRMS (ESI) for $C_{16}H_{13}FNO$ (M+H): 254.0976; Found: 254.0983.



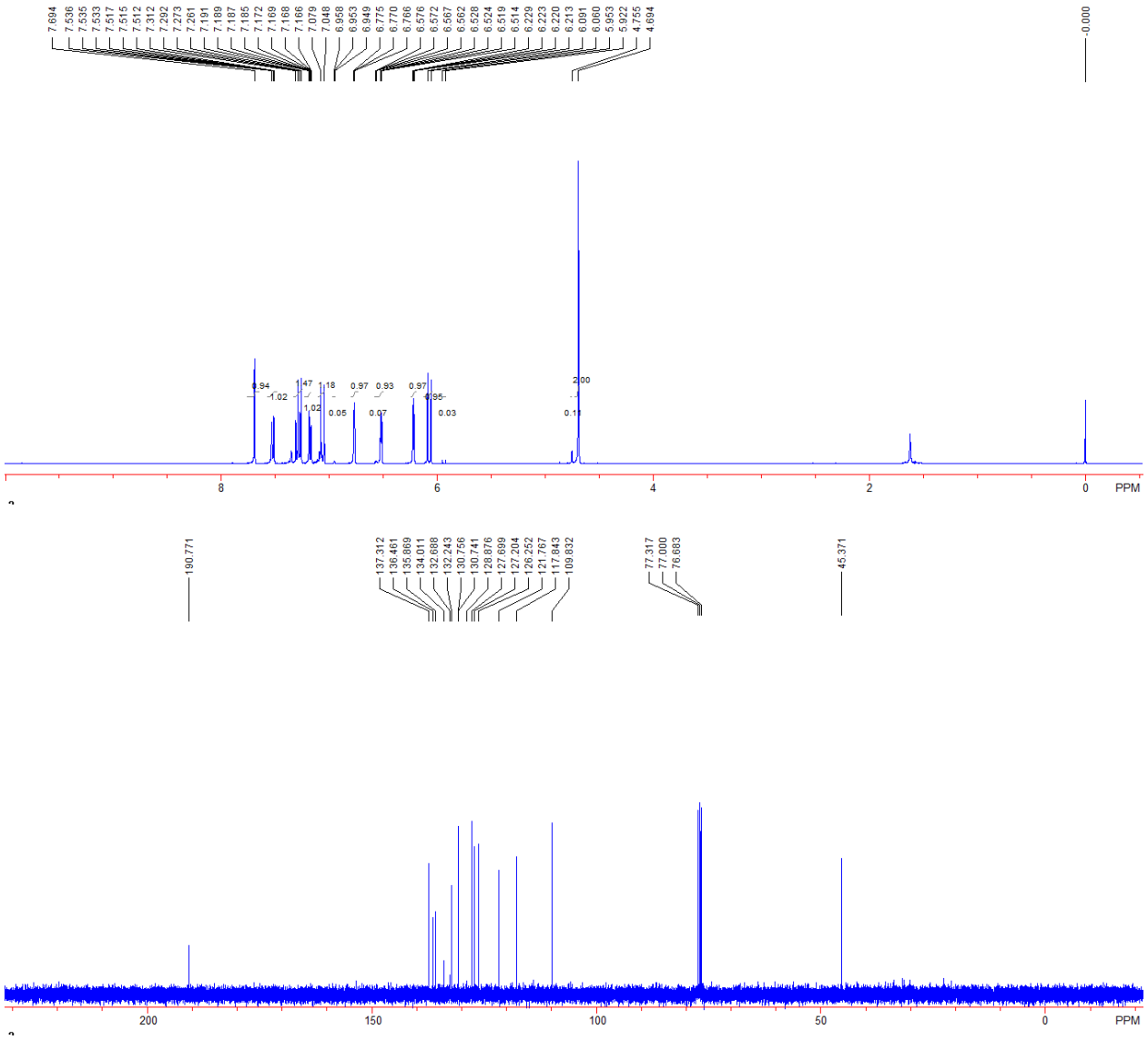
(E)-6-(4-(trifluoromethyl)benzylidene)-5H-pyrrolo[1,2-a]azepin-7(6H)-one 2c: 12 mg, 40%

yield; *E*/*Z* > 20/1 (determined by crude ^{1}H NMR spectroscopy); a yellow solid, m.p. = 166-167 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 4.77 (s, 2H), 6.07 (d, *J* = 12.0 Hz, 1H), 6.26 (m, 1H), 6.55 (d, *J* = 2.4 Hz, 1H), 6.90 (s, 1H), 7.08 (d, *J* = 12.0 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 2H), 7.66 (s, 1H) 7.72 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 45.1, 110.0, 118.0, 120.2 (q, J_{C-F} = 270.0 Hz), 121.6, 125.7 (q, J_{C-F} = 4.0 Hz), 126.2, 129.0, 130.7 (q, J_{C-F} = 32.3 Hz), 130.8, 132.5, 136.4, 138.5, 138.7, 191.4; ^{19}F NMR ($CDCl_3$, 282 MHz, $CFCl_3$): δ -67.540 (s, 3F); IR (neat) ν 2958, 2923, 2853, 1644, 1582, 1472, 1318, 1243, 1081, 916, 859, 824, 730 cm^{-1}; MS (EI) *m/e* (%): 303 [M^{+}] (96.8), 275 (82.0), 274 (100.0), 206 (31.1), 204 (26.3), 130 (43.0), 117 (24.8), 91 (27.2); HRMS (EI) Calcd. for $C_{17}H_{12}NOF_3$ requires (M^{+}) 303.0871, Found: 303.0869.



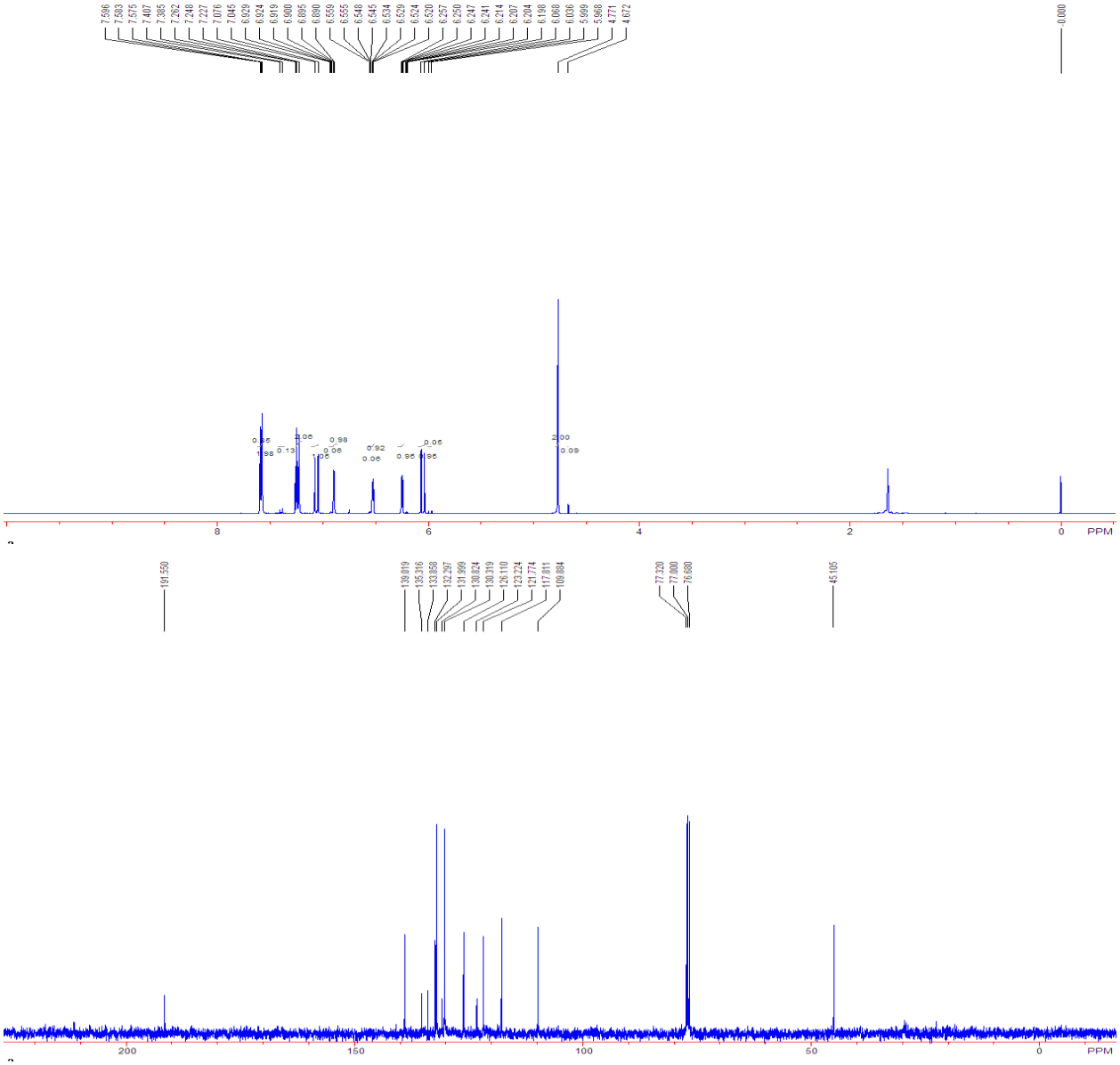


(E)-6-(2,3-dichlorobenzylidene)-5H-pyrrolo[1,2-a]azepin-7(6H)-one 2d: 20 mg, 67% yield; *E*/*Z* > 20/1 (determined by crude ^{1}H NMR spectroscopy); a yellow solid, m.p. = 141-143 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 4.69 (s, 2H), 4.76 (s, 2H) (minor isomer), 5.94 (d, *J* = 12.4 Hz, 1H) (minor isomer), 6.08 (d, *J* = 12.4 Hz, 1H), 6.22 (dd, *J* = 2.8 Hz, 4.0 Hz, 1H), 6.52 (dd, *J* = 2.0 Hz, 4.0 Hz, 1H), 6.57 (dd, *J* = 2.0 Hz, 4.0 Hz, 1H) (minor isomer), 6.77 (t, *J* = 2.0 Hz, 1H), 6.95 (t, *J* = 2.0 Hz, 1H) (minor isomer), 7.06 (d, *J* = 12.4 Hz, 1H), 7.17-7.19 (m, 1H), 7.26-7.31 (m, 1H), 7.51-7.54 (m, 1H), 7.69 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.4, 109.8, 117.8, 121.8, 126.3, 127.2, 127.7, 128.9, 130.7, 130.8, 132.2, 132.7, 134.0, 135.9, 136.5, 137.3, 190.8; IR (neat) ν 2956, 2922, 2853, 1731, 1674, 1568, 1446, 1316, 1222, 1029, 855, 827, 716 cm^{-1}; MS (ESI) m/e 304.0 (M+H); HRMS (ESI) for $C_{16}H_{12}Cl_2NO$ (M+H): 304.0291; Found: 304.0305.



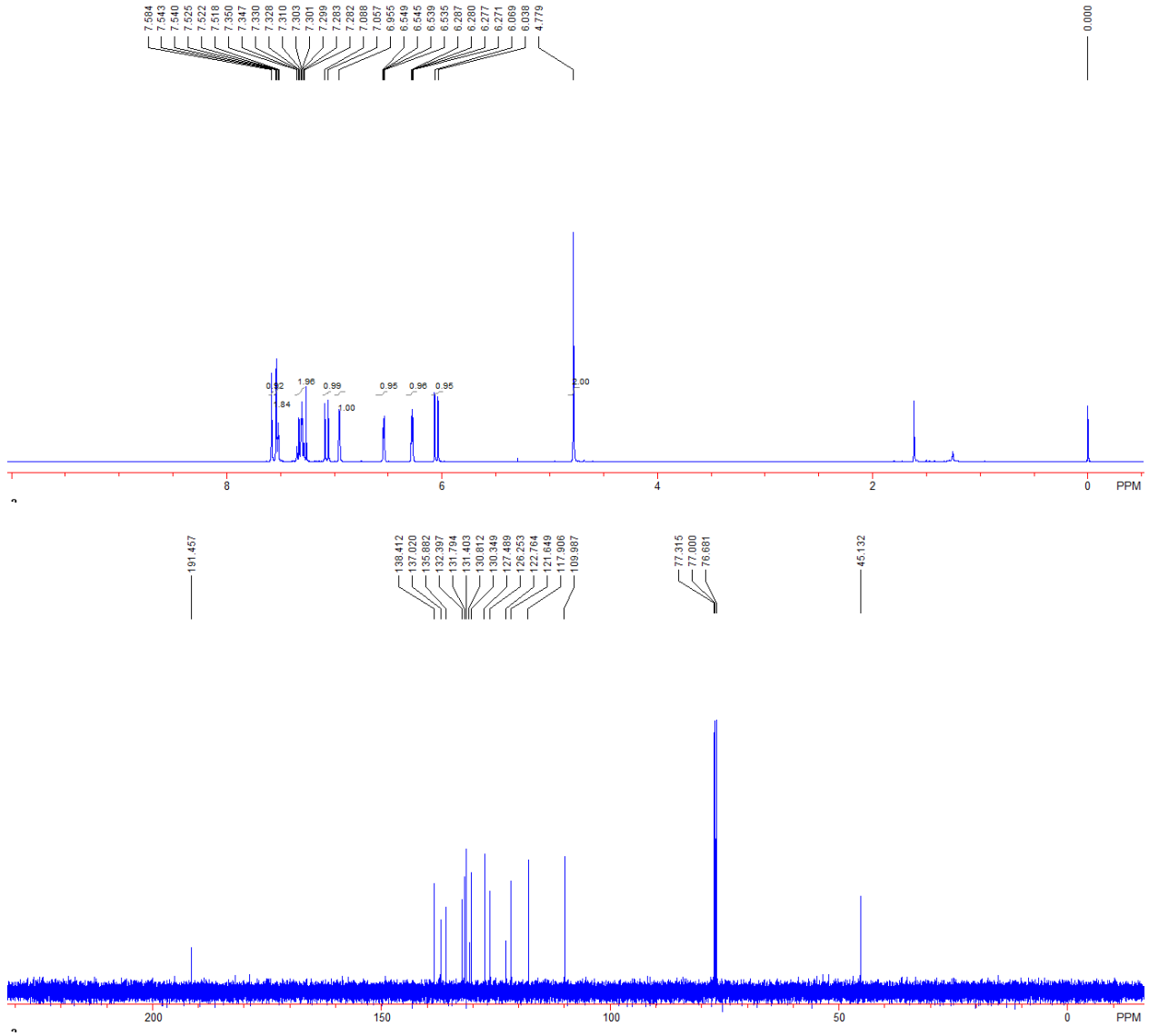
(E)-6-(4-bromobenzylidene)-5H-pyrrolo[1,2-a]azepin-7(6H)-one 2e: 17 mg, 55% yield; *E*/*Z* > 20/1 (determined by crude ^{1}H NMR spectroscopy); a yellow solid, m.p. = 184-185 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 4.67 (s, 2H) (minor isomer), 4.77 (s, 2H), 5.98 (d, *J* = 12.4 Hz, 1H) (minor isomer), 6.05 (d, *J* = 12.4 Hz, 1H), 6.21 (dd, *J* = 2.4 Hz, 4.0 Hz, 1H) (minor isomer), 6.25 (dd, *J* = 2.4 Hz, 4.0 Hz, 1H), 6.53 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H), 6.55 (dd, *J* = 2.4 Hz, 4.0 Hz, 1H) (minor isomer), 6.90 (t, *J* = 2.0 Hz, 1H), 6.92 (t, *J* = 2.0 Hz, 1H) (minor isomer), 7.06 (d, *J* = 12.4 Hz, 1H), 7.24 (d, *J* = 8.4 Hz, 2H), 7.40 (d, *J* = 8.4 Hz, 2H) (minor isomer), 7.58 (s, 1H), 7.59 (d, *J*

= 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.1, 109.9, 117.8, 121.8, 126.1, 129.1, 130.1, 130.9, 132.3, 133.4, 135.0, 135.3, 139.0, 191.6; IR (neat) ν 2922, 2852, 1642, 1570, 1460, 1352, 1216, 1030, 914, 850, 806, 732 cm^{-1}; MS (ESI) m/e 314.0 (M+H); HRMS (ESI) for $C_{16}H_{13}BrNO$ (M+H): 314.0175; Found: 314.0189.

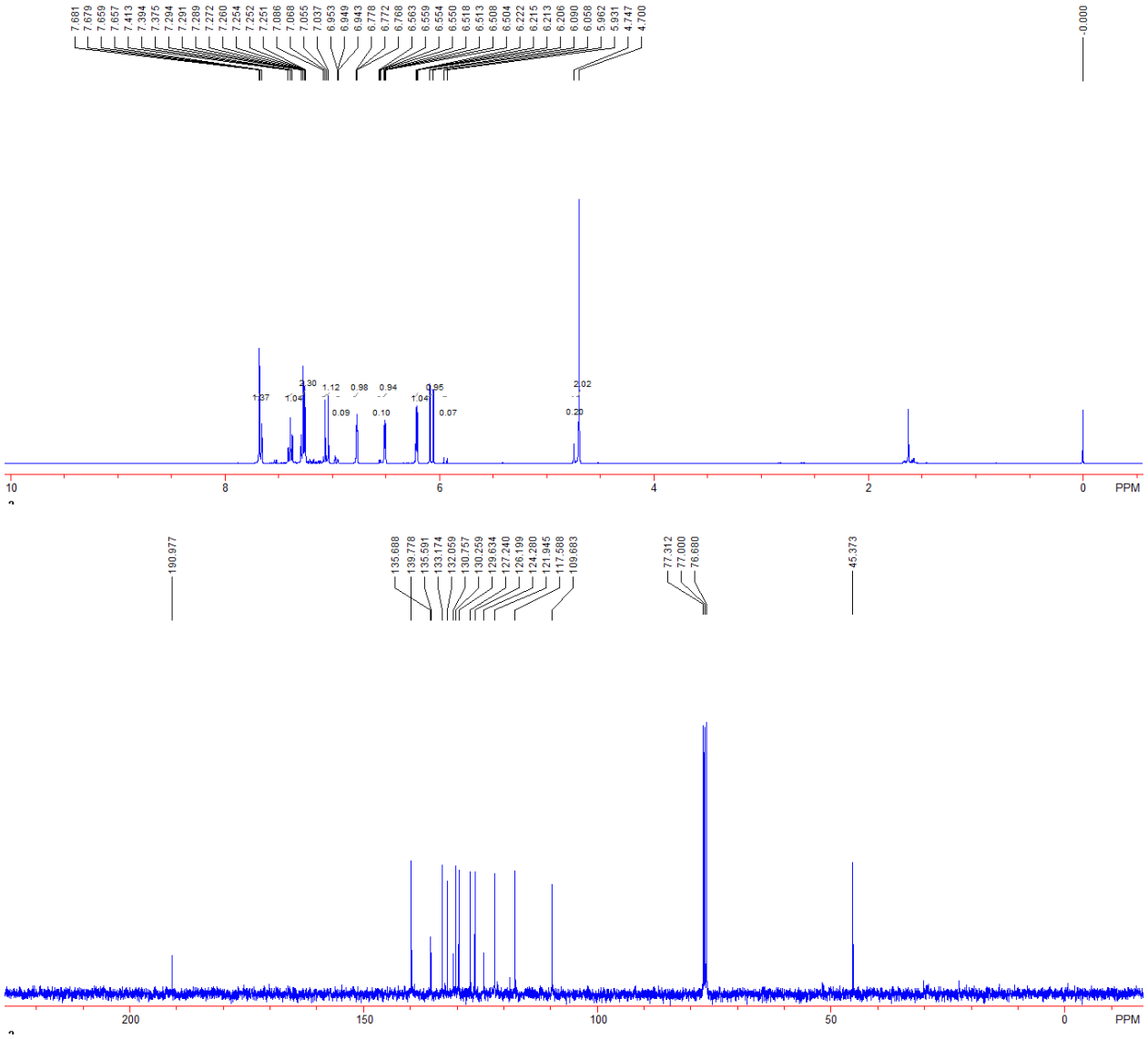


(E)-6-(3-bromobenzylidene)-5H-pyrrolo[1,2-a]azepin-7(6H)-one 2f: 19 mg, 61% yield; *E*/*Z* = 16/1 (determined by crude ^{1}H NMR spectroscopy); a yellow solid, m.p. = 111-112 ^{o}C; ^{1}H NMR

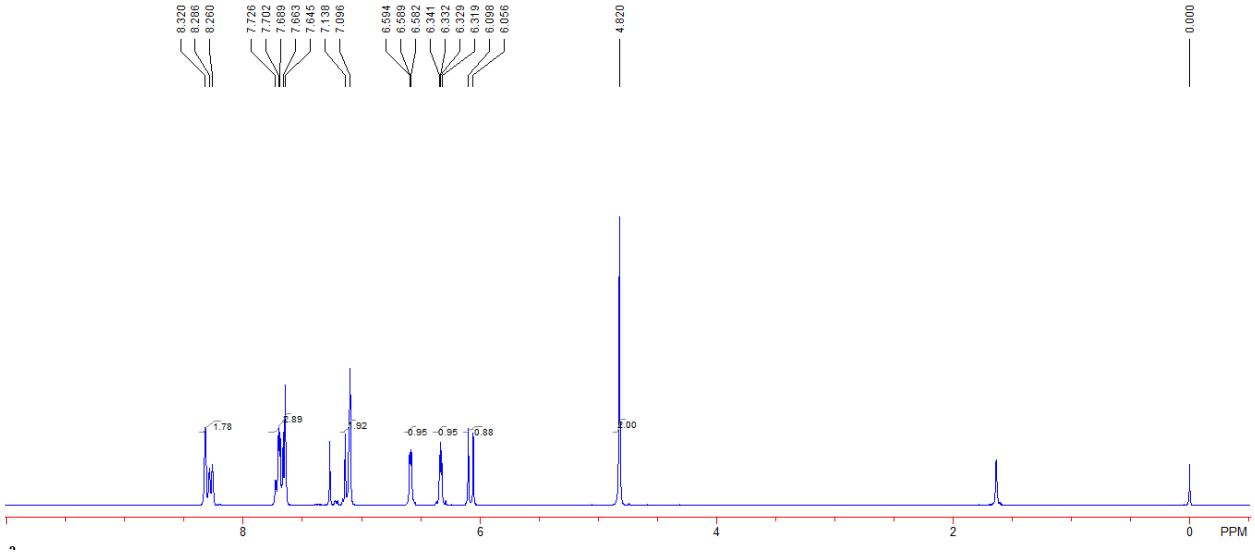
(400 MHz, $CDCl_3$, TMS) δ 4.78 (s, 2H), 6.05 (d, *J* = 12.4 Hz, 1H), 6.28 (dd, *J* = 2.4 Hz, 4.0 Hz, 1H), 6.54 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H), 6.96 (s, 1H), 7.07 (d, *J* = 12.4 Hz, 1H), 7.28-7.35 (m, 2H), 7.52-7.54 (m, 2H), 7.58 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.1, 110.0, 117.9, 121.6, 122.8, 126.3, 127.5, 130.3, 130.8, 131.4, 131.8, 132.4, 135.9, 137.0, 138.4, 191.5; IR (neat) ν 2923, 2852, 1647, 1557, 1466, 1316, 1269, 1078, 930, 876, 827, 798, 734 cm^{-1}; MS (EI) *m/e* (%): 313 [M^+] (99.9), 315 (96.6), 285 (67.7), 206 (71.8), 205 (74.9), 204 (100.0), 130 (69.0), 102 (70.1); HRMS (EI) Calcd. for $C_{16}H_{12}NOBr$ requires (M^+) 313.0102, Found: 313.0103.

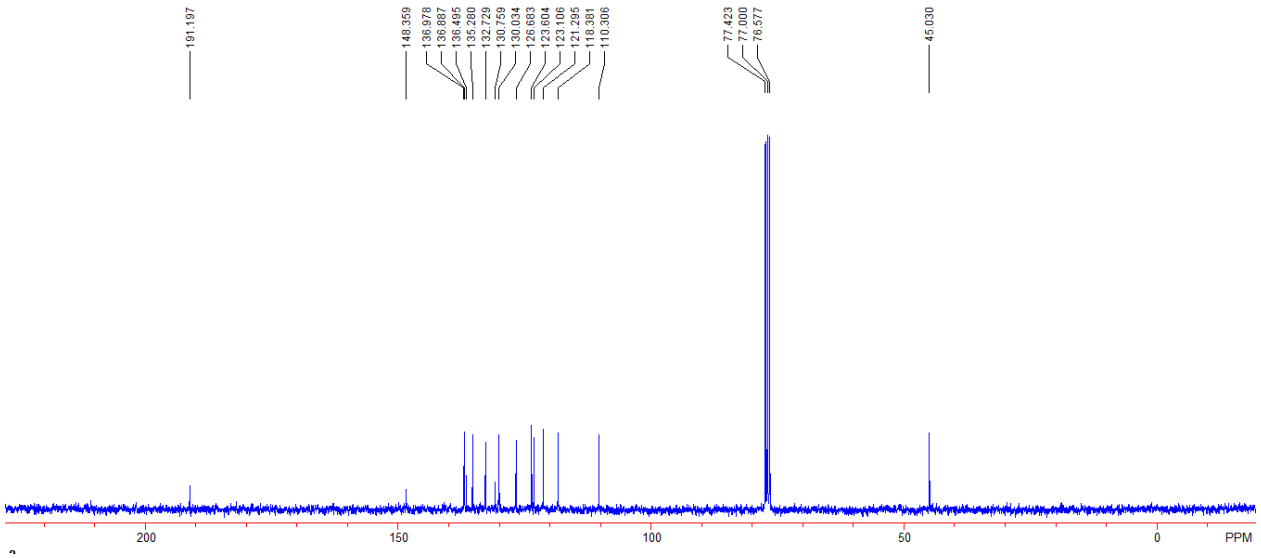


(E)-6-(2-bromobenzylidene)-5H-pyrrolo[1,2-a]azepin-7(6H)-one 2g: 19 mg, 61% yield; *E*/*Z* > 20/1 (determined by crude ^{1}H NMR spectroscopy); a yellow solid, m.p. = 154-156 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 4.70 (s, 2H), 4.75 (s, 2H) (minor isomer), 5.95 (d, *J* = 12.4 Hz, 1H) (minor isomer), 6.07 (d, *J* = 12.4 Hz, 1H), 6.21 (dd, *J* = 2.8 Hz, 4.0 Hz, 1H), 6.51 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H), 6.55 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H) (minor isomer), 6.77-6.78 (m, 1H), 6.94-6.95 (m, 1H) (minor isomer), 7.05 (d, *J* = 12.4 Hz, 1H), 7.07 (d, *J* = 12.4 Hz, 1H) (minor isomer), 7.25-7.29 (m, 2H), 7.38-7.41 (m 1H), 7.66-7.68 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.4, 109.7, 117.6, 121.9, 124.3, 126.2, 127.2, 129.6, 130.3, 130.8, 132.1, 133.2, 135.6, 135.7, 139.8, 191.0; IR (neat) ν 2958, 2924, 2853, 1675, 1617, 1535, 1503, 1460, 1356, 1225, 1020, 990, 871, 829, 736 cm^{-1}; MS (ESI) m/e 314.0 (M+H); HRMS (ESI) for $C_{16}H_{13}BrNO$ (M+H): 314.0175; Found: 314.0190.

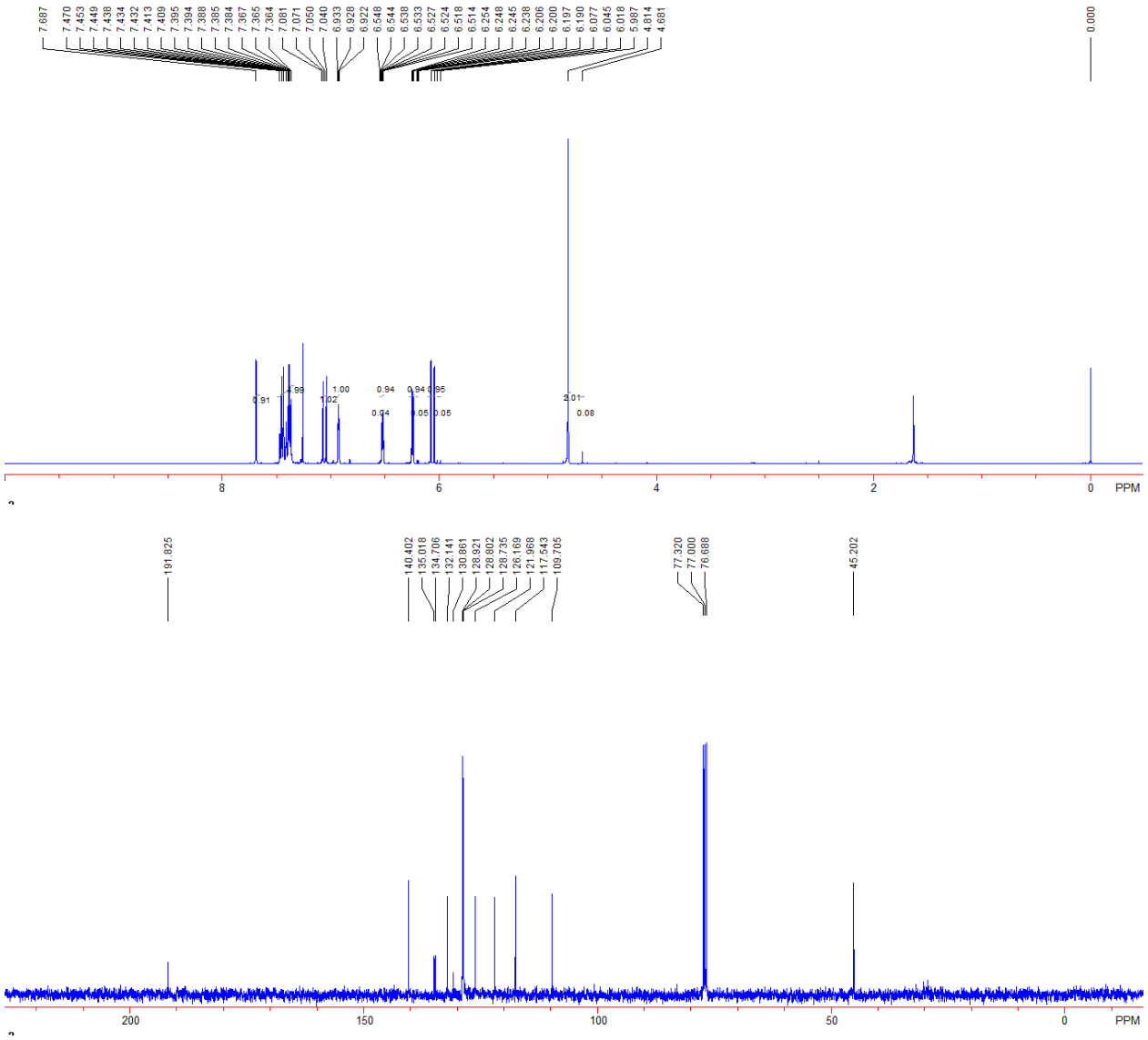


(E)-6-(3-nitrobenzylidene)-5H-pyrrolo[1,2-a]azepin-7(6H)-one 2h: 10 mg, 36% yield; *E*/*Z* = 8/1 (determined by crude ^{1}H NMR spectroscopy); a yellow solid, m.p. = 140-142 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 4.82 (s, 2H), 6.08 (d, *J* = 12.6 Hz, 1H), 6.33 (dd, *J* = 3.0 Hz, 3.9 Hz, 1H), 6.59 (m, 1H), 7.10-7.14 (m, 2H), 7.65-7.73 (m, 3H), 8.27 (d, *J* = 7.8 Hz, 1H), 8.32 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 45.0, 110.3, 118.4, 121.3, 123.1, 123.6, 126.7, 130.0, 130.8, 132.7, 135.3, 136.5, 136.9, 137.0, 148.4, 191.2; IR (neat) ν 2925, 2853, 1644, 1582, 1473, 1351, 1212, 1078, 1027, 831, 731 cm^{-1}; MS (ESI) m/e 281.0 (M+H); HRMS (ESI) for $C_{16}H_{12}N_2NaO_3$ (M+Na): 303.0740; Found: 303.0739.



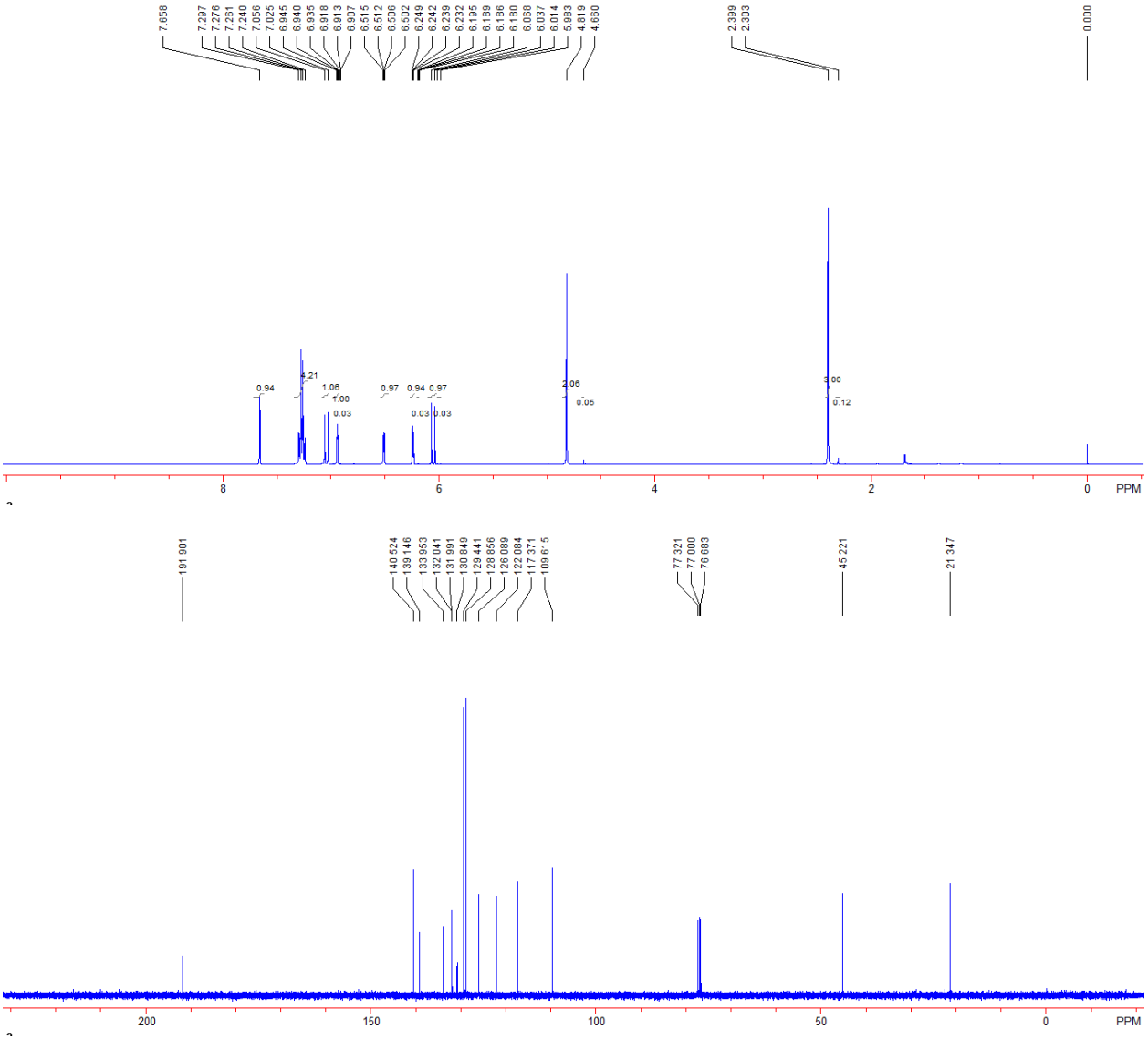


(E)-6-benzylidene-5H-pyrrolo[1,2-a]azepin-7(6H)-one 2i: 17 mg, 74% yield; *E*/*Z* > 20/1 (determined by crude ^{1}H NMR spectroscopy); a yellow solid, m.p. = 116-117 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 4.68 (s, 2H) (minor isomer), 4.81 (s, 2H), 6.00 (d, *J* = 12.4 Hz, 1H) (minor isomer), 6.06 (d, *J* = 12.4 Hz, 1H), 6.20 (dd, *J* = 2.8 Hz, 4.0 Hz, 1H) (minor isomer), 6.25 (dd, *J* = 2.8 Hz, 4.0 Hz, 1H), 6.52 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H), 6.54 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H) (minor isomer), 6.93 (t, *J* = 2.4 Hz, 1H), 7.06 (d, *J* = 12.4 Hz, 1H), 7.07 (d, *J* = 12.4 Hz, 1H) (minor isomer), 7.36-7.47 (m, 5H), 7.69 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.2, 109.7, 117.5, 122.0, 126.2, 128.7, 128.8, 128.9, 130.9, 132.1, 134.7, 135.0, 140.4, 191.8; IR (neat) ν 2956, 2922, 2852, 1730, 1650, 1568, 1518, 1467, 1358, 1241, 1057, 972, 843, 787, 719, 696 cm^{-1}; MS (ESI) m/e 236.1 (M+H); HRMS (ESI) for $C_{16}H_{14}NO$ (M+H): 236.1070; Found: 236.1074.



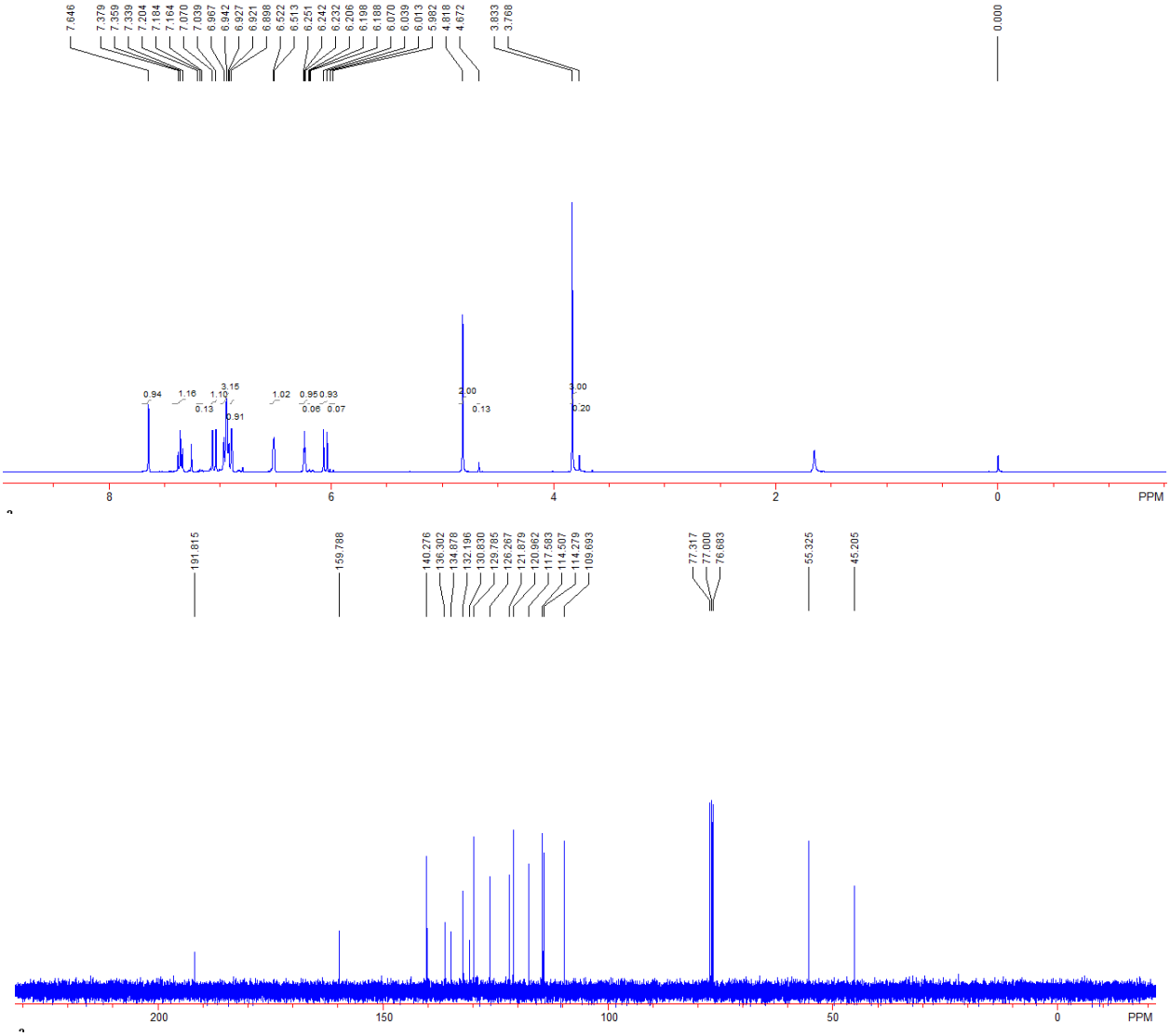
(E)-6-(4-methylbenzylidene)-5H-pyrrolo[1,2-a]azepin-7(6H)-one 2j: 23 mg, 92% yield; *E*/*Z* > 20/1 (determined by crude ^{1}H NMR spectroscopy); a yellow solid, m.p. = 138-139 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.30 (s, 3H) (minor isomer), 2.40 (s, 3H), 4.66 (s, 2H) (minor isomer), 4.82 (s, 2H), 6.00 (d, *J* = 12.4 Hz, 1H) (minor isomer), 6.05 (d, *J* = 12.4 Hz, 1H), 6.19 (dd, *J* = 2.4 Hz, 4.0 Hz, 1H) (minor isomer), 6.24 (dd, *J* = 2.4 Hz, 4.0 Hz, 1H), 6.51 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H), 6.91 (t, *J* = 2.0 Hz, 1H) (minor isomer), 6.94 (t, *J* = 2.0 Hz, 1H), 7.04 (d, *J* = 12.4 Hz, 1H), 7.25 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 2H), 7.66 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ

21.3, 45.2, 109.6, 117.4, 122.1, 122.8, 126.1, 128.9, 129.4, 130.8, 132.0, 134.0, 139.1, 140.5, 191.9; IR (neat) ν 2956, 2923, 2853, 1641, 1585, 1488, 1469, 1374, 1240, 1081, 1013, 853, 820, 731 cm^{-1}; MS (EI) *m/e* (%): 249 [M^+] (17.1), 229 (43.3), 199 (34.6), 165 (100.0), 125 (25.8), 109 (78.8), 91 (25.7), 81 (28.6); HRMS (EI) Calcd. for $C_{17}H_{15}NO$ requires (M^+) 249.1154, Found: 249.1151.

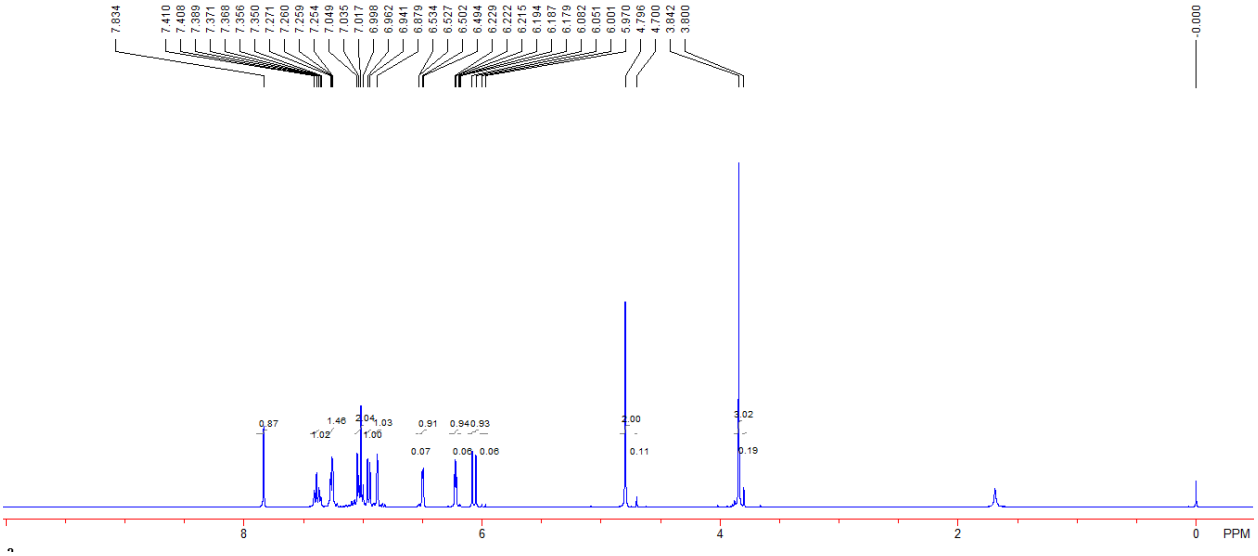


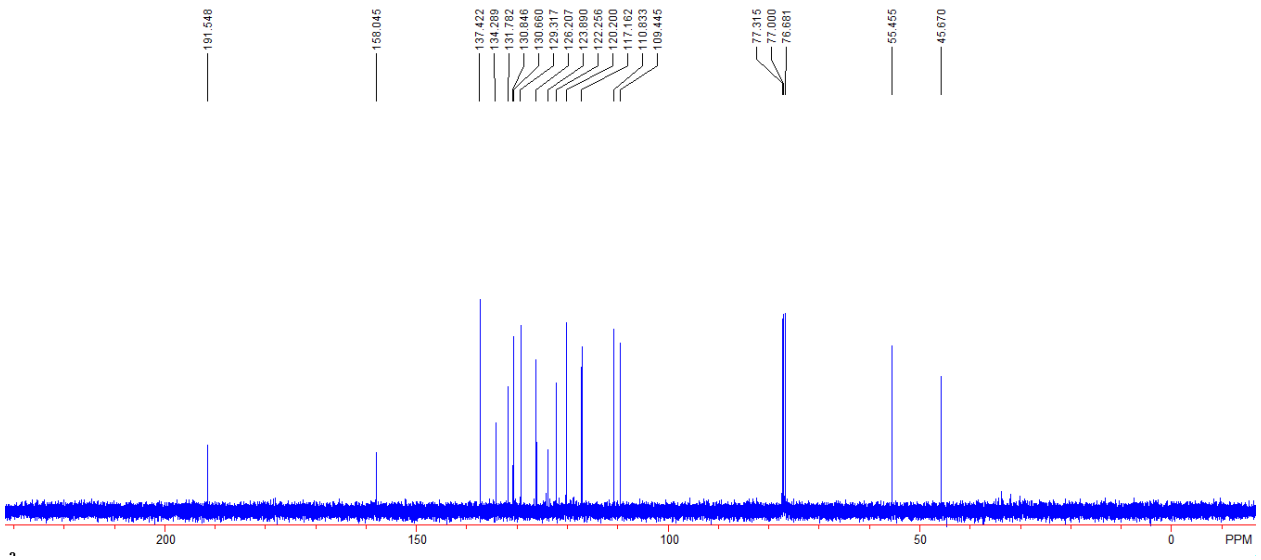
(E)-6-(3-methoxybenzylidene)-5H-pyrrolo[1,2-a]azepin-7(6H)-one 2k: 17 mg, 64% yield; *E*/*Z* > 20/1 (determined by crude ^{1}H NMR spectroscopy); a yellow solid, m.p. = 122-123 ^{o}C; ^{1}H NMR

(400 MHz, $CDCl_3$, TMS) δ 3.77 (s, 3H) (minor isomer), 3.83 (s, 3H), 4.67 (s, 2H) (minor isomer), 4.82 (s, 2H), 6.00 (d, *J* = 12.4 Hz, 1H) (minor isomer), 6.05 (d, *J* = 12.4 Hz, 1H), 6.20 (t, *J* = 4.0 Hz, 1H) (minor isomer), 6.24 (dd, *J* = 4.0 Hz, 1H), 6.51 (d, *J* = 4.0 Hz, 1H), 6.90 (s, 1H), 6.92-6.97 (m, 3H), 7.04 (d, *J* = 12.4 Hz, 1H), 7.18 (t, *J* = 4.0 Hz, 1H) (minor isomer), 7.36 (t, *J* = 4.0 Hz, 1H), 7.65 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.2, 55.3, 109.7, 114.3, 114.5, 117.6, 121.0, 121.9, 126.3, 129.8, 130.8, 132.2, 134.9, 136.3, 140.3, 159.8, 191.8; IR (neat) ν 2958, 2921, 2851, 1698, 1623, 1500, 1480, 1393, 1255, 1037, 941, 858, 824, 777 cm^{-1}; MS (EI) *m/e* (%): 265 [M^+] (100.0), 237 (45.7), 285 (67.7), 206 (21.1), 165 (19.6), 130 (18.7), 115 (17.7), 103 (23.5); HRMS (EI) Calcd. for $C_{17}H_{15}NO_2$requires (M^+) 265.1103, Found: 265.1100.

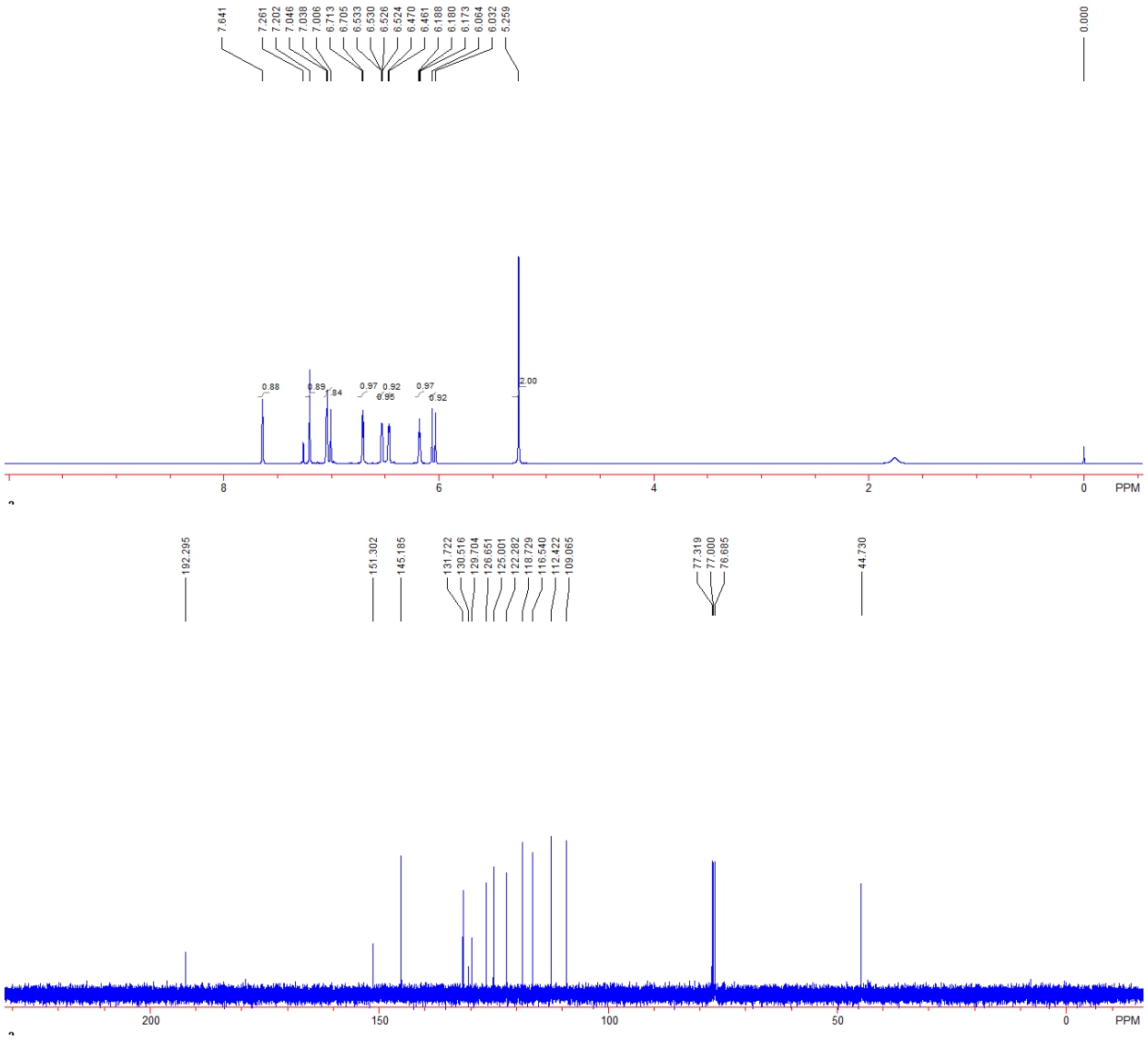


(E)-6-(2-methoxybenzylidene)-5H-pyrrolo[1,2-a]azepin-7(6H)-one 2l: 21 mg, 78% yield; *E*/*Z* > 20/1 (determined by crude ^{1}H NMR spectroscopy); a yellow solid, m.p. = 155-156 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 3.80 (s, 3H) (minor isomer), 3.84 (s, 3H), 4.70 (s, 2H) (minor isomer), 4.80 (s, 2H), 5.99 (d, *J* = 12.4 Hz, 1H) (minor isomer), 6.07 (d, *J* = 12.4 Hz, 1H), 6.19 (t, *J* = 2.8 Hz, 1H) (minor isomer), 6.22 (t, *J* = 2.8 Hz, 1H), 6.50 (d, *J* = 3.2 Hz, 1H), 6.53 (d, *J* = 3.2 Hz, 1H) (minor isomer), 6.88 (s, 1H), 6.95 (d, *J* = 8.4 Hz, 1H), 7.00-7.05 (m, 2H), 7.25-7.27 (m, 1H), 7.35-7.41 (m, 1H), 7.83 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.7, 55.5, 109.4, 110.8, 117.2, 120.2, 122.3, 123.9, 126.2, 129.3, 130.7, 130.8, 131.8, 134.3, 137.4, 158.0, 191.5; IR (neat) ν 2956, 2927, 1697, 1623, 1480, 1457, 1391, 1225, 1046, 938, 785 cm^{-1}; MS (EI) *m/e* (%): 265 [M^{+}] (50.2), 235 (19.6), 234 (100.0), 204 (17.1), 131 (41.5), 115 (17.8), 91 (18.0), 77 (17.0); HRMS (EI) Calcd. for $C_{17}H_{15}NO_2$ requires (M^{+}) 265.1103, Found: 265.1104.



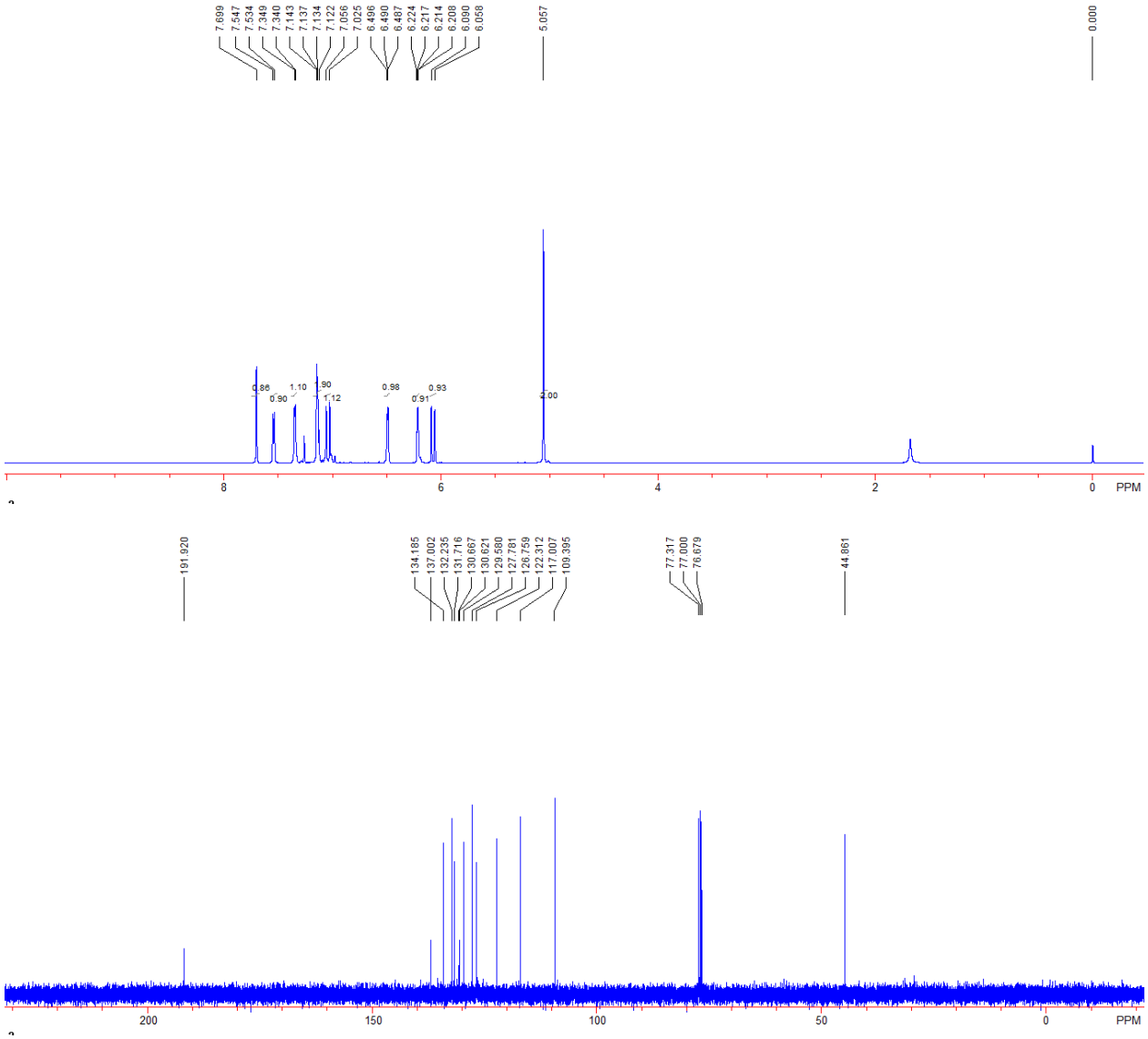


(E)-6-(furan-2-ylmethylene)-5H-pyrrolo[1,2-a]azepin-7(6H)-one 2m: 20 mg, 83% yield; *E*/*Z* > 20/1 (determined by crude ^{1}H NMR spectroscopy); a yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 5.26 (s, 2H), 6.05 (d, *J* = 12.8 Hz, 1H), 6.18 (t, *J* = 2.8 Hz, 1H), 6.47 (d, *J* = 3.6 Hz, 1H), 6.53 (dd, *J* = 0.8 Hz, 2.4 Hz, 1H), 6.71 (d, *J* = 3.2 Hz, 1H), 7.02 (d, *J* = 12.8 Hz, 1H), 7.05 (s, 1H), 7.20 (s, 1H), 7.64 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 44.7, 109.1, 112.4, 116.5, 118.7, 122.3, 125.0, 126.7, 129.7, 130.5, 131.7, 145.2, 151.3, 191.3; IR (neat) ν 2923, 2856, 1708, 1648, 1578, 1468, 1329, 1241, 1072, 962, 884, 829, 725 cm^{-1}; MS (EI) *m/e* (%): 225 [M^+] (72.9), 197 (37.2), 196 (35.1), 168 (100.0), 167 (44.7), 165 (21.6), 109 (28.3), 91 (24.0); HRMS (EI) Calcd. for $C_{14}H_{11}NO_2$ requires (M^+) 225.0790, Found: 225.0793.



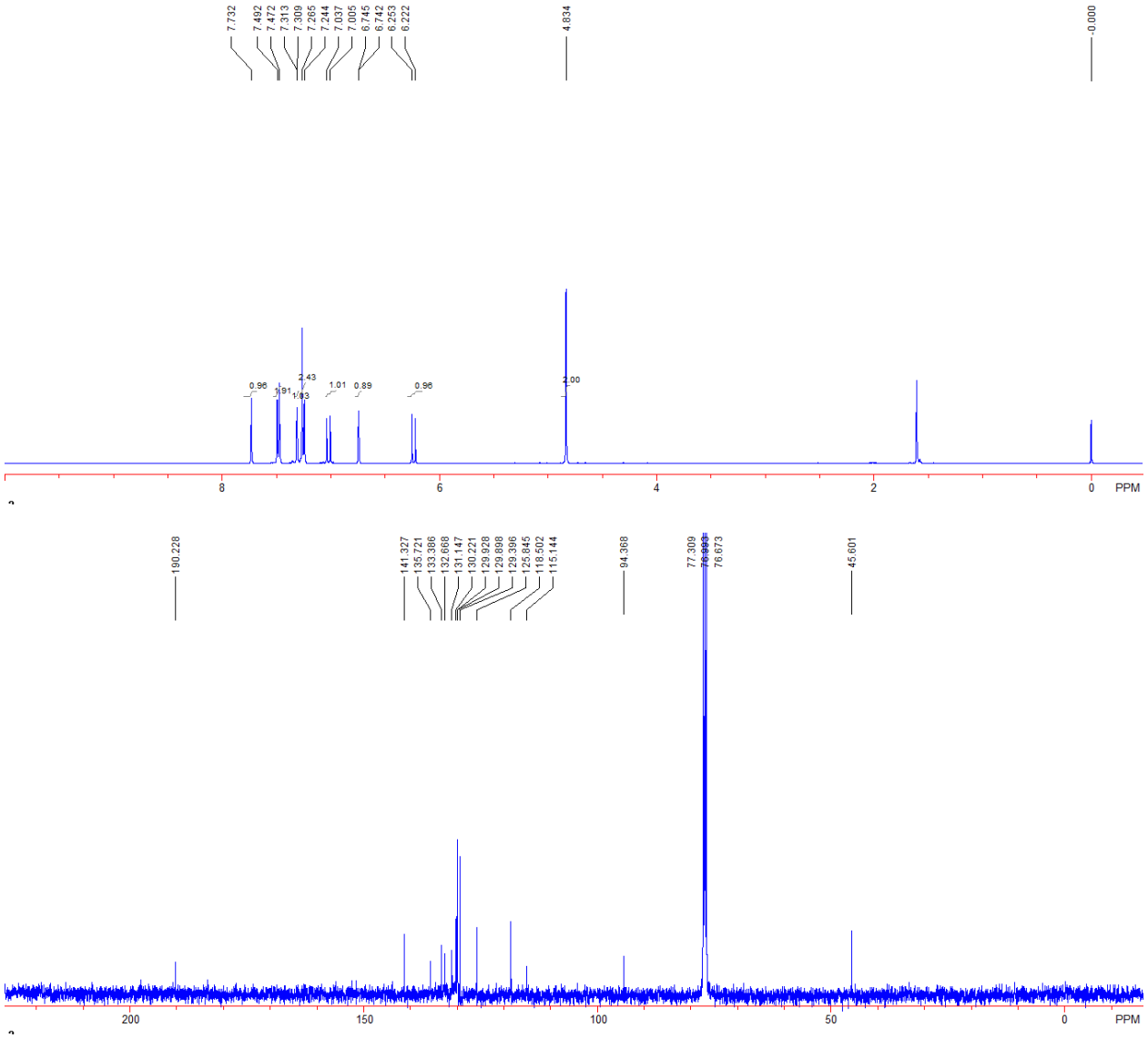
(E)-6-(thiophen-2-ylmethylene)-5H-pyrrolo[1,2-a]azepin-7(6H)-one 2n: 20 mg, 83% yield; *E*/*Z* > 20/1 (determined by crude ^{1}H NMR spectroscopy); a yellow solid, m.p. = 137-138 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 5.06 (s, 2H), 6.07 (d, *J* = 12.4 Hz, 1H), 6.22 (dd, *J* = 2.4 Hz, 4.0 Hz, 1H), 6.49 (m, 1H), 7.04 (d, *J* = 12.4 Hz, 1H), 7.12-7.14 (m, 2H), 7.34 (d, *J* = 3.6 Hz, 1H), 7.54 (d, *J* = 5.2 Hz, 1H) 7.70 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 44.9, 109.4, 117.0, 122.3, 126.8, 127.8, 129.6, 130.6, 130.7, 131.7, 132.2, 137.0, 134.2, 191.9; IR (neat) ν 2956, 2921, 28532, 1638, 1574, 1464, 1364, 1274, 1048, 967, 845, 809, 715 cm^{-1}; MS (EI) *m/e* (%): 241 [M^{+}] (100.0), 213

(60.4), 212 (99.6), 180 (39.0), 121 (50.3), 97 (32.8), 57 (33.4), 55 (34.2); HRMS (EI) Calcd. for $C_{14}H_{11}NOS$ requires (M^+) 241.0561, Found: 241.0558.



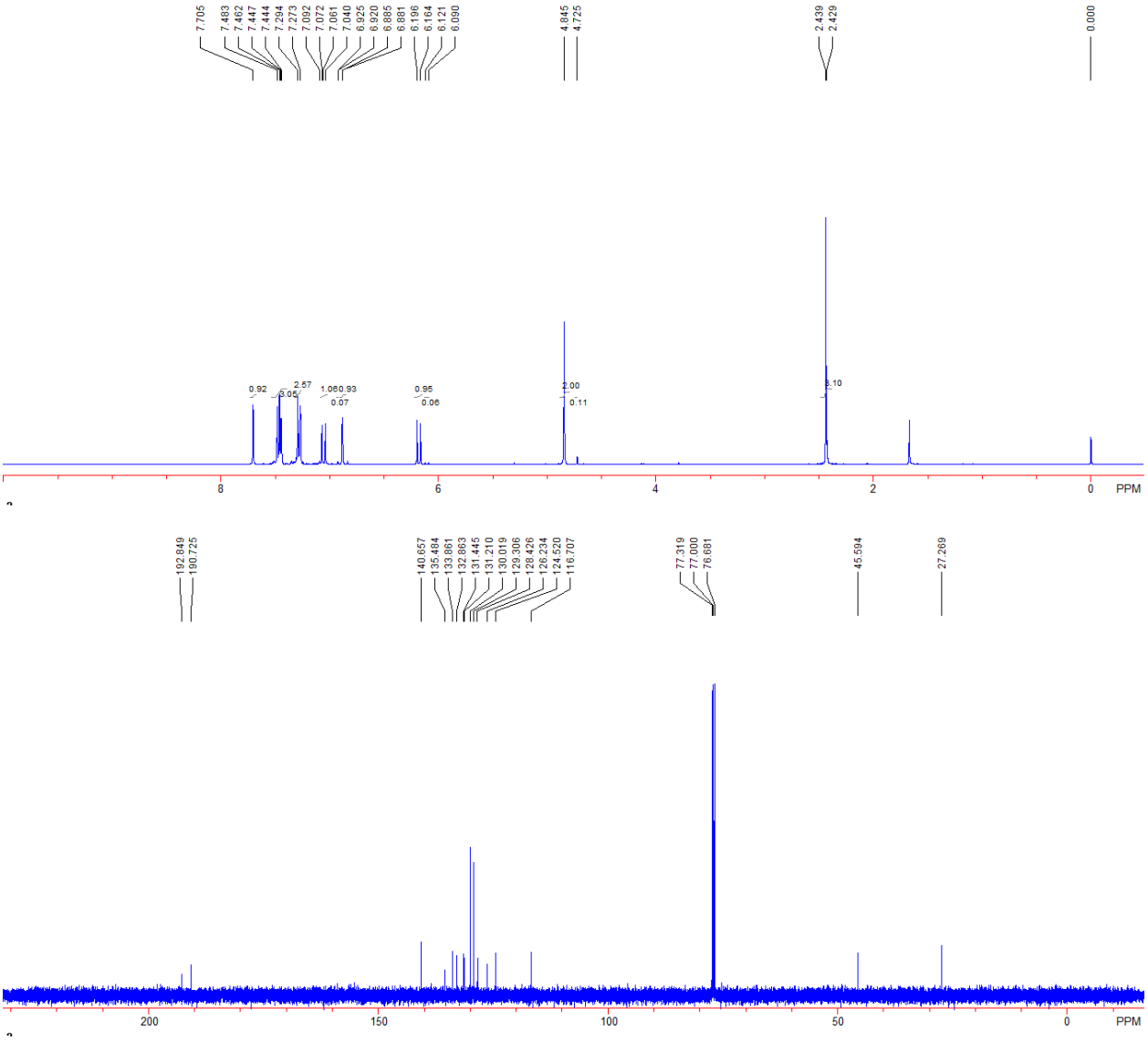
(E)-6-(4-chlorobenzylidene)-7-oxo-6,7-dihydro-5H-pyrrolo[1,2-a]azepine-2-carbonitrile 2o: 17 mg, 55% yield; *E*/*Z* = 15/1 (determined by crude ^{1}H NMR spectroscopy); a yellow solid, m.p. = 207-209 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 4.83 (s, 2H), 6.24 (d, *J* = 12.4 Hz, 1H), 6.74 (d, *J* = 1.2 Hz, 1H), 7.02 (d, *J* = 12.4 Hz, 1H), 7.25 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 1.2 Hz, 1H), 7.48

(d, J = 8.4 Hz, 2H), 7.73 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.6, 94.4 115.1, 118.5, 125.8, 129.4, 129.8, 129.9, 130.2, 131.1, 132.7, 133.4, 135.7, 141.3, 190.2; IR (neat) ν 2924, 2227, 1652, 1601, 1539, 1490, 1448, 1374, 1250, 1094, 983, 835, 785, 737 cm^{-1}; MS (EI) *m/e* (%): 294 [M^+] (51.4), 293 (27.1), 266 (42.7), 259 (40.5), 231 (41.9), 121 (27.0), 115 (100.0), 114 (25.8); HRMS (EI) Calcd. for $C_{17}H_{11}N_2OCl$ requires (M^+) 294.0560, Found: 294.0558.

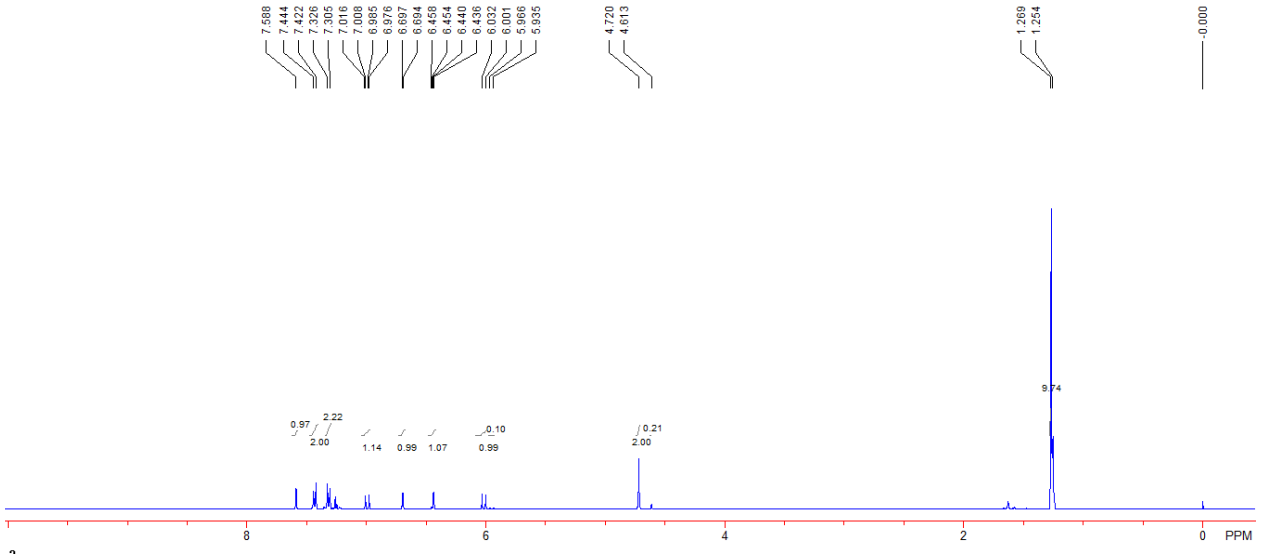


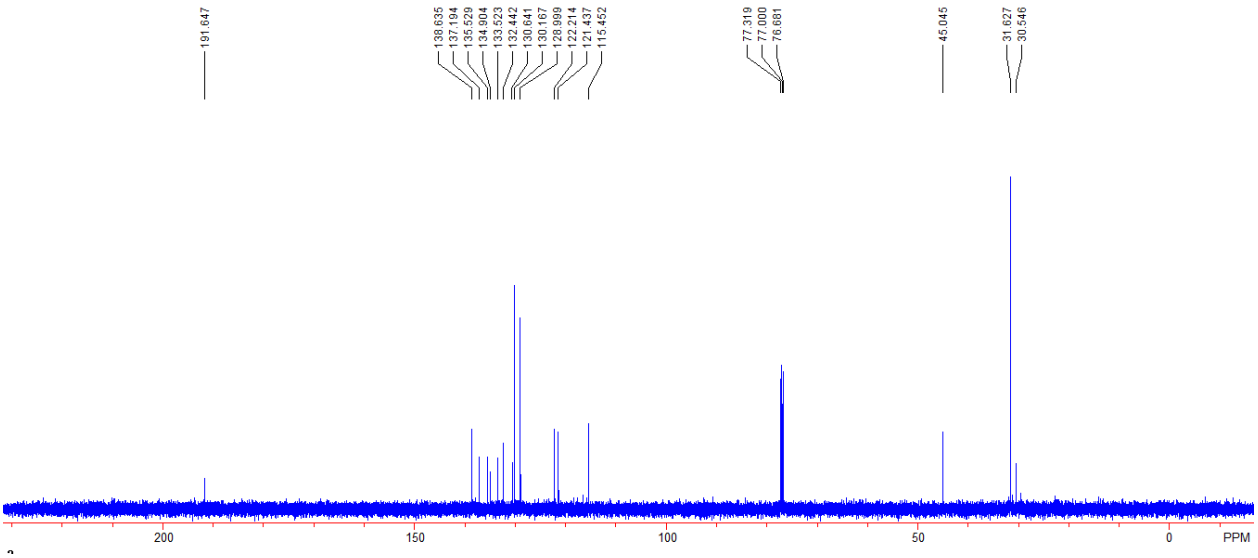
(E)-2-acetyl-6-(4-chlorobenzylidene)-5H-pyrrolo[1,2-a]azepin-7(6H)-one 2p: 13 mg, 39%

yield; *E*/*Z* = 11/1 (determined by crude ^{1}H NMR spectroscopy); a yellow solid, m.p. = 167-169 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.43 (s, 3H) (minor isomer), 2.44 (s, 3H), 4.73 (s, 2H) (minor isomer), 4.85 (s, 2H), 6.11 (d, *J* = 12.4 Hz, 1H) (minor isomer), 6.18 (d, *J* = 12.4 Hz, 1H), 6.88 (d, *J* = 1.6 Hz, 1H), 6.92 (d, *J* = 1.6 Hz, 1H) (minor isomer), 7.06 (d, *J* = 12.4 Hz, 1H), 7.08 (d, *J* = 12.4 Hz, 1H) (minor isomer), 7.28 (d, *J* = 8.4 Hz, 2H), 7.45 (d, *J* = 1.6 Hz, 1H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.71 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.3, 45.6, 116.7, 124.5, 126.2, 128.4, 129.3, 130.0, 131.2, 131.4, 132.9, 133.9, 135.5, 140.7, 190.7, 192.8; IR (neat) ν 2958, 2924, 2853, 1652, 1595, 1488, 1450, 1389, 1254, 1200, 1091, 932, 840, 785, 736 cm^{-1}; MS (EI) *m/e* (%): 311 [M^+] (100.0), 268 (53.1), 204 (35.4), 146 (94.1), 131 (34.9), 118 (33.8), 115 (53.4), 63 (36.4); HRMS (EI) Calcd. for $C_{18}H_{14}NO_2Cl$ requires (M^+) 311.0713, Found: 311.0709.



(E)-2-(tert-butyl)-6-(4-chlorobenzylidene)-5H-pyrrolo[1,2-a]azepin-7(6H)-one 2q: 24 mg, 78% yield; *E*/*Z* = 17/1 (determined by crude ^{1}H NMR spectroscopy); a yellow solid, m.p. = 102-104 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.25 (s, 9H) (minor isomer), 1.27(s, 9H), 4.61 (s, 2H) (minor isomer), 4.72(s, 2H), 5.95 (d, *J* = 12.4 Hz, 1H) (minor isomer), 6.02 (d, *J* = 12.4 Hz, 1H), 6.44 (d, *J* = 1.6 Hz, 1H), 6.46 (d, *J* = 1.6 Hz, 1H) (minor isomer), 6.70 (d, *J* = 1.6 Hz, 1H), 6.99 (d, *J* = 12.4 Hz, 1H), 7.00 (d, *J* = 12.4 Hz, 1H) (minor isomer), 7.32 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 2H), 7.59 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.5, 31.6, 45.0, 115.5, 121.4, 122.2, 129.0, 130.2, 130.6, 132.4, 133.5, 134.9, 135.5, 137.2, 138.6, 191.6; IR (neat) ν 2956, 2924, 2853, 1644, 1587, 1488, 1430, 1364, 1290, 1092, 966, 832, 780, 717 cm^{-1}; MS (EI) *m/e* (%): 325 [M^+] (53.2), 312 (36.1), 311 (27.0), 310 (100.0), 160 (50.5), 124 (29.5), 55 (27.1), 41 (24.7); HRMS (EI) Calcd. for $C_{20}H_{20}NOCl$ requires (M^+) 325.1233, Found: 325.1231.

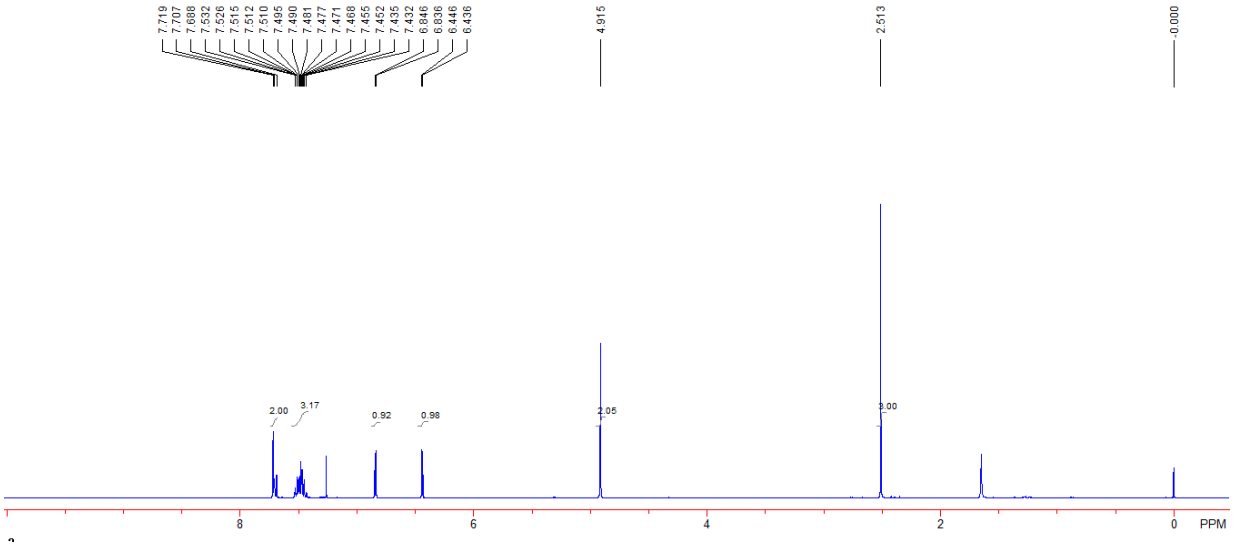


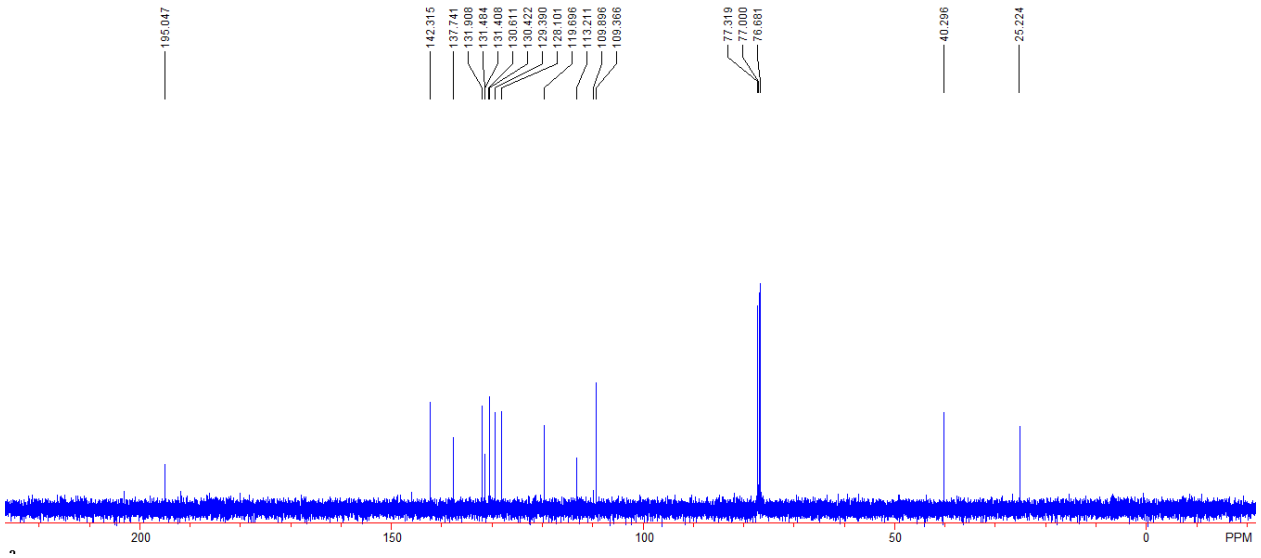


General Procedure for the synthesis of 3

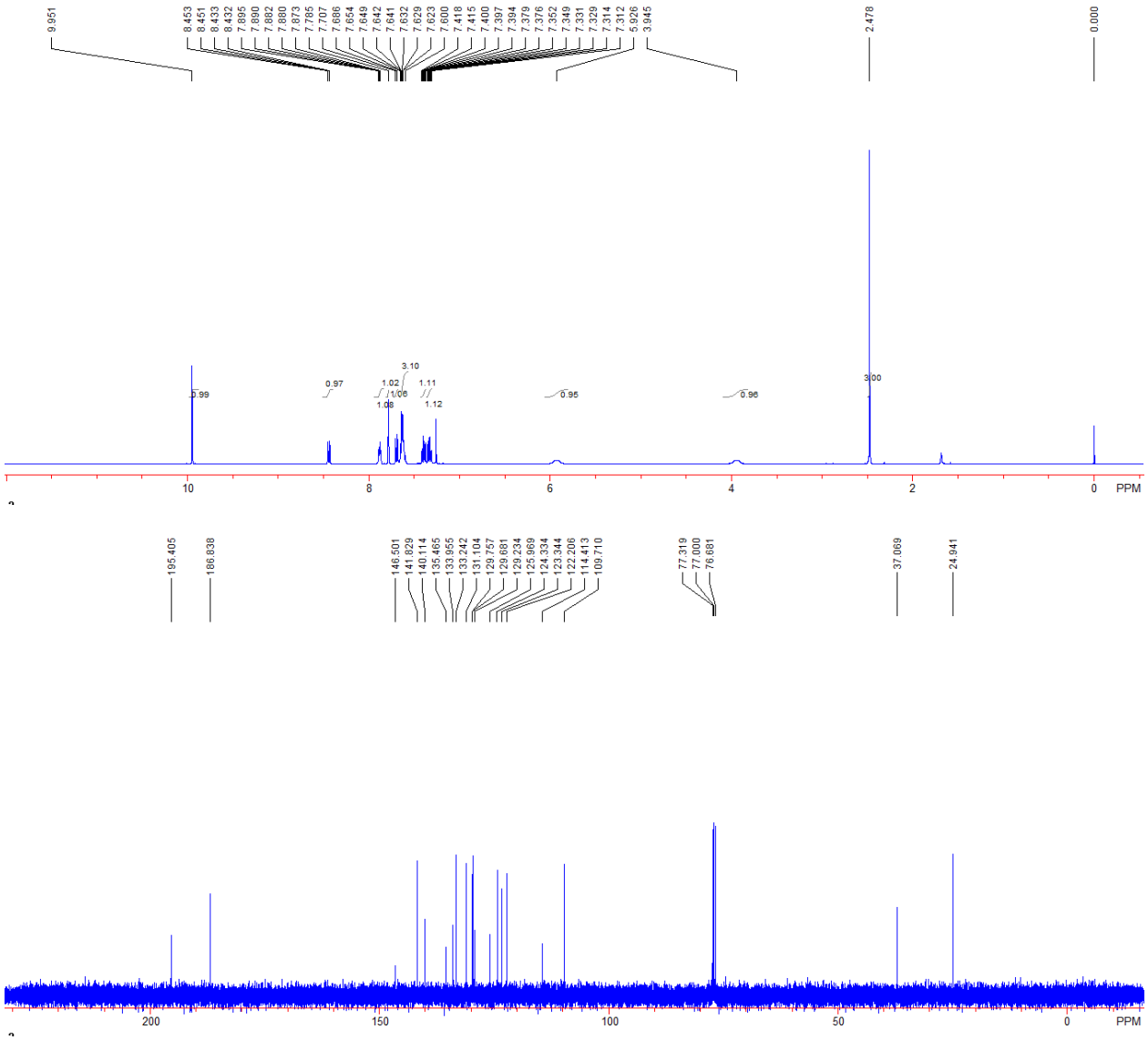
To a reaction tube charged with $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), JohnPhos (19 mg, 0.02 mmol), and tetrabutylammonium acetate (45 mg, 0.15 mmol) was added a solution of **1r** (33 mg, 0.1 mmol) in DMF (1.0 mL) via a syringe, the mixture was stirred at 100 ^{o}C until **1r** had been consumed by TLC analysis. After being cooled to room temperature, the mixture was dissolved in 20 mL of EtOAc and washed with H_2O. The organic phase was dried over anhydrous Na_2SO_4 and comcentrated under reduced pressure. The crude material was purified by silica gel column chromatography (elution with PE/EA = 4/1) to give product **3a** in 72% yield (18 mg).

6-acetyl-5H-benzo[c]pyrrolo[1,2-a]azepine-3-carbonitrile 3a: 18 mg, 72% yield; a yellow solid, m.p. = 177-178 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.51 (s, 3H), 4.92 (s, 2H), 6.44 (d, *J* = 4.0 Hz, 1H), 6.84 (d, *J* = 4.0 Hz, 1H), 7.43-7.53 (m, 3H), 7.70 (d, *J* = 7.6 Hz, 1H), 7.72 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.2, 40.3, 109.4, 109.9, 113.2, 119.7, 128.1, 129.4, 130.4, 130.6, 131.4, 131.5, 131.9, 137.7, 142.3, 195.0; IR (neat) ν 2919, 2209, 1659, 1629, 1532, 1504, 1477, 1382, 1247, 1096, 988, 782, 754, 737 cm^{-1}; MS (ESI) m/e 266.1 (M+H_2O); HRMS (ESI) for $C_{16}H_{12}N_2NaO$ (M+Na): 271.0842; Found: 271.0849.



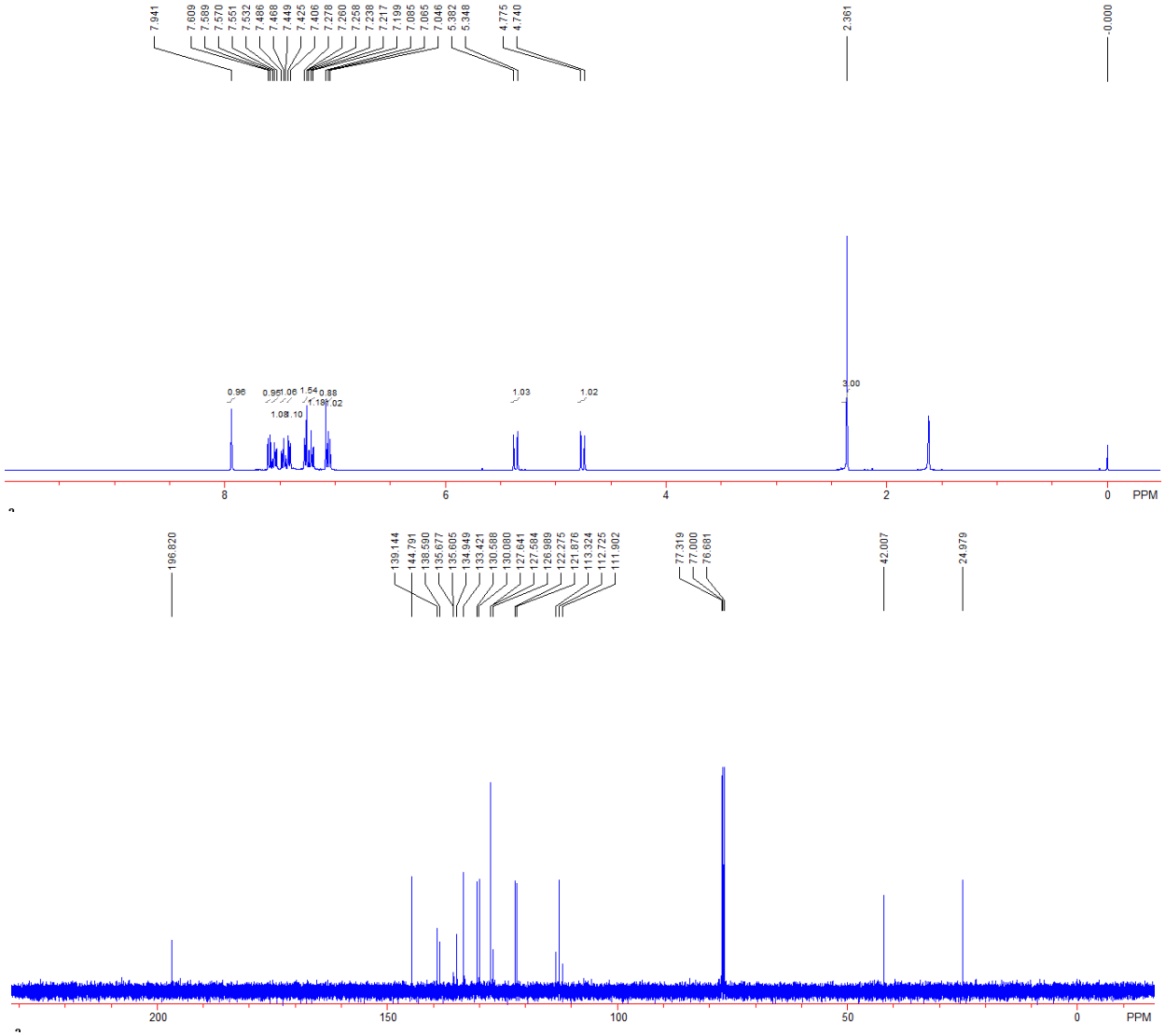


6-acetyl-7H-benzo[3,4]azepino[1,2-a]indole-13-carbaldehyde 3b: 28 mg, 93% yield; a yellow solid, m.p. = 199-200 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.48 (s, 3H), 3.95 (s, 1H), 5.93 (s, 1H), 7.31-7.35 (m, 1H), 7.38-7.42 (m, 1H), 7.60-7.65 (m, 3H), 7.70 (d, *J* = 8.4 Hz, 1H), 7.79 (s, 1H), 7.87-7.90 (m, 1H), 8.43-8.45 (m, 1H), 9.95 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.9, 37.1, 109.7, 114.4, 122.2, 123.3, 124.3, 126.0, 129.2, 129.7, 129.8, 131.1, 133.2, 134.0, 135.5, 140.1, 141.8, 146.5, 186.8, 195.4; IR (neat) ν 2881, 2820, 1649, 1524, 1460, 1388, 1247, 1040, 938, 872, 823, 737 cm^{-1}; MS (ESI) m/e 302.1 (M+H); HRMS (ESI) for $C_{20}H_{16}NO_2$ (M+H): 302.1176; Found: 302.1184.

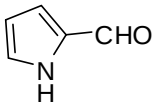


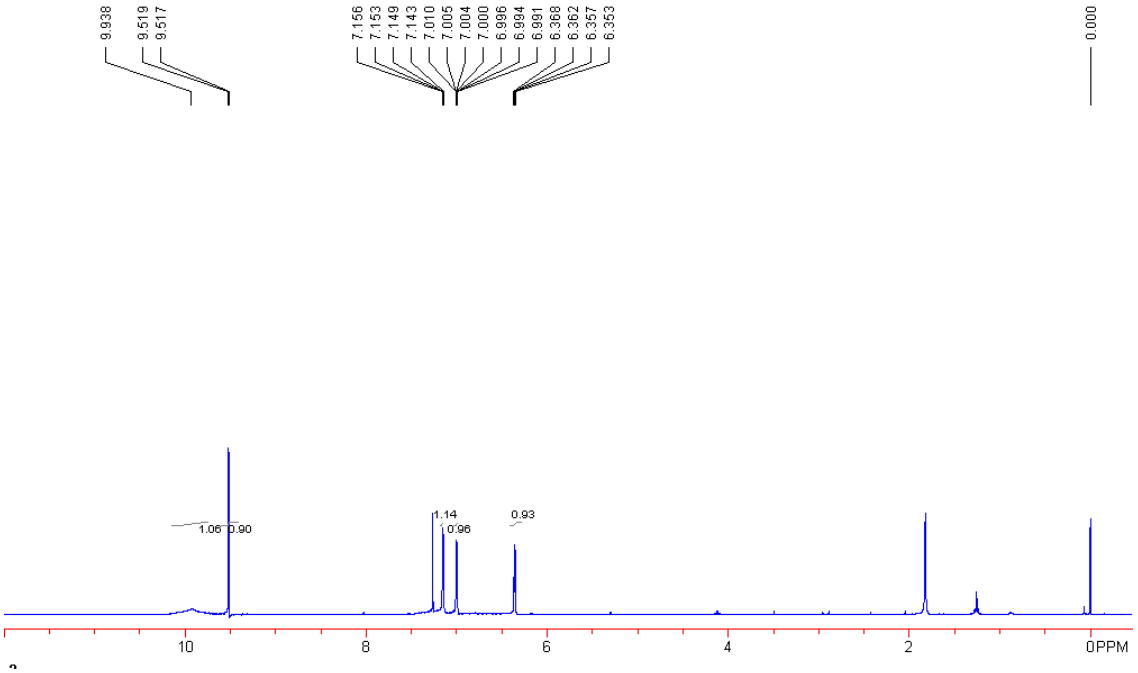
(E)-5-acetyl-4H-benzo[4,5]azocino[3,2,1-hi]indole-2-carbonitrile 3c: 18 mg, 60% yield; a yellow solid, m.p. = 203-205 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.36 (s, 3H), 4.76 (d, *J* = 14.0 Hz, 1H), 5.37 (d, *J* = 14.0 Hz, 1H), 7.06 (d, *J* = 7.6 Hz, 1H), 7.09 (s, 1H), 7.20-7.24 (m, 1H), 7.26-7.28 (m, 1H), 7.42 (d, *J* = 7.6 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 1H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.60 (d, *J* = 7.6 Hz, 1H), 7.94 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.0, 42.0, 111.9, 112.7, 113.3, 121.9, 122.3, 127.0, 127.6, 127.7, 130.1, 130.6, 133.4, 134.9, 135.6, 135.7, 138.6, 139.1, 144.8,

196.8; IR (neat) ν 2999, 2950, 2225, 1671, 1634, 1527, 1477, 1447, 1382, 1244, 1095, 950, 814, 782, 734 cm^{-1}; MS (ESI) m/e 316.0 ($M+H_2O$); HRMS (ESI) for $C_{20}H_{14}N_2NaO$ ($M+Na$): 321.0998; Found: 321.1005.

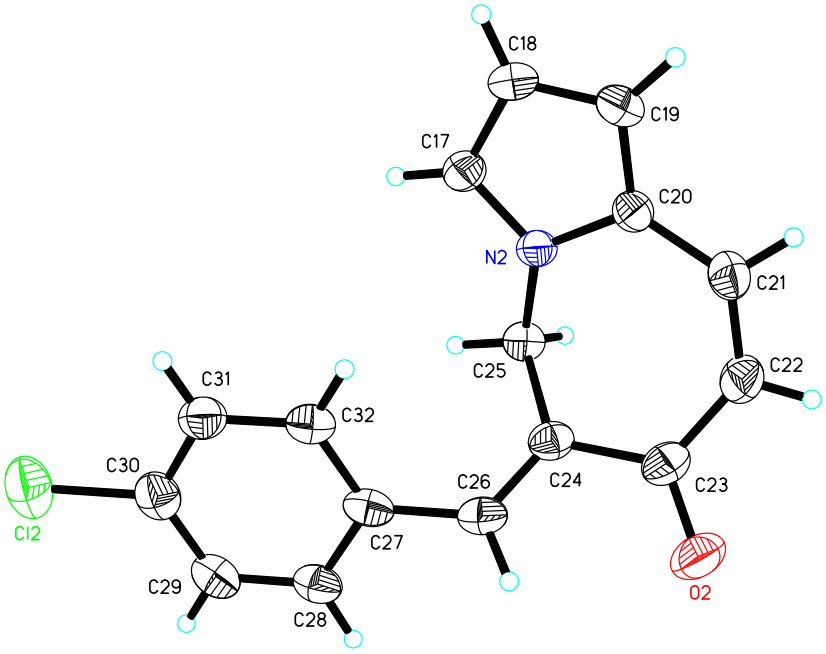


^{1}H NMR spectra of the isolated trace amount of pyrrole-2-carbaldehyde





X-ray crystal data of 2a



The crystal data of **2a** have been deposited in CCDC with number 834094. Empirical Formula: $C_{16}H_{12}ClNO$; Formula Weight: 269.72; Crystal Color, Habit: colorless, Crystal Dimensions: 0.397 x 0.365 x 0.113 mm; Crystal System: Monoclinic; Lattice Parameters: a = 15.803(4)Å, b = 8.275(2)Å, c = 22.001(6)Å, $\alpha = 90^{o}$, $\beta = 110.987(5)^{o}$, $\gamma = 90^{o}$, V = 2686.1(13)$Å^3$; Space group: P2(1)/n; Z = 8; D_{calc}= 1.334 g/cm^3; F_{000} = 1120; Final R induces [I>2sigma(I)]: R1 = 0.1110; wR2 = 0.3533.